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Iodoferrocene as partner in *N*-arylation of amides

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In this study, we developed a convenient methodology for the *N*-arylation of various acetamides, benzamides and related compounds by iodoferrocene. Optimization of the reaction was first performed from acetamide on the basis of the achievements in the benzene series. Next, the identified conditions (use of copper(I) iodide, *N,N'*-dimethylethylenediamine, tripotassium phosphate in dioxane at 110 °C for 14 h) were applied to different aliphatic/aromatic primary and cyclic/acyclic secondary amides in order to determine the scope of the reaction, thus easily generating a small library of ferrocene amides.

Introduction

The Goldberg condensation, which is the copper-catalysed *N*-arylation of amides using aromatic halides, has been the topic of numerous studies since its discovery in the early 1900's.¹ The original protocol requiring harsh reaction conditions (stoichiometric amounts of copper salts, high temperatures and long reaction times), smoother variants have been developed,^{2,4} either involving palladium-catalysed processes^{5, 6} or by identification of suitable chelating ligands for copper catalysis.⁷⁻⁹

The group of Buchwald contributed to the development of an efficient and general system based on copper catalysis for the *N*-arylation (or -heteroarylation) of amides using iodides.¹⁰ It consists in a combination of an air stable copper(I) salt (copper(I) iodide giving the best results) and an aliphatic 1,2-diamine (such as *N,N'*-dimethylethylenediamine and racemic *trans*-1,2-cyclohexanediamine) in the presence of a base (either of low solubility in the solvent used¹¹ such as tripotassium phosphate and potassium carbonate, or delivered gradually if soluble such as potassium hexamethyldisilazide).¹² Studies dedicated to the mechanism showed that the rate determining step is the reaction between the aryl iodide and a 1,2-diamine ligated copper(I) amidate,^{13, 14} and that the *N*-arylation does not take place with bis-amido copper(I) species.¹⁵ As a consequence, both the 1,2-diamine and the amide involved can modulate the overall reactivity of the active species and thus impact the reaction outcome. Concerning this first step, two pathways are generally proposed. One involves a rate determining single electron transfer from the amidate copper(I) to the aryl iodide; the product is next formed by halide transfer to copper(II), radical recombination giving a copper(III) species, and reductive elimination. The other starts with the rate determining formation of an η^2 complex between the copper(I) amidate and the aryl iodide before oxidative addition to a copper(III) species and reductive elimination.¹³

In 2014, the group of Ribas showed that, owing to its coordinating ability, dimethylsulfoxide (DMSO) used as solvent can favourably replace the ligand in such reactions while the dimethyl anion generated *in situ* can play a role as base or ligand.¹⁶ The involvement of copper(I) species in the catalytic cycle was

confirmed, with copper(I) iodide or triflate being the best sources. Regarding the iodo partner, an electron-withdrawing group at the *para* position of iodobenzene seems to favour the reaction (e.g. full conversion for the reaction between 1-iodo-4-nitrobenzene and 2-pyrrolidinone at only 90 °C), when compared with an electron-donating group (e.g. 89% conversion for the same reaction with 4-iodotoluene). While it is established that electron-deficient aryl iodides are more easily activated, the effect of the nature of the amido group on the course of the reaction is more difficult to detect.¹² Different amides, including secondary ones that are less reactive than the primary ones, were evaluated in 24 h reaction with iodobenzene using copper(I) iodide (0.1 equiv) and tripotassium phosphate (2 equiv).¹⁶ According to the authors, amide deprotonation is not rate limiting; instead, stabilization of a putative aryl-Cu(III)-amido would be more relevant in the mechanism.¹⁷⁻²¹ This is in agreement with findings of Hartwig and his group who discarded pathways involving electron transfer to afford a radical anion and subsequent halide dissociation in favour of arylcopper(III) intermediates.¹⁵

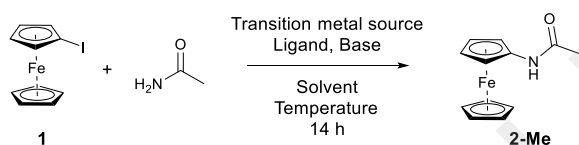
Due to specificities such as three-dimensional structure and redox behaviour, ferrocenes cannot be considered as classical aromatic compounds in numerous reactions. While *N*-arylation of amides has been largely developed with various aromatic and heteroaromatic halides, the corresponding reaction between amides and halogenated derivatives of electron-rich ferrocene has been scarcely explored. Indeed, whereas iodoferrocene reacts with imides in the presence of copper(I) oxide (for example with phthalimide at the reflux temperature of pyridine,²² or with L-proline hydantoin in DMSO at 120 °C²³), its reaction with amides is much less documented.

A very first example was reported in 1983 by Herberhold and co-workers who prepared triferrocenylamine from acetamide by successive sequences of deprotonation using sodium amide and coupling with bromoferrocene in the presence of copper(I) bromide and pyridine in toluene at reflux.²⁴ By employing similar reaction conditions, the group of Bildstein mono-*N*-arylated *N,N'*-diacetyl-1,2-phenylenediamine with bromoferrocene (62% yield); however all attempts of *N,N'*-diarylation failed, a result attributed to steric hindrance.²⁵ To the best of our knowledge, *N*-arylation of amides using iodoferrocene has only been addressed by Bolm and co-workers in 2007 with the successful reactions of iodoferrocene with both acetamide and benzamide in the presence of copper(I) iodide and potassium *tert*-butoxide in DMSO at 90 °C.²⁶

In the continuation of our studies dedicated to the synthesis of ferrocene amides and the evaluation of their properties,²⁷ we here report our efforts to identify an efficient protocol for copper-catalysed C-N coupling between amides and iodoferrocene.

Results and discussion

In the frame of studies dedicated to the synthesis of antiproliferative agents associated with ROS generation, Csámpai and co-workers recently studied the coupling between 6-ferrocenyl-3-pyridazinone and iodoferrocene.²⁸ By using copper(I) iodide, *N,N'*-dimethylethylenediamine (DMEDA) and tripotassium phosphate in dimethylformamide at 110 °C, which proved to be the best reaction conditions, a moderate 33% yield of a mixture of *O*- (major) and *N*- (minor) arylation products was observed and attributed to the steric bulk associated with iodoferrocene. The use of palladium complexes such as (Ph₃P)₂PdCl₂ or (dppf)PdCl₂ (dppf = 1,1'-bis(diphenylphosphino)ferrocene) gave similar results, when used in the presence of potassium carbonate. At the very beginning of our study, we tried to identify in a quite similar approach which of the transition metals, palladium or copper, would be more appropriate for this purpose. In order to find an efficient method to couple amides with iodoferrocene (**1**), we started from acetamide and evaluated different protocols optimized in the benzene series (Scheme 1).



Scheme 1 Optimization plan.

Initially, we tested conditions reported by Yin and Buchwald to couple iodo- and bromobenzenes with a large range of amides in the presence of palladium catalysts.²⁹ Thus, iodoferrocene (**1**) was reacted with acetamide in the presence of dipalladium(0) tris(dibenzylideneacetone) (Pd₂(dba)₃; 2 mol%), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos; 6 mol%) and cesium carbonate (1.4 equiv) in dioxane at 100 °C for 14 h. However, under these conditions, the expected product **2-Me** was not detected and **1** was recovered. The reaction was similarly attempted from bromo- and chloroferrocene, also without success. In order to favour the precipitation of the iodide, cesium carbonate was also replaced by silver acetate or thallium carbonate, but without variation.

In 2008, the group of Buchwald reported a water-mediated catalyst activation protocol which allows the amidation of aryl chlorides in very good yields.^{30, 31} However, no reaction took place (only traces of deiodination) when the three halogenoferrocenes were treated by palladium(II) acetate (Pd(OAc)₂; 2 mol%), 2-(dicyclohexylphosphino)-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl (BrettPhos; 4 mol%), water (4 mol%) and tripotassium phosphate (1.4 equiv) in *tert*-butanol at 110 °C for 14 h by following this protocol.

Inspired by both the use of bulky electron-rich phosphines in cross-coupling³² and the use of electron-rich phosphines for ferroceneamine arylation,³³ we next attempted the same coupling by employing Pd(OAc)₂ (3 mol%), di(1-adamantyl)butylphosphine (cataCXium® A; 6 mol%) and silver carbonate (2 equiv) in dioxane at 110 °C for 14 h. However, none of the halogenoferrocenes was converted into **2-Me**, dehalogenation being the only change observed in the case of iodoferrocene. By replacing silver carbonate by silver acetate, the same observations were made. Interestingly, from the different halogenoferrocenes, the use of thallium carbonate as base led to traces of an unknown product incorporating ferrocene and phosphine as shown by NMR. To get insight into the nature of this compound, we reacted iodoferrocene with stoichiometric amounts of Pd(OAc)₂ and cataCXium® in the presence of thallium carbonate (2 equiv) but without acetamide. This led to the isolation of the same compound, tentatively assigned as a stable palladium complex (see ESI).

We next decided to combine palladium(II) trifluoroacetate (Pd(tfa)₂; 8 mol%), used for the amination of electron-rich heteroaromatic halides³⁴ or the amidation of aromatic chlorides,³⁵ with Xantphos (8 mol%) and cesium carbonate (1.4 equiv) in toluene at 110 °C. However, **2-Me** was never detected after 14 h reaction from the different halogenoferrocenes. Finally, Pd(tfa)₂ (5 mol%) and cataCXium® A (10 mol%) were employed with potassium *tert*-butoxide as base at the reflux of toluene, but the different halogenoferrocenes were fully recovered.

These disappointing results observed with palladium catalysts led us to turn to copper-based systems from which the use of stoichiometric amounts becomes possible. As above, in order to find an efficient method to couple amides with iodoferrocene, we started from acetamide and evaluated different protocols employed in the benzene series (Table 1).

First, we selected a system developed by Buchwald and co-workers for the coupling between amides and iodobenzenes involving copper(I) iodide, DMEDA and tripotassium phosphate in dioxane.¹² The reaction between iodoferrocene (**1**) and acetamide was first attempted in the presence of stoichiometric copper(I) iodide, DMEDA and tripotassium phosphate in dioxane at 110 °C; under these conditions, the monoarylated **2-Me** was isolated in 83% yield (entry 1). Because the rest was ferrocene, the same reaction was carried out at 90 °C (entry 2). In this case, **2-Me** was produced in a similar 82% yield, the rest being a mixture of ferrocene and **1**. However, our attempts to reduce the amount of copper(I) iodide failed (entry 3), as already noticed previously in the ferrocene series.^{26, 28}

Xu and Wolf employed catalytic copper(I) oxide and cesium carbonate to couple primary amides with iodobenzenes in *N*-methylpyrrolidinone (NMP) at 90 °C.³⁶ In our case, by replacing dioxane with NMP, the yield dropped to 46% (entry 4). We thus kept dioxane as solvent and attempted to replace tripotassium phosphate with cesium carbonate; the reaction worked at both 110 and 90 °C (entries 5 and 6), but the yields appeared to be slightly lower than before due to competitive deiodination (with ferrocene found in 16-17% estimated yield).

Cesium fluoride has been proposed by Phillips and co-workers as an efficient alternative to bases to *N*-arylate

propanamide by 1-chloro-4-iodobenzene in the presence of copper(I) iodide, DMEDA and cesium fluoride in tetrahydrofuran at room temperature.³⁷ However, in our case, this led to the desired product **2-Me** in a lower 54% yield (entry 7), partly due to competitive deiodination (with ferrocene obtained in about 17% yield) and recovery of **1** (about 5%).

In the same vein, Hosseinzadeh, Tajbakhsh and co-workers quantitatively formed the expected coupled product by reaction between benzamide and iodobenzene in the presence of copper(I) iodide, 1,10-phenanthroline and potassium fluoride on alumina in toluene at reflux for 1.5 h.³⁸ However, when adapted, these conditions were hardly transposed to the reaction between acetamide and iodoferrocene, with the expected product **2-Me** only formed in a 17% yield with the recovery of about 72% of **1** (entry 8). 1,10-Phenanthroline was also tested as ligand, but the reactivity of **1** proved to be low under these conditions (69% of **1** recovered) and **2-Me** was only isolated in a low 10% yield (entry 9).

Glycine was also identified by Liu, Guo and co-workers as a potent ligand to *N*-arylate various amides with iodobenzenes. For example, the reaction between acetamide and iodobenzene gave the expected derivative in 95% yield in the presence of copper(I) iodide (5 mol %), glycine (0.2 equiv) and tripotassium phosphate (2.5 equiv) in dioxane at 100 °C for 24 h.³⁹ However, when transposed to iodoferrocene (**1**), a moderate 21% yield was recorded for **2-Me** (entry 10).

Table 1 Optimization of the *N*-arylation of acetamide with iodoferrocene (**1**).

Entry	Ligand	Base/Other	Solvent, Temp.	Yield (%) ^a
1	DMEDA	K ₃ PO ₄	Dioxane, 110 °C	83 ^b
2	DMEDA	K ₃ PO ₄	Dioxane, 90 °C	82 ^c (64) ^d
3 ^e	DMEDA	K ₃ PO ₄	Dioxane, 90 °C	56 ^{f,c} (58) ^{g,c}
4	DMEDA	K ₃ PO ₄	NMP, 110 °C	46 ^f
5	DMEDA	Cs ₂ CO ₃	Dioxane, 110 °C	74 ^b
6	DMEDA	Cs ₂ CO ₃	Dioxane, 90 °C	78 ^b
7	DMEDA	CsF	Dioxane, 110 °C	54 ^c
8	1,10-phenanthroline	KF on Al ₂ O ₃ ^h	Toluene, 110 °C	17 ^f
9	1,10-phenanthroline	K ₃ PO ₄	Dioxane, 110 °C	10 ^f
10	glycine	K ₃ PO ₄	Dioxane, 110 °C	21 ^c
11	-	K ₃ PO ₄	Dioxane, 90 °C	0 ^f
12 ⁱ	DMEDA	K ₃ PO ₄	Dioxane, 90 °C	70 ^j

^a After purification (see experimental part). In all these reactions, 1,1'-biferrocene was formed in <2% yield. ^b The rest was mainly ferrocene. ^c The rest was mainly recovered **1** and ferrocene. ^d Performed on a 5 mmol scale instead of 1 mmol for the other reactions. ^e By using 0.5 equiv of CuI and 0.5 equiv of DMEDA. ^f The rest was mainly recovered **1**. ^g With 48 h reaction time. ^h Only 1 equiv was used. ⁱ From bromoferrocene; the rest was starting bromoferrocene and ferrocene. ^j The rest was mainly bromoferrocene and ferrocene.

All these results led us to maintain copper(I) iodide, DMEDA (1 equiv each) and tripotassium phosphate (2 equiv) in dioxane at 90 °C for 14 h as the best reaction conditions to pursue the

study with other amides. The usefulness of DMEDA was evidenced (entry 11), and the conditions were successfully tested with bromoferrocene, allowing **2-Me** to be obtained in a promising 70% yield (entry 12). Unsurprisingly due to precedents in the literature,⁴⁰ applying the optimized conditions to 1,1'-diiodoferrocene or 1,1'-dibromoferrocene did not afford the ferrocene diamide but only product **2-Me** (formed in about 40 or 20% yield, respectively). Finally, all along these experiments, and even when employing only 0.55 equivalent of acetamide, bis-coupling of the amide was never observed, suggesting a much more difficult reaction from the secondary amides than from the primary ones.

With these optimized conditions in hand, we next turned our attention to the use of different amides to perform the *N*-arylation of iodoferrocene (**1**), and we first considered the reactivity of substituted acetamides (Table 2). When the methyl group of acetamide was replaced by cyclopropyl and more sterically hindered *tert*-butyl groups, the yield of the reaction respectively dropped to 57% (product **2-cPr**, entry 2) and 50% (product **2-tBu**, entry 3). These results are in accordance with previous studies invoking steric hindrance of the amide as partly responsible for the narrow scope of copper-catalysed *N*-arylation of amides.⁴¹

Table 2 Reaction between iodoferrocene (**1**) and aliphatic primary amides.

Entry	Amide (Substituent X)	Product, Yield (%) ^a
1		 2-Me , 82 ^b
2		 2-cPr , 57 (13; 14) ^b
3		 2-tBu , 50 ^b
4		 2-H , 26 ^c (33; 1) ^b
5		 2-CH₂NEt₂ , 33 (7; 11) ^b
6		0
7		 2-CF₃ , 10 ^d , 56 ^e

^a After purification (see experimental part). ^b The rest was mainly recovered **1** and ferrocene; for some reactions, the respective yields are given in brackets. ^c *N,N*-Diferrocenylformamide was also isolated in 11% yield. ^d Bare ferrocene was mainly formed. ^e By using CuI (1 equiv) and *t*BuOK (2 equiv) in DMSO at 90 °C for 14 h.

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1		 2-Me , 82 ^b
2		 2-cPr , 57 (13; 14) ^b
3		 2-tBu , 50 ^b
4		 2-H , 26 ^c (33; 1) ^b
5		 2-CH2NEt2 , 33 (7; 11) ^b
6		 0
7		 2-CF3 , 10 ^d , 56 ^e

^a After purification (see experimental part). ^b The rest was mainly recovered **1** and ferrocene; for some reactions, the respective yields are given in brackets. ^c *N,N*-Diferrocenylformamide was also isolated in 11% yield. ^d Bare ferrocene was mainly formed. ^e By using CuI (1 equiv) and *t*BuOK (2 equiv) in DMSO at 90 °C for 14 h.

Replacing acetamide by less hindered formamide led to the coupled product **2-H** in a modest 26% yield, partly due to the formation of the *N,N*-diarylated derivative (entry 4). While successful reactions have been documented in the benzene series,⁴² there is to the best of our knowledge no corresponding reactions reported in the ferrocene series. However, examples in which *N*-substituted formamides are coupled with iodoferrocenes are reported under similar conditions,⁴³ explaining why single *N*-arylation is difficult in this case.

Because of the similarity of *N*-ferrocenylated diethylaminoacetamide with anaesthetic molecules,⁴⁴ we attempted the corresponding amidation using iodoferrocene. Under our conditions, the expected product **2-CH₂NEt₂** was isolated in 33% yield (entry 5). In contrast with trichloroacetamide which did not react at all (entry 6), trifluoroacetamide was converted into **2-CF₃** in a low 10% yield (entry 7). However, inspired by the *N*-arylation of acetamide by iodoferrocene reported by Bolm and co-workers,²⁶ we also treated a mixture of trifluoroacetamide and iodoferrocene by copper(I) iodide and potassium *tert*-butoxide in DMSO at 90 °C, and observed the formation of **2-CF₃** in 56% yield (entry 7). By

N-arylating the two copper(I)-amido complexes [(dppf)CuN(C₆H₄-4-OMe)C(=O)Me] and [(dppf)CuN(C₆H₄-4-OMe)C(=O)CF₃] with iodobenzene in dimethylformamide, Liu, Feng and co-workers noticed a slightly better yield for the latter, result explained by a more stabilized copper(I)-amido complex due to F...Cu interaction.⁴⁵ It can be tentatively rationalized that, upon reacting iodoferrocene with trifluoroacetamide, a more stable amidate complex might be formed when using the CuI/DMEDA combination compared to the CuI/DMSO combination. Thus, it appears that the method developed by Bolm is more suitable for an acetamide bearing strong electron-withdrawing groups. It might avoid the formation of bare ferrocene which is an important side reaction that takes place in this case by using our protocol. Finally, we attempted to *N*-arylate cyanoacetamide and *tert*-butyl carbamate (not shown), but without success due to the formation of an unidentified product under our conditions. The activated methylene group of the former and unfavourable electronic or steric factors for the later could be advanced to rationalize these results.

We next studied the reactivity of benzamides and related compounds (Table 3). Ribas and co-workers showed that, under the coupling conditions they proposed (0.1 equiv of copper(I) iodide and 2 equiv of tripotassium phosphate in DMSO), benzamide (almost complete conversion at 90 °C) is more reactive towards iodobenzene than acetamide (complete conversion at 130 °C).¹⁶ With the method here optimized for iodoferrocene, the yield obtained for benzamide (70%, product **2-Ph**, entry 1) proved to be slightly lower than for acetamide (82%, product **2-Me**, Table 2, entry 1), as previously noticed by Bolm and co-workers (70% yield in the case of acetamide and 57% from benzamide).²⁶

In the course of their study on the reactivity of secondary benzamides with methyl 2-iodobenzoate, Wu, Shang and co-workers showed a substituent onto the benzamide ring has an existing (4-nitro < H) but moderate impact on the course of the reaction, even when located next to the amide function.⁴¹ Here, in the presence of an electron-donating group on the primary benzamide (a 4-methoxy), no significant yield change was noticed (77%, product **2-4OMe**, entry 2). While the presence of an electron-withdrawing 4-nitro group seems to reduce the yield (56%, product **2-4NO₂**, entry 3), good results were observed with 3-methoxy (80%, product **2-3OMe**, entry 4) and 3-chloro (85%, product **2-3Cl**, entry 5) although they all should exhibit the same electron-withdrawing effect. This difference might result from the lower solubility of the product formed from 4-nitrobenzamide.

Unlike 4-fluorobenzamide which allowed **2-4F** to be formed in a good yield (79%, entry 6), 4- and 2-bromobenzamide failed in providing the expected derivatives (entries 7 and 8). While steric hindrance can be proposed to explain the low reactivity of 2-bromobenzamide, it can hardly be advanced in the case of the 4-bromo isomer. Since bromo-substituted benzamides are known to react with methyl 2-iodobenzoate,⁴¹ the lower reactivity of iodoferrocene associated with the high propensity of bromobenzamides to undergo side reactions under the conditions used could be responsible for this result. We evaluated the catalytic system used by Bolm and co-workers²⁶ for this coupling, but this failed to provide the expected

derivative (entry 8). It confirmed that 2-bromobenzamide (which is an activated aromatic halide) can react under these conditions as bromoferrocene was also identified at the end of this reaction.

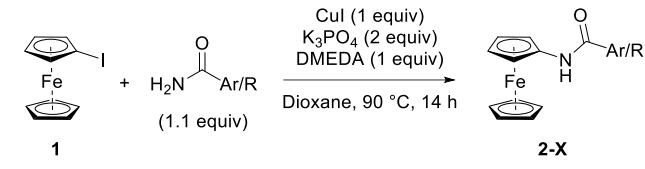
When more sterically hindered 2-methylbenzamide was employed, a lower but still acceptable 63% yield was recorded under the same reaction conditions (product **2-2Me**, entry 9). However, in the case of 2-naphthylamide, the reason for the low 22% yield observed is no more steric hindrance, but rather the low solubility of **2-Naph** making its purification less obvious (entry 10). While using electron-rich/-donating ferrocenyl and 2-thienyl easily led to the coupled products **2-Fc** and **2-2Th** (respective yields of 78 and 93%, entries 11 and 12), using isonicotinamide which possesses an electron-poor/-withdrawing 4-pyridyl ring delivered **2-4Py** in a moderate 49% yield (entry 13).

It is worth mentioning that a satisfying yield was also noticed with the phenyl group separated from the primary amide function through a double bond (76%, product **2-Acry**, entry 14), but not through a triple bond (entry 15). These results were predictable since primary acrylamides have already been employed as coupling partners in copper-catalysed *N*-arylation under similar conditions⁴⁶ but primary propiolamides have, to the best of our knowledge, never being used in such reactions.

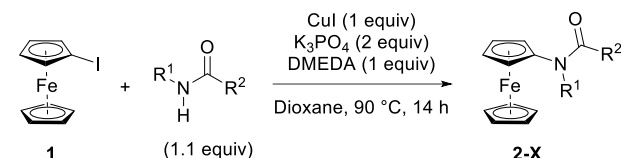
We next turned our attention to the *N*-arylation of secondary amides (Table 4) which is known to be highly substrate-dependent.⁴⁷ In a study dedicated to the discovery of a suitable ligand to couple secondary benzamides with methyl 2-iodobenzoate, Wu, Shang and co-workers identified steric hindrance and poor nucleophilicity as responsible for the very few examples reported in the literature.⁴¹ In the reaction using copper(I) iodide and tripotassium phosphate (2 equiv) in DMSO for 24 h, acyclic secondary amides are reported as able to react with iodobenzene at 130 °C for 24 h in the following order: *N*-methylacetamide (84% conversion) > *N*-ethylacetamide (67% conversion) > *N*-phenylbenzamide (15% conversion); in contrast, cyclic 2-pyrrolidinone can be completely converted at only 110 °C.¹⁶

In the present study, we submitted a mixture of iodoferrocene and 2-pyrrolidinone to our optimized conditions, and isolated the expected product **2-Pyrr** in a high 89% yield (entry 1). It is no accident that 2-pyrrolidinone has been employed in different studies dedicated to the mechanism of copper-catalysed *N*-arylations; indeed, lactams of smaller or larger size such as 2-azetidinone (product **2-Azet**), 2-piperidinone (product **2-Pipe**) and hexahydro-2-azepinone (product **2-Azep**) also gave the expected products, but with less success (entries 2-4). It is worth noting that these conditions are not suitable for the coupling of both isatin and phthalimide with iodoferrocene (not shown).

Table 3 Reaction between iodoferrocene (**1**) and aromatic primary amides.

Entry	Ar/R (Substituent G)	Product, Yield (%) ^a
		
1	G = H	2-Ph , 70 ^b , 79 ^{b,c}
2	G = OMe	2-4OMe , 77 (1; 19) ^b
3	G = NO ₂	2-4NO₂ , 56 (2; 10) ^b
4	G = OMe	2-3OMe , 80 ^d (<5; <5) ^b
5	G = Cl	2-3Cl , 85 (0; 11) ^b , 65 ^e (0; 6) ^b
6	G = F	2-4F , 79 (2; 12) ^b
7	G = Br	traces (66; 5) ^b
8	G = Br	traces (64; 10) ^{b,f}
9	G = Me	2-2Me , 63 (<5; <5) ^b
10		2-Naph , 22 ^g
11		2-Fc , 78 ^g
12		2-2Th , 93 (0; 5) ^b
13		2-4Py , 49 (1; 17) ^b
14		2-Acry , 76 (6; 16) ^b
15		0 (26; 15) ^b

^a After purification (see experimental part). ^b The rest was mainly recovered **1** and ferrocene; for some reactions, the respective yields are given in brackets. ^c Performed on a 6 mmol scale instead of 1 mmol for the other reactions. ^d Performed on a 2 mmol scale. ^e Performed on a 5 mmol scale. ^f By using CuI (1 equiv) and tBuOK (2 equiv) in DMSO at 90 °C for 14h, recovered **1** (24%), ferrocene (13.5%) and bromoferrocene (8%) were obtained. ^g **1** and ferrocene were not recovered.

Table 4 Reaction between iodoferrocene (**1**) and cyclic secondary amides.


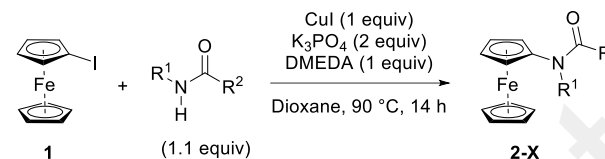
Entry	Amide	Product, Yield (%) ^a
1		 2-Pyrr , 89 ^b
2		 2-Azet , 66 ^b
3		 2-Pipe , 46 ^b
4		 2-Azep , 32 ^b

^a After purification (see experimental part). ^b The rest was mainly recovered **1** and ferrocene.

We next turned our attention to more challenging acyclic secondary amides (Table 5). In the course of their study dedicated to the *N*-arylation of *N*-aryl benzamides, Wu, Shang and co-workers showed that the outcome of the reaction depends both on the aryl group itself (less hindered phenyl > 1-naphthyl) and on the substituent present on this aryl group (e.g. no reaction in the presence of a 4-nitro group) or even on the position of this substituent (higher yields when it is remote from the carboxamide function, e.g. 4-chloro > 2-chloro).⁴¹ We tested our conditions for the reaction between iodoferrocene and an acetamide bearing a hindered ferrocenyl group onto nitrogen; by this way, **2-AcFc** was isolated in 8% yield from **2-Me** (entry 1), a yield much more lower than from acetamide (82%). Similarly, when compared with the reactions from 3-methoxy- and 3-chlorobenzamide (80 and 85% yield, respectively), the *N*-arylation of the corresponding *N*-methyl benzamides proceeded in much more lower yields of 9% (product **2-3OMeMe**, entry 2) and 12% (product **2-3ClMe**, entry 3). In such challenging reactions, ferrocene was competitively produced to a significant extent due to the low reactivity of these secondary amides.

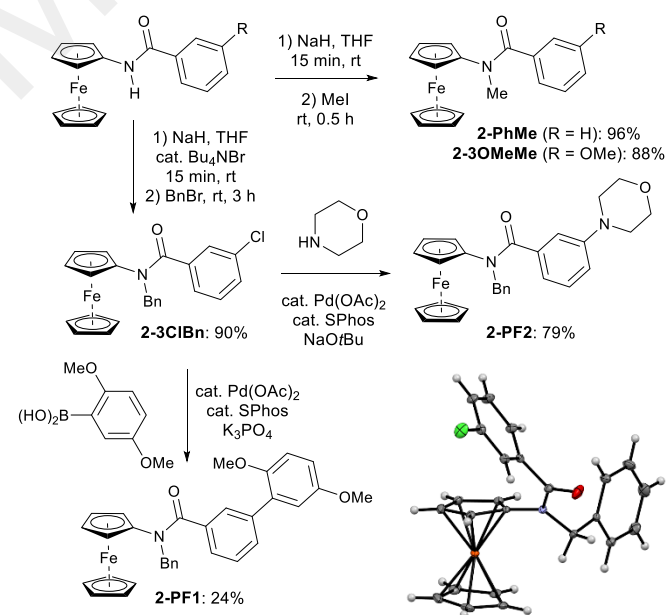
As a consequence, the preferred route towards *N*-ferrocenyl-*N*-alkyl acetamides seems to be the *N*-alkylation of *N*-ferrocenyl benzamides rather than the *N*-ferrocenylation of *N*-methyl benzamides. We confirmed this assumption by *N*-methylating or -benzylating the *N*-ferrocenyl benzamides **2-Ph**, **2-3OMe** and **2-3ClPh**, thus affording the ferrocenyl-based tertiary amides **2-PhMe**, **2-3OMeMe** and **2-3ClBn** in 70–76% overall yields from the required iodoferrocene and primary carboxamides. Finally, by taking advantage of the chloro group present, post-functionalization was studied and we successfully

performed a palladium-catalysed Suzuki coupling with 2,5-dimethoxyphenylboronic acid to access **2-PF1** and a Buchwald-Hartwig amination with morpholine to furnish **2-PF2** (Scheme 2).

Table 5 Reaction between iodoferrocene (**1**) and acyclic secondary amides.


Entry	Amide	Product, Yield (%) ^a
1		 2-AcFc , 8 ^b
2		 2-3OMeMe , 9 ^c (24; 39) ^b
3		 2-3ClMe , 12 ^c (22; 35) ^b

^a After purification (see experimental part). ^b The rest was mainly recovered **1** and ferrocene; for some reactions, the corresponding yields are given in brackets. ^c By performing the reaction on a 5 mmol scale.

**Scheme 2** Alternative way to *N*-alkyl-*N*-ferrocenylbenzamides; Post-functionalization and ORTEP diagram (30% probability) of *N*-benzyl-*N*-ferrocenylbenzamide (**2-3ClBn**).

Most of the ferrocenecarboxamides derivatives obtained through this study were crystalline solids and their structures at the solid state were studied by X-ray diffraction (see ESI). While **2-Me** and **2-CF₃** feature H-bonds strings as observed with all the secondary carboxamides, differences between the two compounds are present. Indeed, two molecules were found in

the asymmetric unit of **2-Me** while only one for **2-CF₃**. Furthermore, while the packing structure of **2-Me** revealed 3 strings of H-bonds, two being parallel and almost perpendicular to the third one, only two parallel H-bond strings are noticed for **2-CF₃**. Finally, in a same string, the methyl groups of **2-Me** are arranged in pairs pointing in opposite direction while the trifluoromethyls point in the same direction in **2-CF₃**. Otherwise, the structures of **2-Me** and **2-CF₃** are very similar: they both share staggered conformation (C1-Cg...Cg-C1', Cg being the centroid of the respective Cp ring, 22.0 ° and 13.6 ° for **2-Me** while 14.1 ° for **2-CF₃**) and have close Cp-carboxamide torsion angles (22.1 ° and 19.8 ° for **2-Me**, 26.4 ° for **2-CF₃**).

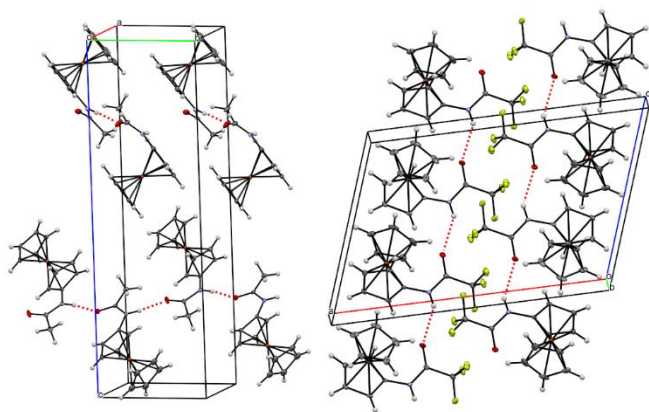


Figure 1 Packing of **2-Me** and **2-CF₃** observed at the solid state highlighting the hydrogen bonds observed as red dotted lines (thermal ellipsoids shown at the 30% probability level).

Experimental

All the reactions were performed under an argon atmosphere in dried Schlenk tubes. Column chromatography separations were achieved on silica gel (40-63 μm). Melting points were measured on a Kofler apparatus. IR spectra were taken on a Perkin-Elmer Spectrum 100 spectrometer. ¹H and ¹³C Nuclear Magnetic Resonance (NMR) spectra were recorded either on a Bruker Avance III spectrometer at 300 MHz and 75 MHz respectively, or a Bruker Avance III spectrometer at 400 MHz and 100 MHz respectively, or even on a Bruker Avance III HD spectrometer at 500 MHz and 126 MHz respectively. ¹H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ¹³C chemical shifts are relative to the central peak of the solvent signal.⁴⁸ Unless otherwise stated, all reagents are commercially available and used as received. Dioxane was continuously refluxed and freshly distilled from sodium-benzophenone under argon and transferred by using a syringe. Iodoferrocene,^{27, 49} bromoferrocene,⁵⁰ chloroferrocene,⁵⁰ KF on Al₂O₃,⁵¹ ferrocenecarboxamide⁵² and (diethylamino)acetamide⁴⁴ were prepared as described previously. 3-[5-(1,3-Benzodioxolyl)]-2-propenamide was prepared by adapting a protocol described.⁵² *N*-Methyl-3-methoxybenzamide and *N*-methyl-3-chlorobenzamide were prepared by reacting 3-methoxybenzoyl chloride and 3-chlorobenzoyl chloride, respectively, with methylamine.⁵³

Crystallography. The X-ray diffraction data were collected for the compounds **2-Me**, **2-cPr**, **2-CH₂NET₂**, **2-Ph**, **2-4OMe**, **2-4NO₂**, **2-3Cl**, **2-4F**, **2-4Py**, **2-Pyrr**, **2-Azet**, **2-Pipe**, **2-Azep**, **2-AcFc**, **2-3OMeMe**, **2-3ClMe**, **2-CF₃**, **2-PhMe** and **2-3ClBn** at 150(2) K on a D8 VENTURE Bruker AXS diffractometer equipped with a (CMOS) PHOTON 100 detector by using Mo-Kα radiation (λ = 0.71073 Å; multilayer monochromator). The structure was solved by dual-space algorithm using the *SHELXT* program,⁵⁴ and then refined with full-matrix least-square methods based on *F*² (*SHELXL* program).⁵⁵ All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. Except hydrogen atoms linked to nitrogen atoms (in the case of **2-Ph**, **2-4NO₂**, **2-4F**, **2-4Py**, **2-CH₂NET₂**, **2-cPr**, **2-CF₃**, **2-3Cl**, **2-4OMe**) and **2-Me**) that were introduced in the structural models through Fourier difference maps analysis, 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 ORTEP-3 (version 2.02).⁵⁶

General procedure 1. Iodoferrocene (**1**; unless otherwise specified in the product description, 1.0 mmol), CuI (0.19 g, 1.0 mmol), K₃PO₄ (0.42 g, 2.0 mmol), DMEDA (0.11 mL, 1.0 mmol) and the amide (1.1 mmol) were introduced in a degassed Schlenk tube and dissolved in dioxane (2 mL). The reaction mixture was stirred under argon and heated at 90 °C for 14 h. It was then allowed to cool to room temperature before addition of water (10 mL). After extraction with AcOEt (3 x 20 mL), drying over MgSO₄ and evaporation of the solvent under reduced pressure, the coupling product was purified by chromatography over silica gel (the eluent is given in the product description).

***N*-Ferrocenylacetamide (2-Me; mixture of rotamers).** The general procedure 1 starting from acetamide (65 mg) gave **2-Me** (eluent: hexane-AcOEt 60:40) in 82% yield (0.20 g) as an orange solid: mp 178-180 °C (lit.⁵⁷ 158-167 °C); IR (ATR) 747, 800, 998, 1103, 1285, 1371, 1386, 1478, 1568, 1650, 3088, 3257 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 1.94 (s, 3H, Me), 3.91 (t, 2H, *J* = 1.9 Hz, H3 and H4), 4.09 (s, 5H, Cp), 4.60 (t, 2H, *J* = 1.9 Hz, H2 and H5), 8.46 (br s, 1H, NH); ¹H NMR (CDCl₃, only main rotamer described) 2.06 (s, 3H, Me), 3.98 (s, 2H, H3 and H4), 4.15 (s, 5H, Cp), 4.57 (s, 2H, H2 and H5), 7.05 (br s, 1H, NH); ¹³C NMR (CDCl₃) δ 24.1 (CH₃), 61.8 (2CH, C2 and C5), 64.7 (2CH, C3 and C4), 69.2 (5CH, Cp), 96.5 (C, C1, C-N), 168.6 (C, C=O); MS (EI, 70 eV): 243 [M]. These data are similar to those reported previously.⁵⁷

Crystal data for 2-Me. C₁₂H₁₃FeNO, *M* = 243.08, monoclinic, *P* 2₁, *a* = 5.9103(2), *b* = 7.4810(2), *c* = 23.4895(8) Å, β = 92.4820(10)°, *V* = 1037.61(6) Å³, *Z* = 4, *d* = 1.556 g cm⁻³, μ = 1.422 mm⁻¹. A final refinement on *F*² with 4398 unique intensities and 247 parameters converged at ω*R*(*F*²) = 0.0891 (*R*(*F*) = 0.0351) for 4272 observed reflections with *I* > 2σ(*I*). CCDC 2014635.

***N*-(Ferrocenyl)cyclopropanecarboxamide (2-cPr).** The general procedure 1 starting from cyclopropanecarboxamide (94 mg) gave **2-cPr** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.37) in 57% yield (0.15 g) as an orange solid: mp 174-176 °C; IR (ATR) 726, 760, 807, 859, 882, 932, 960, 999, 1022, 1038, 1104, 1202, 1215, 1262, 1382, 1404, 1441, 1475, 1542, 1644, 3083, 3249 cm⁻¹; ¹H NMR (CDCl₃) δ 0.78-0.82 (m, 2H, CH₂), 1.02-1.06 (m, 2H, CH₂), 1.36-1.41 (m, 1H, CH-CH₂), 4.00 (s, 2H, H3 and H4),

4.17 (s, 5H, Cp), 4.59 (s, 2H, H2 and H5), 6.79 (br s, 1H, NH); ¹³C NMR (CDCl₃) δ 7.8 (2CH₂), 15.5 (CH-CH₂), 61.5 (2CH, C2 and C5), 64.6 (2CH, C3 and C4), 69.4 (5CH, Cp), 95.2 (C, C1, C-N), 171.8 (C, C=O); MS (EI, 70 eV): 269 [M], 201 [M-C(O)cPr+H]. **Crystal data for 2-cPr.** C₁₄H₁₅FeNO, *M* = 269.12, monoclinic, *C* 2/*c*, *a* = 29.192(3), *b* = 8.5607(8), *c* = 9.4060(9) Å, β = 92.452(4)°, *V* = 2348.5(4) Å³, *Z* = 8, *d* = 1.522 g cm⁻³, μ = 1.265 mm⁻¹. A final refinement on *F*² with 2689 unique intensities and 157 parameters converged at ω*R*(*F*²) = 0.0746 (*R*(*F*) = 0.0265) for 2445 observed reflections with *l* > 2σ(*l*). CCDC 2014636.

***N*-Ferrocenylpivalamide (2-tBu).** The general procedure 1 starting from pivalamide (0.11 g) gave **2-tBu** (eluent: hexane-AcOEt 90:10) in 50% yield (0.14 g) as an orange solid: mp 250-252 °C; IR (ATR) 807, 928, 1002, 1106, 1183, 1247, 1360, 1478, 1547, 1649, 2963, 3298 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 1.23 (s, 9H, tBu), 3.90 (t, 2H, *J* = 2.0 Hz, H3 and H4), 4.07 (s, 5H, Cp), 4.71 (t, 2H, *J* = 2.0 Hz, H2 and H5), 8.10 (br s, 1H, NH); ¹³C NMR ((CD₃)₂CO) δ 27.8 (3CH₃, CMe₃), 39.8 (C, CMe₃), 61.8 (2CH, C2 and C5), 64.5 (2CH, C3 and C4), 69.6 (5CH, Cp), 97.5 (C, C1, C-N), 176.8 (C, C=O); MS (EI, 70 eV): 285 [M], 220 [M-Cp]. The ¹H NMR data are similar to those reported previously.⁵⁸

***N*-Ferrocenylformamide (2-H; 2.8:1 (cis/trans) mixture of rotamers).** The general procedure 1 starting from formamide (44 μL) gave **2-H** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.21) in 26% yield (60 mg) as an orange solid: mp 82-84 °C (lit.⁵⁹ 86-87 °C); IR (ATR) 712, 817, 928, 1001, 1020, 1050, 1104, 1167, 1207, 1267, 1388, 1410, 1510, 1654, 1683, 2889, 3085, 3253 cm⁻¹; ¹H NMR ((CD₃)₂SO) the signals of the main rotamer are marked by an asterisk δ 3.97* and 4.02 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.12* and 4.17 (s, 5H, Cp), 4.35 and 4.57* (t, 2H, *J* = 1.8 Hz, H2 and H5), 8.08* (d, 1H, *J* = 1.6 Hz, CHO) and 8.44 (d, 1H, *J* = 11.3 Hz, CHO), 9.28 (d, 1H, *J* = 11.3 Hz, NH) and 9.49* (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 59.9 and 60.9* (2CH, C2 and C5), 64.0* and 64.5 (2CH, C3 and C4), 68.8* and 69.0 (5CH, Cp), 93.7* and 95.4 (C, C1, C-N), 159.2* and 163.1 (C, C=O). ***N,N*-Diferrocenylformamide** was similarly isolated (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.75) in 11% yield (45 mg) as an orange solid: mp 155-157 °C; IR (ATR) 808, 909, 964, 998, 1028, 1058, 1105, 1171, 1211, 1298, 1356, 1408, 1460, 1674 (s), 2917, 3092 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.01 (s, 2H, H3' and H4'), 4.08 (s, 5H, Cp or Cp'), 4.30 (s, 5H, Cp or Cp'), 4.33 (s, 2H, H3 and H4), 4.47 (s, 2H, H2' and H5'), 4.51 (s, 2H, H2 and H5), 9.24 (s, 1H, CHO); ¹³C NMR ((CD₃)₂SO) δ 61.9 (2CH, C2' and C5'), 64.2 (2CH, C3' and C4'), 65.9 (2CH, C3 and C4), 66.1 (2CH, C2 and C5), 68.9 (5CH, Cp or Cp'), 69.4 (5CH, Cp or Cp'), 98.5 (C, C1 or C1', C-N), 98.6 (C, C1 or C1', C-N), 164.1 (C, C=O).

2-(Diethylamino)-*N*-ferrocenylacetamide (2-CH₂NEt₂). The general procedure 1 starting from iodoferrocene (0.31 g) and using 2-(diethylamino)acetamide (0.14 g) gave **2-CH₂NEt₂** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.31) in 33% yield (0.10 g) as an orange solid: mp 103-105 °C; IR (ATR) 723, 818, 930, 1000, 1034, 1068, 1104, 1163, 1199, 1232, 1262, 1288, 1365, 1388, 1451, 1471, 1537, 1659, 2804, 2934, 2971, 3110, 3284 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 1.03 (t, 6H, *J* = 7.1 Hz, 2Me), 2.57 (q, 4H, *J* = 7.1 Hz, 2CH₂-Me), 3.01 (s, 2H, CH₂-C=O), 3.95 (s, 2H, H3 and H4), 4.09 (s, 5H, Cp), 4.70 (s, 2H, H2 and H5), 8.93 (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 12.0 (2CH₃), 47.8 (2CH₂, 2CH₂-Me), 57.2 (CH₂, CH₂-C=O), 60.7 (2CH, C2 and C5), 63.8

(2CH, C3 and C4), 68.6 (5CH, Cp), 95.0 (C, C1, C-N), 169.3 (C, C=O); MS (EI, 70 eV): 314 [M]. **Crystal data for 2-CH₂NEt₂.** C₁₆H₂₂FeN₂O, *M* = 314.20, monoclinic, *P* 2₁/*c*, *a* = 12.7745(16), *b* = 11.0716(16), *c* = 10.5180(12) Å, β = 94.122(4)°, *V* = 1483.8(3) Å³, *Z* = 4, *d* = 1.407 g cm⁻³, μ = 1.013 mm⁻¹. A final refinement on *F*² with 3384 unique intensities and 186 parameters converged at ω*R*(*F*²) = 0.1092 (*R*(*F*) = 0.0420) for 2856 observed reflections with *l* > 2σ(*l*). CCDC 2014637.

***N*-Ferrocenylbenzamide (2-Ph).** The general procedure 1, but performed on a 6.0 mmol scale, starting from benzamide (0.78 g, 6.6 mmol) gave **2-Ph** (eluent: hexane-AcOEt 60:40) in 79% yield (1.4 g) as an orange solid: mp 188-190 °C (lit.²⁶ 179-181 °C); IR (ATR) 692, 816, 1000, 1285, 1367, 1475, 1495, 1557, 1643, 3307 cm⁻¹; ¹H NMR (CDCl₃) δ 4.15 (s, 2H, H3 and H4), 4.24 (s, 5H, Cp), 4.81 (s, 2H, H2 and H5), 7.14 (br s, 1H, NH), 7.44-7.56 (m, 3H, H2', H4' and H6'), 7.80 (d, 2H, *J* = 7.7 Hz, H3' and H5'); ¹³C NMR (CDCl₃) δ 61.8 (2CH, C2 and C5), 65.0 (2CH, C3 and C4), 69.6 (5CH, Cp), 95.4 (C, C1, C-N), 127.0 (2CH, C3' and C5'), 128.9 (2CH, C2' and C6'), 131.8 (CH, C4'), 134.9 (C, C1'), 165.7 (C, C=O); MS (EI, 70 eV): 305 [M], 240 [M-Cp]. These data are similar to those reported previously.²⁶ **Crystal data for 2-Ph.** C₁₇H₁₅FeNO, *M* = 305.15, orthorhombic, *P* c c n, *a* = 10.2809(14), *b* = 26.782(4), *c* = 9.9687(13) Å, *V* = 2744.8(7) Å³, *Z* = 8, *d* = 1.477 g cm⁻³, μ = 1.092 mm⁻¹. A final refinement on *F*² with 3135 unique intensities and 185 parameters converged at ω*R*(*F*²) = 0.0650 (*R*(*F*) = 0.0273) for 2814 observed reflections with *l* > 2σ(*l*). CCDC 2014639.

***N*-Ferrocenyl-4-methoxybenzamide (2-4OMe).** The general procedure 1 starting from 4-methoxybenzamide (0.17 g) gave **2-4OMe** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.45) in 77% yield (0.27 g) as an orange solid: mp 179-181 °C; IR (ATR) 669, 762, 813, 841, 892, 938, 1002, 1029, 1106, 1126, 1176, 1209, 1255, 1285, 1310, 1348, 1365, 1388, 1411, 1465, 1475, 1509, 1552, 1607, 1631, 2052, 2836, 2932, 2960, 3068, 3099, 3302 (br) cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 3.83 (s, 3H, OMe), 3.99 (t, 2H, *J* = 1.9 Hz, H3 and H4), 4.11 (s, 5H, Cp), 4.79 (t, 2H, *J* = 1.7 Hz, H2 and H5), 7.03 (d, 2H, *J* = 8.8 Hz, H3' and H5'), 7.90 (d, 2H, *J* = 8.8 Hz, H2' and H6'), 9.10 (s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 55.4 (CH₃, OMe), 61.0 (2CH, C2 and C5), 63.8 (2CH, C3 and C4), 68.8 (5CH, Cp), 96.1 (C, C1, C-N), 113.5 (2CH, C3' and C5'), 126.9 (C, C1', C-C=O), 129.2 (2CH, C2' and C6'), 161.6 (C, C4', C-OMe), 164.3 (C, C=O). **Crystal data for 2-4OMe.** C₁₈H₁₇FeNO₂, *M* = 335.17, monoclinic, *P* 2₁/*c*, *a* = 14.3999(12), *b* = 10.4832(7), *c* = 10.1885(9) Å, β = 98.290(3)°, *V* = 1522.0(2) Å³, *Z* = 4, *d* = 1.463 g cm⁻³, μ = 0.997 mm⁻¹. A final refinement on *F*² with 3581 unique intensities and 204 parameters converged at ω*R*(*F*²) = 0.1975 (*R*(*F*) = 0.0761) for 3003 observed reflections with *l* > 2σ(*l*). CCDC 2014640.

***N*-Ferrocenyl-4-nitrobenzamide (2-4NO₂).** The general procedure 1 starting from 4-nitrobenzamide (0.18 g) gave **2-4NO₂** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.60) in 56% yield (0.21 g) as a dark purple solid: mp 242-245 °C; IR (ATR) 710, 738, 802, 824, 851, 867, 895, 928, 1105, 1278, 1341, 1365, 1387, 1494, 1519, 1552, 1600, 1645, 2924, 3317 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.05 (t, 2H, *J* = 1.7 Hz, H3 and H4), 4.15 (s, 5H, Cp), 4.81 (t, 2H, *J* = 1.7 Hz, H2 and H5), 8.14 (d, 2H, *J* = 8.7 Hz, H2' and H6'), 8.35 (d, 2H, *J* = 8.7 Hz, H3' and H5'), 10.09 (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 61.4 (2CH, C2 and C5), 64.2 (2CH, C3

and C4), 68.9 (5CH, Cp), 95.1 (C, C1, C-N), 123.5 (2CH, C3' and C5'), 128.9 (2CH, C2' and C6'), 140.3 (C, C1', C-C=O), 149.0 (C, C4', C-NO₂), 163.1 (C, C=O). **Crystal data for 2-4NO₂**. C₁₇H₁₄FeN₂O₃, *M* = 350.15, orthorhombic, *Pbcn*, *a* = 18.433(3), *b* = 10.1869(16), *c* = 15.329(3) Å, *V* = 2878.4(9) Å³, *Z* = 8, *d* = 1.616 g cm⁻³, *μ* = 1.065 mm⁻¹. A final refinement on *F*² with 3282 unique intensities and 212 parameters converged at $\omega R(F^2) = 0.0899$ (*R*(*F*) = 0.0353) for 2721 observed reflections with *I* > 2σ(*I*). CCDC 2014641.

***N*-Ferrocenyl-3-methoxybenzamide (2-3OMe)**. The general procedure 1, but on a 2 mmol scale, starting from 3-methoxybenzamide (0.34 g) gave **2-3OMe** (eluent: petroleum ether-AcOEt 90:10; *R*_f = 0.25) in 80% yield (0.56 g) as an orange solid: mp 160-161 °C; IR (ATR) 692, 713, 749, 806, 825, 866, 880, 899, 921, 932, 1002, 1036, 1076, 1108, 1184, 1228, 1257, 1281, 1351, 1366, 1385, 1450, 1472, 1490, 1553, 1581, 1600, 1635, 2837, 2972, 3104, 3332 cm⁻¹; ¹H NMR (CDCl₃) δ 3.87 (s, 3H, OMe), 4.07 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.20 (s, 5H, Cp), 4.74 (t, 2H, *J* = 1.8 Hz, H2 and H5), 7.07 (ddd, 1H, *J* = 8.0, 2.6 and 1.3 Hz, Ar), 7.21 (br s, 1H, NH), 7.31 (dd, 1H, *J* = 7.7 and 1.3 Hz, Ar), 7.34-7.41 (m, 2H, Ar); ¹³C NMR (CDCl₃) δ 55.7 (CH₃, OMe), 61.8 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 69.4 (5CH, Cp), 94.9 (C, C1, C-N), 112.5 (CH, Ar), 118.0 (CH, Ar), 118.6 (CH, Ar), 129.8 (CH, Ar), 136.4 (C, C1', C-C=O), 160.2 (C, C3', C-OMe), 165.4 (C, C=O).

3-Chloro-*N*-ferrocenylbenzamide (2-3Cl). The general procedure 1 starting from 3-chlorobenzamide (0.17 g) gave **2-3Cl** (eluent: petroleum ether-AcOEt 90:10; *R*_f = 0.38) in 85% yield (0.23 g) as an orange solid: mp 170-172 °C; IR (ATR) 671, 699, 747, 777, 801, 815, 827, 881, 911, 936, 1003, 1017, 1035, 1105, 1136, 1270, 1292, 1349, 1365, 1389, 1407, 1480, 1558, 1597, 1643, 3096, 3301 cm⁻¹; ¹H NMR (CDCl₃) δ 4.09 (s, 2H, H3 and H4), 4.21 (s, 5H, Cp), 4.75 (s, 2H, H2 and H5), 7.29 (br s, 1H, NH), 7.39 (t, 1H, *J* = 7.7 Hz, H5'), 7.49 (d, 1H, *J* = 7.7 Hz, H4'), 7.67 (d, 1H, *J* = 7.6 Hz, H6'), 7.79 (s, 1H, H2'); ¹³C NMR (CDCl₃) δ 61.9 (2CH, C2 and C5), 65.1 (2CH, C3 and C4), 69.5 (5CH, Cp), 94.8 (C, C1, C-N), 125.1 (CH, C6'), 127.3 (CH, C2'), 130.2 (CH, C5'), 131.8 (CH, C4'), 135.1 (C, C3'), 136.6 (C, C1', C-C=O), 164.3 (C, C=O). **Crystal data for 2-3Cl**. C₁₇H₁₄ClFeNO, *M* = 339.59, monoclinic, *P* 2₁/*c*, *a* = 14.4453(9), *b* = 10.4926(5), *c* = 10.0119(6) Å, *β* = 105.996(2) °, *V* = 1458.74(14) Å³, *Z* = 4, *d* = 1.546 g cm⁻³, *μ* = 1.213 mm⁻¹. A final refinement on *F*² with 3327 unique intensities and 193 parameters converged at $\omega R(F^2) = 0.0720$ (*R*(*F*) = 0.0310) for 2899 observed reflections with *I* > 2σ(*I*). CCDC 2014642.

***N*-Ferrocenyl-4-fluorobenzamide (2-4F)**. The general procedure 1 starting from 4-fluorobenzamide (0.15 g) gave **2-4F** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.80) in 79% yield (0.27 g) as an orange solid: mp 211-213 °C; IR (ATR) 671, 723, 758, 807, 836, 857, 893, 931, 998, 1024, 1037, 1096, 1104, 1124, 1159, 1229, 1282, 1300, 1310, 1349, 1367, 1389, 1408, 1477, 1505, 1561, 1601, 1640, 3109, 3272 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.01 (t, 2H, *J* = 1.6 Hz, H3 and H4), 4.13 (s, 5H, Cp), 4.79 (t, 2H, *J* = 1.6 Hz, H2 and H5), 7.34 (t, 2H, *J* = 8.9 Hz, H3' and H5'), 7.99 (dd, 2H, *J* = 8.7 and 5.6 Hz, H2' and H6'), 9.74 (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 61.1 (2CH, C2 and C5), 63.9 (2CH, C3 and C4), 68.8 (5CH, Cp), 95.7 (C, C1, C-N), 115.2 (d, 2CH, *J* = 21.8 Hz, C3' and C5'), 130.0 (d, 2CH, *J* = 9.1 Hz, C2' and C6'), 131.2 (d, C, *J* =

2.3 Hz, C1', C-C=O), 163.8 (C, C=O), 163.9 (d, C, *J* = 249 Hz, C4', C-F); MS (EI, 70 eV): 323 [M], 258 [M-Cp]. **Crystal data for 2-4F**. C₁₇H₁₄FFeNO, *M* = 323.14, monoclinic, *P* 2₁/*c*, *a* = 10.7882(11), *b* = 14.3983(13), *c* = 9.0245(9) Å, *β* = 102.111(4) °, *V* = 1370.6(2) Å³, *Z* = 4, *d* = 1.566 g cm⁻³, *μ* = 1.108 mm⁻¹. A final refinement on *F*² with 3149 unique intensities and 193 parameters converged at $\omega R(F^2) = 0.0631$ (*R*(*F*) = 0.0248) for 2895 observed reflections with *I* > 2σ(*I*). CCDC 2014643.

***N*-Ferrocenyl-2-methylbenzamide (2-2Me)**. The general procedure 1 starting from 2-methylbenzamide (0.15 g) gave **2-2Me** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.73) in 63% yield (0.21 g) as an orange solid: mp 186-188 °C; IR (ATR) 670, 701, 726, 793, 815, 926, 1008, 1028, 1055, 1105, 1131, 1155, 1180, 1223, 1293, 1333, 1354, 1368, 1402, 1422, 1446, 1487, 1574, 1598, 1628, 2933, 3094 cm⁻¹; ¹H NMR (CDCl₃) δ 2.51 (s, 3H, Me), 4.05 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.21 (s, 5H, Cp), 4.71 (t, 2H, *J* = 1.8 Hz, H2 and H5), 6.86 (br s, 1H, NH), 7.21-7.24 (m, 1H, Ar), 7.26-7.27 (m, 1H, H3'), 7.33 (dd, 1H, *J* = 7.3 and 1.2 Hz, Ar), 7.39 (d, 1H, *J* = 7.6 Hz, H6'); ¹³C NMR (CDCl₃) δ 20.0 (CH₃), 61.7 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 69.4 (5CH, Cp), 94.8 (C, C1, C-N), 126.0 (CH, C4' or C5'), 126.6 (CH, C6'), 130.2 (CH, C4' or C5'), 131.3 (CH, C3'), 136.3 and 136.7 (C, C2', C-Me and C, C1', C-C=O), 168.1 (C, C=O).

