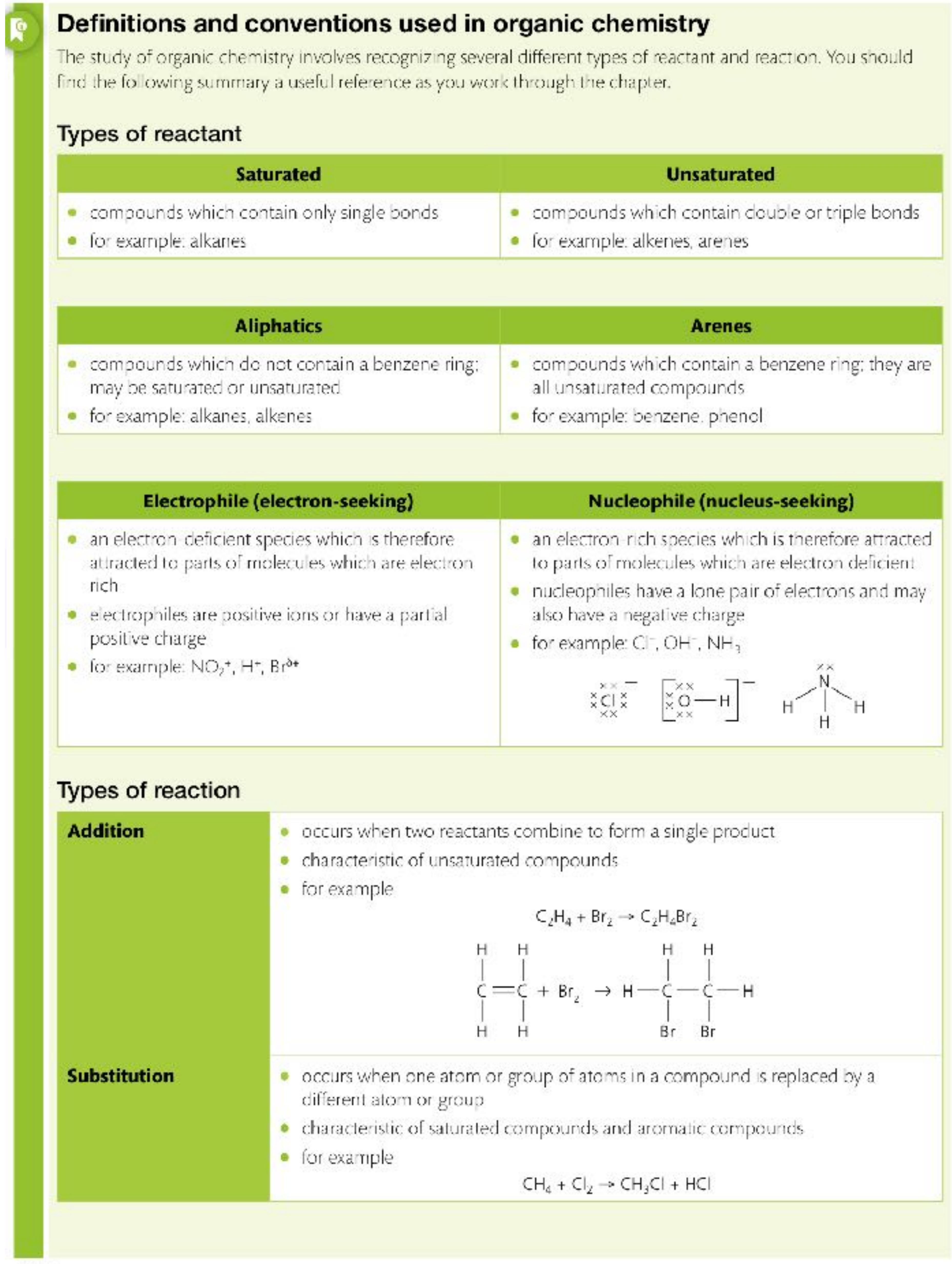
Organic Chemistry

Unit 10

What do I need to know ***before*** we get started?

- Substituents and/or alkyl chains up to 6 carbons
  - meth, eth, prop, but, pent, hex
- Functional Groups (p. 470)
  - FLASH CARDS
  - You may have these from earlier in the year.

Some Conventional Organic Chemistry Terminology



Definitions and conventions used in organic chemistry

The study of organic chemistry involves recognizing several different types of reactant and reaction. You should find the following summary a useful reference as you work through the chapter.

Types of reactant

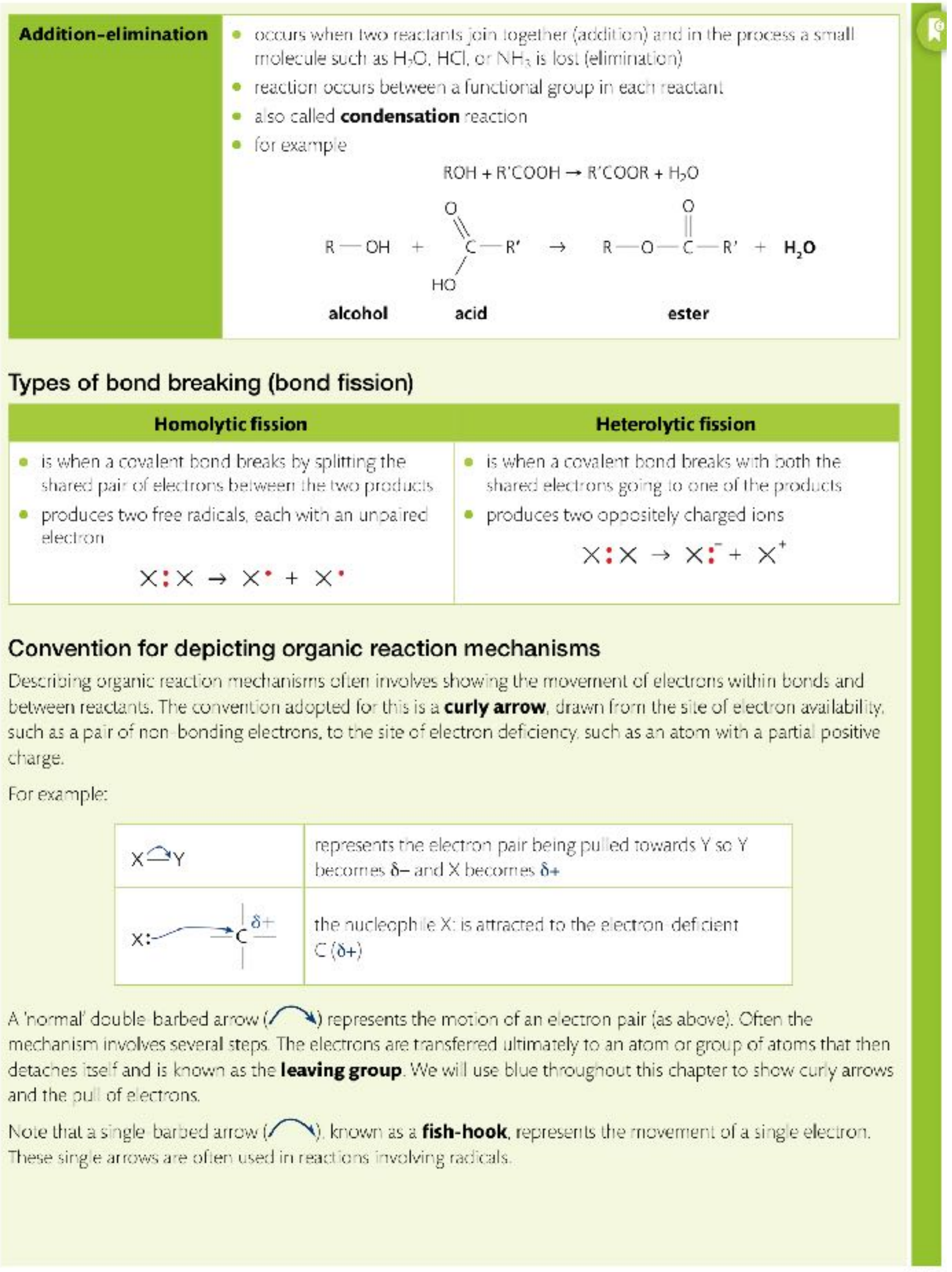
Saturated	Unsaturated
- compounds which contain only single bonds - for example: alkanes	- compounds which contain double or triple bonds - for example: alkenes, arenes

Aliphatics	Arenes
- compounds which do not contain a benzene ring: may be saturated or unsaturated - for example: alkanes, alkenes	- compounds which contain a benzene ring: they are all unsaturated compounds - for example: benzene, phenol

Electrophile (electron-seeking)	Nucleophile (nucleus-seeking)
- an electron-deficient species which is therefore attracted to parts of molecules which are electron rich - electrophiles are positive ions or have a partial positive charge - for example: NO_2^+, H^+, $Br^{\delta+}$	- an electron-rich species which is therefore attracted to parts of molecules which are electron deficient - nucleophiles have a lone pair of electrons and may also have a negative charge - for example: Cl^-, OH^-, NH_3

Types of reaction

Addition	- occurs when two reactants combine to form a single product - characteristic of unsaturated compounds - for example $C_2H_4 + Br_2 \rightarrow C_2H_4Br_2$
Substitution	- occurs when one atom or group of atoms in a compound is replaced by a different atom or group - characteristic of saturated compounds and aromatic compounds - for example $CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$



Addition-elimination	- occurs when two reactants join together (addition) and in the process a small molecule such as H_2O, HCl, or NH_3 is lost (elimination) - reaction occurs between a functional group in each reactant - also called **condensation** reaction - for example $ROH + R'COOH \rightarrow R'COOR + H_2O$ **alcohol** **acid** **ester**

Types of bond breaking (bond fission)

Homolytic fission	Heterolytic fission
- is when a covalent bond breaks by splitting the shared pair of electrons between the two products - produces two free radicals, each with an unpaired electron $X{:}X \rightarrow X^{\bullet} + X^{\bullet}$	- is when a covalent bond breaks with both the shared electrons going to one of the products - produces two oppositely charged ions $X{:}X \rightarrow X{:}^- + X^+$

Convention for depicting organic reaction mechanisms

Describing organic reaction mechanisms often involves showing the movement of electrons within bonds and between reactants. The convention adopted for this is a **curly arrow**, drawn from the site of electron availability, such as a pair of non-bonding electrons, to the site of electron deficiency, such as an atom with a partial positive charge.

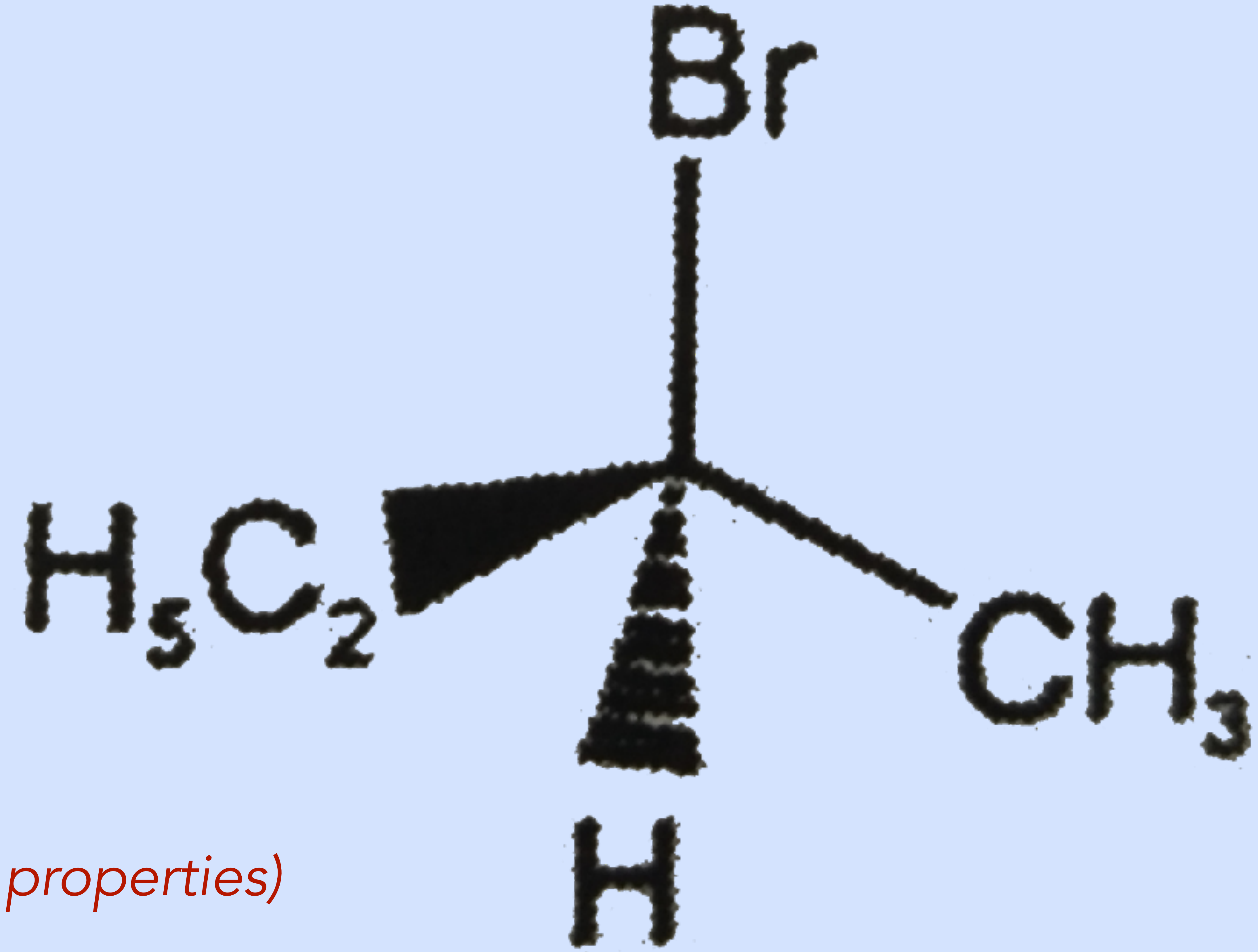
For example:

$X \overset{\curvearrowright}{-} Y$	represents the electron pair being pulled towards Y so Y becomes δ− and X becomes δ+
$X{:} \longrightarrow C^{\delta+}$	the nucleophile X: is attracted to the electron-deficient C (δ+)

A 'normal' double-barbed arrow ($\curvearrowright$) represents the motion of an electron pair (as above). Often the mechanism involves several steps. The electrons are transferred ultimately to an atom or group of atoms that then detaches itself and is known as the **leaving group**. We will use blue throughout this chapter to show curly arrows and the pull of electrons.

Note that a single-barbed arrow ($\curvearrowright$), known as a **fish-hook**, represents the movement of a single electron. These single arrows are often used in reactions involving radicals.

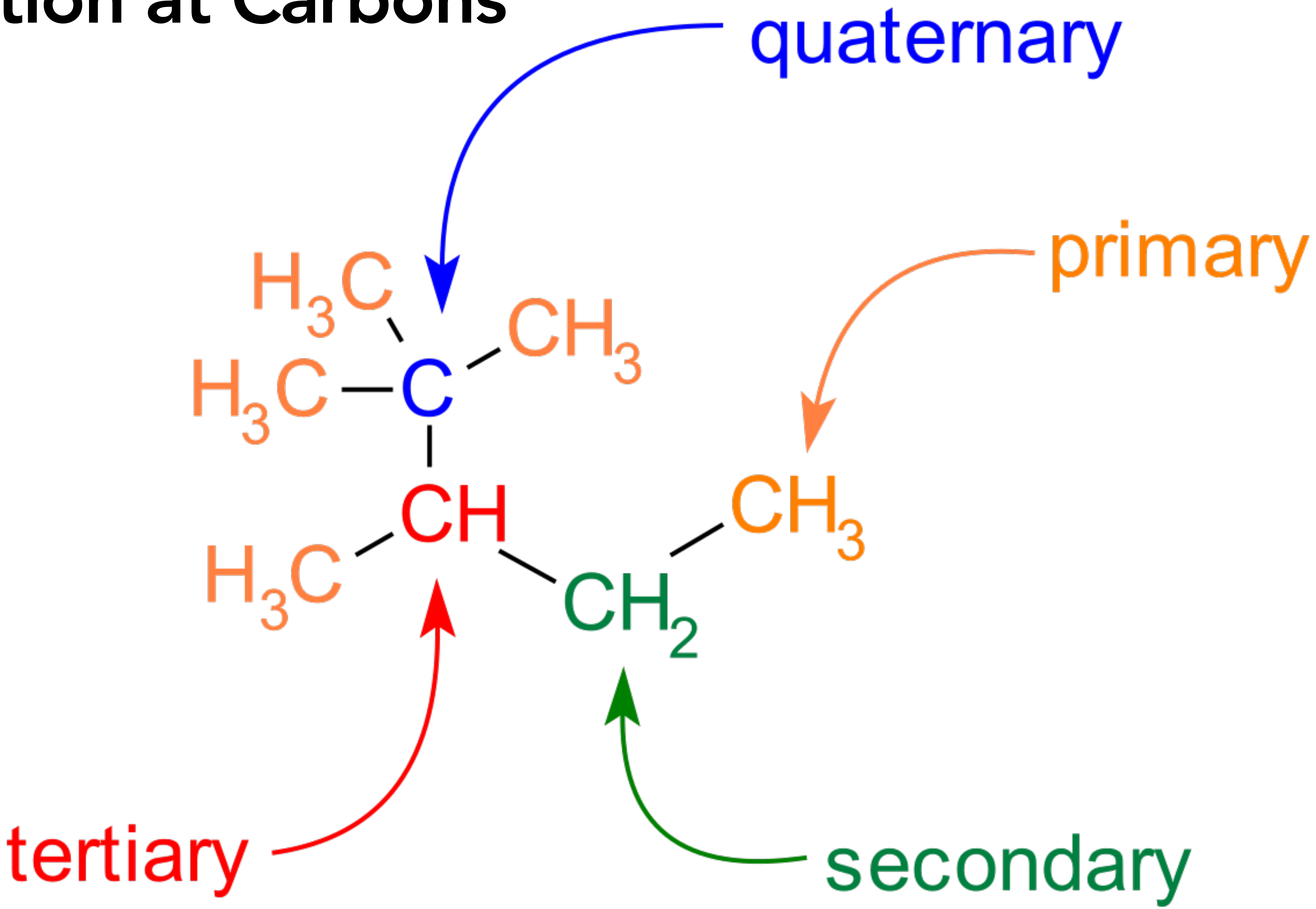
10.1 Fundamentals of Organic Chemistry



- Homologous Series - *Alkanes, Alkenes, Alkynes*
- Formulas (empirical, molecular and structural)
- Nomenclature (*IUPAC* rules)
- Functional Groups - *Flash Cards*
- Isomers - *same molecular formula, different structures (and properties)*
- *Primary, Secondary & Tertiary Compounds (examples)*
- Trends in Physical Properties - *mostly boiling point due to IMFs*
- *Arenes (i.e. Benzene)*

Substitution at Carbons

So What?



quaternary

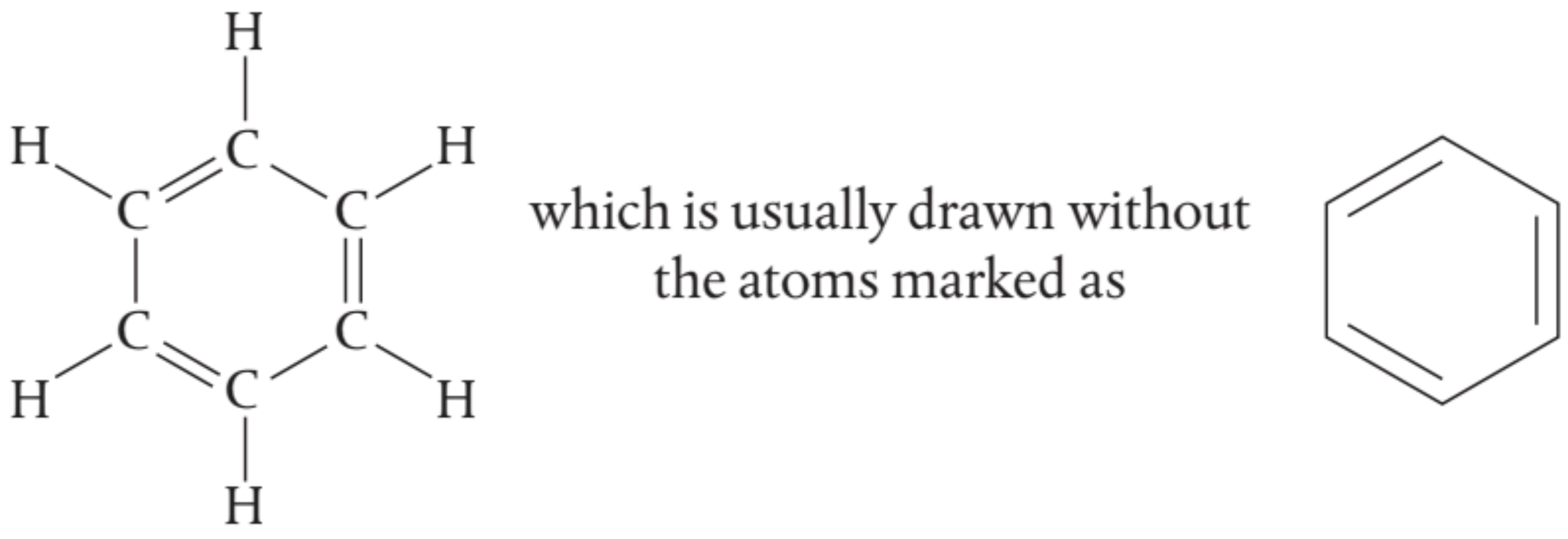
primary

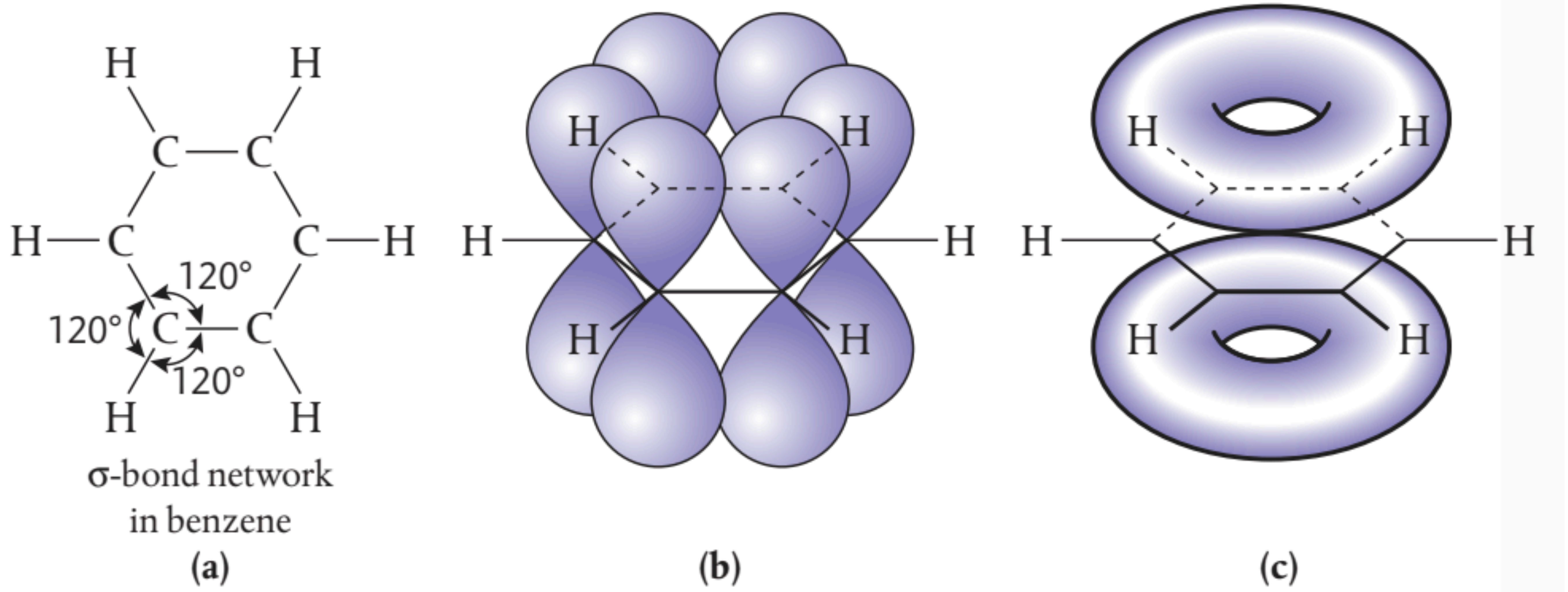
tertiary

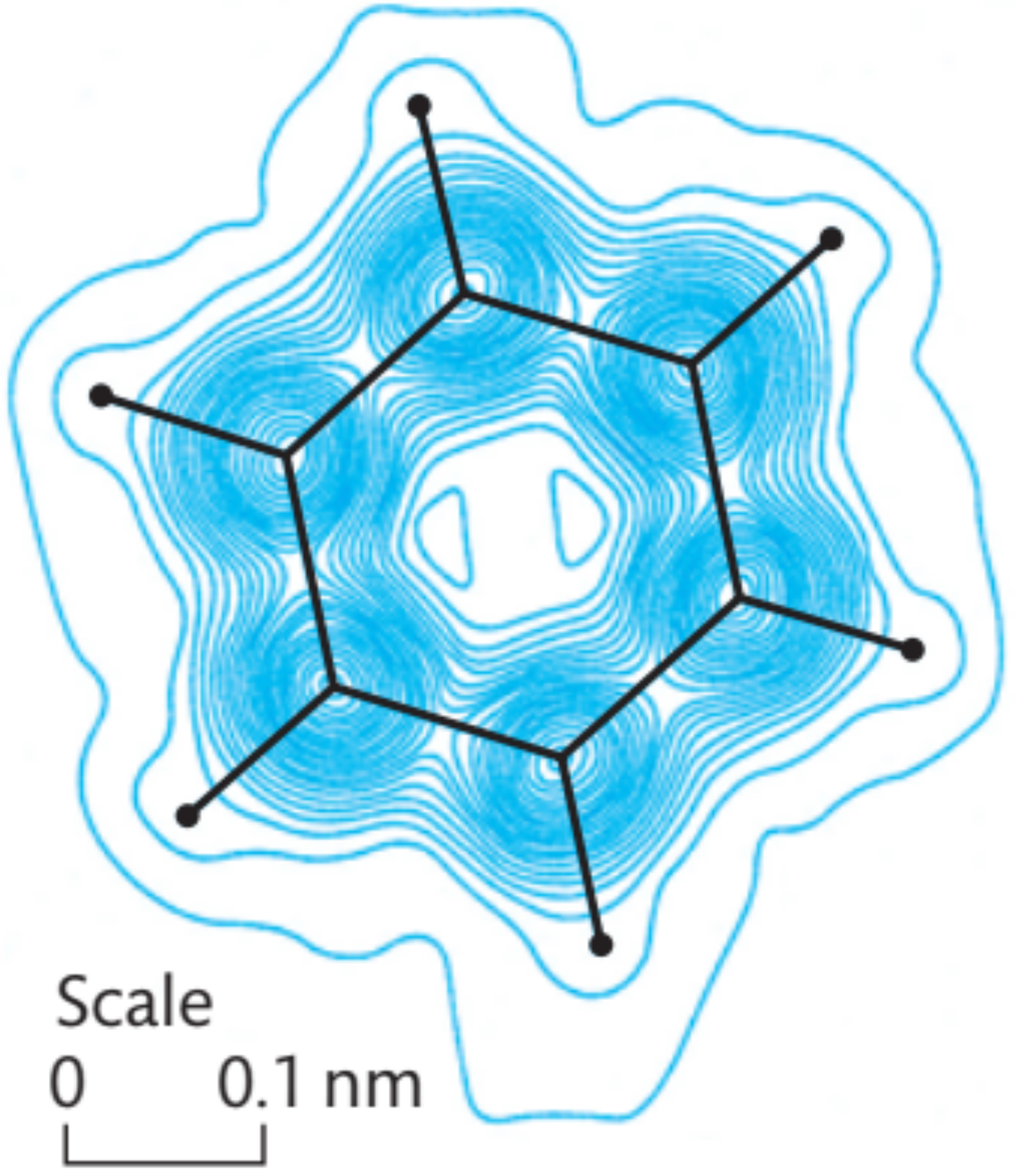
secondary

Benzene - C_6H_6

- When an aromatic functional group $–C_6H_5$ (**IUPAC name - phenyl**)
- Aromatics - generally ringed, alternating single/double bonded hydrocarbons


which is usually drawn without the atoms marked as


σ-bond network in benzene
(a)
(b)
(c)



10.2 Functional Group Chemistry

- Alkanes, Alkenes, Alkynes - *Saturation, Combustion, Substitution Reactions, Addition Reactions*
- Halogenoalkanes
- Polymers
- Benzene
- Alcohols

Alkanes vs Alkenes

- alkenes undergo addition (*across the double bond*) where alkanes will not (*substitution reactions instead*)
- burning (combustion) of alkenes is dirtier (sootier flame due to higher C:H ratio)
- Aromatic Compounds - Benzene Ring
  - Highly unsaturated - very smoky flame
  - Greenhouse gases, global warming, global dimming (smog in polluted air)

Substitution Reactions of Alkanes - *Halogenation*

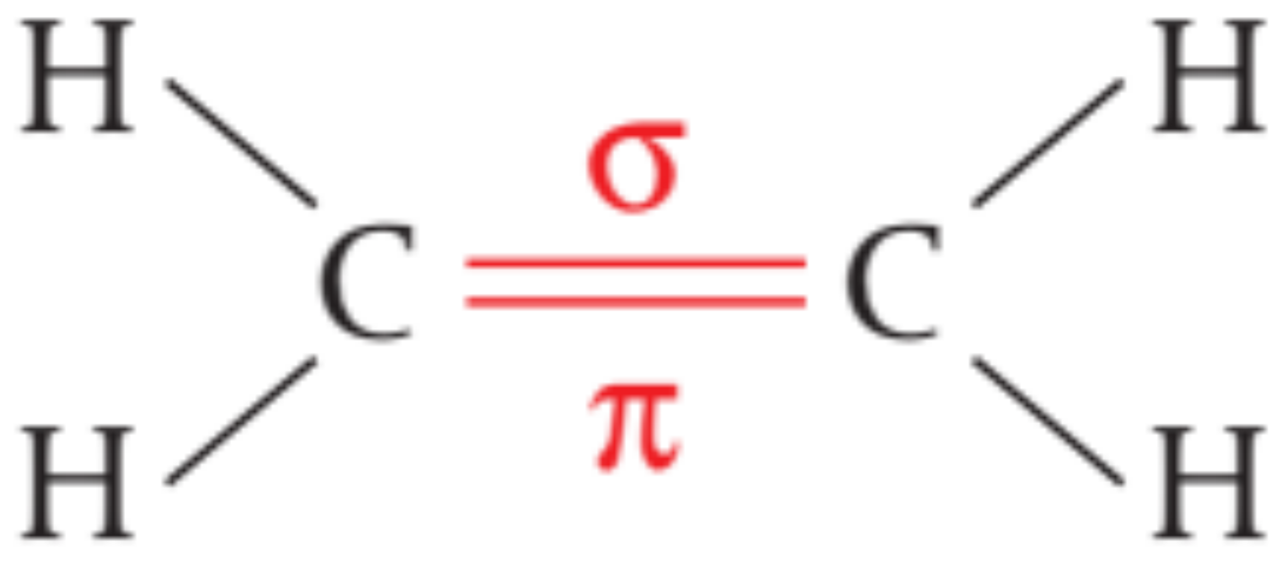
$$CH_{4(g)} + Cl_{2(g)} \xrightarrow{\text{uv light}} CH_3Cl_{(g)} + HCl_{(g)}$$

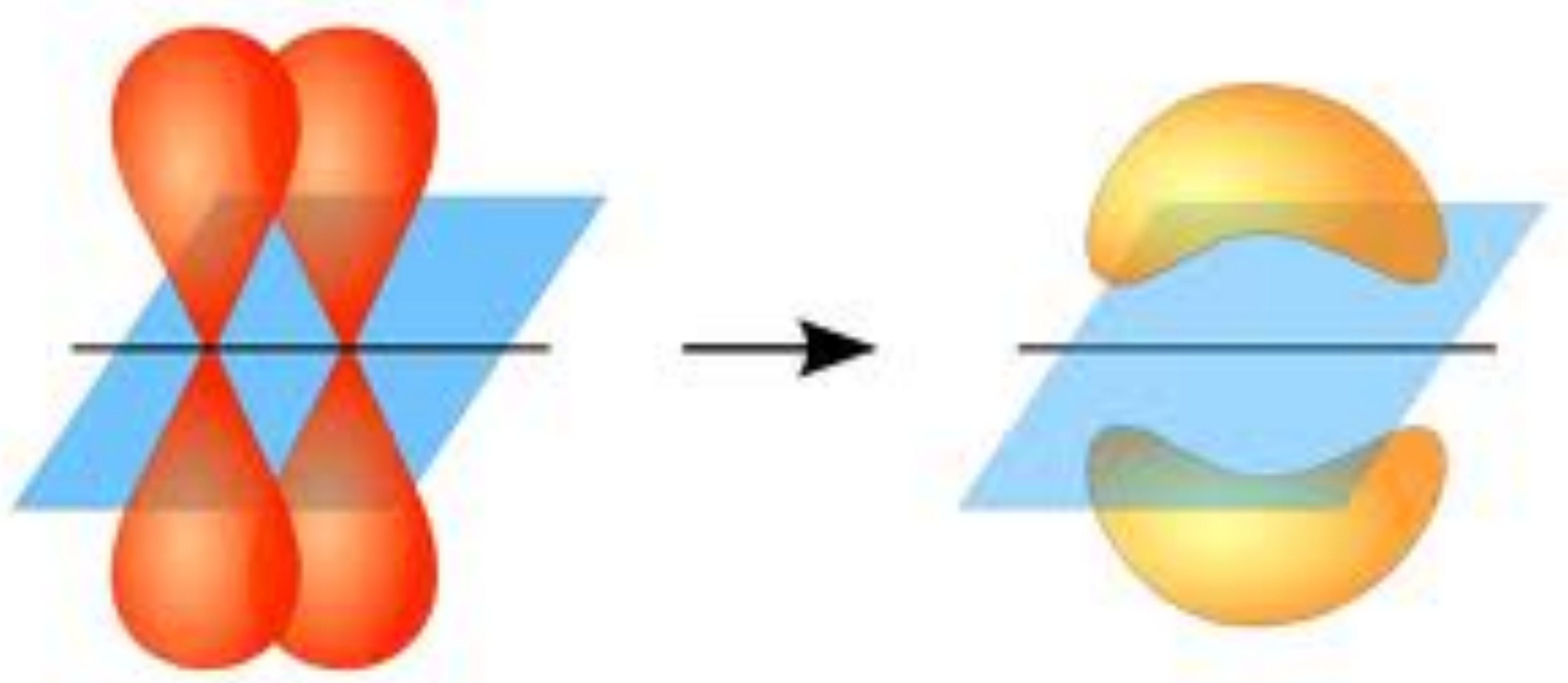
- Reaction Mechanism - sequence of steps in a chemical reaction
    - Initiation - creating the free radical
    - Propagation - both use and produce free radicals
    - Termination - removing free radicals from the mixture

Hexane + Br_2 (in dark vs in UV light): Qualitative observations?

Alkenes - *Addition (Electrophilic)*

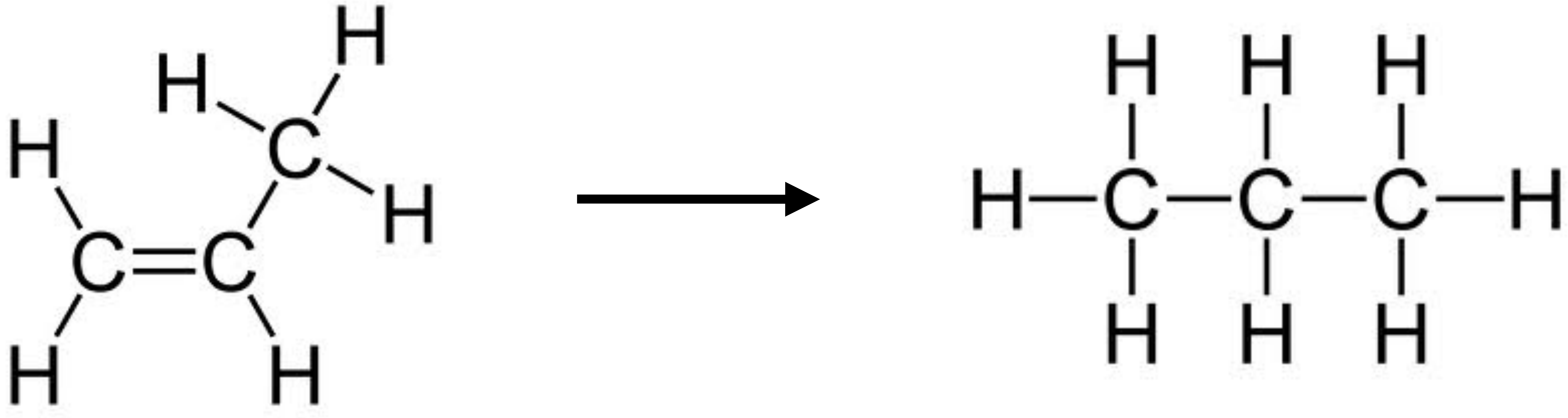
- double bonded carbons - one sigma bond and one pi bond
- Addition Reaction - attacks the *weaker* pi bond, leaving the sigma bond with some species added to the carbons





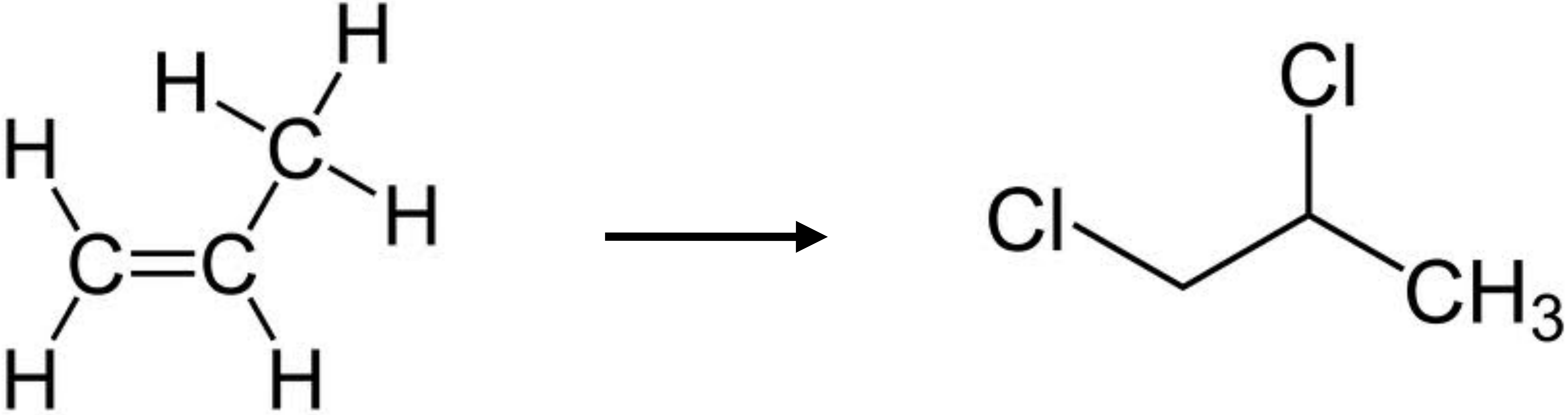
Hydrogenation

- $CH_2CHCH_3 + H_2 \xrightarrow{\text{Ni catalyst @ 150°C}} CH_3CH_2CH_3$



Addition of Halogens

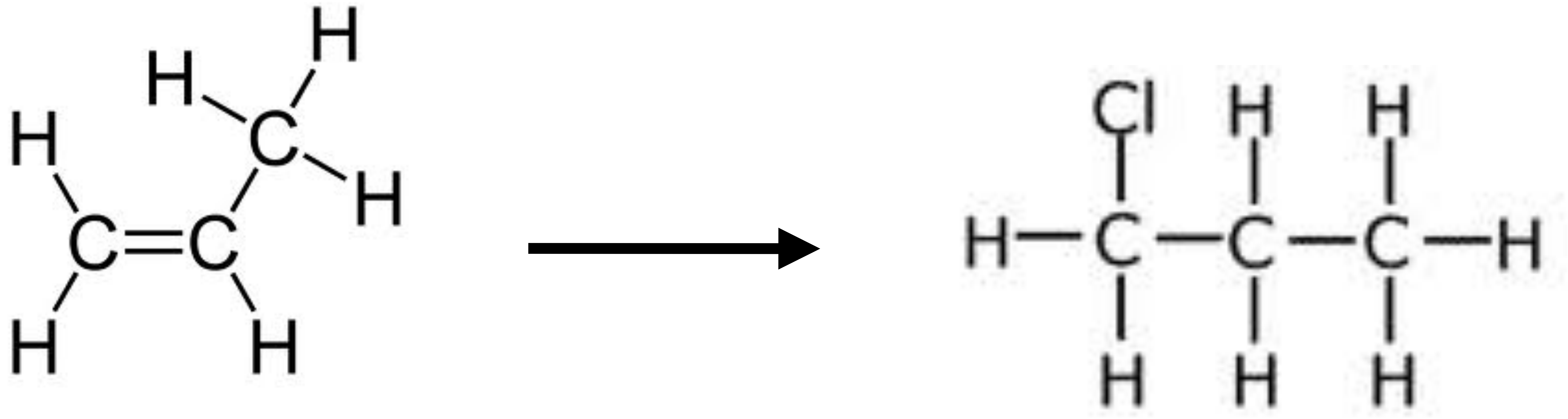
$CH_2CHCH_3 + Cl_2 \rightarrow CH_2ClCHClCH_3$



Addition of Hydrogen Halides

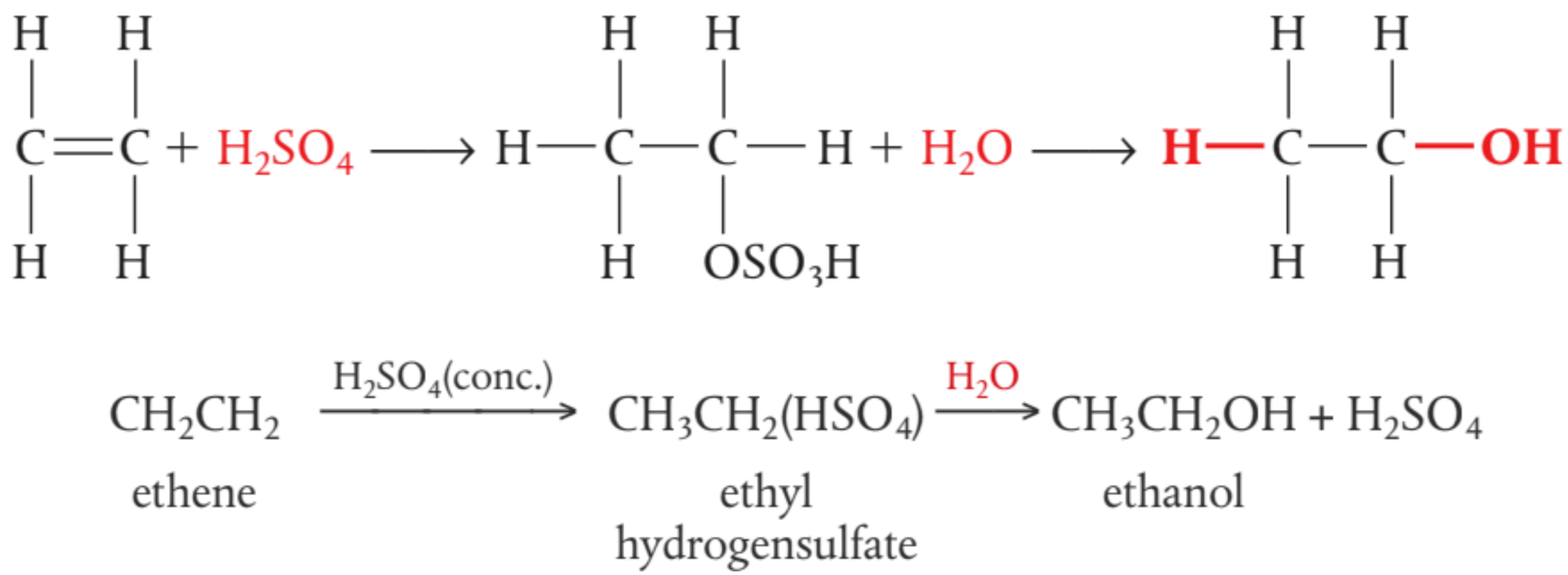
$CH_2CHCH_3 + HCl \longrightarrow CH_2ClCH_2CH_3$

- This is only one possible product and *may not be the most likely*
- More to come regarding stability of intermediates and products



Addition of Water

- mechanism on the board

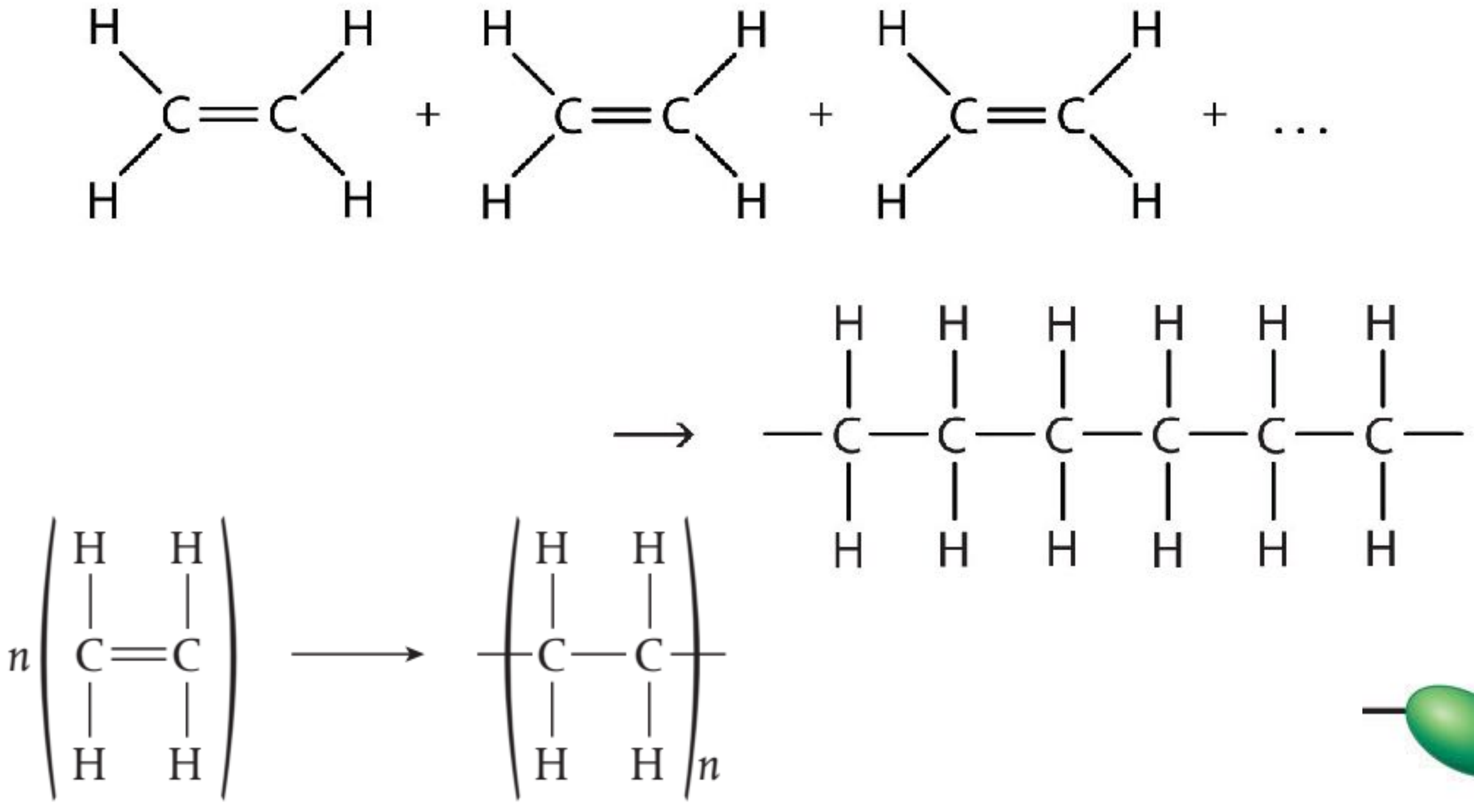


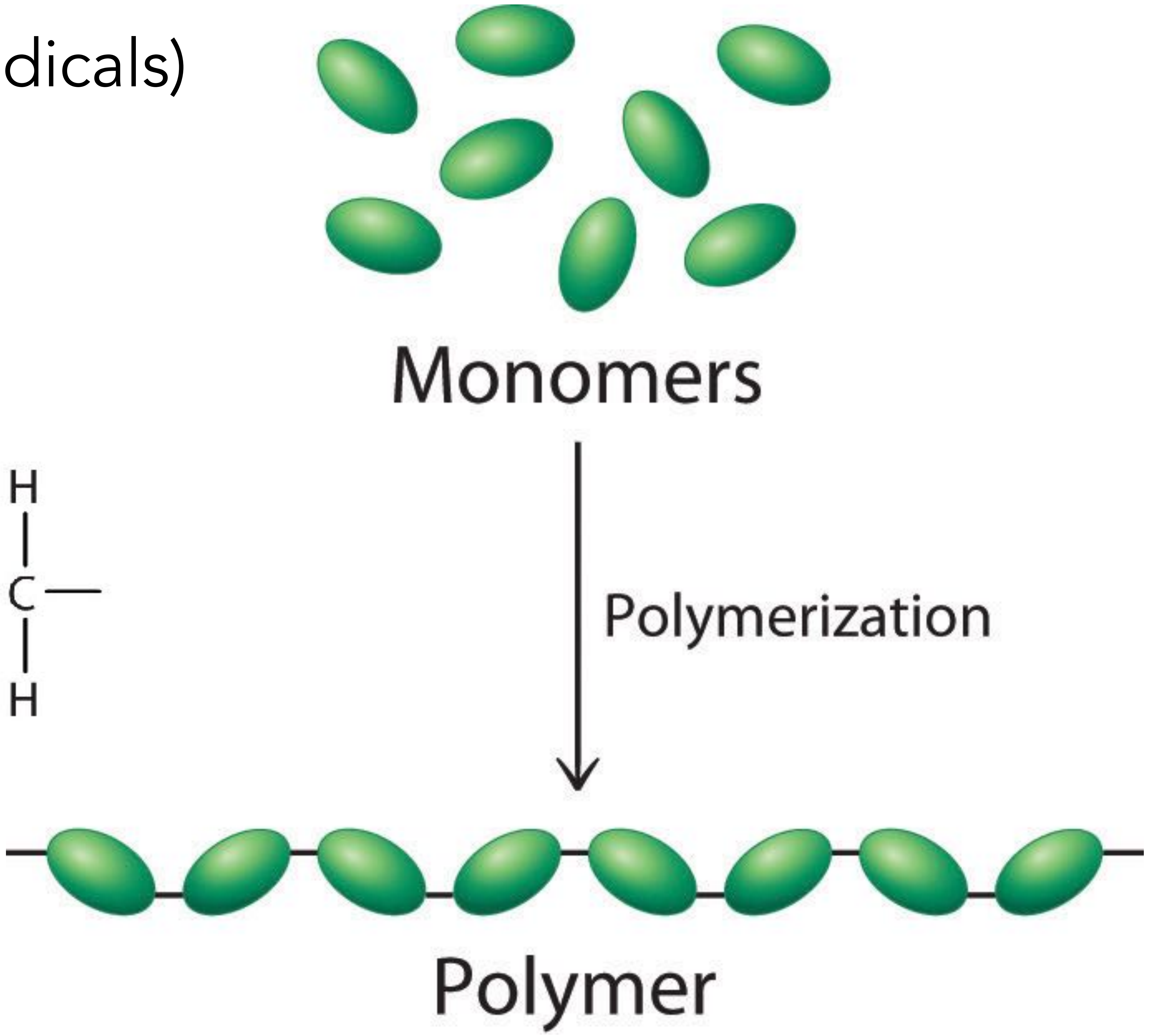
$$\mathrm{H_2C{=}CH_2} + \mathrm{H_2SO_4} \longrightarrow \mathrm{H{-}CH_2{-}CH_2(OSO_3H)} + \mathrm{H_2O} \longrightarrow \mathrm{H{-}CH_2{-}CH_2{-}OH}$$

$$\underset{\text{ethene}}{\mathrm{CH_2CH_2}} \xrightarrow{\mathrm{H_2SO_4(conc.)}} \underset{\text{ethyl hydrogensulfate}}{\mathrm{CH_3CH_2(HSO_4)}} \xrightarrow{\mathrm{H_2O}} \underset{\text{ethanol}}{\mathrm{CH_3CH_2OH}} + \mathrm{H_2SO_4}$$

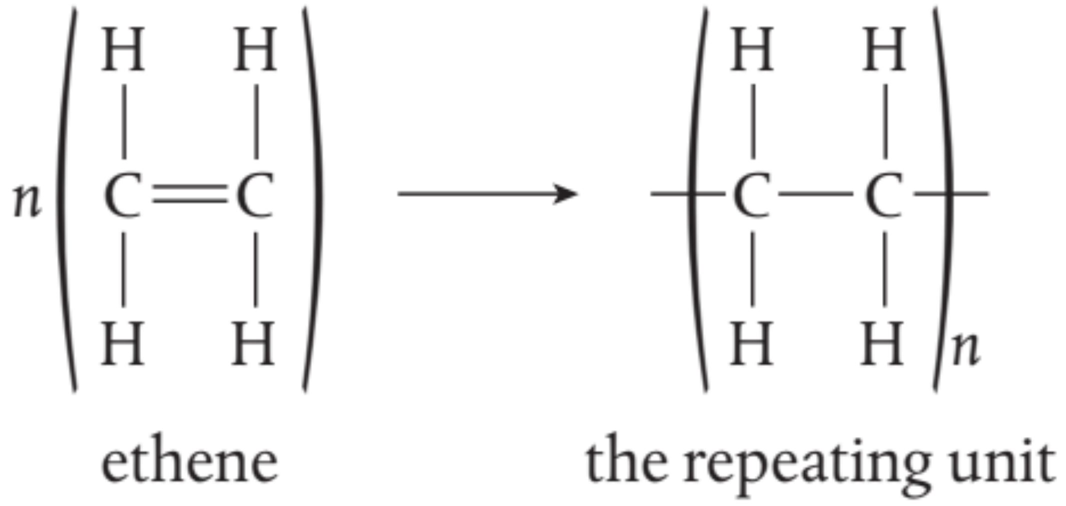
Polymerization

- alkenes readily undergo sequential addition reactions to create long chains
- mechanism for chloroethene (via free radicals)





Challenge

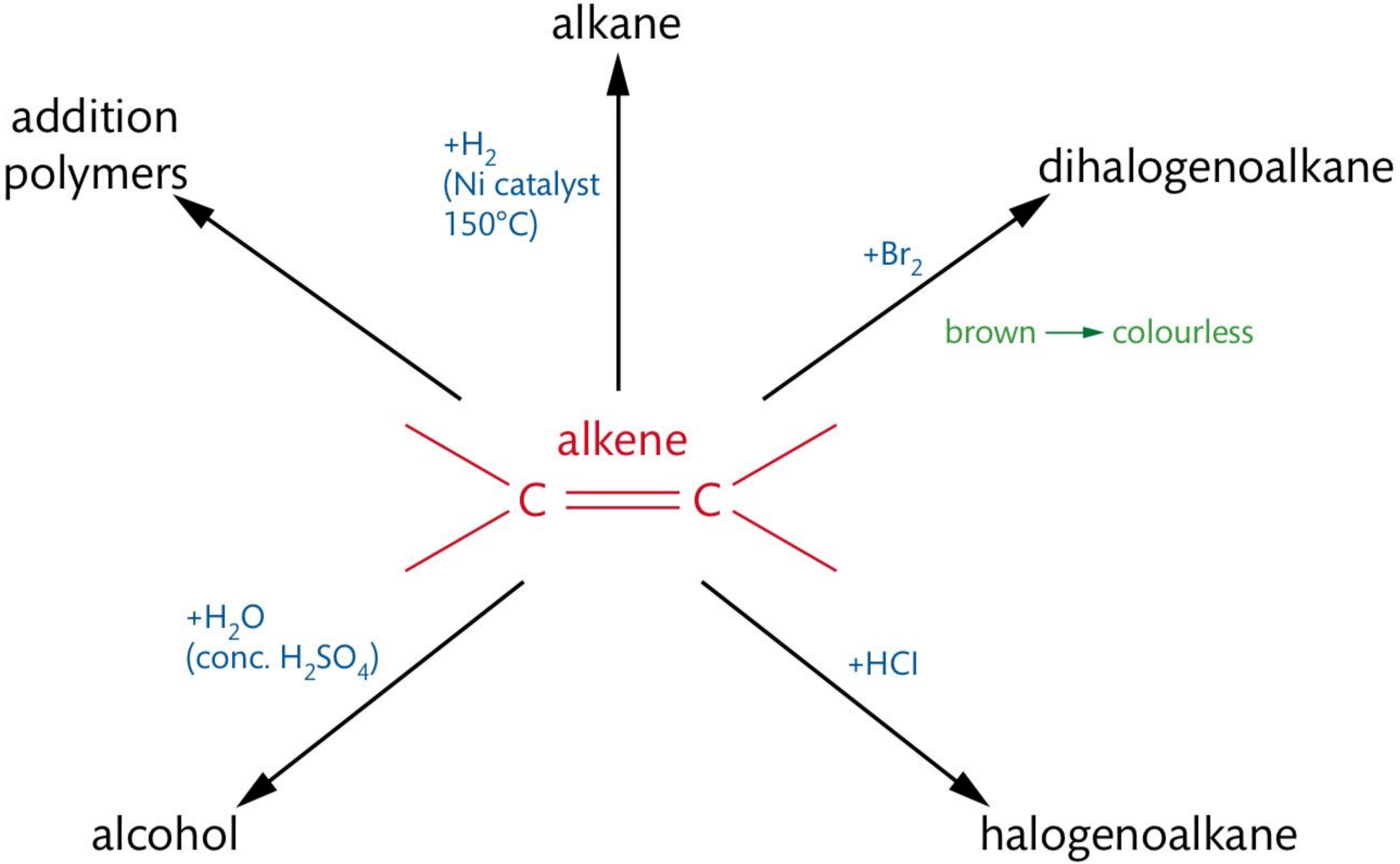


ethene the repeating unit

- Draw the repeating unit of polystyrene if the formula of the monomer is $C_6H_5CHCH_2$ *(Hint: draw the structure of the monomer first)*

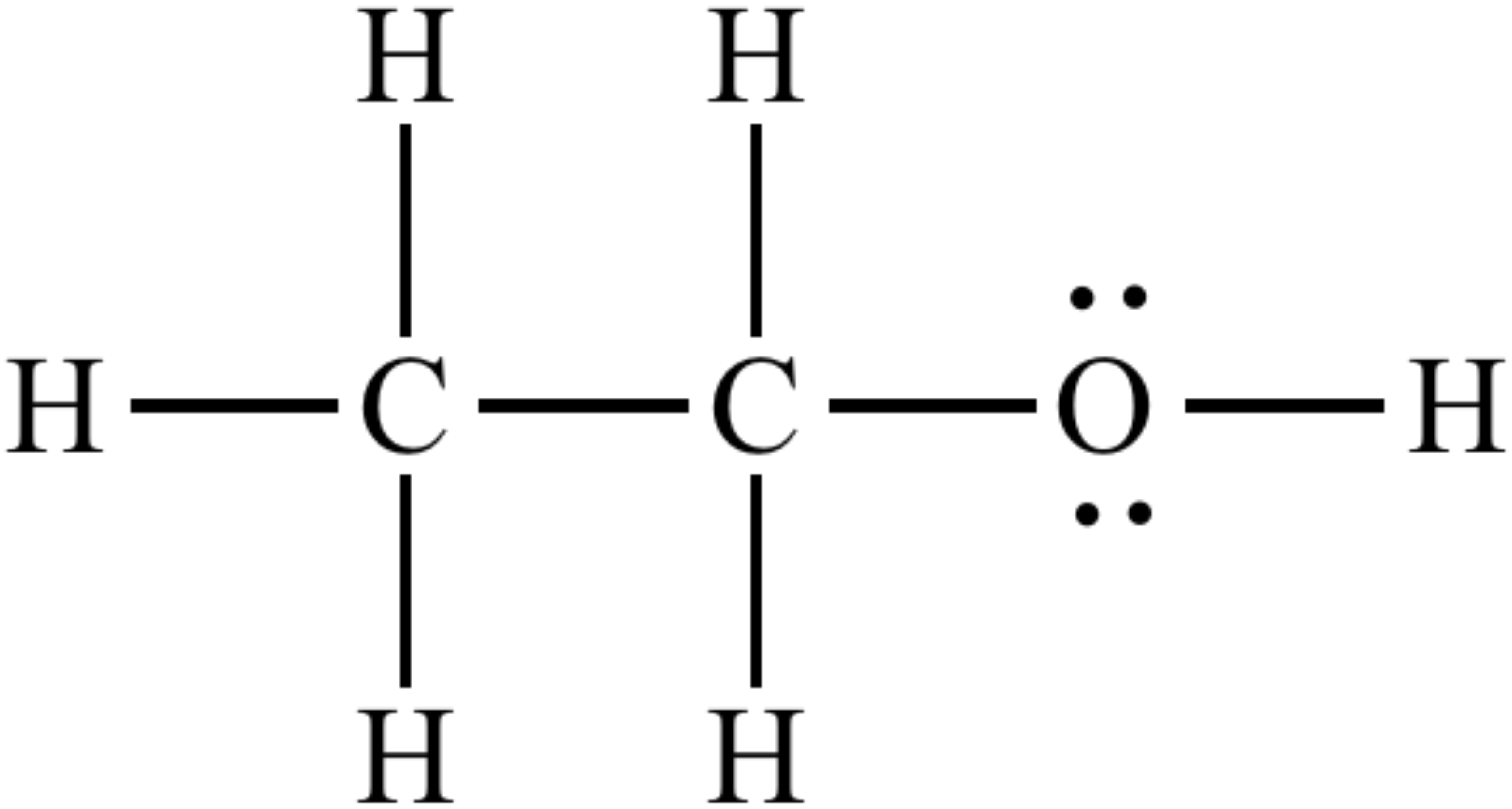
1 PETE	2 HDPE	3 PVC	4 LDPE	5 PP	6 PS	7 OTHER
polyethylene terephthalate	high-density polyethylene	polyvinyl chloride	low-density polyethylene	polypropylene	polystyrene	other plastics, including acrylic, polycarbonate, polyactic fibers, nylon, fiberglass
soft drink bottles, mineral water, fruit juice containers and cooking oil	milk jugs, cleaning agents, laundry detergents, bleaching agents, shampoo bottles, washing and shower soaps	trays for sweets, fruit, plastic packing (bubble foil) and food foils to wrap the foodstuff	crushed bottles, shopping bags, highly-resistant sacks and most of the wrappings	furniture, consumers, luggage, toys as well as bumpers, lining and external borders of the cars	toys, hard packing, refrigerator trays, cosmetic bags, costume jewellery, audio cassettes, CD cases, vending cups	an example of one type is a polycarbonate used for CD production and baby feeding bottles
						

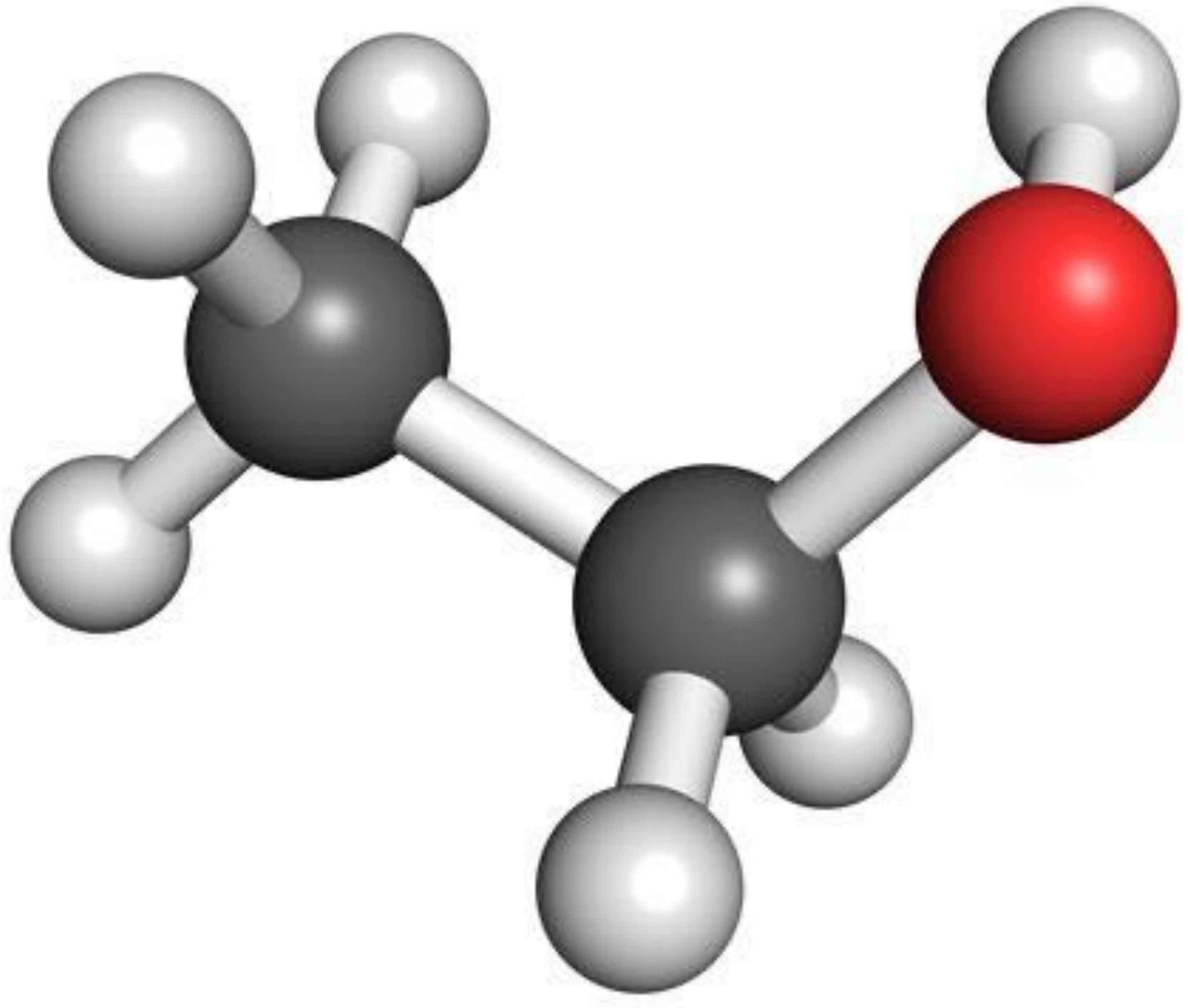
Alkenes - *Electrophilic Addition*



Alcohols

- –OH functional group ***(polar)*** increases solubility of alkanes with similar molecular mass
- most common alcohol is C_2H_5OH (ethanol) - readily soluble in water





Combustion of Alcohols

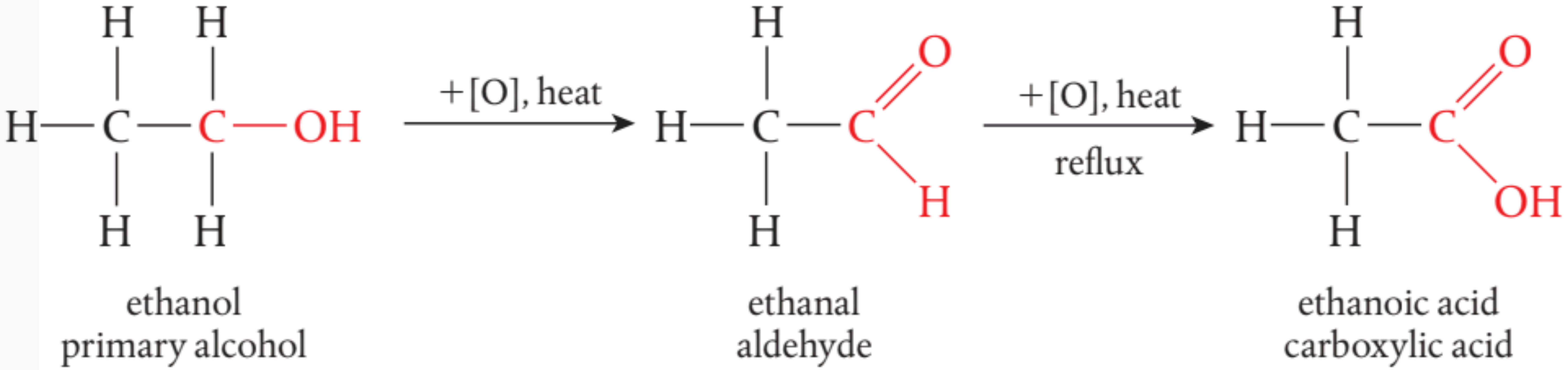
- Alcohols will burn to produce CO_2 and H_2O, just like other hydrocarbons.

$$CH_3CH_2OH + 3O_2 \rightarrow 2CO_2 + 3H_2O \qquad \Delta H = -1360\ \text{kJ/mol}$$

Oxidation of alcohols *(different than combustion)*

- when looking to oxidize an alcohol, use an oxidizing agent (acidified potassium dichromate, colored)

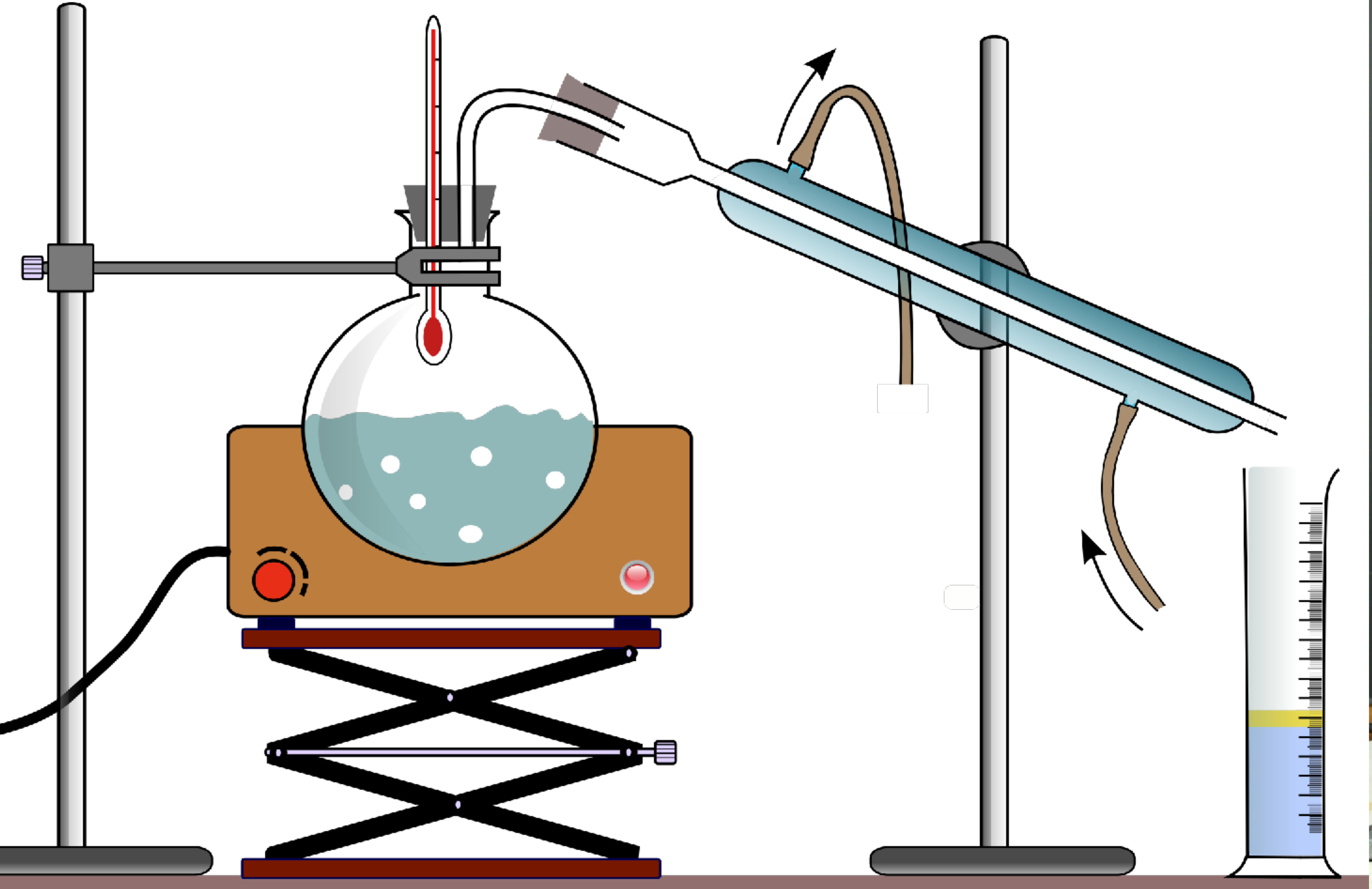
- **Primary** Alcohol Oxidation - 2 step - aldehyde to a carboxylic acid



$$\text{ethanol (primary alcohol)} \xrightarrow{+[\mathrm{O}],\ \text{heat}} \text{ethanal (aldehyde)} \xrightarrow[\text{reflux}]{+[\mathrm{O}],\ \text{heat}} \text{ethanoic acid (carboxylic acid)}$$

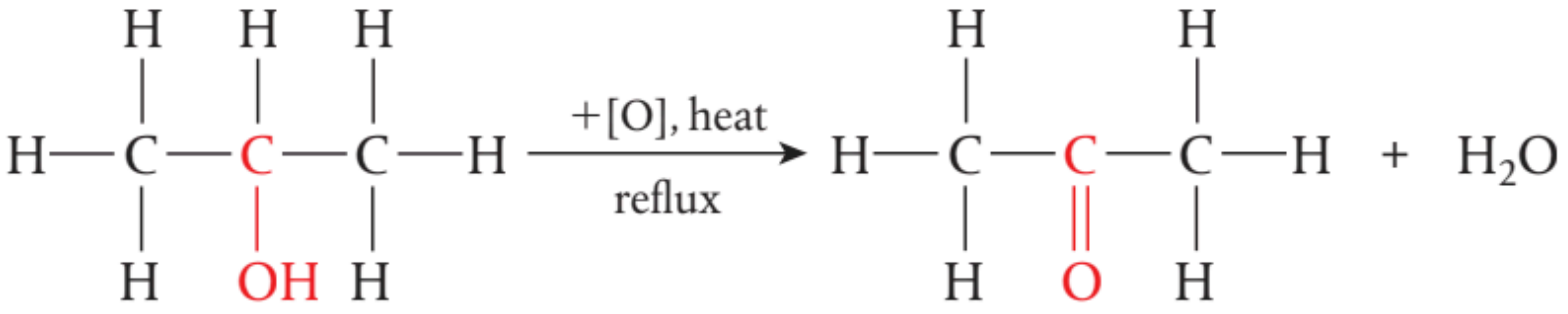
$$\mathrm{H^+/Cr(VI)} \longrightarrow \mathrm{Cr(III)}$$

Reflux vs Distillation



Secondary Alcohols

- oxidized to ketones by a similar process



$CH_3CHOHCH_3$
propan-2-ol

$(CH_3)_2CO$
propanone

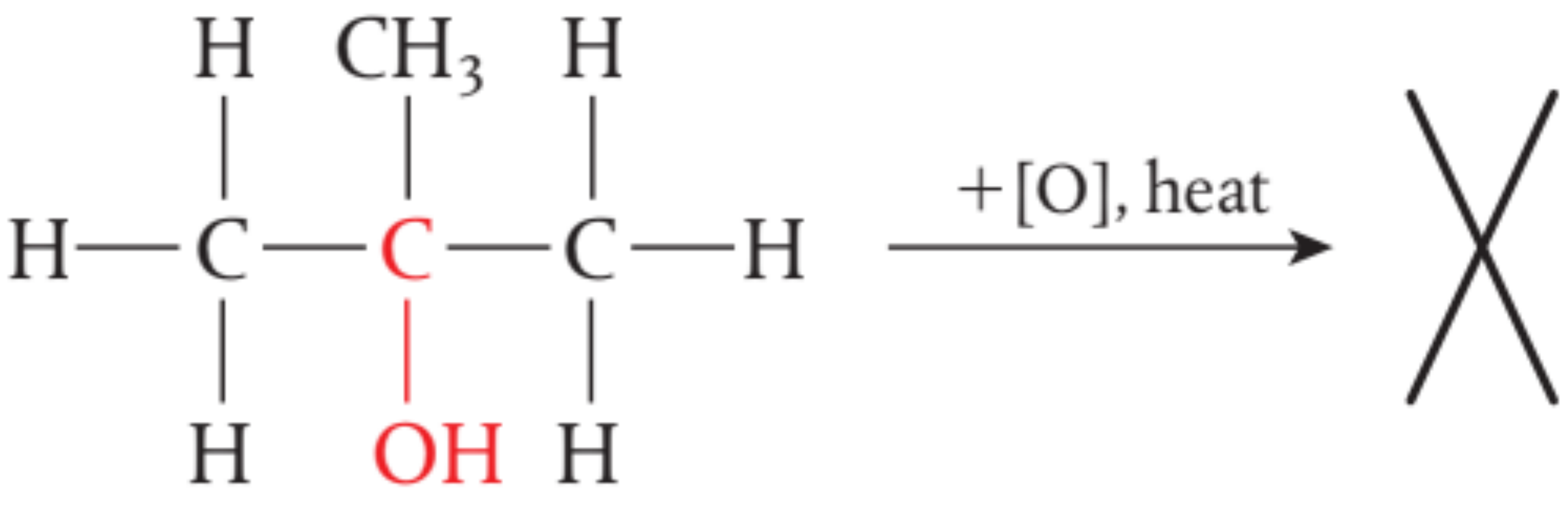
$$\text{propan-2-ol} \xrightarrow[\text{reflux}]{+\,[O],\ \text{heat}} \text{propanone} \quad + \quad H_2O$$

$$CH_3CHOHCH_3 \qquad\qquad (CH_3)_2CO$$

$$H^+/Cr(VI) \longrightarrow Cr(III)$$

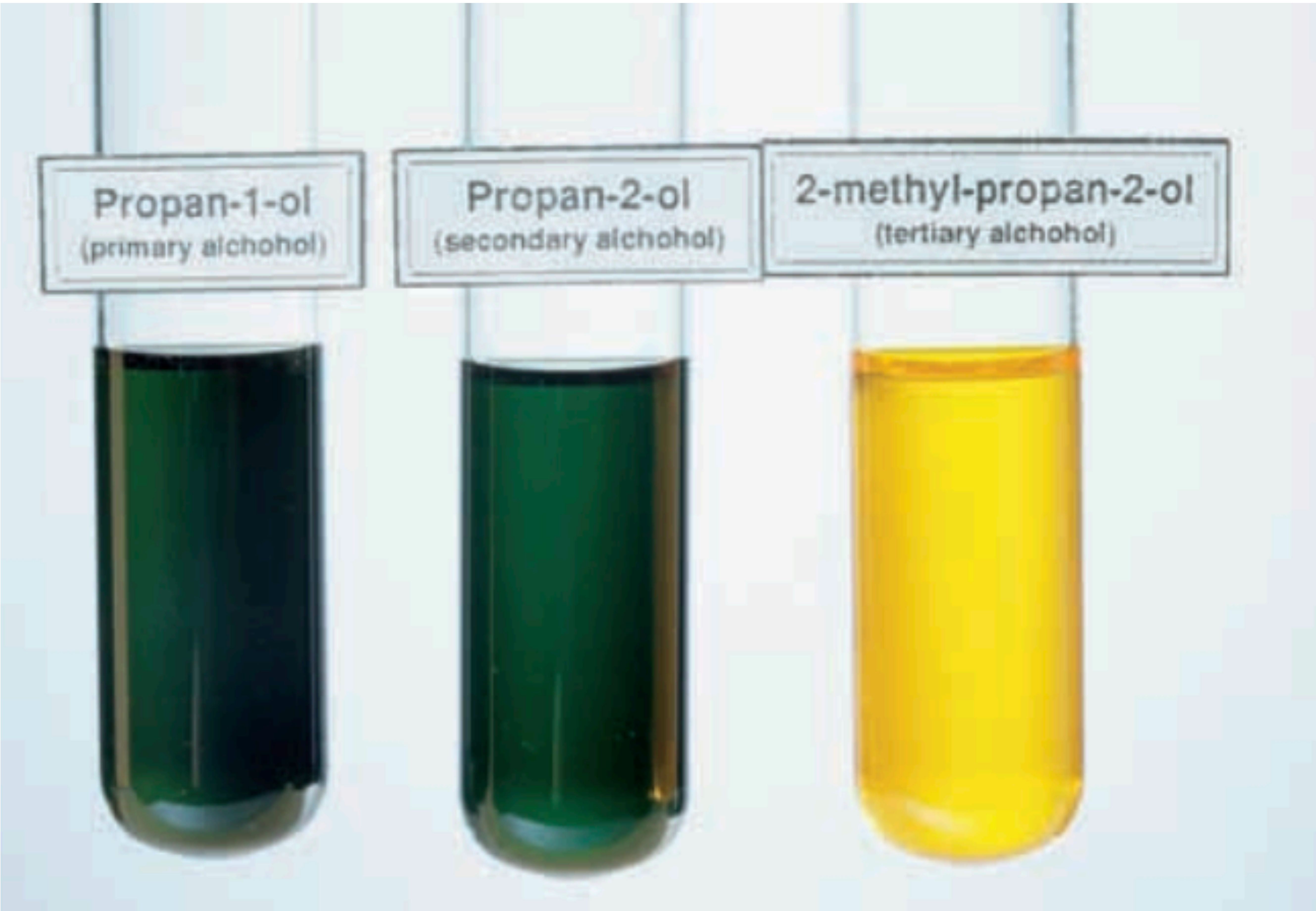
Tertiary Alcohols

- not readily oxidized under comparable conditions
  - would involve breaking the carbon skeleton (LOTS OF ENERGY!!!)



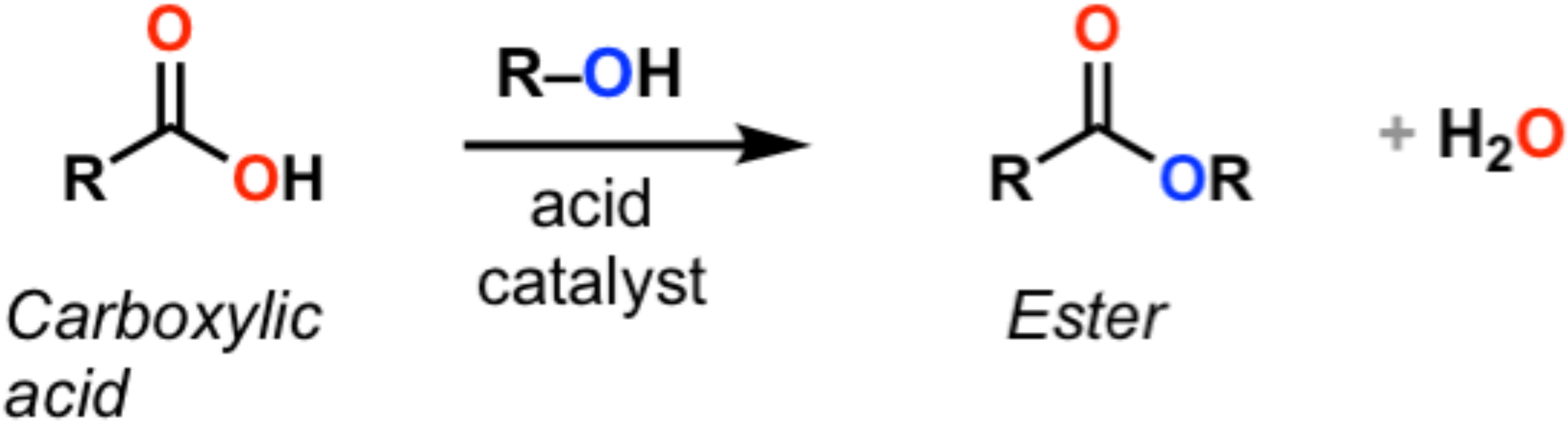
2-methylpropan-2-ol

no reaction



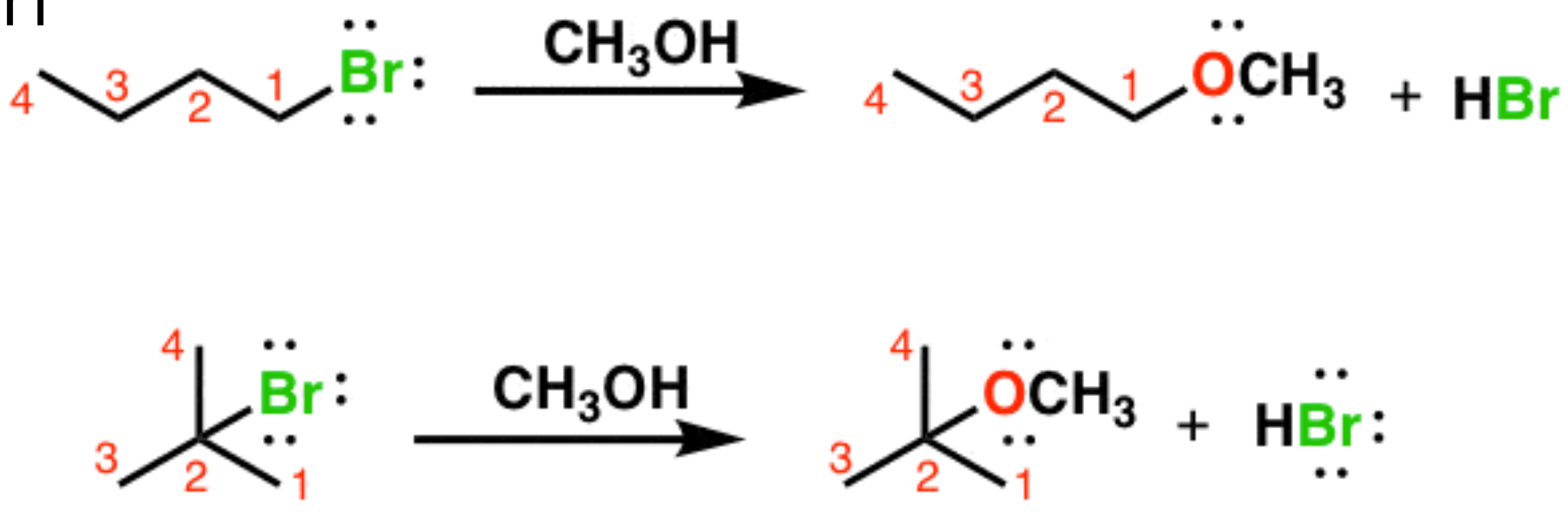
Esterification

- Carboxylic acids and alcohols **condense** to form esters



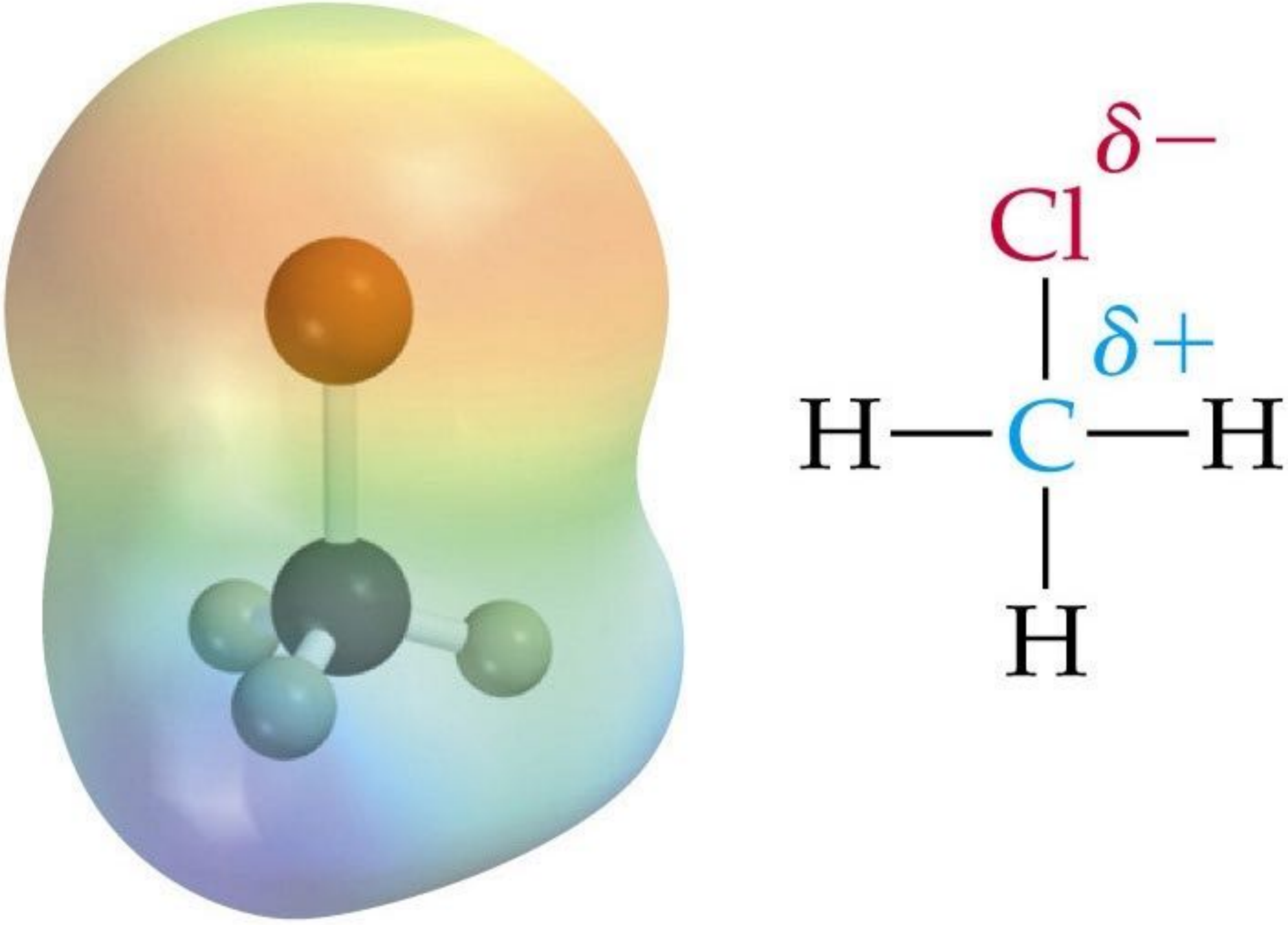
Halogenoalkanes - (nucleophilic substitution)

- Saturated, polar molecules
- the carbon in this molecule is considered “electron poor”
- ***nucleophile*** - reactants that are **<u>electron rich</u>** and are attracted to regions of electron deficiency
- leads to a reaction where the substitution of the halogen occurs
- called Nucleophilic Substitution
  - shorthand - S_N



*rate depends on concentration of alkyl halide **and** CH_3OH*

*rate depends on concentration of alkyl halide **only***



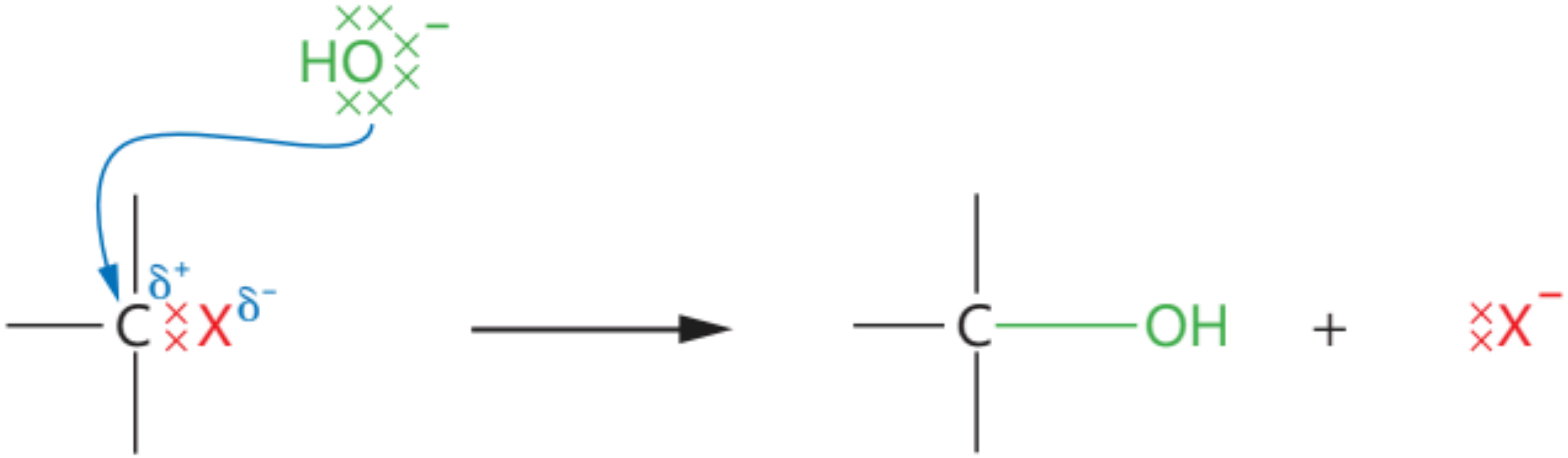
Chloromethane, CH_3Cl
(electron-poor carbon)

20.1 Types of Organic Reactions

- Nucleophilic Substitution Reactions
- Electrophilic Addition Reactions
- Electrophilic Substitution Reactions
- Reduction Reactions

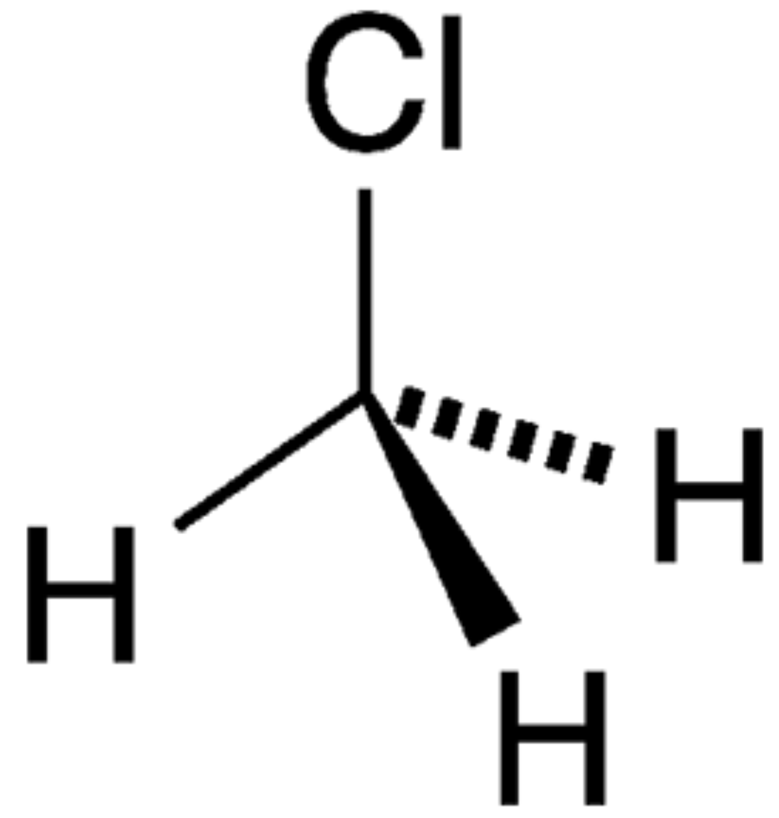
Nucleophilic Substitution Reactions - Halogenoalkanes

- Exact mechanism depends on whether we have a 1°, 2° or 3° halogenoalkane
- Typical reactions are with aqueous sodium hydroxide (NaOH) to produce alcohols.
- Can be done with water but the reaction happens more slowly (*water isn't as good a nucleophile*)



$R{-}X$	+	OH^-	→	$R\text{-}OH$	+	X^-
halogenoalkane		nucleophile		substituted product		leaving group, halide ion

Primary Halogenoalkanes - S_N2 Mechanism

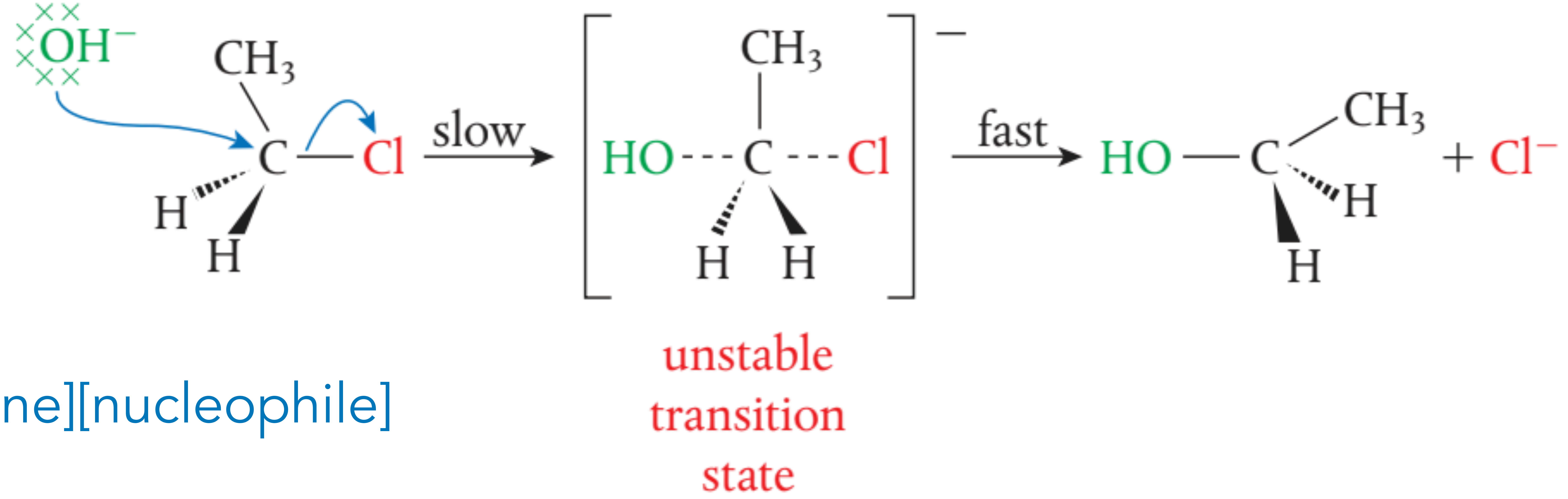


- Overall reaction occurs with NaOH:

$CH_3Cl + OH^- \longrightarrow CH_3OH + Cl^-$

- Since hydrogen atoms are small, there are no “blockers” for the carbon to defend itself

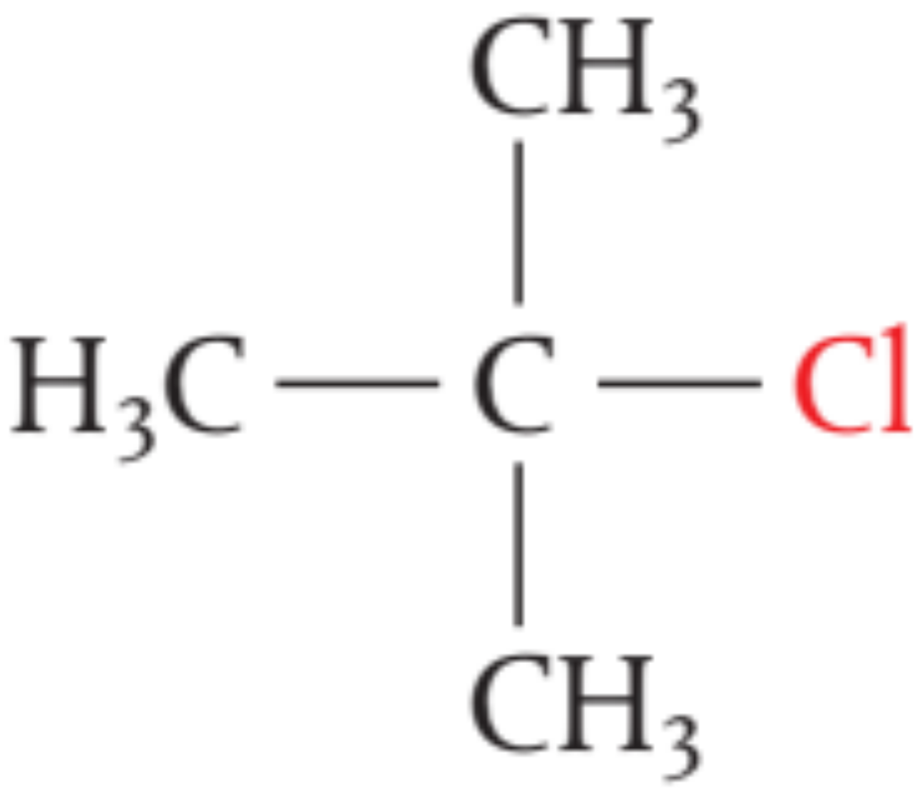
- Use polar aprotic (*no protons*) solvents (acetonitrile, acetone, toluene)

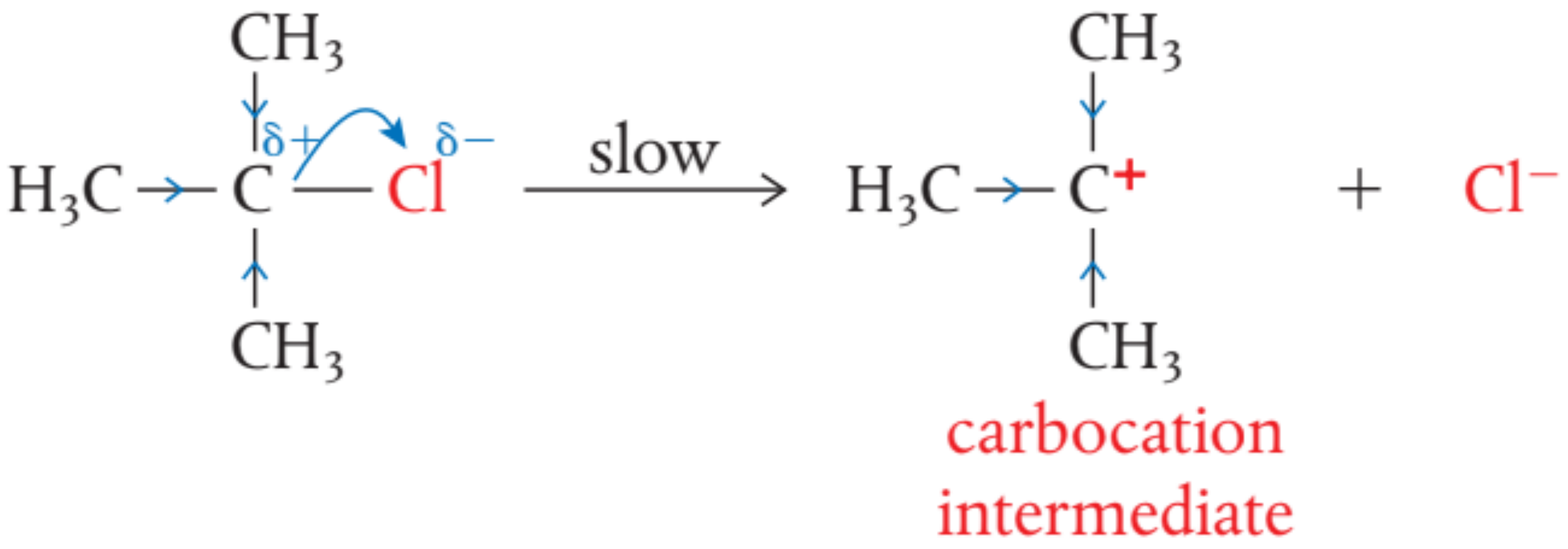


rate = k[halogenoalkane][nucleophile]

Tertiary Halogenoalkane: S_N1 Mechanism

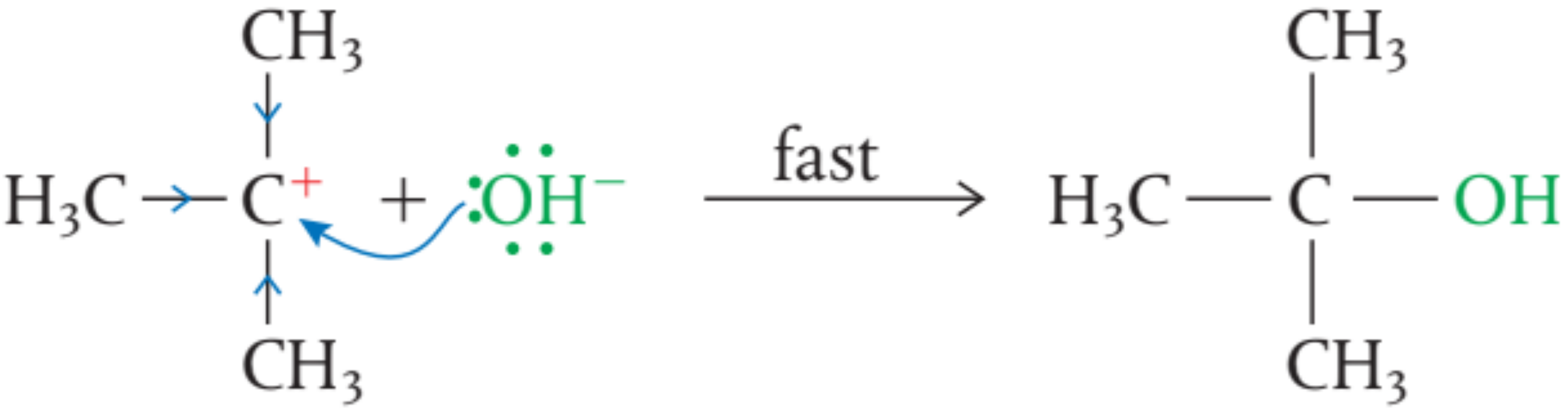
- The presence of 3 alkyl groups…what is happening?





rate = k[halogenoalkane]

carbocation is stabilized by a **positive inductive effect**.



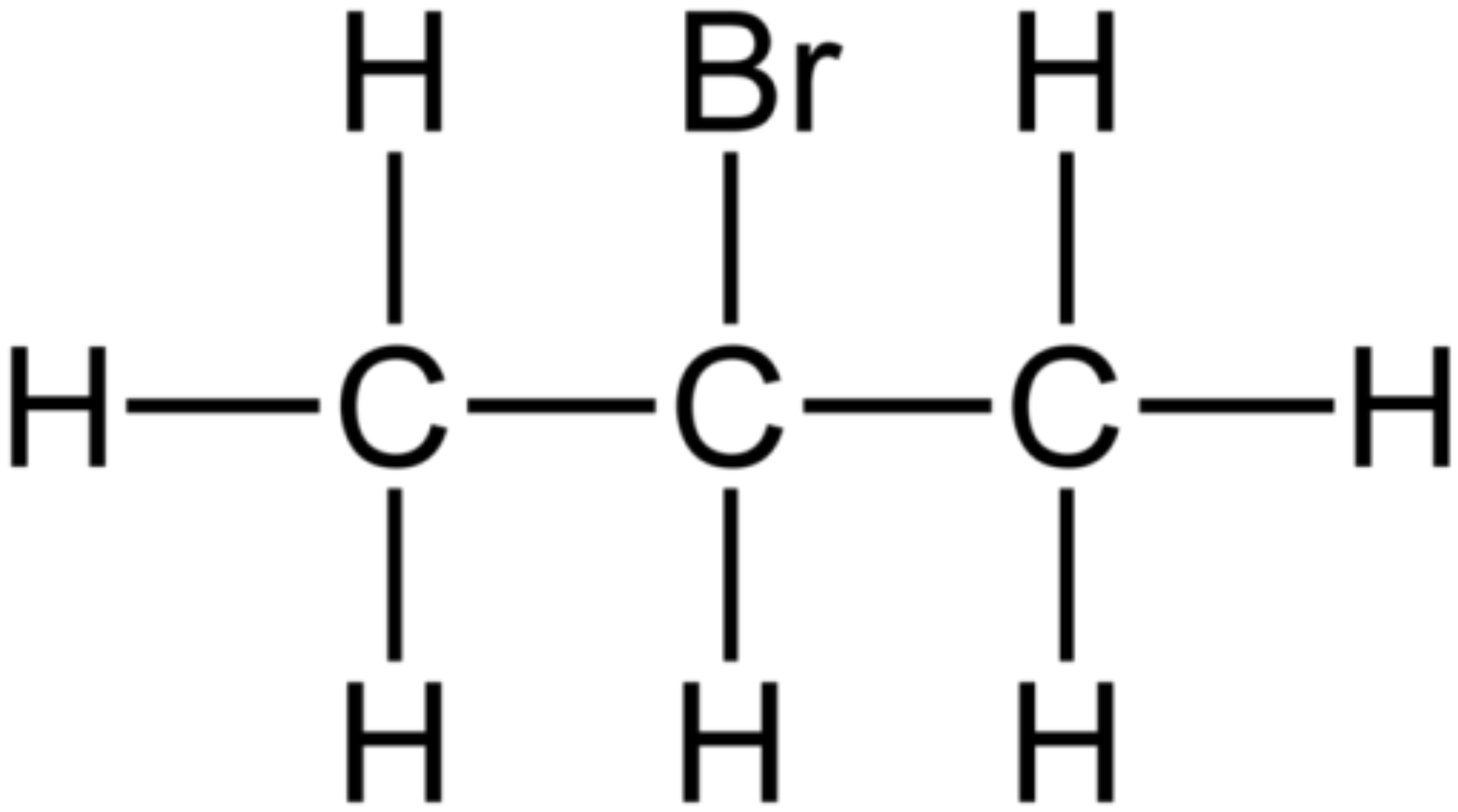
This is called **steric hindrance** - bulky carbon atoms make it difficult for an incoming group to attack the carbon atom

Secondary Halogenoalkanes?

- Do 2° halogenoalkanes undergo an S_N1 or S_N2 mechanism ?

YES!

- Experimental evidence shows they undergo a mixture of both mechanisms.



Nucleophilic Substitution Reactions

- Organic Reactions are very **slow**
  - Rate of reaction is important and studied heavily
    - Experiments show that S_N1 is faster than S_N2 reaction

- Which is the fastest rate of reaction…?
  - (primary, secondary, or tertiary?)

Tertiary > Secondary > Primary

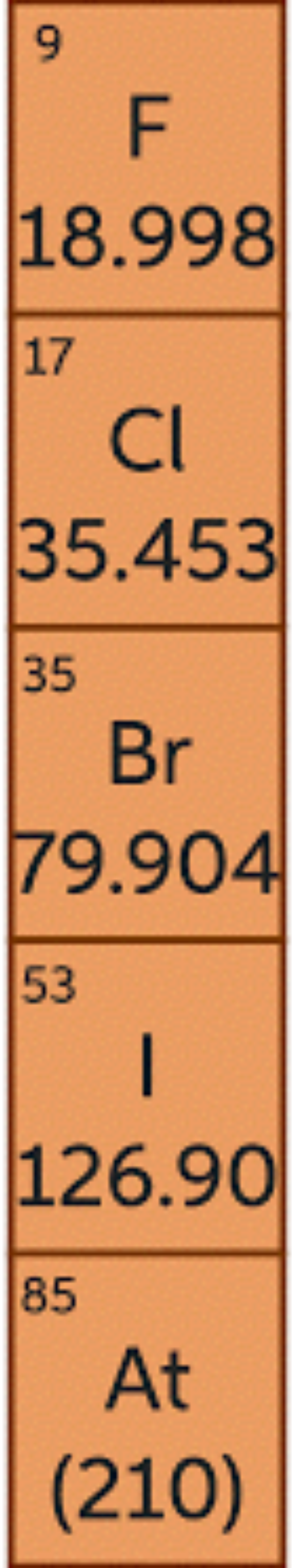
Comparison of Rates of Nucleophilic Substitution Reactions

Tertiary > Secondary > Primary

1. Effect of the mechanism ($S_N1 > S_N2$)
2. Influence of the leaving group (halogen)
   - Polarity of the C-Halogen bond
     - *fluoroalkane > chloroalkane > bromoalkane > iodoalkane*
   - **Strength of the C-Halogen bond**
     - C–F > C–Cl > C–Br > ***C–I (fastest)***

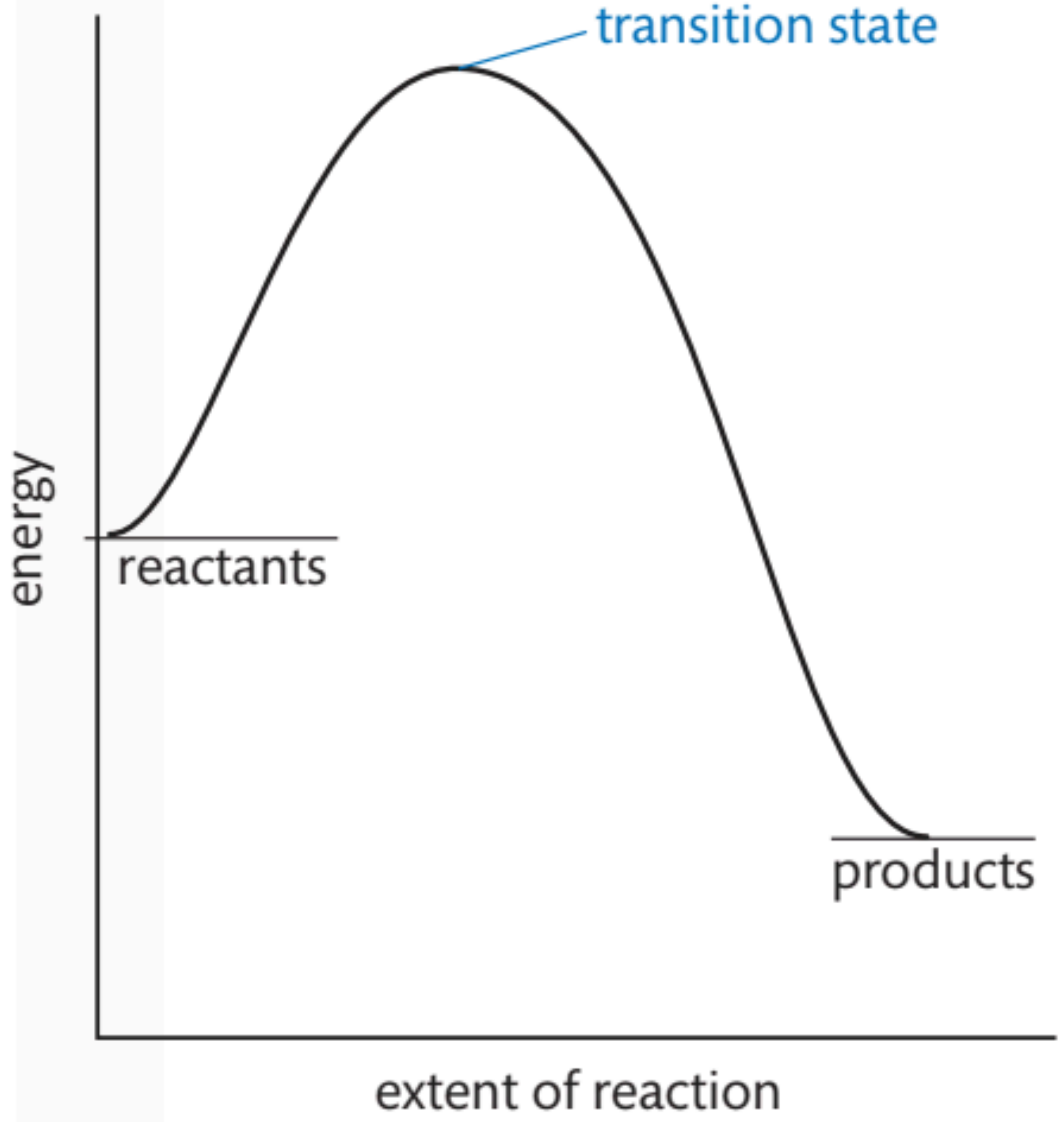
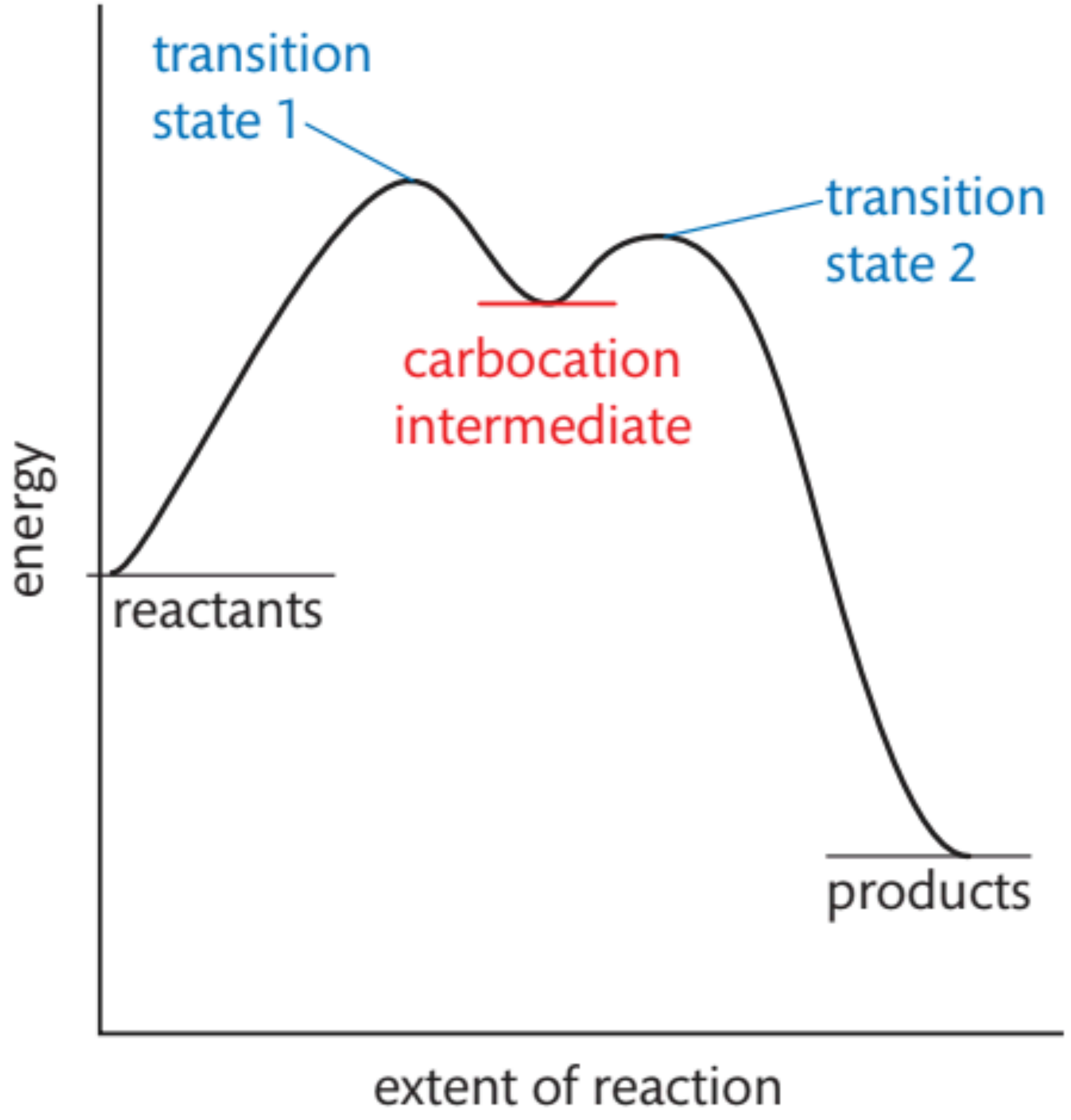
Nucleophilic Substitution Reactions

- Polarity - electronegativity decreases down a group (from F to Cl to Br to I)
  - Carbon is less and less electron deficient - less vulnerable to nucleophilic attack
- Strength - as bond strength decreases down the group, the breakage of this bond is easier (iodoalkane is the most reactive, fluorine is the least)



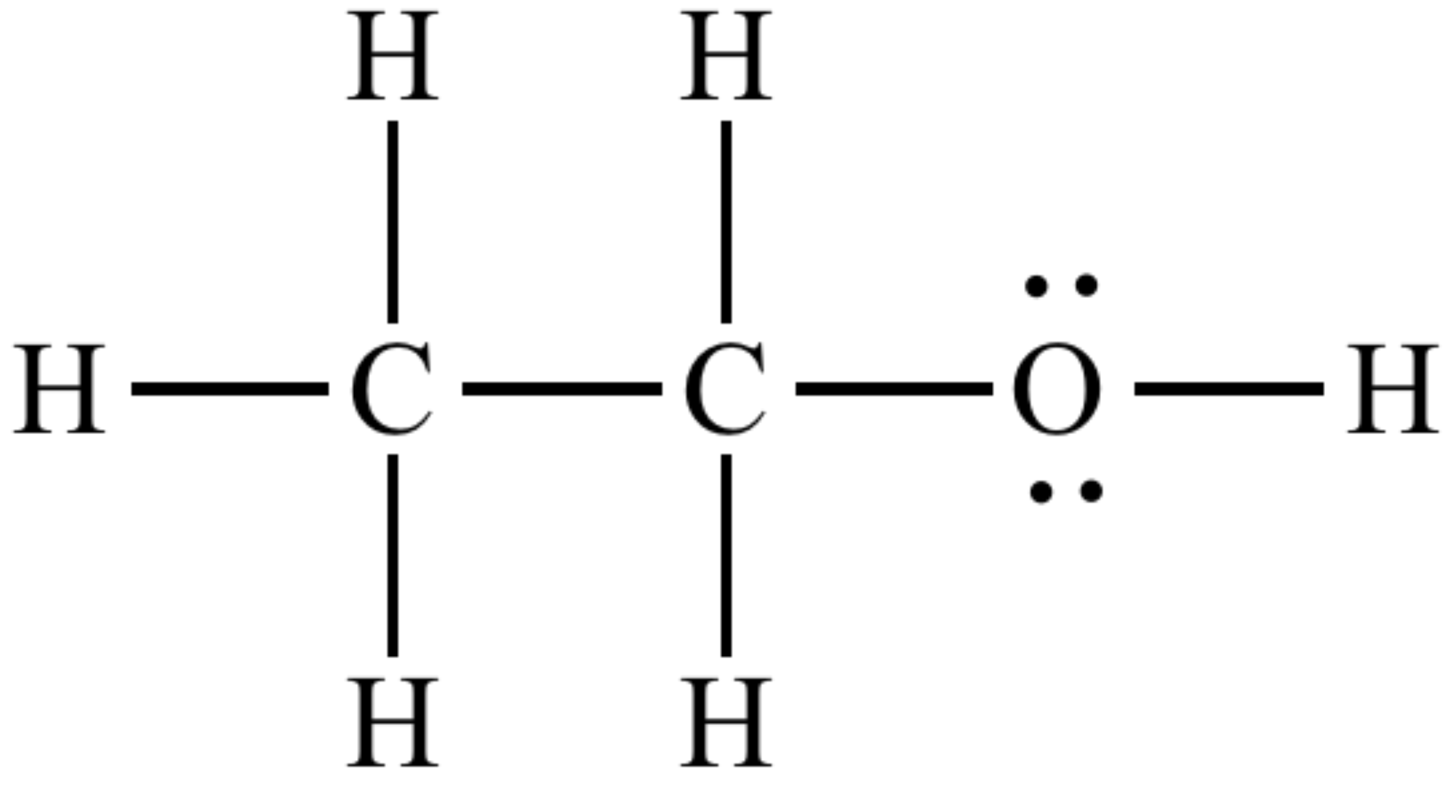
Nucleophilic Substitution Reactions

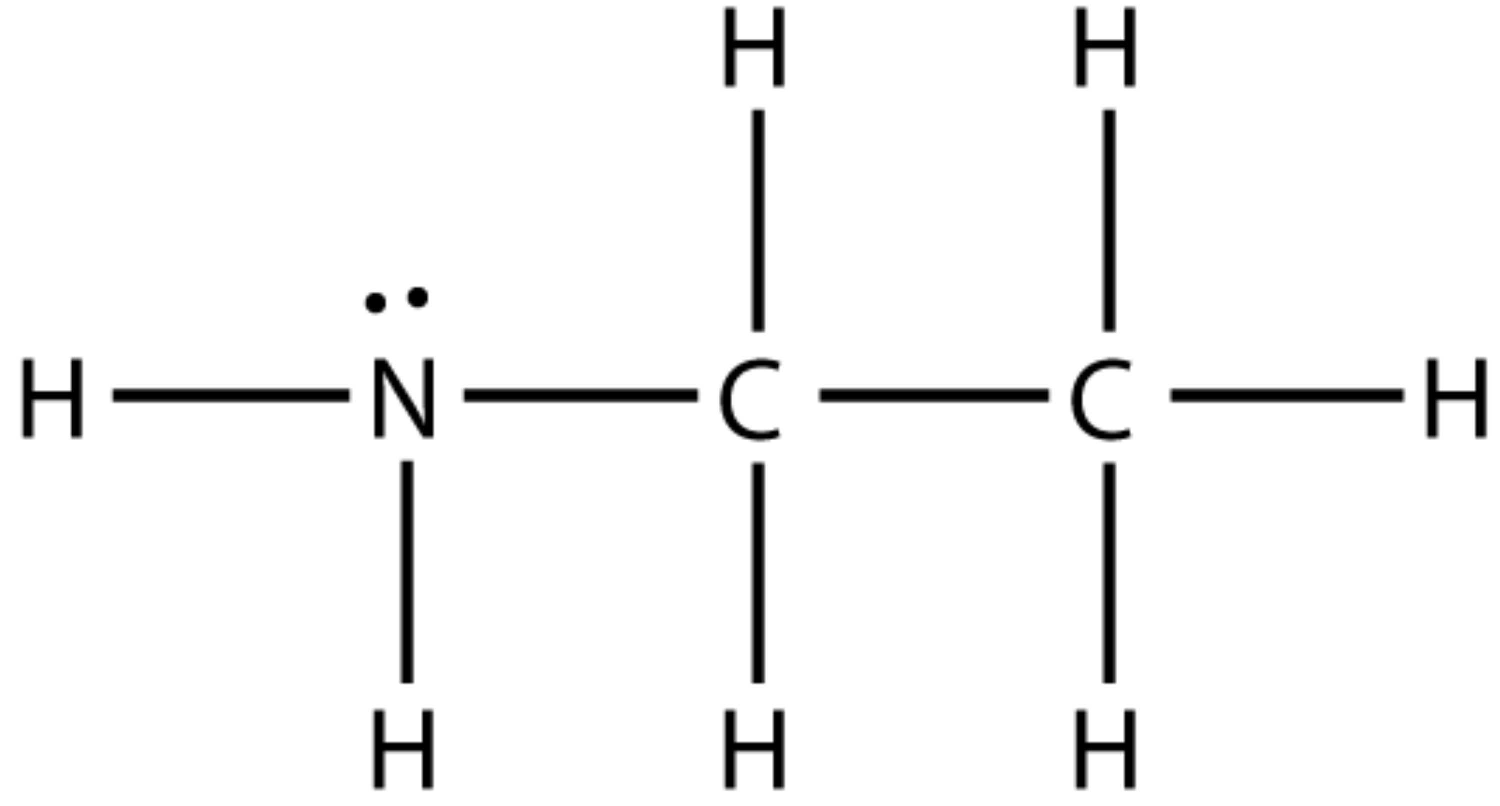
- Based on the reaction data:
  - **Strength is more important**
- Relative rate of reaction
  - iodoalkanes > bromoalkanes > chloroalkanes > fluoroalkanes

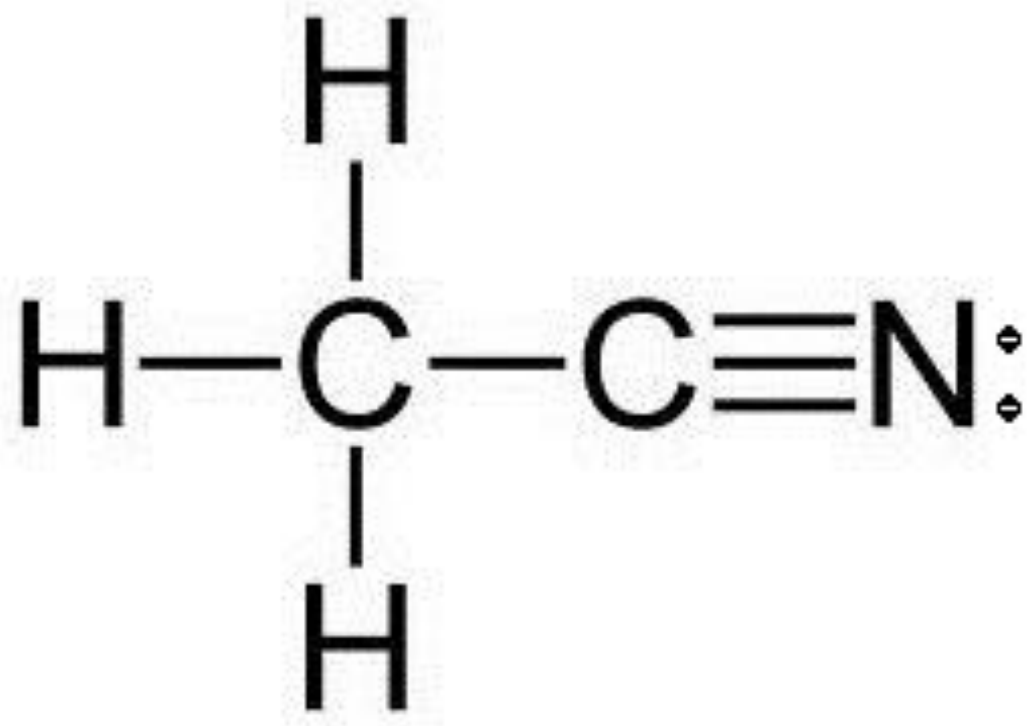
	S_N2	S_N1
Favoured by	primary halogenoalkanes	tertiary halogenoalkanes
Nature of mechanism	concerted one-step mechanism with unstable transition state	two-step reaction via carbocation intermediate
Relative rate	lower	higher
Favoured solvent	polar, aprotic	polar, protic
Reaction profile		

Nucleophilic Substitution Reactions

- These reactions are vital to many organic reactions
- Allow for different synthetic reagents to be used
- Conversions from halides to:
  - Alcohol
  - Amine
  - Nitrile



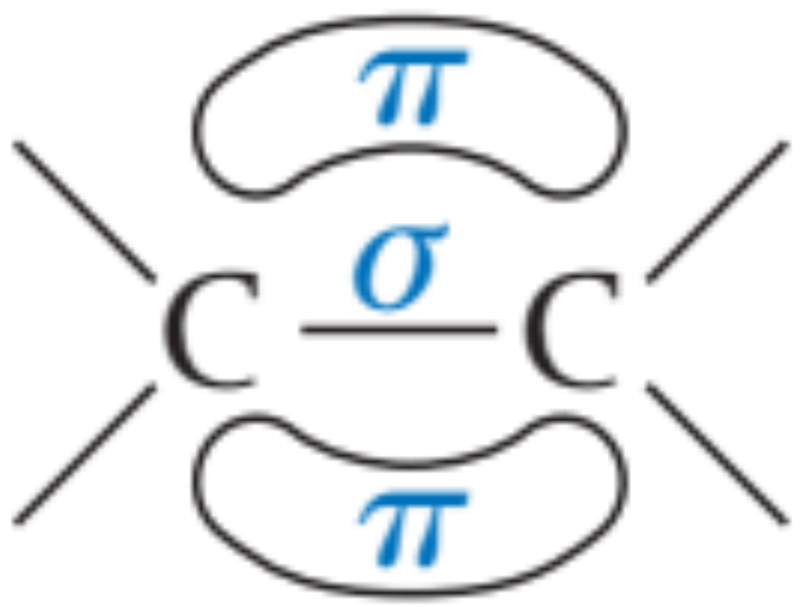




Conversion into Alcohol

- Bromoethane and NaOH → ethanol and NaBr
  - Class of alcohol produced will match class of halide used in reaction
- This will work with water, but is better with a base (OH^-).

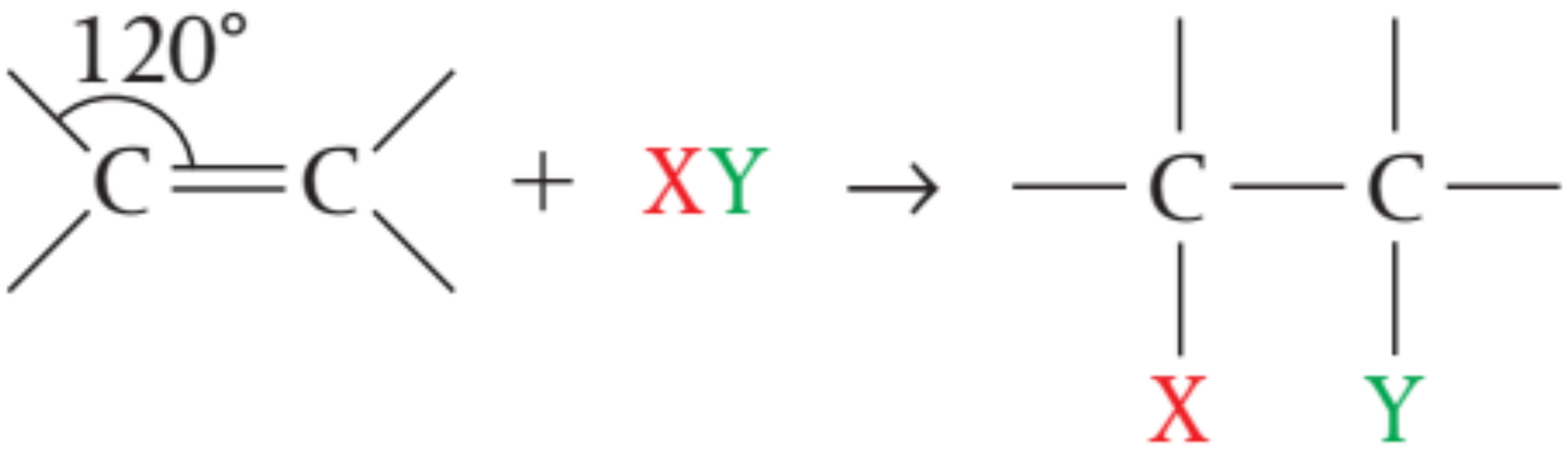
Electrophilic Addition: alkenes



- sp^2 hybridized carbons (120˚ bond angle) result in an open structure - easy for groups to attack.

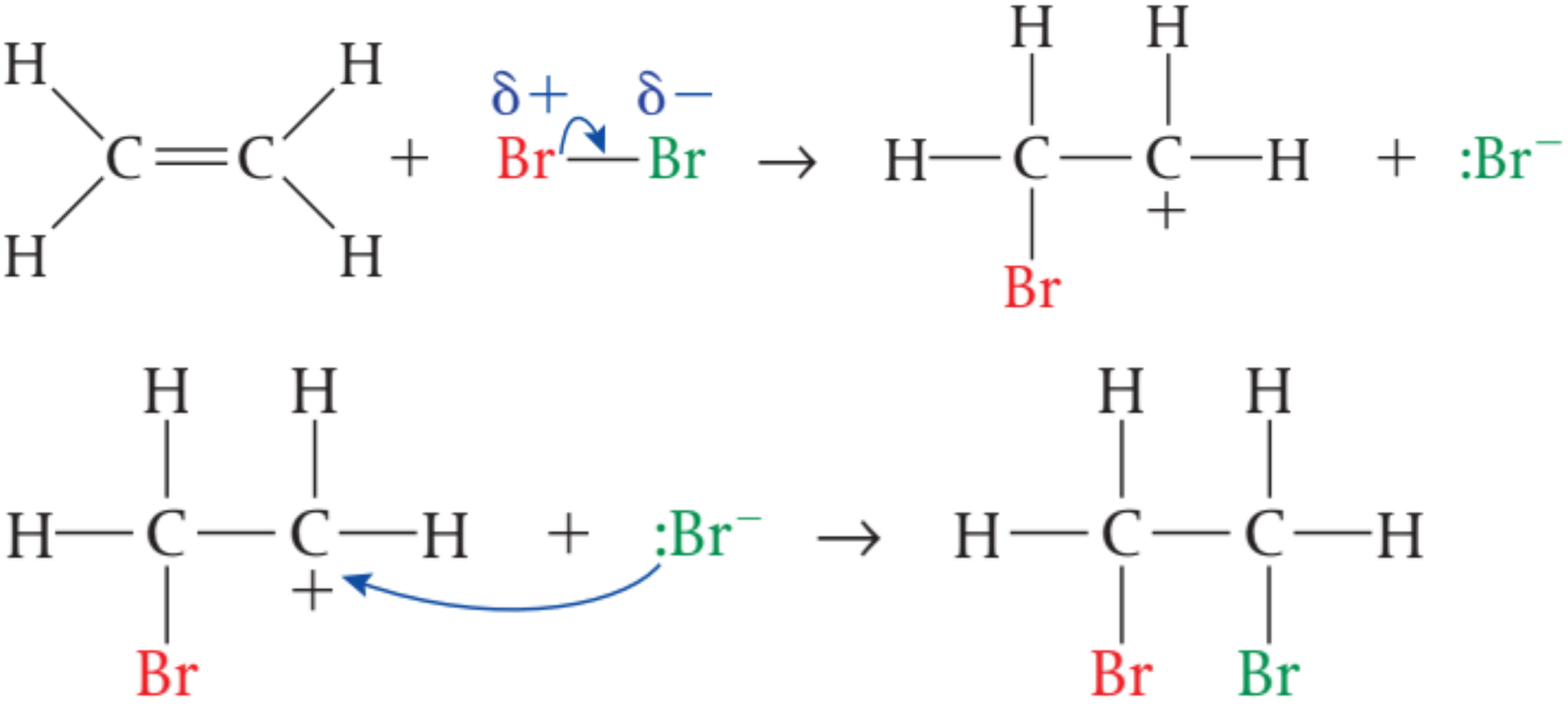
- The pi (π) bond has electron *density above and below*. Weaker bond (less closely associated with nucleus).

- The pi (π) bonds are attractive to **electrophiles** (species either electron deficient or that become electron deficient in the presence of a pi bond).



Electrophilic Addition: alkenes

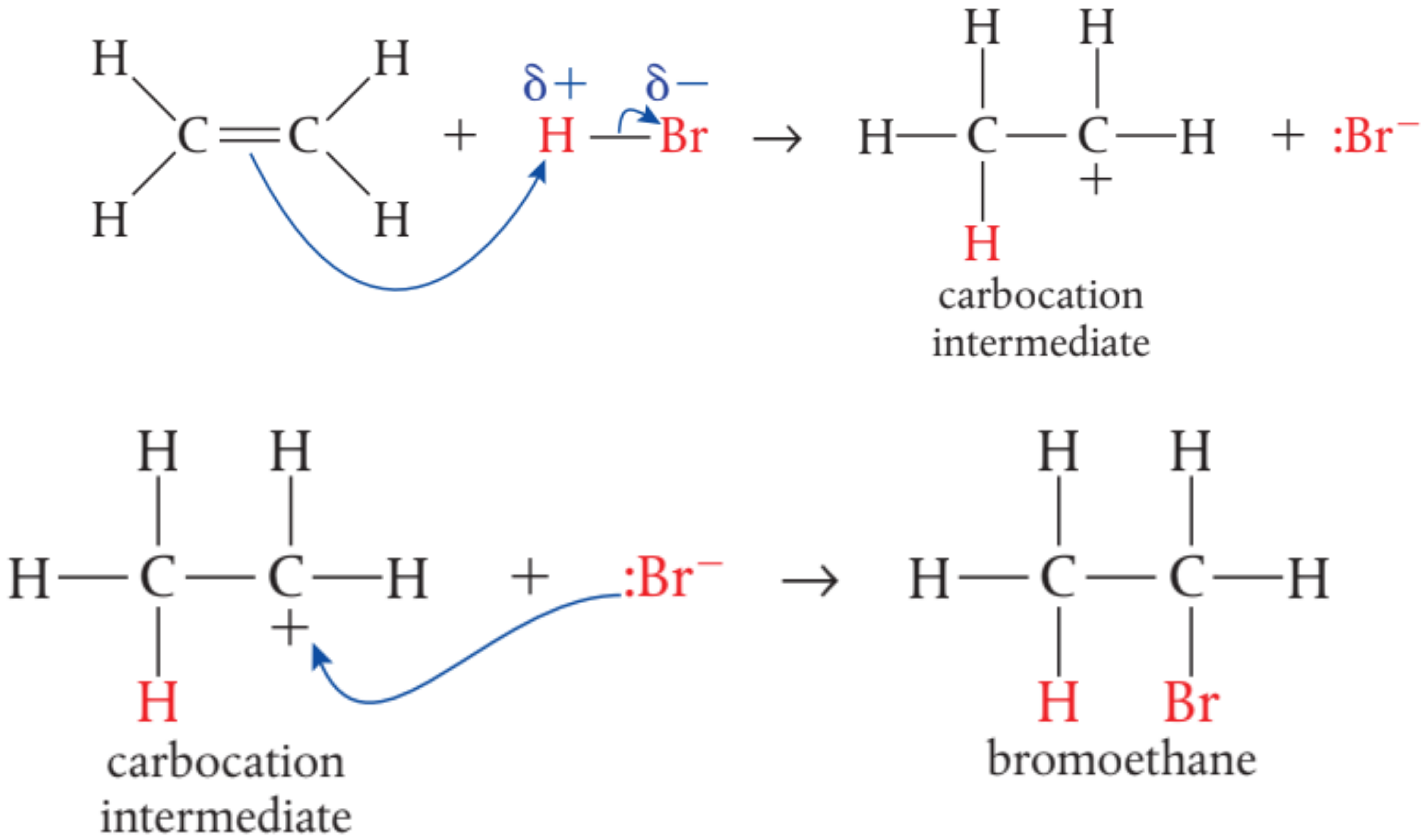
- Ethene + bromine



1,2-dibromoethane

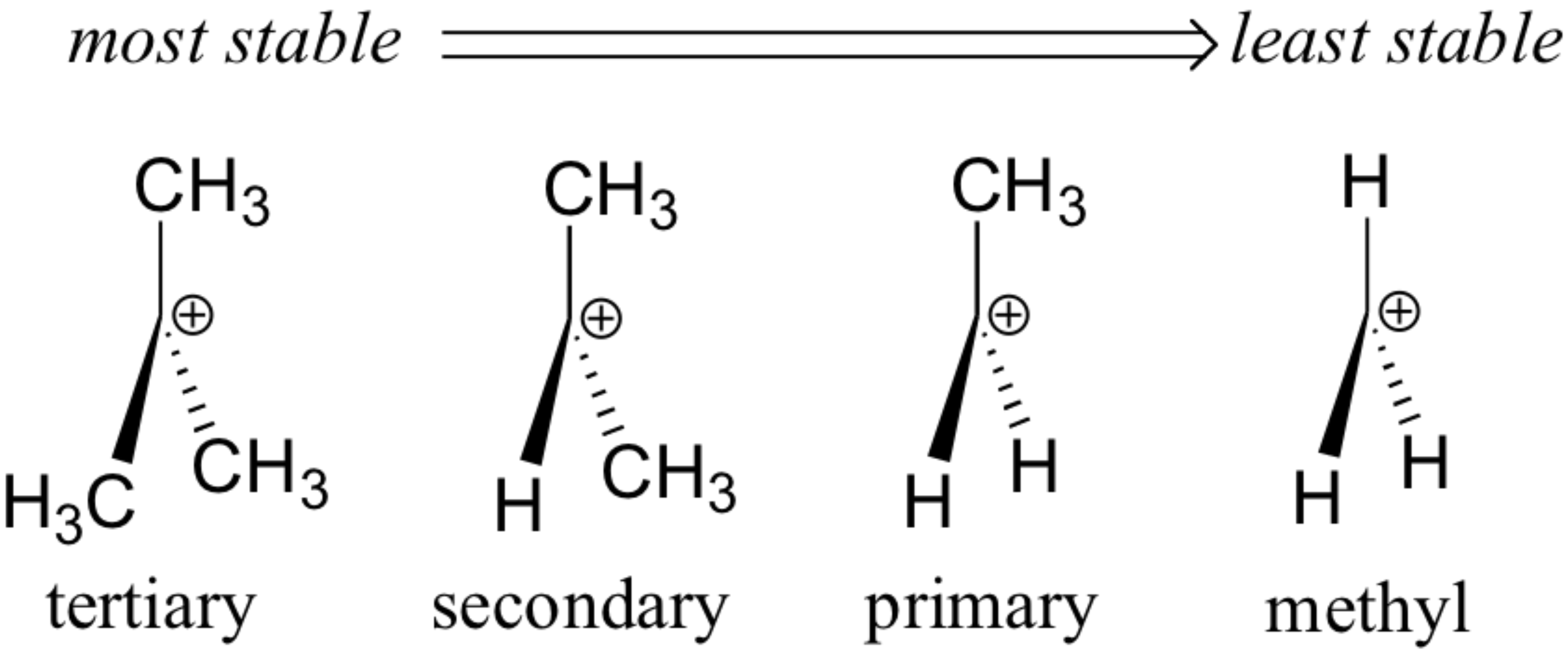
Electrophilic Addition: alkenes

- Ethene + hydrogen bromide



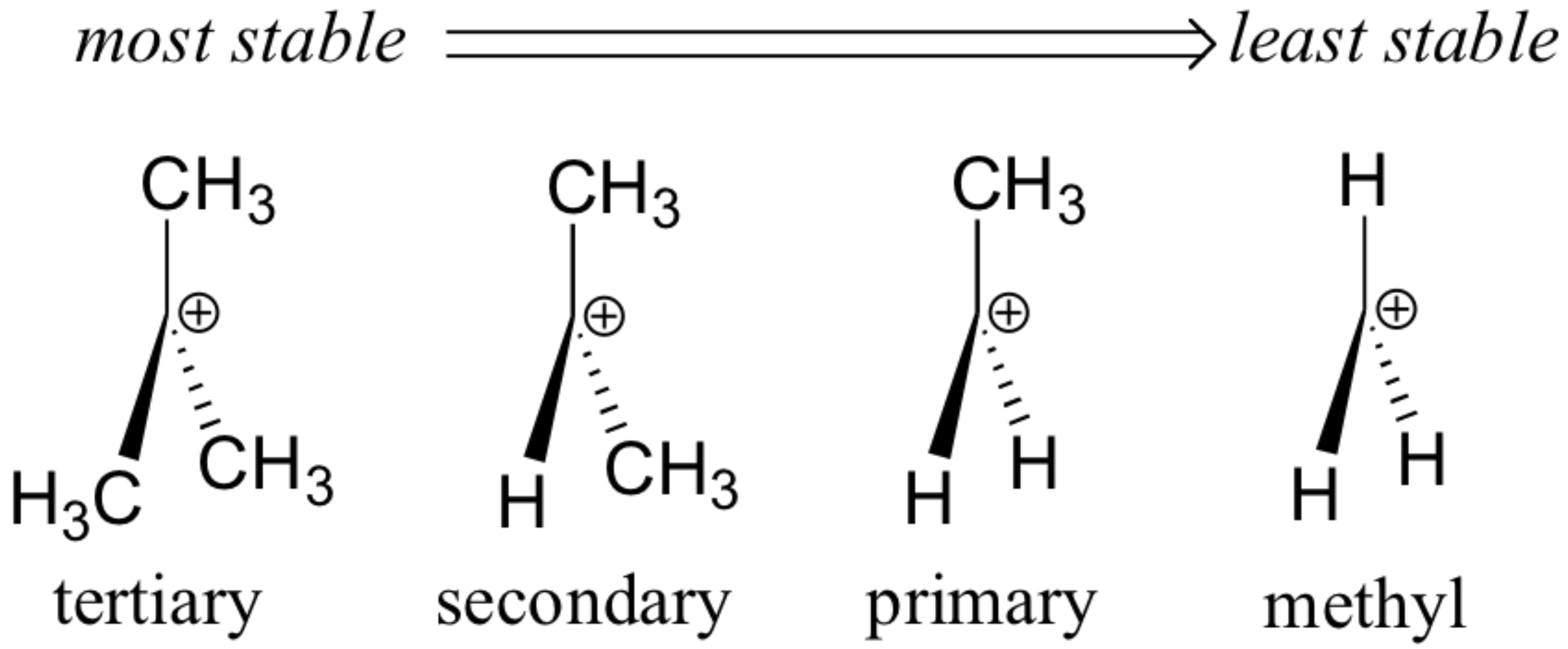
Electrophilic Addition: alkenes

- Propene + hydrogen bromide (asymmetric addition)
  - **Markovnikov's rule (STABILITY)**
  - **Positive Inductive Effects (stabilization of carbocations)**



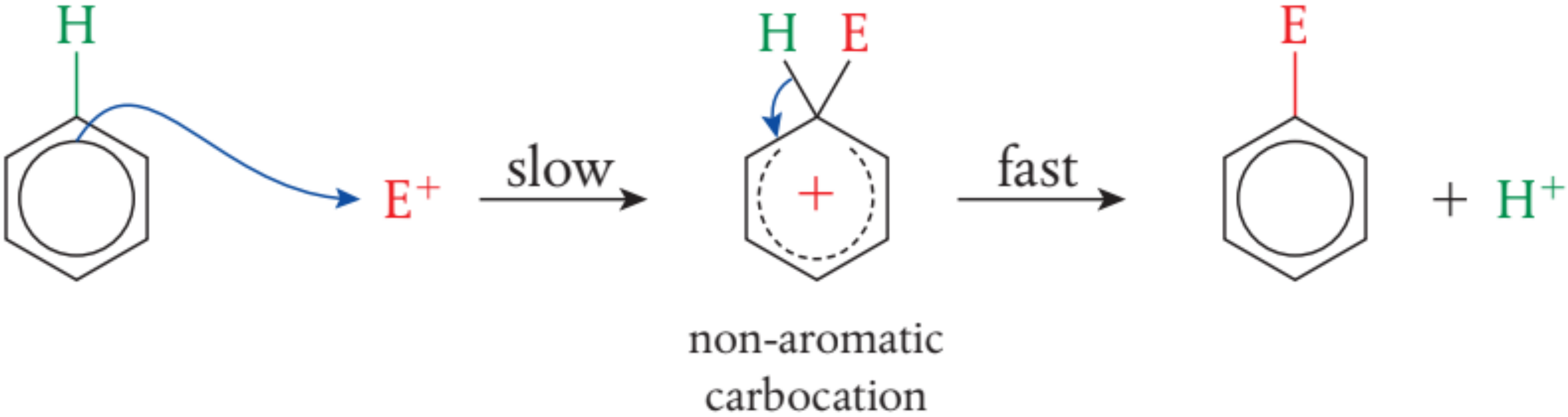
Electrophilic Addition: alkenes (Markovnikov's Rule)

- Propene + hydrogen bromide (asymmetric addition)



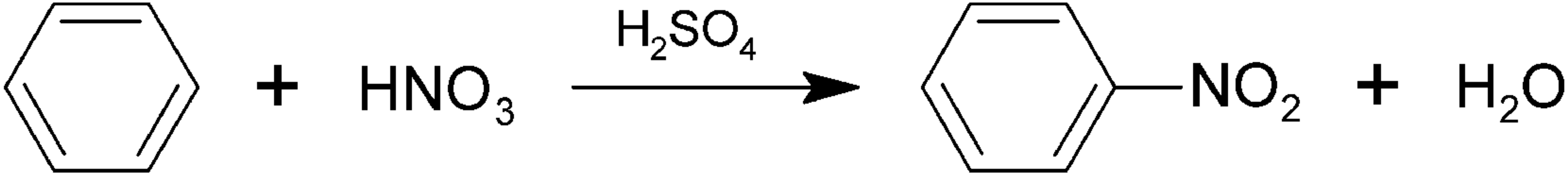
Electrophilic Substitution: benzene

- Benzene attractive to electrophiles.
- High activation energy so slow reaction

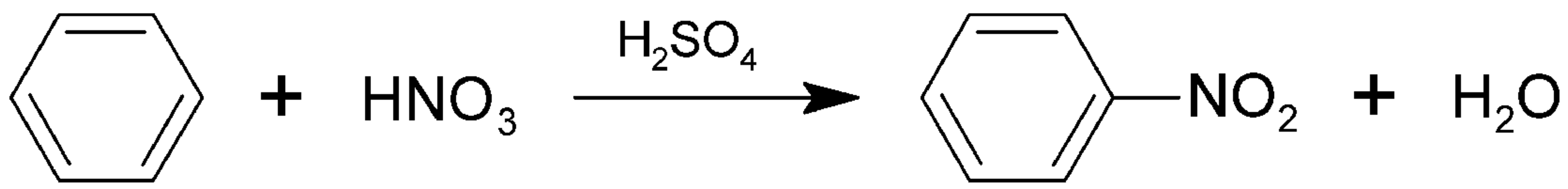


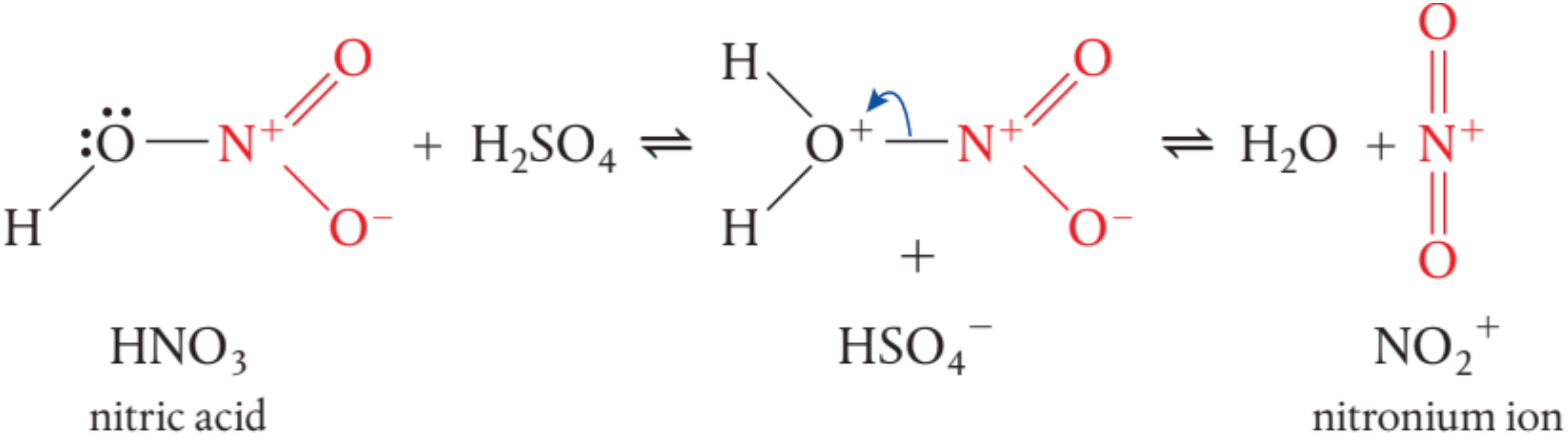
EAS: Nitration of benzene

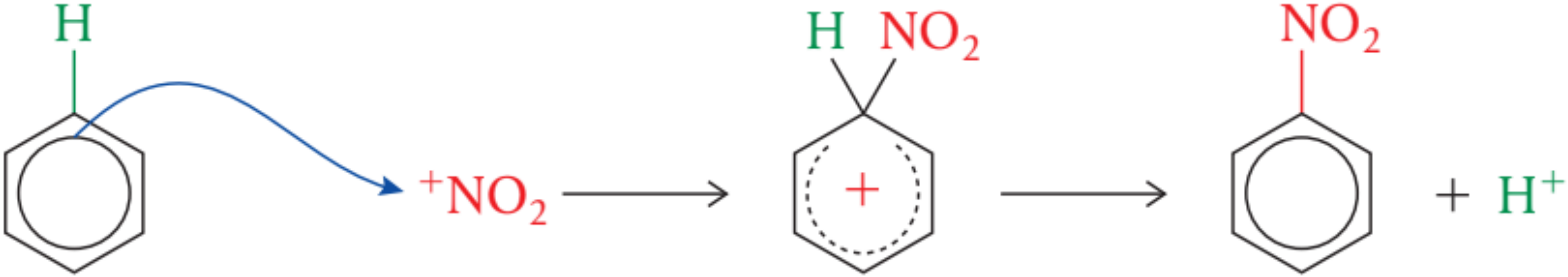
- substitution of –H by –NO_2
- **Nitrating mixture:** conc. HNO_3 and conc. H_2SO_4



EAS: Nitration of benzene







Reduction Reactions

- Oxidation Review
  - Primary alcohol → aldehyde → carboxylic acid
  - Secondary alcohol → ketone
- **Reduction** - reverse the process (2 oxidizing agents)
  1. Sodium borohydride ($NaBH_4$ in aqueous or alcoholic solution)
  2. Lithium aluminum hydride ($LiAlH_4$ in anhydrous conditions, diethyl ether followed by aqueous acid)

Reduction Reactions

- Reduction of carboxylic acids
  - $NaBH_4$ is the safer reagent, but it's not strong enough to reduce acids so we use $LiAlH_4$ instead.

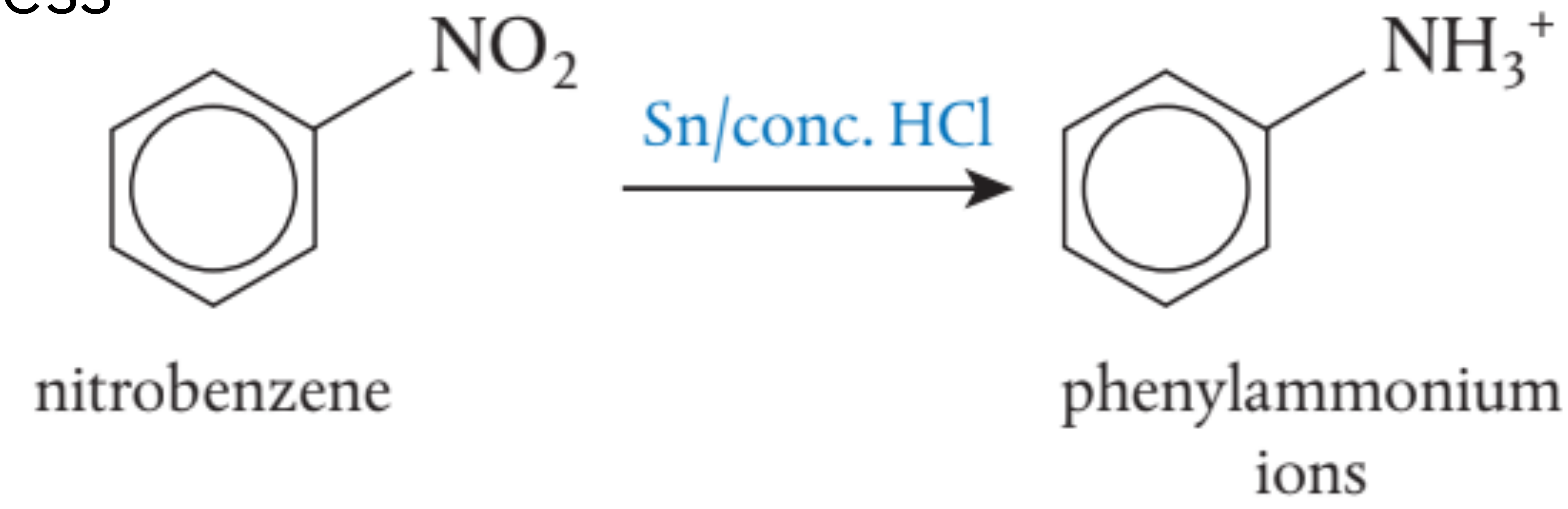
CH_3COOH	$\xrightarrow{[+H]}$	CH_3CHO	$\xrightarrow{[+H]}$	CH_3CH_2OH
ethanoic acid		ethanal		ethanol
carboxylic acid		aldehyde		primary alcohol

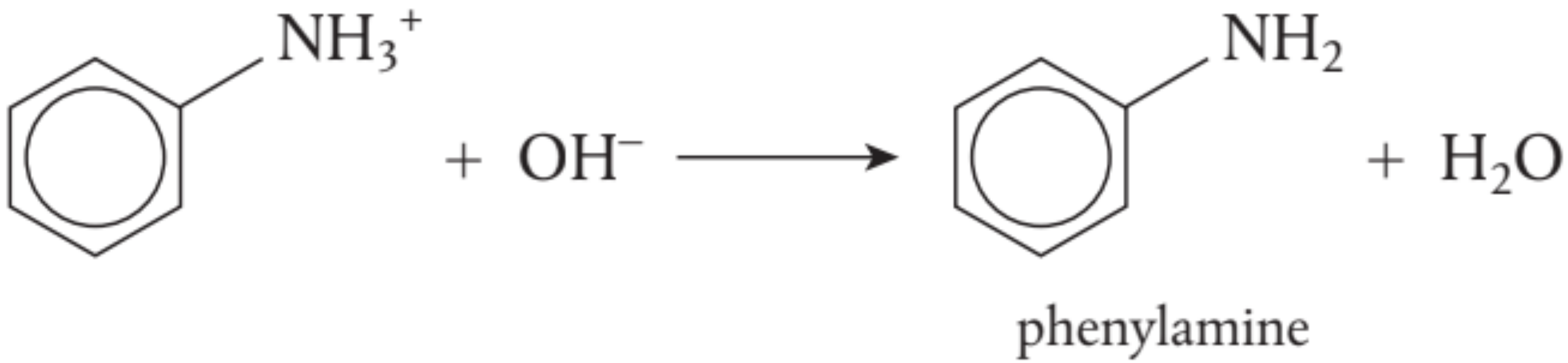
  - <u>Conditions</u>: heat with $LiAlH_4$ in dry ether. The reaction cannot be stopped at the aldehyde as it reacts too readily with $LiAlH_4$.

$(CH_3)_2CO$	$\xrightarrow{[+H]}$	$(CH_3)_2CHOH$
propanone		propan-2-ol
ketone		secondary alcohol

Reduction Reactions

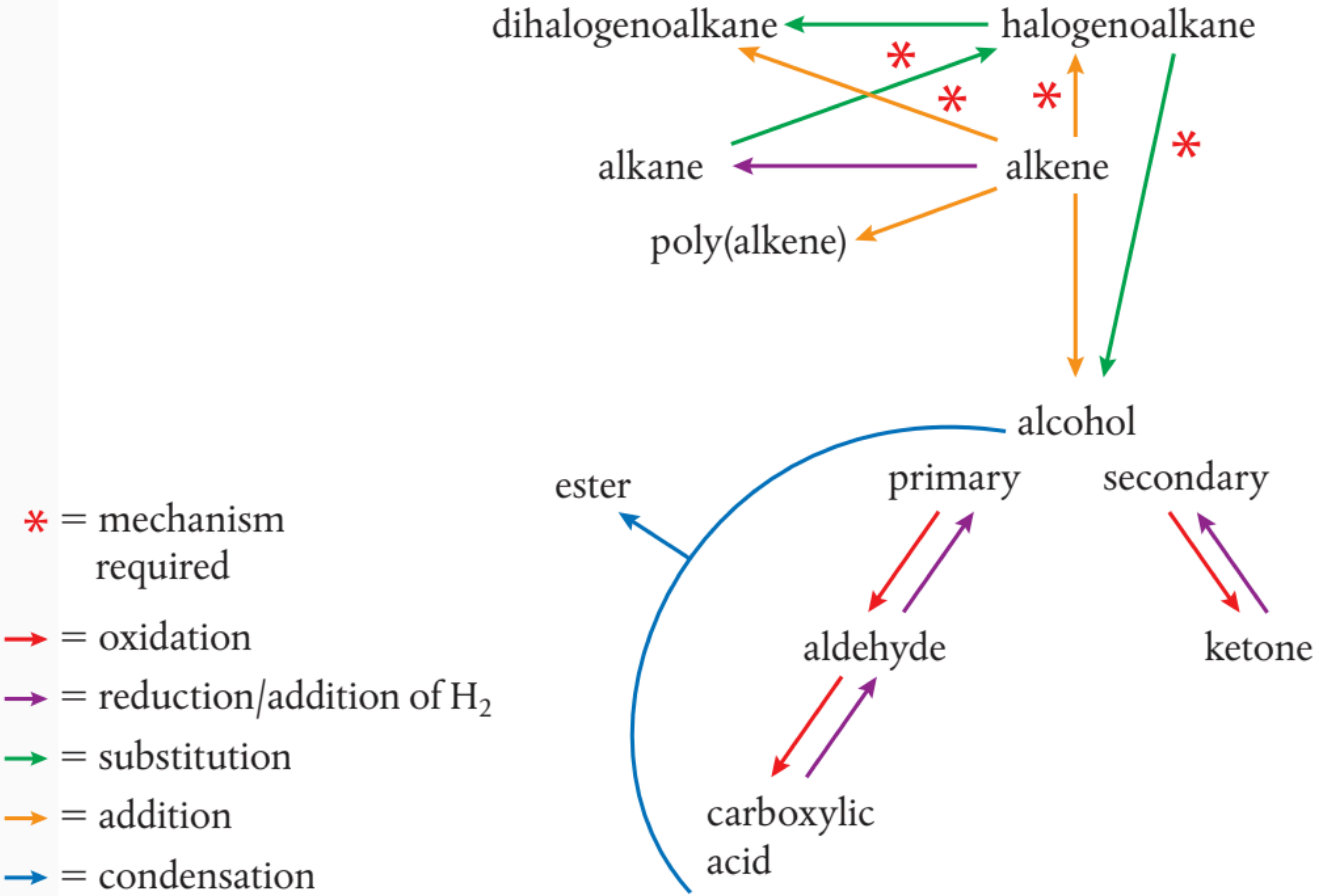
- Reduction of nitrobenzene
  - 2 stage process





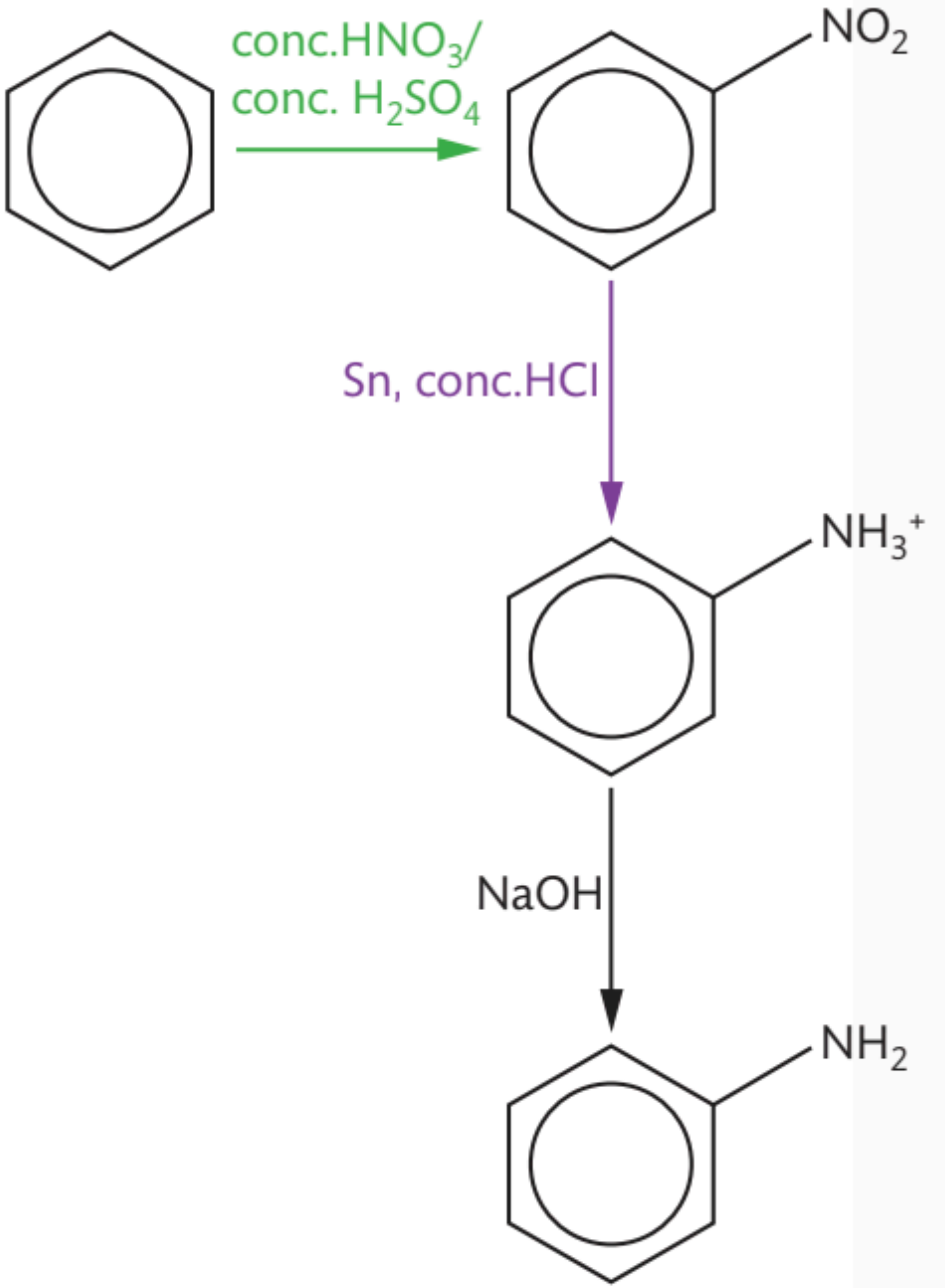
20.2 Synthetic Routes

- Synthesis of an organic compound stems from a readily available starting material via series of discrete steps.
- Functional group interconversions are the basis of such synthetic routes.
- Retro-synthesis of organic compounds (reverse reactions)


dihalogenoalkane
halogenoalkane
alkane
alkene
poly(alkene)
alcohol
primary
secondary
ester
aldehyde
ketone
carboxylic acid
* = mechanism required
→ = oxidation
→ = reduction/addition of H_2
→ = substitution
→ = addition
→ = condensation

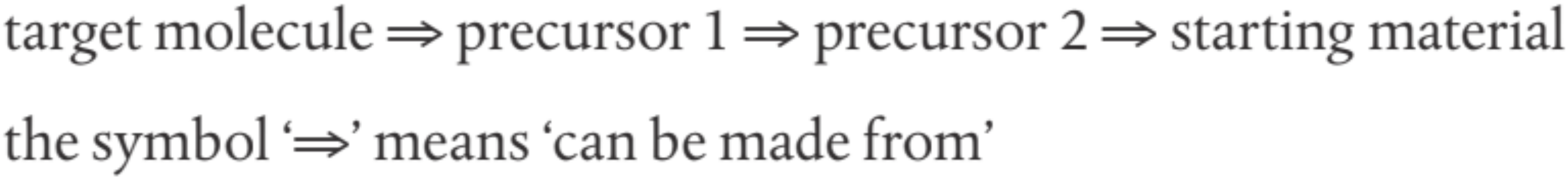
Synthetic Route

Nitration of Benzene



Retro-synthesis - working backwards

- Target molecules (E.J. Corey, MIT, 1990 Nobel Prize winner)
- Work backwards to starting materials (precursors)



target molecule ⇒ precursor 1 ⇒ precursor 2 ⇒ starting material

the symbol '⇒' means 'can be made from'

target molecule ⇒ precursor 1 ⇒ precursor 2 ⇒ starting material

the symbol '⇒' means 'can be made from'

EXAMPLE: You are required to make butanone starting from any alkene of your choice. Show the steps involved in retro-synthesis to determine the identity of the alkene.

20.3 Stereoisomerism

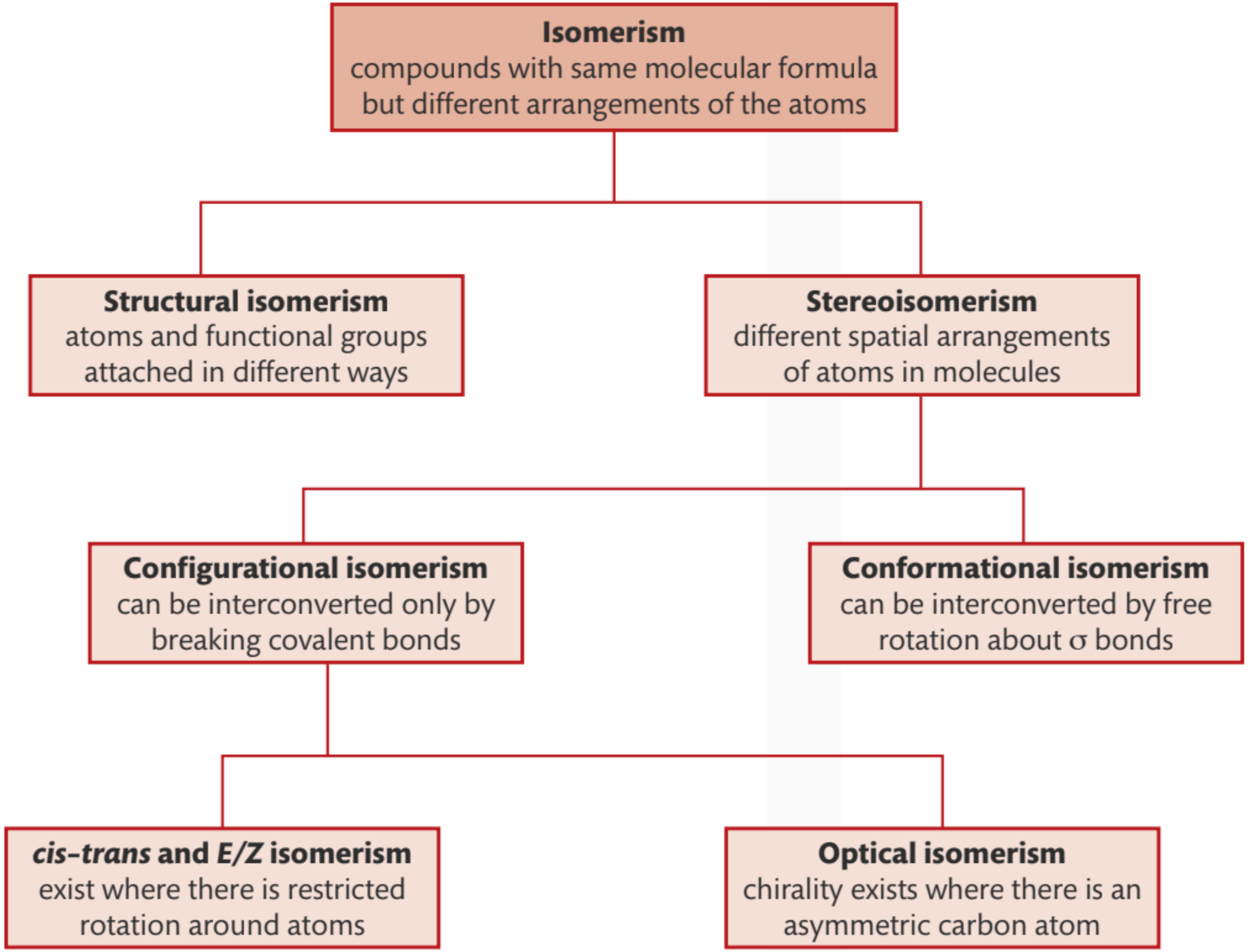
- Stereoisomers
- Configurational Isomers
- Cis-trans Isomers (and E/Z isomers)
- Chiral Carbons
- Optical Activity
- Enantiomers
- Racemic Mixtures

Stereoisomers

- Stereoisomers are subdivided

1. Conformational isomers - interconversion by rotation about a σ bond
2. Configurational isomers - breaking and reforming a bond.
   - cis-trans and E/Z
   - Optical isomer - *chirality*

Build: 2-butene



Isomerism
compounds with same molecular formula but different arrangements of the atoms

Structural isomerism
atoms and functional groups attached in different ways

Stereoisomerism
different spatial arrangements of atoms in molecules

Configurational isomerism
can be interconverted only by breaking covalent bonds

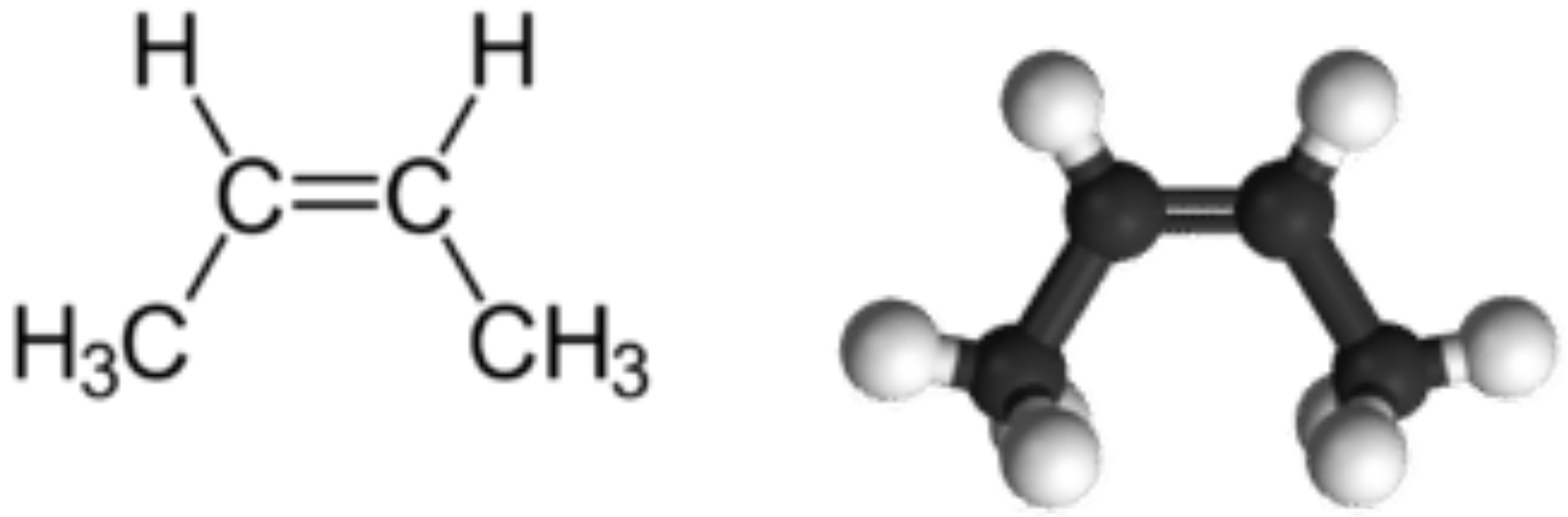
Conformational isomerism
can be interconverted by free rotation about σ bonds

***cis–trans* and *E/Z* isomerism**
exist where there is restricted rotation around atoms

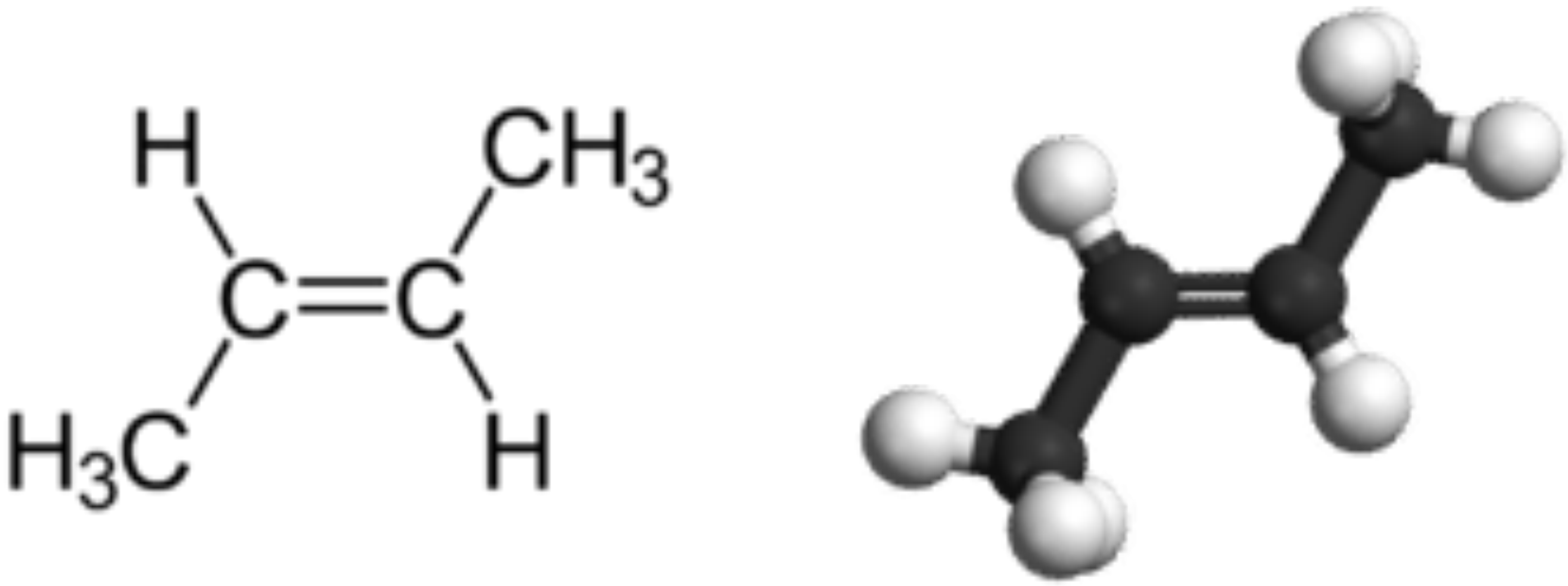
Optical isomerism
chirality exists where there is an asymmetric carbon atom

Build: 2-butene

cis-2-butene

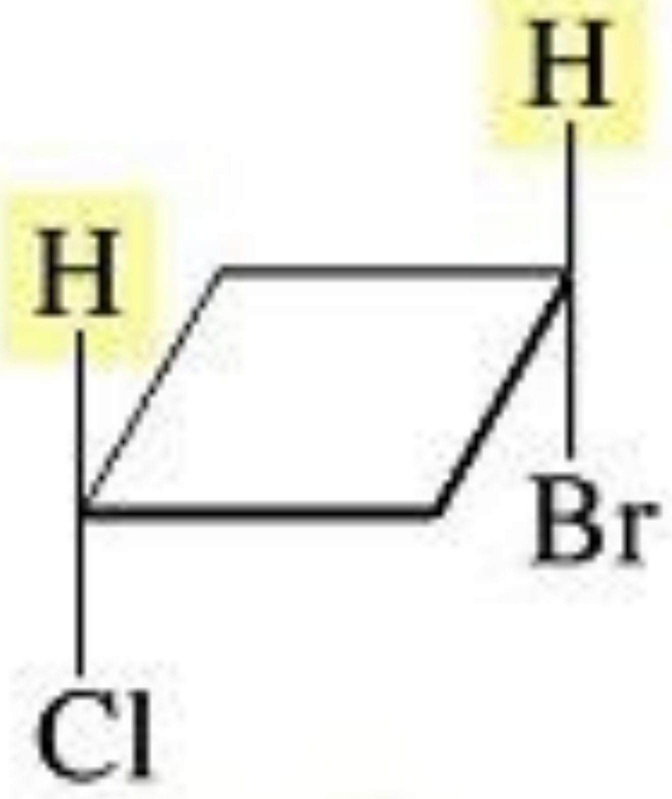


trans-2-butene

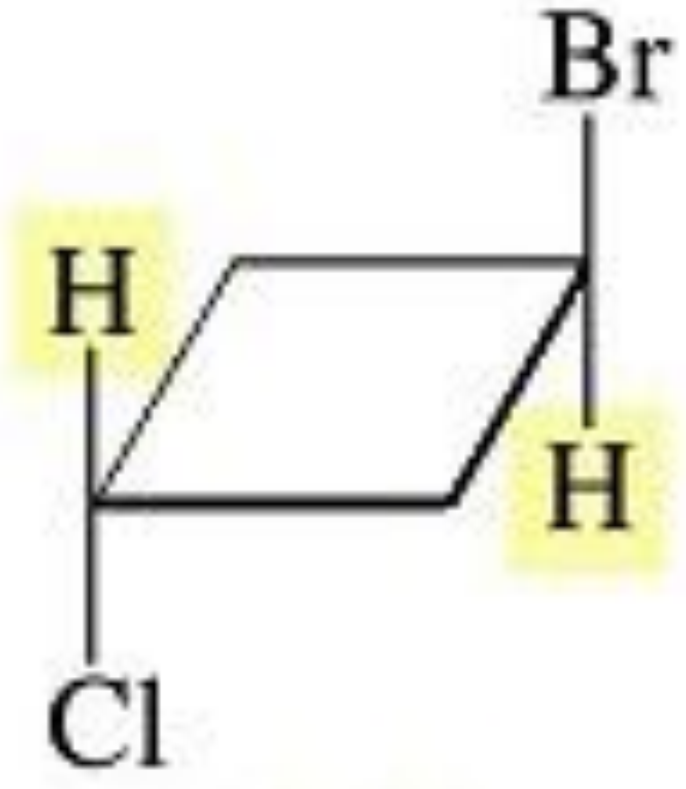


Cyclic molecules

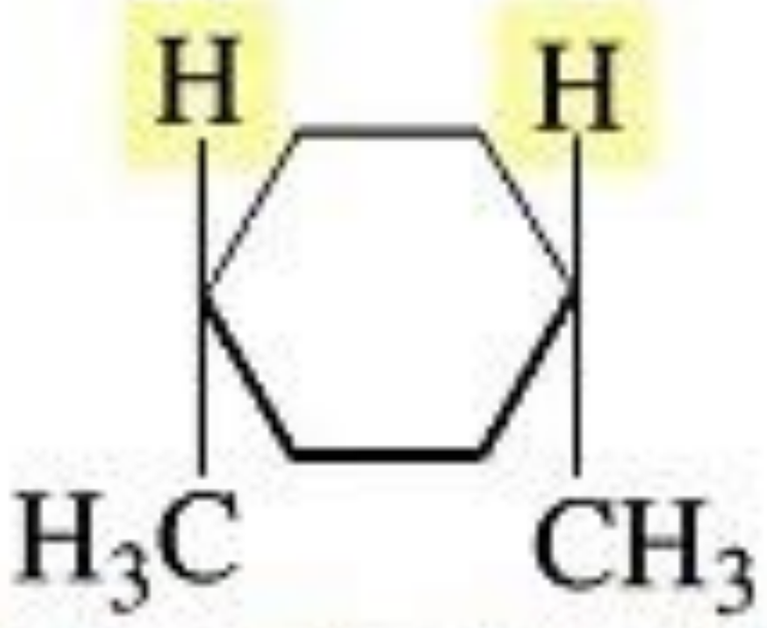
- Ring of carbon atoms which prevent rotation
- Textbook gives several examples (p. 517)



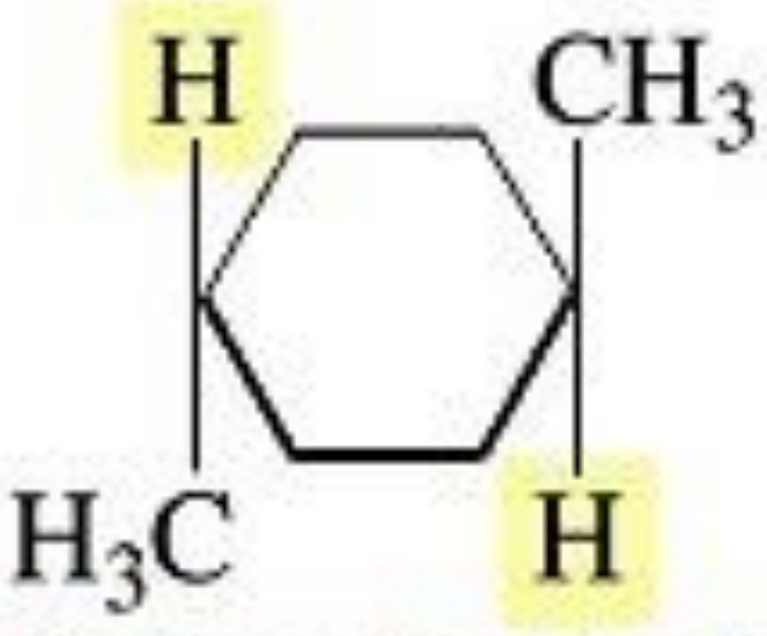
cis-1-bromo-3-chlorocyclobutane



trans-1-bromo-3-chlorocyclobutane



cis-1,4-dimethylcyclohexane



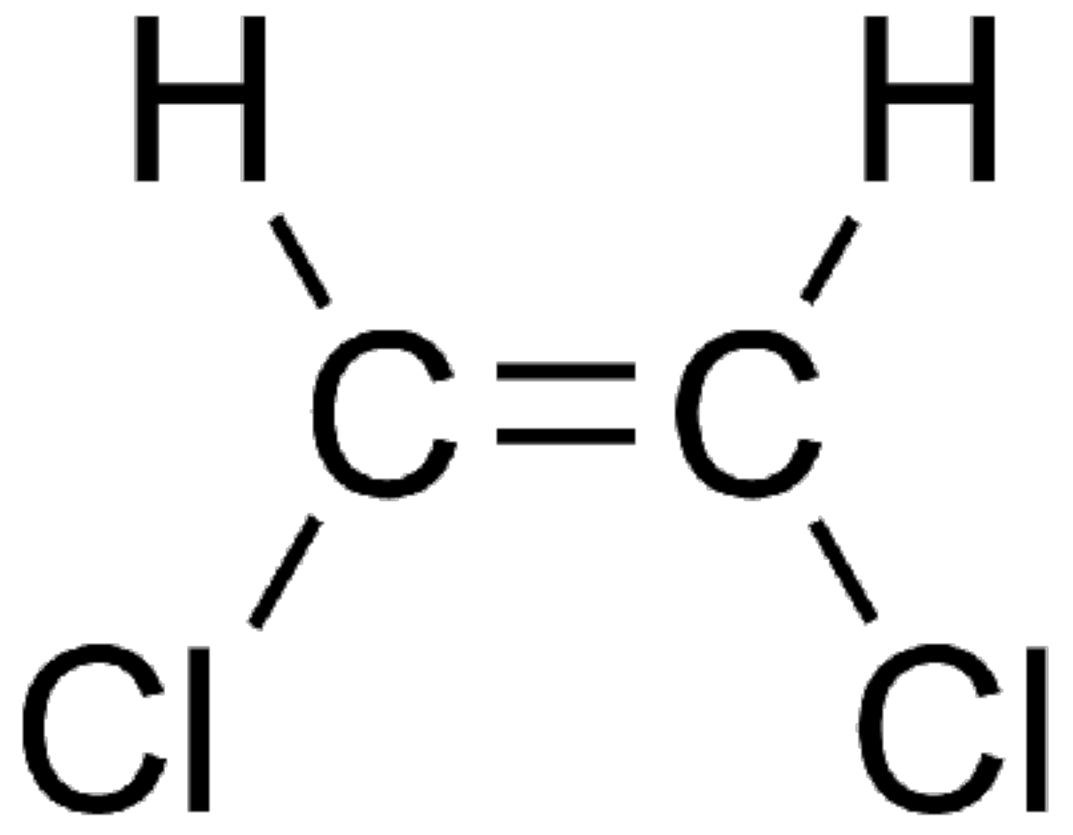
trans-1,4-dimethylcyclohexane

Now, you try it!

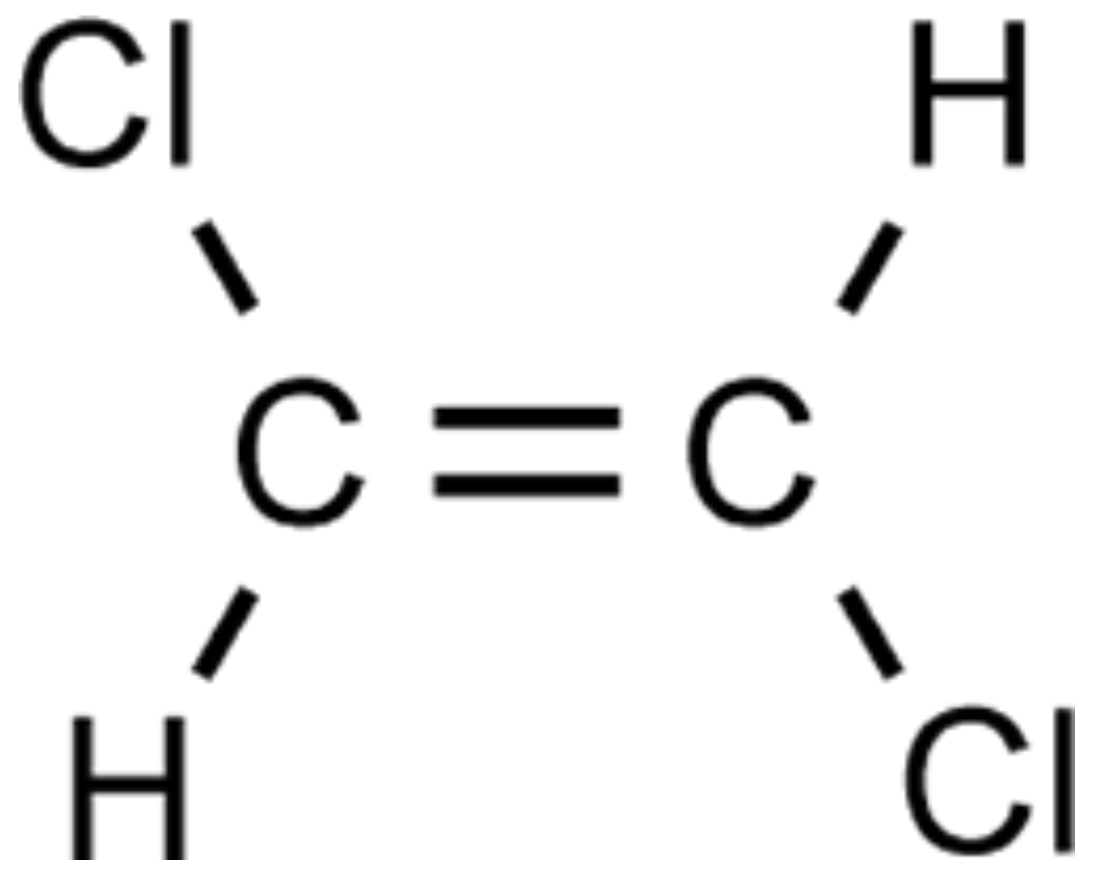
- Draw and name the *cis-trans* isomers of butenedioic acid.

Physical Properties

- Depend on:
  - Polarity
  - Shape or symmetry
- Name these and…
  - What intermolecular forces will these undergo?
  - Which will have a higher boiling point?

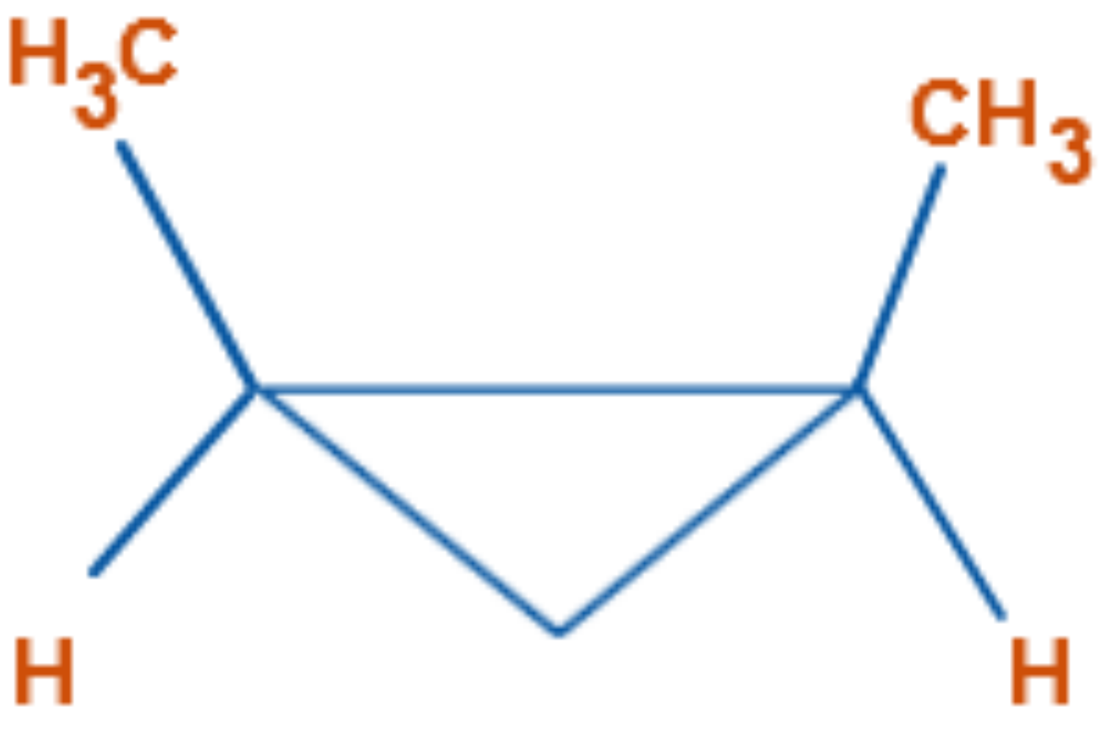


60.2°C

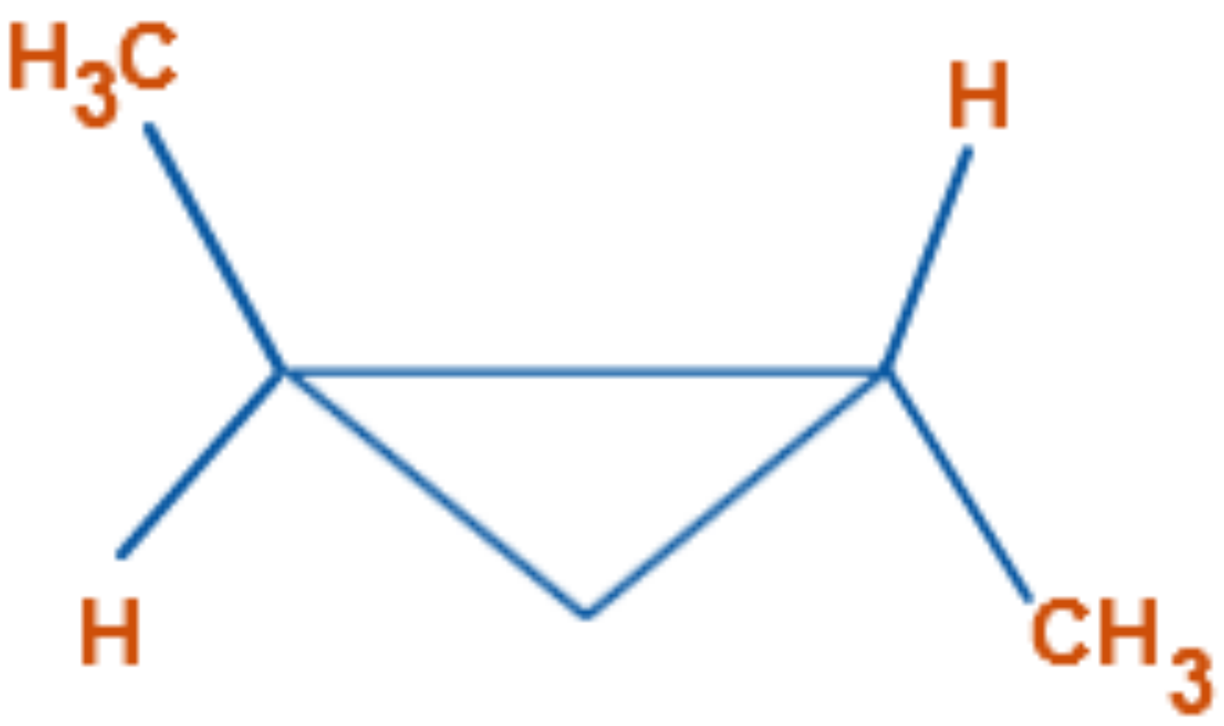


48.5°C

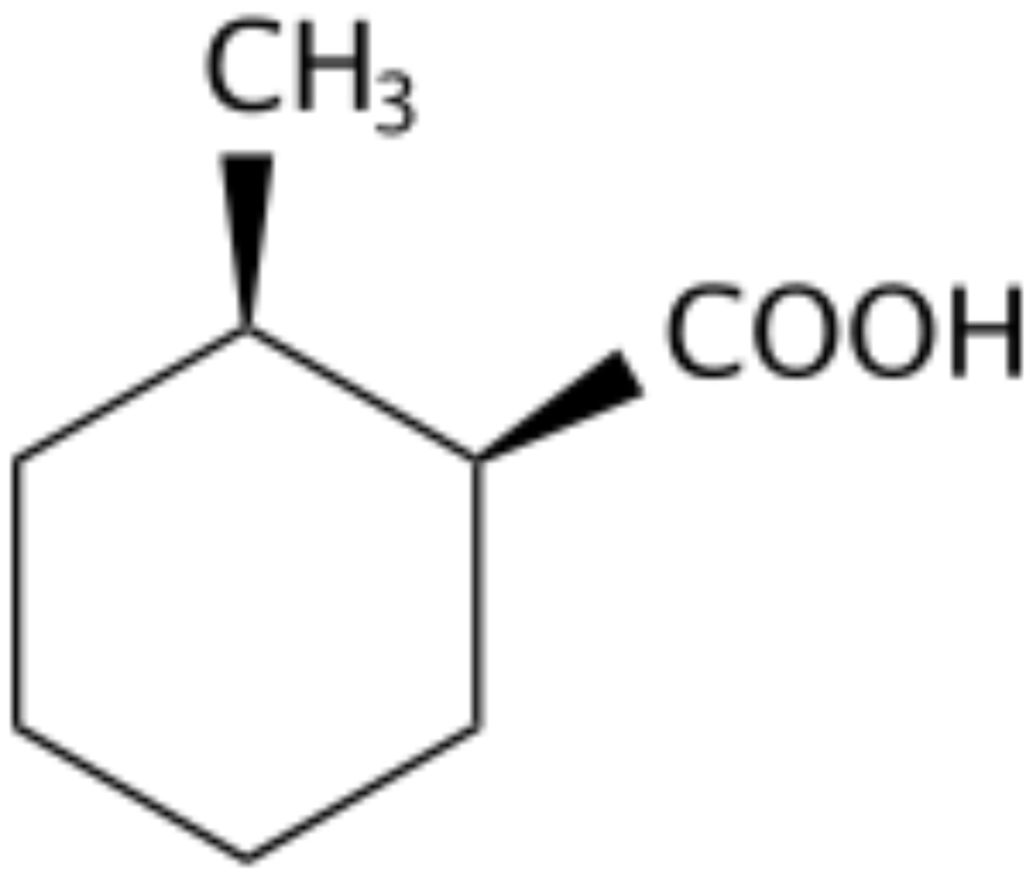
Physical Properties



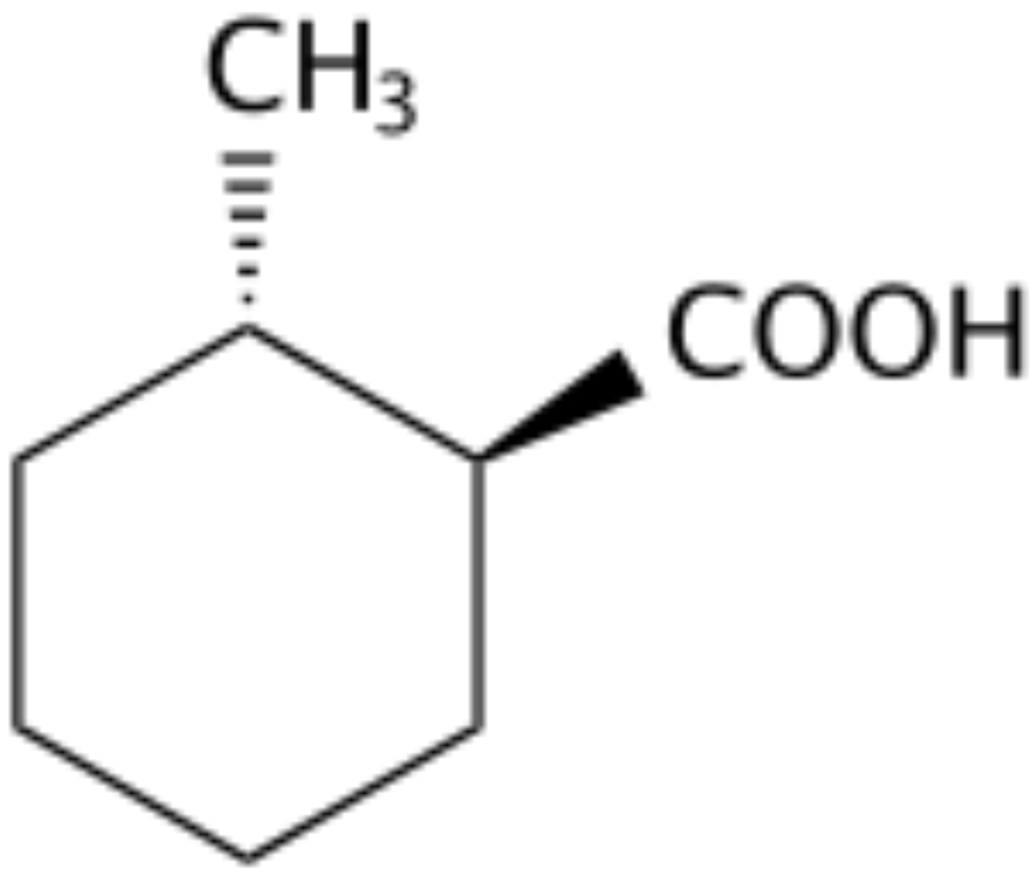
Cis - 1,
2 - dimethyloyolopropane
(bp^{o}37 C)



Trans - 1,
2 - dimethyloyolopropane
(bp 29^{o}C)



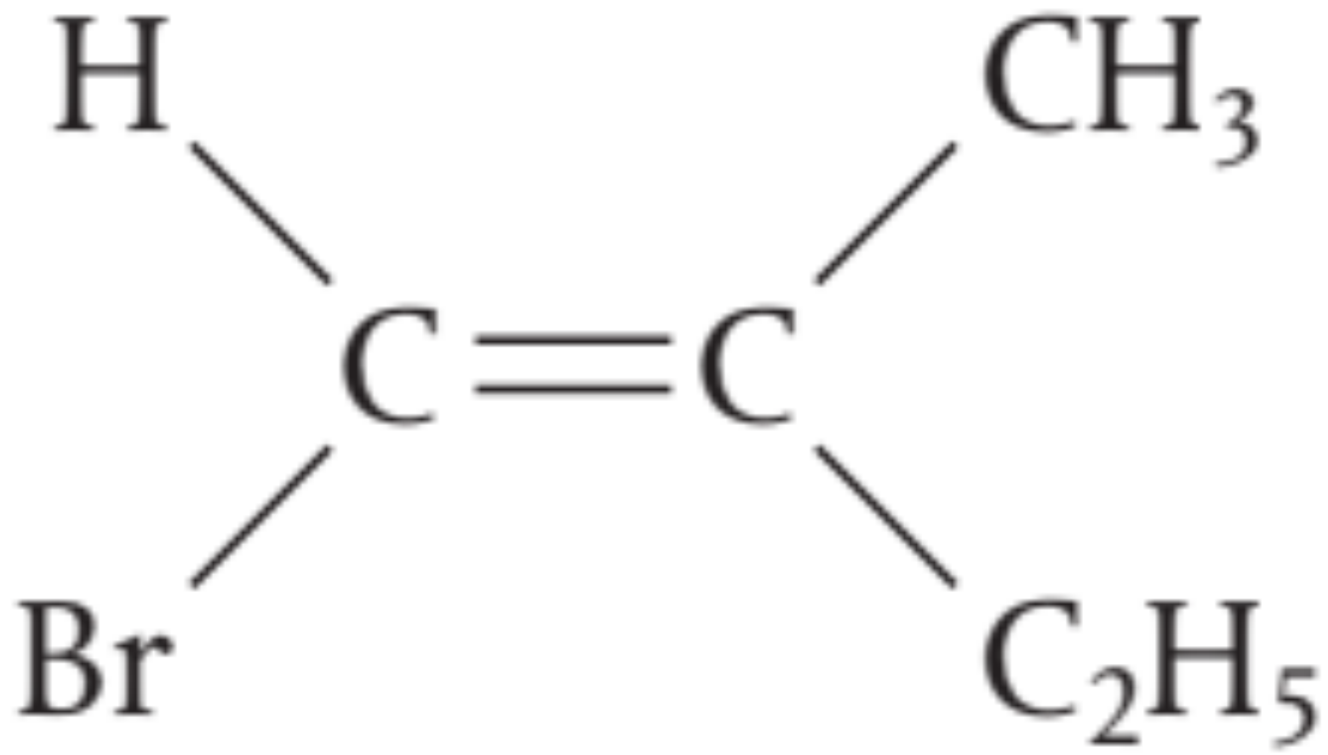
cis



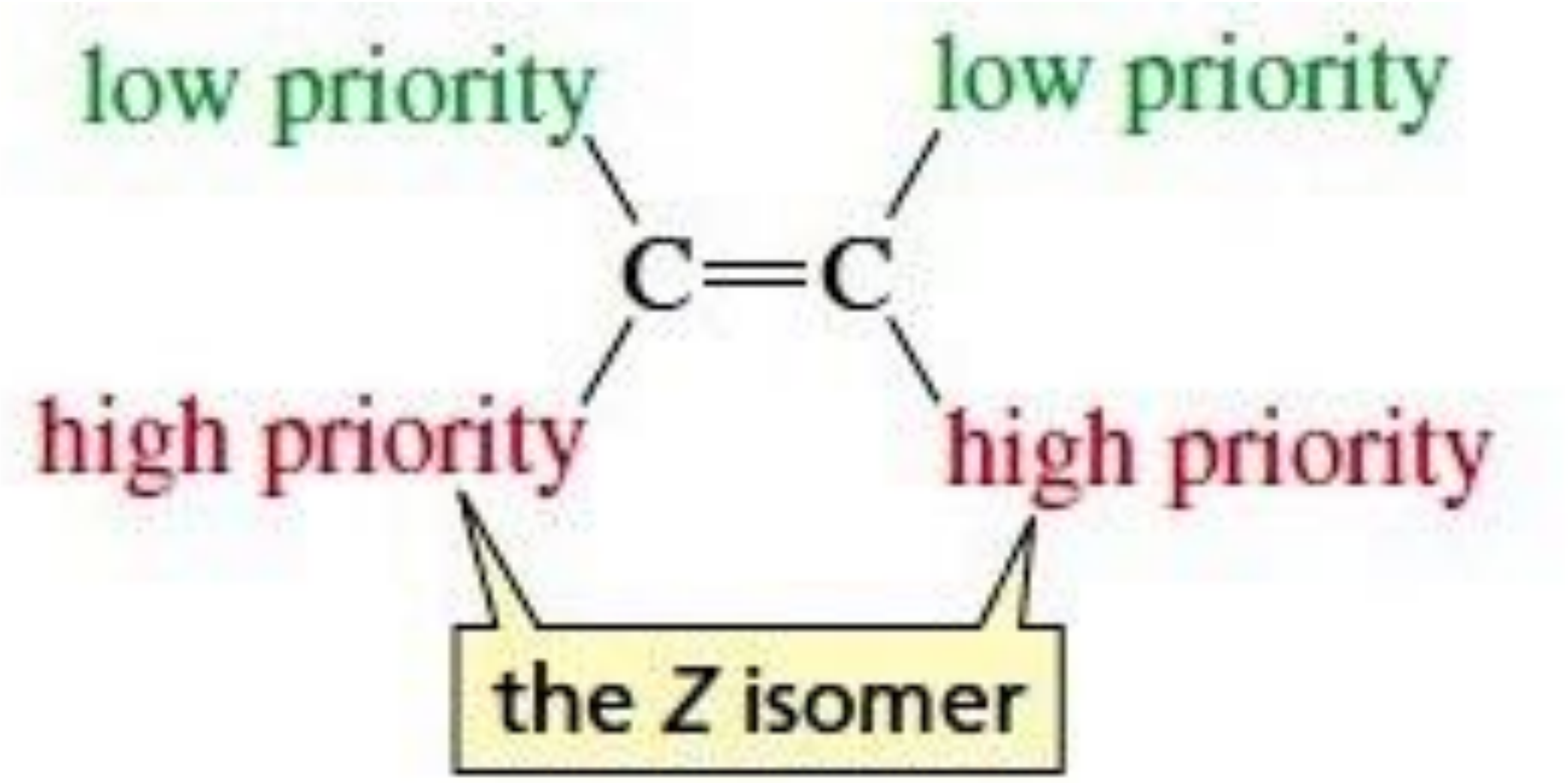
trans

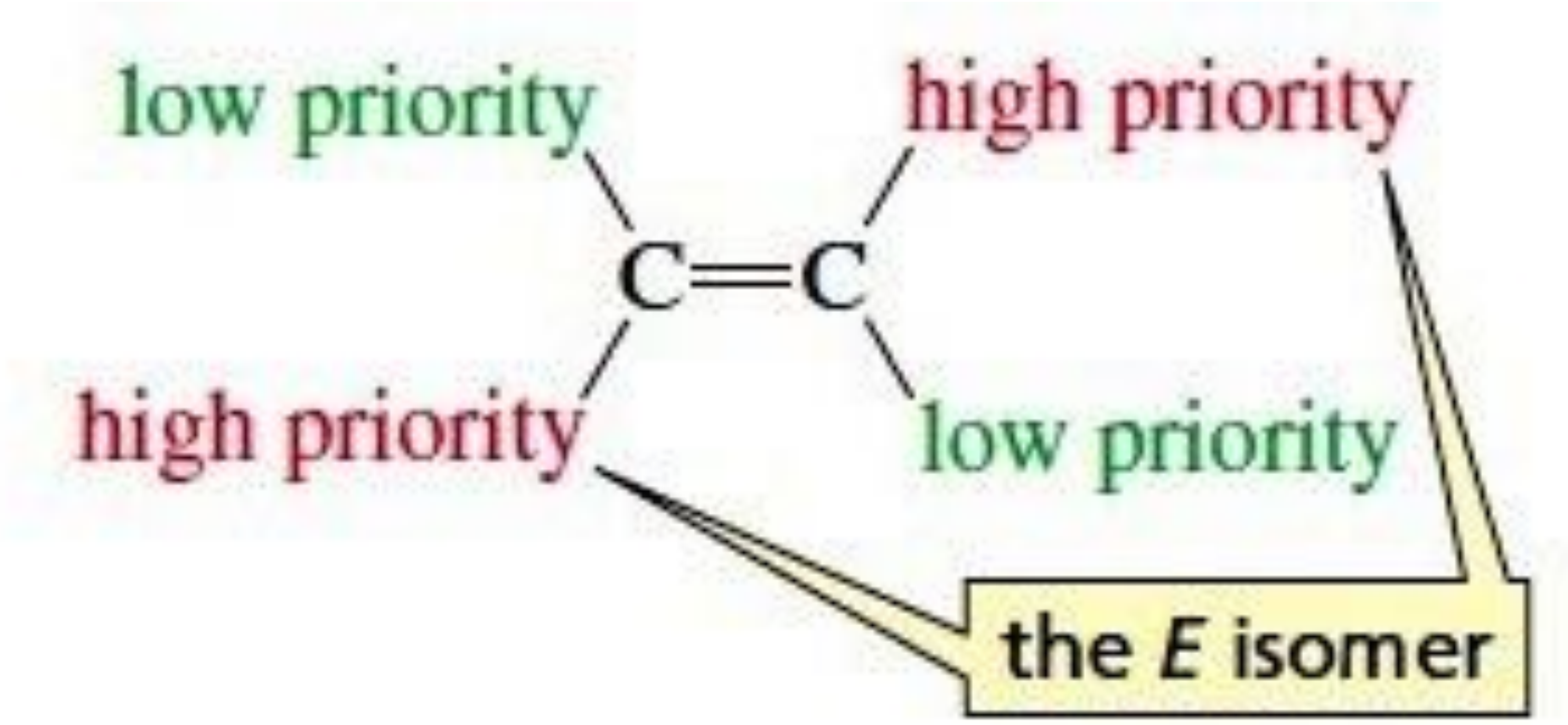
What happens when *cis-trans* doesn't work?

- When the doubly bonded carbons are also bonded to more than one other group.
  - ***E/Z*** designation - based on Cahn-Ingold-Prelog rules of priority
    - Higher atomic number = greater priority



1-bromo-2-methylbut-1-ene



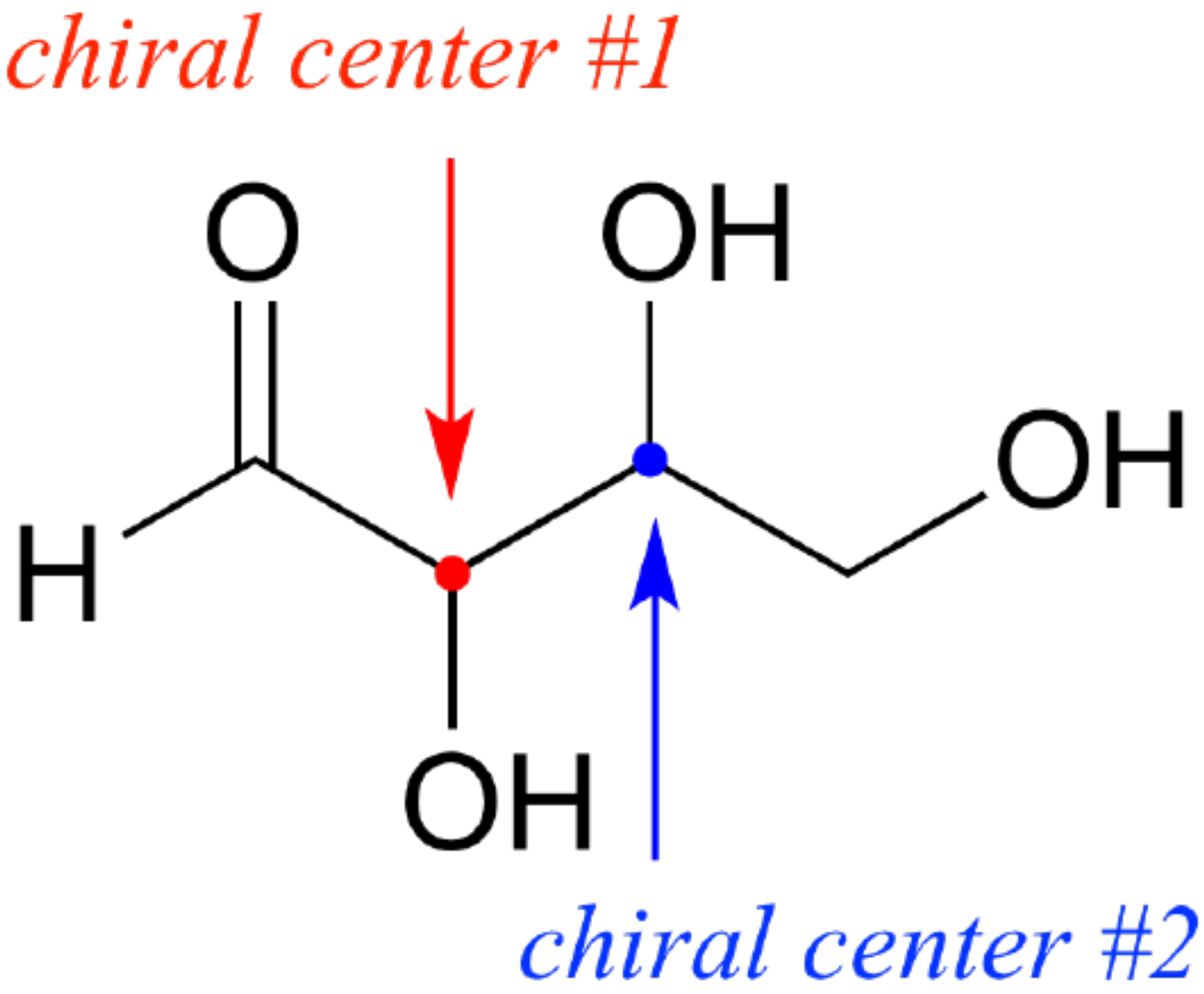


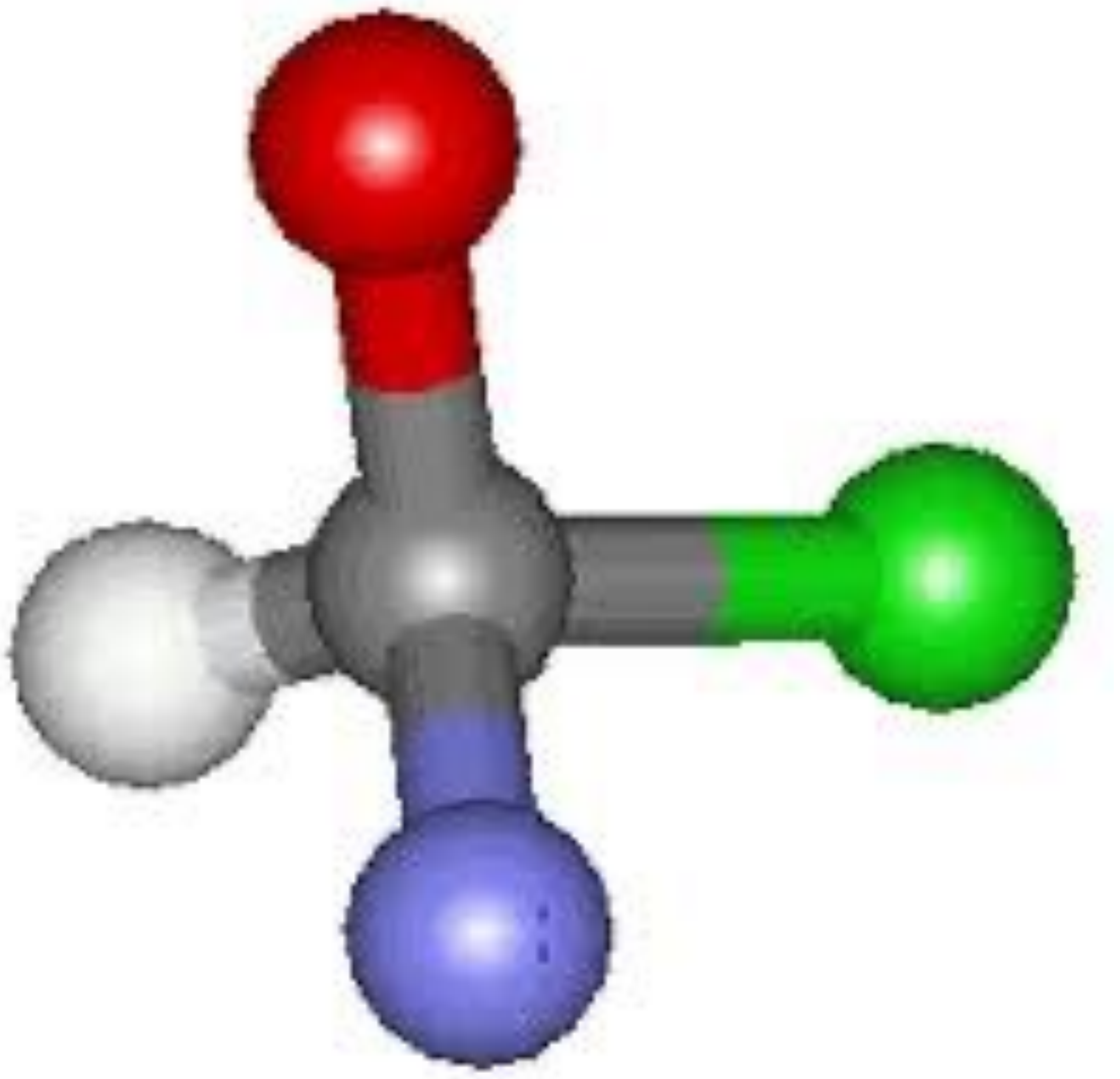
Example - *E/Z* Isomers

- Draw and name, using the *E/Z* convention, the two stereoisomers of 3-methylpent-2-ene.

Optical Isomers

- A carbon atom attached to four different atoms or groups is known as asymmetric or **chiral (a chiral centre)**.



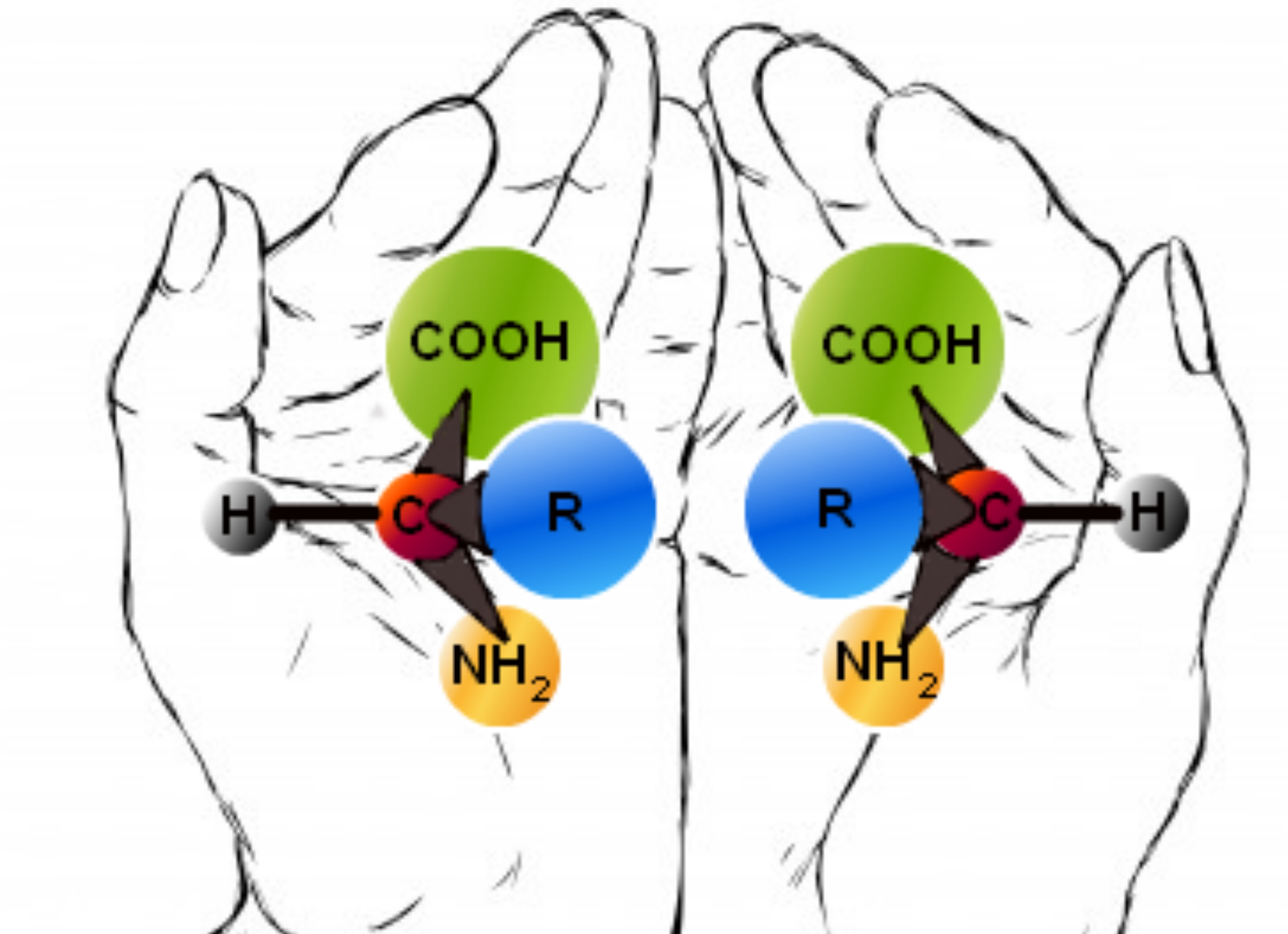


Optical Isomers

- Can be arranged in two different 3-D configurations that are mirror images of each other (***enantiomers***)
  - non-superimposable mirror images
  - known as optical isomerism
  - an equal mixture of two enantiomers is called a **racemic mixture**.

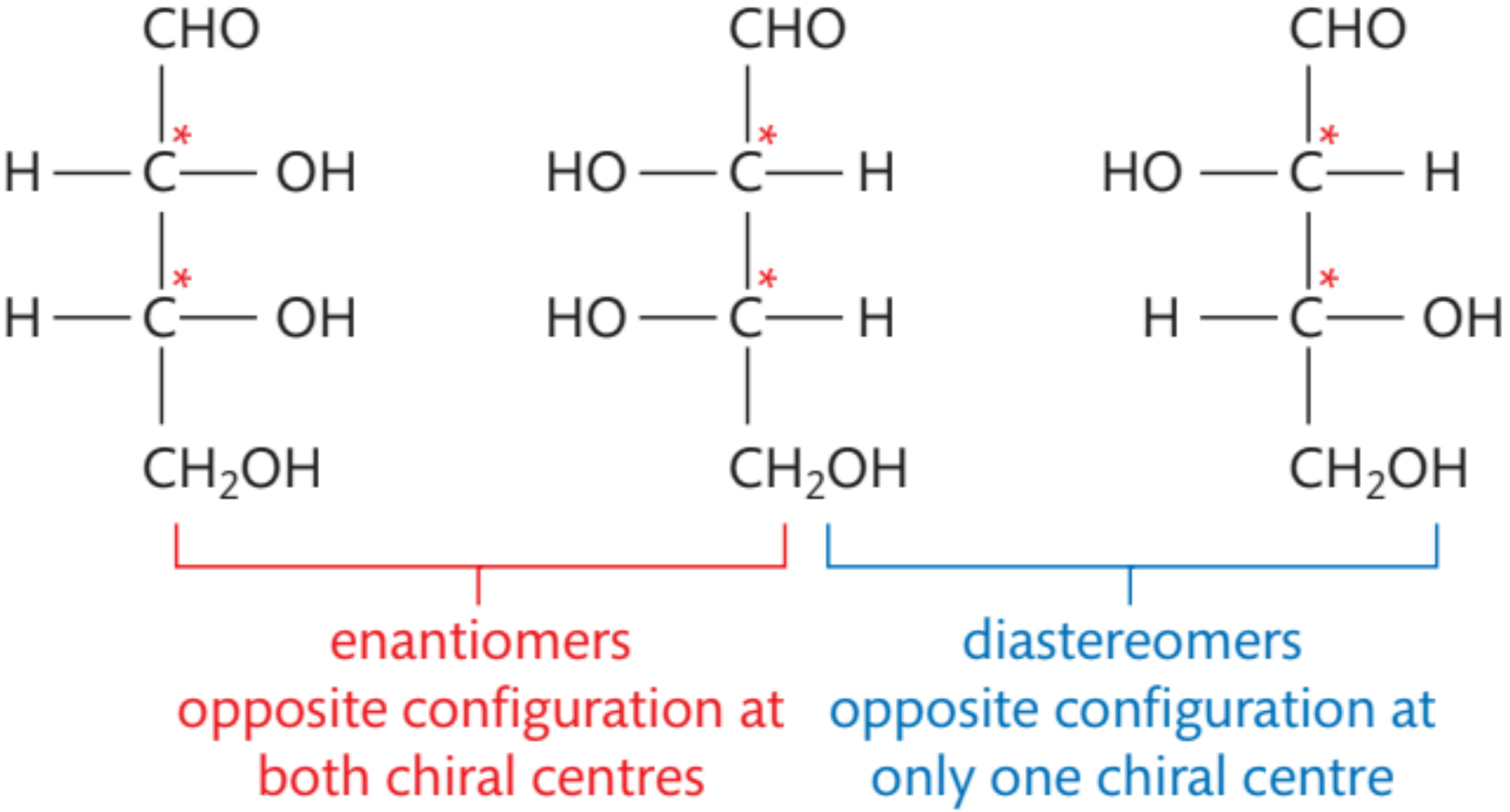
The term refers to the way the isomers react with *plane polarized light*

They are chiral molecules with NO plane of symmetry



Multiple Chiral Centers - Diastereomers

- When molecules have different configurations at one or more, *but not all*, chiral centers.
- They are not always mirror images of each other.

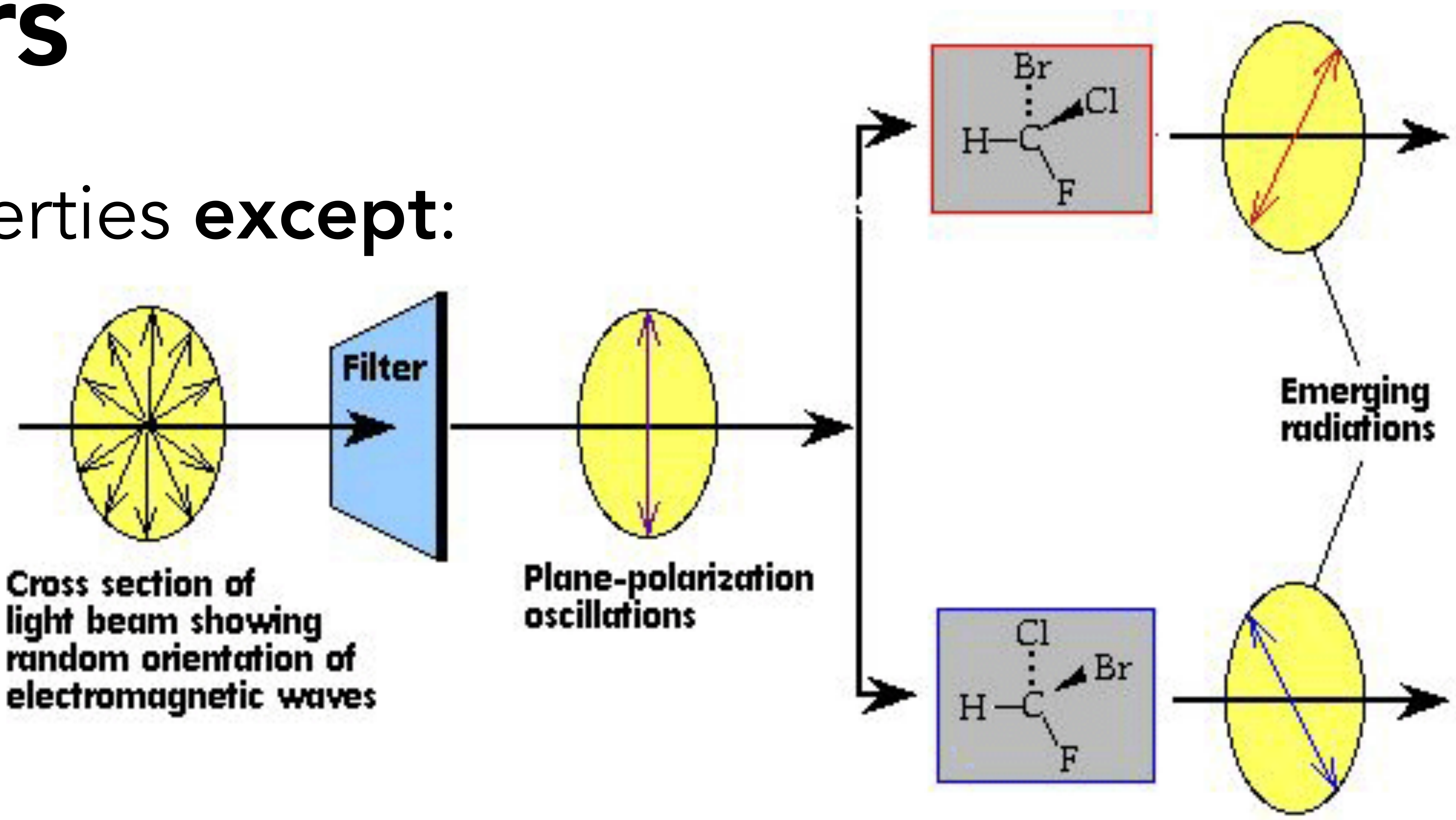


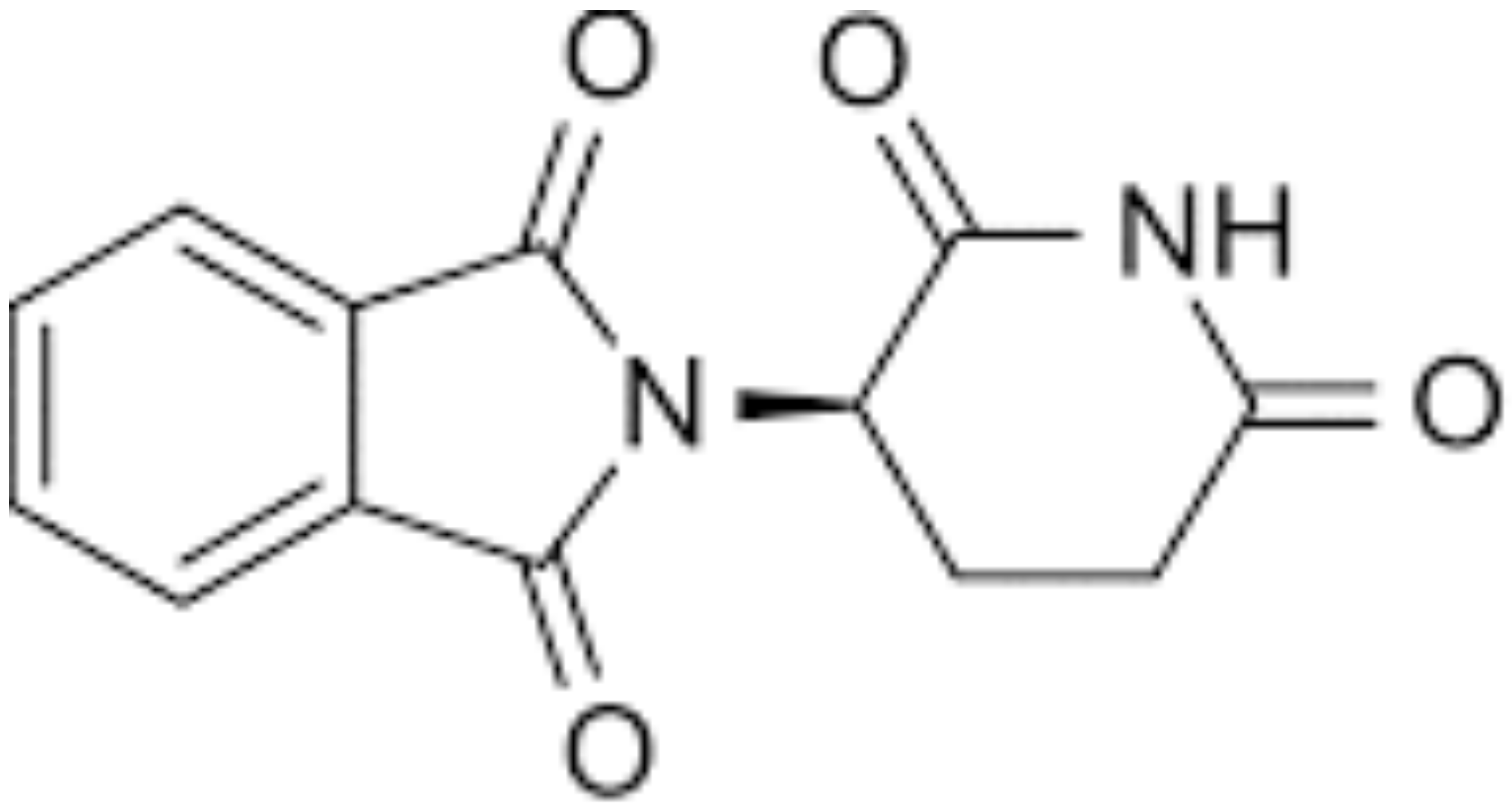
How do I know it's an optical isomer?

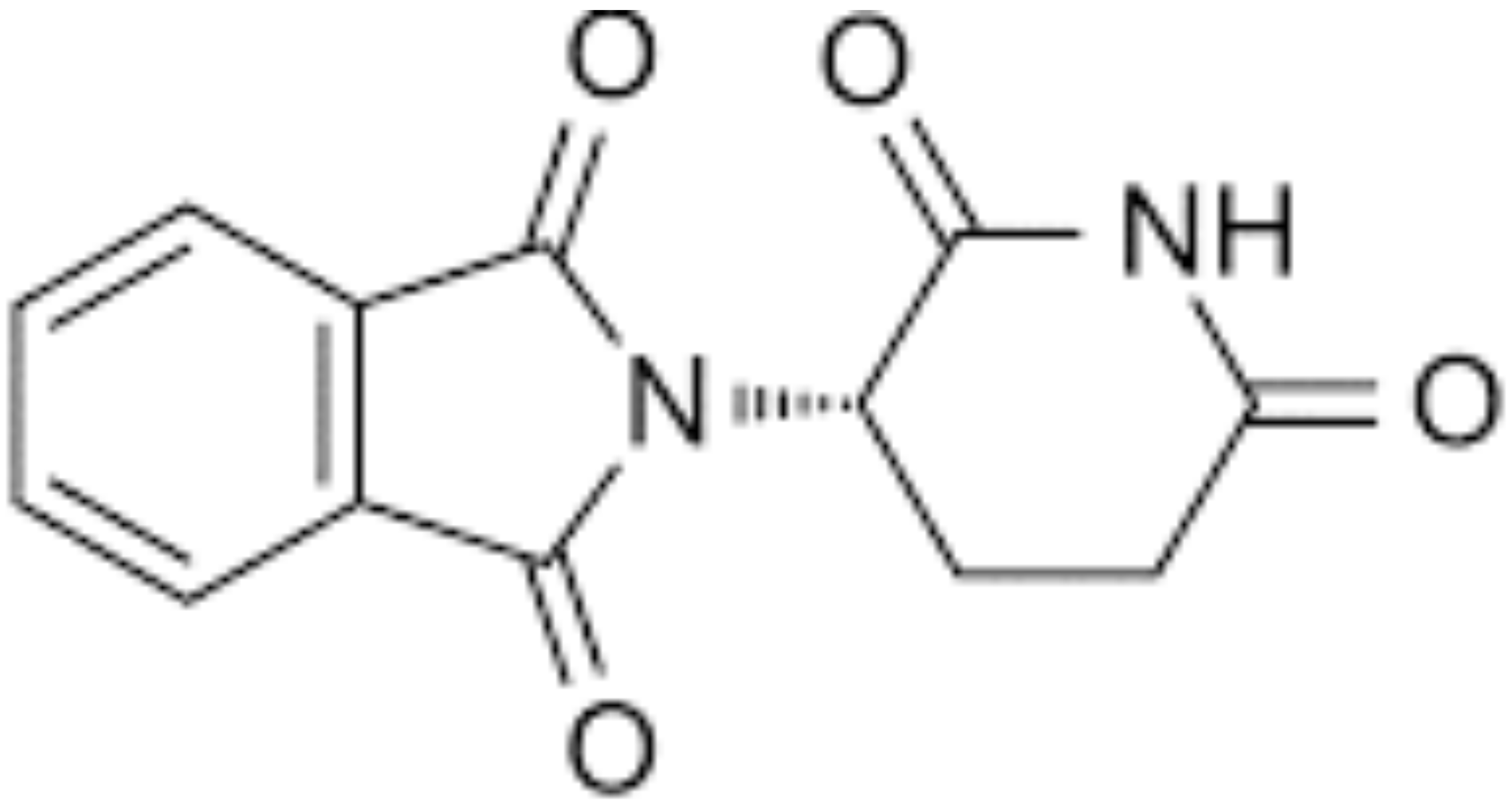
- Find the C atom with four different groups bonded to it. It is useful to mark the ***CHIRAL*** carbon with an asterisk.
    - Draw butan-2-ol. Find the chiral carbon. Mark it with an asterisk.
    - Draw 2-chlorobutane. Find the chiral carbons and mark it with an asterisk.

Properties of Optical Isomers

- Have identical physical and chemical properties **except**:
  - Optical activity
  - Reactivity with other chiral molecules
    - optical purity
    - tase/smell receptors




(R)-thalidomide


(S)-thalidomide