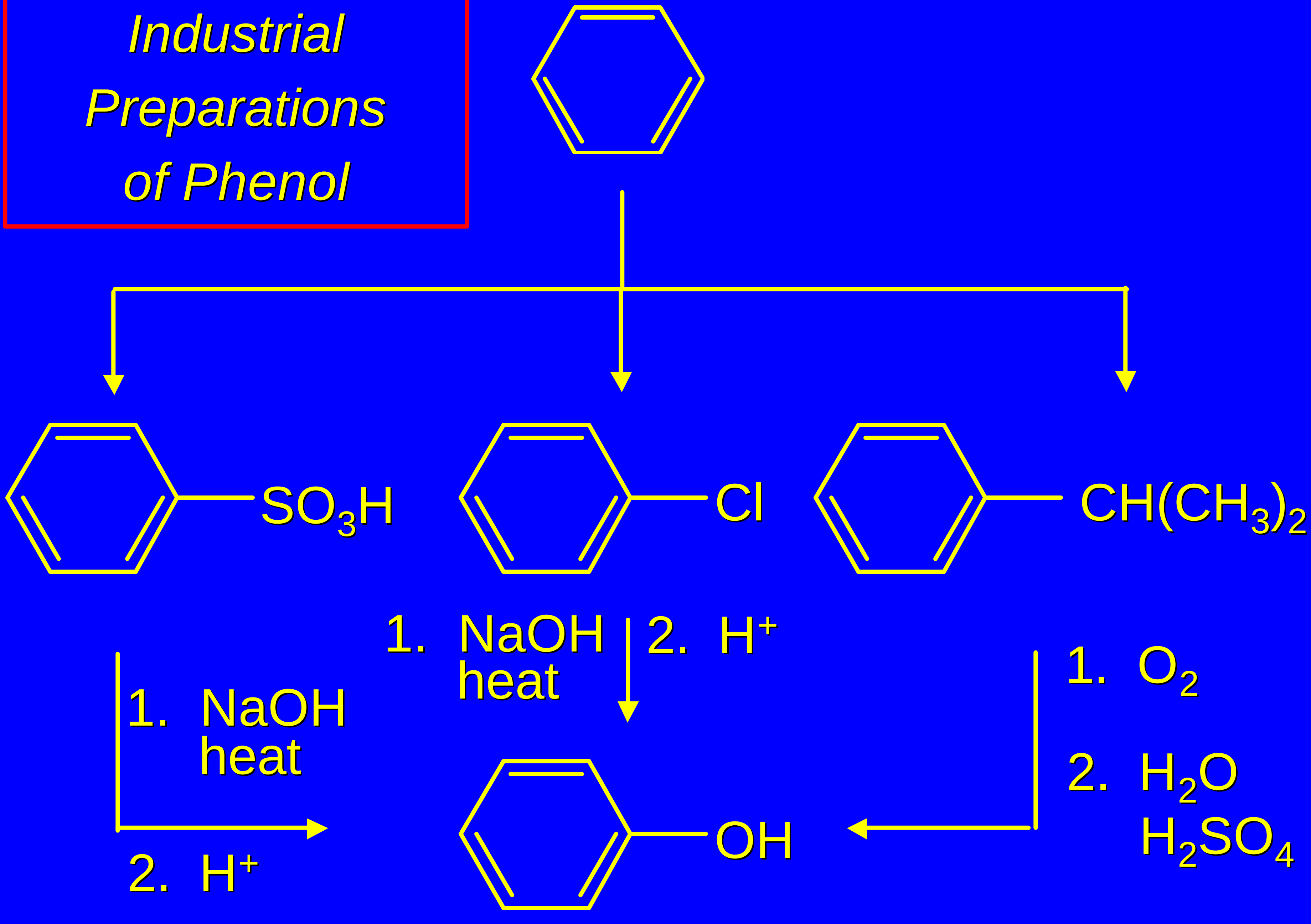
24.6
Sources of Phenols

Phenol is an important industrial chemical.

Major use is in phenolic resins for adhesives and plastics.

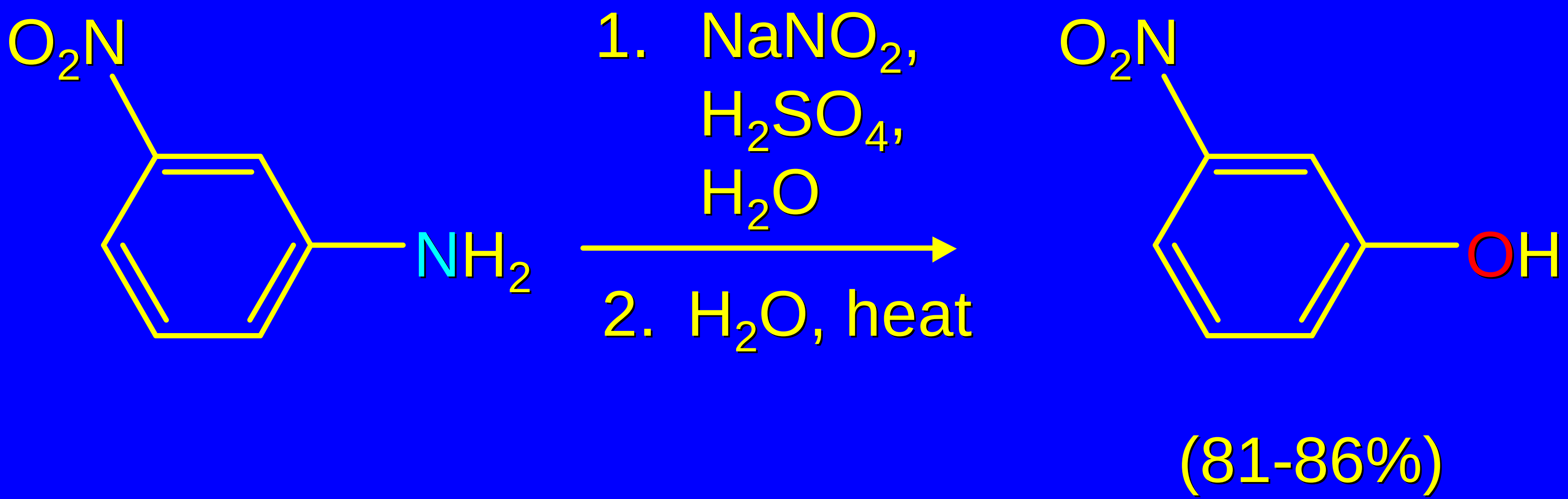
Annual U.S. production is about 4 billion pounds per year.

Industrial Preparations of Phenol



Laboratory Synthesis of Phenols

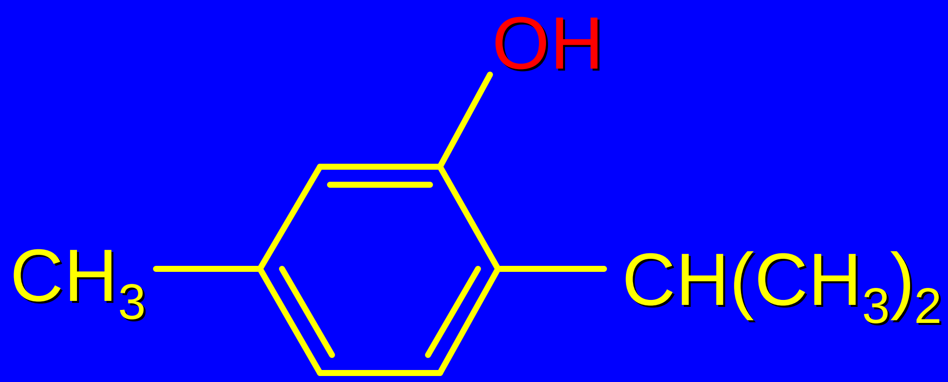
from arylamines via diazonium ions



24.7
Naturally Occurring Phenols

Many phenols occur naturally

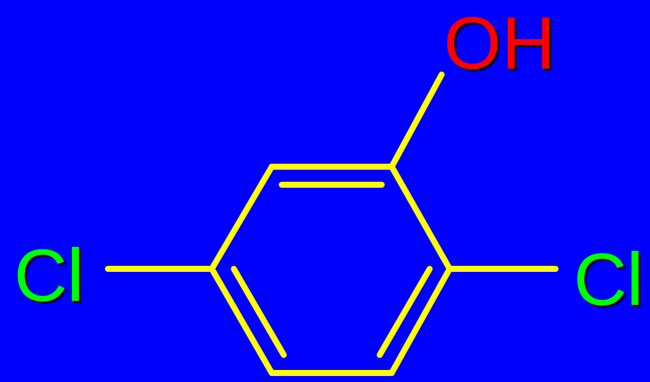
Example: Thymol



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

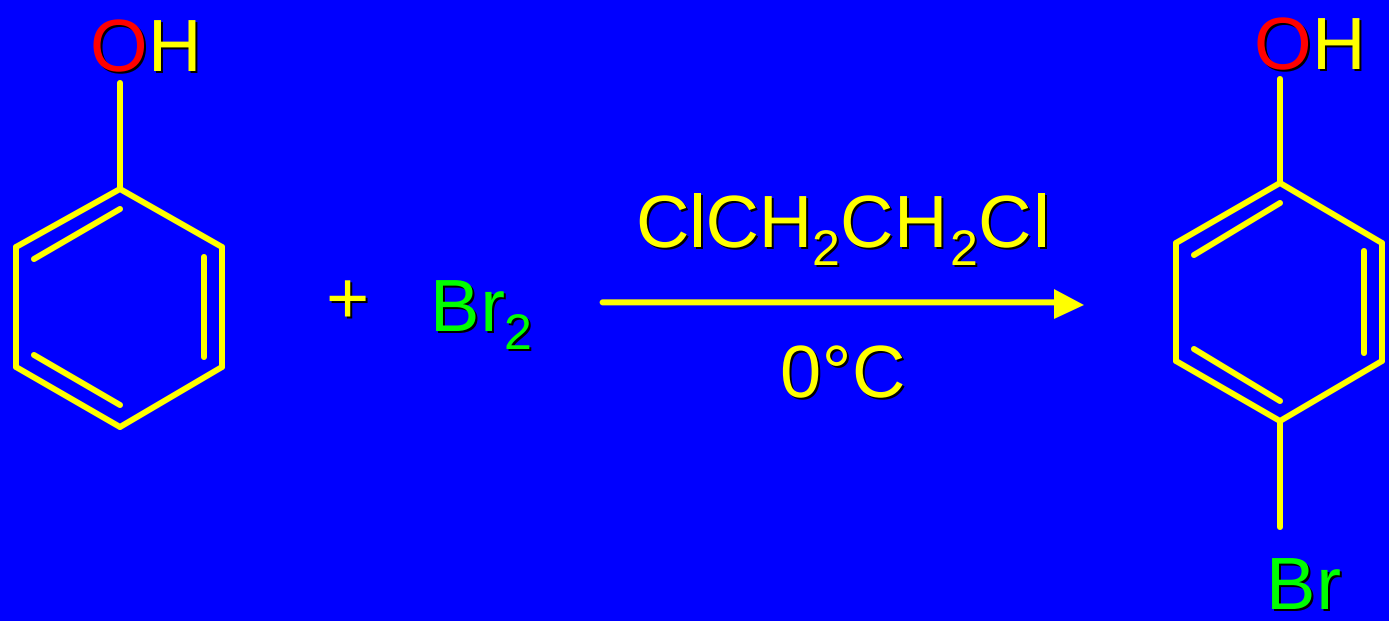
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

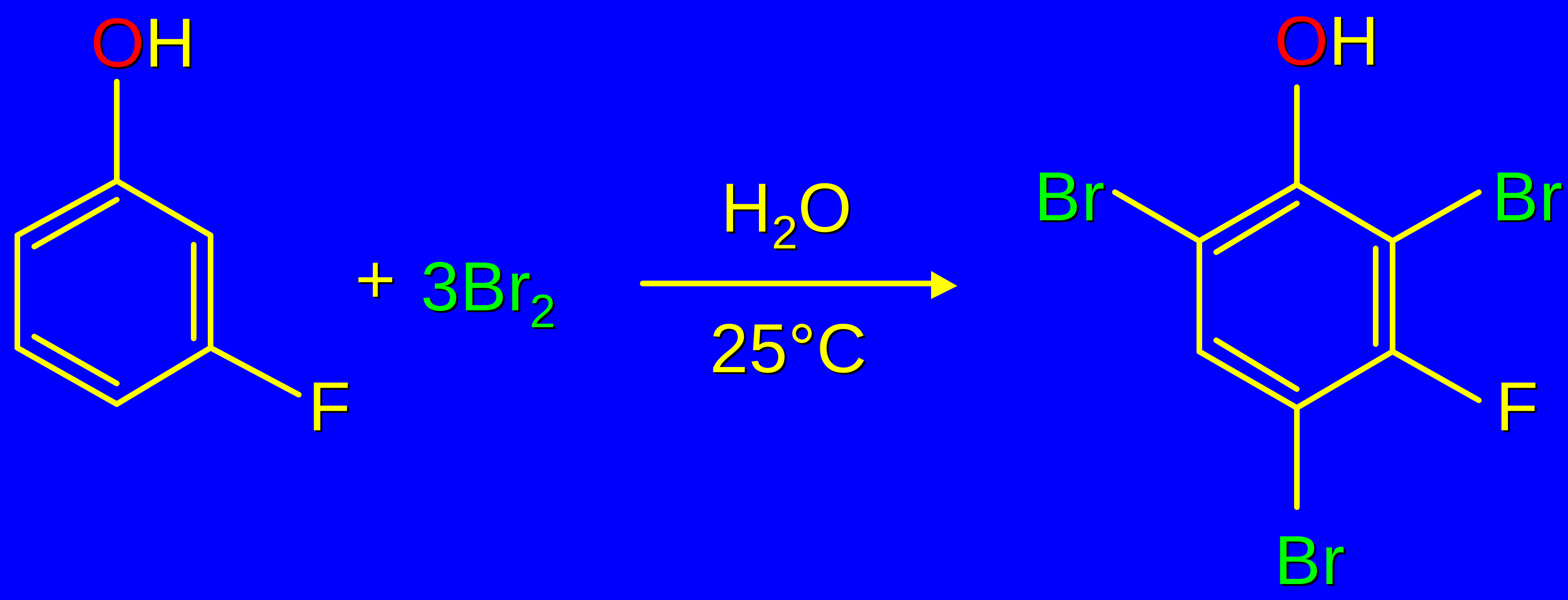
Halogenation



(93%)

monohalogenation in nonpolar solvent
(1,2-dichloroethane)

Halogenation



(95%)

multiple halogenation in polar solvent (water)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

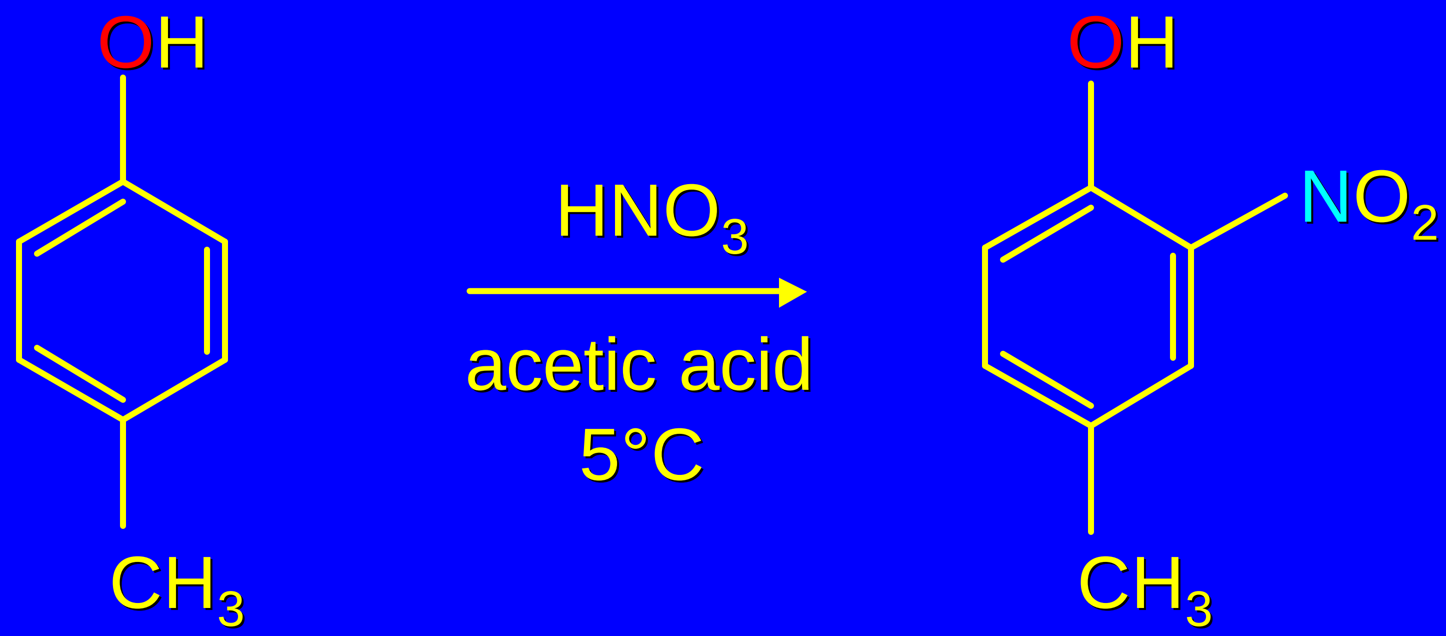
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Nitration



OH group controls regiochemistry

(73-77%)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

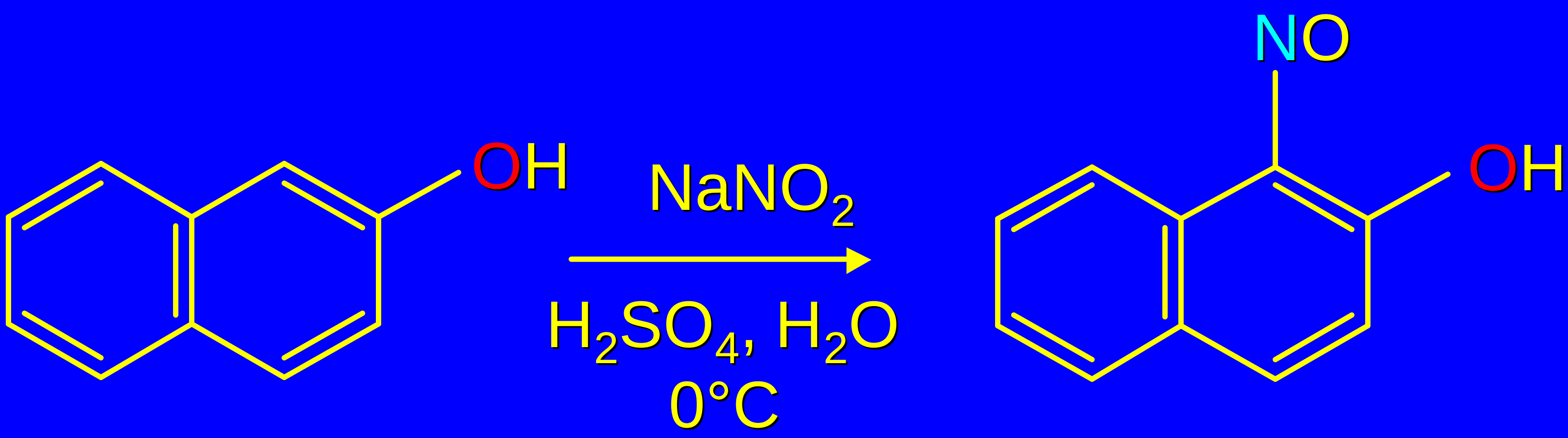
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Nitrosation



(99%)

only strongly activated rings undergo nitrosation when treated with nitrous acid

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

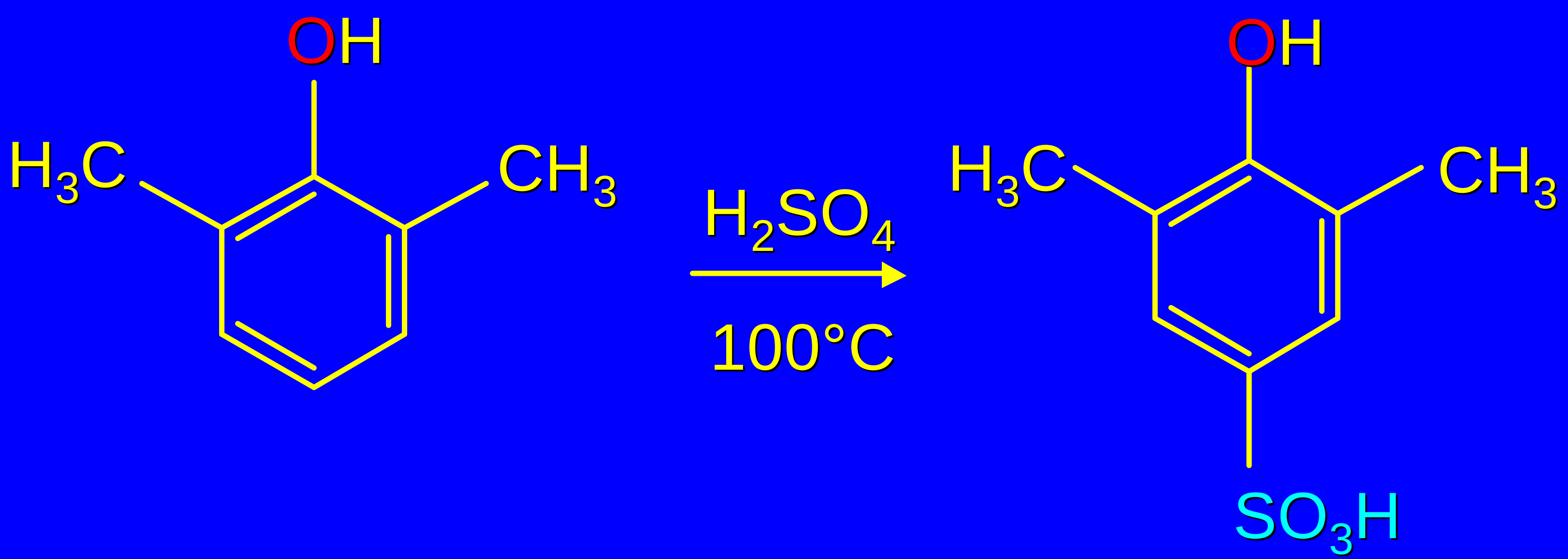
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Sulfonation



OH group controls regiochemistry

(69%)

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

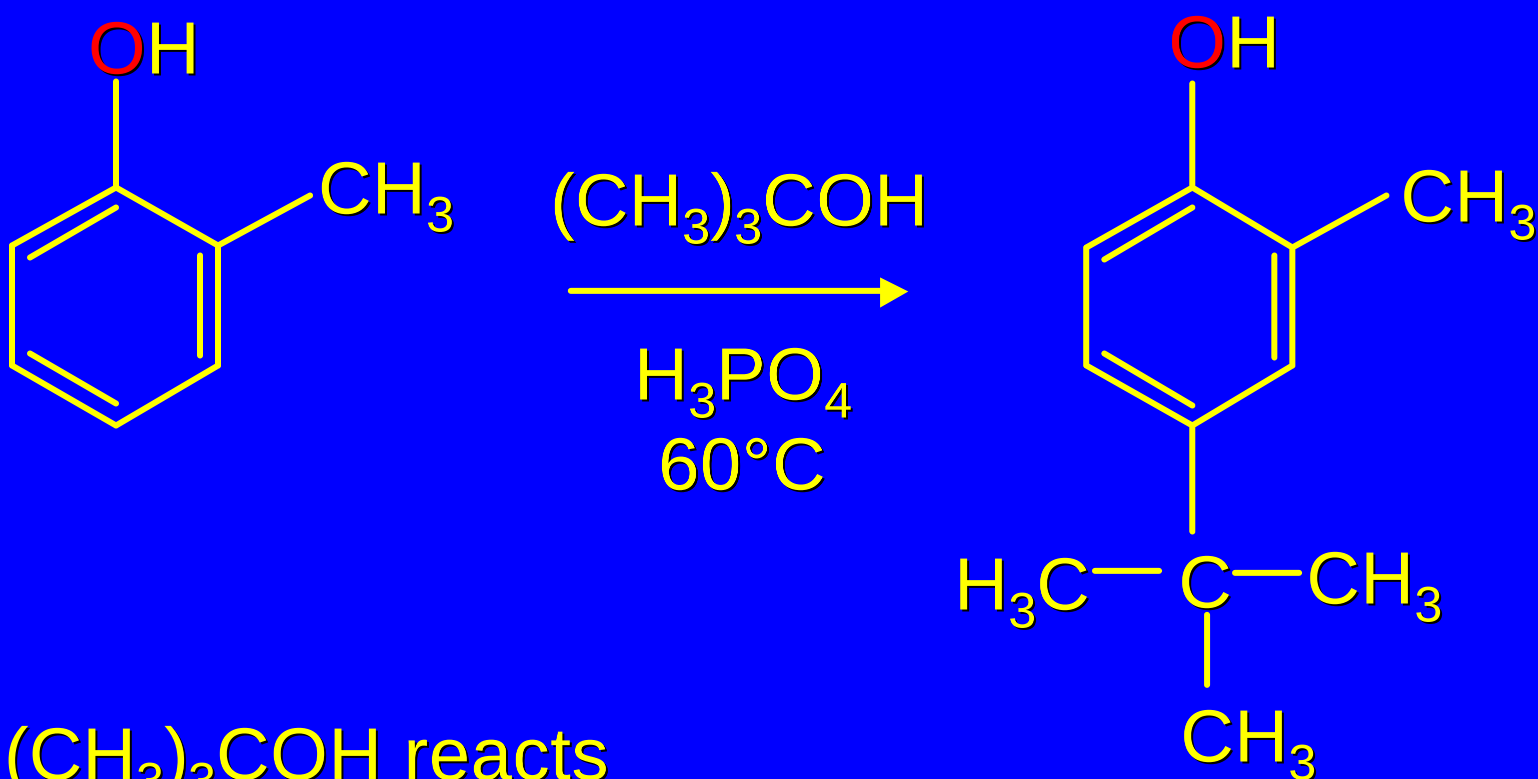
Nitrosation

Sulfonation

Friedel-Crafts Alkylation

Friedel-Crafts Acylation

Friedel-Crafts Alkylation



(63%)

$(CH_3)_3COH$ reacts with H_3PO_4 to give $(CH_3)_3C^+$

Electrophilic Aromatic Substitution in Phenols

Halogenation

Nitration

Nitrosation

Sulfonation

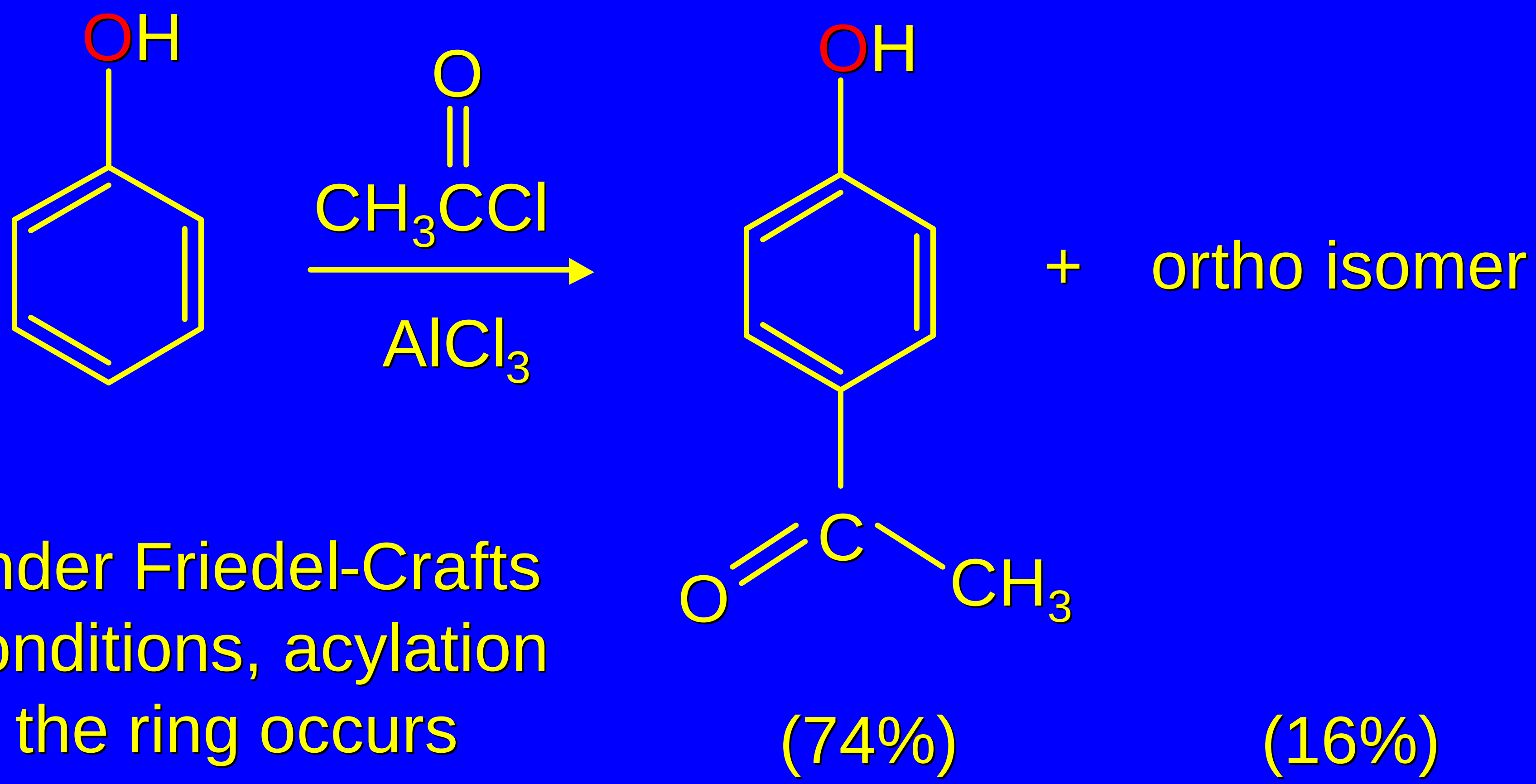
Friedel-Crafts Alkylation

Friedel-Crafts Acylation

24.9
Acylation of Phenols

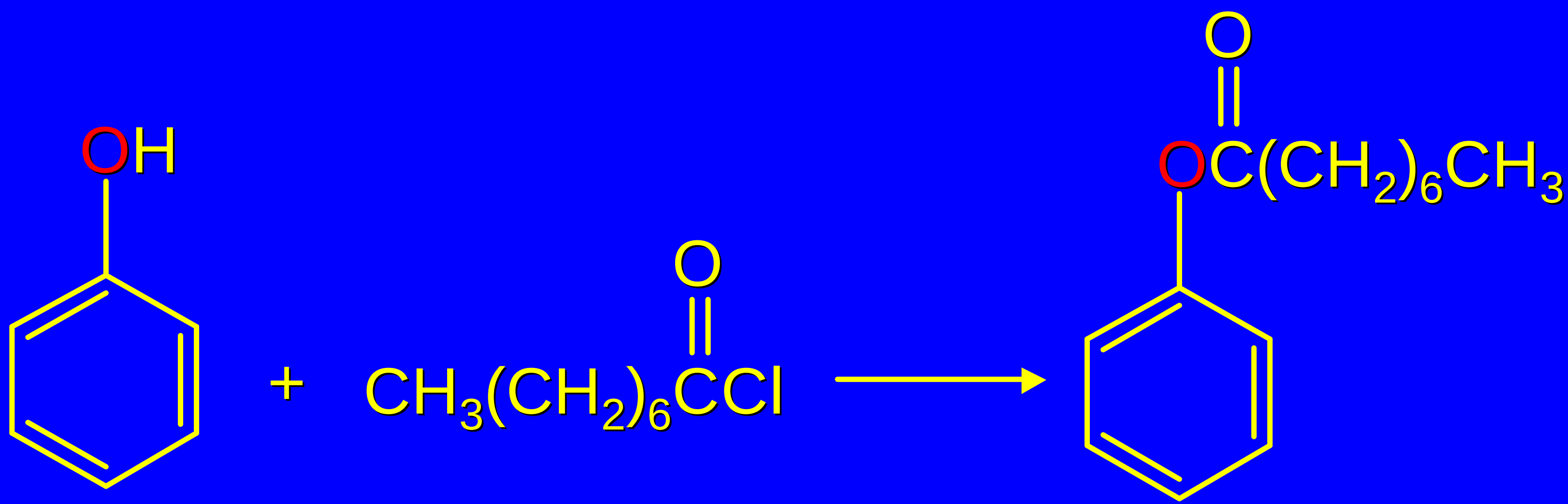
Acylation can take place either on the ring by electrophilic aromatic substitution or on oxygen by nucleophilic acyl substitution

Friedel-Crafts Acylation



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

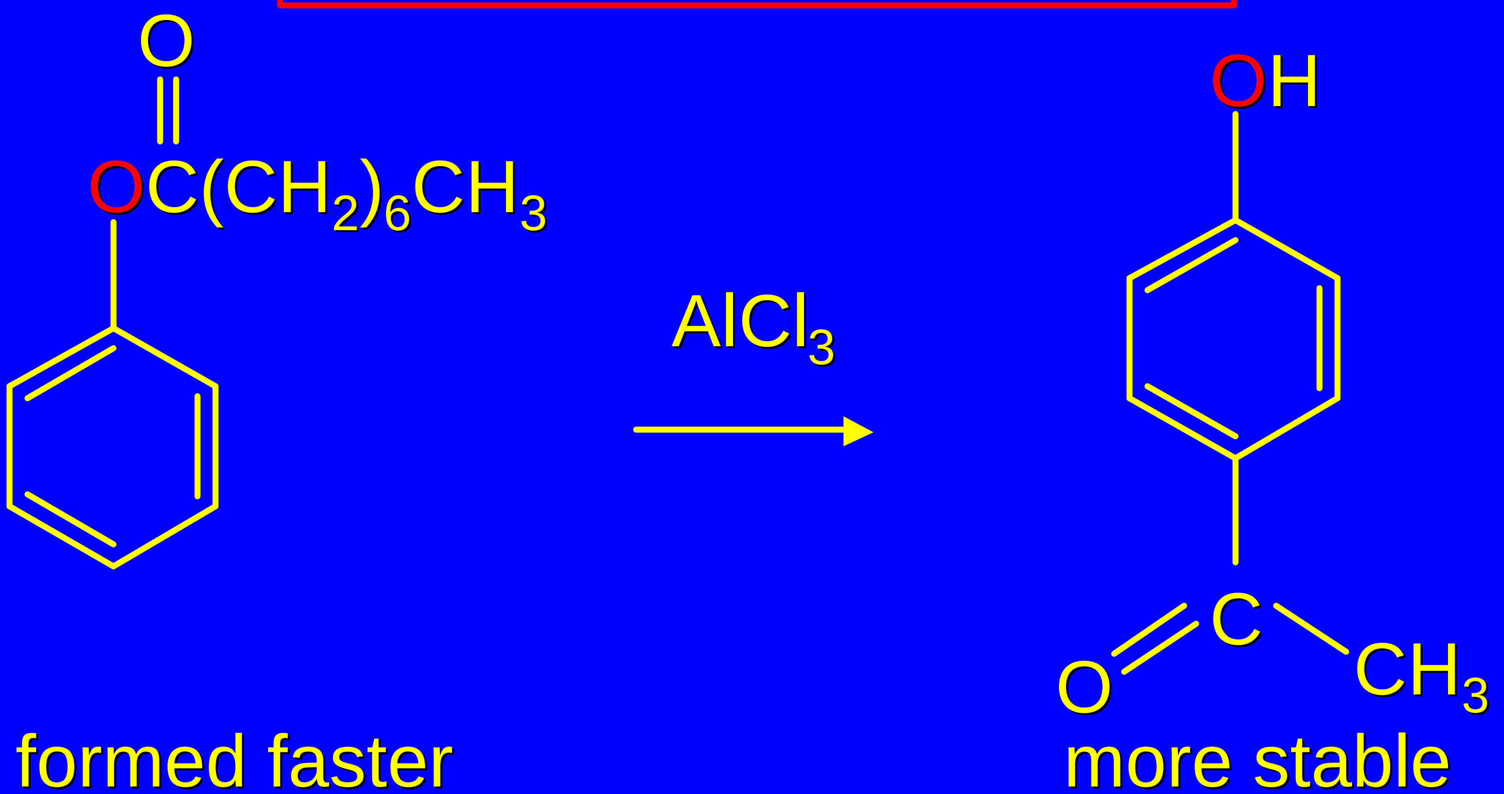
O-Acylation



(95%)

in the absence of $AlCl_3$, acylation of the hydroxyl group occurs (O-acylation)

O- versus C-Acylation

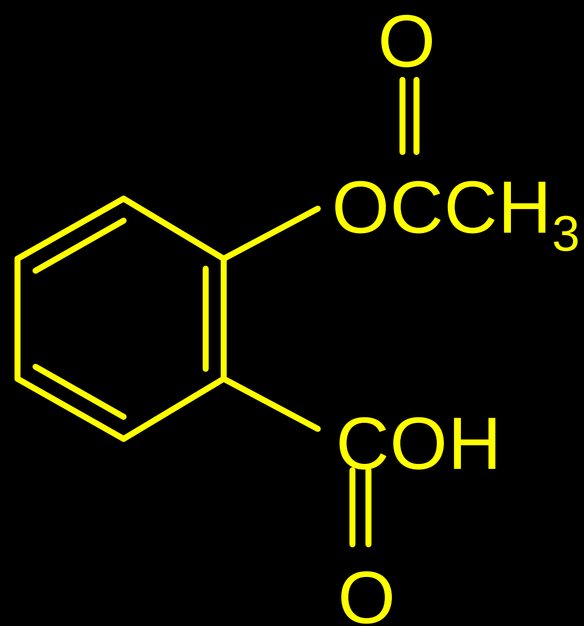


O-Acylation is kinetically controlled process; C-acylation is thermodynamically controlled

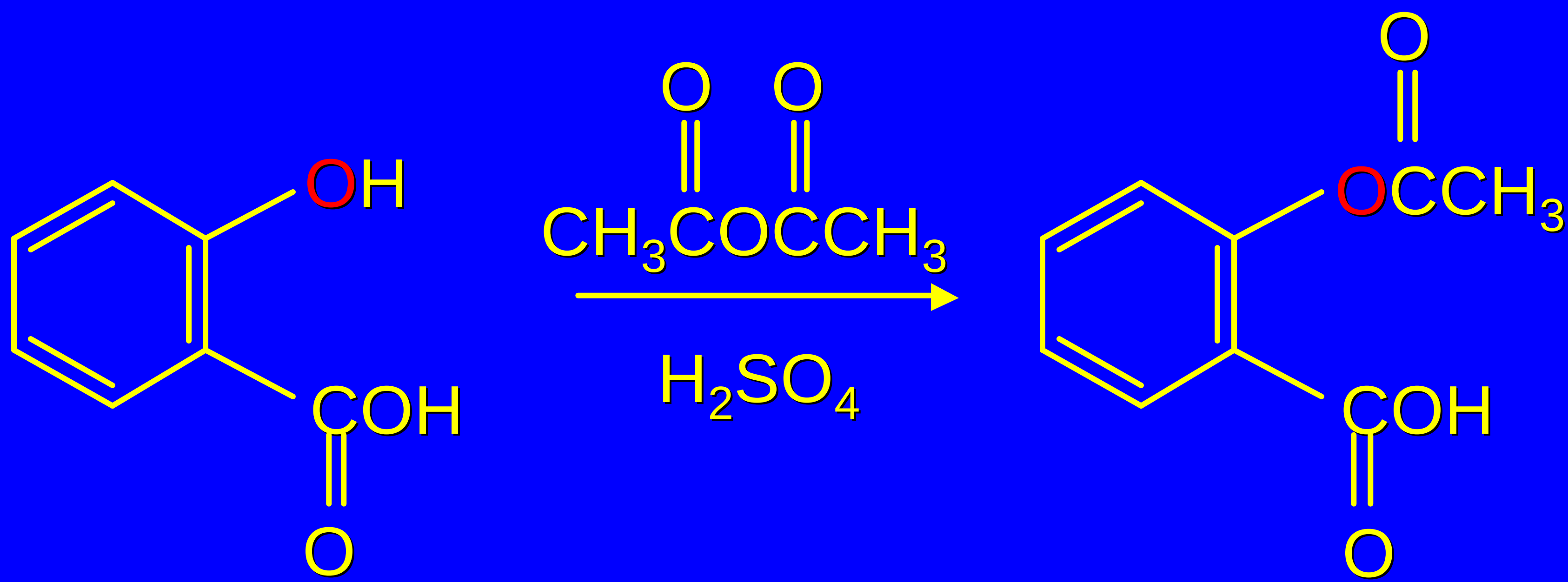
$AlCl_3$ catalyzes the conversion of the aryl ester to the aryl alkyl ketones; this is called the Fries rearrangement

24.10
Carboxylation of Phenols

Aspirin and
the
Kolbe-Schmitt
Reaction

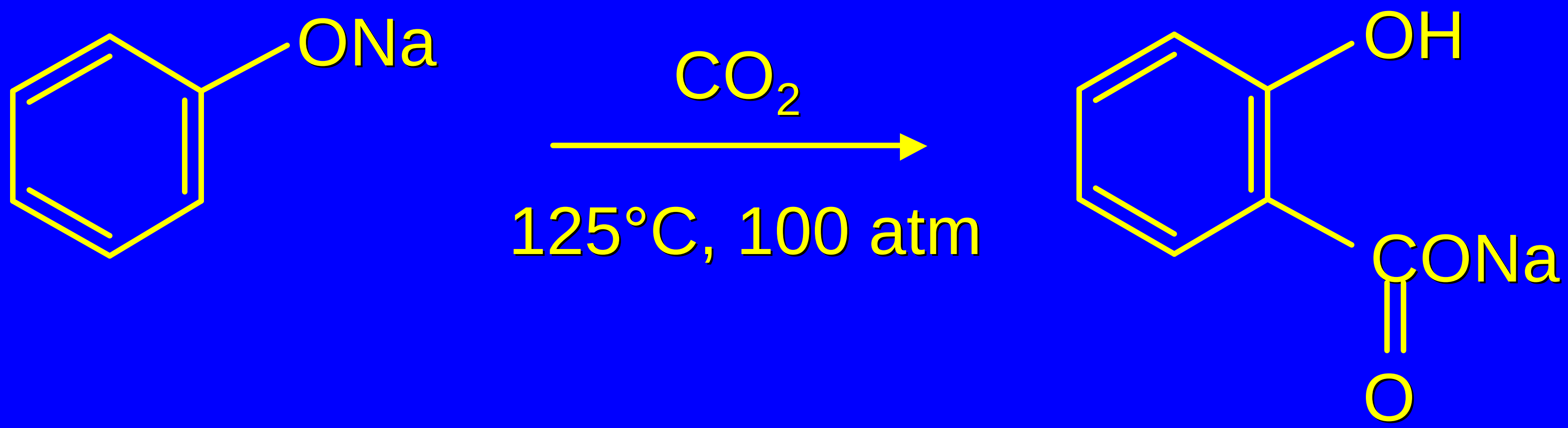


Aspirin is prepared from salicylic acid



how is salicylic acid prepared?

Preparation of Salicylic Acid

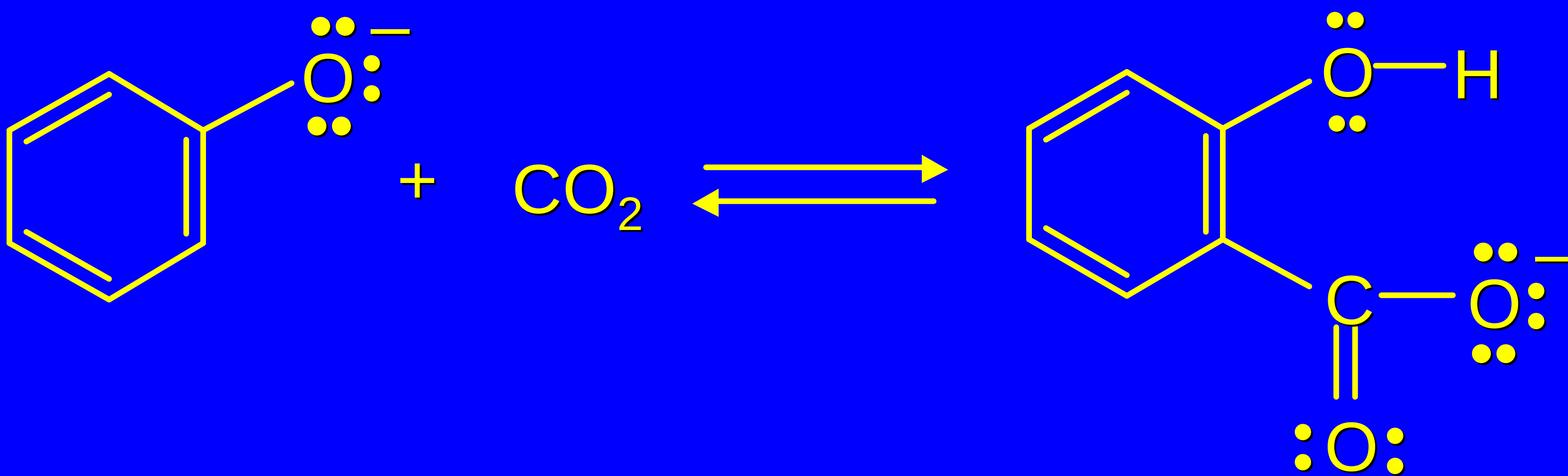


called the Kolbe-Schmitt reaction

acidification converts the sodium salt shown above to salicylic acid

What Drives the Reaction?

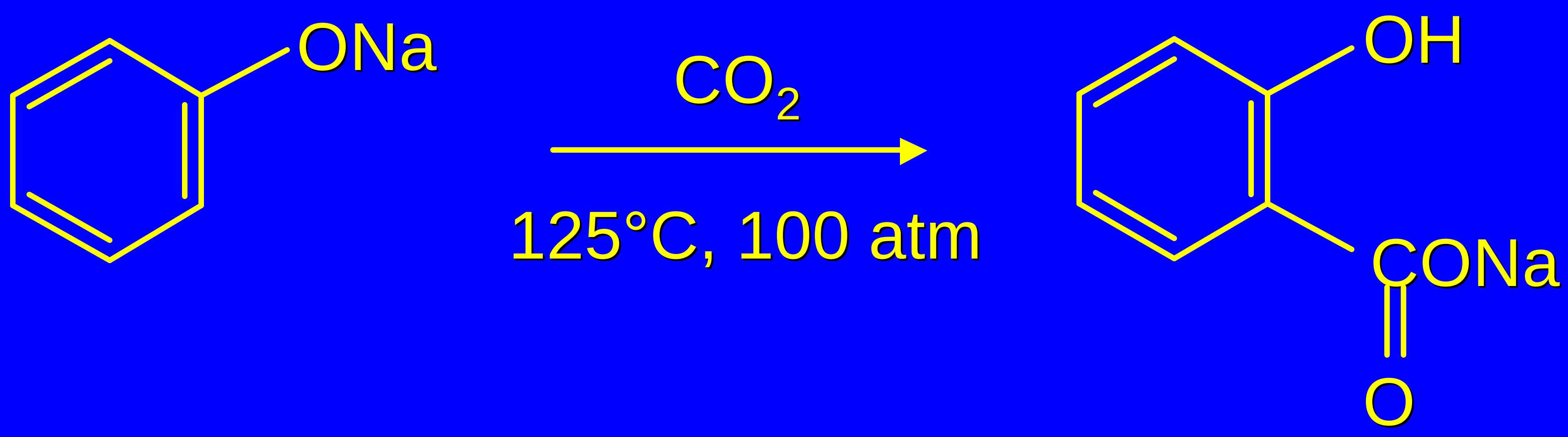
acid-base considerations provide an explanation:
stronger base on left; weaker base on right



stronger base:
pK_a of conjugate
acid = 10

weaker base:
pK_a of conjugate
acid = 3

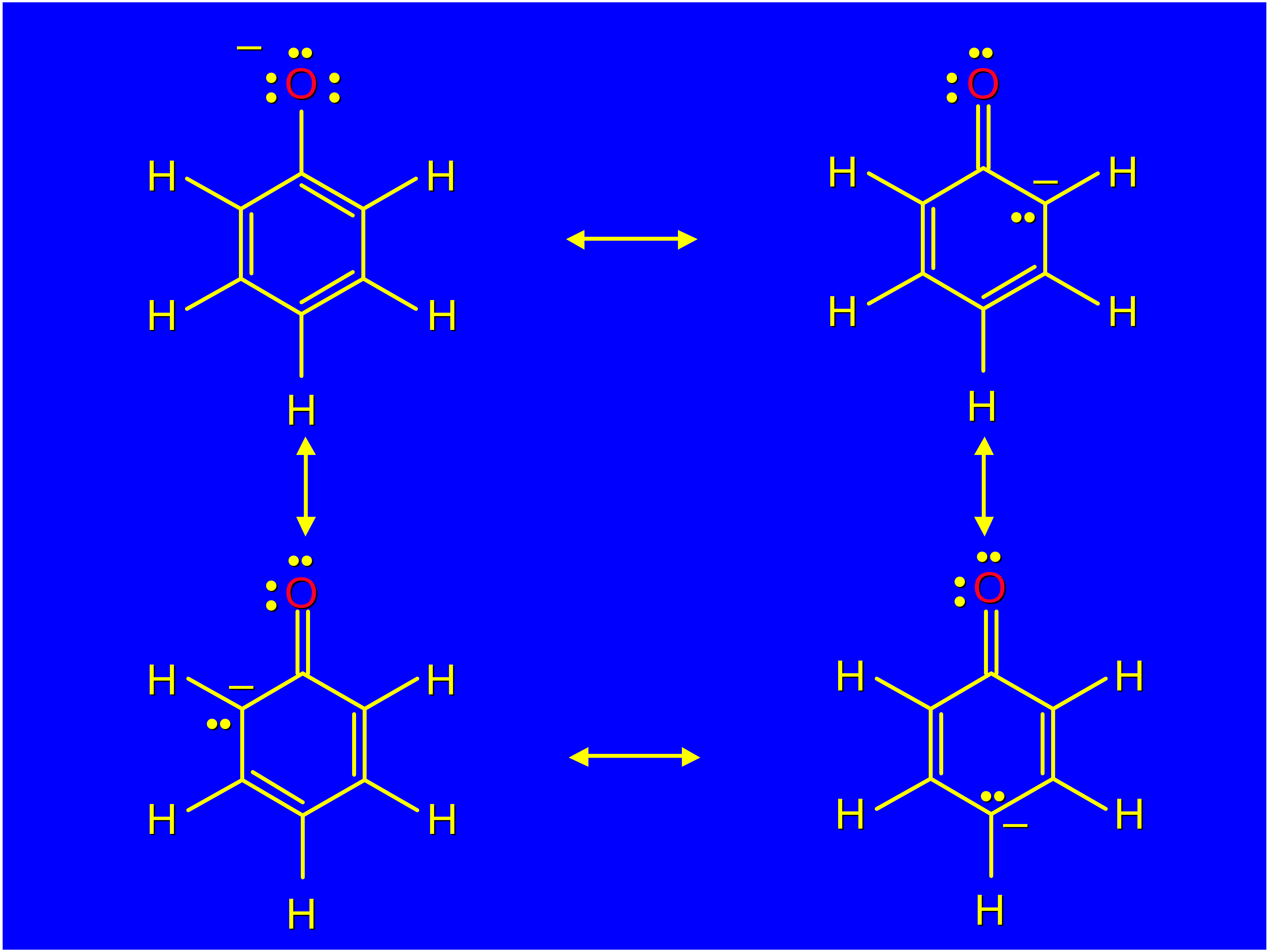
Preparation of Salicylic Acid



how does carbon-carbon bond form?

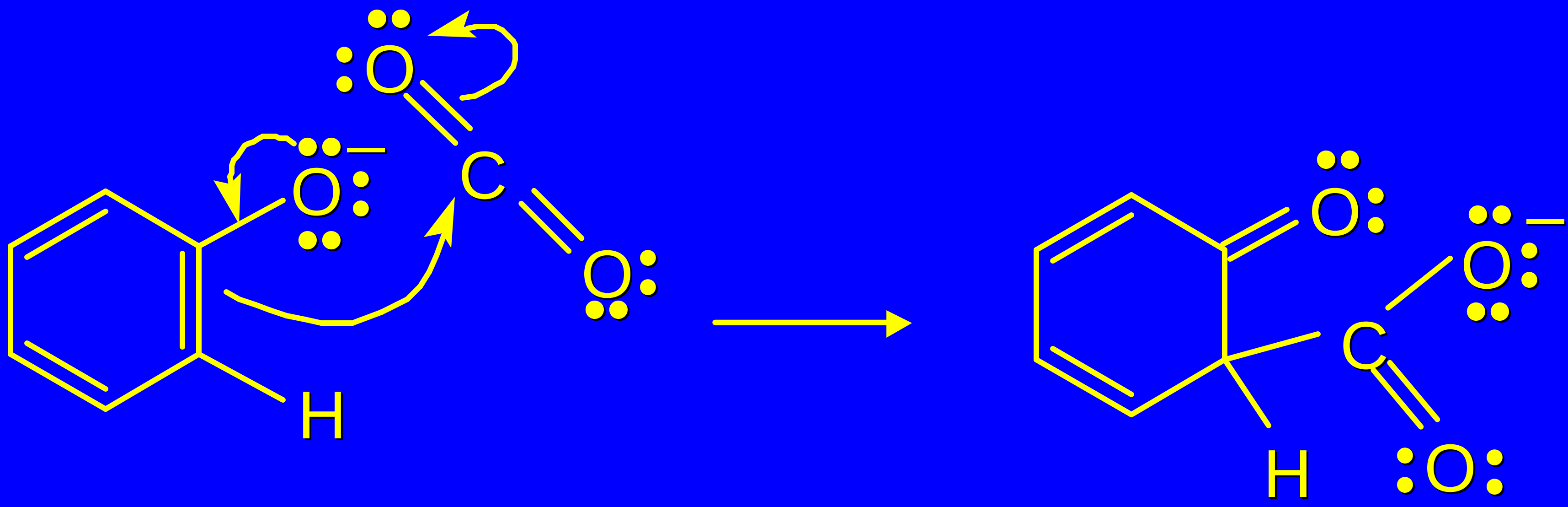
recall electron delocalization in phenoxide ion

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

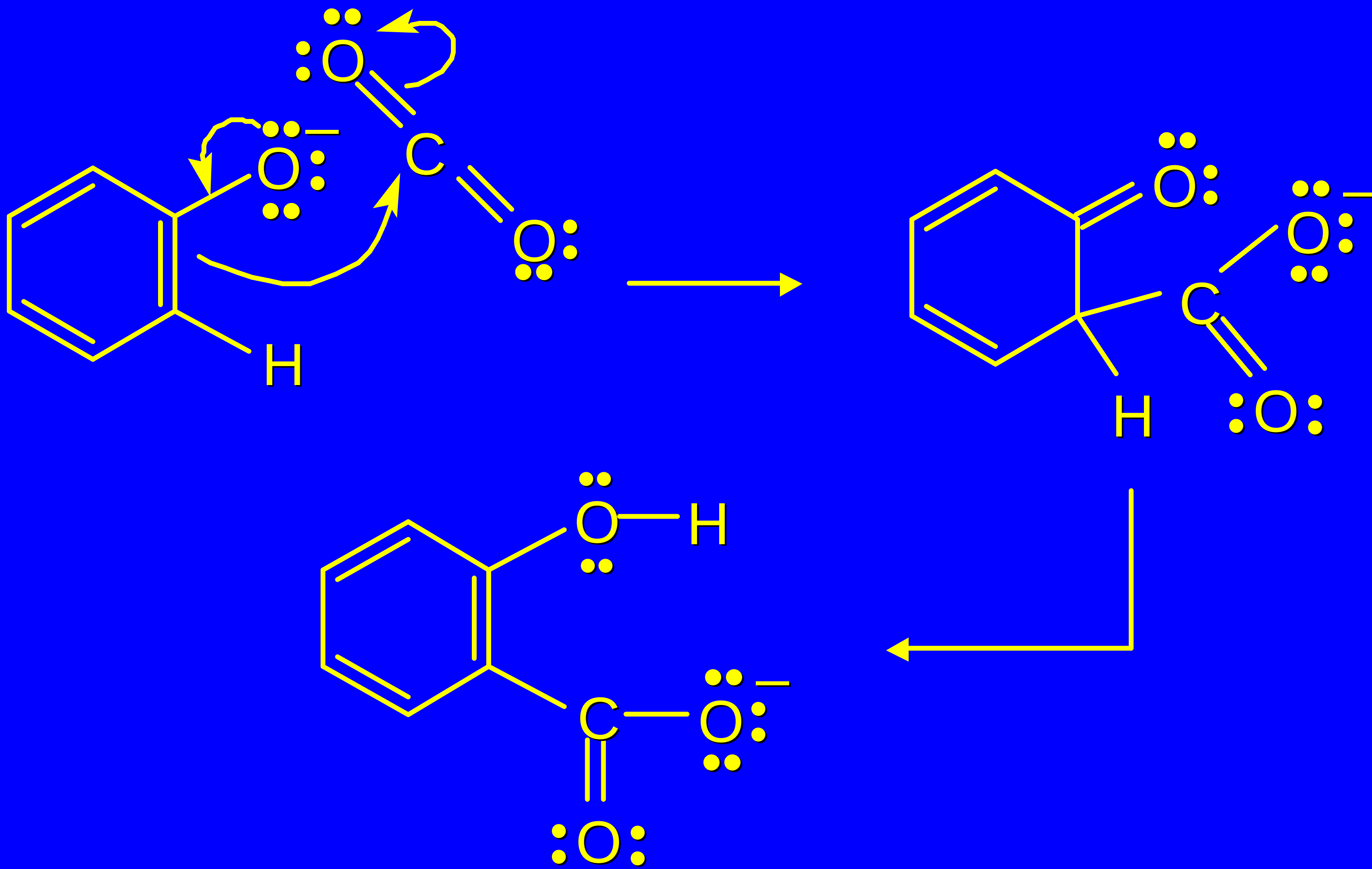


O
H
H
H
H
H

Mechanism of ortho Carboxylation

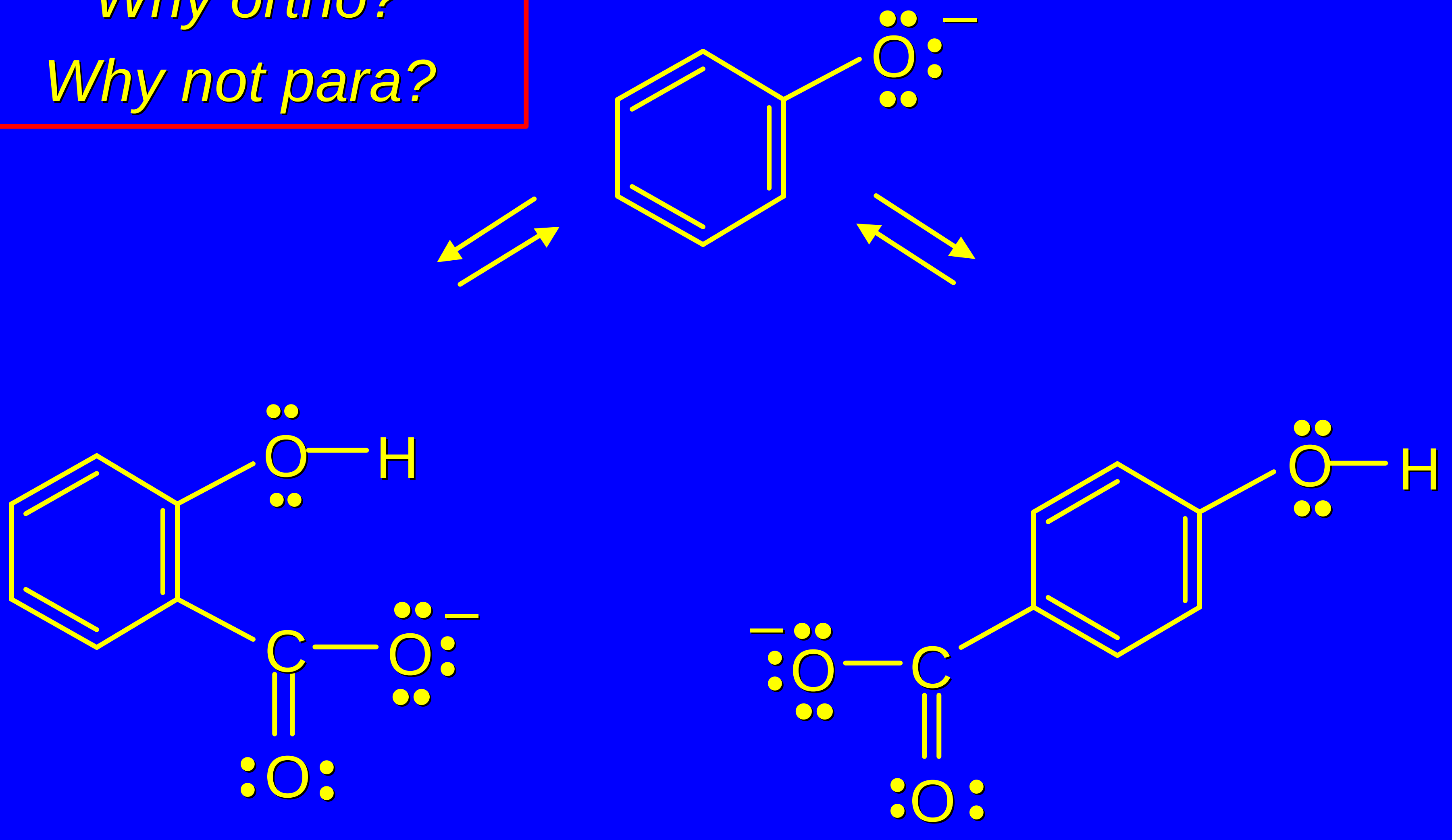


Mechanism of ortho Carboxylation

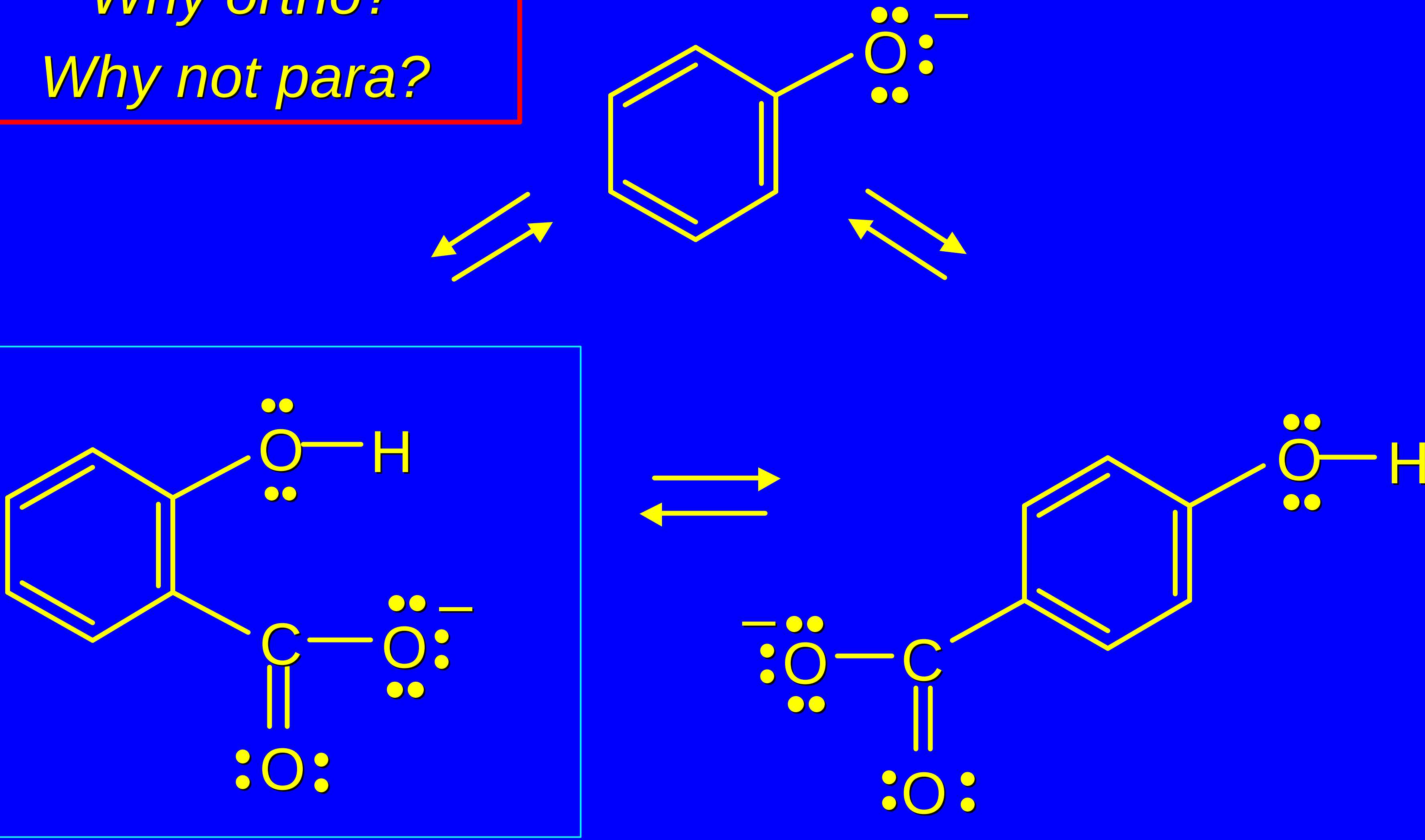


Why ortho?

Why not para?



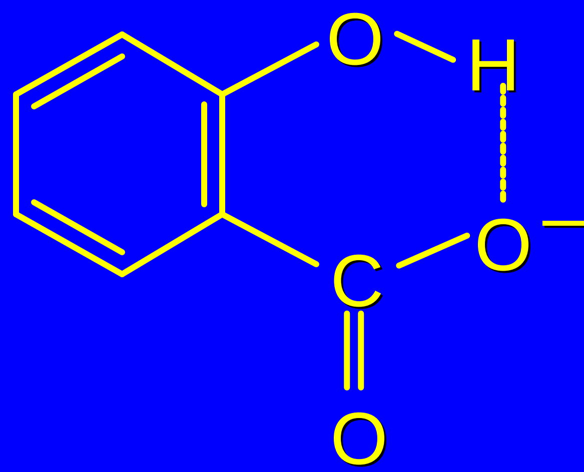
Why ortho?
Why not para?



weaker base:
pK_a of conjugate acid = 3

stronger base:
pK_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.