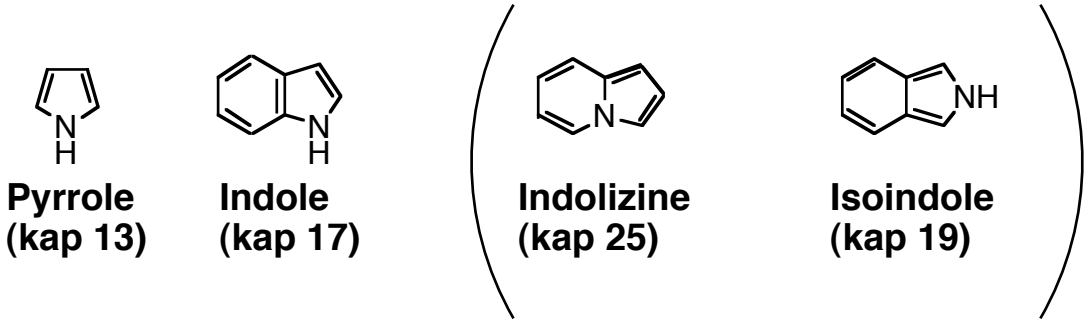
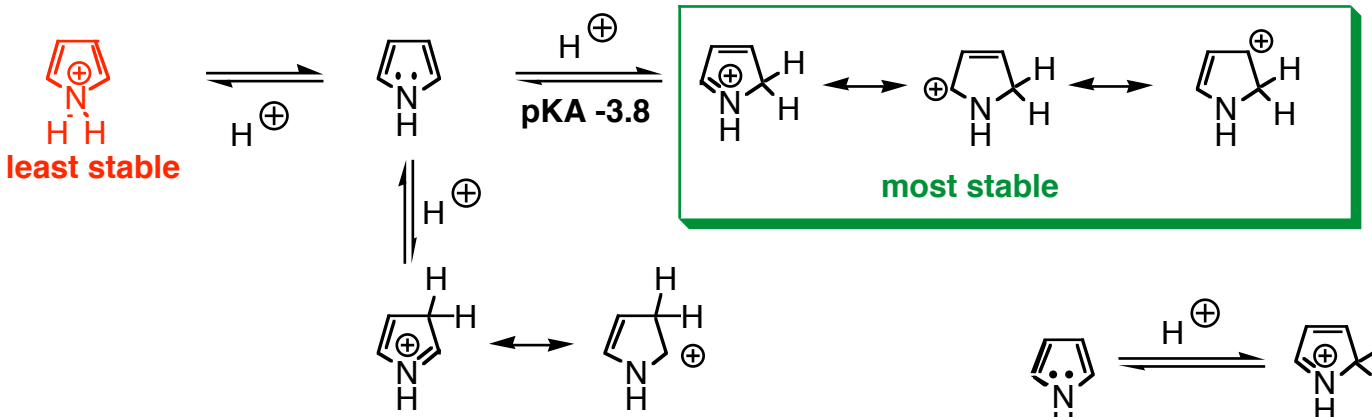
Chapter 13
Pyrroles

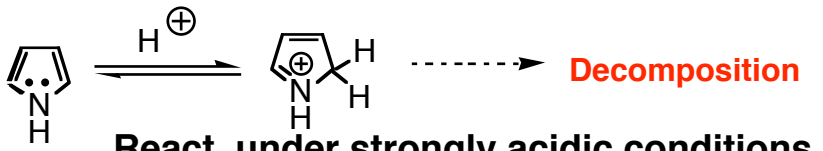


Reaction with electrophiles - Protonation

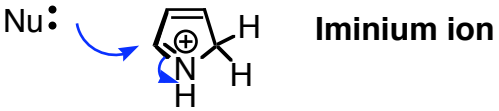


Protonated pyrroles ≈ iminium ions

Reactive intermediates in many react.



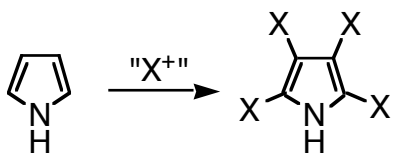
React. under strongly acidic conditions

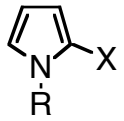


Reaction with electrophiles - E-fil Ar. Subst.

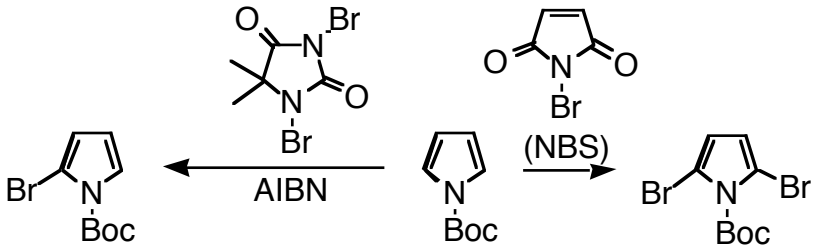
- **Nitration**
- **Sulfonation**
- **Halogenation**
- **FC-acylation**
- **(FC-alkylation)**

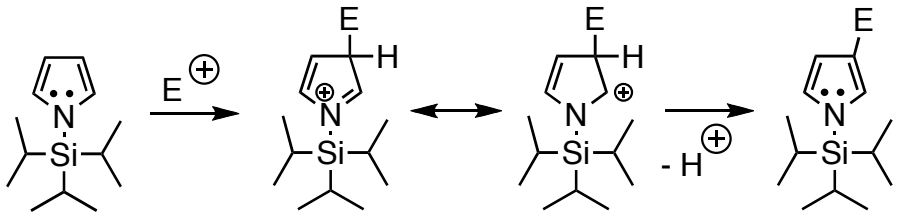
-Halogenation



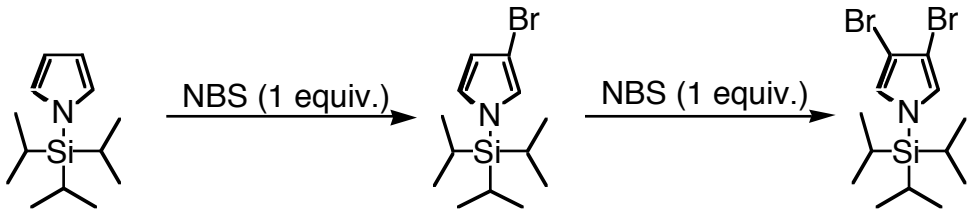


R=H: Unstable
R=EWG (i.e. Boc): More stable

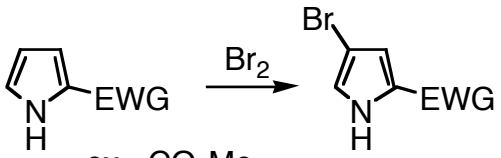




Steric hindrance in 2-pos.



Steric hindrance in 2/5-pos.

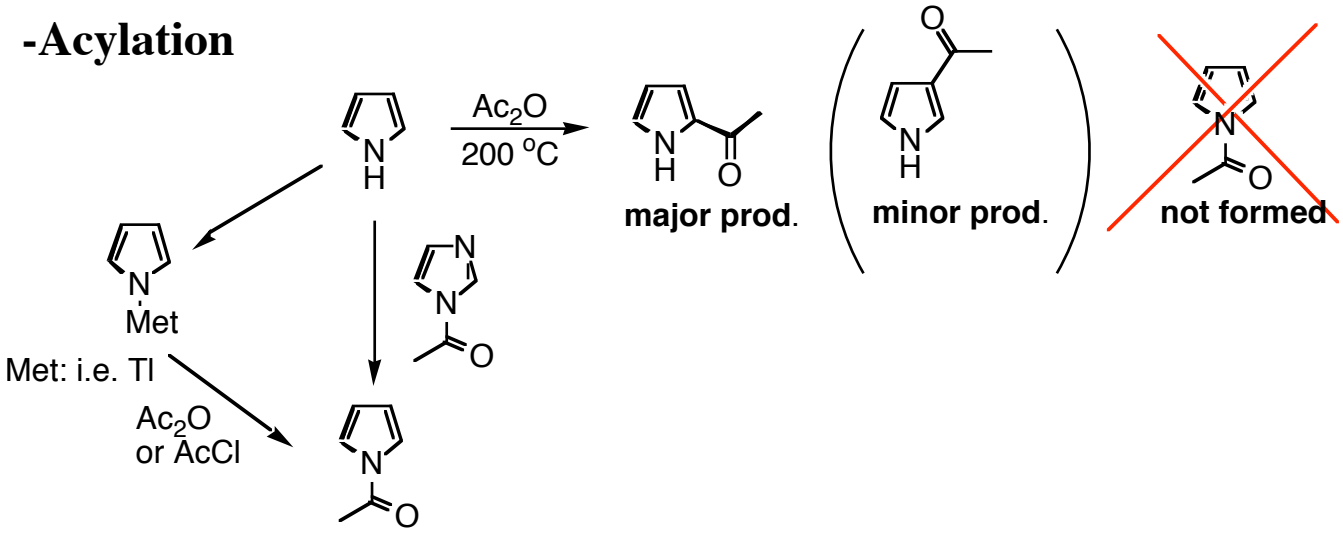


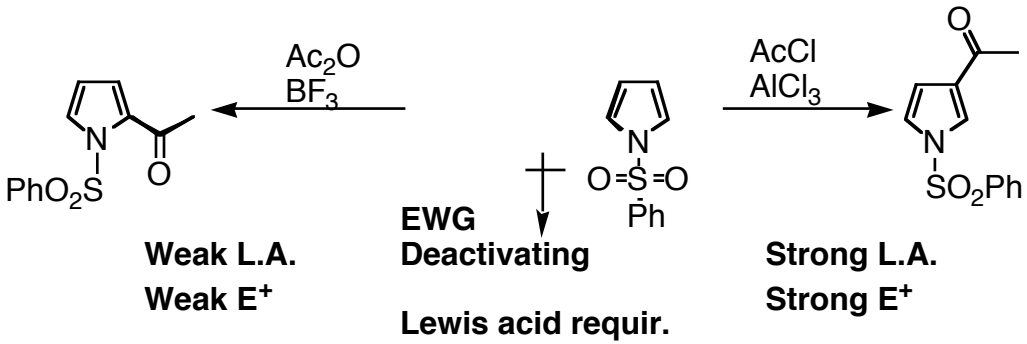
ex. -CO_2Me

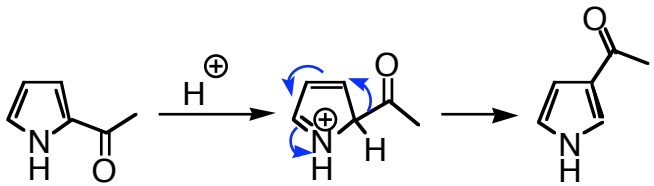
deactivating

m-directing

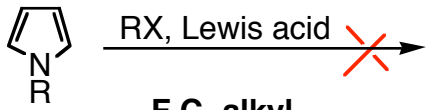
-Acylation





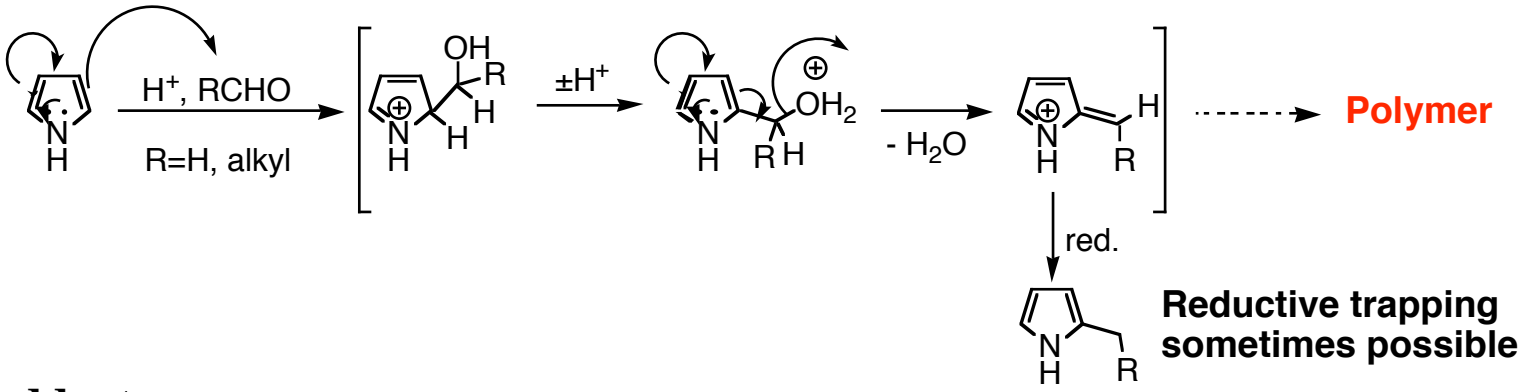


-Alkylation

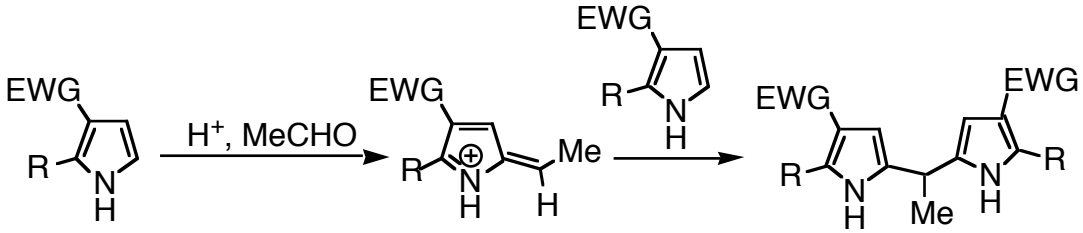


Low reactivity, unselective, polymerization etc

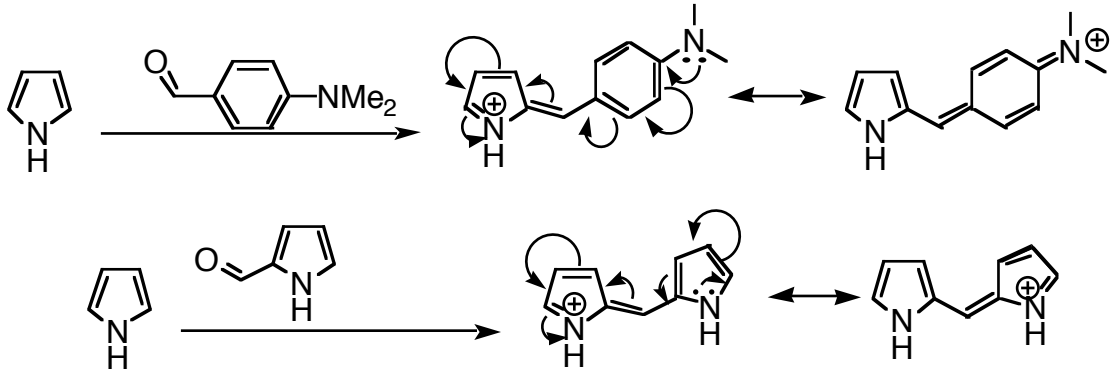
Reaction with electrophiles - Condensation with aldehydes / ketones



