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Halide-Mediated *Ortho*-Deprotonation Reactions Applied to the Synthesis of 1,2- and 1,3-Disubstituted Ferrocene Derivatives

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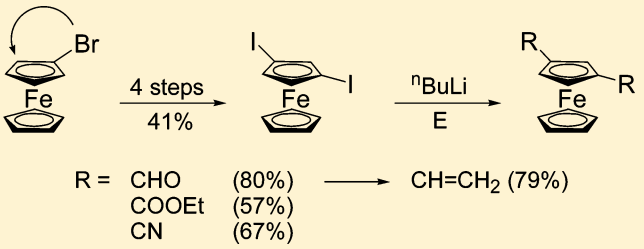
Supporting Information

ABSTRACT: The *ortho*-deprotonation of halide-substituted ferrocenes by treatment with lithium tetramethylpiperidide (LiTMP) has been investigated. Iodo-, bromo-, and chloro-substituted ferrocenes were easily deprotonated adjacent to the halide substituents. The synthetic applicability of this reaction was, however, limited by the fact that, depending on the temperature and the degree of halide substitution, scrambling of both iodo and bromo substituents at the ferrocene core took place. Iodoferrocenes could not be transformed selectively into *ortho*-substituted iodoferrocenes since, in the presence of LiTMP, the iodo substituents scrambled efficiently even at −78 °C, and this process had occurred before electrophiles had been added. Bromoferrocene and certain monobromo-substituted derivatives, however, could be efficiently *ortho*-deprotonated at low temperature and reacted with a number of electrophiles to afford 1,2- and 1,2,3-substituted ferrocene derivatives. For example, 2-bromo-1-iodoferrocene was synthesized by *ortho*-deprotonation of bromoferrocene and reaction with the electrophiles diiodoethane and diiodotetrafluoroethane, respectively. In this and related cases the iodide scrambling process and further product deprotonation due to the excess LiTMP could be suppressed efficiently by running the reaction at low temperature and in inverse mode. In contrast to the low-temperature process, at room temperature bromo substituents in bromoferrocenes scrambled in the presence of LiTMP. Chloro- and 1,2-dichloroferrocene could be *ortho*-deprotonated selectively, but in neither case was scrambling of a chloro substituent observed. As a further application of this *ortho*-deprotonation reaction, a route for the synthesis of 1,3-disubstituted ferrocenes was developed. 1,3-Diiodoferrocene was accessible from bromoferrocene in four steps. On a multigram scale an overall yield of 41% was achieved. 1,3-Diiodoferrocene was further transformed into symmetrically 1,3-disubstituted ferrocenes (1,3-R_2Fc; R = CHO, COOEt, CN, CH═CH_2).



INTRODUCTION

Ferrocene derivatives have found broad application in a number of different fields including catalysis, bioorganometallic chemistry, and material sciences, and all of these areas have been reviewed extensively.[1−4] For applications in catalysis, besides achiral 1,1′-heteroannularly substituted ferrocenes, chiral homoannularly 1,2-substituted derivatives are mainly used. As a consequence, a huge number of methodologies have been developed for the synthesis of 1,2-disubstituted ferrocenes.[1c,d]

The majority of these approaches make use of *ortho*-directing groups. For example, both *N*,*N*-dimethylaminomethylferrocene[5] and chloroferrocene[6] can be *ortho*-deprotonated by treatment with *n*-butyllithium, and the lithiated intermediates can be further reacted with electrophiles to afford 1,2-disubstituted products (Scheme 1).

Recently, we reported on biferrocene diphosphines as ligands for hydrogenation catalysts.[7] The ligand synthesis was achieved by a Negishi coupling reaction, and for this purpose racemic 2-bromo-1-iodoferrocene was required. In this context we questioned whether this derivative could be synthesized in one step from commercially available bromoferrocene. As reported by Butler in 1999,[8] in analogy to bromoarenes,[9] bromoferrocene and 1,1′-dibromoferrocene can be *ortho*-deprotonated with LDA (lithium diisopropylamide). Further reaction of the lithiated intermediates with a number of electrophiles gave *ortho*-substituted bromo- or 1,1′-dibromoferrocenes with moderate yields. We subsequently showed that the *ortho*-deprotonation of bromoferrocenes can be significantly

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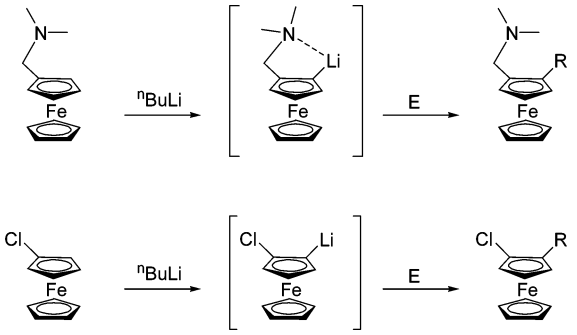
Scheme 1



improved by using LiTMP (lithium 2,2,6,6-tetramethylpiperidide) in place of LDA and by optimizing the reaction conditions.[10] This approach allowed access to a variety of enantiopure 1,2,3- and 1,3-substituted ferrocenes.[10,11]

Two methods for the preparation of racemic 2-bromo-1-iodoferrocene have been reported to date, and these were developed by Butler[12] and Mongin/Krishna,[13] respectively. Butler's procedure starts from 1,1′-dibromoferrocene, which affords the desired product after consecutive treatment with BuLi, LiTMP, and ICF_2CF_2I. According to Mongin/Krishna, bromoferrocene can be deprotonated with a mixture of LiTMP and $Zn(TMP)_2$. Subsequent reaction with iodine gave 2-bromo-1-iodoferrocene in 64% yield. However, significant amounts of byproducts were formed in both types of reaction.

Only in a few cases has bromoferrocene been used as the starting material for *ortho*-deprotonation reactions.[8,13,14] As a consequence, we questioned whether its scope of application could be extended not only to the synthesis of other 1,2-disubstituted ferrocenes but also to 1,3- or higher-substituted derivatives.

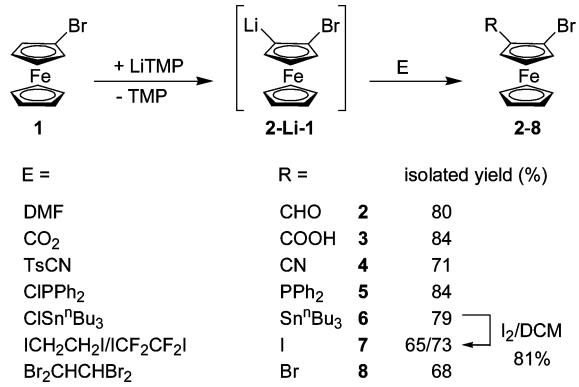
In this work we show how bromoferrocene can be *ortho*-deprotonated selectively by LiTMP and subsequently transformed into a variety of 1,2-di-, 1,2,3-tri-, and 1,3-disubstituted ferrocene derivatives and how the formation of certain byproducts can be suppressed. In addition, the possibility of using this methodology to transform selectively iodo- and chloroferrocenes into their *ortho*-substituted derivatives was evaluated.

RESULTS AND DISCUSSION

***Ortho*-Deprotonation of Bromoferrocenes.** Treatment of bromoferrocene (**1**) with 1.5 equiv of LiTMP and subsequent reaction with one of the electrophiles DMF, CO_2, TsCN, $ClPPh_2$, or $ClSn^nBu_3$ provided the 1,2-disubstituted products **2**–**6** selectively in 71–84% isolated yield (Scheme 2).[15] Products with other substitution patterns were not detected in any case. During optimization of the reaction conditions it was noticed that the conversion of bromoferrocene (**1**) to products depended significantly on the bromoferrocene/LiTMP ratio. For example, when bromoferrocene was reacted with 1, 1.25, 1.5, or 2 equiv of LiTMP and when $ClSn^nBu_3$ was subsequently used as the electrophile, the conversion of bromoferrocene to the product 2-bromo-1-tributylstannylferrocene (**6**) increased from 75% to 84%, 90%, and 93%, as determined by NMR spectroscopy. On the basis of these data we considered a LiTMP/substrate ratio of 1.5:1 to be a suitable compromise.

Interestingly, when bromoferrocene was reacted with 1.5 equiv of LiTMP and iodine or 1,2-diiodoethane were added to

Scheme 2. Synthesis of 2-Substituted Bromoferrocenes



the reaction mixture, not only the desired product 2-bromo-1-iodoferrocene (**7**) but also the trisubstituted derivative 2-bromo-1,3-diiodoferrocene (**9**) and other differently substituted monobromo-iodoferrocenes were obtained (Scheme 3). The structural integrity of **9** was confirmed by an X-ray diffraction study (Figure 1).

In this particular case, one might assume that the electrophile (I_2 or ICH_2CH_2I) reacts faster with *ortho*-lithiated bromoferrocene **2-Li-1** to form the desired product **7** than with the excess LiTMP still present in the reaction mixture. This would allow excess LiTMP to further *ortho*-deprotonate **7** next to either the bromo or the iodo substituent. Subsequent reaction with the electrophile would lead to products **9** and **11**, respectively. Similarly, **12** would be formed from **9**. Only **10** would not be accessible from **1** through a sequence of *ortho*-deprotonation/iodination reactions, but this could result from an iodide scrambling process (a detailed discussion is provided below). It appeared, however, that all byproducts were formed in routes that involve compound **7** as the intermediate. On the basis of this assumption, the reaction was carried out in the inverse mode (slow addition of lithiated **1** to the electrophile).

The *ortho*-lithiated bromoferrocene **2-Li-1** was added slowly at −78 °C to a solution of either ICH_2CH_2I or ICF_2CF_2I in THF, and this reversal of the addition completely suppressed the formation of byproducts to give **7** in 65% and 73% isolated yield, respectively (Scheme 2). Running the reaction in the inverse mode ensures that during the whole reaction period the electrophile is present in large excess rather than LiTMP.

Alternatively, 2-bromo-1-iodoferrocene (**7**) could be obtained in 81% yield and with excellent purity by reaction of **6** in CH_2Cl_2 with a solution of iodine in CH_2Cl_2 (Scheme 4). The use of 1,1,2,2-tetrabromoethane as the electrophile and running the reaction in the inverse mode also allowed access to 1,2-dibromoferrocene (**8**)[14c] in 68% yield (Scheme 2).

We subsequently attempted to carry out a further selective *ortho*-deprotonation on 2-substituted bromoferrocenes. It is clear that a second *ortho*-deprotonation can be expected to take place selectively only if the substituent adjacent to the bromo substituent does not itself show *ortho*-directing properties. Examples of such reactions have been reported previously by Butler,[16] our group,[10,11a] and others.[11b,c]

In this work the 2-bromo-1-tributylstannylferrocene derivative **6** was reacted with LiTMP, and the lithiated intermediate was quenched with $ClSn^nBu_3$ to provide the 1,2,3-trisubstituted product **13** in good yield (76–82%, Scheme 4). However, when 2-bromo-1-iodoferrocene (**7**) was *ortho*-deprotonated with LiTMP and subsequently reacted with ICH_2CH_2I, besides the

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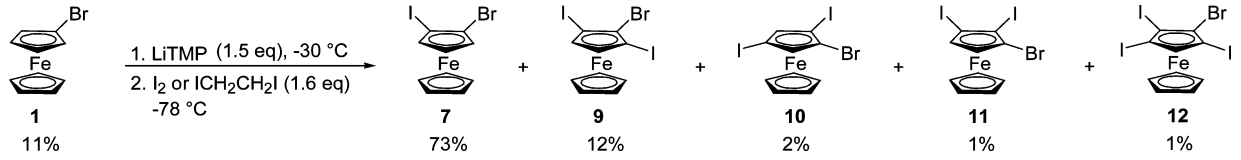
Scheme 3



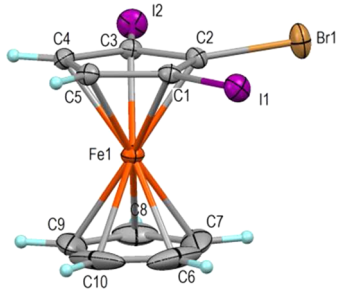
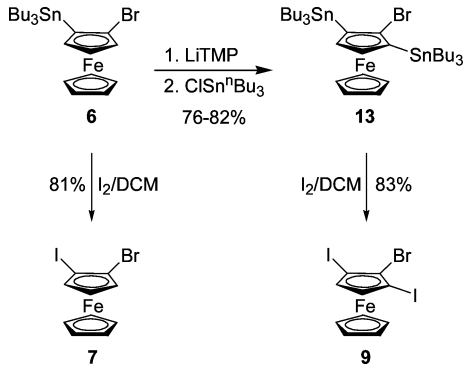
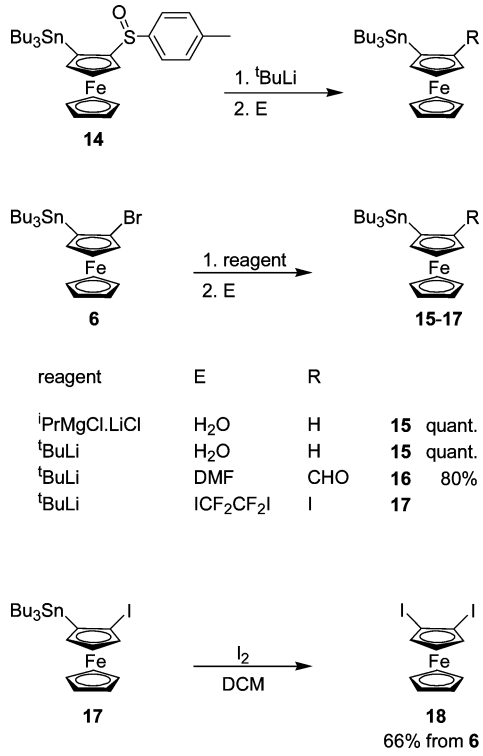


Figure 1. Molecular structure of **9** with thermal ellipsoids at the 50% probability level.

Scheme 4



Scheme 5



starting material and bromoferrocene a selection of five additional monobromo-iodoferrocenes were detected by NMR spectroscopy together with two unidentified byproducts, with the desired product 2-bromo-1,3-diiodoferrocene (**9**) being only a minor component (15%). In this case, the formation of byproducts could not be suppressed by carrying out the reaction in the inverse mode (for a discussion of this reaction see below). Nevertheless, in analogy to the synthesis of **7**, product **9** could be obtained by reaction of **13** with iodine in 83% yield (Scheme 4).

While a wide variety of 1,2-disubstituted ferrocenes can easily be obtained by *ortho*-deprotonation of suitable monosubstituted precursors, 1,3-disubstituted derivatives are significantly more difficult to synthesize. Only Brown and co-workers had reported a methodology that allowed the selective *meta*-deprotonation of a monosubstituted ferrocene derivative.[17] In the majority of cases 1,3-disubstituted ferrocenes have been prepared by removal of the central substituent of a 1,2,3-trisubstituted precursor.[6a,10,16,18]

We therefore questioned whether the bromo substituent of derivative **13** could be replaced selectively by a proton. It is well known from the work of Kagan[19] that the use of ^{t}BuLi followed by treatment with an appropriate electrophile leads to the selective exchange of the 4-tolylsulfinyl group of **14** (Scheme 5, top), and, as a consequence, it seemed likely that the bromide of **13** could also be exchanged with other groups, including a proton.

In order to identify an appropriate reagent, the model compound 2-bromo-1-tributylstannylferrocene (**6**) was first reacted with $NaBH_4$, $LiAlH_4$, $Pd(H_2)$, ^{i}PrMgCl·LiCl, ^{n}BuLi, PhLi, and ^{t}BuLi, and the reaction mixtures were quenched with water. Only with ^{i}PrMgCl·LiCl and ^{t}BuLi could the bromide be exchanged quantitatively with a proton without harming the tributylstannyl residue (**15**, Scheme 5). For practical applications additional electrophiles were applied. Treatment of **6** with 1.5 equiv of ^{t}BuLi followed by quenching with either DMF or ICF_2CF_2I gave derivatives **16**[20] (80%) and **17**, respectively. Derivative **17** was further transformed into 1,2-diiodoferrocene **18**[8a,12,21] (66% based on **6**; Scheme 5, bottom).

On the basis of the results obtained with **6**, removal of the bromo substituent of **13** was attempted with ^{i}PrMgCl·LiCl and ^{t}BuLi. Reaction of **13** at −78 °C with ^{t}BuLi and CH_3OH as the proton source worked best, and the 1,3-disubstituted product **19** was isolated in almost quantitative yield. Treatment of **19** with I_2 in CH_2Cl_2 gave 1,3-diiodoferrocene (**20**)[22] (69%, based on **13**, Scheme 6).

In summary, 1,3-diiodoferrocene (**20**) was accessible in gram quantities from commercially available bromoferrocene (**1**) in four steps with an overall yield of 41−44%. It is clear that **20** constitutes a valuable starting material for the synthesis of a variety of 1,3-disubstituted ferrocene derivatives. For example, both iodides could be exchanged quantitatively by treatment with ^{n}BuLi (4 equiv) at −78 °C. Reactions of the lithiated

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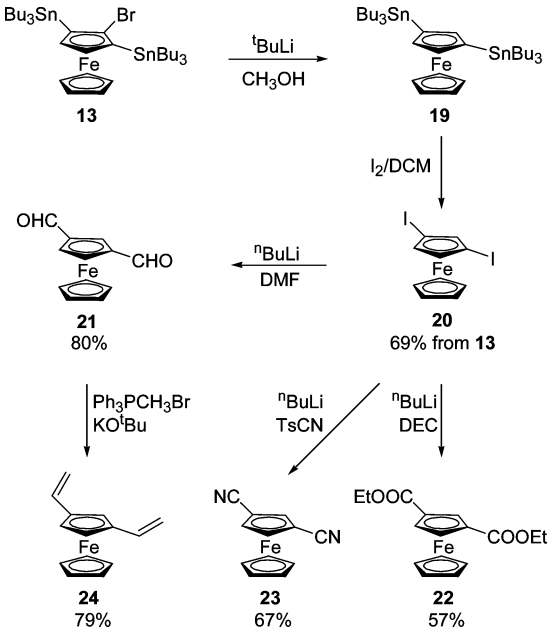
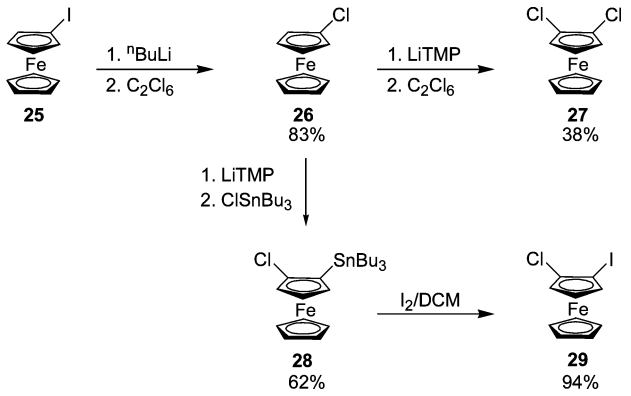
Scheme 6



intermediate with dimethylformamide (DMF), diethyl carbonate (DEC), and tosylcyanide (TsCN) led to derivatives **21**–**23** in 80%, 57%, and 67% yield, respectively. Furthermore, dialdehyde **21**[23] was transformed into 1,3-divinylferrocene (**24**) (79% yield), a derivative that may be of interest in materials chemistry.

***Ortho*-Deprotonation of Chloro- and Iodoferrocenes.** Since the use of LiTMP allowed bromoferrocene (**1**) to be selectively *ortho*-deprotonated and further transformed into a variety of 2-substituted bromoferrocenes, we questioned whether this methodology could also be applied to chloroferrocene (**26**) and iodoferrocene (**25**) (Scheme 7).

Scheme 7



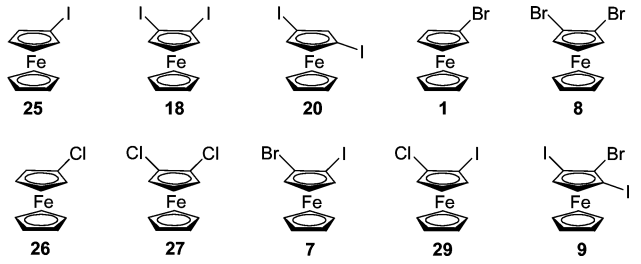
According to a recent report, chloroferrocene (**26**) was *ortho*-deprotonated with LiTMP, and hexachloroethane was added to the lithiated intermediate.[24] This reaction resulted in 1,2-dichloroferrocene (**27**) (Scheme 7) along with higher-substituted derivatives such as 1,2,3-trichloroferrocene.

