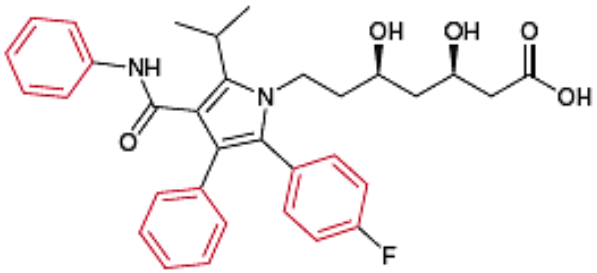
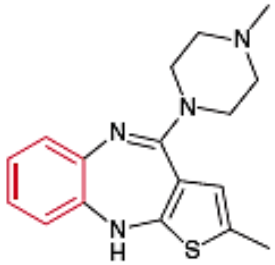
Organic Chemistry II
1st Semester, Year 2
Lectures 1 & 2

Aromatic Compounds and Their Reactions 1

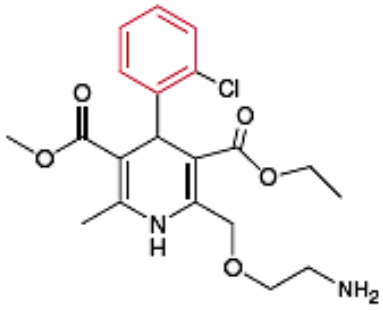
Based on Organic Chemistry, T.W. GRAHAM SOLOMONS and CRAIG B. FRYHLE **10e. & Organic Chemistry,** DAVID KLEIN, 2nd e.



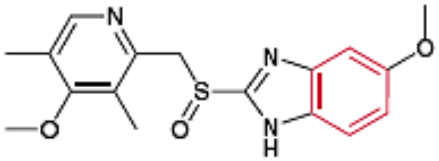
Lipitor
(atorvastatin)
Lowers cholesterol levels and reduces risk of heart attack and stroke



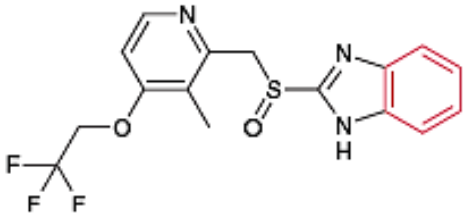
Zyprexa
(olanzapine)
An antipsychotic used in the treatment of schizophrenia and bipolar disorder



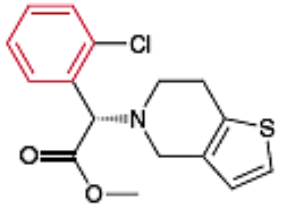
Norvasc
(amlodipine)
Used in the treatment of angina and high blood pressure



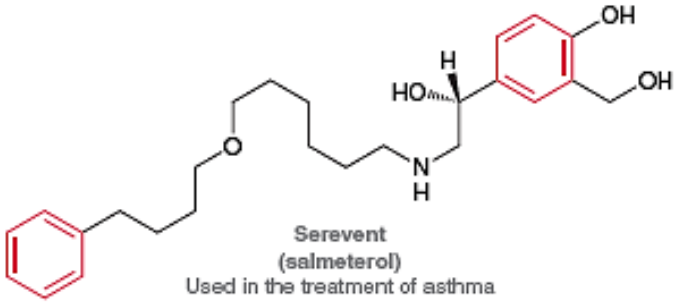
Nexium
(omeprazole)
A proton-pump inhibitor used in the treatment of ulcers and acid reflux



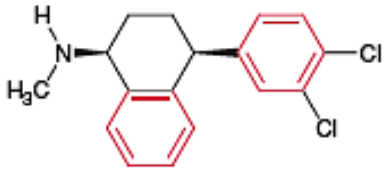
Prevacid
(lansoprazole)
A proton-pump inhibitor used in the treatment of ulcers and acid reflux



Plavix
(clopidogrel)
An antiplatelet agent (prevents formation of blood clots) used in the treatment of coronary artery disease



Serevent
(salmeterol)
Used in the treatment of asthma

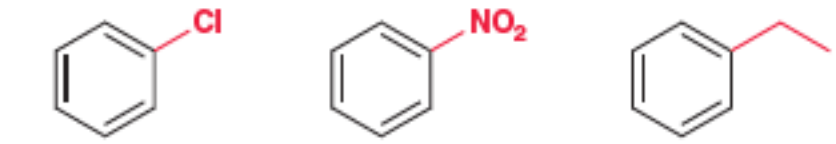


Zoloft
(sertraline)
Used in the treatment of depression

Nomenclature of Benzene Derivatives

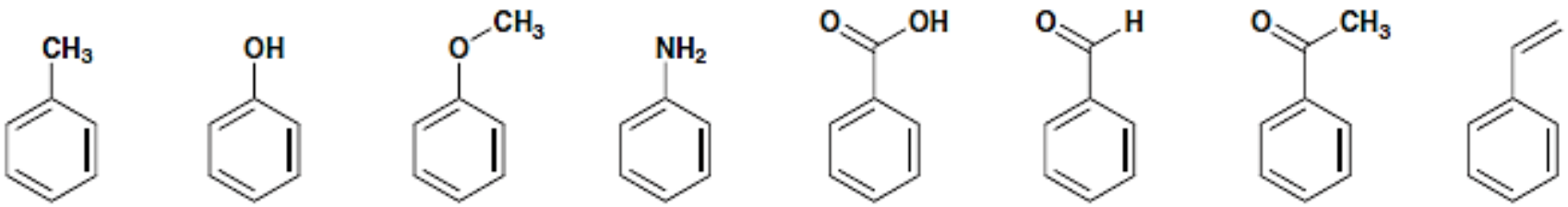
Monosubstituted Derivatives of Benzene:

Monosubstituted derivatives of benzene are named systematically using benzene as the parent and listing the substituent as a prefix. Below are several examples.



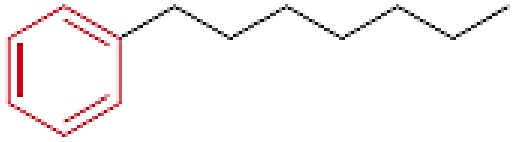
Chlorobenzene Nitrobenzene Ethylbenzene

The following are some monosubstituted aromatic compounds that have common names accepted by IUPAC. You must commit these names to memory, as they will be used extensively throughout the remaining chapters.



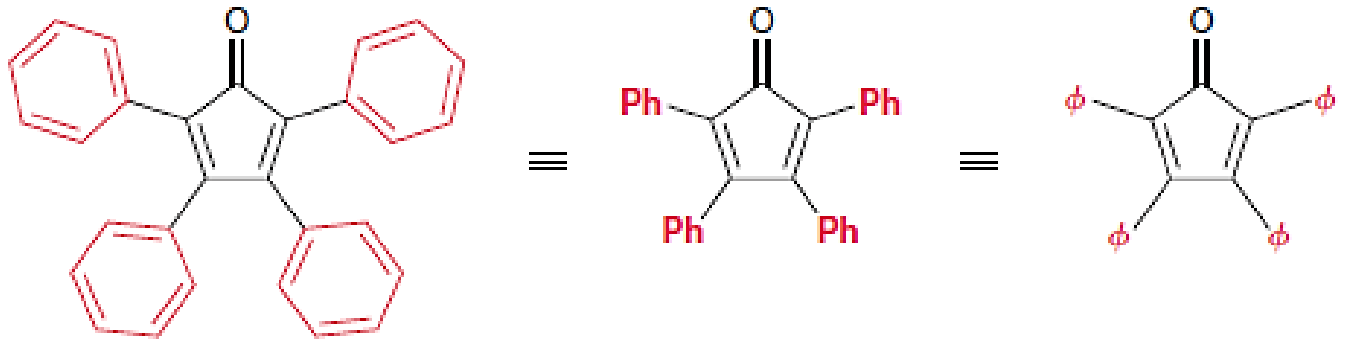
Toluene Phenol Anisole Aniline Benzoic acid Benzaldehyde Acetophenone Styrene

If the substituent is larger than the benzene ring (i.e., if the substituent has more than six carbon atoms), then the benzene ring is treated as a substituent and is called a **phenyl group**.



1-Phenylheptane

The presence of phenyl groups is often indicated with the letters **Ph** or with the Greek letter phi (ϕ)

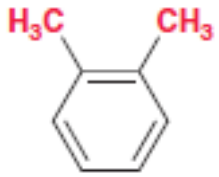


Tetraphenylcyclopentadienone

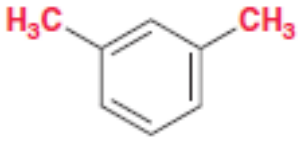
Phenyl groups bearing substituents are sometimes indicated with the letters **Ar**, indicating the presence of an aromatic ring.

Disubstituted Derivatives of Benzene

Dimethyl derivatives of benzene are called xylene, and there are three constitutionally isomeric xylenes.



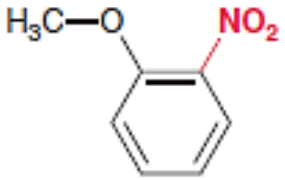
ortho-Xylene
(1,2-dimethylbenzene)



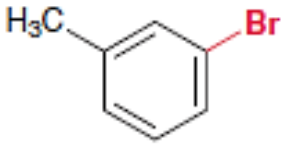
meta-Xylene
(1,3-dimethylbenzene)

para-Xylene
(1,4-dimethylbenzene)

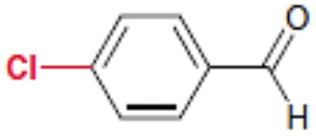
These isomers differ from each other in the relative positions of the methyl groups and can be named in two ways: (1) using the descriptors ***ortho***, ***meta***, and ***para*** or (2) using locants (i.e., 1,3 is the same as *meta*). Both methods can be used when the parent is a common name:



ortho-Nitroanisole
(2-Nitroanisole)



meta-Bromotoluene
(3-Bromotoluene)



para-Chlorobenzaldehyde
(4-Chlorobenzaldehyde)

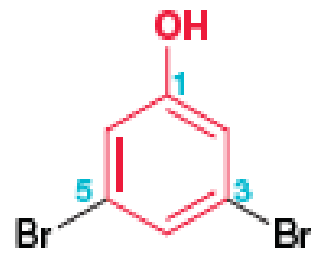
Polysubstituted Derivatives of Benzene

The descriptors *ortho*, *meta*, and *para* cannot be used when naming an aromatic ring bearing three or more substituents.

When naming a polysubstituted benzene ring, we will follow the same four-step process used for naming alkanes, alkenes, alkynes, and alcohols.

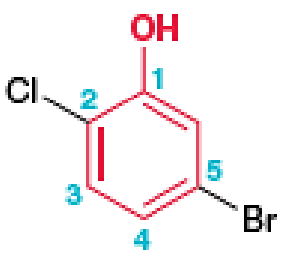
1. Identify and name the parent.
2. Identify and name the substituents.
3. Assign a locant to each substituent.
4. Arrange the substituents alphabetically.

When identifying the parent, it is acceptable (and common practice) to choose a common name.

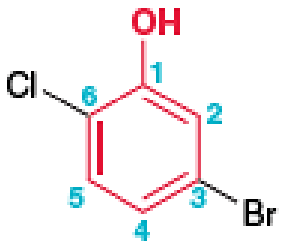


3,5-Dibromophenol

Correct

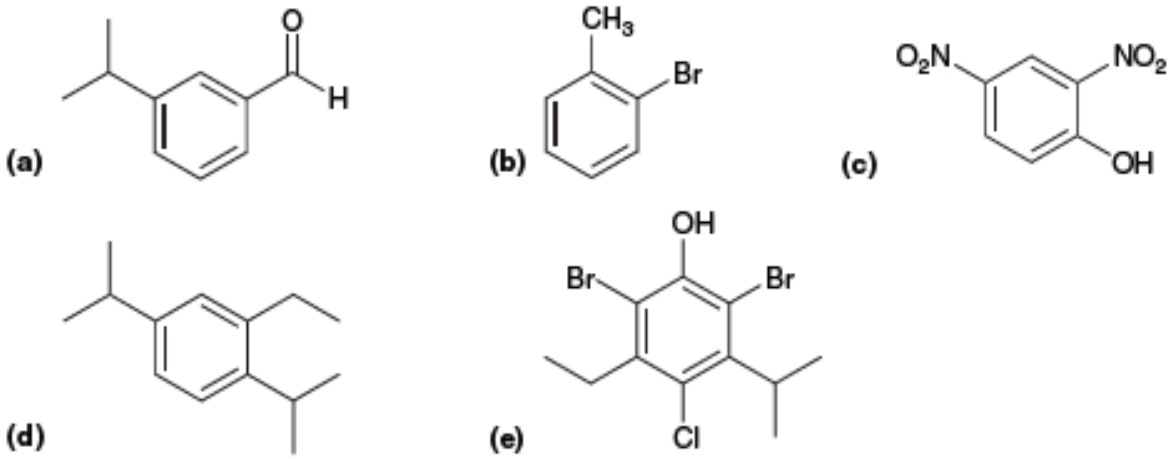


Incorrect



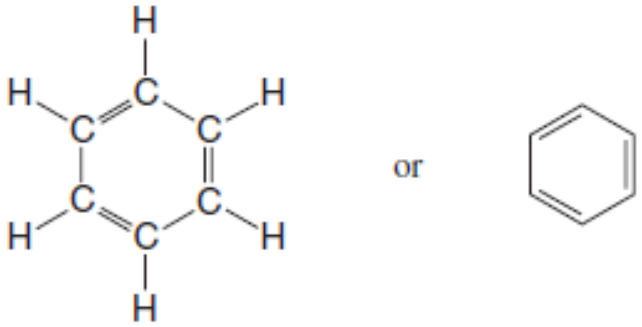
Homework:

Provide a systematic name for each of the following compounds:



The Kekulé Structure for Benzene:

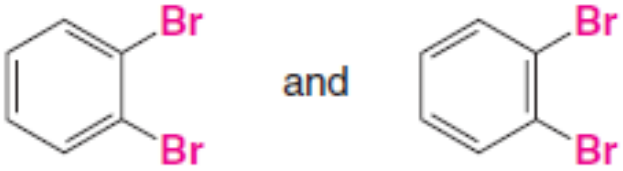
- In 1825, Michael Faraday isolated benzene from the oily residue left by illuminating gas in London street lamps. Further investigation showed that the molecular formula of this compound was C_6H_6: a hydrocarbon comprised of six carbon atoms and six hydrogen atoms.
- August Kekulé proposed that benzene was a rapidly equilibrating mixture of two compounds, each containing a six-membered ring with three alternating π bonds.
- In the Kekulé description, the bond between any two carbon atoms is sometimes a single bond and sometimes a double bond.
- These structures are known as Kekulé structures.



The Kekulé formula for benzene

A problem soon arose with the **Kekulé structure**, however.

The Kekulé structure predicts that there should be two different 1,2-dibromobenzenes, but there are not. In one of these hypothetical compounds (below), the carbon atoms that bear the bromines would be separated by a single bond, and in the other they would be separated by a double bond.



These 1,2-dibromobenzenes do not exist as isomers.

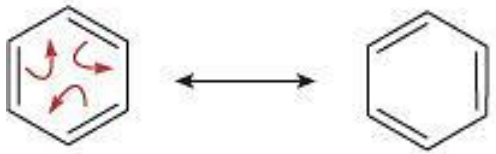
- *Only one 1,2-dibromobenzene has ever been found, however.*

To accommodate this objection, Kekulé proposed that the two forms of benzene (and of benzene derivatives) are in a state of equilibrium and that this equilibrium is so rapidly established that it prevents isolation of the separate compounds.

Thus, the two 1,2-dibromobenzenes would also be rapidly equilibrated, and this would explain why chemists had not been able to isolate the two forms:

There is no such equilibrium between benzene ring bond isomers.

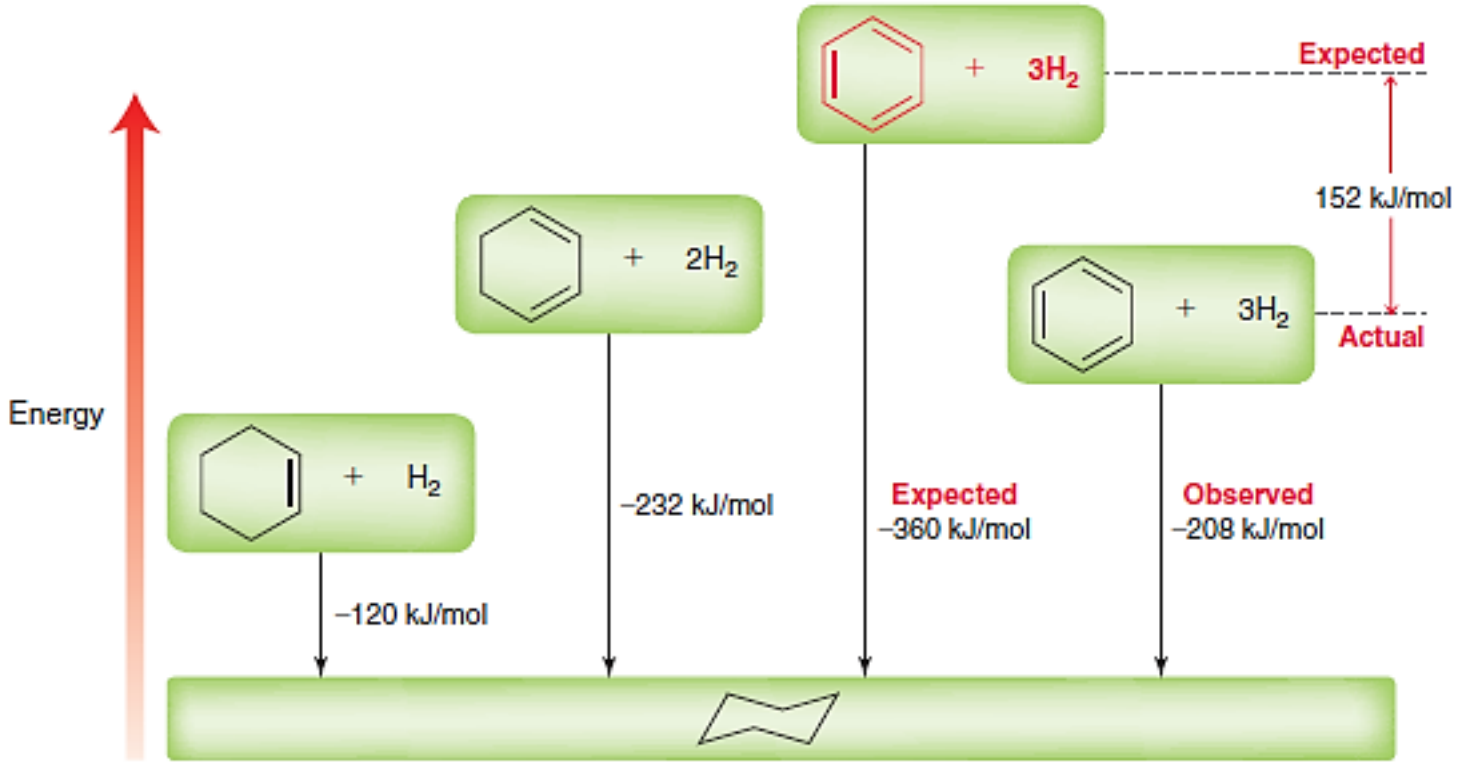
- We now know that this proposal was also incorrect and that *no such equilibrium exists*.



The hybrid

The electrons in the π bonds are **delocalized** around the ring.

Stability of Benzene

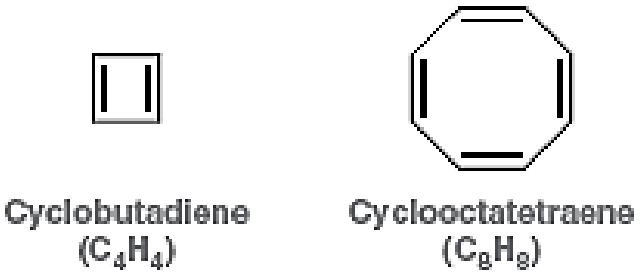


An energy diagram comparing the heats of hydrogenation for cyclohexene, cyclohexadiene, and benzene.

The difference between the expected value (-360) and the observed value (-208) is 152 kJ/mol, which is called the ***stabilization energy*** of benzene. This value represents the amount of stabilization associated with aromaticity.

Hückel's Rule

We might expect the following two compounds to exhibit aromatic stabilization like benzene:

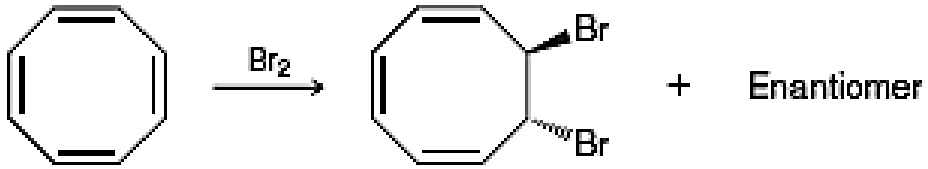


Cyclobutadiene (C_4H_4)

Cyclooctatetraene (C_8H_8)

After all, they are similar to benzene in that each compound is comprised of a ring of alternating single and double bonds.

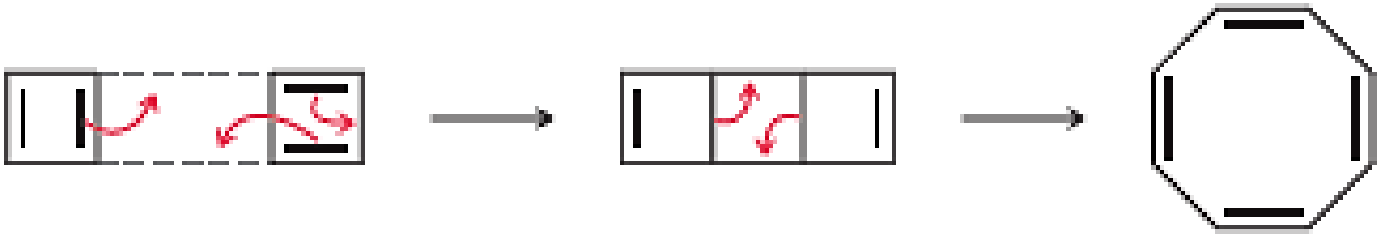
The reactivity of cyclooctatetraene (C_8H_8) suggests that cyclooctatetraene does not exhibit the same stability exhibited by benzene. For example, the compound readily undergoes addition reactions, such as bromination.



Cyclobutadiene (C_4H_4) also does not exhibit aromatic stability.

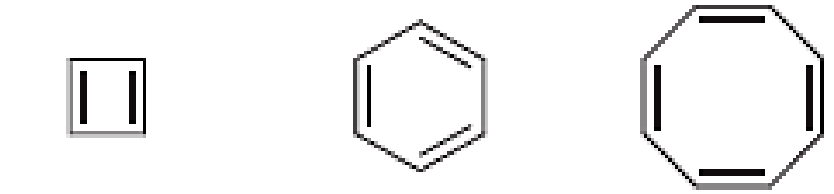
It is extremely unstable and resisted all attempts to prepare it until the second half of the twentieth century. Cyclobutadiene is so unstable that it reacts with itself at -78°C in a Diels-Alder reaction.

The Diels-Alder reaction generates an initial tricyclic product that is also unstable and rapidly rearranges to form cyclooctatetraene.



The presence of a fully conjugated ring of *p* electrons is not the sole requirement for aromaticity; the number of π electrons in the ring is also important.

Specifically, we have seen that an odd number of electron pairs is required for aromaticity.



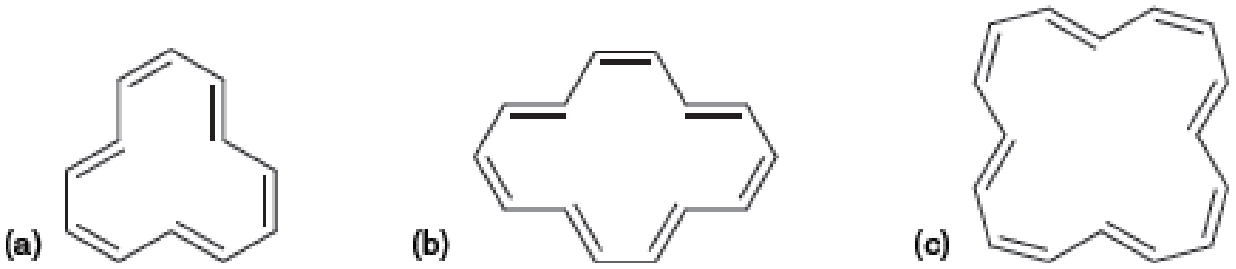
The requirement for an odd number of electron pairs is called **Hückel's rule**.

Specifically, a compound can only be aromatic if the number of π electrons in the ring is 2, 6, 10, 14, 18, and so on.

This series of numbers can be expressed mathematically as **4*n* + 2**, where ***n*** is a whole number.

Homework:

Predict whether each of the following compounds should be aromatic:



The Criteria for Aromaticity

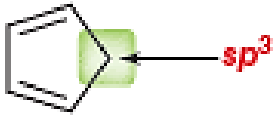
Benzene is not the only compound that exhibits aromatic stabilization. A compound will be aromatic if it satisfies the following two criteria:

1. The compound must contain a ring comprised of continuously overlapping *p* orbitals.

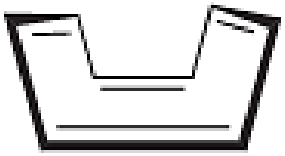
2. The number of p electrons in the ring must be a Hückel number. Compounds that fail the first criterion are called **nonaromatic**.

Below are three examples, each of which fails the first criterion for a different reason.

Not a ring



Not a continuous system of *p* orbitals

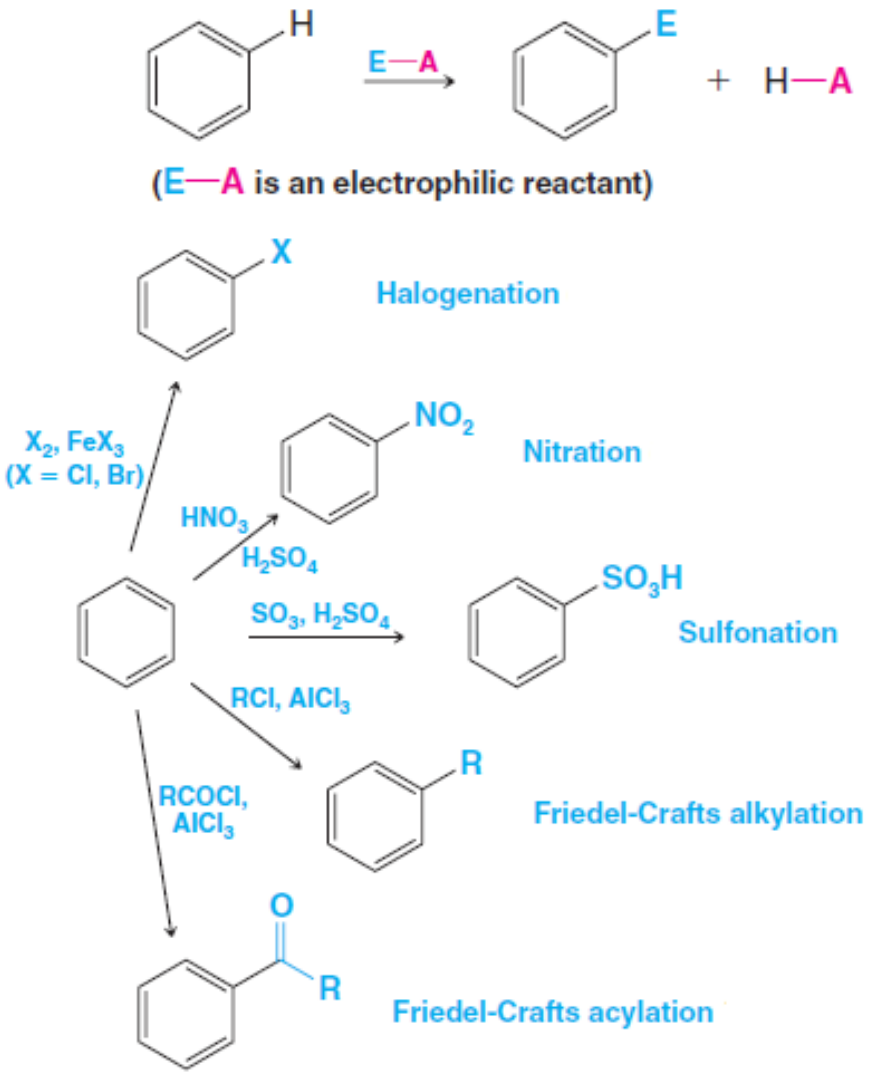


Molecule is not planar, so the *p* orbitals are not overlapping

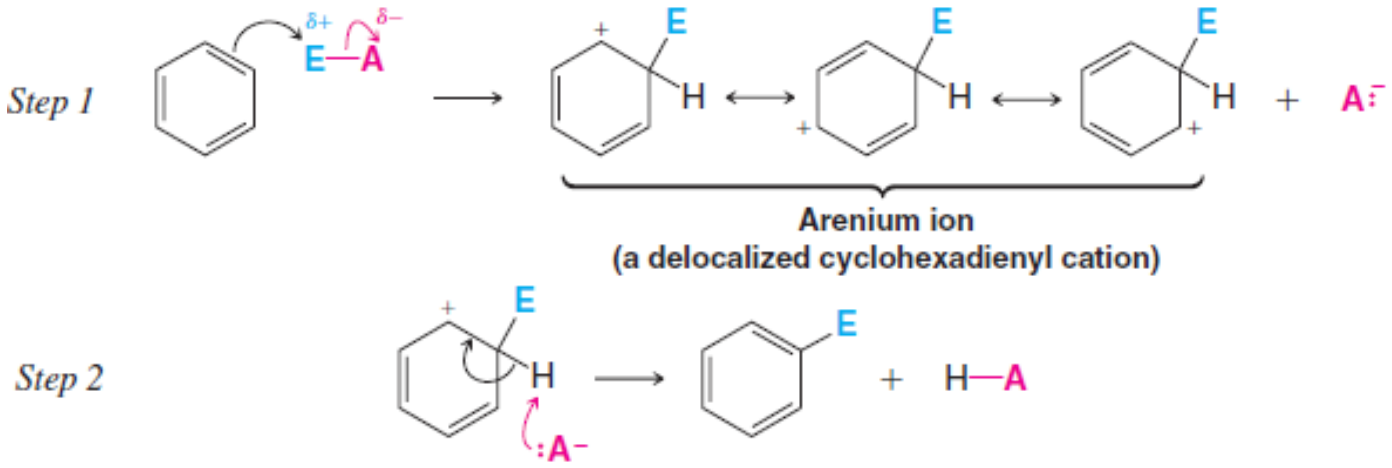
Compounds that satisfy the first criterion but have 4*n* electrons (rather than 4*n* + 2) are **antiaromatic**.

Reactions of Aromatic Compounds

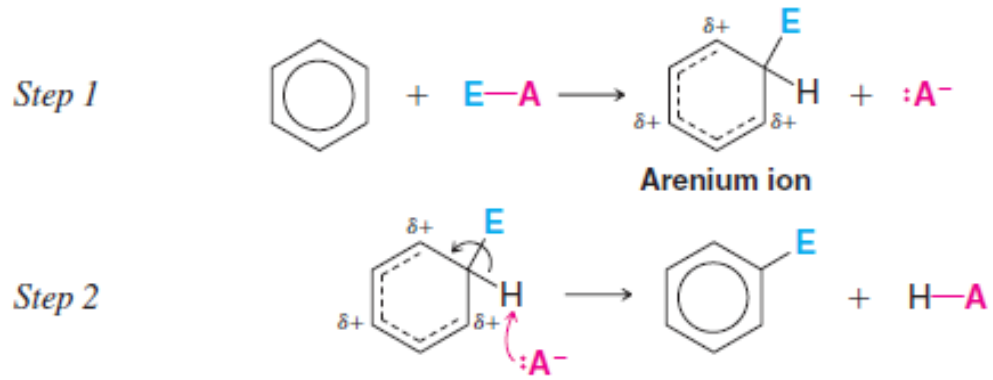
Electrophilic Aromatic Substitution Reactions:



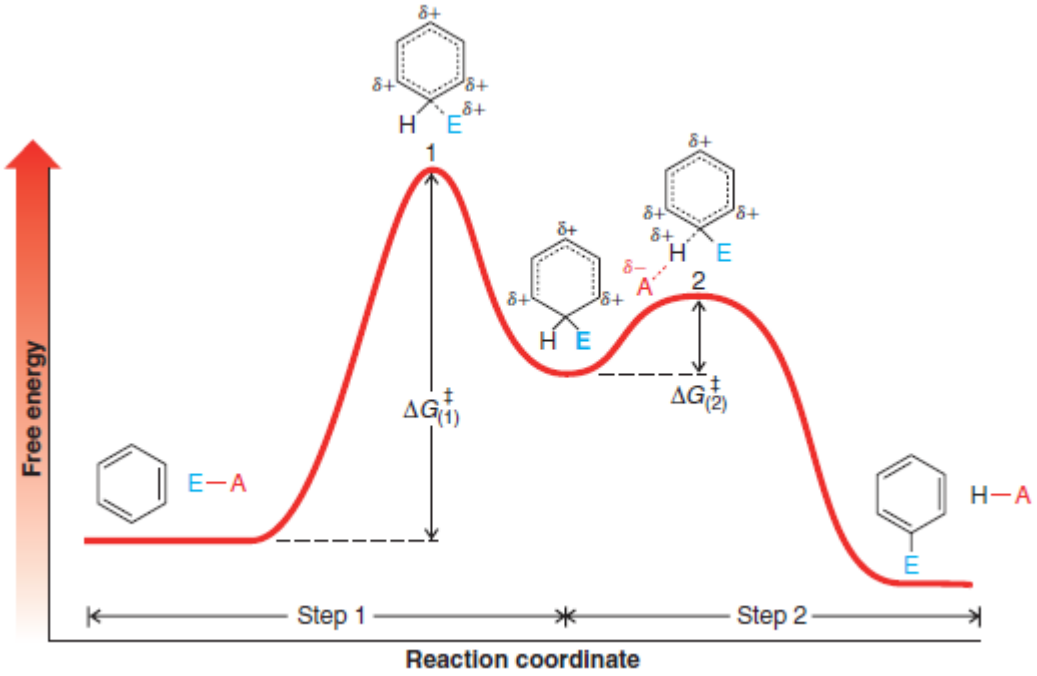
Mechanism of Electrophilic Aromatic Substitution



For brevity, we can show the mechanism using the hybrid formula for benzene:

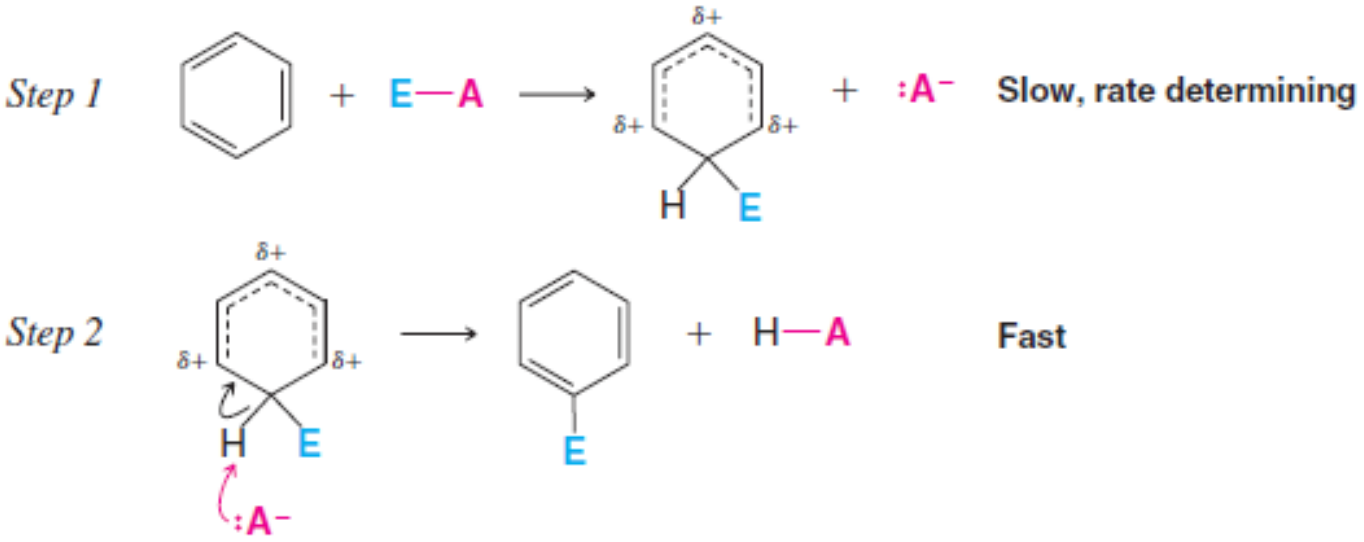


There is firm experimental evidence that the arenium ion is a true *intermediate* in electrophilic substitution reactions. It is not a transition state. This means that in a free-energy diagram the arenium ion lies in an energy valley between two transition states.



The reaction leading from benzene and an electrophile to the arenium ion is highly endothermic, because the aromatic stability of the benzene ring is lost. The reaction leading from the arenium ion to the substituted benzene, by contrast, is highly exothermic because it restores aromaticity to the system.

Of the following two steps, step 1 (the formation of the arenium ion) is usually the rate determining step in electrophilic aromatic substitution because of its higher free energy of activation:



Step 2, the removal of a proton, occurs rapidly relative to step 1 and has no effect on the overall rate of reaction.