

Amines

Amines

The most important of the organic compounds showing appreciable basicity

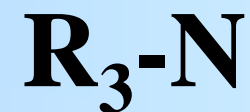
Amines



primary



secondary

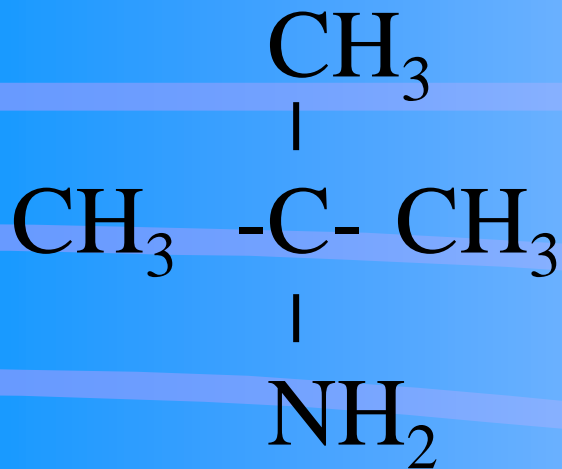


tertiary

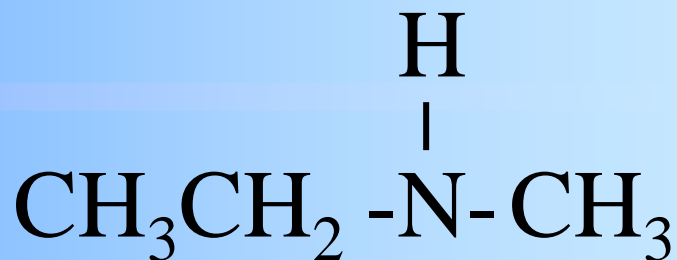
The R group may be either **alkyl** or **aryl**

Nomenclature

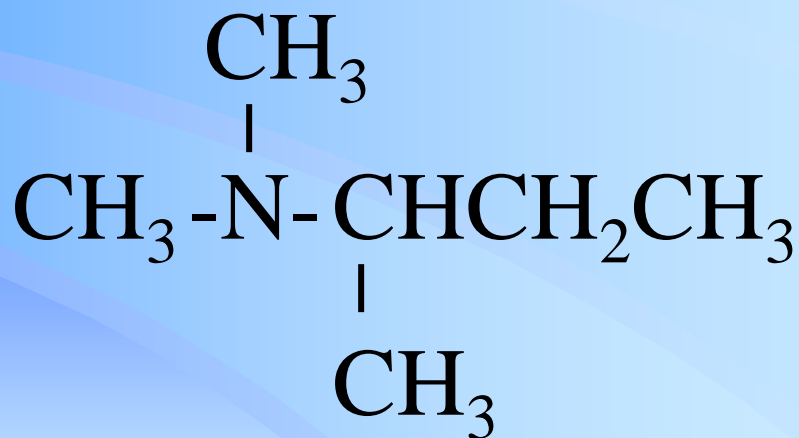
- Aliphatic amines are named by naming the alkyl group followed by the word **-amine**
- Complicated amines are named by prefixing **amino-** to the name of the parent chain
- Aromatic amines are named as derivative of the simplest aromatic amine, **aniline**
- Salts of amines are named by replacing **-amine** by **-ammonium** (or **-aniline** by **-anilinium**)



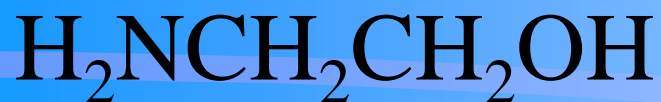
tert-Butylamine



Ethylmethylamine

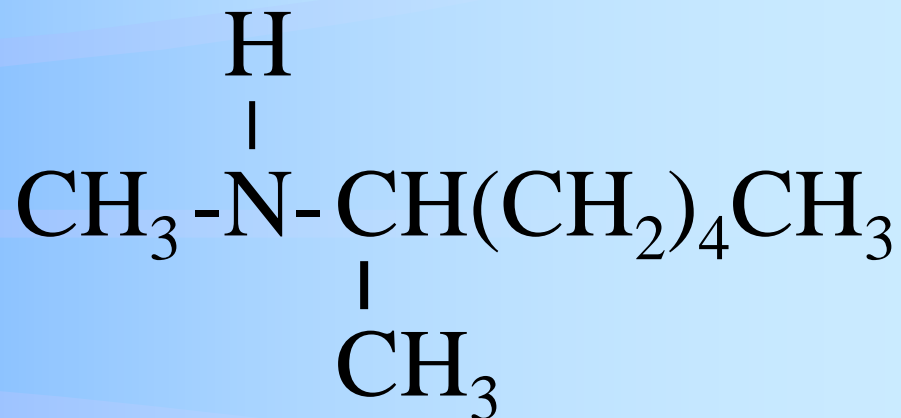


sec-Butyldimethylamine



2-Aminoethanol

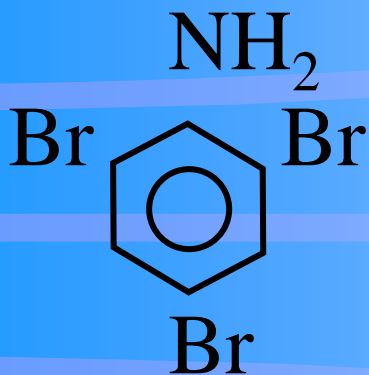
Ethanolamine



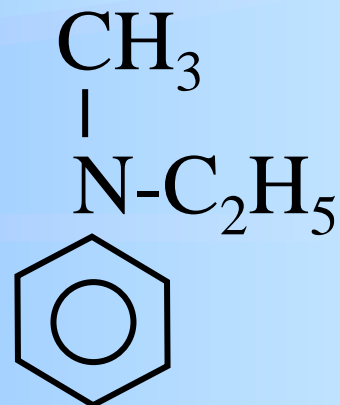
2-(N-Methylamino)heptane



γ -Aminobutyric acid



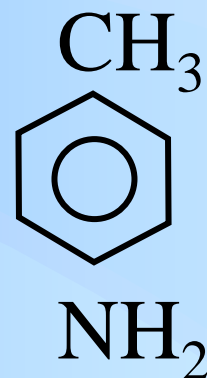
2,4,6-Tribromoaniline



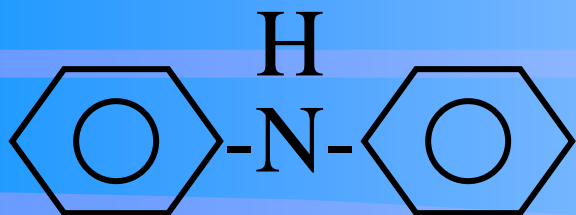
N-Ethyl-N-methylaniline



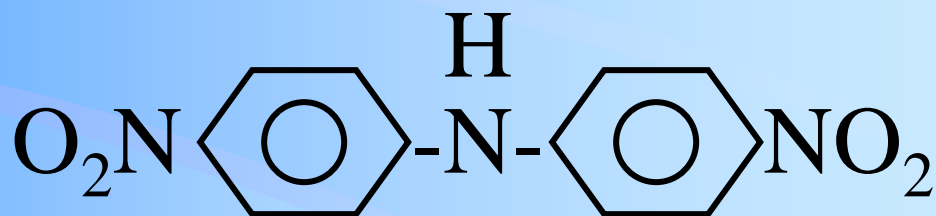
p-Nitroso-N,N-dimethylaniline



p-Toluidine



Diphenylamine



4,4'-Dinitrodiphenylamine



Ethylammonium sulfate



Trimethylammonium nitrate



Anilinium chloride

Physical Properties

- Polar compounds
- Form intermolecular hydrogen bonds
- Higher boiling points than nonpolar compounds
- Lower boiling points than alcohols or carboxylic acids
- Quite soluble in water

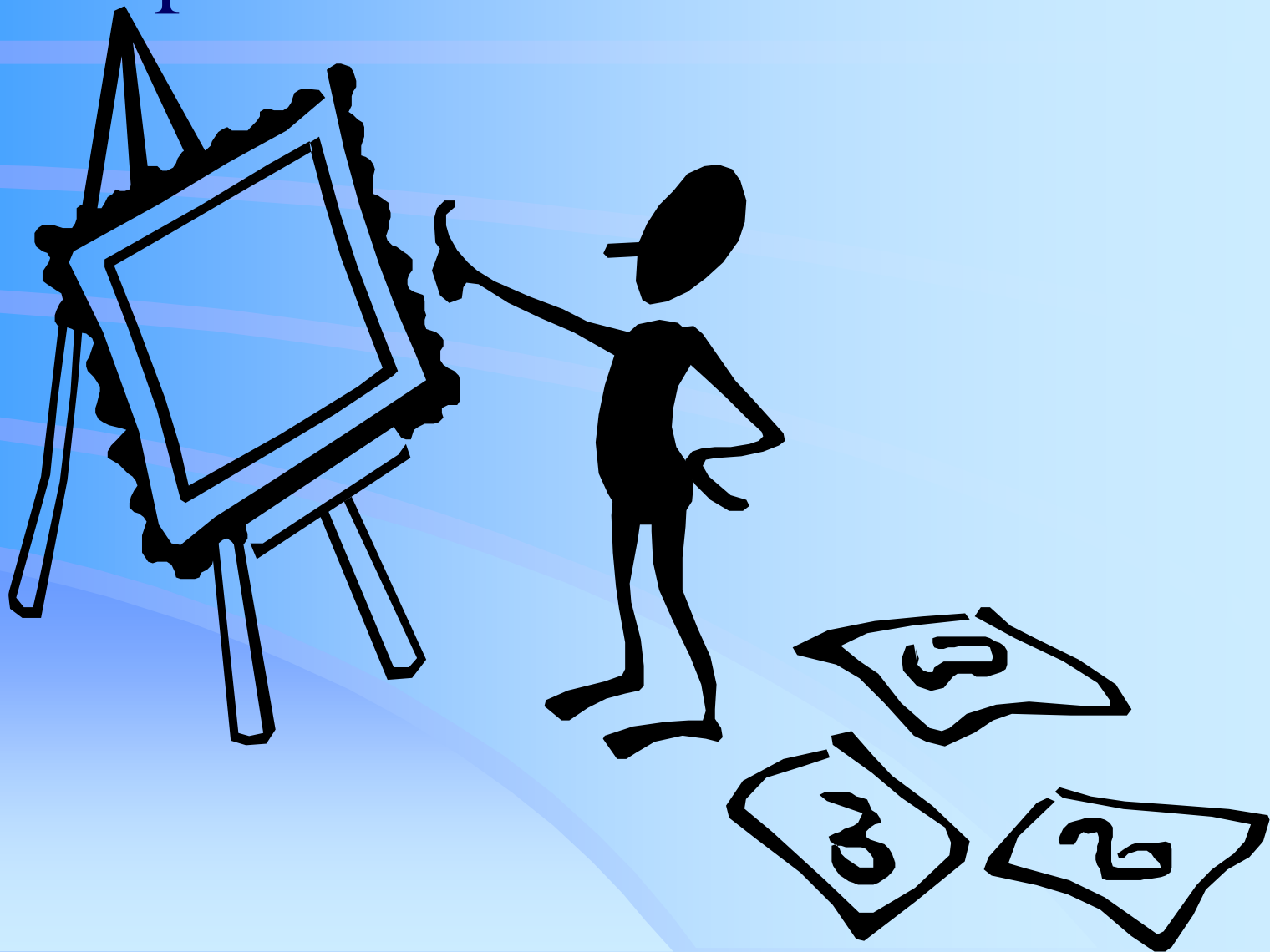
Physical Properties

- Methyl amines & ethyl amines smell like ammonia
- Higher alkyl amines have a “fishy” smell
- Aromatic amines are generally very toxic; they are absorbed through the skin, often with fatal results
- Aromatic amines are oxidized by air

Stereochemistry of Nitrogen

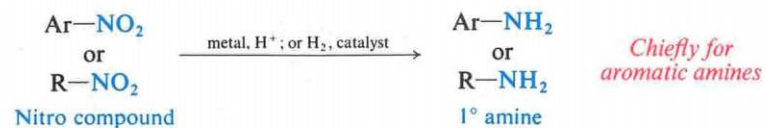
- Nitrogen uses sp^3 hybridized orbitals
- Tetrahedral shape
 - one orbital is a pair of nonbonding electrons
 - the three remaining orbitals overlap s orbitals of hydrogen or carbon
- Approximate bond angles of 109°
- Quaternary ammonium salts use all four sp^3 orbitals to form bonds

Preparation of Amines

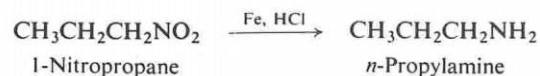
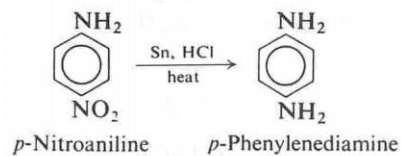
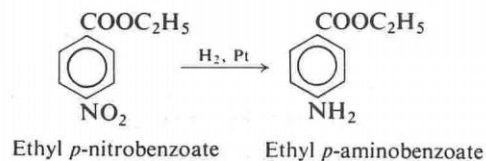


PREPARATION OF AMINES

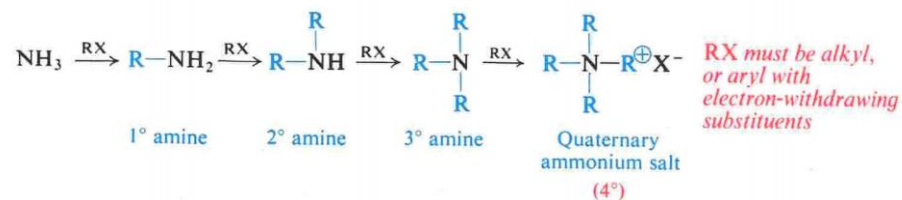
1. Reduction of nitro compounds. Discussed in Sec. 22.9.



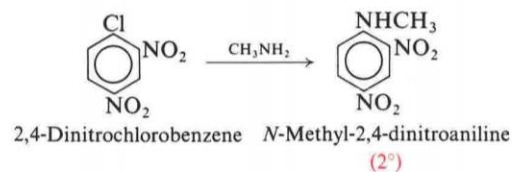
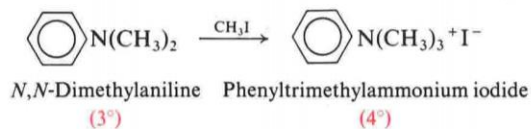
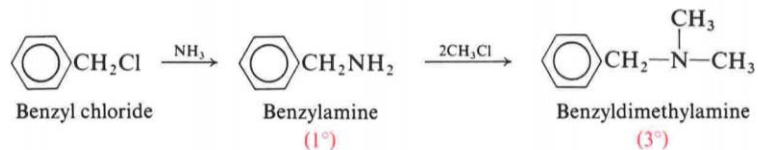
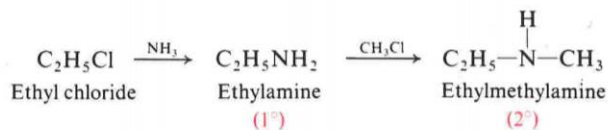
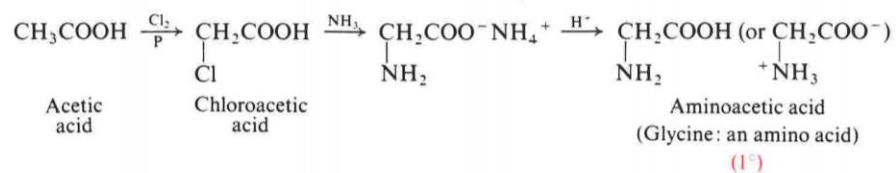
Examples:



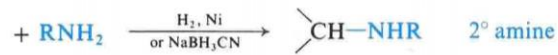
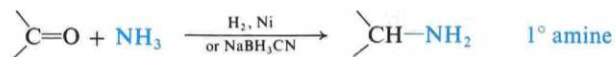
2. Reaction of halides with ammonia or amines. Discussed in Secs. 22.10 and 22.13.



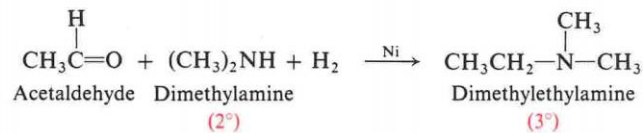
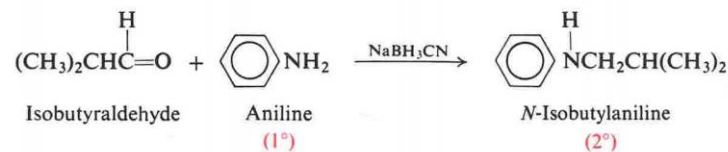
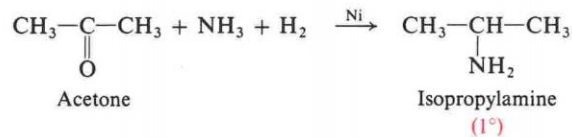
Examples:



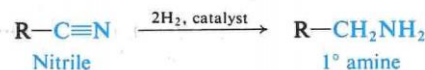
3. Reductive amination. Discussed in Sec. 22.11.



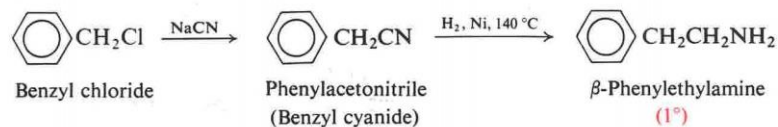
Examples:



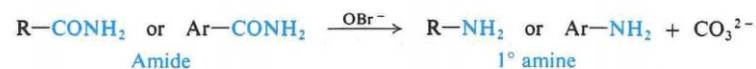
4. Reduction of nitriles. Discussed in Sec. 22.8.



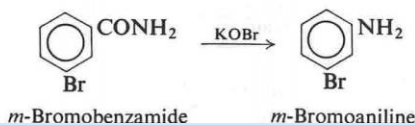
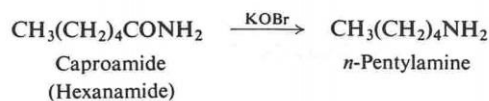
Examples:



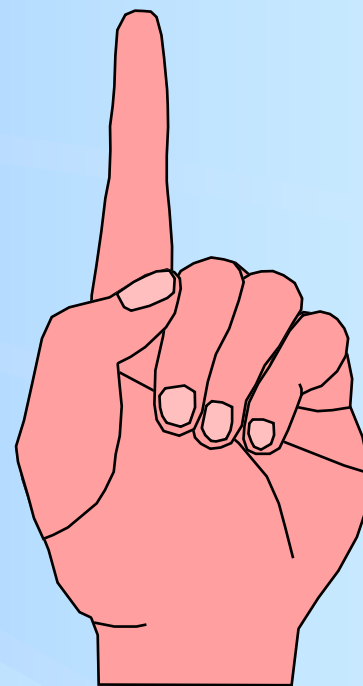
5. Hofmann degradation of amides. Discussed in Secs. 22.15–22.17.



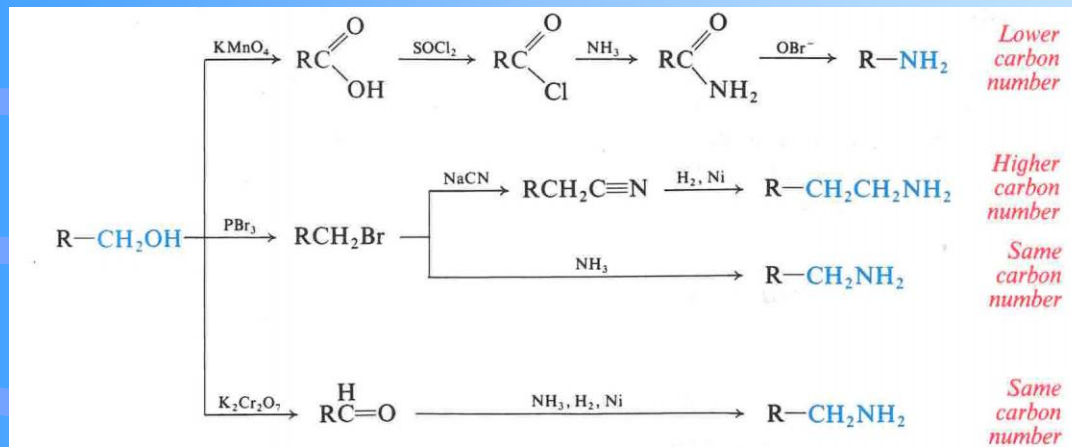
Examples:



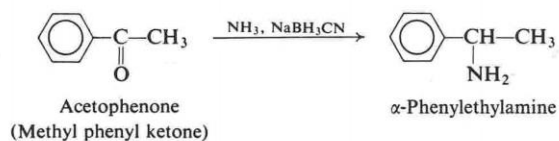
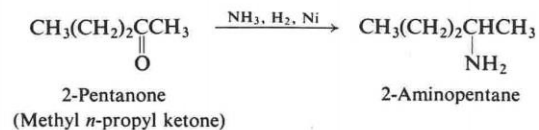
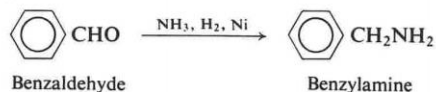
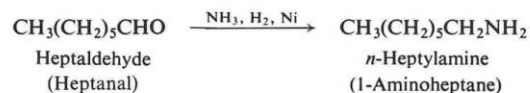
The tendency of nitrogen to share its nonbonding electrons underlies the entire chemical behavior of amines



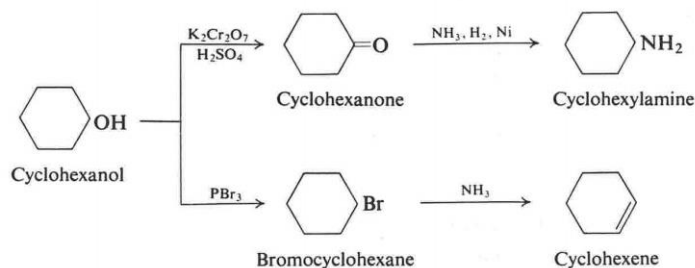
Hofmann Degradation of Amides



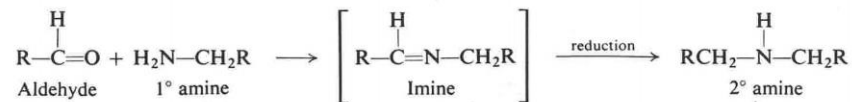
Reductive amination has been used successfully with a wide variety of aldehydes and ketones, both aliphatic and aromatic. For example:



Reductive amination of ketones yields amines containing a *sec*-alkyl group; such amines are difficult to obtain by ammonolysis because of the tendency for *sec*-alkyl halides to undergo elimination. For example, cyclohexanone is converted into cyclohexylamine in good yield, whereas ammonolysis of bromocyclohexane yields only cyclohexene.



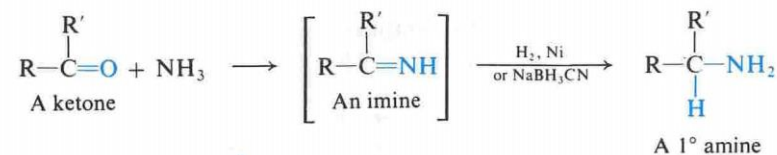
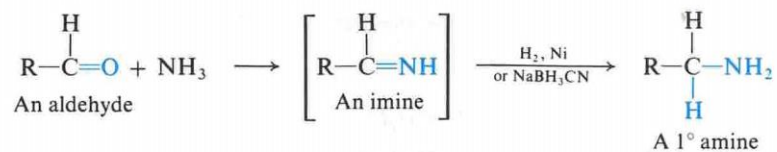
During reductive amination the aldehyde or ketone can react not only with ammonia but also with the primary amine that has already been formed, and thus yield a certain amount of secondary amine. The tendency for the reaction to go



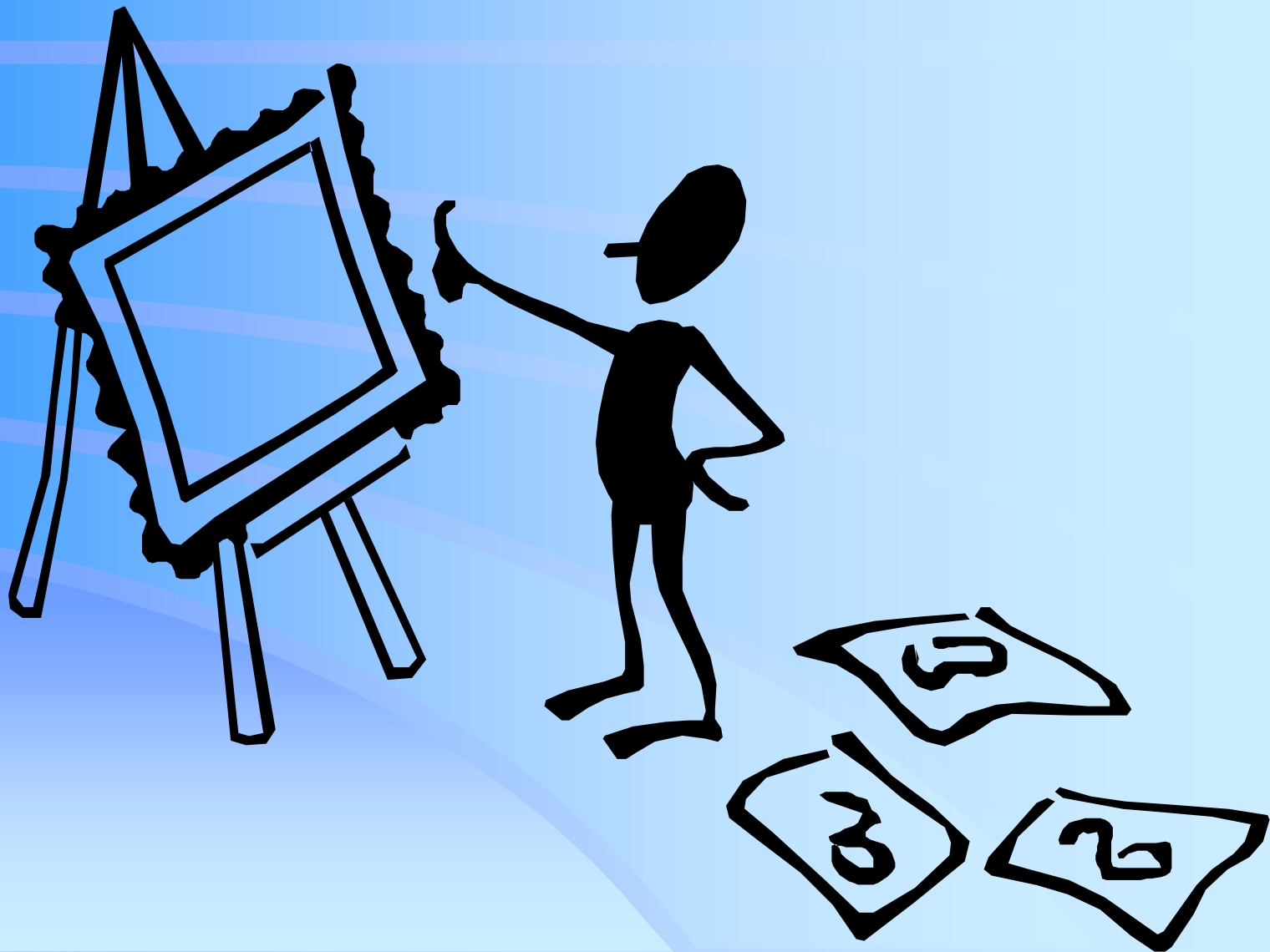
beyond the desired stage can be fairly well limited by the proportions of reactants employed and is seldom a serious handicap.

Reductive amination

Many aldehydes (RCHO) and ketones (R₂CO) are converted into amines by **reductive amination**: reduction in the presence of ammonia. Reduction can be accomplished catalytically or by use of sodium cyanohydridoborate, NaBH₃CN. Reaction involves reduction of an intermediate compound (an *imine*, RCH=NH or R₂C=NH) that contains a carbon–nitrogen double bond.

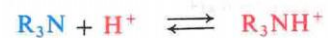


Reactions of Amines

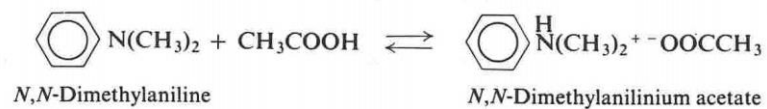
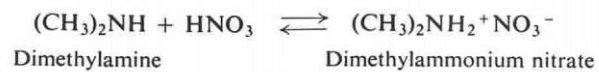
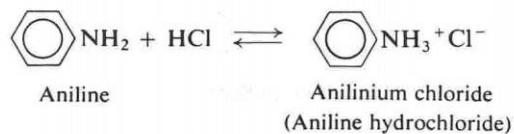


REACTIONS OF AMINES

1. **Basicity. Salt formation.** Discussed in Secs. 22.5 and 23.2–23.4.



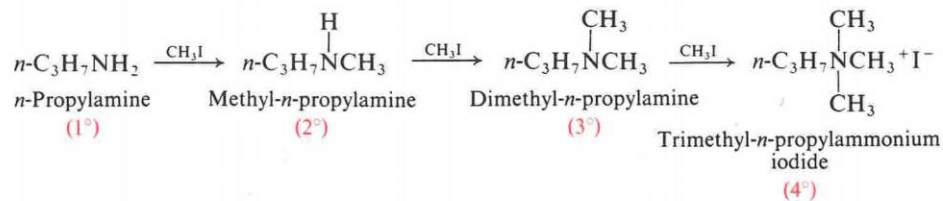
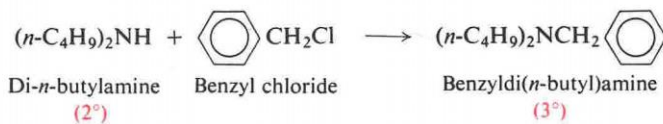
Examples:



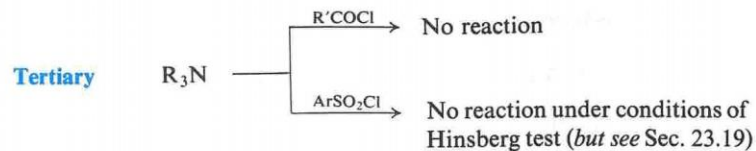
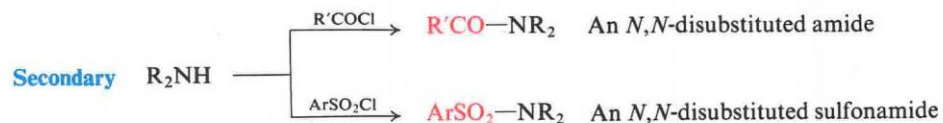
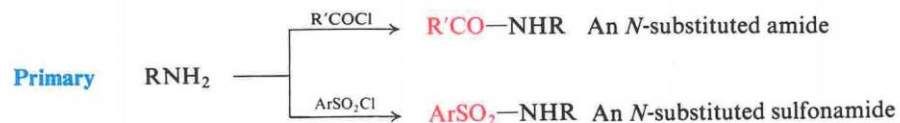
2. Alkylation. Discussed in Secs. 22.13 and 23.5.



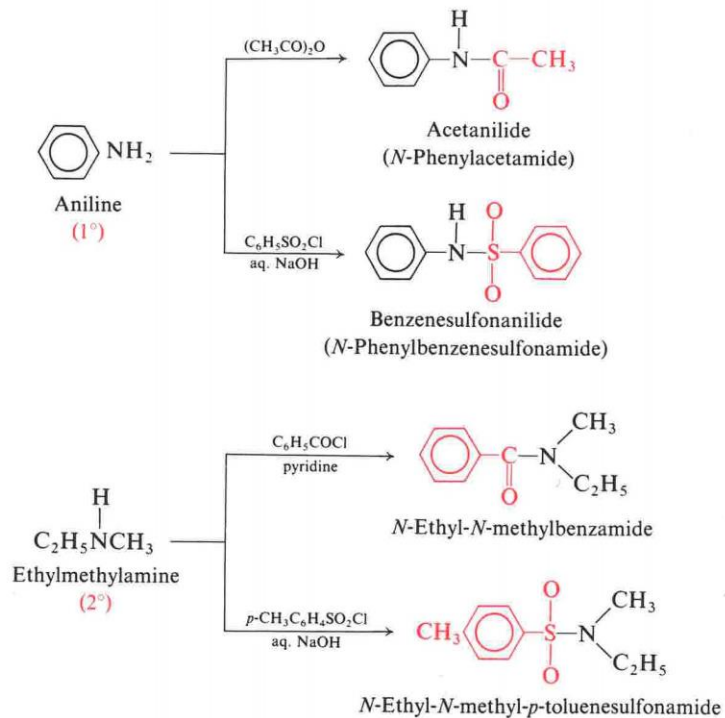
Examples:



3. Conversion into amides. Discussed in Sec. 23.7.



Examples:

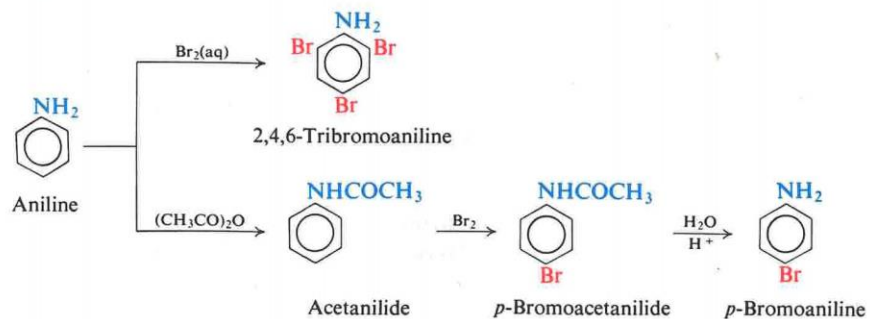


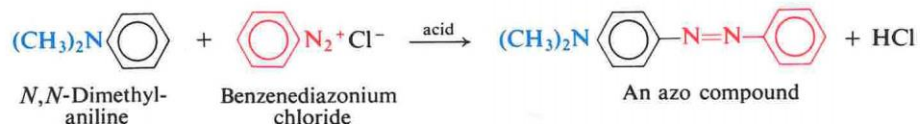
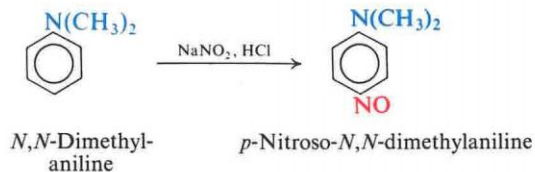
4. Ring substitution in aromatic amines. Discussed in Secs. 23.8, 23.11 and 23.18.

$\left. \begin{array}{l} -\text{NH}_2 \\ -\text{NHR} \\ -\text{NR}_2 \end{array} \right\}$ Activate powerfully, and direct *ortho, para* in electrophilic aromatic substitution

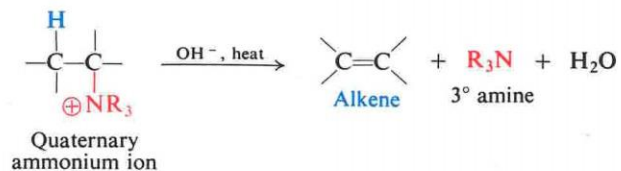
$-\text{NHCOR}$: Less powerful activator than $-\text{NH}_2$

Examples:

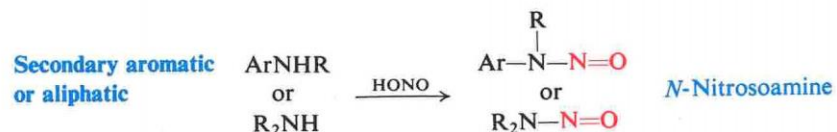




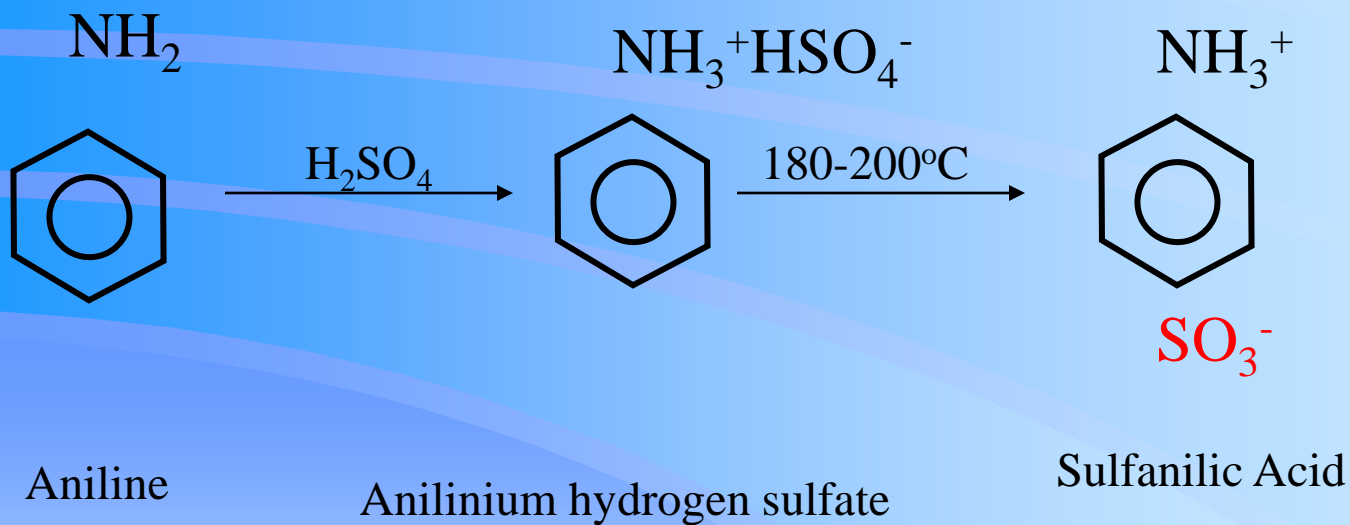
5. Hofmann elimination from quaternary ammonium salts. Discussed in Secs. 23.5–23.6.



6. Reactions with nitrous acid. Discussed in Secs. 23.11–23.12.



Sulfonation of Aromatic Amines



- Aniline is usually sulfonated by “baking” the salt, anilinium hydrogen sulfate at 180 to 200°C.
- The chief product is para isomer.
- *P*-aminobenzenesulfonic acid – known as sulfanilic acid

Sulfanilamide – The Sulfa Drugs

- The amide of sulfanilic acid (sulfanilamide) and certain related substituted amides are of medical importance.
- Sulfa drugs
- Make up a considerable portion of the output of the pharmaceutical industry.
- Prepare by reacting a sulfonyl chloride with ammonia or an amine.

Sulfanilamide – The Sulfa Drugs

- The presence in a sulfonic acid molecule of an amino group poses a special problem: if sulfanilic acid were converted to the acid chloride, the sulfonyl group of one molecule could attack the amino group of another to form an amide linkage.
- This problem is solved by protecting the amino group through acetylation prior to the preparation of the sulfonyl chloride.

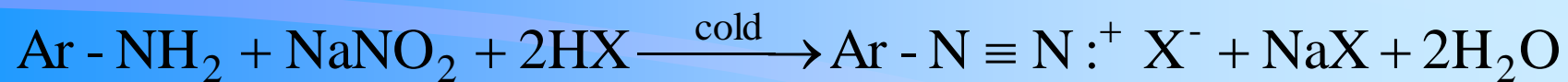
Diazonium Salt



Diazonium Salt

When a **primary aromatic amine**, dissolved or suspended in cold aqueous mineral acid, is treated with sodium nitrite, a **diazonium salt** is formed

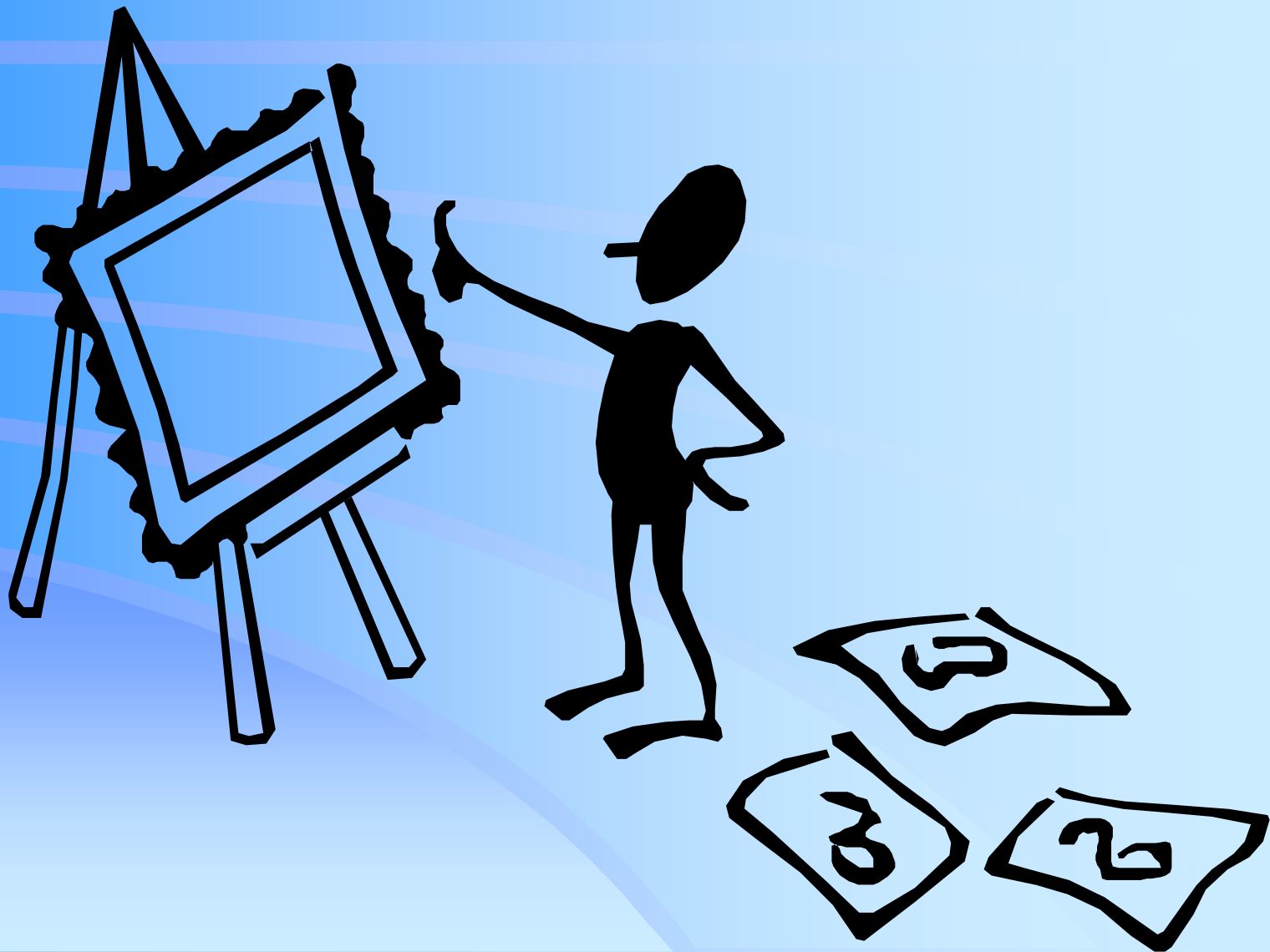
Diazonium Salt



Reactions of Diazonium Salts

- Replacement: nitrogen is lost
- Coupling:

Reactions of Diazonium Salts

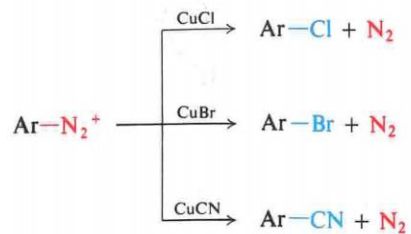


REACTIONS OF DIAZONIUM SALTS

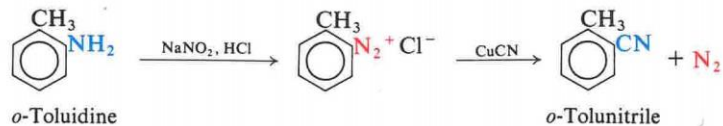
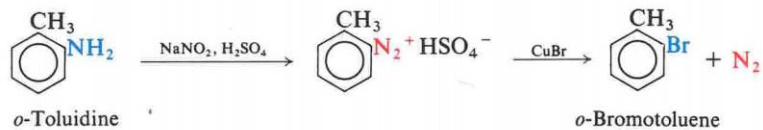
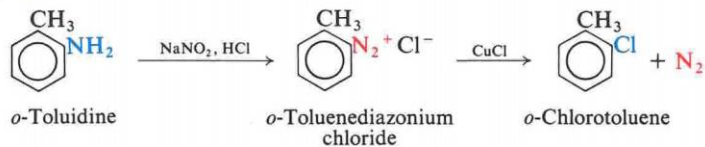
1. Replacement of nitrogen



(a) Replacement by $-\text{Cl}$, $-\text{Br}$, and $-\text{CN}$. Sandmeyer reaction. Discussed in Secs. 23.13–23.14.



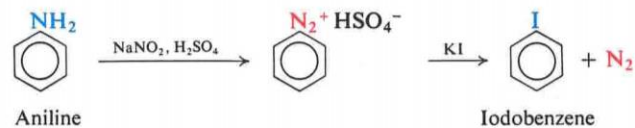
Examples:



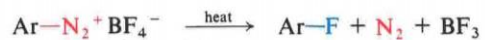
(b) Replacement by —I. Discussed in Sec. 23.13.



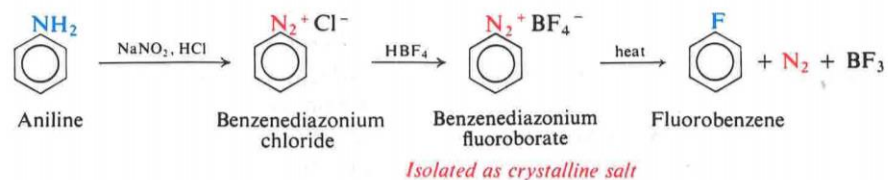
Example:



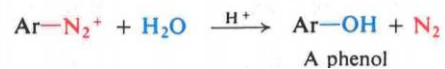
(c) Replacement by —F. Discussed in Sec. 23.13.



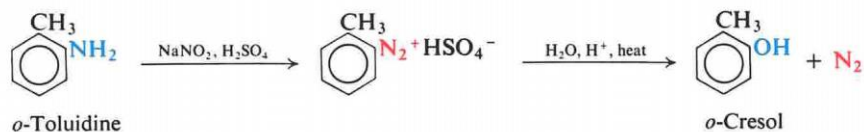
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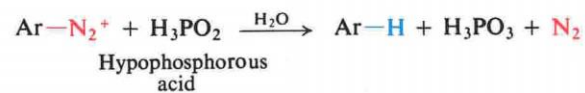
(d) Replacement by —OH. Discussed in Sec. 23.15.



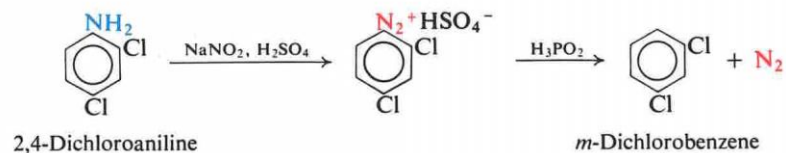
Example:



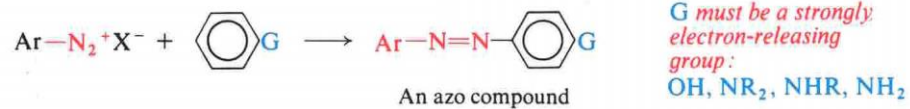
(e) Replacement by —H. Discussed in Sec. 23.16.



Example:



2. Coupling. Discussed in Sec. 23.18.



Example:

