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Iron-Catalyzed Borylation of Alkyl, Allyl, and Aryl Halides: Isolation of an Iron(I) Boryl Complex

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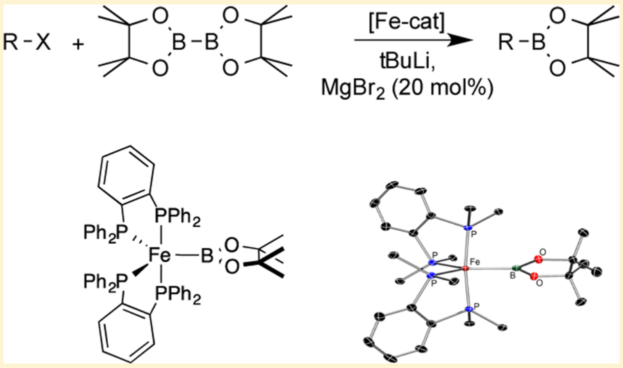
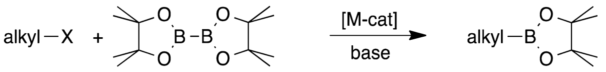
Supporting Information

ABSTRACT: Activation of B_2pin_2 with ^{t}BuLi facilitates the Fe-catalyzed borylation of alkyl, allyl, benzyl, and aryl halides via the formation of Li[B_2pin_2(^{t}Bu)] (**1**). The reaction of **1** with a representative iron phosphine precatalyst generates the unique iron(I) boryl complex [Fe(Bpin)(dpbz)$_2$] (**2**).



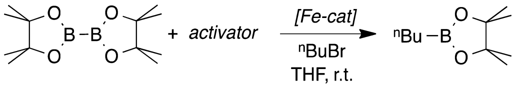
Alkylboronic acid derivatives are of great synthetic interest and can be prepared by a variety of methods.[1] A recent and highly attractive methodology, developed originally by Marder and co-workers,[2] relies on the borylation of alkyl halides with diboron esters, in particular bis(pinacolato)diboron (B_2pin_2) (Scheme 1). Originally, this method required Cu catalysts,[2,3] but the scope has been expanded to include Pd-,[4] Ni-,[5] and, most recently, Zn-based catalysts.[6] The equivalent iron-catalyzed process is highly desirable due to iron's low cost and toxicity.[7] We report that both phosphine-containing and coligand-free iron-based catalysts can be employed in the reaction to excellent effect. Furthermore, we show that a unique iron(I) boryl complex can be isolated under catalytically relevant conditions.

Scheme 1



From optimization studies (Table 1) it was clear that the barrier to success lay with the transfer of the boryl group from B_2pin_2 to the iron center. Initial attempts at coupling ^{n}BuBr with B_2pin_2, activated with KF, KO^{t}Bu, or NEt_3 in the presence of $MgBr_2$ (20 mol %), gave little or none of the desired product. Alkyl anions have been shown to be useful activating agents in the iron-catalyzed Suzuki coupling of arylboronic pinacol esters,[8] and this approach proved fruitful here, particularly when ^{t}BuLi was exploited in the presence of cocatalytic $MgBr_2$ (entry 5).

Table 1. Optimization of Iron-Catalyzed Borylation[a]



entry	[Fe-cat]	activator	yield, %[b]
1	[$FeCl_2$(dppe)]	KF + $MgBr_2$[c]	0
2		KO^{t}Bu + $MgBr_2$[c]	3
3		NEt_3 + $MgBr_2$[c]	6
4		EtMgBr	38
5		^{t}BuLi + $MgBr_2$[c]	71
6	[$FeCl_2$(dppe)][d]		71
7	$FeBr_2$		80
8	$FeBr_2$ + xantphos		85
9	$FeBr_2$ + dcpe		90
10	[$FeCl_2$(dcpe)]		90
11	none		0
12	[$FeCl_2$(dcpe)]	$MgBr_2$[c]	0
13	[$FeCl_2$(dcpe)][e]	^{t}BuLi + $MgBr_2$[c]	88
14	[$FeCl_2$(dcpe)]	^{t}BuLi	71
15		^{t}BuLi + $AlBr_3$[c]	69
16		^{t}BuLi + $ZnBr_2$[c]	77

[a] ^{t}BuBpin produced as coproduct, observed by GC-MS. [b] By GC (dodecane standard). [c] 20 mol % with respect to ^{n}BuBr. [d] From 99.99% purity $FeCl_2$. [e] 6 mol % [Fe].

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Surprisingly, an increase in yield was observed in the *absence* of added ligand (entry 7). Indeed, most of the P- or N-based ligands we surveyed either hindered the catalysis or gave no improvement in yield in comparison to "coligand-free" conditions (see Table S1 in the Supporting Information).[9] Only xantphos (4,5-bis(diphenylphosphino)-9,9-dimethylxanthene) and dcpe (1,2-bis(dicyclohexylphosphino)ethane) gave higher yields (entries 8−10) than the phosphine-free system. Both iron and ^{t}BuLi (entries 11 and 12) were found to be essential for the reaction, while an iron precatalyst made from high-purity $FeCl_2$ gave the same result as that obtained with reagent grade $FeCl_2$. In the absence of $MgBr_2$ the yield dropped significantly (entry 14). Replacing $MgBr_2$ with either $AlBr_3$ or $ZnBr_2$ gave little or no improvement in activity in comparison with ^{t}BuLi alone.

Table 2 summarizes the borylation of a range of substrates. Typically, with more reactive substrates (allyl, benzyl, and secondary alkyl halides) we obtained higher yields under coligand-free conditions in comparison to those when $[FeCl_2(dcpe)]$ was used, whereas with primary alkyl halides, better activity was seen in the presence of the phosphine (see Table S2 (Supporting Information) for full data).[9] Gratifyingly we obtained some, albeit modest, activity with aryl bromides, a class of substrate that can prove challenging for iron catalysis. Here the best precatalyst proved to be $[FeCl_2(dppe)]$.

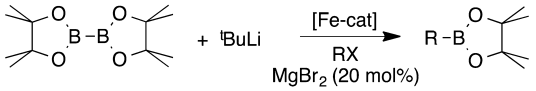
Next we turned our attention to garnering mechanistic insights, starting first with identifying the activated borylating reagent. The reaction of B_2pin_2 with ^{t}BuLi in THF (Scheme 2) gave a solution of a compound we assign as the borate ion $Li[B_2pin_2({}^{t}Bu)]$ (**1**).

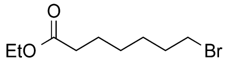
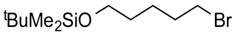
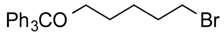
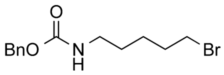
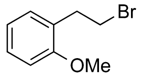
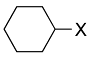
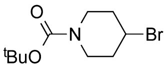
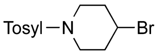
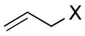
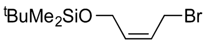
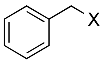
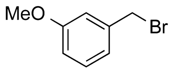
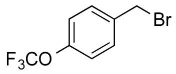
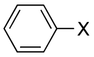
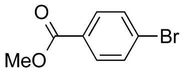
The solution of compound **1** showed two peaks in its ^{11}B NMR spectrum, a broad peak at δ 39.1 and a sharper peak at δ 6.4 similar to those observed previously for the related anion $[B_2pin_2(OMe)]^-$ (δ 35.0 and 5.9).[10] After the solvent was removed, the solubility of the isolated solid **1** was poor. Despite this, its reaction with ^{n}BuBr, catalyzed by $[FeCl_2(dcpe)]$, still gave ^{n}BuBpin in 85% yield, strongly suggesting that **1** is the borylating species. In effect, **1** behaves as a "masked" boryl anion stabilized by coordination to an alkylboronic ester.[11]

As we previously observed in iron-catalyzed Suzuki coupling reactions, phosphine-free precatalysts gave black, heterogeneous reaction mixtures.[8b] In contrast, the reaction of ^{n}BuBr with **1** catalyzed by $[FeCl_2(dcpe)]$ in THF gave a pale yellow, homogeneous solution, allowing us to undertake initial-rate kinetic studies. These were performed at 5 °C unless specified otherwise. The initial rate of the reaction was found to be independent of [**1**] over the range investigated,[9] indicating that **1** was not involved in the rate-limiting step. For a reaction run at 2.5 mM precatalyst concentration we observed no turnover with an $[MgBr_2]_0 = 8.3$ mM. However, by $[MgBr_2]_0 = 12.5$ mM the rate rose significantly, after which point further addition of $MgBr_2$ led to only a slight increase in rate. We have yet to ascertain the role(s) played by the $MgBr_2$, but it is interesting to note that a nontrivial dependence on $[MgBr_2]$ was also observed in Fe-catalyzed Suzuki coupling.[8b]

The initial rate showed an approximately first order dependence on the concentration of the precatalyst, $[FeCl_2(dcpe)]$. Adding extra dcpe proved to be hugely deleterious to the reaction, so much so that we needed to increase the temperature of the reaction to 30 °C and double the concentration of iron precatalyst in order to be able to record meaningful rates. Under these conditions, the addition of 0.5 equiv of dcpe led to an approximately 40-fold decrease in initial rate, beyond which point an approximately inverse first-order dependence on [dcpe] was observed. A previously

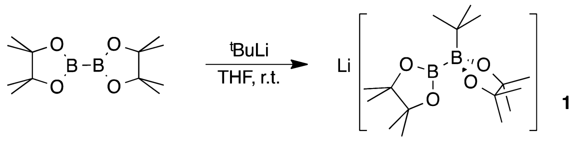
Table 2. Borylation of Alkyl, Benzyl, Allyl, and Aryl Halides[a]



Entry	RX	catalyst	Yield, %[b]
1		$[FeCl_2(dcpe)]$	77
2			59
3			69
4			67
5			73
6	^{n}BuBr		90[c]
7	^{n}BuCl		24[c]
8	^{n}BuI	$FeBr_2$	78[c]
9	 X = Br		78[c]
10	X = Cl		24[c]
11	X = I		70[c]
12			70
13			71
14	 X = Br		87[d]
15	X = Cl		58[d]
16	X = I		63[d]
17			69
18	 X = Br		95[d]
19	X = Cl		85[d]
20			75
21			71
22	 X = Br	$[FeCl_2(dppe)]$	18[a,e]
23	X = I		11[a,e]
24	X = Cl		5[a,e]
25			33[a,e]

[a] Conditions: THF solution of B_2pin_2 (2.8 mmol) and ^{t}BuLi (2.8 mmol) added to a THF solution of RX (2 mmol), $MgBr_2$ (0.4 mmol), and iron precatalyst (3 mol %, unless otherwise indicated), stirred at room temperature for 1 h. [b] Isolated yield, unless otherwise stated. [c] Determined by GC (dodecane internal standard). [d] Determined by ^{1}H NMR (1,3,5-$(MeO)_3C_6H_3$ internal standard). [e] 40 °C, 5 mol % Fe.

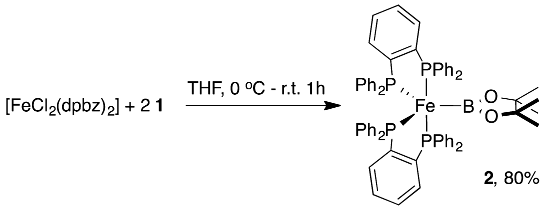
Scheme 2



observed inverse first-order dependence of rate on diphosphine concentration in a related iron-catalyzed Suzuki coupling[8b] was attributed to a pre-equilibrium between a stable bis-diphosphine complex and a reactive mono-diphosphine species immediately prior to the rate-determining step: the oxidation of the latter species by the alkyl halide substrate. Here the effect of added phosphine is far more pronounced and may indicate that the active species is in fact diphosphine-free. In this scenario, the phosphine would presumably stabilize resting state species and thus prevent catalyst degradation: much the same role as we previously proposed for chelating diamine ligands in iron-catalyzed Kumada cross-coupling reactions.[12]

While it might be presumed that the reactions proceed via the formation of iron boryl intermediates, we wished to examine whether such species could indeed be formed under catalytically relevant conditions. Under phosphine-free conditions, the reaction of $FeBr_2$ with excess **1** at room temperature led to the immediate formation of a black suspension.[13] Although yellow to red homogeneous solutions could be obtained at −78 °C on varying the B:Fe ratio from 3:1 through to 5:1, these species underwent rapid decomposition on slight warming. So far we have not been able to isolate any species from these reactions due to their extreme thermal sensitivity; therefore, we focused instead on the equivalent reactions of **1** with Fe phosphine complexes. The reaction of $[FeCl_2(dpbz)_2]$ (dpbz = 1,2-bis(diphenylphospino)benzene) with **1** led to a rapid change from a yellow suspension to a deep red solution, and we were able to isolate the iron(I) boryl complex **2** in good yield (Scheme 3).

Scheme 3. Formation of an Fe(I) Boryl Complex



The single-crystal X-ray structure of **2** is shown in Figure 1 (top). The gross structure is very similar to those of other Fe(I) complexes we have reported of the type $[FeX(PP)_2]$, where X = aryl, halide and PP = dpbz, dppe.[14] To the best of our knowledge, this is both the first example of a boryl ligand on an Fe(I) center (the vast majority of Fe boryl complexes contain Fe(II))[15] and the first example of an iron boryl species supported solely by phosphine ligands. The Fe−B bond length (2.065(3) Å) is similar to those at the longer end of the range reported for iron(II) boryl complexes.[15]

Complex **2** is paramagnetic (μ_{eff} = 1.73 μ_B, Evans method, THF, room temperature),[16] consistent with an $S = {}^1/_2$ spin state, and is NMR silent. The X-band EPR spectrum of complex **2** (Figure 1, bottom left) is significantly more broadened and lacking in resolved hyperfine structure in comparison to the spectra of related $[FeX(PP)_2]$ (X = halide, aryl) complexes,[8b,12,14] presumably as a result of superhyperfine coupling to ^{31}P and both superhyperfine and quadrupolar coupling to $^{10,11}B$. A density functional theory (B3LYP-D2)[9] analysis of the ground-state structure of **2** gave a geometry and electronic structure consistent with low-spin Fe(I) character (Figure 1, bottom right). The Mulliken spin density corresponding to the unpaired electron is located primarily on the Fe atom (86.7%), with only very small contributions from the ligating P and B atoms and the other ligand atoms.

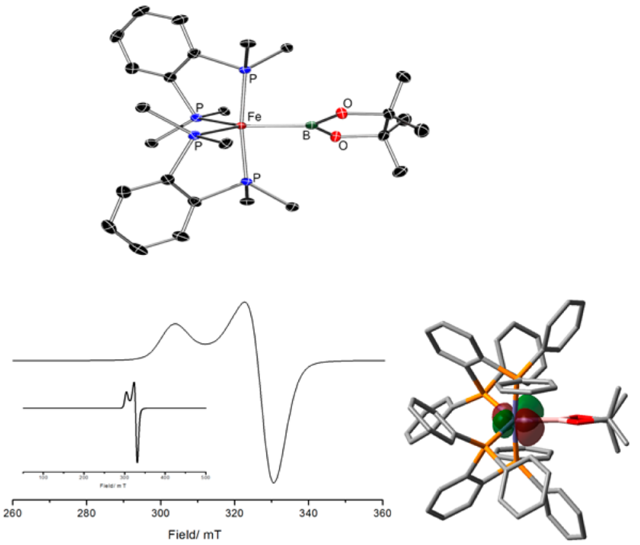


Figure 1. (top) X-ray structure of **2**, with H atoms and C atoms except for the ipso-C atoms of Ph residues omitted. Ellipsoids were set at 50% probability. (bottom left) X-band EPR spectrum (THF, 140 K) of **2**. (bottom right) Calculated SOMO (isovalue ±0.05 (electron/bohr^3)$^{1/2}$) of low-spin **2**.[9]

Unsurprisingly, in view of the highly deleterious effect on the rate of reaction of having >1 diphosphine ligand present in the catalytic reaction, complex **2** showed poor activity as a catalyst in the coupling of ^nBuBr with **1**, giving only 16% of ^nBuBpin after 16 h. This suggests that **2** is not an active catalyst but rather that it slowly converts to an active species. This presumably occurs on reaction with **1**, since complex **2** showed no reaction with a stoichiometric amount of ^nBuBr in the absence of **1** after 16 h.

In summary, the iron-catalyzed borylation of a range of alkyl, allyl, benzyl, and aryl halides can be achieved. Preliminary mechanistic investigations indicate that overcoordination by chelating diphosphines slows the rate enormously. Conversely, the stabilization provided by phosphine ligation allows the isolation of a unique iron(I) boryl complex, the formation of which shows that the activated borate **1** is sufficiently reducing to be able to access oxidation states below Fe(II), adding to the range of nucleophiles that yield Fe(I) under catalytically relevant conditions.[17] We are currently exploring both the scope of the reaction and the mechanism in detail.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, tables, and CIF and xyz files giving experimental details, spectroscopic data, and DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

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