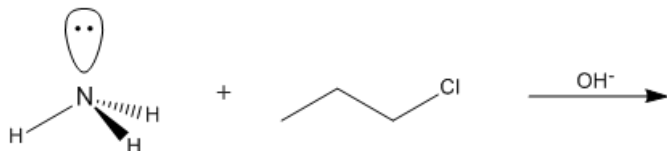


CLUTCH

www.clutchprep.com

CONCEPT: AMINE ALKYLATION

Alkyl halides are susceptible to nucleophilic attack by amines. This mechanism is called _____

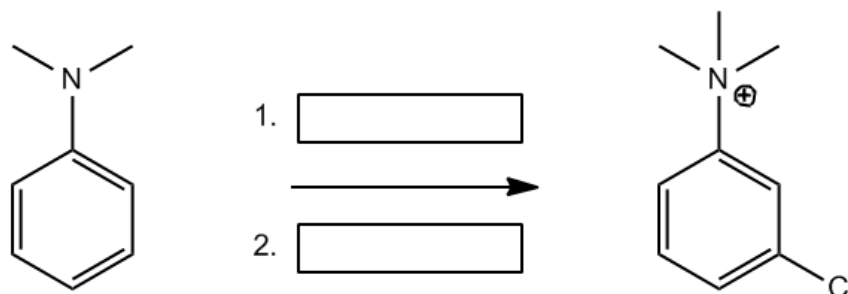


However, this reaction has little synthetic value because multiple alkylations will usually occur:

- The only way to avoid is will excessive amounts of amine.

Amine Polyalkylation Mechanism:

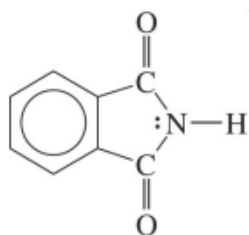
EXAMPLE: Propose a synthesis for the following compound.



CONCEPT: GABRIEL SYNTHESIS

Potassium phthalimide is a secondary diamide that can yield primary amines in much better yield when treated with

1. _____ (to turn it into a strong nucleophile)
2. _____ (back-side attack)
3. _____ (to attack the carbonyls)



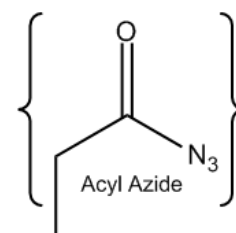
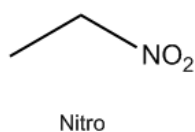
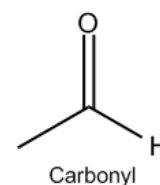
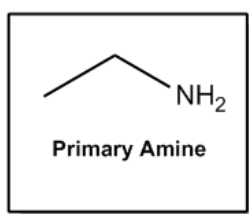
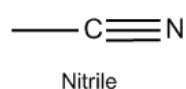
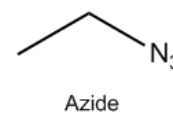
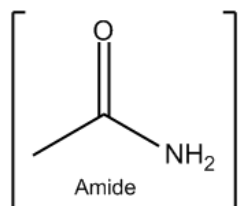
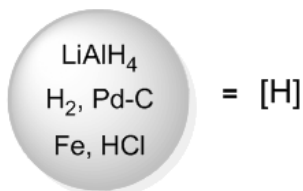
Phthalimide

Gabriel Synthesis Mechanism:

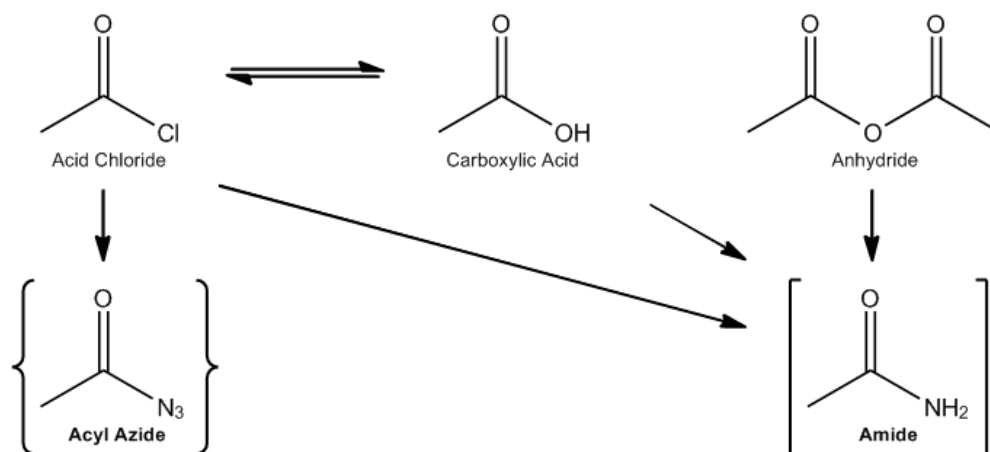
CONCEPT: AMINES BY REDUCTION

Amines By Reduction

Common Reducing Agents



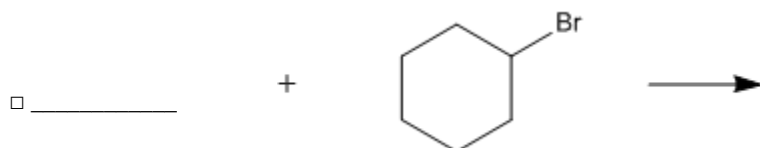
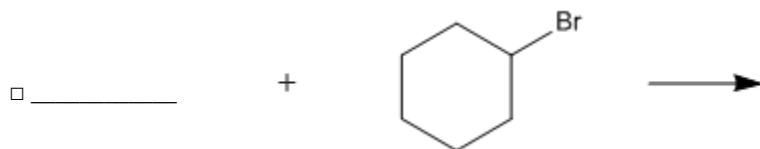
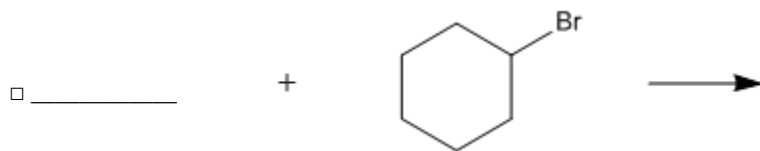
Carboxylic Acid Derivative Conversions



CONCEPT: NITROGENOUS NUCLEOPHILES

Three of the reagents used in *amines by reduction* can be found as excellent nucleophiles.

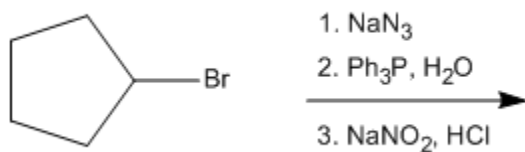
- They can participate in _____ reactions when there is a good leaving group present.



Additionally, _____ can act on acid chlorides to produce _____ (not an S_N2 mech, we'll get to it later!)



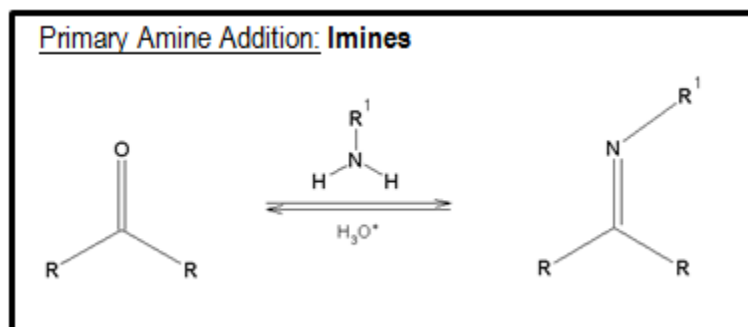
EXAMPLE: Provide the major product for the following reaction.



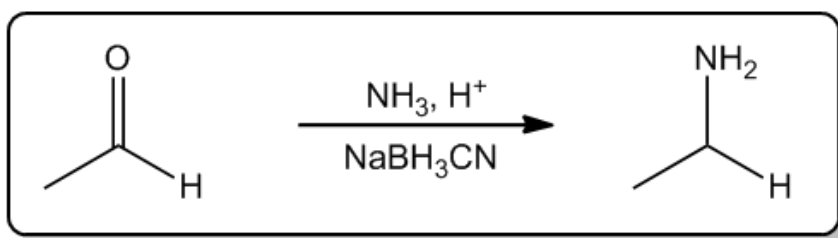
CONCEPT: REDUCTIVE AMINATION

Recall that ketones and aldehydes can react with primary amines in acidic conditions to form *imines*.

