Course Chem 345
Lecturer Gellman
Day Monday
Date 4/20/2015
Notes Taken By Leslie
Total # of Pages 5

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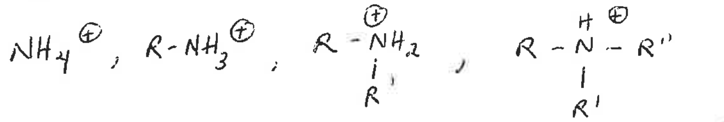
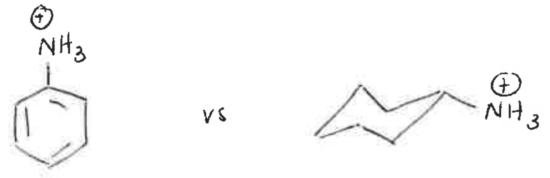
Recall: acid-base behavior of amines...


$NH_4^{\oplus}$, $R-NH_3^{\oplus}$; $R-\overset{\oplus}{N}H_2-R$, $R-\overset{H\ \oplus}{N}(R')-R''$

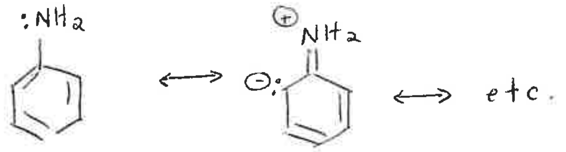
} pKa ~ 9-11 (if R ≡ ~~sample~~ simple alkyl)



pKa ~5

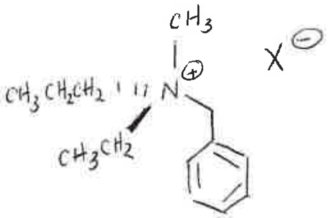
pKa ~11

⇓ loss of e- lone pair delocalization in conjugate acid form...



∴ Predict substituent effects on acidity / basicity

4° ammonium ions, e.g.,



Nucleophilic reactivity of amines

i) S_N2 reactivity: $\ddot{N}H_3$, 1°, 2°, 3° amines are often good nucleophiles

∴ Difficulty introducing just a single substituent via S_N2 rxn

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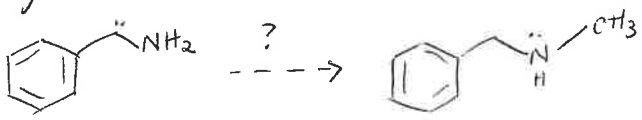
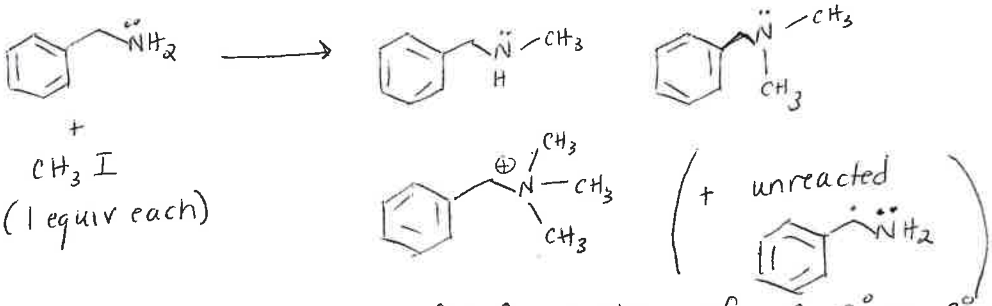
Nucleophilic reactivity of amines

1) S_N2 reactivity continued

Challenge:

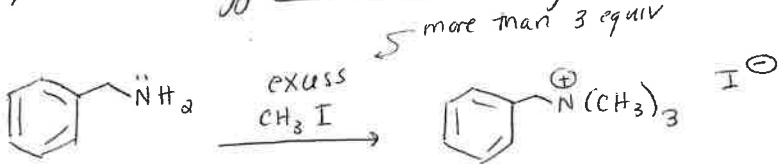


Problem:



- Thus S_N2 strategy typically not useful for synthesis of 1°, 2° or 3° amines (from less-substituted amines).
- However, S_N2 strategy <u>is useful</u> for synthesis of 4° ammonium ions

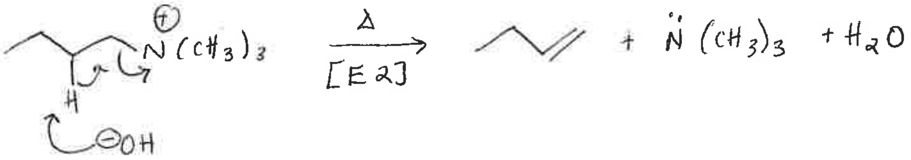
E.g.,



"Exhaustive alkylation / elimination" for controlled degradation:

First lets talk about:

Elimination rxns of 4° ammonium ions



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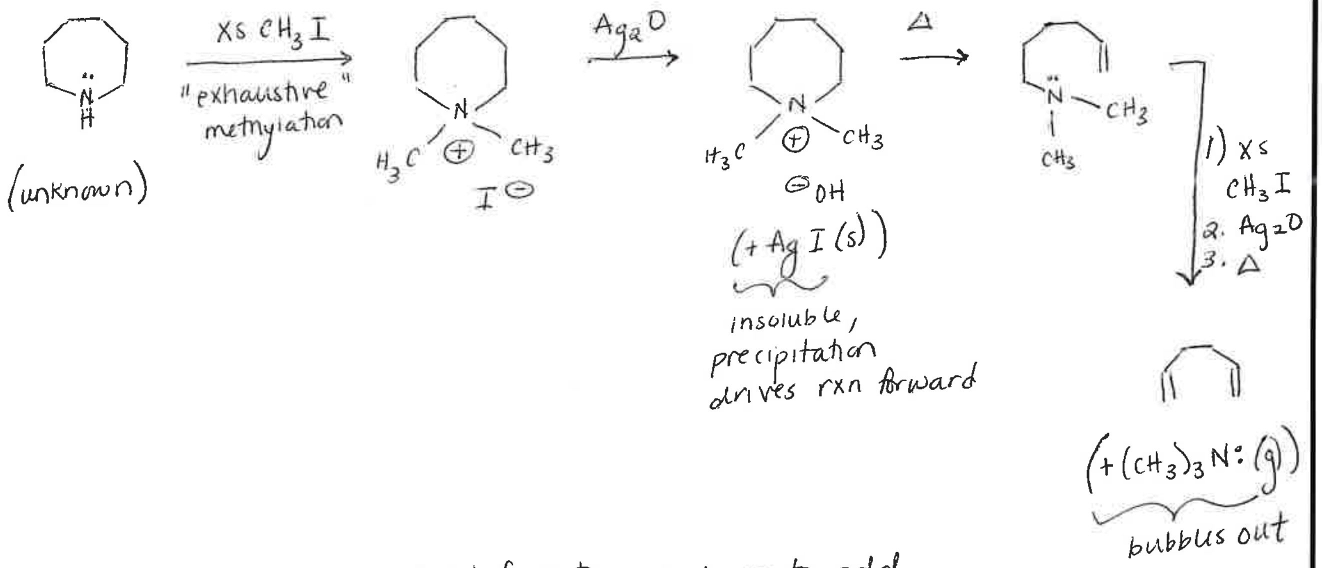
"Exhaustive alkylation / elimination" for controlled degradation:

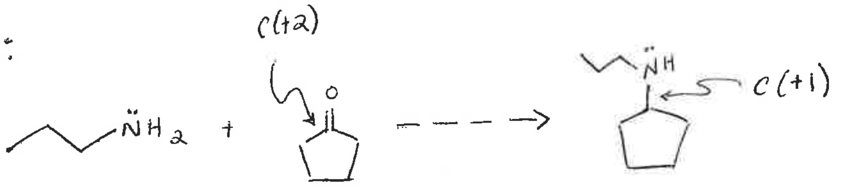
application — amine structure identification.



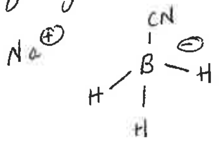
Strategies for controlled C-N bond formation, or how to add a single carbon substituent to amine N.

Reductive amination:

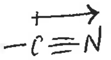
Ex (overall):



Reducing agent: $NaBH_3CN$



CN is e^- withdrawing, so less reactive source of "$H\!:^{\ominus}$"



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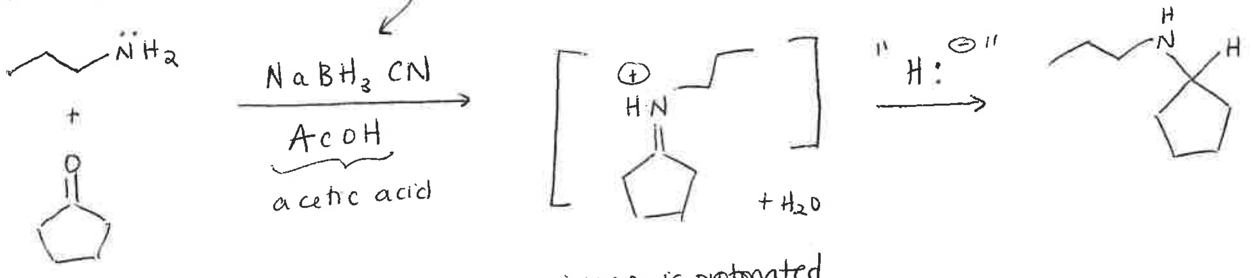
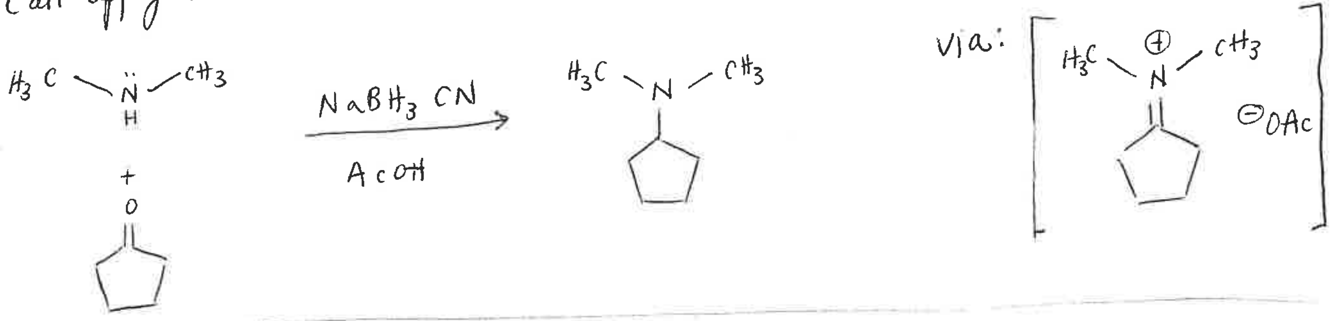
Reductive amination

does not reduce ketone bc of attenuated reactivity!



imine is protonated under acidic conditions gives you: "iminium" ion

Can apply to 2° amines:



Formation of diazonium ions and their rxns:

Overall:

$$R-\ddot{N}H_2 + HNO_2 + H^{\oplus} \longrightarrow \overbrace{R-\overset{\oplus}{N}\equiv N:}^{\text{diazonium ion}} \quad (+\ 2H_2O)$$

Note: N_2 is the very best leaving group. Thus, diazonium ions are a good source of carbocations

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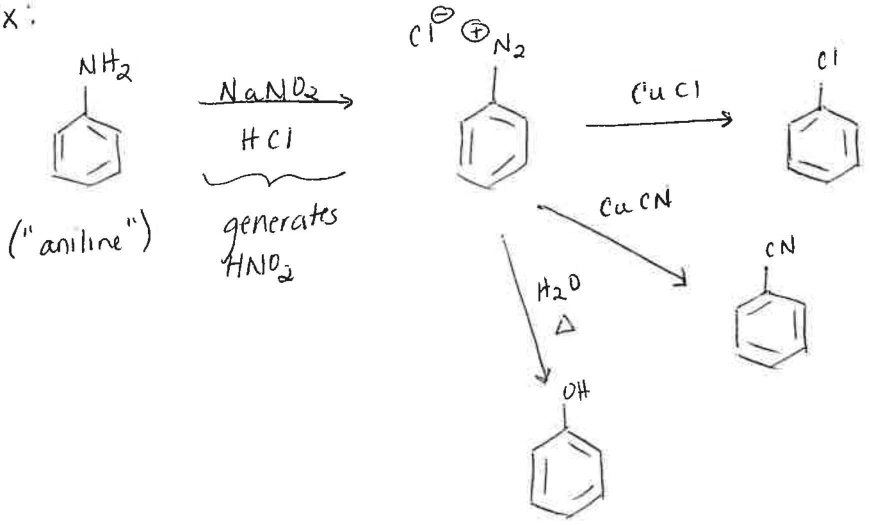
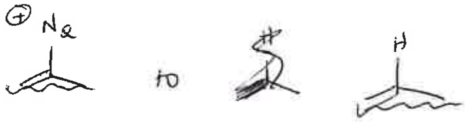
Focus on aryl diazonium very useful reactivity...

Ex:



Can convert



use: