

24.6

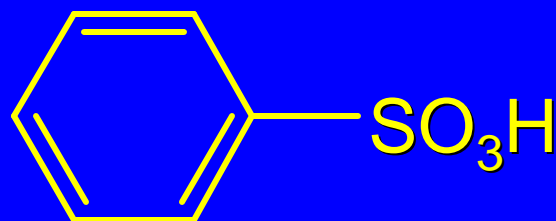
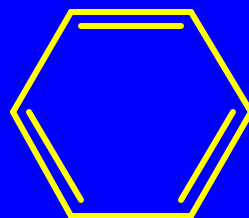
Sources of Phenols

Phenol is an important industrial chemical.

Major use is in phenolic resins for adhesives and plastics.

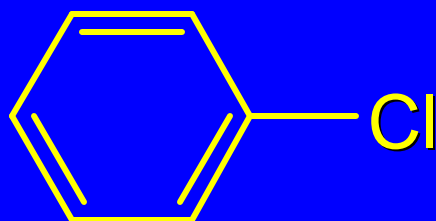
Annual U.S. production is about 4 billion pounds per year.

Industrial Preparations of Phenol



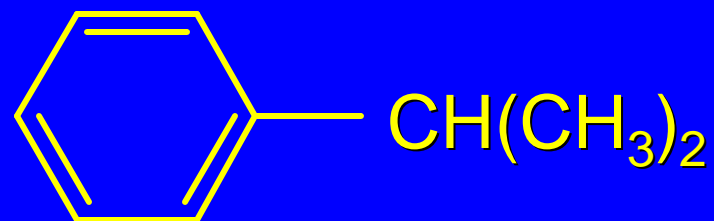
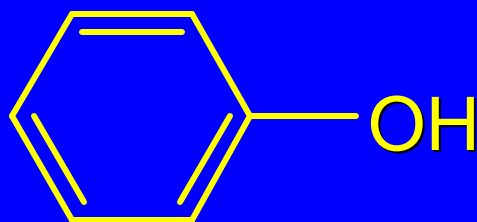
1. NaOH
heat

2. H^+



1. NaOH
heat

2. H^+

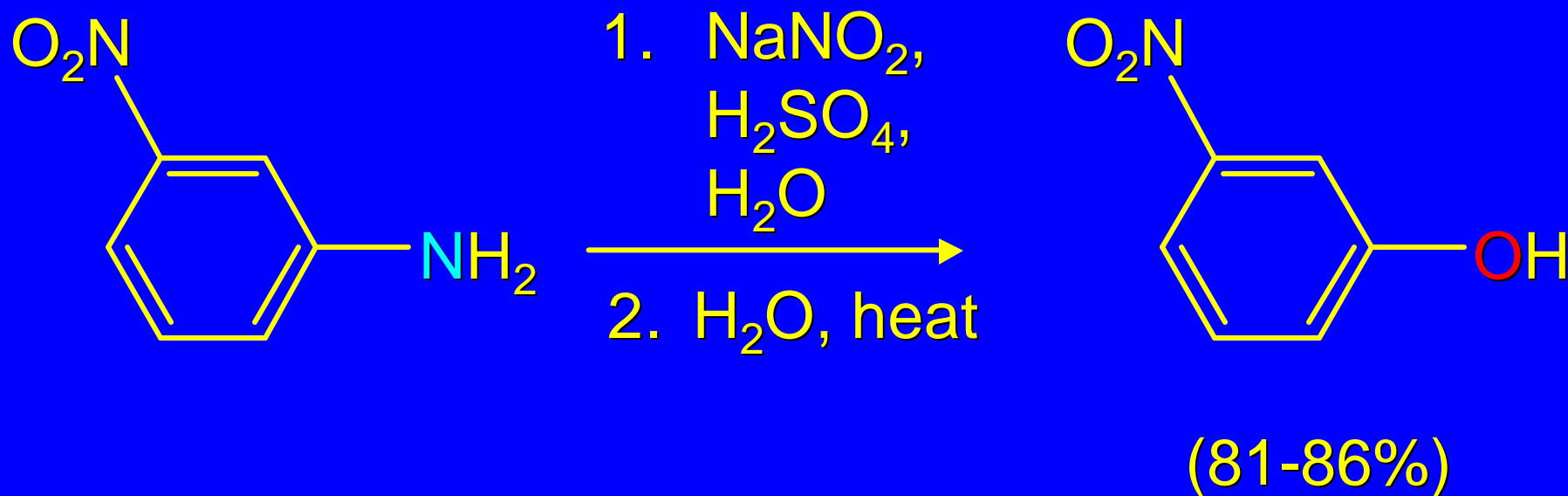


1. O_2

2. H_2O
 H_2SO_4

Laboratory Synthesis of Phenols

from arylamines via diazonium ions

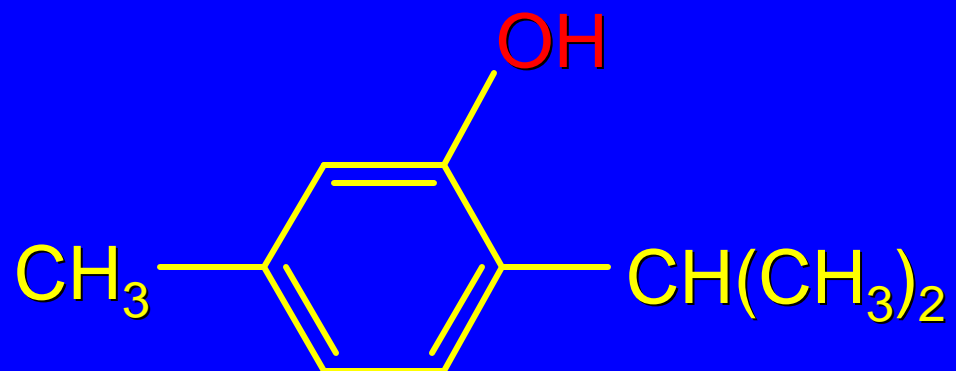


24.7

Naturally Occurring Phenols

Many phenols occur naturally

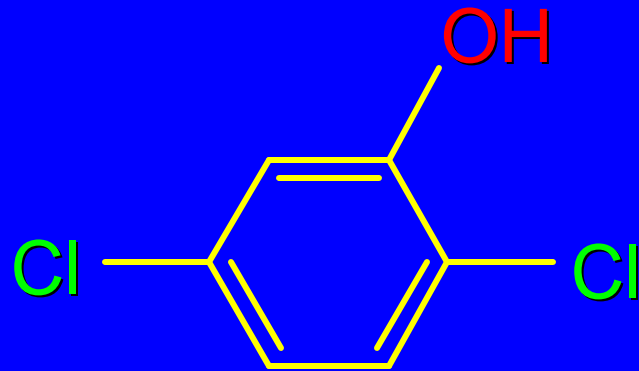
Example: Thymol



Thymol

(major constituent of oil of thyme)

Example: 2,5-Dichlorophenol



2,5-Dichlorophenol
(from defensive secretion of
a species of grasshopper)

24.8

Reactions of Phenols:
Electrophilic Aromatic
Substitution

*Hydroxyl group strongly activates the ring
toward electrophilic aromatic substitution*

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

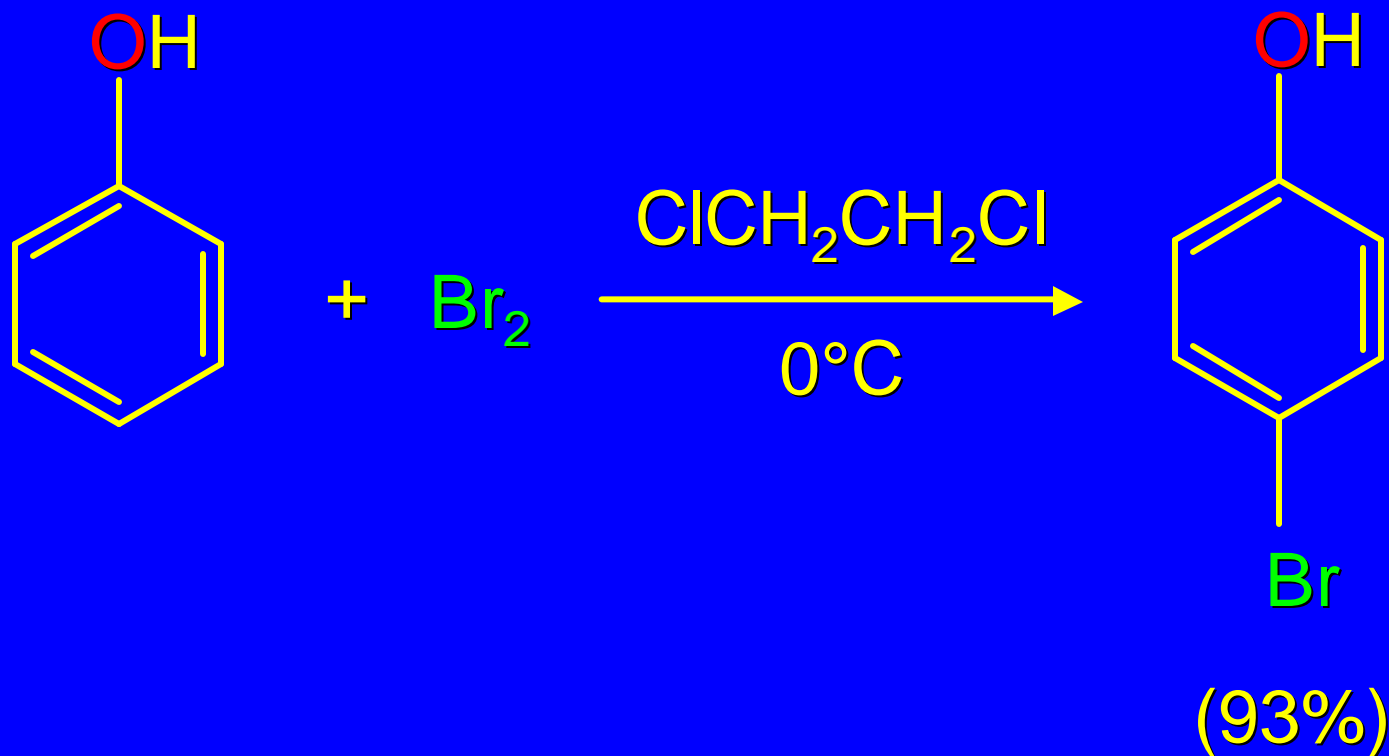
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

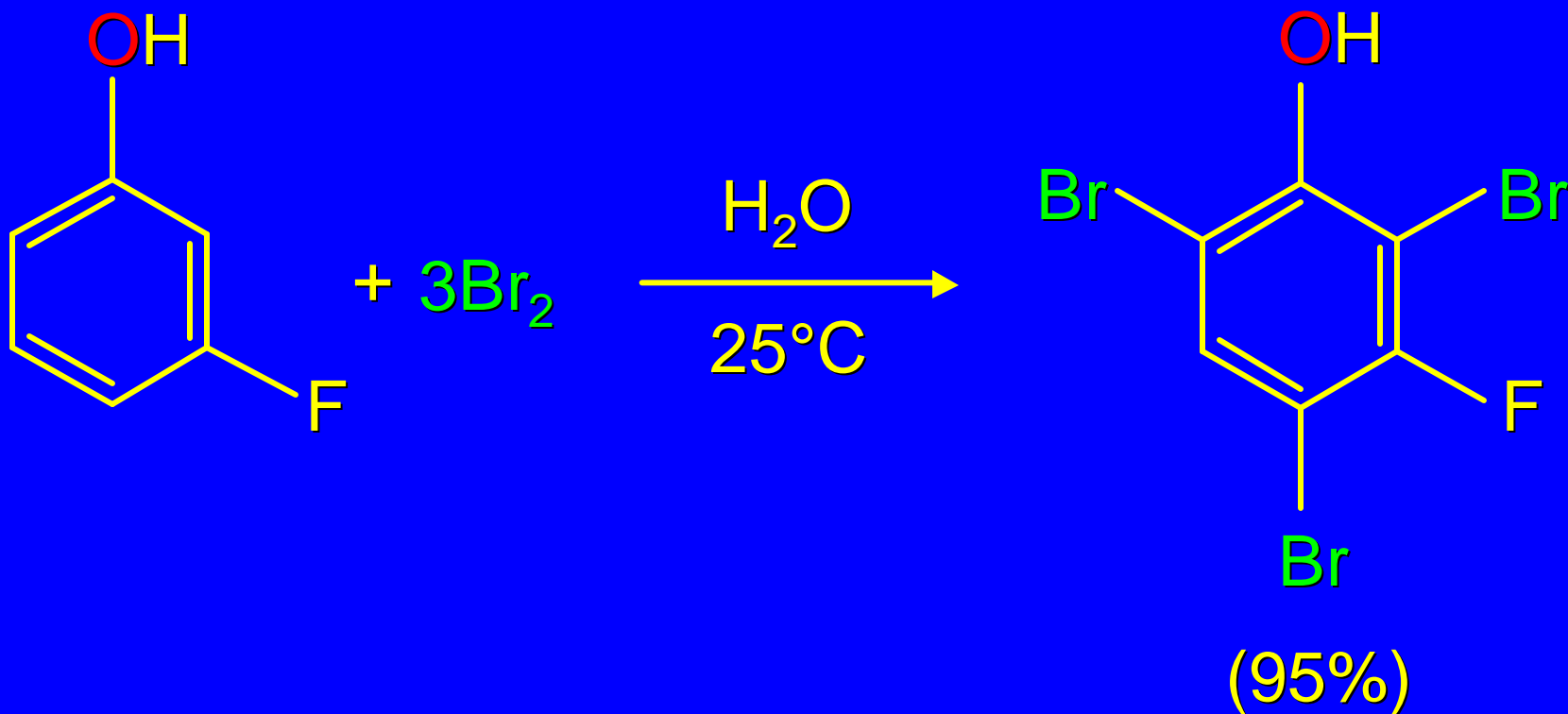
Friedel-Crafts Acylation

Halogenation



monohalogenation in nonpolar solvent
(1,2-dichloroethane)

Halogenation



multiple halogenation in polar solvent
(water)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

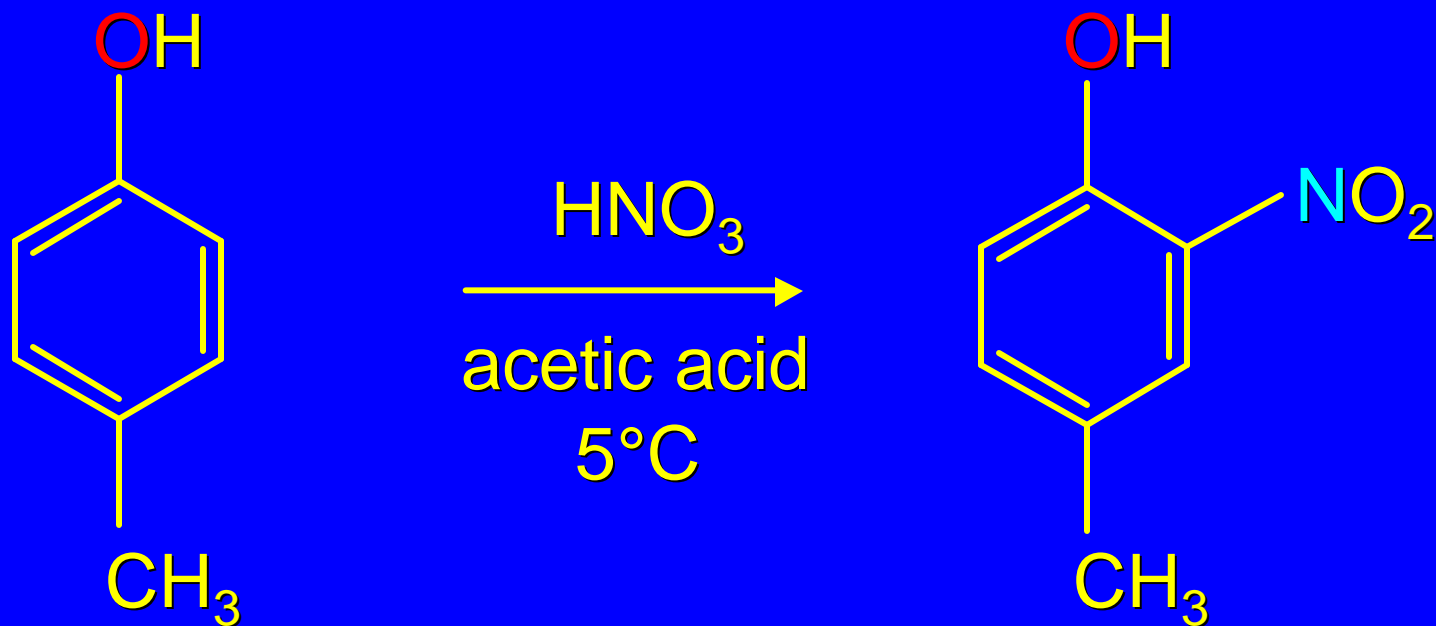
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Nitration



