

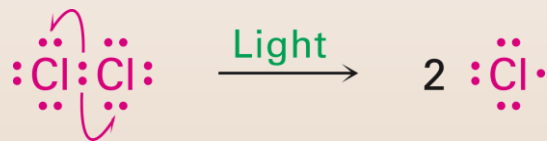
Free Radical Reactions

1 - Mechanisms

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Radical Reactions

- Radicals are formed from homolytic cleavage.



- This breakage requires energy.
- 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.
- Radicals are high in energy therefore reactive.
- Free radical mechanism involves three steps:
 - Initiation (needs an initiator)
 - Propagation
 - Termination (needs a terminator or quencher)

Radical Reactions – Mechanism 1

- **Initiation** – homolytic formation of two reactive species with unpaired electrons. Peroxides are also good initiators as the O-O bond is low in energy.



- *Peroxides:*
Step 1: $\text{R}-\ddot{\text{O}}-\ddot{\text{O}}-\text{R} \longrightarrow \text{R}-\ddot{\text{O}}\cdot + \cdot\ddot{\text{O}}-\text{R}$
 A dialkyl peroxide Two alkoxy radicals

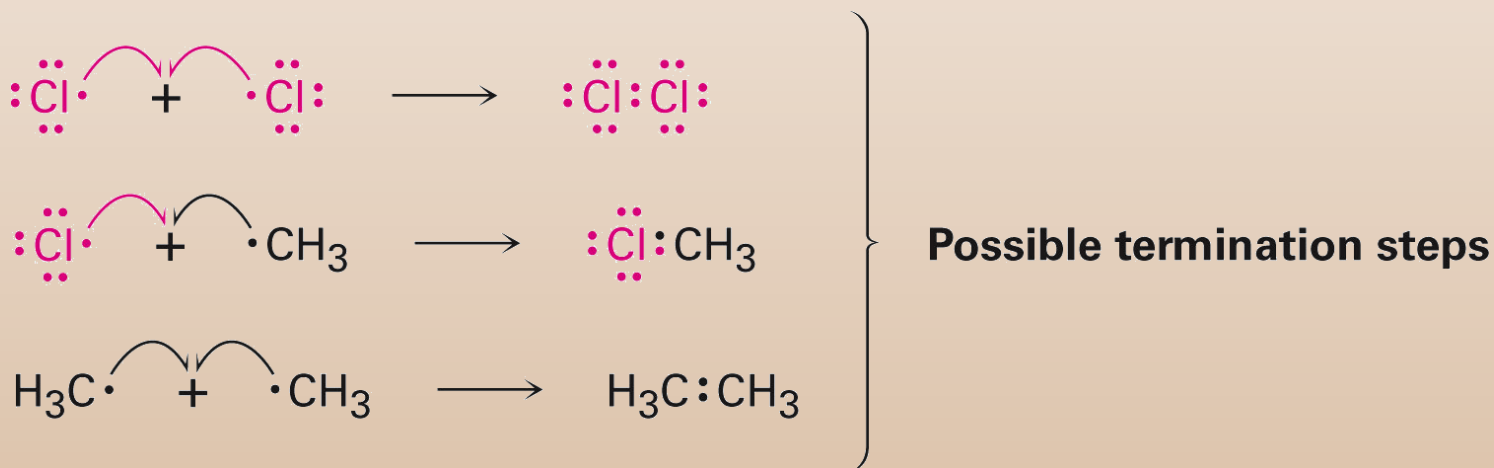


- **Propagation** – reaction with molecule to generate radical. There has to be a radical in the product. Example - reaction of chlorine atom with methane to give HCl and $\text{CH}_3\cdot$



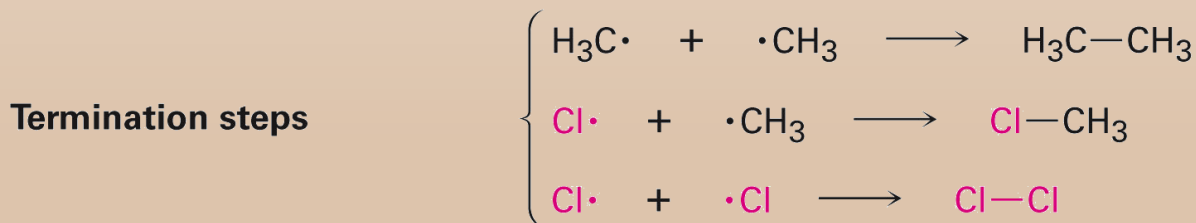
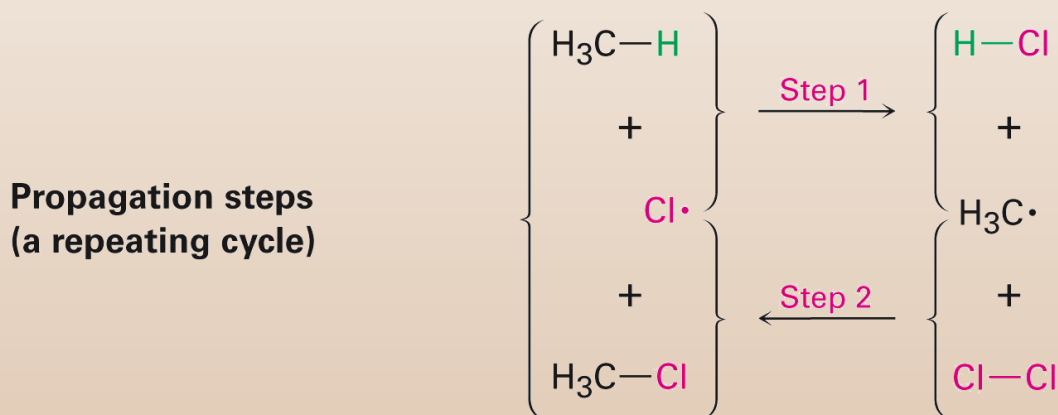
Radical Reactions – Mechanism 2

- **Termination** – combination of two radicals to form a stable product.
- The key point is that there should be no radical in the products.
- Example:



Radical Mechanism

Here is a summarized version of the mechanism.

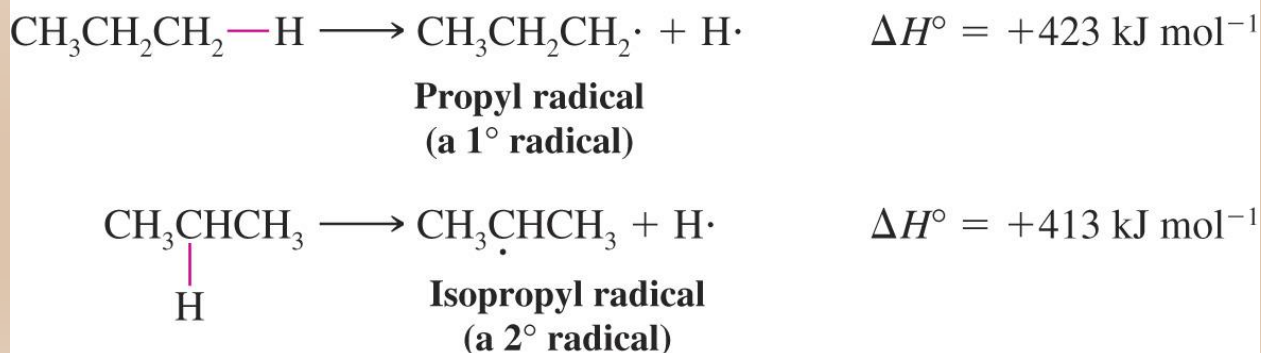


Reaction Energetics

- Atoms have higher energy (are less stable) than the molecules they can form (The formation of covalent bonds is exothermic)
- Breaking covalent bonds requires energy (*i.e.* is endothermic)

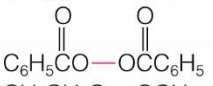
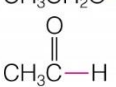


- A Cl-Cl bond requires less energy than H-H bond; due to bond energy.
- It is easier to form a more stable radical e.g. isopropyl than a propyl radical; this is due to stability of the radical.



Bond Energies

- We can calculate the energetics of a reaction hence the products can be predicted.
- It is useful information to also chose the right starting materials for a reaction. E.g. a Br-Br bond easier to break than a Cl-Cl bond so Br₂ is a better halogenation initiator.

