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Practical chromatography-free synthesis of 2-iodo-*N*,*N*-diisopropyl-ferrocenecarboxamide and further transformations

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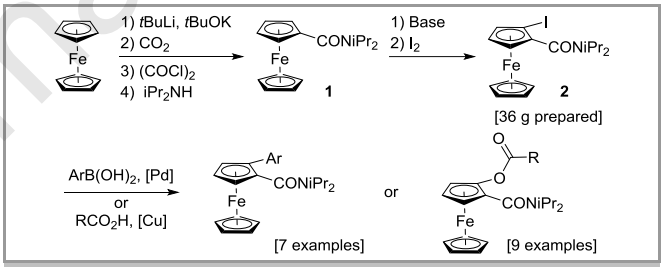
Abstract An efficient procedure able to deliver grams of racemic and enantioenriched 2-iodo-*N*,*N*-diisopropylferrocenecarboxamide without chromatographic purification was developed. To introduce the halogen, two procedures, one using the *n*BuLi-TMEDA chelate and one using a lithium amide in the presence of $ZnCl_2$ as *in situ* trap were developed. Further functionalization by Suzuki-Miyaura and Ullman-type cross-couplings was investigated to access a variety of ferrocene derivatives.

Key words Ferrocene, carboxamide, large scale synthesis, deprotometalation, Suzuki-Miyaura cross-coupling, Ullmann-type cross-coupling

Discovered in 1951, ferrocene is currently one of the most important organometallic scaffolds with multiple applications in redox sensing, catalysis, materials science and medicinal chemistry.[1] Due to its planar chirality when two different substituents are located on the same ring of a ferrocene, the search for asymmetric syntheses has been a recurring question in metallocene science.[2] The diastereoselective ortho-deprotometalation (D*o*M) is a powerful methodology but implies multiple steps to install and remove, when possible, the chiral directing group. Therefore, only a few directing groups are usually used in this strategy.[3] Enzymatic and chemical kinetic resolution have been investigated with various levels of success but are not general.[4] Recent years have witnessed the emergence of catalytic asymmetric ferrocene C-H bond activation.[5] However, due to the use of an expensive catalytic system and, although growing, still limited functionalization scope, this approach remains limited. The enantioselective D*o*M of monosubstituted ferrocenes is another approach which relies on the ability of a chiral base to discriminate between both enantiotopic protons. Although various substrates have been evaluated over the years,[6] *N*,*N*-diisopropylferrocenecarboxamide (**1**) afforded the best results when treated with the *n*BuLi-(-)-sparteine chelate before interception with an electrophile.[7] Even if the availability and prices of sparteine enantiomers have varied over time, (+)-sparteine has remained the most expensive for a long period.[8] Therefore, the use of O'Brien's (+)-sparteine surrogate was required to deliver the opposite enantiomer of 2-substituted ferrocenecarboxamide with high level of stereocontrol.[9] It should be pointed out that, though **1** has mainly been functionalized by deprotolithiation, its deproto-mercuration,[10] -cupration[11] and –zincation[12] have also be reported to prepare compounds that are otherwise hardly accessible.

In the frame of our ongoing research program dedicated to the synthesis of original ferrocene derivatives,[13] we required large quantities of 2-iodo-*N*,*N*-diisopropylferrocenecarboxamide (**2**) in both racemic and enantioenriched forms. Although already reported in the literature, the protocols relying on chromatographic purification were not compatible with the scale required here.

Here we describe the chromatography-free large scale synthesis of **(±)-2** and the gram-scale synthesis of **(S_p)-2** (Scheme 1). The usefulness of **2** in organic synthesis was further demonstrated by its functionalization through palladium-catalyzed Suzuki-Miyaura and copper-mediated Ullmann-type cross-couplings.



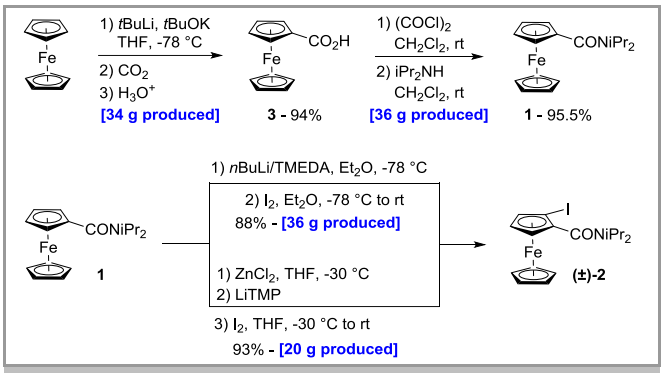
Scheme 1 Gram-scale synthesis of **(±)-** and **(S_p)-2** and their further functionalization.

Commercially available ferrocenecarboxylic acid (**3**) remaining expensive, our synthesis starts from ferrocene, which is metallated using an excess of *t*BuLi in the presence of a catalytic amount of *t*BuOK, as described by Mueller-Westerhoff (Scheme 2).[14] Upon metallation completion, gaseous carbon dioxide is passed through the reaction mixture to afford, after acidic work-up, ferrocenecarboxylic acid (**3**) in 94% yield (34 g in a single batch). It was subsequently converted into *N*,*N*-diisopropylferrocenecarboxamide (**1**) by a two-step process: formation of the acyl chloride by treatment with an excess of oxalyl chloride in the presence of catalytic amounts of dimethylformamide (DMF) and reaction with diisopropylamine. In our optimized protocol, which does not require anhydrous conditions, the crude product can be obtained in a couple of hours. Usually purified by column chromatography, we found that a simple recrystallization of the crude reaction mixture from heptane affords analytically pure product in 95.5% yield. Racemic deprotometalation of compound **1** can be performed using *n*BuLi in the presence of *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA) to enhance its reactivity in diethyl ether. We briefly studied the possibility to carry out this transformation with the more reactive *s*BuLi in THF at -78 °C;

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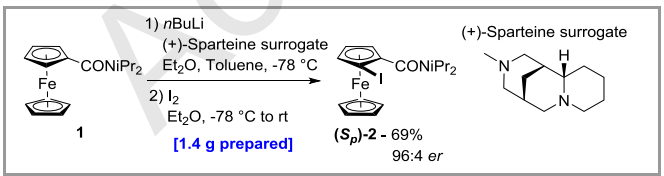
however, moderate yields (68% on average), resulting from the formation of multiple by-products, were obtained. Therefore, the deprotometalation with the *n*BuLi-TMEDA chelate in diethyl ether at cryogenic temperature was performed, followed by iodine interception. After a traditional work-up and removal of insoluble by-products, a simple recrystallization allowed the isolation of 36 g of the title product **(±)-2** in a single batch (88% yield).

For practical reasons, we have also developed another large scale synthesis of **(±)-2** by following the *in situ* trapping strategy.[15] Therefore, we reacted **1** with LiTMP (TMP = 2,2,6,6-tetramethylpiperidide) in the presence of anhydrous $ZnCl_2$ as the *in situ* trap in THF before interception with iodine. By following a similar work-up and crystallization purification protocol, we isolated 20 g of **(±)-2** in a single batch (93% yield).



Scheme 2 Column chromatography-free multi-gram synthesis of compound **(±)-2**.

Having established a reliable multi-gram access toward **(±)-2**, we turned our attention to its enantioenriched form. As the use of O'Brien's (+)-sparteine surrogate has not yet been attempted on **1**, we thought it interesting to secure this way. However, and even though (+)-sparteine surrogate is easily available from natural sources,[16] performing the asymmetric deprotometalation of **1** at a scale similar to that of the racemic one was economically not viable. By following O'Brien's protocol,[9] we therefore prepared 1.4 g of **(S_p)-2** (69% yield) with an enantiomeric ratio (er) of 96:4 as determined by chiral HPLC (Scheme 3). Interestingly, a simple recrystallization increases the er up to 99:1. Initially inferred by optical rotation measurement, the absolute configuration of **(S_p)-2** was confirmed by X-ray diffraction analysis (see SI).

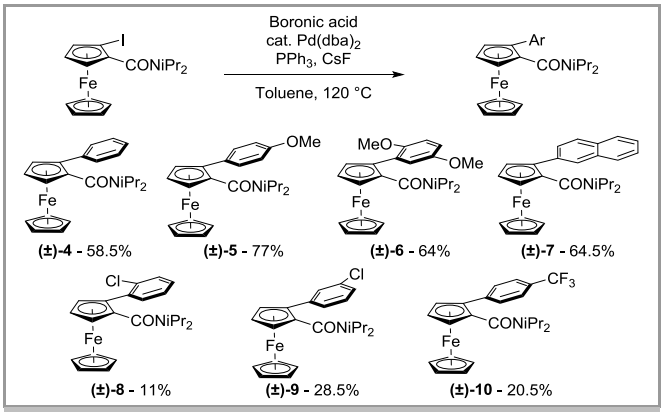


Scheme 3 Enantioselective synthesis of compound **(S_p)-2**.

Therefore, assuming that (-)-sparteine or (+)-sparteine surrogate are accessible in sufficient quantities, ten or so grams of the enantioenriched ferrocene **2** can be prepared in a few days without recurring to chromatographic purification. This is especially relevant with the (+)-sparteine surrogate which can be used in catalytic amount without major drop in the er.

Although we previously demonstrated the usefulness of **2** to access original 3-iodo-*N*,*N*-diisopropylferrocenecarboxamide through a halogen 'dance' reaction,[13, 17] the functionalization of the former was not extensively studied. In 2014, Kumar has reported an original example of a *t*BuOK-mediated sp^3 C-H bond functionalization to access lactams in 96% yield from **(±)-2**.[18] Earlier, Snieckus showed that the Suzuki-Miyaura cross-coupling of **(R_p)-2** under aqueous conditions afforded the desired biaryl product in low yield but with unchanged enantiomeric ratio (31% yield, 98:2 er).[7] More recently, Anderson showed the ability of Cu_2O to perform an Ullmann-type cross-coupling between **(R_p)-2** and either phthalimide or acetic acid.[19] The positive optical rotation recorded clearly indicated that enantioenriched products were obtained but without further indication of the enantiomeric ratio.

Therefore, we thought it interesting to apply Suzuki-Miyaura reaction conditions able to deliver the desired products in higher yields. The full transfer of chiral information being already reported, we focussed our study on racemic compounds. As aqueous reaction conditions seem to promote dehalogenation instead of the desired coupling reaction on such substrates, we successfully switched to anhydrous conditions. Therefore, reacting **(±)-2** with phenylboronic acid in the presence of $Pd(dba)_2$ (dba = dibenzylideneacetone), PPh_3 and CsF in toluene smoothly afforded the title product **(±)-4** in 58% yield (Scheme 4). Following the general reactivity trend of boronic acids in the Suzuki-Miyaura cross-coupling,[20] the electron-rich ones afforded higher yields (compounds **(±)-5-7**), while a major yield drop was noticed with the chlorinated and trifluoromethylated ones (compounds **(±)-8-10**). In these cases, moderate conversions as well as competitive dehalogenation were noticed. The use of ferroceneboronic acid,[21] 2-thienylboronic acid or 4-nitrophenylboronic acid only led to recovery of starting material or degradation.



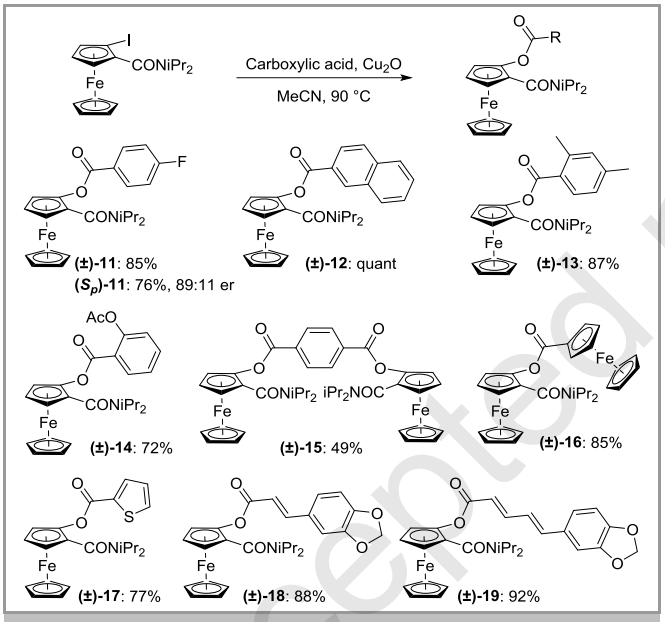
Scheme 4 Suzuki-Miyaura cross-coupling between **(±)-2** and various boronic acids.

Advanced NMR studies and X-ray diffraction analyses revealed similar structures in solution and in the solid state, probably due to the reduced degree of freedom for steric reasons (see SI). As a result, all peaks of the ^1H NMR spectra of compounds **(±)-4-10** are well resolved while the isopropyl signals are usually broad singlets in the ferrocenecarboxamide series. In all studied cases, the phenyl ring appears tilted relative to the Cp ring while the C=O bond of the amide always points down toward the iron atom. Furthermore, one methyl of each isopropyl group points toward the aromatic ring while the other points toward the ferrocene

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moiety. Depending on the substituent on the phenyl ring, some degree of rotation around the FcC-ArC bond was noticed.

To complete this study, we finally extended the scope of the copper-mediated C-O bond formation between **2** and carboxylic acids. When reacting **(±)-2** with a slight excess of 4-fluorobenzoic acid in the presence of Cu_2O, we isolated **(±)-11** in 85% yield (Scheme 5). Similarly, from **(S_p)-2** (87:13 er), **(S_p)-11** was obtained in 76% yield and almost unchanged er ratio (89:11). Having established the full transfer of chiral information, we evaluated the reaction between **(±)-2** and other coupling partners. 2-Naphthoic, 2,4-dimethylbenzoic and 2-acetoxybenzoic acids all afforded the corresponding esters **(±)-12-14** in good yields while terephthalic acid led to the bis-ester **(±)-15** in 49% yield. The reaction was also found to be compatible with ferrocenecarboxylic and 2-thiophenecarboxylic acids (products **(±)-16** and **(±)-17**, respectively). However, 2-picolinic acid and phenylpropiolic acids only led to recovery of starting material. Finally, acrylic acid derivatives such as 3,4-methylenedioxycinnamic acid and piperic acid were successfully converted into the corresponding esters **(±)-18** and **(±)-19** (88% and 92% yield, respectively).



Scheme 5 Ullmann-type cross-coupling between **(±)-2** or **(S_p)-2** and various carboxylic acids.

In conclusion, we have reported reaction conditions able to deliver grams of 2-iodo-*N*,*N*-diisopropylferrocenecarboxamide **(±)-** or **(S_p)-2** from cheap ferrocene without chromatographic purification. Two protocols, one using the *n*BuLi-TMEDA chelate and one using LiTMP in the presence of $ZnCl_2$ as an *in situ* trap were therefore successfully developed. Further elaboration through Suzuki-Miyaura or Ullmann-type cross-coupling reactions afforded biarylic and ester derivatives in moderate to good yields.

General Considerations. Unless otherwise stated, all the reactions were performed under an argon atmosphere with anhydrous solvents using Schlenk technics. THF and Et_2O were distilled over sodium-benzophenone, acetonitrile and toluene were distilled over CaH_2. Unless otherwise stated, all reagents were used without prior purification. All organolithiated reagents were titrated before use.[22] *t*BuOK (99.99% quality) was purchased from Sigma-Aldrich and used without further purification. Column chromatography separations were achieved on silica gel (40-63 µm). All Thin Layer Chromatographies (TLC) were performed on aluminum backed plates pre-coated with silica gel (Merck, Silica Gel 60 F254). They were visualized by exposure to UV light. Melting points were measured on a Kofler bench. IR spectra were taken on a Perkin-Elmer Spectrum 100 spectrometer. ^1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded either (i) on a Bruker Avance III spectrometer at 300 MHz and 75.4 MHz, respectively, or (iii) on a Bruker Avance III HD at 500 MHz and 126 MHz, respectively. ^1H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ^{13}C chemical shifts are relative to the central peak of the solvent signal. Cp refers to the unsubstituted cyclopentadienyl ring on ferrocene. Optical rotations were recorded at 20 °C on a Perkin Elmer 341 polarimeter. Enantiomeric ratios (er) were determined by chiral HPLC on a ThermoFischer Ultimate 3000 apparatus. $ZnCl_2$ was recrystallized from dioxane in the presence of zinc dust and dried under high vacuum at 150 °C overnight. (+)-Sparteine surrogate was prepared according to O'Brien and was distilled over CaH_2 before use.[16] Piperic acid was prepared according to Singh.[23]

Safety Considerations. Due to its high pyrophoric character, *t*BuLi needs to be used only under inert conditions (anhydrous, nitrogen or argon atmosphere) and by people well trained to the manipulation of reactive organometallics. Due to the inherent dangers of using cryogenic temperatures, experiments should be performed by well-trained people.

Procedures

Ferrocenecarboxylic acid (3)

[CAS Reg. No. 1271-42-7]

Ferrocene (29.8 g, 160 mmol, 1.00 equiv) and *t*BuOK (1.79 g, 16.0 mmol, 0.100 equiv) were introduced into a 2 L flame-dried round-bottom flask which was then subjected to three cycles of vacuum/argon. Anhydrous THF (1.23 L) was introduced by cannula and the reaction mixture was stirred at rt until dissolution of all solids. The reaction mixture was cooled between -85 and -80 °C (external temperature) in an acetone/liquid nitrogen bath. *t*BuLi (1.6 M, 320 mmol, 200 mL, 2.00 equiv) was then introduced dropwise by cannula keeping the temperature of the bath between -85 and -80 °C. After addition, the reaction mixture was stirred at the same temperature for 1 h. Gaseous CO_2 (dried by bubbling through concentrated H_2SO_4 and passing through an anhydrous $CaCl_2$ column) was bubbled into the reaction mixture for 30 min, keeping the temperature of the bath between -85 and -80 °C. The reaction mixture was then allowed to warm to -15 °C, keeping the flask into the bath, with a continued bubbling of CO_2. At -15 °C, bubbling of CO_2 was stopped, the cooling bath was removed and the reaction mixture was warmed to rt. Water (200 mL) was slowly added to the reaction mixture which was then extracted with 10% NaOH (6 x 150 mL). The combined aqueous layers were backwashed with Et_2O (4 x 250 mL), cooled to 0 °C (ice-water bath) and acidified with HCl (35%) until pH 1 was reached. **Caution**: vigorous evolution of CO_2 occurred upon acidification. The resulting solids were filtered on a sintered-glass funnel (porosity 3), washed with water (5 x 250 mL) and pentane (1 x 250 mL), wringing the solid under vacuum between each wash. The resulting solid was dried overnight under high-vacuum (2 mbar) using P_2O_5 trap to give the title product as an orange solid (34.6 g, 94%). R_f (PET-EtOAc 75:25) = 0.30. Mp 208-210 °C (decomp.). Analytical data analogous to those reported previously.[24]

ν_{max} (film)/cm^{-1} 2882 (br), 1651, 1474, 1282, 1158, 1029, 936, 914, 834, 740.

^1H NMR (500 MHz, DMSO-d^6): δ (ppm) 12.15 (br s, 1H, CO_2H), 4.69 (s, 2H, 2 x FcCH), 4.43 (s, 2H, 2 x FcCH), 4.21 (s, 5H, Cp).

^{13}C NMR (126 MHz, DMSO-d^6): δ (ppm) 172.1 (CO_2H), 71.8 (FcC), 71.0 (2 x FcCH), 69.9 (2 x FcCH), 69.5 (Cp).

***N*,*N*-Diisopropylferrocenecarboxamide (1)**

[CAS Reg. No. 169830-46-0]

Compound **3** (27.6 g, 120 mmol, 1.00 equiv) was introduced into a 1 L round-bottom flask equipped with a bubbler and an addition funnel. CH_2Cl_2 (undried standard quality, 480 mL) and dimethylformamide (undried standard quality, 0.50 mL, 425 mg, 5.80 mmol, 50.0 equiv) were introduced and the resulting orange suspension was stirred at rt. Oxalyl chloride (25.4 mL, 38.1 g, 300 mmol, 2.50 equiv) was added dropwise over 20 min. **Caution**: evolution of CO and CO_2 required to work under a well-ventilated fume hood. After addition, the addition funnel was washed with CH_2Cl_2 (10.0 mL) and the reaction mixture was then stirred at rt for 30 min. **Remark**: as the reaction proceeds, the orange solid slowly dissolves leading to a dark-red solution of FcCOCl. All volatiles were removed under vacuum using a rotary evaporator and the resulting oil was kept under high vacuum (2 mbar) for 5 min before being dissolved in CH_2Cl_2 (undried standard quality, 480 mL). Diisopropylamine (50.5 mL, 36.4 g, 360 mmol,

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3.00 equiv) was added dropwise over 30 min. **Caution**: a slightly exothermic reaction was noticed, however not high enough for solvent boiling. After addition, the reaction mixture was stirred for an additional 30 min at rt. All volatiles were removed under vacuum using a rotary evaporator and the resulting oil was kept under high vacuum (2 mbar) for 5 min. Et_2O (500 mL) was added and the reaction mixture was washed with HCl (1.0 M aq., 150 mL). **Remark**: in case of emulsion formation, filtration over cotton wool can be done. The aqueous layer was backwashed with Et_2O (100 mL). The combined organic layers were washed with NaOH (5%, 150 mL), water (150 mL), brine (150 mL), dried over $MgSO_4$, filtered over a pad of Celite (⌀ 6, h 4 cm, sintered glass funnel porosity 3) and concentrated under vacuum to give the crude product. The residue was transferred into a 250 mL round-bottom flask using heptane (65 mL). The solution was heated at reflux, allowed to cool to rt and then kept at -20 °C overnight. Using a cannula, the solution was pumped off from the solid which was washed with cooled pentane (-30 °C, 1 x 15 mL). The resulting solid was dried under high-vacuum (2 mbar) to give the title product as an orange solid (35.9 g, 95.5%). R_f (eluent: PET-EtOAc 75:25) = 0.65. Mp 73-75 °C. Analytical data analogous to those reported previously.[13]

ν_{max} (film)/cm^{-1} 3084, 2972, 1627, 1463, 1423, 1369, 1317, 1200, 1151, 1135, 1105, 1041, 1025, 823, 806.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.58 (br s, 1H, CH), 4.52 (t, *J* = 1.7 Hz, 2H, 2 x FcCH), 4.22 (t, *J* = 1.7 Hz, 2H, 2 x FcCH), 4.19 (s, 5H, Cp), 3.38 (br s, 1H, CH), 1.44 (br s, 6H, 2 x CH_3), 1.18 (br s, 6H, 2 x CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 169.5 (C=O), 81.4 (FcC), 70.1 (2 x FcCH), 69.8 (Cp), 68.9 (2 x FcCH), 49.6 (CH), 46.4 (CH), 21.3 (4 x CH_3).

Mass: 313 [M], 213 [M-$NiPr_2$].

(±)-2-iodo-*N*,*N*-diisopropylferrocenecarboxamide ((±)-2) by using *n*BuLi-TMEDA

[CAS Reg. No. 344927-04-4]

TMEDA (21.0 mL, 16.3 g, 140 mmol, 1.50 equiv, freshly distilled over $CaCl_2$ and stored over KOH pellets) and anhydrous Et_2O (430.0 mL) were introduced into a 2 L flame-dried round-bottom flask under argon. The reaction mixture was cooled to between -85 and -80 °C (external temperature) in an acetone/liquid nitrogen bath. *n*BuLi (1.4 M, 100 mL, 140 mmol, 1.50 equiv) was then introduced dropwise by cannula, keeping the temperature of the bath between -85 and -80 °C. After addition, the reaction mixture was stirred at the same temperature for 15 min. Compound **2** (29.2 g, 93.3 mmol, 1.00 equiv) was introduced into a separate 1 L flame-dried round-bottom flask which was subjected to three cycles of vacuum/argon. Anhydrous Et_2O (430 mL) was added and the solution was stirred until dissolution of all solids. The solution of **1** was transferred into the *n*BuLi-TMEDA solution dropwise by cannula, keeping the temperature of the bath between -85 and -80 °C. The flask was washed with 10.0 mL of anhydrous Et_2O, also transferred by cannula. After addition, the reaction mixture was stirred at the same temperature for 1 h. Iodine (47.4 g, 187 mmol, 2.00 equiv) was introduced in a separate 1 L flame-dried round-bottom flask under argon and was dissolved into anhydrous Et_2O (800 mL). The iodine solution was transferred to the lithioferrocene solution dropwise by cannula, keeping the temperature of the bath between -85 and -80 °C. The flask was washed with 10.0 mL of anhydrous Et_2O, also transferred by cannula. The reaction mixture was then allowed to warm to -15 °C, keeping the flask into the bath. At -15 °C, the cooling bath was removed and the reaction mixture was warmed to rt. **Remark**: at this stage, the reaction mixture can be kept at -20 °C overnight before work-up if required. Half of the solvent was removed under vacuum and EtOAc (800 mL) was added. The reaction mixture was washed with $Na_2S_2O_3$ (sat. aq., 2 x 150 mL), water (2 x 150 mL), brine (1 x 150 mL), dried over $MgSO_4$, filtered over cotton wool and concentrated under vacuum using a rotary evaporator. The resulting oil was dissolved in hot heptane/EtOAc (80:20) solution and was hot filtered over a pad of silica (⌀ 6, h 4 cm, sintered glass funnel porosity 3), which was washed with the same hot solvent until the filtrate was colourless. The filtrate was then concentrated under vacuum using a rotary evaporator to give the crude product. This was dissolved into heptane (100 mL), the solution was heated at reflux, allowed to cool to rt and then kept at -20 °C overnight. Using a cannula, the solution was pumped off from the solid which was washed with cooled pentane (-30 °C, 2 x 40 mL). The solution was pumped off using a cannula. The resulting solid was dried under high-vacuum (2 mbar) to give the title product as an orange solid (35.9 g, 88%). R_f (eluent: PET-EtOAc 80:20) = 0.68. Mp 137-139 °C. Analytical data analogous to those reported previously.[13]

