

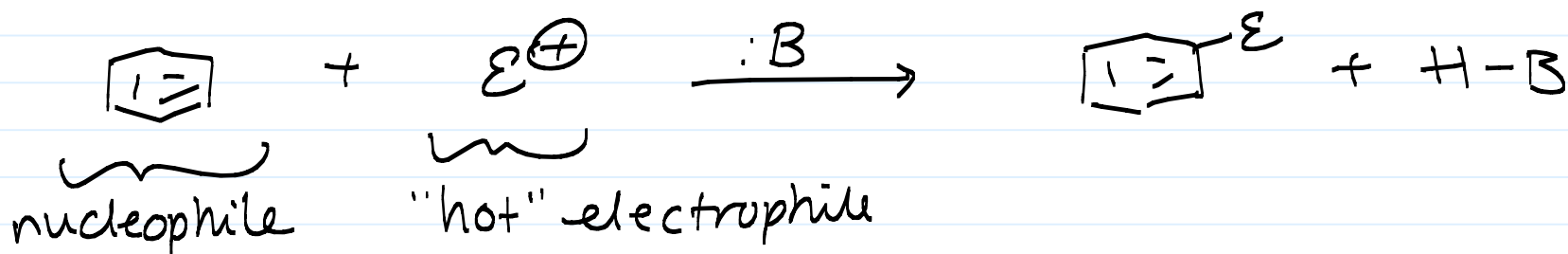
Other Methods of Aromatic Substitution

1) Nucleophilic Aromatic Substitution

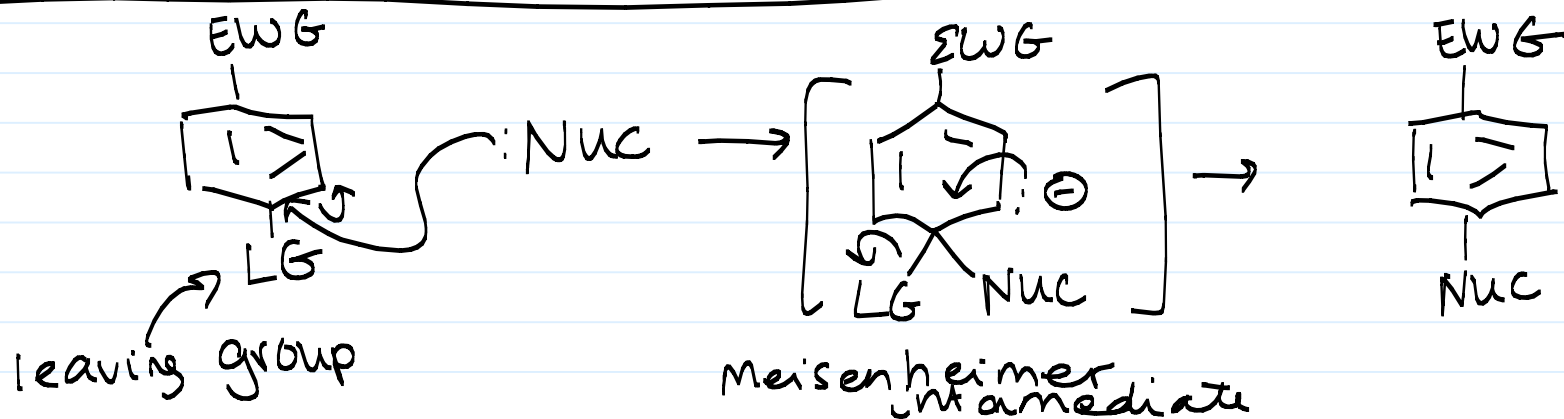
2) Transition Metal Catalysis → Heck Reaction

Nucleophilic Aromatic Substitution (S_NAr)

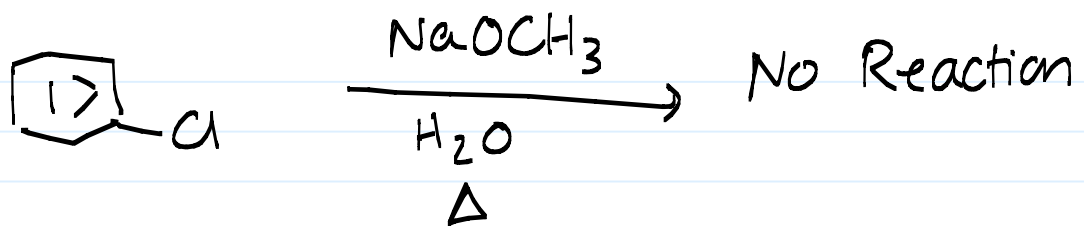
Recall: Electrophilic Aromatic Substitution

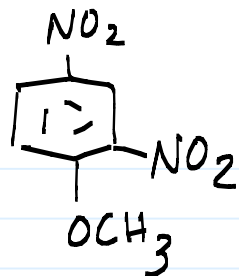
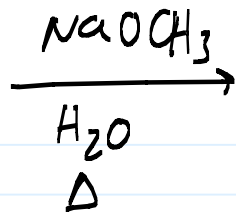
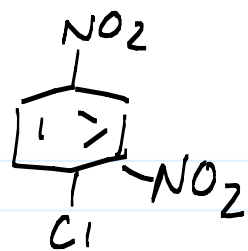


Nucleophilic Aromatic Substitution → Electron-poor aromatic ring



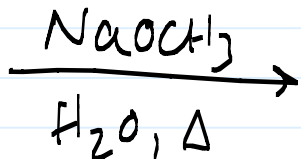
Must be electron-poor:



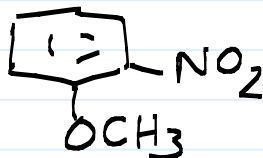
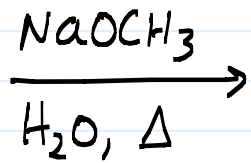
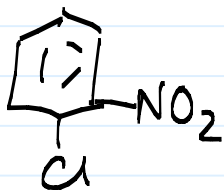


Relative Rates

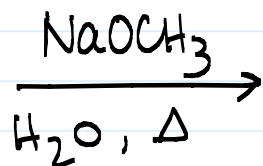
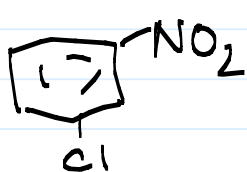
115,000 ← Whoa!



3.4

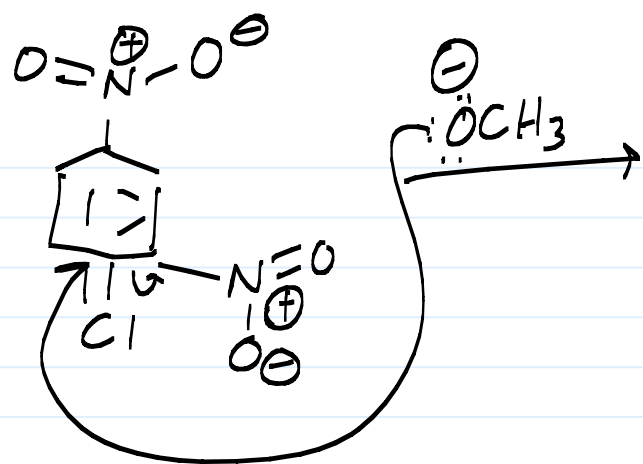


1.0

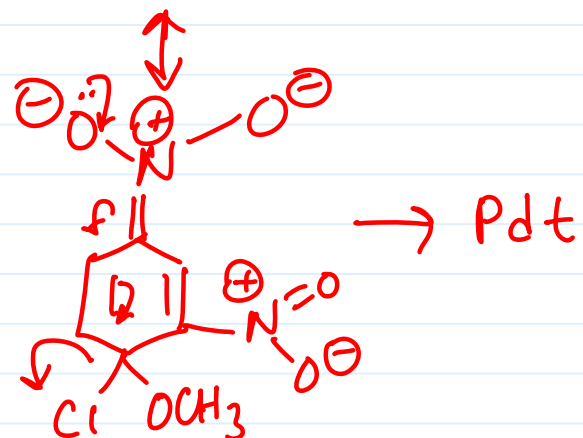
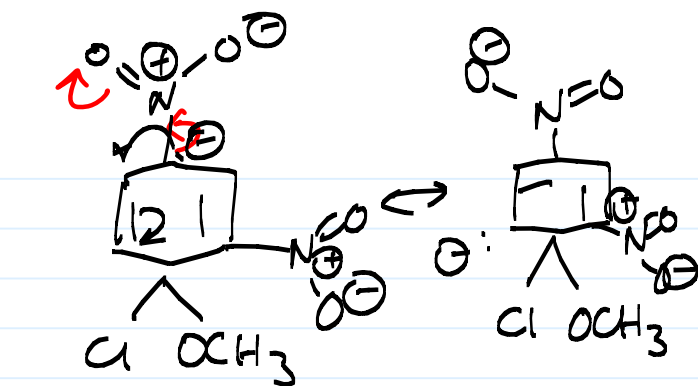
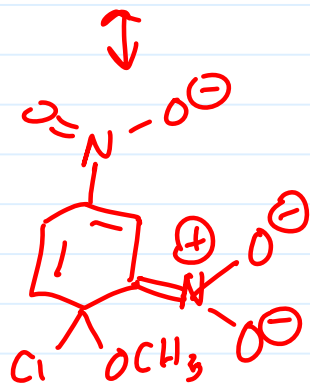
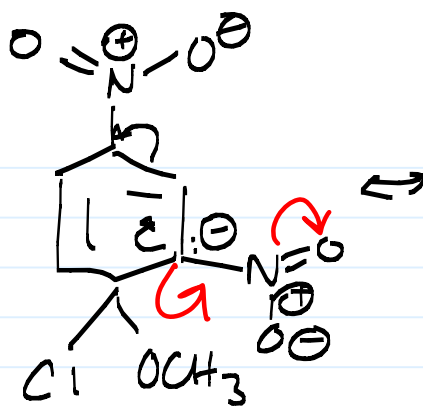


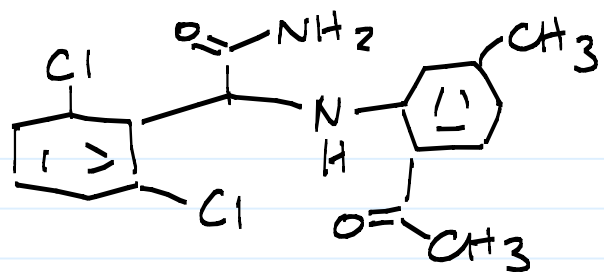
No Rxn!

0.0

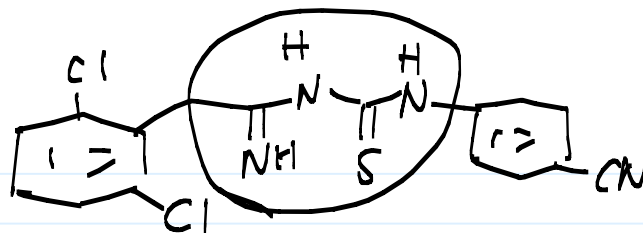


EWG's stabilize
negative charge.

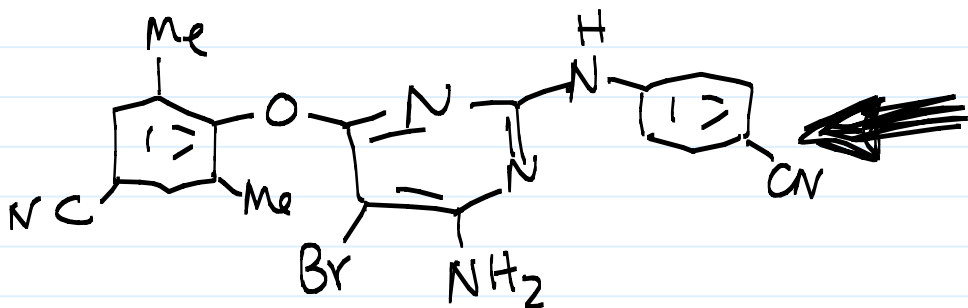




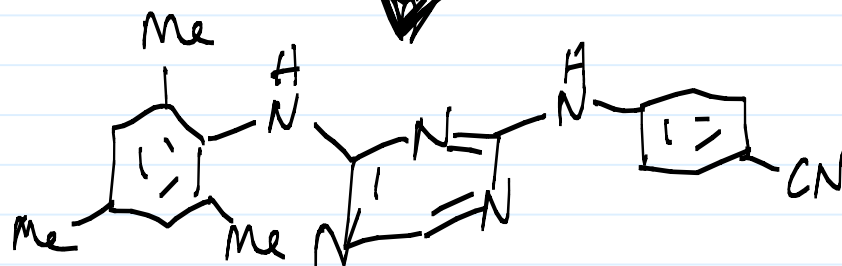
loviride
 $IC_{50} = 13 \text{ nM}$



$IC_{50} = 2.5 \text{ nM}$
 hydrolytic instability



active against double mutants!
 Intelence
 $IC_{50} = 0.4 \text{ nM}$



$IC_{50} = 0.3 \text{ nM}$
 inactive against double mutants "

Synthesis of Intelence:

