ORGANOMETALLICS

Mechanistic Insights and the Origin of Regioselective Borylation in an Iridium-Catalyzed Alkyl C(sp³)–H Bond Functionalization

Chandan Patel,* Vibin Abraham, and Raghavan B. Sunoj*

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India

S Supporting Information

ABSTRACT: Iridium-catalyzed *ortho* benzylic $C(sp^3)$ -H borylation of (2-propylphenyl)dimethylsilane, using bis-(ethylene glycolato)diborane as borylating agent, is investigated using B3LYP-D3 density functional theory. The reaction is found to proceed, first, through a very facile oxidative addition of a Si-H bond at the Ir center. This is followed by reductive elimination of ethylene-glycolborane. The subsequent C-H activation step, accompanied by elimination of a nother molecule of ethylene-glycolborane, leads to formation of a racemic mixture of four diastereomeric chiral iradacycle intermediates. The ensuing chirality at the metal center is accompanied by stereodifferentiation of the two



enantiotopic hydrogen atoms due to steric interaction between the alkyl group and the boryl ligands. Our calculations also correctly predict the experimentally observed regioselectivity. The propensity for C–H bond activation was found to be in the order benzylic $C(sp^3)$ –H > terminal alkyl $C(sp^3)$ –H > ortho $C(sp^2)$ –H of the aryl > secondary internal $C(sp^3)$ –H bonds. This is succeeded by oxidative addition of bis(ethylene glycolato)diborane at the Ir center. The resulting Ir(III) (bpy)trisboryl species then undergoes borylation at the benzyllic carbon. The relative free energies of the transition states for C–H activation and C–B bond formation are found to be comparable.

INTRODUCTION

Development and application of methodologies for C–H bond activation has been an active area of research in organic chemistry for several years.^{1–3} However, functionalization of $C(sp^3)$ –H bonds is usually difficult owing to its relatively inert and nonpolar nature. Further, development of stereoselective versions of $C(sp^3)$ –H functionalization reactions is of particular interest to chemists. In this regard, transition-metalcatalyzed C–H bond activation reactions provide ample opportunities to develop stereoselective variants by using chiral ligands at the metal center.

Among various strategies employed for C-H activation, catalytic borylation of alkanes is specifically impressive, as the newly formed C-B bond in the resulting alkylboron product can be transformed into multiple functional groups.^{4,5} Preparation of alkylboron reagents typically involves reaction of organometallic nucleophiles such as Grignard reagents with boron electrophiles⁶ or via cross-coupling of alkyl electrophiles with boron reagents.^{7,8} Recently, transition-metal-catalyzed functionalization of C-H bonds with bis(pinacolato)diboron $(B_2 pin_2)$ has emerged as an effective methodology, particularly for borylation of $C(sp^2)$ -H bonds.⁹ However, borylation of C(sp³)–H bonds still suffers from lower turnover numbers and typically demands the use of an excess amount of substrate. In addition, the regioselectivity of $C(sp^3)$ -H borylation generally remained limited to primary C-H bonds, as borylation at secondary C-H bonds is much harder to accomplish.^{10,1}

Recently, catalytic systems comprising $[Ir(COD)OMe]_2$ (COD = 1,5-cyclooctadiene) and 1,10-phenanthroline derived ligands have gained prominence for functionalization of secondary C–H bonds in a range of compounds such as cyclic ethers, cyclopropanes, cyclic amides, and alkylpyridines.^{12–15} In addition, the use of hydrosilyl (–SiR₂H) as a directing group in this iridium-catalyzed borylation of secondary benzylic C–H bonds opens up new opportunities, as both hydrosilyl and boryl groups in the ensuing product could suitably be transformed into multiple functional groups (Figure 1).^{5,16} The hydrosilyl group has earlier been successfully employed as a directing group in C(sp²)–H borylation of arenes.^{17,18}

In keeping with our current research efforts toward understanding the mechanism of transition-metal-catalyzed C–H activation reactions,^{19,20} we became interested in examining the mechanism of $[Ir(COD)OMe]_2$ -catalyzed borylation of (2-propylphenyl)dimethylsilane (A) as shown in Scheme 1.²¹ Studies on Ir-catalyzed borylations of secondary $C(sp^3)$ –H bonds are seldom found in the literature. Further, the reaction holds promise as it offers a high degree of regiocontrol even with various substituents present on the alkyl chain of A. The borylation at the benzylic C–H bond on the alkyl chain is preferred over that of the phenyl, which itself can

Special Issue: Hydrocarbon Chemistry: Activation and Beyond

Received: June 23, 2016



Figure 1. Representative set of organic transformations that can be performed on Bpin and SiMe₂H groups.

Scheme 1. Iridium-Catalyzed Borylation of (2-Propylphenyl)dimethylsilane^{21a}



^aStructures shown in red have been used to model the reaction in the present study.

undergo C-H activation under similar reaction conditions. This reaction is additionally interesting, as it involves borylation of a secondary $C(sp^3)$ -H bond, which is relatively harder to functionalize, with a high degree of regiocontrol. In addition, this reaction shows little influence of the electronic properties of the aryl ring on the yield, further increasing its substrate scope. These two features render higher synthetic utility to the final product (P), as it can offer access to a number of other, different compounds through suitable manipulation of the boryl and the silvl functional groups. It should also be noted that use of HBpin, instead of $B_2 pin_2$, as the boron reagent decreases the yield of the reaction. These observations raise some pertinent questions such as (1) what is the origin of the observed regioselectivity? (2) what is the role of the hydrosilyl group as an effective directing group? and (3) why is HBpin less effective and why does it result in a lower yield?

COMPUTATIONAL DETAILS

All calculations have been performed using the Gaussian09 quantum chemical program.²² Full geometry optimizations followed by frequency calculations on the stationary points were carried out to ascertain the nature of the stationary points as minima or first-order saddle points. We employed the hybrid density functional B3LYP^{23,24} with Grimme's dispersion correction $(D3)^{25}$ in combination with the Los Alamos pseudopotential basis set (LANL2DZ)^{26,27} for iridium and the 6-31G^{**} basis set²⁸⁻³¹ for all other atoms. All transition states (TSs) were characterized by only one imaginary frequency pertaining to the desired reaction coordinate. These TSs were further verified by performing intrinsic reaction coordinate (IRC) calculations at the same level of theory.³² Solvent effects were taken into account using the SMD solvation model with tetrahydrofuran (THF) as the dielectric continuum.³³ For better accuracy, we also calculated Gibbs free energies using the range-separated hybrid functional ω -B97XD with a much larger basis set, which is $6-311++G^{**}$ for all atoms except for iridium, for which LANL2TZ(f) is used.³⁴ In addition, we also employed the rigid-rotor harmonic oscillator (RRHO) model for a more accurate computation of vibrational entropy.³⁵ For consistency,

all structures and energies reported have been obtained after full geometry optimization in the solvent phase at the SMD_{THF}/B3LYP-D3/6-31G**,LANL2DZ(Ir) level unless stated otherwise.

RESULTS AND DISCUSSION

In this section, we describe the mechanistic details of how a secondary $C(sp^3)$ -H bond of *ortho*-propyl(dimethylsilyl)benzene undergoes borylation with bis(ethylene glycolato)diborane (B₂eg₂) using [Ir(COD)OMe]₂ as the transition metal precatalyst and 2,2'-bipyridine (bpy) as a ligand (Scheme 1). Under the reaction conditions, the iridium(I) complex converts to Ir(III)(bpy)tris(boryl) complex 1, which then serves as the active catalyst.³⁶⁻³⁹ An alternative scenario where the Ir(I)(bpy)(boryl) complex acts as the active species is also considered. However, this pathway, summarized in Figure S10 of the Supporting Information, is found to be of higher energy.

The broad features of the mechanism are depicted in Scheme 2. For convenience of discussion, the mechanism can be envisaged to involve six distinct steps as follows: (i) silvlation, in which the Ir center of the active catalyst (1) undergoes an oxidative addition to the Si-H bond of the substrate A to generate intermediate 2; (ii) H-Beg elimination, where intermediate 2 isomerizes to intermediate 2', which is followed by a reductive elimination of a molecule of H-Beg, furnishing a 16-electron intermediate 3; (iii) C-H activation, in which intermediate 3 first rearranges to another geometry denoted as 4, where the benzylic C-H bond develops a weak interaction with the Ir center; this is followed by an oxidative addition of Ir to the benzylic C-H bond and a concomitant reductive elimination of a molecule of H-Beg to yield iridacycle 5; (iv) C–B bond formation, in which intermediate 5 can undergo oxidative insertion to a new molecule of B₂eg₂ to generate another intermediate, 6, which then undergoes the desired C_{benzylic}-B bond formation through reductive elimination, resulting in intermediate 7; (v) H-Beg addition, where one molecule of H–Beg released earlier in the 2'-3 conversion can now oxidatively add to the Ir center in 7 to form intermediate 8', which can then isomerize to form 8; it can be noted that intermediates 8 and 8' are the borylated versions of 2 and 2', respectively, noted in the earlier steps of the catalytic cycle; (vi) Si-H elimination, in which the final step involves the reductive elimination of the borylated product from the iridium center such that the active catalyst 1 is regenerated.