***N*-Ferrocenyl-2-naphthalenecarboxamide (2-Naph)**. The general procedure 1 starting from 2-naphthalenecarboxamide (0.19 g) gave **2-Naph** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.60) in 22% yield (82 mg) as an orange solid: mp 208-210 °C; IR (ATR) 682, 711, 761, 773, 811, 821, 863, 905, 937, 957, 1003, 1017, 1028, 1108, 1133, 1201, 1236, 1256, 1273, 1293, 1350, 1366, 1387, 1475, 1506, 1556, 1628, 1637, 3103, 3315 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.04 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.16 (s, 5H, Cp), 4.85 (t, 2H, *J* = 1.8 Hz, H2 and H5), 7.60-7.65 (m, 2H, Ar), 7.99-8.04 (m, 3H, Ar), 8.08 (dd, 1H, *J* = 6.8 and 2.1 Hz, Ar), 8.52 (s, 1H, H1'), 9.91 (s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 61.2 (2CH, C2 and C5), 64.0 (2CH, C3 and C4), 68.8 (5CH, Cp), 95.9 (C, C1, C-N), 124.3 (CH, Ar), 126.8 (CH, Ar), 127.5 (CH, Ar), 127.6 (CH, Ar), 127.6 (CH, Ar), 127.9 (CH, Ar), 128.9 (CH, Ar), 132.1 (C, Ar), 132.1 (C, Ar), 134.1 (C, Ar), 164.9 (C, C=O).

***N*-(Ferrocenyl)ferrocenecarboxamide (2-Fc)**. The general procedure 1 starting from ferrocenecarboxamide (0.25 g) gave **2-Fc** (eluent: petroleum ether-AcOEt 50:50; *R*_f = 0.11) in 78% yield (0.34 g) as an orange solid: mp 202-204 °C (lit.⁶⁰ 210-230 °C (dec.)); IR (ATR) 674, 692, 766, 809, 840, 877, 933, 1000, 1019, 1042, 1052, 1107, 1153, 1222, 1247, 1286, 1349, 1362, 1385, 1411, 1453, 1484, 1554, 1633, 3102, 3315 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 3.99 (br s, 2H, H3 and H4), 4.13 (s, 5H, Cp or Cp'), 4.21 (s, 5H, Cp or Cp'), 4.41 (t, 2H, *J* = 1.7 Hz, H3' and H4'), 4.74 (br s, 2H, H2 and H5), 4.91 (t, 2H, *J* = 1.7 Hz, H2' and H5'), 8.92 (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 60.6 (2CH, C2 and C5), 63.6 (2CH, C3 and C4), 68.3 (2CH, C2' and C5'), 68.8 (5CH, Cp or Cp'), 69.4 (5CH, Cp or Cp'), 70.2 (2CH, C3' and C4'), 76.8 (C, C1', C-C=O), 96.4 (C, C1, C-N), 167.2 (C, C=O).

***N*-Ferrocenyl-2-thiophenecarboxamide (2-2Th)**. The general procedure 1 starting from 2-thiophenecarboxamide (0.14 g) gave **2-2Th** (eluent: petroleum ether-AcOEt 80:20; *R*_f = 0.30) in 93% yield (0.31 g) as an orange solid: mp 199-201 °C; IR (ATR) 667, 724, 741, 753, 809, 824, 855, 931, 1001, 1020, 1032, 1049, 1080, 1106, 1218, 1250, 1285, 1353, 1368, 1387, 1418,

1475, 1558, 1621, 3010, 3105, 3300 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.02 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.13 (s, 5H, Cp), 4.74 (t, 2H, *J* = 1.8 Hz, H2 and H5), 7.18 (dd, 1H, *J* = 4.8 and 3.8 Hz, H4'), 7.80 (dd, 1H, *J* = 5.1 and 0.9 Hz, H5'), 7.89 (d, 1H, *J* = 3.4 Hz, H3'), 9.73 (br s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 61.0 (2CH, C2 and C5), 64.0 (2CH, C3 and C4), 68.8 (5CH, Cp), 95.5 (C, C1, C-N), 127.9 (CH, C4'), 128.4 (CH, C3'), 131.1 (CH, C5'), 140.2 (C, C2', C-C=O), 159.4 (C, C=O); MS (EI, 70 eV): 311 [M], 246 [M-Cp], 207.

***N*-Ferrocenylisonicotinamide (2-4Py).**⁶¹ The general procedure 1 starting from isonicotinamide (0.13 g) gave **2-4Py** (eluent: petroleum ether-AcOEt 50:50; *R_f* = 0.11) in 49% yield (0.16 g) as a red solid: mp 176-178 °C; IR (ATR) 662, 684, 751, 814, 827, 841, 900, 933, 1002, 1018, 1036, 1065, 1106, 1130, 1222, 1289, 1349, 1367, 1389, 1409, 1473, 1496, 1548, 1598, 1645, 3100, 3301 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.05 (t, 2H, *J* = 1.7 Hz, H3 and H4), 4.14 (s, 5H, Cp), 4.80 (t, 2H, *J* = 1.7 Hz, H2 and H5), 7.82 (d, 2H, *J* = 4.6 Hz, H3' and H5'), 8.77 (br s, 2H, H2' and H6'), 10.03 (s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 61.3 (2CH, C2 and C5), 64.2 (2CH, C3 and C4), 68.9 (5CH, Cp), 95.0 (C, C1, C-N), 121.3 (2CH, C3' and C5'), 141.5 (C, C4'), 150.2 (2CH, C2' and C6'), 163.2 (C, C=O); MS (EI, 70 eV): 306 [M], 241 [M-Cp]. **Crystal data for 2-4Py.** C₁₆H₁₄FeN₂O, *M* = 306.14, orthorhombic, *P* b c a, *a* = 10.5061(12), *b* = 9.9738(12), *c* = 25.333(3) Å, *V* = 2654.5(5) Å³, *Z* = 8, *d* = 1.532 g cm⁻³, *μ* = 1.131 mm⁻¹. A final refinement on *F*² with 3011 unique intensities and 184 parameters converged at ω*R*(*F*²) = 0.0959 (*R*(*F*) = 0.0413) for 2406 observed reflections with *l* > 2σ(*l*). These X-ray data are as reported previously (XOTTIL, CCDC 1035326).⁶¹

3-(5-(1,3-Benzodioxolyl))-*N*-ferrocenylacrylamide (2-Acry). The general procedure 1 starting from 3-(5-(1,3-benzodioxolyl))acrylamide (0.21 g) gave **2-Acry** (eluent: petroleum ether-AcOEt 50:50; *R_f* = 0.58) in 76% yield (0.30 g) as a red solid: mp 175-177 °C; IR (ATR) 700, 723, 749, 811, 855, 878, 933, 973, 1000, 1039, 1102, 1133, 1187, 1218, 1250, 1358, 1369, 1387, 1410, 1447, 1487, 1504, 1561, 1601, 1649, 1733, 2885, 3079, 3288 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 4.00 (t, 2H, *J* = 1.9 Hz, H3 and H4), 4.11 (s, 5H, Cp), 4.67 (t, 2H, *J* = 1.9 Hz, H2 and H5), 6.08 (s, 2H, CH₂), 6.51 (d, 1H, *J* = 15.6 Hz, Hα), 6.97 (d, 1H, *J* = 8.1 Hz, H7'), 7.10 (dd, 1H, *J* = 8.1 and 1.4 Hz, H6'), 7.16 (d, 1H, *J* = 1.4 Hz, H4'), 7.42 (d, 1H, *J* = 15.6 Hz, Hβ), 9.49 (s, 1H, NH); ¹³C NMR ((CD₃)₂SO) δ 60.9 (2CH, C2 and C5), 64.0 (2CH, C3 and C4), 68.8 (5CH, Cp), 95.4 (C, C1, C-N), 101.4 (CH₂), 106.2 (CH, C4'), 108.6 (CH, C7'), 120.1 (CH, Cα), 123.3 (CH, C6'), 129.2 (C, C5'), 138.8 (CH, Cβ), 147.9 (C, Cα), 148.5 (C, Cβ), 163.5 (C, C=O).

***N*-Ferrocenyl-2-pyrrolidinone (2-Pyrr).** The general procedure 1 starting from 2-pyrrolidinone (84 μL) gave **2-Pyrr** (eluent: hexane-AcOEt 60:40) in 89% yield (0.24 g) as an orange solid: mp 126-128 °C; IR (ATR) 797, 828, 1000, 1021, 1101, 1212, 1297, 1382, 1416, 1495, 1682 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 2.12 (quint, 2H, *J* = 7.0 Hz, H4'), 2.35 (t, 2H, *J* = 7.0 Hz, H3'), 3.71 (t, 2H, *J* = 7.0 Hz, H5'), 4.00 (s, 2H, H3 and H4), 4.15 (s, 5H, Cp), 4.75 (s, 2H, H2 and H5); ¹³C NMR ((CD₃)₂CO) δ 18.8 (CH₂, C4'), 32.6 (CH₂, C3'), 48.9 (CH₂, C5'), 60.6 (2CH, C2 and C5), 65.0 (2CH, C3 and C4), 69.3 (5CH, Cp), 97.9 (C, C1, C-N), 173.9 (C, C=O); MS (EI, 70 eV): 269 [M], 204 [M-Cp]. **Crystal data for 2-Pyrr.** C₁₄H₁₅FeNO, *M* = 269.12, orthorhombic, *P* b c a, *a* = 9.8360(12), *b* = 8.3860(10), *c* = 28.171(3) Å, *V* = 2323.6(5) Å³, *Z* = 8, *d* = 1.539 g cm⁻³, *μ* = 1.278 mm⁻¹. A final refinement on *F*² with 2662

unique intensities and 154 parameters converged at ω*R*(*F*²) = 0.0832 (*R*(*F*) = 0.0352) for 2360 observed reflections with *l* > 2σ(*l*). CCDC 2014644.

***N*-Ferrocenyl-2-azetidinone (2-Azet).** The general procedure 1 starting from 2-azetidinone (78 mg) gave **2-Azet** (eluent: hexane-AcOEt 60:40) in 66% yield (0.17 g) as an orange solid: mp 136-138 °C; IR (ATR) 797, 809, 1002, 1017, 1157, 1339, 1353, 1378, 1408, 1509, 1728, 2903, 2967 cm⁻¹; ¹H NMR (CDCl₃) δ 3.00 (t, 2H, *J* = 4.2 Hz, H4'), 3.43 (t, 2H, *J* = 4.2 Hz, H3'), 4.00 (s, 2H, H3 and H4), 4.21 (s, 5H, Cp), 4.47 (s, 2H, H2 and H5); ¹³C NMR (CDCl₃) δ 36.9 (CH₂, C4'), 39.5 (CH₂, C3'), 59.1 (2CH, C2 and C5), 64.7 (2CH, C3 and C4), 68.9 (5CH, Cp), 94.4 (C, C1, C-N), 164.9 (C, C=O); MS (EI, 70 eV): 255 [M], 227, 213. **Crystal data for 2-Azet.** C₁₃H₁₃FeNO, *M* = 255.09, monoclinic, *P* 2₁/c, *a* = 14.1641(13), *b* = 9.6057(8), *c* = 8.2368(8) Å, β = 106.643(3) °, *V* = 1073.72(17) Å³, *Z* = 4, *d* = 1.578 g cm⁻³, *μ* = 1.378 mm⁻¹. A final refinement on *F*² with 2472 unique intensities and 146 parameters converged at ω*R*(*F*²) = 0.0629 (*R*(*F*) = 0.0224) for 2304 observed reflections with *l* > 2σ(*l*). CCDC 2014645.

