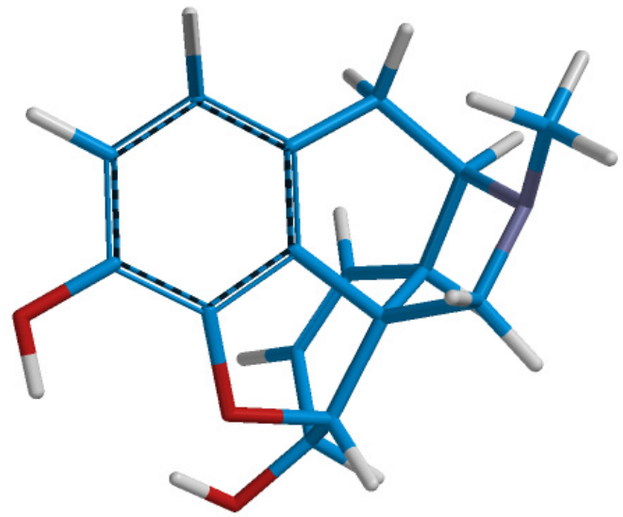
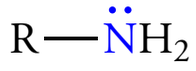
23

Amines and Amides

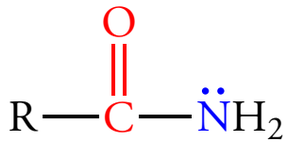


Morphine

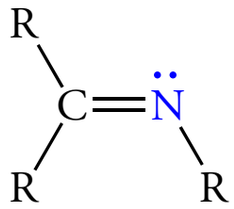
23.1 ORGANIC NITROGEN COMPOUNDS



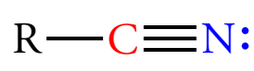
(an amine)



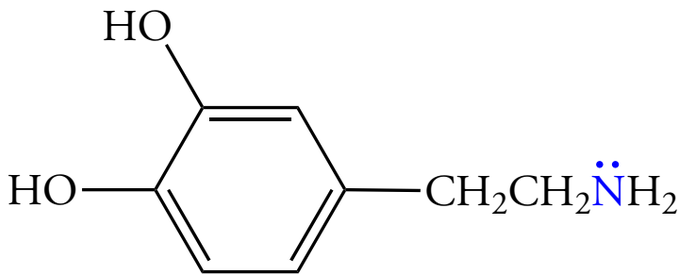
(an amide)



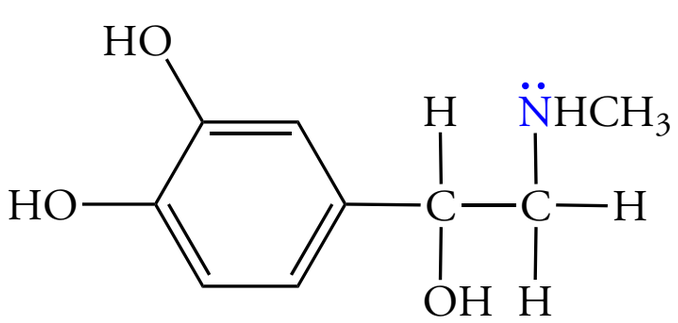
(an imine)



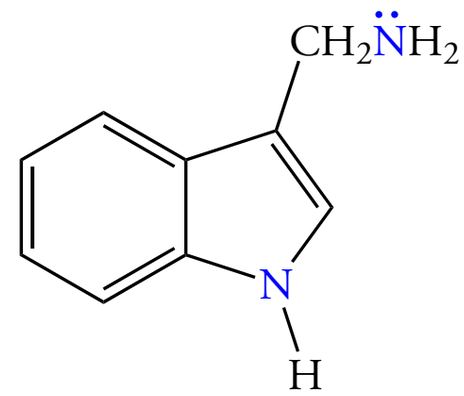
(a nitrile)



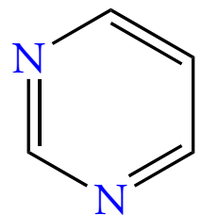
dopamine



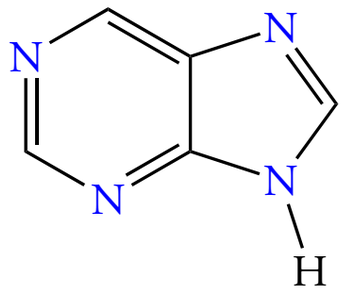
epinephrine



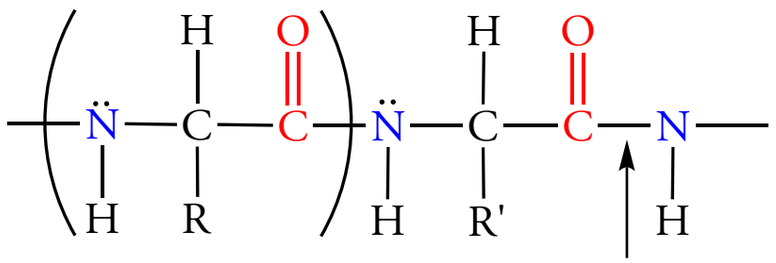
seratonin



pyrimidine



purine

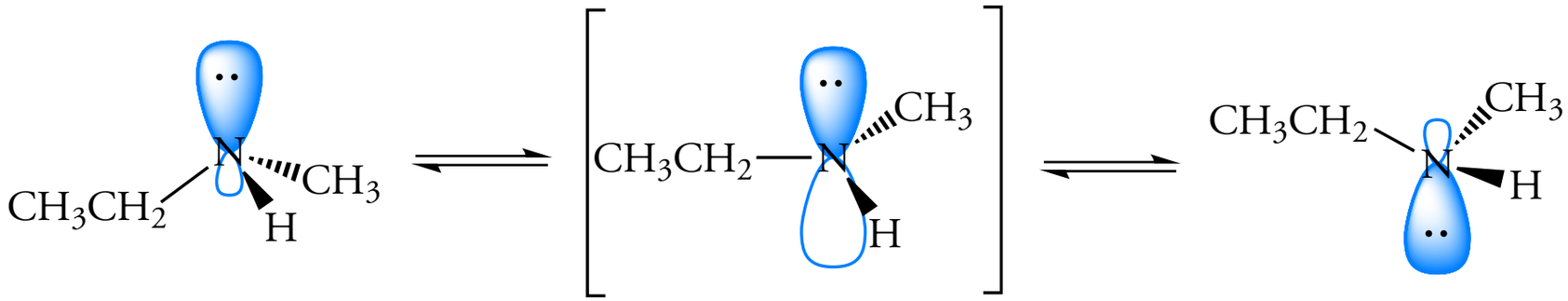


(an amino acyl group)

(an amide bond,
or peptide bond)

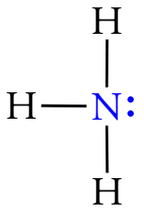
23.2 BONDING AND STRUCTURE OF AMINES

Nitrogen Inversion of Amines

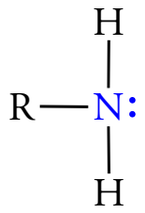


planar transition state

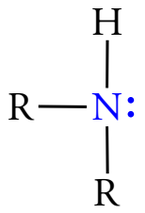
23.3 CLASSIFICATION AND NOMENCLATURE OF AMINES



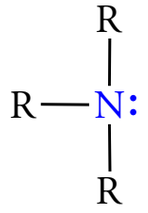
ammonia



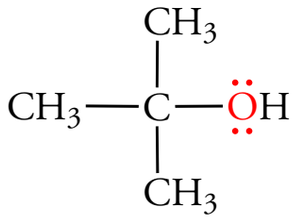
primary (1°) amine



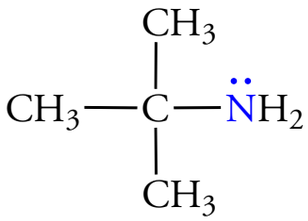
secondary (2°) amine



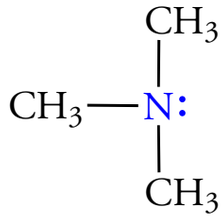
tertiary (3°) amine



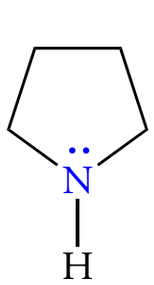
tert-butyl alcohol
(a tertiary alcohol)



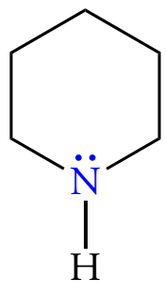
tert-butylamine
(a primary amine)



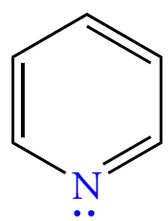
trimethylamine
(a tertiary amine)



pyrrolidine
(a secondary amine)



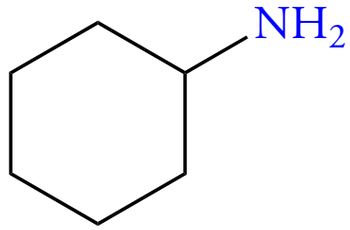
piperidine
(a secondary amine)



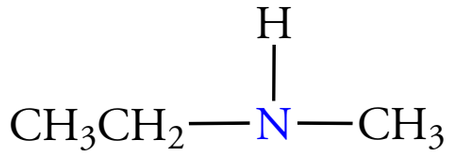
pyridine
(a tertiary amine)

23.3 CLASSIFICATION AND NOMENCLATURE OF AMINES

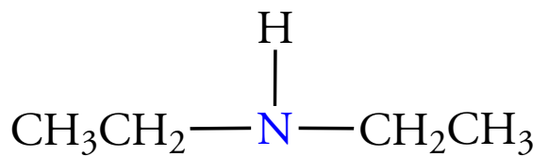
Common Names of Amines



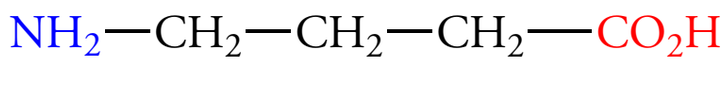
cyclohexylamine



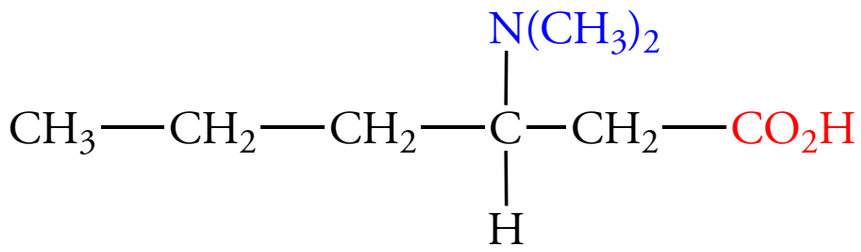
ethylmethylamine



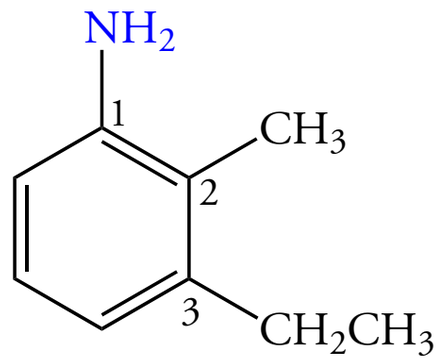
diethylamine



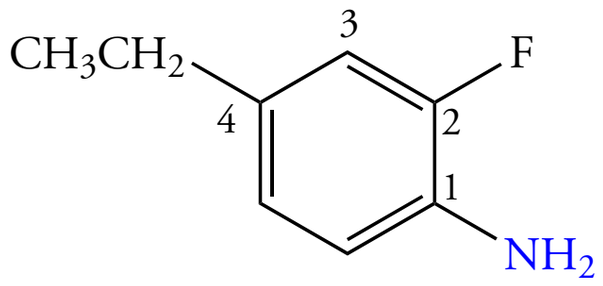
γ-aminobutryic acid



β-(N,N-dimethylamino)caproic acid



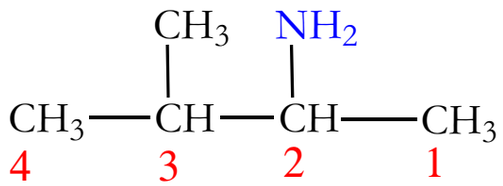
3-ethyl-2-methylaniline



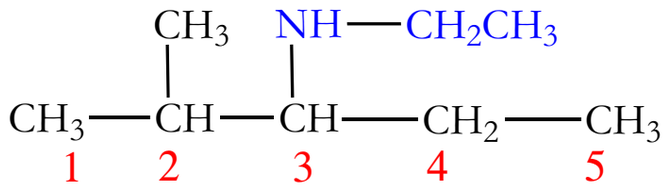
4-ethyl-2-fluorolaniline

23.3 CLASSIFICATION AND NOMENCLATURE OF AMINES

Systematic Names of Amines



3-methyl-2-butanamine



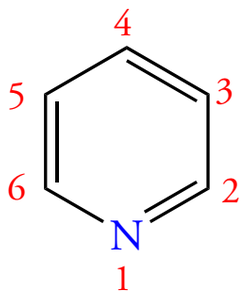
N-ethyl-2-methyl-3-pentanamine

aziridine

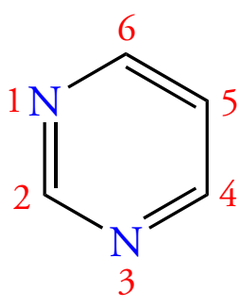
azetidine

pyrrolidine

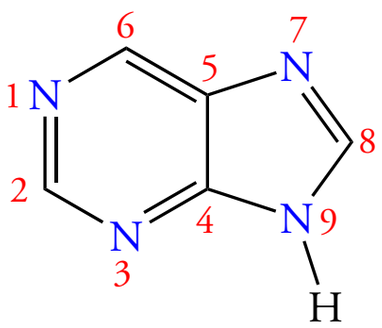
piperidine



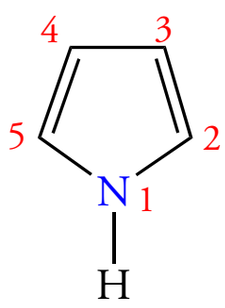
pyridine



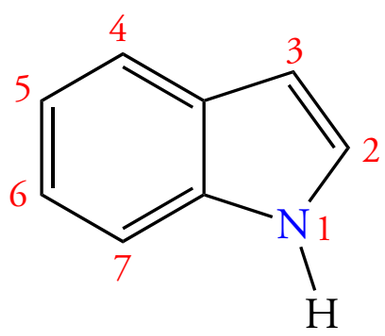
pyrimidine



purine



pyrrole



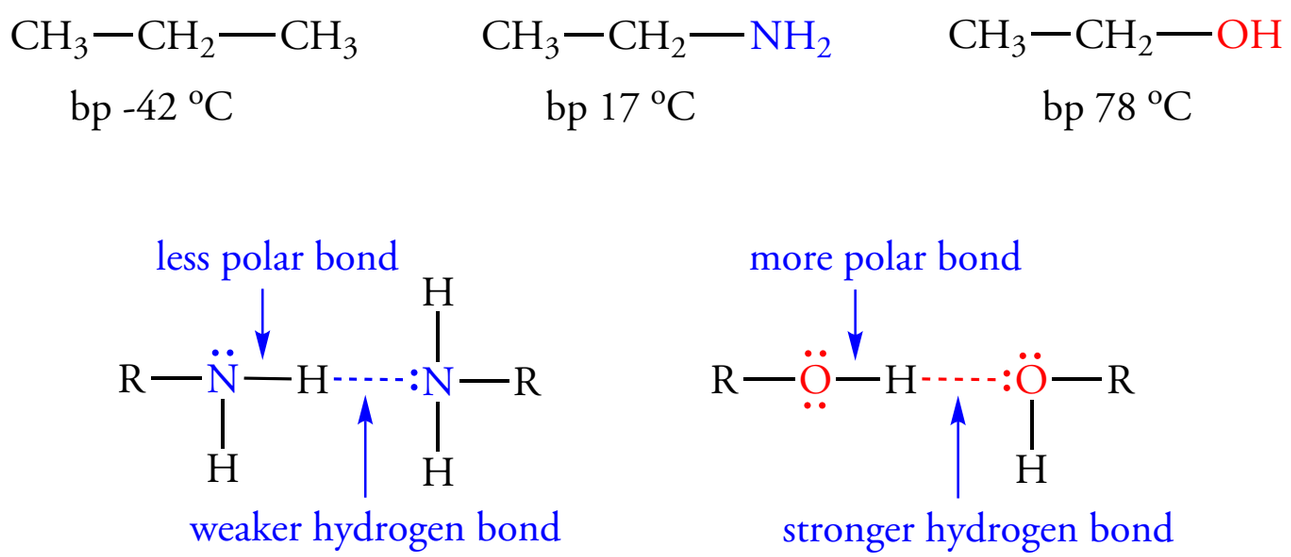
indole

23.4 PHYSICAL PROPERTIES OF AMINES

Melting Points and Boiling Points of Amine

Table 23.1
Boiling Points of Amines

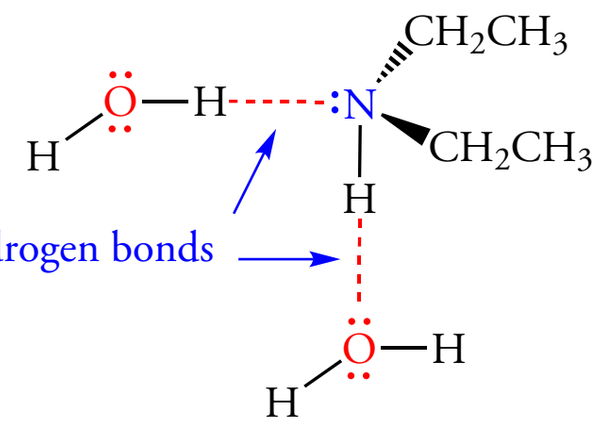
Name	Boiling Point, °C
methylamine	-7
ethylamine	17
propylamine	48
isopropylamine	33
butylamine	77
isobutylamine	68
sec-butylamine	63
tert-butylamine	45
cyclohexylamine	134
dimethylamine	7
ethylmethylamine	37
diethylamine	56
dipropylamine	111
trimethylamine	3
triethylamine	90
tripropylamine	156



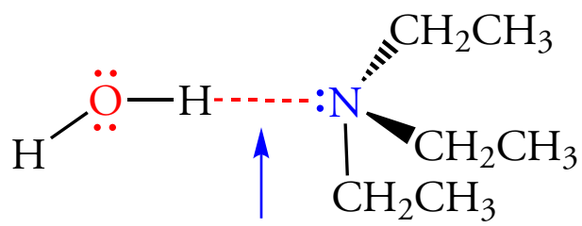
23.5 BASICITY OF AMINES

$$pK_b + pK_a = 14$$

	NH_3	$CH_3CH_2NH_2$	$(CH_3CH_2)_2NH$	$(CH_3CH_2)_3N$
pK_b	4.7	3.60	3.01	3.24



Two water-amine hydrogen bonds to diethylamine.



One water-amine hydrogen bond to triethylamine.

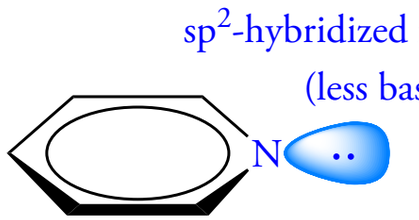
23.5 BASICITY OF AMINES

Table 23.1
Basicity of Amines

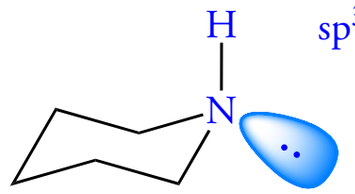
Name	K_b	pK_b
methylamine	4.3×10^{-4}	3.37
ethylamine	4.4×10^{-4}	3.36
propylamine	4.7×10^{-4}	3.33
isopropylamine	4.0×10^{-4}	3.40
butylamine	4.8×10^{-4}	3.22
cyclohexylamine	4.7×10^{-4}	3.33
dimethylamine	5.3×10^{-4}	3.28
diethylamine	9.8×10^{-4}	3.01
dipropylamine	1.0×10^{-3}	3.00
trimethylamine	5.5×10^{-5}	4.26
triethylamine	5.7×10^{-4}	3.24
tripropylamine	4.5×10^{-4}	3.35

23.5 BASICITY OF AMINES

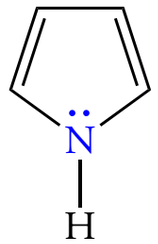
Heterocyclic Amines



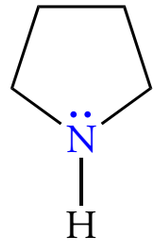
pyridine
pK_b 8.75



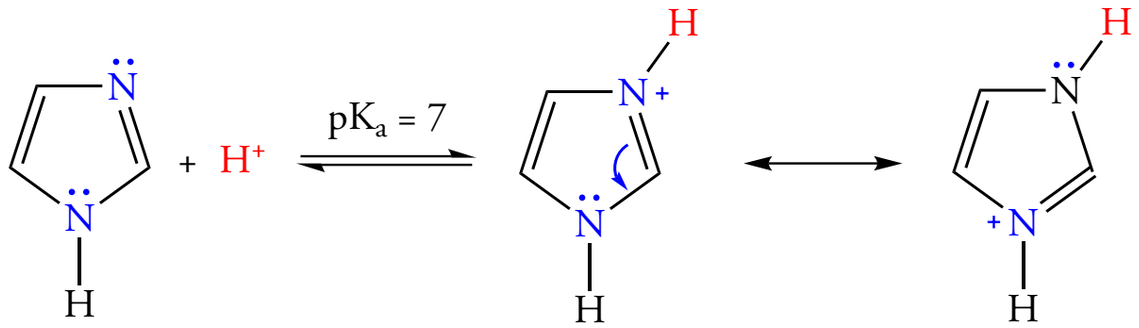
piperidine
pK_b 2.88



pyrrole
pK_b 15



pyrrolidine
pK_b 2.73

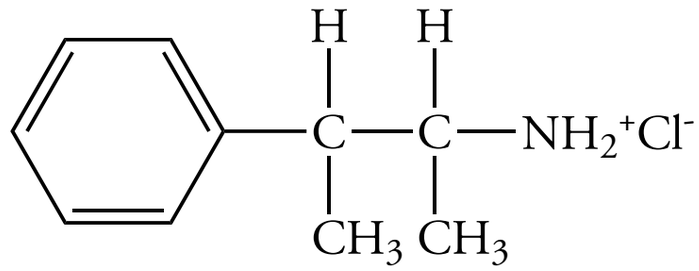


imidazole

resonance-stabilized imidazolium ion

23.6 SOLUBILITY OF AMMONIUM SALTS

$$RNH_2 + HCl \rightleftharpoons RNH_3^+Cl^-$$



ephedrine hydrochloride

$$CH_3(CH_2)_6CH_2\underset{\text{(insoluble in water)}}{NH_2} + HCl \longrightarrow \underset{\text{(soluble in water)}}{CH_3(CH_2)_6CH_2NH_3^+Cl^-}$$

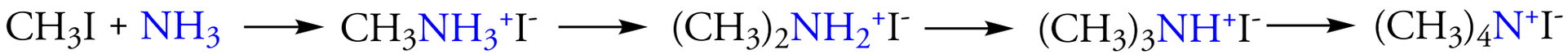
$$CH_3(CH_2)_6CH_2Cl + HCl \xrightarrow{X} \text{no reaction}$$

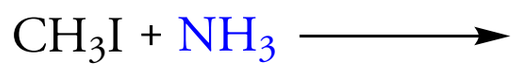
(insoluble in water)

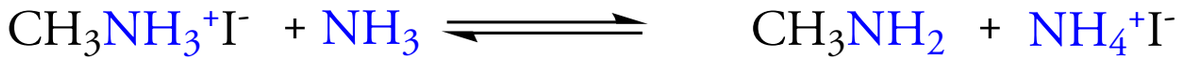
$$\underset{\text{(soluble in water)}}{CH_3(CH_2)_6CH_2NH_3^+} + OH^- \longrightarrow \underset{\text{(insoluble in water)}}{CH_3(CH_2)_6CH_2NH_2} + H_2O$$

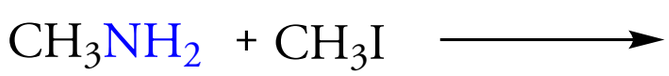
23.7 SYNTHESIS OF AMINES BY SUBSTITUTION REACTIONS

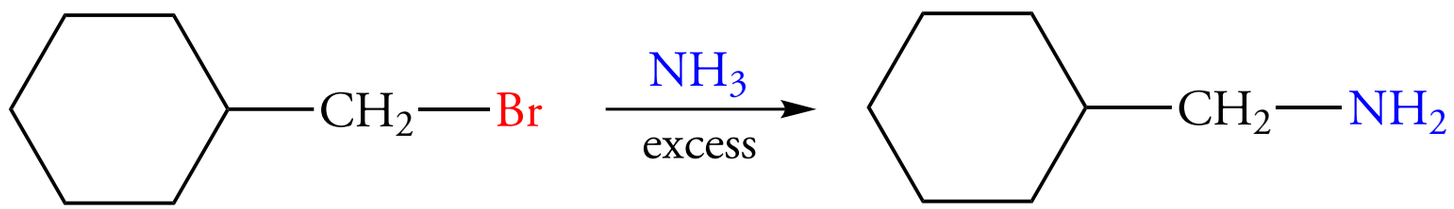
Alkylation of Amines by Alkyl Halides





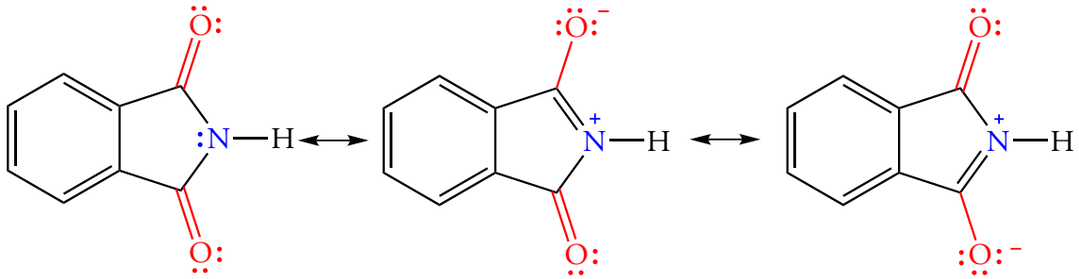






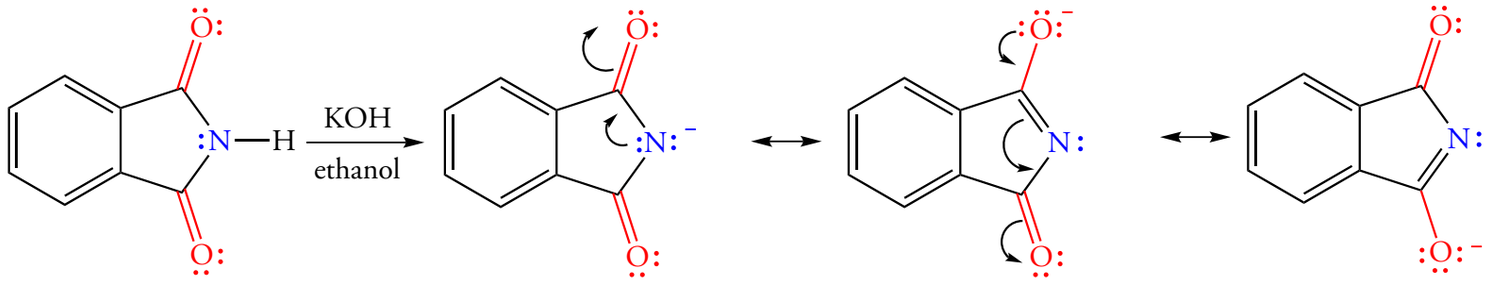
23.7 SYNTHESIS OF AMINES BY SUBSTITUTION REACTIONS

Gabriel Synthesis

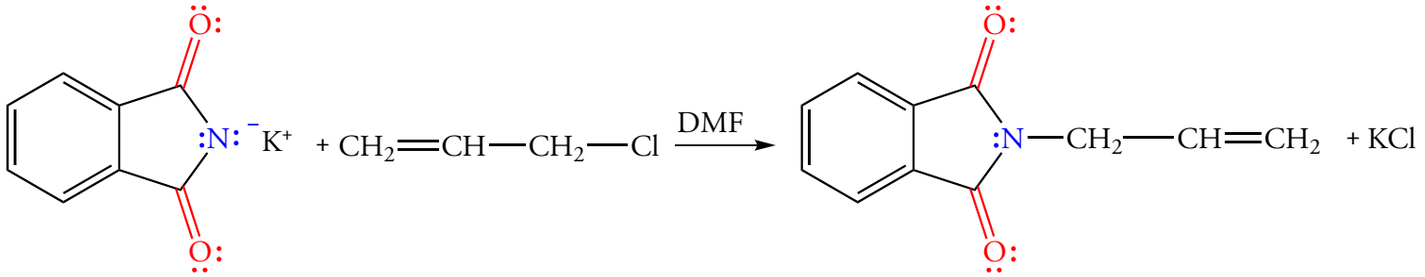


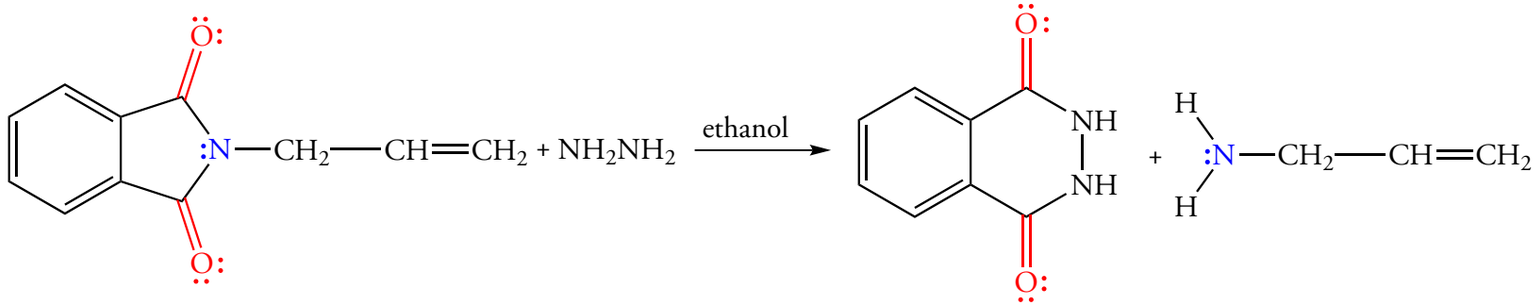
phthalimide

dipolar resonance forms



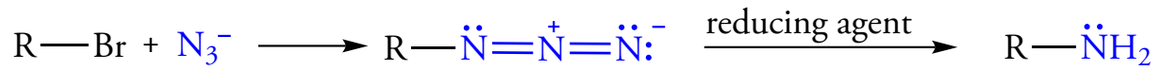
resonance-stabilized conjugate base

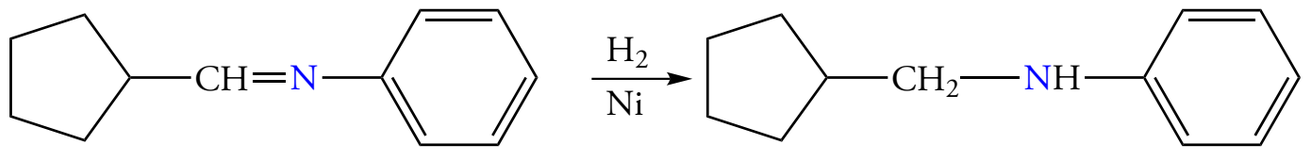


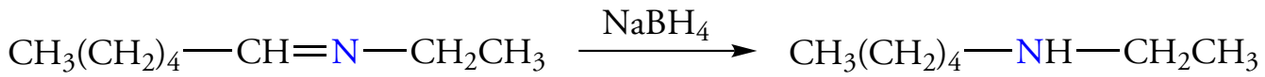


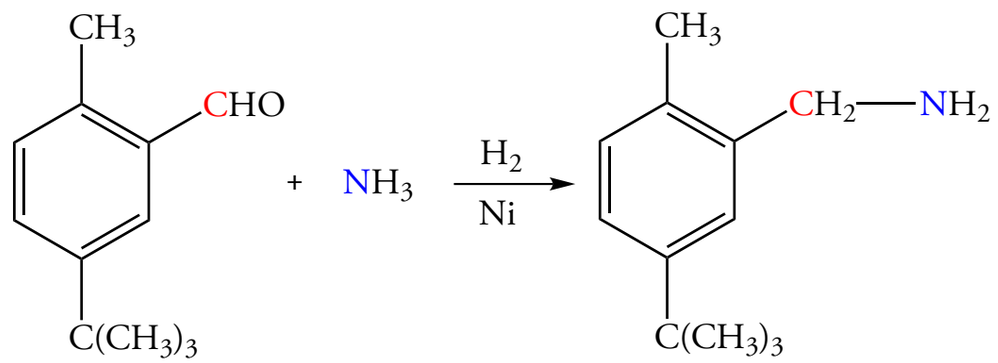
23.8 SYNTHESIS OF AMINES BY REDUCTION REACTIONS

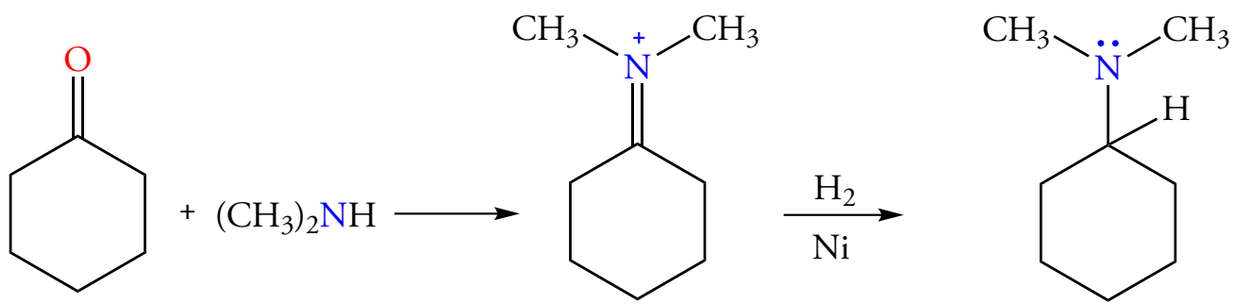
Reduction of Azides and Imines

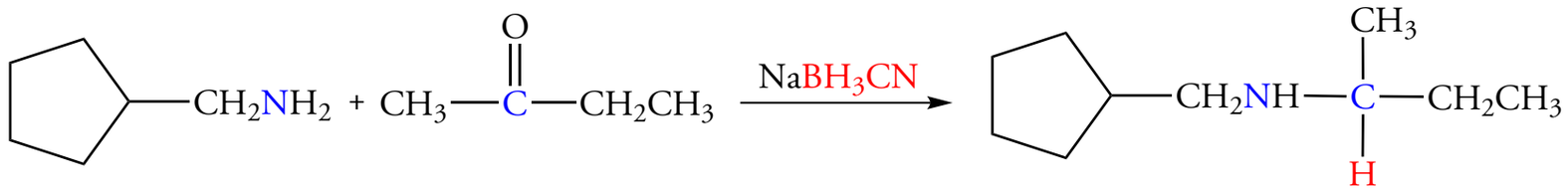






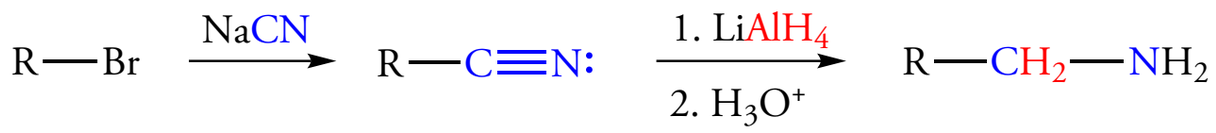


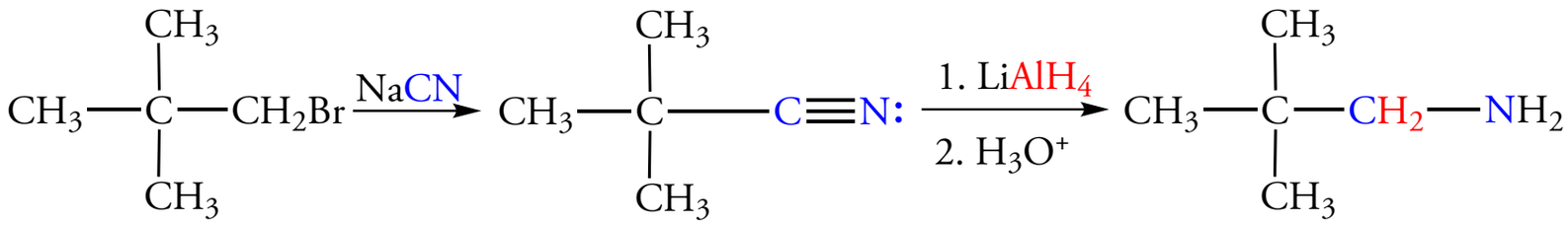


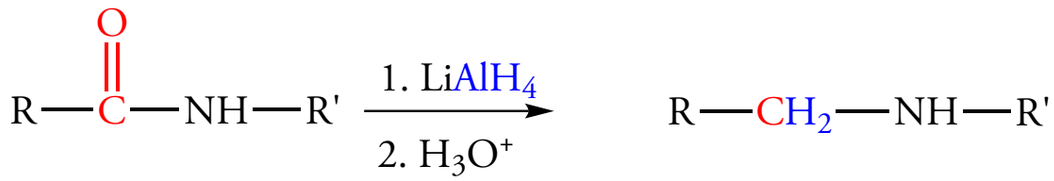


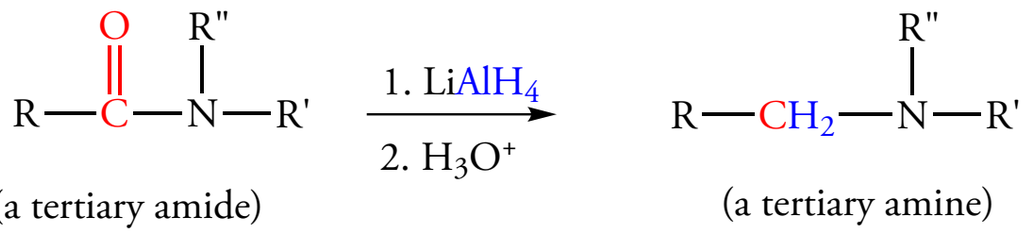
23.8 SYNTHESIS OF AMINES BY REDUCTION REACTIONS

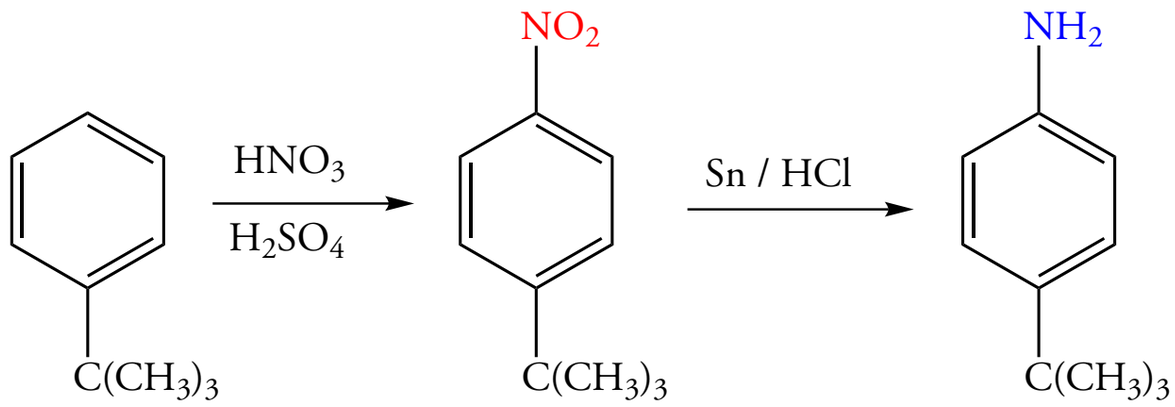
Reduction of Nitriles and Amines and Nitro Compounds



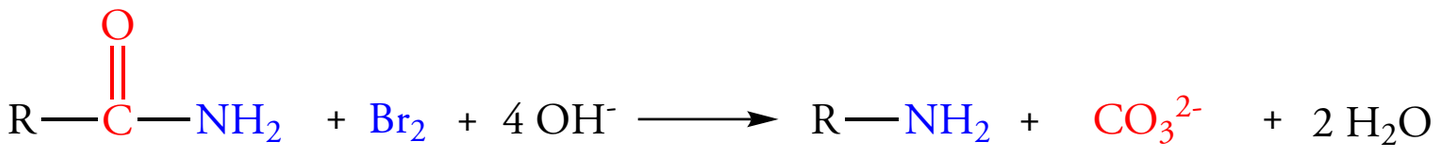


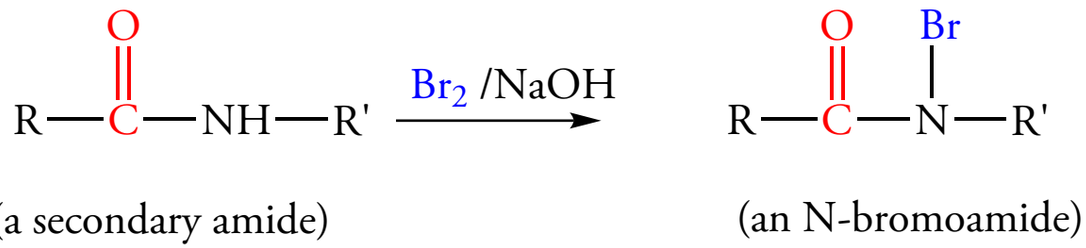




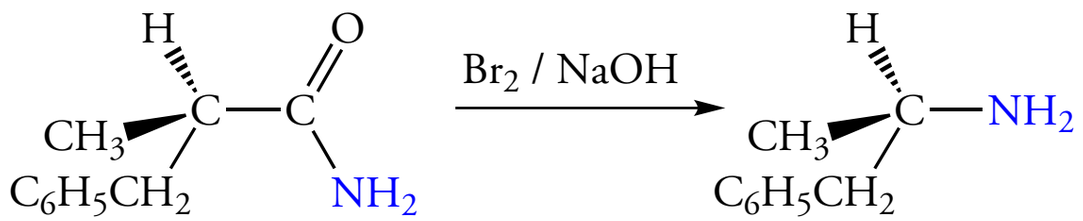


23.9 THE HOFMANN REARRANGEMENT

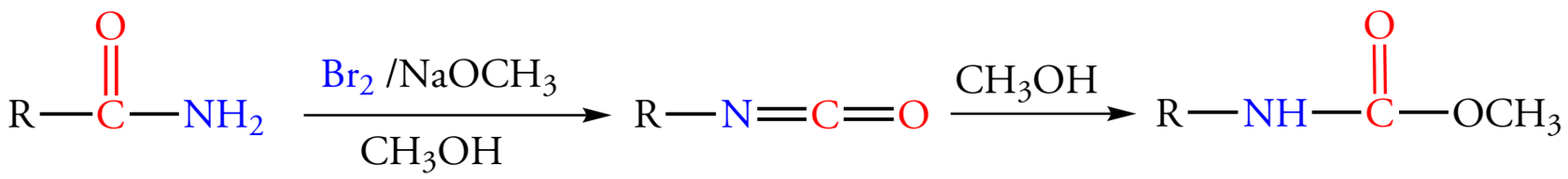




(a secondary amide) (an N-bromoamide)



(R)-2-methyl-3-phenylpropanamide (R)-1-phenyl-2-propanamine

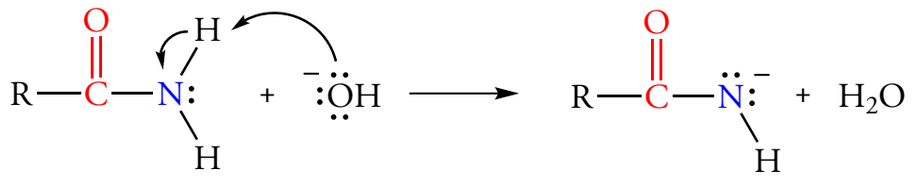


(an isocyanate) a methyl N-alkylcarbamate

23.9 THE HOFMANN REARRANGEMENT

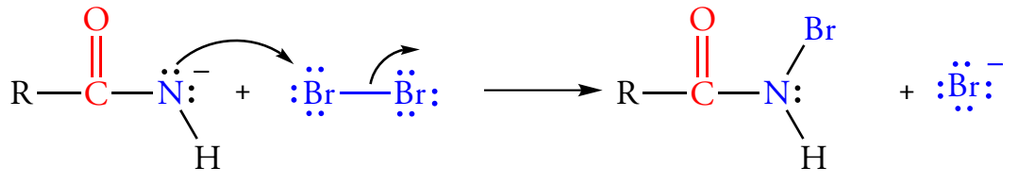
Mechanism of the Hofmann Rearrangement

Step 1.



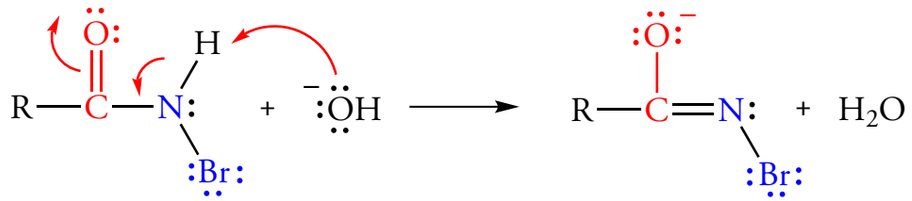
(resonance-stabilized ion)

Step 2.



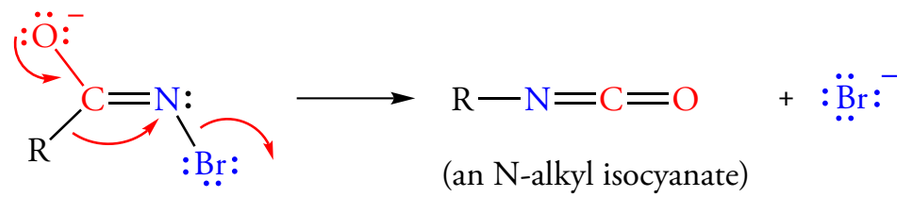
(an N-bromoamide)

Step 1.



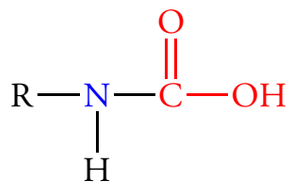
(conjugate base of an N-bromoamide)

Step 2.



(an N-alkyl isocyanate)

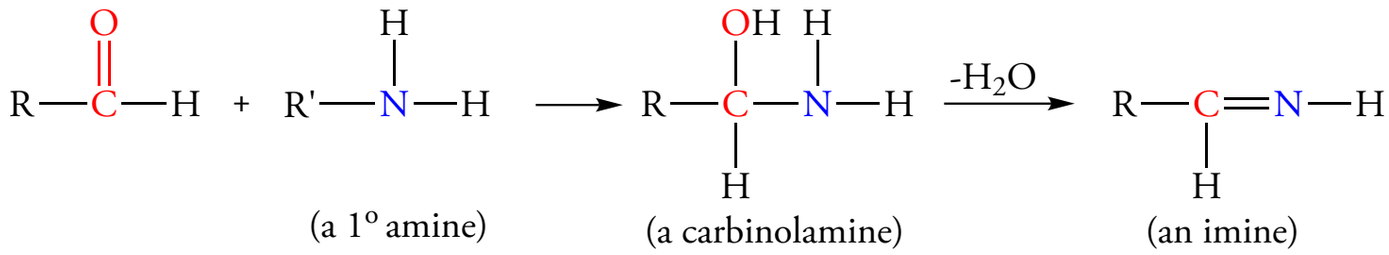
Step 1. $R-N=C=O + H_2O \longrightarrow$

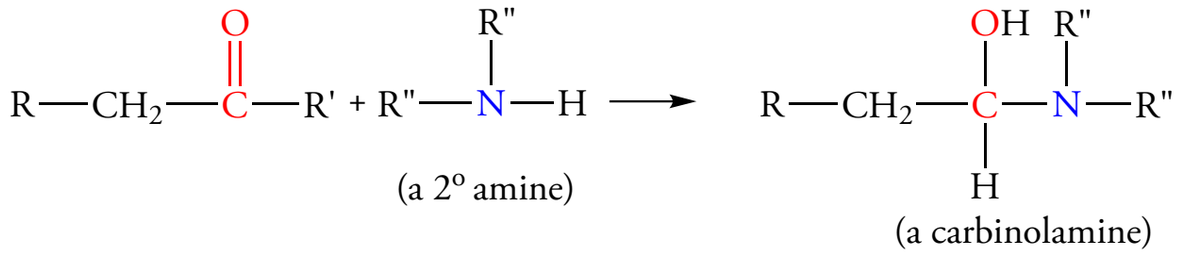


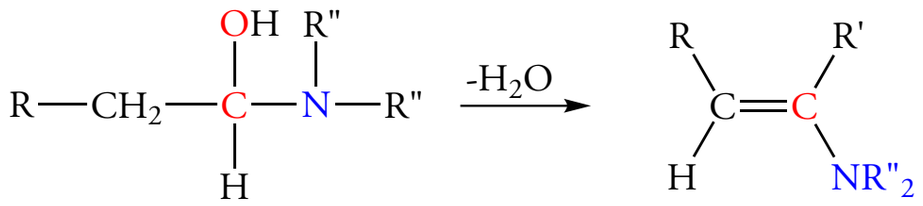
(a carbamic acid)

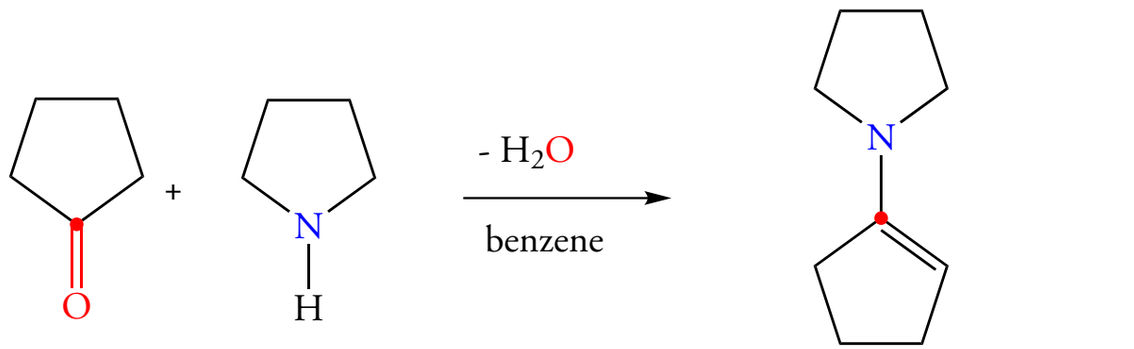
Step 2. $R-\underset{\underset{H}{|}}{N}-\overset{\overset{O}{\|}}{C}-OH + 2\ OH^- \longrightarrow R-NH_2 + CO_3^{2-} + H_2O$

23.11 ENAMINES



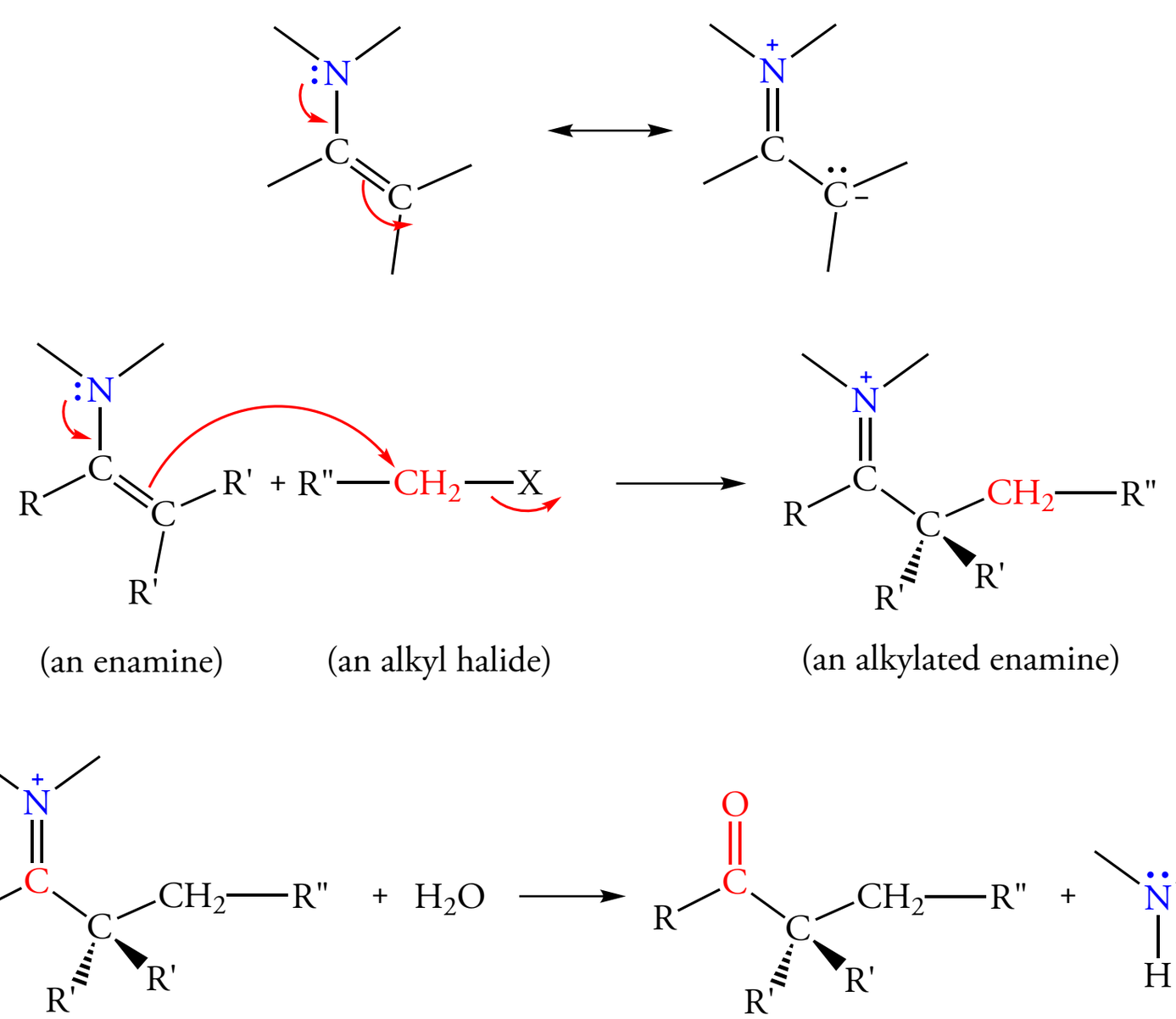






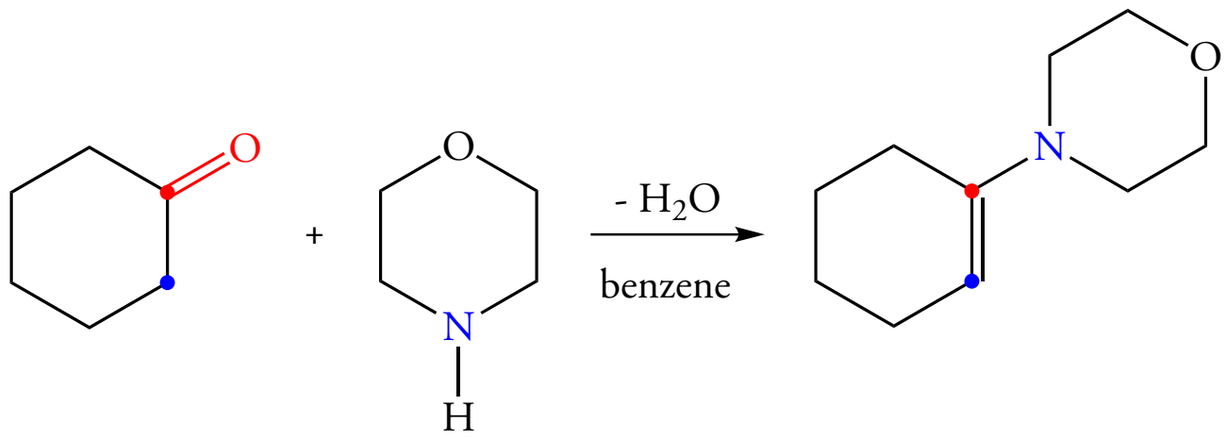
23.11 ENAMINES

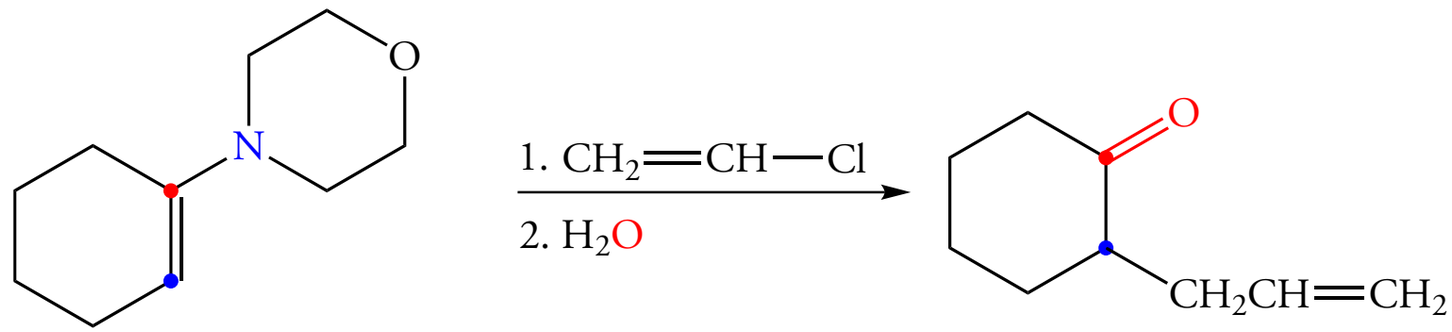
Alkylation of Enamines

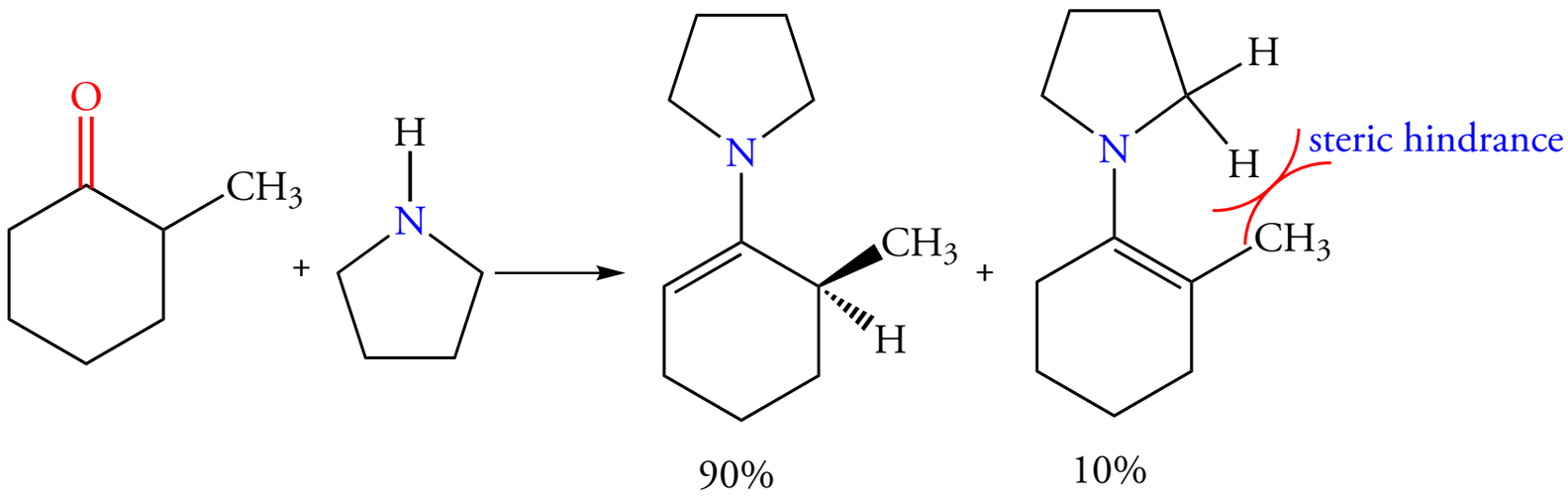


23.11 ENAMINES

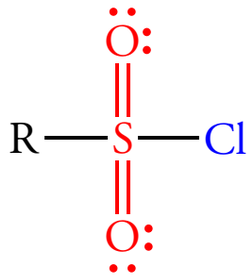
Alkylation of Enamines



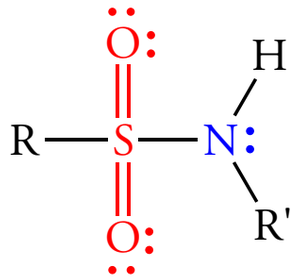




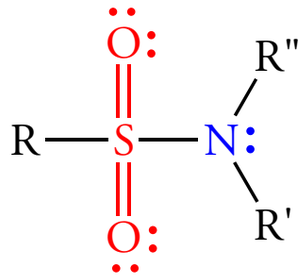
23.12 SULFONAMIDES



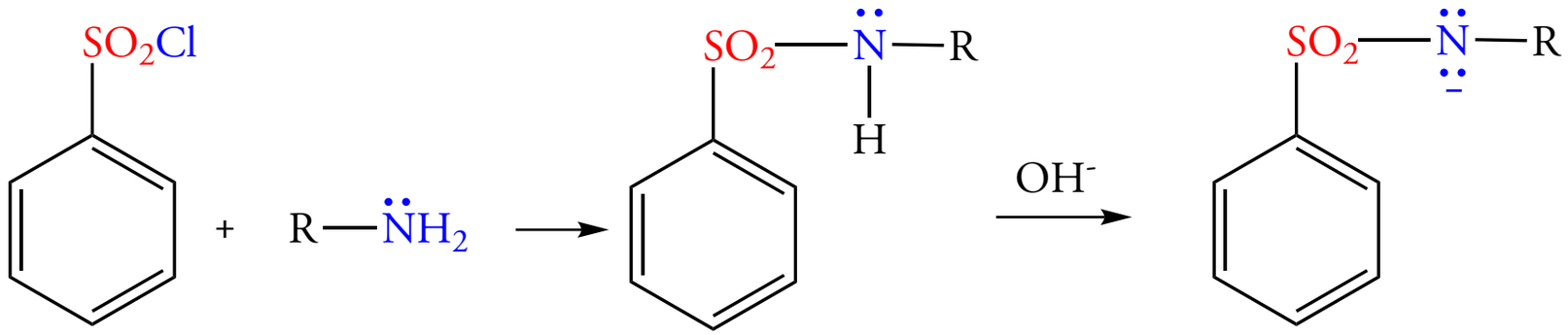
a sulfonyl chloride



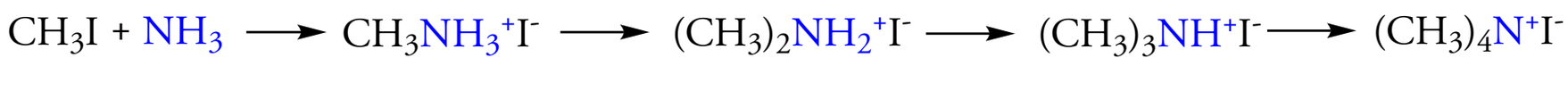
sulfonamide of a 1° amine

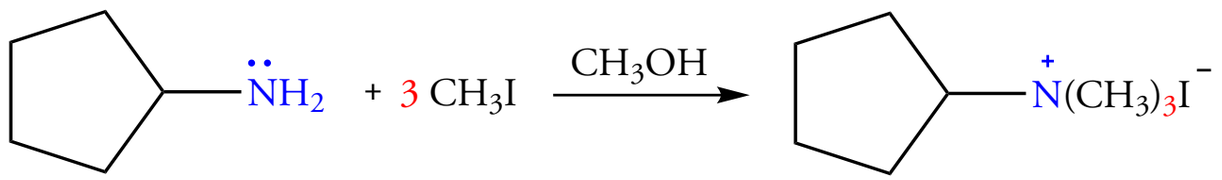


sulfonamide of a 2° amine



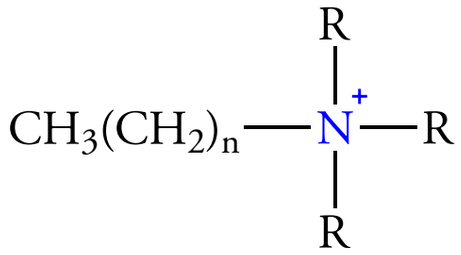
23.13 QUATERNARY AMMONIUM SALTS



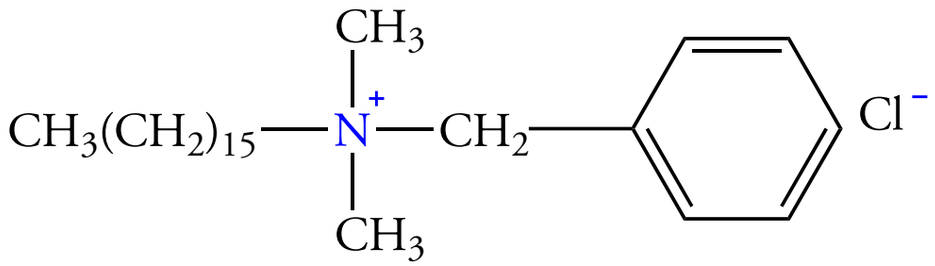


23.13 QUATERNARY AMMONIUM SALTS

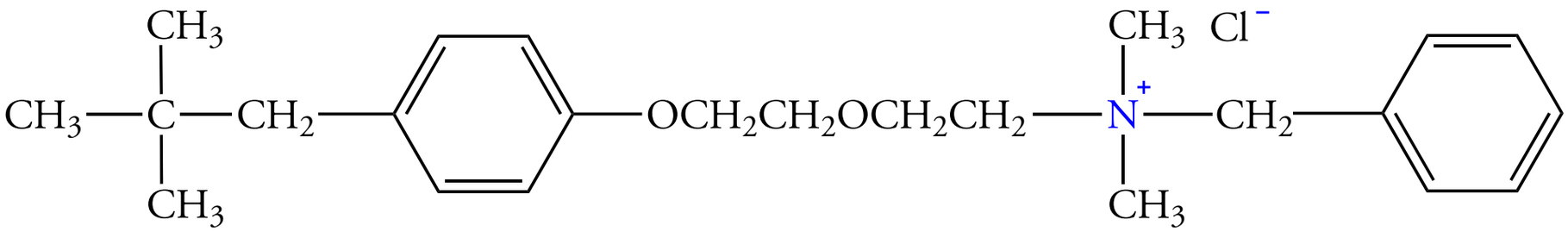
Invert Soaps



(an invert soap)



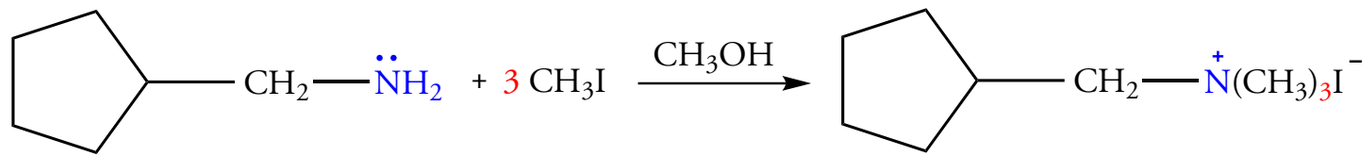
benzalkonium chloride



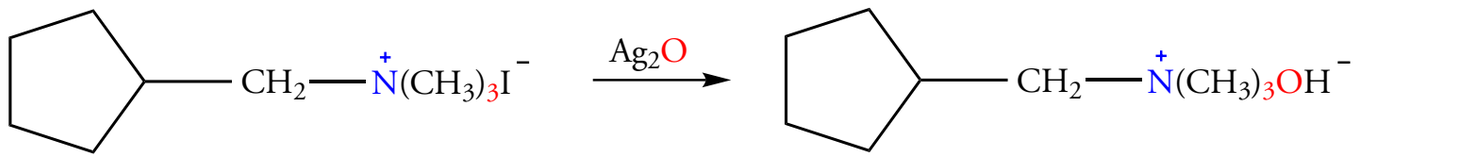
benzethonium chloride

23.13 QUATERNARY AMMONIUM SALTS

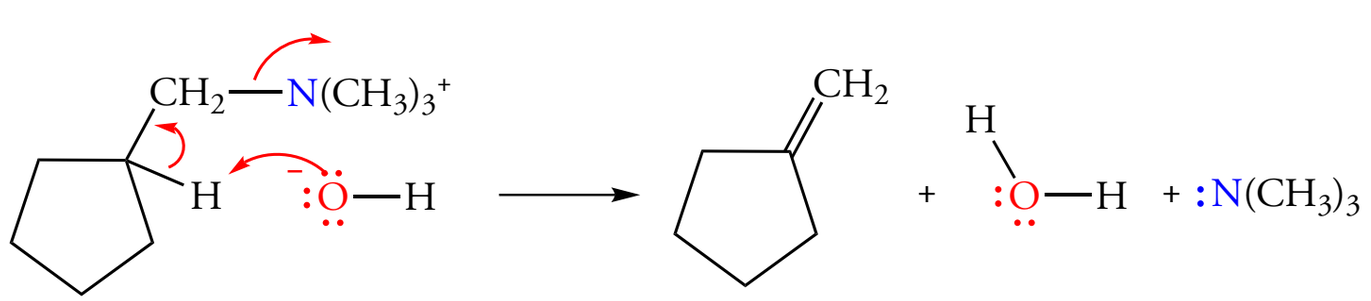
The Hofmann Elimination

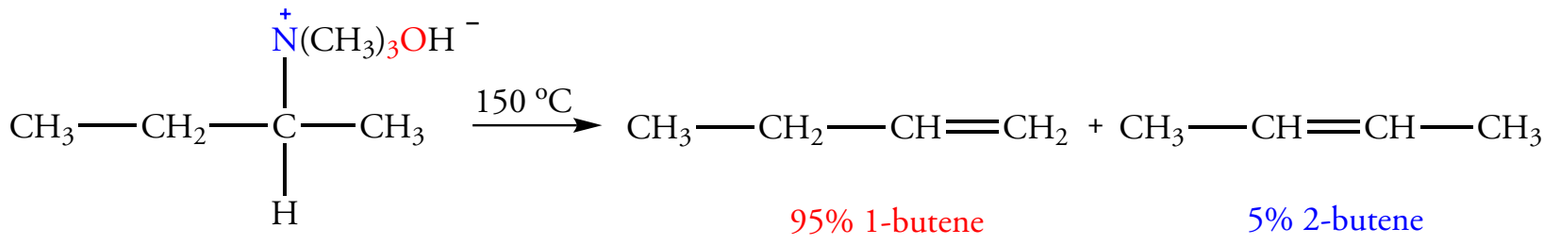


(cyclopentylmethyl)trimethylammonium iodide

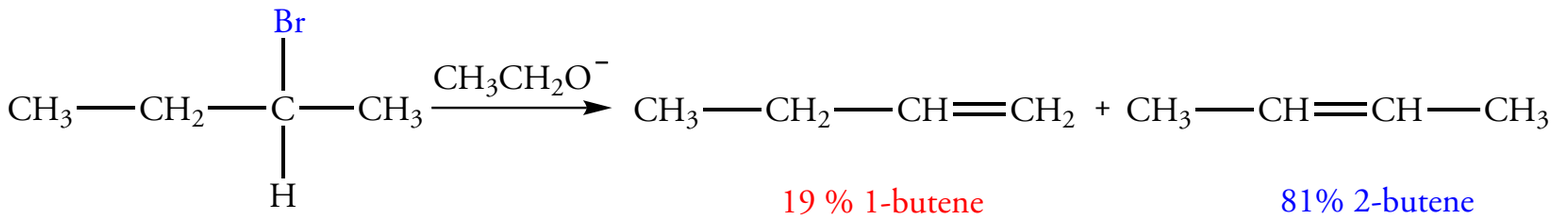


(cyclopentylmethyl)trimethylammonium hydroxide





95% 1-butene 5% 2-butene



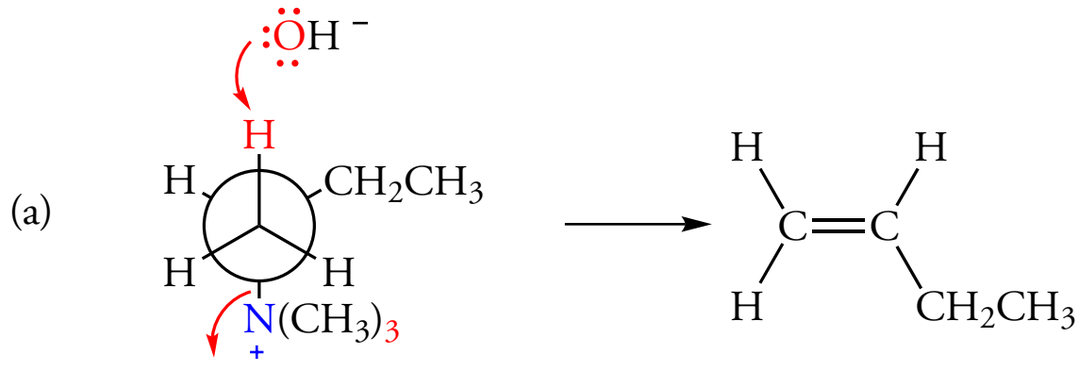
19 % 1-butene 81% 2-butene

Figure 23.1
The Hofmann Elimination

(a) The abstraction of a hydrogen atom at C-1 occurs from a conformation that has no steric crowding of the trimethylammonium group.

(b) The abstraction of a hydrogen atom at C-2 occurs from a conformation in which the C-4 methyl group and the trimethylammonium ion are gauche. The product is *trans*-2-butene.

(c) In this conformation the C-4 methyl group and the trimethylammonium ion are gauche. However, the C-4 and C-1 methyl groups are also gauche. The cis-2-butene product is formed in smaller amount than the *trans*-2-butene derived from (b).

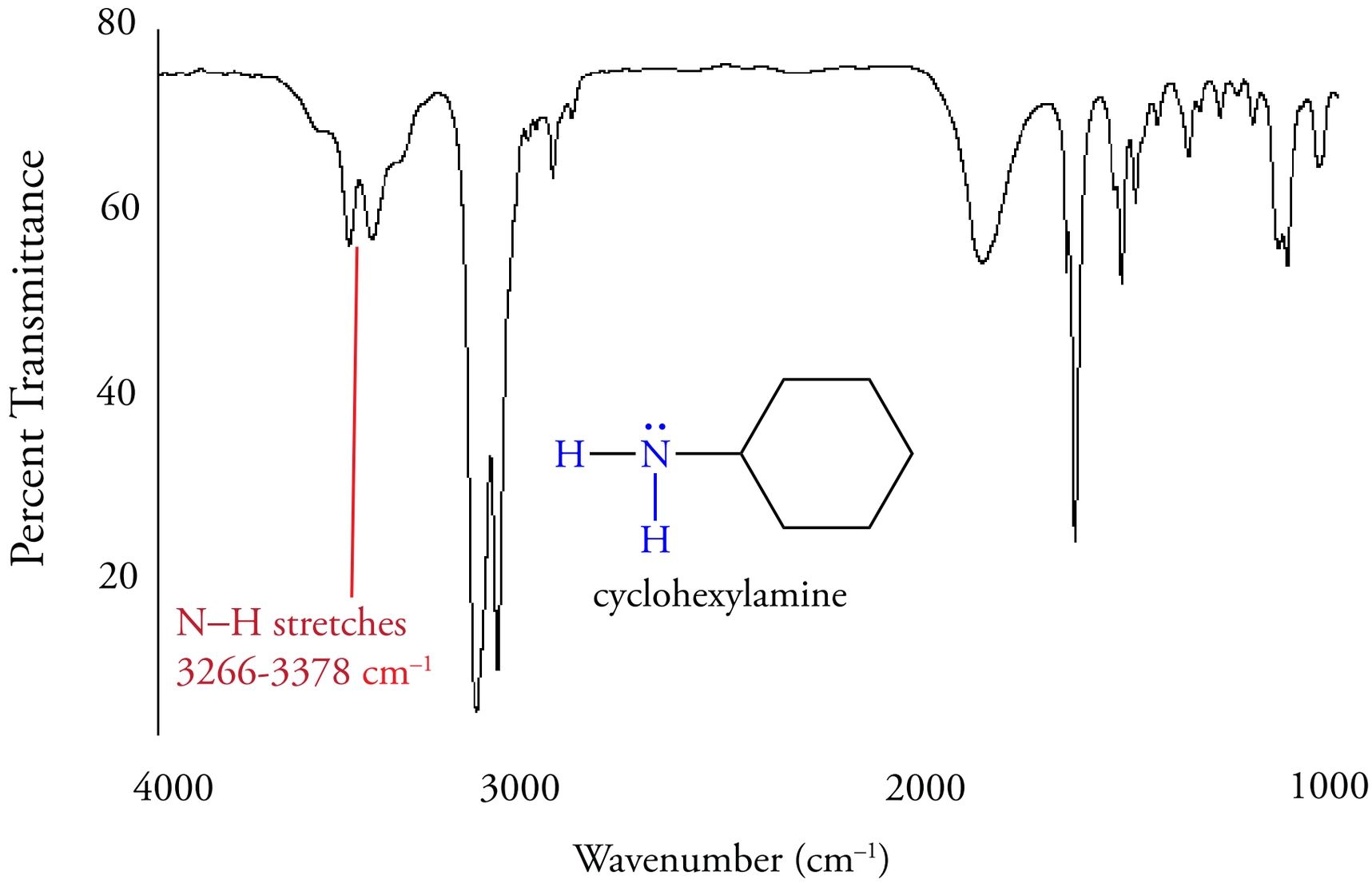


23.14 SPECTROSCOPY OF AMINES

Infrared Spectroscopy

Figure 23.2 Infrared Spectrum of a Primary Amine

Primary amines have two absorptions in the IR in the 3200-3380 cm^{-1} region, as shown for cyclohexylamine.



23.14 SPECTROSCOPY OF AMINES

Infrared Spectroscopy

Figure 23.3 Infrared Spectrum of a Secondary Amine

Secondary amines have one absorption in the IR in the 3200-3380 cm^{-1}, region as shown for diethylamine.

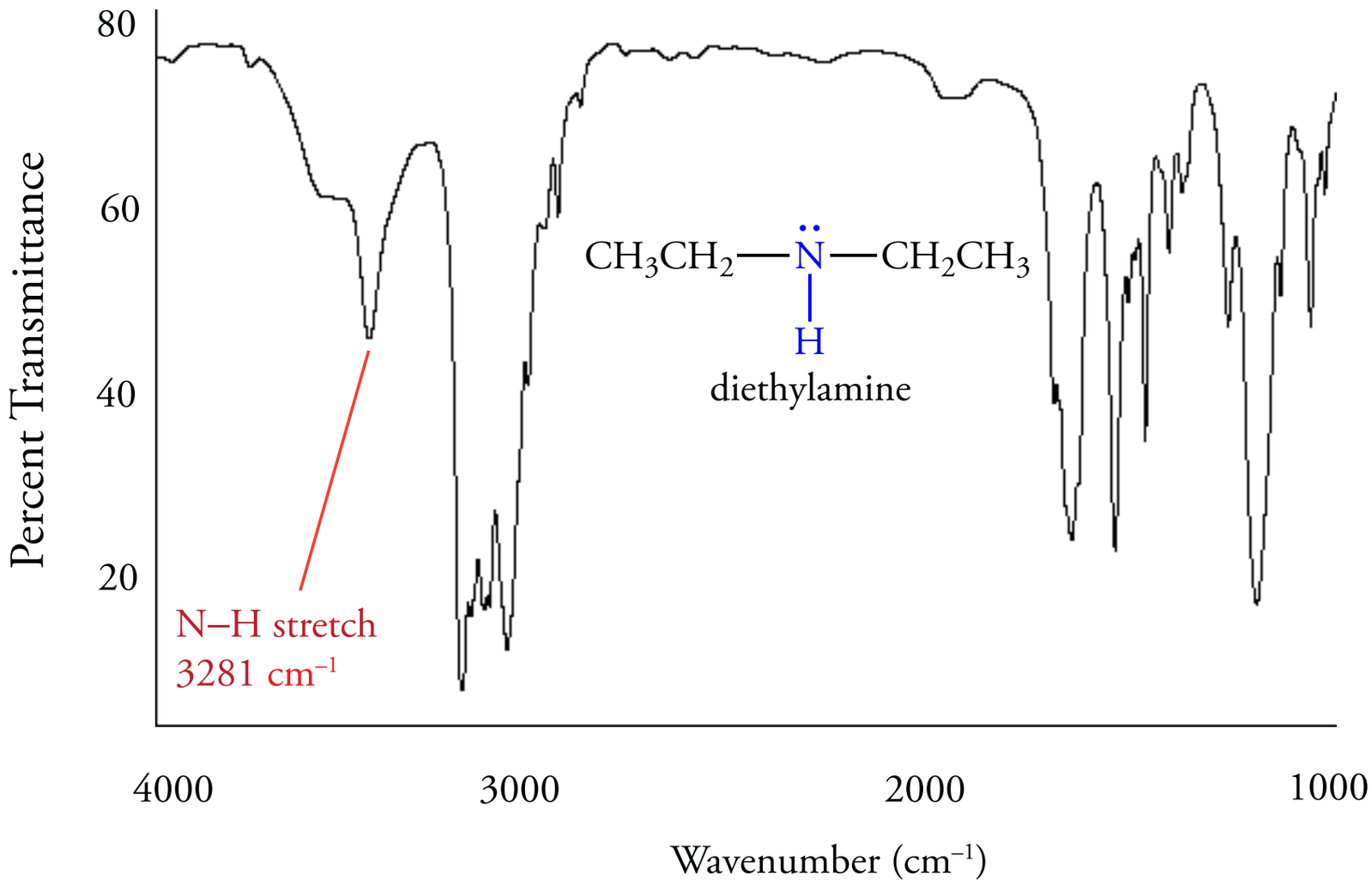
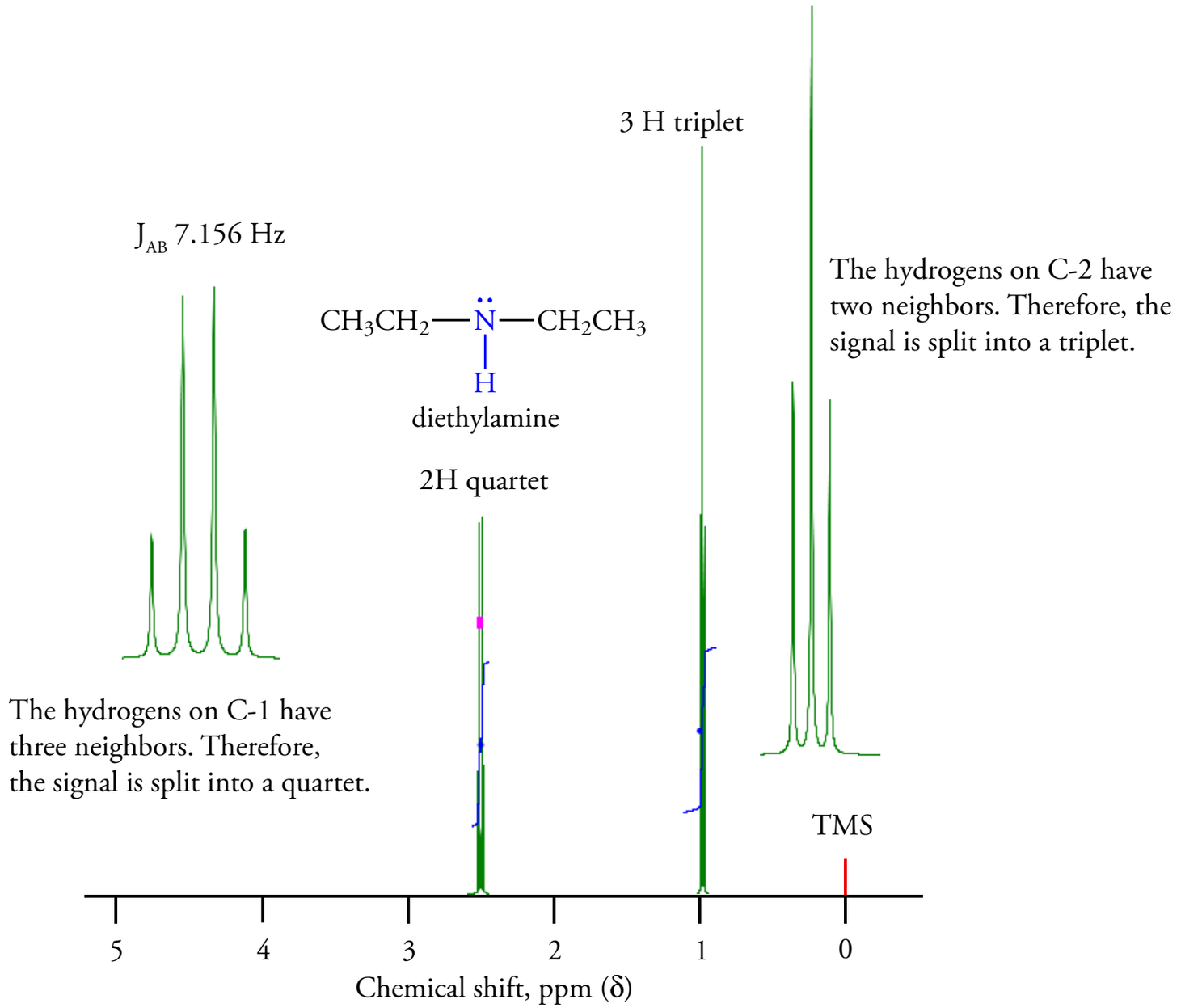


Figure 23.4 NMR Spectrum of Diethylamine

The alkyl hydrogens of primary amines have about the same chemical shifts as those of alkanes. When a small amount of D_2O is added to the sample, the N—H hydrogen exchanges with D_2O, and the N-H resonance disappears.



23.14 SPECTROSCOPY OF AMINES

C-13 NMR Spectroscopy