



INTERNATIONAL COLLEGE
OF PHARMACEUTICAL
INNOVATION

国际创新药学院

Fundamentals of Medicinal and Pharmaceutical Chemistry

FUNCHEM.18 Alkenes in nature and reactions of alkenes.

Professor Dan Wu

DATE: 15 November 2024

Learning outcomes

At the end of this lecture, the learner will be able to

- Recall and describe the general structure and bonding in alkenes.
- Recall and apply the rules of IUPAC method of nomenclature to name and identify alkenes.
- Recall and explain the general reactivity of alkenes.
- Interpret and apply the correct use of curved arrows in representing electron movement in reaction mechanisms.
- Recall and explain the reaction profile, products, and mechanism of reactions of symmetrical and unsymmetrical alkenes with acids.
- Recall and explain the products and mechanism of hydrogenation and halogenation of alkenes.
- Recall and explain the relative reactivity of substituted alkenes.
- Identify and explain geometric isomerism in alkenes.
- Describe examples of alkene geometric isomerism in biological systems.
- Recall the synthesis of alkenes from halides and from alcohols.

Recommended reading

- Organic chemistry with biological application
(John McMurry)
- Chapter 7

Halogenation of Alkenes: Electrophilic Addition

Alkenes add Cl_2 or Br_2 instantaneously in the dark at room temperature.
 F_2 adds violently.

A chemical test which distinguishes alkenes from alkanes involves the use of Br_2 in CCl_4 which is a dark red-brown solution.

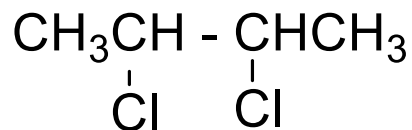
Addition of excess alkene will decolourise this instantly.

This will not happen with alkanes (no double bond present).

Halogenation of Alkenes

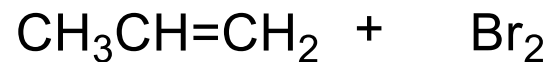


$\text{CCl}_4(\text{solvent})$

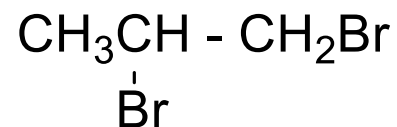


2,3-dichlorobutane

and



$\text{CCl}_4(\text{solvent})$



1,2-dibromopropane

Relative Rates of Alkene Bromination

Ethene	$\text{H}_2\text{C}=\text{CH}_2$	1
Propene	$\text{CH}_3\text{CH}=\text{CH}_2$	61
2-Methylprop-1-ene	$(\text{CH}_3)_2\text{C}=\text{CH}_2$	5400
2,3-Dimethyl-2-butene	$(\text{CH}_3)_2\text{C}=\text{C}(\text{CH}_3)_2$	920,000

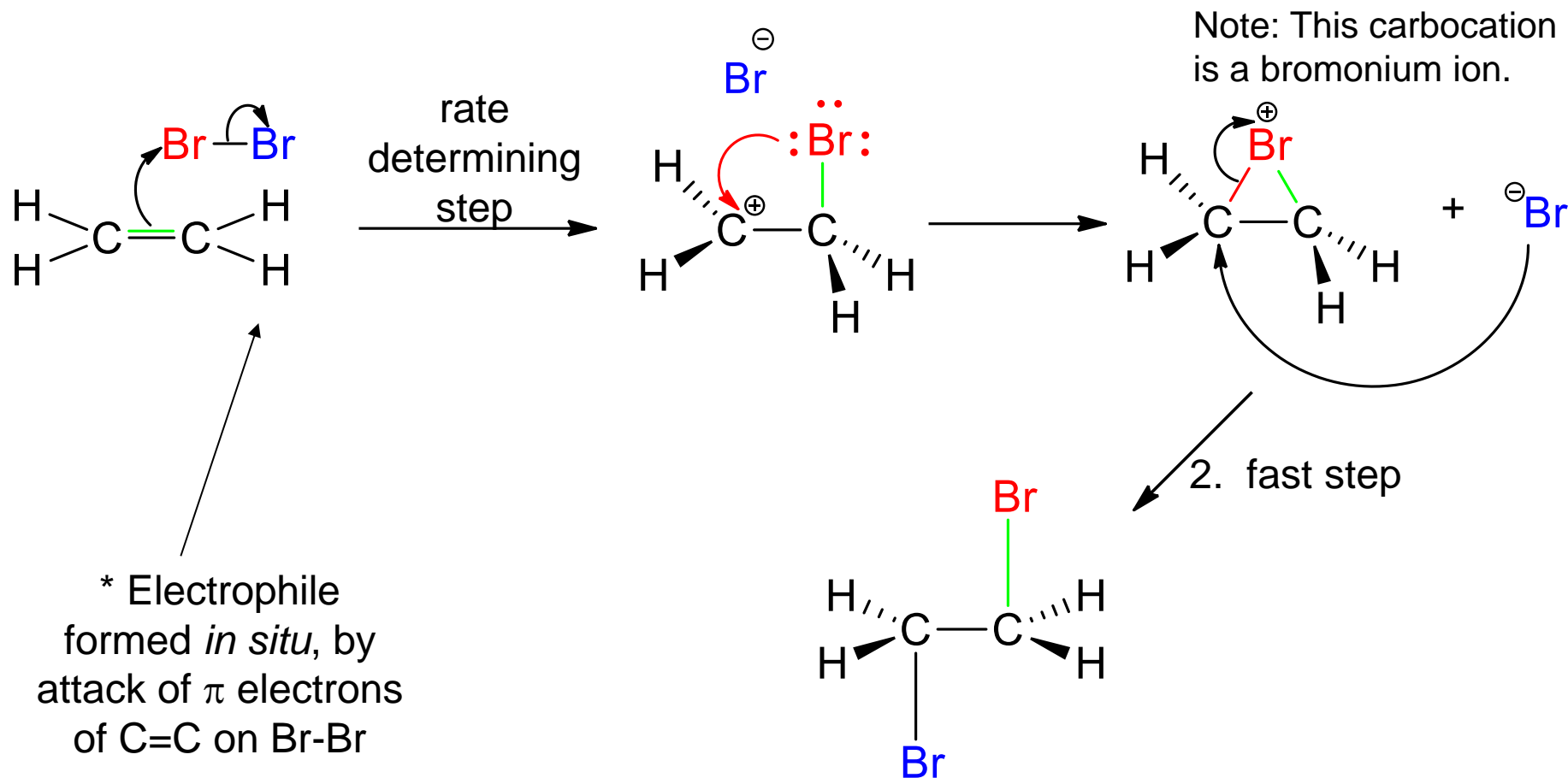
More highly substituted double bonds react faster