In this case we also noticed that on running the reaction in the inverse mode the formation of higher-substituted derivatives could be suppressed to a very high extent. In addition to 1,2-dichloroferrocene (**27**) (38% yield), 2-chloro-1-tributylstannylferrocene (**28**) (62%) was prepared and further transformed into 2-chloro-1-iodoferrocene (**29**)[25] (94%).

In contrast to chloroferrocene (**26**), iodoferrocene (**25**)[26] could not be transformed selectively into its 2-substituted derivatives. When **25** was deprotonated with LiTMP and subsequently reacted with an electrophile, regardless of the mode of addition, a variety of products were formed in all cases. For example, the use of ICH_2CH_2I as the electrophile led to a number of differently substituted iodoferrocenes in addition to ferrocene itself.

In order to gain further insights into the reactivity of differently substituted halo-ferrocenes, the *ortho*-deprotonation of 10 substrates with LiTMP was investigated (Chart 1). All

Chart 1



substrates were deprotonated under comparable conditions with LiTMP, and the lithiated species were reacted further with either CH_3OH, CD_3OD, ICH_2CH_2I, $ClSn^nBu_3$, or Cl_3CCCl_3. The results of these reactions are summarized in Table 1.

Each substrate was deprotonated with 1.5 equiv of LiTMP at the temperature indicated, and the reaction mixture was cooled to −78 °C. The reaction was then quenched with CH_3OH or CD_3OD or continued in the straight or inverse mode with one of the electrophiles listed in Table 1 (for details see the Experimental Section and the Supporting Information).

The results obtained after quenching with CH_3OH clearly show that, regardless of the reaction conditions applied, all iodo-substituted derivatives (**7**, **9**, **18**, **20**, **25**, and **29**; Table 1, entries 1, 4, 6, 18, 19, and 23–26) resulted in a mixture of products. For example, the reaction of 1,2-diiodoferrocene (**18**) with LiTMP (Scheme 8; Table 1, entry 4) resulted, after quenching with CH_3OH, in a mixture of five (including starting material) out of seven possible iodo-substituted ferrocenes, with 1,3-diiodoferrocene (**20**) being the main component (67%). For a compilation of all possible homoannularly substituted iodo- and bromoferrocenes see Chart 2 (top).

These results indicate that even in the absence of an external iodide source an intermolecular iodide transfer reaction had taken place. In each case, LiTMP had clearly induced an intermolecular iodide scrambling process. Such general reaction behavior, and especially the fact that LiTMP had isomerized 1,2-diiodoferrocene (**18**) to 1,3-diiodoferocene (**20**), is reminiscent of the so-called "halogen dance" reaction, which is particularly well documented for halide-substituted aromatic heterocycles.[27] Typically, a base-like LiTMP induces an isomerization process that involves deprotonation, lithium/halide exchange, and protonation steps.

The fact that LiTMP already scrambled the iodo substituents of iodoferrocenes before an electrophile had been added to the reaction mixture clearly indicates that a selective *ortho*-substitution of iodoferrocenes cannot be expected. This fact

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Table 1. Deprotonation of Substrates with LiTMP and Reaction with Electrophiles CH_3OH, ICH_2CH_2I, Cl_3CCCl_3, and $ClSn^nBu_3$[a]

Entry	Substrate		Electrophile[b]	Deproton. Temp.[c] (°C)	Reaction mode	Reaction Temp.[b] (°C)	Products (% conversion)[d]
1 2 3		**25**	CH_3OH ICH_2CH_2I ICH_2CH_2I	–30 –30 –30	straight inverse straight	–78 –78 –78	**FeCp$_2$**(38); **18**(7); **20**(25); **25**(24); bpr(6); **FeCp$_2$** (38); **18**(12); **20**(tr); **25**(16); **30**(11); **31**(19); bpr(4); **FeCp$_2$** (38); **18**(18); **20**(tr); **25**(5); **30**(8); **31**(19); **32**(6); bpr(6);
4 5		**18**	CH_3OH ICH_2CH_2I	–30 –30	straight straight	–78 –78	**18**(9); **20**(67); **25**(12); **30**(6); **31**(6); **18**(2); **20**(3); **25**(11); **30**(44); **31**(29); **32**(11);
6 7		**20**	CH_3OH ICH_2CH_2I	–30 –30	straight straight	–78 –78	**18**(7); **20**(86); **25**(5); **30**(tr); **31**(2); **18**(4); **20**(tr); **25**(2); **30**(16); **31**(62); **32**(16);
8 9 10 11		**1**	CH_3OH ICH_2CH_2I ICH_2CH_2I $ClSn^nBu_3$	–30 –30 –30 –30	straight inverse straight straight	–78 –78 –78 –78	**1**(100); **1**(12); **7**(88); **9**(tr); **1**(11); **7**(73); **9**(12); **10**(2); **11**(1); **12**(1); **1**(10); **6**(90);
12 13		**8**	CH_3OH CH_3OH	–30 –30/r.t.	straight straight	–78 –78	**1**(3); **8**(94); **34**(tr); **35**(3); **36**(tr); **1**(28); **8**(6); **34**(38); **35**(1); **36**(25); **37**(2);
14 15		**26**	Cl_3CCCl_3 $ClSn^nBu_3$	–30 –30	inverse inverse	–78 –78	**26**(17); **27**(83); **26**(19); **28**(81);
16 17		**27**	CH_3OH CH_3OH	–30 –30/r.t.	straight straight	–78 –78	**27**(100); **27**(100);
18 19 20 21 22		**7**	CH_3OH CH_3OH ICH_2CH_2I ICH_2CH_2I ICH_2CH_2I	–30 –30/r.t. –30 –30 –30	straight straight straight straight straight	–78 –78 –78 –30 r.t.	**1**(7); **7**(26); **9**(1); **10**(6); **39**(60); **FeCp$_2$** (2); **1**(27); **7**(8); **8**(8); **34**(4); **39**(51);[e] **1**(tr); **7**(8); **9**(16); **10**(13); **11**(13); **12**(46); **42**(1); bpr(3); **1**(2); **7**(22); **9**(20); **10**(20); **11**(17); **12**(16); **42**(tr); bpr(3); **1**; **7**–**12**; **30**–**32**; **35**–**37**; **42**; several bpr;
23 24		**29**	CH_3OH CH_3OH	–30 –30/r.t.	straight straight	–78 –78	**26**(2); **29**(13); **44**(22); **45**(6); **46**(9); **48** (48);[e] **26**(3); **29**(27); **44**(26); **45**(9); **46**(11); **48** (24);[e]
25 26 27		**9**	CH_3OH CH_3OH ICH_2CH_2I	–30 –30/r.t. –30	straight straight straight	–78 –78 –78	**9**(4); **10**(63); **11**(14); **12**(5); **39**(11); bpr(3); **7**–**12**; **18**; **20**; **30**–**32**; **34**; **36**; several bpr; **7**(tr); **10**(2); **11**(1); **12**(89); **42**(5); bpr(3).

[a]Substrate:LiTMP = 1:1.5. [b]Addition of electrophile at −78 °C followed by a reaction period at the given temperature. [c]Deprotonation with LiTMP: −78 °C (30 min) + −30 °C (3 h) + [rt (1 h)]. [d]bpr: unidentified byproducts; tr: traces. [e]Iodide balance does not fit because of significant product degradation during the reaction period.

became even clearer when CD_3OD was used to quench the deprotonation reaction of **18**.

According to ^1H and ^{13}C NMR spectroscopy, the product mixture contained—in addition to all protonated products (**18**, **20**, **25**, **30**, **31**; Scheme 8, top)—at least five additional deuterated derivatives that must be the result of the reaction of lithiated intermediates with CD_3OD (Scheme 8, bottom).

In a similar way to **18**, identical deuteration experiments were carried out with the iodo-substituted substrates **7**, **9**, **20**, and **25** (Supporting Information, Table S3, entries 1−3, 5−7), and in each case mixtures of protonated and deuterated products were obtained. This indicates that after deprotonation not only had an iodide scrambling occurred but also this process led to a mixture of lithiated intermediates. It is clear that the reaction of such a mixture with an electrophile would lead to complex product mixtures.

The bromo-substituted ferrocenes were investigated next. The reactivity of the bromo substituent of bromoferrocene (**1**) and derivatives **7**, **8**, and **9** depended on the reaction temperature as well as on the number of bromo substituents. Only starting material was recovered when bromoferrocene (**1**) was deprotonated with LiTMP at −30 °C and then reacted with CH_3OH (Table 1, entry 8). As discussed above, the use of other electrophiles resulted exclusively in 1,2-substituted bromoferrocenes, and this indicates that the deprotonation reaction had occurred exclusively at one of the *ortho*-positions (Scheme 2). However, when 1,2-dibromoferrocene (**8**) was treated at −30 °C with LiTMP, a slow reaction took place that led to a mixture of four products, with the starting material still being the major component (94%; Scheme 9, top; Table 1, entry 12). When the deprotonation of **8** was carried out at room temperature, a mixture of six (including starting material)

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Scheme 8. Deprotonation of 18 with LiTMP Followed by Protonation with CH_3OH (Top) or Deuteration with CD_3OD (Bottom)

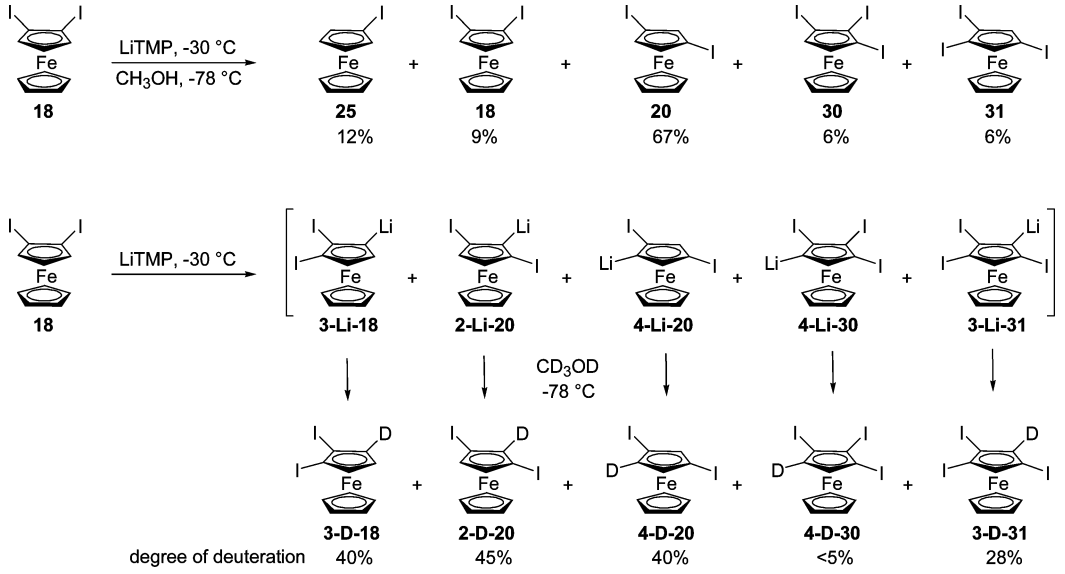
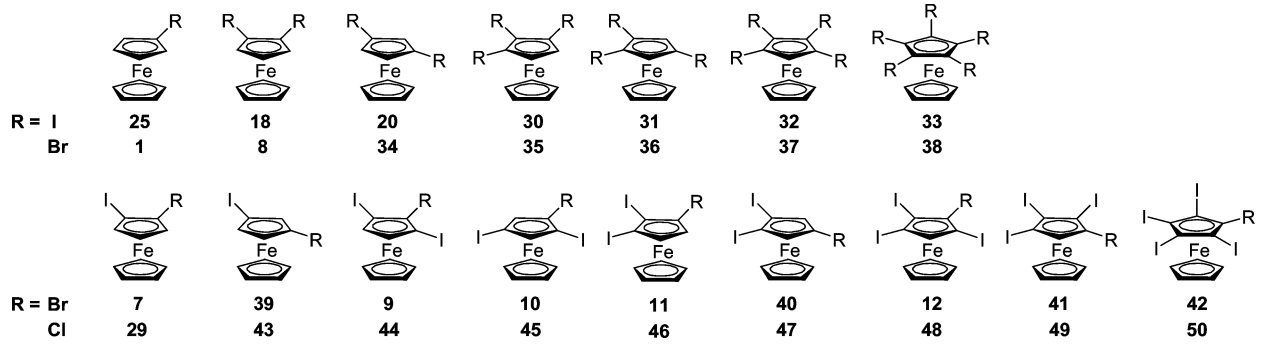
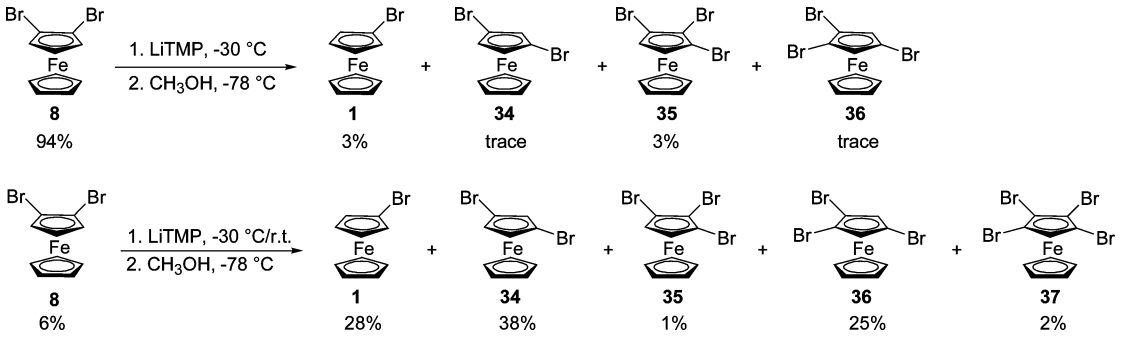


Chart 2. Substitution Patterns of All Possible Homoannularly Substituted Iodo- and Bromoferrocenes (Top) and Monobromoiodo- and Monochloroiodoferrocenes (Bottom)



Scheme 9. Deprotonation of 8 with LiTMP at −30 °C (Top) and −30 °C → rt (Bottom) Followed by Quenching with CH_3OH



out of seven bromo-substituted ferrocenes (Chart 2) was obtained, with the starting material now being a minor component (6%; Scheme 9, bottom; Table 1, entry 13). In summary, at −30 °C the bromo substituent of *ortho*-deprotonated bromoferrocene (**1**) did not exchange, while those in 1,2-dibromoferrocene did, albeit at a very slow rate. At room temperature extensive bromide scrambling took place.

The monobromo-substituted derivatives 2-bromo-1-iodoferrocene (**7**) and 2-bromo-1,3-diiodoferrocene (**9**) showed very similar behavior. At a deprotonation temperature of −30 °C only the iodides scrambled (Table 1, entries 18, 25). At room temperature, in addition to the iodides, the bromides also exchanged (Table 1, entries 19, 26).

For example, when derivative **7** was deprotonated with LiTMP at −30 °C and subsequently reacted at −78 °C with ICH_2CH_2I (described above), five additional monobromoiodoferrocenes were obtained besides starting material and bromoferrocene (**1**) (Table 1, entry 20). After addition of the electrophile the reaction temperature was raised to 20 °C, and, in this case, a complex mixture of more than 14 products was obtained; these included iodoferrocenes, bromoferrocenes, and bromoiodoferrocenes (Table 1, entry 22).

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In contrast to the bromo substituents of **7**, **8**, and **9**, the chlorides of 1,2-dichloroferrocene (**27**) and 2-chloro-1-iodoferrocene (**29**) did not exchange either at −30 °C or at room temperature. In the case of **27** only starting material was recovered (Table 1, entries 16, 17), while **29** gave nearly identical mixtures of monochloro-iodoferrocenes at both temperatures (Table 1, entries 23, 24).

CONCLUSIONS

Chloroferrocene (**26**) and bromoferrocene (**1**) can be deprotonated easily by treatment with LiTMP at −30 °C. Subsequent reactions with electrophiles led selectively to *ortho*-substituted bromo- and chloroferrocenes. On using chloroferrocene as the substrate, excellent selectivity could be achieved only when the reaction was carried out in inverse mode instead of straight mode. Otherwise higher-substituted derivatives were formed. On employing bromoferrocene (**1**), most reactions could be carried out in straight mode, and only some electrophiles (e.g., ICH_2CH_2I, ICF_2CF_2I, Cl_3CCCl_3) required the inverse reaction mode. For example, deprotonated bromoferrocene reacted with ICH_2CH_2I in inverse mode to afford the desired 2-bromo-1-iodoferrocene, whereas in straight mode the formation of several higher-substituted products was observed. It seems reasonable to assume that in the latter case the excess of LiTMP present in the reaction mixture deprotonates the product, which reacts further to give higher-substituted derivatives. On carrying out the reaction in inverse mode, however, the presence of a large excess of electrophile is ensured rather than LiTMP during the whole reaction period.

In contrast to bromo- and chloroferrocene (**1** and **26**), iodoferrocene (**25**) could not be substituted selectively. Although deprotonation with LiTMP occurred easily, even in the absence of an additional electrophile, the iodo substituent of deprotonated iodoferrocene scrambled, and this process resulted, after protonation with H_2O or CH_3OH, in a mixture of ferrocene plus a number of differently substituted iodoferrocenes. Such a scrambling process at −30 °C was observed for all iodo-substituted ferrocenes tested, including 2-bromo-1-iodoferrocene (**7**) and 2-bromo-1,3-diiodoferrocene (**9**). Therefore, these derivatives and their analogues could not be substituted selectively.

In contrast to bromoferrocene (**1**), at −30 °C the bromides of deprotonated 1,2-dibromoferrocene (**8**) scrambled very slowly, whereas at room temperature this process was fast and led to six out of seven differently substituted bromoferrocenes (including starting material). This finding shows that the scrambling process depends not only on temperature but also on the degree of substitution. Higher levels of halo substitution clearly ease this scrambling process.

The chlorides of the deprotonated chloro-substituted ferrocenes chloroferrocene (**26**), 1,2-dichloroferrocene (**27**), and 2-chloro-1-iodoferrocene (**29**) did not scramble, even at room temperature.

It is clear that in order to achieve high selectivity it is necessary to suppress efficiently both the scrambling process and product deprotonation.

The fact that bromoferrocene (**1**) can be *ortho*-deprotonated with LiTMP without bromide scrambling allowed the selective synthesis of a number of 2-substituted bromoferrocenes. The product 2-bromo-1-tributylstannylferrocene (**6**) was found to be particularly useful since it could be further *ortho*-deprotonated adjacent to the bromo substituent and then reacted to afford 1,3-bis(tributylstannyl)-2-bromoferrocene (**13**). A further two-step transformation gave 1,3-diiodoferrocene (**20**) (41−44% overall yield, based on **1**), which we consider to be a very valuable starting material for the synthesis of a variety of 1,3-disubstituted ferrocenes. For example, on using ^{n}BuLi both iodides of **20** could be exchanged quantitatively. Reaction of the 1,3-dilithiated ferrocene with DMF, diethyl carbonate, and tosylcyanide gave the corresponding 1,3-disubstituted aldehyde **21** (80%), ester **22** (57%), and cyanide **23** (67%), respectively. Since ferrocenyl iodides can be easily transformed to provide other functional groups or can be subjected to different coupling reactions, a variety of additional 1,3-disubstituted ferrocenes should now be accessible via 1,3-diiodoferrocene.

EXPERIMENTAL SECTION

General Details. All reactions were carried out under an argon atmosphere using standard Schlenk techniques and dry solvents. Solvents and solutions were degassed by three freeze−pump−thaw cycles. Column chromatography was performed either on silica gel (Merck, 40−63 μm) or on aluminum oxide (Merck, aluminum oxide 90). Eluents heptane (heptane fraction), ethyl acetate (EA), and dichloromethane (DCM) were of technical grade and were distilled before use. NMR spectra were recorded in $CDCl_3$; chemical shifts are referenced to $CHCl_3$ (^{1}H: 7.26 ppm) and $CDCl_3$ (^{13}C: 77.0 ppm). ^{31}P NMR spectra are referenced to 85% H_3PO_4 (^{31}P: 0 ppm). For the assignment of peaks, the following abbreviations are used: s = singlet, bs = broad singlet, d = doublet, t = triplet, pt = pseudotriplet, q = quartet, dd = doublet of doublets, m = multiplet. Coupling constants in ^{13}C NMR spectra are due to ^{31}P−^{13}C, ^{117}Sn−^{13}C, or ^{119}Sn−^{13}C coupling. High-resolution mass spectra were recorded on an ESI-Qq aoTOF MS system. A commercial source of bromoferrocene (**1**) that contained 5% ferrocene was dried under vacuum (rt, 0.5 Torr, 3 h) before use. For running reactions at −30 °C (±4 °C) an FT900 immersion cooler was used.

Lithium 2,2,6,6-Tetramethylpiperidide. To a degassed solution of 2,2,6,6-tetramethylpiperidine (2.26 g, 16 mmol) in THF (9.5 mL) was added dropwise at 0 °C a solution of ^{n}BuLi (9.4 mL, 1.6 M in hexane, 15 mmol), and the clear yellow solution (referred to as LiTMP in THF/hexane) was stirred at the same temperature for 30 min.

*1-Bromo-2-formylferrocene (**2**).* To a degassed solution of bromoferrocene (**1**) (0.566 g, 2.14 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of LiTMP (3.20 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. To the resulting orange-red suspension was added neat DMF (1.561 g, 21.36 mmol), and stirring was continued for 90 min at −30 °C. The reaction mixture was warmed to rt, quenched by the addition of water (20 mL), and extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with brine (3 × 20 mL) and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane/Et_2O = 1:1) gave product **2** in 80% yield (0.500 g, 1.707 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.33 (s, 5H, Cp′), 4.60 (bt, J = 2.7 Hz, 1H, H4), 4.82 (dd, J_1 = 2.7 Hz, J_2 = 1.5 Hz, 1H, Cp), 4.85 (dd, J_1 = 2.7 Hz, J_2 = 1.5 Hz, 1H, Cp), 10.17 (bs, 1H, CHO). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 66.6 (Cp), 71.1 (Cp), 72.1 (5C, Cp′), 75.0 (Cp), 75.6 (C2), 80.0 (C1), 192.8 (CHO). HR-MS (ESI in MeOH/MeCN): m/z $[M]^+$ calcd for $C_{11}H_9BrFeO$ 291.9186; found 291.9195. For additional spectroscopic data see refs 15 and 28.

*1-Bromo-2-hydroxycarbonylferrocene (**3**).* To a degassed solution of bromoferrocene (**1**) (0.491 g, 1.85 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of LiTMP (2.78 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for 3 h at −30 °C. The resulting orange-red suspension was transferred via a Teflon cannula onto 300 g of crushed dry ice. The reaction mixture was stirred until it reached rt, and to the orange-brown solution was added aqueous NaOH (15 mL, 0.5 M). The phases were separated, and the organic phase was extracted twice with NaOH (25 mL, 0.5 M). The combined aqueous phases were acidified at rt to pH 3 by

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addition of *ortho*-phosphoric acid (80%). The precipitate was filtered off, dissolved in ethyl acetate, and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave 84% of product **3** (0.483 g, 1.56 mmol) as orange crystals. Mp: 165 °C, dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.32 (s, 5H, Cp′), 4.43 (t, J = 2.8 Hz, 1H, H4), 4.74 (dd, J_1 = 1.5 Hz, J_2 = 2.8 Hz, 1H, H5), 4.87 (dd, J_1 = 1.5 Hz, J_2 = 2.8 Hz, 1H, H3), COOH proton not observed. ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 70.2, 70.3 (2C, C3+C4), 72.7 (5C, Cp′), 75.4 (C5), 78.3 (C1), 174.8 (COOH), signal of C2 not observed. HR-MS (ESI in MeOH/MeCN): m/z [M + Na]$^+$ calcd 330.9033 for $C_{11}H_9BrFeNaO_2$, found 330.9023.

*1-Bromo-2-cyanoferrocene (**4**).* To a degassed solution of bromoferrocene (**1**) (0.484 g, 1.83 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of LiTMP (2.74 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C and subsequently transferred within 10 min via a Teflon cannula to a degassed solution of tosylcyanide (0.671 g, 3.71 mmol) in THF (3.5 mL), which had been precooled to −78 °C. The reaction mixture was stirred for an additional 30 min at −78 °C and for 40 min at rt. The reaction mixture was quenched by the addition of water (20 mL), and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with brine (3 × 20 mL) and dried over $MgSO_4$. Column chromatography on silica gel (heptane/EA = 1:1) gave product **4** in 71% yield (0.377 g, 1.30 mmol) as orange-brown crystals. Mp: 112−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.36 (t, J = 2.8 Hz, 1H, H4), 4.40 (s, 5H, Cp′), 4.64 (dd, J_1 = 1.3 Hz, J_2 = 2.8 Hz, 1H, H3), 4.66 (dd, J_1 = 1.3 Hz, J_2 = 2.8 Hz, 1H, H5). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 69.5 (C4), 70.6 (C3), 72.7 (C5), 73.2 (5C, Cp′), 79.2 (C1), 118.4 (CN), signal of C2 not observed. HR-MS (ESI, MeOH/MeCN): m/z [M + Na]$^+$ calcd 311.9087 for $C_{11}H_8BrFeNNa$, found 311.9082.

*1-Bromo-2-diphenylphosphinoferrocene (**5**).* To a degassed solution of bromoferrocene (**1**) (1.000 g, 3.775 mmol) in THF (15 mL) was added dropwise at −78 °C a solution of LiTMP (5.663 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 4 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C, and neat chlorodiphenylphosphine (1.664 g, 7.542 mmol) was added. The reaction mixture was stirred for an additional 30 min at −78 °C and for 16 h at rt. The reaction mixture was quenched by the addition of water (30 mL), and the aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with brine (3 × 20 mL) and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane/Et_2O = 9:1) gave product **5** in 84% yield (1.419 g, 3.160 mmol) as a yellow powder. Mp: 175 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.64 (dd, J_1 = 1.5 Hz, J_2 = 2.5 Hz, 1H, H3), 4.16 (s, 5H, Cp′), 4.24 (t, J = 2.5 Hz, 1H, H4), 4.66−4.69 (m, 1H, H5), 7.14−7.22 (m, 2H, Ph^A-*ortho*), 7.23−7.30 (m, 3H, Ph^A-*meta* + Ph^A-*para*), 7.36−7.43 (m, 3H, Ph^B-*meta* + Ph^B-*para*), 7.51−7.59 (m, 2H, Ph^B-*ortho*). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 68.6 (C4), 69.9 (d, J = 4.5 Hz, C3), 71.7 (5C, Cp′), 73.1 (d, J = 2.3 Hz, C5), 84.9 (d, J = 30.7 Hz, C1), 128.0 (Ph^A-*para*), 128.58, 128.64, 128.66, 128.73 (4C, Ph^A *meta* + Ph^B *meta*), 129.3 (Ph^B-*para*), 132.2 (d, J = 18.4 Hz, 2C, Ph^A-*ortho*), 135.0 (d, J = 21.5 Hz, 2C, Ph^B-*ortho*), 136.9 (d, J = 9.2 Hz, Ph^B-*ipso*), 138.6 (d, J = 11.1 Hz, Ph^A-*ipso*), signal of C2 not observed. ^{31}P NMR (162 MHz, $CDCl_3$): δ −18.9 (PPh_2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 447.9679 for $C_{22}H_{18}BrFeP$, found 447.9672. For additional spectroscopic data see ref 12.

*2-Bromo-1-tributylstannylferrocene (**6**).* To a degassed solution of bromoferrocene (**1**) (11.15 g, 42.09 mmol) in THF (110 mL) was added dropwise at −78 °C a solution of LiTMP (63.14 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C, and neat chlorotributylstannane (24.41 g, 74.99 mmol) was added. The reaction mixture was stirred at this temperature for an additional 90 min and subsequently quenched by the addition of methanol (50 mL). The organic phase was diluted with Et_2O (500 mL), washed with water (2 × 300 mL) and brine (2 × 300 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **6** in 79% yield (18.39 g, 33.20 mmol) as a dark orange-red oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.92 (t, J = 7.4 Hz, 9H, CH_3), 1.08−1.19 (m, 6H, CH_2), 1.34−1.41 (m, 6H, CH_2), 1.53−1.67 (m, 6H, CH_2), 3.90−3.93 (m, 1H, H5), 4.16 (s, 5H, Cp′), 4.20−4.22 (m, 1H, H4), 4.54−4.55 (m, 1H, H3). ^{13}C{^{1}H} NMR (150.9 MHz, $CDCl_3$): δ 10.6 (J_1 = 337 Hz, J_2 = 353 Hz, 3C, CH_2), 13.7 (3C, CH_3), 27.4 (J_1 = 59.2 Hz, J_2 = 62.1 Hz, 3C, CH_2), 29.2 (J = 19.0 Hz, 3C, CH_2), 69.4 (J = 29.4 Hz, C4), 70.4 (5C, Cp′), 72.3 (J = 22.8 Hz, C3), 72.9 (C1), 73.5 (J = 37.3 Hz, C5), 86.1 (C2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 554.0294 for $C_{22}H_{35}BrFeSn$; found 554.0283.

*2-Bromo-1-iodoferrocene (**7**). Method A.* To a degassed solution of bromoferrocene (**1**) (0.500 g, 1.89 mmol) in THF (5 mL) was added dropwise at −78 °C a solution of LiTMP (2.83 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C and subsequently transferred within 15 min via a Teflon cannula to a degassed and precooled (−78 °C) solution of ICH_2CH_2I (1.064 g, 3.775 mmol) in THF (5 mL). Stirring was continued for 90 min at −78 °C. The reaction mixture was quenched by the addition of methanol (2 mL) and diluted with Et_2O (20 mL). The organic phase was washed with water (2 × 20 mL) and brine (2 × 20 mL) and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **7** in 65% yield (0.476 g, 1.22 mmol) as orange crystals. On a 5 g scale compound **7** was isolated in 63% yield.

The use of IF_2CCF_2I as the electrophile (1.336 g, 3.776 mmol, 5 mL THF) gave **7** in 73% isolated yield (0.535 g, 1.37 mmol).

