Stereoselective functionalisation of *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-alkyl-1,3-oxazolidin-5-ones: asymmetric synthesis of (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids and (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid†

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Treatment of a range of *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-alkyl-1,3-oxazolidin-5-ones with LDA followed by the addition of allyl bromide promotes highly stereoselective allylation (>98% de) at the 4-position of the oxazolidinone ring *anti* to the stereodirecting 2-ferrocenyl group. Hydrolysis of the resultant 4,4-disubstituted oxazolidinones (>98% de) yields enantiomeric (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids in high ee. Furthermore, the aldol reaction of the lithium enolate of *cis*-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one with benzaldehyde followed by *in situ O*-protection affords *O*-protected aldol products in >98% de, with hydrolysis affording (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid in >98% de.

Introduction

Enantiomerically pure α,α-disubstituted α-amino acids are recognised as important building blocks in the *de novo* design of peptides and proteins,[1] with their synthesis presenting a considerable challenge for chemists due to the stereogenic quaternary carbon contained within their structure.[2] Among the many methods used for their preparation in homochiral form, the self-regeneration of stereocentres (SRS) concept introduced by Seebach[3] using oxazolidinones and imidazolidinones as effective chiral templates is perhaps the most widely applied in synthesis.[4] Although of widespread synthetic utility, this strategy is inherently limited. Primarily, cyclisation of the α-amino acid derived imine to yield the parent oxazolidinone proceeds with incomplete stereoselectivity, requiring purification of the predominant *cis*-oxazolidinones to homogeneity before their use in synthesis. Only the *cis*-isomer is generally available in sufficient quantity by this route for synthetic applications, although access to both *cis*- and *trans*-oxazolidinones in a highly stereoselective fashion would be advantageous, leading to either enantiomer of the desired quaternary amino acid from the same enantiomer of the starting α-amino acid. Furthermore, the disubstituted oxazolidinone products from alkylation require relatively forcing hydrolysis conditions to liberate the free α,α-disubstituted α-amino acid.

In order to solve these inherent limitations and extend the utility of this powerful strategy, previous investigations from this laboratory on 2-ferrocenyl-1,3-oxazolidin-5-ones[5] have introduced *cis*-(2*S*,4*S*)-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one as an efficient chiral template for the asymmetric synthesis of a range of α-alkyl-α-methyl-α-amino acids in high ee.[5a,b] In the preceding manuscript[6] we demonstrated that both *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-ones can be prepared stereoselectively under thermodynamic and kinetic control respectively from imines derived from α-amino acids. We detail herein the elaboration of these *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-ones to the asymmetric synthesis of (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids in enantiomerically pure form from the same amino acid starting material. The further application of this strategy to the synthesis of (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid is also delineated.

Results and discussion

Stereoselective allylation reactions of *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-alkyl-1,3-oxazolidin-5-ones: asymmetric synthesis of (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids

Unsaturated α-amino acids can be considered useful chiral synthons[7] and important building blocks in the synthesis of biologically active peptides and peptides isosteres.[8] In particular, α-allyl-α-amino acids have been synthesised by alkylation of glycine and alanine synthons[9] or using chiral auxiliaries,[10] among other methods.[11]

Initial studies within this area focused upon the stereoselective allylation of the *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-methyl oxazolidinones **1** and **3**, which were prepared under thermodynamic and kinetic control, respectively, from the alanine derived ferrocenyl imine and pivaloyl chloride. Deprotonation of *cis*-oxazolidinone **1** with 1.0 eq of LDA at −78 °C, followed by addition of allyl bromide at −78 °C and subsequent warming to rt overnight, generated (2*S*,4*R*)-2-ferrocenyl-3-pivaloyl-4-allyl-4-methyl-1,3-oxazolidin-5-one **2** in >98% de,[12] and in 85% yield as

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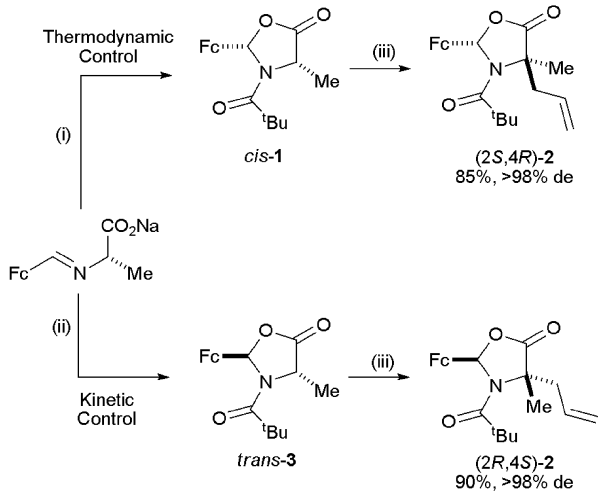
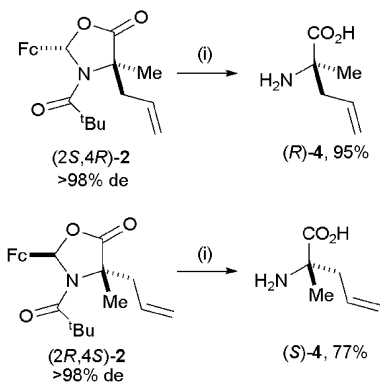
a single diastereoisomer after purification. Following an identical procedure, allylation of the enolate of *trans*-oxazolidinone **3** gave (2*R*,4*S*)-**2** in >98% de, and in 90% yield and >98% de after purification (Scheme 1).



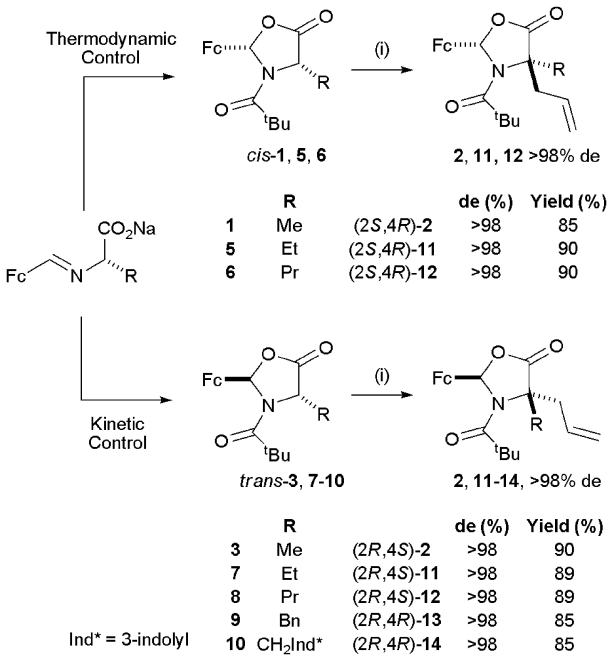
Scheme 1 *Reagents and conditions:* (i) ^{t}BuCOCl (1.0 eq), CH_2Cl_2, 4 Å molecular sieves, −15 °C to rt, 16 h; (ii) ^{t}BuCOCl (1.0 eq), CH_2Cl_2, 4 Å molecular sieves, −78 °C, 16 h; (iii) LDA (1.5 eq), THF, −78 °C then allyl bromide (1.5 eq), THF, −78 °C to rt.

Subsequent hydrolysis of oxazolidinones (2*S*,4*R*)-**2** and (2*R*,4*S*)-**2** with the acidic ion exchange resin Amberlyst-15[5b] gave (*R*)- and (*S*)-2-amino-2-methylpent-4-enoic acid **4** in 95 and 77% yield respectively (Scheme 2). Amino acids (*R*)- and (*S*)-**4** showed spectroscopic properties consistent with the literature {for (*R*)-**4**: mp 296–299 °C; lit.[13] mp 300 °C (dec.); $[\alpha]_D^{25}$ +24.1 (*c* 0.7 in MeOH); for (*S*)-**4**: $[\alpha]_D^{25}$ −29.0 (*c* 0.4 in MeOH; lit.[14] $[\alpha]_D^{20}$ −25.7 (*c* 0.8 in MeOH)}, consistent with this deprotection protocol proceeding without racemisation of the amino acid fragment.



