Organocopper chemistry

- **Types of organocuprates**

Organocopper reagents – RCu

Lower-order cuprates – RCu(CN)Li R_2CuLi

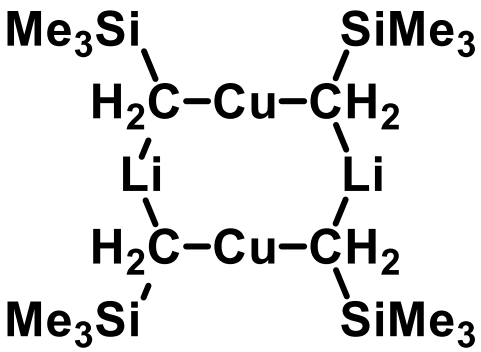
Higher-order cuprates – $(R_3Si)_2Cu(CN)Li_2$

$R^1R^2Cu(CN)Li_2$ $R_2Cu(SCN)Li_2$

$R^1R^2Cu(CN)LiMgX$ $R_2Cu(CN)Li_2$

$R_2Cu(CN)Li_2$ reacts faster in S_N then R_2CuLi

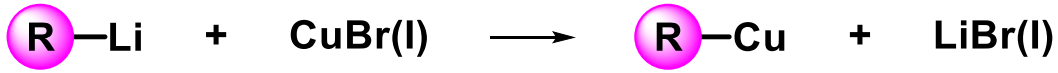
- **Structure of homocuprate (X-ray)**



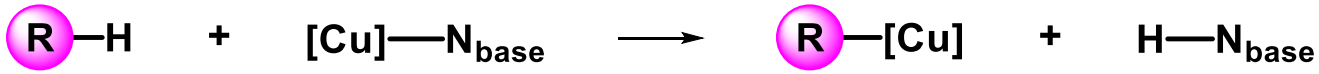
Organocopper chemistry

➢ Synthesis of organocuprates

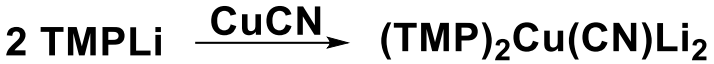
- **By transmetallation**



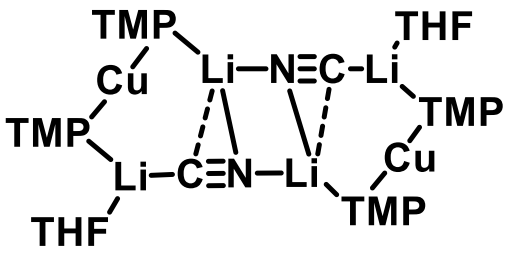
- **By deprotocupration**



○ **Formation of Lipshutz base**



○ **Structure of Lipshutz base (X-ray)**



○ **Other bases**

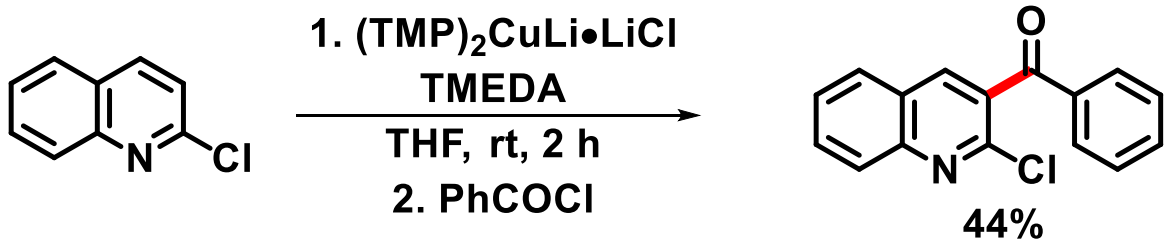
$(Ph_2N)_2Cu(NPh_2)Li_2 \bullet 2Et_2O$ $(TMP)_2CuLi$ $RCu(TMP)Li$

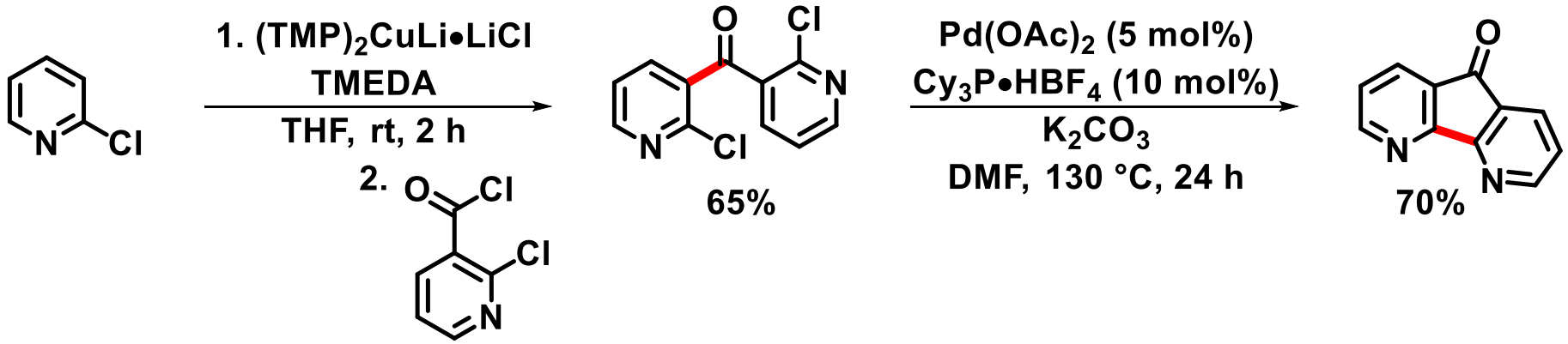
For review see: Dalton Trans. **2014**, *43*, 14181

Organocopper chemistry

➢ Synthesis of organocuprates

- **Deprotocupration – Selected examples**





Tetrahedron **2013**, *69*, 10123

Organocopper chemistry

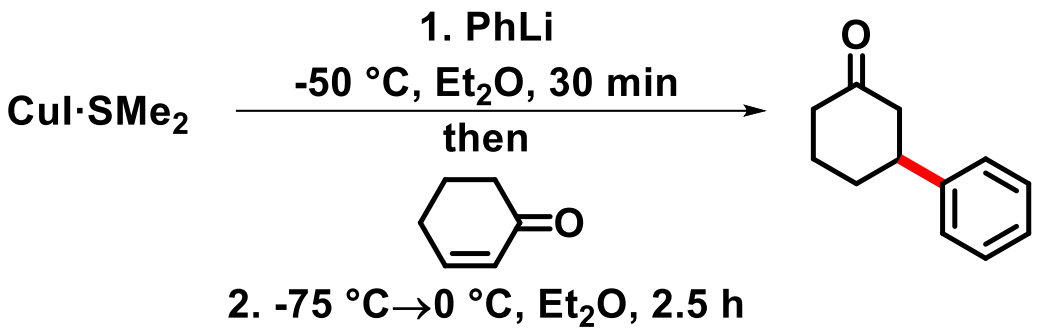
➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

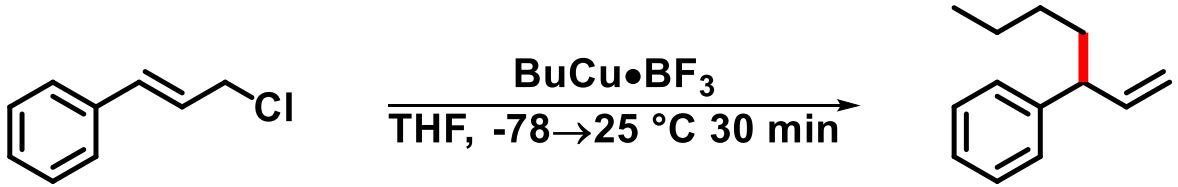
○ **Organocopper reagents (RCu)**

✓ **Easily available**

$$\text{R–Li} + \text{CuBr(I)} \longrightarrow \text{R–Cu} + \text{LiBr(I)}$$



Tetrahedron **1989**, *45*, 425



94%

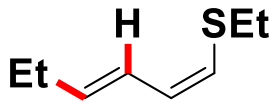
J. Am. Chem. Soc. **1977**, *99*, 8068

○ **Dry RCu may be explosive!**

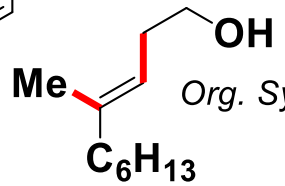
Organocopper chemisty

➢ Chemistry of organocuprates (from organolithium reagents)

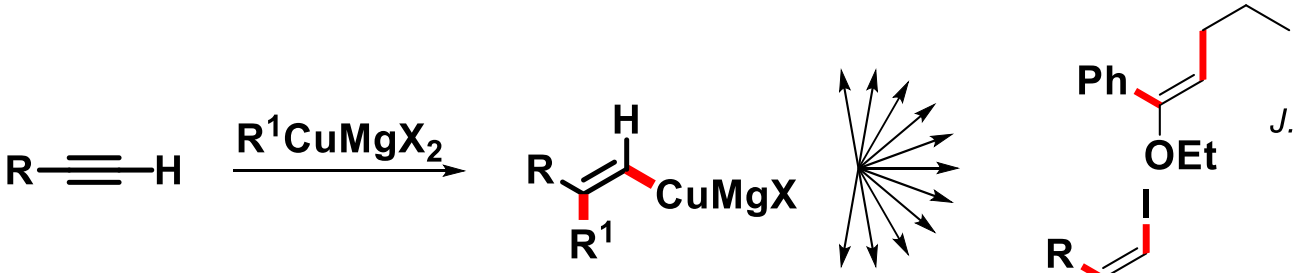
- **Stoichiometric reactions**
  - **Organocopper reagents (RCu) - Alkyne carbocupration**
- **Catalytic reactions**

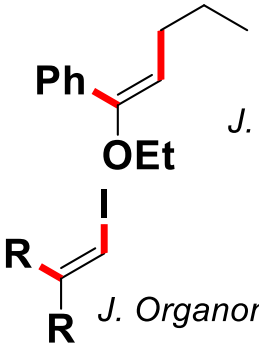


J. Organomet. Chem. **1975**, *96*, 471



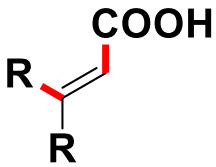
Org. Synth. **1985**, *64*, 1





J. Organomet. Chem. **1986**, *301*, 247

J. Organomet. Chem. **1974**, *77*, 269



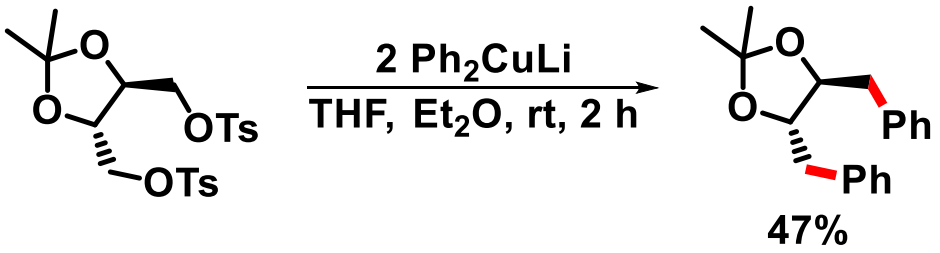
J. Organomet. Chem. **1973**, *54*, C53

Organocopper chemistry

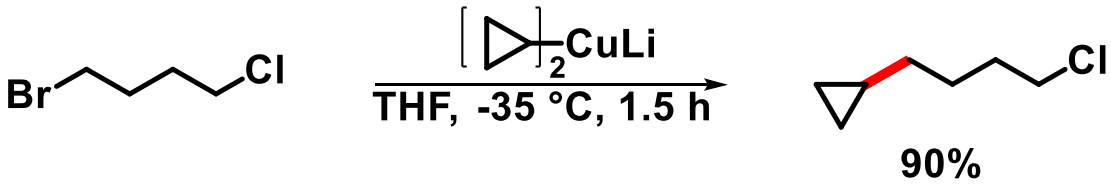
➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

○ **Gilman reagent in alkylation reactions (S_N2)**



Experimentia **1982**, *38*, 70



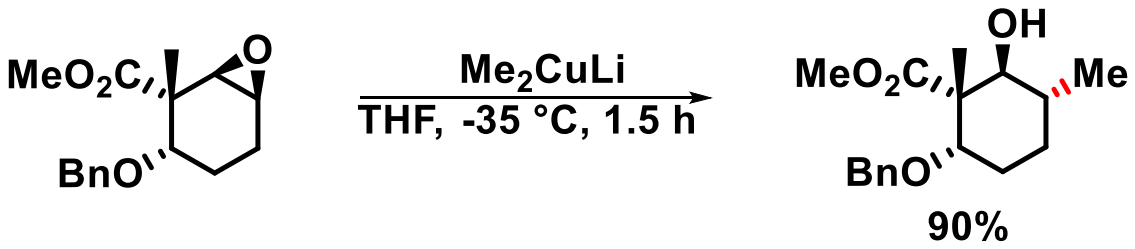
Bull. Chem. Soc. Jpn. **1976**, *40*, 1989

Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

○ **Gilman reagent in alkylation reactions (S_N2)**



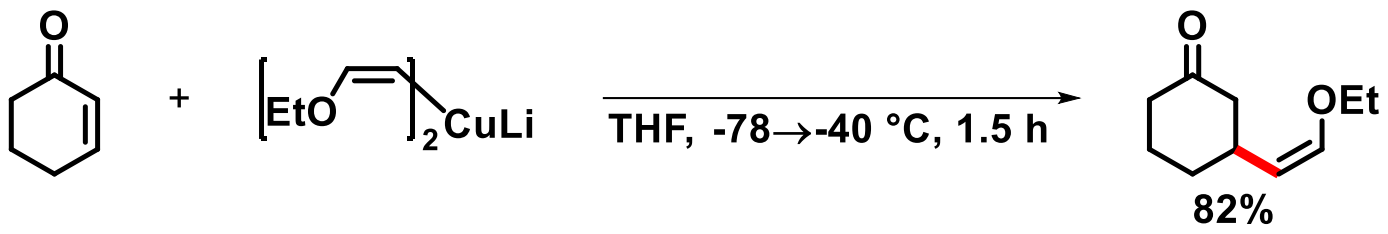
Perkin I **1982**, 2885

Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

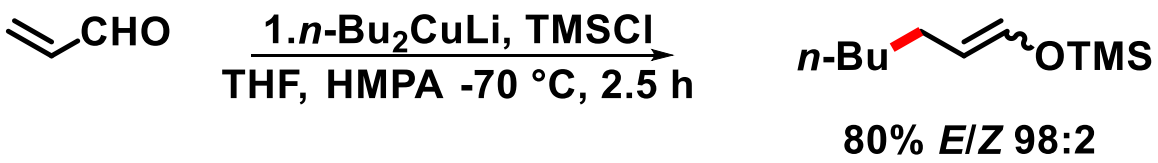
- **Stoichiometric reactions**
- **Catalytic reactions**

○ Organocuprates and 1,4-addition



J. Am. Chem. Soc. **1977**, *99*, 7365

✓ **1,4-Addition in the presence of additives (TMSCl, BF_3•Et_2O)**



Tetrahedron **1989**, *45*, 349

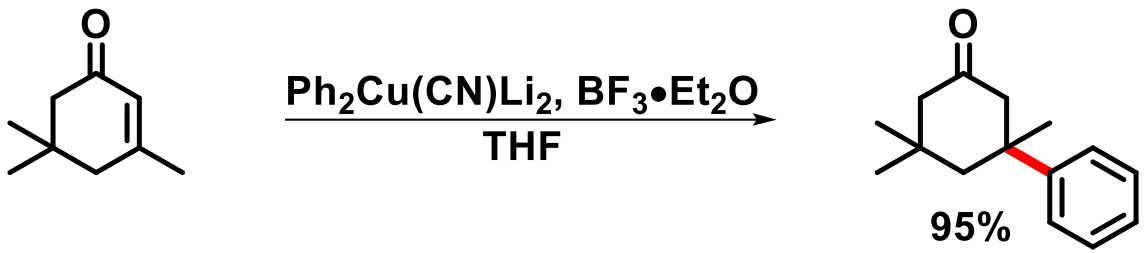
Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

○ Cuprates and 1,4-addition

○ 1,4-Addition in the presence of additives (TMSCl, $BF_3 \bullet Et_2O$)



Tet. Lett. **1984**, *25*, 5959

○ How do aditives work?

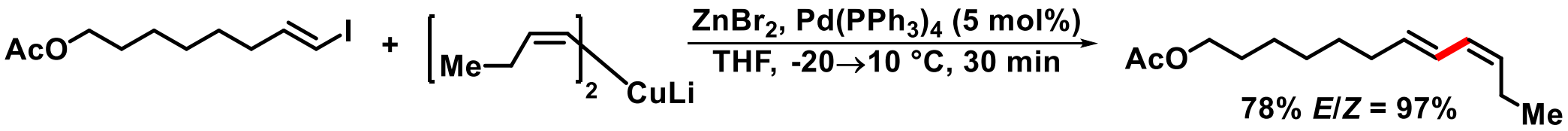
$$[R_2CuLi]_2 + 2\,BF_3 \rightleftharpoons R_3Cu_2Li + BF_3 + RLi \bullet BF_3$$

Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

  - **Gilman reagent and cross-coupling reactions**



Tetrahedron **1984**, 40, 2741.

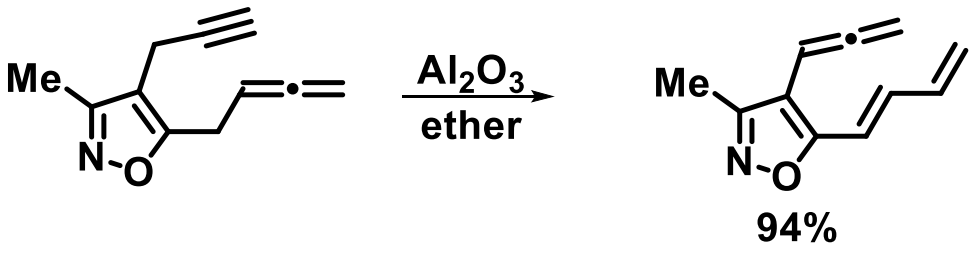
Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

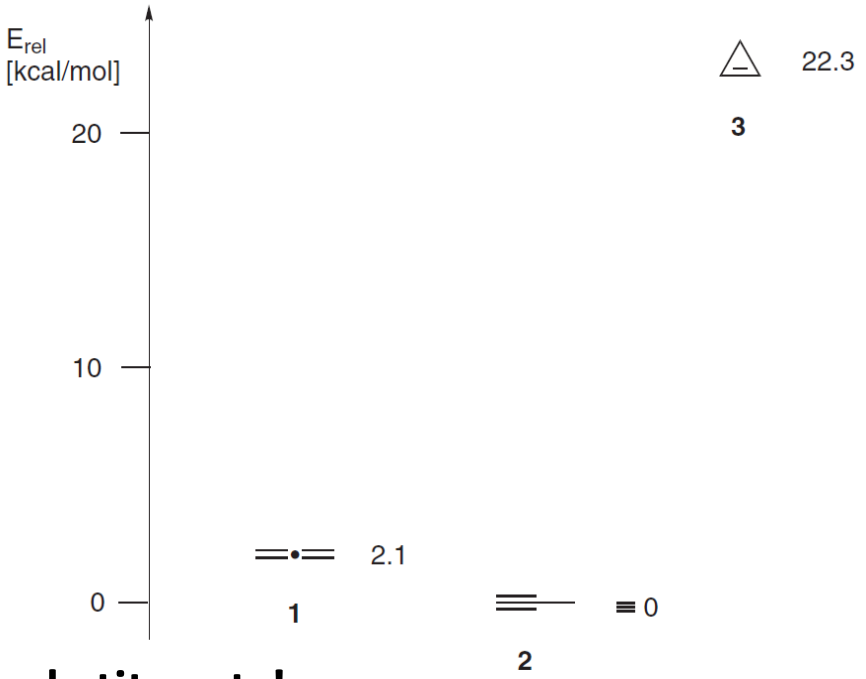
○ **Gilman reagent for the synthesis of allenes**

✓ **Synthesis of allenes by isomerization**



J. Org. Chem. **1969**, *34*, 3248

✓ **Relative energies of propa-1,3-diene and its isomers**



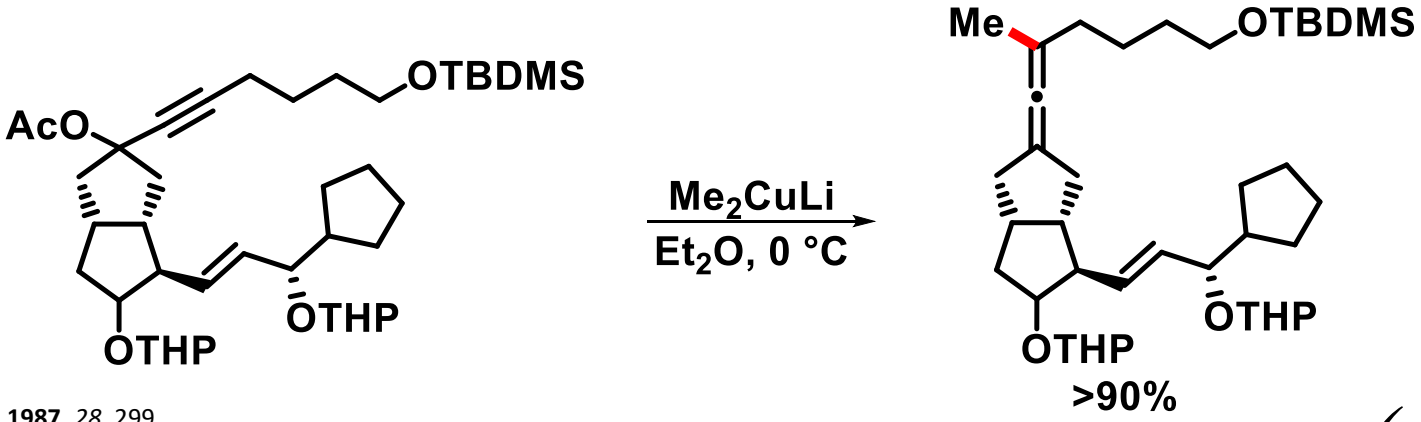
✓ **The course of isomerization is governed by the properties of substituents!**

Organocopper chemistry

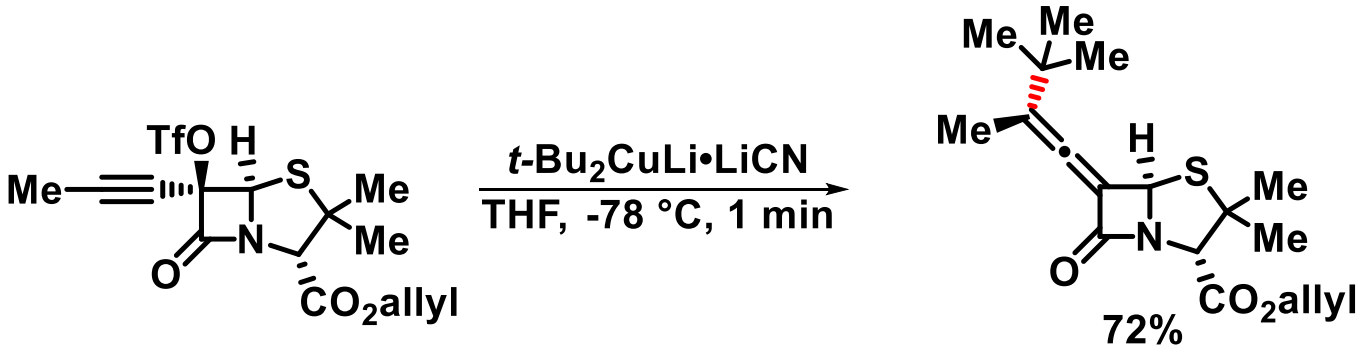
➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

○ **Gilman reagent for the synthesis of allenes**

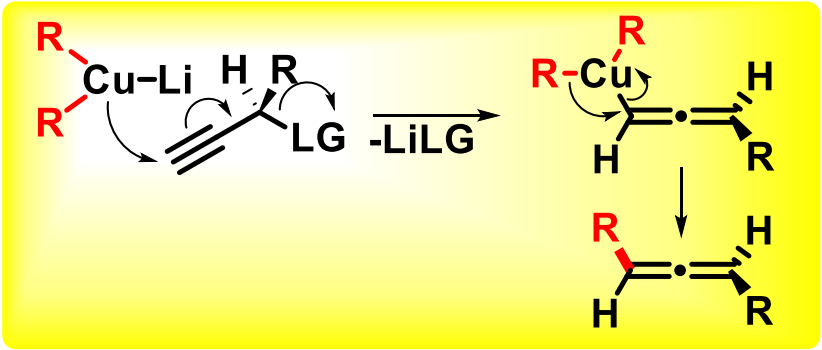


Tetrahedron Lett. **1987**, *28*, 299



J. Org. Chem. **1993**, *58*, 1325

✓ **Mechanistic proposal**

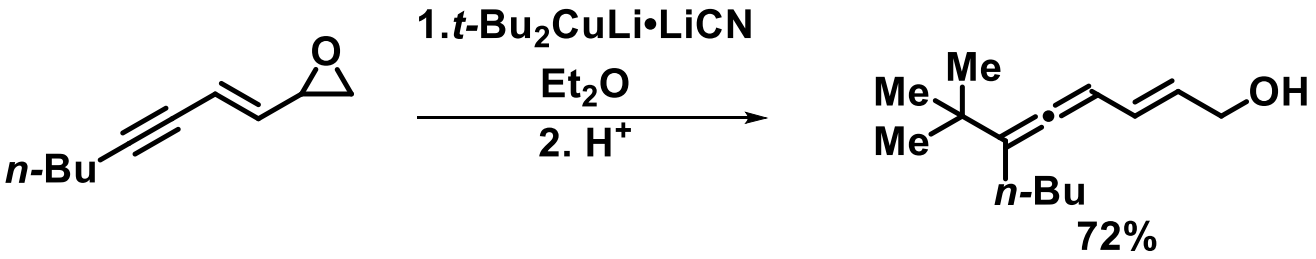


Organocopper chemistry

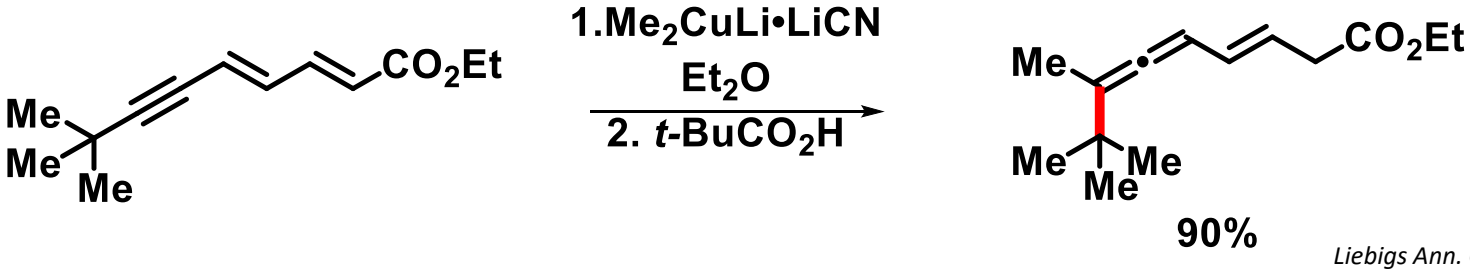
➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**

○ **Gilman reagent for the synthesis of allenes**



Eur. J. Org. Chem. **1999**, 267



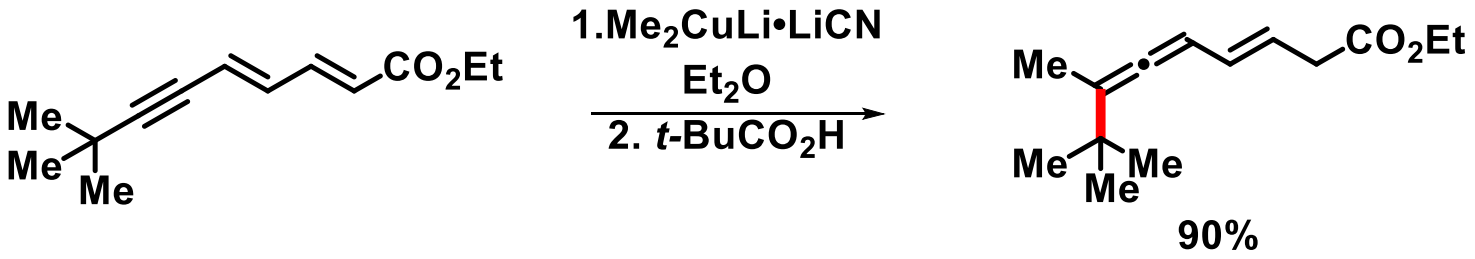
Liebigs Ann. Chem. **1996**, 1487

Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

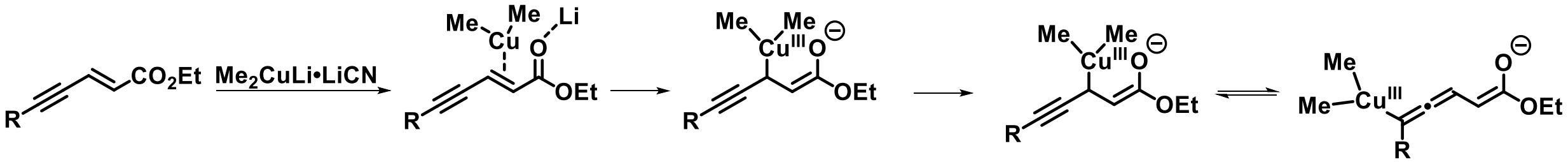
- **Stoichiometric reactions**
- **Catalytic reactions**

○ **Gilman reagent for the synthesis of allenes**



Liebigs Ann. Chem. **1996**, 1487

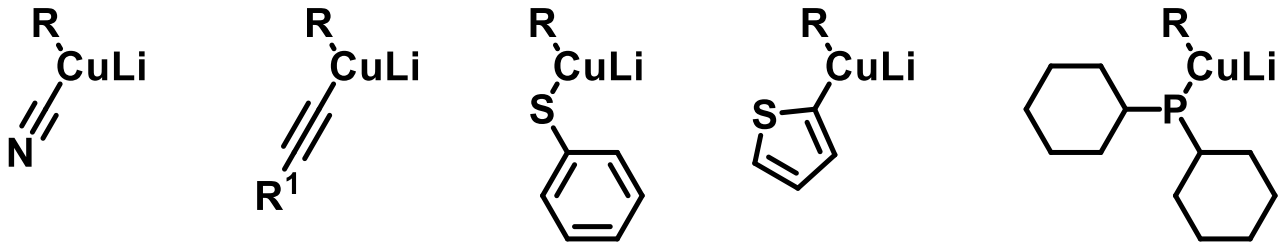
✓ **Mechanistic proposal**

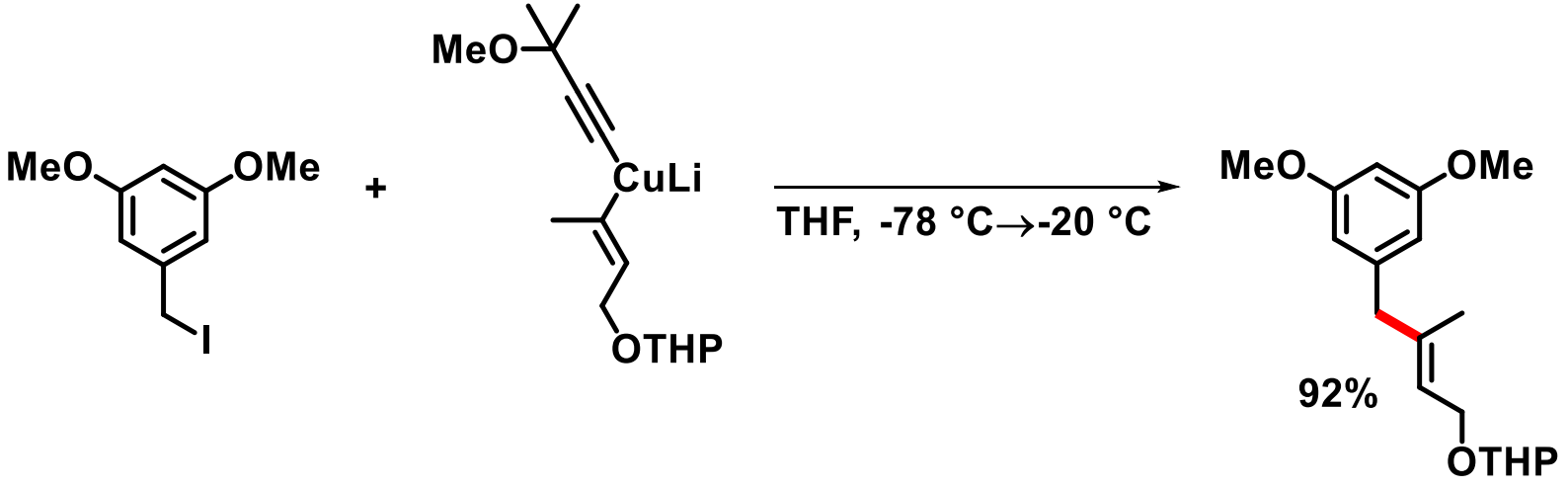


Organocopper chemistry

➢ Chemistry of organocuprates (from organolithium reagents)

- **Stoichiometric reactions**
  - **Mixed cuprates**
- **Catalytic reactions**



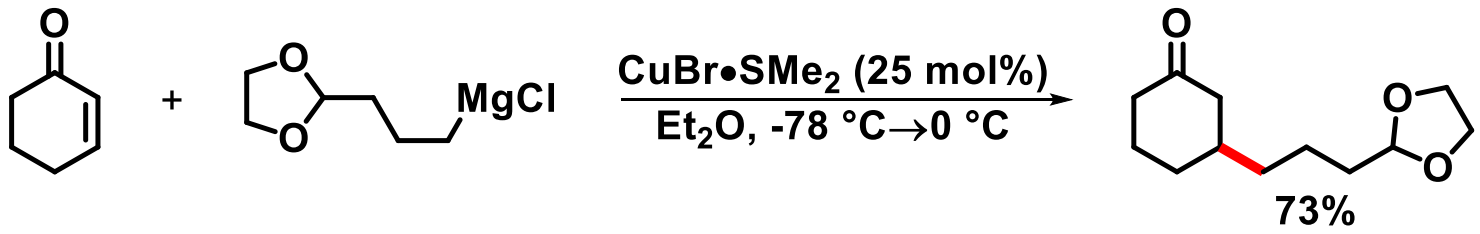


J. Org. Chem. **1978**, *43*, 3418

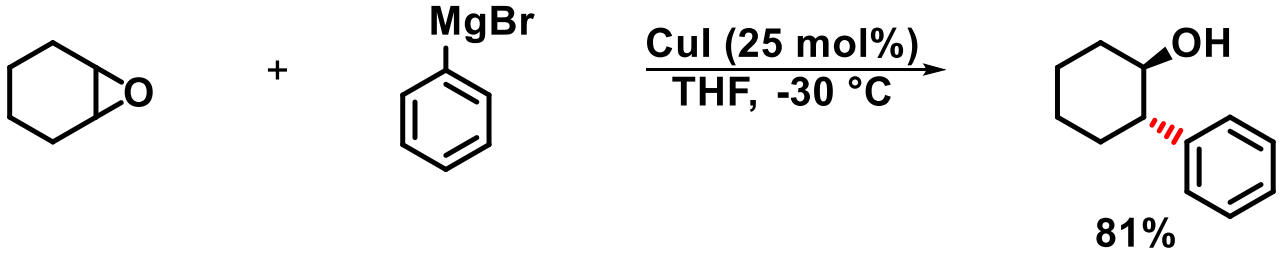
Organocopper chemistry

➢ Chemistry of organocuprates (from Grignard reagents)

- **Stoichiometric reactions**
- **Catalytic reactions reactions**



J. Org. Chem. **1982**, *47*, 5045

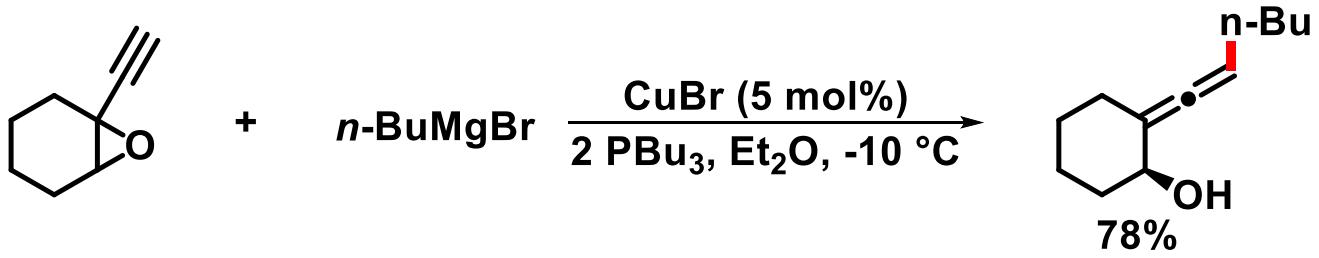


J. Org. Chem. **1986**, *51*, 4779

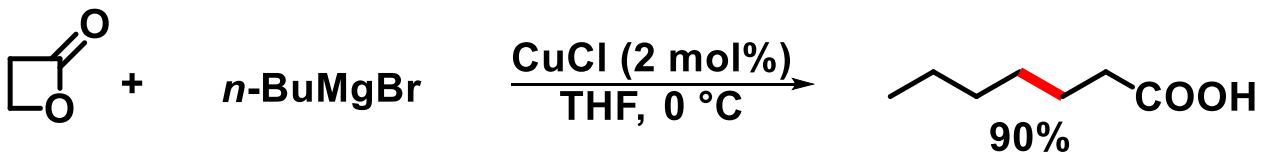
Organocopper chemistry

➢ Chemistry of organocuprates (from Grignard reagents)

- **Stoichiometric reactions**
- **Catalytic reactions**



Tetrahedron Lett. **1989**, *30*, 2387

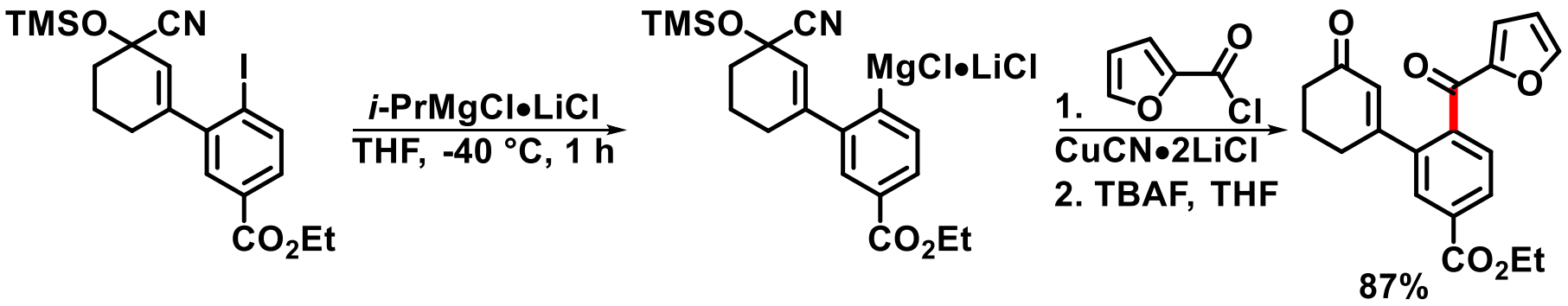


Chem. Lett. **1980**, *571*

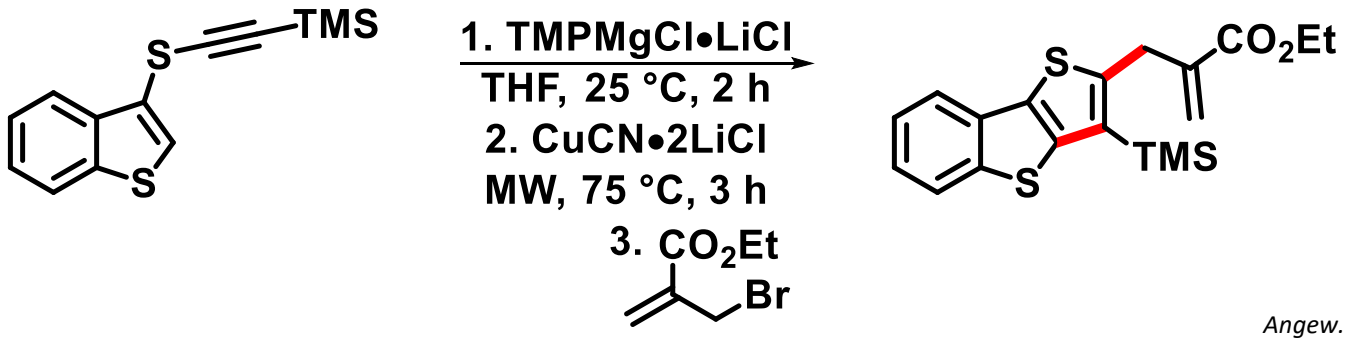
Organocopper chemistry

➢ Chemistry of organocuprates (from Grignard reagents)

- **Stoichiometric reactions**
  - **Functionalized Grignard reagents**
- **Catalytic reactions**



Org. Lett., **2006**, *8*, 617

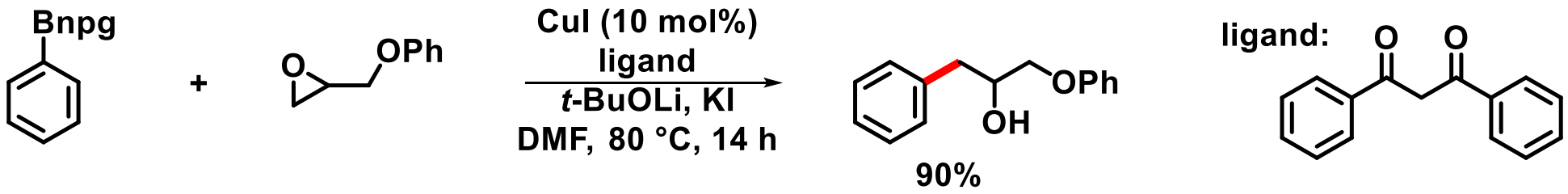


Angew. Chem. Int. Ed., **2012**, *51*, 1958

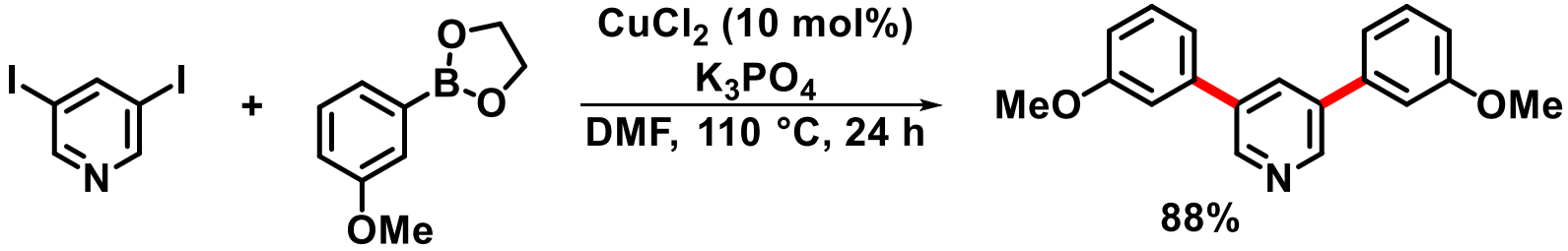
Organocopper chemistry

➢ Copper-catalyzed reactions

- **Copper-catalyzed cross-couplings**



Chem. Commun. **2015**, *51*, 2388

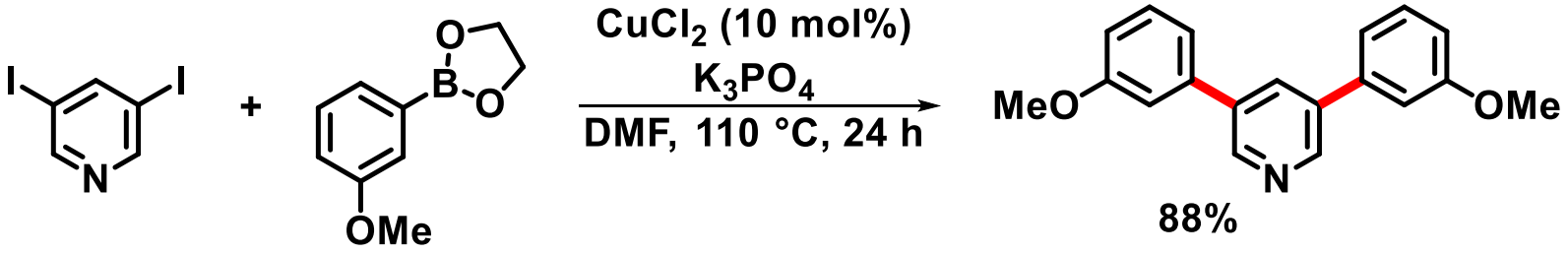


Org. Lett. **2017**, *19*, 3974

Organocopper chemistry

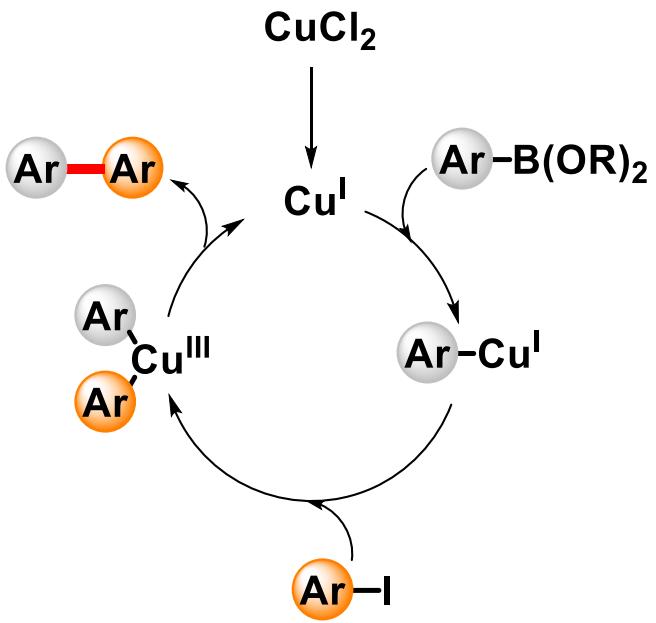
➢ Copper-catalyzed reactions

- **Copper-catalyzed cross-couplings**



Org. Lett. **2017**, *19*, 3974

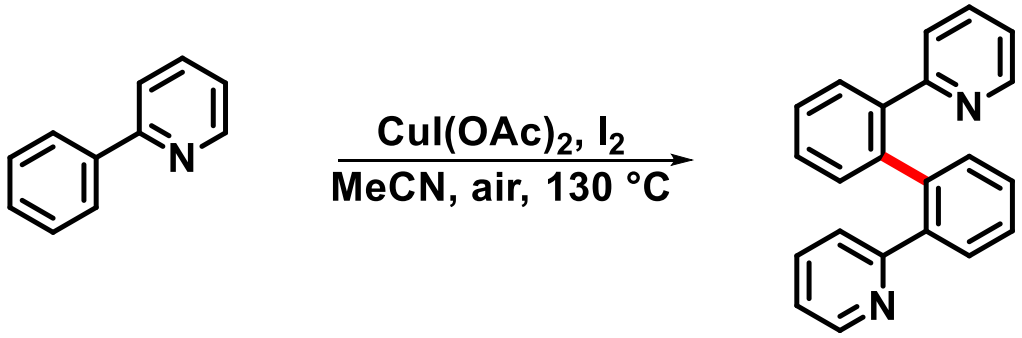
- **Proposed mechanism**



Organocopper chemistry

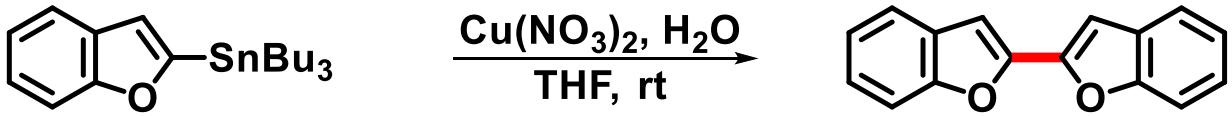
➢ Copper-catalyzed reactions

- **Copper-catalyzed homo-couplings**



85%

Tetrahedron **2009**, *65*, 3085



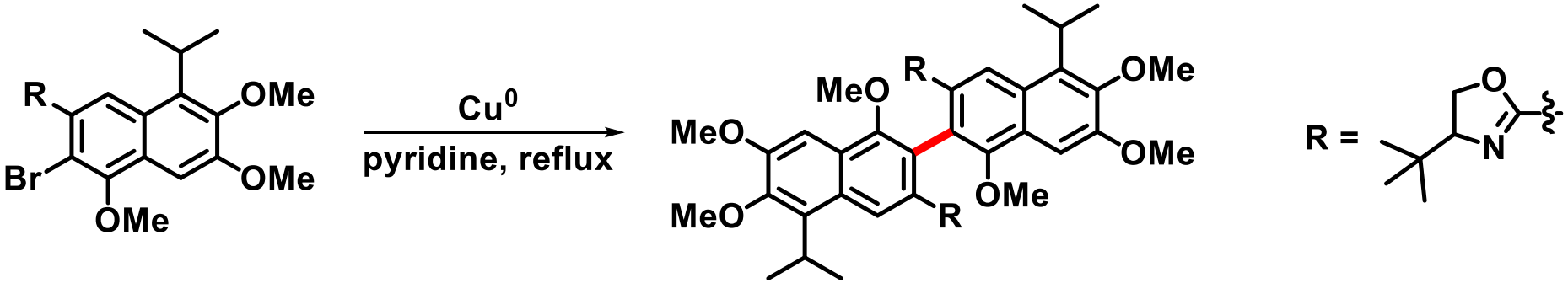
52%

J. Org. Chem. **1971**, *36*, 10

Organocopper chemistry

➢ Copper-catalyzed reactions

- **Copper-catalyzed homo-couplings**
  - **Ullmann homocoupling**



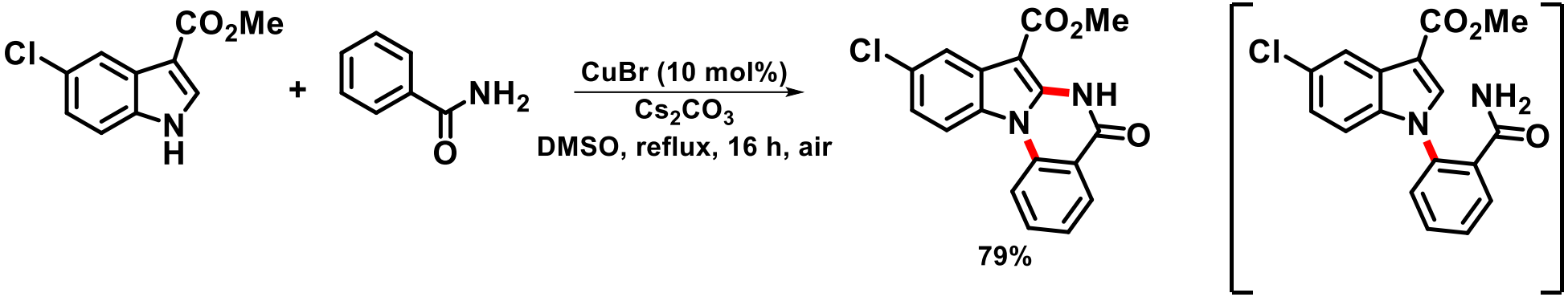
Tetrahedron **1996**, *37*, 791

Organocopper chemistry

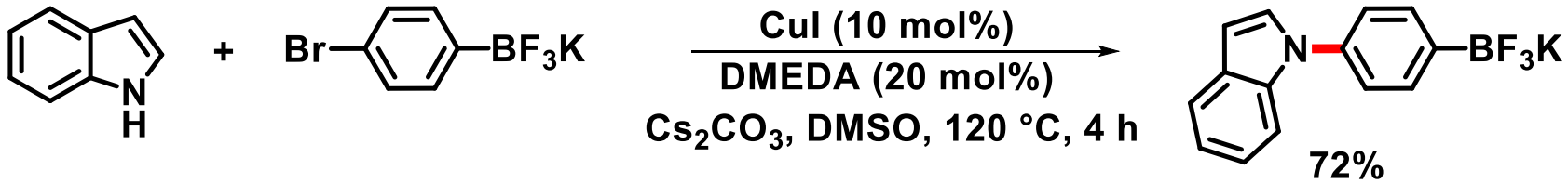
➢ Copper-catalyzed reactions

- **Copper-catalyzed C–N bond formation**

○ **Ullmann condensation**



Org. Chem. Front. **2017**, *4*, 2124



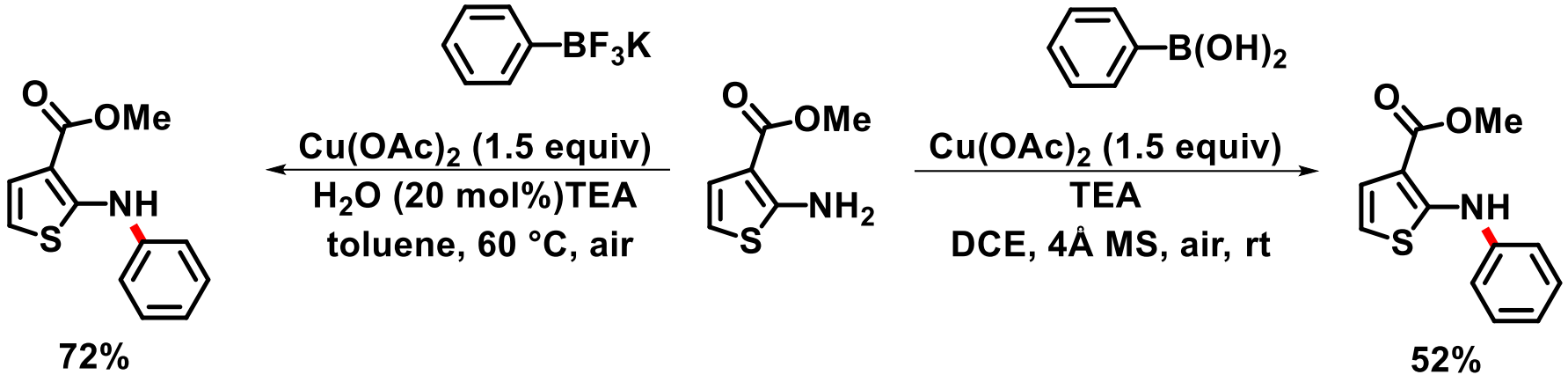
Bull. KoreanChem. Soc. **2013**, *34*, 42

Organocopper chemistry

➢ Copper-catalyzed reactions

- Copper-catalyzed C–N bond formation

○ Chan-Lam reaction

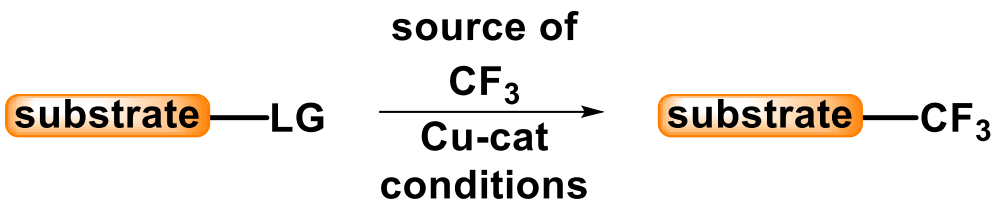


Tetrahedron Lett. **2015**, *56*, 6839

Organocopper chemisty

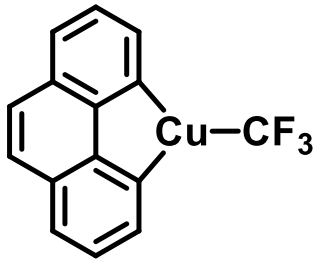
➢ Copper-catalyzed reactions

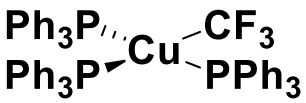
- **Copper-catalyzed trifluoromethylation**



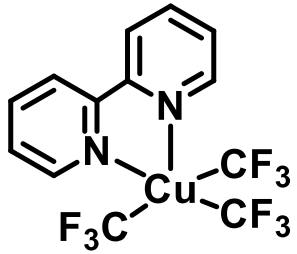
○ **Selected stable trifluoromethylation complexes**

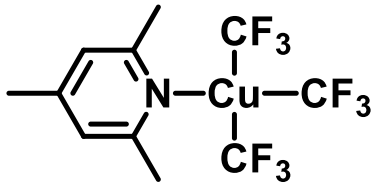
✓ **Cu^{I}**





✓ **Cu^{III}**



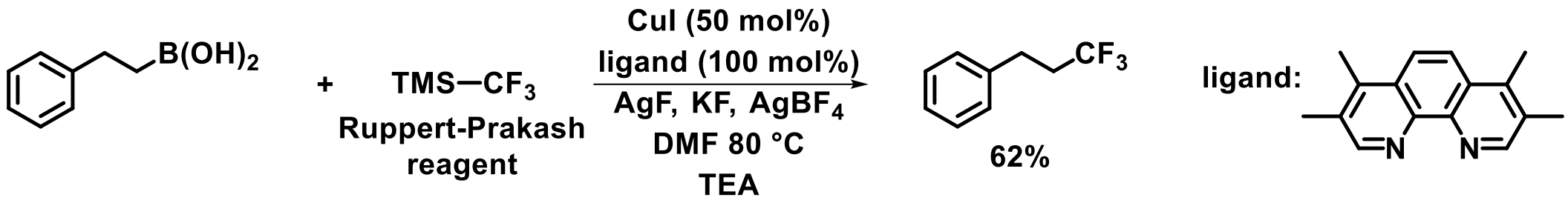


Organocopper chemisty

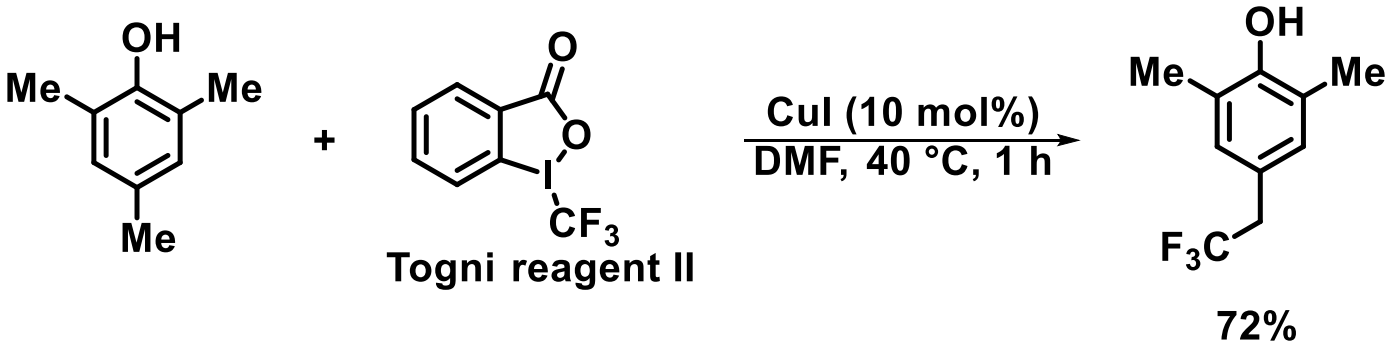
➢ Copper-catalyzed reactions

- **Copper-catalyzed trifluoromethylation**

○ **Selected examples**



Ang. Chem. Int. Ed. **2012**, *51, 12551*



Chem. Comunn. **2015**, *51, 16675*