Dr. Davies Chem. 2320 Amine Synthesis

- I. Synthesis of Primary (1°) amines R-NH<sub>2</sub>
  - A. Addition of excess ammonia to a primary alkyl halide:

 $NH_3 + H_3C$  OTs  $H_3C$   $NH_2 + NH_4OTs$  (salt) (excess)

B. Reductive amination:



Ketones yield 2°C adjacent to 1° amine, while Aldehydes yield 1°C adjacent to 1° amine.

C. Reduction of amides:



D. Addition of sodium azide to a primary or secondary alkyl halide, tosylate or epoxide:



E. Cyanide additions followed by reduction:



## F. Gabriel amine synthesis (1887, Siegmund Gabriel, Berlin)



G. Reduction of a nitro group:

$$\begin{array}{c} \bigoplus_{\substack{n \in \mathbb{N} \\ n \in \mathbb{N} \\$$

H. Hofmann Rearrangement (RAR):

$$R = 1^{\circ}, 2^{\circ}, 3^{\circ} \text{ alkyl or aryl}$$

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- II. Synthesis of Secondary  $(2^{\circ})$  amines  $R_2NH$ 
  - A. Reductive amination (Reduce imine to a secondary amine):



B. Reduction of a secondary amide:



- III. Synthesis of Tertiary  $(3^{\circ})$  amines  $R_3N$ 
  - A. Reductive amination (Reduce iminium ion to a tertiary amine)



B. Reduction of a tertiary amide:



C. Worth mentioning - Hofmann elimination produces a tertiary amine. See notes