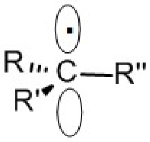
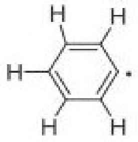
Free-Radicals:

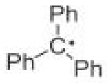
A **free radical**: **is a species that has one or more unpaired electrons**. The **total magnetic moment** is **zero** in the **species where all electrons** are **paired**. In **radicals**, however, since there are **one** or **more unpaired electrons**, there is a **net magnetic moment** and the radicals are **paramagnetic**. **Free radicals** are usually **detected** by **electron spin resonance**, which is also termed **electron paramagnetic resonance**.

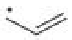


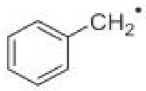
Examples:

$\dot{C}H_3$ $CH_2{=}\dot{C}H$







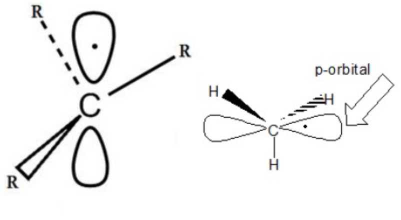


Structure and Geometry of Free Radicals:

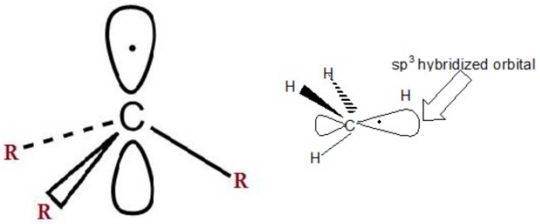
Simple alkyl radicals have:

a) **Planar (trigonal) structure**, i.e., **sp^2 bonding with the odd electron in a p orbital**.

b) The **pyramidal structure** is **another possibility** when the **bonding may be sp^3 and the odd electron is in a sp^3 orbital**.

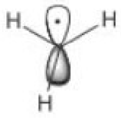


Trigonal structure

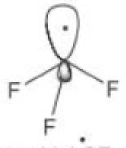


Pyramidal structure SP^3

Examples:



Planar $\dot{C}H_3$ radical

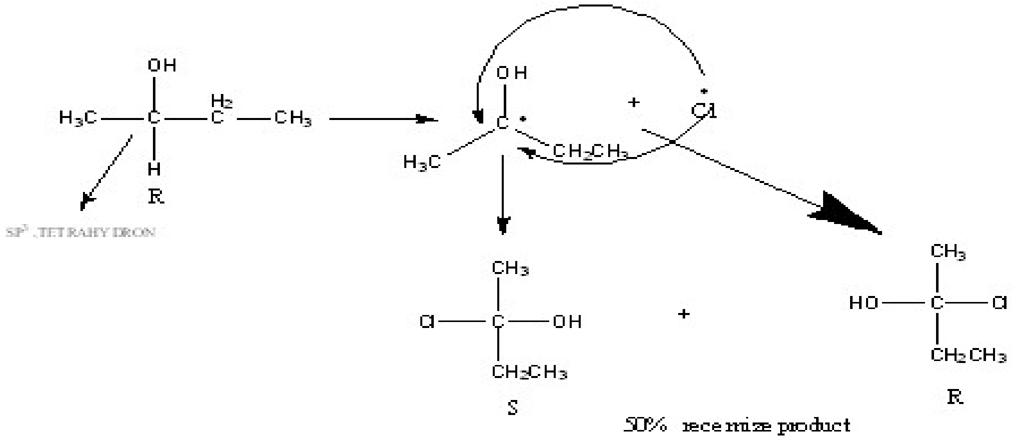


Pyramidal $\dot{C}F_3$ radical

- **Unlike carbocations, the free radicals can be generated at the bridgehead showing that pyramidal geometry for radicals is also possible and that free radicals need to be planar**.

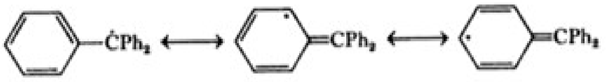
The **planar structure** is in keeping with the loss of activity when a free radical is generated at a **chiral center**. Thus, a **planar radical** will be **attacked at either face** after its formation with **equal probability to give enantiomers**.

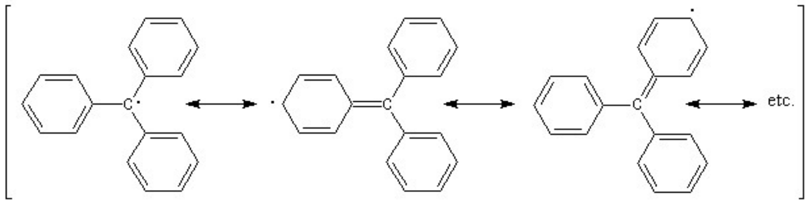
Example:



Stability of Free Radicals:

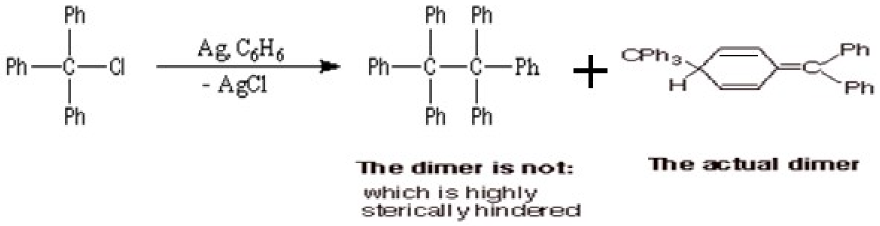
As in the case of **carbocation**, the **stability** of **free radicals is tertiary > secondary > primary** and is **explained based on hyperconjugation** (**radicals are electrophilic**, and **therefore they are stabilized by alkyl groups**). The **stabilizing** effects in **allylic radicals and benzyl radicals are due to vinyl and phenyl groups in terms of resonance structures** (**the C is attached to a C=C π bond or a benzene ring by resonance**). Bond dissociation energies show that 19 kcal/mol less energy is needed to form the benzyl radical from toluene than the formation of methyl radical from methane. The **triphenyl methyl** type radicals are no doubt **stabilized** by **resonance**; however, the **major cause of their stability is the steric hindrance to dimerization**.



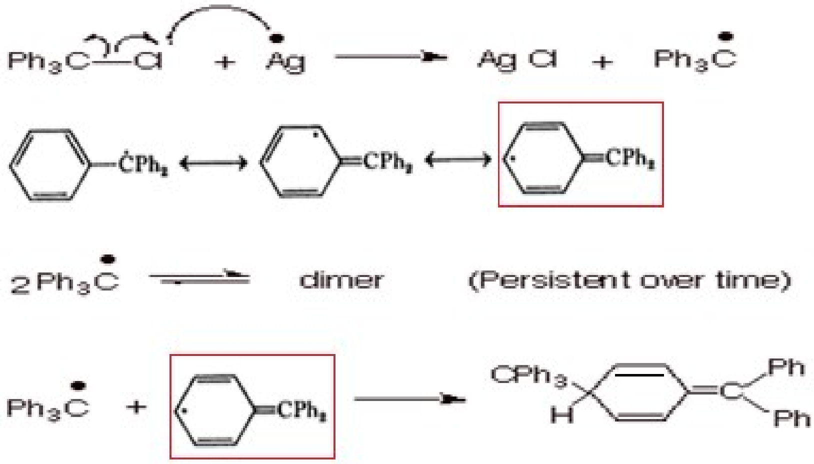


Example:

Example:

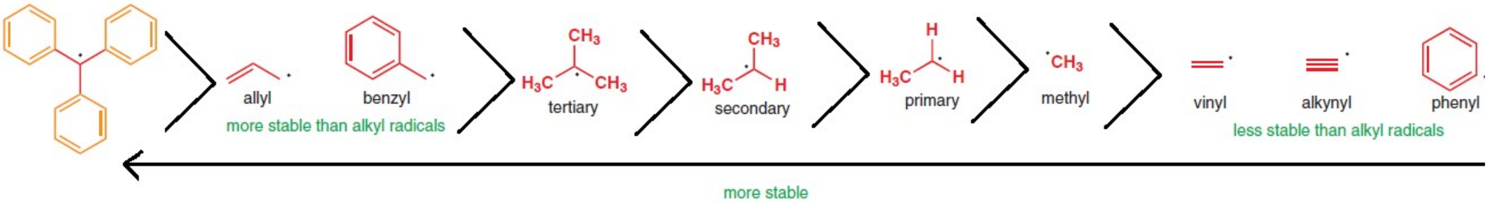


Mechanism:

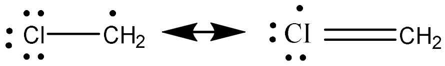


A **radical is a seven-electron intermediate** that adopts a flat, sp^2 structure although it has four electron groups; the **lone electron resides** in a **half-filled p-orbital**. This **sp^2 structure allows radicals to delocalize the single electron through resonance**.

Ease of formation of free radicals } Benzyl > allyl > 3° > 2° >1° > $CH_3^{\cdot}$ > vinyl



- **Cl, S increased stability** of free radical because it's **content empty orbital and resonance**.



Bond cleavage is the splitting of chemical bonds:

There are **two types** of bond cleavage:

1- **Heterolytic cleavage**: **one atom gets both of the shard electrons** (this cleavage is given **ionic species**).

$$X{-}Y \longrightarrow \overset{\oplus}{X} + \overset{\ominus}{Y}$$

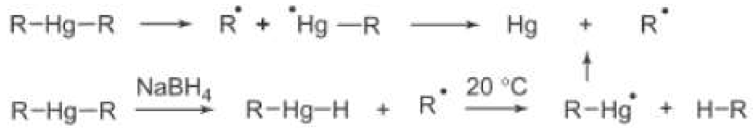
Example:

$$H{-}Cl \xrightarrow{\text{Heterolysis}} H^+ + Cl^-$$

2- **Homolytic cleavage**: **The two electrons in the bond are divided equally between the products (this cleavage is given free radical).** Radicals are **intermediates** with an **unpaired electron** (**highly reactive**, **short-lived species**, **electrophile**).

$$X{-}Y \xrightarrow[\text{or peroxid}]{\text{heat or light}} \overset{\bullet}{X} + \overset{\bullet}{Y}$$

Example: Homolysis of organometallic compounds



Example:

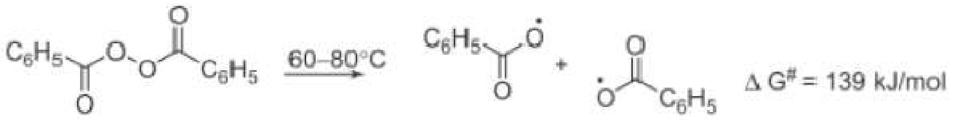
$$H{-}Cl \xrightarrow{\text{Homolysis}} H\bullet + Cl\bullet$$

Formation of Free Radicals:

Three general methods are used for the generation of free radicals:

1- Thermal Generation.

Examples:



Peroxyoxalate

2- Photochemical Generation.

Examples:

$$Cl{-}Cl \xrightarrow{\text{Light } (h\nu)} 2\ Cl^{\bullet} \qquad \Delta G^{\#} = 243\ \text{kJ/mol}$$

$$Br{-}Br \xrightarrow{\text{Light } (h\nu)} 2\ Br^{\bullet} \qquad \Delta G^{\#} = 192\ \text{kJ/mol}$$

$$I{-}I \xrightarrow{\text{Light } (h\nu)} 2\ I^{\bullet} \qquad \Delta G^{\#} = 151\ \text{kJ/mol}$$

$$RO{-}Cl \xrightarrow{\text{Light } (h\nu)} RO^{\bullet} + Cl^{\bullet}$$

Alkyl hypochlorite

$$RO{-}N{=}O \xrightarrow{\text{Light } (h\nu)} RO^{\bullet} + NO^{\bullet}$$

Alkyl nitrite

Example: Cleavage of the cyclic azo compound to produce a **biradical**

3- Redox Generation.

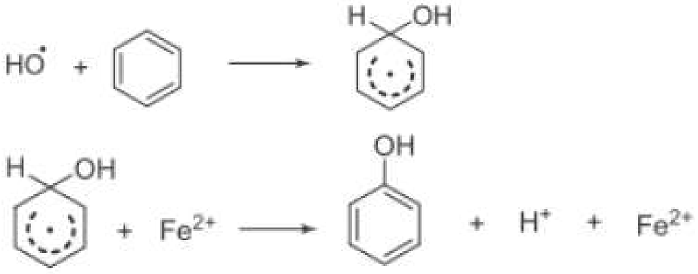
Examples:

$$Fe^{2+} + R_2NCl \longrightarrow Fe^{3+} + Cl^{-} + R_2N^{\bullet}$$

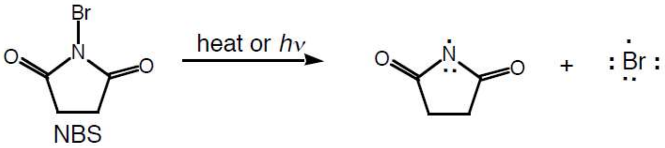
$$Fe^{2+} + ROOH \longrightarrow Fe^{3+} + OH^{-} + RO^{\bullet}$$

Example: Oxidation of benzene

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + HO^{-} + HO^{\bullet}$$



- **NBS** (**N-bromosuccinimide**) is often **used** as the **Br source** in **free radical brominations**.

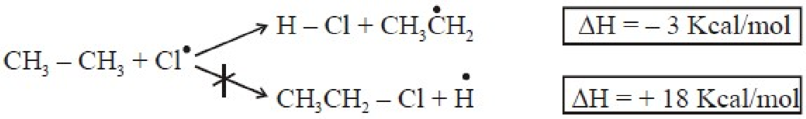


Reactivity:

1- Reactivity for Aliphatic Substrates:

It is the abstraction step that determines which product will be formed in a chain reaction. A free radical almost always abstracts a univalent (hydrogen or halogen) and never a tetra or tera covalent atom, and seldom a divalent one.

Example: a reaction between a chlorine free radical and ethane gives an ethyl radical, not a hydrogen free radical:



The main reaction to this is steric. A univalent atom is much more exposed to attack by the incoming radical than an atom with a higher valency. Another reason is that in many cases abstraction of a univalent atom is energetically more favored.

Group sequence in reaction with Br and Cl:

Cl :more reactive ,less selective

$MeH < MeCH_2H < (CH_3)_2CH_2 < (Me)_3CH < PhCH_3 < Ph_2CH_2 < Ph_3CH$

$\longrightarrow$

Br less reactive :more selective

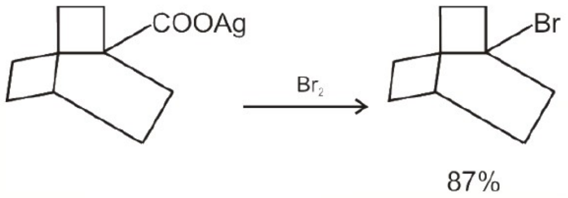
2- The compound containing electron withdrawing substituents:

Example: Z-CH_2CH_3 (Z = COOH, COCl, COOR, SO_2Cl or CX_3 position is **attached predominantly** or β) the exclusively in free radical halogenations. This is **because electron withdrawing groups highly) positions**. Compounds like acetic acid and acetyl chloride are **not attacked** at α deactivate (all. This is **because halogen atoms are electrophilic radicals and look for positions of high electron density**. Hydrogen's on carbon atoms next to the electron withdrawing groups

have low electron densities; therefore, the attack is avoided at this position.

3- Reactivity at the bridgehead:

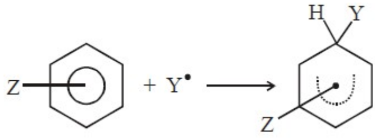
There are many free-radical reactions which have been observed at bridge head carbons.



However treatment of norbornane with sulfuryl chloride and benzoyl peroxide give mostly 2-chloronorbornane, though the bridgehead position is tertiary. Thus the final result is that while bridge head free-radical substitution is possible, it is not preferred, presumably because of the strain involved.

4- Reactivity In Aromatic Substrates:

Free radical substitution at an aromatic carbon seldom takes place by a mechanism in which a ring of hydrogen is abstracted to give an aryl radical. Usually, the mechanism is similar to that of aromatic electrophilic and nucleophilic substitutions.



- All substituents **increase reactivity at *ortho* and *para* positions as compared to that of benzene**. There is **no great difference between electron-donating and electron-withdrawing groups**. This is because radicals are neutral species and are not influenced by the polar properties of the substrate to any significant extent. Furthermore, it has been shown that both electron-donating and electron-withdrawing groups stabilize a free radical.

5- Reactivity of radical halogenations of alkanes:

There are two components to understanding the selectivity of radical halogenations of alkanes:

a- reactivity of R-H system:

The strength of the R-H varies slightly depending on whether the H is 1^o, 2^o or 3^o. The following table shows the **bond dissociation energy** which is the energy required to break the bond in a homolytic fashion, generating $R^\cdot$ and $H^\cdot$

Type	R-H	kJ/mol	kcal/mol	
	CH_3-H	435	104	**Note how the bonds get weaker as we move down the table, so the $R^{\cdot}$ also get easier to form, with 3° being the easiest.**
1°	CH_3CH_2-H	410	98	
2°	$(CH_3)_2$CH-H	397	95	
3°	$(CH_3)_3$C-H	265		

b- <u>Reactivity of $X^{\cdot}$ (Halogen radical, $X^{\cdot}$):</u>

1- Bromine radicals are less reactive than chlorine radicals.

2- $Br^{\cdot}$ tends to be more selective in its reactions, and prefers to react with the weaker R-H bonds.

3- The more reactive chlorine radical is less discriminating in what it reacts with.