We have examined an exhaustive set of possibilities for each mechanistic event as described in Scheme 1. For the sake of clarity, only the lowest energy pathway is presented here.⁴⁰ Each elementary step involved in the mechanism is discussed in succession in the following sections. The active catalyst 1 is a 16-electron square pyramidal species with a vacant axial coordination site for the incoming substrate. The first step is an oxidative addition of 1 to alkyl benzene A. There are two likely sites for the oxidative insertion of the iridium catalyst: (a) to the Si-H bond of the dimethyl silyl group or (b) to the benzylic C–H bond of the *ortho*-propyl chain.³⁹ We notice that the relatively weaker Si-H bond of the hydrosilyl group is a more preferred site for oxidative addition via $TS(1-2)_{ax}$ as compared to that at the benzylic C-H bond. This transition state is preceded by a weakly interacting catalyst-substrate prereacting complex (PRC1), as shown in Figure 2. Geometric features reveal a π -stacking interaction between the bipyridine ligand on the catalyst and the aryl ring of the substrate. In addition, the Si-H group of the substrate is found to exhibit a weak interaction with the Ir center, with an H…Ir distance of

Scheme 2. Important Steps Involved in the Mechanism of Borylation at the $C(sp^3)$ -H Bond of the Alkyl Benzene A



2.01 Å. Both these interactions result in a modest stabilization of **PRC1** by -3.8 kcal/mol relative to the separated species, **1** and **A**.

A comparison between the geometries of PRC1 and TS(1–2)_{ax} reveals that when the hydrosilyl group approaches the metal center from the axial position, the incoming hydride ligand pushes one of the equatorial boryl ligands (B2) toward the axial position (Figure 2).⁴¹ In addition, the distance between the incoming hydride ligand and the boron atom of B2 was found to be 2.17 Å, implying a weak interaction between the two atoms. Such H…B interaction is usually attributed as arising due to a favorable orbital interaction between the empty p-orbitals of the boron and the incoming hydride.^{36,37,39,42-44} This interaction is found to be even stronger in intermediate 2_{ax} as evident through a shorter H–B distance (1.79 Å).

The relative energy of the $TS(1-2)_{ax}$ is found to be 1.8 kcal/ mol relative to the infinitely separated 1 and A, implying that the oxidative addition to the Si-H bond is quite facile. An alternative possibility, wherein the active catalyst first reacts with another molecule of $B_2(eg)_2$ to form an 18-electron Ir(V)(bpy)penta(boryl) complex, is found to go through a transition state 4.1 kcal/mol higher than $TS(1-2)_{ax}$. In addition, intermediate 2_{ax} was found to be lower in energy than the Ir(V) (bpy)penta(boryl) complex by 4.5 kcal/mol. Thus, the formation of intermediate 2_{ax} is both kinetically and thermodynamically more favored over the formation of the Ir(V)(bpy)penta(boryl) species.⁴⁵ Yet another possibility is a direct oxidative addition of Ir catalyst to the benzylic C–H bond through a concerted TS, without the involvement of the Si–H bond. This TS is found to be ~26 kcal/mol higher in energy than $TS(1-2)_{av}$ ⁴⁶ again indicating that the initial activation of the Si–H bond is indeed more favorable than the activation of the benzylic C–H bond in the present reaction.

Intermediate 2_{ax} is an 18-electron species and, as such, cannot participate in C-H activation of the Ir-bound substrate. Therefore, it is expected that such an intermediate first converts to a 16-electron species via a reductive elimination of a molecule of H-Beg. At first glance, it appears reasonable that the hydride can be transferred to the boron atom of one of the two Beg ligands in the near vicinity (B1 or B2, Figure 2). However, the corresponding TS remained elusive, even after repeated attempts. Two independent relaxed potential energy surface (PES) scans, one by varying the H…B distance and another by varying the Ir…B distance, have been carried out. In both these cases, the resulting PES indicated the absence of a TS for the expulsion of H–Beg from 2_{ax}^{47} Subsequently, we have looked into the possibility of a reductive elimination of the Beg ligand (B3) from the axial position (axial, with respect to the Si atom). In order for this step to occur, intermediate 2_{ax} should first isomerize to another geometry, $2'_{ax}$ via TS(2- $2')_{ax}$. Intermediates $2'_{ax}$ is ~4 kcal/mol higher in energy than 2_{ax} and differs primarily in the disposition of the hydride relative the N-Ir-N equatorial plane (Figure 2). As seen in



Figure 2. SMD_{THF}/B3LYP-D3/6-31G**, LANL2DZ(Ir)-optimized geometries of important stationary points for the oxidative insertion of **1** to the Si–H bond of the substrate. All distances are in angstroms. Only important H atoms are shown for clarity.

Figure 2, the hydride ligand in 2_{ax} is located roughly in the N– Ir–N plane and enjoys a weak interaction with the **B2** ligand. However, in $2'_{ax}$ the hydride is slightly pushed toward the axial position with a N–Ir–N–H dihedral angle around -156.5° and occupying a position adjacent to the **B1** and **B3** ligands (Figure 2). It can be noted here that in $2'_{ax}$ the hydride tends to develop a weak interaction with the **B1** ligand with a H…B_{B1} distance of 1.60 Å. The hydride ligand can then transfer to the axial Beg ligand **B3** via $TS(2'-3)_{ax}$. The relative energy for $TS(2'-3)_{ax}$ is only 1.7 kcal/mol, implying that the reductive elimination of a molecule of H–Beg is very facile from intermediate $2'_{ax}$.

The reductive elimination of H-Beg from $2'_{ax}$ leads to the formation of a 16-electron species, 3_{ax} . In this intermediate, the benzylic C-H bond could get suitably positioned near the iridium center such that an oxidative insertion will result in an iridacycle intermediate, 5_{ax} . A couple of interesting aspects pertaining to regio- and stereoselectivities associated with this step are worth considering at this juncture. First, a total of four different C-H bonds in 3_{ax} could, in principle, participate in the oxidative addition, as shown in Figure 3. These include the $C(sp^2)$ -H bond of the aryl ring, secondary $C(sp^3)$ -H bonds at the C1 and C2 positions of the propyl chain, and the remaining primary $C(sp^3)$ -H bond at the terminal C3 position. Second, an interesting feature relates to the different stereoisomeric forms of 3_{ax} by suitable substitution. In the present scenario, as described in Figure 3, two conformers of 3_{ax} are interconvertible through a rotation around the Si-C_{phenyl} or Ir-Si bonds and hence are expected to be present in equal proportion. However, by installing substituents at appropriate sites on the substrate or on the catalyst framework, if rotation around these bonds could be restricted, one could envisage ensuing intermediates with different configurations depending upon



Figure 3. Potential stereodifferentiation in the oxidative addition to the benzylic secondary $C(sp^3)$ -H bond in 3_{ax} . Molecules with the same configuration at the benzylic carbon are shown in the same color. The notation for the absolute configuration (R/S) in $5_{axR/S}$ refers to configuration at the benzylic carbon.

which one of the diastereotopic C-H bonds participates in the oxidative insertion. Molecular insights of this kind could provide a useful starting point for developing asymmetric versions of this reaction.

Figure 4 shows the optimized geometries of TSs for the oxidative addition to each of the above-mentioned C–H bonds. The IRC calculations, which enable a careful walk-down from the transition state, on these TSs reveal that they are preceded by a high-energy intermediate, 4_{ax} . In 4_{axy} the **B1** ligand



Figure 4. SMD_{THF}/B3LYP-D3/6-31G^{**}, LANL2DZ(Ir)-optimized geometries and relative Gibbs free energies of transition states for the oxidative insertion to various C–H bonds at C1(a,b), C4(c), C2(d,e), and C4(f). Values in square brackets are the relative free energies (in kcal/mol) of corresponding TSs with respect to the infinitely separated reactants. All distances are in angstroms. Only important H atoms are shown for improved clarity.

occupies the axial position and the C–H bond is found to participate in an agostic interaction with the Ir center. More importantly, the IRC calculations further conveyed that the oxidative insertion to the C–H is accompanied by a concomitant reductive elimination of the axial Beg ligand **B1** as H–Beg.

It is of interest to compare the relative abilities of various C– H bonds, described earlier, in this vital oxidative addition step. While the geometric and energetic features can be gleaned from Figure 4, a succinct comparison by using the relative Gibbs free energies of various C–H activation transition states is provided in Figure 5. The oxidative addition to the benzylic secondary



Figure 5. Relative Gibbs free energies (in kcal/mol, given in parentheses) for the oxidative insertion of iridium to various C–H bonds in intermediate **4**.

C(sp³)-H is the most favorable option, which is in accordance with the final product observed in the experimental studies.²¹ The energetic preference for the oxidative insertion to various C-H bonds exhibits the following order: benzylic C(sp³)-H > terminal alkyl C(sp³)-H > *ortho* C(sp²)-H of the aryl > secondary C(sp³)-H bonds at the C2 position. This regiochemical preference can be traced to a combination of factors such as the acidity of the C-H involved, ring strain, and 1,3-interactions between substituents of the metallacycle.

The oxidative addition to the $C1(sp^3)$ -H bond is more favored than all other C-H bonds by about ~2 kcal/mol. Interestingly, the computed Wiberg bond indices are found to be in the order C1-H < C4-H < C2-H < C3-H, with the lowest value for $C1(sp^3)$ -H as compared to other C-H bonds in the reactant R (see Table S2 in the Supporting Information for more details). Between the remaining two $C(sp^3)$ -H bonds, the oxidative addition to the terminal $C3(sp^3)$ -H bond is more favored, owing to the involvement of a less strained seven-membered TS (Figure 4f). In addition, on the basis of Wiberg indices, the oxidative addition to the $C4(sp^2)$ -H bond is expected to be more favorable than the oxidative addition to the C2-H/C3-H bond. However, the strain in the fourmembered TS geometry is also expected to be the highest in this case. A combination of these two factors energetically places this TS in between the TSs for the oxidative addition to C3-H and C2-H bonds. We have also attempted to determine an approximate value of the percentage yield on the basis of the computed energetics. The theoretical yield for our system is found to be ~78% at the B3LYP-D3 and 69% at the ω -B97XD levels of theory (with RRHO correction, as described in the Computational Details), which compares quite well with the experimentally observed yield (61%) for our model ligand (L2 in Scheme 1) with B_2pin_2 as borylating agent.48

The oxidative addition to the benzylic $C(sp^3)$ -H bond as described in the previous sections provides iridacycle intermediate 5_{ax} , which on subsequent reductive elimination provides the borylated product. As 5_{ax} is a 16-electron species, it should first convert to an 18-electron species through an oxidative addition with $B_2(eg)_2$, to form Ir(III)(bpy)tris(boryl)complex 6_{ax} via $TS(5-6)_{ax}$, as shown in Figure 6. This step is similar to the oxidative addition of the active catalytic species 1 to $B_2(eg)_2$ noted in the early part of the catalytic cycle described in the previous sections. In the trisboryl intermediate 6_{ax} one of the boryl ligands (B5) coordinated to the metal center participates in a C-B bond formation via $TS(6-7)_{ax}$.



Figure 6. $SMD_{THF}/B3LYP-D3/6-31G^{**}$, LANL2DZ(Ir)-optimized geometries of transition states for reductive elimination leading to the C–B bond formation.

The borylation of the iridium-bound benzylic carbon takes place through this process. It is important to note here that the approach of the boryl ligand is from the same side as that of the iridium-benzylic carbon bond. Hence, the borylation occurs with retention of configuration at C1. The relative energy of $TS(6-7)_{ax}$ is found to be ~31 kcal/mol.

After the C-B bond formation leading to borylation, the resulting intermediate 7_{ax} should now undergo a reductive elimination, to regenerate the active catalyst 1 and the borylated version of the substrate (product P). It should be noted here that intermediate 7_{ax} is essentially the product P with a Si-H bond oxidatively added at the Ir center and is structurally similar to 3_{ax} , discussed in the earlier section. Therefore, the mechanism for the regeneration of the active catalyst from 7_{ax} should be regarded essentially as the reverse of that for the formation of 3_{ax} . The geometric features of stationary points involved in the conversion of 7_{ax} to 1 and P are similar to that for the formation of 3_{ax}^{49} Intermediate 7_{ax} first undergoes an oxidative addition to a molecule of H-Beg (released earlier in the catalytic cycle) to generate $\mathbf{8'}_{axv}$ which is structurally similar to $2'_{ax}$ with the hydride ligand pushed toward the axial boryl ligand. $8'_{ax}$ subsequently isomerizes via $TS(8'-8)_{ax}$ to furnish 8_{ax} which is structurally similar to 2_{ax} with the hydride ligand remaining nearly coplanar with the N-Ir-N plane (Figure 7). This is followed by the reductive elimination of the Si-H bond to furnish the product P and active catalyst 1 via $TS(8-1)_{ax}$ which has similar geometric features to $TS(1-2)_{ax}$.

The overall energetic details of the catalytic cycle can be gleaned from the Gibbs free energy profile diagram given in

Figure 8. The barrier height for the oxidative insertion to the benzylic $C(sp^3)$ -H bond through $TS(4-5)_{ax}$ is found to be the largest, implying that the C-H activation step is likely to be the rate-determining step in the present reaction. This prediction is in accordance with previous studies concerning borylation of C-H bonds.^{36,50} The predicted exoergic formation of certain bis-Ir(III)boryl intermediates $(3_{ax} \text{ and } 7_{ax})$ during the catalytic cycle suggests that such species could become potentially detectable. Overall, the reaction is found to be mildly exoergic, as notable from the change in Gibbs free energies for the \mathbf{R} + $B_2(eg)_2 \rightarrow P + H-Beg$ conversion in the presence of active catalyst 1. Here, the borylation at the benzylic position of the propyl chain takes place when the reactant ortho-propyl-(dimethylsilyl)benzene (R) is converted to the borylated product (P). It can also be noticed that the formation of 3_{ax} is crucial to the C-H activation step, and it involves the elimination of a molecule of H-Beg. Thus, the use of H-Beg or HBpin as the borylating agent, instead of B2pin2, can result in a reduction of the concentration of vital species 3_{ax} in the catalytic cycle. The situation is comparable to the experimentally observed lower overall yield of the reaction with HBpin as compared to that with B₂pin₂.

CONCLUSION

We have investigated the mechanism of an iridium-catalyzed regioselective borylation of ortho-propyl(dimethylsilyl)benzene using the SMD_{THE}/B3LYP-D3/6-31G** level of theory. The precatalyst $Ir(I)[(COD)(OMe)]_2$ is converted to an active catalyst by the action of bis(ethylene glycolato)diborane $(B_2 eg_2)$ in the presence of bipyridine ligand during the initial phase of the reaction. The active catalyst Ir(III)(bpy)tris(boryl) complex enters the catalytic cycle through the formation of a catalyst-substrate complex, where it interacts with the Si-H bond of the substrate. Structural and energetic features of various intermediates and transition states involved in the formation of the product have been established. In particular, an important question of how high site-selective monoborylation could be accomplished has been addressed with the help of relative energies of the corresponding transition states. The borylation of the benzylic secondary C(sp³)-H bond has been identified as the most preferred site for the C-H activation and borylation. The most preferred pathway has been found to involve six key steps such as (i) oxidative addition of the active catalyst to the Si-H bond of substrate, (ii) reductive elimination of a molecule of H-Beg, (iii) another oxidative



Figure 7. SMD_{THF}/B3LYP-D3/6-31G**, LANL2DZ(Ir)-optimized geometries of transition states for regeneration of catalyst after C–B bond formation.



Figure 8. Gibbs free energy profile for benzylic $C(sp^2)$ -H borylation of *ortho*-propyl dimethylsilyl benzene (**R**) using Ir(III)tris(boryl) complex (1) as the active catalyst obtained using the SMD_{THF}/B3LYP-D3/6-31G**, LANL2DZ(Ir) level of theory. All energies are in kcal/mol. Values in parentheses are Gibbs free energies at 353.15 K obtained at the ω -B97XD/6-311++G**,LANL2TZ(f)//SMD_{THF}/B3LYP-D3/6-31G** level of theory inclusive of RRHO correction.

addition of iridium to the benzylic $C(sp^3)$ -H bond and a concomitant elimination of a molecule of H-Beg, (iv) oxidative addition of B₂eg₂ followed by a reductive elimination through borylation (C-B formation), (v) uptake of a H-Beg molecule through oxidative addition (H-Beg addition), and (vi) reductive elimination of the final borylated product through a Si-H bond formation. Steps v and vi are reverse of i and ii and are essential for regeneration of active catalyst. The C-H activation of a benzylic secondary $C(sp^3)$ -H bond was found to be most favorable due to a combination of electronic and steric effects.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organo-met.6b00513.

Optimized geometries, additional schemes, figures, tables, and structural details of the transition states (PDF)

Text file of all the Cartesian coordinates of stationary points in a format for convenient visualization (XYZ)

AUTHOR INFORMATION

Corresponding Authors

*E-mail (C. Patel): chandanz@gmail.com. *E-mail (R. B. Sunoj): sunoj@chem.iitb.ac.in.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

C.P. acknowledges a postdoctoral fellowship from IIT Bombay. The SpaceTime supercomputing facility at IIT Bombay is gratefully acknowledged for providing generous computing time.

REFERENCES

- (1) Hartwig, J. F. Nature 2008, 455, 314-322.
- (2) Balcells, D.; Clot, E.; Eisenstein, O. Chem. Rev. 2010, 110, 749-823.
- (3) Labinger, J. A.; Bercaw, J. E. Nature 2002, 417, 507-514.
- (4) Hall, D. G. Structure, Properties and Preparation of Boronic Acid Derivatives: Overview of their Reactions and Applications In Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005; Vol. 2.
- (5) Crudden, C. M.; Edwards, D. Eur. J. Org. Chem. 2003, 2003, 4695-4712.
- (6) Brown, H. C.; Bhat, N. G.; Somayajilb, V. Organometallics 1983, 2, 1311-1316.
- (7) Yang, C.-T.; Zhang, Z.-Q.; Tajuddin, H.; Wu, C.-C.; Liang, J.; Liu, J.-H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. Angew. Chem. **2012**, *124*, 543–547.
- (8) Dudnik, A. S.; Fu, G. C. J. Am. Chem. Soc. 2012, 134, 10693-10697.
- (9) Hartwig, J. F. Acc. Chem. Res. 2012, 45, 864-873.
- (10) Ohmura, T.; Torigoe, T.; Suginome, M. J. Am. Chem. Soc. 2012, 134, 17416–17419.
- (11) Murphy, J. M.; Lawrence, J. D.; Kawamura, K.; Incarvito, C.; Hartwig, J. F. J. Am. Chem. Soc. **2006**, 128, 13684–13685.
- (12) Liskey, C. W.; Hartwig, J. F. J. Am. Chem. Soc. 2012, 134, 12422-12425.
- (13) Liskey, C. W.; Hartwig, J. F. J. Am. Chem. Soc. 2013, 135, 3375–3378.
- (14) Kawamorita, S.; Miyazaki, T.; Iwai, T.; Ohmiya, H.; Sawamura,
 M. J. Am. Chem. Soc. 2012, 134, 12924–12927.
- (15) Kawamorita, S.; Murakami, R.; Iwai, T.; Sawamura, M. J. Am. Chem. Soc. **2013**, 135, 2947–2950.
- (16) Chernyak, N.; Dudnik, A. S.; Huang, C.; Gevorgyan, V. J. Am. Chem. Soc. 2010, 132, 8270-8272.
- (17) Boebel, T. A.; Hartwig, J. F. J. Am. Chem. Soc. 2008, 130, 7534–7535.
- (18) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. J. Am. Chem. Soc. 2010, 132, 4068-4069.
- (19) Anand, M.; Sunoj, R. B. Organometallics 2012, 31, 6466-6481.
- (20) Anand, M.; Sunoj, R. B. Org. Lett. 2012, 14, 4584-4587.

(21) Cho, S. H.; Hartwig, J. F. J. Am. Chem. Soc. 2013, 135, 8157-8160.

(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V; Cioslowski, J.; Fox, D. J. Gaussian09; Gaussian Inc.: Wallingford, CT, 2009.

