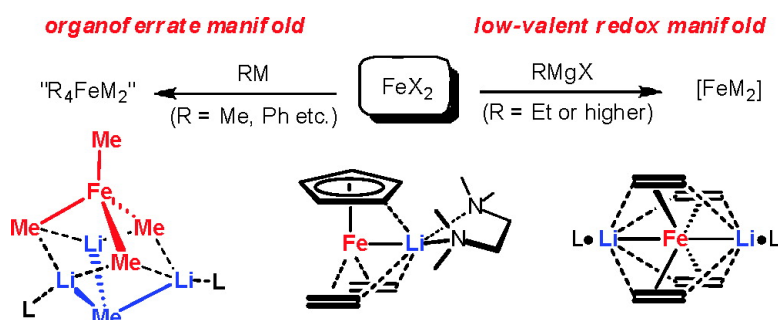Article

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Preparation, Structure, and Reactivity of Nonstabilized Organoiron Compounds. Implications for Iron-Catalyzed Cross Coupling Reactions

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Abstract: A series of unprecedented organoiron complexes of the formal oxidation states -2, 0, $+1$, $+2$, and $+3$ is presented, which are largely devoid of stabilizing ligands and, in part, also electronically unsaturated (14-, 16-, 17- and 18-electron counts). Specifically, it is shown that nucleophiles unable to undergo β-hydride elimination, such as MeLi, PhLi, or PhMgBr, rapidly reduce Fe(3+) to Fe(2+) and then exhaustively alkylate the metal center. The resulting homoleptic organoferrate complexes [(Me$_4$Fe)(MeLi)][Li(OEt$_2$)]$_2$ (**3**) and [Ph$_4$Fe][Li(Et$_2$O)$_2$][Li(1,4-dioxane)] (**5**) could be characterized by X-ray crystal structure analysis. However, these exceptionally sensitive compounds turned out to be only moderately nucleophilic, transferring their organic ligands to activated electrophiles only, while being unable to alkylate (hetero)aryl halides unless they are very electron deficient. In striking contrast, Grignard reagents bearing alkyl residues amenable to β-hydride elimination reduce FeX$_n$ ($n = 2, 3$) to clusters of the formal composition [Fe(MgX)$_2$]$_n$. The behavior of these intermetallic species can be emulated by structurally well-defined lithium ferrate complexes of the type [Fe(C$_2$H$_4$)$_4$][Li(tmeda)]$_2$ (**8**), [Fe(cod)$_2$][Li(dme)]$_2$ (**9**), [CpFe(C$_2$H$_4$)$_2$][Li(tmeda)] (**7**), [CpFe(cod)][Li(dme)] (**11**), or [Cp*Fe(C$_2$H$_4$)$_2$][Li(tmeda)] (**14**). Such electron-rich complexes, which are distinguished by short intermetallic Fe−Li bonds, were shown to react with aryl chlorides and allyl halides; the structures and reactivity patterns of the resulting organoiron compounds provide first insights into the elementary steps of low valent iron-catalyzed cross coupling reactions of aryl, alkyl, allyl, benzyl, and propargyl halides with organomagnesium reagents. However, the acquired data suggest that such C−C bond formations can occur, a priori, along different catalytic cycles shuttling between metal centers of the formal oxidation states Fe(+1)/Fe(+3), Fe(0)/Fe(+2), and Fe(−2)/Fe(0). Since these different manifolds are likely interconnected, an unambiguous decision as to which redox cycle dominates in solution remains difficult, even though iron complexes of the lowest accessible formal oxidation states promote the reactions most effectively.

Introduction

The formation of carbon−carbon as well as carbon-heteroatom bonds by metal-catalyzed cross coupling is arguably one of the most important chemical innovations of the second half of the 20th century.[1−3] Its use is so pervasive that it is actually difficult to find any advanced synthesis that does not take recourse to this methodology at some point. After many rounds of optimization, cross coupling has also been widely embraced by chemical industry,[4] even though expensive noble metals and sometimes even more expensive ligands are required. It is the use of palladium which dominates the field, due to the many favorable attributes of this late transition metal. This impressive success story would not have been possible without the ever increasing insights into the underpinning organometallic chemistry of palladium and its immediate neighbors.[5]

Cross coupling in general, however, is by no means confined to the use of group 10 metals. In fact, one may see the immediate

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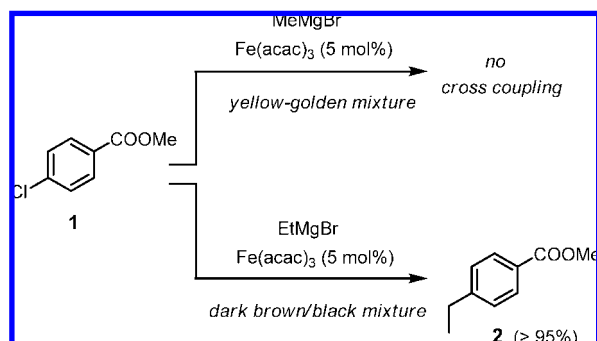
roots of the field in early contributions to organonickel chemistry,[6] which themselves were predated by notable reports on the use of iron salts for the cross coupling of Grignard reagents with various organic electrophiles.[7–9] These results found surprisingly little echo for a long period of time,[10] in part because they were overshadowed by the triumph of their nickel- and palladium-based relatives discovered shortly thereafter. It is only recently that iron-catalyzed processes regain considerable attention,[11] paralleled by an equally growing interest in the use of cobalt for similar purposes.[12] This may be ascribed to the fact that iron salts are cheap, readily accessible, generally nontoxic, environmentally benign, and surprisingly effective in certain cases. Even the most simple iron salts are able to promote notoriously difficult transformations.[13–24] Illustrative examples are the smooth activation of aryl *chlorides*[14] as well as of unactivated primary and secondary *alkyl* halides[19–21] which are particularly challenging substrates in the cross coupling arena.

Despite these impressive preparative advances, a mechanistic understanding for iron-catalyzed cross coupling is virtually nonexistent. Because the actual catalysts are usually generated in situ as ill-defined but highly sensitive and short-lived entities, their true nature remains largely unknown. Not even a consensus

on the formal oxidation states of the operating species has been reached, with catalytic cycles shuttling between $Fe(-2)/Fe(0)$,[14] $Fe(0)/Fe(+2)$,[8d,13c] or $Fe(+1)/Fe(+3)$[8c,d,25] being proposed in the literature. Yet other authors favored mechanisms devoid of any such redox manifolds, invoking nucleophilic organoferrate complexes of different composition as the relevant intermediates in analogy to the well established principles governing, for example, organocopper chemistry.[26,27]

Another reason why the mechanistic understanding has evolved at a surprisingly slow pace must be seen in the general lack of knowledge about structure and reactivity of organoiron derivatives devoid of stabilizing ligands.[28,29] Because of their exceptional sensitivity, only very few such compounds have

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Scheme 1. Illustration of the Strikingly Different Behavior of MeMgBr and EtMgBr in Iron Catalyzed Cross Coupling Reactions

Scheme 2. Proposed Elementary Steps Leading to the Formation of an "Inorganic Grignard Reagent" of Iron

previously been characterized and none of them has ever been tested for its capacity to react with organic electrophiles. Overall, the chemistry of "low valent" iron represents a largely void terrain on the organometallic landscape. Even though we were apprehensive that its systematic cartography will be far from trivial, we decided to venture into this challenging area and managed to obtain a series of organoiron complexes, which are not only unprecedented in structural terms but also relevant in the context of cross coupling chemistry. The results of this investigation are summarized below.[20,36]

Results and Discussion

Empirical Evidence. Our work in the field of iron catalysis commenced with the puzzling observation that MeMgBr and EtMgBr exhibit strikingly different behavior in attempted cross coupling reactions with aryl chlorides (Scheme 1).[14a,c,d] Specifically, treatment of methyl 4-chlorobenzoate **1** with EtMgBr (or higher alkyl Grignard reagents) in the presence of Fe(acac)$_3$ or FeCl$_n$ ($n = 2, 3$) as precatalyst affords the desired product **2** in virtually quantitative yield within minutes at ≤ 0 °C, whereas MeMgBr essentially fails to react even under more forcing conditions. Remarkably, the appearance of the reaction mixtures is also noticeably different: whereas the use of MeMgBr leads to intensely yellow-colored solutions that only slowly turn dark, the addition of EtMgBr instantaneously generates a brown/black and turbid mixture, which may eventually evolve to black-violet as the reaction proceeds.

These stunning differences might be interpreted in light of previous conclusions drawn by Bogdanović and co-workers, who suggested that anhydrous FeX$_2$ reacts with RMgX to give
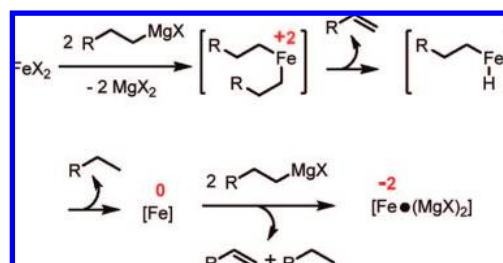
dark-brown bimetallic clusters of the formal composition [Fe(MgX)$_2$]$_n$, provided that the R group of the chosen Grignard reagent is able to undergo β-hydride elimination (Scheme 2).[30] Although a direct spectroscopic characterization of this particular "inorganic Grignard reagent" is missing,[31,32] it has been rigorously proven that *4 equiv* of RMgX are consumed on reaction with an Fe(2+) salt. Likewise, the amount and composition of the released gas derived from the organic residue R (alkene/alkane = 1:1, cf. Scheme 2),[33] as well as the amount of H$_2$SO$_4$ needed to titrate the resulting precipitate, are consistent with an empirical formula [Fe(MgX)$_2$]$_n$.[30] Apparently, the reduction of FeX$_n$ effected by the Grignard reagent does not stop once a zerovalent iron species is generated, but ultimately leads to compounds in which the iron center is distinguished by a *formally negative* oxidation state and a d^{10} electron configuration.

Obviously, MeMgBr cannot follow the Bogdanović activation pathway for its inability to undergo β-hydride elimination. As a consequence, one might expect that this and related nucleophiles merely alkylate the Fe(n+) ($n = 2, 3$) center, generating metastable organoferrate complexes of unknown composition that do not react with chlorobenzoate **1** but are able to transfer their organic residues to more reactive substrates such as acid chlorides, enol triflates, or very electron-deficient heteroarenes.[14d]

Based on these empirical data, we proposed that iron-catalyzed cross coupling reactions might occur by, at least, two distinctly different mechanisms (Scheme 3).[14] Whereas MeMgX supposedly generates discrete organoferrate complexes as reactive intermediates, EtMgBr and higher homologues give rise to low-valent iron cluster species (step A) that activate aryl halides or related substrates. In a formal sense, the reaction of [Fe(MgX)$_2$]$_n$ with an organic halide (step B) constitutes a σ-bond metathesis rather than a "conventional" oxidative insertion, although this formalism is not meant to imply any mechanistic

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(32) The term "inorganic Grignard reagent" for [Fe(MgX)$_2$]$_n$ reflects the fact that Mg has formally inserted into the Fe–X bonds of the starting iron salt FeX$_2$.

(33) Small amounts of the product derived from homocoupling of the Grignard reagent were also observed.

Scheme 3. Proposed Basic Scenarios for Iron Catalyzed Cross Coupling Reactions: Organoferrate Manifold versus a "Non-Canonical" Mechanism Involving a Low-Valent Intermetallic Catalyst
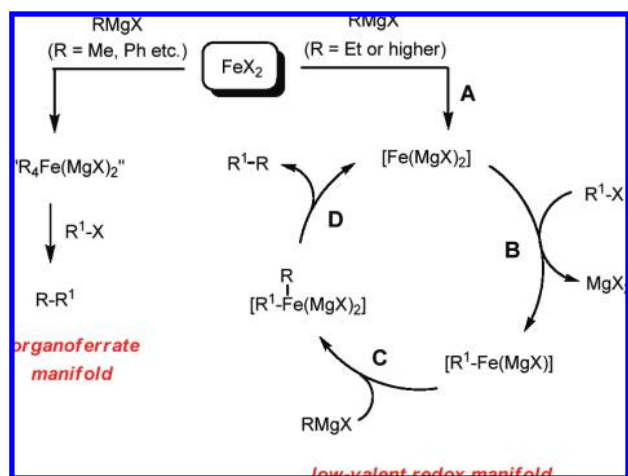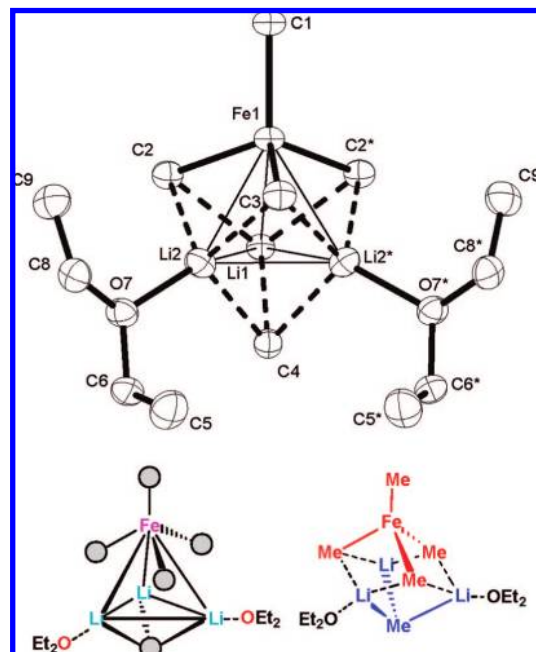

detail. Because such a process does not generate an organoiron halide, the subsequent reaction with RMgX must occur by alkylation rather than by regular transmetalation of the intermediate primarily formed (step C). The resulting diorganoiron species then undergoes reductive elimination (step D) to afford the product and regenerate the catalyst. It was the purpose of this study to scrutinize both distinct elementary scenarios shown in Scheme 3 by the isolation of pertinent organoiron compounds.

Organoferrate Manifold. It has been repeatedly proposed in the literature that homoleptic nonstabilized alkyliron species and/ or organoferrate complexes of different composition are formed on reaction of FeX_n ($n = 2, 3$) with various organolithium or organomagnesium halide reagents.[26,34] Importantly, however, the relevance of any such a putative intermediate for cross coupling has never been rigorously confirmed. Only the rapid reduction of $FeCl_3$ to $FeCl_2$ on treatment with the first equivalent of MeLi or MeMgBr is formally secured.[35]

Kochi et al. emphasized that the catalytic species produced from the reaction of Fe(3+) salts and methyl donors is unusually labile and strongly discouraged attempts at isolation.[7c] Challenged by this authoritative statement, we reacted ethereal solutions of $FeCl_3$ with excess MeLi at low temperatures and managed to isolate the resulting iron complex as an *exceptionally* sensitive red solid which vigorously ignites in air and rapidly decomposes when allowed to reach ∼0 °C. Solutions in THF show the characteristic bright yellow color also observed in iron-catalyzed reactions of MeMgX in this solvent.[14d]

Careful recrystallization from Et_2O at low temperatures (−40 °C → −78 °C) furnished crystals suitable for X-ray crystal structure analysis.[36,37] The remarkable constitution of the

(34) (a) Corey, E. J.; Posner, G. H. *Tetrahedron Lett.* **1970**, *11*, 315. (b) Corey, E. J.; Yamamoto, H.; Herron, D. K.; Achiwa, K. *J. Am. Chem. Soc.* **1970**, *92*, 6635. (c) Kauffmann, T.; Laarmann, B.; Menges, D.; Neiteler, G. *Chem. Ber.* **1992**, *125*, 163. (d) Kauffmann, T.; Voss, K.-U.; Neiteler, G. *Chem. Ber.* **1993**, *126*, 1453.

(35) Berthold, H. J.; Spiegl, H. J. *Z. Anorg. Allg. Chem.* **1972**, *391*, 193.

(36) Preliminary communication: Fürstner, A.; Krause, H.; Lehmann, C. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 440.

(37) Attempts to characterize the product formed from $FeCl_3$ and MeLi were reported by Spiegl et al., who proposed a ferrate complex of the composition [Me_4Fe][$Li(OEt_2)_2$] essentially based on titration experiments; cf. Spiegl, H. J.; Groth, G.; Berthold, H. J. *Z. Anorg. Allg. Chem.* **1973**, *398*, 225. Failed attempts to crystallize the compound were reported by other authors; cf. ref 26.

Figure 1. Structure of the iron "super-ate" complex **3** in the solid state; anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.[36] The graphical representation on the bottom left side emphasizes the tetrahedral framework of the metal cluster decorated by methyl groups represented as balls, whereas the representation on the bottom right-hand side interprets this compound as consisting of a ferrate entity with an intertwined lithium "cap" incorporating an extra methyl group devoid of direct contacts with the iron center.

homoleptic iron complex **3** in the solid state is shown in Figure 1. The Fe(+2) center is surrounded by four methyl groups in an almost ideal tetrahedral arrangement.[38] However, the Fe−C1 distance is shorter (2.095(4) Å) than the distances between Fe and the other methyl groups (average 2.185(4) Å) which show additional short contacts to three lithium atoms. Together with the iron center, these lithium atoms form a tetrahedral metal framework with C_{3v} symmetry. As evident from Figure 1, three of the four sides of this cluster are capped in a μ^3-fashion by the methyl groups of the ferrate unit; most strikingly, however, the fourth face is capped by an additional methyl group (C4) *devoid* of any direct contact to the iron atom. The coordination sphere of two of the three lithium atoms is completed by contacts with two Et_2O ligands, whereas the third lithium forms a close contact of 2.301(6) Å to the carbon atom of the terminal Fe-methyl group of a neighboring molecule.

Overall, the product derived from $FeCl_3$ and MeLi analyses as [(Me_4Fe)(MeLi)][$Li(OEt_2)$]$_2$ (**3**).[37] As such, **3** represents the first *alkyl*-ate complex of iron devoid of any stabilizing ligands that has been structurally characterized and adds one more example to the very small family of homoleptic iron complexes with η^1-bound carbon entities other than CO that are reasonably well characterized.[28,39–41] Its gross structure can be interpreted as consisting of a ferrate unit with an intertwined lithium cap

(38) The average C−Fe−C angle is 109(3)°.

(39) [($RC\equiv C$)$_6Fe$]K$_4$: Nast, R.; Urban, F. *Z. Anorg. Allg. Chem.* **1956**, *287*, 17.

(40) (a) Homoleptic, nonstabilized Fe(0) complexes with aryl ligands: [Ph_4Fe^0][$Li(OEt_2)_4$]: Bazhenova, T. A.; Lobkovskaya, R. M.; Shibaeva, R. P.; Shilov, A. E.; Shilova, A. K.; Gruselle, M.; Leny, G.; Tchoubar, B. *J. Organomet. Chem.* **1983**, *244*, 265. (b) For a complex of the putative composition [$Fe(PhLi)_5$] see: Sarry, B.; Noll, S. *Z. Anorg. Allg. Chem.* **1972**, *394*, 141.

or, alternatively, as a heavily alkylated tetrahedral metallic frame which is reminiscent of the structure of methyllithium tetramer in the solid state (Figure 1).[42]

Compound **3** was found unable to alkylate chlorobenzoate **1a** (X = Cl) and even iodobenzoate **1b** (X = I) to any appreciable extent (<20%, cf. Table 1, entry 1).[43] It does react, however, with more activated substrates such as acid chlorides and enol triflates to give the corresponding products in good yields (Table 1). **3** also turned out to be an effective single-electron-transfer agent capable of inducing homocoupling reactions of aryl bromides (entry 5)[44] and is sufficiently basic to effect the vinylogous deprotonation of enones ("Kharasch deconjugation", entry 6).[45] Overall, the reactivity profile of pure **3** toward a set of representative electrophiles corresponds very nicely to the results obtained when the exact same compounds are reacted with MeMgBr and catalytic amounts of Fe(acac)$_3$ in THF.[14d,36,46,47] We therefore believe that iron-catalyzed processes involving methyl donors proceed via ferrate complexes such as **3** as the actual reactive intermediates formed in situ, provided that these reactions are carried out at low temperatures.

As the behavior of PhMgX in iron-catalyzed cross coupling reactions is quite similar to that of MeMgX,[14] one might expect that arylmagnesium halides also lead to ferrate complexes as the pertinent intermediates. In fact, treatment of FeCl$_3$ in Et$_2$O with a large excess of PhLi at low temperature affords the brownish-purple, pyrophoric, and thermally highly unstable complex [Ph$_4$Fe][Li(OEt$_2$)]$_4$ (**4**). This compound has already previously been characterized by X-ray crystallography as the first and, to our knowledge, only ate-complex of Fe(0) known to date (Figure 2).[40a] In contrast to the organoferrate complexes

(41) (a) Homoleptic, nonstabilized Fe(2+) or Fe(3+) complexes with aryl ligands: [(Naphthyl)$_4$Fe][Li(OEt$_2$)]$_2$: Bazhenova, T. A.; Lobkovskaya, R. M.; Shibaeva, R. P.; Shilova, A. K.; Gruselle, M.; Leny, G.; Deschanps, E *J. Organomet. Chem.* **1983**, *244*, 375. (b) [(Mesityl)$_3$Fe]-[Li(dioxane)$_{0.25}$]: Seidel, W.; Lattermann, K.-J. *Z. Anorg. Allg. Chem.* **1982**, *488*, 69. (c) [(C$_6$Cl$_5$)$_4$Fe^{III}][Li(thf)$_4$]: Alonso, P. J.; Arauzo, A. B.; Forniés, J.; García-Monforte, M. A.; Martín, A.; Martínez, J. I; Menjón, B.; Rillo, C.; Sáiz-Garitaonandia, J. J. *Angew. Chem., Int. Ed* **2006**, *45*, 6707. (d) [Fe$_2$(mesityl)$_2$(μ-mesityl)$_2$]: Müller, H; Seidel, W.; Görls, H. *J. Organomet. Chem.* **1993**, *445*, 133. See also:(e) Klose, A.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C.; Re, N. *J. Am. Chem. Soc.* **1994**, *116*, 9123. (f) [(Mesityl)$_2$Fe(dme)]: Müller, H.; Seidel, W.; Görls, H. *Z. Anorg. Allg. Chem.* **1996**, *622*, 756. (g) [Ph$_2$Fe(H)$_2$][Li(OEt$_2$)]$_4$: Bazhenova, T. A.; Kachapina, L. M.; Shilov, A. E.; Antipin, M. Y.; Struchkov, Y. T. *J. Organomet. Chem.* **1992**, *428*, 107. (h) [(fc)$_3$Fe$_2$][Li(tmeda)]$_2$ (fc = ferrocenyl): Sänger, I.; Heilmann, J. B.; Bolte; M.; Lerner, H.-W.; Wagner, M. *Chem. Commun.* **2006**, 2027.

(42) (a) Weiss, E.; Hencken, G. *J. Organomet. Chem.* **1970**, *21*, 265. (b) Review on the structure of organolithium compounds: Setzer, W. N.; Schleyer, P. v. R. *Adv. Organomet. Chem.* **1985**, *24*, 353. (c) Streitwieser, A.; Bachrach, S. M.; Dorigo, A.; Schleyer, P. v. R. In *Lithium Chemistry*; Sapse, A.-M., Schleyer, P. v. R., Eds.; Wiley: New York, 1995; p 1.

(43) For a convenient alternative protocol allowing for the methylation of aryl halides, see:(a) Fürstner, A.; Seidel, G. *Tetrahedron* **1995**, *51*, 11165.

(44) For a study on Ullmann-type coupling reactions effected by a putative complex "Me$_4$FeLi$_2$" generated in situ, see:(a) Ohwada, T.; Uchiyama, M.; Matsumoto, Y.; Nakamura, S.; Kobayashi, N.; Yamashita, N.; Matsumiya, A.; Sakamoto, T. *J. Am. Chem. Soc.* **2004**, *126*, 8755.

(45) Kharasch, M. S.; Tawney, P. O. *J. Am. Chem. Soc.* **1941**, *63*, 2308. For a more detailed discussion of the role of **3** in the Kharasch deconjugation reaction, see ref 36.

(46) Fürstner, A.; Hannen, P. *Chem.—Eur. J.* **2006**, *12*, 3006.

(47) (a) Hamajima, A.; Isobe, M. *Org. Lett.* **2006**, *8*, 1205. (b) Scheerer, J. R.; Lawrence, J. F.; Wang, G. C.; Evans, D. A. *J. Am. Chem. Soc.* **2007**, *129*, 8968. (c) Maulide, N.; Vanherck, J.-C.; Markó, I. E. *Eur. J. Org. Chem.* **2004**, 3962. (d) Dickschat, J. S.; Reichenbach, H.; Wagner-Döbler, I.; Schulz, S. *Eur. J. Org. Chem.* **2005**, 4141. (e) Hocek, M.; Dvoráková, H. *J. Org. Chem.* **2003**, *68*, 5773. (f) Hocek, M.; Pohl, R. *Synthesis* **2004**, 2869.

Table 1. Representative Reactions Induced by the "Super-ate Complex" **3**[a]

Nr	Substrate	Product	Yield
1			< 20% (X = Cl, I)
2			60%
3			70%
4			80%
5			83%
6			45%[b,c]

[a] All reactions were performed in THF at −40 → −30 °C, unless stated otherwise. [b] In Et$_2$O at −20°C. [c] The enolate primarily formed was trapped with TMSCl; the yield refers to the dimethylacetal derivative formed on treatment of the crude enol silane with HC(OMe)$_3$ and BF$_3$·Et$_2$O in CH$_2$Cl$_2$ at −78°C; cf. ref 36.
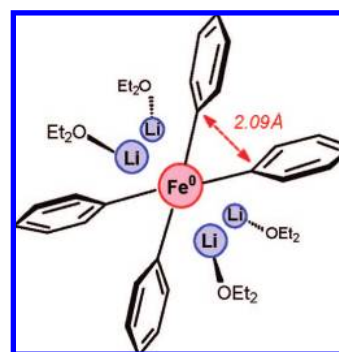
Figure 2. Schematic presentation of the planar rectangular structure of the zerovalent tetraphenylferrate complex [Ph$_4$Fe][Li(OEt$_2$)]$_4$ (**4**) in the solid state.[40a]

of Fe(2+), in which the central metal is tetrahedrally surrounded by the organic ligands, the Fe(0) center in **4** is distinguished by a planar-rectangular coordination geometry which brings two pairs of phenyl groups into close proximity and may hence facilitate their reductive elimination. In any case, this remarkable complex proves that even zerovalent iron centers can be exhaustively alkylated under notably mild conditions; note that such an alkylation also constitutes one of the key steps of the noncanonical cross coupling mechanism depicted in Scheme 3 (step C).
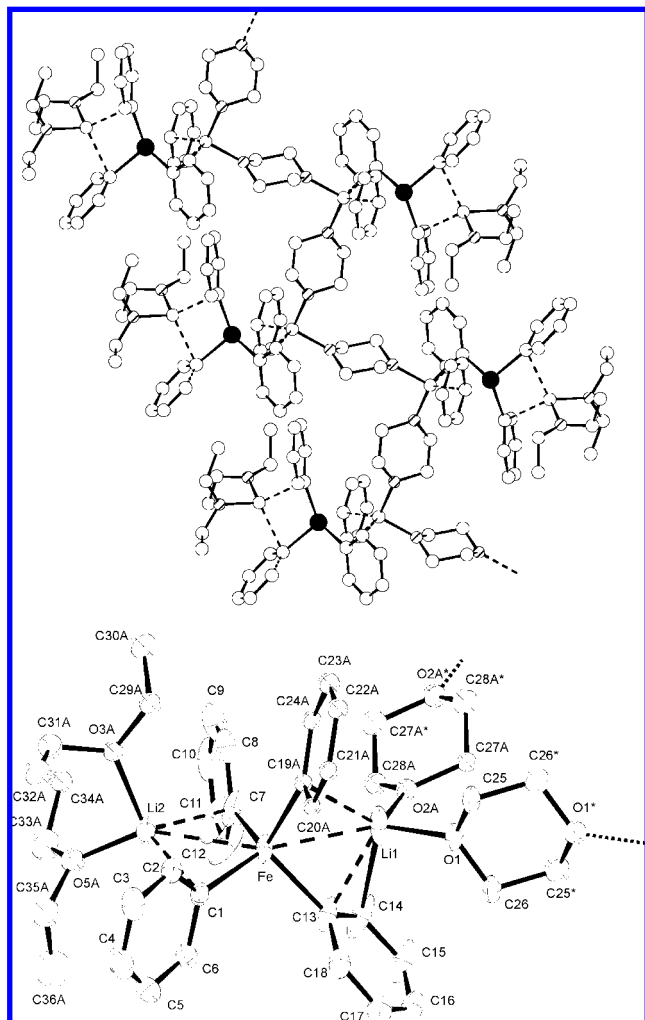
Figure 3. Structure of the organoferrate complex **5** in the solid state.[48] Top: Section of the coordination network, with dioxane molecules linking the adjacent [Ph$_4$Fe]Li$_2$ units, whereas Et$_2$O caps the second lithium atom. Bottom: Ortep plot of an individual organoferrate unit. Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.

Upon limiting the amount of PhLi in the reaction with FeCl$_2$ to 4 equiv, however, we were able to intercept for the first time the putative precursor of the Fe(0) complex **3**, that is the corresponding tetraphenylferrate complex incorporating an Fe(+2) center. After numerous attempts, crystals of this mustard-colored, highly pyrophoric solid suitable for X-ray structure analysis could be grown.[48,49] As can be seen from Figure 3, the product analyzes as [Ph$_4$Fe][Li(Et$_2$O)$_2$][Li(1,4-dioxane)] (**5**). One of the lithium counterions carries two molecules of diethyl ether, whereas the other lithium atom is coordinated to 1,4-dioxane serving as a bridging ligand between the individual ferrate entities. In contrast to the methyl-ate complex **3** described above, the molecular structure of **5** is not determined by a tetrahedral metallic frame; rather, each individual organoferrate moiety comprises a slightly bent Li–Fe–Li unit (dihedral angle 156.38(16)°) characterized by

short intermetallic contacts between the iron and the lithium centers (2.690(5) Å). The lithium atoms entertain short contacts to the C$_{ipso}$ positions of two phenyl rings each, which surround the iron center in an almost ideal tetrahedral arrangement.

Complexes **4** and **5** thermally decompose with formation of biphenyl as the major product. Biphenyl can also be generated in essentially quantitative yield upon treatment of **5** with a suitable oxidant such as 1,2-dichloroethane, iodine, or even dry air.[50] Since biphenyl formation usually plagues iron-catalyzed cross coupling reactions of PhMgX with less activated substrates under the standard conditions, we take this as an indication that tetraphenylferrate complexes may be passed through, the decomposition of which is as fast as or even faster than productive aryl transfer to an electrophilic partner.[51] It is notable, however, that **4** and **5** catalyze the cross coupling of PhMgBr with cyclohexyl bromide, a reaction which is difficult to achieve by more conventional means (see below).

Low-Valent Redox Regimen. The data summarized above advocate the notion that donors unable to undergo β-hydride elimination primarily lead to organoferrate complexes such as **3**–**5**, which alkylate activated electrophiles but are not sufficiently nucleophilic to transfer their organic residues to aryl chlorides such as **1**. Since **1** and related substrates, however, react with exceptional ease with EtMgBr or higher homologues at or even below room temperature, it is most unlikely that related organoferrate complexes account for these results. A representative case is the formation of 4-nonylbenzoic acid ester **6**, a valuable precursor to a liquid crystalline material, which requires less than 10 min at 0 °C when performed on a >15 g scale (Scheme 4).[15,52]

As suggested by Bogdanović, EtMgX is thought to convert FeX$_n$ ($n = 2, 3$) into low-valent iron clusters of the formal composition [Fe(MgX)$_2$]$_n$ or [Fe(MgX$_2$)$_2$]$_n$,[30,31] either of which might be sufficiently nucleophilic to react with aryl chlorides, sulfonates, or other suitable partners (Scheme 5). Alkylation of the resulting organoiron complexes by the remaining RMgX in solution followed by reductive coupling affords the desired product Ar–R and regenerates the catalytically competent iron

(48) For further details concerning the crystal structures described in this paper, see the Supporting Information.

(49) For a previous attempt to isolate the ate complex derived from PhLi and FeCl$_2$, see: Taube, R.; Stransky, N. *Z. Chem* **1977**, *17*, 427. The microcrystalline compound was analyzed as [Ph$_4$Fe]Li$_2$(dioxane)$_{2.5}$ according to combustion analysis and titration with iodine.

(50) (a) This may explain the effective iron-catalyzed homocoupling of Grignard reagents reported in the recent literature; cf. Cahiez, G.; Chaboche, C.; Mahuteau-Betzer, F.; Ahr, M. *Org. Lett.* **2005**, *7*, 1943. (b) Cahiez, G.; Moyeux, A.; Buendia, J.; Duplais, C. *J. Am. Chem. Soc.* **2007**, *129*, 13788. (c) Nagano, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 491.

(51) In this context, reference is made to a remarkable recent improvement, which allows undesired homocoupling of aryl Grignard reagents to be significantly reduced, thus resulting in a much more productive cross coupling with aryl halides. This procedure is based on the use of FeF$_3$(H$_2$O)$_n$ in combination with an N-heterocyclic carbene ligand, which are pretreated with EtMgBr prior to addition of ArMgX and Ar'Cl as the actual coupling partners; cf. ref 17. In view of our results on the behavior of per-arylated ferrate species, one may speculate that the fluoride ligands at the iron center limit or even suppress the formation of ferrate complexes bearing more than one aryl entity and hence minimize the parasite homocoupling process.

(52) (a) For applications of iron-catalyzed cross coupling reactions in total syntheses reported by our group, see: Fürstner, A.; Leitner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 308. (b) Scheiper, B.; Glorius, F.; Leitner, A.; Fürstner, A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11960. (c) Fürstner, A.; De Souza, D.; Parra-Rapado, L.; Jensen, J. T. *Angew. Chem., Int. Ed.* **2003**, *42*, 5358. (d) Fürstner, A.; Turet, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 3462. (e) Fürstner, A.; De Souza, D.; Turet, L.; Fenster, M. D. B.; Parra-Rapado, L.; Wirtz, C.; Mynott, R.; Lehmann, C. W. *Chem.–Eur. J.* **2007**, *13*, 115. (f) Fürstner, A.; Kirk, D.; Fenster, M. D. B.; Aïssa, C.; De Souza, D.; Nevado, C.; Tuttle, T.; Thiel, W.; Müller, O. *Chem.–Eur. J.* **2007**, *13*, 135. (g) Fürstner, A.; Kirk, D.; Fenster, M. D. B.; Aïssa, C.; De Souza, D.; Müller, O. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 8103. (h) See also refs 46 and 63b,c.

Scheme 4. Large Scale Adaptable Iron-Catalyzed Cross Coupling of a Higher Alkyl Grignard Reagent with a Functionalized Aryl Chloride
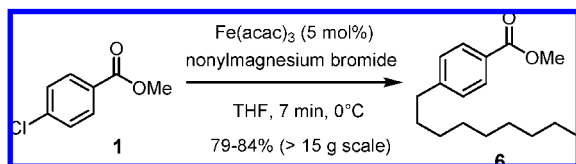
species. However, one must not overlook that exceedingly electron-rich low valent iron species could also be prone to single electron transfer processes, thus opening additional redox cycles passing through odd-numbered formal oxidation states. Likewise, the homolysis of Fe–R bonds might lead into such odd-numbered regimens and hence result in overly complex and as yet completely uncharted reaction manifolds. Only one of many different conceivable intertwined scenarios is depicted in Scheme 5.

At present, it seems merely impossible to unravel even the most basic features of such a complex scenario at the molecular level, in particular if one starts with an in situ generated catalyst which itself is ill-defined and may be only one of many iron species present in the mixture. Therefore, the replacement of the putative clusters $[Fe(MgX)_2]_n$ or $[Fe(MgX_2)_2]_n$ by structurally well characterized intermetallic complexes, which are more readily amenable to mechanistic studies, was considered to be of prime importance. A family of remarkable iron–olefin complexes pioneered by Jonas and co-workers seemed ideally suited for this purpose.[53–57]

The required compounds can be prepared on a large scale by successive removal of the cyclopentadienyl (Cp) rings from inexpensive ferrocene under reducing conditions in the presence of suitable olefin traps (Scheme 6). Specifically, the use of ethylene affords the Fe(0) complex **7** as the primary product, whereas more stringent conditions lead to the tetraethylene ferrate complex **8** in which the iron center is d^{10} configured, formally exhibiting the oxidation state −2. Both compounds are obtained in respectable yields in multigram quantities as highly air-sensitive crystalline materials upon complexation of the escorting lithium counterions with tmeda. Ethene can be replaced by cyclooctadiene (COD), which affords the slightly more robust complex **10** that can also be obtained in a tmeda-free form as the corresponding DME adduct **11**; the analogous

Fe(−2) complex **9** is equally available. Ferrate complexes of the pentamethylcyclopentadienyl (Cp*) series are obtained by a slightly different synthesis route using complex **13** as a convenient starting material (Scheme 7).[55] Even though all of these complexes are highly sensitive to air and moisture, they can be stored for years under an inert atmosphere in a freezer without noticeable decomposition.

The structure of **8** in the solid state is highly informative (Figure 4).[58] The most striking features are the remarkably short Li···Fe distances of only 2.02−2.08 Å as well as the rather short contacts between the lithium atoms and the ethylene ligands which indicate strong ion pairing. The C=C bonds are significantly elongated (1.432(5) and 1.447(5) Å) compared with the theoretical value of free ethylene (1.34 Å), implying a significant back-donation of electron density from the central metal to the empty π^*-orbitals. Nevertheless, the olefins remain kinetically labile, thus imparting a rather "bare" character onto the very electron-rich iron center. The presence of distinctive intermetallic bonds, the low formal oxidation state and d^{10} electron configuration of the iron center, as well as the ready availability of "free" coordination sites upon release of the kinetically labile olefins, suggest that complex **8** and its relatives represent *structural* mimics of the intermetallic clusters of the putative composition $[Fe(MgX)_2]_n$ formed in situ, which are likely distinguished by the exact same attributes.[59]

Tables 2 and 3 provide strong evidence that **8** also constitutes a *functional* surrogate for the in situ catalyst. Specifically, iron species generated from Fe(acac)$_3$ or FeCl$_3$ in the presence or absence of additional ligands behave much like this structurally well-defined lithium ferrate complex in the cross coupling of the representative aryl chloride **18** with two different alkyl Grignard reagents, as well as in the even more challenging cross coupling of cyclohexyl bromide (**20**) with an assortment of ArMgX reagents. The analogous COD complex **9** and even the Fe(0) complex **7** are similarly effective but require a somewhat higher temperature. In striking contrast, however, Collman's reagent Na$_2$Fe(CO)$_4$ failed to afford any of the desired product even on prolonged stirring, most likely because the tightly bound CO ligands cannot vacate the coordination sites required for productive cross coupling.[60] Of all complexes investigated, the Fe(−2) complex **8** with the least stable ligand sphere turned out to be the best catalyst, allowing the reaction of **20** with ArMgX to be performed at −20 °C within minutes (see also below).

(53) (a) Jonas, K. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 295. (b) Jonas, K.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 520. (c) Jonas, K. *Pure Appl. Chem.* **1990**, *62*, 1169.
(54) (a) Jonas, K.; Schieferstein, L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 549. (b) Jonas, K.; Schieferstein, L.; Krüger, C.; Tsay, Y.-H. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 550. (c) Schieferstein, L. Dissertation, Ruhr-Universität Bochum, 1978. (d) Klusmann, P. Dissertation, Ruhr-Universität Bochum, 1993.
(55) Jonas, K.; Klusmann, P.; Goddard, R. *Z. Naturforsch., B: Chem. Sci.* **1995**, *50*, 394.
(56) (a) For the use of complexes **7** and **10** as catalysts in cycloisomerization reactions, a discussion of their X-ray structures, as well as detailed procedures for their large scale preparation, see: Fürstner, A.; Martín, R.; Majima, K. *J. Am. Chem. Soc.* **2005**, *127*, 12236. (b) Fürstner, A.; Majima, K.; Martín, R.; Krause, H.; Kattnig, E.; Goddard, R.; Lehmann, C. W. *J. Am. Chem. Soc.* **2008**, *130*, 1992.
(57) (a) For other structurally defined iron ate complexes, see the following for leading references: Brennessel, W. W.; Jilek, R. E.; Ellis, J. E. *Angew. Chem., Int. Ed* **2007**, *46*, 6132. (b) Döring, M.; Uhlig, E. *Z. Chem.* **1986**, *26*, 449. (c) Rosa, P.; Mézailles, N.; Ricard, L.; Mathey, F.; Le Floch, P.; Jean, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1251. (d) Ellis, J. E.; Chen, Y. S. *Organometallics* **1989**, *8*, 1350. (e) Ellis, J. E. *Adv. Organomet. Chem.* **1990**, *31*, 1.

(58) The structure of **8** has previously been communicated by Jonas; cf. ref 54b. Apparently **8** exhibits polymorphism, since these authors reported a primitive orthorhombic unit cell (*Pbcn* with $a = 12.279(1)$, $b = 13.069(1)$, and $c = 16.336(2)$ Å. The comparison of the bond lengths between the earlier room temperature structure and the present 100 K structure shows differences around 0.01 to 0.02 Å. Unfortunately no atomic coordinates of the structure published in 1979 are available for a more detailed comparison. However, it is noteworthy that for the previous structure two unit cell edges are halved compared to the present unit cell, while one is doubled. No transformation between the present F-centered and the earlier primitive unit cell was found.
(59) (a) The notion that clusters of the type $[Fe(MgX)_2]_n$ should have an intermetallic bond between Fe and Mg of largely covalent character comes from the crystal structure of $[(dppeCpFe)−(MgBr)(thf)_3]$, which has a highly covalent bond Fe−Mg bond of 2.593(7) Å length, as well as from spectroscopic data recorded for $[(CO)_2CpFe−MgBr(thf)_n]$; cf.: Felkin, H.; Knowles, P. J.; Meunier, B.; Mitschler, A.; Ricard, L.; Weiss, R. *J. Chem. Soc., Chem. Commun.* **1974**, 44. (b) Felkin, H.; Knowles, P. J.; Meunier, B. *J. Organomet. Chem.* **1978**, *146*, 151. (c) Burlitch, J. M.; Ulmer, S. W. *J. Organomet. Chem.* **1969**, *19*, P21. (d) McVicker, G. B *Inorg. Chem.* **1975**, *14*, 2087. (e) EXAFS data of other inorganic Grignard reagents $[M(MgX)_n]$ are also in line with largely covalent intermetallic bonds; cf. ref 31.
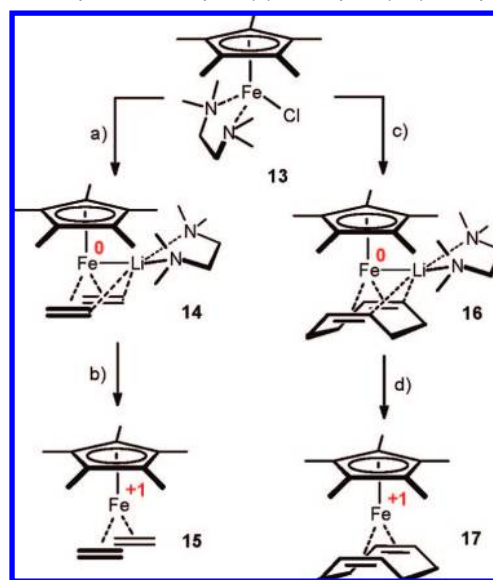
Scheme 5. One of Many Conceivable Scenarios of Interconnected Catalytic Redox Cycles
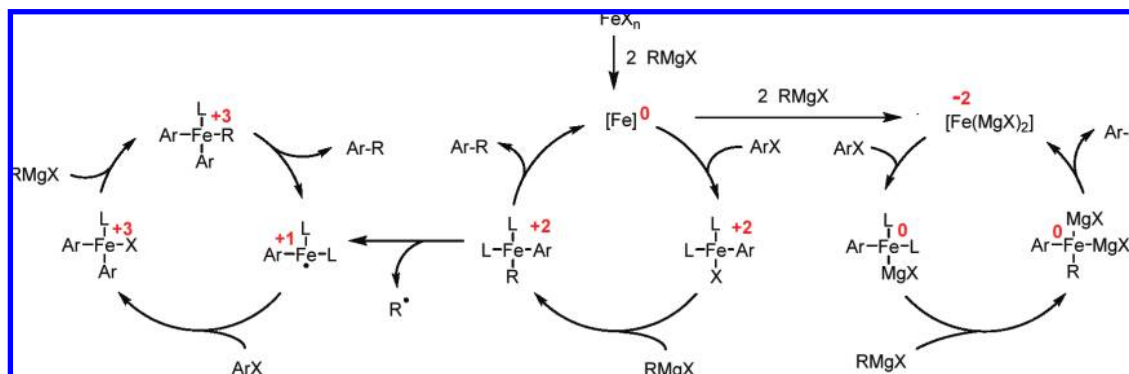
Scheme 6. Preparation of Lithium Ferrate Complexes and Products Derived Thereof[a,b]
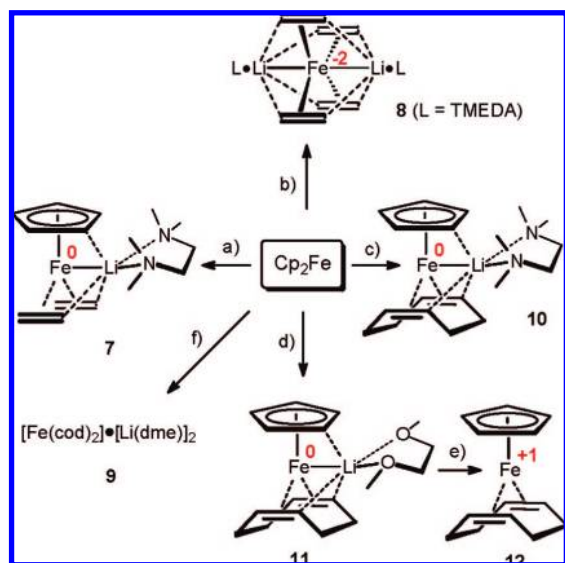
[a] The red numbers indicate the *formal* oxidation states of the iron centers. [b] Reagents and conditions: (a) Li, ethylene (1 bar), THF, −50 °C → 0 °C, then *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (tmeda); 45% (23 g scale); (b) Li, ethylene (5−8 bar), 20 °C, then tmeda, 43% (12 g scale); (c) (i) Li, COD, THF, −50 °C, (ii) tmeda, Et₂O, RT, 75%; (d) Li, COD, DME, −50 °C → RT, 97% (85 g scale) [50% after recrystallization, 11 g scale]; (e) Ph₃CCl, pentane, −35 °C → RT, 70%; (f) Li, DME, ethylene (4−6 bar), RT, then COD, 70 °C, 22% (>27 g scale).

Scheme 7. Preparation of Cp*Fe(0) and Cp*Fe(+1) Complexes[a,b]

[a] The red numbers indicate the *formal* oxidation states of the iron centers. [b] Reagents and conditions: (a) Li, ethylene, THF, −78 °C → RT, then tmeda, 63%, cf. ref 55; (b) 1,2-dichloroethane, pentane, 78%, cf. ref 55; (c) Li, COD, THF, −78 °C → RT, then tmeda, 70%; (d) 1,2-dichloroethane, 75%.

Preparative Results. Next, we set out to explore the scope and limitations of the surprisingly facile cross coupling of alkyl halides with aromatic Grignard reagents. Such reactions are particularly challenging due to the high barrier to oxidative addition and the proclivity of the once formed metal alkyl complexes toward β-hydride elimination. Actually, it took several rounds of careful optimization of the ligand sets until appropriate conditions were found to allow such substrates to undergo cross coupling with the aid of palladium or nickel

complexes.[61] Therefore it is particularly striking that low-valent iron effects such transformations with remarkable ease.[19,20] The unprecedentedly high reaction rates translate into an excellent chemoselectivity profile, since primary and secondary alkyl bromides and iodides can be cross coupled in the presence of a variety of functional groups that are a priori susceptible to Grignard reagents. Representative examples are compiled in Tables 4 and 5 (the full list is contained in the Supporting Information). From these data it can be deduced that the reaction is compatible with ketones, esters, enoates, alkyl and aryl chlorides, aryl bromides, nitriles, isocyanates, ethers, acetals, pinacol boronates, trialkylsilyl groups, and even terminal and internal epoxides. Equally striking is the fact that tertiary amines do not interfere, indicating low Lewis acidity of the operating catalyst, if any. In contrast to the well behaved α-bromo ester shown in entry 12, however, an α-bromo ketone was decomposed (cf. Chart 1).

Despite previous reports on iron-catalyzed reactions of allylic phosphates and sulfones,[10k,34b] cross couplings of the more

(60) (a) Na₂Fe(CO)₄ oxidatively inserts into a variety of organic electrophiles, with the substrate reactivity resembling classical S_N2 processes. However, it is not sufficiently active to insert into nonactivated aryl halides under mild conditions; cf.: Collman, J. P. *Acc. Chem. Res.* **1975**, *8*, 342. (b) Ellis, J. E. *Organometallics* **2003**, *22*, 3322. (c) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed.; University Science Books: Mill Valley, CA, 1987. (d) It is noteworthy, however, that the corresponding Fe(0) complex [CpFe(CO)₂]Na was reported to react with certain aryl and vinyl halides; cf.: King, R. B. *Acc. Chem. Res.* **1970**, *3*, 417.

(61) (a) Reviews : Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525. (b) Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674. (c) Cárdenas, D. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 384.
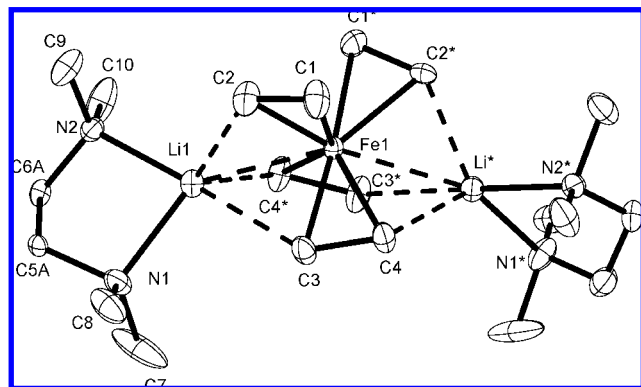
Figure 4. Structure of the lithium tetra(ethylene)ferrate complex **8** in the solid state; disorder of the tmeda ligand is not shown for clarity. Selected distances (Å) and angles (deg): Fe1−C1 2.020(5), Fe1−C2 2.078(4), Fe1−C3 2.032(5), Fe1−C4 2.057(4), Fe1−Li1 2.586(5), Li1−N1 2.198(5), Li1−N2 2.173(5), C1−Fe1−C1* 88.6(4), C2−Fe1−C2* 111.6(2), C3−Fe1−C3* 92.0(3), C4−Fe1−C4* 115.4(2), Li1−Fe1−Li1 147.3(2).

Table 2. Comparison of the Catalytic Competence of an Iron Catalyst Generated in Situ with That of the Structurally Defined Lithium Ferrate Complex **8** in the Cross Coupling of an Aryl Chloride
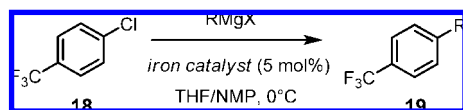
entry	iron catalyst	R	yield
1	Fe(acac)₃	n-C₆H₁₃	80%
2	**8**		85%
3	Fe(acac)₃	n-C₁₄H₂₉	94%
4	**8**		91%

Table 3. Comparison of the Catalytic Competence of Iron Catalysts Generated in Situ with That of Different Structurally Defined Lithium Ferrate Complexes in the Cross Coupling of Cyclohexyl Bromide with an Assortment of Aromatic Grignard Reagents
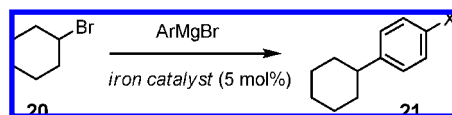
entry	iron catalyst	conditions	X	yield	ref
1	Fe(acac)₃	Et₂O, reflux	Me	69%	19b
2	FeCl₃, 2 PCy₃	Et₂O, reflux	Me	85% (GC)	19d
3	FeCl₃, tmeda	Et₂O, reflux	Me	90%	19f
4	FeCl₃, tmeda	THF, 25 °C	Me	96%	19a
5	FeCl₃, tmeda	THF, 0 °C	H	99%	19a
6	FeCl₃, tmeda	THF, 25 °C	OMe	99%	19a
7	**8**	THF, −20 °C	H	94%	
8	**8**	THF, −20 °C	H	61%[a]	
9	**8**	THF, −20 °C	Me	90%	
10	**8**	THF, −20 °C	OMe	95%	
11	**9**	THF, 0 °C → RT	H	87%	
12	**7**	THF, 0 °C → RT	H	81%	
13	Na₂Fe(CO)₄	THF, RT	H	0%	

[a] Using PhLi instead of PhMgBr.

abundant allylic halides with Grignard reagents have not been thoroughly investigated. The selected examples summarized in Table 5 show that complex **8** is highly adequate for this purpose (for the full list, consult the Supporting Information). In all cases investigated, the aryl moiety was introduced at the least hindered site of the electrophilic partner. Proparylic and benzylic

Table 4. Selected Examples of Cross Coupling Reactions of Alkyl Halides with Aromatic Grignard Reagents Catalyzed by the Lithium Ferrate Complex **8** (for the Full Table, See the Supporting Information)[a,b]

Nr	Substrate	Product	Yield
1			95% (X = OMe)
2			67% (X = Cl)[c]
3			93% (X = Ph)[c]
4			86% (X = NMe₂)
5			77%
6			94%
7			93%[d]
8			58%[e]
9			74%
10			84%
11			91%
12			87%
13			83%
14			90%
15			86%
16			68%
17			85%[c]
18			92%
19			66%
20			56%

[a] Complex **8** (5 mol%), THF, −20 °C, unless stated otherwise. [b] Isolated yield of pure product; variable amounts of Ar−Ar derived from the homocoupling of the ArMgX reagent were removed by flash chromatography. [c] At 0°C. [d] The product is racemic. [e] Exo/endo = 94:6.

substrates are also suited, with essentially no allenic byproduct being formed in the former series. This is remarkable in view of early reports on the use of iron catalysts for the conversion of propargyl halides into variously substituted allene derivatives.[62,63]

Table 5. Selected Examples of Cross Coupling Reactions of Allylic, Benzylic and Propargylic Halides with Aromatic Grignard Reagents Catalyzed by the Lithium Ferrate Complex **8** (for the Full Table, See the Supporting Information)[a,b]

Nr	Substrate	Product	Yield
1			87%
2			84%
3			95%
4			96%[c]
5			80%[d]
6			62%
7			96%[e]
8			87%

[a] Complex **8** (5 mol%), THF, −20 °C [b] Isolated yield of pure product; variable amounts of biphenyl were removed by flash chromatography; [c] Using 2.2 equiv of PhMgBr. [d] E/Z = 4.4:1. [e] Traces of allenic byproducts were removed by flash chromatography.

Chart 1. Unsuccessful Substrates
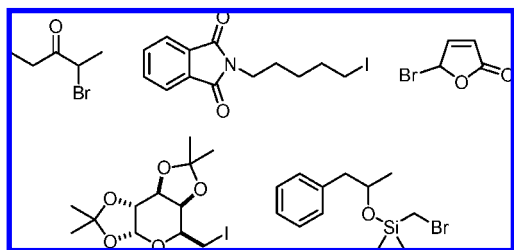
In contrast to primary iodides or bromides, the corresponding chlorides and tosylates were found unreactive under the same conditions; tertiary halides also remain unchanged.[64,65] Further limitations were encountered with the substrates displayed in Chart 1, which either failed to react or were decomposed. The reasons are not entirely clear, in particular for the phthalimide derivative, since chemically much more labile functional groups caused no problems (cf. Tables 4 and 5).

Additional data suggest that single electron transfer (s.e.t.) processes intervene in iron-catalyzed alkyl−aryl cross coupling,

Scheme 8[a]

[a] Reagents and conditions: complex **8** (5 mol%), PhMgBr, THF, 0 °C; 85% (**23**, X = I, dr = 10:1); 54% (**23**, X = Br, dr = 10:1); 89% (**25**); 77% (**27**, dr = 1.8:1); 73% (**29**, dr = 4:1); quant. (**31**, GC).

at least in certain cases.[66,67] Specifically, optically pure (R)-2-bromooctane (98% ee) is racemized upon reaction with PhMgBr in the presence of catalytic amounts of **8** (Table 4, entry 7). Although the configurational lability of an organometallic intermediate en route to the product might account for this result, a radical intermediate seems more likely. This view is supported by the fact that iodoacetals **22**, **26**, and **28** undergo 5-exo-trig(dig) ring closure with or without subsequent cross coupling (Scheme 8). It is of note, however, that the conformationally less biased but otherwise closely related substrate **24** does not cyclize, thus illustrating the subtleties of the system.[68] Cyclopropylmethyl iodide **30** as another relevant probe molecule afforded ring opened **31** as the only detectable product, in addition to biphenyl derived from the homocoupling of the Grignard reagent.[69,70]

(62) (a) Pasto, D. J.; Hennion, G. F.; Shults, R. H.; Waterhouse, A.; Chou, S.-K. *J. Org. Chem.* **1976**, *41*, 3496. (b) Pasto, D. J.; Chou, S.-K.; Waterhouse, A.; Shults, R. H.; Hennion, G. F. *J. Org. Chem.* **1978**, *43*, 1385. (c) Hashmi, A. S. K.; Szeimies, G. *Chem. Ber.* **1994**, *127*, 1075.

(63) (a) According to our investigations, this allene synthesis is rather limited in scope. A much more effective and versatile approach uses propargyl epoxides as the substrates, which stereoselectively convert to the corresponding allenes on treatment with Grignard reagents and catalytic amounts of Fe(acac)₃ through directed delivery of the nucelophile; cf.: Fürstner, A.; Méndez, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 5355. (b) For applications of this method in total synthesis, see: Lepage, O.; Kattnig, E.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 15970. (c) Fürstner, A.; Kattnig, E.; Lepage, O. *J. Am. Chem. Soc.* **2006**, *128*, 9194.

(64) The fact that *tert*-halides are inert is somewhat surprising if one assumes that radical intermediates may be involved in such iron-catalyzed processes.
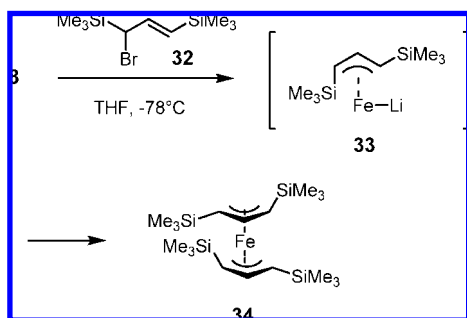
(65) Tertiary halides can be cross coupled with certain Grignard reagents in the presence of silver salts by a reaction that is believed to involve radical intermediates; cf.: Tamura, M.; Kochi, J. *J. Am. Chem. Soc.* **1971**, *93*, 1483.

(66) Early CIDNP experiments suggested the interference of radicals in iron-catalyzed processes; cf. ref 25.

(67) For evidence that radical intermediates are involved in the Ni-catalyzed cross coupling reaction of alkyl halides, see:(a) Andersen, T. J.; Jones, G. D.; Vicic, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 8100. (b) Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8790.

(68) For related experiments, see ref 181.

Scheme 9

Scheme 10[a]

[a] Reagents and conditions: (a) cyclooctenyl bromide, pentane, −20 °C → 0 °C, 16 h, 50%; (b) CO (1 atm), Et₂O, −78 °C → 0 °C, 70%; (c) allyl chloride, pentane, −20 °C → 0 °C, 16 h, 43%.

Figure 5. Structure of the cyclooctenyliron(+2) complex **36** in the solid state. Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.[48]

Mechanistic Studies: Oxidative Addition. The data summarized above corroborate a close structural as well as functional relationship between the in situ catalyst systems generated from FeX$_n$ and RMgX and the structurally well-defined lithium ferrate complexes pioneered by Jonas. Therefore the latter were used to investigate the basic features of the proposed catalytic redox cycles for which no direct experimental evidence yet exists.

To this end, we set out to explore whether such highly electron-rich iron species are capable of "inserting"[76] into the different types of substrates amenable to iron-catalyzed cross coupling or if they solely transfer electrons and trigger radical processes. As an initial foray, complex **8** was exposed to the 1,3-bis-silylated allyl bromide **32**,[71] which afforded the 14-electron complex **34** in a virtually instantaneous reaction as judged by the characteristic color change from olive-green to dark red (Scheme 9). The resulting product was identified by comparison with an authentic sample;[72] to the best of our knowledge, **34** is the only fully characterized homoleptic, monomeric bis-allyl iron complex known in the literature.[72,73] Its η^3-coordinated allyl segments adopt an eclipsed conformation with the bulky silyl substituents being *syn,anti*-disposed, thus providing effective steric shielding for the electron deficient metal center.[74] In any case, the formation of this unusual complex shows that ferrate **8** can deliver up to four electrons in reactions with suitable organic partners.

Next, we turned our attention to the behavior of the formally zerovalent ferrate **7** and its Cp* analogue **14**. Both complexes were found to insert smoothly into allylic halides even at −20 °C to give the corresponding dark red allyl complexes **36** and **38**, respectively (Scheme 10).[54c,d] As evident from the structure of **36** in the solid state (Figure 5),[48] one of the labile ethylene ligands of the starting complex is retained during the reaction. Under *rigorously* inert conditions, the insertion of **7** into cyclooctenyl bromide (**35**) in THF-d_8 could also be monitored by NMR spectroscopy. Within the limits of detection, **36** is the

only product formed, which retains a π-allyl character in solution. The signals of the cyclooctenyl ring in the ^{13}C NMR spectrum are temperature dependent, likely indicating an equilibrium between different conformers of the medium-sized ring. The kinetic lability of the bound olefin is evident from the fact that the ^{13}C NMR spectrum of **36** shows traces of free ethylene in solution, even when recorded at −80 °C; as expected, this ligand is easily displaced by CO at −78 °C to give the more stable complex **37**[54c] (Scheme 10).

Whereas the allyl subunit embedded into the bulky cyclooctenyl ring of **36** is "*exo*" oriented (Figure 5), the NMR data of **38** recorded at −30 °C in THF-d_8 suggest that the unsubstituted π-allyl ligand adopts an "*endo*" conformation, directing the *meso*-proton toward the Cp* ring. This is deduced from the characteristic high field shift of the *meso*- and the *syn*-protons
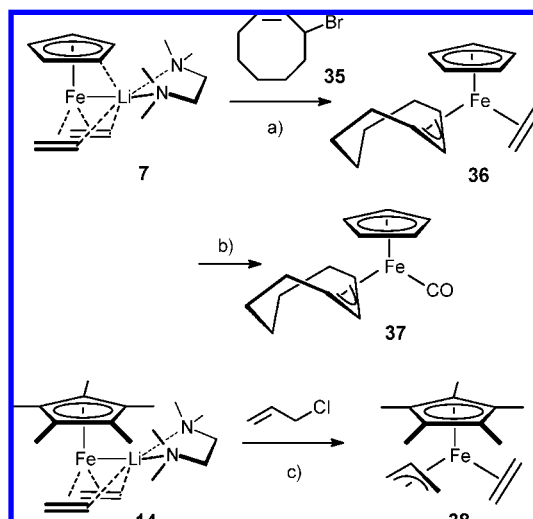
(69) For related experiments with cyclopropylmethyl iodide, see: Bedford, R. B.; Betham, M.; Bruce, D. W.; Davis, S. A.; Frost, R. M.; Hird, M. *Chem. Commun.* **2006**, 1398.

(70) For the rate constants of cyclopropylmethyl radical ring opening, see: Newcomb, M.; Johnson, C. C.; Manek, B.; Varick, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 10915.
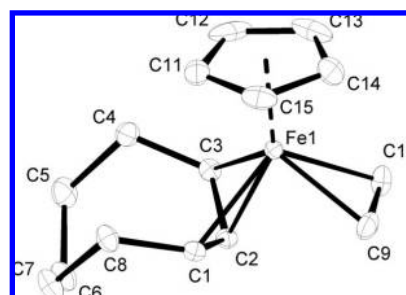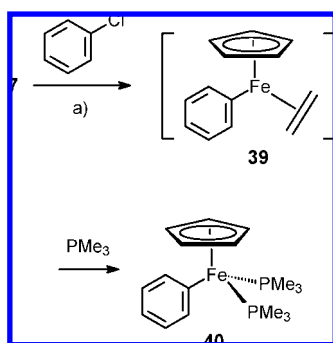
(71) Fraenkel, G.; Chow, A.; Winchester, W. R. *J. Am. Chem. Soc.* **1990**, *112*, 1382.

(72) The diallyliron complex **34** was characterized by X-ray crystallography. The data obtained for the sample prepared according to Scheme 9 were identical with those reported in the literature: Smith, J. D.; Hanusa, T. P.; Young, V. G *J. Am. Chem. Soc.* **2001**, *123*, 6455.

(73) Tris(π-allyl)iron has been briefly mentioned, but a full characterization is missing; cf.: Wilke, G.; Bogdanović, B.; Hardt, P.; Heimbach, P.; Keim, W.; Kröner, M.; Oberkirch, W.; Tanaka, K.; Steinrücke, E.; Walter, D.; Zimmermann, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 151.

(74) (a) We suppose that this effective steric shielding is the reason why the 14-electron complex **34** could not be alkylated with Grignard reagents. Sterically less hindered but otherwise closely related bis-allyl complexes of, e.g., palladium and nickel are known to react readily with RMgX or R₂Mg; cf.: Bogdanović, B.; Huckett, S. C.; Wilczok, U.; Rufińska, A *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1513. (b) Holle, S.; Jolly, P. W.; Mynott, R.; Salz, R. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1982**, *37*, 675. This propensity is believed to be essential for nickel-catalyzed cross coupling of Grignard reagents with alkyl halides; see: Terao, J.; Kambe, N. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 663.

Scheme 11[a]

[a] Reagents and conditions: chlorobenzene, PMe₃ (2 equiv), THF, 20 °C, 18%.

Figure 6. Structure of the phenyliron complex **40** in the solid state.[48] Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.

Scheme 12. Proposed Oxidative Insertion/Redistribution Pathway of Benzylic Substrates According to Sen and Coworkers[78]

($\delta_H = 0.38$ and 0.78 ppm, respectively) relative to the *anti*-protons ($\delta_H = 2.81$ ppm). Likewise, the recorded coupling constant $^2J_{\text{H-}syn,\text{H-}anti} = 2.5$ Hz is consistent with this assignment.[75]

After firmly establishing the ability of Jonas-type lithium ferrate species to "insert"[76] into allylic substrates, we set out to investigate whether such reagents are also able to activate aromatic halides. Slightly electron-deficient aryl chlorides are an important class of substrates amenable to iron-catalyzed cross coupling with alkyl Grignard reagents (cf. Table 2).[14,15,52] Gratifyingly, we were able to prove that complex **7** undergoes oxidative addition to chlorobenzene, a substrate known to require special ligands of high donor capacity and steric demand if to be activated by Pd(0).[1–3] However, the putative ethylene complex **39** as the primary product could not be obtained in pure form but had to be trapped with Me₃P (Scheme 11).[77] The structure of the resulting adduct **40** in the solid state is depicted in Figure 6.[48]

At this point it is interesting to compare our results with those previously reported by Sen and co-workers who investigated the reaction of the analogous COD complex **10** with benzyl bromide (Scheme 12).[78] These authors assumed formation of the benzyliron complex **42** as the primary product, most likely via two consecutive single-electron transfer steps. In the presence of tmeda, however, **42** is believed to undergo ligand redistribution with formation of ferrocene and the tmeda-stabilized tetrahedral diorganoiron species **43**. Although no rigorous structural proof for **43** could be obtained,[79,80] extensive NMR studies with partially deuterated substrates support the proposed constitution of this paramagnetic species. This ligand stabilized diorganoiron compound reacts with excess benzyl or
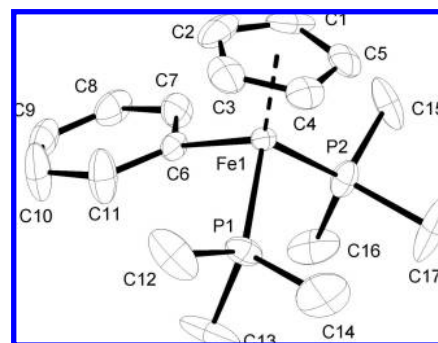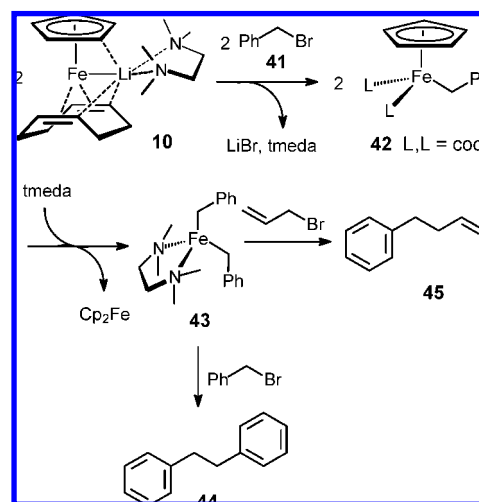
allyl bromide to give bibenzyl **44** or 4-phenyl-1-butene **45**, respectively. Although stoichiometric and performed in the absence of Grignard reagent, these results may be a useful entry point into examinations of the essential role tmeda plays in some of the iron-based protocols presently available.[13c,19a] Moreover, it is tempting to speculate that they represent a link between the redox manifolds of iron-catalyzed cross coupling chemistry and the organoiron/organoferrate regimen outlined in the previous section of this paper in which the formal oxidation state of the iron center remains unchanged throughout the catalytic transformation.

High Valent Redox Manifold. Despite the clean formation of the allyliron(2+) complex **38** on treatment of **14** with allyl chloride (1 equiv, Scheme 10), it was noticed that **38** reacts further when excess allyl chloride is present in the mixture, resulting in a formal single-electron oxidation with formation of the corresponding Fe(3+) allyl complex **46** and hexadiene as the organic byproduct (Scheme 13).[81,54d] Even though this

(75) (a) For reference data, see inter alia: ref 77a. (b) Faller, J. W.; Johnson, B. V.; Dryja, T. P. *J. Organomet. Chem.* **1974**, *65*, 395. (c) Faller, J. W.; Chen, C. C.; Mattina, M. J.; Jakubowski, A. *J. Organomet. Chem.* **1973**, *52*, 361.

(76) Note that the reaction of a Jonas-type lithium ferrate complex with an organic halide *formally* constitutes a σ-bond metathesis and not a conventional oxidative insertion.

(77) (a) Similar experiments were reported by Lehmkuhl et al., even though no crystal structures of the iron complexes could be obtained. These authors show that **7** is equally amenable to oxidative insertion into vinyl chlorides: Lehmkuhl, H.; Mehler, G.; Benn, R.; Rufínska, A.; Schroth, G.; Krüger, C.; Raabe, E. *Chem. Ber.* **1987**, *120*, 1987. (b) Benn, R.; Brenneke, H.; Frings, A.; Lehmkuhl, H.; Mehler, G.; Rufinska, A.; Wildt, T. *J. Am. Chem. Soc.* **1988**, *110*, 5661. (c) For an alternative synthesis and use of such complexes as catalysts in Kharasch-type homocoupling reactions, see: Felkin, H.; Meunier, B. *J. Organomet. Chem.* **1978**, *146*, 169.

(78) (a) Hill, D. H.; Sen, A. *J. Am. Chem. Soc.* **1988**, *110*, 1650. (b) Hill, D. H.; Parvez, M. A.; Sen, A. *J. Am. Chem. Soc.* **1994**, *116*, 2889.

(79) (a) Alkyl iron complexes stabilized by nitrogen-based ligands are known in the literature; see ref 29 and the following for leading references and literature cited therein : Bart, S. C.; Hawrelak, E. J.; Schmisseur, A. K.; Lobkovsky, E.; Chirik, P. J. *Organometallics* **2004**, *23*, 237. (b) Lau, W.; Huffman, J. C.; Kochi, J. K. *Organometallics* **1982**, *1*, 155.

(80) Related disproportionation reactions were also suggested by Hayashi to participate in iron-catalyzed C–C bond formations; cf. ref 19b.

(81) Because of the volatility of hexadiene, its presence could only be confirmed by GC/MS.

Scheme 13^a
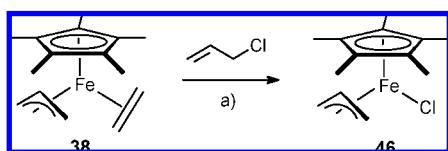
^a Reagents and conditions: (a) allyl chloride, Et₂O, 0 °C, 24 h, 61%.
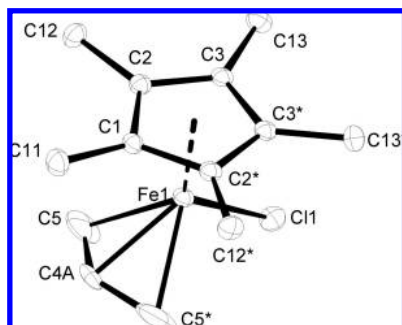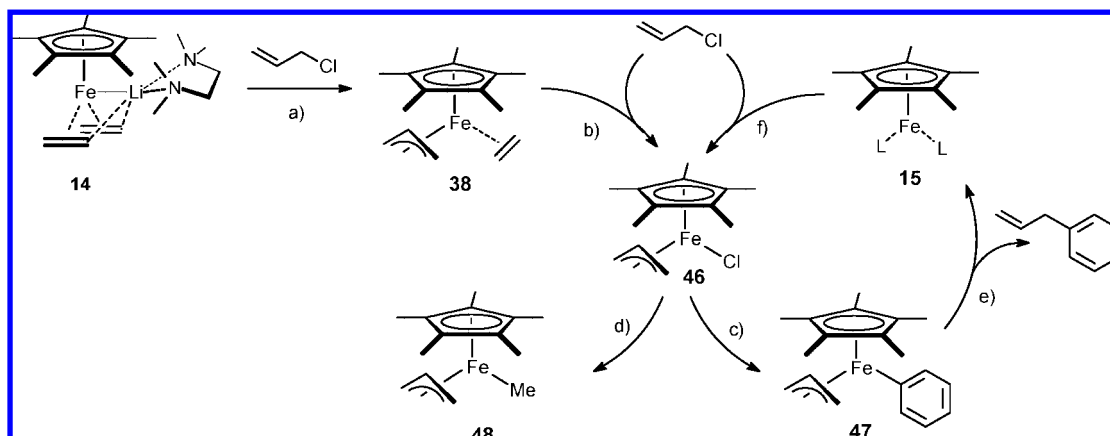

Figure 7. Structure of the 17-electron allyliron(3+) complex **46** in the solid state; the allyl ligand is disordered.[48] Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.

transformation is slower than the formation of **38** itself, it affords analytically pure **46** as dark red plates in good yield. The crystal structure of this remarkable example of an allyliron(+3) complex featuring a 17-electron count is depicted in Figure 7.[48]
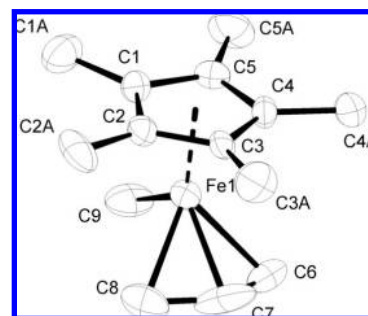
This result implies that radical processes, as manifested, for example, in the 5-*exo*-trig(dig) cyclization of the iodoacetals depicted in Scheme 8, not only may intervene during the initial reaction of an organic halide with a lithium ferrate complex[78] but also can be triggered after an organoiron complex has been formed.[82]

With different organoiron complexes at hand, we set out to investigate their reactivity toward different nucleophiles. Specifically, treatment of **46** with PhMgBr or PhLi in Et₂O at low temperature affords a new compound, which corresponds to the 17e-triorganoiron species **47** according to MS data and elemental analysis (Scheme 14). However, no single crystals of this paramagnetic species suitable for X-ray structure analysis could be obtained; therefore the analogous reaction with MeLi was

Figure 8. Structure of the 17-electron organoiron complex **48** in the solid state.[48] Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.
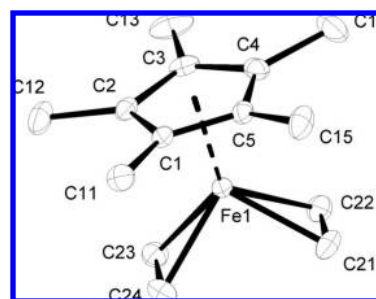
Figure 9. Structure of the 17-electron Fe(+1) bisethylene complex **15** in the solid state.[48] Anisotropic displacement parameter ellipsoids are drawn at the 50% probability level.

carried out, which resulted in the crystalline product **48** that was unambiguously characterized (Figure 8).[48]

When kept at ambient temperature, samples of **47** in THF decomposed with time, generating allylbenzene as the expected cross coupling product together with several minor byproducts derived from the Cp* ligand.[83] In an attempt to identify the corresponding [Cp*Fe(1+)] template that must have been concomitantly released in this reductive elimination process, we managed to obtain complex **15** (L = ethene),[55] provided that ethylene was present in the reaction mixture. The identity of this open shell Fe(1+) complex could again be rigorously proven by single-crystal X-ray diffraction analysis (Figure 9).[48] As **15** reacts cleanly with allyl chloride in ethereal solution to

Scheme 14. Experimental Evidence for the Cross Coupling of Allyl Chloride by an Fe(1+)/Fe(3+) Redox Couple that Is Innately Connected with Lower-Valent Organoiron Precursors^a

^a Reagents and conditions: (a) allyl chloride, pentane, −20 °C → 0 °C, 16 h, 43%, cf. Scheme 9; (b) allyl chloride, Et₂O, 0 °C, 24 h, 61%, cf. Scheme 13; (c) PhLi or PhMgBr, Et₂O, −35 °C, 2 h; (d) MeLi, pentane, −78 °C → 0 °C, ca. 70%; (e) THF-*d*₈, ethene (1 atm), ambient temperature, 46% (NMR, allylbenzene), see text; (f) allyl chloride, Et₂O, −40 °C, 20 h, 58%.
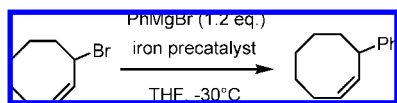
Table 6. Comparison of the Catalytic Competence of Different Structurally Defined Organoiron Complexes for the Cross Coupling of Cyclooctenyl Bromide

entry	complex (loading)	formal oxidation state	t^a	yield[b]
1	**8** (5%)	−2	<20 min	81%
2	**7** (5%)	0	18 h	39%
3	**36** (10%)	+2	18 h	33%

[a] Time necessary to reach complete conversion of the substrate. [b] Isolated yield of pure product; variable amounts of biphenyl were removed by flash chromatography.

Table 7. Comparison of the Catalytic Competence of Different Structurally Defined Organoiron Complexes for the Cross Coupling of Methyl 4-Bromocrotonate
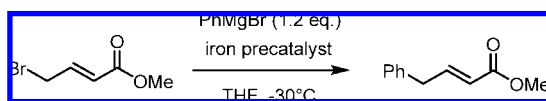
| entry	complex (loading)	formal oxidation state	t^a	yield[b]
1	**8** (5%)	−2	<10 min	94%
2	**7** (5%)	0	30 min	45%
3	**15** (10%)	+1	30 min	50%
4	**36** (10%)	+2	30 min	46%
5	**46** (10%)	+3	30 min	73%

[a] Time necessary to reach complete conversion of the substrate. [b] Isolated yield of pure product; variable amounts of biphenyl were removed by flash chromatography.

regenerate the corresponding Fe(3+) complex **46**, one might claim unequivocal experimental proof for all elementary steps of an iron-based catalytic cycle that results in cross coupling of an allylic halide with a phenyl donor (Scheme 14).

Question of the Operative Catalytic Cycle. At first sight, the data summarized in Scheme 14 suggest that a catalytic process shuttling between Fe(1+) and Fe(3+) results in the cross coupling of allylic halides and related substrates with polar organometallic reagents; this conclusion corresponds nicely to Kochi's original proposal assuming an Fe(+1)/Fe(+3) based redox mechanism.[8] Although our results show beyond doubt that such a pathway *may* be populated, we believe that this particular manifold makes a minor contribution to productive cross coupling under our standard reaction conditions, if any.

Tables 6 and 7 compare the different molecularly defined iron complexes prepared during this study in two representative model reactions. While all of them are catalytically competent, their efficiency is strikingly different. Thus, the Fe(−2) species **8** outperforms all compounds incorporating iron in higher formal oxidation states (0, +1, +2, and +3) in terms of yield and reaction rate. This difference is particularly pronounced with cyclooctenyl bromide as the substrate. The superiority of the Fe(−2) complex in catalytic cross coupling mirrors the results obtained in the stoichiometric experiments, wherein only **8**

Scheme 15. Alkylative Displacement of Ethylene from a Cobalt Template by a Grignard Reagent (R = Ph, Me)[85]
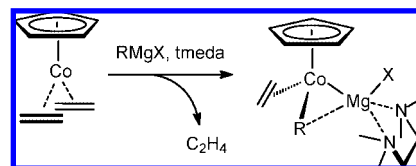
underwent an exceptionally rapid (<5 min) insertion into allylic halides (cf. Scheme 9), whereas all transformations involving higher valent iron complexes shown in Scheme 14 proceeded on the time scale of hours or even days.

This huge differential in reactivity suggests that the preparative cross coupling experiments summarized in Tables 4 and 5 (for the full list, see the Supporting Information), all of which occur within minutes, not only start off with a highly reduced species but also effectively regenerate such an entity during the course of the reaction, as originally proposed by our group.[14,20] Other manifolds shuttling between Fe(0)/Fe(+2) or Fe(+1)/Fe(+3), though accessible and viable, are too slow to account for the recorded preparative data. Whether or not they may be involved in the iron-catalyzed reactions following experimental set-ups developed by other groups, however, cannot be decided at this point.

Open Questions. Although this study allowed us for the first time to garner information on the structure and reaction characteristics of several new types of unstabilized organoiron compounds, many questions of immediate relevance for a better understanding of iron-catalyzed cross coupling still remain unanswered. The following aspects are most daunting:

(1) To which extent are unstabilized organoiron complexes prone to ligand exchange? Are such redistribution processes triggered by external ligands, do they explain the effect of additives (e.g., tmeda) or donor solvents (e.g., NMP),[78,80] and might they even cause a mechanistic switch from the redox to an organoferrate manifold?

(2) It remains largely unknown if and how low valent organoiron species react with the Grignard reagent in solution. The molecular structure of complex **4** is the only confirmed evidence for our assumption that even Fe(0) centers can be (exhaustively) alkylated by such donors under mild conditions.[84] Moreover, an example from the cobalt series might also be relevant, which illustrates an unusual alkylative displacement of ethylene (Scheme 15).[85] It will be interesting to see whether or not low-valent iron ethene complexes show similar behavior.

(3) Grignard reagents are privileged donors in iron-catalyzed cross coupling reactions. While it seems likely that organolithium reagents effect some uncatalyzed metal halogen exchange processes with the aryl or alkyl halide substrates and are hence less adequate,[86] the exact role played by the magnesium cation remains unclear and deserves further scrutiny.

(4) Finally, it should be mentioned that the decomposition pathways of low valent and/or nonstabilized organoiron compounds are essentially unknown.

(82) For a similar conclusion, proposing the generation of radicals by homolysis of a diorganoiron intermediate primarily formed, see ref 18i.

(83) According to GC/MS, these byproducts show mass peaks of $m/z =$ 134, 136, and 212, which formally correspond to [Cp*-2], [Cp*], and [Cp*+Ph], respectively. The structures of these compounds have not been analyzed any further.

(84) Additional support comes from our previous observation that finely dispersed Rieke iron slowly dissolves on exposure to the solution of a Grignard reagent to afford a dark brown and catalytically competent iron species of unknown constitution; cf. ref 14a.

(85) Jonas, K.; Koepe, G.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1986**, 25, 923.

(86) Attempted reaction of methyl 4-bromocrotonate with PhLi in the presence of catalytic amounts of complex **8** affords bromobenzene as the major product.

Conclusions

This investigation provides compelling evidence that iron-catalyzed cross coupling reactions can occur along more than one pathway. The unusual molecular structures of complexes **3−5** show that Grignard reagents unable to undergo β-hydride elimination primarily lead to homoleptic organoferrate species, which cannot alkylate aryl chlorides but react with more highly activated substrates such as acid chlorides, enol triflates, or certain electron-deficient heteroaryl halides. On the other hand, treatment with FeX_2 with EtMgX or higher alkyl Grignard reagents likely affords intermetallic clusters of the type $[Fe(MgX)_2]_n$. Their behavior can be mimicked by structurally well-defined lithium ferrate complexes of the type pioneered by Jonas,[53,56] bearing only kinetically labile olefin ligands. Such electron-rich and highly nucleophilic complexes cleanly react with prototype substrates amenable to catalytic cross coupling, as witnessed by the isolation and characterization of a host of exceptionally sensitive and unprecedented organoiron species devoid of stabilizing ligands.

Moreover, we were able to demonstrate that the entire range of formal oxidation states of iron ranging from −2 to +3 is potentially traversed under the conditions of prototype cross coupling experiments. This implies that different intertwined catalytic cycles might be populated, the kinetic characteristics of which can so far only be estimated at best. Future investigations should therefore attempt to develop ligand sets and/or reaction conditions that allow the different redox manifolds to be rigorously dissected in order to impose better control and garner even higher selectivities. Finally, our data suggest that the highest reactivity might be found in the area of organoiron complexes, in which the central metal is in the lowest conceivable formal oxidation states. Although it will require exceptional preparative and analytical skills to chart this largely unexplored terrain in more detail, fundamental insights will almost certainly reward the efforts of the brave.

Supporting Information Available: Full experimental section, including spectroscopic and analytical data of all new compounds as well as additional information concerning the crystal structures reported in this paper. This material is available free of charge via the Internet at http://pubs.acs.org

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