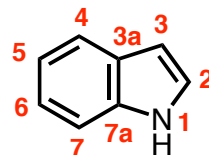
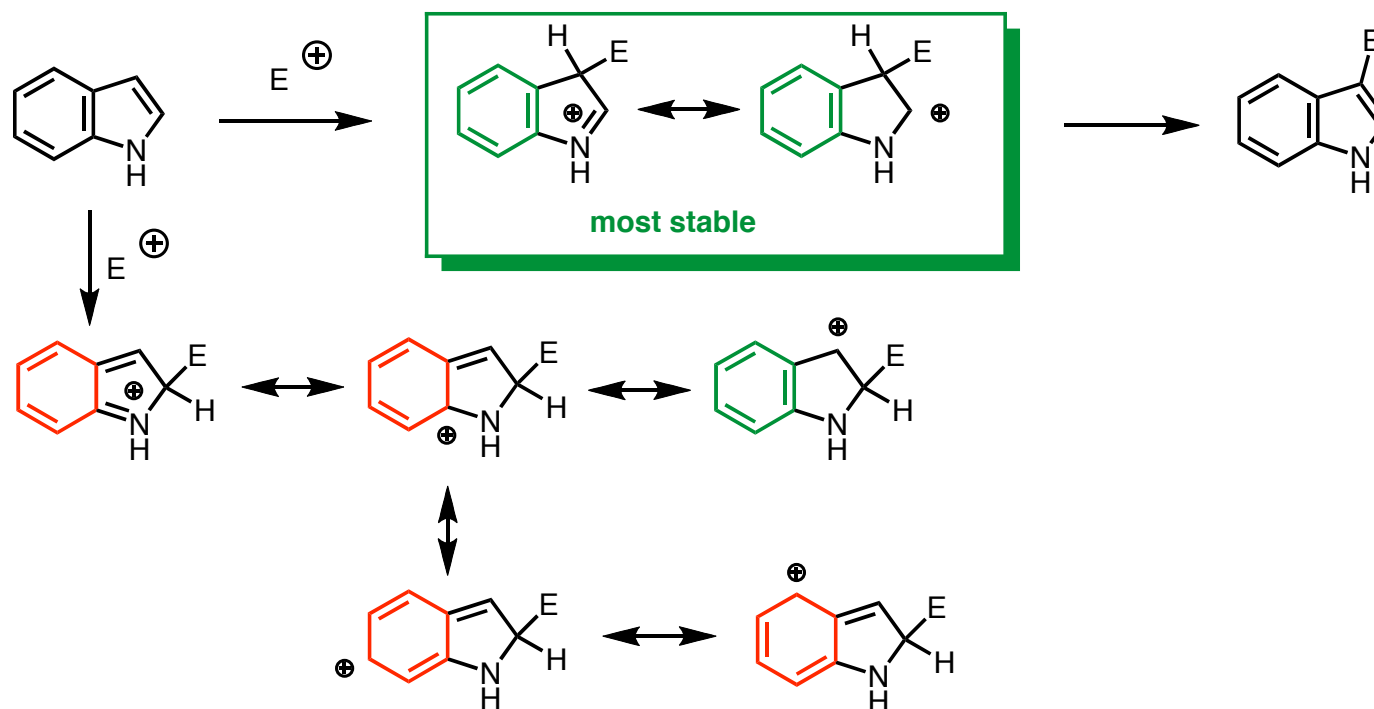


INDOLES

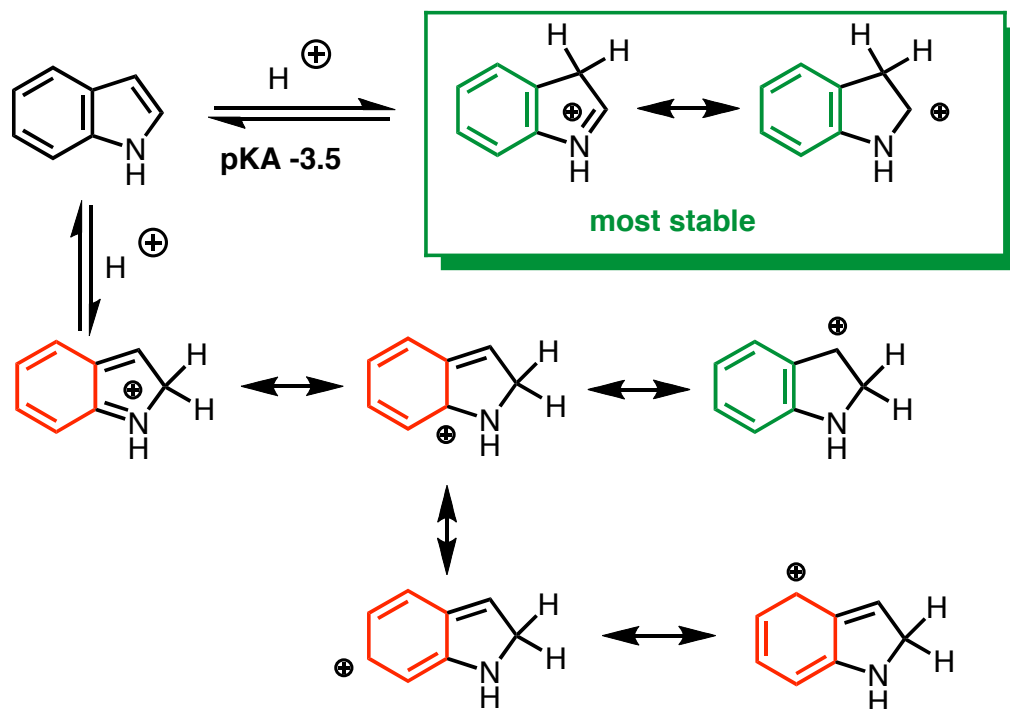


Reaction with electrophiles - Reacts preferably at C-3 !!



Protonation

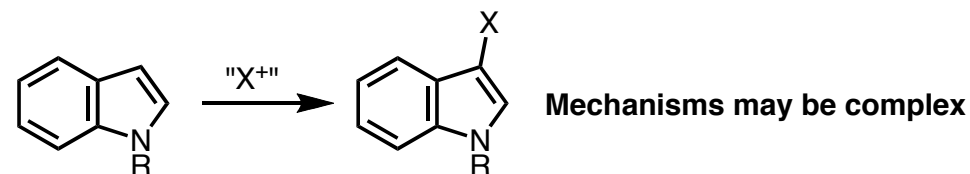
Weak base, pKa ca as for pyrrol



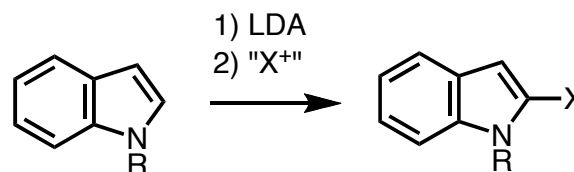
Nitration

at C-3

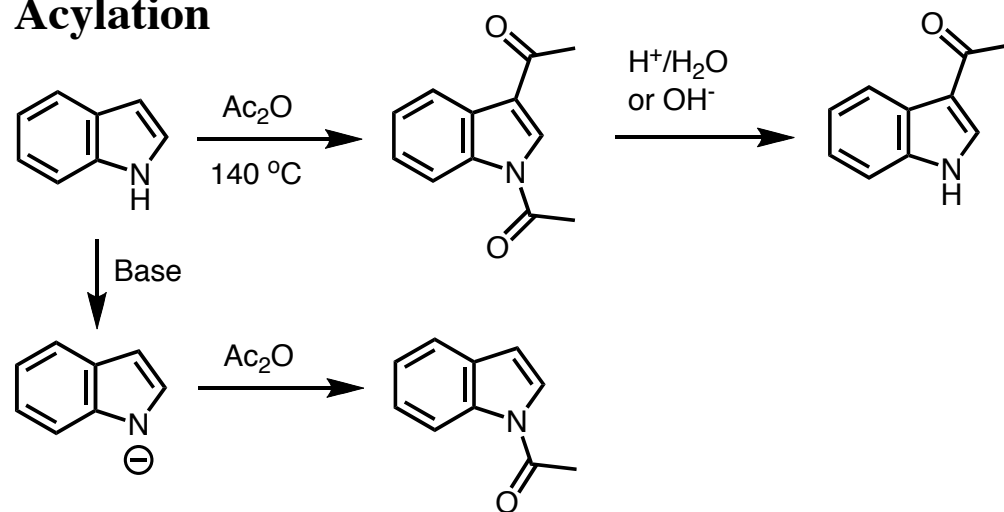
Halogenation



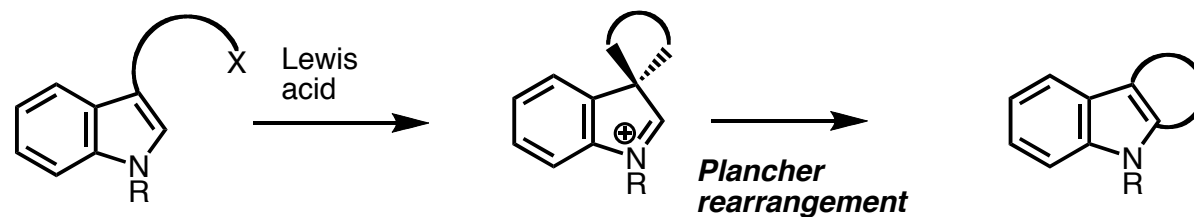
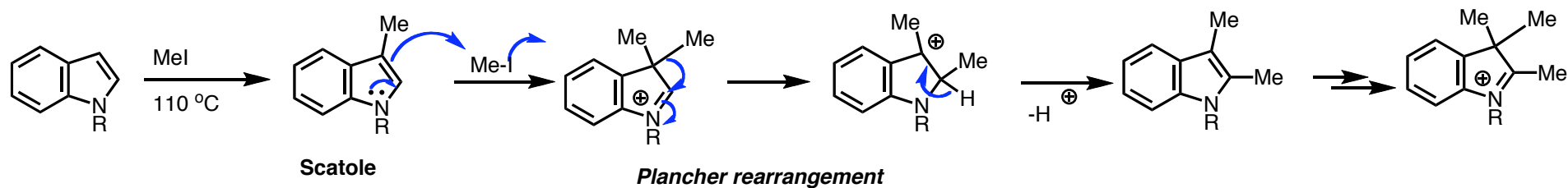
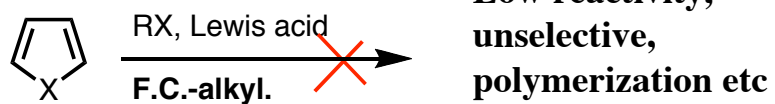
Haloindoles (esp. 2-halo-) **unstable**



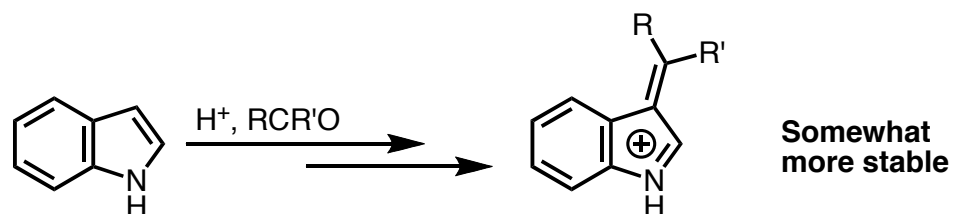
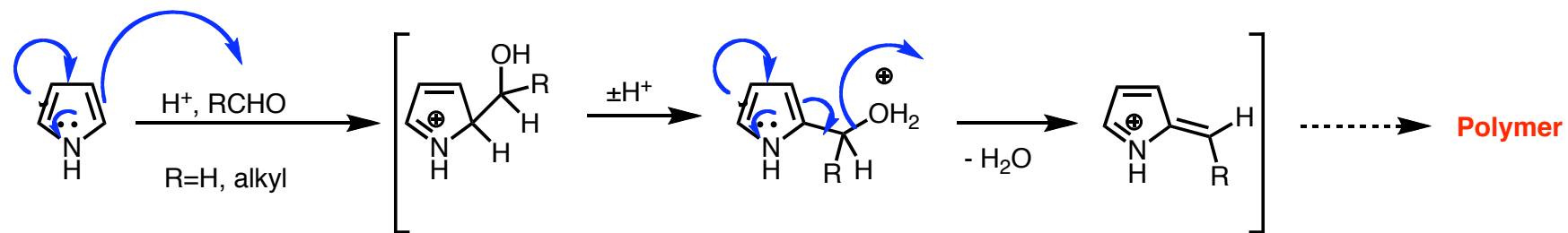
Acylation



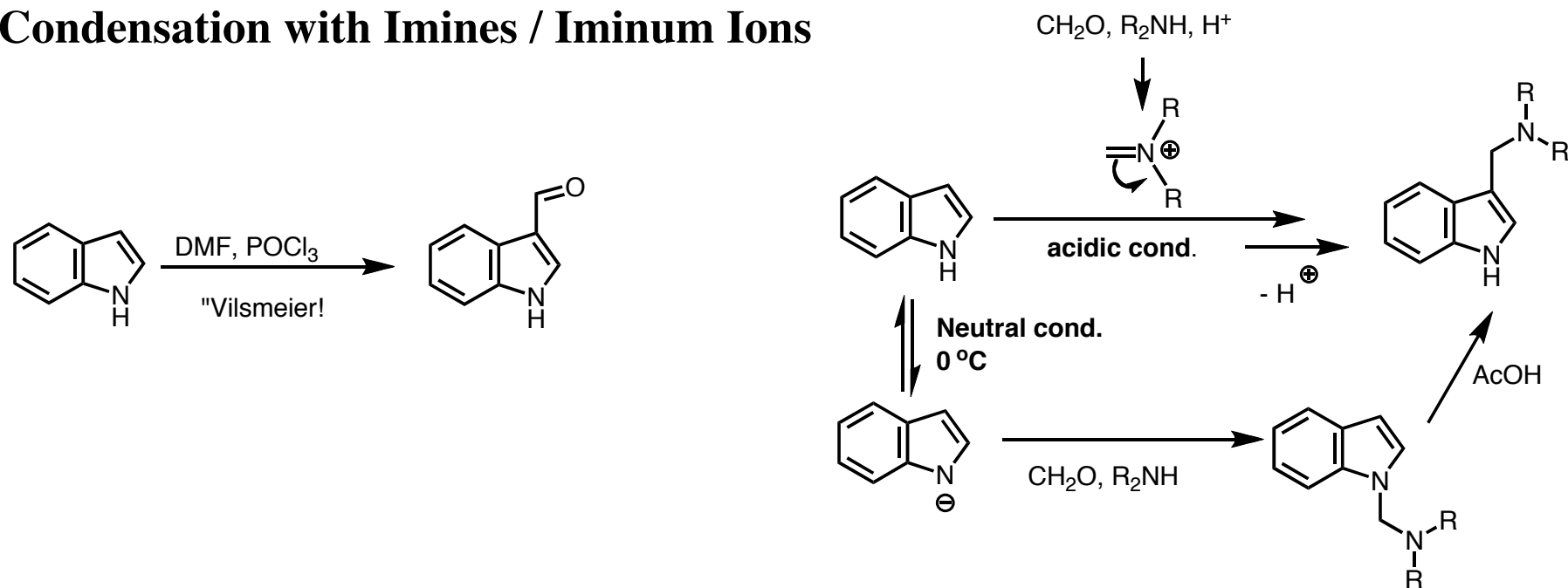
Alkylation



Condensation with aldehydes / ketones

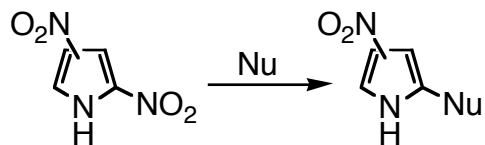


Condensation with Imines / Iminium Ions



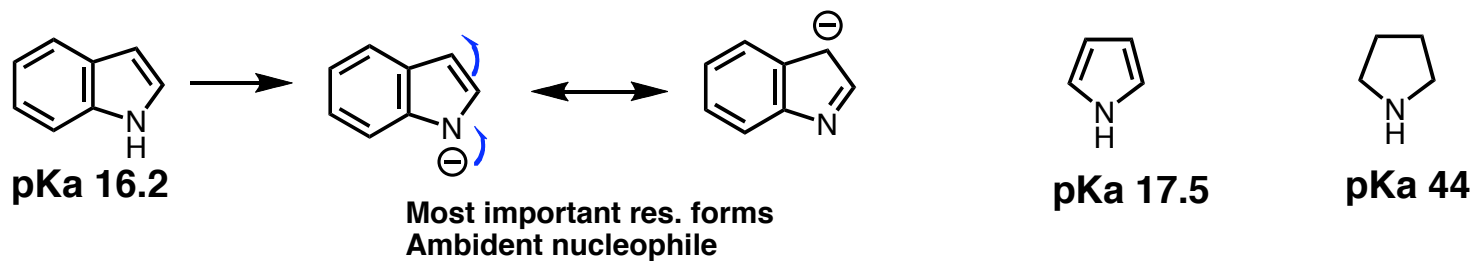
Reaction with nucleophiles

Electron rich ring - not very reactive towards Nu



Indole: React. In benzene ring preferred

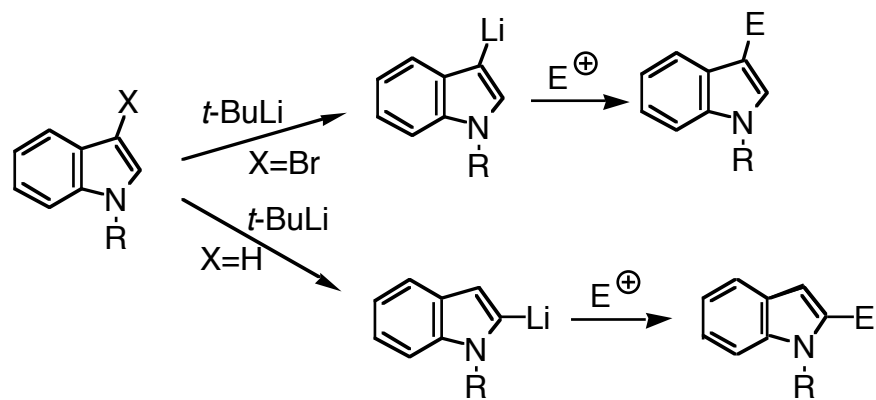
Reaction with base and further react. with E-files



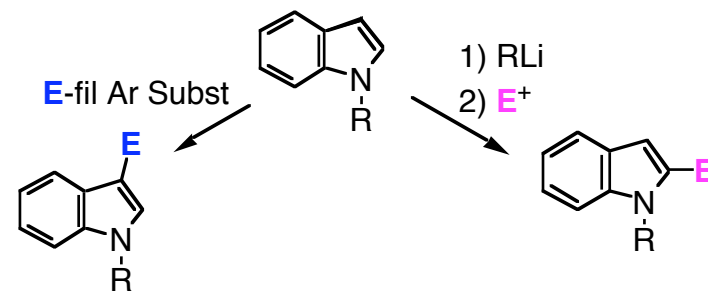
React at N: Polar solvents
Ionic (Na, K counter ions)

React at C: Less polar solvents
More covalent bound metal (Grignard etc)

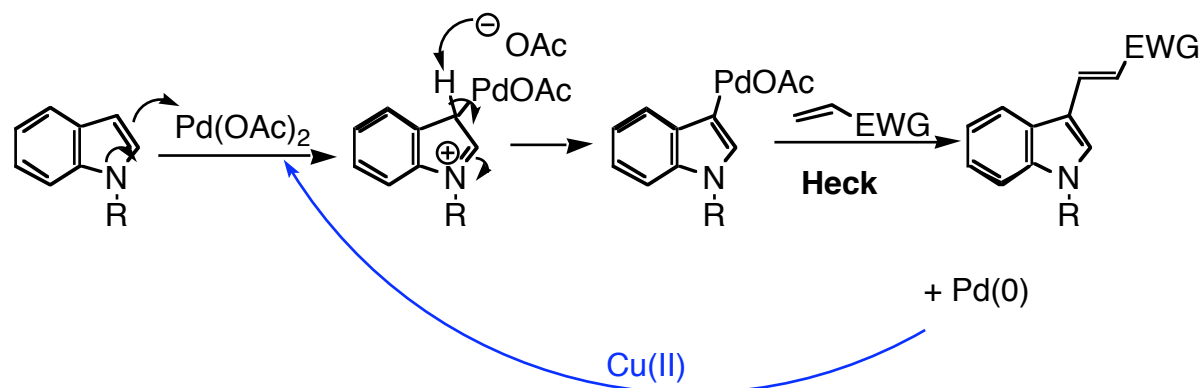
C-metallation and further react.



Simple routes to 2- or 3-subst. indoles



Electrophilic Palladation

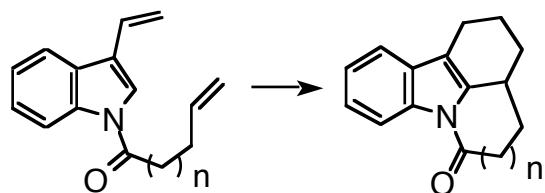
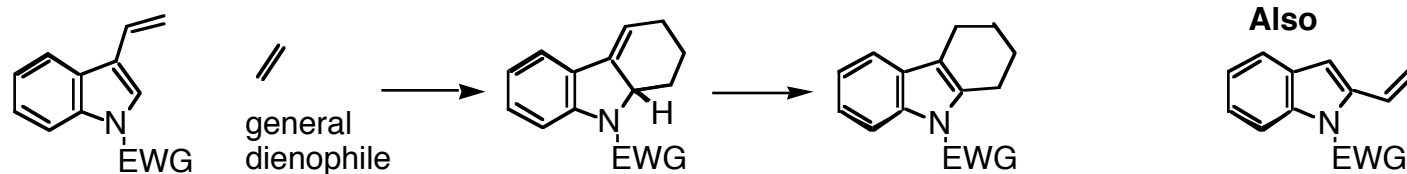


Cyclo Additions

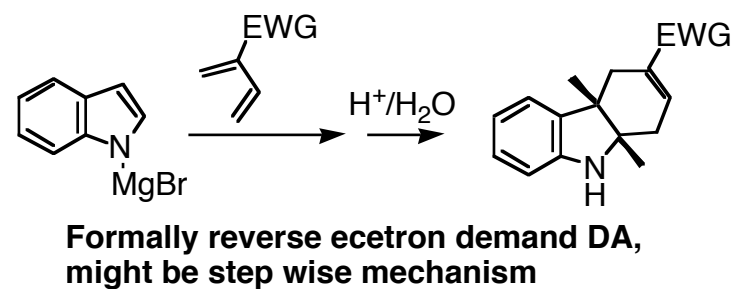
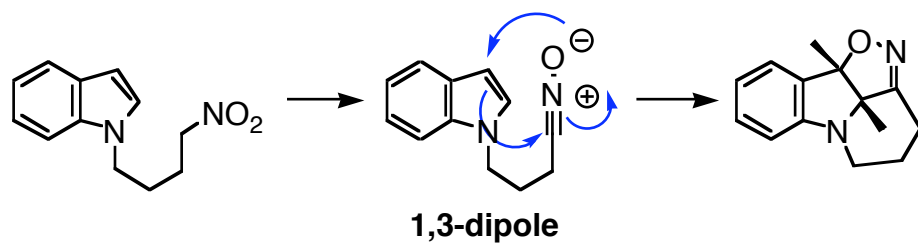
Indole as diene (4 π component)



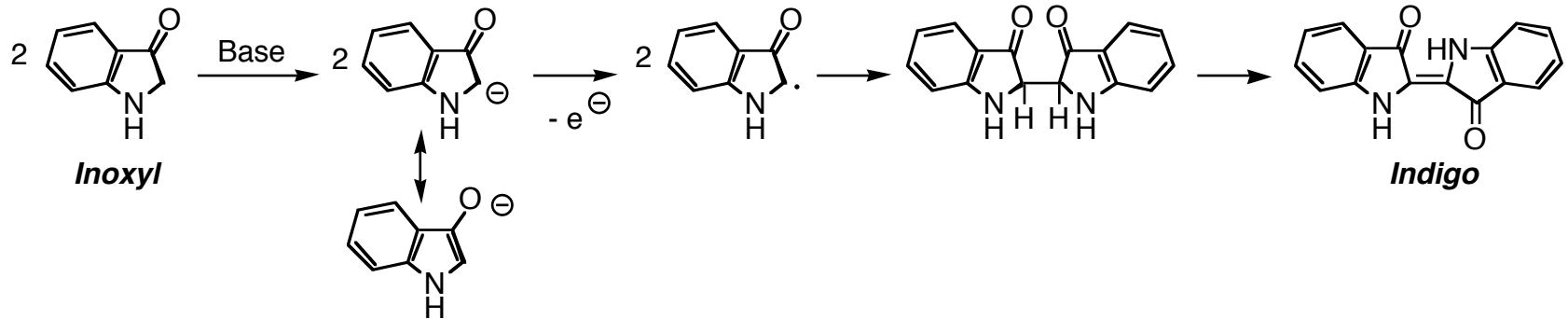
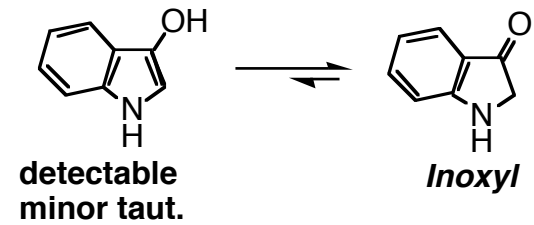
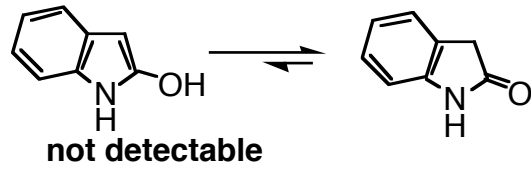
Vinylindole as diene



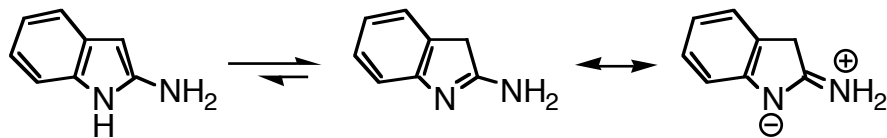
Indole as dienophile (2 π component)



Oxyindoles

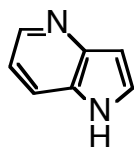
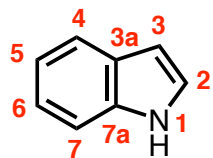


Aminoindoles

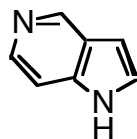


3-Amino - unstable

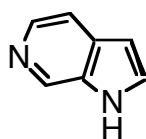
Azaindoles (Pyrrolopyridines)



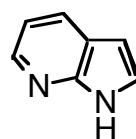
4-azaindole



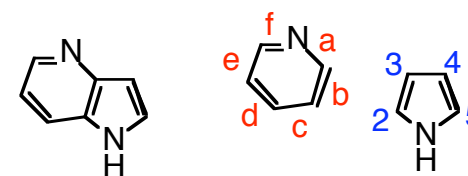
5-azaindole



6-azaindole



7-azaindole

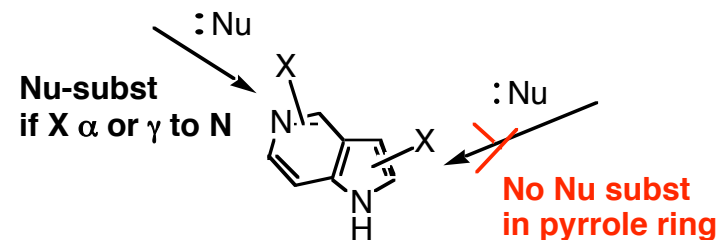
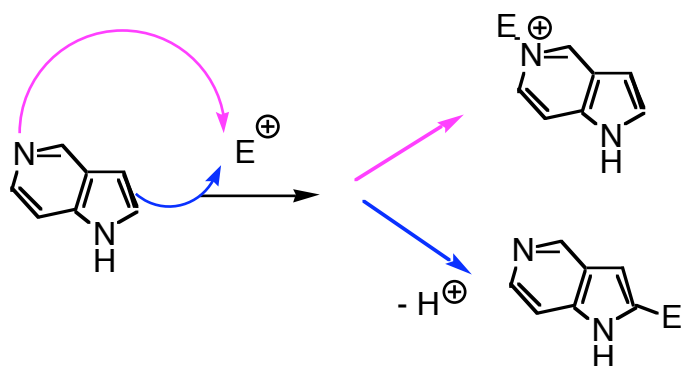


pyrrolo[2,3-b]pyridine

largest ring

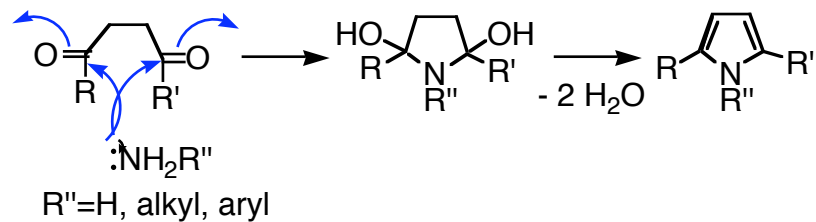
5-membered ring \approx pyrrol (less electron rich)

6-membered ring \approx pyridine (more electron rich)

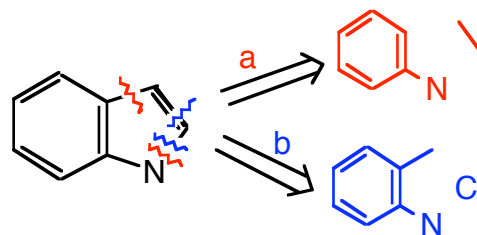
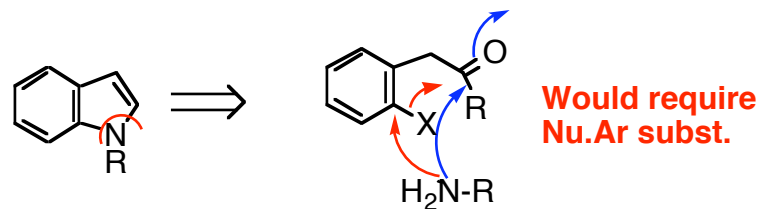


Synthesis of Indoles

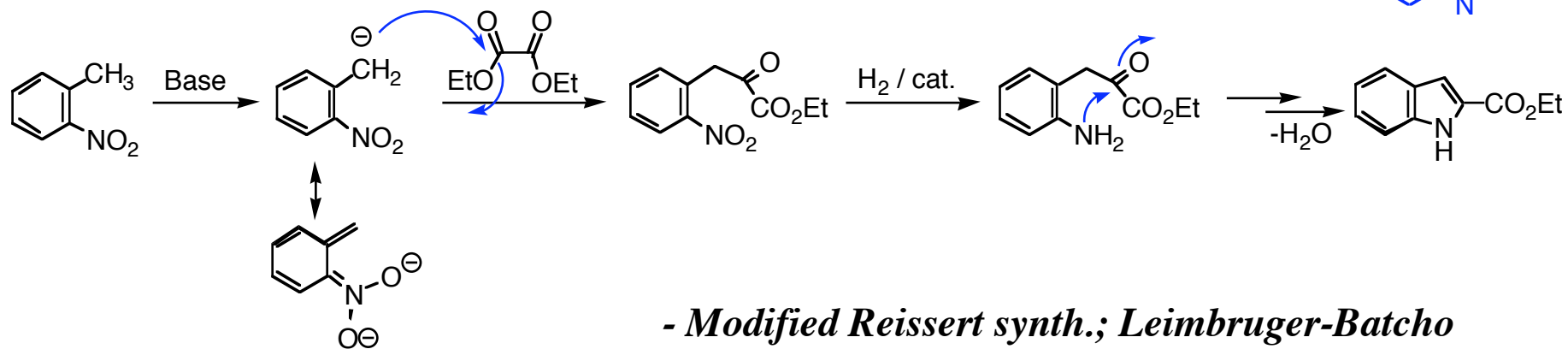
Paal-Knorr synth.



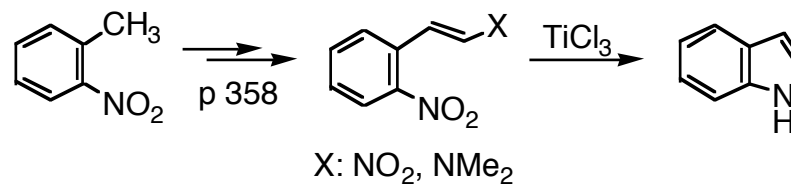
Not useful for indoles



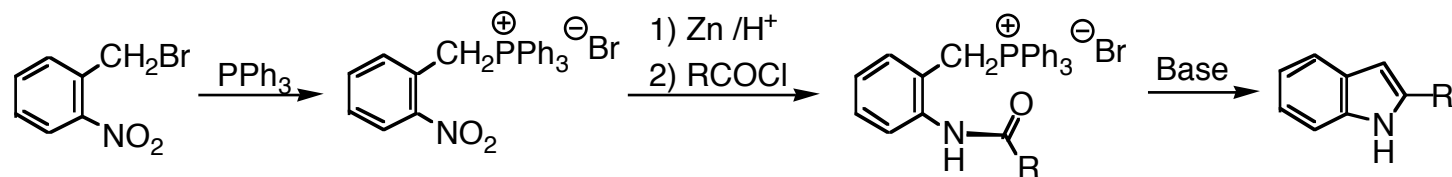
Strategy b
-Reissert synth.



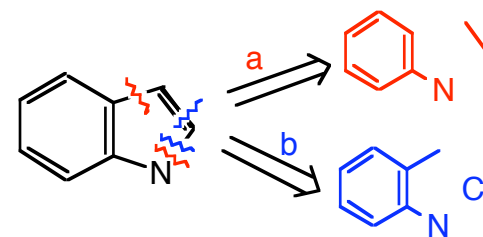
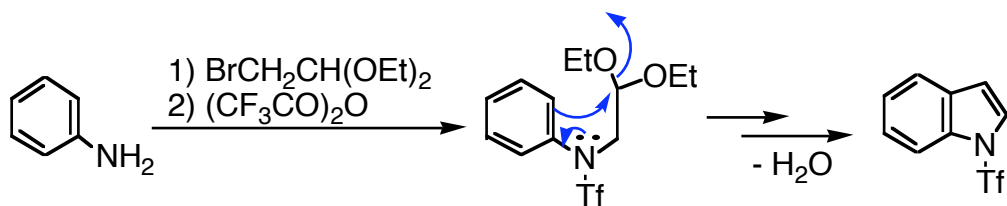
- Modified Reissert synth.; Leimbruger-Batcho



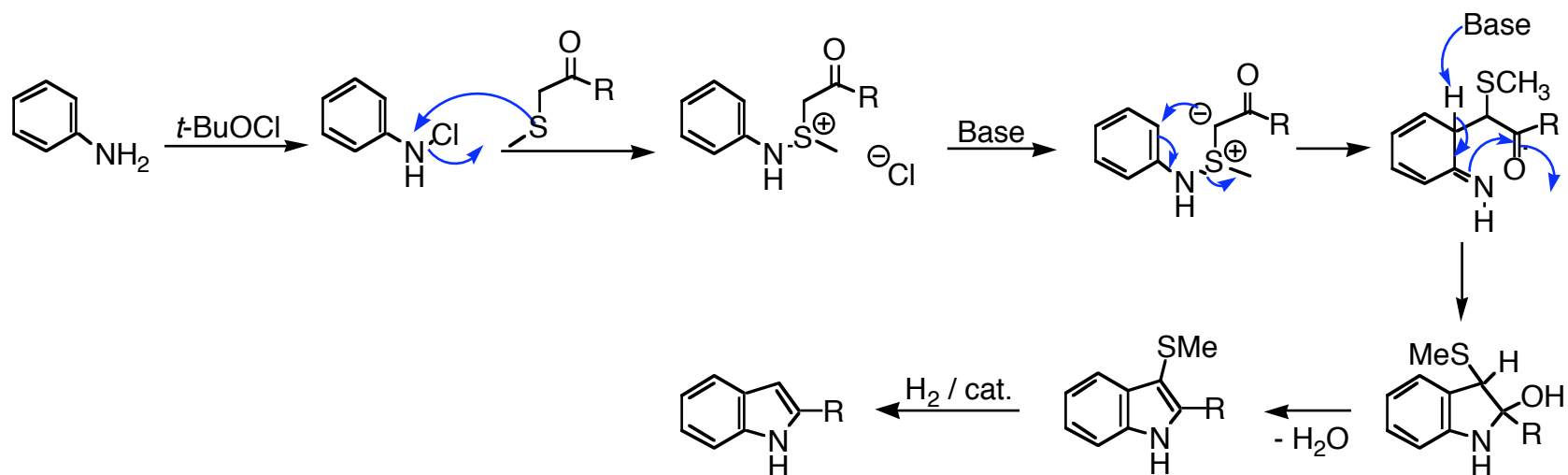
-Madelung synth.



Strategy a
-Bischler synth.

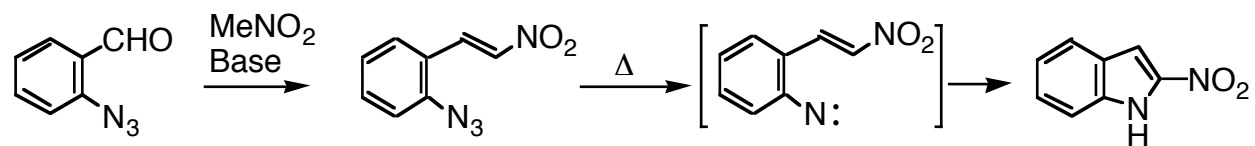
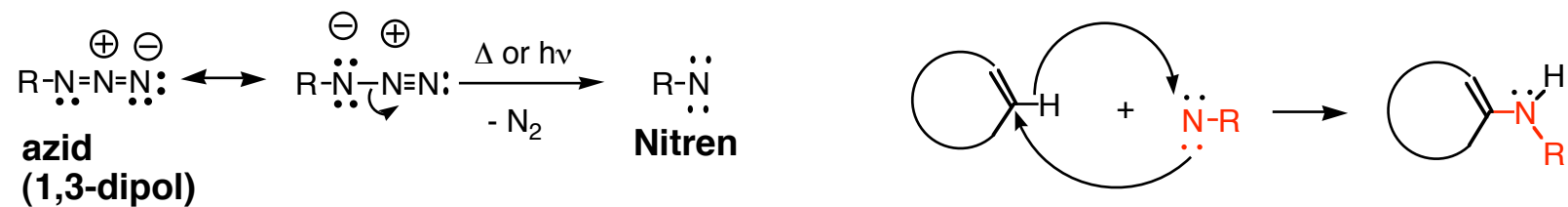


-Gassman synth.

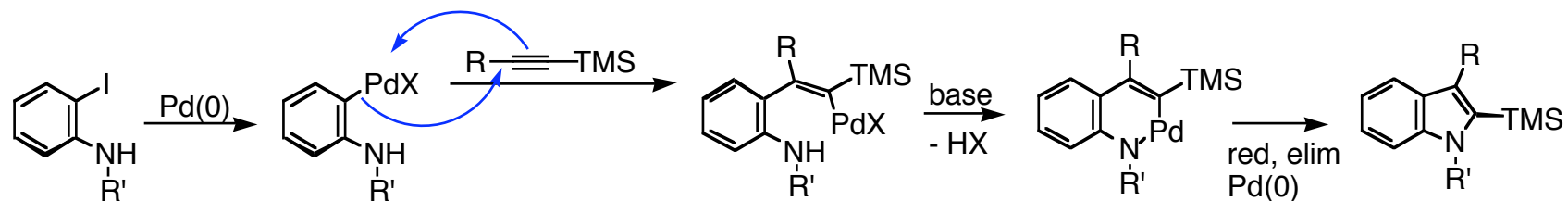
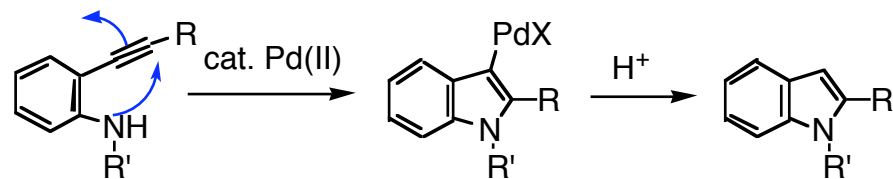


Miscellaneous indol syntheses

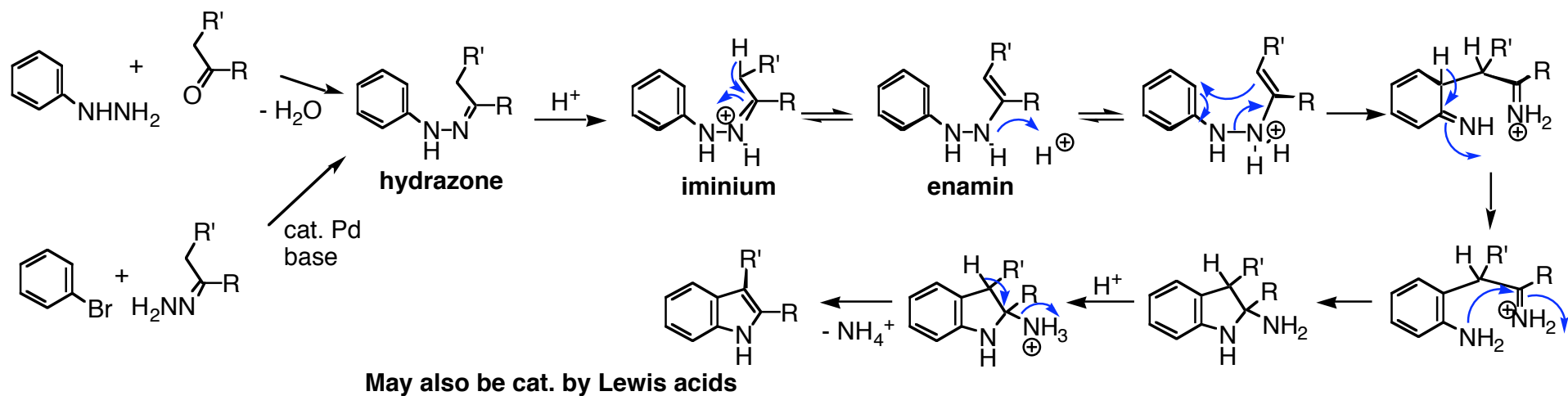
Reaction with nitrenes



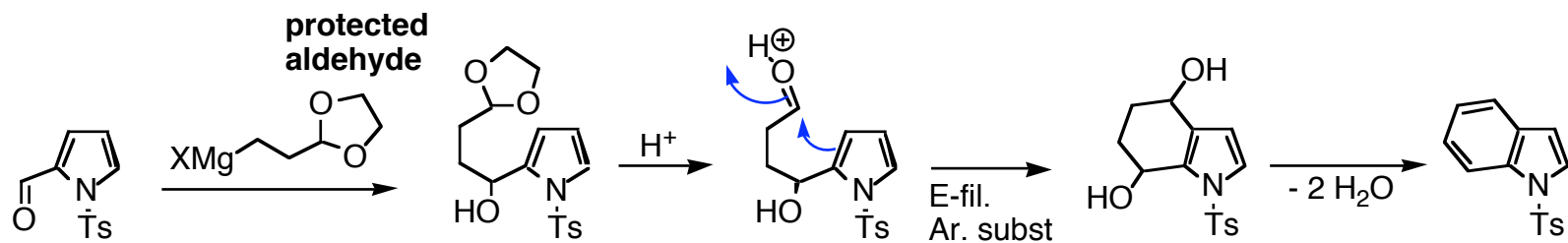
Synthesis from aminoalkynes



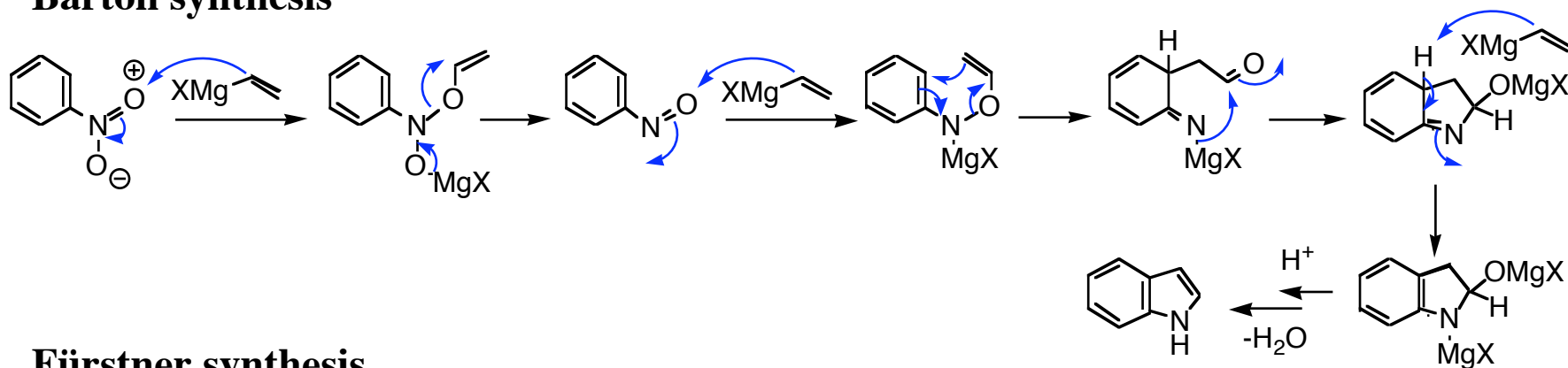
Fischer indol synthesis



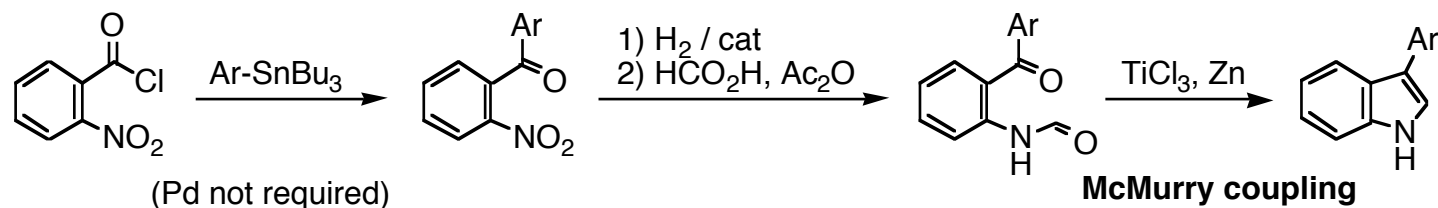
Synthesis from pyrroles



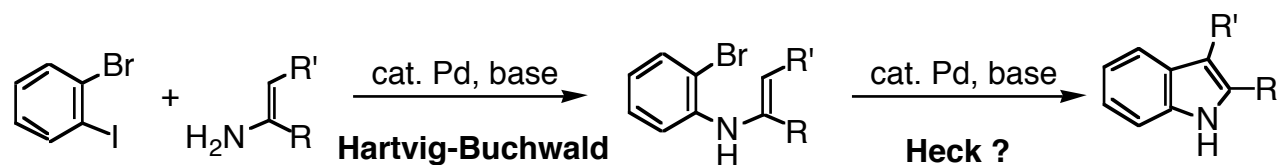
Bartoli synthesis



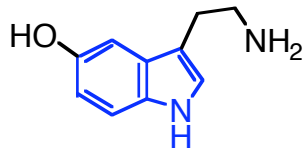
Fürstner synthesis



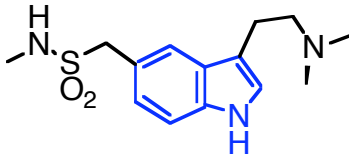
Pd-cat. couplings



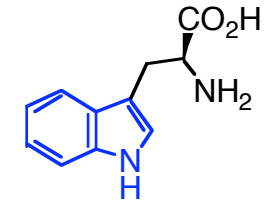
Bioactive Indoles



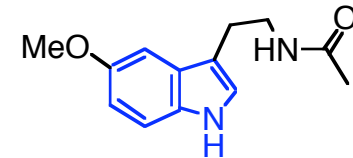
Serotonin
Neurotransmitter



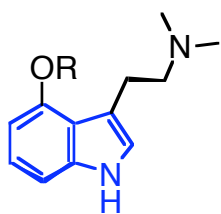
Sumatriptan, Imigran®
Drug against Migraine
serotonin reseptor antagonist



Tryptophan
Essential amino acid



Melatonin
Hormone



Halucinogens from *Psilocybe* sopper

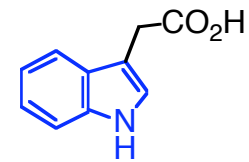
R=H: **Psilocin**
R=PO₃H: **Psilocybin** $\xrightarrow{\text{in vivo}}$

Serotoninagonists,
not broken down in the body
strong, continuous nerve impulse

Psilocybe semilanceata
(Spiss fleinsopp)



Psilocybe Mexicana

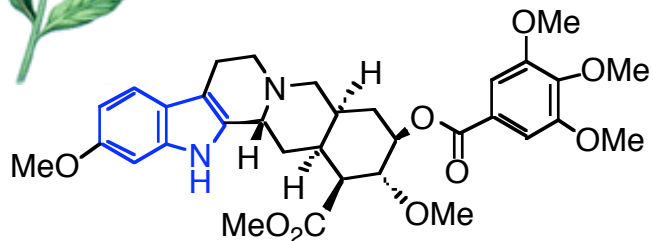


Auxine
Plant growth hormone

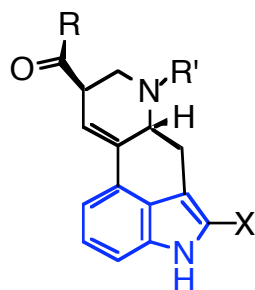
Bioactive Indoles



Rauwolfia serpentina
India, Thailand etc



Reserpine
from *Rauwolfia sp.*
Reduce blood pressure



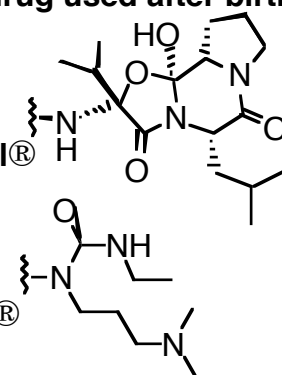
Secal alkaloids and derivatives
from *Claviceps purpurea* (mold)

X=H, R'=Me, R=OH: **Lysergic acid**
X=H, R'=Me, R=NEt₂: **LSD**

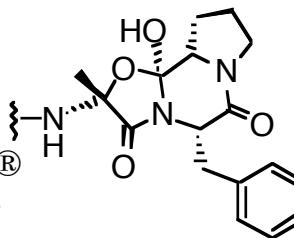
X=H, R'=Me, R=-NHCH(Et)CH₂OH: **Metylergometrin**,
Uterus contractions, drug used after birth

X=Br, R'=Me, R=
Bromokriptin, Parlodel®
Prolactine inhibitor

X=H, R'=Allyl, R=
Kabergolin, Dostinexl®
Prolactine inhibitor



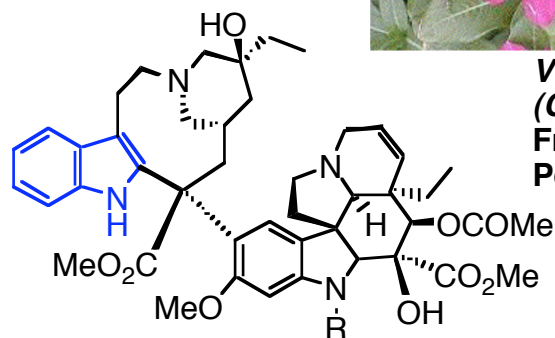
X=H, R'=Me, R=
Ergotamin, Anervanel®
Drug against migraine



Vinca alkaloids
from *Vinca rosea*
Anticancer comp.



Vinca rosea
(*Cathartus roseus*)
From Madagaskar
Perivinkle



R=-Me: **Vinblastin, Oncovin®**
R=-CHO: **Vinkristin, Velbe®**