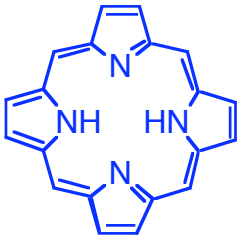
2:1 adducts

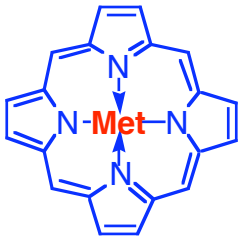


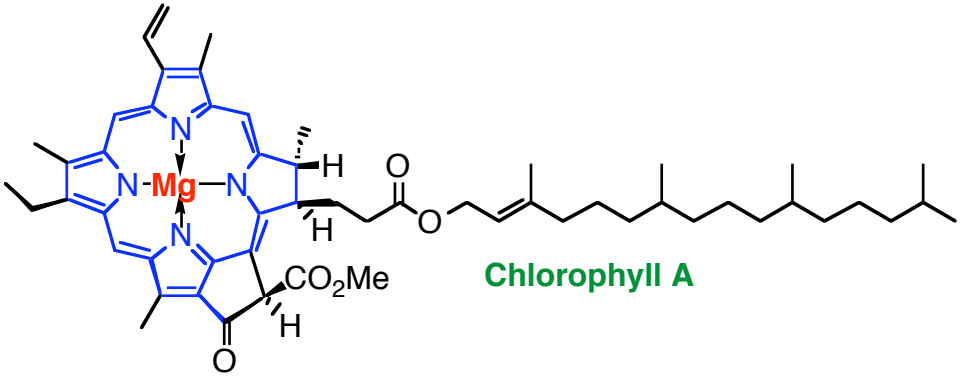
With electron rich arylaldehydes



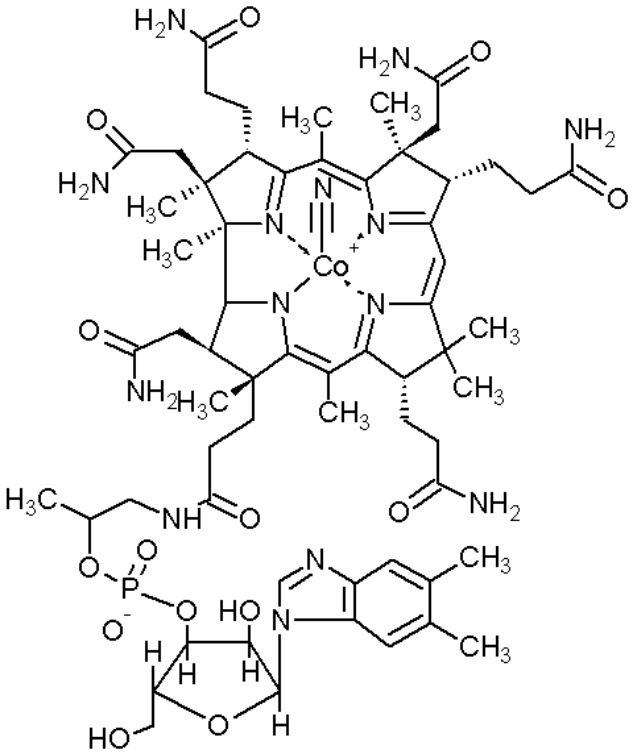
Application in Porphyrine Synthesis

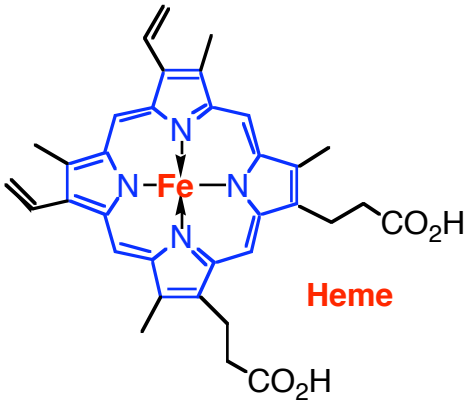




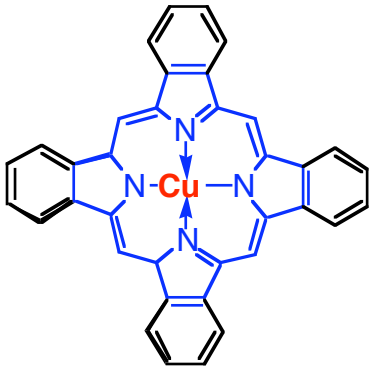


Vit. B12



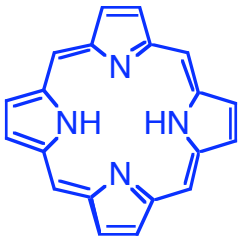


- **Hemoglobine**
- **Myoglobine**
- **Cytochromes**

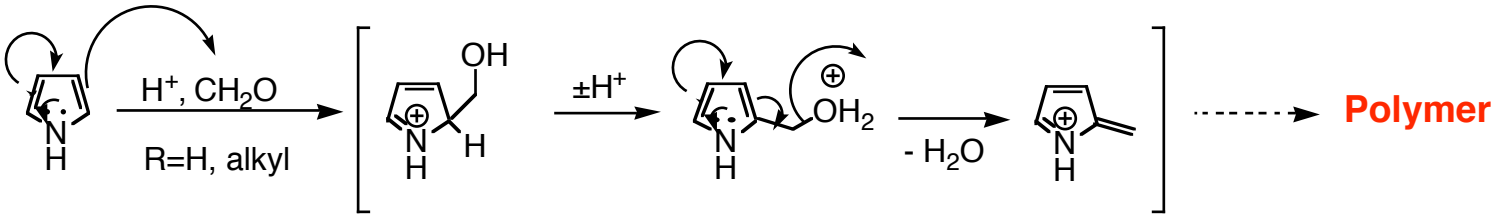


Copper Phtalocyanin
Blue synthetic dye

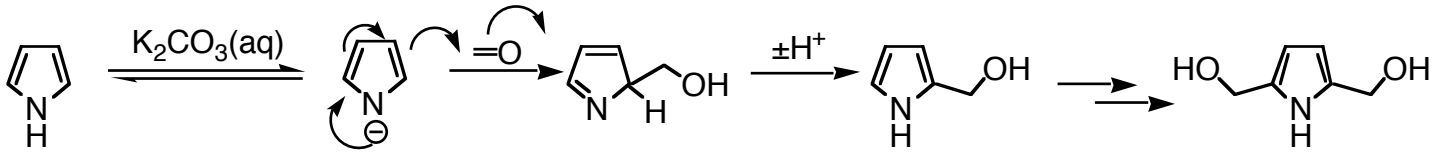
Application in Porphyrine Synthesis



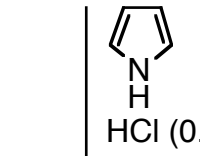
React. under acidic conditions

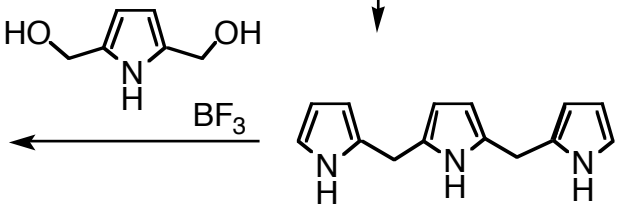


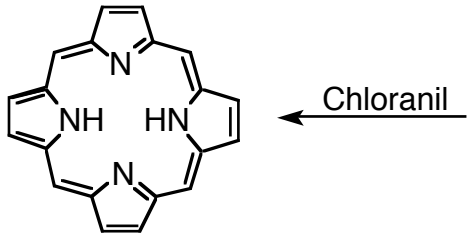
React. under alkaline conditions



No highly reactive iminium salts

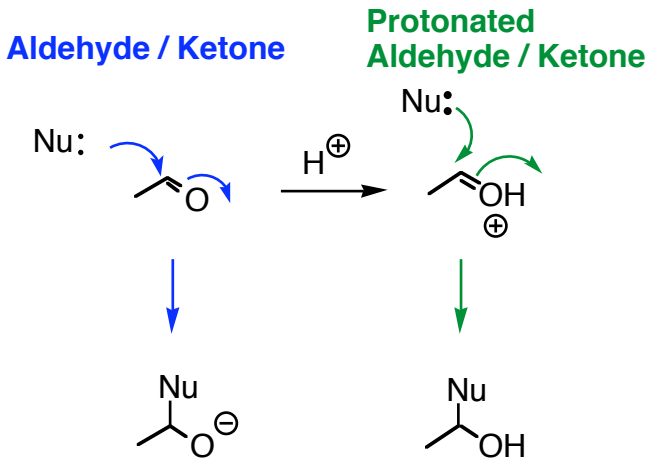


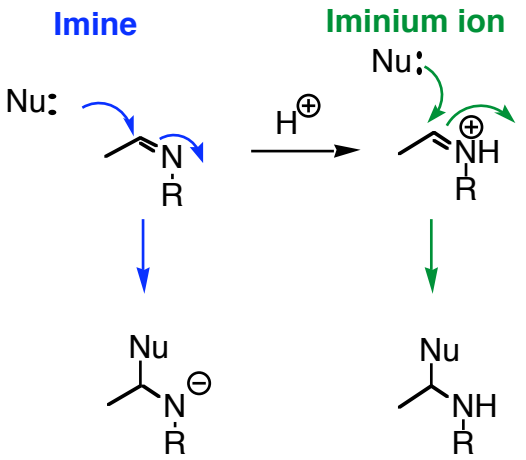




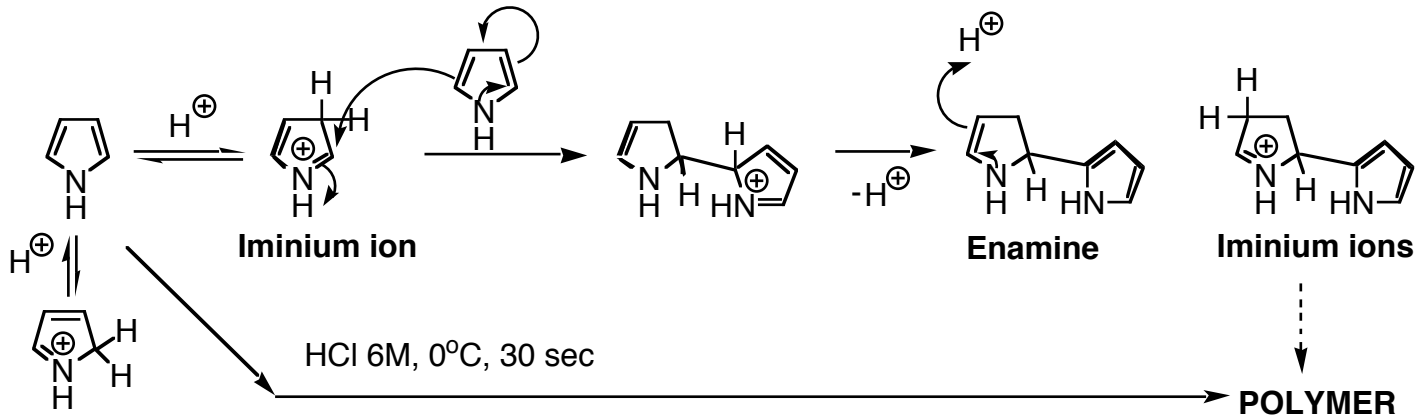
Porphyrin **Porphyrinogen**

Reaction with electrophiles - Condensation with Imines / Iminum Ions

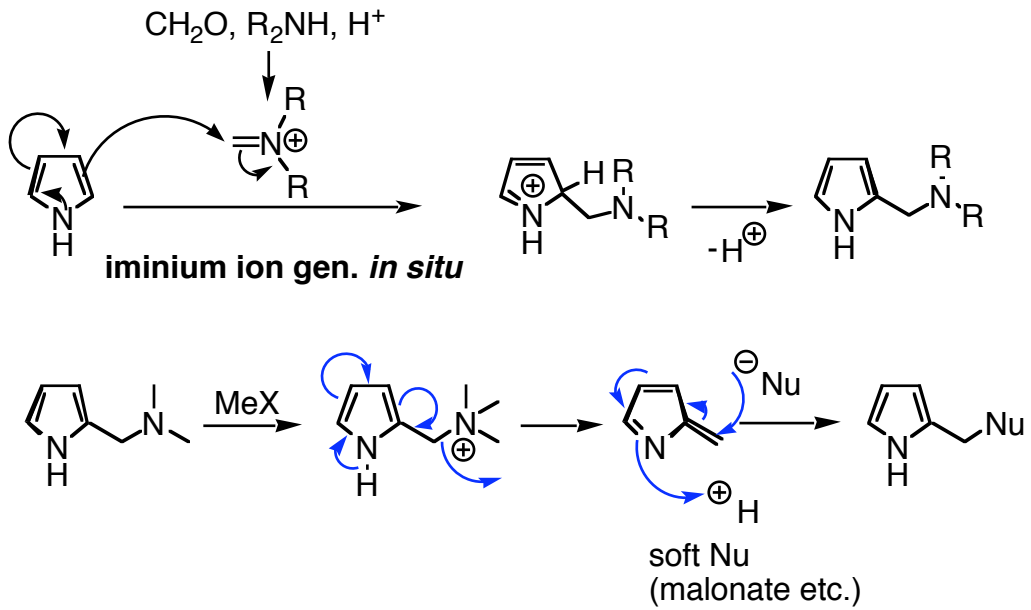




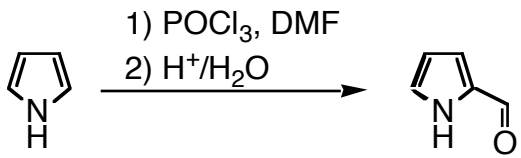
Pyrrole unstable in acidic media



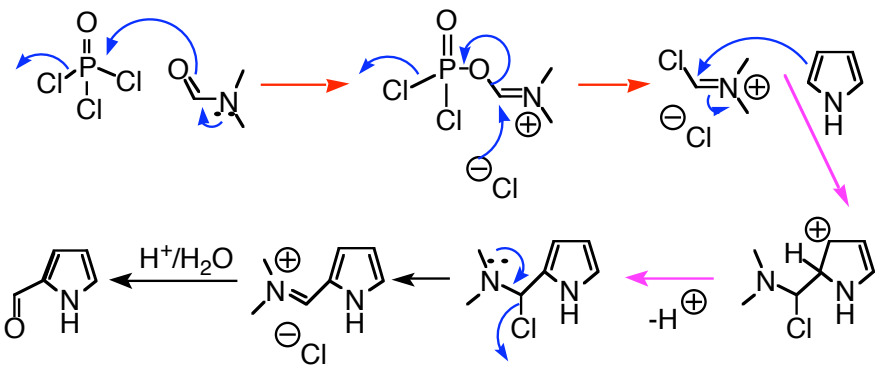
Mannich react.



Vilsmeier react. (Vilsmeier-Haack): Formylation

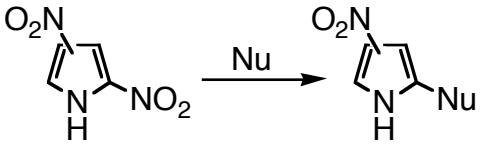


Generation of Vilsmeier reagent
E-fil Ar. subst.
Hydrolysis of iminium salt

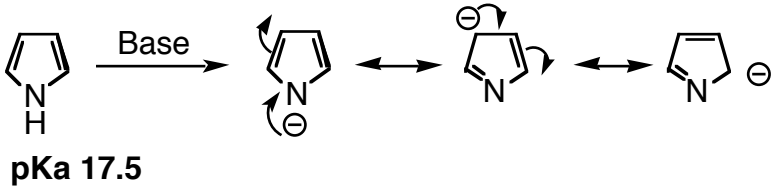


Reaction with nucleophiles

Electron rich ring - not very reactive towards Nu

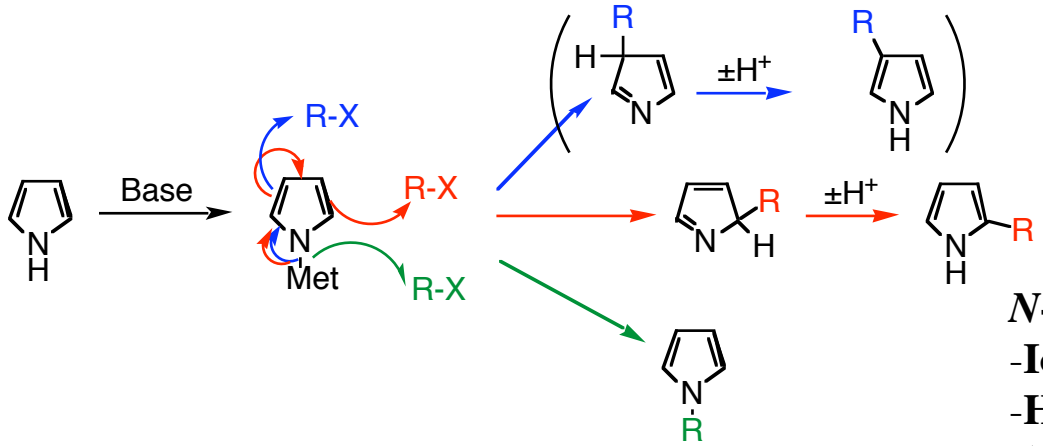


Reaction with base and further react. with E-files



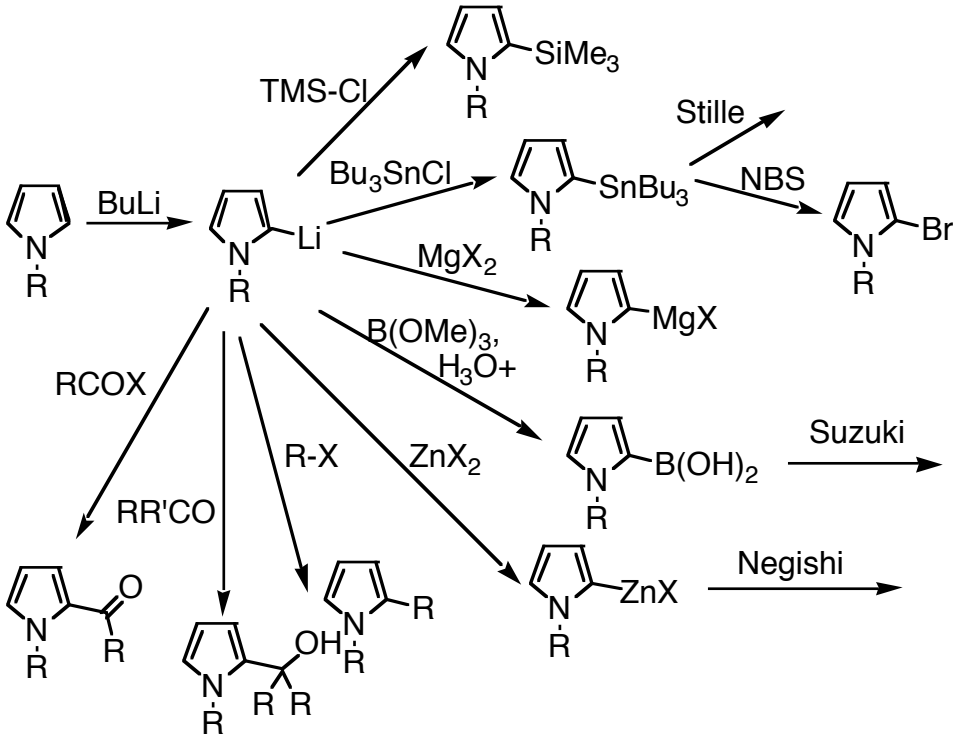
pKa 17.5

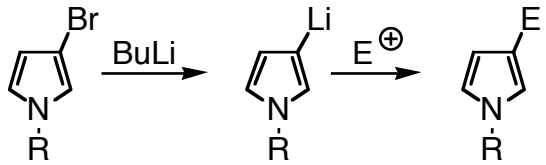
pKa 44



***N*-alkylation favoured by:**
-Ionic N-Met bond (Li)
-High solvating power of solvent
(DMF, DMSO etc., crown ethers, PTC)

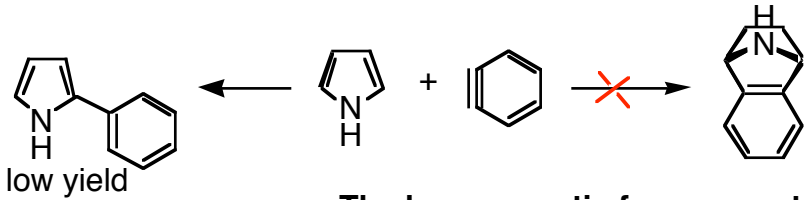
C-metallation and further react.



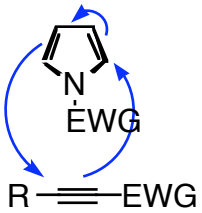


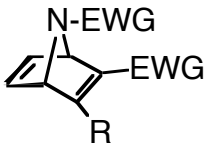
Cyclo Additions

Pyrrole as diene (4π component)



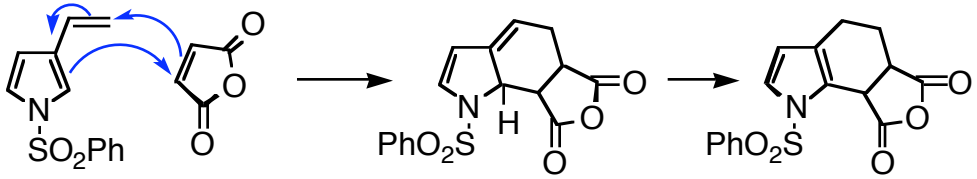
The less aromatic furane reacts





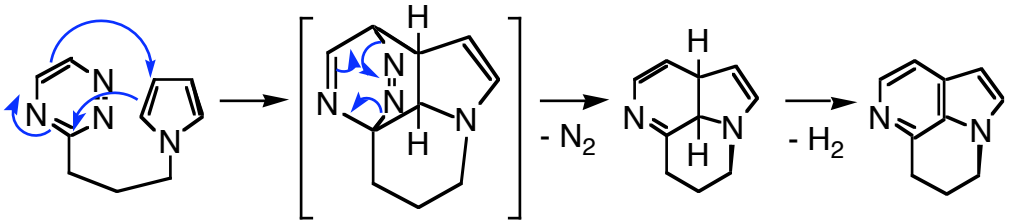
EWG: Less interact. Between Lone pair on N and "diene"

Vinylpyrrole as diene

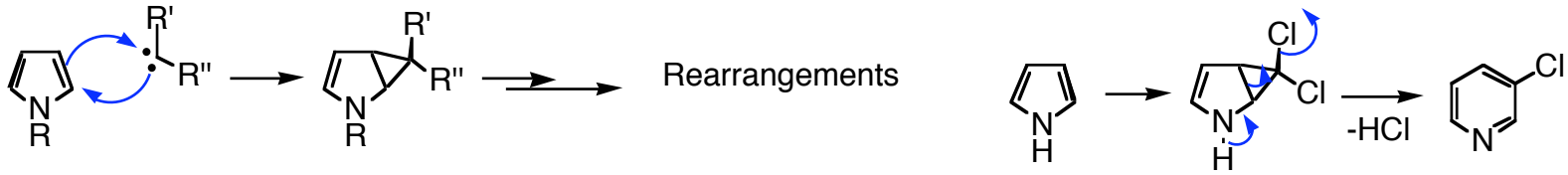


Pyrrole as dienophile (2π component)

A few intramolek. ex.

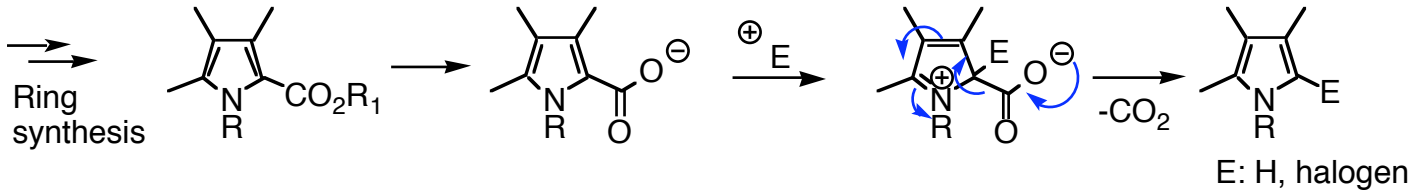


Reaction with carbenes / carbenoids

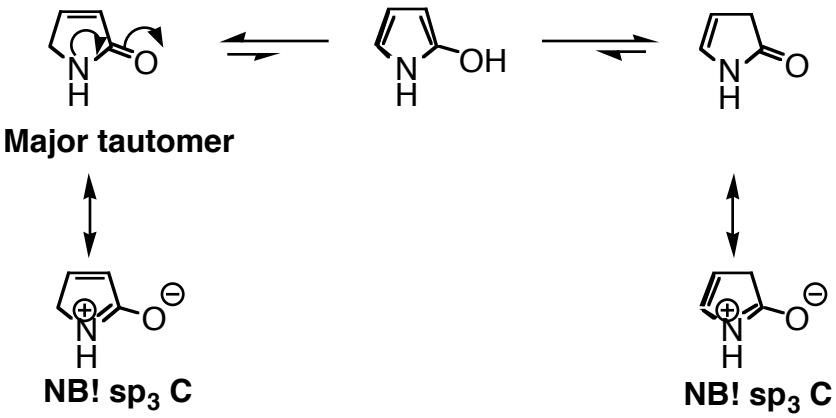


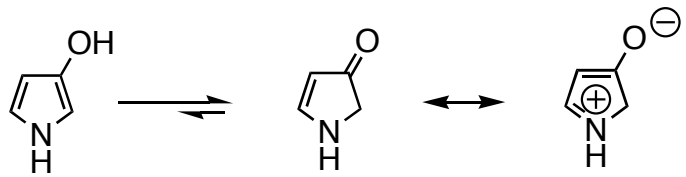
Indoles: No cyclopropanes isolated from carben(oid) react.

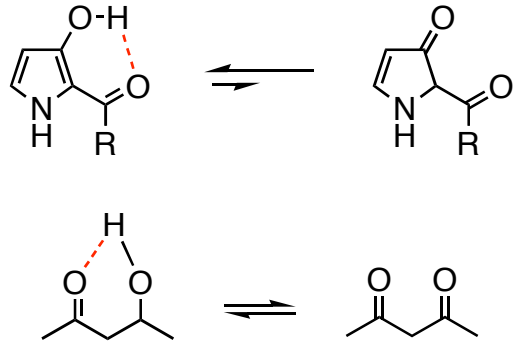
Pyrrole Carboxylic Acids



Oxypyrroles





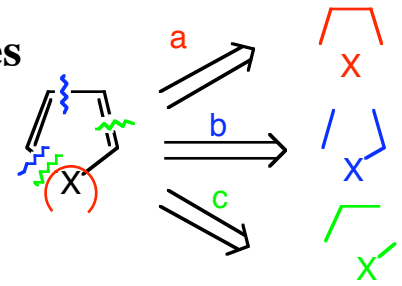


Aminopyrroles

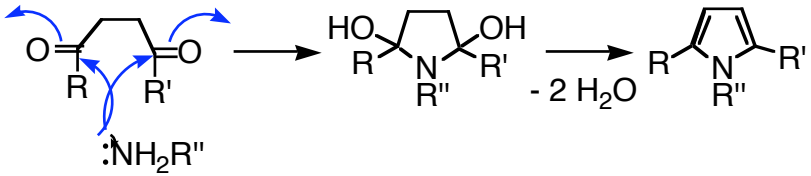
-Amino (not iminoform) - unstable

Synthesis of Pyrroles

Carbonyl condensations (c.f. chapt. 3) - Pyrroles



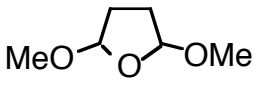
Strategy a; Paal-Knorr synth.

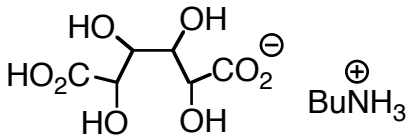


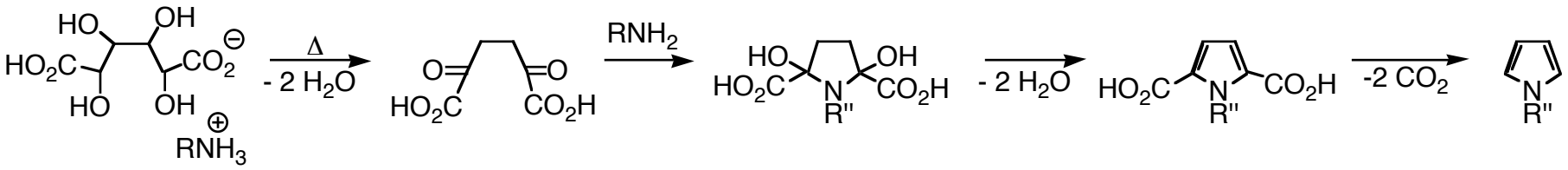
R"=H, alkyl, aryl

R, R' = H:  **Unstable**

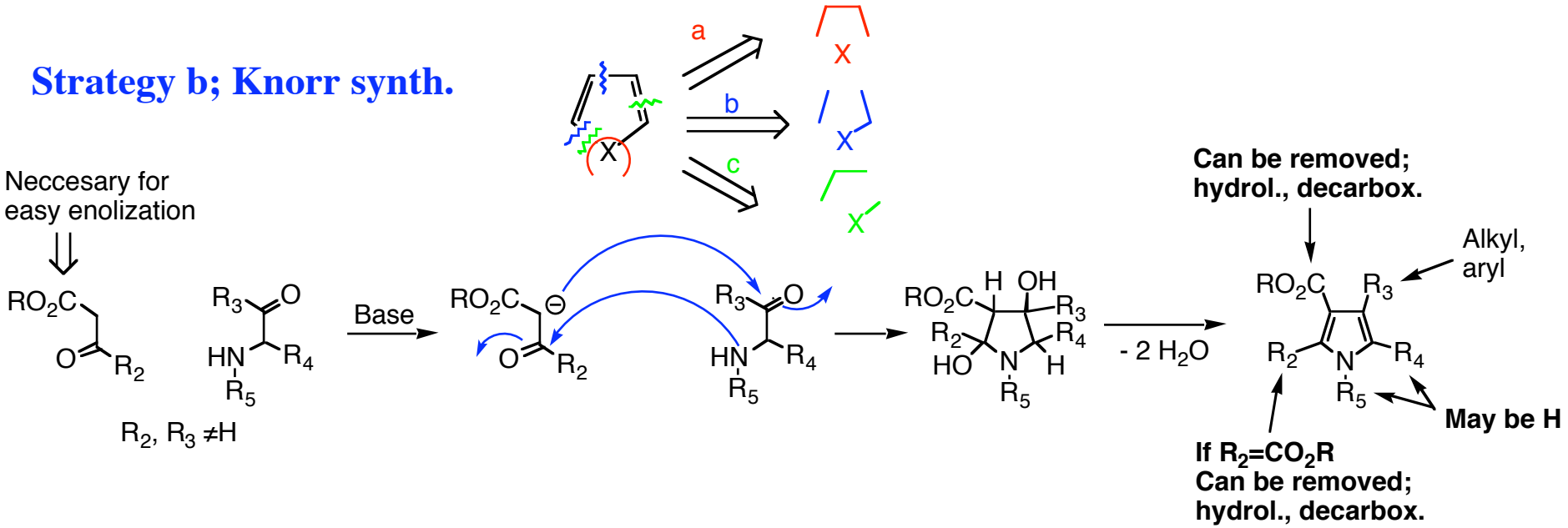
Synthons:



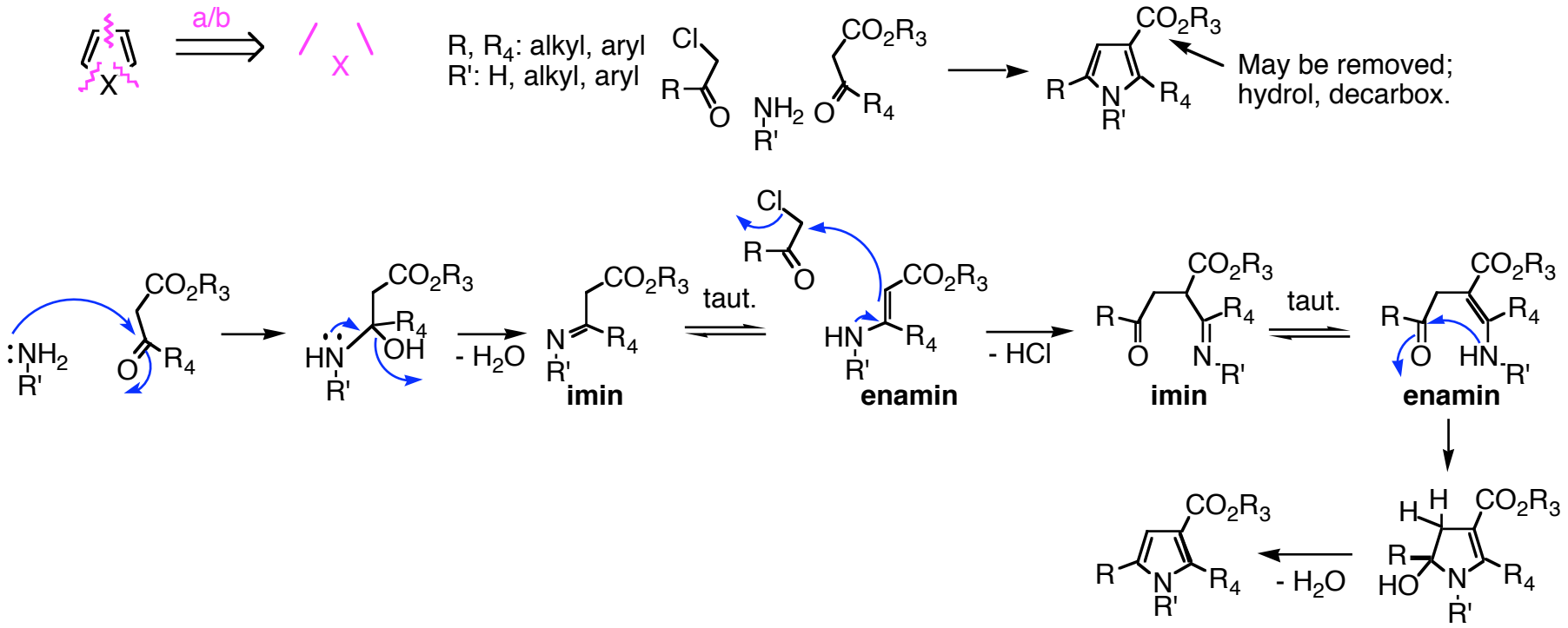




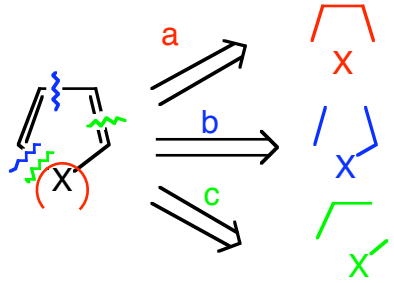
Strategy b; Knorr synth.

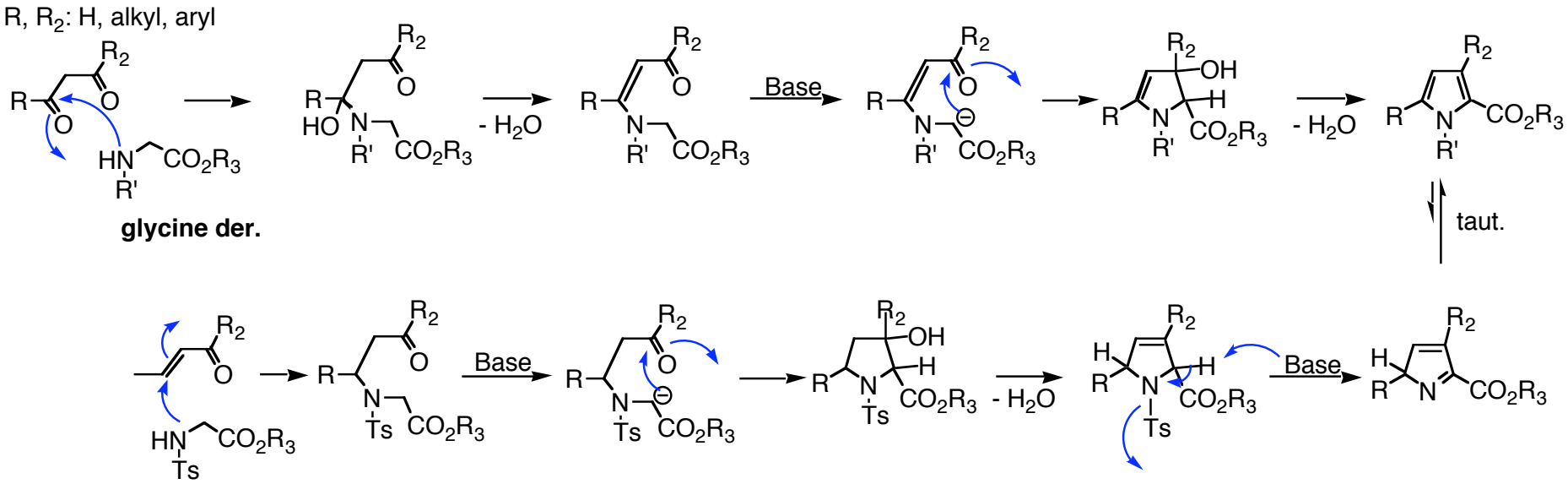


Strategy a and b combined; Hantzsch synth.

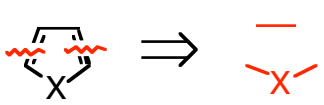


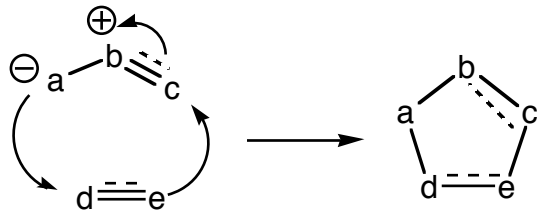
Strategy c



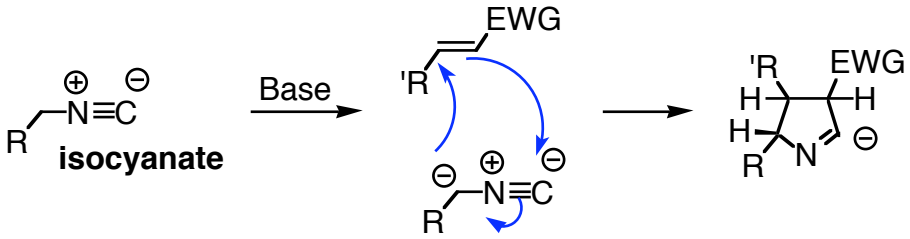


Cycloadditions with 1,3-dipoles (c.f. chapt. 3)





Reaction with isocyanide

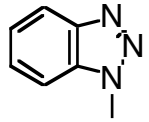


R=Ts (TsMIC)
R=Benzotriazolyl (BetMIC)
R=-CO_2R

EWG= NO_2, COR

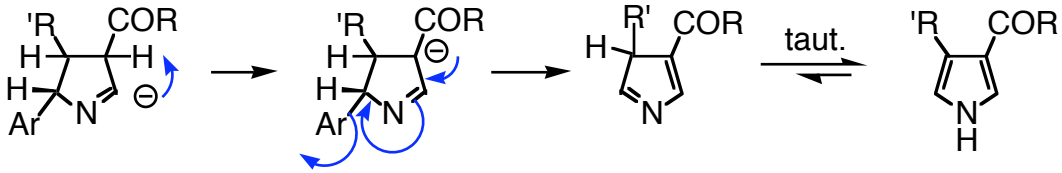
MIC: methyl isocyanate

Bet:



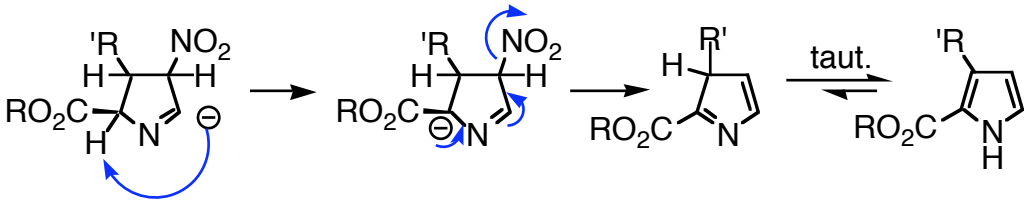
Alt. I; van Leusen synth.

R: Ts or Bet (Good leaving groups)
EWG: -COR

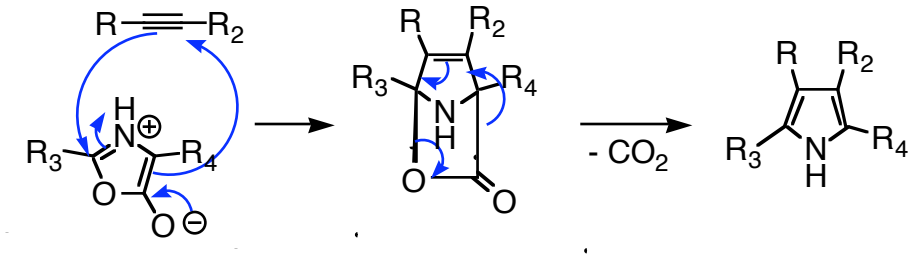


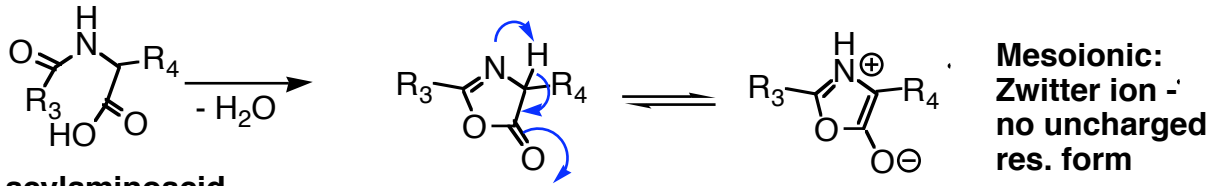
Alt. II; Barton Zard synth.

R: -CO2R
EWG: -NO_2



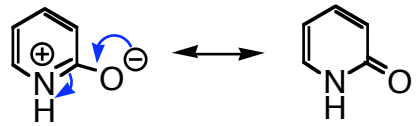
Reaction with mesoionic oxido-oxazoliums





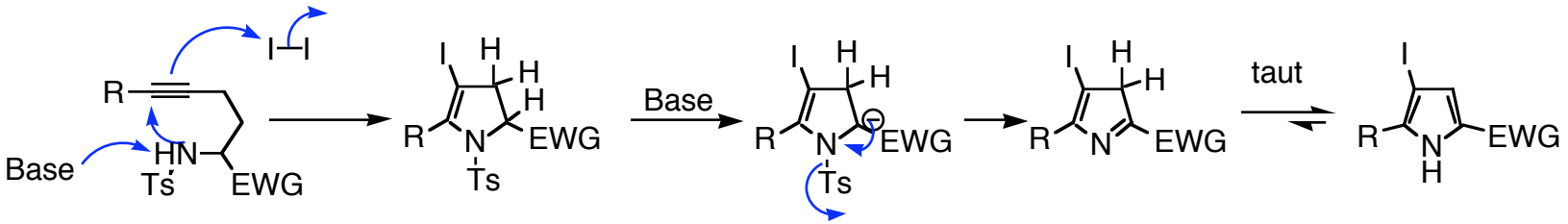
***N*-acylaminoacid**

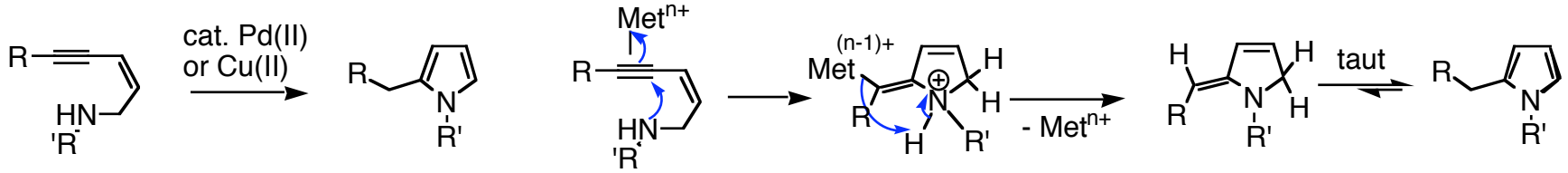
Mesoionic:
Zwitter ion -
no uncharged
res. form



Not mesoionic

Synthesis from aminoalkynes





R: alkyl, alkenyl