Chapter 25: Amines

♦ General facts

- Amines are organic nitrogen compounds having the general structure RNH_2, R_2NH, or R_3N, with a lone pair of electrons on N (25.1).
- Amines are named using the suffix *-amine* (25.3).
- All amines have polar C–N bonds. Primary (1°) and 2° amines have polar N–H bonds and are capable of intermolecular hydrogen bonding (25.4).
- The lone pair on N makes amines strong organic bases and nucleophiles (25.8).

♦ Summary of spectroscopic absorptions (25.5)

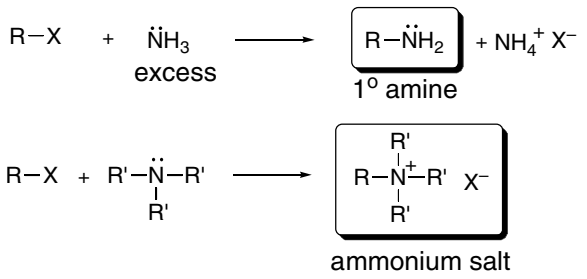
Mass spectra	Molecular ion	Amines with an odd number of N atoms give an odd molecular ion.
IR absorptions	N–H	3300–3500 cm^{-1} (two peaks for RNH_2, one peak for R_2NH)
^{1}H NMR absorptions	NH	0.5–5 ppm (no splitting with adjacent protons)
	CH–N	2.3–3.0 ppm (deshielded Csp^3–H)
^{13}C NMR absorption	C–N	30–50 ppm

♦ Comparing the basicity of amines and other compounds (25.10)

- Alkylamines (RNH_2, R_2NH, and R_3N) are more basic than NH_3 because of the electron-donating R groups (25.10A).
- Alkylamines (RNH_2) are more basic than arylamines ($C_6H_5NH_2$), which have a delocalized lone pair from the N atom (25.10B).
- Arylamines with electron-donor groups are more basic than arylamines with electron-withdrawing groups (25.10B).
- Alkylamines (RNH_2) are more basic than amides ($RCONH_2$), which have a delocalized lone pair from the N atom (25.10C).
- Aromatic heterocycles with a localized electron pair on N are more basic than those with a delocalized lone pair from the N atom (25.10D).
- Alkylamines with a lone pair in an sp^3 hybrid orbital are more basic than those with a lone pair in an sp^2 hybrid orbital (25.10E).

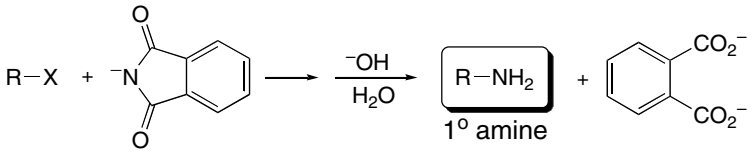
♦ Preparation of amines (25.7)

[1] Direct nucleophilic substitution with NH_3 and amines (25.7A)



- The mechanism is S_N2.
- The reaction works best for CH_3X or RCH_2X.
- The reaction works best to prepare 1° amines and ammonium salts.

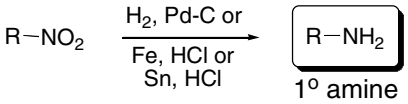
[2] Gabriel synthesis (25.7A)



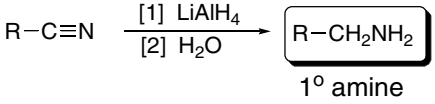
- The mechanism is S_N2.
- The reaction works best for CH_3X or RCH_2X.
- Only 1° amines can be prepared.

[3] Reduction methods (25.7B)

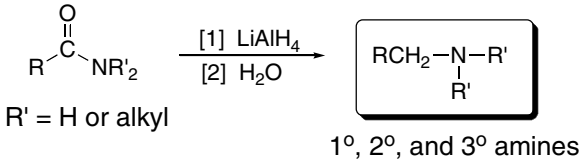
[a] From nitro compounds



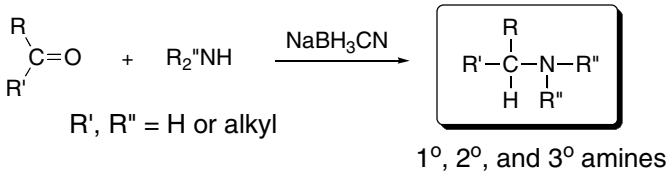
[b] From nitriles



[c] From amides



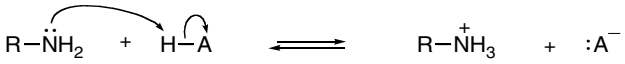
[4] Reductive amination (25.7C)



- Reductive amination adds one alkyl group (from an aldehyde or ketone) to a nitrogen nucleophile.
- Primary (1°), 2°, and 3° amines can be prepared.

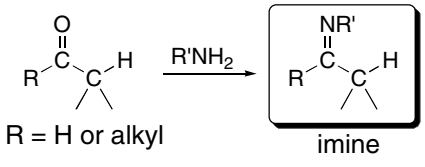
♦ Reactions of amines

[1] Reaction as a base (25.9)

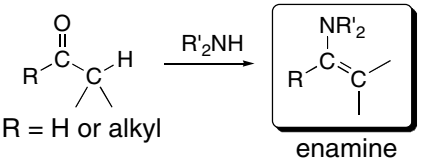


[2] Nucleophilic addition to aldehydes and ketones (25.11)

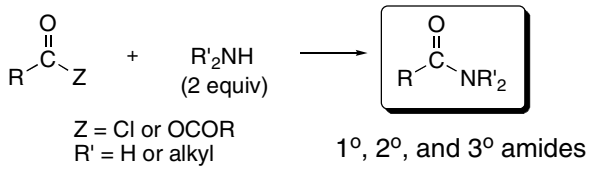
With 1° amines:



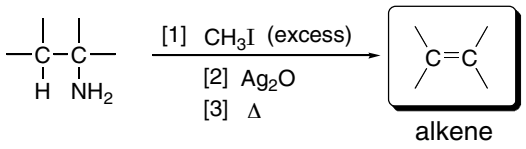
With 2° amines:



[3] Nucleophilic substitution with acid chlorides and anhydrides (25.11)



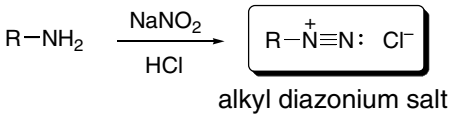
[4] Hofmann elimination (25.12)



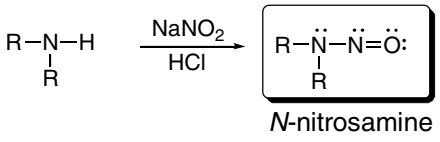
- The less substituted alkene is the major product.

[5] Reaction with nitrous acid (25.13)

With 1° amines:

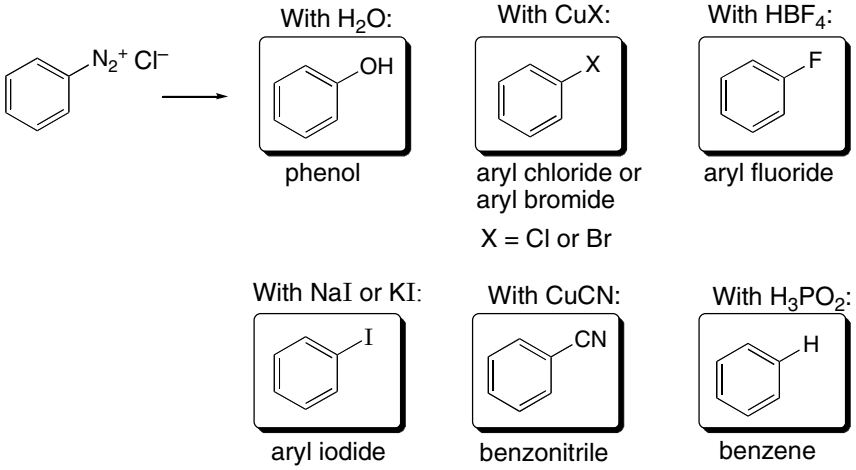


With 2° amines:

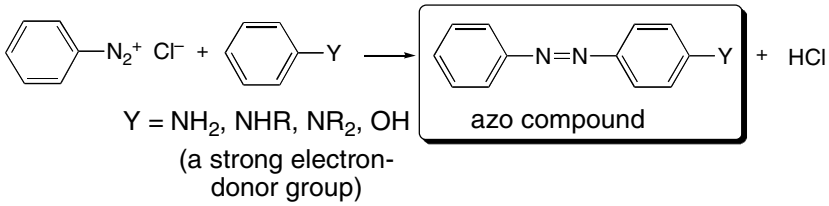


♦ Reactions of diazonium salts

[1] Substitution reactions (25.14)

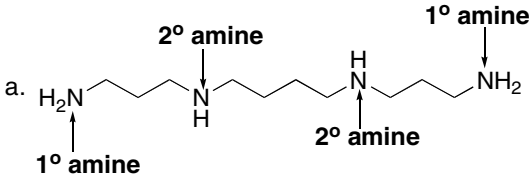


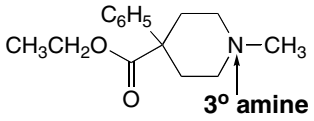
[2] Coupling to form azo compounds (25.15)



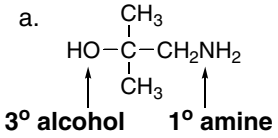
Chapter 25: Answers to Problems

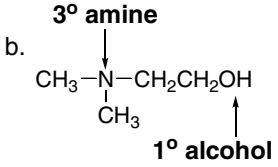
25.1 Amines are classified as 1°, 2°, or 3° by the number of alkyl groups bonded to the *nitrogen* atom.

a. 

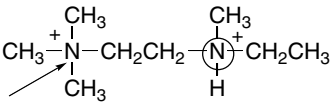
b. 

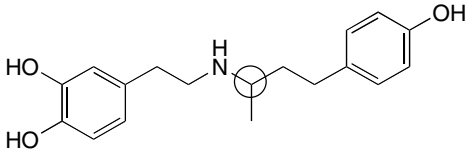
25.2

a. 

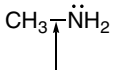
b. 

25.3 The N atom of a quaternary ammonium salt is a stereogenic center when the N is surrounded by four different groups. All stereogenic centers are circled.

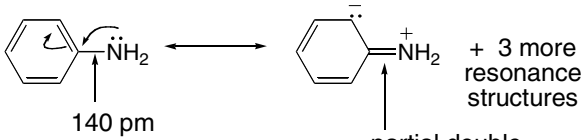
a. 
N has 3 similar groups.

b. 

25.4


147 pm

The C–N bond is formed from two sp^3 hybridized atoms and the lone pair is localized on N.

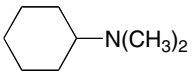


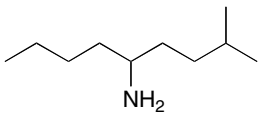
Because the lone pair on N can be delocalized on the benzene ring, the C–N bond has partial double bond character, making it shorter. Both the C and N atoms must be sp^2 hybridized (+ have a *p* orbital) for delocalization to occur. The higher percent *s*-character of the orbitals of both C and N shortens the bond as well.

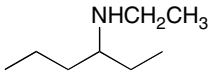
25.5

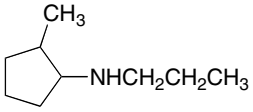
a. $CH_3CH_2CH(NH_2)CH_3$
2-butanamine
or
sec-butylamine

b. $(CH_3CH_2CH_2CH_2)_2NH$
dibutylamine

c. 
N,N-dimethylcyclohexanamine

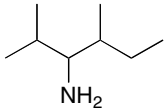
d. 
2-methyl-5-nonanamine

e. 
N-ethyl-3-hexanamine

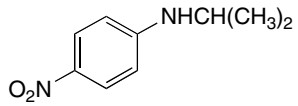
f. 
2-methyl-*N*-propylcyclopentanamine

25.6 An **NH_2** group named as a substituent is called an **amino group**.

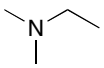
a. 2,4-dimethyl-3-hexanamine



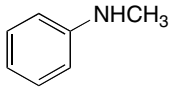
c. *N*-isopropyl-*p*-nitroaniline



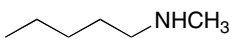
e. *N,N*-dimethylethylamine



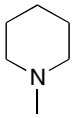
g. *N*-methylaniline



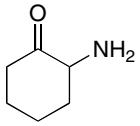
b. *N*-methylpentylamine



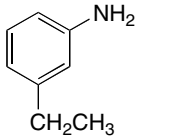
d. *N*-methylpiperidine



f. 2-aminocyclohexanone

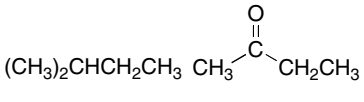


h. *m*-ethylaniline

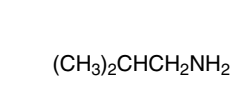


25.7 Primary (1°) and 2° amines have higher bp's than similar compounds (like ethers) incapable of hydrogen bonding, but lower bp's than alcohols that have stronger intermolecular hydrogen bonds. Tertiary amines (3°) have lower boiling points than 1° and 2° amines of comparable molecular weight because they have no N–H bonds.

a.



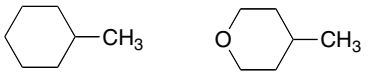
alkane
lowest boiling point



ketone
intermediate boiling point

amine
N–H can hydrogen bond.
highest boiling point

b.



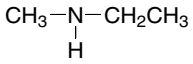
alkane
lowest boiling point

ether
intermediate boiling point

amine
N–H can hydrogen bond.
highest boiling point

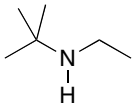
25.8 1° Amines show *two* N–H absorptions at 3300–3500 cm^{-1}. 2° Amines show *one* N–H absorption at 3300–3500 cm^{-1}.

molecular weight = 59
one IR peak = 2° amine

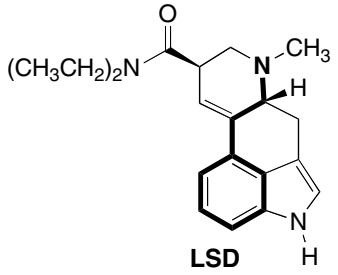


25.9 **The NH signal occurs between 0.5 and 5.0 ppm.** The protons on the carbon bonded to the amine nitrogen are deshielded and typically absorb at 2.3–3.0 ppm. The NH protons are not split.

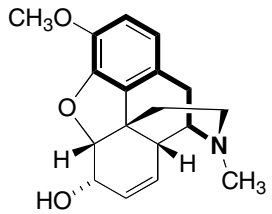
molecular formula $C_6H_{15}N$
^1H NMR absorptions (ppm):
- 0.9 (singlet, 1 H) ⟶ NH
- 1.10 (triplet, 3 H) ⟶ CH_3 adjacent to CH_2
- 1.15 (singlet, 9 H) ⟶ $(CH_3)_3C$
- 2.6 (quartet, 2 H) ⟶ CH_2 adjacent to CH_3



25.10 The atoms of 2-phenylethylamine are in bold.

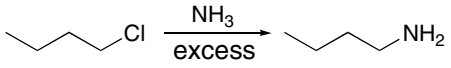
a. 

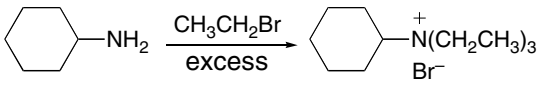
LSD
lysergic acid diethyl amide

b. 

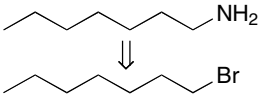
codeine

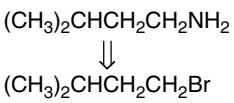
25.11 S_N2 reaction of an alkyl halide with NH_3 or an amine forms an amine or an ammonium salt.

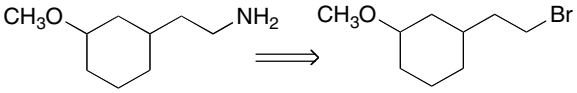
a. 

b. 

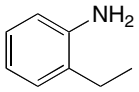
25.12 The Gabriel synthesis converts an alkyl halide into a 1° amine by a two-step process: nucleophilic substitution followed by hydrolysis.

a. 

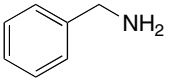
b. 

c. 

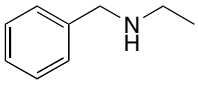
25.13 The Gabriel synthesis prepares 1° amines from alkyl halides. Since the reaction proceeds by an S_N2 mechanism, the halide must be CH_3 or 1°, and X can't be bonded to an sp^2 hybridized C.

a. 

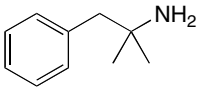
aromatic
An S_N2 does not occur on an aryl halide.
cannot be made by Gabriel synthesis

b. 

can be made by Gabriel synthesis

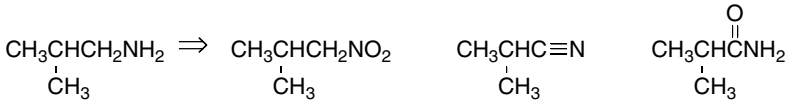
c. 

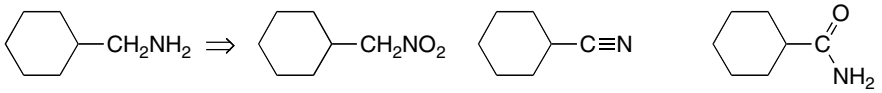
2° amine
cannot be made by Gabriel synthesis

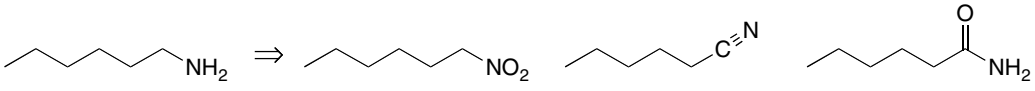
d. 

N on 3° C
An S_N2 does not occur on a 3° RX.
cannot be made by Gabriel synthesis

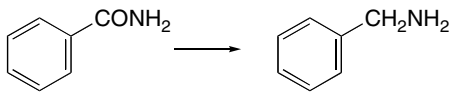
25.14 **Nitriles are reduced to 1° amines with $LiAlH_4$. Nitro groups are reduced to 1° amines** using a variety of reducing agents. **Primary (1°), 2°, and 3° amides are reduced to 1°, 2°, and 3° amines** respectively, using $LiAlH_4$.

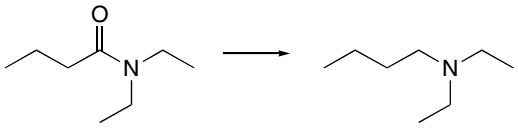
a. 

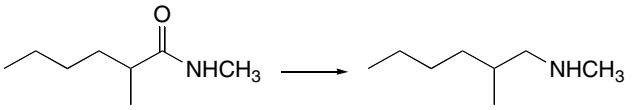
b. 

c. 

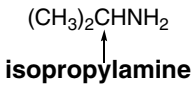
25.15 **Primary (1°), 2°, and 3° amides are reduced to 1°, 2°, and 3° amines** respectively, using $LiAlH_4$.

a. 

b. 

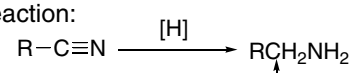
c. 

25.16



isopropylamine

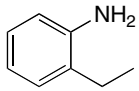
General reaction:



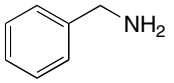
The amine needs 2 H's here.

The C bonded to the N must have 2 H's for the amine to be formed by reduction of a nitrile.

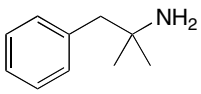
25.17 Only amines with a CH_2 or CH_3 bonded to the N can be made by reduction of an amide.

a. 

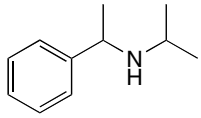
N bonded to benzene cannot be made by reduction of an amide

b. 

N bonded to CH_2 can be made by reduction of an amide

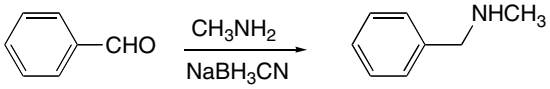
c. 

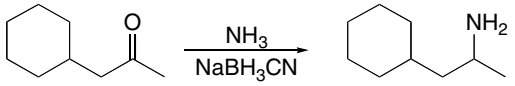
N bonded to a 3° C cannot be made by reduction of an amide

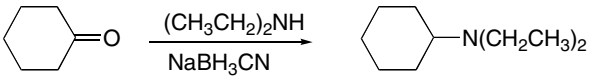
d. 

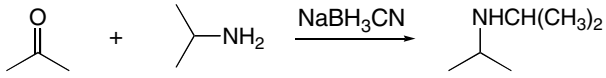
N on 2° C on both sides cannot be made by reduction of an amide

25.18 Reductive amination is a two-step method that converts aldehydes and ketones into 1°, 2°, and 3° amines. Reductive amination replaces a C=O by a C–H and C–N bond.

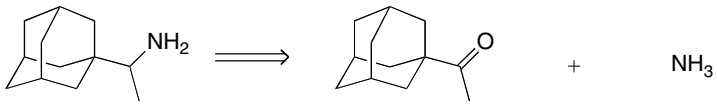
a. 

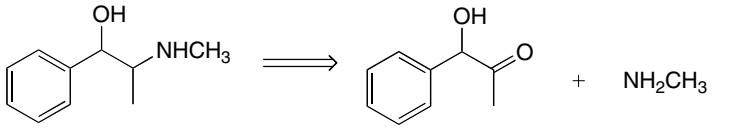
b. 

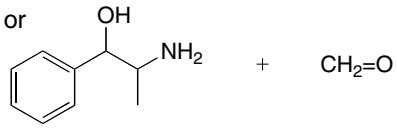
c. 

d. 

25.19

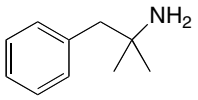
a. 

b. 

or 

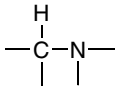
25.20

a.



phentermine

Only amines that have a C bonded to a H and N atom can be made by reductive amination; that is, an amine must have the following structural feature:



In phentermine, the C bonded to N is not bonded to a H, so it cannot be made by reductive amination.

b. systematic name: 2-methyl-1-phenyl-2-propanamine

25.21 The pK_a of many protonated amines is 10–11, so the pK_a of the starting acid must be **less than 10** for equilibrium to favor the products. Amines are thus readily protonated by strong inorganic acids like HCl and H_2SO_4, and by carboxylic acids as well.

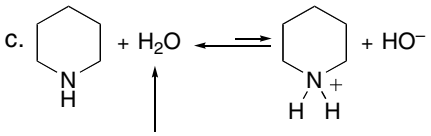
a. $CH_3CH_2CH_2CH_2{-}NH_2 + HCl \rightleftharpoons CH_3CH_2CH_2CH_2{-}\overset{+}{N}H_3 + Cl^-$

pK_a = –7 p$K_a \approx$ 10 weaker acid products favored

b. $C_6H_5COOH + (CH_3)_2NH \rightleftharpoons (CH_3)_2\overset{+}{N}H_2 + C_6H_5COO^-$

pK_a = 4.2 pK_a = 10.7 weaker acid products favored

c.

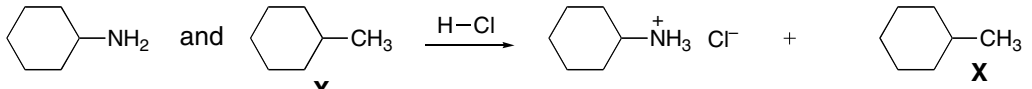


pK_a = 15.7 weaker acid reactants favored p$K_a \approx$ 10

25.22 An amine can be separated from other organic compounds by converting it to a water-soluble ammonium salt by an acid–base reaction. In each case, the extraction procedure would employ the following steps:

- Dissolve the amine and either **X** or **Y** in CH_2Cl_2.
- Add a solution of 10% HCl. The amine will be protonated and dissolve in the aqueous layer, while **X** or **Y** will remain in the organic layer as a neutral compound.
- Separate the layers.

a.



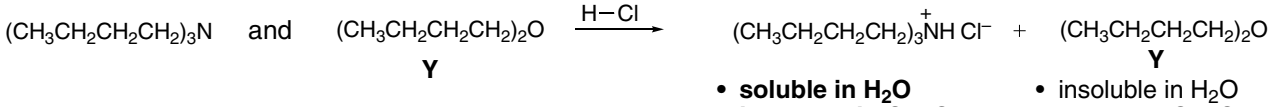
X

- **soluble in H_2O**
- **insoluble in CH_2Cl_2**

X

- insoluble in H_2O
- soluble in CH_2Cl_2

b.



Y

- **soluble in H_2O**
- **insoluble in CH_2Cl_2**

Y

- insoluble in H_2O
- soluble in CH_2Cl_2

25.23 Primary (1°), 2°, and 3° alkylamines are more basic than NH_3 because of the electron-donating inductive effect of the R groups.

a. $(CH_3)_2NH$ and NH_3

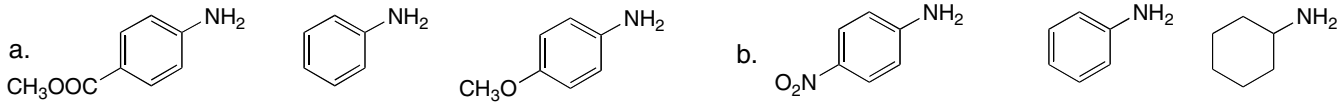
2° alkylamine
CH_3 groups are electron donating.
stronger base

b. $CH_3CH_2NH_2$ and $ClCH_2CH_2NH_2$

1° alkylamine
stronger base

1° alkylamine
Cl is electron withdrawing.
weaker base

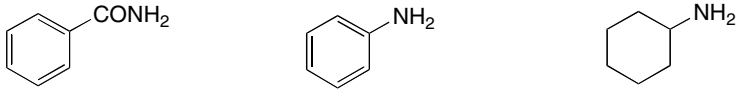
25.24 Arylamines are less basic than alkylamines because the electron pair on N is delocalized. Electron-donor groups add electron density to the benzene ring making the arylamine more basic than aniline. Electron-withdrawing groups remove electron density from the benzene ring, making the arylamine less basic than aniline.



a. electron-withdrawing group **least basic** | arylamine **intermediate basicity** | electron-donating group **most basic**

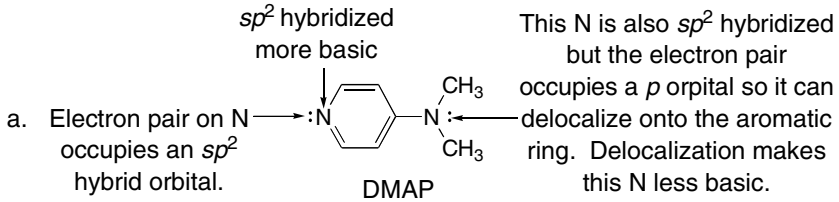
b. electron-withdrawing group **least basic** | arylamine **intermediate basicity** | alkylamine **most basic**

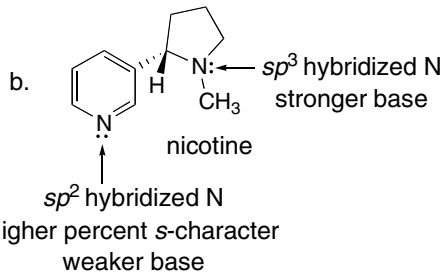
25.25 Amides are much less basic than amines because the electron pair on N is highly delocalized.



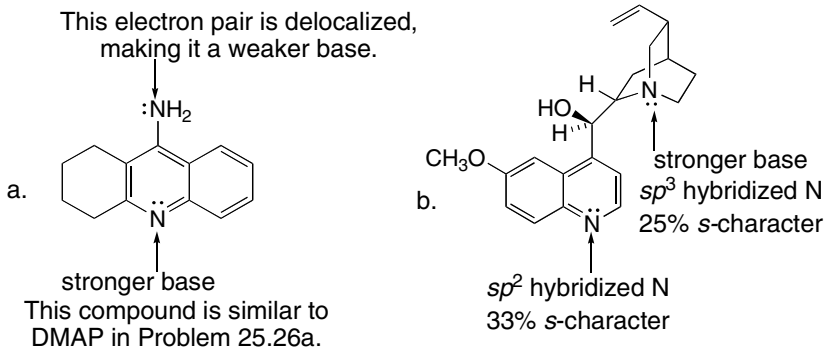
amide **least basic** | arylamine **intermediate basicity** | alkylamine **most basic**

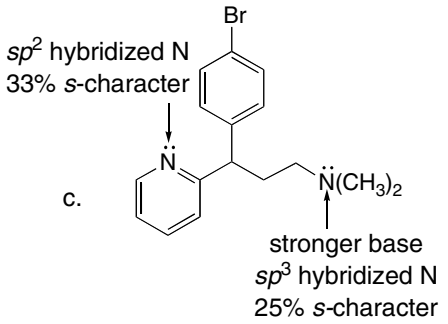
25.26



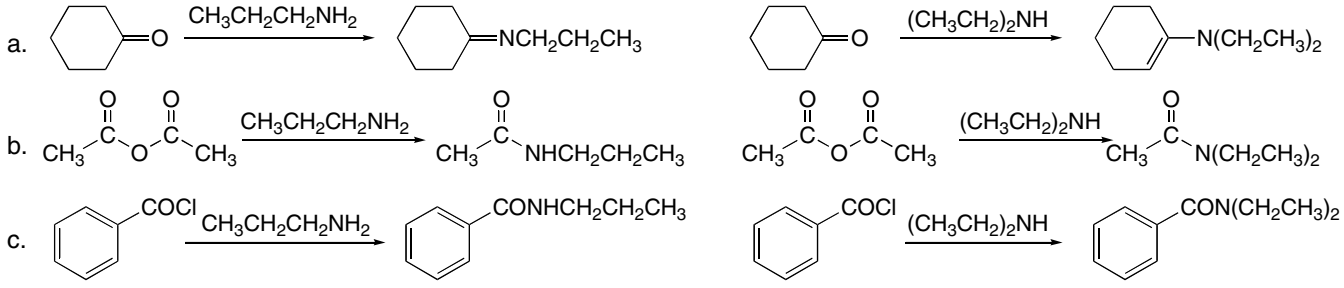


25.27

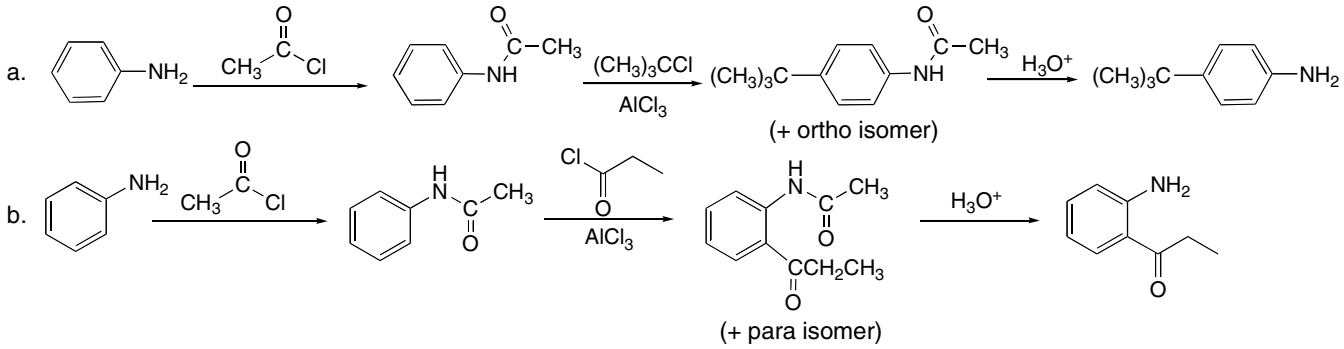




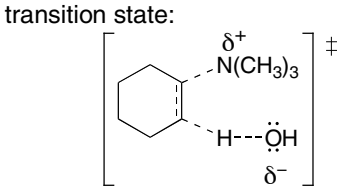
25.28 Amines attack carbonyl groups to form products of nucleophilic addition or substitution.



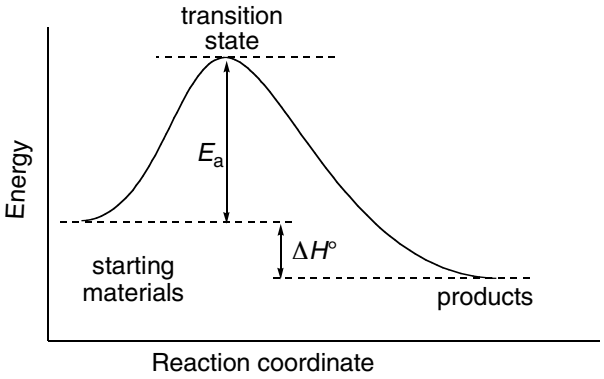
25.29 [1] Convert the amine (aniline) into an amide (acetanilide).
[2] **Carry out the Friedel–Crafts reaction.**
[3] **Hydrolyze the amide** to generate the free amino group.



25.30



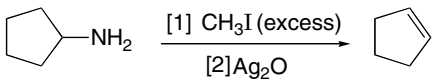
(no 3-D geometry shown here)



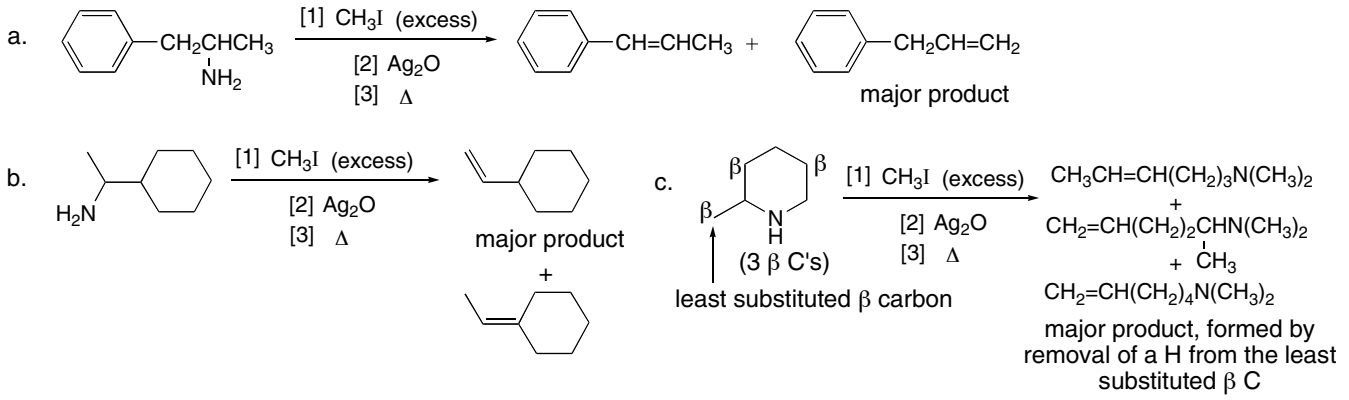
25.31

a. $CH_3CH_2CH_2CH_2{-}NH_2 \xrightarrow[[2]Ag_2O\ [3]\ \Delta]{[1]\ CH_3I\ (excess)} CH_3CH_2CH{=}CH_2$

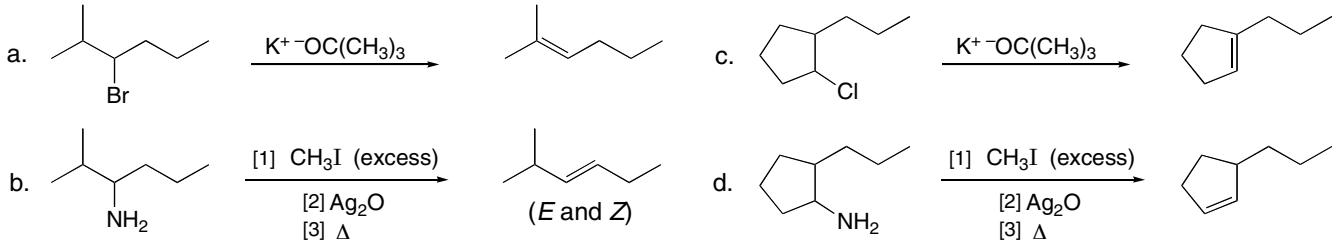
b. $(CH_3)_2CHNH_2 \xrightarrow[[2]Ag_2O\ [3]\ \Delta]{[1]\ CH_3I\ (excess)} CH_3CH{=}CH_2$

c. 

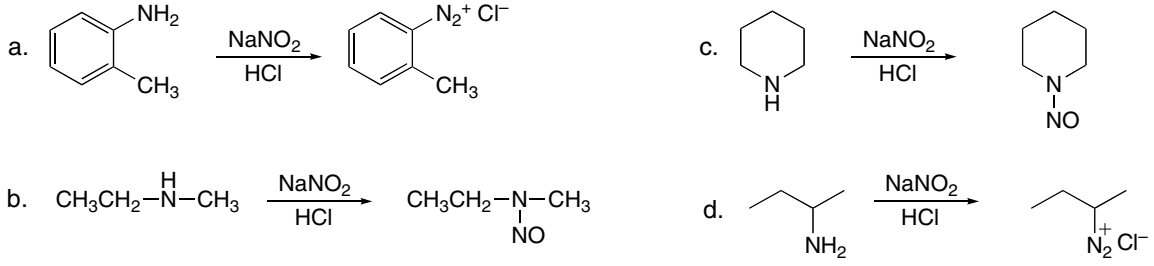
25.32 In a Hofmann elimination, the base removes a proton from the less substituted, more accessible β carbon atom, because of the bulky leaving group on the nearby α carbon.



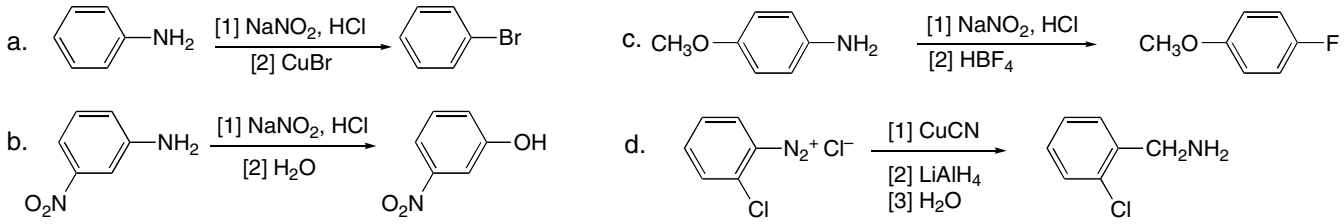
25.33



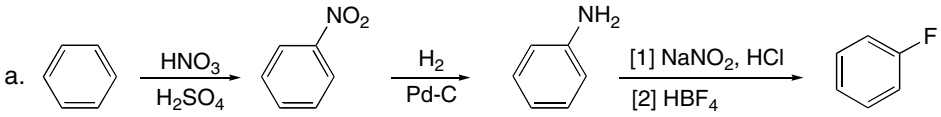
25.34

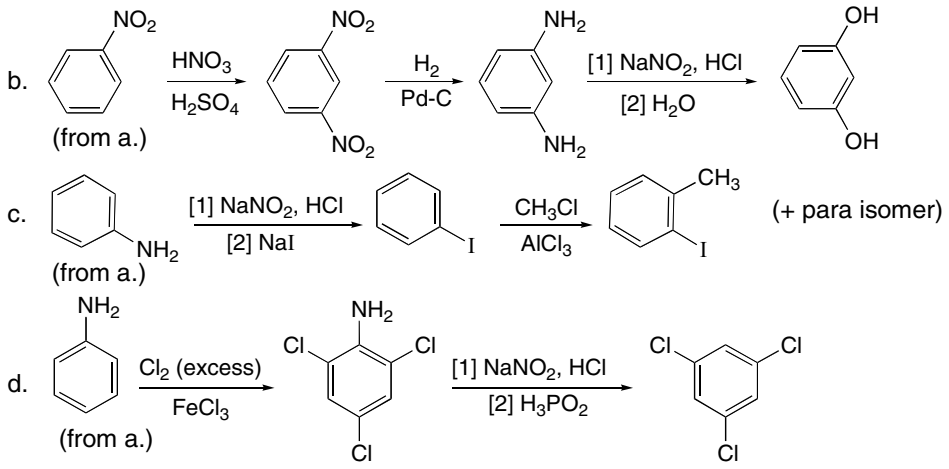


25.35

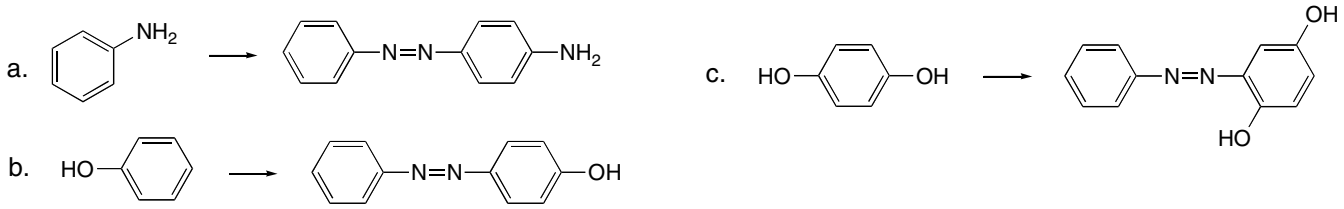


25.36

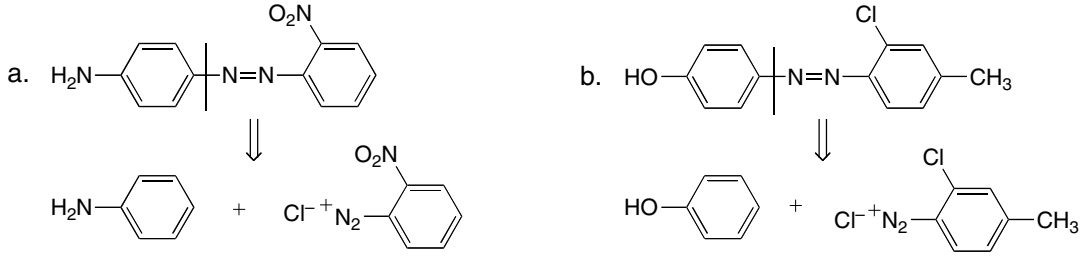




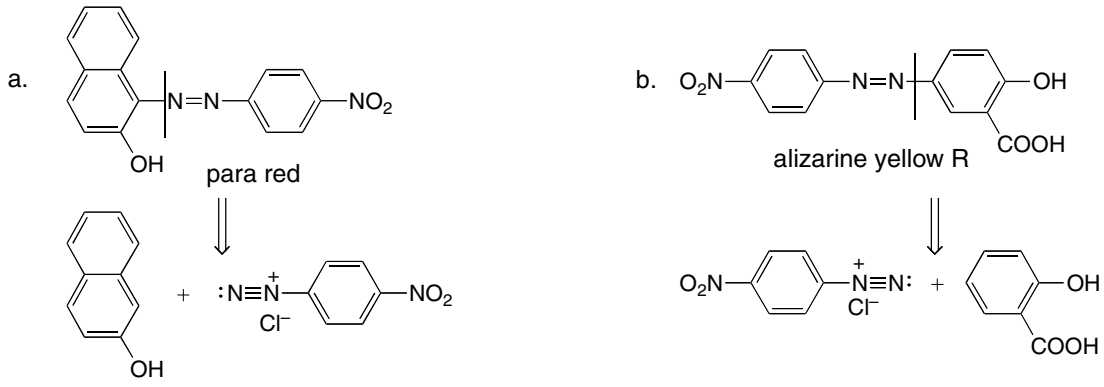
25.37



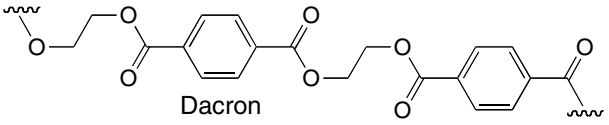
25.38 To determine what starting materials are needed to synthesize a particular azo compound, always divide the molecule into two components: **one has a benzene ring with a diazonium ion, and one has a benzene ring with a very strong electron-donor group.**



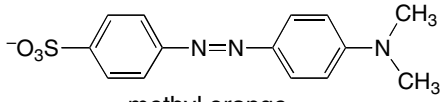
25.39



25.40



Dacron

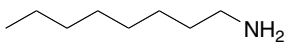


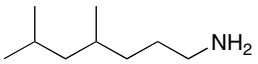
methyl orange

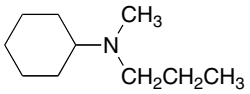
To bind to fabric, methyl orange (an anion) needs to interact with positively charged sites. Since Dacron is a neutral compound with no cationic sites on the chain, it does not bind methyl orange well.

25.41

a. $CH_3NHCH_2CH_2CH_2CH_3$
N-methyl-1-butanamine
(*N*-methylbutylamine)

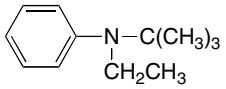
b. 
1-octanamine
(octylamine)

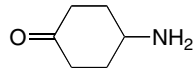
c. 
4,6-dimethyl-1-heptanamine

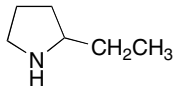
d. 
N-methyl-*N*-propylcyclohexanamine

e. $(CH_3CH_2CH_2)_3N$
tripropylamine

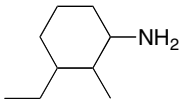
f. $(C_6H_5)_2NH$
diphenylamine

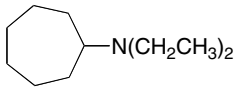
g. 
N-*tert*-butyl-*N*-ethylaniline

h. 
4-aminocyclohexanone

i. 
2-ethylpyrrolidine

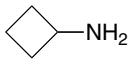
j. $CH_3CH_2CH_2CH(NH_2)CH(CH_3)_2$
2-methyl-3-hexanamine

k. 
3-ethyl-2-methylcyclohexanamine

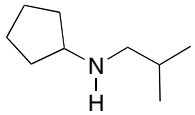
l. 
N,*N*-diethylcycloheptanamine

25.42

a. cyclobutylamine

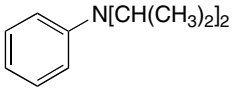


b. *N*-isobutylcyclopentylamine

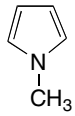


c. tri-*tert*-butylamine
$N[C(CH_3)_3]_3$

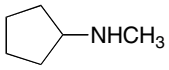
d. *N*,*N*-diisopropylaniline



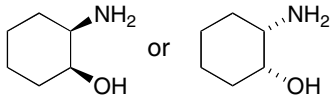
e. *N*-methylpyrrole



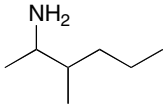
f. *N*-methylcyclopentylamine



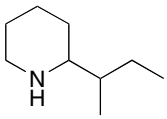
g. *cis*-2-aminocyclohexanol



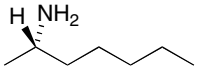
h. 3-methyl-2-hexanamine



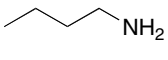
i. 2-*sec*-butylpiperidine

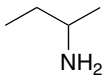


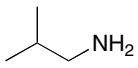
j. (2*S*)-2-heptanamine



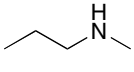
25.43

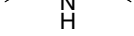

1-butanamine

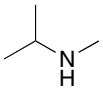

2-butanamine

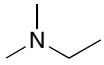

2-methyl-1-propanamine


2-methyl-2-propanamine

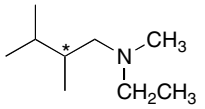

N-methyl-1-propanamine


diethylamine

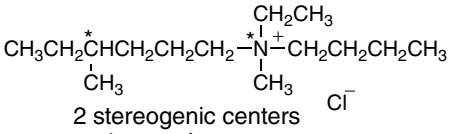

N-methyl-2-propanamine


N,*N*-dimethylethanamine

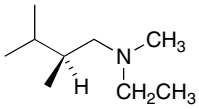
25.44 [* denotes a stereogenic center.]

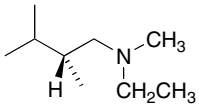
a. 

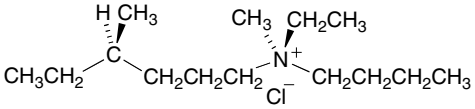
1 stereogenic center
2 stereoisomers

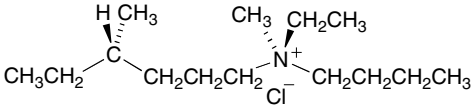
b. 

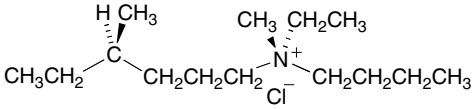
2 stereogenic centers
4 stereoisomers

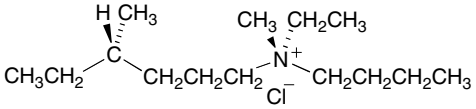












25.45

a. $(CH_3CH_2)_2NH$ or 

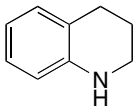
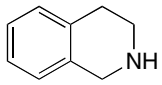
sp^3 hybridized N **stronger base** | sp^2 hybridized N **weaker base**

b. $HCON(CH_3)_2$ or $(CH_3)_3N$

amide **weaker base** | alkylamine **stronger base**

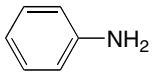
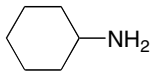
c. $(CH_3CH_2)_2NH$ or $(ClCH_2CH_2)_2NH$

2° alkylamine **stronger base** | 2° alkylamine Cl is electron withdrawing. **weaker base**

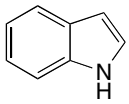
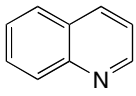
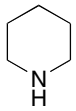
d.  or 

weaker base (delocalized electron pair on N) | **stronger base**

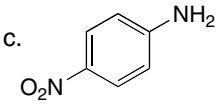
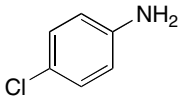
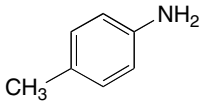
25.46

a.  NH_3 

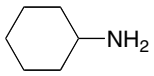
arylamine **least basic** | **intermediate basicity** | alkylamine **most basic**

b.   

delocalized electron pair on N **least basic** | sp^2 hybridized N **intermediate basicity** | sp^3 hybridized N **most basic**

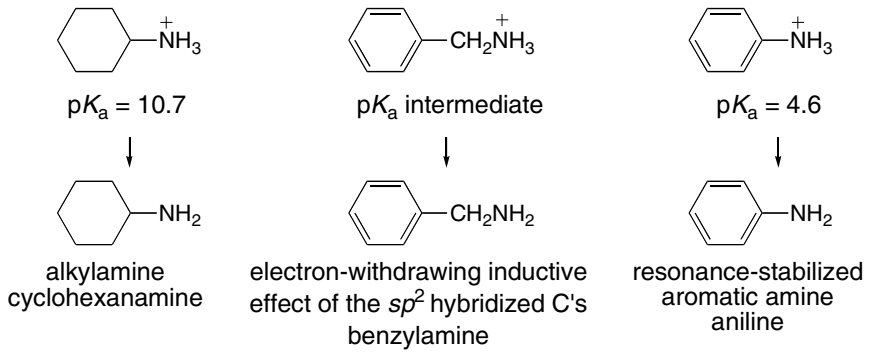
c.   

electron-withdrawing group **least basic** | **intermediate basicity** | electron-donating group **most basic**

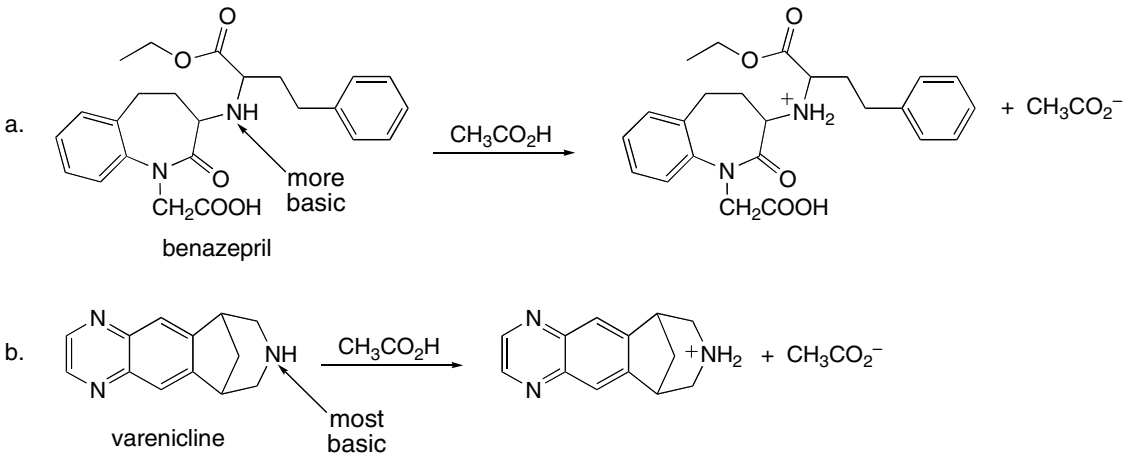
d. $(C_6H_5)_2NH$ $C_6H_5NH_2$ 

diarylamine **least basic** | arylamine **intermediate basicity** | alkylamine **most basic**

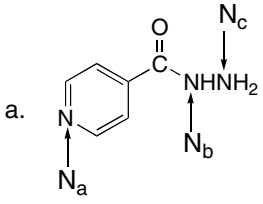
25.47 The electron-withdrawing inductive effect of the phenyl group stabilizes benzylamine, making its conjugate acid more acidic than the conjugate acid of cyclohexanamine. The conjugate acid of aniline is more acidic than the conjugate acid of benzylamine, since loss of a proton generates a resonance-stabilized amine, $C_6H_5NH_2$.



25.48 The most basic N atom is protonated on treatment with acid.



25.49



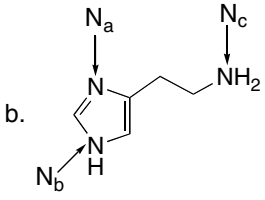
$N_b < N_a < N_c$

Order of basicity: $N_b < N_a < N_c$

N_b – The electron pair on this N atom is delocalized on the O atom; least basic.

N_a – The electron pair on this N atom is not delocalized, but is on an sp^2 hybridized atom.

N_c – The electron pair on this N atom is on an sp^3 hybridized N; most basic.



$N_b < N_a < N_c$

Order of basicity: $N_b < N_a < N_c$

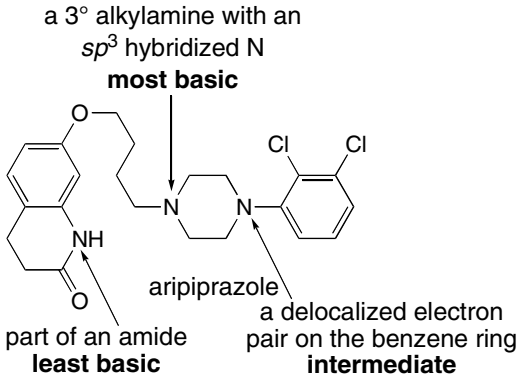
N_b – The electron pair on this N atom is delocalized on the aromatic five-membered ring; least basic.

N_a – The electron pair on this N atom is not delocalized, but is on an sp^2 hybridized atom.

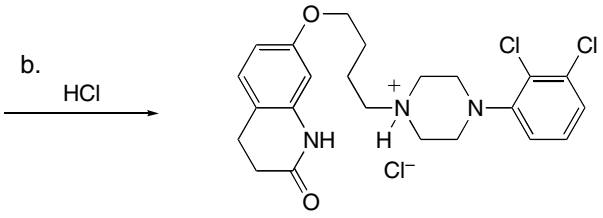
N_c – The electron pair on this N atom is on an sp^3 hybridized N; most basic.

25.50 The most basic N atom is protonated on treatment with acid.

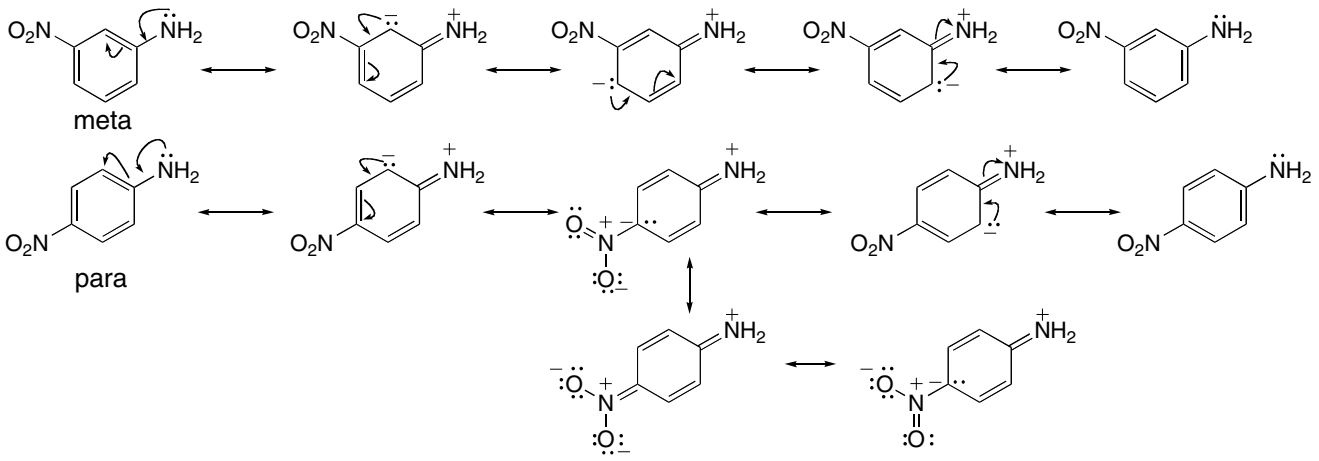
a.



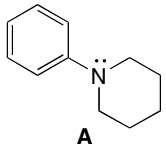
b.



25.51 The para isomer is the weaker base because the electron pair on its NH_2 group can be delocalized onto the NO_2 group. In the meta isomer, no resonance structure places the electron pair on the NO_2 group, and fewer resonance structures can be drawn:

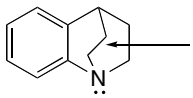


25.52



A

pK_a of the conjugate acid = 5.2
stronger conjugate acid
weaker base
The electron pair of this arylamine is delocalized on the benzene ring, decreasing its basicity.

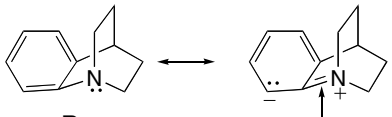


This two-carbon bridge makes it difficult for the lone pair on N to delocalize on the aromatic ring.

B

pK_a of the conjugate acid = 7.29
weaker conjugate acid
stronger base

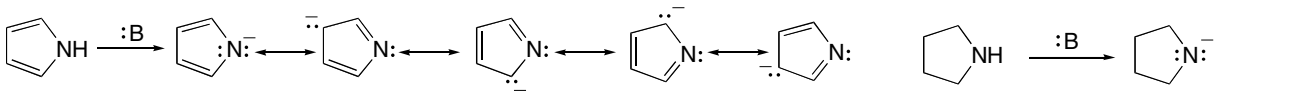
Resonance structures that place a double bond between the N atom and the benzene ring are destabilized. Since the electron pair is more localized on N, compound **B** is more basic.



B

Geometry makes it difficult to have a double bond here.

25.53



pyrrole
pK_a = 23
stronger acid

weaker conjugate base
The electron pair is delocalized, decreasing the basicity. The N atom is sp^2 hybridized.

pyrrolidine
pK_a = 44
weaker acid

stronger conjugate base
The electron pair is not delocalized on the ring. The N atom is sp^3 hybridized.

25.54

a. $C_6H_5CH_2CH_2CH_2Br \xrightarrow[\text{excess}]{NH_3} C_6H_5CH_2CH_2CH_2NH_2$

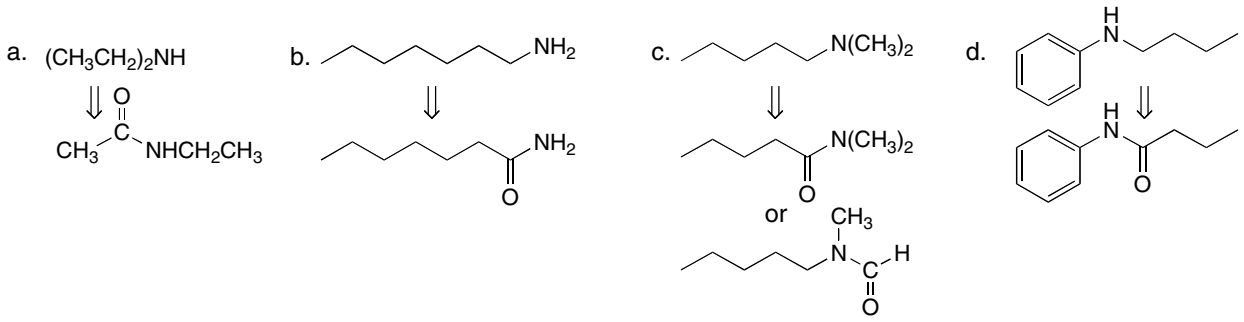
b. $C_6H_5CH_2CH_2Br \xrightarrow{NaCN} C_6H_5CH_2CH_2CN \xrightarrow[[2]\ H_2O]{[1]\ LiAlH_4} C_6H_5CH_2CH_2CH_2NH_2$

c. $C_6H_5CH_2CH_2CH_2NO_2 \xrightarrow[Pd\text{-}C]{H_2} C_6H_5CH_2CH_2CH_2NH_2$

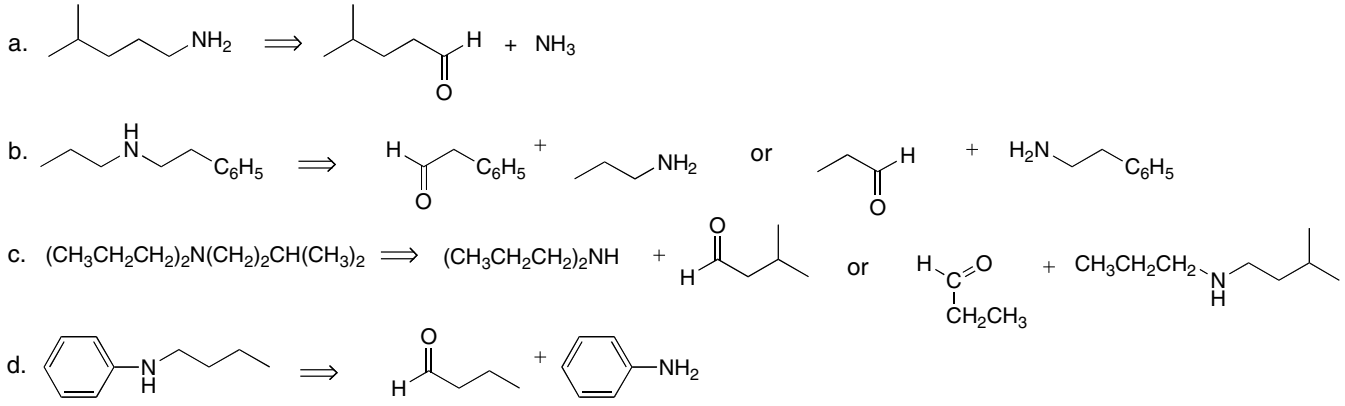
d. $C_6H_5CH_2CH_2CONH_2 \xrightarrow[[2]\ H_2O]{[1]\ LiAlH_4} C_6H_5CH_2CH_2CH_2NH_2$

e. $C_6H_5CH_2CH_2CHO \xrightarrow[NaBH_3CN]{NH_3} C_6H_5CH_2CH_2CH_2NH_2$

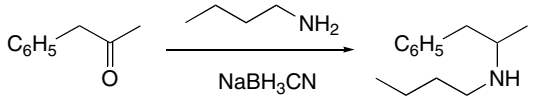
25.55

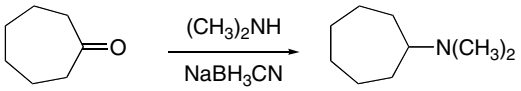


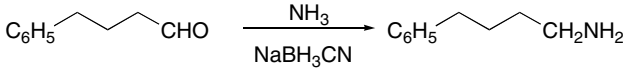
25.56 In reductive amination, one alkyl group on N comes from the carbonyl compound. The remainder of the molecule comes from NH_3 or an amine.

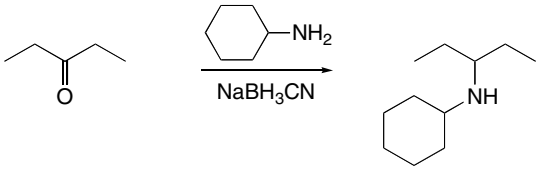


25.57

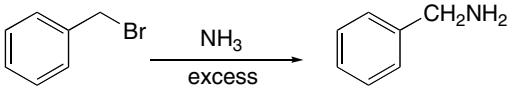
a. 

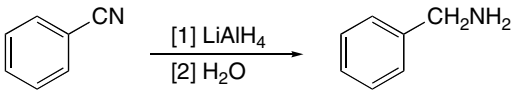
b. 

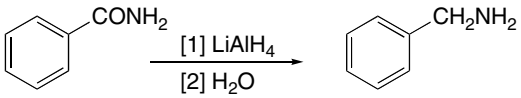
c. 

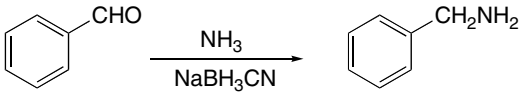
d. 

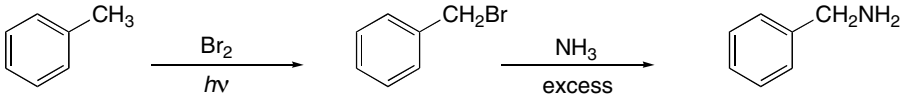
25.58

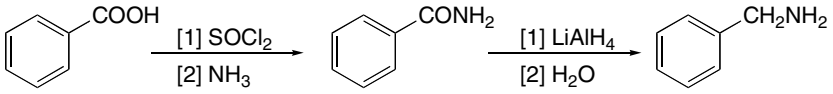
a. 

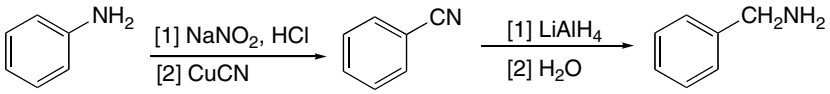
b. 

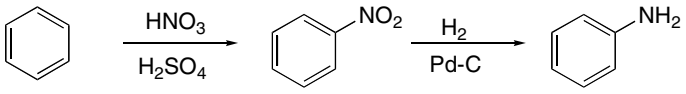
c. 

d. 

e. 

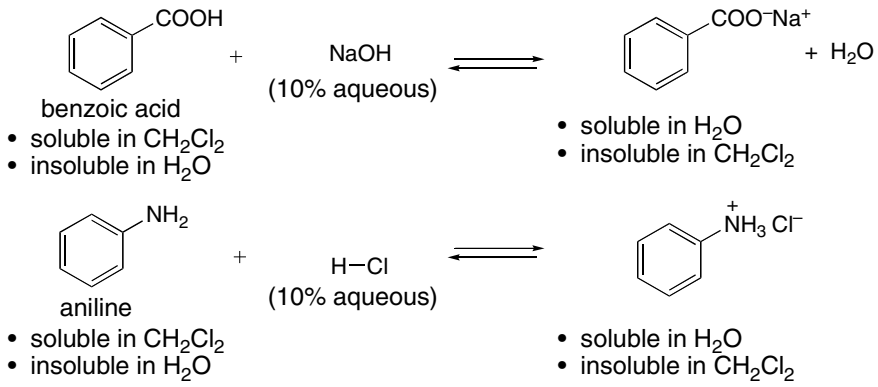
f. 

g. 

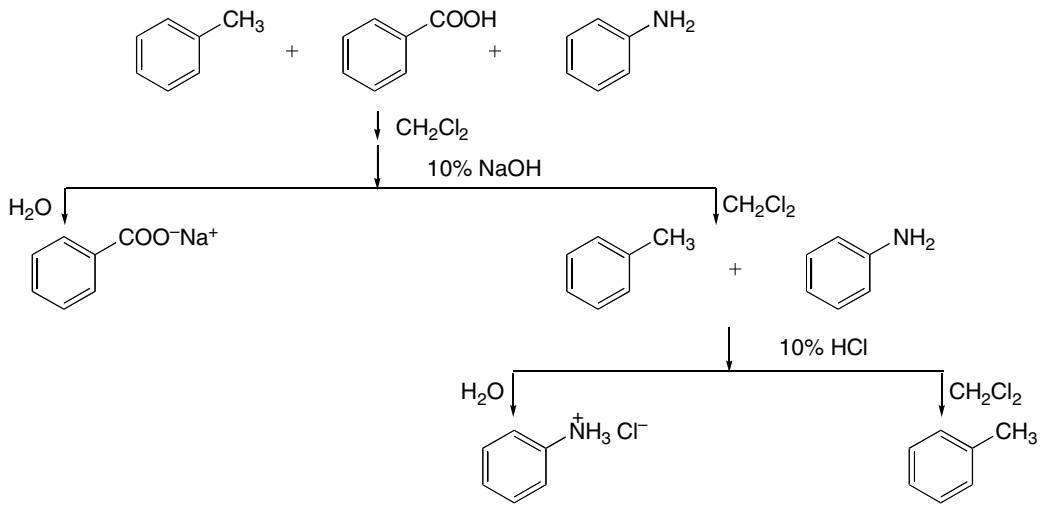
h. 

Then as in (g).

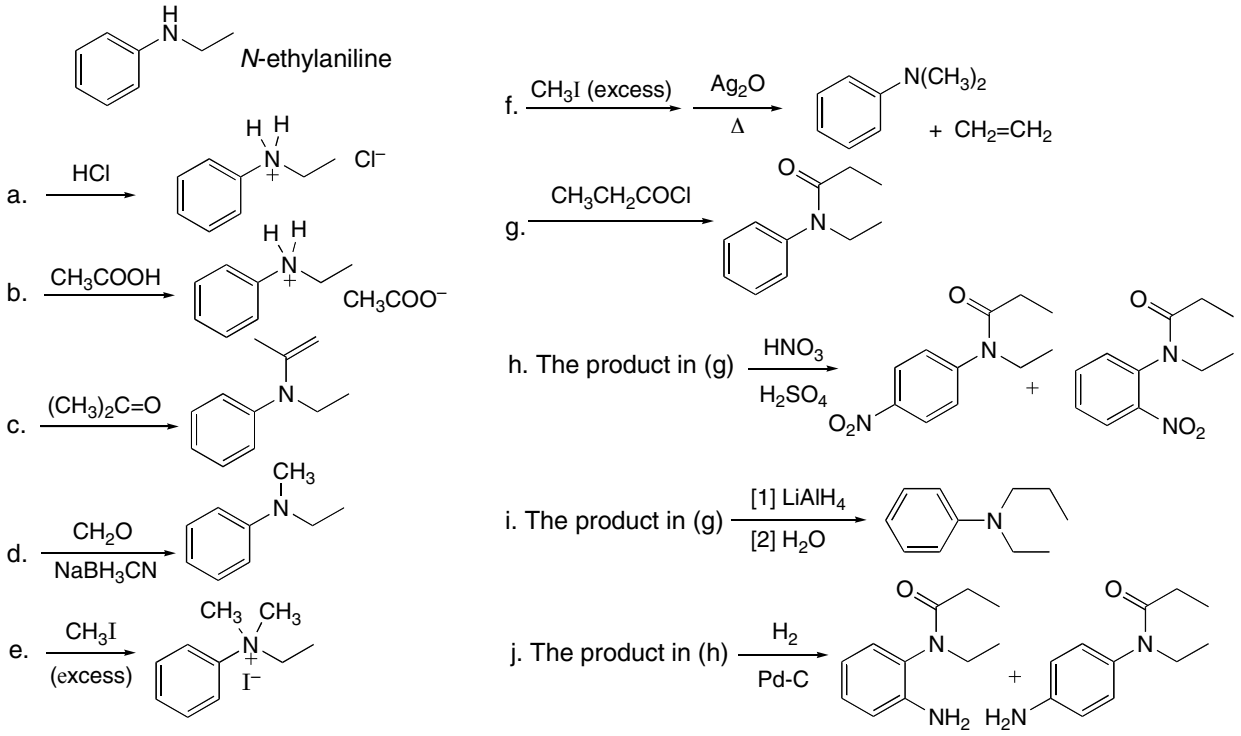
25.59 Use the directions from Answer 25.22. Separation can be achieved because benzoic acid reacts with aqueous base and aniline reacts with aqueous acid according to the following equations:



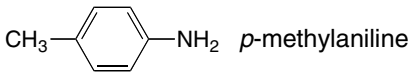
Toluene ($C_6H_5CH_3$), on the other hand, is not protonated or deprotonated in aqueous solution so it is always soluble in CH_2Cl_2 and insoluble in H_2O. The following flow chart illustrates the process.

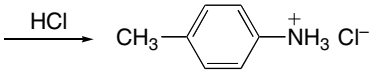


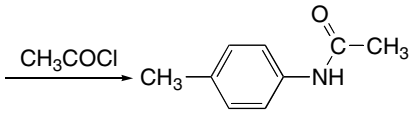
25.60

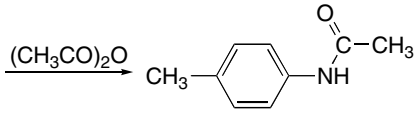


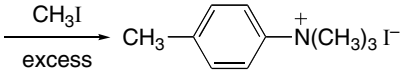
25.61

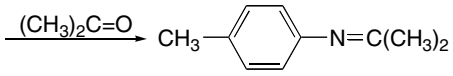


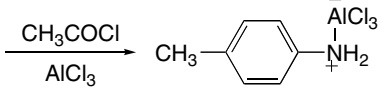
a. 

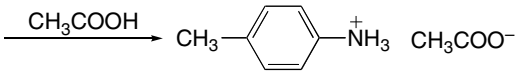
b. 

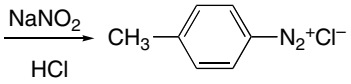
c. 

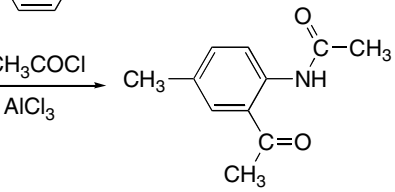
d. 

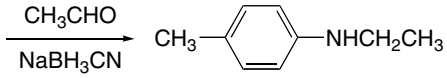
e. 

f. 

g. 

h. 

i. Step (b), then 

j. 

25.62

a. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow{ClCOC_6H_5} CH_3CH_2CH_2CH_2NHCOC_6H_5$

b. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow{O=C(CH_2CH_3)_2} CH_3CH_2CH_2CH_2N=C(CH_2CH_3)_2$

c. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow[\text{[2] } Ag_2O\text{ [3] } \Delta]{\text{[1] } CH_3I \text{ (excess)}} CH_3CH_2CH{=}CH_2$

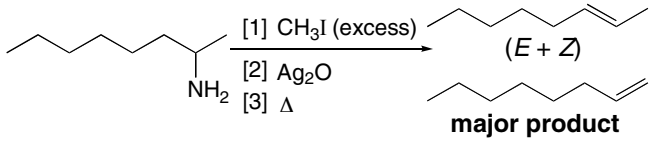
d. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow[NaBH_3CN]{C_6H_5CHO} CH_3CH_2CH_2CH_2NHCH_2C_6H_5$

e. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow[CH_3CHO]{NaBH_3CN} CH_3CH_2CH_2CH_2NHCH_2CH_3$

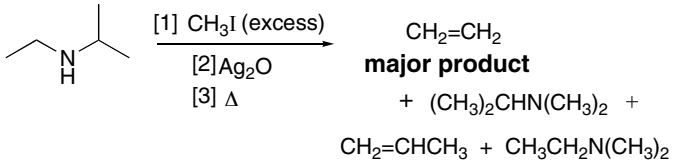
f. $CH_3CH_2CH_2CH_2NH_2 \xrightarrow[\text{excess}]{CH_3I} [CH_3CH_2CH_2CH_2N(CH_3)_3]^+I^-$

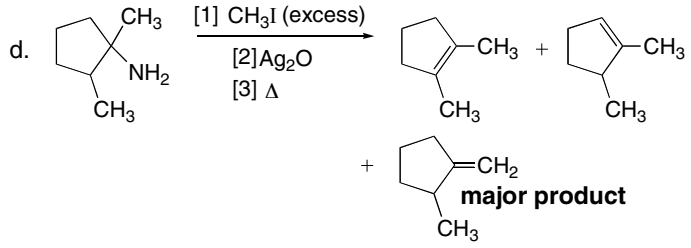
25.63

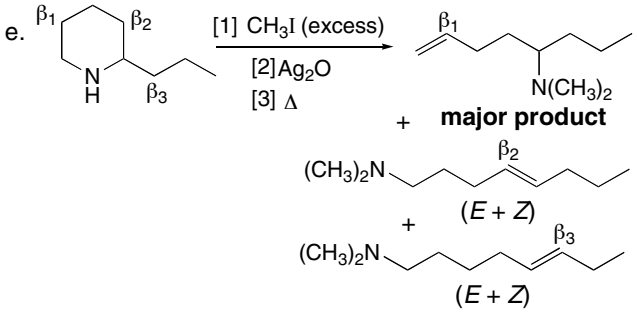
a. $CH_3(CH_2)_6NH_2 \xrightarrow[\text{[2]}Ag_2O\text{ [3] } \Delta]{\text{[1] } CH_3I \text{ (excess)}} CH_3(CH_2)_4CH{=}CH_2$

b. 

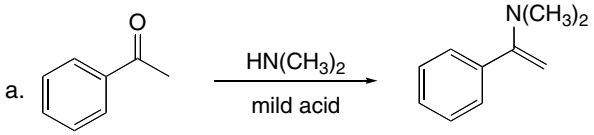
major product

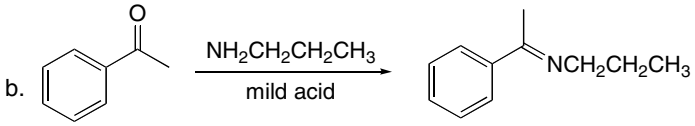
c. 

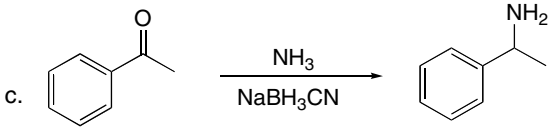
d. 

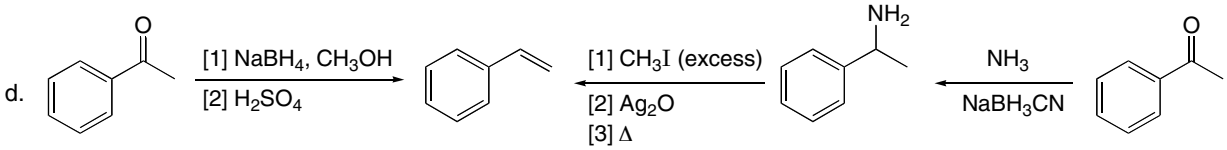
e. 

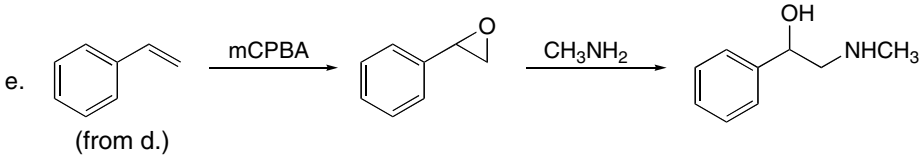
25.64

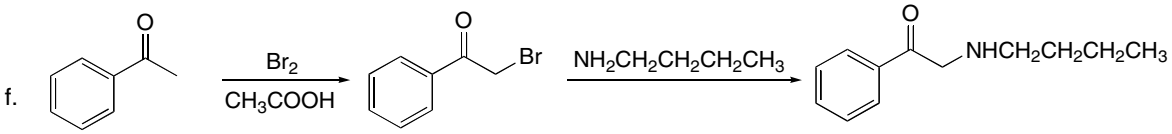
a. 

b. 

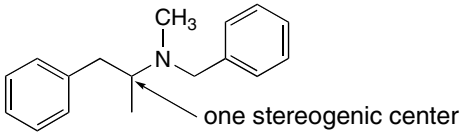
c. 

d. 

e. 

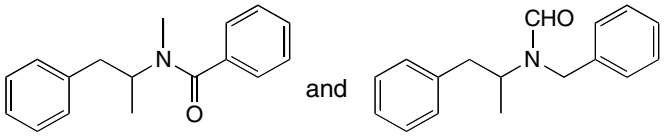
f. 

25.65

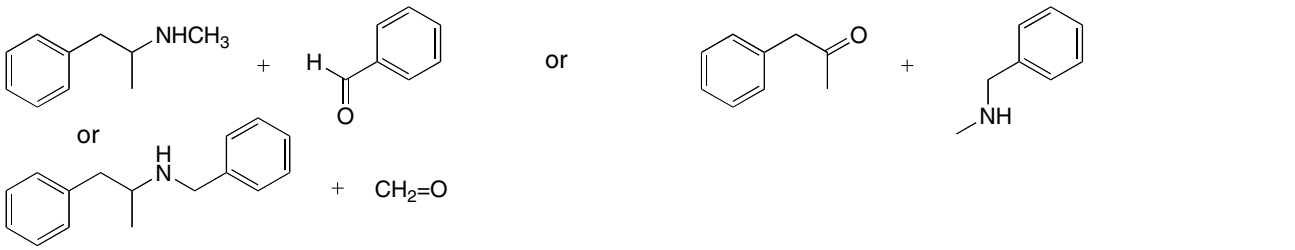
a. 

benzphetamine

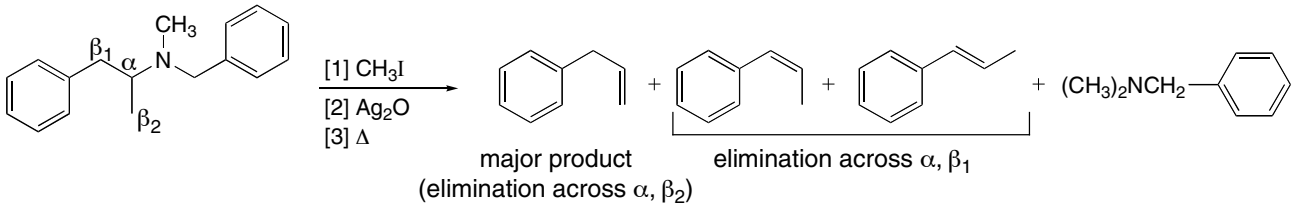
b. Amides that can be reduced to benzphetamine:



c. Amines + carbonyl compounds that form benzphetamine by reductive amination:



d.



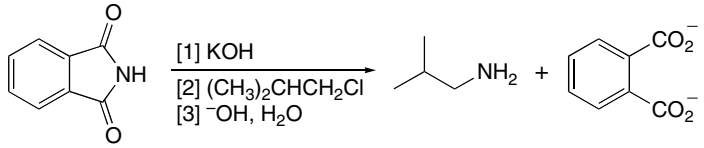
major product (elimination across α, β_2)

elimination across α, β_1

25.66

a. $C_6H_5CH_2CH_2Cl \xrightarrow[\text{excess}]{NH_3} C_6H_5CH_2CH_2NH_2$

b.



c. $Br{-}C_6H_4{-}NO_2 \xrightarrow[HCl]{Sn} Br{-}C_6H_4{-}NH_2$

d. $(CH_3)_2CHCN \xrightarrow[[2]\ H_2O]{[1]\ LiAlH_4} (CH_3)_2CHCH_2NH_2$

e. $C_6H_5CONHCH_2CH_3 \xrightarrow[[2]\ H_2O]{[1]\ LiAlH_4} C_6H_5CH_2NHCH_2CH_3$

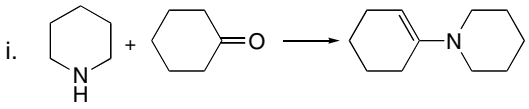
f. $C_6H_5CH_2CH_2NH_2 + (C_6H_5CO)_2O \longrightarrow$

$C_6H_5CH_2CH_2NHCOC_6H_5 + C_6H_5CH_2CH_2NH_3^+\ C_6H_5COO^-$

g. $C_4H_8NH \xrightarrow[HCl]{NaNO_2} C_4H_8N{-}N{=}O$

h. $C_4H_8NH + C_6H_5CHO \xrightarrow{NaBH_3CN} C_4H_8N{-}CH_2C_6H_5$

i.

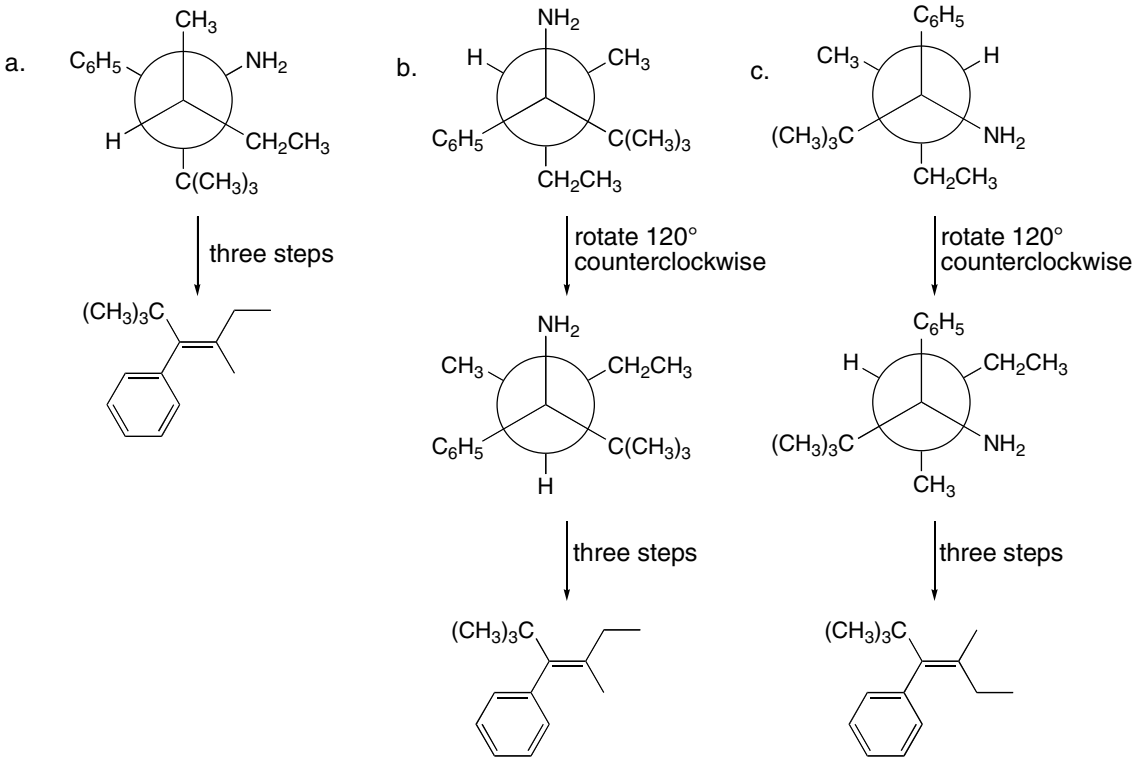


j. $CH_3CH_2CH_2{-}N(H){-}CH(CH_3)_2 \xrightarrow[[2]\ Ag_2O\ [3]\ \Delta]{[1]\ CH_3I\ (excess)}$

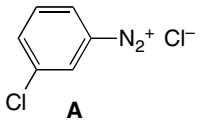
$CH_3CH{=}CH_2 + (CH_3)_2NCH(CH_3)_2$

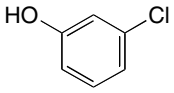
$CH_3CH_2CH_2N(CH_3)_2$

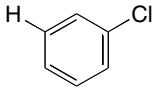
25.67 NH_2 and H must be anti for the Hofmann elimination. Rotate around the C–C bond so the NH_2 and H are anti.

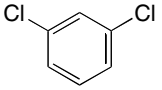


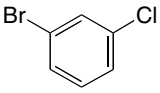
25.68

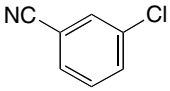


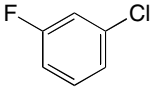
a. H_2O 

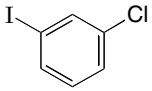
b. H_3PO_2 

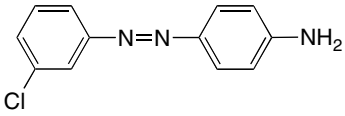
c. CuCl 

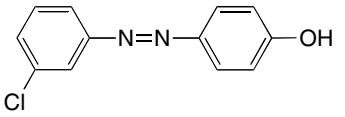
d. CuBr 

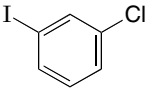
e. CuCN 

f. HBF_4 

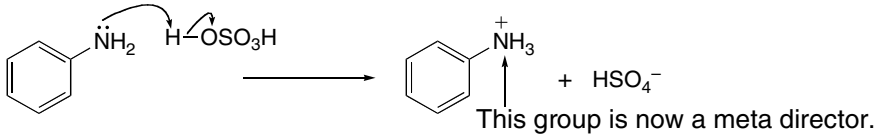
g. NaI 

h. $C_6H_5NH_2$ 

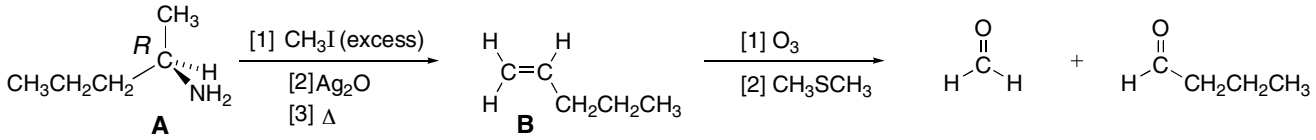
i. C_6H_5OH 

j. KI 

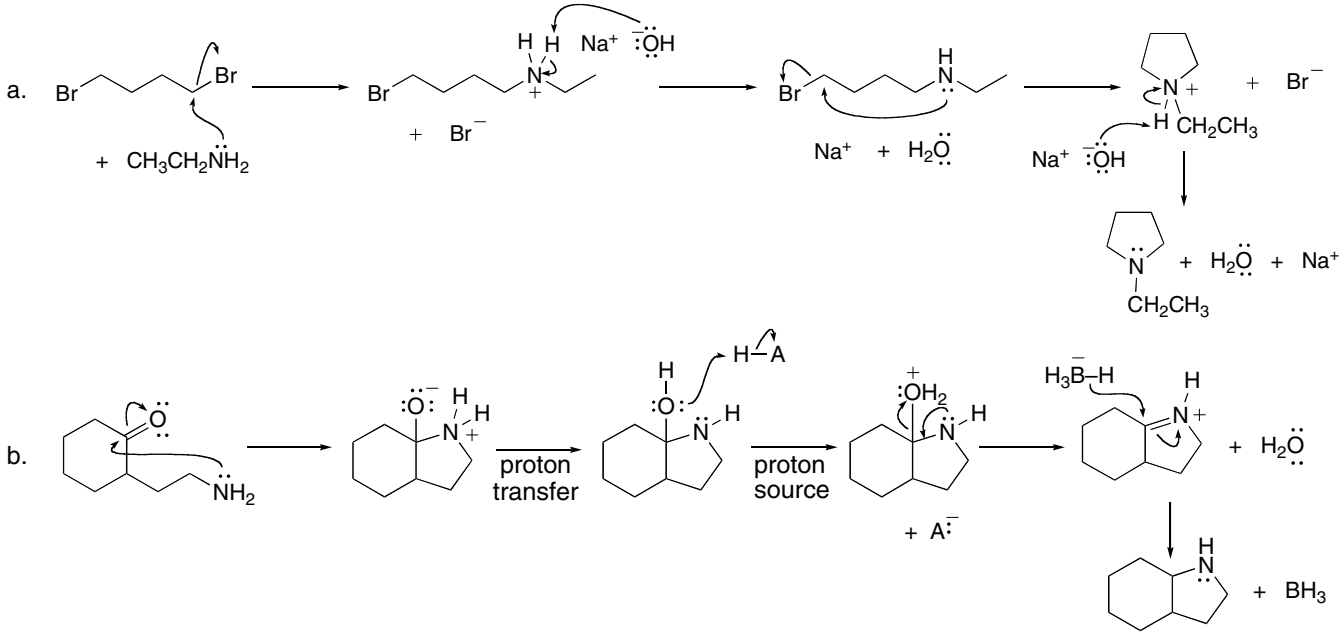
25.69 Under the acidic conditions of the reaction, aniline is first protonated to form an ammonium salt that has a positive charge on the atom bonded to the benzene ring. The $-NH_3^+$ is now an electron-withdrawing meta director, so a significant amount of meta substitution occurs.



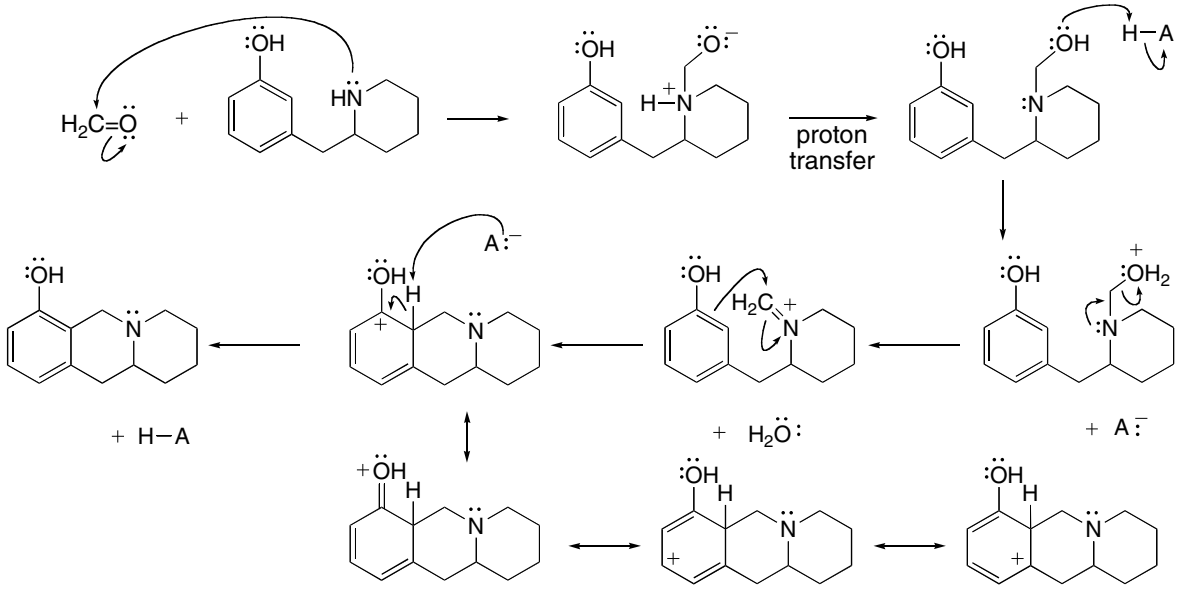
25.70



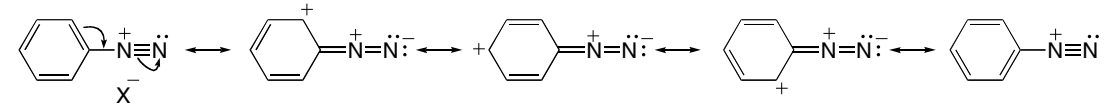
25.71



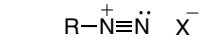
25.72



25.73



aryl diazonium salt

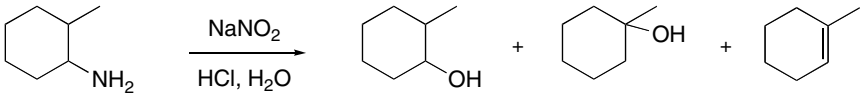


alkyl diazonium salt

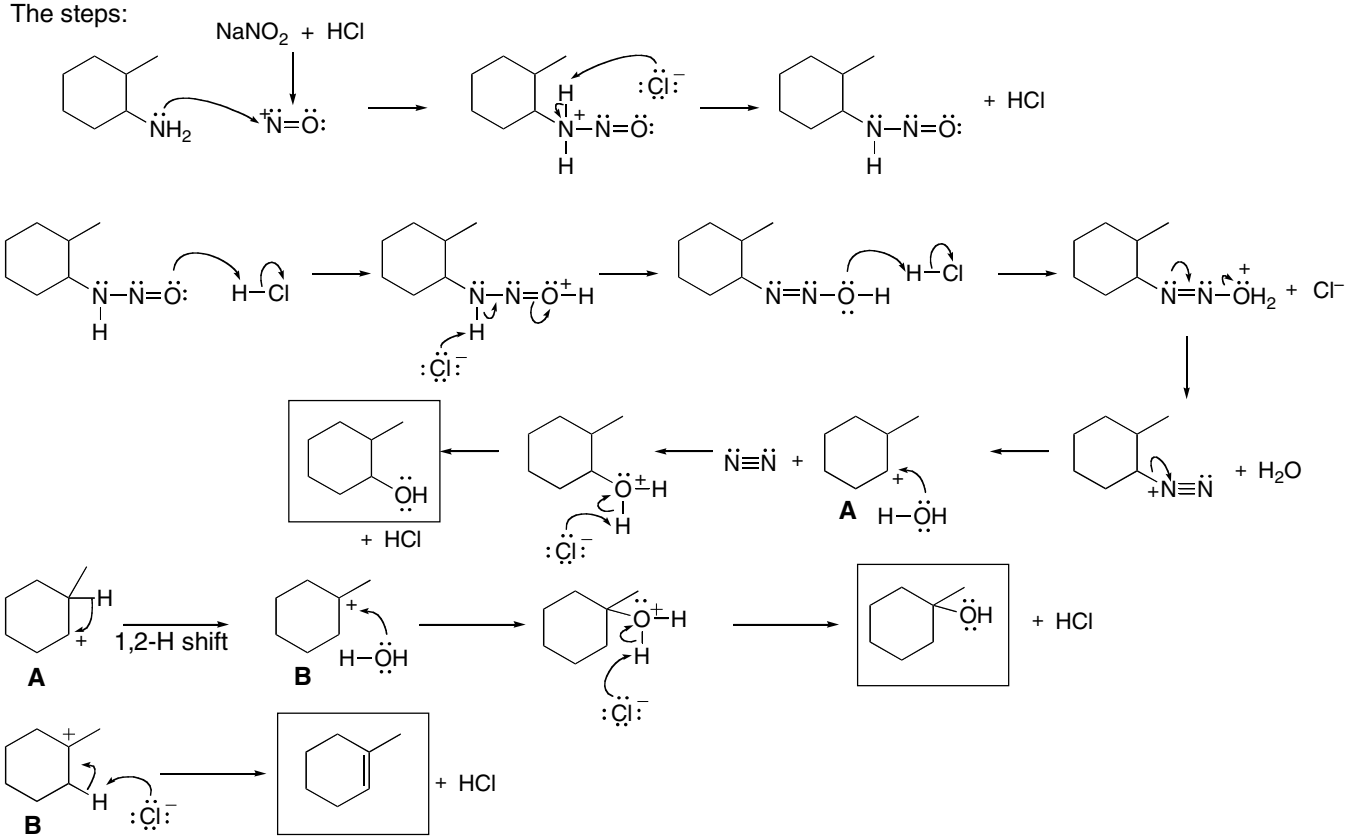
The N_2^+ group on an aromatic ring is stabilized by resonance, whereas the alkyl diazonium salt is not.

25.74

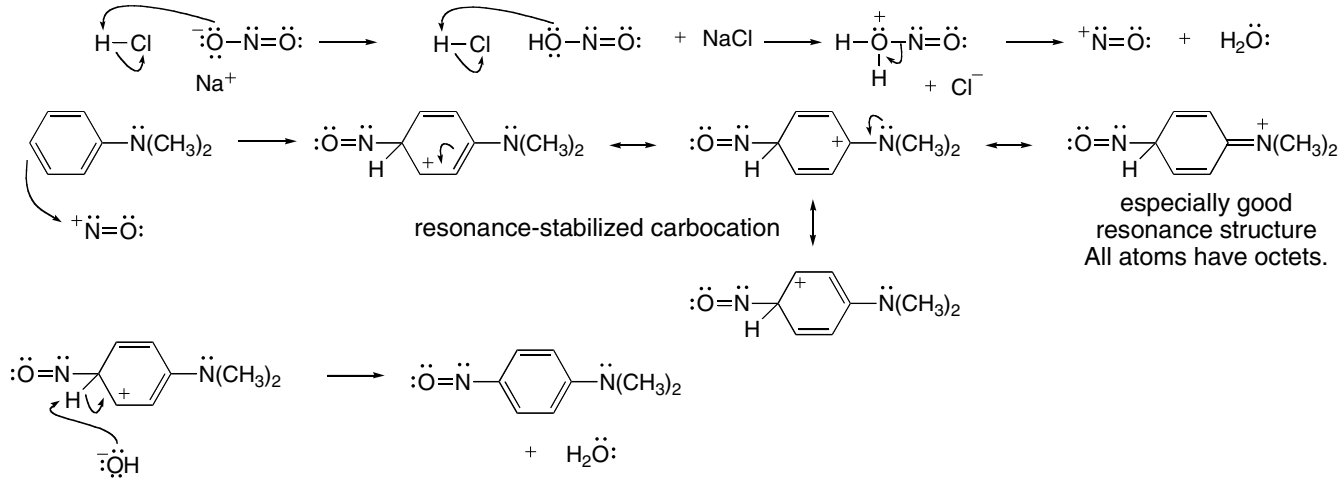
Overall reaction:



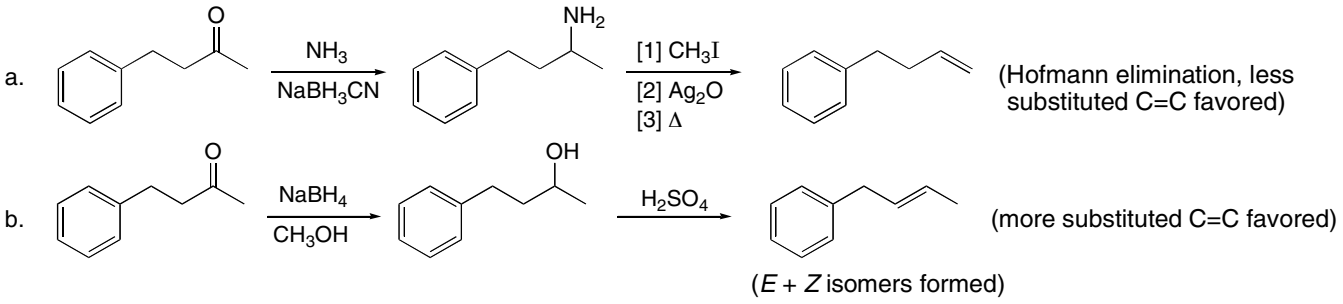
The steps:



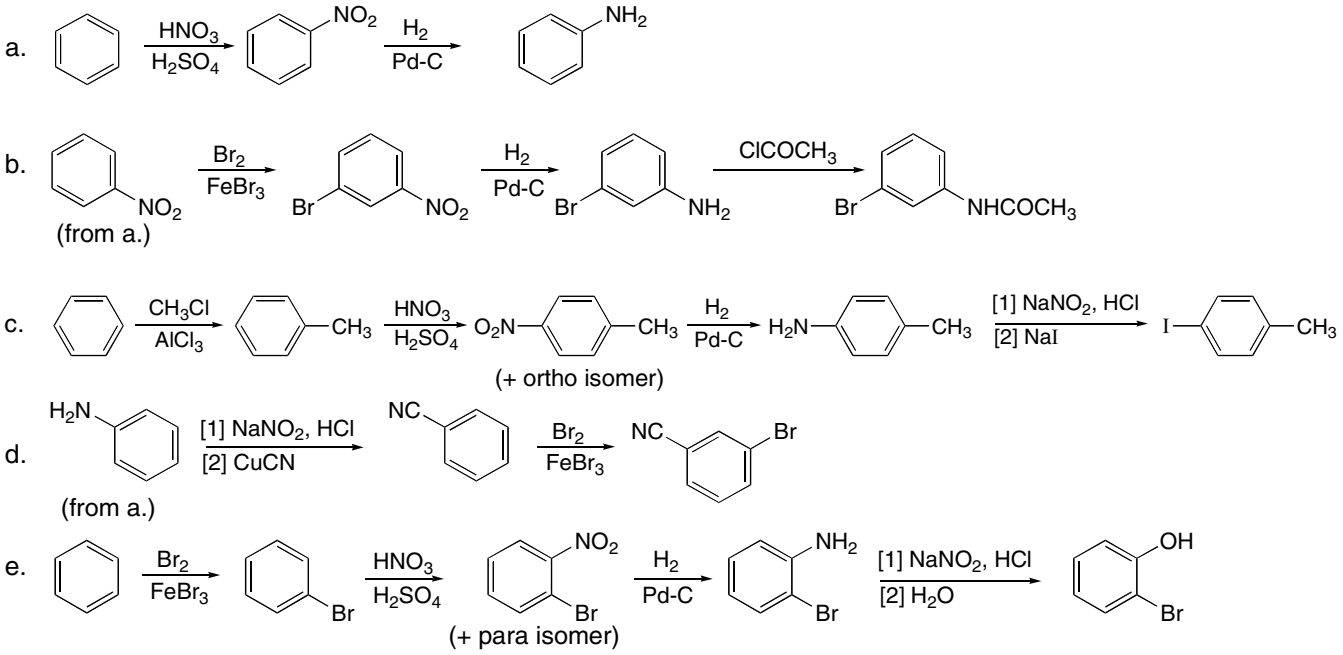
25.75 A nitrosonium ion ($^{+}$NO) is a weak electrophile so electrophilic aromatic substitution occurs only with a strong electron-donor group that stabilizes the intermediate carbocation.

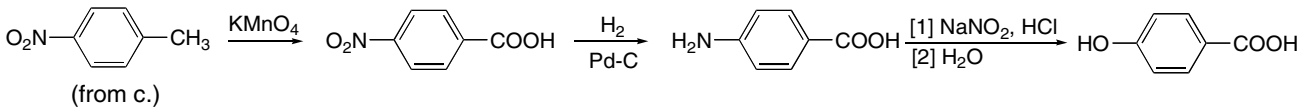


25.76

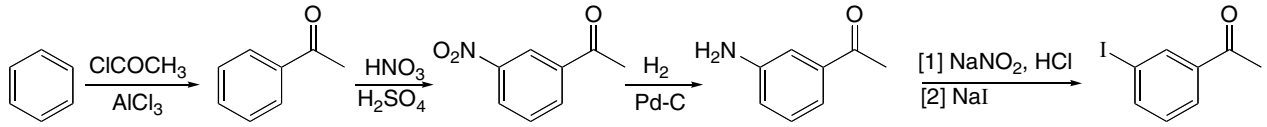


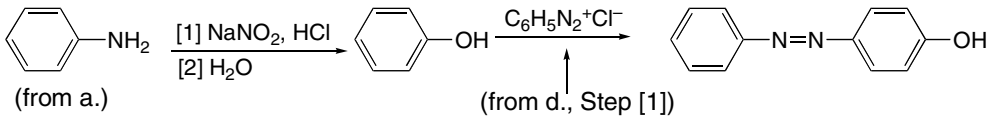
25.77



f. 

(from c.)

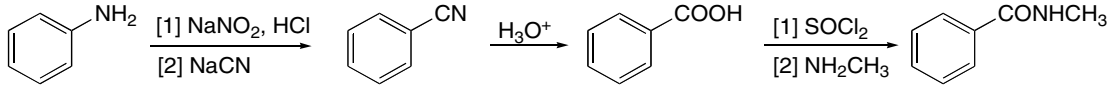
g. 

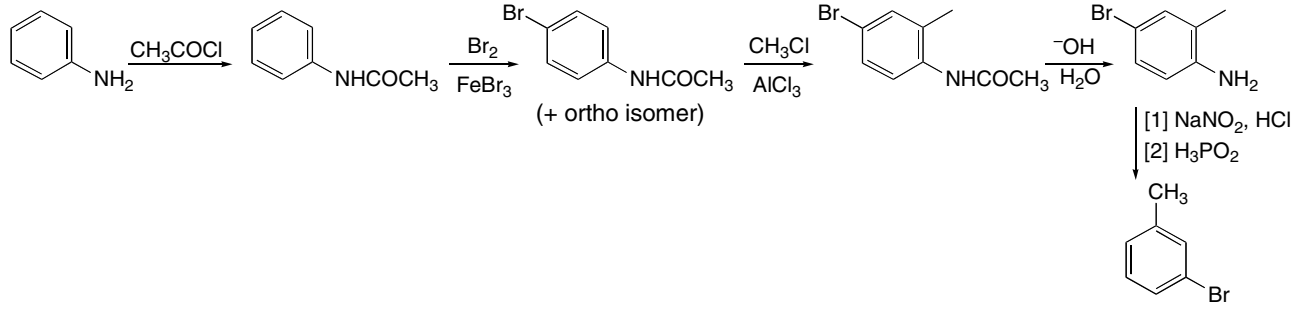
h. 

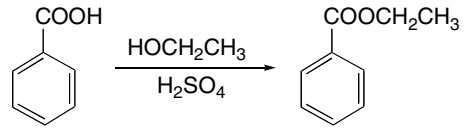
(from a.)

(from d., Step [1])

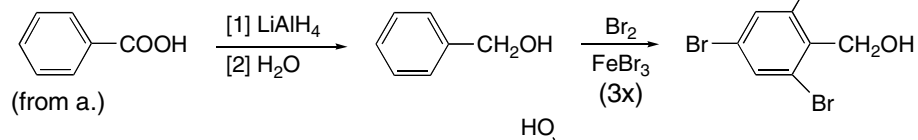
25.78

a. 

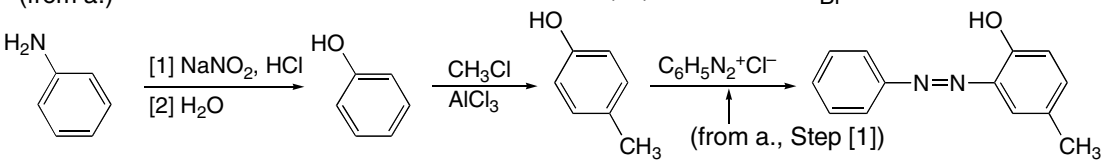
b. 

c. 

(from a.)

d. 

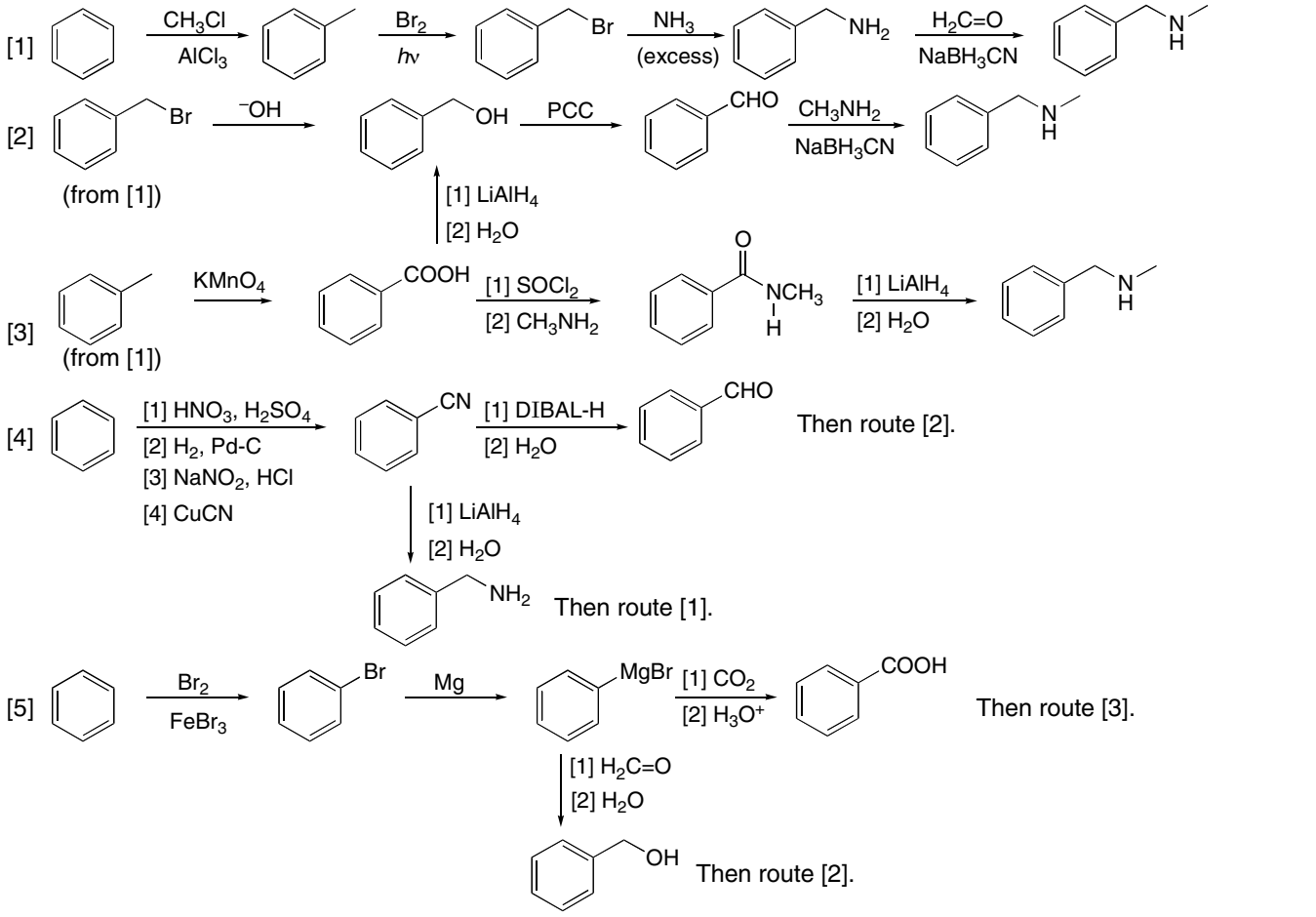
(from a.)

e. 

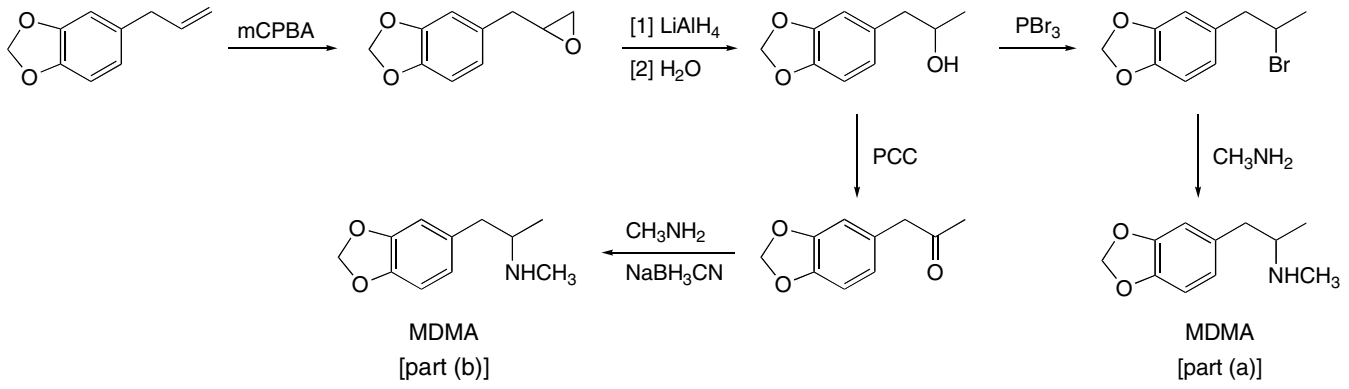
(from a., Step [1])

(+ ortho isomer)

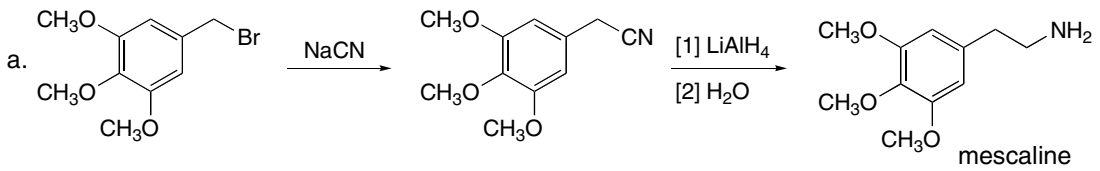
25.79



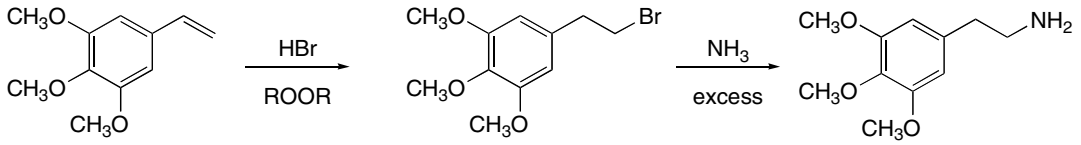
25.80



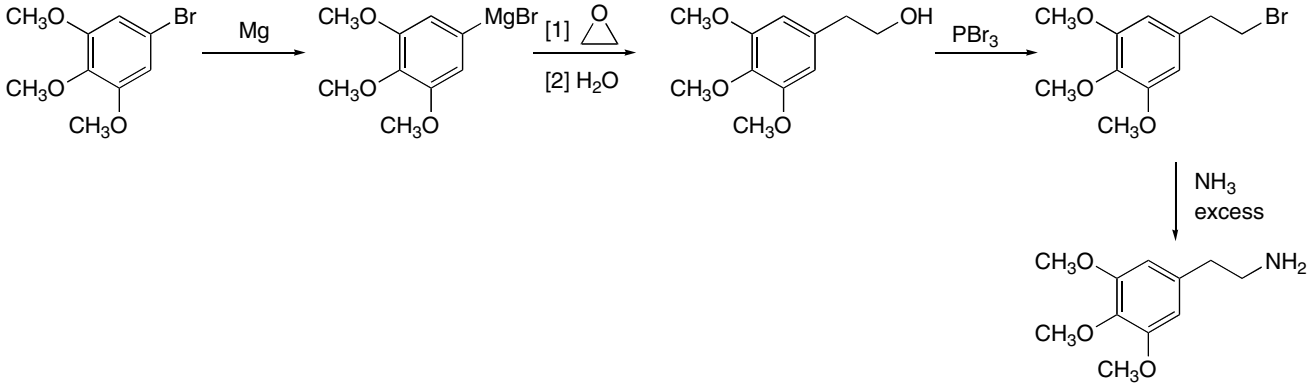
25.81



b.

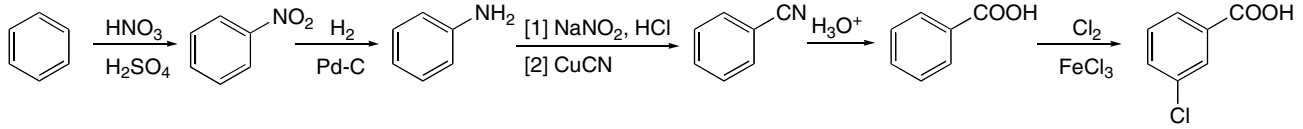


c.

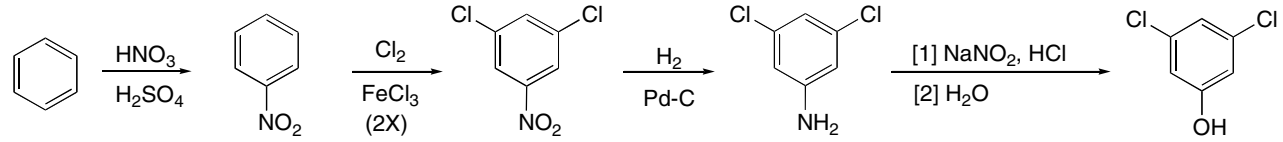


25.82

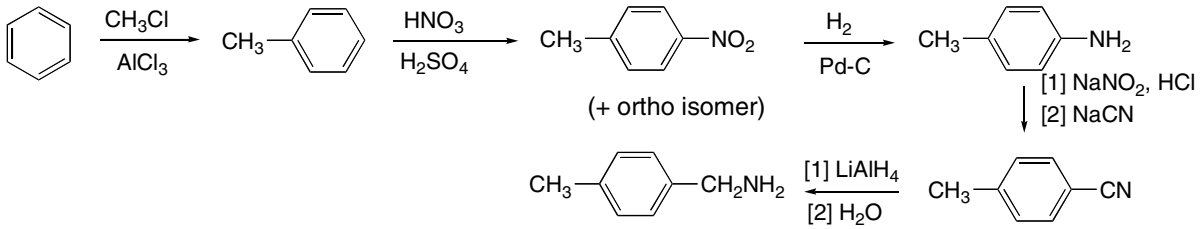
a.



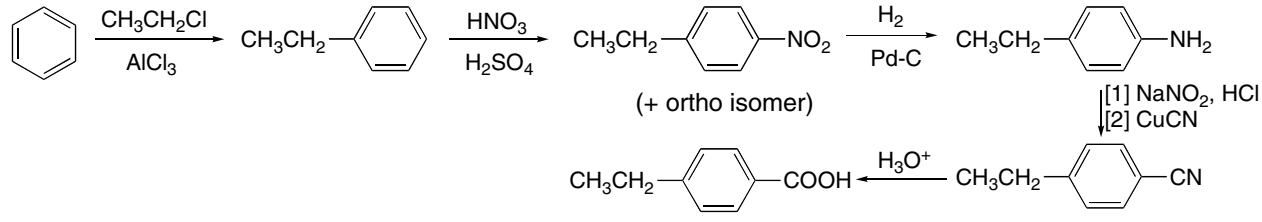
b.



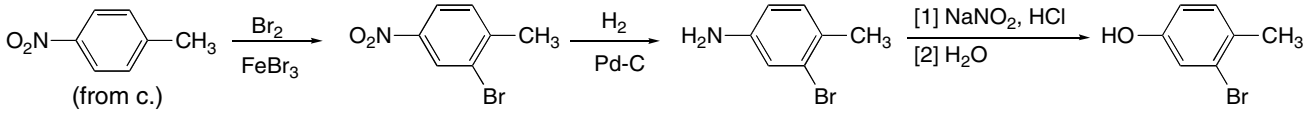
c.



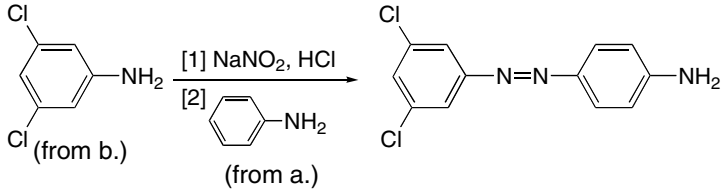
d.



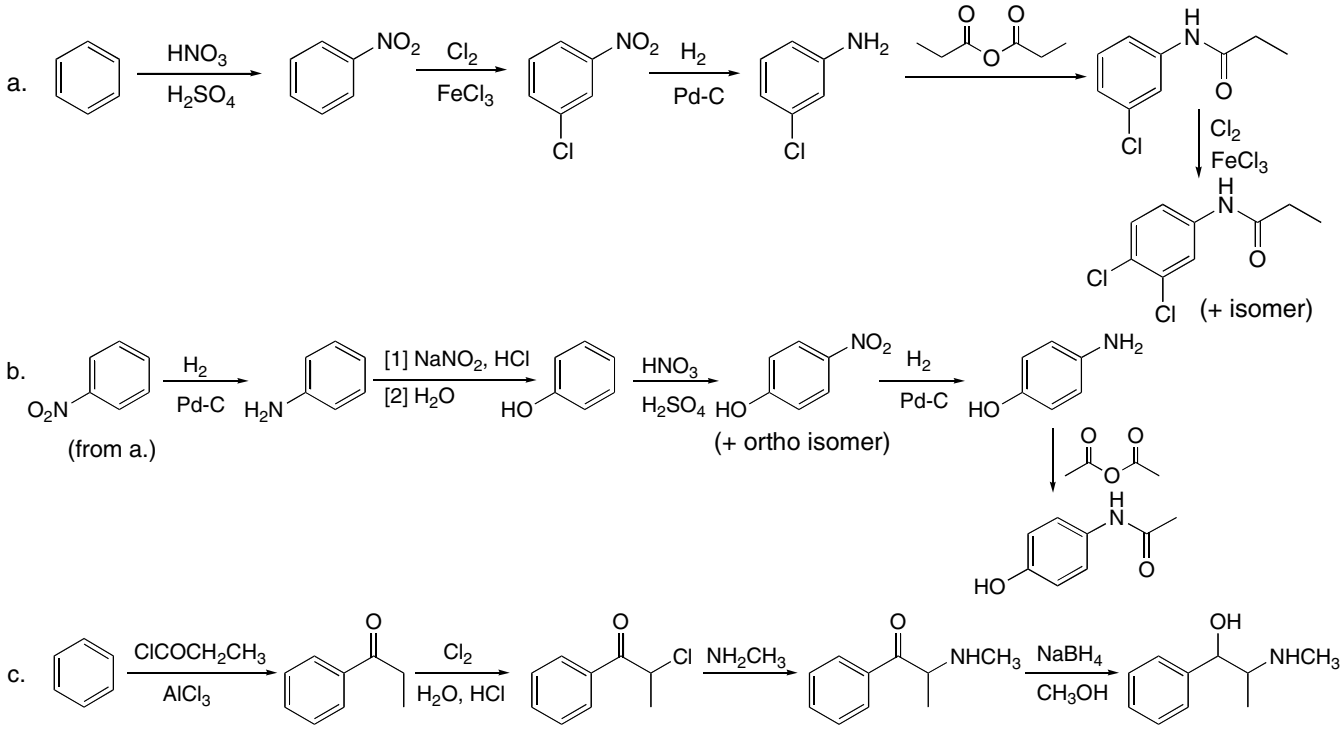
e.



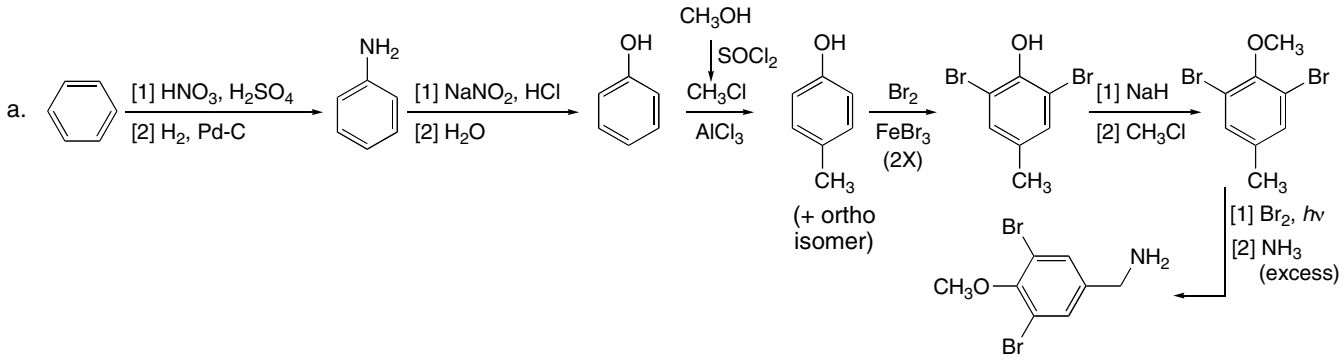
f.

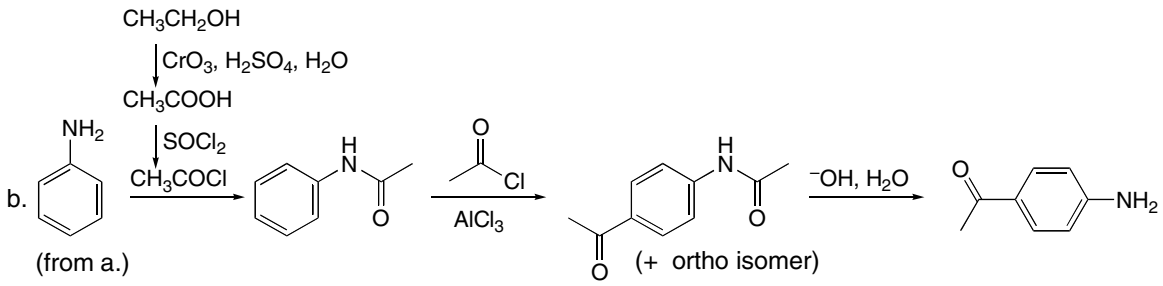


25.83

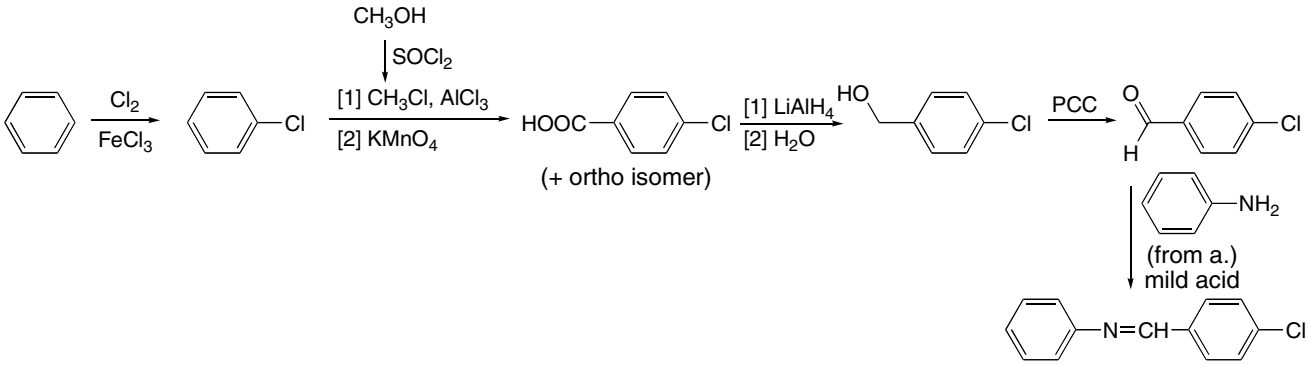

a.
HNO3
H2SO4
NO2
Cl2
FeCl3
NO2
Cl
H2
Pd-C
NH2
Cl
O
O
O
H
N
O
Cl
Cl2
FeCl3
H
N
O
Cl
Cl
(+ isomer)
b.
O2N
(from a.)
H2
Pd-C
H2N
[1] NaNO2, HCl
[2] H2O
HO
HNO3
H2SO4
HO
NO2
(+ ortho isomer)
H2
Pd-C
NH2
HO
O
O
O
H
N
O
HO
c.
ClCOCH2CH3
AlCl3
O
Cl2
H2O, HCl
O
Cl
NH2CH3
O
NHCH3
NaBH4
CH3OH
OH
NHCH3

25.84

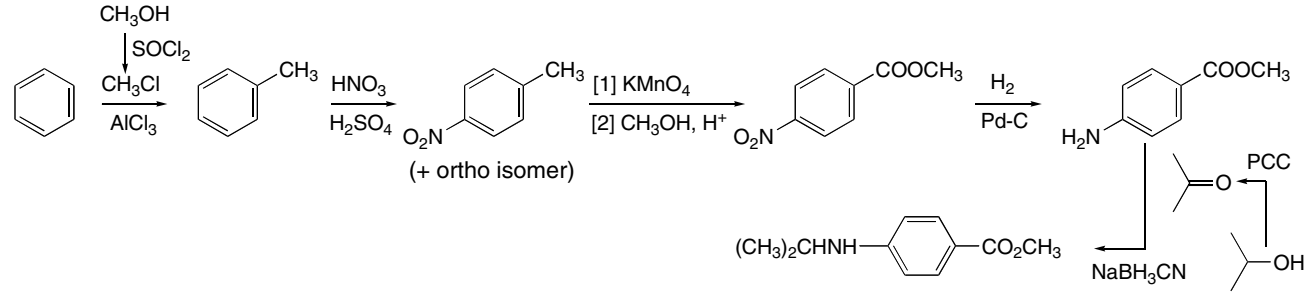

a.
[1] HNO3, H2SO4
[2] H2, Pd-C
NH2
[1] NaNO2, HCl
[2] H2O
OH
CH3OH
SOCl2
CH3Cl
AlCl3
OH
CH3
(+ ortho isomer)
Br2
FeBr3
(2X)
Br
OH
Br
CH3
[1] NaH
[2] CH3Cl
Br
OCH3
Br
CH3
[1] Br2, hν
[2] NH3
(excess)
Br
NH2
CH3O
Br


CH3CH2OH
CrO3, H2SO4, H2O
CH3COOH
b.
NH2
(from a.)
SOCl2
CH3COCl
H
N
O
O
Cl
AlCl3
H
N
O
O
(+ ortho isomer)
−OH, H2O
O
NH2

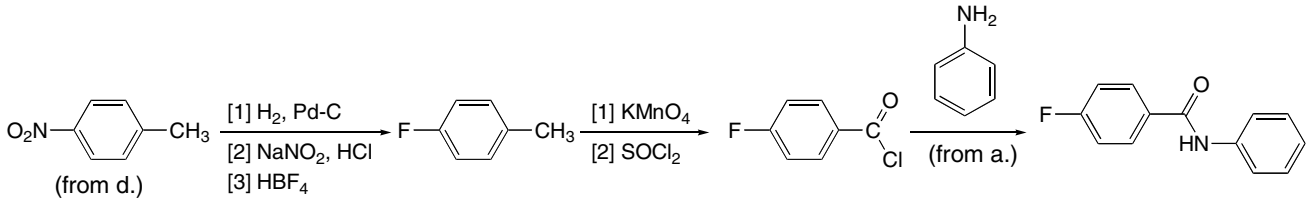
c.



d.

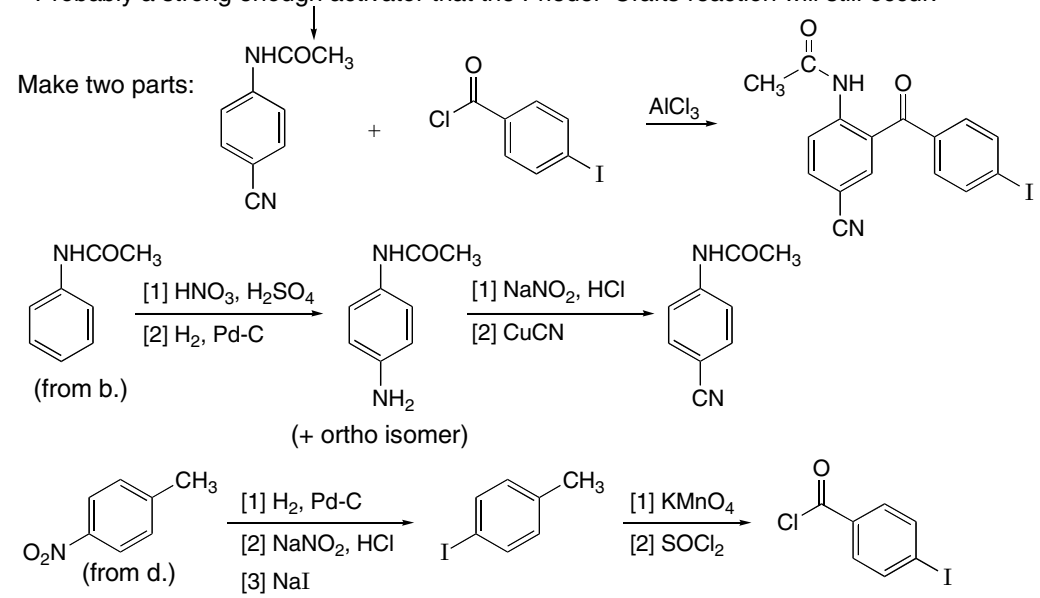


e.



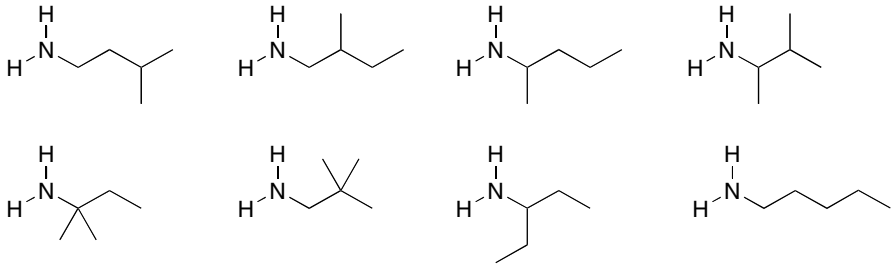
Probably a strong enough activator that the Friedel–Crafts reaction will still occur.

f.

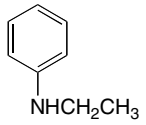


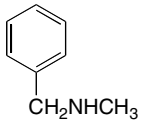
25.85

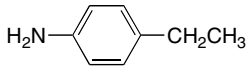
molecular weight = 87
$C_5H_{13}N$
two IR peaks = 1° amine



25.86





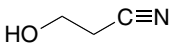


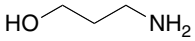
Compound **A**: $C_8H_{11}N$
IR absorption at 3400 cm^{-1} → 2° amine
^1H NMR signals at (ppm):
1.3 (triplet, 3 H) CH_3 adjacent to 2 H's
3.1 (quartet, 2 H) CH_2 adjacent to 3 H's
3.6 (singlet, 1 H) amine H
6.8–7.2 (multiplet, 5 H) benzene ring

Compound **B**: $C_8H_{11}N$
IR absorption at 3310 cm^{-1} → 2° amine
^1H NMR signals at (ppm):
1.4 (singlet, 1 H) amine H
2.4 (singlet, 3 H) CH_3
3.8 (singlet, 2 H) CH_2
7.2 (multiplet, 5 H) benzene ring

Compound **C**: $C_8H_{11}N$
IR absorption at 3430 and
3350 cm^{-1} → 1° amine
^1H NMR signals at (ppm):
1.3 (triplet, 3 H) CH_3 near CH_2
2.5 (quartet, 2 H) CH_2 near CH_3
3.6 (singlet, 2 H) amine H's
6.7 (doublet, 2 H) } para disubstituted
7.0 (doublet, 2 H) } benzene ring

25.87

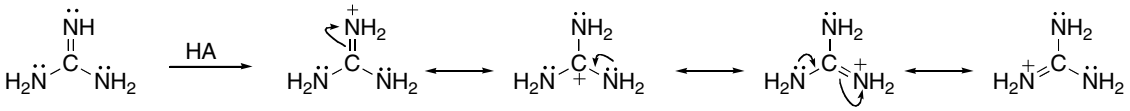




Compound **D**:
Molecular ion at m/z = 71: C_3H_5NO (possible formula)
IR absorption at 3600–3200 cm^{-1} → OH
2263 cm^{-1} → CN
Use integration values and the molecular formula to determine the number of H's that give rise to each signal.
^1H NMR signals at (ppm):
2.6 (triplet, 2 H) CH_2 adjacent to 2 H's
3.2 (singlet, 1 H) OH
3.9 (triplet, 2 H) CH_2 adjacent to 2 H's

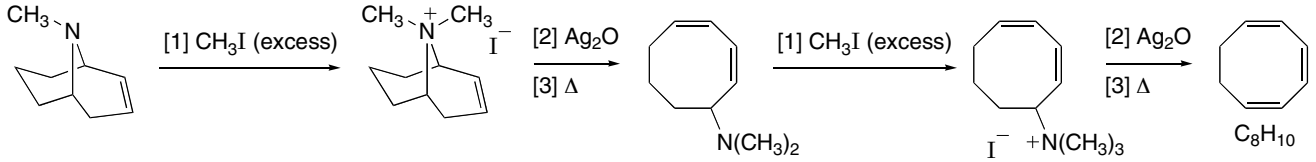
Compound **E**:
Molecular ion at m/z = 75: C_3H_9NO (possible formula)
IR absorption at 3600–3200 cm^{-1} → OH
3636 cm^{-1} → N–H of amine
^1H NMR signals at (ppm):
1.6 (quintet, 2 H) CH_2 split by 2 CH_2's
2.5 (singlet, 3 H) NH_2 and OH
2.8 (triplet, 2 H) CH_2 split by CH_2
3.7 (triplet, 2 H) CH_2 split by CH_2

25.88 Guanidine is a strong base because its conjugate acid is stabilized by resonance. This resonance delocalization makes guanidine easily donate its electron pair; thus it's a strong base.



guanidine pK_a = 13.6

25.89

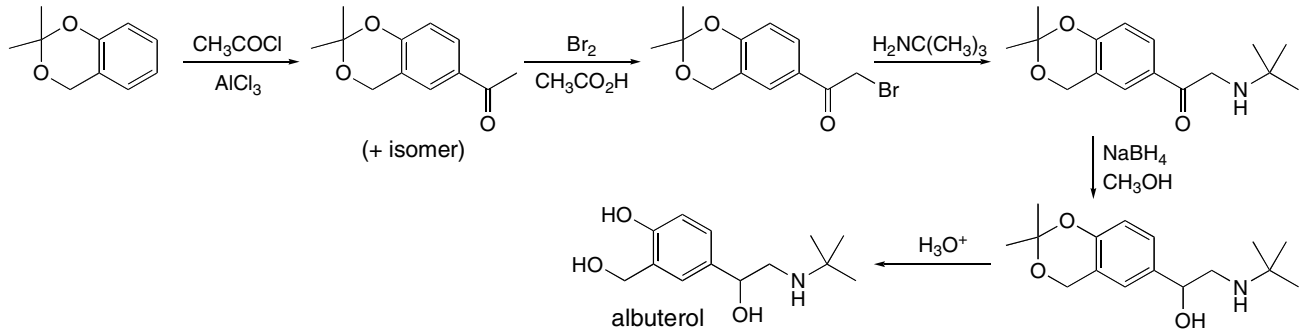


Y

25.90

One possibility:

a.



b.