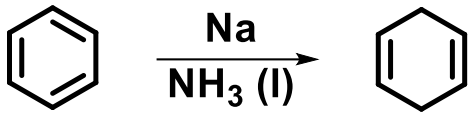
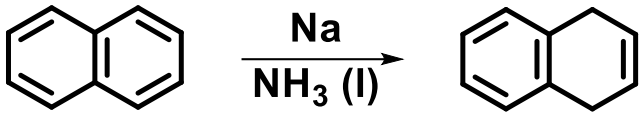
Dearomative reactions

➢ Dearomative reactions in traditional chemistry

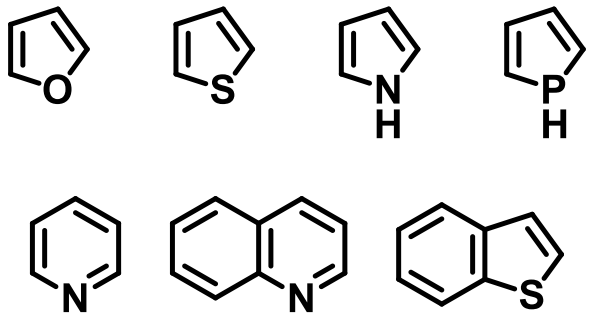
- **Birch reduction**





➢ Transition-metal-catalyzed dearomatization

- ○ **Activated substrates**

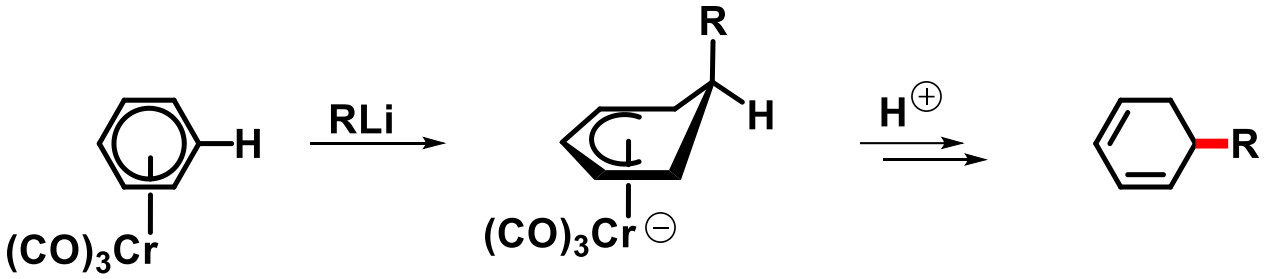


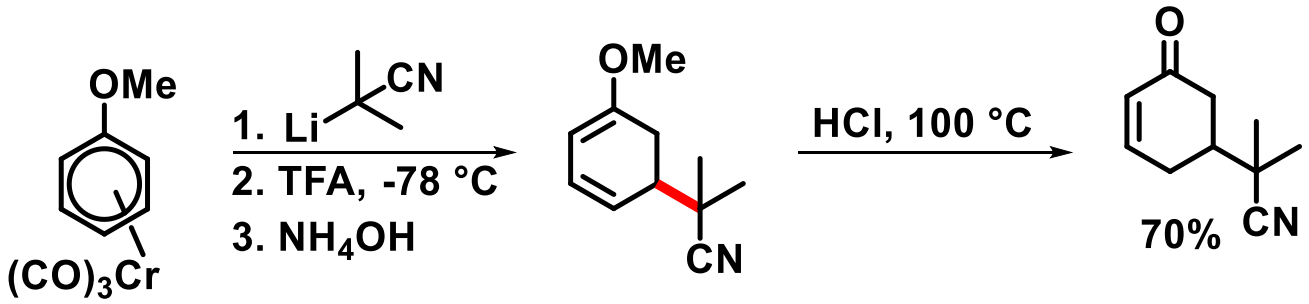
- ○ **Nonactivated substrates**

Dearomative reactions

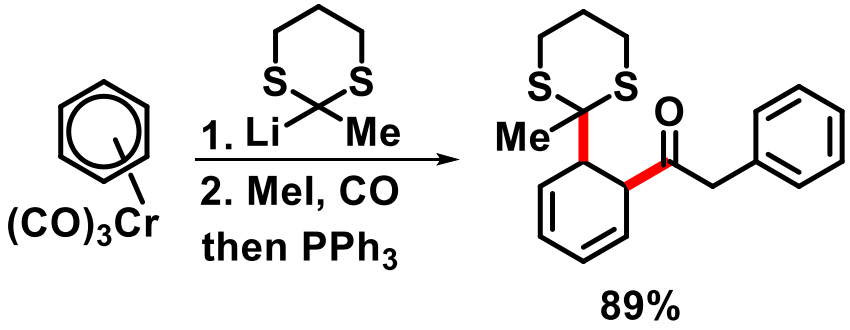
➢ Chemistry of η^6-arene complexes

- **Transition-metal-mediated dearomative reactions**





J. Org. Chem. **1979**, *44, 3275*

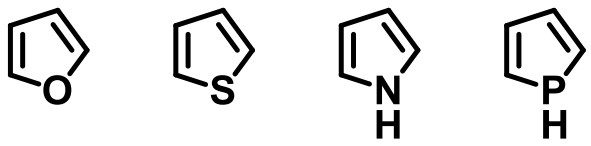


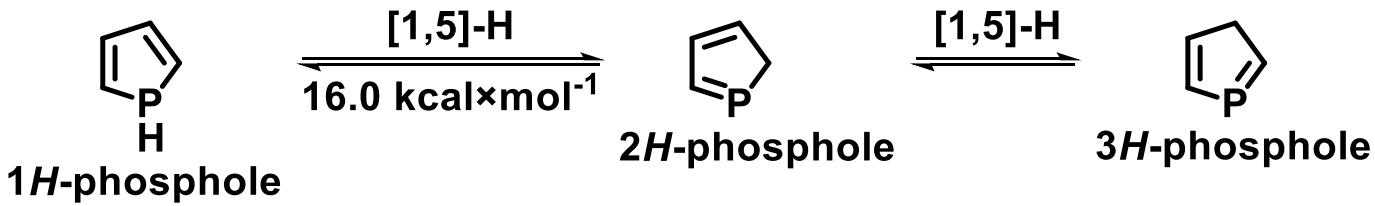
J. Chem. Soc., Chem. Comunn. **1983**, *1320*

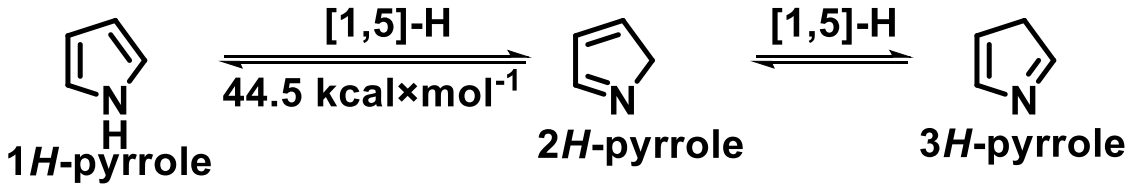
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Aromaticity of five-membered heterocycles**



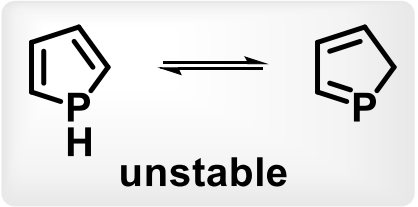


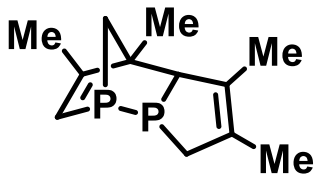


Dearomative reactions

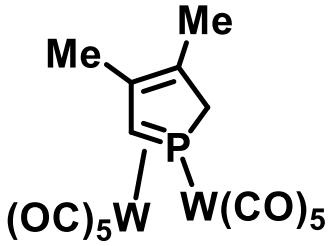
➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of phospholes – 2*H*-phospholes**



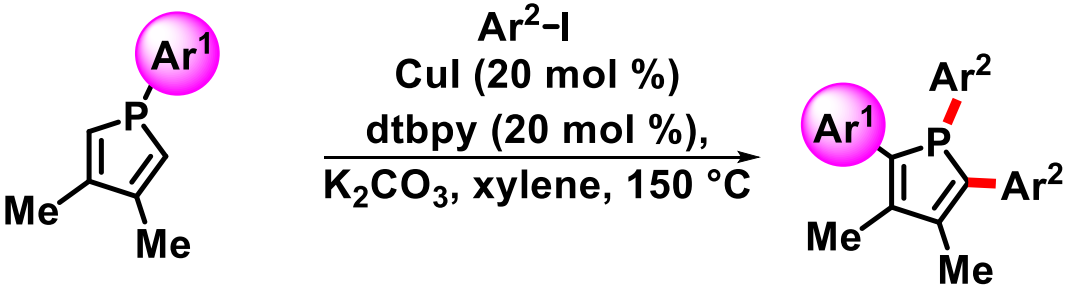


stable dimer



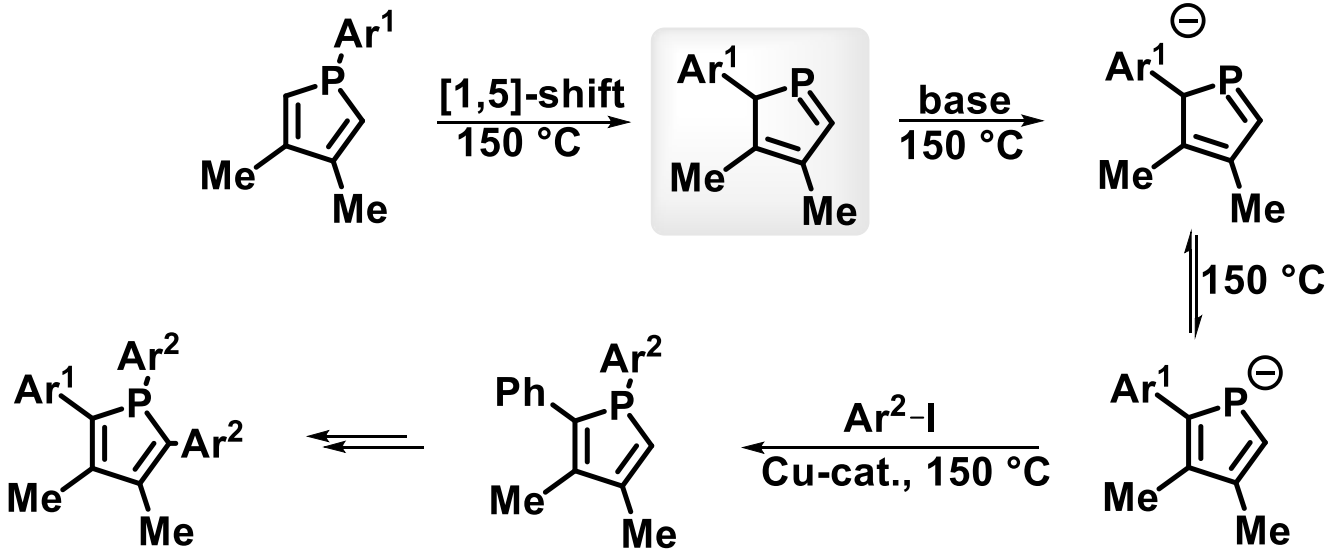
stable

○ **Arylation of phosphole via 2*H*-phospholes**



Org. Lett. **2020**, *22*, 2187

✓ **Proposed mechanism**

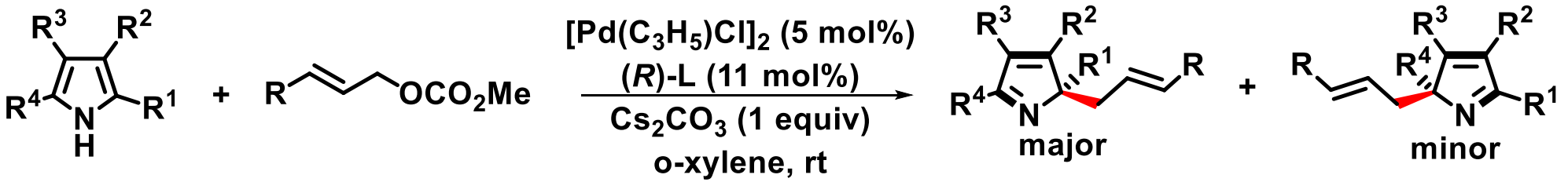


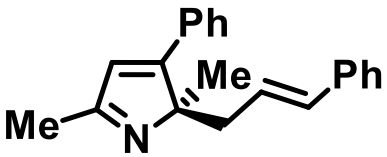
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

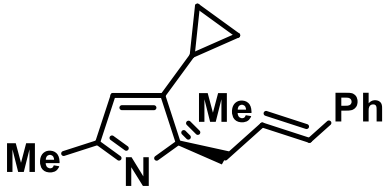
- **Dearomative modificaton of 1*H*-pyrroles**

○ **Synthesis of 2*H*-pyrroles**

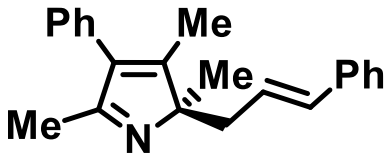




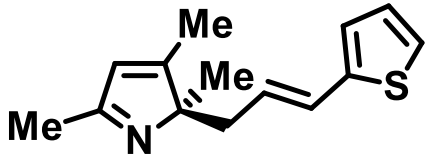
86%, 91% ee
r.r. = 94/6



90%, 91% ee
r.r. = 95/5



92%, 93% ee
r.r. = 76/24



77%, 97% ee
r.r. = 94/6

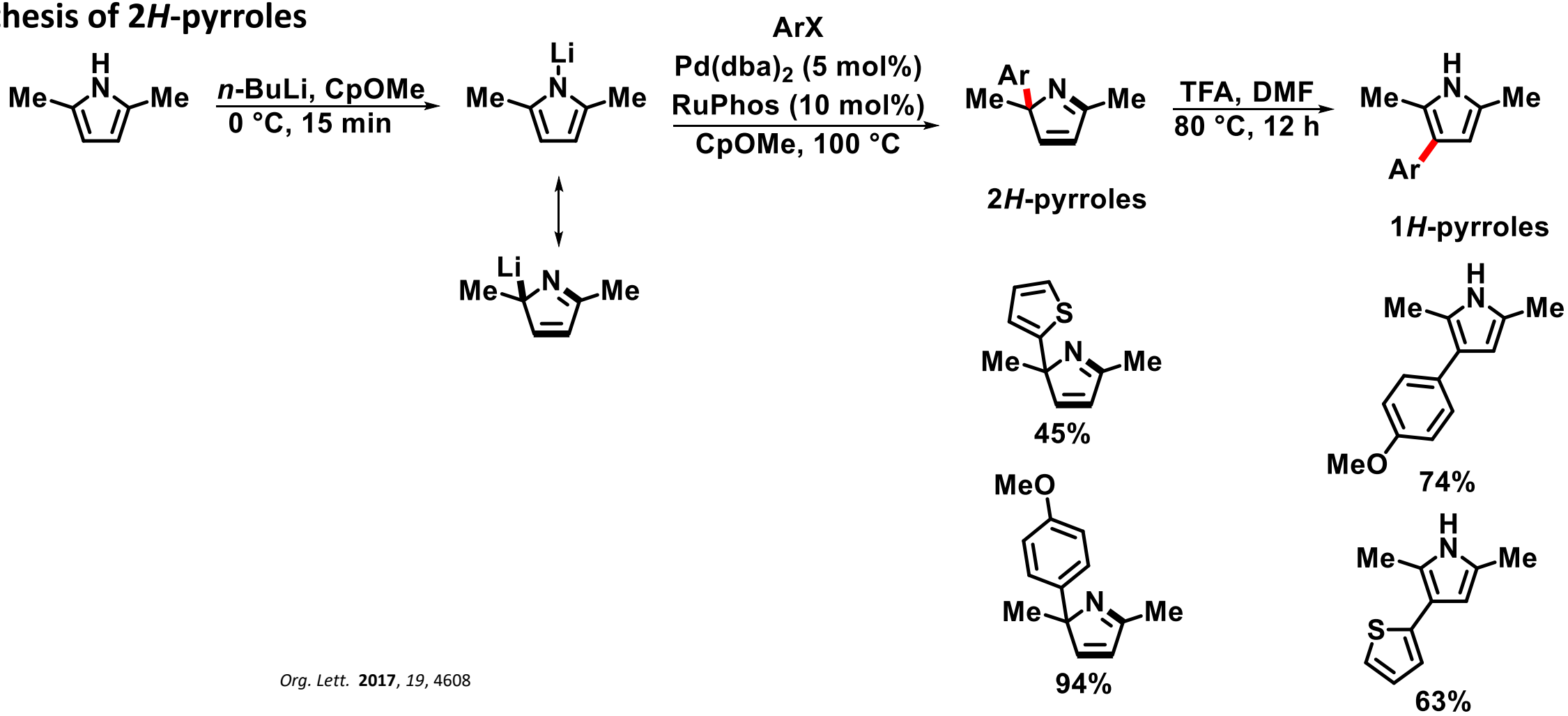
J. Am. Chem. Soc. **2014**, *136*, 6590

Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of 1*H*-pyrroles**

○ **Synthesis of 2*H*-pyrroles**



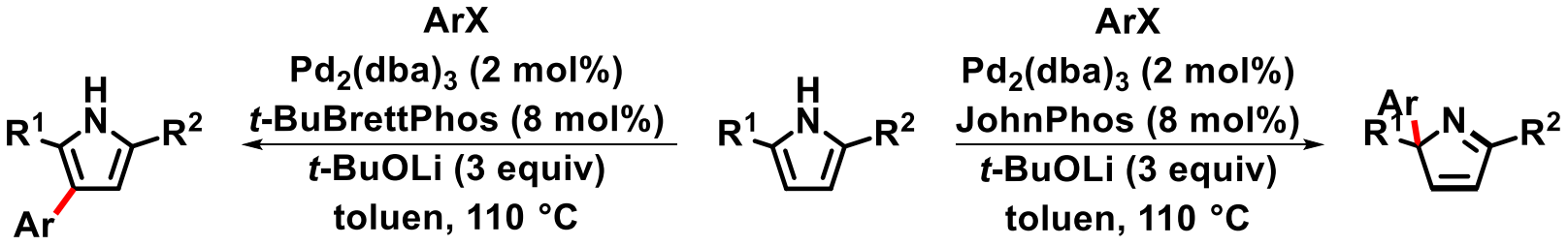
Org. Lett. **2017**, *19*, 4608

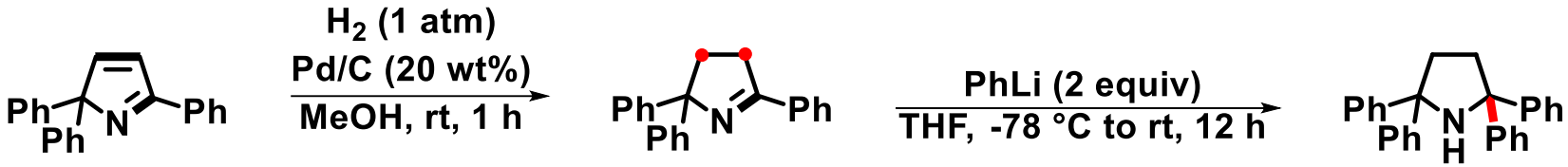
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of 1*H*-pyrroles**

○ **Synthesis of 2*H*-pyrroles**





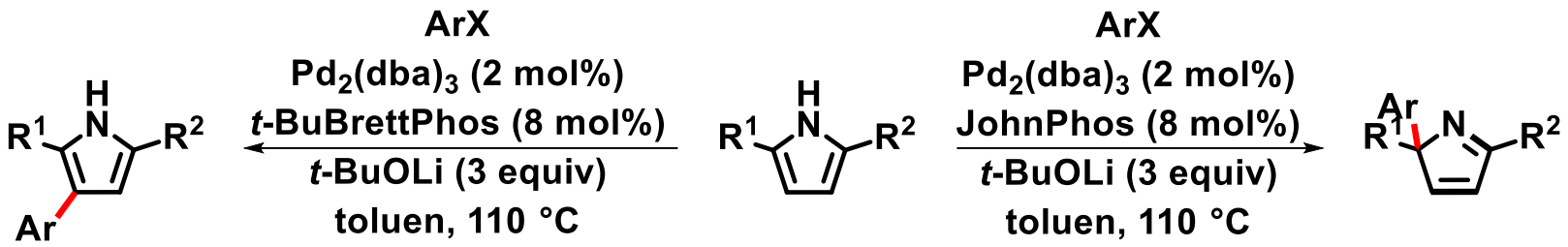
Org. Lett. **2019**, *21*, 6972

Dearomative reactions

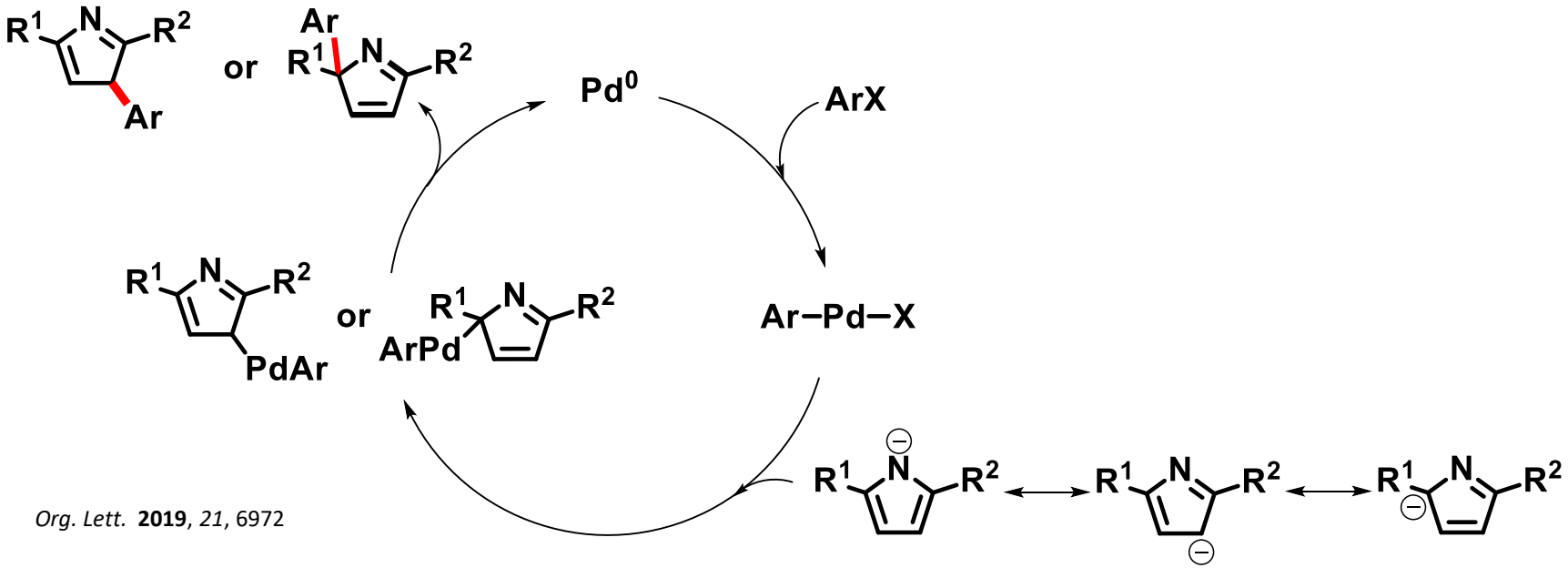
➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of 1*H*-pyrroles**

○ Synthesis of 2*H*-pyrroles



✓ Proposed mechanism



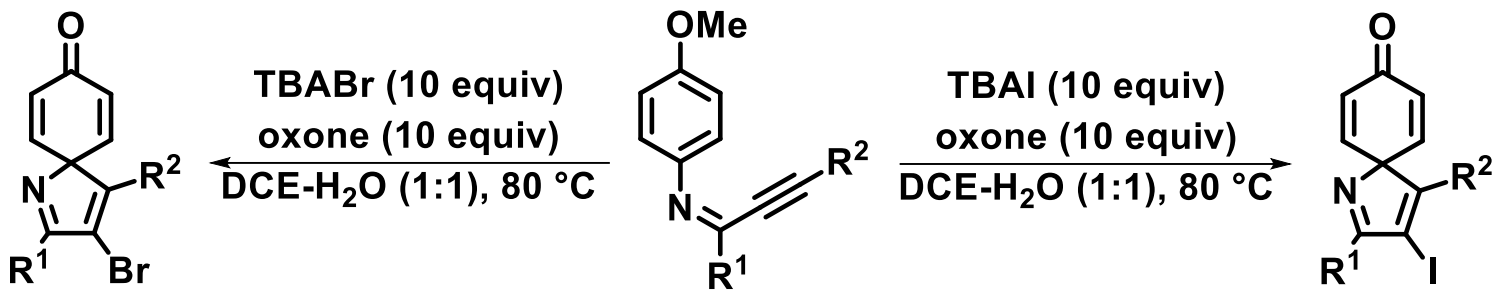
Org. Lett. **2019**, *21*, 6972

Dearomative reactions

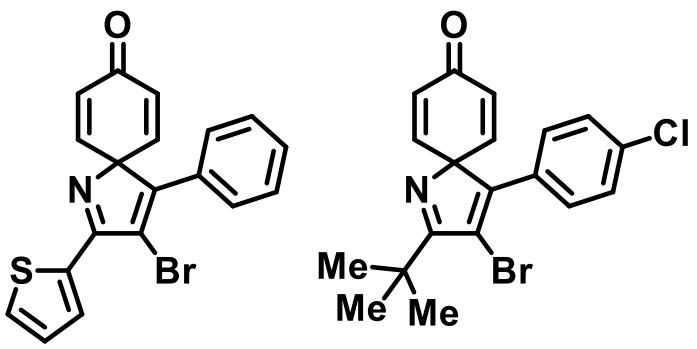
➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of 1*H*-pyrroles**

○ Transition-metal-free synthesis of 2*H*-pyrroles

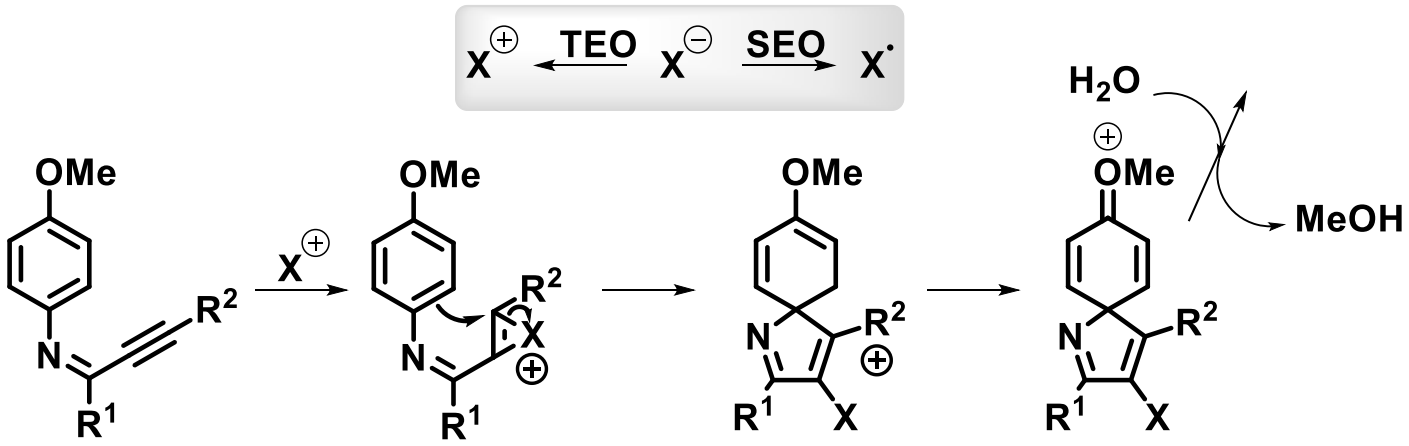


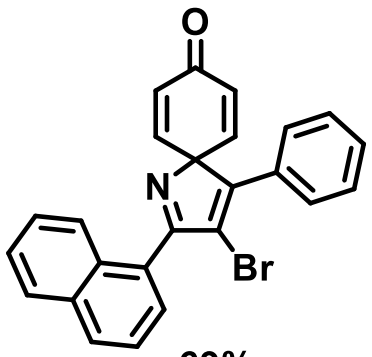
✓ Selected examples



69% 71%

✓ Proposed mechanism





69%

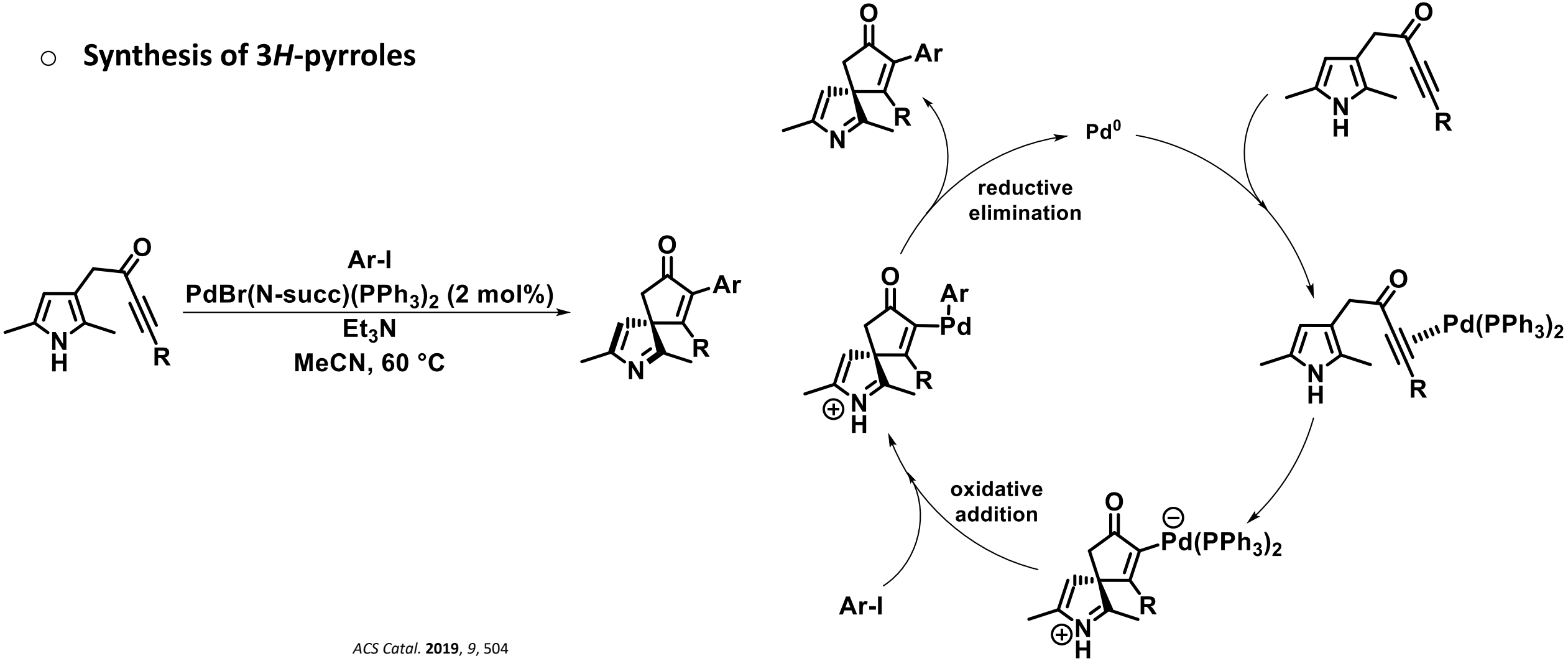
Synthesis **2020**, *52*, 609

Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of 1*H*-pyrroles**

○ **Synthesis of 3*H*-pyrroles**

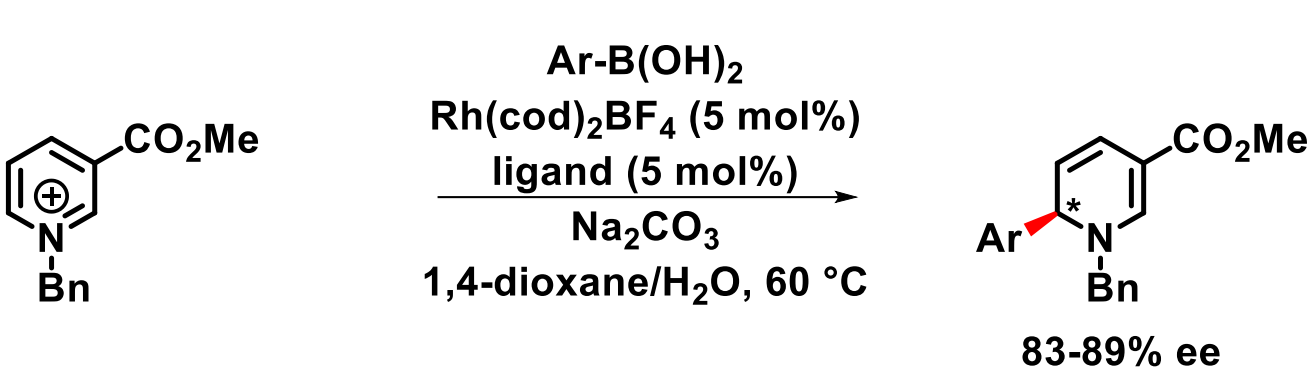


ACS Catal. **2019**, *9*, 504

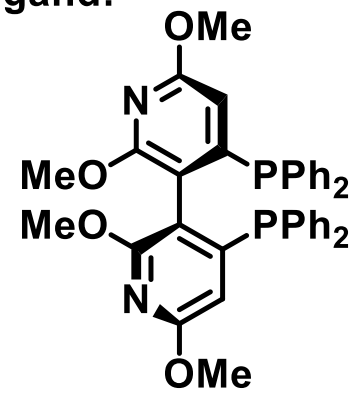
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

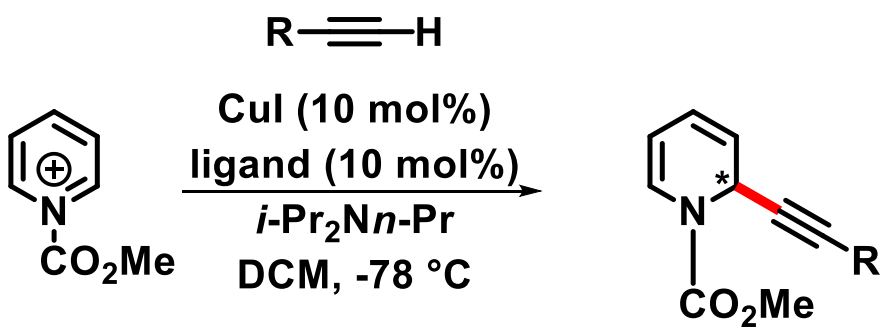
- **Dearomative modificaton of pyridines**



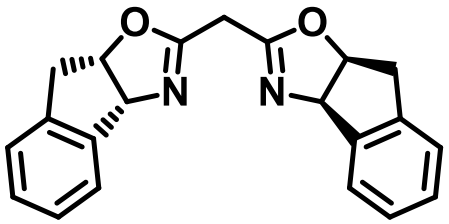
ligand:



J. Am. Chem. Soc. **2011**, *133*, 2878



ligand:

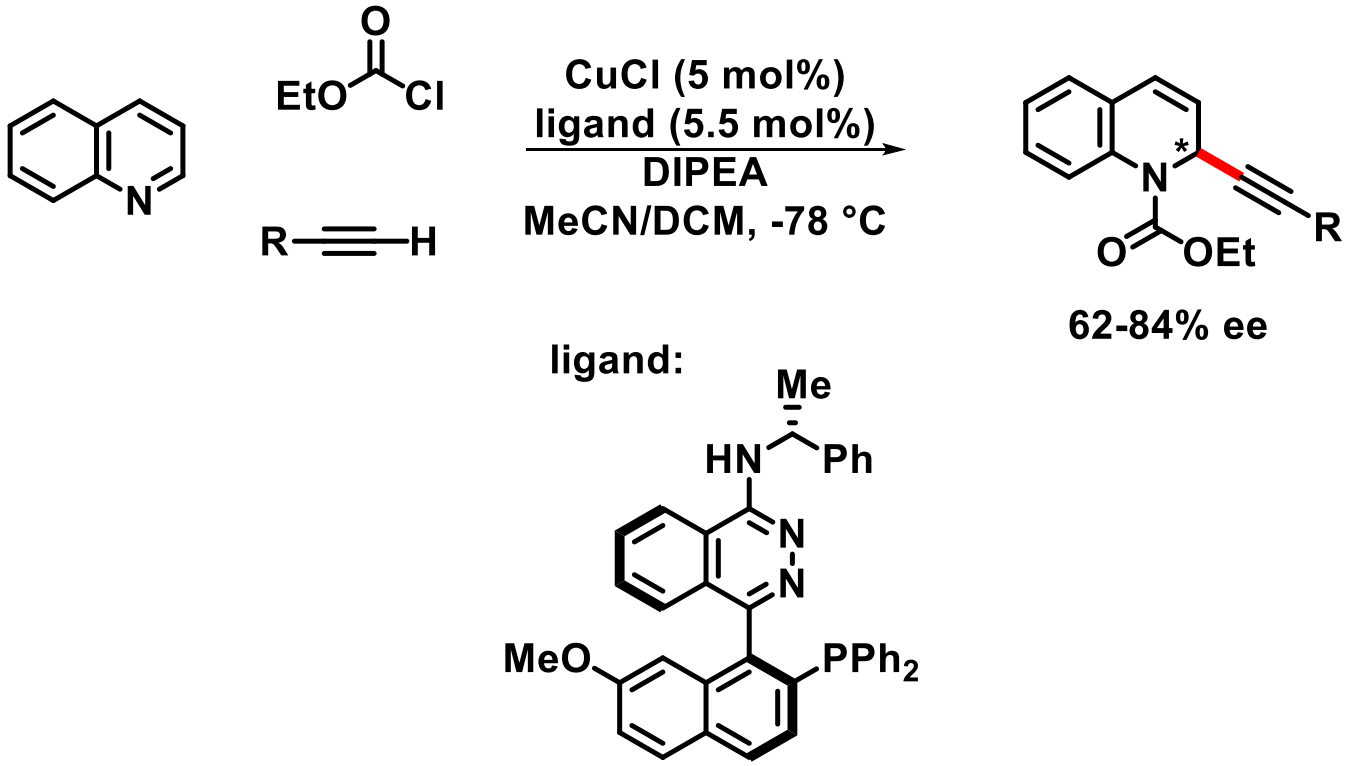


J. Am. Chem. Soc. **2007**, *129*, 9300

Dearomative reactions

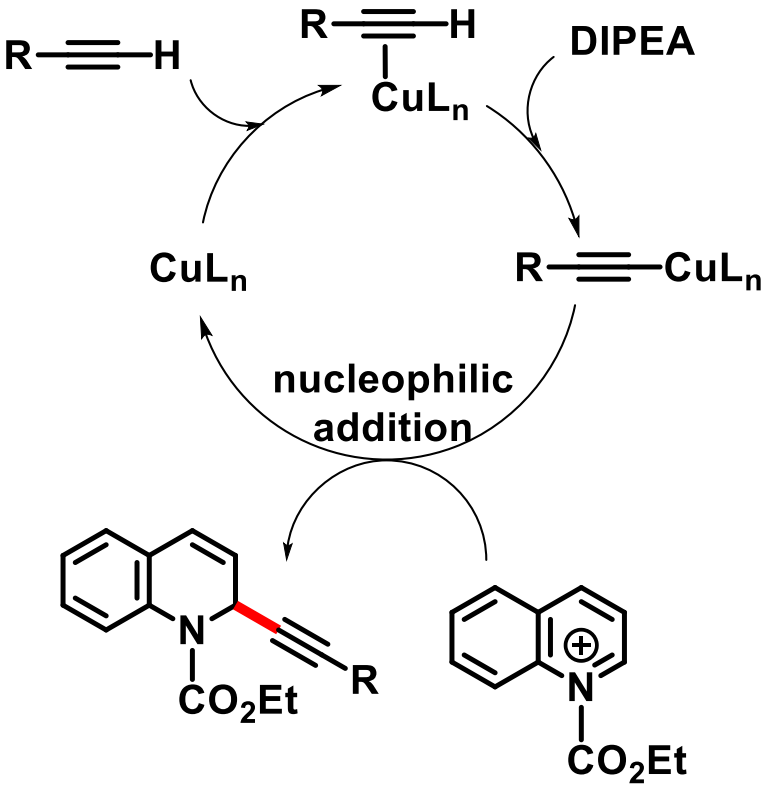
➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of quinolines and isoquinolines**



J. Org. Chem. **2008**, *73*, 1906

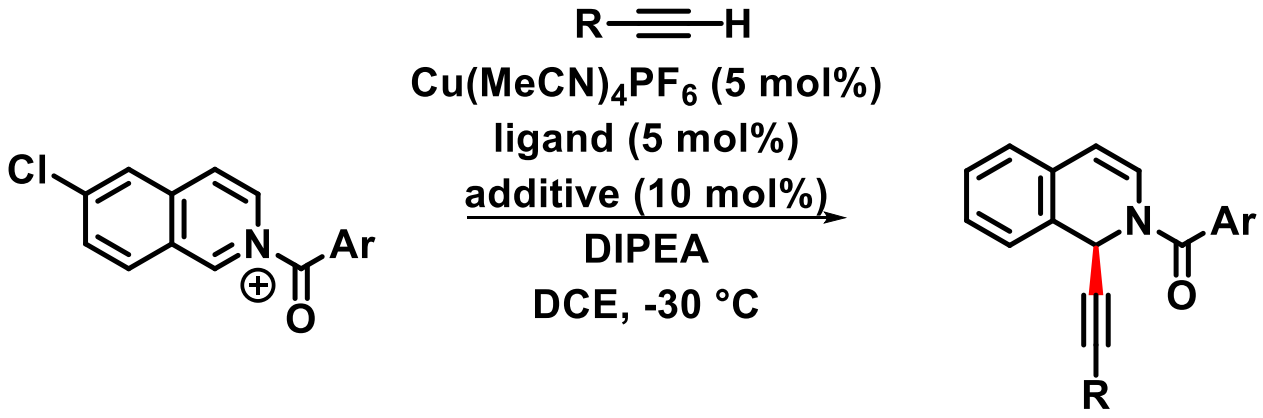
- **Proposed mechenism**



Dearomative reactions

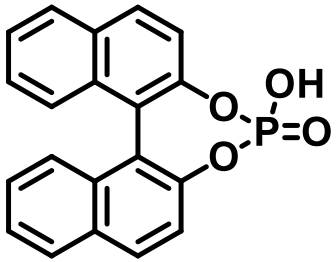
➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of quinolines and isoquinolines**

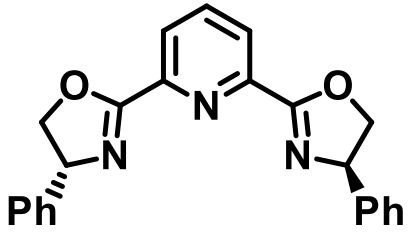


82-96% ee

additive:



ligand:

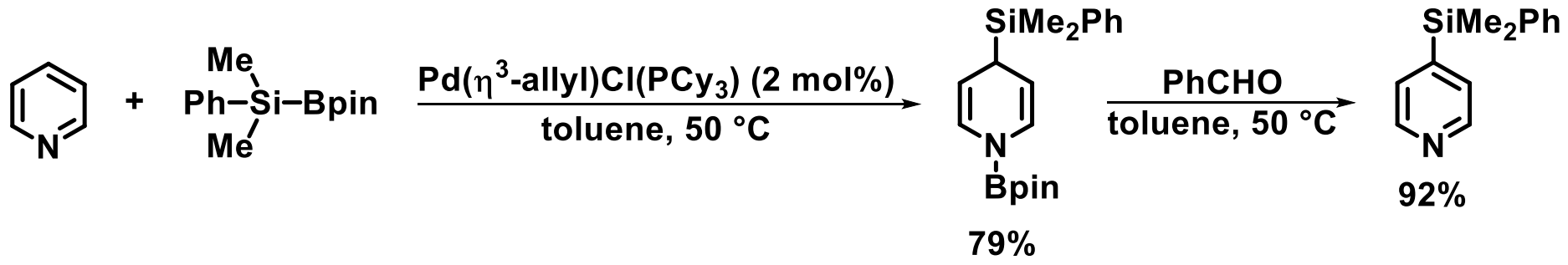


Org. Chem. Front. **2020**, *7*, 829

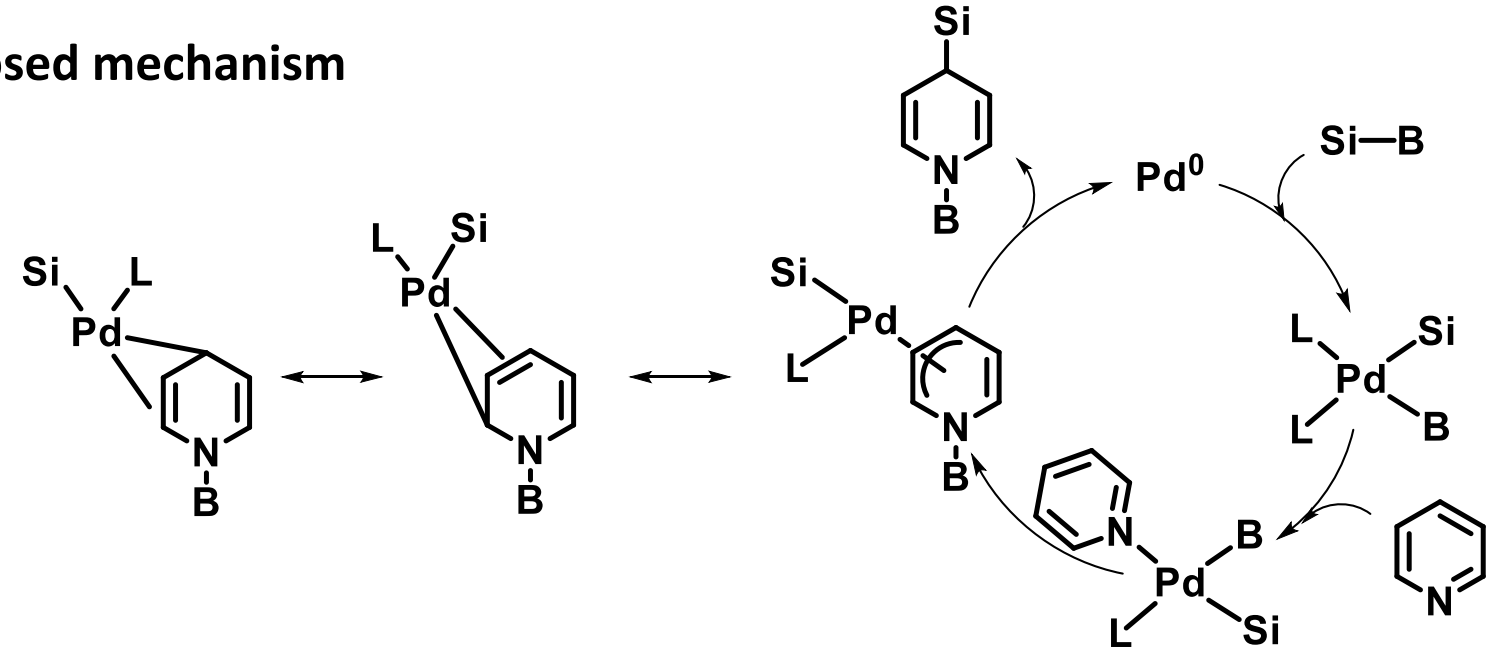
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

- **Dearomative modificaton of pyridine at position 4**



○ **Proposed mechanism**

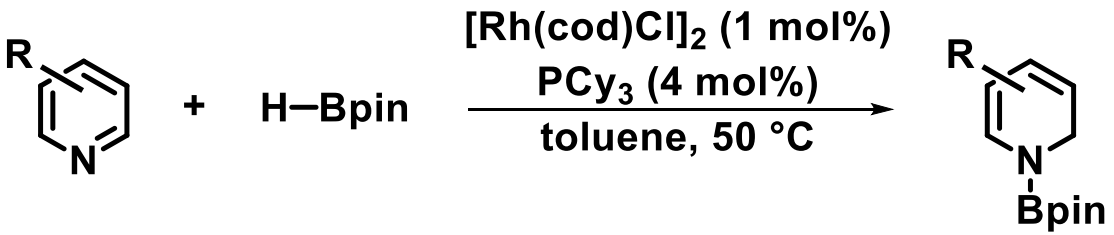


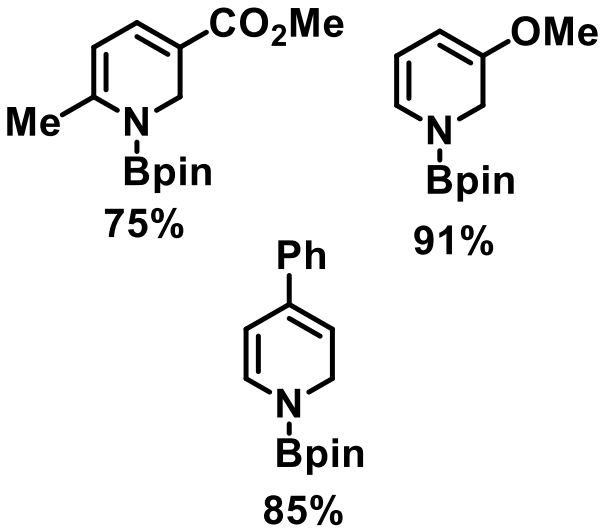
J. Am. Chem. Soc. **2011**, *133*, 7324

Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of heterocycles

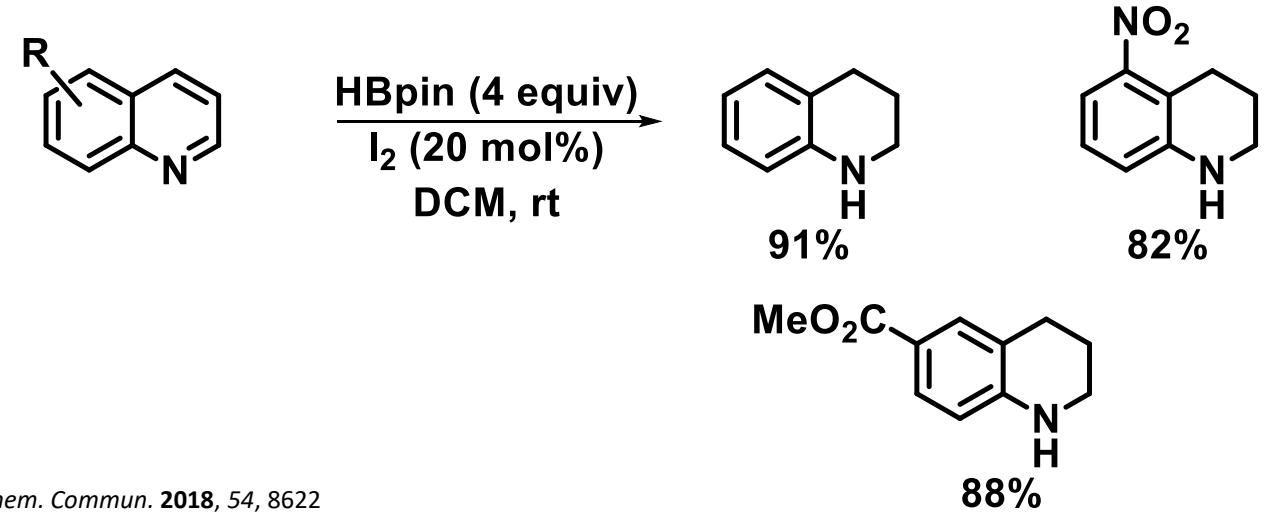
- **Dearomative hydroboration of pyridine-based heterocycles**





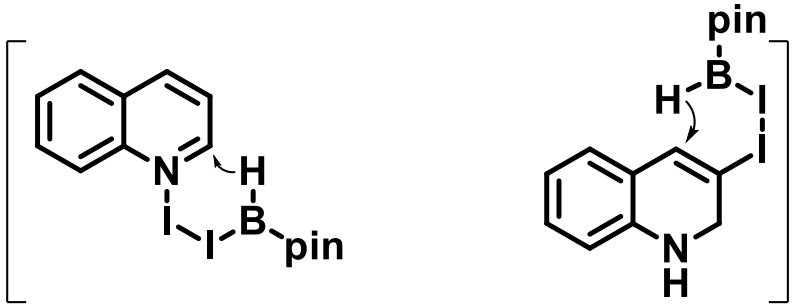
J. Am. Chem. Soc. **2012**, *134* 3699

- **Transition-metal-free alternative**



Chem. Commun. **2018**, *54*, 8622

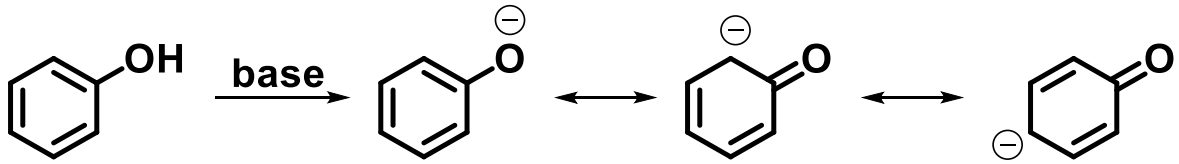
- **Proposed intermediates**



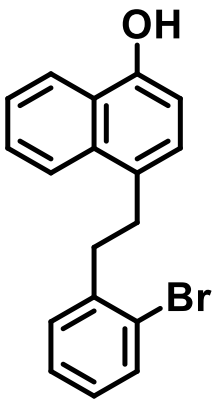
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of phenols

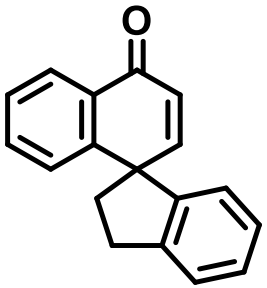
- **Phenol as ambident nucleophile**



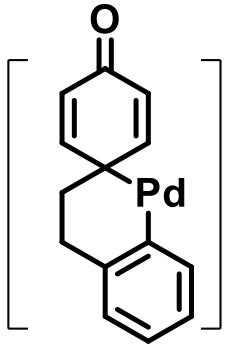
- **Transition-metal-catalyzed intramolecular C-arylation**



$Pd(OAc)_2$ (4 mol%)
ligand (12 mol%)
H_2O, K_2CO_3
dioxane, 80 °C



99%

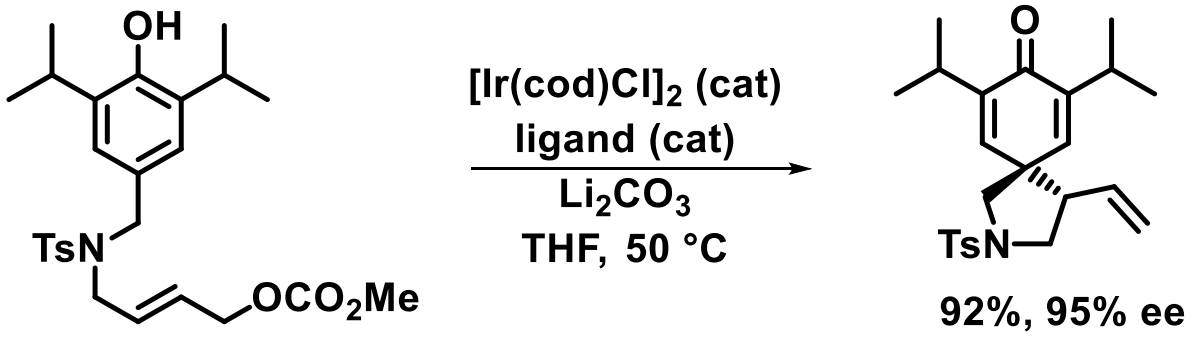


J. Am. Chem. Soc. **2011**, *133*, 9282

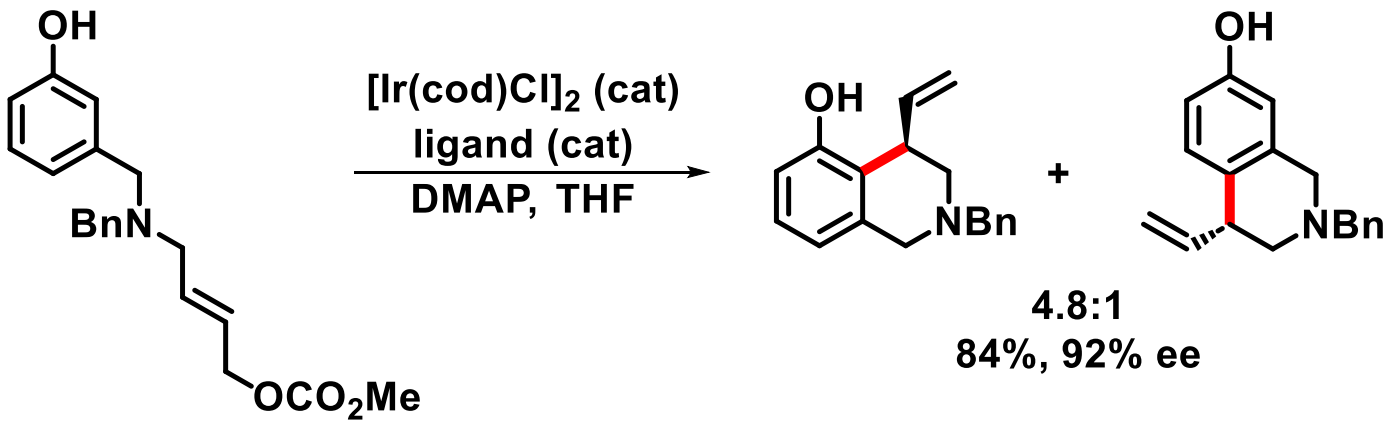
Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of phenols

- **Transition-metal-catalyzed intramolecular Tsuji-Trost reaction**



Angew. Chem., Int. Ed. **2011**, *50*, 4455

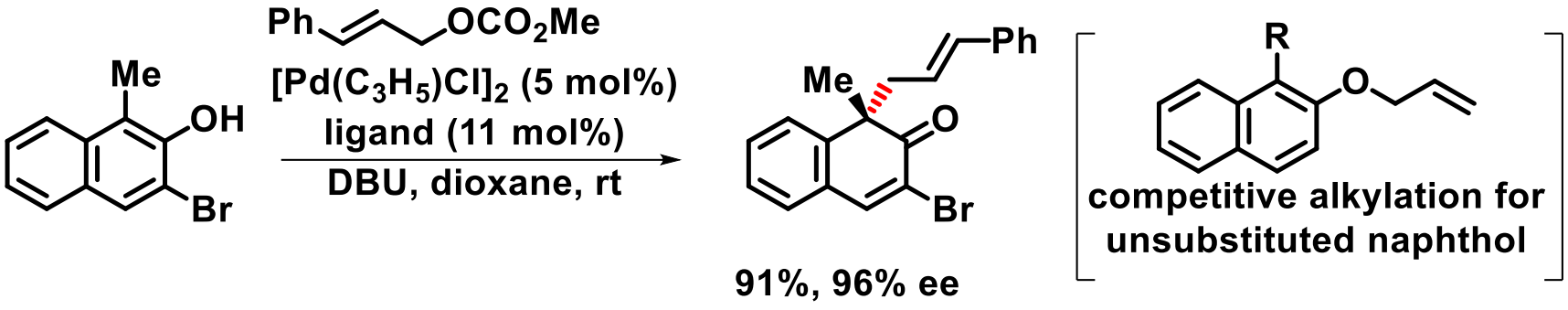


Org. Lett. **2012**, *14*, 2579

Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of phenols

- **Transition-metal-catalyzed intermolecular Tsuji-Trost reaction**

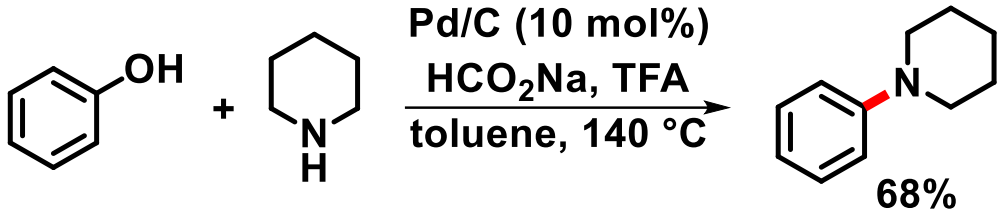


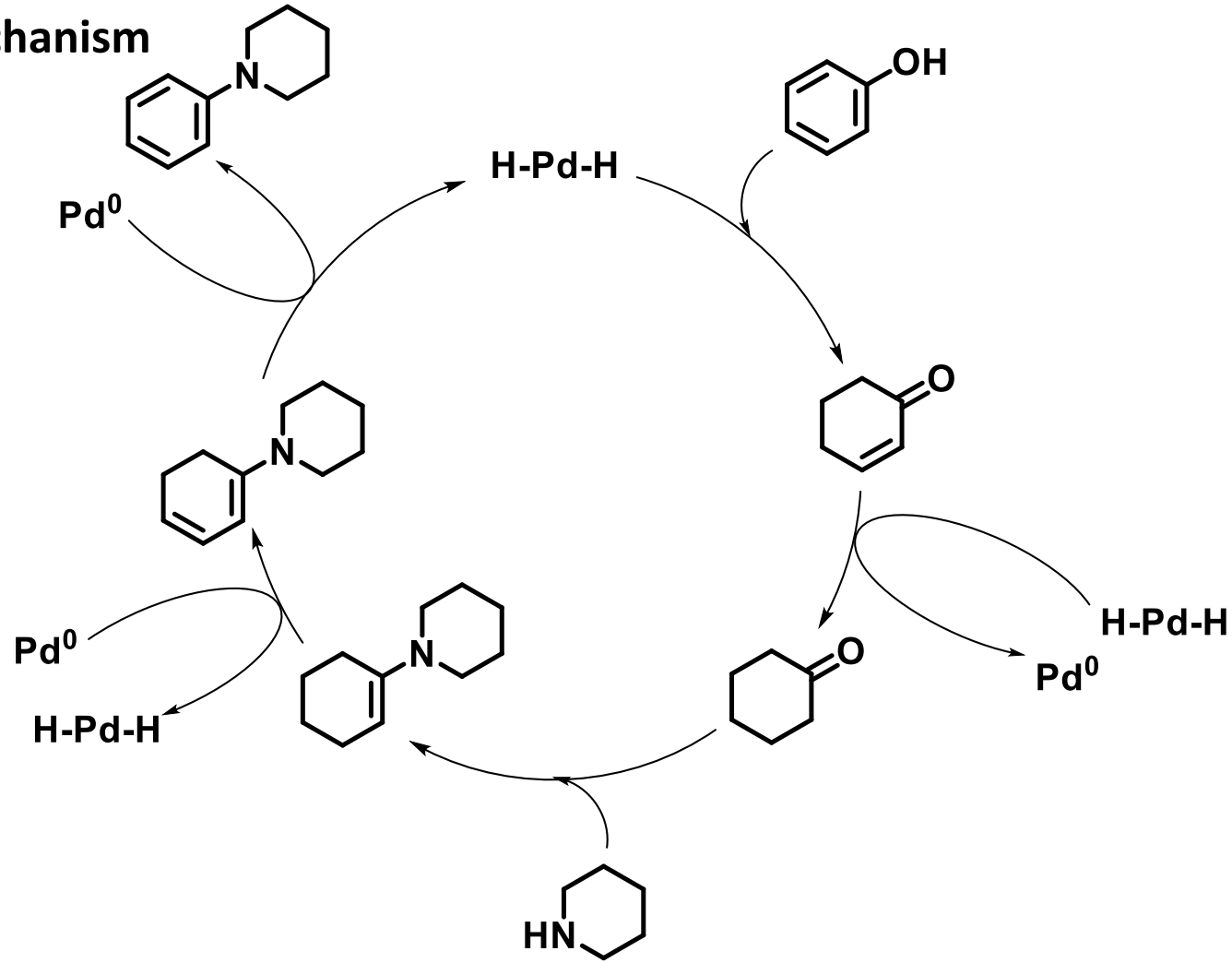
Angew. Chem. Int. Ed. **2013**, *52*, 1

Dearomative reactions

➢ Transition-metal-catalyzed dearomative functionalization of phenols

- **Dearomatization-rearomatization strategy for palladium catalyzed cross-coupling reactions**
  - **Proposed mechanism**



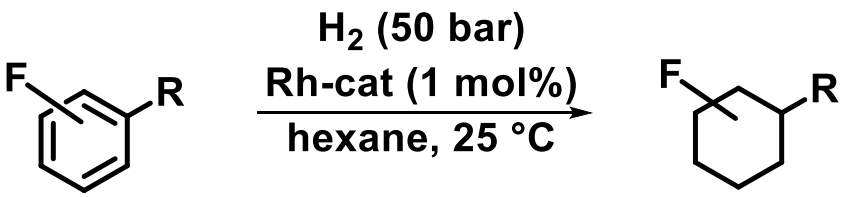


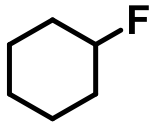
Angew. Chem. Int. Ed. **2015**, *54*, 14487

Dearomative reactions

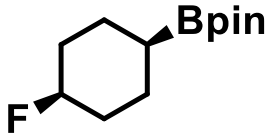
➢ Dearomative reactions of nonactivated substrates

- **Transition-metal-catalyzed hydrogenation**

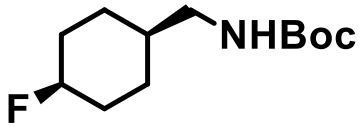




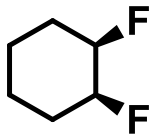
90%



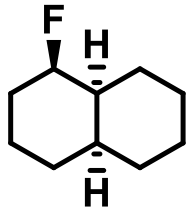
88%, 9:1 dr



90%, 7:1 dr



96%, 17:1 dr



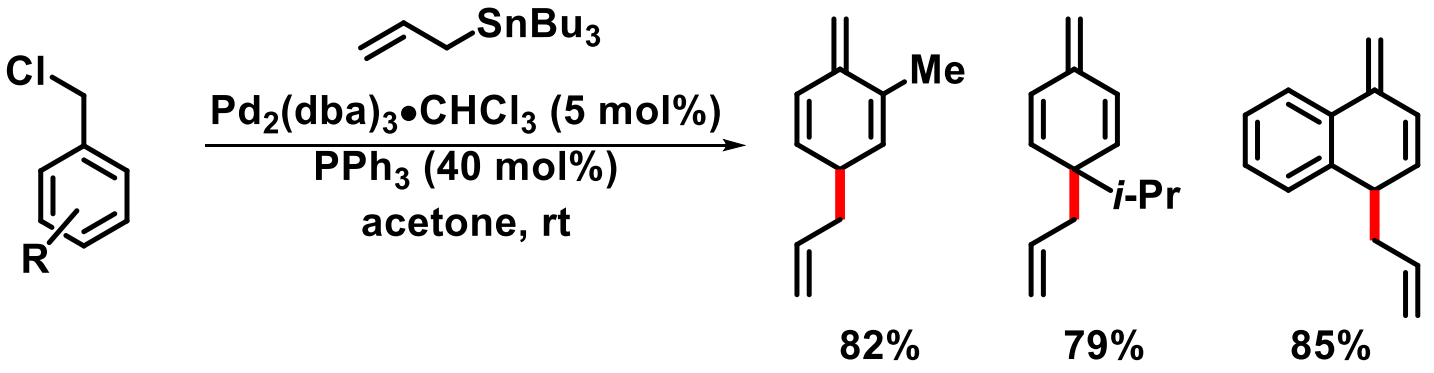
74%, 6:1 dr

Science **2017**, *357*, 908

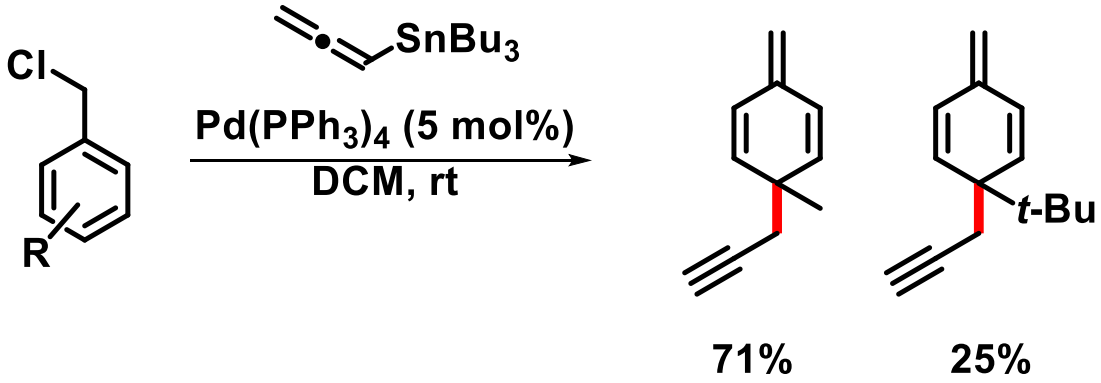
Dearomative reactions

➢ Dearomative reactions of nonactivated substrates

- **Transition-metal-catalyzed dearomative reactions**



J. Am. Chem. Soc. **2001**, *123*, 759

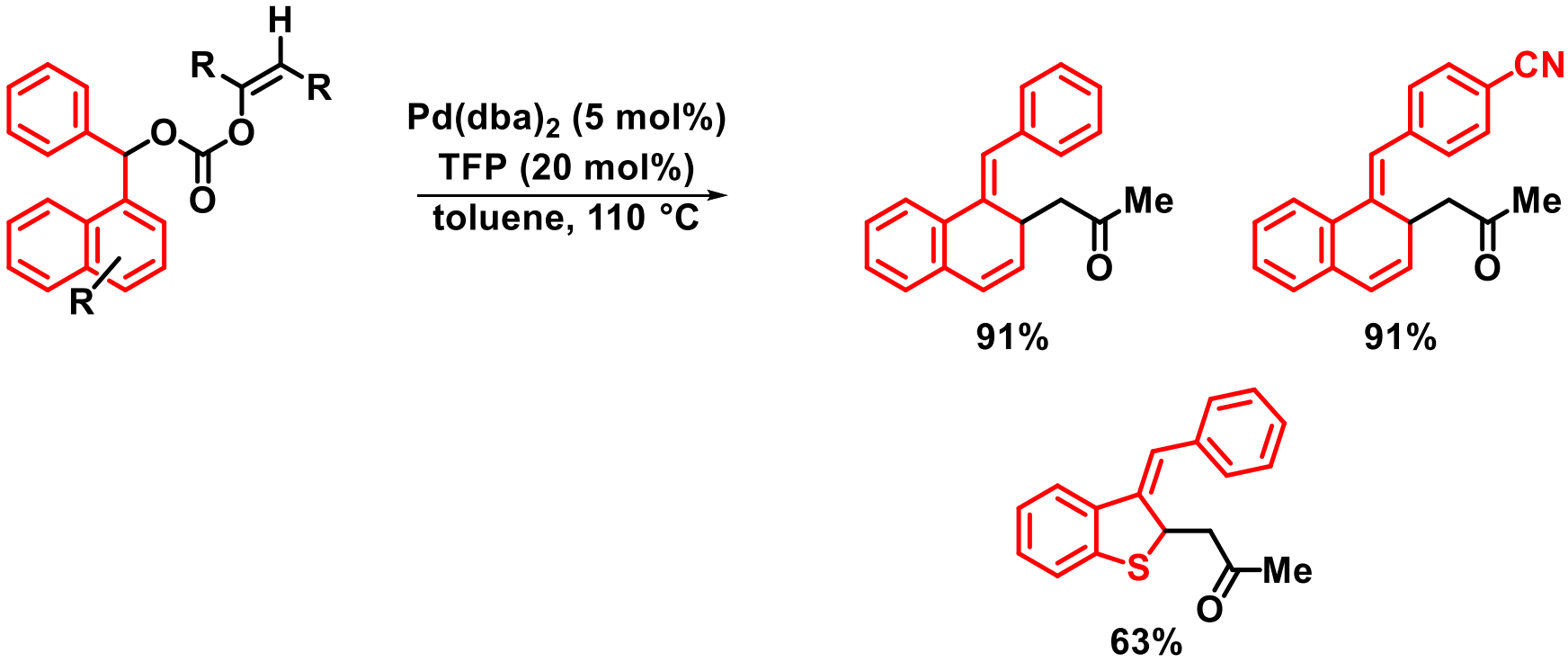


J. Org. Chem. **2010**, *75*, 2619

Dearomative reactions

➢ Dearomative reactions of nonactivated substrates

- **Transition-metal-catalyzed dearomative reactions**



Chem. Commun. **2016**, *52*, 7695