# Aromatic Compounds

Organic Chemistry

## Pharmacy College/ 2nd Stage

Dr.Sham Wali Qurban

17.1 Introduction to Aromatic Compounds

Many derivatives of benzene were originally isolated from the fragrant balsams obtained from trees and plants, and these compounds were therefore described as being **aromatic** in reference to their pleasant odors. Over time, chemists discovered that many derivatives of benzene are, in fact, odorless.
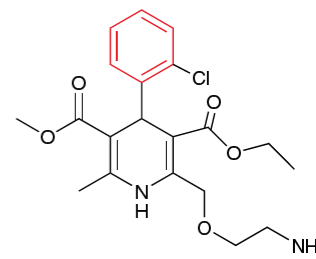
- Benzene rings are a particularly common structural feature in drugs. All of the following top-selling drugs contain the benzene-like aromatic ring
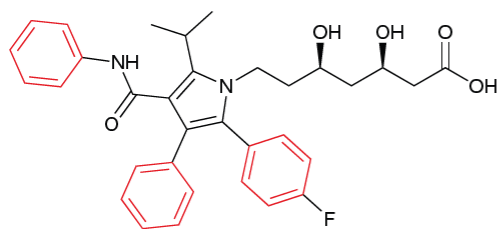
Lipitor (atorvastatin)
Lowers cholesterol levels and reduces risk of heart attack and stroke
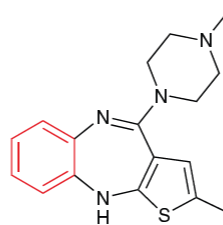
Zyprexa (olanzapine)
An antipsychotic used in the treatment of schizophrenia and bipolar disorder

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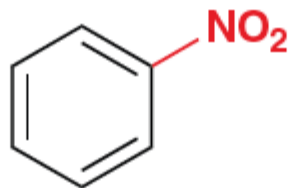Used in the treatment of angina and high blood pressure

17.2 Nomenclature of Benzene Derivatives

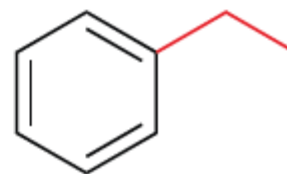**Monosubstituted Derivatives of Benzene**

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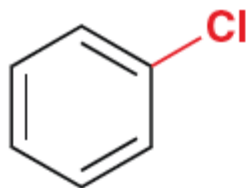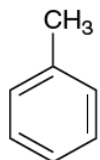

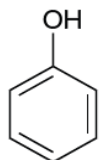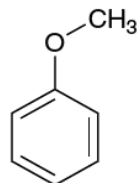**Chloro**benzene   **Nitro**benzene   **Ethyl**benzene

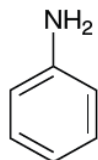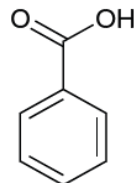The following are some monosubstituted aromatic compounds that have common names accepted by IUPAC.
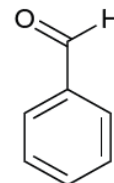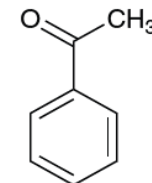

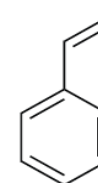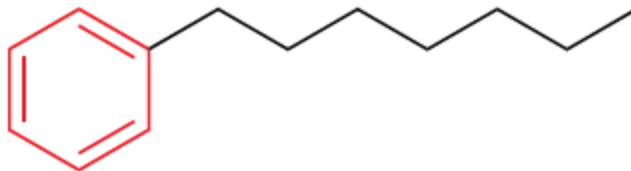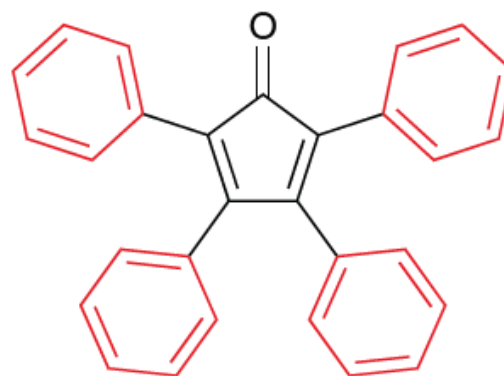Toluene   Phenol   Anisole   Aniline   Benzoic acid   Benzaldehyde   Acetophenone   Styrene

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

1-Phenylheptane

The presence of a phenyl group is often indicated with the abbreviation Ph.

Tetraphenylcyclopentadienone
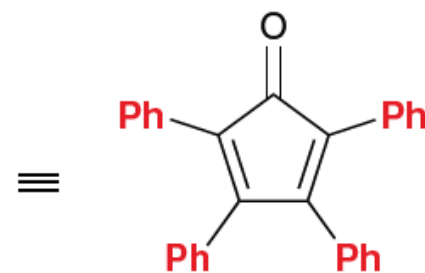
Disubstituted Derivatives of Benzene

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

ortho-Xylene
(1,2-dimethylbenzene)

meta-Xylene
(1,3-dimethylbenzene)
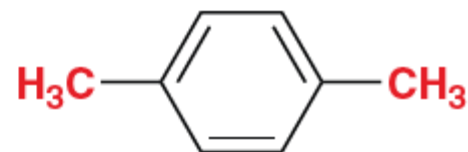
para-Xylene
(1,4-dimethylbenzene)
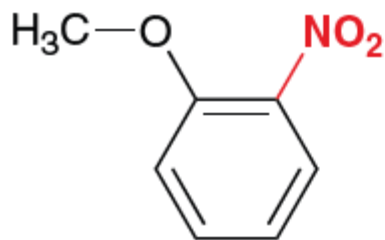
ortho-Nitroanisole
(2-Nitroanisole)
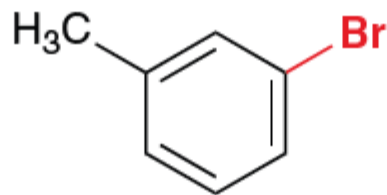
meta-Bromotoluene
(3-Bromotoluene)
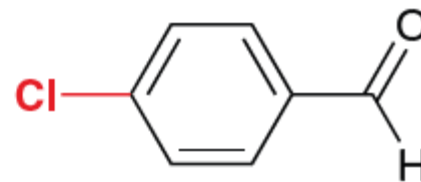
para-Chlorobenzaldehyde
(4-Chlorobenzaldehyde)

Polysubstituted Derivatives of Benzene

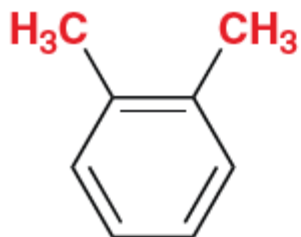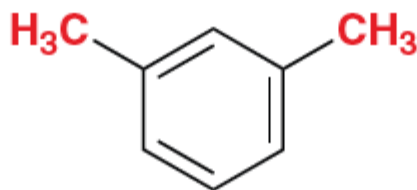When naming a **polysubstituted benzene ring**, we will follow the same four-step process used for naming alkanes, alkenes, alkynes, and alcohols.

1. Identify and name the parent.

2. Identify and name the substituents.

3. Assign a locant to each substituent.

4. Arrange the substituents alphabetically.

3,5-Dibromophenol

Correct

Incorrect
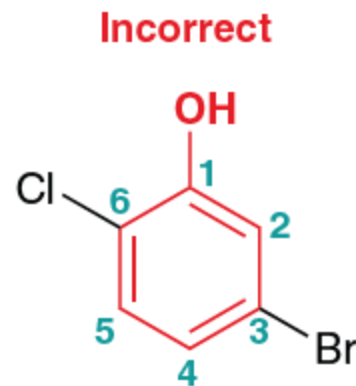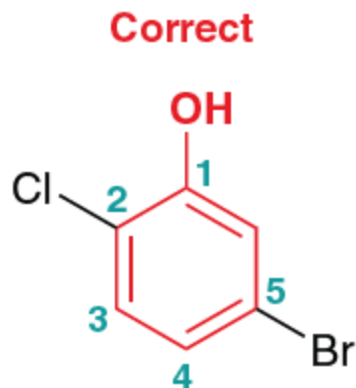
17.1 naming a polysubstituted benzene
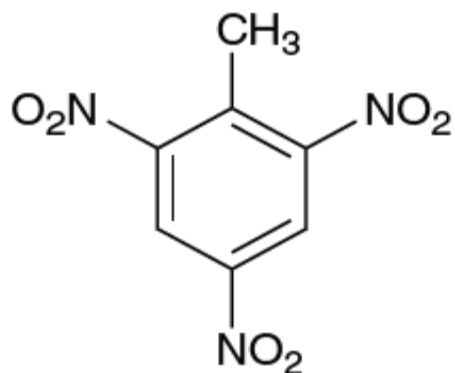
STEP 1

Identify and name the parent.

STEPS 2 AND 3

Identify the substituents and assign locants.

STEP 4

Arrange the substituents alphabetically.

2,4,6-Trinitrotoluene

17.1 Provide a systematic name for each of the following compounds:

(a)

(b)
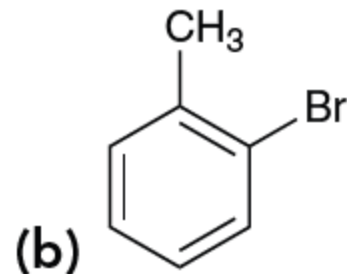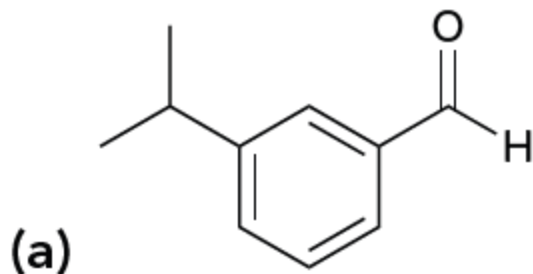
17.3 For each of the following compounds, draw its structure:

(a) 2,6-Dibromo-4-chloroanisole

(b) *meta*-Nitrophenol

17.3 Structure of 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.

In 1866, August Kekule used his recently published structural theory of matter to propose a structure for benzene. Specifically, he proposed a ring comprised of alternating double and single bonds.
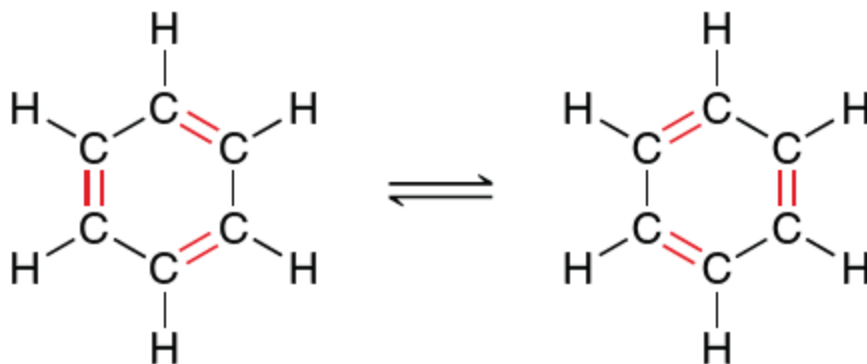
Kekule described the exchange of double and single bonds to be an equilibrium process.
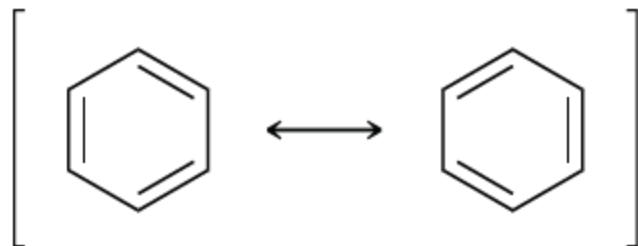
The resonance does not describe the motion of electrons, but rather, resonance is the way that chemists deal with the inadequacy of bond-line drawings.

The problem is that each C-C bond is neither a single bond nor a double bond, nor is it vibrating back and forth between these two states. Instead, each **C=C** bond has a bond order of 1.5, exactly midway between a single bond and a double bond.

To avoid drawing resonance structures, benzene is often drawn like this:
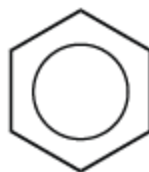
17.4 Stability of Benzene

Evidence for Unusual Stability

There is much evidence that aromatic rings are particularly stable, much more so than expected. Below, we will explore two pieces of evidence for this stability.

Alkenes readily undergo addition reactions. We might therefore expect benzene to undergo a similar reaction, perhaps even three times But in fact, **no reaction is observed**
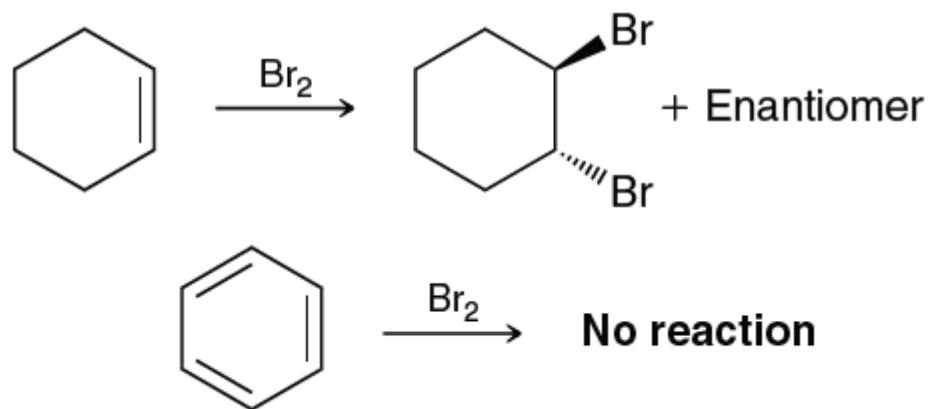
The aromatic ring apparently exhibits a special stability that would be lost if an addition reaction were to occur.

The stability of aromatic rings is also observed when comparing heats of hydrogenation for several similar compounds.

$\Delta H° = -120$ kJ/mol

(100%)

Expected:
$\Delta H° = -360$ kJ/mol

Actual:
$\Delta H° = -208$ kJ/mol

(100%)
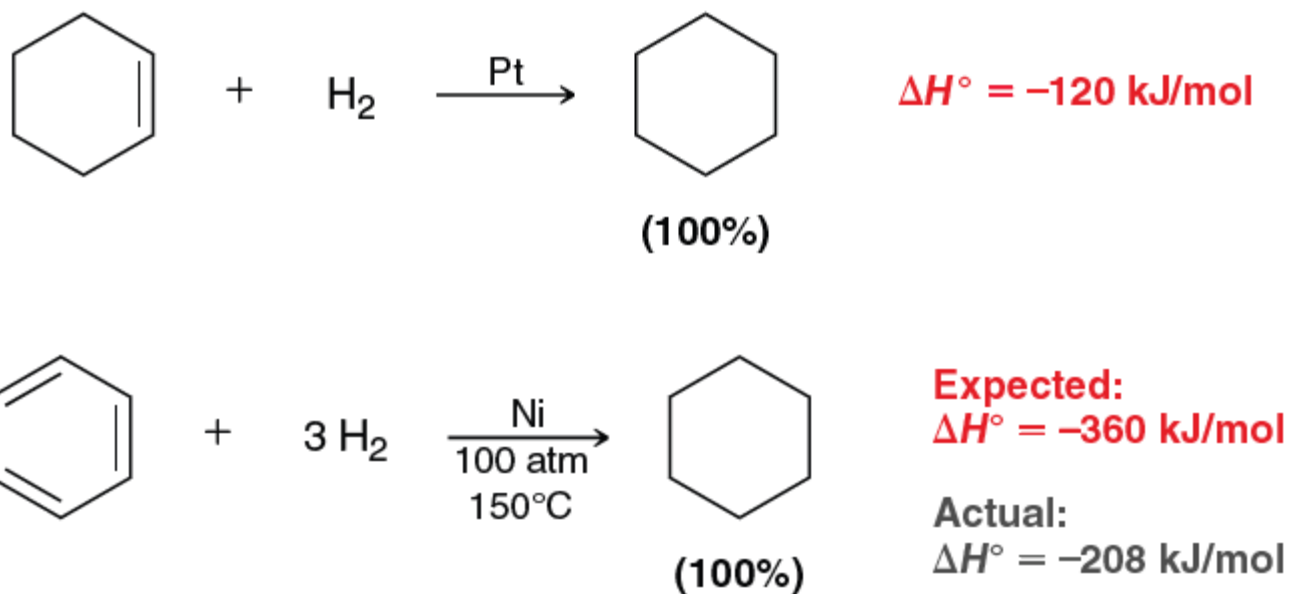
The difference between the expected value (−360) and the observed value (−208) is **152 kJ/mol**, which is called the *stabilization energy* of benzene. This value represents the amount of stabilization associated with aromaticity.
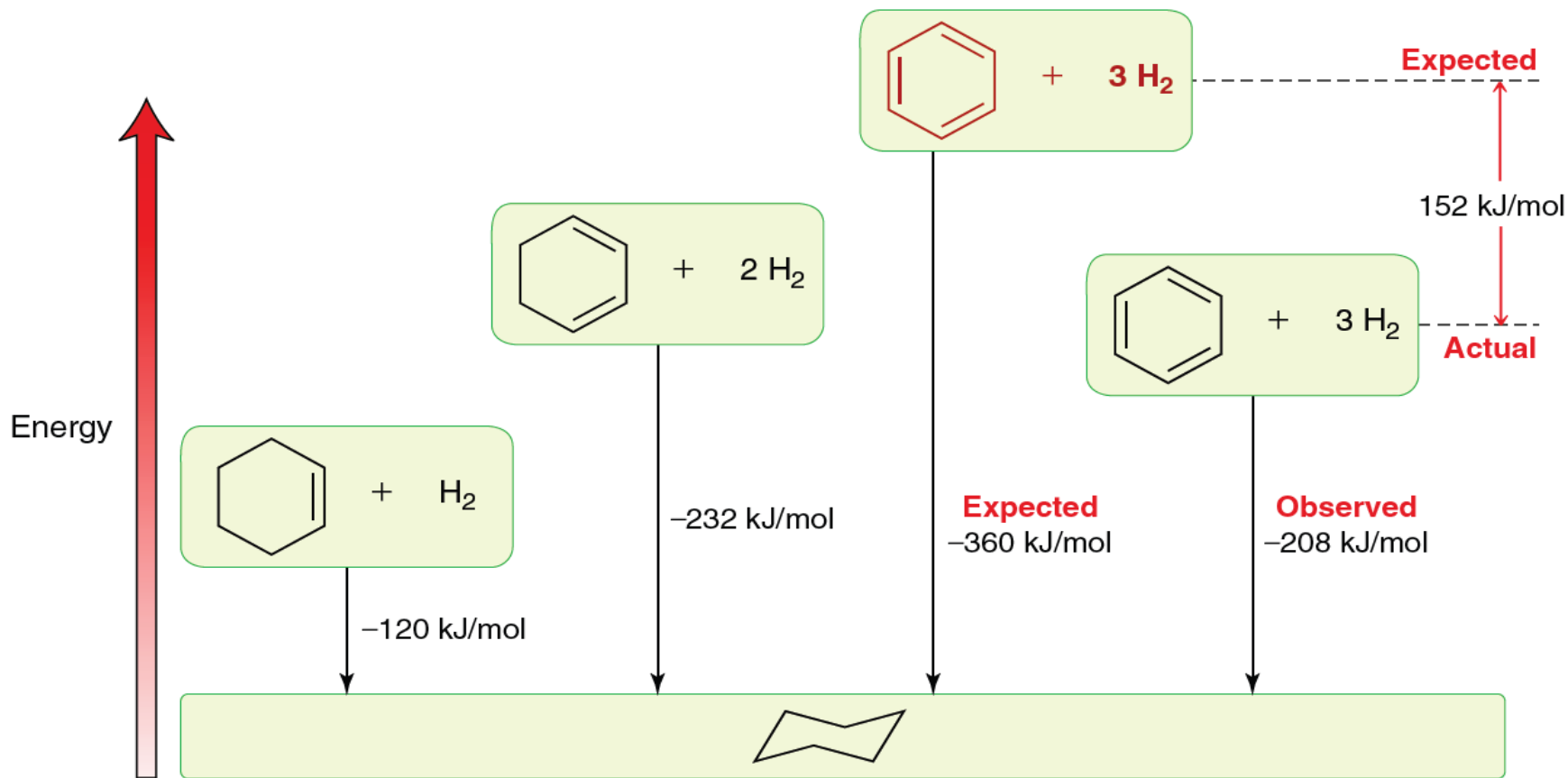
FIGURE 17.1

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

Source of Stability
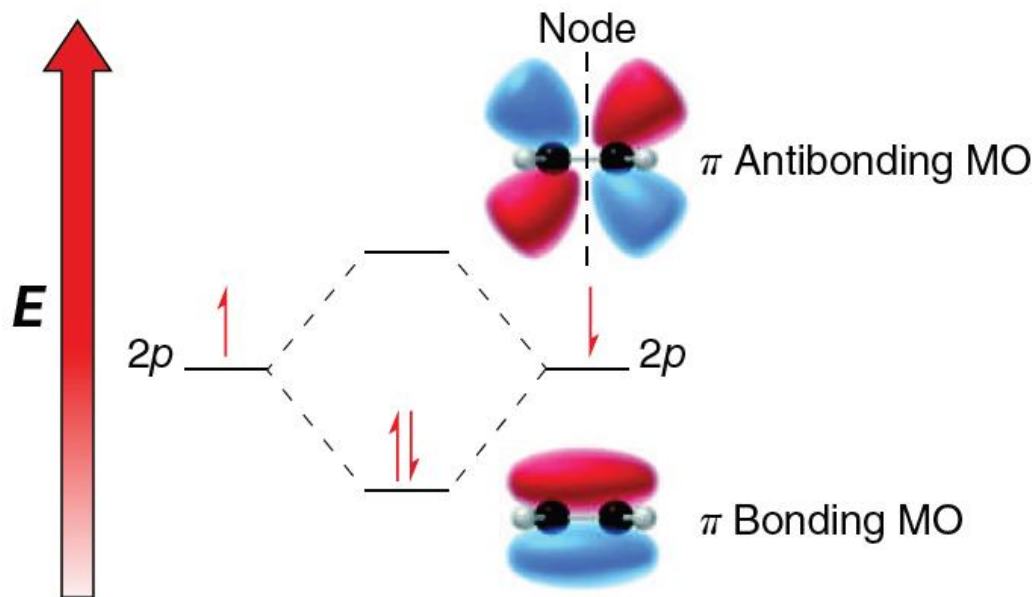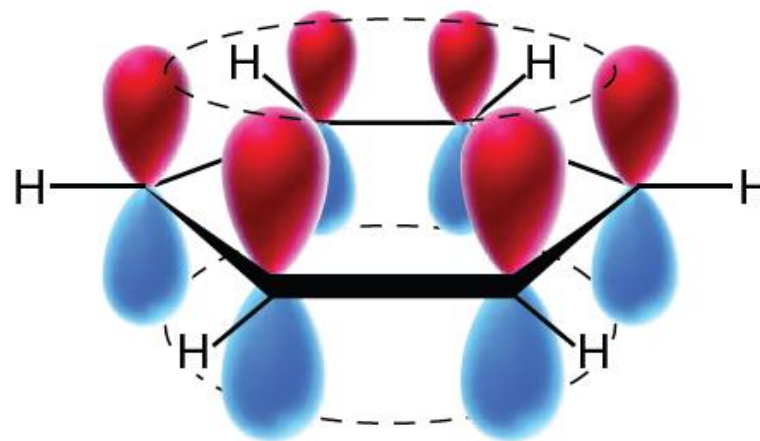
FIGURE 17.2
The molecular orbitals of a π bond.

Node
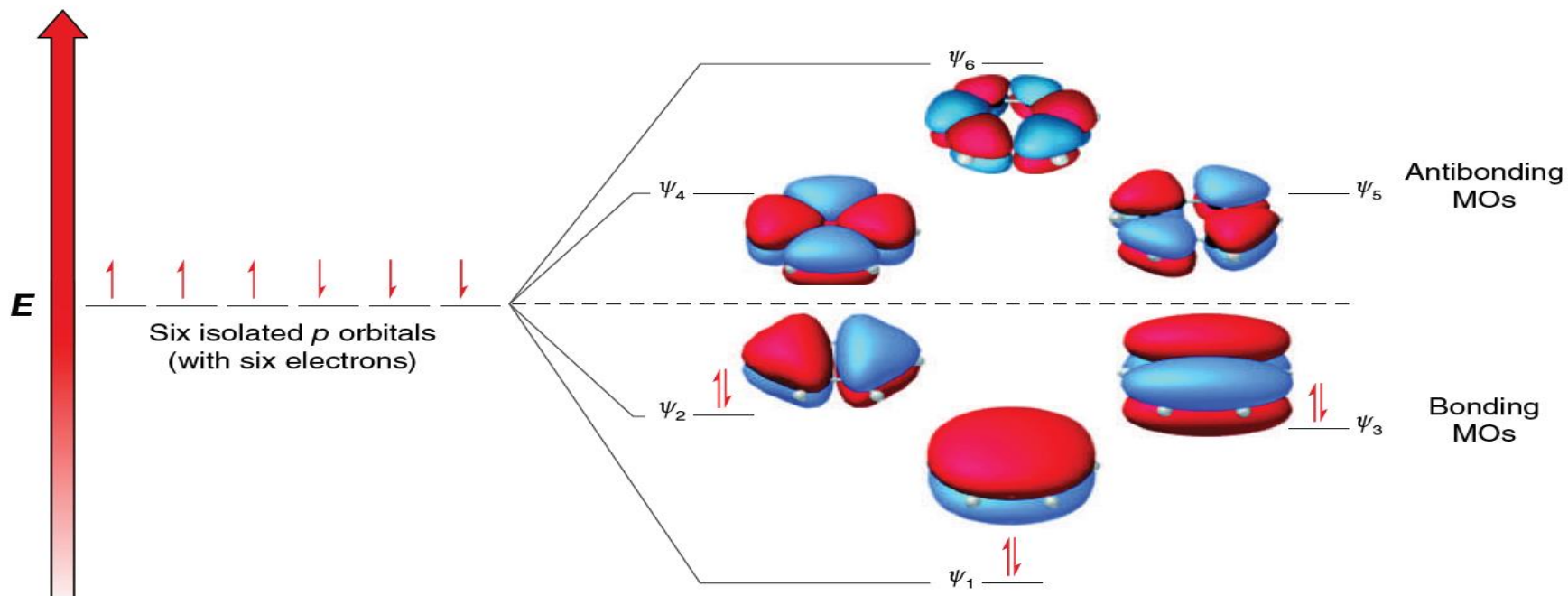
π Antibonding MO

E

2p

2p

π Bonding MO

FIGURE 17.3
The *p* orbitals of benzene overlap continuously around the ring.

➢ There are six molecular orbitals, each of which is associated with the entire molecule (rather than being associated with any specific bond).

➢ Three of the six MOs (those below the dashed line) are **bonding MOs**, while the other three MOs (those above the dashed line) are **antibonding MOs**.

➢ Since each MO can contain two electrons, the three bonding MOs can collectively accommodate up to six π electrons.

➢ By occupying the bonding MOs, all six electrons achieve a lower energy state and are delocalized. Since the bonding MOs are filled with paired electrons while the antibonding MOs are empty, benzene is said to have a closed-shell electron configuration, and this is the source of the stabilization energy associated with benzene.

Hückel's Rule

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

Cyclobutadiene
(C_4H_4)

Cyclooctatetraene
(C_8H_8)
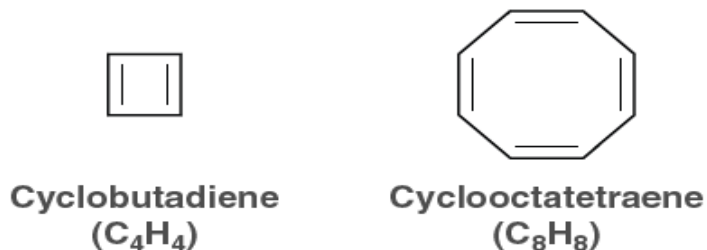
The reactivity of this compound suggests that cyclooctatetraene does not exhibit the same stability exhibited by benzene.

Br_2 → + Enantiomer
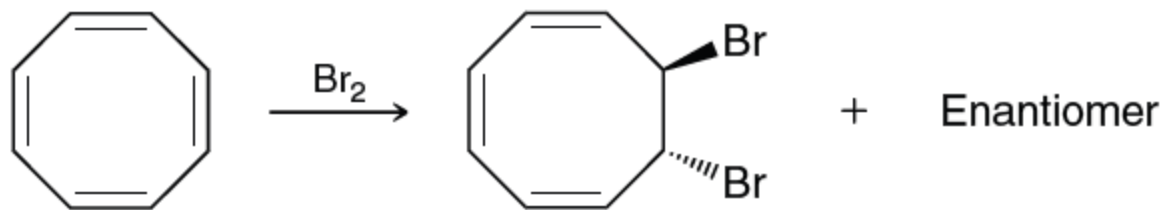
Cyclobutadiene is so unstable that it reacts with itself at −78°C in a Diels–Alder reaction.
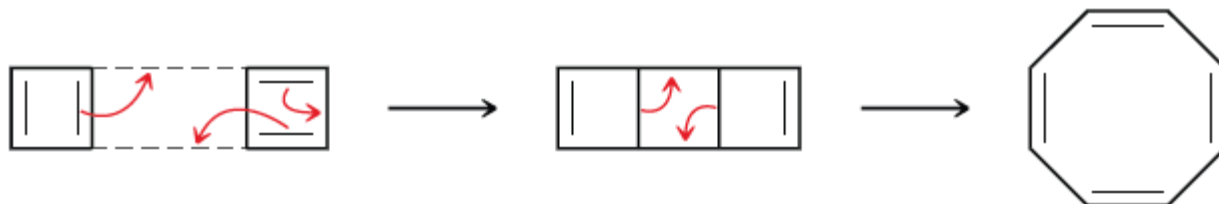
These observations indicate that the presence of a fully conjugated ring of π electrons is not the sole requirement for aromaticity; the number of π electrons in the ring is also important. Specifically, we have seen that an odd number of electron pairs is required for aromaticity.

2 pairs of
π electrons

3 pairs of
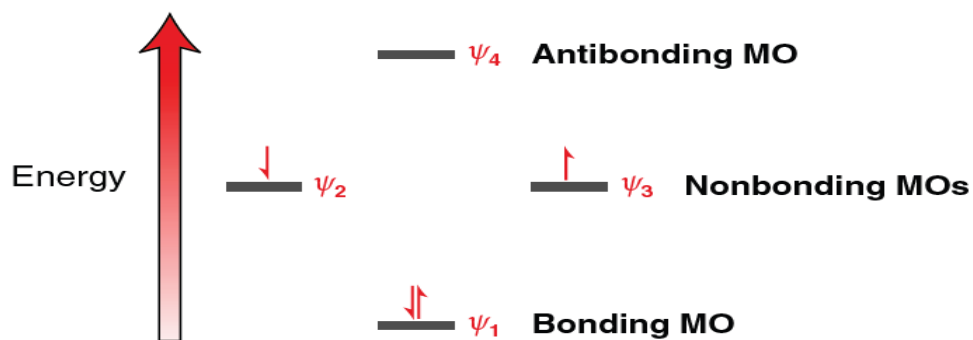π electrons

4 pairs of
π electrons
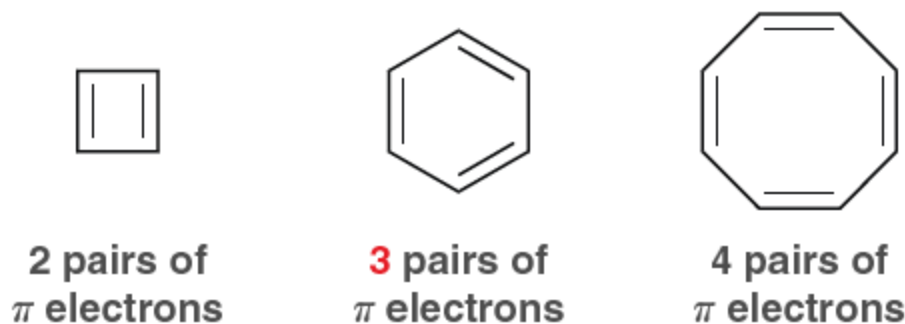
The requirement for an odd number of electron pairs is the basis for **Hückel's rule**, which states that a compound can only be aromatic if the number of π electrons in the ring is 2, 6, 10, 14, 18, and so on. This series of numbers can be expressed mathematically as **4n+ 2**, where n is a whole number.
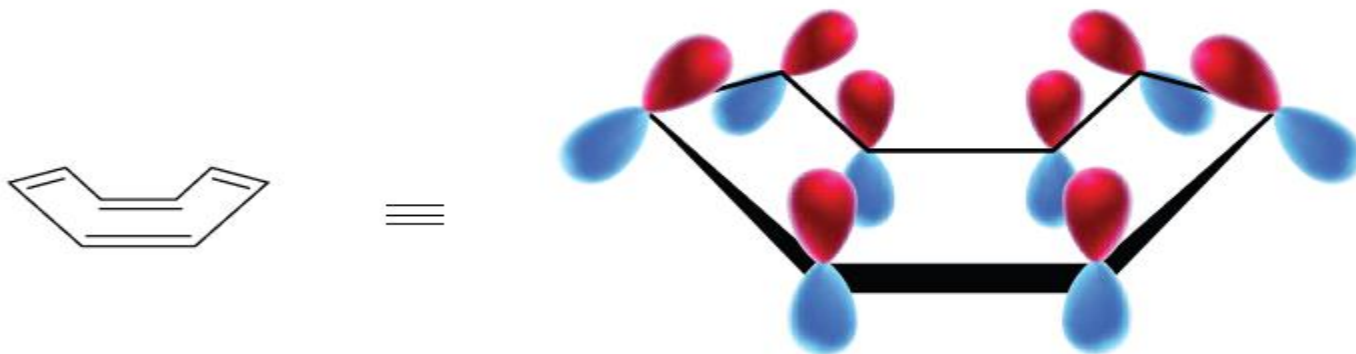
MO Theory and Frost Circles
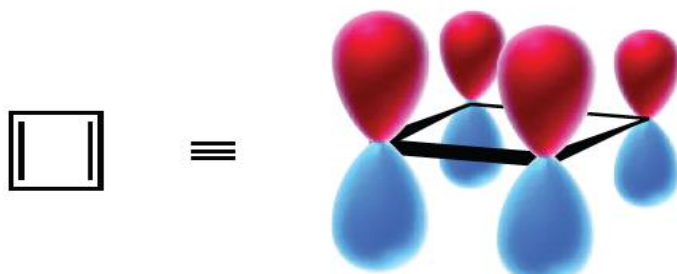
According to MO theory, these four atomic orbitals are replaced with four molecular orbitals, with the relative energy levels shown in Figure 17.6.
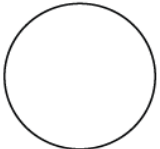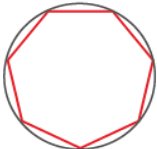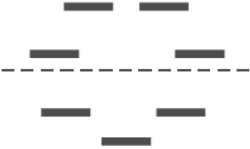

In the case of **benzene**, all of the π electrons are paired in bonding MOs, giving a closed-shell electron configuration. In contrast, **square cyclobutadiene** (Figure 17.6) lacks a closed-shell electron configuration, and this is the source of its instability. Due to its unusual instability, this compound is said to be **antiaromatic**.

ψ_8

ψ_6 $\qquad$ ψ_7 **Antibonding MOs**

Energy ψ_4 - - - - - ψ_5 - - - - **Nonbonding MOs**

ψ_2 $\qquad$ ψ_3 **Bonding MOs**

ψ_1
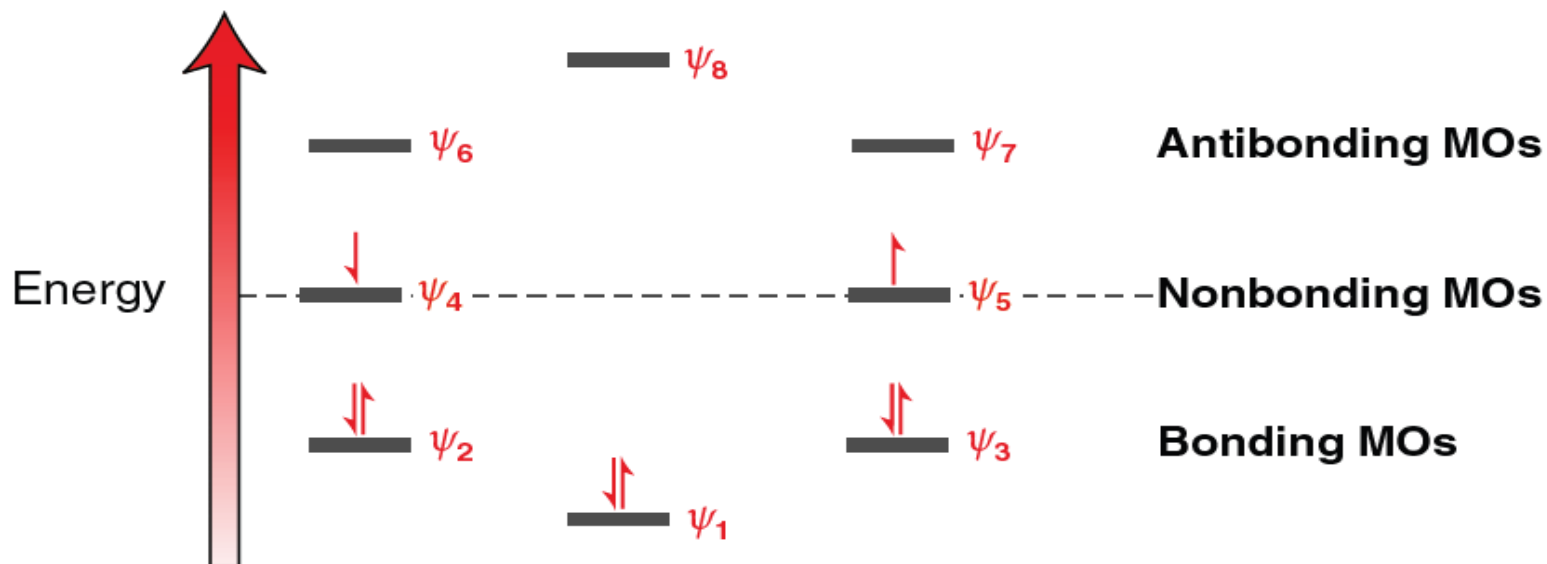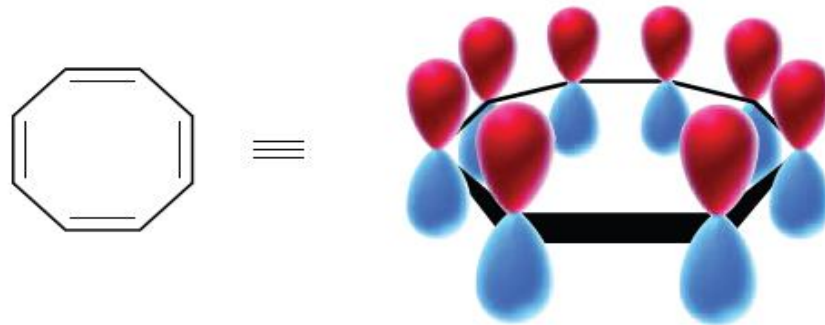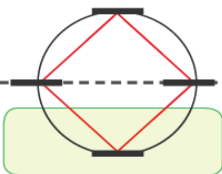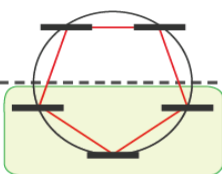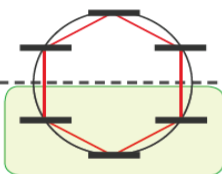
Two of the electrons are unpaired and occupy nonbonding orbitals. Once again, this open-shell electron configuration is expected to be unstable, and the compound should be **antiaromatic**. But the compound can avoid this unnecessary instability by assuming a tub shape

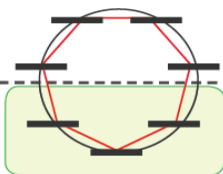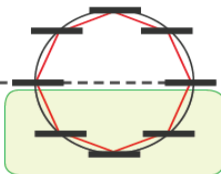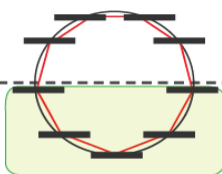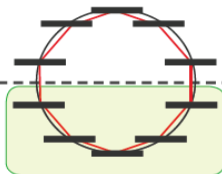| STEP 1 Draw a circle.	STEP 2 Inscribe a polygon, making sure that one of the connecting points is at the bottom of the circle.	STEP 3 Draw a horizontal line at each point of intersection.	STEP 4 Draw a dotted horizontal line through the center of the circle, and then erase the circle and polygon.	STEP 5 Identify all bonding MOs (below the line), nonbonding MOs (on the line), and antibonding MOs (above the line).

This method was first developed by Arthur Frost (Northwestern University), and it is referred to as a **Frost circle**.

Four-membered ring	Five-membered ring	Six-membered ring	Seven-membered ring	Eight-membered ring	Nine-membered ring	Ten-membered ring
1 Bonding MO	3 Bonding MOs	3 Bonding MOs	3 Bonding MOs	3 Bonding MOs	5 Bonding MOs	5 Bonding MOs

# 17.5 Aromatic Compounds Other Than Benzene

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 π electrons in the ring must be a Huckel 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
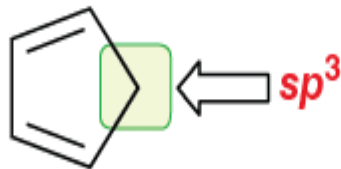
Not a continuous system
of *p* orbitals

sp^3

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

Compounds that satisfy the first criterion but have $4n$ π electrons (rather than $4n+ 2$) are **antiaromatic**. In practice, there are very few examples of antiaromatic compounds, because most compounds can change their geometry to avoid being antiaromatic,
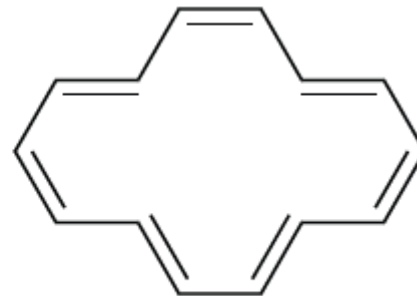
Annulenes

Annulenes are compounds consisting of a single ring containing a fully conjugated π system.
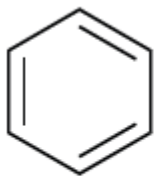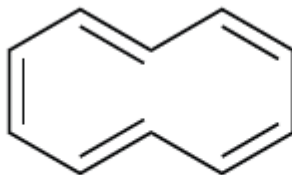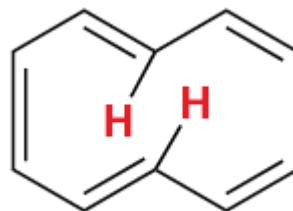

[6]Annulene   [10]Annulene   [14]Annulene

[10]annulene does not meet the first criterion for aromaticity. It is nonaromatic.

the hydrogen atomspositioned inside the ring (shown in red) experience a steric interaction that forces the compound out of planarity

[14]annulene is nonplanar, it does indeed exhibit aromatic stabilization, because the deviation from planarity is not too great.

[18]Annulene has been found to be nearly planar, and is therefore aromatic, as we would expect.

Aromatic Ions

Three bonding MOs can accommodate six π electrons
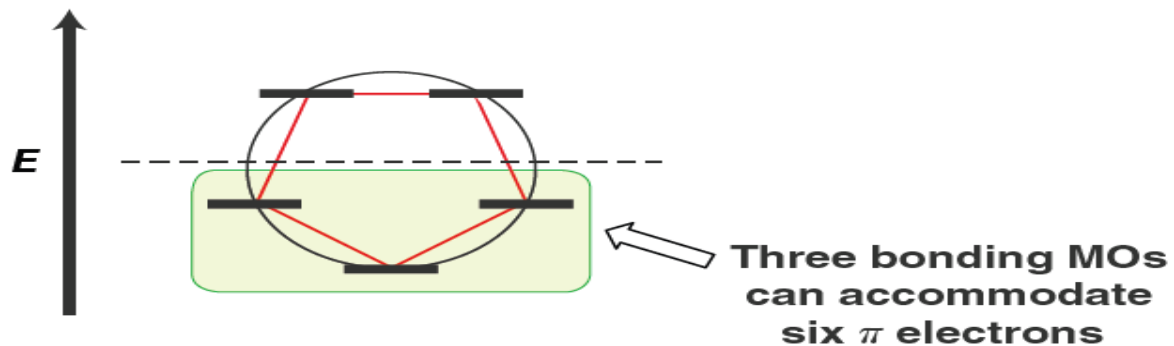
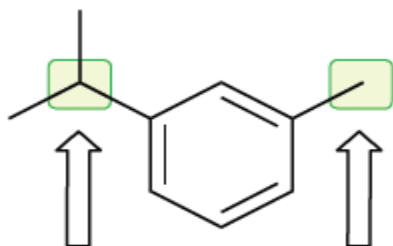**The resulting anion, called the cyclopentadienyl anion, has five resonance structures.**

In order to have six π electrons in a seven-membered ring, one of the carbon atoms must possess an empty *p* orbital (a carbocation). The resulting ion is called the tropylium cation, and it has seven resonance structures.
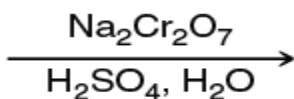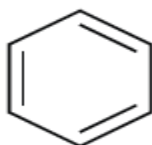
Three bonding MOs can accommodate six π electrons
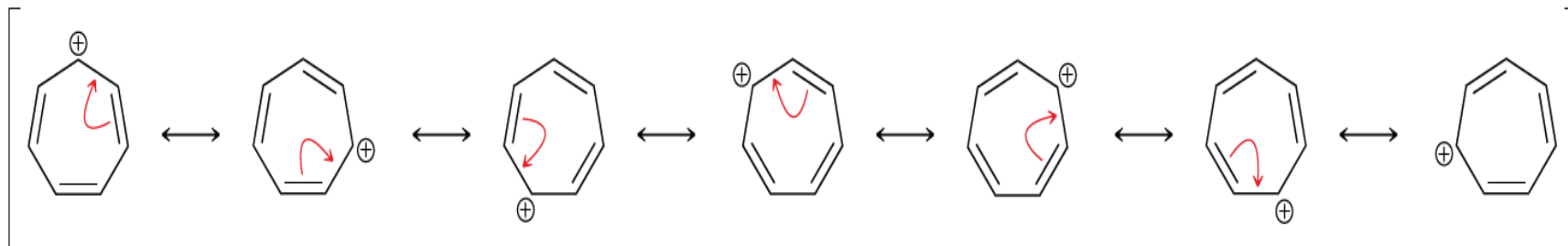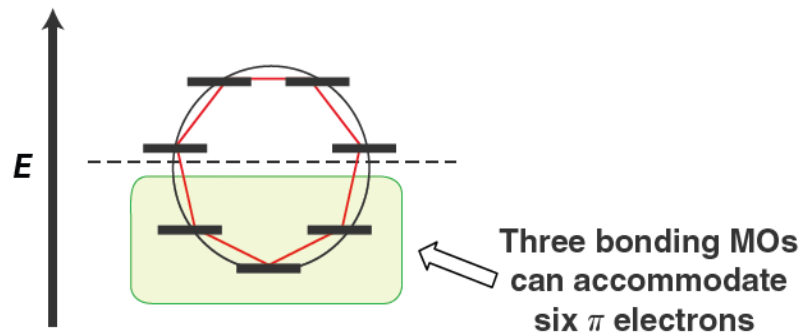
17.6 Reactions at the Benzylic Position

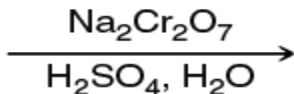Any carbon atom attached directly to a benzene ring is called a **benzylic position**:
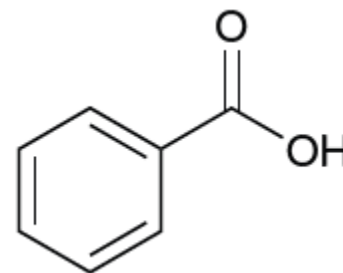

Benzylic positions

Oxidation

Na$_2$Cr$_2$O$_7$ / H$_2$SO$_4$, H$_2$O → **No reaction**

KMnO$_4$ / H$_2$O, heat → ... H$_3$O$^+$ →
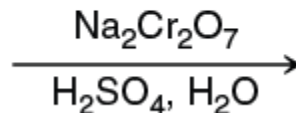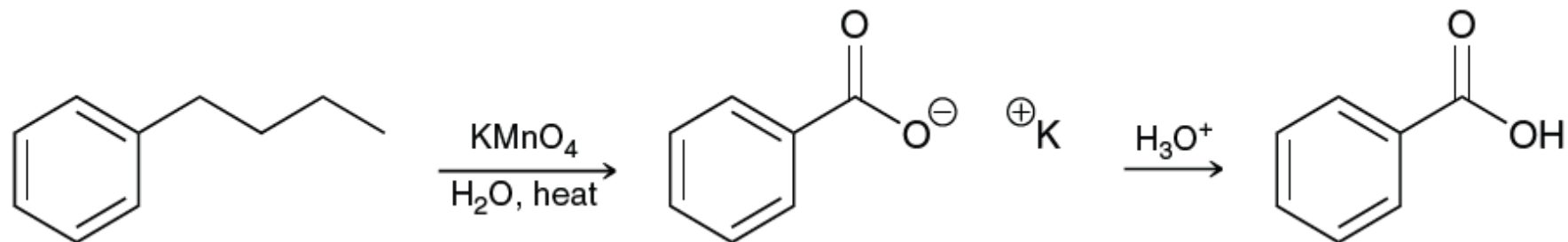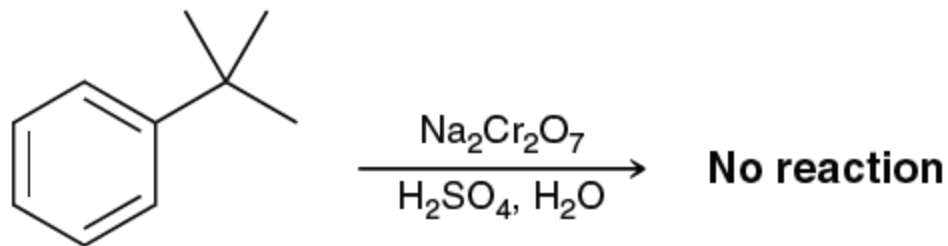
Free-Radical Bromination

NBS, heat
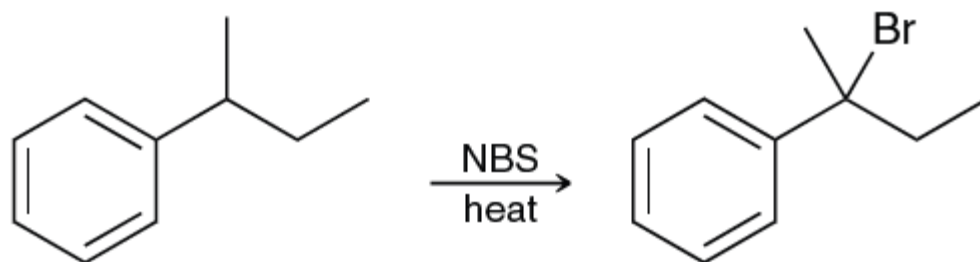
The reaction is highly regioselective (bromination occurs primarily at the benzylic position) due to resonance stabilization of the intermediate benzylic radical.

Substitution Reactions of Benzylic Halides

benzylic halides undergo S_N1 reactions rapidly.
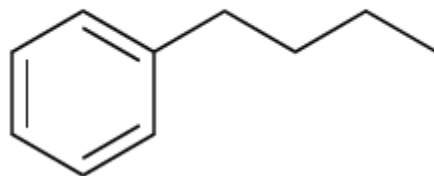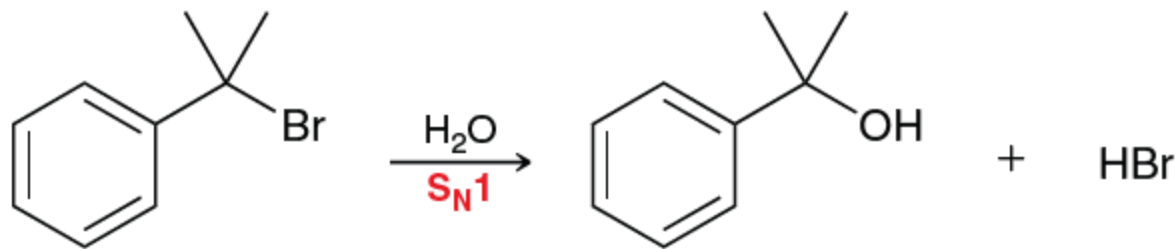

The relative ease of the reaction is attributed to the stability of the carbocation intermediate. Specifically, a benzylic carbocation is resonance stabilized.
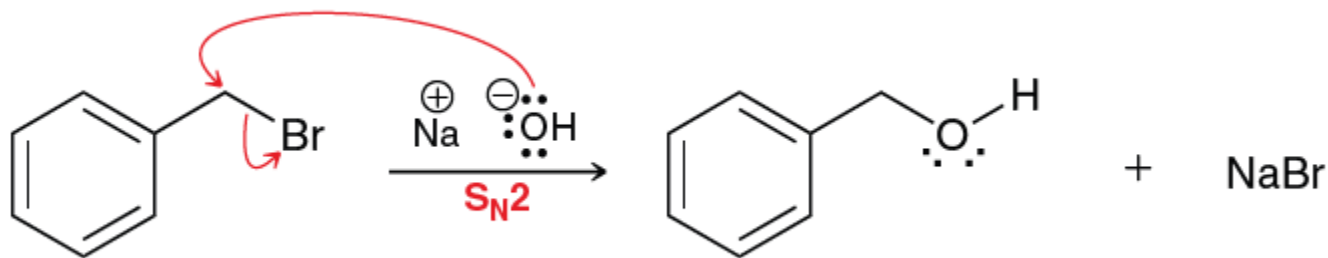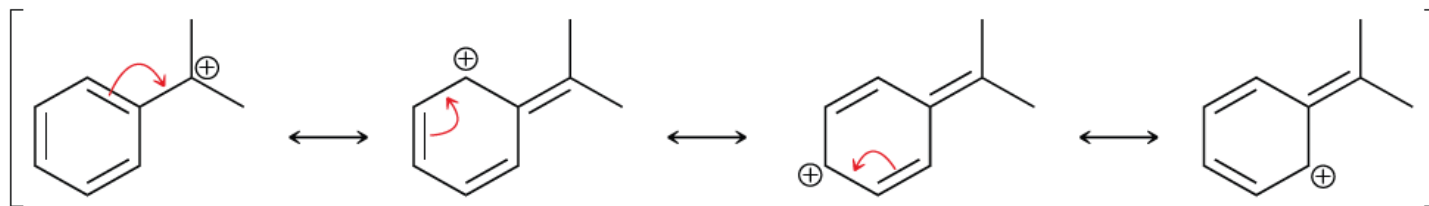
Elimination Reactions of Benzylic Halides

The relative ease of the reaction is attributed to the stability of the carbocation intermediate (a benzylic carbocation)

The relative ease of the reaction is attributed to the low energy of the transition state as a result of conjugation between the forming double bond and the aromatic ring.

17.4 Propose an efficient synthesis for the following transformation:

17.7 Reduction of Benzene and Its Derivatives:

Hydrogenation
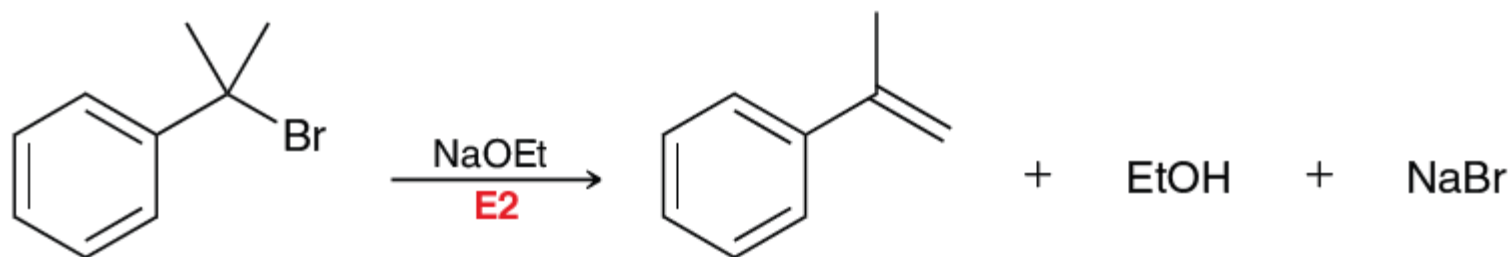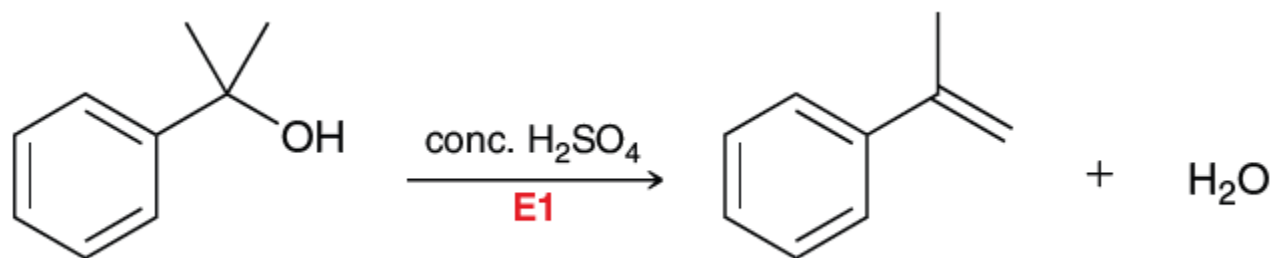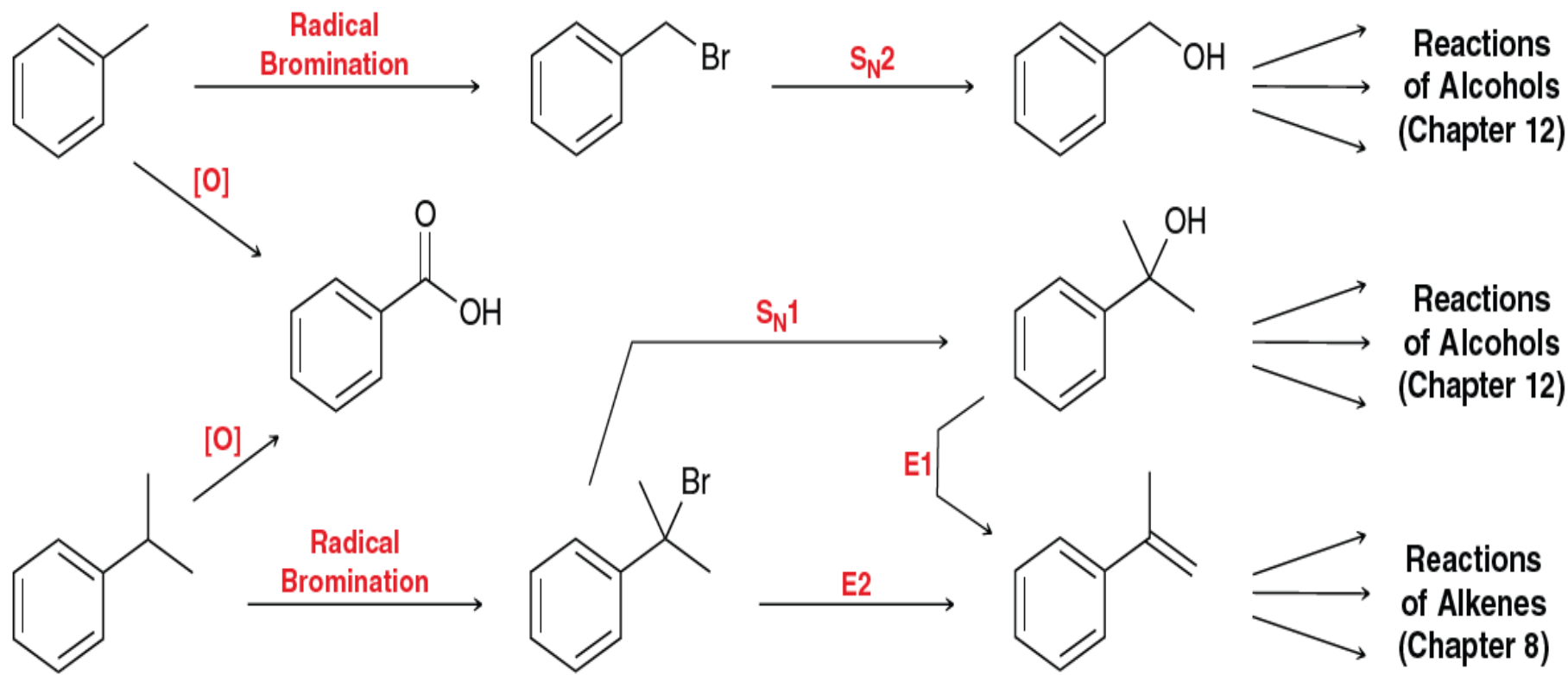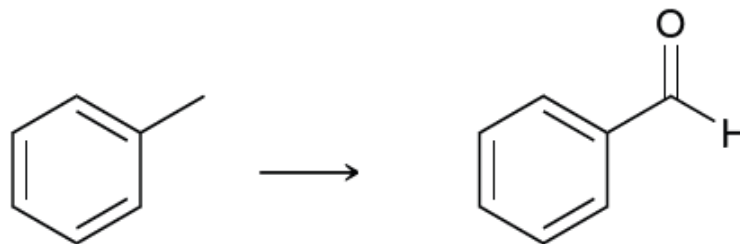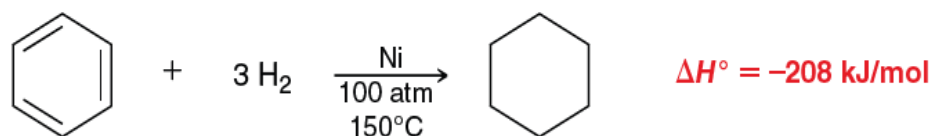
Recall from Section 17.4 that under forcing conditions benzene will react with three equivalents of molecular hydrogen to produce cyclohexane:

$$\text{benzene} + 3\ H_2 \xrightarrow[\substack{100\ \text{atm} \\ 150°C}]{\text{Ni}} \text{cyclohexane} \qquad \Delta H° = -208\ \text{kJ/mol}$$

With some catalysts and under certain conditions, it is possible to hydrogenate a vinyl group selectively in the presence of an aromatic ring:

$$\text{styrene} + H_2 \xrightarrow[\substack{2\ \text{atm} \\ 25°C}]{\text{Pt}} \text{ethylbenzene} \qquad \Delta H° = -117\ \text{kJ/mol}$$

(100%)
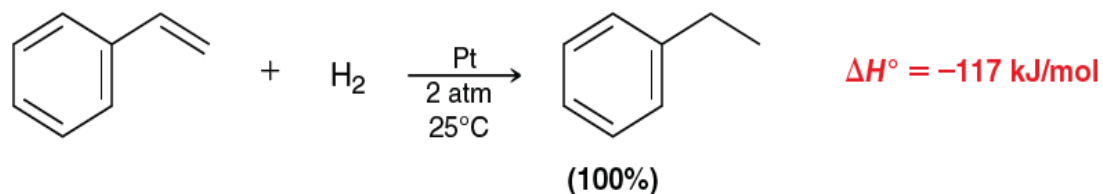
The vinyl group is reduced, but the aromatic ring is not. Notice that ΔH for this reaction is slightly lower than what we expect for a double bond (-120 kJ/mol), which can be attributed to the fact that the double bond is conjugated in this case.

Birch Reduction
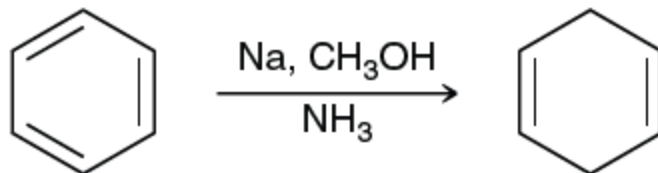
MECHANISM 17.1 THE BIRCH REDUCTION

Nucleophilic attack	Proton transfer	Nucleophilic attack	Proton transfer

A single electron is transferred from the sodium atom to the aromatic ring

A radical anion

Methanol donates a proton to the radical anion, generating a radical intermediate
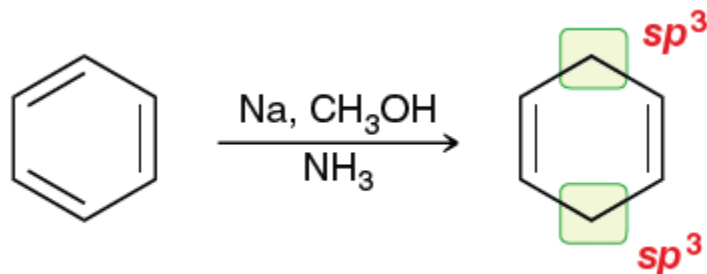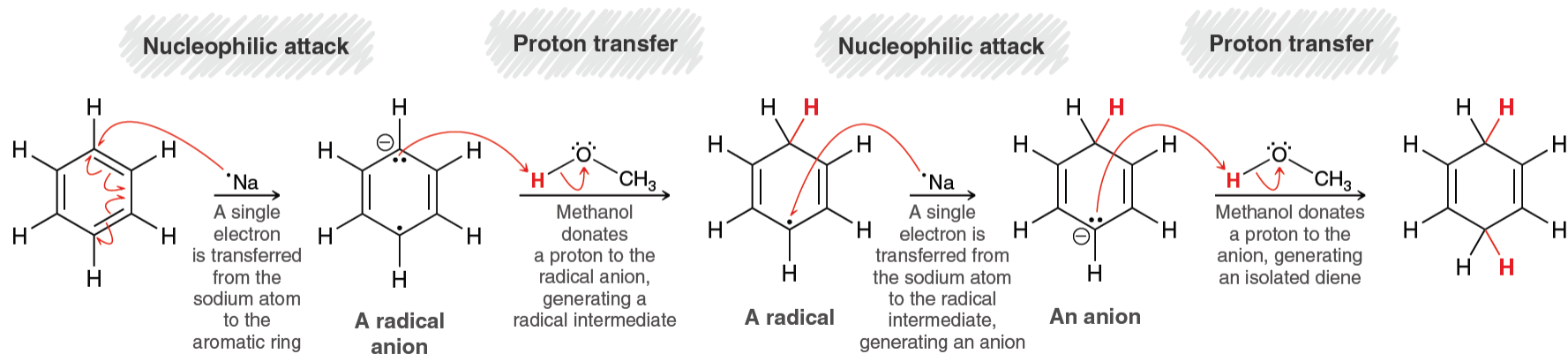
A radical

A single electron is transferred from the sodium atom to the radical intermediate, generating an anion

An anion

Methanol donates a proton to the anion, generating an isolated diene

sp^3

sp^3
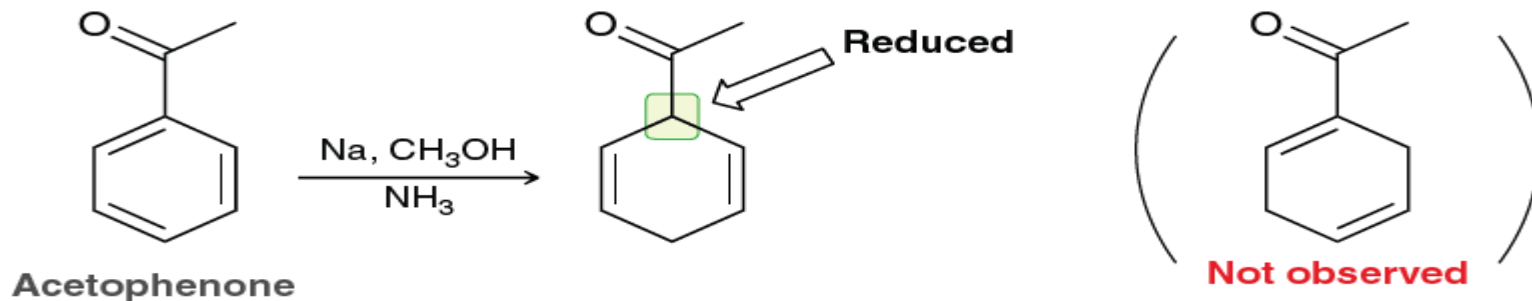
When an alkylbenzene is treated with Birch conditions, the carbon atom connected to the alkyl group is not reduced:
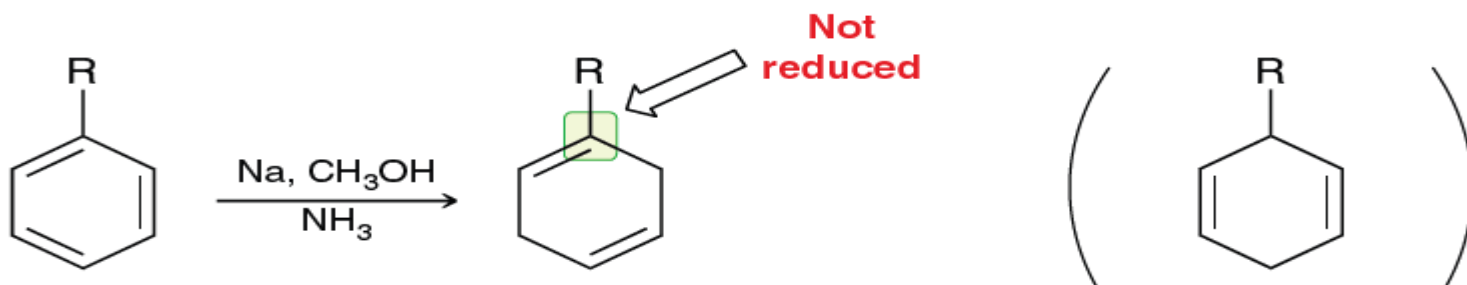
Why not? Recall that alkyl groups are electron donating. This effect destabilizes the radical anion intermediate that is necessary to generate the product that is not observed.

The carbonyl group is electron withdrawing via resonance. This electron- withdrawing effect stabilizes the intermediate that is necessary to generate the observed product.

17.5 Predict the major product obtained when the following compound is treated with Birch conditions:

Carbonyl group is electron withdrawing

Alkyl group is electron donating

Will be reduced

Will not be reduced

Na
CH$_3$OH
NH$_3$