OH group controls
regiochemistry

(73-77%)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

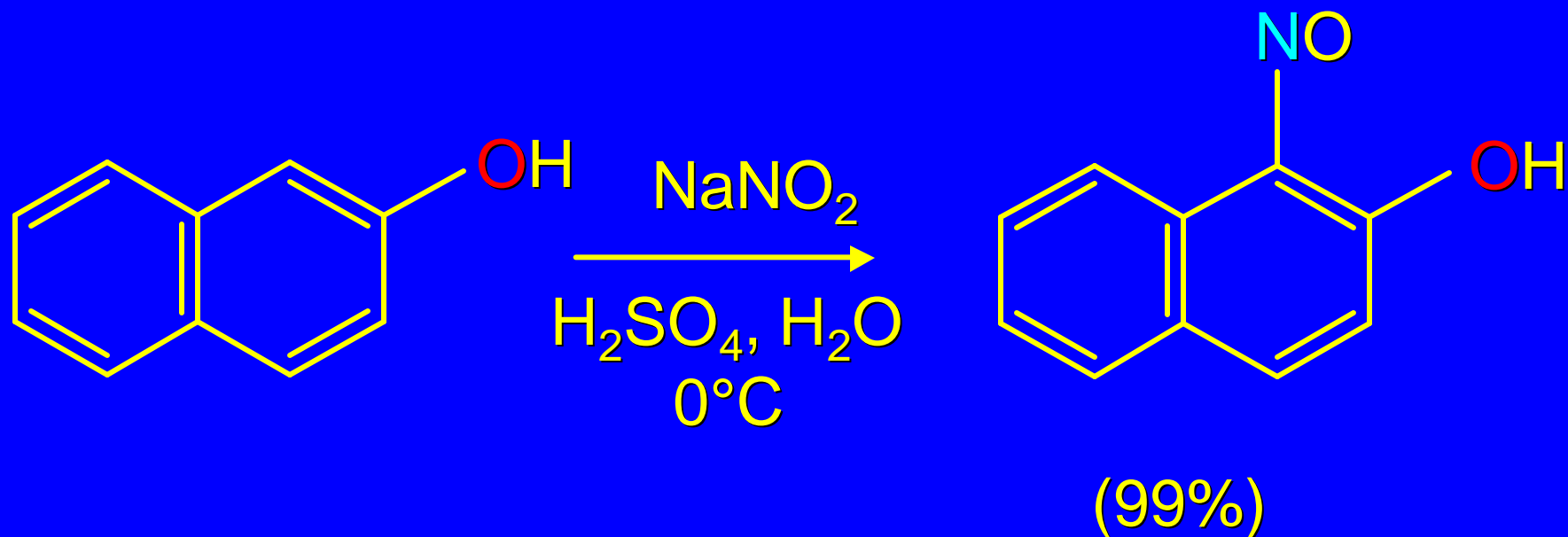
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Nitrosation



only strongly activated rings undergo nitrosation when treated with nitrous acid

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

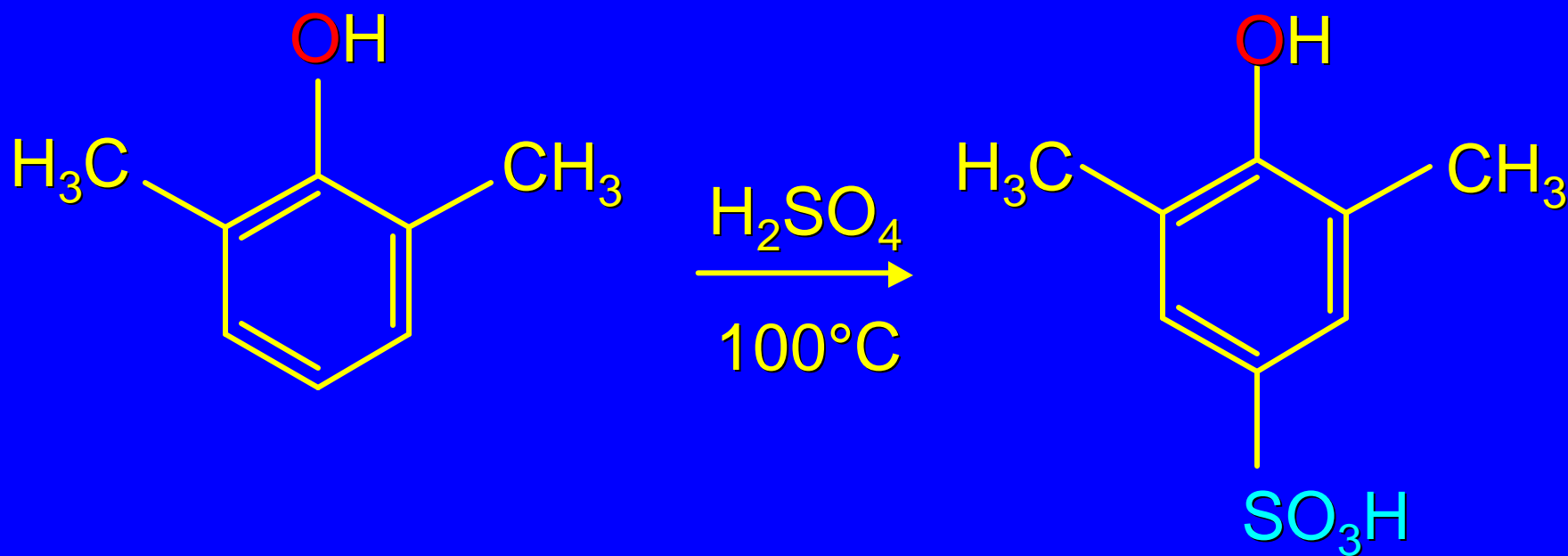
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Sulfonation



OH group controls
regiochemistry

(69%)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

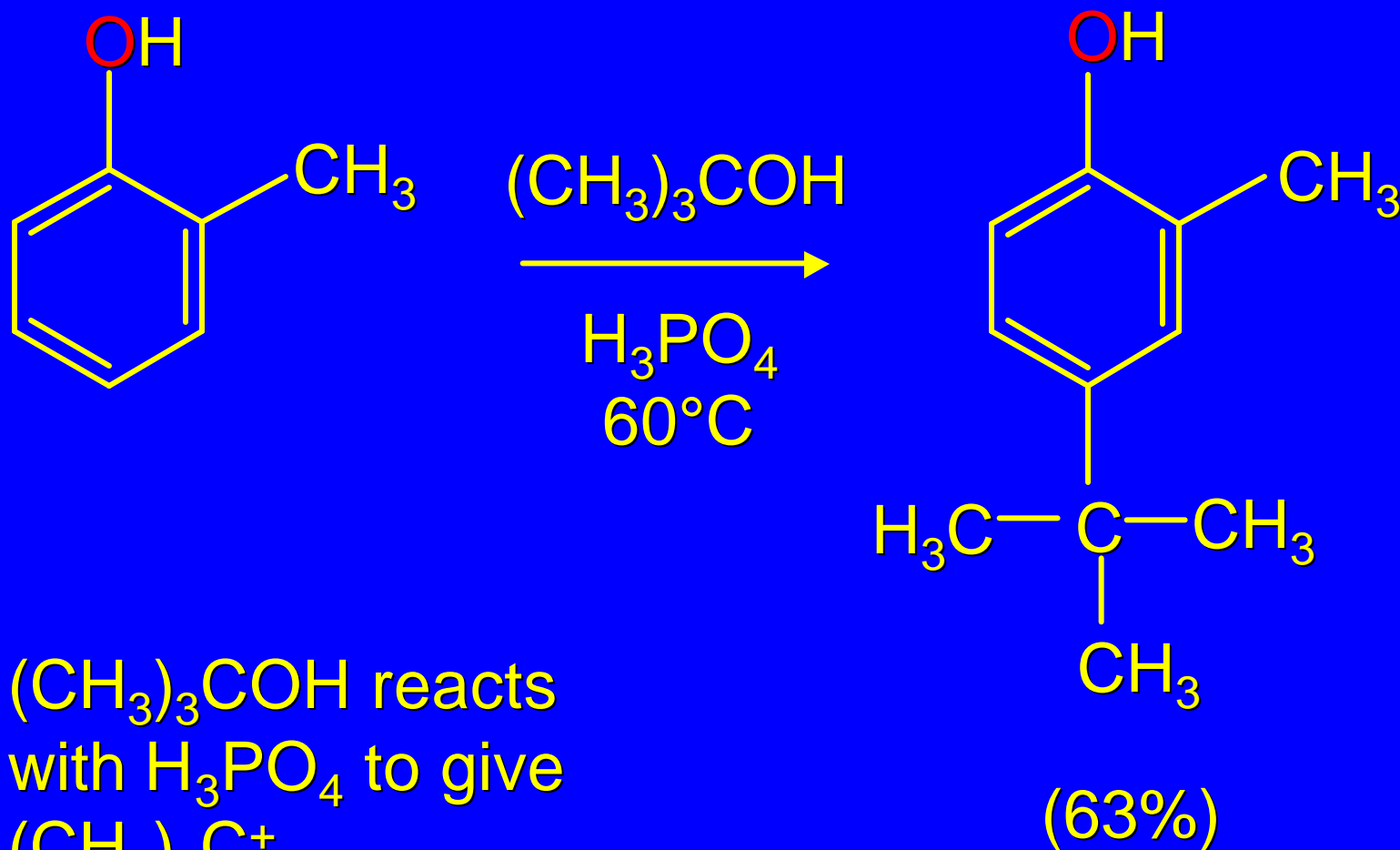
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Friedel-Crafts Alkylation



(CH₃)₃COH reacts
with H₃PO₄ to give
(CH₃)₃C⁺

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

Nitrosation

Sulfonation

Friedel-Crafts Alkylation

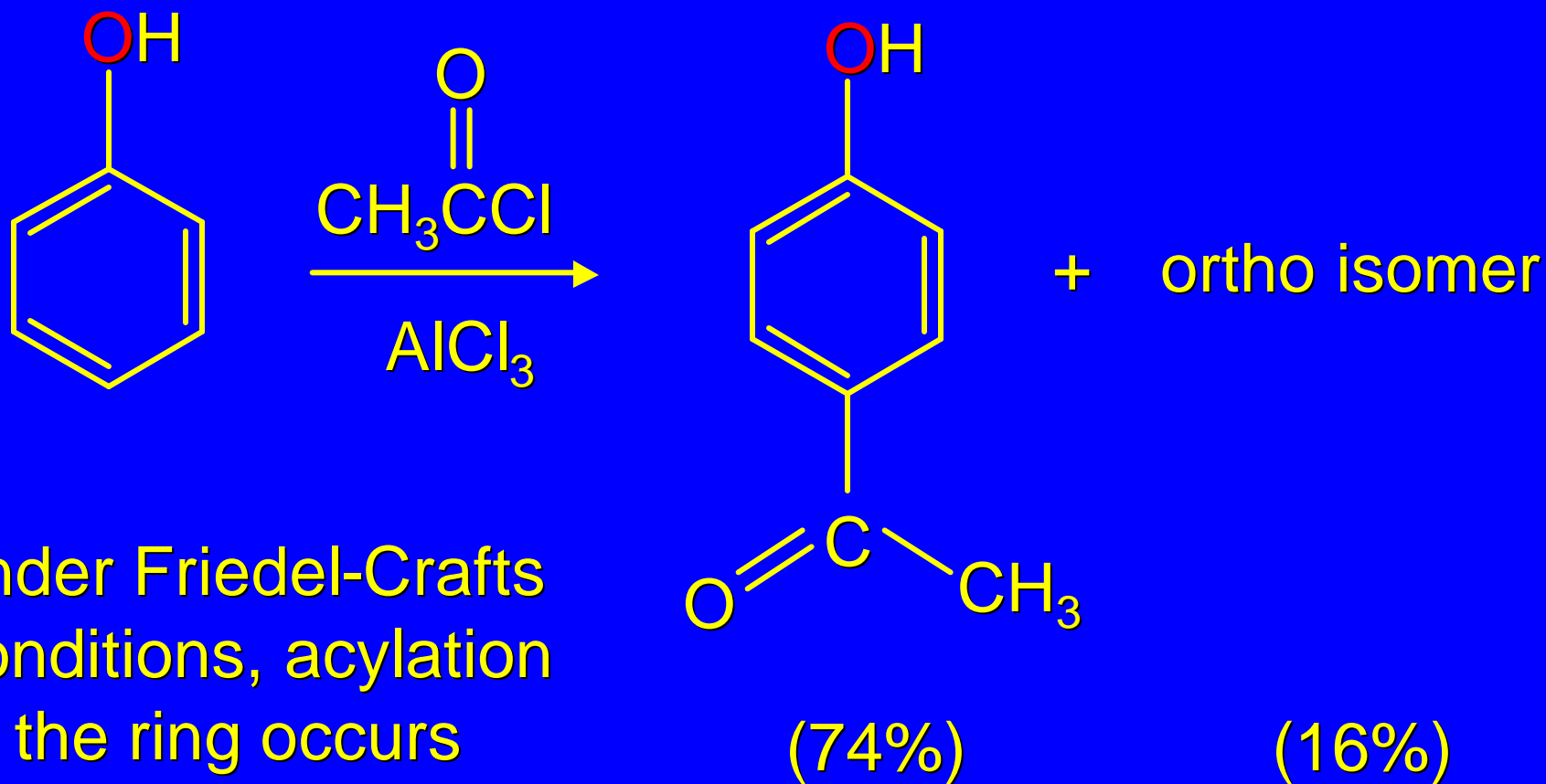
Friedel-Crafts Acylation

24.9

Acylation of Phenols

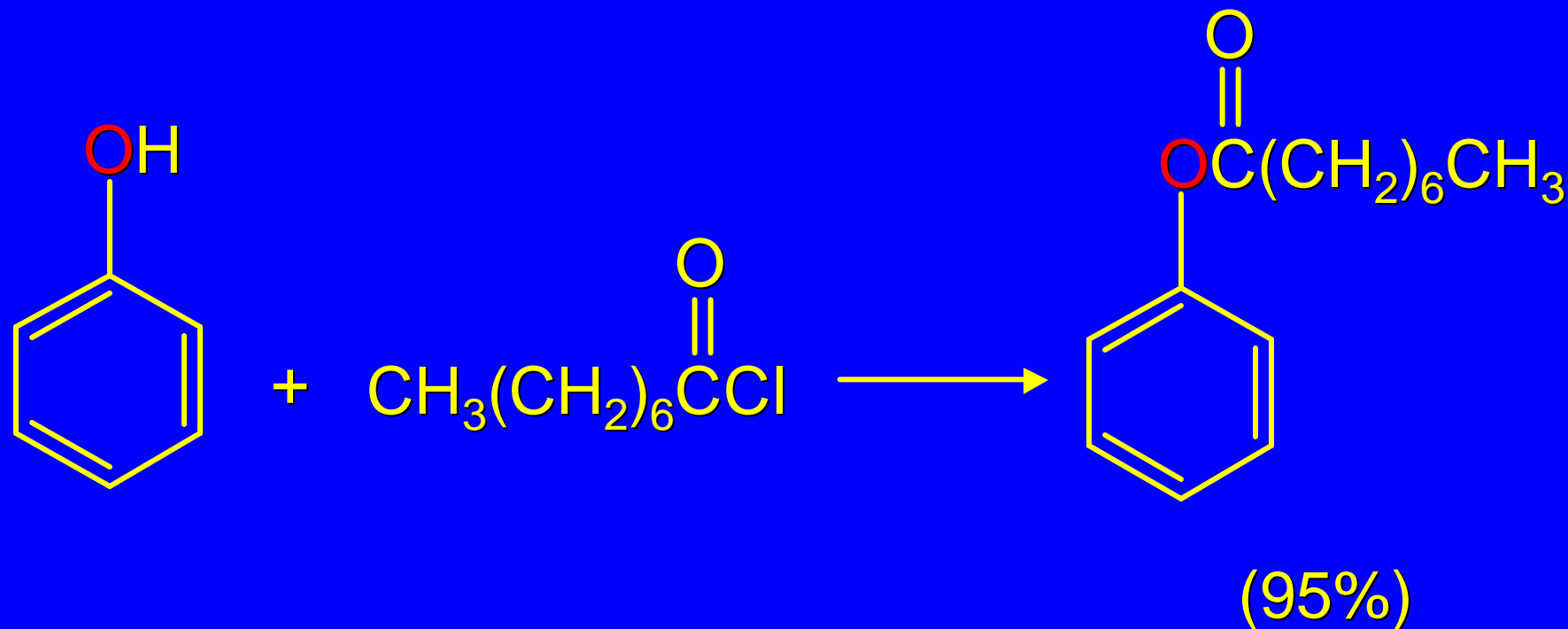
Acylation can take place either on the ring by electrophilic aromatic substitution or on oxygen by nucleophilic acyl substitution

Friedel-Crafts Acylation



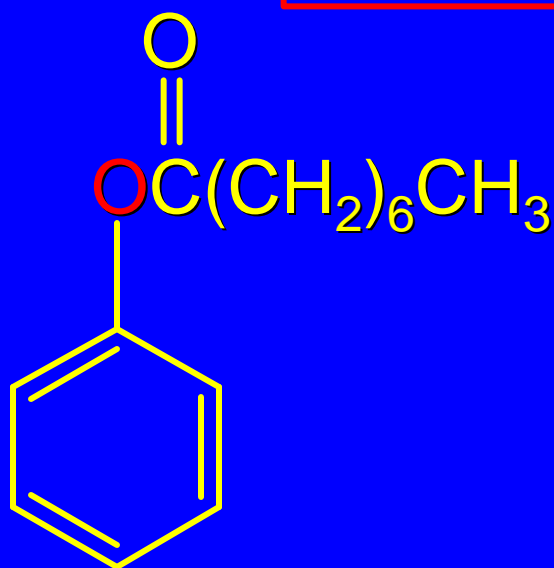
under Friedel-Crafts conditions, acylation of the ring occurs (C-acylation)

O-Acylation

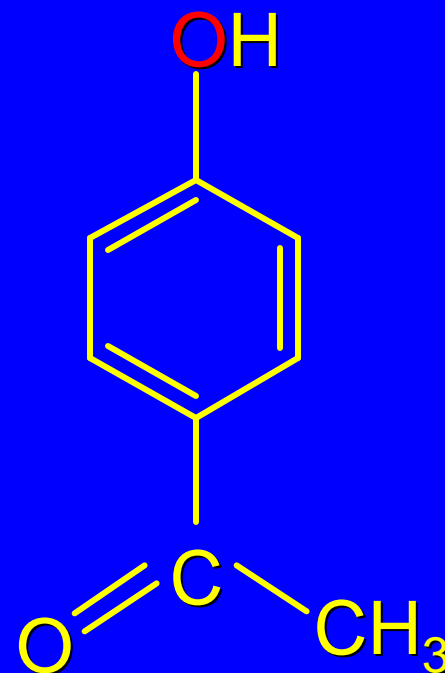


in the absence of AlCl₃, acylation of the hydroxyl group occurs (O-acylation)

O- versus C-Acylation



formed faster



more stable

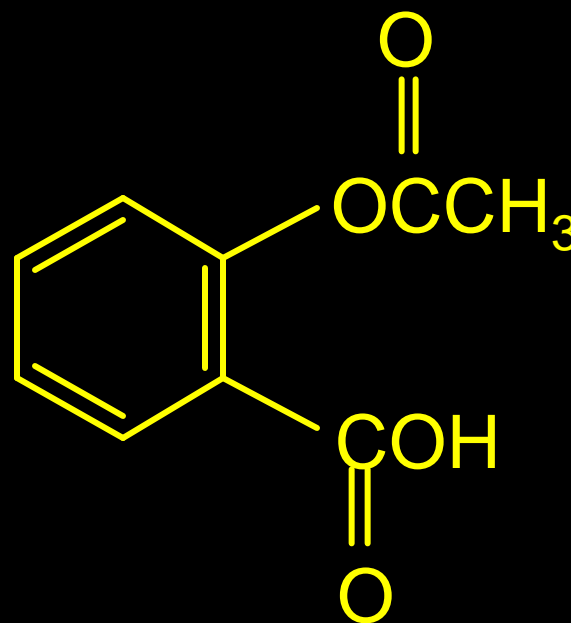
O-Acylation is kinetically controlled process; C-acylation is thermodynamically controlled

AlCl_3 catalyzes the conversion of the aryl ester to the aryl alkyl ketones; this is called the Fries rearrangement

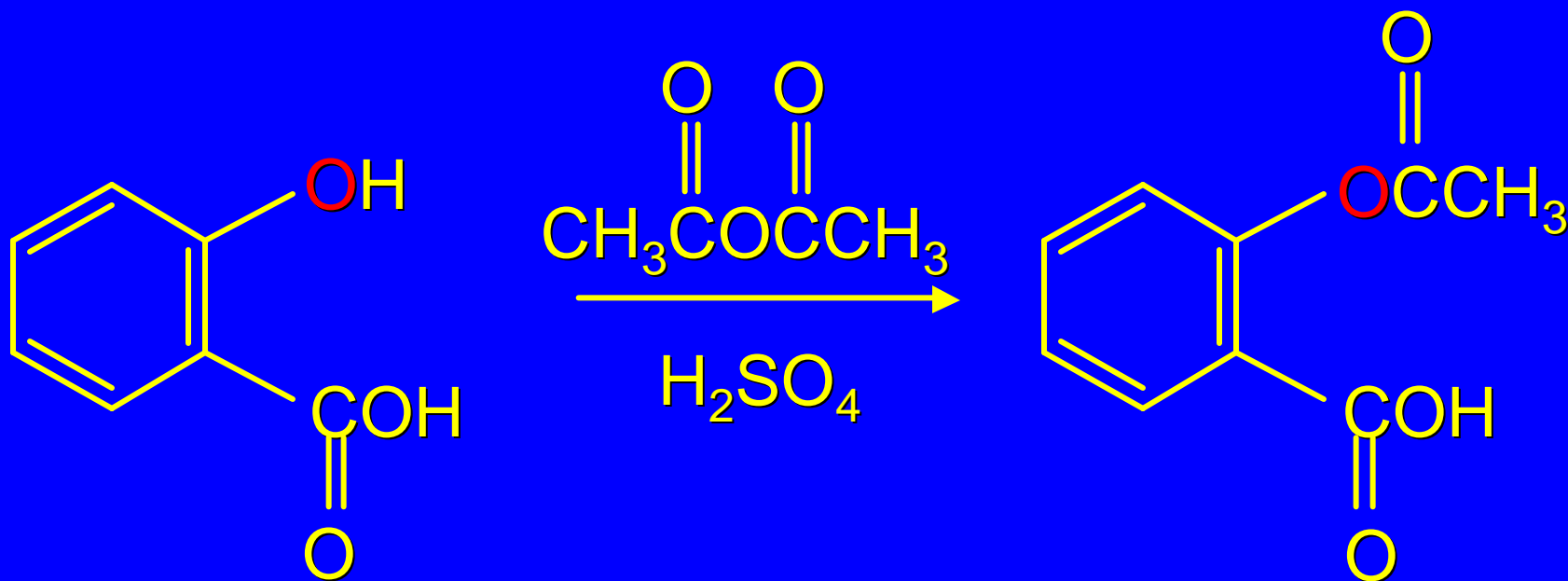
24.10

Carboxylation of Phenols

Aspirin and
the
Kolbe-Schmitt
Reaction

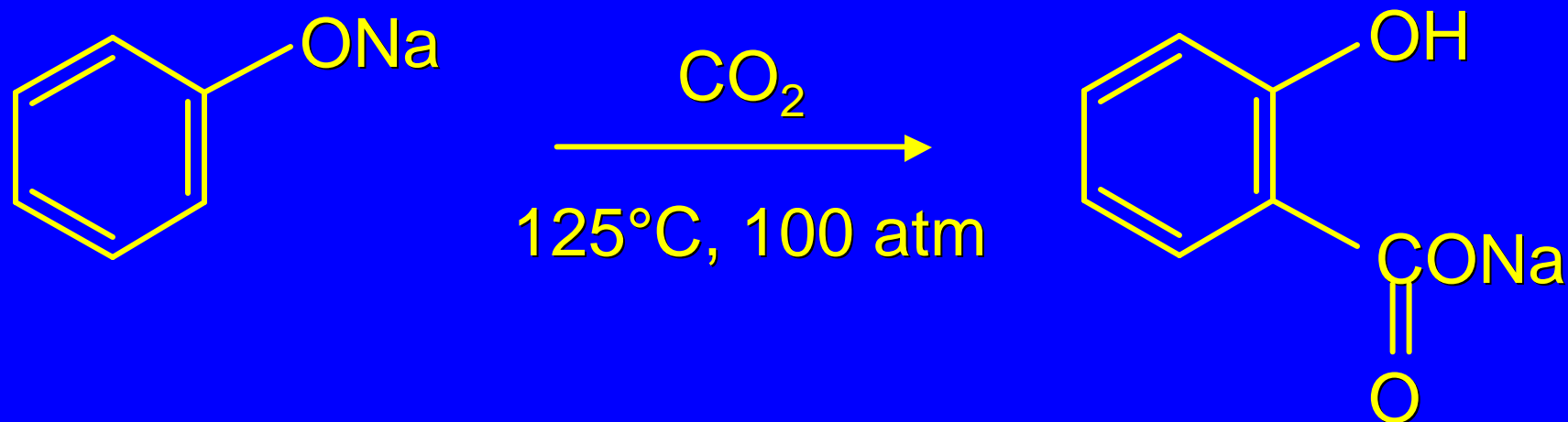


Aspirin is prepared from salicylic acid



how is salicylic acid prepared?

Preparation of Salicylic Acid

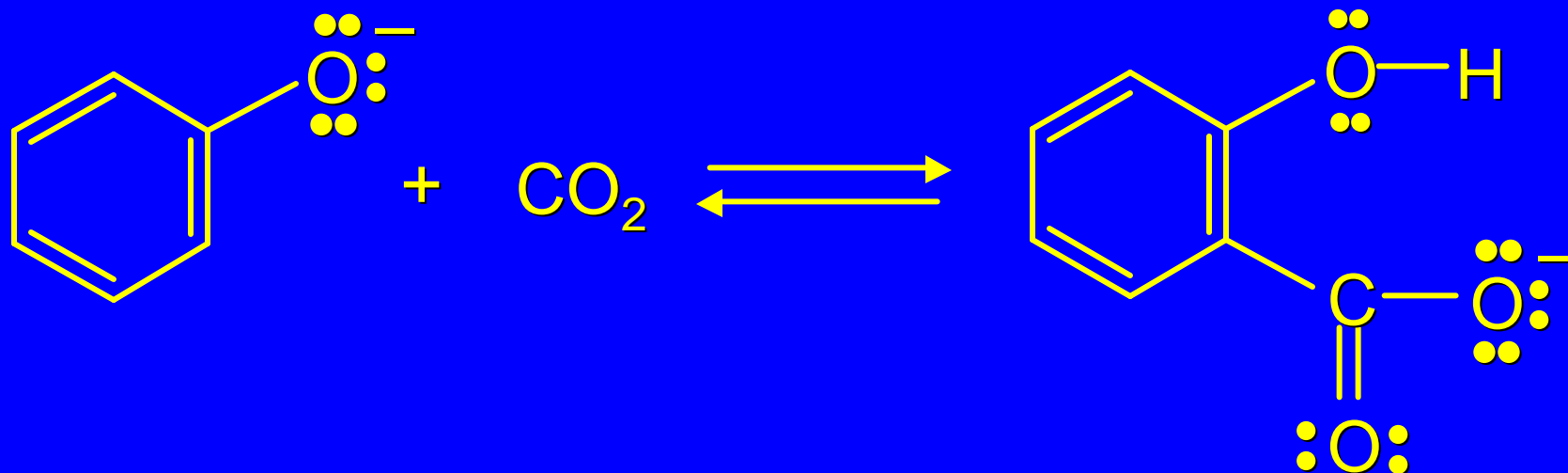


called the Kolbe-Schmitt reaction

acidification converts the sodium salt shown above to salicylic acid

What Drives the Reaction?

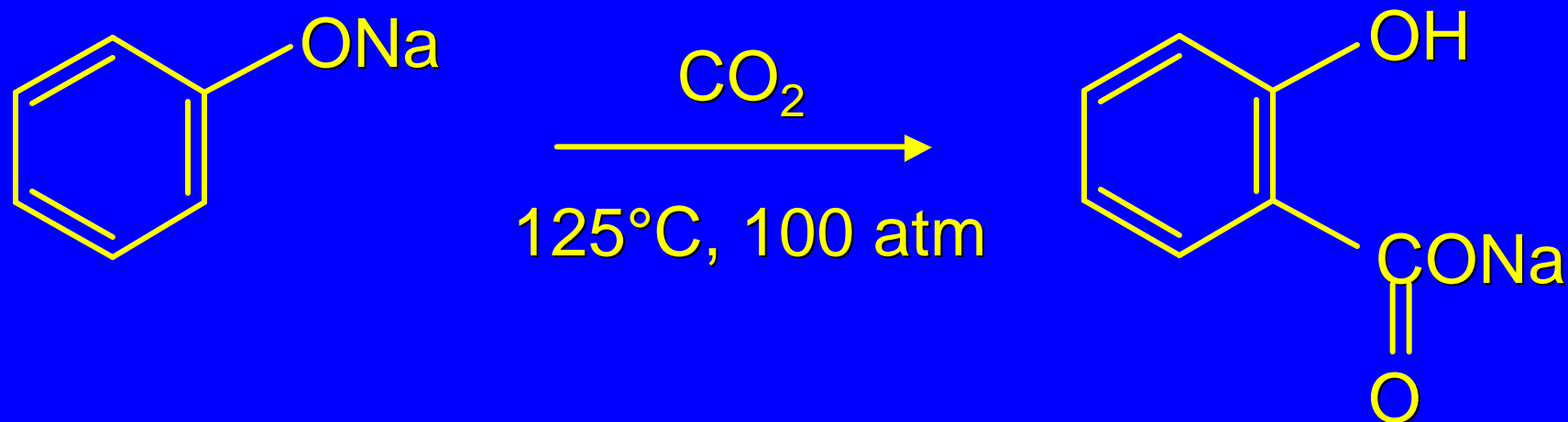
acid-base considerations provide an explanation:
stronger base on left; weaker base on right



stronger base:
 $\text{p}K_a$ of conjugate
acid = 10

weaker base:
 $\text{p}K_a$ of conjugate
acid = 3

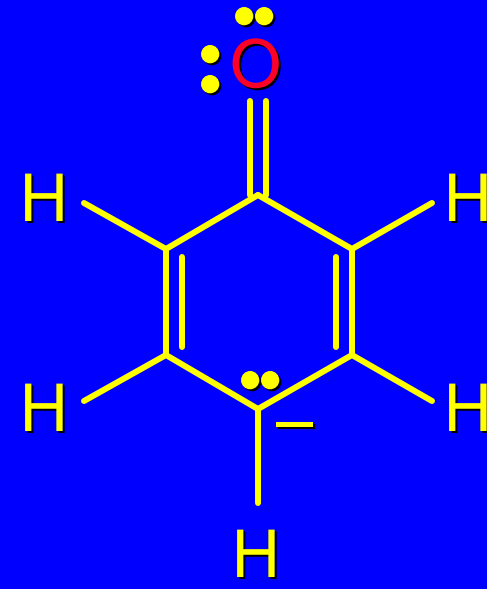
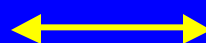
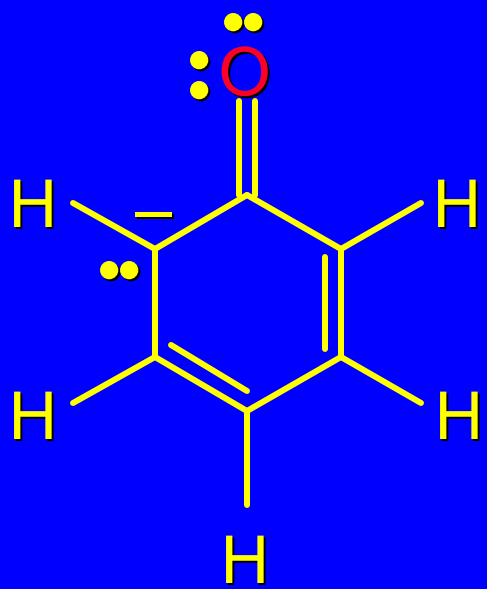
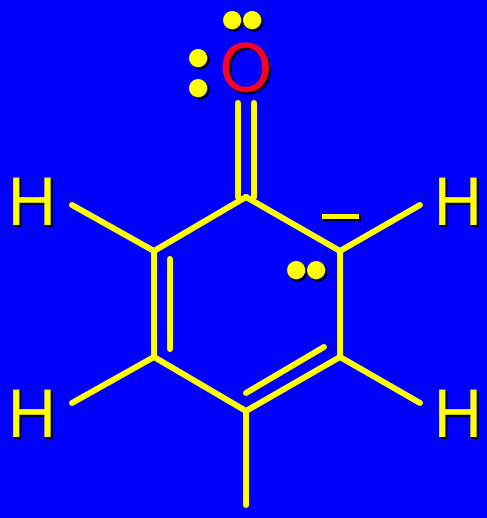
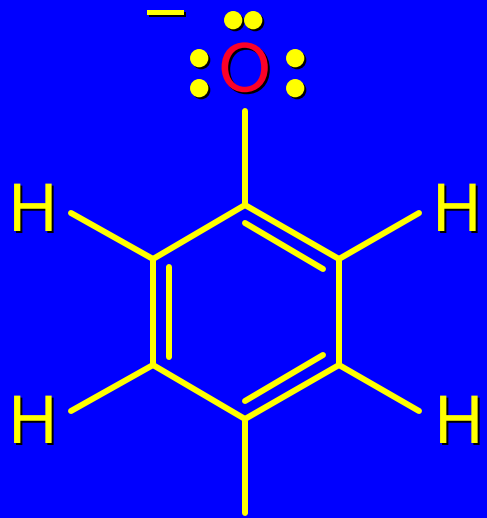
Preparation of Salicylic Acid



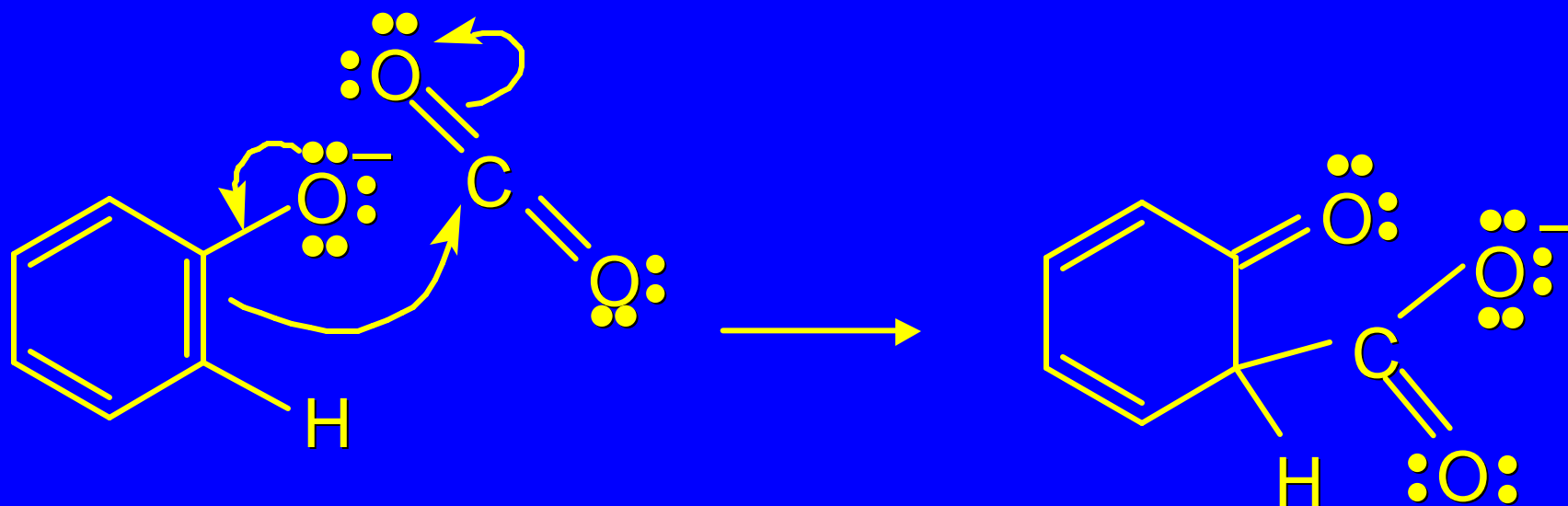
how does carbon-carbon bond form?

recall electron delocalization in phenoxide ion

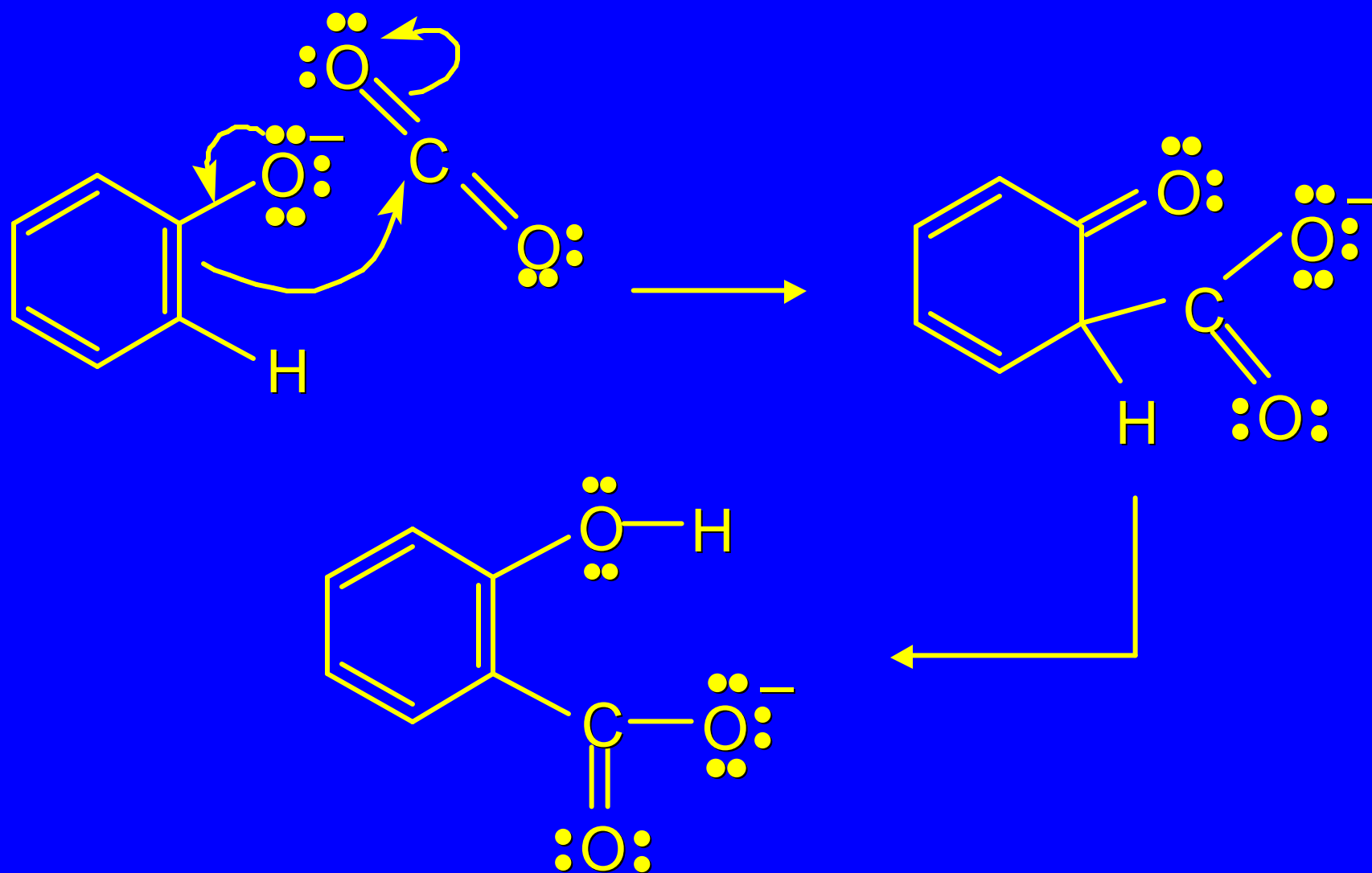
negative charge shared by oxygen and by the ring carbons that are ortho and para to oxygen



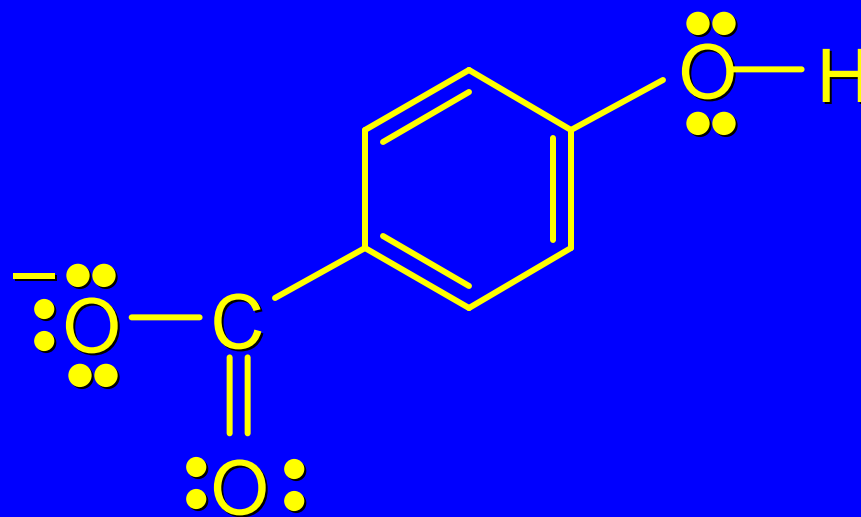
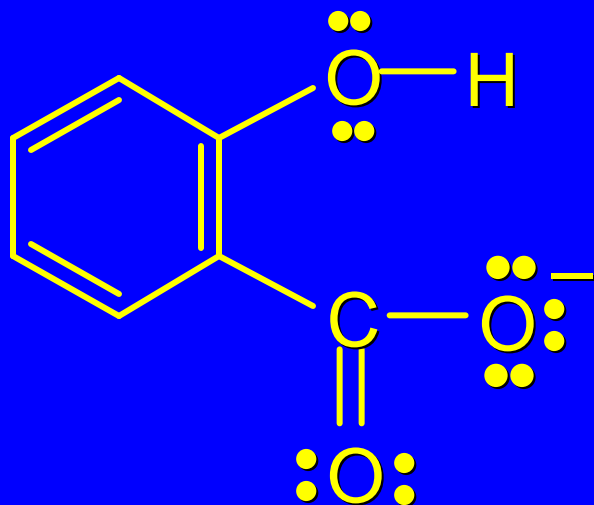
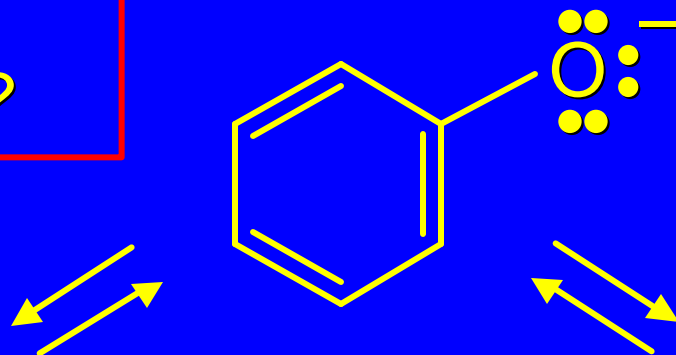
Mechanism of ortho Carboxylation



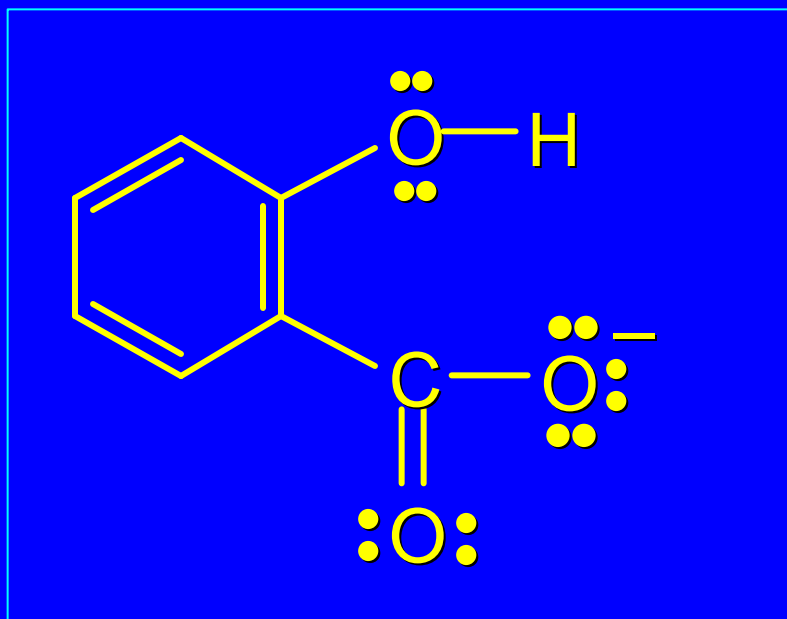
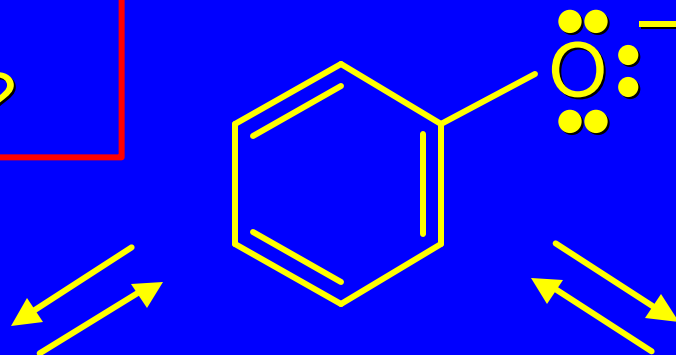
Mechanism of ortho Carboxylation



*Why ortho?
Why not para?*



*Why ortho?
Why not para?*

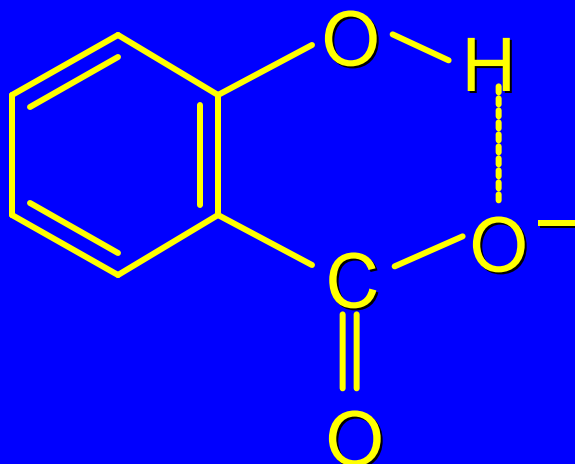


weaker base:
 $\text{p}K_a$ of conjugate acid = 3



stronger base:
 $\text{p}K_a$ of conjugate acid = 4.5

Intramolecular Hydrogen Bonding in Salicylate Ion



Hydrogen bonding between carboxylate and hydroxyl group stabilizes salicylate ion. Salicylate is less basic than para isomer and predominates under conditions of thermodynamic control.