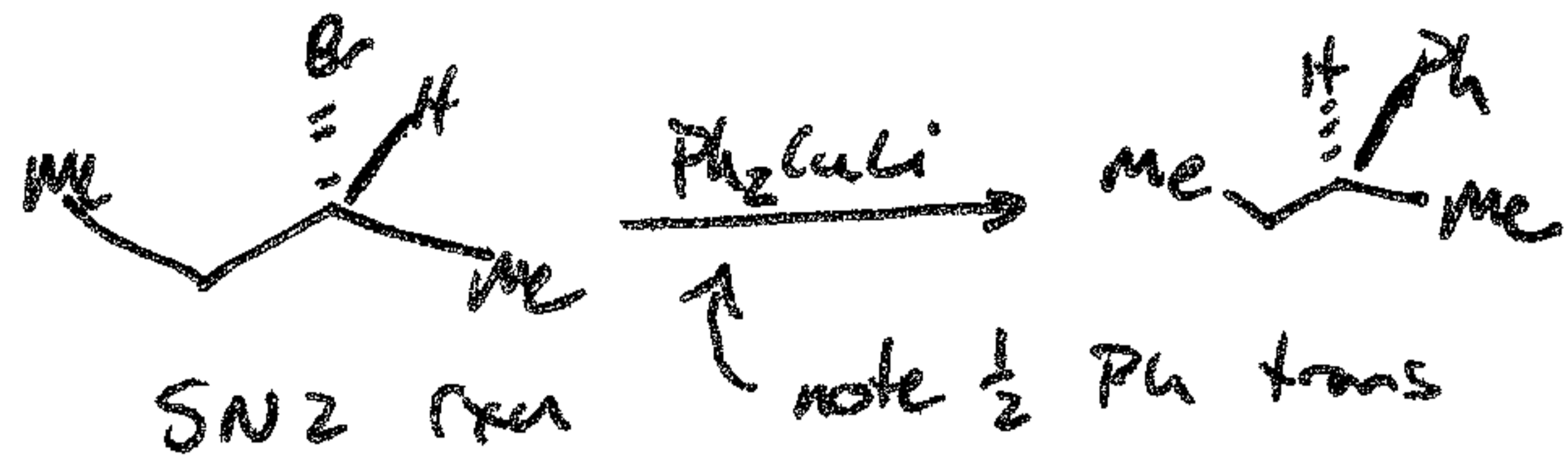


metal mediated substitution Reactions



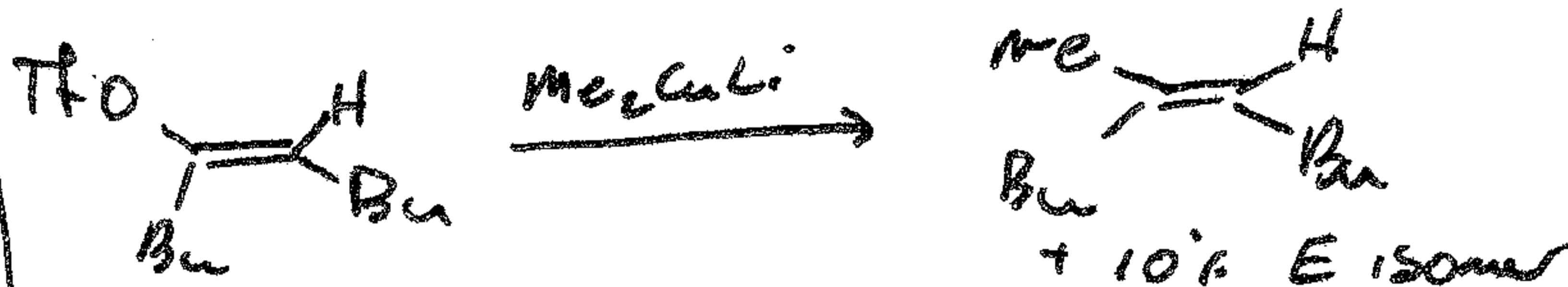
$1^\circ > 2^\circ > 3^\circ$

TfO ~ TsO ~ I > Br > Cl

Mech not clear

Rev: Comp. Org Synth, Vol 3, section 1.5

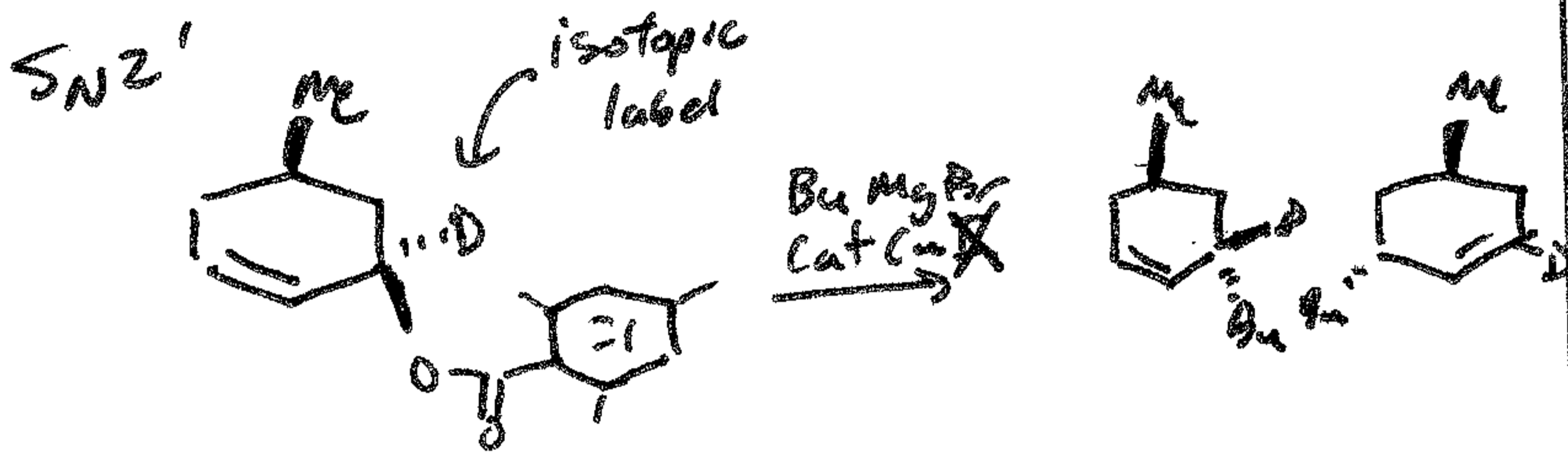
Also sp<sup>2</sup> systems



TL, 1980, 21, 4313

Also works w/ ArX

But not used very often now... see later

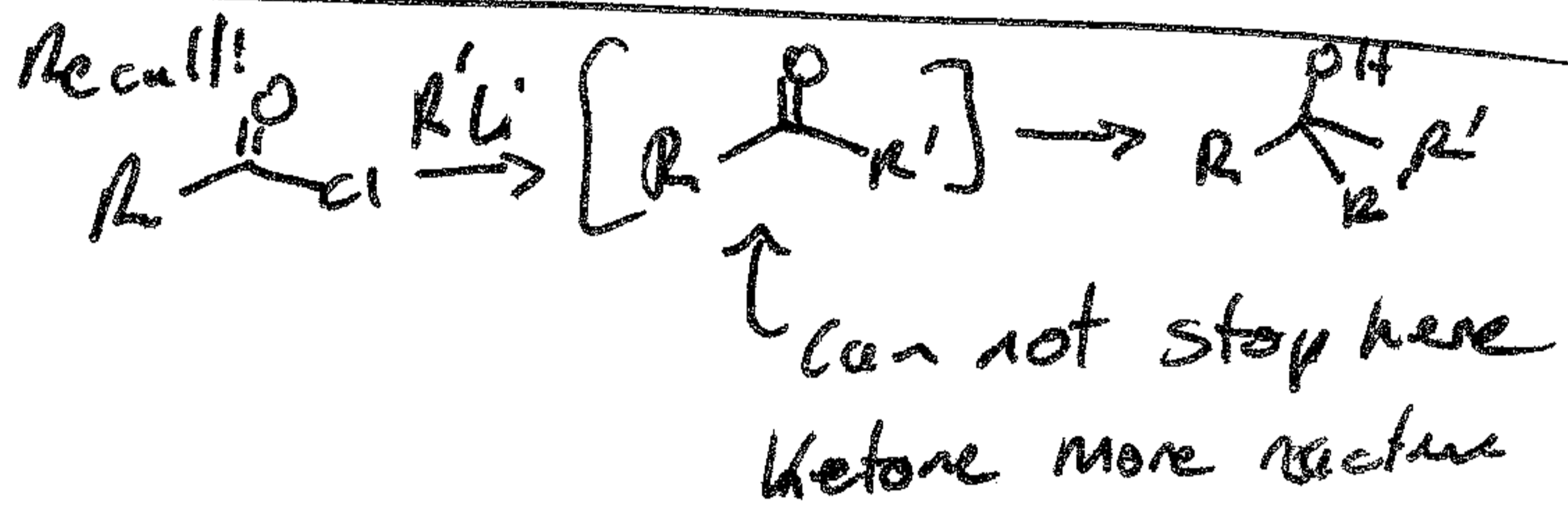
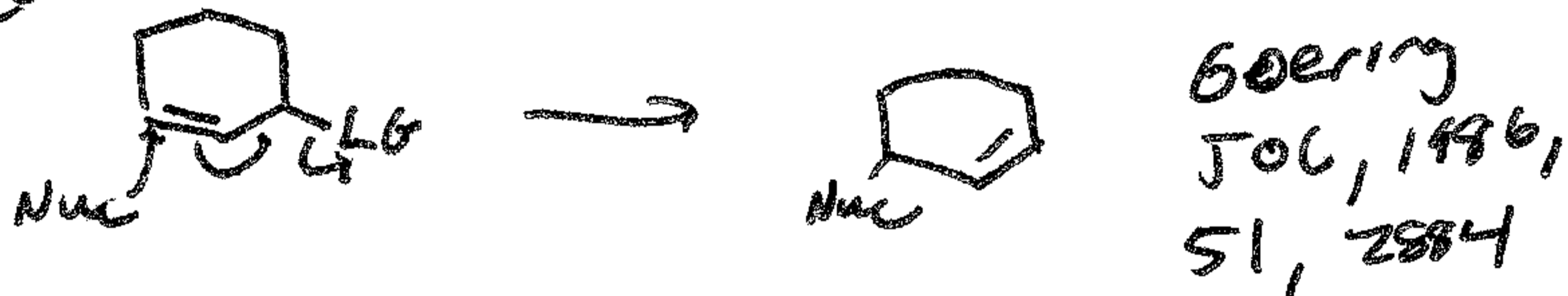
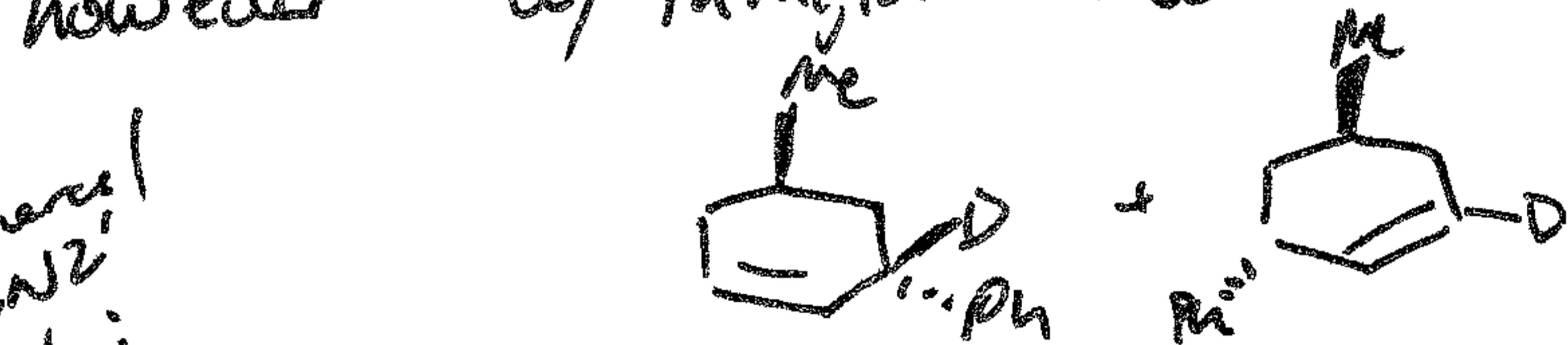


