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Synthesis of planar chiral ferrocenyl 1,3-diamines and 1,3-amino ethers

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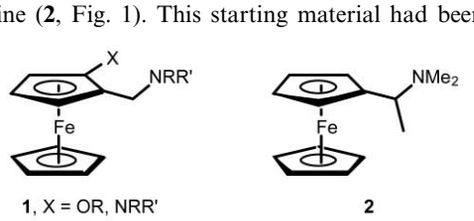
The efficient syntheses of novel planar chiral 1,3-diamines and 1,3-amino ethers with an oxy or amino function directly bound to the cyclopentadienyl ring of ferrocene has been developed. The key reaction is the Cu_2O promoted substitution of (*pR*)-*N*,*N*-diisopropyl-2-iodoferrocenecarboxamide with either phthalimide or AcOH to introduce nitrogen or oxygen functionality onto the cyclopentadienyl ring. The enantiomerically pure iodoferrocene derivative is available from the known enantioselective *ortho*-lithiation of *N*,*N*-diisopropylferrocenecarboxamide with *n*-BuLi–sparteine. In the course of these studies the synthesis of a novel C_2 symmetric C-2 dimer of *N*,*N*-dimethyl-1-ferrocenylethylamine was characterised by single crystal X-ray diffraction.

Introduction

The development of asymmetric catalysis has relied in part on the invention of unique ligand architectures ultimately to control stereoselectivity. Planar chiral ligands used in metal centred asymmetric catalysis have been shown to be a powerful stereocontrol element in the efficient production of enantio-enriched materials. The most well known planar chiral bidentate chelate ligands at present are based upon the ferrocene motif.[1,2] Since the first report of chelate ligands in this class were shown to give modest enantioselectivities in rhodium-catalysed hydrosilylations of ketones,[3] numerous studies have been undertaken to improve these results. These studies have collectively investigated the diverse architecture and possible permutations of functional groups around the ferrocene unit.[1,4] We wish to investigate amino alcohol and diamine planar chiral ligands, based on a ferrocene motif, which possesses an oxy or amino function directly bound to a cyclopentadienyl ligand, in various metal catalysed asymmetric processes. Although hydroxy and amino ferrocene have been synthesised there are no reports of chelate ligands based in part on these potential donor sites. The amino ferrocene derivative in particular may exhibit interesting donor capabilities based on a correlation with its basicity which, due to opposing resonance stabilisation by the Cp ring and a positive inductive effect from the ferrocenyl group, lies between that of aniline and 1-ferrocenylethylamine.[5] In this publication we report our development of the synthesis of planar chiral chelate ligands of amino and oxy ferrocene with a pendant amino side chain. These new variants have the flexibility to become platforms for other chiral ligands.

Results and discussion

Our initial attempts to access ligand systems of type **1** were from the readily available racemic *N*,*N*-dimethyl-1-ferrocenylethylamine (**2**, Fig. 1). This starting material had been introduced by Ugi and coworkers[6,7] and has proven particularly effective for the synthesis of enantiomerically pure planar chiral ferrocene ligands by resolution of **2**.[8]



1, X = OR, NRR' **2**

Fig. 1

The most direct entry to an aminoferrocene derivative we thought would be *via* electrophilic amination of *ortho*-lithiated **2**. The diastereoselective *ortho*-lithiation of **2** is very reliable,[7] but treatment with benzylhydroxylamine,[9] *N*,*N*-dimethyl-*O*-(methylsulfonyl)hydroxylamine,[10] or *N*,*O*-bis(trimethylsilyl)-hydroxylamine (*via* the corresponding cyano cuprate),[11] gave only recovered starting material. A three step synthesis of aminoferrocene from ferrocene has been reported that proceeds *via* the coupling of ferroceneboronic acid with copper phthalimide in 13% overall yield.[12] In addition the synthesis of the corresponding boronic acid of **2** would also allow investigation of direct *N*-arylation.[13] Despite following a procedure for the synthesis of 2-(*N*,*N*-dimethylaminomethyl)ferroceneboronic acid which proceeded in 64% yield[14] we were unable to synthesise the corresponding boronic acid of **2**, again only recovering starting material. The preparation of enantiomerically pure 2-aminoferrocenecarboxylic acid *via* a 2-nitroferrocenyloxazoline has been reported by Richards and coworkers.[15] Analogous nitration of lithiated **2** at a melting THF/N_2O_4 interface[16] gave an air unstable oil that by ^1H and ^{13}C NMR was consistent with a 1-ferrocenylethylamine *ortho*-substituted with an electron withdrawing group which we tentatively assigned structure **3** (Scheme 1). The crude mixture of **3** was hydrogenated to give an orange solid that displayed new spectroscopic characteristics indicative of a mono-*ortho*-substituted **2**. Single crystal X-ray diffraction revealed the product to be the racemic C_2 symmetric dimer (*S**,*pS**,*S**,*pS**)-**4**‡ formed in 31% yield.

Compound (*S**,*pS**,*S**,*pS**)-**4** is the homocoupled product arising from the dimerisation of identical enantiomers from the expected diastereoselective *ortho*-lithiation of (±)-**2**. The other expected (*S**,*pS**,*R**,*pR**)-diastereoisomer (formed from the dimerisation of opposite enantiomers from the diastereoselective *ortho*-lithiation of (±)-**2**) and a small amount of the (*R**,*pR**,*R*,*pS**)-diastereomer (formed from the minor diastereoisomer of *ortho*-lithiated (±)-**2** combining with the major diastereoisomer of *ortho*-lithiated (±)-**2**) have been reported,[17] but were not isolated in our experiment. We postulate that this unique bis-ferrocenyl amine is formed from the ferrocenyl nitro

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‡ CCDC reference number 218360. See http://www.rsc.org/suppdata/ob/b3/b307014j/ for crystallographic files in .cif or other electronic format.

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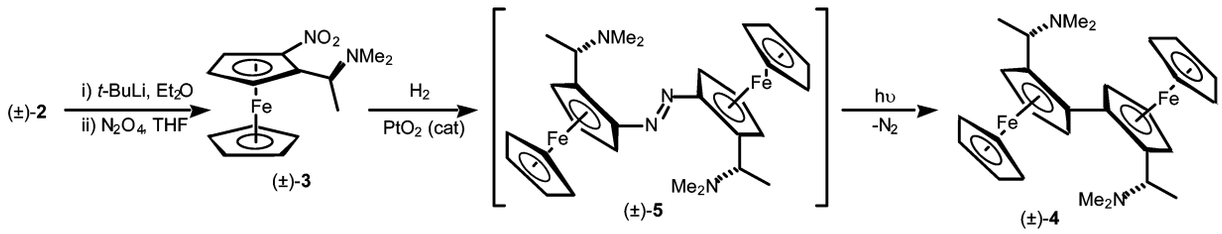


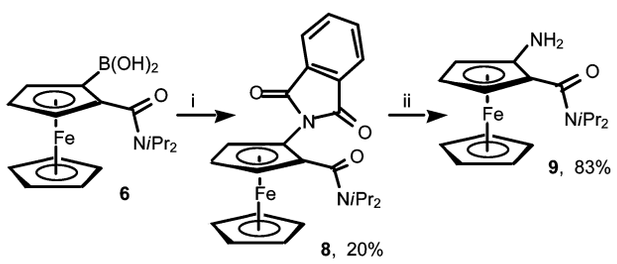
Scheme 1

compound **3** which under the reducing conditions was transformed into azo compound **5**.[18] The azo compound might then photolytically extrude nitrogen[19] to yield the C_2 symmetric dimer **4**. This dimer may exhibit interesting coordinating properties like its bis-phosphine analogue[20] and these studies are underway.

