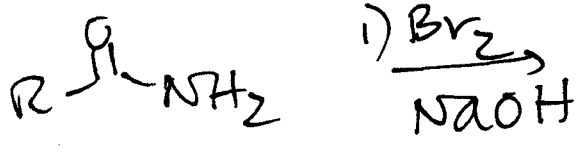
Hofmann Rearrangement – 1° amides only



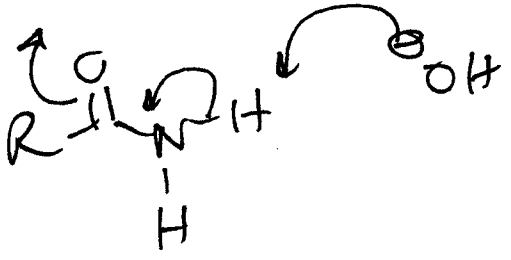
$R-NH_2$ + $(CO_2 + H_2O)$

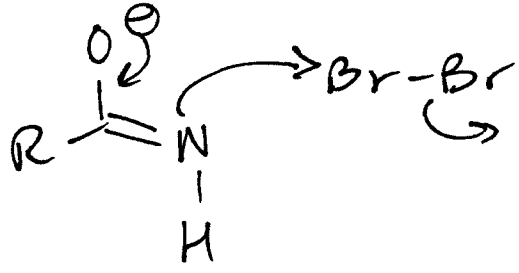
1° amine

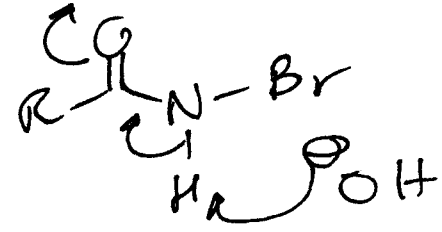
$+ \bar{O}H$

HCO_3^- etc.

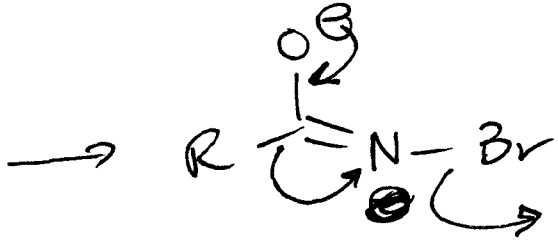
mechanism:

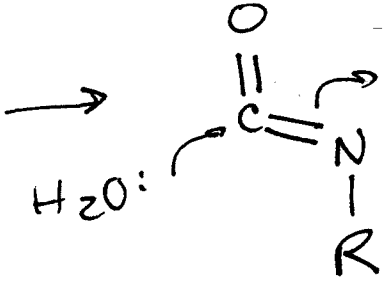




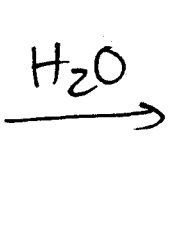


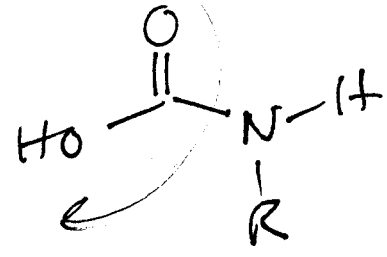
N-bromo amide





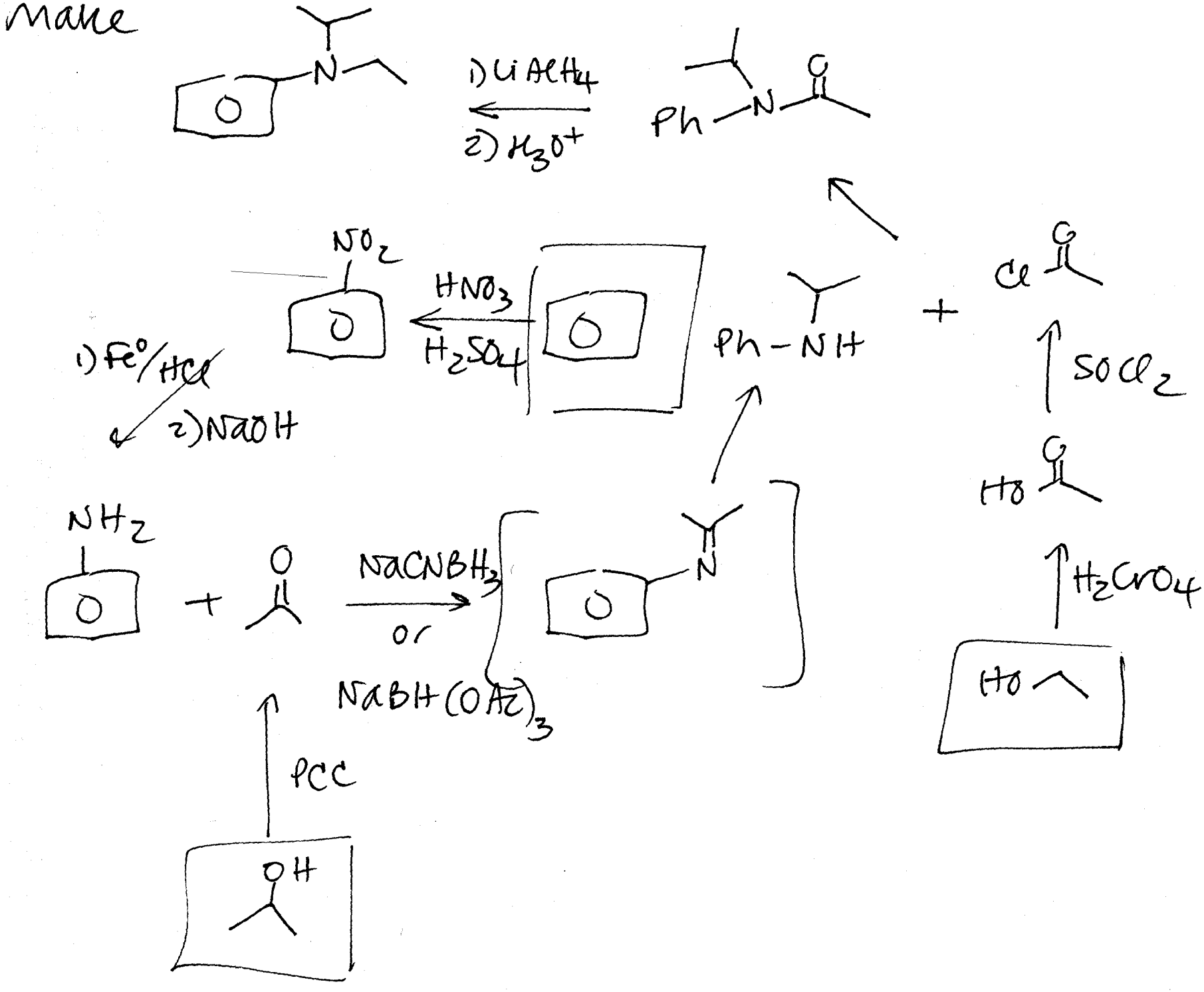
an isocyanate





a carbamic acid (unstable)

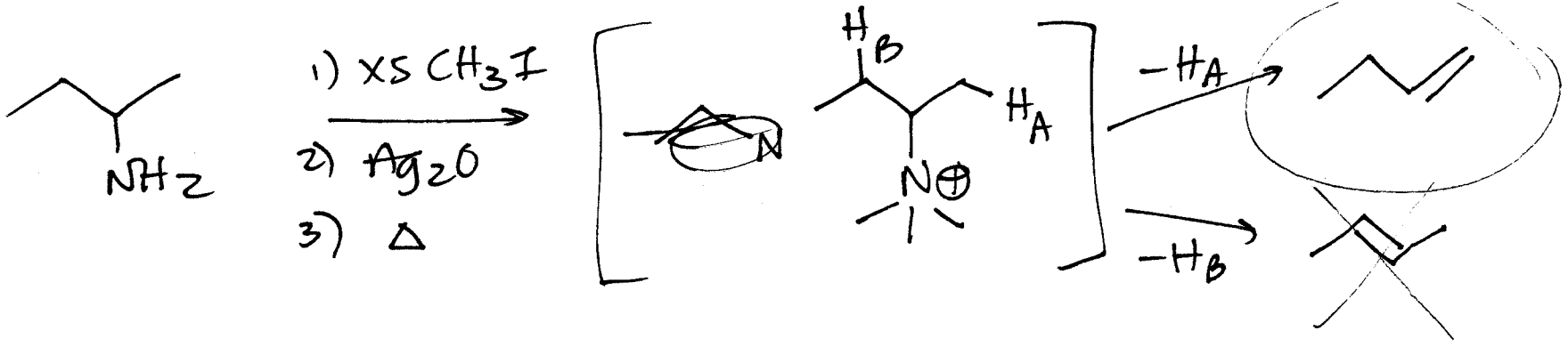
etc. + RNH_2


Make
1) LiAlH4
2) H3O+
Ph
N
O
NO2
HNO3
H2SO4
1) Fe°/HCl
2) NaOH
NH2
NaCNBH3
or
NaBH(OAc)3
PCC
OH
Ph-NH
+
Cl
SOCl2
HO
H2CrO4

Reactions of Amines – bases + nucleophiles

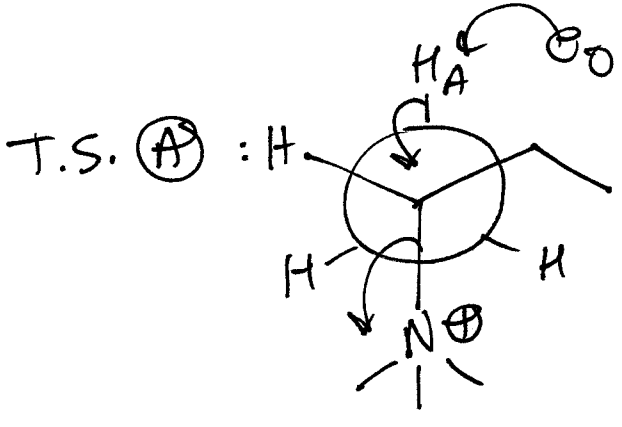
1. Rxn w/ aldehydes + ketones → imines + enamines
2. Rxn w/ acyl chlorides, esters, etc. → amides
3. Rxn w/ alkyl halides (S_N2) – most useful is exhaustive methylation (react w/ xs CH_3I)

4. Hofmann Elimination – specific to 4° ammonium salts.

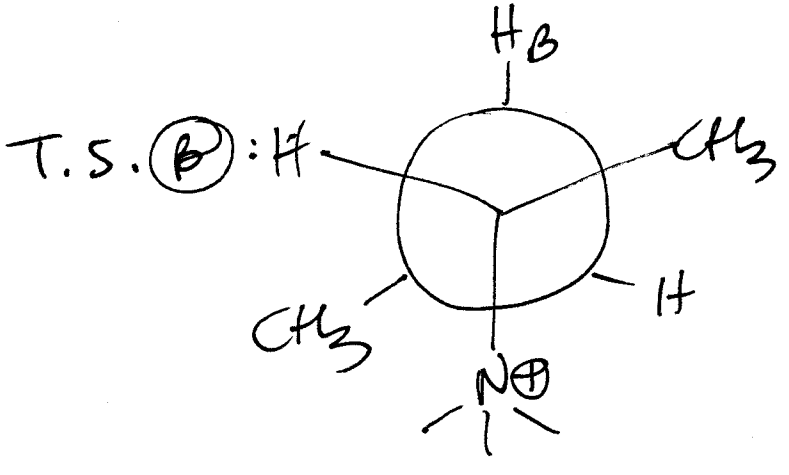


Hofmann elimination does not follow Zaitsev's rule - instead, we get the less substituted alkene.

Why? could be electronics (see book); it could be sterics. Both give the same answer.



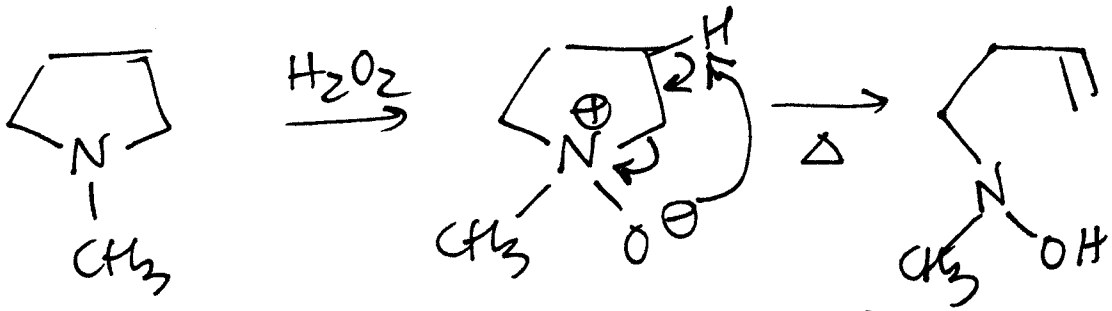
sterically less hindered



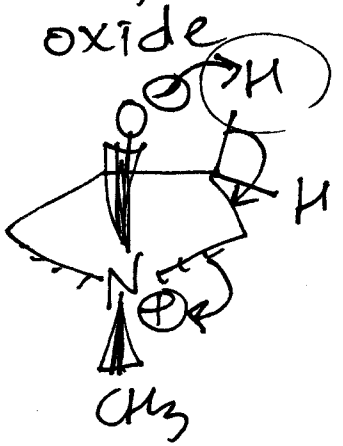
5. Oxidation of Amines – use H_2O_2 or mCPBA

1°/2° amines → nothing useful

3° amine



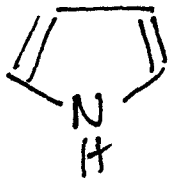
tertiary amine oxide



* Cope elimination
  syn-elimination

6. Recall diazotization rxns

Aromatic Heterocyclic compounds

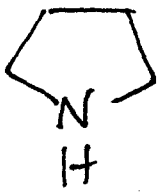


pyrrole

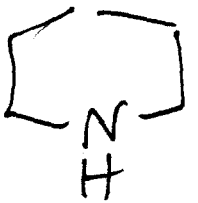
furan

thiophene

pyridine



pyrrolidine



piperidine

* these aromatics also do EAS.

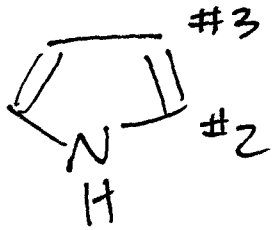
pyrrole > furan > thiophene > benzene

> nitrobenzene > pyridine

very reactive

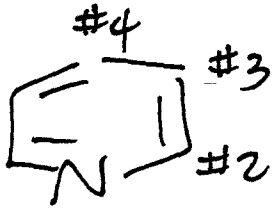
not very reactive

5-membered heterocycles



EAS is preferred @ #2
(sigma complex is more stable)

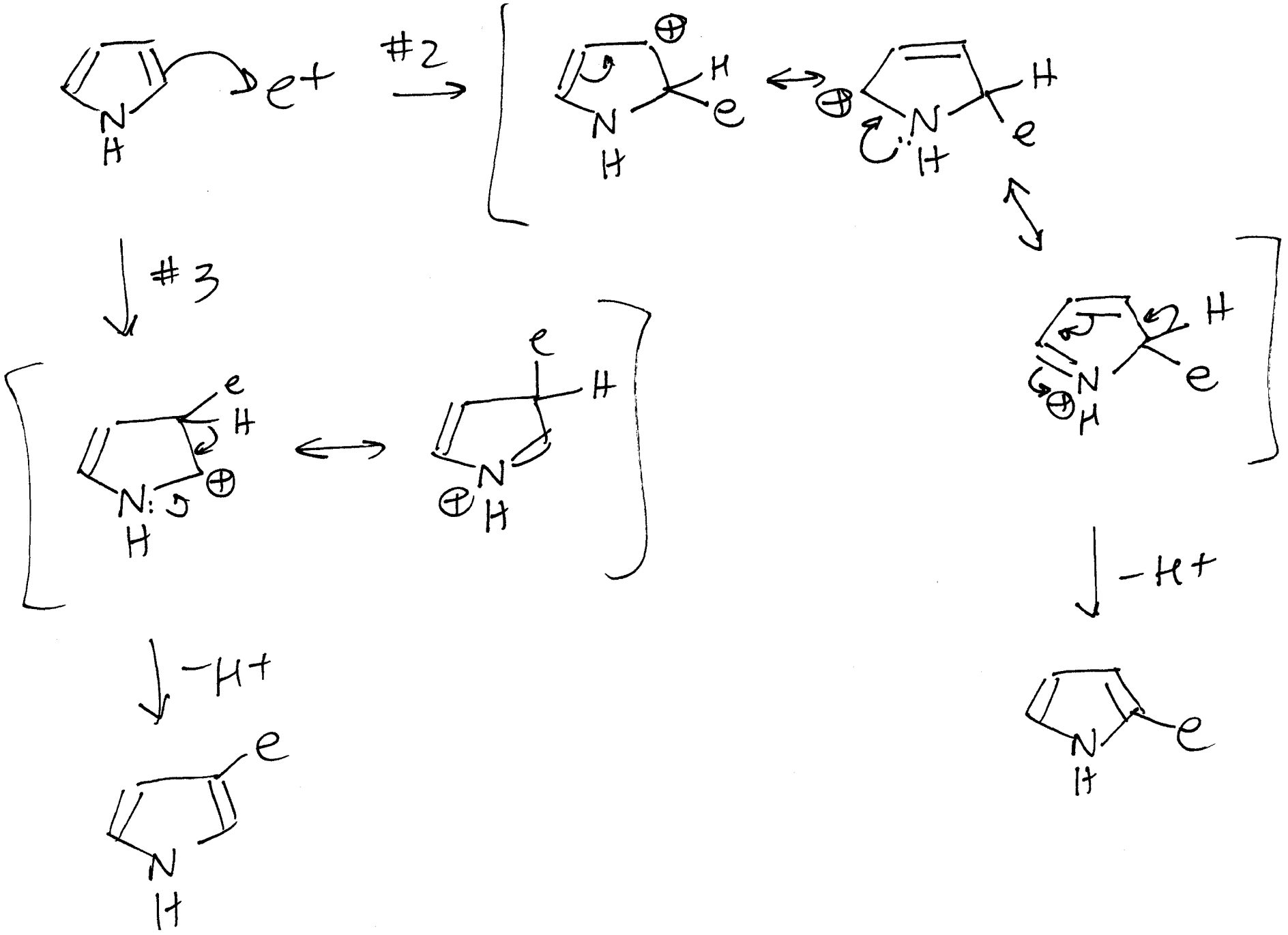
6-membered heterocycles



EAS is preferred @ #3

sigma complexes for rxn @ #2 + #4
have N w/o complete octet <u>and</u> w/ a ⊕

[SKIP nucleophilic aromatic substitution]


e+
#2
#3
-H+
-H+