



CLASSIFICATIONS AND REACTIONS INVOLVING CARBON RADICALS

Key words: radicals, stability, addition, cyclization reactions, polymerization





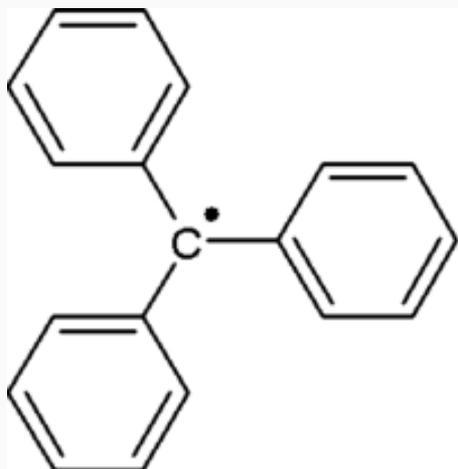
INTRODUCTION

In this module an overview of carbon radicals are given. Some preliminary examples of their structure, properties and reactions are provided. Since this topic is expected to be part of physical organic and other domains, only a brief account is presented.



CARBON RADICALS

The first organic free radical identified was **triphenylmethyl radical** formed by abstraction of chlorine by silver metal .



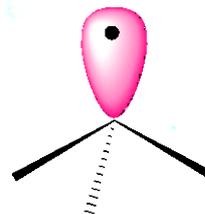
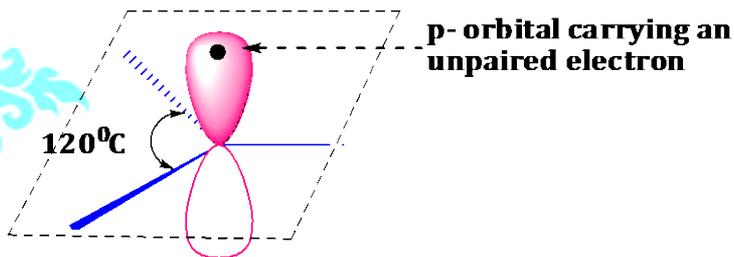
This species was discovered by **Moses Gomberg** in 1900 at the University of Michigan USA.



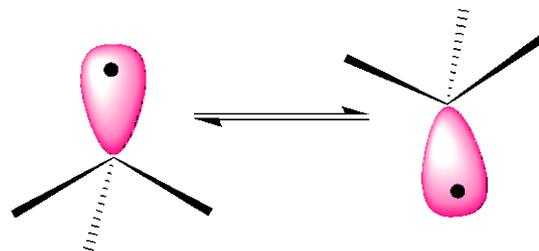
- A **radical** is a **reactive intermediate** with a **single unpaired electron**, having very short lifetime .
- Radical reaction are **non-ionic reactions** judged by the **frontier molecular orbital approach** (and not the nucleophilicity or electrophilicity concept).
- It is generated by **homolysis** of a **covalent bond**.
- Radical is represented by atom with one dot.
- Electronic movements involving radicals are represented using half headed fishhook arrows.
- Carbon radical is a neutral carbon species with three single bonds and one unpaired electron.

STRUCTURE OF RADICAL

- A carbon radical is sp^2 hybridized with an unpaired single electron occupying an unhybridised p-orbital, having trigonal pyramidal or planar geometry possessing an angle of 120° .



sp^2 Hybridised carbon having rigid pyramidal geometry.

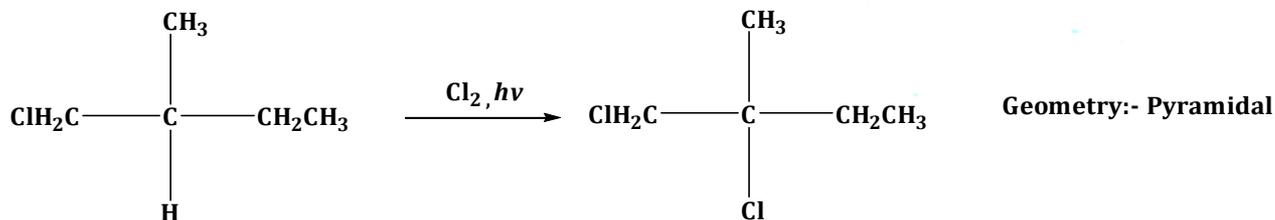


Flexible pyramidal geometry

- In most of the cases the pyramidal geometry is observed, especially when heteroatom's are π electron donating substituent or electronegative groups like fluorine or oxygen are present. However, some of the lower group of alkyl class like methyl possess planar geometry, t-butyl show pyramidal geometry with a slight characteristics of planar geometry.
- The energy required to invert the geometry is very low in the case of flexible pyramidal geometry.

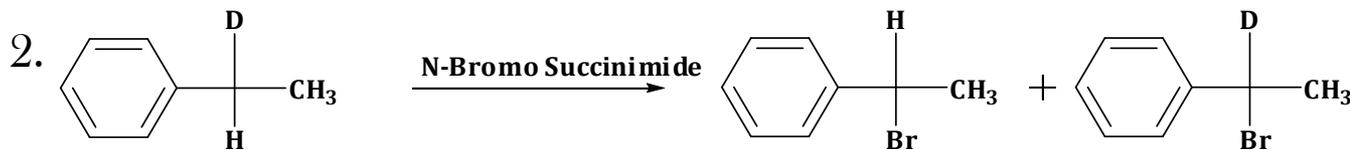
PREDICTION OF GEOMETRIES.

- Geometries can be very well predicted from the product stereochemistry.
- Rigid pyramidal geometry of structure give product with retention of configuration .
- Planar or rapidly inverting radical will give racemised product.
- Examples :-1.



(+)-1-Chloro-2-methyl butane.

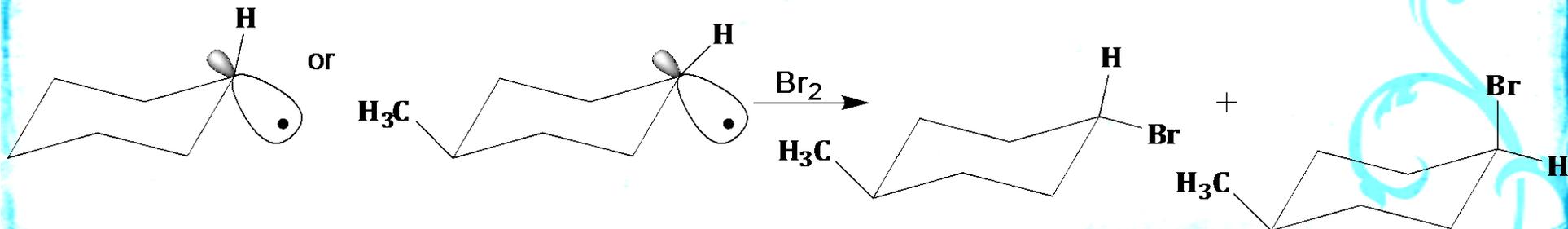
(±)-1,2-dichloro-2-methyl butane.



99.7 % racemization

Geometry:- Pyramidal

However in case of cyclic compound the stereochemistry is not retained. Cis and trans isomers both independently give cis or trans isomer .

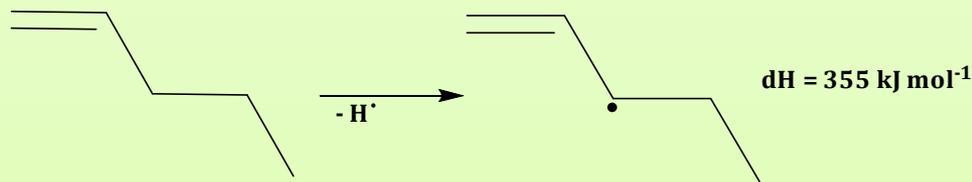
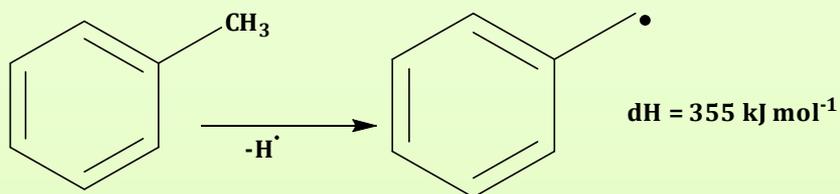


STABILITY OF RADICAL

Radicals are produced by heat or light or by the action of peroxide. Once a radical is produced, it will attack another species and would try to abstract a hydrogen radical or bind with another radical or with a π electron, forming σ bond in all the cases,

Radicals are formed when they are exposed to sufficiently high energy (in the form of heat or light) to break the bond between the two atoms.

The increased substitution will improve the stability of radical formed, and lesser will be the energy required for its formation.



Allyl radical
 $dH = 369 \text{ kJ mol}^{-1}$

$(\text{CH}_3)_3\text{C}^\bullet$
Tertiary
butyl radical
 $dH = 400 \text{ kJ mol}^{-1}$

$(\text{CH}_3)_2\text{CH}^\bullet$
Secondary
radical
 $dH = 431 \text{ kJ mol}^{-1}$

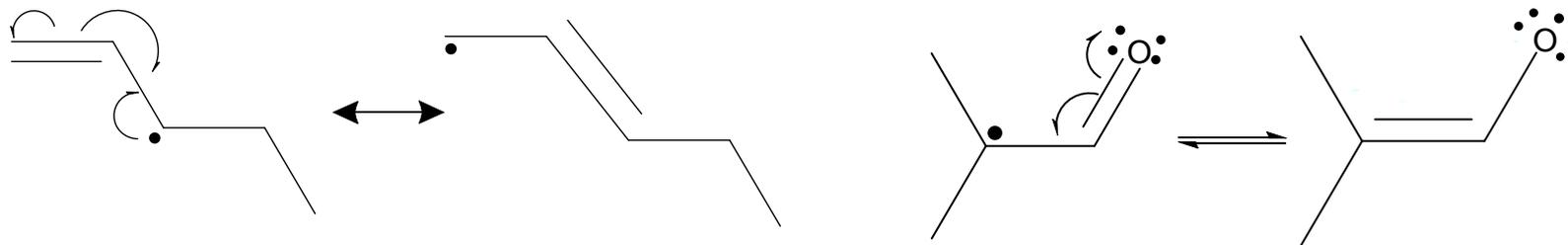
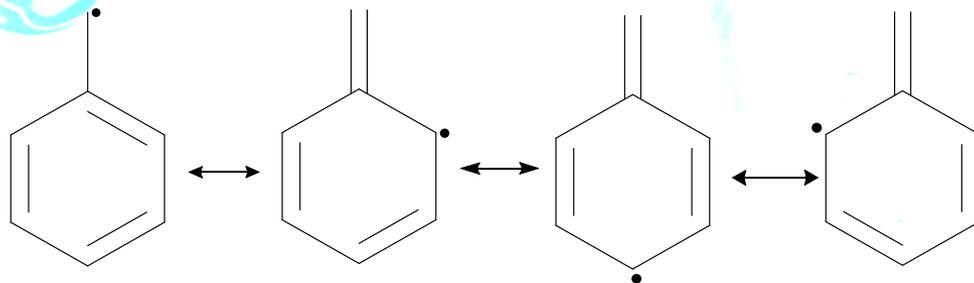
$\text{CH}_3\text{CH}_2\text{CH}_2^\bullet$
Primary
radical
 $dH = 423 \text{ kJ mol}^{-1}$

$\text{CH}_2=\text{CH}^\bullet$
Vinyl
radical
 $dH = 465 \text{ kJ mol}^{-1}$

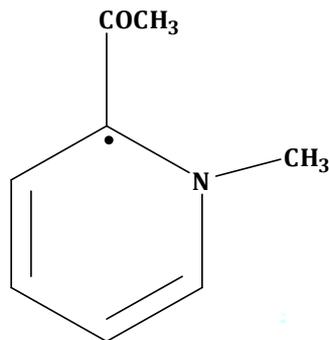
$\text{C}_6\text{H}_5^\bullet$
 $dH = 460.55 \text{ kJ mol}^{-1}$

Hence stability decreases from allylic and benzylic radical to vinylic and phenyl radical.

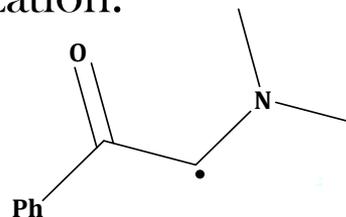
- The higher stability of radical in the case of benzyl and allyl through resonance stabilization. This type of stabilization is not present in case of phenyl or vinyl radical.



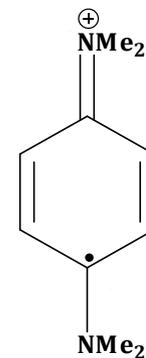
- When both electron donating and withdrawing groups are present in the same molecule, with a suitable separation between them, it can provide additional stabilization known as captodative stabilization.



J.Hermolin , M. Levin, JAC 1991 103: 4795



F. M. Welle , H.D. Beckhaus
& G.Ruchardt
liebigs Ann 1997: 155



Wruster's salt

Carbocation

- Carbocation are electron deficient species with 6 electrons accounting for a lower stability and higher energy state.
- The stability is supported by alkyl group, pi bonding electron or lone pair .
- In a chemical reaction when carbocation MO or AOs interact with filled MO or AOs the electrons are placed in lower energy bonding orbital .

Radical

- Radicals possess 7 electrons with a better stability due to lesser energy compared with carbocation hence lower member of radical are existent.
- Stability resulting from alkyl pi bonding or lone pair is relatively negligible, however there is assisted stability in case of benzylic radical.
- When a radical interact the two electrons are placed one in lower energy and one in higher energy antibonding orbital.

THE FMO APPROACH FOR RADICAL REACTIVITY

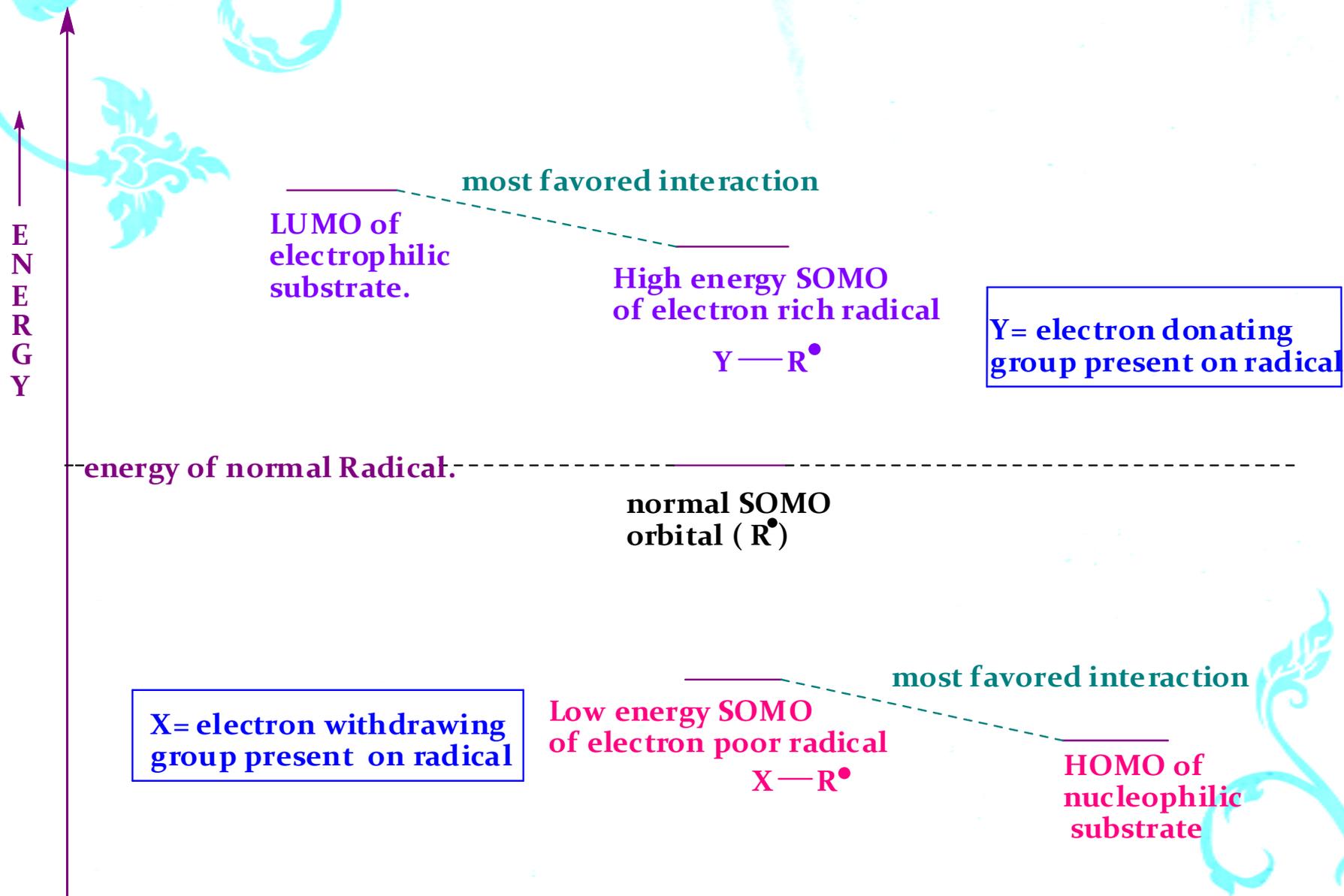
- As we know that radical reactions are non ionic reactions in which energy of the orbitals involved are most important for reactivity.
- Radical posses a single unpaired electron typically in a p -orbital known as **SOMO** (Singly Occupied Molecular Orbital), which is quite higher in energy. Any factor that **decreases this energy** will result in **increased radical stability** and **decreased reactivity**. This factor is more precisely presented by the electron donating or withdrawing group attached with radical carbon,

Interaction of radicals with electrophilic and nucleophilic substrate,

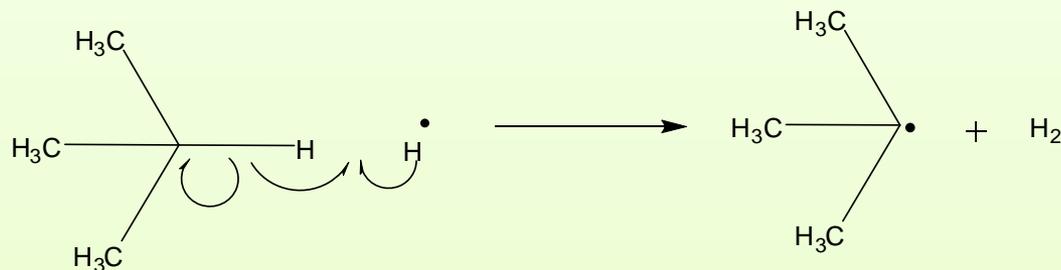
Radical having lower energy SOMO can accept an electron and can best interact with the HOMO of the incoming substrate having nucleophilic character.

Radical having higher energy SOMO is ready to give away the electron. It will best interact with the LUMO of the incoming substrate having electrophilic character.

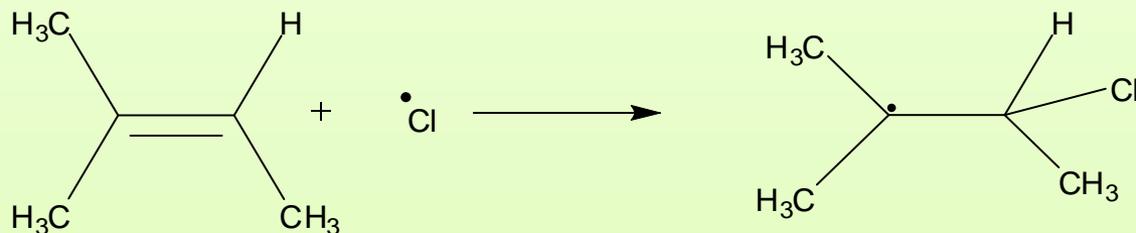
• ENERGY DIAGRAM OF INTERACTION OF RADICAL.



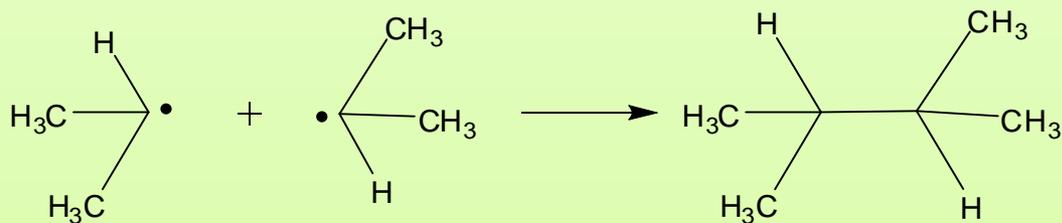
- **Reactions of free radicals**
- Consider a radical **R** undergoing a reaction.



- The addition to alkene result in radical initiation step where the molecule of reactant alkene form a radical which then attack another similar molecule resulting in a polymer.



- Radical combination leading to termination

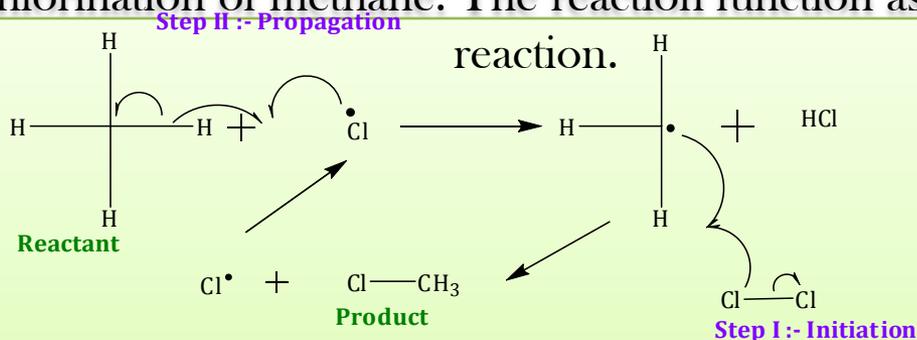


CLASSIFICATION OF RADICAL REACTIONS

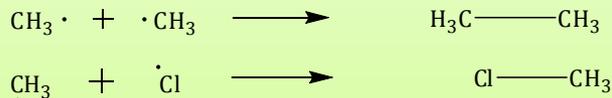
- Radical are generally very reactive species with a short lifetime. If the reaction rate can be controlled, selectivity of radical reactions can be improved. Radicals can undergo,
 - Substitution
 - Addition
 - Rearrangement
 - Auto-oxidation
 - Single electron transfer (SET).

SUBSTITUTION REACTIONS: This radical reaction involves substitution of smaller molecules, (e.g., chlorination of methane). The reaction function as a chain substitution reaction

- This radical reaction involve substitution of smaller molecules , the well known evident reaction is chlorination of methane. The reaction function as a chain substitution



Step III :- Termination



ADDITION REACTIONS.

- Addition reactions are carried out in the presence of **tinbutyl hydrides** and its higher analogs. Addition reaction of alkenes in the presence of radicals are extensively used in carbon- carbon bond formation reactions in organic chemistry.
- This reaction can further be classified as,

1. **Direct addition**

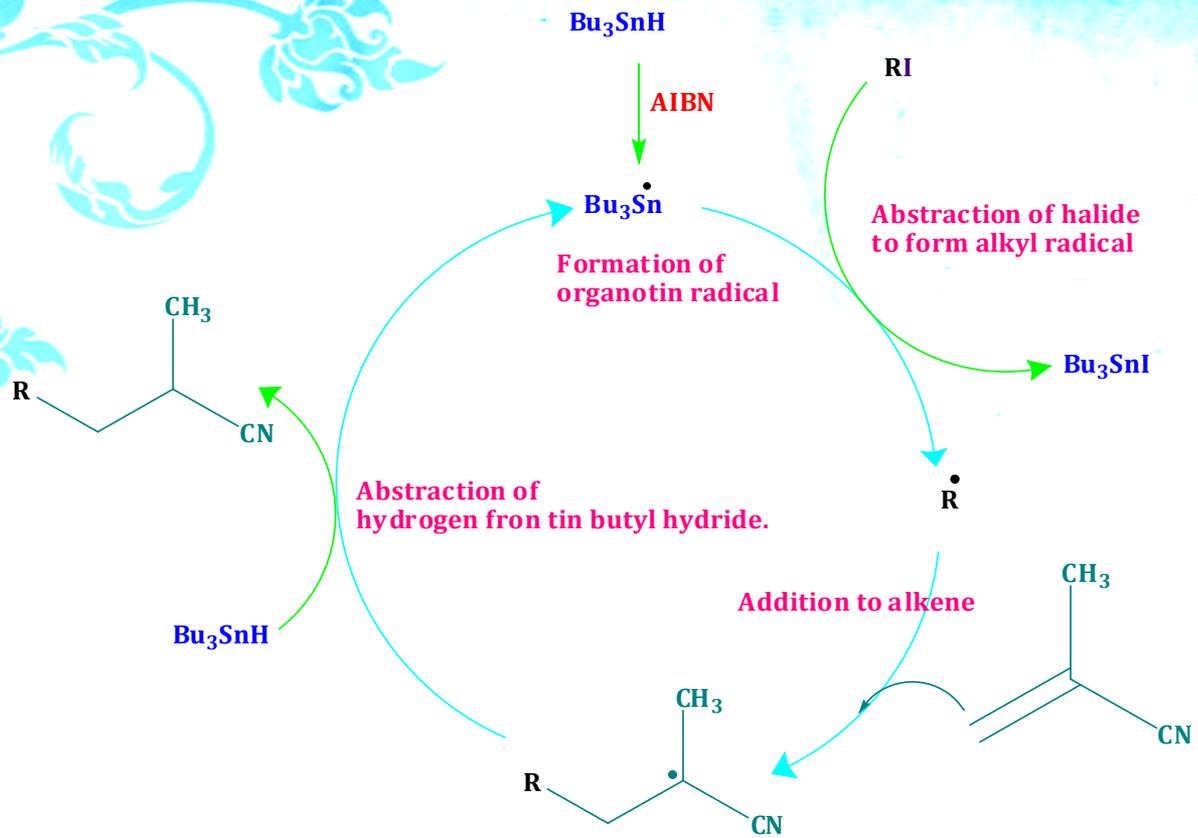
2. **Intramolecular cyclizations.**

➤ **Direct additions:-**

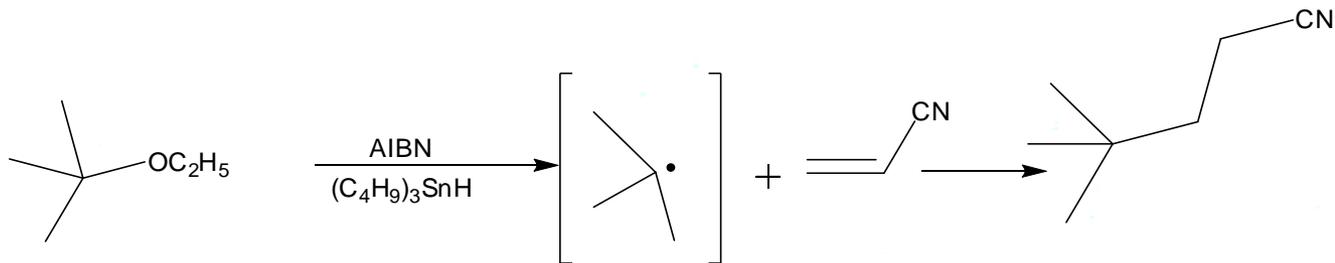
These reactions take place following the anti-Markovnikov's rule of addition.

The peculiar characteristic of the reaction is the product radical do not abstract the halogen from the alkyl halide, but abstract a proton from tinbutyl hydride. This tinbutyl hydride radical will then abstract a halogen from alkyl halide.

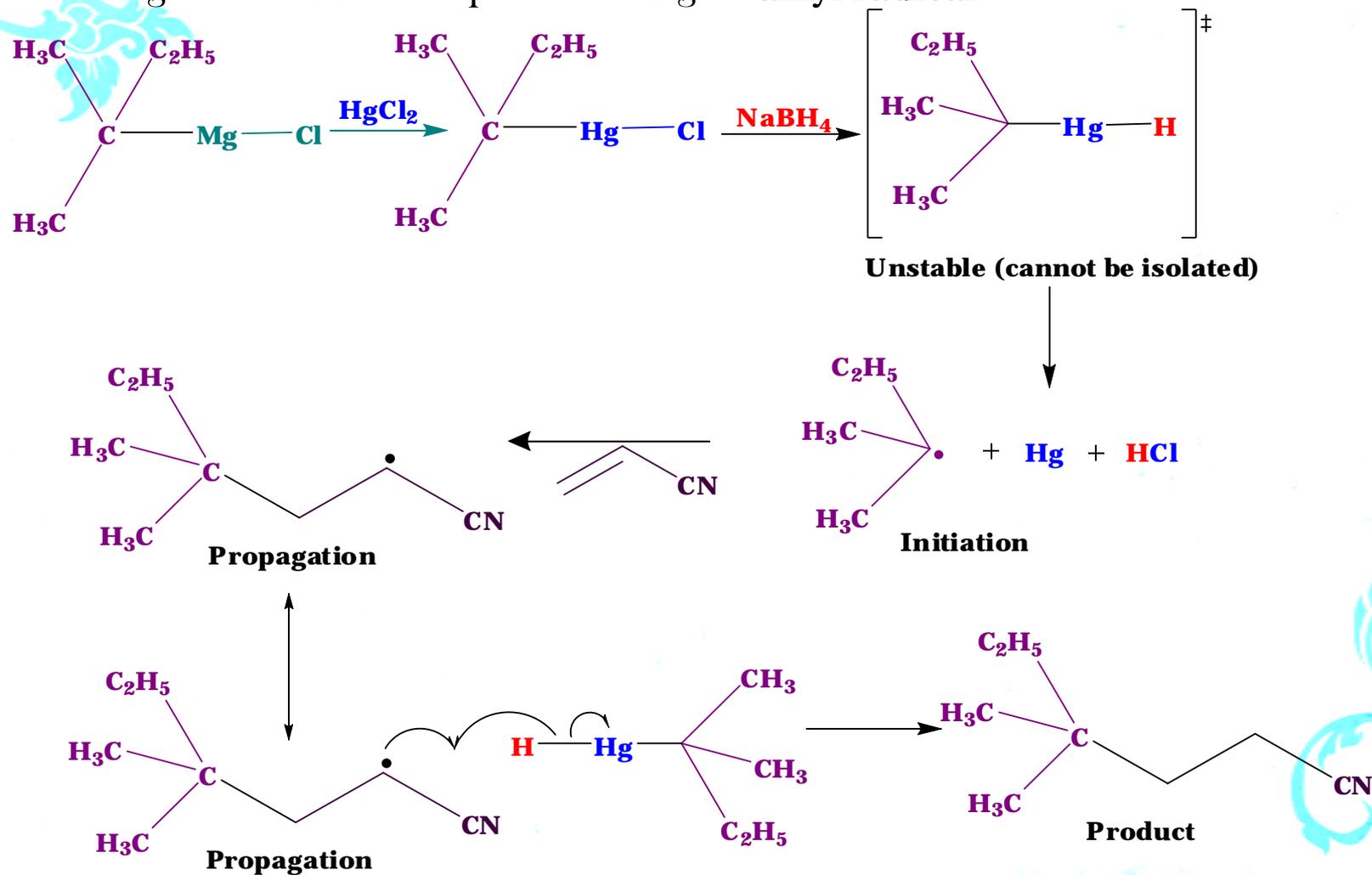
This can be explained through this cyclic mechanism,



• Example :-



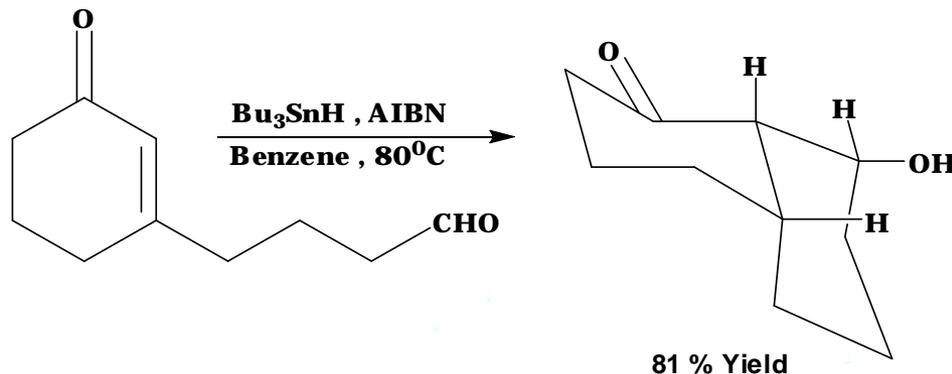
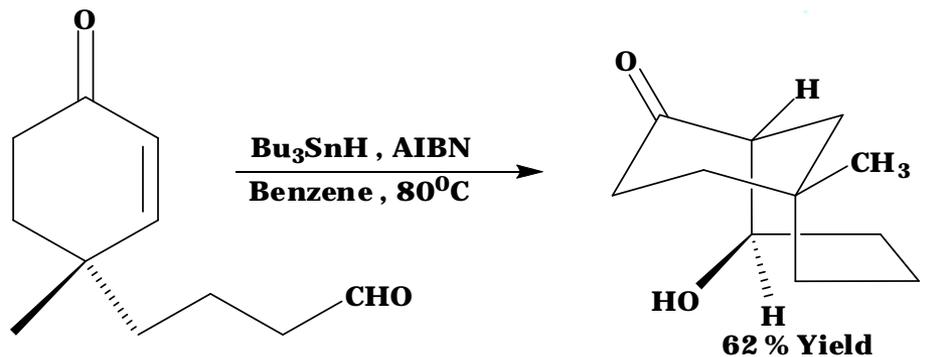
- Alkylations can even be performed using **alkyl mercuries**, this can be done by subjecting **alkyl mercury halides** to **reduction** in the presence of **Sodium Borohydride** leading to **unstable alkyl mercury hydride** which then disintegrate at room temperature to give **alkyl radical**.



• Addition reaction involving enones

- Attack occurs on the terminal alkene at that carbon away from the carbonyl carbon (Reason:- the high energy **Singly Occupied Molecular Orbital** of radical can best interact with FMOs or more specifically **the LUMO of electrophilic alkene** just slightly higher in energy).

- Example :-



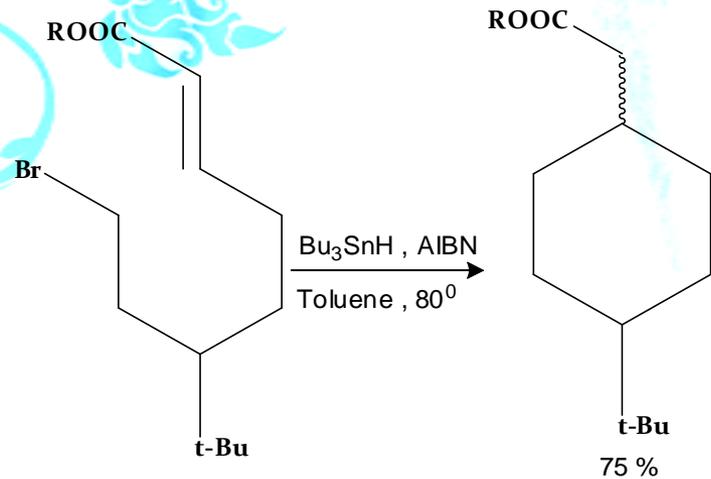
In radical addition the stereochemistry of reactant is conserved in product, here in case of cyclohexanone derivatives (e.g. 1) the stereochemistry is conserved.

Enholm, E. J.; Whitley, P. E.; Xie, Y. *J. Org. Chem.* 1996, 61, 5384.

● Intramolecular cyclizations

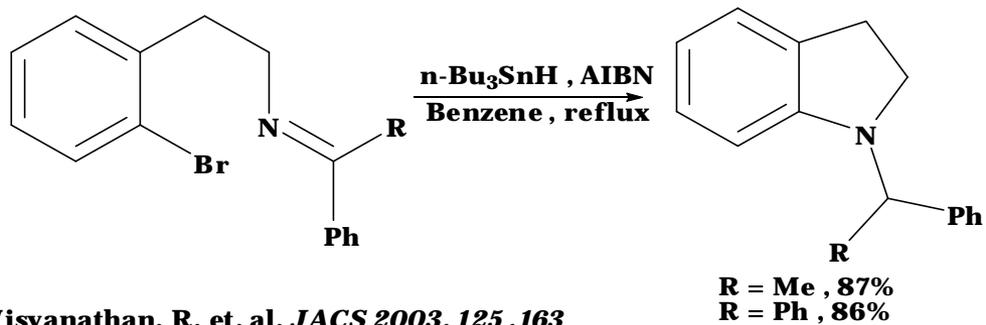
- Intramolecular radical cyclizations are very important steps in a large family of cyclization reactions.
- Radical cyclizations occur in a chain of three or more carbons attached at one end to a radical and another end to an alkene.
- These reactions is not driven by excess quantity of reagent, whatever be the substituent present on the radical or alkene part, the reaction is driven by radical trap which is typically a double bond present in the same molecule.
- The cyclization occurs such that the resultant intermediate has the radical site outside the ring and not in the ring (for stereoelectronic reasons). As per the stereoelectronic factors, to release or minimize strain, the radical should approach a double bond at nearly 109° angle (an essential factor for formation of sp^3 carbon).
- According to the above explanation, it would be feasible to approach the inner carbon attached to chain and not the terminal carbon which is far away from radical (if we try to do so, it will result in a highly strained structure, sterically unfavorable).

- Examples :-1.

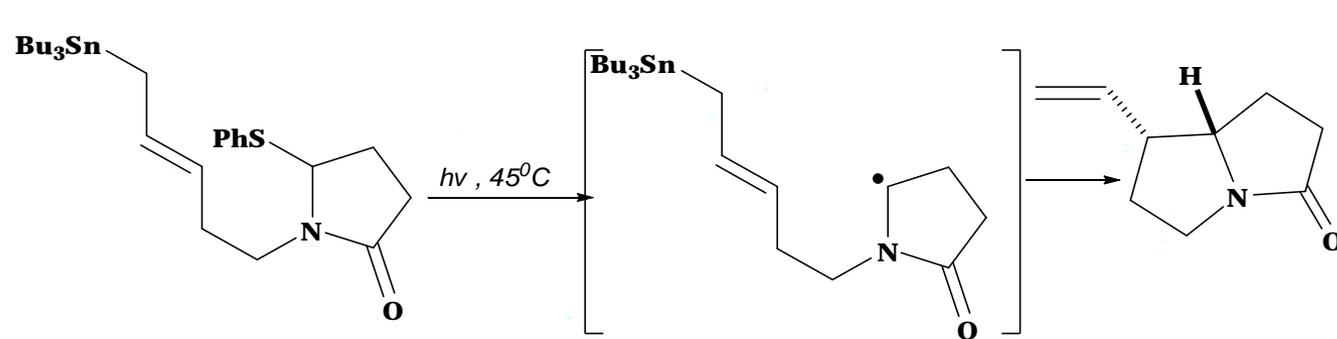


- Heteroatom in radical cyclization

- 1.

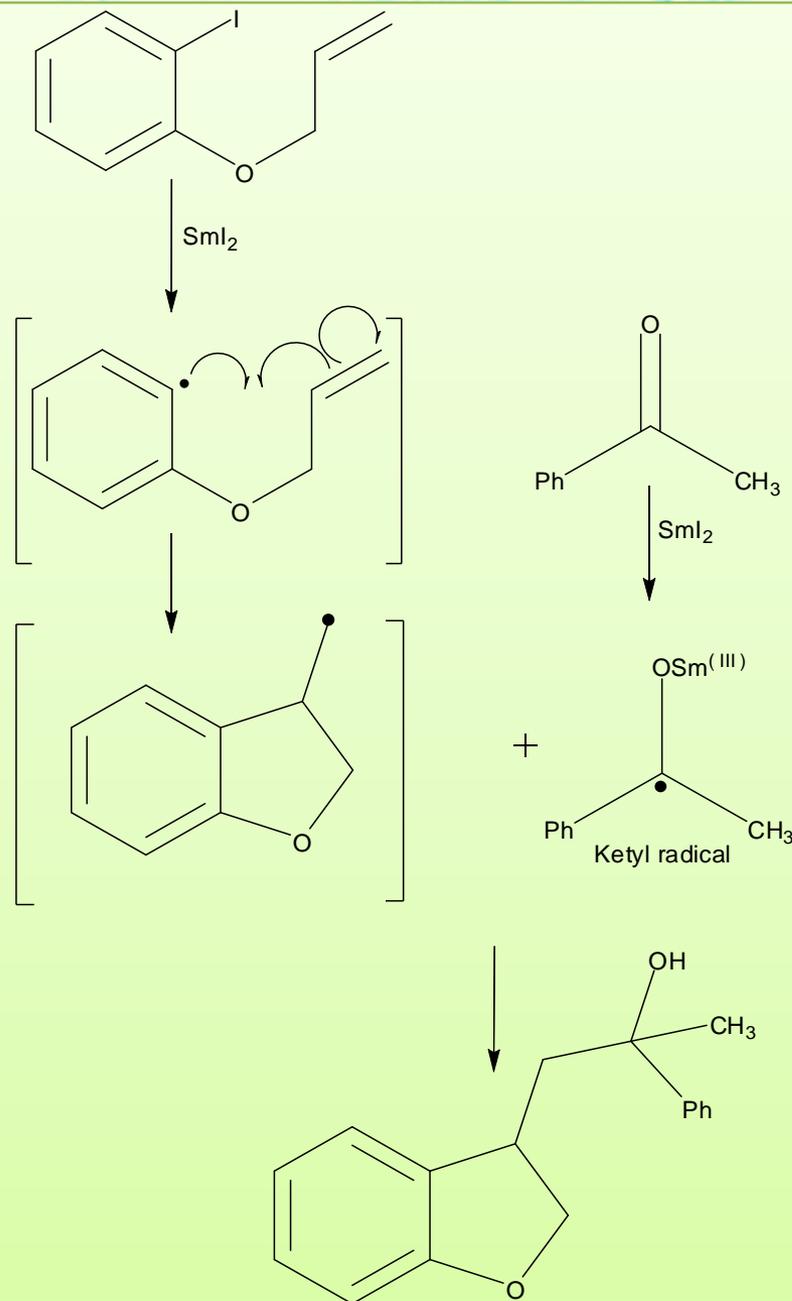


- 2.



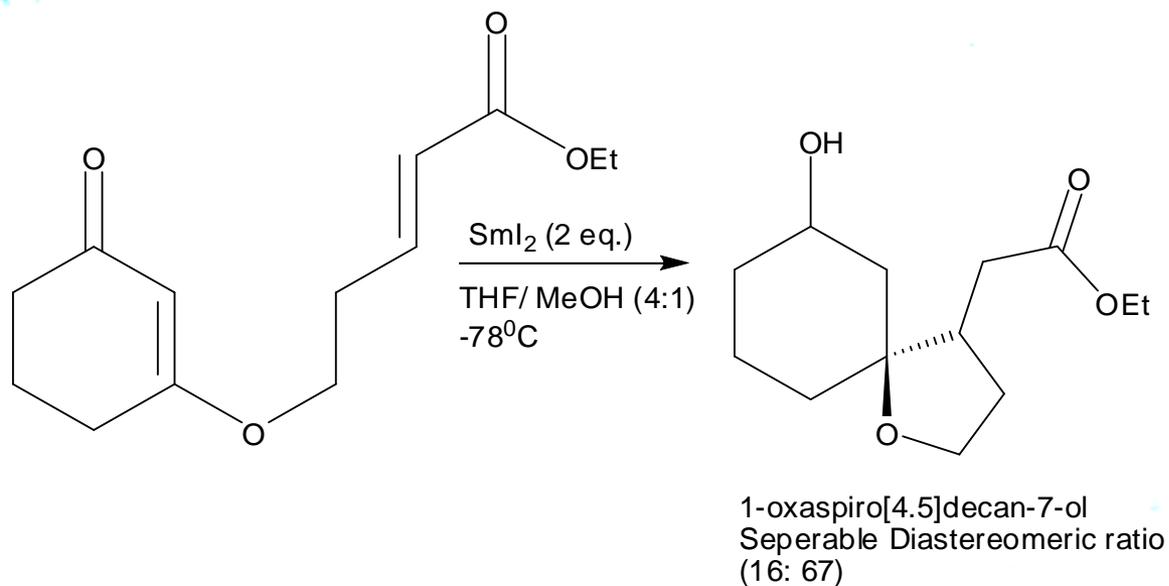
SAMARIUM IODIDE MEDIATED RADICAL CYCLIZATIONS.

- Samarium di-iodide is an excellent catalyst for synthesis of cyclic systems. The reaction follows similar type of ring closure as in the case of tributyl hydride.
- The reaction is carried out using THF as the solvent in presence of Hexamethylphosphoramide (HMPA).
- Samarium complex is added to the substrate to be cyclized. HMPA is added separately to the ketone to form ketyl radical. The cyclic radical was then added to reaction mixture to obtain the final product in good yield.



- Examples :-

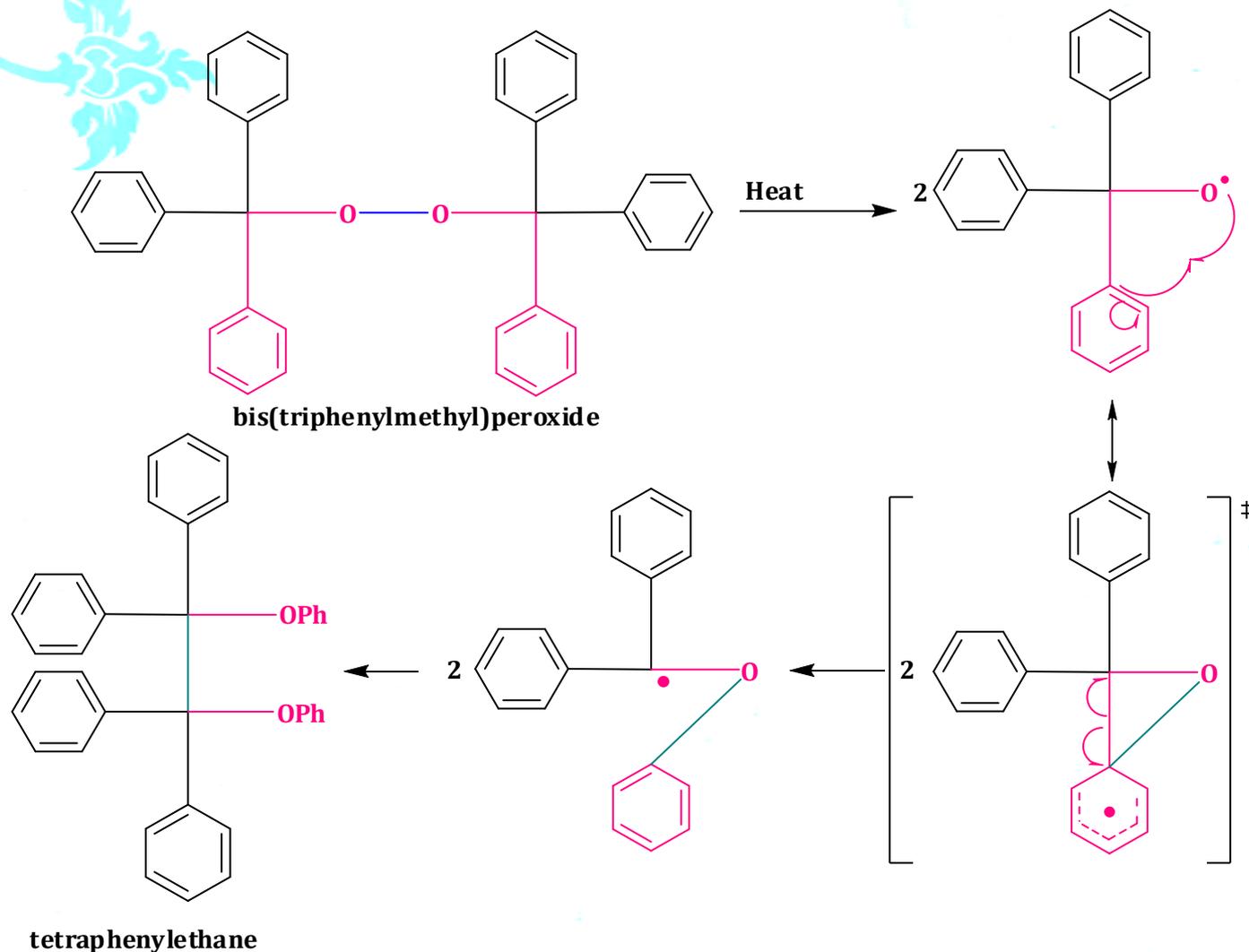
- Intramolecular cyclization of mixed enone-enoate for preparation of spirocyclic ethers.



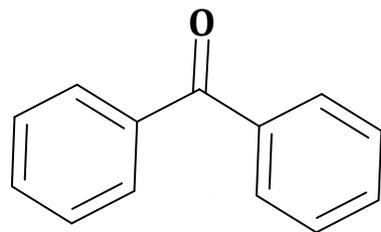
J. Meng et al. / Tetrahedron Letters 52 (2011) 928–931 929

REARRANGEMENT REACTIONS

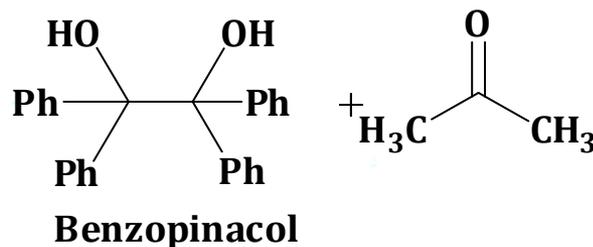
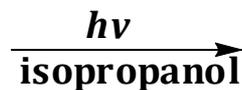
- The first type of 1,2- radical rearrangement reported by Heinrich Otto Wieland was the conversion of bis(triphenylmethyl)peroxide to the tetraphenylethane.



- Unlike carbocations, radicals undergo migrations less readily.
- In the above mentioned example and similar type of 1,2- rearrangements, the transition state involves bonding to three atoms simultaneously.
- In a radical reaction, the odd electron present in the transition state is stabilized by a pi electron system (In the above example, the benzene ring provide stabilization).
- An another class of reaction exhibited by radical when they are quite stabilized are **coupling reactions**, in some cases the radical have longer lifetimes, leading to **radical coupling reactions**.
- The most familiar reaction is conversion of Benzophenone to Benzopinacol , the reaction is quite easy to set i.e. mixing the reactant with isopropanol which act as the hydrogen donor as well as the solvent & is set conveniently in UV or visible light to obtain the crystalline benzopinacol .



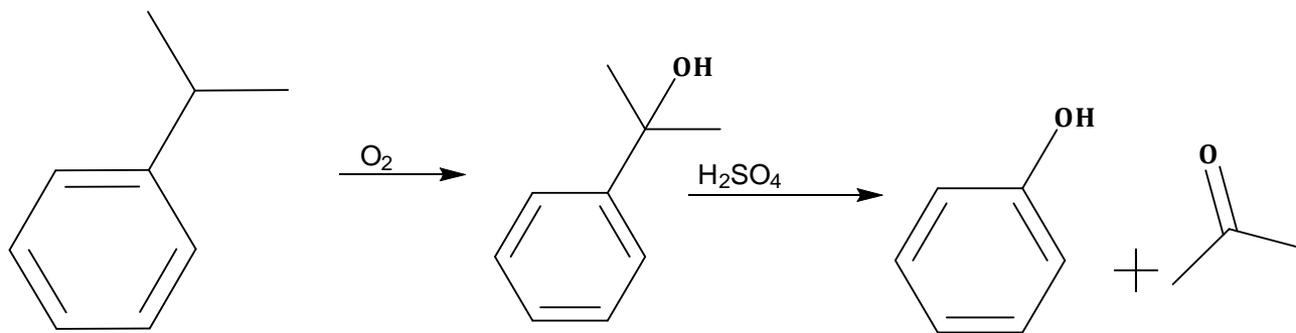
Benzophenone



Benzopinacol

AUTO-OXIDATION REACTIONS

- The reaction of radicals involving molecular oxygen in the presence of UV radiation to form peroxides and hydroperoxides are called oxidation reactions.
- E.g., cumene process for synthesis of phenol and acetone from benzene and propylene,



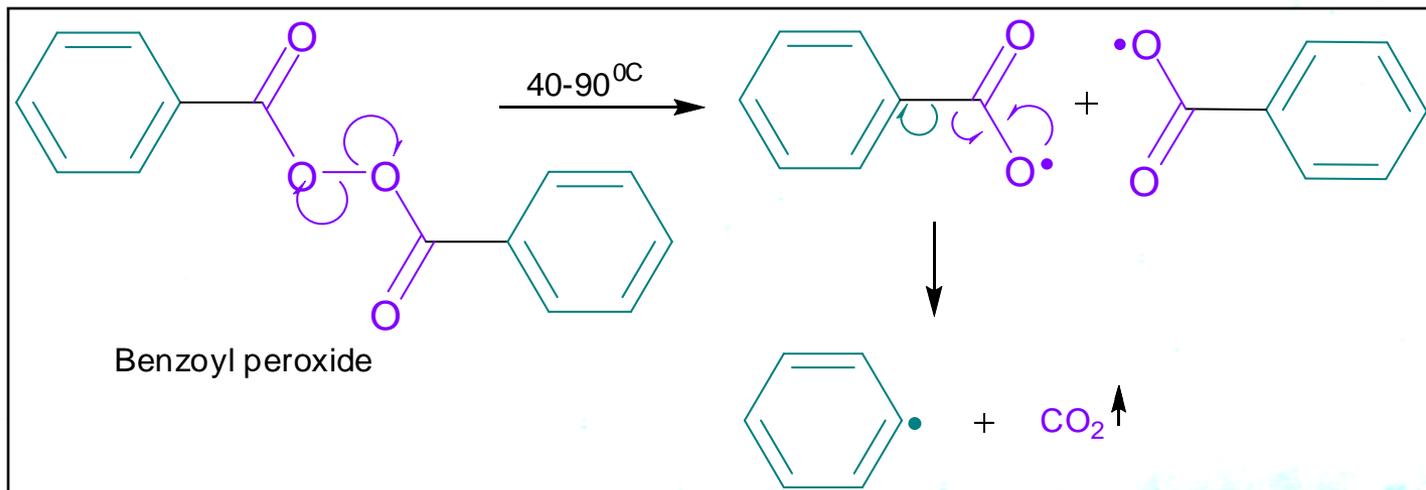
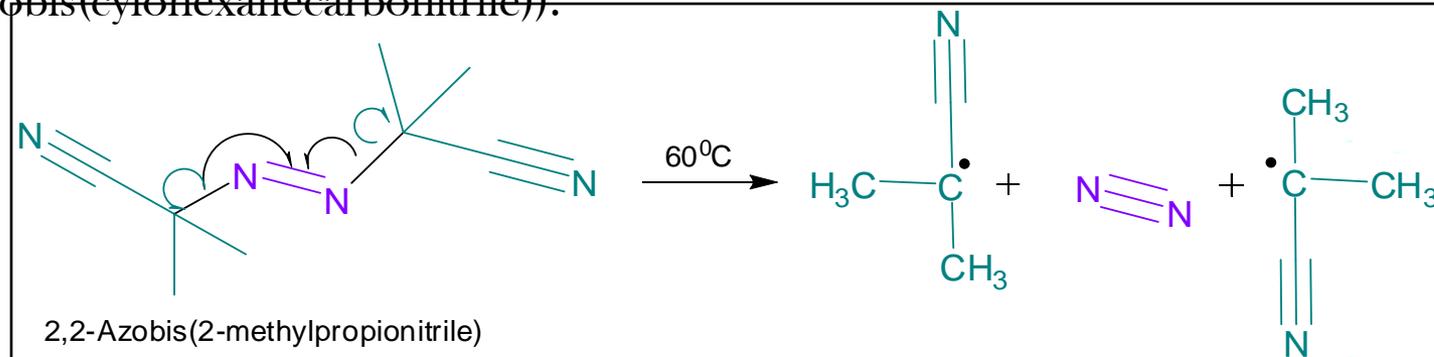
cumene

RADICALS IN POLYMERIZATION

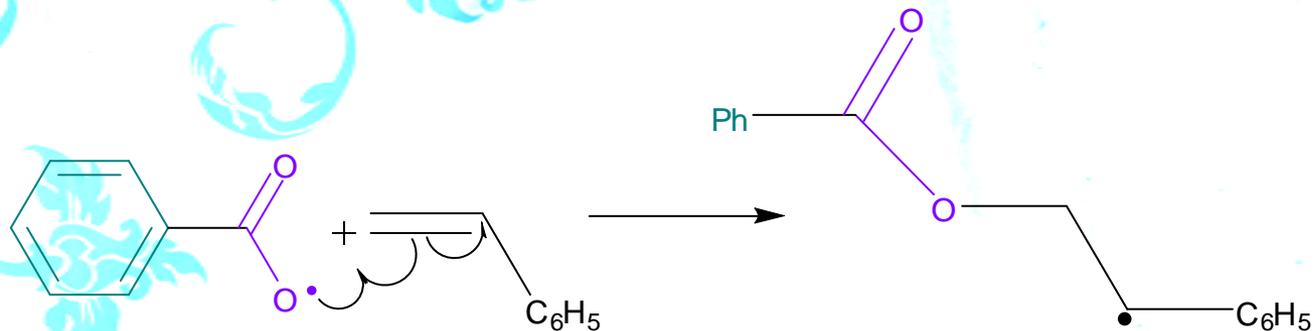
- Polystyrene, poly(methyl methacrylate), poly(vinyl acetate) and branched polyethylene are commonly synthesized by radical polymerization.
- Radical Polymerization involve three major steps
- **Initiation**:- starting a radical process i.e., formation of monomer radical.
- **Propagation**:- the newly-formed activated monomer attacks and attaches to the double bond of another monomer repeatedly to form a long polymer chain.
- **Termination**:-stopping the process of addition of monomer at the required step to isolate the chain.

INITIATION

- It involves thermal decomposition of weak bonds (like in peroxides or azo compounds), which further attack the monomers to create a radical site on the monomer. This step occurs in a solvent cage i.e., solvent do not take part in the reaction
- The process can be initiated by peroxide (t-butyl and cumyl hydroperoxides, t-butyl perbenzoate etc.) or AIBN (or its analogues like 2,20-azobis(2,4-dimethylpentanenitrile), 4,40-azobis(4-cyanovaleric acid), and 1,10-azobis(cyclohexanecarbonitrile)).

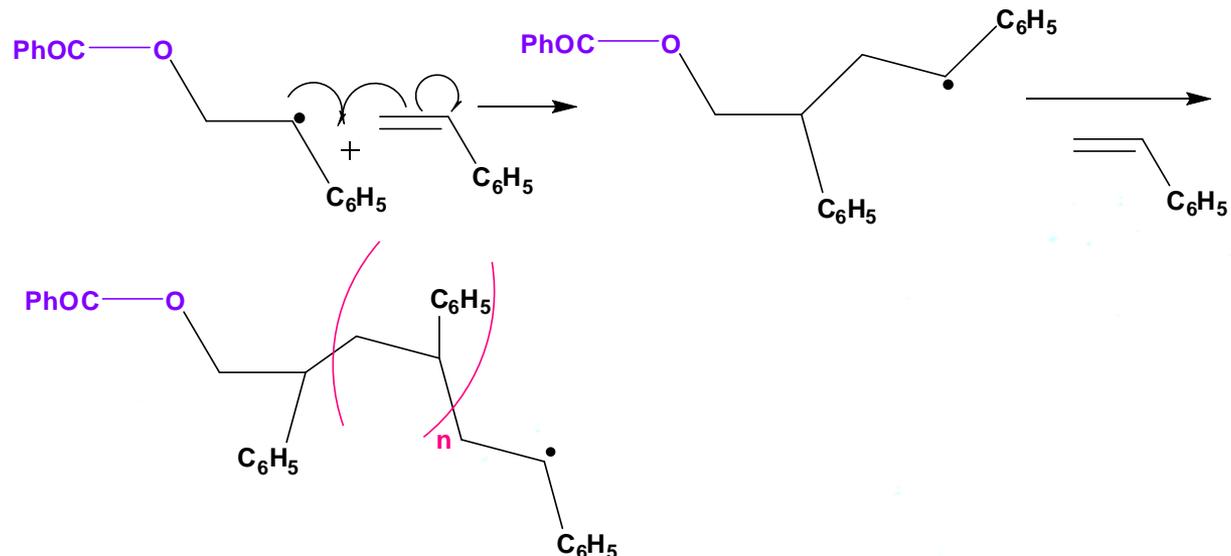


- The **initiation** step in the polymerization of polystyrene



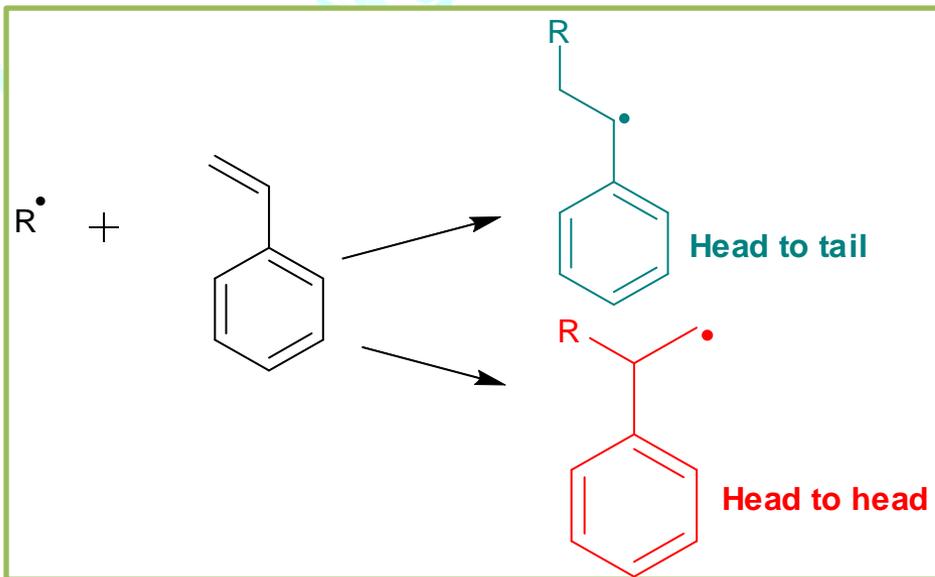
The free radical attacks the monomer creating a new radical site on the monomer through which it attacks another monomer in the **propagation** step leading to a chain formation.

PROPAGATION



The propagation step continues till a required molecular weight of polymer is obtained.

- During the addition of free radical (R) to monomer there can be two types of interactions 'head-to-head' or 'head-to-tail'



The addition occur as per two considerations :-

Stabilizing effect offered by the substituent on the monomer

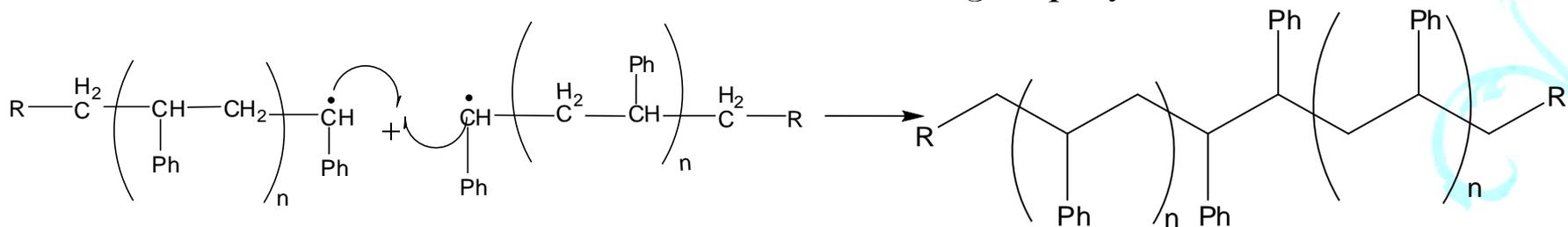
Steric effect at the addition site which favor addition at the least substituted carbon.

According to following preferences the head to tail addition is favored in most cases.

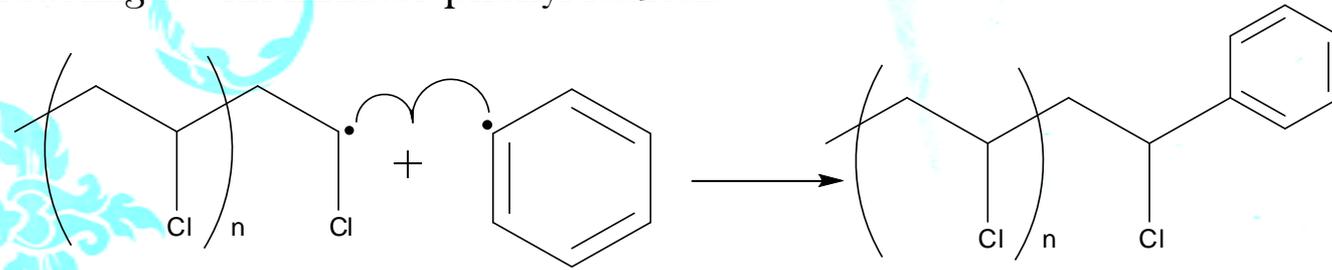
TERMINATION :-

It is the final step for completing polymerization. It can be achieved by following methods.

1. Combination :- this method result in doubling of polymer chain



2. Combination with initiator radical :- Poly- vinyl chloride polymerization can be terminated by reacting it with initiator phenyl radical.



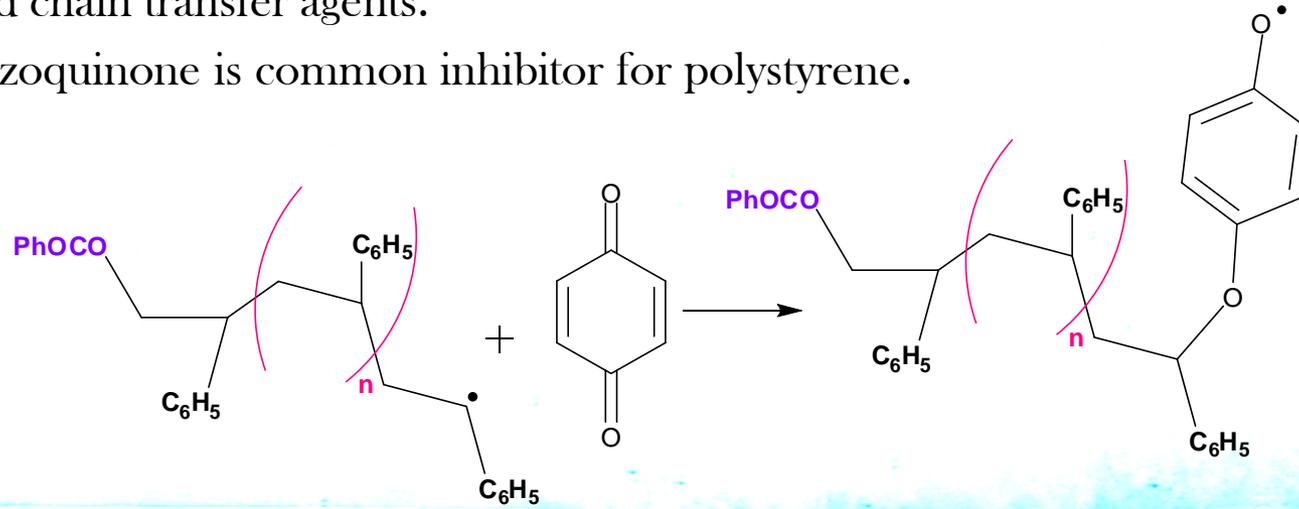
3. Use of inhibitors or retarders:-

Inhibitors stop every radical, and polymerization is completely ceased until they are consumed.

Retarders, on the other hand, are less efficient and halt a portion of radicals. In this case, polymerization continues at a slower rate.

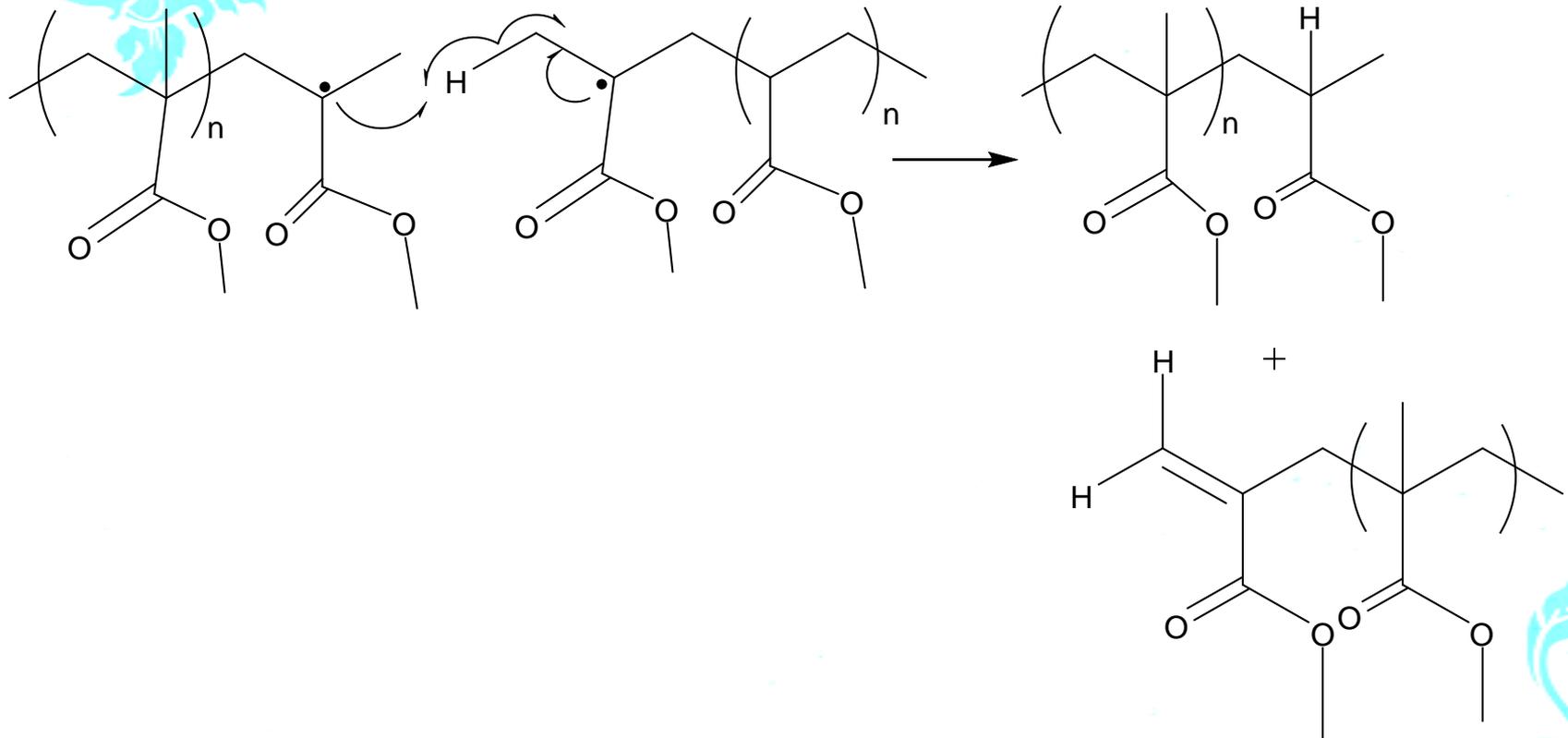
Inhibitor or retarders are compounds which combine with polymer chain by giving it electron and form a radical site on itself which can be stabilized by resonance. They are better called chain transfer agents.

E.g. Benzoquinone is common inhibitor for polystyrene.



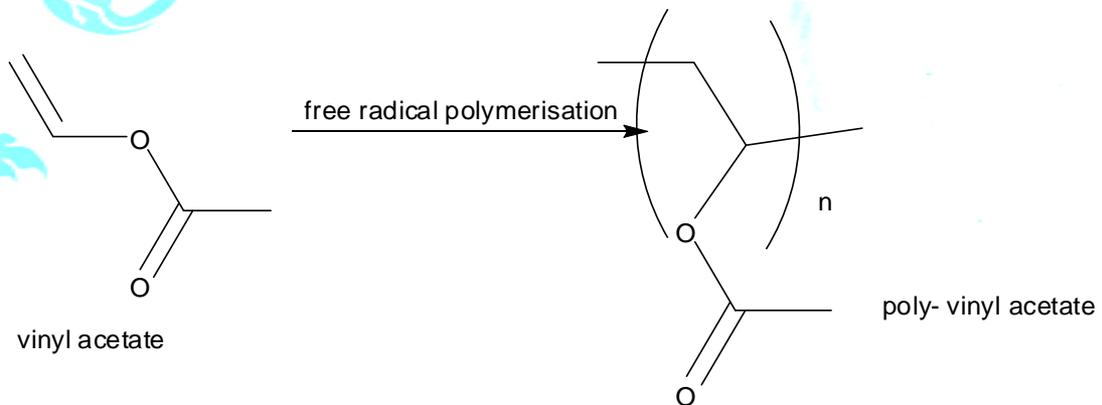
4. Disproportion :- In disproportion a hydrogen present on the carbon next to the radical site is abstracted by another radical centre to form alkene at one end and saturated carbon at the other end.

Termination by disproportion in poly- methyl acrylate.



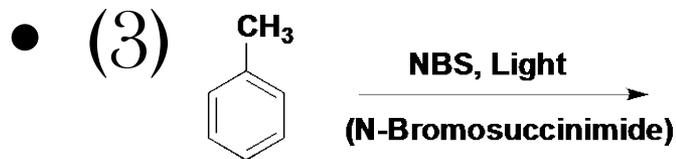
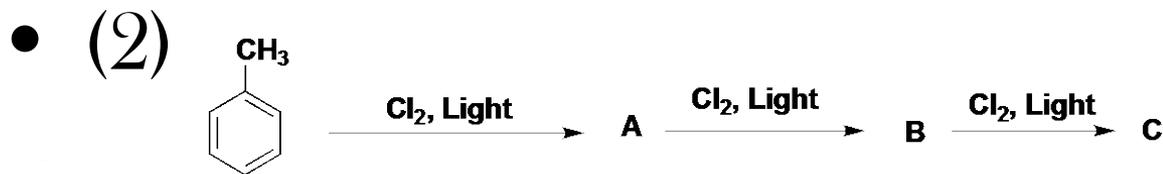
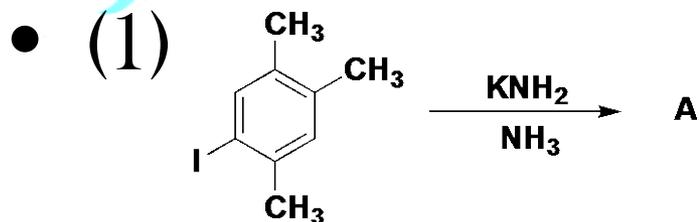
EXAMPLES

- Synthesis of poly(vinyl acetate) from vinyl acetate .



PRACTICE PROBLEMS

- Identify the product of the following reactions



ANSWERS

