Amines II. Reactions

REACTIONS OF AMINES

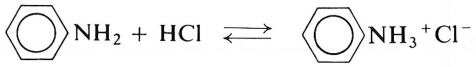
1. Basicity. Salt formation. Discussed in Secs. 22.5 and 23.2–23.4.

$$RNH_2 + H^+ \rightleftharpoons RNH_3^+$$

$$R_2NH + H^+ \rightleftharpoons R_2NH_2^+$$

$$R_3N + H^+ \rightleftharpoons R_3NH^+$$

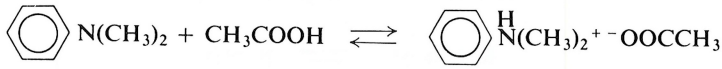
Examples:



Aniline — Anilinium chloride (Aniline hydrochloride)

$$(CH_3)_2NH + HNO_3 \rightleftharpoons (CH_3)_2NH_2^+NO_3^-$$

Dimethylamine — Dimethylammonium nitrate



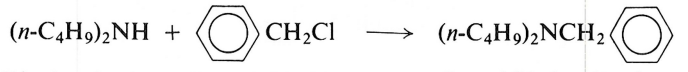
N,*N*-Dimethylaniline — *N*,*N*-Dimethylanilinium acetate

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

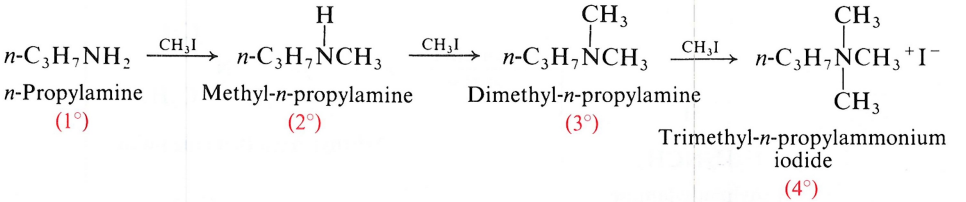
$$RNH_2 \xrightarrow{RX} R_2NH \xrightarrow{RX} R_3N \xrightarrow{RX} R_4N^+X^-$$

$$ArNH_2 \xrightarrow{RX} ArNHR \xrightarrow{RX} ArNR_2 \xrightarrow{RX} ArNR_3^+X^-$$

Examples:



Di-*n*-butylamine (2°) + Benzyl chloride → Benzyldi(*n*-butyl)amine (3°)



n-Propylamine (1°) → Methyl-*n*-propylamine (2°) → Dimethyl-*n*-propylamine (3°) → Trimethyl-*n*-propylammonium iodide (4°)

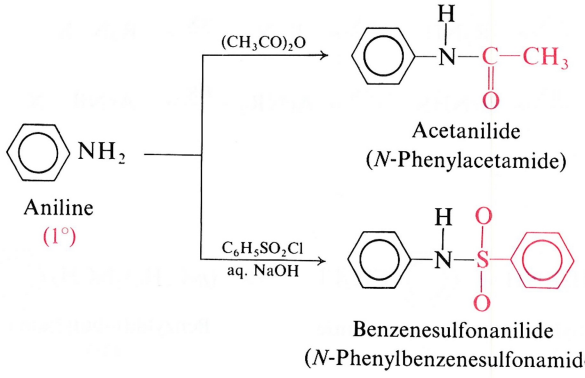
3. Conversion into amides. Discussed in Sec. 23.7.

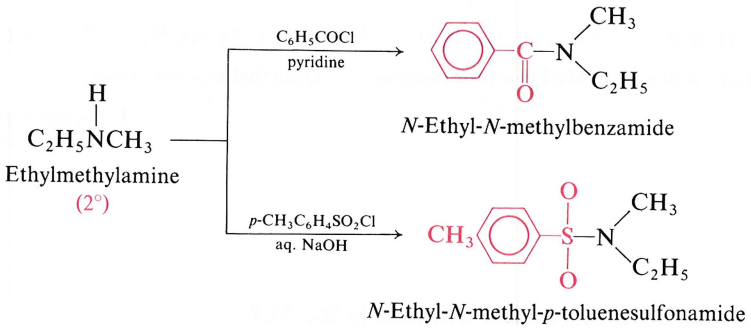
Primary RNH_2

- $\xrightarrow{R'COCl}$ $R'CO—NHR$ An *N*-substituted amide
- $\xrightarrow{ArSO_2Cl}$ $ArSO_2—NHR$ An *N*-substituted sulfonamide

Secondary R_2NH

- $\xrightarrow{R'COCl}$ $R'CO—NR_2$ An *N*,*N*-disubstituted amide
- $\xrightarrow{ArSO_2Cl}$ $ArSO_2—NR_2$ An *N*,*N*-disubstituted sulfonamide



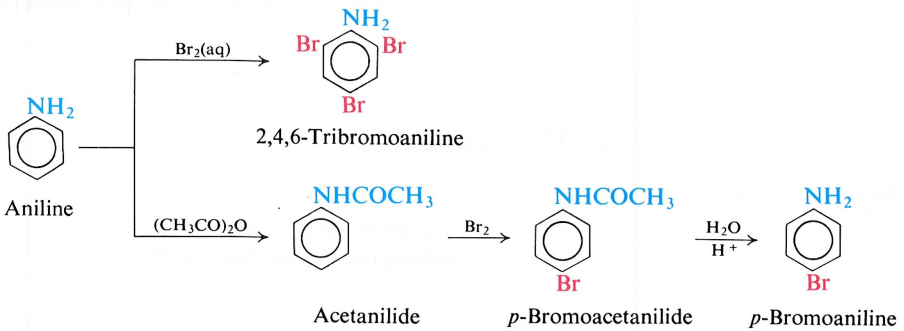


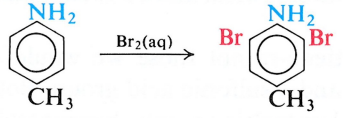
4. Ring substitution in aromatic amines. Discussed in Secs. 23.8, 23.11 and 23.18.

$-NH_2$, $-NHR$, $-NR_2$: Activate powerfully, and direct *ortho*, *para* in electrophilic aromatic substitution

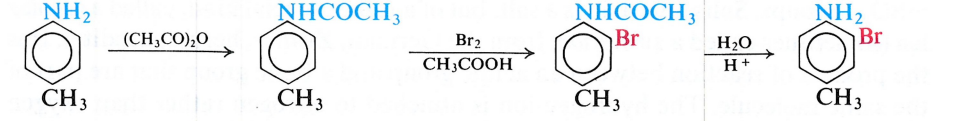
$-NHCOR$: Less powerful activator than $-NH_2$

Examples:

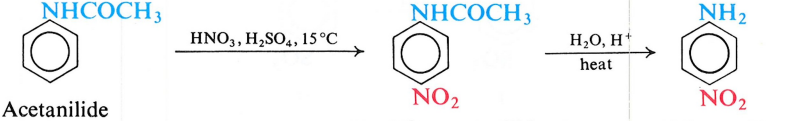




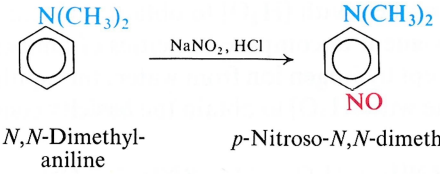
p-Toluidine 3,5-Dibromo-4-aminotoluene



p-Toluidine Aceto-*p*-toluidide 3-Bromo-4-aminotoluene

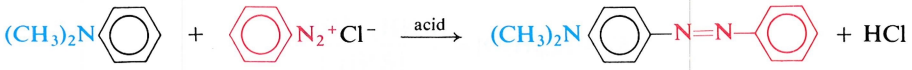


Acetanilide *p*-Nitroacetanilide *p*-Nitroaniline



N,*N*-Dimethyl-aniline

p-Nitroso-*N*,*N*-dimethylaniline

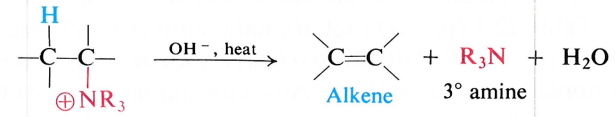


N,*N*-Dimethyl-aniline

Benzenediazonium chloride

An azo compound

5. Hofmann elimination from quaternary ammonium salts.

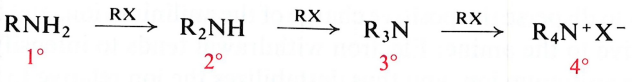


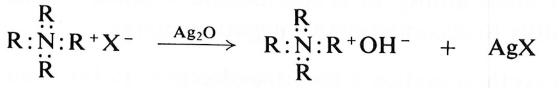
Quaternary ammonium ion

Alkene

3° amine

Quaternary ammonium salts.



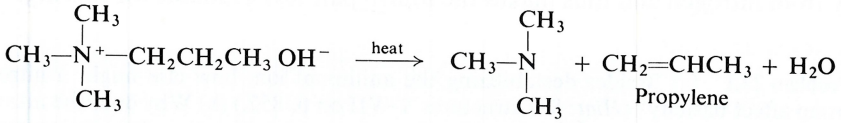


Quaternary ammonium salt

Quaternary ammonium hydroxide

Insoluble

When a quaternary ammonium hydroxide is heated strongly (to 125 °C or higher), it decomposes to yield water, a tertiary amine, and an alkene. Trimethyl-*n*-propylammonium hydroxide, for example, yields trimethylamine and propylene:

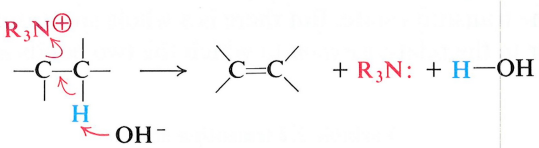


Trimethyl-*n*-propylammonium hydroxide

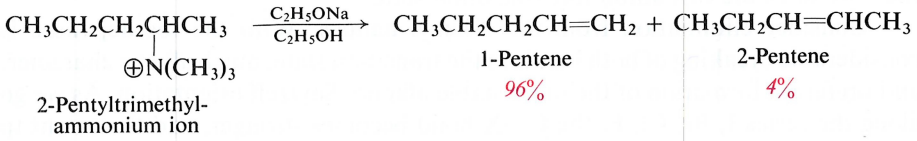
Trimethylamine

Propylene

Rection Mechanism



E2 elimination: Hofmann orientation. The variable E2 transition state



2-Pentyltrimethylammonium ion

1-Pentene 96%

2-Pentene 4%

We see that the preferred product here is the *least* branched alkene, 1-pentene. Such orientation is called **Hofmann orientation**, since it was first observed by Hofmann in studying this particular kind of reaction.

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

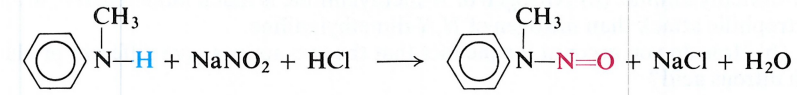
Primary aromatic $ArNH_2 \xrightarrow{HONO} Ar{-}N{\equiv}N^+$ Diazonium salt

Primary aliphatic $RNH_2 \xrightarrow{HONO} [R{-}N{\equiv}N^+] \xrightarrow{H_2O} N_2$ + mixture of alcohols and alkenes

Secondary aromatic or aliphatic

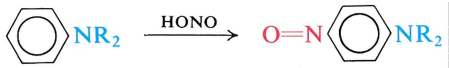
$$\begin{matrix} ArNHR \\ \text{or} \\ R_2NH \end{matrix} \xrightarrow{HONO} \begin{matrix} Ar{-}\underset{\displaystyle R}{\underset{|}{N}}{-}N{=}O \\ \text{or} \\ R_2N{-}N{=}O \end{matrix}$$

N-Nitrosoamine

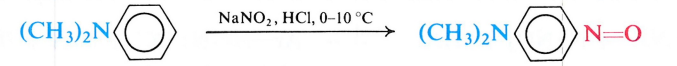


N-Methylaniline — *N*-Nitroso-*N*-methylaniline

Tertiary aromatic



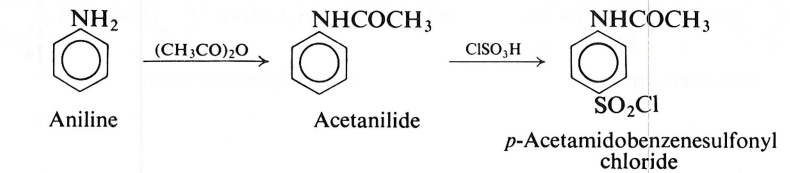
p-Nitroso compound

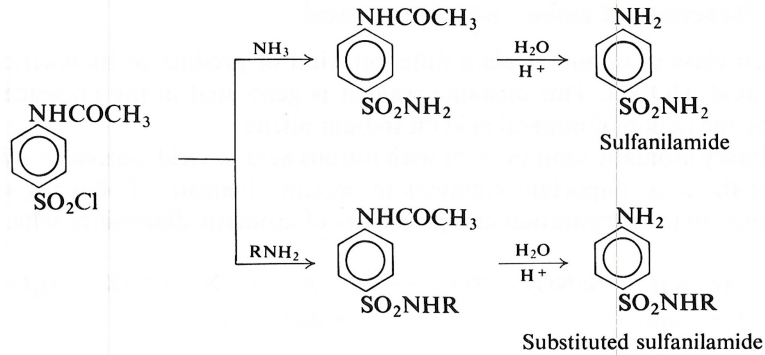


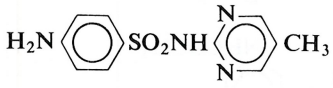
N,*N*-Dimethylaniline — *p*-Nitroso-*N*,*N*-dimethylaniline

23.10 Sulfanilamide. The sulfa drugs

The amide of sulfanilic acid (*sulfanilamide*) and certain related substituted amides are of considerable medical importance as the *sulfa drugs*.







Sulfamerazine

Succinoylsulfathiazole