Electrophilic Aromatic Substitution

Benzene

- Source of electrons -thus- a base
- Other reactants are deficient in electrons - thus- electrophilic reagents or acids
- Typical reactions of benzene rings are electrophilic substitution reactions

ELECTROPHILIC AROMATIC SUBSTITUTION

Ar = *aryl*, any aromatic group with attachment directly to ring carbon

1. Nitration. Discussed in Sec. 15.8.

$$ArH + HONO_2 \xrightarrow{H_2SO_4} Ar{-}NO_2 + H_2O$$

A nitro compound

2. Sulfonation. Discussed in Sec. 15.9.

$$ArH + HOSO_3H \xrightarrow{SO_3} Ar{-}SO_3H + H_2O$$

A sulfonic acid

3. Halogenation. Discussed in Sec. 15.11.

$$ArH + Cl_2 \xrightarrow{Fe} Ar{-}Cl + HCl$$

An aryl chloride

$$ArH + Br_2 \xrightarrow{Fe} Ar{-}Br + HBr$$

An aryl bromide

4. Friedel–Crafts alkylation. Discussed in Sec. 15.10.

$$ArH + RCl \xrightarrow{AlCl_3} Ar{-}R + HCl$$

An alkylbenzene

5. Friedel–Crafts acylation. Discussed in Sec. 18.5.

$$\underset{\text{An acyl chloride}}{ArH + RCOCl} \xrightarrow{AlCl_3} \underset{\text{A ketone}}{Ar{-}COR} + HCl$$

6. Protonation. Discussed in Sec. 15.12.

$$ArSO_3H + H^+ \xrightarrow{H_2O} Ar{-}H + H_2SO_4$$ *Desulfonation*

$$ArH + D^+ \xrightarrow{D_2O} Ar{-}D + H^+$$ *Hydrogen exchange*

7. Nitrosation. Discussed in Secs. 23.11 and 24.11.

$$ArH + HONO \longrightarrow \underset{\text{A nitroso compound}}{Ar{-}N{=}O} + H_2O$$ *Only for highly reactive* ArH

8. Diazo coupling. Discussed in Sec. 23.18.

$$\underset{\text{A diazonium salt}}{ArH + Ar'N_2^+X^-} \longrightarrow \underset{\text{An azo compound}}{Ar{-}N{=}NAr'} + HX$$ *Only for highly reactive* ArH

9. Kolbe reaction. Discussed in Sec. 24.12. *Only for phenols*

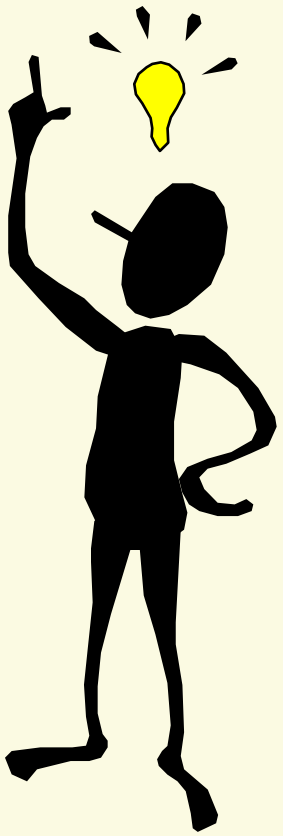
10. Reimer–Tiemann reaction. Discussed in Sec. 24.13. *Only for phenols* ■

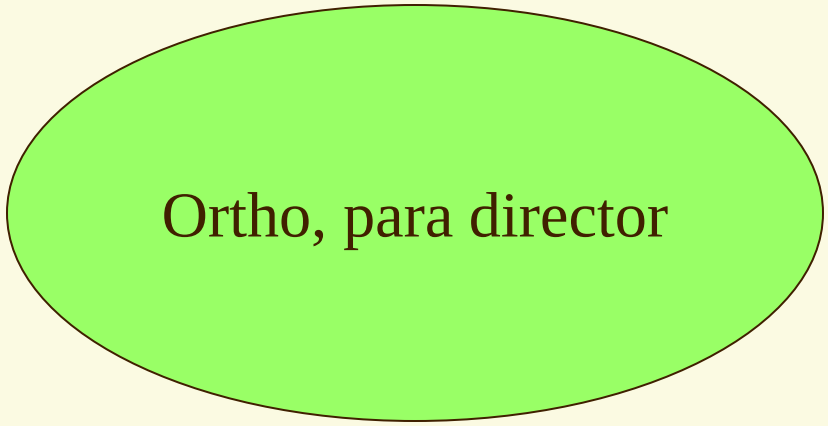
Effect of Substituent Groups

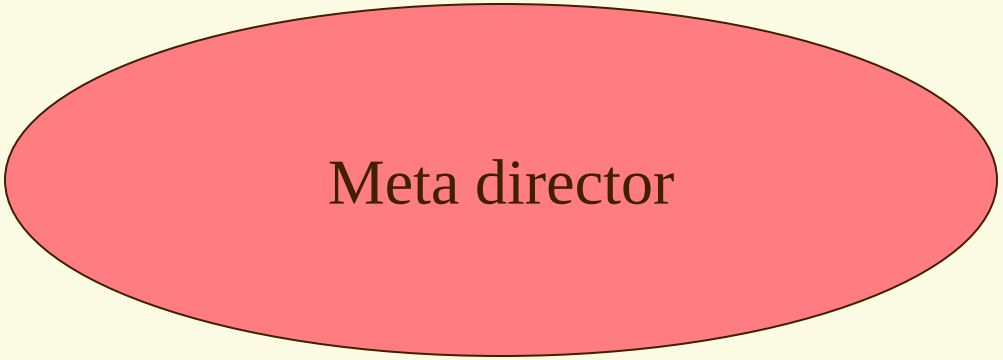
- Substitued groups direct the attach of a second group to the *ortho* or *para* positions
- Substitued groups direct the attach of a second group to the *meta* position
- Affects reactivity
- Affects orientation

Activating groups -
make the ring more reactive

Deactivating group -
makes the ring less reactive




Ortho, para director


Meta director

Effect of Groups on Electrophilic Aromatic Substitution

Activating: Ortho,para directors

Strongly activating

$-NH_2$ ($-NRH$, $-NR_2$)

$-OH$

Effect of Groups on Electrophilic Aromatic Substitution

Activating: Ortho,para directors

Moderately activating

-OCH_3 (-OC_2H_5, etc.)

-$NHCOCH_3$

Effect of Groups on Electrophilic Aromatic Substitution

Activating: Ortho,para directors

Weakly activating

- C_6H_5

-CH_3 (-C_2H_5, etc.)

Effect of Groups on Electrophilic Aromatic Substitution

Deactivating: Meta directors

- $-NO_2$
- $-N(CH_3)_3^+$
- -CN
- -COOH (-COOR)
- $-SO_3H$
- -CHO, -COR

Effect of Groups on Electrophilic Aromatic Substitution

- Deactivating: Ortho,para directors

  -F, -Cl, -Br, -I

Table 15.3 EFFECT OF GROUPS ON ELECTROPHILIC AROMATIC SUBSTITUTION

Activating: *Ortho, para* directors

Strongly activating

—NH_2 (—NHR, —NR_2)
—OH

Moderately activating

—OCH_3 (—OC_2H_5, etc.)
—$NHCOCH_3$

Weakly activating

—C_6H_5
—CH_3 (—C_2H_5, etc.)

Deactivating: *Meta* directors

—NO_2
—$N(CH_3)_3^+$
—CN
—COOH (—COOR)
—SO_3H
—CHO, —COR

Deactivating: *Ortho, para* directors

—F, —Cl, —Br, —I

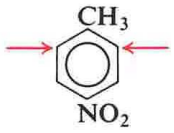
Orientation in Disubstituted Benzenes

- Strongly activating groups generally win out over deactivating or weakly activating groups.
- There is often little substitution between two groups that are meta to each other.

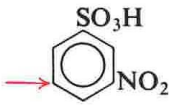
15.6 Orientation in disubstituted benzenes

The presence of two substituents on a ring makes the problem of orientation more complicated, but even here we can frequently make very definite predictions.

First of all, the two substituents may be located so that the directive influence of one *reinforces* that of the other; for example, in I, II, and III the orientation clearly must be that indicated by the arrows.



I



II

III

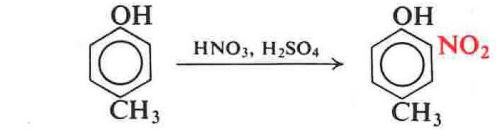
On the other hand, when the directive effect of one group *opposes* that of the other, it may be difficult to predict the major product; in such cases complicated mixtures of several products are often obtained.

Even where there are opposing effects, however, it is still possible in certain cases to make predictions in accordance with the following generalizations.

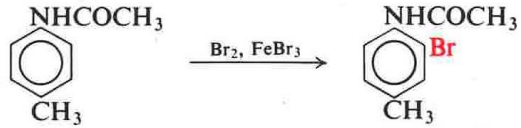
(a) *Strongly activating groups generally win out over deactivating or weakly activating groups.* The differences in directive power in the sequence

$$-NH_2, -OH > -OCH_3, -NHCOCH_3 > -C_6H_5, -CH_3 > \textit{meta}\text{ directors}$$

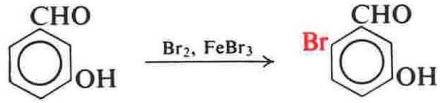
are great enough to be used in planning feasible syntheses. For example:



Sole product

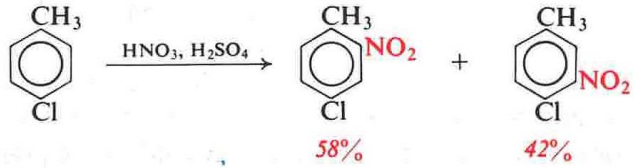


Chief product

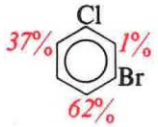


Chief product

There must be, however, a fairly large difference in the effects of the two groups for clear-cut results; otherwise one gets results like these:

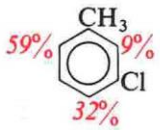


(b) *There is often little substitution between two groups that are meta to each other.* In many cases it seems as though there just is not enough room between two groups located *meta* to each other for appreciable substitution to occur there, as illustrated by IV and V:



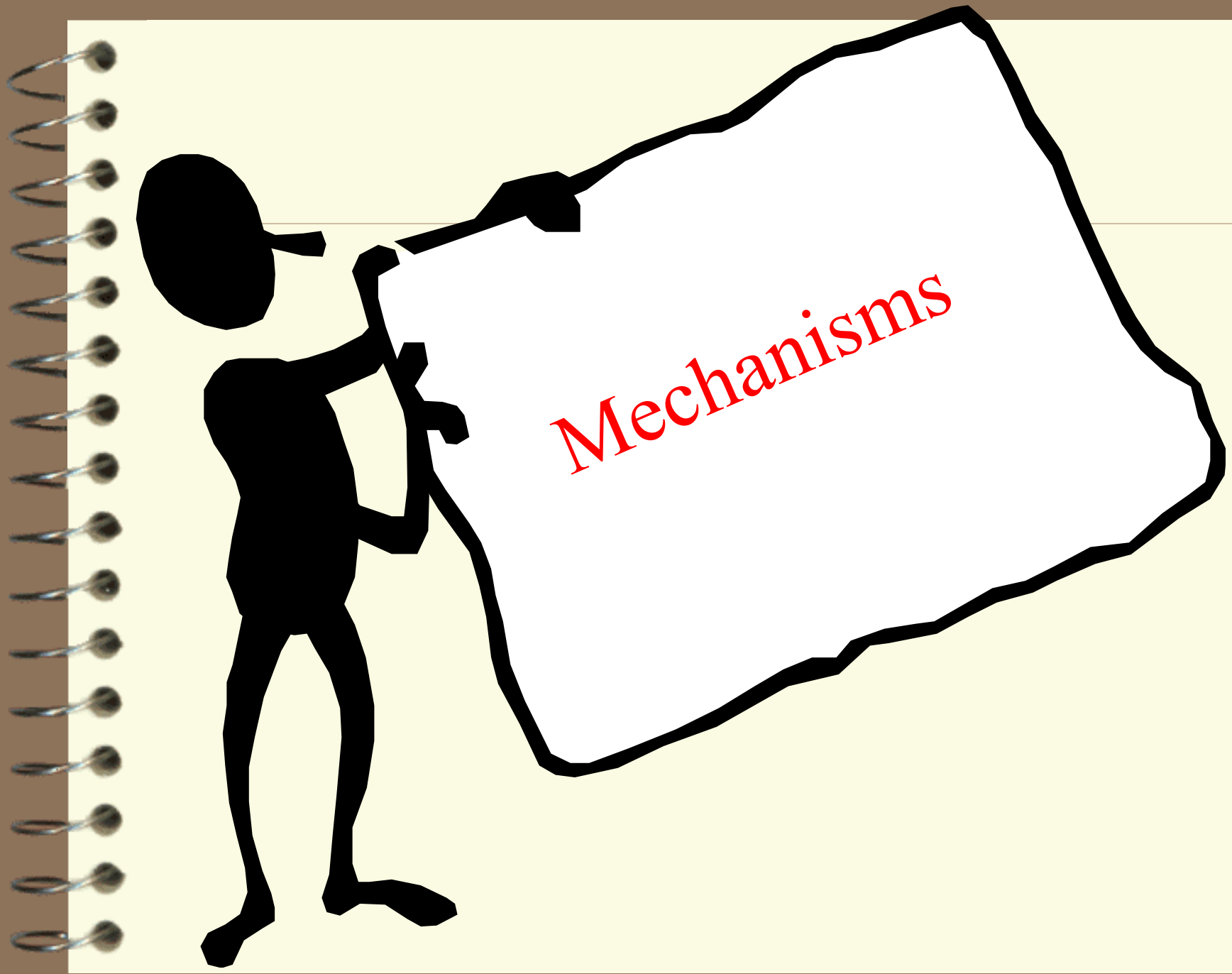
Nitration

IV



Nitration

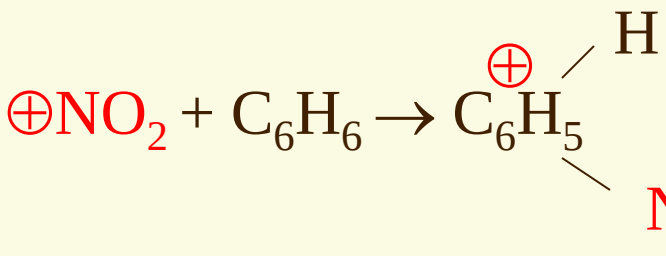
V

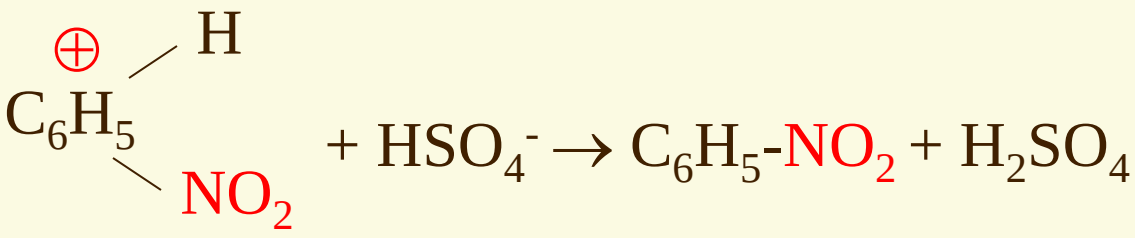

Mechanisms

Nitration

$$HONO_2 + 2H_2SO_4 \leftrightarrow H_3O^+ + 2HSO_4^- + \oplus NO_2$$

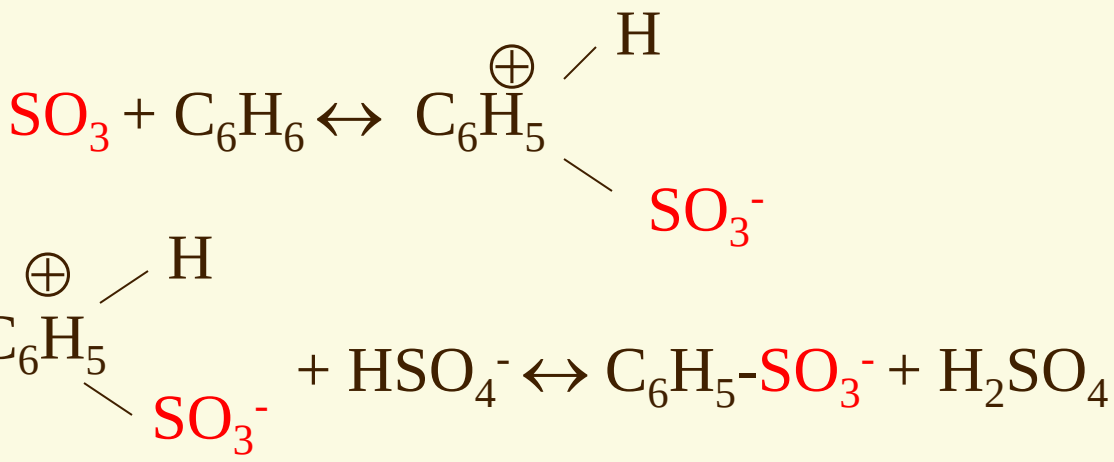
Nitronium ion



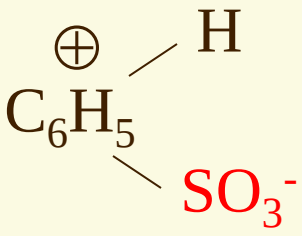


Sulfonation

$$2H_2SO_4 \leftrightarrow H_3O^+ + HSO_4^- + SO_3$$



$$SO_3 + C_6H_6 \leftrightarrow C_6H_5\text{-}SO_3^-$$



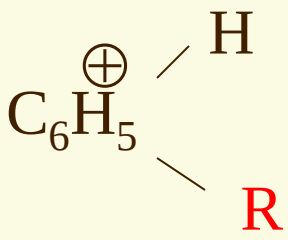
$$+ HSO_4^- \leftrightarrow C_6H_5\text{-}SO_3^- + H_2SO_4$$

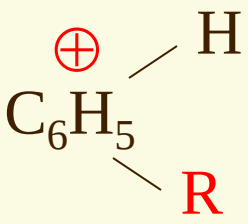
$$C_6H_5\text{-}SO_3^- + H_3O^+ \leftrightarrow C_6H_5\text{-}SO_3H + H_2O$$

Equilibrium far to the left

Friedel-Crafts Alkylation

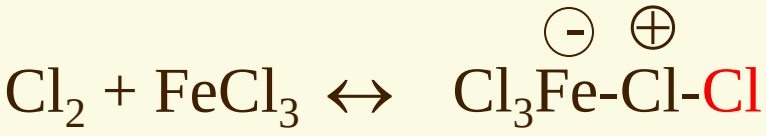
$$RCl + AlCl_3 \leftrightarrow AlCl_4^- + R^{\oplus}$$

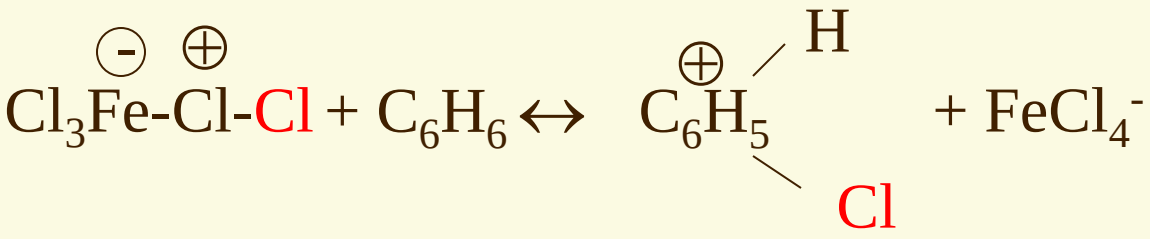
$$R^{\oplus} + C_6H_6 \leftrightarrow$$ 

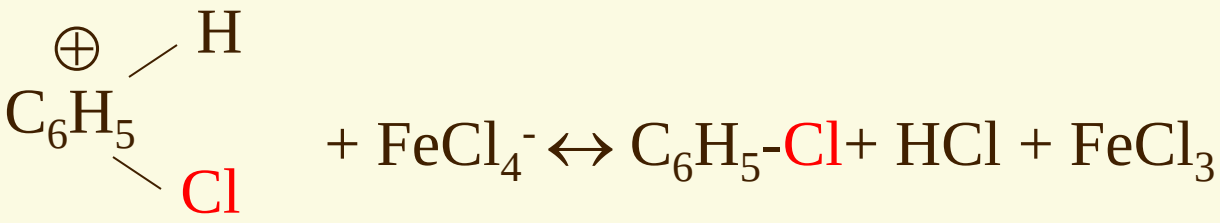
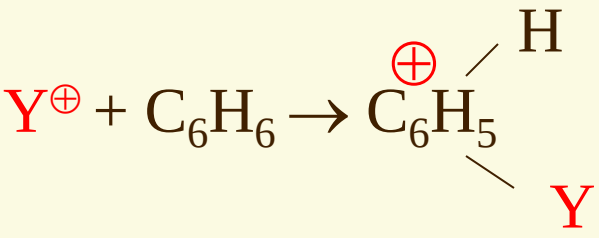
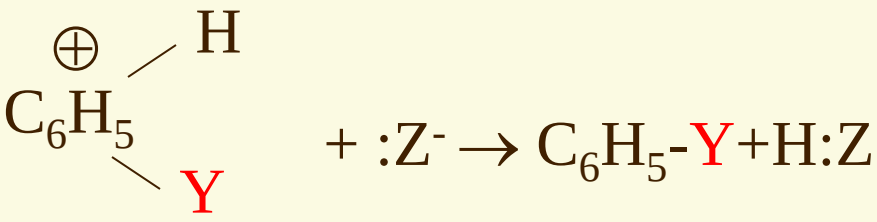


$$+ AlCl_4^- \leftrightarrow C_6H_5\text{-}R + HCl + AlCl_3$$

Halogenation







A Summary