The use of a Curtius rearrangement to introduce the desired amino substituent[21] was thwarted by our inability to form the precursor amino amide from direct treatment of lithiated **2** with TMS-isocyanate[22] or *via* the amino acid with solid CO_2.[23] Our attention briefly turned to the introduction of an *ortho*-hydroxy group into **2**. The synthesis of 2-(*N*,*N*-dimethylaminomethyl)-ferrocenol had been reported from the corresponding iodide by treatment with AcOH and Cu_2O.[24] Treatment of 2-iodo-*N*,*N*-dimethyl-1-ferrocenylethylamine[25] under identical conditions led to an intractable mixture of products.

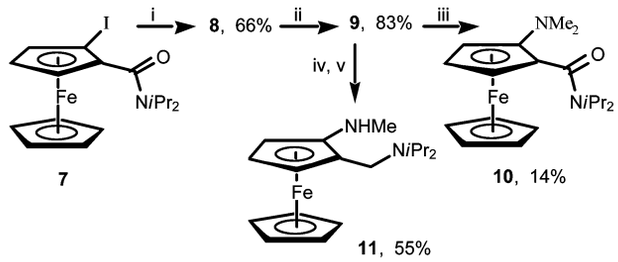
It became apparent that the popular starting material **2**, which has been used successfully for many planar chiral ligand syntheses, was not going to be useful for the synthesis of ligands **1**. However from our efforts we were able to conceive that the introduction of amino and oxygen functionalities directly onto the Cp ring of ferrocene looked most promising from the treatment of a ferrocenyl boronic acid derivative with copper phthalimide[12] and treatment of an iodoferrocenyl derivative with AcOH and Cu_2O[24] respectively. We concluded that our lack of success in our previous efforts was due to the basic amino side chain and that this could be remedied by using a similar ferrocene starting material that possessed a much less basic nitrogen side chain.

The enantiomerically pure boronic acid **6** and iodo derivative **7** of *N*,*N*-diisopropylferrocenecarboxamide have been prepared by *ortho*-lithiation with *n*-butyllithium and (−)-sparteine and quenching with a suitable electrophile in high enantioselectivity.[26] We envisaged that the amide nitrogen would be less likely to interfere in subsequent reactions due to the reduced availability of its lone pair. Treatment of **6**[26] with copper phthalimide in refluxing acetone gave a disappointing 20% yield of the desired substitution product **8** (Scheme 2). The phthalimide was successfully deprotected to give the amine **9** in 83% yield.



Scheme 2 *Reagents*: i, copper phthalimide, acetone; ii, $H_2NNH_2{\cdot}H_2O$, EtOH.

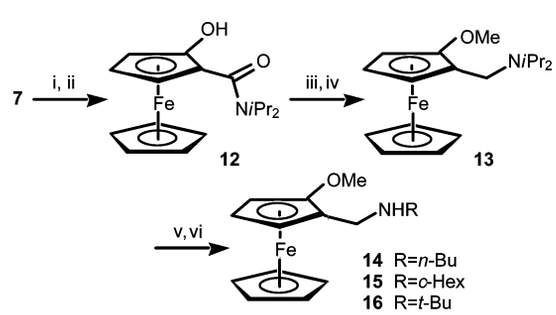
The yield of this amination was not synthetically useful. Attempts at Buchwald–Hartwig type palladium catalysed amination[27] of the corresponding iodide **7** were unfruitful. However treatment of **7**[26] with phthalimide and Cu_2O under modified reaction conditions, in which pyridine was replaced with MeCN, gave a 66% yield of **8** after refluxing overnight (Scheme 3). Deprotection proceeded as before, but alkylation of the primary amine could not be achieved by standard reductive amination. Eschweiler–Clarke *N*,*N*-dimethylation[28] gave only a low 14% yield of diamine **10**. The mono-*N*-methyl ligand **11** was achieved by first Boc protection and then reduction with $LiAlH_4$ which also reduced the amide to a pendant diisopropylaminomethyl substituent.



Scheme 3 *Reagents and conditions*: i, phthalimide, Cu_2O, MeCN, 14 h, 82 °C; ii, $H_2NNH_2{\cdot}H_2O$, EtOH; iii, H_2CO, HCO_2H; iv, Boc_2O, DMAP, CH_2Cl_2, 60%; v, $LiAlH_4$, THF, 67 °C, 91%.

Although this diamine is the first of its kind, its synthesis is limited with respect to diversity. The exchange of the diisopropyl substituent would require selective activation,[29] which is hard to conceive. However the cyclopentadienyl amine was unreactive towards alkylation. A more fruitful strategy in future could be to use an *ortho* directing amide that possessed a removable group.[30]

With respect to structural diversity, the synthesis of potential chelate ligands based on oxy-substituted ferrocene derivatives with a pendant amino side chain became more attractive. Treatment of **7** with AcOH and Cu_2O gave the acetate substitution product in 85% yield (Scheme 4). Hydrolysis with ethoxide ion gave the hydroxyferrocene derivative **12** (88% yield), which was more stable than anticipated.[31] This may be attributed to a favourable hydrogen bond between the hydroxy and the amide carbonyl group as evidenced by the hydroxy group's chemical shift of δ 9.68 in the ^{1}H NMR spectrum.[32] The alcohol was smoothly methylated with NaH and MeI (80%) and the amide successfully reduced with $LiAlH_4$ (81%) to give the desired oxyferrocene derivative with a pendant amino side chain **13**.



Scheme 4 *Reagents and conditions*: i, AcOH, Cu_2O, MeCN, 85%; ii, aq. NaOH, EtOH, 88%; iii) NaH, THF, MeI, 80%; iv) $LiAlH_4$, Et_2O, 81%; v) MeI, MeCN; vi) RNH_2, MeCN, R = *n*-Bu, 64%, R = *c*-Hex 72%, R = *t*-Bu, 49% over two steps.

We were also able to show that the pendant diisopropylamine side chain could be substituted with other amines. Quaternisation with MeI followed by treatment with *n*-butylamine, cyclohexylamine or *tert*-butylamine gave the potential chelating ligands **14**–**16** in good yields.

