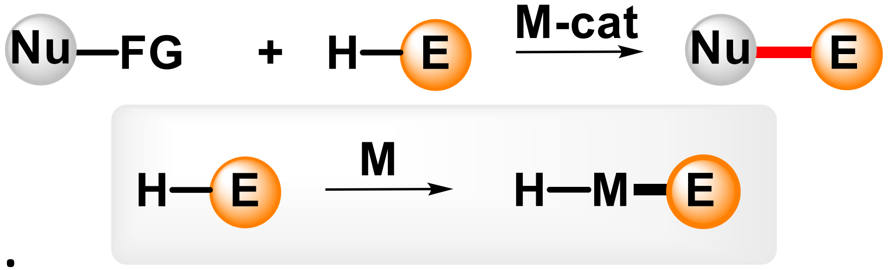
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

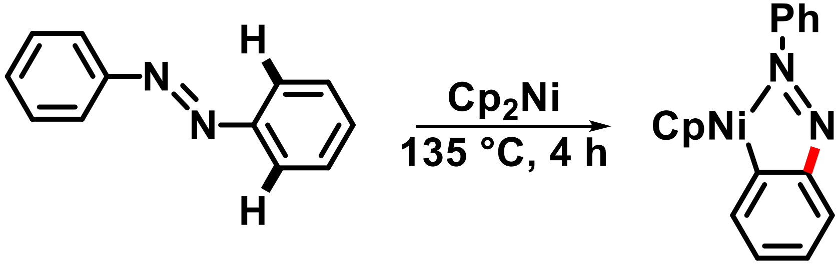
➢ C–H activation



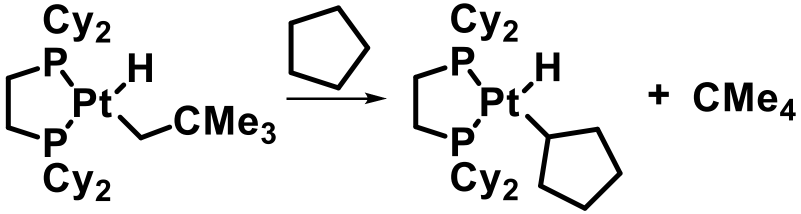
- Transition-metal-free C–H activation:

- Transition metal mediated C–H activation

○ Intramolecular C–H activation (cyclometallation):



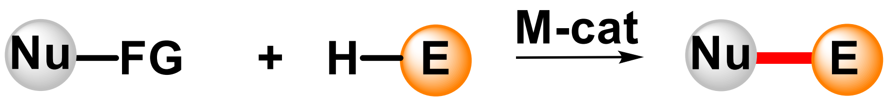
○ Intermolecular C–H activation:

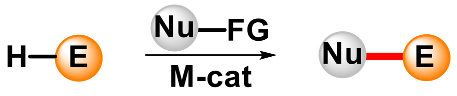


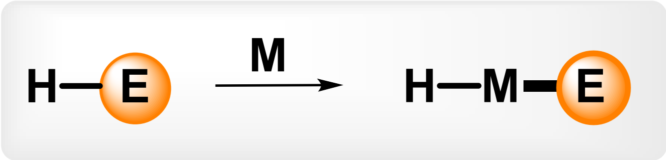
UCT PRAGUE

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

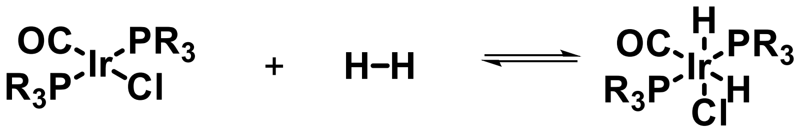
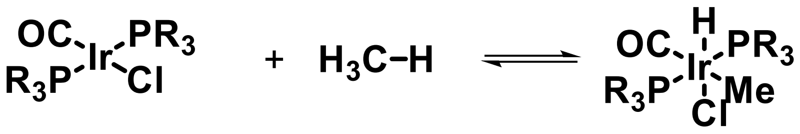
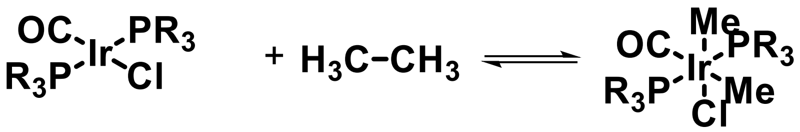
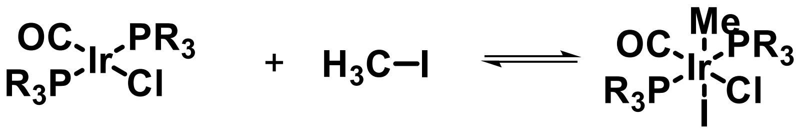
➢ C–H activation



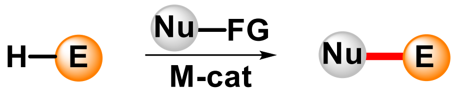




- **Thermodynamics of oxidative addition for Vaska´s complex**

	Estimated ΔH (kcal/mol)	Estimated ΔG (kcal/mol)
	-15	-6
	-2	+3
	-4	+6
	-35	-25

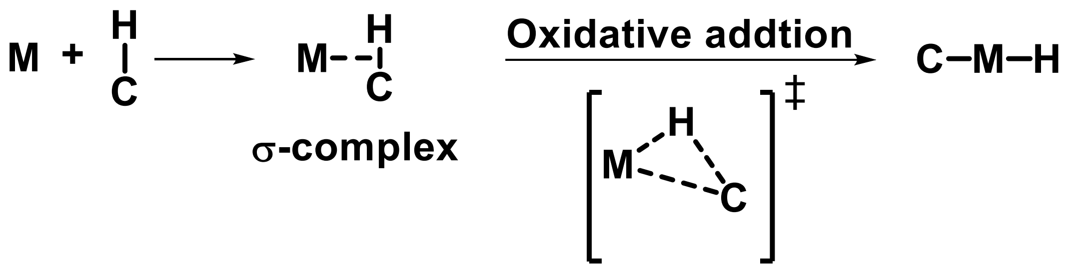
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



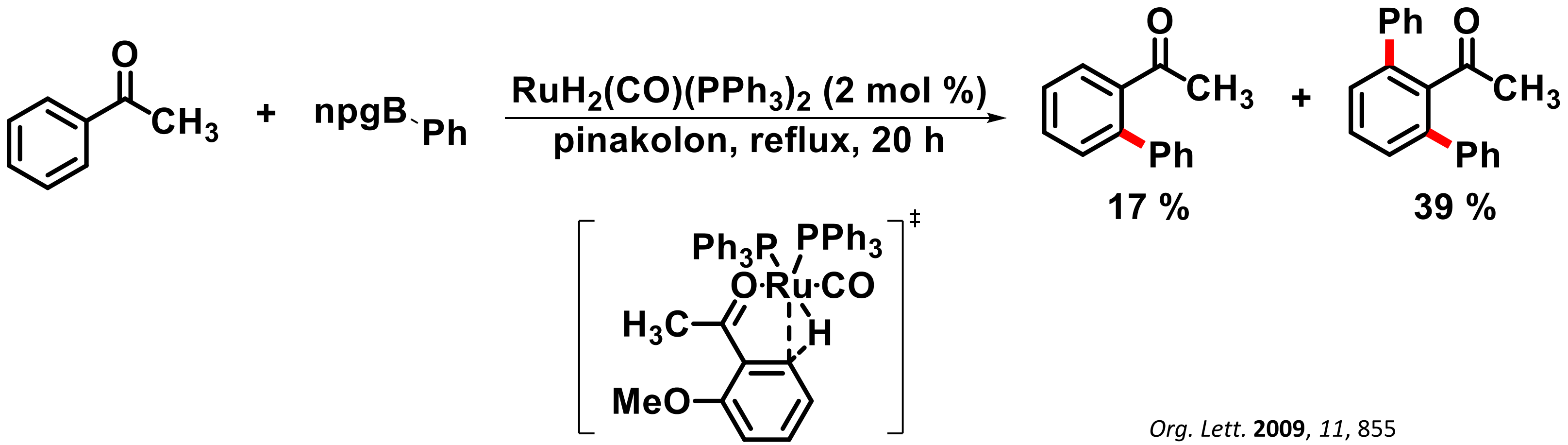
➢ C–H activation

- Mechanism of C–H activation

  - Concerted mechanism



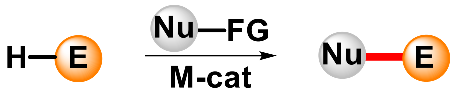
  - Selected example

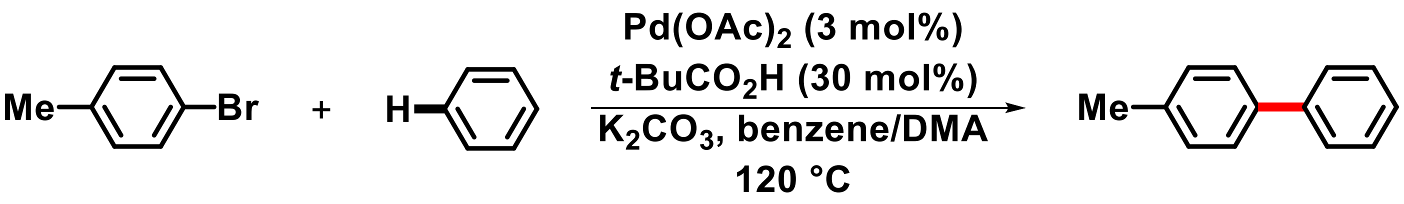


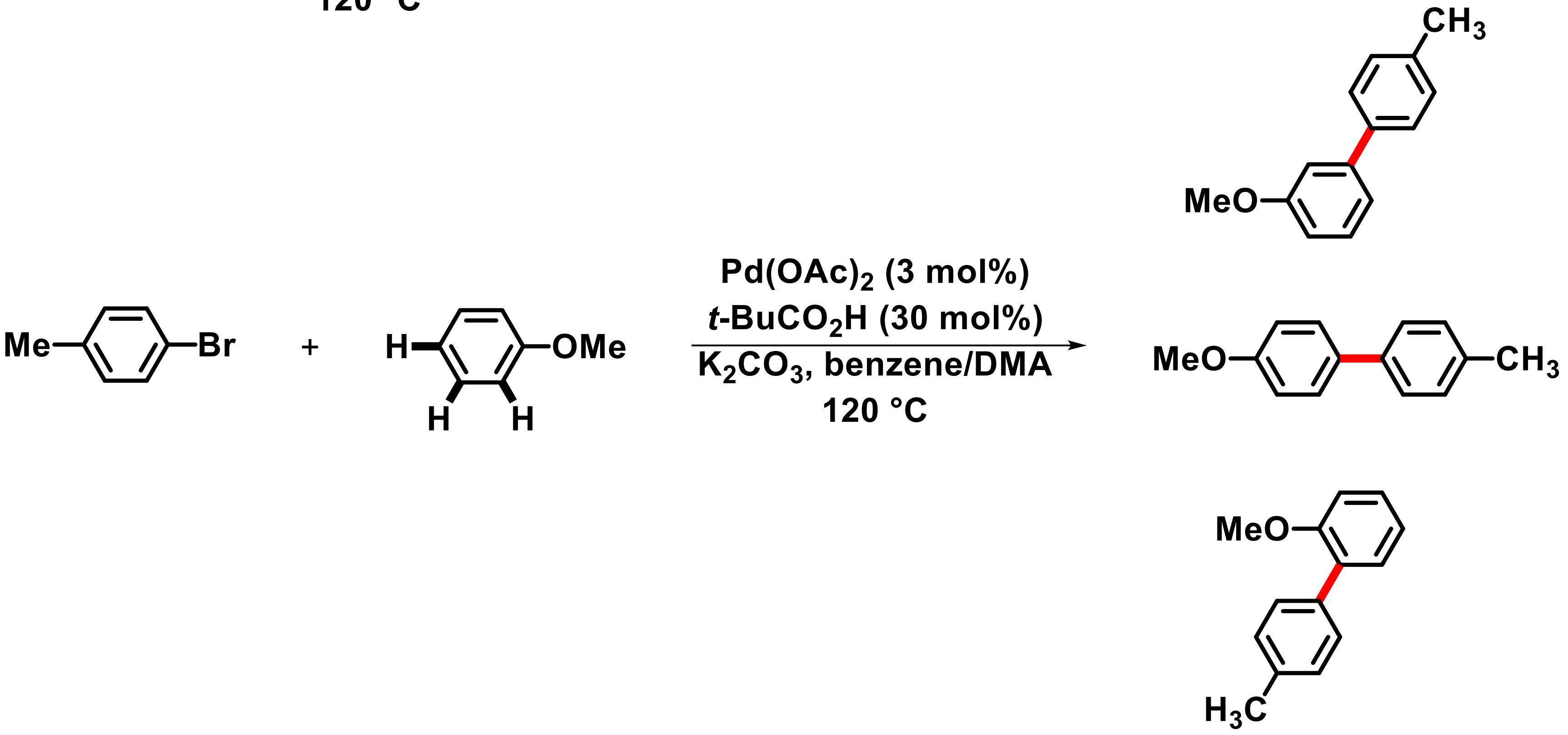
Org. Lett. **2009**, *11*, 855

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

➢ C–H activation







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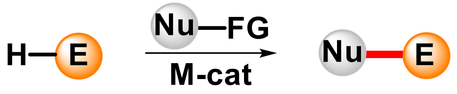
J. Am. Chem. Soc. **2006**, *128*, 16496

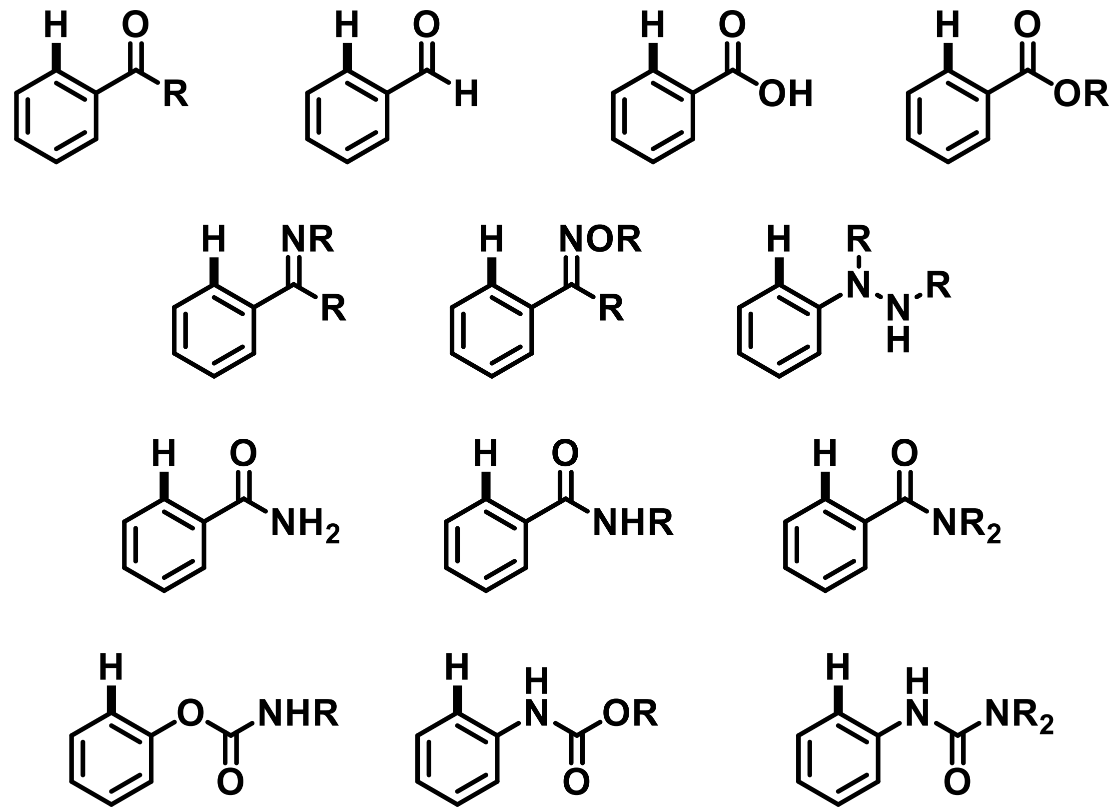
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

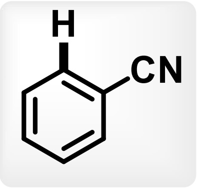


➢ C–H activation

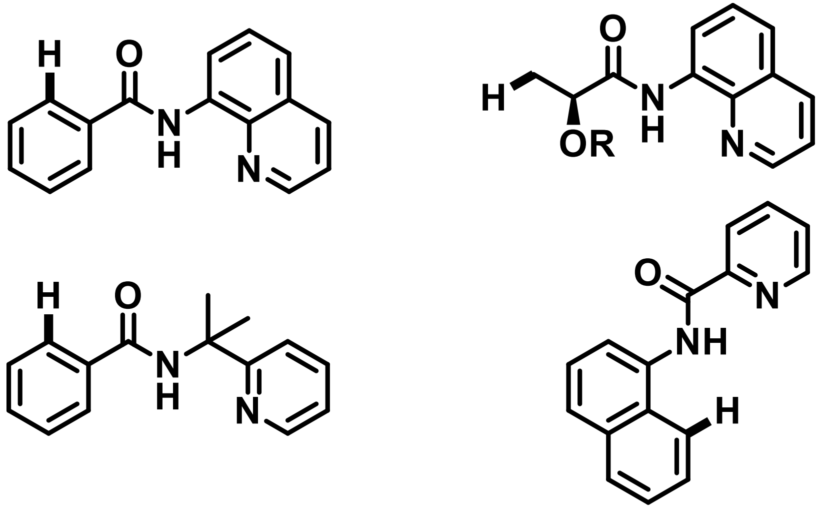
- Directing groups

  - ○ Monodentade directing groups

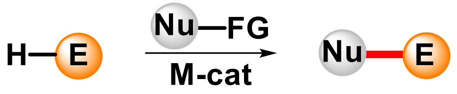




  - ○ Bidentate directing groups

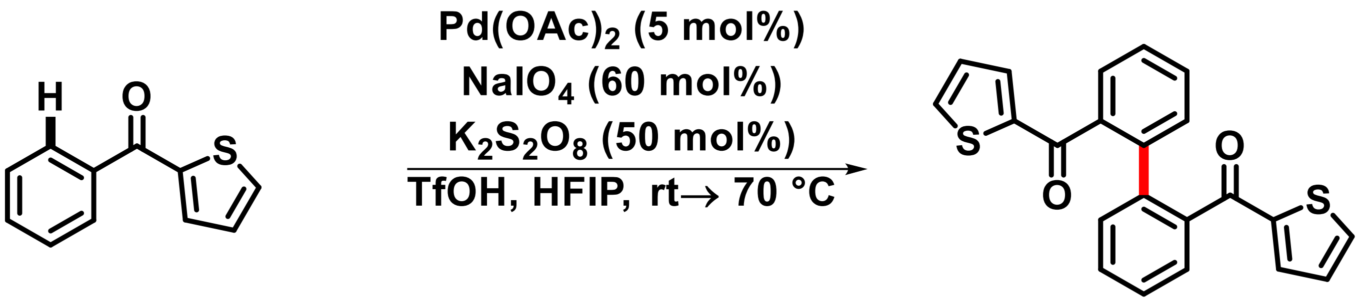


Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



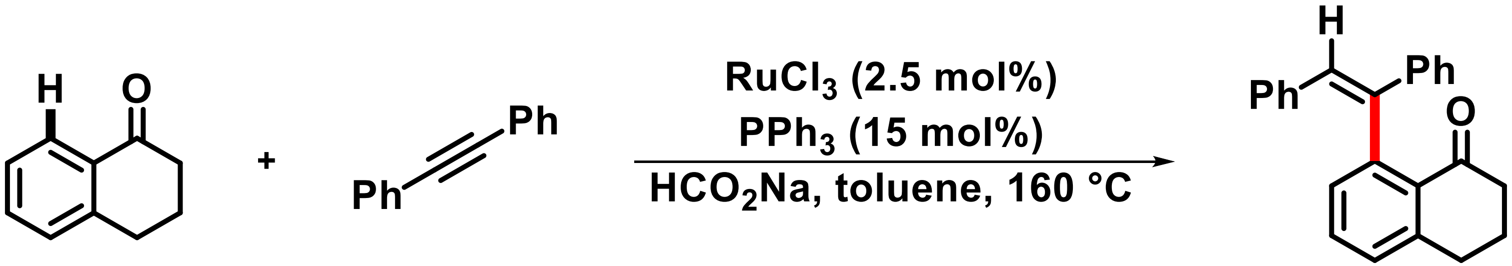
➢ C–H activation

- *Ortho* directing groups



50%

Org. Lett. **2015**, *17*, 4456



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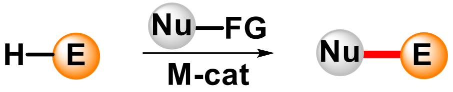
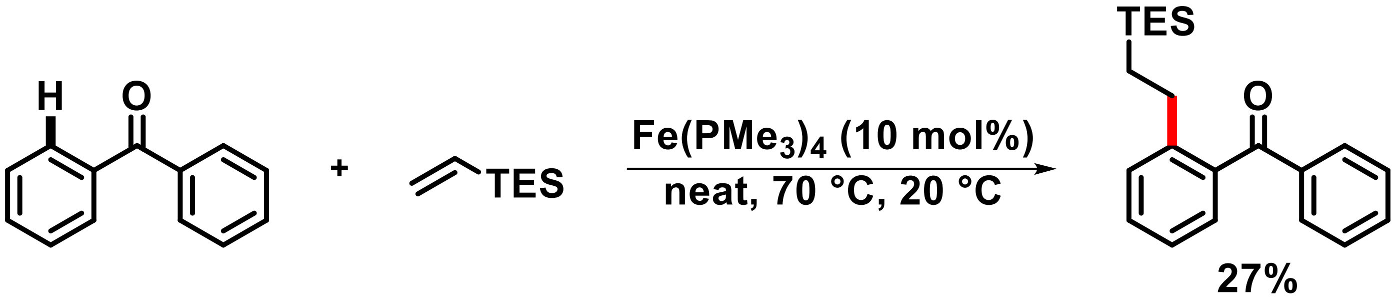
Chem. Commun. **2016**, *52*, 9715

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

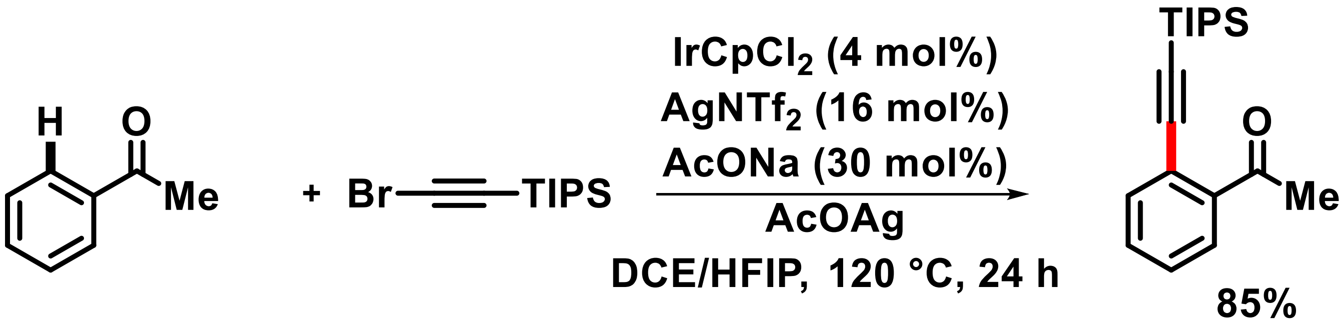


➢ C–H activation

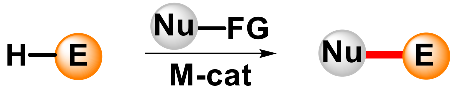
- *Ortho* directing groups



J. Am. Chem. Soc. **2017**, *139*, 14849

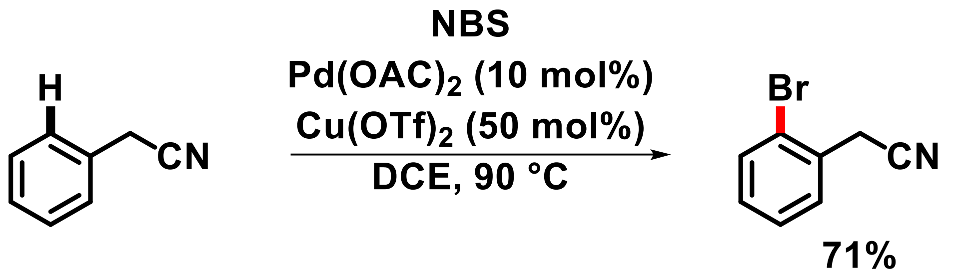


J. Org. Chem. **2017**, *82*, 13003

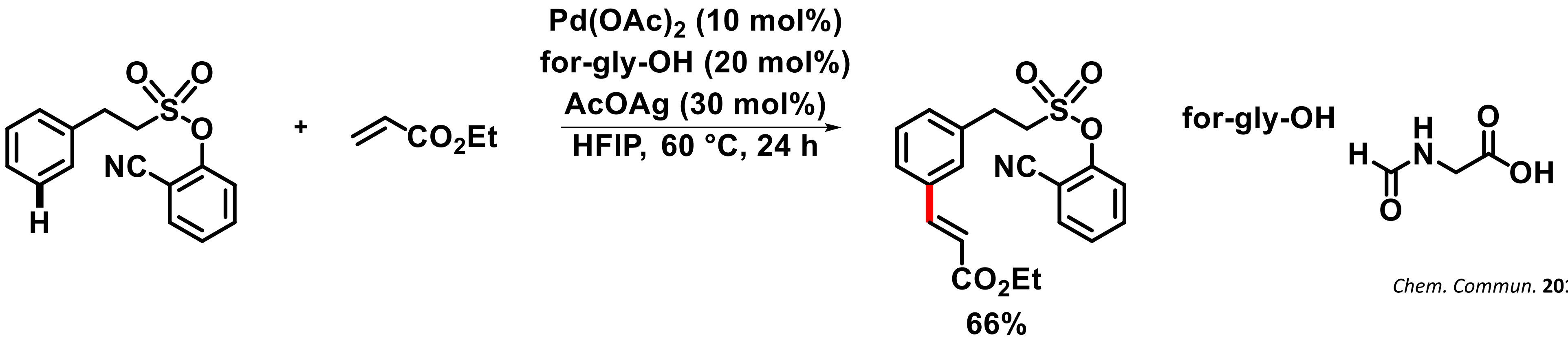


➢ C–H activation

- *Meta*-directing groups

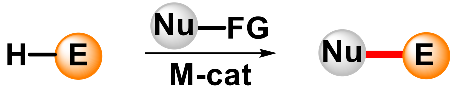


J. Org. Chem. **2017**, *82*, 1114



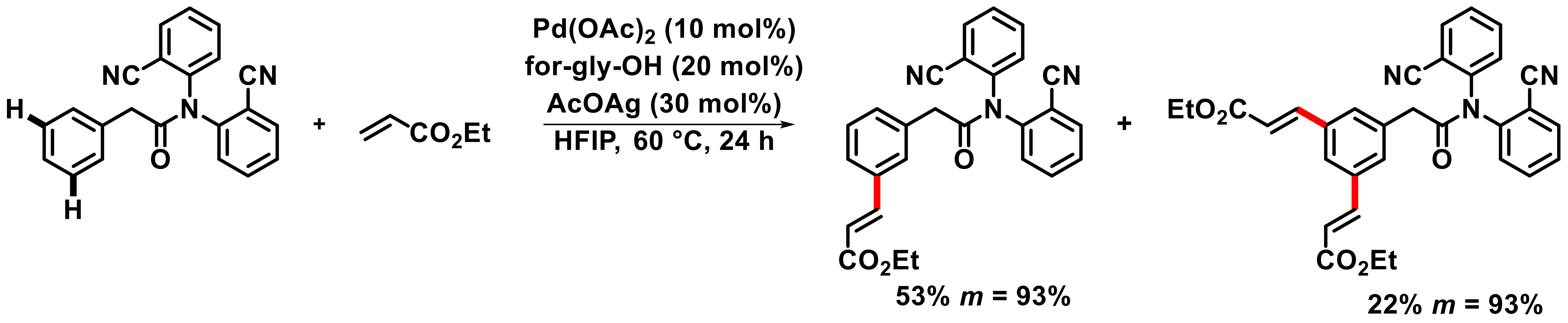
Chem. Commun. **2016**, *52*, 13916

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ C–H activation

- *Meta*-directing groups



Angew. Chem., Int. Ed. **2015**, *54*, 888

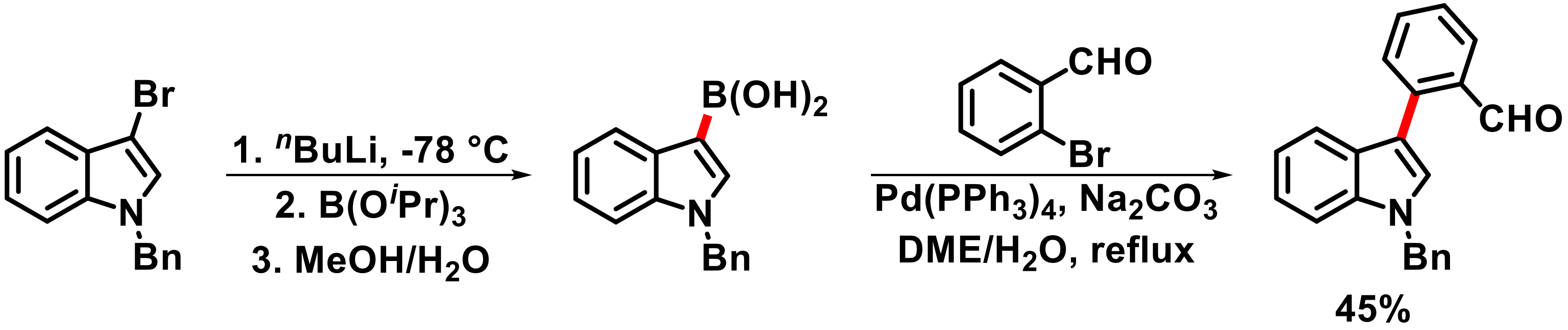
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

➢ C–H activation

Ar—H —[TM-cat, $(Bpin)_2$]→ Ar—Bpin

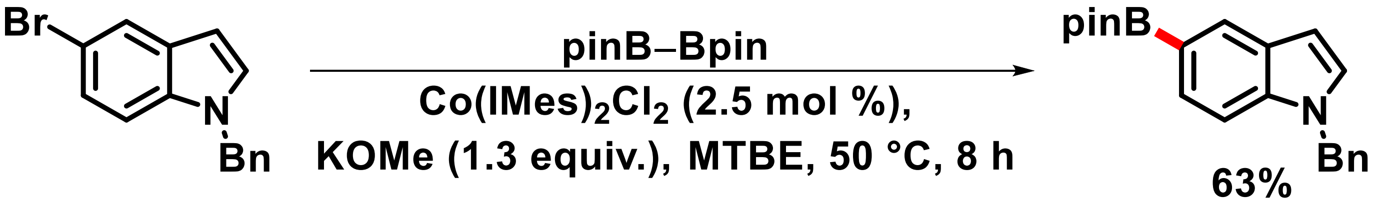
- C–H borylation

  - ○ **Traditional transition-metal-free borylation**



Tetrahedron **2008**, *64*, 9033

  - ○ **Miyaura borylation**

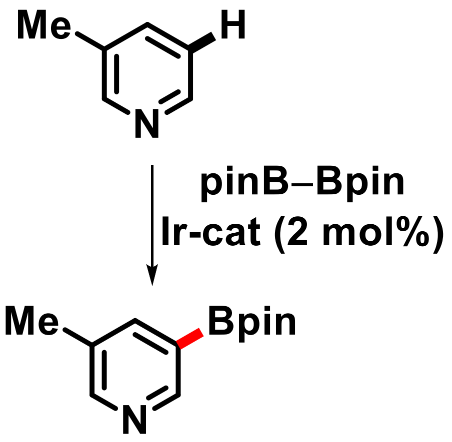


ACS Catal. **2018**, *8*, 4049

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

➢ C–H activation

- **C–H borylation**



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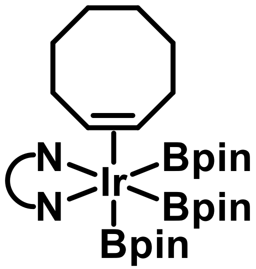
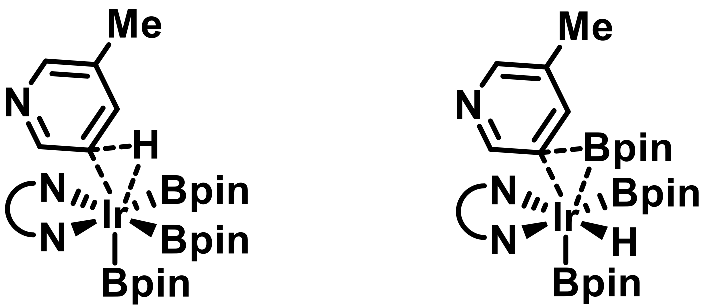
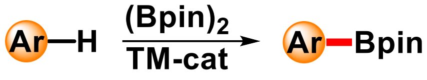


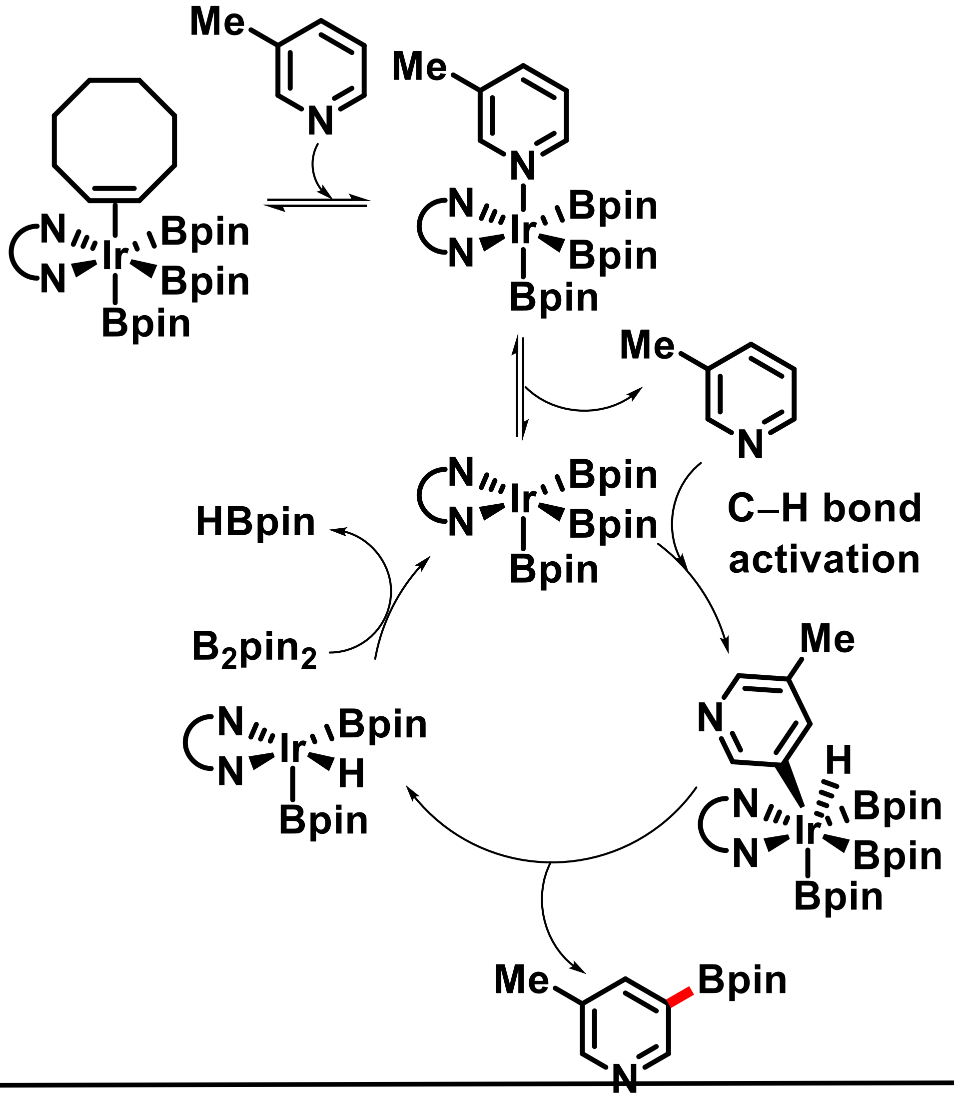
○ **Calculated transition states for C–H activation**



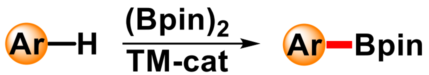
J. Am. Chem. Soc. **2014**, *136*, 4287

○ **Proposed mechanism**



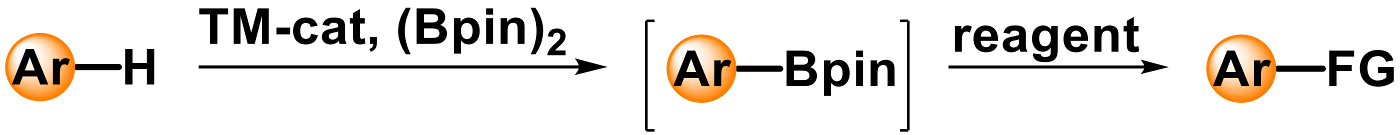


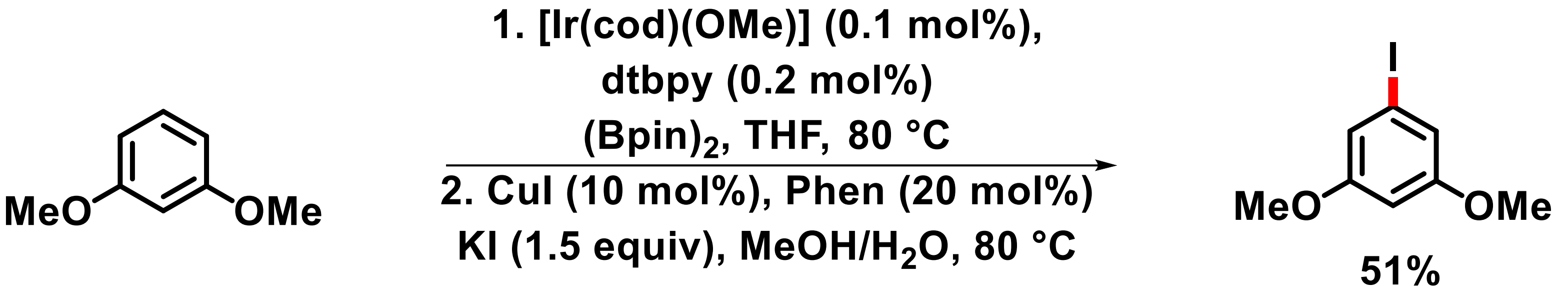
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ C–H activation

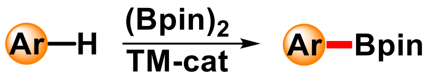
- C–H borylation – Selected applications



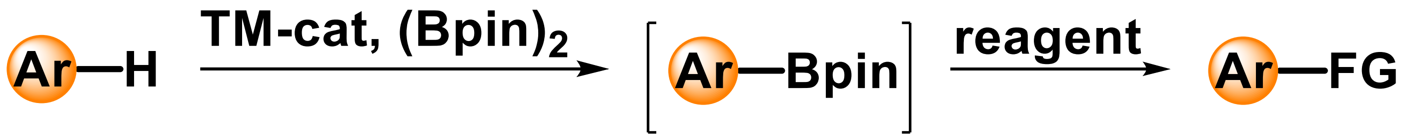


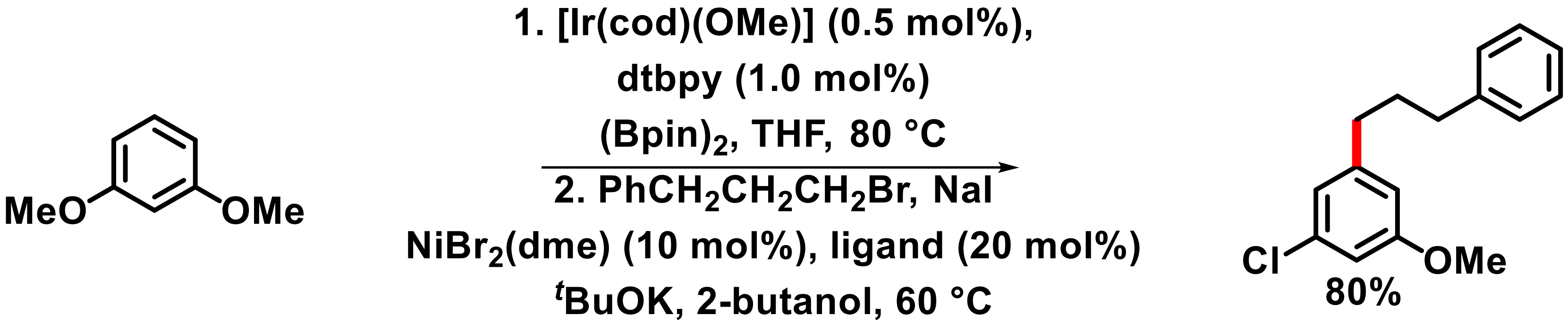
Org. Lett. **2013**, *15*, 140

➢ C–H activation



- C–H borylation – Selected applications

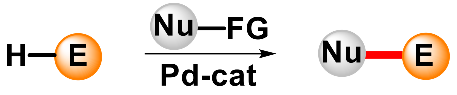




Angew. Chem. Int. Ed. **2013**, *15*, 933

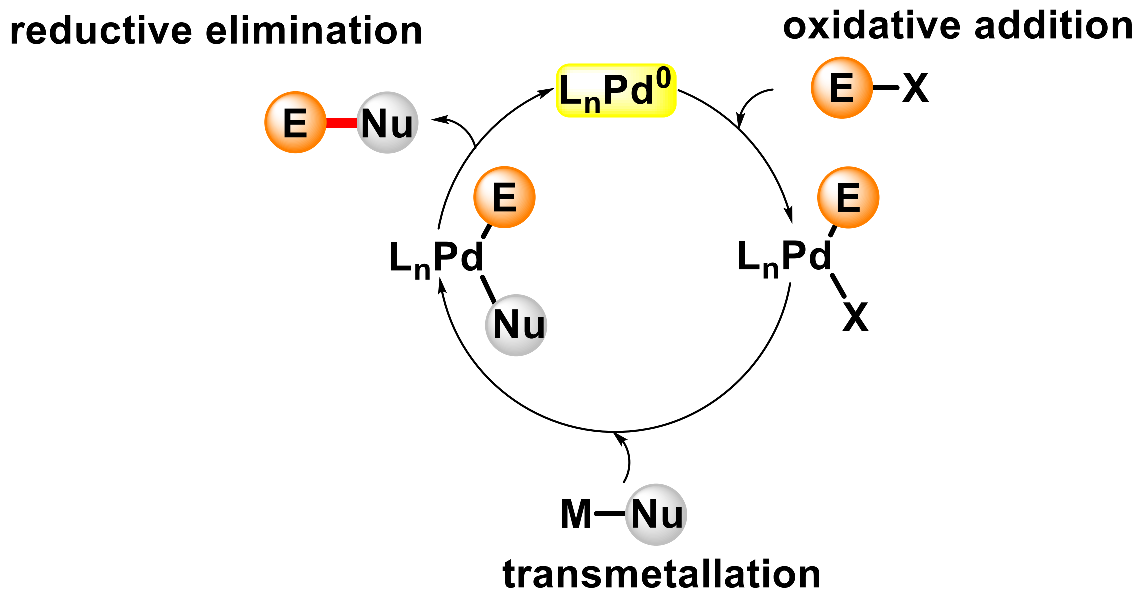
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

➢ C–H activation

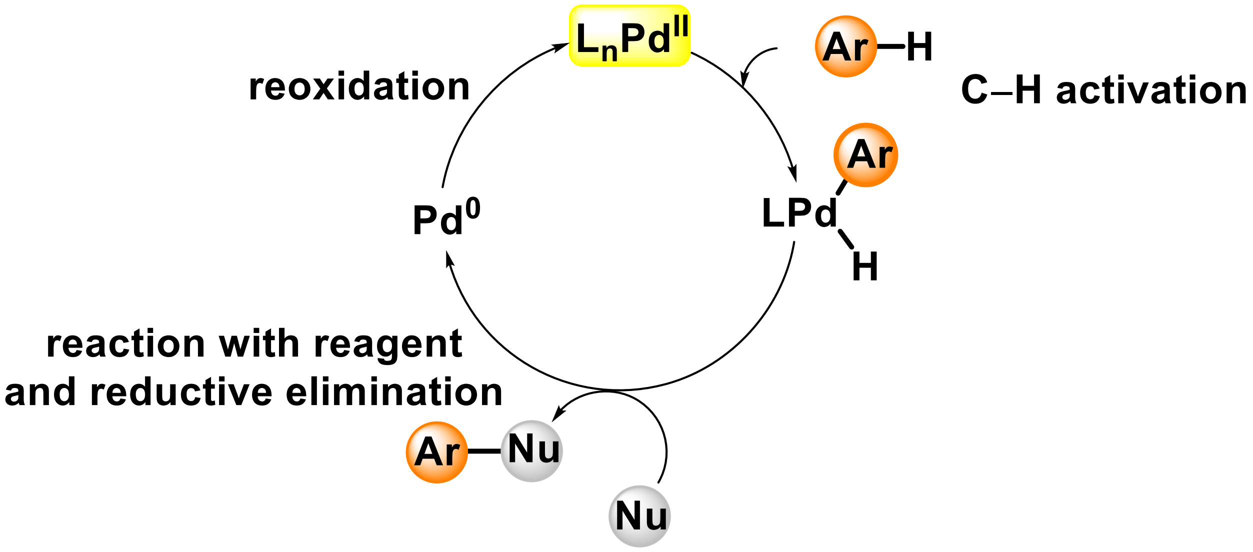


- Palladium catalyzed C–H activation

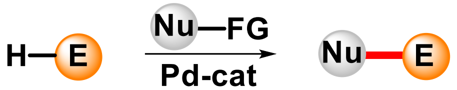
○ Traditional cross-coupling $Pd^0/Pd^{II}/Pd^0$:



○ Oxidative C–H activation $Pd^{II}/Pd^0/Pd^{II}$ catalysis:

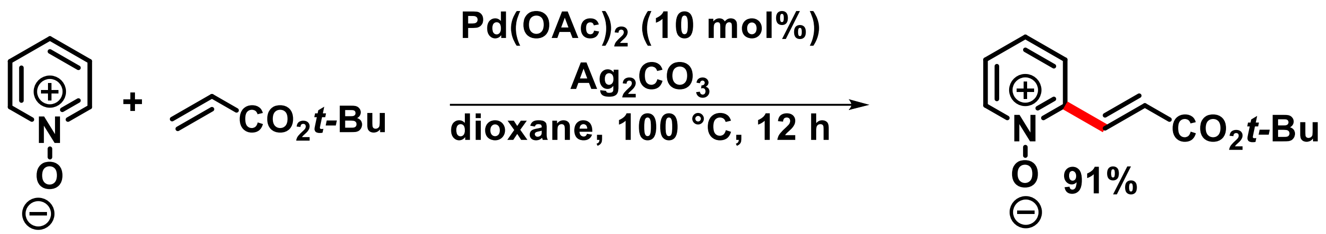


Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

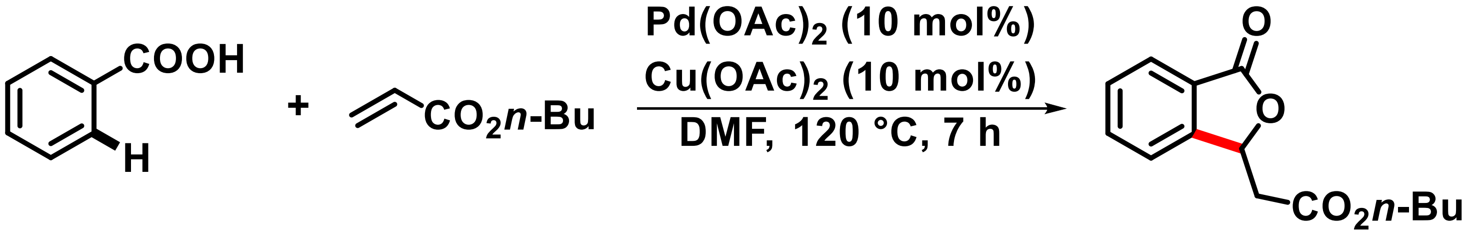


➢ C–H activation

- Selected examples for $Pd^{II}/Pd^{0}/Pd^{II}$ cat. cycle

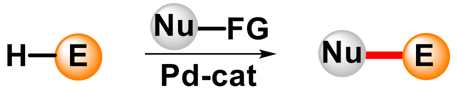


J. Am. Chem. Soc. **2008**, 130, 9254



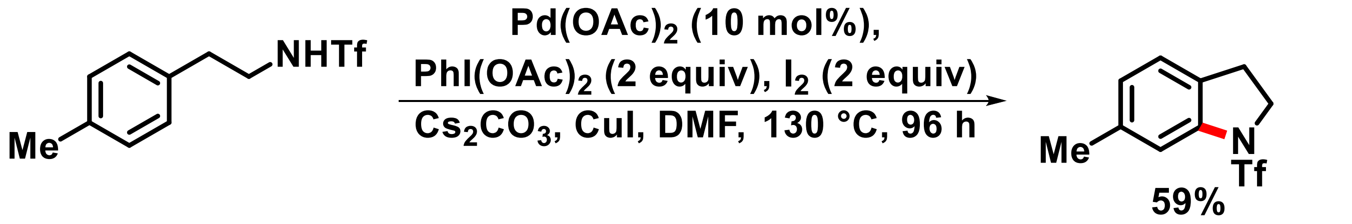
J. Org. Chem. **1998**, 63, 5211

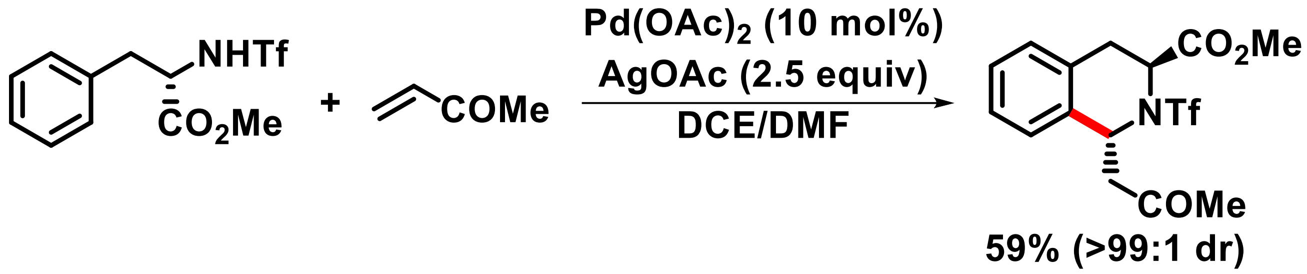
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ C–H activation

- Selected examples for $Pd^{II}/Pd^{0}/Pd^{II}$ cat. cycle

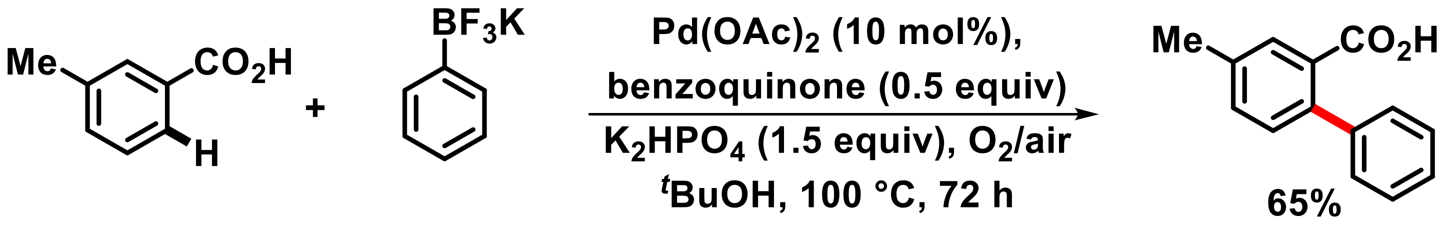




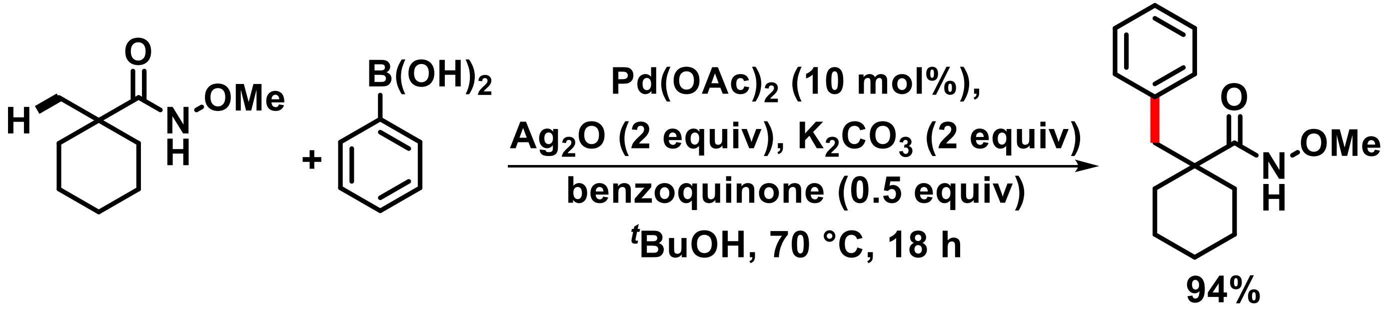
Angew. Chem. Int. Ed. **2008,** 47, 6452

➢ C–H activation

- C–H activation with organometallic reagents – Merged catalytic cycle

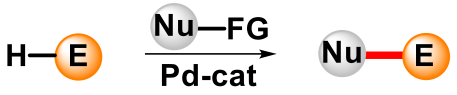


J. Am. Chem. Soc. **2008**, *130*, 17676



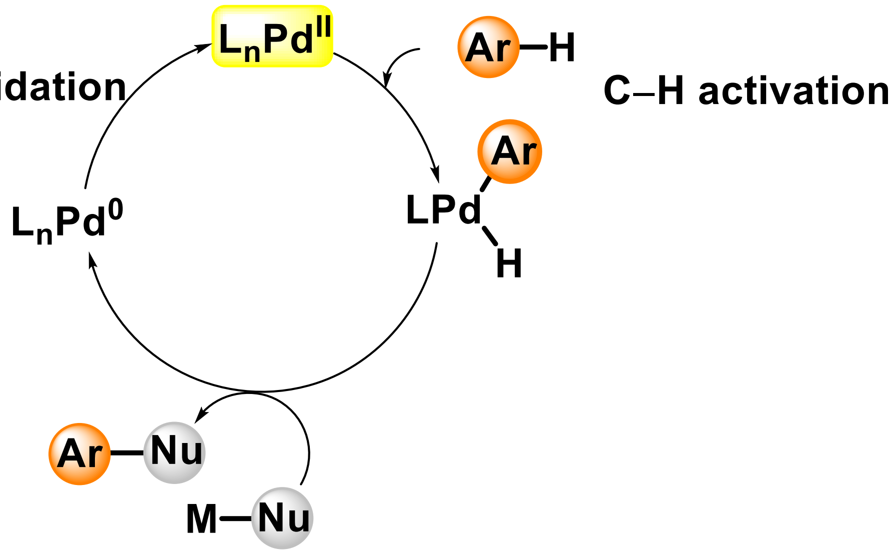
J. Am. Chem. Soc. **2008**, *130*, 7190

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



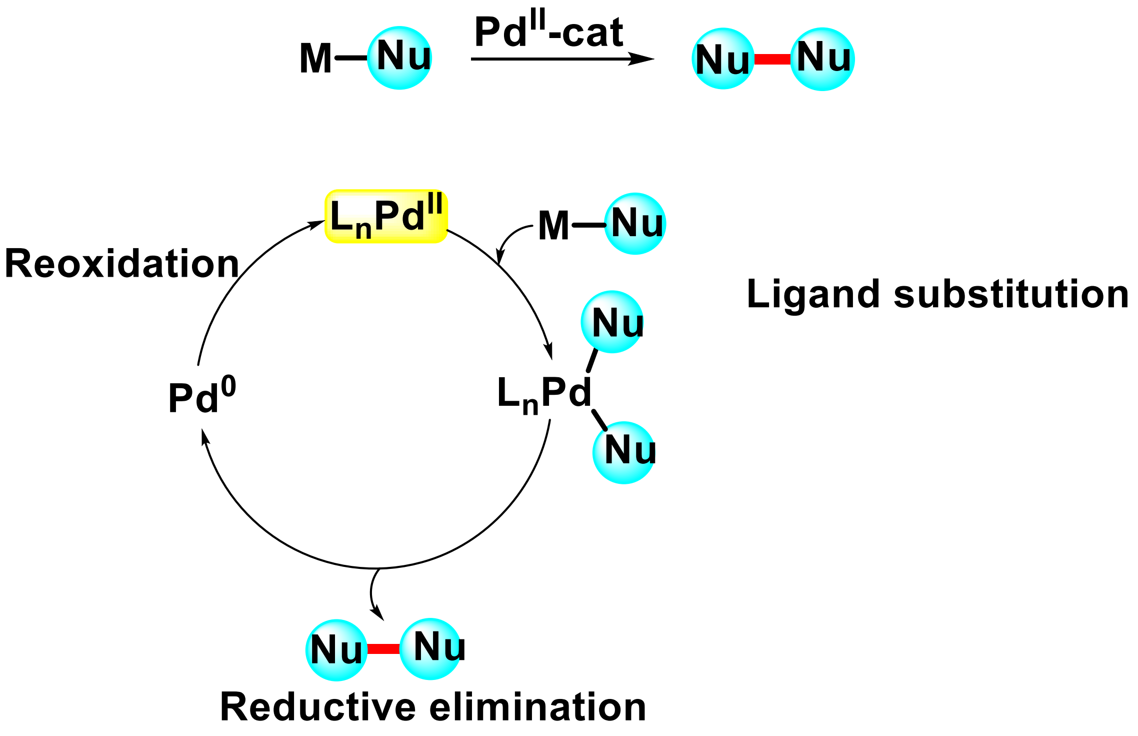
C–H activation

- C–H activation with organometallic reagents
  - Catalytic cycle

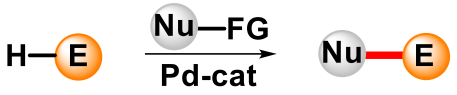


Reaction with organometallic reagent (M = $B(OR)_2$, SnR_3, etc) and reductive elimination