Scheme 2 *Reagents and conditions:* (i) Amberlyst-15 at pH 2–4, acetone : H_2O (9 : 1), rt, 16 h then ion exchange chromatography.

The synthesis of (*R*)- and (*S*)-2-amino-2-methylpent-4-enoic acid in this manner indicates that both enantiomers of 2-alkyl-2-aminopent-4-enoic acids are available from a single enantiomer of a given α-amino acid using this methodology. In order to demonstrate the generality of this approach, a range of *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-alkyl oxazolidinones **5–10**[6] were treated with LDA to give the corresponding enolates, and subsequently alkylated with allyl bromide. In each case, analysis of the crude reaction product indicated good conversion to the desired 4-alkyl-4-allyl oxazolidinones in >98% de, with subsequent purification giving **11–14** in 85–90% yield and as single diastereoisomers in each case (Scheme 3).



	R		de (%)	Yield (%)
1	Me	(2*S*,4*R*)-**2**	>98	85
5	Et	(2*S*,4*R*)-**11**	>98	90
6	Pr	(2*S*,4*R*)-**12**	>98	90

	R		de (%)	Yield (%)
3	Me	(2*R*,4*S*)-**2**	>98	90
7	Et	(2*R*,4*S*)-**11**	>98	89
8	Pr	(2*R*,4*S*)-**12**	>98	89
9	Bn	(2*R*,4*R*)-**13**	>98	85
10	CH_2Ind*	(2*R*,4*R*)-**14**	>98	85

Scheme 3 *Reagents and conditions:* (i) LDA (1.5 eq), THF, −78 °C then allyl bromide (1.5 eq), THF, −78 °C to rt.

In the racemic series, single crystal X-ray crystallographic analysis of **11** (obtained by stereoselective allylation of (2*RS*,4*SR*)-**5** using the standard protocol) confirmed the assigned relative configuration (Fig. 1).

Subsequent hydrolysis of the enantiomeric oxazolidinones (2*S*,4*R*)- and (2*R*,4*S*)-**11**, and (2*S*,4*R*)- and (2*R*,4*S*)-**12** with Amberlyst-15[5b] under standard conditions gave (*R*)- and (*S*)-2-amino-2-ethylpent-4-enoic acid **15**, and (*R*)- and (*S*)-2-amino-2-propylpent-4-enoic acid **16**, respectively, in good yield. The ee of amino acids **15** and **16** was assigned as >98% ee on the assumption that no racemisation of the amino acid fragment had occurred during this acid catalysed deprotection step (Scheme 4).

Attempted hydrolysis of oxazolidinone (2*R*,4*R*)-**13** under these standard conditions proved problematic giving, at 80% conversion, an approximate 50 : 50 mixture of the desired (*R*)-2-amino-2-benzylpent-4-enoic acid **17** (isolated in 25% yield after purification) and *N*-pivaloyl (*R*)-2-amino-2-benzylpent-4-enoic acid **18**. Fortunately, *N*-pivaloyl **18** could be converted to the desired free amino acid (*R*)-**17** by refluxing in HCl, giving **17** in 53% yield after ion exchange chromatography (Scheme 5). As the ready hydrolysis of oxazolidinones in this system is thought to be due to neighbouring group participation of the ferrocenyl group,[5b] the isolation of *N*-pivaloyl amino acid **18** indicates that other hydrolysis manifolds may compete with the neighbouring group participation mechanism in this case (Scheme 5).[5b]

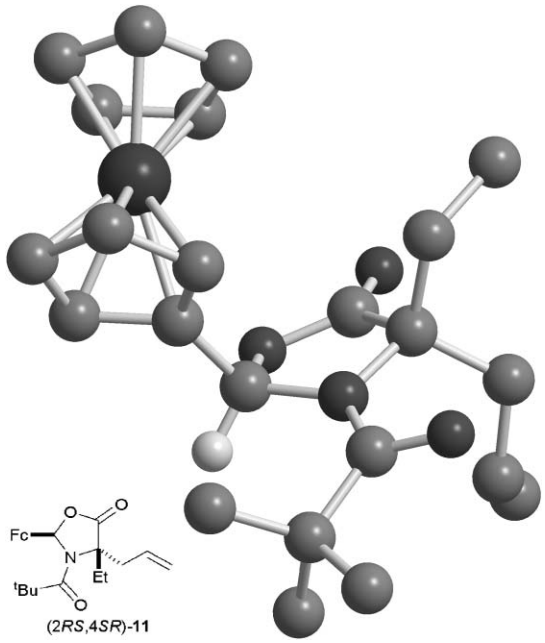
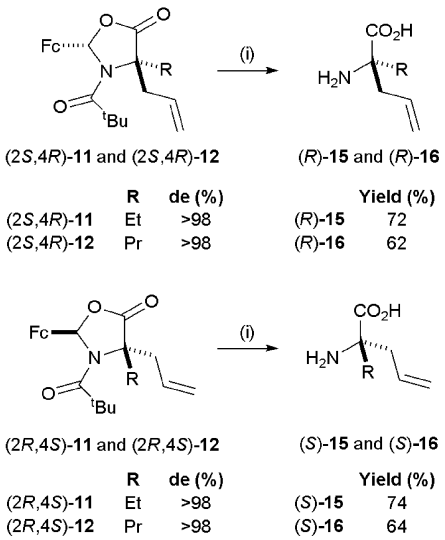


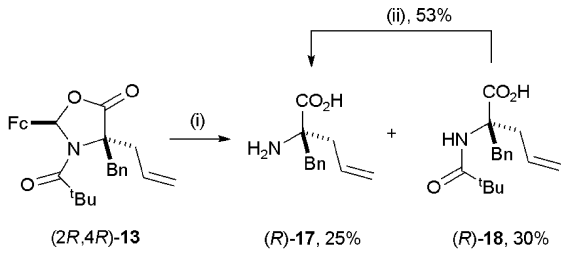
Fig. 1 Chem 3D representation of the X-ray crystal structure of (2*RS*,4*SR*)-**11** (some H atoms omitted for clarity).



Scheme 4 *Reagents and conditions:* (i) Amberlyst-15 at pH 2–4, acetone : H_2O (9 : 1), rt, 16 h then ion exchange chromatography.

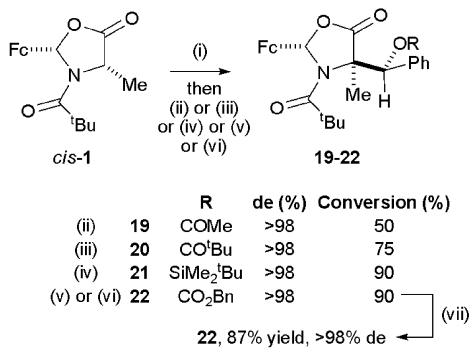
Stereoselective aldol reactions of (2*S*,4*S*)-*cis*-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one: asymmetric synthesis of (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid

Having demonstrated stereoselective allylation of the enolate derived from both *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-methyl oxazolidinones, the ability of the enolate derived from *cis*-**1** to undergo stereoselective aldol reactions was investigated. It was envisaged that this approach would allow the stereoselective synthesis of the β-hydroxy-α-amino acid molecular class, a component of a number of biologically active compounds,[15] to which only limited asymmetric routes have been developed.[16,17]



Scheme 5 *Reagents and conditions:* (i) Amberlyst-15 at pH 2–4, acetone : H_2O (9 : 1), rt, 16 h; (ii). HCl, reflux then ion exchange chromatography.

Following the successful allylation reaction protocol, deprotonation of *cis*-**1** with LDA at −78 °C, followed by addition of benzaldehyde and subsequent warming to rt gave only a complex mixture of decomposition products. Assuming these decomposition products were the result of an initial aldol reaction, followed by a retro-aldol decomposition pathway, a range of reactive electrophiles designed to trap the initially formed aldol product were added after the addition of benzaldehyde to the enolate. In this protocol, the use of acetyl chloride and pivaloyl chloride gave 50% and 75% conversion respectively to the corresponding aldol products **19** and **20** as single diastereoisomers in each case. However, the use of *tert*-butyldimethylsilyl chloride, benzyl chloroformate, or dibenzyl dicarbonate as the *O*-protecting agent proved superior, giving approximately 90% conversion to the desired *O*-protected aldol products **21** and **22** as single diastereoisomers (Scheme 6).



Scheme 6 *Reagents and conditions:* (i) LDA (1.0 eq), THF, −78 °C then PhCHO (1.3 eq), THF, −78 °C; (ii) MeCOCl (1.3 eq), THF, −78 °C to rt; (iii) ^{t}BuCOCl (1.3 eq), THF, −78 °C to rt; (iv) ^{t}BuMe$_2$SiCl (1.3 eq), THF, −78 °C to rt; (v) BnOCOCl (1.3 eq), THF, −78 °C to rt; (vi) (BnOCO)$_2$O (1.3 eq), THF, −78 °C to rt; (vii) recrystallisation.

Crystallisation of the crude reaction product from the use of benzyl chloroformate in this reaction protocol afforded (2*S*,4*R*,1′*S*)-**22** as a single diastereoisomer in 87% yield (Scheme 6). X-Ray crystallographic analysis of **22** confirmed the relative *cis*-configuration of the 2-ferrocenyl and the 4-methyl oxazolidinone substituents, with the absolute (2*S*,4*R*,1′*S*)-configuration of the aldol product **22** following from the known (*S*)-configuration of the C(2) stereocentre (Fig. 2).

The stereoselective formation of **22** as the only diastereoisomer in this aldol protocol is consistent with the stereochemical outcome of related aldol reactions of oxazolidinone enolates described by

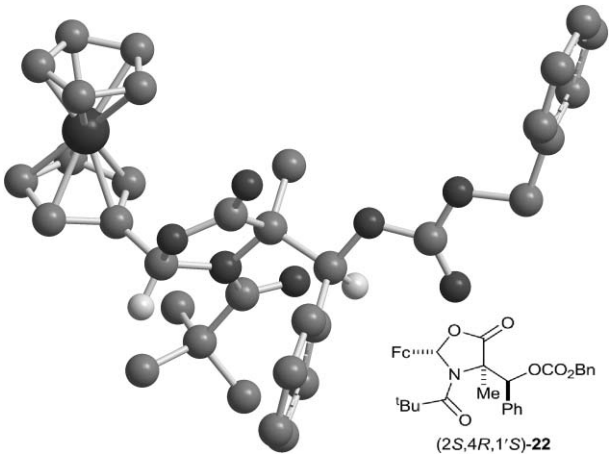
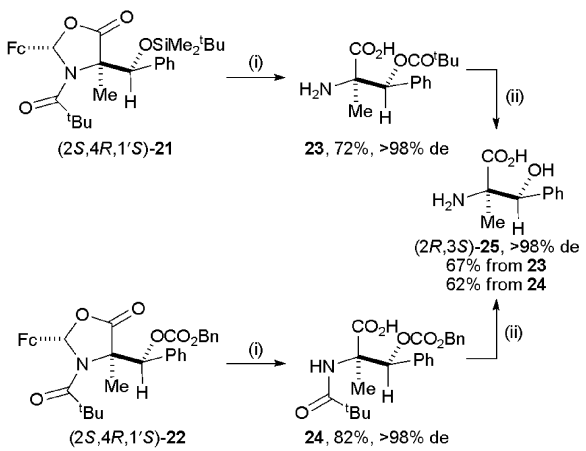


Fig. 2 Chem 3D representation of the X-ray crystal structure of (2*S*,4*R*,1′*S*)-**22** (some H atoms omitted for clarity).

Seebach *et al.*[18] The configurations within aldol products **19–21** were assigned by analogy to that proven for **22**.

The further application of this aldol protocol using either acetaldehyde or pivalaldehyde gave complex mixtures of products, so subsequent investigations focused upon deprotection of **21** and **22** to (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid. Hydrolysis of *O*-TBDMS protected aldol product **21** (>98% de) with Amberlyst-15 under standard conditions yielded *O*-pivaloyl ester **23** in 72% yield and >98% de,[19] which upon treatment with conc. HCl at reflux gave (2*R*,3*S*)-**25** in >98% de and 67% yield after purification by ion exchange chromatography. Treatment of *O*-Cbz protected aldol product **22** (>98% de) with Amberlyst-15 gave *N*-pivaloyl-*O*-Cbz **24** in 82% yield and >98% de, which also gave (2*R*,3*S*)-**25** upon treatment with conc. HCl at reflux in >98% de and 62% yield after ion exchange chromatography (Scheme 7).



Scheme 7 *Reagents and conditions:* (i) Amberlyst-15 at pH 2–4, acetone : H_2O (9 : 1), rt, overnight; (ii) HCl, reflux then ion exchange chromatography.

Conclusions

In conclusion, treatment of a range of *cis*- and *trans*-2-ferrocenyl-3-pivaloyl-4-alkyl-1,3-oxazolidin-5-ones with LDA, followed by the addition of allyl bromide, promotes highly stereoselective allylation (>98% de) at the 4-position of the oxazolidinone ring *anti* to the stereodirecting 2-ferrocenyl group. Hydrolysis of the resultant 4,4-disubstituted oxazolidinones (>98% de) yields enantiomeric (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids in high ee. The aldol reaction of the lithium enolate of *cis*-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one with benzaldehyde followed by *in situ O*-protection affords *O*-protected aldol products in >98% de, with hydrolysis affording (2*R*,3*S*)-2-amino-2-methyl-3-hydroxy-3-phenylpropanoic acid in >98% de. The further application of this strategy for the asymmetric synthesis of enantiomerically pure stereodefined chiral building blocks is currently underway in this laboratory.

Experimental

General experimental

All reactions were performed under a nitrogen atmosphere. THF and diethyl ether were distilled under nitrogen from sodium benzophenone ketyl. Methanol was distilled from $Mg(OMe)_2$. Petroleum refers to light petroleum (bp 40–60 °C) and was redistilled before use. All ethanol used was 'absolute ethanol'. Allyl bromide and benzaldehyde were distilled before use. Diisopropylamine was distilled from and stored over potassium hydroxide pellets.

Melting points (mp) were obtained using a Thermogalen™ III, Griffin Gallenkamp or Swiss Flawil melting point apparatus and are uncorrected.

Optical rotations were measured with a Perkin-Elmer 241 polarimeter with a thermally jacketted 10 cm cell. Concentrations (*c*) are given in g/100 mL and specific rotations [α] are given in units of 10^{-1} deg cm^2 g^{-1}.

Infrared spectra were recorded as KBr discs on a Perkin-Elmer 1750 Fourier Transform spectrometer. Absorptions are recorded in wavenumbers (cm^{-1}). Only diagnostic peaks are quoted.

^{1}H NMR spectra were recorded at 200 MHz on a Varian Gemini 200 or a Bruker AC200 spectrometer, at 300 MHz on a Bruker WH300 spectrometer, at 400 MHz on a Bruker AC400 spectrometer and at 500 MHz on a Bruker AM500 or AMX500 spectrometer. Chemical shifts (δ_H) are quoted in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual solvent peak. Spectra recorded in D_2O are referenced to internal 1,4-dioxane. Coupling constants (*J*) were recorded in Hertz to the nearest 0.5 Hz. Carbon magnetic resonance spectra (^{13}C NMR) were recorded at 50.3 MHz on a Varian Gemini 200 or a Bruker AC200 spectrometer, at 100.6 MHz on a Bruker AC400 spectrometer and at 125.7 MHz on a Bruker AM500 or AMX500 spectrometer using DEPT editing. Chemical shifts (δ_C) are quoted in ppm downfield from tetramethylsilane and referenced to the corresponding deuterated solvent.

Low resolution mass spectra (*m*/*z*) were recorded on a VG Micromass ZAB 1F, a VG Masslab 20–250, a GCMS Trio-1, a VG BIO Q, an APCI Platform or a Finnigan MAT95S spectrometer, with only molecular ions (M^+), fragments from molecular ions and major peaks being reported. Accurate mass analyses (HRMS) were performed on a VG AutoSpec spectrometer.

Microanalyses were performed on a Carlo Erba 1106 combustion elemental analyser.

Thin layer chromatography was performed on Merck aluminium sheets coated with 0.2 mm silica gel 60 F_{254}. Column chromatography was performed on silica gel (Kieselgel 60), Amberlyst-15 (wet) or Dowex (50WX8-200) resin.

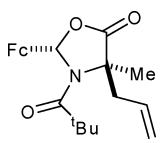
Diastereomeric excesses were determined by ^{1}H NMR analysis of the crude reaction mixtures.

Crystallographic analyses. The crystal was mounted on a glass fibre using a drop of perfluoropolyether oil. It was then plunged into a cold nitrogen stream using an Oxford Cryosystems CRYOSTREAM cooling system. The data were collected on an Enraf-Nonius DIP 2020 image-plate diffractometer (ω scans, DIP 2000 software) and the images were processed using the DENZO[20] and SCALEPACK suite of programs. Data were corrected for Lorentz and polarisation effects. A partial absorption correction is implied by multi-frame scaling of the image-plate data using equivalent reflections. The structure was solved by direct methods (SIR92)[21] giving all non-hydrogen atom positions. The structure was refined using full-matrix least-squares procedures with anisotropic thermal parameters for all non-hydrogen atoms. The hydrogen atoms were placed in calculated positions during the final cycles of refinement. A three parameter Chebychev[22] weighting scheme and corrections for anomalous dispersion were applied to all data. All crystallographic calculations were carried out using CRYSTALS[23] on a PC/AT computer. Neutral atom scattering factors were taken from International Tables for X-ray Crystallography.[24]

General procedure 1 for allylation of oxazolidinones

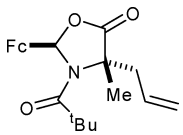
BuLi (1.6 M in hexanes, 1.0 eq for **1**, **5** and **6**, 1.5 eq for **3** and **7–10**) was added dropwise to a stirred solution of diisopropylamine (1.1 eq for **1**, **5** and **6**, 1.65 eq for **3** and **7–10**) in THF at 0 °C and stirred for 15 min. The resulting solution was cooled to −78 °C and then transferred *via* cannula to a precooled (−78 °C) solution of the corresponding oxazolidinone (1.0 eq) in THF. Allyl bromide (1.3 eq) was added dropwise and the solution was stirred overnight and allowed to warm to rt. The reaction mixture was concentrated *in vacuo*. Several portions of Et_2O were added and quickly passed through a sinter containing layers of celite and silica. The Et_2O solution was concentrated *in vacuo*. The product was purified by washing with cold pentane.

(2*S*,4*R*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-methyl-1,3-oxazolidin-5-one (2*S*,4*R*)-2



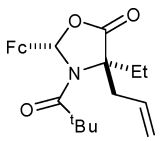
Following *general procedure 1*, **1** (2.25 g, 6.09 mmol) gave (2*S*,4*R*)-**2** as orange crystals (2.12 g, 85%, >98% de); $C_{22}H_{27}FeNO_3$ requires C, 64.6; H, 6.7; N, 3.4%; found C, 64.5; H, 6.9; N, 3.4%; mp 167–169 °C; $[\alpha]_D^{25}$ −218 (*c* 1.0 in $CHCl_3$); ν_{max} (KBr) 3090 (C–H), 1795 (OC=O), 1651 (NC=O), 1640 (C=C), 1353, 1186; δ_H (300 MHz, $CDCl_3$) 1.05 (9H, s, CMe_3), 1.92 (3H, s, C(4)*Me*), 2.53 (1H, dd, *J* 14.0, 6.0, CH_AH$_B$CH=CH$_2$), 3.36 (1H, dd, *J* 14.0, 9.0, CH$_A$$H_B$CH=CH$_2$), 4.20–4.32 (4H, m, *Cp*), 4.23 (5H, s, *Cp′*), 5.12 (1H, d, *J* 12.0, CH=CH_AH$_B$), 5.13 (1H, d, *J* 17.0, CH=CH$_A$$H_B$), 5.47–5.61 (1H, m, C*H*=CH$_2$), 6.66 (1H, s, C(2)*H*); δ_C (50 MHz, $CDCl_3$) 22.9 (C(4)*Me*), 28.7 (CMe_3), 39.6 (*C*H$_2$CH=CH$_2$), 41.1 (*C*Me$_3$), 64.7 (*C*(4)), 67.4, 68.1, 69.1, 69.2 (*Cp*, *Cp′*), 86.5 (*C*(2)), 89.8 (*Cp*), 120.0 (CH=*C*H$_2$), 131.6 (*C*H=CH$_2$), 175.5, 176.0 (*C*(5), N*C*O); *m*/*z* (EI$^+$) 410 ([M + H]$^+$, 13%), 409 (73), 280 (37), 121 (57), 57 (100).

(2*R*,4*S*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-methyl-1,3-oxazolidin-5-one (2*R*,4*S*)-2



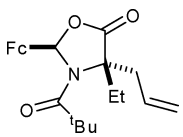
Following *general procedure 1*, **3** (100 mg, 0.27 mmol) gave (2*R*,4*S*)-**2** as orange crystals (100 mg, 90%, >98% de); mp 116–119 °C; $[\alpha]_D^{25}$ +214 (*c* 0.1 in $CHCl_3$).

(2*S*,4*R*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-ethyl-1,3-oxazolidin-5-one (2*S*,4*R*)-11



Following *general procedure 1*, **5** (0.63 g, 1.64 mmol) gave (2*S*,4*R*)-**11** as orange crystals (0.62 g, 90%, >98% de); Found C, 65.0; H, 6.9; N, 3.2%; $C_{23}H_{29}FeNO_3$ requires C 65.3, H 6.9, N 3.3%; mp 103–107 °C; $[\alpha]_D^{25}$ −209 (*c* 0.2 in $CHCl_3$); ν_{max} (KBr) 3080, 2973 (C–H), 1786 (OC=O), 1641 (NC=O), 1360, 1180; δ_H (400 MHz, $CDCl_3$) 1.03 (9H, s, CMe_3), 1.11 (3H, t, *J* 7.5, CH$_2$CH_3), 2.35–2.44 (2H, m, CH_2CH$_3$), 2.57 (1H, dd, *J* 13.5, 6.0, CH_AH$_B$CH=CH$_2$), 3.27 (1H, dd, *J* 13.5, 9.0, CH$_A$$H_B$CH=CH$_2$), 4.22–4.35 (4H, m, *Cp*), 4.26 (5H, s, *Cp′*), 5.11 (1H, s, CH=CH_AH$_B$), 5.15 (1H, d, *J* 4.0, CH=CH$_A$$H_B$), 5.50–5.61 (1H, m, C*H*=CH$_2$), 6.58 (1H, s, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 9.3 (CH$_2$*C*H$_3$), 28.6 (CMe_3), 29.7 (*C*H$_2$CH$_3$), 37.3 (*C*H$_2$CH=CH$_2$), 41.2 (*C*Me$_3$), 67.8, 68.7 (*Cp*), 68.9 (*C*(4)), 69.0, 69.1 (*Cp*), 69.3 (*Cp′*), 86.8 (*C*(2)), 89.0 (*Cp*), 120.2 (CH=*C*H$_2$), 131.8 (*C*H=CH$_2$), 174.1, 176.3 (*C*(5), N*C*O); *m*/*z* (APCI$^+$) 424 ([M + H]$^+$, 100%), 294 (29), 215 (30), 122 (27).

(2*R*,4*S*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-ethyl-1,3-oxazolidin-5-one (2*R*,4*S*)-11



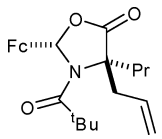
Following *general procedure 1*, **7** (0.67 g, 1.75 mmol) gave (2*R*,4*S*)-**11** as orange crystals (0.66 g, 89%, >98% de); mp 98–101 °C; $[\alpha]_D^{25}$ +213 (*c* 0.2 in $CHCl_3$).

X-Ray crystal structure data for (2*RS*,4*SR*)-11

[$C_{23}H_{29}Fe_1N_1O_3$]: M = 423.3, triclinic, space group $P\bar{1}$, a = 9.462(1) Å, b = 10.432(1) Å, c = 11.673(1) Å, α = 73.144(3)°,

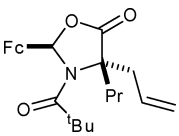
$\beta = 85.380(3)°$, $\gamma = 65.358(3)°$, $V = 1001.21$ Å^3, $Z = 2$, $\mu = 0.77$ mm^{-1}, yellow block crystal dimensions $0.25 \times 0.20 \times 0.20$ mm. A total of 4752 reflections were measured for $5 < \theta < 27$ and 2799 reflections were used in the refinement. Refinement on F: the final parameters were $wR_2 = 0.0463$ and $R_1 = 0.0488$ [$I > 4\sigma(I)$]. CCDC 679349.

(2*S*,4*R*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-propyl-1,3-oxazolidin-5-one (2*S*,4*R*)-12



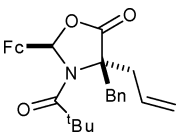
Following *general procedure 1*, **6** (432 mg, 1.09 mmol) gave (2*S*,4*R*)-**12** as orange crystals (428 mg, 90%, >98% de); mp 123–125 °C; $[\alpha]_D^{23}$ −292 (*c* 0.1 in $CHCl_3$); ν_{max} (KBr) 2971 (C–H), 1783 (OC=O), 1634 (NC=O), 1353, 1179; δ_H (400 MHz, $CDCl_3$) 0.98 (3H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.02 (9H, s, CMe_3), 1.43–1.55 (1H, m, $CH_2CH_AH_BCH_3$), 1.62–1.71 (1H, m, $CH_2CH_AH_BCH_3$), 2.26 (1H, dt, *J* 13.0, 4.5, $CH_AH_BCH_2CH_3$), 2.34 (1H, dt, *J* 13.0, 5.0, $CH_AH_BCH_2CH_3$), 2.55 (1H, dd, *J* 13.5, 6.0, $CH_AH_BCH{=}CH_2$), 3.29 (1H, dd, *J* 13.5, 9.0, $CH_AH_BCH{=}CH_2$), 4.22–4.35 (4H, m, *Cp*), 4.25 (5H, s, *Cp′*), 5.11 (1H, s, $CH{=}CH_AH_B$), 5.14 (1H, d, *J* 3.5, $CH{=}CH_AH_B$), 5.49–5.60 (1H, m, $CH{=}CH_2$), 6.57 (1H, s, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 14.3 ($CH_2CH_2CH_3$), 17.9 ($CH_2CH_2CH_3$), 28.5 (CMe_3), 37.6, 38.7 ($CH_2CH_2CH_3$, $CH_2CH{=}CH_2$), 41.1 (CMe_3), 67.7 (*Cp*), 68.4 (*C*(4)), 68.7, 68.8, 68.9 (*Cp*), 69.2 (*Cp′*), 86.7 (*C*(2)), 88.9 (*Cp*), 120.1 ($CH{=}CH_2$), 131.7 ($CH{=}CH_2$), 174.1, 176.2 (*C*(5), N*C*O); *m*/*z* (FAB$^+$) 437 ([M]$^+$, 100%), 196 (18), 57 (27); HRMS (ESI$^+$) $C_{24}H_{32}FeNO_3$ ([M + H]$^+$) requires 438.1731; found 438.1745.

(2*R*,4*S*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-propyl-1,3-oxazolidin-5-one (2*R*,4*S*)-12



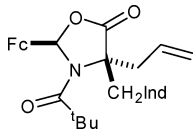
Following *general procedure 1*, **8** (164 mg, 0.41 mmol) gave (2*R*,4*S*)-**12** as orange crystals (160 mg, 89%, >98% de); mp 122–125 °C; $[\alpha]_D^{25}$ +270 (*c* 0.1 in $CHCl_3$).

(2*R*,4*R*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-benzyl-1,3-oxazolidin-5-one (2*R*,4*R*)-13



Following *general procedure 1*, **9** (0.96 g, 2.16 mmol) gave (2*R*,4*R*)-**13** as orange crystals (901 mg, 86%, >98% de); mp 120–123 °C; $[\alpha]_D^{26}$ +324 (*c* 0.2 in $CHCl_3$); ν_{max} (KBr) 2965 (C–H), 1786 (OC=O), 1640 (NC=O), 1362, 1298, 1186; δ_H (500 MHz, $CDCl_3$) 0.93 (9H, s, CMe_3), 2.53 (1H, dd, *J* 13.5, 5.5, $CH_AH_BCH{=}CH_2$), 3.35 (1H, d, *J* 13.0, CH_AH_BPh), 3.40 (1H, dd, *J* 13.5, 9.5, $CH_AH_BCH{=}CH_2$), 3.90 (1H, d, *J* 13.0, CH_AH_BPh), 3.88–3.92 (1H, m, *Cp*), 4.05–4.06 (1H, m, *Cp*), 4.15–4.17 (1H, m, *Cp*), 4.31–4.33 (1H, m, *Cp*), 4.16 (5H, s, *Cp′*), 5.19 (1H, d, *J* 14.0, $CH{=}CH_AH_B$), 5.23 (1H, dd, *J* 14.0, 2.0, $CH{=}CH_AH_B$), 5.64–5.72 (1H, m, $CH{=}CH_2$), 6.27 (1H, s, C(2)*H*), 7.28–7.35 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 27.5 (CMe_3), 39.3, 41.7 (CH_2Ph, $CH_2CH{=}CH_2$), 40.7 (CMe_3), 67.2, 67.4, 68.7 (*Cp*), 69.2 (*Cp′*), 71.2 (*Cp*), 71.7 (*C*(4)), 86.3 (*Cp*), 88.1 (*C*(2)), 120.9 ($CH{=}CH_2$), 127.2, 128.5, 130.8, 131.3 ($CH{=}CH_2$, *p*-, *o*-, *m*-*Ph*) 136.6 (*i*-*Ph*), 173.1, 177.2 (*C*(5), N*C*O); *m*/*z* (APCI$^+$) 486 ([M + H]$^+$, 100%); HRMS (FI$^+$) $C_{28}H_{31}FeNO_3$ ([M]$^+$) requires 485.1653; found 485.1643.

(2*R*,4*R*)-2-Ferrocenyl-3-pivaloyl-4-allyl-4-(indol-3′-ylmethyl)-1,3-oxazolidin-5-one (2*R*,4*R*)-14

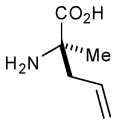


Following *general procedure 1*, **10** (168 mg, 0.35 mmol) gave, after purification *via* flash column chromatography (eluent 30–40 °C petrol/Et_2O, 8 : 2), (2*R*,4*R*)-**14** as orange crystals (147 mg, 81%, >98% de); mp 59–63 °C; $[\alpha]_D^{23}$ +257 (*c* 0.8 in $CHCl_3$); ν_{max} (KBr) 3325 (N–H), 2958, 2917 (C–H), 1786 (OC=O), 1637 (NC=O), 1372, 1303, 1190; δ_H (500 MHz, $CDCl_3$) 0.97 (9H, s, CMe_3), 2.60 (1H, dd, *J* 15.5, 5.5, $CH_AH_BCH{=}CH_2$), 3.46 (1H, dd, *J* 13.5, 9.5, $CH_AH_BCH{=}CH_2$), 3.64 (1H, d, *J* 14.5, CH_AH_BInd), 3.77–4.28 (4H, m, *Cp*), 4.00 (5H, s, *Cp′*), 4.07 (1H, d, *J* 14.5, CH_AH_BInd), 5.17–5.22 (2H, m, $CH{=}CH_2$), 5.63–5.72 (1H, m, $CH{=}CH_2$), 6.31 (1H, s, C(2)*H*), 7.11 (1H, d, *J* 2.5, *Ar*), 7.13, 7.21 (2H, 2dt, *J* 7.5, 1.0, *Ar*), 7.42 (1H, dd, *J* 7.5, 1.0, *Ar*), 7.78 (1H, d, *J* 7.5, *Ar*), 8.35 (1H, br s, N*H*); δ_C (125 MHz, $CDCl_3$) 27.8 (CMe_3), 32.2, 39.0 (CH_2Ind, $CH_2CH{=}CH_2$), 40.9 (CMe_3), 67.3, 67.5, 68.3, 70.8 (*Cp*), 69.1 (*Cp′*), 71.5 (*C*(4)), 86.7 (*Cp*), 87.9 (*C*(2)), 110.6, 110.8, 119.8, 120.1 (*Ar*), 120.7 ($CH{=}CH_2$), 122.1, 124.7, 128.4 (*Ar*), 131.7 ($CH{=}CH_2$), 135.8 (*Ar*), 174.2, 177.2 (*C*(5), N*C*O); *m*/*z* (APCI$^+$) 525 ([M + H]$^+$, 100%); HRMS (FI$^+$) $C_{30}H_{32}FeN_2O_3$ ([M]$^+$) requires 524.1762; found 524.1749.

General procedure 2 for hydrolysis of oxazolidinones 2

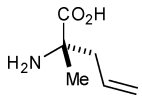
A column was filled with distilled water and Amberlyst-15 was added slowly and in several portions into the column. The column was prepared by washing with distilled water up to pH 2–4 and then with acetone/water 9 : 1. The corresponding oxazolidinone **2** was dissolved in acetone/water 9 : 1; a gentle warming was sometimes required to complete dissolution. The resulting solution was poured into the column and left for 12 h. The Amberlyst column was eluted with acetone/water 9 : 1, the acetone was concentrated *in vacuo* and the aqueous solution was extracted with ether. The ether solution was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica gel, petroleum/ether 9 : 1) to yield ferrocenecarboxaldehyde. The Amberlyst column was also eluted with 2 M NH_4OH. The aqueous solution was concentrated *in vacuo* to yield the free α-amino acid, which was purified by ion-exchange column chromatography using Dowex (50WX8-200), to yield the expected (*R*)- and (*S*)-2-alkyl-2-aminopent-4-enoic acids **4**.

(*R*)-2-Amino-2-methylpent-4-enoic acid (*R*)-4[13,25]



Following *general procedure 2*, (2*S*,4*R*)-**2** (1.84 g, 4.50 mmol) gave ferrocenecarboxaldehyde (0.82 g, 85%) and (*R*)-**4** as white crystals (0.55 g, 95%); mp 296–299 °C; {lit.[25] mp 308 °C, lit.[13] mp 300 °C (dec.)}; $[\alpha]_D^{25}$ +24.1 (*c* 0.7 in MeOH); {lit.[25] $[\alpha]_D^{20}$ +14.2 (*c* 1.0 in 1 M HCl)}; ν_{max} (KBr) 3509 (N–H, br), 3021 (O–H, br), 1645 (C=O), 1575, 1545; δ_H (200 MHz, D_2O) 1.47 (3H, s, CH_3), 2.43 (1H, dd, *J* 14.5, 8.0, C(3)H_AH_B), 2.65 (1H, dd, *J* 14.5, 6.5, C(3)H_AH_B), 5.25 (1H, d, *J* 18.0, C(5)H_AH_B), 5.26 (1H, d, *J* 13.0, C(5)H_AH_B), 5.64–5.83 (1H, m, C(4)*H*); δ_C (125 MHz, D_2O) 21.9 (*C*H_3), 41.3 (*C*(3)), 60.9 (*C*(2)), 121.3 (*C*(5)), 130.6 (*C*(4)), 176.4 (*C*(1)); *m*/*z* (CI^+) 130 ([M + H]$^+$, 100%), 88 (21), 84 (17); HRMS (ESI^+) $C_6H_{12}NO_2$ ([M + H]$^+$) requires 130.0868; found 130.0865.

(*S*)-2-Amino-2-methylpent-4-enoic acid (*S*)-4[13,14,25]

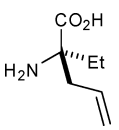


Following *general procedure 2*, (2*R*,4*S*)-**2** (346 mg, 0.85 mmol) gave ferrocenecarboxaldehyde (134 mg, 74%) and (*S*)-**4** as white crystals (84 mg, 77%); mp 262–266 °C; {lit.[25] mp 308 °C, lit.[13] mp 300°C (dec.)}; $[\alpha]_D^{25}$ −29.0 (*c* 0.4 in MeOH); {lit.[25] $[\alpha]_D^{20}$ −14.4 (*c* 1.3 in 1 M HCl); lit.[25] $[\alpha]_D^{20}$ −28.5 (*c* 1.3 in H_2O); lit.[13] $[\alpha]_D^{20}$ −17.6 (*c* 1.3 in 1 M HCl); lit.[13] $[\alpha]_D^{20}$ −25.7 (*c* 0.8 in MeOH).

General procedure 3 for hydrolysis of oxazolidinones 11–13

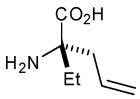
The corresponding oxazolidinone was dissolved in acetone/water 9 : 1; a gentle warming was sometimes required to complete dissolution. Amberlyst-15 was prepared by washing with distilled water up to pH 2–4, then with acetone/water 9 : 1 and added to the solution of the oxazolidinone. The reaction mixture was placed under argon and, to ensure the complete exclusion of oxygen, argon was bubbled through the reaction mixture for 10 min. The reaction mixture was left under a positive pressure of argon for 12 h and then poured into a column. The Amberlyst column was eluted with acetone/water (9 : 1) and the acetone was concentrated *in vacuo*. The aqueous solution was extracted with ether and the ether solution was concentrated *in vacuo* to yield ferrocenecarboxaldehyde, sometimes together with traces of the corresponding *N*-pivaloyl 2-alkyl-2-aminopent-4-enoic acid. At any rate, they could be separated and purified by flash column chromatography (silica gel, petroleum/ether 9 : 1, followed by ethyl acetate/methanol 4 : 1). The Amberlyst column was also eluted with 2 M NH_4OH. The aqueous solution was concentrated *in vacuo* to yield the free 2-aminopent-4-enoic acid, which was purified by Dowex (50WX8-200) ion-exchange column chromatography.

(*R*)-2-Amino-2-ethylpent-4-enoic acid (*R*)-15



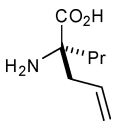
Following *general procedure 3*, (2*S*,4*R*)-**11** (420 mg, 0.99 mmol) gave ferrocenecarboxaldehyde (168 mg, 79%) and (*R*)-**15** as white crystals (102 mg, 72%); mp 237–241 °C; $[\alpha]_D^{27}$ +36.2 (*c* 0.3 in MeOH); ν_{max} (KBr) 3426 (br, N–H), 3031 (br, O–H), 1603 (C=O), 1394; δ_H (500 MHz, D_2O) 0.88 (3H, t, *J* 7.5, CH_2CH_3), 1.68–1.77 (1H, m, CH_AH_BCH$_3$), 1.82–1.92 (1H, m, CH$_A$$H_BCH_3$), 2.41 (1H, dd, *J* 14.5, 8.5, C(3)H_AH_B), 2.60 (1H, dd, *J* 14.5, 6.5, C(3)H_AH_B), 5.21 (1H, s, C(5)H_AH_B), 5.23 (1H, s, C(5)H_AH_B), 5.65–5.73 (1H, m, C(4)*H*); δ_C (125 MHz, D_2O) 7.3 (CH_2CH_3), 28.9 (CH_2CH_3), 40.3 (*C*(3)), 65.2 (*C*(2)), 121.4 (*C*(5)), 130.6 (*C*(4)), 175.4 (*C*(1)); *m*/*z* (APCI$^+$) 144 ([M + H]$^+$, 100%), 102 (97); HRMS (ESI^+) $C_7H_{14}NO_2$ ([M + H]$^+$) requires 144.1024; found 144.1026.

(*S*)-2-Amino-2-ethylpent-4-enoic acid (*S*)-15



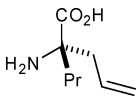
Following *general procedure 3*, (2*R*,4*S*)-**11** (372 mg, 0.88 mmol) gave ferrocenecarboxaldehyde (148 mg, 79%) and (*S*)-**15** as white crystals (93 mg, 74%); mp 225–228 °C; $[\alpha]_D^{27}$ −36.2 (*c* 0.3 in MeOH).

(*R*)-2-Amino-2-propylpent-4-enoic acid (*R*)-16[26]



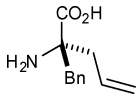
Following *general procedure 3*, (2*S*,4*R*)-**12** (531 mg, 1.21 mmol) gave ferrocenecarboxaldehyde (205 mg, 79%) and (*R*)-**16** as white crystals (118 mg, 62%); mp 215–218 °C; {lit.[26] mp 208–210 °C}; $[\alpha]_D^{22}$ +14.5 (*c* 0.2 in MeOH); ν_{max} (KBr) 3436 (N–H, br), 3140 (O–H, br), 2963 (C–H), 1607 (C=O), 1392; δ_H (500 MHz, D_2O) 0.87 (3H, t, *J* 7.0, $CH_2CH_2CH_3$), 1.14–1.22 (1H, m, $CH_2CH_AH_BCH_3$), 1.31–1.38 (1H, m, $CH_2CH_AH_BCH_3$), 1.68 (1H, dt, *J* 13.5, 4.5, $CH_AH_BCH_2CH_3$), 1.80 (1H, dt, *J* 13.5, 4.5, $CH_AH_BCH_2CH_3$), 2.43 (1H, dd, *J* 14.5, 8.5, C(3)H_AH_B), 2.61 (1H, dd, *J* 14.5, 6.5, C(3)H_AH_B), 5.21 (1H, m, C(5)H_AH_B), 5.24 (1H, s, C(5)H_AH_B), 5.65–5.74 (1H, m, C(4)*H*); δ_C (125 MHz, D_2O) 13.3 ($CH_2CH_2CH_3$), 16.7 ($CH_2CH_2CH_3$), 37.9, 40.6 (*C*(3), $CH_2CH_2CH_3$), 64.7 (*C*(2)), 121.5 (*C*(5)), 130.5 (*C*(4)), 175.5 (*C*(1)); *m*/*z* (APCI$^+$) 158 ([M + H]$^+$, 8%), 116 (12), 112 (100); HRMS (ESI^+) $C_8H_{16}NO_2$ ([M + H]$^+$) requires 158.1181; found 158.1180.

(*S*)-2-Amino-2-propylpent-4-enoic acid (*S*)-16[26]



Following *general procedure 3*, (2*R*,4*S*)-**12** (321 mg, 0.73 mmol) gave ferrocenecarboxaldehyde (127 mg, 81%) and (*S*)-**16** as white crystals (74 mg, 64%); mp 238–243 °C; {lit.[26] mp 208–210 °C}; $[\alpha]_D^{25}$ −31.5 (*c* 0.3 in MeOH).

(*R*)-2-Amino-2-benzylpent-4-enoic acid (*R*)-17[27]

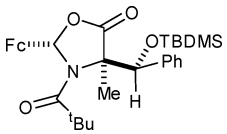


Following *general procedure 3*, (2*R*,4*R*)-**13** (560 mg, 1.15 mmol) gave ferrocenecarboxaldehyde (193 mg, 78%) and (*R*)-**17** as white crystals (59 mg, 25%); mp 165–168 °C; $[\alpha]_D^{22}$ −19.6 (*c* 1.0 in H_2O); {lit.[27] for (*S*)–enantiomer $[\alpha]_D$ +27.3 (*c* 1.0 in H_2O)}; ν_{max} (KBr) 3401 (br, N–H), 3140, 3048 (br, O–H), 1621 (C=O), 1496, 1403; δ_H (500 MHz, CD_3OD) 2.49 (1H, dd, *J* 14.5, 8.5, C(3)H_AH_B), 2.78 (1H, dd, *J* 14.5, 6.5, C(3)H_AH_B), 2.95 (1H, d, *J* 14.0, CH_AH_BPh), 3.31 (1H, d, *J* 14.0, CH_AH_BPh), 5.23–5.29 (2H, m, C(5)H_2), 5.83–5.91 (1H, m, C(4)*H*), 7.21–7.39 (5H, m, *Ph*); δ_C (125 MHz, CD_3OD) 42.1, 42.9 (*C*(3), CH_2Ph), 65.9 (*C*(2)), 121.4 (*C*(5)), 128.6, 129.8, 131.4, 131.5 (*C*(4), *Ph*), 135.8 (*i-Ph*), 174.6 (*C*(1)); *m*/*z* (APCI$^+$) 206 ([M + H]$^+$, 100%), 189 (10), 164 (21), 145 (28); HRMS (ESI$^+$) $C_{12}H_{16}NO_2$ ([M + H]$^+$) requires 206.1181; found 206.1183. Unreacted (2*R*,4*R*)-**13** and the corresponding *N*-pivaloyl amino acid were also isolated and converted into the free α-amino acid in 46 and 53% yield, respectively, by refluxing in concentrated HCl overnight.

General procedure 4 for aldol reaction of (2*S*,4*S*)-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one 1

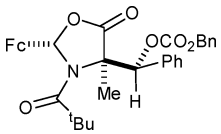
1.6 M *n*-Butyl lithium (1.0 eq) was added dropwise to a stirred solution of diisopropylamine (1.1 eq) in THF at 0 °C and stirred for 15 min. The resulting solution was cooled to −78 °C and then transferred *via* cannula to a precooled (−78 °C) solution of **1** (1.0 eq) in THF. Then, benzaldehyde (1.3 eq) was added dropwise and the solution was stirred for 3 h at −78 °C. The corresponding trapping agent (1.3 eq) was added and the solution was stirred overnight and allowed to warm up to room temperature. The reaction mixture was concentrated *in vacuo.* Several portions of ether were added and quickly passed through a sinter containing layers of celite and silica. The ether solution was concentrated *in vacuo* to yield the corresponding aldol products **19–22**. Then the product was purified by flash column chromatography and/or recrystallisation.

(2*S*,4*R*,1′*S*)-4-[1′-(*tert*-Butyldimethylsilyloxy)benzyl]-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one 21



Following *general procedure 4*, **1** (1.76 g, 4.77 mmol), BuLi (1.6 M in hexanes, 2.98 mL, 4.77 mmol), diisopropylamine (0.73 mL, 5.24 mmol), benzaldehyde (0.63 mL, 6.20 mmol) and TBDMSCl (0.93 g, 6.20 mmol) gave **21** in >98% de. The crude product was washed with cold pentane and purified *via* flash column chromatography (silica gel, petroleum/ether 9 : 1) to yield **21** as a waxy solid, contaminated with trace amounts of impurities (2.45 g, 87%); δ_H (200 MHz, $CDCl_3$) 0.26 (3H, s, Si*Me*), 0.29 (3H, s, Si*Me*), 0.95 (9H, s, SiCMe_3), 1.22 (9H, s, COCMe_3), 1.37 (3H, s, C(4)*Me*), 4.14 (5H, s, *Cp′*), 4.36–4.66 (4H, m, *Cp*), 5.80 (1H, s, C*H*Ph), 6.21 (1H, s, C(2)*H*), 7.26–7.49 (5H, m, *Ph*); *m*/*z* (APCI$^+$) 476 (35%), 330 (100), 289 (45), 144 (74); HRMS (ESI$^+$) $C_{32}H_{44}FeNO_4Si$ ([M + H]$^+$) requires 590.2389; found 590.2380.

(2*S*,4*R*,1′*S*)-4-[1′-(Benzyloxycarbonyloxy)benzyl]-2-ferrocenyl-3-pivaloyl-4-methyl-1,3-oxazolidin-5-one 22

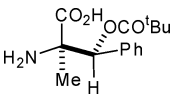


Following *general procedure 4*, **1** (1.55 g, 4.20 mmol), BuLi (1.6 M in hexanes, 2.62 mL, 4.20 mmol), diisopropylamine (0.65 mL, 4.62 mmol), benzaldehyde (0.55 mL, 5.46 mmol) and benzyl chloroformate (0.78 mL, 5.46 mmol) gave **22** as yellow needles (2.23 g, 87%, >98% de); Found C, 67.1; H, 5.9; N, 2.1%; $C_{34}H_{35}FeNO_6$ requires C, 67.0; H, 5.8; N, 2.3%; mp 157–159 °C; $[\alpha]_D^{23}$ +168 (*c* 0.5 in $CHCl_3$); ν_{max} (KBr) 3090, 2970 (C–H), 1791 (OC=O), 1755 (O_2C=O), 1628 (NC=O), 1258; δ_H (200 MHz, $CDCl_3$) 0.85 (9H, s, CMe_3), 2.17 (3H, s, C(4)*Me*), 4.20–4.28 (4H, m, *Cp*), 4.27 (5H, s, *Cp′*), 5.12 (1H, d, *J* 12.0, CH_AH_BPh), 5.21 (1H, d, *J* 12.0, CH_AH_BPh), 5.91 (1H, s, C*H*Ph), 6.59 (1H, s, C(2)*H*), 7.27–7.38 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 20.7 (C(4)*Me*), 28.0 (CMe_3), 41.1 (*C*Me$_3$), 66.5 (*C*(4)), 68.0, 68.5, 68.6, 69.4 (*Cp*, *Cp′*), 69.9 (CH_2Ph), 77.7 (*C*HPh), 86.3 (*C*(2)), 89.0 (*Cp*), 127.8, 128.5, 128.6, 129.4 (*p-*, *o-*, *m-Ph*), 135.3, 135.6 (*i-Ph*), 154.5, 171.3, 177.1 (*C*(5), N*C*O, O*C*OO); *m*/*z* (APCI$^+$) 610 ([M + H]$^+$, 100%), 475 (10), 330 (39), 229 (14). HRMS (ESI$^+$) $C_{34}H_{36}FeNO_6$ ([M + H]$^+$) requires 610.1892; found 610.1900.

X-Ray crystal structure data for (2*S*,4*R*,1′*S*)-22

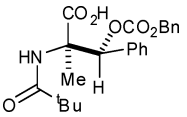
[$C_{34}H_{35}Fe_1N_1O_6$]: $M = 609.5$, monoclinic, space group $P\,2_1$, $a = 11.422(1)$ Å, $b = 8.778(1)$ Å, $c = 15.357(1)$ Å, $\beta = 107.526(3)°$, $V = 1468.41$ Å^3, $Z = 2$, $\mu = 0.56$ mm^{-1}, orange block crystal dimensions $0.40 \times 0.30 \times 0.20$ mm. A total of 8634 reflections were measured for $5 < \theta < 27$ and 3143 reflections were used in the refinement. Refinement on F: the final parameters were $wR_2 = 0.0372$ and $R_1 = 0.0373$ [$I > 3\sigma(I)$]. CCDC 679348.

(2*R*,3*S*)-2-Amino-2-methyl-3-pivaloyloxy-3-phenylpropanoic acid 23



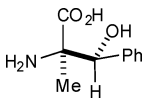
Following *general procedure 3*, **21** (471 mg, 0.80 mmol) gave ferrocenecarboxaldehyde (138 mg, 81%) and (2*R*,3*S*)-**23** as white crystals (161 mg, 72%); mp 113–115 °C; $[\alpha]_D^{22}$ −33.5 (*c* 0.8 in MeOH); ν_{max} (KBr) 3382, 2964 (br, N–H, O–H, C–H), 1720 (C=O), 1624 (C=O), 1050 (C–O), 703; δ_H (200 MHz, D_2O) 0.84 (9H, s, CMe_3), 1.38 (3H, s, C(2)*Me*), 4.98 (1H, s, C(3)*H*), 7.00–7.24 (5H, m, *Ph*); δ_C (125 MHz, CD_3OD) 21.4 (C(2)*Me*), 27.7 (*C*Me_3), 39.8 (*C*Me$_3$), 64.0 (*C*(2)), 77.1 (*C*(3)), 128.3, 128.6, 128.7 (*p-*, *o-*, *m-Ph*), 142.6 (*i-Ph*), 178.8, 179.9 (*C*(1), O*C*O^{t}Bu); *m*/*z* (APCI$^-$) 278 ([M − H]$^-$, 11%), 172 (100); HRMS (ESI$^+$) $C_{15}H_{22}NO_4$ ([M + H]$^+$) requires 280.1548; found 280.1540.

(2*R*,3*S*)-2-Methyl-2-pivaloylamino-3-benzyloxycarbonyloxy-3-phenylpropanoic acid 24



Following *general procedure 3*, **22** (0.96 g, 1.58 mmol) gave ferrocenecarboxaldehyde (0.26 g, 78%) and (2*R*,3*S*)-**24** as light brown solid (0.54 g, 82%); mp 114–122 °C; $[\alpha]_D^{24}$ –28.3 (*c* 0.9 in MeOH); ν_{max} (KBr) 3390 (br, N–H, O–H), 2962 (C–H), 1756 (OC=O), 1656 (amide I), 1516 (amide II), 1254; δ_H (200 MHz, $CDCl_3$) 1.15 (9H, s, CMe_3), 1.60 (3H, s, C(2)*Me*), 5.21 (1H, d, *J* 12.0, CH_AH_BPh), 5.21 (1H, d, *J* 12.0, CH_AH_BPh), 6.28 (1H, s, C(3)*H*), 7.31–7.41 (10H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 18.9 (C(2)*Me*), 27.3 (CMe_3), 39.2 (*C*Me_3), 64.1 (*C*(2)), 70.1 (CH_2Ph), 81.7 (*C*(3)), 128.0, 128.2, 128.7, 129.2 (*p*-, *o*-, *m*-*Ph*), 135.2, 136.0 (*i*-*Ph*), 155.1 (O_2C=O), 178.2, 178.9 (*C*(1), N*C*O); *m*/*z* (APCI$^+$) 414 ([M + H]$^+$, 9%), 262 (100), 134 (34); HRMS (ESI$^+$) $C_{23}H_{28}NO_6$ ([M + H]$^+$) requires 414.1916; found 414.1937.

(2*R*,3*S*)-2-Amino-2-methyl-3-hydroxy-3-phenylpropanoic acid 25[17,28,29]



23 (357 mg, 1.28 mmol) was dissolved in concentrated HCl (50 mL) and refluxed. The crude product was purified by ion-exchange column chromatography using Dowex (50WX8-200) to give (2*R*,3*S*)-**25** as white crystals (167 mg, 67%); mp 215–216 °C; {lit.[28] mp 249 °C (dec.); lit.[29] mp 243 °C (dec.)}; $[\alpha]_D^{26}$ +19.3 (*c* 0.4 in MeOH); {lit.[17] $[\alpha]_D^{25}$ +33.0 (*c* 0.35 in H_2O)}; ν_{max} (KBr) 3154 (br, O–H, N–H), 1634 (C=O), 1497, 1394, 1363, 708; δ_H (200 MHz, D_2O) 1.08 (3H, s, C(2)*Me*), 4.93 (1H, s, C(3)*H*), 7.21–7.28 (5H, m, *Ph*); δ_C (125 MHz, D_2O) 19.0 (C(2)*Me*), 65.3 (*C*(2)), 75.3 (*C*(3)), 127.6, 129.0, 129.2 (*p*-, *o*-, *m*-*Ph*), 137.6 (*i*-*Ph*), 175.8 (*C*(1)); *m*/*z* (APCI$^-$) 194 ([M–H]$^-$, 100%), 111 (7); HRMS (ESI$^+$) $C_{10}H_{14}NO_3$ ([M + H]$^+$) requires 196.0973; found 196.0980.

24 (320 mg, 0.77 mmol), when subjected to the above hydrolysis procedure, also yielded (2*R*,3*S*)-**25** as white crystals (94 mg, 62%); mp 217–220 °C; $[\alpha]_D^{23}$ +21.0 (*c* 0.6 in MeOH).

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