# Chapter 23
# Amines

## Review of Concepts

Fill in the blanks below. To verify that your answers are correct, look in your textbook at the end of Chapter 23. Each of the sentences below appears verbatim in the section entitled *Review of Concepts and Vocabulary*.

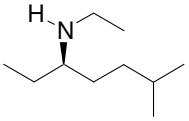
- Amines are _____, _____, or _____, depending on the number of groups attached to the nitrogen atom.
- The lone pair on the nitrogen atom of an amine can function as a _____ or _____.
- The basicity of an amine can be quantified by measuring the p$K_a$ of the corresponding _____.
- Aryl amines are less basic than alkyl amines, because the lone pair is _____.
- Pyridine is a stronger base than pyrrole, because the lone pair in pyrrole participates in _____.
- An amine moiety exists primarily as _____ at physiological pH.
- The **azide synthesis** involves treating an _____ with sodium azide, followed by _____.
- The _____ **synthesis** generates primary amines upon treatment of potassium phthalimide with an alkyl halide, followed by hydrolysis or reaction with $N_2H_4$.
- Amines can be prepared via **reductive amination**, in which a ketone or aldehyde is converted into an imine in the presence of a _____ agent, such as **sodium cyanoborohydride** ($NaBH_3CN$).
- Amines react with acyl halides to produce _____.
- In the **Hofmann elimination**, and amino group is converted into a better leaving group which is expelled in an ____ process to form an _____.
- Primary amines react with a nitrosonium ion to yield a _____ **salt** in a process called **diazotization**.
- **Sandmeyer reactions** utilize copper salts (CuX), enabling the installation of a halogen or a _____ group.
- In the **Schiemann reaction**, an aryl diazonium salt is converted into a fluorobenzene by treatment with _____.
- Aryldiazonium salts react with activated aromatic rings in a process called _____ **coupling**, to produce colored compounds called _____ **dyes**.
- A _____**cycle** is a ring that contains atoms of more than one element.
- Pyrrole undergoes electrophilic aromatic substitution reactions, which occur primarily at C__.

## Review of Skills

Fill in the blanks and empty boxes below. To verify that your answers are correct, look in your textbook at the end of Chapter 23. The answers appear in the section entitled *SkillBuilder Review*.

### 23.1 Naming an Amine

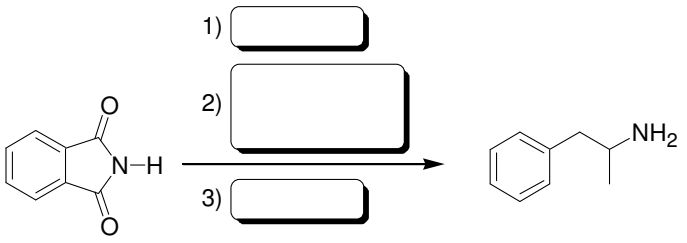
*PROVIDE A SYSTEMATIC NAME FOR THE FOLLOWING COMPOUND*




*1) IDENTIFY THE PARENT*
*2) IDENTIFY AND NAME SUBSTITUENTS*
*3) ASSIGN LOCANTS TO EACH SUBSTITUENT*
*4) ALPHABETIZE*
*5) ASSIGN CONFIGURATION*

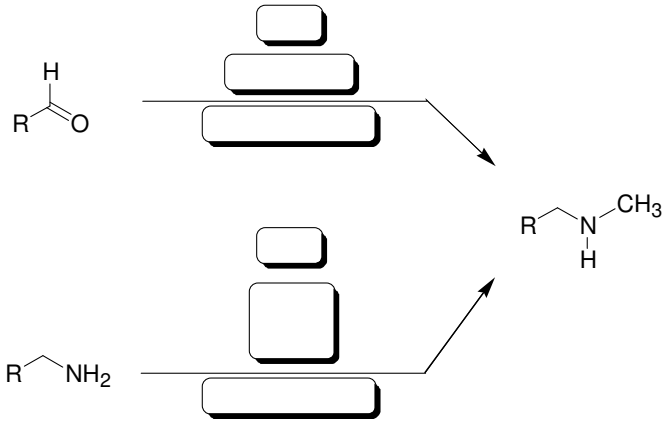
### 23.2 Preparing a Primary Amine via the Gabriel Reaction

*IDENTIFY REAGENTS THAT WILL ACHIEVE THE FOLLOWING TRANSFORMATION:*

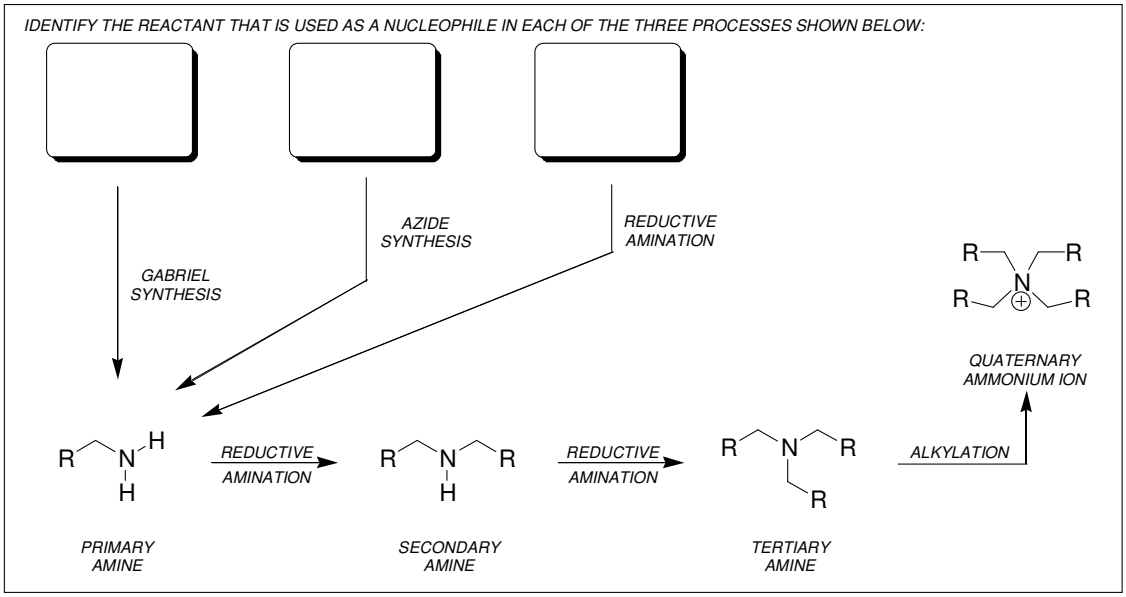



### 23.3 Preparing an Amine via a Reductive Amination

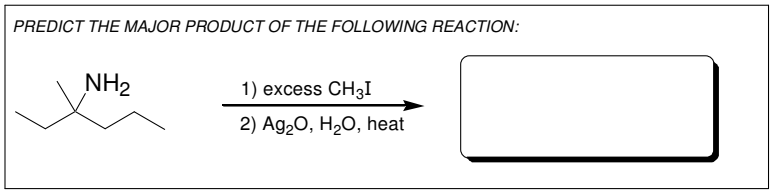
*IDENTIFY REAGENTS THAT WILL ACHIEVE EACH OF THE FOLLOWING TRANSFORMATIONS:*



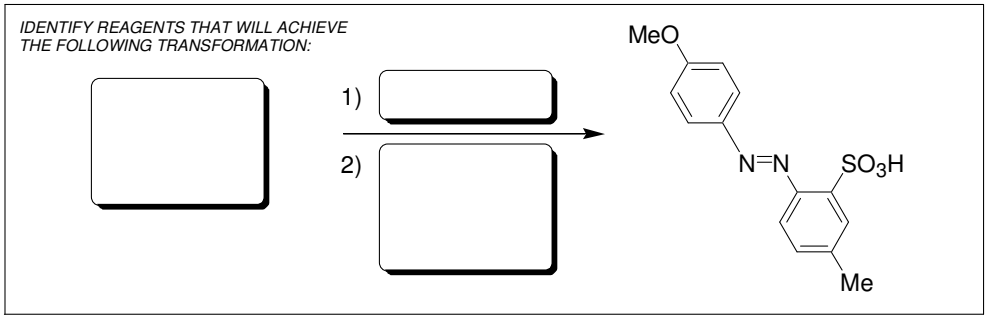
## 23.4 Synthesis Strategies




## 23.5 Predicting the Product of a Hofmann Elimination



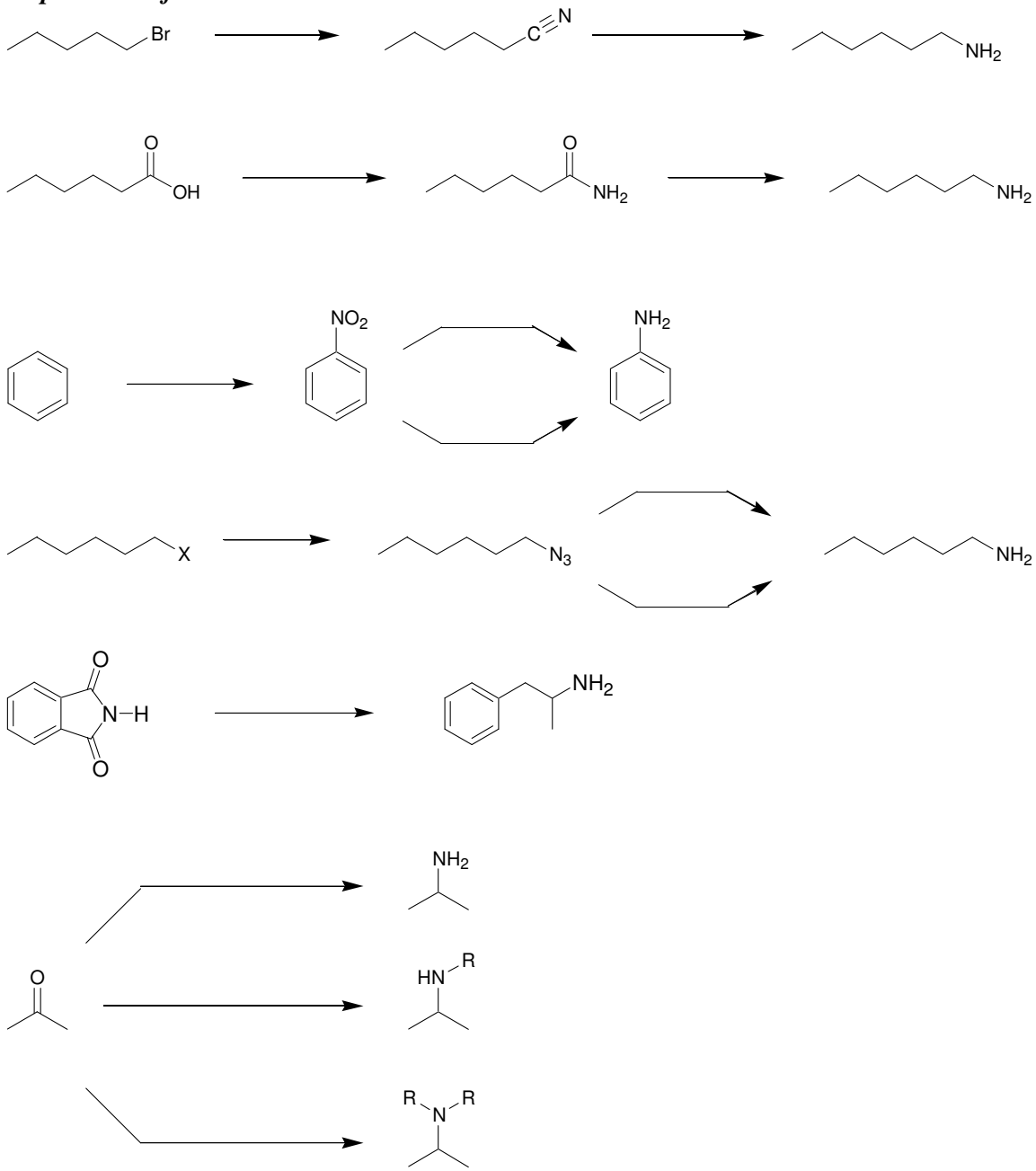

## 23.6 Determining the Reactants for Preparing an Azo Dye



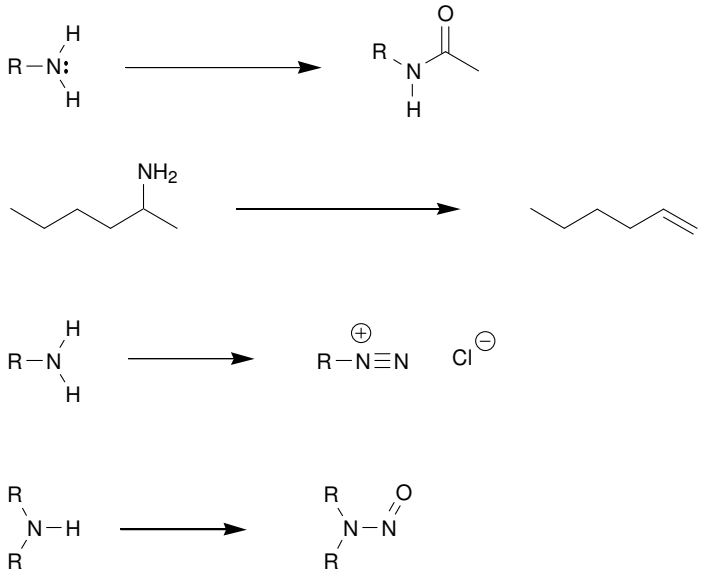
## Review of Reactions

Identify the reagents necessary to achieve each of the following transformations. To verify that your answers are correct, look in your textbook at the end of Chapter 23. The answers appear in the section entitled *Review of Reactions*.