w/ 10% CuCl  
CuCN

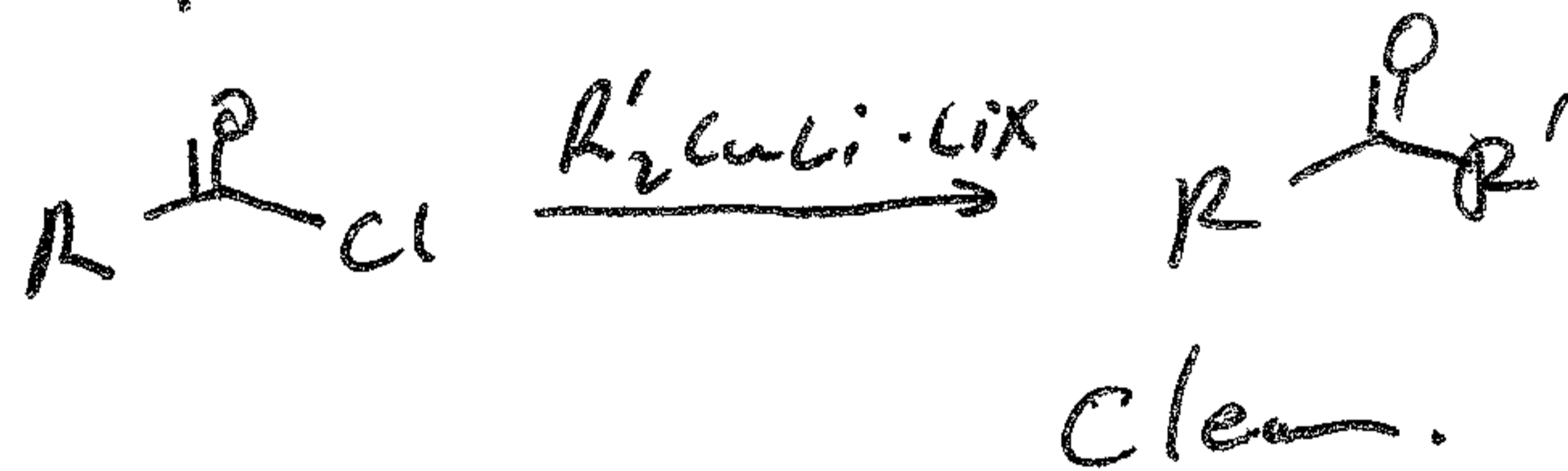
61% + 39%  
100% + 0%

however w/ PhMgBr + CuCN

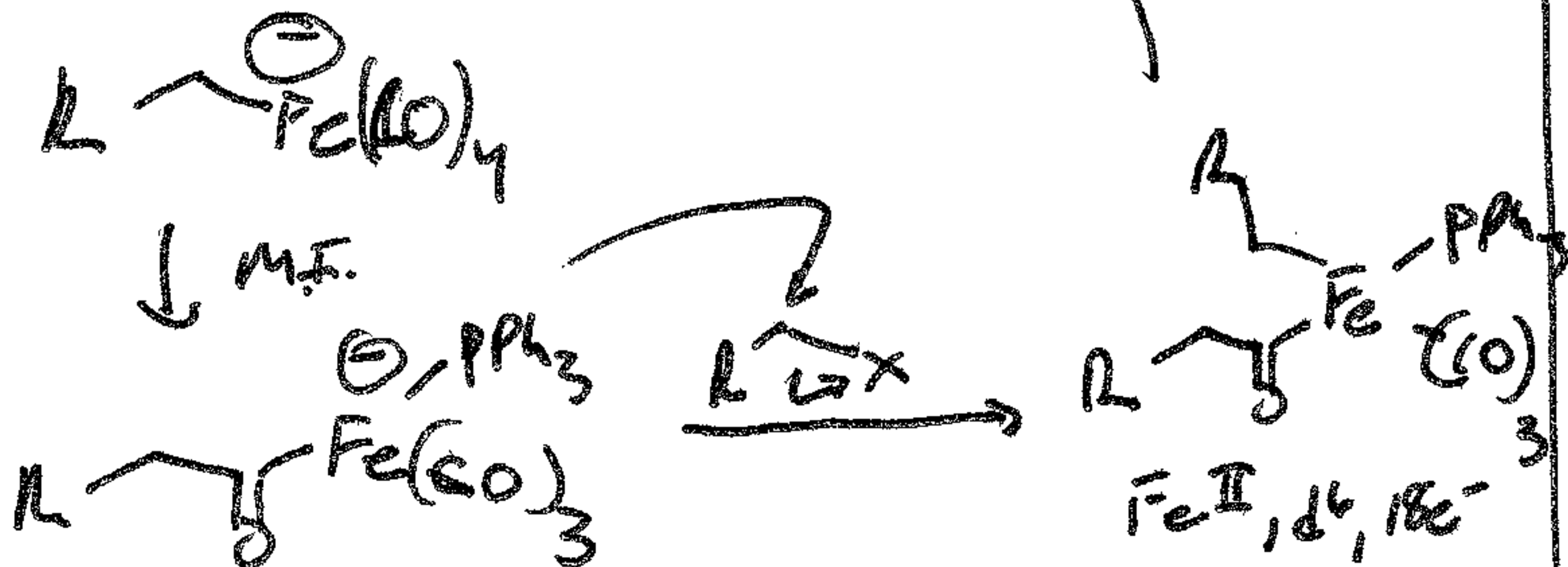
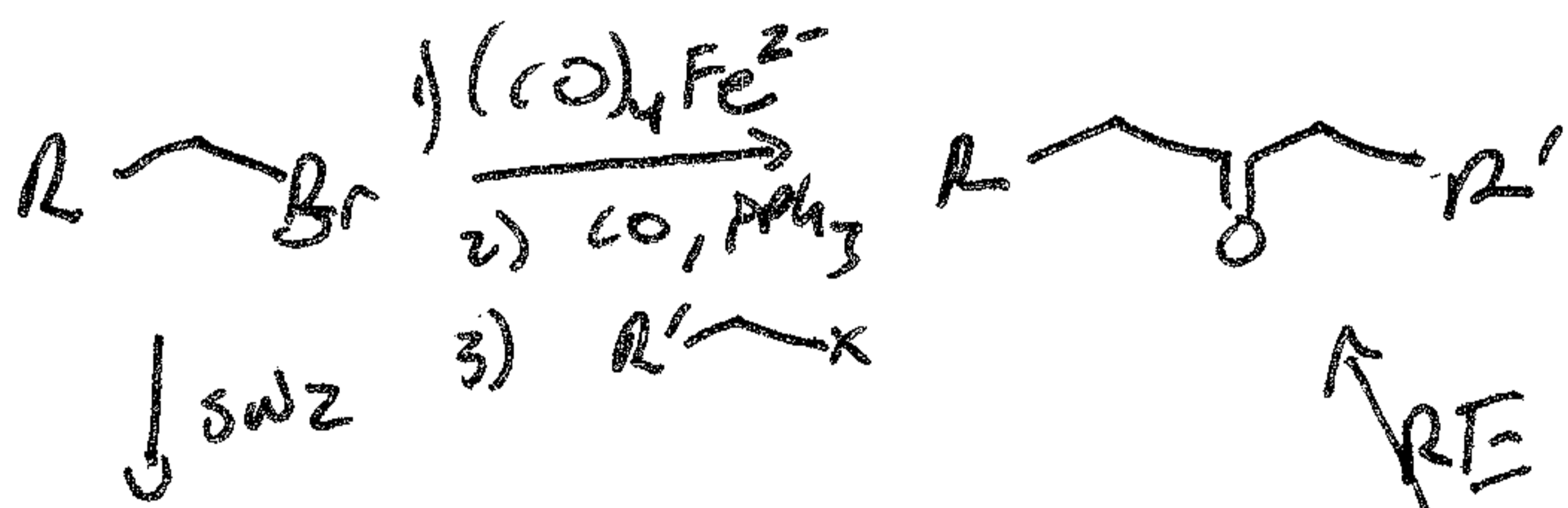
General SN2' mech:



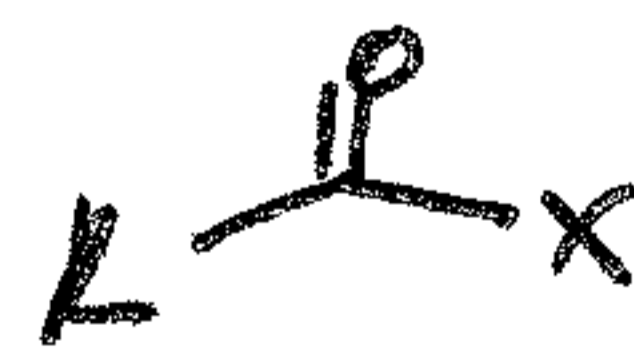
cuprate



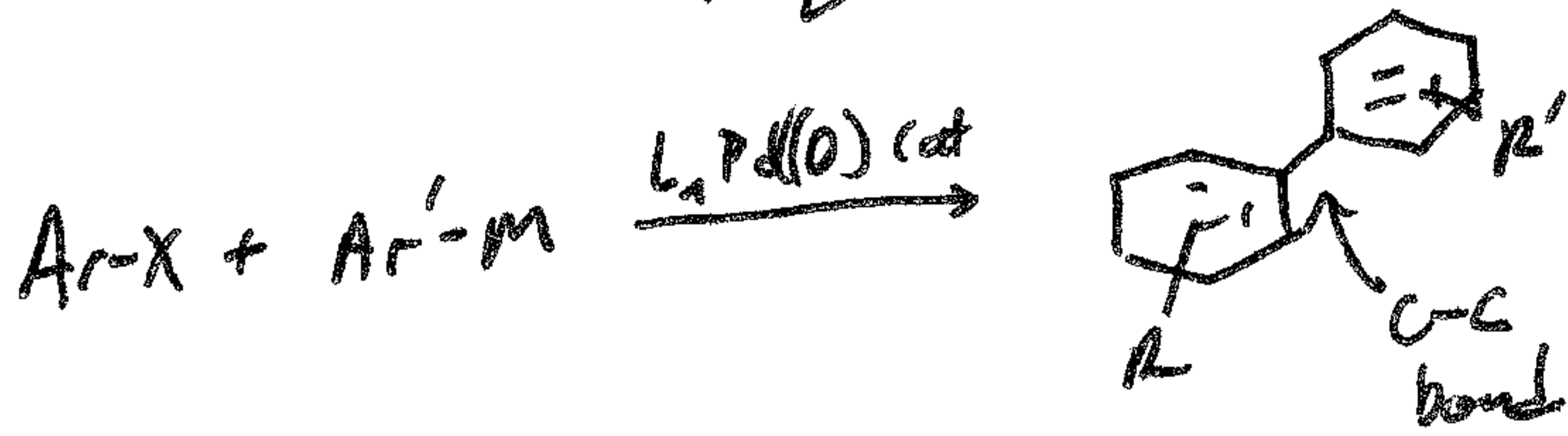
collman's reagent ( $\text{Fe}^{2+}, d^6, 18e^-$ )



Also works w/

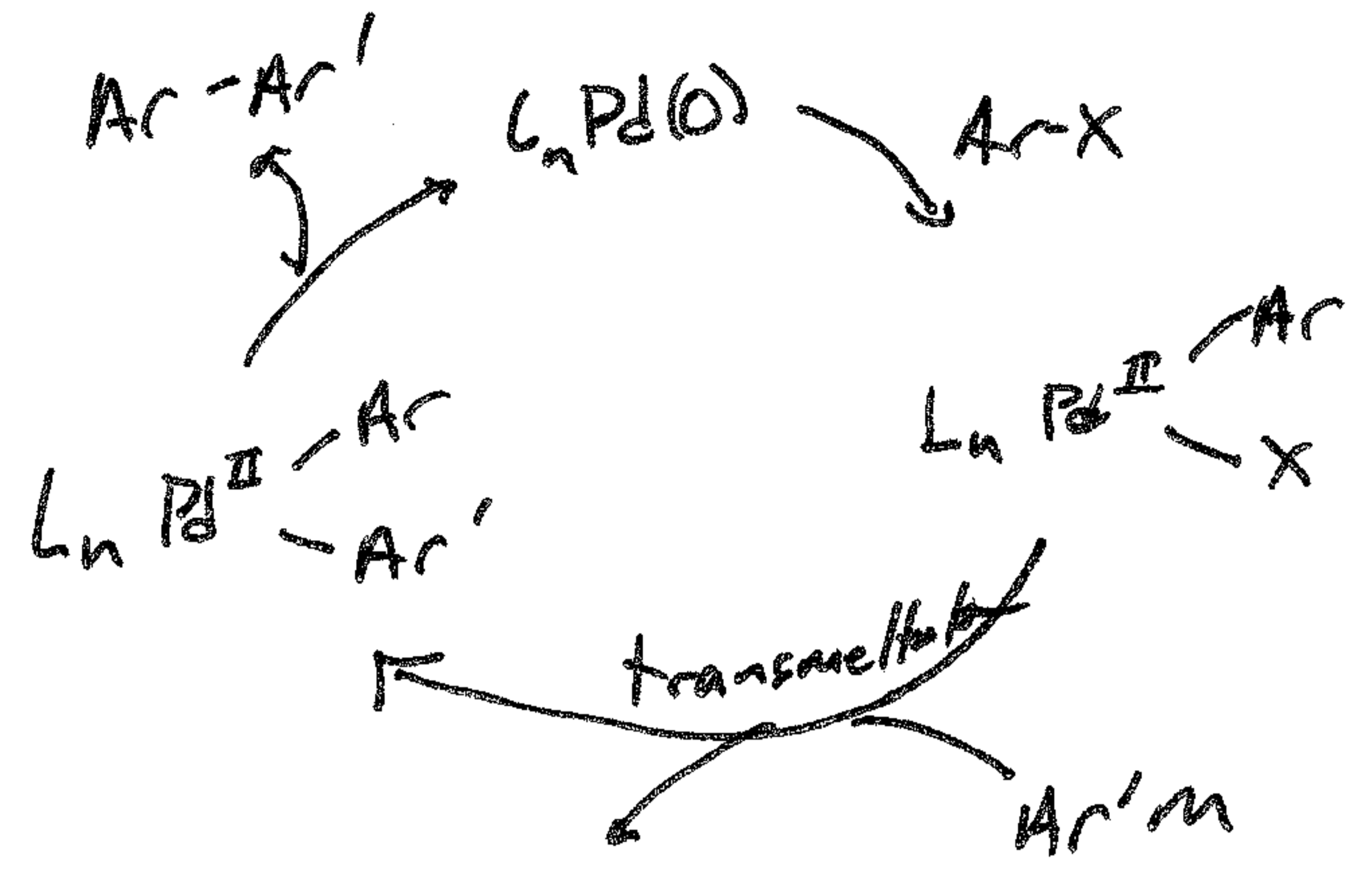


**Pd (Ni) Cross coupling chem**



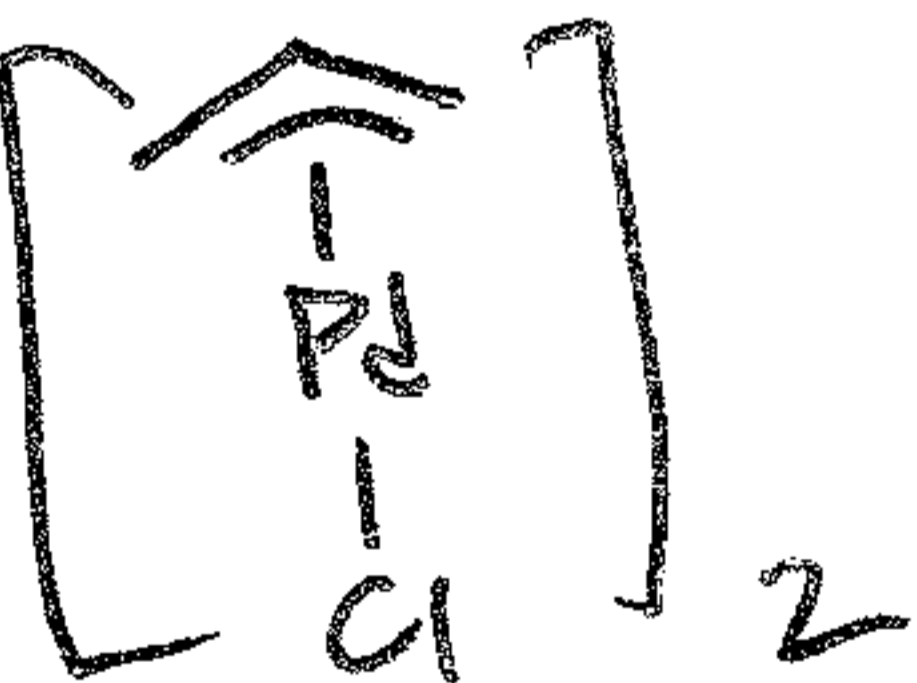
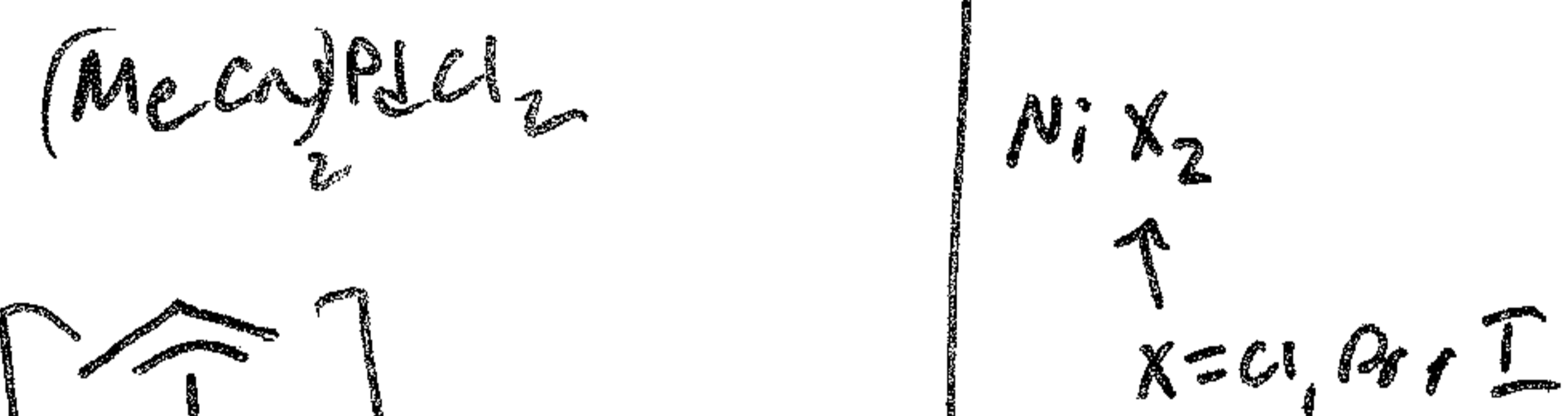
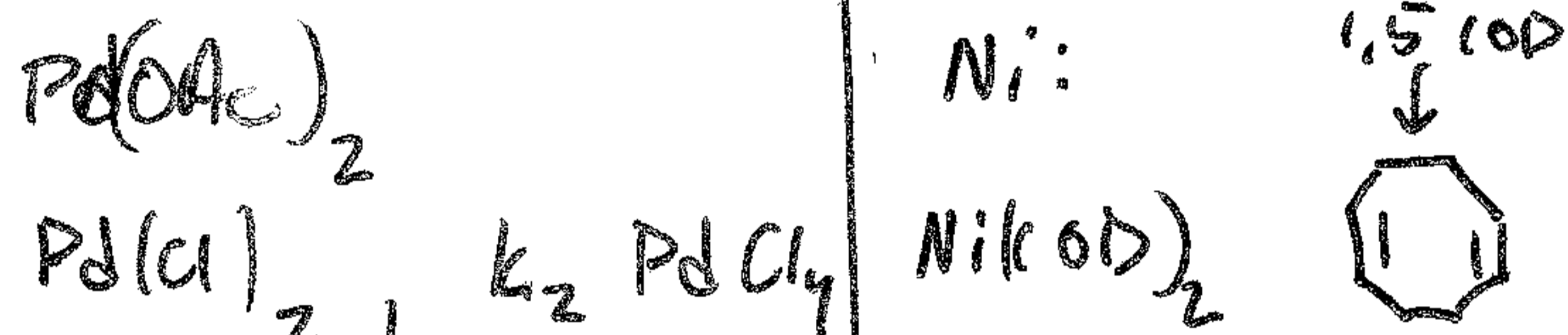
X = TFO > I > Br > OTS ~ Cl

- M =
- SnR<sub>3</sub> (Stille Rxn)
  - B(OR)<sub>2</sub> or BBH<sub>2</sub> w/ Base Suzuki
  - SiR<sub>3</sub> Hiyama
  - MgX Kumada-Corriu
  - ZnBr Negishi



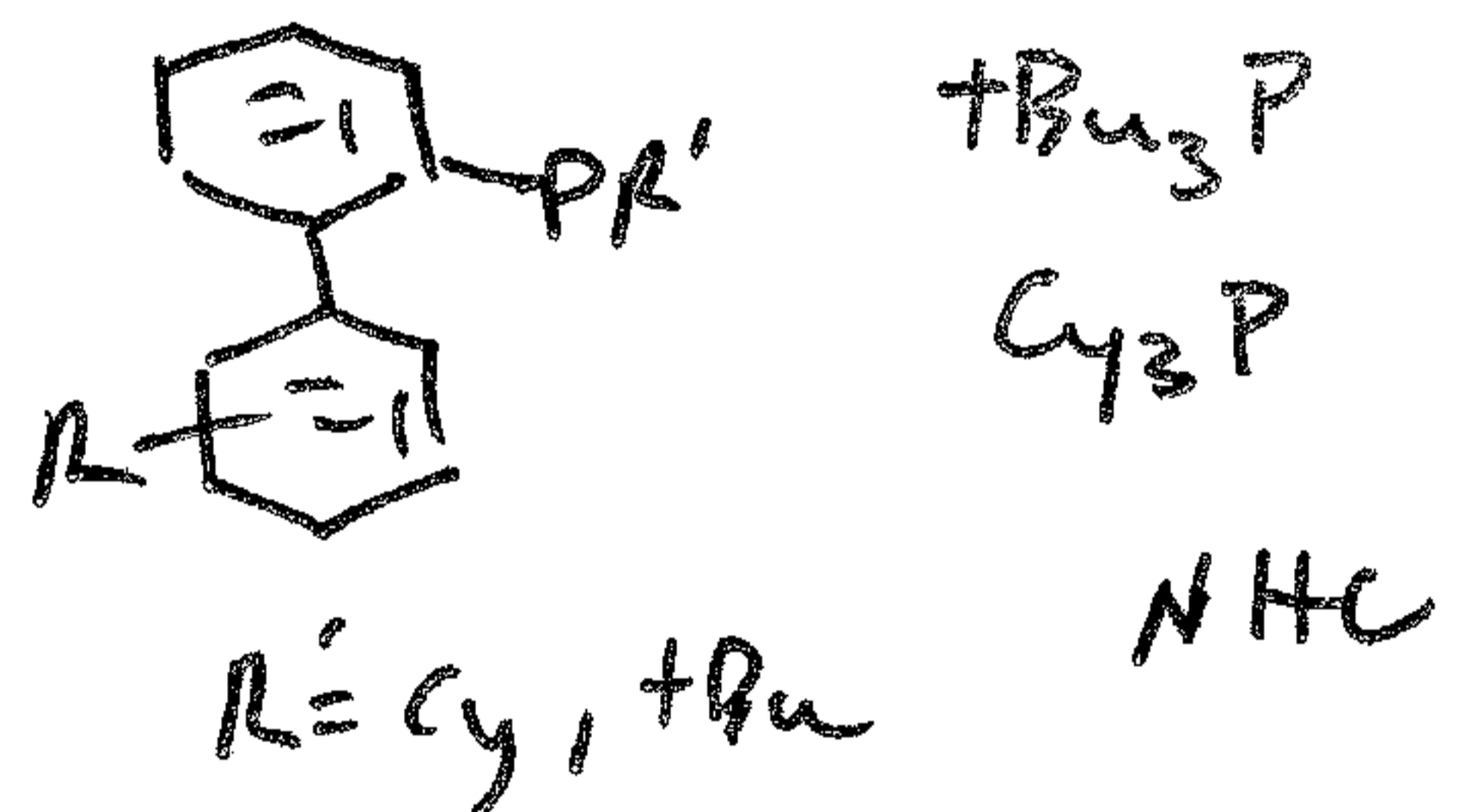
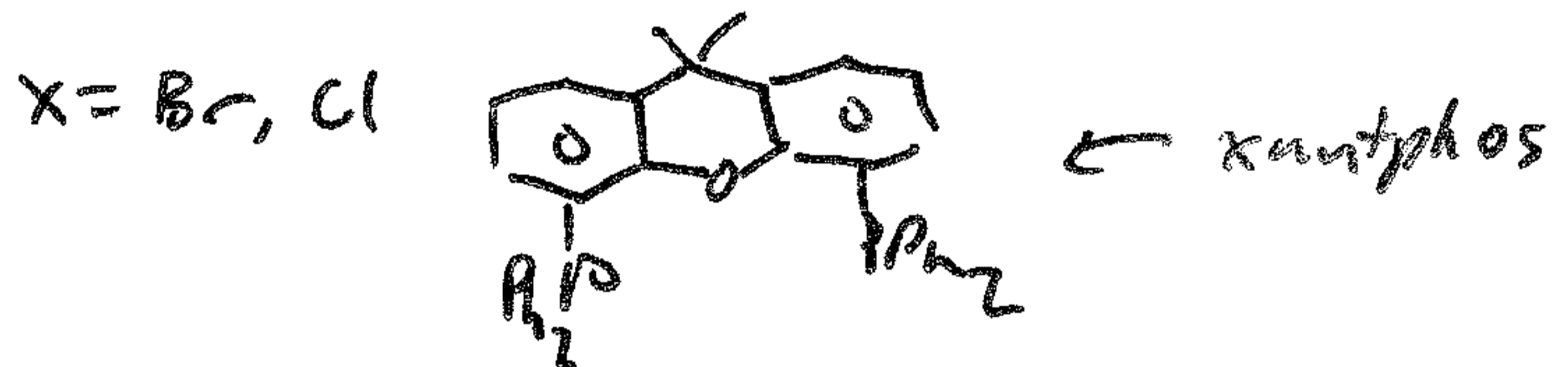
Also works w/ vinyl systems

**Pd sources (often reduced in situ)**



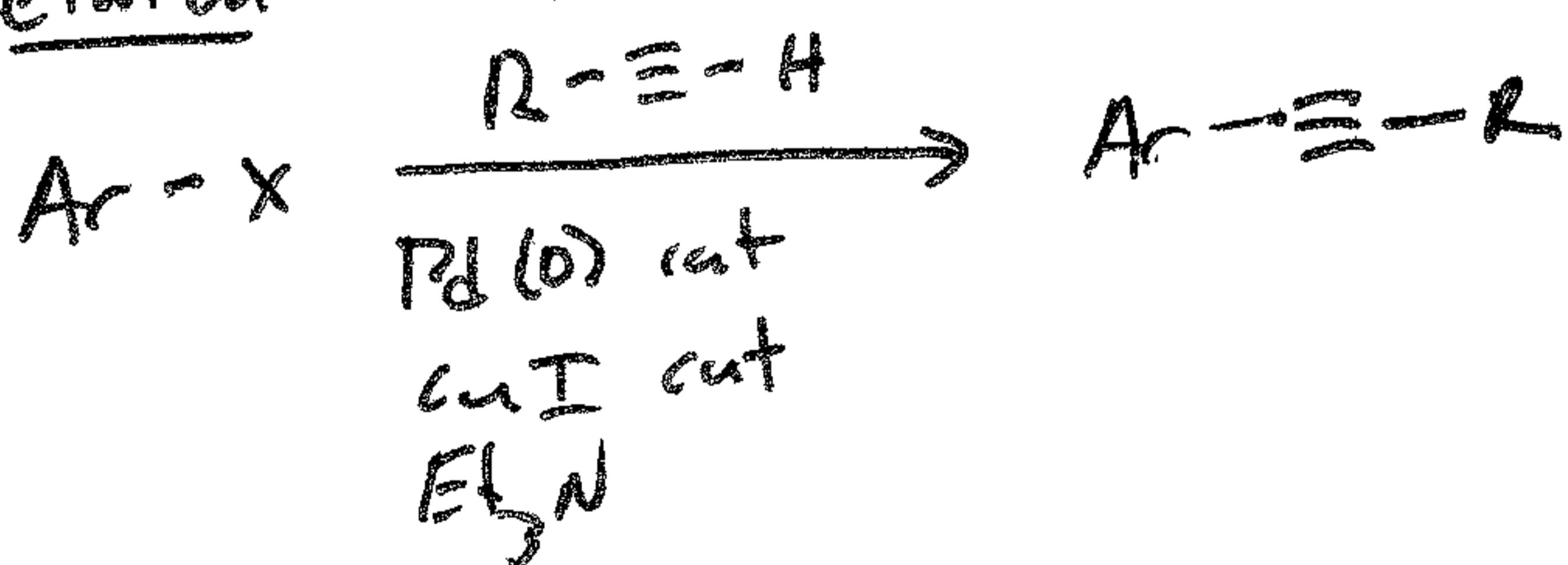
**Ligands**

X = TFO, I, sometimes Br  
 PPh<sub>3</sub>, P(tol)<sub>3</sub>, etc. dppe, dppf

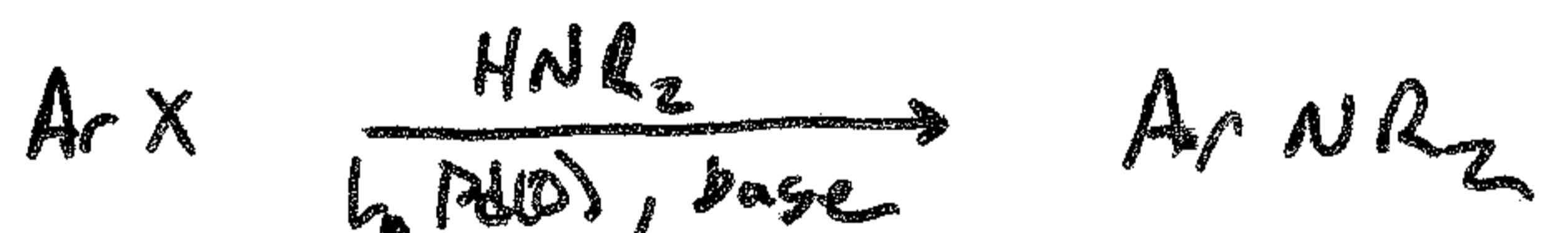


**Related**

**Sonogashira**



in situ formation of

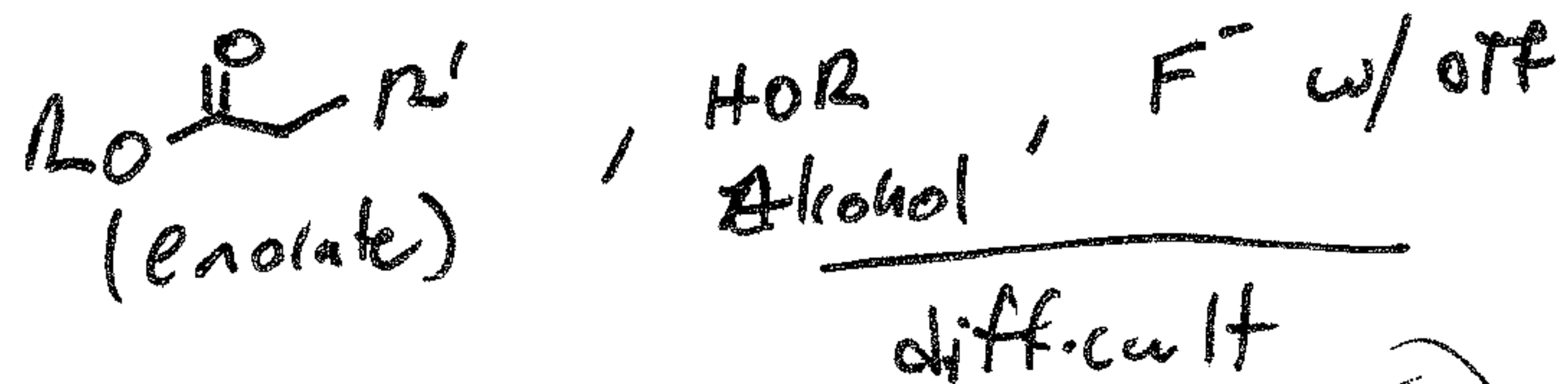


X = Br, Cl, OTf

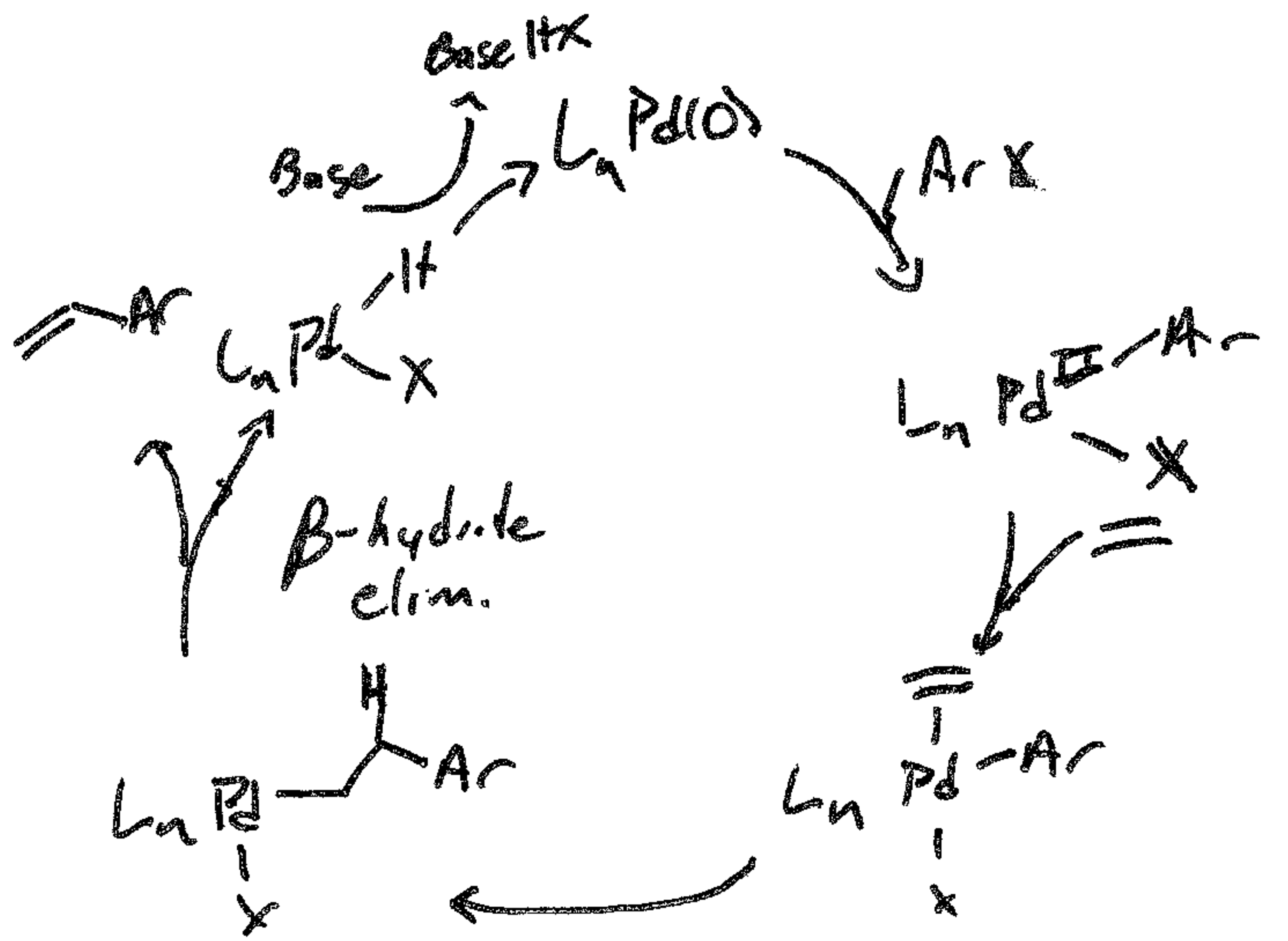
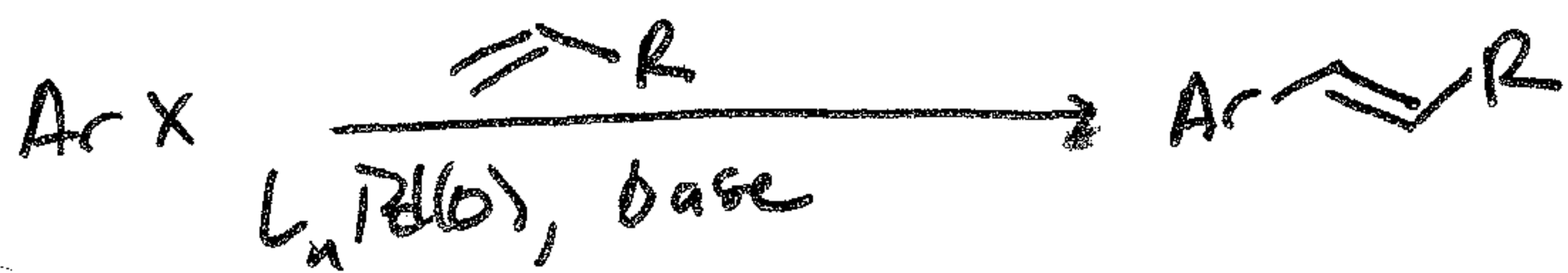
Recently I

Buchwald Hartwig  
 Buchwald ACIE, 2008, 47, 6338  
 Hartwig Acc. Chem Res, 2008, 41, 1534

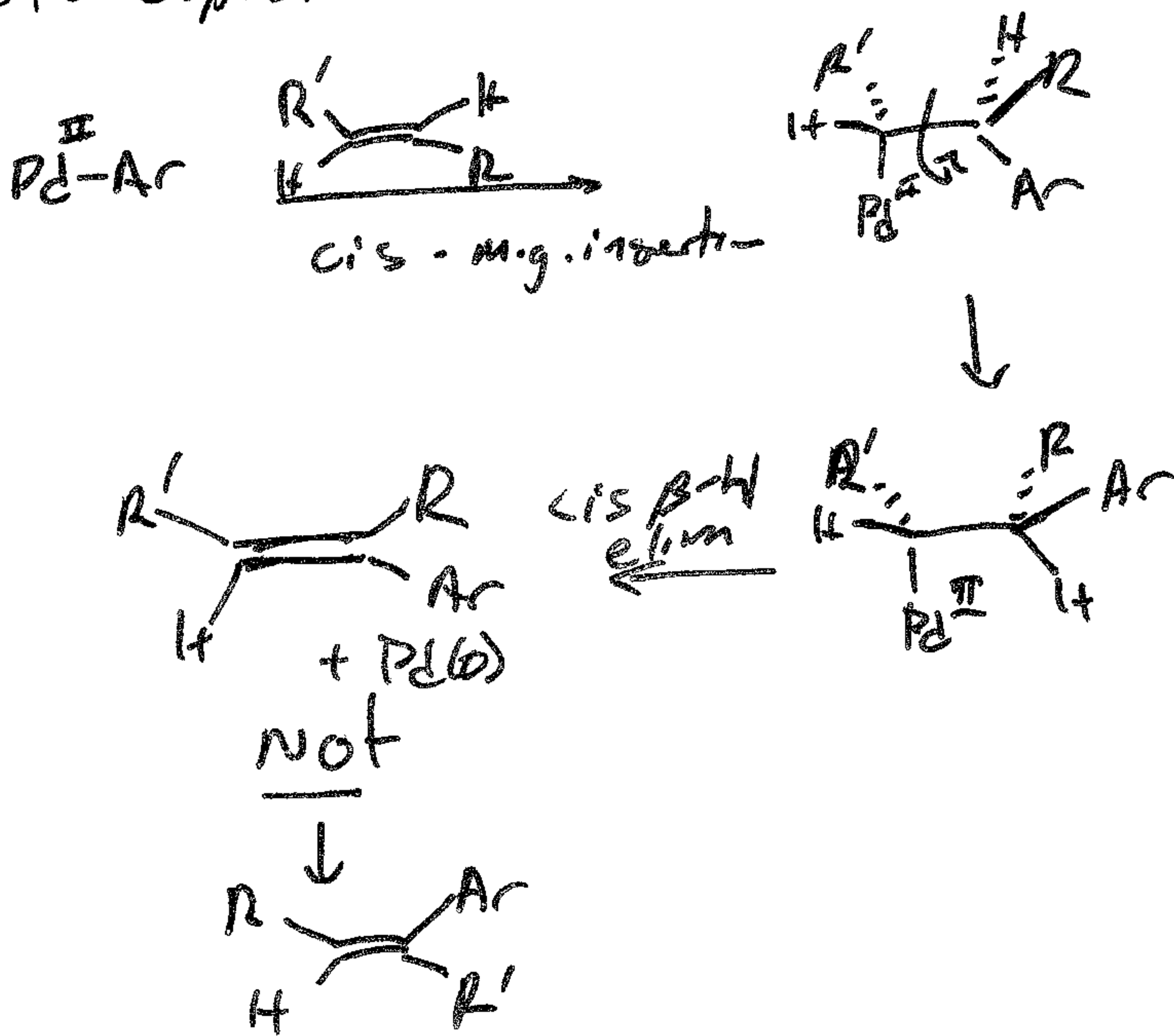
**Other nucleophiles**



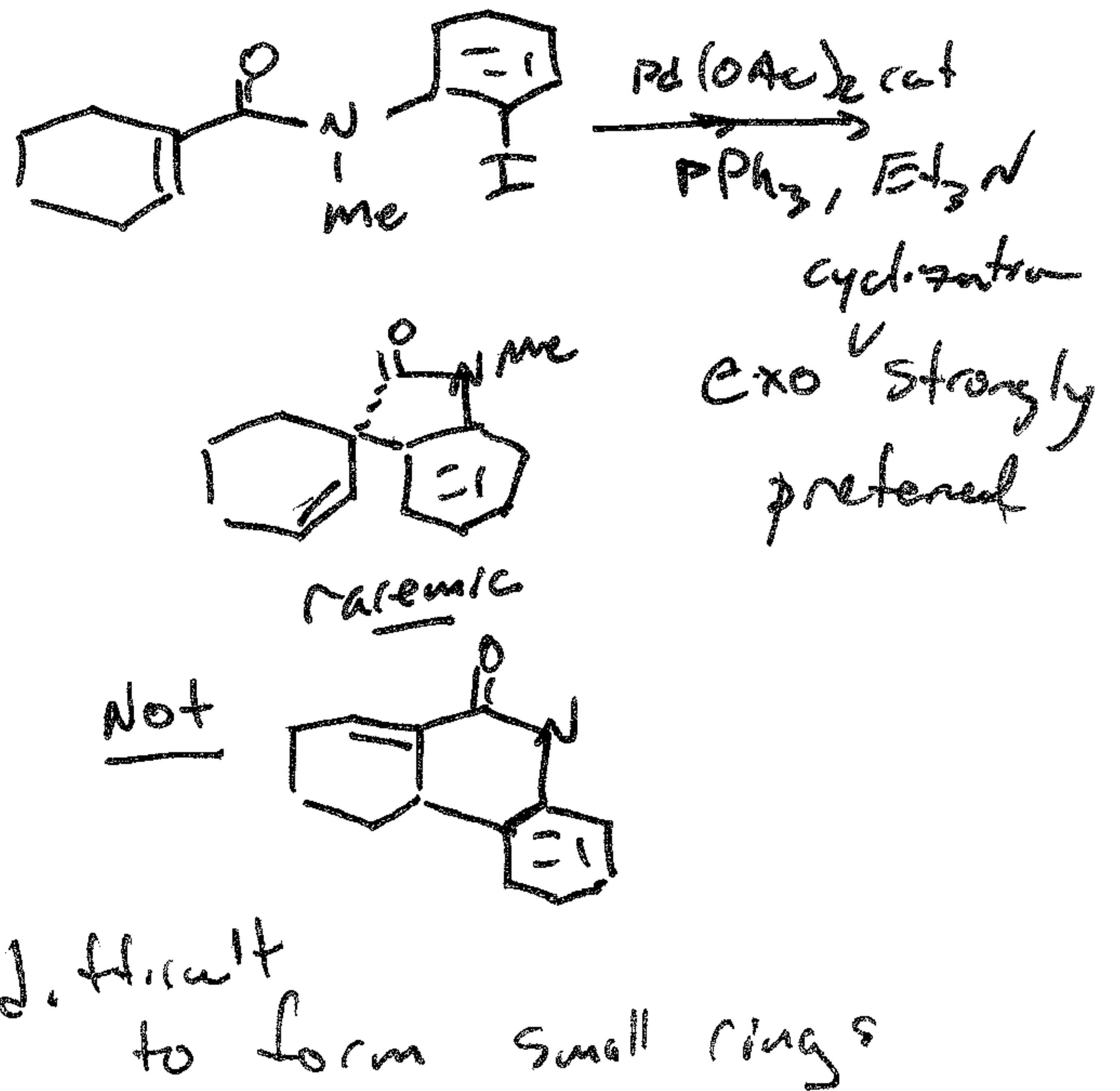
# Alkenes as Nuc: Heck Rxn



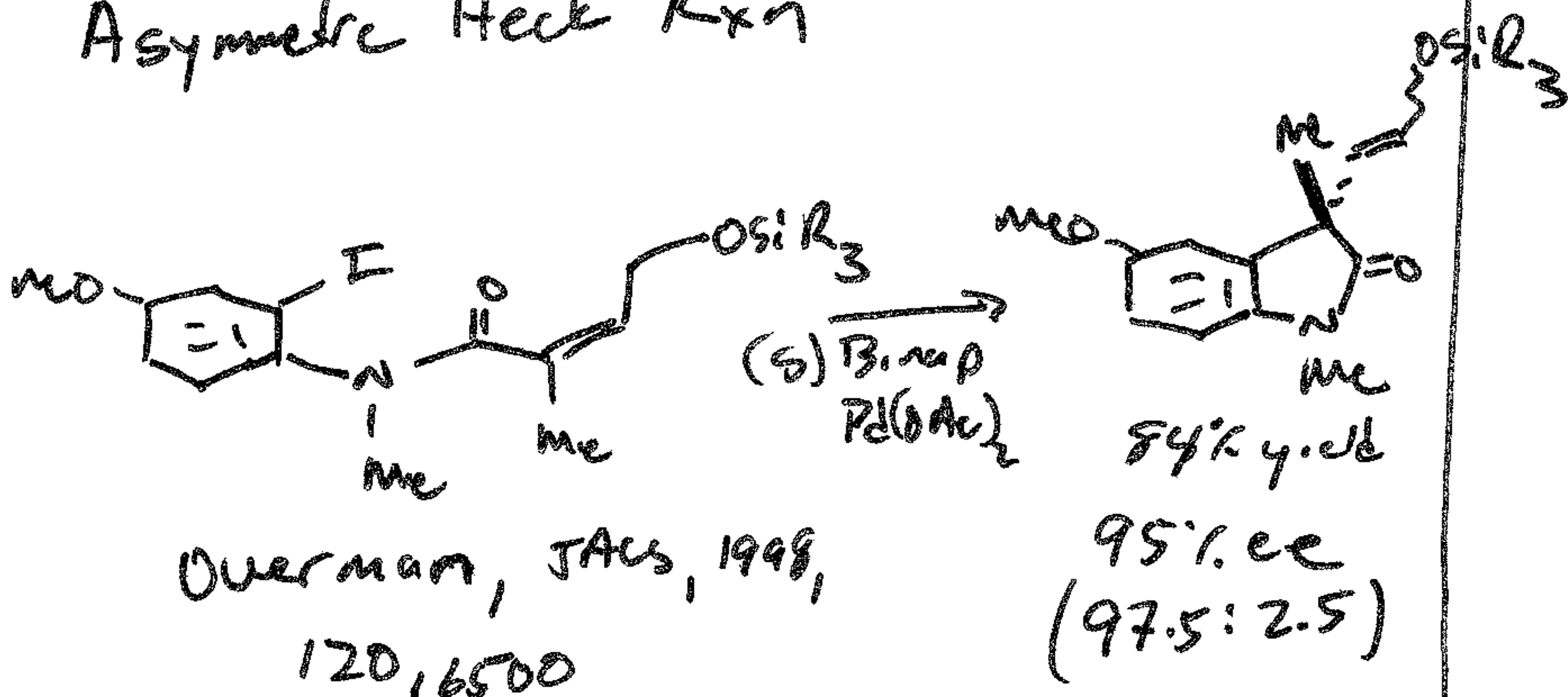
# Stereospecific



# Intramolecular

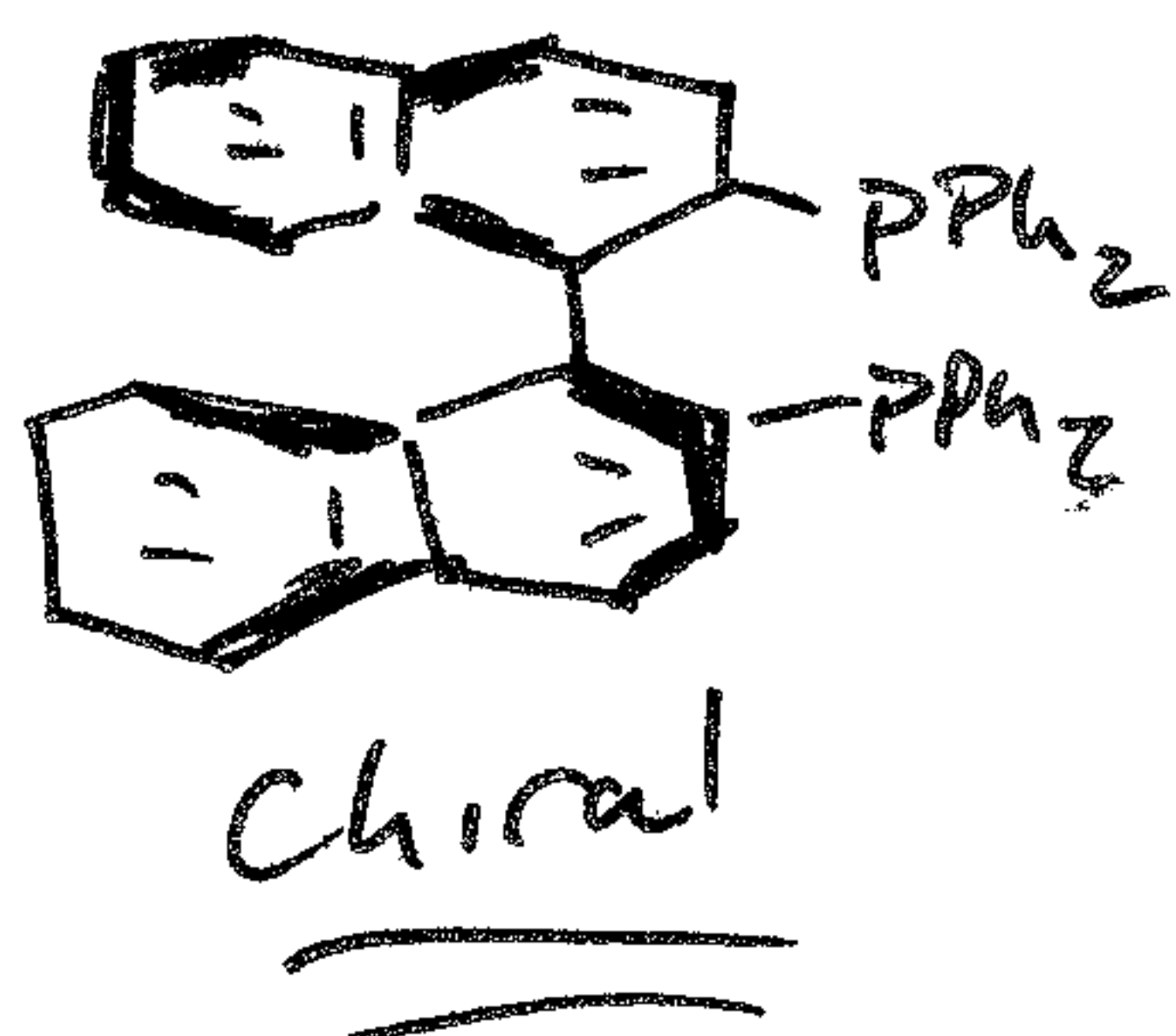


# Asymmetric Heck Rxn



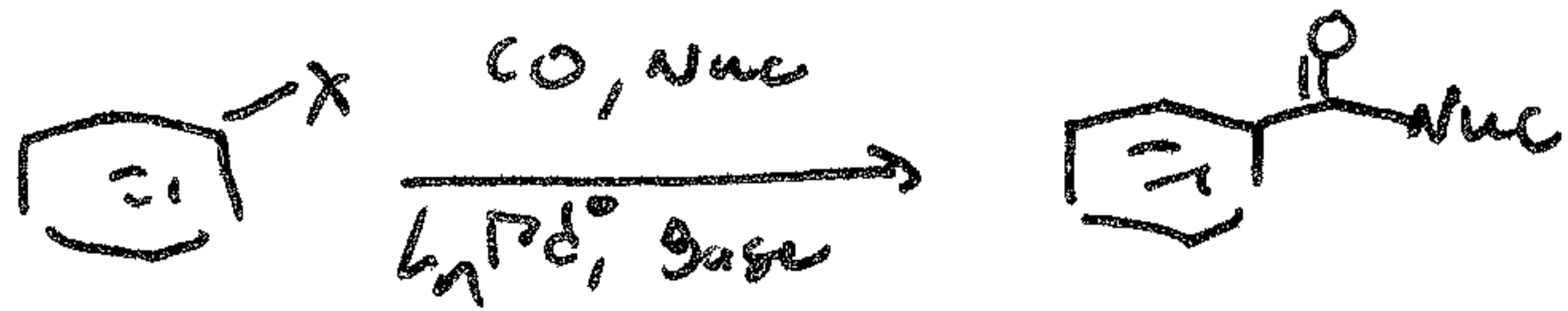
Also Shibasaki has contributed to this area

# Binap



Can be resolved.

# Hack carbonylation

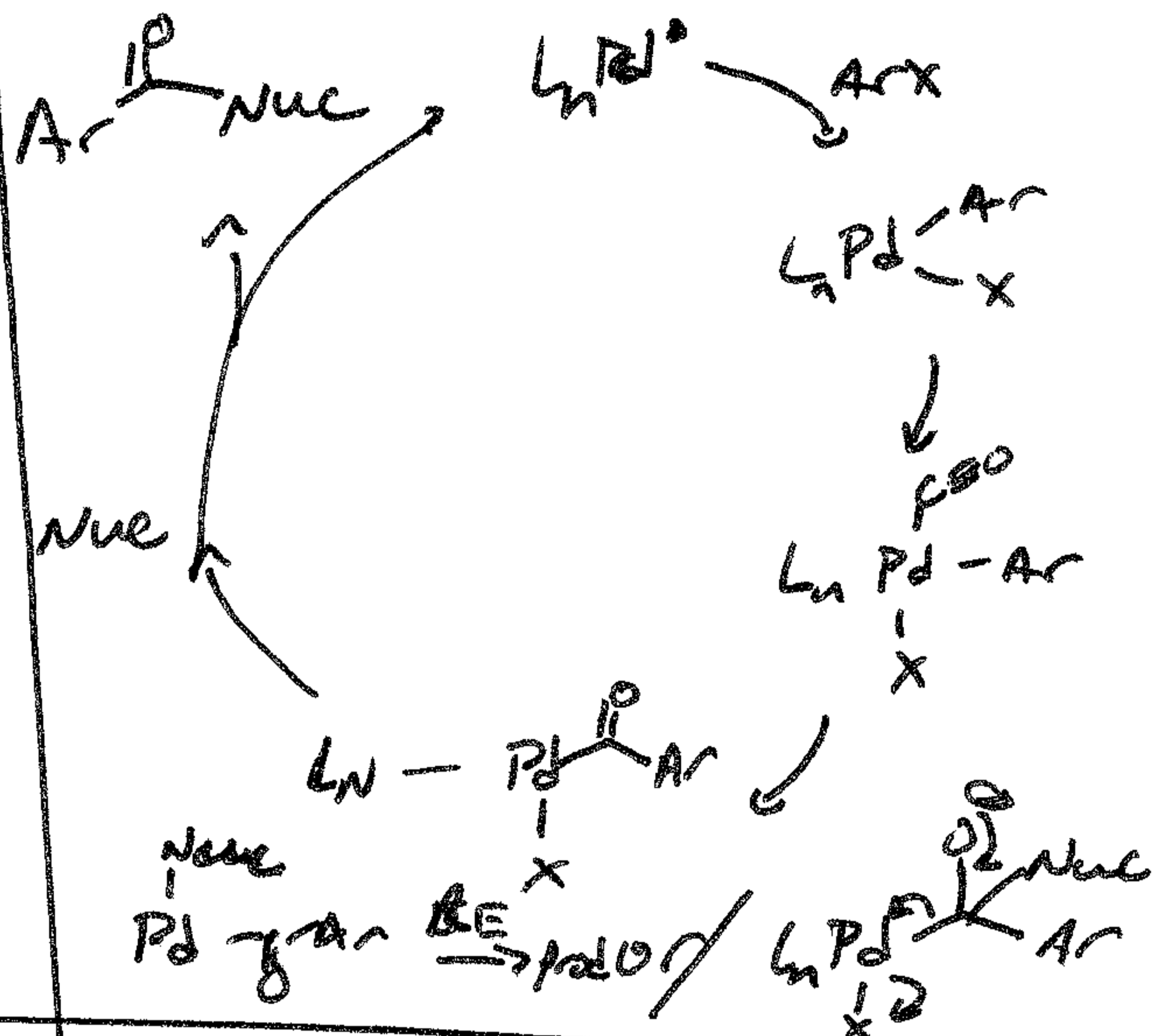


X = I,  $\text{PPh}_3$  etc

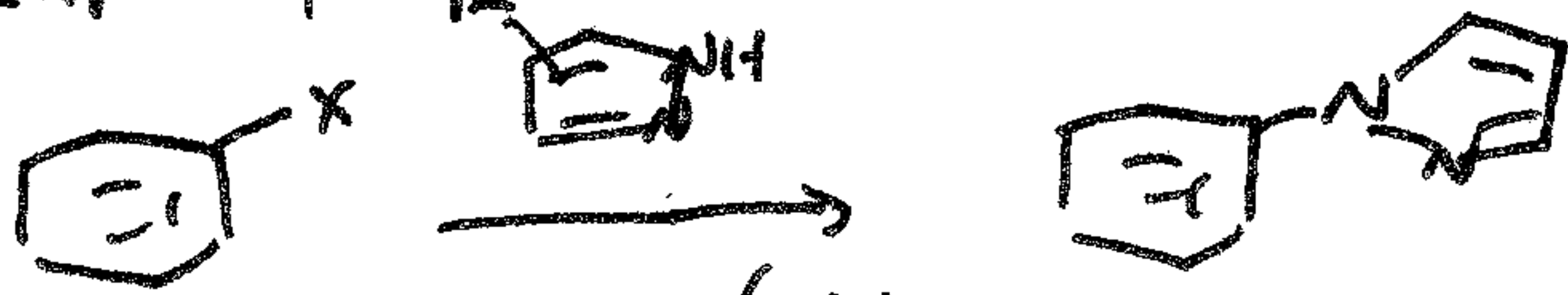
Br Xantphos



Nuc : amine, alcohol,  $\text{Bu}_3\text{SnH}$



Ullmann / Goldberg



X = I, Br

CuI (cat)  
Ligand (cat)



good for weakly basic N-Nuc

amide, heterocycles etc

limited to ArI & ArBr

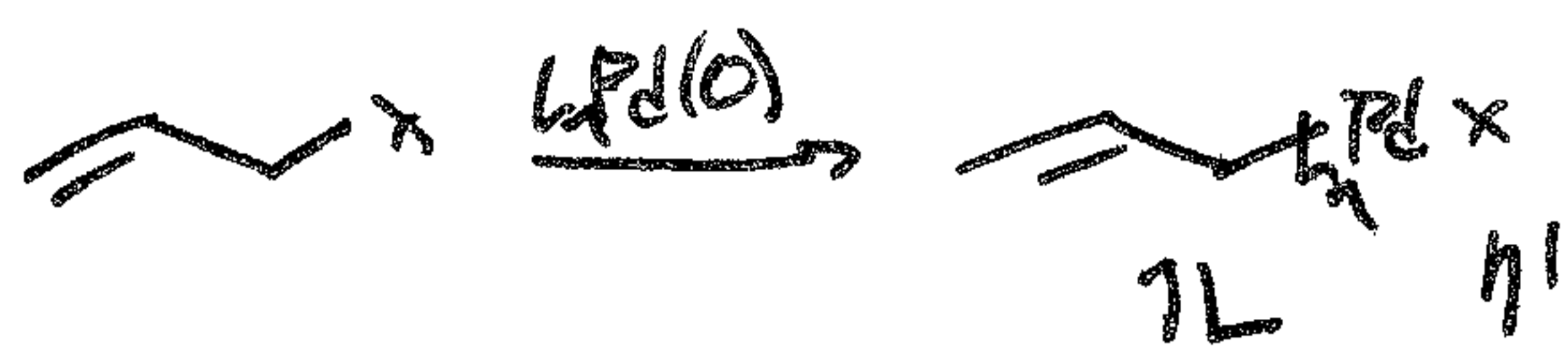
Buchwald - cat

Reading

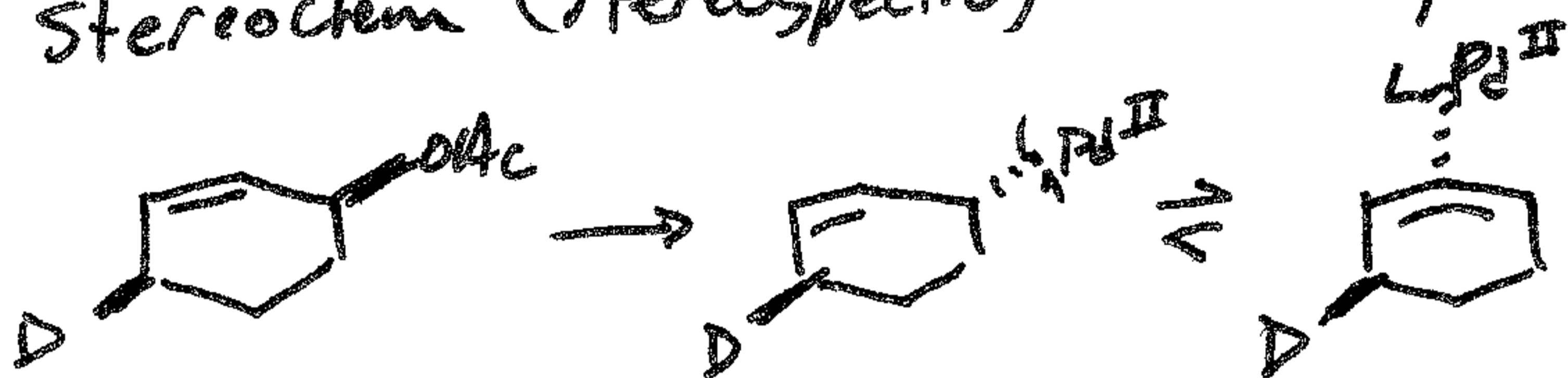
12.1

Ch. 1

$\pi$ -allyl Chem (Trost Tsuji)

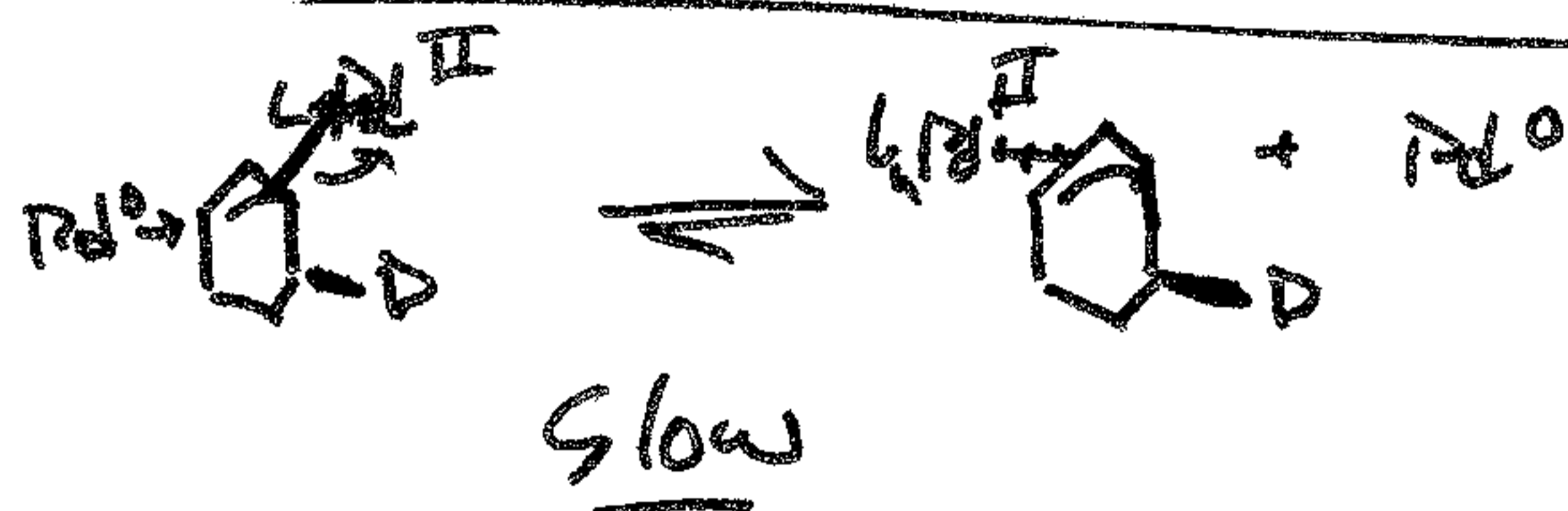
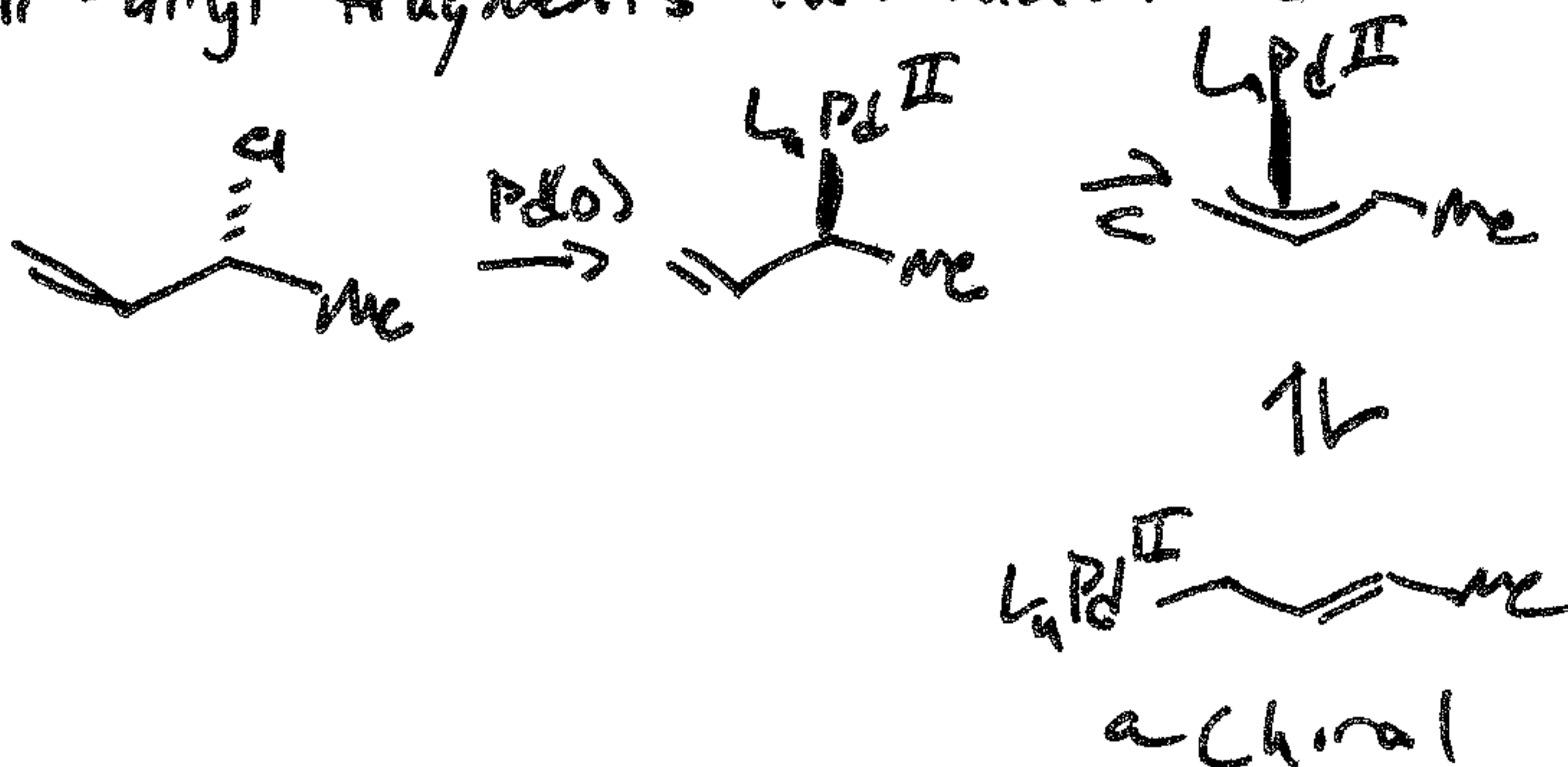


Stereochem (stereospecific)



Backside attack

$\pi$ -allyl fragments can racemize:

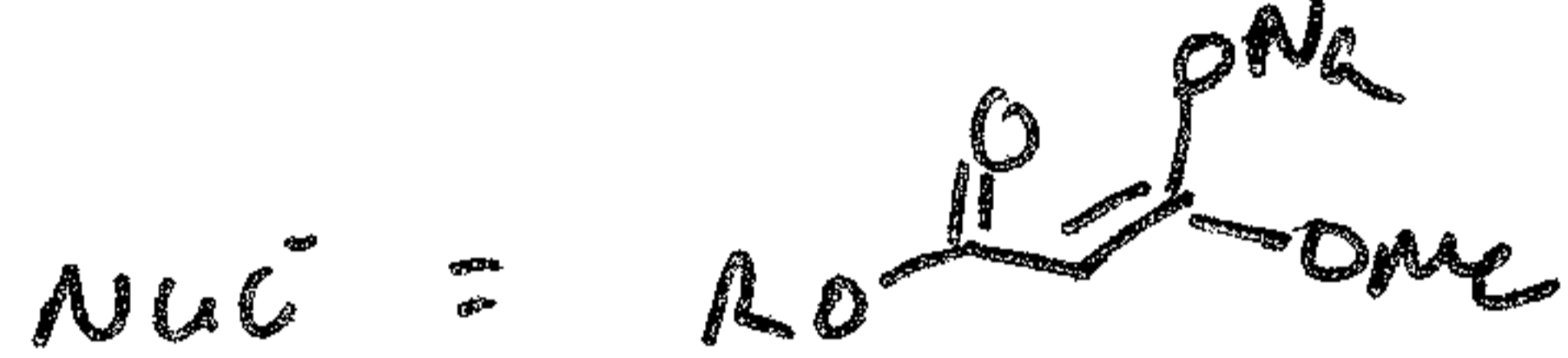
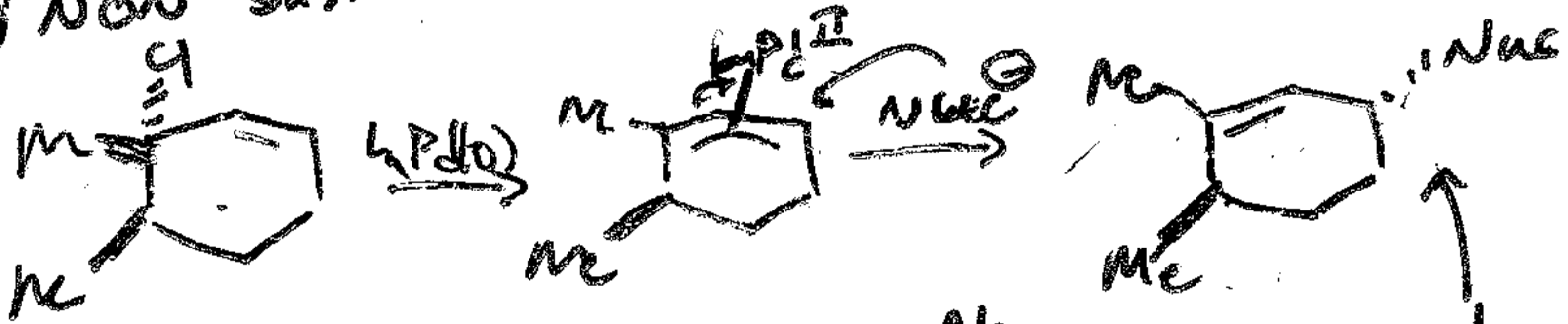


Rxn w/ Nucleophiles Also stereospecific

2 types

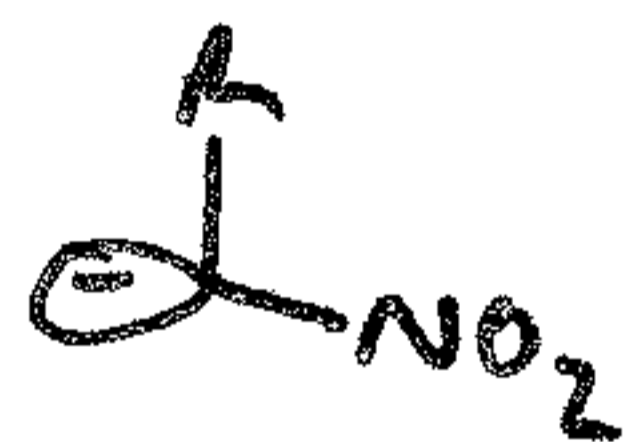
1) Non-basic

$\Delta G^\ddagger \geq 25$  (dmsO)



amines

PhO^-

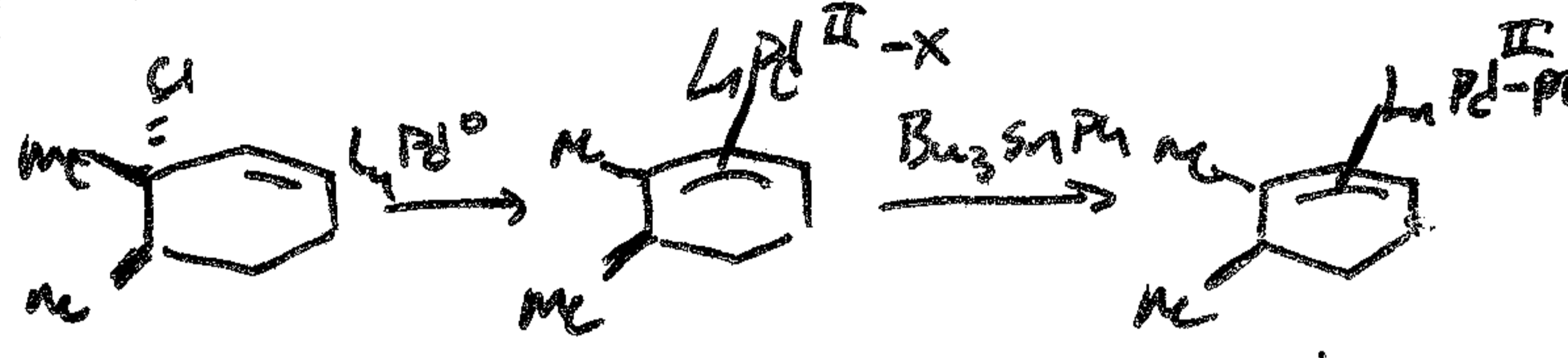


etc

not less sub. side of  $\pi$ -allyl

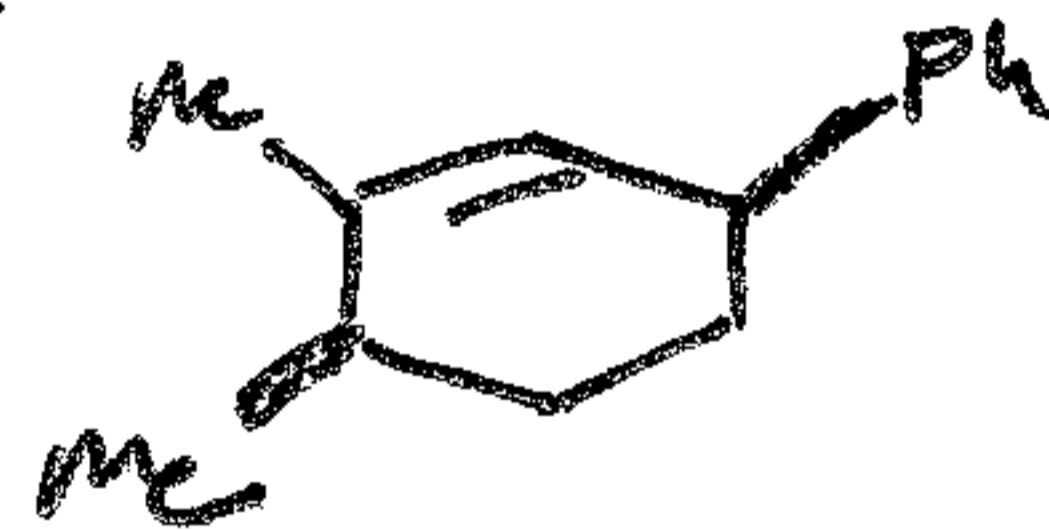
double backside displacement = retention.

2) transmetalation



TM occurs w/

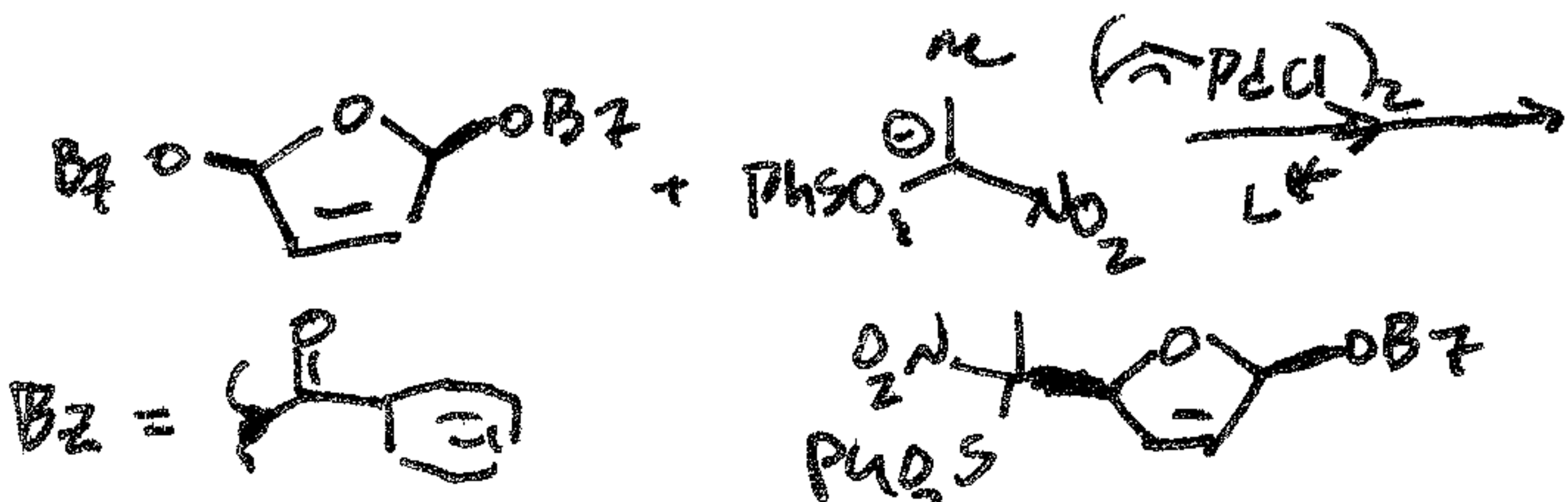
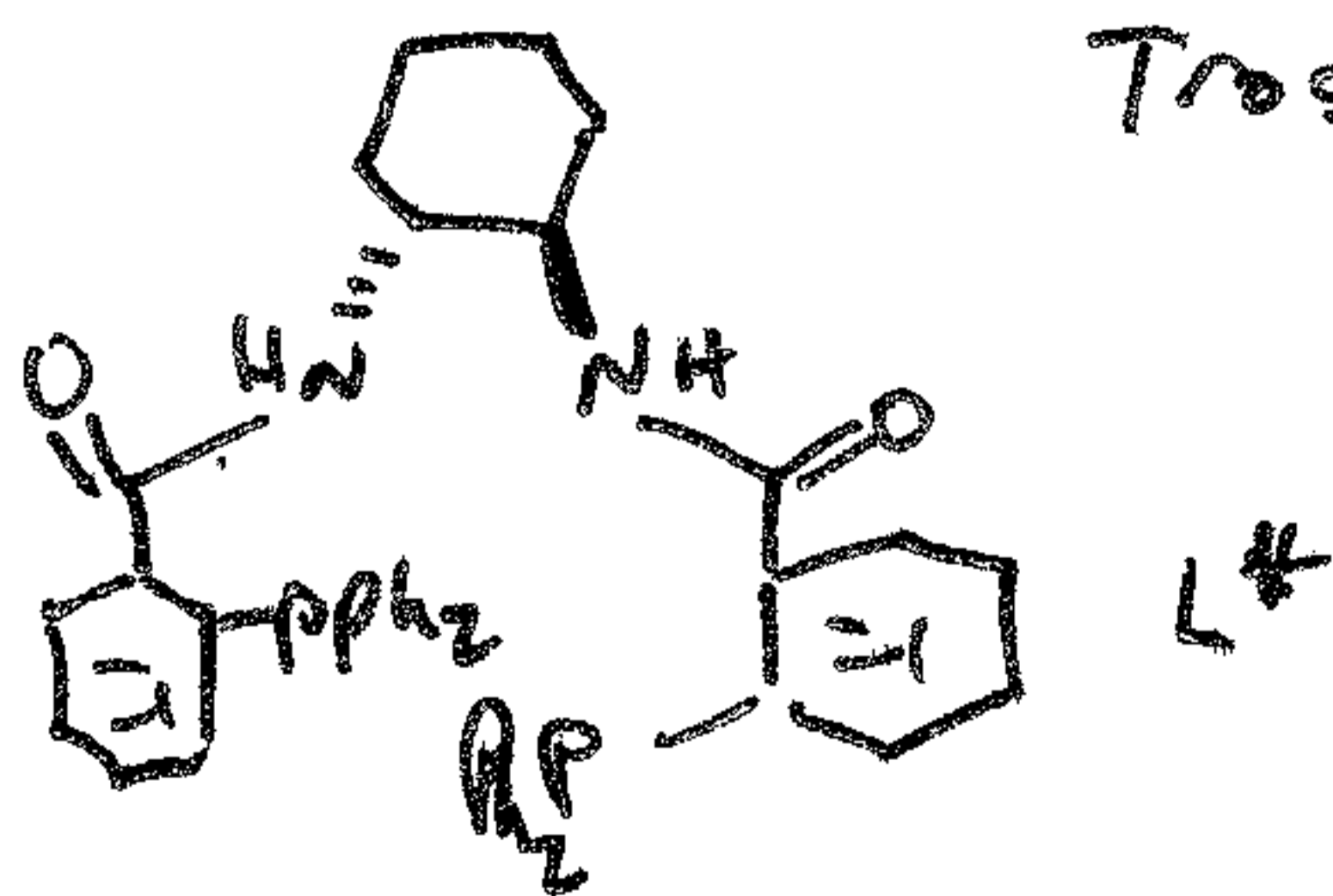
R\_3SnR, R\_3BH\_2, etc...



net inversion

Asy. Variant very important

Trost modular Ligand "TML"



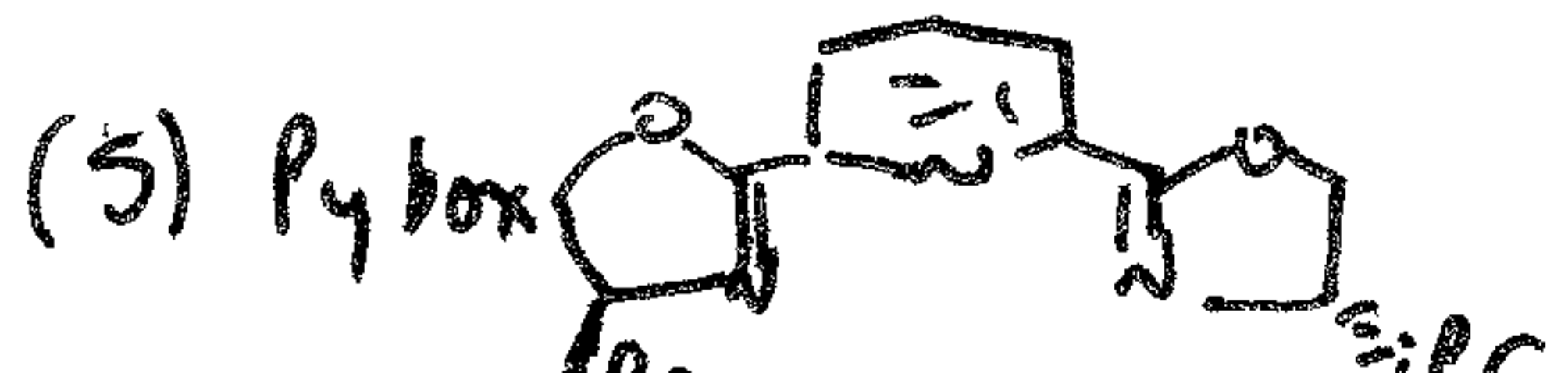
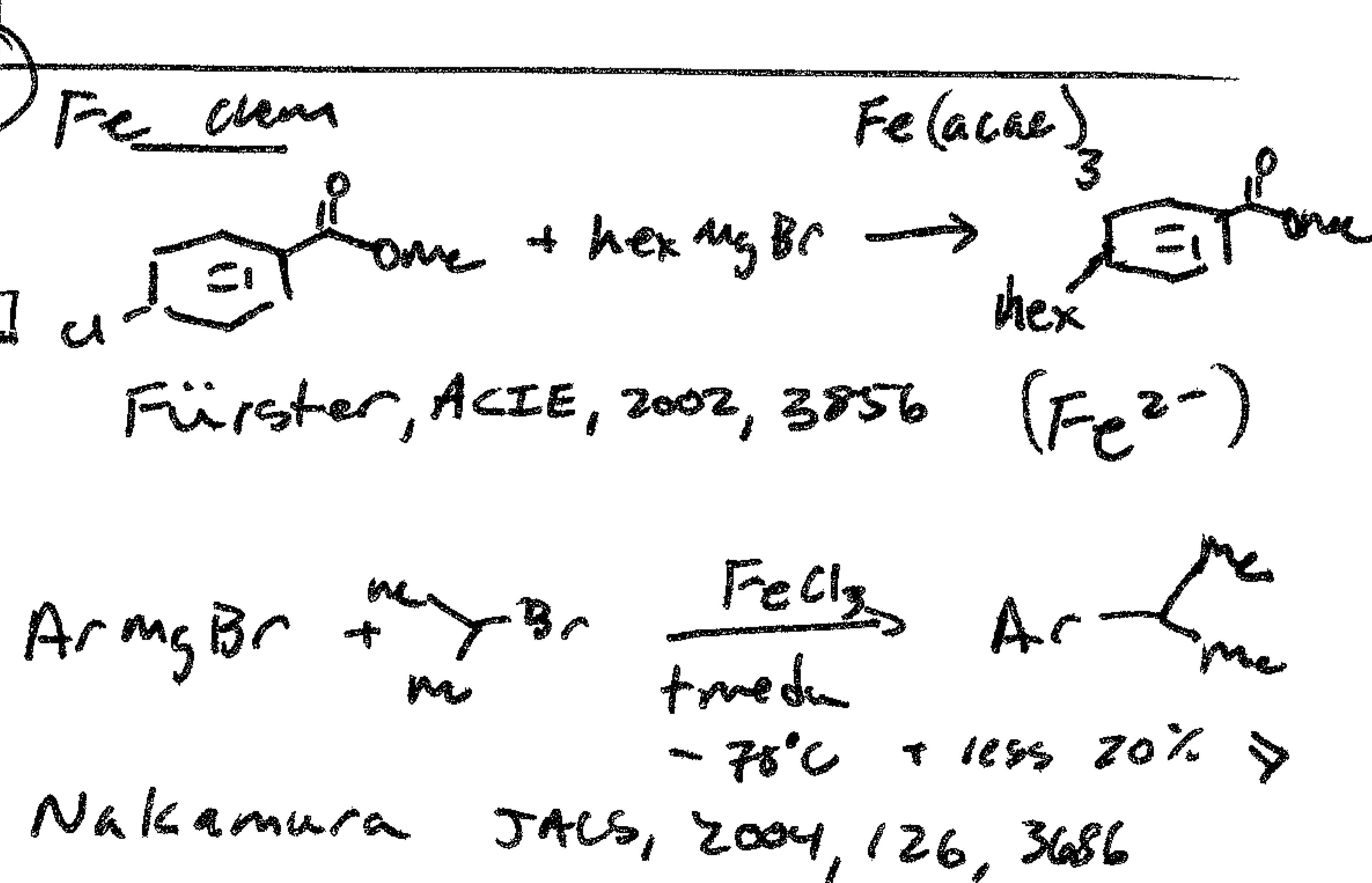
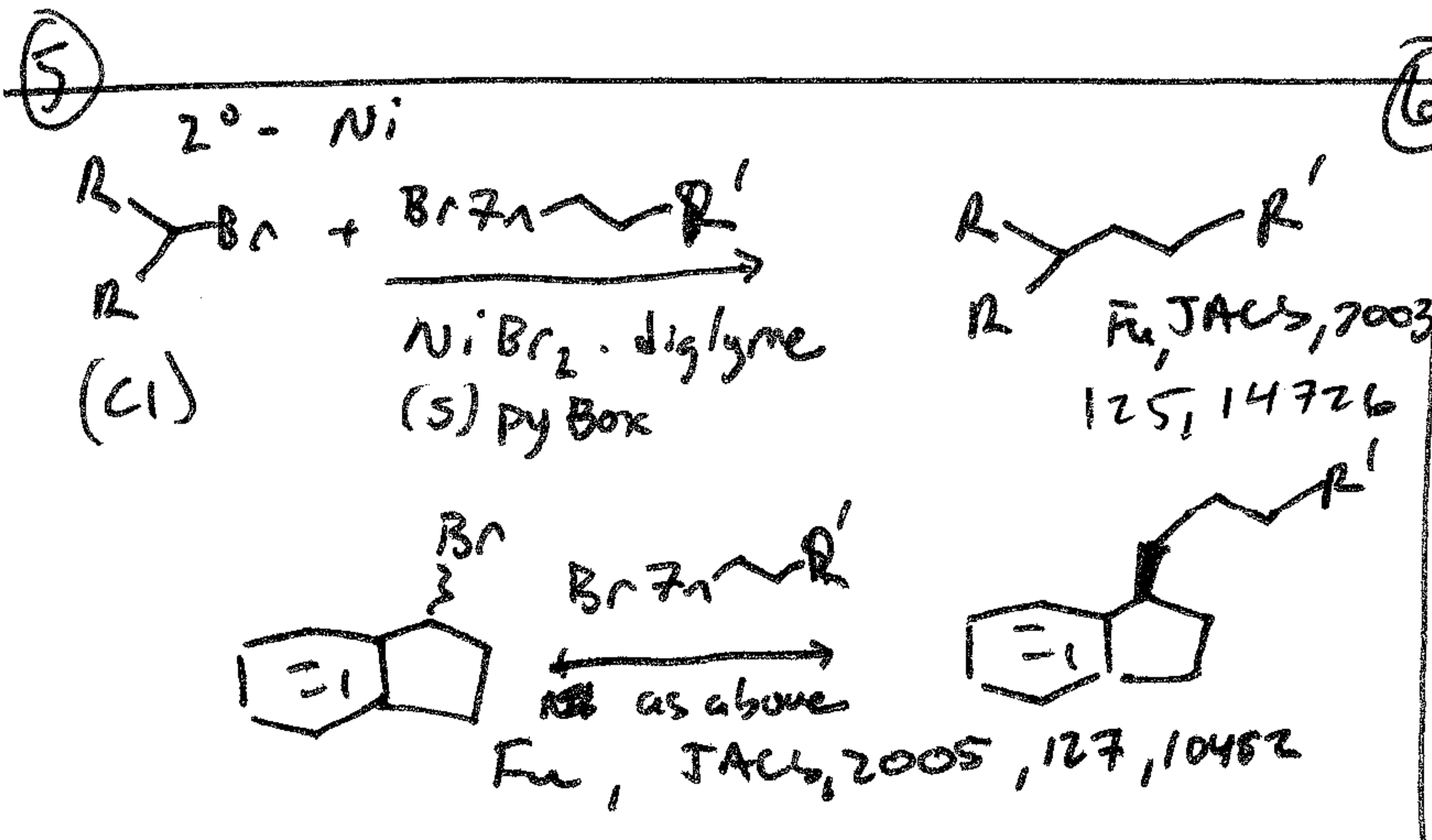
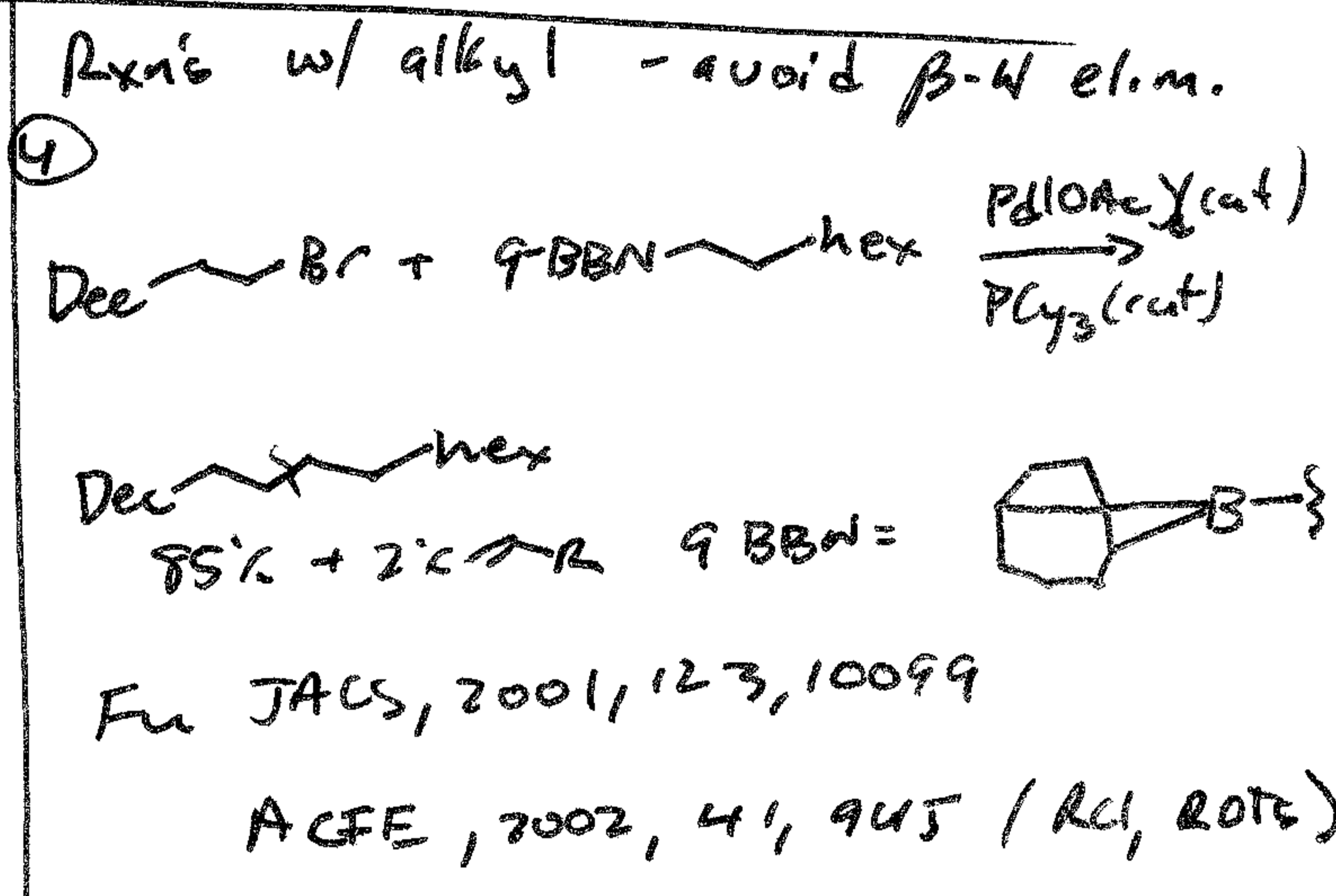
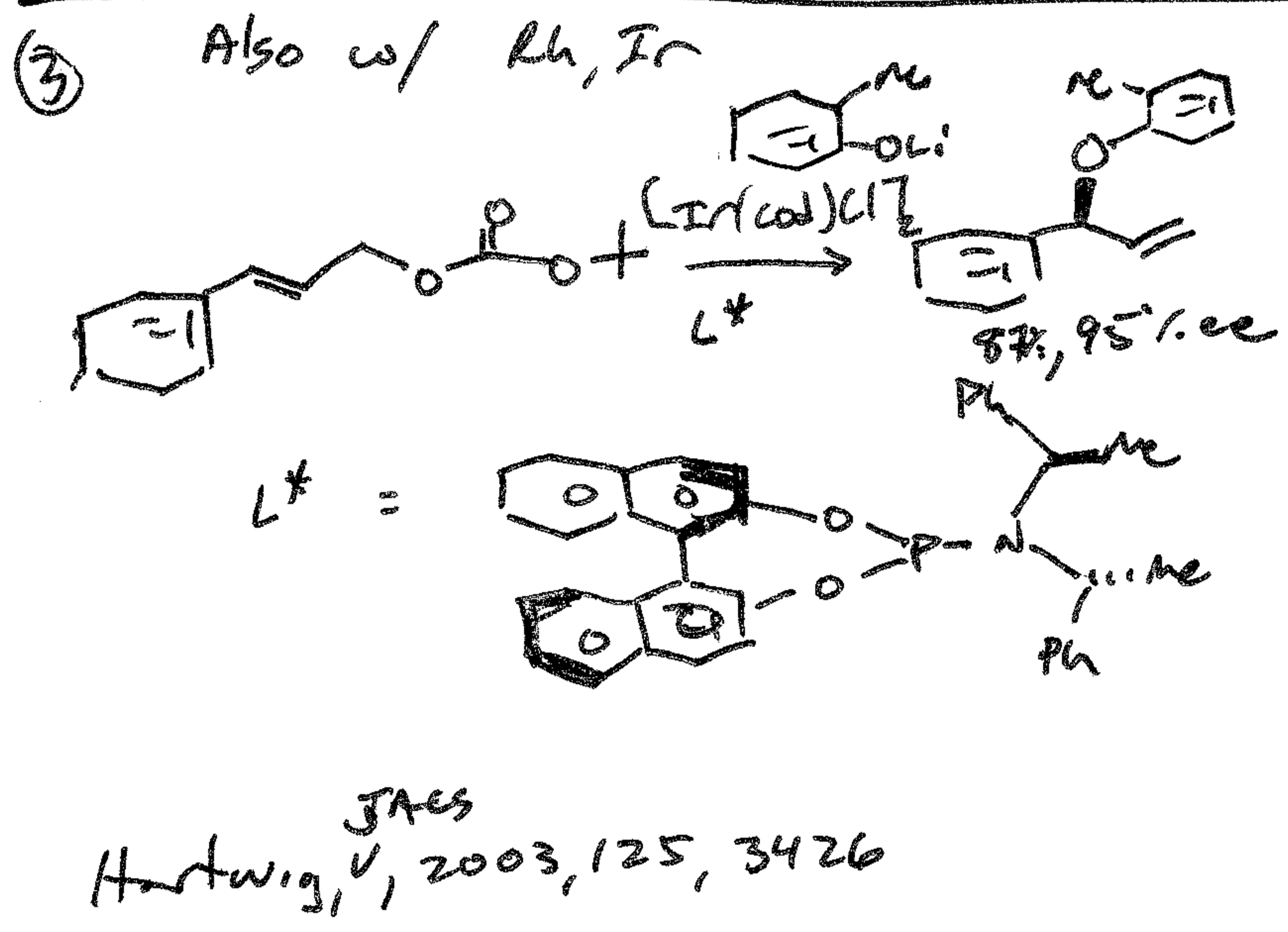
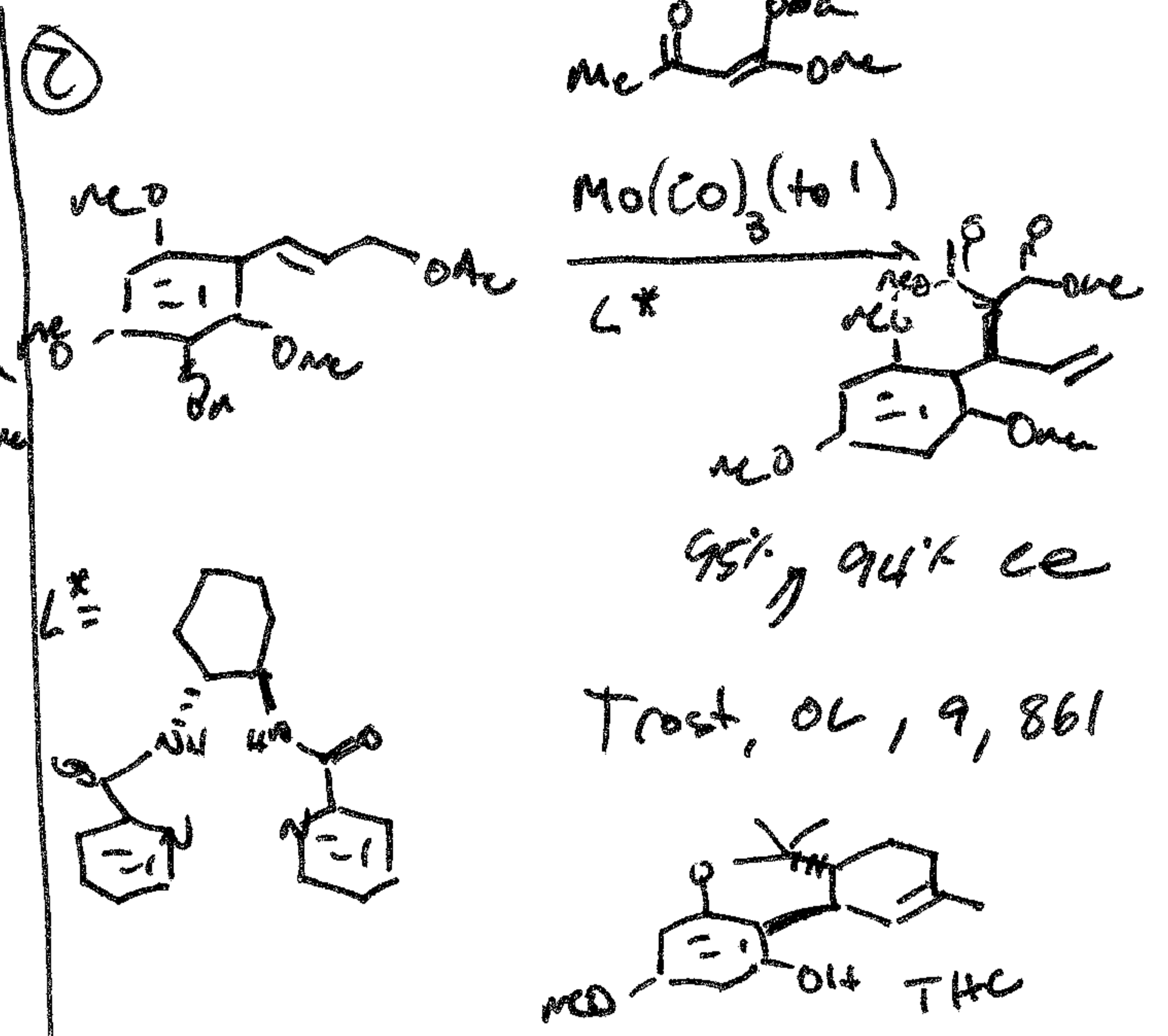
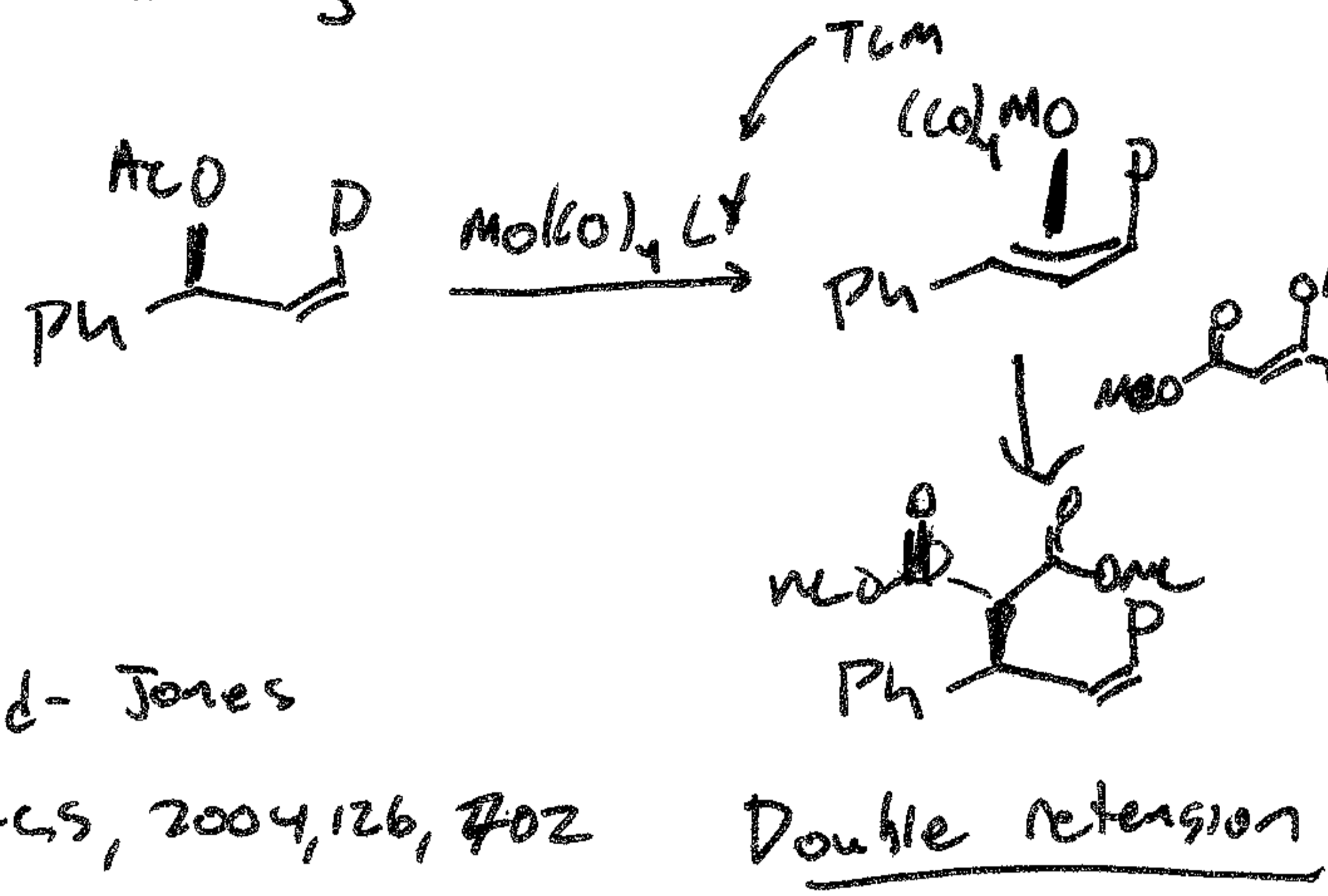
Trost Chem Rev 2003, 103, 2921

Acc. Chem Res. 2006, 39, 747

Lloyd-Jones <sup>JACS</sup> 2009, 131, 9945

Stereoselectivity in AAA rxn.

① Other metals  
Mo or allyl



⑤