$A:B \longrightarrow A\cdot + B\cdot$			
Bond Broken (shown in red)	kJ mol ⁻¹	Bond Broken (shown in red)	kJ mol ⁻¹
H—H	436	(CH ₃) ₂ CH—Br	298
D—D	443	(CH ₃) ₂ CH—I	222
F—F	159	(CH ₃) ₂ CH—OH	402
Cl—Cl	243	(CH ₃) ₂ CH—OCH ₃	359
Br—Br	193	(CH ₃) ₂ CHCH ₂ —H	422
I—I	151	(CH ₃) ₃ C—H	400
H—F	570	(CH ₃) ₃ C—Cl	349
H—Cl	432	(CH ₃) ₃ C—Br	292
H—Br	366	(CH ₃) ₃ C—I	227
H—I	298	(CH ₃) ₃ C—OH	400
CH ₃ —H	440	(CH ₃) ₃ C—OCH ₃	348
CH ₃ —F	461	C ₆ H ₅ CH ₂ —H	375
CH ₃ —Cl	352	CH ₂ =CHCH ₂ —H	369
CH ₃ —Br	293	CH ₂ =CH—H	465
CH ₃ —I	240	C ₆ H ₅ —H	474
CH ₃ —OH	387	HC≡C—H	547
CH ₃ —OCH ₃	348	CH ₃ —CH ₃	378
CH ₃ CH ₂ —H	421	CH ₃ CH ₂ —CH ₃	371
CH ₃ CH ₂ —F	444	CH ₃ CH ₂ CH ₂ —CH ₃	374
CH ₃ CH ₂ —Cl	353	CH ₃ CH ₂ —CH ₂ CH ₃	343
CH ₃ CH ₂ —Br	295	(CH ₃) ₂ CH—CH ₃	371
CH ₃ CH ₂ —I	233	(CH ₃) ₃ C—CH ₃	363
CH ₃ CH ₂ —OH	393	HO—H	499
CH ₃ CH ₂ —OCH ₃	352	HOO—H	356
CH ₃ CH ₂ CH ₂ —H	423	HO—OH	214
CH ₃ CH ₂ CH ₂ —F	444	(CH ₃) ₃ CO—OC(CH ₃) ₃	157
CH ₃ CH ₂ CH ₂ —Cl	354		139
CH ₃ CH ₂ CH ₂ —Br	294	CH ₃ CH ₂ O—OCH ₃	184
CH ₃ CH ₂ CH ₂ —I	176	CH ₃ CH ₂ O—H	431
CH ₃ CH ₂ CH ₂ —OH	395		364
CH ₃ CH ₂ CH ₂ —OCH ₃	355		
(CH ₃) ₂ CH—H	413		
(CH ₃) ₂ CH—F	439		
(CH ₃) ₂ CH—Cl	355		

"Data compiled from the *National Institute of Standards (NIST) Standard Reference Database Number 69*, July 2001 Release, accessed via *NIST Chemistry WebBook* (<http://webbook.nist.gov/chemistry/>) and the *CRC Handbook of Chemistry and Physics*, 3rd Electronic Edition (updated from content in the 81st print edition), accessed via *Knovel Engineering and Scientific Online References* (<http://www.knovel.com>). DH° values were obtained directly or calculated from heat of formation (H_f) data using the equation $DH^\circ[A-B] = H_f[A\cdot] + H_f[B\cdot] - H_f[A-B]$.

Comparison of Halogenation

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

- **Fluorination** has a very low value for E_{act} in the first step and ΔH° is extremely exothermic therefore fluorination reactions are explosive
- **Chlorination and bromination** have increasingly higher values of E_{act} and lower overall ΔH° values which makes these halogenation reactions less vigorous
- **Iodination** has a prohibitively high value for E_{act} of the first step and the reaction does not occur

FLUORINATION

	ΔH° (kJ mol ⁻¹)	E_{act} (kJ mol ⁻¹)
Chain Initiation		
$\text{F}_2 \longrightarrow 2 \text{F}\cdot$	+159	+159
Chain Propagation		
$\text{F}\cdot + \text{CH}_4 \longrightarrow \text{HF} + \text{CH}_3\cdot$	-130	+5.0
$\text{CH}_3\cdot + \text{F}_2 \longrightarrow \text{CH}_3\text{F} + \text{F}\cdot$	-302	Small
Overall $\Delta H^\circ = -432$		

CHLORINATION

	ΔH° (kJ mol ⁻¹)	E_{act} (kJ mol ⁻¹)
Chain Initiation		
$\text{Cl}_2 \longrightarrow 2 \text{Cl}\cdot$	+243	+243
Chain Propagation		
$\text{Cl}\cdot + \text{CH}_4 \longrightarrow \text{HCl} + \text{CH}_3\cdot$	+8	+16
$\text{CH}_3\cdot + \text{Cl}_2 \longrightarrow \text{CH}_3\text{Cl} + \text{Cl}\cdot$	-109	Small
Overall $\Delta H^\circ = -101$		

BROMINATION

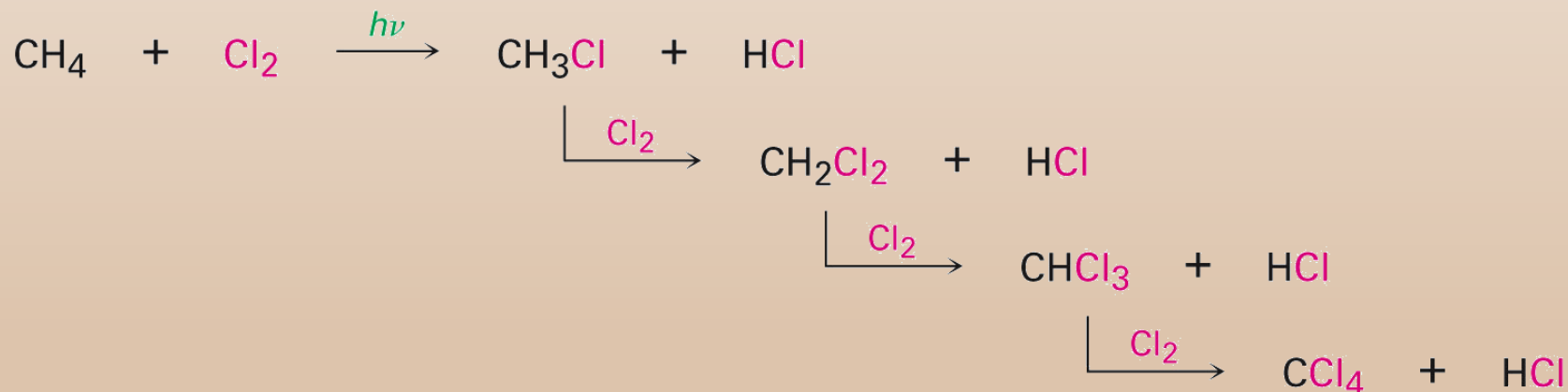
	ΔH° (kJ mol ⁻¹)	E_{act} (kJ mol ⁻¹)
Chain Initiation		
$\text{Br}_2 \longrightarrow 2 \text{Br}\cdot$	+193	+193
Chain Propagation		
$\text{Br}\cdot + \text{CH}_4 \longrightarrow \text{HBr} + \text{CH}_3\cdot$	+74	+78
$\text{CH}_3\cdot + \text{Br}_2 \longrightarrow \text{CH}_3\text{Br} + \text{Br}\cdot$	-100	Small
Overall $\Delta H^\circ = -26$		

IODINATION

	ΔH° (kJ mol ⁻¹)	E_{act} (kJ mol ⁻¹)
Chain Initiation		
$\text{I}_2 \longrightarrow 2 \text{I}\cdot$	+151	+151
Chain Propagation		
$\text{I}\cdot + \text{CH}_4 \longrightarrow \text{HI} + \text{CH}_3\cdot$	+142	+140
$\text{CH}_3\cdot + \text{I}_2 \longrightarrow \text{CH}_3\text{I} + \text{I}\cdot$	-89	Small
Overall $\Delta H^\circ = +53$		

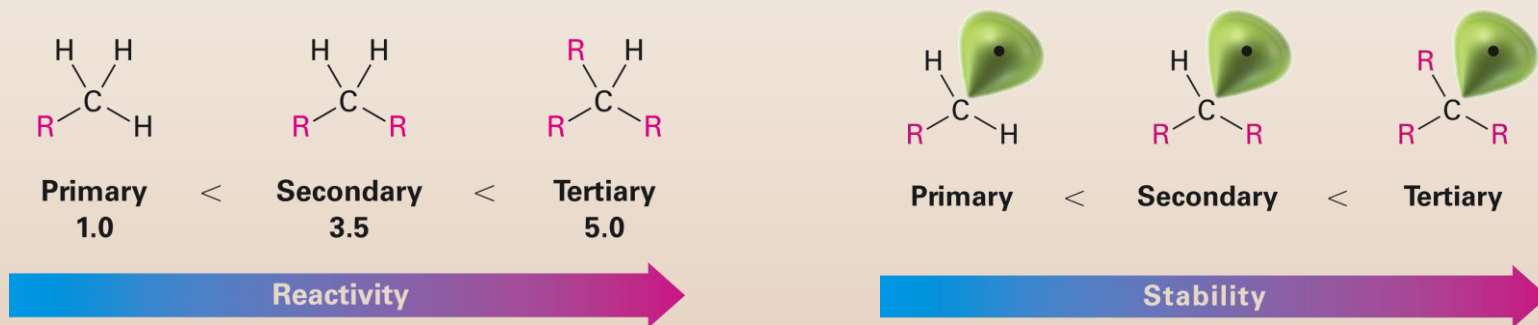
Radical Reactions - Properties

- Alkane + Cl₂ or Br₂, heat or light replaces C-H with C-X but gives mixtures
 - Hard to control
 - Via free radical mechanism
- It is usually not a good idea to plan a synthesis that uses this method

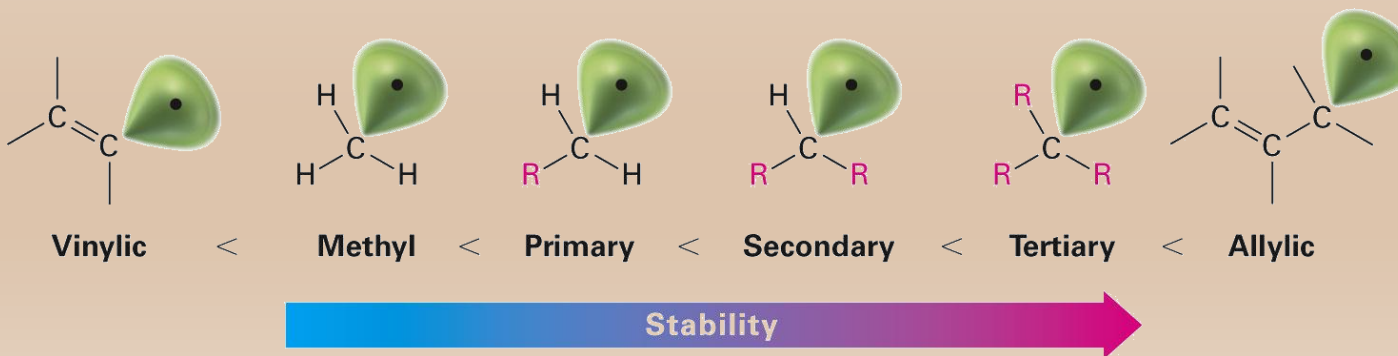


Reactivity of Radicals

- Based on quantitative analysis of reaction products, relative reactivity of radical intermediates are estimated

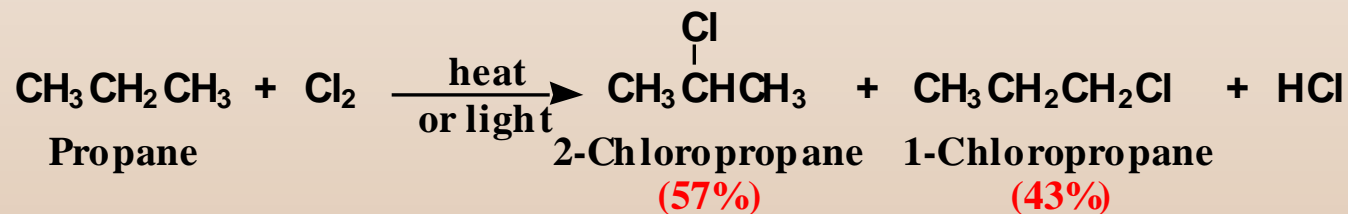
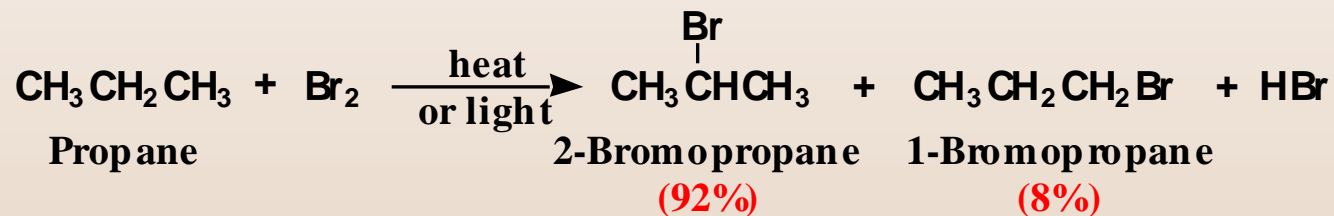