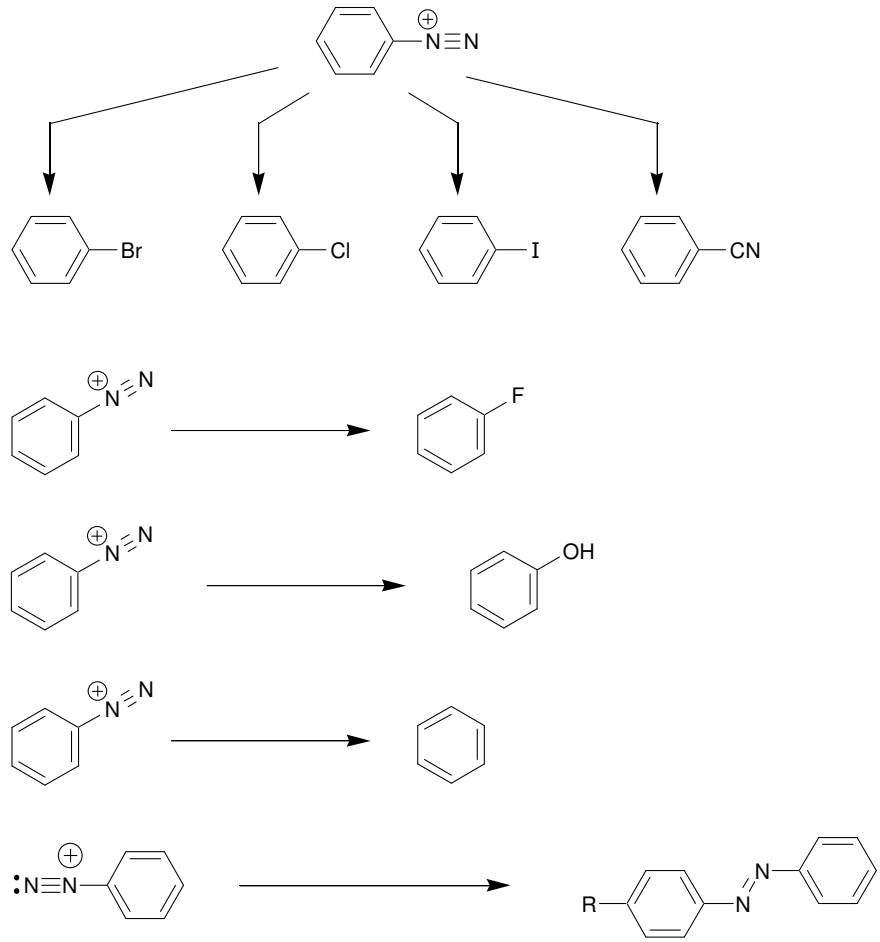
***Preparation of Amines***



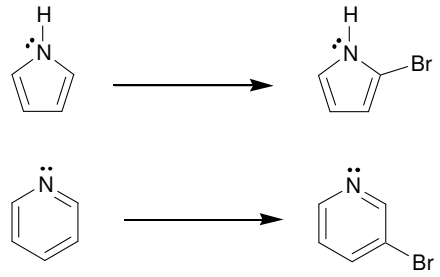
### *Reactions of Amines*



### *Reactions of Aryldiazonium Salts*



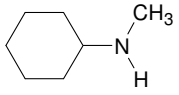
***Reactions of Nitrogen Heterocycles***

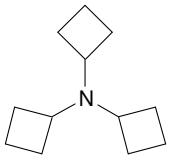


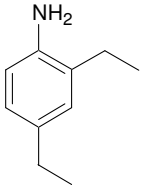

## Solutions

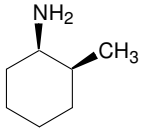
**23.1.**
a) 3,3-dimethyl-1-butanamine
b) cyclopentylamine
c) *N,N*-dimethylcyclopentylamine
d) triethylamine
e) (*1S,3R*)-3-isopropylcyclohexanamine
f) (*1S, 3S*)-3-aminocyclohexanol

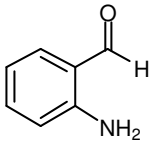
**23.2.**

a) 

b) 

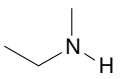
c) 

d) 

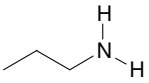
e) 


**23.3.**

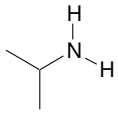
trimethylamine



ethyl methyl amine

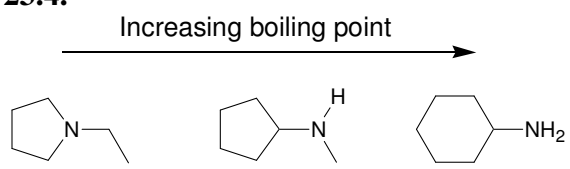


propylamine

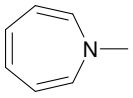
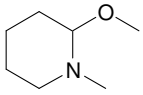
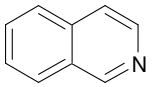


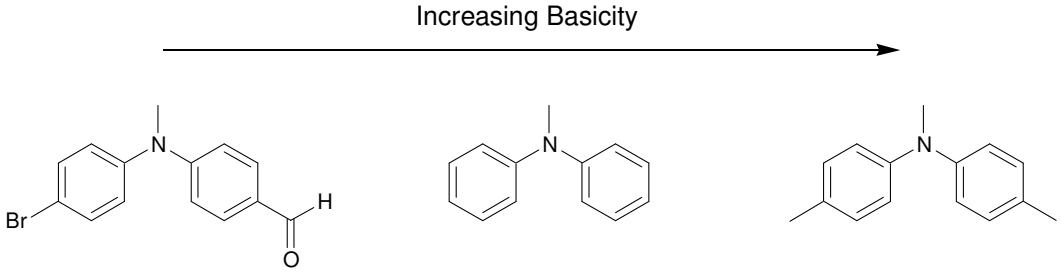
isopropylamine

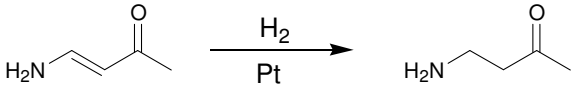
**23.4.**

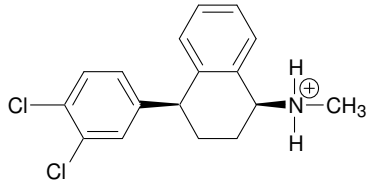


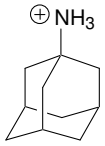
**23.5.**
a) No. This compound has eight carbon atoms and only one functional group.
b) Yes.
c) Yes.

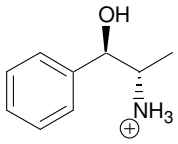
**23.6.**
a) 
b) 
c) 
d) 

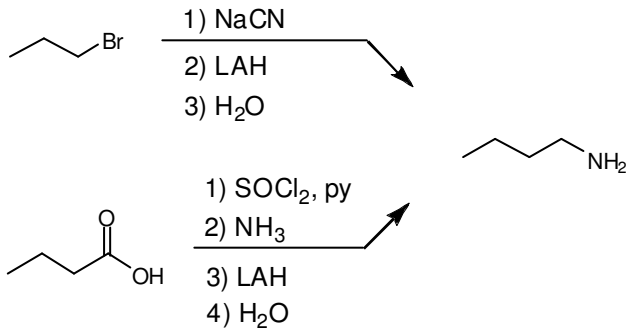
**23.7.**



**23.8.** In the reactant, the lone pair of the amino group is delocalized via resonance. In the product, the lone pair of the amino group is localized.


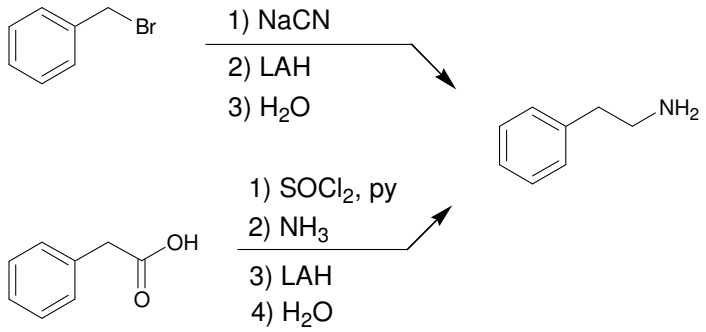

**23.9.**
a) 

b) 

c) 


**23.10.**
a)


b)

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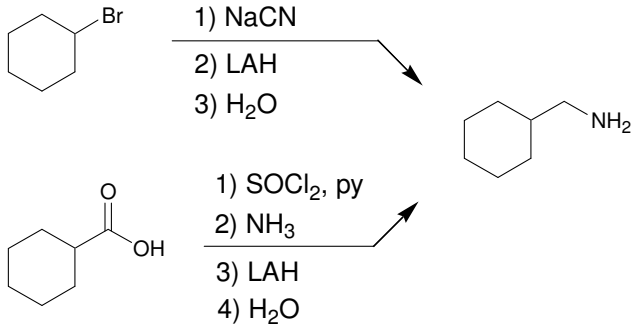
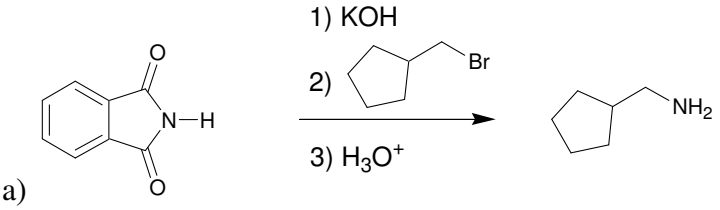



**23.11.** This compound cannot be prepared from an alkyl halide or a carboxylic acid, using the methods described in this section, because there are two methyl groups at the alpha position (the carbon atom connected to the amino group). These two methyl groups cannot be installed with either of the synthetic methods above, because both methods produce an amine with two alpha protons.

**23.12.**

a)

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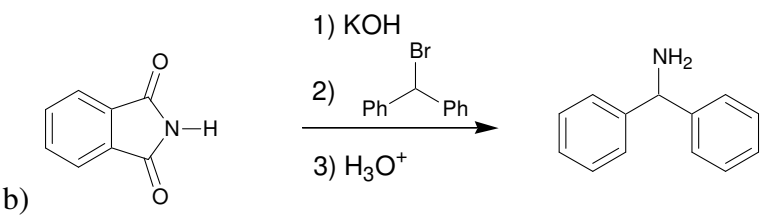

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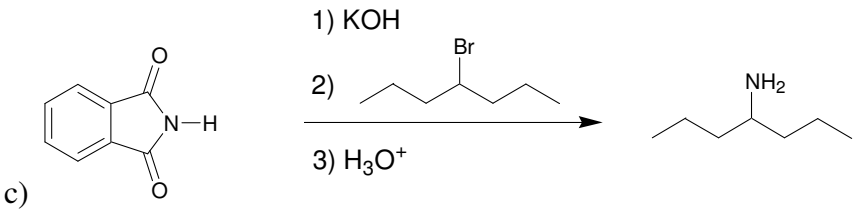
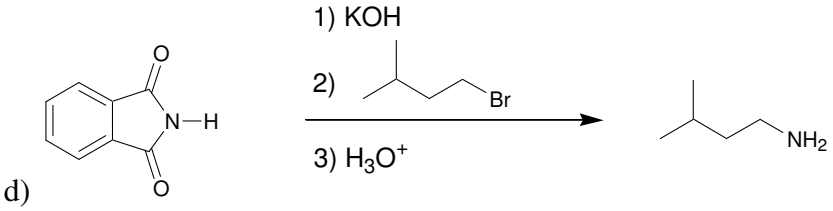
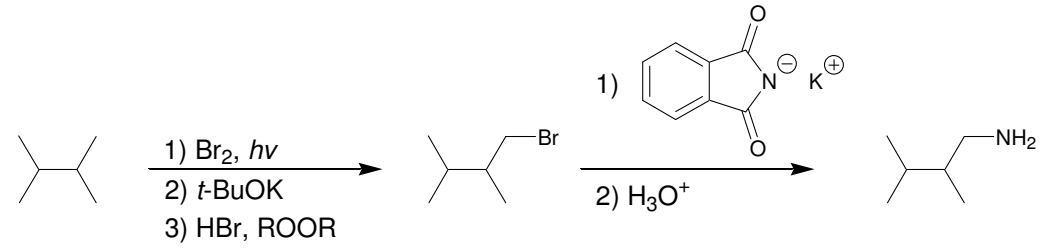



d)




**23.13.**

a)

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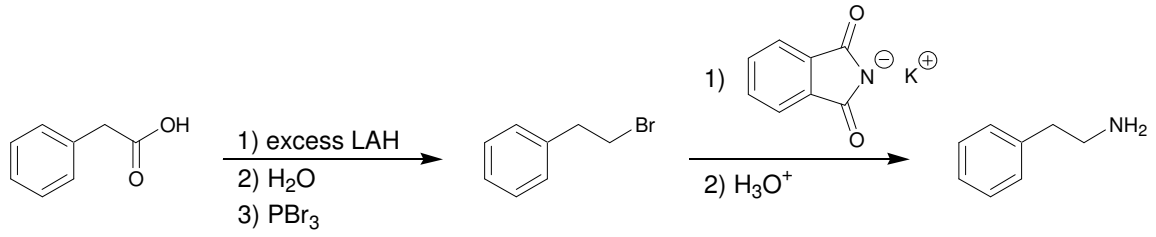
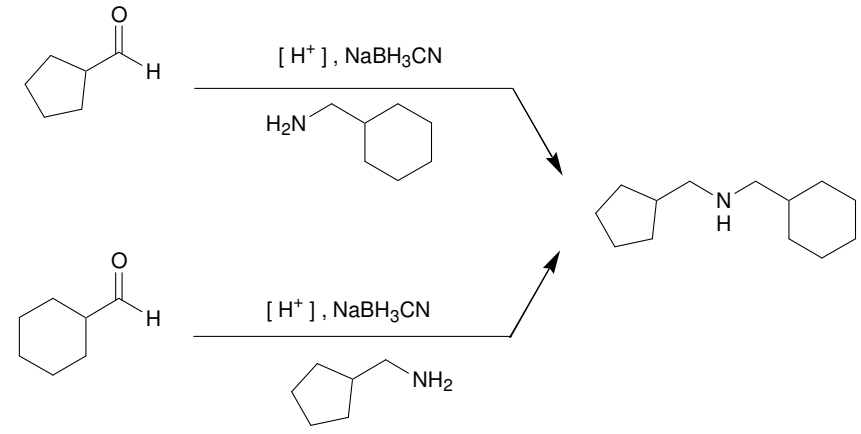
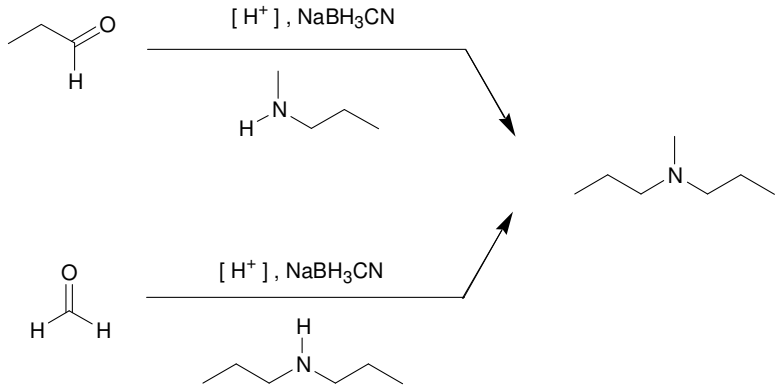



**23.14.**

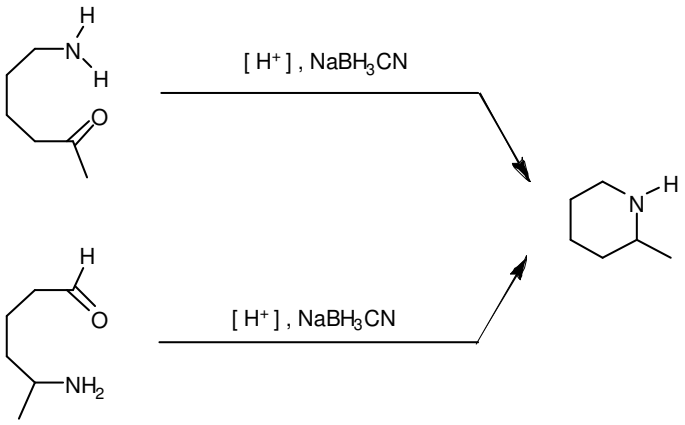
a)



b)




c)

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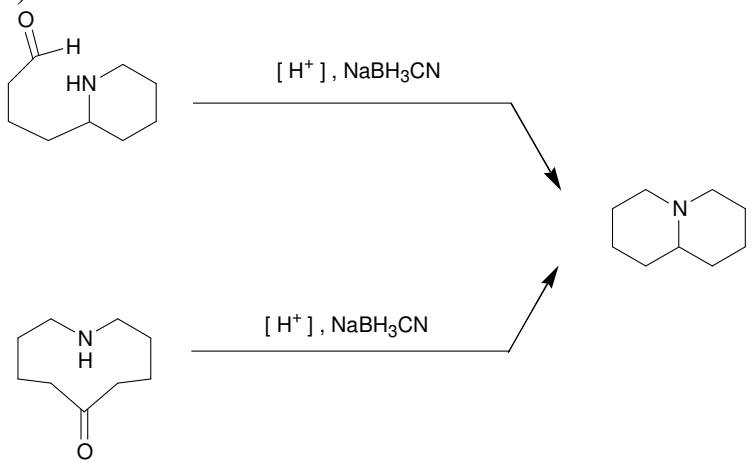

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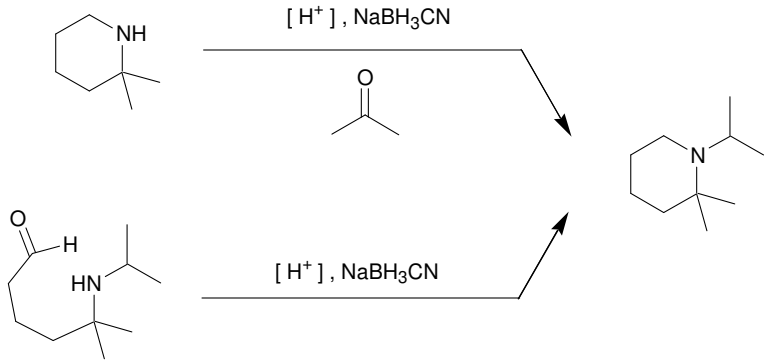
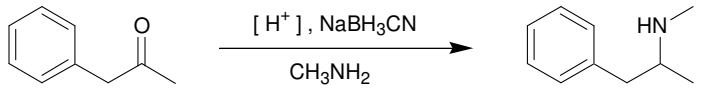
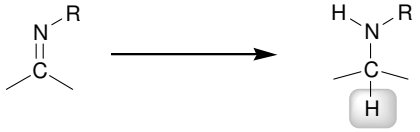


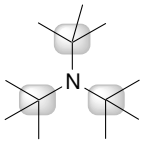

**23.15.**




**23.16.** The last step of reductive amination is the reduction of a C=N bond. That step introduces a proton on the alpha position (the carbon atom that is connected to the nitrogen atom in the product):

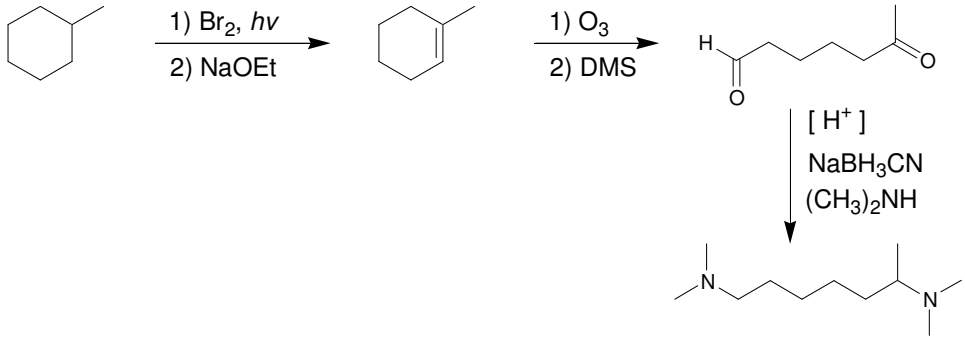



As a result, the product of a reductive amination must have at least one proton at the alpha position. In the case of tri-*tert*-butyl amine, there are three alpha positions, and none of them bears a proton. Each of the alpha positions has three alkyl groups and no protons.



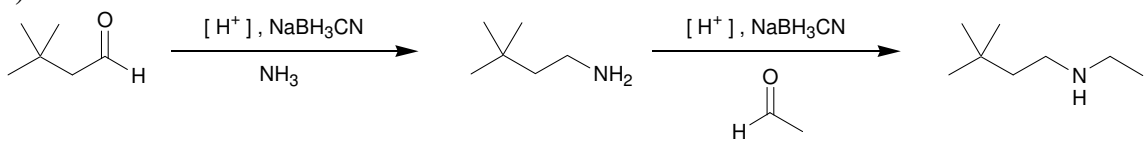

Therefore, this compound cannot be made with a reductive amination.

**23.17.**

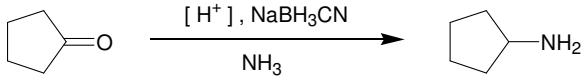


**23.18.**

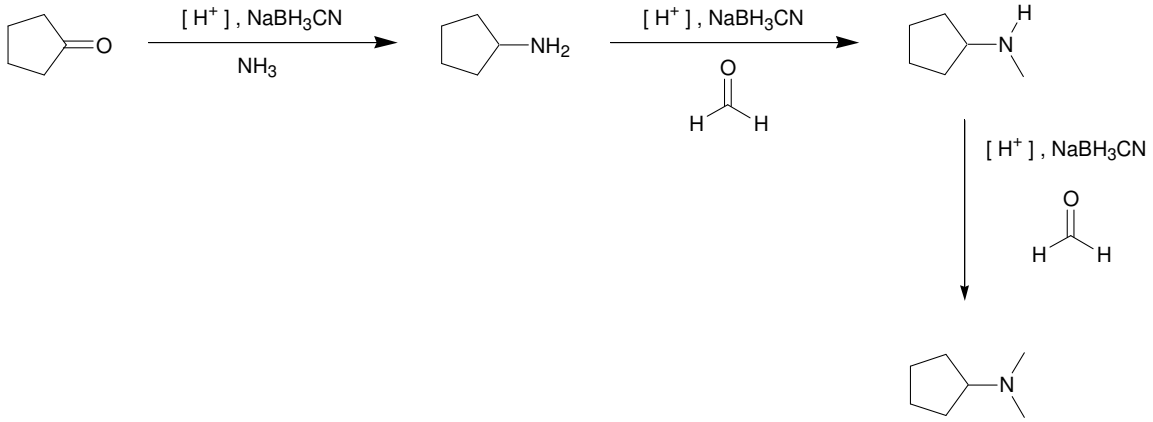
a)


O
H
[ H+ ] , NaBH3CN
NH3
NH2
[ H+ ] , NaBH3CN
O
H
N
H

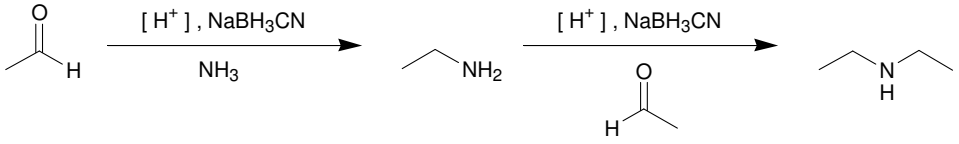
b)


O
[ H+ ] , NaBH3CN
NH3
NH2

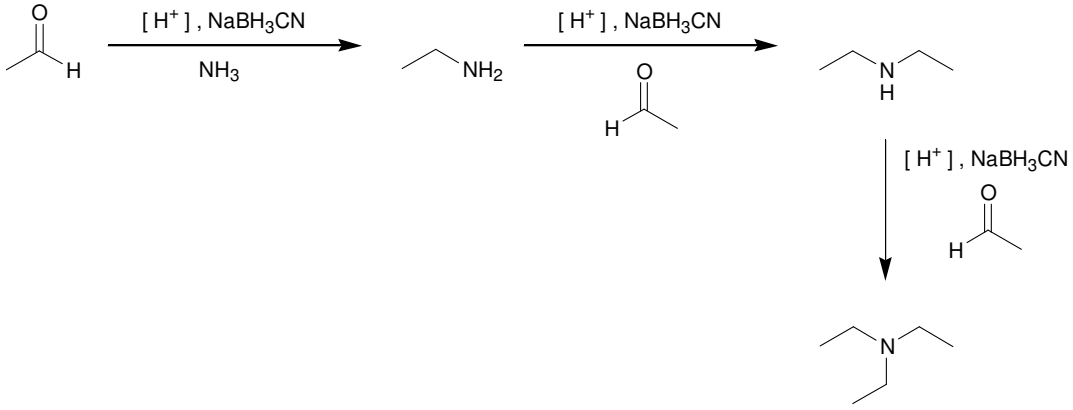
c)


O
[ H+ ] , NaBH3CN
NH3
NH2
[ H+ ] , NaBH3CN
O
H
H
H
N
[ H+ ] , NaBH3CN
O
H
H
N

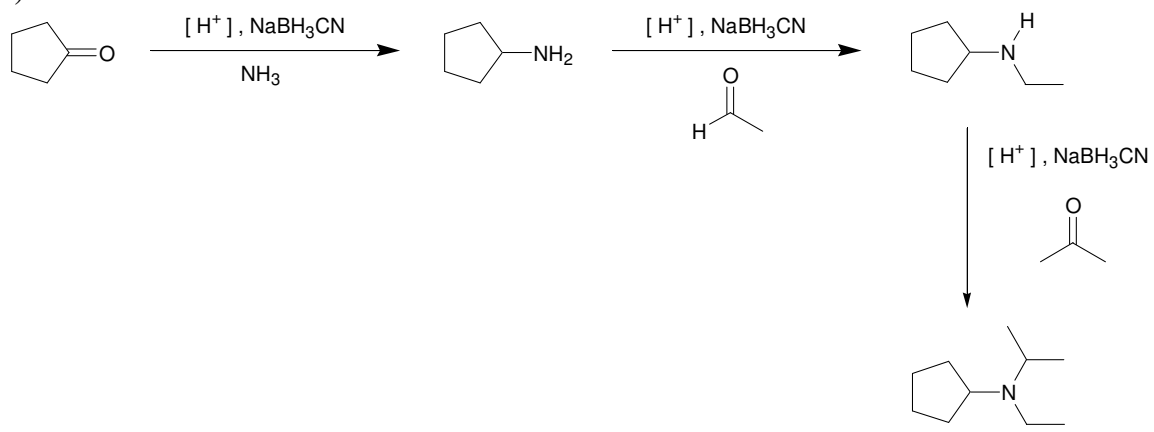
d)


O
H
[ H+ ] , NaBH3CN
NH3
NH2
[ H+ ] , NaBH3CN
O
H
N
H

e)

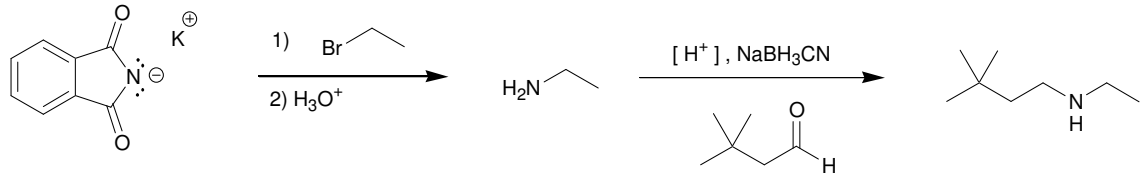

O
H
[ H+ ] , NaBH3CN
NH3
NH2
[ H+ ] , NaBH3CN
O
H
N
H
[ H+ ] , NaBH3CN
O
H
N

f)

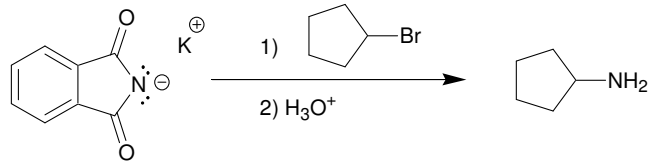



**23.19.** The first alkyl group is installed via a Gabriel synthesis, and the remaining alkyl groups are installed via reductive amination processes. For most of the following syntheses, there is a choice regarding which group to attach via the initial Gabriel synthesis. In such cases, the least sterically hindered group is chosen (the group whose installation involves the least hindered alkyl halide):

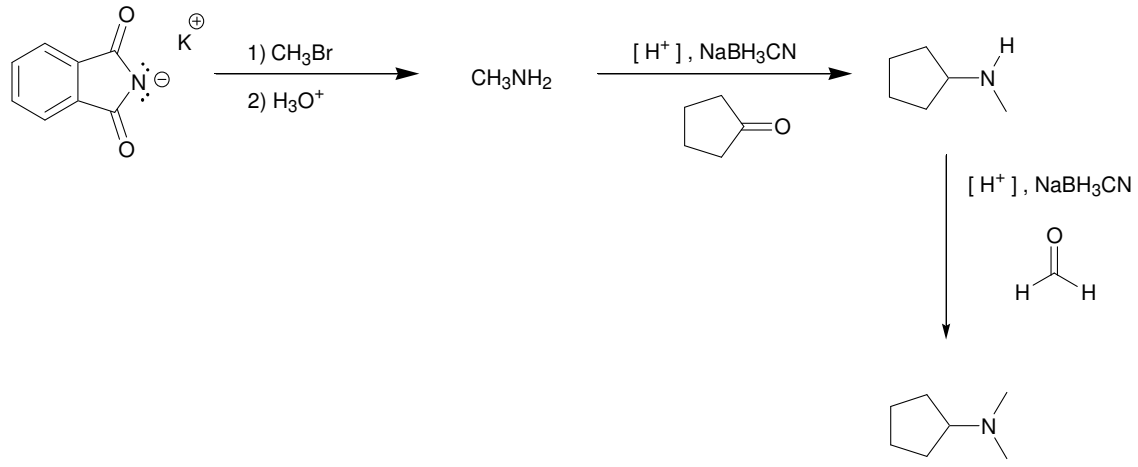
a)



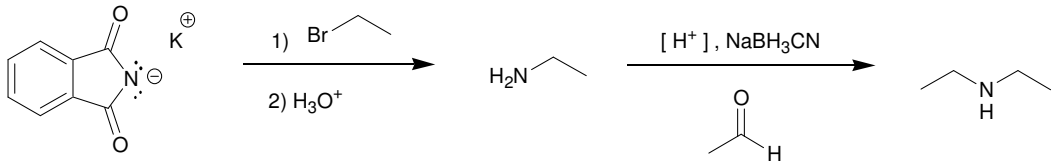

b)



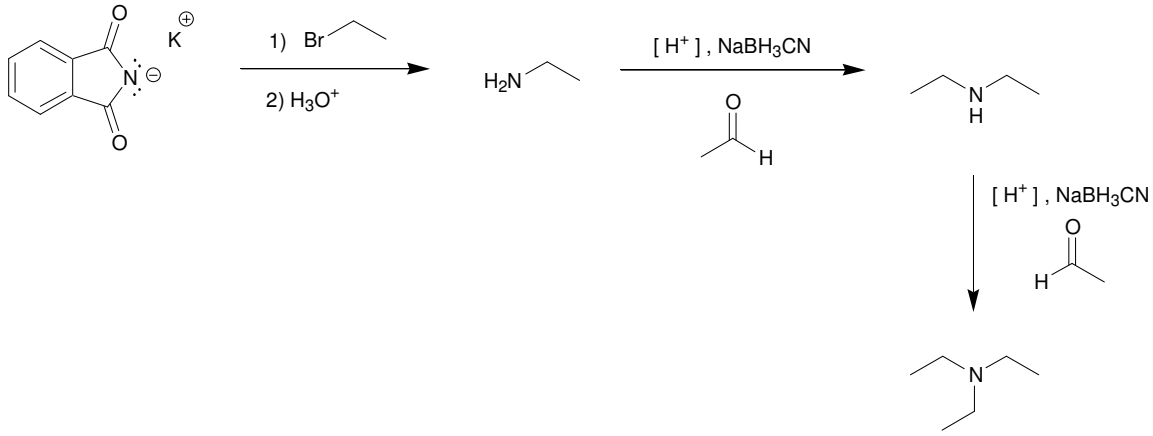

c)



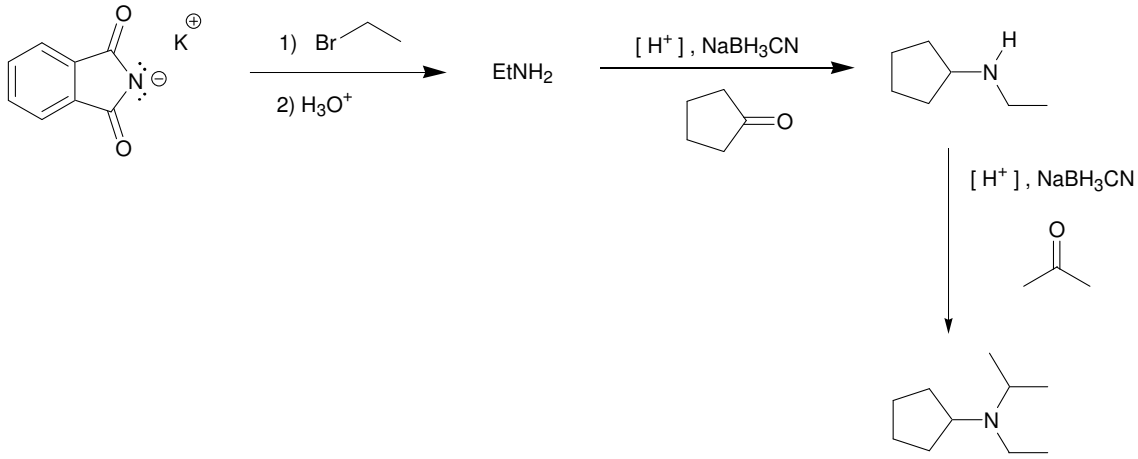
d)




e)

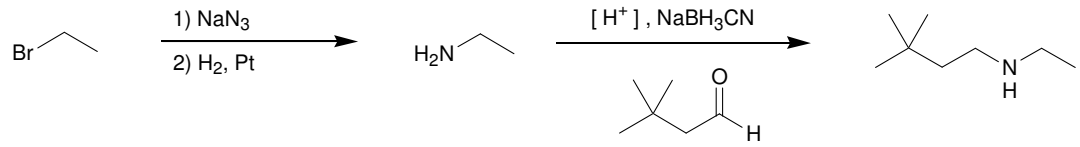



f)

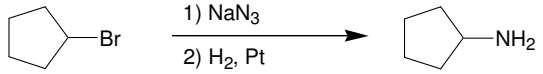



**23.20.** The first alkyl group is installed via an azide synthesis, and the remaining alkyl groups are installed via reductive amination processes. For most of the following syntheses, there is a choice regarding which group to attach via the initial azide synthesis. In such cases, the least sterically hindered group is chosen (the group whose installation involves the least hindered alkyl halide):

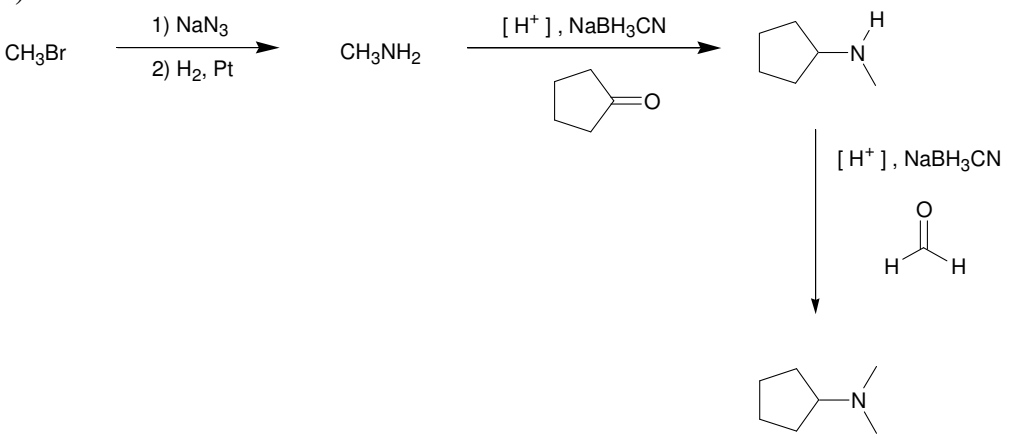
a)



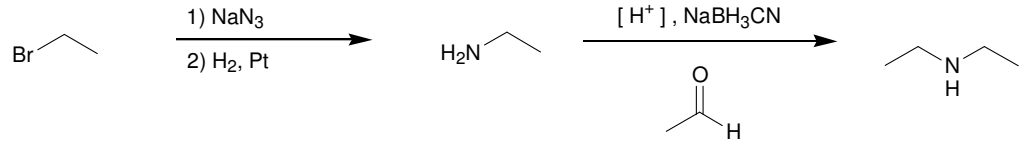
b)


Br
1) NaN3
2) H2, Pt
NH2

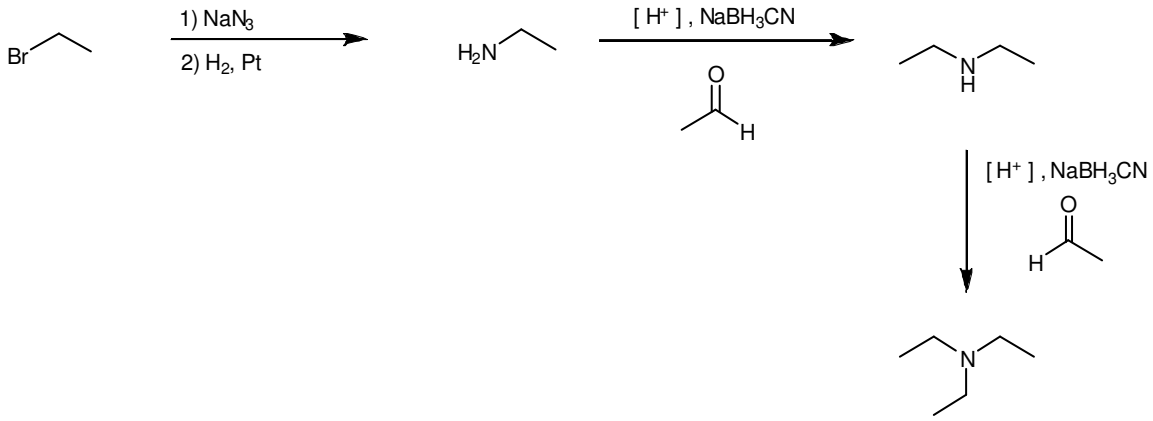
c)


CH3Br
1) NaN3
2) H2, Pt
CH3NH2
[ H+ ] , NaBH3CN
O
H
N
[ H+ ] , NaBH3CN
O
H
H
N

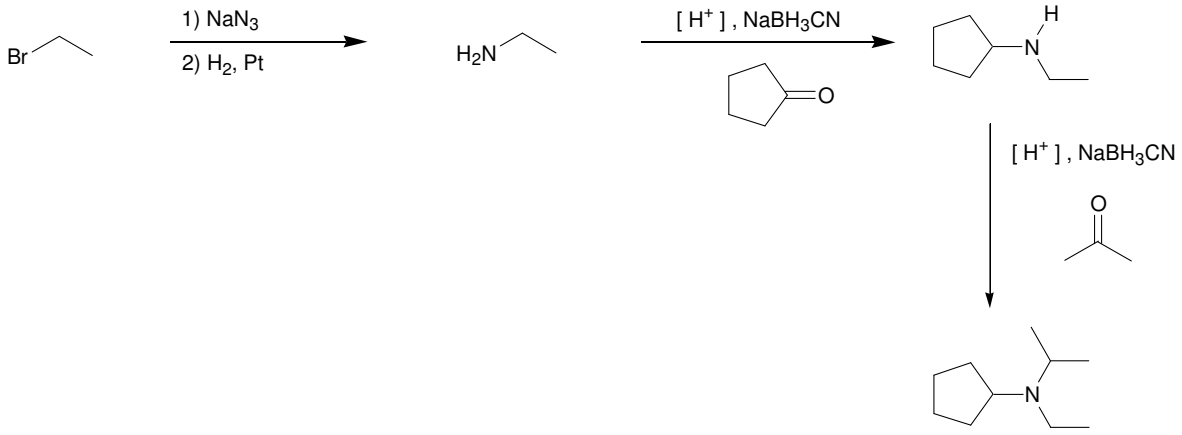
d)


Br
1) NaN3
2) H2, Pt
H2N
[ H+ ] , NaBH3CN
O
H
N
H

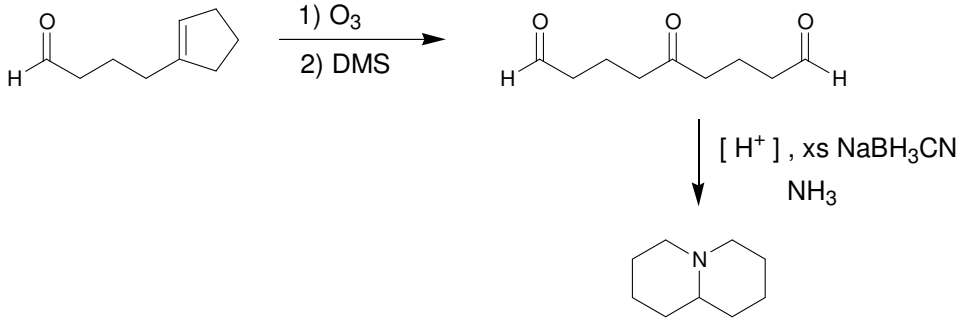
e)


Br
1) NaN3
2) H2, Pt
H2N
[ H+ ] , NaBH3CN
O
H
N
H
[ H+ ] , NaBH3CN
O
H
N

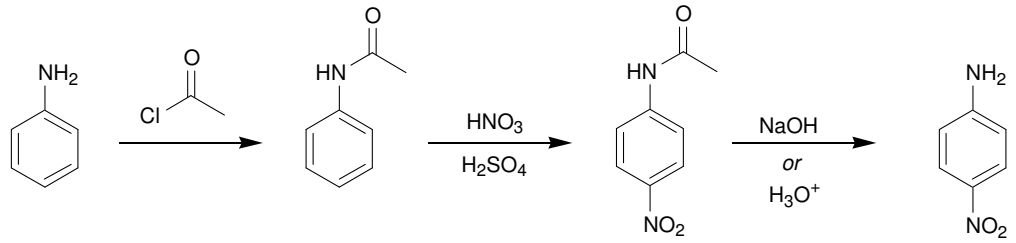
f)



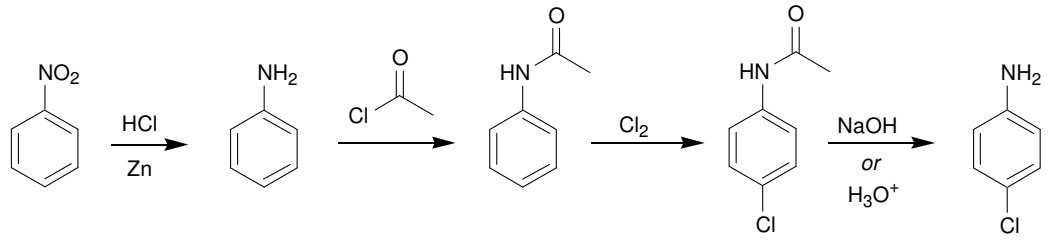

**23.21.**



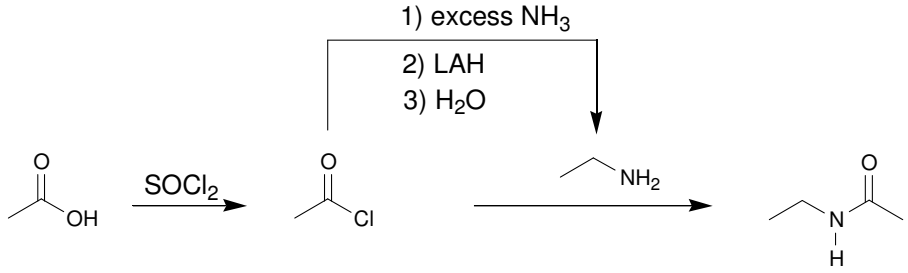

**23.22.**




**23.23.**

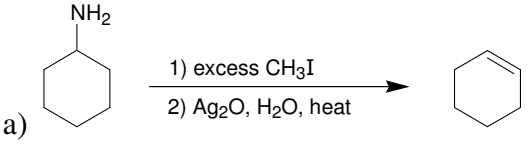


**23.24.**

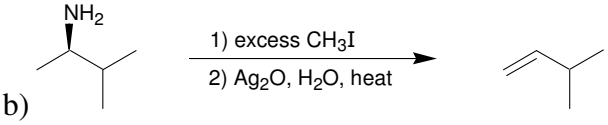



**23.25.**

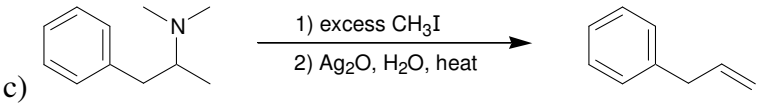
a)



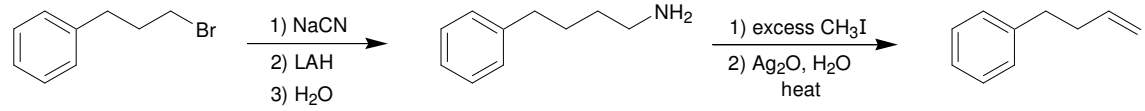

b)



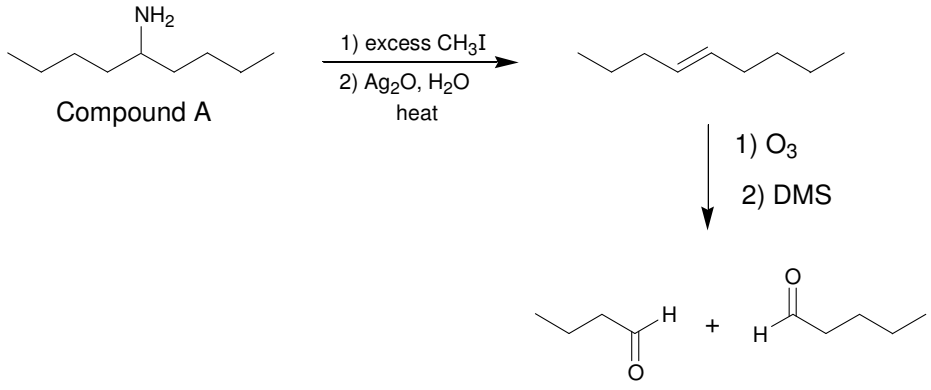

c)



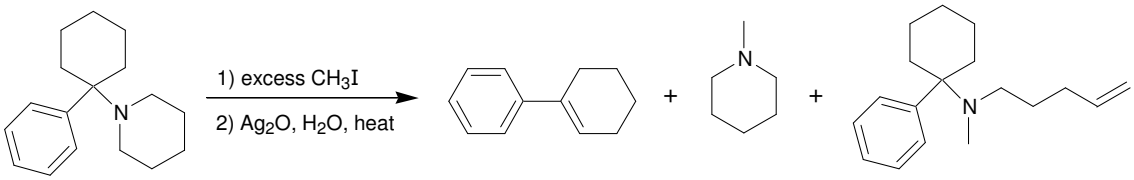

**23.26.**



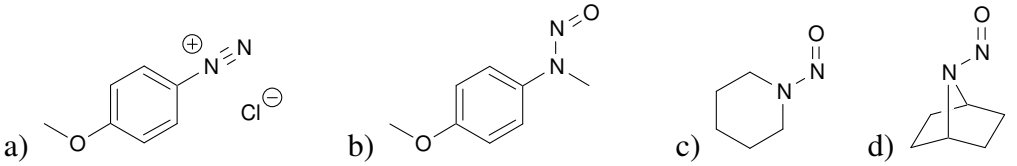

**23.27.**



**23.28.**

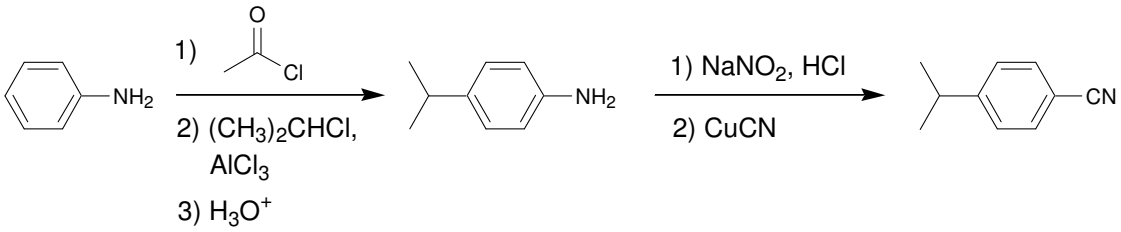



**23.29.**

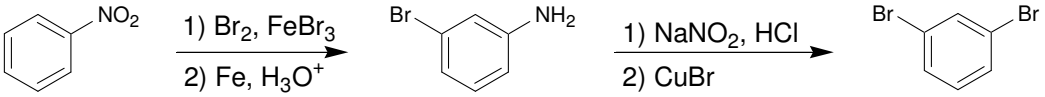



**23.30.**

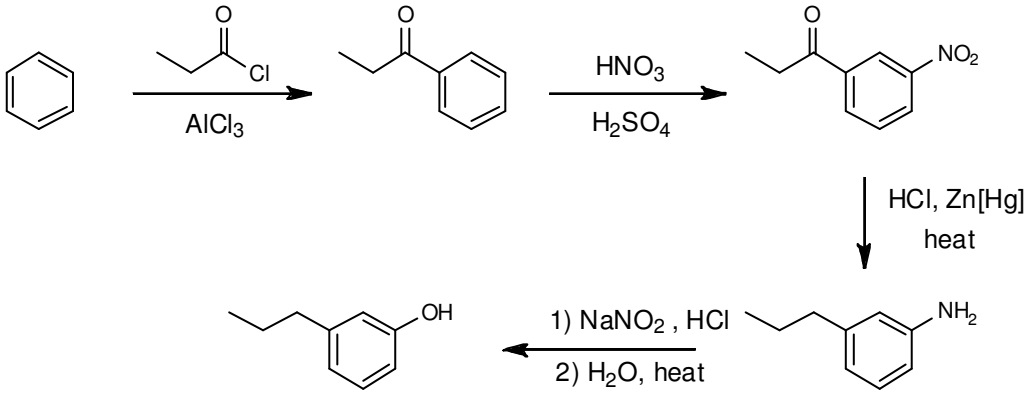
a)



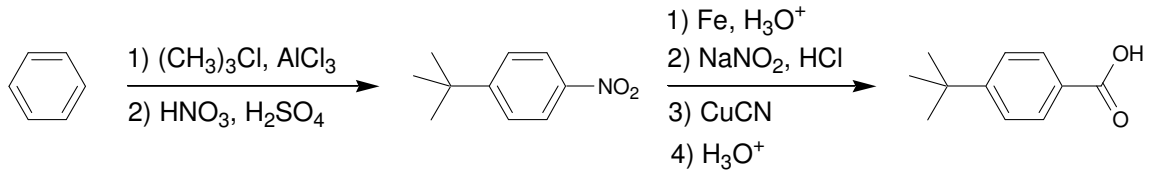

b)



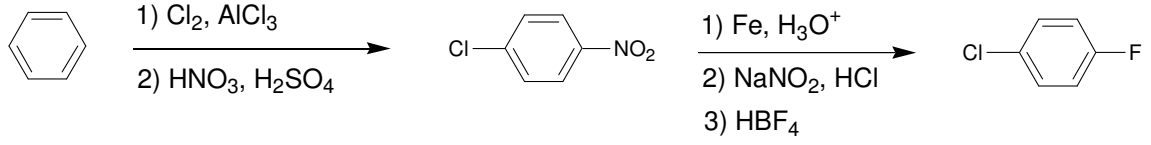

c)



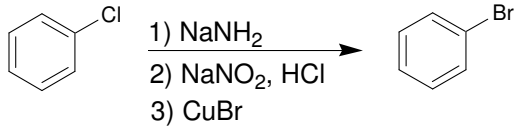
d)


1) $(CH_3)_3Cl$, $AlCl_3$
2) $HNO_3$, $H_2SO_4$
$NO_2$
1) Fe, $H_3O^+$
2) $NaNO_2$, HCl
3) CuCN
4) $H_3O^+$
OH
O

e)

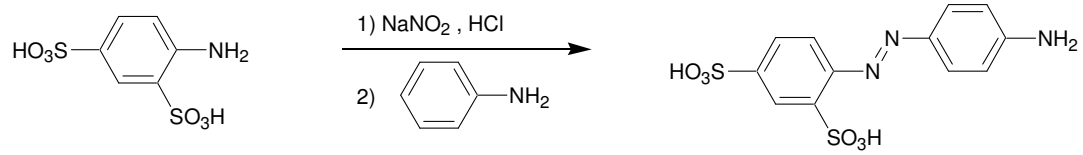

1) $Cl_2$, $AlCl_3$
2) $HNO_3$, $H_2SO_4$
Cl
$NO_2$
1) Fe, $H_3O^+$
2) $NaNO_2$, HCl
3) $HBF_4$
Cl
F

f)

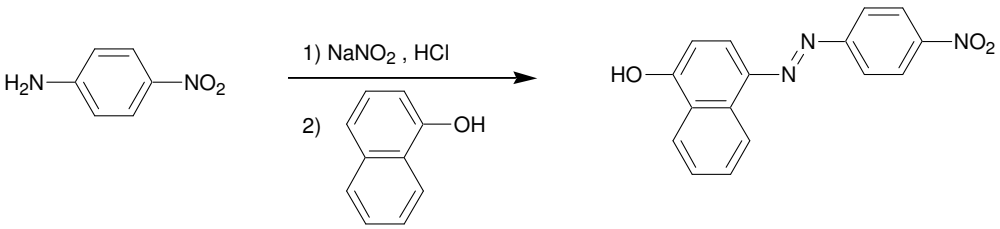

Cl
1) $NaNH_2$
2) $NaNO_2$, HCl
3) CuBr
Br

**23.31.**

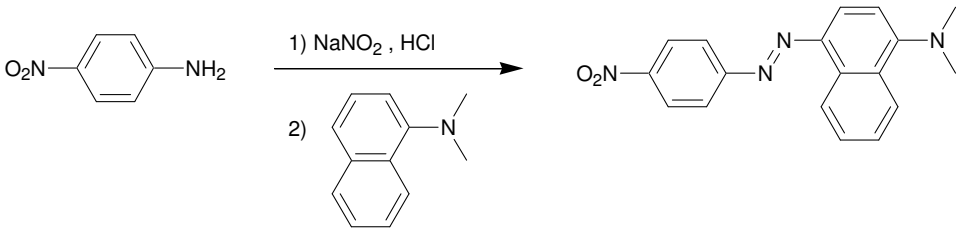
a)


$HO_3S$
$NH_2$
$SO_3H$
1) $NaNO_2$ , HCl
2)
$NH_2$
$HO_3S$
N
N
$NH_2$
$SO_3H$

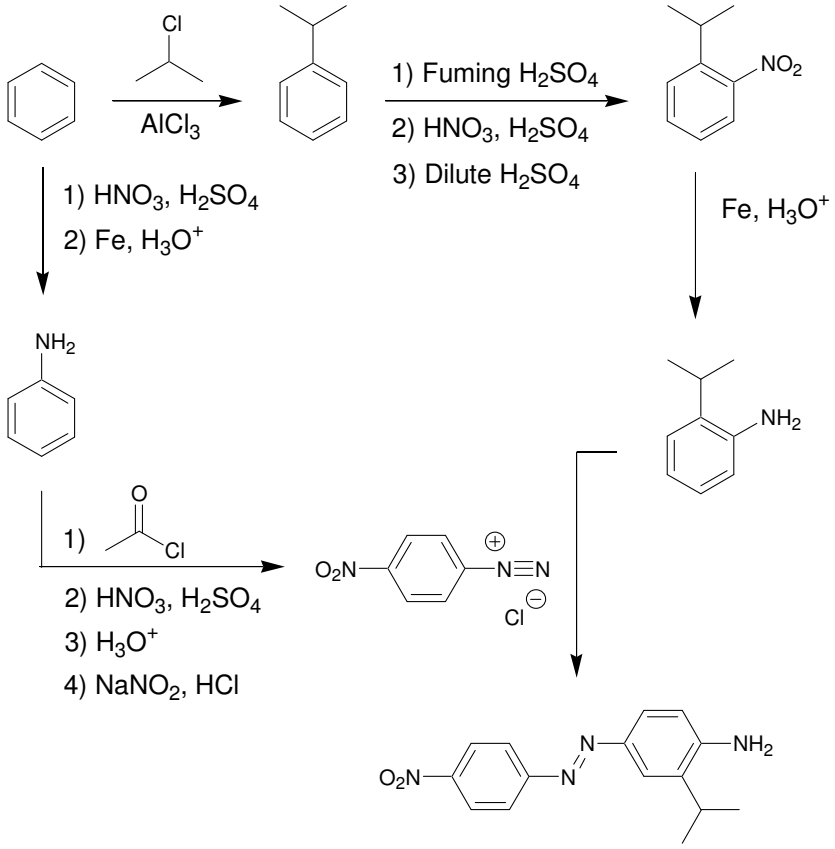
b)


$H_2N$
$NO_2$
1) $NaNO_2$ , HCl
2)
OH
HO
N
N
$NO_2$

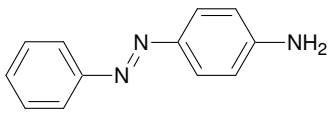
c)

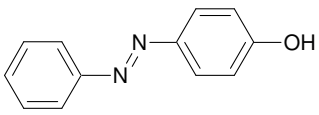

$O_2N$
$NH_2$
1) $NaNO_2$ , HCl
2)
N
$O_2N$
N
N
N

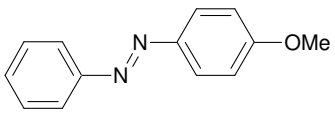
**23.32.**



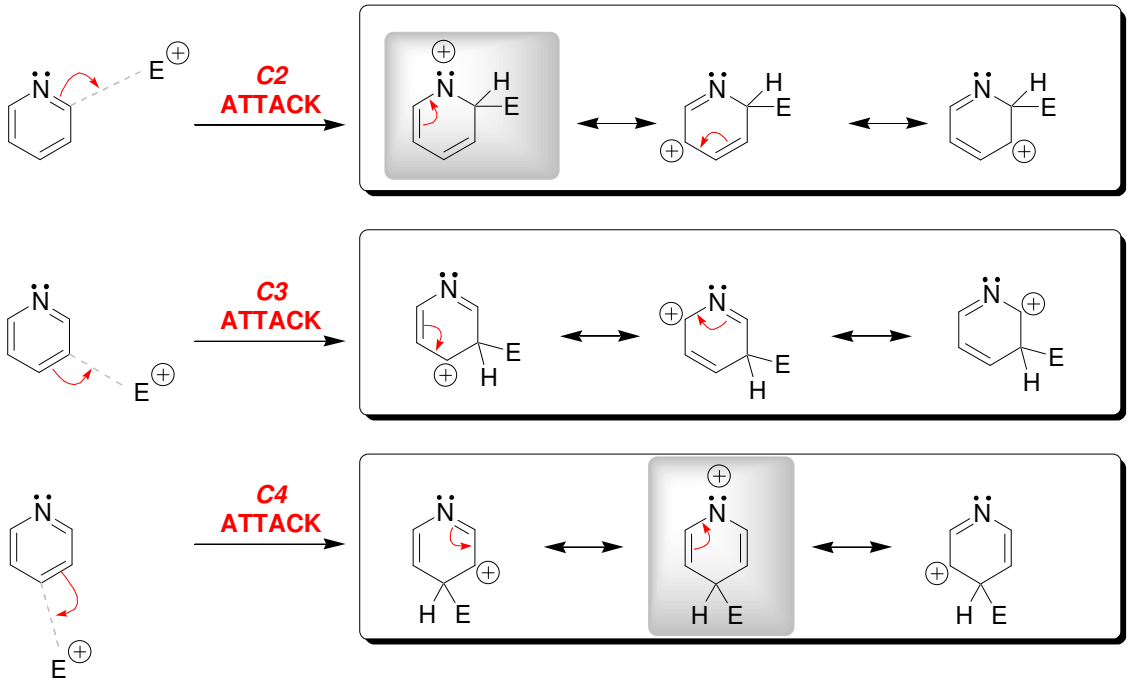

**23.33.**

a) 

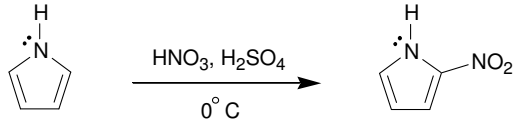

b) 


c) 

**23.34.** Attack at either C2 or C4 generates an intermediate that exhibits a resonance structure with a nitrogen atom that lacks an octet (highlighted below). Attack at C3 generates a more stable intermediate:




**23.35.**




**23.36.**

a) The second compound will have an N-H stretching signal between 3300 and 3500 $cm^{-1}$. The first compound will not have such a signal.

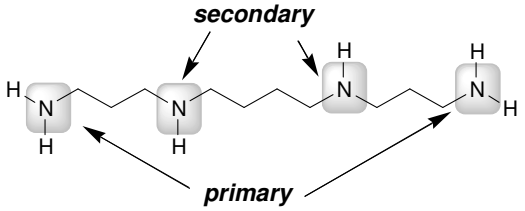
b) When treated with HCl, the first compound will be protonated to form an ammonium salt that will produce an IR signal between 2200 and 3000 $cm^{-1}$. The second compound is not an amine and will not exhibit the same behavior.

**23.37.**

a) The $^1H$ NMR spectrum of the first compound will have a singlet resulting from the N-methyl group. $^1H$ NMR spectrum of the second compound will not have any singlets.

b) The $^1H$ NMR spectrum of the first compound will have six signals, while the $^1H$ NMR spectrum of the second compound will have only three signals.

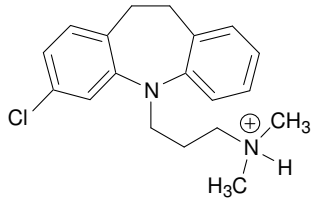
**23.38.**



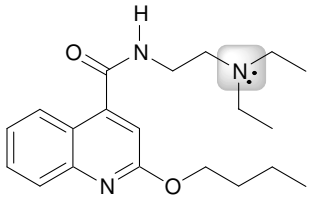

**23.39.**

a) The lone pair that is farthest away from the rings is the most basic, because its lone pair is localized. The lone pair of the other nitrogen atom is delocalized via resonance.

b)



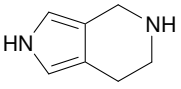
**23.40.**



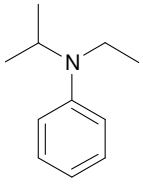
**23.41.**

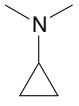
a) 

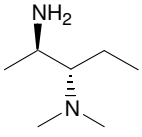
b) 

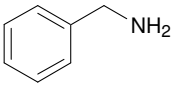
c) 

**23.42.**

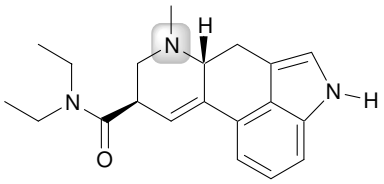
a) 

b) 

c) 

d) 

**23.43.** Only one of the nitrogen atoms has a localized lone pair (highlighted in the following structure). The other two nitrogen atoms have delocalized lone pairs.



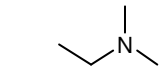
**23.44.**

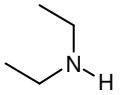
a) two b) two c) one

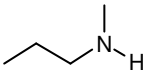
**23.45.**

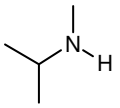
a) 2,2,3,3-tetramethyl-1-hexanamine
b) (*S*)-4-amino-2,2-dimethylcyclohexanone
c) dicyclobutylmethylamine
d) 3-bromo-2,6-dimethylaniline
e) *N*,*N*-dimethyl-3-propylaniline
f) 2,5-diethyl-*N*-methyl pyrrole

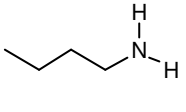
**23.46.**

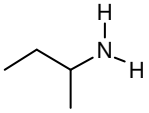

ethyldimethylamine

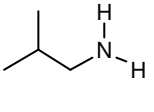

diethylamine

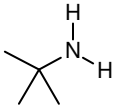

methylpropylamine


isopropylmethylamine

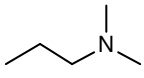

1-butanamine

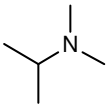

2-butanamine

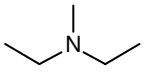

2-methyl-
1-propanamine


2-methyl-
2-propanamine

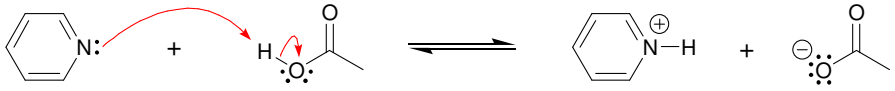
**23.47.** None of these compounds are chiral.


dimethylpropylamine

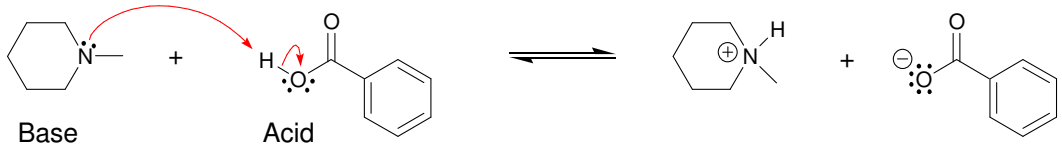

isopropyldimethylamine


diethylmethylamine

**23.48.**

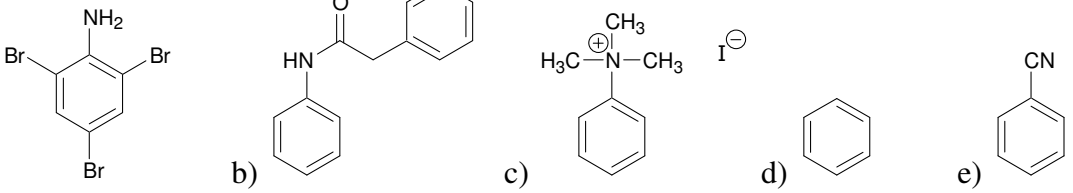


a) Base Acid



b) Base Acid

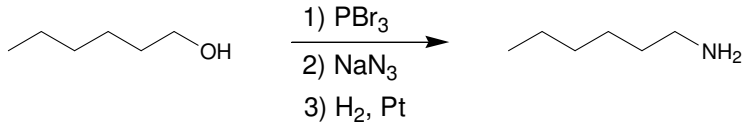
**23.49.**



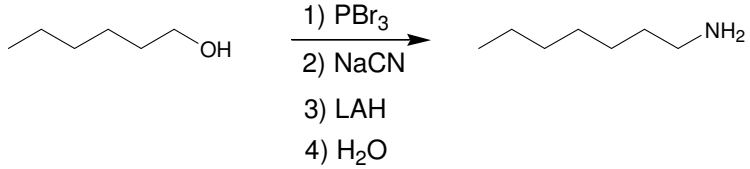
a) b) c) d) e)

**23.50.**

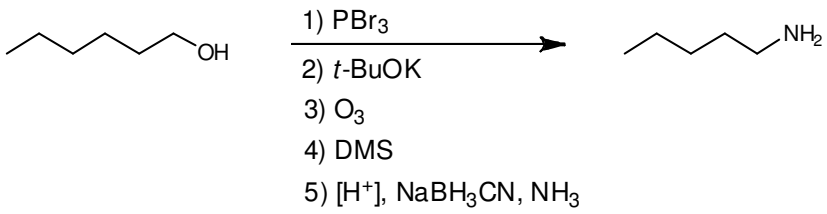
a)




b)

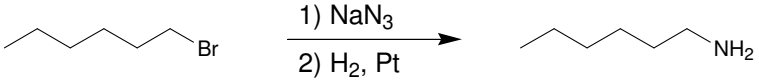



c)

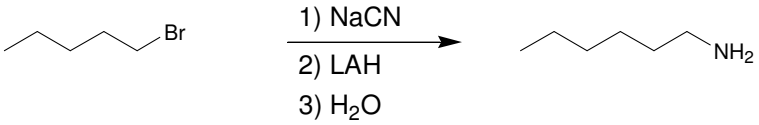


**23.51.**

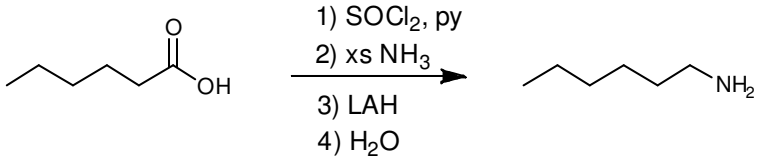
a)



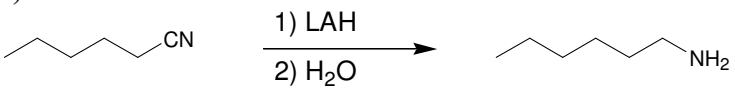

b)




c)

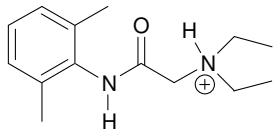



d)

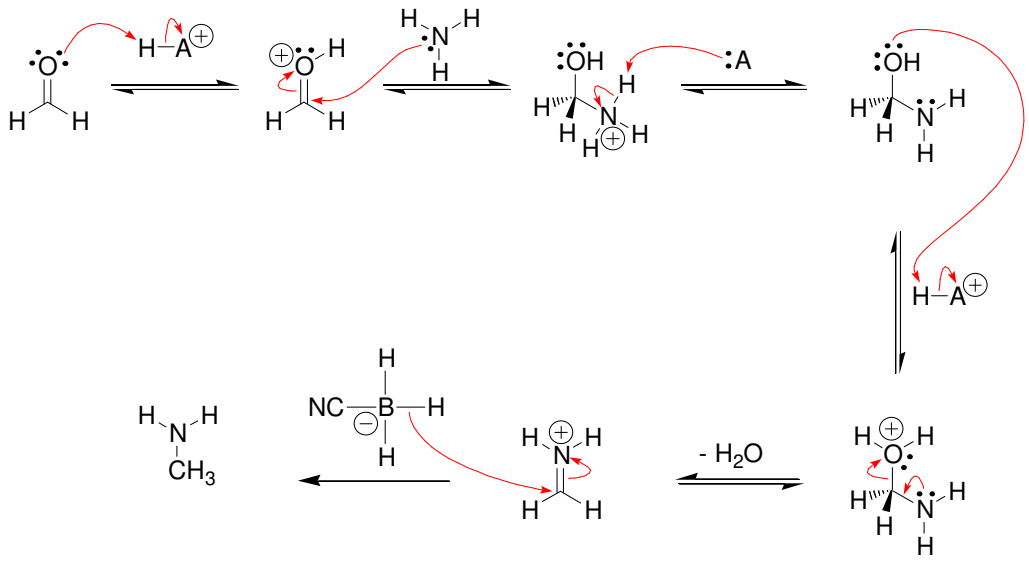



**23.52.** Aziridine has significant ring strain, which would increase significantly during pyramidal inversion. This provides a significant energy barrier that prevents pyramidal inversion at room temperature.

**23.53.**




**23.54.**



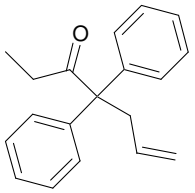
**23.55.** In acidic conditions, the amino group is protonated to give an ammonium ion. The ammonium group is a powerful deactivator and meta-director.

**23.56.**

a) The presence of the nitro group in the para position helps stabilize the conjugate base via resonance. As seen in chapter 19, this effect only occurs when the nitro group is in the ortho and para positions.

b) The basicity of *ortho*-nitroaniline should be closer in value to *para*-nitroaniline.

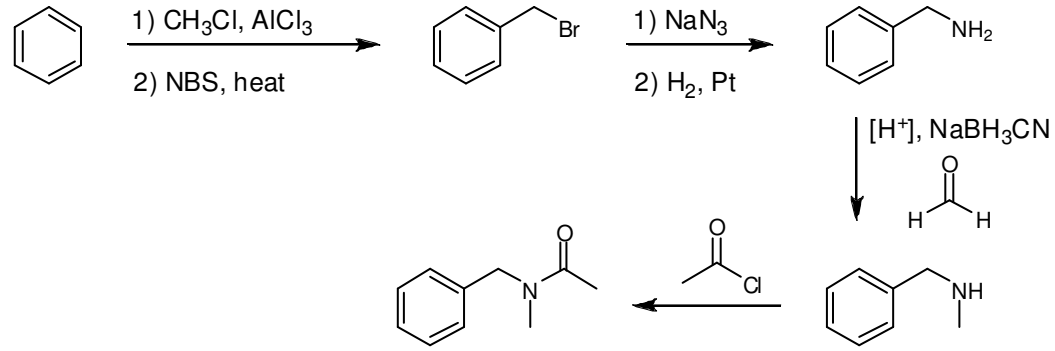
**23.57.**



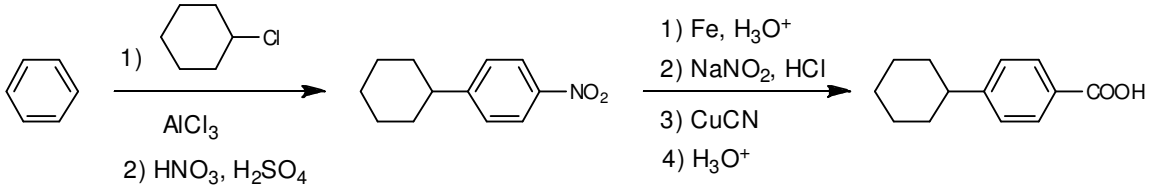

**23.58.** Protonation of the oxygen atom gives a resonance stabilized cation (as seen in chapter 20). In contrast, protonation of the nitrogen atom gives a cation that is not resonance stabilized.

**23.59.**

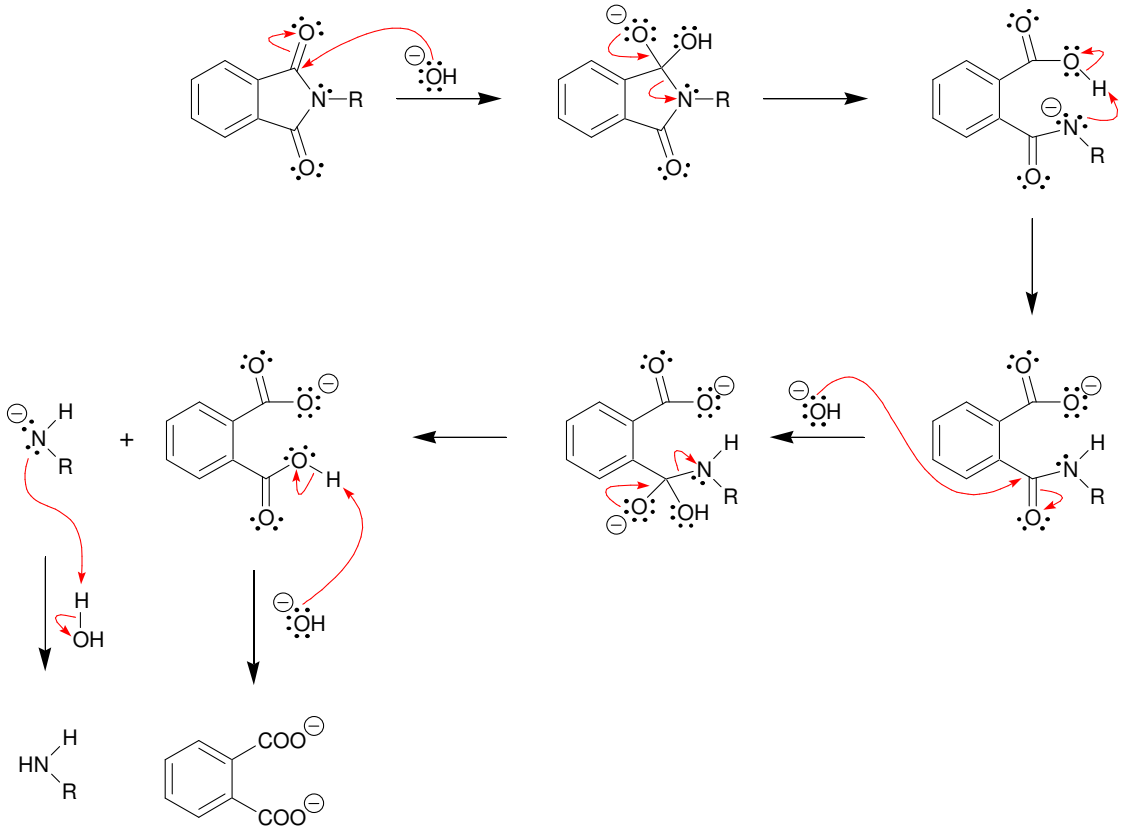
a)



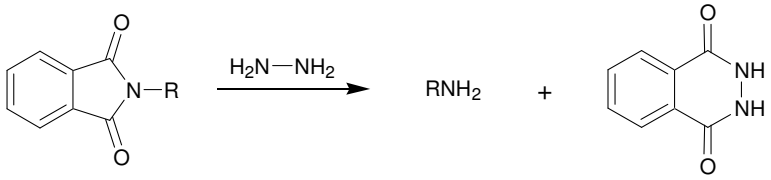

b)



**23.60.**

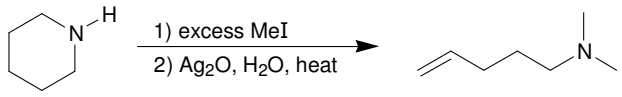


**23.61.**

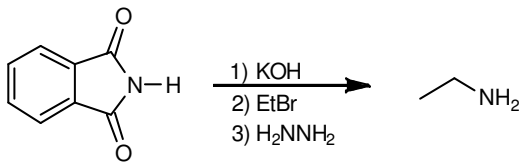



**23.62.**

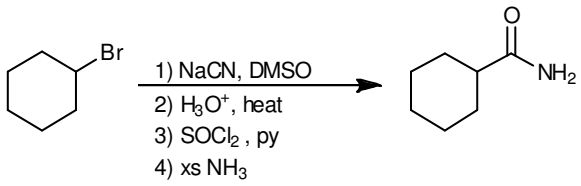
a)



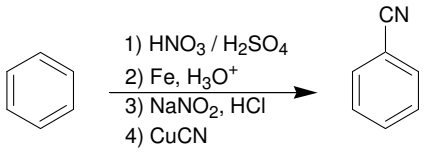

b)



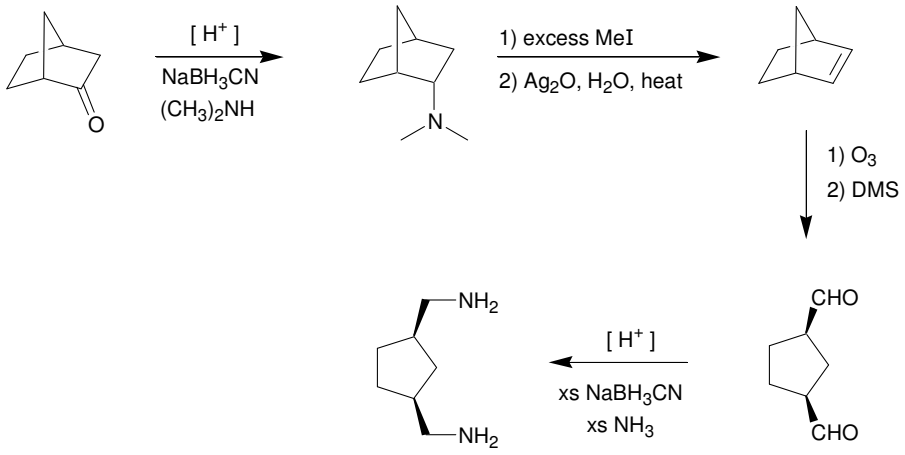
c)



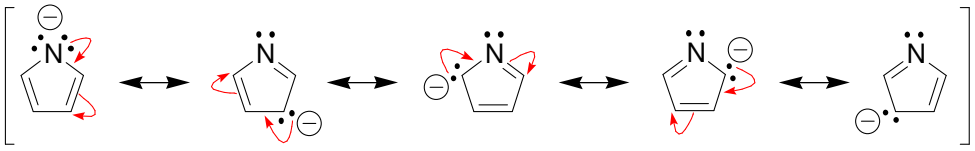

d)



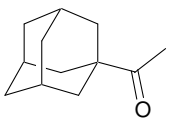

**23.63.**



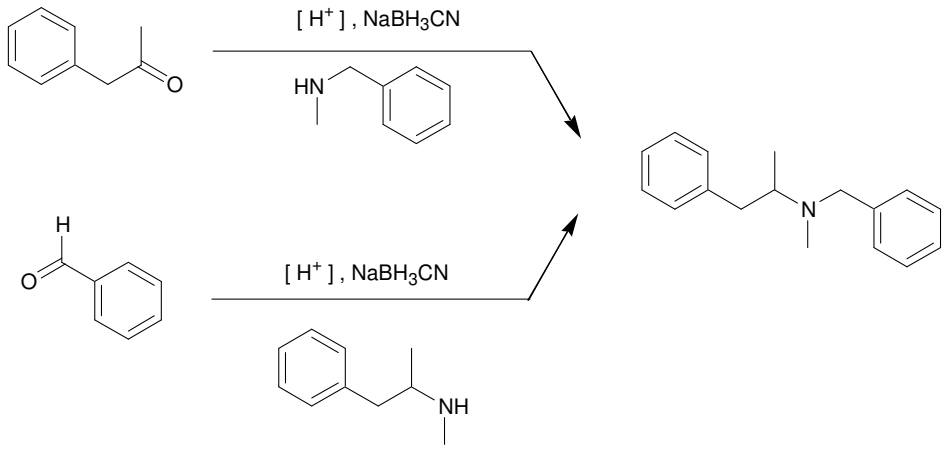

**23.64.** The conjugate base of pyrrole is highly stabilized because it is an aromatic anion and it is resonance stabilized, spreading the negative charge over all five atoms of the ring:



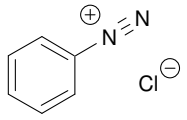

**23.65.**

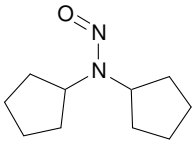


**23.66.**

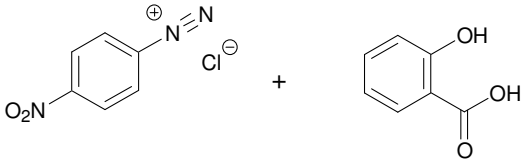



**23.67.**

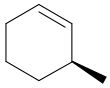
a) 

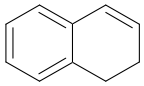

b) 


**23.68.**

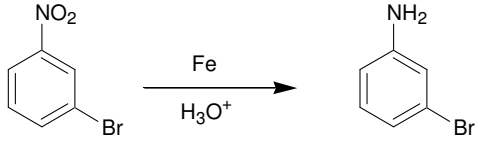



**23.69.**

a) 

b) 

**23.70.**

a) 

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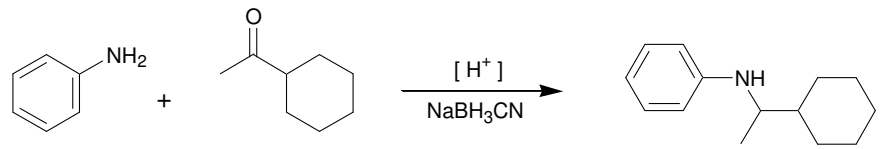
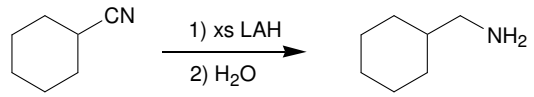
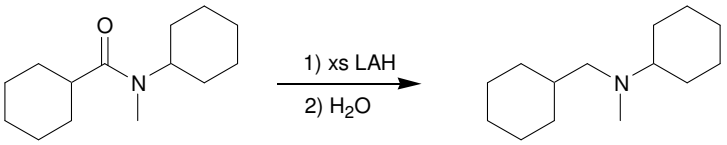



c)

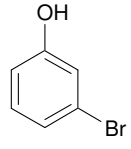



d)

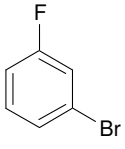



**23.71.**

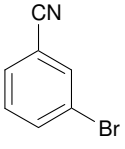
a)



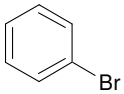

b)



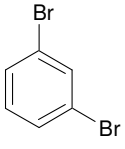

c)



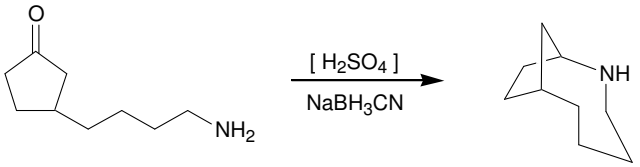

d)




e)

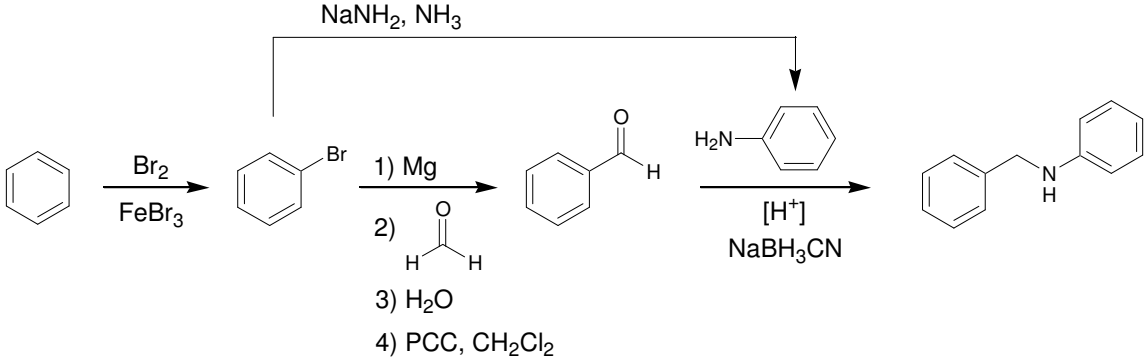



**23.72.**

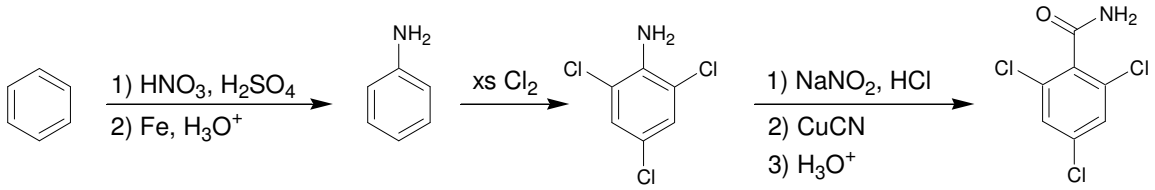



**23.73.**

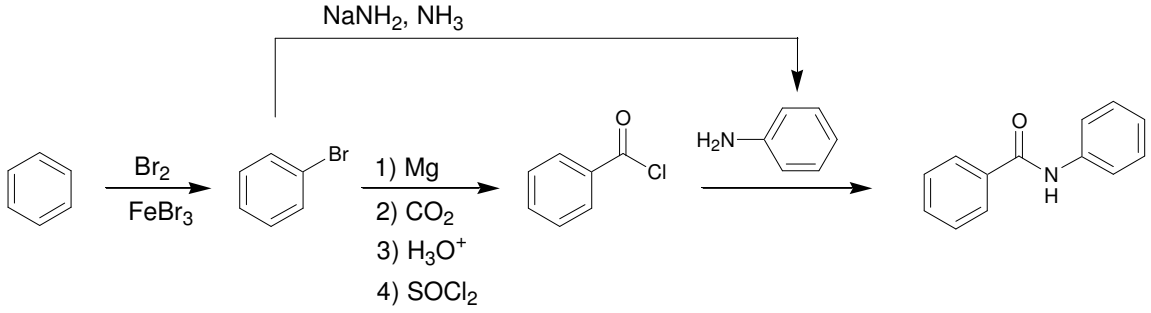
a)



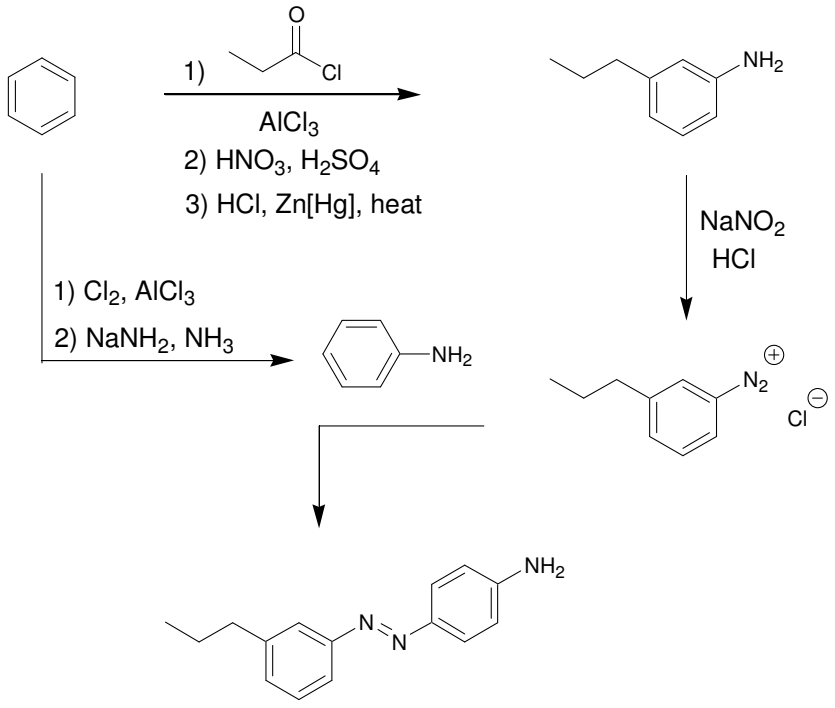
b)


1) HNO3, H2SO4
2) Fe, H3O+
NH2
xs Cl2
Cl
Cl
Cl
1) NaNO2, HCl
2) CuCN
3) H3O+
O
NH2
Cl
Cl
Cl

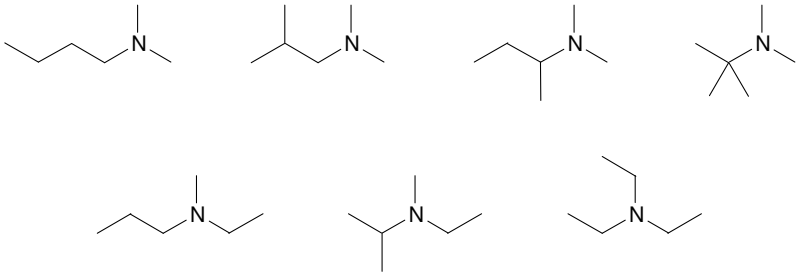
c)


NaNH2, NH3
Br2
FeBr3
Br
1) Mg
2) CO2
3) H3O+
4) SOCl2
O
Cl
H2N
O
N
H

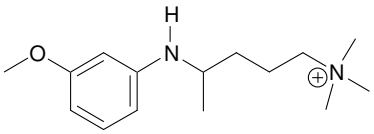
d)


O
1)
Cl
AlCl3
2) HNO3, H2SO4
3) HCl, Zn[Hg], heat
NH2
NaNO2
HCl
1) Cl2, AlCl3
2) NaNH2, NH3
NH2
N2
Cl
NH2
N
N

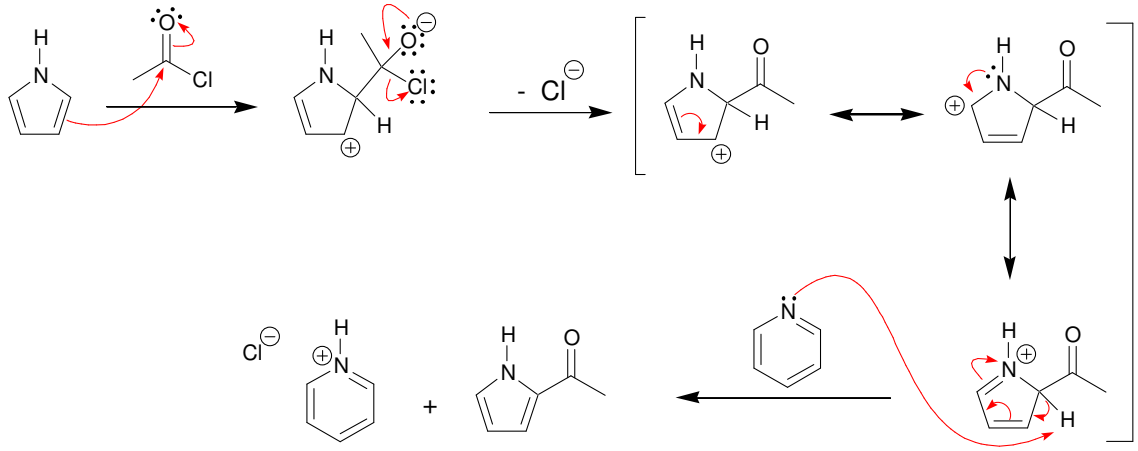
**23.74.** The IR data indicates that we are looking for structures that lack an N-H bond (i.e tertiary amines):



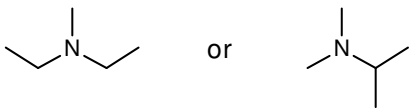
**23.75.**



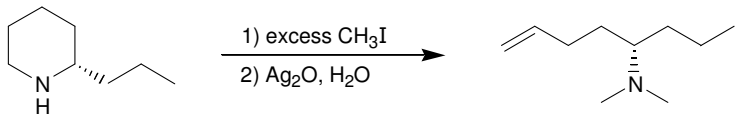
**23.76.**



**23.77.** The compound is a tertiary amine with the appropriate symmetry that provides for only three signals:

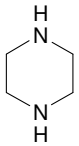


**23.78.**

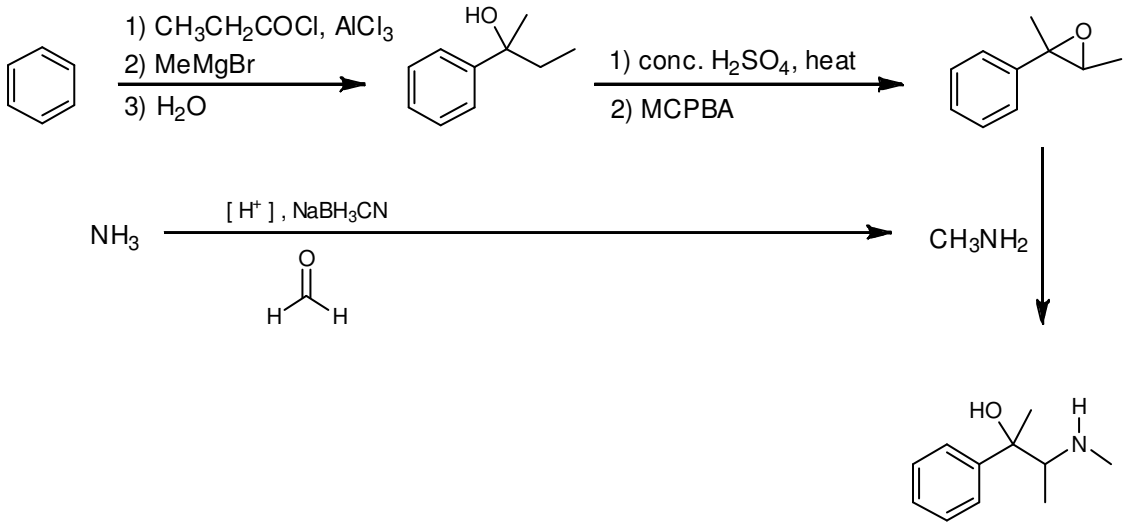


Coniine

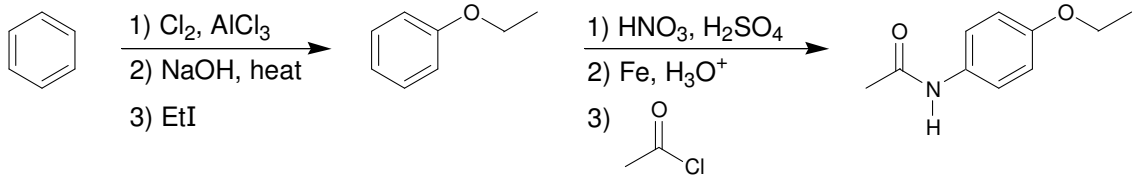
**23.79.**



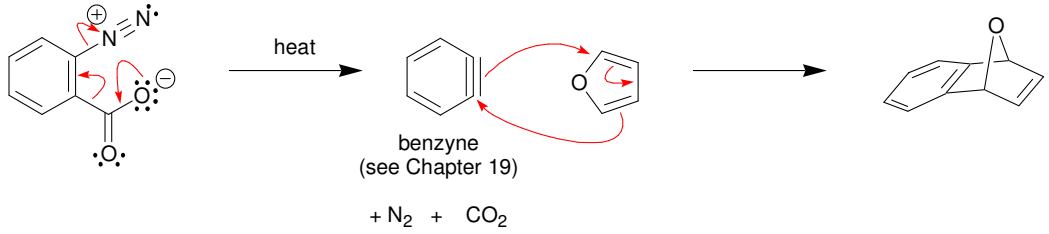
**23.80.**



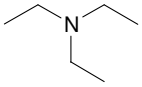

**23.81.**



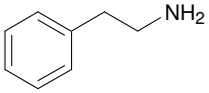

**23.82.**



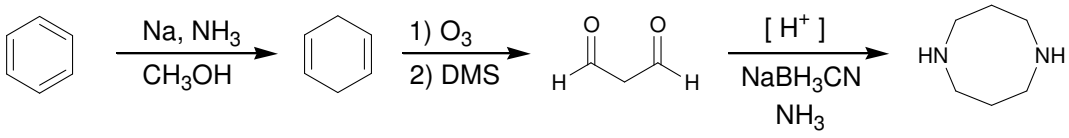
**23.83.**



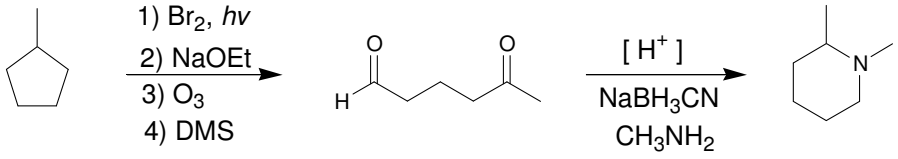

**23.84.**



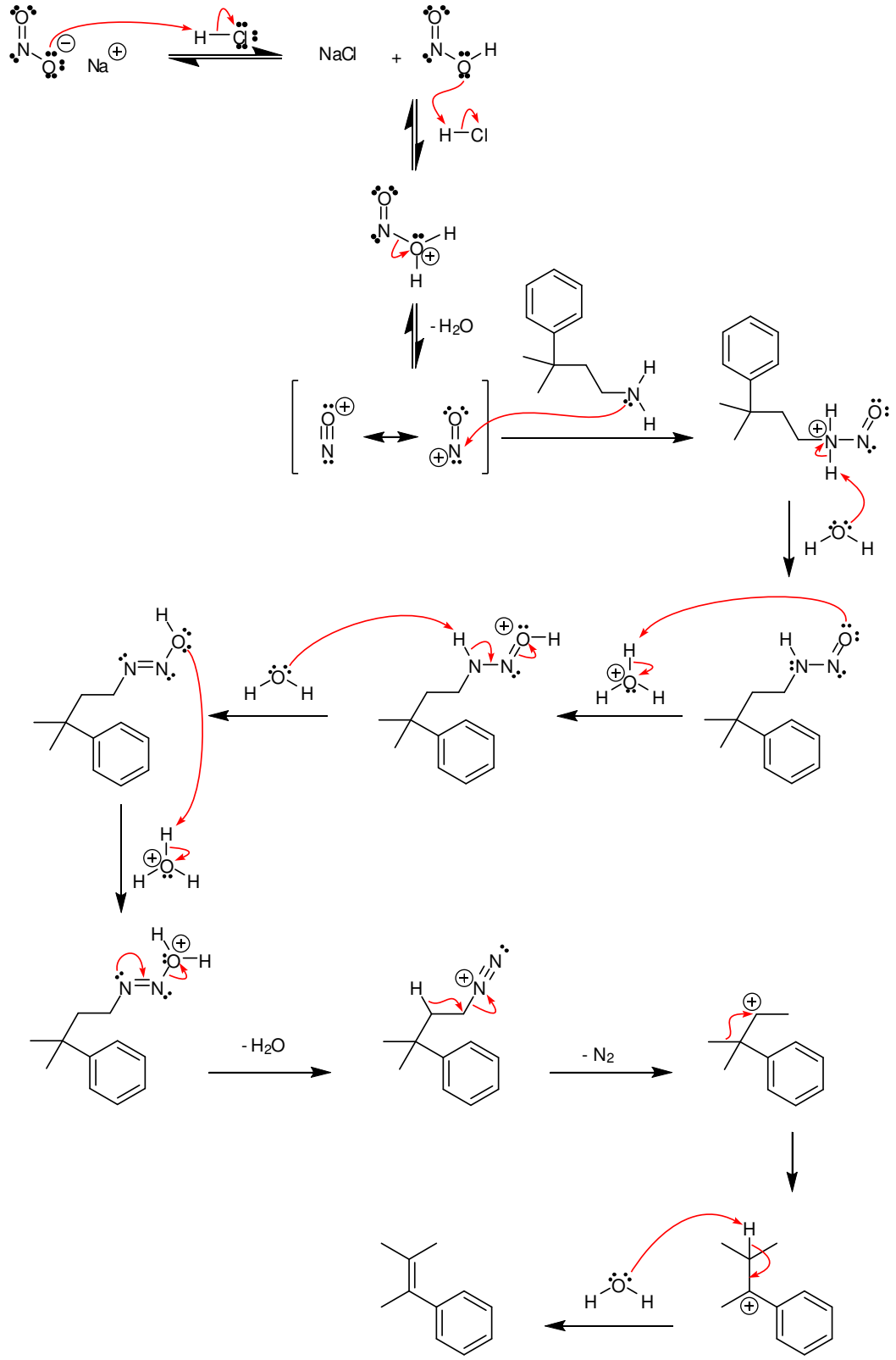

**23.85.**




**23.86.**



**23.87.**



**23.88.** Protonation of the nitrogen highlighted below results in a cation that is highly resonance stabilized. Protonation of either of the other nitrogen atoms would not result in a resonance stabilized cation: