Free Radical Reactions
1 – Introduction and Mechanism

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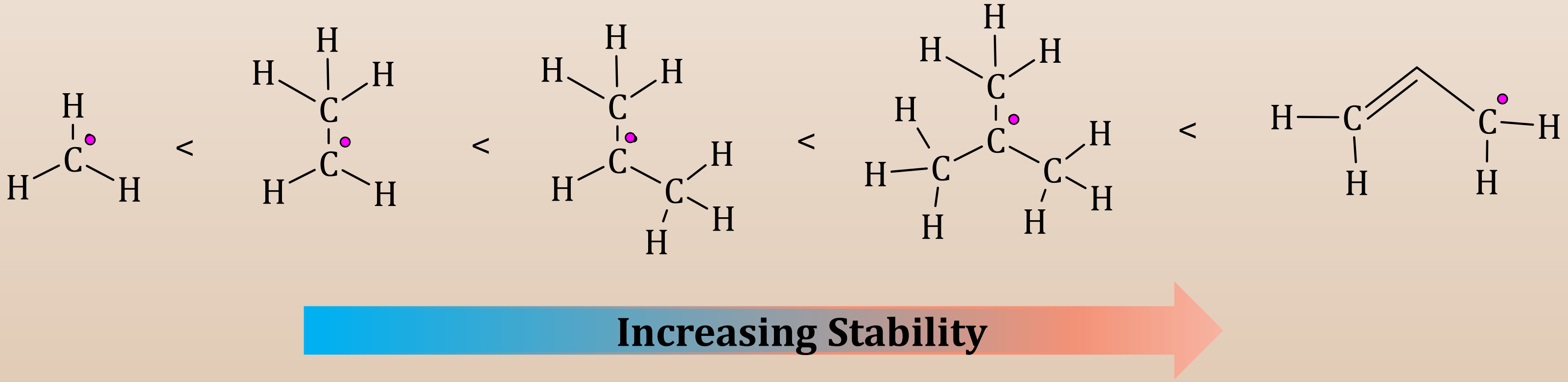
Radical Reactions - Introduction

Radicals are formed from homolytic cleavage, which is a bond breakage with equal sharing of electrons. Note here that half headed arrows are used to show movement of one electron. The radicals formed are neutral.

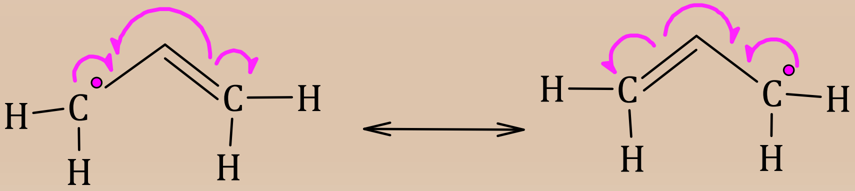
- This breakage requires energy hence bond energy is an important consideration – weaker bonds require less energy and will react easily, e.g. H-Cl easier to break than H-F.
- The radicals formed have high energy and are therefore reactive.
- Free radical reaction mechanism involves three steps:
  - Initiation (needs an initiator)
  - Propagation
  - Termination (needs a terminator or quencher)

Stability of Radicals

Just like carbocations, radical intermediates are also, primary (1^o), secondary, (2^o), tertiary, (3^o) and allylic in nature. 3^o are generally the most stable, however resonance leads to more stability, thus allylic radicals are even more stable than 3^o. This stability has to be kept in mind when determining major products in a reaction.

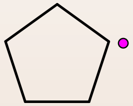


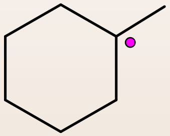
Resonance in an allylic radical. Note again the half headed arrows.



Solved Problem: Stability of radicals

Arrange the following radicals in order of their stability.


1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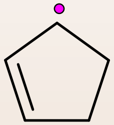
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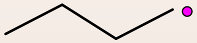

4

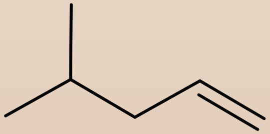
ANSWER

3 > 2 > 1 > 4

Notes: 3^{o} is allylic radical, 2 is 3^{o}, 1 is 2^{o} and 4 is 1^{o} thus least stable.

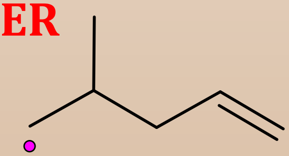
Solved Problem: Stability of radicals

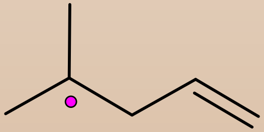
Write all the radicals for the following compound and identify which radical will give the major product.

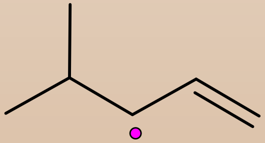


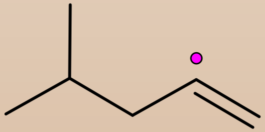
ANSWER

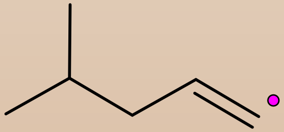
a)


1
1^{o}

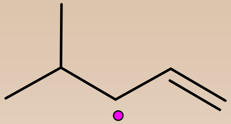

2
3^{o}


3
allylic


4
2^{o}


5
allylic

b)

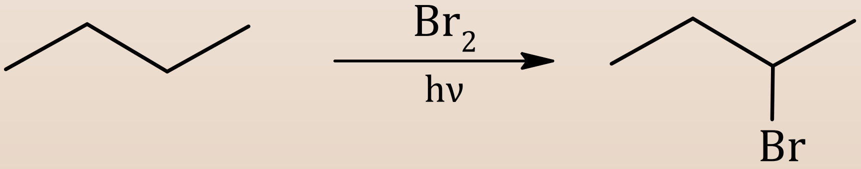


Notes: This is the 2^{o} allylic radical and it will give the major product.

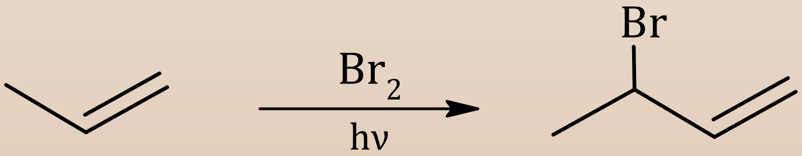
Types of Radical Reactions

The reactions listed below can be carried out by radical mechanism. The feasibility of the reaction is determined by the energetics. We will cover more details of each reaction as we learn more. I have used only bromine here but that is not the only reagent used.

1) Substitution: The most stable radical gives the product. H is substituted for Br.

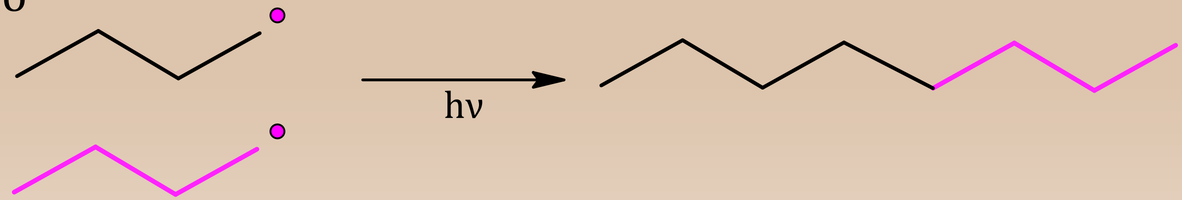


2) Allylic Substitution: This is specifically an allylic substitution of a H.



3) Addition: This a traditional addition reaction, however, it is anti-Markovnikov's addition of Br.

4) Coupling: This is adding two alkyl radicals to form a longer chain alkane.



Reaction Energetics

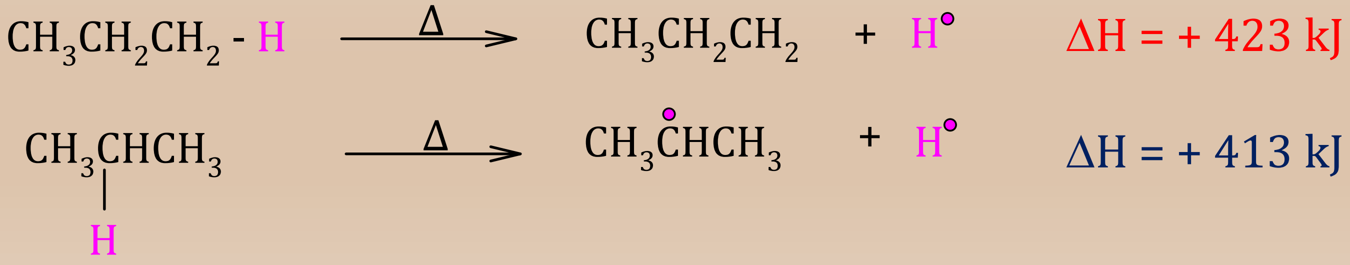
Atoms have higher energy (are less stable) than the molecules they form. This is because formation of covalent bonds is exothermic. During free radical reactions, covalent bonds are broken, which then is endothermic process.

- Breaking a H-H bond is harder than Cl-Cl bond due to H-H having higher bond energy.

$$H-H \longrightarrow H\bullet + H\bullet \qquad \Delta H = +\,436\ kJ/mol$$

$$Cl-Cl \longrightarrow Cl\bullet + Cl\bullet \qquad \Delta H = +\,243\ kJ/mol$$

- Bond breakage in C-H bonds is determined by which radical formed is more stable, e.g., isopropyl requires less energy than a propyl radical due to stability of the 2° radical.



$$CH_3CH_2CH_2-H \xrightarrow{\Delta} CH_3CH_2CH_2 + H^{\bullet} \qquad \Delta H = +\,423\ kJ$$

$$CH_3\underset{\substack{|\\H}}{C}HCH_3 \xrightarrow{\Delta} CH_3\overset{\bullet}{C}HCH_3 + H^{\bullet} \qquad \Delta H = +\,413\ kJ$$

Bond Energies

The energies in a reaction can be calculated by using the bond energy values hence the products can be predicted.

- This becomes important so the correct starting material is chosen for a reaction, e.g., a Br-Br bond easier to break than a Cl-Cl bond so Br_2 is a better halogenation initiator.
- The next slide goes over the energetics of various halogens.

Comparison of Halogenation

The order of reactivity is based on the values of E_{act} for the first step of chain propagation and ΔH^o for the entire chain propagation.

- ***Fluorination*** **-** ΔH^o is extremely exothermic therefore fluorination reactions are explosive.
- ***Chlorination and bromination*** have lower overall ΔH^o values which makes these halogenation reactions less vigorous.
- ***Iodination*** has a prohibitively high activation energy hence the reaction does not occur.

Reaction	**ΔH**	**ΔH_{total}**
$F_2 \longrightarrow 2F\bullet$	+159	**-432**
$F\bullet + CH_4 \longrightarrow HF + CH_3\bullet$	-130	
$CH_3\bullet + F_2 \longrightarrow CH_3F + F\bullet$	-302	
$Cl_2 \longrightarrow 2Cl\bullet$	+243	**-101**
$Cl\bullet + CH_4 \longrightarrow HCl + CH_3\bullet$	+8	
$CH_3\bullet + Cl_2 \longrightarrow CH_3Cl + Cl\bullet$	-109	
$Br_2 \longrightarrow 2Br\bullet$	+193	**-26**
$Br\bullet + CH_4 \longrightarrow HBr + CH_3\bullet$	+74	
$CH_3\bullet + Br_2 \longrightarrow CH_3Br + Br\bullet$	-100	
$I_2 \longrightarrow 2I\bullet$	+151	**+53**
$I\bullet + CH_4 \longrightarrow HI + CH_3\bullet$	+142	
$CH_3\bullet + I_2 \longrightarrow CH_3I + I\bullet$	-89	

Radical Reaction Mechanism 1– Initiation

1) **Initiation** – Homolytic cleavage leading to formation of two reactive species with unpaired electrons (radicals). This process requires energy which can be provided in form of light or heat. Light can be written as hν which is Planck's equation ($E = h\nu$). Heat is represented by the symbol, Delta, Δ, on the arrow. It does not specify the actual temperature.

Molecules used as initiators should have weak bond energy. Common examples of these are bromides, chlorides and peroxides.

Halides: Chlorine and bromine molecules are used as initiators as their bonds have low energy.

Peroxides*:* Peroxides are also good initiators as the O-O bond is low in energy. RO-OR, alkyl peroxides will form alkoxy radicals (•OR).

Two hydroxy radicals

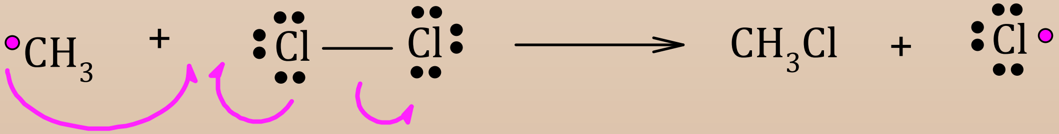
Radical Reaction Mechanism 2- Propagation

2) Propagation – In this step, the initiator radical reacts with the substrate molecule to generate the radical of the substrate. Propagation steps are identified by having a radical in the product.

Examples:

Reaction of chlorine radical with methane gives HCl and •CH_3, a methyl radical.

And a methyl radical reacting with chlorine. In both cases a radical is part of the products.

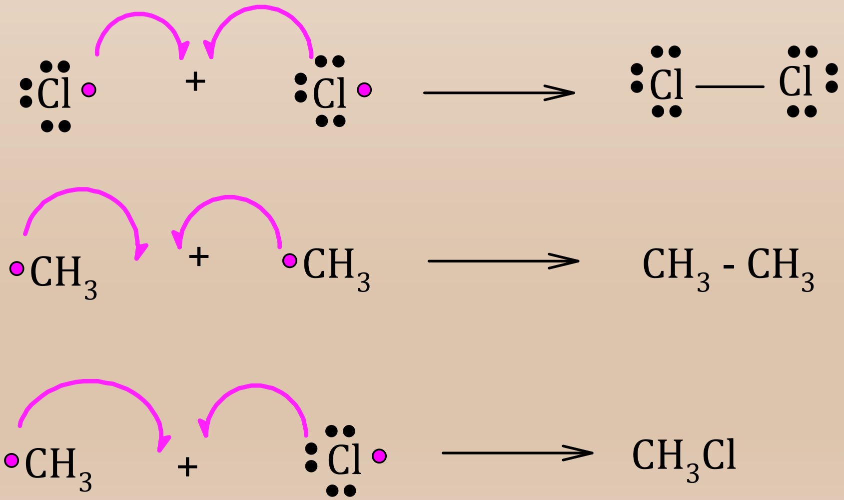


Radical Reaction Mechanism 3 - Termination

3) Termination – This step is to stop the free radical reaction from continuing. The products should not have any radicals left in this step.

- The reaction here is the combination of two radicals to form an unreactive compound. It is possible to have coupling reactions here.
- The key point is that there should no radical in the products.
- In some cases, a terminator, or quencher, is added to stop the reaction from going any further.

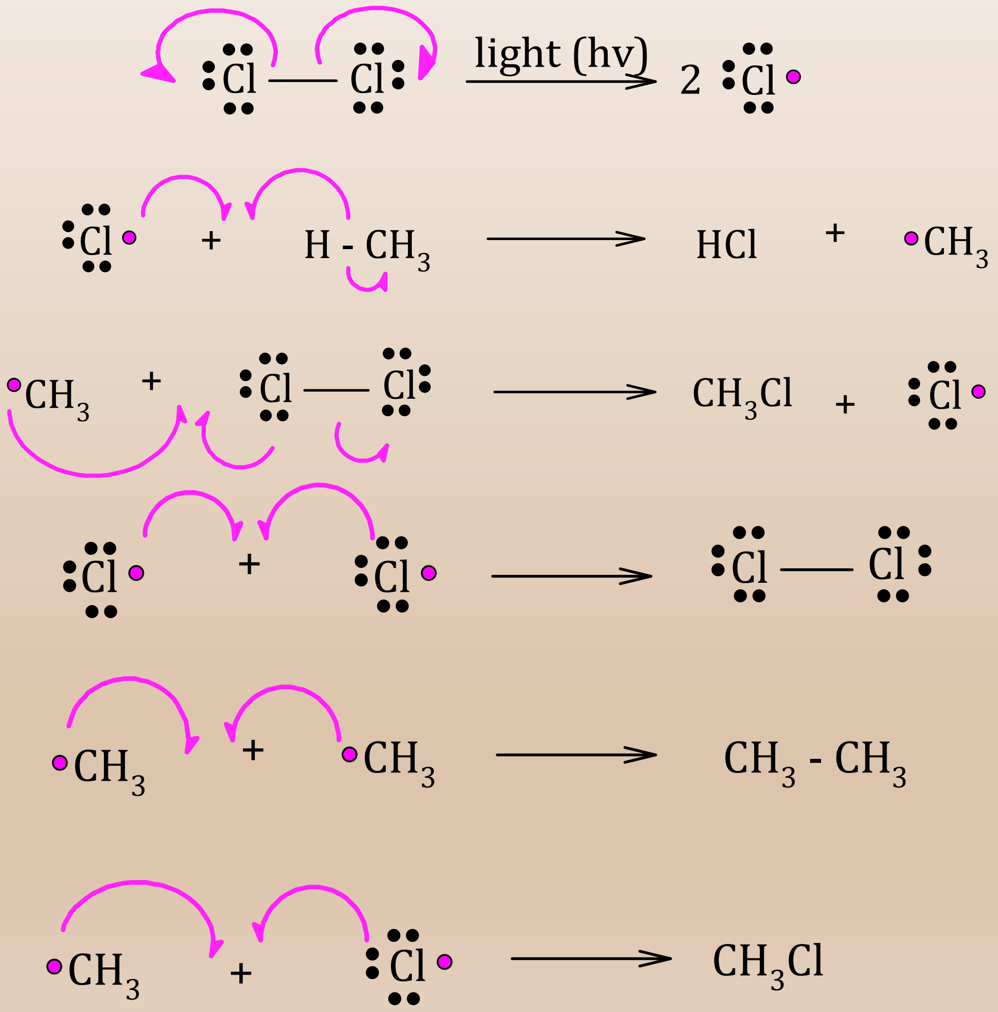
Examples:



Radical Mechanism - Summary

Overall Reaction

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$



Initiation

$$Cl - Cl \xrightarrow{\text{light (hv)}} 2\ Cl\cdot$$

Propagation

$$Cl\cdot + H - CH_3 \longrightarrow HCl + \cdot CH_3$$

$$\cdot CH_3 + Cl - Cl \longrightarrow CH_3Cl + Cl\cdot$$

Termination (any one of these)

$$Cl\cdot + Cl\cdot \longrightarrow Cl - Cl$$

$$\cdot CH_3 + \cdot CH_3 \longrightarrow CH_3 - CH_3$$

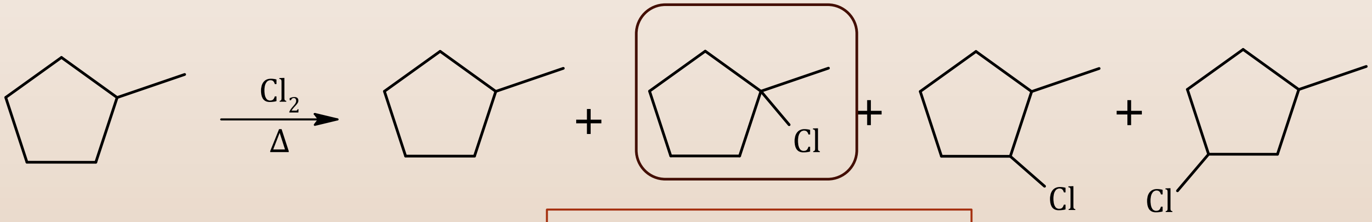
$$\cdot CH_3 + Cl\cdot \longrightarrow CH_3Cl$$

Solved Problem: Writing reaction mechanism for radical reactions.

Write all the products that can be formed in the free radical reaction of methylcyclopentane with chlorine. Give the mechanism for the formation of the major product.

ANSWER

Products formed



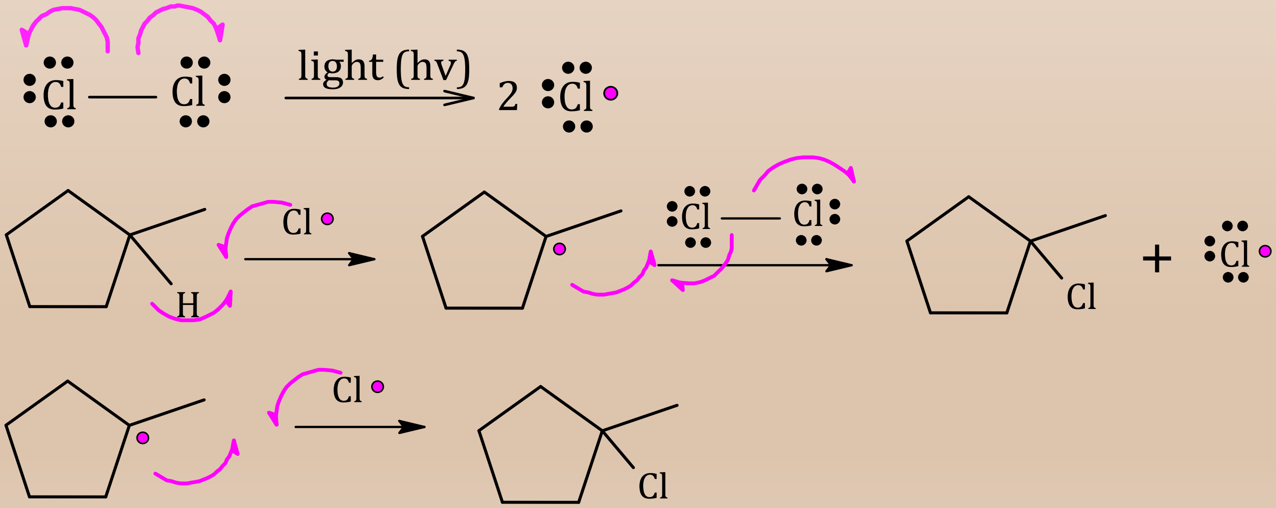
Major product as it is formed from 3° radical.

Mechanism

Initiation: Use chlorine as initiator as it has weaker bonds.

Propagation: Form product while showing free radicals in the products.

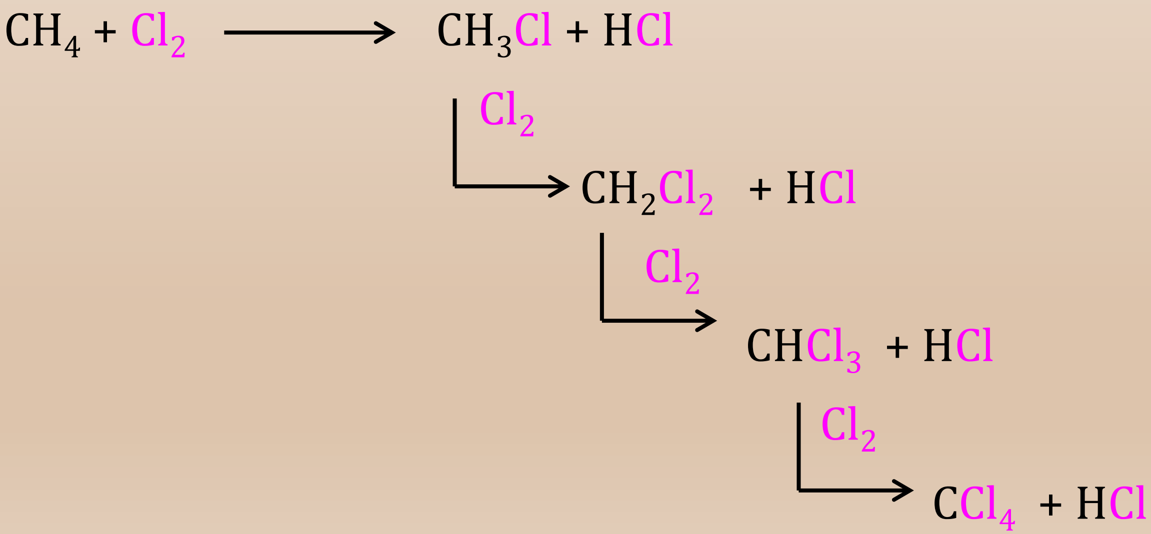
Termination: Product should not have radicals.



Properties Radical Reactions – Reactivity

Small alkanes on reaction with Cl_2 or Br_2, in presence of heat or light will form halogenated alkanes but mixtures are produced since the reaction is hard to control via the free radical mechanism.

- If only methyl chloride is the desired product, then using free radical reaction is not a good way to make it as the reaction can continue on until tetrachloromethane is formed.
- Mixture of products are generally separated by simple or fractional distillations if products are liquids.



$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

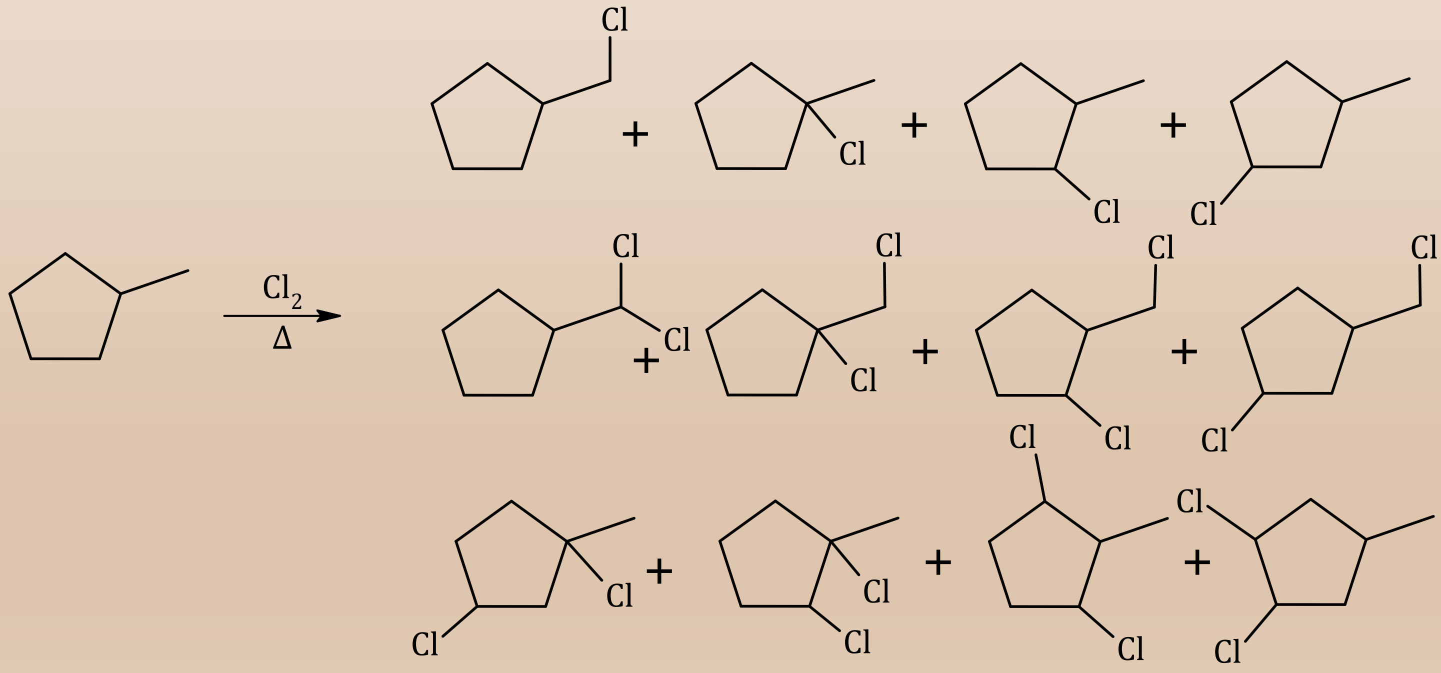
$$CH_3Cl \xrightarrow{Cl_2} CH_2Cl_2 + HCl$$

$$CH_2Cl_2 \xrightarrow{Cl_2} CHCl_3 + HCl$$

$$CHCl_3 \xrightarrow{Cl_2} CCl_4 + HCl$$

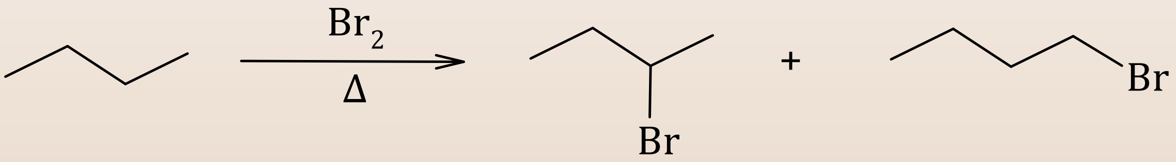
Disubstitutions of Alkanes

Free radical reactions are high energy reactions and are hard to control. When carrying out halogenations with alkanes many constitutional isomers can be formed along with mono- and di- or multi-substitution products. Generally, the more stable radical will give the major product while others are formed in minor quantities. Below are just the mono and some disubstitution products shown for the chlorination of methylcycloxane. It is better to avoid such reactions.



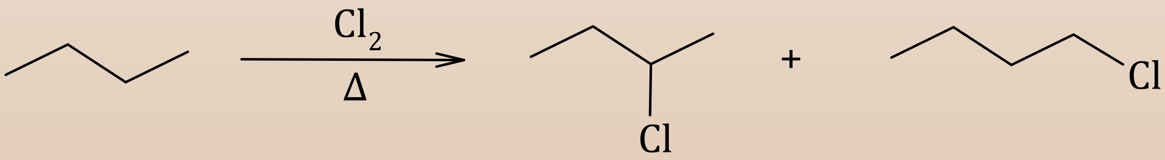
Regioselectivity of Bromine

Free radical reaction is more selective with bromine than chlorine since bromination is a slower reaction because of higher stability of bromine radical.



major product

minor product

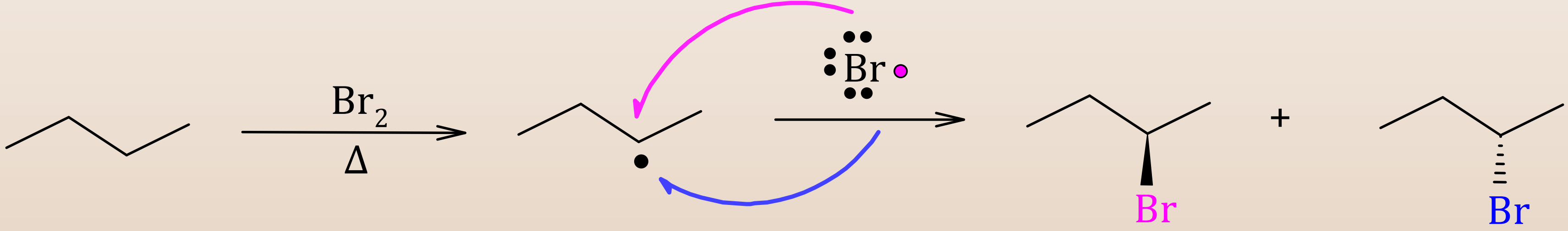


Both almost equal in proportion

- Regioselectivity is 3° > 2° > 1°.
  - for bromination, approximately 1600:80:1
  - for chlorination, approximately 5:4:1

Stereochemistry of Products

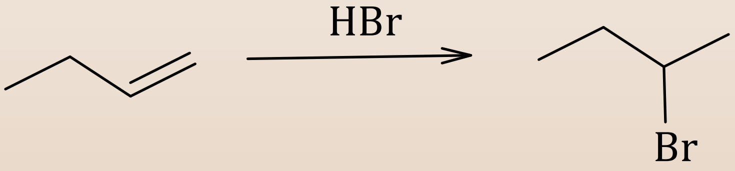
The carbon radical is sp^2 hybridized therefore trigonal planar hence the radical (Br or Cl) can approach from above or below the plane thus the product is a racemic mixture.



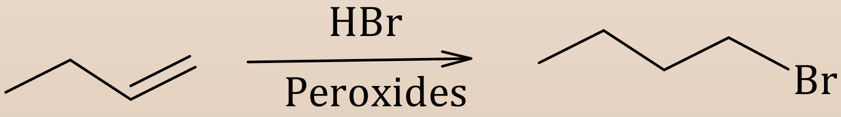
Racemic products can add to the complication of separating the products, as now chiral resolution is carried out to separate the enantiomers.

Radical Addition on Alkenes - Bromination

Traditional addition of HBr to alkenes gives Markovnikov addition, however in case of free radical mechanism the product is anti-Markovnikov. Addition of HCl and HI is only Markovnikov's addition.

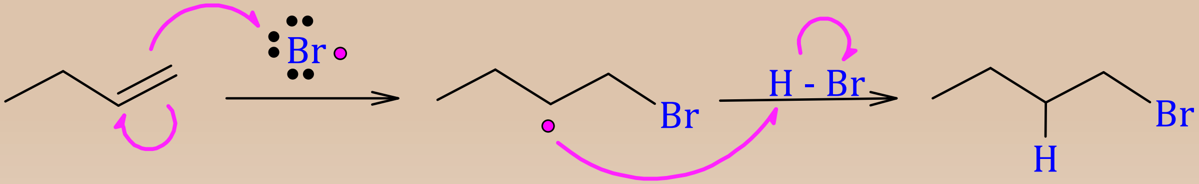


Markovnikov's Product



Anti-Markovnikov's Product

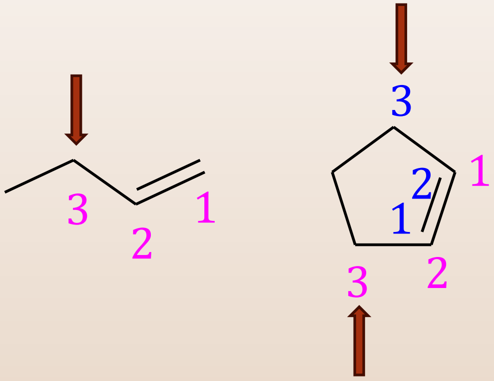
Mechanism shows that the bromine radical will react with the primary carbon to form the more stable 2^o radical. In the second step HBr reacts with the radical to add the H to the more stable radical forming the anti-Markovnikov product.

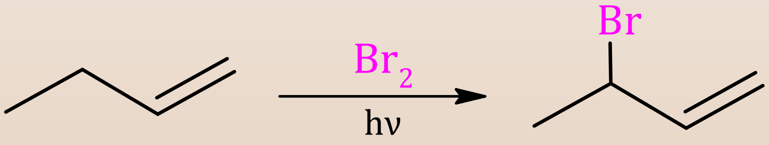


Allylic Substitution - Bromination

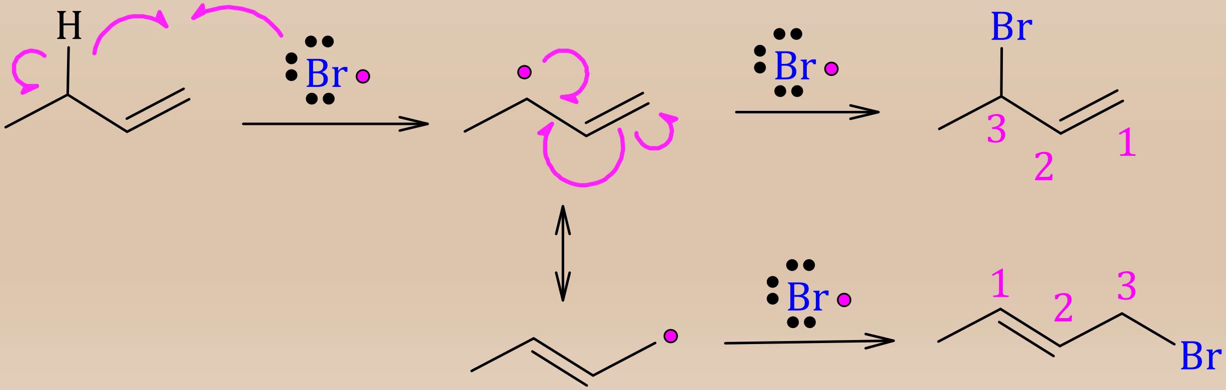
Allylic bromination is very specific free radical reaction on alkenes with bromine. Bromination occurs on the allylic position only.

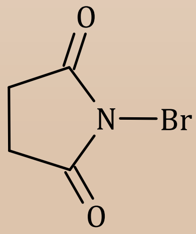
- "Allylic" carbon is the 3rd carbon from the start of the double bond.





Mechanism: The bromine radical abstracts the allylic hydrogen as it leads to the allylic radical which is resonance stabilized. The next bromine radical will then bond in the allylic position of the radical intermediate. Two common reagents used to carry out this reaction are Br_2/hν, or N-bromosuccinimide (NBS).





N-bromosuccinimide
(NBS)

Chain Reaction

Chain reaction is another name for propagation steps.

- Once the radicals are formed it is hard to control their reactions which results in a continuous loop of reactions.
- Chain reactions can be stopped only by terminators or quenchers (or removing the energy source).

Last Word

When carrying out free radical reactions, do not break any C-C bonds. Only C-H bonds are broken during the reaction due to their lower bond energy.

Key Concepts

- Synthesis of alkyl halides from
  - Alkenes
  - Alkynes
  - Alkanes
- Free radical reactions
  - Homolytic cleavage
  - Initiation
  - Propagation
  - Termination
- Stability of radicals
- Energetics of reactions
- Regioselectivity of bromine (NBS)
- Allyl radical and resonance
- Chain reaction