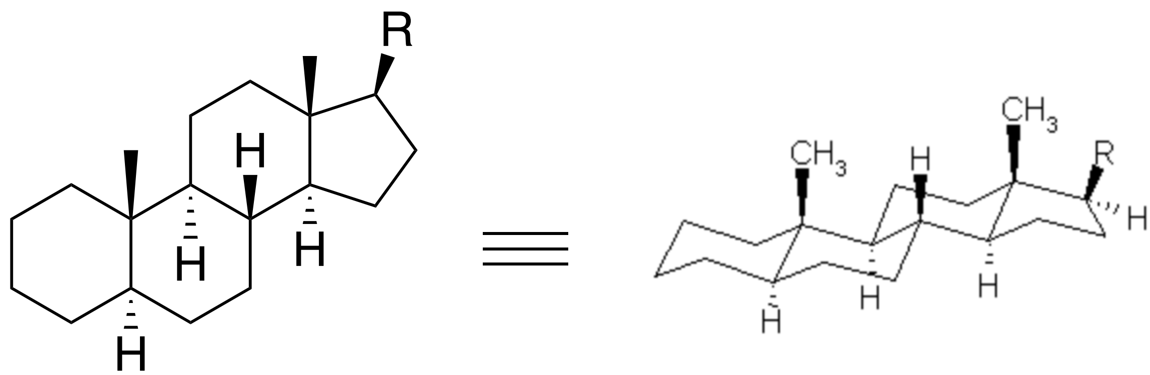
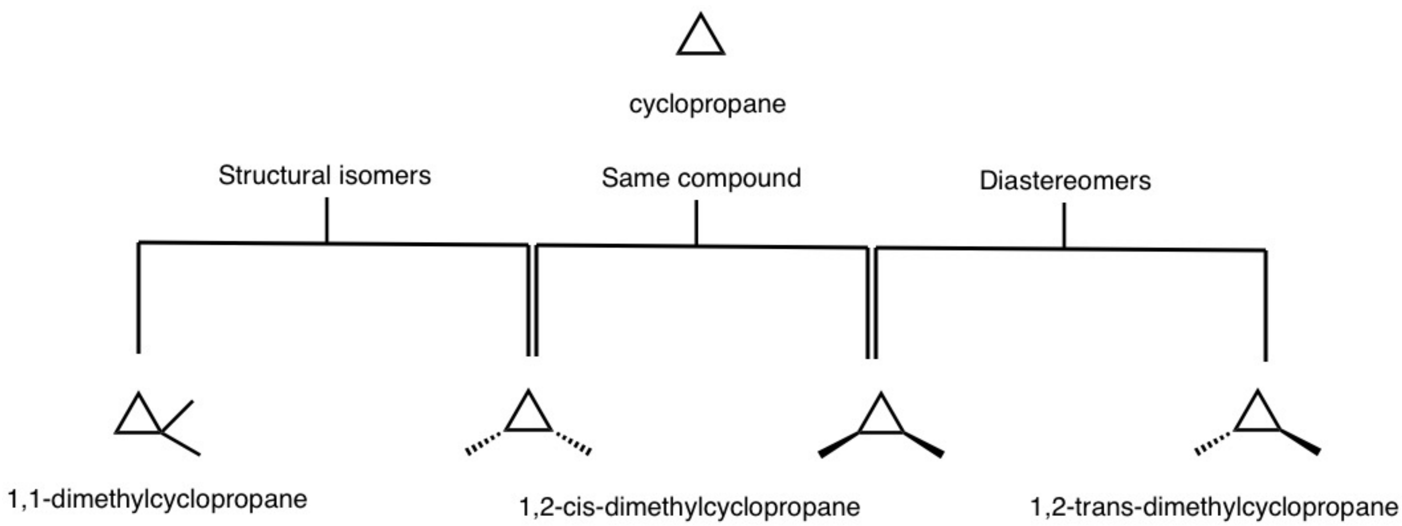
Review/Polycyclic aliphatic compounds

Steroid:



Cyclopropane



When naming the compounds above, it is necessary to describe the location of the two methyl groups even if they are located on the same substituent because all of these are dimethylcyclopropanes (i.e. from left to right: **1,1**-dimethyl-, **1,2-cis-**dimethyl-, **1,2-trans**-dimethyl- cylcopropane).

Reactions of alkanes

1) Combustion:

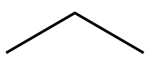
$$R\text{-}H + O_2 \xrightarrow{\Delta = \textbf{heat}} CO_2 + H_2O$$

R = any alkyl group

General formula for combustion reactions:

$$C_nH_{2n+2} + \left(\frac{3n}{2} + \frac{1}{2}\right) O_2 \longrightarrow (n+1)\ H_2O + n\ CO_2$$

e.g. propane



$CH_3CH_2CH_3$ $\quad 5O_2 \xrightarrow{\Delta} 3CO_2 + 4H_2O$

2) Halogenation of alkanes

$$R\text{-}H + X_2 \xrightarrow{\textbf{h}\nu} R\text{-}X + HX$$

R = any alkyl group, R-X = alkyl halide / haloalkane (X= Cl, Br, F); F_2 is the most reactive and I_2 fails to react.
h = Planck’s constant 6.6 x10^{-34} joules-sec
ν = frequency of light
E = **hν, are the symbols we use to describe light energy**

In this course, we will be focused on chlorination and bromination.

Substitution reaction (via radicals) – Substitute H with X

e.g. Chlorination of methane

$$CH_4 + Cl_2 \xrightarrow{h\upsilon} CH_3Cl + HCl$$

methane → methyl chloride / chloromethane

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

methylene chloride
dichloromethane

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

chloroform
trichloromethane

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

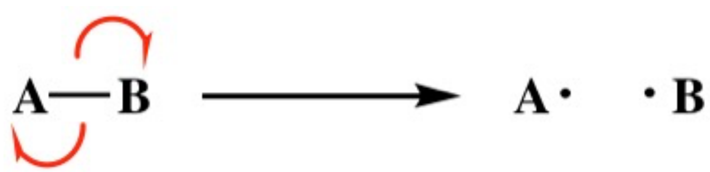
carbon tetrachloride
tetrachloromethane

Mechanism of reaction:

- Step by step description (proposal) of a reaction process (hypothetical and difficult to "prove")

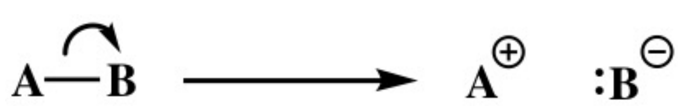
Two kinds of mechanism

1. **Homolytic** (radical): One electron goes to each atom once the bond in broken. e.g. Free radical halogenation of alkanes



The red half arrows above describe the movement of one electron, full arrows describe movement of lone pairs.

2. **Heterolytic** (polar reaction): The electron pair goes to one of the atoms once the bond is broken. e.g. Addition reactions of alkenes; elimination reactions

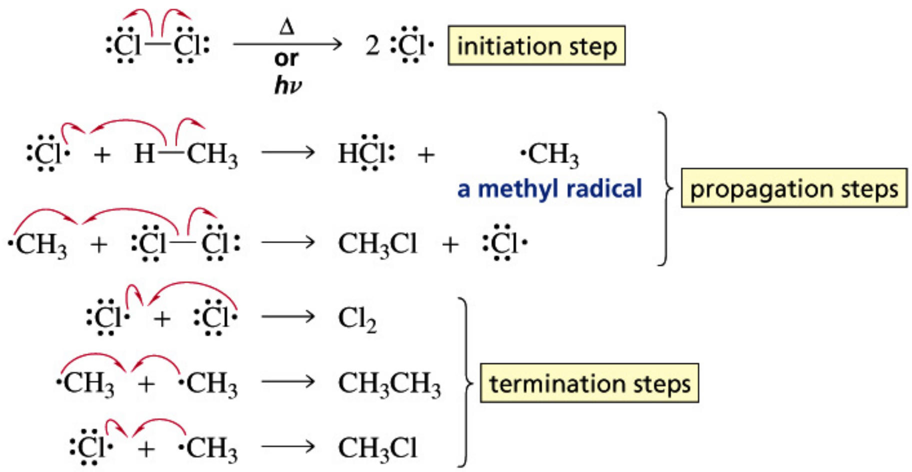


Homolytic reactions are less common than heterolytic reactions

- Initiated by heat (Δ) or by light (hυ)

Mechanism of halogenation of CH_4:

$$CH_4 + X_2 \xrightarrow{h\upsilon} CH_3X + HX$$



Propagation is the main step within the process. The termination step is the combination of radicals and is quite rare during the progress of the reaction, yet any one of the three listed can occur to terminate the reaction.

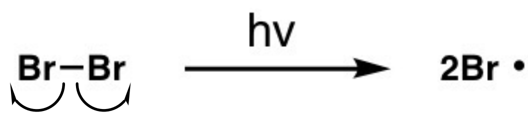
<u>Note</u>: The above mechanism also applies to other halogens (F, Cl, Br; not I)

Example: Ethane (analogous)

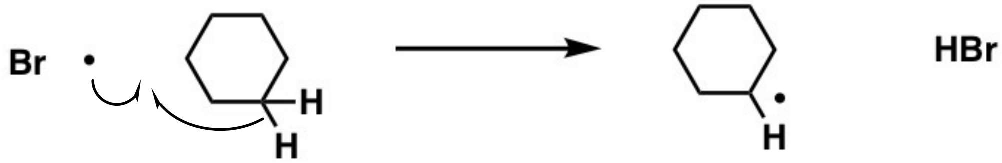
$$H_3C - CH_3 \xrightarrow[h\nu]{Cl_2} CH_3\text{-}CH_2\text{-}Cl + HCl$$

Example: Bromination of cyclohexane
(step 1 is **initiation**, steps 2 and 3 are **propagation steps** that are the main process. Other steps are **termination** steps that shut down the reaction

Step 1

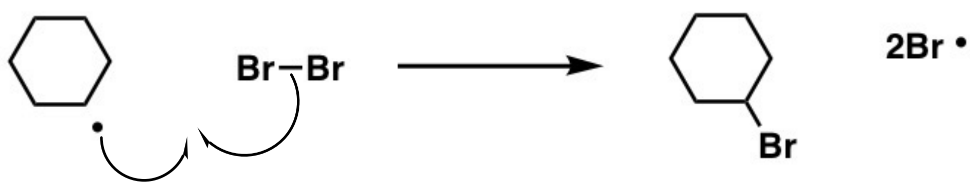


Step 2

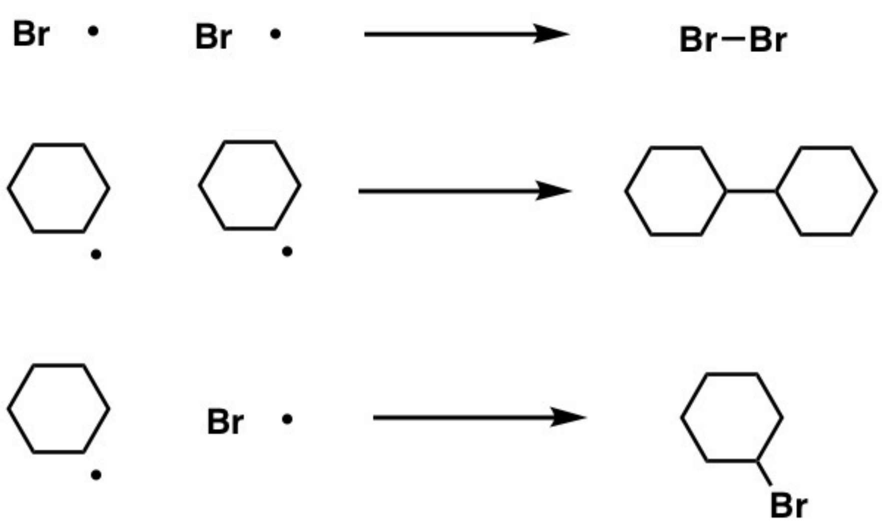


Rate Determining Step (RDS)

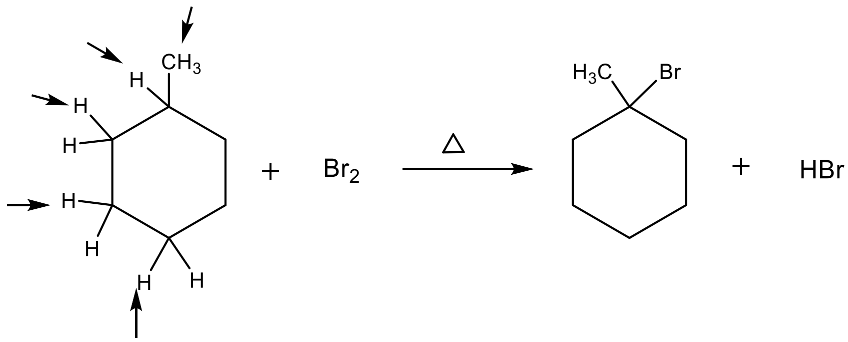
Step 3



Terminations



Example: Methylcyclohexane

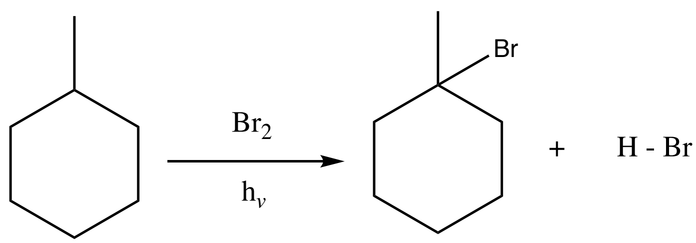


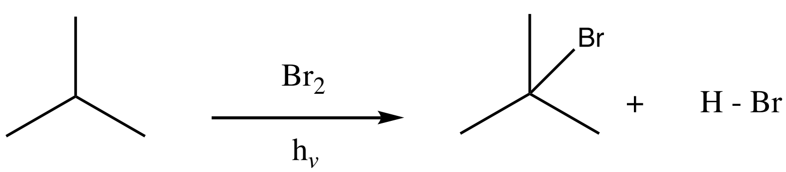
Other Examples:

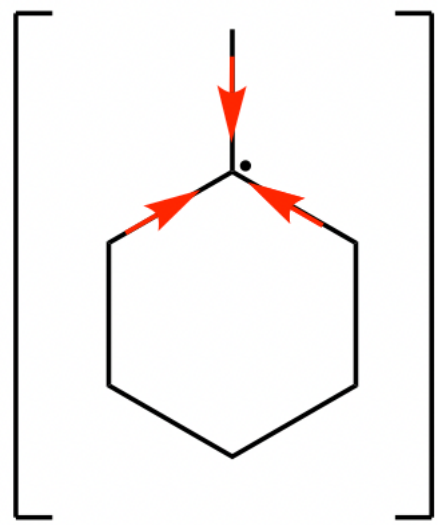
Alkyl Groups Donate electrons and stabilize

Intermediate Radical

is NOT a transition state





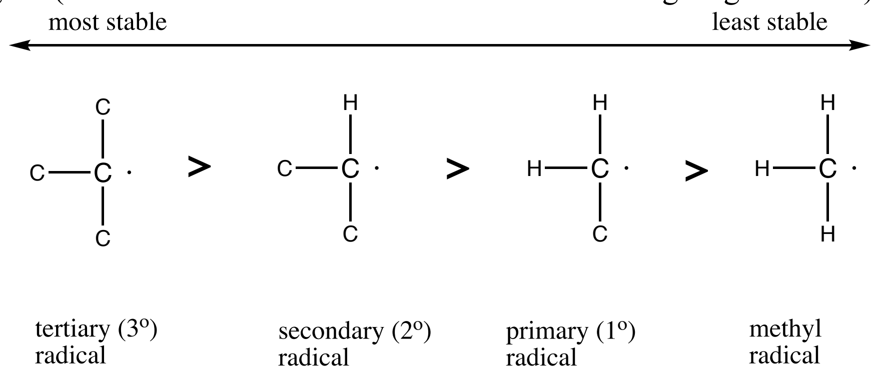


The reaction can utilize either heat (Δ) or light (hν)

Different types of hydrogen can be pulled from a methylcyclohexane in a radical halogenation reaction to give various products. However, one main product is obtained. This is explained in terms of the stability of the radical formed during the reaction process.

Stability of radicals:

- Stability increases with alkyl substitution
- Alkyl groups are polarizable and donate electrons to electron deficient sites better than hydrogens (this is called **inductive effect** and occurs through sigma bonds)

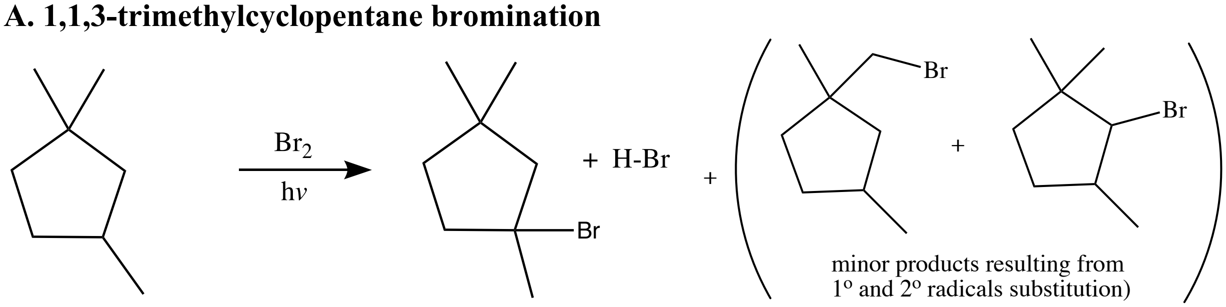


Or it can be summarized from least to most stable radicals:

$\cdot CH_3$	<	$\cdot CH_2R$	<	$\cdot CHR_2$	<	$\cdot CR_3$
methyl radical (least stable)		primary (1°) radical		secondary (2°) radical		tertiary (3°) radical (most stable)

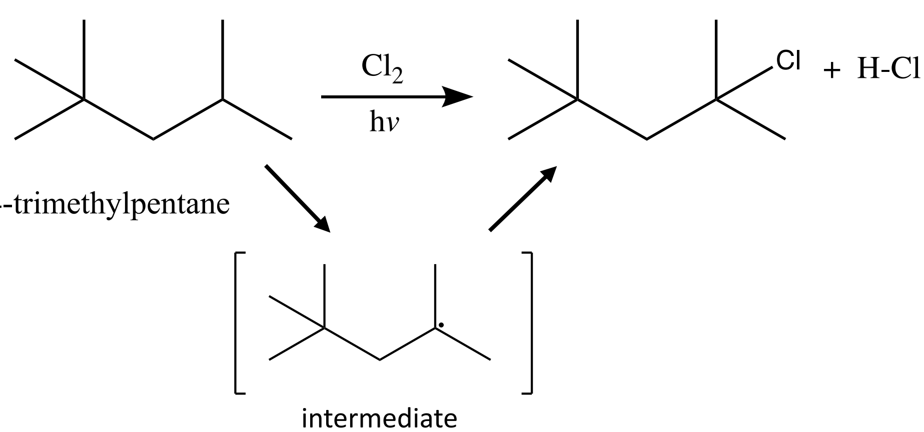
More Examples

A. 1,1,3-trimethylcyclopentane bromination



1,1,3-trimethylcyclopentane

B. 2,2,4-trimethylpentane chlorination

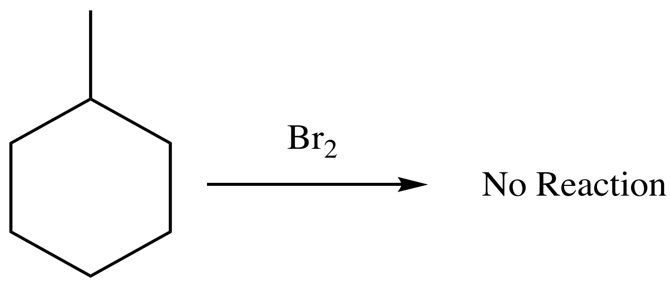


RECALL:

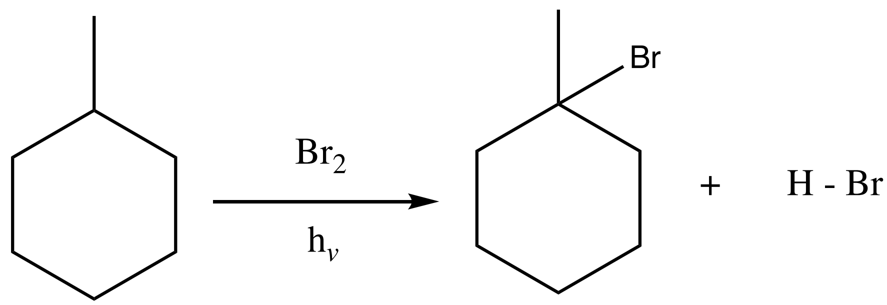
Halogenation of alkanes:

- requires light or heat to cause a reaction between the starting material and halogen.

Example:

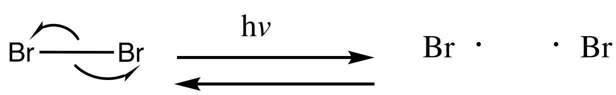


- requires light or heat to cause a reaction between the starting material and halogen.

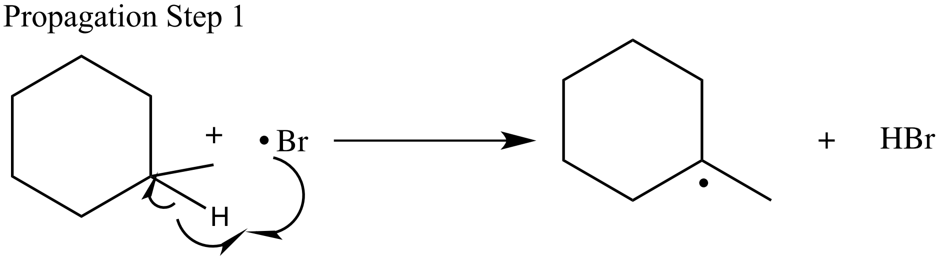


C_7H_{14}

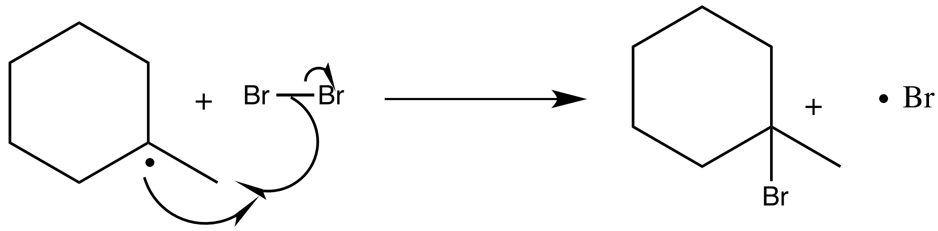
Initiation Step:



Propagation Step 1

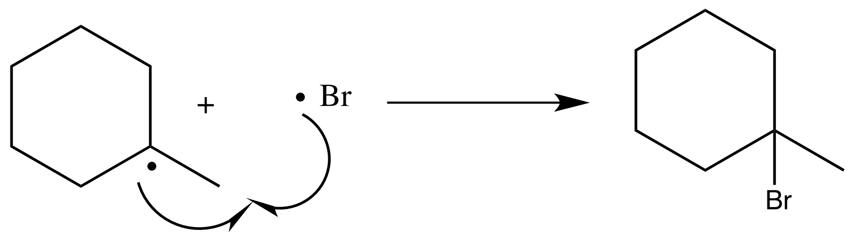


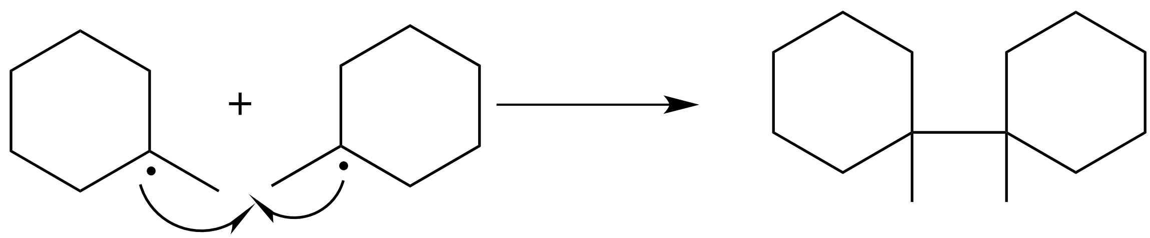
Propagation Step 2



Termination Step: Radicals Recombine

-Very minor component of the reaction



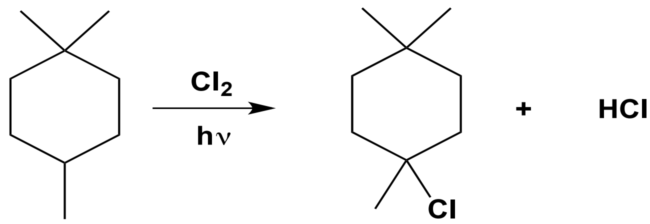


Two alkyl radicals combining is highly unlikely because the chances of them finding one another is very low (they are low in concentration) – above also very crowded (steric effect)

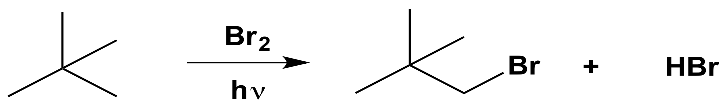
Stability of radicals:

- Stability increases with alkyl substitution
- Alkyl groups are polarizable and donate electrons to electron deficient sites better than hydrogens (this is called **inductive effect** and occurs through sigma bonds)

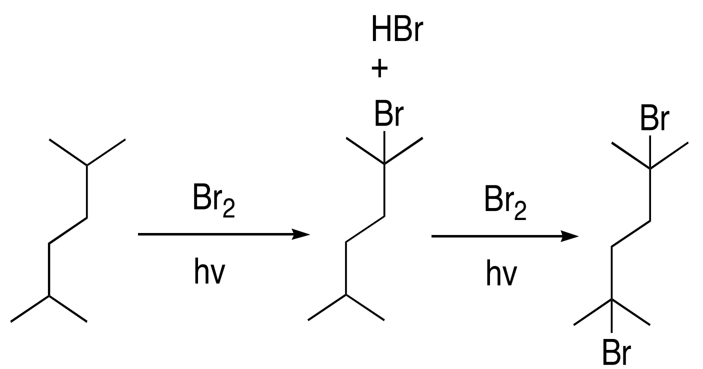
More Examples:



1,1,4-trimethylcyclohexane



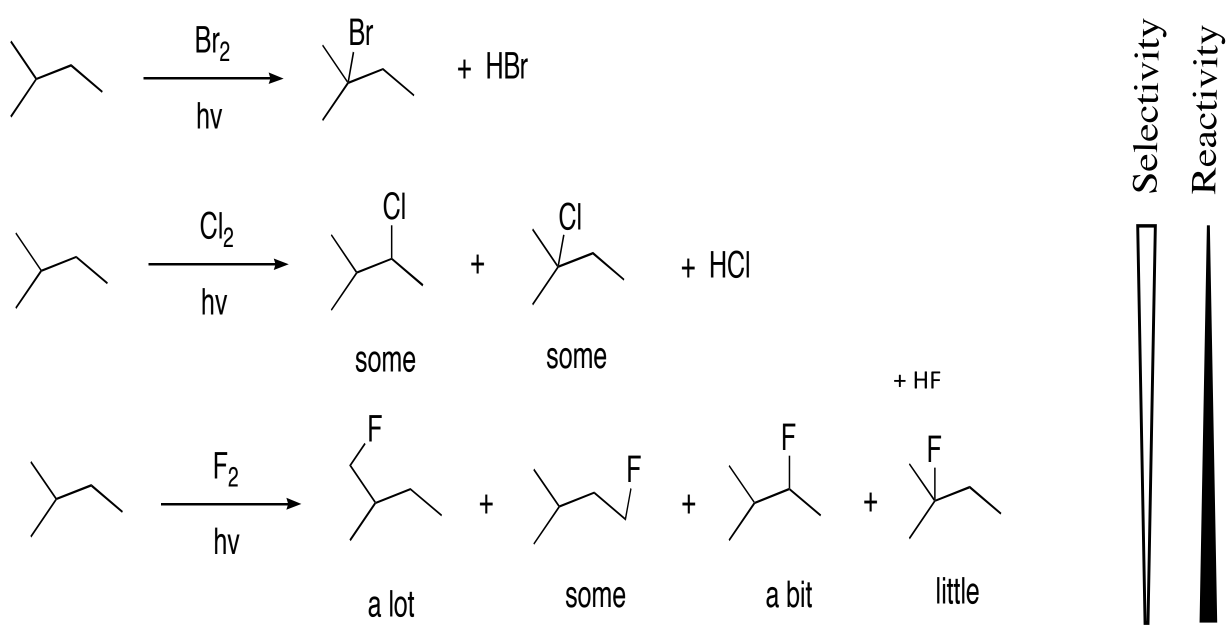
Neopentane
(2,2-dimethylpropane)



2, 5-dimethylhexane

<u>Reactivity and Selectivity (Hammond Postulate)</u>

e.g. Halogenation of 2-methylbutane



NOTE:
More reactive reagents give less selective products
Less reactive reagents give more selective products

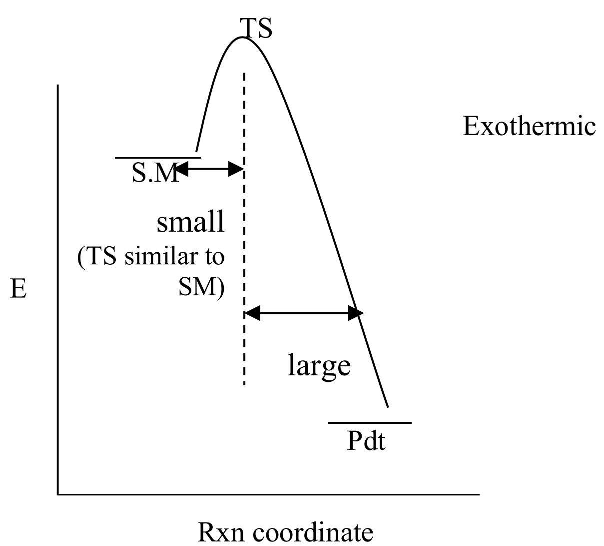
I_2 does not react as above

For Exothermic Reactions
-The transition state (TS) resembles the starting material (SM)

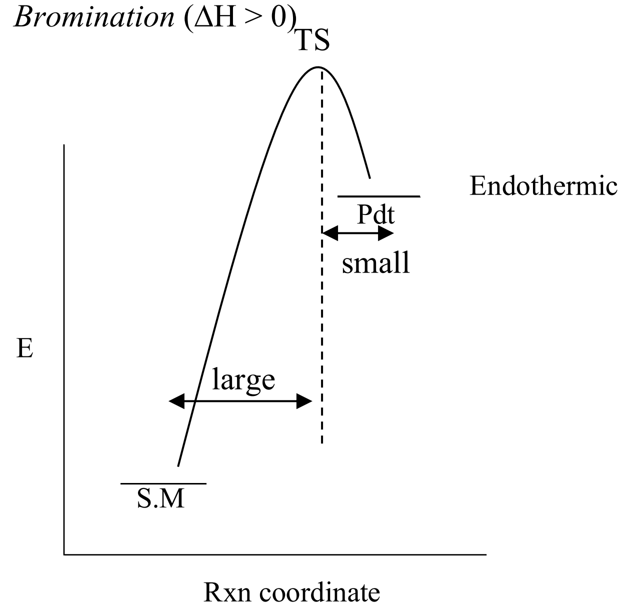
For Endothermic Reactions
-The transition state (TS) resembles the products (Pdt)

Energy Diagrams for Halogenation Reactions

Fluorination ($\Delta H < 0$)

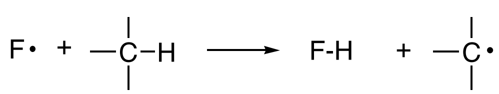


Bromination ($\Delta H > 0$)

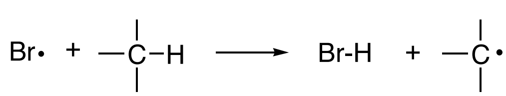


E = energy
TS = transition state
SM = starting material

Reactivity TREND:
$F_2 > Cl_2 > Br_2 >> I_2$ Iodine does not react



$\Delta H = -35$ kcal/mole
Exothermic



$\Delta H = +16$ kcal/mole
Endothermic

Selectivity TREND:

Br• > Cl• > F•

most selective — least selective

endothermic — exothermic

Bromine atom "searches" the molecule to create the most stable radical
Fluorine atom is small and feels the loss of an electron much more than bromine

- Fluorine is less precise and reacts immediately

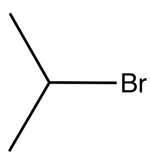
Naming of Alkyl Halides = Haloalkanes

CH_3Cl	CH_2Cl_2	$CHCl_3$	CCl_4
Methyl chloride Chloromethane	Methylene chloride Dichloromethane	Chloroform Trichloromethane	Carbon tetrachloride Tetrachloromethane

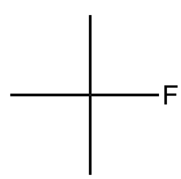
Structure and Nomenclature

1) Find longest chain with largest number of branches
2) Number from end so as to give 1^{st} halogen the lowest number
3) Name prefix with "halo" (chloro, bromo, iodo, fluoro) OR name alkyl and add halide (chloride, bromide, iodide, fluoride) as the suffix

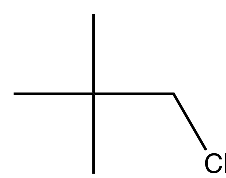
Examples:



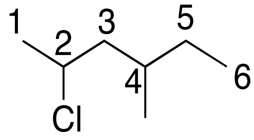
Isopropyl Bromide
2-Bromopropane



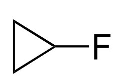
tert-Butyl fluoride
2-Fluoro-2-methylpropane



Neopentyl chloride
1-Chloro-2,2-dimethylpropane

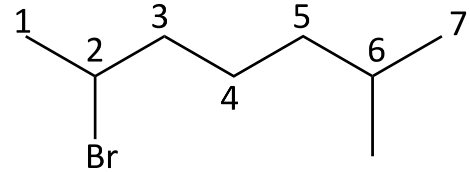


2 -chloro -4-methylhexane

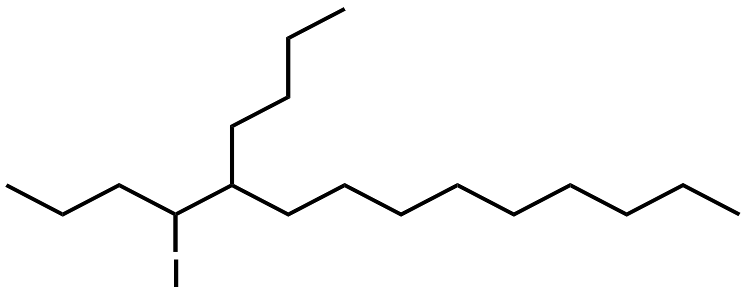


Fluorocyclopropane

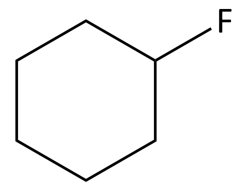
Cyclopropyl fluoride



2-bromo-6-methylheptane



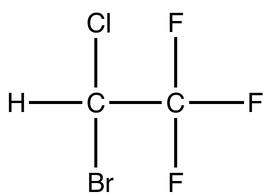
5-Butyl-4-iodotetradecane



cyclohexyl fluoride
1-fluorocyclohexane

Applications of Haloalkanes

1.) Halothane (anesthetic)



1,1,1-trifluoro-2-bromo-2-chloroethane