Conclusion

Efficient syntheses of novel planar chiral 1,3-diamines and 1,3-amino alcohols with an oxy or amino function directly bound to the cyclopentadienyl ring of ferrocene have been reported. The enantiomerically pure ligands were derived from the enantioselective *ortho*-lithiation of *N*,*N*-diisopropylferrocenecarboxamide developed by Snieckus *et.al.*[26] The enantiomeric systems could be prepared by using a silicon blocking group in the enantioselective *ortho*-lithiation reaction.[26] These new ligands are currently being assayed for effectiveness in asymmetric catalytic processes and are being used as starting materials for more complex planar chiral ligand systems. Results from these studies will be reported in due course.

Experimental

Unless otherwise stated all reactions were carried out under an atmosphere of nitrogen. All glassware was flame dried and allowed to cool under a stream of nitrogen before use. THF was distilled under an atmosphere of dry nitrogen from potassium benzophenone ketyl. Diethyl ether was distilled under a dry atmosphere of nitrogen from sodium benzophenone ketyl. All other reagents were purified or dried according to standard literature methods. Solutions of alkyllithiums were standardised with *N*-pivaloyl-*o*-toluidine.[33] Water was distilled. Thin layer chromatography was performed on Polygram® SIL G/UV_{254} 0.25 mm silica gel precoated plastic sheets with fluorescent indicator. Sheets were visualised using ultra violet light (254 nm) and/or $KMnO_4$ or anisaldehyde solutions. Flash column chromatography was carried out using Fluorochem silica gel 60, 35–70 μ. Optical rotations were recorded on a Jasco DIP370 Digital Polarimeter and are reported in deg cm^2 g^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded as dilute solutions in deuteriochloroform unless otherwise stated. All chemical shifts (δ) are quoted in ppm and coupling constants (J) in Hz. Coupling constants are recorded as observed in the spectrum without averaging. ^{13}C multiplicities were assigned using a DEPT sequence. Residual signals from the solvents were used as an internal reference. Mass spectra were acquired on a VG micromass 70E, VG Autospec or Micromass LCTOF spectrometer. Melting points are uncorrected and were recorded on a Reichert melting point apparatus. Elemental analyses were performed by the microanalysis service of the School of Chemistry, University of Nottingham on an Exeter Analytical Inc. CE440 elemental analyzer.

(±)-2-Nitro-*N*,*N*-dimethyl-1-ferrocenylethylamine (±)-3

To a solution of (+)-**2** (1.06 g, 4.1 mmol) in Et_2O (40 mL) in a 500 mL Schlenk flask at −78 °C was added *tert*-butyllithium (3.3 mL of a 1.6 M soln in hexane, 5.3 mmol) dropwise and the reaction mixture left to stir for 1 h before being allowed to warm to rt. The Et_2O was removed *in vacuo* and the residue was dissolved in THF (40 mL). The reaction mixture was then frozen in as thin a layer as possible, around the walls of the flask, using a liquid nitrogen bath and placed under a static vacuum. Dinitrogen tetraoxide (0.38 g, 4.1 mmol, 1.0 equiv.) was condensed, as a blue solid, into a pre-weighed, evacuated Schlenk flask using an acetone–dry ice bath. The flask was then allowed to warm to room temperature to give a brown gas. A piece of Portex™ tubing fitted with a needle was attached to the flask and used to condense the gas into the reaction vessel. The reaction mixture was then warmed rapidly using a methanol bath and agitated vigorously. The pale brown frozen solution turned a deep red colour and the reaction was complete within 2 minutes. The excess dinitrogen tetraoxide and THF were removed *in vacuo* and the residue was dissolved in CH_2Cl_2. The CH_2Cl_2 solution was then filtered, washed with H_2O, dried (Na_2SO_4) and concentrated *in vacuo* yielding 1.04 g of red oil.

In one experiment this seemingly air unstable oil was purified by flash column chromatography to give four main fractions. All but the third fraction (in order of polarity) oxidised rapidly and gave broad NMR spectra thought to be due to paramagnetism. The third fraction (60 mg) was a 1 : 1 mixture of **3** with starting material from which NMR data was recorded before decomposition. The data below is a listing of the peaks assigned to **3**. δ_H (400 MHz) 1.55 (3H, d, J 6.9, CH_3), 2.08 (6H, s, $N(CH_3)_2$), 4.11 (6H, s, CH_5 Cp + CH Cp_{subs}), 4.48 (1H, m, CH Cp_{subs}), 4.63 (1H, q, J 6.9, CH), 5.25 (1H, s, CH Cp_{subs}); δ_C (100 MHz) 15.5 (CH_3), 40.4 (2C, $N(CH_3)_2$), 54.4 (CH), 68.0 (CH Cp_{subs}), 70.1 (CH Cp_{subs}), 72.3 (CH Cp_{subs}), 87.4 (C Cp_{subs}).

(*S**,*pS**,*S**,*pS**)-2,2′-Bis[1-(*N*,*N*-dimethylamino)ethyl]-1,1′-biferrocene (*S**,*pS**,*S**,*pS**)-4

To a solution of the crude nitration reaction mixture (1.04 g, theoretically 3.4 mmol) in EtOH (100 mL) was added PtO_2 (0.099 g, 0.44 mmol). The reaction flask was stirred under H_2 at atmospheric pressure and rt for 2 h. The reaction mixture was filtered through Celite™ and concentrated *in vacuo*, yielding 0.87 g of brown oil. Flash column chromatography (gradient elution 4% CH_2Cl_2–1% Et_3N–95% MeOH to 50% Et_3N–MeOH) gave (±)-**2** (0.29 g) and the dimer (*S**,*pS**,*S**,*pS**)-**4** (0.33 g, 31%) as a brown–orange solid. Mp = 145–147 °C; ν_{max} 2933 (C–H), 2775, 1601, 1455, 1366, 1106 cm^{-1}; δ_H (400 MHz) 1.37 (6H, d, J 6.8, $CH(NMe_2)CH_3$), 1.80 (12H, s, $N(CH_3)_2$), 3.68 (2H, q, J 6.8, $CH(NMe_2)CH_3$), 4.15 (2H, s, CH Cp_{subs}), 4.24 (10H, s, CH Cp_{unsubs}), 4.44 (2H, s, CH Cp_{subs}); δ_C (100 MHz) 14.5 (2C, $CH(NMe_2)CH_3$), 40.4 (4C, $N(CH_3)_2$), 55.7 (2C, $CH(NMe_2)CH_3$), 65.8 (2C, CH Cp_{subs}), 67.0 (2C, CH Cp_{subs}), 69.7 (10C, CH Cp_{unsubs}), 85.9, 90.4; HRMS (FAB^+) $C_{28}H_{37}Fe_2N_2$ calcd. 513.1655, found 513.1651 (MH^+); anal. calcd. for $C_{28}H_{36}Fe_2N_2$: C, 65.65; H, 7.08; N, 5.47; found: C, 65.16; H, 7.11; N, 5.42%.

Crystal structure determination of (*S**,*pS**,*S**,*pS**)-4 ‡

Crystal data: $C_{28}H_{36}Fe_2N_2$, M = 512.29, triclinic, a = 10.517(4), b = 10.678(4), c = 12.532(5) Å, α = 104.199(4), β = 100.115(4), γ = 112.747(3)°, U = 1199.3(9) $Å^3$, T = 150(2) K, space group $P\bar{1}$ (No. 2), Z = 2, D_c = 1.419 g cm^{-3}, μ = 1.228 mm^{-1}, 5358 unique reflections measured, corrected for absorption (R_{int} 0.020) and used in all calculations. Final R_1 [$4515F > 4\sigma(F)$] = 0.0261 and wR (all F^2) = 0.0694.

(*pR*)-2-[2-(*N*,*N*-Diisopropylcarbamoyl)ferrocenyl]phthalimide 8 from 6

A suspension of **6**[26] (3.80 g, 10.6 mmol) and copper phthalimide[12] (7.57 g, 21.3 mmol) in acetone (100 mL) was refluxed for 2 h then allowed to cool to rt overnight. The reaction mixture was concentrated *in vacuo* and the residue was taken up in EtOAc. This solution was filtered in order to remove the copper salts. The organic layer was then washed successively with 10% KOH (2 × 50 mL), H_2O (50 mL), 10% AcOH (2 × 50 mL), H_2O (50 mL) then brine (2 × 50 mL). The organics were then dried ($MgSO_4$), and concentrated *in vacuo* to yield an orange solid. Purification by column chromatography (10% EtOAc–hexane) yielded **8** (0.960 g, 20%) as a pale brown solid. Mp = 218–220 °C; R_f = 0.40 (30% EtOAc–hexane); $[a]_D$ = +146.3 (c = 1.08, $CHCl_3$); ν_{max} 1722 (C=O phthalimide), 1617 (C=O ferrocenyl amide), 1462, 1372, 1317 cm^{-1}; δ_H (400 MHz) 1.23 (6H, br s, $NCH(CH_3)_2$), 1.40 (3H, br, $NCH(CH_3)_2$), 1.46 (3H, br, $NCH(CH_3)_2$), 3.40 (1H, br s, $NCHMe_2$), 4.28 (1H, t,

J 2.6, C*H* Cp_{subs}), 4.39 (6H, s, 5C*H* Cp_{unsubs} and C*H* Cp_{subs}), 4.52 (1H, dd, *J* 2.4, 1.4, C*H* Cp_{subs}), 4.60 (1H, br s, NC*H*Me_2), 7.71 (2H, dd, *J* 5.4, 3.0, C*H* phthalimide), 7.85 (2H, dd, *J* 5.4, 3.0, C*H* phthalimide); δ_C (100 MHz) 20.6 (2C, br, NCH(CH_3)$_2$), 20.8 (1C, br, NCH(CH_3)$_2$), 21.6 (1C, br, NCH(CH_3)$_2$), 45.9 (1C, N*C*HMe_2), 50.5 (1C, N*C*HMe_2), 64.8 (1C, *C*H Cp_{subs}), 65.0 (1C, *C*H Cp_{subs}), 65.2 (1C, *C*H Cp_{subs}), 71.8 (5C, *C*H Cp_{unsubs}), 80.2 (1C, *C*C=ON^{i}Pr$_2$), 88.8 (1C, *C*N Cp_{subs}), 123.2 (2C, *C*H phthalimide), 132.3 (2C, *C* phthalimide), 134.0 (2C *C*H phthalimide), 166.9 (2C, *C*=O phthalimide), 167.2 (1C, C*C*=ON^{i}Pr$_2$); *m*/*z* (EI$^+$) 458 (100%, M$^+$), 330 (10%), 266 (14%), 119 (12%); HRMS $C_{25}H_{20}FeN_2O_3$ calcd. 458.1293, found 458.1288; anal. calc. for $C_{25}H_{20}FeN_2O_3$: C, 65.51; H, 5.72; N, 6.11; found: C, 65.41; H, 5.53; N, 6.06%.

($_p$*R*)-2-[2-(*N*,*N*-Diisopropylcarbamoyl)ferrocenyl]phthalimide 8 from 7

A stirred solution of **7**[26] (4.94 g, 11.3 mmol), Cu_2O (966 mg, 6.75 mmol) and phthalimide (1.99 g, 13.5 mmol) in MeCN (68 mL) was refluxed for 14 h. The reaction mixture was allowed to cool to rt and concentrated *in vacuo*. The residue was taken up in EtOAc (70 mL) and filtered to remove copper salts. The filtrate was washed with 2 M NaOH (2 × 50 mL), brine (2 × 50 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography gave **8** (3.40 g, 66%) whose spectroscopic data were identical to that prepared from **6**.

($_p$*R*)-2-(*N*,*N*-Diisopropylcarbamoyl)ferrocenylamine 9

To a solution of **8** (1.20 g, 2.62 mmol) in EtOH (50 mL) was added $NH_2NH_2{\cdot}H_2O$ (1.3 mL, 26 mmol). The reaction mixture was refluxed for 30 min then allowed to cool to rt before being quenched with H_2O (50 mL). The reaction mixture was extracted with Et_2O (3 × 40 mL) and then the Et_2O layer was extracted with 15% HCl (3 × 30 mL). The aqueous layer was basified with 2 M NaOH and extracted with Et_2O (3 × 40 mL). The Et_2O layer was then dried ($MgSO_4$), and concentrated *in vacuo* to yield **9** (0.860 g, 83%) as a dark brown crystalline solid. Mp = 125–127 °C; R_f = 0.20 (40% EtOAc–hexane); $[\alpha]_D$ = −8.82 (*c* = 1.03, $CHCl_3$); ν_{max} 3419 and 3326 (N–H), 1581 (C=O), 1463, 1370, 1336 cm^{-1}; δ_H (400 MHz) 1.4 (12H, br, N(CH(C*H*$_3$)$_2$)$_2$), 3.5–4.5 (2H, br, NC*H*Me_2), 3.75 (2H, s, N*H*$_2$), 3.90 (1H, t, *J* 2.6, C*H* Cp_{subs}), 4.08 (1H, dd, *J* 2.6, 1.4, C*H* Cp_{subs}), 4.12 (5H, s, C*H* Cp_{unsubs}), 4.17 (1H, dd, *J* 2.6, 1.4, C*H* Cp_{subs}); δ_C (100 MHz) 21.3 (br, *C*H$_3$), 21.7 (*C*H$_3$), 45–50 (2C, br, N*C*HMe_2), 58.8 (1C, *C*H Cp_{subs}), 62.5 (1C, *C*H Cp_{subs}), 62.7 (1C, *C*H Cp_{subs}), 67.1 (1C, *C*C=ON^{i}Pr$_2$), 70.8 (5C, *C*H Cp_{unsubs}), 111.4 (1C, *C*NH_2 Cp_{subs}), 171.3 (1C, C*C*=ON^{i}Pr$_2$); *m*/*z* (FAB$^+$) 328 (100%, M$^+$), 228 (18%), 200 (8%); HRMS $C_{17}H_{24}FeN_2O$ calcd. 328.1238, found 328.1247; anal. calcd. for $C_{17}H_{24}FeN_2O$: C, 62.17; H, 7.37; N, 8.54; found: C, 62.25; H, 7.21; N, 8.63%.

($_p$*R*)-*N*,*N*-Dimethyl-2-(*N*′,*N*′-diisopropylcarbamoyl)ferrocenylamine 10

To a solution of (±)-**9** (500 mg, 1.52 mmol) in formaldehyde (1.1 mL of a 40% w/v aqueous solution, 15 mmol) was added HCO_2H (1.2 mL of a 98% aqueous solution, 30 mmol). The reaction mixture was allowed to cool to rt and diluted with H_2O (5 mL), basified with 2 M NaOH and extracted with Et_2O. The Et_2O layer was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc–1% Et_3N–hexane) gave (±)-**10** (75 mg, 14%) as a pale brown crystalline solid. Mp = 115.9–17.2 °C; R_f = 0.68 (40% EtOAc–petrol); ν_{max} 2964 (C–H), 1621 (C=O), 1456, 1369, 1320, 1039 cm^{-1}; δ_H (400 MHz) 0.93 (3H, d, *J* 6.7, NCH(C*H*$_3$)$_2$), 1.08 (3H, d, *J* 6.6, NCH(C*H*$_3$)$_2$), 1.45 (3H, d, *J* 6.8, NCH(C*H*$_3$)$_2$), 1.48 (3H, d, *J* 6.8, NCH(C*H*$_3$)$_2$), 2.59 (6H, s, N(C*H*$_3$)$_2$), 3.39 (1H, septet, *J* 6.8, NC*H*Me_2), 3.80 (1H, septet, *J* 6.8, NC*H*Me_2), 3.82 (1H, dd, *J* 2.4, 1.6, C*H* Cp_{subs}), 3.87 (1H, t, *J* 2.5, C*H* Cp_{subs}), 4.06 (1H, dd, *J* 2.5, 1.6, C*H* Cp_{subs}) 4.42 (5H, s, C*H* Cp_{unsubs}); δ_C (100 MHz) 19.7 (NCH(*C*H$_3$)$_2$), 20.5 (NCH(*C*H$_3$)$_2$), 20.9 (NCH(*C*H$_3$)$_2$), 21.0 (NCH(*C*H$_3$)$_2$), 43.6 (2C, N(*C*H$_3$)$_2$), 45.7 (N*C*HMe_2), 50.5 (N*C*HMe_2), 56.9 (*C*H Cp_{subs}), 61.3 (*C*H Cp_{subs}), 66.1 (*C*H Cp_{subs}), 68.4 (5C, *C*H Cp_{unsubs}), 75.9 (*C*C=ON^{i}Pr$_2$), 111.7 (*C*NMe_2), 168.4 (C*C*=ON^{i}Pr$_2$); *m*/*z* (FAB$^+$) 356 (100%, M$^+$), 256 (19%), 147 (13%), 73 (53%); HRMS $C_{19}H_{28}FeN_2O$ calcd. 356.1551, found 356.1559; anal. calcd. for $C_{19}H_{28}FeN_2O$: C, 64.05; H, 7.92; N, 7.86; found: C, 64.20; H, 7.80; N, 7.82%.

($_p$*R*)-*N*-*tert*-Butoxycarbonyl-2-(*N*′,*N*′-diisopropylcarbamoyl)ferrocenylamine

A mixture of **9** (0.378 g, 1.15 mmol), Boc_2O (0.329 g, 1.50 mmol) and DMAP (0.020 g, 0.16 mmol) in CH_2Cl_2 (4.0 mL) was stirred at rt overnight. The reaction mixture was concentrated *in vacuo* and purified by column chromatography (20% EtOAc–hexane) to give Boc protected-**9** (0.292 g, 60%) as an orange solid. Mp = 132–134 °C; R_f = 0.35 (40% EtOAc–hexane); $[\alpha]_D$ = +505.6 (*c* = 0.99, $CHCl_3$); ν_{max} 3343 (N–H), 2973 (C–H), 1711 (C=O Boc), 1595 (C=O amide), 1454, 1369, 1346, 1315, 1159 cm^{-1}; δ_H (400 MHz) 1.2–1.6 (12H, br, NCH(C*H*$_3$)$_2$), 1.51 (9H, s, (C=O)OC(C*H*$_3$)$_3$), 3.2–3.8 (1H, br, N(C*H*Me_2), 4.10 (2H, m, C*H* Cp_{subs}), 4.17 (5H, s, C*H* Cp_{unsubs}), 4.3–5.0 (1H, br, NC*H*Me_2), 5.33 (1H, s, C*H* Cp_{subs}), 8.18 (1H, s, N*H*); δ_C (100 MHz) 21.4 (CH(*C*H$_3$)$_2$), 28.5 (C(*C*H$_3$)$_3$), 50 (br, *C*HMe_2), 62.4 (*C*H Cp_{subs}), 63.7 (*C*H Cp_{subs}), 64.9 (*C*H Cp_{subs}), 66.5, 70.7 (*C*H Cp_{unsubs}), 79.7, 100.6, 153.5 (C=O), 171.6 (C=O); *m*/*z* (FAB$^+$) 428 (100%, M$^+$), 328 (78%), 228 (19%); HRMS $C_{22}H_{32}FeN_2O_3$ calcd. 428.1762, found 428.1752; anal. calcd. for $C_{22}H_{32}FeN_2O_3$: C, 61.69; H, 7.53; N, 6.54; found: C, 61.53; H, 7.51; N, 6.42%.

($_p$*R*)-2-(*N*′-Methylamino)-*N*,*N*-(diisopropyl)ferrocenylmethylamine 11

To a stirred solution of Boc protected-**9** (1.00 g, 2.33 mmol) in THF (12 mL) was added a solution of $LiAlH_4$ (9.3 mL of a 1 M soln in THF, 9.3 mmol) at rt. The reaction mixture was refluxed for 14 h before cooling to rt and quenched by the cautious dropwise addition of H_2O (0.5 mL), then 2 M NaOH (0.5 mL) and a further portion of water (1.5 mL) with vigorous stirring. The mixture was filtered, the filtrate washed with water (3 × 10 mL) and extracted with 1 M HCl. The acid layer was basified with 2 M NaOH and extracted with Et_2O (3 × 10 mL). The Et_2O layers were washed with brine (3 × 10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (40% EtOAc–1% Et_3N–59% hexane) gave **11** as an orange oil (697 mg, 91%); R_f = 0.20 (50% EtOAc–1% Et_3N–49% hexane); $[\alpha]_D$ = +344.5 (*c* = 1.00, $CHCl_3$); ν_{max} 3370 (N–H), 2931 (C–H), 1731, 1364, 1118, 1046, 998 cm^{-1}; δ_H (400 MHz) 0.96 (6H, d, *J* 6.6, NCH(C*H*$_3$)$_2$), 1.03 (6H, d, *J* 6.7, NCH(C*H*$_3$)$_2$), 2.73 (3H, d, *J* 5.8, NHC*H*$_3$), 3.08 (2H, septet, *J* 6.6, NC*H*Me_2), 3.30 (1H, d, *J* 5.7, N*H*Me), 3.37 (1H, d, *J* 14.0, C*H*$_2$N^{i}Pr$_2$), 3.74 (2H, s, 2 × C*H* Cp_{subs}), 3.76 (1H, d, *J* 14.4, C*H*$_2$N^{i}Pr$_2$), 3.86 (1H, s, CCp_{subs}), 4.08 (5H, s, C*H* Cp_{unsubs}); δ_C (100 MHz) 19.2 (NCH(*C*H$_3$)$_2$), 21.7 (NCH(*C*H$_3$)$_2$), 33.7 (NHC*H*$_3$), 43.4 (*C*H$_2$), 46.6 (2C, N*C*HMe_2), 52.7 (*C*H Cp_{subs}), 60.2 (*C*H Cp_{subs}), 65.5 (*C*H Cp_{subs}), 68.4 (5C, *C*H Cp_{unsubs}), 73.8 (*C*CH$_2$), 113.1 (*C*NHMe); *m*/*z* (FAB$^+$) 328 (100%, M$^+$), 227 (58%), 114 (28%); HRMS $C_{18}H_{28}FeN_2$ calcd. 328.1602, found 328.1619.

($_p$*R*)-2-(*N*,*N*-Diisopropylcarbamoyl)ferrocenyl acetate

To a flask containing Cu_2O (0.694 g, 4.85 mmol) was added a solution of **7** (3.38 g, 7.70 mmol) in MeCN (50 mL), AcOH (0.53 mL, 9.2 mmol) and the mixture refluxed for 2.5 h. After cooling to rt the reaction mixture was filtered and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL) and washed

with sat. aq. NH_4Cl (2 × 50 mL) and brine (2 × 50 mL) then dried ($MgSO_4$) and concentrated *in vacuo* to yield a golden brown oil. Purification by flash column chromatography (10% EtOAc–hexane) gave a pale brown oil which solidified on standing. Recrystallisation from hexane gave 2-(*N*,*N*-diisopropylcarbamoyl)ferrocenyl acetate (2.44 g, 85%) as golden brown crystals. Mp = 94–96 °C; R_f = 0.55 (30% EtOAc–hexane); $[\alpha]_D$ = +107.4 (*c* = 1.10, $CHCl_3$); ν_{max} 2968 (C–H), 1754 (C=O ferrocenyl acetate), 1620 (C=O ferrocenyl amide), 1462, 1370, 1322 cm^{-1}; δ_H (400 MHz) 1.1 (6H, br s, NCH(CH_3)$_2$), 1.5 (6H, br s, NCH(CH_3)$_2$), 2.18 (3H, s, C=OCH_3), 3.39 (1H, br s, NC*H*Me$_2$), 3.98 (1H, t, *J* 2.6, C*H* Cp$_{subs}$), 4.10 (2H, dd and br s, *J* 2.6, 1.4, C*H* Cp$_{subs}$ and NC*H*Me$_2$), 4.36 (5H, s, C*H* Cp$_{unsubs}$), 4.42 (1H, dd, *J* 2.6, 1.4, C*H* Cp$_{subs}$); δ (100 MHz) 20.9 (4C, br, NCH(*C*H$_3$)$_2$), 21.2 (1C, OC=O*C*H$_3$), 46.0 (1C, br, N*C*HMe$_2$), 50.6 (1C, br, N*C*HMe$_2$), 61.0 (1C, *C*H Cp$_{subs}$), 61.9 (1C, *C*H Cp$_{subs}$), 62.8 (1C, *C*H Cp$_{subs}$), 71.3 (5C, *C*H Cp$_{unsubs}$), 79.3 (1C, *C*C=ON^{i}Pr$_2$), 115.2 (1C, *C*OC=OCH$_3$), 166.1 (1C, *C*=O), 169.9 (1C, *C*=O); *m*/*z* (FAB$^+$) 371 (100%, M$^+$), 329 (30%), 228 (12%); HRMS $C_{19}H_{25}FeNO_3$ calcd. 371.1184, found 371.1159; anal. calcd. for $C_{19}H_{25}NFeO_3$: C, 61.47; H, 6.79; N, 3.77; found: C, 61.58; H, 6.78; N, 3.58%.

($_p$*R*)-*N*,*N*-Diisopropyl-2-hydroxyferrocenecarboxamide 12

To a solution of 2-(*N*,*N*-diisopropylcarbamoyl)ferrocenyl acetate (8.67 g, 23.3 mmol) in EtOH (230 mL) was added a solution of NaOH (1.4 g, 35 mmol) in H_2O (35 mL). The reaction mixture was stirred at rt for 30 min before being quenched with sat. aq. NH_4Cl (200 mL). The resultant mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organics were washed with H_2O (2 × 100 mL) and then brine (2 × 100 mL) before being dried ($MgSO_4$). Concentration *in vacuo* gave **12** (6.74 g, 88%) as a dark brown solid. Mp = 104–106 °C; R_f = 0.65 (30% EtOAc–hexane); ν_{max} 3196 (O–H, H-bonded), 2967 (C–H), 1588 (C=O), 1503, 1345, 1209, 816 cm^{-1}; δ_H (400 MHz) 1.2–1.6 (12H, br, NCH(CH_3)$_2$), 3.4–3.6 (1H, br, NC*H*Me$_2$), 3.93 (1H, t, *J* 2.8, C*H* Cp$_{subs}$), 4.04 (1H, s, C*H* Cp$_{subs}$), 4.17 (5H, s, C*H* Cp$_{unsubs}$), 4.45 (1H, s, C*H* Cp$_{subs}$), 4.7–4.8 (1H, br s, NC*H*Me$_2$), 9.68 (1H, s, exchanges with D_2O, O*H*); δ_C (100 MHz) 21.2 (4C, br, NCH(*C*H$_3$)$_2$), 46.9 (1C, br, NC*H*Me$_2$), 49.2 (1C, br, NC*H*Me$_2$), 58.0 (1C, *C*H Cp$_{subs}$), 59.6 (1C, *C*C=ON^{i}Pr$_2$), 61.8 (1C, *C*H Cp$_{subs}$), 62.6 (1C, *C*H Cp$_{subs}$), 70.3 (5C, *C*H Cp$_{unsubs}$), 128.8 (1C, *C*OH), 174.9 (1C, C*C*=ON^{i}Pr$_2$); *m*/*z* (FAB$^+$) 329 (100%, M$^+$), 228 (15%), 200 (13%); HRMS $C_{17}H_{23}FeNO_2$ calcd. 329.1078, found 329.1105; anal. calcd. for $C_{17}H_{23}NFeO_2$: C, 62.04; H, 7.04; N, 4.26; found: C, 61.92; H, 7.04; N, 4.26%.

($_p$*R*)-*N*,*N*-Diisopropyl-2-methoxyferrocenecarboxamide

To a slurry of NaH (60% in mineral oil, 0.687 g, 17.1 mmol) in THF (20 mL) at 0 °C was added a solution of **12** (3.77 g, 11.5 mmol) in THF (120 mL). The reaction mixture was stirred at 0 °C for 45 min before the addition of MeI (1.4 mL, 23 mmol). The reaction mixture was allowed to warm slowly to rt overnight. The solvents were removed *in vacuo* and the residue was dissolved in Et_2O (150 mL). The organics were washed with H_2O (3 × 100 mL) and the aqueous phase then extracted with Et_2O (2 × 50 mL). The combined Et_2O layers were washed with brine (2 × 150 mL) then dried ($MgSO_4$). Concentration *in vacuo* yielded *N*,*N*-diisopropyl-2-methoxyferrocenecarboxamide (3.14 g, 80%) as a pale orange solid. Mp = 132–134 °C; R_f = 0.60 (30% EtOAc–hexane); $[\alpha]_D$ = +210.4 (*c* = 0.96, $CHCl_3$); ν_{max} 2966 (C–H), 2234, 1616 (C=O), 1413, 1323, 1257, 1136, 1049, 819 cm^{-1}; δ_H (400 MHz) 1.0–1.2 (6H, br d, NCH(CH_3)$_2$), 1.49 (6H, br s, NCH(CH_3)$_2$), 3.40 (1H, br s, N(C*H*Me$_2$), 3.71 (3H, s, OCH_3), 3.84 (1H, t, *J* 2.5, C*H* Cp$_{subs}$), 4.03 (2H, dd and br s, *J* 2.5, 1.5, C*H* Cp$_{subs}$ and N(C*H*Me$_2$), 4.11 (1H, dd, *J* 2.6, 1.5, C*H* Cp$_{subs}$), 4.34 (5H, s, C*H* Cp$_{unsubs}$); δ_C 21.2 (4C, br, N(CH(*C*H$_3$)$_2$)$_2$), 46.1 (1C, br, N*C*HMe$_2$), 50.6 (1C, br, N*C*HMe$_2$), 52.7 (1C, O*C*H$_3$), 58.2 (1C, *C*H Cp$_{subs}$), 60.3 (1C, *C*H Cp$_{subs}$), 64.3 (1C, *C*H Cp$_{subs}$), 70.2 (5C, *C*H Cp$_{unsubs}$), 76.3 (1C, *C*C=ON^{i}Pr$_2$), 125.0 (1C, *C*OCH$_3$), 167.1 (1C, C*C*=ON^{i}Pr$_2$); *m*/*z* (FAB$^+$) 343 (100%, M$^+$), 243 (6%), 86 (3%); HRMS $C_{18}H_{25}NO_2Fe$ calcd. 343.1235, found 343.1219; anal. calc. for $C_{18}H_{25}FeNO_2$: C, 62.99; H, 7.34; N, 4.08; found: C, 62.90; H, 7.18; N, 4.03%.

($_p$*R*)-*N*,*N*-Diisopropyl-2-methoxyferrocenylmethylamine 13

To a slurry of $LiAlH_4$ (0.995 g, 26.2 mmol) in Et_2O (15 mL) at 0 °C was added a solution of *N*,*N*-diisopropyl-2-methoxyferrocenecarboxamide (3.00 g, 8.74 mmol) in Et_2O (65 mL) and the reaction refluxed for 14 h. The reaction mixture was then cooled to 0 °C and H_2O (1 mL) was added cautiously dropwise, followed by 2 M NaOH (1 mL) then a further portion of water (3 mL) with vigorous stirring. The granular precipitate was filtered and washed with Et_2O (10 mL). The organic layer was extracted with a 10% solution of phosphoric acid (3 × 50 mL). The acidic aqueous layer was basified with 2 M NaOH and extracted with Et_2O (3 × 50 mL). The Et_2O layer was then washed with brine (2 × 50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give **13** (2.32 g, 81%) as an orange oil. R_f = 0.70 (50% EtOAc–1% Et_3N–49% hexane); $[\alpha]_D$ = +182.7 (*c* = 1.04, $CHCl_3$); ν_{max} 2964 (C–H), 2820 (O–CH_3), 1492, 1418, 1289, 1204, 1050 (C–O) cm^{-1}; δ_H (400 MHz) 0.99 (6H, d, *J* 6.6, NCH(CH_3)$_2$), 1.02 (6H, d, *J* 6.6, NCH(CH_3)$_2$), 3.04 (2H, septet, *J* 6.6, N(C*H*Me$_2$)$_2$), 3.44 (1H, d, *J* 14.3, CpCH_2N^{i}Pr$_2$), 3.58 (1H, d, *J* 14.3, CpCH_2N^{i}Pr$_2$), 3.66 (3H, s, OCH_3), 3.71 (1H, t, *J* 2.6, C*H* Cp$_{subs}$), 3.94 (1H, dd, *J* 2.5, 1.4, C*H* Cp$_{subs}$), 4.00 (1H, s, C*H* Cp$_{subs}$), 4.12 (5H, s, C*H* Cp$_{unsubs}$); δ_C (100 MHz) 20.5 (2C, NCH(*C*H$_3$)$_2$), 21.5 (2C, N(CH*C*H$_3$)$_2$), 41.1 (1C, *C*H$_2$), 47.6 (1C, O*C*H$_3$), 52.3 (1C, *C*H Cp$_{subs}$), 58.0 (2C, *C*H), 59.7 (1C, *C*H Cp$_{subs}$), 65.1 (1C, *C*H, Cp$_{subs}$), 69.0 (5C, *C*H Cp$_{unsubs}$), 77.3 (1C, *C*CH$_2$N^{i}Pr$_2$), 126.0 (1C, *C*OCH$_3$); *m*/*z* (FAB$^+$) 329 (100%, M$^+$), 229 (62%), 114 (11%); HRMS $C_{18}H_{27}NOFe$ calcd. 329.1442, found 329.1443; anal. calcd. for $C_{18}H_{27}FeNO$: C, 65.66; H, 8.26; N, 4.25; found: C, 65.68; H, 8.26; N, 4.24%.

General procedure for substitution of –N^{i}Pr$_2$ for primary amine [29]

To a solution of tertiary ferrocenylamine in MeCN (5 mL mmol^{-1}) was added MeI (60 equiv.). The reaction mixture was stirred at rt for 1.5 h before the volatiles were removed *in vacuo*. The residue was dissolved in MeCN (5 mL mmol^{-1}) and a primary amine (30 equiv.) was added. The reaction mixture was stirred at rt for 14 h before removal of the solvents *in vacuo*. The residue was taken up in CH_2Cl_2 (5 mL mmol^{-1}) and washed with H_2O (2 × 50 mL) and brine (2 × 50 mL) then dried ($MgSO_4$), and concentrated *in vacuo*.

