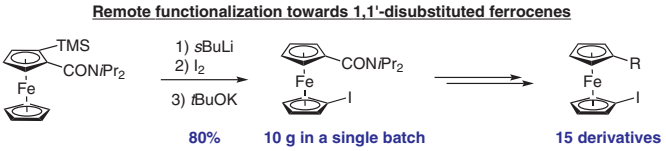
Synthesis L. Kadari et al. PSP

Remote Deprotometalation-Iodolysis of *N*,*N*-Diisopropyl-2-trimethylsilylferrocenecarboxamide: A New Route Toward 1,1′-Disubstituted Ferrocenes

Lingaswamy Kadari[a,b]
Thierry Roisnel[a]
William Erb*[a]
Palakodety Radha Krishna*[b]
Florence Mongin[a]

[a] Univ Rennes, CNRS, ISCR (Institut des Sciences Chimiques de Rennes)-UMR 6226, 35000 Rennes, France
william.erb@univ-rennes1.fr
[b] Organic Synthesis and Process Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500007, India
prkgenius@iict.res.in



Received: 19.05.2020
Accepted after revision: 08.06.2020
Published online: 01.07.2020
DOI: 10.1055/s-0040-1707175; Art ID: ss-2020-f0274-psp

Abstract The 1,1′-disubstitution is currently the most frequent substitution pattern encountered in the ferrocene series. Here an original access based on the remote deprotometalation of *N*,*N*-diisopropyl-2-trimethylsilylferrocenecarboxamide is reported. The key intermediate, 1′-iodo-*N*,*N*-diisopropylferrocenecarboxamide, was prepared in multiple grams and was further functionalized toward fifteen 1′-substituted iodoferrocenes.

Key words ferrocene, 1,1′-disubstitution, carboxamide, remote functionalization, functional group manipulation

The discovery of ferrocene in 1952 has profoundly changed the organometallic chemistry landscape and this sandwich compound remains one of the most important organometallic scaffolds.[1] Among the various substitution patterns explored in ferrocene chemistry, the most popular is the 1,1′-disubstitution, with applications in catalysis,[2] material science,[3] and bio-inorganic chemistry.[3a,4]

1,1′-Disubstituted ferrocenes with the same substituents can easily be obtained by two complementary approaches: (1) the ferrocene core assembly from the corresponding monosubstituted cyclopentadienes[5] and (2) the double deprotometalation-electrophilic trapping sequence from ferrocene.[6] However, while 1′-substituted iodoferrocenes represent an important family of precursors to unsymmetrical compounds,[7] they cannot be directly prepared by one of the above mentioned approaches. Therefore, the most popular synthetic routes currently rely on the halogen/Li or Sn/Li mono-exchange of such 1,1′-disubstituted ferrocenes. Buttler initially reported the mono I/Li exchange from 1,1′-diiodoferrocene using *n*BuLi, followed by an electrophilic trapping step (Scheme 1, approach a, R = CO_2H, $SnBu_3$).[8] However, low yields were obtained (28–32%), linked with the highly sensitive nature of the reaction as expressed in a footnote. Similar low yields were recorded by Christmann, Sarkar, and Heretsch using tosyl azide as the electrophile[9] while Lentz and later Nijhuis, both using tributyltin chloride, managed to isolate 1-iodo-1′-tributylstannylferrocene in good yields (77 and 84%, respectively).[10] The concentration was proposed as being an important reaction parameter in such reactions,[11] and the development of a flow-based approach partially solved this issue.[9] From 1,1′-bis(tributylstannyl)ferrocene, Wright reported a controlled Sn/Li mono-exchange by using *n*BuLi before interception with an electrophile.[12] However, iodine cannot be introduced this way due to a competitive Sn/I exchange leading to mixtures of products. Therefore, another substituent needs to be introduced first, before performing the final Sn/I exchange using iodine. Such approach was illustrated with success during the synthesis of 1′-iodoferrocenecarboxaldehyde (Scheme 1, approach b, R = CHO).[13] Finally, Dong developed a mono Li/Br exchange-electrophilic trapping sequence from 1,1′-dibromoferrocene;[14] this was used by Ilyashenko as the key step in the synthesis of 1-bromo-1′-iodoferrocene (78% yield; Scheme 1, approach c, R = Br).[11]

The other strategies toward 1′-substituted iodoferrocene start from monosubstituted ferrocenes and rely on functionalizations at the unsubstituted cyclopentadienyl (Cp) ring, remote from the substituent. The regioselective aromatic electrophilic substitution of iodoferrocene using acetyl chloride in the presence of iron trichloride was first attempted by Richards.[15] However, the expected 1,1′-disubstituted product was not obtained due to competitive deiodination observed under the reaction conditions. However, by using *N*-methylformanilide in the presence of phosphorus oxychloride, Yuan managed to isolate the corresponding 1′-iodoferrocenecarboxaldehyde in a moderate 61% yield (Scheme 1, approach d, R = CHO).[16]

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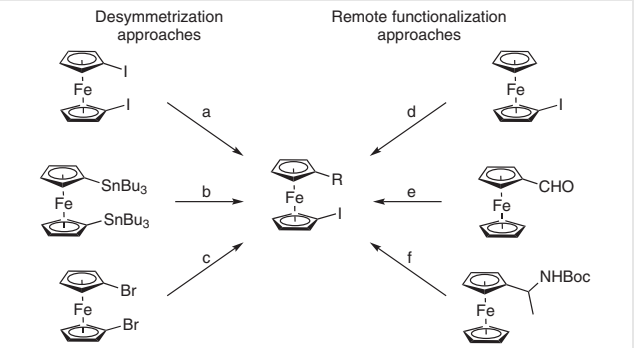


Scheme 1 Reported approaches toward 1′-substituted iodoferrocenes. *Reagents and conditions*: a) i. *n*BuLi, ii. CO_2 or nBu_3SnCl; b) i. *n*BuLi; ii. Me_2NCHO, iii. I_2; c) i. *n*BuLi; ii. I_2; d) PhN(Me)CHO, $POCl_3$; e) i. *N*-methylpiperazine Li salt, ii. *t*BuLi, iii. I_2; f) i. *n*BuLi; ii. I_2.

The use of directing groups able to reroute the classical *ortho*-deprotometalation to the unsubstituted Cp ring represents the second approach in the remote functionalization strategy. Balavoine and Manoury reported the reaction of the lithium salt of *N*-methylpiperazine with ferrocenecarboxaldehyde, followed by a deprotolithiation-electrophilic trapping sequence toward 1′-iodoferrocenecarboxaldehyde in a moderate 50% yield (Scheme 1, approach e, R = CHO).[17] The *N*-methylpiperazine acts as a protecting group for the aldehyde (temporary formation of the hemiaminal salt) and as the directing group with methylated nitrogen atom. More recently, Chong revealed a similar behavior for *N*-Boc protected α-methylated aminomethylferrocene in deprotolithiation and managed to obtain the corresponding iodinated derivative in a 71% yield [Scheme 1, approach f, R = CH(Me)NHBoc].[18]

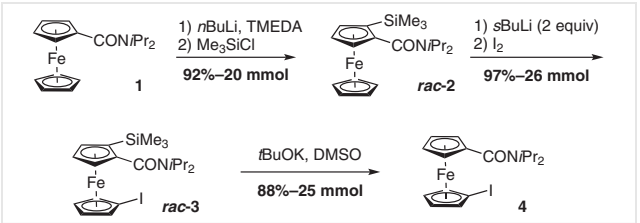
A few other catalytic desymmetrizations of 1,1′-diiodoferrocene have been reported, based on Stille,[10a,19] Sonogashira,[20] Suzuki–Miyaura,[21] and Ulmann[22] cross-couplings and by aminocarbonylation.[23] However, the selectivity is often an issue in such transformations, leading to mixtures of products.

In the frame of ongoing studies dedicated to the synthesis of original ferrocene derivatives,[24] we required an access to different 1′-substituted iodoferrocene derivatives. We initially focused our work on the mono-exchange of 1,1′-diiodoferrocene by using *n*BuLi, as this approach has the potential to easily deliver many derivatives by varying the electrophile.[8] However, regardless of the reaction conditions, only traces of the desired products were invariably obtained while 1,1′-bis-functionalized derivatives and mixtures of 1,1′-diiodoferrocene, iodoferrocene, and ferrocene were mainly obtained. We briefly evaluated the Manoury approach,[17] but failed to obtain significant amounts of the title products by using iodine as the electrophile. Moderate success was encountered in our attempts to achieve a mono Sn/Li exchange from 1,1′-bis(tributylstannyl)ferrocene[12] by using *n*BuLi and either methyl chloroformate or dimethylformamide as the electrophile (22 or 25% yield, respectively). However, as we recognized that the synthesis of the targeted compounds would require the manipulation of large quantities of toxic stannylated products, the need for another original approach emerged.

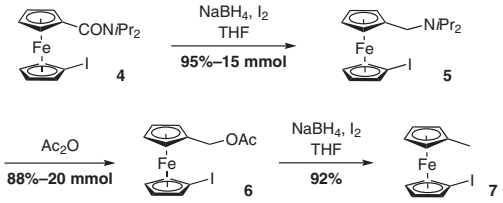
In his seminal paper on the enantioselective deprotometalation of *N*,*N*-diisopropylferrocenecarboxamide,[25] Snieckus reported that the introduction of a trimethylsilyl group at position 2 was able to reroute a further deprotometalation to the unsubstituted Cp ring. While a similar behavior was also noticed by Richards on ferrocene oxazolines,[26] this remote functionalization has never been considered as a valuable synthetic tool. Therefore, our plan was to use a silyl group to temporarily protect the position next to the carboxamide and favor the remote deprotometalation to introduce iodine onto the unsubstituted ring. Final deprotection of the silyl group would afford the targeted 1,1′-disubstituted ferrocenes.

We first deprotolithiated *N*,*N*-diisopropylferrocenecarboxamide (**1**)[27] by using the *n*BuLi·TMEDA (TMEDA: *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) chelate before intercepting the lithiated intermediate with trimethylsilyl chloride toward the ferrocene *rac*-**2**, isolated in a 92% yield (Scheme 2). To reach the iodinated derivative *rac*-**3**, we initially applied the Snieckus reaction conditions by using *s*BuLi (1.2 equiv) in THF at cryogenic temperature (–80 to –78 °C) before addition of iodine as the electrophile.[25] However, the title product was isolated in a disappointing 50% yield together with recovered starting material. While recourse to the more reactive *s*BuLi·TMEDA chelate improved the conversion to 95%, formation of inseparable by-products was noticed. However, the use of 2 equivalents of *s*BuLi at cryogenic temperature (–80 to –78 °C) led to a complete conversion and the ferrocene *rac*-**3** was isolated in a 95% yield on a 1 mmol scale. Pleasingly, the yield remained constant upon scaling up (97% yield on a 26 mmol scale). Although the trimethylsilyl group is usually removed upon treatment with fluorides,[28] we found that *rac*-**3** was reluctant to desilylation under smooth reaction conditions (2 equivalents of tetrabutylammonium fluoride at room temperature) and that decomposition occurred upon heating. However, the use of a stoichiometric amount of potassium *tert*-butoxide in dimethyl sulfoxide afforded **4** in a promising 70% yield after only 5 minutes.[29] Evaluation of other reaction conditions revealed a complete conversion with increased amount of potassium *tert*-butoxide, reaction time, and concentration, delivering **4** in an 80% yield on a 1 mmol scale. Furthermore, it was possible to scale-up the reaction up to 25 mmol with a slightly better yield (88%, 10 g of product **4** made in a single batch).

Clues about the origin of this remote functionalization can be found in the solid-state structure of compound *rac*-**2**. Indeed, to release the steric pressure generated between the diisopropyl and trimethysilyl moieties, the C=O bond of the carboxamide needs to be almost perpendicular to the



Scheme 2 Remote functionalization strategy toward the 1,1′-disubstituted ferrocene **4**



Scheme 3 Functional group manipulation toward the methylated derivative **7**

Cp ring (Figure 1, right and S.I.). As shown by a variable temperature ^{1}H NMR study (see S.I.), rotation of the C=O to reach the conformation favorable to the *ortho*-deprotometalation (C=O parallel with the Cp ring, Figure 1, left), is too energetic. Therefore, the only reaction observed is the remote deprotometalation, probably favored by the C=O bound pointing toward the unsubstituted Cp ring to guide the approach of the lithiated base (Figure 1, right).

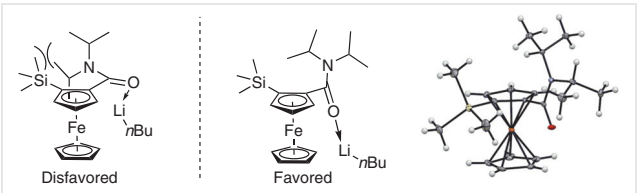
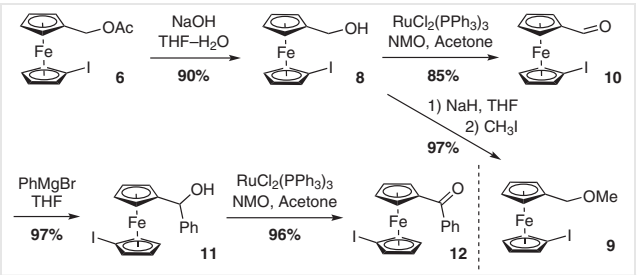


Figure 1 Rationalization of the origin of the remote deprotometalation

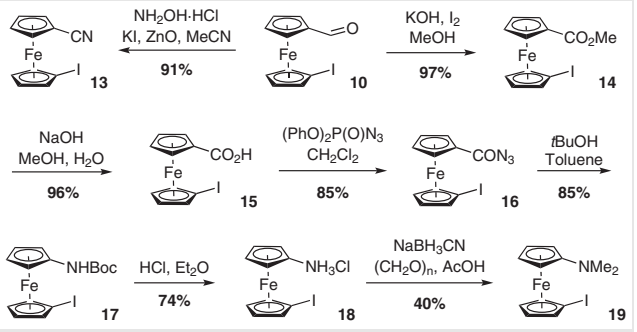
With a reliable protocol toward **4** in hands, we next focused our attention onto the carboxamide transformation. While the borane-mediated reduction of similar substrates is well known,[25,30] transformation of the resulting diisopropylamine moiety did not receive much attention[31] until we recently documented the substitution of this bulky amine for an acetate.[32] Consequently, the carboxamide **4** was reduced by an excess of borane (generated in situ from sodium borohydride and iodine) in refluxing tetrahydrofuran to deliver **5** in a 95% yield (Scheme 3). The substitution step then occurred smoothly in neat acetic anhydride at 160 °C for 1 hour and **6** was isolated in a 88% yield on a 20 mmol scale (6.7 g of compound in a single batch). During the reduction of **4** to **5**, traces of a by-product, tentatively assigned to be 1-iodo-1′-methylferrocene (**7**), were noticed. To validate its structure, we engaged the acetate in another borane reduction and indeed isolated **7** in a 92% yield.

Saponification of the acetate **6** with sodium hydroxide in a tetrahydrofuran/water mixture at 80 °C led to the isolation of the alcohol **8** in a 90% yield (Scheme 4). It should be noted that the use of methanol/water mixtures in such reaction should be avoided as variable amounts of the methyl ether **9** can be formed as a side-product. However, it is possible to obtain **9** in an almost quantitative yield by the deprotonation of the alcohol using sodium hydride followed by the interception of the alkoxide with methyl iodide. The known aldehyde **10** then was prepared by a ruthenium-mediated oxidation in the presence of *N*-methylmorpholine oxide initially described by Sharpless.[33] Addition of phenylmagnesium bromide to the aldehyde afforded the alcohol **11** in a 97% yield, which was finally converted into the known ketone **12** in a 96% yield by following the same ruthenium-mediated oxidation protocol.



Scheme 4 Functional group manipulation toward the ketone **12** (NMO: *N*-methylmorpholine oxide)

While condensation of the aldehyde **10** with hydroxylamine followed by dehydration led to 1′-iodoferrocenecarbonitrile (**13**) in 91% yield (Scheme 5),[34] it is known that such substrates are difficult to oxidize under classical conditions.[35] However, reaction of **10** with iodine in the presence of potassium hydroxide[36] in methanol led to the ester **14** in a very good 97% yield. The acid **15** was easily made by saponification in 96% yield and it was further reacted with diphenylphosphoryl azide by following our recently developed protocol[37] toward the acyl azide **16**, isolated in an 85% yield. Curtius rearrangement at 110 °C in the presence of *tert*-butyl alcohol to intercept the intermediate isocyanate allowed the isolation of the Boc-protected aminoferrocene **17** (85% yield). Removal of the protecting group was easily done by using an ethereal solution of HCl at room temperature toward **18**, isolated in a 74% yield as its HCl salt. Although salts of aminoferrocene derivatives are known to be more stable when compared to the free base, storage of **18** in a closed vessel without specific protection led to decomposition. A double reductive amination[38] with paraformaldehyde in the presence of an excess of sodium cyanoborohydride was finally performed toward the sensitive dimethylaminoferrocene **19**, isolated in a 40% yield.



Scheme 5 Functional group manipulation toward the dimethylaminoferrocene derivative **19**

In conclusion, we have reported a new route toward 1′-substituted iodoferrocenes based on a remote deprotometalation observed more than 20 years ago and never exploited. By following this methodology, grams of our key substrate, 1′-iodo-*N*,*N*-diisopropylferrocenecarboxamide, were prepared and further functionalized towards fifteen 1,1′-disubstituted ferrocenes, most of them being fully described for the first time.

Unless otherwise stated, all the reactions were performed under an argon atmosphere with anhydrous solvents using Schlenk technics. THF and Et_2O were distilled over Na-benzophenone, DMSO and toluene were distilled over CaH_2, and acetone and MeOH were dried by prolonged contact over activated 3Å molecular sieves.[39] Unless otherwise stated, all reagents were used without prior purification. All organolithiated reagents were titrated before use.[40] *t*BuOK (99.99% quality) was purchased from Sigma-Aldrich and used without further purification. Column chromatography separations were achieved on silica gel (40–63 µm). All TLC analyses were performed on aluminum backed plates pre-coated with silica gel (Merck, Silica Gel 60 F254). They were visualized by exposure to UV light. Melting points were measured on a Kofler bench. IR spectra were taken on a PerkinElmer Spectrum 100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded either (i) on a Bruker Avance III spectrometer at 300 MHz and 75.4 MHz, respectively, or (ii) on a Bruker Avance III at 400 MHz and 100 MHz, respectively or (iii) on a Bruker Avance III HD at 500 MHz and 126 MHz, respectively. ^{1}H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ^{13}C chemical shifts are relative to the central peak of the solvent signal. Cp refers to the unsubstituted cyclopentadienyl ring of ferrocene.

N,*N*-Diisopropyl-2-trimethylsilylferrocenecarboxamide (*rac*-2) [CAS Reg. No. 173910-99-1]

TMEDA (4.50 mL, 3.49 g, 30.0 mmol, 1.50 equiv, freshly distilled over $CaCl_2$ and stored over KOH pellets) and anhyd Et_2O (90.0 mL) were introduced into a flame-dried round-bottom flask under argon. The reaction mixture was cooled between –80 and –78 °C (external temperature) in an acetone/liquid N_2 bath. *n*BuLi (1.4 M, 21.4 mL, 30.0 mmol, 1.50 equiv) was then introduced dropwise by syringe. After addition, the reaction mixture was stirred at the same temperature for 15 min. Compound **1** (6.26 g, 20.0 mmol, 1.00 equiv) was introduced into a separate flame-dried round-bottom flask, which was subjected to three cycles of vacuum/argon. Anhyd Et_2O (90.0 mL) was added and the solution was stirred until dissolution of all solids. The solution of **1** was transferred into the *n*BuLi·TMEDA chelate solution dropwise by cannula keeping the temperature between –80 and –78 °C. The flask was washed with anhyd Et_2O (10 mL), also transferred by cannula. After addition, the reaction mixture was stirred at the same temperature for 1 h. Me_3SiCl (5.10 mL, 4.34 g, 40.0 mmol, 2.00 equiv) was added dropwise by syringe keeping the temperature between –80 and –78 °C. The mixture was then allowed to warm to –15 °C, keeping the flask into the bath. At –15 °C, the cooling bath was removed and the mixture was warmed to rt. H_2O (100 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 75 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PE/EtOAc (80:20) to give the title product *rac*-**2** as an orange solid; yield: 7.12 g (92%); mp 108–110 °C.

Analytical data analogous to those reported previously.[25]

IR (film): 2966, 1628, 1441, 1368, 1328, 1278, 1243, 1148, 1035, 833, 807, 753 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.34 (dd, *J* = 1.2, 2.3 Hz, 1 H, H5), 4.29 (t, *J* = 2.3 Hz, 1 H, H4), 4.27 (s, 5 H, Cp), 4.13 (dd, *J* = 1.2, 2.3 Hz, 1 H, H3), 4.11 (br s, 1 H, CH), 3.39 (br s, 1 H, CH), 1.45 (br s, 6 H, 2 × CH_3), 1.11 (br s, 6 H, 2 × CH_3), 0.27 [s, 9 H, $Si(CH_3)_3$].

^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.9 (C=O), 92.3 (C1), 73.7 (C2), 73.5 (C3), 69.9 (Cp + C5), 69.4 (C4), 50.1 (CH), 45.9 (CH), 21.1 (2 × CH_3), 20.9 (2 × CH_3), 0.7 [$Si(CH_3)_3$].

rac-**2** was also characterized by X-ray structural data.[41]

1′-Iodo-*N*,*N*-diisopropyl-2-trimethylsilylferrocenecarboxamide (*rac*-3)

*s*BuLi (1.2 M, 43.3 mL, 52.0 mmol, 2.00 equiv) was added dropwise to a solution of *rac*-**2** (10.0 g, 26.0 mmol, 1.00 equiv) in anhyd Et_2O (300 mL) between –80 and –78 °C. The reaction mixture was stirred at the same temperature for 1 h after addition. I_2 (19.8 g, 78.0 mmol, 3.00 equiv) was introduced in a separate flame-dried round-bottomed flask under argon and was dissolved in anhyd Et_2O (300 mL). The I_2 solution was transferred by cannula into the reaction mixture. The flask was washed with anhyd Et_2O (10 mL), also transferred by cannula. After addition, the reaction mixture was stirred at the same temperature for 30 min before being warmed to rt. A sat. aq solution of $Na_2S_2O_3$ (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PE/EtOAc (99:1) to give the title product *rac*-**3** as an orange oil; yield: 12.9 g (97%).

IR (film): 2961, 2866, 1626, 1442, 1368, 1326, 1274, 1244, 1150, 1034, 830, 809, 756 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.51 (s, 1 H, FcH), 4.40 (s, 1 H, FcH), 4.38 (s, 1 H, FcH), 4.29 (s, 1 H, H5), 4.28 (s, 1 H, FcH), 4.25 (s, 1 H, H4), 4.08 (s, 1 H, H3), 3.98 (br s, 1 H, CH), 3.38 (br s, 1 H, CH), 1.46 (br s, 6 H, 2 × CH_3), 1.07 (br s, 6 H, 2 × CH_3), 0.26 [s, 9 H, $Si(CH_3)_3$].

^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.2 (C=O), 93.5 (C1), 77.4 (C3), 76.7 (FcCH), 75.6 (C2), 75.3 (FcCH), 73.9 (C4), 73.6 (C5), 72.1 (FcCH), 71.6 (FcCH), 50.3 (CH), 45.8 (CH), 40.4 (C1′), 21.2 (2 × CH_3), 20.8 (2 × CH_3), 0.7 [$Si(CH_3)_3$].

MS: *m*/*z* = 511 [M], 496 [M – CH_3].

1′-Iodo-*N*,*N*-diisopropylferrocenecarboxamide (4) [CAS Reg. No. 2407448-99-9]

*t*BuOK (5.72 g, 51.0 mmol, 2.00 equiv) was added to a solution of *rac*-**3** (13.0 g, 25.5 mmol, 1.00 equiv) in DMSO (76.5 mL) and the reaction mixture was stirred for 10 min at rt. Cold H_2O (200 mL) was added to the reaction mixture, which was extracted with EtOAc (4 × 70 mL). The combined organic layers were washed with brine (4 × 50 mL), dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography using PE/EtOAc (85:15) to give the title product **4** as an orange solid; yield: 9.92 g (88%); mp 58–60 °C.

IR (film): 2964, 1615, 1459, 1368, 1315, 1201, 1043, 1029, 862, 825, 804, 762 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.49 (t, *J* = 1.9 Hz, 2 H, H2, H5), 4.46 (br s, 1 H, CH), 4.41 (t, *J* = 1.9 Hz, 2 H, H2′, H5′), 4.26–4.24 (m, 4 H, H3, H4, H3′, H4′), 3.41 (br s, 1 H, CH), 1.47 (br s, 6 H, 2 × CH_3), 1.21 (br s, 6 H, 2 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5 (C=O), 83.5 (C1), 76.5 (C2′, C5′), 73.1 (C2, C5), 72.2 (C3, C4), 71.3 (C3′, C4′), 49.8 (CH), 46.4 (CH), 40.1 (C1′), 21.3 (4 × CH_3).

MS: *m*/*z* = 439 [M], 339 [M – N*i*Pr$_2$].

1-(*N*,*N*-Diisopropylaminomethyl)-1′-iodoferrocene (5)

$NaBH_4$ (2.84 g, 75.0 mmol, 5.00 equiv) was introduced into a flame-dried round-bottom flask equipped with a bubbler, and THF (75.0 mL) was added before the reaction mixture was cooled to 0 °C. I_2 (9.14 g, 36.0 mmol, 2.40 equiv) was introduced into a separate flame-dried round-bottom flask under argon and was dissolved into anhyd THF (30.0 mL). The I_2 solution was transferred into the $NaBH_4$ suspension dropwise by cannula. **Remark**: vigorous evolution of H_2 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 **4** (6.60 g, 15.0 mmol, 1.00 equiv) was then added portionwise to the BH_3·THF solution, which was then stirred overnight at reflux **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 aq NaOH (10%, 75 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. The mixture was cooled to rt and the layers were separated. The aqueous layer was further extracted with EtOAc (2 × 50 mL). The combined organic layers were extracted with aq 1 M HCl (3 × 50 mL). The combined aqueous layers were washed with Et_2O (2 × 50 mL) and basified with solid K_2CO_3 until pH 8 was reached. The mixture was extracted with EtOAc (2 × 60 mL) and the combined organic layers were dried ($MgSO_4$), filtered on Celite (washed with EtOAc until the filtrate was colorless), and concentrated under vacuum using a rotary evaporator to give the pure product **5** as an orange oil; yield: 6.08 g (95%).

IR (film): 3090, 2961, 1684, 1461, 1380, 1360, 1200, 1164, 1136, 1115, 1018, 861, 823, 807 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.31 (t, *J* = 1.6 Hz, 2 H, H2′, H5′), 4.15 (t, *J* = 1.6 Hz, 2 H, H2, H5), 4.10 (d, *J* = 1.6 Hz, 2 H, H3′, H4′), 4.09 (d, *J* = 1.6 Hz, 2 H, H3, H4), 3.47 (s, 2 H, CH_2), 3.04 (sept, *J* = 6.7 Hz, 2 H, 2 × CH), 1.02 (d, *J* = 6.7 Hz, 12 H, 4 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 90.4 (C1), 75.1 (C2′, C5′), 72.9 (C2, C5), 70.6 (C3, C4), 69.4 (C3′, C4′), 47.7 (2 × CH), 43.4 (CH_2), 41.0 (C1′), 21.0 (4 × CH_3).

MS: *m*/*z* = 439 [M], 339 [M – N*i*Pr$_2$].

1-(Acetoxymethyl)-1′-iodoferrocene (6)

Compound **5** (8.53 g, 20.0 mmol, 1.00 equiv) was dissolved into Ac_2O (76.2 mL, 82.3 g, 800 mmol, 40.0 equiv) at rt and the resulting solution was stirred at 160 °C in a pre-heated bath for 1 h. The reaction mixture was cooled to 0 °C and EtOAc (150 mL) was added before pouring the mixture onto ice (200 mL). Solid K_2CO_3 was added under stirring until pH 8 was reached. **Caution**: small portions of K_2CO_3 should be added each time as vigorous evolution of gas occurred. The layers were separated and the aqueous layer was extracted with EtOAc (75 mL). The combined organic layers were washed with H_2O (75 mL), brine (50 mL), dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (95:5) to give the title product **6** as an orange solid; yield: 6.75 g (88%); mp 54–56 °C.

IR (film): 3090, 2961, 1684, 1461, 1380, 1360, 1200, 1164, 1136, 1115, 1018, 861, 823, 807 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.91 (s, 2 H, CH_2), 4.39 (t, *J* = 1.7 Hz, 2 H, H2′, H5′), 4.22 (m, 2 H, H3, H4), 4.21 (m, 2 H, H2, H5), 4.15 (t, *J* = 1.7 Hz, 2 H, H3′, H4′), 2.05 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.9 (C=O), 82.9 (C1), 75.3 (C2′, C5′), 72.6 (C3, C4), 72.0 (C2, C5), 69.5 (C3′, C4′), 62.2 (CH_2), 39.9 (C1′), 21.1 (CH_3).

MS: *m*/*z* = 439 [M], 339 [M – N*i*Pr$_2$].

1-Iodo-1′-methylferrocene (7) [CAS Reg. No. 31833-00-8]

Compound **6** (384 mg, 1.00 mmol, 1.00 equiv) was added portionwise to a solution of BH_3 in THF (1.0 M, 5.00 mL, 5.00 mmol, 5.00 equiv) at rt before the reaction mixture was heated at reflux 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 a solution of aq 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. The reaction mixture was cooled to rt and the layers were separated. The aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were washed with H_2O (10 mL), brine (10 mL), dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (95:5) to give the title product **7** as an orange oil; yield: 300 mg (92%).

IR (film): 3087, 2918, 1476, 1453, 1403, 1382, 1368, 1342, 1227, 1144, 1039, 1022, 860, 822, 804 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.31 (t, *J* = 1.6 Hz, 2 H, H2, H5), 4.11 (t, *J* = 1.6 Hz, 2 H, H3, H4), 4.09 (t, *J* = 1.7 Hz, 2 H, H3′, H4′), 4.04 (t, *J* = 1.7 Hz, 2 H, H2′, H5′), 2.01 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 85.7 (C1′), 75.2 (C2, C5), 72.4 (C2′, C5′), 70.3 (C3′, C4′), 69.5 (C3, C4), 40.9 (C1), 14.2 (CH_3).

MS: *m*/*z* = 326 [M].

1′-Iodoferrocenemethanol (8) [CAS Reg. No. 224456-53-5]

NaOH (2.04 g, 51.0 mmol, 3.00 equiv) was dissolved in H_2O (55.0 mL) and a solution of compound **6** (6.50 g, 17.0 mmol, 1.00 equiv) in THF (30.0 mL) was added at rt. The reaction mixture was heated at 80 °C for 2 h in a pre-heated bath. The mixture was cooled to rt and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary

evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (95:5) to give the title product **8** as an orange solid; yield: 5.23 g (90%); mp 58–60 °C.

Analytical data analogous to those reported previously.[13]

IR (film): 3325, 3097, 2925, 2863, 1402, 1379, 1343, 1235, 1143, 1040, 996, 922, 862, 825, 738 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.40–4.39 (m, 4 H, H2′, H5′, CH_2), 4.19 (s, 4 H, H2, H3, H4, H5), 4.16 (t, *J* = 1.8 Hz, 2 H, H3′, H4′), 1.78 (br s, 1 H, OH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 89.6 (C1), 75.0 (C2′, C5′), 71.4 (C2, C5 or C3, C4), 70.9 (C2, C5 or C3, C4), 69.3 (C3′, C4′), 60.3 (CH_2), 40.1 (C1′).

MS: *m*/*z* = 342 [M], 264.

1-Iodo-1′-(methoxymethyl)ferrocene (9)

NaH (60% dispersion in oil, 120 mg, 3.00 mmol, 3.00 equiv) was added portionwise to a solution of compound **8** (342 mg, 1.00 mmol, 1.00 equiv) in THF (5.00 mL) at 0 °C. After addition, the cooling bath was removed and the reaction mixture was stirred for 1 h at rt. The mixture was cooled to 0 °C and MeI (250 µL, 568 mg, 4.00 mmol, 4.00 equiv) was added dropwise. After addition, the cooling bath was removed and the mixture was stirred for 1 h at rt. The mixture was cooled to 0 °C and sat. aq NH_4Cl (10 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 ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (80:20) to give the title product **9** as an orange oil; yield: 346 mg (97%).

IR (film): 3089, 2920, 2887, 2813, 1447, 1402, 1379, 1344, 1234, 1187, 1175, 1085, 1038, 1021, 899, 862, 824, 809 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.36 (s, 2 H, H2, H5), 4.25 (s, 2 H, CH_2), 4.19 (s, 4 H, H2′, H3′, H4′, H5′), 4.13 (s, 2 H, H3, H4), 3.34 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 84.8 (C1′), 75.1 (C2, C5), 72.4 (C2′, C5′ or C3′, C4′), 71.7 (C2′, C5′or C3′, C4′), 70.2 (CH_2), 69.4 (C3, C4), 57.9 (CH_3), 40.1 (C1).

MS: *m*/*z* = 356 [M].

1′-Iodoferrocenecarboxaldehyde (10) [CAS Reg. No. 176100-20-2]

NMO (5.04 g, 43.0 mmol, 3.50 equiv) was placed in a Schlenk tube, which was heated at 90 °C under high vacuum for 3 h before being cooled to rt. In a separate Schlenk tube, compound **8** (4.22 g, 12.3 mmol, 1.00 equiv) was dissolved in acetone (120 mL) and this solution was cannulated onto NMO. $RuCl_2(PPh_3)_3$ (589 mg, 0.61 mmol, 0.05 equiv) was added in one portion and the reaction mixture was stirred at rt for 1 h, shielded from light. The mixture was concentrated under vacuum using a rotary evaporator. Aq 1 M HCl (40 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2 using PE/EtOAc (80:20) with 1% of NEt_3 to give the title product **10** as a red solid; yield: 3.57 g (85%); mp 31–33 °C.

Analytical data analogous to those reported previously.[13]

IR (film): 3096, 2801, 2761, 1673, 1658, 1455, 1368, 1343, 1242, 1026, 824, 740 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 10.00 (s, 1 H, CHO), 4.77 (t, *J* = 2.0 Hz, 2 H, H2, H5), 4.59 (t, *J* = 2.0 Hz, 2 H, H3, H4), 4.50 (t, *J* = 1.9 Hz, 2 H, H2′, H5′), 4.26 (t, *J* = 1.9 Hz, 2 H, H3′, H4′).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.4 (CHO), 80.6 (C1), 76.4 (C3, C4), 76.3 (C2′, C5′), 72.4 (C2, C5), 70.6 (C3′, C4′), 39.4 (C1′).

1-[Hydroxy(phenyl)methyl]-1′-iodoferrocene (11)

A solution of phenylmagnesium bromide in THF (0.90 M, 2.10 mL, 1.90 mmol, 0.95 equiv) was added dropwise to a solution of compound **10** (680 mg, 2.00 mmol, 1.00 equiv) in THF (20.0 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 monitored by TLC. After consumption of the starting material, sat. aq NH_4Cl (20 mL) was added and the mixture was warmed to rt before being extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (80:20) to give the title product **11** as a red solid; yield: 812 mg (97%); mp 76–78 °C.

Splitting of some ferrocene peaks was noticed in both ^1H and ^{13}C NMR spectrum as previously observed in chiral ferrocenemethanol derivatives.[42]

IR (film): 3470, 1490, 1449, 1377, 1179, 1047, 1018, 806, 716 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 2 H, H2″, H6″), 7.35–7.32 (m, 2 H, H3″, H5″), 7.28–7.26 (m, 1 H, H4″), 5.59 (d, *J* = 3.2 Hz, 1 H, CH), 4.46 (m, 1 H, H2′ or H5′), 4.45 (m, 1 H, H2′ or H5′), 4.27 (dd, *J* = 1.8, 3.3 Hz, 1 H, H2 or H5), 4.21 (m, 2 H, H3, H4), 4.19 (m, 2 H, H3′, H4′), 4.14 (dd, *J* = 1.8, 3.3 Hz, 1 H, H2 or H5), 2.44 (d, *J* = 3.3 Hz, 1 H, OH).

^1H NMR (500 MHz, DMSO-d_6): δ = 7.38 (d, *J* = 7.7 Hz, 2 H, H2″, H6″), 7.31 (t, *J* = 7.7 Hz, 2 H, H3″, H5″), 7.22 (t, *J* = 7.7 Hz, 1 H, H4″), 5.50–5.48 (m, 2 H, OH + CH), 4.44 (m, 1 H, FcCH), 4.40 (m, 1 H, FcCH), 4.27 (m, 1 H, FcCH), 4.18 (m, 2 H, FcCH), 4.08 (m, 1 H, FcCH), 4.06 (m, 1 H, FcCH), 3.94 (m, 1 H, FcCH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.4 (C1″), 128.4 (C3″, C5″), 127.7 (C4″), 126.4 (C2″, C6″), 95.2 (C1), 75.3 (C2′ or C5′), 75.2 (C2′ or C5′), 71.9 (CH), 71.5 (C3 or C4), 71.3 (C3 or C4), 70.3 (C2 or C5), 69.6 (C3′ or C4′), 69.5 (C3′ or C4′), 68.9 (C2 or C5), 40.1 (C1′).

1-Benzoyl-1′-iodoferrocene (12) [CAS Reg. No. 1884149-19-2]

NMO (351 mg, 3.00 mmol, 3.00 equiv) was placed in a Schlenk tube, which was heated at 90 °C under high vacuum for 3 h before cooling to rt. In a separate Schlenk tube, compound **11** (418 mg, 1.00 mmol, 1.00 equiv) was dissolved in acetone (10.0 mL) and this solution was cannulated onto NMO. $RuCl_2(PPh_3)_3$ (47.9 mg, 50.0 µmol, 0.05 equiv) was added in one portion and the reaction mixture was stirred at rt for 1 h, shielded from light. Volatiles were removed under vacuum using a rotary evaporator. Aq 1 M HCl (20 mL) was added and the mixture was extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (80:20) with 1% of NEt_3 to give the title product **12** as a red oil; yield: 400 mg (96%).

Analytical data analogous to those reported previously.[10b]

IR (film): 1635, 1447, 1438, 1374, 1282, 1168, 1048, 1024, 852, 828, 797, 724 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 2 H, H2″, H6″), 7.55 (t, *J* = 7.2 Hz, 1 H, H4″), 7.47 (t, *J* = 7.6 Hz, 2 H, H3″, H5″), 4.90 (t, *J* = 1.9 Hz, 2 H, H2, H5), 4.55 (t, *J* = 1.9 Hz, 2 H, H3, H4), 4.41 (t, *J* = 1.8 Hz, 2 H, H2′, H5′), 4.19 (t, *J* = 1.8 Hz, 2 H, H3′, H4′).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 198.2 (C=O), 139.6 (C1″), 131.8 (C4″), 128.4 (C3″, C5″), 128.3 (C2″, C6″), 79.7 (C1), 76.6 (C2′, C5′), 76.1 (C3, C4), 74.0 (C2, C5), 71.4 (C3′, C4′), 40.0 (C1′).

1′-Iodoferrocenecarbonitrile (13) [CAS Reg. No. 32876-20-3]

Compound **10** (0.68 g, 2.00 mmol, 1.00 equiv), $NH_2OH{\cdot}HCl$ (181 mg, 2.60 mmol, 1.30 equiv), KI (0.53 g, 2.00 mmol, 1.00 equiv), and ZnO (0.16 mg, 2.00 mmol, 1.00 equiv) were introduced in a Schlenk tube, which was subjected to three cycles of vacuum/argon. MeCN (10.0 mL) was added and the reaction mixture was stirred at 80 °C for 2 h. The mixture was cooled to rt and 5% aq $Na_2S_2O_3$ (2.00 mL) was added and stirring was continued for 5 min. The mixture was filtered and the resulting solids were washed with EtOAc (10 mL). H_2O (10 mL) was added to the combined filtrates, which were extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography, using PE/EtOAc (90:10) to give the title product **13** as a dark red solid; yield: 0.61 g (91%); mp 39–41 °C.

IR (film): 3101, 3087, 2224, 1406, 1381, 1346, 1233, 1023, 865, 845, 812 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.62 (t, *J* = 1.9 Hz, 2 H, H2, H5), 4.55 (t, *J* = 1.9 Hz, 2 H, H2′, H5′), 4.39 (t, *J* = 1.9 Hz, 2 H, H3, H4), 4.34 (t, *J* = 1.9 Hz, 2 H, H3′, H4′).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 119.2 (C≡N), 77.0 (C2′, C5′), 74.4 (C2, C5), 74.2 (C3, C4), 71.7 (C3′, C4′), 54.1 (C1), 39.8 (C1′).

MS: *m*/*z* = 337 [M], 210 [M – I], 183.

Methyl 1′-Iodoferrocenecarboxylate (14) [CAS Reg. No. 31869-23-5]

KOH (2.53 g, 45.0 mmol, 6.00 equiv) was added to a solution of compound **10** (2.51 g, 7.50 mmol, 1.00 equiv) in MeOH (98.0 mL) at 0 °C. I_2 (5.71 g, 22.5 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, aq 1 M HCl (30 mL) was added, and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with sat. aq $Na_2S_2O_3$ (20 mL), H_2O (10 mL), brine (10 mL), dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2, using PE/EtOAc (90:10) to give the title product **14** as an orange solid; yield: 2.69 g (97%); mp 75–77 °C.

IR (film): 2942, 1706, 1465, 1375, 1344, 1273, 1191, 1139, 1030, 696, 865, 843, 819, 773 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.78 (t, *J* = 1.9 Hz, 2 H, H2, H5), 4.41 (t, *J* = 1.7 Hz, 2 H, H2′, H5′), 4.38 (t, *J* = 1.9 Hz, 2 H, H3, H4), 4.17 (t, *J* = 1.7 Hz, 2 H, H3′, H4′), 3.82 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (C=O), 76.2 (C2′, C5′), 74.4 (C3, C4), 73.5 (C1), 72.7 (C2, C5), 70.7 (C3′, C4′), 51.8 (CH_3), 40.4 (C1′).

MS: *m*/*z* = 370 [M].

1′-Iodoferrocenecarboxylic Acid (15) [CAS Reg. No. 31832-98-1]

NaOH (1.40 g, 35.0 mmol, 5.00 equiv) dissolved in H_2O (42.0 mL) was added to a solution of compound **14** (2.60 g, 7.00 mmol, 1.00 equiv) in MeOH (35.0 mL) at rt and the reaction mixture was heated at 80 °C in a pre-heated bath for 75 min. The mixture was cooled to rt and MeOH 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 filtered and washed with cold (0 °C) H_2O (2 × 5 mL) and pentane (10 mL). Drying the solid under high vacuum with a P_2O_5 trap afforded the title product **15** as a dark red solid; yield: 2.39 g (96%); mp 153–155 °C.

IR (film): 3108, 2857 (br), 2636, 2562, 1667, 1482, 1296, 1166, 1025, 840, 745 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.86 (s, 2 H, H2, H5), 4.48 (s, 2 H, H2′, H5′), 4.47 (s, 2 H, H3, H4), 4.28 (s, 2 H, H3′, H4′). Acid proton missing.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.9 (C=O), 76.5 (C2′, C5′), 75.4 (C3, C4), 73.2 (C2, C5), 72.1 (C1), 71.2 (C3′, C4′), 40.3 (C1′).

1′-Iodoferrocenoyl Azide (16)

Et_3N (4.32 mL, 3.14 g, 31.0 mmol, 5.00 equiv) was added to a solution of compound **15** (2.20 g, 6.20 mmol, 1.00 equiv) in CH_2Cl_2 (12.0 mL) at 40 °C. Diphenylphosphoryl azide (1.47 mL, 1.88 g, 6.82 mmol, 1.10 equiv) was added dropwise to the reaction mixture, which was then kept at the same temperature for 10 min. The mixture was cooled to rt and aq 1 M HCl (30 mL) was added. The mixture was extracted with Et_2O (2 × 30 mL) and the combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2 using pentane/Et_2O (90:10) to give the title product **16** as a red solid; yield: 2.02 g (85%); mp 102–104 °C.

IR (film): 2146, 1673, 1452, 1372, 1261, 1191, 1052, 989, 829, 818 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.81 (t, *J* = 1.9 Hz, 2 H, H2, H5), 4.49 (t, *J* = 1.9 Hz, 2 H, H3, H4), 4.47 (t, *J* = 1.8 Hz, 2 H, H2′, H5′), 4.24 (t, *J* = 1.8 Hz, 2 H, H3′, H4′).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.0 (C=O), 76.6 (C2′, C5′), 75.7 (C3, C4), 74.5 (C1), 72.8 (C2, C5), 71.1 (C3′, C4′), 40.7 (C1′).

1-(*tert*-Butoxycarbonyl)amino-1′-iodoferrocene (17)

tert-BuOH (2.40 mL, 1.85 g, 25.0 mmol, 5.00 equiv) was added to a solution of compound **16** (1.85 g, 5.00 mmol, 1.00 equiv) in toluene (31.0 mL) at rt and the reaction mixture was heated at 100 °C for 1 h in a pre-heated oil bath. The mixture was cooled to rt and volatiles were removed under vacuum to give the crude product. This was purified by column chromatography, using PE/EtOAc (90:10) to give the title product **17** as an orange solid; yield: 1.81 g (85%); mp 100–102 °C.

IR (film): 3354, 2147, 1697, 1550, 1389, 1366, 1252, 1157, 1073, 1028, 867, 808 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.86 (br s, 1 H, NH), 4.42 (br s, 2 H, H2, H5), 4.38 (s, 2 H, H2′, H5′), 4.13 (s, 2 H, H3′, H4′), 3.98 (s, 2 H, H3, H4), 1.51 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (126 MHz, $CDCl_3$): δ = 153.3 (C=O), 97.5 (C1), 80.3 [$C(CH_3)_3$], 75.6 (C2′, C5′), 69.7 (C3′, C4′), 67.1 (C3, C4), 62.9 (C2, C5), 42.6 (C1′), 28.5 [$C(CH_3)_3$].

1′-Iodoferrocenamine Hydrochloride (18)

A solution of HCl in Et_2O (≈ 5.00 M, 24.0 mL, 120 mmol, 40.0 equiv) was added to a solution of compound **17** (1.28 g, 3.00 mmol, 1.00 equiv) in Et_2O (30.0 mL) and the reaction mixture was stirred at rt for 2 h. The resulting solid was quickly filtered and washed with Et_2O (2 ×

10 mL) and pentane (10 mL), and dried under high vacuum to give the title product **18** as an orange solid; yield: 800 mg (74%); mp 146–148 °C.

IR (film): 2802, 2601, 2569, 1672, 1608, 1521, 1469, 1375, 1143, 1023, 855, 833, 818 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.84 (br s, 3 H, NH_3^+), 4.61 (s, 2 H, H2′, H5′), 4.43 (s, 2 H, H2, H5), 4.39 (s, 2 H, H3′, H4′), 4.13 (s, 2 H, H3, H4).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 89.2 (C1), 75.7 (C2′, C5′), 71.1 (C3′, C4′), 70.1 (C3, C4), 65.7 (C2, C5), 39.0 (C1′).

1-(Dimethylamino)-1′-iodoferrocene (19)

$NaBH_3CN$ (754 mg, 12.0 mmol, 6.00 equiv) was added portionwise to a solution of compound **18** (727 mg, 2.00 mmol, 1.00 equiv) and paraformaldehyde (720 mg, 24.0 mmol, 12.0 equiv) in glacial AcOH (6.00 mL) at rt. The reaction mixture was stirred for 4 h before additional portions of paraformaldehyde (120 mg, 4.00 mmol, 2.00 equiv) and $NaBH_3CN$ (120 mg, 2.00 mmol, 1.00 equiv) were added to the mixture, which was stirred at rt overnight. EtOAc (20 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 (2 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered over cotton wool, and concentrated under vacuum using a rotary evaporator to give the crude product. This was purified by column chromatography over SiO_2 using PE/EtOAc (80:20 to 70:30) to give the title product **19** as an orange solid; yield: 284 mg (40%); mp 52–54 °C.

IR (film): 3094, 2922, 1628, 1598, 1487, 1445, 1422, 1367, 1354, 1333, 1293, 1052, 1028, 1008, 814, 792, 726, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.52 (s, 2 H, H2′, H5′), 4.24 (s, 2 H, H3′, H4′), 3.97 (s, 2 H, H3, H4), 3.71 (s, 2 H, H2, H5), 2.66 (br s, 6 H, 2 × CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 117.2 (C1), 73.1 (C2′, C5′), 67.8 (C3′, C4′), 66.9 (C3, C4), 58.1 (C2, C5), 42.4 (2 × CH_3), 40.6 (C1′).

Funding Information

This work was supported by the Université de Rennes 1 and CNRS.

Acknowledgment

The authors would like to acknowledge Région Bretagne for a postdoctoral fellowship grant (L. K.). We gratefully acknowledge the Fonds Européen de Développement Régional (FEDER; D8 VENTURE Bruker AXS diffractometer) and Thermofisher (generous gift of 2,2,6,6-tetramethylpiperidine). This research has been performed as part of the Indo-French 'Joint Laboratory for Natural Products and Synthesis towards Affordable Health'. The authors would like to acknowledge Mehdi Tazi for growing crystals of compound *rac*-**2**.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1707175.

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