***N*-Ferrocenyl-2-piperidinone (2-Pipe).** The general procedure 1 starting from 2-piperidinone (97 μL) gave **2-Pipe** (eluent: hexane-AcOEt 60:40) in 46% yield (0.13 g) as an orange solid: mp 104-106 °C; IR (ATR) 791, 825, 1000, 1167, 1304, 1333, 1462, 1643, 2942 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 1.80 (quint, 2H, *J* = 6.1 Hz, H4'), 1.92 (quint, 2H, *J* = 5.9 Hz, H5'), 2.35 (t, 2H, *J* = 6.8 Hz, H3'), 3.71 (t, 2H, *J* = 5.9 Hz, H6'), 4.00 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.15 (s, 5H, Cp), 4.72 (t, 2H, *J* = 1.8 Hz, H2 and H5); ¹³C NMR ((CD₃)₂CO) δ 21.7 (CH₂, C4'), 24.0 (CH₂, C5'), 34.2 (CH₂, C3'), 49.9 (CH₂, C6'), 63.0 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 69.4 (5CH, Cp), 101.3 (C, C1, C-N), 169.2 (C, C=O); MS (EI, 70 eV): 283 [M], 218 [M-Cp]. **Crystal data for 2-Pipe.** C₁₅H₁₇FeNO, *M* = 283.14, orthorhombic, *P* b c a, *a* = 10.0250(13), *b* = 8.8225(10), *c* = 27.727(3) Å, *V* = 2452.3(5) Å³, *Z* = 8, *d* = 1.534 g cm⁻³, *μ* = 1.215 mm⁻¹. A final refinement on *F*² with 2793 unique intensities and 163 parameters converged at ω*R*(*F*²) = 0.0724 (*R*(*F*) = 0.0305) for 2385 observed reflections with *l* > 2σ(*l*). CCDC 2014646.

***N*-Ferrocenylhexahydro-2-azepinone (2-Azep).** The general procedure 1 starting from hexahydro-2-azepinone (0.12 g) gave **2-Azep** (eluent: hexane-AcOEt 60:40) in 32% yield (95 mg) as an orange solid: mp 102-104 °C; IR (ATR) 710, 803, 967, 1032, 1185, 1215, 1258, 1385, 1410, 1466, 1643, 2928 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 1.66 (quint, 2H, *J* = 4.8 Hz, H4'), 1.75-1.81 (m, 4H, H5' and H6'), 2.55-2.58 (m, 2H, H3'), 3.90-3.92 (m, 2H, H7'), 4.01 (t, 2H, *J* = 1.8 Hz, H3 and H4), 4.17 (s, 5H, Cp), 4.54 (t, 2H, *J* = 1.8 Hz, H2 and H5); ¹³C NMR ((CD₃)₂CO) δ 24.4 (CH₂, C4'), 29.4 and 30.2 (2CH₂, C5' and C6'), 38.7 (CH₂, C3'), 52.0 (CH₂, C7'), 63.7 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 69.4 (5CH, Cp), 101.9 (C, C1, C-N), 174.8 (C, C=O); MS (EI, 70 eV): 297 [M], 232 [M-Cp]. **Crystal data for 2-Azep.** C₁₆H₁₉FeNO, *M* = 297.17, monoclinic, *C* 2/c, *a* = 20.788(3), *b* = 13.387(2), *c* = 10.5242(13) Å, β = 114.189(4) °, *V* = 2671.6(7) Å³, *Z* = 8, *d* = 1.478 g cm⁻³, *μ* = 1.119 mm⁻¹. A final refinement on *F*² with 3051 unique intensities and 172 parameters converged at ω*R*(*F*²) = 0.0696 (*R*(*F*) = 0.0288) for 2630 observed reflections with *l* > 2σ(*l*). CCDC 2014647.

***N,N*-Diferrocenylacetamide (2-AcFc).** The general procedure 1 starting from *N*-ferrocenylacetamide (0.27 g) gave **2-AcFc** (eluent: hexane-AcOEt 60:40) in 8% yield (36 mg) as an

orange solid: mp 171–173 °C; IR (ATR) 800, 818, 1001, 1017, 1106, 1226, 1280, 1312, 1363, 1455, 1672, 2928, 3103 cm⁻¹; ¹H NMR (CDCl₃) δ 1.99 (s, 3H, Me), 4.06 (s, 10H, Cp), 4.11 (s, 4H, H3 and H4), 4.44 (s, 4H, H2 and H5); ¹³C NMR (CDCl₃) δ 24.4 (CH₃), 64.6 (4CH, C3 and C4), 66.6 (4CH, C2 and C5), 69.7 (10CH, Cp), 102.9 (2C, C1, C-N), 171.1 (C, C=O); MS (EI, 70 eV): 427 [M], 207. The NMR data are as reported previously.²⁴ **Crystal data for 2-AcFc.** C₂₂H₂₁Fe₂NO, *M* = 427.10, monoclinic, *P* 2₁/*n*, *a* = 17.0141(13), *b* = 10.6656(9), *c* = 20.1450(16) Å, β = 107.428(3) °, *V* = 3487.8(5) Å³, *Z* = 8, *d* = 1.627 g cm⁻³, μ = 1.674 mm⁻¹. A final refinement on *F*² with 8038 unique intensities and 471 parameters converged at ω*R*(*F*²) = 0.0853 (*R*(*F*) = 0.0341) for 6945 observed reflections with *l* > 2σ(*l*). CCDC 2014648.

***N*-Ferrocenyl-3-methoxy-*N*-methylbenzamide (2-3OMeMe).** The general procedure 1, but on a 5 mmol scale, starting from 3-methoxy-*N*-methylbenzamide (0.90 g) gave **2-3OMeMe** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.36) in 9% yield (165 mg) as a red glue oil: IR (ATR) 663, 693, 745, 788, 819, 877, 932, 1009, 1041, 1105, 1123, 1160, 1216, 1249, 1288, 1333, 1353, 1367, 1429, 1452, 1483, 1580, 1599, 1634, 2835, 2936, 3090 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 3.42 (br s, 3H, Me), 3.66 (s, 3H, OMe), 4.01 (s, 2H, H3 and H4), 4.11 (br s, 2H, H2 and H5), 4.26 (s, 5H, Cp), 6.74 (br s, 2H, H2' and H6'), 6.90 (d, 1H, *J* = 6.6 Hz, H4'), 7.18 (br s, 1H, H5'); ¹³C NMR ((CD₃)₂SO) δ 39.0 (CH₃, NMe), 55.5 (CH₃, OMe), 64.3 (2CH, C2 and C5), 65.1 (2CH, C3 and C4), 69.2 (5CH, Cp), 102.8 (C, C1, C-N), 113.6 (CH, C2'), 115.9 (CH, C4'), 120.5 (CH, C6'), 129.4 (CH, C5'), 138.2 (C, C1', C-C=O), 159.0 (C, C3', C-OMe), 169.8 (C, C=O). **Crystal data for 2-3OMeMe.** C₁₉H₁₉FeNO₂, *M* = 349.20, monoclinic, *P* 2₁, *a* = 8.9424(5), *b* = 9.3918(6), *c* = 18.8587(12) Å, β = 94.385(2) °, *V* = 1579.22(17) Å³, *Z* = 4, *d* = 1.469 g cm⁻³, μ = 0.964 mm⁻¹. A final refinement on *F*² with 6715 unique intensities and 419 parameters converged at ω*R*(*F*²) = 0.1996 (*R*(*F*) = 0.0804) for 6266 observed reflections with *l* > 2σ(*l*). CCDC 2014649.

3-Chloro-*N*-ferrocenyl-*N*-methylbenzamide (2-3ClMe). The general procedure 1, but on a 5 mmol scale, starting from 3-chloro-*N*-methylbenzamide (0.95 g) gave **2-3ClMe** (eluent: petroleum ether-AcOEt 70:30; *R*_f = 0.53) in 12% yield (225 mg) as a red solid: mp 138–140 °C; IR (ATR) 666, 683, 728, 760, 806, 853, 891, 917, 1001, 1027, 1050, 1106, 1130, 1222, 1295, 1331, 1354, 1369, 1411, 1478, 1563, 1631, 2928 cm⁻¹; ¹H NMR ((CD₃)₂SO) δ 3.43 (br s, 3H, Me), 4.03 (s, 2H, H3 and H4), 3.87–4.21 (br s, 2H, H2 and H5), 4.28 (s, 5H, Cp), 7.12 (br s, 1H, Ar), 7.22 (br s, 1H, Ar), 7.29 (br s, 1H, Ar), 7.39 (br s, 1H, Ar); ¹³C NMR ((CD₃)₂SO) δ 38.6 (CH₃), 64.1 (2CH, C2 and C5), 64.8 (2CH, C3 and C4), 68.8 (5CH, Cp), 102.1 (C, C1, C-N), 126.5 (CH, Ar), 127.7 (CH, Ar), 129.4 (CH, Ar), 129.7 (CH, Ar), 132.5 (C, Ar), 138.4 (C, Ar), 168.0 (C, C=O); MS (EI, 70 eV): 353 [M], 288 [M-Cp]. **Crystal data for 2-3ClMe.** C₁₈H₁₆ClFeNO, *M* = 353.62, triclinic, *P* -1, *a* = 10.3749(11), *b* = 11.6955(13), *c* = 13.3758(12) Å, α = 109.852(3), β = 100.413(3), γ = 91.180(4) °, *V* = 1495.5(3) Å³, *Z* = 4, *d* = 1.571 g cm⁻³, μ = 1.187 mm⁻¹. A final refinement on *F*² with 6806 unique intensities and 399 parameters converged at ω*R*(*F*²) = 0.1001 (*R*(*F*) = 0.0391) for 6090 observed reflections with *l* > 2σ(*l*). CCDC 2014650.

General procedure 2. Iodoferrocene (**1**; unless otherwise specified in the product description, 1.0 mmol), CuI (0.19 g, 1.0 mmol), *t*BuOK (0.11 g, 2.0 mmol) and the amide (1.1 mmol)

were introduced in a degassed Schlenk tube and dissolved in DMSO (2 mL). The reaction mixture was stirred under argon and heated at 90 °C for 14 h. It was then allowed to cool to room temperature before addition of water (10 mL). After extraction with AcOEt (3 x 20 mL), drying over MgSO₄ and evaporation of the solvent under reduced pressure, the coupling product was purified by chromatography over silica gel (the eluent is given in the product description).

***N*-(Ferrocenyl)trifluoroacetamide (2-CF₃).** The general procedure 2 starting from trifluoroacetamide (0.11 g) gave **2-CF₃** (eluent: petroleum ether-AcOEt 90:10; *R*_f = 0.48) in 56% yield (0.165 g) as an orange solid: mp 37–38 °C; IR (ATR) 802, 821, 903, 1001, 1106, 1144, 1170, 1256, 1314, 1474, 1559, 1701, 3106, 3325 cm⁻¹; ¹H NMR ((CD₃)₂CO) δ 4.08 (t, 2H, *J* = 2.0 Hz, H3 and H4), 4.16 (s, 5H, Cp), 4.76 (t, 2H, *J* = 2.0 Hz, H2 and H5), 9.93 (br s, 1H, NH); ¹³C NMR ((CD₃)₂CO) δ 62.6 (2CH, C2 and C5), 65.8 (2CH, C3 and C4), 70.1 (5CH, Cp), 93.5 (m, C, C1, C-N), 117.0 (q, C, *J* = 288 Hz, CF₃), 155.3 (q, C, *J* = 39.1 Hz, C=O); ¹⁹F NMR ((CD₃)₂CO) δ -76.1; ¹⁹F NMR (CDCl₃) δ -75.6; MS (EI, 70 eV): 297 [M]. The ¹H NMR data are similar to those reported previously.⁵⁸ **Crystal data for 2-CF₃.** C₁₂H₁₀F₃FeNO, *M* = 297.06, monoclinic, *P* 2₁/*c*, *a* = 15.261(3), *b* = 7.4670(11), *c* = 10.2018(16) Å, β = 109.261(6) °, *V* = 1097.5(3) Å³, *Z* = 4, *d* = 1.798 g cm⁻³, μ = 1.400 mm⁻¹. A final refinement on *F*² with 2466 unique intensities and 166 parameters converged at ω*R*(*F*²) = 0.0720 (*R*(*F*) = 0.0333) for 2147 observed reflections with *l* > 2σ(*l*). CCDC 2014638.

General procedure 3. The *N*-ferrocenylbenzamide (1.0 mmol) was dissolved in THF (8 mL) and treated by NaH (~60% dispersion in mineral oil; 0.12 g, 3.0 mmol). After 15 min at room temperature, MeI (0.43 g, 0.19 mL, 3.0 mmol) was added and the reaction mixture was stirred for 0.5 h at room temperature. It was then cooled to 0 °C before addition of water (10 mL). After extraction with AcOEt (3 x 20 mL) and drying over MgSO₄, the product was purified by chromatography over silica gel (the eluent is given in the product description).

***N*-Ferrocenyl-*N*-methylbenzamide (2-PhMe).** The general procedure 2 starting from *N*-ferrocenylbenzamide (0.31 g) gave **2-PhMe** (eluent: petroleum ether-AcOEt 70:30) in 96% yield (0.31 g) as an orange solid: mp 132–134 °C; IR (ATR) 670, 701, 726, 762, 793, 816, 826, 926, 1008, 1028, 1055, 1105, 1132, 1155, 1180, 1223, 1293, 1333, 1354, 1368, 1402, 1422, 1446, 1487, 1574, 1598, 1628, 1979, 2854, 2923, 3031, 3095 cm⁻¹; ¹H NMR (CDCl₃) δ 3.53 (s, 3H, Me), 3.96 (s, 2H, H3 and H4), 4.00 (br s, 2H, H2 and H5), 4.23 (s, 5H, Cp), 7.19–7.30 (m, 5H, Ph); ¹³C NMR (CDCl₃) δ 38.9 (CH₃, NMe), 64.2 (2CH, C2 and C5), 65.0 (2CH, C3 and C4), 69.1 (5CH, Cp), 102.9 (C, C1, C-N), 127.8 and 128.5 (CH, C2' and C6', and CH, C3' and C5'), 129.8 (CH, C4'), 136.3 (C, C1', C-C=O), 171.0 (C, C=O); MS (EI, 70 eV): 319 [M], 254 [M-Cp], 207. The IR and ¹H NMR data are as reported previously.⁶² **Crystal data for 2-PhMe.** C₁₈H₁₇FeNO, *M* = 319.17, monoclinic, *P* 2₁/*c*, *a* = 9.6323(9), *b* = 10.0838(12), *c* = 15.0175(18) Å, β = 95.784(4) °, *V* = 1451.2(3) Å³, *Z* = 4, *d* = 1.461 g cm⁻³, μ = 1.036 mm⁻¹. A final refinement on *F*² with 3316 unique intensities and 191 parameters converged at ω*R*(*F*²) = 0.0699 (*R*(*F*) = 0.0263) for 3050 observed reflections with *l* > 2σ(*l*). CCDC 2014651.

***N*-Ferrocenyl-3-methoxy-*N*-methylbenzamide (2-3OMeMe).** The general procedure 2 starting from *N*-ferrocenyl-3-methoxybenzamide (0.34 g) gave **2-3OMeMe** (eluent: petroleum ether-AcOEt 70:30; Rf = 0.36) in 88% yield (33 mg) as a red glue oil. The analyses are as reported before in the present paper.

***N*-Benzyl-3-chloro-*N*-ferrocenylbenzamide (2-3ClBn).** Sodium hydride (60% in mineral oil, 0.33 g, 7.5 mmol) was added to a solution of 3-chloro-*N*-ferrocenylbenzamide (**2-3Cl**; 0.85 g, 2.5 mmol) and tetrabutylammonium bromide (80 mg, 0.25 mmol) in tetrahydrofuran (40 mL) at room temperature, and the reaction mixture was stirred for 15 min. Benzyl bromide (0.89 mL, 7.5 mmol) was added and the reaction mixture was stirred at room temperature for 3 h. Water (20 mL) was added and the reaction mixture was extracted with AcOEt (3 x 20 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under reduced pressure. Purification by chromatography over silica gel (eluent: petroleum ether-AcOEt 90:10 to 70:30) gave **2-3ClBn** in 90% yield (0.97 g) as an orange solid: Rf (petroleum ether-AcOEt 80:20) = 0.40; mp 129-131 °C; IR (ATR) 664, 695, 719, 744, 758, 794, 823, 845, 881, 898, 923, 1001, 1016, 1026, 1076, 1104, 1233, 1293, 1311, 1333, 1349, 1377, 1404, 1421, 1456, 1475, 1495, 1566, 1631, 1645, 3096 cm⁻¹; ¹H NMR (CDCl₃) δ 3.90 (br s, 2H, H2 and H5), 3.95 (s, 2H, H3 and H4), 4.20 (s, 5H, Cp), 5.35 (br s, 2H, CH₂), 7.14-7.15 (m, 2H, Ar), 7.27-7.32 (m, 2H, Ar), 7.34 (s, 1H, H2'), 7.39-7.40 (m, 4H, H2'', H3'', H5'' and H6''); ¹³C NMR (CDCl₃) δ 55.8 (CH₂), 64.8 (2CH, C2 and C5), 65.1 (2CH, C3 and C4), 69.3 (5CH, Cp), 103.7 (C, C1, C-N), 126.6 (CH, Ar), 126.8 (CH, Ar), 127.4 (2CH, C2'' and C6''), 128.7 (CH, Ar), 128.9 (2CH, C3'' and C5''), 129.1 (CH, C2'), 130.1 (CH, Ar), 134.0 (C, C3', C-Cl), 138.1 (C, Ar), 138.4 (C, Ar), 169.3 (C, C=O). **Crystal data for 2-3ClBn.** C₂₄H₂₀ClFeNO, *M* = 429.71, triclinic, *P* -1, *a* = 10.9882(5), *b* = 12.9018(5), *c* = 14.8228(5) Å, α = 99.381(2), β = 91.4120(10), γ = 109.2600(10)°, *V* = 1950.30(13) Å³, *Z* = 4, *d* = 1.463 g cm⁻³, μ = 0.925 mm⁻¹. A final refinement on *F*² with 8850 unique intensities and 505 parameters converged at ω*R*(*F*²) = 0.0730 (*R*(*F*) = 0.0321) for 7363 observed reflections with *l* > 2σ(*l*). CCDC 2014652.

***N*-Benzyl-3-(2,5-dimethoxyphenyl)-*N*-ferrocenylbenzamide (2-PF1).** *N*-benzyl-3-chloro-*N*-ferrocenylbenzamide (**2-3ClBn**; 0.21 g, 0.5 mmol), 2,5-dimethoxybenzeneboronic acid (0.14 g, 0.75 mmol), palladium(II) acetate (1.1 mg, 5 μmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos; 4.1 mg, 10 μmol) and tripotassium phosphate (0.21 g, 1.0 mmol) were charged in a degassed Schlenk. Tetrahydrofuran (1.0 mL) was added and the reaction mixture was heated at 60 °C for 14 h. The reaction mixture was cooled to room temperature. Water (5 mL) was added and the reaction mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under reduced pressure. Purification by column chromatography over silica gel (eluent: petroleum ether-AcOEt-Et₃N 69:30:1) gave **2-PF1** in 24% yield (0.14 g) as an orange solid: Rf (petroleum ether-AcOEt 80:20) = 0.37; mp 58-60 °C; IR (ATR) 697, 718, 808, 908, 999, 1025, 1040, 1052, 1106, 1149, 1178, 1216, 1259, 1307, 1336, 1374, 1407, 1475, 1502, 1578, 1602, 1637, 2249, 2832,

2932 cm⁻¹; ¹H NMR (CDCl₃) δ 3.68 (s, 3H, C2''-OMe), 3.77 (s, 3H, C5''-OMe), 3.96 (s, 2H, H3 and H4), 4.00 (br s, 2H, H2 and H5), 4.22 (s, 5H, Cp), 5.38 (br s, 2H, CH₂), 6.66 (d, 1H, *J* = 2.9 Hz, H6''), 6.83 (dd, 1H, *J* = 8.9 and 2.9 Hz, H4''), 6.88 (d, 1H, *J* = 8.9 Hz, H3''), 7.27-7.31 (m, 2H, H5' and H6'), 7.35-7.38 (m, 3H, H3'', H4'' and H5''), 7.39-7.41 (m, 3H, H2' and H2''), 7.53 (d, 1H, *J* = 7.6 Hz, H4'); ¹³C NMR (CDCl₃) δ 55.7 (CH₂), 56.0 (CH₃, C5'''-OMe), 56.5 (CH₃, C2'''-OMe), 64.7 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 69.2 (5CH, Cp), 104.3 (C, C1, C-N ferrocenyl), 113.1 (CH, C3'''), 113.8 (CH, C4'''), 116.5 (CH, C6'''), 126.8 (C2'' and C6''), 127.2 (CH, C6'), 127.3 (CH, C4''), 127.6 (CH, C5'), 128.9 (2CH, C3'' and C5''), 129.4 (CH, C2'), 131.0 (C, C3'), 131.4 (CH, C4'), 136.1 (C, C1', C-C=O), 138.0 (C, C1'''), 138.7 (C, C1'', C-CH₂), 150.9 (C, C2''), 153.9 (C, C5'''), 170.8 (C, C=O).

***N*-Benzyl-*N*-ferrocenyl-3-(*N*-morpholino)benzamide (2-PF2).** *N*-benzyl-3-chloro-*N*-ferrocenylbenzamide (**2-3ClBn**; 0.21 g, 0.5 mmol), palladium(II) acetate (1.1 mg, 5 μmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (SPhos; 4.1 mg, 10 μmol) and sodium *tert*-butoxide (64 mg, 0.65 mmol) were charged in a degassed Schlenk. Morpholine (52.5 μL) and tetrahydrofuran (1.0 mL) were added and the reaction mixture was heated at 85 °C for 14 h. The reaction mixture was cooled to room temperature. Water (5 mL) was added and the reaction mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtrated over cotton wool and concentrated under reduced pressure. Purification by column chromatography over silica gel (eluent: petroleum ether-AcOEt-Et₃N 69:30:1; Rf = 0.19) gave **2-PF2** in 79% yield (0.19 g) as an orange solid: mp 66-68 °C; IR (ATR) 664, 695, 747, 792, 817, 864, 920, 946, 1000, 1028, 1069, 1106, 1120, 1146, 1242, 1263, 1305, 1338, 1374, 1408, 1439, 1475, 1576, 1598, 1638, 2855, 2959 cm⁻¹; ¹H NMR (CDCl₃) δ 3.01 (t, 4H, *J* = 4.8 Hz, 2CH₂-N morpholino), 3.80 (t, 4H, *J* = 4.8 Hz, 2CH₂-O), 3.92 (s, 2H, H3 and H4), 3.96 (br s, 2H, H2 and H5), 4.19 (s, 5H, Cp), 5.33 (br s, 2H, CH₂-N benzyl), 6.82 (d, 1H, *J* = 7.8 Hz, H6'), 6.85 (dd, 1H, *J* = 7.8 and 2.4 Hz, H4'), 6.87 (s, 1H, H2'), 7.12 (t, 1H, *J* = 7.8 Hz, H5'), 7.27-7.29 (m, 1H, H4''), 7.36-7.39 (m, 4H, H2'', H3'', H5'' and H6''); ¹³C NMR (CDCl₃) δ 49.3 (2CH₂, CH₂-N morpholino), 55.7 (CH₂, CH₂-N benzyl), 64.5 (2CH, C2 and C5), 64.9 (2CH, C3 and C4), 66.9 (2CH₂, CH₂-O morpholino), 69.2 (5CH, Cp), 104.1 (C, C1), 116.0 (CH, C2'), 117.5 (CH, C4'), 120.3 (CH, C6'), 126.8 and 128.9 (2CH, C2'' and C6'', and 2CH, C3'' and C5''), 127.2 (CH, C4''), 128.7 (CH, C5'), 137.0 (C, C1', C-C=O), 138.8 (C, C1'', C-CH₂ benzyl), 150.8 (C, C3', C-N morpholino), 171.0 (C, C=O).

Conclusions

Thus, while it is not suitable to forge C-N bonds between iodoferrocene and partners such as benzylamine, pyrazole and imidazole, our protocol allows for the coupling of iodoferrocene with primary and cyclic secondary amides to rapidly deliver libraries of ferrocene amide derivatives. It is complementary to the method developed by Bolm to create C-N bonds between iodoferrocene and azoles or, as we have shown in the present paper, between iodoferrocene and an acetamide bearing electron-withdrawing groups. Extension of these results to the copper-catalysed amidation with substituted iodoferrocenes is

currently under investigation in the lab and will be reported in due course.

Conflicts of interest

There are no conflicts to declare.

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