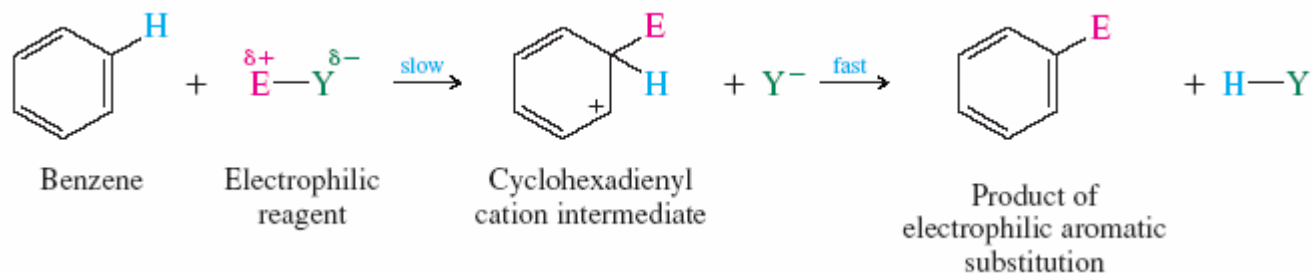


# Reactions of Arenes: Electrophilic Aromatic Substitution

## SUMMARY

Section 12.1 On reaction with electrophilic reagents, compounds that contain a benzene ring undergo **electrophilic aromatic substitution**. Table 12.1 in Section 12.1 and Table 12.3 in this summary give examples.

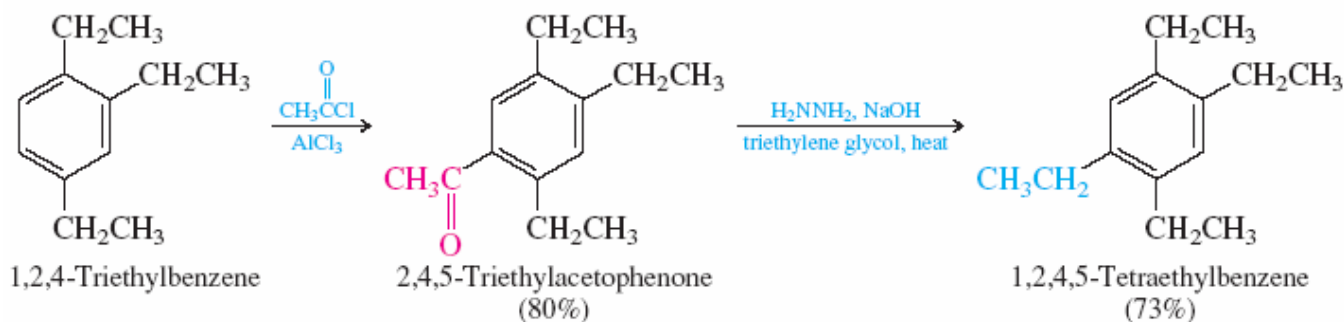
Section 12.2 The mechanism of electrophilic aromatic substitution involves two stages: attack of the electrophile on the  $\pi$  electrons of the ring (slow, rate-determining), followed by loss of a proton to restore the aromaticity of the ring.



Sections 12.3–12.5 See Table 12.3

Sections 12.6–12.7 See Tables 12.3 and 12.4

Section 12.8 Friedel–Crafts acylation, followed by Clemmensen or Wolff–Kishner reduction is a standard sequence used to introduce a primary alkyl group onto an aromatic ring.

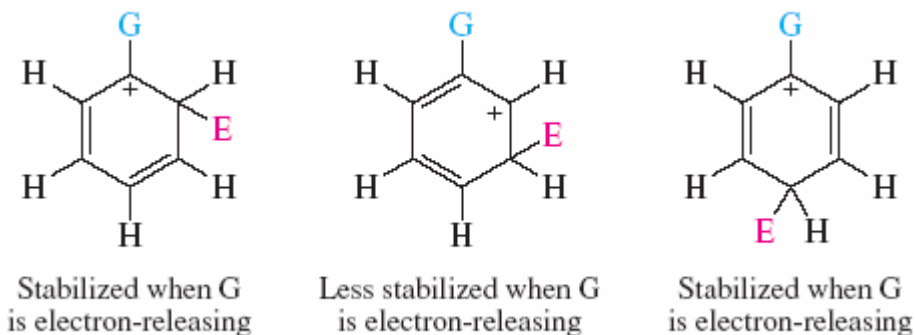


Section 12.9 Substituents on an aromatic ring can influence both the *rate* and *regioselectivity* of electrophilic aromatic substitution. Substituents are classified as *activating* or *deactivating* according to whether they cause the ring to react more rapidly or less rapidly than benzene. With respect to regioselectivity, substituents are either *ortho*, *para*-directing or *meta*-directing. A methyl group is activating and ortho, para-directing. A trifluoromethyl group is deactivating and meta-directing.

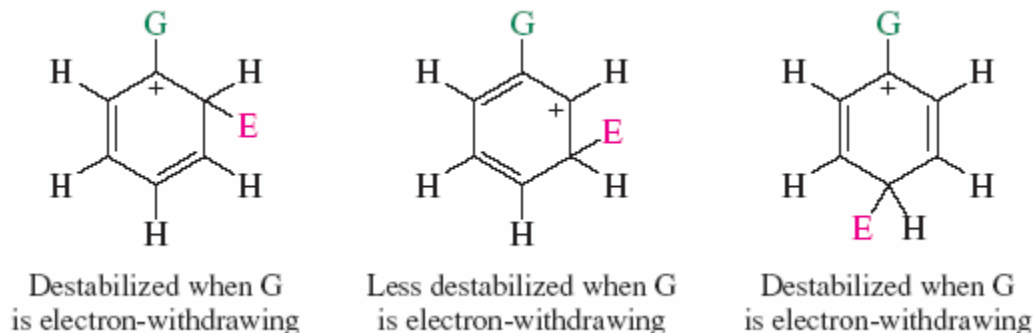
Sections How substituents control rate and regioselectivity in electrophilic aromatic

12.10–12.14

substitution results from their effect on carbocation stability. An electron-releasing substituent stabilizes the cyclohexadienyl cation intermediates corresponding to ortho and para attack more than meta.



Conversely, an electron-withdrawing substituent destabilizes the cyclohexadienyl cations corresponding to ortho and para attack more than meta. Thus, meta substitution predominates.

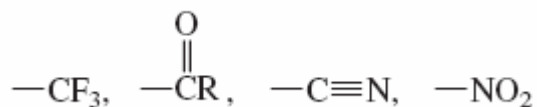


Substituents can be arranged into three major categories:

**1. Activating and ortho, para-directing:** These substituents stabilize the cyclohexadienyl cation formed in the rate-determining step. They include  $-OR$ ,  $OAr$ , and related species. The most strongly activating members of this group are bonded to the ring by a nitrogen or oxygen atom that bears an unshared pair of electrons.

**2. Deactivating and ortho, para-directing:** The halogens are the most prominent members of this class. They withdraw electron density from all the ring positions by an inductive effect, making halobenzenes less reactive than benzene. Lone-pair electron donation stabilizes the cyclohexadienyl cations corresponding to attack at the ortho and para positions more than those formed by attack at the meta positions, giving rise to the observed regioselectivity.

**3. Deactivating and meta-directing:** These substituents are strongly electron-withdrawing and destabilize carbocations. They include  $-NO_2$  and related species. All the ring positions are deactivated, but because the *meta* positions are deactivated less than the ortho and para, meta substitution is favored.



Section 12.15 When two or more substituents are present on a ring, the regioselectivity of electrophilic aromatic substitution is generally controlled by the directing effect of the more powerful *activating* substituent.

- Section 12.16 The order in which substituents are introduced onto a benzene ring needs to be considered in order to prepare the desired isomer in a multistep synthesis.
- Section 12.17 Polycyclic aromatic hydrocarbons undergo the same kind of electrophilic aromatic substitution reactions as benzene.
- Section 12.18 Heterocyclic aromatic compounds may be more reactive or less reactive than benzene. Pyridine is much less reactive than benzene, but pyrrole, furan, and thiophene are more reactive.