($_p$*R*)-*N*-Butyl-2-methoxyferrocenylmethylamine 14

Reaction of **13** (5.38 g, 16.3 mmol) with *n*-butylamine (48 mL, 490 mmol) according to the general procedure, after purification by flash column chromatography (49% EtOAc–1% Et_3N–49% hexane) gave, in order of elution **13** (1.13 g, 21%) followed by **14** (3.15 g, 64%) as a pale brown oil. R_f = 0.72 (49% EtOAc–1% Et_3N–49% hexane); $[\alpha]_D$ = +274.3 (*c* = 1.04, $CHCl_3$); ν_{max} 3323 (N–H), 3096, 2925 (C–H), 2184, 1495, 1419, 1284, 1049 (C–O), 819 cm^{-1}; δ_H (400 MHz) 0.90 (3H, t, *J* 7.3, CH_2CH_3), 1.33 (3H, m, N*H* and $CH_2CH_2CH_3$), 1.46 (2H, m, $CH_2CH_2CH_3$), 2.60 (2H, m, NHCH_2CH$_2$), 3.42 (1H, d, *J* 13.0, CpCH_2N^{i}Pr$_2$), 3.65 (3H, s, OCH_3), 3.74 (1H, t, *J* 2.6, C*H* Cp$_{subs}$), 3.78 (1H, d, *J* 13.0, CpCH$_a$H$_b$N^{i}Pr$_2$) 3.93 (1H, dd, *J* 2.6, 1.4, C*H* Cp$_{subs}$), 3.98 (1H, dd, *J* 2.6, 1.4, C*H* Cp$_{subs}$), 4.13 (5H, s, C*H* Cp$_{unsubs}$); δ_C (100 MHz) 14.2 (1C, CH$_2$*C*H$_3$), 20.7 (1C, CH$_2$*C*H$_2$CH$_3$), 32.4 (1C, *C*H$_2$CH$_2$CH$_3$), 46.5 (1C, NH*C*H$_2$CH$_2$), 49.4 (1C, Cp*C*H$_2$NH^{n}Bu), 52.3 (1C, *C*H Cp$_{subs}$), 57.6 (1C, O*C*H$_3$), 59.8 (1C, *C*H Cp$_{subs}$), 63.9 (1C, *C*H Cp$_{subs}$), 68.9 (5C, *C*H Cp$_{unsubs}$), 75.4 (1C, *C*CH$_2$NH^{n}Bu), 126.3 (1C,

$COCH_3$); *m/z* (FAB$^+$) 301 (34%, M$^+$), 243 (24%), 229 (100%), 73 (44%); HRMS $C_{16}H_{23}FeNO$ calcd. 301.1129, found 301.1139; anal. calc. for $C_{16}H_{23}FeNO$: C, 63.76; H, 7.70; N, 4.65; found: C, 63.40; H, 7.59; N, 4.78%.

($_p$*R*)-*N*-Cyclohexyl-2-methoxyferrocenylmethylamine 15

Reaction of **13** (500 mg, 1.52 mmol) with cyclohexylamine (5.2 mL, 45 mmol) according to the general procedure, after purification by flash column chromatography (30% EtOAc–1% Et_3N–69% hexane), gave **13** (81 mg, 16%) followed by **15** (360 mg, 72%) as an orange oil. R_f = 0.50 (50% EtOAc–1% Et_3N–49% hexane); ν_{max} 3306 (N–H), 2841, (C–H), 2662, 2506, 1715, 1643, 1456, 1368, 1350, 1093, 1058, 996, 890 cm^{-1}; δ_H 1.1–1.2 (5H, m, *c*-Hex), 1.27 (1H, br s, N*H*), 1.60 (1H, m, *c*-Hex), 1.72 (2H, m, *c*-Hex), 1.88 (2H, m, *c*-Hex), 2.47 (1H, m, NHC*H*c-Hex), 3.48 (1H, d, *J* 12.9, CpCH_2NHc-Hex), 3.65 (3H, s, OCH_3), 3.74 (1H, t, *J* 2.6, C*H* Cp_{subs}), 3.78 (1H, d, *J* 12.9, CpCH_2NHc-Hex), 3.93 (1H, dd, *J* 2.6, 1.4, C*H* Cp_{subs}), 3.98 (1H, dd, *J* 2.6, 1.4, C*H* Cp_{subs}), 4.13 (5H, s, C*H* Cp_{unsubs}); δ_C (400 MHz) 25.06 (CH_2, *c*-Hex), 25.10 (CH_2, *c*-Hex), 26.2 (CH_2, *c*-Hex), 33.4 (CH_2, *c*-Hex), 33.6 (CH_2, *c*-Hex), 43.3 (CH_2NHc-Hex), 52.2 (*C*H, *c*-Hex), 56.2 (*C*H Cp_{subs}), 57.5 (O*C*H$_3$), 59.7 (*C*H Cp_{subs}), 63.6 (*C*H Cp_{subs}), 68.8 (5C, *C*H Cp_{unsubs}), 75.5 (*C*CH$_2$NHc-Hex), 126.1 (*C*OCH$_3$); *m/z* (FAB$^+$) 327 (100%, M$^+$), 229 (97%), 73 (11%), 55 (11%); HRMS $C_{18}H_{25}FeNO$ calcd. 327.1286, found 327.1310.

($_p$*R*)-*N*-*tert*-Butyl-2-methoxyferrocenylmethylamine 16

Reaction of **13** (883 mg, 2.68 mmol) with *tert*-butylamine (8.45 mL, 80.5 mmol) according to the general procedure, after purification by flash column chromatography (20% EtOAc–1% Et_3N–79% hexane), gave **13** (115 mg, 13%) followed by **16** (398 mg, 49%) as an orange oil. R_f = 0.22 (50% EtOAc–1% Et_3N–49% hexane); $[\alpha]_D$ = +275.3 (*c* = 0.98, $CHCl_3$); ν_{max} 3307 (N–H), 2961 (C–H), 1490, 1364, 1130, 1104, 1050, 1000 cm^{-1}; δ_H (400 MHz) 1.15 (9H, s, NHC(CH_3)$_3$), 1.25 (1H, br s, N*H*^{t}Bu), 3.41 (1H, d, *J* 11.8, CpCH_2NH^{t}Bu), 3.65 (3H, s, OCH_3), 3.67 (1H, d, *J* 11.8, CpCH_2NH^{t}Bu), 3.72 (1H, t, *J* 2.6, C*H* Cp_{subs}), 3.96 (2H, m, C*H* Cp_{subs}), 4.12 (5H, s, C*H* Cp_{unsubs}); δ_C (100 MHz) 29.1 (3C, C(*C*H$_3$)$_3$), 39.4 (Cp*C*H$_2$NH^{t}Bu), 50.6 (*C*(CH$_3$)$_3$), 52.3 (*C*H Cp_{subs}), 57.6 (O*C*H$_3$), 59.7 (*C*H Cp_{subs}), 63.4 (*C*H Cp_{subs}), 68.8 (5C, *C*H Cp_{unsubs}), 76.3 (Cp*C*H$_2$NH^{t}Bu), 126.0 (*C*OCH$_3$); *m/z* (FAB$^+$) 301 (100%, M$^+$), 229 (80%), 57 (16%); HRMS $C_{16}H_{23}FeNO$ calcd. 301.1129, found 301.1150; anal. calc. for $C_{16}H_{23}FeNO$: C, 63.76; H, 7.70; N, 4.65; found: C, 63.78; H, 7.58; N, 4.38%.

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