# Catalytic Asymmetric Synthesis of Chiral Tertiary Organoboronic Esters through Conjugate Boration of *β*-Substituted Cyclic Enones

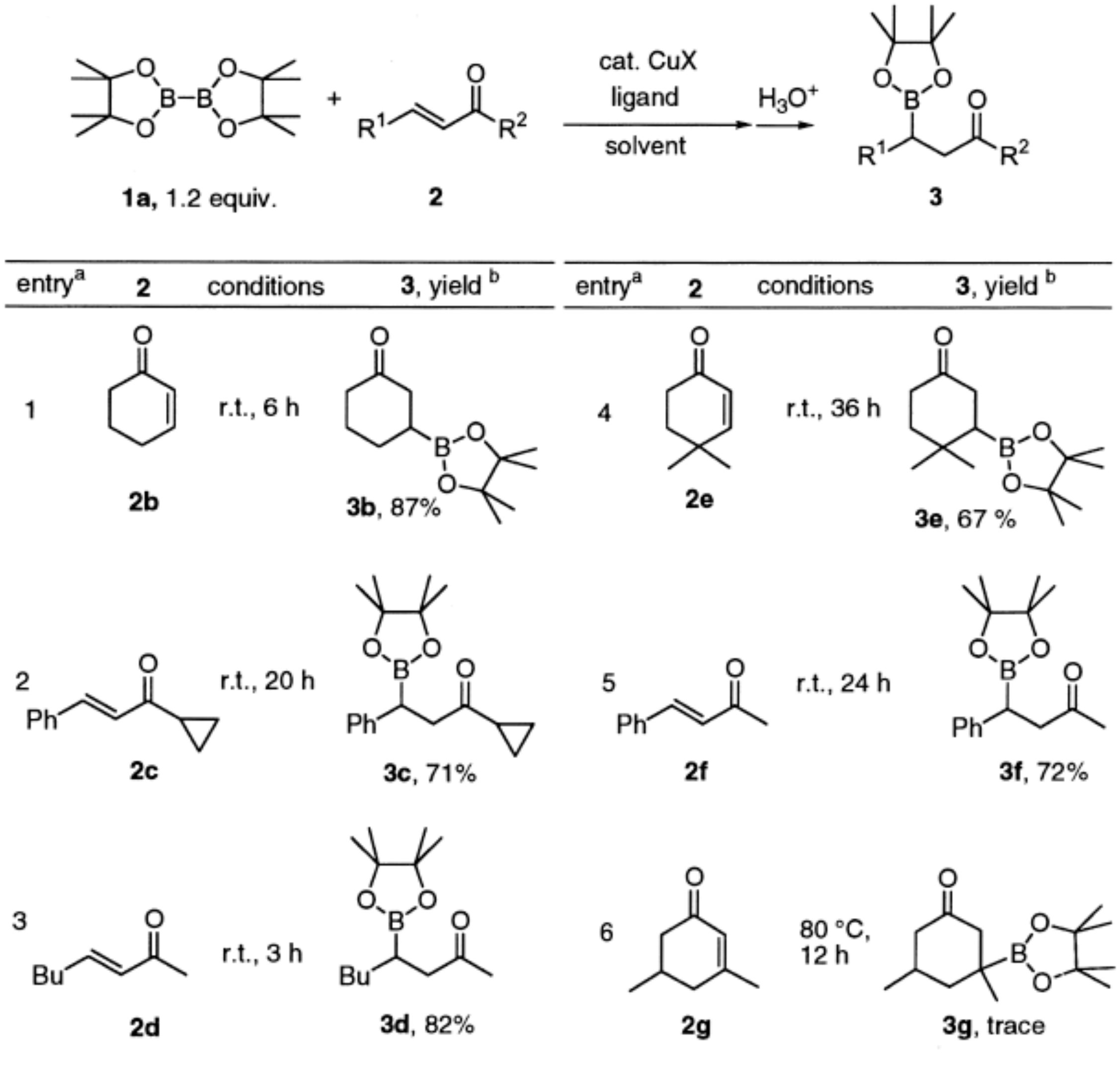
*J. Am. Chem. Soc.,* Article ASAP

DOI: 10.1021/ja9045839

Yong Guan

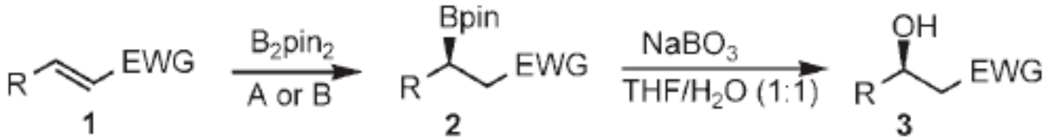
2009-08-14

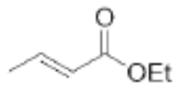
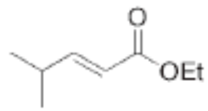
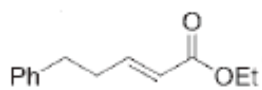
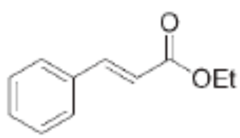
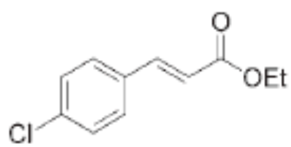
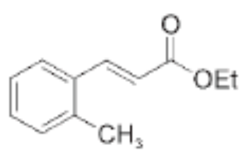
# Racemic System

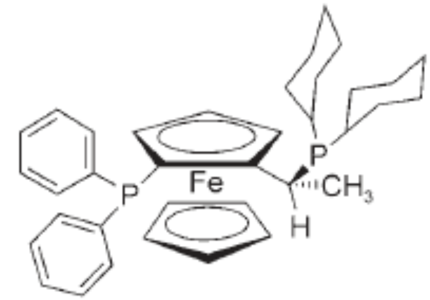



Ito, H.; Yamanaka, H.; Tateiwa, J.; Hosomi, A. *Tetrahedron Lett.* **2000,** *41*, 6821.

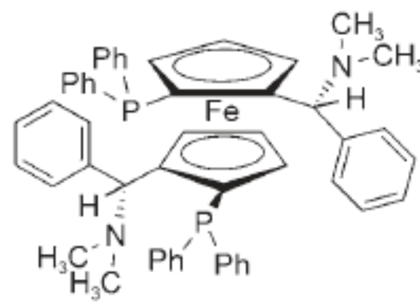
# Catalytic Asymmetric Boration of Acyclic $\alpha,\beta$-Unsaturated Esters and Nitriles




| Entry | Substrate | Condition[b] | Yield of **2** [%][c] | *ee* of **3** [%][d] |
|---|---|---|---|---|
| 1 |  **1a** | A | 94 | 90 (*R*) |
| 2 |  **1b** | A | 92 | 91 (*S*) |
| 3 |  **1c** | A | 97 | 89 |
| 4 |  **1d** | A | 93 | 90 (*S*) |
| 5 | | B | 94 | 87 (*S*) |
| 6 |  **1e** | A | 90 | 91 (*S*) |
| 7 |  **1f** | A | 87 | 88 |



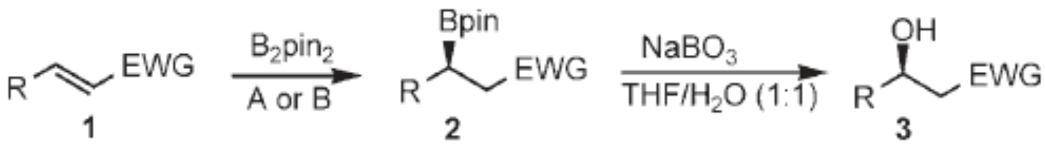
L1 (*R*)-(*S*)-josiphos

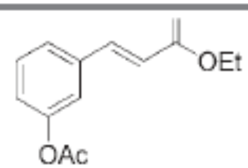
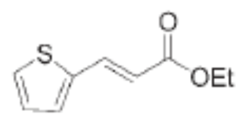
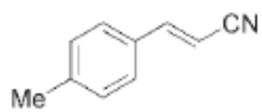
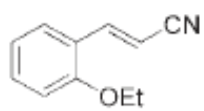
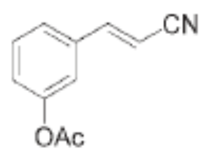


