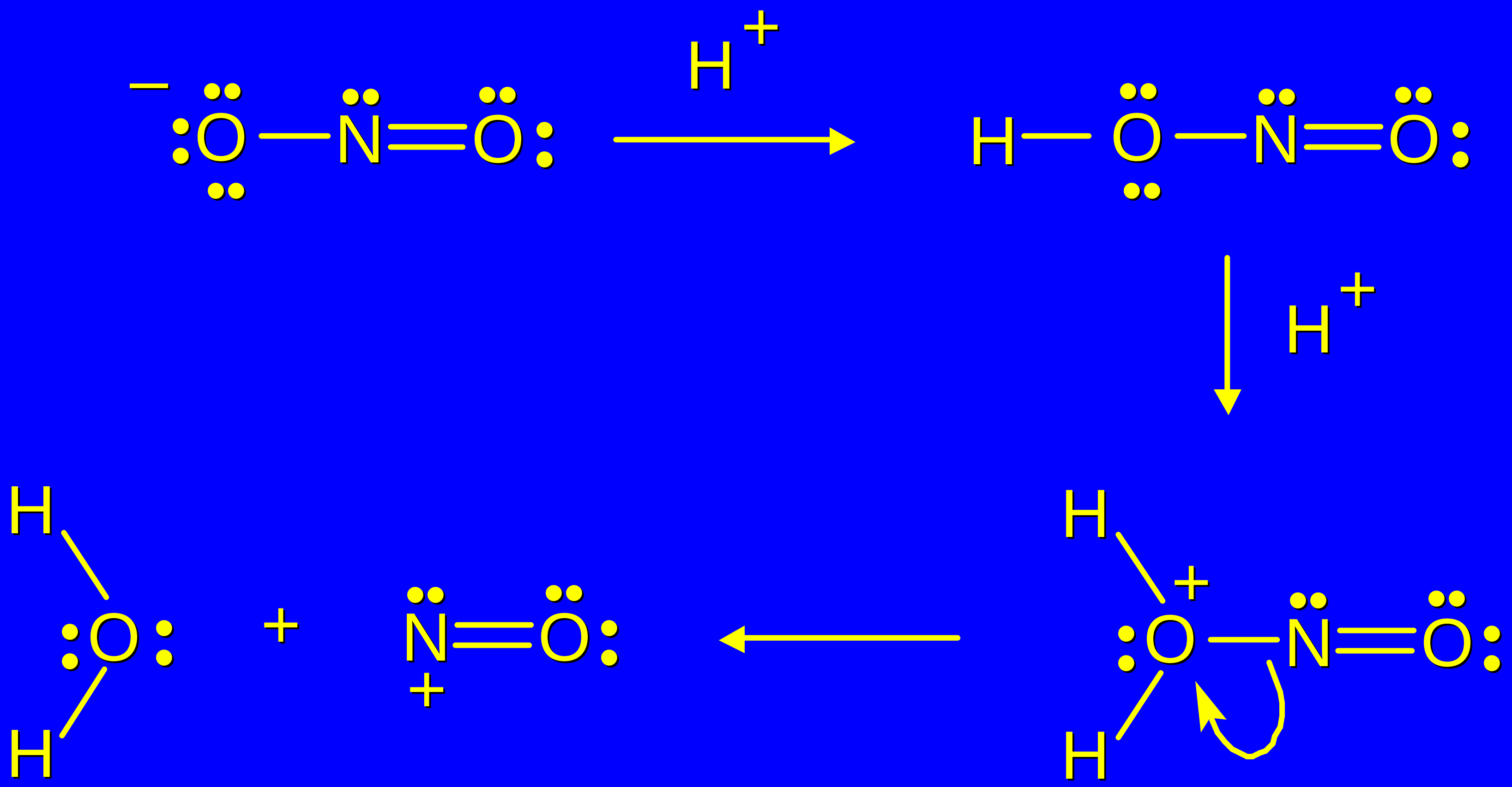
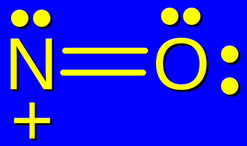
22.16

Nitrosation of Alkylamines

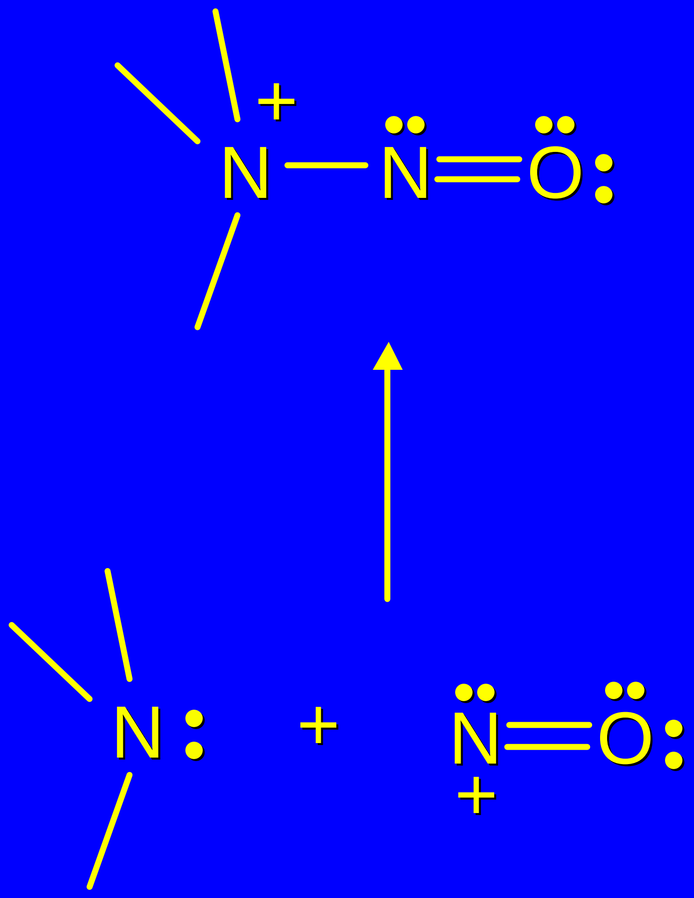
Nitrite Ion, Nitrous Acid, and Nitrosyl Cation



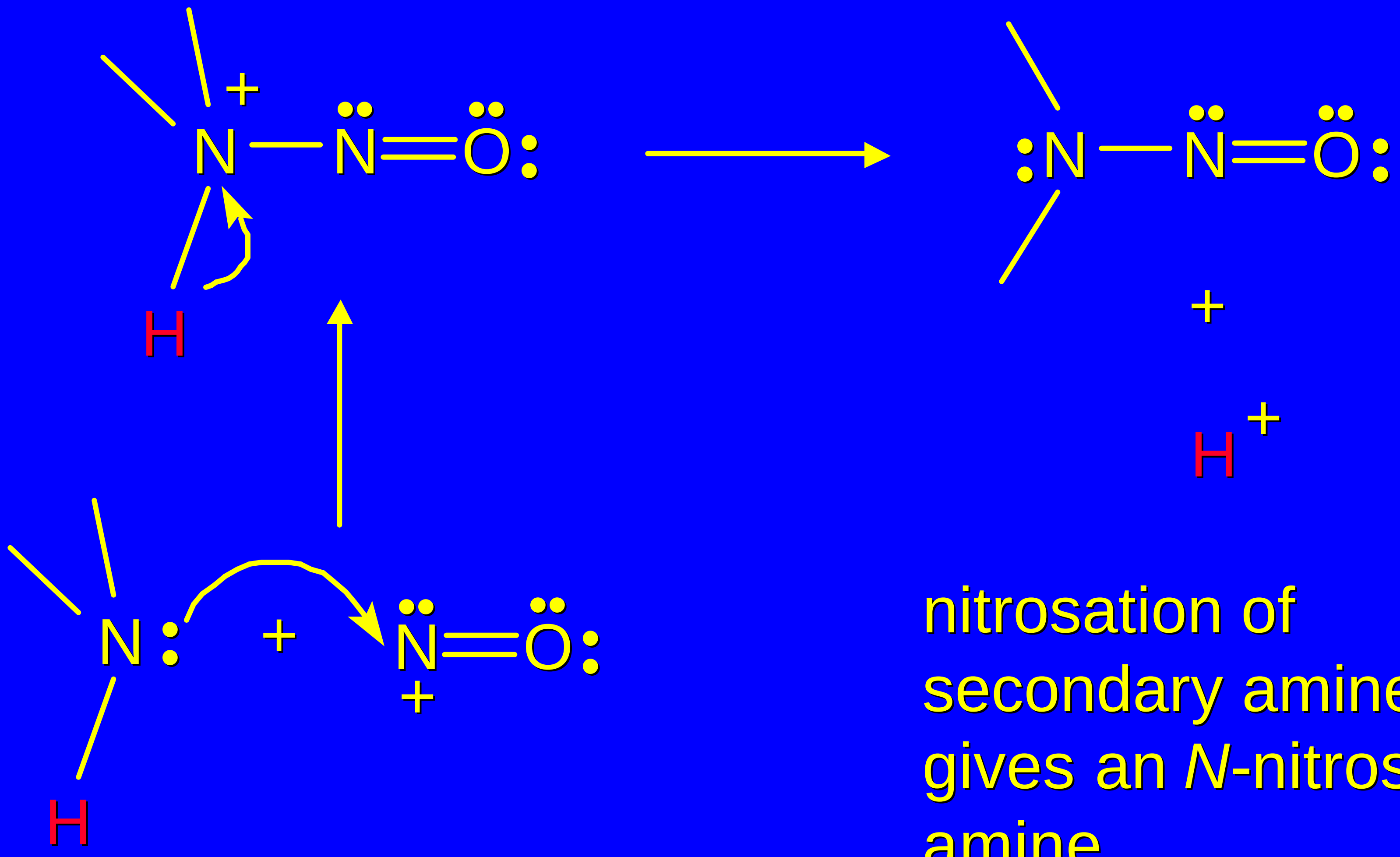
Nitrosyl Cation and Nitrosation



Nitrosyl Cation and Nitrosation

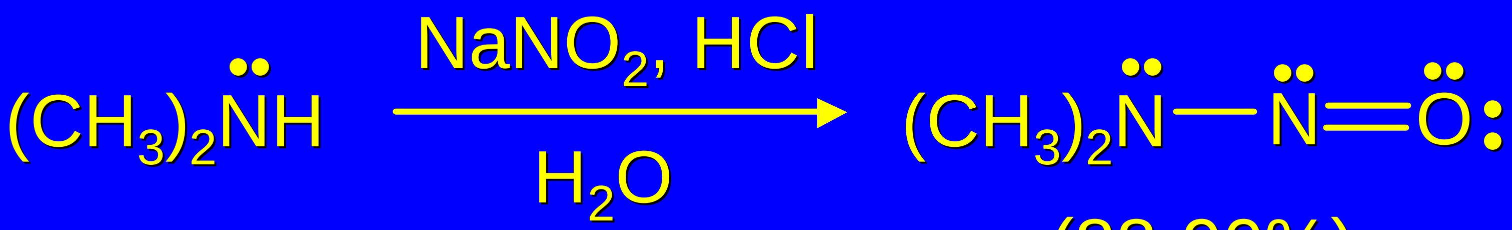


Nitrosation of Secondary Alkylamines



nitrosation of secondary amines gives an *N*-nitroso amine

Example



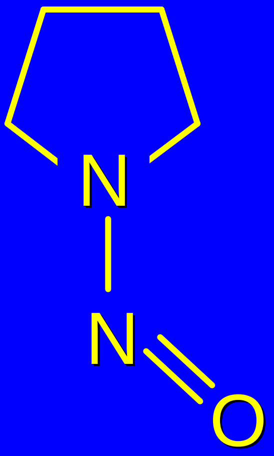
$$(CH_3)_2\ddot{N}H \xrightarrow[H_2O]{NaNO_2,\ HCl} (CH_3)_2\ddot{N}-\ddot{N}=\ddot{O}:$$

(88-90%)

Some N-Nitroso Amines

$(CH_3)_2N-N=O$

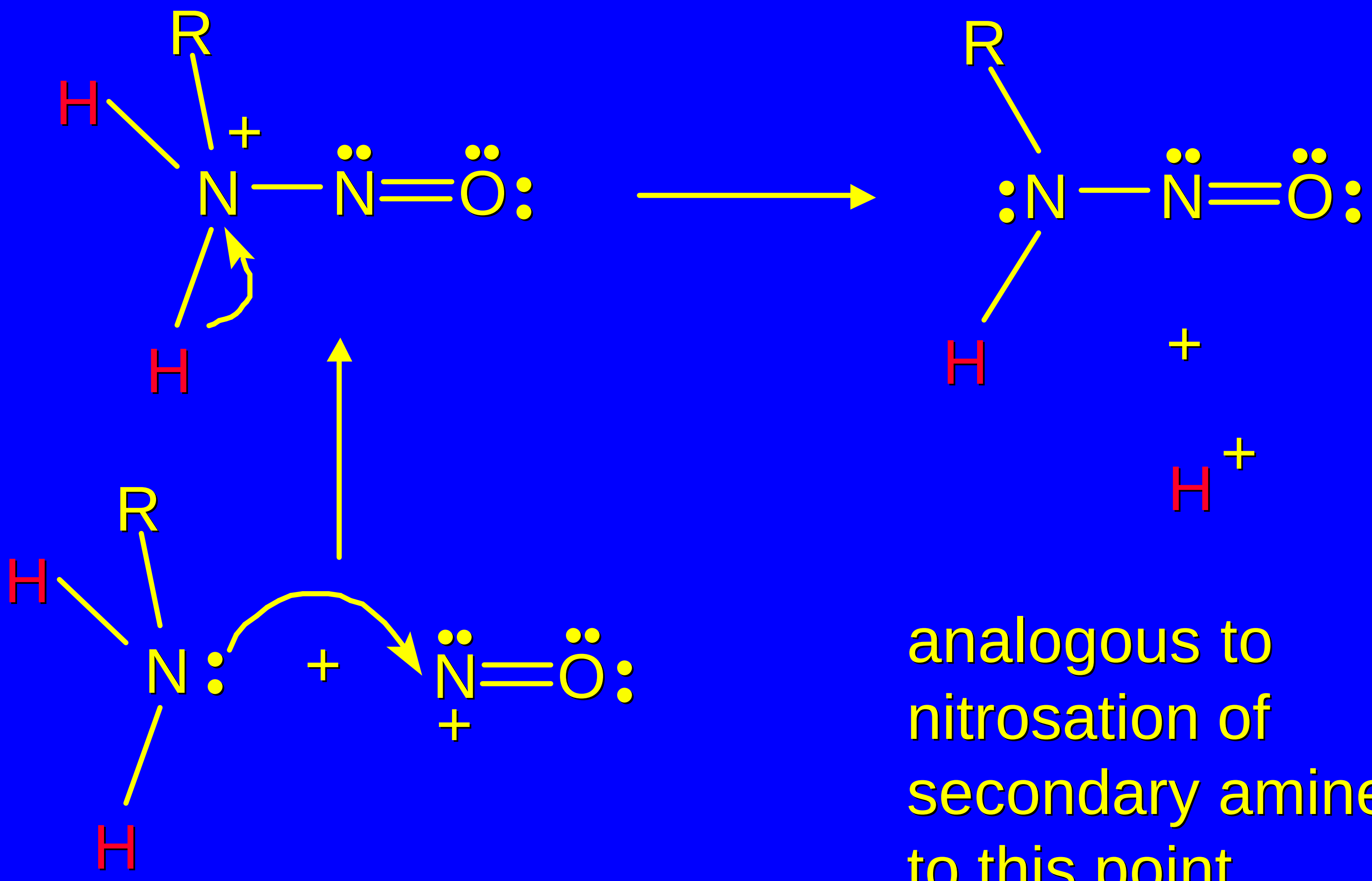
N-nitrosodimethylamine
(leather tanning)



N-nitrosopyrrolidine
(nitrite-cured bacon)

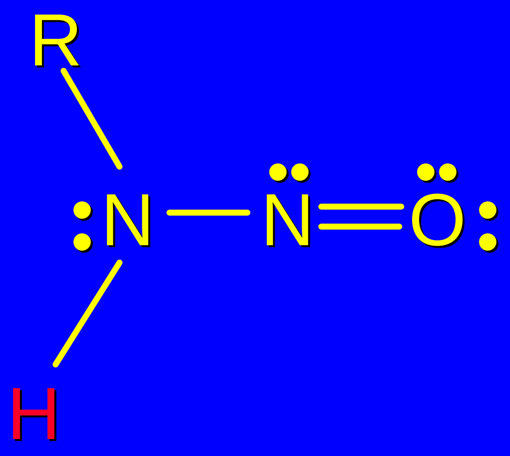
N-nitrosonornicotine
(tobacco smoke)

Nitrosation of Primary Alkylamines



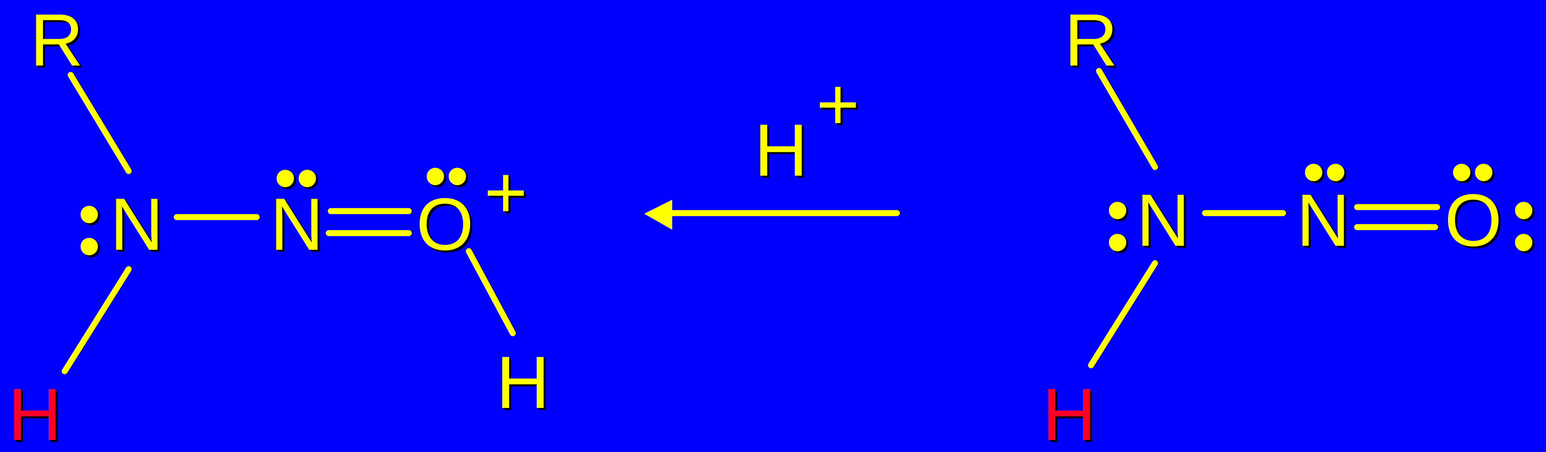
analogous to
nitrosation of
secondary amines
to this point

Nitrosation of Primary Alkylamines

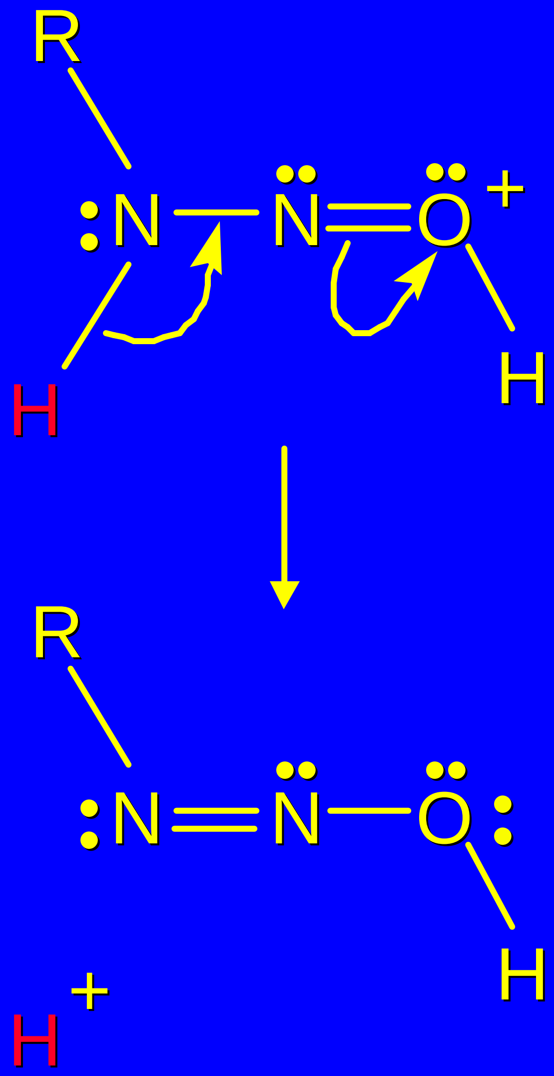


this species reacts further

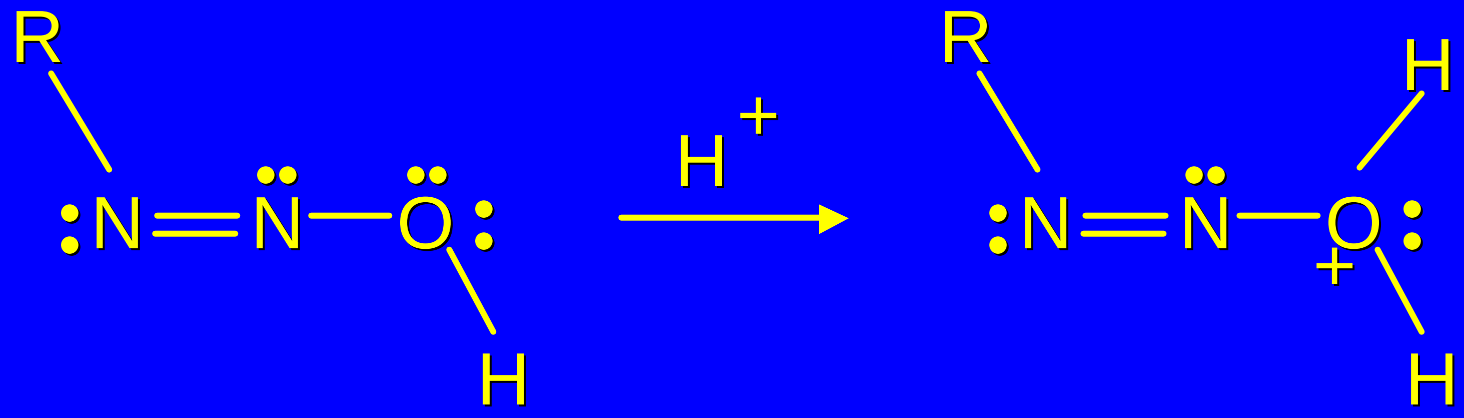
Nitrosation of Primary Alkylamines



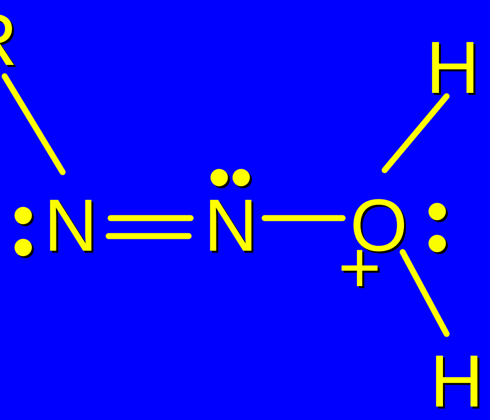
Nitrosation of Primary Alkylamines



Nitrosation of Primary Alkylamines



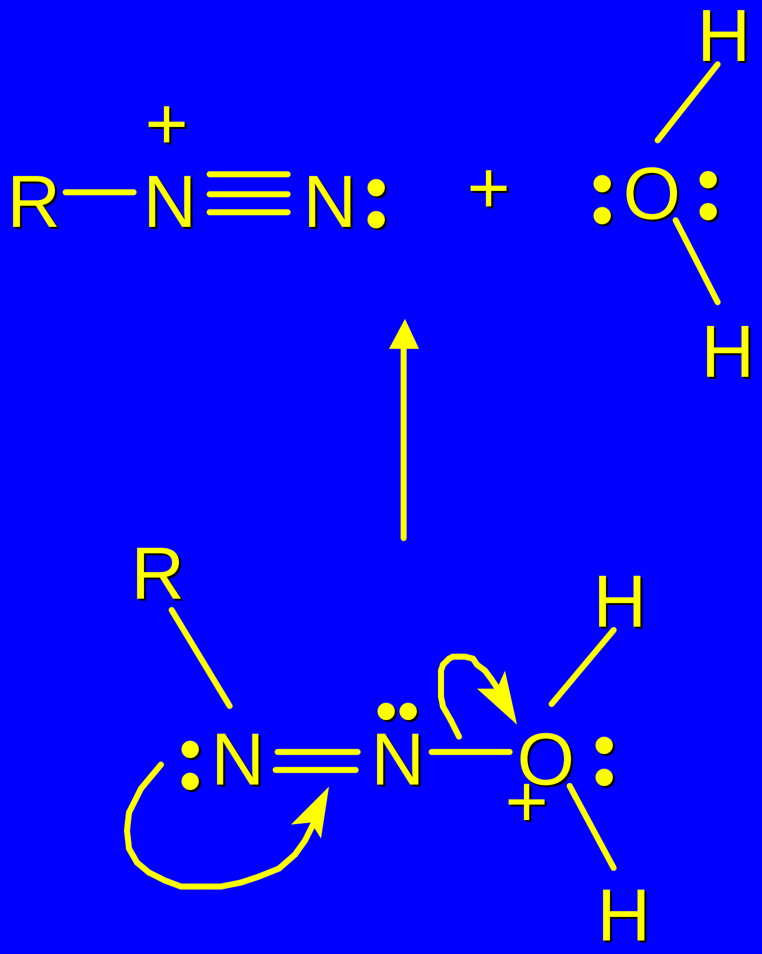
Nitrosation of Primary Alkylamines



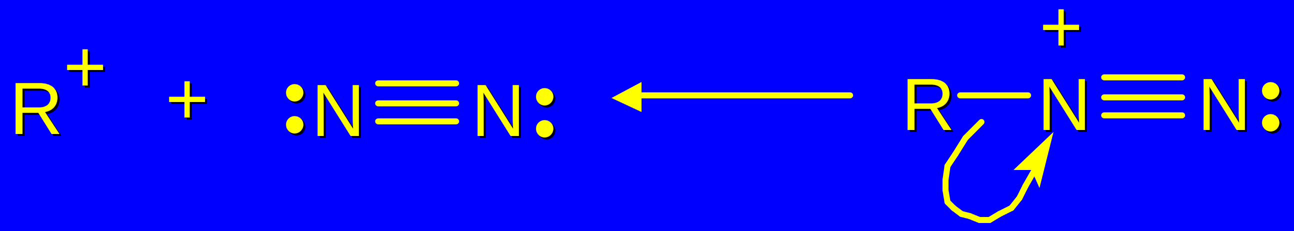
Nitrosation of Primary Alkylamines

nitrosation of a primary alkylamine gives an alkyl diazonium ion

process is called *diazotization*



Alkyl Diazonium Ions



$$R^{+} + :N\equiv N: \longleftarrow R-\overset{+}{N}\equiv N:$$

alkyl diazonium ions
readily lose N_2 to
give carbocations

Example: Nitrosation of 1,1-Dimethylpropylamine

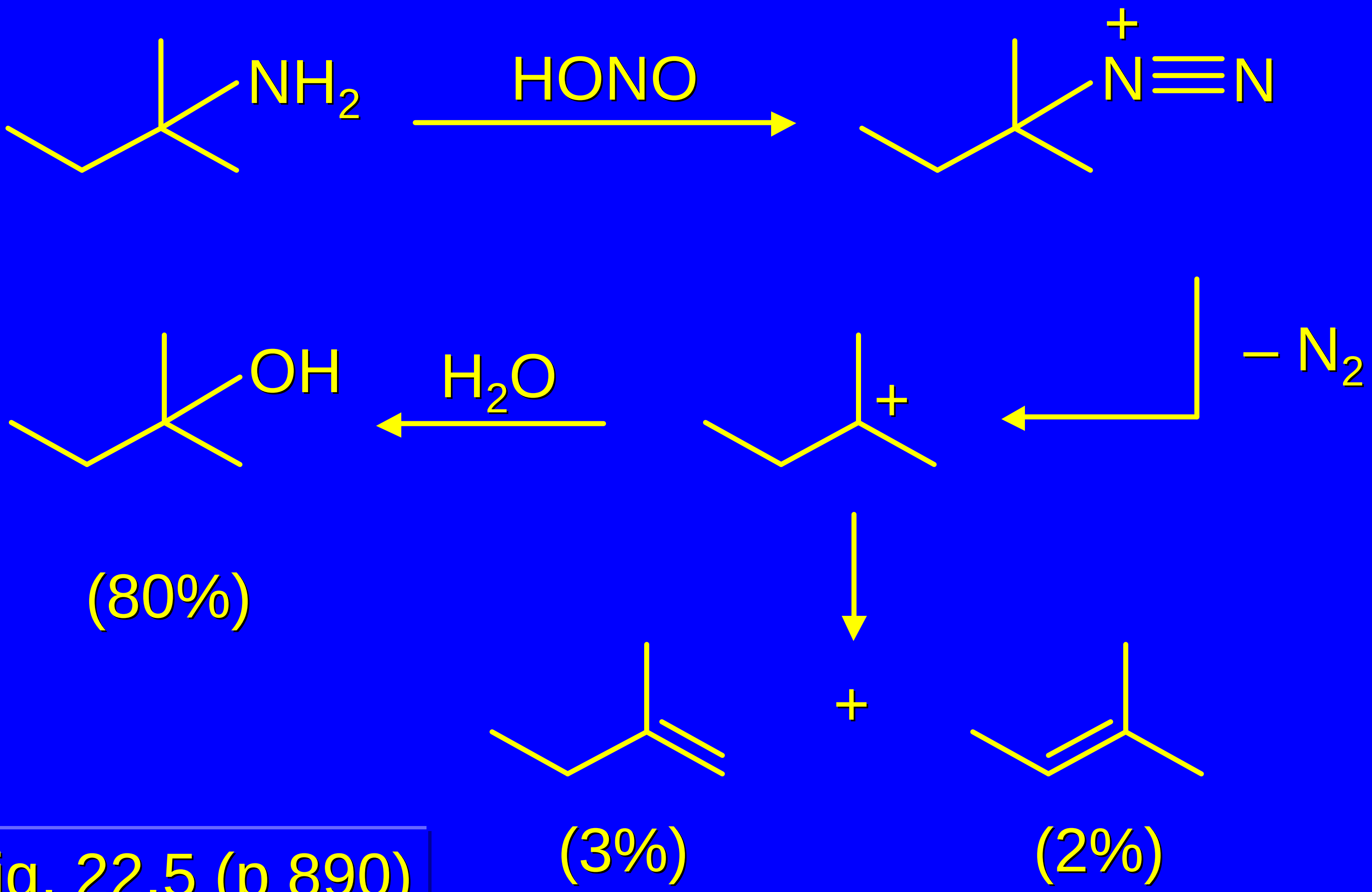
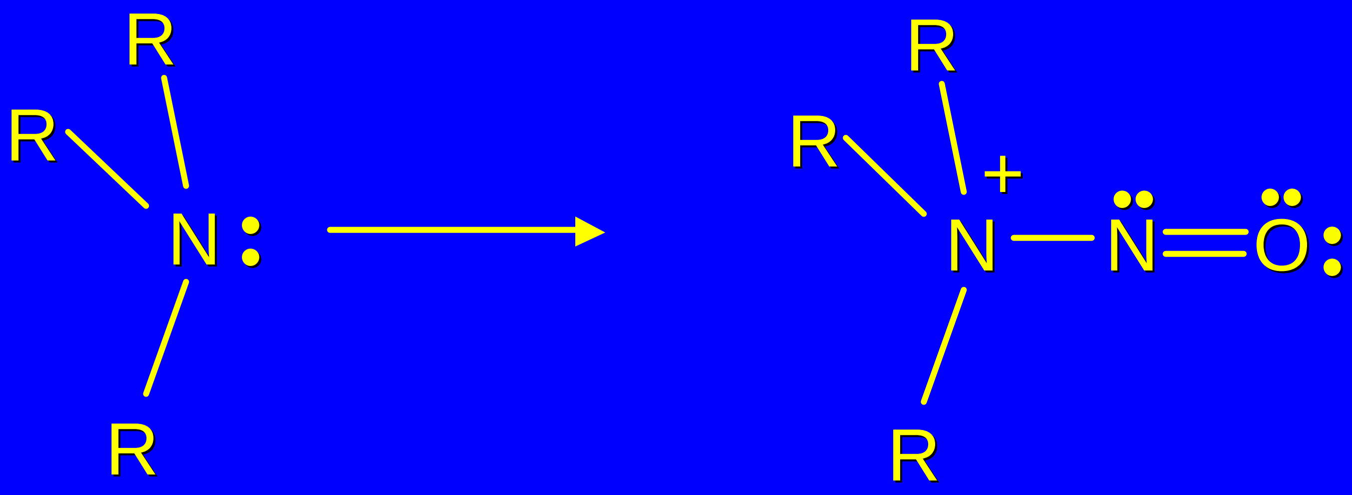


Fig. 22.5 (p 890)

Nitrosation of Tertiary Alkylamines

There is no useful chemistry associated with the nitrosation of tertiary alkylamines.

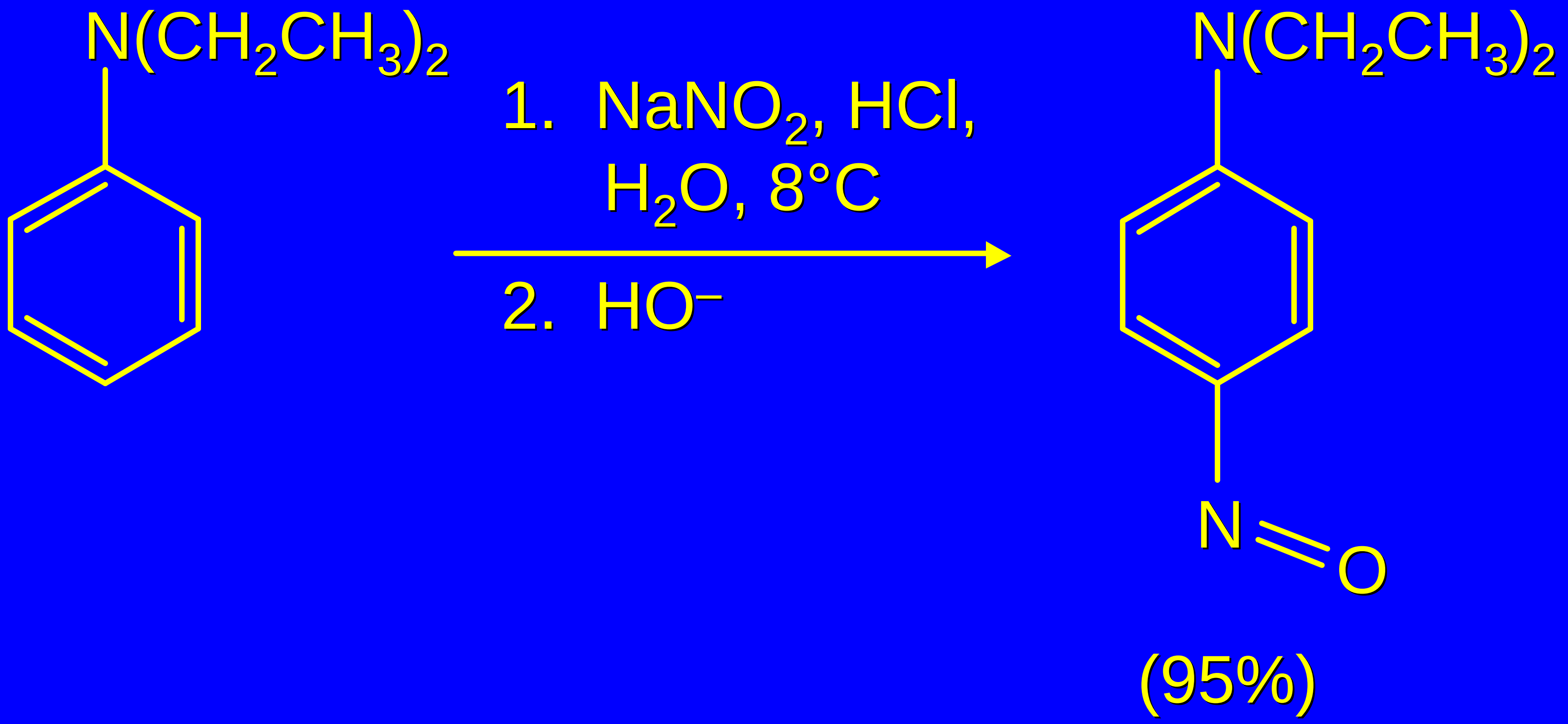


22.17

Nitrosation of Arylamines

Nitrosation of Tertiary Arylamines

reaction that occurs is
electrophilic aromatic substitution



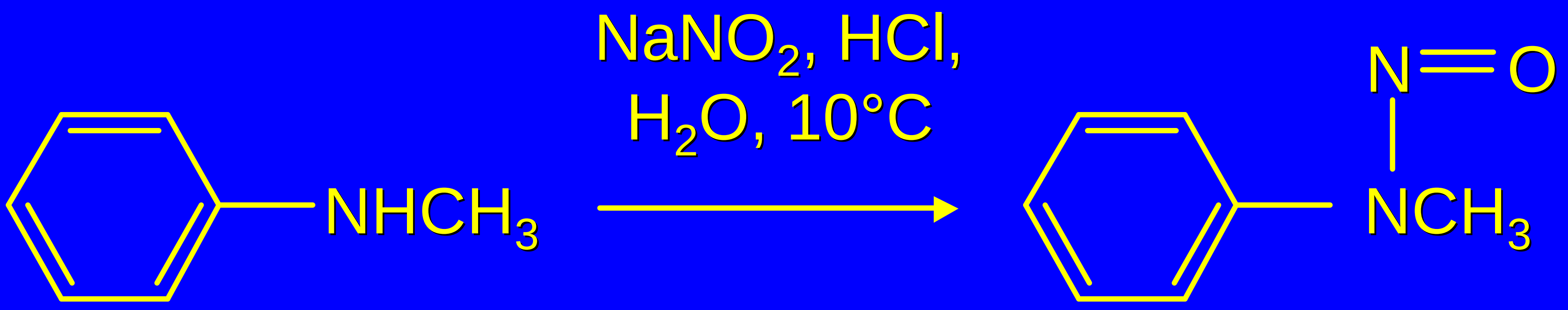
1. $NaNO_2$, HCl, H_2O, 8°C
2. HO^-

(95%)

Nitrosation of N-Alkylarylamines

similar to secondary alkylamines;

gives *N*-nitroso amines



(87-93%)

Nitrosation of Primary Arylamines

gives aryl diazonium ions

aryl diazonium ions are much more stable than alkyl diazonium ions

most aryl diazonium ions are stable under the conditions of their formation (0-10°C)

Nitrosation of Primary Arylamines

gives aryl diazonium ions

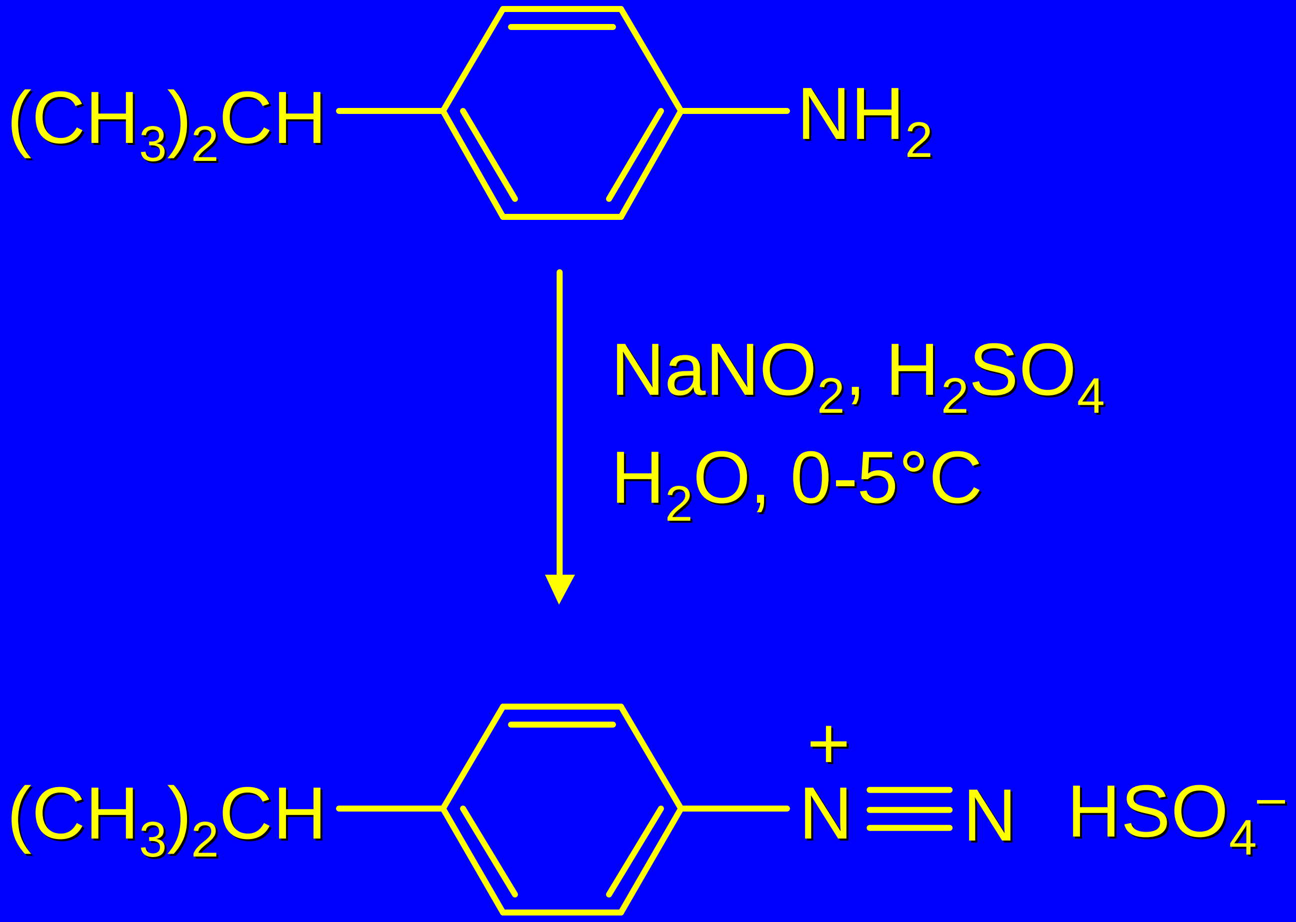
aryl diazonium ions are much more stable than alkyl diazonium ions

most aryl diazonium ions are stable under the conditions of their formation (0-10°C)

$$R\overset{+}{N}\equiv N \xrightarrow{\text{fast}} R^{+} + N_2$$

$$Ar\overset{+}{N}\equiv N \xrightarrow{\text{slow}} Ar^{+} + N_2$$

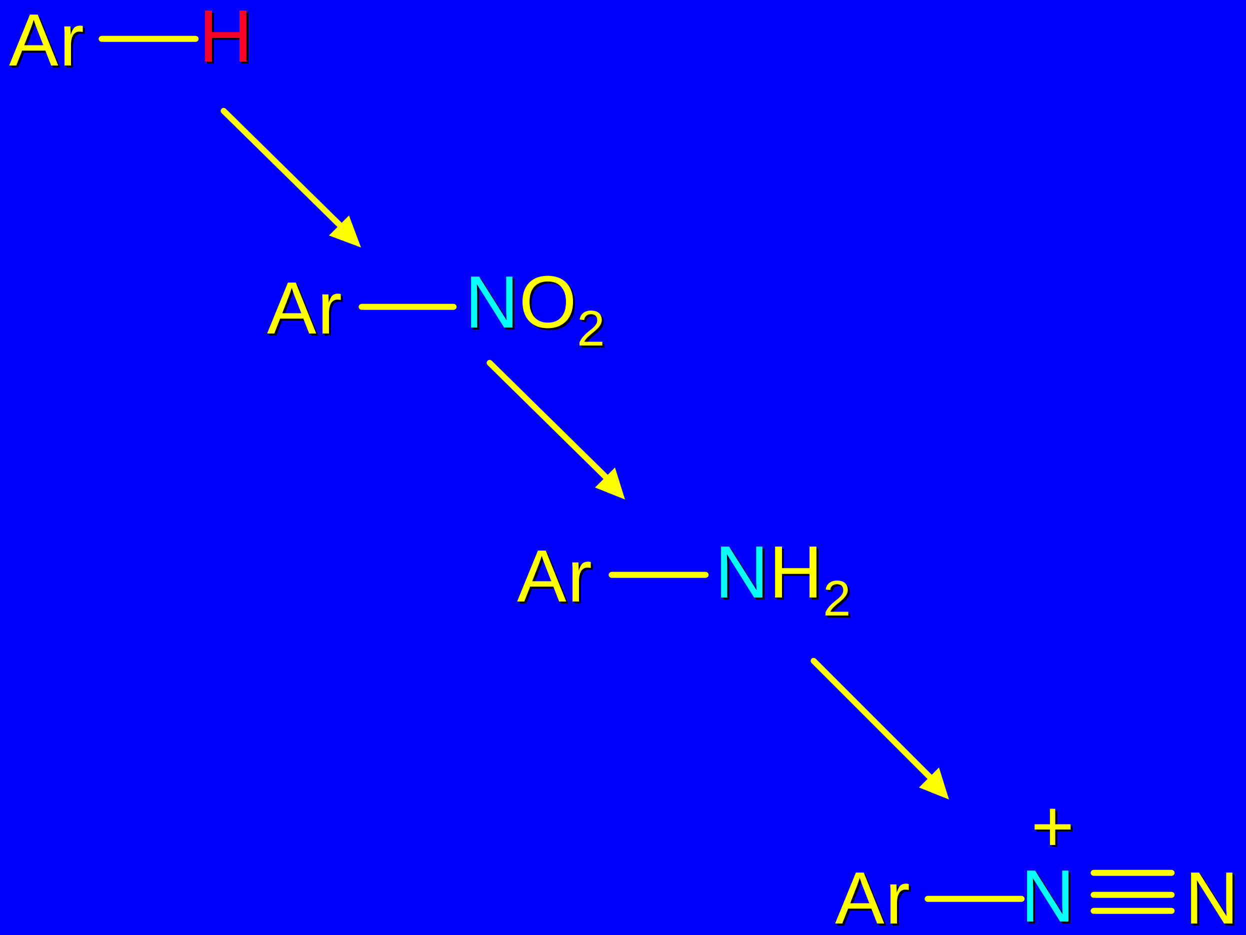
Example:



$NaNO_2$, H_2SO_4

H_2O, 0-5°C

Synthetic Origin of Aryl Diazonium Salts

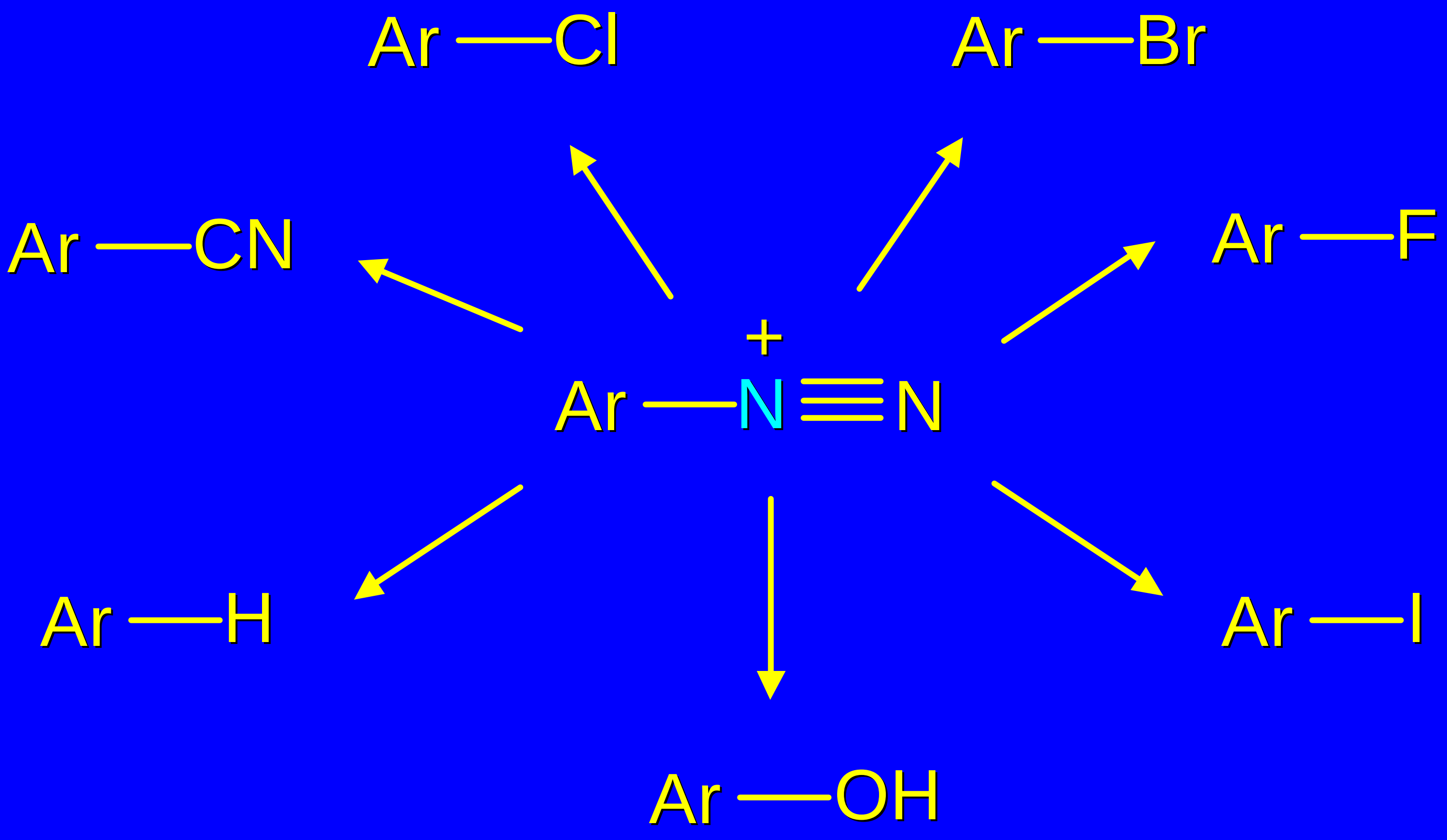


$$\mathrm{Ar{-}H} \rightarrow \mathrm{Ar{-}NO_2} \rightarrow \mathrm{Ar{-}NH_2} \rightarrow \mathrm{Ar{-}\overset{+}{N}{\equiv}N}$$

22.18

Synthetic Transformations of Aryl Diazonium Salts

Transformations of Aryl Diazonium Salts



$\mathrm{Ar-\overset{+}{N}\equiv N}$

Ar—Cl

Ar—Br

Ar—CN

Ar—F

Ar—H

Ar—I

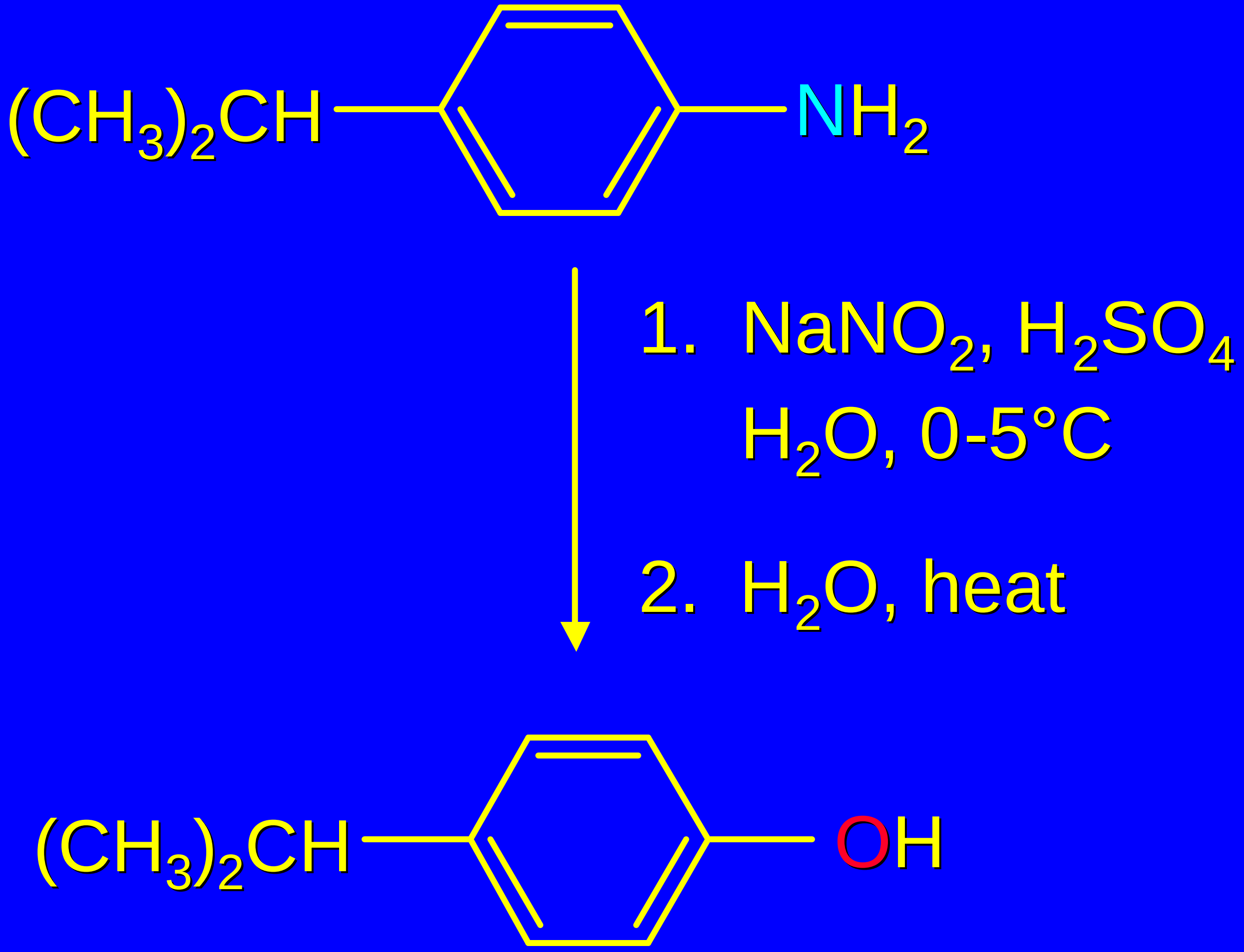
Ar—OH

Preparation of Phenols

hydrolysis of a diazonium salt

$$\mathrm{Ar}-\overset{+}{\mathrm{N}}\equiv\mathrm{N} \xrightarrow{H_2O,\ \text{heat}} \mathrm{Ar}-\mathrm{OH}$$

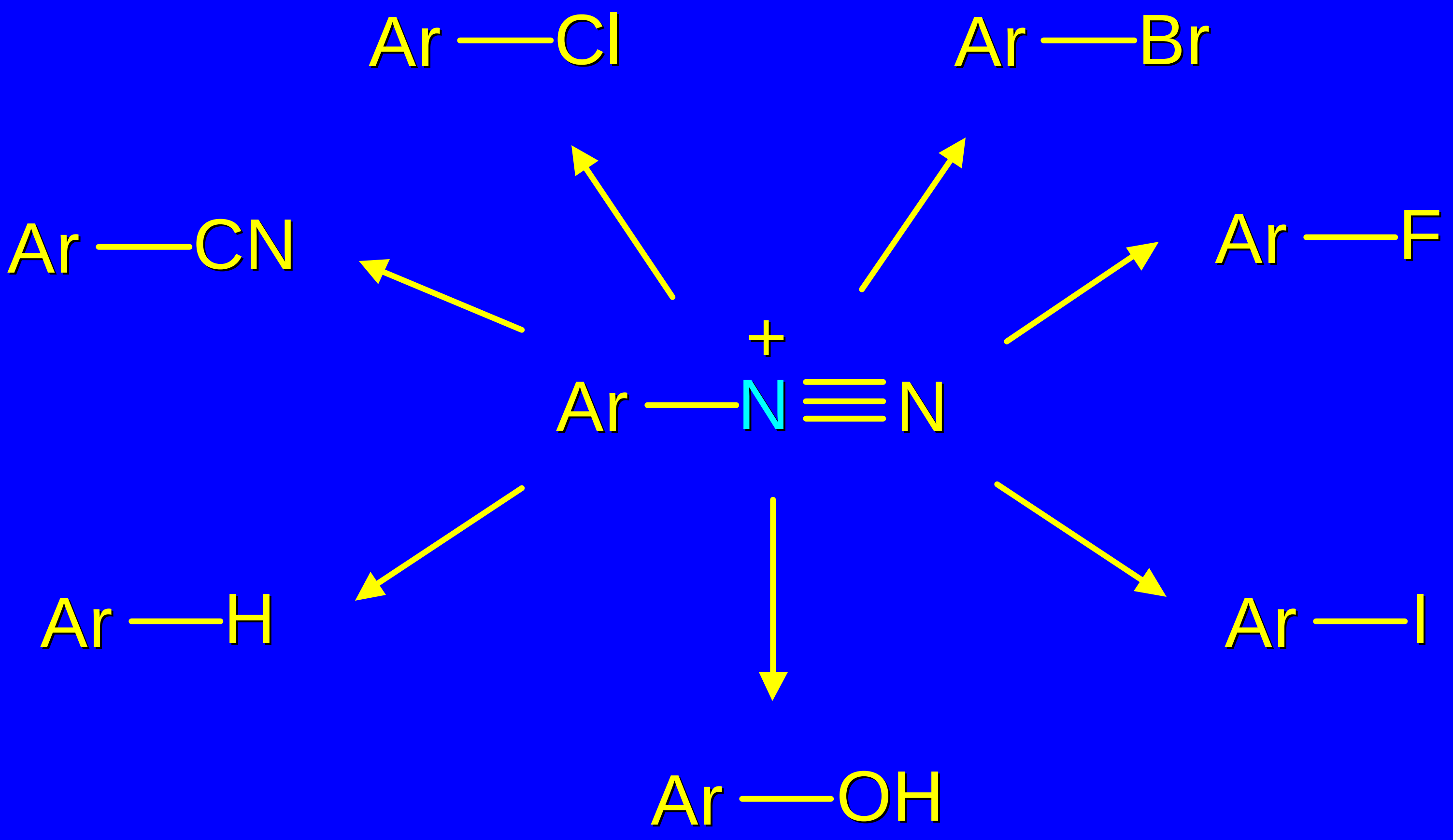
Example



1. $NaNO_2$, H_2SO_4
   H_2O, 0-5°C
2. H_2O, heat

(73%)

Transformations of Aryl Diazonium Salts



$Ar-Cl$

$Ar-Br$

$Ar-CN$

$Ar-F$

$Ar-\overset{+}{N}\equiv N$

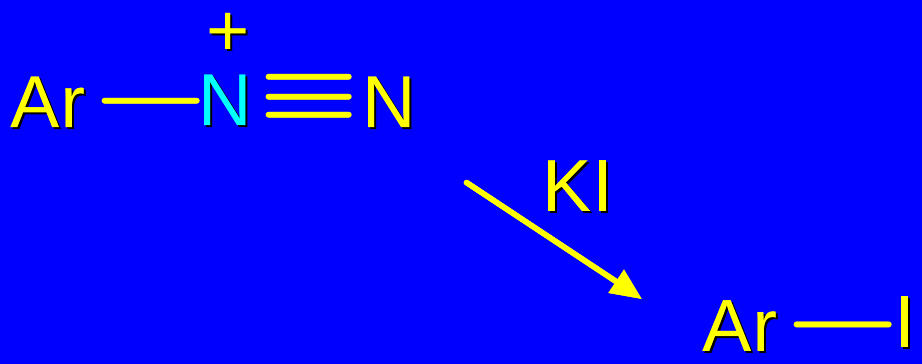
$Ar-H$

$Ar-I$

$Ar-OH$

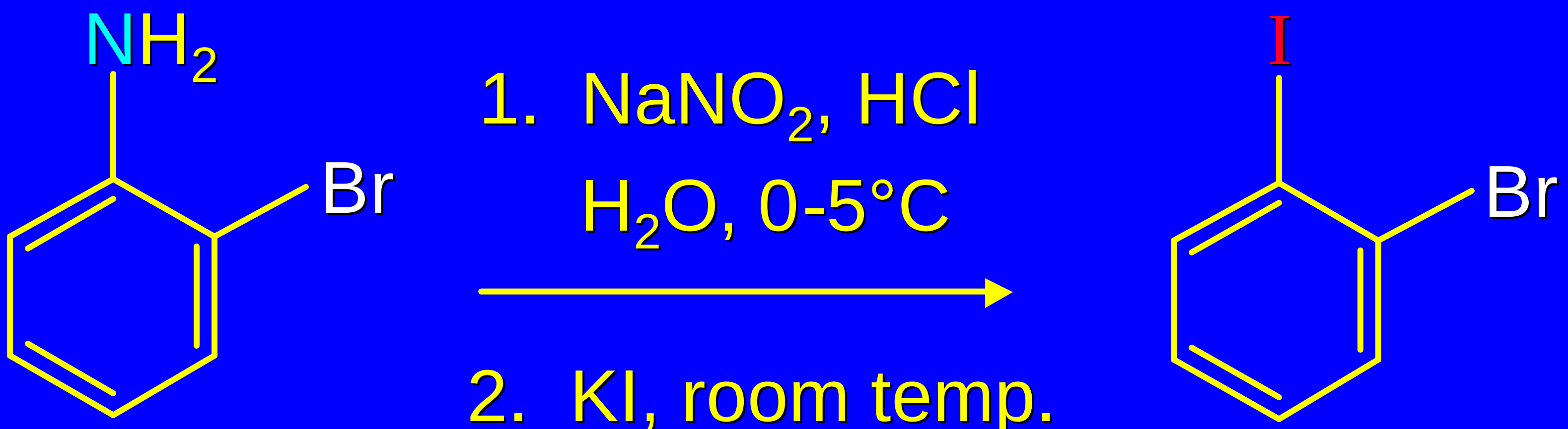
Preparation of Aryl Iodides

reaction of an aryl diazonium salt with potassium iodide



$$\mathrm{Ar}-\overset{+}{\mathrm{N}}\equiv\mathrm{N}\xrightarrow{\mathrm{KI}}\mathrm{Ar}-\mathrm{I}$$

Example



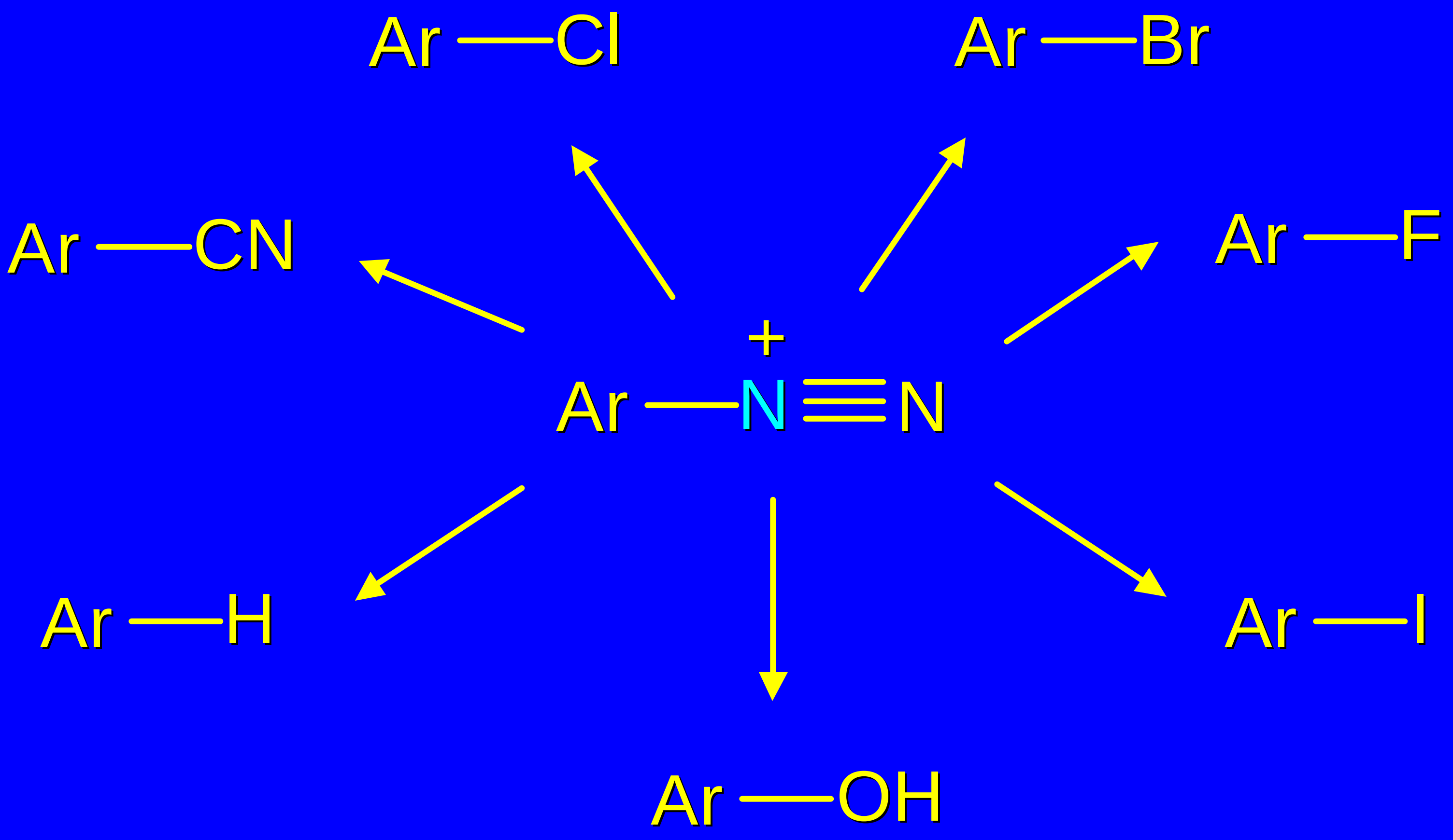
1. $NaNO_2$, HCl

H_2O, 0-5°C

2. KI, room temp.

(72-83%)

Transformations of Aryl Diazonium Salts



Ar—Cl

Ar—Br

Ar—CN

Ar—F

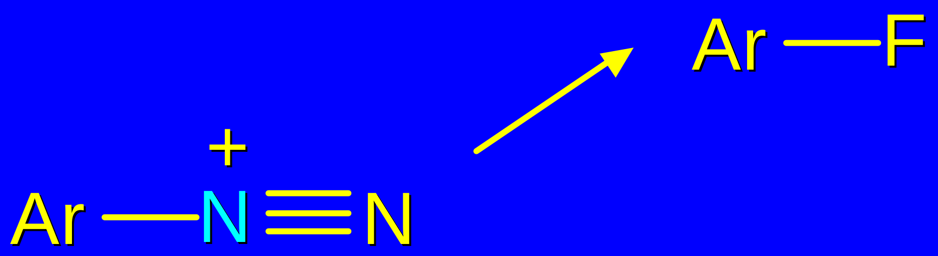
$Ar-\overset{+}{N}\equiv N$

Ar—H

Ar—I

Ar—OH

Preparation of Aryl Fluorides

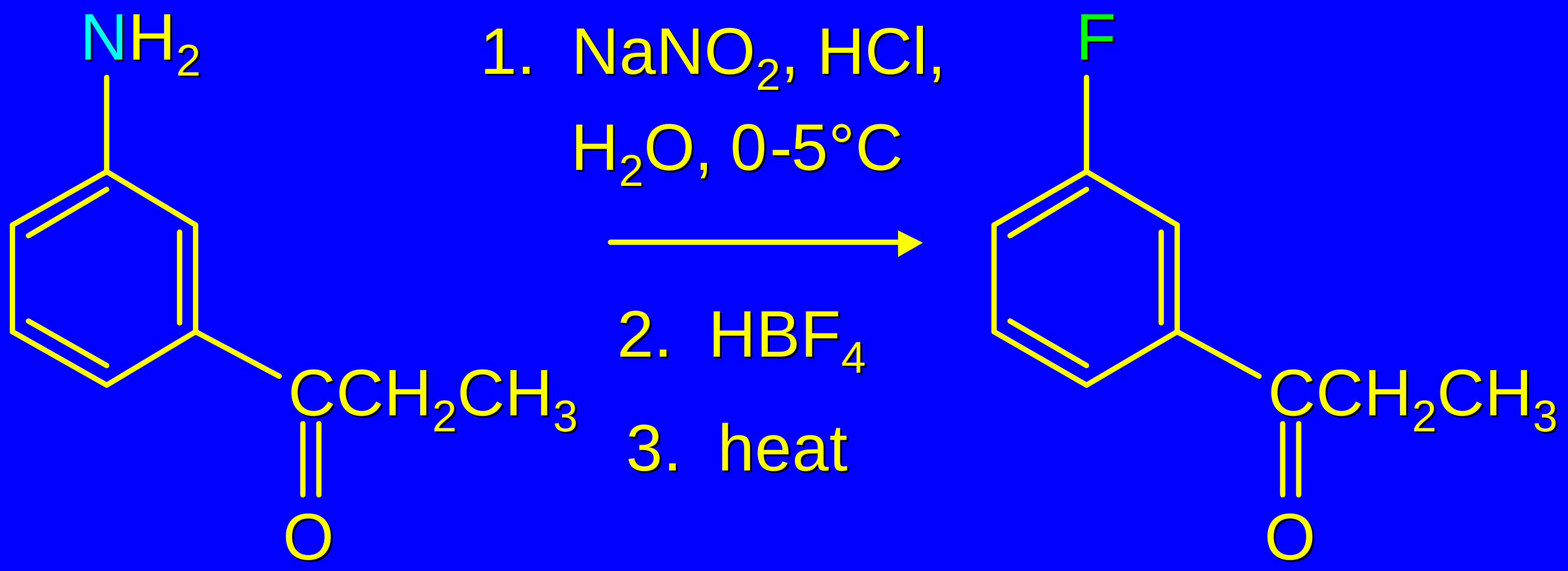


$$Ar-\overset{+}{N}\equiv N \longrightarrow Ar-F$$

heat the tetrafluoroborate salt of a diazonium ion;

process is called the Schiemann reaction

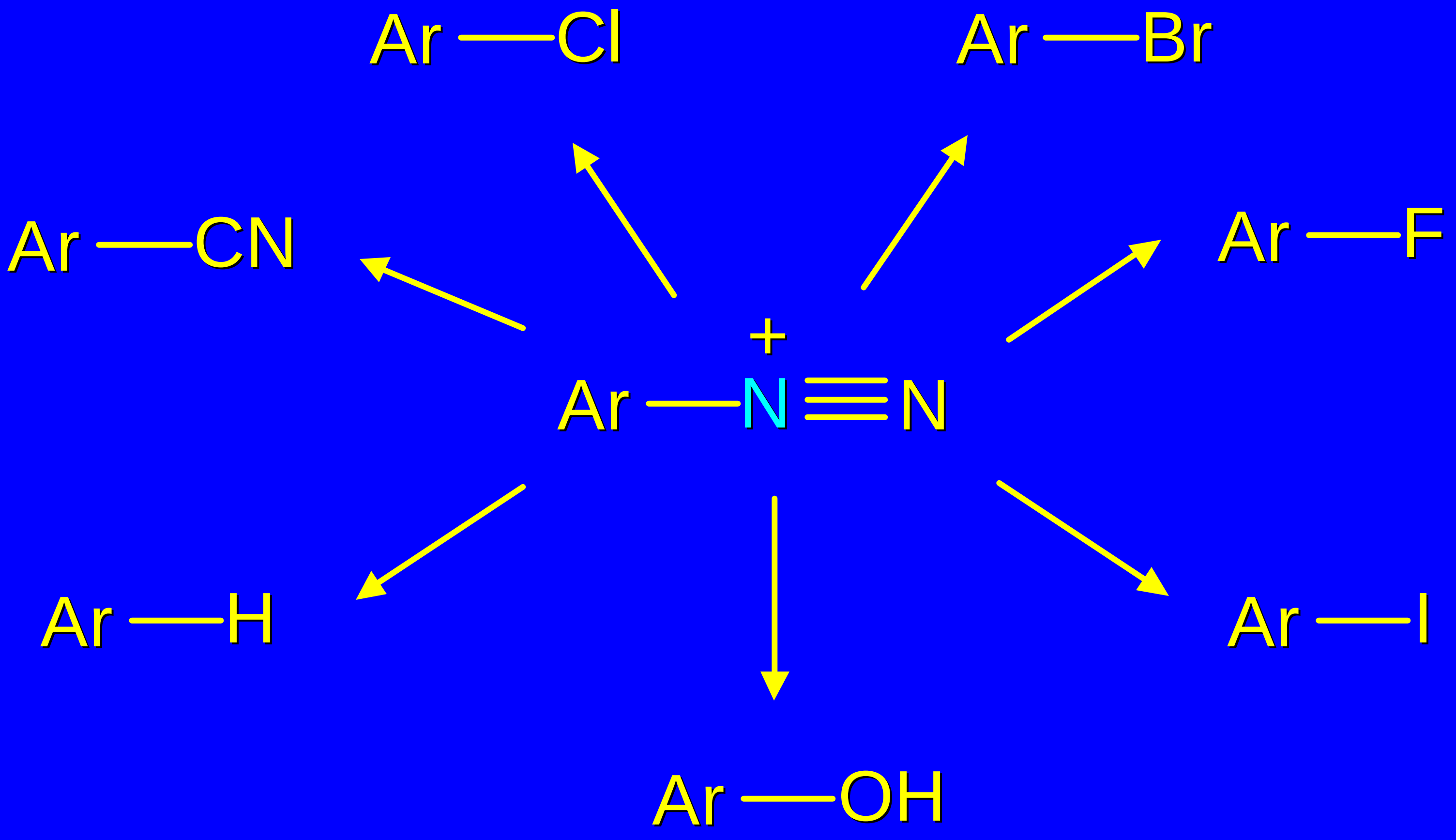
Example



1. $NaNO_2$, HCl, H_2O, 0-5°C
2. HBF_4
3. heat

(68%)

Transformations of Aryl Diazonium Salts



Ar—Cl

Ar—Br

Ar—CN

Ar—F

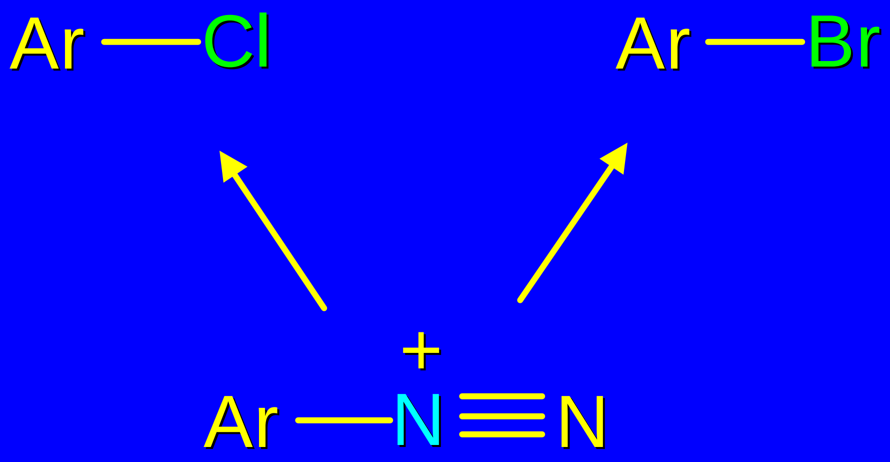
$\mathrm{Ar-\overset{+}{N}\equiv N}$

Ar—H

Ar—I

Ar—OH

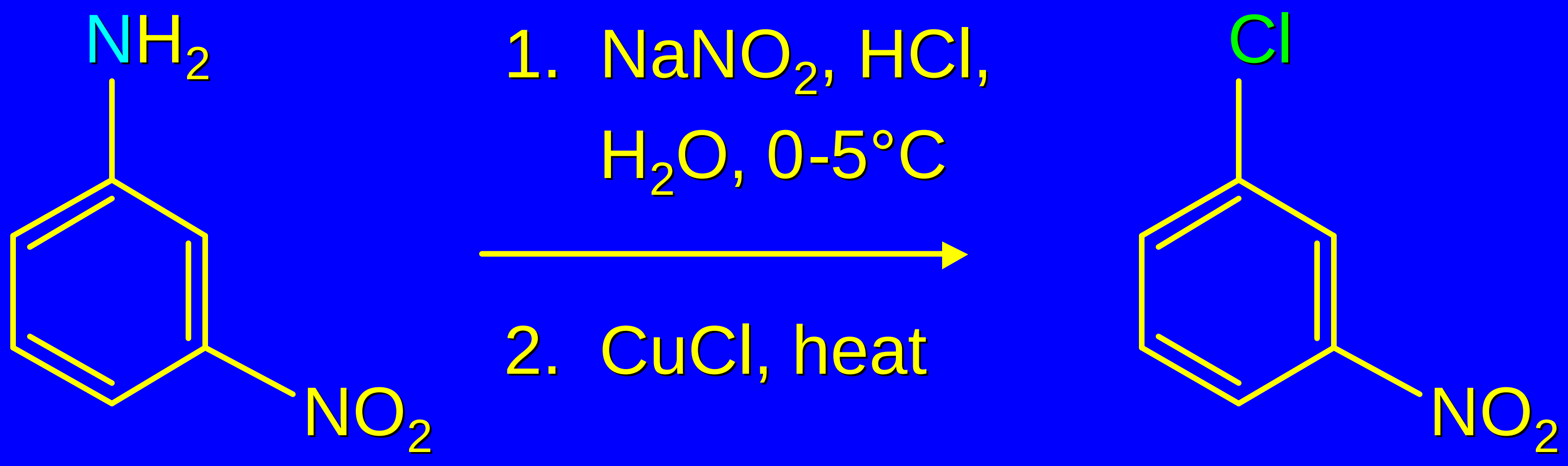
Preparation of Aryl Chlorides and Bromides



aryl chlorides and aryl bromides are prepared by heating a diazonium salt with copper(I) chloride or bromide

substitutions of diazonium salts that use copper(I) halides are called *Sandmeyer reactions*

Example

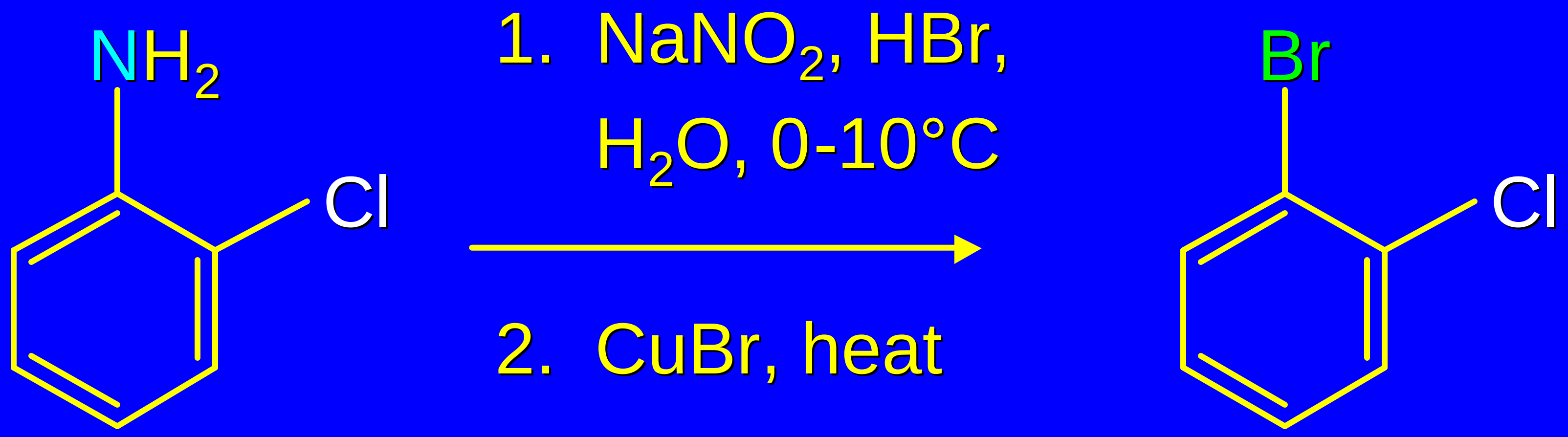


1. $NaNO_2$, HCl, H_2O, 0-5°C

2. CuCl, heat

(68-71%)

Example

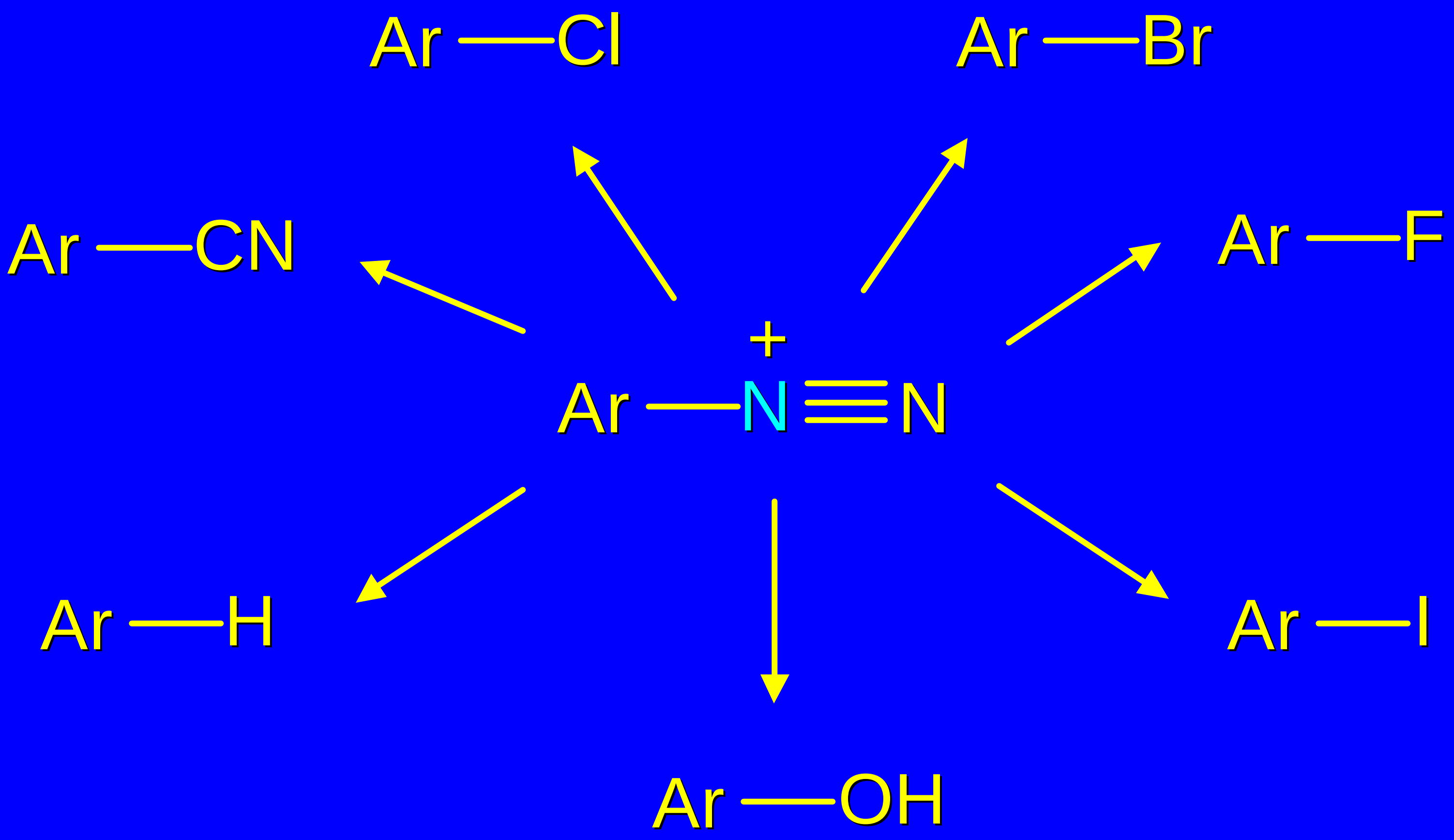


1. $NaNO_2$, HBr,
   H_2O, 0-10°C

2. CuBr, heat

(89-95%)

Transformations of Aryl Diazonium Salts



$\mathrm{Ar{-}\overset{+}{N}{\equiv}N}$

$\mathrm{Ar{-}Cl}$

$\mathrm{Ar{-}Br}$

$\mathrm{Ar{-}CN}$

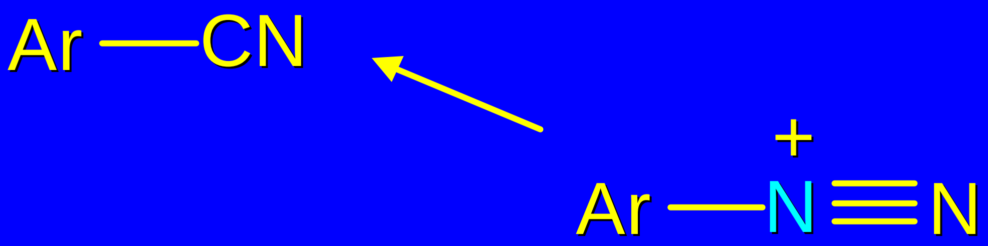
$\mathrm{Ar{-}F}$

$\mathrm{Ar{-}H}$

$\mathrm{Ar{-}I}$

$\mathrm{Ar{-}OH}$

Preparation of Aryl Nitriles

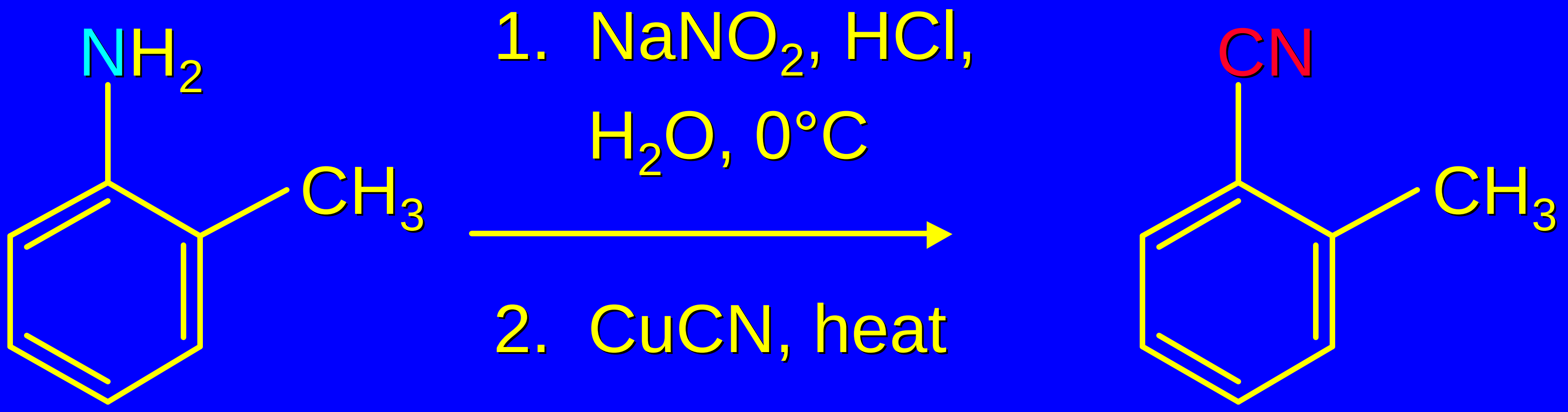


$$\mathrm{Ar{-}CN} \leftarrow \mathrm{Ar{-}\overset{+}{N}{\equiv}N}$$

aryl nitriles are prepared by heating a diazonium salt with copper(I) cyanide

this is another type of Sandmeyer reaction

Example

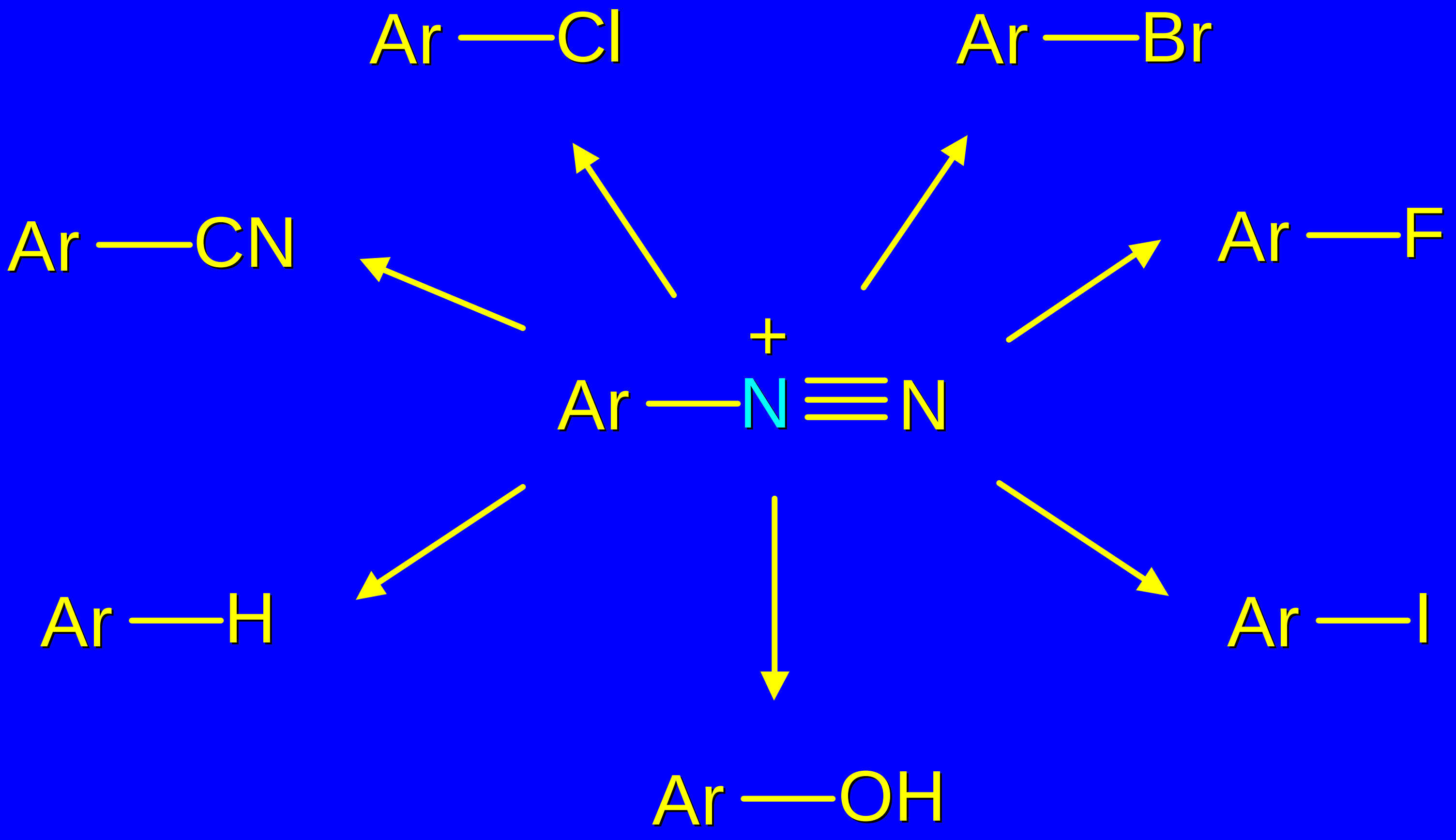


1. $NaNO_2$, HCl, H_2O, 0°C

2. CuCN, heat

(64-70%)

Transformations of Aryl Diazonium Salts


Ar—Cl

Ar—Br

Ar—CN

Ar—F

$Ar-\overset{+}{N}\equiv N$

Ar—H

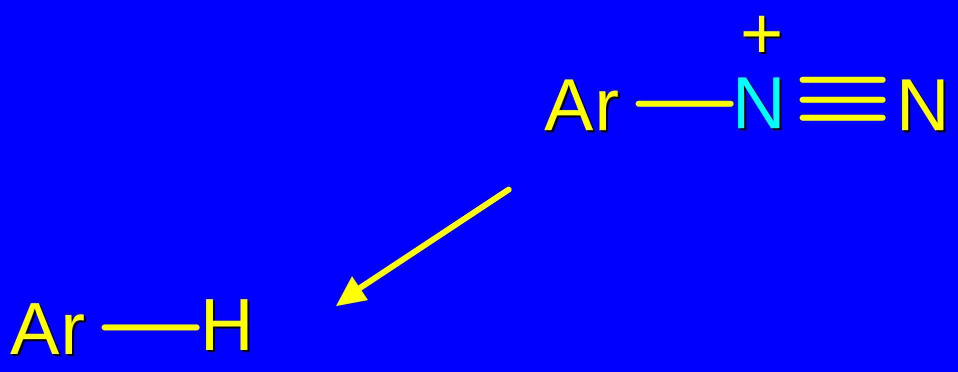
Ar—I

Ar—OH

Transformations of Aryl Diazonium Salts

hypophosphorous acid (H_3PO_2) reduces diazonium salts; ethanol does the same thing

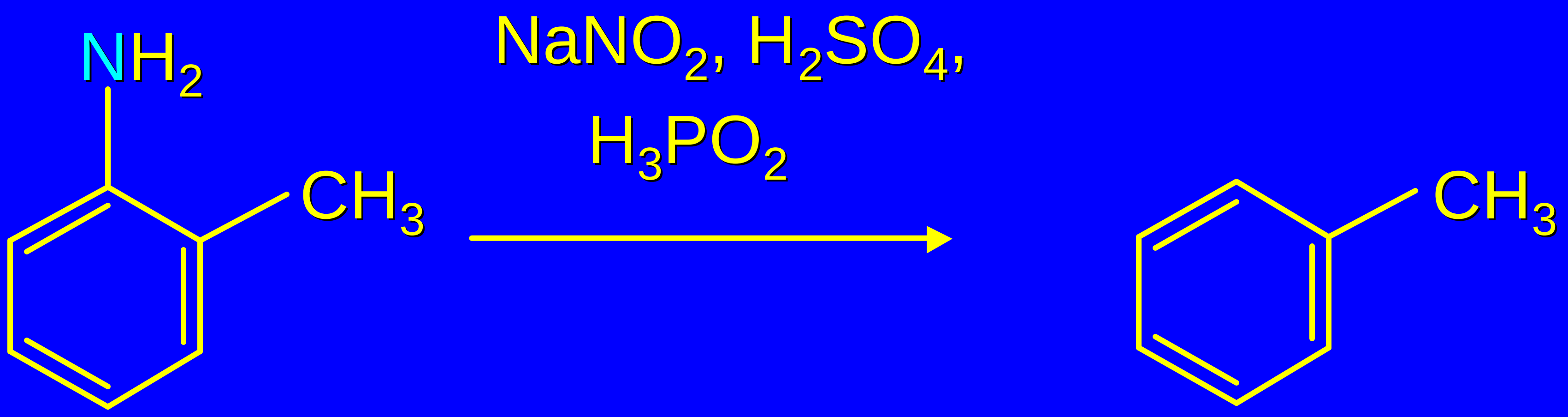
this is called *reductive deamination*



$$Ar-\overset{+}{N}\equiv N$$

$$Ar-H$$

Example

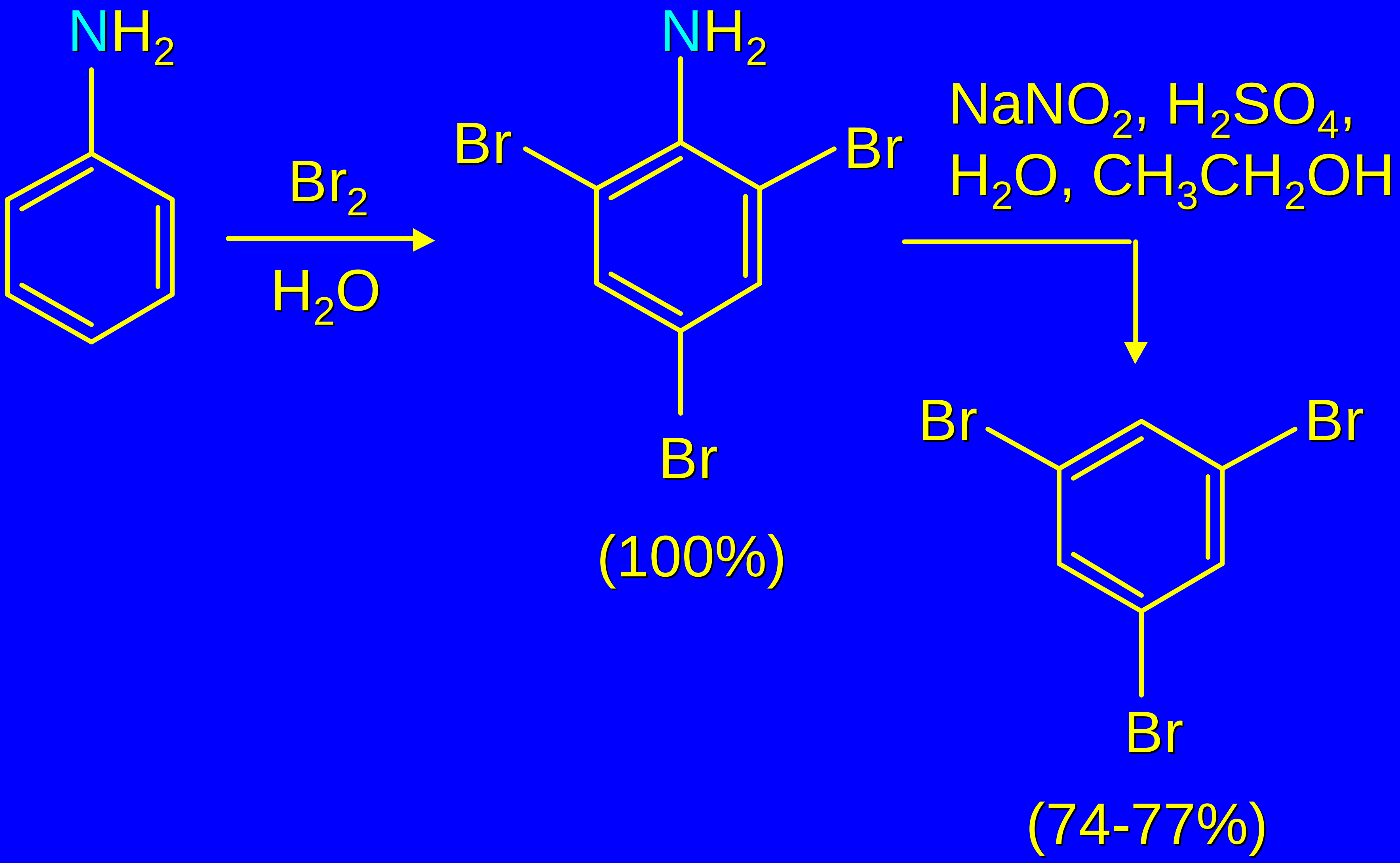


(70-75%)

Value of Diazonium Salts

1) allows introduction of substituents such as OH, F, I, and CN on the ring
2) allows preparation of otherwise difficultly accessible substitution patterns

Example


NH_2
Br_2
H_2O
NH_2
Br
Br
Br
(100%)
$NaNO_2$, H_2SO_4,
H_2O, CH_3CH_2OH
Br
Br
Br
(74-77%)

22.19

Azo Coupling

Azo Coupling

Diazonium salts are weak electrophiles.

React with strongly activated aromatic compounds by electrophilic aromatic substitution.

Azo Coupling

Diazonium salts are weak electrophiles.

React with strongly activated aromatic compounds by electrophilic aromatic substitution.

$$\mathrm{Ar}-\overset{+}{\mathrm{N}}\equiv\mathrm{N} \;+\; \mathrm{Ar'}-\mathrm{H} \longrightarrow \mathrm{Ar}-\mathrm{N}=\mathrm{N}-\mathrm{Ar'}$$

an azo compound

Ar' must bear a strongly electron-releasing group such as OH, OR, or NR_2.

Example