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Functionalization of 3-Iodo-*N*,*N*-diisopropylferrocene-carboxamide, a Pivotal Substrate to Open the Chemical Space to 1,3-Disubstituted Ferrocenes

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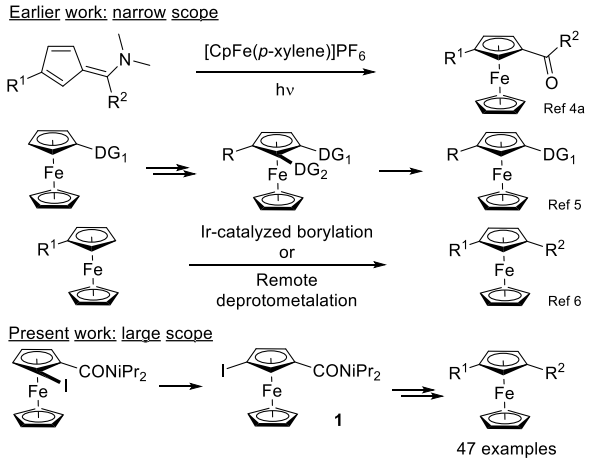
Abstract. From 2-iodo-*N*,*N*-diisopropylferrocene-carboxamide, the halogen 'dance' reaction was applied to deliver gram quantities of the 3-iodo isomer. The latter was successfully functionalized by Ullmann-type and Suzuki-Miyaura cross-couplings to build C-O and C-C bonds, respectively. Lithium/iodine exchange-electrophilic trapping sequences were also implemented to provide ferrocenes bearing valuable functional groups. Borane-mediated carboxamide reduction was next studied on selected substrates to deliver the corresponding amino derivatives in moderate to excellent yields. One of them, 1-(*N*,*N*-diisopropylaminomethyl)-3-iodoferrocene, was used as a substrate to access various iodoferrocene derivatives. Not only this work constitutes a general entry into the world of 1,3-disubstituted ferrocenes, but it also extends the chemical space available around this original scaffold.

Keywords: Ferrocene; Carboxamide; Halogen migration; Suzuki-Miyaura cross-coupling; Ullmann-type cross-coupling

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Introduction

Discovered in 1951,[1] ferrocene is currently one of the most important organometallic scaffold with multiple applications in redox sensing, catalysis, material science and medicinal chemistry.[2] However, while monosubstituted, 1,1'- and 1,2-disubstituted derivatives are easily prepared by electrophilic substitution or deprotometalation/electrophilic trapping sequences, a general approach towards 1,3-disubstituted derivatives remains elusive in spite of their potential for specific applications.[3] Construction of the ferrocene core from substituted cyclopentadienes is a first, although lengthy, strategy (Scheme 1, top).[4] All the other approaches are currently based on the functionalization of monosubstituted ferrocenes. Direct electrophilic substitution being hardly regioselective, the main strategies currently rely on deprotometalation. The iterative installation and removal of ortho-directing groups (Cl, Br, sulfoxide) was proposed by Slocum, Butler, Weissensteiner, Top, Jaouen and Nicolosi.[5] Although diastereoenriched products can be made, syntheses remain lengthy and with a poor atom economy. Even though catalytic and stoichiometric remote C-H transformations were reported by Plenio, Brown and Manners, these approaches suffer from a narrow scope concerning both substrates and reaction conditions.[6]



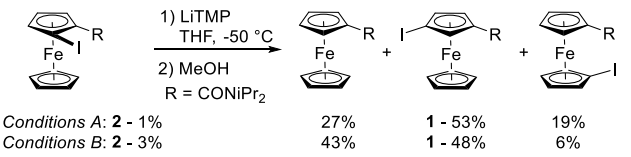
Scheme 1. Selected approaches toward 1,3-disubstituted ferrocenes.

An original approach relies on the base-triggered isomerization of 2-halogeno substituted compounds into their 3-halogeno isomers, namely the halogen 'dance' reaction (H.D.).[7] Initially reported in the ferrocene series as a side reaction by Mongin in 2010,[8] it was later studied by Weissensteiner on 1,2-dihalogenoferrocenes.[5f] However, the extensive scrambling noticed refrained the development of this approach which remained more like a chemical curiosity than a synthetically useful reaction in the ferrocene series.

Recently, we identified carboxamide and fluorine as pivotal groups to control the H.D. reaction in the ferrocene series.[9] However, due to very strong C-F bond, fluorine can hardly be converted into other functional groups. The chemistry of carboxamides being more developed, compound **1** was selected as a potential common precursor toward various 1,3-disubstituted ferrocenes. Therefore, here we report the catalytic and stoichiometric conversion of **1** into an unprecedented diversity of 1,3-disubstituted ferrocene derivatives (Scheme 1, bottom).

Results and Discussion

The required 2-iodo-*N*,*N*-diisopropylferrocene-carboxamide (**2**)[10] can easily be prepared on a multigram scale by following our chromatography-free approach.[11] As the halogen 'dance' reaction to convert **2** into **1** was previously optimized on a 1 to 2 mmol scale,[9a] a gram-scale synthesis was here required. The reaction on a small scale can be carried out by using a slight excess of LiTMP (TMP = 2,2,6,6-tetramethylpiperidide) in THF (THF = tetrahydrofuran) at –50 °C for 14 h.[9a] However, we found that upon scaling-up, the reaction time could be dramatically reduced, provided that a specific methanol quenching was applied (Scheme 2). When the reaction was conducted on a 10 mmol scale at –50 °C for 14 h, it appeared necessary to warm the reaction mixture to room temperature for 5 min before addition of methanol while we previously quenched at –50 °C (*Conditions A*). Indeed, a product distribution in favor of **1** was noticed by GC-MS analysis of the crude reaction mixture by following the new protocol (see SI). However, if methanol was added at –50 °C after only 2 h (*Conditions B*), a similar amount of **1** was detected by GC-MS analysis while warming to rt was detrimental to the yield. Therefore, expensive apparatus able to keep cryogenic temperature for long reaction time was not required anymore and, by following our new protocol B, a 13 mmol scale reaction was easily performed to provide 2 g of pure **1** in a single batch (35% yield).[12] Once our gram-scale approach toward **1** was secured, we studied its functionalization in catalytic and stoichiometric transformations.



Scheme 2. Halogen 'dance' reaction from compound **2**. Ratios calculated on the crude reaction mixtures by GC-MS analysis. *Conditions A*: 14 h reaction time, warm to room temperature for 5 min, addition of methanol at –50 °C. *Conditions B*: 2 h reaction time, addition of methanol at –50 °C.

Previously, we successfully investigated the behavior of 2-iodo-*N*,*N*-diisopropylferrocene-carboxamide (**2**) in Ullmann-type and Suzuki-Miyaura cross-coupling reactions.[11] In spite of the steric hindrance resulting from the bulky carboxamide, good yields were obtained. Because 1,3-disubstituted ferrocenes are less common than their 1,2- isomers, we were interested in evaluating the reactivity of **1** under similar conditions. Indeed, different steric and electronic factors between the two isomers might influence the reaction outcome. It is known that NMR chemical shifts can be helpful to predict reactivity trends. Indeed, by recording ^{1}H NMR shifts for the parent non-halogenated arenes, Handy has shown that cross-coupling reactions are generally favored at the most deshielded position.[13] Similarly, it is possible to correlate the reactivity in cross-coupling with the ^{13}C NMR shifts of the carbons bearing the halogens, the most reactive position corresponding to the most deshielded carbon.[14] Accordingly, we recorded the ^{1}H and ^{13}C NMR spectra of ferrocenes **1**, **2** and their parent non iodinated compound. On the basis of the Hα and Hβ chemical shifts of both isomers, it was deduced that cross-coupling should be favored on the 2-iododerivative **2**. Although small differences are observed between the two carbons bearing iodine in ^{13}C NMR spectroscopy, the same conclusion can be drawn. Thus, by excluding the steric factors, cross-coupling of the 2-iodo isomer **2** should be favored.

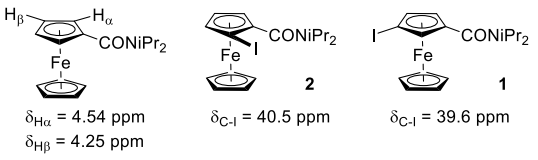


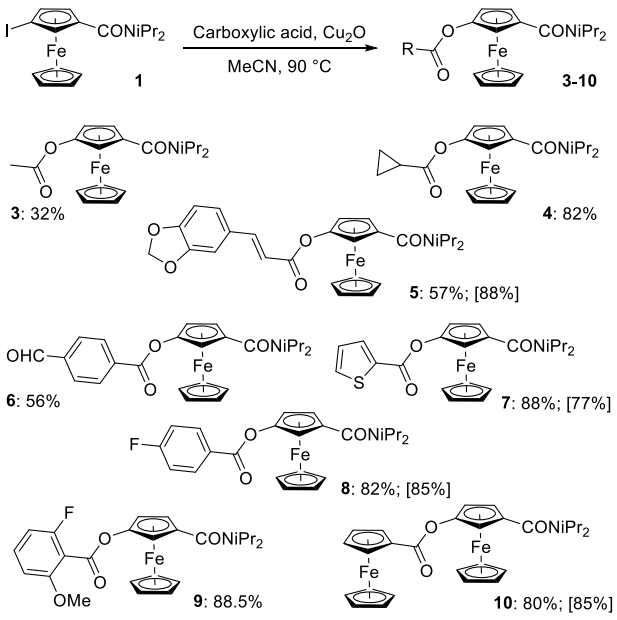
Figure 1. Comparison of ^{1}H and ^{13}C NMR shifts of compounds **1** and **2** and their parent non-iodinated compound. Data recorded in $CDCl_3$.

Therefore, **1** was reacted with various carboxylic acids in the presence of copper(I) oxide at acetonitrile reflux toward the esters **3**-**10** (Scheme 3). While the use of acetic acid gave an unexpected low yield of **3** (32%), cyclopropylcarboxylic acid afforded **4** in a better 82% yield. Moderate yields were noticed for

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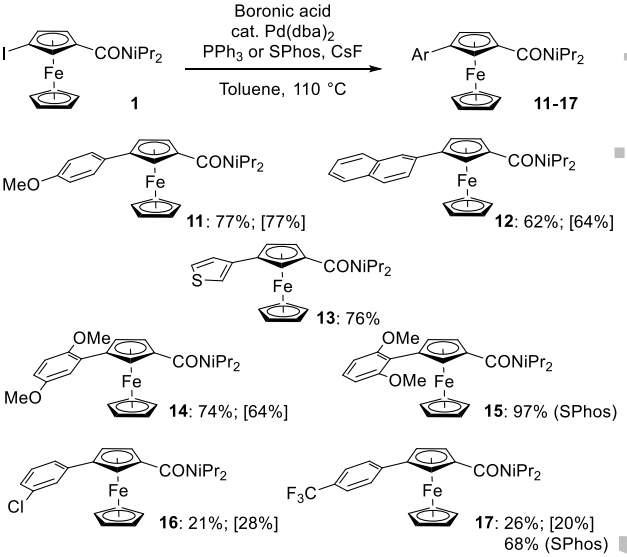
3,4-methylenedioxycinnamic and 4-formylbenzoic acids (products **5** and **6**), a result that could be due to the presence of a reactive olefin or to oxidation. Better results were noticed when more stable carboxylic acids were evaluated, and esters **7**-**10** were isolated in yields ranging from 80 to 88%. Picolinic and isonicotinic acids were found to be non-reactive under these reaction conditions.[15]



Scheme 3. Ullmann-type cross-coupling of compound **1**. Yields in brackets refer to the reaction from the 2-iodo isomer **2**, taken from ref 11.

From these selected examples, both isomers seem to share a similar level of reactivity under these conditions, except for the coupling of 3,4-methylenedioxycinnamic acid. The origin of such differences is hard to explain although it should be mentioned that strict anaerobic reaction conditions need to be respected. Indeed, inconsistent yields were noticed when reacting **1** if the solvent was not thoroughly degassed while the coupling of **2** was less sensitive. Contrary to the 1,3-disubstituted derivative **1**, the carboxamide group of **2** might help stabilize reactive intermediates during the catalytic cycle involving ligand-less conditions.

Suzuki-Miyaura cross-coupling was next performed on **1** by using our previously reported conditions which involve the use of $Pd(dba)_2$ (dba = dibenzylideneacetone), triphenylphosphine as the ligand and CsF as the base at toluene reflux.[9a] Though we previously reported the coupling of 4-methoxyphenylboronic acid under similar conditions in 46% yield, careful re-evaluation of reaction conditions provided **11** in an optimized 77% yield. 2-Naphthyl-, 2,5-dimethoxyphenyl- and 3-thiophenylboronic acids similarly afforded the original biaryl derivatives **12**-**14** in good yields while the coupling of the more sterically demanding 2,6-dimethoxyphenylboronic acid required the use of SPhos as ligand (compound **15**, 97% yield).[16] As usually observed,[17] the coupling of electron-poor substrates (3-chloro- and 4-(trifluoromethyl)phenylboronic acids) proved to be challenging as low yields were recorded for compounds **16** and **17** (21% and 26% respectively). It is worth noting that, for the latter, the use of SPhos as ligand considerably improved the reaction efficiency (68% yield). However, whatever the ligand used, couplings of the three isomeric pyridinylboronic acids led to the formation of multiple by-products without traces of the title products.



Scheme 4. Suzuki-Miyaura cross-coupling of compound **1**. Yields in brackets refer to the reaction from the 2-iodo isomer **2**, taken from ref 11.

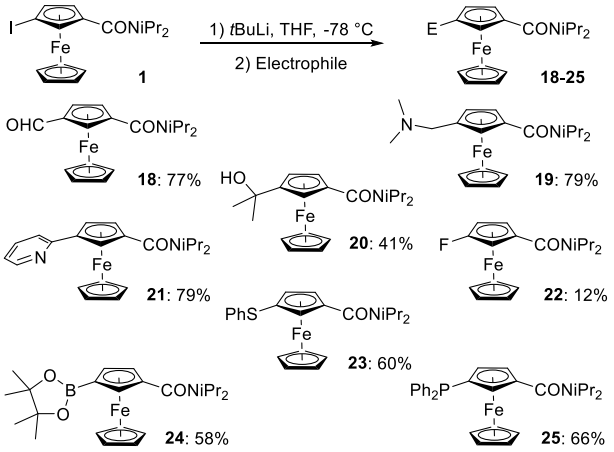
Again, by applying these Suzuki-Miyaura reaction conditions, both isomers appear to have a similar reactivity. The larger difference was noticed upon coupling 2,5-dimethoxyphenylboronic acid, in which steric factors might be an important parameter.

Since the pioneering work of Corey and Seebach on the lithium/halogen exchange,[18] this reaction has become a general way to functionalize organic bromides and iodides.[7a,19] To extend the range of 1,3-disubstituted ferrocenes available, we performed such reaction from **1** in THF at cryogenic temperature before trapping the corresponding lithiated intermediate with suitable electrophiles. By using *n*BuLi as lithiation reagent and dimethylformamide as electrophile, the corresponding aldehyde **18** was isolated in 68% yield, together with unreacted **1** (Scheme 5). Efficient lithium/halogen exchange can be achieved by using 2 equivalents of *t*BuLi, one to realize the exchange and the second to convert the formed *t*BuI into unreactive isobutene.[18] Therefore, by using *t*BuLi, we noticed the formation of the aldehyde **18** in an improved 77% yield. With the same reaction conditions, using Eschenmoser's salt and acetone as electrophiles led to the derivatives **19** and **20** in 79 and 41% yield, respectively. It was also

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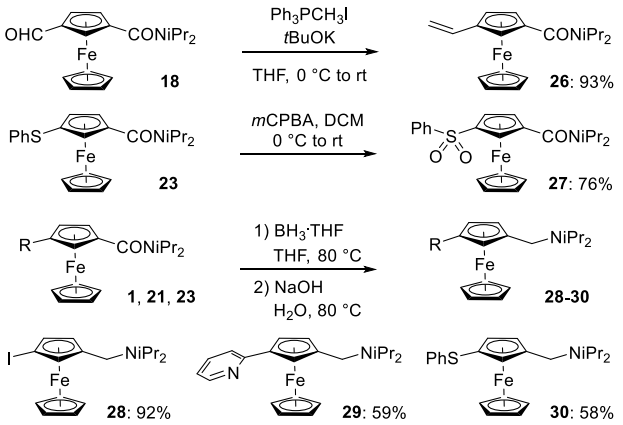
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possible to transmetalate the lithio intermediate with $ZnCl_2$·TMEDA (TMEDA = *N*,*N*,*N*',*N*'-tetramethylethylenediamine) and perform a Negishi cross-coupling toward the 2-pyridinyl derivative **21** that we failed to obtain by Suzuki-Miyaura coupling. Synthesis of the fluorinated ferrocene **22** by using *N*-fluorobenzenesulfonimide (NFSI) proved to be tricky concerning both the reaction and the purification process. Indeed, fluorination of substituted ferrocenes currently remains an unmet challenge.[9c,20] Furthermore, due to similar polarities between **1** and **22**, an efficient purification was hard to achieve. By using phenyl disulfide, triisopropylborate and chlorodiphenylphosphine as electrophiles, the original derivatives **23**-**25** were isolated in moderate yields.



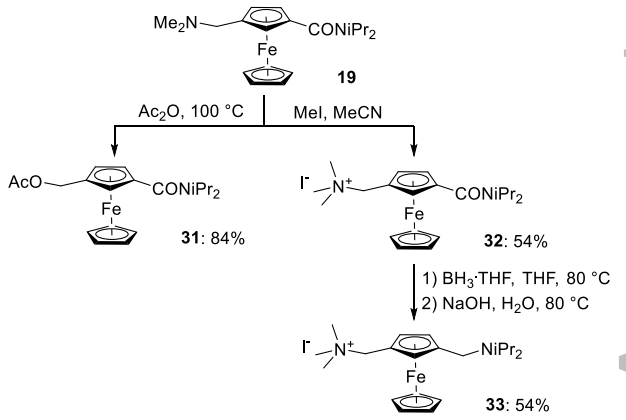
Scheme 5. Lithium/iodine exchange-electrophilic trapping sequence from compound **1**.

Selected compounds obtained by the lithium/iodide exchange-electrophilic trapping sequence were appealing for further elaboration. As vinylferrocene derivatives can be easily polymerized,[21] we first investigated the synthesis of an original 3-substituted vinylferrocene. Therefore, we reacted the aldehyde **18** with methylenetriphenylphosphorane (formed *in situ* by reaction of methyltriphenylphosphonium iodide and potassium *tert*-butoxide)[22] and isolated the vinylferrocene **26** in 93% yield (Scheme 6). Treatment of the sulfide **23** with 3-chloroperbenzoic acid was then attempted and the corresponding sulfone **27**, although of limited stability in solution, was isolated in a good 76% yield. Although the bulky *N*,*N*-diisopropylcarboxamide is known to be inert under various reaction conditions, it can be reduced by using borane.[10] Therefore, the ferrocenes **1**, **21** and **23** were treated with an excess of BH_3·THF complex to furnish, after basic hydrolysis, the corresponding amino derivatives **28**-**30** in moderate to excellent yields.



Scheme 6. Functional group manipulation from compounds **1**, **18**, **21** and **23**.

From the dimethylaminomethylated derivative **19**, it was possible to perform either the substitution for an acetate (**31**, 84% yield) or the quaternarization (**32**, 54% yield) by reaction with acetic anhydride and methyl iodide, respectively (Scheme 7). Such derivatives can be used for the well-described introduction of *P*-, *O*- and *N*-based nucleophiles,[23] however, we were eager to evaluate the behavior of **32** in reduction conditions. Indeed, it was reported by Manoury that ammonium derivatives do not react with borane,[24] but this was never attempted on such derivatives. Therefore, we reacted **32** with a 5-fold excess of BH_3.THF complex and obtained, after basic hydrolysis, the amino-ammonium derivative **33**. Although isolated in a moderate 54% yield, it can be mentioned that this compound should be hardly reachable by the selective methylation of the parent diamino derivative.

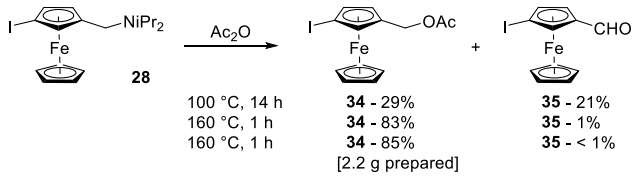


Scheme 7. Functional group manipulation from compound **19**.

Although borane-mediated reduction of the carboxamide into the *N*,*N*-diisopropylamino derivative **28** is possible, being able to substitute this bulky amine for another substituent would greatly enhance the chemical diversity accessible. To the best

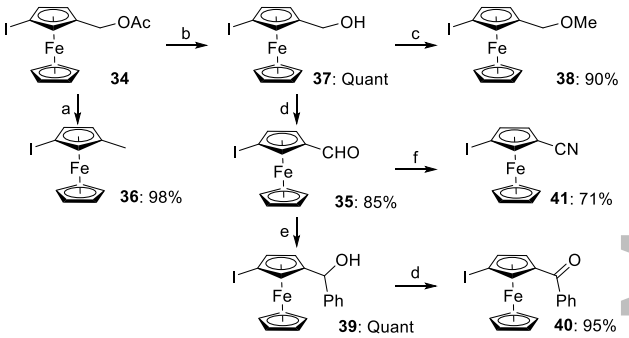
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of our knowledge, such transformation was only attempted by Anderson on non-halogenated 1,2-disubstituted ferrocenes.[25] We were eager to evaluate the Anderson's conditions to transform the diisopropylamine into an acetate. As no experimental details were reported apart from the temperature, we set up an overnight reaction from **28** by using a large excess of acetic anhydride at 100 °C (Scheme 8). Surprisingly, although full conversion was reached, we only isolated the acetate **34** and the unexpected aldehyde **35** in low yields (29 and 21% respectively). Although the oxidation of (dimethylaminomethyl)ferrocene derivatives is reported by using manganese dioxide,[26] it is difficult to rationalize the formation of **34** as no oxidant other than air dioxygen can be identified. Compared with Anderson's study, the iodine atom present on **28** might reduce product stability and impair the desired reaction for electronic reasons, explaining the side reaction and low yield recorded. We reasoned that increasing the temperature might speed up the reaction toward **34** at the expense of aldehyde formation. Pleasingly, after 1 h at 160 °C, full conversion was observed and the title product was isolated in 83% yield on a 1 mmol scale with only traces of the aldehyde. Furthermore, it was possible to scale-up the reaction and isolate up to 2 g of acetate in a single batch in a similar 85% yield. However, it should be mentioned that reaction time needs to be carefully respected as prolonged heating invariably leads to lower yields.



Scheme 8. Substitution of the diisopropylamino group from compound **28**.

Once a reliable access towards **34** secured, we were eager to study the functional group conversion in order to access various 3-substituted iodoferrocene derivatives. We initially extended the reduction scope of the borane·THF complex[24] by directly converting the acetate into a methyl group in an almost quantitative yield (compound **36**; Scheme 9). Then, saponification was first performed in a methanol-water mixture in the presence of an excess of sodium hydroxide. However, in addition to the alcohol **37**, a variable amount of the methylated ether **38** was also obtained. To avoid this side reaction, saponification was done in a THF-water mixture to deliver **37** in a quantitative yield. The alcohol **37** was methylated toward **38** by deprotonation with sodium hydride and subsequent trapping with methyl iodide (90% yield), validating the structure of the methylated ether. The oxidation of the alcohol into the aldehyde **35** was next attempted. Though reactions are known with stoichiometric amounts of chromium derivatives,[27] we were more interested in green approaches. Thus IBX-mediated oxidation in refluxing ethyl acetate was first attempted[28] with moderate success (21% of **35** isolated). However, the $RuCl_2PPh_2$-*N*-methylmorpholine oxide (NMO) system gave a much better result as the title product was isolated in a reproducible 85% yield after 2 h at room temperature.[29] Although **35** was of limited stability in acidic media, it could be isolated by column chromatography in 85% yield. Addition of the suitable Grignard reagent occurred in a quantitative way toward the alcohol **39**, isolated as an inseparable mixture of diastereoisomers in a 1:2 ratio. Therefore, the mixture was oxidized toward the keto derivative **40** using the same $RuCl_2PPh_3$-NMO system as before. Although of limited stability in acidic media, **40** was isolated in 95% yield as a red oil, which proved stable over time after filtration on basic alumina. From the aldehyde, we also prepared the nitrile derivative **41** by *in situ* condensation with hydroxylamine followed by dehydration in 71% yield.[30]

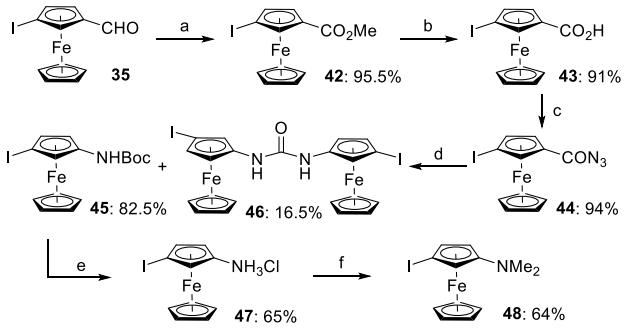


Scheme 9. Functional group manipulation from acetate **34**. Reactions conditions: a) i) BH_3·THF, THF, 80 °C; ii) NaOH, H_2O, 80 °C; b) NaOH, THF, H_2O, 80 °C; c) i) NaH, THF, 0 °C to rt; ii) MeI, THF, 0 °C to rt; d) NMO, $RuCl_2PPh_3$, acetone, rt; e) PhMgBr, THF, –78 °C to –40 °C; f) $NH_2OH.HCl$, KI, ZnO, MeCN, 80 °C.

Based on Kagan's report that 2-iodoferrocenecarboxaldehyde is surprisingly difficult to oxidize to the carboxylic acid,[31] we applied Yamada's oxidation protocol (KOH, I_2 in methanol) to access the methylated ester **42** in 95.5% yield (Scheme 10).[32] The direct oxidation of **35** to the carboxylic acid **43** in similar aqueous conditions was then attempted but resulted in very low conversion even on prolonged reaction time. However, **43** was obtained in 91% yield by a simple saponification of the corresponding methylated ester. Eager to access amino derivatives, we reacted **43** with diphenylphosphoryl azide (DPPA) by following a recently developed protocol[33] to isolated the acyl azide **44** in 94% yield. A Curtius rearrangement in the presence of *tert*-butanol was then successfully performed toward the Boc-protected amino derivative **45** which was isolated in 82.5% yield together with the symmetric urea **46** (16.5% yield). The formation

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of the latter can be rationalized by thermolysis of the intermediate isocyanate leading, after proton abstraction from the reaction mixture, to the corresponding amine, able to react with another isocyanate molecule.[34] Acidic deprotection (HCl in Et_2O) was next done toward **47** which was isolated as its salt (65% yield) to avoid the instability issues experienced with some aminoferrocene derivatives. A double reductive amination[35] was finally done toward the dimethylamino derivative **48**, isolated in 64% yield.



Scheme 10. Functional group manipulation toward dimethylaminoferrocene derivative **48**. Reactions conditions: a) KOH, I_2, MeOH, 0 °C to rt; b) NaOH, THF, H_2O, 80 °C; c) DPPA, NEt_3, DCM, 40 °C; d) *t*BuOH, toluene, 110 °C; e) HCl, Et_2O, rt; f) $(CH_2O)_n$, $NaBH_3CN$, AcOH, rt.

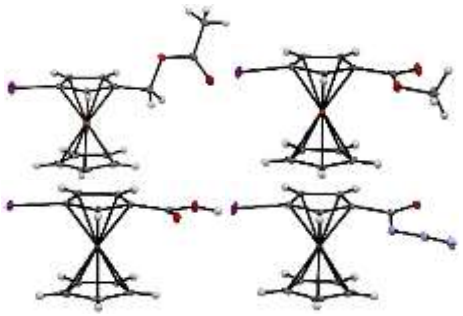


Figure 2. From left to right, top to bottom: molecular structure of compounds **34**, **42-44** (thermal ellipsoids shown at the 30% probability level).

Having prepared a large library of original 1,3-disubstituted ferrocene derivatives, we were looking forward to initiate their physicochemical characterization, starting with advanced NMR studies. Indeed, tables of ^1H and ^{13}C chemical shifts of some ferrocene derivatives have been sporadically reported in the literature.[36] While ^1H tables can be useful to predict the chemical shifts of monosubstituted, 1,1'- and 1,2-disubstituted ferrocenes, they are not always detailed enough to provide accurate predictions of non-symmetric 1,3-disusbtituted ferrocenes (Figure 3, top). Furthermore, similar tables of ^{13}C chemical shifts do not usually cover a wide range of functional groups, and predictions are less accurate than from ^1H NMR data (Figure 3, bottom). Therefore, we initially recorded ^1H and ^{13}C spectra of all new compounds containing the carboxamide moiety and, whenever possible, performed the full attribution based on short and long range correlations.

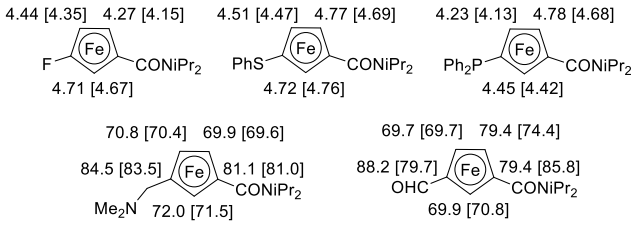


Figure 3. Experimental and calculated[35] (in brackets) ^1H (top) and ^{13}C (bottom) chemical shifts of selected compounds in $CDCl_3$.

Instead of making lists of chemical shifts, we reported the values relative to *N*,*N*-diisopropylferrocenecarboxamide in order to more easily evaluate the effect of the additional substituent at the 3-position.

Very small differences were noticed between the esters **3-10** concerning the ^1H and ^{13}C chemical shifts of ferrocene hydrogens (see SI, Table S1). Therefore, it seems that the effect of the substituent on the aromatic ring is not transferred through the ester linkage. The only trend observed in ^1H NMR is that the aromatic esters appear as stronger electron withdrawing groups than the aliphatic ones.

For the phenyl-substituted ferrocenes **11-17**, larger differences were noticed, clearly indicating that the substituent effect is transmitted to the organometallic core (Table 1).[37] In ^1H spectra, all ferrocene hydrogens were deshielded, the effect being more pronounced upon the iterative introduction of methoxy substituents (compounds **11**, **14** and **15**). As expected, the phenyl ring introduced onto ferrocene has a decreasing impact on the substituted Cp (Cp = cyclopentadienyl) ring hydrogens in the order H2 > H4 > H5 while little effect was noticed on the unsubstituted Cp ring. On ^{13}C spectra, larger shifts, especially for quaternary carbons, were noticed when compared with the monosubstituted phenylferrocenes.[38] Therefore, an additional effect of the other substituent should be taken into account.

For the remaining 1,3-disubstituted ferrocenes bearing the *N*,*N*-diisopropylcarboxamide group, compared to the previously reported table,[35c] small differences were noticed in ^1H chemical shifts (Table 2). No general trends could be identified although it should mentioned that the average of H2 and H4 shifts is close to the value observed for H_α in monosubstituted ferrocenes. By ^{13}C NMR spectroscopy, the electron-withdrawing nature of the aldehyde, 2-pyridinyl and sulfone substituents was confirmed (effect more pronounced on C_β than on C_α relative to the substituents). As observed for fluoroferrocene,[39] C_α (C2 and C4) and C_β (C1 and C5) became more shielded while C_{ipso} (C3) was

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strongly deshielded. The larger differences between the shifts of C2 and C4 were noticed for the iodo and the two sulfur-containing derivatives although no clear explanation can be currently advanced.

Table 1. Changes in chemical shifts,[a] relative to *N*,*N*-diisopropylferrocenecarboxamide, for the compounds **11**-**17**.

	δ (ppm)									
Compound	H2	H4	H5	Cp	C1	C2	C3	C4	C5	Cp
11	0.47	0.42	0.10	-0.11	0.4	-1.7	17.9	-2.0	0.1	1.6
12	0.65	0.60	0.19	-0.17	1.4	-1.2	17.3	-1.6	0.7	1.8
13	0.44	0.39	0.08	-0.09	0.5	-1.2	13.3	-1.5	0.0	1.6
14	0.68	0.61	0.13	-0.09	0.3	1.1	14.5	0.7	0.2	1.6
15	0.75	0.70	0.16	-0.10	-1.3	3.2	10.5	3.2	-0.04	1.3
16	0.51	0.47	0.15	-0.08	1.6	-1.3	15.7	-1.7	0.8	1.9
17	0.58	0.52	0.18	-0.09	2.1	-0.9	15.1	-1.6	0.9	1.9

[a] Spectra recorded in $CDCl_3$. Cp = unsubstituted cyclopentadienyl ring.

Table 2. Changes in chemical shifts,[a] relative to *N*,*N*-diisopropylferrocenecarboxamide, for the 1,3-disubstituted ferrocenes **1**, **18**-**27**.

	δ (ppm)									
Compound	H2	H4	H5	Cp	C1	C2	C3	C4	C5	Cp
1	0.19	0.23	-0.03	0.04	1.6	5.6	-29.3	2.2	5.2	3.2
18	0.51	0.59	0.41	0.13	-1.9	-0.1	19.3	0.8	5.1	1.9
19	-0.04	-0.02	-0.06	-0.09	-0.2	2.0	15.6	1.9	-0.1	0.5
20	0.07	0.04	-0.01	0.04	-0.7	-1.8	32	-2.6	0.7	0.5
21	0.73	0.78	0.22	-0.10	2.5	-1.1	15.6	-1.41	1.6	1.7
22	0.17	0.19	-0.27	0.11	-7.5	-12.2	65.9	-11.9	-6.7	1.4
23	0.18	0.26	0.23	0.12	2.1	6.0	8.4	3.3	5.5	1.8
24	0.13	nd	nd	0.01	5.5	4.4	nd	nd	nd	0.6
25	-0.09	-0.02	0.24	-0.06	2.6	4.5	8.8	4.8	2.6	1.2
26	0.22	-0.08	0.06	-0.04	0.7	-1.4	15.5	-1.6	0.5	0.3
27	0.46	0.51	0.21	0.33	9.7	0.5	16.0	3.8	-0.4	2.9

[a] Spectra recorded in $CDCl_3$. nd: not determinated. Cp = unsubstituted cyclopentadienyl ring.

Conclusion

In conclusion, from the easily accessible 2-iodo-*N*,*N*-diisopropylferrocenecarboxamide, optimization of a halogen 'dance' reaction afforded its 1,3-disubstituted isomer in gram quantities. We first established the similar reactivity of both isomers in Ullmann-type and Suzuki-Miyaura cross-couplings. Lithium/iodine exchange-electrophilic trapping sequences then afforded original carboxamide derivatives which could be reduced with borane to the corresponding diisopropylaminomethylated compounds. The substitution of the bulky amine in acetic anhydride was established and the original acetate derivative was further functionalized to access iodoferrocene derivatives bearing various functional groups. Tables of NMR chemical shifts increments were finally established for more accurate predictions in the ferrocenecarboxamide series. Therefore, by establishing such synthetic methodologies, a wide range of 1,3-disubstituted ferrocenes can now be easily made to find applications in many aspects of chemistry from sensing to catalysis.

Experimental Section

General Considerations. Unless otherwise stated, all reactions were performed under an argon atmosphere with anhydrous solvents using Schlenk technics. THF was distilled over sodium/benzophenone, acetone and methanol were dried by prolonged contact over activated 3Å molecular sieve,[40] acetonitrile, toluene, dioxane and dichloromethane were distilled over CaH_2. 2,2,6,6-Tetramethylpiperidine was distilled over CaH_2 under argon and stored over KOH pellets. Unless otherwise stated, all reagents were used without prior purification. All organolithiated reagents were titrated before use.[41] Column chromatography separations were achieved on silica gel (40-63 μm). All Thin Layer Chromatographies (TLC) were performed on aluminium 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 (a) on a Bruker Avance III spectrometer at 300 MHz and 75.4 MHz, respectively, or (b) Bruker Avance III HD at 400 MHz and 100 MHz, respectively, or (c) 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. Broad signals for the isopropyl groups were usually observed in the ferrocenecarboxamide series. They might result from

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restricted bond rotation as proposed by Petter[42] and Erb[9a] on *N*,*N*-dimethylferrocenecarboxamide and *N*,*N*-diisopropylferrocene-carboxamide. Compound **2** was prepared according to Erb.[11] $ZnCl_2$·TMEDA was prepared according to Mongin.[43]

Safety Considerations. Due to its high pyrophoric character, *t*BuLi need to be used only under inert conditions (anhydrous, nitrogen or argon atmosphere) and by people well trained to the manipulation of reactive organometallics.

Crystallography. For **34**, **42**, **43** and **44**, the X-ray diffraction data were collected using D8 VENTURE Bruker AXS diffractometer at the temperature given in the crystal data. The samples were studied with monochromatized Mo-Kα radiation (λ = 0.71073 Å). The structure was solved by dual-space algorithm using the *SHELXT* program,[44] and then refined with full-matrix least-square methods based on F^2 (*SHELXL*).[45] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. The molecular diagrams were generated by MERCURY (version 3.9).

3-Iodo-N,N-diisopropylferrocenecarboxamide (1). TMPH (2.42 mL, 2.02 g, 14.3 mmol, 1.10 equiv) and anhydrous THF (13.0 mL) were introduced into a 100 mL flame-dried Schlenk tube under argon. The reaction mixture was cooled between –15 and –10 °C (external temperature) in an ice/NaCl bath. *n*BuLi (1.4 M, 10.2 mL, 14.3 mmol, 1.10 equiv) was then introduced dropwise by syringe. After addition, the reaction mixture was stirred at the same temperature for 5 min. The Schlenk tube was transferred into a –50 °C cooled bath and was stirred for 5 more minutes before introduction of compound **2** (5.71 g, 13.0 mmol, 1.00 equiv) as a solid in one portion. After addition, the reaction mixture was stirred at –50 °C for 2 h. Methanol (7 mL) was added in one portion and the reaction mixture was then allowed to warm to rt out of the cooling bath. HCl (1.0 M aq., 30 mL) was added and the layers were separated. The aqueous layer was backwashed with EtOAc (1 x 20 mL) and the combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude which consists in a mixture of *N*,*N*-diisopropylferrocenecarboxamide (R_f = 0.42 in cyclohexane-iPrOAc 78:22), 2-iodo-*N*,*N*-diisopropyl-ferrocenecarboxamide (R_f = 0.58 in cyclohexane-iPrOAc 78:22), 3-iodo-*N*,*N*-diisopropyl-ferrocenecarboxamide (R_f = 0.50 in cyclohexane-iPrOAc 78:22) and 1'-iodo-*N*,*N*-diisopropylferrocenecarboxamide (R_f = 0.45 in cyclohexane-iPrOAc 78:22). This was purified by column chromatography over SiO_2, using cyclohexane/AcOiPr (78:22) to give the title product **3** (1.99 g, 35%). Analytical data analogous to those reported previously.[9a] R_f (eluent: cyclohexane/iPrOAc 78:22) = 0.50. Mp 111-113 °C. ν_{max} (film)/cm^{-1} 2959, 1602, 1457, 1368, 1323, 1302, 1221, 1208, 1154, 1037, 875, 843, 826, 804, 763. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.73 (s, 1H, H2), 4.58 (s, 1H, H4), 4.51 (s, 1H, H5), 4.44 (br s, 1H, H8), 4.25 (s, 5H, H6), 3.42 (br s, 1H, H8), 1.45 (br s, 6H, H9), 1.20 (br s, 6H, H9). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 167.8 (C7), 82.8 (C1), 75.6 (C2), 75.2 (C5), 73.0 (C6), 71.1 (C4), 49.9 (C8), 46.5 (C8), 39.6 (C3), 21.2 (C9). Mass: 439 [M], 339 [M-$NiPr_2$].

General procedure A: Ullmann-type cross-coupling from 1.

Compound **1** (219 mg, 0.50 mmol, 1.00 equiv), carboxylic acid (0.60 mmol, 1.20 equiv) and Cu_2O (85.8 mg, 0.60 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.

*3-(Acetoxy)-N,N-diisopropylferrocenecarboxamide (**3**).* By following the general procedure A, using acetic acid (35.0 µL), compound **3** was obtained after column chromatography (PET-EtOAc, 70:30, 1% of NEt_3) as an orange oil (60.0 mg, 32%). R_f (eluent: PET-EtOAc 70:30) = 0.38. ν_{max} (film)/cm^{-1} 2965, 2929, 1756, 1440, 1368, 1332, 1317, 1202, 1158, 1140, 1034, 1008, 955, 818, 805. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.80 (s, 1H, H2), 4.55 (s, 1H, H4), 4.49 (br s, 1H, H8), 4.41 (s, 1H, H5), 4.27 (5H, H6), 3.43 (br s, 1H, H8), 2.17 (s, 3H, H11), 1.32 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.1 (C7 or C10), 168.7 (C7 or C10), 115.4 (C3), 76.1 (C1), 71.3 (C6), 65.5 (C5), 62.5 (C2), 61.9 (C4), 49.4 (C8), 46.6 (C8), 21.4 (C11), 21.3 (C9). HRMS (ESI) calcd for $C_{19}H_{26}FeNO_3$ $[M+H]^+$ 372.1262; found 372.1613.

*3-(Cyclopropyloyl)-N,N-diisopropylferrocenecarboxamide (**4**).* By following the general procedure A, using cyclopropylcarboxylic acid (47.8 µL), the title product was obtained after column chromatography (PET-EtOAc, 80:20, 1% of NEt_3) as an orange oil (164 mg, 82%). R_f (eluent: PET-EtOAc 70:30) = 0.55. ν_{max} (film)/cm^{-1} 2955, 1746, 1613, 1440, 1374, 1332, 1317, 1143, 1134, 1097, 1033, 917, 818, 805. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.79 (t, *J* = 1.1 Hz, 1H, H2), 4.56 (dd, *J* = 1.3, 2.6 Hz, 1H, H4), 4.49 (br s, 1H, H8), 4.41 (dd, *J* = 1.5, 2.7 Hz, 1H, H5), 4.26 (s, 5H, H6), 3.45 (br s, 1H, H8), 1.71 (m, 1H, H11), 1.32 (br s, 12H, H9), 1.08 (m, 2H, H12), 0.96 (m, 2H, H12). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 173.1 (C10), 168.8 (C7), 115.6 (C3), 75.9 (C1), 71.2 (C6), 65.5 (C5), 62.4 (C2), 61.9 (C4), 49.6 (C8), 46.5 (C8), 21.3 (C9), 13.2 (C11), 9.3 (C12). HRMS (ESI) calcd for $C_{21}H_{28}FeNO_3$ $[M+H]^+$ 398.1413; found 398.1402.

*N,N-Diisopropyl-3-(3,4-methylenedioxycinnamoyl)ferrocene-carboxamide (**5**).* By following the general procedure A, using 3,4 methylenedioxycinnamic acid (115 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20 to 70:30, 1% of NEt_3) as an orange solid (145 mg, 57%). R_f (eluent: PET-EtOAc 70:30) = 0.47. Mp 139-141 °C. ν_{max} (film)/cm^{-1} 2964, 2925, 1728, 1602, 1490, 1446, 1368, 1318, 1251, 1144, 1122, 1105, 1033, 980, 921, 853, 806, 758. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.66 (d, *J* = 15.9 Hz, 1H, H12), 7.06 (s, 1H, H14), 7.04 (d, *J* = 7.8 Hz, 1H, H17 or H18), 6.82 (d, *J* = 7.8 Hz, 1H, H17 or H18), 6.32 (d, *J* = 15.9 Hz, 1H, H11), 6.01 (s, 2H, H19), 4.90 (s, 1H, H2), 4.66 (s, 1H, H4), 4.56 (br s, 1H, H8), 4.46 (s, 1H, H5), 4.29 (s, 5H, H6), 3.44 (br s, 1H, H8), 1.33 (br s, 12 H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.8 (C7), 165.3 (C10), 150.1 (C15 or C16), 148.6 (C15 or C16), 146.0 (C12), 128.7 (C17 or C18), 125.0 (C13), 115.6 (C3), 115.0 (C11), 108.7 (C17 or C18), 106.6 (C14), 101.8 (C19), 76.0 (C1), 71.3 (C6), 65.6 (C5), 62.4 (C2), 61.9 (C4), 49.6 (C8), 46.3 (C8), 21.3 (C9). HRMS (ESI) calcd for $C_{27}H_{30}FeNO_5$ $[M+H]^+$ 504.1468; found 504.1438.

*3-(4-Formylbenzoyl)-N,N-diisopropylferrocenecarboxamide (**6**).* By following the general procedure A, using 4-formylbenzoic acid (90.1 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20 to 70:30, 1% of NEt_3) as an orange oil (129 mg, 56%). R_f (eluent: PET-EtOAc 70:30) = 0.35. ν_{max} (film)/cm^{-1} 2966, 1738, 1705, 1507, 1441, 1333, 1318, 1251, 1200, 1142, 1089, 1064, 1033, 1015, 821, 752, 728. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 10.02 (s, 1H, H15), 8.16 (s, *J* = 8.2 Hz, 2H, H12), 7.90 (d, *J* = 8.2 Hz, 2H, H13), 4.88 (s, 1H, H2), 4.63 (m, 1H, H4), 4.52 (br s, 1H, H8), 4.40 (m, 1H, H5), 4.22 (s, 5H, H6), 3.35 (br s, 1H, H8), 1.25 (br s , 12H, H9). ^{13}C NMR (75.4

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MHz, $CDCl_3$): δ (ppm) 191.5 (C15), 168.5 (C7), 163.8 (C10), 139.6 (C14), 134.4 (C10), 130.6 (C12), 129.7 (C13), 115.8 (C3), 76.5 (C1), 71.4 (C6), 65.7 (C5), 62.4 (C2), 61.8 (C4), 49.7 (C8), 46.5 (C8), 21.3 (C9). HRMS (ESI) calcd for $C_{25}H_{28}FeNO_4$ $[M+H]^+$ 462.1362; found 462.1351.

*N,N-Diisopropyl-3-(2-thiophenoyl)ferrocenecarboxamide (**7**).* By following the general procedure A, using 2-thiophenecarboxylic acid (76.9 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20 to 70:30, 1% of NEt_3) as an orange oil (195 mg, 88.5%). R_f (eluent: PET-EtOAc 70:30) = 0.45. ν_{max} (film)/cm^{-1} 2965, 726, 1510, 1442, 1409, 1357, 1332, 1318, 1245, 114, 1085, 1054, 1034, 819, 737. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.89 (d, *J* = 3.7 Hz, 1H, H12), 7.64 (d, *J* = 4.9 Hz, 1H, H14), 7.15 (t, *J* = 4.4 Hz, 1H, H13), 4.94 (s, 1H, H2), 4.70 (s, 1H, H4), 4.61 (br s, 1H, H8), 4.48 (s, 1H, H5), 4.31 (s, 5H, H6), 3.44 (br s, 1H, H8), 1.34 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.7 (C7), 160.3 (C10), 134.4 (C12), 133.5 (C14), 132.9 (C11), 128.2 (C13), 115.7 (C3), 76.3 (C1), 71.4 (C6), 65.7 (C5), 62.3 (C2), 61.8 (C4), 49.7 (C8), 46.6 (C8), 21.3 (C9). HRMS (ESI) calcd for $C_{22}H_{26}FeNO_3S$ $[M+H]^+$ 440.0977; found 440.0955.

*3-(4-Fluorobenzoyl)-N,N-diisopropylferrocenecarboxamide (**8**).* By following the general procedure A, using 4-fluorobenzoic acid (84.1 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20, 1% of NEt_3) as an orange oil (188 mg, 92%). R_f (eluent: PET-EtOAc 70:30) = 0.50. ν_{max} (film)/cm^{-1} 2966, 1737, 1603, 1507, 1441, 1333, 1318, 1255, 1238, 1153, 1086, 1051, 852, 818, 759, 729. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.0 (dd, *J* = 5.5, 8.7 Hz, 2H, H12), 7.06 (t, *J* = 8.5 Hz, 2H, H13), 4.84 (s, 1H, H2), 4.60 (dd, *J* = 1.4, 2.4 Hz, 1H, H4), 4.48 (br s, 1H, H8), 4.39 (dd, *J* = 1.7, 2.4 Hz, 1H, H5), 4.21 (5H, H6), 3.34 (br s, 1H, H8), 1.24 (br s , 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.6 (s, C7), 166.2 (d, *J* = 254.7 Hz, C14), 163.9 (s, C10), 132.6 (d, *J* = 9.5 Hz, C12), 125.6 (d, *J* = 2.5 Hz, C11), 115.9 (d, *J* = 22.2 Hz, C13), 115.7 (s, C3), 76.3 (s, C1), 71.3 (s, C6), 65.7 (s, C5); 62.5 (s, C2), 61.9 (s, C4), 49.7 (s, C8), 46.5 (s, C8), 21.3 (s, C9). ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) -104.5 (s). HRMS (ESI) calcd for $C_{24}H_{27}FFeNO_3$ $[M+H]^+$ 452.1319; found 452.1293.

*3-(2-Fluoro-6-methoxybenzoyl)-N,N-diisopropylferrocene-carboxamide (**9**).* By following the general procedure A, using 2-fluoro-6-methoxybenzoic acid (102 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20 to 70:30, 1% of NEt_3) as an orange oil (225 mg, 93%). R_f (eluent: PET-EtOAc 70:30) = 0.32. Mp 111-113 °C. ν_{max} (film)/cm^{-1} 2967, 1750, 1614, 1472, 1438, 1318, 1286, 1247, 1083, 1050, 792, 728. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.26 (m, 1H, H14), 6.67-6.62 (m, 2H, H13 and H15), 4.90 (t, *J* = 1.4 Hz, 1H, H2), 4.68 (dd, *J* = 1.4, 2.6 Hz, 1H, H4), 4.47 (br s, 1H, H8), 4.35 (dd, *J* = 1.6, 2.6, 1H, H5), 4.22 (s, 5H, H6), 3.78 (s, 3H, H17), 3.34 (br s, 1H, H8), 1.23 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.7 (C7), 160.4 (d, *J* = 251.3 Hz, C16), 161.6 (C10), 158.3 (d, *J* = 6.7 Hz, C12), 132.4 (d, *J* = 10.5 Hz, H15), 115.8 (s, C3), 111.6 (d, *J* = 19.1 Hz, C11), 108.3 (d, *J* = 21.6 Hz, C15), 107.1 (d, *J* = 2.6 Hz, C13), 76.1 (s, C1), 71.3 (C6), 65.6 (s, C5), 62.3 (C2), 61.8 (C4), 56.4 (C17), 49.5 (C8), 46.6 (C8), 21.2 (C9). ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) -113.3 (s). HRMS (ESI) calcd for $C_{25}H_{29}FFeNO_4$ $[M+H]^+$ 482.1425; found 482.1397.

*3-(Ferrocenoyl)-N,N-diisopropylferrocenecarboxamide (**10**).* By following the general procedure A, using ferrocenecarboxylic acid (138 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20, 1% of NEt_3) as an orange oil (219 mg, 80%). R_f (eluent: PET-EtOAc 70:30) = 0.48. ν_{max} (film)/cm^{-1} 2965, 1728, 1612, 1436, 1372, 1332, 1317, 1267, 1255, 1142, 1102, 1017, 1001, 818, 750. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.90 (t, *J* = 1.4 Hz, 1H, H2), 4.87 (t, *J* = 1.9 Hz, 2H, H12), 4.64 (dd, *J* = 1.4, 2.6 Hz, 1H, H4), 4.60 (br s, 1H, H8), 4.46 (t, *J* = 1.9 Hz, 2H, H13), 4.44 (dd, *J* = 1.5, 2.4 Hz, 1H, H5), 4.30 (s, H6 or H14), 4.24 (s, H6 or H14), 3.41 (br s, 1H, H8), 1.44 (br s, 6H, H9), 1.24 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.0 (C7), 168.9 (C10), 115.8 (C3), 76.0 (C1), 72.0 (C13), 71.3 (C6 or C14), 70.6 (C12), 70.3 (C11), 70.1 (C6 or C14), 65.4 (C5), 62.6 (C2), 61.9 (C4), 49.8 (C8), 46.5 (C8), 21.3 (C9). HRMS (ESI) calcd for $C_{28}H_{32}Fe_2NO_3$ $[M+H]^+$ 542.1075; found 542.1053.

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General procedure B: Suzuki-Miyaura cross-coupling from 1.

Compound **1** (219 mg, 0.50 mmol, 1.00 equiv), boronic acid (2.00 mmol, 4.00 equiv), $Pd(dba)_2$ (14.4 mg, 25.0 µmol, 0.05 equiv), ligand (0.10 mmol, 0.20 equiv) and CsF (152 mg, 1.00 mmol, 2.00 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 110 °C (external temperature) in a pre-heated oil bath. The reaction mixture was cooled to rt and was diluted with H_2O (10 mL). The reaction mixture was extracted with EtOAc (2 x 10 mL), the combined organic layers were dried over $MgSO_4$, filtrated on cotton wool and concentrated under vacuum on 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-3-(4-methoxyphenyl)ferrocenecarboxamide ***(11)***. By following the general procedure B, using 4-methoxyphenylboronic acid (304 mg) and triphenylphosphine (26.2 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange solid (162 mg, 77%). Analytical data analogous to those reported.[9a] R_f (eluent: PET-EtOAc 70:30) = 0.42. Mp 128-130 °C. ν_{max} (film)/cm^{-1} 2963, 1609, 1525, 1472, 1451, 1437, 1372, 1341, 1320, 1271, 1246, 1177, 1157, 108, 1035, 830, 805, 790, 762. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.42 (d, J = 8.4 Hz, 2H, H11), 6.86 (d, J = 8.4 Hz, 2H, H12), 5.01 (s, 1H, H2), 4.71 (br s, 1H, H8), 4.67 (s, 1H, H4), 4.64 (s, 1H, H5), 4.10 (s, 5H, H6), 3.82 (s, 3H, H14), 3.45 (br s, 1H, H8), 1.48 (br s, 6H, H9), 1.26 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.4 (C7), 158.5 (C13), 130.3 (C10), 127.3 (C11), 114.1 (C12), 86.8 (C3), 81.7 (C1), 71.4 (C6), 70.1 (C5), 68.3 (C2), 66.9 (C4), 55.4 (C14), 49.7 (C8), 46.5 (C8), 21.3 (C9). HRMS (ESI) calcd for $C_{24}H_{30}FeNO_2$ $[M+H]^+$ 420.1620; found 420.1600.

N,N-Diisopropyl-3-(2-naphthyl)ferrocenecarboxamide ***(12)***. By following the general procedure B, using 2-naphthylboronic acid (344 mg) and triphenylphosphine (26.2 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange oil (136 mg, 62%). R_f (eluent: PET-EtOAc 80:20) = 0.31. ν_{max} (film)/cm^{-1} 2965, 1601, 1460, 1440, 1358, 1324, 1213, 1159, 1106, 1040, 910, 815, 747, 727. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.88 (s, 1H, H1), 7.81-7.77 (m, 3H, 3 x ArCH), 7.64 (dd, *J* = 1.5, 8.6 Hz, 1H, H19), 7.48-7.42 (m, 2H, 2 x ArCH=, 5.19 (t, *J* = 1.4 Hz, 1H, H2), 4.85 (dd, *J* = 1.5, 2.4 Hz, 1H, H4), 4.73 (dd, *J* = 1.3, 2.4 Hz, 1H, H5), 4.62 (br s, 1H, H8), 4.04 (s, 5H, H5), 3.40 (br s, 1H, H8), 1.30 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.2 (C7), 135.9 (C10), 133.7 (C12 or C13), 132.4 (C12 or C13), 128.1 (ArCh), 127.9 (ArCH), 127.7 (ArCH), 126.5 (ArCH), 125.6 (ArCH), 125.1 (C19), 124.0 (C11), 86.2 (C3), 82.7 (C1), 71.6 (C6), 70.7 (C5), 68.8 (C2), 67.3 (C4), 49.5 (C8), 46.5 (C8), 21.3 (C9). Mass: 439 [M], 339 [M-$NiPr_2$], 312 [M-$CONiPr_2$ + H]. HRMS (ESI) calcd for $C_{27}H_{30}FeNO$ $[M+H]^+$ 440.1677; found 440.1689.

N,N-Diisopropyl-3-(3-thiophenyl)ferrocenecarboxamide ***(13)***. By following the general procedure B, using 3-thiopheneboronic acid (255 mg) and triphenylphosphine (26.2 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange oil (150 mg, 76%). R_f (eluent: PET-EtOAc 80:20) = 0.29. ν_{max} (film)/cm^{-1} 2965, 1605, 1449, 1369, 1323, 1254, 1159, 1105, 1042, 1001, 846, 818, 807, 778, 749. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.30 (dd, J = 2.9, 4.9 Hz, 1H, H13), 7.21-7.19 (m, 2H, H10 and H12), 4.98 (t, J = 1.2 Hz, 1H, H2), 4.64 (m, 1H, H4), 4.63 (br s, 1H, H8), 4.62 (m, m, 1H, H5), 4.12 (s, 5H, H6), 3.46 (br s, 1H, H8), 1.36 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.2 (C7), 139.1 (C11), 126.6 (C10), 125.8 (C13), 118.6 (C12), 82.2 (C3), 81.8 (C1), 71.4 (C6), 70.0 (C5), 68.8 (C2), 67.4 (C4), 49.5 (C8), 46.5 (C8), 21.3 (C9). Mass: 395 [M], 295 [M-$NiPr_2$], 268 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{21}H_{26}FeNO_5$ $[M+H]^+$ 396.1079; found 396.1068.

3-(2,5-Dimethoxyphenyl)-N,N-diisopropylferrocenecarboxamide ***(14)***. By following the general procedure B, using 2,5-dimethoxyphenylboronic acid (364 mg) and triphenylphosphine (26.2 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as a red solid (183 mg, 74%). R_f (eluent: PET-EtOAc 80:20) = 0.33. Mp 46-50 °C. ν_{max} (film)/cm^{-1} 2963, 2933, 1608, 1508, 1453, 1435, 1358, 1331, 1262, 1213, 1159, 1040, 1023, 805, 762, 732. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.11 (d, *J* = 3.1 Hz, 1H, H15), 6.83 (d, *J* = 8.9 Hz, 1H, H12), 6.75 (dd, *J* = 3.1, 8.9 Hz, 1H, H13), 5.22 (t, *J* = 1.4 Hz, 1H, H2), 4.86 (dd, *J* = 1.4, 2.5 Hz, 1H, H4), 4.75 (br s, 1H, H8), 4.67 (dd, *J* = 1.4, 2.5 Hz, 1H, H5), 4.12 (s, 5H, H6), 3.85 (s, 3H, H17), 3.81 (s, 3H, H16), 3.74 (br s, 1H, H8), 1.37 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 169.6 (C7), 153.6 (C14), 151.3 (C11), 127.6 (C10), 115.3 (C15), 112.3 (C12), 111.9 (C13), 83.4 (C3), 81.6 (C1), 71.4 (C6), 71.1 (C2), 70.2 (C5), 69.6 (C4), 56.1 (C17), 55.8 (C16), 49.6 (C8), 46.5 (C8), 21.4 (C9). Mass: 449 [M], 349 [M-$NiPr_2$]. HRMS (ESI) calcd for $C_{25}H_{32}FeNO_3$ $[M+H]^+$ 450.1726; found 450.1698.

3-(2,6-Dimethoxyphenyl)-N,N-diisopropylferrocenecarboxamide ***(15)***. By following the general procedure B, using 2,6-dimethoxyphenylboronic acid (364 mg) and SPhos (41.0 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange oil which solidify on standing (219 mg, 97%). R_f (eluent: PET-EtOAc 80:20) = 0.45. Mp 145-147 °C. ν_{max} (film)/cm^{-1} 2963, 1606, 1593, 1585, 1472, 1432, 1368, 1337, 1269, 1244, 1104, 1038, 807, 781, 726. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.19 (t, *J* = 8.4 Hz, 1H, H13), 6.60 (d, *J* = 8.4 Hz, 1H, H12), 5.29 (t, *J* = 1.3 Hz, 1H, H2), 4.95 (dd, *J* = 1.3, 2.5 Hz, 1H, H4), 4.79 (br s, 1H, H8), 4.70 (dd, *J* = 1.6, 2.5 Hz, 1H, H5), 4.11 (s, 5H, H6), 3.87 (s, 6H, H14), 3.45 (br s, 1H, H8), 1.44 (br s, 6H, H9), 1.31 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 170.3 (C7), 158.3 (C11), 127.4 (C13), 114.3 (C10), 104.3 (C12), 79.9 (C1), 79.4 (C3), 73.2 (C2), 72.1 (C4), 71.1 (C6), 69.6 (C5), 55.7 (C14), 49.5 (C8), 46.4 (C8), 21.4 (C9). HRMS (ESI) calcd for $C_{25}H_{32}FeNO_3$ $[M+H]^+$ 450.1726; found 450.1696.

3-(3-Chlorophenyl)-N,N-diisopropylferrocenecarboxamide ***(16)***. By following the general procedure B, using 3-chlorophenylboronic acid (313 mg) and triphenylphosphine (26.2 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange oil (43.1 mg, 21%). R_f (eluent: PET-EtOAc 70:30) = 0.33. ν_{max} (film)/cm^{-1} 2964, 2928, 1609, 1596, 1444, 1369, 1325, 1281, 1160, 1105, 1041, 819, 805, 783, 747. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.44 (t, *J* = 1.8 Hz, 1H, H11), 7.36 (dt, *J* = 1.4, 7.6 Hz, 1H, H15), 7.23 (t, *J* = 7.6 Hz, 1H, H14), 7.18 (dq, *J* = 1.2, 7.8 Hz, 1H, H13), 5.05 (t, *J* = 1.5 Hz, 1H, H2), 4.72 (dd, *J* = 1.5, 2.5 Hz, 1H, H4), 4.69 (dd, *J* = 1.5, 2.5 Hz, 1H, H5), 4.62 (br s, 1H, H8), 4.13 (s, 5H, H6), 3.46 (br s, 1H, H8), 1.49 (br s, 6H, H9), 1.25 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 168.9 (C7), 140.7 (C10), 134.5 (C12), 129.8 (C14), 126.4 (C13), 126.1 (C11), 124.3 (C15), 84.6 (C3), 82.9 (C1=, 71.7 (C6), 70.8 (C5), 68.7 (C2), 67.2 (C4), 49.9 (C8), 46.5 (C8), 21.3 (C9). Mass: 423 [M], 323 [M-$NiPr_2$], 296 [M-$CONiPr_2$ + H]. HRMS (ESI) calcd for $C_{23}H_{27}ClFeNO$ $[M+H]^+$ 424.1125; found 424.1106.

N,N-Diisopropyl-3-(4-trifluoromethylphenyl)ferrocenecarboxamide ***(17)***. By following the general procedure B, using 4-trifluoromethylphenylboronic acid (379 mg) and SPhos (41.0 mg), the title product was obtained after column chromatography (PET-EtOAc, 80:20) as an orange oil (156 mg, 68%). Analytical data analogous to those reported.[9a] R_f (eluent: PET-EtOAc 80:20) = 0.25. ν_{max} (film)/cm^{-1} 2967, 1614, 1467, 1445, 1320, 1284, 1160, 1119, 1105, 1067, 1039, 842, 821, 807. ^{1}H NMR (500 MHz, $CDCl_3$): δ

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(ppm) 7.55 (br s, 4H, H11 and H12), 5.12 (s, 1H, H2), 4.77 (s, 1H, H'), 4.72 (s, 1H, H5), 4.61 (br s, 1H, H8), 4.12 (s, 5H, H6), 3.46 (br s, 1H, H8), 1.49 (br s, 6H, H9), 1.25 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 168.7 (C7), 142.8 (s, C10), 128.3 (q, *J* = 32.2 Hz, C13), 126.2 (s, C11), 125.6 (q, *J* = 2.4 Hz, C12), 124.5 (q, *J* = 272.2 Hz, C14), 84.0 (s, C3), 83.4 (C1), 71.7 (C6), 70.9 (C5), 69.1 (C2), 67.3 (C4), 49.9 (C8), 46.5 (C8), 21.3 (C9). ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) -62.4 (s). HRMS (ESI) calcd for $C_{24}H_{27}F_3FeNO$ $[M+H]^+$ 458.1389; found 458.1361.

General procedure C: halogen/metal exchange-electrophilic trapping sequence from 1.

*t*BuLi (1.6 M, 1.25 mL, 2.00 mmol, 2.00 equiv) was added dropwise to a solution of compound **1** (439 mg, 1.00 mmol, 1.00 equiv) in THF (5.00 mL) at –78 °C. After addition, the reaction mixture was stirred at –78 °C for 15 min. The required electrophile was added at once. The reaction mixture was stirred at –78 °C for 15 min before being warmed to rt. After work-up, described for each product, purification by column chromatography over SiO_2, using PET-EtOAc (proportions given for each product) afforded the title product.

*3-Formyl-N,N-diisopropylferrocenecarboxamide (**18**).* By following the general procedure C, dimethylformamide (232 µL, 219 mg, 3.00 mmol, 3.00 equiv) was used as the electrophile. Once at rt, water (5 mL) was added and the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (80:20) with 2% of NEt_3 to give the title product as a red solid (262 mg, 77%). R_f (eluent: PET-EtOAc 80:20) = 0.20. Mp 107-110 °C. ν_{max} (film)/cm^{-1} 2965, 1667, 1601, 1453, 1368, 1337, 1310, 1254, 1216, 1160, 1082, 1040, 829, 805, 745. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.94 (s, 1H, H10), 5.05 (t, *J* = 1.3 Hz, 1H, H2), 4.95 (dd, *J* = 1.0, 2.3 Hz, 1H, H5), 4.84 (dd, *J* = 0.9, 2.4 Hz, 1H, H4), 4.38 (br s, 1H, H8), 4.34 (s, 5H, H6), 3.45 (br s, 1H, H8), 1.47 (br s, 6H, H9), 1.19 (br s, 6H, H9). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 193.1 (C10), 167.1 (C7), 88.2 (C3), 79.4 (C1), 75.1 (C5), 71.7 (C6), 69.9 (C2), 69.7 (C4), 50.2 (C8), 46.5 (C8), 21.3 (C9), 21.0 (C9). Mass: 341 [M], 241 [M-$NiPr_2$], 213 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{18}H_{24}FeNO_2$ $[M+H]^+$ 342.1151; found 342.1145.

*3-(N,N-Dimethylaminomethyl)-N,N-diisopropylferrocenecarboxamide (**19**).* By following the general procedure C, dimethylmethylideneammonium iodide (370 mg, 2.00 mmol, 2.00 equiv) was used as the electrophile. Once at rt, aqueous K_2CO_3 (sat. 5 mL) was added and the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (30:70 to 10:90) with 2% of NEt_3 to give the title product as a brown solid (294 mg, 79%). R_f (eluent: PET-EtOAc 20:80, 10 drops of NEt_3 per 10 mL of eluent) = 0.28. Mp 59-62 °C. ν_{max} (film)/cm^{-1} 2970, 2929, 2766, 1511, 1445, 1372, 1351, 1336, 1315, 1255, 1202, 1158, 1132, 1039, 1020, 833, 814, 807, 762. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.56 (br s, 1H, H8), 4.50 (t, *J* = 1.3 Hz, 1H, H2), 4.48 (dd, *J* = 1.6, 2.4 Hz, 1H, H5), 4.23 (dd, *J* = 1.5, 2.2 Hz, 1H, H4), 4.12 (s, 5H, H6), 3.37 (br s, 1H, H8), 3.22 (s, 2H, H10), 2.13 (s, 6H, H11), 1.40 (br s, 6H, H9), 1.16 (br s, 6H, H9). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.2 (C7), 84.5 (C3), 81.1 (C1), 72.0 (C2), 70.8 (C4), 70.3 (C6), 69.9 (C5), 59.0 (C10), 49.5 (C8), 46.3 (C8), 44.9 (C11), 21.2 (C9). Mass: 370 [M], 326 [M-NMe_2], 242 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{20}H_{31}FeN_2O$ $[M+H]^+$ 371.1780; found 371.1770.

*3-(Hydroxydimethylmethyl)-N,N-diisopropylferrocenecarboxamide (**20**).* By following the general procedure C, acetone (293 µL, 232 mg, 4.00 mmol, 4.00 equiv) was used as the electrophile. Once at rt, water (5 mL) was added and the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (95:5 to 90:10) to give the title product as an orange oil (152 mg, 41%). R_f (eluent: PET-EtOAc 70:30) = 0.34. ν_{max} (film)/cm^{-1} 3399 (br), 2970, 1594, 1459, 1369, 1331, 1315, 1268, 1160, 1133, 1107, 1035, 820, 807. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.61 (t, *J* = 1.5 Hz, 1H, H2), 4.57 (br s, 1H, H8), 4.53 (dd, *J* = 1.5, 2.5 Hz, 1H, H5), 4.29 (dd, *J* = 1.5, 2.5 Hz, 1H, H4), 4.25 (s, 5H, H6), 3.43 (br s, 1H, H8), 2.00 (br s, 1H, OH), 1.52 (s, 3H, H11), 1.48 (s, 3H, H11), 1.47 (br s, 6H, H9), 1.22 (br s, 6H, H9). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.1 (C7), 100.9 (C3), 80.6 (C1), 70.3 (C6), 69.3 C5), 69.0 (C10), 68.2 (C2), 66.3 (C4), 49.6 (C8), 46.4 (C8), 31.1 (C11), 30.9 (C11), 21.3 (C9). Mass: 354 [M-H_2O], 253 [M-$NiPr_2$-H_2O], 226 [M-$CONiPr_2$-H_2O]. HRMS (ESI) calcd for $C_{20}H_{30}FeNO_2$ $[M+H]^+$ 372.1620; found 372.1613.

*N,N-Diisopropyl-3-(2-pyridinyl)ferrocenecarboxamide (**21**).* By following the general procedure C, $ZnCl_2$·TMEDA (253 mg, 1.00 mmol, 1.00 equiv) was used as the electrophile. Once at rt, $PdCl_2$ (14.2 mg, 0.08 mmol, 0.08 equiv), DPPF (44.4 mg, 0.08 mmol, 0.08 equiv) and 2-chloropyridine (378 µL, 454 mg, 4.00 mmol, 4.00 equiv) were added and the reaction mixture was stirred at 80 °C in a pre-heated oil bath overnight. The reaction mixture was cooled to rt and water (10 mL) was added. The reaction mixture was extracted with EtOAc (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (60:40) with 2% of NEt_3 to give the title product as a red solid (309 mg, 79%). R_f (eluent: PET-EtOAc 60:40, 5 drops of NEt_3 per 10 mL of eluent) = 0.43. Mp 117-119 °C. ν_{max} (film)/cm^{-1} 2974, 1622, 1586, 1497, 1448, 1425, 1371, 1322, 1287, 1151, 1103, 1039, 832, 808, 786, 762, 743. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.50 (ddd, *J* = 0.9, 1.6, 4.8 Hz, 1H, H14), 7.58 (dt, *J* = 1.8, 7.8 Hz, 1H, H12), 7.43 (dt, *J* = 1.0, 7.8 Hz, 1H, H11, 7.08 (ddd, *J* = 0.9, 1.0, 4.8 Hz, 1H, H13), 5.27 (t, *J* = 1.3 Hz, 1H, H2), 5.03 (dd, *J* = 1.3, 2.4 Hz, 1H, H4), 4.76 (dd, *J* = 1.3, 2.4 He, 1H, H5), 4.61 (br s, 1H, H8), 4.11 (s, 5H, H6), 3.46 (br s, 1H, H8), 1.41 (br s, 6H, H9), 1.29 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.8 (C7), 158.4 (C10), 149.5 (C14), 136.2 (C12), 126.0 (C13), 120.3 (C11), 84.5 (C3), 83.8 (C1), 71.6 (C5), 71.5 (C6), 68.9 (C2), 67.8 (C4), 49.9 (C8), 46.5 (C8), 21.3 (C9). Mass: 390 [M], 290 [M-$NiPr_2$], 262 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{22}H_{27}FeN_2O$ $[M+H]^+$ 391.1467; found 391.1457.

*3-Fluoro-N,N-diisopropylferrocenecarboxamide (**22**).* By following the general procedure C, the solution of lithioferrocene in THF was cannulated onto a solution of NFSI (630 mg, 2.00 mmol, 2.00 equiv) in THF (4 mL) at –30 °C. After addition, the reaction mixture was stirred at –30 °C for 15 min before water (5 mL) was added. The reaction mixture was warmed to rt and was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using cyclohexane-EtOiPr (78:22) to give the title product as an orange oil (41.0 mg, 12%). R_f (eluent: cyclohexane-iPrOAc 78:22) = 0.60. ν_{max} (film)/cm^{-1} 2965, 1612, 1445, 1369, 1331, 1315, 1211, 1157, 1136, 1106, 1033, 1002, 953, 818, 805, 760. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.71 (s, 1H, H2), 4.54 (br s, 1H, H8), 4.44 (s, 1H, H4), 4.32 (s, 5H, H6), 4.27 (s, 1H, H5), 3.42 (br s, 1H, H8), 1.41 (br s, 6H, H9), 1.25 (br s, 6H, H9). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 168.6 (s, C7), 134.8 (d, *J* = 270.5 Hz, C3), 73.8 (s, C1), 71.2 (s, C6), 63.3 (d, *J* = 2.7 Hz, H5), 57.8 (d, *J* = 14.6 Hz, C2), 57.3 (d,

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J = 15.3 Hz, C4), 49.7 (s, C8), 46.5 (C8), 21.3 (C9). ^{19}F NMR (376 MHz, $CDCl_3$): -185.5 (s). HRMS (ESI) calcd for $C_{17}H_{23}FFeNO$ $[M+H]^+$ 332.1108; found 332.1099.

*N,N-Diisopropyl-3-(phenylthio)ferrocenecarboxamide (**23**).* By following the general procedure C starting from **1** (1.09 g, 2.5 mmol, 1.00 equiv), the solution of lithioferrocene in THF was cannulated onto a solution of phenyldisulfide (1.09 g, 5.00 mmol, 2.00 equiv) in THF (5 mL) at –78 °C. After addition, the reaction mixture was stirred at –78 °C for 15 min before being warmed to rt. Aqueous NaOH (5%, 10 mL) was added and the reaction mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with aqueous NaOH (5%, 3 x 10 mL), dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (95:5 to 90:10) to give the title product as an orange solid (632 mg, 60%). R_f (eluent: PET-EtOAc 90:10) = 0.26. Mp 110-112 °C. ν_{max} (film)/cm^{-1} 2955, 1615, 1447, 1374, 1329, 1293, 1208, 1152, 1126, 1106, 1034, 823, 806, 760, 735. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.22-7.17 (m, 2H, H12), 7.11-7.05 (m, 3H, H11 and H13), 4.77 (dd, *J* = 1.3, 2.4 Hz, 1H, H5), 4.72 (t, *J* = 1.3 Hz, 1H, H2), 4.60 (br s, 1H, H8), 4.51 (dd, *J* = 1.3, 2.4 Hz, 1H, H4), 4.33 (s, 5H, H6), 3.46 (br s, 1H, H8), 1.44 (br s, 6H, H9), 1.26 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.1 (C7), 140.1 (C10), 128.8 (C12), 126.4 (C11), 125.4 (C13), 83.4 (C1), 77.3 (C3), 76.0 (C2), 75.5 (C5), 72.2 (C4), 71.6 (C6), 49.8 (C8), 46.5 (C8), 21.3 (C9). Mass: 421 [M], 321 [M-$NiPr_2$], 294 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{23}H_{28}FeNOS$ $[M+H]^+$ 422.1235; found 422.1219.

*N,N-Diisopropyl-3-(pinacolboryl)ferrocenecarboxamide (**24**).* By following the general procedure C, the solution of lithioferrocene in THF was cannulated onto a solution of triisopropylborate (692 µL, 564 mg, 3.00 mmol, 3.00 equiv) in THF (3 mL) at –78 °C. After addition, the reaction mixture was stirred at –78 °C for 15 min before being warmed to rt. Methanol (2 mL) was added to the reaction mixture which was stirred at rt for 1 h. Volatiles were removed under vacuum using a rotary evaporator and THF (10.0 mL) was added to the residue. Pinacol (236 mg, 2.00 mmol, 2.00 equiv) was added and the reaction mixture was stirred at rt for 1h. Volatiles were removed under vacuum using a rotary evaporator, THF (10.0 mL) was added to the residue which was stirred at rt overnight. The reaction mixture was concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (80:20) to give the title product as an orange solid (253 mg, 58%). R_f (eluent: PET-EtOAc 80:20) = 0.27. Mp 127-129 °C. ν_{max} (film)/cm^{-1} 2973, 1521, 1484, 1454, 1370, 1330, 1306, 1273, 1200, 1142, 1120, 1034, 965, 855, 809, 753. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.76 (dd, *J* = 1.1, 2.2 Hz, 1H, H4 or H5), 4.67 (t, *J* = 1.1 Hz, 1H, H2), 4.48 (dd, *J* = 1.1, 2.2 Hz, 1H, H4 or H5), 4.41 (br s, 1H, H8), 4.22 (s, 5H, H6), 3.42 (br s, 1H, H8), 1.42 (br s, 6H, H9), 1.33 (s, 12H, H11), 1.24 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.8 (C7), 86.8 (C1), 83.4 (C10), 74.4 (C2 and C4 or C5), 74.1 (C4 or C5), 70.4 (C6), 49.7 (C8), 46.2 (C8), 25.1 (C11), 25.0 (C11), 21.3 (C9). C3 is not observed to due quadrupolar coupling. ^{11}B NMR (96.2 MHz, $CDCl_3$): δ (ppm) 32.8 (s). Mass: 439 [M], 339 [M-$NiPr_2$]. HRMS (ESI) calcd for $C_{23}H_{35}BFeNO_3$ $[M+H]^+$ 440.2054; found 440.2033.

*N,N-Diisopropyl-3-(diphenylphospino)ferrocenecarboxamide (**25**).* By following the general procedure C, chlorodiphenylphosphine (370 µL, 441 mg, 2.00 mmol, 2.00 equiv) was used as the electrophile. Once at rt, methanol (3 mL) was added and the reaction mixture was concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (10:1) with 1% of NEt_3 to give the title product as an orange solid (332 mg, 66%). R_f (eluent: PET-EtOAc 90:10) = 0.34. Mp 152-153 °C. ν_{max} (film)/cm^{-1} 2960, 1506, 1457, 1433, 1369, 1318, 1207, 1069, 1035, 908, 820, 805, 727. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.42 (m, 10H, ArCH), 4.78 (dd, *J* = 1.3, 2.2 hz, 1H, H4), 4.62 (br s, 1H, H8), 4.45 (dd, *J* = 1.5, 3.0 Hz, 1H, H2), 4.23 (dd, *J* = 2.2, 3.7 Hz, 1H, H4), 4.15 (s, 5H, H6), 3.44 (br s, 1H, H8), 1.44 (br s, 6H, H9), 1.23 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 168.8 (s, C7), 138.8 (d, *J* = 9.6 Hz, C10), 138.5 (d, *J* = 9.6 Hz, C10'), 133.7 (d, *J* = 10.8 Hz, ArCH), 133.4 (d, *J* = 11.0 Hz, ArCH), 128.8 (d, *J* = 7.5 Hz, ArCH), 128.4 (d, *J* = 4.5 Hz, ArCH), 128.3 (d, *J* = 4.5 Hz, ArCH), 83.9 (d, *J* = 3.1 Hz, C1), 77.7 (s, C3), 74.5 (d, *J* = 13.6 Hz, C2), 73.7 (d, *J* = 15.8 Hz, C4), 72.6 (d, *J* = 3.5 Hz, C5), 71.0 (s, C6), 49.7 (s, C8), 46.5 (s, C8), 21.3 (s, C9). ^{31}P NMR (121 MHz, $CDCl_3$): δ (ppm) -17.2 (s). Mass: 497 [M], 397 [M-$NiPr_2$], 369 [M-$CONiPr_2$]. HRMS (ESI) calcd for $C_{29}H_{33}FeNOP$ $[M+H]^+$ 498.1644; found 498.1620.

*N,N-Diisopropyl-3-vinylferrocenecarboxamide (**26**).* *t*BuOK (50.5 mg, 0.45 mmol, 1.50 equiv) was added portionwise to a suspension of methyltriphenylphosphonium iodide (182 mg, 0.45 mmol, 1.50 equiv) in THF (2 mL) at 0 °C. After addition, the yellow solution was stirred at 0 °C for 10 min. A solution of compound **18** (103 mg, 0.30 mmol, 1.00 equiv) in THF (2 mL) was added dropwise. After addition, the reaction mixture was warmed to rt and stirred for 30 min. Water (10 mL) was added and the reaction mixture was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-AcOEt (90:10 to 80:20) with 1% of NEt_3 to give the title product as an orange oil (95.0 mg, 93%). R_f (eluent: PET-EtOAc 80:20) = 0.44. ν_{max} (film)/cm^{-1} 2966, 2237, 1605, 1455, 1369, 1329, 1315, 1248, 1211, 1157, 1036, 923, 907, 819, 807, 726. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.43 (dd, *J* = 17.5, 10.7 Hz, 1H, H10), 5.39 (dd, *J* = 17.5, 0.7 Hz, 1H, H11), 5.07 (dd, *J* = 10.7, 0.7 Hz, 1H, H11), 4.76 (s, 1H, H2), 4.64 (br s, 1H, H8), 4.60 (s, 1H, H5), 4.46 (s, 1H, H4), 4.17 (s, 5H, H6), 3.43 (br s, 1H, H8), 1.46 (br s, 6H, H9), 1.24 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.2 (C7), 133.9 (C10), 112.3 (C11), 84.4 (C3), 82.0 (C1), 71.1 (C6), 70.5 (C5), 68.6 (C2), 67.3 (C4), 49.7 (C8), 46.4 (C8), 21.3 (C9). Mass: 339 [M], 239 [M-$NiPr_2$], 211 [M-$CONiPr_2$].

*N,N-Diisopropyl-3-(phenylsulfonyl)ferrocenecarboxamide (**27**).* *m*CPBA (129 mg, 0.75 mmol, 3.00 equiv) was added in three portions to a solution of compound **23** (105 mg, 0.25 mmol, 1.00 equiv) in DCM (1.5 mL) at 0 °C. After 5 min at 0 °C, the reaction mixture was warmed to rt and stirred for 1 h. Water (5 mL) was added to the reaction mixture which was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with aqueous NaOH (5%, 10 mL), dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (75:25) to give the title product as a brown solid (86 mg, 76%). R_f (eluent: PET-EtOAc 70:30) = 0.56. Mp 146-148 °C. ν_{max} (film)/cm^{-1} 2966, 1615, 1447, 1304, 1150, 1088, 819, 761, 722. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.86 (d, *J* = 7.7 Hz, 2H, H11), 7.53 (t, *J* = 7.7 Hz, 1H, H13), 4.76 (t, *J* = 7.7 Hz, 2H, H12), 5.00 (s, 1H, H2), 4.76 (s, 1H, H4), 4.75 (s, 1H, H5), 4.54 (s, 5H, H6), 4.39 (br s, 1H, H8), 3.43 (br s, 1H, H8), 1.45 (br s, 6H, H89), 1.18 (br s, 6H, H9). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 166.8 (C7), 142.8 (C10), 132.9 (C13), 129.2 (C12), 126.9 (C11), 91.0 (C1), 84.9 (C3), 72.7 (C4 and C6), 70.5 (C2), 69.6 (C5), 49.9 (C8), 46.6 (C8), 21.4 (C9), 20.9 (C9). Mass: 453 [M], 353 [M-$NiPr_2$]. HRMS (ESI) calcd for $C_{23}H_{28}FeNO_3S$ $[M+H]^+$ 454.1134; found 454.1111.

*1-(N,N-Diisopropylaminomethyl)-3-iodoferrocene (**28**).* $NaBH_4$ (1.90 g, 50.0 mmol, 5.00 equiv) and anhydrous THF (50.0 mL) were introduced under argon into a 250 mL round-bottom flask equipped with a bubbler and the reaction mixture was cooled to 0 °C. Iodine (6.10 g, 24.0 mmol, 2.40 equiv) was introduced into a separate 50 mL

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flame-dried round-bottom flask under argon and was dissolved into anhydrous THF (20.0 mL). The iodine solution was transferred into the $NaBH_4$ suspension dropwise by cannula. **Remark**: evolution of hydrogen occurred during the addition. After addition, the reaction mixture was allowed to warm to rt out of the cooling bath and was stirred for 1 h, giving a colorless solution of BH_3·THF. Compound **1** (4.40 g, 10.0 mmol, 1.00 equiv) was then added portionwise to the BH_3·THF solution which was then stirred overnight at reflux (heating mantle, external temperature 80 °C). **Remark**: the use of PTFE sleeve is strongly recommended to avoid blockage of the ground glass joints. The reaction mixture was cooled to 0 °C and a solution of NaOH (10%, 50 mL) was added dropwise. **Caution**: as a vigorous evolution of gas was noticed, the first drops of NaOH solution should be added slowly. After addition, the reaction mixture was stirred at reflux for 1 h (heating mantel, external temperature 80 °C). The reaction mixture was cooled to rt and the layers were separated. The aqueous layer was extracted with Et_2O (1 x 50 mL). The combined organic layers were washed with water (1 x 50 mL), brine (1 x 50 mL), dried over $MgSO_4$, filtrated 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 (70:30) with 10 mL of NEt_3 per litre of eluent to give the title product as an orange oil (3.91 g, 92%).
Another work-up affording pure product without column chromatography was also developed. After basic hydrolysis and 1 h heating at reflux, the reaction mixture was cooled to rt and the layers were separated. The aqueous layer was further extracted with EtOAc (2 x 50 mL). The combined organic layers were extracted with HCl (1.0 M aq., 3 x 50 mL). The combined aqueous layers were washed with Et_2O (2 x 50 mL) and basified with solid K_2CO_3 until pH 8 was reached. The mixture was extracted with EtOAc (2 x 60 mL) and the combined organic layers were dried over $MgSO_4$, filtrated on celite (washed with EtOAc until the filtrate was colorless), and concentrated under vacuum using a rotary evaporator to give the pure product. From compound **1** (6.20 g, 14.2 mmol), 4.90 g of **28** were obtained as an orange oil (80.5%). Analytical data analogous to those reported previously.[9a] R_f (eluent: PET/EtOAc 70:30) = 0.61. ν_{max} (film)/cm^{-1} 3094, 2961, 2868, 1683, 1462, 1379, 1361, 1202, 1189, 1159, 1106, 1000, 870, 817. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.46 (s, 1H, H2), 4.31 (dd, *J* = 2.0, 1.2 Hz, 1H, H4), 4.20 (t, *J* = 1.2 Hz, 1H, H5), 4.13 (s, 5H, H6), 3.41 (d, *J* = 14.6 Hz, 1H, H7), 3.34 (d, *J* = 14.6 Hz, 1H, H7), 3.03 (sept, *J* = 6.6 Hz, 2H, H8), 1.00 (d, *J* = 6.6 Hz, 6H, H9), 0.98 (d, *J* = 6.6 Hz, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 90.0 (C1), 75.9 (C2), 73.7 (C4), 71.7 (C6), 70.1 (C5), 47.6 (C8), 43.9 (C7), 39.8 (C3), 21.0 (C9). Mass: 425 [M], 325 [M-$NiPr_2$].

*1-(N,N-Diisopropylaminomethyl)-3-(2-pyridinyl)ferrocene (**29**).* BH_3.THF (1M in THF, 5.85 mL, 5.85 mmol, 7.60 equiv) was added to a solution of compound **21** (390 mg, 0.77 mmol, 1.00 equiv) in THF (5.00 mL) at rt. The reaction mixture was stirred for 15 min before being heated at 80 °C overnight. **Remark**: the use of PTFE sleeve is strongly recommended to avoid blockage of the ground glass joints. The reaction mixture was cooled to 0 °C and aqueous NaOH (5%, 10 mL) was added dropwise. **Caution**: as a vigorous evolution of gas was noticed, the first drops of NaOH solution should be added slowly. The reaction mixture was heated at 80 °C for 1 h before being cooled to rt. The reaction mixture was extracted with EtOAc (2 x 5 mL), the combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (90:10) with 2% of NEt_3 to give the title product as a red oil (169.3 mg, 59%). R_f (eluent: PET-EtOAc 80:20, 10 drops of NEt_3 per 10 mL of eluent) = 0.50. ν_{max} (film)/cm^{-1} 2962, 1587, 1563, 1498, 1465, 1418, 1360, 1202, 1150, 1105, 1000, 815, 784, 739. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.49 (d, *J* = 4.8 Hz, 1H, H14), 7.54 (dt, *J* = 1.7, 7.8 Hz, 1H, H12), 7.38 (d, *J* = 7.8 Hz, 1H, H11), 7.03 (ddd, *J* = 0.7, 4.8, 7.2 Hz, 1H, H13), 4.99 (s, 1H, H2), 4.82 (s, 1H, H4), 4.45 (s, 1H, H5), 3.99 (s, 5H, H6), 3.53 (d, *J* = 14.3 Hz, 1H, H7), 3.46 (d, *J* = 14.3 Hz, 1H, H7), 3.09 (sept, *J* = 6.6 Hz, 2H, H8), 1.03 (d, *J* = 606 Hz, 6H, H9), 1.02 (d, *J* = 6.6 Hz, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 159.7 (C10), 149.4 (C14), 135.9 (C12), 120.4 (C13), 120.0 (C11), 91.2 (C1), 82.8 (C3), 71.6 (C5), 70.2 (C6), 69.1 (C2), 66.5 (C4), 47.5 (C8), 44.2 (C7), 21.1 (C9), 20.9 (C9). HRMS (ESI) calcd for $C_{22}H_{29}FeN_2$ $[M+H]^+$ 377.1675; found 377.1664.

*1-(N,N-Diisopropylaminomethyl)-3-(phenylthio)ferrocene (**30**).* BH_3.THF (1M in THF, 3.50 mL, 3.50 mmol, 5.00 equiv) was added to a solution of compound **23** in THF (5.00 mL) at rt. The reaction mixture was stirred for 15 min before being heated at 80 °C overnight. **Remark**: the use of PTFE sleeve is strongly recommended to avoid blockage of the ground glass joints. The reaction mixture was cooled to 0 °C and aqueous NaOH (5%, 10 mL) was added dropwise. **Caution**: as a vigorous evolution of gas was noticed, the first drops of NaOH solution should be added slowly. The reaction mixture was heated at 80 °C for 1 h before being cooled to rt. The reaction mixture was extracted with EtOAc (2 x 5 mL) and the combined organic layers were extracted with aqueous HCl (1M, 2 x 10 mL). The combined aqueous layers were washed with Et_2O (15 mL) before solid K_2CO_3 was added portionwise until pH 10 was reached. The aqueous layers were extracted with EtOAc (2 x 10 mL), dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the title product as a yellow solid (165 mg, 58%). R_f (eluent: PET-EtOAc 80:20, 5 drops of NEt_3 per 10 mL of eluent) = 0.40. Mp 58-61 °C. ν_{max} (film)/cm^{-1} 2951, 1581, 1479, 1456, 1437, 1371, 1359, 1186, 1151, 1105, 1025, 817, 735. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.17 (t, *J* = 8.0 Hz, 2H, H12), 7.07-7.02 (m, 3H, H11 and H13), 4.48 (s, 1H, H2), 4.41 (s, 1H, H5), 4.32 (s, 1H, H4), 4.22 (s, 5H, H6), 3.50 (d, *J* = 15.0 Hz, 1H, H7), 3.45 (d, *J* = 15.0 Hz, 1H, H7), 3.09 (sept, *J* = 6.5 Hz, 2H, H8), 1.04 (d, *J* = 6.5 Hz, 6H, H9), 1.03 (d, *J* = 6.5 Hz, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 141.2 (C10), 128. (C12), 125.6 (C11), 124.7 (C13), 91.6 (C1) 76.5 (C2), 74.6 (C3), 74.3 (C4), 71.5 (C5), 70.3 (C6), 48.1 (C8), 44.1 (C7), 21.1 (C9), 20.9 (C9). Mass: 407 [M], 307 [M-$NiPr_2$]. HRMS (ESI) calcd for $C_{23}H_{30}FeNS$ $[M+H]^+$ 408.1443; found 408.1430.

*3-(Acetoxymethyl)-N,N-diisopropylferrocenecarboxamide (**31**).* A solution of **19** (148.0 mg, 0.40 mmol, 1.00 equiv) in acetic anhydride (945 µL, 1.02 g, 10.0 mmol, 25.0 equiv) was heated at 100 °C for 1 h. The reaction mixture was cooled to rt, poured onto an ice/water mixture and solid K_2CO_3 was added until pH 10 was reached. The reaction mixture was extracted with EtOAc (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PET-EtOAc (80:20 to 70:30) with 2% of NEt_3 to give the title product as an orange solid (130 mg, 84%). R_f (eluent: PET-EtOAc 80:20) = 0.32. Mp 87-89 °C. ν_{max} (film)/cm^{-1} 2962, 1744, 1595, 1454, 1369, 1337, 1263, 1229, 1211, 1037, 1022, 947, 845. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.89 (d, *J* = 12.3 Hz, 1H, H10), 4.85 (d, *J* = 12.3 Hz, 1H, H10), 4.65 (t, *J* = 1.2 Hz, 1H, H2), 4.58 (dd, *J* = 1.7, 2.3 Hz, 1H, H5), 452 (br s, 1H, H8), 4.36 (dd, *J* = 1.4, 2.1 Hz, 1H, H4), 4.22 (s, 5H, H6), 3.42 (br s, 1H, H8), 2.04 (s, 3H, H12), 1.41 (br s, 6H, H9), 1.25 (br s, 6H, H9). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 170.9 (C11), 168.7 (C7), 82.3 (C3), 82.1 (C1), 71.5 (C2), 70.7 (C5), 70.5 (C6), 70.2 (C4), 62.6 (C10), 49.6 (C8), 46.5 (C8), 21.3 (C9), 21.1 (C12). HRMS (ESI) calcd for $C_{20}H_{28}FeNO_3$ $[M+H]^+$ 386.1413; found 386.1405.

*3-(Diisopropylaminocarbonyl)ferrocenylmethyl)trimethyl-ammonium iodide (**32**).* Iodomethane (129.0 µL, 294 mg, 2.07 mmol, 3.00 equiv) was added to a solution of **19** (257 mg, 0.69 mmol, 1.00 equiv) in MeCN (4.00 mL) and the reaction mixture was stirred at rt for 30 min. Volatiles were removed under vacuum using a rotary evaporator to give the crude product. This was triturated in Et_2O (6 mL) and

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the resulting solids were filtrated under vacuum. Solids were washed with Et_2O (6 mL) before being dried under high vacuum to give the title product as an orange solid (352 mg, quant). R_f (eluent: PET-EtOAc 50:50) = 0.00. Mp 120-124 °C. ν_{max} (film)/cm^{-1} 3446 (br), 2965, 1597, 1475, 1455, 1369, 1325, 1252, 1209, 1158, 1036, 876, 807. ^{1}H NMR (300 MHz, DMSO-d^6): δ (ppm) 4.84 (s, 1H, H2), 4.66 (s, 2H, H4 and H5), 4.54 (br s, 1H, H8), 4.49 (d, *J* = 13.6 Hz, 1H, H10), 4.43 (d, *J* = 13.6 Hz, 1H, H10), 4.29 (s, 5H, H6), 3.50 (br s, 1H, H8); 2.96 (s, 9H, H11), 1.28 (br s, 12H, H9). ^{13}C NMR (75.4 MHz, DMSO-d^6): δ (ppm) 166.6 (C7), 82.8 (C3), 74.1 (C1), 73.7 (C2), 72.8 (C4 or C5), 71.3 (C4 or C5), 70.5 (C6), 64.9 (C10), 51.5 (C11), 49.1 (C8), 45.4 (C8), 20.8 (C9). HRMS (ESI) calcd for $C_{21}H_{33}FeN_2O$ [M-I+H]$^+$ 385.1942; found 385.1941.

*3-(Diisopropylaminomethyl)ferrocenylmethyl)trimethyl-ammonium iodide (**33**).* BH_3·THF (1M in THF, 3.15 mL, 3.15 mmol, 5.00 equiv) was added to a solution of compound **32** (350 mg, 0.68 mmol, 1.00 equiv) in THF (5.00 mL) at rt. The reaction mixture was stirred for 15 min before being heated at 80 °C overnight. **Remark**: the use of PTFE sleeve is strongly recommended to avoid blockage of the ground glass joints. The reaction mixture was cooled to 0 °C and aqueous NaOH (5%, 10 mL) was added dropwise. **Caution**: as a vigorous evolution of gas was noticed, the first drops of NaOH solution should be added slowly. The reaction mixture was heated at 80 °C for 1 h before being cooled to rt. The reaction mixture was extracted with EtOAc (2 x 5 mL), the combined organic layers were dried over $MgSO_4$, filtrated over cotton wool and concentrated under vacuum using a rotary evaporator to give the crude product. This was triturated in Et_2O (4 mL) and the resulting solids were filtrated under vacuum. Solids were washed with Et_2O (4 mL) before being dried under high vacuum to give the title product as a yellow solid (185 mg, 54%). R_f (eluent: PET-EtOAc 50:50) = 0.00. Mp 163-165 °C. ν_{max} (film)/cm^{-1} 2963, 1476, 1375, 1360, 1202, 1169, 1140, 1103, 988, 977, 872, 818, 809. ^{1}H NMR (300 MHz, DMSO-d^6): δ (ppm) 4.51 (s, 1H, H2), 4.38 (br s, 4H, H4, H5 and H10), 3.45 (d, *J* = 14.8 Hz, 1H, H7), 3.39 (d, *J* = 14.8 Hz, 1H, H7), 2.99 (sept, *J* = 6.6 Hz, 2H, H8), 2.91 (s, 9H, H11), 0.96 (d, *J* = 6.6 Hz, 6H, H9), 0.95 (d, *J* = 6.6 Hz, 6H, H9). ^{13}C NMR (75.4 MHz, DMSO-d^6): δ (ppm) 91.4 (C3), 72.9 (C2), 72.1 (C1), 70.8 (C4 or C5), 70.7 (C4 or C5), 69.4 (C6), 65.6 (C10), 51.3 (C11), 47.4 (C8), 43.2 (C7), 20.8 (C9), 20.7 (C9). HRMS (ESI) calcd for $C_{21}H_{35}FeN_2$ [M-I+H]$^+$ 371.2149; found 371.2156.

*1-(Acetoxymethyl)-3-iodoferrocene (**34**).* Compound **28** (4.20 g, 10.0 mmol, 1.00 equiv) was dissolved into acetic anhydride (38.0 mL, 41.2 g, 400 mmol, 40.0 equiv) at rt and the resulting solution was stirred at reflux (heating mantel, external temperature 160 °C) for 1 h. The reaction mixture was cooled to 0 °C and EtOAc (100 mL) was added before pouring the reaction mixture onto ice (200 mL). Solid K_2CO_3 was added under stirring until pH 8 was reached. **Caution**: as vigorous evolution of gas occurred, only small portions of K_2CO_3 should be added each time. The layers were separated and the aqueous layer was extracted with EtOAc (1 x 50 mL). The combined organic layers were washed with water (1 x 50 mL), brine (1 x 50 mL), dried over $MgSO_4$, filtrated 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 give the title product as an orange solid (3.3 g, 85.5%). R_f (eluent: PET/EtOAc 10:1) = 0.58. Mp 78-80 °C. ν_{max} (film)/cm^{-1} 3094, 2926, 1732, 1370, 1219, 1001, 932, 871, 822. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.82 (d, *J* = 12.0 Hz, 1H, H7), 4.77 (d, *J* = 12.0 Hz, 1H, H7), 4.53 (s, 1H, H2), 4.43 (dd, *J* = 2.2, 1.1, 1H, H4), 4.26 (dd, *J* = 2.2, 1.1, 1H, H5), 4.18 (s, 5H, H6), 2.03 (s, 3H, H9). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 170.7 (C8), 82.5 (C1), 75.9 (C2), 75.3 (C4), 71.7 (C6), 70.4 (C5), 62.1 (C7), 39.7 (C3), 21.1 (C9). Mass: 384 [M], 325 [M-OAc], 180. HRMS (ESI) calcd for $C_{11}H_{10}FeI$ [M-OAc]$^+$ 324.9177; found 324.9179. **Crystal data for 34**. $C_{13}H_{13}FeIO_2$, *M* = 383.98, *T* = 150(2) K; monoclinic *P* 2$_1$/*c* (I.T.#14), a = 17.145(2), b = 7.7567(9), c = 10.0111(13) Å, β = 105.232(5) °, *V* = 1284.6(3) Å^3. *Z* = 4, *d* = 1.985 g.cm^{-3}, μ = 3.563 mm^{-1}. A final refinement on F^2 with 2926 unique intensities and 155 parameters converged at $\omega R(F^2)$ = 0.0585 ($R(F)$ = 0.0254) for 2649 observed reflections with $I > 2\sigma(I)$. CCDC 1898625.

*3-Iodoferrocenecarboxaldehyde (**35**).* *N*-Methylmorpholine-*N*-oxide (NMO, 1.60 g, 13.3 mmol, 3.50 equiv) was placed in a Schlenk tube which was heated at 90 °C (oil bath, external temperature) under high vacuum for 3 h before being cooled to rt. In a separate Schlenk tube, compound **37** (1.30 g, 3.80 mmol, 1.00 equiv) was dissolved in acetone (38.0 mL) and this solution was cannulated onto NMO. $RuCl_2(PPh_3)_3$ (182 mg, 0.20 mmol, 0.05 equiv) was added in one portion and the reaction mixture was stirred at rt for 2 h, shielded from light. The reaction mixture was concentrated under vacuum using a rotary evaporator. HCl (1.0 M aq., 20 mL) was added and the reaction mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtrated 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 (80:20) to give the title product as a red oil (1.10 g, 85%). Analytical data analogous to those reported previously.[5e] R_f (eluent: PET/EtOAc 90:10) = 0.34. ν_{max} (film)/cm^{-1} 3095, 2820, 1683, 1666, 1445, 1377, 1307, 1236, 1002, 873, 828, 744. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.87 (s, 1H, H7), 5.05 (s, 1H, H2), 4.83 (s, 1H, H4), 4.79 (s, 1H, H5), 4.29 (s, 5H, H6). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 192.3 (C7), 80.0 (C1), 79.7 (C4), 75.9 (C2), 72.6 (C6), 70.5 (C5), 41.3 (C3). Mass: 340 [M], 184 [FcH].

*1-Iodo-3-methylferrocene (**36**).* Compound **34** (576.0 mg, 1.5 mmol, 1.0 equiv) was added portionwise to a solution of BH_3 in THF (1.0 M, 7.50 mL, 7.50 mmol, 5.00 equiv) at rt before the reaction mixture was heated at reflux overnight (heating mantel, external temperature 80 °C). **Remark**: the use of PTFE sleeve is strongly recommended to avoid blockage of the ground glass joints. The reaction mixture was cooled to 0 °C and a solution of NaOH (10%, 10 mL) was added dropwise. **Caution**: as a vigorous evolution of gas occurs, the first drops of NaOH solution should be added slowly. After addition, the reaction mixture was stirred at reflux for 1 h (heating mantel, external temperature 80 °C). The reaction mixture was cooled to rt and the layers were separated. The aqueous layer was extracted with EtOAc (1 x 20 mL). The combined organic layers were washed with water (1 x 20 mL), brine (1 x 20 mL), dried over $MgSO_4$, filtrated 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 (15:1) to give the title product as an orange oil (483 mg, 98.5%). R_f (eluent: PET/EtOAc 10:1) = 0.84. ν_{max} (film)/cm^{-1} 3093, 2916, 1635, 1452, 1369, 1338, 1236, 1105, 1029, 1000, 870, 818. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.32 (s, 1H, H2), 4.27 (q, *J* = 2.1, 1.4 Hz, 1H, H5), 4.10 (s, 5H, H6), 4.04 (t, *J* = 1.4 Hz, 1H, H4), 1.92 (s, 3H, H7). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 85.2 (C3), 75.7 (C2), 73.6 (C5), 71.8 (C6), 69.9 (C4), 39.7 (C1), 14.7 (C7). Mass: 326 [M]. HRMS (ESI) calcd for $C_{11}H_{11}FeI$ [M]$^+$ 325.9249; found 325.9242.

*1-(Hydromethyl)-3-iodoferrocene (**37**).* NaOH (480 mg, 12.0 mmol, 3.00 equiv) was dissolved in H_2O (13.0 mL) and THF (7.0 mL) at rt. Compound **34** (1.50 g, 4.00 mmol, 1.00 equiv) was added and the reaction mixture was heated overnight (heating mantel, external temperature 80 °C). The reaction mixture was cooled to rt, water (20 mL), followed by EtOAc (30 mL) were added. The layers were separated and the aqueous layer was extracted with EtOAc (20 mL). The combined organic layers were dried over $MgSO_4$, filtrated 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 (70:30 to 50:50) to give the title product

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as an orange oil (1.30 g, quant). R_f (eluent: PET/EtOAc 90:10) = 0.08. ν_{max} (film)/cm^{-1} 3322, 2922, 2852, 1714, 1461, 1409, 1361, 1242, 1105, 1028, 998, 870, 820. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.51 (s, 1H, H2), 4.43 (s, 1H, H4), 4.28 (s, 2H, H7), 4.25 (s, 1H, H5), 4.21 (s, 5H, H6). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 89.3 (C1), 74.8 (C4), 74.4 (C2), 71.6 (C6), 68.7 (C5), 60.4 (C7), 39.7 (C1). Mass: 342 [M]. HRMS (ESI) calcd for $C_{11}H_{11}FeIO$ $[M]^+$ 341.9198; found 341.9189.

*1-Iodo-3-(methoxymethyl)ferrocene (**38**).* Sodium hydride (60% dispersion in oil, 259 mg, 6.00 mmol, 3.00 equiv) was added portionwise to a solution of compound **37** (684 mg, 2.00 mmol, 1.00 equiv) in THF (10.0 mL) at 0 °C. After addition, the cooling bath was removed and the reaction mixture was stirred for 1 h. The reaction mixture was cooled to 0 °C and iodomethane (373.5 µL, 852 mg, 6.00 mmol, 3.00 equiv) was added dropwise. After addition, the cooling bath was removed and the reaction mixture was stirred for 1 h. The reaction mixture was cooled to 0 °C and NH_4Cl (aq. sat., 20 mL) was added dropwise. EtOAc (10 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc (10 mL) and the combined organic layers were dried over $MgSO_4$, filtrated 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 (90:10) to give the title product as an orange oil (643 mg, 90%). R_f (eluent: PET/EtOAc 90:10) = 0.56. ν_{max} (film)/cm^{-1} 3093, 2920, 2885, 2814, 1645, 1448, 1384, 1362, 1221, 1192, 1171, 1104, 1087, 1066, 1000, 870, 819. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm) 4.50 (s, 1H, H2), 4.41 (dd, *J* = 2.1, 1.4 Hz, 1H, H5), 4.23 (t, *J* = 1.4 Hz, 1H, H4), 4.17 (s, 5H, H6), 4.15 (s, 1H, H7), 4.12 (s, 1H, F7), 3.31 (s, 3H, H8). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 84.6 (C3), 75.7 (C2), 74.9 (C5), 71.6 (C6), 70.3 (C7), 70.0 (C4), 58.0 (C8), 39.8 (C1). Mass: 356 [M]. HRMS (ESI) calcd for $C_{12}H_{13}FeIO$ $[M]^+$ 355.9355; found 355.9348.

*3-Iodo-α-Phenylferrocenemethanol (**39**).* A solution of phenylmagnesium bromide in THF (0.30 M, 4.20 mL, 1.30 mmol, 0.95 equiv) was added dropwise to a solution of compound **35** (453 mg, 1.30 mmol, 1.00 equiv) in THF (13.0 mL) at –78 °C. Keeping the flask in the cooling bath, the reaction mixture was allowed to warm slowly to –40 °C and the progress of the reaction was checked by TLC. After consumption of the starting material, NH_4Cl (sat. aq., 20 mL) was added and the reaction mixture was warmed to rt before being extracted with EtOAc (2 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtrated 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 (90:10 to 80:20) to give the title product as an orange oil as a 1:2 mixture of diastereoisomers (575 mg, quant.). R_f (eluent: PET/EtOAc 12:1) = 0.23 and 0.15. ν_{max} (film)/cm^{-1} 3356 (br), 1645, 1492, 1451, 1371, 1219, 1195, 1106, 1066, 999, 872, 821, 739, 698. Mixture of two diastereoisomers (minor indicated with *).^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.39-7.35 (m, 8H, 4 x ArH + 4 x ArH*), 7.33-7.27 (m, 2H, ArH + ArH*), 5.44 (s, 1H, H7*), 5.42 (s, 1H, H7), 4.49 (s, 1H, FcCH), 4.43-4.42 (m, 3H, FcCH + 2 x FcCH*), 4.26-4.25 (m, 1H, FcCH*), 4.24 (s, 5H, H6), 4.23 (s, 5H, H6*), 4.18-4.17 (m, 1H, FcCH), 2.37 (br s, 1H, OH), 2.35 (br s, 1H, OH*). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 142.9 (ArC + ArC*), 128.5 (2 x ArCH + 2 x ArCH*), 127.9 (ArCH + ArCH*), 126.3 (2 x ArCH + 2 x ArCH*), 94.7 (C3), 94.5 (C3*), 74.6 (FcCH), 74.5 (FcCH*), 73.8 (FcCH*), 72.9 (FcCH), 71.8 (C7 + C7* + C6 + C6*), 68.0 (FcCH), 67.0 (FcCH*), 39.9 (C3*), 39.8 (C3). Mass: 1st dia: 402 [M-HO+H], 2nd dia: 416 [M-2H]. HRMS (ESI) calcd for $C_{17}H_{14}FeI$ $[M\text{-}HO]^+$ 400.9489; found 400.9478.

*1-Benzoyl-3-iodoferrocene (**40**).* *N*-Methylmorpholine-*N*-oxide (NMO, 330 mg, 2.80 mmol, 3.00 equiv) was placed in a Schlenk tube which was heated at 90 °C (oil bath, external temperature) under high vacuum for 3 h before being cooled to rt. In a separate Schlenk tube, compound **39** (395 mg, 0.90 mmol, 1.00 equiv) was dissolved in acetone (10.0 mL) and this solution was cannulated onto NMO. $RuCl_2(PPh_3)_3$ (45.0 mg, 50 µmol, 0.05 equiv) was added in one portion and the reaction mixture was stirred at rt for 10 min, shielded from light. The reaction mixture was concentrated up to 3 mL and this residue was purified by column chromatography over SiO_2, shielded from light, using PET/EtOAc (90:10) to give the crude product. This was purified by column chromatography over alumina, shielded from light, using EtOAc (9:1) to give the title product as a red oil (371 mg, 95%). R_f (eluent: PET/EtOAc 80:20) = 0.60. ν_{max} (film)/cm^{-1} 3095, 1635, 1597, 1446, 1431, 1376, 1312, 1272, 1169, 1068, 1001, 958, 855, 825, 723, 695. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (dd, *J* = 8.2, 1.1 Hz, 2H, H9), 7.56 (td, *J* = 7.6, 1.5 Hz, 1H, H11), 7.47 (t, *J* = 7.6 Hz, 2H, H10), 5.12 (s, 1H, H2), 4.92 (dd, *J* = 2.4, 1.2 Hz, 1H, H5), 4.82 (dd, *J* = 2.4, 1.2 Hz, 1H, H4), 4.22 (s, 5H, H6). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 197.8 (C7), 139.3 (C8), 131.9 (C11), 128.5 (C10), 128.1 (C9), 79.0 (C4), 78.9 (C1), 77.7 (C2), 73.2 (C6), 72.3 (C5), 41.3 (C3). Mass: 416 [M]. HRMS (ESI) calcd for $C_{17}H_{14}FeIO$ $[M+H]^+$ 416.9433; found 416.9420.

*3-Iodoferrocenecarbonitrile (**41**).* Compound **35** (500 mg, 1.50 mmol, 1.00 equiv), hydroxylamine hydrochloride (146 mg, 2.10 mmol, 1.40 equiv), potassium iodide (250 mg, 1.50 mmol, 1.00 equiv) and zinc oxide (123 mg, 1.50 mmol, 1.00 equiv) were introduced in a Schlenk tube which was subjected to three cycles of vacuum/argon. Acetonitrile (40.0 mL) was added and the reaction mixture was stirred at 80 °C for 2 h (heating mantle, external temperature). The reaction mixture was cooled to rt, $Na_2S_2O_3$ (sat. aq., 20.0 mL) and EtOAc (20 mL) were added and the phases were separated. The aqueous layer was extracted with EtOAc (20 ml). The combined organic layers were dried over $MgSO_4$, filtrated 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 (90:10) to give the title product as an orange oil (325 mg, 71%). R_f (eluent: PET/EtOAc 90:10) = 0.62. ν_{max} (film)/cm^{-1} 3102, 2921, 2225, 1668, 1412, 1375, 1239, 1107, 1035, 1001, 920, 874, 825, 729. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.89 (s, 1H, H2), 4.65 (s, 1H, H5), 4.63 (s, 1H, H4), 4.36 (s, 5H, H6). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 118.8 (C7), 77.5 (C2 or C4), 77.4 (C2 or C4), 73.6 (C6), 72.7 (C5), 53.3 (C1), 38.6 (C3). Mass: 337 [M], 210 [M-I]. HRMS (ESI) calcd for $C_{11}H_8FeIN$ $[M]^+$ 336.9051; found 336.9037.

*Methyl 3-iodoferrocenecarboxylate (**42**).* Potassium hydroxide (1.10 g, 19.2 mmol, 6.00 equiv) was added to a solution of compound **(±)-35** (1.10 g, 3.20 mmol, 1.00 equiv) in methanol (42.0 mL) at 0 °C. Iodine (2.40 g, 9.60 mmol, 3.00 equiv) was added to the reaction mixture which was warmed to rt and stirred for 1 h. Volatiles were removed under vacuum and EtOAc (20 mL), followed by $Na_2S_2O_3$ (sat. aq., 20 mL) were added to the residue. Layers were separated and the aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were washed with water (10 mL), dried over $MgSO_4$, filtrated 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 (90:10) to give the title product as an orange solid (1.10 g, 95.5%). R_f (eluent: PET/EtOAc 90:10) = 0.50. Mp 82-86 °C (decomp.). ν_{max} (film)/cm^{-1} 1705, 1463, 1318, 1278, 1195, 1156, 1052, 826, 771. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 5.05 (s, 1H, H2), 4.79 (dd, *J* = 2.3, 1.0 Hz, 1H, H4), 4.63 (dd, *J* = 2.3, 1.0 Hz, 1H, H5), 4.22 (s, 5H, H6), 3.79 (s, 3H, H8). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 171.0 (C7), 77.9 (C5), 76.4 (C2), 72.7 (C6), 72.1 (C1), 71.1 (C4), 51.9 (C8), 40.0 (C3). Mass: 370 [M]. HRMS (ESI) calcd for $C_{12}H_{11}FeIO_2$ $[M]^+$ 369.9148; found 369.9142. **Crystal data for 42**. $C_{12}H_{11}FeIO_2$, *M* = 369.96, *T* = 150(2) K, triclinic *P* 1 (I.T.#1), a = 5.7618(5), b = 7.2423(7), c = 7.9769(8) Å, α = 95.378(4), β = 97.805(4), γ = 112.497(3) °, *V* = 300.80(5) Å^3. *Z* = 1, *d* = 2.042 g.cm^{-3}, µ = 3.800 mm^{-1}. A final refinement on F^2 with 2485 unique

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intensities and 147 parameters converged at $\omega R(F^2)$ = 0.0431 ($R(F)$ = 0.0201) for 2447 observed reflections with $I > 2\sigma(I)$. CCDC 1898626.

*3-Iodoferrocenecarboxylic acid (**43**).* NaOH (400 mg, 10.0 mmol, 5.00 equiv) in H_2O (12.0 mL) was added to a solution of compound **42** (739 mg, 2.00 mmol, 1.00 equiv) in methanol (10.0 mL) at rt and the reaction mixture was heated at 80 °C (heating mantle, external temperature) for 75 min. The reaction mixture was cooled to rt and methanol was removed under vacuum using a rotary evaporator. The resulting solution was cooled to 0 °C and HCl (35% aq.) was added dropwise until pH 1 was reached. The resulting solid was filtrated and washed with cooled (0 °C) water (2 x 5 mL) and pentane (10 mL). Drying the solid under high vacuum with a P_2O_5 trap afforded the title product as an orange solid (652 mg, 91%). R_f (eluent: PET/EtOAc 80:20) = 0.12. Mp 178-181 °C (decomp.). ν_{max} (film)/cm^{-1} 3094, 2926, 1732, 1370, 1219, 1001, 932, 871, 822. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.12 (s, 1H, H2), 4.86 (s, 1H, H4 or H5), 4.71 (s, 1H, H4 or H5), 4.29 (s, 5H, H6). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 177.9 (C7), 78.7 (C4 or C5), 76.8 (C2), 73.1 (C6), 71.6 (C4 or C5), 70.7 (C1), 40.3 (C3). HRMS (ESI) calcd for $C_{11}H_9FeIO_2$ [M]$^+$ 355.8997; found 355.8996. **Crystal data for 43**. $C_{11}H_9FeIO_2$, M = 355.93, T = 150 K; triclinic P -1 (I.T.#2), a = 5.7011(7), b = 8.2537(11), c = 11.9895(16) Å, α = 98.303(5), β = 98.159(5), γ = 99.877(4) °, V = 541.88(12) Å^3. Z = 2, d = 2.181 g.cm^{-3}, μ = 4.214 mm^{-1}. A final refinement on F^2 with 2471 unique intensities and 130 parameters converged at $\omega R(F^2)$ = 0.0547 ($R(F)$ = 0.0235) for 2300 observed reflections with $I > 2\sigma(I)$. CCDC 1898627.

*3-Iodoferrocenoyl azide (**44**).* Triethylamine (1.20 mL, 809.5 mg, 8.00 mmol, 5.00 equiv) was added to a solution of compound **43** (569 mg, 1.60 mmol, 1.00 equiv) in CH_2Cl_2 (3.0 mL) at 40 °C (heating mantle, external temperature). Diphenylphosphoryl azide (379 µL, 484 mg, 1.80 mmol, 1.10 equiv) was added dropwise to the reaction mixture which was then kept at the same temperature for 10 min. The reaction mixture was cooled to rt and HCl (1.0 M aq., 20 mL) was added. The reaction mixture was extracted with Et_2O (2 x 20 mL) and the combined organic layers were dried over $MgSO_4$, filtrated 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 pentane/Et_2O (10:1) to give the title product as a red solid (574 mg, 94%). R_f (eluent: PET/EtOAc 80:20) = 0.71. Mp 109-112 °C (decomp.). ν_{max} (film)/cm^{-1} 2934, 2151, 1681, 1443, 1316, 1264, 1204, 1086, 991, 820. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 5.07 (s, 1H, H2), 4.82 (dd, J = 2.5, 1.3 Hz, 1H, H4), 4.74 (dd, J = 2.5, 1.3 Hz, 1H, H5), 4.27 (s, 5H, H6). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 176.0 (C7), 79.3 (C5), 76.5 (C2), 73.2 (C6), 71.3 (C4), 40.7 (C3). One FcC signal is missing. **Crystal data for 44**. $C_{11}H_8FeIN_3O$, M = 380.95, T = 150(2) K, monoclinic P $2_1/n$ (I.T.#14), a = 5.7536(7), b = 27.123(3), c = 7.4761(8) Å, β = 93.045(4) °, V = 1165.0(2) Å^3. Z = 4, d = 2.172 g.cm^{-3}, μ = 3.929 mm^{-1}. A final refinement on F^2 with 2676 unique intensities and 154 parameters converged at $\omega R(F^2)$ = 0.0587 ($R(F)$ = 0.0255) for 2581 observed reflections with $I > 2\sigma(I)$. CCDC 1898628.

*1-(tert-Butoxycarbonyl)amino-3-iodoferrocene (**45**) and N,N'-di(3-iodoferrocenyl)urea (**46**).* tBuOH (311 µL, 241 mg, 3.20 mmol, 2.50 equiv) was added to a solution of compound **44** (495 mg, 1.30 mmol, 1.00 equiv) in toluene (8.0 mL) and the reaction mixture was heated at 110 °C (heating mantel, external temperature) for 1 h. The reaction mixture was cooled to rt and directly purified by column chromatography over SiO_2, using PET/EtOAc (10:1 to 60:40) to give the title product and the corresponding symmetric urea. The title product **45** was obtained as an orange solid (458 mg, 82.5%). R_f (eluent: PET/EtOAc 80:20) = 0.71. Mp 150-153 °C (decomp.). ν_{max} (film)/cm^{-1} 3323 (br), 2978, 1694, 1528, 1366, 1236, 1155, 1105, 1046, 1023, 907, 869, 818, 727. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 5.81 (s, 1H, NH), 4.77 (s, 1H, H2), 4.42 (s, 1H, H5), 4.21 (s, 1H, H4), 4.18 (s, 5H, H8), 1.50 (s, 9H, H9). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 153.1 (C7), 96.5 (C1), 80.5 (C8), 72.3 (C6), 70.5 (C4), 67.1 (C2), 61.3 (C5), 37.6 (C3), 28.4 (C9). HRMS (ESI) calcd for $C_{15}H_{18}FeINO_2$ [M]$^+$ 426.9726; found 426.9719. The bis-urea **46** (mixture of stereoisomers) was isolated as an orange solid (74.0 mg, 16.5%). R_f (eluent: PET/EtOAc 80:20) = 0.30. Mp 176-178 °C (decomp.). ν_{max} (film)/cm^{-1} 3295 (br), 3094, 1640, 1562, 1473, 1375, 1226, 1106, 1001, 907, 868, 819, 729. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.58 (br s, 2H, 2 x NH), 4.74 (s, 2H, H2), 4.48 (s, 2H, H5), 4.39 (s, 2H, H4), 4.28 (s, 10H, H6). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (ppm) 154.5 (C7), 95.7 (C1), 72.7 (C6), 71.8 (C4), 68.9 (C2), 63.6 (C5), 37.7 (C3). HRMS (ESI) calcd for $C_{21}H_{18}Fe_2I_2N_2O$ [M]$^+$ 679.8207; found 679.8216.

*3-Iodoferrocenamine hydrochloride (**47**).* HCl in Et_2O (5.0 M, 8.00 mL, 40.0 mmol) was added to a solution of compound **45** (427 mg, 1.00 mmol, 1.00 equiv) in Et_2O (10 mL) and the reaction mixture was stirred at rt for 2 h. The resulting solid was quickly filtrated and washed with Et_2O (2 x 10 mL) and pentane (10 mL) and dried under high vacuum to give the title product as a yellow solid (236 mg, 65%). R_f (eluent: PET/EtOAc 80:20) = 0.00. Mp 160-165 °C (decomp.). ν_{max} (film)/cm^{-1} 2811 (br), 2568, 2005, 1529, 1463, 1409, 1367, 1106, 1030, 1000, 868, 827. ^{1}H NMR (400 MHz, DMSO-d^6): δ (ppm) 9.96 (br s, 3H, NH_3^+), 4.73 (s, 1H, H2), 4.50 (s, 1H, H4), 4.47 (s, 1H, H5), 4.33 (s, 5H, H6). ^{13}C NMR (100 MHz, DMSO-d^6): δ (ppm) 88.6 (C1), 72.3 (C5 + C6), 69.4 (C2), 64.7 (C4), 36.2 (C3).

*1-(Dimethylamino)-3-iodoferrocene (**48**).* Sodium cyanoborohydride (196 mg, 3.10 mmol, 6.00 equiv) was added portionwise to a solution of compound **47** (190 mg, 0.50 mmol, 1.00 equiv) and paraformaldehyde (187 mg, 6.20 mmol, 12.0 equiv) in glacial acetic acid (reagent grade quality, 1.50 mL) at rt. The reaction mixture was stirred for 4 h. Paraformaldehyde (31.2 mg, 1.00 mmol, 2.00 equiv) and sodium cyanoborohydride (32.6 mg, 0.50 mmol, 1.00 equiv) were added to the reaction mixture which was stirred at rt overnight. EtOAc (10 mL) was added, followed by solid K_2CO_3 until pH 8 was reached. The layers were separated and the aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were dried over $MgSO_4$, filtrated 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 pentane/Et_2O (10:1) to give the title product as an orange solid (118 mg, 64%). R_f (eluent: PET/EtOAc 80:20) = 0.56. Mp 48-50 °C. ν_{max} (film)/cm^{-1} 2953, 2855, 2829, 2784, 1510, 1450, 1422, 1333, 1301, 1221, 1140, 1102, 1077, 1037, 996, 865, 805. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.26 (s, 5H, H6), 4.19 (dd, J = 2.1, 1.2 Hz, 1H, H4), 4.03 (t, J = 1.2 Hz, 1H, H2), 3.76 (t, J = 2.1 Hz, 1H, H5), 2.53 (s, 6H, H7). ^{13}C NMR (126 MHz, $CDCl_3$): δ (ppm) 115.7 (C1), 70.4 (C6), 69.8 (C4), 61.8 (C2), 55.3 (C5), 42.2 (C7), 39.7 (C3). Mass: 355 [M], 172.

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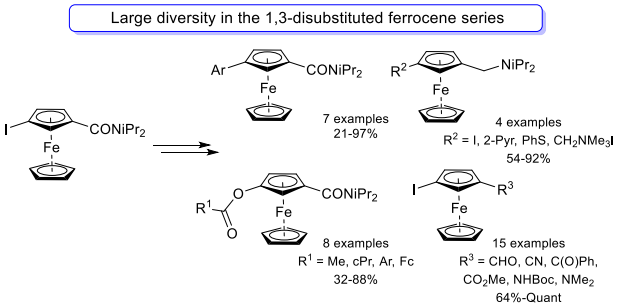
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FULL PAPER

Functionalization of 3-Iodo-*N*,*N*-diisopropylferrocenecarboxamide, a Pivotal Substrate to Open the Chemical Space to 1,3-Disubstituted Ferrocenes

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