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Relevance of single-transmetallated resting states in iron-mediated cross-couplings: unexpected role of σ -donating additives

Lidie Rousseau,^[a,b] Nadia Touati,^[c] Laurent Binet,^[c] Pierre Thuéry,^[b] and Guillaume Lefèvre^[a]*

[a] Chimie ParisTech, PSL University, CNRS, Institute of Chemistry for Life and Health Sciences, CSB2D, 75005 Paris, France

[b] Université Paris-Saclay, CEA, CNRS, NIMBE, 91191 Gif-sur-Yvette cedex, France

[c] ChimieParisTech, Université PSL, CNRS, Institut de Recherche de Chimie-Paris (IRCP), PCMTH, 75005 Paris, France

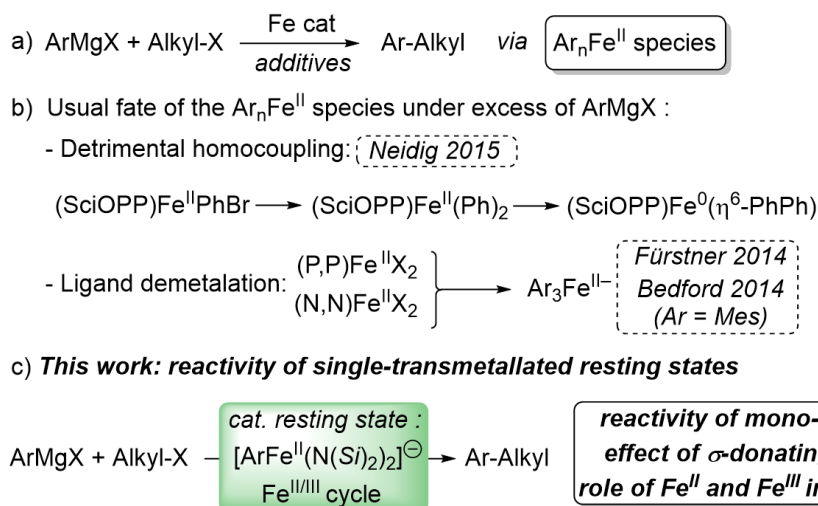
KEYWORDS. iron catalysis • cross-coupling • mechanisms • single-electron transfer • transmetallation

ABSTRACT. Control of the transmetallation degree of organoiron(II) species is a critical parameter in numerous Fe-catalyzed cross-couplings to ensure the success of the process. In this report, we however demonstrate that selective formation of mono-transmetallated Fe^{II} species during the catalytic regime counter-intuitively does not ensure alone an efficient suppression of the nucleophile homocoupling side reaction. It is conversely showed that a fine control of the transmetallation degree of the transient Fe^{III} intermediates obtained after activation of alkyl

electrophiles by single-electron-transfer (SET), achievable using σ -donating additives, accounts for the selectivity of the cross-coupling pathway. This report shows for the first time that both coordination spheres of Fe^{II} resting states and Fe^{III} short-lived intermediates must be efficiently tuned during the catalytic regime to ensure high coupling selectivities.

INTRODUCTION. Over the past decades, Fe-catalyzed cross-coupling reactions have been intensely developed, thanks to the pioneer work of Kochi^{1a-b}, followed by Cahiez^{1c}, Fürstner^{1d-e}, Nakamura^{1f-g} and Bedford.^{1h-i} Despite the significant ecologic and economic advantages displayed by this metal for its catalytic applications in synthetic chemistry,² unveiling the mechanistic facets of the related systems remains a challenging issue, especially due to the short lifetimes of the active species.³ The Kumada cross-coupling, involving Grignard reagents as nucleophiles, is by far the most developed Fe-catalyzed coupling reaction (see Scheme 1a). The key role of aryliron(II) species in aryl-alkyl cross-coupling has been established to date for numerous systems, the activation of the electrophile proceeding by a single electron transfer (SET) between the latter and the aryliron(II), leading to coupling mechanisms based on a $\text{Fe}^{\text{II}}/\text{Fe}^{\text{III}}$ sequence.⁴ It is not uncommon though that such reactions present undesired byproducts such as homocoupling of either the Grignard reagent, or of the organic electrophile, or even both. This is particularly true when the nucleophile is a sterically unhindered aryl Grignard reagent (ArMgX). It was previously reported that *in situ* formation of organoiron(II) species with ratios $\text{Ar}:\text{Fe} > 1$ often leads to homocoupling of the nucleophile or to formation of *ate*- Fe^{II} species with decoordination of the ligand (Scheme 1b).^{1i,5} Strict control of the transmetallation degree of well-defined Fe^{II} precursors has thus been often presented as a key to minimize the formation of Grignard homocoupling.⁵ It is generally admitted that formation of undertransmetallated Fe^{II} resting states can be achieved by slow rate addition of the Grignard in the bulk medium,⁶ or by

using suitable coordination frameworks involving σ -donating additives, thus hampering multiple Mg-to-Fe^{II} transmetallations. Classic examples are the aryl-aryl coupling systems developed by Nakamura and Duong, which efficiently suppressed Grignard homocoupling by associating iron salts with N-Heterocycle Carbenes (NHCs) and fluoride^{7a} or alkoxide salts.^{7b}



Scheme 1. a) classical Fe-catalyzed Kumada reaction involving an aryl Grignard reagent and an alkyl electrophile; b) usual fate of $\text{Ar}_n\text{Fe}^{\text{II}}$ species in the presence of an excess of ArMgX ; c) single-transmetallated catalytic resting state investigated in this work ($\text{Si} = \text{SiMe}_2\text{Ph}$).

From a mechanistic standpoint, single-transmetallated species are often elusive in the catalytic process, evolving towards multiple transmetallated intermediates. The latter can also lead to lower oxidation states at various stages of the catalysis (Scheme 1b). Based on these reports, it is thus difficult to evaluate the exact effect of the controlled formation of single-transmetallated Fe^{II} intermediates on coupling selectivities.

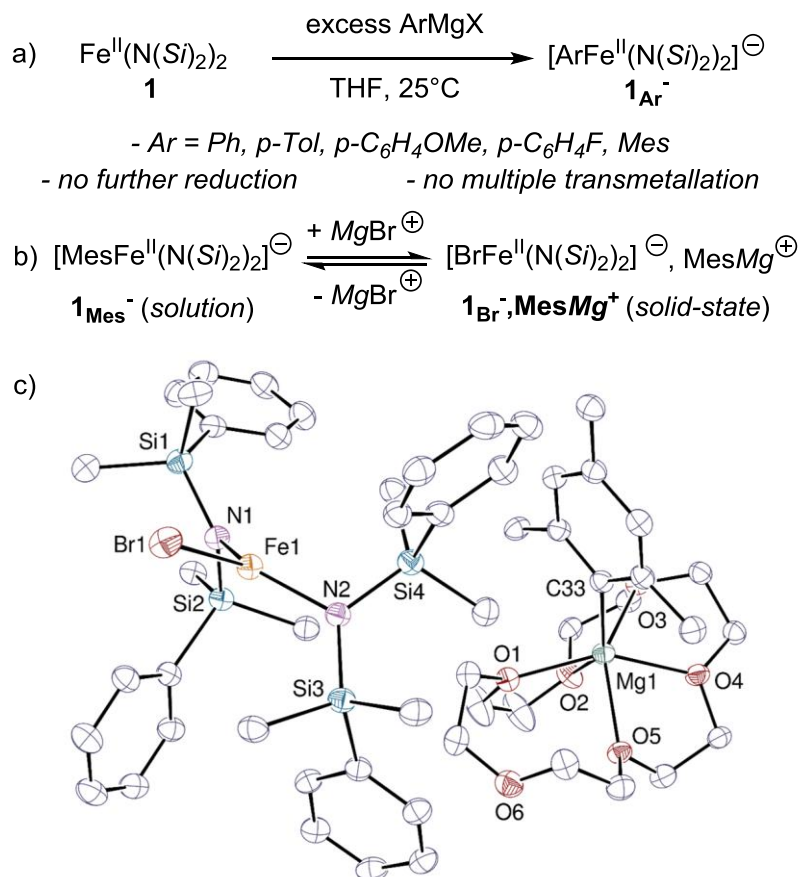
In this work, we report that *N*-bis-silylamide complex $[\text{Fe}^{\text{II}}(\text{N}(\text{Si})_2)_2]$ (**1**, $\text{Si} = \text{SiMe}_2\text{Ph}$) provides a robust framework which undergoes a single transmetallation in the presence of excess of aryl Grignard reagents, affording mono-transmetallated species $[\text{ArFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ (**1**_{Ar}⁻, Scheme 1c). The latter is able to catalyze Kumada aryl-alkyl cross-coupling with alkyl halides as electrophiles. We demonstrate that although **1**_{Ar}⁻ remains the single Fe^{II} resting state during catalytic regime, this does not ensure significant suppression of homocoupling side-products, unlike the general mechanistic pattern so far admitted. On the other hand, we bring evidence that σ -donating additives such as fluoride anions allow to limit homocoupling, thanks to a control of the transmetallation degree of transient organoiron(III) intermediates formed at a later stage of the catalytic process. These results are supported by paramagnetic ¹H NMR, cyclic voltammetry, as well as EPR experiments.

RESULTS AND DISCUSSION. Our first goal was to select a suitable Fe^{II} precursor which i) selectively undergoes single transmetallation in the presence of an excess of aryl Grignard reagents and ii) efficiently achieves aryl-alkyl catalytic cross-couplings with alkyl halides. Several well-defined monoaryllron(II) species have been structurally characterized in the past, involving a variety of σ -donating ligands (e.g. 1,2-diphosphines, 1,2-diamines (Scheme 1b), Bopa-Ph pincers^{5b}, β -diketiminates,^{8a} NHCs,^{8b} tris(pyrazolyl)borates,^{8c} N-silylamides,^{8d} ...). However, the behaviour of those species in the presence of an excess of ArMgX was either not investigated, or an evolution towards multiple transmetallations was described (Scheme 1b).

We first investigated the reactivity of Fe^{II} complexes stabilized by sterically crowded *N*-silylamide and *O*-aryloxy ligands, ($[\text{Fe}^{\text{II}}(\text{tmeda})(\text{Cl})(\text{N}(\text{SiMe}_3)((2\text{-Ph})\text{C}_6\text{H}_4))]$ (**2**) and $[\text{Fe}^{\text{II}}(\text{tmeda})(\text{Cl})(\text{O}((2,4\text{-Ph}_2)\text{C}_6\text{H}_3))]$ (**3**), see Figures S1-2 for XRD characterization), anticipating that those σ -donating frameworks would prevent multiple transmetallations with

ArMgBr (Ar = Mes, Ph).⁹ However, both complexes underwent partial or total ligand demetallation upon reaction with an excess of MesMgBr, leading to $[\text{Mes}_3\text{Fe}^{\text{II}}]^-$ (see Figures S3-4). On the other hand, iron(II) *N*-bis-silylamide $[\text{Fe}^{\text{II}}(\text{N}(\text{Si})_2)_2]$ (**1**)¹⁰ proved to undergo a single transmetallation upon addition of an excess of ArMgX (Ar = Ph, *p*-Tol, *p*-MeOC₆H₄, *p*-FC₆H₄, Mes), no demetallation being observed. Heteroleptic monoaryliiron(II) *ate*-complexes $[\text{ArFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ (**1**_{Ar}⁻) could thus be characterized in solution by action of the corresponding Grignard reagent on **1** (Scheme 2a). ¹H NMR data for those high-spin Fe^{II} species are in agreement with less bulky analogues (see Figures S5-9).^{8c,11} Importantly, ¹H NMR speciation showed that **1** underwent almost quantitative transmetallation with 1 equiv. ArMgBr for Ar = Ph, *p*-Tol, *p*-MeOC₆H₄, and *p*-FC₆H₄ to afford **1**_{Ar}⁻. Moreover, the latter species remained intact upon addition of a large excess of ArMgX (up to 10 equiv., see Figure S10), and underwent neither further transmetallation nor reduction to lower oxidation states. This behavior strongly differs from the other well-defined Fe^{II} precursors used as coupling catalysts (Scheme 1b).^{5c,11,12} Selective obtention of single-transmetallated aryliron(II) from **1** mostly originates from two factors. First, the stabilization of the Fe^{II} precursor **1** by two mono-anionic ligands leads to the building of an overall formal negative charge at the iron in **1**_{Ar}⁻ upon first transmetallation. For electrostatic reasons, this may discourage the feasibility of a second transmetallation which would lead to a dianionic species $[\text{Ar}_2\text{Fe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^{2-}$, with a formal double negative charge at the iron. A second factor hampering formation of double-transmetallated species is the high steric pressure brought by the *N*-bis-silylamide moieties around the metal. In this regard, bulkiness of this ligand even hampers full transmetallation of bulky aryl Grignard reagents such as MesMgBr with **1**. As a consequence of the steric hindrance, an equilibrium was observed between species $[\text{MesFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ (**1**_{Mes}⁻) and free complex **1** upon addition of 1 equiv.

MesMgBr onto **1**, leading to a transmetallation ratio $\mathbf{1}_{\text{Mes}^-}/\mathbf{1} = 70/30$ (Figure S9). This equilibrium was reflected in the solid state, since the halide complex $[\text{BrFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ ($\mathbf{1}_{\text{Br}^-}$) was observed in the solid-state associated to the MesMg^+ counter-cation ($(\mathbf{1}_{\text{Br}^-}, \text{MesMg}^+)$,



Scheme 2b-c).

Scheme 2. a) selective formation of $\mathbf{1}_{\text{Ar}^-}$ by transmetallation between **1** and ArMgBr (p-Tol = *para*-tolyl, Mes = 2,4,6-C₆H₂Me₃); b) equilibrium between $\mathbf{1}_{\text{Mes}^-}$ (solution) and $\mathbf{1}_{\text{Br}^-}, \text{MesMg}^+$ (solid-state), Mg = Mg(18-C-6)²⁺; c) solid-state molecular structure of $\mathbf{1}_{\text{Br}^-}, \text{MesMg}^+$ with 30% probability displacement ellipsoids shown; hydrogen atoms are omitted.

Complex **1** providing a single-transmetallated stable species ($\mathbf{1}_{Ar^-}$) in the presence of an excess of aryl Grignard reagents, its performance as a catalyst for aryl-alkyl cross-coupling was investigated. **1** was able to catalyze cross-coupling between PhMgBr and $n\text{-C}_6\text{H}_{13}\text{I}$ under smooth conditions at long reaction times (43% cross-coupling yield; 24 h at 0°C were required to reach full $n\text{-C}_6\text{H}_{13}\text{I}$ conversion, Table 1, Entry 1). When radical clock 1-bromohexene was used as a coupling partner along with PhMgBr, benzylcyclopentane was formed as a coupling product (18% yield, 25% conversion). Detection of this product, albeit in a small yield, probes a radical activation of the alkyl electrophile, in line with previously reported iron-catalyzed aryl-alkyl coupling systems.⁴

$$\text{Ar[M]} + n\text{-C}_6\text{H}_{13}\text{I} \xrightarrow[\text{y TBAT}]{\text{Fe}^{\text{II}}(\text{N}(\text{Si})_2)_2, \text{ conditions (a,b,c)}} \text{Ar-C}_6\text{H}_{13} + \text{Ar-Ar}$$

Entry	Ar[M] and conditions		y = 0		y = 5		R
			% cc	r	% cc	r	
1	PhMgBr	a	43	1.4	48	1.6	1.1
2	PhMgBr	b	59	1.6	62	2.6	1.6
3	<i>p</i> -C ₆ H ₄ MeMgCl	b	47	1.5	37	2.8	1.9
4	<i>m</i> -MeC ₆ H ₄ MgBr	b	35	1.1	42	2.0	1.8
5	<i>p</i> -MeOC ₆ H ₄ MgBr	b	39	2.2	29	3.2	1.5
6	<i>p</i> -FC ₆ H ₄ MgBr	b	71	6.4	44	6.3	1.0
7	Ph ₂ Mn	c	20	0.8	35	1.4	1.7
8	(<i>p</i> -C ₆ H ₄ Me) ₂ Mn	c	26	0.6	32	0.9	1.5
9	(<i>m</i> -C ₆ H ₄ Me) ₂ Mn	c	21	0.7	25	1.1	1.6
10	(<i>p</i> -MeOC ₆ H ₄) ₂ Mn	c	22	0.6	28	1.8	1.2
11	(<i>p</i> -FC ₆ H ₄) ₂ Mn	c	25	1.6	30	1.4	0.9

Conditions : (a) Fe:ArMgX: $n\text{-C}_6\text{H}_{13}\text{I}$ = 0.05:1:1, 0°C , 24h; (b) Fe:ArMgX: $n\text{-C}_6\text{H}_{13}\text{I}$ = 1:1:10, 0°C , 5h; (c) Fe:Ar₂Mn: $n\text{-C}_6\text{H}_{13}\text{I}$ = 0.05:0.5:1, 0°C , 24h; $r = n(\text{Ar-C}_6\text{H}_{13})/n(\text{Ar-Ar})$; $y = n(\text{TBAT})/n(\text{Fe})$; $R = r(y = 5)/r(y = 0)$; TBAT : *n*-tetrabutylammonium difluorotriphenylsilicate.

Table 1. Evolution of cross-coupling (cc) yield between Ar[M] and $n\text{-C}_6\text{H}_{13}\text{I}$ mediated by **1** in the absence or the presence of TBAT as fluoride source.

Activation of the alkyl electrophile by $[\text{ArFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ ($\mathbf{1}_{\text{Ar}}^-$) thus involves a first single-electron-transfer (SET) step leading to an alkyl radical and a transient organoiron(III) intermediate (Scheme 3a). ^1H NMR monitoring demonstrated that the consumption rate of $\mathbf{1}_{\text{Ph}}^-$ in the presence of an excess of $n\text{-C}_6\text{H}_{13}\text{I}$ is first order in $\mathbf{1}_{\text{Ph}}^-$ (Figure S11), strengthening the hypothesis of a monometallic $\text{Fe}^{\text{II}}/\text{Fe}^{\text{III}}$ activation, by contrast with Hu's system in which a transmetallation between two monoarylliron(II) species affording an active bis-arylliron(II) is the rate-determining step, leading to an overall second order in iron.^{5b} However, although single-transmetallated species $\mathbf{1}_{\text{Ph}}^-$ is stable in the presence of an excess of PhMgBr , homocoupling side-reaction significantly occurred. 30% of PhPh were indeed detected in catalytic conditions (Entry 1, conditions a). This prompted us to investigate the reactivity of species $\mathbf{1}_{\text{Ar}}^-$ towards an excess of $n\text{-C}_6\text{H}_{13}\text{I}$, in the absence of additional Grignard reagent (conditions b). Surprisingly, the cross-coupling *vs* homocoupling ratio r also remained low in those conditions (r ranking between 1.1 and 2.2, Entries 2-5), except when $p\text{-C}_6\text{H}_4\text{FMgBr}$ was used ($r = 6.4$, Entry 6). Formation of notable quantities of ArAr bisaryl by reaction of mono-aryl species $\mathbf{1}_{\text{Ar}}^-$ and $n\text{-C}_6\text{H}_{13}\text{I}$ demonstrates that, contrary to the widespread idea,^{5,6,13} the control of the transmetallation of the iron(II) resting state is not enough to efficiently hamper formation of bisaryls in Fe-mediated aryl-alkyl couplings.

TBAT was observed under catalytic conditions with Grignard reagents (conditions a, see Table S2). From a mechanistic standpoint, the absence of interaction between $[\text{PhFe}^{\text{II}}(\text{N}(\text{Si})_2)_2]^-$ and F^- was ascertained by ^1H NMR (see Figure S12), confirming again that the control of the iron(II) resting state coordination sphere alone does not fully govern the occurrence of homocoupling. These results are in stark contrast with the current mechanistic picture rationalizing the competition between Fe-catalyzed aryl-alkyl cross-coupling and nucleophile homocoupling. The commonly reported hypothesis is indeed that fluoride anions actually bound to the organoiron(II) resting states to avoid multiple transmetallations, and thus suppress the homocoupling process.¹³ Consequently, homocoupling of the Grignard reagent is not mediated by a bielectronic $\text{Fe}^{\text{II}}/\text{Fe}^0$ sequence, which suggests that this side process involves later-stage intermediates, formed after the electron transfer between $\mathbf{1}_{\text{Ph}}^-$ and the electrophile.

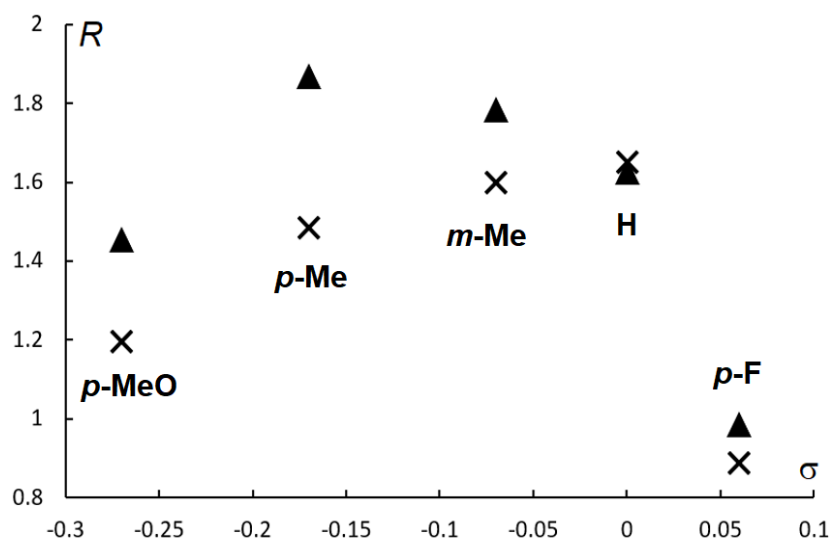


Figure 1. evolution of the R ratio as a function of the Hammett σ constant for cross-coupling between n -hexyl iodide and ArMgX (\blacktriangle , conditions b) or $\text{Ar}_2[\text{Mn}]$ (\times , conditions c).

In order to reproduce the one-electron oxidation of $\mathbf{1}_{\text{Ph}}^-$ by the organic halide, the former was subjected to reaction with a ferrocenium salt ($[\text{Cp}_2\text{Fe}][\text{PF}_6]$, Scheme 3b). When $\mathbf{1}_{\text{Ph}}^-$ was treated by an excess (5.6 equiv.) of $[\text{Cp}_2\text{Fe}][\text{PF}_6]$, only 7% of biphenyl PhPh were detected, whereas 25% of PhPh were obtained by treating $\mathbf{1}_{\text{Ph}}^-$ with 0.5 equiv. $[\text{Cp}_2\text{Fe}][\text{PF}_6]$. This suggests that, in the latter case, half quantity of $\mathbf{1}_{\text{Ph}}^-$ is oxidized into $[\text{PhFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$, which reacts with remaining $\mathbf{1}_{\text{Ph}}^-$ to afford the bis-arylated species $[\text{Ph}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$ after a Fe^{II} -to- Fe^{III} aryl transmetallation. Biphenyl is then formed from $[\text{Ph}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$ in a two-electron reductive elimination process (Scheme 3b).¹⁴ However, $[\text{Fe}^{\text{I}}(\text{N}(\text{Si})_2)_2]^-$ ($\mathbf{4}^-$) obtained after reductive elimination could not be observed by ^1H NMR. ^1H NMR monitoring showed disappearance of $\mathbf{4}^-$ upon treatment by PhMgBr , suggesting that the former might undergo ligand demetallation in the presence of PhMgBr followed by decomposition (see Fig. S14). The reactivity of the Fe^{III} species obtained after the SET between $\mathbf{1}_{\text{Ph}}^-$ and organic electrophiles (Scheme 3a) was then investigated by cyclic voltammetry, mimicking the redox processes during electrophile activation. $\mathbf{1}_{\text{Ph}}^-$ displayed a reversible $\text{Fe}^{\text{II}}/\text{Fe}^{\text{III}}$ oxidation signal at $E_{\text{p},\text{O}1} = -0.32 \text{ V vs Fc}^{0/+}$, associated with the reduction peak $E_{\text{p},\text{R}1} = -0.52 \text{ V vs Fc}^{0/+}$, observed on the reverse scan (Figure 2a).¹⁵ The quasi-reversibility observed for this system ($i_{\text{p},\text{R}1}/i_{\text{p},\text{O}1} \sim 0.7$ at $0.1 \text{ V}\cdot\text{s}^{-1}$) suggests that $[\text{PhFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$, formed after 1-electron oxidation of $\mathbf{1}_{\text{Ph}}^-$, is stable at the timescale of the cyclic voltammetry. This species is reduced in the diffusion layer of the electrode on the reverse scan at R_1 , leading back to complex $\mathbf{1}_{\text{Ph}}^-$ (Figure 2c). $\mathbf{1}_{\text{Ph}}^-$ is less easily oxidized than similar species described by Deng ($[(\text{IPr}_2\text{Me}_2)_2\text{Fe}^{\text{II}}\text{Ph}_2]$, $E_{\text{ox}} = -0.93 \text{ V vs Fc}^{0/+}$)^{16a} or Tonzetich ($[(\text{IPr})\text{Fe}^{\text{II}}(\text{CH}_2\text{Ph})_2]$, $E_{\text{ox}} = -0.86 \text{ V vs Fc}^{0/+}$),^{16b} themselves used as cross-coupling catalysts, explaining the long reaction times required to reach full *n*-hexyl iodide conversions using catalyst **1** (Table 1).

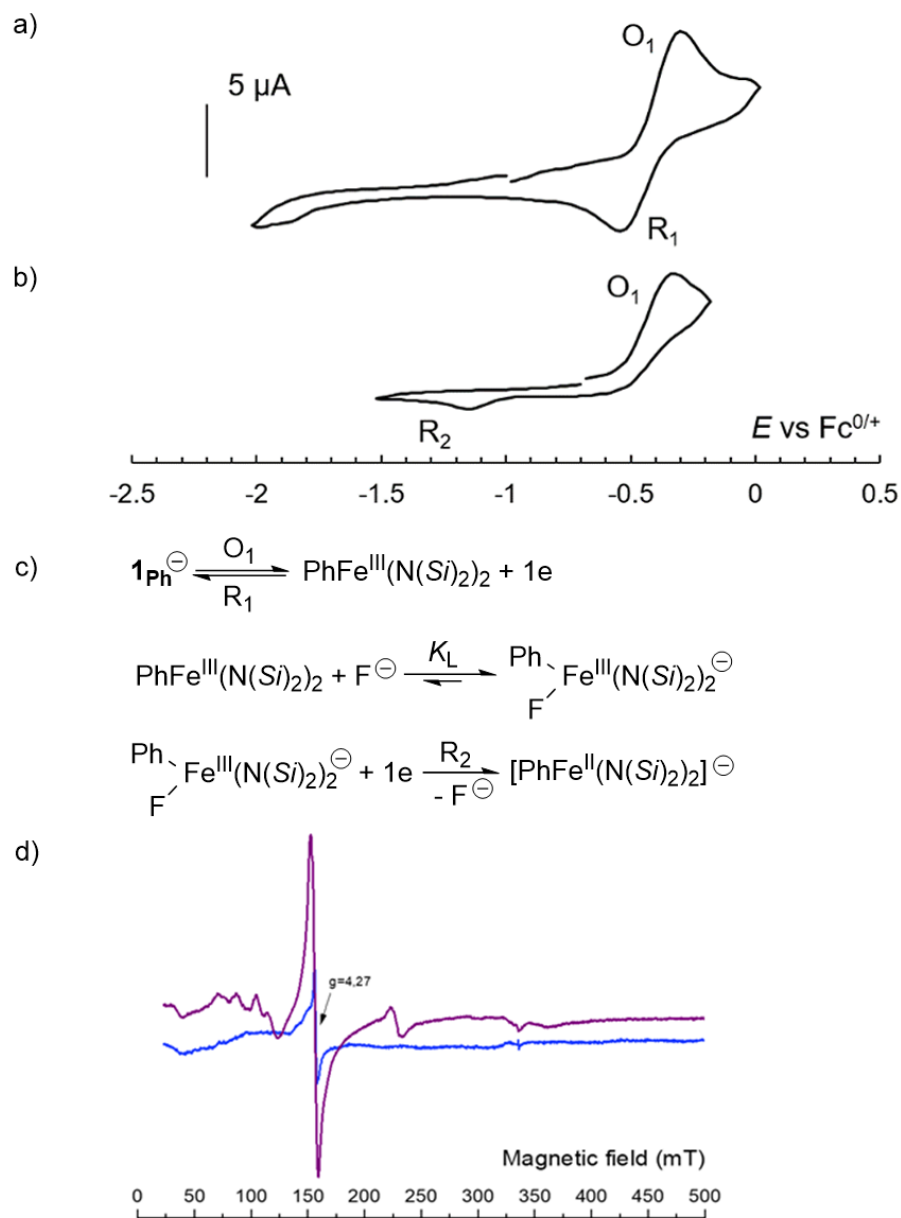


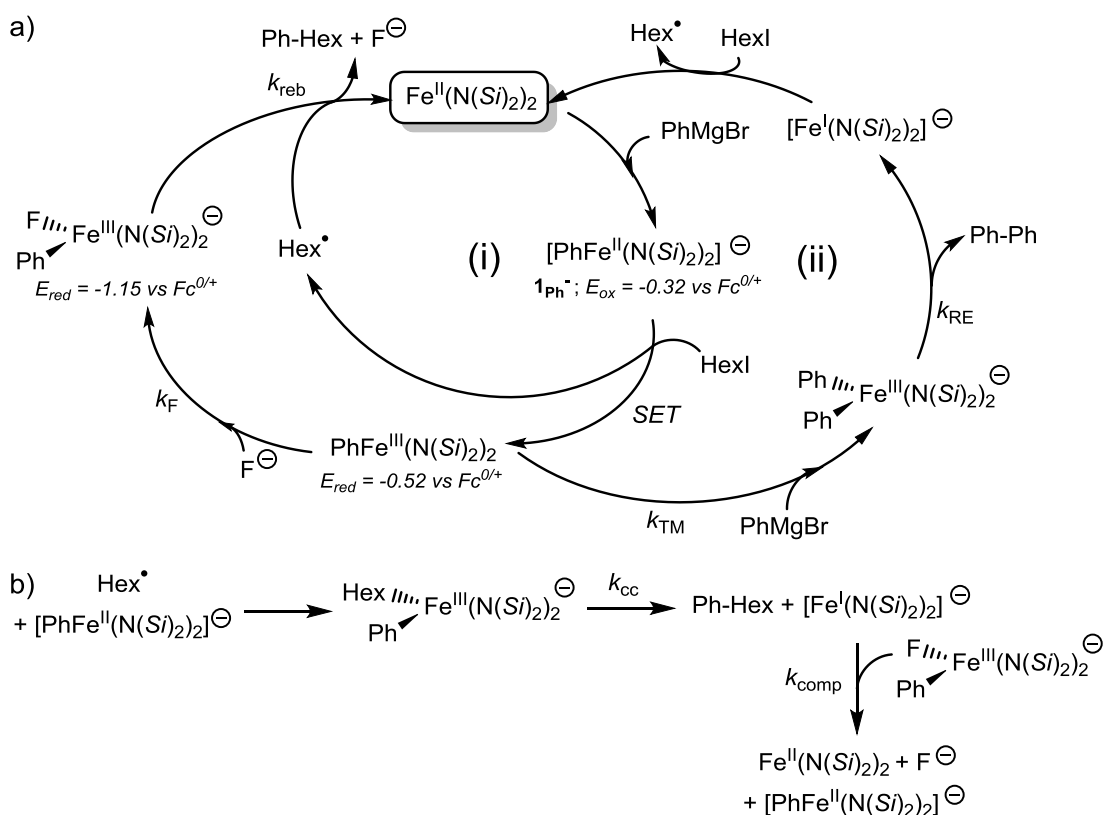
Figure 2. cyclic voltammetry performed in THF at 22°C at a gold disk electrode ($d = 2$ mm) in the presence of $n\text{Bu}_4\text{N}^+$, BPh_4^- (0.05 M) as a supporting electrolyte (scan rate = 0.1 $\text{V}\cdot\text{s}^{-1}$) of a solution of a) $\mathbf{1}_{\text{Ph}}^-$, MgBr^+ (6.5 mM); b) same as a) after addition of 1.2 equiv. of TBAT; c) related redox events; d) cw-EPR spectrum (0.02:1 2-MeTHF:THF glass, $T = 10$ K) of a solution of $\mathbf{1}$ treated by 10 equiv. PhMgBr and 10 equiv. $n\text{-C}_6\text{H}_{13}\text{I}$ in the absence (blue) or the presence (purple) of 5 equiv. TBAT, frozen after 5 min at 20°C.

When $\mathbf{1}_{\text{Ph}}^-$ was subjected to addition of 1.2 equiv. of TBAT, its oxidation potential remained unchanged (Figure 2b). This confirms the absence of reaction of $\mathbf{1}_{\text{Ph}}^-$ with fluoride salts, excluding formation of any new Fe^{II} species featuring a $\text{F}-\text{Fe}^{\text{II}}$ ligation. However, oxidation peak O_1 became irreversible and reduction peak R_1 fully disappeared, while a new reduction peak developed at potential R_2 ($E_{\text{p,R}2} = -1.15 \text{ V vs Fc}^{0/+}$, Figure 2b). In other words, $[\text{PhFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$, generated at the O_1 potential, reacts with the fluoride source to afford a new complex, reduced at the more negative R_2 potential. This strongly suggests that $[\text{PhFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$ reacts with F^- to afford a new species featuring a $\text{F}-\text{Fe}^{\text{III}}$ ligation, less easily reduced than $[\text{PhFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$ (Figure 2c). This stabilization of the Fe^{III} oxidation state in the presence of fluorides is mirrored by EPR analysis of the catalytic medium, which shows an increase of the high-spin Fe^{III} intermediates concentration by ca. 5 (Figure 2d, $g = 4.27$).

Taken together, these results demonstrate that σ -donating additives such as fluoride anions actually act in this system as ancillary ligands to the Fe^{III} intermediate $[\text{ArFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$, obtained after the SET step between the alkyl iodide and the organoiron(II) resting state $\mathbf{1}_{\text{Ar}}^-$, and not as Fe^{II} ligands. This $\text{F}-\text{Fe}^{\text{III}}$ ligation allows the blocking of a Fe^{III} coordination site and hampers a second transmetallation between the latter and an aryl nucleophile $\text{Ar}[\text{M}]$. Formation of a bisarylliron(III) intermediate $[\text{Ar}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$ is thus prevented, which limits the amount of bisaryl formed by reductive elimination.

Monoarylliron(III) intermediate $[\text{ArFe}^{\text{III}}\text{F}(\text{N}(\text{Si})_2)_2]^-$ is then involved in the last step of the coupling process, that is the formation of the C—C bond. The first scenario which can occur is a classic radical rebound of the alkyl radical Alk^\bullet with the Fe^{III} -ligated Ar group (Scheme 4a, cycle (i)), affording the coupling product and regenerating complex $\mathbf{1}$, as described by Tonzetich for similar NHC-ligated systems.^{16b} A second scenario is the radical addition of Alk^\bullet onto $\mathbf{1}_{\text{Ar}}^-$,

leading to the cross-coupling after a $\text{Fe}^{\text{II}}/\text{Fe}^{\text{III}}/\text{Fe}^{\text{I}}$ sequence. This hypothesis is sustained by the formation of 35% of coupling product $\text{Ph-}n\text{C}_{11}\text{H}_{23}$ when $\mathbf{1}_{\text{Ph}}^-$ is treated by an excess of lauroyl peroxide (LPO) under thermal conditions, allowing generation of free radical $n\text{-C}_{11}\text{H}_{23}^\bullet$ (Scheme 3c; 16% of $\text{Ph-}n\text{C}_{11}\text{H}_{23}$ are also detected in the absence of thermal activation, in a coupling process initiated by oxidation of $\mathbf{1}_{\text{Ph}}^-$ by LPO). This suggests that in-situ-generated radical $n\text{-C}_{11}\text{H}_{23}^\bullet$ is able to react with $\mathbf{1}_{\text{Ph}}^-$ to afford the heteroleptic species $[(\text{Ph})(n\text{C}_{11}\text{H}_{23})\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$, which leads after reductive elimination to $\text{Ph-}n\text{C}_{11}\text{H}_{23}$ and $[\text{Fe}^{\text{I}}(\text{N}(\text{Si})_2)_2]^-$ ($\mathbf{4}^-$). A comproportionation reaction between $\mathbf{4}^-$ and $[\text{ArFe}^{\text{III}}\text{F}(\text{N}(\text{Si})_2)_2]^-$ can then occur, leading to $\mathbf{1}$ and $\mathbf{1}_{\text{Ar}}^-$, which both re-enter the catalytic cycle as summarized in Scheme 4b.¹⁷

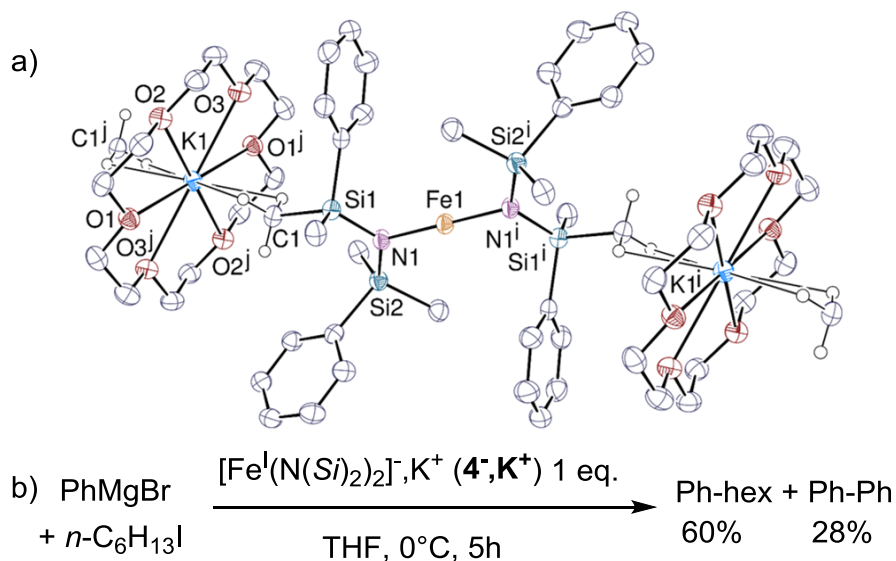


Scheme 4. a) Mechanisms of the formation of (i) Ph-Hex by cross-coupling between PhMgBr and $n\text{-C}_6\text{H}_{13}\text{I}$ involving the classical radical rebound as final step and (ii) Ph-Ph by

homocoupling, in the presence of a fluoride source and with $\mathbf{1_{Ph}^-}$ as resting state; b) alternative coupling mechanism featuring a $\text{Fe}^{\text{II}}/\text{Fe}^{\text{III}}/\text{Fe}^{\text{I}}$ sequence, followed by a $\text{Fe}^{\text{I}}/\text{Fe}^{\text{III}}$ comproportionation.

Role of fluoride additives is thus to enhance the stability of the intermediate $[\text{ArFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$ and to prevent the transmetallation leading to $[\text{Ar}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$. By hampering the homocoupling process (Scheme 4a, cycle (ii)), they allow an efficient closure of the cross-coupling cycle through the rebound (Scheme 4a, cycle (i)) and $\text{Fe}^{\text{I}}/\text{Fe}^{\text{III}}$ comproportionation (Scheme 4b) steps. This also explains the bell-shaped dependence of the role of fluoride anions on the cross-coupling ratio (R , Figure 1) with the Hammett parameters of the nucleophile substituents ($\text{Ar}[\text{M}]$, Table 1). Nucleophiles bearing electron-rich aryl groups easily afford the double-transmetallated symmetric species $[\text{Ar}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$ regardless of the presence of F^- , quickly entering cycle (ii). After a fast reductive elimination, bisaryl ArAr is obtained (k_{TM} and $k_{\text{RE}} \gg k_{\text{F}}$). This behavior is similar to the reductive elimination of electron-rich bisaryls in symmetric $[(\text{P},\text{P})\text{Pt}^{\text{II}}\text{Ar}_2]$, faster than that of electron-poor analogues.¹⁸ On the other hand, nucleophiles involving electron-poor aryl groups do not easily provide $[\text{Ar}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si})_2)_2]^-$, reductive elimination of the corresponding bisaryl also being a slow process. In that case, single transmetallated $\text{Ar}-\text{Fe}^{\text{III}}$ species quickly completes cross-coupling process, following either the rebound (Scheme 4a, cycle (i)) or the comproportionation (Scheme 4b) path (k_{TM} and $k_{\text{RE}} \ll k_{\text{F}}$, k_{reb} and k_{comp}), regardless of the presence of fluorides. A low influence of fluoride additives on the r ratio is thus observed for both electron-rich and poor Ar groups, leading to R values close to 1 (Figure 1). However, fluoride anions efficiently block the transmetallation of aryl groups with intermediate electronic effects onto $[\text{ArFe}^{\text{III}}(\text{N}(\text{Si})_2)_2]$, leading to an improvement of the cross-

coupling selectivity (R values > 1 , Figure 1).¹⁹ Formation of bisaryls by cycle (ii) nevertheless allows to re-enter the main cross-coupling cycle (i). Two-electron reductive elimination from $[\text{Ar}_2\text{Fe}^{\text{III}}(\text{N}(\text{Si}i)_2)_2]^-$ indeed affords $[\text{Fe}^{\text{I}}(\text{N}(\text{Si}i)_2)_2]^-$ ($\mathbf{4}^-$), which was synthesized, characterized by X-Ray diffraction (associated to the $\text{K}(\mathbf{18-C-6})^+$ counter-cation), and proved to be an efficient cross-coupling promotor (Scheme 5, stoichiometric experiment). Evans speciation moreover showed that $\mathbf{4}^-$ displays a high-spin Fe^{I} center ($S = 3/2$; $\mu_{\text{eff}} = 5.02 \mu_{\text{B}}$, $\mu_{\text{s.o.}} = 3.87 \mu_{\text{B}}$), akin to the recently reported analogue $[\text{Fe}^{\text{I}}(\text{N}(\text{SiMe}_3)_2)_2]^-$ ($\mu_{\text{eff}} = 5.12 \mu_{\text{B}}$).²⁰ As suggested by a recent report by Werncke *et al.*, a SET step between $\mathbf{4}^-$ and $n\text{-C}_6\text{H}_{13}\text{I}$ should quickly occur, allowing the formation of $\mathbf{1}$, which can re-enter the cross-coupling process (Scheme 4, last step of cycle (ii)).^{8d}



Scheme 5. a) solid state molecular structure of $\mathbf{4}^-$, $(\mathbf{18-C-6})\text{K}^+$ obtained by reduction of $\mathbf{1}$ with 1 equiv. KC_8 . Displacement ellipsoids shown at 50% probability, hydrogen atoms omitted; b) cross-coupling between PhMgBr and $n\text{-C}_6\text{H}_{13}\text{I}$ mediated by $\mathbf{4}^-$, K^+ .

CONCLUSION. We demonstrated that bulky *N*-bis-silylamides used as Fe^{II} ligands provide robust frameworks which selectively afford single-transmetallated aryliron(II) species as resting states in Fe-catalyzed aryl-alkyl cross-couplings. Unlike the currently admitted mechanistic picture, we proved that access to single-transmetallated Fe^{II} resting states is a non-sufficient condition to impede the usual bisaryls side-products formation. Bisaryls are indeed also significantly formed by reductive elimination from transient bis-aryliron(III) intermediates obtained after activation of the alkyl halide. Hampering multiple transmetallations at the Fe^{III} stage can be performed using σ -donating additives such as fluoride anions, limiting the formation of bisaryls. A fine control of the Fe^{III} coordination sphere therefore proves to be a critical parameter to access a good cross-coupling selectivity, in addition to a control of the Fe^{II} resting states coordination sphere (multiple transmetallations at the Fe^{II} stage being also controlled by either the coordination sphere of the latter, or also by the use of suitable σ -donating additives). In a general way, this shows that design of the coordination sphere of transient oxidized iron intermediates in those couplings is as essential as the design of the resting state itself.

ASSOCIATED CONTENT

Supporting information (PDF): general procedures, ¹H NMR spectra, kinetics plots, CIF files.

The corresponding files are available free of charge.

AUTHOR INFORMATION

Corresponding Author

*E-mail: guillaume.lefevre@chimieparistech.psl.eu

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Table of contents:

Control of the transmetalation of iron(II) resting states in Fe-catalyzed cross-coupling has long been told to be the key of a good coupling selectivity, by hampering homocoupling process. We demonstrate in this work, using a rare example of single-transmetalated iron(II) resting state, that a significant part of the homocoupling originates from organoiron(III) intermediates. A fine control of the iron(III) transmetalation degree can be achieved thanks to fluoride anions, at the origin of the coupling efficiency.