Method B. To a degassed solution of 2-bromo-1-tributylstannylferrocene (**6**) (1.048 g, 1.892 mmol) in DCM (6 mL) was added at rt via a Teflon cannula a degassed solution of I_2 (0.568 g, 2.24 mmol) in DCM (14 mL). The reaction mixture was stirred for 16 h at rt, quenched with saturated aqueous $Na_2S_2O_3$ (10 mL), and diluted with water (10 mL). The aqueous phase was extracted with Et_2O (2 × 5 mL), and the combined organic phases were washed with brine (2 × 20 mL). The solvents were removed under reduced pressure, and to the residue were added KF (3 g) and methanol (10 mL). The resulting suspension was stirred for 30 min and filtered through a plug of aluminum oxide (eluent DCM), and the solvents were removed under reduced pressure. The residue was taken up in Et_2O (30 mL), washed with water (3 × 10 mL) and brine (10 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **7** in 81% yield (0.600 g, 1.54 mmol) as orange-brown crystals. Mp: 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19 (t, J = 2.6 Hz, 1H, H4), 4.22 (s, 5H, Cp′), 4.43 (dd, J_1 = 2.6 Hz, J_2 = 1.4 Hz, 1H, H5), 4.52 (dd, J_1 = 2.6 Hz, J_2 = 1.4 Hz, 1H, H3). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 46.2 (C1), 68.4 (C4), 69.6 (C3), 73.59 (C5), 73.62 (5C, Cp′), 84.5 (C2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 389.8204 for $C_{10}H_8BrFeI$, found 389.8204. For additional spectroscopic data see refs 12 and 13.

*1,2-Dibromoferrocene (**8**).* To a degassed solution of bromoferrocene (**1**) (1.000 g, 3.775 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of LiTMP (5.663 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C and subsequently transferred dropwise via a Teflon cannula to a degassed solution of $Br_2CHCHBr_2$ (2.610 g, 7.551 mmol) in THF (6 mL) that had been precooled to −78 °C. The reaction mixture was stirred for an additional 90 min at −78 °C and subsequently quenched by the addition of methanol (2 mL). The organic phase was diluted with Et_2O (30 mL), washed with brine (3 × 30 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **8** in 68% yield (0.878 g, 2.55 mmol) as orange-red crystals. Mp: 91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.11 (t, J = 2.7 Hz, 1H, H4), 4.26 (s, 5H, Cp′), 4.44 (d, J = 2.7 Hz, 2H, H3 + H5). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 65.9 (C4), 68.9 (2C, C3 + C5), 73.2 (5C, Cp′), 80.3 (2C, C1 + C2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 343.8322 for $C_{10}H_8Br_2Fe$, found 343.8309. For additional spectroscopic data see ref 14c.

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*2-Bromo-1,3-diiodoferrocene (**9**).* To a degassed solution of 1,3-bis(tributylstannyl)-2-bromoferrocene (**13**) (1.008 g, 1.196 mmol) in DCM (6 mL) was added at rt via a Teflon cannula a degassed solution of I_2 (1.233 g, 4.858 mmol) in DCM (30 mL). The reaction mixture was stirred for 16 h at rt, quenched with saturated aqueous $Na_2S_2O_3$ (10 mL), and diluted with water (10 mL). The aqueous phase was extracted with Et_2O (2 × 10 mL), and the combined organic phases were washed with brine (2 × 30 mL). The solvents were removed under reduced pressure, and to the residue were added KF (12 g) and methanol (20 mL). The resulting suspension was stirred for 30 min and filtered through a plug of aluminum oxide (eluent DCM), and the solvents were removed under reduced pressure. The residue was taken up in Et_2O (30 mL), washed with water (3 × 10 mL) and brine (10 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **9** in 83% yield (0.515 g, 0.997 mmol) as orange-red crystals. Mp: 150−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (s, 5H, Cp′), 4.56 (s, 2H, C4 + C5). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 44.1 (2C, C1 + C3), 74.6 (2C, C4 + C5), 76.6 (5C, Cp′), 90.9 (C2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 515.7170 for $C_{10}H_7BrFeI_2$, found 515.7173. The X-ray crystal structure determination of **9** confirmed the 2-bromo-1,3-diiodo substitution pattern and is reported in the Supporting Information.

*3-Bromo-1,2,4-triiodoferrocene (**12**) and 2-Bromo-1,3,4,5-tetraiodoferrocene (**42**).* To a degassed solution of 2-bromo-1,3-diiodoferrocene (**9**) (0.991 g, 1.92 mmol) in THF (10 mL) was added dropwise at −78 °C a solution of LiTMP (2.88 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C, and to this mixture was added a degassed solution of ICH_2CH_2I (1.100 g, 3.903 mmol) in THF (6 mL). Stirring at −78 °C was continued for 1 h, and the reaction mixture was quenched with methanol (3 mL). The organic phase was diluted at rt with Et_2O (25 mL) and ethyl acetate (25 mL), washed with water (2 × 50 mL) and brine (2 × 50 mL), and dried over $MgSO_4$. Column chromatography on silica (heptane) gave, in the main fraction, pure product **12** in 51% yield (0.628 g, 0.977 mmol) as orange crystals. A second fraction (0.231 g) contained derivative **42** with a purity of 90%. **12**: Mp: 111−115 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.19 (s, 5H, Cp′), 4.99 (s, 1H, H5). $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 45.1 (1C, C1/C4), 50.9 (1C, C4/C1), 56.8 (1C, C2), 79.4 (5C, Cp′), 79.6 (C5), 90.5 (C3). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 641.6136 for $C_{10}H_6BrFeI_3$, found 641.6128. **42**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.15 (s, 5H, Cp′). $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 56.5 (2C, CI), 62.0 (2C, CI), 82.3 (5C, Cp′), 90.7 (CBr). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 767.5103 for $C_{10}H_5BrFeI_4$, found 767.5100.

*1,3-Bis(tributylstannyl)-2-bromoferrocene (**13**).* To a degassed solution of 2-bromo-1-tributylstannylferrocene (**6**) (18.00 g, 32.49 mmol) in THF (180 mL) was added dropwise at −78 °C a solution of LiTMP (48.74 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C, and neat chlorotributylstannane (32.40 g, 58.49 mmol) was added. Stirring of the reaction mixture was continued for 16 h, and during this period the reaction mixture was allowed to warm slowly to rt. The reaction was quenched with methanol (50 mL), and the organic phase was diluted with Et_2O (500 mL), washed with water (2 × 300 mL) and brine (2 × 300 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave 76% of product **13** (20.90 g, 24.79 mmol) as a dark red-brown oil. On using 1 g of **6**, the product **13** was isolated in 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 7.3 Hz, 18H, CH_3), 1.04−1.22 (m, 12H, CH_2), 1.30−1.43 (m, 12H, CH_2), 1.49−1.69 (m, 12H, CH_2), 4.04 (s, 2H, H4 + H5), 4.10 (s, 5H, Cp′). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 10.7 (6C, CH_2), 13.7 (6C, CH_3), 27.4 (6C, CH_2), 29.2 (6C, CH_2), 70.2 (5C, Cp′), 75.1 (2C, C1 + C3), 75.6 (2C, C4 + C5), 95.0 (C2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 844.1350 for $C_{34}H_{61}FeBrSn_2$, found 844.1342.

*2-Formyl-1-tributylstannylferrocene (**16**).* To a degassed solution of 2-bromo-1-tributylstannylferrocene (**6**) (0.500 g, 0.903 mmol) in THF (5 mL) was added at −78 °C ^{t}BuLi (0.8 mL, 1.7 M in heptane, 1.36 mmol). The mixture was stirred for 30 min at −78 °C, and neat DMF (0.660 g, 9.03 mmol) was added. The reaction mixture was stirred for 15 min at −78 °C and for 1 h at rt. The reaction was quenched with water (10 mL) and diluted with Et_2O (50 mL). The organic phase was washed with water (2 × 30 mL) and brine (2 × 30 mL) and dried over $MgSO_4$. Column chromatography on silica (CH_2Cl_2/heptane = 7:3) gave product **16** in 80% yield (0.363 g, 0.722 mmol) as a dark orange-red solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 7.3 Hz, 9H, CH_3), 0.99−1.12 (m, 6H, CH_2), 1.30−1.41 (m, 6H, CH_2), 1.51−1.62 (m, 6H, CH_2), 4.22 (s, 5H, Cp′), 4.46−4.51 (m, 1H, H5), 4.72−4.76 (m, 1H, H4), 4.90−4.94 (m, 1H, H3), 9.94 (1H, CHO). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 10.7 (3C, CH_2), 13.7 (3C, CH_3), 27.4 (3C, CH_2), 29.2 (3C, CH_2), 69.4 (C4), 70.4 (5C, Cp′), 72.3 (C3), 72.9 (C1), 73.5 (C5), 86.1 (C2), 194.6 (CHO). HR-MS (ESI, MeOH/MeCN): m/z $[M - Bu]^+$ calcd 447.0433 for $C_{19}H_{27}FeOSn$, found 447.0439. For additional spectroscopic data see refs 20, 28a, and 29.

*1-Iodo-2-tributylstannylferrocene (**17**).* To a degassed solution of 2-bromo-1-tributylstannylferrocene (**6**) (1.998 g, 3.607 mmol) in THF (15 mL) was added at −78 °C ^{t}BuLi (3.2 mL, 1.7 M in heptane, 5.44 mmol). The mixture was stirred for 30 min at −78 °C, and the reaction mixture was added via a Teflon cannula to a precooled (−78 °C) solution of ICF_2CF_2I (1.978 g, 5.590 mmol) in THF (10 mL). Stirring was continued for 90 min, and the reaction mixture was quenched with methanol (3 mL). The reaction mixture was warmed quickly to rt and was diluted with Et_2O (50 mL). The organic phase was washed with an aqueous solution of sodium bisulfite (30 mL), water (2 × 30 mL), and brine (3 × 30 mL) and dried over $MgSO_4$. The solvents were removed, and the raw material contained 88% of the desired product **17**. An analytical sample was purified by column chromatography on aluminum oxide (heptane). On a larger scale chromatographic separation of product **17** from byproduct tributylstannylferrocene (**15**) was unsuccessful, and the raw material was therefore used without further purification in the synthesis of 1,2-diiodoferrocene (**18**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, J = 7.4 Hz, 9H, CH_3), 1.06−1.24 (m, 6H, CH_2), 1.32−1.44 (m, 6H, CH_2), 1.51−1.70 (m, 6H, CH_2), 3.96−3.99 (m, 1H, H5), 4.13 (s, 5H, Cp′), 4.24−4.28 (m, 1H, H4), 4.55−4.58 (m, 1H, H3). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 10.8 (J_1 = 336 Hz, J_2 = 353 Hz, 3C, CH_2), 13.7 (3C, CH_3), 27.4 (J_1 = 59.1 Hz, J_2 = 61.8 Hz, 3C, CH_2), 29.2 (J = 19.0 Hz, 3C, CH_2), 50.51 (C2), 70.8 (5C, Cp′), 70.9 (C4), 75.4 (C5), 77.4 (C3), 73.6 (C1). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 602.0155 for $C_{22}H_{35}FeISn$, found 602.0144.

*1,2-Diiodoferrocene (**18**).* To a degassed solution of 1-iodo-2-tributylstannylferrocene (**17**) (raw material obtained from 3.607 mmol of **6**) in DCM (20 mL) was added at rt via a Teflon cannula a degassed solution of I_2 (1.007 g, 3.968 mmol) in DCM (22 mL). The reaction mixture was stirred for 16 h at rt, quenched with saturated aqueous $Na_2S_2O_3$ (5 mL), and diluted with water (10 mL). The aqueous phase was extracted with Et_2O (2 × 20 mL), and the combined organic phases were washed with brine (2 × 30 mL). The solvents were removed under reduced pressure, and to the residue were added KF (2 g) and methanol (30 mL). The resulting suspension was stirred for 30 min and filtered through a plug of aluminum oxide (eluent DCM), and the solvents were removed under reduced pressure. The residue was taken up in Et_2O (30 mL), washed with water (3 × 10 mL) and brine (10 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **18** (1.043 g, 2.382 mmol) as yellow crystals in 66% overall yield (based on **6**). Mp: 46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18 (s, 5H, Cp′), 4.25 (t, J = 2.5 Hz, 1H, H4), 4.51 (d, J = 2.5 Hz, 2H, H3 + H5). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 51.9 (2C, C1 + C2), 70.5 (C4), 74.1 (5C, Cp′), 74.6 (2C, C3 + C5). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 437.8065 for $C_{10}H_8FeI_2$, found 437.8051. For additional spectroscopic data see refs 21a, 21b, and 30.

*1,3-Bis(tributylstannyl)ferrocene (**19**).* To a degassed solution of 1,3-bis(tributylstannyl)-2-bromoferrocene (**13**) (5.758 g, 6.830 mmol) in THF (50 mL) was added at −78 °C within 5 min ^{t}BuLi (8.5 mL, 1.7 M in heptane, 14.5 mmol). The mixture was stirred for 15 min at −78 °C, and methanol (24 mL) was added. To the reaction mixture

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was added at rt water (80 mL), and the phases were separated. The aqueous phase was extracted twice with Et_2O (100, 50 mL). The combined organic phases were washed with brine (100 mL) and dried over $MgSO_4$. Removal of the solvents under reduced pressure gave a mixture of the desired product **19** in 95% yield together with 2% of 1,1′-bis(tributylstannyl)ferrocene as a byproduct (total yield: 5.070 g, 6.635 mmol, 97%). The byproduct could not be removed by column chromatography on aluminum oxide (heptane), and the product mixture was therefore used without further purification in the synthesis of 1,3-diiodoferrocene (**20**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, J = 7.4 Hz, 18H, CH_3), 0.99−1.05 (m, 12H, CH_2), 1.30−1.42 (m, 12H, CH_2), 1.54−1.64 (m, 12H, CH_2), 3.82−3.85 (m, J = 3.7 Hz, 1H, H2), 4.04 (s, 5H, Cp′), 4.17−4.20 (m, J = 0.9 Hz, 2H, H4 + H5). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 10.3 (J_1 = 330 Hz, J_2 = 345 Hz, 6C, CH_2), 13.7 (6C, CH_3), 27.4 (J = 66 Hz, 6C, CH_2), 29.2 (J = 19.7 Hz, 6C, CH_2), 67.9 (5C, Cp′), 71.0 (2C, C1 + C3), 76.3 (2C, C4 + C5), 80.9 (C2). HR-MS (ESI in MeOH/MeCN): m/z [M]$^+$ calcd 766.2245 for $C_{34}H_{62}FeSn_2$, found 766.2248.

*1,3-Diiodoferrocene (**20**).* To a degassed solution of 1,3-bis-(tributylstannyl)ferrocene (**19**) (raw material obtained from 6.830 mmol of **13**) in DCM (42 mL) was added within 1 h at rt a degassed solution of I_2 (3.810 g, 15.01 mmol) in DCM (84 mL). The reaction mixture was stirred for 16 h at rt, quenched with saturated aqueous $Na_2S_2O_3$ (15 mL), and diluted with water (100 mL). The phases were separated, the organic phase was washed with water (100 mL) and brine (100 mL) and dried over $MgSO_4$, and the solvents were removed under reduced pressure. To the residue were added KF (6 g) and methanol (80 mL). The resulting suspension was stirred for 30 min, and filtered through a plug of aluminum oxide (wetted with methanol), and the solvents were removed under reduced pressure. The residue was taken up in heptane (80 mL) and filtered through a short plug of aluminum oxide, and the solvent was removed under reduced pressure. Column chromatography on aluminum oxide (heptane) gave product **20** in 69% overall yield (based on **13**) as yellow crystals (2.065 g, 4.717 mmol). Mp: 52−54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (s, 5H, Cp′), 4.43 (d, J = 1.2 Hz, 2H, H4 + H5), 4.67 (t, J = 1.2 Hz, 1H, H2). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 39.1 (2C, C1 + C3), 74.0 (5C, Cp′), 75.4 (2C, C4 + C5), 80.0 (C2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 437.8065 for $C_{10}H_8FeI_2$, found 437.8058.

*1,3-Diformylferrocene (**21**).* To a degassed solution of 1,3-diiodoferrocene (**20**) (1.000 g, 2.284 mmol) in THF (16 mL) was added at −78 °C ^{n}BuLi (6 mL, 1.6 M in hexane, 9.6 mmol). The mixture was stirred for 15 min at −78 °C, and neat DMF (3.339 g, 45.68 mmol) was added. The reaction mixture was stirred for an additional 70 min at −78 °C. The cooling bath was removed, and water (2 mL) was added. As the mixture warmed to rt the color changed to dark red. Water (10 mL) and Et_2O (20 mL) were added, the phases were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with brine (2 × 30 mL) and dried over $MgSO_4$. Column chromatography on silica (CH_2Cl_2 → CH_2Cl_2/EA = 100:2.5) gave product **21** in 80% yield (0.443 g, 1.83 mmol) as a dark red solid. Mp: 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (s, 5H, Cp′), 5.14 (d, J = 1.3 Hz, 2H, H4 + H5), 5.41 (t, J = 1.3 Hz, 1H, H2), 10.0 (s, 2H, CHO). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 71.09 (C2), 74.14 (5C, Cp′), 73.3 (2C, C4 + C5), 83.1 (2C, C1 + C3), 192.1 (2C, CHO). HR-MS (ESI, MeOH/MeCN): m/z [M + Na]$^+$ calcd 264.9928 for $C_{12}H_{10}FeNaO_2$, found 264.9929. For additional spectroscopic data see ref 23.

*1,3-Bis(ethoxycarbonyl)ferrocene (**22**).* To a degassed solution of 1,3-diiodoferrocene (**20**) (2.000 g, 4.568 mmol) in THF (32 mL) was added at −78 °C ^{n}BuLi (12 mL, 1.6 M in hexane, 19.2 mmol). The suspension was stirred for 15 min at −78 °C and then added to a degassed and precooled (−78 °C) solution of diethyl carbonate (20.51 g, 174 mmol) in THF (20 mL). The reaction mixture was stirred for an additional 2 h at −78 °C. The cooling bath was removed, and ethanol (5 mL) was added. Water (20 mL) and Et_2O (50 mL) were added at rt, and the phases were separated. The organic phase was washed with brine (3 × 30 mL) and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane/EA = 9:1 → 17:3) gave product **22** in 57% yield (0.860 g, 2.61 mmol) as a yellow-orange solid. Mp: 99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.3 Hz, 6H, CH_3), 4.24 (s, 5H, Cp′), 4.29 (q, J = 7.3 Hz, 4H, CH_2), 4.98 (d, J = 1.4 Hz, 2H, H4 + H5), 5.43 (t, J = 1.4 Hz, 1H, H2). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 14.5 (2C, CH_3), 60.5 (2C, CH_2), 71.3 (5C, Cp′), 71.9 (C2), 72.7 (2C, C4 + C5), 74.4 (2C, C1 + C3), 170.1 (2C, CO). HR-MS (ESI, MeOH/MeCN): m/z [M + Na]$^+$ calcd 353.0452 for $C_{16}H_{18}FeNaO_4$, found 353.0450.

*1,3-Dicyanoferrocene (**23**).* To a degassed solution of 1,3-diiodoferrocene (**20**) (0.250 g, 0.571 mmol) in THF (4 mL) was added at −78 °C ^{n}BuLi (1.5 mL, 1.6 M in hexane, 2.4 mmol). The mixture was stirred for 15 min at −78 °C, and the resulting suspension was added to a degassed and precooled (−78 °C) solution of tosylcyanide (0.620 g, 3.42 mmol) in THF (10 mL). The reaction mixture was stirred for 30 min at −78 °C and for an additional 75 min at rt. To the reaction mixture were added aqueous NaOH (2 mL, 1 M) and Et_2O (10 mL), and the phases were separated. The organic phase was washed with NaOH (2 × 10 mL, 1 M), aqueous NH_4Cl (10 mL), water (2 × 10 mL), and brine (2 × 10 mL) and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane/EA = 4:1) gave product **23** in 67% yield (0.090 g, 0.381 mmol) as an orange solid. Mp: 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.56 (s, 5H, Cp′), 4.89 (d, J = 1.3 Hz, 2H, H4 + H5), 5.14 (t, J = 1.3 Hz, 1H, H2). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 55.2 (2C, C1 + C3), 73.2 (5C, Cp′), 73.7 (2C, C4 + C5), 74.2 (C2), 117.5 (2C, CN). HR-MS (ESI, MeOH/MeCN): m/z [M + H]$^+$ calcd 237.0115 for $C_{12}H_9FeN_2$, found 237.0101.

*1,3-Diethenylferrocene (**24**).* A suspension of [$MePPh_3$]Br (1.007 g, 2.819 mmol), KO^{t}Bu (0.316 g, 2.82 mmol), and dibenzo-18-crown-6 (0.004 g, 0.011 mmol) in THF (3.7 mL) was stirred at rt for 3 h, and to this suspension was added via a Teflon cannula a solution of 1,3-diformylferrocene (**21**) (0.325 g, 1.34 mmol) in THF (6.3 mL). Stirring at rt was continued for 16 h. To the reaction mixture were added water (5 mL) and Et_2O (10 mL). The phases were separated, and the organic phase was washed with water (2 × 10 mL) and brine (2 × 10 mL) and dried over $MgSO_4$. Column chromatography on silica (heptane) gave product **24** in 79% yield (0.253 g, 1.06 mmol) as a yellow solid. Mp: 27 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.04 (s, 5H, Cp′), 4.40 (d, J = 1.4 Hz, 2H, H4 + H5), 4.59 (t, J = 1.4 Hz, 1H, H2), 5.03 (dd, J_1 = 10.7 Hz, J_2 = 1.5 Hz, 2H, CH), 5.36 (dd, J_1 = 17.5 Hz, J_2 = 1.5 Hz, 2H, C*H*H), 6.43 (dd, J_1 = 17.5 Hz, J_2 = 10.7 Hz, 2H, CH*H*). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 65.12 (C2), 67.4 (2C, C4 + C5), 70.4 (5C, Cp′), 84.2 (2C, C1 + C3), 111.3 (2C, CH_2), 134.4 (2C, CH). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 238.0445 for $C_{14}H_{14}Fe$, found 238.0436.

*Chloroferrocene (**26**).* To a degassed solution of iodoferrocene (**25**)[26c] (3.000 g, 9.618 mmol) in THF (20 mL) was added at −78 °C ^{n}BuLi (6.6 mL, 1.6 M in hexane, 10.56 mmol). The mixture was stirred for 15 min at −78 °C and then transferred via a Teflon cannula to a precooled (−78 °C) solution of Cl_3CCCl_3 (2.732 g, 11.54 mmol) in THF (10 mL). The reaction mixture was stirred for an additional 90 min at −78 °C. Methanol (2 mL) was added, and the reaction mixture was warmed to rt. Water (10 mL) and Et_2O (20 mL) were added, and the phases were separated. The organic phase was washed with water (2 × 20 mL) and brine (2 × 20 mL) and dried over $MgSO_4$. In order to remove excess Cl_3CCCl_3 by sublimation, the residue (2.354 g) was transferred to a Kugelrohr distillation apparatus and held for 15 min at 50 °C and at a pressure of 0.1 Torr. The remaining solid (2.221 g) was subjected to column chromatography on aluminum oxide (heptane) to give chloroferrocene (**26**) containing 2% ferrocene in 83% yield (1.754 g, 7.955 mmol) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (pt, 2H, Cp), 4.23 (s, 5H, Cp′), 4.38 (pt, 2H, Cp). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 66.0 (2C, Cp), 67.8 (2C, Cp), 70.2 (5C, Cp′), 92.4 (C1). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 219.9742 for $C_{10}H_9ClFe$, found 219.9732. For additional spectroscopic data see, for example, ref 24.

*1,2-Dichloroferrocene (**27**).* To a degassed solution of chloroferrocene (**26**) (2.505 g, 11.36 mmol) in THF (30 mL) was added dropwise at −78 °C a solution of LiTMP (17.04 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for

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an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C and transferred dropwise within 75 min via a Teflon cannula to a degassed solution of Cl_3CCCl_3 (4.575 g, 19.33 mmol) in THF (17 mL) that had been precooled to −78 °C. The reaction mixture was stirred for 1 h at −78 °C and subsequently quenched by the addition of methanol (6 mL). The organic phase was diluted with Et_2O (50 mL), washed with water (100 mL) and brine (100 mL), and dried over $MgSO_4$. Removal of the solvents gave a mixture of product and starting material that could not be fully separated by column chromatography on aluminum oxide (heptane). Recrystallization of a fraction (2.085 g, **27**/**26** = 9:1) from heptane (5 mL) gave a precipitate (1.450 g) that was again recrystallized from heptane (8 mL). The final yellow product **27** (1.107 g, 4.343 mmol, 38%) contained 1.2% starting material **26**. Mp: 71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.99 (t, J = 2.7 Hz, 1H, H4), 4.27 (s, 5H, Cp′), 4.37 (d, J = 2.7 Hz, 2H, H3 + H5). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 62.9 (C4), 65.9 (2C, C3 + C5), 72.5 (5C, Cp′), 91.1 (2C, C1 + C2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 253.9352 for $C_{10}H_8Cl_2Fe$, found 253.9344. For additional spectroscopic data see ref 24.

*2-Chloro-1-tributylstannylferrocene (**28**).* To a degassed solution of chloroferrocene (**26**) (1.982 g, 8.989 mmol) in THF (20 mL) was added dropwise at −78 °C a solution of LiTMP (13.48 mmol) in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and for an additional 3 h at −30 °C. The resulting orange-red suspension was cooled to −78 °C and added dropwise to a precooled (−78 °C) solution of chlorotributylstannane (5.120 g, 15.73 mmol) in THF (15 mL). The reaction mixture was stirred at this temperature for an additional 90 min and subsequently quenched with methanol (5 mL). The organic phase was diluted at rt with Et_2O (50 mL), washed with water (2 × 50 mL) and brine (2 × 50 mL), and dried over $MgSO_4$. Column chromatography on aluminum oxide (heptane) gave product **28** in 62% yield (2.855 g, 5.603 mmol) as a dark orange-red oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.92 (t, J = 7.3 Hz, 9H, CH_3), 1.04−1.22 (m, 6H, CH_2), 1.32−1.43 (m, 6H, CH_2), 1.50−1.69 (m, 6H, CH_2), 3.85−3.89 (m, 1H, H5), 4.17 (s, 5H, Cp′), 4.17−4.19 (m, 1H, H4), 4.50−4.52 (m, 1H, H3). $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 10.5 (J_1 = 338 Hz, J_2 = 354 Hz, 3C, CH_2), 13.7 (3C, CH_3), 27.4 (J = 60.2 Hz, 3C, CH_2), 29.2 (J = 19.5 Hz, 3C, CH_2), 68.5 (J = 30.94 Hz, C4), 69.7 (C3), 70.0 (5C, Cp′), 70.3 (C1), 72.3 (J = 35.2 Hz, C5), 99.3 (C2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 510.0799 for $C_{22}H_{35}ClFeSn$, found 510.0772.

*2-Chloro-1-iodoferrocene (**29**).* To a degassed solution of 2-chloro-1-tributylstannylferrocene (**28**) (2.855 g, 5.603 mmol) in DCM (25 mL) was added at rt via a Teflon cannula a degassed solution of I_2 (0.568 g, 2.24 mmol) in DCM (35 mL). The reaction mixture was stirred for 16 h at rt, quenched with saturated aqueous $Na_2S_2O_3$ (5 mL), and diluted with water (30 mL). The aqueous phase was extracted with Et_2O (2 × 10 mL), and the combined organic phases were washed with brine (2 × 75 mL) and dried over $MgSO_4$. The solvents were removed under reduced pressure, and to the residue were added KF (3 g) and methanol (60 mL). The resulting suspension was stirred for 30 min and filtered through a plug of aluminum oxide (wetted with methanol), and the solvents were removed under reduced pressure. The residue was taken up in heptane (50 mL) and filtered again through a short plug of aluminum oxide. Column chromatography on aluminum oxide (heptane) gave product **29** in 94% yield (1.825 g, 5.269 mmol) as yellow-orange crystals. Mp: 59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (t, J = 2.7 Hz, 1H, H4), 4.23 (s, 5H, Cp′), 4.37 (dd, J_1 = 2.7 Hz, J_2 = 1.5 Hz, 1H, H5), 4.50 (dd, J_1 = 2.7 Hz, J_2 = 1.5 Hz, 1H, H3). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 43.3 (C1), 67.0, 67.1 (2C, C3 + C4), 72.7 (C5), 73.3 (5C, Cp′), 96.6 (C2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 345.8709 for $C_{10}H_8ClFeI$, found 345.8701.

Typical Deprotonation and Scrambling Experiments (Table 1). To a degassed solution of substrate **1**, **7**−**9**, **18**, **20**, **25**−**27**, and **29** (1.00 mmol) in THF (3.5 mL) was added dropwise (via a cannula; 30 drops/min) at −78 °C a solution of 1.5 mmol of LiTMP in THF/hexane. The reaction mixture was stirred for 30 min at −78 °C and 3 h at −30 °C and was subsequently cooled to −78 °C.

Method A. To the resulting suspension was added via a syringe either CH_3OH (1 mL) or CD_3OH (1 mL), and the reaction mixture was warmed to rt and diluted with Et_2O (10 mL).

Method B (Straight Mode). To the resulting suspension was added at −78 °C 2.0 mmol of an electrophile [neat $ClSn^nBu_3$ via a syringe; a solution of ICH_2CH_2I, ICF_2CF_2I, or Cl_3CCCl_3 in THF (3.5 mL) via a cannula]. The reaction mixture was stirred for 90 min at the stated reaction temperature (Table 1), quenched by the addition of CH_3OH (2 mL), and diluted with Et_2O (10 mL).

Method C (Inverse Mode). The resulting suspension was added dropwise via a cannula to a precooled (−78 °C) solution of 2 mmol of electrophile in THF (3.5 mL). The reaction mixture was stirred for 90 min at the stated reaction temperature (Table 1), quenched by the addition of CH_3OH (2 mL), and diluted with Et_2O (10 mL).

The organic phase was washed with water (2 × 10 mL) and brine (2 × 10 mL) and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was analyzed by NMR spectroscopy. For product distributions see Table 1 and Table S3 (Supporting Information); for the corresponding NMR data see Supporting Information.

*X-ray Structure Determination of 2-Bromo-1,3-diiodoferrocene (**9**).* Orange prismatic crystals of **9** suitable for X-ray diffraction were obtained from acetone by evaporation. Single-crystal X-ray data were collected at T = 100 K on a Bruker Kappa APEX2 CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.710 73 Å) and fine sliced 0.5° ω- and φ-scan frames covering a complete Ewald sphere with θ_{max} = 30°. The frames were integrated with the program SAINT, and corrections for absorption and $\lambda/2$ effects were applied with the program SADABS. After structure solution with the program SHELXS97 by direct methods, refinement on F^2 was carried out with the program SHELXL (version 2014/6). Non-hydrogen atoms were refined anisotropically. All H atoms were placed in calculated positions and thereafter refined as riding. The crystal structure was checked with the program PLATON.[31] For crystallographic data and atomic parameters in CIF format as well as structural relationships see the Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information

Figures, tables with geometric data, and a CIF for **9** as well as figures of NMR spectra of starting materials and products are given. Further NMR data for *ortho*-deprotonation reactions as well as the results of deuteration experiments are listed. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00464.

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Notes

The authors declare no competing financial interest.

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