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Catalytic borylation of methane

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Abstract

Despite steady progress in catalytic methods for the borylation of hydrocarbons, methane has not yet been subject to this transformation. Here we report the iridium-catalyzed borylation of methane using bis(pinacolborane) in cyclohexane solvent. Initially, trace amounts of borylated products were detected with phenanthroline-coordinated Ir complexes. A combination of experimental high-pressure and high-throughput screening, and computational mechanism discovery techniques helped to rationalize the foundation of the catalysis and identify improved phosphine-coordinated catalytic complexes. Optimized conditions of 150°C and 3500-kilopascal pressure led to yields as high as ~52%, turnover numbers of 100, and improved chemoselectivity for monoborylated versus diborylated methane.

Activation of methane is challenging because it is nonpolar, has strong sp^3 C-H bonds, is sparingly soluble in both polar and non-polar solvents, and has very high ionization energies and very low triple, boiling, and flashing points (1–8). Homogeneous catalysts that convert methane to products that could be used as liquid fuels are known, but these systems often require strong electrophiles and, in some cases, superacids and/or powerful oxidants (1, 2, 9–17). Chemoselectivity is another limitation in methane activation and functionalization. For instance, H_3C-R (R = functional group) products resulting from methane activation and functionalization have more reactive C-H bonds than methane itself, hence often resulting in poor selectivity, overfunctionalization, and overoxidation.

The pioneering work by Hartwig, Marder, and Smith on C-H bond borylation inspired our investigation into the catalytic functionalization of methane using a similar approach (18). Whereas stoichiometric and catalytic borylations of alkanes show marked selectivity for monoborylation of terminal methyl groups (18), analogous reactions with methane have not

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Experimental procedures, spectroscopic measurements, and theoretical calculations are provided in the supplementary materials.

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been thoroughly explored, despite this reaction being known for more than a decade. Fundamentally important is that the methyl-derived product is arguably a form of a mildly nucleophilic methyl transfer reagent, which complements the chemistry observed in electrophilic activation reactions in Shilov-type chemistry (9). Theory predicts that borylation of hydrocarbons with a borane (Eq. 1) is thermoneutral, whereas the weaker B-B bond in diboron reagents provides an enthalpic driving force of at least 12 kcal/mol, as shown in Eq. 2 (18). These considerations led us to pursue the catalytic borylation of methane using diboron reagents such as B₂pin₂ (pin = pinacolate).

Iridium systems are particularly promising for C-H activation of methane (1,2), and some of the most active borylation catalysts use this transition metal (18). Therefore, we focused our attention on the commercially available iridium reagents [Ir(COD)(μ-Cl)]₂, [Ir(COD)(μ-OMe)]₂ (COD = 1,5-cyclooctadiene), and (MesH)Ir(Bpin)₃ (MesH = mesitylene) (19), modifying them with a range of nitrogen-based ligands, some of which are summarized in Table 1. Suitable catalyst and reaction conditions were identified systematically by means of a high-pressure, high-throughput reactor (see fig. S1 for details). Both [Ir(COD)(μ-OMe)]₂ and (MesH)Ir(Bpin)₃ complexes gave some conversion to borylated methane products in cyclohexane (CyH) or tetrahydrofuran (THF) at pressures as low as 2068 kPa. Product yields were determined by gas chromatography-mass spectrometry (GC-MS) techniques with mesitylene as an internal standard

Ir(I) precatalysts with supporting ligand combinations were exposed for 16 hours at 120°C to 2068 kPa of methane and B₂pin₂. Our results indicate that L3 (3,4,7,8-tetramethyl-1,10-phenanthroline) is the best nitrogen ligand. Among the products detected in the reaction mixture were H₃CBpin (**1**), H₂C[Bpin]₂ (**2**), HBpin (**3**), and H₃COBpin. We also observed the production of O[Bpin]₂. Because hydrolysis of **1** and **2** is very slow on the basis of control experiments, we propose O[Bpin]₂ to derive from a combination of hydrolysis of **3** during aerobic workup and analysis by GC-MS, as well as decomposition of B₂pin₂ or **3**. The decomposition of B₂pin₂ may be metal-catalyzed, as ring-opening of pinacolborane with Ir catalysts has been documented recently (20). We did not observe any tri- or tetraborylated methyl products, H_{4-x}C[Bpin]_x (x = 3 or 4), whereas borylation of the solvent is barely detected under our conditions. Increasing CH₄ pressures in small increments to 8274 kPa did not improve the mono- or diborylation reaction appreciably. Although gem-diborylation of alkanes is unknown, the gemdiborylation of benzylic groups has been documented (21, 22). Because three boryl moieties become incorporated into the active catalyst, as illustrated in Fig. 1, the diboron additive has an immediate impact on the reactivity. For instance, no reaction takes place when B₂cat₂ (cat: catechol) is used instead of

B₂pin₂, which is consistent with previous experimental and computational studies showing that borylation is favored for more electron-rich catalysts (23,24).

The observed lower yield of **3** compared to **1** and **2** may be due to a second, slower borylation cycle that consumes **3** (Eq. 1). Consistent with our findings, we have observed that **3** can be used as a reactant replacing B₂(pin)₂, but this reaction is much slower at 120°C (table S7). Other diboron reagents, such as B₂(OH)₄ or B₂(NMe₂)₄, produced complex mixtures of products with intractable precipitates.

Table 1 summarizes some of our screening results with the most promising chelating polypyridyl ligands. The use of ligands L1 and L2 gave detectable amounts of H₃CBpin, whereas the best results were obtained with L3 (3,4,7,8-tetramethyl-1, 10-phenanthroline), which showed yields as high as 4.1% and chemoselectivity ratios of mono- versus diborylated products **1:2** as high as 4:1. Surprisingly, even [Ir(COD)(μ-OMe)]₂ without exogenous ligand resulted in some borylation (<1%) but overall (25), the results listed in Table 1 suggest these systems to be stoichiometric with respect to methane borylation (supplementary text). Likewise, increasing the temperature to 150°C did not improve the reaction (table S6).

The mechanism of methane borylation was modeled with density functional theory calculations on the Ir-phenanthroline system, and the proposed catalytic cycle is summarized in Fig. 1. Before catalysis can take place, the [Ir(COD)(μ-X)]₂ (X[−] = OMe or Cl) undergoes a series of ligand substitutions to ultimately yield (phen)Ir(Bpin)₃ (phen = 1,10-phenanthroline). This complex is the most plausible resting state of the catalyst and consists of an Ir(III)-*d*⁶ center in a pseudo-square-pyramidal coordination geometry labeled as **a** (see Fig. 2). The catalytic cycle commences with weak binding of methane at the empty coordination site to give the intermediate complex **b**, followed by oxidative addition traversing the likely rate-determining transition state **b-TS** at 25.9 kcal/mol (26). The iridium center in this intermediate **c** adopts a rare, but not unprecedented, seven-coordinate geometry (27). Next, the hydride and borane ligands swap position to give access to **c-iso** that can undergo reductive elimination of the boryl-methane product **1** to afford the Ir(III)-complex **d**, which reacts with another equivalent of the diboron source to regenerate the catalyst resting state **a**. We considered several alternative mechanisms, most notably a σ-bond metathesis pathway (28), but found that the mechanism shown in Fig. 1 is energetically most favorable. A detailed analysis of the computational results suggested a potential optimization strategy: As the H-CH₃ bond is cleaved at the transition state **b-TS**, the Ir-center must undergo formally an oxidation from Ir(III) to Ir(V). Therefore, the hard N-based Lewis base ligands may not provide the ideal supporting ligand framework, as these ligands tend to decrease the polarizability of the valence electrons of the metal. Softer Lewis bases, such as the phosphine analogs of the N ligands, seemed likely to prove beneficial by increasing the polarizability of the metal.

We tested the simple qualitative rationale from our computer model by exploring whether phosphine ligands offered improved reactivity toward C-B bond formation. Initial screens showed that phosphine ligands do not result in any notable borylation at 120°C with 2068 to 3447 kPa of methane, but at 150°C the dmpe ligand (Me₂PCH₂CH₂PMe₂) improved the

reaction substantially. Table 2 summarizes the best results from our screening. Varying catalyst loadings from 0.5 to 25 mole percent (mol %) led to conversion yields as high as 52% and catalytic turnover numbers (TONs) up to 104 with selectivity of 3:1 for monoborylated product **1** versus **2**. Increasing the mol % of catalyst resulted in lower conversion, though the selectivity for mono- versus diborylation (**1**:**2** ratio) of methane increased to as high as 9:1 (entry 1). Pressures below 1379 kPa afforded lower conversions, whereas pressures above 3447 kPa did not greatly improve the overall yield of products. Reactions required 16 hours for completion, and control experiments using similar amounts of dmpe/[Ir(COD)(μ -Cl)]₂ and **1** as a reagent with 40 equivalents of B₂(pin)₂ (with or without methane) did yield the diborylated product **2**. This result implies that the yield of monoborylation product is always greater than for diborylation with the dmpe scaffold.

An inverse relationship between precatalyst concentration and borylation conversion has previously been observed in borylations with [Ir(COD)(μ -Cl)]₂ precatalysts and N-chelating ligands, but no explanation was provided for this behavior (29). Recently, Finke and co-workers have analyzed similar counterintuitive behavior in hydrogenations with Ziegler-type nanoparticle catalysts prepared from Ir precatalysts (30). Likewise, benzene borylation has been described with Ir nanoparticles at 80°C with activities that are considerably lower than those for homogeneous catalysts (31). Both of these Ir nanoparticle-catalyzed reactions are poisoned by Hg. In our case, Hg addition to the reactions listed in Table 2 did not suppress catalysis. In addition, borylations with dmpe and phenanthrolinebased ligands at 150°C with identical precatalyst loadings and concentrations give very different conversions (table S6). These observations are consistent with a homogeneous process in which the nature of the ligand affects catalysis. Lastly, methane activation over Ir/ZrO₂ has been described, but high temperatures (~600°C) are typically required for these processes (32).

Because dmpe/[Ir(COD)(μ -Cl)]₂ afforded the cleanest yield of monoborylated product **1**, we conducted isotopic labeling studies using ¹³CH₄-enriched methane (99% atom enriched, 1379 kPa) to unambiguously establish that methane gas is the source of methyl in **1**. As anticipated, GC-MS results conclusively established the formation of **1**-¹³C as the only product derived from ¹³CH₄ borylation (fig. S7), excluding the possibility of pinacol or solvent degradation as possible sources of CH₃. Mechanistically, we expect the phosphine system to follow the same route outlined above for the polypyridyl systems.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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26. All energies discussed are obtained from calculations without any corrections for concentration differences. That is, all calculations assume standard conditions. In reality, the substrate concentrations are a few orders of magnitude higher than the concentration of the catalyst. Thus, Le Chatelier's principle will give rise to a lowering of all free energies by a few kcal/mol. As a result, our computed barrier of 25.9 kcal/mol must be considered an upper bound estimate. The real barrier will be a few kcal/mol lower because of the concentration differential.
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Fig. 1. Proposed cycle for the monoborylation of methane with 1,10-phenanthroline as a supporting ligand

Fig. 2. Computed structures of catalytic cycle states in Fig. 1
Nonessential hydrogens are omitted for clarity.

1, 10-phenanthroline ligands used in the borylation of methane

The ligands were added in a 2:1 ratio relative to dimeric Ir reagent and in a 1:1 ratio relative to independently prepared (MesH) Ir(Bpin)₃. Solvent was either tetrahydrofuran (THF) or cyclohexane (CyH). Results with other ligands are shown in table S4.

Table 2
Variations of catalyst loading and time with the ligand dmpe for the borylation of methane

The ligand dmpe ($\text{Me}_2\text{PCH}_2\text{CH}_2\text{PMe}_2$) was used in a 2:1 ratio relative to the Ir precatalyst $[\text{Ir}(\text{COD})(\mu\text{-Cl})_2]$ in cyclohexane (CyH) under 3447 kPa of CH_4 .

$\text{CH}_4 + \text{B}_2\text{pin}_2 \xrightarrow[\text{3447 kPa}]{\begin{array}{c} [\text{Ir}(\text{COD})(\mu\text{-Cl})_2]_2 \\ \text{dmpe} \\ \text{CyH, X hours} \\ 150^\circ\text{C} \\ - \text{ClBpin} \end{array}} \begin{array}{c} \text{H}_3\text{C-Bpin} + \text{H}_2\text{C(Bpin)}_2 + \text{HBpin} + \text{O(Bpin)}_2 \\ \mathbf{1} \qquad \mathbf{2} \qquad \mathbf{3} \end{array}$					
Entry	Loading (mol %)	Time (hours)	Percent yield	1:2	TON
1	25	16	9.4	9:1	<1
2	10	16	16	5:1	~1
3	5.0	16	23	5:1	4
4	1.0	16	25	5:1	25
5	0.5	16	52	3:1	104
6	25	6	17	7:1	<1
7	10	6	25	7:1	~2
8	5.0	6	27	6:1	5
9	1.0	6	21	8:1	21
10	0.5	6	28	6:1	56
11	10	2	22	3:1	22
12	5.0	2	27	4:1	5
13	1.0	2	24	4:1	24
14	0.5	2	16	2:1	32