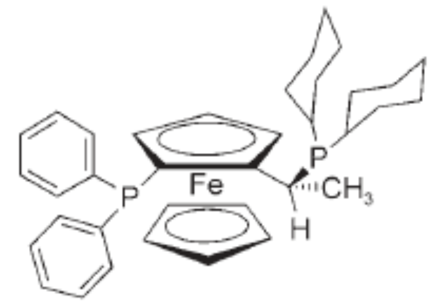
L2 (*R*)-(*S*)-NMe$_2$-PPh$_2$-mandyphos

Lee, J.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 145.

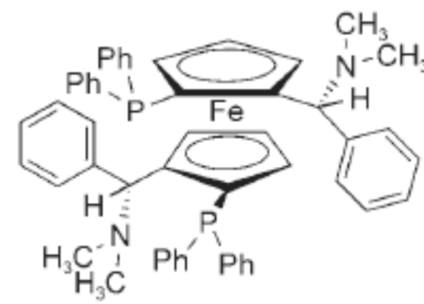
# Catalytic Asymmetric Boration of Acyclic $\alpha,\beta$-Unsaturated Esters and Nitriles




| Entry | Substrate | | Condition[b] | Yield of **2** [%][c] | *ee* of **3** [%][d] |
|---|---|---|---|---|---|
| 8 |  | **1g** | A | 95 | 87 |
| 9 | | | B | 89 | 84 |
| 10 |  | **1h** | A | 93 | 82 |
| 11 |  | **1i** | A | 94 | 90 (*S*) |
| 12 |  | **1j** | A | 90 | 92 |
| 13 |  | **1k** | B | 94 | 91 |



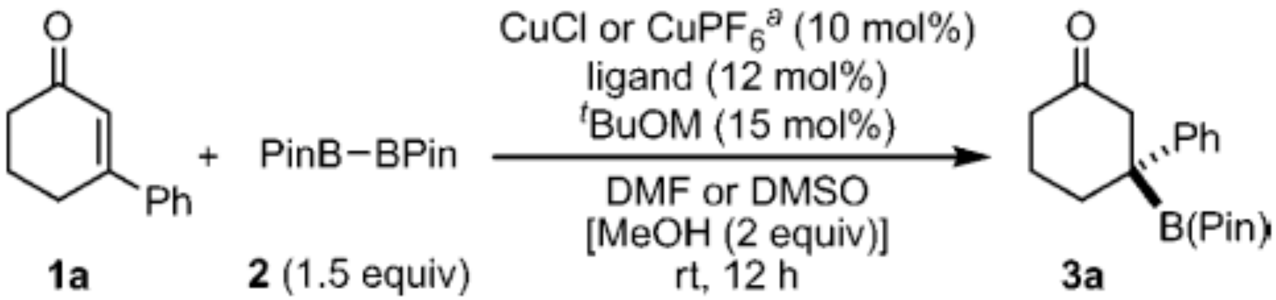

L1 (*R*)-(*S*)-josiphos

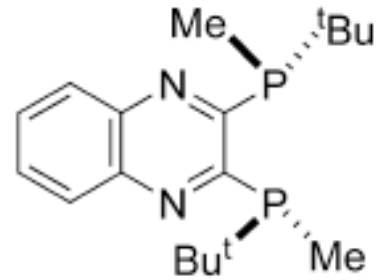



L2 (*R*)-(*S*)-$NMe_2$-$PPh_2$-mandyphos

Lee, J.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 145.

# Optimization



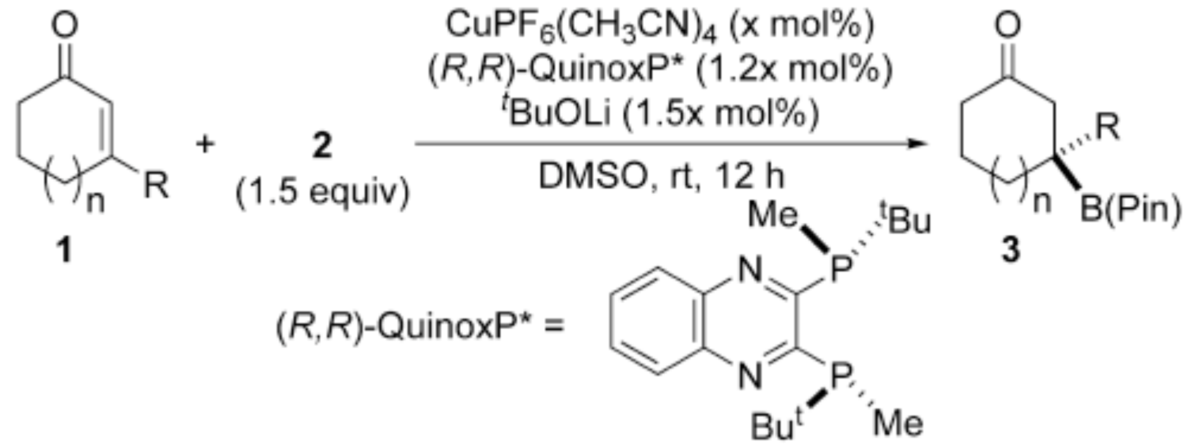




QuinoxP*

| entry | M | ligand | solv. | MeOH | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|---|
| 1 | Na | *rac*-BINAP | DMF | – | 10 | – |
| 2 | Li | *rac*-BINAP | DMF | – | 55 | – |
| 3 | Li | *rac*-BINAP | DMSO | + | 11 | – |
| 4 | Li | tol-BINAP | DMF | – | 82 | 48 |
| 5 | Li | DTBM-SEGPHOS | DMF | – | 23 | 11 |
| 6 | Li | Ph-BPE | DMF | – | 90 | 27 |
| 7 | Li | JOSIPHOS | DMF | – | 55 | 20 |
| 8 | Li | QuinoxP* | DMF | – | 78 | 91 |
| 9 | Li | QuinoxP* | DMSO | – | 90 | 98 |
| 10[d] | Li | QuinoxP* | DMSO | – | 88 | 98 |
| 11[d] | Na | QuinoxP* | DMSO | – | 61 | 96 |
| 12[d] | K | QuinoxP* | DMSO | – | 57 | 93 |

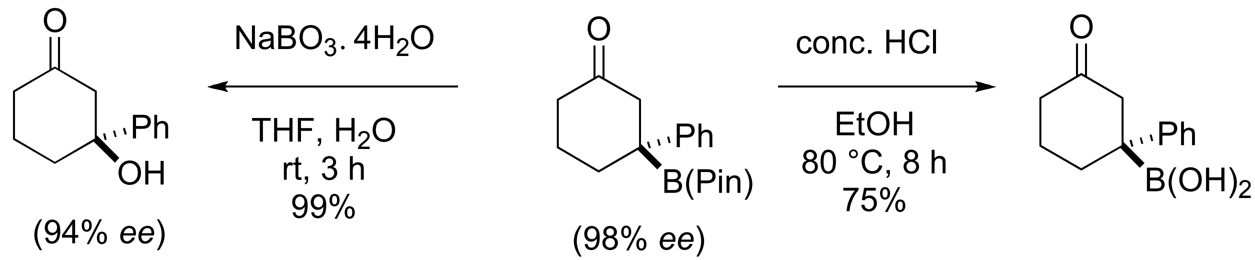
[a] In entry 1, CuCl was used. In other entries, $CuPF_6(CH_3CN)_4$ was used. [b] Isolated yield. [c] Determined by chiral GC. [d] 5 mol % of catalyst.

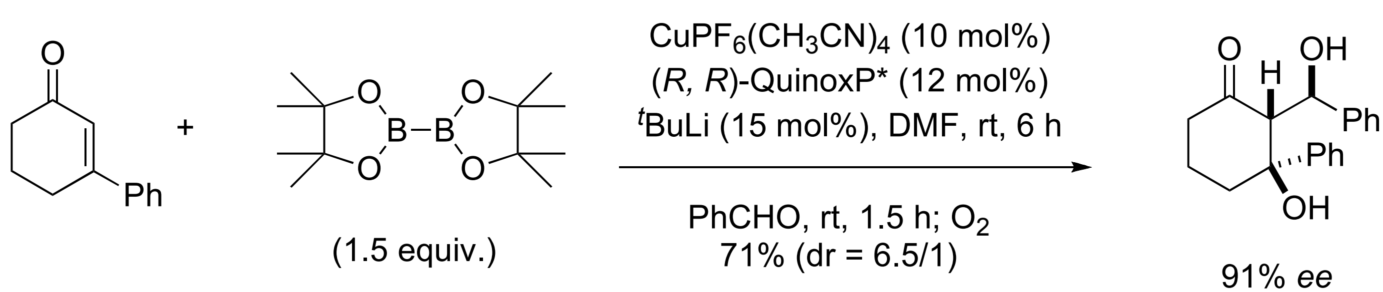
# Substrate Scope



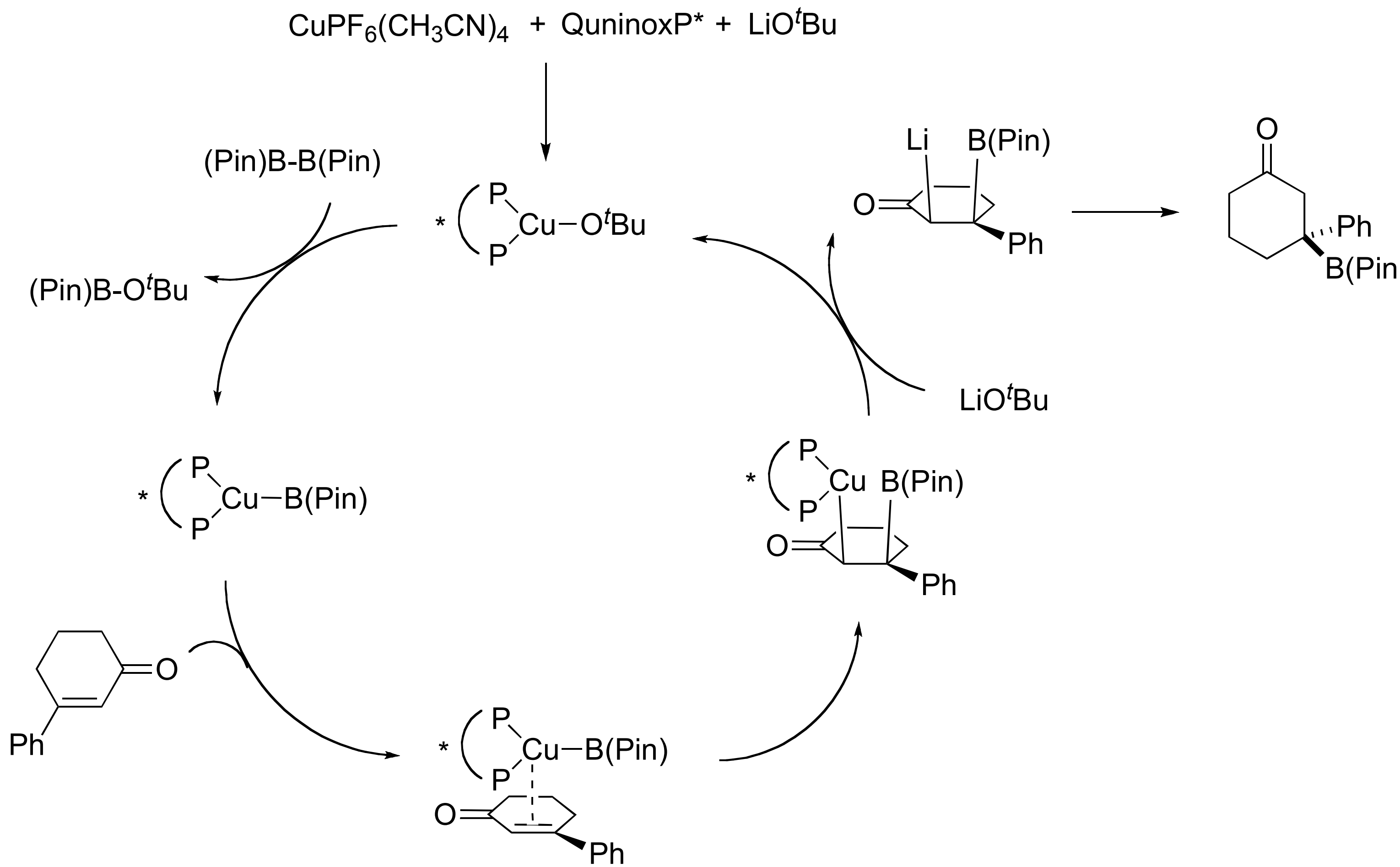

| entry | substrate | *x* (mol %) | yield (%)[a] | ee (%)[b] |
|---|---|---|---|---|
| 1 | R = Ph, *n* = 1 (**1a**) | 5 | 88 | 98[d] |
| 2 | R = *p*-MeO-$C_6H_4$, *n* = 1 (**1b**) | 10 | 84 | 93 |
| 3 | R = *p*-Me-$C_6H_4$, *n* = 1 (**1c**) | 10 | 86 | 95 |
| 4 | R = *p*-F-$C_6H_4$, *n* = 1 (**1d**) | 5 | 80 | 93 |
| 5 | R = *m*-MeO-$C_6H_4$, *n* = 1 (**1e**) | 10 | 83 | 95 |
| 6 | R = *m*-Me-$C_6H_4$, *n* = 1 (**1f**) | 10 | 89 | 98 |
| 7[c] | R = Me, *n* = 1 (**1g**) | 5 | 91 | 81 |
| 8 | R = $^i$Pr, *n* = 1 (**1h**) | 10 | 91 | 94 |
| 9 | R = $^i$Bu, *n* = 1 (**1i**) | 10 | 92 | 85 |
| 10 | R = Ph, *n* = 0 (**1j**) | 10 | 85 | 98 |
| 11 | R = $^i$Bu, *n* = 0 (**1k**) | 10 | 94 | 70 |
| 12 | R = Ph, *n* = 2 (**1l**) | 10 | 99 | 98 |

# Transformations and Extension



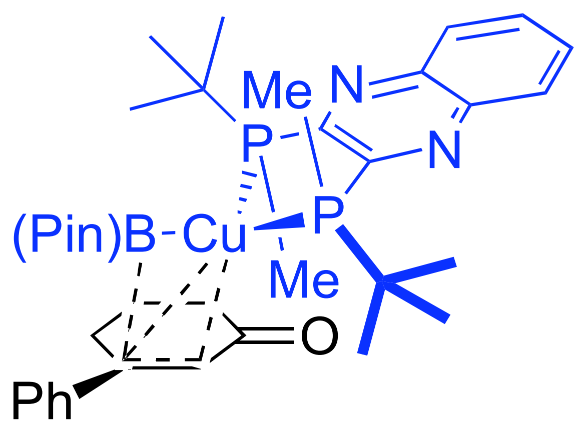



# Mechanism

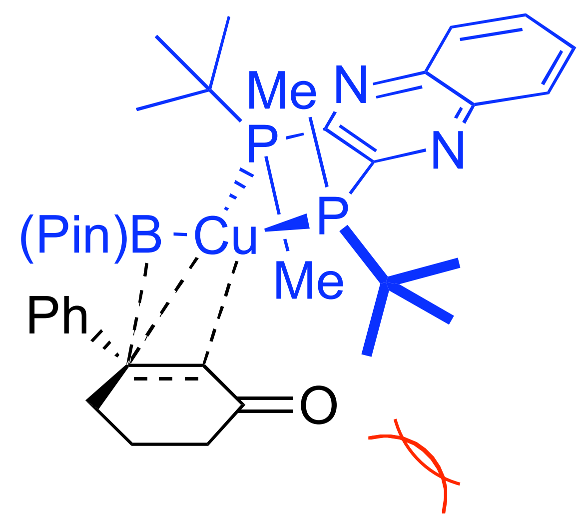



Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem.Soc.* **2007**, *129*, 14856.

# Transition States




**Favored TS**




**Unfavored TS**


Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem.Soc.* **2007**, *129*, 14856.

# THANK YOU