C-H Activation for the Construction of C-B bonds

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1. Introduction

2. Stoichiometric Borylation
   2.1. Iron
   2.2. Tungsten

3. Metal-Catalyzed Borylation
   3.1. Rhenium
   3.2. Ruthenium
   3.3. Rhodium
   3.4. Iridium

4. Application

5. Conclusion
1. Introduction

Common Syntheses of Arylboronate Esters and Acids

Thermodynamic of Methane Borylation with $B_2(OR)_4$ or HB(OR)$_2$
2. Stoichiometric Borylation

2.1. Iron

- Summary of the Reactions of the Iron Boryl Complex \( \text{CpFe(CO)}_2(\text{Bcat}) \)
2.2. Tungsten

- Reactions of Cp*W(CO)₃(Bcat’) with Various Alkanes

- Proposed mechanism for the reaction of Cp*W(CO)₃(Bcat’) with alkanes
3. Metal-catalyzed Borylation

3.1. Rhenium

- Cp*Re-Catalyzed Borylation of Alkanes

\[ R-H \text{ (neat)} + B_2pin_2 \xrightarrow{2.4-5.0 \text{ mol\% } Cp*Re(CO)_3} \xrightarrow{hv, CO, 25^\circ C} R-Bpin + HBpin \]

- Proposed mechanism for Cp*Re-Catalyzed Alkanes Borylation
3.2. Ruthenium

- **Borylation of Octane with $\text{B}_2\text{pin}_2$ catalyzed Ru complexes**

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Yield$^a$</th>
<th>Conversion$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Cp*RuCl$_2$)$_2$</td>
<td>98% (75%)$^b$</td>
<td>99%</td>
</tr>
<tr>
<td>[Cp*RuCl]$_4$</td>
<td>65%</td>
<td>99%</td>
</tr>
<tr>
<td>Cp*Ru(H)(COD)</td>
<td>58%</td>
<td>80%</td>
</tr>
<tr>
<td>Cp*Ru(Cl)(TMEDA)</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>[Cp*Ru(OMe)$_2$]$_2$</td>
<td>7%</td>
<td>65%</td>
</tr>
<tr>
<td>(COD)Ru(2-methylallyl)$_2$</td>
<td>7%</td>
<td>59%</td>
</tr>
<tr>
<td>Ru(acac)$_3$</td>
<td>4%</td>
<td>76%</td>
</tr>
</tbody>
</table>

$^a$ Determined by GC. $^b$ Isolated yield in parentheses. $^c$ 5 mol % Ru used.

- **Ru-Catalyzed Terminal Borylation of Heteroatom-Containing Substrates**

The reaction of arenes with $\text{B}_2\text{pin}_2$ in the presence of Cp*Ru-complexes did not form functionalized products in good yields.
3.3. Rhodium

- Rh-catalyzed Borylation of Aliphatic Substrates

More electron-deficient C-H bonds in aliphatic substrates undergo borylation catalyzed by Cp*Rh(η^4-C_6Me_6) faster than more electron-rich C-H bonds.

The presence of heteroatoms, such as nitrogen and oxygen, are known to activate the C-H bond α to the heteroatom toward cleavage by many metal complexes. However this property of the heteroatoms did not override the preference of the catalyst for the functionalization of the least hindered of the primary C-H bonds.

- Electronic Effect on Aliphatic Borylation
• Rh-catalyzed Borylation of Arenes

\[
\text{Ar} - R + \text{HBPin} \quad \xrightarrow{2 \text{ mol\% } \text{Cp}^*\text{Rh}(\eta^4\text{-C}_8\text{H}_8)}\quad \text{Ar} - \text{pinB}^- \\
150^\circ \text{C} \quad \text{% yield (para:meta:ortho)}
\]

- Me - Bpin 72% (1.00:1.93:0.15)
- Me₂N - Bpin 65% (1.00:1.74:0.04)
- F₂ - Bpin 46%
- EtO₂C - Bpin yield not determined 1.00:1.74:0.29
- Me - Bpin 86%
- Me - Bpin 73%
- F₃C - Bpin 41%

• Rh-Catalyzed Benzylic Borlation of Toluene

\[
\text{Me} - \text{Me} + \text{HBPin} \quad \xrightarrow{[\text{RhCl}[(\text{PPh}_3)_2](\text{N}_2)]} \quad \text{Me} - \text{Me} - \text{Me} - \text{Me} + \text{Me} - \text{Me} - \text{Me} - \text{Me} + \text{Me} - \text{Me} - \text{Me} - \text{Me} \quad \text{17% (smp. 1:4:3:13)}
\]

\[
\text{Me} - \text{Me} + \text{HBPin} \quad \xrightarrow{[\text{RhCl}(\text{PPh}_3)_2](\text{N}_2)]} \quad \text{Me} - \text{Me} - \text{Me} - \text{Me} + \text{Me} - \text{Me} - \text{Me} - \text{Me} + \text{Me} - \text{Me} - \text{Me} - \text{Me} \quad \text{40%}
\]

