Carbon-carbon double bond as substituents

Free Radical Halogenation of Alkenes

- Free radical halogenation of alkenes is a fundamental organic transformation that involves the substitution of a hydrogen atom by a halogen atom (usually chlorine or bromine) through a free radical mechanism.
- This reaction can occur at allylic positions (the carbon atoms adjacent to the double bond), as direct halogenation of the double bond typically leads to addition rather than substitution.
- Therefore, free radical halogenation of alkenes is particularly important when discussing allylic halogenation.

Reaction Conditions and Halogenation Reagents

- **Common halogens used**: Chlorine (Cl_2) or Bromine (Br_2).
- **Initiation method**: Usually requires heat or light (hv) or a radical initiator like AIBN (azobisisobutyronitrile) or benzoyl peroxide.
- **Solvent**: Typically carried out in non-polar solvents like CCl_4 or inert gases to prevent unwanted side reactions.
- **Reactivity of halogens**:
  - **Chlorine** is more reactive but less selective.
  - **Bromine** is less reactive but more selective, making it preferable for controlled reactions.

Mechanism

The process occurs via a chain mechanism involving three main steps:

1. **Initiation**
   - The halogen molecule undergoes homolytic cleavage when exposed to heat or light, generating two halogen radicals:

$$Cl_2 \xrightarrow{hv} 2 \cdot Cl$$

2. **Propagation**
   - The halogen radical abstracts an allylic hydrogen (a hydrogen attached to a carbon adjacent to the C=C bond), producing an allyl radical:

$$Cl \cdot + CH_2 = CHCH_3 \rightarrow HCl + \cdot CH_2CH = CH_2$$

   - This allylic radical then reacts with another halogen molecule to form the allyl halide and regenerate the halogen radical:

$$\cdot CH_2CH = CH_2 + Cl_2 \rightarrow CH_2ClCH = CH_2 + \cdot Cl$$

   - This regenerates the chain-carrying radical and continues the chain process.
3. **Termination**

- Two radicals combine to terminate the reaction, though this is relatively rare compared to the propagation steps.

Selectivity and Stability

- Allylic positions are favored because the resulting allylic radical is resonance-stabilized.
- The stability of the intermediate radical determines the site of halogenation.
- The reaction is regioselective — it selectively occurs at positions that lead to the most stable intermediate radical.

Limitations and Issues

- **Over-halogenation**: Excess halogen can lead to multiple substitutions.
- **Competing reactions**: Halogenation across the double bond (addition) can compete under certain conditions, especially in the absence of radical initiators.
- **Stereochemical considerations**: Since the allyl radical is planar and symmetric, it can lead to mixtures of stereoisomers if not controlled.

Example

- Allylic bromination of propene with NBS (N-Bromosuccinimide) in the presence of light:

$$CH_2 = CHCH_3 + NBS \xrightarrow{hv} CH_2 = CHCH_2Br$$

- This is a preferred method because NBS provides a low steady-state concentration of Br_2, favoring allylic substitution over addition.

Comparison of Free Radical Substitution with Free Radical Addition

- Understanding the difference between free radical substitution and free radical addition is essential for predicting product outcomes, especially when dealing with alkenes and alkynes.
- These two reaction types operate via radical pathways but differ significantly in their mechanism, substrates, intermediates, and products.

Free Radical Substitution

Definition

- In this type of reaction, a radical replaces an atom or group (typically hydrogen or halogen) on a molecule. It's a substitution because one group is replaced by another.

Common Example

- Allylic bromination of alkenes using NBS is a classic example. Another is the halogenation of alkanes.

Mechanism Outline

- **Initiation**: Generation of free radicals.
- **Propagation**: Radical abstracts a hydrogen or group, forms a new radical.
- **Termination**: Two radicals recombine.

Requirements

- Requires a radical initiator (heat/light/AIBN).
- Preferential at **allylic or benzylic** positions due to resonance stabilization.
- The substrate should have easily abstractable hydrogens.

Product

- A hydrogen (or another atom) is replaced by a halogen or another radical-bearing group.

Free Radical Addition

Definition

- This reaction involves the addition of radicals across a double or triple bond, forming new sigma bonds and eliminating the pi bond.

Common Example

- Anti-Markovnikov addition of HBr to alkenes in the presence of peroxides is a classical example.

Mechanism Outline

- Initiation: Peroxide decomposes into alkoxy radicals which initiate the chain.
- Propagation: Radical adds to the double bond forming a new carbon radical, which then abstracts a halogen.
- Termination: Radical recombination.

Requirements

- Needs a source of radicals (often peroxides).
- Works best with electron-rich alkenes.
- Usually involves electrophilic radicals adding to nucleophilic alkenes.

Regioselectivity

- In contrast to ionic addition, radical addition often follows Anti-Markovnikov orientation due to the stability of the carbon radicals formed.
- **For example:**

$$CH_2 = CHCH_3 + HBr \xrightarrow{ROOR} CH_3CHBrCH_3$$

Key Differences

Feature	Radical Substitution	Radical Addition
Type of reaction	Replacement of atom/group	Addition across a multiple bond
Substrate type	Usually alkanes or allylic alkenes	Alkenes or alkynes
Site of reactivity	Allylic, benzylic, tertiary hydrogens	Double or triple bonds
Radical intermediate	Formed by H-abstraction	Formed by radical addition to pi bond
Orientation	Depends on radical stability	Often Anti-Markovnikov
Control methods	Light, heat, radical initiators	Peroxides and heat
Products	Haloalkanes (e.g., allyl halide)	Addition products (e.g., haloalkanes)

Free Radical Substitution In Alkenes

Fundamental Concepts

- Free radical substitution in alkenes primarily refers to the replacement of a hydrogen atom at an allylic position (adjacent to a C=C double bond) with a halogen or another group via a radical mechanism.
- This is in contrast to electrophilic addition reactions, which target the double bond itself.
- The allylic position in an alkene is particularly reactive in radical substitution due to the resonance stabilization of the resulting allyl radical.

Mechanism Overview

- The substitution process generally follows a radical chain mechanism consisting of **initiation, propagation, and termination** steps.

These are discussed in detail below.

1. Initiation

- A halogen source (Cl_2 or Br_2) or halogen donor (e.g., NBS) is homolytically cleaved under the influence of light or heat to generate halogen radicals.

$$Br_2 \xrightarrow{hv} 2 \cdot Br$$

- Or, using NBS (N-Bromosuccinimide):

$$NBS + ROOR \xrightarrow{hv} Br \cdot + \text{Succinimide-radical}$$

2. Propagation

- A halogen radical abstracts a hydrogen atom from the allylic position of the alkene, forming an **allyl radical**, which is resonance-stabilized.

$$\mathbf{Br\cdot + CH_2 = CHCH_3 \rightarrow HBr + \cdot CH_2CH = CH_2}$$

- The resulting allyl radical reacts with a Br_2 molecule (or similar halogen donor), yielding the **allylic halide** product and regenerating a halogen radical.

$$\mathbf{\cdot CH_2CH = CH_2 + Br_2 \rightarrow CH_2BrCH = CH_2 + Br\cdot}$$

- This maintains the chain propagation.

3. Termination

- This occurs when two radicals combine, ending the chain process:

$$\mathbf{Br\cdot + \cdot CH_2CH = CH_2 \rightarrow CH_2BrCH = CH_2}$$

- Or other radical-radical combinations.

Regioselectivity and Resonance

- Allylic radicals are resonance stabilized, which means they have delocalized electrons across the π-system:

$$\mathbf{\cdot CH_2CH = CH_2 \rightleftharpoons CH_2 = CH\cdot CH_2}$$

- This delocalization allows for multiple sites of substitution, potentially leading to isomeric products if the substrate has more than one allylic position. For example:

$$\mathbf{CH_2 = CHCH_2CH_3 \xrightarrow{NBS,hv} CH_2 = CHCHBrCH_3 + CH_2 = CHCH_2CH_2Br}$$

- Here, substitution can occur at either end of the resonance-stabilized allylic radical.

Role of NBS

- NBS is a key reagent for selective allylic bromination. It acts as a slow, steady source of Br_2 in low concentration, which minimizes side reactions like addition to the double bond.
- NBS is particularly favored for its:
  - Selectivity
  - Efficiency in forming mono-brominated products
  - Clean reaction profiles

Substrate Scope

- Radical substitution in alkenes is typically limited to:
  - Allylic and benzylic hydrogens
  - Tertiary hydrogens (due to high radical stability)
  - Not favored for primary non-allylic alkenes or unactivated alkanes

Synthetic Applications

First Hope

FREE PREVIEW

Click here to visit our website

PHARMACY PREMIUM NOTES

Complete subject and semesters are available on FirstHope app only.

Scan or click here

Click here to get the app >

Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram >

Scan or click here

@FirstHopeNotes

Instagram

@firsthope.official

Click here to follow >

YouTube channel

FirstHope-Pharmacy / Live streams

Click here to watch >

WhatsApp channel

Follow FirstHope on WhatsApp

Click here to join >

FirstHope website

firsthope.co.in

Click here to visit >

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.