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B. Pharm Semester-II

Subject Name: Pharmaceutical Organic Chemistry I
Subject Code: BP202TP

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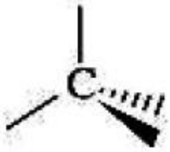
Alkane

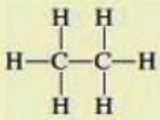
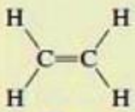
- Alkanes are the simplest type of organic compounds and member of a larger class of organic compounds called saturated hydrocarbons that contains **only carbon–carbon single bonds**.
- Alkanes have the general molecular formula CnH2n+2.
- we can determine the number of hydrogen's in the molecule and its molecular formula. For example, decane, with ten carbon atoms, must have (2×10)+ 2= 22 hydrogen atoms and a molecular formula of $C_{10}H_{22}$.

Molecular Formula	Structural formula	Name
CH_4	CH_4	Methane
C_2H_6	CH3 – CH_3	Ethane
C_3H_8	CH3 – CH_2–CH3	Propane
C_4H_{10}	CH3 – CH_2–CH2–CH_3	Butane
C_5H_{12}	CH3 – CH_2–CH2–CH_2–CH_3	Pentane
C_6H_{14}	CH3 – CH_2–CH2–CH_2–CH_2–CH_3	Hexane
C_7H_{16}	CH3 – CH_2–CH2–CH_2–CH_2–CH_2–CH_3	Heptane
C_8H_{18}	CH3 – CH_2–CH2–CH_2–CH_2–CH_2–CH_2–CH_3	octane

• Hybridization:

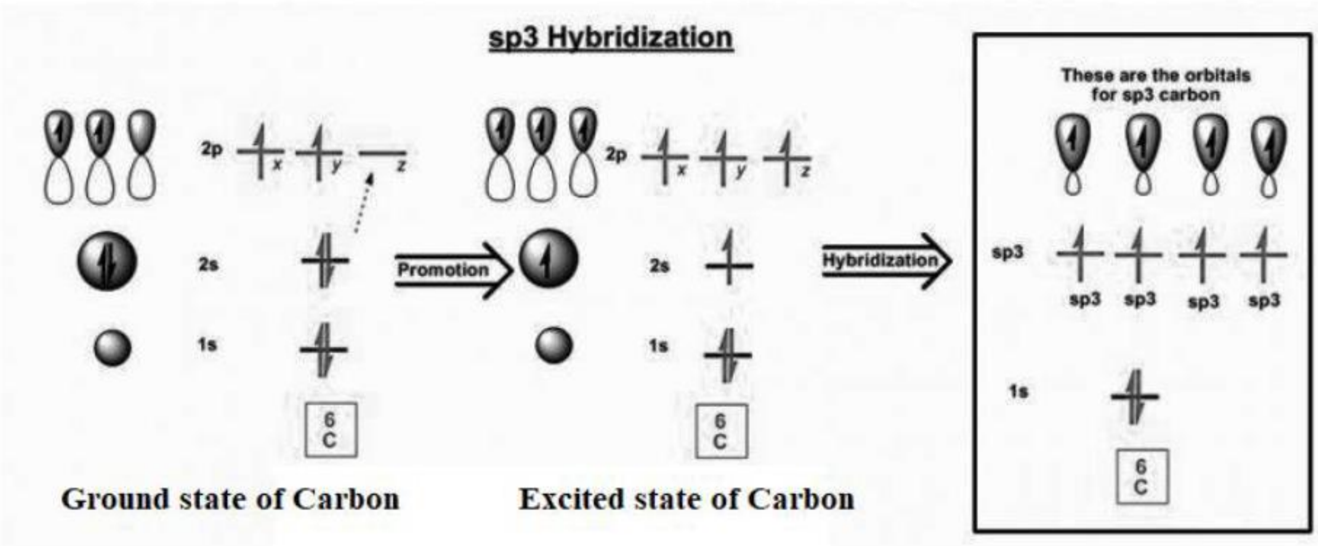
- Hybridization and general principles explain how covalent bonding in organic chemistry is possible.
- Hybridization happens when atomic orbitals mix to form a new atomic orbital. The new orbital can hold the same total number of electrons as the old ones. The properties and energy of the new, hybridized orbital are an 'average of the original unhybridized orbitals.
- *Types of Hybridization*:

Type of hybrid	*sp3 hybridization*	*sp2 hybridization*	*sp hybridization*
Diagram			
Atomic orbitals used	s, p, p, p	s, p, p	s, p
Orbitals Combined	s-orbital + 3 p-orbitals	s-orbital + 2 p-orbitals	s-orbital + 1 p-orbital
Resulting Orbitals	4 sp^3 orbitals (no p-orbitals)	3 sp^2 orbitals + 1 p-orbital	2 sp orbitals + 2 p-orbitals
Number of hybrid orbitals formed	4	3	2
Number of atoms bonded to the C	4	3	2
Geometry	tetrahedral	flat triangular	Linear
Ideal angle	109.5^0	120^0	180^0
Bonds	single bonds	double bonds	triple bonds

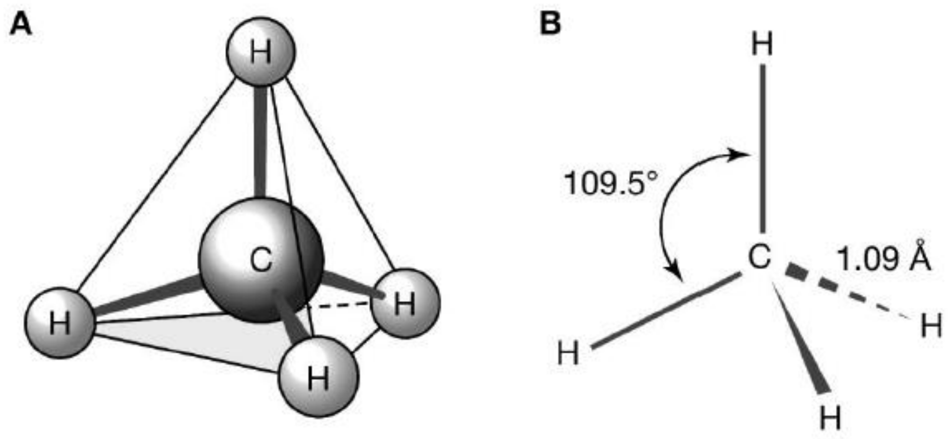
Molecule	Hybridization of carbon	Bond angles	Length of C—C bond (Å)	Strength of C—C bond (kcal/mol)	Strength of C—C bond (kJ/mol)	Length of C—H bond (Å)	Strength of C—H bond (kcal/mol)	Strength of C—H bond (kJ/mol)
 ethane	sp^3	109.5°	1.54	90	377	1.10	101	423
 ethene	sp^2	120°	1.33	174	720	1.08	111	466
H—C≡C—H ethyne	sp	180°	1.20	231	967	1.06	131	548

- **sp^3 Hybridization**

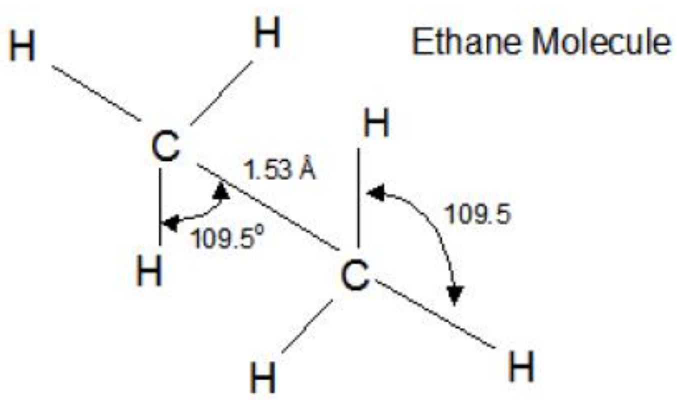
- The process of formation of 4 equivalent orbitals from hybridization or mixing up of one '**S**' and three '**P**' orbitals is known as sp^3 hybridization. sp^3 hybrid orbitals and properties of sigma bonds.
- ***Characteristics:***
    - sp^3 has 25% s and 75% p character
    - The 4 sp^3 hybrids point towards the corners of a tetrahedron at 109.5^0 to each other
    - Each sp^3 hybrid is involved in a s bond.



- ***Bond Angle and Bond Length of Methane***

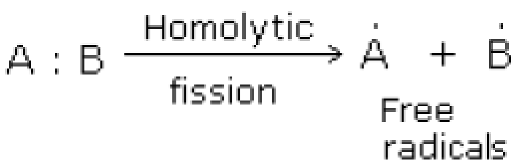


- ***Bond Angle and Bond Length of Ethane***



<u>**Free Radical**</u>

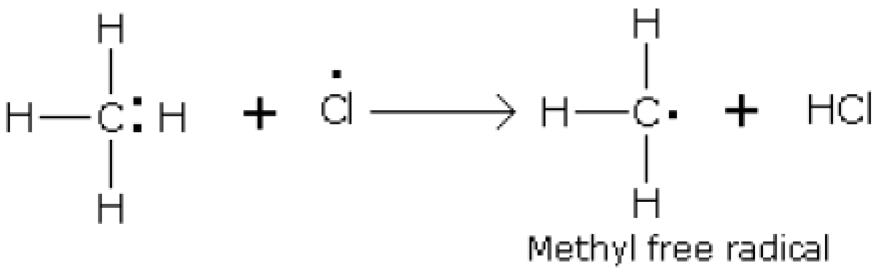
A free radical may be defined as an atom or group of atoms having an unpaired electron. Free radicals are produced during the homolytic fission of a covalent bond.



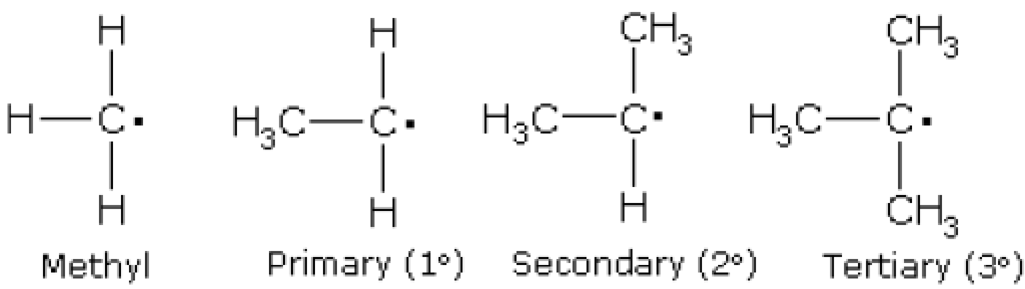
Free radicals are very reactive as they have strong tendency to pair up their unpaired electron with another electron from wherever available. These pairs are very short lived and occur only as reaction intermediates during reactions. - For example, dissociation of chlorine gas in the presence of ultra-violet light produces chlorine free radicals:

$$Cl : Cl \xrightarrow{u.\ v.} \dot{Cl} + \dot{Cl}$$

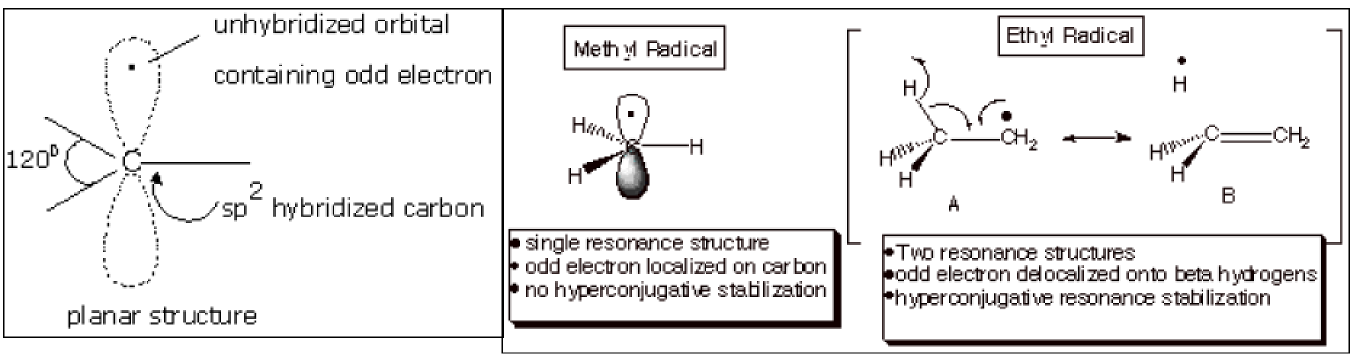
The alkyl free radical may be obtained when free radical chlorine attacks methane.



Free radicals may be classified as primary, secondary or tertiary depending upon whether one, two or three carbon atoms are attached to the carbon atom carrying the odd electron:



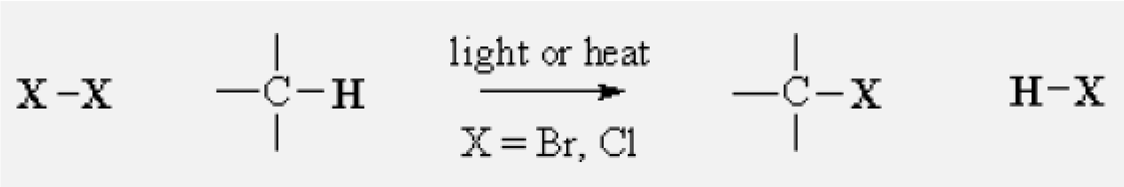
- ***Structure of alkyl free radical:*** The carbon atom in alkyl free radicals involves **sp^2 hybridization**. Therefore, it has a **planar structure**. Three hybrid orbitals are used in the formation of three **s-bonds** with three **H atoms** or **alkyl group**. The unpaired electron is present in unhybridized **p orbital**.



Halogenation of Alkanes (Free Radical Substitution Reaction)

The reaction of a halogen with an alkane in the presence of ultraviolet (UV) light or heat leads to the formation of a haloalkane (alkyl halide). An example is the chlorination of methane.

- Radical Halogenation of Alkanes (Reaction type: Free Radical Substitution)



Summary:

- When treated with Br_2 or Cl_2, radical substitution of R-H generates the alkyl halide and HX.
- Alkane R-H relative reactivity order: tertiary > secondary > primary > methyl.
- Halogen reactivity $F_2 > Cl_2 > Br_2 > I_2$
- Only chlorination and bromination are useful in the laboratory.
- Bromination is selective for the R-H that gives the most stable radical.
- Chlorination is less selective

- ***Mechanism Of Halogenation***	*Radical chain mechanism for reaction of methane with Cl_2*
Initiation Step $X_2 \xrightarrow{uv} X\bullet + X\bullet$ **Propagation Steps** $RH + X\bullet \longrightarrow R\bullet + HX$ $R\bullet + X_2 \longrightarrow RX + X\bullet$ **Termination Steps** $X\bullet + X\bullet \longrightarrow X_2$ $X\bullet + R\bullet \longrightarrow RX$ $R\bullet + R\bullet \longrightarrow R\text{-}R$	• **Chain - initiating steps**: steps in which the chain reaction starts $Cl{-}Cl \xrightarrow{energy} 2\ Cl\bullet$ • **Chain propagating steps**: steps which keep to the reaction going $Cl\bullet + CH_4 \longrightarrow CH_3\bullet + HCl$ $CH_3\bullet + Cl_2 \longrightarrow CH_3Cl + Cl\bullet$ • **Chain - terminating**: steps which might occur which causes the chain reaction to stop $Cl\bullet + Cl\bullet \longrightarrow Cl_2$ $CH_3\bullet + CH_3 \longrightarrow C_2H_6$ $CH_3\bullet + Cl\bullet \longrightarrow CH_3C$

INHIBITORS

- Inhibitor - a substance which slows down or stops a reaction even though the inhibitor is present in small amounts.
- Inhibition period - time during which the inhibitor lasts.
- Example: If oxygen is present during halogenation, the oxygen slows down the reaction.

$$CH_3\bullet + O_2 \longrightarrow CH_3-O-O\bullet$$

less reactive than $CH_3\bullet$

- This breaks the cycle (propagating steps) and slows down the reaction.
- When the oxygen molecules are all reacted (inhibition period), the reaction then speeds up.

Paraffin

Paraffin‟s, more commonly referred to as alkanes, are the chemical family of saturated hydrocarbons.

- The general formula **CnH2n+2**, **C** being a carbon atom, **H** a hydrogen atom, and „**n**‟ an integer.

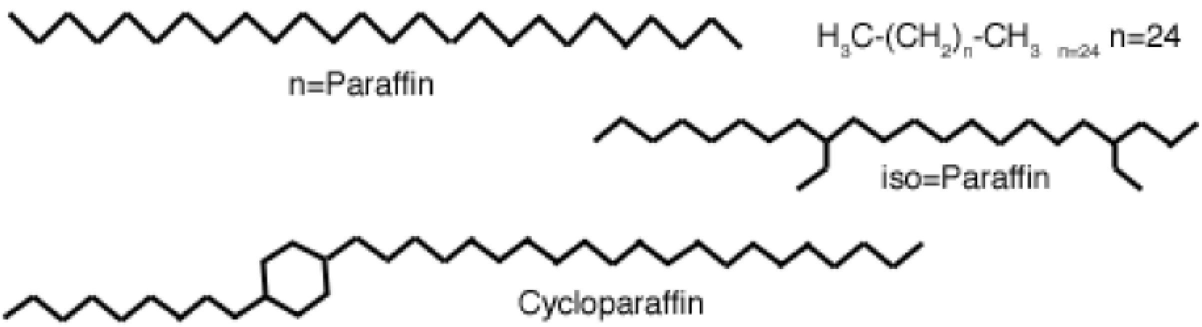
- The paraffin‟s are major constituents of natural gas and petroleum.

- Paraffin‟s containing fewer than 5 carbon atoms per molecule are usually gaseous at room temperature, those having 5 to 15 carbon atoms are usually liquids, and the straight-chain paraffins having more than 15 carbon atoms per molecule are solids.

- Branched-chain paraffin‟s have a much higher octane number rating than straight-chain paraffin‟s and, therefore, are the more desirable constituents of gasoline.

- The hydrocarbons are immiscible with water. All paraffin‟s are colourless.

- Paraffin is a strong-smelling liquid which is used as a fuel in heaters, lamps, and engines.



Paraffin wax

- It is also known as American English paraffin, is a white wax obtained from petrol or coal. It is used to make candles and in beauty treatments.

- The term "**wax**" simply refers to saturated hydrocarbons that contain more than 16 carbon atoms in the paraffin series (**C16-C40**) and are in solid state at room temperature. Chemically, natural waxes are defined as long chain esters, monohydric (one hydroxyl group), or alcohols with long chain fatty acids. The majority of the waxes present in crude oil are considered synthetic paraffin waxes with non-oxidized saturated alkanes.

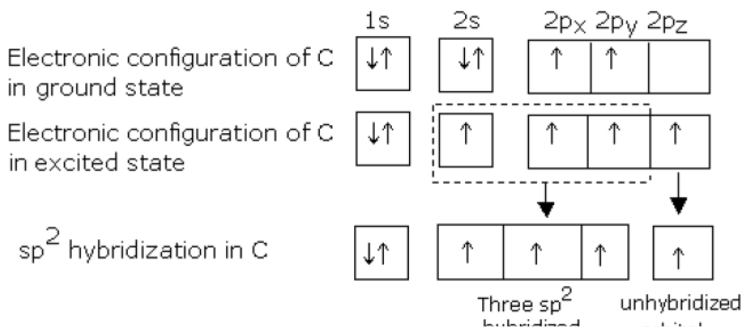
Uses of Paraffin

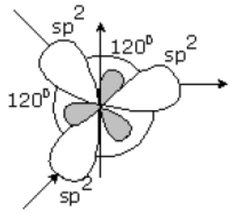
- Medicinal liquid paraffin, also known as ***paraffinum liquidum***, is a very highly refined mineral oil used in cosmetics and for medical purposes.
- Liquid paraffin has many uses in the medical field. Because liquid paraffin passes through the body's intestinal tract without being absorbed, it can be used as a laxative to limit the amount of water removed from the stool and ease constipation.
- Liquid paraffin is considered to have a limited usefulness as an occasional laxative.
- Liquid paraffin will reveal that this common personal care ingredient is used in many skin products, including creams, lotions, lip balm, soap, and even eczema ointments.
- In burns treatment that involved covering the affected area with a combination of waxes and oils including paraffin wax; this petroleum-derived substance created a barrier for the skin to heal and was seen as a very effective treatment.
- Paraffin wax were developed, the most popular of which was giving hot wax baths to patients suffering from a variety of ailments, in particular rheumatism and joint pain. The wax would be used to soften the skin and the intense heat would soothe the muscles and ready them for massage treatment.
- White soft paraffin with liquid paraffin is used as a barrier cream by providing a layer of oil on the surface of the skin to prevent water evaporating from the skin surface. It is an emollient, sometimes known as skin lubricant. It is used to soothe, smooth and hydrate the skin.

❖ sp^2 hybridization in alkenes

✓ Structure of Alkene:

- In alkenes, two carbon atoms are bonded through a double bond in the parent chain. The formation of a double bond in alkenes is illustrated below by taking the simplest alkene, ethene, as a typical example.
- Ethene can be described by the molecular formula C_2H_4. Each carbon atom in this molecule has three points of attachment and therefore, each carbon atom in ethene is **sp^2 hybridized**.

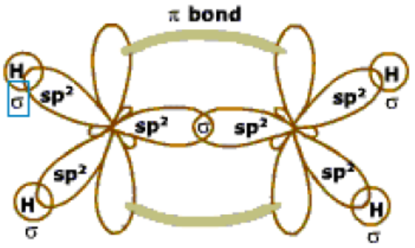


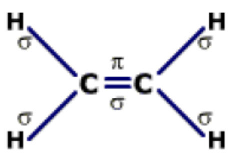


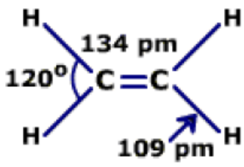
The sp2 hybridization of carbon orbital

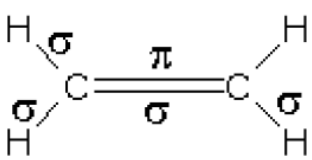
✓ The sp^2 hybridization of carbon orbital

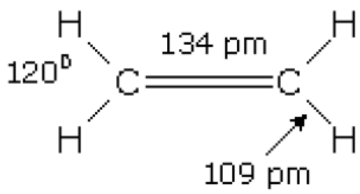
- The three sp^2 hybrid orbitals lie in a plane and are inclined to each other at an angle of **120°** (see above figure). One of the **p orbitals** (say **2pz**) on each carbon atom is left unhybridized.
- The three **sp^2** hybrid orbitals form **three sigma (s) bonds**: two with H-atoms and one with the adjacent carbon atom. This results in a planar structure. The two partially filled unhybridized **p orbitals** of the two carbon atoms overlap side-ways to form a **pi bond** as shown:











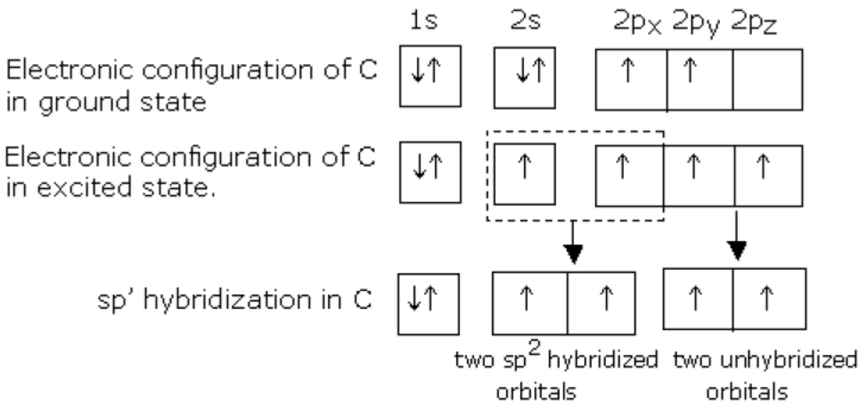
Simplified representation of ethene molecule

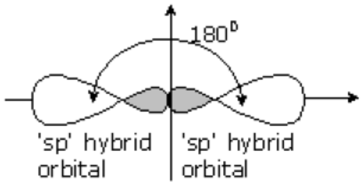
- Side-ways overlap of unhybridized pz orbitals of the two carbon atoms leading to the formation of a p bond
- Therefore, in ethene, the carbon-carbon double bond (=) is a combination of a **sigma** (s) and a **pi bond** (p). The simple structural formula of ethene is written as shown above.

❖ sp hybridization in alkyne

✓ Structure of Alkyne:

- In alkynes, the two carbon atoms in the parent chain are bonded through a triple bond. The formation of triple bond in alkynes is illustrated below by taking ethyne (acetylene) as a typical example.
- Ethyne (acetylene) can be described by the molecular formula C_2H_2. As each carbon atom in this molecule has two points of attachments, each carbon atoms in ethyne (acetylene) is ***sp* hybridized**.

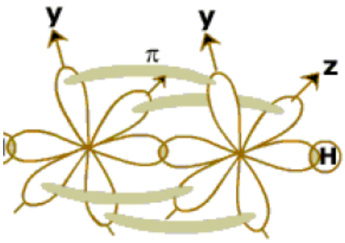


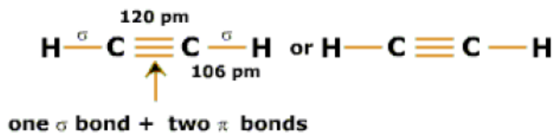


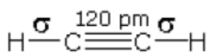
***sp* hybridization of carbon orbitals**

The two ***'sp'* hybrid orbitals** are oriented at an angle of **180°** to each other, while the two p orbitals (p_y and p_z) on each carbon are left unhybridized. These orbitals are at right angles to each other as well as to the ***sp* hybrid orbitals**.

One of the ***'sp'* hybrid orbitals** overlaps with the ***'sp'* hybrid orbital** of the other carbon atom to form a ***sp-sp* sigma** bond. The remaining two ***sp* hybrid orbitals** of the two carbon atoms overlap with the ***s* orbitals** of two hydrogen atoms to form **two sigma bonds**. The unhybridized p_y and p_z **orbitals** of two carbon atoms overlap laterally to form **two *p* bonds**. The combination of one (*sp-sp*) **sigma bond**, and two (*p-p*) ***p* bonds** gives rise to the **triple** (≡) bond. **Two *p*-electron** clouds merge into each other to form a cylindral ***p-p* electron cloud**.







Ethyne molecule representation

Formation of a triple bond between two carbon atoms due to sideways overlap of the unhybridized orbitals

> **How to Convert Picometer (pm) to Angstrom (A)**
>
> 1 **pm** = 0.01 **A**
>
> 1 **A** = 100 **pm**
>
> **Example: convert 15 pm to A**:
>
> 15 pm = 15 × 0.01 A = 0.15 A