- Allylic radical is stabilized by resonance, hence even more stable than tertiary radical.



Regioselectivity

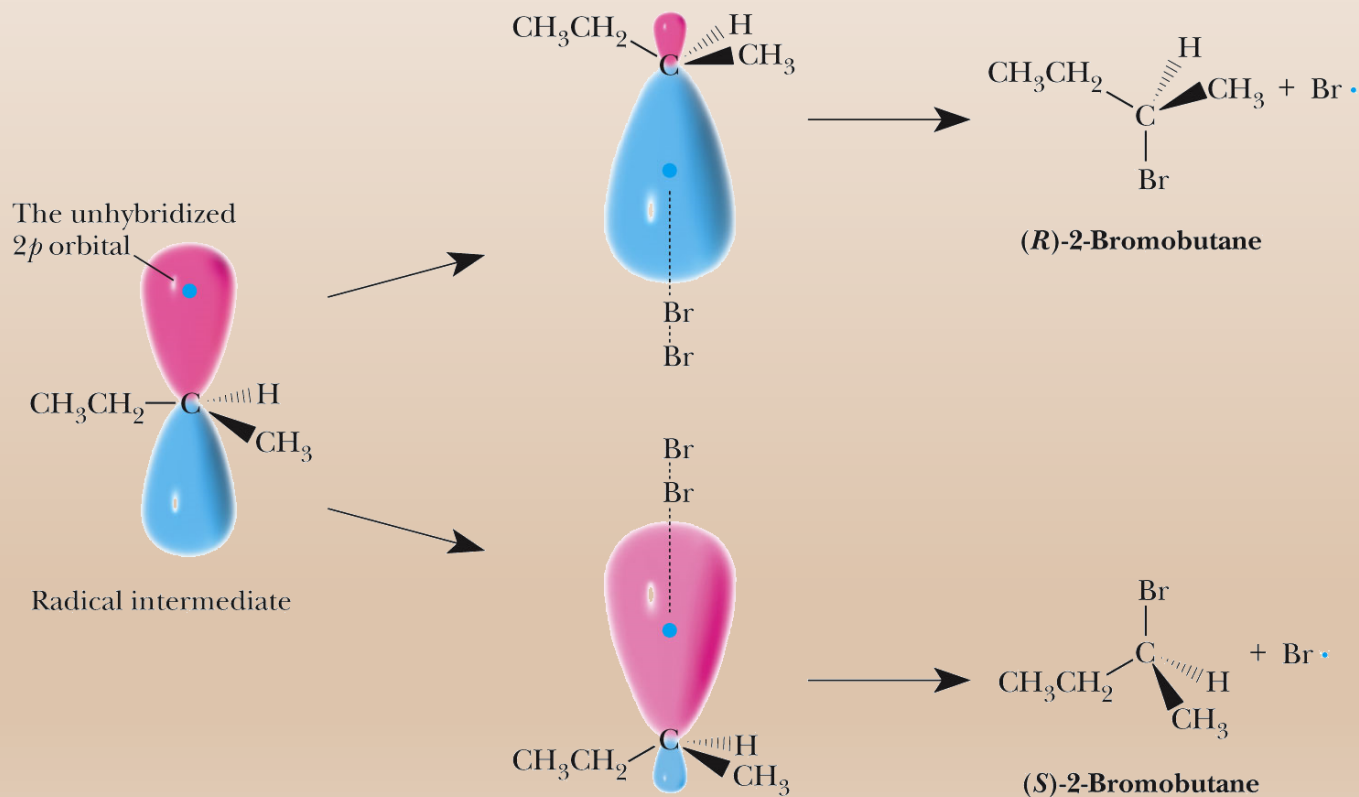
- Reaction is more selective with bromine than chlorine



- Regioselectivity is $3^\circ > 2^\circ > 1^\circ$.
 - for bromination, approximately 1600:80:1
 - for chlorination, approximately 5:4:1

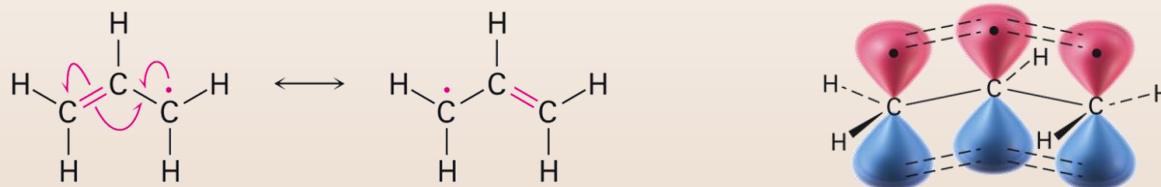
Stereochemistry

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

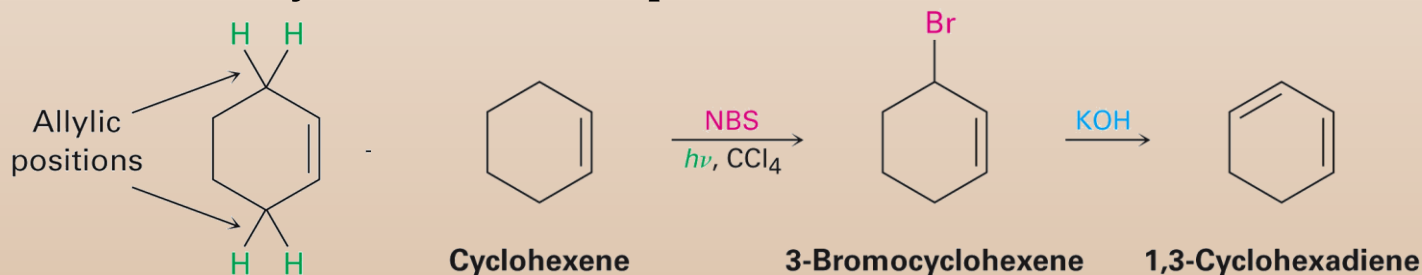


Allylic Radical

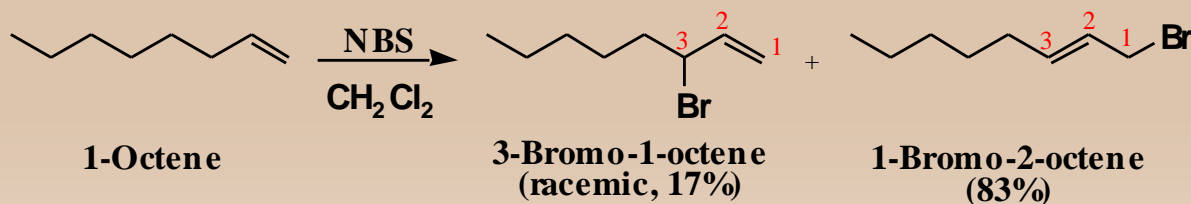
- Three electrons are delocalized over three carbons



- Allylic bromination with NBS creates an allylic bromide
- Reaction of an allylic bromide with base produces a conjugated diene, useful in the synthesis of complex molecules



- Another example:

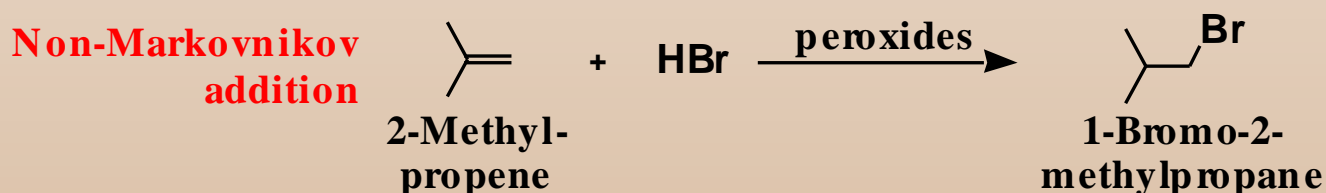
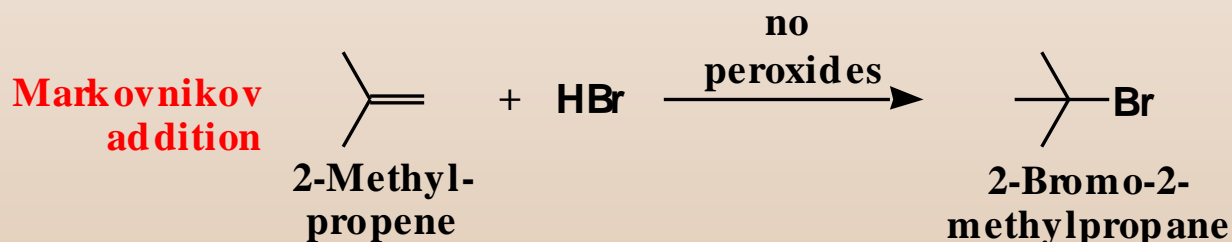


Chain Reaction

- Chain reactions are also another name for propagation steps
- Once the radicals are formed it is hard to control their reactions
- Chain reactions can be stopped only by terminators or quenchers (or removing the energy source)

Radical Addition on Alkenes

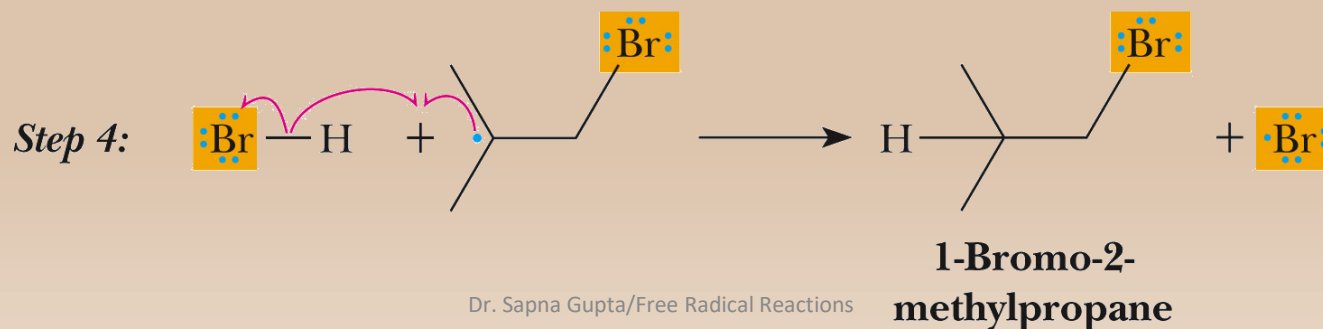
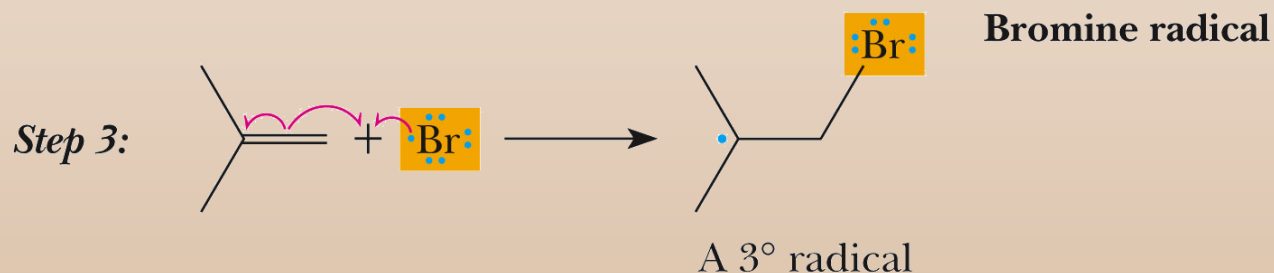
- Addition of HBr to alkenes gives either Markovnikov addition or anti-Markovnikov addition depending on reaction conditions.
 - Markovnikov addition occurs when radicals are absent.
 - non-Markovnikov addition occurs when peroxides or other sources of radicals are present.



- Addition of HCl and HI is only Markovnikov's addition.

Mechanism of Alkene Radical Reaction

- The key difference in the mechanism is in the chain propagation.
- Adding Br radical on the less substituted carbon gives a more stable radical.



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