Alkyl groups on the double bond make it more “electron rich”

Mechanism for Addition of Br₂ to Ethene

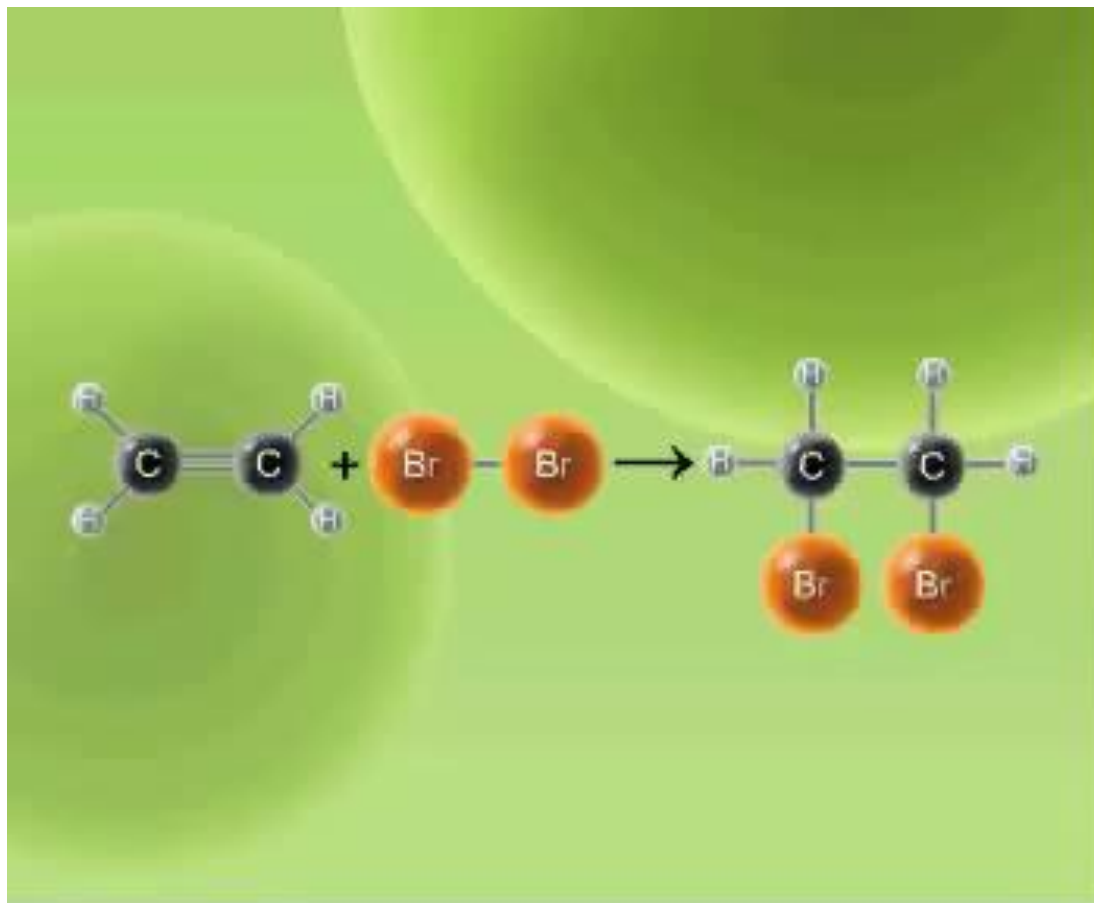
Reaction is an electrophilic addition and involves 2 steps:

1. a rate determining step (addition of electrophile*, Br[⊕])



Note: same mechanism for Cl₂

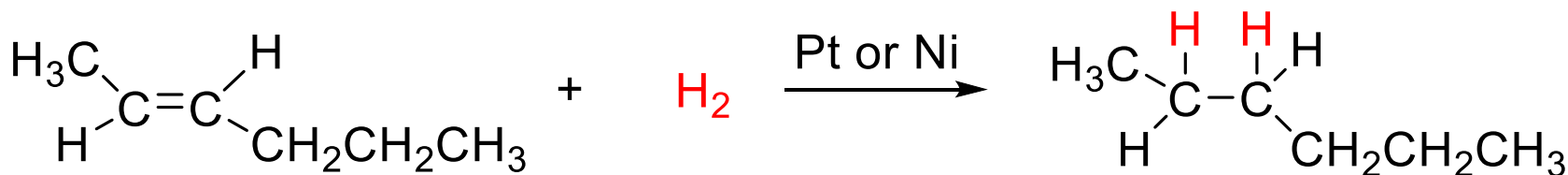
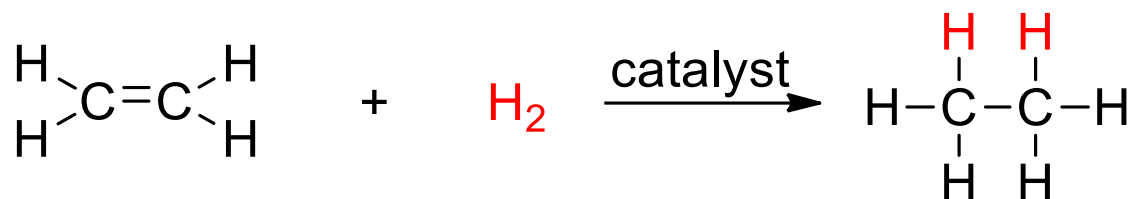
Another Look at the Mechanism for Addition of Br_2 to Ethene



Note: the bromonium ion step is not shown in the animation

Hydrogenation of Alkenes

This involves addition of H_2 to the alkene dissolved in a suitable solvent and requires a finely powdered metal catalyst eg. Ni, Pd or Pt suspended in the solution. This is an example of heterogeneous catalysis (catalyst not dissolved).



Note: This is NOT an electrophilic addition

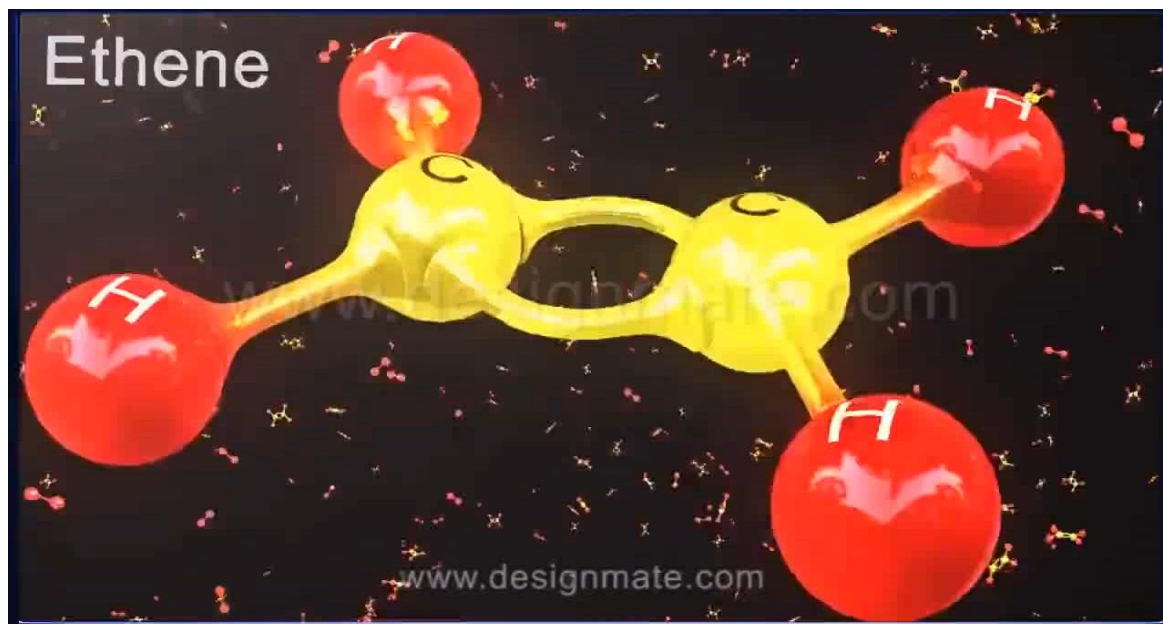
Hydrogenation of Alkenes - Mechanism

Mechanism involves adsorption of H_2 molecules onto metal surface

H atoms in H_2 form weak bonds with metal atoms – this breaks the H-H bond.

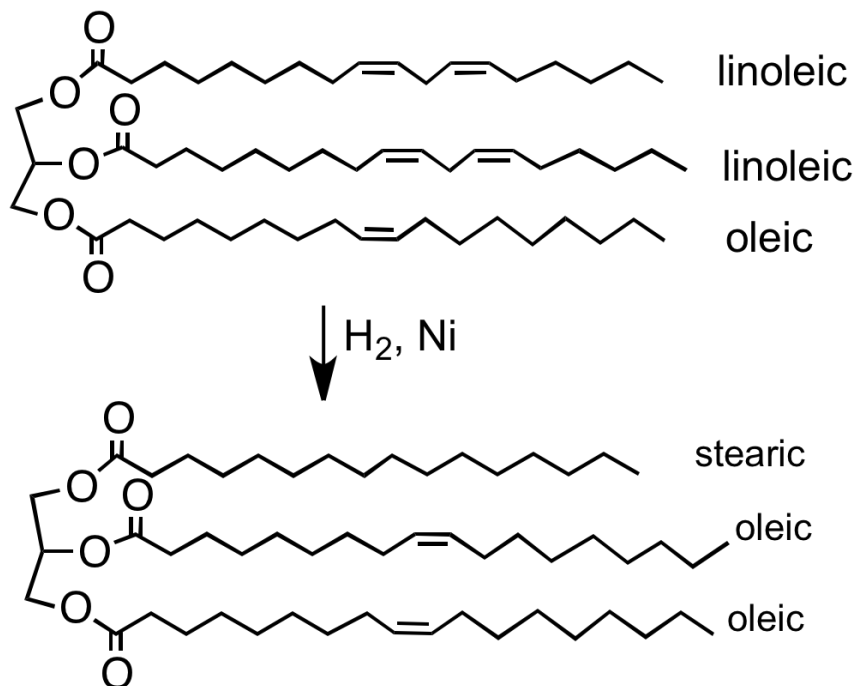
Alkene also adsorbs and binds to the metal surface.

H-H bond then breaks into atoms which add to the alkene



Note: the H atoms add at the same side of the double bond

Partial Hydrogenation of Plant Oils produces Margarines



Most of the $\text{C}=\text{C}$ double bonds are removed in this process, which elevates the melting point of the product

Geometric (Cis / Trans or E / Z) Isomerism

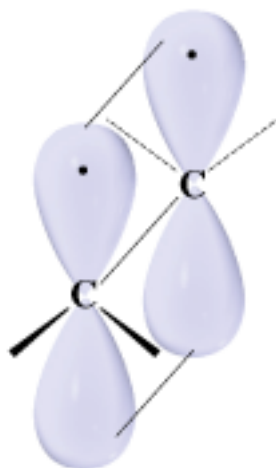
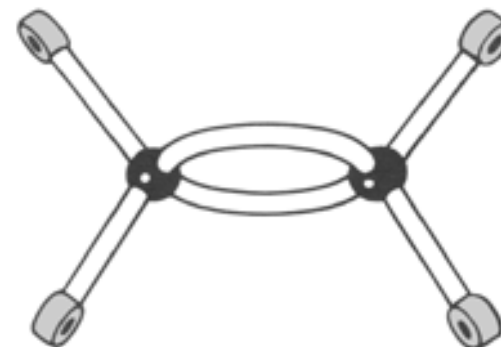
In general, geometric isomerism occurs in the following situations:

1. Some substituted alkenes.
2. Some substituted cycloalkanes (eg. disubstituted on different carbons).
3. Some square planar and octahedral complexes having different ligands eg. $\text{PtCl}_2(\text{NH}_3)_2$.

Geometric (Cis / Trans or E / Z) Isomerism in Alkenes

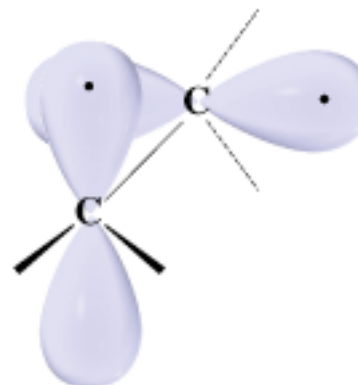
Geometric isomerism occurs in alkenes because there is not free rotation around the carbon-carbon double bond.

The π bond would break if rotation occurred.



π bond
(p orbitals are parallel)

90°
rotation

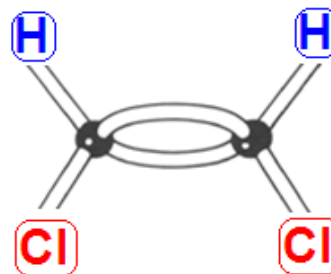


broken π bond after rotation
(p orbitals are perpendicular)

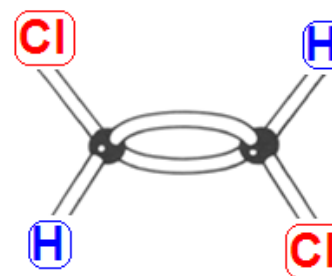
Geometric (Cis / Trans) Isomerism in Alkenes

The presence of a carbon-carbon double bond can create two possible structures.

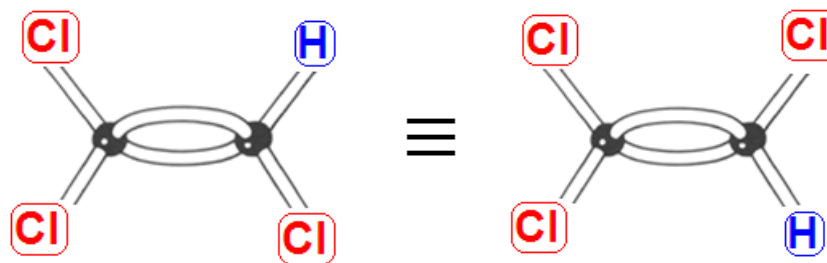
cis isomer - two identical groups, one on each C, on same side of double bond



trans isomer - two identical groups, one on each C, on opposite sides of double bond

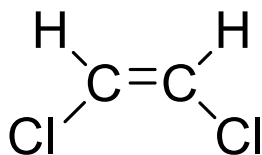
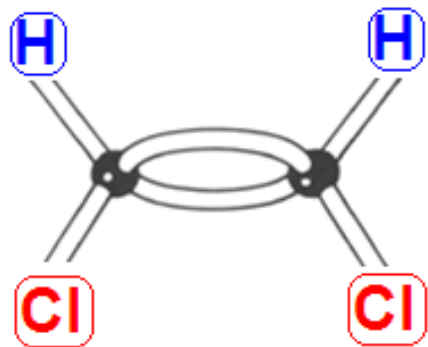


Each carbon must have two different groups for these isomers to occur.



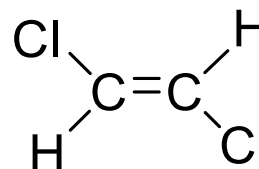
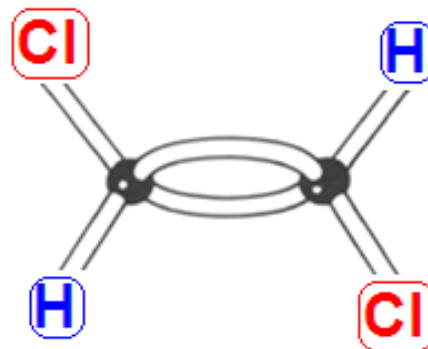
Geometric isomerism not possible.

Geometric (Cis / Trans or E / Z) Isomerism in Alkenes



cis-1,2-dichloroethene

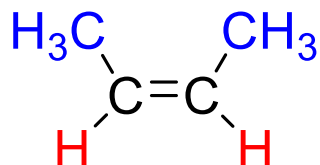
b.p. 60 °C; m.p. – 80 °C



trans- 1,2-dichloroethene

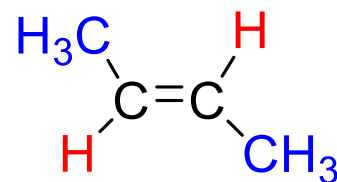
b.p. 47 °C; m.p. -50 °C

Geometric (Cis / Trans or E / Z) Isomerism in Alkenes



cis-2-butene

b.p. 3.7 °C, m.p. -139 °C



trans-2-butene

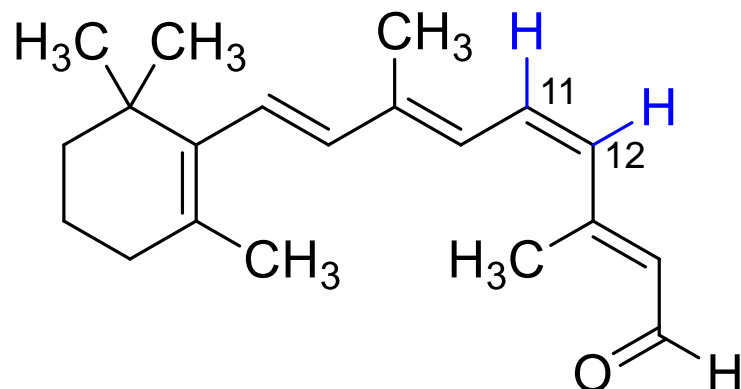
b.p. 0.3 °C, m.p. -106 °C

Geometric isomers of alkenes can be interconverted by breaking the C-C π bond, then rotating around the C-C σ bond and reforming the π bond.

This can be done if sufficient energy is provided,
e.g. using light (photochemically) or heat (thermally).

Alkene Isomerisation and the Chemistry of Vision

11-*cis*-retinal is a chromophore (light absorbing group) involved in vision



11-*cis*-retinal is a penta-ene and also an aldehyde.

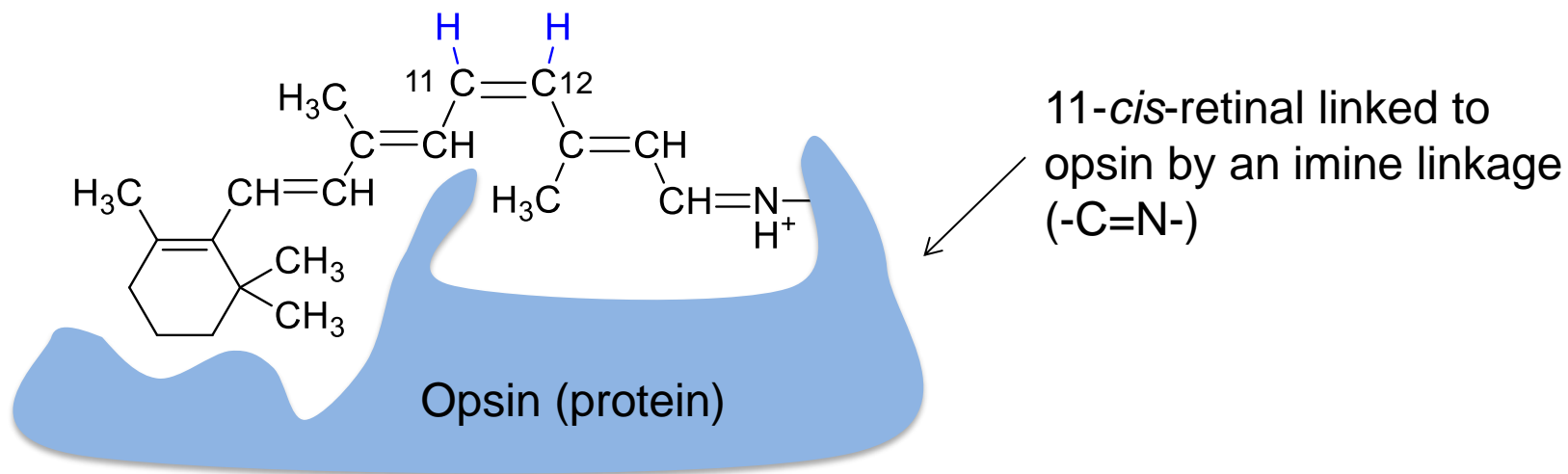
In rod cells in the cornea it is combined with the protein opsin (via the aldehyde) to give rhodopsin which is responsible for vision.

The primary event involves isomerisation at the C(11)-C(12) double bond.

Rhodopsin

Rod cells in the eye contain a red pigment called rhodopsin

This is obtained by reaction of the aldehyde 11-*cis*-retinal with an amino group from the protein Opsin forming an imine ($-\text{C}=\text{N}-$) functional group linkage.

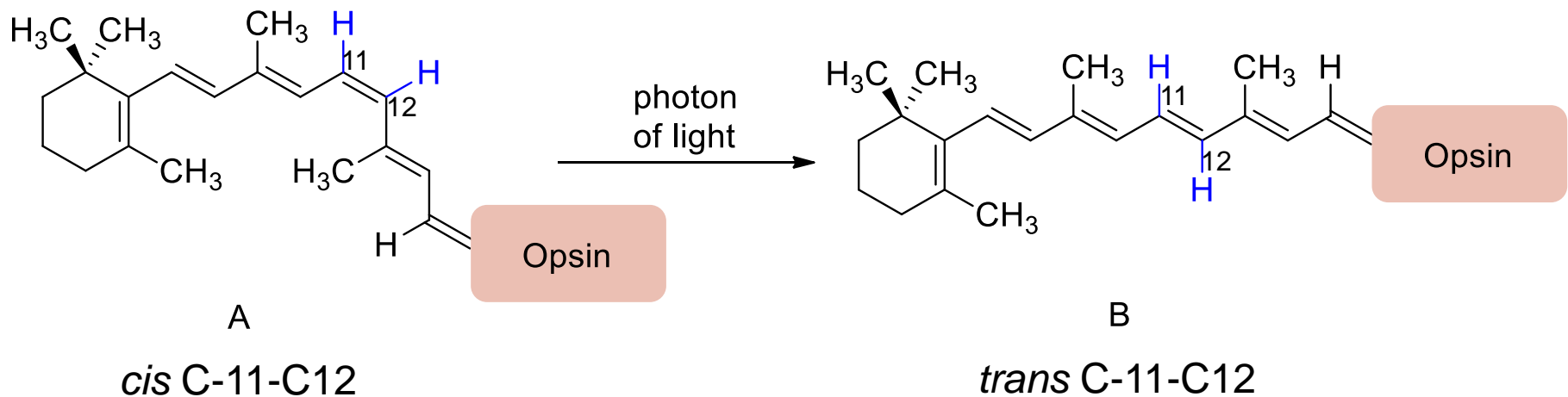
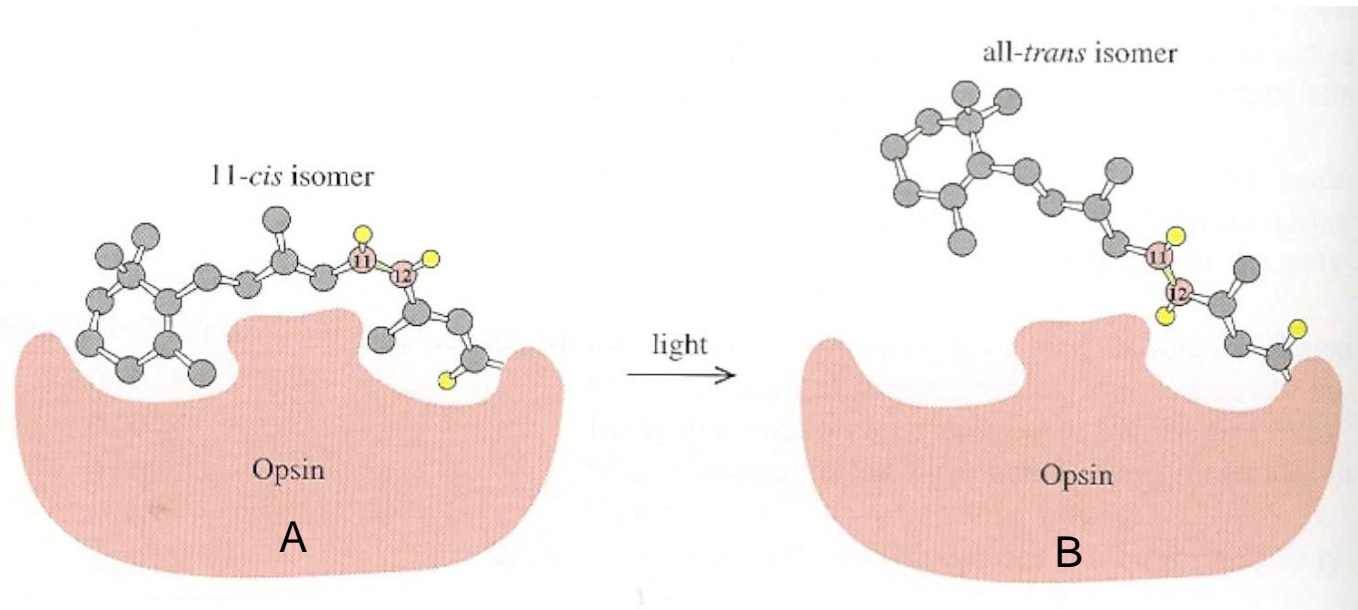


Rhodopsin, a red, light-sensitive pigment found in the rod cells in the retina of the eye, can isomerize to the *trans* isomer. This change in geometry triggers a response in the rod nerve cells that is transmitted to the brain and perceived as vision.

Note: Aldehydes react with amines to give imines (mechanism in carbonyl compounds lecture, next semester).

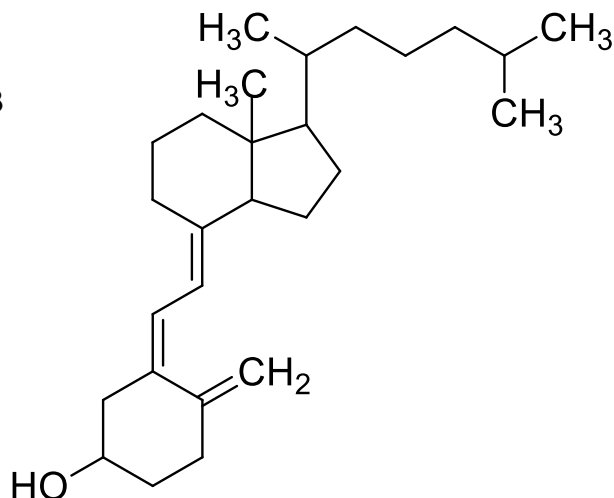
Isomerisation of Rhodopsin to Lumirhodopsin

Light is converted into atomic motion which gives rise to a nerve impulse which is perceived as vision.



Other Important Biological Alkenyl Compounds

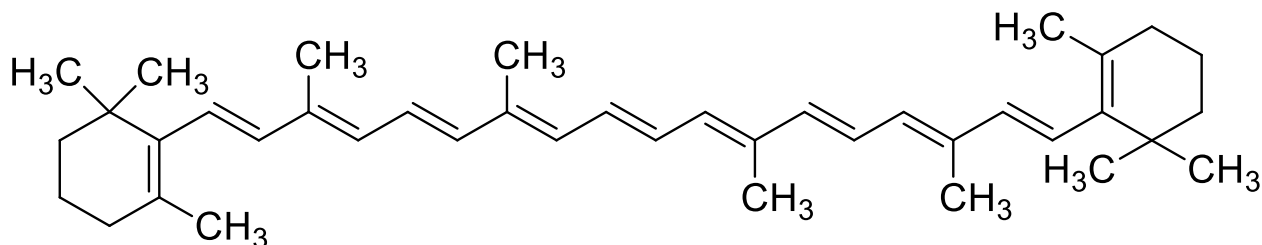
Vitamin D₃



enhances intestinal absorption of
calcium, iron, magnesium, and zinc

sunshine vitamin, synthesised in the skin from cholesterol with adequate sun
exposure

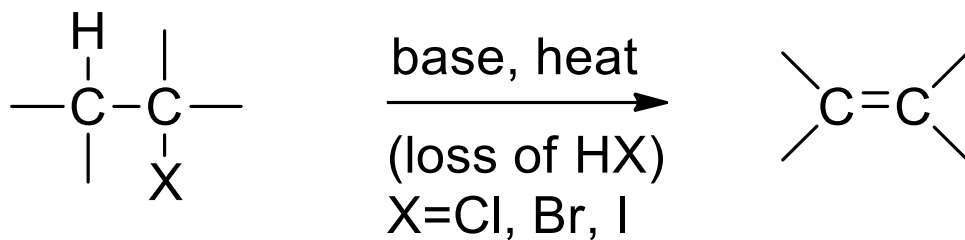
β-Carotene



responsible for the orange colour of carrots and many other fruits and vegetables

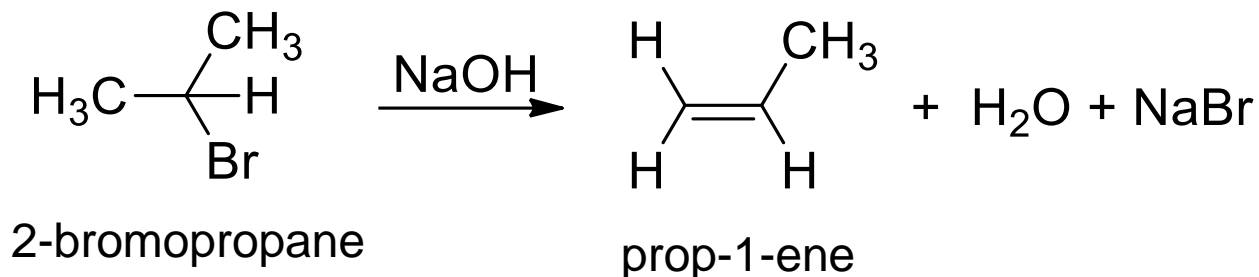
Synthesis of Alkenes

Dehydrohalogenation of alkyl halides (elimination)

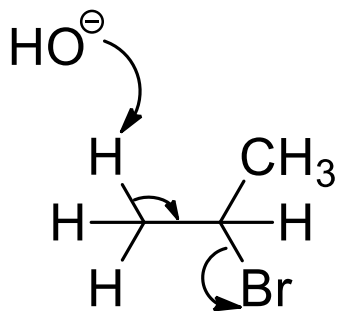


Note: This is the reverse of the HX addition reaction shown in the previous lecture.

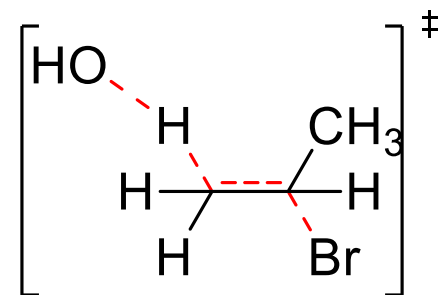
Synthesis of Propene



Reaction Mechanism
(three steps occur simultaneously)



Transition State

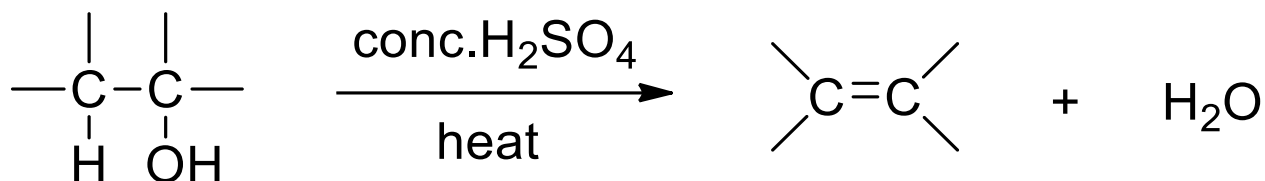


Hydroxide base begins to remove a neighbouring hydrogen, at the same time as the alkene double bond starts to form, and the Br group starts to leave.

Simultaneous breaking of C-H and C-Br bonds while forming C-C π bond.

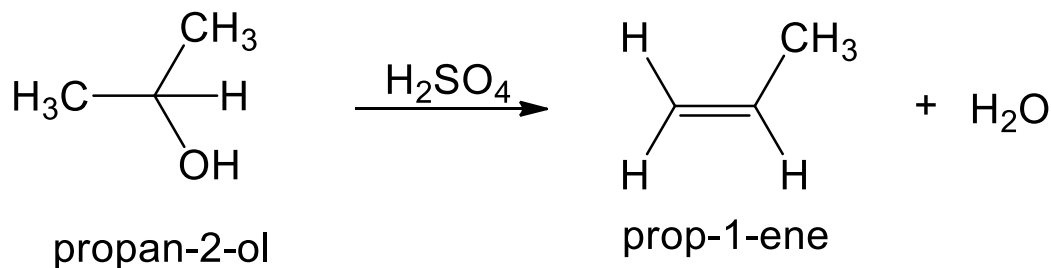
Synthesis of Alkenes

dehydration of alcohols (elimination reaction)

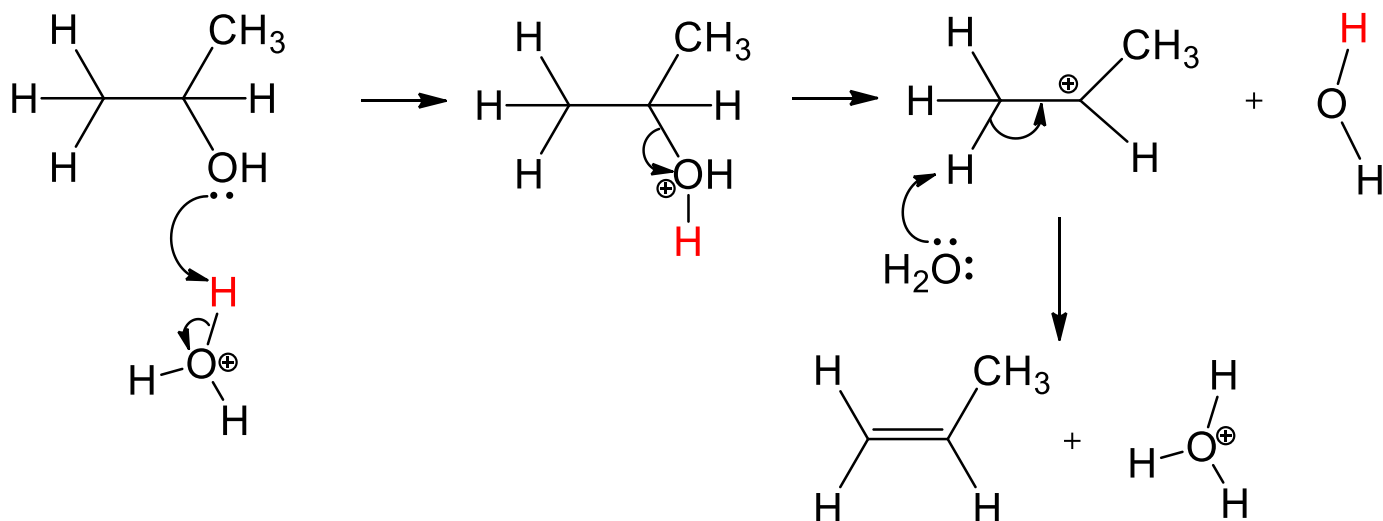


Requires harsh acidic conditions with tertiary alcohols being the most reactive, followed by secondary alcohols with primary alcohols being the least reactive.

Synthesis of Propene



Reaction Mechanism (three steps)



- In the presence of water: $\text{H}_2\text{SO}_4 + \text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{HSO}_4^-$
- Protonation of OH group by strong acid
- Carbon oxygen bond breaks forming a carbocation
- Deprotonation of C-H by water forming the double bond

Practice Example

reaction of 2-bromobutane with sodium hydroxide produces a mixture of two alkenes A and B

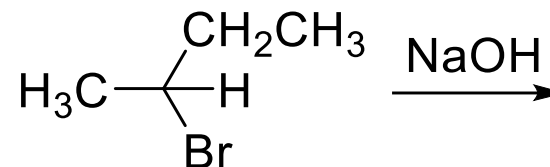


2-bromobutane

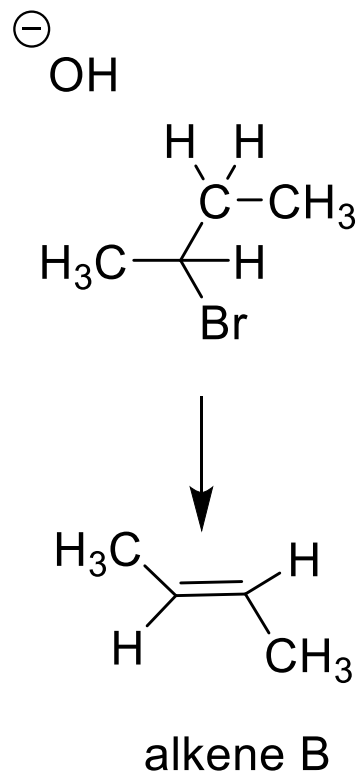
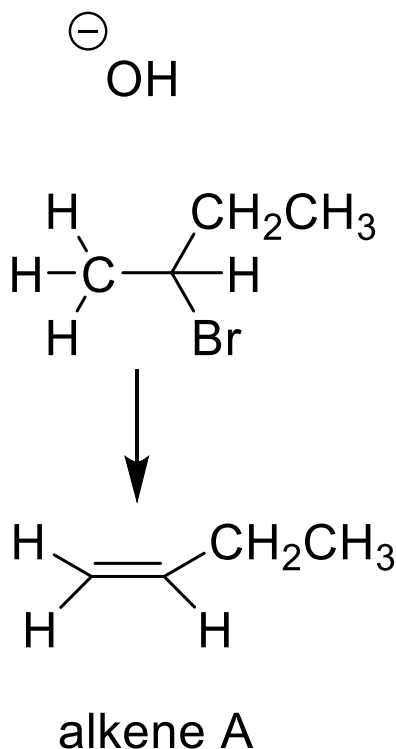
- i) Give the structures of alkenes A and B and describe the reaction mechanism by which they are produced.

Answer

Give the structures of alkenes A and B



First draw out all the key C-H bonds then identify the HBr to be eliminated



Can you add in the curly arrows to complete the mechanism?

Learning outcomes

At the end of this lecture, the learner will be able to

- Recall and describe the general structure and bonding in alkenes.
- Recall and apply the rules of IUPAC method of nomenclature to name and identify alkenes.
- Recall and explain the general reactivity of alkenes.
- Interpret and apply the correct use of curved arrows in representing electron movement in reaction mechanisms.
- Recall and explain the reaction profile, products, and mechanism of reactions of symmetrical and unsymmetrical alkenes with acids.
- Recall and explain the products and mechanism of hydrogenation and halogenation of alkenes.
- Recall and explain the relative reactivity of substituted alkenes.
- Identify and explain geometric isomerism in alkenes.
- Describe examples of alkene geometric isomerism in biological systems.
- Recall the synthesis of alkenes from halides and from alcohols.