- Possible side reaction

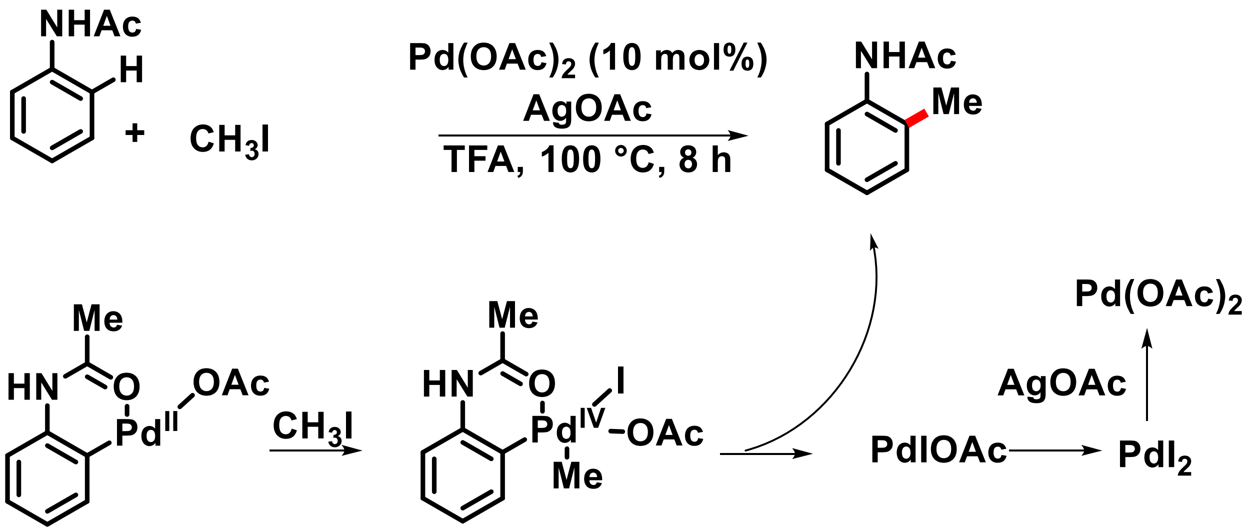


Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

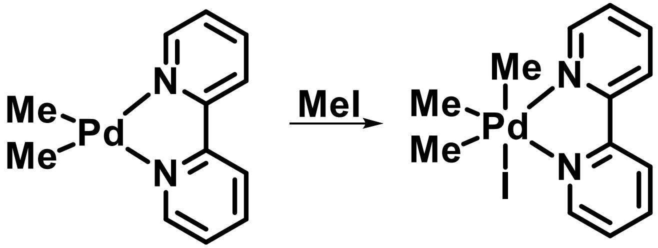


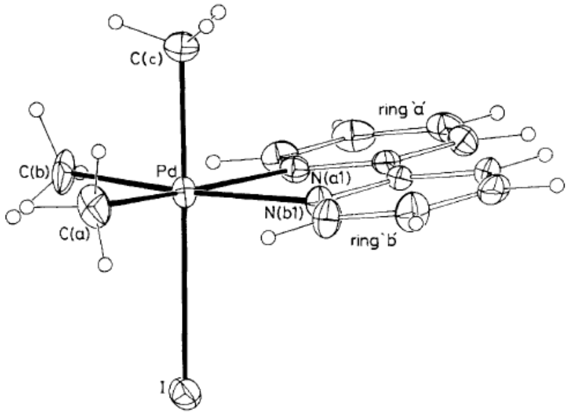
➢ C–H activation

- Pd^{II}/Pd^{IV} catalytic cycle



J. Am. Chem. Soc. **1984,** 106, 5759

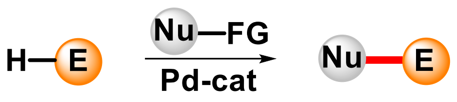




J. Chem. Soc. Chem. Commun. **1986,** 1722

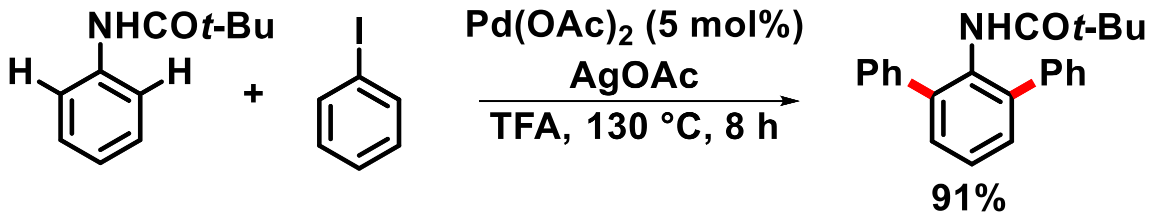
UCT PRAGUE

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



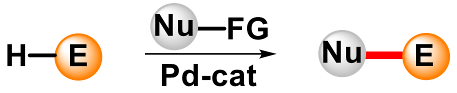
➢ C–H activation

- Pd^{II}/Pd^{IV} catalytic cycle



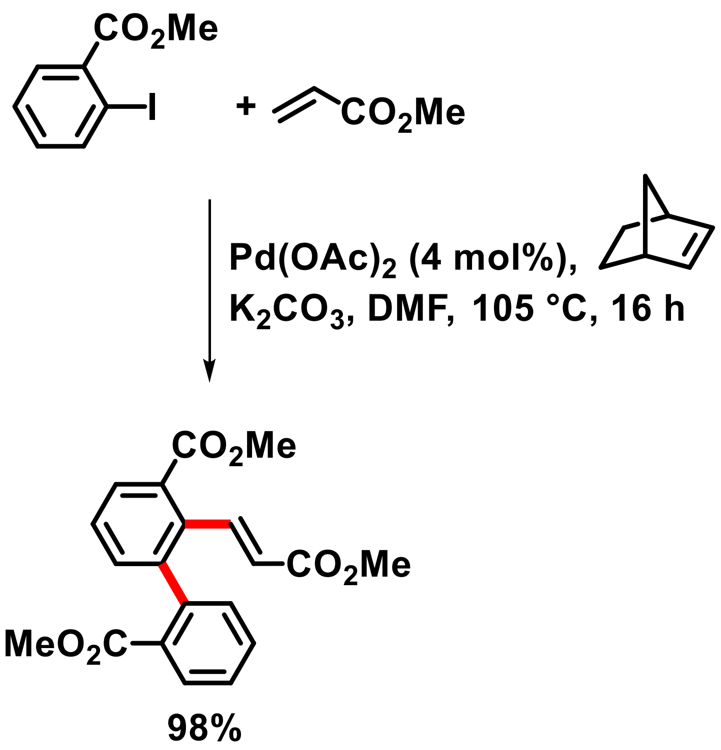
J. Am. Chem. Soc. **2005**, 127, 13154

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



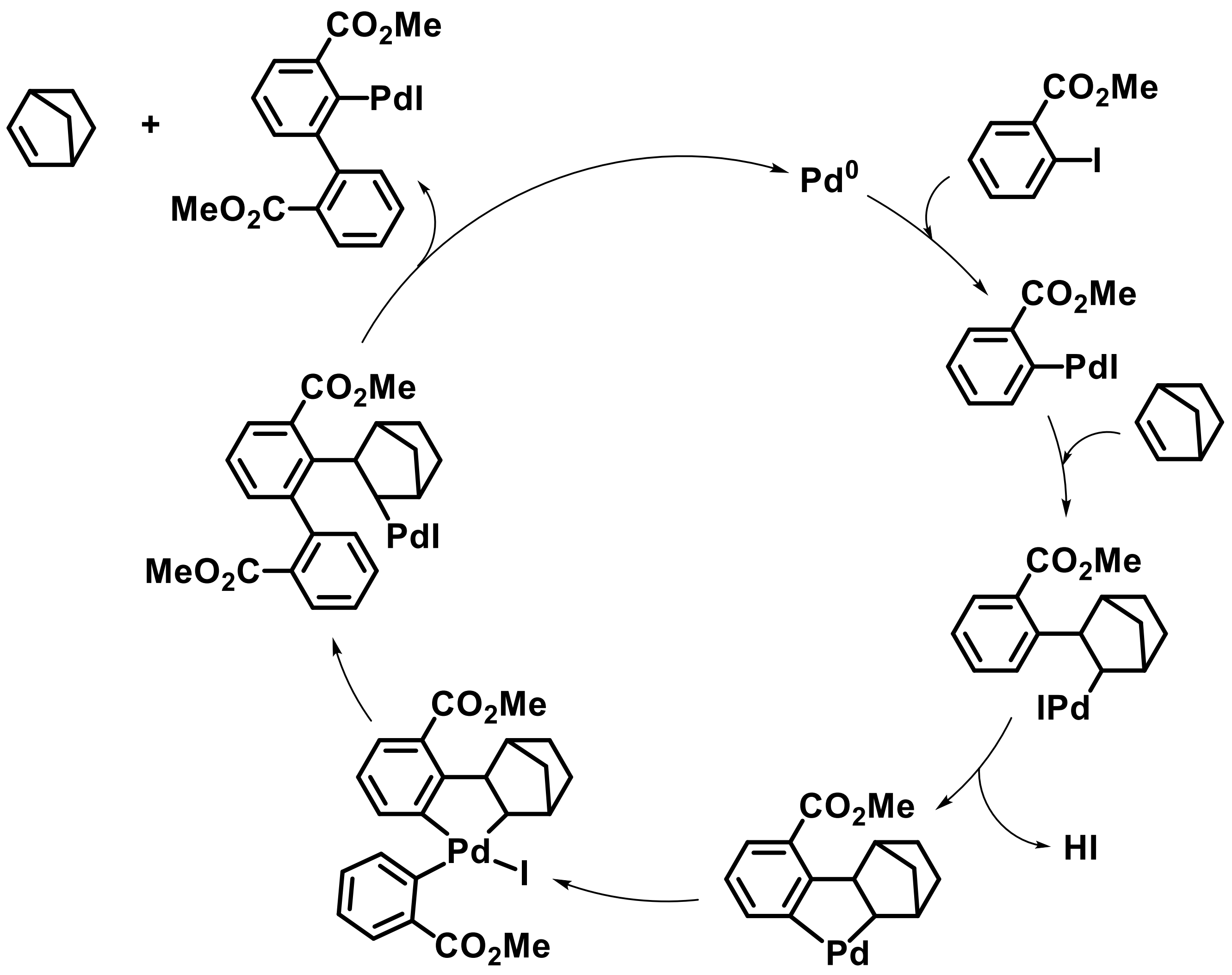
➢ C–H activation

- Pd^{II}/Pd^{IV} catalytic cycle – Catellani reaction



Synthesis **2003,** 2671

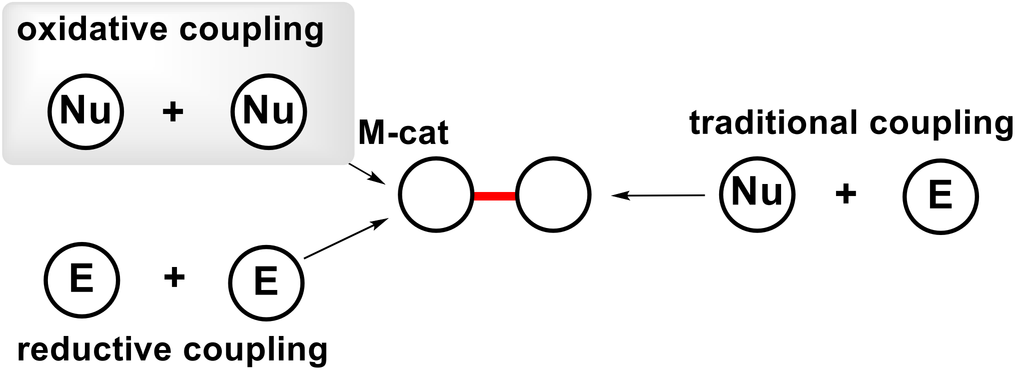
○ Proposed mechanism



Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

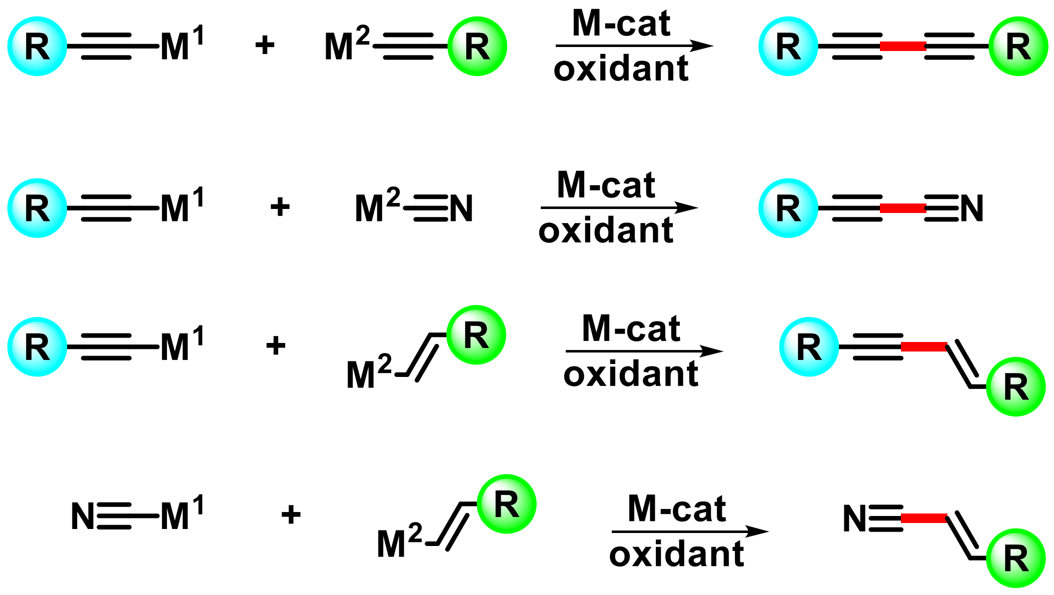
oxidative coupling

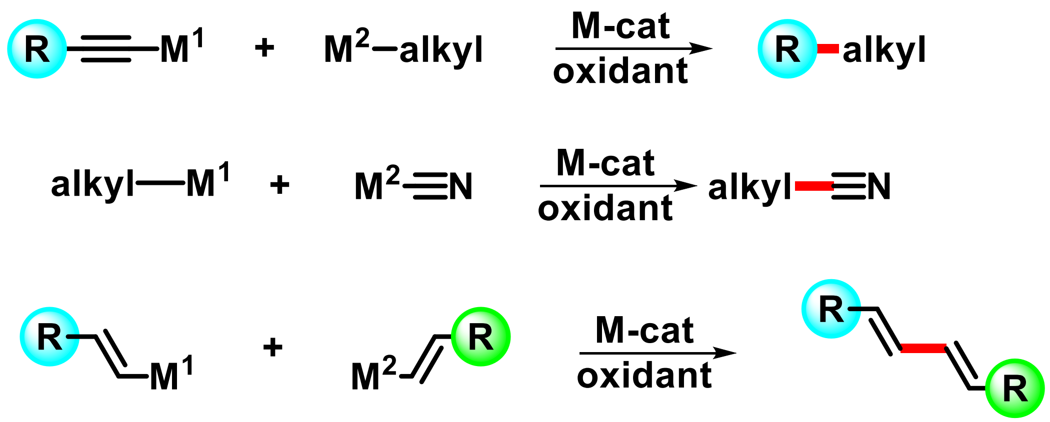
➢ Oxidative cross-coupling



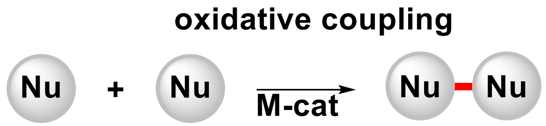
- Common oxidants:

Di(*terc*-butyl)peroxide (DTBP)
terc-butylhydroperoxide (TBHP)
Benzoquinone/O_2, O_2
$Cu(OAc)_2$, AgOAc



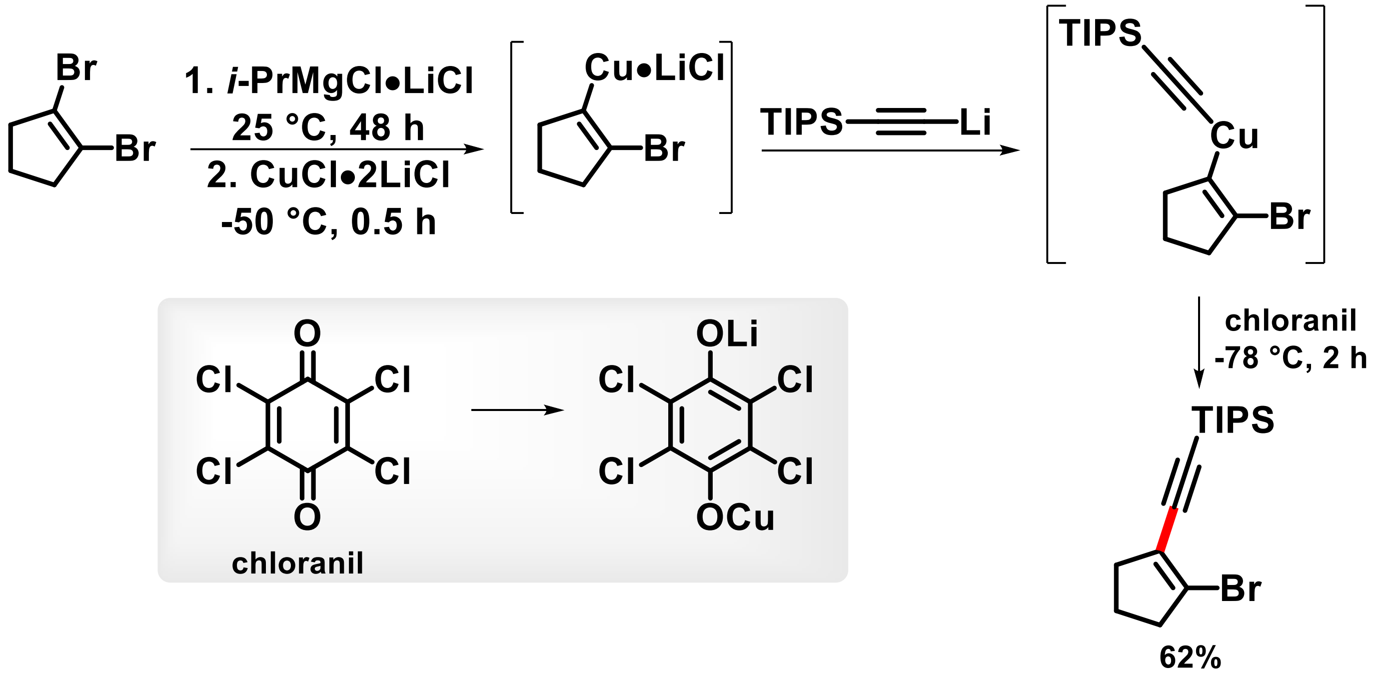


Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ Oxidative cross-coupling

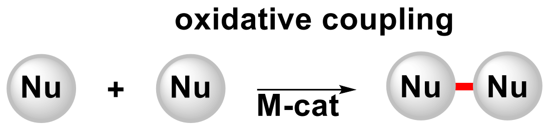
- Selected examples



- Stoichiometric reaction

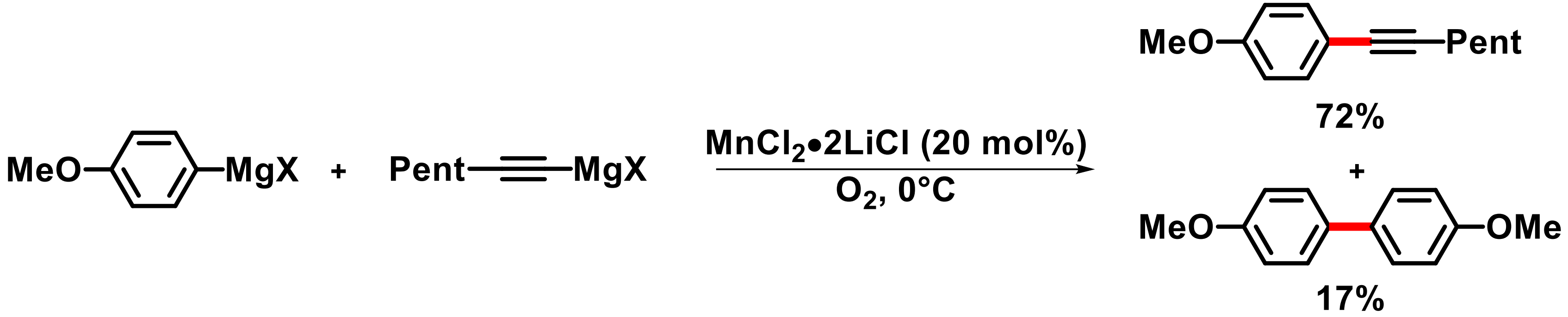
Angew. Chem. Int. Ed. **2007**, *46*, 9093

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ Oxidative cross-coupling

- Selected examples – catalytic reactions



Angew. Chem., Int. Ed. **2009**, *48*, 6731

- Other organometals

ArZnCl / R_3In
$PdCl_2(MeCN)_2$/DPEPhos
desyl chloride

Angew. Chem., Int. Ed. **2009**, *48*, 2969

ArZnCl / RC≡$CSnBu_3$
$Pd(dba)_2$ (2.5 mol%)
desyl chloride

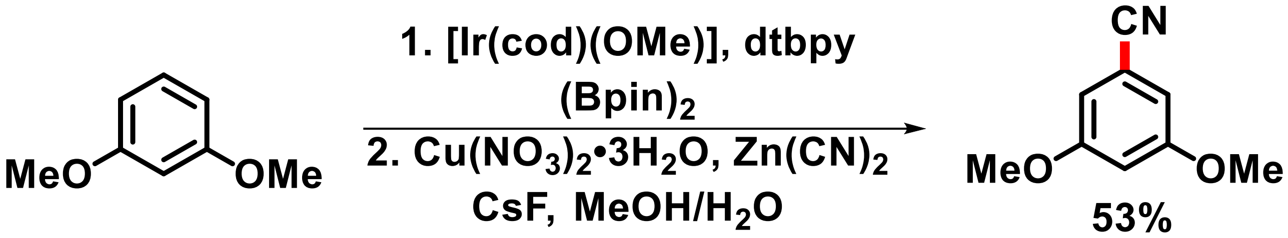
J. Am. Chem. Soc. **2006**, *128*, 15048

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

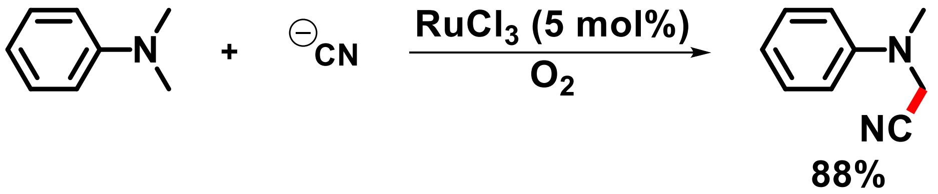
oxidative coupling

➢ Oxidative cross-coupling

- Selected examples – catalytic reactions

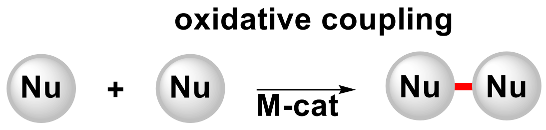


J. Am. Chem. Soc. **2010**, *132*, 11389



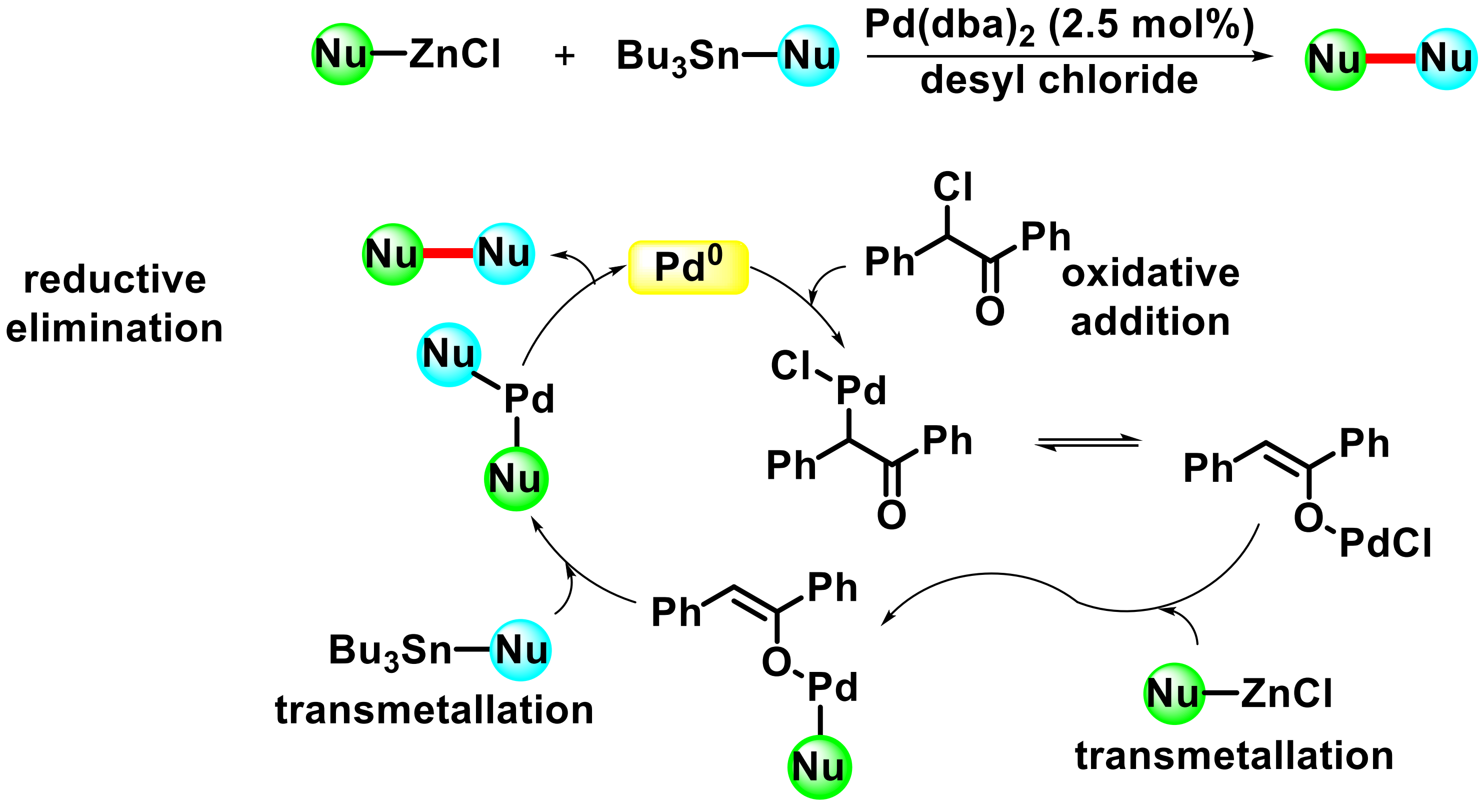
J. Am. Chem. Soc. **2003**, *125*, 15312

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

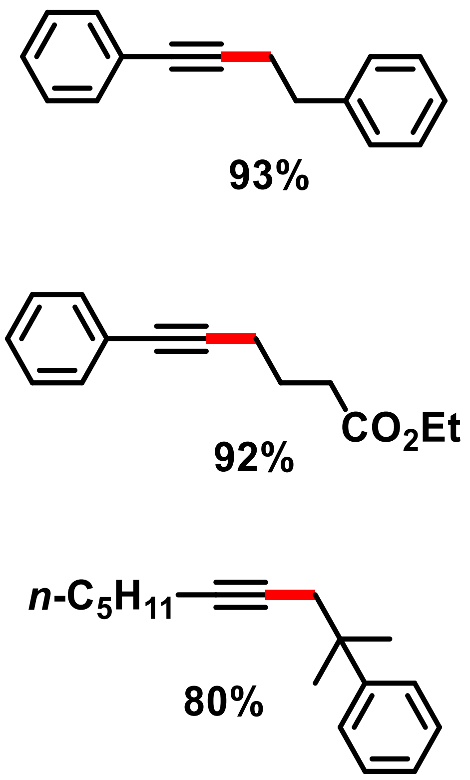


➢ Oxidative cross-coupling

- Mechanism of oxidative cross-coupling



○ **Selected examples**



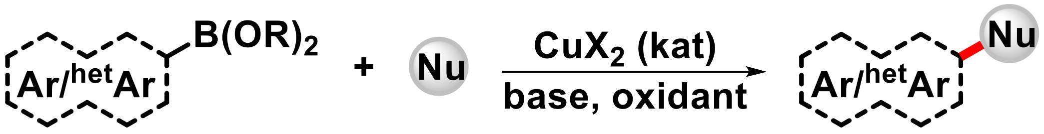
J. Am. Chem. Soc. **2006**, *128*, 15048

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

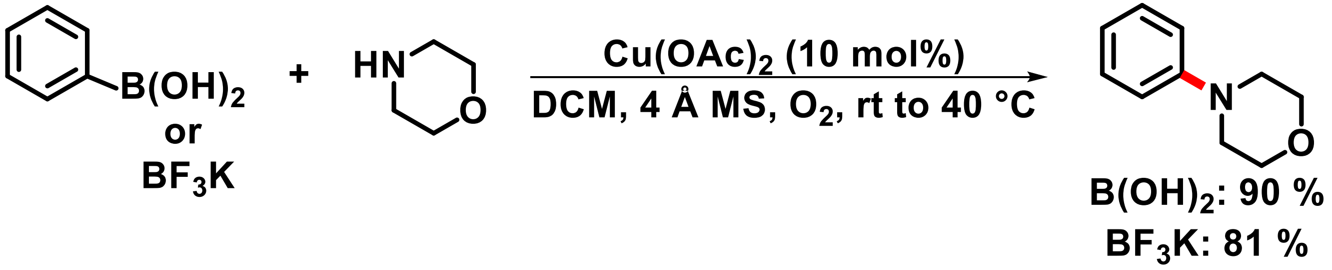
oxidative coupling

➢ Oxidative cross-coupling

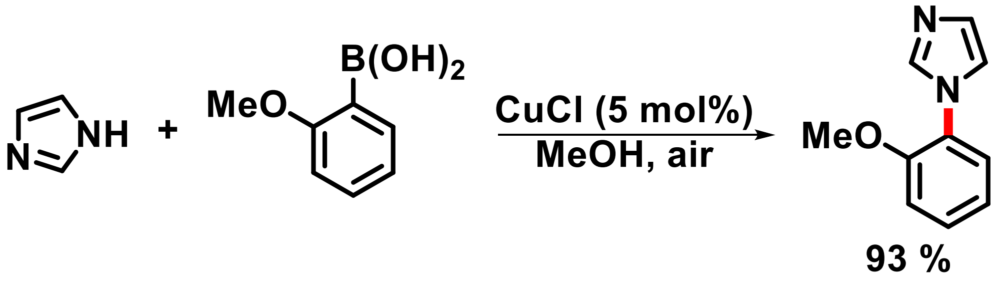
- Chan-Lam reaction



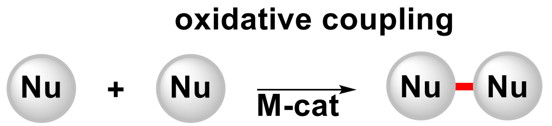
Nu = amine, alcohol



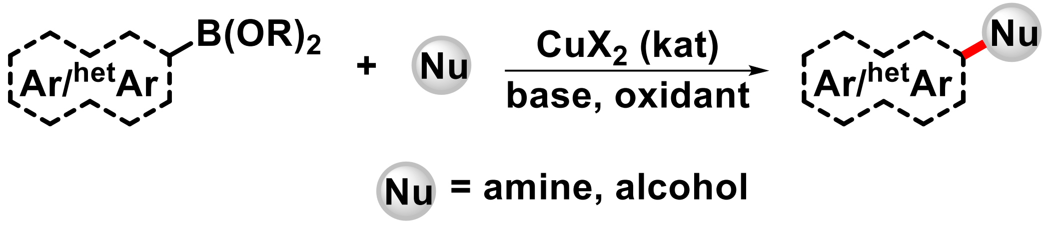
Org. Lett. **2003**, *5*, 4397

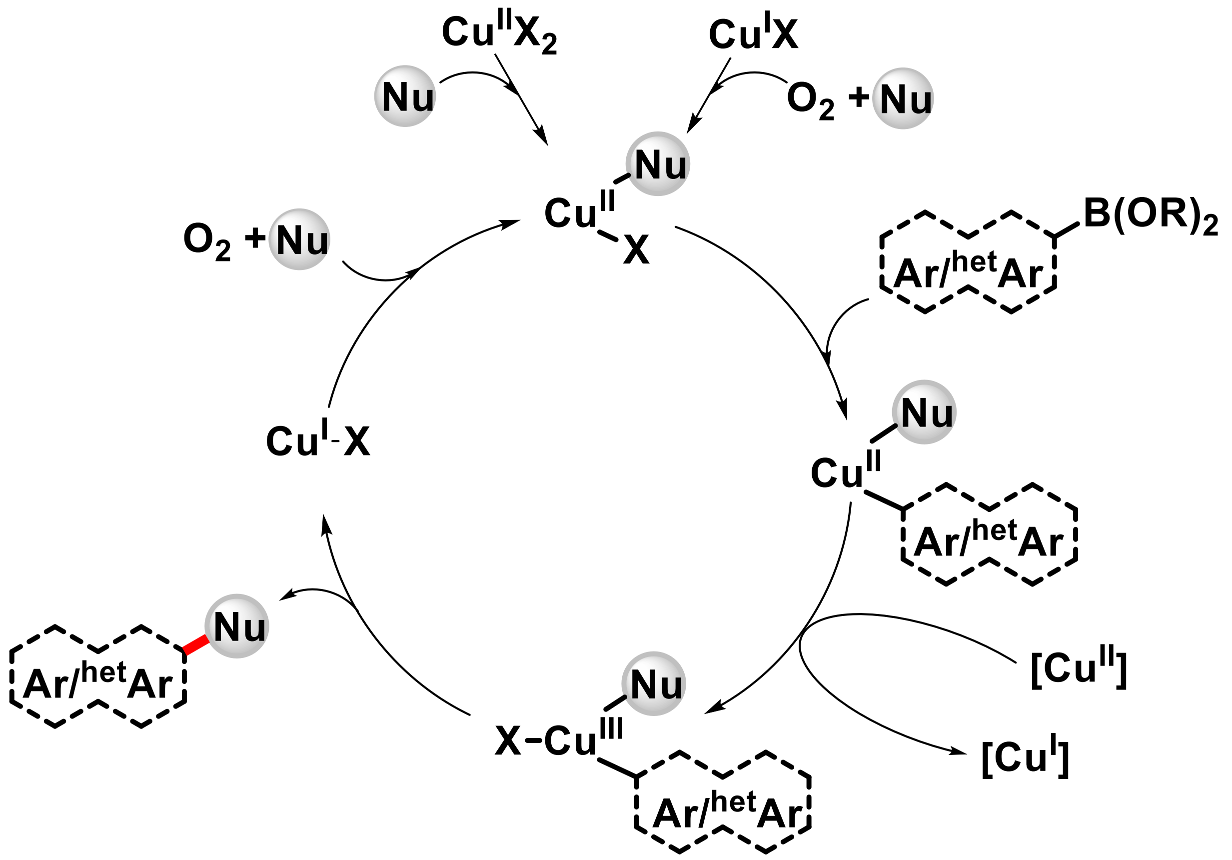


Chem. Commun. **2004**, 188



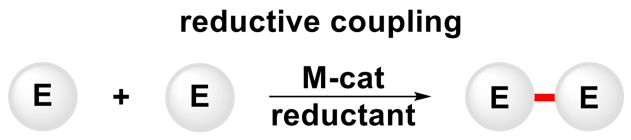
- Oxidative cross-coupling
  - Chan-Lam reaction
    - Mechanism

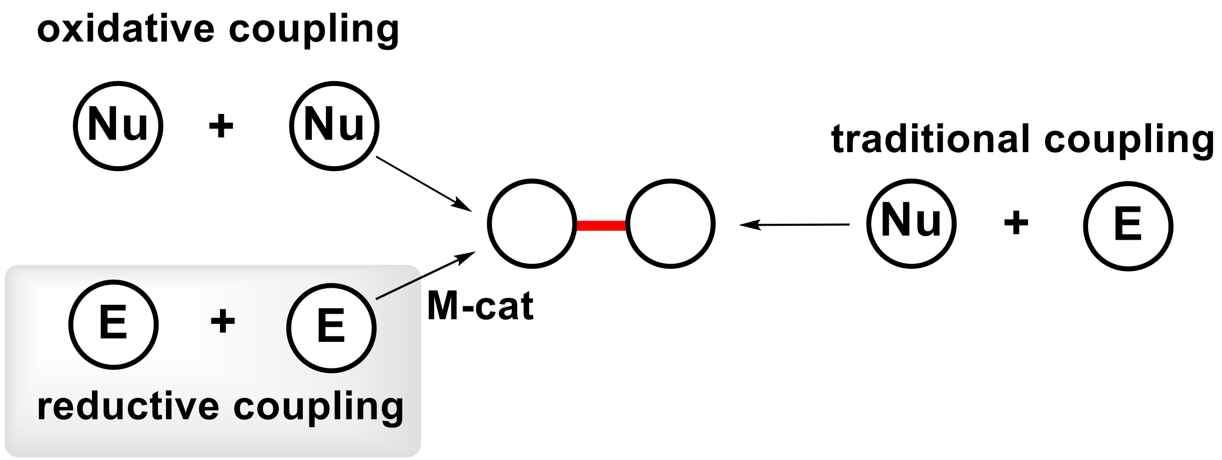




Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

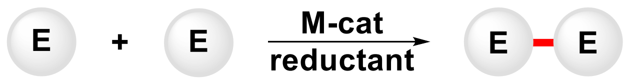
➢ Reductive cross-coupling





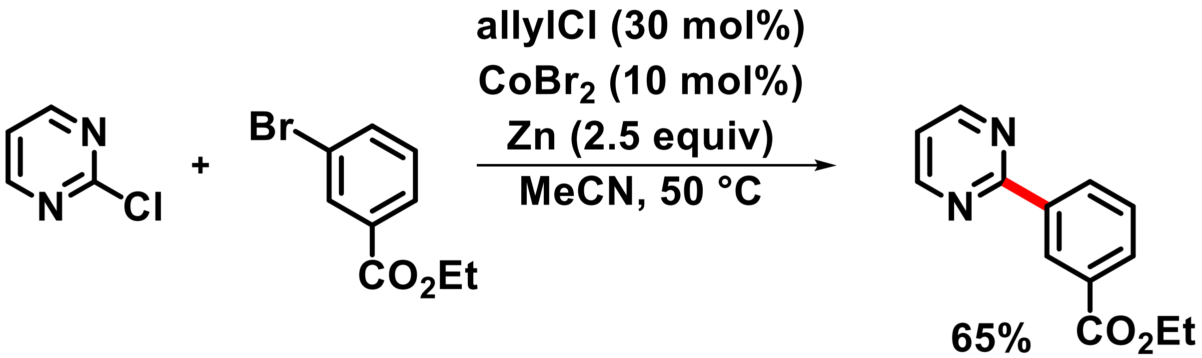
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

reductive coupling

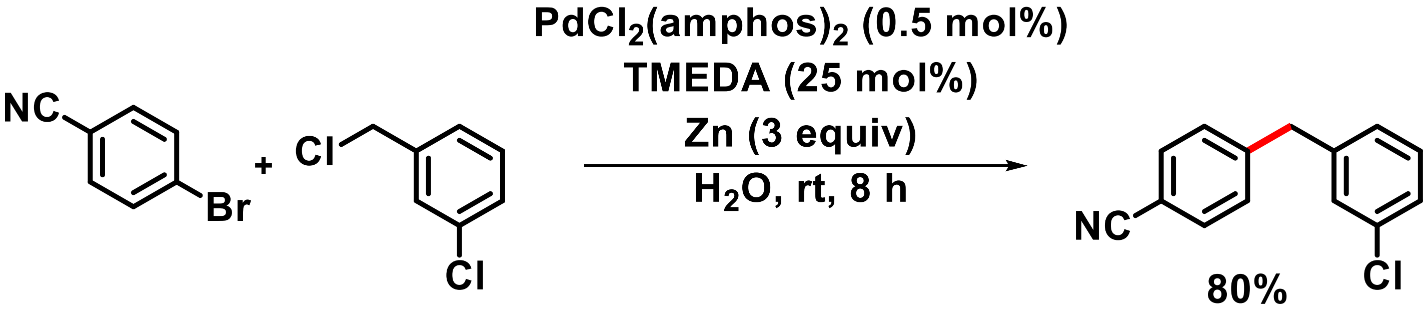


➢ Reductive cross-coupling

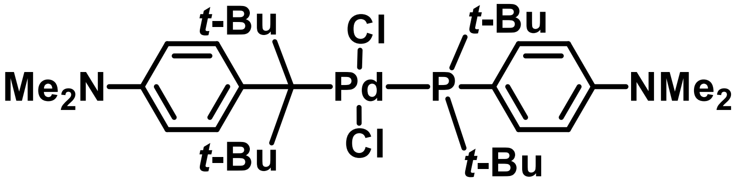
- Selected examples



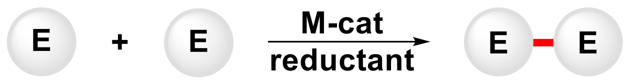
J. Org. Chem. **2009**, *74*, 3221



$PdCl_2(amphos)_2$

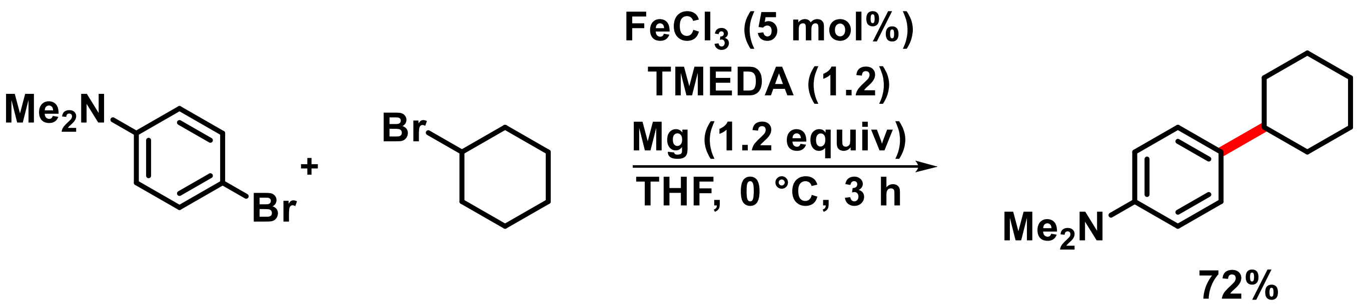


Chem. Commun. **2010**, *46*, 562

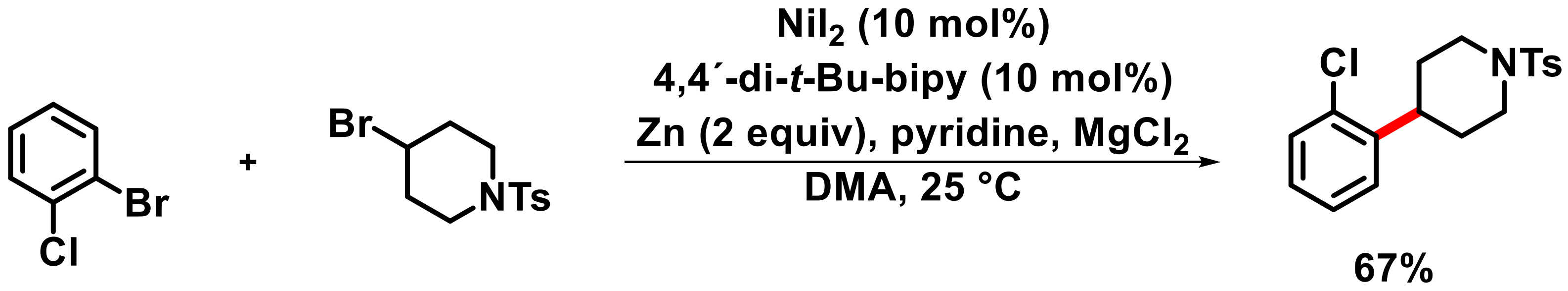


➢ Reductive cross-coupling

- Selected examples

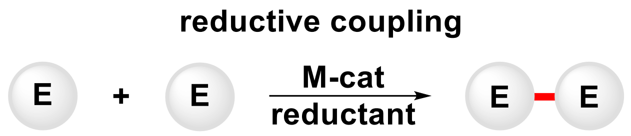


Angew. Chem. Int. Ed. **2009**, *48*, 607



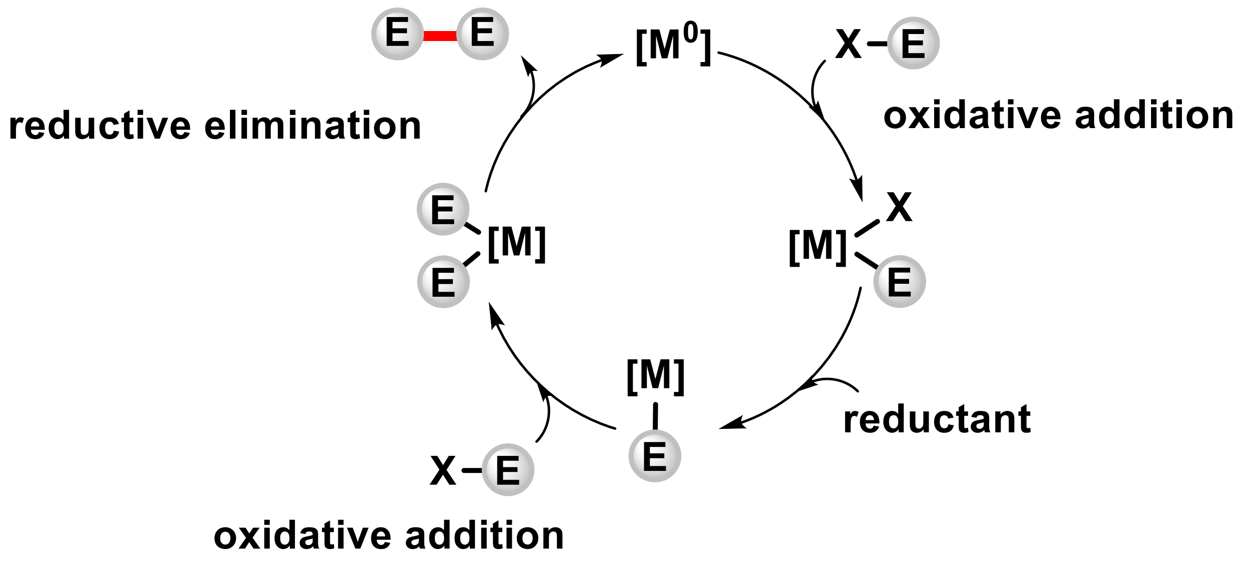
Org. Lett. **2012**, *14*, 3352

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



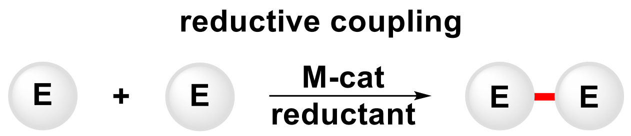
➢ Reductive cross-coupling

- General mechanism of reductive cross-coupling



- ○ Typical reductant: Zn, Mg , Cu

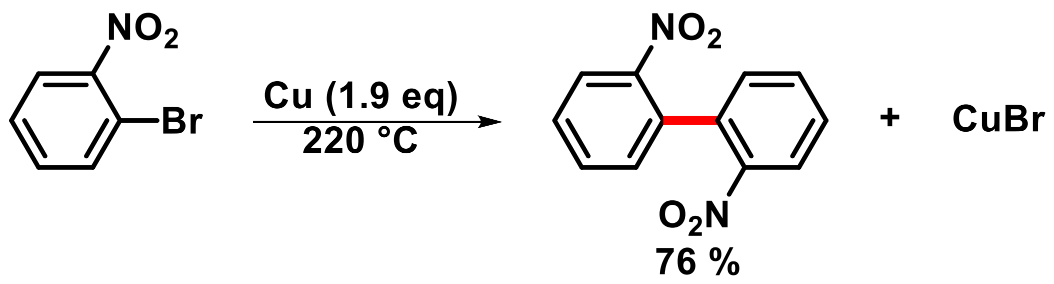
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



➢ Reductive cross-coupling

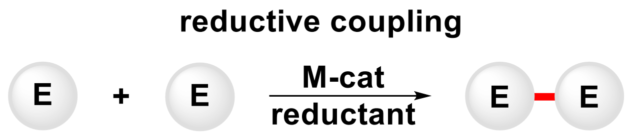
- Ullmann reaction

  - The first dimerization was published in 1901



Ber. Dtsch. Chem. Ges. **1901** , *34* , 2174

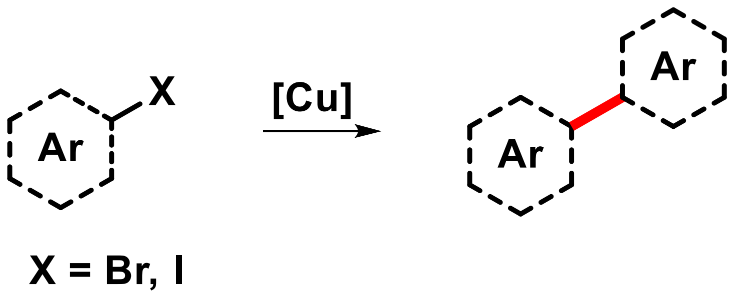
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