• Two Potential Mechanisms

\[
[\text{L}_2\text{RhCl}(\text{N}_2)] + \text{HBPin} \quad \xrightarrow{\text{N}_2} \quad \text{L}_2\text{Rh}(\text{H})(\text{Bpin}) \quad \xrightarrow{\text{ClBpin}} \quad \text{PhMe}
\]

\[
\text{L}_2\text{RhCl}(\text{H})(\text{Bpin}) \quad \xrightarrow{\text{H}_2} \quad \text{L}_2\text{RhCl}(\text{H})(\text{Bpin}) \quad \xrightarrow{\text{HBpin}} \quad \text{L}_2\text{Rh}(\text{Bpin}) \quad \xrightarrow{\text{H}_2} \quad \text{L}_2\text{Rh}(\text{Bpin}) \quad \xrightarrow{\text{Bpin}} \quad \text{PhMe}
\]
3.4. Iridium

- Arene Borylation

I. Arene Borylation with Iridium catalysts containing Phosphine Ligands

Proposed Mechanism
II. Arene Borylation with Iridium catalysts containing Bipyridine Ligands

\[
\text{ArH} + \text{B}_2\text{pin}_2 \xrightleftharpoons[3.0 \text{ mol}\% \text{ bpy}]{1.5 \text{ mol}\% [\text{Ir(COD)Cl}_2]} \xrightarrow{80 \degree \text{C, } 16 \text{ h}} 2 \text{ArBpin} + \text{H}_2
\]

<table>
<thead>
<tr>
<th>product</th>
<th>yield %</th>
<th>product</th>
<th>yield %</th>
<th>product</th>
<th>yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Me-}\text{Bpin})</td>
<td>95</td>
<td>(\text{Me-}\text{Me-Bpin})</td>
<td>83</td>
<td>(\text{Me-}\text{Bpin})</td>
<td>86</td>
</tr>
<tr>
<td>(\text{MeO-}\text{Bpin})</td>
<td>95 (1:74:25) ((\sigma: m: \rho))</td>
<td>(\text{MeO-}\text{Me-Bpin})</td>
<td>86</td>
<td>(\text{Me-}\text{Bpin})</td>
<td>72</td>
</tr>
<tr>
<td>(\text{Me-}\text{Bpin})</td>
<td>82 (0:69:31) ((\sigma: m: \rho))</td>
<td>(\text{Cl-}\text{Bpin})</td>
<td>83</td>
<td>(\text{Me-}\text{Bpin})</td>
<td>73</td>
</tr>
<tr>
<td>(\text{F}_3\text{C-Bpin})</td>
<td>80 (0:70:30) ((\sigma: m: \rho))</td>
<td>(\text{Me-}\text{Me-Bpin})</td>
<td>58</td>
<td>(\text{Br-}\text{Bpin})</td>
<td></td>
</tr>
</tbody>
</table>

\[
\text{B}_2\text{pin}_2 + 2 \text{FG} \xrightarrow[3.0 \text{ mol}\% \text{ bipyridine ligand}]{1.5 \text{ mol}\% [\text{Ir(COD)(OMe)}_2]} \text{room temperature} \xrightarrow{\text{H}_2} \text{FG-}\text{Bpin}
\]

Steric effect

Electronic effect
II. Arene Borylation with Iridium catalysts containing Bipyridine Ligands

It was faster in nonpolar solvents, such as hexane, than in more coordination, more polar solvents, such as dimethyl ether (DME), and dimethyl formamide (DMF).
Heteroarene Borylation

\[
\text{B}_2\text{pin}_2 + 2 \text{X} \xrightarrow{1.5 \text{ mol}\% \text{[Ir(COD)Cl]_2}, \text{3.0 mol}\% \text{dtbpy}} \text{octane, 80}^\circ\text{C} \rightarrow \text{H}_2 + 2 \text{pinB-X}
\]

