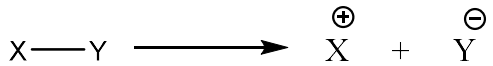
Free-Radical Chemistry: Structure and Mechanism:

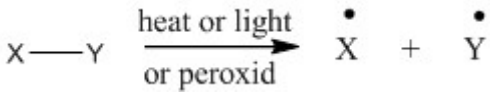
A free radical: is any molecular species capable of independent existence that **contains** an **unpaired electron** in an atomic orbital.

Bond cleavage is the splitting of chemical bond: There are **two types** of bond cleavage:

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



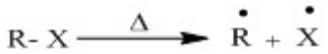
2- **Homolytic cleavage**: **The two electrons in the bond are divided equal between the products (this cleavage is generated Free radical).** Radicals are **intermediates** with an **unpaired electron** (**highly reactive**, **short-lived species**, **electrophile**).



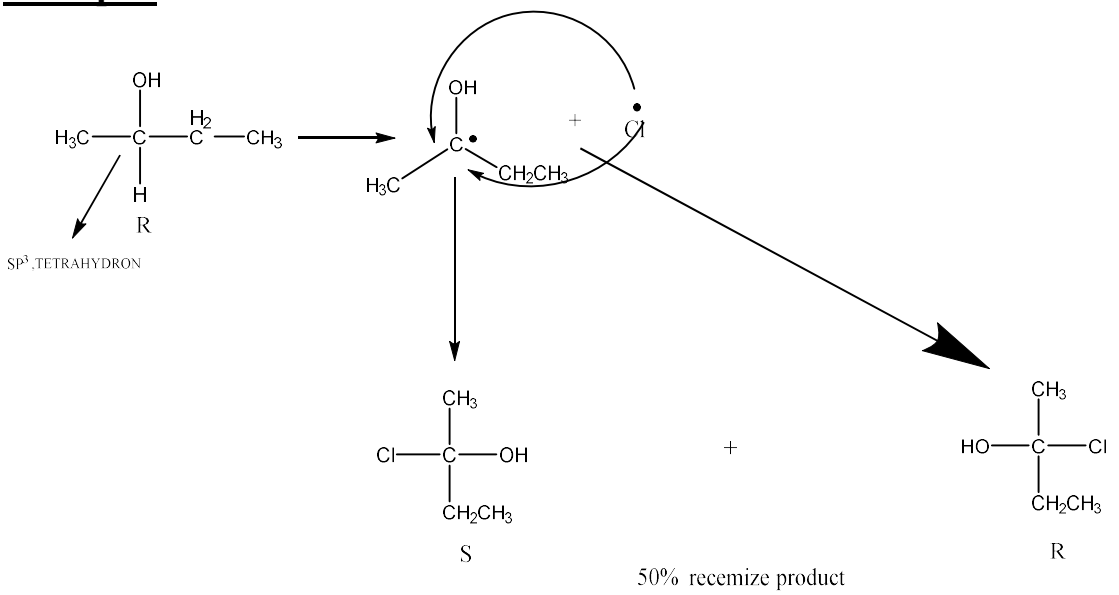
Formation of Free Radicals: **Three** general methods are used for the generation of free radicals:

1- **Thermal** Generation. 2-**Photochemical** Generation. 3-**Redox** Generation.

- When R-X **chiral** compound, **R take place at achiral carbon**, **racemization** is almost observed **because free radical (do not retain configuration).**



Example:

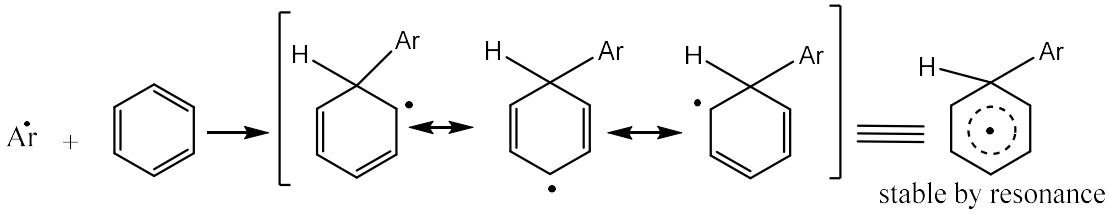


- When compound is **aromatic** :

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

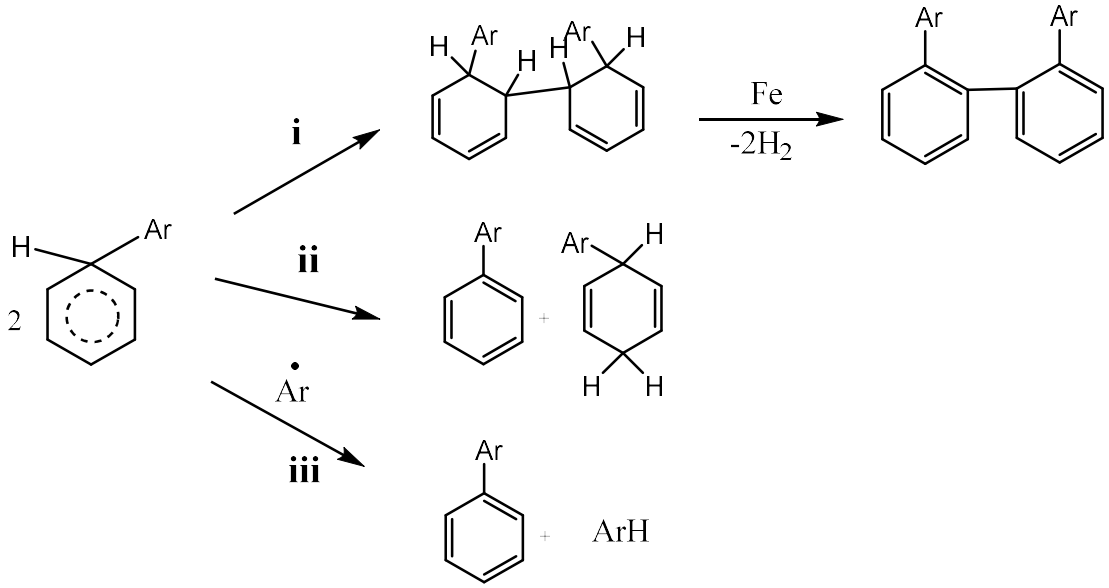
The product can be explained a **mechanism** similar to that of **electrophilic aromatic substitution**. In the **first step**, the radical Ar˙ attacks the ring in much the same way as would an electrophile or nuclophile.

Mechanism:



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

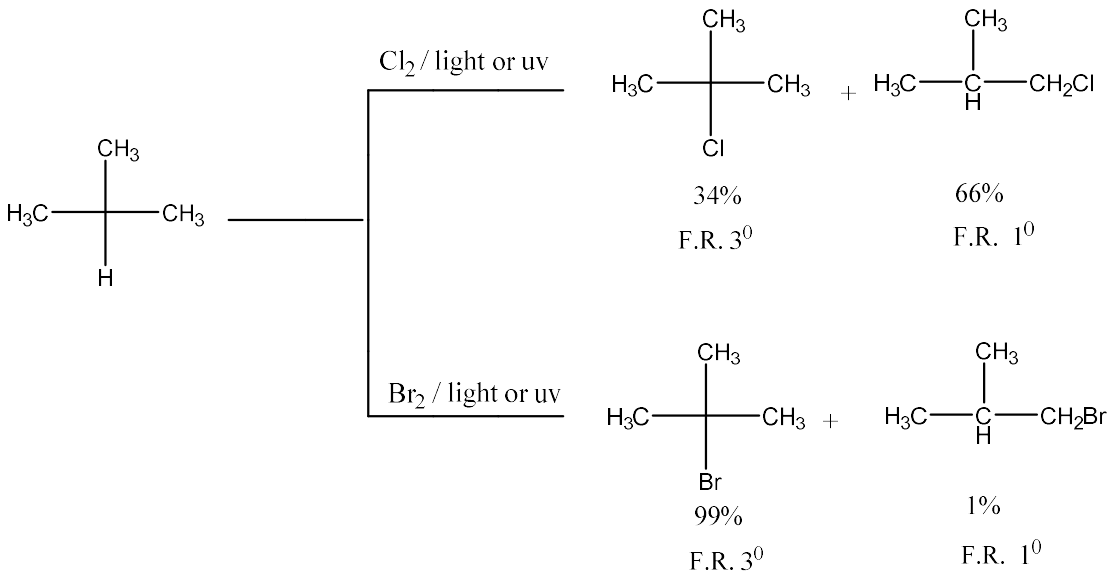
a- By simple to give i.
b- By disproportionation to give ii.
c- If species Ar˙ is present that abstracts hydrogen by abstraction to give iii.



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:

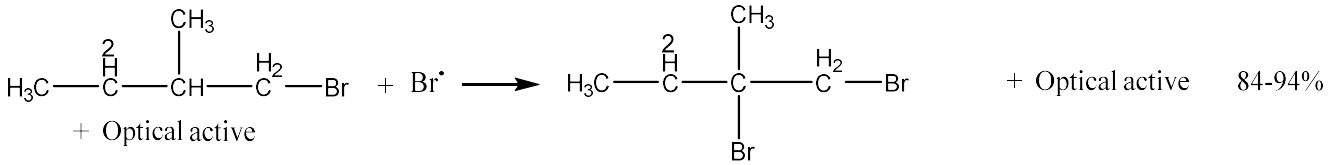


Neighbouring Group Assistance in Free Radical Reactions:

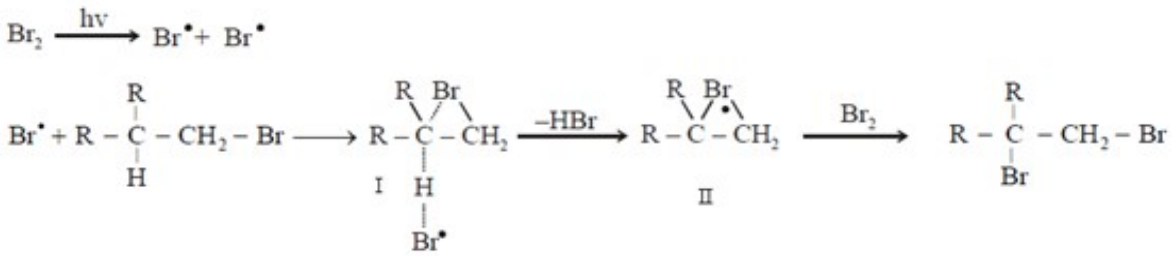
In certain cases it has been shown that free radical reactions are accelerated by the presence of neighbouring group.

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

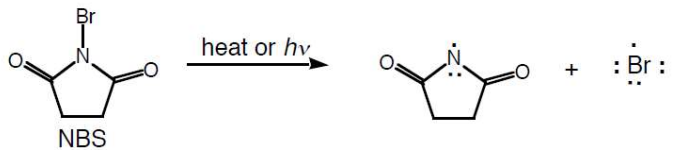
Example: **Bromination** of alkyl bromide give **84-94%** substitution at the carbon adjacent to the bromine already in the molecule positions close to a polar group, such as bromine, should actually be **deactivated electron withdrawing field effect** of the bromine, the unusual **regioselectivity**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



Mechanism:

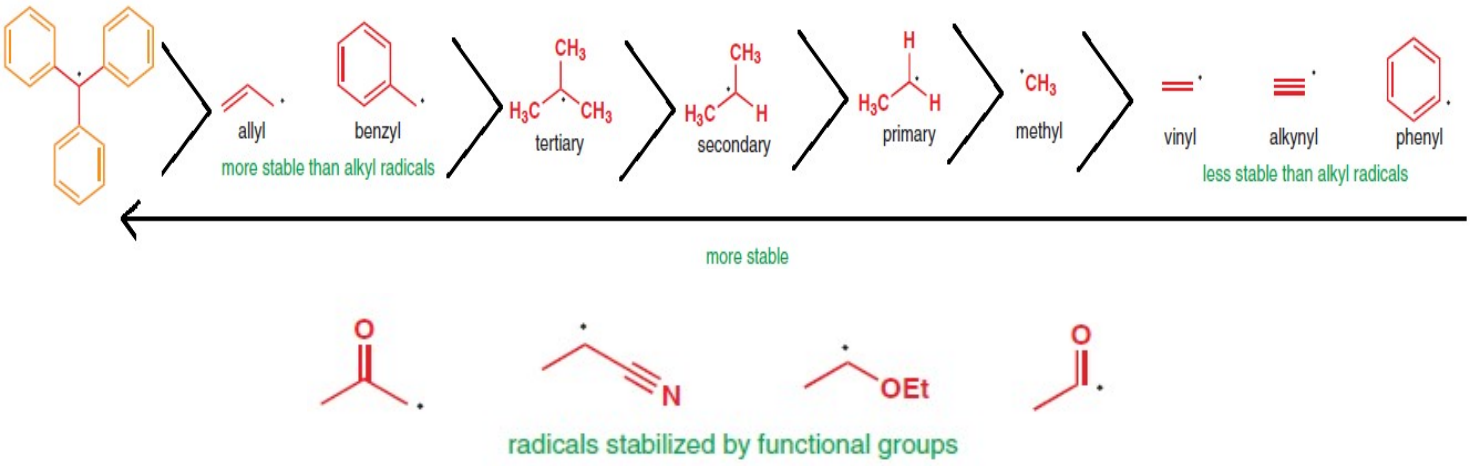


- **NBS** (**N-bromosuccinimide**) is often **used** as the **Br source** in **free radical brominations**.

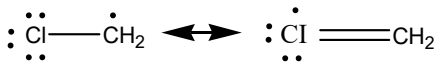


Radical stability:

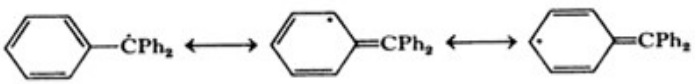
The H atom that is removed is best **allylic** or **benzylic** (**the C is attached to a C=C π bond or to a benzene ring by resonance**). the order of reactivity of H atoms is stability:



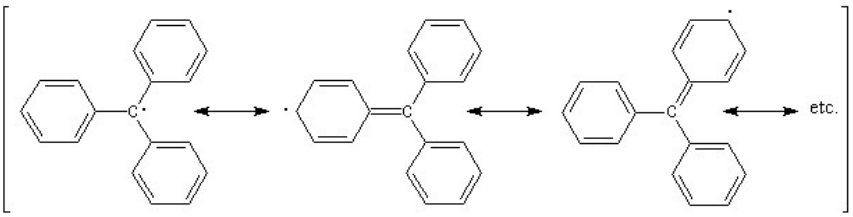
- **CI, S increased stability** of free radical because it's **content empty orbital and resonance**.



The e.s.r. spectra of triphenylmethyl radicals indicate that there is considerable delocalization of the unpaired electron onto the *ortho*- and *para*-positions of the phenyl rings (iii). The extent of delocalization of the unpaired electron was not, however, very much greater for triphenylmethyl radicals than for diphenylmethyl or benzyl radicals ·

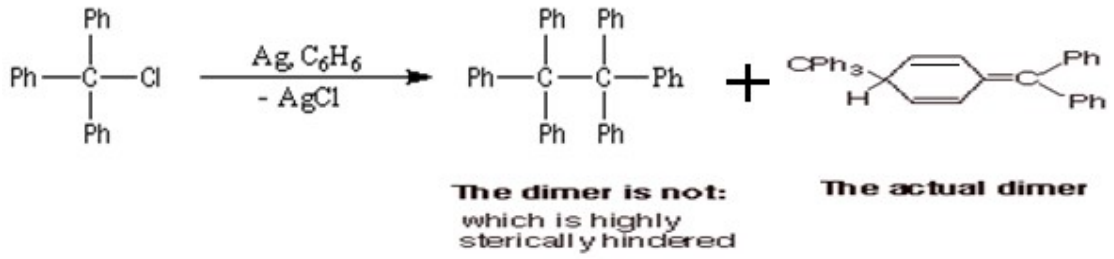


(iii).

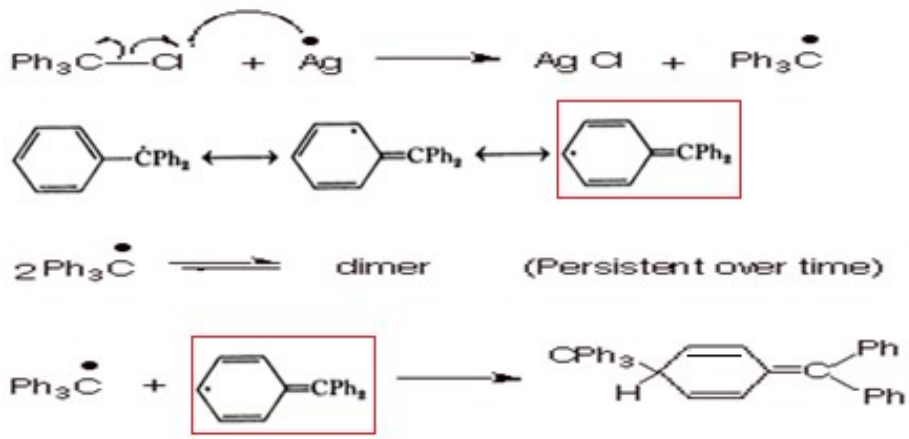


The stability of triphenylmethyl radicals must thus be due more to steric influences which prevent dimerization rather than delocalization of the unpaired electron. That the unpaired electron is not that much more extensively delocalized in the triphenylmethyl radical than the benzyl radical arises from the lack of coplanarity of the phenyl groups in the former.

Example:



Mechanism:

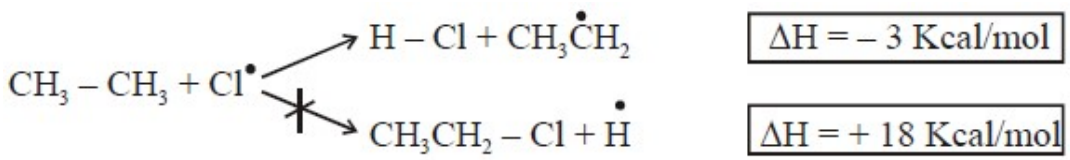


Reactivity:

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 teracovalent 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 for 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 favoured.

Group sequence in reaction with Br and Cl:

Cl :more reactive ,less selective

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

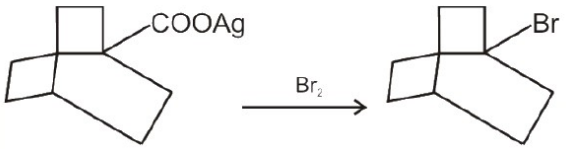
Br less reactive :more selective

2- **<u>The compound containing electron withdrawing substituents:</u>**

<u>Example:</u> $Z\text{-}CH_2CH_3$ (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**. Compound 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**. Hydrogens on carbon atoms next to the electron with drawing groups **have low electron densities**; therefore, the attack is avoided at this position.

3- **<u>Reactivity at the bridgehead:</u>**

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



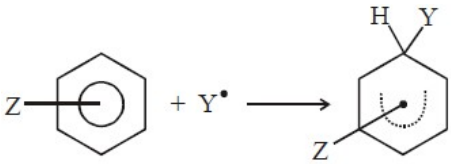
87%

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- **<u>Reactivity In Aromatic Substrates:</u>**

Free radical substitution at an aromatic carbon seldom takes place by a mechanism in which a ring hydrogen is abstracted to give an aryl radical.

Usually the mechanism is similar to that of aromatic electrophilic and nuleophilic 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. Further-more, it has been shown that both electron donating and electron-with drawing groups stabilise a free radical.

5- **Reactivityof 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°, 2° or 3°. The following table shows the **bond dissociation energy** that is the energy required to break the bond in a homolytic fashion, generating R· and H·

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· also get easier to form, with 3° being the easiest.**
1°	CH_3CH_2-H	410	98	
2°	$(CH_3)_2CH$-H	397	95	
3°	$(CH_3)_3C$-H	265		

b- Reactivity of X· (Halogen radical, X·):

1- Bromine radicals are less reactive than chlorine radicals.

2- Br· 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.

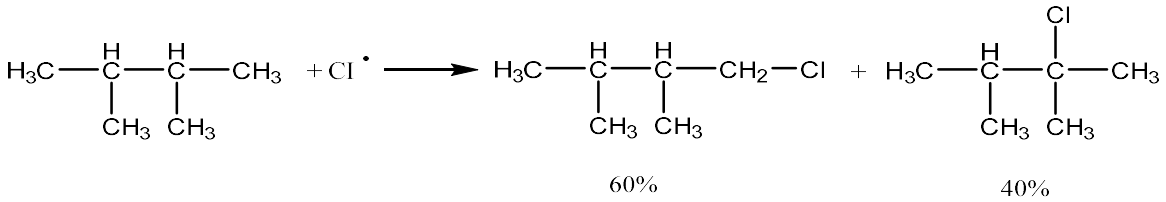
	Br	Cl
1°	1	1
2°	82	3.9
3°	1640	5.2

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°.

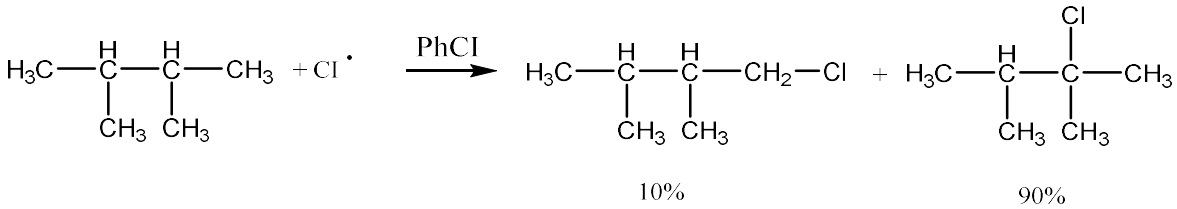
6- **<u>The effect of solvent on reactivity:</u>**

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

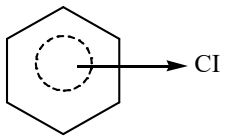
a- Aliphatic solvent:



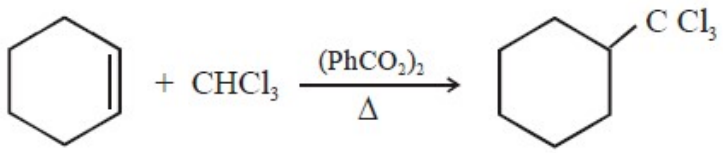
b- Aromatic solvent:



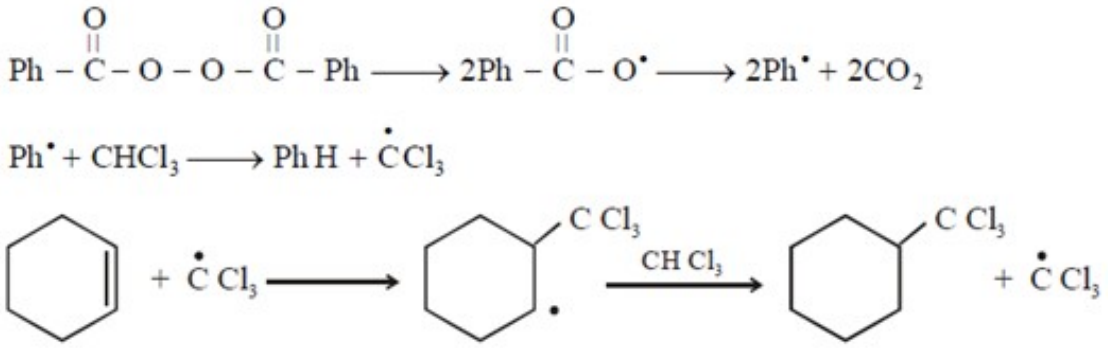
This result is attributed to complex formation between the aromatic solvent and the chlorine atom that makes the chlorine more selective:



<u>Example:</u>



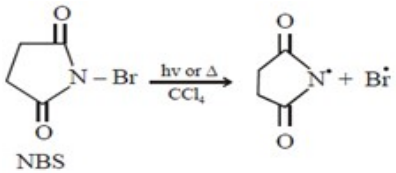
<u>Mechanism:</u>



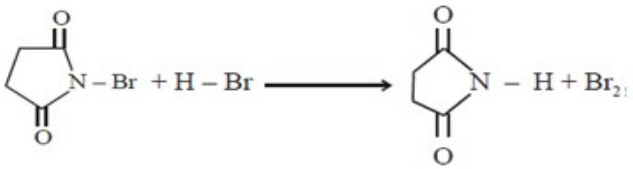
Example:

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

Mechanism:



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

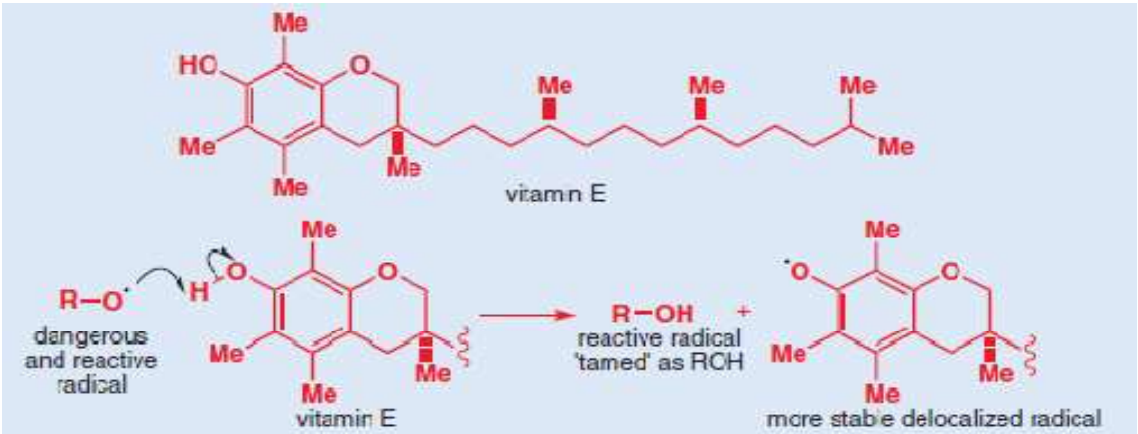


$$\dot{C}H_2-CH=CH_2 + Br_2 \longrightarrow Br-CH_2-CH=CH_2 + \dot{Br}$$

Example:

$$\underset{\text{Propane}}{CH_3CH_2CH_3} \xrightarrow[\text{light, } 127^\circ]{Br_2} \underset{3\%}{CH_3CH_2CH_2Br} \quad \text{and} \quad \underset{97\%}{CH_3\underset{\underset{Br}{|}}{C}HCH_3}$$

Radical reactions in biology:

Vitamin E tames radicals

Many of the molecules that make up the structure of human tissue are susceptible to homolysis in intense light, and the body makes use of sophisticated chemistry to protect itself from the action of the reactive radical products. Vitamin E plays an important role in the 'taming' of these radicals: abstraction of H from the phenolic hydroxyl group produces a relatively stable radical that does no further damage.