(23) Becke, A. D. Phys. Rev. A: At, Mol., Opt. Phys. 1988, 38, 3098-3100.

(24) Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B: Condens. Matter Mater. Phys. **1988**, 37, 785-789.

(25) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. J. Chem. Phys. 2010, 132.15410410.1063/1.3382344

- (26) Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 270-283.
- (27) Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 299-310.
- (28) Hariharan, P. C.; Pople, J. A. Theor. Chim. Acta 1973, 28, 213–22210.1007/BF00533485.
- (29) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. Chem. Informationsdienst **1982**, 77,
- 3654–3665.
- (30) Rassolov, V. A.; Pople, J. A.; Ratner, M. A.; Windus, T. L. J. Chem. Phys. **1998**, 109, 1223–1229.
- (31) Rassolov, V. A.; Ratner, M. A.; Pople, J. A.; Redfern, P. C.; Curtiss, L. A. J. Comput. Chem. 2001, 22, 976–984.

(32) (a) Fukui, K. Acc. Chem. Res. 1981, 14, 363-368. (b) Gonzalez, C.; Schlegel, H. B. J. Chem. Phys. 1989, 90, 2154-2161.

- (33) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. J. Phys. Chem. B 2009, 113, 6378-6396.
- (34) Chai, J.-D.; Head-Gordon, M. Phys. Chem. Chem. Phys. 2008, 10, 6615–6620.
- (35) Grimme, S. Chem. Eur. J. 2012, 18, 9955-9964.

(36) Li, Q.; Liskey, C. W.; Hartwig, J. F. J. Am. Chem. Soc. 2014, 136, 8755–8765.

(37) Tamura, H.; Yamazaki, H.; Sato, H.; Sakaki, S. J. Am. Chem. Soc. **2003**, *125*, 16114–16126.

- (38) Vanchura, B. A., III; Preshlock, S. M.; Roosen, P. C.; Kallepalli, V. A.; Staples, R. J.; Maleczka, R. E., Jr.; Singleton, D. A.; Smith, M. R., III *Chem. Commun.* **2010**, *46*, 7724–7726.
- (39) Roosen, P. C.; Kallepalli, V. A.; Chattopadhyay, B.; Singleton, D. A.; Maleczka, R. E., Jr.; Smith, M. R., III *J. Am. Chem. Soc.* 2012, 134, 11350–11353.

(40) Other possibilities arising due to differing configuration of ligands around the metal center are presented in Figures S6 and S7, and the corresponding energetics are provided in Table S1 in the Supporting Information.

(41) In an earlier study on the C–H bond activation of chlorosilanes, an oxidative insertion of Ir(I) catalyst at the primary $C(sp^3)$ –H bonds has been considered. See: Huang, G.; Kalek, M.; Liao, R. -Z; Himo, F. *Chem. Sci.* **2015**, *6*, 1735–1746.

(42) Webster, C. E.; Fan, Y.; Hall, M. B.; Kunz, D.; Hartwig, J. F. J. Am. Chem. Soc. 2003, 125, 858-859.

(43) Vanchura, B. A., III; Preshlock, S. M.; Roosen, P. C.; Kallepalli, V. A.; Staples, R. J.; Maleczka, R. E., Jr.; Singleton, D. A.; Smith, M. R., III *Chem. Commun.* **2010**, *46*, 7724–7726.

(44) Hartwig, J. F.; Cook, K. S.; Hapke, M.; Incarvito, C. D.; Fan, Y.; Webster, C. E.; Hall, M. B. *J. Am. Chem. Soc.* **2005**, *127*, 2538–2552. (45) Interestingly, in a previous study on primary $C(sp^3)$ –H borylation of chlorosilanes by $Ir(Me_4$ -phen)(Bpin)₃ as the active catalyst, the Ir(V) (bpy)penta(boryl) species was noted as the lowest energy intermediate and was proposed to be the resting state of the catalyst. 39

(46) Geometry and energy of this stationary point are provided in Figure S8 in the Supporting Information.

(47) The details of the potential energy surfaces are provided in Figure S9 in the Supporting Information.

(48) Details of how the yields were calculated are included in the Supporting Information.

(49) Additional geometric details are provided in Figures S3–S5 in the Supporting Information.

(50) Huang, G.; Kalek, M.; Liao, R.-Z.; Himo, F. Chem. Sci. 2015, 6, 1735–1746.