<table>
<thead>
<tr>
<th>product</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>pinB-S</td>
<td>83(^a)</td>
</tr>
<tr>
<td>pinB-S-Me</td>
<td>91</td>
</tr>
<tr>
<td>pinB-N</td>
<td>92</td>
</tr>
<tr>
<td>pinB-F</td>
<td>83(^a)</td>
</tr>
<tr>
<td>pinB-S</td>
<td>89</td>
</tr>
<tr>
<td>Bpin</td>
<td>42(^a,b,c)</td>
</tr>
<tr>
<td>pinB-H</td>
<td>67(^a)</td>
</tr>
<tr>
<td>pinB-O</td>
<td>91</td>
</tr>
<tr>
<td>pinB-N</td>
<td>84(^b)</td>
</tr>
</tbody>
</table>

\(^a\) Diborylated products were produced in 12–17\% yield.\(^b\) Reaction conducted at 100 \(^\circ\)C.\(^c\) Ratio of 3- and 4-boryl pyridine was 67:33.
- **Indole Borylation**

\[
\begin{align*}
R - \text{Indole} + 1.5\text{HBpin} & \xrightarrow{1.5\text{mol}\%\ [\text{Ir}(\text{COD})(\text{OMe})_2\text{]}_2, 3\text{mol}\%\ \text{dbpy}} \text{hexanes, 60 }^\circ\text{C} \quad \text{Bpin} \\
\text{product} & \quad \% \text{yield} & \quad \text{product} & \quad \% \text{yield} & \quad \text{product} & \quad \% \text{yield} \\
\text{Bpin} & \quad 78\% & \quad \text{Bpin} & \quad 83\% & \quad \text{Bpin} & \quad 90\% \\
\text{Bpin} & \quad 91\% & \quad \text{Bpin} & \quad 82\% & \quad \text{Bpin} & \quad 45\% \\
\text{Bpin} & \quad 88\% & \quad \text{Bpin} & \quad 64\% & \quad \text{Bpin} & \quad 76\% \\
\text{Bpin} & \quad 82\% & \quad \text{Bpin} & \quad 79\% & \quad \text{Bpin} & \quad 69\% \\
\text{Bpin} & \quad 92\% & \quad \text{Bpin} & \quad 90\% & \\
\end{align*}
\]
• Proposed Mechanism for the Iridium-Catalyzed Borylation of Arenes
4. Application

- One-Pot Syntheses of Organic Compounds

I. One-Pot Syntheses of Phenols and Arylamines
II. One-Pot Syntheses of Aryl Bromides and Aryl Chlorides

<table>
<thead>
<tr>
<th>entry</th>
<th>product</th>
<th>yield</th>
<th>entry</th>
<th>product</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Br 61%</td>
<td>6</td>
<td>Me</td>
<td>Br 75%</td>
</tr>
<tr>
<td></td>
<td>MeO</td>
<td>Cl 75%</td>
<td>11</td>
<td>Br</td>
<td>Br 80%</td>
</tr>
<tr>
<td>2</td>
<td>Br 65%</td>
<td></td>
<td>7</td>
<td>Br 65%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MeO</td>
<td>Cl 65%</td>
<td>12a</td>
<td>Br</td>
<td>Br 72%</td>
</tr>
<tr>
<td>3</td>
<td>Br 62%</td>
<td></td>
<td>8</td>
<td>Br 67%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F3C</td>
<td></td>
<td>13oa</td>
<td>Br</td>
<td>Br 51%</td>
</tr>
<tr>
<td>4</td>
<td>Br 75%</td>
<td></td>
<td>9a</td>
<td>Br</td>
<td>Br 74%</td>
</tr>
</tbody>
</table>
|       | F3C     |       |       | Me      | Piv 0%
| 5     | Br 59%  |       | 10f   | Br      | Br 57% |

- Average isolated yield from two experiments. All reactions were run on a 2.0 mmol scale. 
- 0.5 mol % 1 and 1.0 mol % 2 were used.
- Contained 2% pinacol by 1H NMR spectroscopy. 
- 3.0 mol % 1 and 6.0 mol % 2 used. 
- 1.0 mol % 1 and 2.0 mol % 2 used.
- 2.0 mol % 1 and 4.0 mol % 2 used.
III. Conversion of Arenes to Arylboronic Acids and Potassium Aryltrifluoroborates

Borylation of arene was carried out on a 10 mmol scale using 0.1% [Ir(COD)Cl]₂ and 0.2% dtbpy in THF at 80 °C. NaIO₄ (15.0 mmol) was added to 5 mmol of crude ArBpin in a 4:1 THF/H₂O mixture. Isolated yields on a 5 mmol scale of arene.
1. In contrast to many of these methods, the borylation of aryl C-H bonds occurs under mild conditions, with high turnover numbers and with a broad tolerance for functional groups.

2. Considering the rapid development of this C-H borylation chemistry, one can anticipate that further advances will lead to C-H bond functionalizations with main group reagents that will lead, in turn, to additional, widely used synthetic methods.
Thank you