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

Christina Y. Tang, William Smith, Amber L. Thompson, Dragoslav Vidovic, and Simon Aldridge*

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, indenvl; 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 B₂pin₂ as the boron reagent of choice (pin = pinacolato, OCMe₂CMe₂O), with Ir^{III}-tris(Bpin) complexes thought to be key catalytic intermediates.^[5] C-B bond formation proceeds through either M-B/C-H o 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)₂Cl}₂] (coe = cyclooctene) which leads to the transfer of a BH₃ fragment from LiBH₄ 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 LiBH₄ in diethyl ether generates the known compound IMes⁻BH₃ (**2**) in 75% yield.^[12] By contrast, the reaction of **1** with [{Ir(coe)₂Cl}₂] (0.25 equiv of dimer)/excess LiBH₄, 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 [ArCH₂BH₃]⁻ function (Scheme 1).

 [*] Dr. C. Y. Tang, W. Smith, Dr. A. L. Thompson, Dr. D. Vidovic, Dr. S. Aldridge
Inorganic Chemistry Laboratory, Department of Chemistry
University of Oxford, South Parks Road, Oxford, OX1 3QR (UK)
Fax: (+44) 1865-272-690
E-mail: simon.aldridge@chem.ox.ac.uk
Homepage: http://users.ox.ac.uk/~quee1989/

- [**] We thank the EPSRC for funding and for access to the National Mass Spectrometry facility, Swansea University.
 - Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201006320.



Scheme 1. Syntheses of **2** and **3** through borane complexation with or without additional C-H activation. Key reagents and conditions: a) LiBH₄ (10 equiv), diethyl ether, 20 °C, 6 h, 75 %; b) [{Ir(coe)₂Cl}₂] (0.25 equiv), THF, then LiBH₄ (40 equiv), diethyl ether, 7 d, 42 %.

The formation of **3** is suggested by ¹¹B NMR spectroscopy which reveals two quartet resonances (at $\delta_{\rm B}$ -35.1, ${}^{1}J_{\rm BH}$ = 81 Hz and -27.4 ppm, ${}^{1}J_{BH} = 78$ Hz), the former being similar to that reported for 2 ($\delta_{\rm B}$ -36.8 ppm, ${}^{1}J_{\rm BH}$ = 88 Hz),^[12b] the latter consistent with other examples of [RBH₃]⁻ species [e.g. $\delta_{\rm B} - 26.8 \text{ ppm}, {}^{1}J_{\rm BH} = 79 \text{ Hz for } (2\text{-naphthyl})\text{BH}_{3}^{-1}.$ ^[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 BH₃ and [ArCH₂BH₃]⁻ units of one $[(IMes'BH_3)BH_3]^-$ moiety, and the other two in the [ArCH₂BH₃]⁻ 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 $3 \cdot C_6 H_5 F$. 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).

Angew. Chem. Int. Ed. 2011, 50, 1359-1362

Communications

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

In order to probe the mechanistic steps leading to benzylic borylation in **3**, the stepwise reactions of **1** with $[{Ir(coe)_2Cl}_2]$ and LiBH₄ have been investigated (Scheme 2). Thus, the



Scheme 2. Iridium-mediated conversion of 1 to 3. Key reagents and conditions: a) [{ $Ir(coe)_2CI$ }_2] (0.47 equiv of dimer), THF, 7 d at 20°C, 45%; b) (from 1) [{ $Ir(coe)_2CI$ }_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) [{ $Ir(coe)_2CI$ }_2] (0.25 equiv of dimer), THF, 60 h at 20°C, 68%; d) PMe₃ (excess), toluene, 1 h at 20°C, 61%; e, f) (from 5) LiBH₄ (4 equiv), diethyl ether, 12 h at 20°C, 45%.

interaction of 1 with [{Ir(coe)₂Cl}₂] in THF under a dinitrogen atmosphere proceeds sequentially to the formation of the planar tetra-coordinate Ir^{I} complexes $[Ir(IMes)(N_2)(\eta^2$ 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 ¹H NMR resonance at $\delta_{\rm H}$ -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 PMe₃ which yields [Ir(IMes)(IMes')HCl(PMe₃)] (6). Complex **6** features *trans* bis(NHC) and benzyl/chloride ligand pairs within a pseudo-octahedral complex. Moreover the PMe₃ ligand gives rise to a doublet in the ³¹P NMR spectrum, with a coupling constant (${}^{2}J_{PH} = 185$ 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. ¹H and ¹¹B NMR measurements are consistent with the proposed structure. The former reveals five high-field signals at 20 °C [at $\delta_{\rm H}$ –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 ¹¹B spectrum shows a broad resonance at $\delta_{\rm B}$ –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 ¹H NMR resonances are strongly reminiscent of those found for related IrIII complexes featuring η^2 -coordinated (charge neutral) aminoboranes {for example, $\delta_{\rm H}$ –15.50 (2H, IrH), –5.83 ppm (2H, IrHB) for [Ir- $(IMes)_2(H)_2(\eta^2-H_2BNiPr_2)]^+$ and the solid-state structure of 8 (Figure 2) features a similar Ir⁻⁻B distance for the η^2 -bound



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).

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 -H₃B·NMe₃)]⁺).^[9b,16] In the case of **8**, the borylated product can be liberated from the metal coordination sphere by the use of excess LiBH₄ and extended reaction times, thereby generating the bis(BH₃) system **3**; the second equivalent of borane presumably offers a potent alternative Lewis acid center for NHC coordination [cf. Ir^{III}].

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 -H₂BNCy₂)]⁺, which features the neutral aminoborane H₂BNCy₂ η^2 -ligated to the same [Ir(IMes)-(IMes')(H)]⁺ fragment.^[9b] That said, the anionic BH₄⁻ 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 $[Ir(IMes)_2(H)(X)(\eta^2-BH_4)]$. To this end we have been successful in synthesizing $[Ir(IMes)_2(H)_2(\eta^2-BH_4)]$ (9) by reaction of **4b** with the more soluble borohydride source $[nBu_4N][BH_4]$ in diethyl ether. Crystallographic and spectroscopic studies of this complex (Figure 3) are consistent with



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).

trans-Ir(IMes)₂, *cis*-Ir(H)(X) and Ir(η^2 -BH₄) motifs analogous to those proposed for **7**. Moreover, the alkyl migration step converting the proposed intermediate **7** into **8** finds precedent among d⁶ 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 tetracoordinate boron centers.^[19] Related migration of alkyl substituents from f-block metals to boron to give alkyltrihydroborates has also been reported.^[20]

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) LiBH₄ 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** C₆H₅F): C₄₈H₆₃B₄FLi₂N₄, *M*_r 772.18, tetragonal, *P*4₁2₁2, *a* = 17.3197(2), *c* = 16.1346(2) Å, *V* = 4839.9(1) Å³, *Z* = 4, ρ_c = 1.060 Mg m⁻³, *T* = 150 K, λ = 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 reflec-

tions $[F^2 > 2\sigma(F^2)]$ and $R_1 = 0.0422$, $wR_2 = 0.1071$ for all unique reflections. Max./min. residual electron densities: $0.18/-0.25 \text{ e} \text{ Å}^{-3}$.

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, a=94.860(1), $\beta=93.489(1)$, $\gamma=117.875(1)^\circ$, V=1874.2(1) Å³, 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, $\beta = 96.567(1)^\circ$, V = 3980.3(1) Å³, Z = 4, $\rho_c = 1.365 \text{ Mg m}^{-3}$, 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).

Received: October 8, 2010 Published online: December 29, 2010

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

- For a comprehensive recent review of C-H borylation chemistry, see: I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* 2010, *110*, 890-931.
- [2] See, for example: Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine (Ed.: D. G. Hall), Wiley-VCH, Weinheim, 2005.
- [3] a) J.-Y. Cho, M. K. Tse, D. Holmes, R. E. Maleczka, Jr., M. R. Smith III, *Science* 2002, 295, 305-308; b) T. Ishiyama, J. Takagi, K. Ishida, N. Miyaura, N. R. Anastasi, J. F. Hartwig, *J. Am. Chem. Soc.* 2002, 124, 390-391.
- [4] For representative examples, see: a) R. E. Maleczka, Jr., F. Shi, D. Holmes, M. R. Smith III, J. Am. Chem. Soc. 2003, 125, 7792– 7793; b) D. N. Coventry, A. S. Batsanov, A. E. Goeta, J. A. K. Howard, T. B. Marder, R. N. Perutz, Chem. Commun. 2005, 2172–2174; c) J. M. Murphy, X. Liao, J. F. Hartwig, J. Am. Chem. Soc. 2007, 129, 15434–15435; d) C. C. Tzschucke, J. M. Murphy, J. F. Hartwig, Org. Lett. 2007, 9, 761–764.
- [5] For relevant iridium-tris(Bpin) and related complexes see reference [3b] and: a) P. Nguyen, H. P. Blom, S. A. Westcott, N. J. Taylor, T. B. Marder, J. Am. Chem. Soc. 1993, 115, 9329– 9330; b) T. M. Boller, J. M. Murphy, M. Hapke, T. Ishiyama, N. Miyaura, J. F. Hartwig, J. Am. Chem. Soc. 2005, 127, 14263– 14278; c) C. W. Liskey, C. S. Wei, D. R. Pahls, J. F. Hartwig, Chem. Commun. 2009, 5603–5605; d) G. A. Chotana, B. A. Vanchura II, M. K. Tse, R. J. Staples, R. E. Maleczka, Jr., M. R. Smith III, Chem. Commun. 2009, 5731–5733.
- [6] H. Tamura, H. Yamazaki, H. Sato, S. Sakaki, J. Am. Chem. Soc. 2003, 125, 16114–16126.
- [7] a) S. Shimada, A. S. Batsanov, J. A. K. Howard, T. B. Marder, *Angew. Chem.* 2001, 113, 2226–2229; *Angew. Chem. Int. Ed.* 2001, 40, 2168–2171; b) W. H. Lam, K. C. Lam, Z. Lin, S. Shimada, R. N. Perutz, T. B. Marder, *Dalton Trans.* 2004, 1556– 1562.
- [8] C. Y. Tang, W. Smith, D. Vidovic, A. L. Thompson, A. B. Chaplin, S. Aldridge, *Organometallics* 2009, 28, 3059–3066.
- [9] a) C. Y. Tang, A. L. Thompson, S. Aldridge, Angew. Chem. 2010, 122, 933–937; Angew. Chem. Int. Ed. 2010, 49, 921–925; Angew.

Communications

Chem. **2010**, *122*, 933–937; b) C. Y. Tang, A. L. Thompson, S. Aldridge, J. Am. Chem. Soc. **2010**, *132*, 10578–10591.

- [10] For previous reports of benzylic C–H borylation see reference [7] and: a) J.-Y. Cho, C. N. Iverson, M. R. Smith III, *J. Am. Chem. Soc.* 2000, 122, 12868–12869; b) T. Ishiyama, K. Ishida, J. Takagi, N. Miyaura, *Chem. Lett.* 2001, 30, 1082–1083.
- [11] For a report of arene borylation using HBpin and [(NHC)₂M-(cod)]⁺ complexes (M = Rh or Ir) see: G. D. Frey, C. F. Rentzsch, D. von Preysing, T. Scherg, M. Mühlhofer, E. Herdtweck, W. A. Herrmann, J. Organomet. Chem. 2006, 691, 5725 5738.
- [12] IMes·BH₃ has previously been prepared from BH₃ thf or BH₃ SMe₂. Synthesis and crystal structure: a) T. Ramnial, H. Jong, I. D. McKenzie, M. Jennings, J. A. C. Clyburne, *Chem. Commun.* **2003**, 1722–1723; ¹¹B NMR data: b) Y. Yamaguchi, T. Kashiwabara, K. Ogata, Y. Miura, Y. Nakamura, K. Kobayashi, T. Ito, *Chem. Commun.* **2004**, 2160–2161.
- [13] ¹¹B resonances at -27 and -36 ppm have been reported for (2-naphthyl)BH₃⁻ and (C₆F₅)BH₃⁻, respectively: a) M. R. Biscoe, R. Breslow, J. Am. Chem. Soc. 2003, 125, 12718-12719; ¹¹B signals in the range + 2 to -7 ppm have been reported for η²-bound PhBH₃⁻ ligands: b) F.-C. Liu, J.-H. Chen, S.-C. Chen, K.-Y. Chen, G.-H. Lee, S.-M. Peng, J. Organomet. Chem. 2005, 690, 291-300.
- [14] The analogous rhodium complex [Rh(IMes)(IMes')HCl] has previously been reported by Nolan and co-workers under similar conditions: a) J. Huang, E. D. Stevens, S. P. Nolan, Organo-

metallics **2000**, *19*, 1194–1197. For related IMes C–H activation chemistry, see: b) R. F. R. Jazzar, S. A. Macgregor, M. F. Mahon, S. P. Richards, M. K. Whittlesey, *J. Am. Chem. Soc.* **2002**, *124*, 4944–4945; c) O. Torres, M. Martín, E. Sola, *Organometallics* **2009**, *28*, 863–870.

- [15] By means of comparison, a *trans* ²J_{PH} coupling constant of 153.5 Hz has been reported for *mer*-[Ir(PMe₃)₃H(2-py)Cl]: H. E. Selnau, J. S. Merola, *Organometallics* **1993**, *12*, 1583–1591.
- [16] One other example of an η²-benzyltrihydroborate complex has been structurally characterized: S. Nlate, P. Guenot, S. Sinbandhit, L. Toupet, C. Lapinte, V. Guerchais, *Angew. Chem.* **1994**, *106*, 2294–2296; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2218– 2219.
- [17] The sole example of a structurally characterized Ir^{III} borohydride complex reported to date, features a dinuclear Ir(μ:η¹,η¹-BH₄)Ir unit: T. M. Gilbert, F. J. Hollander, R. G. Bergman, J. Am. Chem. Soc. **1985**, 107, 3508–3516.
- [18] A number of systems of the type [Ir(PR₃)₂(H)₂(BH₄)] have been reported in conjunction with bulky phosphines and their thermal decomposition pathways analyzed, although no structural data are available: a) H. D. Empsall, E. Mentzer, B. L. Shaw, *J. Chem. Soc. Chem. Commun.* **1975**, 861–862; b) T. J. Marks, J. R. Kolb, *Chem. Rev.* **1976**, 76, 263–293.
- [19] E. Khaskin, P. Y. Zavalij, A. N. Vedernikov, J. Am. Chem. Soc. 2008, 130, 10088-10089.
- [20] G. Rossetto, M. Porchia, F. Ossola, P. Zanella, R. D. Fischer, J. Chem. Soc. Chem. Commun. 1985, 1460-1461.