AMINES

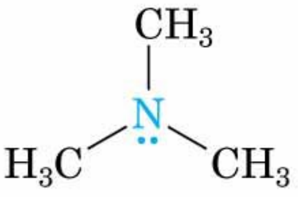
LECTURER:HIBA MUSHTAQ AHMED

AMINES – ORGANIC NITROGEN COMPOUNDS

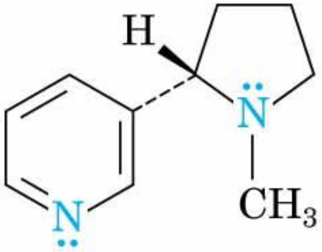
Organic derivatives of ammonia, NH_3,

Nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic

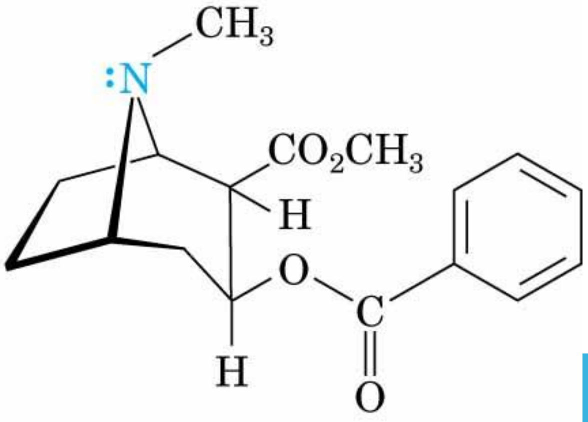
Occur in plants and animals



Trimethylamine



Nicotine



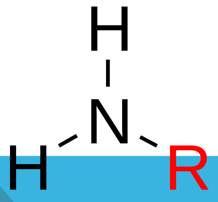
Cocaine

NAMING AMINES

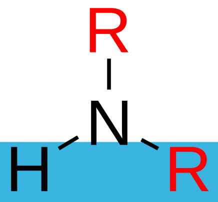
Alkyl-substituted (alkylamines) or aryl-substituted (arylamines)

Classified:

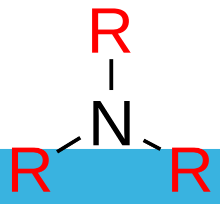
- 1° (RNH_2) primary amine
- 2° (R_2NH) secondary amine
- Tertiary amine 3° (R_3N)



Primary



Secondary

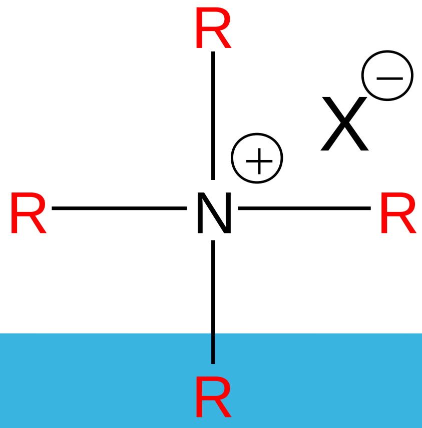


Tertiary

QUATERNARY AMMONIUM IONS

A nitrogen atom with four attached groups is positively charged

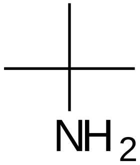
Compounds are quaternary ammonium salts



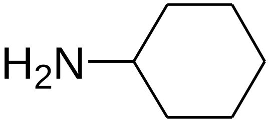
$$\mathrm{R-\overset{\overset{\displaystyle R}{|}}{\underset{\underset{\displaystyle R}{|}}{N^{\oplus}}}-R}\quad \mathrm{X^{\ominus}}$$

IUPAC NAMES – SIMPLE AMINES

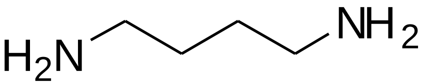
For simple amines, the suffix *-amine* is added to the name of the alkyl substituent



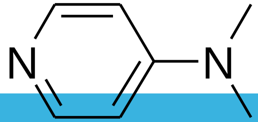
tert-butylamine



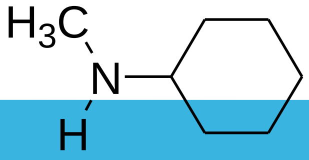
cyclohexanamine



1,4-butandiamine



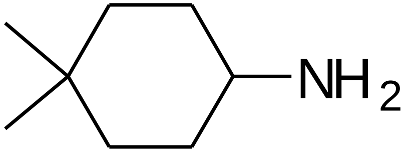
N,N-Dimethyl-4-aminopyridine



N-Methyl-Cyclohexanamine

IUPAC NAMES – “-AMINE” SUFFIX

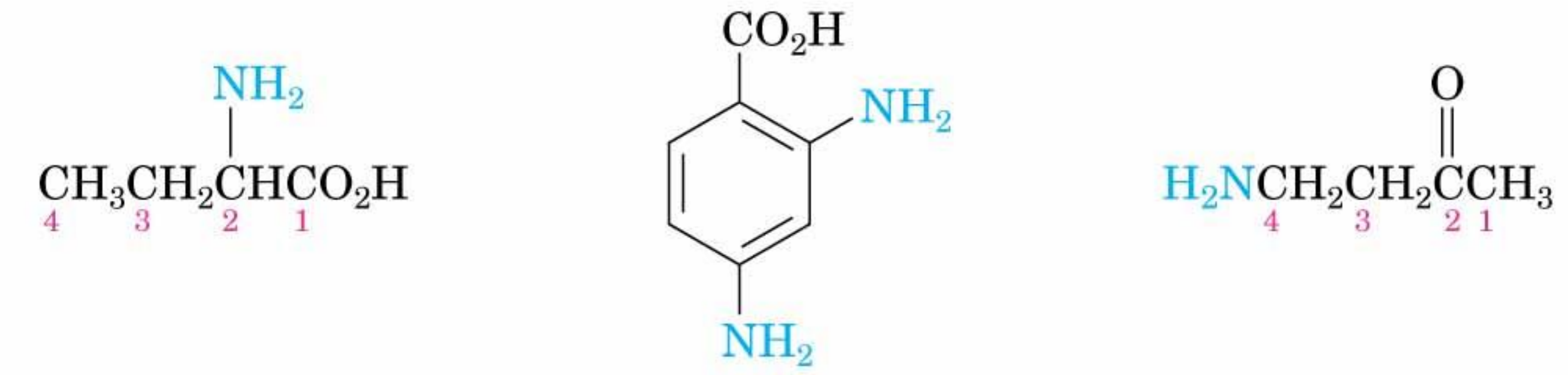
The suffix -*amine* can be used in place of the final -*e* in the name of the parent compound



4,4-Dimethylcyclohexanamine

IUPAC NAMES – AMINES WITH MORE THAN ONE FUNCTIONAL GROUP

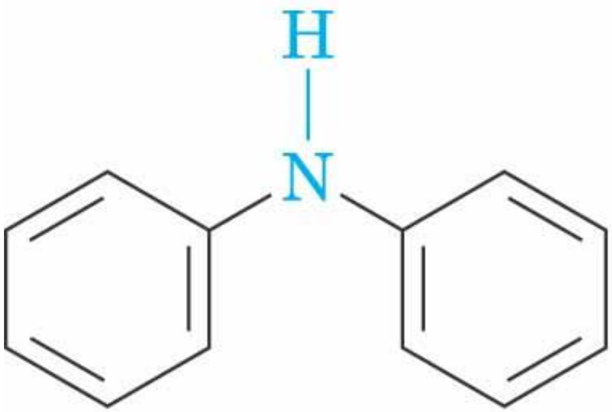
Consider the —NH_2 as an *amino* substituent on the parent molecule



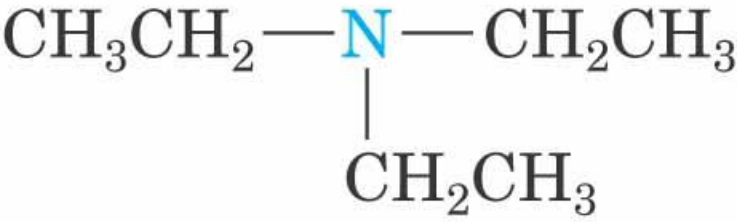
2-Aminobutanoic acid 2,4-Diaminobenzoic acid 4-Amino-2-butanone

IUPAC NAMES – MULTIPLE ALKYL GROUPS

Symmetrical secondary and tertiary amines are named by adding the prefix *di*- or *tri*- to the alkyl group



Diphenylamine



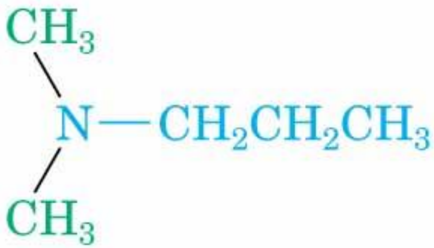
$$CH_3CH_2-\underset{\displaystyle CH_2CH_3}{\underset{|}{N}}-CH_2CH_3$$

Triethylamine

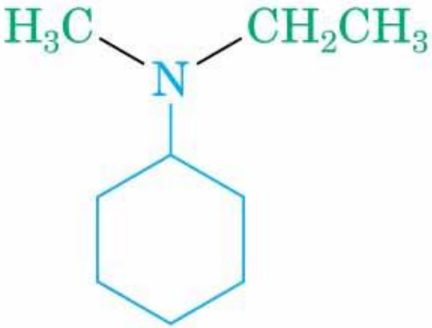
IUPAC NAMES – MULTIPLE, DIFFERENT ALKYL GROUPS

Named as *N*-substituted primary amines

Largest alkyl group is the parent name, and other alkyl groups are considered *N*-substituents



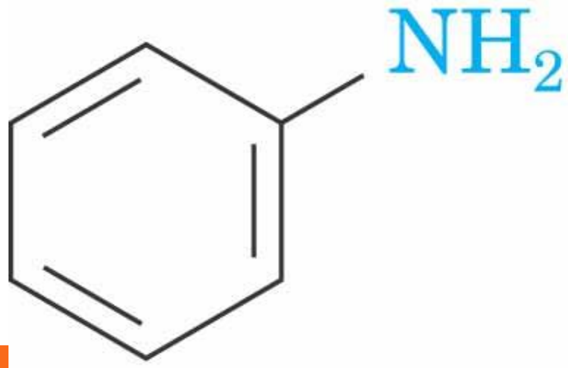
***N,N*-Dimethylpropylamine**
(propylamine is the parent name; the two methyl groups are substituents on nitrogen)



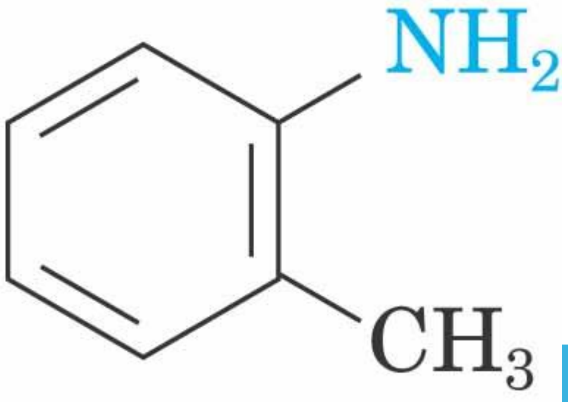
***N*-Ethyl-*N*-methylcyclohexylamine**
(cyclohexylamine is the parent name; methyl and ethyl are *N*-substituents)

COMMON NAMES

- Alkylamines do not have common names unless they are biological molecules
- Simple arylamines have common names



Aniline

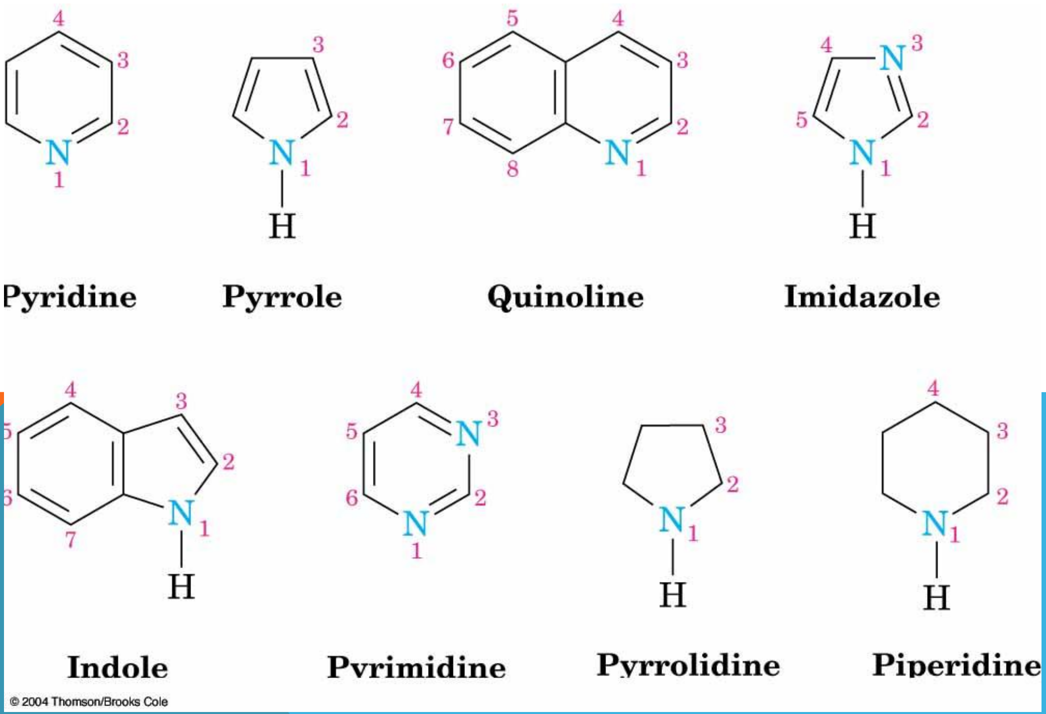


***o*-Toluidine**

COMMON NAMES OF HETEROCYCLIC AMINES

If the nitrogen atom occurs as part of a ring, the compound is designated as being heterocyclic

Each ring system has its own parent name



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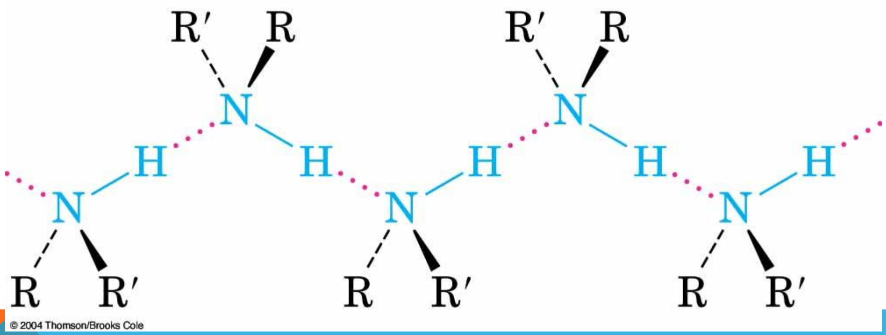
AMINES FORM H-BONDS

Amines with fewer than five carbons are water-soluble

Primary and secondary amines form hydrogen bonds, increasing their boiling points



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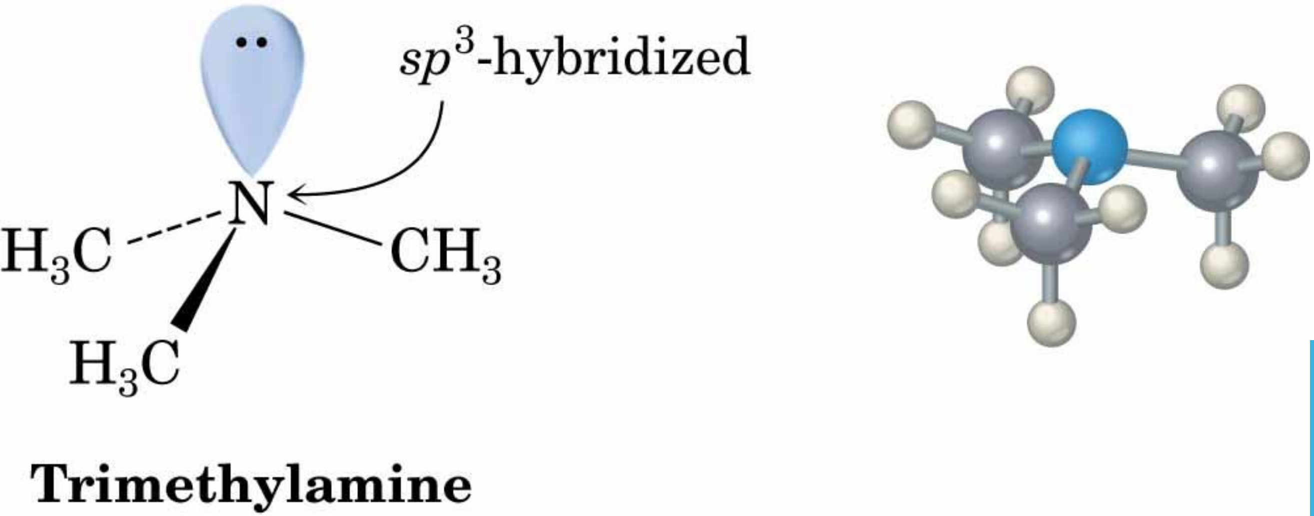
STRUCTURE AND BONDING IN AMINES

Bonding to N is similar to that in ammonia

- N is *sp*^{3}-hybridized
- C–N–C bond angles are close to 109° tetrahedral value



Trimethylamine

PROPERTIES AND SOURCES OF AMINES

Simple methylated amines from reaction of NH_3 with CH_3OH and alumina catalyst

Yields a mixture of monomethylated, dimethylated, and trimethylated products that are easily separated by distillation

$$NH_3 + CH_3OH \xrightarrow[450^{\circ}C]{Al_2O_3} CH_3NH_2 + CH_3\overset{\overset{H}{|}}{N}CH_3 + CH_3\overset{\overset{CH_3}{|}}{N}CH_3$$

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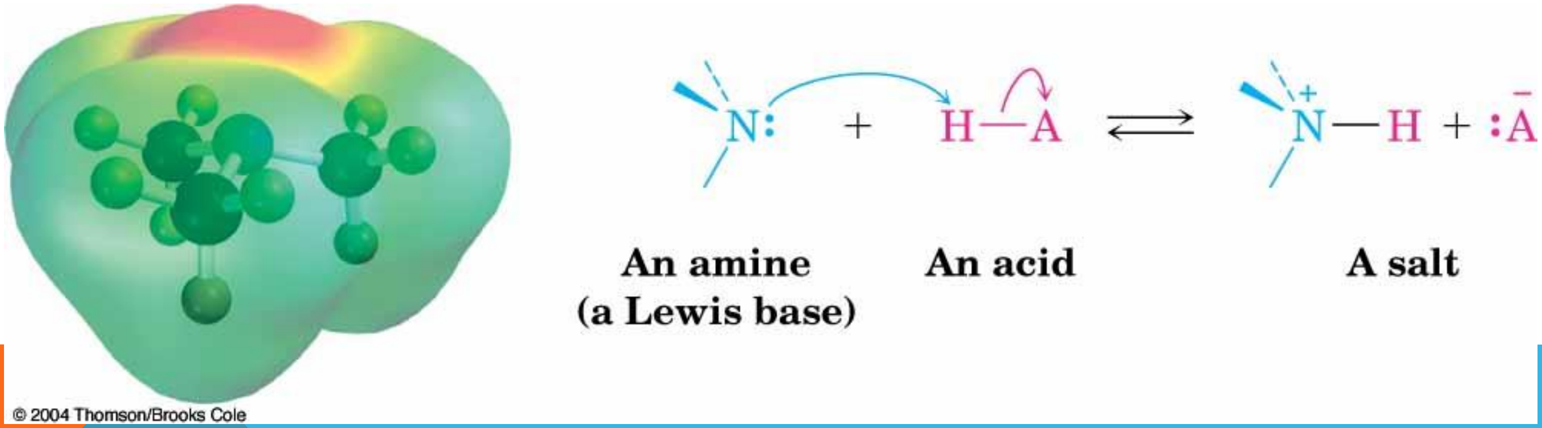
BASICITY OF AMINES

The lone pair of electrons on nitrogen makes amines basic and nucleophilic

They react with acids to form acid–base salts and they react with electrophiles



RELATIVE BASICITY

Amines are stronger bases than alcohols, ethers, or water

Amines establish an equilibrium with water in which the amine becomes protonated and hydroxide is produced

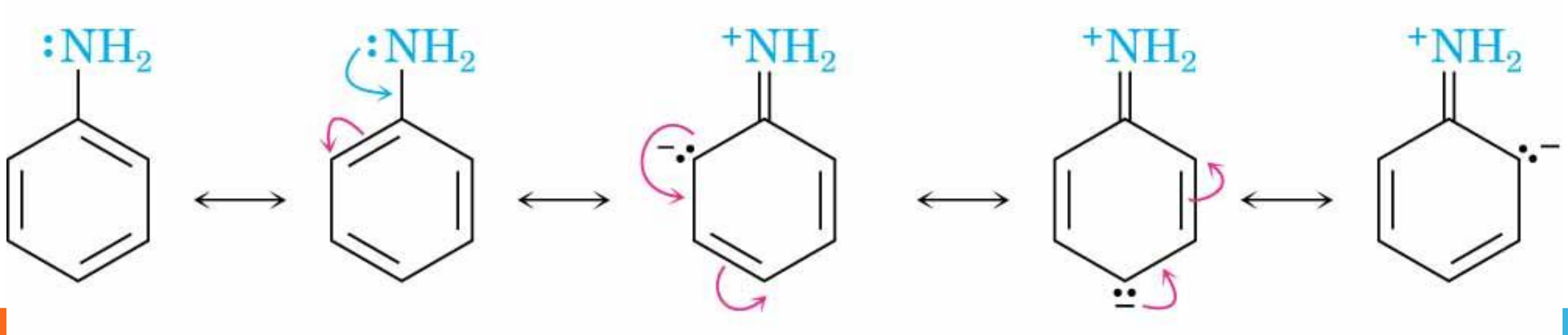
The most convenient way to measure the basicity of an amine (RNH_2) is to look at the acidity of the corresponding ammonium ion (RNH_3^+)

$$RNH_3^+ \xrightleftharpoons{K_a} RNH_2 + H^+$$

$$pK_a = pH - \log ([RNH_2])/[RNH_3^+])$$

BASICITY OF SUBSTITUTED ARYLAMINES

The N lone-pair electrons in arylamines are delocalized by interaction with the aromatic ring π electron system and are less able to accept H^+ than are alkylamines



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GENERAL PATTERNS OF BASICITY

Table 24.1: pK_a values of ammonium ions

Most simple alkylammmonium ions have pK_a's of 10 to 11

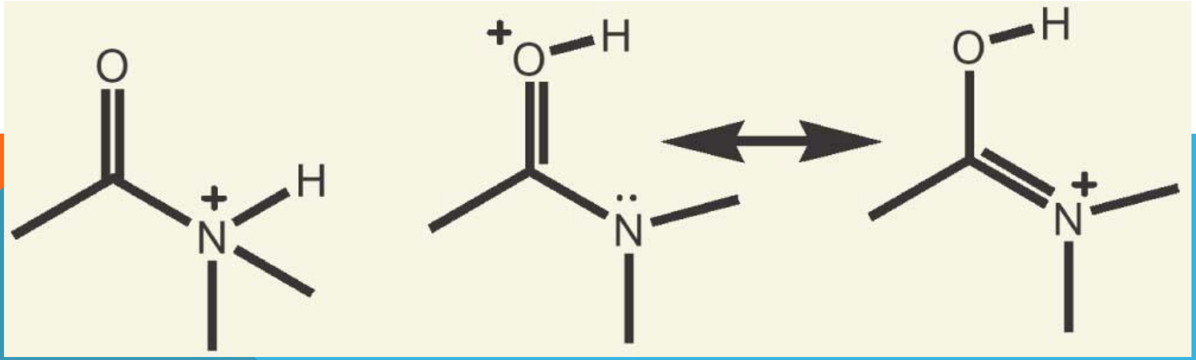
Arylamines and heterocyclic aromatic amines are considerably less basic than alkylamines (conjugate acid pK_a 5 or less)

AMIDES

Amides ($RCONH_2$) in general are not proton acceptors except in very strong acid

The C=O group is strongly electron-withdrawing, making the N a very weak base

Addition of a proton occurs on O but this destroys the double bond character of C=O as a requirement of stabilization by N



SUBSTITUTED ARYLAMINES

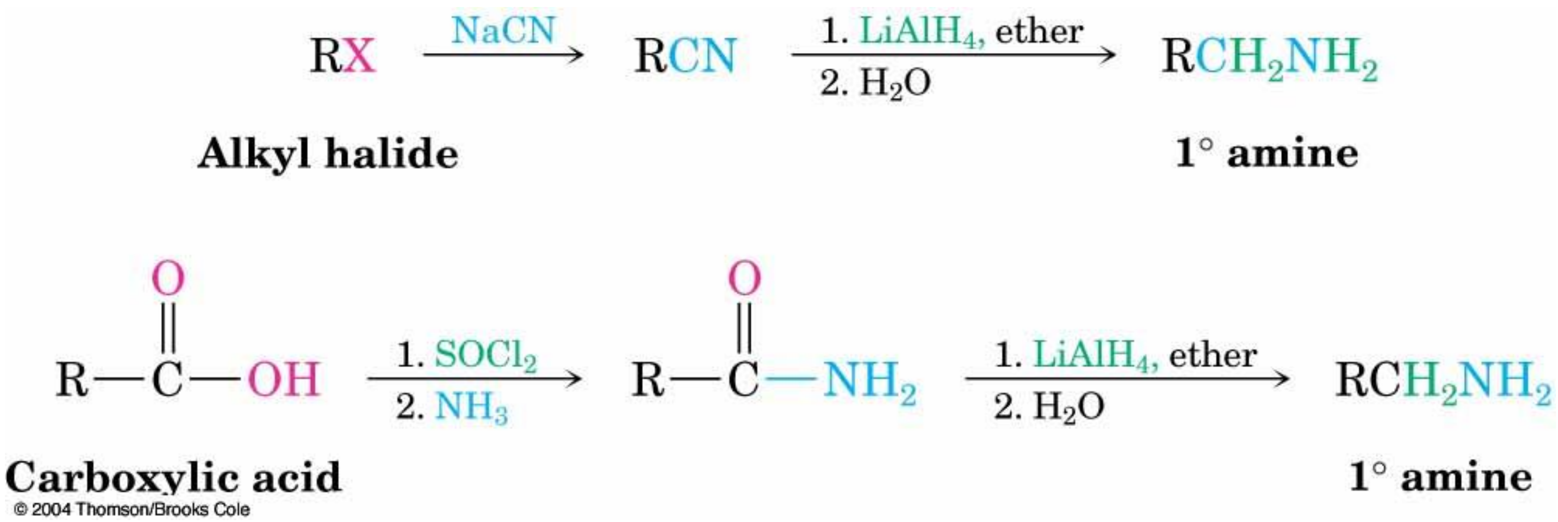
Can be more basic or less basic than aniline

Electron-donating substituents (such as —CH_3, —NH_2, —OCH_3) increase the basicity of the corresponding arylamine

Electron-withdrawing substituents (such as —Cl, —NO_2, —CN) decrease arylamine basicity

SYNTHESIS OF AMINES

Reduction of nitriles and amides (review)



$$RX \xrightarrow{NaCN} RCN \xrightarrow[\text{2. } H_2O]{\text{1. } LiAlH_4\text{, ether}} RCH_2NH_2$$

$$R-\overset{\overset{O}{\|}}{C}-OH \xrightarrow[\text{2. } NH_3]{\text{1. } SOCl_2} R-\overset{\overset{O}{\|}}{C}-NH_2 \xrightarrow[\text{2. } H_2O]{\text{1. } LiAlH_4\text{, ether}} RCH_2NH_2$$

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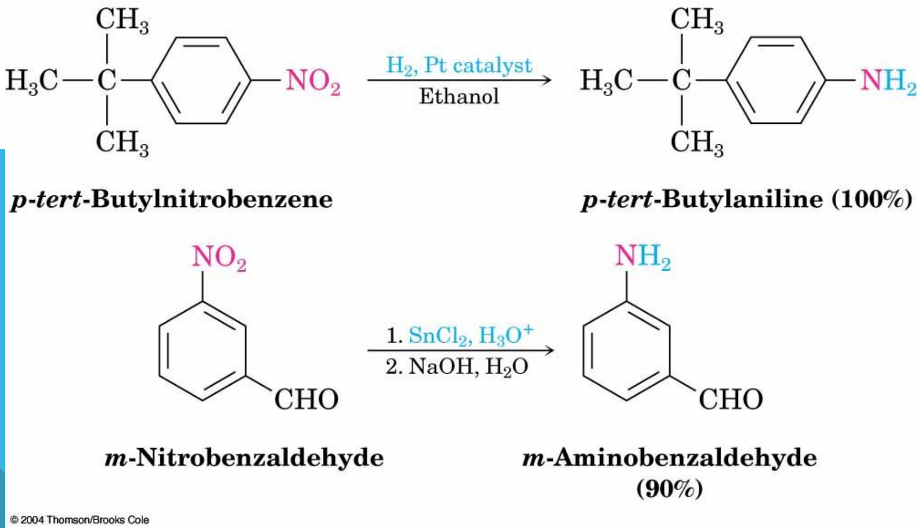
REDUCTION ARYL NITRO COMPOUNDS

Arylamines are prepared from nitration of an aromatic compound and reduction of the nitro group

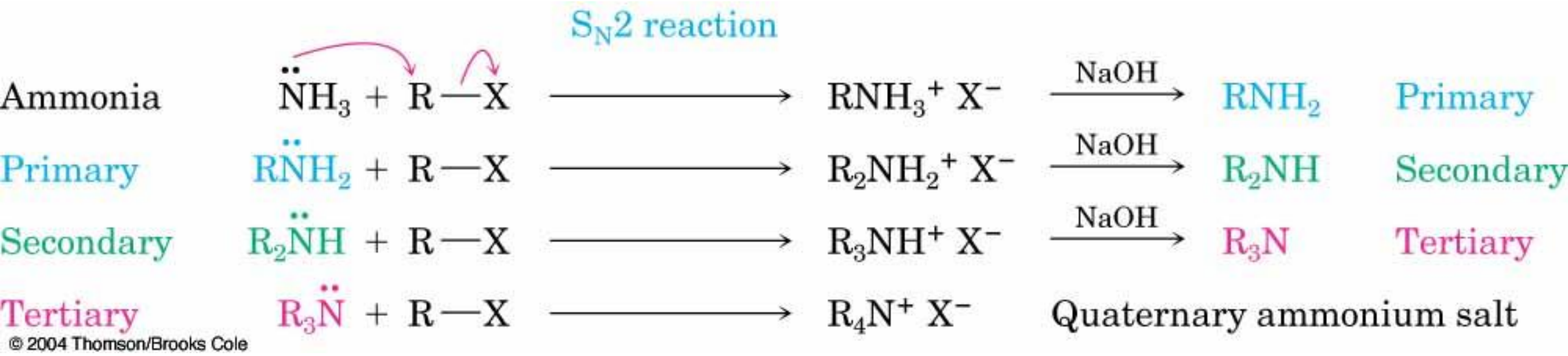
Reduction by catalytic hydrogenation over platinum is suitable if no other groups can be reduced

Iron, zinc, tin, and tin(II) chloride are effective in acidic solution



SN2 REACTIONS OF ALKYL HALIDES

Ammonia and other amines are good nucleophiles



S_N2 reaction

Ammonia $\ddot{N}H_3 + R{-}X \longrightarrow RNH_3^+\ X^- \xrightarrow{NaOH} RNH_2$ Primary

Primary $R\ddot{N}H_2 + R{-}X \longrightarrow R_2NH_2^+\ X^- \xrightarrow{NaOH} R_2NH$ Secondary

Secondary $R_2\ddot{N}H + R{-}X \longrightarrow R_3NH^+\ X^- \xrightarrow{NaOH} R_3N$ Tertiary

Tertiary $R_3\ddot{N} + R{-}X \longrightarrow R_4N^+\ X^-$ Quaternary ammonium salt

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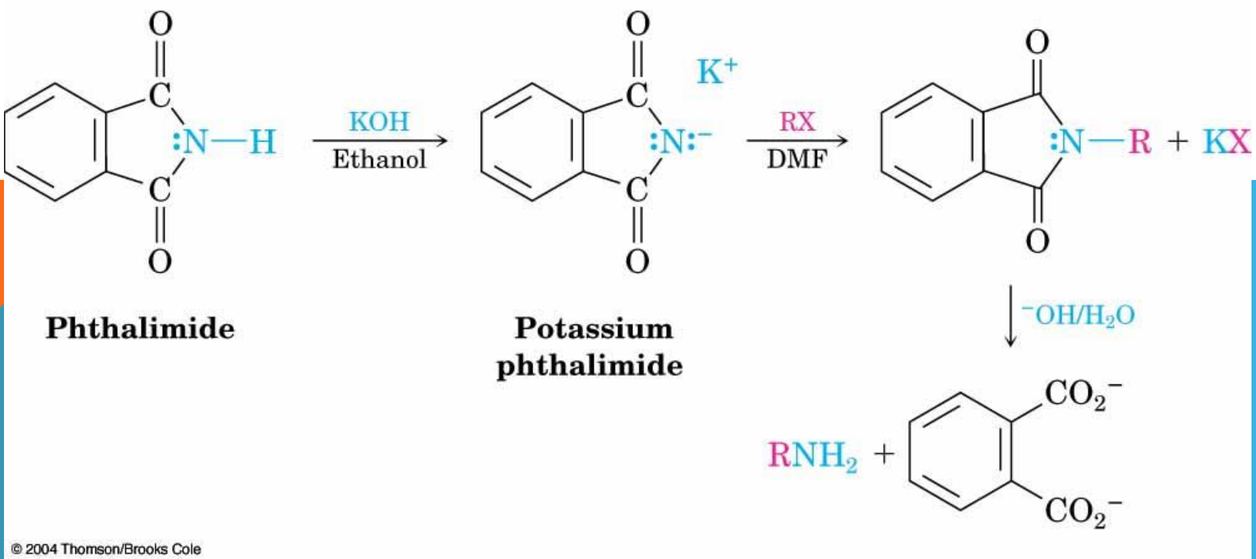
GABRIEL SYNTHESIS OF PRIMARY AMINES

A *phthalimide* alkylation for preparing a primary amine from an alkyl halide

The N-H in imides (—CONHCO—) can be removed by KOH followed by alkylation and hydrolysis



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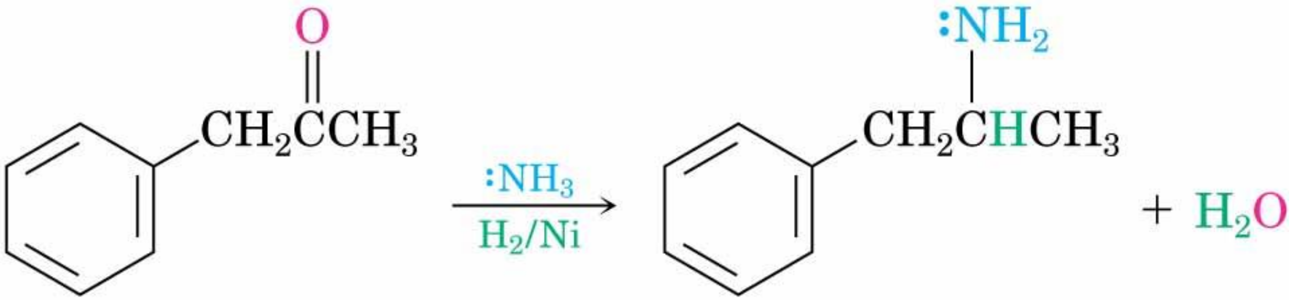
REDUCTIVE AMINATION OF ALDEHYDES AND KETONES

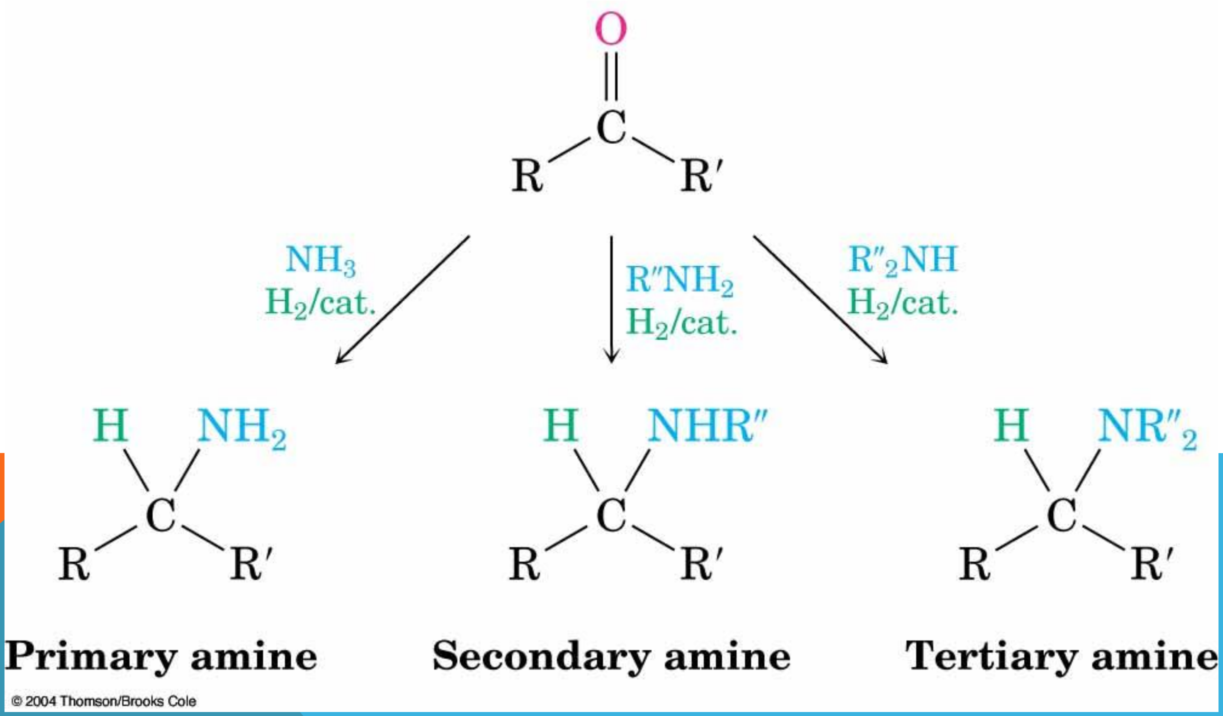
Treatment of an aldehyde or ketone with ammonia or an amine in the presence of a reducing agent



Phenyl-2-propanone **Amphetamine**

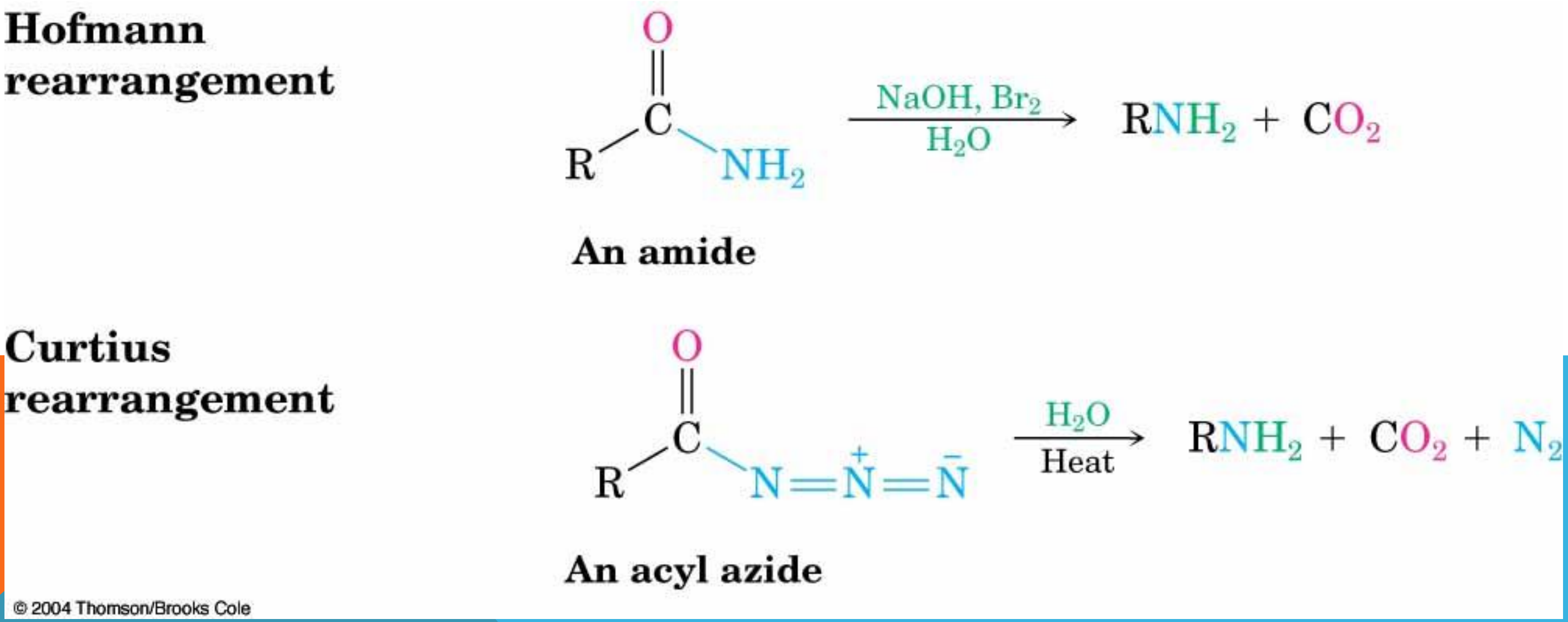
REDUCTIVE AMINATION IS VERSATILE

Ammonia, primary amines, and secondary amines yield primary, secondary, and tertiary amines, respectively



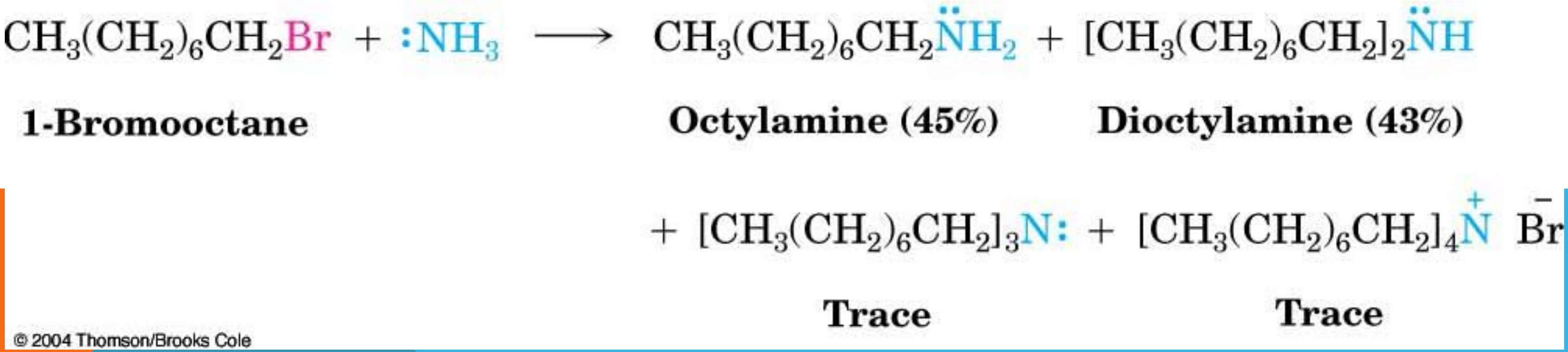
HOFMANN AND CURTIUS REARRANGEMENTS

Carboxylic acid derivatives can be converted into primary amines with loss of one carbon atom by both the Hofmann rearrangement and the Curtius rearrangement



UNCONTROLLED MULTIPLE ALKYLATION

Primary, secondary, and tertiary amines all have similar reactivity, the initially formed monoalkylated substance undergoes further reaction to yield a mixture of products



$$CH_3(CH_2)_6CH_2Br + :NH_3 \longrightarrow CH_3(CH_2)_6CH_2\ddot{N}H_2 + [CH_3(CH_2)_6CH_2]_2\ddot{N}H$$

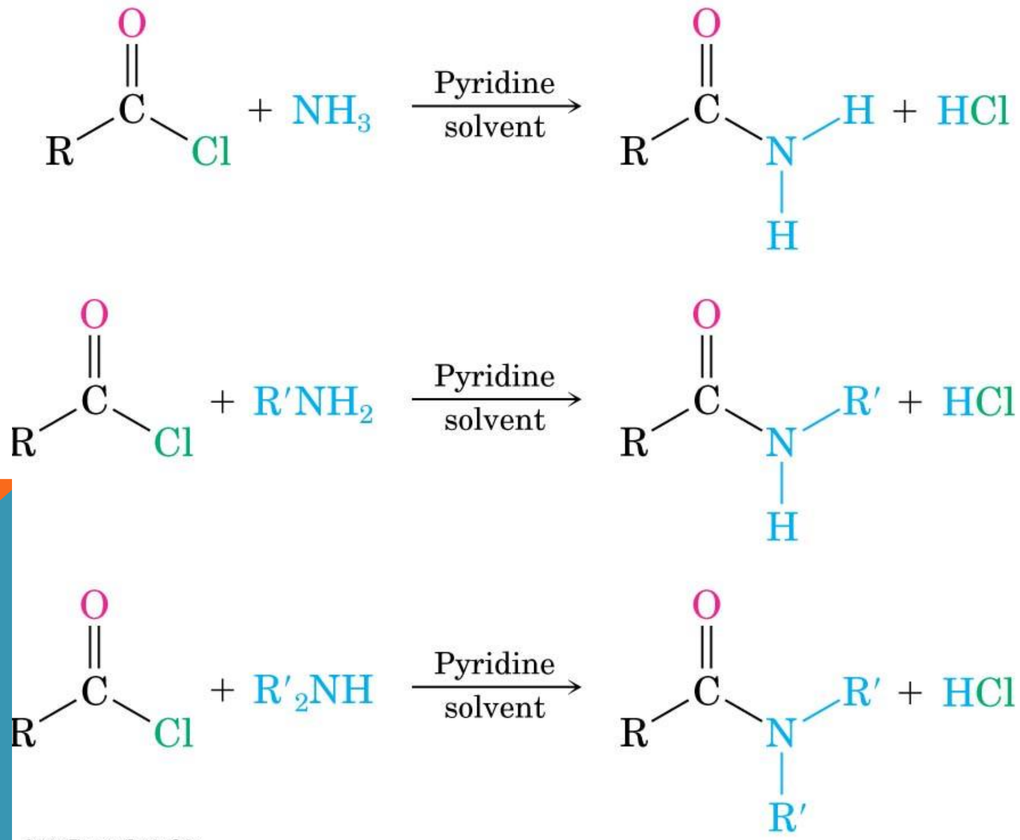
1-Bromooctane **Octylamine (45%)** **Dioctylamine (43%)**

$$+ [CH_3(CH_2)_6CH_2]_3N: + [CH_3(CH_2)_6CH_2]_4\overset{+}{N}\ \overset{-}{Br}$$

Trace **Trace**

REACTIONS OF AMINES

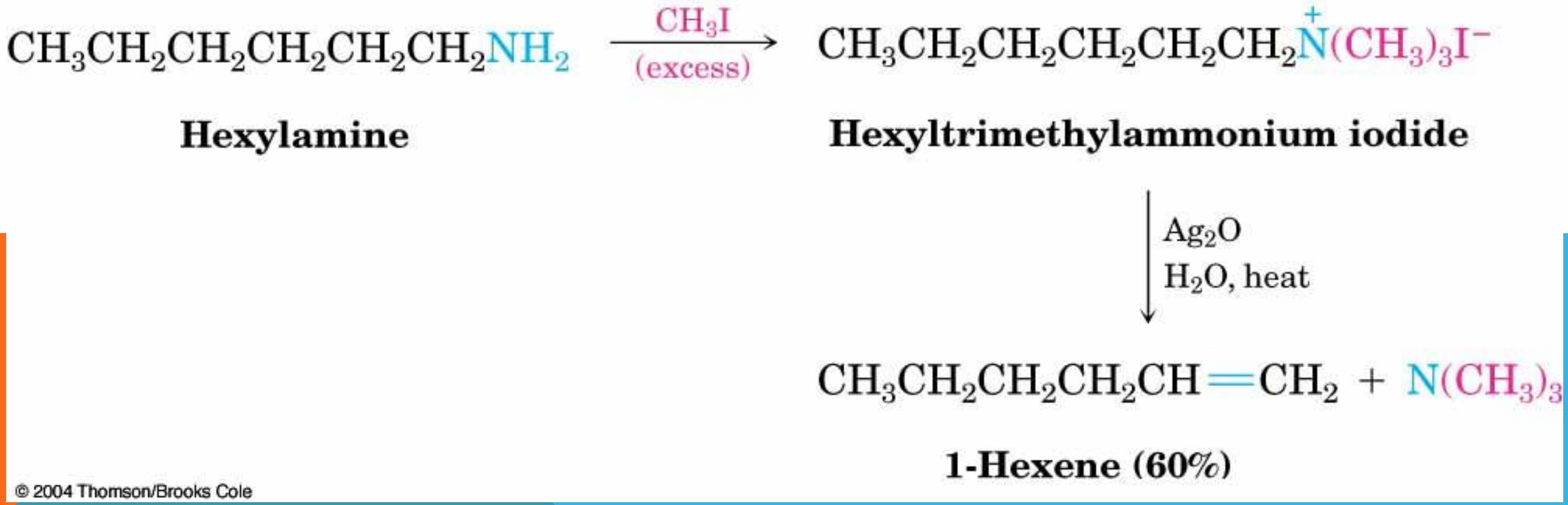
Alkylation and acylation have already been presented



HOFMANN ELIMINATION

Converts amines into alkenes

NH_2^- is very a poor leaving group so it converted to an alkylammonium ion, which is a good leaving group



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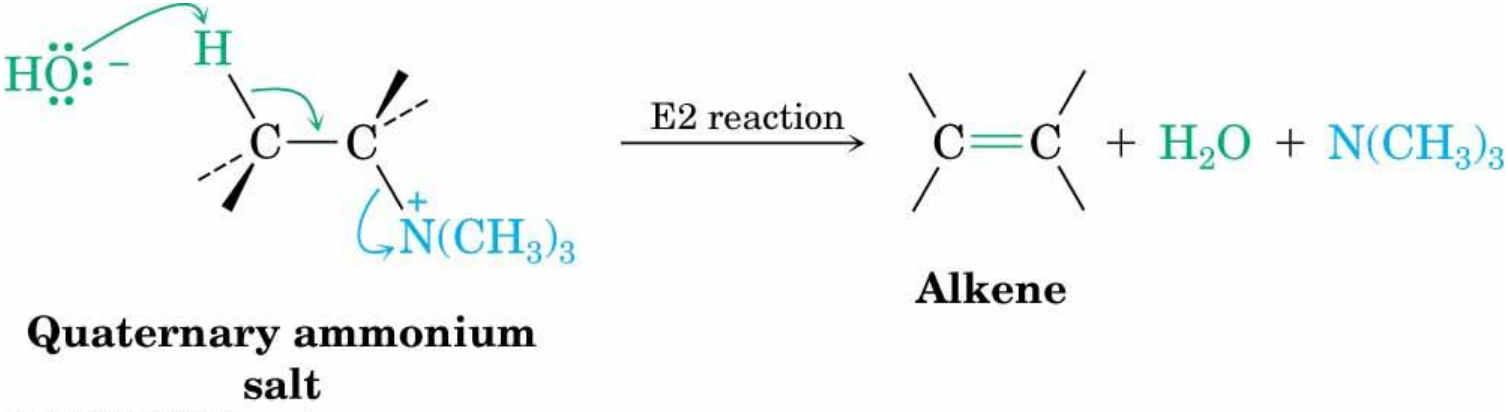
SILVER OXIDE IS USED FOR THE ELIMINATION STEP

Exchanges hydroxide ion for iodide ion in the quaternary ammonium salt, thus providing the base necessary to cause elimination



ORIENTATION IN HOFMANN ELIMINATION

We would expect that the *more* highly substituted alkene product predominates in the E2 reaction of an alkyl halide (Zaitsev's rule)

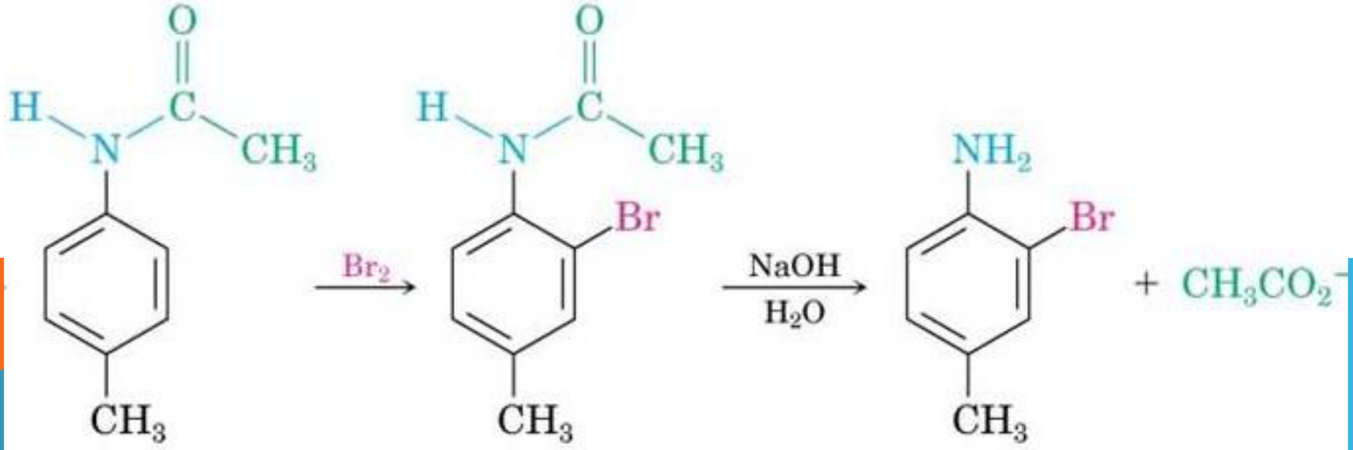
However, the *less* highly substituted alkene predominates in the Hofmann elimination due to the large size of the trialkylamine leaving group

The base must abstract a hydrogen from the most sterically accessible, least hindered position

REACTIONS OF ARYLAMINES

Amino substituents are strongly activating, ortho- and para-directing groups in electrophilic aromatic substitution reactions

Reactions are controlled by conversion to amide



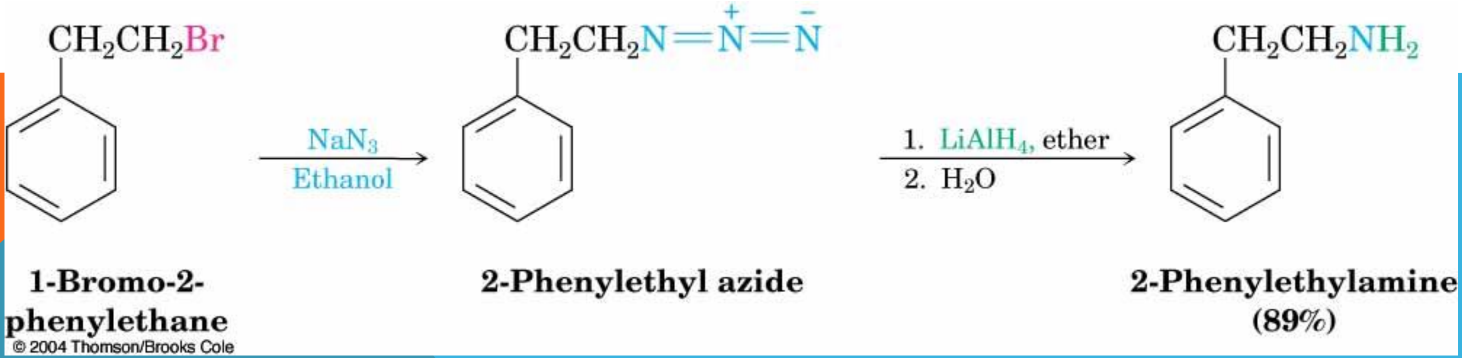
2-Bromo-4-methyl-aniline (79%)

SELECTIVE PREPARATION OF PRIMARY AMINES: THE AZIDE SYNTHESIS

Azide ion, N_3^- displaces a halide ion from a primary or secondary alkyl halide to give an alkyl azide, RN_3

Alkyl azides are not nucleophilic (but they are explosive)

Reduction gives the primary amine



1-Bromo-2-phenylethane

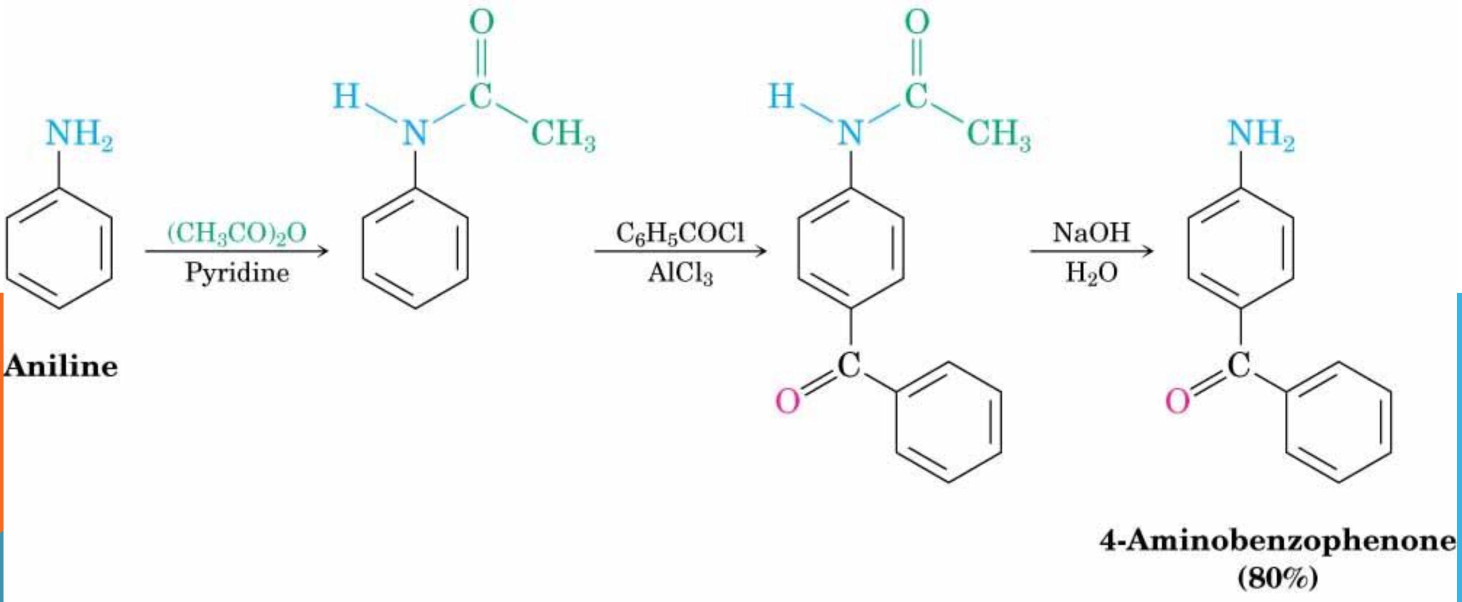
2-Phenylethyl azide

2-Phenylethylamine (89%)

ARYLAMINES ARE NOT USEFUL FOR FRIEDEL-CRAFTS REACTIONS

The amino group forms a Lewis acid–base complex with the $AlCl_3$ catalyst, preventing further reaction

Therefore we use the corresponding amide



Aniline

4-Aminobenzophenone (80%)

DIVERSE REACTIONS OF ARENEDIAZONIUM SALTS

Sequence of (1) nitration, (2) reduction, (3) diazotization, and (4) nucleophilic substitution leads to many different products

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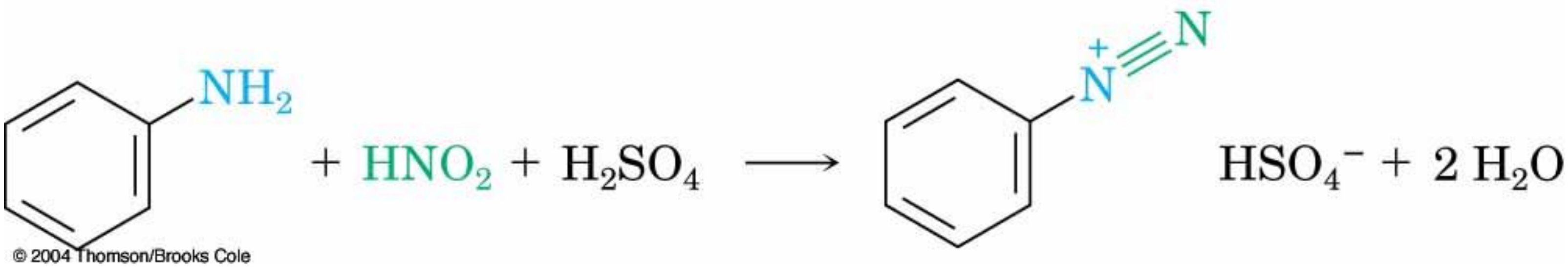
DIAZONIUM SALTS: THE SANDMEYER REACTION

Primary arylamines react with HNO_2, yielding stable arenediazonium salts



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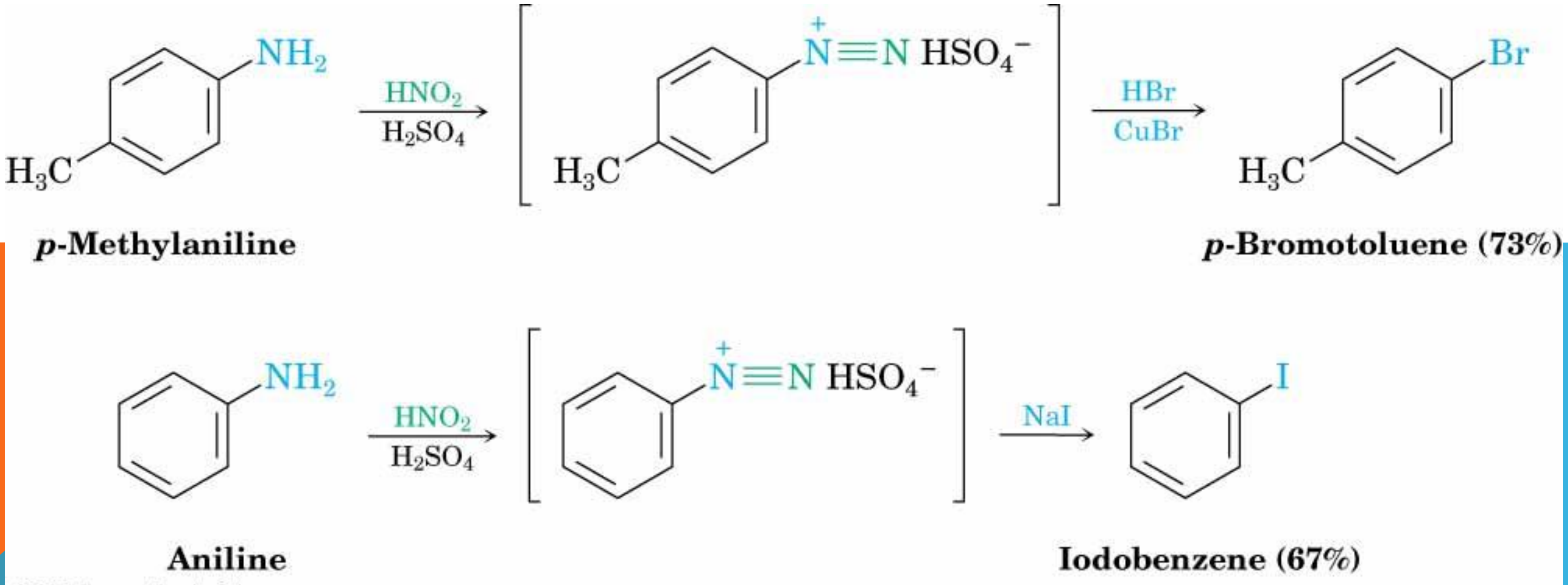
PREPARATION OF ARYL HALIDES

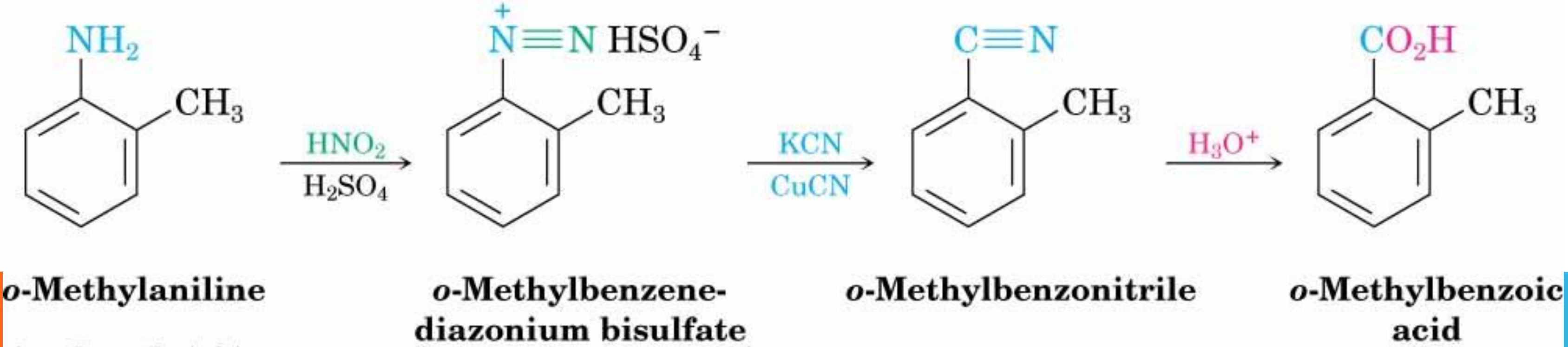
Reaction of an arenediazonium salt with CuCl or CuBr gives aryl halides (Sandmeyer Reaction)

Aryl iodides form from reaction with NaI without a copper(I) salt



ARYL NITRILES AND CARBOXYLIC ACIDS

An arenediazonium salt and CuCN yield the nitrile, ArCN, which can be hydrolyzed to ArCOOH



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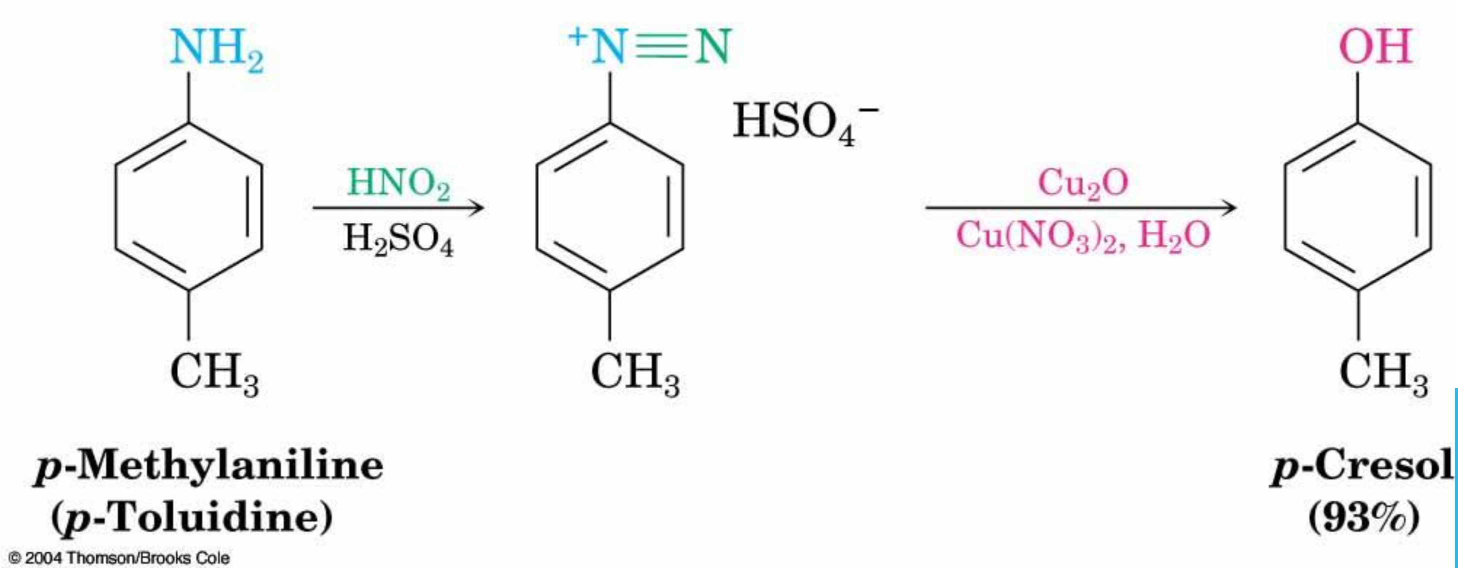
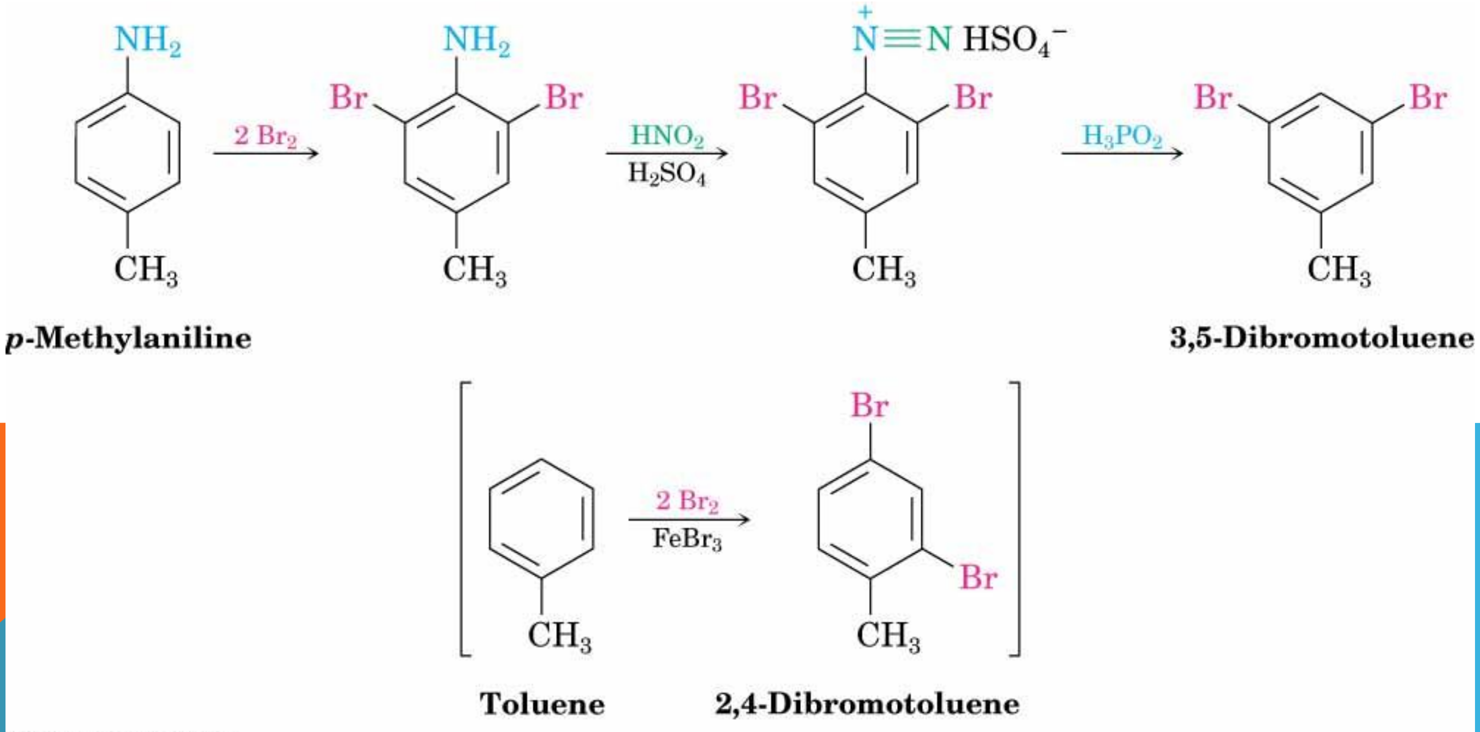
FORMATION OF PENOLS (AROH)

From reaction of the arenediazonium salt with copper(I) oxide in an aqueous solution of copper(II) nitrate



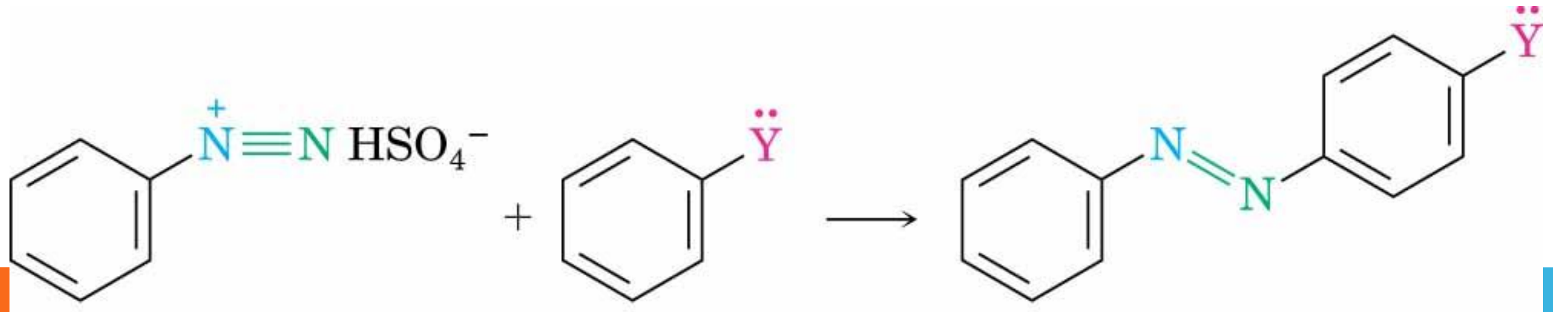
REDUCTION TO A HYDROCARBON

By treatment of a diazonium salt with hypophosphorous acid, H_3PO_2



DIAZONIUM COUPLING REACTIONS

Arenediazonium salts undergo a coupling reaction with activated aromatic rings, such as phenols and arylamines, to yield brightly colored azo compounds, Ar—N=N—Ar′

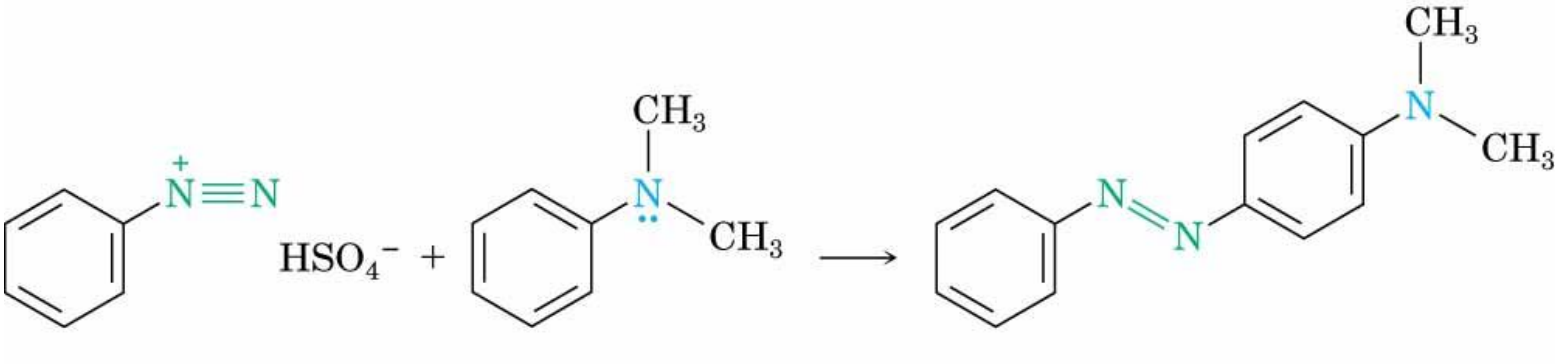


An azo compound

where $Y = -OH$ or $-NR_2$

AZO DYES

Azo-coupled products have extended π conjugation that lead to low energy electronic transitions that occur in visible light (dyes)



Benzenediazonium bisulfate **N,N-Dimethylaniline** ***p*-(Dimethylamino)azobenzene (yellow crystals, mp 127°C)**

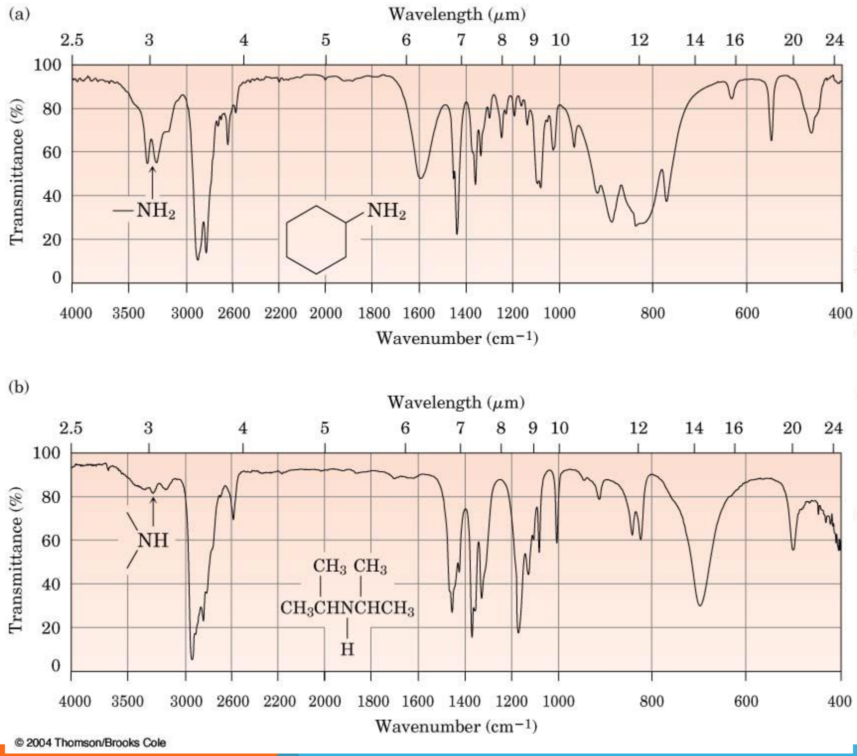
SPECTROSCOPY OF AMINES - INFRARED

Characteristic N–H stretching absorptions 3300 to 3500 cm^{-1}

Amine absorption bands are sharper and less intense than hydroxyl bands

- Protonated amines show an ammonium band in the range 2200 to 3000 cm^{-1}

EXAMPLES OF INFRARED SPECTRA



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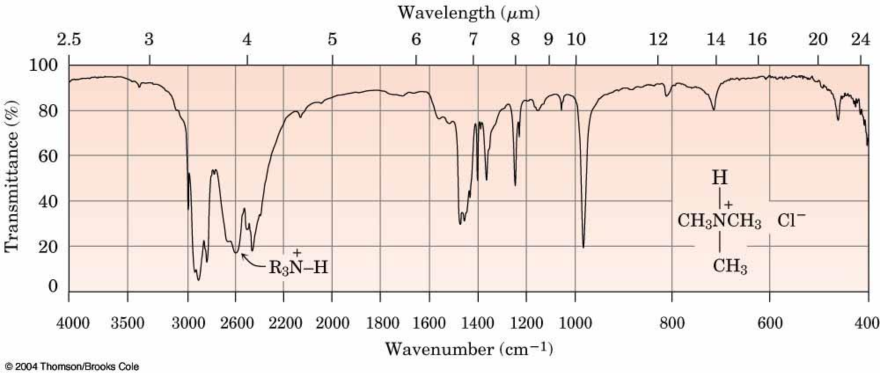

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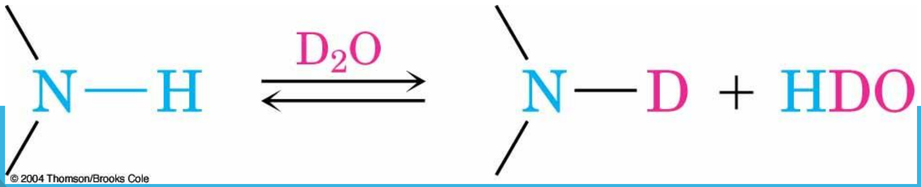
NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

N–H hydrogens appear as broad signals without clear-cut coupling to neighboring C–H hydrogens

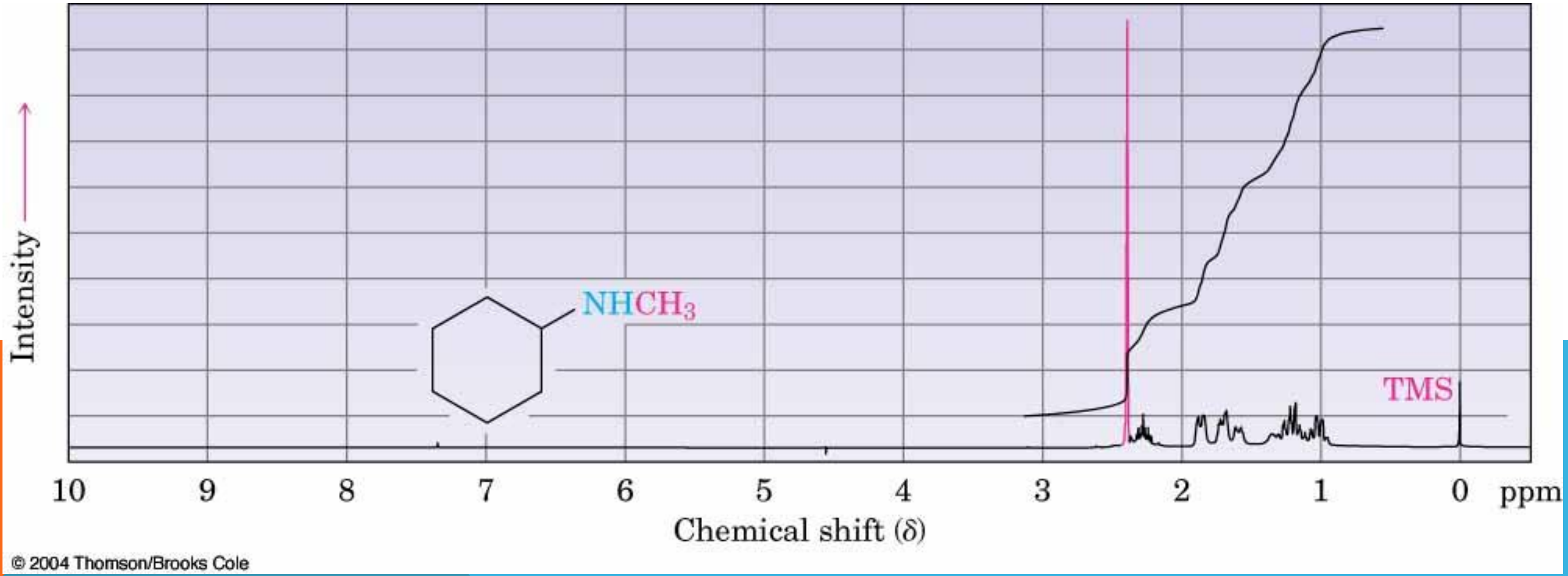
In D_2O exchange of N–D for N–H occurs, and the N–H signal disappears



CHEMICAL SHIFT EFFECTS

Hydrogens on C next to N and absorb at lower field than alkane hydrogens

N-CH_3 gives a sharp three-H singlet at δ 2.2 to δ 2.6



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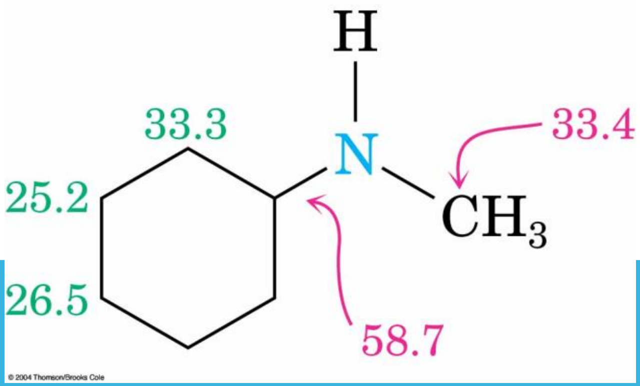
^{13}C NMR

Carbons next to amine N are slightly deshielded - about 20 ppm downfield from where they would absorb in an alkane



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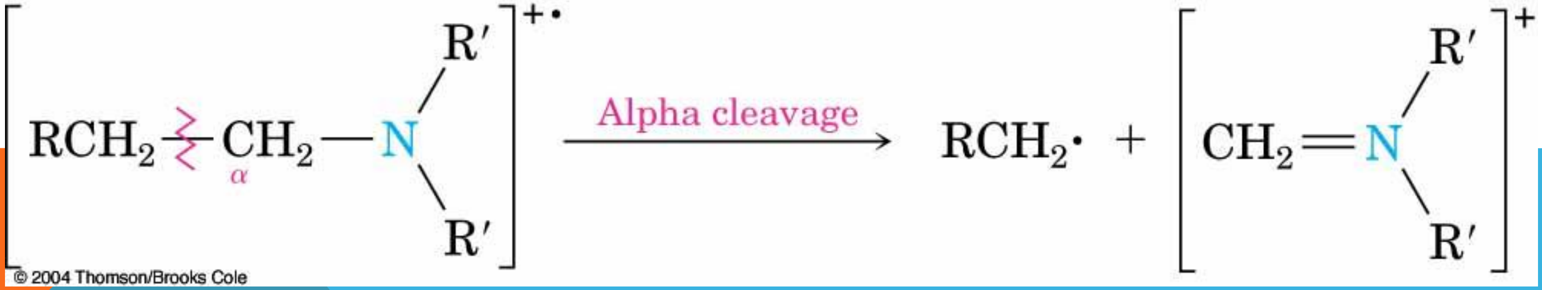
MASS SPECTROMETRY

Since N is a compound with an odd number of nitrogen atoms has an odd-numbered molecular weight and a corresponding parent ion

Alkylamines cleave at the C–C bond nearest the nitrogen to yield an alkyl radical and a nitrogen-containing cation



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MASS SPECTRUM OF N-ETHYLPROPYLAMINE

The two modes of a cleavage give fragment ions at *m/z* = 58 and *m/z* = 72.