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Iridium-catalysed regioselective borylation of carboranes via direct B-H activation

Ruofei Cheng¹, Zaozao Qiu¹ & Zuowei Xie^{1,2}

Carboranes are carbon-boron molecular clusters, which can be viewed as three-dimensional analogues to benzene. They are finding many applications in medicine, materials and organometallic chemistry. On the other hand, their exceptional thermal and chemical stabilities, as well as 3D structures, make them very difficult to be functionalized, in particular the regioselective functionalization of BH vertex among ten similar B-H bonds. Here we report a very efficient iridium-catalysed borylation of cage B(3,6)-H bonds of *o*-carboranes with excellent yields and regioselectivity using bis(pinacolato)diboron (B₂pin₂) as a reagent. Selective cage B(4)-H borylation has also been achieved by introducing a bulky TBDMS (*tert*-butyldimethylsilyl) group to one cage carbon vertex. The resultant 3,6-(Bpin)₂-*o*-carboranes are useful synthons for the synthesis of a wide variety of B(3,6)-difunctionalized *o*-carboranes bearing cage B-X (X = O, N, C, I and Br) bonds.

¹Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China. ²Department of Chemistry and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. Correspondence and requests for materials should be addressed to Z.Q. (email: qiuzz@sioc.ac.cn).

icosahedral carboranes are carbon–boron molecular clusters, sharing many features with benzene such as aromaticity, high thermal and chemical stability^{1,2}. On the other hand, carboranes have their own unique characteristics such as spherical geometry and hydrophobic molecular surface^{1,2}, which make them attractive building blocks for boron neutron capture therapy agents in medicine^{3–6}, functional units in supramolecular design/materials^{7–17} and versatile ligands in coordination/organometallic chemistry^{18–23}. These research activities have drawn growing interests in the selective functionalization of carboranes^{1,2,24–26}.

Classic routes to functionalized carboranes rely on the polarized cage C–H/B–H bonds: the weakly acidic C–H proton (pK_a ~23) and basic B–H hydride¹. Accordingly, cage C–H bonds can be deprotonated by strong bases, followed by reactions with electrophiles to give carbon-substituted carboranes^{1,2}, and cage B–H bonds are subjected to electrophilic substitution reactions, leading to the formation of cage boron-substituted carborane derivatives with the reaction rate B(9,12)–H > B(8,10)–H > B(4,5,7,11)–H (refs 1,27). However, the B(3,6)-disubstituted *o*-carboranes cannot be prepared by electrophilic substitution reactions. They are generally achieved via multistep reaction of deboration–capping–deboration–capping (Fig. 1)^{1,28,29}.

Very recently, we have developed –COOH guided transition metal-catalysed regioselective B(4)-alkenylation³⁰, -alkynylation³¹, -amination³² and -hydroxylation³³, as well as B(4,5)-dialkylation³⁴ and -diarylation³⁵ of *o*-carboranes. In contrast, transition metal-catalysed B(3,6)-difunctionalization of *o*-carboranes is much less studied^{36,37}, although transition metal promoted B(3)–H activation in *o*-carboranes has been well documented^{38–44}.

Encouraged by transition metal-catalysed C–H borylation and application of the resultant boronate esters/boronic acids in C–C/C–O/C–N/C–halogen bond forming process^{45–47}, we initiated a research program to study transition metal-catalysed direct cage B–H borylation of *o*-carboranes and the results are reported in this study (Fig. 1).

Results

B(3,6)-diborylation of *o*-carboranes. The optimization of reaction conditions for the following reactions was summarized in Supplementary Tables 1 and 2. The initial reaction of

o-carborane (**1a**) with B₂pin₂ ([B(OCMe₂CMe₂O)]₂) in the presence of 3.5 mol% [(cod)IrCl]₂ (cod = 1,5-cyclooctadiene) in tetrahydrofuran (THF) gave 3-Bpin-1,2-C₂B₁₀H₁₁ (**2a**) in 60% gas chromatography (GC) yield. It was later found that the ligands played an important role in the reaction^{48,49}. Addition of 0.21 equiv. of pyridine (Py) significantly increased the reaction efficiency, leading to the formation of **2a** and 3,6-(Bpin)₂-1,2-C₂B₁₀H₁₀ (**3a**) in 23% and 67% GC yields, respectively. Replacement of Py by 2-Me- and 4-Me-Py resulted in 98% and 95% GC yields of **3a**. Increasing the steric hindrance of Py derivatives led to much lower yields of **3a**. It was noted that bipyridine ligands commonly used in C–H borylation led to the formation of inseparable geometrical isomers of mono-, di- and tri-borylated products (see Supplementary Table 2). Other Ir(I) complexes such as [(cod)Ir(OMe)]₂, (cod)Ir(acac), (cod)₂IrBF₄ and (cod)₂IrB[3,5-(CF₃)₂C₆H₃]₄ also worked well, giving very good to excellent yields of **3a**, whereas the Ir(III) complexes such as [Cp*IrCl₂]₂ and IrCl₃, as well as [(cod)RhCl]₂ and Pd(OAc)₂ showed poor or no catalytic activity. On the other hand, HBpin did not give any borylation product. Extensive screening of solvents, catalyst loadings, reaction temperatures and molar ratios of ligand/B₂pin₂ led to the optimal reaction conditions shown entry 6 of Supplementary Table 1.

The substrate scope was then examined under the optimized reaction conditions and the results were compiled in Table 1. The borylation efficiency was generally very high regardless of the nature of substituents on cage B(9,12) of *o*-carboranes (**3a–3m**). It was noted that the double bond in 9-vinyl-*o*-carborane (**1k**) underwent hydroboration with HBpin, a byproduct of B–H borylation (vide infra), to afford **3k** in 91% isolated yield with excellent regioselectivity, probably owing to steric effect of *o*-carboranyl moiety. The B(3,6)-diborylation efficiency of 4-*I*-*o*-C₂B₁₀H₁₁ (**1n**) was lower than other substrates likely to be due to steric effect of vicinal iodo group. In fact, both the mono- and diborylation products **2n** and **3n** were observed by GC–mass spectrometry with a molar ratio of 25:75. The bulkier substituents at the B(4) position such as 4-Ph and 4-(Ph)CH = (Ph)C or at B(4,7) positions such as 4,7-*I*₂ can block the B(3)-borylation, giving **2o**, **2p** and **2q** in 76–89% isolated yields, respectively. For 3-Ph-*o*-C₂B₁₀H₁₁, the expected monoborylation product **2r** was isolated in 89% yield. It was noteworthy that substituents on cage C had a significant impact on the borylation

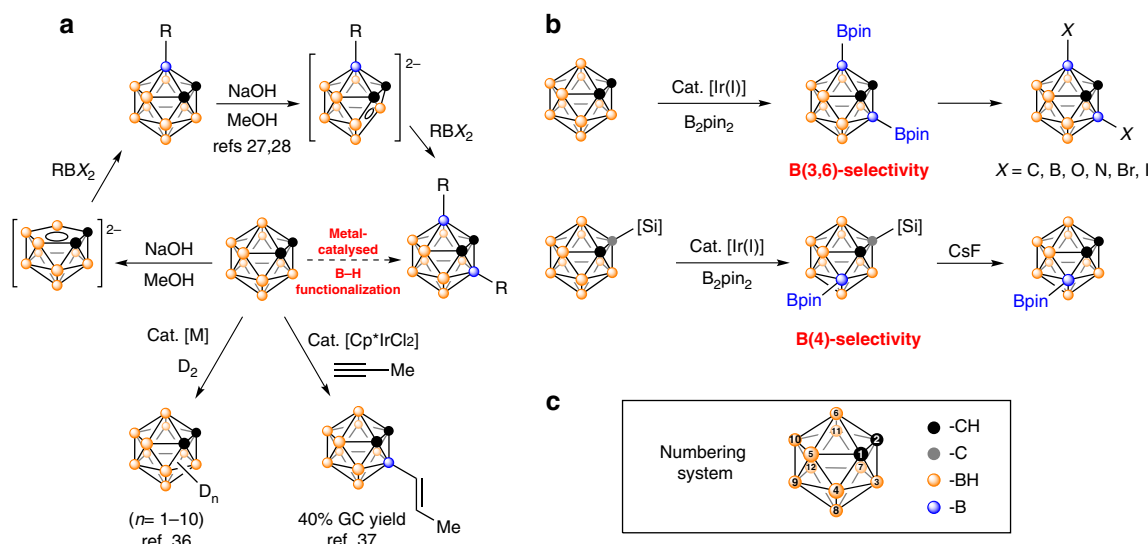
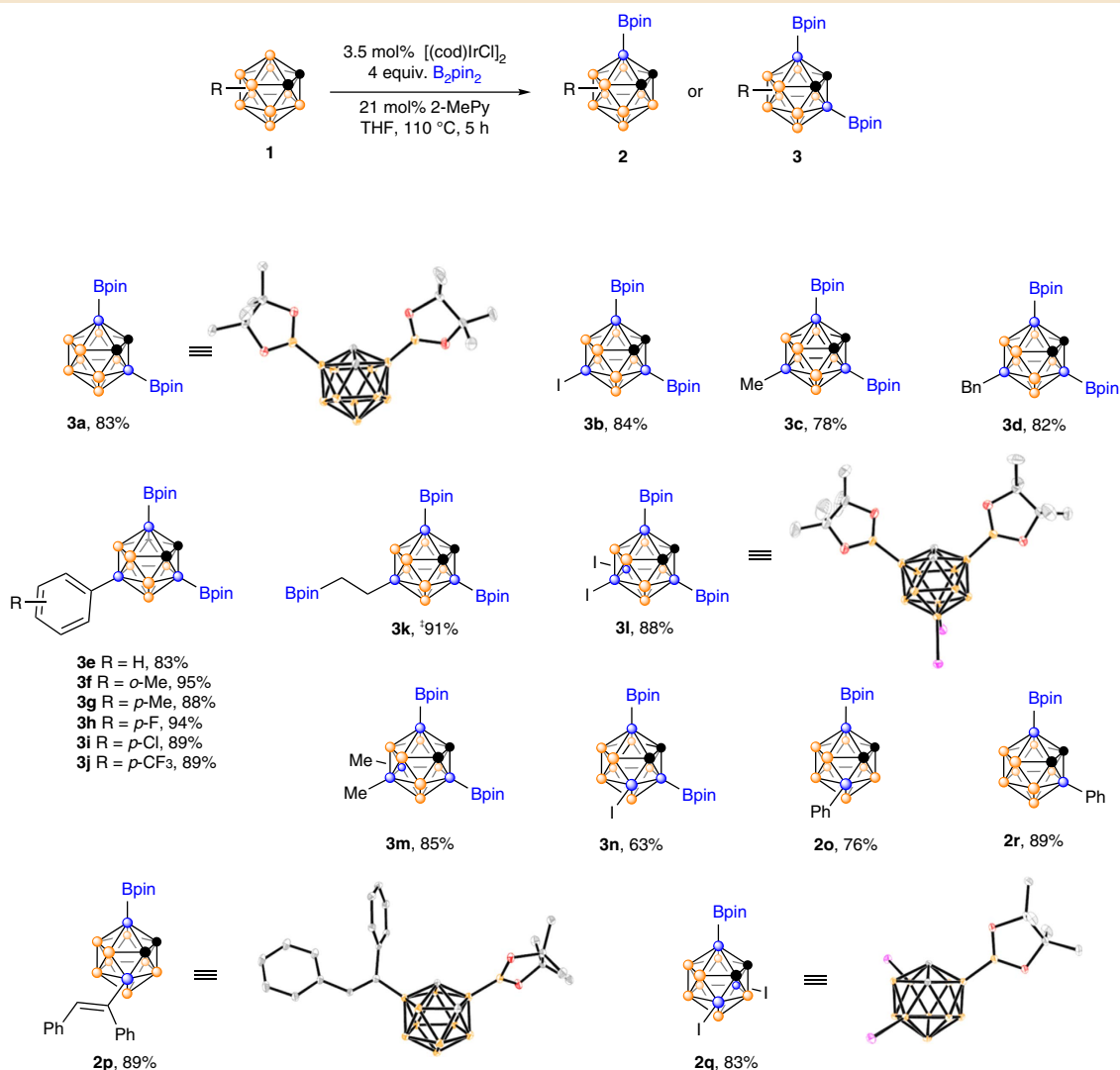


Figure 1 | Functionalization of B(3,6)-H bonds in *o*-carboranes (Bpin = B(OCMe₂CMe₂O), B₂pin₂ = pinB-Bpin). (a) Known methods for B(3) and B(3,6) functionalization. (b) This work: Iridium-catalysed regioselective borylation of carboranes via direct B–H activation. (c) Numbering system of *o*-carborane.

Table 1 | Substrate scope for selective cage B–H borylation of *o*-carboranes^{*,†}.

*Reactions were conducted on 0.5 mmol scale in a closed flask at 110 °C (bath temperature) for 5 h.

†Isolated yields.

‡9-Vinyl-*o*-carborane (**1k**) was used as a starting material.

reaction. For example, 1-Me-*o*-C₂B₁₀H₁₁ gave an inseparable mixture of geometrical isomers and no borylation with 1,2-Me₂-*o*-C₂B₁₀H₁₀ was observed.

We also examined the gram-scale borylation reaction. Under the optimal reaction conditions, treatment of **1a** (1.44 g, 10 mmol) with B₂pin₂ (10.16 g, 40 mmol) in THF (50 ml) afforded 3.75 g of **3a** (95% isolated yield).

In a similar manner, reaction of *m*-C₂B₁₀H₁₂ (**4**) with 1.5 equiv. of B₂pin₂ in the presence of 3.5 mol% [(cod)IrCl]₂ and 21 mol% 2-methylpyridine (2-MePy) in THF at 80 °C for 5 h gave 2-Bpin-*m*-carborane (**5**) in 74% isolated yield (see Supplementary Table 3 and Supplementary Fig. 6). On the other hand, under the same reaction conditions, *p*-carborane afforded an inseparable mixture of mono-, di- and triborylated products.

B(4)-borylation of *o*-carboranes. The aforementioned results clearly show that bulky substituents such as Ph (**2o** in Table 1) and C(Ph)=CH(Ph) (**2p** in Table 1) can completely block the borylation of *ortho*-BH vertices, suggesting the importance of steric factors. We wondered whether Ir-catalysed regioselective

cage B(4)-H borylation in *o*-carboranes could be achieved by introducing a bulky substituent at the cage C position. Accordingly, 1-trimethylsilyl-*o*-carborane was chosen as the model substrate for initial screening and the results were compiled in Supplementary Table 4. It was found that 2,2'-bipyridine (2,2'-bipy) derivatives were better ligands than monodentate Pys as the latters caused partial desilylation of 1-trimethylsilyl-*o*-carborane. The screening results indicated clearly that substrates with bulkier silyl groups can efficiently block the *ortho*-B–H activation, resulting in higher regioselectivity. If 2-TBDMS-*o*-carboranes **6** (TBDMS = *tert*-butyldimethylsilyl) were used as starting materials and 2,2'-bipy as the ligand, the desired product 4-Bpin-2-TBDMS-*o*-carboranes **7a–c** were isolated in 89–92% yields. Subsequently, the TBDMS group can be easily removed by caesium fluoride (CsF) under very mild condition to give the corresponding compound **8** in *ca.* 94% isolated yield (Fig. 2).

Transformation of **3a.** Although it has been well documented that Bpin can be replaced by a wide variety of functional groups^{45–47}, the chemical properties of cage B–Bpin bonds have

not been explored thus far. To illustrate the synthetic applications of B-borylated-*o*-carboranes, various transformations of **3** in an example of **3a** were studied and the results were outlined in Fig. 3. Suzuki–Miyaura cross-coupling of **3a** with PhBr in the presence of 20 mol% Pd(PPh₃)₄ and 3 equiv. of Cs₂CO₃ gave 3,6-diphenyl-*o*-carborane (**9**) in 81% isolated yield. Treatment of **3a** with CH₂=CHCH₂Cl in the presence of Pd(dba)₂ (dba, dibenzylideneacetone) at room temperature afforded **10** in 87% yield. Surprisingly, replacement of Cs₂CO₃ by ^tBuOK, reaction of **3a** with PhBr in the presence of Pd(PPh₃)₄ produced 3,6-Br₂-*o*-C₂B₁₀H₁₀ (**11a**) in 73% yield. Similarly, 3,6-I₂-*o*-C₂B₁₀H₁₀ (**11b**) was prepared in 78% isolated yield if PhI was used as coupling agent. It is not clear at this stage why ^tBuOK can alter the coupling partner in these cross-coupling reactions. The two Bpin moieties in **3a** were readily replaced by acetoxy groups using Cu(OAc)₂/KF in CH₃CN under 1 atm of O₂. 3,6-(NH₂)₂-*o*-

C₂B₁₀H₁₀ (**13**) was prepared in 90% isolated yield by treatment of **3a** with *in situ* generated MeONH⁻ in THF. Reaction of **3a** with TMSN₃ in the presence of KF and CuCl gave 3,6-(N₃)₂-*o*-C₂B₁₀H₁₀ (**14**) in 83% yield. Double click reaction of **14** with EtO₂CC≡CCO₂Et afforded 3,6-ditriazolyl-*o*-carborane (**15**) in 83% yield. In addition, carboranylboronic acid 3,6-[B(OH)₂]₂-*o*-C₂B₁₀H₁₀ (**16**) was also synthesized from **3a** in 85% isolated yield.

Compounds **2**, **3**, **5** and **7–16** were fully characterized by ¹H, ¹³C and ¹¹B nuclear magnetic resonance (NMR) spectroscopy, as well as elemental analyses. The molecular structures of **2a**, **2p**, **2q**, **3a**, **3l**, **5**, **7c**, **8a** and **15** were further confirmed by single-crystal X-ray analyses.

Mechanistic study. To shed some light on the reaction mechanism of the first Ir-catalysed regioselective cage B–H borylation, NMR reactions (Fig. 4) were carried out in *d*₈-THF, which were monitored by ¹H and ¹¹B NMR spectra (see Supplementary Figs 12–16 for detail). The following results were observed: (1) dissociation of [(cod)IrCl]₂ in the presence of 2-MePy generated a monomeric species (cod)IrCl(2-MePy) (**A**) (Fig. 4, eq. a). (2) B₂pin₂ underwent rapid oxidative addition reaction on Ir(I) species in the presence of 2-MePy to generate a Ir(III) species^{50,51} and release ClBpin that was trapped by THF to form ROBpin (see Supplementary Fig. 14)^{52,53}. However, no reaction was observed by treatment of [(cod)IrCl]₂ with **1a** or HBpin under the same reaction conditions (Fig. 4, eq. b and d). (3) Under the optimal reaction conditions, both **2a** and HBpin were observed by ¹H and ¹¹B NMR at the initial stage. As the reaction proceeded, **3a** gradually appeared at the expense of **2a**. These results suggested that the borylation proceeded stepwise (Fig. 4, eq. e). (4) The Ir(III) complex (η⁶-MesH)Ir(Bpin)₃ (ref. 54) was found to catalyse the diborylation of **1a** equally well as [(cod)IrCl]₂ did to give **3a** in 98% GC yield (Fig. 4, eq. f). (5) B(3,6)–H bonds were more reactive than B(4,5,7,11)–H ones in the above borylation, suggesting that the activation of cage B–H bond may proceed via oxidative addition pathway^{1,36–39,55–57}, instead of electrophilic substitution mechanism^{30–35} as the electron density in *o*-carborane follows the trend: B(3,6) < B(4,5,7,11) < B(8,10) < B(9,12)^{1,27}.

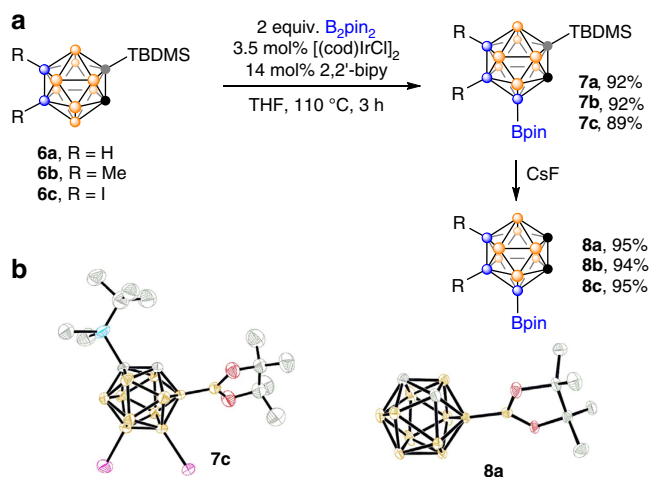


Figure 2 | Synthesis of 4-Bpin-*o*-carboranes. (a) Ir-catalysed regioselective B(4)–H borylation in *o*-carboranes by introducing a bulky substituent at the cage C position. (b) Molecular structures of **7c** and **8a**.

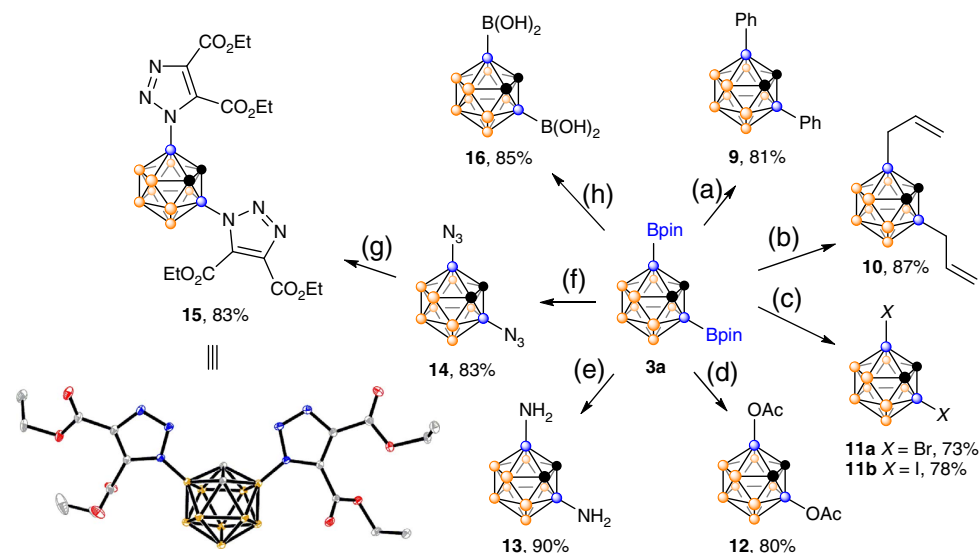


Figure 3 | Chemical transformations of **3a.** Reaction conditions: (a) PhBr (3 equiv.), Pd(PPh₃)₄ (20 mol%), Cs₂CO₃ (3 equiv.), cyclohexane, 150 °C (bath), 8 h. (b) Allyl chloride (6 equiv.), Pd(dba)₂ (20 mol%), Cs₂CO₃ (3 equiv.), toluene, room temperature, 24 h. (c) PhX (3 equiv.), Pd(PPh₃)₄ (10 mol%), ^tBuOK (3 equiv.), THF, 80 °C, 24 h. (d) Cu(OAc)₂ (6 equiv.), KF (6 equiv.), CH₃CN, 80 °C, 12 h, under 1 atm of O₂. (e) MeONHLi, THF, 80 °C, 8 h. (f) TMSN₃ (2.4 equiv.), CuCl (2.1 equiv.), KF (2.4 equiv.), THF, 60 °C, 24 h. (g) Diethyl acetylenedicarboxylate (2.4 equiv.), toluene, 95 °C. (h) 1) DEA (diethanolamine, 2.5 equiv.), Et₂O, room temperature, 18 h, 2) HCl aq. (0.5 M, excess).

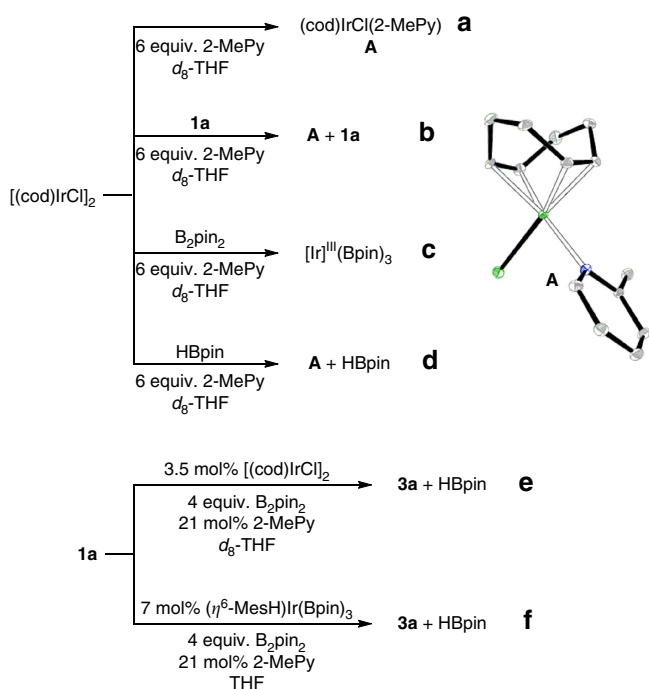


Figure 4 | Mechanistic investigations. Control experiments. (a) Stoichiometric reaction of $[(cod)IrCl]_2$ with 2-MePy. (b) Stoichiometric reaction of $[(cod)IrCl]_2$ with 2-MePy and *o*-carborane (**1a**). (c) Stoichiometric reaction of $[(cod)IrCl]_2$ with 2-MePy and B_2pin_2 . (d) Stoichiometric reaction of $[(cod)IrCl]_2$ with 2-MePy and HBpin. (e) Standard catalytic borylation reaction of **1a** monitored by 1H and ^{11}B NMR. (f) $(\eta^6-MesH)Ir(Bpin)_3$ catalysed borylation reaction of **1a**.

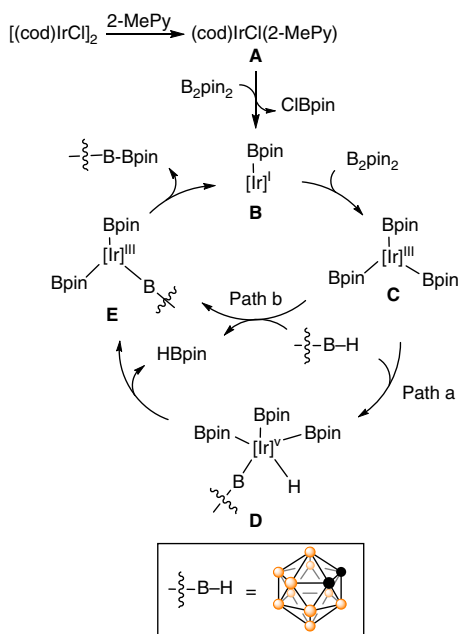


Figure 5 | Proposed reaction mechanism. The ligand on iridium has been omitted for clarity.

On the basis of the aforementioned experimental results and literature work^{30,36,45–57}, a proposed mechanism for the borylation reaction is shown in Fig. 5. Dissociation of $[(cod)IrCl]_2$ in the presence of 2-MePy ligand generates a monomeric active

species $(cod)IrCl(2-MePy)$ (**A**), which undergoes oxidative addition with B_2pin_2 , followed by reductive elimination to form Ir(I)-Bpin **B** and release ClBpin^{50,58,59}, entering the catalytic cycle. Oxidative addition of B_2pin_2 on **B** gives the Ir(III) intermediate **C**⁴⁸, followed by another oxidative addition of the most electron-deficient cage B(3)–H bond^{1,36,37} to afford **D** (path a). Reductive elimination yields the intermediate **E** and HBpin. Alternatively, electrophilic substitution of Ir(III) species in **C** on cage B–H yields the intermediate **E** and release one equivalent of HBpin (path b)³⁰. Reductive elimination generates cage boron-borylated product **2** (ref. 48). Compound **2** undergoes another catalytic borylation cycle to afford cage B(3,6)-diborylated product **3**. As the electron-deficient cage B(3,6)–H bonds preferentially undergo oxidative addition reaction with transition metal species over other more electron-rich cage B–H bonds^{1,36,37}, path a is believed to be more favourable over path b.

In summary, a very efficient and regioselective Ir-catalysed diborylation of cage B(3,6)–H bonds in carboranes has been developed. This serves as a new methodology for the regioselective generation of a series of B(3,6)-diborylated- or B(3)-borylated-*o*-carboranes. Selective B(4)-borylation of cage B(4)–H bond has also been achieved by introducing a TBDMS group to the cage carbon position. The resultant *B*-borylated carboranes can be conveniently converted to a variety of functionalized carboranes bearing cage B–X ($X = Br, I$), B–O, B–C(sp^2), B–C(sp^3), B–NH₂ and B–N₃ bonds that otherwise cannot be prepared by other known methods. This work opens up a new way for efficient and regioselective functionalization of carboranes, which may be extended to other boron cluster systems.

Methods

Preparation of B(3,6)-diborylated- or B(3)-borylated-*o*-carboranes (**3** or **2**).

An oven-dried Schlenk flask was charged with *o*-carborane (**1**) (0.5 mmol), B_2pin_2 (508 mg, 2.0 mmol), $[(cod)IrCl]_2$ (12 mg, 0.0175 mmol) and 2-MePy (10.3 mg, 0.105 mmol), followed by dry THF (5 ml). The flask was closed under an atmosphere of nitrogen and stirred at 110 °C (bath temperature) for 5 h. After hydrolysis with water (10 ml) and extraction with diethyl ether (10 ml \times 3), the ether solutions were combined and concentrated to dryness *in vacuo*. The residue was subjected to flash column chromatography on silica gel (230–400 mesh) using *n*-hexane and ethyl acetate (10/1 in v/v) as eluent to give a mixture of product and B_2pin_2 . Removal of B_2pin_2 via sublimation at 90 °C under vacuum (0.1 torr) gave a pure product **2o-r** or **3a-n**.

B(4)-borylated-carboranes (8**).** Compound **7** was prepared from 1-TBDMS-*o*-carboranes **6** (0.5 mmol), B_2pin_2 (254 mg, 1.0 mmol), $[(cod)IrCl]_2$ (12 mg, 0.0175 mmol) and 2,2'-bipy (22 mg, 0.07 mmol) in THF (5 ml) at 110 °C (bath temperature) for 3 h, using the same procedure reported for **3**. To a solution (2 ml) of **7** (0.3 mmol) (acetone for **7a** and **7b**; MeOH/DCM (2/1 in v/v) for **7c**) was added CsF (182 mg, 1.2 mmol). The mixture was stirred at room temperature (for 1 h for **7a** and **7b**, and 20 min for **7c**). After filtration and removal of the solvent under vacuo, the residue was subjected to flash column chromatography on silica gel (230–400 mesh) using *n*-hexane/Et₃N (5/1 in v/v) as eluent to give product **8**.

For NMR spectra and single-crystal X-ray structures of the compounds in this study, see Supplementary Figs 1–5, 7–11 and 17–178.

Data availability. X-ray crystallographic data for compounds **2a**, **2p**, **2q**, **3a**, **3l**, **5**, **7c**, **8a** and **15**, and complex **A** have been deposited at the Cambridge Crystallographic Data Centre as CCDC 1500326–1500335, respectively (<http://www.ccdc.cam.ac.uk/pages/Home.aspx>). The authors declare that the data supporting the findings of this study are available within the article (and Supplementary Information files) and also are available from the corresponding author on request.

References

- Grimes, R. M. *Carboranes* 2nd edn (Academic Press, 2011).
- Hosmane, N. S. *Boron Science: New Technologies and Applications* (CRC, 2012).
- Hawthorne, M. F. The role of chemistry in the development of boron neutron capture therapy of cancer. *Angew. Chem. Int. Ed. Engl.* **32**, 950–984 (1993).

- Soloway, A. H. *et al.* The chemistry of neutron capture therapy. *Chem. Rev.* **98**, 1515–1562 (1998).
- Armstrong, A. F. & Valliant, J. F. The bioinorganic and medicinal chemistry of carboranes: from new drug discovery to molecular imaging and therapy. *Dalton Trans.* 4240–4251 (2007).
- Issa, F., Kassiou, M. & Rendina, L. M. Boron in drug discovery: carboranes as unique pharmacophores in biologically active compounds. *Chem. Rev.* **111**, 5701–5722 (2011).
- Jude, H. *et al.* Coordination-driven self-assemblies with a carborane backbone. *J. Am. Chem. Soc.* **127**, 12131–12139 (2005).
- Dash, B. P., Satapathy, R., Gaillard, E. R., Maguire, J. A. & Hosmane, N. S. Synthesis and properties of carborane-appended C3-symmetrical extended π systems. *J. Am. Chem. Soc.* **132**, 6578–6587 (2010).
- Wee, K.-R. *et al.* Carborane-based optoelectronically active organic molecules: wide band gap host materials for blue phosphorescence. *J. Am. Chem. Soc.* **134**, 17982–17990 (2012).
- Cioran, A. M. *et al.* Mercaptocarborane-capped gold nanoparticles: electron pools and ion traps with switchable hydrophilicity. *J. Am. Chem. Soc.* **134**, 212–221 (2012).
- Shi, C. *et al.* Variable photophysical properties of phosphorescent iridium(III) complexes triggered by *closo*- and *nido*-carborane substitution. *Angew. Chem. Int. Ed.* **52**, 13434–13438 (2013).
- Prokhorov, A. M. *et al.* Brightly luminescent Pt(II) pincer complexes with a sterically demanding carboranyl-phenylpyridine ligand: a new material class for diverse optoelectronic applications. *J. Am. Chem. Soc.* **136**, 9637–9642 (2014).
- Naito, H., Morisaki, Y. & Chujo, Y. *o*-Carborane-based anthracene: a variety of emission behaviors. *Angew. Chem. Int. Ed.* **54**, 5084–5087 (2015).
- Guo, J. *et al.* *o*-Carborane functionalized pentacenes: synthesis, molecular packing and ambipolar organic thin film transistors. *Chem. Commun.* **51**, 12004–12007 (2015).
- Mukherjee, S. & Thilagar, P. Boron clusters in luminescent materials. *Chem. Commun.* **52**, 1070–1093 (2016).
- Schwartz, J. J. *et al.* Surface dipole control of liquid crystal alignment. *J. Am. Chem. Soc.* **138**, 5957–5967 (2016).
- Furue, R., Nishimoto, T., Park, I. S., Lee, J. & Yasuda, T. Aggregation-induced delayed fluorescence based on donor/acceptor-tethered Janus carborane triads: unique photophysical properties of nondoped OLEDs. *Angew. Chem. Int. Ed.* **55**, 7171–7175 (2016).
- Xie, Z. Advances in the chemistry of metallocarboranes of f-block elements. *Coord. Chem. Rev.* **231**, 23–46 (2002).
- Xie, Z. Cyclopentadienyl-carboranyl hybrid compounds: a new class of versatile ligands for organometallic chemistry. *Acc. Chem. Res.* **36**, 1–9 (2003).
- Spokoyny, A. M. *et al.* Facile insertion of Rh and Ir into a boron-phenyl bond, leading to boryl/bis(phosphine) PBP Pincer complexes. *J. Am. Chem. Soc.* **131**, 9482–9483 (2009).
- Spokoyny, A. M. *et al.* A coordination chemistry dichotomy for icosahedral carborane-based ligands. *Nat. Chem.* **3**, 590–596 (2011).
- El-Hellani, A. & Lavallo, V. Fusing N-heterocyclic carbenes with carborane anions. *Angew. Chem. Int. Ed.* **53**, 4489–4493 (2014).
- Eleazer, B. J., Smith, M. D., Popov, A. A. & Peryshkov, D. V. (BB)-carboryne complex of ruthenium: synthesis by double B–H activation at a single metal center. *J. Am. Chem. Soc.* **138**, 10531–10538 (2016).
- Qiu, Z. Recent advances in transition metal-mediated functionalization of *o*-carboranes. *Tetrahedron Lett.* **56**, 963–971 (2015).
- Olid, D., Núñez, R., Viñas, C. & Teixidor, F. Methods to produce B–C, B–P, B–N and B–S bonds in boron clusters. *Chem. Soc. Rev.* **42**, 3318–3336 (2013).
- Dziedzic, R. M. *et al.* B–N, B–O, and B–CN bond formation via palladium-catalyzed cross-coupling of *B*-bromo-carboranes. *J. Am. Chem. Soc.* **138**, 9081–9084 (2016).
- Dixon, D. A., Kleier, D. A., Halgren, T. A., Hall, J. H. & Lipscomb, W. N. Localized orbitals for polyatomic molecules. The *closo* boron hydrides $B_nH_n^{2-}$ and carboranes $C_2B_n-2H_n$. *J. Am. Chem. Soc.* **77**, 6226–6237 (1977).
- Teixidor, F. *et al.* Are methyl groups electron-donating or electron-withdrawing in boron clusters? Permethylated *o*-carborane. *J. Am. Chem. Soc.* **127**, 10158–10159 (2005).
- Yamazaki, H., Ohta, K. & Endo, Y. Regioselective synthesis of triiodo-*o*-carboranes and tetraiodo-*o*-carborane. *Tetrahedron Lett.* **46**, 3119–3122 (2005).
- Quan, Y. & Xie, Z. Iridium catalyzed regioselective cage boron alkenylation of *o*-carboranes via direct cage B–H activation. *J. Am. Chem. Soc.* **136**, 15513–15516 (2014).
- Quan, Y., Tang, C. & Xie, Z. Palladium catalyzed regioselective B–C(sp) coupling via direct cage B–H activation: synthesis of B(4)-alkynylated *o*-carboranes. *Chem. Sci.* **7**, 5838–5845 (2016).
- Lyu, H., Quan, Y. & Xie, Z. Transition metal catalyzed direct amination of cage B(4)–H bond in *o*-carboranes: synthesis of tertiary, secondary, and primary *o*-carboranyl amines. *J. Am. Chem. Soc.* **138**, 12727–12730 (2016).
- Lyu, H., Quan, Y. & Xie, Z. Rhodium-catalyzed regioselective hydroxylation of cage B–H bonds of *o*-carboranes with O_2 or air. *Angew. Chem. Int. Ed.* **55**, 11840–11844 (2016).
- Lyu, H., Quan, Y. & Xie, Z. Palladium-catalyzed direct dialkenylation of cage BH bonds in *o*-carboranes through cross-coupling reactions. *Angew. Chem. Int. Ed.* **54**, 10623–10626 (2015).
- Quan, Y. & Xie, Z. Palladium-catalyzed regioselective diarylation of *o*-carboranes by direct cage B–H activation. *Angew. Chem. Int. Ed.* **55**, 1295–1298 (2016).
- Hoel, E. L., Talebinasab-Savari, M. & Hawthorne, M. F. Deuterium exchange at terminal boron-hydrogen bonds catalyzed by certain transition metal complexes. A qualitative study of selectivity and mechanism. *J. Am. Chem. Soc.* **99**, 4356–4367 (1977).
- Mirabelli, M. G. L. & Sneddon, L. G. Transition-metal-promoted reactions of boron hydrides. Cp*Ir-catalyzed reactions of polyhedral boranes and acetylenes. *J. Am. Chem. Soc.* **110**, 449–453 (1988).
- Hoel, E. L. & Hawthorne, M. F. Intramolecular oxidative addition of iridium to a boron-hydrogen bond of a complexed carboranylphosphine. *J. Am. Chem. Soc.* **95**, 2712–2713 (1973).
- Hoel, E. L. & Hawthorne, M. F. Preparation of B- σ -carboranyl iridium complexes by oxidative addition of terminal boron-hydrogen bonds to iridium(I) species. *J. Am. Chem. Soc.* **97**, 6388–6395 (1975).
- Herberhold, M., Yan, H., Milius, W. & Wrackmeyer, B. Rhodium-induced selective B(3)/B(6)-disubstitution of *ortho*-carborane-1,2-dithiolate. *Angew. Chem. Int. Ed.* **38**, 3689–3691 (1999).
- Liu, D. *et al.* Hydrogen-mediated metal-carbon to metal-boron bond conversion in metal-carboranyl complexes. *J. Am. Chem. Soc.* **130**, 16103–16110 (2008).
- Zhang, R. *et al.* Cobalt-promoted B–H and C–H activation: facile B–C coupling of carboranedithiolate and cyclopentadienyl. *J. Am. Chem. Soc.* **134**, 10341–10344 (2012).
- Yao, Z.-J. *et al.* Iridium-mediated regioselective B–H/C–H activation of carborane cage: a facile synthetic route to metallocycles with a carborane backbone. *J. Am. Chem. Soc.* **136**, 2825–2832 (2014).
- Kirlikovali, K. O. *et al.* Luminescent metal complexes featuring photophysically innocent boron cluster ligands. *Chem. Sci.* **7**, 5132–5138 (2016).
- Mkhalid, I. A. I., Barnard, J. H., Marder, T. B., Murphy, J. M. & Hartwig, J. F. C–H activation for the construction of C–B bonds. *Chem. Rev.* **110**, 890–931 (2010).
- Hartwig, J. F. Borylation and silylation of C–H bonds: a platform for diverse C–H bond functionalizations. *Acc. Chem. Res.* **45**, 864–873 (2012).
- Neeve, E. C., Geier, S. J., Mkhalid, I. A. I., Westcott, S. A. & Marder, T. B. Diboron(4) compounds: from structural curiosity to synthetic workhorse. *Chem. Rev.* **116**, 9091–9161 (2016).
- Corcoran, Jr E. W. & Sneddon, L. G. Transition-metal-promoted reactions of boron hydrides. Platinum(II) bromide catalyzed borane and carborane dehydrodimerization reactions: a new synthetic route to boron-boron linked multicage boranes and carboranes. *J. Am. Chem. Soc.* **106**, 7793–7800 (1984).
- Corcoran, Jr E. W. & Sneddon, L. G. Transition-metal-promoted reactions of boron hydrides. Platinum(II) bromide catalyzed cage growth and dehydrocoupling reactions of diborane with small polyhedral carboranes and boranes: Synthesis of a new arachno carborane, 5,6-C₂B₆H₁₂, and the diborane-coupled compounds 2:1',2'-[1,6-C₂B₄H₅][B₂H₅] and 2:1',2'-[B₅H₈][B₂H₅]. *J. Am. Chem. Soc.* **107**, 7446–7450 (1985).
- Boller, T. M. *et al.* Mechanism of the mild functionalization of arenes by diboron reagents catalyzed by iridium complexes. Intermediacy and chemistry of bipyridine-ligated iridium trisboryl complexes. *J. Am. Chem. Soc.* **127**, 14263–14278 (2005).
- Irvine, G. J. *et al.* Transition metal-boryl compounds: synthesis, reactivity, and structure. *Chem. Rev.* **98**, 2685–2722 (1998).
- Ramachandran, P. V., Zou, M.-F. & Brown, H. C. Efficient synthesis of B-iododialkyl- and B-alkyldiiodoboranes as their acetonitrile complexes: application for the enolboration – Aldolization of ethyl ketones. *Helv. Chim. Acta* **85**, 3027–3032 (2002).
- Wang, Y. *et al.* N-Heterocyclic olefin stabilized borenium cations. *Organometallics* **32**, 6639–6642 (2013).
- Merola, J. S. & Kacmarcik, R. T. Synthesis and reaction chemistry of (η^2 -Indenyl)(cyclooctadiene)iridium: migration of indenyl from iridium to cyclooctadiene. *Organometallics* **8**, 778–784 (1989).
- Tamura, H., Yamazaki, H., Sato, H. & Sakaki, S. Iridium-catalyzed borylation of benzene with diboron. Theoretical elucidation of catalytic cycle including unusual iridium(V) intermediate. *J. Am. Chem. Soc.* **125**, 16114–16126 (2003).

56. Tajuddin, H. *et al.* Iridium-catalyzed C–H borylation of quinolines and unsymmetrical 1,2-disubstituted benzenes: insights into steric and electronic effects on selectivity. *Chem. Sci.* **3**, 3505–3515 (2012).
57. Green, A. G., Liu, P., Merlic, C. A. & Houk, K. N. Distortion/interaction analysis reveals the origins of selectivities in iridium-catalyzed C–H borylation of substituted arenes and 5-membered heterocycles. *J. Am. Chem. Soc.* **136**, 4575–4583 (2014).
58. Ishiyama, T. *et al.* Mild iridium-catalyzed borylation of arenes. High turnover numbers, room temperature reactions, and isolation of a potential intermediate. *J. Am. Chem. Soc.* **124**, 390–391 (2002).
59. Tobisu, M., Kinuta, H., Kita, Y., Remond, E. & Chatani, N. Rhodium(I)-catalyzed borylation of nitriles through the cleavage of carbon-cyano bonds. *J. Am. Chem. Soc.* **134**, 115–118 (2012).

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Author contributions

R.C. carried out the experiments and structural determination of the reaction products, and prepared the Supplementary Information. Z.Q. and Z.X. conceived and designed the concepts and experiments, as well as prepared the manuscript.

Additional information

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