

OC2

KING'S
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Synthesis

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Amine Synthesis

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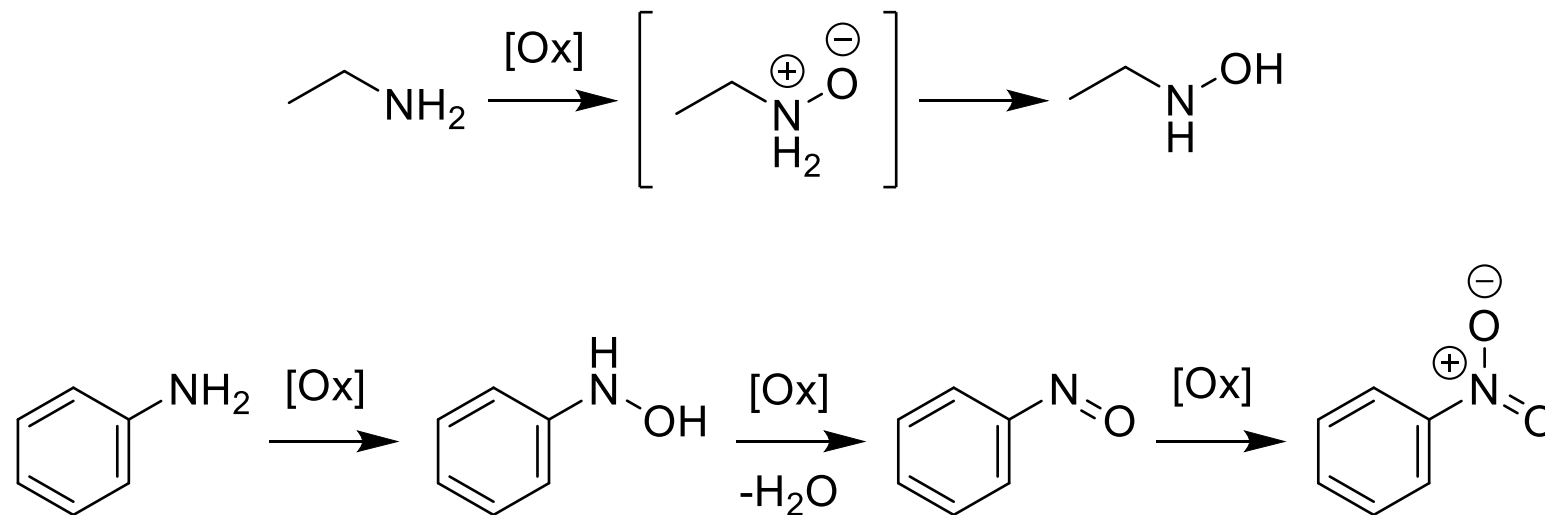
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<http://bojdyslab.org>

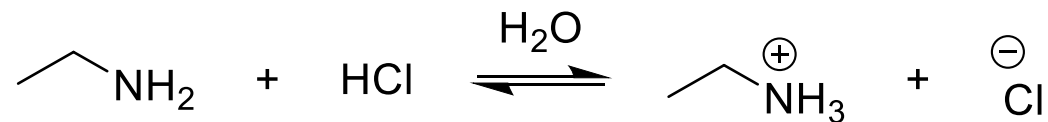
@mjbojdys

Reactivity of Amines

Amines (aliphatic and aromatic) are prone to oxidation

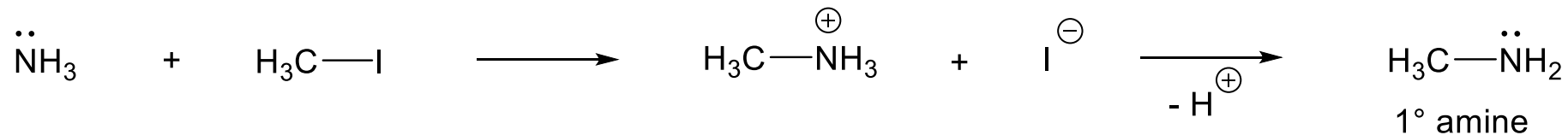


However, amines react quantitatively with strong acids to form water-soluble salts (for purification, and ox. stability):

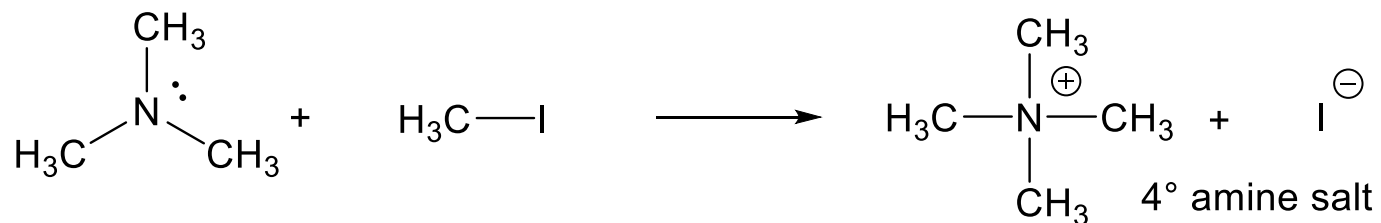
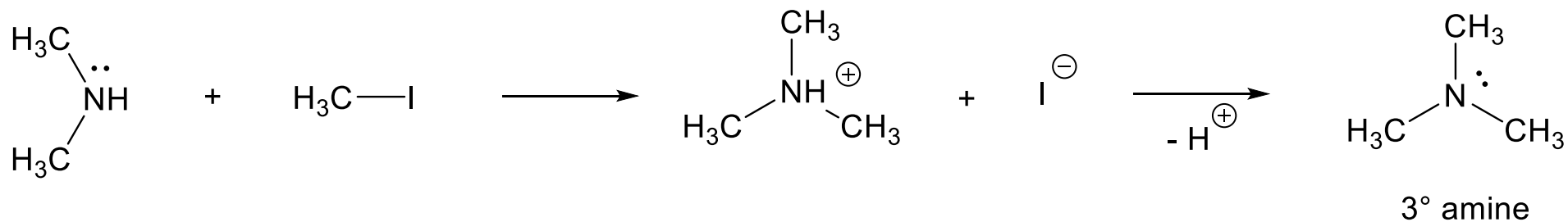
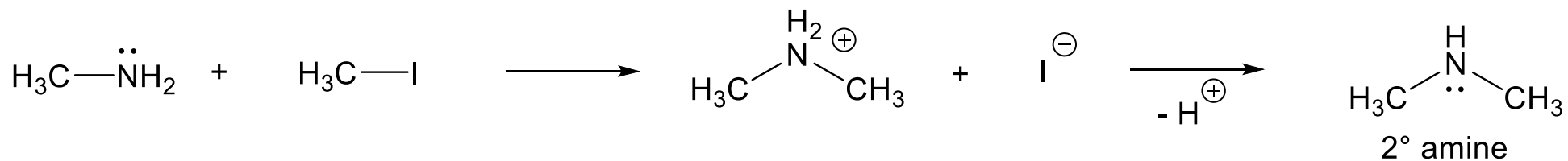


Amine Synthesis

Might try alkylation of ammonia...



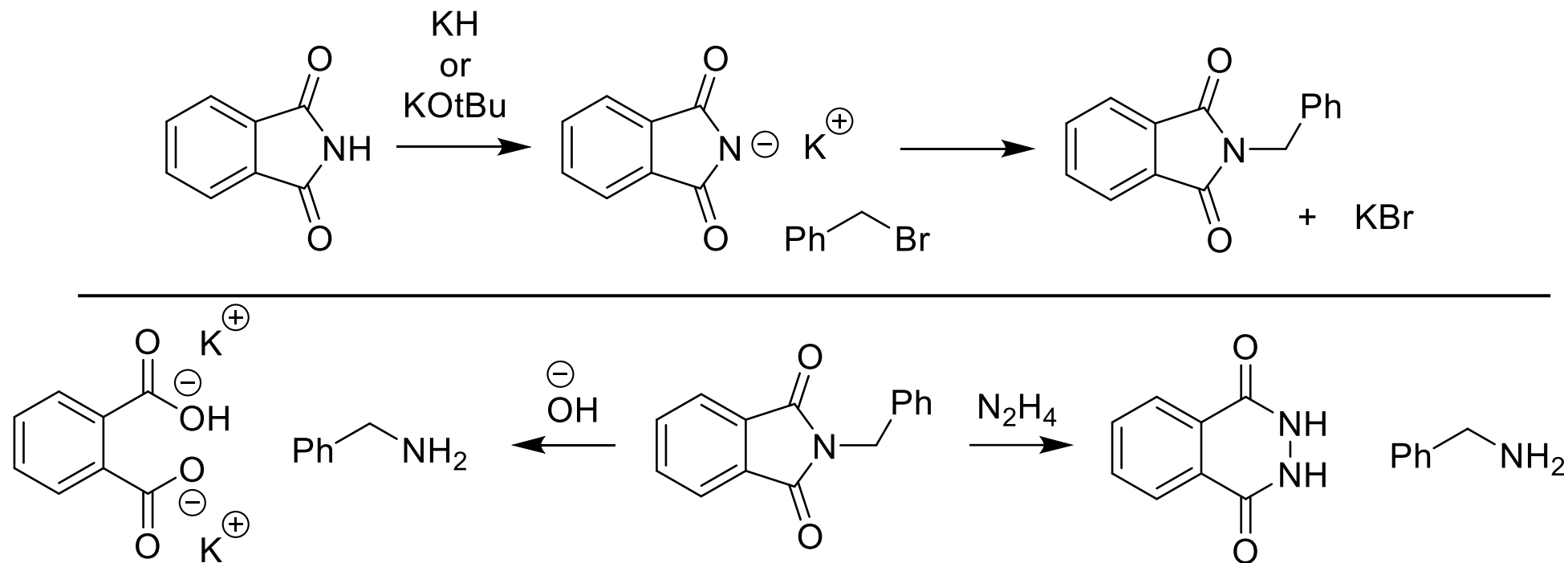
... however, such alkylations rapidly lead to a mix of products:



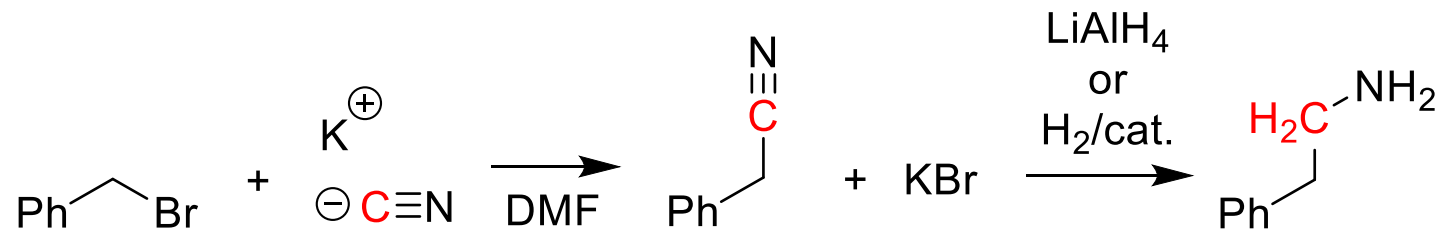
(1) Amine Synthesis

Better routes:

- alkylation of phthalimide anion (Gabriel Method)

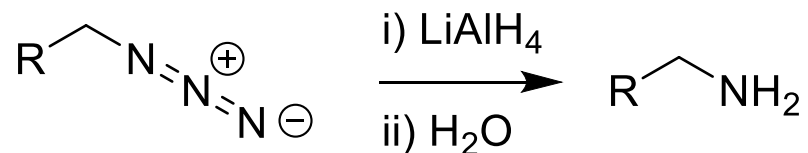
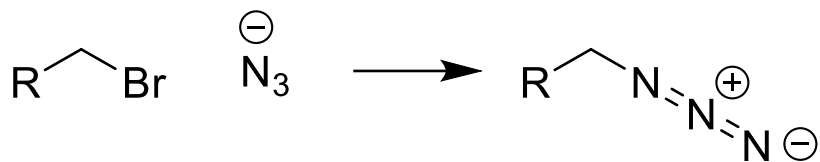
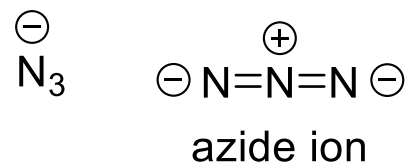


- Alkylation of nitrile anion (by homologation; insertion of a e.g. a CH₂-group after reduction)



(2) Amine Synthesis

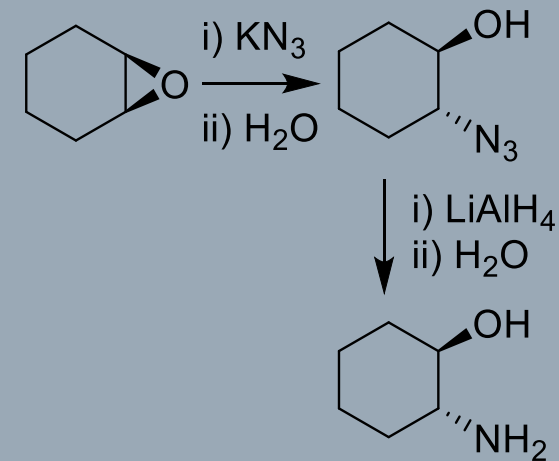
- alkylation of azide ion



or
 $\text{H}_2/\text{Pd@C}$

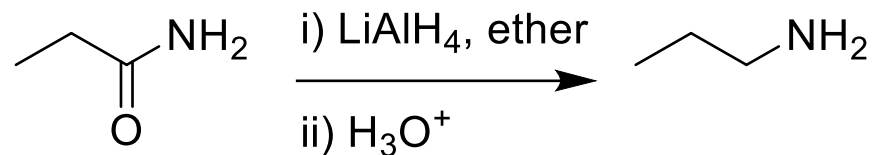
NOTE:

Azide can open epoxides to make β -aminoalcohols

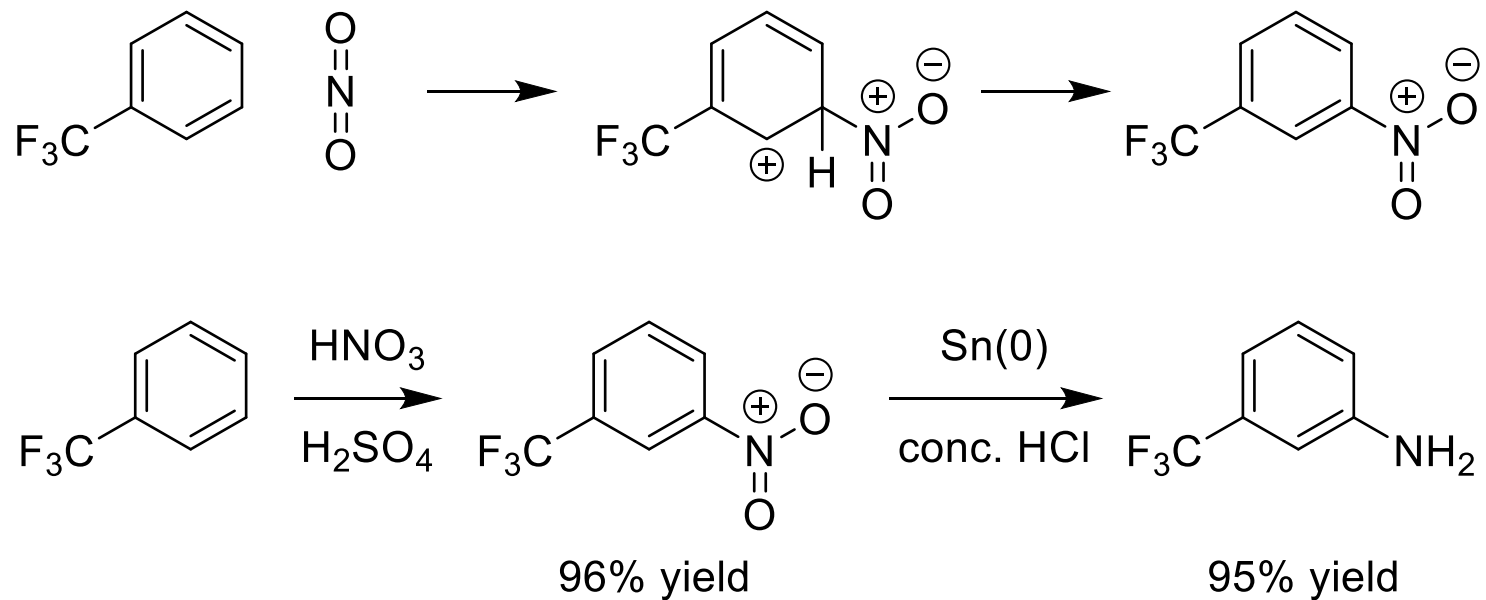


(3) Amine Synthesis

- reduction of amides (with strong reductants such as lithium aluminium hydride or borane (in the presence of Lewis Acids, e.g. $\text{BF}_3 \cdot \text{OEt}_2$)

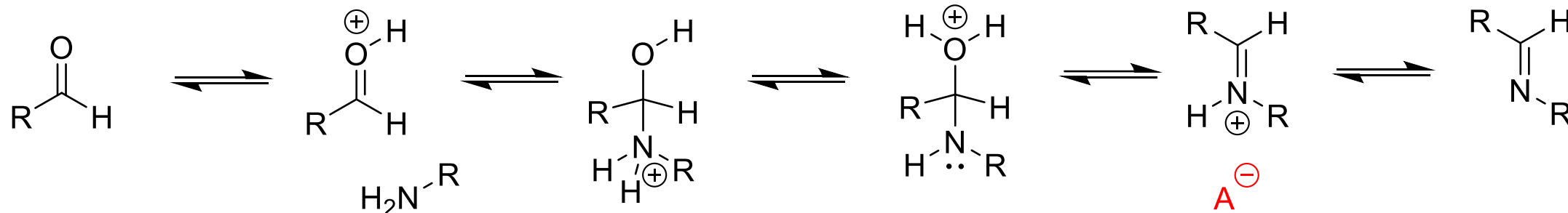


- reduction of aromatic nitro-compounds

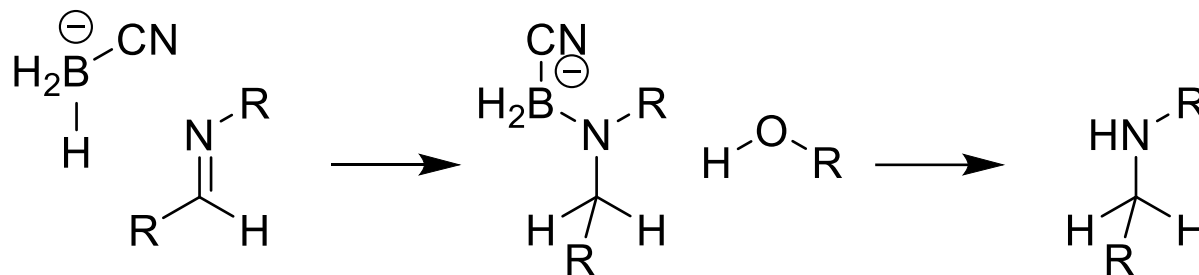


(4) Amine Synthesis

- Addition of nitrogen nucleophiles to aldehydes and ketones (with **acid catalyst**)... first, step-wise:

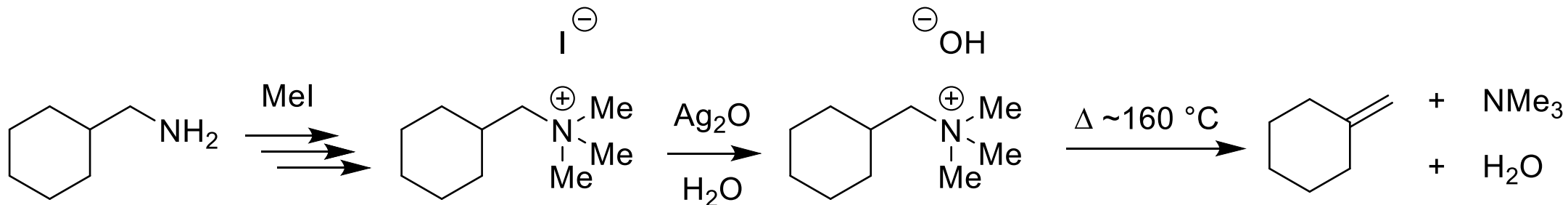


- Or in one-pot using NaCNBH₃ or Na(OAc)BH₃ (i.e. with mild reducing agent that only reduces the imine):

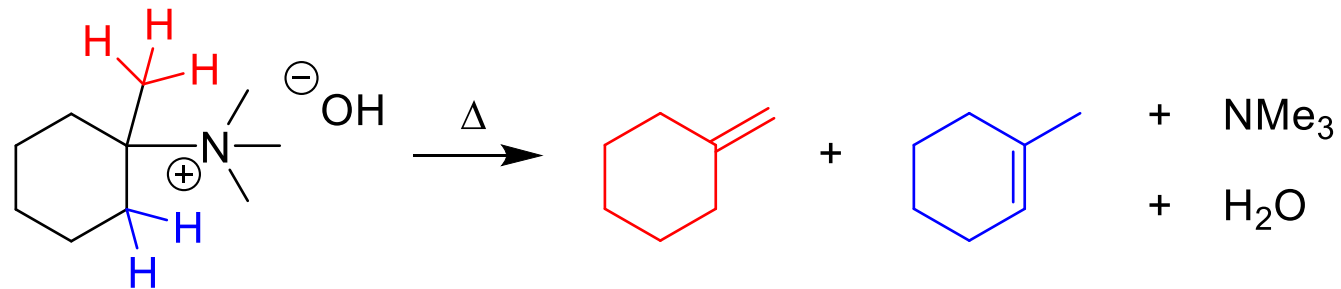


(5) Amine Synthesis

- Hofmann Elimination – thermal decomposition of quaternary ammonium hydroxide



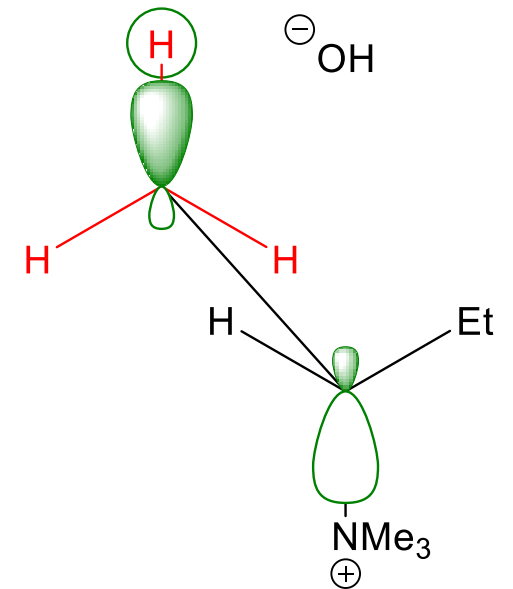
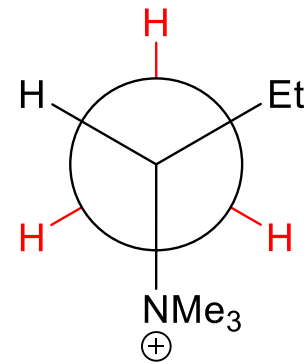
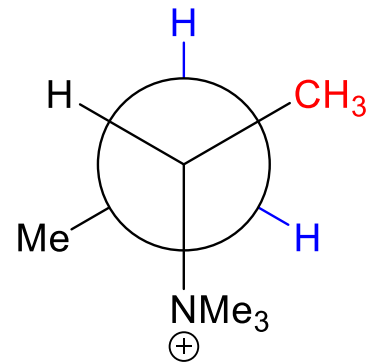
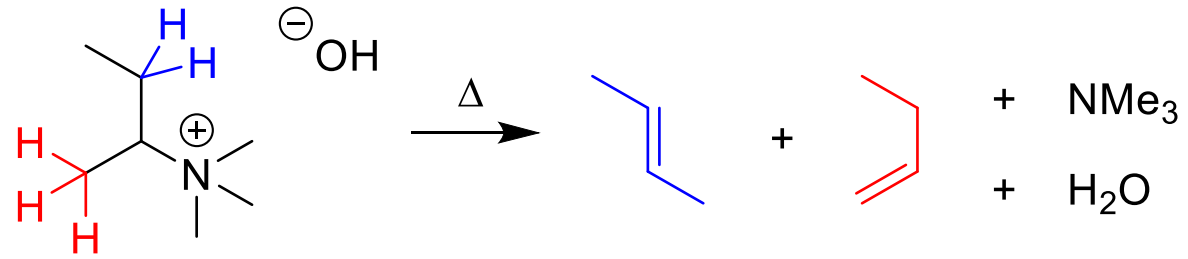
- Regioselectivity – the **least** substituted alkene is the **major** product



(5) Amine Synthesis

- Hofmann Elimination – steric factors and orbital overlap

Consider:



What's next?

Introduction to Protecting Groups

Academic Insights #5

Applying my research to the real world

