Isomerism

Isomerism

- These compounds possess the same molecular formula but differ from each other in physical or chemical properties, and are called Isomers and the phenomenon is termed **Isomerism**
- Since isomers have the same molecular formula, the difference in their properties must be due to different modes of combination or arrangement of atoms within the molecule. There are two main types of isomerism
- **(i)** ***Structural Isomerism*** **and** ***(ii) Stereoisomerism.***

Structural Isomerism

- When the isomerism is simply due to difference in the arrangement of atoms within the molecule without any reference to space, the phenomenon is termed Structural Isomerism. **In other words, the structural isomers are compounds that have the same molecular formula but different structural formulas.**

Types of Structural Isomerism

1. Chain Isomerism
2. Position Isomerism
3. Functional Isomerism
4. Metamersim
5. Tautomerism

Stereoisomerism

- When isomerism is caused by the different arrangements of atoms or groups in space, the phenomenon is called Stereoisomerism (Greek, Stereos = occupying space).
- **The stereoisomers have the same structural formulas but differ in arrangement of atoms in space**. In other words, stereoisomerism is exhibited by such compounds which have identical molecular structure but different configurations. Configuration refers to the 3-dimentional arrangement of atoms that characterizes a particular compound.

Types of Stereoisomerism

Stereoisomerism is of two types

1. **Geometrical or Cis-Trans Isomerism**
2. **Optical Isomerism**

Structural Isomerism

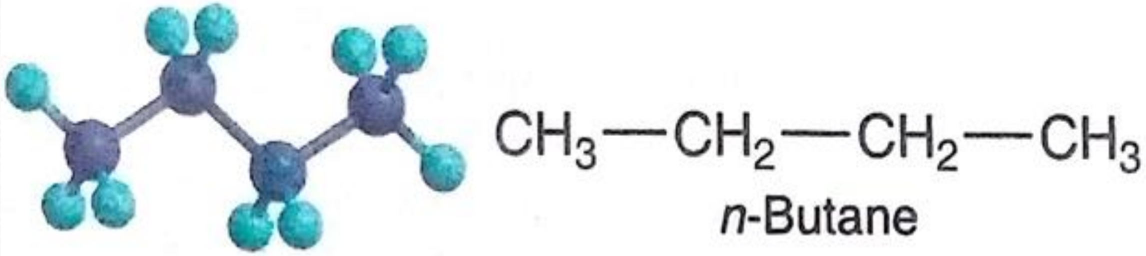
Chain Isomerism

This type of isomerism arises from she difference in the structure of carbon chain which forms the nucleus of the molecule. It is, therefore, named as Chain or Nuclear Isomerism.

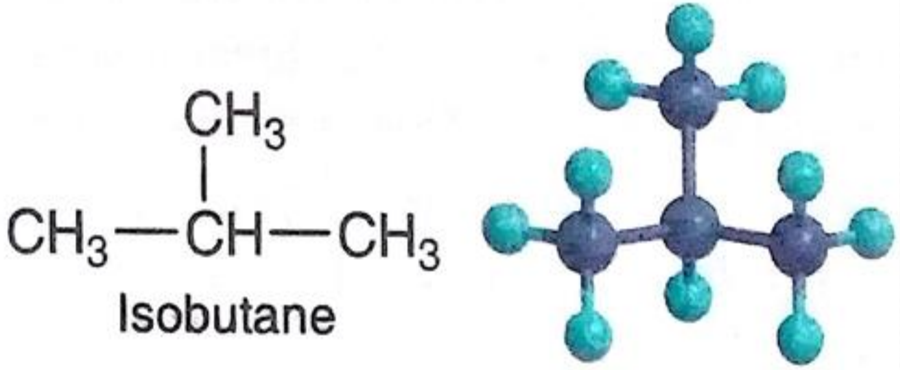
Chain isomers have the same molecular formula but differ in the order in which the carbon atoms are bonded to each other

For example, there are known two butanes which have the same molecular formula (C_4H_{10}) but differ in the structure of the carbon chains in their molecules.

Example 1. *n*-Butane and Isobutane


$CH_3-CH_2-CH_2-CH_3$

n-Butane

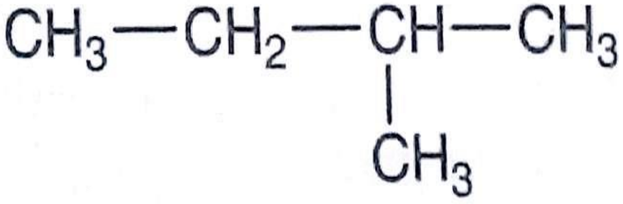

$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{CH}}-CH_3$$

Isobutane

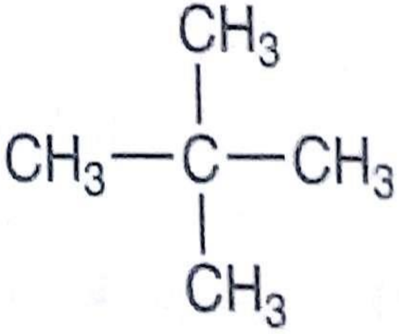
Example 2. 2-Methylbutane and 2,2-Dimethylpropane

$CH_3CH_2CH_2CH_2CH_3$

n-Pentane


$$CH_3-CH_2-\underset{\underset{\displaystyle CH_3}{|}}{CH}-CH_3$$

2-Methylbutane

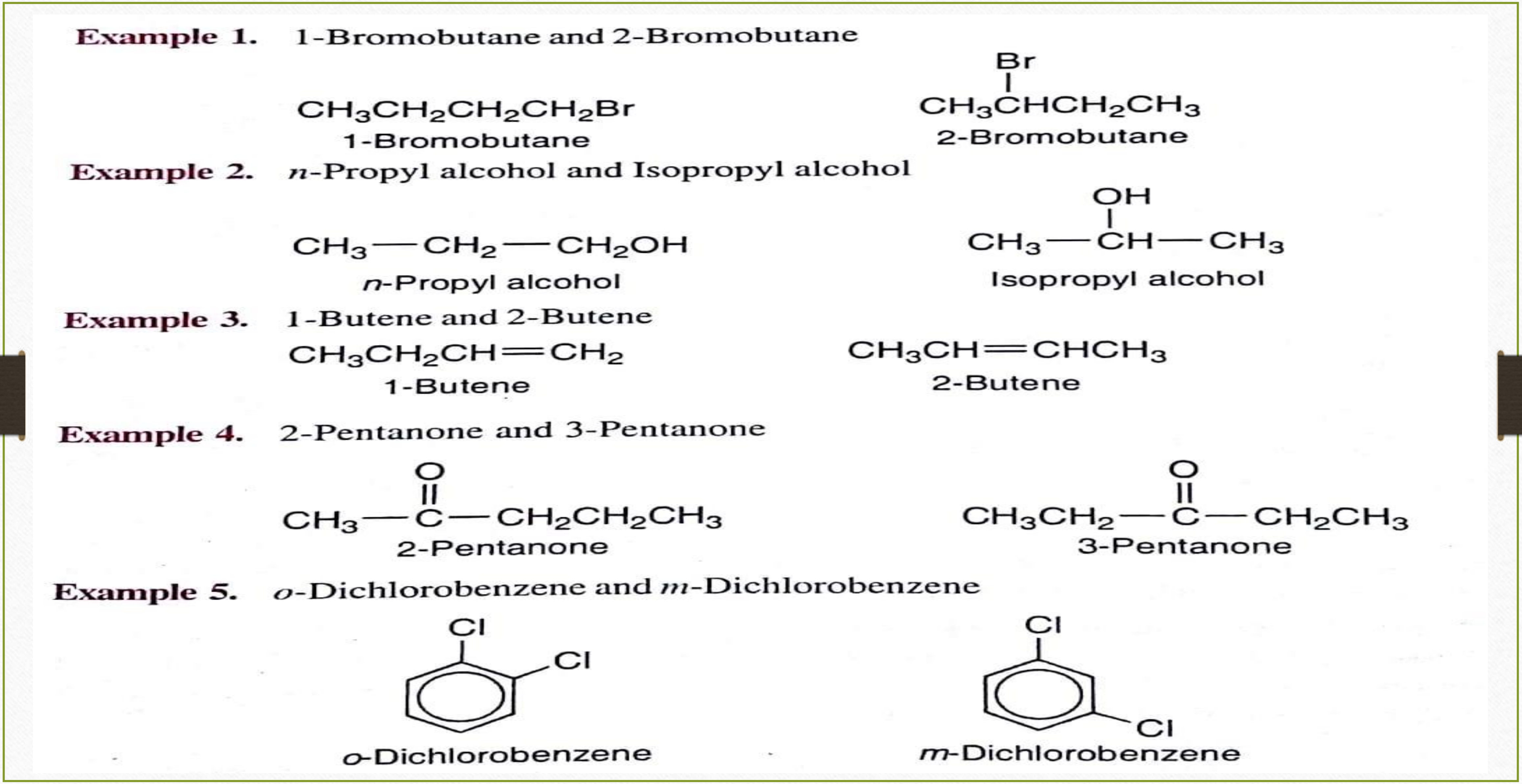

$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{\underset{\underset{\displaystyle CH_3}{|}}{C}}}-CH_3$$

2,2-Dimethylpropane

Position Isomerism

When two or more compounds have structural formulas which differ only in the position of the substituent atom or group on the carbon chain, these are called Position isomers and the phenomenon is termed Positional isomerism.

Simply position isomers have the same molecular formula but differ in the position of a functional group on the carbon chain



Example 1. 1-Bromobutane and 2-Bromobutane

$CH_3CH_2CH_2CH_2Br$

1-Bromobutane

$CH_3\overset{\overset{Br}{|}}{C}HCH_2CH_3$

2-Bromobutane

Example 2. *n*-Propyl alcohol and Isopropyl alcohol

$CH_3-CH_2-CH_2OH$

n-Propyl alcohol

$CH_3-\overset{\overset{OH}{|}}{C}H-CH_3$

Isopropyl alcohol

Example 3. 1-Butene and 2-Butene

$CH_3CH_2CH=CH_2$

1-Butene

$CH_3CH=CHCH_3$

2-Butene

Example 4. 2-Pentanone and 3-Pentanone

$CH_3-\overset{\overset{O}{\|}}{C}-CH_2CH_2CH_3$

2-Pentanone

$CH_3CH_2-\overset{\overset{O}{\|}}{C}-CH_2CH_3$

3-Pentanone

Example 5. *o*-Dichlorobenzene and *m*-Dichlorobenzene

o-Dichlorobenzene

m-Dichlorobenzene

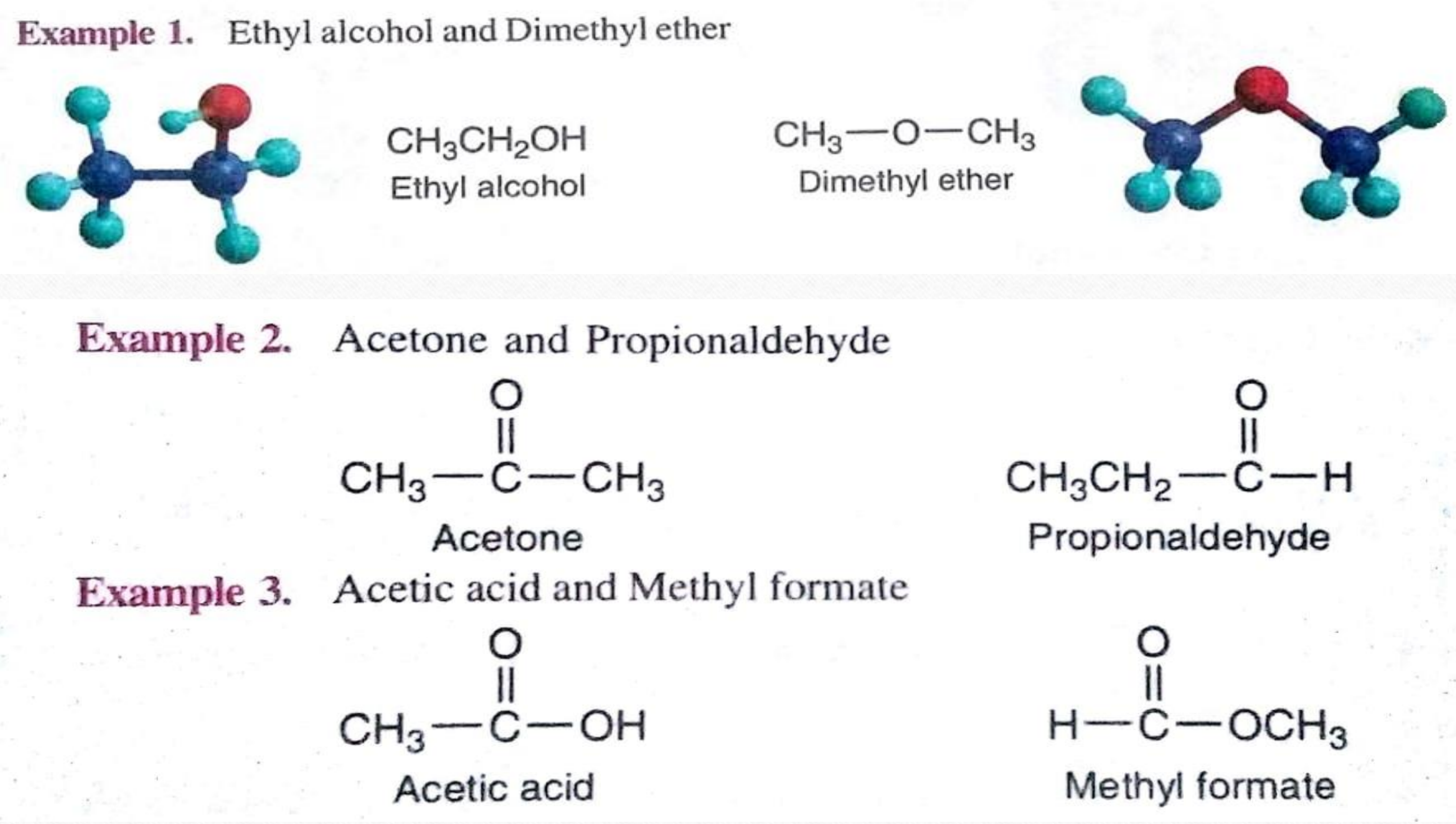
The positional isomerism may also be extended to alkanes and alkynes which differ only in the position of the double or triple bond in their molecules. Thus the molecular formula C_4H_8 stands for two butenes, in which the double bond is different.

Functional Isomerism

When any two compounds have the same molecular formula but possess different functional groups, they are called Functional isomers and the phenomenon is termed Functional isomerism.

In other words substances with the same molecular formula but belonging to different classes of compounds exhibit functional isomerism

Simply, functional isomer have the same molecular formula but different functional groups



Example 1. Ethyl alcohol and Dimethyl ether

CH_3CH_2OH
Ethyl alcohol

CH_3-O-CH_3
Dimethyl ether

Example 2. Acetone and Propionaldehyde

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$

Acetone

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-H$$

Propionaldehyde

Example 3. Acetic acid and Methyl formate

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

Acetic acid

$$H-\overset{\overset{\displaystyle O}{\|}}{C}-OCH_3$$

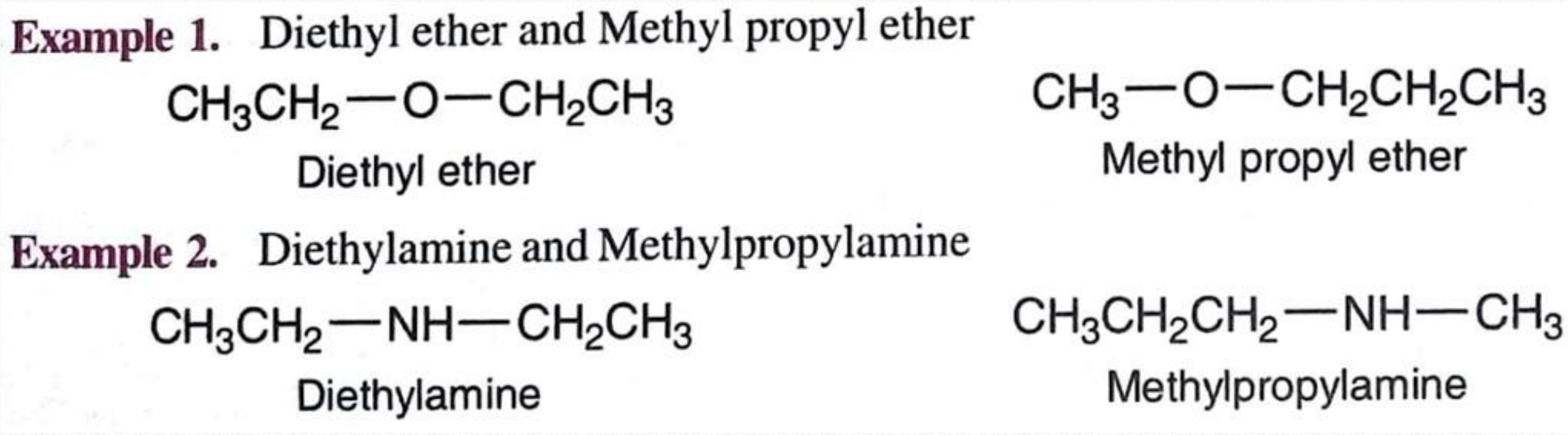
Methyl formate

Metamerism

This type of isomerism is due to the unequal distribution of carbon atoms on either side of the functional group in the molecule of compounds belonging to the same class.

Simply, the unequal distribution of carbon atoms on either side of the functional group are Metamers and the phenomena is Metamerism

Metamerism is shown by members of classes such as ethers, ketones and amines where the central functional group is flanked by two chains. The individual isomers are known as **Metamers**.


Example 1. Diethyl ether and Methyl propyl ether

$CH_3CH_2—O—CH_2CH_3$

Diethyl ether

$CH_3—O—CH_2CH_2CH_3$

Methyl propyl ether

Example 2. Diethylamine and Methylpropylamine

$CH_3CH_2—NH—CH_2CH_3$

Diethylamine

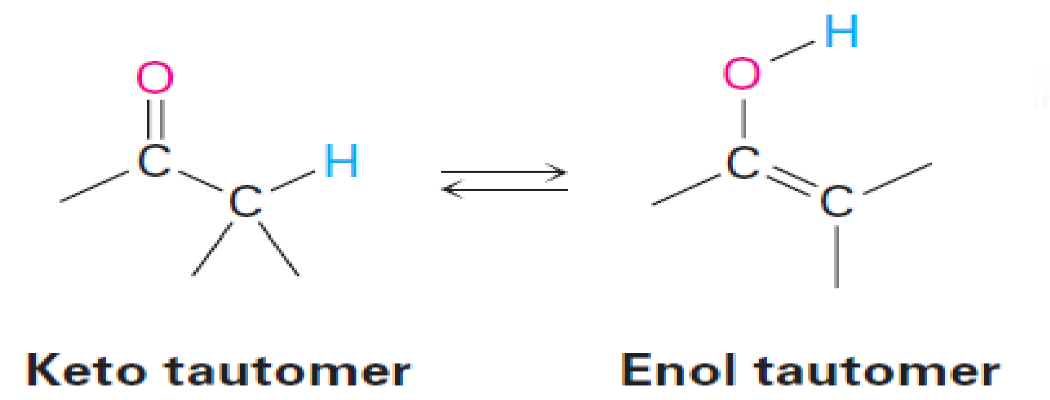
$CH_3CH_2CH_2—NH—CH_3$

Methylpropylamine

Methyl propyl ether and diethyl ether both have the molecular formula $C_4H_{10}O$. The number of carbon atoms attached to the **ethereal group —0—,** is 1 and 3, while 2 and 2 in diethyl ether.

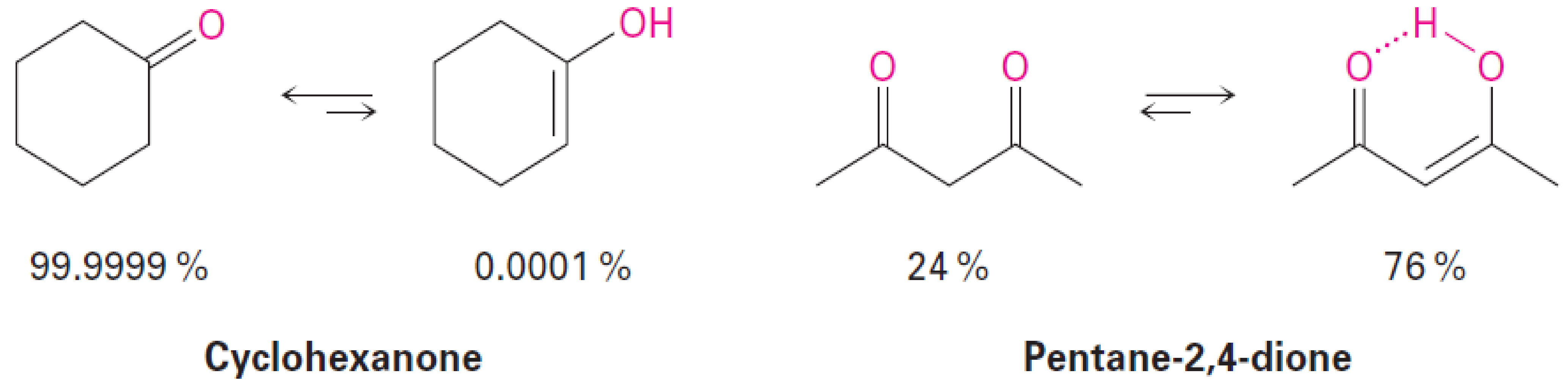
Tautomerism

It is a special type of functional isomerism in which the isomers are in dynamic equilibrium with each other.



A carbonyl compound with a hydrogen atom on its carbon rapidly equilibrates with its corresponding **enol** (*ene ol;* unsaturated alcohol) isomer. This spontaneous interconversion between two isomers, usually with the change in position of a hydrogen, is called ***tautomerism***, from the Greek ***tauto***, meaning "the same," and **meros**, meaning "part." The individual keto and enol isomers are called **tautomers**.

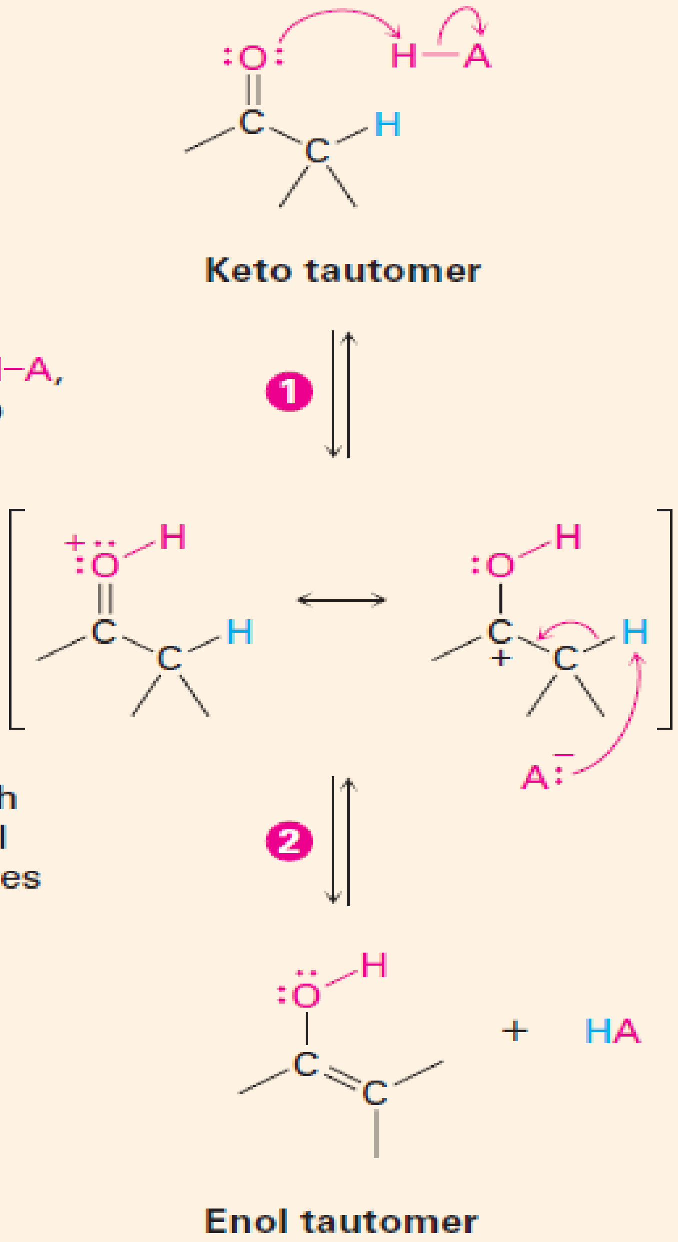
Most monocarbonyl compounds exist almost entirely in the **keto form** at equilibrium, and it’s usually difficult to isolate the pure enol. Cyclohexanone, for example, contains only about 0.0001% of its enol tautomer at room temperature, and the amount of enol tautomer is even less for carboxylic acids, esters, and amides. Only when the enol can be stabilized by conjugation or by intramolecular hydrogen bond formation does the enol sometimes predominate. Thus, pentane-2,4-dione is about 76% enol tautomer.



Keto–enol tautomerism of carbonyl compounds is catalyzed by both acids and bases. Acid catalysis involves protonation of the carbonyl oxygen atom (a Lewis base) to give an intermediate cation that loses H^+ from the **α-carbon** to yield the enol.

Base-catalyzed enol formation occurs because the presence of a carbonyl group makes the hydrogens on the **α-carbon** weakly acidic. Thus, a carbonyl compound can act as an acid and donate one of its **α-hydrogens** to a sufficiently strong base. The resultant resonance-stabilized anion, an enolate ion, is then protonated to yield a neutral compound. If protonation of the enolate ion takes place on the **α-carbon**, the keto tautomer is regenerated and no net change occurs. If, however, protonation takes place on the oxygen atom, then an enol tautomer is formed.

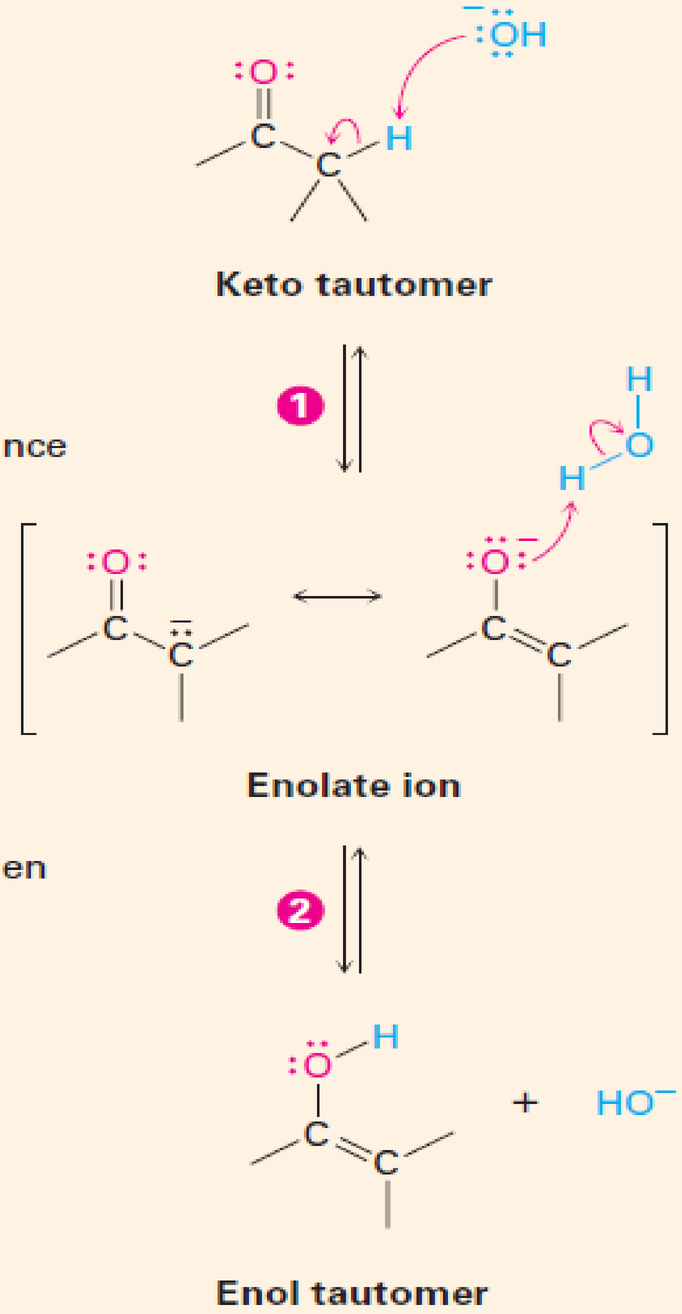
(a) Acidic conditions



① The carbonyl oxygen is protonated by an acid H–A, giving a cation with two resonance structures.

② Loss of H^+ from the α position by reaction with a base A^- gives the enol tautomer and regenerates HA catalyst.

(b) Basic conditions



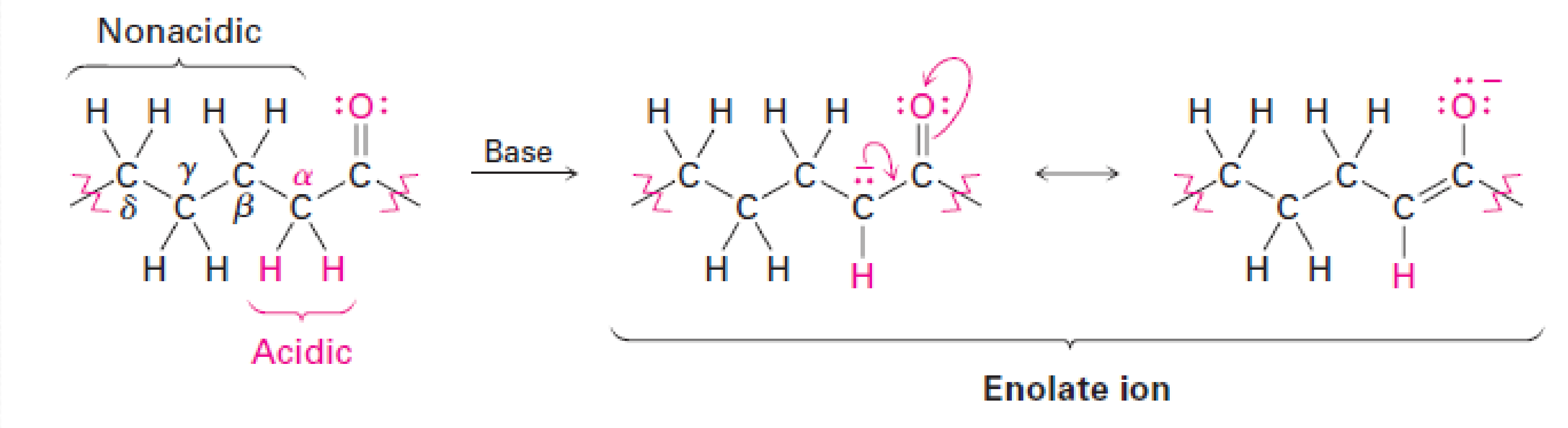
① Base removes the acidic α hydrogen, yielding an enolate ion with two resonance structures.

② Protonation of the enolate ion on oxygen gives the enol and regenerates base catalyst.

(a) Acid catalysis involves initial protonation of the carbonyl oxygen followed by removal **H**$^+$ from the **α**-position.

(b) Base catalysis involves initial deprotonation of the **α**-position to give an enolate ion, followed by reprotonation on oxygen.

Note that only the protons on the **α**-position of carbonyl compounds are acidic. The protons at beta (β), gamma (ϒ), delta, and other positions aren’t acidic because the resulting anions can’t be resonance-stabilized by the carbonyl group.



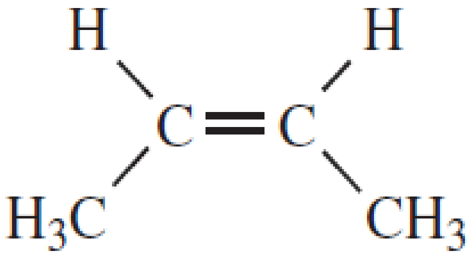
Stereoisomerism

- When isomerism is caused by the different arrangements of atoms or groups in space, the phenomenon is called Stereoisomerism (Greek, Stereos = occupying space).
- **The stereoisomers have the same structural formulas but differ in arrangement of atoms in space**. In other words, stereoisomerism is exhibited by such compounds which have identical molecular structure but different configurations. Configuration refers to the 3-dimentional arrangement of atoms that characterizes a particular compound.

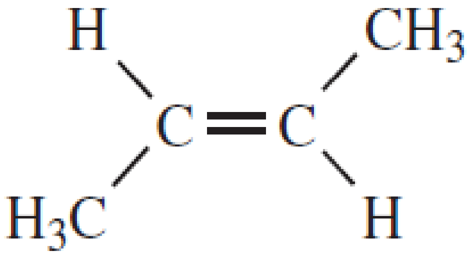
Geometrical (Cis-Trans Isomerism)

Geometrical (Cis-Trans Isomerism)

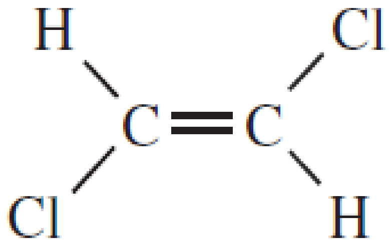
The different geometrical arrangements of the groups about the doubly bonded carbon atom is known as Geometrical isomerism.



cis-2-butene



trans-2-butene



trans-1,2-dichloroethene

When the similar groups lie on the same side it is called the Cis isomer (Latin, cis.=on same side). When similar groups are on the opposite sides, it is called the trains isomer (Latin, trans=across).

Consequently this type of Isomerism is often spoken of as **Cis-Trans Isomerism.**

Geometric isomers possess the same structural formula containing a double bond and differ only in respect of the arrangement of atoms or groups about the double bond.

In general we could say that Geometrical isomerism is shown by alkenes or their derivatives in which two different atoms or groups are attached to each carbon containing the double bond

Geometric Isomerism in Alkenes

The carbon atom of carbon-carbon double bond are sp2 hybridized. The C-C double bond consist of a sigma bond and a pi-bond. The sigma bond is formed via the overlap of sp2 hybrid orbitals, while the pi-bond is formed by the overlap of p-orbitals.

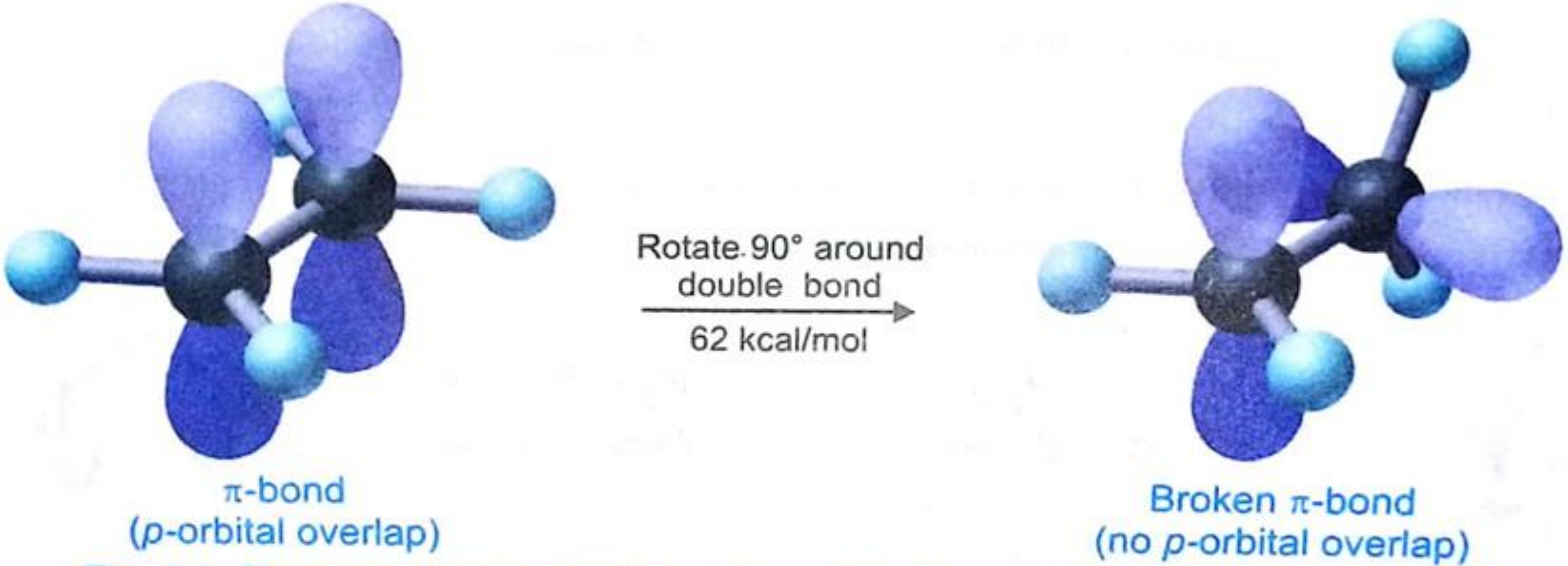
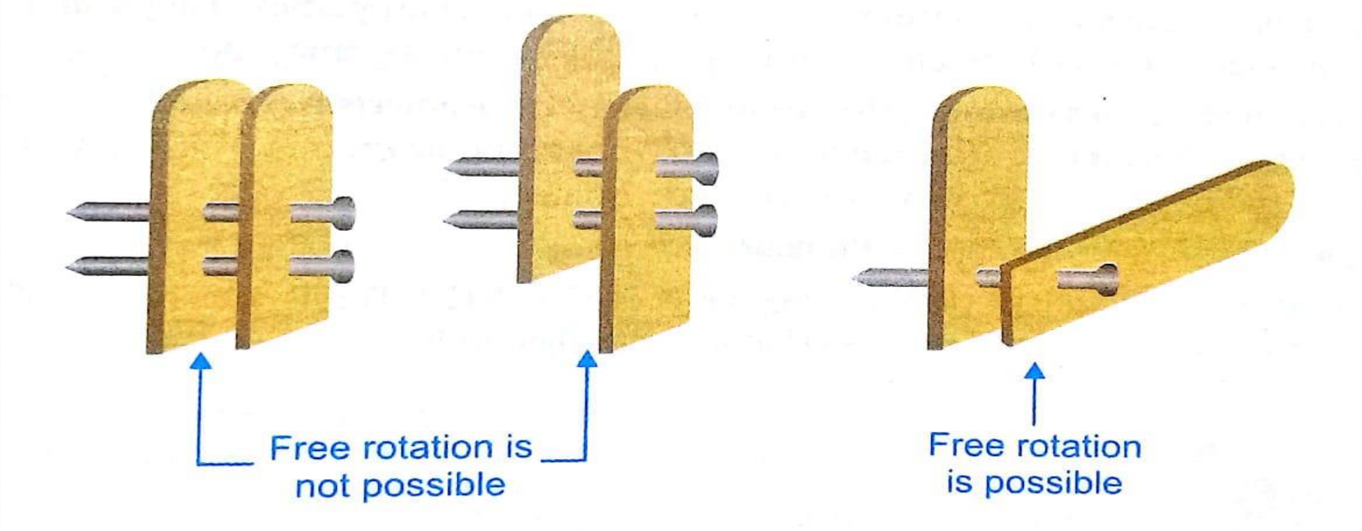


Fig. 4.1. Rotation about π bond is not possible because it would break the π bond.

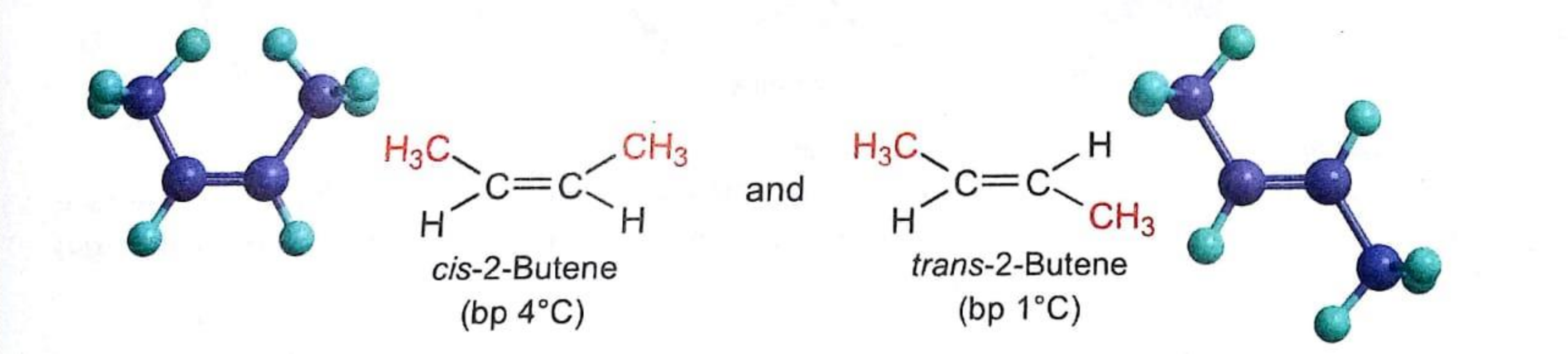
The presence of pi-bond locks the molecule in one position. The two carbon atoms of the C=C bond and the four atoms that are attached to them lie in one plane and their position in space are fixed. Therefore, rotation around the C=C bond is not possible because rotation would break the pi-bond.

This restriction about the carbon double bond is responsible for the geometric isomerism in alkenes.

To understand, take two boards and two nails. Driving one nail through two boards will not prevent free rotation, but once the second nail is used, then the boards cannot be freely rotated.



For example 2-butene exists in two special arrangements i.e., cis-2-butene and trans-2-butene



cis-2-Butene
(bp 4°C)

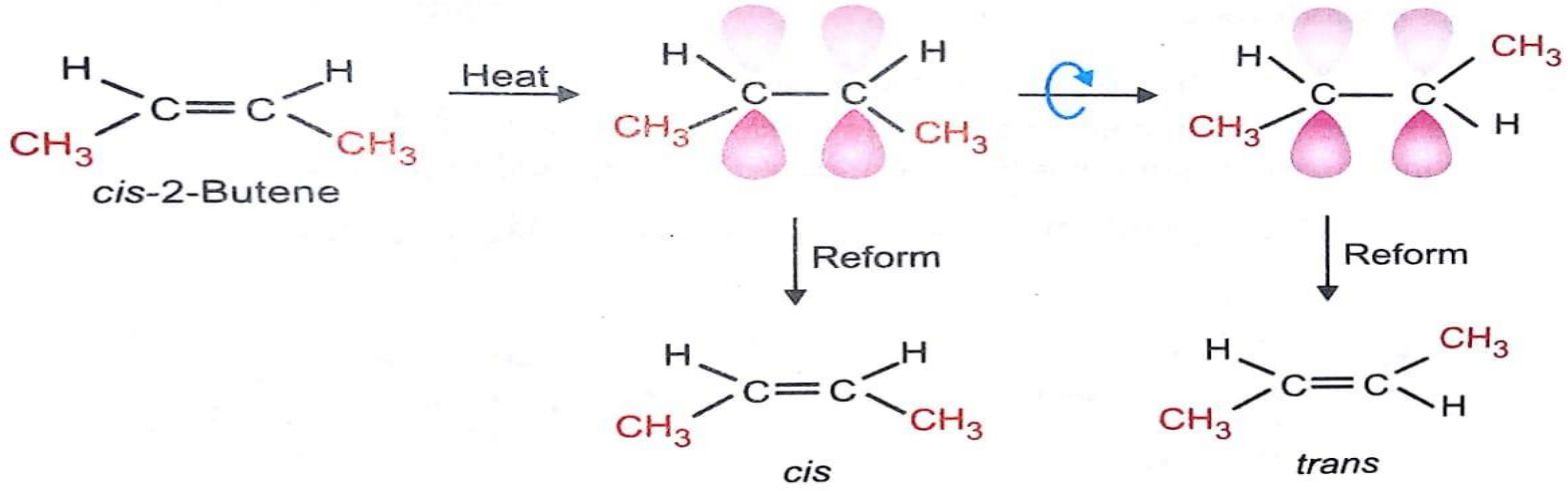
trans-2-Butene
(bp 1°C)

These two compounds are referred to as geometric isomers and are distinguished from each other by the term cis or trans.

The cis isomer is one in which the two similar groups are on the same side of the double bond. While, the trans isomer has two similar groups on the opposite sides of the double bond. Such type of isomerism is therefore often called cis-trans isomerism. These geometric isomers are stereoisomers because they have the same structural formula but different arrangement of atoms in space.

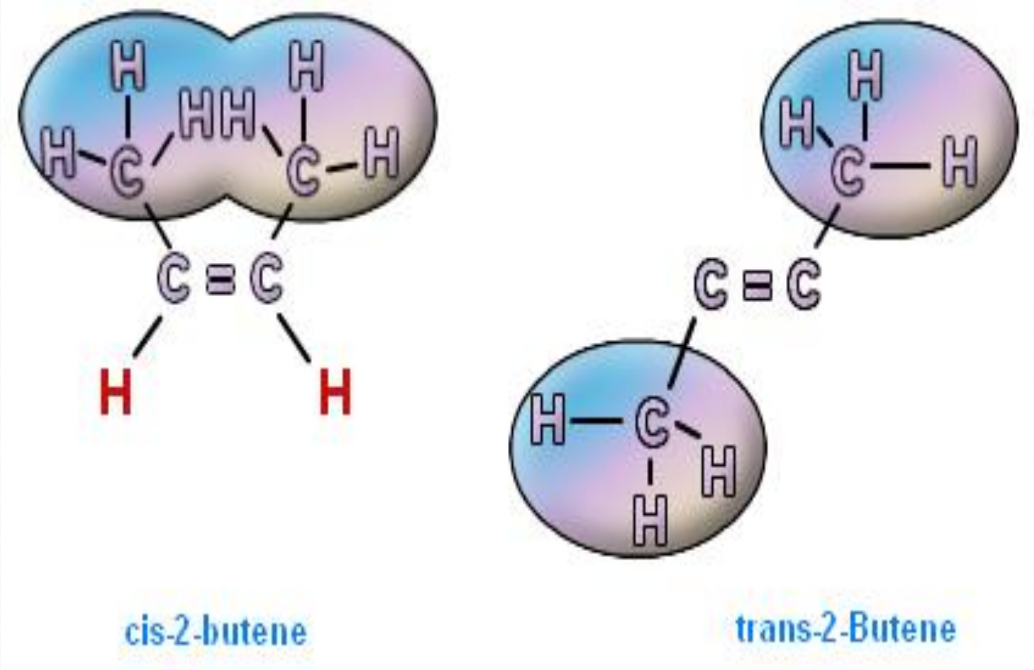
Conversion of cis isomer into trans isomer

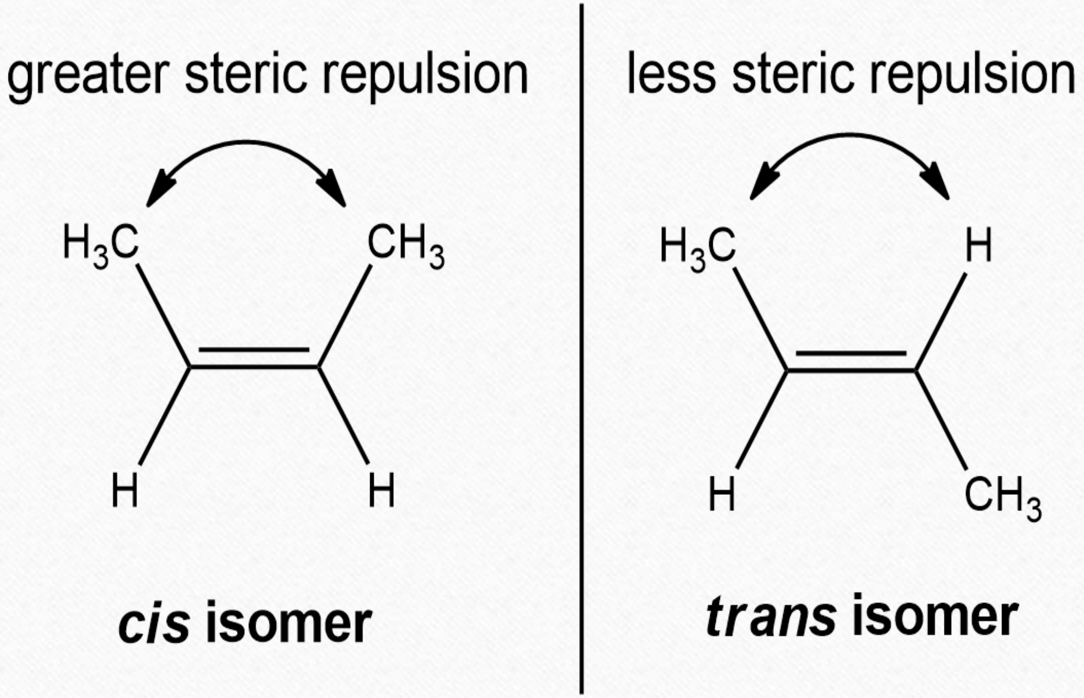
This conversion is only possible if either isomer is heated to a high temperature or it absorb light. The heat supplies about **62 kcal/mole** energy which cause the breaking of pi-bond and thus rotation around the sigma bond become possible. **Upon cooling**, the reformation of pi-bond takes place and gives a mixture of trans and cis isomer. For Example consider cis-2-butene conversion is as follows



Stability

The trans isomers are more stable than the corresponding cis isomer because in cis isomer the bulky groups are on the same side of the double bond. The steric repulsion of the groups make the cis isomer least stable.

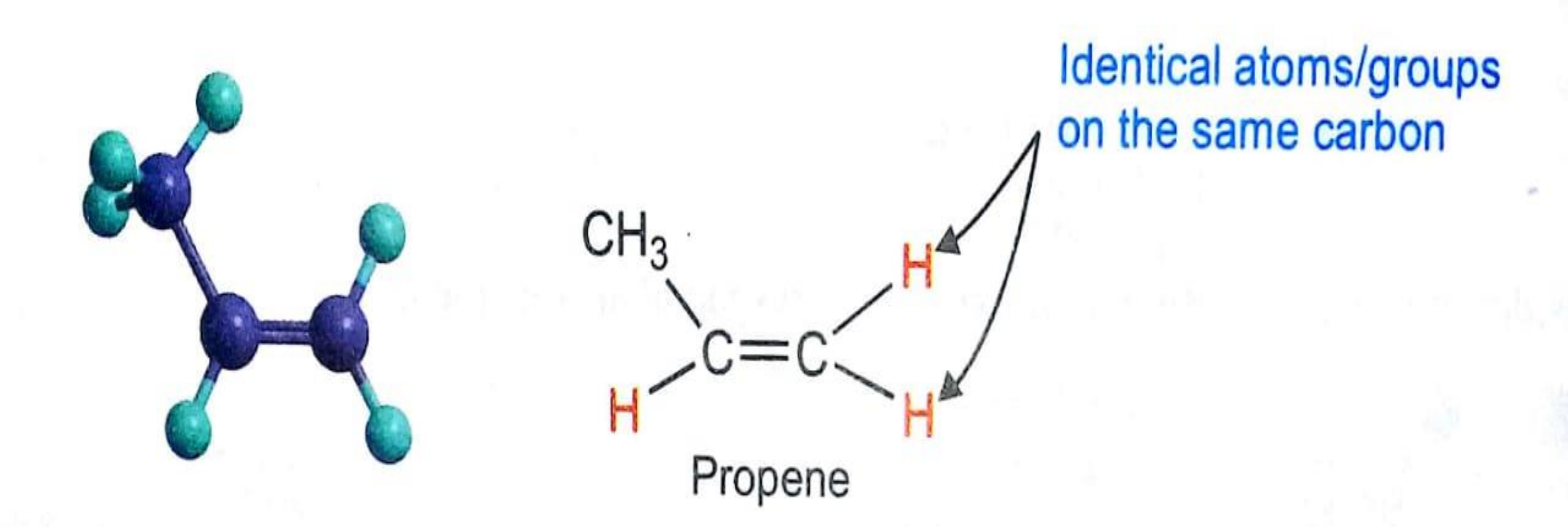




All alkenes do not show geometric isomerism. It is only possible when each double bonded carbon atom is attached to two different atoms or groups.

For example: **Propene $CH_3CH_2=CH_2$**

In propene geometric isomerism is not possible because one carbon on the double bonded carbon has **two identical groups** (H atoms) attached to it.

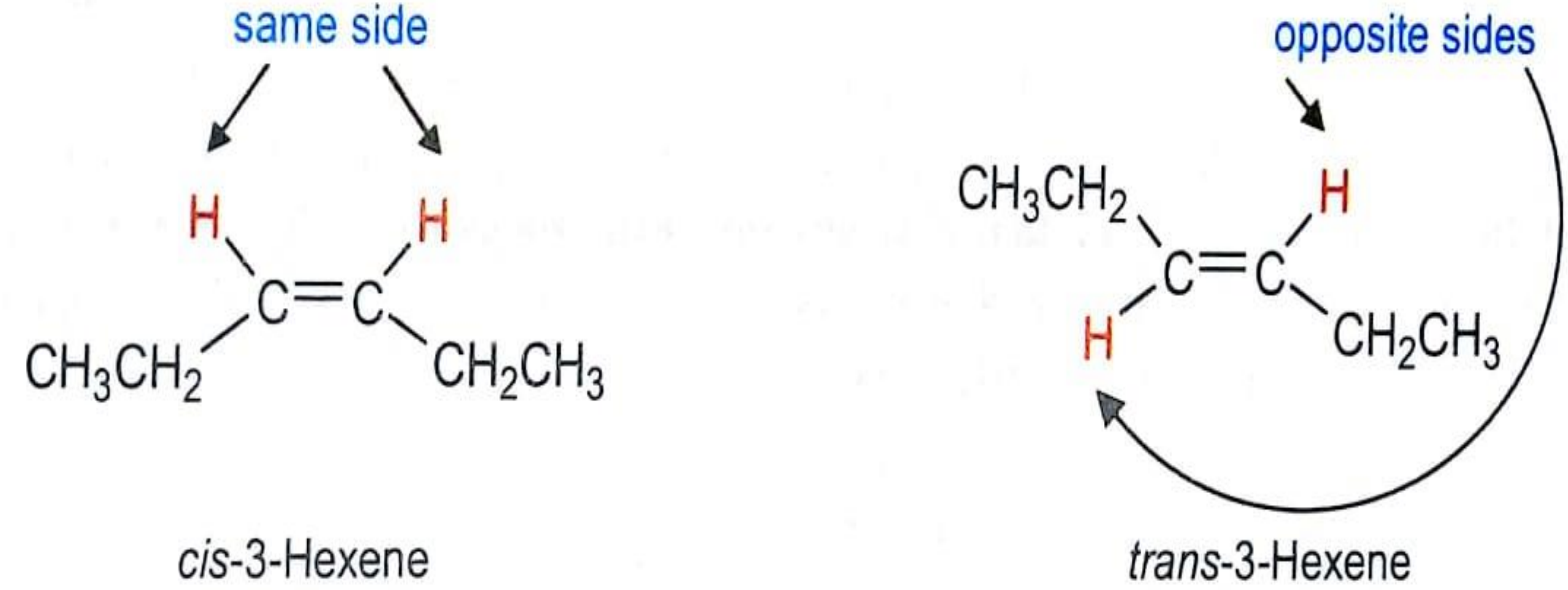


Identical atoms/groups on the same carbon

Propene

3-Hexene $CH_3CH_2CH{=}CHCH_2CH_3$

Geometric isomerism is possible because each double bonded carbon is attached to two **different groups** (CH3CH2 and H) attached to it.

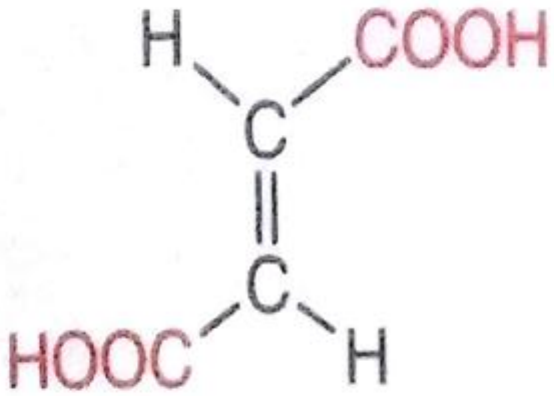


cis-3-Hexene

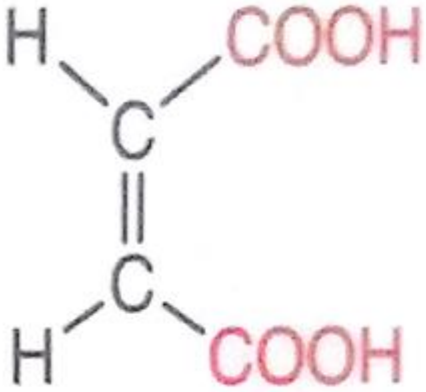
trans-3-Hexene

Butenedioic Acid COOH-CH=CH-COOH

Geometric isomerism is possible because each double bonded carbon is attached to two **different groups** (COOH and H) attached to it.

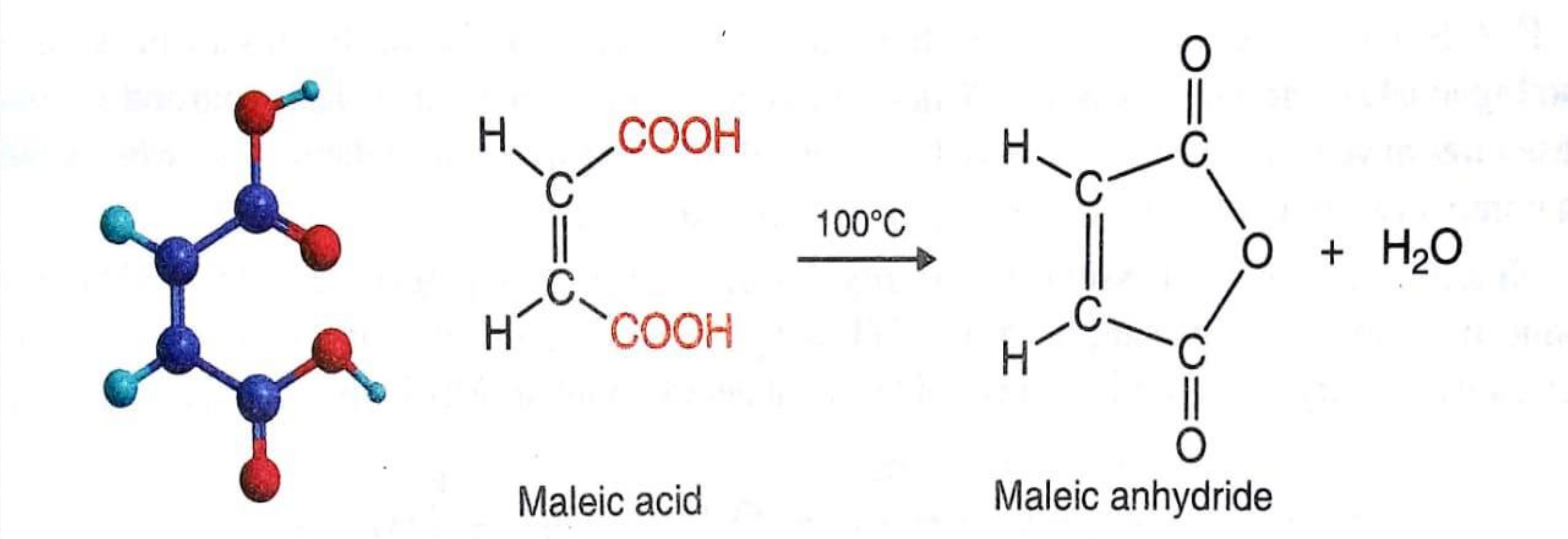


trans-Butenedioic acid
(Fumaric acid)
mp 130°C



cis-Butenedioic acid
(Maleic acid)
mp 288°C

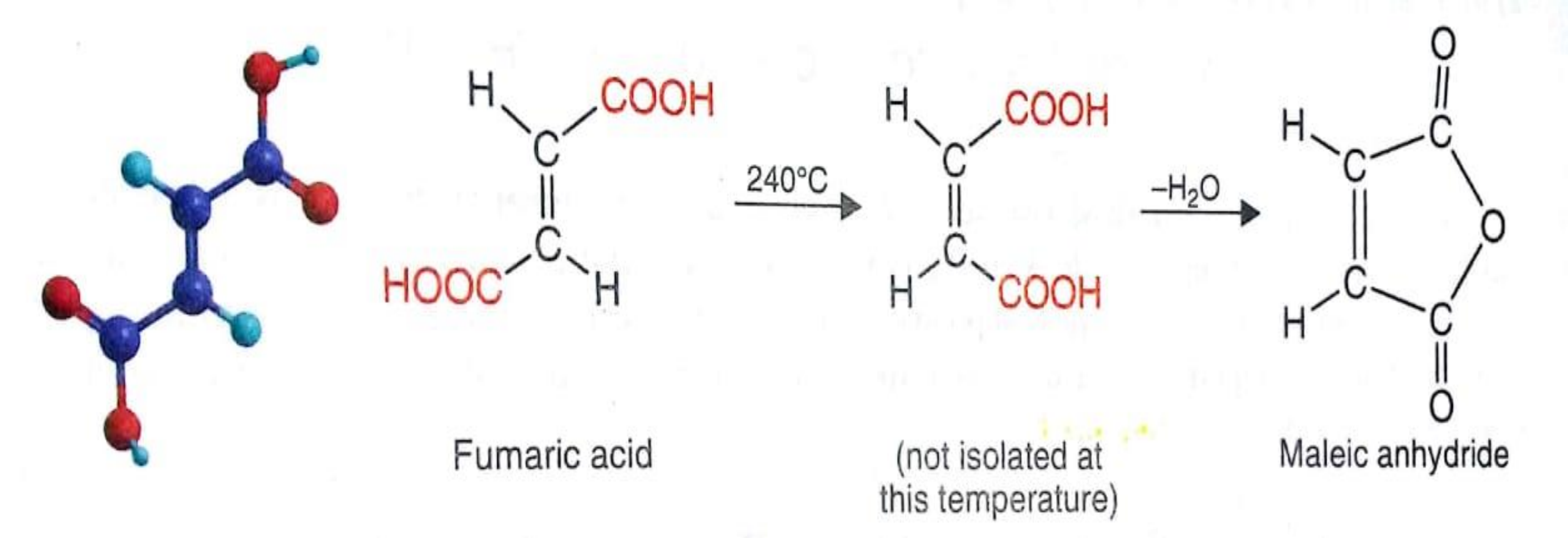
These isomers differ in physical properties such as melting point, dipole moment, and acidities. The trans isomer has no dipole, since it is symmetrical unlike cis isomer. Cis-isomer is strong acid than trans-isomer. In Butenedioic acids even the chemical properties are different because the cis-Butenedioic acid undergoes dehydration at 100 degrees.



Maleic acid

Maleic anhydride

However, the trans-acid does not form anhydride until heated at 240 degrees. At that temperature there is sufficient thermal energy to break the double bond, so that the cis and trans isomers are formed in succession.



Assigning Configurations to Alkenes

- Two systems such as **cis-trans system and E-Z system** can be used to designate the configurations of alkenes
- **Cis-Trans System:** The most common system. Cis-isomer have the substituents on the same side, while trans-isomer have the substituents on the opposite side.
- The configuration of geometric isomers can be designated as cis or trans but for some alkenes, this cis-trans method does not work when there are there are four different groups on the double bond such as BrClC=CFI

(1-bromo-1-chloro-2-fluoro-2-iodoethene)

So in this case then the configuration of these isomers and all other geometrical isomers can be specified by the **E-Z system**.

E-Z System:

This system can be used to specify the configuration about any carbon-carbon double bond unambiguously by using a set of priority rules. This system is devised in 1964 by **R.S. Cahn, C.K. Ingold and V. Prelog.**

Z derived from German, zusammen = together, whereas, **E** from German, entgegen = opposite

- E-alkenes have the groups of highest priority on the opposite sides
- Z-alkenes have the groups of highest priority on the same sides.

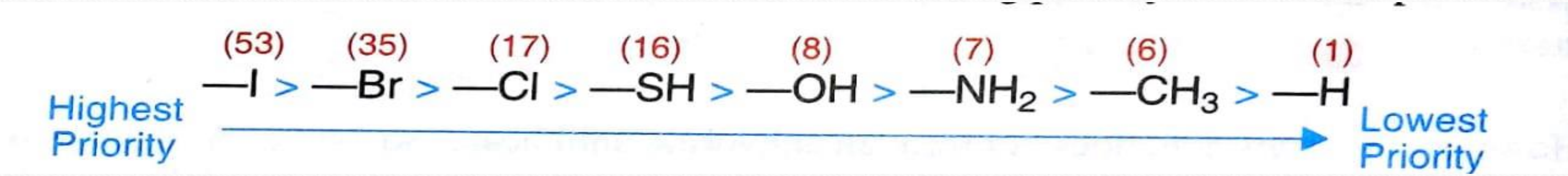
The E-Z system is based on a set of "**priority rules**", which allow you to rank any groups.

The general strategy of the E-Z system is to analyze the two groups at each end of the double bond. At each end, rank the two groups, using the CIP priority rules. Then, see whether the higher priority group at one end of the double bond and the higher priority group at the other end of the double bond are on the same side (Z, from German zusammen = together) or on opposite sides (E, from German entgegen = opposite) of the double bond.

There are four CIP priority rules

Rule 1:

Each atom is assigned a priority. Priority is based on atomic number; higher the atomic number, the higher the priority



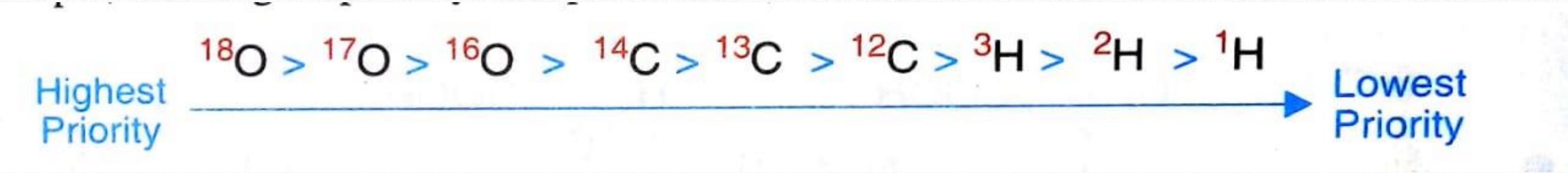
Highest Priority

$\overset{(53)}{\text{—I}} > \overset{(35)}{\text{—Br}} > \overset{(17)}{\text{—Cl}} > \overset{(16)}{\text{—SH}} > \overset{(8)}{\text{—OH}} > \overset{(7)}{\text{—NH}_2} > \overset{(6)}{\text{—CH}_3} > \overset{(1)}{\text{—H}}$

Lowest Priority

Rule 2:

For isotopes, the higher the atomic mass the higher the priority. For example, deuterium (Hydrogen-2) has higher priority than protium (Hydrogen-1)

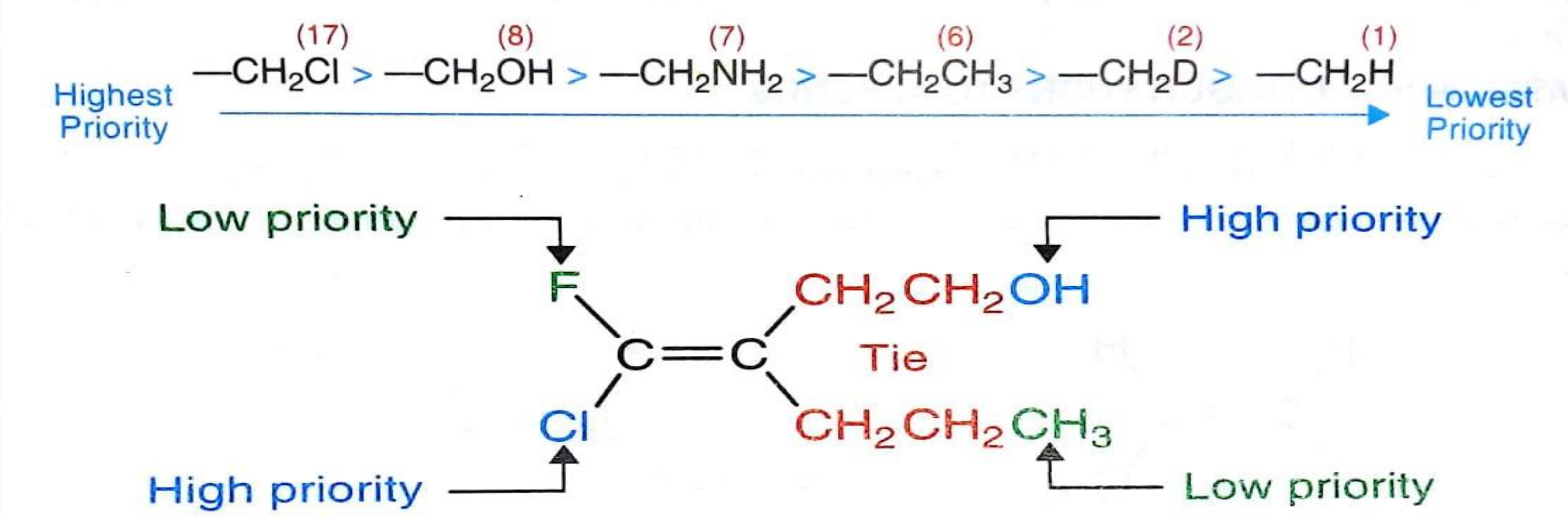


Highest Priority

$^{18}O > ^{17}O > ^{16}O > ^{14}C > ^{13}C > ^{12}C > ^{3}H > ^{2}H > ^{1}H$

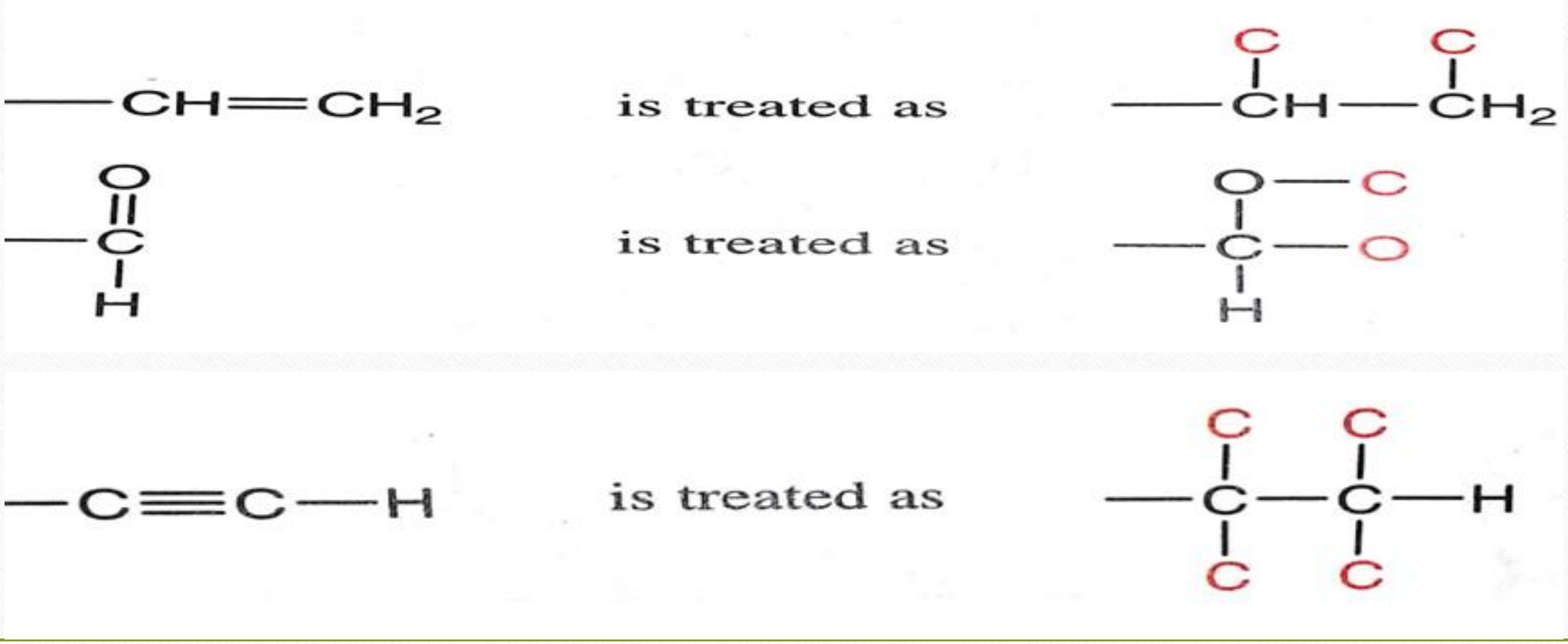
Lowest Priority

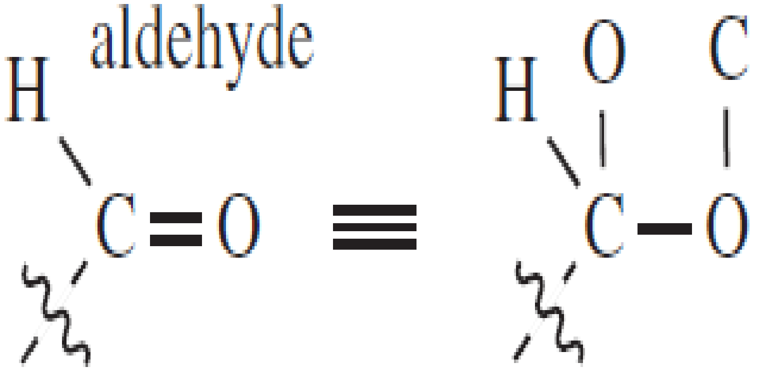
Rule 3: If priority cannot be assigned on the basis of atomic number or atomic mass considering the first atom of a group, then look at the next set of atoms and continue until a priority can be assigned. Priority can be assigned at the first point of difference. If the atoms directly linked to the double bond are the same, then the second, third, fourth, etc. atoms (away from the double bond) are ranked until a difference is found.



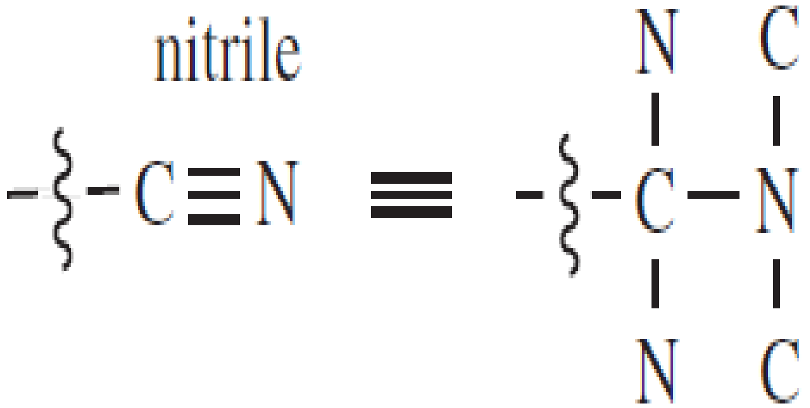
Rule 4: In the case of double or triple bonds, atoms participating in the double or triple bond are considered to be bonded to an equivalent number of similar atoms by single bonds, that is, atoms of double and triple bonds are replicated.

Multiple (double or triple) bonds are assumed to have the same number of single-bonded atoms.



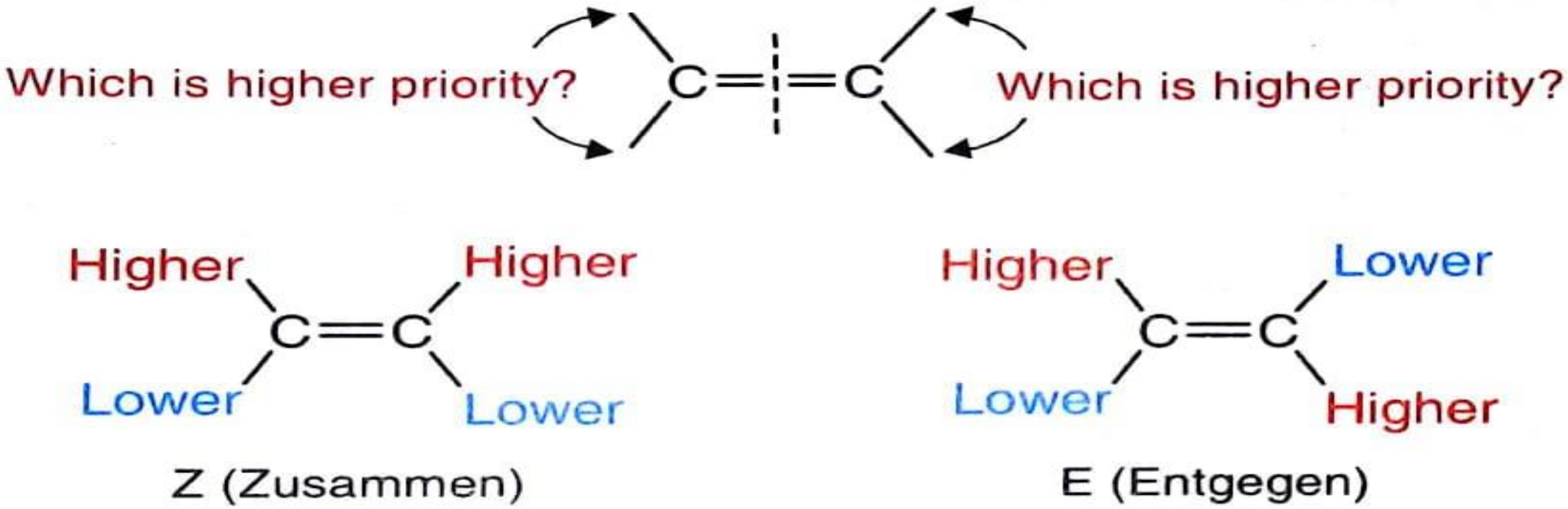


Assume carbon is bonded to two oxygens
Assume oxygen is bonded to two carbons

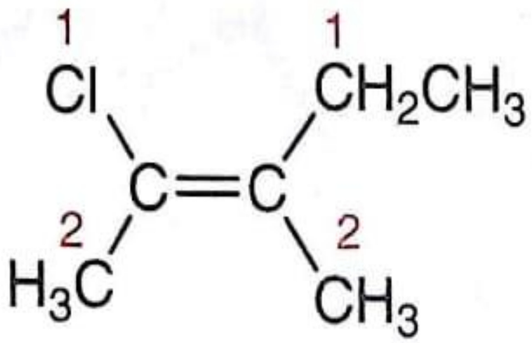


Assume carbon is bonded to three nitrogens
Assume nitrogen is bonded to three carbons

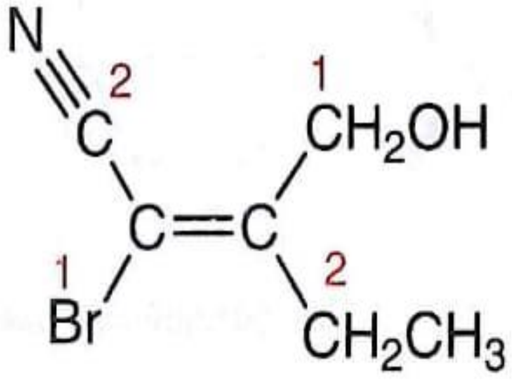
To assign E-Z system, first determine the groups of highest priority on each carbon. If the two highest priority groups are on the same side of the double bond, the configuration is Z. If they are on opposite side of the double bond then the configuration is E.



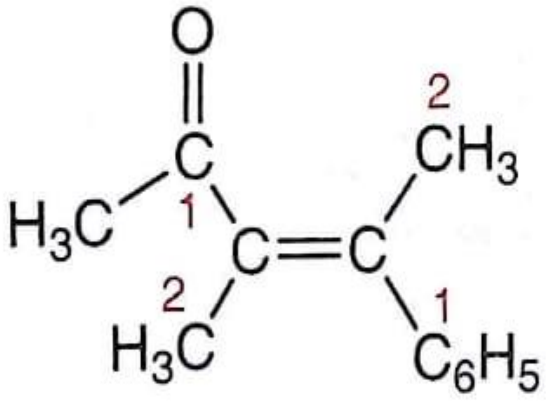
E-alkenes have the groups of highest priority on the *opposite* sides
Z-alkenes have the groups of highest priority on the *same* sides



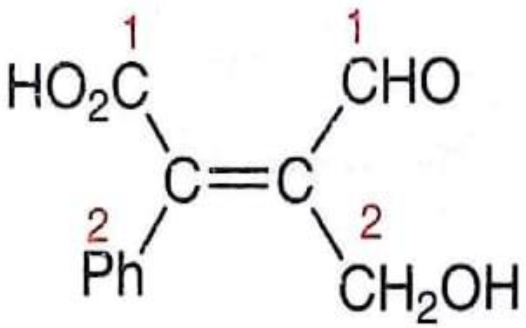
(*Z*)-2-Chloro-3-methyl-2-pentene



(*E*)-2-Bromo-3-hydroxymethyl-2-pentenitrile

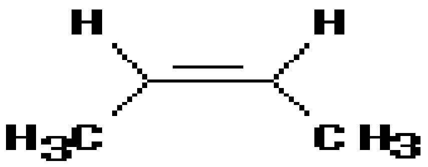


(*E*)-3-Methyl-4-phenyl-3-penten-2-one



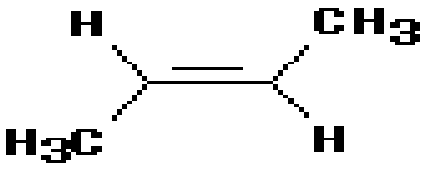
(*Z*)-3-Hydroxymethyl-4-oxo-2-pheny-2-buteonic acid

EXAMPLE 1: BUTENE



cis-2-butene

(Z)-2-butene



trans-2-butene

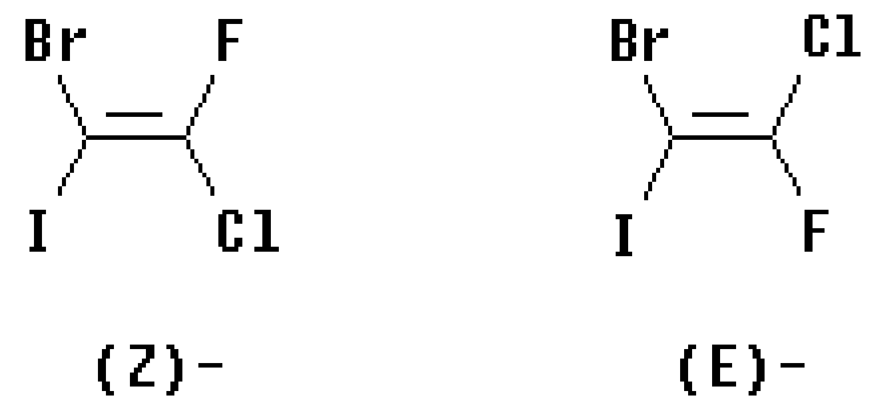
(E)-2-butene

Start with the left hand structure (the cis isomer). On C2 (the left end of the double bond), the two atoms attached to the double bond are C and H. By the CIP priority rules, C is higher priority than H (higher atomic number). Now look at C3 (the right end of the double bond). Similarly, the atoms are C and H, with C being higher priority. We see that the higher priority group is "down" at C2 and "down" at C3. Since the two priority groups are both on the **same** side of the double bond ("down", in this case), they are zusammen = together. Therefore, this is (Z)-2-butene.

Now look at the right hand structure (the trans isomer). In this case, the priority group is "down" on the left end of the double bond and "up" on the right end of the double bond. Since the two priority groups are on **opposite** sides of the double bond, they are entgegen = opposite. Therefore, this is (E)-2-butene.

E-Z will always work, even when cis-trans fails

The figure shows two isomers of an alkene with four different groups on the double bond, **1-bromo-2-chloro-2-fluoro-1-iodoethene.**



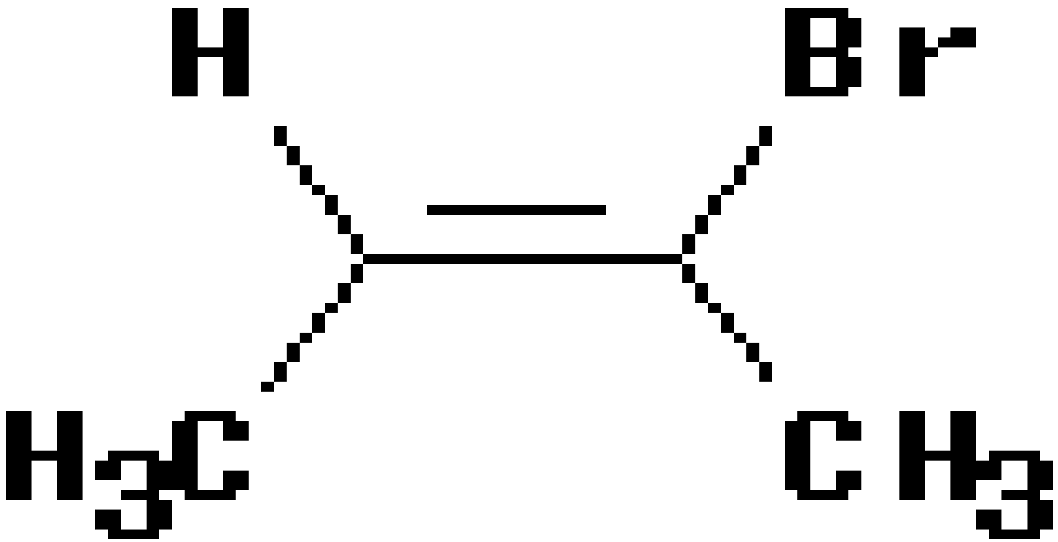
It is impossible to name them as cis or trans. While, the E-Z system works fine.

Consider the left hand structure. On C1 (the left end of the double bond), the two atoms attached to the double bond are Br and I. By the CIP priority rules, I is higher priority than Br (higher atomic number). Now look at C2. The atoms are Cl and F, with Cl being higher priority. We see that the higher priority group is "down" at C1 and "down" at C2. Since the two priority groups are both on the **same** side of the double bond ("down", in this case), they are zusammen = together. Therefore, this is the (Z) isomer. Similarly, the right hand structure is (E).

So the real advantage of the E-Z system is that it will always work. In contrast, the cis-trans system breaks down with many ambiguous cases.

E-Z will work, but may not agree with cis-trans

How you will name 2-bromo-2-butene??



E-Z will work, but may not agree with cis-trans

This molecule is clearly cis. The two methyl groups are on the same side. More rigorously, the "parent chain" is cis.

Now Apply the E-Z system.

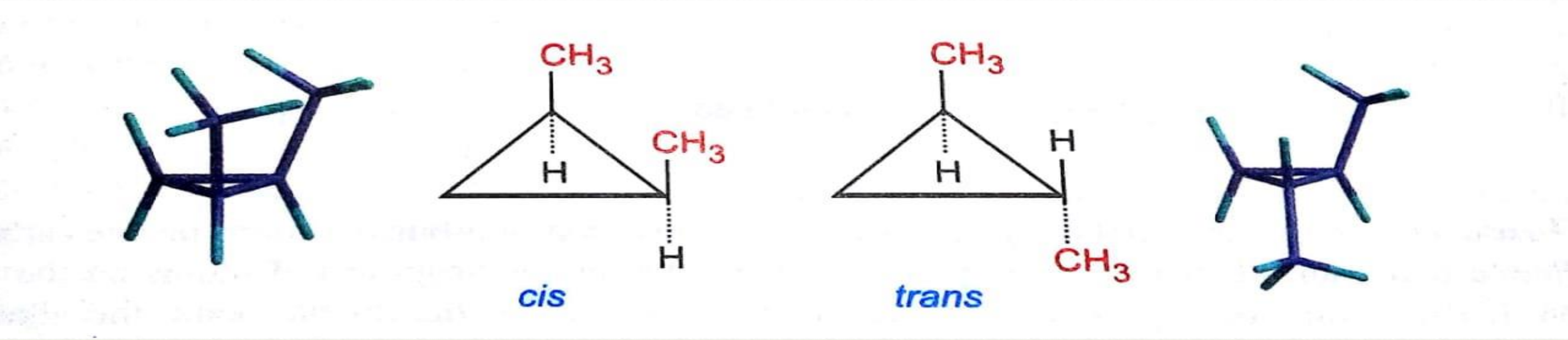
On the left, the methyl is the high priority group -- because the other group is -H. On the right, the methyl is the low priority group -- because the other group is -Br. That is, the high priority groups are $-CH_3$ (left) and -Br (right). Thus the two priority groups are on opposite sides = entgegen = E.

Note:

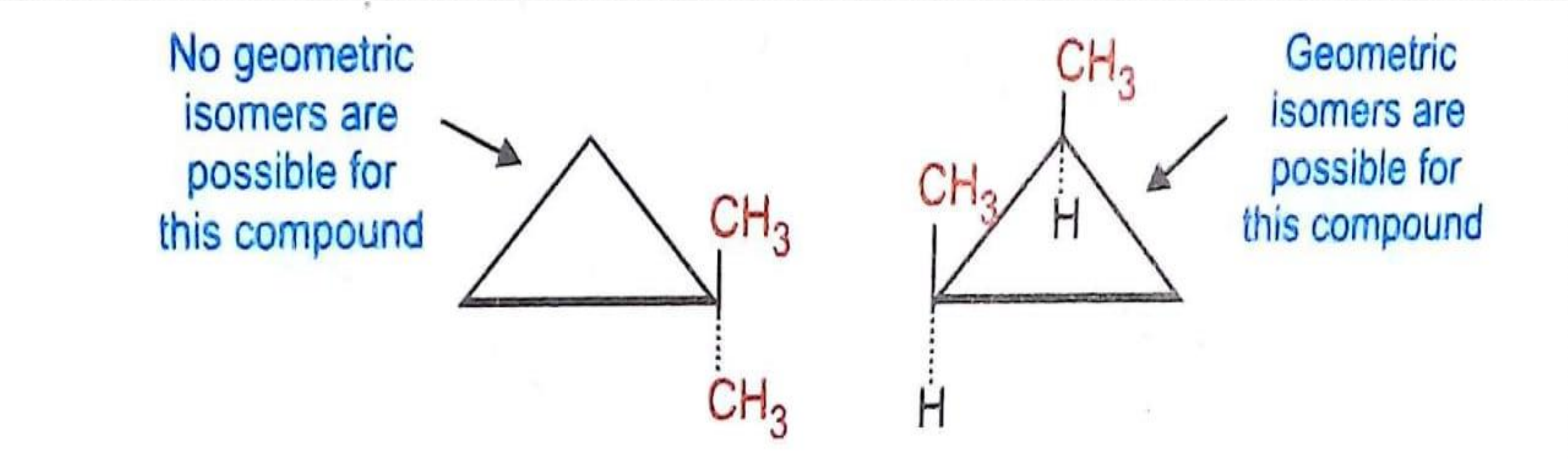
This example should convince you that cis and Z are not synonyms. Cis/trans and E,Z are determined by distinct criteria. There may seem to be a simple correspondence, but it is not a rule. Be sure to determine cis-trans or E,Z separately, as needed.

Geometric Isomerism in Cyclic Compounds

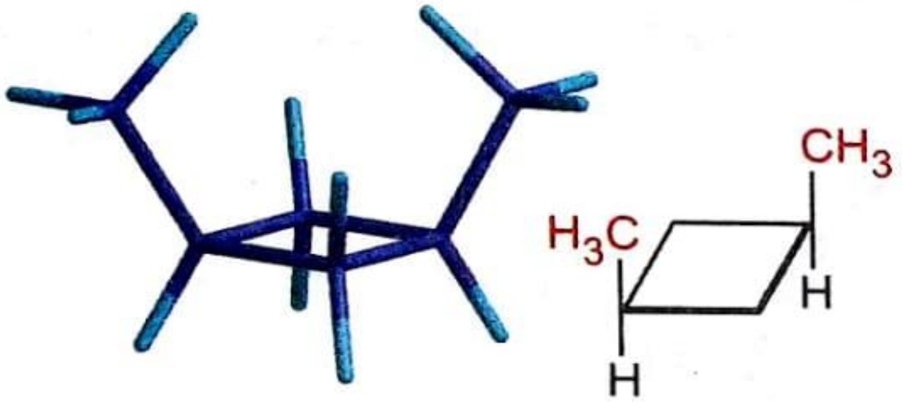
- Geometric isomerism is also possible in cycloalkanes. There can be no rotation about carbon-carbon single bonds forming a ring because rotation would break the bonds and break the ring.
- For example 1,2 dimethylcyclopropane exist in two isomeric forms



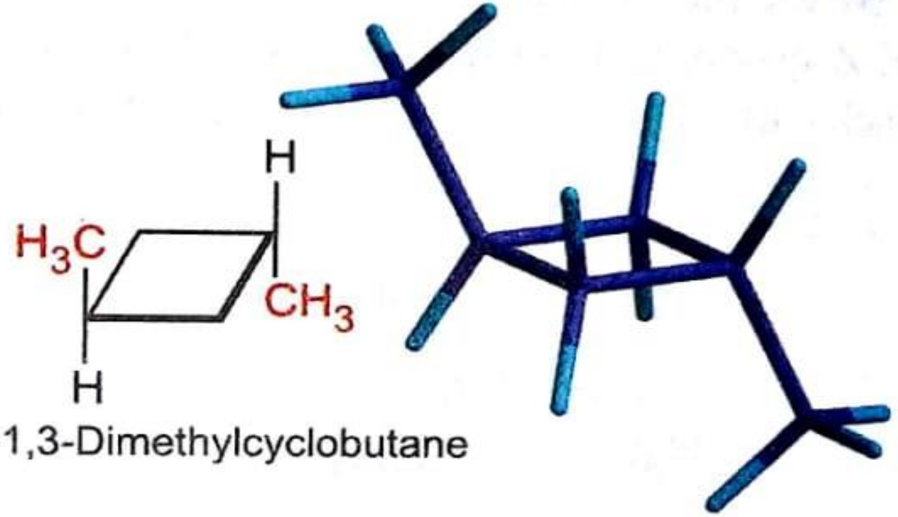
A requirement for geometric isomerism in cyclic compounds is that there must be at least two other groups besides hydrogens on the ring and these must be on different ring carbons.



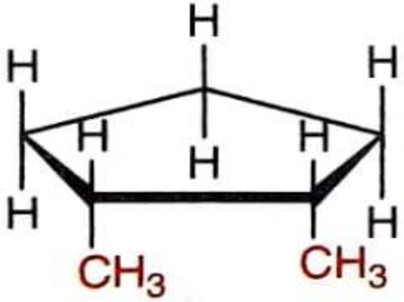
More Examples of Cis-Trans Isomerism



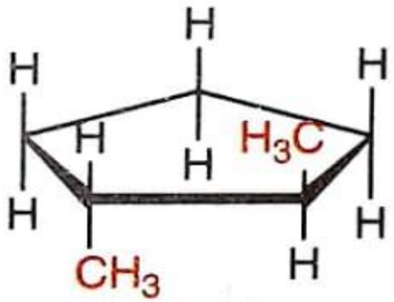
cis-1,3-Dimethylcyclobutane



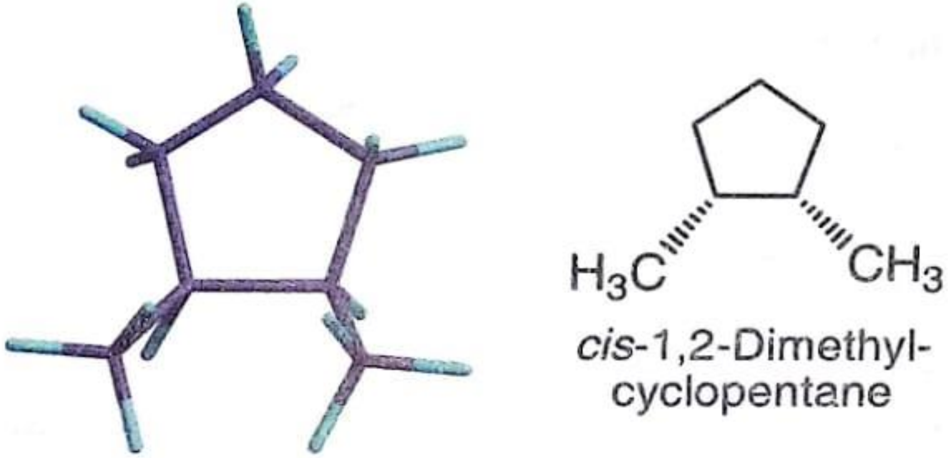
trans-1,3-Dimethylcyclobutane



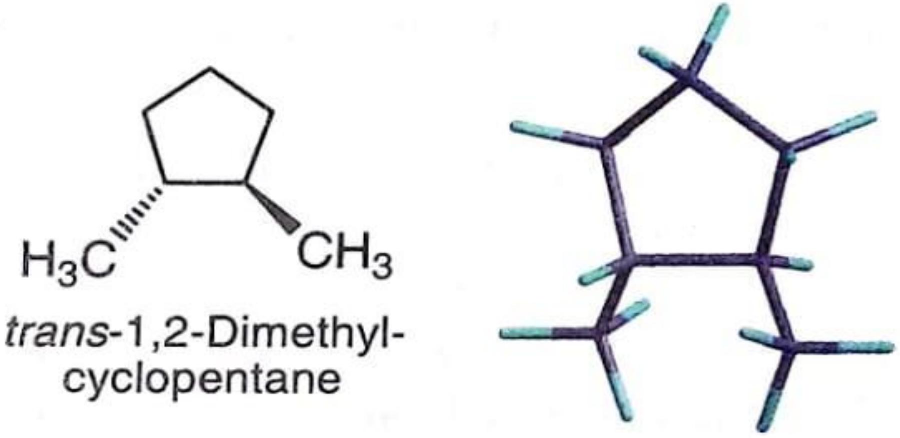
cis-1,2-Dimethylcyclopentane



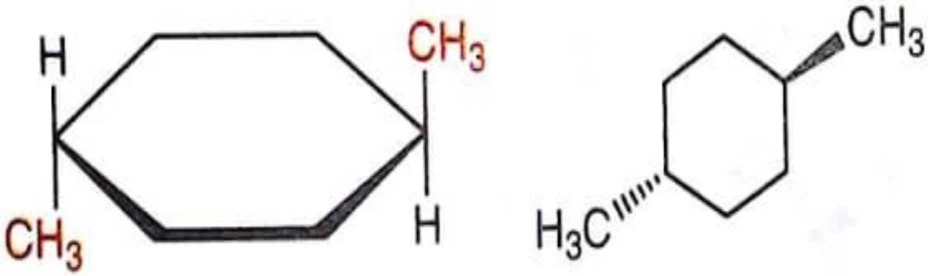
trans-1,2-Dimethylcyclopentane



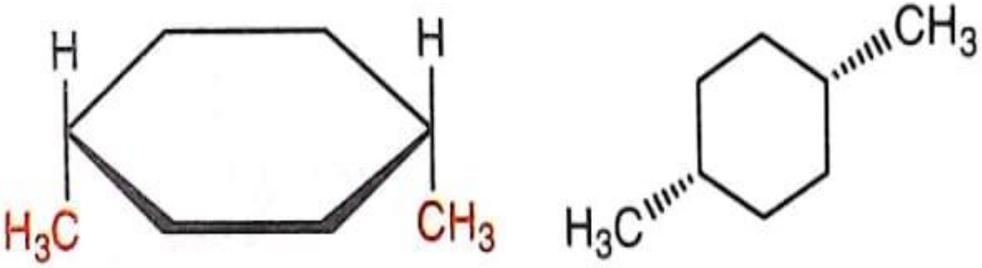
cis-1,2-Dimethylcyclopentane



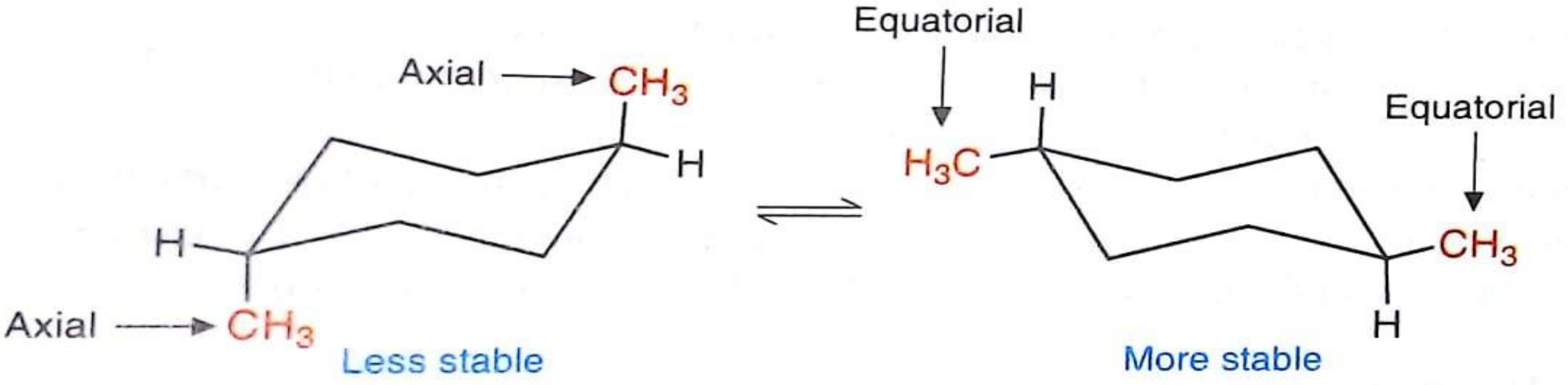
trans-1,2-Dimethylcyclopentane



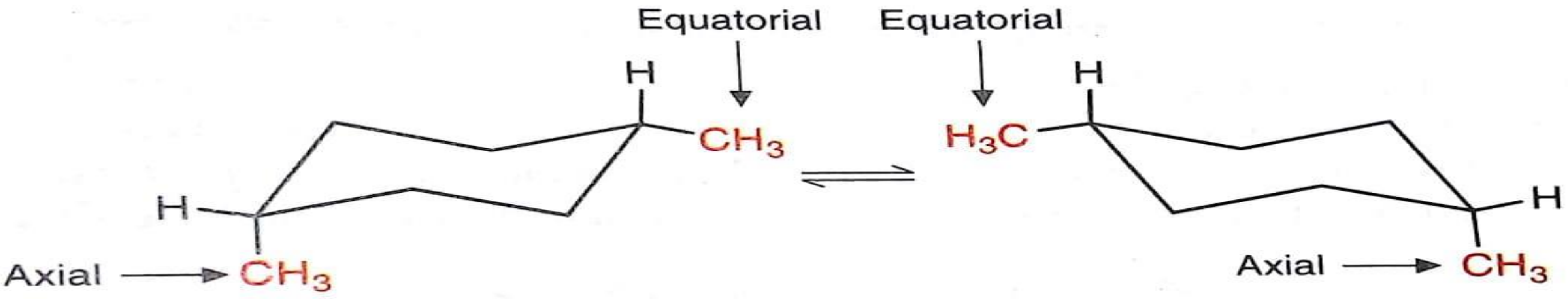
trans-1,4-Dimethylcyclohexane



cis-1,4-Dimethylcyclohexane



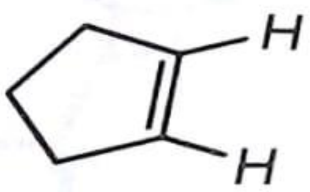
trans-1,4-Dimethylcyclohexane



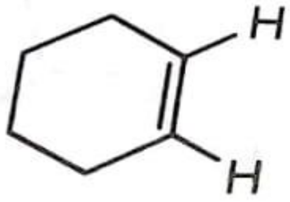
cis-1,4-Dimethylcyclohexane
(These conformations are of equal stability)

Geometric Isomerism in Cycloalkenes

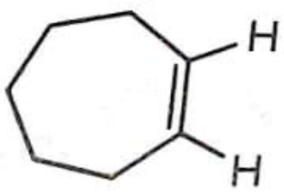
Structure formulas of four Cycloalkenes



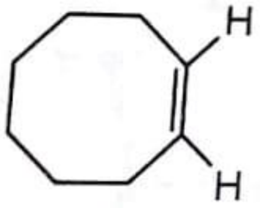
Cyclopentene



Cyclohexene



Cycloheptene



Cyclooctene

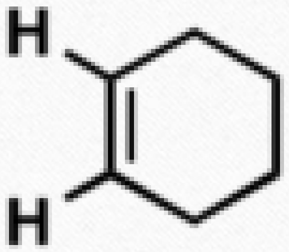
In these representations, the configuration about each double bond is cis. Because of angle strain, it is not possible to have a trans configuration in cycloalkenes of seven or fewer carbons. Therefore, double bonds in cycloalkenes in seven or fewer carbons are exclusively cis rather than trans.

Cis and trans alkenes in rings

Double bonds in cycloalkenes of 7 or fewer carbons are exclusively *cis*.

The *trans* isomers are too strained to stable under ordinary conditions

Cis



Trans

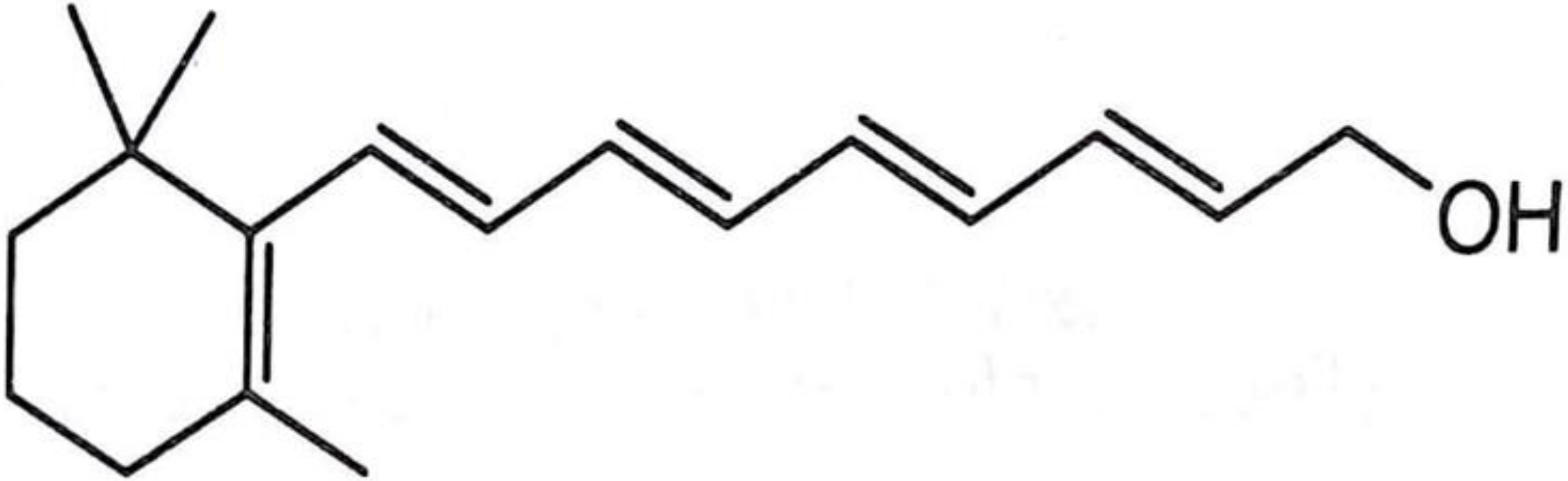
(extremely unstable due to ring strain)

For this reason we can omit the *cis*- when naming "cyclohexene".
A "cis" configuration is assumed.

To date only **trans-cyclooctene** is smallest trans-cycloalkene that has been prepared in pure form and is stable at room temperature. Although in this trans-cycloalkene form there is considerable intramolecular strain.

For an alkene with one carbon-carbon double bond that can show cis-trans isomerism, two cis-trans isomers are possible. So far an alkene with n number of carbon-carbon double bonds, each of which can show cis-trans isomerism, 2^n *cis-trans* isomers are possible.

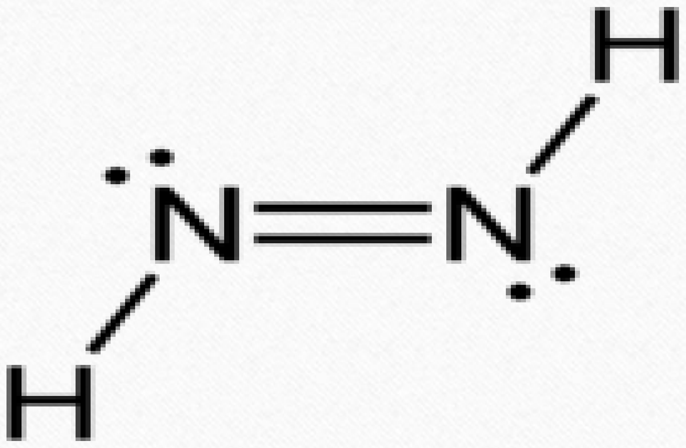
Vitamin A is a biologically important compound for which a number of cis-trans isomers are possible. There are four carbon-carbon double bonds in the chain of carbon atoms bonded to the substituted cycloalkene ring, and each has the potential for cis-trans isomerism. Thus $2^4 = 16$ cis-trans isomers are possible.



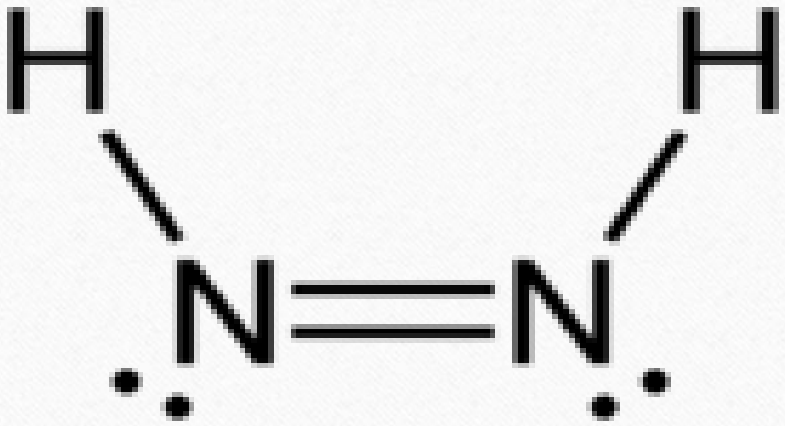
Vitamin A (Retinol)

Geometric Isomerism in Oximes and AZO Compounds

Geometric isomerism is also possible in compounds containing oximes **(C=N)** and Azo compounds **(N=N).** Like alkenes, both double bonded carbon and nitrogen are sp2 hybridized. The lone-pair electrons on nitrogen resides in the sp2 hybrid orbitals. **The lone pair fixes the position of all substituents around C=N and N=N double bonds, thus resulting in geometric isomerism.**

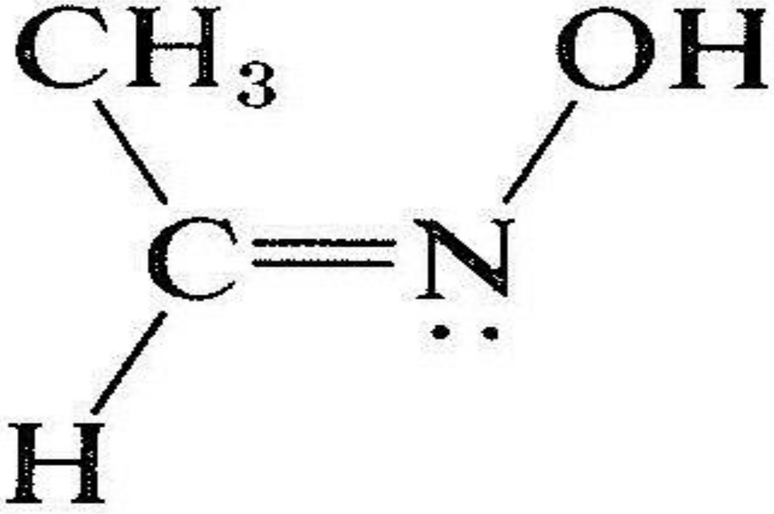


trans-diazene

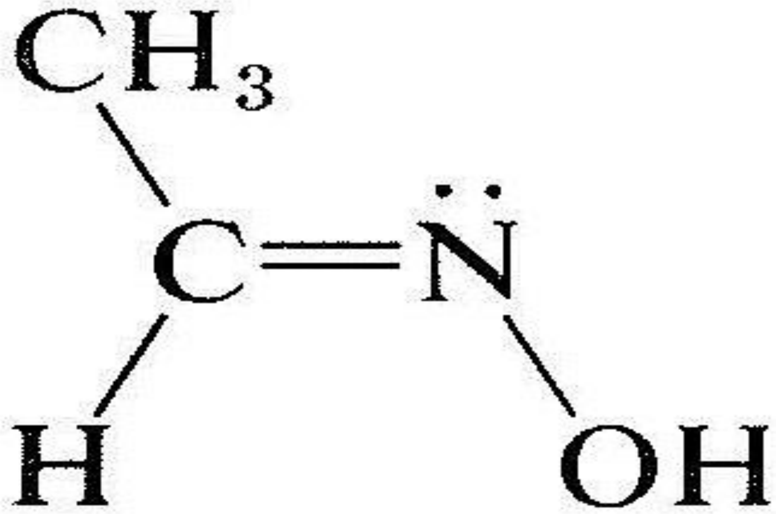


cis-diazene

syn = equivalent to Cis, & anti = equivalent to trans

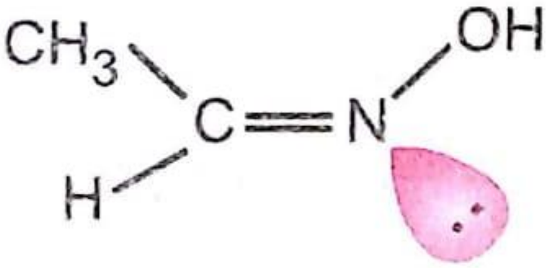


Z (syn)

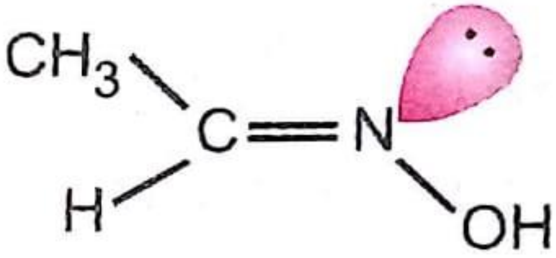


E (anti)

Isomeric Aldoximes :

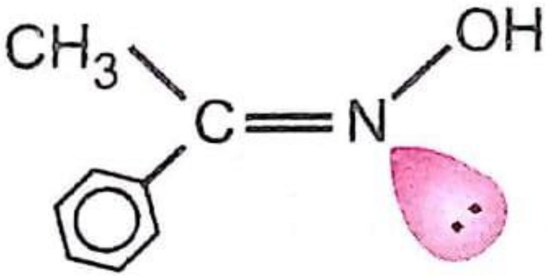


(Z)-Acetoaldoxime

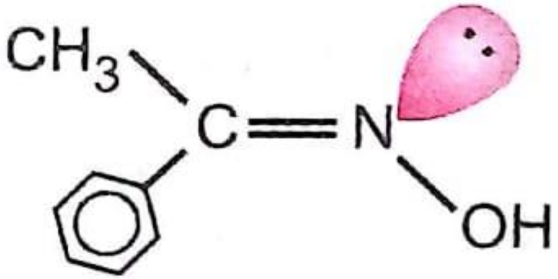


(E)-Acetoaldoxime

Isomeric Ketoximes :



(E)-Acetophenoneoxime



(Z)-Acetophenoneoxime

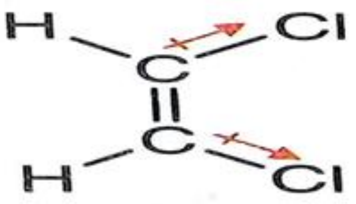
Determination of configuration of isomers

Physical Properties: The difference in the structure of cis and trans isomers is reflected in their physical properties. Some such properties are illustrated below

Dipole moments: The trans isomers have normally less dipole moments than cis isomer. Consider the cis and trans isomers of 1,2-dichloroethylene.

The trans isomer has a dipole moment of zero, because the two bond moments C-Cl bonds are opposed because of the symmetry of the molecule. On the other hand, the cis isomer being non-symmetrical has dipole moment because the bond moments are not opposed here.

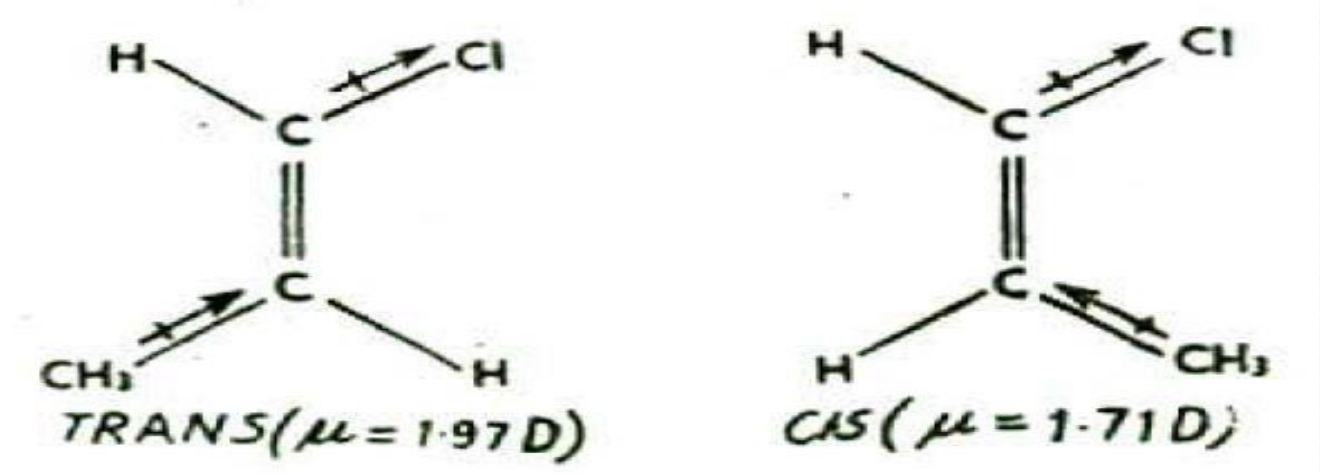
trans ($\mu = 0.01D$)



cis ($\mu = 1.89D$)

In such alkenes which have one polar substituent different from other, the dipole moment will not be normally zero but would be smaller than the corresponding cis isomer.

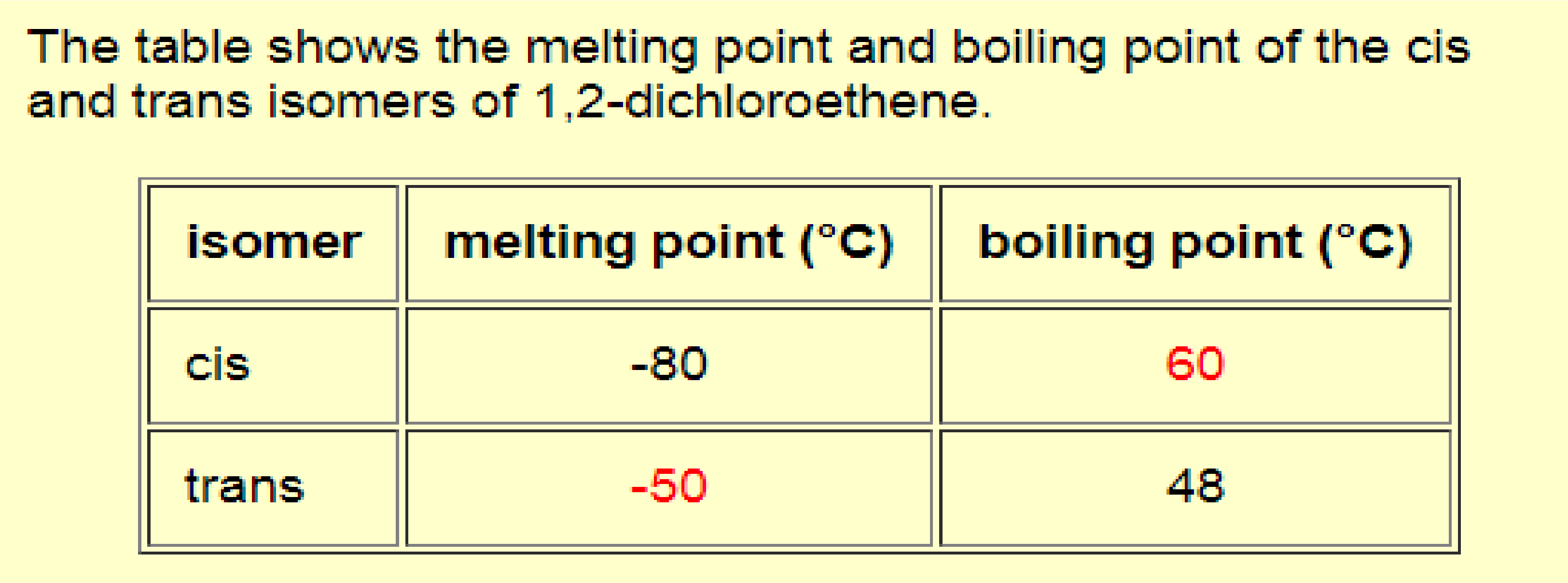
If, however, one substituent is electron-donating and the other electron-withdrawing, the bond moments are fully additive in trans isomer. Thus the trans isomer in this case has a higher dipole moment than the corresponding cis isomer.



Therefore, it is possible to assign configuration to a pair of isomers on the basis of dipole measurements, provided the nature of substituents is known.

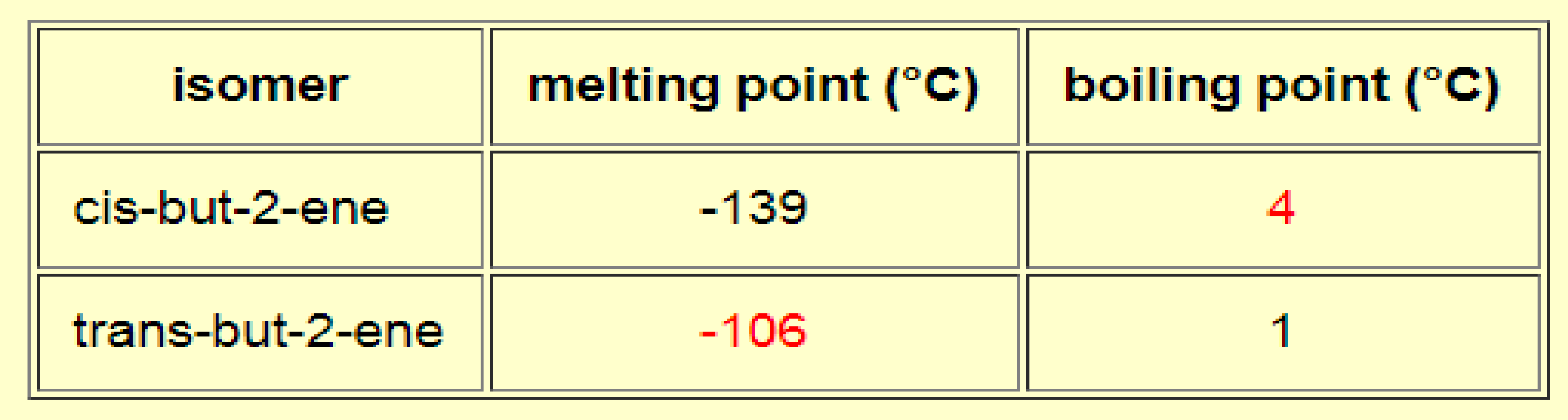
Melting point and related phenomena

In general, a trans isomer has greater symmetry than the corresponding cis isomer. Thus it packs more easily in the crystal lattice and hence has a higher melting point. Cis compounds, on the other hand, have low melting points since they being less symmetrical do not pack well in the crystal lattice. Moreover, the poor packing leads to weaker forces of attraction between the molecules in the crystal lattice. The **weaker forces of attraction** can be easily broken by the dielectric constant of the solvents and hence the cis isomers have greater solubilities than their trans isomers. Cis compounds have also been found to have higher heats of formation and ionization constants as acids.



The table shows the melting point and boiling point of the cis and trans isomers of 1,2-dichloroethene.

isomer	melting point (°C)	boiling point (°C)
cis	-80	60
trans	-50	48

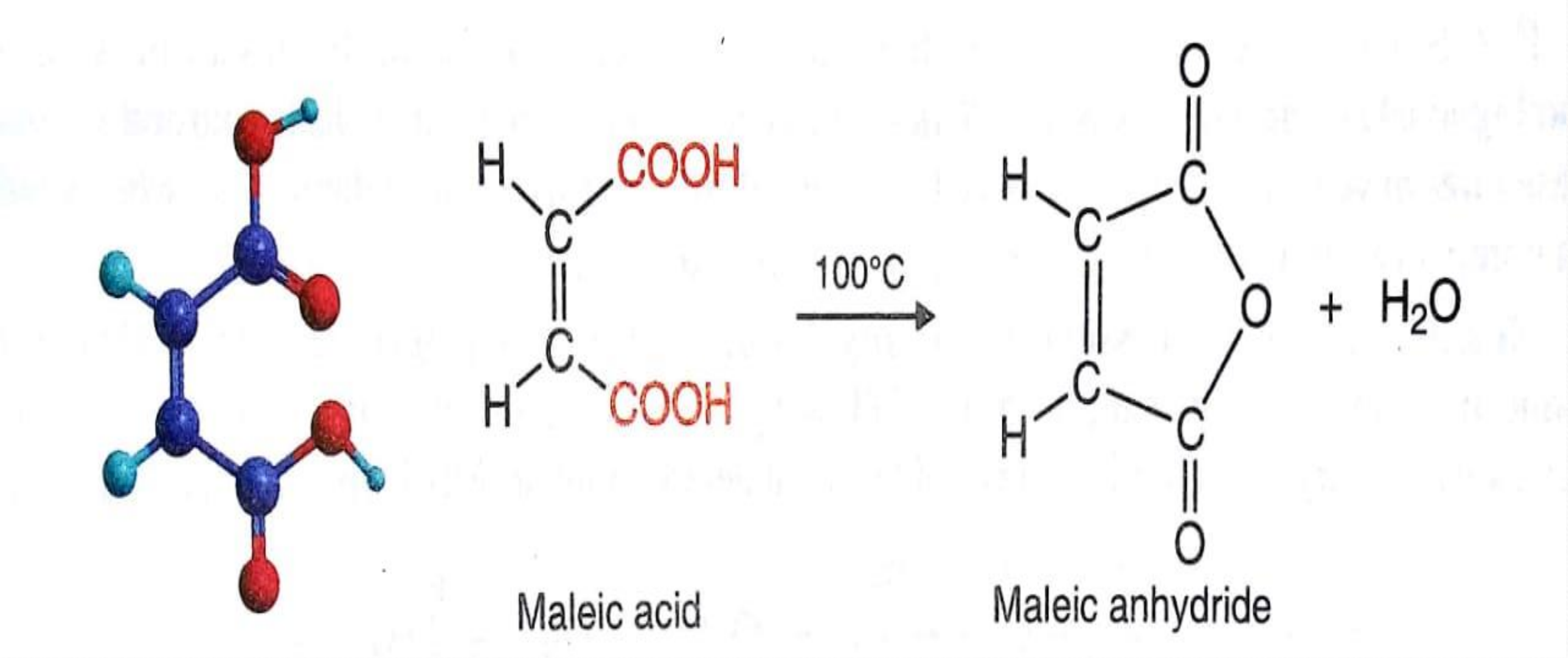


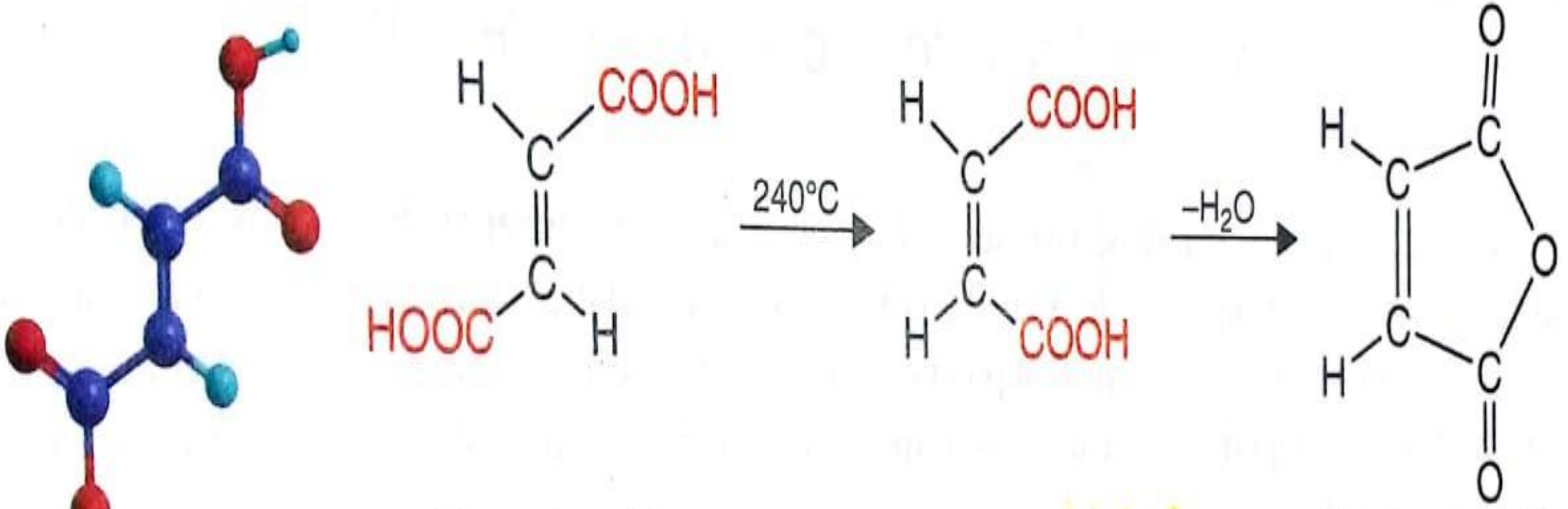
isomer	melting point (°C)	boiling point (°C)
cis-but-2-ene	-139	4
trans-but-2-ene	-106	1

By chemical methods

The formation of a cyclic molecule from an open chain molecule takes place easily only when the reacting groups are close to each other. This fact has been most useful in assigning configuration to *cis-trans* isomers in which the doubly bound carbon atoms carry groups that are capable of reacting with each other, The configuration of maleic and fumaric acids is established on this basis.

Maleic acid readily forms cyclic anhydride whereas fumaric acid does not. This means that in maleic acid the two groups are nearer to each other than they are in fumaric acid. That is, **obviously maleic acid is the cis form and fumaric acid the trans form.**


H
COOH
C
C
H
COOH
Maleic acid
100°C
O
H
C
C
O
+ H2O
C
H
C
O
Maleic anhydride



Fumaric acid

(not isolated at this temperature)

Maleic anhydride

In addition to the methods given above, other physical measurements such as the measurement of the distances between certain atoms by means of **X-rays**, measurement of **absorption spectra** etc., may be of help for deciding upon the configuration in some cases.

Conformational Isomerism

- Conformational isomers are different shapes of the same molecule resulting from rotation around a single C-C bond. They are not different compounds (i.e. they have the same physical and chemical properties) and are readily interconvertible
- **Conformational isomerism** is a form of stereoisomerism in which the **isomers** can be interconverted just by rotations about formally single bonds.

Conformation:

The different arrangements of atoms caused by rotation about a single bond are called conformations.

Conformer:

A *conformer* (or conformational isomer) is a compound with a particular conformation.

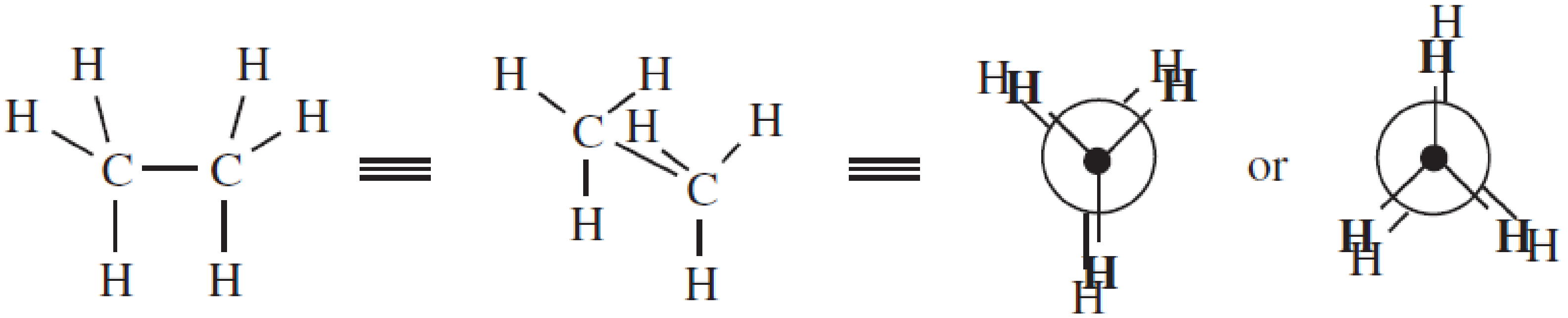
Conformational isomers can be represented by

Sawhorse representations or *Newman projections*.

Conformations of Ethane (CH3-CH3)

Rotation around the C-C bond produces two distinctive conformations.

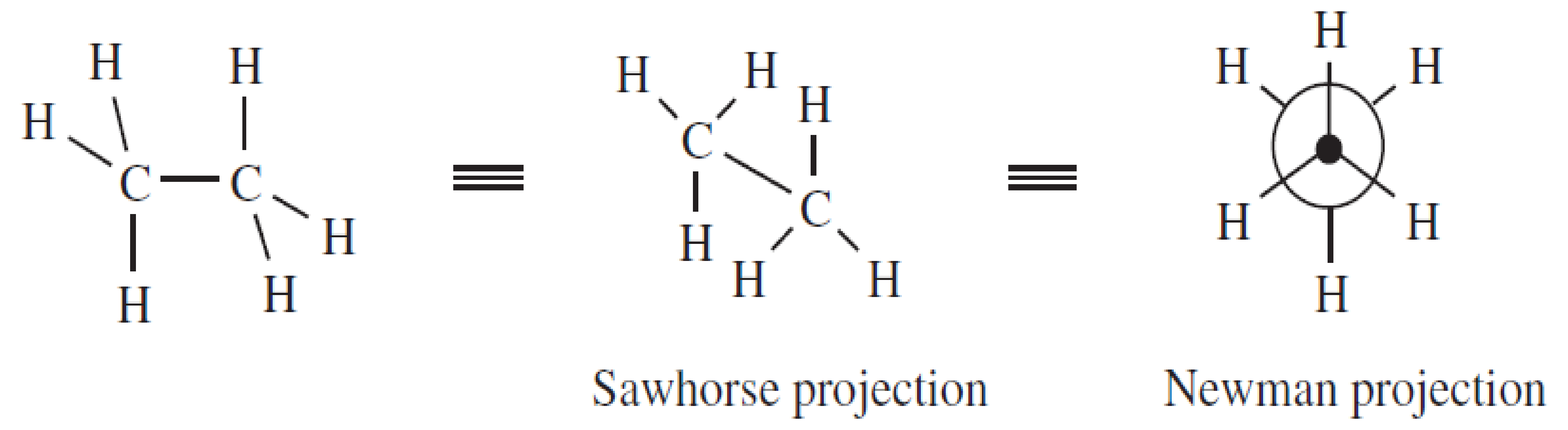
1. **Eclipsed Conformation:** C-H bonds on each carbon atom are as close as possible.



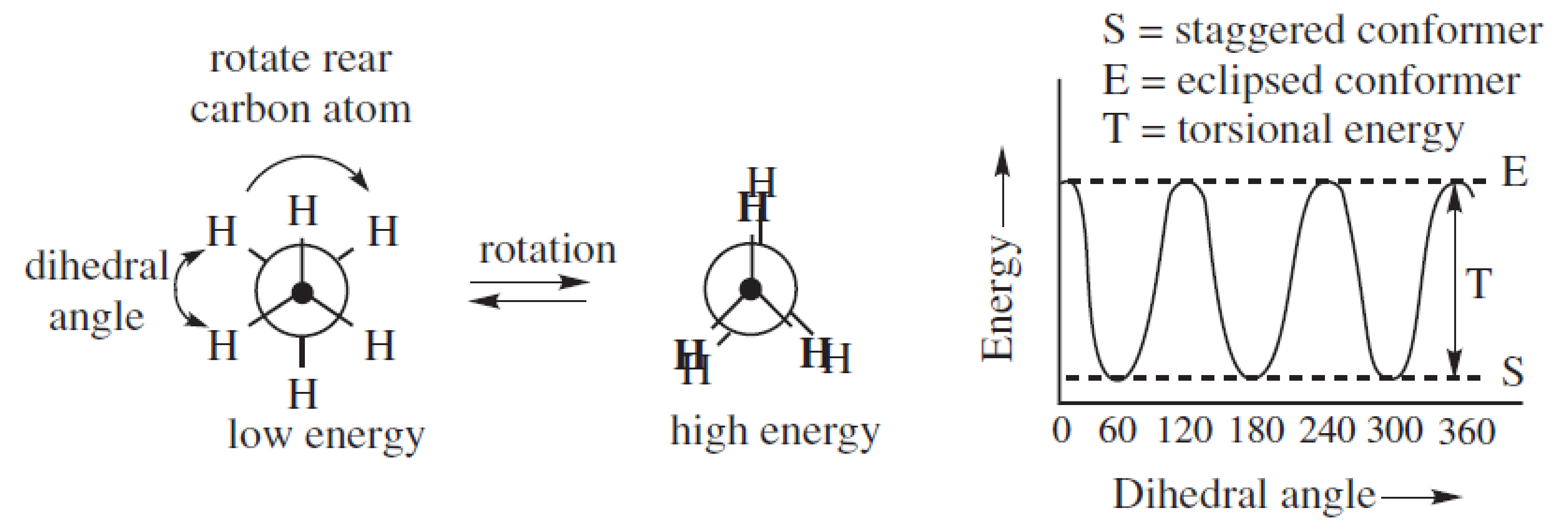
Sawhorse projection
(view the C–C bond from an oblique angle and show all C–H bonds)

Newman projection
(view the C–C bond directly on, show the front carbon atom by a small black circle and the back carbon by a much larger circle. Show all C–H bonds)

2. **Staggered conformation:** C-H bonds on each carbon atom are as far apart as possible.



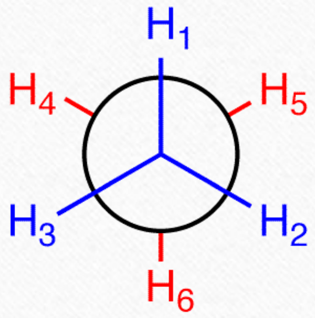
The staggered conformation is more stable as the C-H bonds are further apart. The energy difference between them (12 kJmol−1) is known as the *torsional strain*. This energy difference is relatively small, and hence there is free rotation about the C-C bond at room temperature.



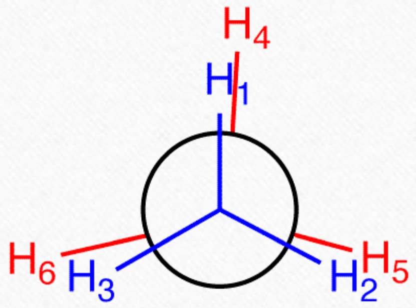
The angle between the front and back hydrogen is dihedral (or torsional) angle.

Torsional Strain

Torsional strain or eclipsing strain is the increase in potential energy of a molecule due to repulsion between electrons in bonds that do not share an atom. Consider two conformations of ethane:



1



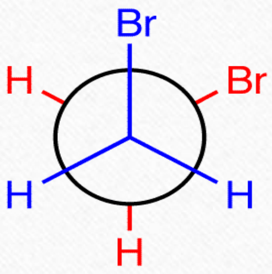
2

The smallest dihedral angle is 60º in **1**; it is 0º in **2**. Thus, two C-H bonds not sharing a carbon atom that are closest to each other (ex: C-H_1 and C-H4) are closer in **2** than in **1**. The repulsion between electrons in bonds that do not share a carbon atom is, therefore, greater in **2** than in **1**. Consequently, torsional strain is greater in **2** than in **1**.

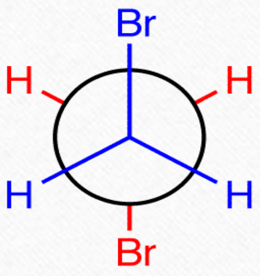
Steric Strain

Steric strain is the increase in potential energy of a molecule due to repulsion between electrons in atoms that are not directly bonded to each other.

Consider two staggered conformations of 1,2-dibromoethane:



1



2

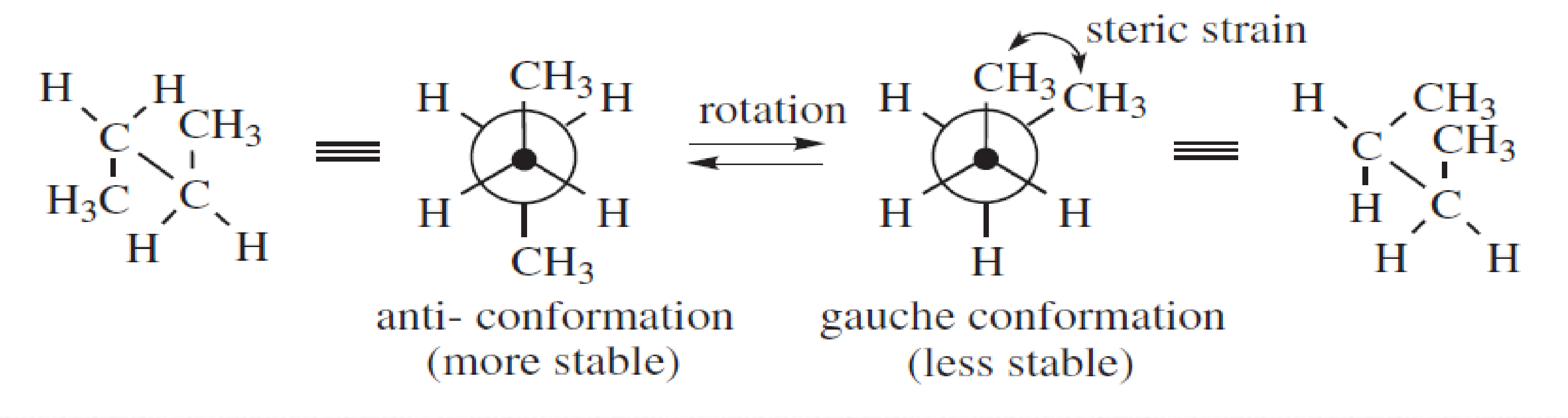
In 1, the Br atoms are closer to each other than they are in 2 (in 1, the dihedral angle between the bromine atoms is 60º; in 2, it is 180º). Thus, the repulsion between electrons in one bromine atom and those in the other is greater in 1 than in 2. Thus, steric strain is greater in 1 than in 2. (Since the Br atoms are pointing in opposite directions in 2, there is no steric strain in 2 due to interaction between the Br atoms.)

Conformations of butane ($CH_3CH_2CH_2CH_3$)

In butane, the staggered conformations do not all have the same energy.

1. The *anti*- (or *antiperiplanar*) *conformation* is the most stable as the two methyl groups are as far apart as possible (180° separation).

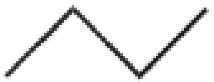
2. The *gauche* (or *synclinal*) *conformation* is higher in energy (by **4 kJmol/mol**) as the two methyl groups are near one another (60° separation), resulting in *steric strain*. Steric strain is the repulsive interaction between two groups, which are closer to one another than their atomic radii allow.



anti- conformation
(more stable)

gauche conformation
(less stable)

The most stable conformation for a straight-chain alkane is a zigzag shape, as the alkyl groups are as far apart as possible. (This is why we draw alkyl chains with a zigzag structure.)



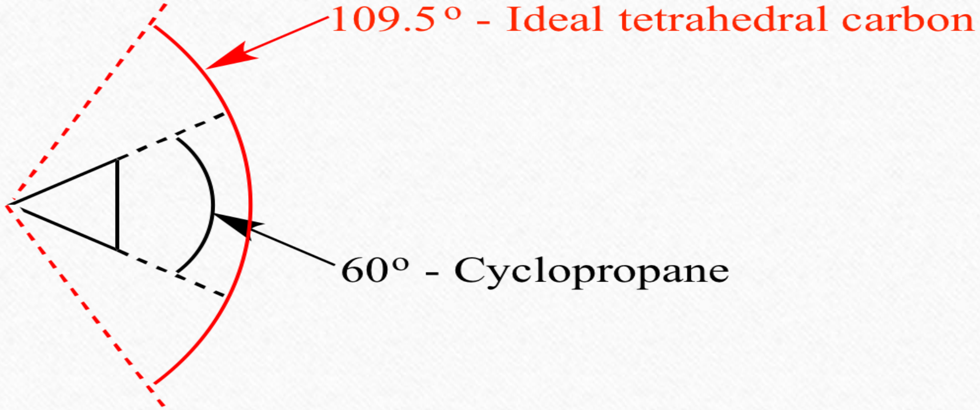
zigzag shape
of butane

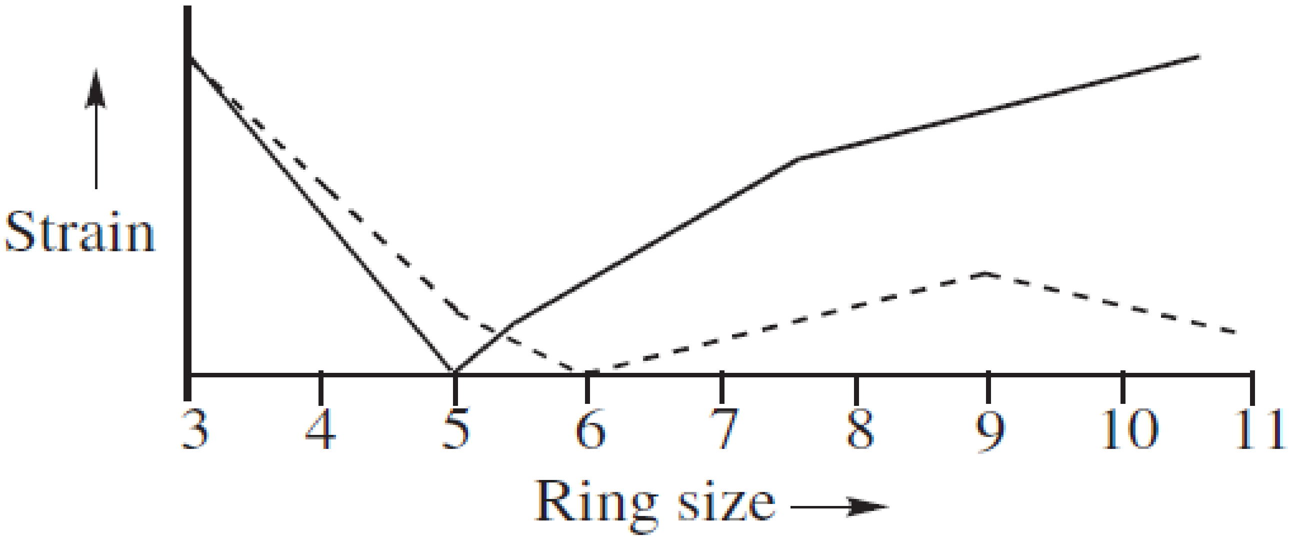
It should be noted that when the methyl groups in butane are eclipsed and are in the same plane (0° separation), this is known as the synperiplanar conformation.

Conformations of cycloalkanes

The shape of cycloalkanes is determined by torsional strain, steric strain and angle strain.

***Angle strain*:** For an sp3 hybridized carbon atom, the ideal bond angle is 109.5° (tetrahedral). Angle strain is the extra energy that a compound has because of non-ideal bond angles (i.e. angles above or below 109.5°) e.g. **Cyclopropane**. Due to the rigidity of the cyclopropane ring it could assume only one conformation, namely the planar conformation.





—— = Angle strain

- - - - = Total strain

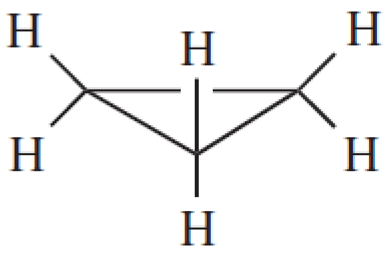
(angle + steric + torsional strain)

A 3-ring has the highest and a planar 5-ring has the lowest angle strain. After 5, the angle strain increases as the ring gets larger

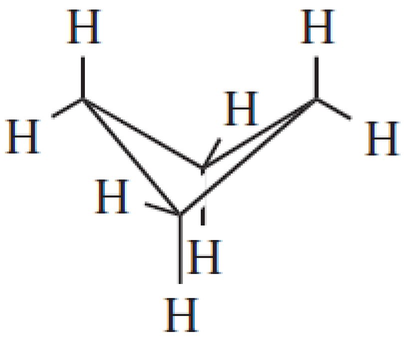
A 3-ring has the highest total strain which reaches a minimum for a 6-ring. The strain increases from 6 to 9 and then decreases

Cyclopentane (5-membered) and cyclohexane (6-membered) rings are therefore the most stable and, consequently, the most easily formed.

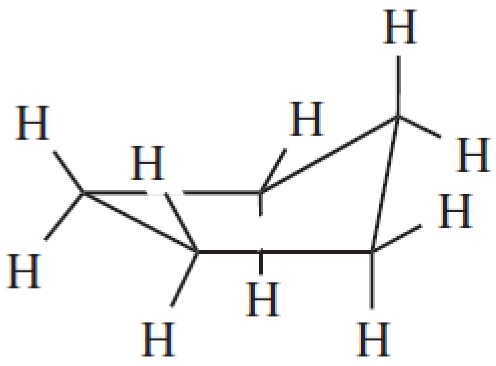
Cycloalkanes can adopt different conformations (or shapes): Cyclopropane is flat, cyclobutane can form a butterfly shape, while cyclopentane can form an open-envelope shape.



cyclopropane
(internal C–C
angle = 60°)



cyclobutane
(butterfly)

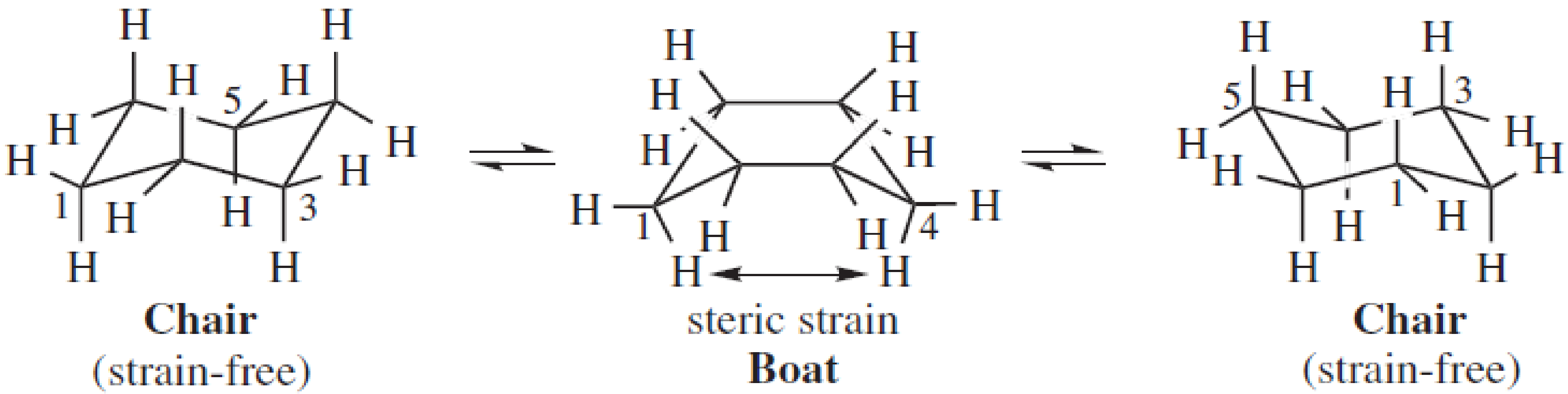


cyclopentane
(open-envelope)

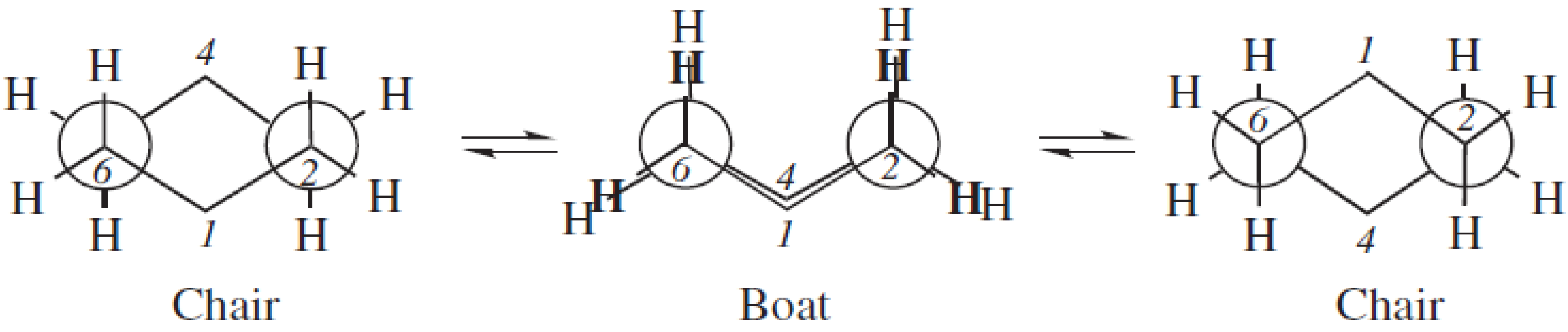
Cyclopropane has to be planar and therefore has very strained bond angles of 60° and a great deal of torsional energy. However, cyclobutane and cyclopentane can adopt non-planar (puckered) shapes which decrease the torsional strain by staggering the C-H bonds. However, this is at the expense of angle strain, and the butterfly and open-envelope shapes represent the best compromise between the two opposing effects.

Cyclohexane

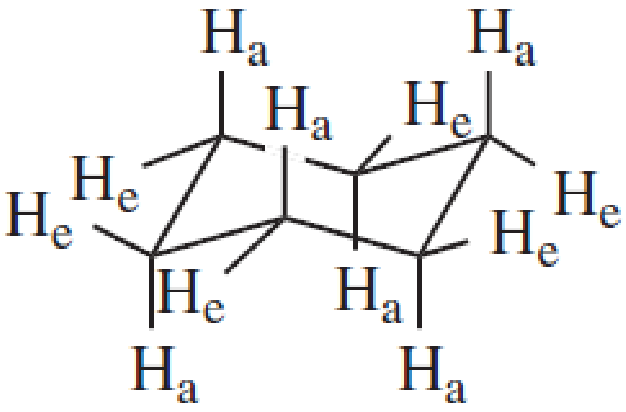
- Cyclohexane adopts the **chair or boat conformations**, which are both free of angle strain. However, the boat conformation is less stable because of steric strain between the C-1 and C-4 hydrogens.
- The two chair forms can interconvert via the boat form in a process known as ***ring-flipping*.**



Newman projections



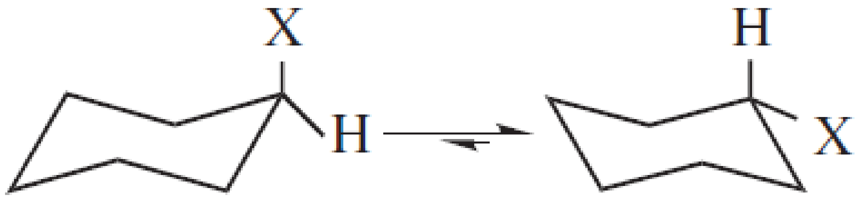
The chair conformation has six *axial* and six *equatorial* hydrogens. On ring-flipping, the axial hydrogens become equatorial and the equatorial hydrogens become axial.



H_a = axial hydrogen (point up and down)

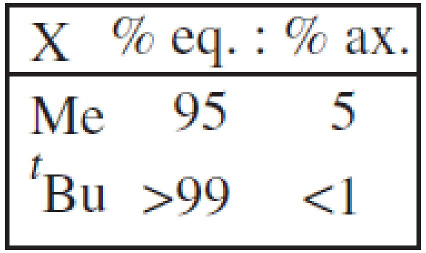
H_e = equatorial hydrogen (point sideways)

If a substituent (X) is present, then this prefers to sit in an *equatorial position*. The equatorial conformer is lower in energy because *steric strain* (or *1,3-diaxial interactions*) raises the energy of the axial conformer. As the size of the X group increases, so does the proportion of the equatorial conformer at equilibrium.

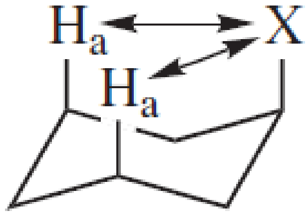


axial conformer

equatorial conformer

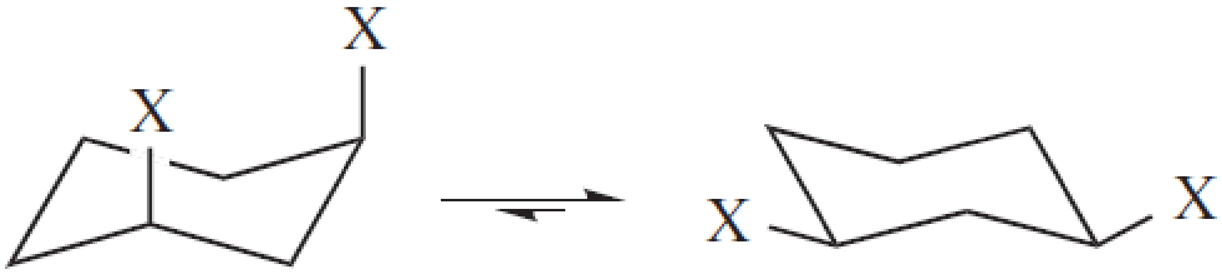


X	% eq. :	% ax.
Me	95	5
^{t}Bu	>99	<1



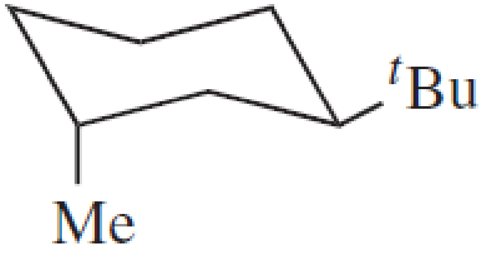
1,3-diaxial interactions (unfavourable)

For disubstituted cyclohexanes, both groups should sit in an equatorial position. When this is not possible, then the largest group (e.g. a *t*-Bu group rather than a Me group) will sit in the equatorial position.



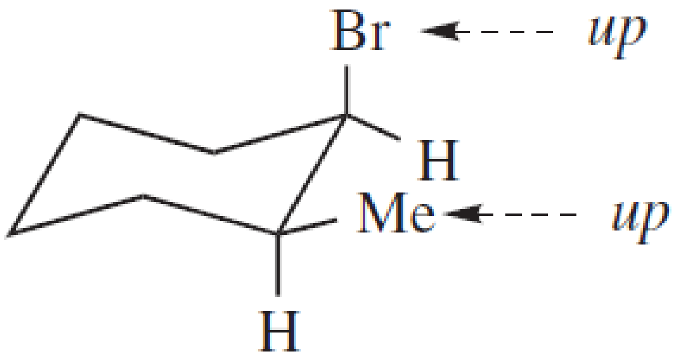
diaxial conformer

diequatorial conformer

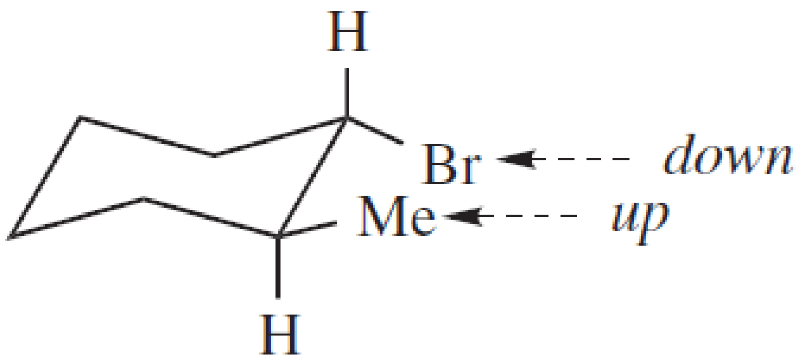


The bulkier ^{t}Bu group prefers the equatorial position

When the two substituents on the ring are *both* pointing up (or *both* pointing down), these cyclic compounds are designated *cis* stereoisomers. When one substituent is pointing up and the other down, these cyclic compounds are designated *trans*-stereoisomers



cis-1-bromo-2-methylcyclohexane



trans-1-bromo-2-methylcyclohexane