WELCOME

TO

This is an Education Platform

We Provide PDF Notes for Pharmacy Students

Web Site http://www.fdspharmacy.in/

You tube https://www.youtube.com/c/FDSpharmacy

Telegram https://t.me/Fdspharmacy

App https://play.google.com/store/apps/details?id=com.FDSPharmacyMedia.FDSPharmacy

E-mail fdspharmacyinfo@gmail.com

PHARMACEUTICAL ORGANIC CHEMISTRY - II

UNIT 1

TOPIC :

- **Benzeneand its derivatives**

  Analytical, synthetic and other evidences in the derivation of structure

  of benzene, Orbital picture, resonance in benzene, aromatic characters, Huckel's rule

BENZENE

→ Benzene is a colorless, highly flammable organic liquid with a pleasant, sweet odor.
→ Its chemical formula is C_6H_6, meaning it contains 6 carbon atoms and 6 hydrogen atoms.
→ Benzene is a hydrocarbon, specifically an aromatic hydrocarbon, because of its stable ring structure and distinct chemical behavior.
→ It has a boiling point of 80°C and a melting point of 5.5°C.
→ Benzene is less dense than water and does not mix with water, but it is soluble in organic solvents like ether, alcohol, and acetone.
→ Natural sources of benzene include volcanic eruptions, forest fires, and crude oil (petroleum).
→ It is also produced during the burning of tobacco, gasoline, and other fossil fuels.
→ Benzene and its derivatives that exhibit similar chemical properties are classified as Aromatic Compounds.
→ The name "aromatic" originally came from the fragrant smell of these compounds, though now it refers to their structure.
→ Benzene is carcinogenic (cancer-causing) and highly toxic to humans, particularly affecting the bone marrow and blood-forming organs.
→ Prolonged exposure to benzene can lead to leukemia and other blood disorders, which is why its use is strictly regulated in industries.

STRUCTURE OF BENZENE

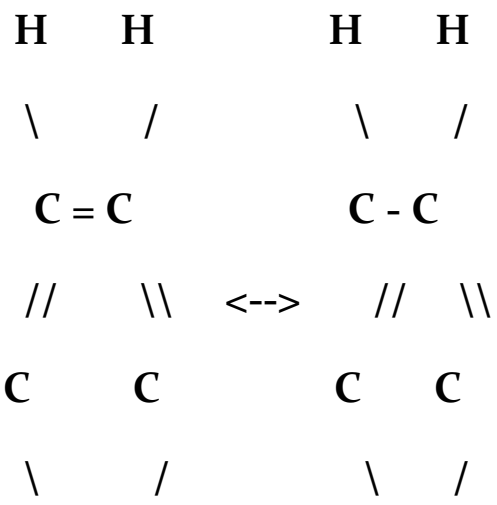
→ The molecular formula of benzene is C_6H_6, which indicates a high degree of unsaturation (fewer hydrogen atoms compared to alkanes).
→ In 1865, Sir August Kekulé proposed the first structural model of benzene.
→ He suggested that benzene is a six-membered carbon ring with three alternating double bonds.
→ This structure became known as the Kekulé Structure of Benzene.

Kekulé's Theory:

- According to Kekulé, each carbon in benzene is sp^2 hybridized and forms:
  - Two sigma (σ) bonds with adjacent carbon atoms.
  - One sigma bond with a hydrogen atom.
- The three double bonds are not fixed but alternate rapidly between positions. This concept was introduced to satisfy the tetravalency of carbon atoms.

Kekulé Structures of Benzene:

- The two resonating forms are shown as:



H H H H

Limitations of Kekulé's Structure:

While Kekulé's model was a major breakthrough, it could **not explain** some key characteristics of benzene:

1. **Equal bond lengths**: In benzene, all six carbon-carbon bonds are equal in length (139 pm), intermediate between single (154 pm) and double bonds (134 pm).
2. **Resistance to addition reactions**: Unlike alkenes, benzene does not undergo typical addition reactions. Instead, it prefers substitution reactions, indicating extra stability.
3. **Heat of hydrogenation**: The observed heat of hydrogenation of benzene is much lower than expected, which shows delocalization of electrons and extra stability.
4. **Unusual stability (Aromaticity)**: The high stability of benzene could not be justified by alternating double bonds.

CHEMICAL REACTIONS

→ Benzene behaves differently from other unsaturated compounds like alkenes.
→ It undergoes substitution reactions instead of addition reactions, which is unusual for a compound containing multiple double bonds.
→ This behavior indicates that benzene is highly stable and aromatic.

Bond Length in Benzene:

- According to Kekulé, benzene has alternating single and double bonds:
  - C–C (single bond) length: 1.54 Å
  - C=C (double bond) length: 1.34 Å
- But experimental studies (like X-ray diffraction) show that all carbon-carbon bonds in benzene are equal, measuring 1.39 Å, which is intermediate between a single and a double bond.
- This uniform bond length suggests electron delocalization across the ring.

Stability of Benzene:

- Benzene is more stable than expected for a compound with three double bonds.
- It does not undergo oxidation easily like other unsaturated compounds.
- For example, strong oxidizing agents readily oxidize alkenes, but benzene resists oxidation, indicating extra stability due to resonance or aromaticity.

EVIDENCES IN THE STRUCTURE OF BENZENE

- Many analytical, synthetic, and chemical evidences support the unique structure of benzene:

Analytical Evidence

→ Based on elemental analysis and molecular weight determination, it was confirmed that benzene contains 6 carbon atoms and 6 hydrogen atoms.

→ Thus, the molecular formula of benzene is C_6H_6.

→ When compared to hexane (C_6H_{14}), which is a fully saturated hydrocarbon, benzene has 8 fewer hydrogen atoms.

→ This indicates that benzene is a highly unsaturated compound.

→ The unsaturation suggests the presence of multiple double bonds (i.e., π-bonds) in the structure of benzene.

→ Despite this unsaturation, benzene does not behave like a typical alkene—it is resistant to addition reactions, which shows its exceptional stability.

→ Therefore, from analytical evidence, it was concluded that benzene must contain delocalized π-electrons or alternating double bonds (as initially proposed), and not isolated double bonds like in alkenes.

Synthetic Evidence

- After confirming that benzene is highly unsaturated (C_6H_6), scientists tried to construct its structure.
- A compound with this formula could, in theory, exist as a straight-chain with multiple double or triple bonds.

Possible Straight-Chain Structures:

1. **$CH_2 = CH - C \equiv C - CH = CH_2$**
2. **$CH_3 - C \equiv C - C \equiv C - CH_3$**

3. **$CH = C - CH_2 - CH_2 - C = CH$**

- However, all these structures were rejected, because benzene does not give the typical reactions of alkenes or alkynes such as:
  - Decolorization of bromine water (Br_2/CCl_4)
  - Oxidation by cold dilute $KMnO_4$ (Baeyer's reagent)
  - Addition reactions with halogens, hydrogen, or water

Other Evidences

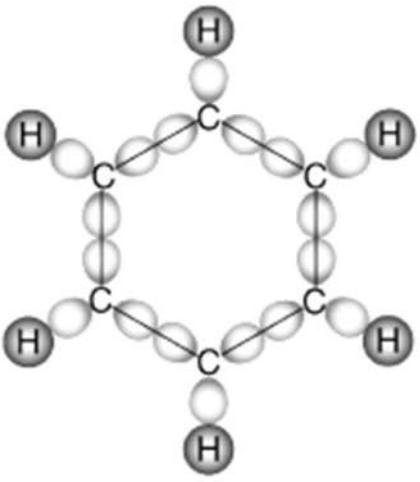
- Benzene reacts with bromine (Br_2) in the presence of a Lewis acid catalyst ($AlCl_3$) to undergo electrophilic substitution, forming bromobenzene.

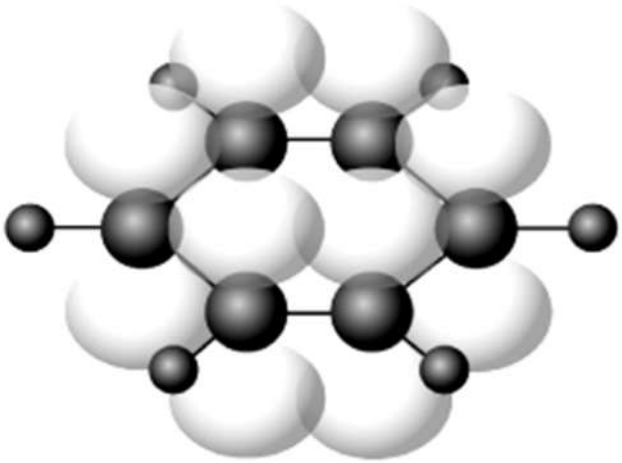
$$C_6H_6 + Br_2 \xrightarrow{AlCl_3} C_6H_5Br + HBr$$

- Only one monosubstituted product (bromobenzene) is formed, regardless of which hydrogen is replaced.
- This experimental observation confirms that all six hydrogen atoms in benzene are chemically equivalent.
- This equivalency is only possible if benzene has a cyclic and symmetrical structure where:
- All six carbon atoms are arranged in a ring, and
- Each carbon is bonded to one hydrogen atom.
- Hence, this further supports the idea that benzene is a closed, cyclic structure with uniform electron distribution.

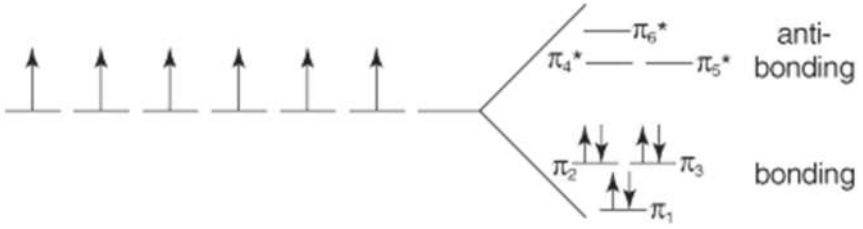
Orbital Picture

- Observations of the benzene molecule, which are all planar, bond to three other atoms, and all bond angles are 120 degrees, indicate that sp 2 hybridization occurs within the molecule.
- A carbon atom with sp2 hybridization has an unhybridized atomic p orbital on its surface.
- By overlapping the sp 2 hybrid orbitals, the ring would be held together with o atom bonds, but by overlapping the atomic p orbitals, the system goes through complete delocalization.
- The molecule is highly stable as a result of this complete delocalization.





- Six atomic orbitals that overlap will generate six orbitals in the molecule, according to molecular orbital theory.
- The bonding orbitals makes up three of these, while the antibonding orbitals makes up the other three.



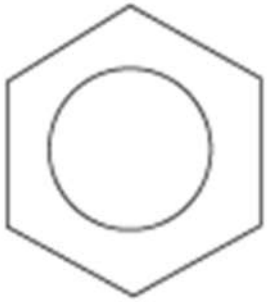
- A bonding combination is one with π 1, π 2, and π3, while an antibonding combination, denoted by π4,π5, and π6, is one with no bonding. Similarly, the bonding orbitals of atoms (π2 and π3) as well as the antibonding orbitals of atoms (π4 and π5) have the same energy. They are called degenerate orbitals.
- Molecular stability is very high due to the electrons in bonding orbitals. Furthermore, all the bonding orbitals are filled and all the electrons have paired spins, so the stability is increased. A molecule which possesses all of these properties is said to have a closed bond shell of delocalized electrons Delocalized electrons in closed bond molecules such as benzene give these molecules excellent stability and a large resonance energy.

Resonance in Benzene

- In modern instrumental studies, it has been confirmed that benzene bonds are all of the same length, or approximately 1.40 pm. Exactly halfway between the lengths of a carbon-carbon single bond (1.46 pm) and carbon-carbon double bonds (1.34 pm), a picometer = 1 x 10-12 meter. In addition, these studies demonstrate that all bond angles on the benzene molecule are equal (120") and that its structure is planar (flat). Benzene's structure can be described by resonance theory and molecular orbital theory
- For the same molecule, there are many possible structures, but according to resonance theory, none are correct. The drawn structures are all made up of the true structure, which is the most stable. The more structures that a molecule can have, the more stable the hybrid structure will be. In a hybrid structure, resonance energy is the difference between the computed energy and the actual energy. The resonance energy of compounds increases with their stability. Two

Kekulé structures can be used to represent the benzene molecule. Both structures are based on strong resonances.

- This hybrid structure could be represented by the following



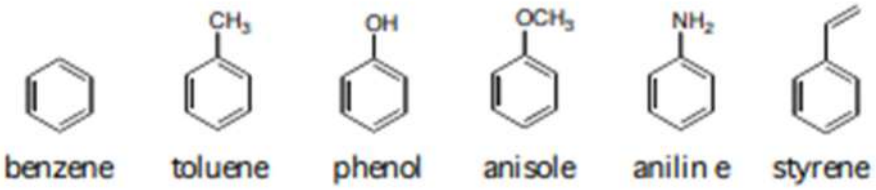
- Electrons move throughout the entire molecule as shown by the circle. Also, conjugated diene systems exhibit delocalized electrons (electrons within molecular orbitals). Diene conjugated systems are stable like benzene Due to its 1,3,5-cyclohexatriene structure, the benzene molecule is more stable than it would otherwise appear. The resonance energy of a molecule (36 kcal/mole) comes from its extra stability

Aromatic Characters

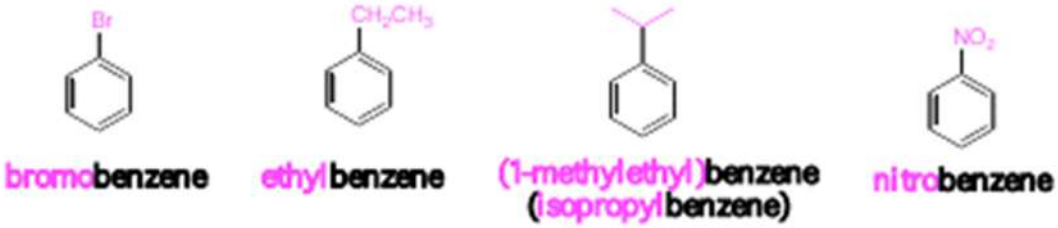
- Compounds that exhibit resonance delocalization of electron resonances, such as benzene, which exhibit special stability.

Naming the Aromatic Characters

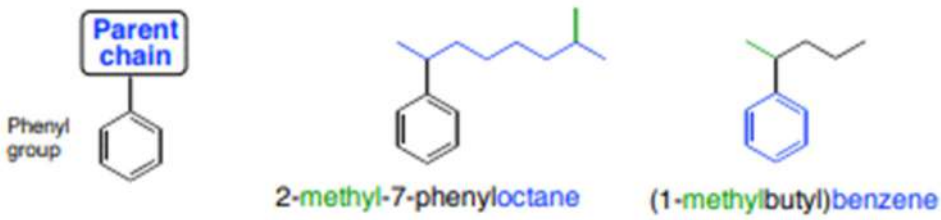
- A large number of names are not systematic



- It is usually called -benzene as a parent name for mono-substituted benzenes, similar to hydrocarbons



- It is referred to as a phenyl group when the benzene ring is attached to a parent chain. In the presence of more than six carbons in the parent chain, the benzene ring is considered a substitute. Where the longest alkyl chain substitute has six or fewer carbons, the benzene ring is the parent



Huckel's Rule

→ According to Huckel's Rule, you can determine if a molecule is aromatic, antiaromatic, or nonaromatic by using the number of n electrons (N) and the physical structure of the ring system.

→ In an aromatic system, you can determine the number of n electrons by using the following algorithm:

$$N=4n+2$$

n here is an integer.

→ Based on the following algorithm, one can determine how many AB electrons there are in an antiaromatic system

$$N=4n$$

n here is an integer

→ Nonaromatic compounds are those that have no continuous ring of conjugated p orbitals in a plane conformation In determining if a ringed molecule is aromatic, Hucker's Rule is a useful first step. It is worth investigating whether the ring must be planar to be aromatic