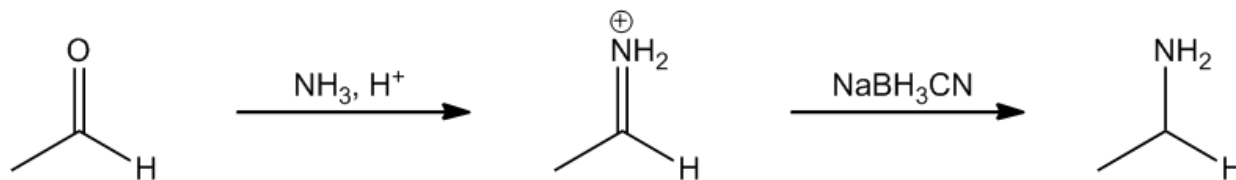
- This mechanism passed through an important intermediate called an *iminium cation*.



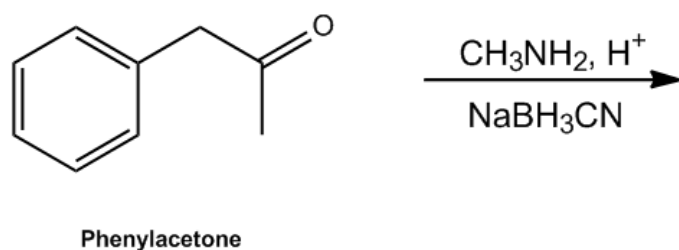
Ketones and aldehydes can be made to form *amines* instead by using the reducing agent, NaBH_3CN on the imine.



- This mechanism starts the same, except for the fact that we **reduce the imine** instead of deprotonating it



EXAMPLE: Provide the major product for the following reaction.

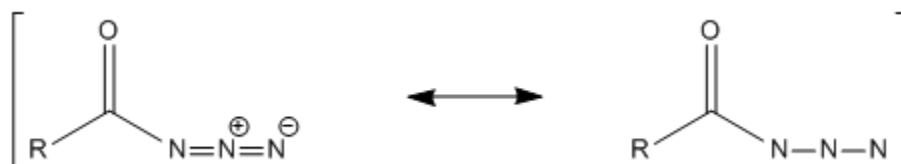


CONCEPT: CURTIUS REARRANGEMENT

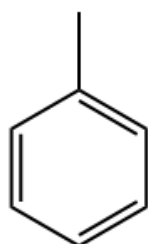
Also known as *Reduction of Acyl Azides*, it is the result of the thermal formation of a reactive intermediate called a **nitrene**.

- Heat drives the rearrangement of the acyl group to a molecule called an isocyanate
- Addition of _____ results in a decarboxylation reaction that liberates _____ and _____

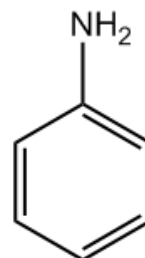
General Mechanism:



EXAMPLE: Propose a synthesis for the following compound.



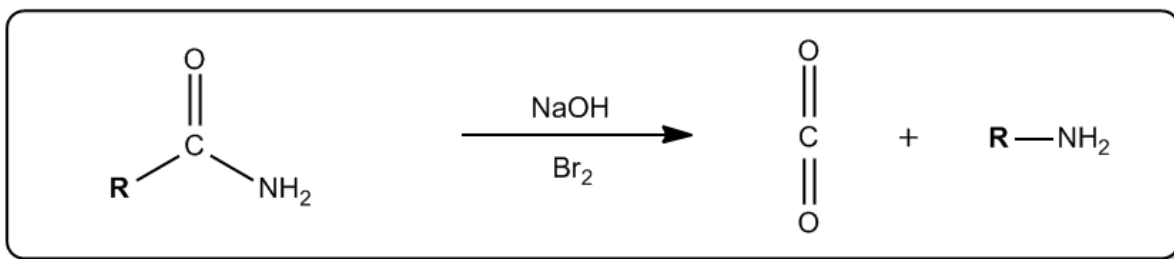
1.
 2.
 3.
 4.
-



CONCEPT: HOFMANN REARRANGEMENT

Also known as *Hofmann Degradation*, it is a method to turn amides into primary amines.

- The amide rearranges to a molecule called an isocyanate
- Liberates _____ as a by-product

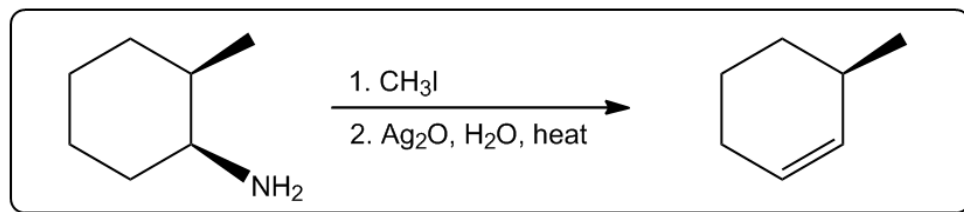


Hofmann Rearrangement Mechanism:

CONCEPT: HOFMANN ELIMINATION

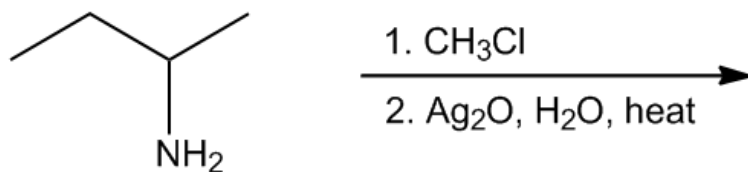
Also known as *exhaustive methylation* or *Hofmann Degradation*.

- This reaction uses amine polyalkylation to produce a Hofmann Elimination product.



Hofmann Elimination Mechanism:

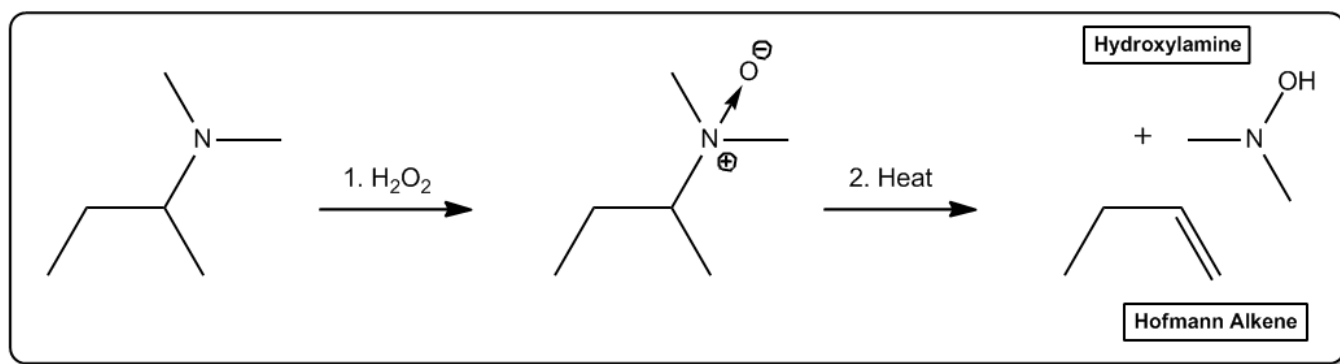
EXAMPLE: Provide the major product for the following reaction.



CONCEPT: COPE ELIMINATION

Amines are easily oxidized. Tertiary amine oxides have the ability to self-eliminate, favoring a *Hofmann Product*.

- The tertiary amine oxide, or *N-oxide*, contains a *dative* (also known as dipolar) covalent bond.
 - This represents that both electrons came from one atom. Denoted as $N \rightarrow O$ in some texts



Cope Elimination Mechanism:

EXAMPLE: Predict the product for the following reaction.

