C–H Borylation

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Iridium-Mediated Borylation of Benzylic C–H Bonds by Borohydride[**]

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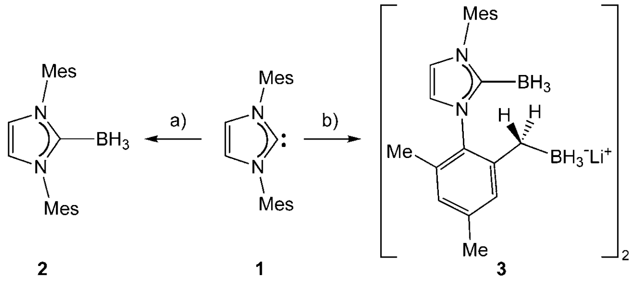
The transition-metal-mediated conversion of C–H to C–B bonds is an exciting recent development in the functionalization of both saturated and unsaturated hydrocarbons.[1] In part this reflects the fact that the resulting borylated compounds (boronic esters or acids) are attractive substrates for further chemistry through a range of established protocols.[2] C–H to C–B conversion in arenes/heteroarenes catalyzed by [{Ir(cod)X}$_2$]/4,4′-di-*tert*-butylbipyridine systems (X = Cl, OMe, indenyl; cod = cyclooctadiene) has been particularly well developed,[1,3] in some cases achieving selectivity for substitution patterns which have proved difficult to access using classical synthetic methods.[4] Typically these borylation protocols utilize HBpin or B$_2$pin$_2$ as the boron reagent of choice (pin = pinacolato, OCMe$_2$CMe$_2$O), with Ir^{III}–tris(Bpin) complexes thought to be key catalytic intermediates.[5] C–B bond formation proceeds through either M–B/C–H σ bond metathesis or through distinct C–H oxidative addition/B–C reductive elimination steps in an Ir^{III}/Ir^{V} cycle.[1,5,6] An alternative mechanism implicating a mono(Bpin) complex and a Rh^{I}/Rh^{III} catalytic cycle has been proposed for benzylic borylation using HBpin.[7]

In recent work we have examined the interaction of rhodium and iridium complexes containing bis(N-heterocyclic carbene) (NHC) ligand sets with boranes.[8,9] In doing so we have discovered an unusual intramolecular C–H borylation process mediated by [{Ir(coe)$_2$Cl}$_2$] (coe = cyclooctene) which leads to the transfer of a BH$_3$ fragment from LiBH$_4$ to a benzylic carbon center.[7,10,11] Here, we investigate the fundamental mechanistic steps which lead to this chemistry.

The reaction of IMes [*N*,*N*′-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene; **1**] with excess LiBH$_4$ in diethyl ether generates the known compound IMes·BH$_3$ (**2**) in 75% yield.[12] By contrast, the reaction of **1** with [{Ir(coe)$_2$Cl}$_2$] (0.25 equiv of dimer)/excess LiBH$_4$, leads to the formation of the lithium salt **3**, in which one of the *ortho*-methyl substituents has undergone additional C–H activation, thereby generating an [ArCH$_2$BH$_3$]$^-$ function (Scheme 1).



Scheme 1. Syntheses of **2** and **3** through borane complexation with or without additional C–H activation. Key reagents and conditions: a) LiBH$_4$ (10 equiv), diethyl ether, 20°C, 6 h, 75%; b) [{Ir(coe)$_2$Cl}$_2$] (0.25 equiv), THF, then LiBH$_4$ (40 equiv), diethyl ether, 7 d, 42%.

The formation of **3** is suggested by ^{11}B NMR spectroscopy which reveals two quartet resonances (at δ_B −35.1, $^1J_{BH}$ = 81 Hz and −27.4 ppm, $^1J_{BH}$ = 78 Hz), the former being similar to that reported for **2** (δ_B −36.8 ppm, $^1J_{BH}$ = 88 Hz),[12b] the latter consistent with other examples of [RBH$_3$]$^-$ species [e.g. δ_B −26.8 ppm, $^1J_{BH}$ = 79 Hz for (2-naphthyl)BH$_3^-$].[13] These spectroscopic inferences were subsequently confirmed by crystallographic studies, with **3** being shown to exist as a centrosymmetric dimer in the solid state (Figure 1). Each lithium center interacts with six BH hydrogen atoms (with distances in the range 1.86–2.24 Å), two of which originate from each of the carbene·BH$_3$ and [ArCH$_2$BH$_3$]$^-$ units of one [(IMes′BH$_3$)BH$_3$]$^-$ moiety, and the other two in the [ArCH$_2$BH$_3$]$^-$ unit of the second. The C–B distances associated with the two different carbon donors are marginally different [1.587(3) and 1.634(3) Å] with the shorter bond

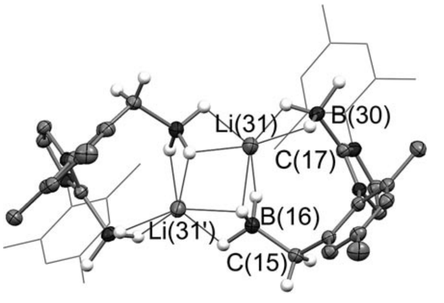


Figure 1. Molecular structure of dinuclear **3**·C$_6$H$_5$F. Hydrogen atoms [except those attached to C(15), B(16) and B(30)] and fluorobenzene solvate omitted (and unactivated mesityl groups shown in wireframe format) for clarity; thermal ellipsoids set at the 40% proability level. Key distances [Å]: C(17)–B(30) 1.587(3), C(15)–B(16) 1.634(3).

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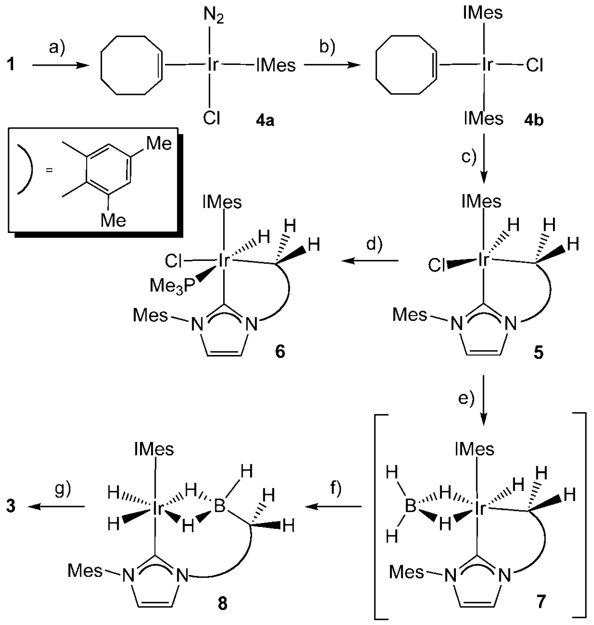
being associated with neutral NHC donor [cf. 1.596(4) Å for **2**].[12a]



Scheme 2. Iridium-mediated conversion of **1** to **3**. Key reagents and conditions: a) [{Ir(coe)$_2$Cl}$_2$] (0.47 equiv of dimer), THF, 7 d at 20 °C, 45 %; b) (from **1**) [{Ir(coe)$_2$Cl}$_2$] (0.23 equiv of dimer), THF, 12 h at 20 °C, 85 %; c) (from **4b**) thermolysis at 65 °C, toluene, 24 h, quantitative by NMR analysis; (from **1**) [{Ir(coe)$_2$Cl}$_2$] (0.25 equiv of dimer), THF, 60 h at 20 °C, 68 %; d) PMe$_3$ (excess), toluene, 1 h at 20 °C, 61 %; e, f) (from **5**) LiBH$_4$ (4 equiv), diethyl ether, 12 h at 20 °C, 48 %; g) (from **5**) LiBH$_4$ (40 equiv), diethyl ether, 7 d at 20 °C, 45 %.

In order to probe the mechanistic steps leading to benzylic borylation in **3**, the stepwise reactions of **1** with [{Ir(coe)$_2$Cl}$_2$] and LiBH$_4$ have been investigated (Scheme 2). Thus, the interaction of **1** with [{Ir(coe)$_2$Cl}$_2$] in THF under a dinitrogen atmosphere proceeds sequentially to the formation of the planar tetra-coordinate Ir^{I} complexes [Ir(IMes)(N$_2$)(η^2-coe)Cl] (**4a**) and [Ir(IMes)$_2$(η^2-coe)Cl] (**4b**), respectively (see Supporting Information for details of both compounds). The structure of **4a** is characterized by a *trans* disposition of IMes and coe ligands, while in **4b** the IMes and coe ligands are *cis*, presumably to accommodate the bulky IMes ligands in a mutually *trans* arrangement. Prolonged reaction in THF leads to loss of the remaining coe ligand and the formation of the Ir^{III} complex [Ir(IMes)(IMes′)HCl] (**5**). Complex **5** features the chelating NHC/benzyl IMes′ ligand, formed by oxidative addition of one of the C–H bonds of a mesityl *ortho*-methyl substituent.[8,14] As such, a mechanism for borylation through initial C–H oxidative addition is plausible. The resulting Ir–H linkage is characterized by a ^{1}H NMR resonance at δ_H −33.14 ppm; methyl activation is also signaled by a significantly more complex pattern of signals in the aliphatic region, and the heavy atom skeleton of **5** was subsequently confirmed crystallographically. Although the location of the hydride ligand could not be determined reliably, further evidence for the identity of **5** was obtained from a trapping reaction with PMe$_3$ which yields [Ir(IMes)(IMes′)HCl(PMe$_3$)] (**6**). Complex **6** features *trans* bis(NHC) and benzyl/chloride ligand pairs within a pseudo-octahedral complex. Moreover the PMe$_3$ ligand gives rise to a doublet in the ^{31}P NMR spectrum, with a coupling constant ($^2J_{PH} = 185$ Hz) characteristic of mutually *trans* hydride and phosphine ligands.[15]

The reaction of **5** with LiBH$_4$ (40 equiv) in diethyl ether leads to the formation of the bis(hydrido)Ir^{III} benzyltrihydroborate complex **8**. ^{1}H and ^{11}B NMR measurements are consistent with the proposed structure. The former reveals five high-field signals at 20 °C [at δ_H −19.60, −18.25, −7.14, −6.74, and −0.42 ppm (all 1 H)] assigned to the two IrH, two IrHB, and one BH protons, respectively. The ^{11}B spectrum shows a broad resonance at δ_B −38.7 ppm, consistent the formation of an [RBH$_3$]$^-$ system (cf. −27.4 ppm for **3**).[13] With due allowance for the lower symmetry, the chemical shifts of the four highest field ^{1}H NMR resonances are strongly reminiscent of those found for related Ir^{III} complexes featuring η^2-coordinated (charge neutral) aminoboranes {for example, δ_H −15.50 (2 H, IrH), −5.83 ppm (2 H, IrHB) for [Ir(IMes)$_2$(H)$_2$(η^2-H$_2$B·N*i*Pr$_2$)]$^+$} and the solid-state structure of **8** (Figure 2) features a similar Ir···B distance for the η^2-bound benzyltrihydroborate ligand to related amineborane complexes [2.253(7) Å vs., for example, 2.230(2) Å for [Ir(IMes)$_2$(H)$_2$(η^2-H$_3$B·NMe$_3$)]$^+$).[9b,16] In the case of **8**, the borylated product can be liberated from the metal coordination sphere by the use of excess LiBH$_4$ and extended reaction times, thereby generating the bis(BH$_3$) system **3**; the second equivalent of borane presumably offers a potent alternative Lewis acid center for NHC coordination [cf. Ir^{III}].

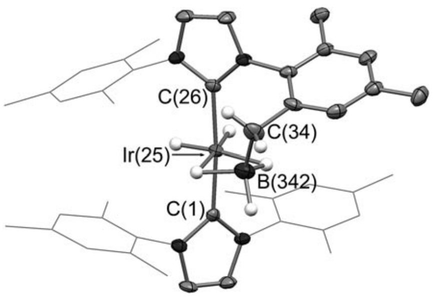


Figure 2. Molecular structure of **8**. Hydrogen atoms [except those attached to Ir(25), C(34) and B(342)] omitted and unactivated mesityl groups shown in wireframe format for clarity; thermal ellipsoids set at the 40 % probability level. Key distances [Å] and angle [°]: Ir(25)···B(342) 2.253(7), C(34)–B(342) 1.679(10); C(1)-Ir(25)-C(26) 174.7(2).

Of interest mechanistically is the route for the formation of **8** from **5**. One possibility is initial salt metathesis to yield the borohydride complex **7**, followed by an intramolecular migration of the tethered benzyl function from iridium to boron. Precedent for a structural motif akin to **7** comes from the crystallographically characterized complex [Ir(IMes)(IMes′)(H)(η^2-H$_2$BNCy$_2$)]$^+$, which features the neutral aminoborane H$_2$BNCy$_2$ η^2-ligated to the same [Ir(IMes)(IMes′)(H)]$^+$ fragment.[9b] That said, the anionic BH$_4^-$ ligand is known to be more strongly reducing than neutral aminoboranes, and given the paucity of mononuclear Ir^{III}

borohydride derivatives in the chemical literature,[17,18] we sought to independently verify the viability of a system of the type [Ir(IMes)$_2$(H)(X)(η^2-BH$_4$)]. To this end we have been successful in synthesizing [Ir(IMes)$_2$(H)$_2$(η^2-BH$_4$)] (**9**) by reaction of **4b** with the more soluble borohydride source [nBu$_4$N][BH$_4$] in diethyl ether. Crystallographic and spectroscopic studies of this complex (Figure 3) are consistent with *trans*-Ir(IMes)$_2$, *cis*-Ir(H)(X) and Ir(η^2-BH$_4$) motifs analogous to those proposed for **7**. Moreover, the alkyl migration step converting the proposed intermediate **7** into **8** finds precedent among d^6 5d metal complexes in the recent work of Vedernikov and co-workers, who report methyl and phenyl group migration between hexa-coordinate Pt^{IV} and tetra-coordinate boron centers.[19] Related migration of alkyl substituents from f-block metals to boron to give alkyltrihydroborates has also been reported:[20]

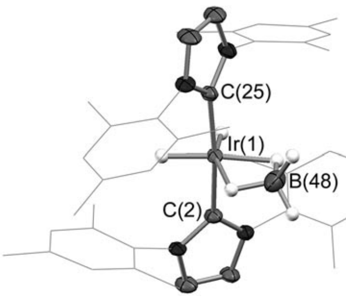


Figure 3. Molecular structure of **9**. Hydrogen atoms [except those attached to Ir(1) and B(48)] omitted and unactivated mesityl groups shown in wireframe format for clarity; thermal ellipsoids set at the 40% probability level. Key distance [Å] and angle [°]: Ir(1)···B(48) 2.248(5); C(2)-Ir(1)-C(25) 173.0(2).

In summary, we report an intramolecular benzylic borylation occurring at the *ortho*-methyl substituent of an ancillary NHC ligand. While selective C–H borylation chemistry is becoming a more widely exploited synthetic method, the current example is intriguing in exploiting simple (and inexpensive) LiBH$_4$ as the boron source. Mechanistically, this chemistry appears to proceed through C–H oxidative addition and subsequent Ir-to-B benzyl migration steps. Further studies aimed at accessing related chemistry for non-tethered substrates [for example, by partnering borohydride sources with Ir^{I} systems capable of intermolecular C–H activation] are currently being investigated and will be reported in due course.

Experimental Section

Included here are crystallographic data for compounds **3**, **8**, and **9**. Synthetic and characterizing data for all new compounds and crystallographic data for **4a**, **4b**, **5**, and **6** are included in the Supporting Information.

Crystallographic data (for **3**·C$_6$H$_5$F): C$_{48}$H$_{63}$B$_4$FLi$_2$N$_4$, M_r 772.18, tetragonal, $P4_12_12$, $a = 17.3197(2)$, $c = 16.1346(2)$ Å, $V = 4839.9(1)$ Å^3, $Z = 4$, $\rho_c = 1.060$ Mg m^{-3}, $T = 150$ K, $\lambda = 0.71073$ Å. 65879 reflections collected, 3156 independent [R(int) = 0.032], which were used in all calculations. $R_1 = 0.0643$, $wR_2 = 0.1128$ for observed unique reflections [$F^2 > 2\sigma(F^2)$] and $R_1 = 0.0422$, $wR_2 = 0.1071$ for all unique reflections. Max./min. residual electron densities: 0.18/−0.25 e Å^{-3}.

Crystallographic data (for **8**): C$_{42}$H$_{51}$BIrN$_4$, M_r 814.92, triclinic, $P\bar{1}$, $a = 11.0741(2)$, $b = 11.4654(3)$, $c = 16.8691(5)$ Å, $\alpha = 94.860(1)$, $\beta = 93.489(1)$, $\gamma = 117.875(1)°$, $V = 1874.2(1)$ Å^3, $Z = 2$, $\rho_c = 1.444$ Mg m^{-3}, $T = 150$ K, $\lambda = 0.71073$ Å. 26047 reflections collected, 8430 independent [R(int) = 0.044], which were used in all calculations. $R_1 = 0.0408$, $wR_2 = 0.1824$ for observed unique reflections [$F^2 > 2\sigma(F^2)$] and $R_1 = 0.0681$, $wR_2 = 0.1824$ for all unique reflections. Max./min. residual electron densities: 1.02/−0.96 e Å^{-3}.

Crystallographic data (for **9**): C$_{42}$H$_{54}$BIrN$_4$, M_r 817.91, monoclinic, $P2_1/n$, $a = 12.6789(1)$, $b = 11.1796(1)$, $c = 28.2664(3)$ Å, $\beta = 96.567(1)°$, $V = 3980.3(1)$ Å^3, $Z = 4$, $\rho_c = 1.365$ Mg m^{-3}, $T = 150$ K, $\lambda = 0.71073$ Å. 51436 reflections collected, 9057 independent [R(int) = 0.031], which were used in all calculations. $R_1 = 0.0334$, $wR_2 = 0.0628$ for observed unique reflections [$F^2 > 2\sigma(F^2)$] and $R_1 = 0.0482$, $wR_2 = 0.0707$ for all unique reflections. Max./min. residual electron densities: 1.77/−1.39 e Å^{-3}.

Further details on the crystal structure investigations may be obtained from the Fachinformationszentrum Karlsruhe (e-mail: crysdata@fiz-karlsruhe.de), on quoting the depository numbers CSD 795296 (**3**), 795300 (**8**), and 805002 (**9**).

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Keywords: boron · borylation · C–H activation · iridium · N-heterocyclic ligands

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