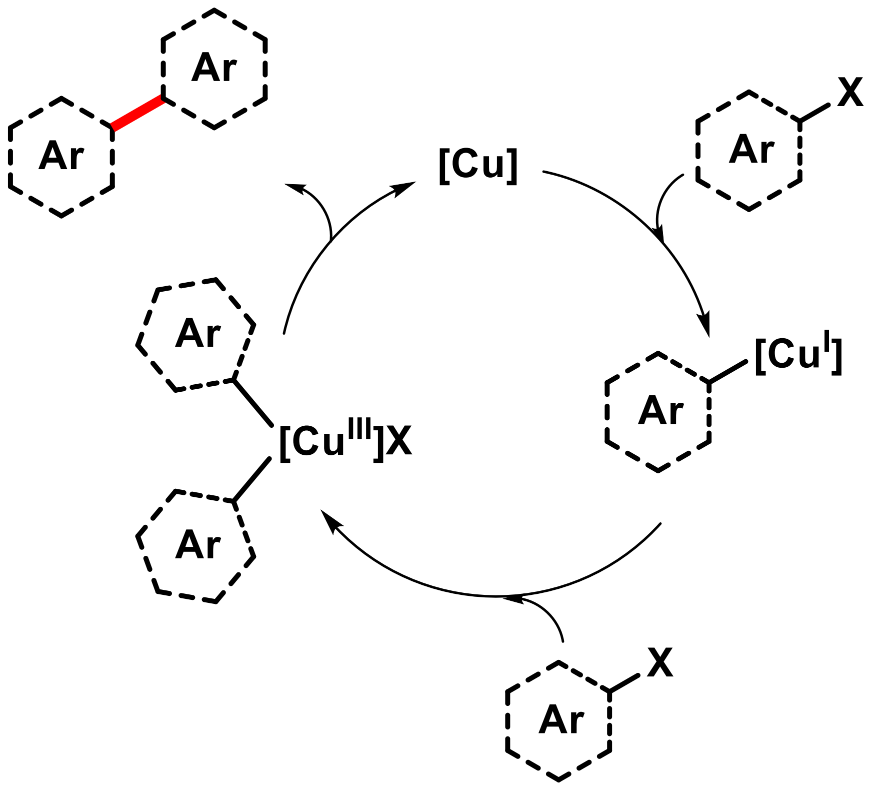


➢ Reductive cross-coupling

- Ullmann reaction

  - General reaction scheme

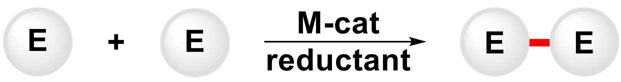




Synthesis **1974**, *20*, 9

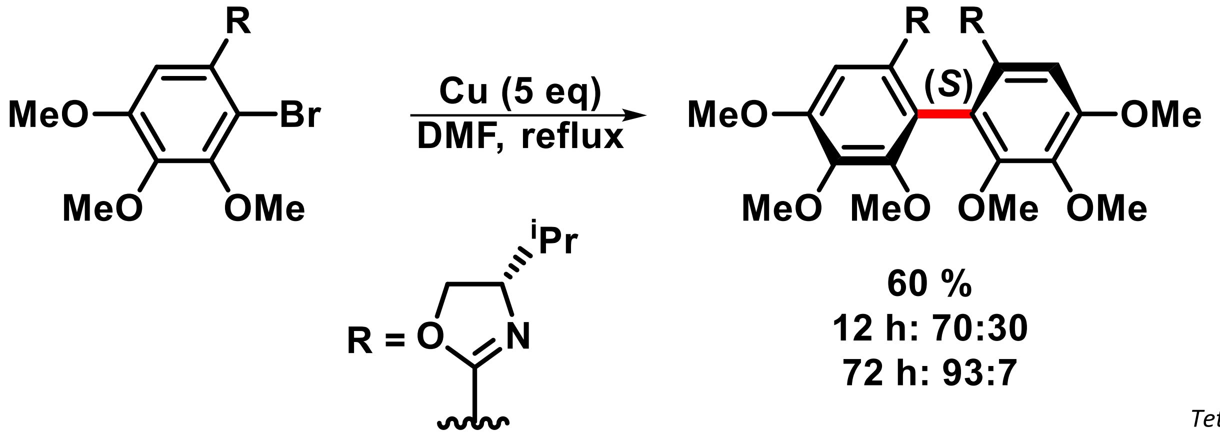
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

reductive coupling

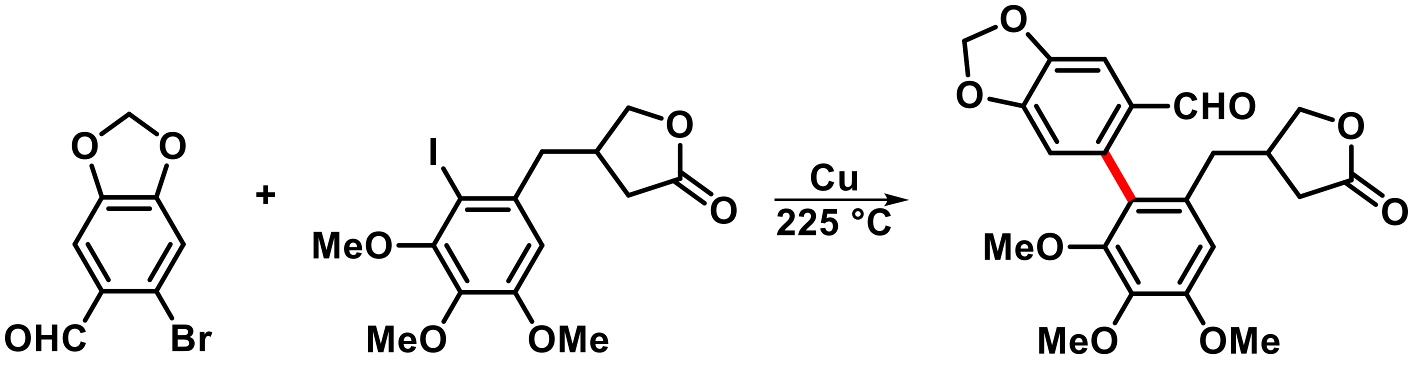


➢ Reductive cross-coupling

- Ullmann reaction
  - Selected examples



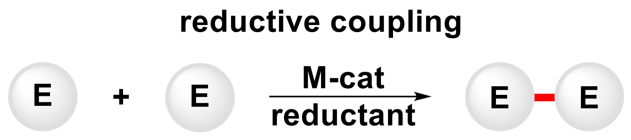
Tetrahedron Lett. **1993**, *34*, 3061



59 %

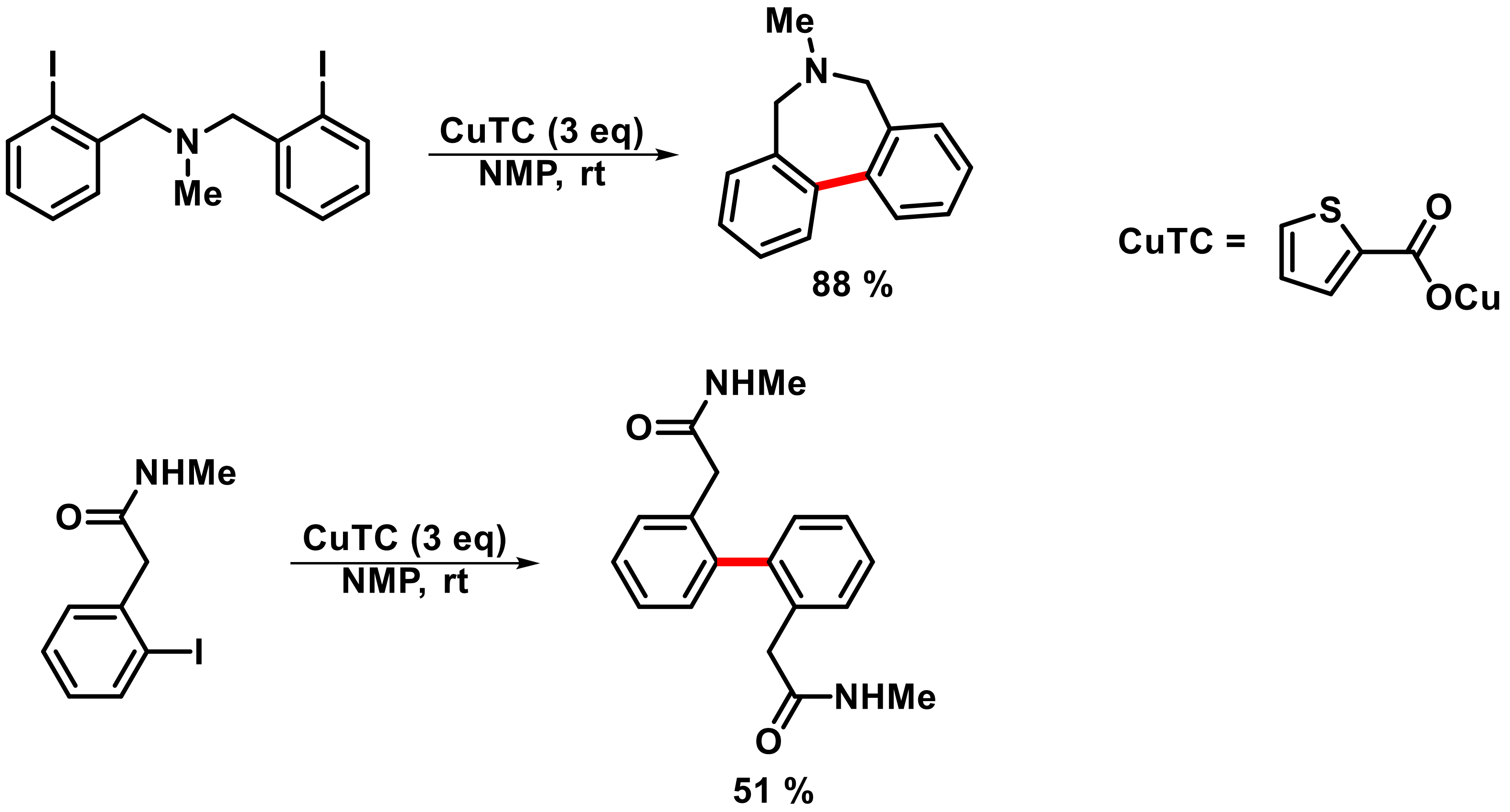
Tetrahedron Lett. **1979**, *20*, 773

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



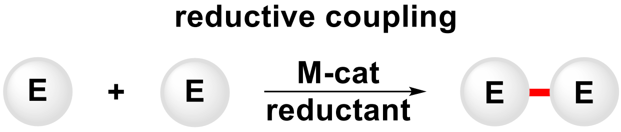
➢ Reductive cross-coupling

- Ullmann reaction
  - Selected examples



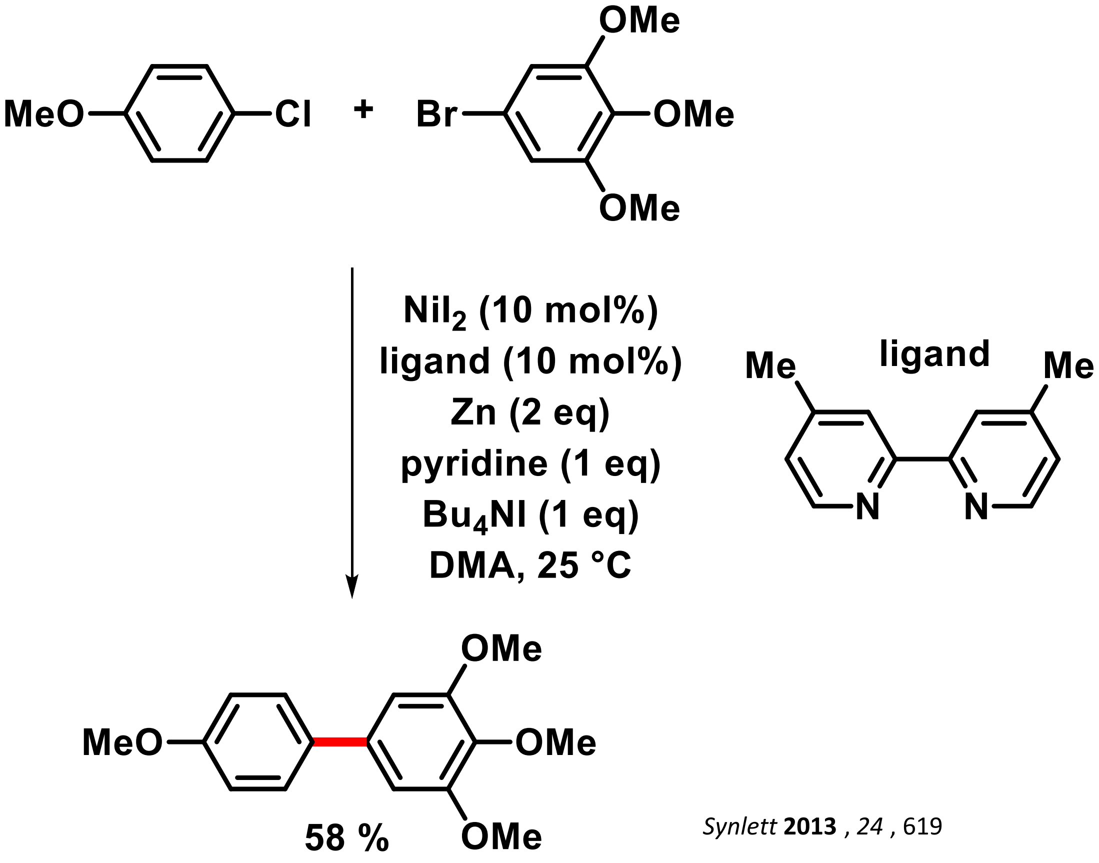
J. Org. Chem. **1997**, *62*, 2312

Formation of C–C Bond by Transition-Metal-Catalyzed Reactions



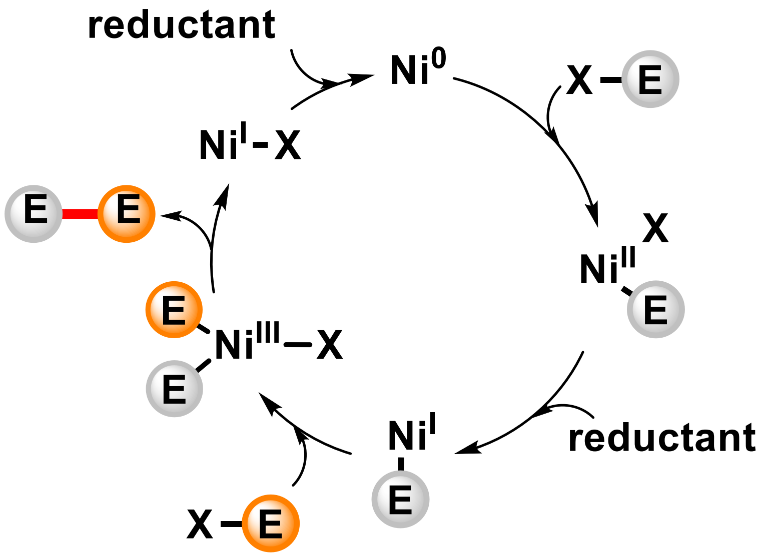
➢ Reductive cross-coupling

- Nickel-catalyzed reactions
  - Selected examples



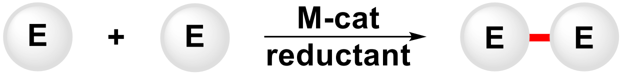
Synlett **2013** , *24* , 619

  - Typical mechanism



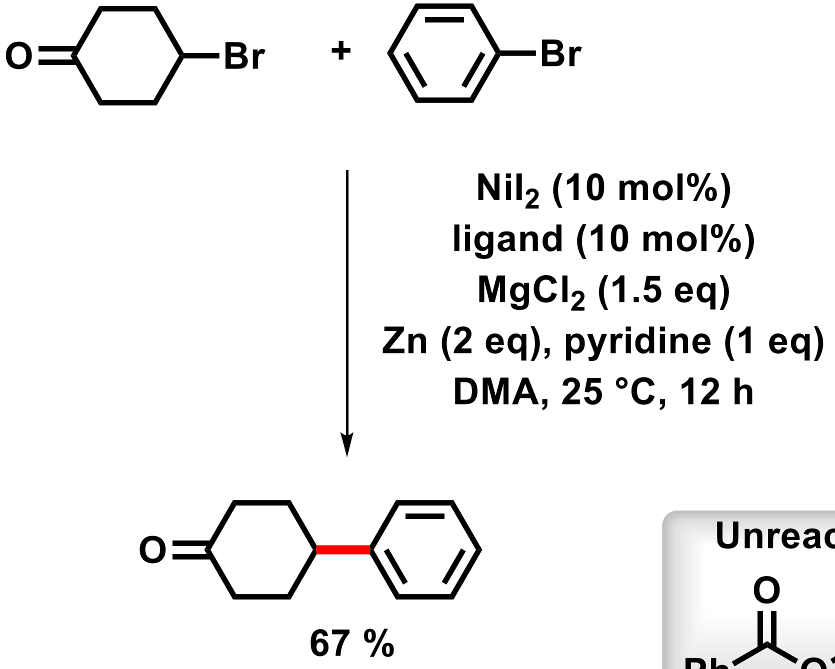
Formation of C–C Bond by Transition-Metal-Catalyzed Reactions

reductive coupling

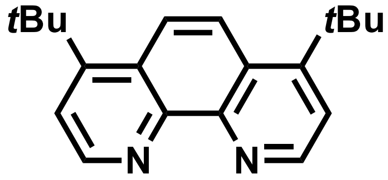


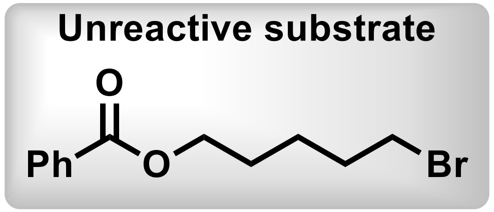
➢ Reductive cross-coupling

- Nickel-catalyzed reactions
  - Selected examples



ligand





Org. Lett. **2012**, *14*, 3352

- Typical mechanism