ν_{max} (film)/cm^{-1} 2971, 1619, 1456, 1368, 1315, 1298, 1206, 1036, 811, 686.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.36 (q, *J* = 1.7, 1.1 Hz, 1H, FcCH), 4.28 (s, 5H, Cp), 4.22 (q, *J* = 2.0, 1.1 Hz, 1H, FcCH), 4.11 (t, *J* = 2.4 Hz, 1H, FcCH), 3.55 (t, *J* = 5.5 Hz, 1H, CH), 3.33 (t, *J* = 5.5 Hz, 1H, CH), 1.45 (s, 6H, 2 x CH_3), 1.03 (d, *J* = 5.5 Hz, 3H, CH_3), 0.92 (d, *J* = 5.5 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 166.3 (C=O), 92.6 (FcC), 73.6 (FcCH), 72.7 (Cp), 67.6 (FcCH), 66.8 (FcCH), 50.8 (CH), 45.9 (CH), 40.5 (FcC-I), 21.0 (2 x CH_3), 20.8 (CH_3), 20.7 (CH_3).

Mass: 439 [M], 311 [M-CO$NiPr_2$], 268.

(±)-2-iodo-*N*,*N*-diisopropylferrocenecarboxamide ((±)-2) by using LiTMP-$ZnCl_2$

[CAS Reg. No. 344927-04-4]

*n*BuLi (1.4 M, 71.4 mL, 100 mmol, 2.00 equiv) was added dropwise by cannula to a solution of TMPH (16.9 mL, 14.1 g, 100 mmol, 2.00 equiv) in THF (80.0 mL) at -20 °C. After addition, the reaction mixture was stirred at the same temperature for 10 min. The reaction mixture was cooled to -30 °C and was cannulated onto a solution of compound **1** (15.7 g, 50.0 mmol, 1.00 equiv) and $ZnCl_2$ (6.81 g, 50.0 mmol, 1.00 equiv) in THF (100 mL) at -30 °C. The LiTMP flask was washed with THF (10 mL). The reaction mixture was warmed to -10 °C over 2h and a solution of iodine (25.4 g, 100 mmol, 2.00 equiv) in THF (130 mL) was added by cannula. The iodine flask was washed with THF (10 mL). The cooling bath was removed and the reaction mixture was warmed to rt. Half of the solvent was removed under vacuum and EtOAc (430 mL) was added. By following a similar work-up procedure as the one described before, adjusting the quantities, the title product was obtained as an orange solid (20.5 g, 93%). Analytical data analogous to those reported above.

(*S*$_p$)-2-iodo-*N*,*N*-diisopropylferrocenecarboxamide ((*S*$_p$)-2)

(+)-Sparteine surrogate (1.16 g, 6.00 mmol, 1.30 equiv) and anhydrous Et_2O (70.0 mL) were introduced into a 250 mL flame-dried round-bottom flask under argon. The reaction mixture was cooled to between -85 and -80 °C (external temperature) in an acetone/liquid nitrogen bath. *n*BuLi (1.4 M, 4.30 mL, 6.00 mmol, 1.30 equiv) was then introduced dropwise by syringe, keeping the temperature of the bath between -85 and -80 °C. After addition, the reaction mixture was stirred at the same temperature for 30 min. Compound **1** (1.40 g, 4.50 mmol, 1.00 equiv) was introduced into a separate 20 mL flame-dried round-bottom flask which was subjected to three cycles of vacuum/argon. Anhydrous toluene (10.0 mL) was added and the solution was stirred until dissolution of all solids had occurred. The solution of **1** was transferred into the *n*BuLi/(+)-Sparteine surrogate solution dropwise by cannula, keeping the temperature of the bath between -85 and -80 °C. The flask was washed with 2.0 mL of anhydrous Et_2O, also transferred by cannula. After addition, the reaction mixture was stirred at the same temperature for 2 h. Iodine (2.30 g, 9.00 mmol, 2.00 equiv) was introduced into a separate 100 mL flame-dried round-bottom flask under argon and was dissolved into anhydrous Et_2O (60.0 mL). The iodine solution was transferred to the lithioferrocene solution dropwise by cannula, keeping the temperature of the bath between -85 and -80 °C. The flask was washed with 5.0 mL of anhydrous Et_2O, also transferred by cannula. The reaction mixture was then allowed to warm to -15 °C, keeping the flask into the bath. At -15 °C, the cooling bath was removed and the reaction mixture was warmed to rt. $Na_2S_2O_3$ (sat. aq., 100 mL), EtOAc (100 mL) and water (50 mL) were added to the reaction mixture, layers were separated and the aqueous one was backwashed with EtOAc (50 mL). The organic layer was washed with H_3PO_4 (5% aq., 3 x 30 mL) and the combined aqueous layers were backwashed with EtOAc (50 mL). The combined organic layers were washed with water (2 x 50 mL), brine (1 x 50 mL), dried over $MgSO_4$, filtered over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PET-EtOAc (10:1 to 9:1) to give the title product as an orange oil (1.4 g, 69%, 96:4 *er*). Analytical data analogous to racemic compound. $[\alpha]_D$ -87.9 (*c* 0.01 in $CHCl_3$). The enantiomeric ratio was determined on Chiralpak IC-3 column, hexane-iPrOH: 98:2, 1.5 mL/min, 20 °C, λ = 254 nm, t (major) = 10.19 min, t (minor) = 7.64 min). Recrystallization from hot heptane as described for the racemic product increased the er to 99:1 as determined by chiral HPLC. CCDC 1898624.

General procedure A: Suzuki-Miyaura cross-coupling of (±)-2

Compound **(±)-2** (242 mg, 0.55 mmol, 1.00 equiv), arylboronic acid (2.20 mmol, 4.00 equiv), $Pd(dba)_2$ (15.8 mg, 27.5 µmol, 5 mol%), CsF (167 mg, 1.10 mmol, 2.00 equiv) and PPh_3 (28.5 mg, 0.11 mmol, 0.20 equiv) were placed in a dried Schlenk tube, subjected to three cycles of vacuum/argon. Toluene (5.00 mL) was added and the reaction mixture was stirred overnight at 120 °C (external temperature) in a pre-heated oil bath. The reaction mixture was cooled to rt, water (10 mL) was added and the reaction mixture was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered over cotton wool and

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concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PET-EtOAc (proportions given for each product) to give the title product.

(±)-*N*,*N*-Diisopropyl-2-phenylferrocenecarboxamide ((±)-4)

By following the general procedure A, using phenylboronic acid (268 mg), **(±)-4** was obtained after column chromatography (PET-EtOAc, 90:10) as an orange solid (125 mg, 58.5%). R_f (eluent: PET-EtOAc 90:10) = 0.54. Mp 134-136 °C. CCDC 1909912.

ν_{max} (film)/cm^{-1} 2965, 1626, 1463, 1442, 1343, 1317, 1304, 1215, 1136, 1105, 1035, 818, 765, 698.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.52 (d, *J* = 8.0 Hz, 2H, 2 x ArCH), 8.23 (m, 2H, 2 x ArCH), 7.17 (d, *J* = 7.1 Hz, 1H, ArCH), 4.45 (dd, *J* = 1.4, 2.0 Hz, 1H, FcCH), 4.41 (dd, *J* = 1.4, 2.0 Hz, 1H, FcCH), 4.24-4.23 (m, 6H, Cp + FcCH), 3.47 (sept, *J* = 6.7 Hz, 1H, CH), 3.19 (sept, *J* = 6.8 Hz, 1H, CH), 1.47 (d, *J* = 6.8 Hz, 3H, CH_3), 1.38 (d, *J* = 6.8 Hz, 3H, CH_3), 0.81 (d, *J* = 6.7 Hz, 3H, CH_3), 0.24 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 168.2 (C=O), 138.3 (ArC), 128.3 (2 x ArCH), 128.2 (2 x ArCH), 126.7 (ArCH), 90.1 (Fc*C*-CO), 84.9 (FcC), 71.4 (Cp), 69.8 (FcCH), 67.0 (FcCH), 64.9 (FcCH), 50.8 (CH), 45.9 (CH), 21.4 (CH_3), 21.1 (CH_3), 19.9 (CH_3), 19.5 (CH_3).

Mass: 389 [M], 289 [M-$NiPr_2$].

(±)-*N*,*N*-Diisopropyl-2-(4-methoxyphenyl)ferrocenecarboxamide ((±)-5)

By following the general procedure A, using 4-methoxyphenylboronic acid (334 mg), **(±)-5** was obtained after column chromatography (PET-EtOAc, 10:1) as an orange solid (197 mg, 77%). R_f (eluent: PET-EtOAc 80:20) = 0.57. Mp 142-144 °C. CCDC 1909910.

ν_{max} (film)/cm^{-1} 2962, 2931, 1625, 1460, 1437, 1341, 1314, 1305, 1289, 1243, 1106, 1027, 906, 845, 815, 734.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.45 (d, *J* = 8.8 Hz, 2H, 2 x ArCH), 6.79 (d, *J* = 8.8 Hz, 2H, 2 x ArCH), 4.41 (dd, *J* = 1.5, 2.2 Hz, 1H, FcCH), 4.38 (dd, *J* = 1.5, 2.2 Hz, 1H, FcCH), 4.23 (s, 5H, Cp), 4.20 (t, *J* = 2.2 Hz, 1H, FcCH), 3.78 (s, 3H, OCH_3), 3.48 (sept, *J* = 6.7 Hz, 1H, CH), 3.20 (sept, *J* = 6.7 Hz, 1H, CH), 1.48 (d, *J* = 6.7 Hz, 3H, CH_3), 1.38 (d, *J* = 6.7 Hz, 3H, CH_3), 0.83 (d, *J* = 6.7 Hz, 3H, CH_3), 0.30 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 168.3 (C=O), 158.6 (ArC-O), 130.4 (ArC), 129.3 (2 x ArCH), 113.7 (2 x ArCH), 89.3 (Fc*C*-CO), 85.1 (FcC), 71.3 (Cp), 69.4 (FcCH), 66.6 (FcCH), 64.9 (FcCH), 55.4 (OCH_3), 50.8 (CH), 45.8 (CH), 21.3 (CH_3), 21.0 (CH_3), 19.9 (CH_3), 19.7 (CH_3).

Mass: 491 [M], 319 [M-$NiPr_2$].

(±)-*N*,*N*-Diisopropyl-2-(2,4-dimethoxyphenyl)ferrocene-carboxamide ((±)-6)

[CAS Reg. No. 173911-02-9]

By following the general procedure A, using 2,4-dimethoxyphenylboronic acid (400 mg), **(±)-6** was obtained after column chromatography (PET-EtOAc, 10:1) as an orange solid (174 mg, 64%). R_f (eluent: PET-EtOAc 80:20) = 0.59. Mp 163-166 °C. Analytical data analogous to those reported previously.[7] CCDC 1909911.

ν_{max} (film)/cm^{-1} 2964, 1625, 1505, 1450, 1341, 1310, 122, 1037, 1104, 809, 735.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.43 (d, *J* = 2.6 Hz, 1H, ArCH), 6.75-6.70 (m, 2H, 2 x ArCH), 4.63 (dd, *J* = 1.5, 2.3 Hz, 1H, FcCH), 4.41 (dd, *J* = 1.5, 2.2 Hz, 1H, FcCH), 4.26 (s, 5H, Cp), 4.25 (t, *J* = 2.2 Hz, 1H, FcCH), 3.79 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.53 (sept, *J* = 6.7 Hz, 1H, CH), 3.16 (sept, *J* = 6.7 Hz, 1H, CH), 1.45 (d, *J* = 6.7 Hz, 3H, CH_3), 1.32 (d, *J* = 6.7 Hz, 3H, CH_3), 0.82 (d, *J* = 6.7 Hz, 3H, CH_3), 0.28 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 168.2 (C=O), 153.3 (ArC-O), 151.5 (ArC-O), 127.1 (ArC), 117.4 (ArCH), 113.5 (ArCH), 112.1 (ArCH), 90.8 (Fc*C*-CO), 81.5 (FcC), 71.3 (Cp), 69.0 (FcCH), 68.7 (FcCH), 66.7 (FcCH), 56.1 (OCH_3), 55.8 (OCH_3), 50.6 (CH), 45.7 (CH), 21.2 (CH_3), 21.1 (CH_3), 20.3 (CH_3), 19.7 (CH_3).

Mass: 449 [M], 349 [M-$NiPr_2$].

(±)-*N*,*N*-Diisopropyl-2-(2-naphthyl)ferrocenecarboxamide ((±)-7)

By following the general procedure A, using 2-naphthylboronic acid (378 mg), **(±)-7** was obtained after column chromatography (PET-EtOAc, 90:10) as an orange solid (156 mg, 64.5%). R_f (eluent: PET-EtOAc 90:10) = 0.43. Mp 218-220 °C. CCDC 1909914.

ν_{max} (film)/cm^{-1} 2966, 1622, 1462, 1334, 1303, 1201, 1134, 1040, 864, 820, 808, 755.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.94 (s, 1H, ArCH), 7.78-7.74 (m, 2H, 2 x ArCH), 7.74 (m, 2H, 2 x ArCH), 7.45-7.40 (m, 2H, 2 x ArCH), 4.61 (dd, *J* = 1.5, 2.3 Hz, 1H, FcCH), 4.49 (dd, *J* = 1.4, 2.3 Hz, 1H, FcCH), 4.32 (t, *J* = 2.3 Hz, 1H, FcCH), 3.55 (sept, *J* = 6.7 Hz, 1H, CH), 3.20 (sept, *J* = 6.8 Hz, 1H, CH), 1.52 (d, *J* = 6.8 Hz, 3H, CH_3), 1.43 (d, *J* = 6.8 Hz, 3H, CH_3), 0.84 (d, *J* = 6.7 Hz, 3H, CH_3), 0.19 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 168.3 (C=O), 136.1 (ArC), 133.6 (ArC), 132.5 (ArC), 127.9 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 127.1 (ArCH), 126.4 (ArCH), 125.8 (ArCH), 125.6 (ArCH), 90.3 (Fc*C*-CO), 84.5 (FcC), 71.5 (Cp), 70.2 (FcCH), 67.3 (FcCH), 65.0 (FcCH), 50.9 (CH), 45.9 (CH), 21.4 (CH_3), 21.1 (CH_3), 20.0 (CH_3), 19.8 (CH_3).

Mass: 439 [M], 339 [M-$NiPr_2$].

(±)-2-(2-Chlorophenyl)-*N*,*N*-diisopropylferrocenecarboxamide ((±)-8)

By following the general procedure A, using 2-chlorophenylboronic acid (344 mg), **(±)-8** was obtained after column chromatography (PET-EtOAc, 10:1) as an orange solid (29.2 mg, 11%). R_f (eluent: PET-EtOAc 90:10) = 0.34. Mp 82-84 °C.

ν_{max} (film)/cm^{-1} 2994, 2960, 2929, 1621, 1461, 1437, 1368, 1339, 1305, 1212, 1195, 1157, 1136, 1035, 1023, 1003, 813, 749.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.03 (dd, *J* = 1.5, 7.8 Hz, 1H, ArCH), 7.29 (dd, *J* = 0.8, 7.8 Hz, 1H, ArCH), 7.22 (dt, *J* = 1.1, 7.7 Hz, 1H, ArCH), 7.16 (dt, *J* = 1.5, 7.7 Hz, 1H, ArCH), 4.70 (dd, *J* = 1.0, 2.0 Hz, 1H, FcCH), 4.46 (dd, *J* = 1.4, 2.0 Hz, 1H, FcCH), 4.31 (t, *J* = 2.4 Hz, 1H, FcCH), 4.29 (s, 5H, Cp), 3.51 (sept, *J* = 6.6 Hz, 1H, CH), 3.13 (sept, *J* = 6.8 Hz, 1H, CH), 1.44 (d, *J* = 6.8 Hz, 3H, CH_3), 1.21 (d, *J* = 6.8 Hz, 3H, CH_3), 0.85 (d, *J* = 6.6 Hz, 3H, CH_3), 0.30 (d, *J* = 6.6 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 167.6 (C=O), 135.9 (ArC), 134.0 (ArCH), 133.5 (ArC), 129.6 (ArCH), 128.0 (ArCH), 126.4 (ArCH), 91.9 (Fc*C*-CO), 83.2 (FcC), 71.5 (Cp), 68.9 (FcCH), 68.8 (FcCH), 66.6 (FcCH), 50.7 (CH), 45.8 (CH), 21.3 (CH_3), 21.2 (CH_3), 19.9 (CH_3), 19.6 (CH_3).

Mass: 313 [M-C_6H_4Cl+H], 213 [$FcCO_2H$].

(±)-2-(3-Chlorophenyl)-*N*,*N*-diisopropylferrocenecarboxamide ((±)-9)

By following the general procedure A, using 3-chlorophenylboronic acid (344 mg), **(±)-9** was obtained after column chromatography (PET-EtOAc, 10:1) as an orange solid (66.6 mg, 28.5%). R_f (eluent: PET-EtOAc 90:10) = 0.46. Mp 133-135 °C. CCDC 1909913.

ν_{max} (film)/cm^{-1} 2972, 1617, 1597, 1461, 1439, 1368, 1341, 1310, 1196, 1136, 1055, 1039, 1005, 819, 810, 798, 768, 687.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.51 (t, *J* = 1.8 Hz, 1H, ArCH), 7.42 (dt, *J* = 1.9, 6.6 Hz, 1H, ArCH), 7.17 (d, *J* = 4.7 Hz, 1H, ArCH), 7.16 (t, *J* = 1.8 Hz, 1H, ArCH), 4.45 (m, 1H, FcCH), 4.44 (m, 1H, FcCH), 4.28 (t, *J* = 2.4 Hz, 1H, FcCH), 4.25 (s, 5H, Cp), 3.47 (sept, *J* = 6.7 Hz, 1H, CH), 3.24 (sept, *J* = 6.8 Hz, 1H, CH), 1.50 (d, *J* = 6.8 Hz, 3H, CH_3), 1.42 (d, *J* = 6.8 Hz, 3H, CH_3), 0.85 (d, *J* = 6.7 Hz, 3H, CH_3), 0.35 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 167.8 (C=O), 140.7(ArC), 134.2 (ArC), 129.5 (ArCH), 127.9 (ArCH), 126.7 (ArCH), 126.3 (ArCH), 90.3 (Fc*C*-CO), 83.2 (FcC), 71.6 (Cp), 70.1 (FcCH), 67.4 (FcCH), 64.9 (FcCH), 50.9 (CH), 46.0 (CH), 21.3 (CH_3), 21.1 (CH_3), 20.0 (CH_3), 19.7 (CH_3).

Mass: 423 [M], 323 [M-$NiPr_2$], 296 [M-$CONiPr_2$ + H].

(±)-*N*,*N*-Diisopropyl-2-(4-trifluoromethylphenyl)ferrocene-carboxamide ((±)-10)

By following the general procedure A, using 4-(trifluoromethyl)phenylboronic acid (417 mg), **(±)-10** was obtained after column chromatography (PET-EtOAc, 10:1) as an orange solid (52.0 mg, 20.5%). R_f (eluent: PET-EtOAc 90:10) = 0.50. Mp 179-181 °C. CCDC 1909915.

ν_{max} (film)/cm^{-1} 2965, 2932, 2234, 1613, 1463, 1319, 1162, 1121, 1106, 1068, 906, 818, 727.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.65 (d, *J* = 8.0 Hz, 2H, 2 x ArCH), 7.49 (d, *J* = 8.0 Hz, 2H, 2 x ArCH), 4.50 (s, 1H, FcCH), 4.47 (s, 1H, FcCH), 4.32 (s, 1H, FcH), 4.25 (s, 5H, Cp), 3.48 (sept, *J* = 6.7 Hz, 1H, CH), 3.25 (sept, *J* = 6.7 Hz, 1H, CH), 1.50 (d, *J* = 6.7 Hz, 3H, CH_3), 1.40 (d, *J* = 6.7 Hz, 3H, CH_3), 0.87 (d, *J* = 6.7 Hz, 3H, CH_3), 0.34 (d, *J* = 6.7 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 167.8 (s, C=O), 142.9 (s, ArC), 128.6 (q, *J* = 32.6 Hz, Ar*C*-CF_3), 128.2 (s, 2 x ArCH), 124.5 (q, *J* = 271.9 Hz, CF_3), 125.2 (q, *J* = 3.5 Hz, 2 x ArCH), 90.7 (s, Fc*C*-CO), 82.9 (s, FcC), 71.7 (s, Cp), 70.3 (s, FcCH), 67.6 (s, FcCH), 65.1 (s, FcCH), 50.9 (s, CH), 46.0 (s, CH), 21.3 (s, CH_3), 21.0 (s, CH_3), 20.1 (s, CH_3), 19.8 (s, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ (ppm) -62.4 (s).

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Mass: 457 [M], 357 [M-$NiPr_2$], 330 [M-$CONiPr_2$ + H].

General procedure B: Ullmann-type cross-coupling of (±)-2

Compound **(±)-2** (263 mg, 0.60 mmol, 1.00 equiv), carboxylic acid (0.72 mmol, 1.20 equiv) and Cu_2O (103 mg, 0.72 mmol, 1.20 equiv) were placed in a dried Schlenk tube, subjected to three cycles of vacuum/argon. Acetonitrile (8.50 mL) was added and the reaction mixture was stirred overnight at 90 °C (external temperature) in a pre-heated oil bath. The reaction mixture was cooled to rt, filtered over a pad of Celite, washed with EtOAc until colorless. The filtrate was concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PET-EtOAc (proportions given for each product) to give the title product.

(±)-*N,N*-Diisopropyl-2-(4-fluorobenzoyl)ferrocenecarboxamide ((±)-11)

By following the general procedure B, using 4-fluorobenzoic acid (101 mg), **(±)-11** was obtained after column chromatography (PET-EtOAc, 10:1 to 90:10, 1% of NEt_3) as an orange solid (230 mg, 85%). R_f (eluent: PET-EtOAc 90:10) = 0.50. Mp 142-144 °C. CCDC 1909916.

ν_{max} (film)/cm^{-1} 2967, 1744, 1736, 1632, 1598, 1507, 1471, 1435, 1371, 1321, 1262, 1246, 1224, 1155, 1134, 1081, 1063, 1041, 1012, 1003, 866, 812, 763, 757, 686.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.10 (dd, *J* = 5.5, 8.9 Hz, 2H, 2 x ArCH), 7.11 (t, *J* = 8.6 Hz, 2H, 2 x ArCH), 4.64 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.38 (s, 5H, Cp), 4.12 (dd, *J* = 1.5, 2.7 Hz, 1H, FcCH), 4.06 (br s, 1H, CH), 4.00 (t, *J* = 2.7 Hz, 1H, FcCH), 3.36 (br s, 1H, CH), 1.45 (br s, 3H, CH_3), 1.37 (br s, 3H, CH_3), 1.05 (br s, 3H, CH_3), 0.99 (br s, 3H, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 166.2 (d, *J* = 254.7 Hz, ArC-F), 165.8 (s, C=O_{amide}), 164.4 (s, C=O_{ester}), 132.7 (d, *J* = 9.4 Hz, 2 x ArCH), 126.0 (d, *J* = 2.8 Hz, ArC), 115.9 (d, *J* = 22.2 Hz, 2 x ArCH), 115.2 (s; FcC-O), 80.1 (s, FcC), 71.4 (s, Cp), 62.8 (s, FcCH), 62.1 (s, FcCH), 61.1 (s, FcCH), 50.7 (s, CH), 46.1 (s, CH), 20.8 (s, 4 x CH_3).

Mass: 451 [M], 328, 229.

(S_p)-*N,N*-Diisopropyl-2-(4-fluorobenzoyl)ferrocenecarboxamide ((S_p)-11)

By following the general procedure B, using (S_p)-2-iodo-*N,N*-diisopropylferrocenecarboxamide (er 87:13, 80.0 mg) and 4-fluorobenzoic acid (30.3 mg), **(S_p)-11** was obtained after column chromatography (PET-EtOAc, 10:1 to 90:10, 1% of NEt_3) as an orange solid (62 mg, 76%, 89:11 er). $[\alpha]_D$ -1.09 (*c* 0.01 in $CHCl_3$). The enantiomeric ratio was determined on Chiralpak IC-3 column, hexane-iPrOH: 98:2, 1.0 mL/min, 20 °C, λ = 254 nm, t (major) = 16.50 min, t (minor) = 19.41 min.

(±)-*N,N*-Diisopropyl-2-(2-naphthoyl)ferrocenecarboxamide ((±)-12)

By following the general procedure B, using 2-naphthoic acid (126 mg), **(±)-12** was obtained after column chromatography (PET-EtOAc, 10:1 to 90:10, 1% of NEt_3) as an orange solid (290 mg, quant.). R_f (eluent: PET-EtOAc 90:10) = 0.43. Mp 145-147 °C.

ν_{max} (film)/cm^{-1} 2978, 1732, 1626, 1472, 1429, 1318, 1265, 1217, 1189, 1134, 1082, 1004, 951, 876, 834, 814, 778.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.67 (s, 1H, ArCH), 8.10 (dd, *J* = 1.7, 8.6 Hz, 1H, ArCH), 7.96 (d, *J* = 8.6 Hz, 1H, ArCH), 7.89 (d, *J* = 6.2 Hz, 1H, ArCH), 7.87 (d, *J* = 5.4 Hz, 1H, ArCH), 7.56 (m, 2H, 2 x ArCH), 4.75 (dd, *J* = 1.4, 2.5 Hz, 1H, FcCH), 4.43 (s, 5H, Cp), 4.16 (dd, *J* = 1.4, 2.5 Hz, 1H, FcCH), 4.08 (br s, 1H, CH), 4.04 (t, *J* = 2.7 Hz, 1H, FcCH), 3.39 (br s, 1H, CH), 1.47 (br s, 6H, 2 x CH_3), 1.02 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 165.8 (s, C=O_{amide}), 165.4 (s, C=O_{ester}), 135.9 (ArC), 132.7 (ArC), 131.8 (ArCH), 129.7 (ArCH), 128.7 (ArCH), 128.5 (ArCH), 127.9 (ArCH), 126.9 (ArCH), 125.5 (ArCH), 114.9 (FcC-O), 80.6 (FcC), 71.4 (Cp), 62.9 (FcCH), 62.1 (FcCH), 61.0 (FcCH), 50.7 (CH), 46.1 (CH), 20.9 (4 x CH_3).

Mass: 313 [M-$C_{11}H_7O_2$ + H].

(±)-*N,N*-Diisopropyl-2-(2,4-dimethylbenzoyl)ferrocenecarboxamide ((±)-13)

By following the general procedure B, using 2,4-dimethylbenzoic acid (108 mg), **(±)-13** was obtained after column chromatography (PET-EtOAc, 90:10, 1% of NEt_3) as an orange solid (242 mg, 87%). R_f (eluent: PET-EtOAc 10:1) = 0.28. Mp 152-154 °C. CCDC 1909919.

ν_{max} (film)/cm^{-1} 2958, 1715,1620, 1463, 1430, 1323, 1288, 1252, 1236,

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.95 (d, *J* = 8.4 Hz, 1H, ArCH), 7.07-7.05 (m, 2H, 2 x ArCH), 4.60 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.39 (s, 5H, Cp), 4.12 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.06 (br s, 1H, CH), 4.00 (t, *J* = 2.6 Hz, 1H, FcCH), 3.35 (br s, 1H, CH), 2.59 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 1.46 (br s, 3H, CH_3), 1.38 (br s, 3H, CH_3), 1.03 (br s, 3H, CH_3), 0.98 (br s, 3H, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 166.2 (C=O), 165.9 (C=O), 143.3 (ArC), 141.0 (ArC), 132.7 (ArCH), 131.7 (ArCH), 126.8 (ArCH), 125.9 (ArC), 114.9 (FcC-O), 80.7 (FcC), 71.3 (Cp), 62.8 (FcCH), 62.1 (FcCH), 61.2 (FcCH), 50.7 (CH), 46.0 (CH), 22.0 (CH_3), 21.6 (CH_3), 20.8 (2 x CH_3).

Mass: 461 [M].

(±)-2-(2-Acetoxyphenyl)-*N,N*-diisopropylferrocenecarboxamide ((±)-14)

By following the general procedure B, using 2-acetoxybenzoic acid (130 mg), **(±)-14** was obtained after column chromatography (PET-EtOAc, 10:1 to 90:10, 1% of NEt_3) as an orange solid (212 mg, 72%). R_f (eluent: PET-EtOAc 90:10) = 0.42. Mp 157-159 °C. CCDC 1909918.

ν_{max} (film)/cm^{-1} 2966, 1764, 1736, 1624, 1604, 1474, 1431, 1321, 1242, 1212, 1182, 1156, 1051, 1002, 911, 818, 754, 696.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.13 (dd, *J* = 1.7, 7.8 Hz, 1H, ArCH), 7.56 (dt, *J* = 1.7, 7.8 Hz, 1H, ArCH), 7.32 (dt, *J* = 1.7, 7.8 Hz, 1H, ArCH), 7.09 (dd, *J* = 1.7, 7.8 Hz, 1H, ArCH), 4.56 (dd, *J* = 1.4, 2.5 Hz, 1H, FcCH), 4.38 (s, 5H, Cp), 4.12 (dd, *J* = 1.4, 2.6 Hz, 1H, FcCH), 4.04 (br s, 1H, CH), 4.00 (t, *J* = 2.6 Hz, 1H, FcCH), 3.34 (br s, 1H, CH), 2.34 (CH_3), 1.44 (br s, 3H, CH_3), 1.38 (br s, 3H, CH_3), 1.02 (br s, 3H, CH_3), 0.96 (br s, 3H, CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.6 (C=$O_{acetate}$), 165.6 (C=O_{amide}), 163.1 (C=O_{ester}), 151.1 (ArC), 134.5 (ArCH), 132.3 (ArCH), 126.3 (ArCH), 124.1 (ArCH), 122.6 (ArC-O), 114.7 (FcC-O), 80.4 (FcC), 71.3 (Cp), 62.9 (FcCH), 62.1 (FcCH), 61.2 (FcCH), 50.6 (CH), 46.0 (CH), 21.2 (CH_3), 20.7 (2 x CH_3).

Mass: 491 [M], 329 [M-$C_9H_7O_3$ + H].

Bis (±)-*N,N*-Diisopropyl-2-(1,4-phenyldioyl)ferrocenecarboxamide ((±)-15)

By following the general procedure B, using terephtalic acid (49.8 mg, 0.30 mmol, 0.50 equiv), **(±)-15** was obtained after column chromatography (PET-EtOAc, 10:1 to 90:10, 1% of NEt_3) as a red solid (193 mg, 49%). R_f (eluent: PET-EtOAc 10:1) = 0.18. Mp 70-75 °C.

ν_{max} (film)/cm^{-1} 2965, 1737, 1627, 1464, 1431, 1319, 1241, 1211, 1134, 1085, 1017, 814, 720.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.18 (s, 2H, 2 x ArCH), 8.17 (s, 2H, 2 x ArCH), 4.69 (dd, *J* = 1.4, 2.4 Hz, 2H, 2 x FcCH), 4.40 (s, 10H, 2x Cp), 4.15 (dd, *J* = 1.2, 2.4 Hz, 2H, 2 x FcCH), 4.09 (br s, 2H, 2 x CH), 4.03 (t, *J* = 2.6 Hz, 2H, 2 x FcCH), 3.39 (br s, 2H, 2 x CH), 1.47 (br s, 6H, 2 x CH_3), 1.41 (br s, 6H, 2 x CH_3), 1.06 (br s, 6H, 2 x CH_3), 1.02 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 165.6 (2 x C=O_{amide}), 164.3 (C=O_{ester}), 164.2 (C=O_{ester}), 133.7 (2 x ArC), 130.0 (4 x ArCH), 115.0 (FcC-O), 114.9 (FcC-O), 79.9 (2 x FcC), 71.3 (2 x Cp), 62.8 (FcCH), 62.7 (FcCH), 62.0 (2 x FcCH), 60.8 (FcCH), 60.7 (FcCH), 55.5 (CH), 50.5 (CH), 45.9 (2 x CH), 20.7 (8 x CH_3).

(±)-*N,N*-Diisopropyl-2-(ferrocenoyl)ferrocenecarboxamide ((±)-16)

By following the general procedure B, using ferrocenecarboxylic acid (165 mg), **(±)-16** was obtained after column chromatography (PET-EtOAc, 90:10, 1% of NEt_3) as an orange solid (277 mg, 85%). R_f (eluent: PET-EtOAc 10:1) = 0.26. Mp 58-62 °C. CCDC 1909917.

ν_{max} (film)/cm^{-1} 2959, 1727, 1626, 1467, 1429, 1374, 1317, 1267, 1245, 1134, 1104, 1027, 1002, 910, 817, 804.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.85 (m, 1H, FcCH), 4.83 (m, 1H, FcCH), 4.61 (dd, *J* = 1.5, 2.5 Hz, 1H, FcCH), 4.43 (t, *J* = 1.7 Hz, 2H, 2 x FcCH), 4.39 (s, 5H, Cp), 4.28 (s, 5H, Cp), 4.09 (dd, *J* = 1.5, 2.5 Hz, 1H, FcCH), 4.02 (br s, 1H, CH), 3.98 (t, *J* = 2.5 Hz, 1H, FcCH), 3.40 (br s, 1H, CH), 1.50 (br s, 6H, 2 x CH_3), 1.05 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.7 (2 x C=O_{ester}), 165.7 (C=O_{amide}), 114.5 (FcC-O), 80.2 (FcC-CO_{amide}), 71.7 (2 x FcCH), 71.1 (Cp), 70.4 (2 x FcCH), 70.3 (FcC-CO_{ester}), 70.0 (Cp), 62.5 (FcCH), 61.9 (FcCH), 60.6 (FcCH), 50.6 (CH), 45.8 (CH), 21.0 (4 x CH_3).

(±)-*N,N*-Diisopropyl-2-(2-thiophenoyl)ferrocenecarboxamide ((±)-17)

By following the general procedure B, using 2-thiophenecarboxylic acid (92.3 mg), **(±)-17** was obtained after column chromatography (PET-EtOAc, 10:1, 1% of NEt_3) as an orange solid (204 mg, 77%). R_f (eluent: PET-EtOAc 90:10) = 0.40. Mp 118-120 °C.

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ν_{max} (film)/cm^{-1} 2966, 1721, 1632, 1615, 1463, 1410, 1357, 1317, 1247, 1223, 1208, 1079, 1057, 1038, 1022, 1001, 812, 742, 735.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.86 (dd, *J* = 1.3, 3.8 Hz, 1H, ArCH), 7.59 (dd, *J* = 1.3, 5.0 Hz, 1H, ArCH), 7.11 (dd, *J* = 3.8, 5.0 Hz, 1H, ArCH), 4.66 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.11 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.04 (br s, 1H, CH), 3.99 (t, *J* = 2.6 Hz, 1H, FcCH), 3.38 (br s, 1H, CH), 1.44 (br s, 6H, 2 x CH_3), 1.02 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 165.6 (C=O_{amide}), 160.5 (C=O_{ester}), 134.4 (ArCH), 133.5 (ArCH), 13.1 (ArC), 128.1 (ArCH), 114.6 (FcC-CO), 80.4 (FcC), 71.4 (Cp), 62.9 (FcCH), 62.1 (FcCH), 60.7 (FcCH), 50.7 (CH), 46.0 (CH), 20.8 (4 x CH_3).

Mass: 439 [M], 328, 229.

(±)-*N,N*-Diisopropyl-2-(3,4-methylenedioxycinnamoyl)ferrocene-carboxamide ((±)-18)

By following the general procedure B, using 3,4-methylenedioxycinnamic acid (138 mg), **(±)-18** was obtained after column chromatography (PET-EtOAc, 90:10, 1% of NEt_3) as an orange solid (267 mg, 88%). R_f (eluent: PET-EtOAc 90:10) = 0.22. Mp 153-155 °C.

ν_{max} (film)/cm^{-1} 2967, 1730, 1628, 1601, 1500, 1490, 1464, 1447, 1430, 1367, 1317, 1299, 1247, 1136, 1119, 1100, 1032, 1006, 926, 817, 751.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 15.9 Hz, 1H, C*H*=CH=CO), 7.04 (d, *J* = 1.7 Hz, 1H, ArCH), 7.01 (dd, *J* = 1.7, 7.9 Hz, 1H, ArCH), 6.80 (d, *J* = 7.9 Hz, 1H, ArCH), 6.34 (d, *J* = 15.9 Hz, 1H, CH=C*H*=CO), 6.00 (s, 2H, CH_2), 4.56 (dd, *J* = 1.4, 2.4 Hz, 1H, FcCH), 4.37 (s, 5H, Cp), 4.11 (dd, *J* = 1.5, 2.6 Hz, 1H, FcCH), 4.05 (br s, 1H, CH), 3.98 (t, *J* = 2.6 Hz, 1H, FcCH), 3.37 (br s, 1H, CH), 1.45 (br s, 6H, 2 x CH_3), 1.04 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 165.9 (C=O), 165.8 (C=O), 150.1 (ArC-O), 148.6 (ArC-O), 145.9 (*C*H=CH=CO), 128.9 (ArC), 125.0 (ArCH), 115.3 (CH=*C*H=CO), 114.8 (FcC-CO), 108.8 (ArCH), 106.8 (ArCH), 101.8 (CH_2), 80.0 (FcC), 71.4 (Cp), 63.0 (FcCH), 62.0 (FcCH), 61.1 (FcCH), 50.7 (CH), 46.1 (CH), 21.0 (4 x CH_3).

(±)-*N,N*-Diisopropyl-2-(piperoyl)ferrocenecarboxamide ((±)-19)

By following the general procedure B, using piperic acid (157 mg), **(±)-19** was obtained after column chromatography (PET-EtOAc, 90:10 to 80:20, 1% of NEt_3) as an orange solid (291 mg, 92%). R_f (eluent: PET-EtOAc 90:10) = 0.23. Mp 59-64 °C.

ν_{max} (film)/cm^{-1} 2965, 1722, 162, 1605, 1489, 1446, 1433, 1368, 1320, 1521, 1227, 1203, 1108, 1036, 997, 928, 814, 754.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.48 (dd, *J* = 10.7, 15.2 Hz, 1H, CH=CH=C*H*=CH=CO), 6.99 (d, *J* = 1.6 Hz, 1H, ArCH), 6.92 (dd, *J* = 1.6, 8.1 Hz, 1H, ArCH), 6.84 (d, *J* = 15.5 Hz, 1H, C*H*=CH=CH=CH=CO), 6.78 (d, *J* = 8.1 Hz, 1H, ArCH), 6.71 (dd, *J* = 10.7, 15.5 Hz, 1H, CH=C*H*=CH=CH=CO), 6.01 (d, *J* = 15.2 Hz, 1H, CH=CH=CH=C*H*=CO), 5.98 (s, 2H, CH_2), 4.56 (dd, *J* = 1.5, 2.5 Hz, 1H, FcCH), 4.37 (s, 5H, Cp), 4.11 (dd, *J* = 1.5, 2.5 Hz, 1H, FcCH), 4.04 (br s, 1H, CH), 3.97 (t, *J* = 2.56 Hz, 1H, FcCH), 3.38 (br s, 1H, CH), 1.46 (br s, 6H, 2 x CH_3), 1.04 (br s, 6H, 2 x CH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 165.9 (C=O_{ester}), 165.7 (C=O_{amide}), 148.9 (ArC-O), 148.5 (ArC-O), 146.4 (CH=CH=*C*H=CH=CO), 141.3 (*C*H=CH=CH=CH=CO), 130.7 (ArC), 124.6 (CH=*C*H=CH=CH=CO), 123.4 (CH=CH=CH=*C*H=CO), 114.6 (FcC-CO), 108.8 (ArCH), 106.2 (ArCH), 101.6 (CH_2), 80.2 (FcC), 71.4 (Cp), 63.1 (FcCH), 62.1 (FcCH), 61.0 (FcCH), 50.7 (CH), 46.0 (CH), 20.9 (4 x CH_3).

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