Bean 7
Chem 3332

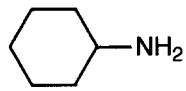
CHAPTER 19: AMINES (omit sections: 7, 8, 11B-D, 14, 16, 17, 24)

- many have important biological activity
- some serve as important synthetic intermediates

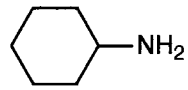
I. Nomenclature

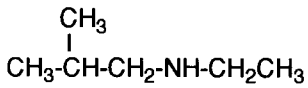
general: $R-NH_2$ R_2NH R_3N

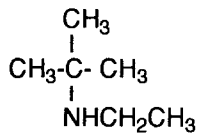
A. Common Names: named as alkyl amines - name of alkyl groups bonded to N + amine

CH_3-NH-CH_2CH_3 $(CH_3CH_2)_3N$ 

B. IUPAC: the suffix "amine" replaces the "e" of the alkane/alkene/alkyne/cycloalkane (alkene) name; for 2° and 3° amines, the largest group is the parent; use "N" to designate substituents on N

CH_3-NH-CH_2CH_3 $(CH_3CH_2)_2N-CH_3CH_2$ 





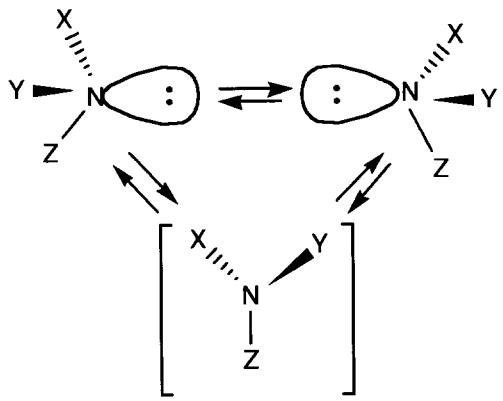
C. When higher priority groups are present, - NH_2 is called "amino".

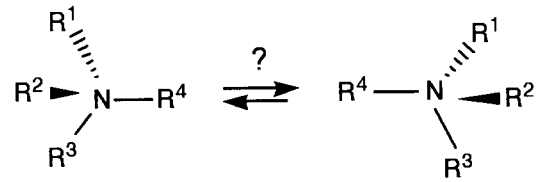
$H_2NCH_2CH_2CH_2OH$ $CH_3CH_2NHCH_2CH_2CH_2CO_2H$

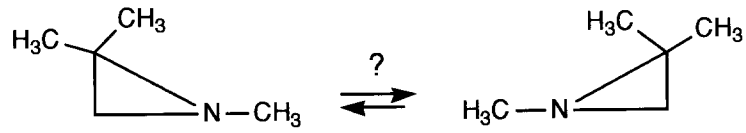
II. Structure/Bonding

chiral or achiral?

Pyramidal Inversion (Walden Inversion):





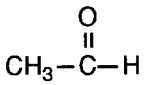


III. Physical Properties

$H_2N\text{-}(CH_2)_4\text{-}NH_2$ $H_2N\text{-}(CH_2)_5\text{-}NH_2$

Boiling Point:

$CH_3\text{-}O\text{-}CH_3$ $CH_3CH_2NH_2$ CH_3CH_2OH

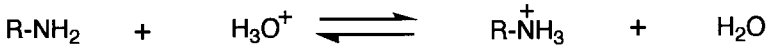


$CH_3\text{-}NH\text{-}CH_3$ $(CH_3)_3N$

IV. Amine Basicity

- ability to accept a proton (Bronsted-Lowry)
- ability to donate an electron pair (Lewis)

Amines are more basic than ethers, alcohols, water. Why?

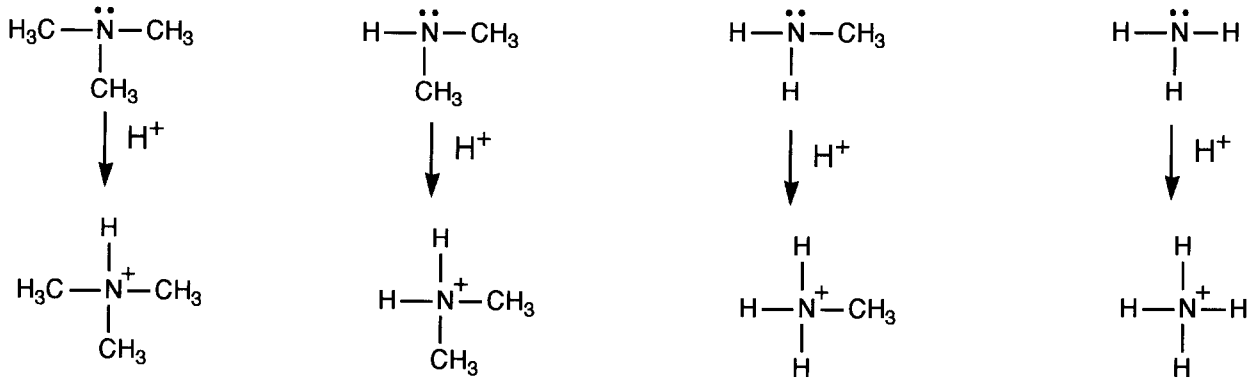


1. Consider stability of species after proton is accepted: Factors that stabilize + charge increase basicity
Factors that destabilize + charge decrease basicity

2. Consider availability of electron pair:

Compare Basicity

Alkyl Amines:

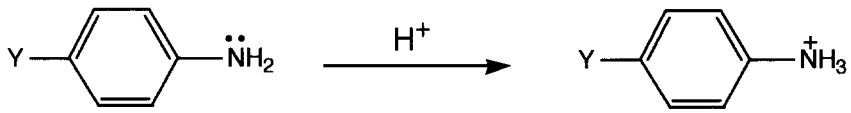


Amine vs Amide:

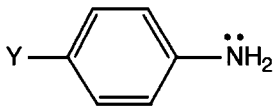
Heterocyclic Amines:

Alkyl vs Aryl:

Substituted Aryl Amines:

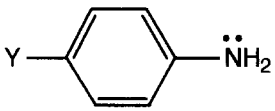


If Y is electron donating:

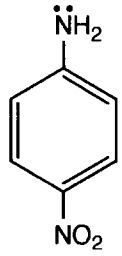


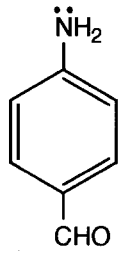
- electron pair of amine is more available
- electron donation stabilizes + charge in product
- increase in basicity

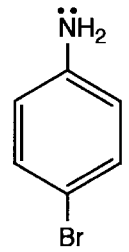
If Y is electron withdrawing:

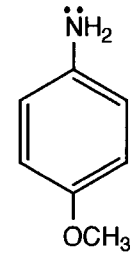


- electron pair of amine is less available
- electron withdrawal destabilizes + charge in product
- decrease in basicity



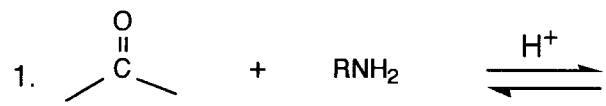


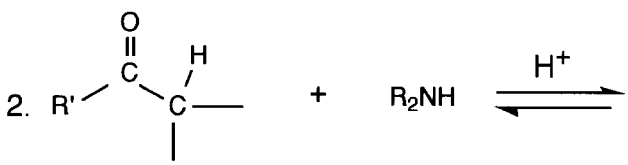




V. Reactions of Amines

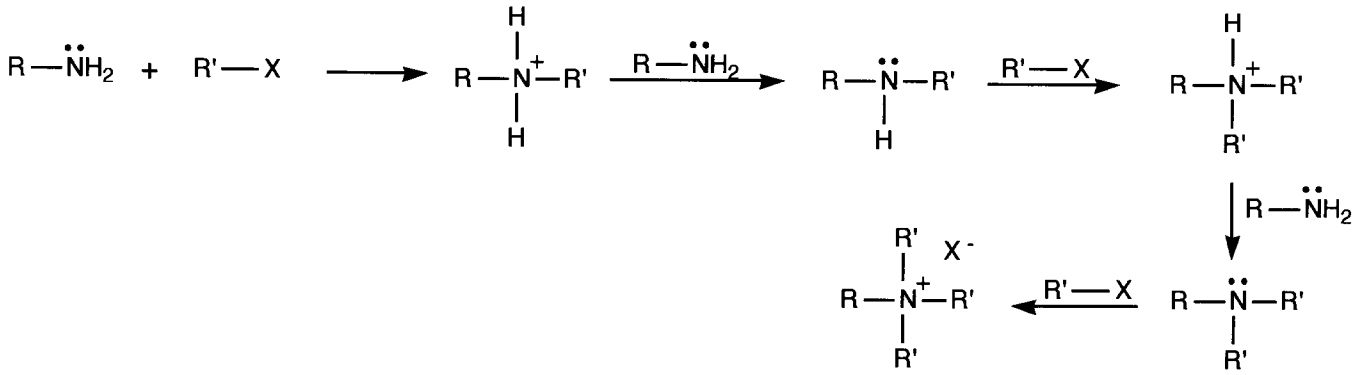
A. Reaction with Aldehydes or Ketones (Review, Ch. 18)





B. Alkylation of Amines by Alkyl Halides

- limited synthetic applications because multiple alkylations occur



Useful cases:

1. $CH_3CH_2—\ddot{N}H_2$ $\xrightarrow{CH_3I\ (xs)}$

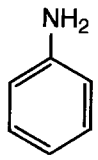
2. $CH_3\underset{Br}{\underset{|}{C}}H—CO_2H + \ddot{N}H_3 \longrightarrow$

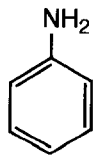
C. Acylation of Amines by Acid Chlorides (Review, Ch. 20/21)

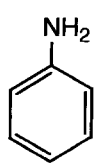
$$R—\ddot{N}H_2 + R—\overset{O}{\overset{\|}{C}}—Cl \longrightarrow$$

D. Electrophilic Aromatic Substitution of Aniline

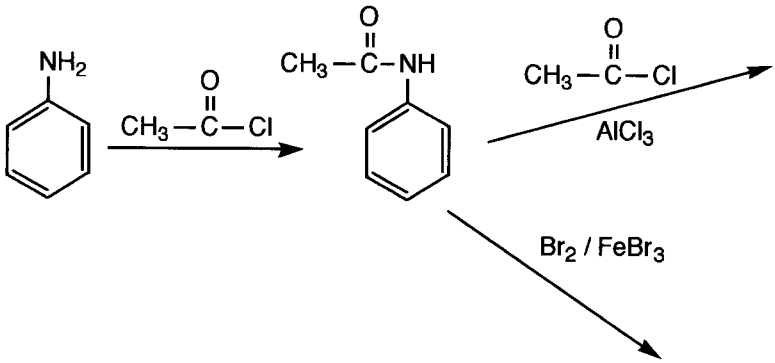
- NH_2 is a powerful activating group and can cause problems with some EAS reactions

1.  $\xrightarrow{Br_2 / H_2O}$

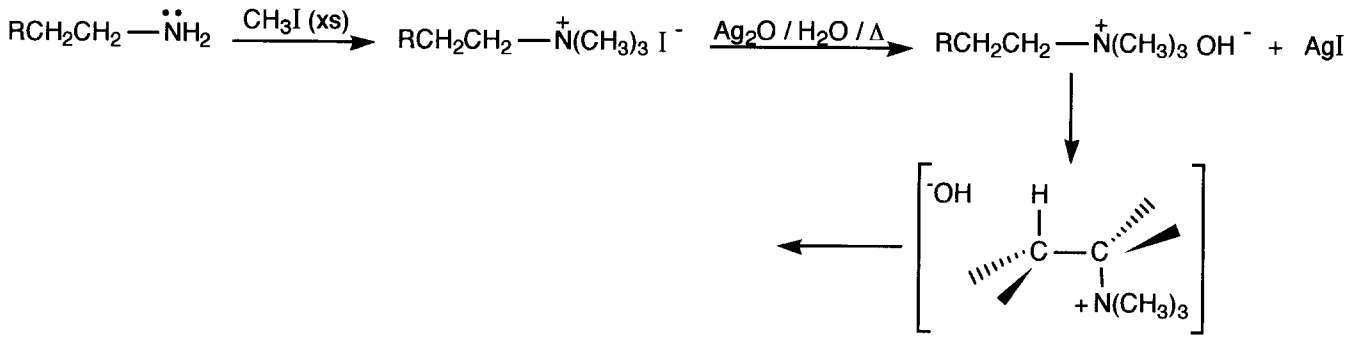
2.  $\xrightarrow[AlCl_3]{CH_3—\overset{O}{\overset{\|}{C}}—Cl}$

3.  $\xrightarrow{H\,NO_3 / H_2SO_4}$

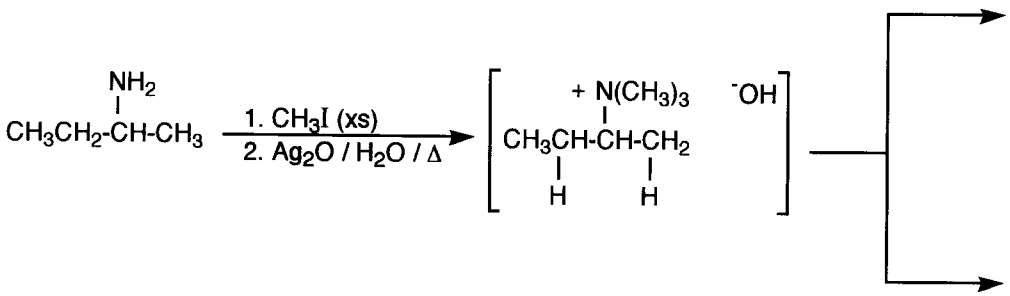
Solution: acylate amino group first, then hydrolyze after desired reaction



E. Hofmann Elimination

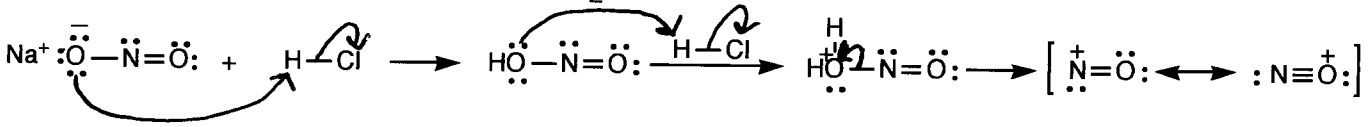


Example:



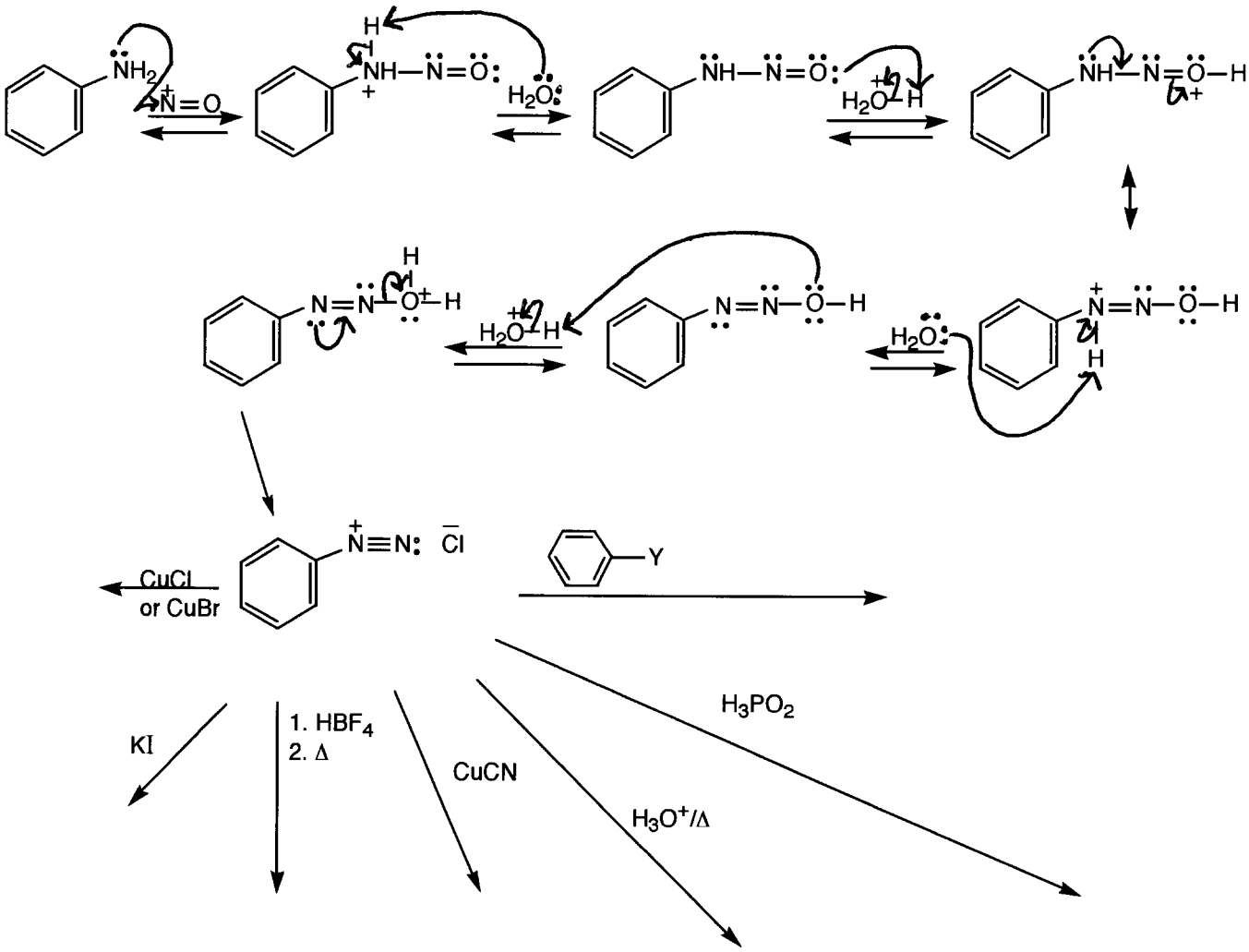
F. Reaction of Amines with Nitrous Acid (HNO_2)

- HNO_2 is not stable; generate from $NaNO_2$ and HCl:

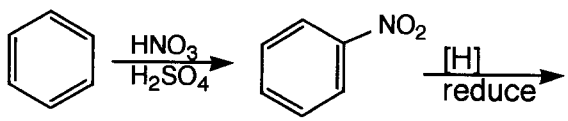


1. Reaction of Alkyl Amines with HNO_2: NOT synthetically useful

2. Reaction of Aryl Amines with HNO_2: VERY useful!



Before examples of arenediazonium salt reactions - The Best Synthesis of Aniline:



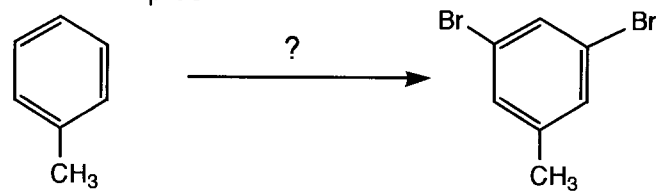
choice of [H]:

1. catalytic reduction: H_2 with Pt, Pd, or Ni

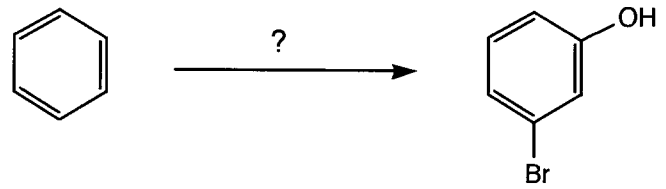
2. "active" metal / acid catalyst: Fe, Zn, Sn, or $SnCl_2$ in acid (followed by base for "free" amine)

Synthesis Examples:

1.

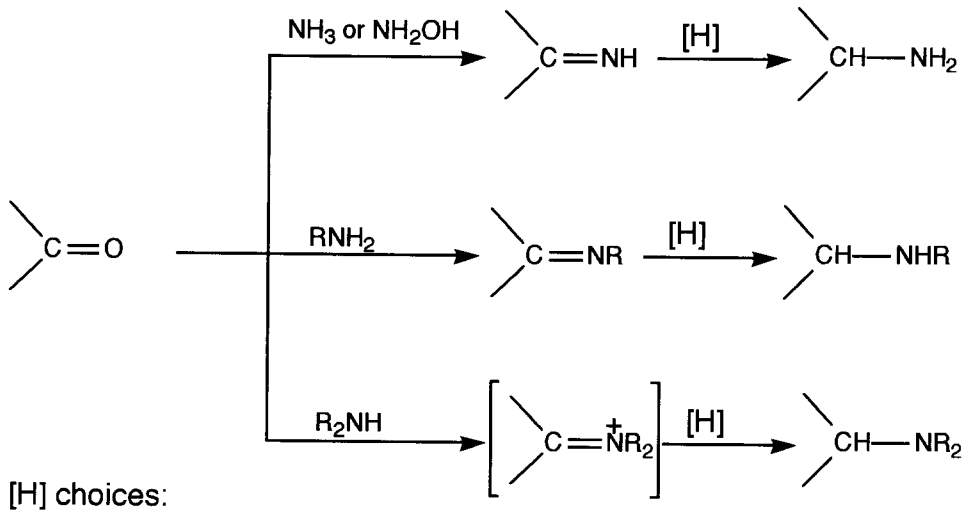


2.



VI. Synthesis of Amines

A. Reductive Aminaton of Aldehydes and Ketones (In true reductive amination, the amine, the reducing agent and the aldehyde or ketone are mixed together.)

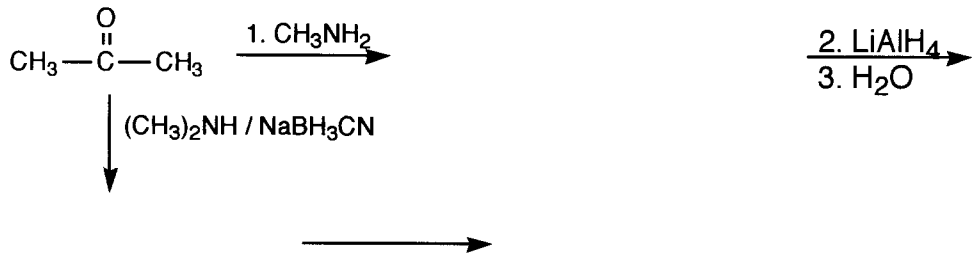


[H] choices:

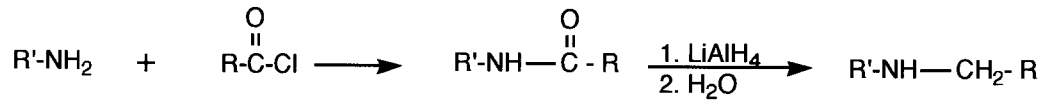
1. $LiAlH_4$ - must be used as a sceond step

2. $NaBH_3CN$ - similar to $NaBH_4$, but does not reduce aldehydes or ketones; used particularly in the formation of 3° amines, because the iminium salt cannot be isolated

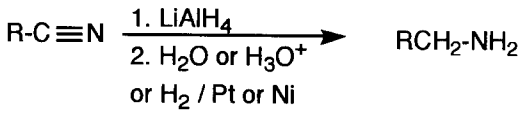
Examples:

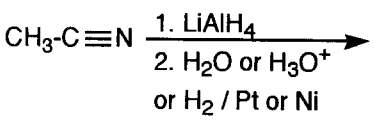


B. Acylation / Reduction (Review)



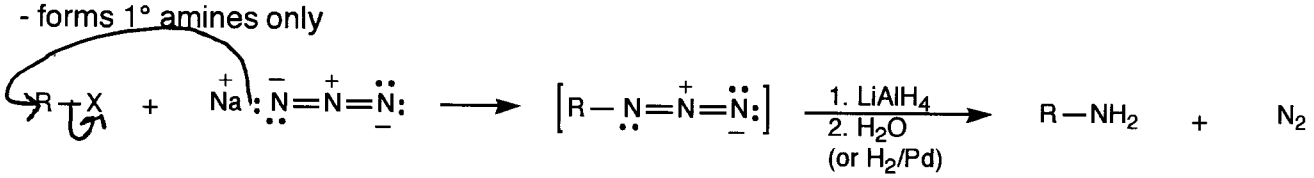
C. Reduction of Nitriles (Review)



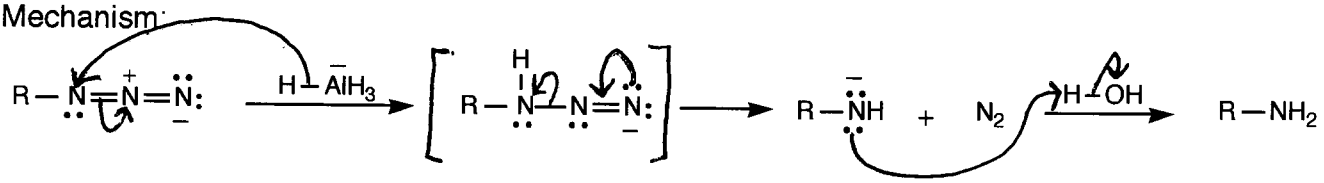


D. Fomation and Reduction of Azides

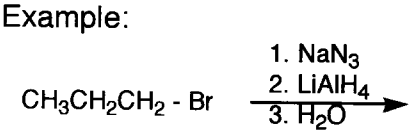
- forms 1° amines only



Mechanism:

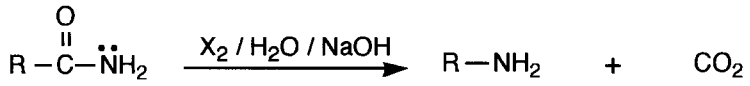


Example:

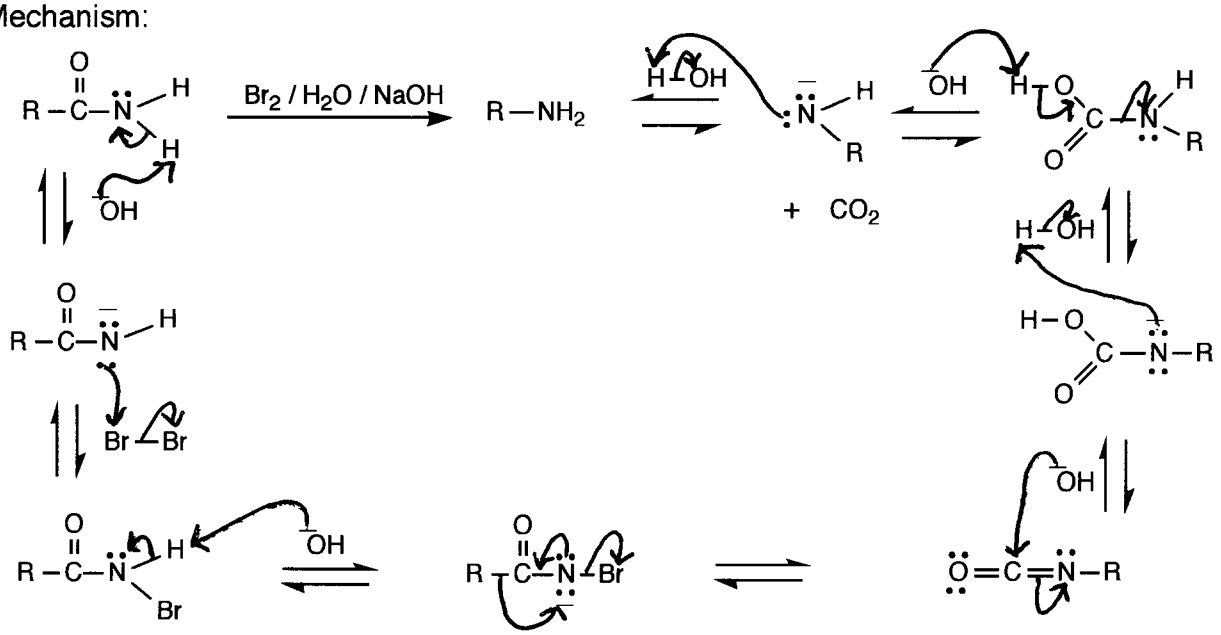


E. Hofmann Rearrangement

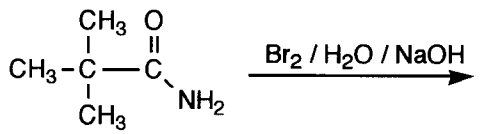
- 1° amide forms a 1° amine that is one carbon smaller and CO_2



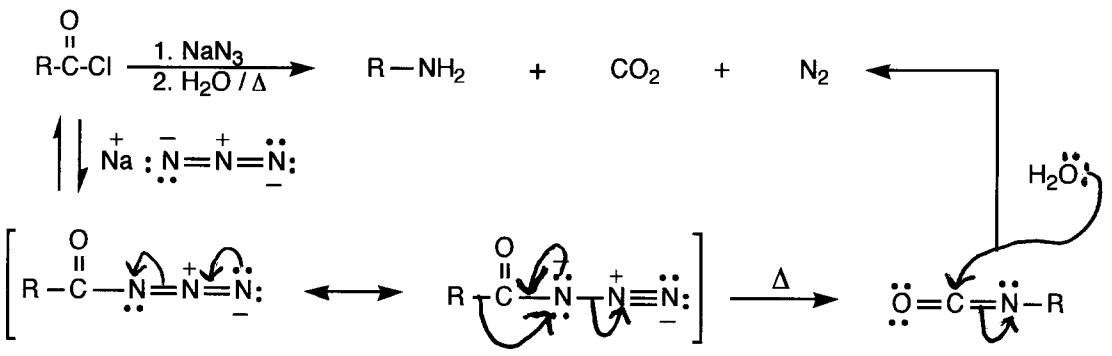
Mechanism:



Example:



F. Curtius Rearrangement (problem 19 - 37) - forms 1° amines; closely related to above process



Example: