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A Practical Procedure for Iron-Catalyzed Cross-Coupling Reactions of Sterically Hindered Aryl-Grignard Reagents with Primary Alkyl Halides

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Abstract: Although iron-catalyzed cross-coupling reactions of arylmagnesium halides with alkyl halides are well established and proceed effectively under a variety of experimental conditions, they often find limitations when working with sterically hindered aryl-Grignard reagents. Outlined in this paper is a practical solution that allows this gap in coverage to be filled. Specifically, it is shown that bis(diethylphosphino)ethane (depe) crafts an effective coordination environment about Fe(+2). This commercially available ligand is slim enough not to interfere with the loading of the iron center even by *ortho,ortho*-disubstituted arylmagnesium halides, yet capable of preventing premature reductive coupling of the resulting organoiron species, which seem to be hardly basic either. The reaction is compatible with various polar functional groups as well as with substrates containing β-heteroatom substituents. Moreover, the procedure even allows encumbered neopentylic electrophiles to be arylated with donors as bulky as mesitylmagnesium bromide, whereas secondary alkyl halides tend to eliminate.

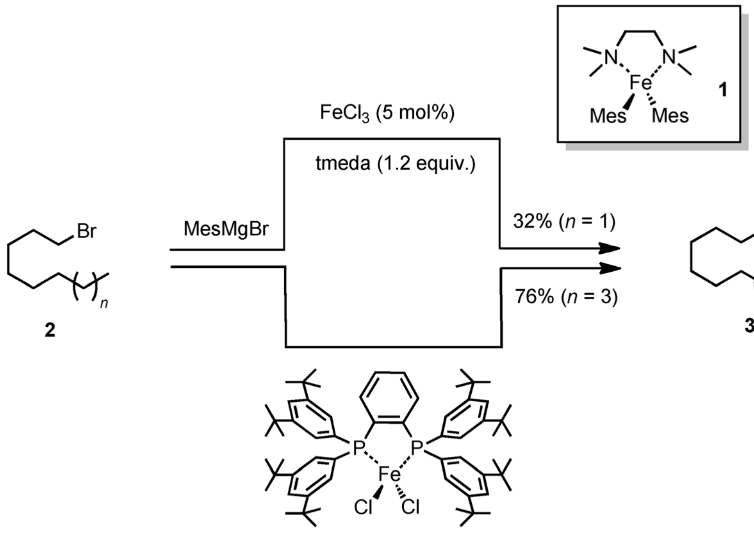
Keywords: alkyl halides; cross-coupling; diphosphines; Grignard reagents; iron; radicals

Introduction

Although the dominance of palladium catalysts over the field of cross-coupling is likely to persist,[1] other metals do provide valuable alternative solutions for specific applications. In this context, the interest in iron was rejuvenated during the last decade because of the obvious benefits that this cheap, benign and readily available metal can provide.[2–12] A particularly valuable facet of its chemistry is the ease with which different iron catalysts promote cross-coupling reactions of alkyl halides,[13–16] which do not belong to the privileged substrates in the realm of palladium catalysis.[17] Such reactions are distinguished by an appreciable functional group tolerance, including many substituents which are *a priori* susceptible to uncatalyzed attack by an organomagnesium species as the most commonly used nucleophilic partners.[13–16,18–23]

This considerable scope notwithstanding, successful cross-coupling reactions of sterically hindered arylmagnesium halides with alkyl halides are conspicuously rare. Even the highly reactive ferrate complex $[Li(tmeda)]_2[Fe(C_2H_4)_4]$ (5 mol%), which effects the reaction of p-XC_6H_4MgBr [X = H, Me, Ph, OMe, Cl, NMe_2, $N(SiMe_3)_2$] with functionalized primary and secondary alkyl halides with remarkable rates at temperatures as low as −20 °C, failed when MesMgBr was used.[18] Likewise, the combination of $FeCl_3$ (5 mol%) and bulky NHC ligands did not allow mesityl groups to be transferred either, although the catalysts formed *in situ* from these components accept even unreactive alkyl chlorides otherwise.[24,25]

Amongst the few cases of successful cross-couplings of hindered arylmagnesium halides, two reports by Nakamura and co-workers stand out (Scheme 1).[26–29] These authors showed that $FeCl_3$ (5 mol%) in the presence of excess tmeda (1.2 equiv.) effects the coupling of 1-bromooctane **2** ($n = 1$) with MesMgBr, albeit in modest yield (32%).[26] A stoichiometric control experiment using the relatively stable iron complex **1** furnished product **3** in 76% yield after 9.5 h at 30 °C, suggesting that **1** might be the competent nucleophile generated *in situ* in the catalytic manifold. Shortly thereafter, the same group demonstrated that complex **4** endowed with a very bulky 1,2-bis{bis[3,5-(di-*tert*-butyl)phenyl]phosphino}benzene [3,5-(t-Bu)$_2$-SciOPP] ligand fares much better in such challenging transformations.[27,28]



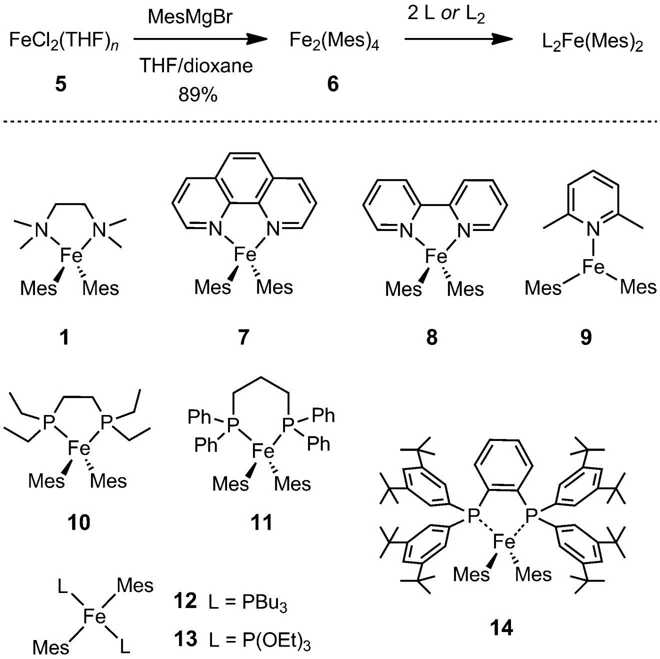
Scheme 1. Important literature precedent for iron-catalyzed cross-coupling reactions of alkyl halides with MesMgBr. Mes = mesityl (2,4,6-$Me_3C_6H_2$-); tmeda = *N,N,N′,N′*-tetramethylethylenediamine.

Outlined below we present a practical alternative solution for iron-catalyzed cross-coupling of *ortho*-substituted aryl-Grignard reagents with primary alkyl halides, based on the use of bis(diethylphosphino)ethane (depe) as ligand for $FeCl_2$. The fact that this low molecular weight catalyst system is uniquely effective for the transfer of sterically hindered nucleophiles such as MesMgBr but hardly useful for slimmer donors has mechanistic significance. Reductive elimination of two encumbered aryl groups from a single iron center is impeded on steric grounds, whereas less bulky nucleophiles likely generate low-valent iron species. This conclusion corroborates our previous view that iron-catalyzed cross-coupling reactions are mechanistically by no means uniform; rather, they can follow different pathways depending on the chosen nucleophiles.[2,18,30]

Results and Discussion

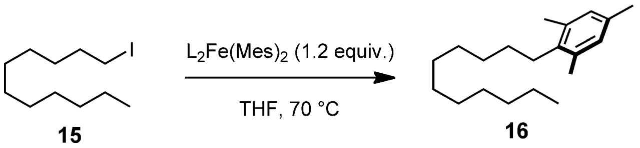
The Stoichiometric Regime

Mechanistic investigations into iron-catalyzed reactions are challenging, not least because of the exceptional sensitivity of many organoiron compounds. One important exception, however, are iron mesityl complexes of the general type $[L_2Fe(Mes)_2]$ (Mes = 2,4,6-trimethylphenyl), many of which are thermally surprisingly stable. They are readily accessible by addition of the appropriate ligand(s) L to the dinuclear complex $[Fe_2(Mes)_4]$ (**6**) (Scheme 2).[31–33] Although many complexes of the general type $[L_2Fe(Mes)_2]$ were fully characterized in structural terms in the past,[34] their reactivity *vis-à-vis* organic electrophiles remains largely unexplored.[35] To fill this gap, we prepared a representative set of complexes of this type by following the literature route (Scheme 2) and engaged them into stoichiometric reactions with different electrophilic partners that are known to be amenable to iron-catalyzed cross-coupling. To calibrate our results, this investigation included complexes **1** and **14**[36] carrying the ligands that had already been successfully used by the Nakamura group.[26,27] More-



Scheme 2. Assortment of iron bis(mesityl) complexes with ancillary ligands of greatly different steric demand and electronic character.

Table 1. Results of the reaction of 1-iodoundecane (**15**) with stoichiometric amounts of different iron mesityl complexes in THF at 70 °C.[a]



Entry	Complex	t [h]	Mes–Mes [%, GC]	**16** [%, GC]
1	**1**	2.5	3	82
2	**6**	2.5	12	66
3	**7**	4	4	83
4	**8**	2	3	54
5	**9**	24	17	65
6[c]	**10**	4[c]	3.7[c]	68[c]
7	**10**	0.5	<1	91
8[d]	**10**	1[d]	1[d]	91[d]
9[e]	**10**	2	2	83[e]
10	**11**	6.5	10	60
11	**12**	2.5	7	<50[b]
12	**13**	2.5	7	63
13	**14**	2.5	<1	77
14	**19**	1	15	66
15	**21**	1	24	43[f]

[a] Unless stated otherwise, the mass balance is made up by mesitylene formed by partial decomposition of the complexes (ref.[39]) and, in some cases, residual starting material; unless stated otherwise, the crude mixture contained <5% of 1-undecene.

[b] The exact determination is difficult because of large amounts of Bu_3P in the GC trace.

[c] The reaction was performed at ambient temperature.

[d] Using only $^1/_2$ equivalent of the complex.

[e] Using 1-bromoundecane as the substrate.

[f] 33% of 1-undecene were detected in the crude mixture.

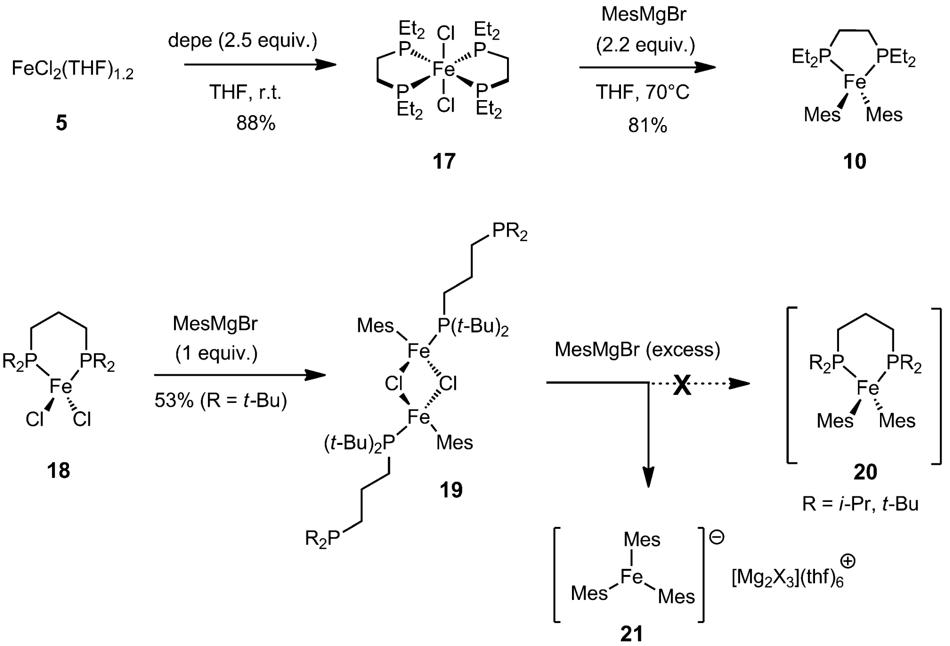
over, three representative complexes of proven constitution bearing monodentate ligands were also included in this screening exercise.[34,37]

Whereas attempted cross-coupling reactions of these iron nucleophiles with representative alkenyl and aryl chlorides were not rewarding,[38] complex **1** reacted cleanly with 1-iodoundecane (**15**) to give product **16**, in line with the result of Nakamura's model study alluded to above.[26] At ambient temperature, the coupling proceeded rather slowly (68% GC after 6 h), but it became effective when performed at 70 °C (82% GC yield after 2.5 h) (Table 1, entry 1).

However, the ability of **1** to react with 1-iodoundecane is not unique and other complexes of the type $[L_2Fe(Mes)_2]$ worked similarly well as long as L_2 is a chelating ligand set; in contrast, the ligandless complex **6** (entry 2) as well as complexes **12** and **13** containing monodentate phosphines or phosphites (entries 11 and 12), respectively, were less productive.[40] As can be seen from the results compiled in Table 1, the yields varied surprisingly little with the electronic character of the ancillary chelate ligand. Thus, the tmeda complex **1** (entry 1) and the 1,10-phenanthroline complex **7** (entry 3) gave an almost identical product distribution, although tmeda is a strong σ-donor whereas phenanthroline has substantial π-acceptor properties; as one might expect, however, the reaction rate was higher for complex **1**. By far the best results in terms of yield, reaction rate and purity of the crude material were obtained with 1,2-bis(diethylphosphino)ethane (depe) as the ligand; virtually no bis(mesityl) formed by reductive coupling of the aryl units of [(depe)Fe(Mes)$_2$] (**10**)[34e] was detected in the crude mixture, thus rendering product isolation very facile. Entry 8 shows that this complex is able to transfer both mesityl groups to the alkyl iodide. Entry 9 illustrates that bromoalkanes are also amenable to cross-coupling with complex **10** with similar efficiency. Comparison of entries 7 and 13 reveals that the depe ligand ($C_{10}H_{24}P_2$, 206.3) clearly outperforms its more engineered cousin 3,5-(t-Bu)$_2$-SciOPP ($C_{62}H_{88}P_2$, 895.6) contained in complex **14**[36] and has the distinct advantage of a much lower molecular weight.

These encouraging results prompted us to study whether complex **10** can also be generated under conditions that emulate the elementary step of a catalytic process more closely than the procedure shown in Scheme 2. In this context, one has to keep in mind that mixing of depe and $FeCl_2$ in THF does not lead to [(depe)FeCl$_2$]; rather, the known 2:1 adduct *trans*-[(depe)$_2$FeCl$_2$] (**17**) is formed, which can be obtained in analytically pure form when 2 equivalents of depe are utilized (Scheme 3).[41,42] Significantly though, treatment of **17** with MesMgBr (2.2 equiv.) in THF at 70 °C releases the excess phosphine and furnishes [(depe)Fe(Mes)$_2$] (**10**) as the only iron-containing complex that could be isolated from the reaction mixture in 81% yield by crystallization. The constitution of this sample and its identity with the material prepared from **6** by the literature route (Scheme 2) was unambiguously proven by X-ray diffraction (Figure 1).[33,43] The ease of formation of **10** from adduct **17** is interpreted in the light of a previous study which suggested that [(depe)$_2$FeCl$_2$] might undergo reversible dissociation of one of the bidentate ligands from the iron center in solution.[42]

Diphosphines that are sterically more encumbered than depe led to a different outcome (Scheme 3, *bottom*). Although they afford 1:1 adducts **18** with $FeCl_2$, treatment with excess MesMgBr in THF does not lead to the putative complexes **20**, likely for steric reasons.[44] Black mixtures were produced instead, from which small amounts of the ate-complex **21** could be isolated by crystallization in one case. Its constitution was confirmed by X-ray diffraction (Figure 2);[33] related mesityl ate-complexes, differing



Scheme 3. Reaction of different [(diphosphine)FeCl$_2$] complexes with MesMgBr in THF.

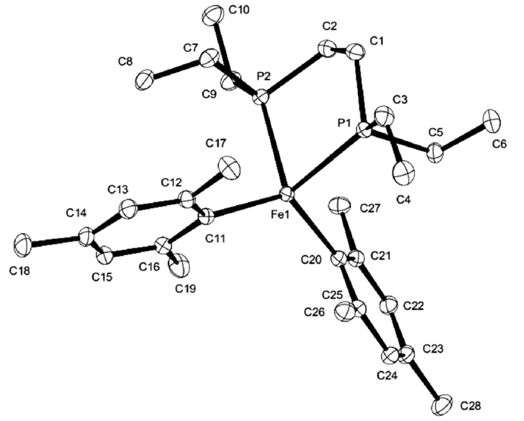


Figure 1. Structure of complex **10**[34e] in the solid state, which was formed by reaction of complex **17** with MesMgBr (Scheme 3).

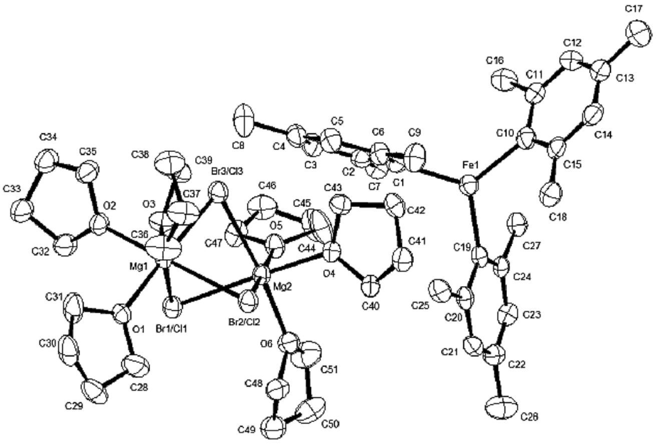


Figure 2. Structure of the tris(mesityl)-ate complex **21** in the solid state; co-crystallized toluene in the unit cell has been removed for clarity (the full structure is shown in the Supporting Information).

only in the escorting cation, are known in the literature.[31a,34f] Next, we checked whether this result has any implications for catalysis:[45] in a catalytic process, the Grignard reagent is necessarily present in large excess relative to the chosen iron precatalyst, at least in the early stages of the reaction. One might therefore speculate that ligand-free **21** could also be generated *in situ* from complexes **17** or **10**. Although **21** reacted with 1-iodoundecane (**15**) to give the product **16**, competing elimination of HI gained prominence, leading to the formation of substantial amounts of 1-undecene (Table 1, entry 15). This result shows that **21** is significantly more basic than **10**, which produced hardly any alkene under otherwise identical conditions (entry 7). Since the catalytic cross-coupling reactions of primary alkyl halides outlined below are not plagued by competing elimination either, we conclude that tris(mesityl)-ate complexes of type **21** cannot be the reigning nucleophiles.[56]

Upon limiting the amount of the MesMgBr to 1 equivalent, the precursor complex **18** (R = *t*-Bu) was converted into the rather unusual halide-bridged dimer **19**, in which the chelate ring has been opened and one of the phosphine units resides unbound on a dangling side arm (Figure 3).[33] This structural feature notwithstanding, **19** reacts with 1-iodoundecane (**15**) to give the desired cross-coupling product **16** in fair yield under the standard conditions of our assay

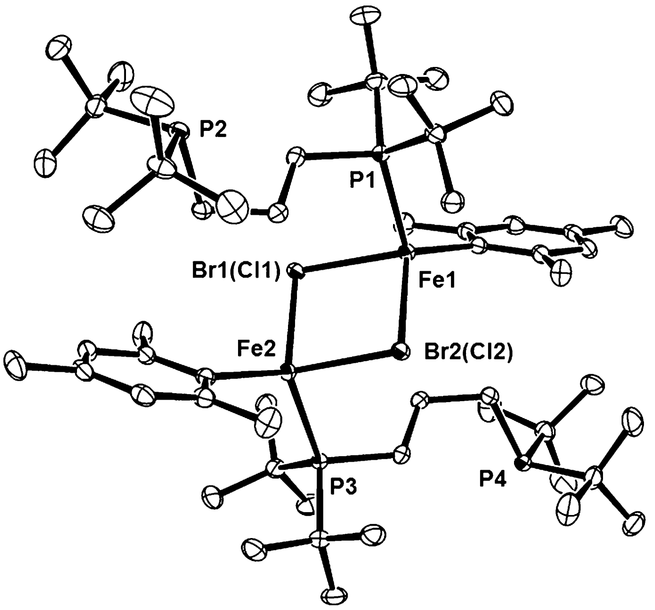


Figure 3. Structure of complex **19** in the solid state.

(entry 14). Yet, the higher efficacy of **10**, the commercial availability of depe and its significantly lower molecular weight suggested that our further studies be focused on this particular complex as the most promising candidate *en route* to a practical catalytic manifold.

Catalytic Cross-Coupling of *ortho*-Substituted Aryl-Grignard Reagents

The favorable outcome of the stoichiometric reactions of various well defined organoiron species is mirrored in the catalytic set-up (Table 2). As expected, [(depe)Fe(Mes)$_2$] (**10**) outperformed the other tested complexes in terms of yield and purity of the crude mixture. Although the reaction proceeded at ambient temperature (Table 2, entry 5), the best result was again obtained at 70 °C (entry 6). Neither the formation of Mes–Mes nor elimination of HI with formation of 1-undecene was a serious complication with this catalyst. 1-Bromoundecane reacted with similar efficiency as its iodinated congener **15** (entry 7), which echoes the results of the stoichiometric regimen. As one might gather from the results outlined above (Scheme 3), there is no need to use the preformed complex **10**; the robust adduct **17** (with and without added FeCl$_2$ meant to sequester the second diphosphine) basically led to the same preparative outcome (entries 8 and 9), which therefore constitutes a convenient and practical choice.

Next, we used this complex as an effective and user-friendly iron source to study the scope of the reaction. To this end, MesMgBr and other sterically hindered aryl-Grignard reagents were cross-coupled with an assortment of primary alkyl iodides and bromides. Good to excellent results were obtained and the compatibility of this method with various polar functional groups was proven (Figure 4). Specifically, esters, ethers, silyl ethers, acetals, nitriles, aryl bromides and perfluoroalkyl chains are tolerated. Two carbohydrate derivatives were also found to react without incident to give products **38** and **39** in high yield. These latter examples, together with the tetrahydropyranyl derivative **37** and chromanes **40** and **41**, demonstrate that the reaction is applicable to alkyl halides bearing β-heteroatom substituents. However, a substrate containing an aromatic nitro group was decomposed, whereas an alkyl halide comprising an internal alkyne

Table 2. Catalytic cross-coupling of MesMgBr with 1-iodoundecane (**15**) as induced by different iron complexes.[a]

Entry	Complex	*t* [h]	Mes–Mes [%, GC]	1-undecene [%, GC]	**16** [%, GC]	**16** [isolated, %]
1	**1**	2.5	1	5	75[b]	nd
2	**7**	2.5	4	13	35	nd
3	**11**	2.5	1	3	80	67
4	**14**	2.5	2	<1	84	79
5[c]	**10**	3[c]	5	4	59[c]	58[c]
6	**10**	2.5	<1	<1	91	88
7[d]	**10**	20	5	2	nd	85[d]
8	**17**	2	<1	<1	nd	83
9	**17**+FeCl$_2$	2	<1	<1	nd	86
10	**18** (R=*t*-Bu)	2.5[e]	4[e]	1	88[e]	84[e]
11	**19**	2	1	2	83	nd

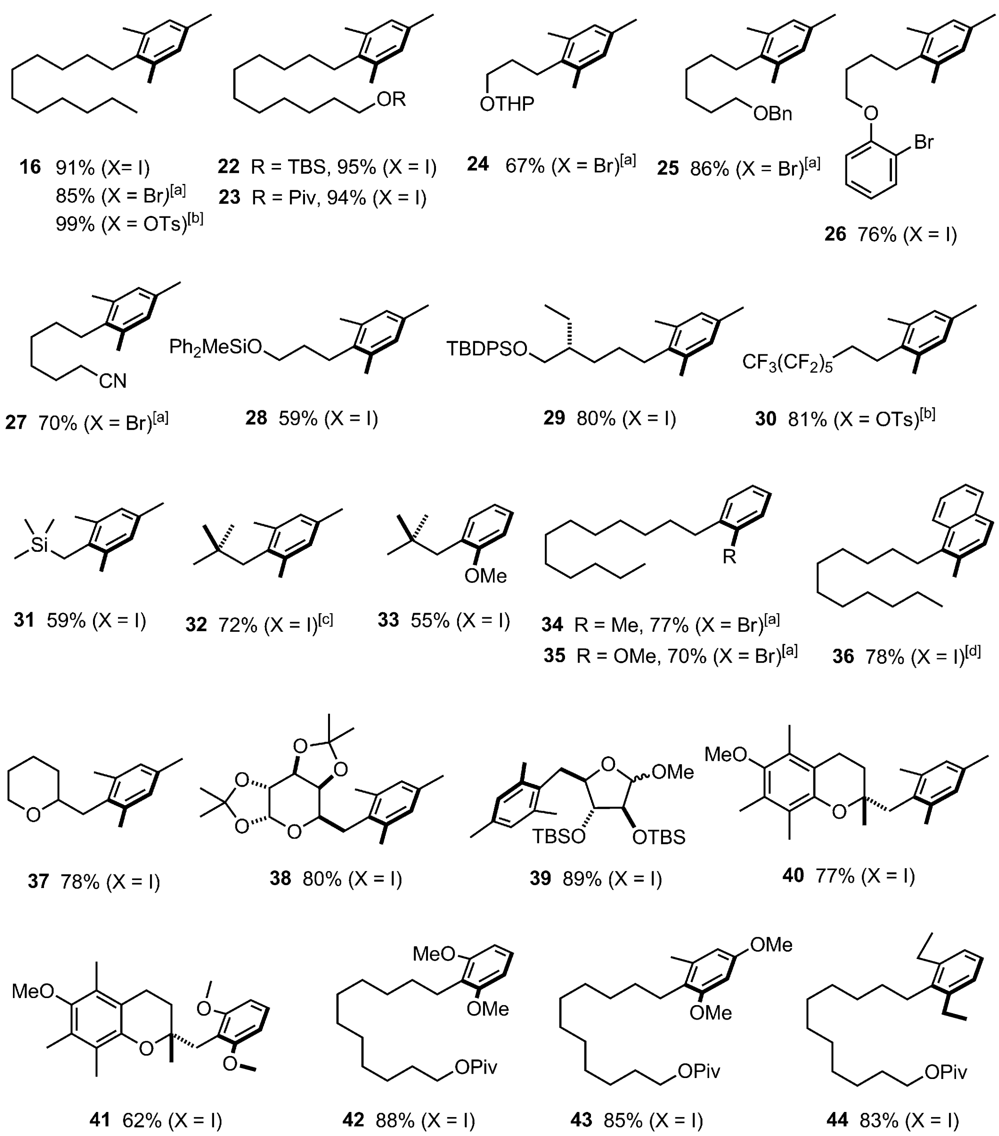
[a] Unless stated otherwise, all reactions were performed with 5 mol% of the iron complex in THF at 70 °C.

[b] When a mixture of FeCl$_2$(THF)$_{1.5}$ (5 mol%) and tmeda (1 equiv.) was used instead of preformed **1**, a GC yield of 63% was reached.

[c] At ambient temperature.

[d] Using 1-bromoundecane as the substrate.

[e] Using 10 mol% of the iron complex; nd=not determined.



16 91% (X= I)
85% (X = Br)[a]
99% (X = OTs)[b]

22 R = TBS, 95% (X = I)
23 R = Piv, 94% (X = I)

24 67% (X = Br)[a]

25 86% (X = Br)[a]

26 76% (X = I)

27 70% (X = Br)[a]

28 59% (X = I)

29 80% (X = I)

30 81% (X = OTs)[b]

31 59% (X = I)

32 72% (X = I)[c]

33 55% (X = I)

34 R = Me, 77% (X = Br)[a]
35 R = OMe, 70% (X = Br)[a]

36 78% (X = I)[d]

37 78% (X = I)

38 80% (X = I)

39 89% (X = I)

40 77% (X = I)

41 62% (X = I)

42 88% (X = I)

43 85% (X = I)

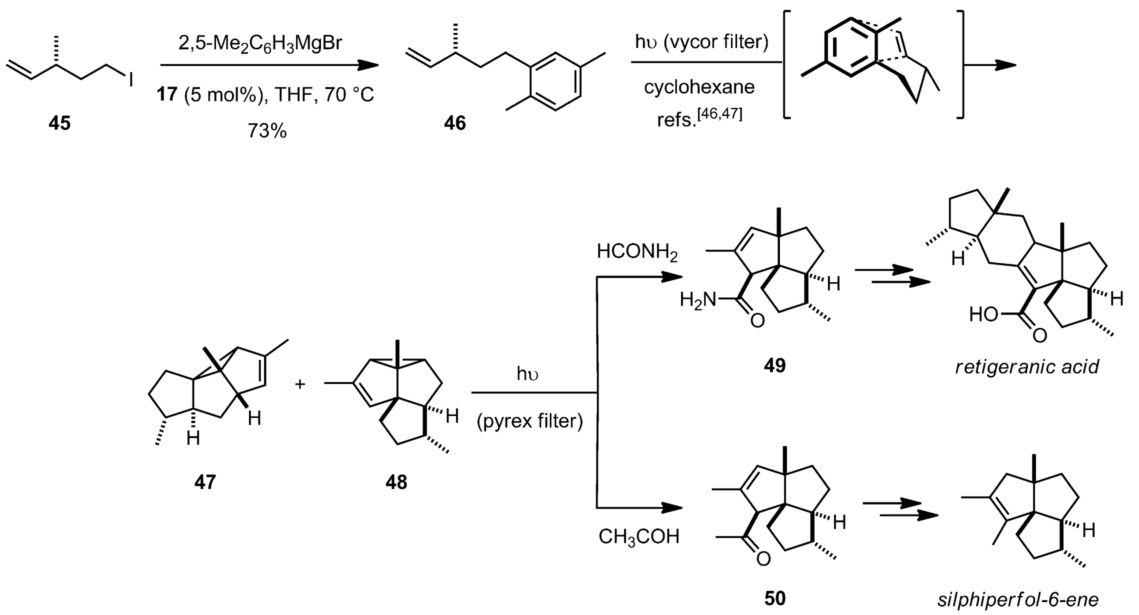
44 83% (X = I)

[a] Starting from the primary bromide.
[b] Starting from the primary tosylate; the reaction was performed in the presence of NaI (10 mol%).
[c] In Et_2O.
[d] GC yield.

Figure 4. Assortment of products formed by iron-catalyzed cross-coupling of primary halides RX with Grignard reagents bearing at least one *ortho*-substituent; unless stated otherwise, all reactions were performed using complex **17** as the precatalyst (5 mol%) in THF at 70 °C.

underwent competitive carbometalation of the π-system; this reaction is currently under investigation.[46]

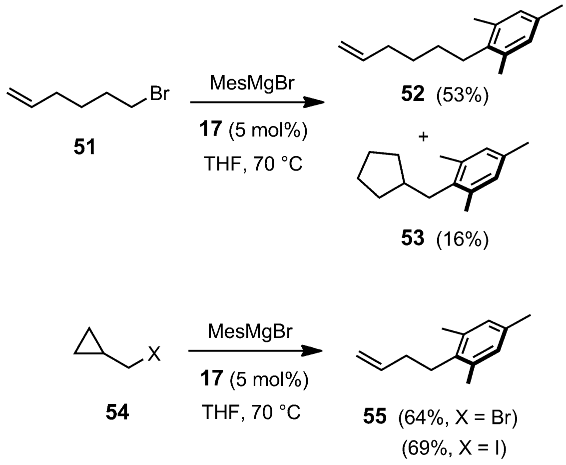
It is rewarding that even sterically hindered electrophilic partners can be coupled, as evident from the successful arylation of neopentyl iodide to afford products **32** and **33** in respectable yields. The equally "neopentylic" environments in **31** and in the crowded chromane derivatives **40** and **41** further illustrate this aspect. In these cases, however, the use of the corresponding iodide was mandatory, although primary bromides and iodides had been found similarly effective otherwise. Primary tosylates *per se* do not react,[47] but they can be used if the reaction mixture is supplemented with catalytic amounts of NaI to ensure *in situ* formation of the corresponding iodide as the actual coupling partner (see products **16** and **30**).[48] Unfortunately though, secondary halides tend to eliminate under the standard conditions, probably due to the elevated temperature of 70 °C that is needed to ensure meaningful reaction rates.



Scheme 4. An iron-catalyzed cross-coupling delivers the starting material for the known *meta*-photocycloaddition that enabled the total syntheses of retigeranic acid and the silphiperfolenes.[50,51]

With regard to the nucleophile, an assortment of sterically hindered aryl-Grignard reagents was successfully used. Specifically, 2,6-disubstituted Grignard reagents other than mesityl-MgBr also reacted cleanly to give the expected coupling products **41**–**44**. Likewise, organomagnesium reagents with only one *ortho*-substituent performed well, as evident from the preparation of compounds **33**–**35**. The scope is further illustrated by the reaction of 2,5-dimethylphenylmagnesium bromide with the unsaturated iodide **45** which gave product **46** in good yield (Scheme 4). Upon irradiation with light of appropriate wave length, this particular compound is known to undergo an intramolecular arene–alkene *meta*-photocycloaddition that engenders a significant increase in structural complexity.[49] As previously reported by Wender and Singh, products **47** and **48** are initially formed in a 1.9:1 ratio; further irradiation (pyrex filter) in the presence of formamide shifts the composition toward isomer **48** which undergoes homolytic cleavage of the cyclopropane ring with concomitant attachment of the amide group.[50] Product **49** thus formed served as the core building block for an elegant total synthesis of retigeranic acid. Replacement of formamide by acetaldehyde delivers product **50**, which opened a concise entry into the angular sesquiterpenes of the silphiperfolene family.[51]

If one takes the amount of homocoupling product Mes–Mes as a proxy for the amount of low-valent iron in solution, one must infer from the data shown in Table 2 that MesMgBr does not reduce the iron salt precursors tested in this study under the chosen reaction conditions to any significant extent.[52] Complex [(depe)Fe(Mes)$_2$] (**10**) and relatives are hence unlikely to operate *via* a regime that involves low-valent iron species.[18] On the other hand, it is equally unlikely that **10** reacts *via* a simple S$_N$2-type alkylation pathway, because primary tosylates *per se* are inert whereas primary halides are well suited substrates.[47] The smooth conversion of neopentylic halides, which tend to perform poorly in S$_N$2-type reactions, also argues for a more involved pathway. It is assumed that the reactions are triggered by single electron transfer, as evident from the conversion of 6-bromo-1-hexene (**51**) into a mixture of **52** and the cyclized isomer **53** (Scheme 5). The faster-ticking radical clock of the cyclopropylmethyl halides **54** resulted in quantitative ring opening prior to C–C bond forma-



Scheme 5. Radical clock experiments.

tion to give **55** as the only product. Collectively, these observations suggest that the coupling of sterically hindered arylmagnesium halides with alkyl halides described herein proceeds *via* a catalytic cycle based upon an Fe(II)/Fe(III) redox couple and the intervention of alkyl radical intermediates. This conclusion basically reiterates the proposal made by Nakamura and co-workers for [(tmeda)Fe(Mes)$_2$] (**1**).[53]

Slimmer Grignard reagents almost certainly react by other pathways.[54] This notion is evident from the fact that **10** is highly effective in catalyzing the cross-coupling of 1-bromoundecane with *o*-MeC_6H_4MgBr to give product **34** in 77% yield (Figure 4), whereas the positional isomer *p*-MeC_6H_4MgBr as well as the parent reagent PhMgBr both performed poorly under otherwise identical conditions (22–32% GC yield). Substantial amounts (25–40%, GC) of Ar–Ar were detected in these cases, which is likely formed by reductive coupling of a transient [(depe)Fe(Ar)$_2$] (Ar = Ph, *para*-tolyl) intermediate with concomitant formation of an Fe(0) species.[54]

Hence we conclude that the commercial and reasonably low molecular weight diphosphine ligand depe crafts a coordination environment about Fe(II) that is particularly effective for the cross-coupling of sterically hindered arylmagnesium halides with alkyl halides. On the one hand, little barrier seems to exist for the crucial diarylation of the central metal even by bulky *ortho,ortho′*-disubstituted Grignard reagents. The resulting loaded complexes such as **10** are averse against reductive ligand coupling, which renders them thermally surprisingly robust. Moreover, they are hardly basic but effective in transferring a single electron to alkyl halides substrate as the likely key step *en route* to the desired cross-coupling products. Since the functional group compatibility is good and even congested starting materials are amenable to productive C–C bond formation, we believe that this methodology provides a benign and practical solution for a challenging problem and should therefore be of interest for advanced organic synthesis.[55,56]

Experimental Section

All experimental details can be found in the Supporting Information. The material includes the structure of complexes **6**, **10**, **17**, **19** and **21** in the solid state, crystallographic abstracts, compound characterization, and copies of spectra of new compounds.

Preparation of 1,3,5-Trimethyl-2-undecylbenzene (16)

Method A: MesMgBr (1 M in THF, 0.97 mL, 0.974 mmol) was added dropwise over 1 h to a stirred solution of 1-iodoundecane (228.9 mg, 0.812 mmol) and [Fe(depe)Mes$_2$] (20.3 mg, 5 mol%, 0.041 mmol) in THF (4 mL) at 70 °C. Once the addition was complete, stirring was continued at this temperature for 30 min before the mixture was allowed to reach ambient temperature. The reaction was quenched with water (20 mL) and the organic phase extracted by MeO-*t*-Bu (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (silica, hexane) to give the title compound as a colorless liquid; yield: 200.2 mg (90%).

Method B: 1-Iodoundecane (44.6 mg, 0.158 mmol) was added to a stirred solution of [Fe(depe)Mes$_2$] (**10**) (102.9 mg, 0.206 mmol) in THF (4 mL). The mixture was stirred at 70 °C until complete conversion of the starting material was reached (the reaction was monitored by GC-MS; the samples were quenched with MeOD). For work-up, the mixture was allowed to reach ambient temperature, the reaction was quenched with water (20 mL) and the organic phase extracted by MeO*t*Bu (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (silica, hexane) to give the title compound as a colorless liquid; yield: 39.4 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.02$ (t, $J = 3.6$ Hz, 3 H), 1.40–1.54 (m, 18 H), 2.36 (s, 3 H), 2.40 (s, 6 H), 2.68 (t, $J = 8.0$ Hz, 2 H), 6.93 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.1$, 19.7, 20.8, 22.7, 29.4, 29.5, 29.6, 29.7, 30.3, 32.0, 128.9, 134.7, 135.8, 136.7; IR (film): $\nu = 2921$, 2853, 1614, 1578, 1484, 1466, 1376, 1205, 1117, 1029, 1012, 849, 721 cm^{-1}; MS (EI): *m/z* (%) = 274 (31), 133 (100), 120 (3), 105 (3), 91 (2), 55 (2), 41 (4); HR-MS (EI): *m/z* = 274.26605, calcd. for $C_{20}H_{34}$ [*M*]: 274.26618.

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References

[1] a) *Metal-Catalyzed Cross-Coupling Reactions*, Vols. 1 and 2 (Eds.: A. de Meijere, F. Diederich), 2nd edn., Wiley-VCH, Weinheim, **2004**; b) *Handbook of Organopalladium Chemistry for Organic Synthesis*, (Ed.: E. Negishi,), Wiley, New York, **2002**.
[2] B. D. Sherry, A. Fürstner, *Acc. Chem. Res.* **2008**, *41*, 1500–1511.
[3] G. Cahiez, S. Marquais, *Pure Appl. Chem.* **1996**, *68*, 53–60.
[4] E. Nakamura, N. Yoshikai, *J. Org. Chem.* **2010**, *75*, 6061–6067.
[5] T. Hatakeyama, K. Ishizuka, M. Nakamura, *J. Synth. Org. Chem. Jpn.* **2011**, *69*, 1282–1297.
[6] E. B. Bauer, *Curr. Org. Chem.* **2008**, *12*, 1341–1369.
[7] W. M. Czaplik, M. Mayer, J. Cvengroš, A. Jacobi von Wangelin, *ChemSusChem* **2009**, *2*, 396–417.

[8] C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Rev.* **2011**, *111*, 1293–1314.

[9] C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217–6254.

[10] H. Shinokubo, K. Oshima, *Eur. J. Org. Chem.* **2004**, 2081–2091.

[11] a) A. Fürstner, *Angew. Chem.* **2009**, *121*, 1390–1393; *Angew. Chem. Int. Ed.* **2009**, *48*, 1364–1367; b) A. Fürstner, R. Martin, *Chem. Lett.* **2005**, *34*, 624–629.

[12] *Iron Catalysis in Organic Chemistry: Reactions and Applications*, (Ed.: B. Plietker), Wiley-VCH, Weinheim, **2008**.

[13] M. Nakamura, K. Matsuo, S. Ito, E. Nakamura, *J. Am. Chem. Soc.* **2004**, *126*, 3686–3687.

[14] T. Nagano, T. Hayashi, *Org. Lett.* **2004**, *6*, 1297–1299.

[15] R. Martin, A. Fürstner, *Angew. Chem.* **2004**, *116*, 4045–4047; *Angew. Chem. Int. Ed.* **2004**, *43*, 3955–3957.

[16] R. B. Bedford, D. W. Bruce, R. M. Frost, J. W. Goodby, M. Hird, *Chem. Commun.* **2004**, 2822–2823.

[17] For pertinent discussions, see: a) A. Rudolph, M. Lautens, *Angew. Chem.* **2009**, *121*, 2694–2708; *Angew. Chem. Int. Ed.* **2009**, *48*, 2656–2670; b) J. Terao, N. Kambe, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 663–672; c) A. C. Frisch, M. Beller, *Angew. Chem.* **2005**, *117*, 680–695; *Angew. Chem. Int. Ed.* **2005**, *44*, 674–688; d) D. J. Cárdenas, *Angew. Chem.* **2003**, *115*, 398–401; *Angew. Chem. Int. Ed.* **2003**, *42*, 384–387.

[18] A. Fürstner, R. Martin, H. Krause, G. Seidel, R. Goddard, C. W. Lehmann, *J. Am. Chem. Soc.* **2008**, *130*, 8773–8787.

[19] a) M. Nakamura, S. Ito, K. Matsuo, E. Nakamura, *Synlett* **2005**, 1794–1798; b) R. B. Bedford, D. W. Bruce, R. M. Frost, M. Hird, *Chem. Commun.* **2005**, 4161–4163; c) K. Bica, P. Gaertner, *Org. Lett.* **2006**, *8*, 733–735; d) R. B. Bedford, M. Betham, D. W. Bruce, A. A. Danopoulos, R. M. Frost, M. Hird, *J. Org. Chem.* **2006**, *71*, 1104–1110; e) R. B. Bedford, M. Betham, D. W. Bruce, S. A. Davis, R. M. Frost, M. Hird, *Chem. Commun.* **2006**, 1398–1400; f) G. Cahiez, V. Habiak, C. Duplais, A. Moyeux, *Angew. Chem.* **2007**, *119*, 4442–4444; *Angew. Chem. Int. Ed.* **2007**, *46*, 4364–4366; g) W. M. Czaplik, M. Mayer, A. Jacobi von Wangelin, *Angew. Chem.* **2009**, *121*, 616–620; *Angew. Chem. Int. Ed.* **2009**, *48*, 607–610; h) S. Kawamura, K. Ishizuka, H. Takaya, M. Nakamura, *Chem. Commun.* **2010**, *46*, 6054–6056; i) T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *J. Am. Chem. Soc.* **2010**, *132*, 10674–10676; j) H. Gao, C. Yan, X.-P. Tao, Y. Xia, H.-M. Sun, Q. Shen, Y. Zhang, *Organometallics* **2010**, *29*, 4189–4192; k) M. Jin, M. Nakamura, *Chem. Lett.* **2011**, *40*, 1012–1014; l) Y. Yamaguchi, H. Ando, M. Nagaya, H. Hinago, T. Ito, M. Asami, *Chem. Lett.* **2011**, *40*, 983–985; m) A. K. Steib, T. Thaler, K. Komeyama, P. Mayer, P. Knochel, *Angew. Chem.* **2011**, *123*, 3361–3365; *Angew. Chem. Int. Ed.* **2011**, *50*, 3303–3307; n) K. Weber, E.-M. Schnöckelborg, R. Wolf, *ChemCatChem* **2011**, *3*, 1572–1577; o) S. Meyer, C. M. Orben, S. Demeshko, S. Dechert, F. Meyer, *Organometallics* **2011**, *30*, 6692–6702; p) X. Lin, F. Zheng, F.-L. Qing, *Organometallics* **2012**, *31*, 1578–1582; q) S. Kawamura, T. Kawabata, K. Ishizuka, M. Nakamura, *Chem. Commun.* **2012**, *48*, 9376–9378.

[20] For analogous iron-catalyzed coupling reactions of alkyl halides with alkenylmetal reagents, see: a) U. H. Brinker, L. König, *Chem. Ber.* **1983**, *116*, 882–893; b) A. Guérinot, S. Reymond, J. Cossy, *Angew. Chem.* **2007**, *119*, 6641–6644; *Angew. Chem. Int. Ed.* **2007**, *46*, 6521–6524; c) G. Cahiez, C. Duplais, A. Moyeux, *Org. Lett.* **2007**, *9*, 3253–3254; d) T. Hatakeyama, N. Nakagawa, M. Nakamura, *Org. Lett.* **2009**, *11*, 4496–4499; e) T. Hashimoto, T. Hatakeyama, M. Nakamura, *J. Org. Chem.* **2012**, *77*, 1168–1173.

[21] For analogous iron-catalyzed coupling reactions of alkyl halides with alkynylmetal reagents, see: T. Hatakeyama, Y. Okada, Y. Yoshimoto, M. Nakamura, *Angew. Chem.* **2011**, *123*, 11165–11168; *Angew. Chem. Int. Ed.* **2011**, *50*, 10973–10976.

[22] Even iron-catalyzed alkyl–alkyl coupling reactions are possible, see: a) K. G. Dongol, H. Koh, M. Sau, C. L. L. Chai, *Adv. Synth. Catal.* **2007**, *349*, 1015–1018; b) T. Hatakeyama, T. Hashimoto, K. K. A. D. S. Kathriarachchi, T. Zenmyo, H. Seike, M. Nakamura, *Angew. Chem.* **2012**, *124*, 8964–8967; *Angew Chem. Int. Ed.* **2012**, *51*, 8834–8837; c) M. Guisán-Ceinos, F. Tato, E. Buñuel, P. Calle, D. J. Cárdenas, *Chem. Sci.* **2013**, *4*, 1098–1104.

[23] For iron-catalyzed cross-coupling of alkyl thioethers and alkyl sulfones with aryl-Grignard reagents, see: S. E. Denmark, A. J. Cresswell, *J. Org. Chem.* **2013**, *78*, 12593–12628.

[24] S. K. Ghorai, M. Jin, T. Hatakeyama, M. Nakamura, *Org. Lett.* **2012**, *14*, 1066–1069.

[25] a) H. Deng, Y. Xing, C. Xia, H. Sun, Q. Shen, Y. Zhang, *Dalton Trans.* **2012**, *41*, 11597–11607; b) C.-L. Xia, C.-F. Xie, Y.-F. Wu, H.-M. Sun, Q. Shen, Y. Zhang, *Org. Biomol. Chem.* **2013**, *11*, 8135–8144.

[26] D. Noda, Y. Sunada, T. Hatakeyama, M. Nakamura, H. Nagashima, *J. Am. Chem. Soc.* **2009**, *131*, 6078–6079.

[27] T. Hatakeyama, Y. Fujiwara, Y. Okada, T. Itoh, T. Hashimoto, S. Kawamura, K. Ogata, H. Takaya, M. Nakamura, *Chem. Lett.* **2011**, *40*, 1030–1032.

[28] S. Kawamura, M. Nakamura, *Chem. Lett.* **2013**, *42*, 183–185.

[29] For successful coupling reactions of arylmagnesium halides bearing one or two *ortho*-substituents with alkyl halides using iron complexes with tailored amino(bisphenolate) or NHC ligands, see: a) R. R. Chowdhury, A. K. Crane, C. Fowler, P. Kwong, C. M. Kozak, *Chem. Commun.* **2008**, 94–96; b) X. Qian, L. N. Dawe, C. M. Kozak, *Dalton Trans.* **2011**, *40*, 933–943; c) K. Hasan, L. N. Dawe, C. M. Kozak, *Eur. J. Inorg. Chem.* **2011**, 4610–4621; d) Z. Mo, Q. Zhang, L. Deng, *Organometallics* **2012**, *31*, 6518–6521.

[30] B. Scheiper, M. Bonnekessel, H. Krause, A. Fürstner, *J. Org. Chem.* **2004**, *69*, 3943–3949.

[31] a) W. Seidel, K.-J. Lattermann, *Z. Anorg. Allg. Chem.* **1982**, *488*, 69–74; b) A. Klose, E. Solari, C. Floriani, A. Chiesa-Villa, C. Rizzoli, N. Re, *J. Am. Chem. Soc.* **1994**, *116*, 9123–9135; c) H. Müller, W. Seidel, H. Görls, *J. Organomet. Chem.* **1993**, *445*, 133–136; d) H. Müller, W. Seidel, H. Görls, *Z. Anorg. Allg. Chem.* **1996**, *622*, 756–758.

[32] Complex **6** was prepared according to the literature (ref.[31]); although the structure of this compound in the solid state is known, our sample differed in that it contained co-crystallized Et_2O in the unit cell; for details see the Supporting Information.

[33] CCDC 973605 (**21**), CCDC 973606 (**6**), CCDC 973607 (**10**), CCDC 973608 (**17**), and CCDC 973609 (**19**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. Short crystallographic abstracts and Figures showing the entire unit cells of these crystal structures can also be found in the Supporting Information.

[34] Depending on the chosen ligand, they exist either as a low-spin/square planar or as high-spin/tetrahedral coordination compounds, although "intermediate" spin states have also been documented, see: a) J. Chatt, B. L. Shaw, *J. Chem. Soc.* **1961**, 285–290; b) B. Machelett, *Z. Chem.* **1976**, *16*, 116–117; c) K.-J. Lattermann, W. Seidel, *Z. Chem.* **1983**, *23*, 31; d) C. P. Magill, C. Floriani, A. Chiesi-Villa, C. Rizzoli, *Inorg. Chem.* **1994**, *33*, 1928–1933; e) E. J. Hawrelak, W. H. Bernskoetter, E. Lobkovsky, G. T. Yee, E. Bill, P. J. Chirik, *Inorg. Chem.* **2005**, *44*, 3103–3111; f) M. Irwin, R. K. Jenkins, M. S. Denning, T. Krämer, F. Grandjean, G. J. Long, R. Herchel, J. E. McGrady, J. M. Goicoechea, *Inorg. Chem.* **2010**, *49*, 6160–6171.

[35] a) One piece of information concerns the reaction of [(dppe)Fe(Mes)$_2$] with CH_2Cl_2, which affords [(dppe)Fe(Mes)Cl] within minutes; unfortunately, the fate of the lost mesityl group has not been determined, *cf.* ref.[34e]; b) for iron-catalyzed reactions of ArMgX with CH_2Cl_2 to give diarylmethane derivatives, see: X. Qian, C. M. Kozak, *Synlett* **2011**, 852–856.

[36] Complex **14** was prepared as an amorphous solid material from **6** as shown in Scheme 2; since no crystals suitable for X-ray diffraction could be grown so far, the assignment is tentative.

[37] For the preparation of the tri-coordinate complex **9**, see: H. Müller, W. Seidel, H. Görls, *Z. Anorg. Allg. Chem.* **1996**, *622*, 1269–1273.

[38] Treatment of (*E*)-1-(2-chlorovinyl)-4-methoxybenzene with a stoichiometric amount of [(tmeda)Fe(Mes)$_2$] (**1**) furnished only small amounts ($<41\%$ GC) of the desired stilbene derivative together with bis(mesityl) (31%) and mesitylene ($\approx 10\%$); other substrates containing $C(sp^2){-}X$ units were equally recalcitrant.

[39] Most of the detected mesitylene is supposed to derive from decomposition of the respective complex, since quenching of the reaction mixture with MeOD after 6 h reaction time led to only marginal deuterium incorporation.

[40] It is currently unclear whether this is a consequence of the fact that these complexes are *trans*-configured in the ground state.

[41] J. Chatt, R. G. Hayter, *J. Chem. Soc.* **1961**, 5507–5511.

[42] M. V. Baker, L. D. Field, T. W. Hambley, *Inorg. Chem.* **1988**, *27*, 2872–2876.

[43] The constitution of **10** was confirmed by single crystal X-ray diffraction; its structure was basically identical to that reported in the literature (ref.[42]), except that two independent molecules were found in the unit cell; for details, see the Supporting Information.

[44] Girolami et al. previously reported that the attempted formation of [L_2Fe(Mes)$_2$] [L_2 = bis(diisopropylphosphino)ethane] from [L_2FeBr_2] failed even when an excess of MesMgX was used; only the corresponding monomesityl complex [L_2Fe(Mes)X] could be isolated, see: A. R. Hermes, G. S. Girolami, *Organometallics* **1987**, *6*, 763–768.

[45] For evidence that ate-complexes may be the actual nucleophiles in certain iron-catalyzed cross-coupling reactions, see: a) A. Fürstner, H. Krause, C. W. Lehmann, *Angew. Chem.* **2006**, *118*, 454–458; *Angew. Chem. Int. Ed.* **2006**, *45*, 440–444; b) C.-L. Sun, A. Fürstner, *Angew. Chem.* **2013**, *125*, 13309–13313; *Angew. Chem. Int. Ed.* **2013**, *52*, 13071–13075; c) see also: B. D. Sherry, A. Fürstner, *Chem. Commun.* **2009**, 7116–7118; d) A. Fürstner, M. Méndez, *Angew. Chem.* **2003**, *115*, 5513–5515; *Angew. Chem. Int. Ed.* **2003**, *42*, 5355–5357.

[46] In this context, a report on iron-catalyzed carbometalation of alkynes is noteworthy that gave good yields only for aryllithium reagents carrying an *ortho*-substituent, see: a) E. Shirakawa, S. Masui, R. Narui, R. Watabe, D. Ikeda, T. Hayashi, *Chem. Commun.* **2011**, *47*, 9714–9716; b) see also: E. Shirakawa, T. Yamagami, T. Kimura, S. Yamaguchi, T. Hayashi, *J. Am. Chem. Soc.* **2005**, *127*, 17164–17165.

[47] 1-Tosyloxyundecane remained unchanged on treatment with stoichiometric **10** under the standard conditions.

[48] For the reaction of arylzinc reagents with alkyl sulfonates in the presence of magnesium halides, see: S. Ito, Y. Fujiwara, E. Nakamura, M. Nakamura, *Org. Lett.* **2009**, *11*, 4306–4309.

[49] a) P. A. Wender, L. Siggel, J. M. Nuss, in: *Comprehensive Organic Synthesis*, (Eds.: B. M. Trost, I. Fleming), Vol. 5, Pergamon Press, Oxford, **1991**, pp. 645–673; b) N. Hoffmann, *Synthesis* **2004**, 481–495.

[50] P. A. Wender, S. K. Singh, *Tetrahedron Lett.* **1990**, *31*, 2517–2520.

[51] P. A. Wender, S. K. Singh, *Tetrahedron Lett.* **1985**, *26*, 5987–5990.

[52] However, MesMgBr is able to reduce iron(II) bis(phosphaethenyl)pyridine complexes to iron(I) species, see: Y. Nakajima, F. Ozawa, *Organometallics* **2012**, *31*, 2009–2015.

[53] Nakamura suggested a cycle shuttling between [(tmeda)Fe(Mes)$_2$] (**1**) and [(tmeda)FeCl(Mes)], *cf.* ref.[26]; our data for complex [(depe)Fe(Mes)$_2$] (**10**) seem to imply that the overall process might be more complex: since **10** is able to transfer *both* mesityl groups, either a second cycle shuttling between a monoaryliron halide and an iron dihalide species or a kinetically competent ligand redistribution process must be involved.

[54] There is no consensus in the literature as to which iron oxidation states are involved in the catalytic cycle, which may in part be explained by the different combinations of ligands, nucleophiles, substrates, additives and solvents that were investigated. For studies suggesting an Fe(I)/Fe(III) cycle, see: a) A. Hedström, U. Bollmann, J. Bravidor, P.-O. Norrby, *Chem. Eur. J.* **2011**, *17*, 11991–11993; b) C. J. Adams, R. B. Bedford,

E. Carter, N. J. Gower, M. F. Haddow, J. N. Harvey, M. Huwe, M. Á. Cartes, S. M. Mansell, C. Mendoza, D. M. Murphy, E. C. Neeve, J. Nunn, *J. Am. Chem. Soc.* **2012**, *134*, 10333–10336; c) R. B. Bedford, E. Carter, P. M. Cogswell, N. J. Gower, M. F. Haddow, J. N. Harvey, D. M. Murphy, E. C. Neeve, J. Nunn, *Angew. Chem.* **2013**, *125*, 1323–1326; *Angew. Chem. Int. Ed.* **2013**, *52*, 1285–1288.

[55] For selected applications of iron catalysis by our laboratory, see: a) A. Fürstner, A. Leitner, *Angew. Chem.* **2003**, *115*, 320–323; *Angew. Chem. Int. Ed.* **2003**, *42*, 308–311; b) B. Scheiper, F. Glorius, A. Leitner, A. Fürstner, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11960–11965; c) G. Seidel, D. Laurich, A. Fürstner, *J. Org. Chem.* **2004**, *69*, 3950–3952; d) A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006–3019; e) A. Fürstner, A. Schlecker, *Chem. Eur. J.* **2008**, *14*, 9181–9191; f) A. Fürstner, E. Kattnig, O. Lepage, *J. Am. Chem. Soc.* **2006**, *128*, 9184–9204.

[56] While this paper was in press, a report was published that claims tris(mesityl)-ate complexes related to **21** to be the actual nucleophiles, see: R. B. Bedford. P. B. Brenner, E. Carter, P. M. Cogswell, M. F. Haddow, J. N. Harvey, D. M. Muzrphy, J. Nunn, C. H. Woddall, *Angew. Chem.* **2014**, *126*, 1835–1839; *Angew. Chem. Int. Ed.* **2014**, *53*, 1804–1808