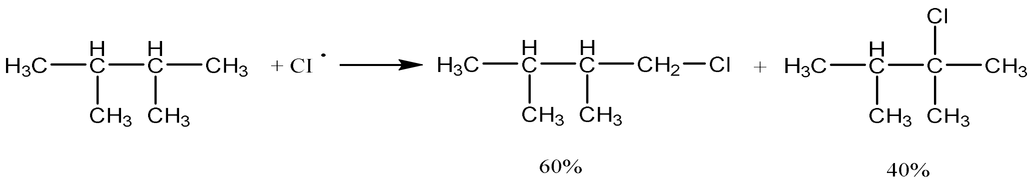
	Br	Cl
1°	1	1
2°	82	3.9
3°	1640	5.2

Bromination is 1640 times more likely to occur at a 3° position than 1°, chlorination is 5.2 times more likely to occur at a 3° position than 1°.

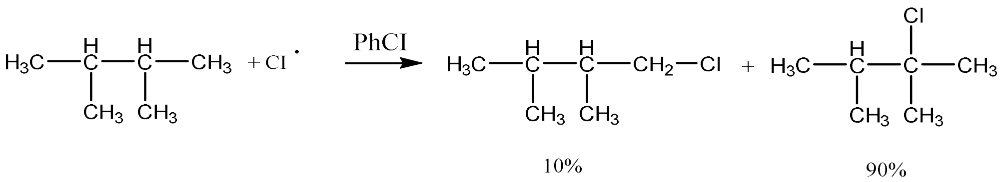
6- **<u>The effect of solvent on reactivity:</u>**

The solvent usually has little effect on free radical, but there are two types solvent which different in attack:

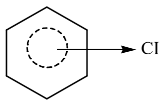
a- Aliphatic solvent:



b- Aromatic solvent:



This result is attributed to complex formation between the aromatic solvent and the chlorine atom that makes the chlorine more selective:

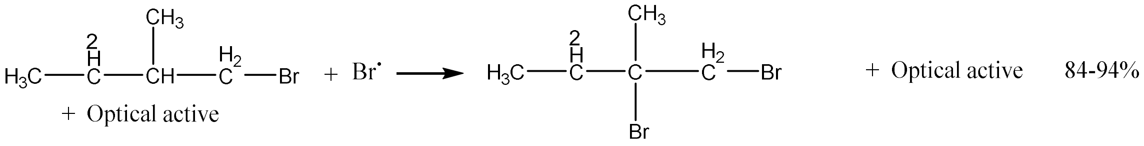


7- Neighbouring Group Assistance in Free Radical Reactions:

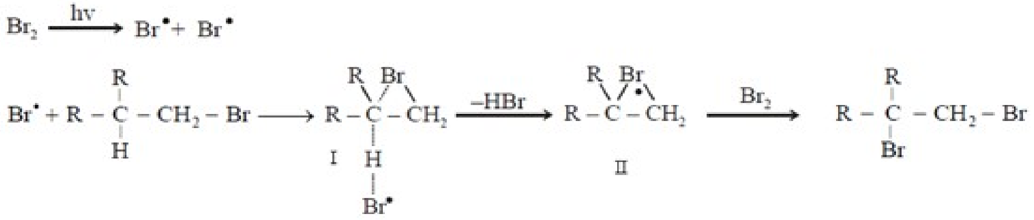
In certain cases it has been shown that free radical reactions are accelerated by the presence of neighbouring group.

- **Optically active** 1- bromo-2-methyl butane give 1,2-dibromo-2-methyl butane with **retention of configuration**.

Example: **Bromination** of alkyl bromide give **84-94%** substitution at the carbon adjacent to the bromine already in the molecule positions close to a polar group, such as bromine, should actually be **deactivated electron withdrawing field effect** of the bromine, the unusual **regioselectivity** is explained by a mechanism in which abstraction assisted by a **neighboring** bromine atom (I), $Br^{\cdot}$ abstract hydrogen from RH, leaving $R^{\cdot}$, when abromine is present in the proper position, it assists this process giving **acyclic intermediate** (**abridged free radical**) (II).



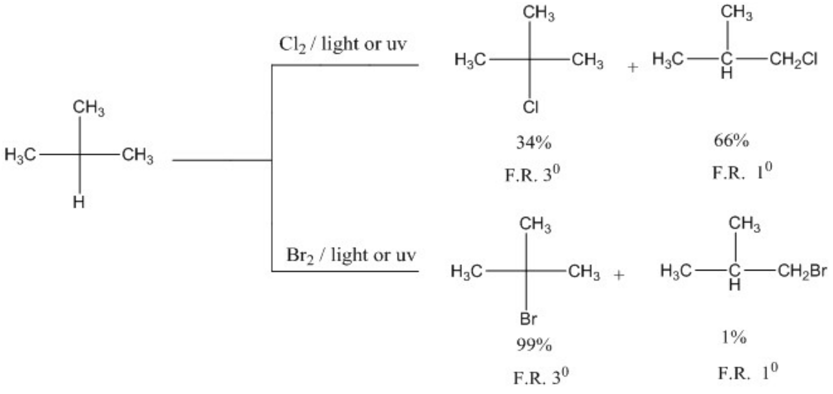
Mechanism:



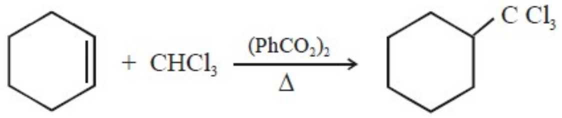
8- Reactivity between chlorine and bromine:

Chlorine is **more reactive** but **less selective** and **does not greatly distinguish between type of hydrogen**, **bromine less reactive** but **more selective**.

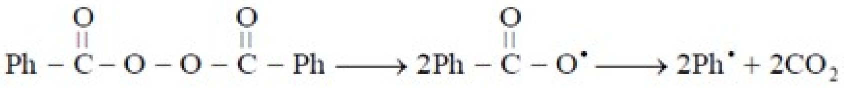
Example:



Example:

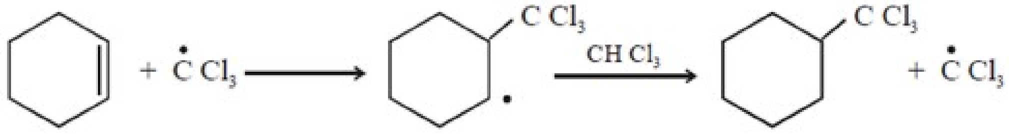


Mechanism:



$$Ph-\overset{O}{\overset{\|}{C}}-O-O-\overset{O}{\overset{\|}{C}}-Ph \longrightarrow 2Ph-\overset{O}{\overset{\|}{C}}-O^{\bullet} \longrightarrow 2Ph^{\bullet}+2CO_2$$

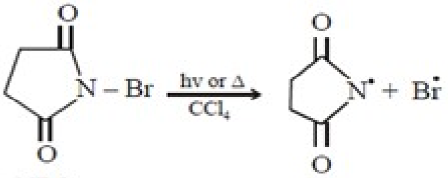
$$Ph^{\bullet}+CHCl_3 \longrightarrow PhH+\dot{C}Cl_3$$



Example:

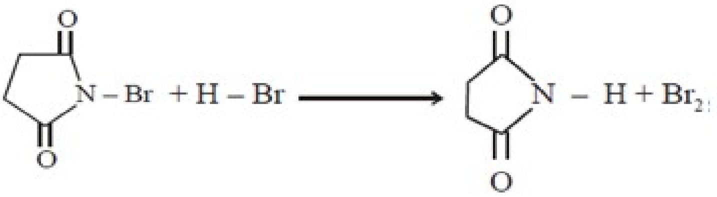
$$CH_3-CH=CH_2 \xrightarrow[hv/CCl_4]{NBS} Br-CH_2-CH=CH_2$$

Mechanism:



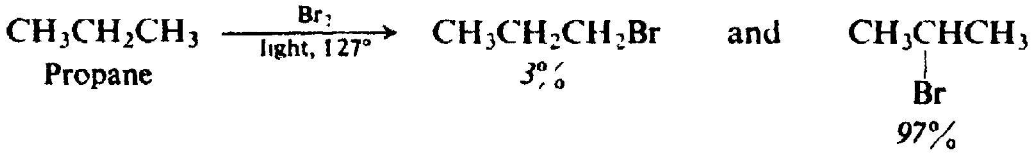
NBS

$$CH_3-CH=CH_2+\dot{B}r \longrightarrow \dot{C}H_2-CH=CH_2+HBr$$



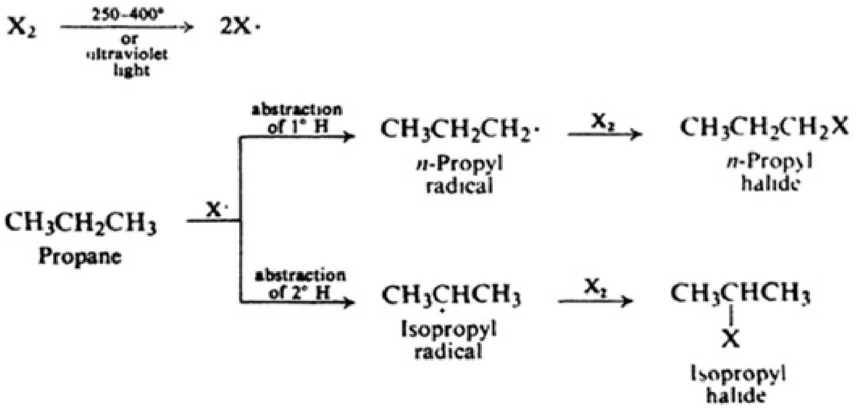
$$\dot{C}H_2-CH=CH_2+Br_2 \longrightarrow Br-CH_2-CH=CH_2 + \dot{B}r$$

Example:



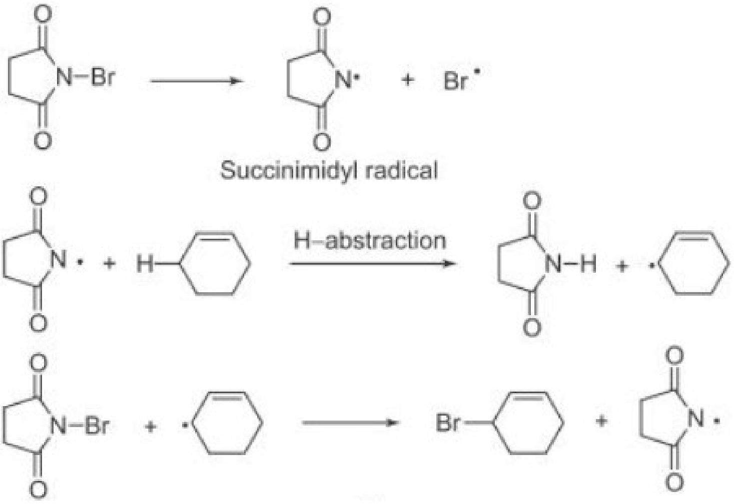
$$\underset{\text{Propane}}{CH_3CH_2CH_3} \xrightarrow[\text{light, 127°}]{Br_2} \underset{3\%}{CH_3CH_2CH_2Br} \quad \text{and} \quad \underset{97\%}{\underset{Br}{\underset{|}{CH_3CHCH_3}}}$$

Mechanism:

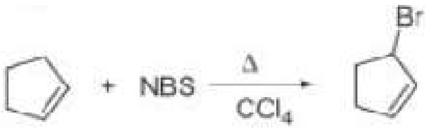


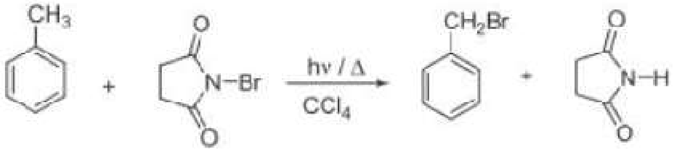
Example:

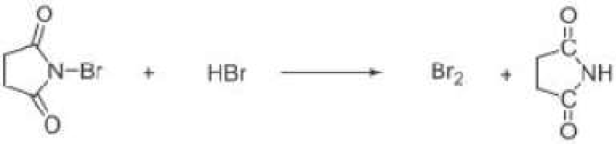
Mechanism:



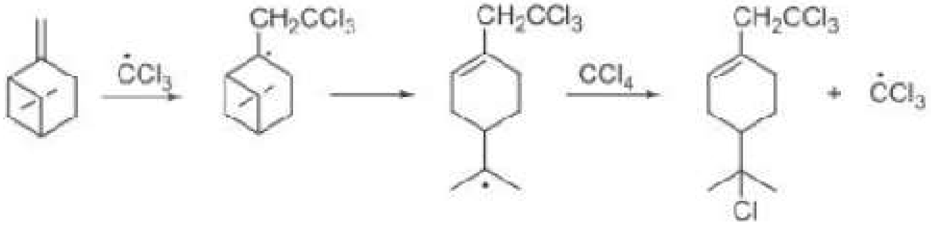
Examples:



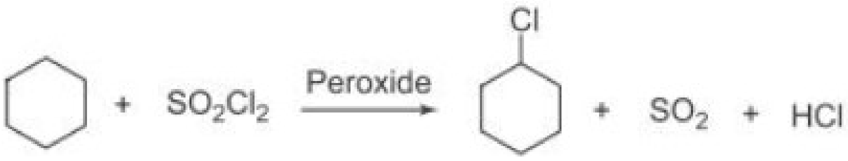




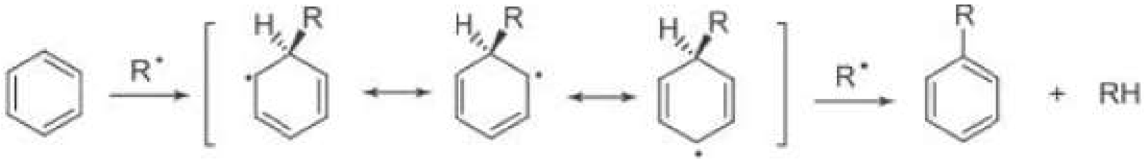
Example: Radical addition of CCl_4 to p-pinene



Example: Chlorination of cyclohexane



Example: Radical addition – elimination reaction

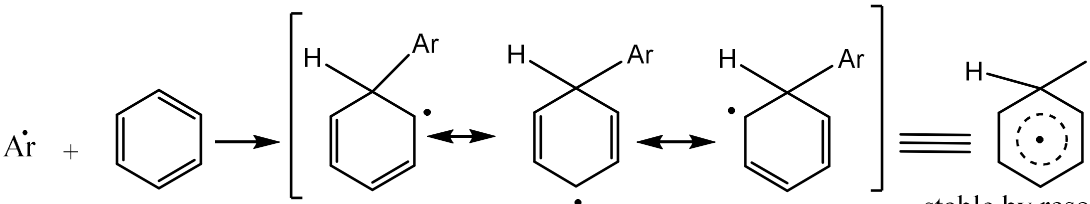


Example: Radical addition – elimination reaction

$$\dot{Ar} + ArH \longrightarrow Ar\text{-}Ar$$

The product can be explained a **mechanism** similar to that of **electrophilic aromatic substitution**. In the **first step**, the radical $Ar^{\cdot}$ attacks the ring in much the same way as would an electrophile or nuclophile.

Mechanism:



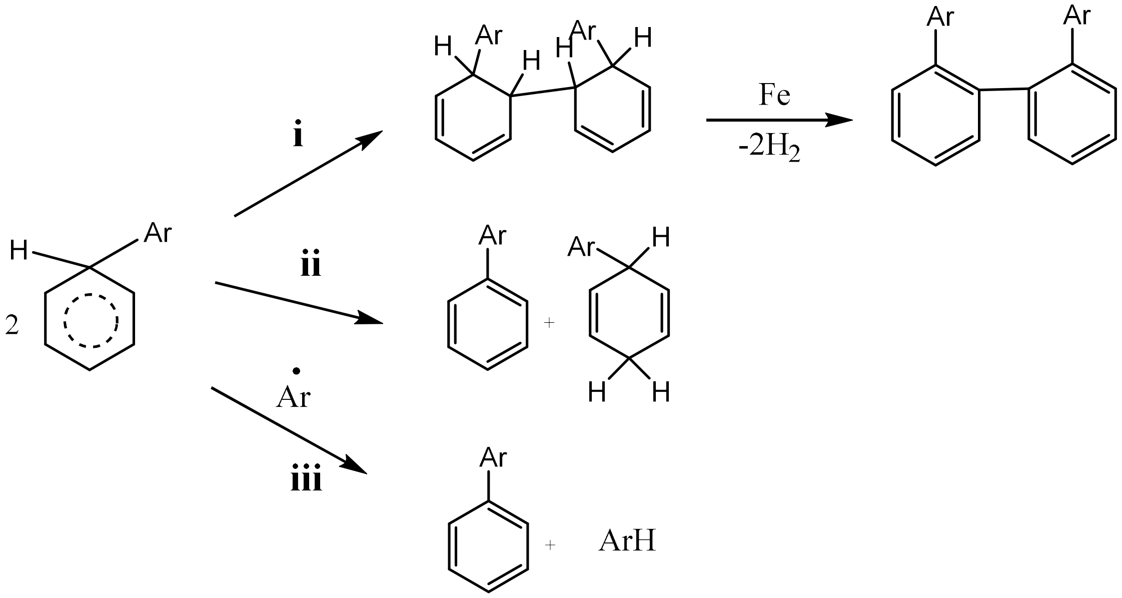
stable by resonance

The reaction can terminate in **three ways**:

a- By simple to give i.

b- By disproportionation to give ii.

c- If species $Ar^{\cdot}$ is present that abstracts hydrogen by abstraction to give iii.


2
H
Ar
i
ii
Ar
iii
H
Ar
H
H
Ar
H
Fe
-2H2
Ar
Ar
Ar
+
Ar
H
H
H
Ar
+
ArH