CHAPTER

26

Optical Isomerism

INTRODUCTION

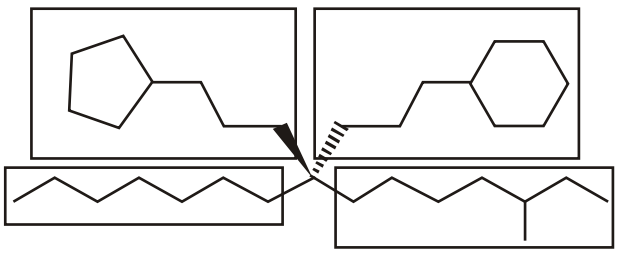
Plane polarised light and optical activity: Certain compounds rotate the plane polarised light (produced by passing ordinary light through Nicol prism) when it is passed through their solutions. Such compounds are called **optically active** compounds. The angle by which the plane polarised light is rotated is measured by an instrument called polarimeter. If the compound rotates the plane polarised light to the right, *i.e.,* clockwise direction, it is called dextrorotatory (Greek for right rotating) or the d-form and is indicated by placing a positive (+) sign before the degree of rotation. If the light is rotated towards left (anticlockwise direction), the compound is said to be laevorotatory or the l-form and a negative (–) sign is placed before the degree of rotation. Such (+) and (–) isomers of a compound are called optical isomers and the phenomenon is termed as **optical isomerism**.

CHIRAL CENTER

- ☞ Those centers which create unsymmetry (chirality) in the molecule are called chiral centers. Chiral center must be sp^3 with 4 different valencies.

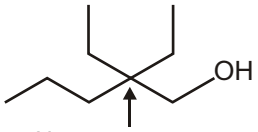
For purposes of this course, we will define a chiral center (stereocenter) as a carbon atom with four different groups on it. For example.

Whenever we look at the four groups connected to an atom, we are looking at the entire molecule, no matter how big those groups are. Consider the following example:



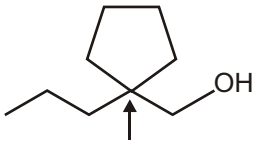
All four of these groups are different.

You must learn how to recognize when an atom has four different groups attached to it. To help you with this, let's begin by seeing the situations that are not chiral center (stereocenter):



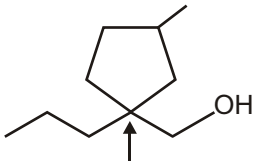
Not a stereocenter

The carbon atom indicated above is not a chiral center (stereocenter) because there are two groups that are the same (there are two ethyl groups). The same is true in the following case:



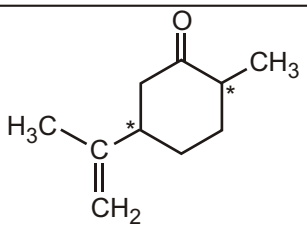
Not a stereocenter

Whether you go around the ring clockwise or counterclockwise, you see the same thing, so this is not a chiral center (stereocenter). If we wanted to make it a chiral center (stereocenter), we could do so by putting a group on the ring:

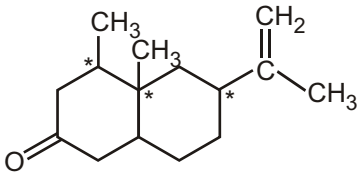


A stereocenter

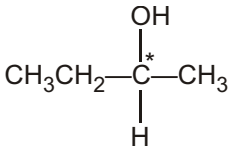
Solved Example



Carvone (spearmint oil)



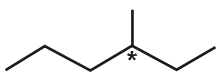
Nootkatone (grapefruit oil)

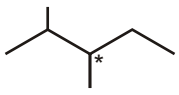


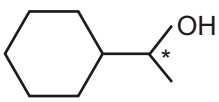
2-Butanol (chiral)

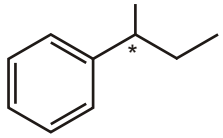
Solved Example

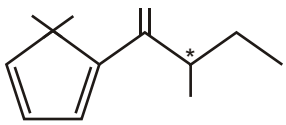
- In each of the compounds below', there is one stereocenter. Find it.

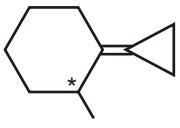
(a) 

(b) 

(c) 

(d) 

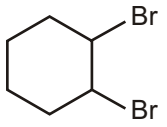
(e) 

(f) 

Stereocenters are marked with asterisck (*)

Solved Example

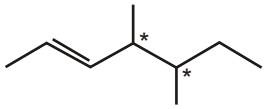
- In the following compound, find all of the chiral center (stereocenters), if any:

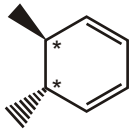


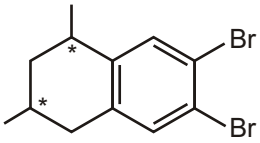
Ans. If we go around the ring, we find that there are only six carbon atoms in this compound. Four of them are CH_2 groups, so we know that they are not chiral center (stereocenters). If we look at the remaining two carbon atoms, we see that each of them is connected to four different groups. They are both chiral center (stereocenters).

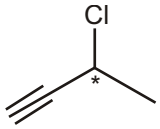
Solved Example

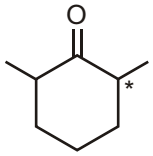
- For each of the compounds below, find all of the chiral center (stereocenters), if any.

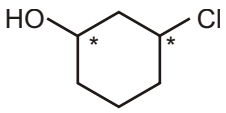
(a) 

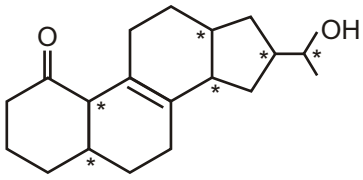
(b) 

(c) 

(d) 

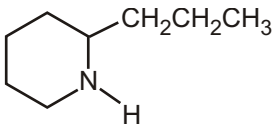
(e) 

(f) 

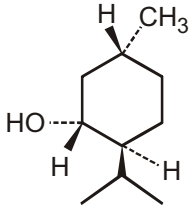
(g) 

Solved Example

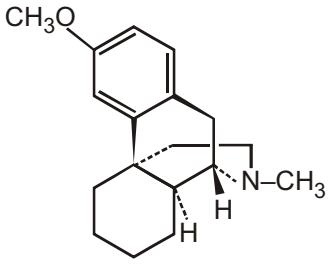
- Which of the following molecules are chiral? Identify the chirality center(s) in each.

(a) 

Coniine
(poison hemlock)

(b) 

Menthol
(flavoring agent)

(c) 

Dextromethorphan
(cough suppressant)

Ans. *a*, *b*, *c*, chiral centers in *a* = 2
b = 3
c = 4

Solved Example

- Which of the following compounds have chiral centers?

(a) $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$

(b) $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

(c) $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}CH_2CH_2CH_3$

(d) CH_3CH_2OH

(e) $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_2CH_3$

(f) $CH_2\!=\!\underset{\displaystyle NH_2}{\underset{|}{C}}HCH_3$

Ans. Only a, c and f has chirality centre (chiral carbon).

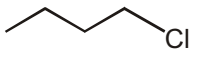
Solved Example

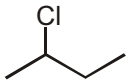
- Which of the following compound is chiral compound ?

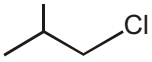
(A) 1-Chlorobutane (B) 2-Chlorobutane

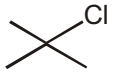
(C) 1-Chloro-2-methyl propane (D) 2-Chloro-2-methyl propane

Ans. (B)

(A) 

(B) 

(C) 

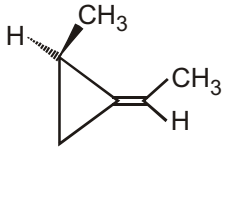
(D) 

STEREOCENTER

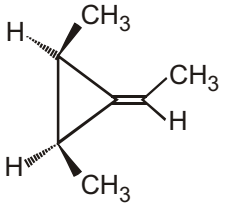
☞ Those centers in a molecule which can show optical or geometrical isomerism are called stereocenters. One Chiralcenter showing optical isomerism means one stereocenters and one bond showing geometrical isomerism means two stereocenters.

Solved Example

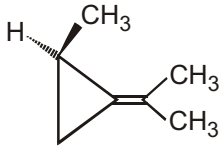
- Find the sum of all the stereocenters that are present in below compounds :



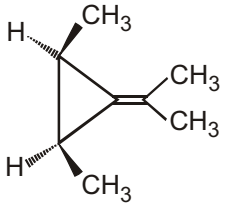
(I)



(II)



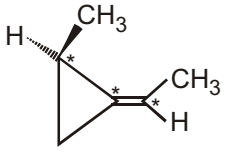
(III)



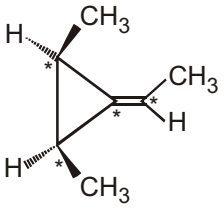
(IV)

(A) 8 (B) 9 (*C) 10 (D) 11

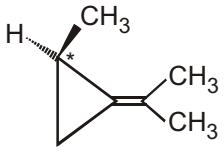
Sol.



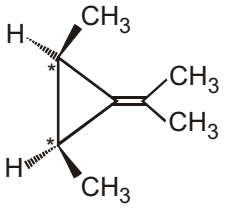
(I)



(II)



(III)

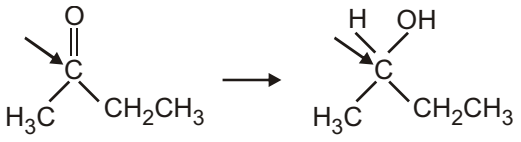


(IV)

Stereocenters are marked with asterisck (*)

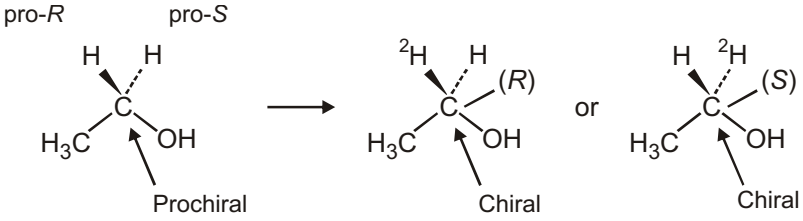
PROCHIRALITY

Closely related to the concept of chirality, and particularly important in biological chemistry, is the notion of prochirality. A molecule is said to be prochiral if it can be converted from achiral to chiral in a single chemical step. For instance, an unsymmetrical ketone like 2-butanone is prochiral because it can be converted to the chiral alcohol 2-butanol by addition of hydrogen.



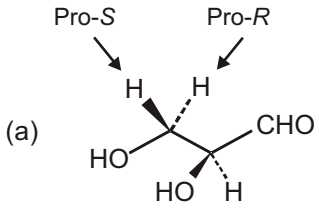
2-Butanone (prochiral) — 2-Butanol (chiral)

Of the two identical atoms in the original compound, that atom whose replacement leads to an *R* chirality center is said to be pro-*R* and that atom whose replacement leads to an *S* chirality center is pro-*S*.

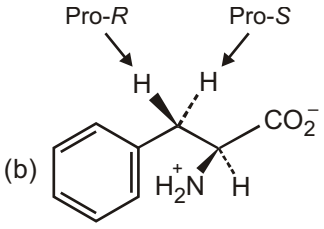


Solved Example

- Identify the indicated hydrogens in the following molecules as pro-*R* or pro-*S* :



(S)-Glyceraldehyde



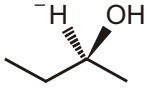
Phenylalanine

R, S CONFIGURATION

Determining the Configuration of a Stereocenter

Now that we can find stereocenters, we must now learn how to determine whether a stereocenter is *R* or *S*. There are two steps involved in making the determination. First, we give each of the four groups a number (from 1 to 4). Then we use the orientation of these numbers to determine the configuration. So, how do we assign numbers to each of the groups?

We start by making a list of the four atoms attached to the stereocenter. Let's look at the following example:



The four atoms attached to the stereocenter are C, C, O, and H. We rank them from 1 to 4 based on atomic number. To do this, we must either consult a periodic table every time or commit to memory a small part of the periodic table — just those atoms that are most commonly used in organic chemistry:

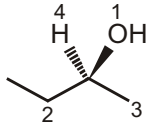
C N O F
P S Cl
Br
I

When comparing the four atoms in the example above, we see that oxygen has the highest atomic number, so we give it the first priority — we give it the number 1. Hydrogen is the smallest atom, so it will always get the number 4 (lowest priority) when a stereocenter has a hydrogen atom. We don't have to worry about what to do if there are two hydrogen atoms, because if there were, it would not be a stereocenter.

We compare the two lists and look for the first point of difference:

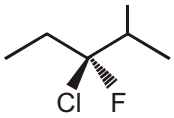
C	H
H	H
H	H

We see the first point of difference immediately: carbon beats hydrogen. So the left side of the stereocenter gets priority over the right side, and the numbering turns out like this:



Solved Example

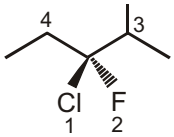
- In the compound below, find the stereocenter, and label the four groups from 1 to 4 using the system of priorities based on atomic number.



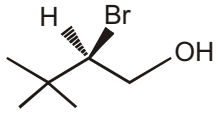
Ans. The four atoms attached to the stereocenter are C, C, Cl, and F. Of these, Cl has the highest atomic number, so its gets the first priority. Then comes F as number 2. We need to decide which carbon atom gets the number 2 and which carbon atom gets the number 3. We do this by listing the three atoms attached to each of them:

Left side	**Right side**
C	C
H	C
H	H

So the right side wins. Therefore, the numbering goes like this :



Also, you should know that we are looking for the first point of difference as we travel out, and we don't add the atomic number. This is best explained with an example:

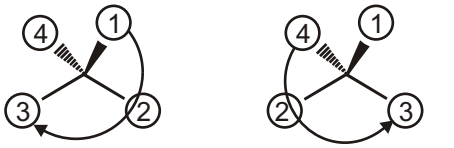


Left side	**Right side**
C	O
C	H
C	H

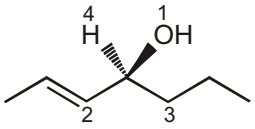
In this case, we do not add the atomic number and say that the left side wins. Rather we go down the list and compare each row. In the first row above, we have C versus O. That's it, end of story—the O wins. It doesn't matter what comes in the next two rows. Always look for the first point of difference. So the priorities so like this:

Now we need to learn how to use this numbering system to determine the configuration of a stereocenter. The idea is simple, but it is difficult to do if you have a hard time closing your eyes and rotating 3D objects in your mind. For those who cannot do this, don't worry. There is a trick. Let's first see how to do it without the trick.

If the number 4 group is pointing away from us (on the dash), then we ask whether 1, 2, and 3 are going clockwise or counterclockwise:



In the example on the left, we see that 1, 2, 3 go clockwise, which is called *R*. In the example on the right, we see that 1, 2, 3 go counterclockwise, which is called *S*. If the molecule is already drawn with the number 4 priority on the dash, then your life is very simple:

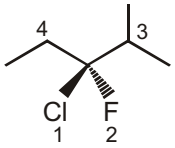


The 4 is already on the dash, so you just look at 1, 2 and 3. In this case, they go counterclockwise, so it is S.

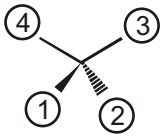
The solid wedges represent bonds that point out of the plane of the paper toward the viewer.

The hatched wedges (dash) represent bonds that point back from the plane of the paper away from the viewer.

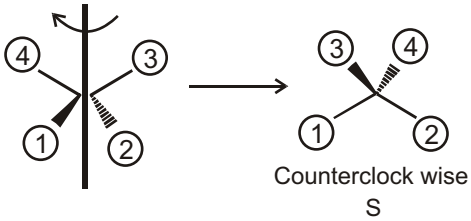
It gets a little more difficult when the number 4 is not on a dash, because then you must rotate the molecule in your mind. For example,



Let's redraw just the stereocenter showing the location of the four priorities:

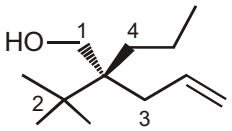


Now we need to rotate the molecule so that the fourth priority is on a dash. To do this, imagine spearing the molecule with a pencil and then rotating the pencil 90º.

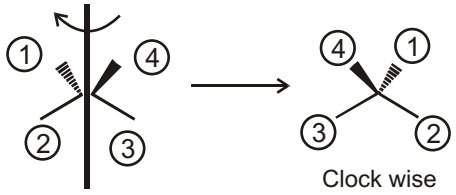


Now the 4 is on a dash, so we can look at 1, 2 and 3, and we see that they go counterclockwise. Therefore, the configuration is *S*.

Let's see one more example:

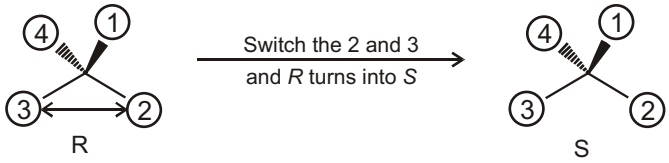


We redraw just the stereocenter showing the location of the four priorities, and then we spear the molecule with a pencil and rotate 180° to put the 4 on a dash:

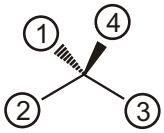


Now, the 4 is on a dash, so we can look at 1, 2 and 3, and we see that they go clockwise. Therefore, the configuration is *R*.

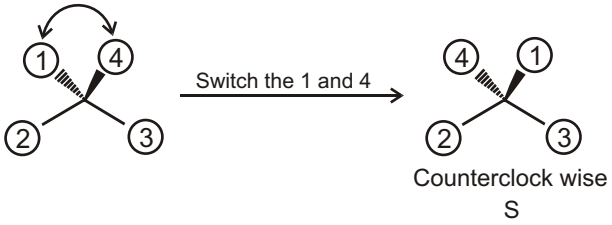
And now, for the trick. If you were able to see all of that, great! But if you had trouble seeing the molecules in 3*D*, there is a simple trick that will help you get the answer every time. To understand how the trick works, you need to realize that if you redraw the molecule so that any two of the four groups are switched, then you have switched the configuration (*R* turns into *S* and *S* turns into *R*):



You can switch any two groups and this will happen. You can use this idea to your advantage. Here is the trick: Switch the number 4 with whatever group is on the dash—then your answer is the opposite of what you see. Let's do an example :

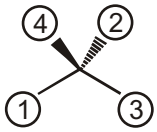


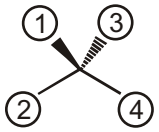
This looks tough because the 4 is on a wedge. But let's do the trick: switch the 4 with whichever group is on the dash; in this case, we switch the 4 with the 1:

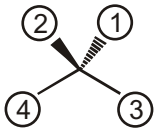


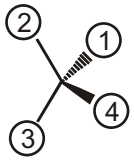
After doing the switch, the 4 is on a dash, and it becomes easy to figure out. It is counterclockwise, w'hich means *S*. We had to do one switch to make it easy to figure out, which means that we changed the configuration. So if it became *S* after the switch, then it must have been *R* before the switch. That's the trick. But be careful. This trick will work every time, but you must not forget that the answer you immediately get is the opposite of the real answer, because you did one switch.

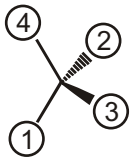
Now, let's practice determining *R* or *S* when you are given the numbers, so that we can make sure you know how to do this step. You can either visualize the molecule in 3D, or you can use the trick—whatever works best for you.

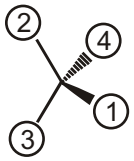
(a) 

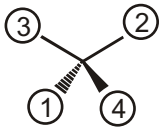
(b) 

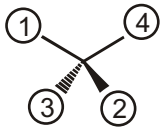
(c) 

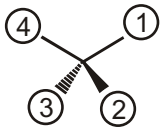
(d) 

(e) 

(f) 

(g) 

(h) 

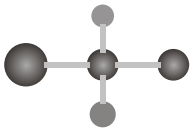
(i) 

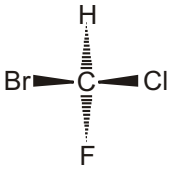
Ans. (a) *S* (b) *R* (c) *S* (d) *R*
(e) *S* (f) *S* (g) *R* (h) *R*
(i) *S*

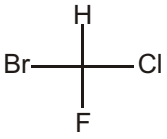
FISCHER PROJECTIONS

It is possible, however, to convey stereochemical information in an abbreviated form using a method devised by the German chemist Emil Fischer.

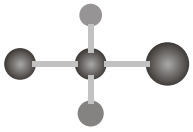
The molecule is oriented so that the vertical bonds at the chirality center are directed away from you and the horizontal bonds point toward you. A projection of the bonds onto the page is a cross. The chirality center lies at the center of the cross but is not explicitly shown.

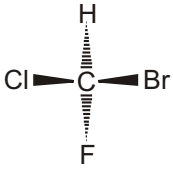


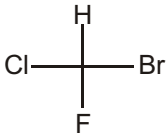




(R)-Bromochlorofluoromethane







(S)-Bromochlorofluoromethane

☞ **How do we assign priority number (1 4) to four different groups attached to stereocenter?**

- ⋆ Higher atomic number precedes lower. *e.g.*, Br > Cl > S > O > N > C > H
- ⋆ For isotopes, higher atomic mass precedes lower. *e.g.*, T > D > H.
- ⋆ If atoms have the same priority, then secondary groups attached are considered. If necessary, the process is continued to the next atom in the chain.

e.g., $—CH_2—CH_3$ $—CH_2—H$

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

First atom is carbon in both cases; consider the second atom: second atom is carbon in both cases; consider the next atom(s): carbon directly bonded to two further carbons has higher priority than carbon directly bonded to just one further carbon

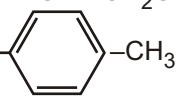
Solved Example

- Assign priority numbers to the following groups :

(a) —CH_2OH — CH_3 — CH_2CH_2OH — H

(b) —CH O — OH — CH_3 — CH_2OH

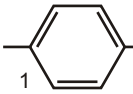
(c) —$CH(CH_3)_2$ — CH_2CH_2Br — Cl — $CH_2CH_2CH_2Br$

(d) —CH CH_2 — CH_2CH_3  –CH_3

Ans. (a) —CH_2OH (1) —CH_3 (3) —CH_2CH_2OH (2) —H (4)

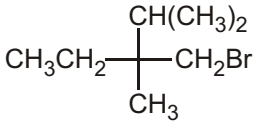
(b) —CH=O (2) —OH (1) —CH_3 (4) —CH_2OH (3)

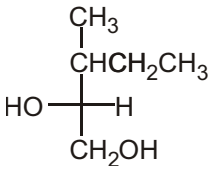
(c) —$CH(CH_3)_2$ (2) —CH_2CH_2Br (3) —Cl (1) —$CH_2CH_2CH_2Br$ (4)

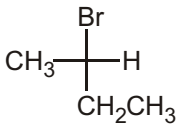
(d) —CH=CH_2 (2) — CH_2CH_3 (3)  (1) — CH_3 (4)

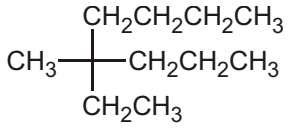
Solved Example

- Indicate whether each of the following structures has the *R* configuration or the *S* configuration.

(a) 

(b) 

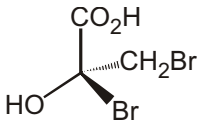
(c) 

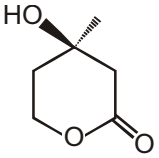
(d) 

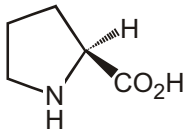
Ans. (a) *S* (b) *R* (c) *S* (d) *S*

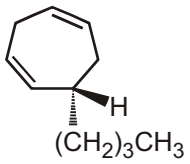
Solved Example

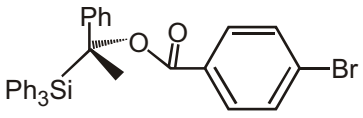
- Assign *R* / *S* configuration at each stereogenic centre in the following molecules :

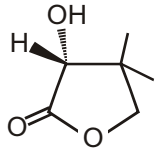
(a) 

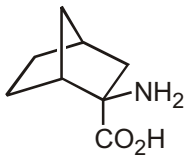
(b) 

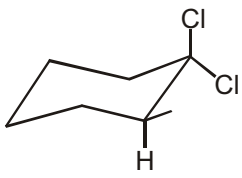
(c) 

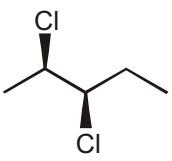
(d) 

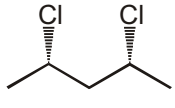
(e) 

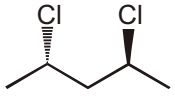
(f) 

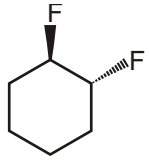
(g) 

(h) 

(i) 

(j) 

(k) 

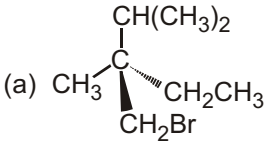
(l) 

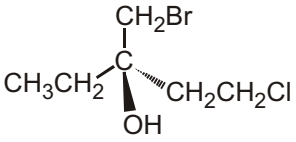
(m) 

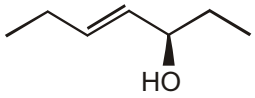
Ans. (a) *S* (b) *R* (c) *S* (d) *S*
(e) *R* (f) *R* (g) *R* (h) *S*
(i) 2*R*, 3*R* (j) 2*S*, 4*R* (k) 2*S*, 4*S* (l) 1*R*, 2*R*
(m) 1*R*, 2*S*

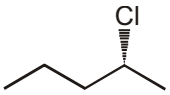
Solved Example

- Indicate whether each of the following structures has the R configuration or the S configuration:

(a) 

(b) 

(c) 

(d) 

Ans. (a) *R* (b) *R* (c) *R* (d) *R*

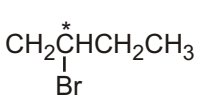
☑ SPECIAL TOPIC

ENANTIOMERS

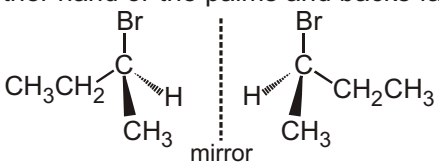
Drawing Enantiomers

Enantiomers are two compounds that are nonsuperimposable mirror images. Let's first clear up the term "enantiomers," since students will often use this word incorrectly in a sentence. Let's compare it to people again. If two boys are born to the same parents, those boys are called brothers. Each one is the brother of the other. If you had to describe both of them, you say that they are brothers. Similarly, when you have two compounds that are non-super imposable mirror images, they are called enantiomers. Each one is the en-antiomer of the other. Together, they are a pair of enantiomers. But what do we mean by "nonsuperimposable mirror images"?

A compound with a chirality center, such as 2-bromobutane can exist as two different isomers. Because the two isomers are different, they cannot be superimposed. The two isomers are analogous to a left and a right hand. You cannot superimpose your left hand on your right hand. When you try to superimpose them, either the thumb of one hand lies on top of the little finger of the other hand or the palms and backs face opposite directions.

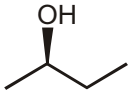


2-bromobutane

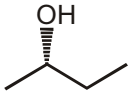


the two isomers of 2-bromobutane
a pair of enantiomers

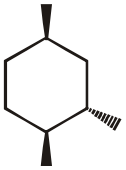
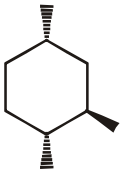
The simplest way to draw an enantiomer is to redraw the carbon skeleton, but invert all stereocenters. In other words, change all dashes into wedges and change all wedges into dashes. For example,



The compound above has a stereocenter (what is the configuration?). If we wanted to draw the enantiomer, we would redraw the compound, but we would turn the wedge into a dash:

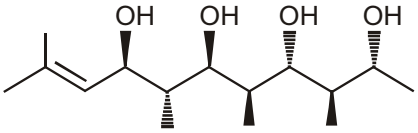


This is a pretty simple procedure for drawing enantiomers. It works for compounds with many stereocenters just as easily. For example,

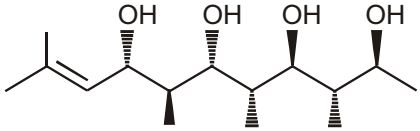
The enantiomer of  is 

Solved Example

- The enantiomer of the following compound :

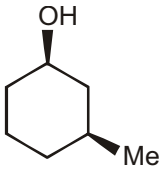


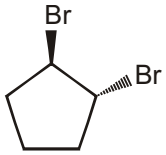
Sol. Redraw' the molecule, but invert every stereocenter. Convert all wedges into dashes, and convert all dashes into wedges :

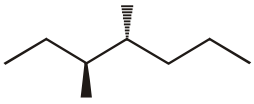


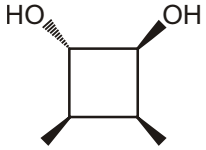
Solved Example

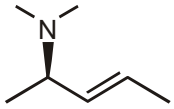
- Draw the enantiomer of each of the following compounds.

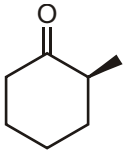
(a) 

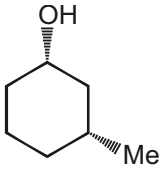
(b) 

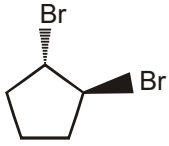
(c) 

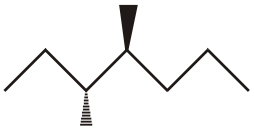
(d) 

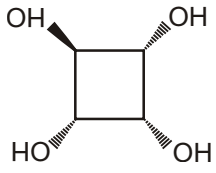
(e) 

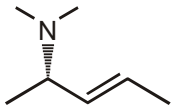
(f) 

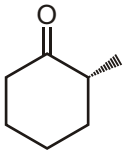
Ans. (a) 

(b) 

(c) 

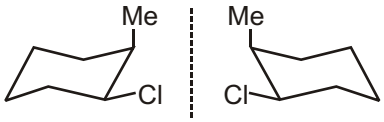
(d) 

(e) 

(f) 

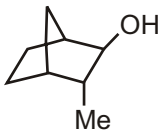
There is another way to draw enantiomers. In the previous method, we placed an imaginary mirror behind the compound, and we looked into that mirror to see the reflection. In the second method for drawing enantiomers, we place the imaginary mirror on the side of the compound, and we look into the mirror to see the reflection. Let's see an example:

But that is a lot of steps to go through when there is a simpler way to draw' the enantiomer—just put the imaginary mirror on the side (there is no need to actually draw the mirror), and draw' the enantiomer like this:

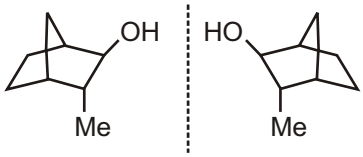


Solved Example

- Draw the enantiomer of the following compound :

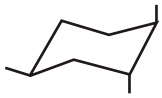


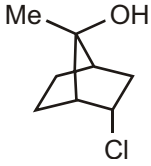
Ans. This is a rigid bicyclic system, and the dashes and wedges are not shown. Therefore, we will use the second method for drawing enantiomers. We will place the mirror on the side of the compound, and draw what would appear in the mirror:

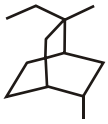


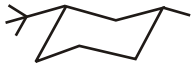
Solved Example

- Draw the enantiomer of each of the following compounds.

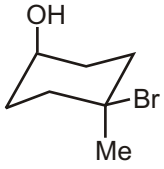
(a) 

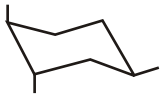
(b) 

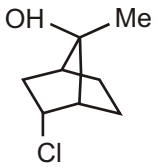
(c) 

(d) 

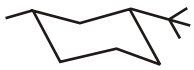
(e) 

(f) 

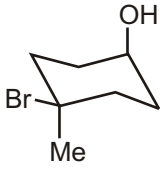
Ans. (a) 

(b) 

(c) 

(d) 

(e) 

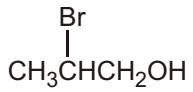
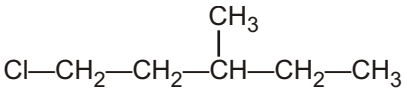
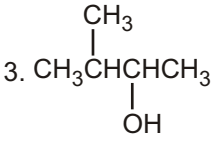
(f) 

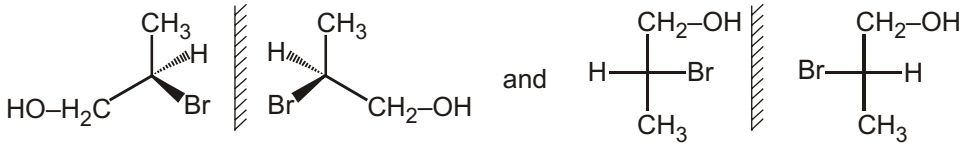
ENANTIOMERS

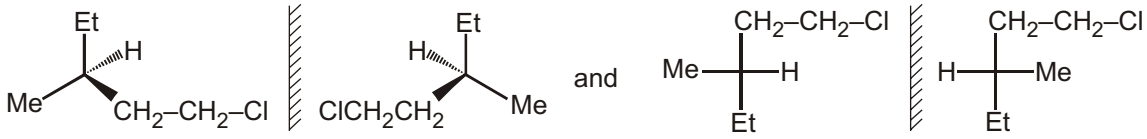
☞ Enantiomers have identical physical properties, except for the direction of rotation of the plane of polarized light.

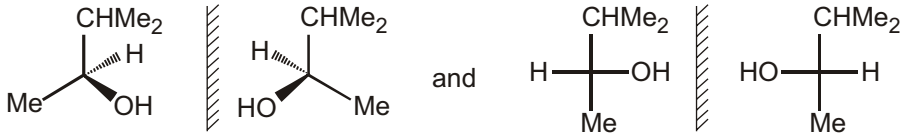
Solved Example

▸ Draw enantiomers for each of the following compounds using :
(a) Perspective formulas (b) Fischer projections

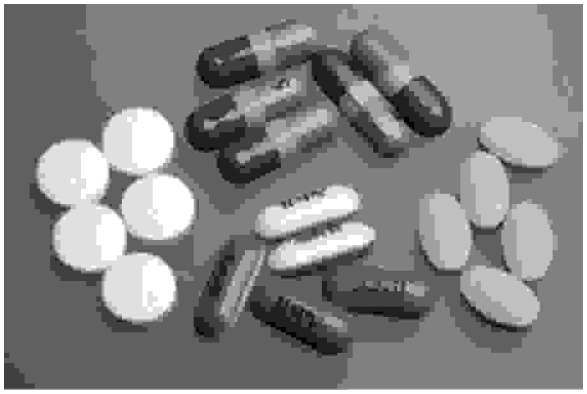
1. 
2. 
3. 

Ans. 1. 

2. 

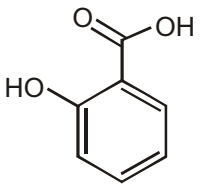
3. 

DRUGS BIND TO THEIR RECEPTORS

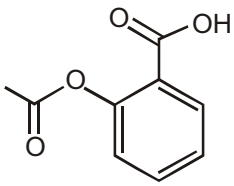


Many drugs exert their physiological effects by binding to specific sites, called receptors , on the surface of certain cells. A drug binds to a receptor using the same kinds of bonding interactions—van der Waals interactions, dipole–dipole interactions, hydrogen bonding—that molecules use to bind to each other. The most important factor in the interaction between a drug and its receptor is a snug fit. Therefore, drugs with similar shapes and properties, which causes them to bind to the same receptor, have similar physiological effects. For example, each of the compounds shown here has a nonpolar, planar, six-membered ring and substituents with similar polarities. They all have anti-inflammatory activity and are known as NSAIDs (non-steroidal anti-inflammatory agents).

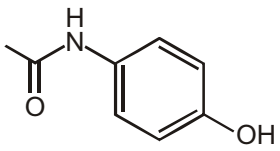
Salicylic acid has been used for the relief of fever and arthritic pain since 500 b.c. In 1897, acetylsalicylic acid (known by brand names such as Bayer Aspirin, Bufferin, Anacin, Ecotrin, and Ascriptin) was found to be a more potent anti-inflammatory agent and less irritating to the stomach; it became commercially available in 1899.



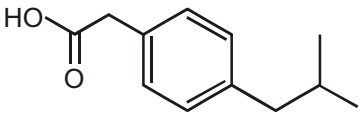
salicyclic acid



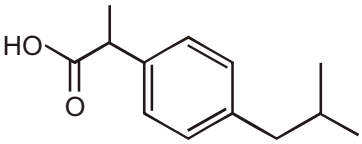
acetylsalicylic acid



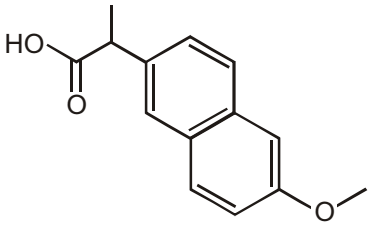
acetaminophen
(Tylenol)



ibufenac



ibuprofen
(Advil)

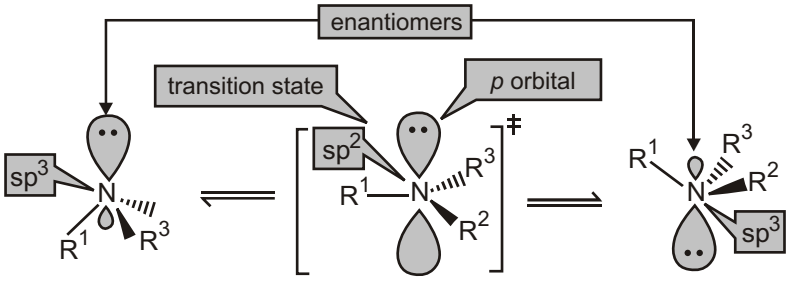


naproxen
(Aleve)

Changing the substituents and their relative positions on the ring produced acetaminophen (Tylenol), which was introduced in 1955. It became a widely used drug because it causes no gastric irritation. However, its effective dose is not far from its toxic dose. Subsequently, ibufenac emerged; adding a methyl group to ibufenac produced ibuprofen (Advil), which is a much safer drug. Naproxen (Aleve), which has twice the potency of ibuprofen, was introduced in 1976.

Chiral Drugs

Until relatively recently, most drugs with one or more asymmetric centers have been marketed as racemic mixtures because of the difficulty of synthesizing single enantiomers and the high cost of separating enantiomers. In 1992, however, the Food and Drug Administration (FDA) issued a policy statement encouraging drug companies to use recent advances in synthesis and separation techniques to develop single-enantiomer drugs. Now most new drugs sold are single enantiomers. Drug companies have been able to extend their patents by marketing a single enantiomer of a drug that was previously available only as a racemate (see page 303). If a drug is sold as a racemate, the FDA requires both enantiomers to be tested because drugs bind to receptors and, since receptors are chiral, the enantiomers of a drug can bind to different receptors (Section 6.18). Therefore, enantiomers can have similar or very different physiological properties. Examples are numerous. Testing has shown that (*S*)-(+)-ketamine is four times more potent an anesthetic than (*R*)-(–)-ketamine, and the disturbing side effects are apparently associated only with the (*R*)-(–)-enantiomer. Only the *S* isomer of the beta-blocker propranolol shows activity; the *R* isomer is inactive. The *R* isomer of Prozac, an antidepressant, is better at blocking serotonin but is used up faster than the R isomer. The activity of ibuprofen, the popular analgesic marketed as Advil, Nuprin, and Motrin, resides primarily in the (*S*)-(+)-enantiomer. Heroin addicts can be maintained with (–)- acetylmethadol for a 72-hour period compared to 24 hours with racemic methadone. This means less frequent visits to an outpatient clinic, because a single dose can keep an addict stable through an entire weekend . Prescribing a single enantiomer spares the patient from having to metabolize the less potent enantiomer and decreases the chance of unwanted drug interactions. Drugs that could not be given as racemates because of the toxicity of one of the enantiomers can now be used. For example, (*S*)-penicillamine can be used to treat Wilson's disease even though (*R*)-penicillamine causes blindness.



amine inversion

Why Are Drugs So Expensive?

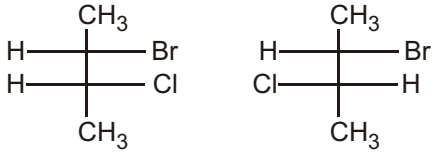
The average cost of launching a new drug is $1.2 billion. The manufacturer has to recover this cost quickly because the patent has to be filed as soon as the drug is first discovered. Although a patent is good for 20 years, it takes an average of 12 years to bring a drug to market after its initial discovery, so the patent protects the discoverer of the drug for an average of 8 years. It is only during the eight years of patent protection that drug sales can provide the income needed to cover the initial costs as well as to pay for research on new drugs.

Why does it cost so much to develop a new drug? First of all, the Food and Drug Administration (FDA) has high standards that must be met before a drug is approved for a particular use. An important factor leading to the high price of many drugs is the low rate of success in progressing from the initial concept to an approved product. In fact, only 1 or 2 of every 100 compounds tested become lead compounds. A lead compound is a compound that shows promise of becoming a drug. Chemists modify the structure of a lead compound to see if doing so improves its likelihood of becoming a drug. For every 100 structural modifications of a lead compound, only one is worthy of further study. For every 10,000 compounds evaluated in animal studies, only 10 will get to clinical trials. Clinical trials consist of three phases. Phase I evaluates the effectiveness, safety, side effects, and dosage levels in up to 100 healthy volunteers; phase II investigates the effectiveness, safety, and side effects in 100 to 500 volunteers who have the condition the drug is meant to treat; and phase III establishes the effectiveness and appropriate dosage of the drug and monitors adverse reactions in several thousand volunteer patients. For every 10 compounds that enter clinical trials, only 1 satisfies the increasingly stringent requirements to become a marketable drug.

☑ SPECIAL TOPIC

DIASTEREOMERS

Let's start off with a simple case where we only have two stereocenters. Consider the two compounds below:

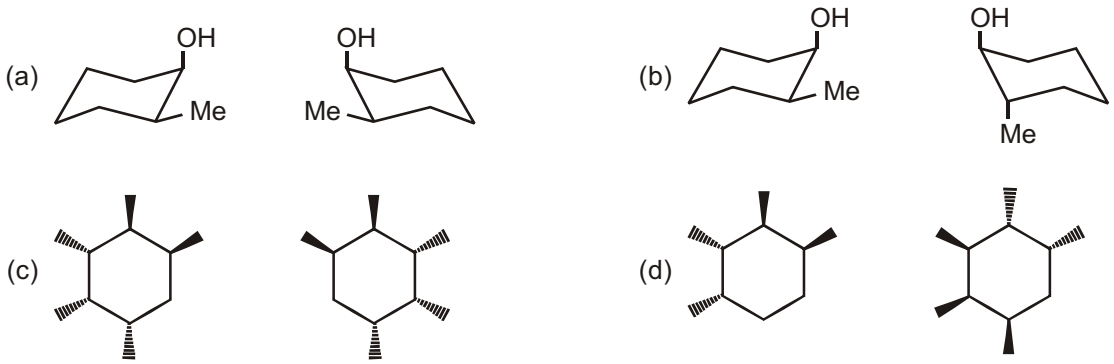


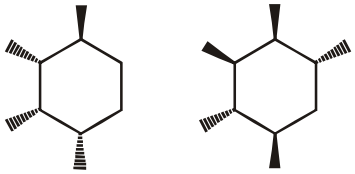
We can clearly see that they are not the same compound. In other words, they are nonsuperimposable. But, they are not mirror images of each other. The top stereocenter has the same configuration in both compounds. If they are not mirror images, then they are not enantiomers. So what is their relationship? They are called di-astereomers.

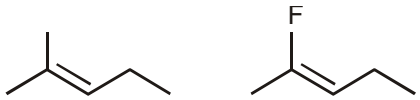
Diastereomers are any compounds that are nonsuperimposable stereoisomers that are not mirror images of each other.

Solved Example

- For each pair compounds below, determine whether the pair are enantiomers or diastereomers.

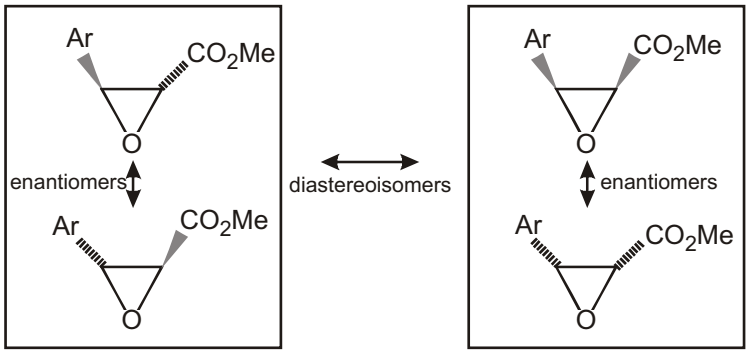


(e) 

(f) 

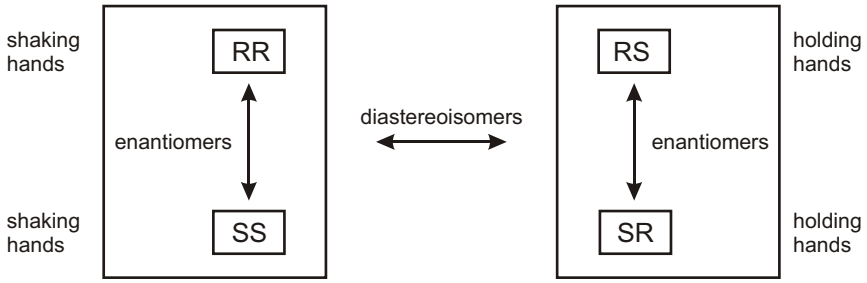
Ans. (a) Enantiomers (b) Diastereomers (c) Enantiomers (d) Different compounds
(e) Different compound (f) Different compounds

If a compound is chiral, it can exist as two enantiomers. We've just drawn the two enantiomers of each of the diastereoisomers of our epoxide. This set of four structures contains two diastereoisomers (stereoisomers that are not mirror images). These are the two different chemical compounds, the cis and trans epoxides, that have different properties. Each can exist as two enantiomers (stereoisomers that are mirror images) indistinguishable except for rotation. We have two pairs of diastereoisomers and two pairs of enantiomers. When you are considering the stereochemistry of a compound, always distinguish the diastereoisomers first and then split these into enantiomers if they are chiral.

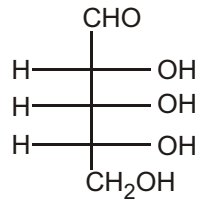


trans epoxide cis epoxide

We can illustrate the combination of two stereogenic centres in a compound by considering what happens when you shake hands with someone. Hand-shaking is successful only if you each use the same hand! By convention, this is your right hand, but it's equally possible to shake left hands. The overall pattern of interaction between two right hands and two left hands is the same: a right-handshake and a left-handshake are enantiomers of one another; they differ only in being mirror images. If, however, you misguidedly try to shake your right hand with someone else's left hand you end up holding hands. Held hands consist of one left and one right hand; a pair of held hands have totally different interactions from pair of shaking hands; we can say that holding hands is a diastereoisomer of shaking hands. We can summarize the situation when we have two hands, or two chiral centres, each one *R* or *S*.



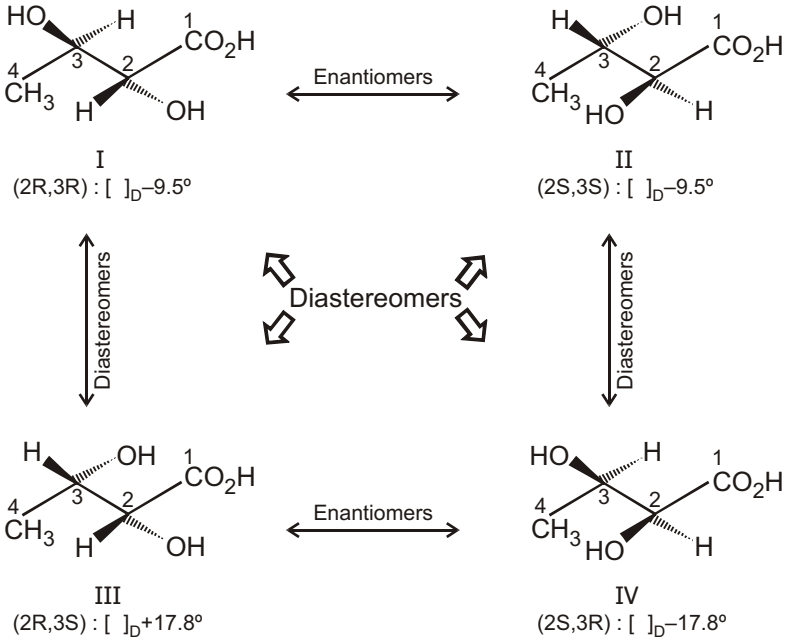
What about compounds with more than two stereogenic centres? The family of sugars provides lots of examples. Ribose is a 5-carbon sugar that contains three stereogenic centres. The enantiomer shown here is the one used in the metabolism of all living things and, by convention, is known as D-ribose. The three stereogenic centres of D-ribose have the *R* configuration. In theory we can work out how many 'stereoisomers' there are of a compound with three stereogenic centres simply by noting that there are 8 (2^3) ways of arranging *R* and *S*.



RRR	RRS	RSR	RSS
SSS	SSR	SRS	SRR

But this method blurs the all-important distinction between diastereoisomers and enantiomers. In each case, the combination in the top row and the combination directly below it are enantiomers (all three centres are inverted); the four columns are diastereoisomers. Three stereogenic centres therefore give four diastereoisomers, each a pair of two enantiomers.

Chiral Molecules with Two Chirality Centers



I
(2R,3R) : $[\ ]_D$–9.5°

II
(2S,3S) : $[\ ]_D$–9.5°

III
(2R,3S) : $[\ ]_D$+17.8°

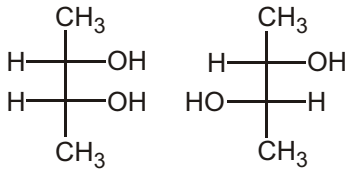
IV
(2S,3R) : $[\ ]_D$–17.8°

Solved Example

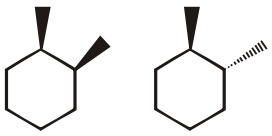
- Which of the following pair are diastereomers?

(A) cis-2-Butene,trans-2-Butene

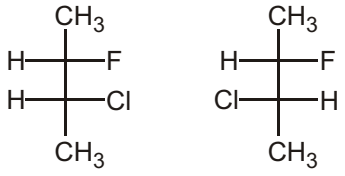
(B)



(C)

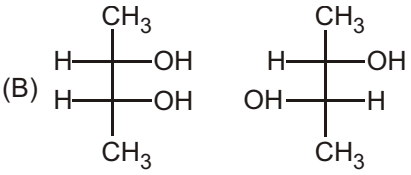


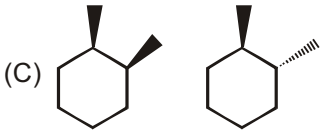
(D)

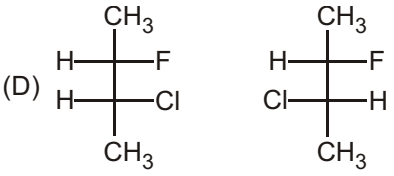


Ans. (A, B, C, D)

Sol. (A) 

(B) 

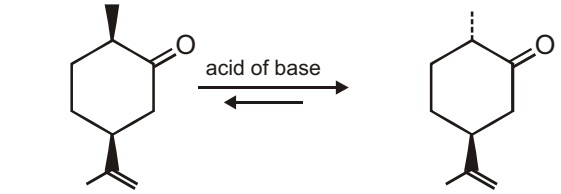
(C) 

(D) 

Diastereomers are not mirror image of each other

Interconversion of monoterpene stereoisomers through enolization

On heating with either acid or base, the monoterpene ketone **isodihydrocarvone** is largely converted into one product only, its stereoisomer **dihydrocarvone.**

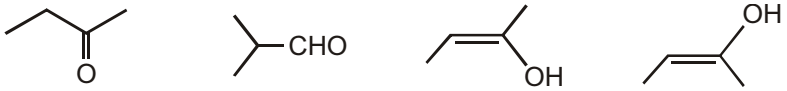


(–)-isodihydrocarvone (–)-dihydocarvone

There are two chiral centres in isodihydrocarvone, but only one of these is adjacent to the carbonyl group and can participate in enolization. Under normal circumstances, we might expect to generate an equimolar mixture of two diastereoisomers. This is because two possible configurations could result from the chiral centre a to the carbonyl, whereas the other centre is going to stay unchanged.

Solved Example

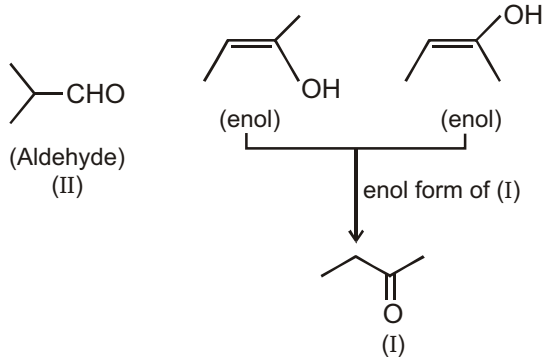
- Predict the correct relationship between given compounds :



(I) (II) (III) (IV)

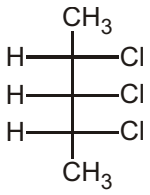
(A) (I) and (II) are tautomers of each other.
(B) (III) and (IV) are enol form of compound (II)
(C) (II) and [(III), (IV)] are functional isomers
(D) (I) and (II) will give same enol forms.

Sol. (C)



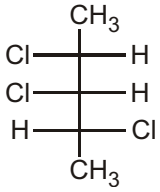
Solved Example

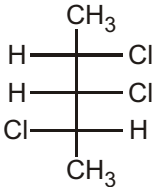
- Number of diastereomer of given compound :

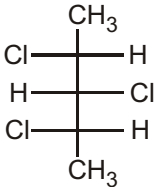


(A) 2
(B) 3
(C) 4
(D) 6

Sol.



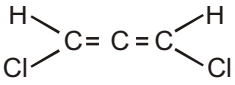


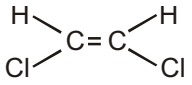


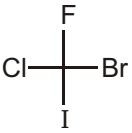
3

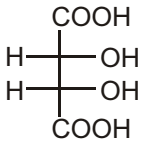
Solved Example

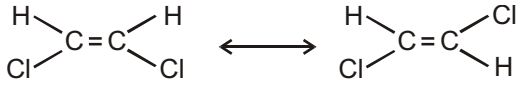
- Which of the following can exist in diastereomeric form?

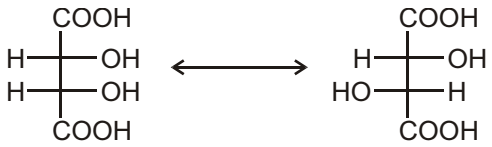
(A) 

(B) 

(C) 

(D) 

Sol. (B)  ; diastereomers

(D)  ; diastereomers

(meso)-tartaric acid

☑ SPECIAL TOPIC

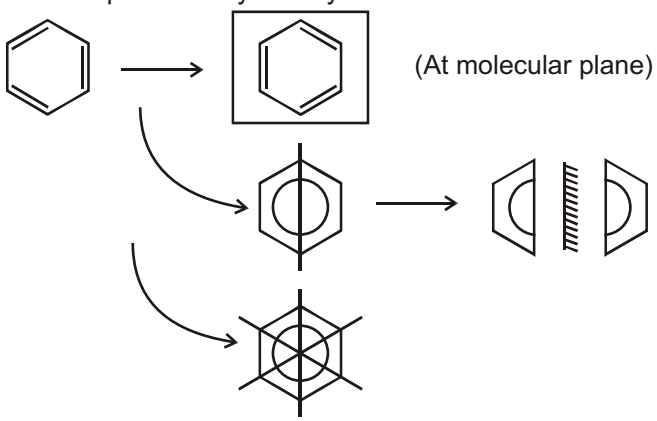
PLANE OF SYMMETRY

Plane of symmetry ( ) : An imaginary plane which bisects the molecule into two equal halves is called as plane of symmetry. It is also known as internal mirror plane.

Only one plane of symmetry in any conformer of compound is sufficient for optical inactivity.

Solved Example

- Benzene molecule has total 7 planes of symmetry.



(At molecular plane)

Solved Example

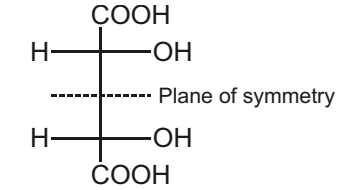
- Most of the alphabets from A to Z have a molecular plane (horizontal) and a vertical plane. The vertical plane is shown as follows :

A	B	C	D	E	F	G	H	I	J	K
✓	✓	✓	✓	✓	×	×	✓✓	✓✓	×	✓
L	M	N	O	P	Q	R	S	T	U	V
×	✓	×	✓✓	×	×	×	×	✓	✓	✓
W	X	Y	Z							
✓	✓✓	✓	×							

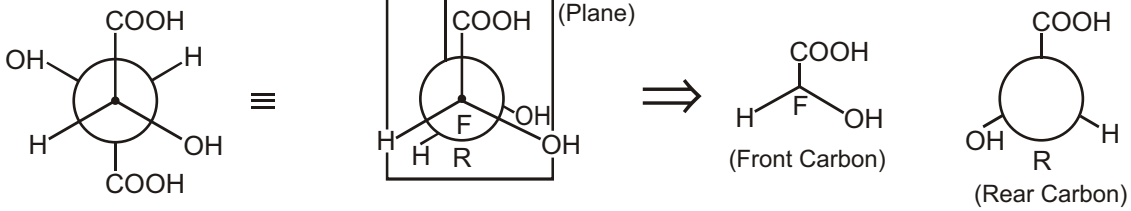
✓ One plane
✓✓ Two or more planes
× No plane

Solved Example

- Mesotartaric acid :



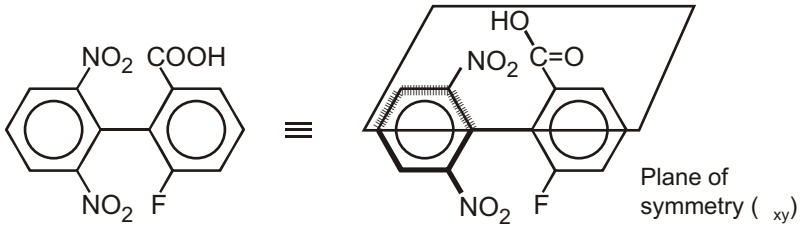
(Fischer Projection Formula)



(Newman Formula) (Front Carbon) (Rear Carbon)

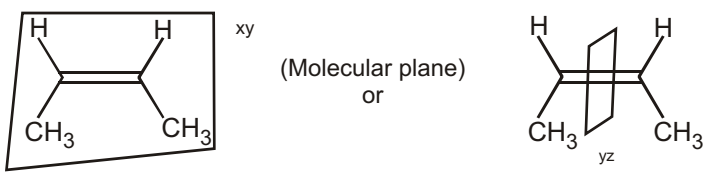
Solved Example

- A tetrasubstituted biphenyl



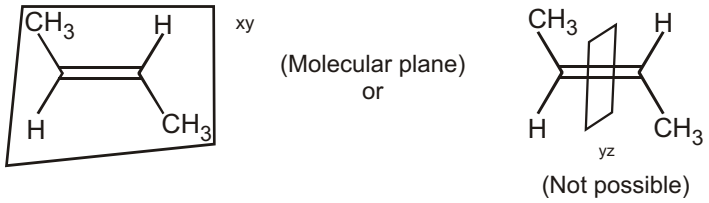
Solved Example

- Cis 2-butene



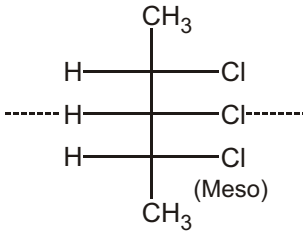
Solved Example

- Trans 2-butene



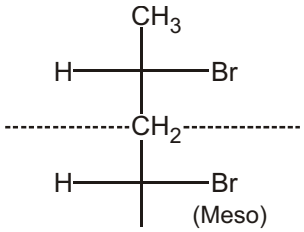
Solved Example

- 2,3,4-trichloropentane



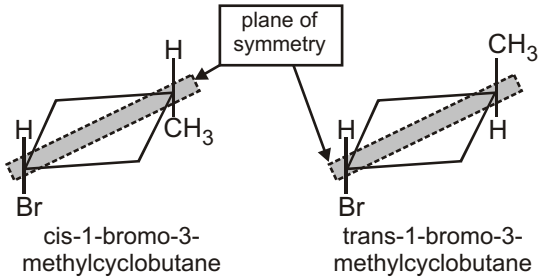
Solved Example

- 2,4-dibromopentane



Solved Example

-



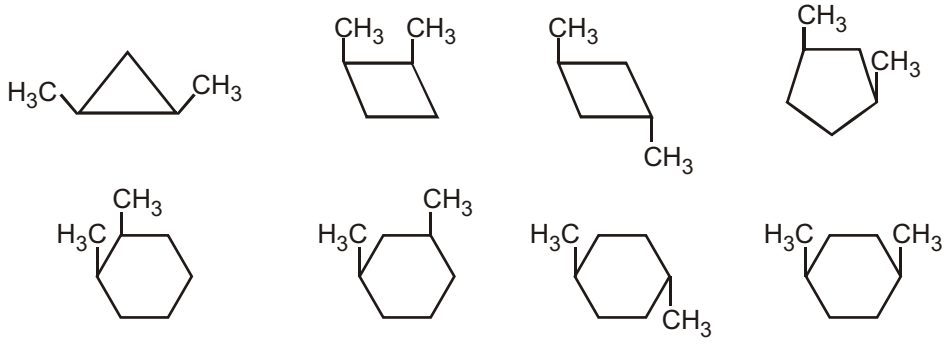
A molecule that has a nonidentical mirror image, such as either enantiomer of 2-bromobutane, is said to be **chiral** (ky-ral). A chiral molecule does not contain a plane of symmetry. A **plane of symmetry** is a plane that cuts a molecule into two halves, each of which is the mirror image of the other.

Chiral objects do not contain a plane of symmetry

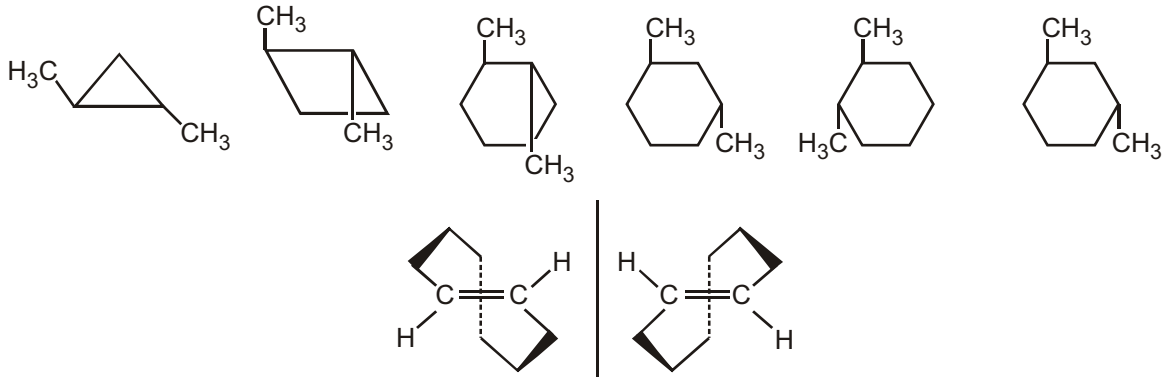
A molecule or object that does contain a plane of symmetry is said to be achiral (ayky-ral). If you cut the object in two halves along the plane of symmetry, the left half is the mirror image of the right half. A fork and a table each has a plane of symmetry, so they are achiral.

Solved Example

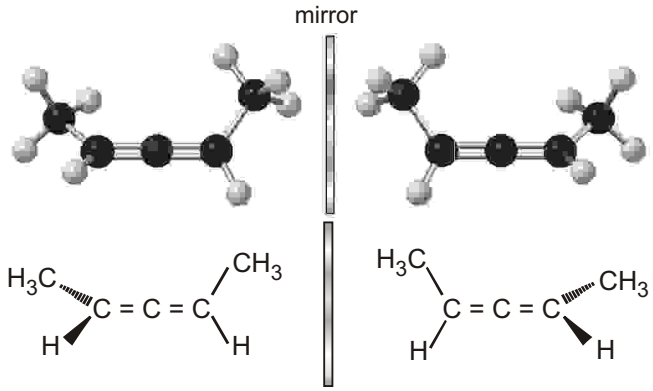
- Achiral structures :



Chiral structures



These conformations are nonsuperimposable mirror images, and they do not interconvert. They are enantiomers, and they can be separated and isolated. Each of them is optically active, and they have equal and opposite specific rotations.



enantiomers of penta-2,3-diene

Solved Example

- 

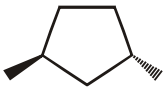
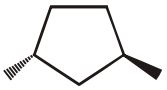
(A) (B) (C) (D)

Which of the following will be optically active?

(A) Pure (A)
(B) pure (C)
(C) an equal mixture of (A) and (B)
(D) pure (D)

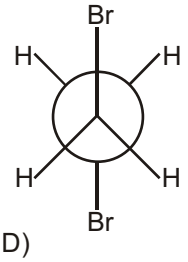
Ans. (A)

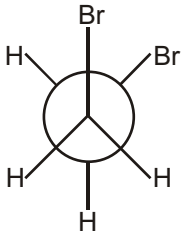
Sol.

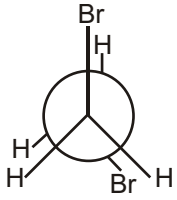
Compound	POS	optically active
 (A)	✗	✔
 (B)	✗	✔
 (C)	✔	✗
 (D)	✔	✗

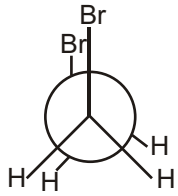
Solved Example

- Which of the following conformer has presence of plane of symmetry

(A) 

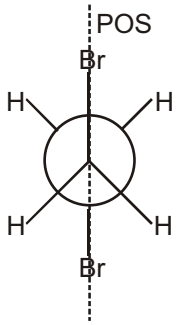
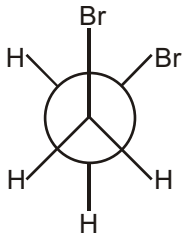
(B) 

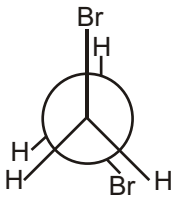
(C) 

(D) 

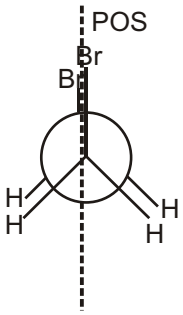
Sol. (A,D)

Sol.

Compound	POS
(A) 	✔
(B) 	✗

(C) 

✗

(D) 

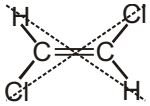
✗

☑ SPECIAL TOPIC

CENTER OF SYMMETRY (COS)

An imaginary center in a molecule through which if we draw two lines in opposite direction and they meet the same atom after the same distance (this rule should applicable for each atom in molecule). Then molecule is said to have center of symmetry it also called center of inversion (Ci).

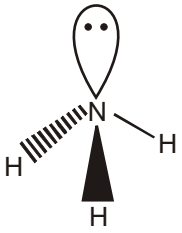
This operation is only applicable for three-dimensional formula and not for Fisher projection formula.



Point of symmetry

Solved Example

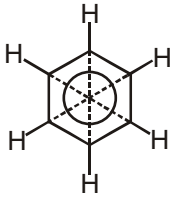
- Ammonia molecule



COS absent

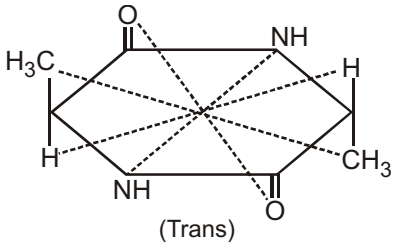
Solved Example

- Benzene molecule



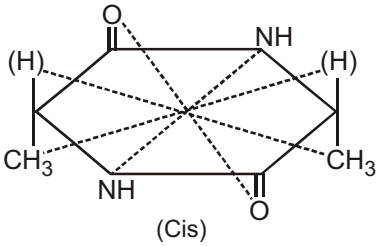
COS present

Solved Example



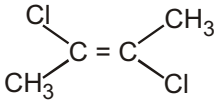
(Trans)
COS present

Solved Example



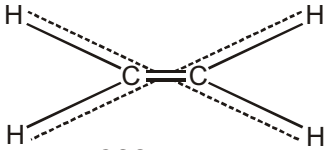
(Cis)
COS absent

Solved Example



COS present

Solved Example



COS present

☑ SPECIAL TOPIC

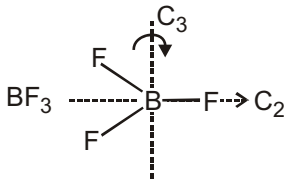
AXIS OF SYMMETRY (C_n)

An imaginary axis (passing through center) in a molecule through which if we rotate the molecule by a certain minimum angle ( ) and if molecule is again reappear than the molecule is said to have axis of symmetry

It is represented as C_n where n $\frac{360}{\quad}$.

AOS has nothing to do with optical activity. All objects of universe have (C_1) one AOS which is called natural axis of symmetry.

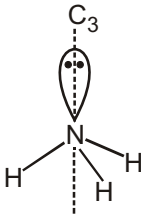
Solved Example



n = 360/120 = 3

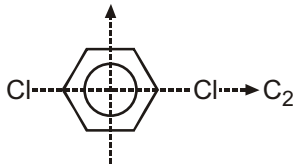
Therefore, C_n C_3 axis.

Solved Example



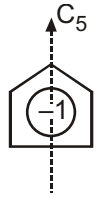
If there are two or more types of C_n axes, then the axis with higher value of n is the main axis.

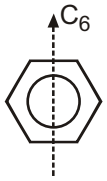
Solved Example

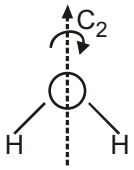


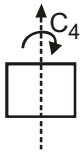
If there are two or more possible AOS with the same value of n, then preference is given to the axis that passes through more no. of atoms.

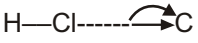
Solved Example

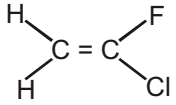




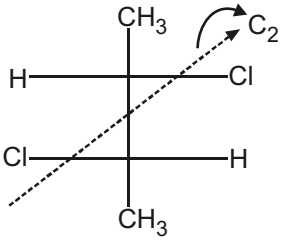




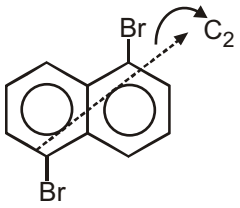


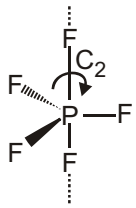


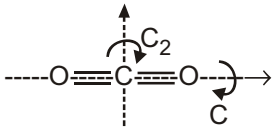
(AOS (absent)

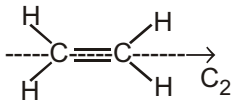


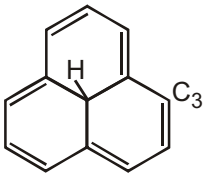
(In Fisher projection formula, AOS is visible.)

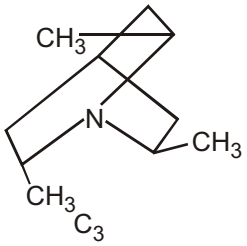






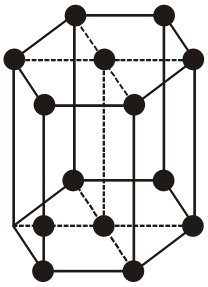
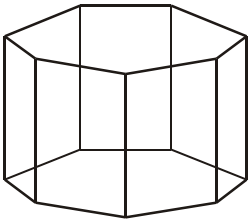
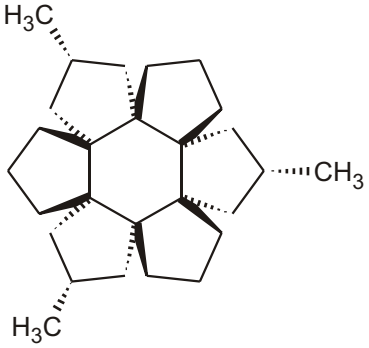






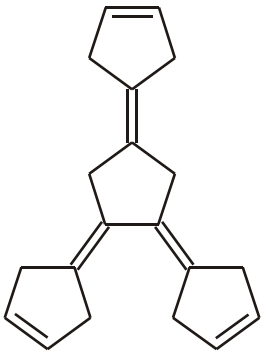
Solved Example

- **Match the Column**

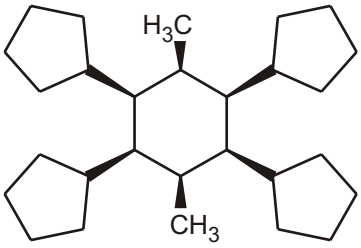
Column-I	**Column-II**
(A) C_2-axis of symmetry	(P) 
(B) C_3-axis of symmetry	(Q) 
(C) Plane of symmetry	(R) 

(D) Centre of symmetry

(S)

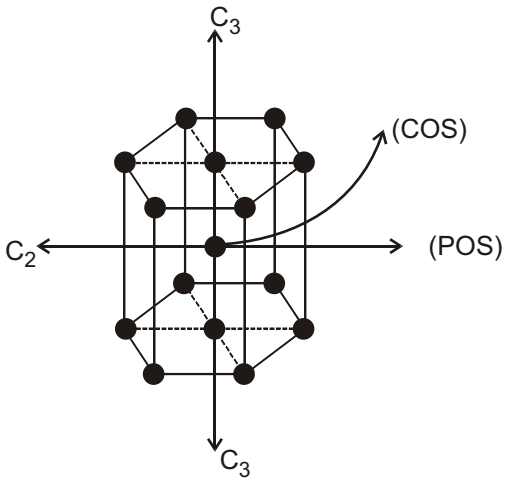


(T)



Ans. A P,Q,S,T; B PR; C PQRST; D P;

Sol.



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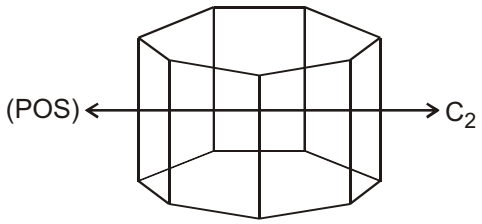

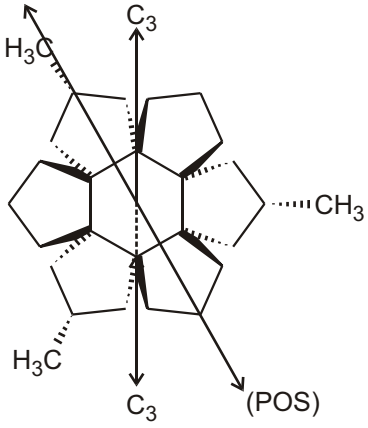

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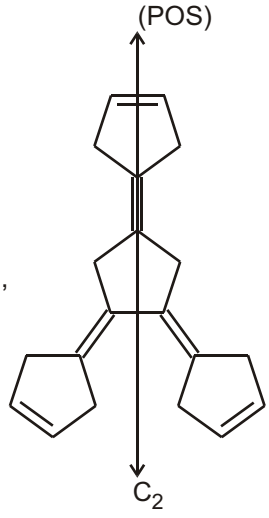

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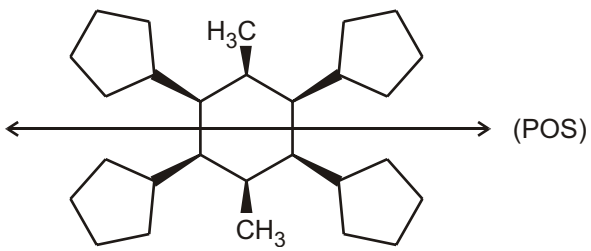
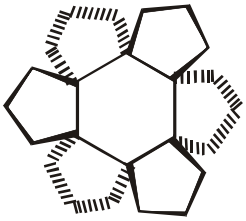
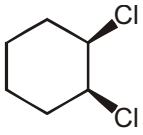
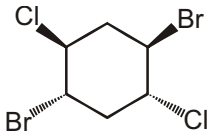
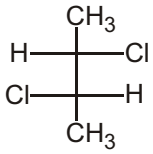
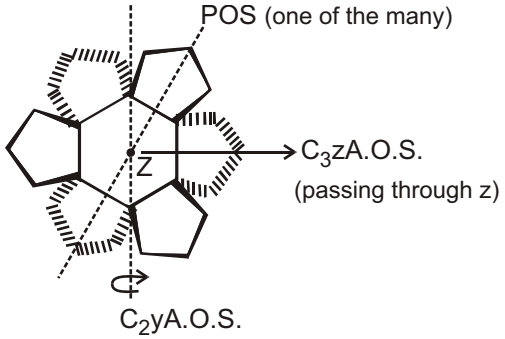


Solved Example

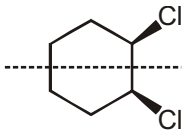
- **Match the Column**

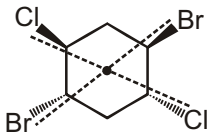
Column-I	**Column-II**
(A) 	(P) Centre of symmetry
(B) 	(Q) C_2 axis of symmetry
(C) 	(R) Plane of symmetry
(D) 	(S) Optically active
	(T) C_3 axis of symmetry

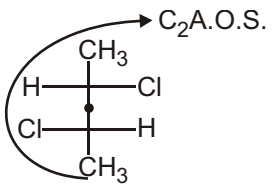
Ans. A P, Q, R, T; B R; C P; D Q, S

Sol. (A) 

Molecule possess C.O.S. with centre z.

(B) 
P.O.S.

(C) 
C.O.S. present

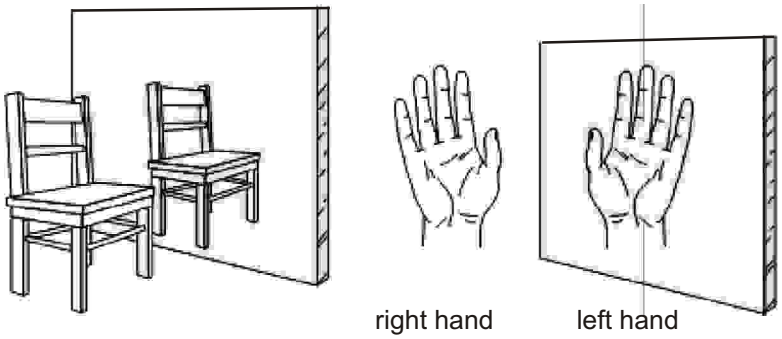
(D) 

Optically active

☑ SPECIAL TOPIC

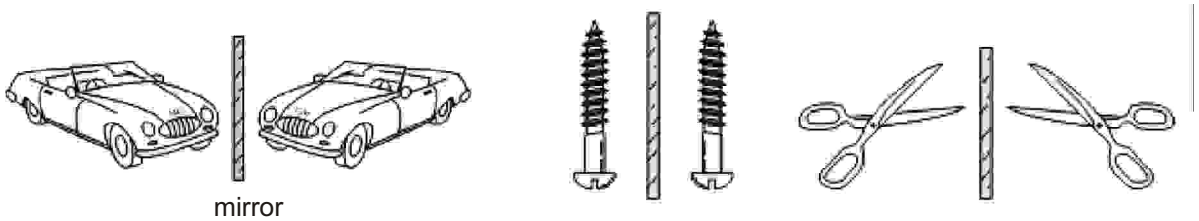
CHIRALITY

The discovery of stereochemistry was one of the most important breakthroughs in the structural theory of organic chemistry. Stereochemistry explained why several types of isomers exist, and it forced scientists to propose the tetrahedral carbon atom.



right hand left hand

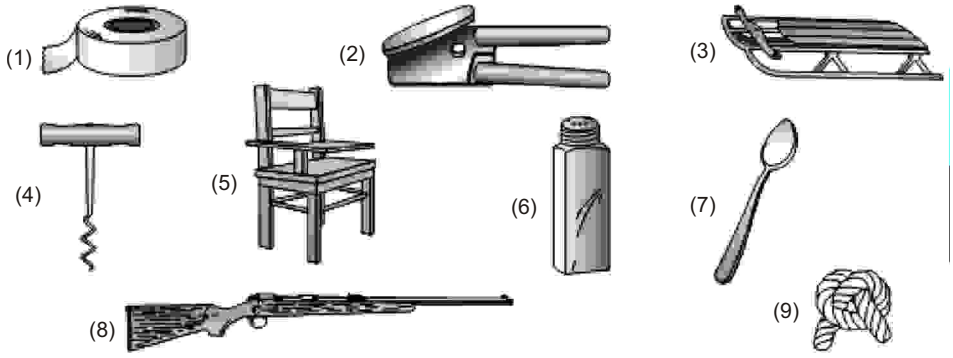
Use of a mirror to test for chirality. An object is chiral if its mirror image is different from the original object.



mirror mirror mirror

Common chiral objects. Many objects come in “left-handed” and “right-handed” versions.

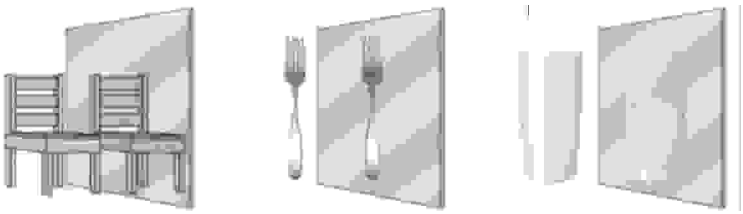
Determine whether the following objects are chiral or achiral.



(4, 6, 8 are chiral)

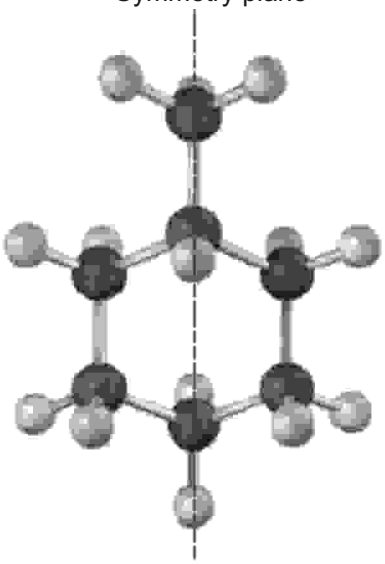
Why can’t you put your right shoe on your left foot? Why can’t you put your right glove on your left hand? It is because hands, feet, gloves, and shoes have right-handed and lefthanded forms. An object with a right-handed and a left-handed form is said to be chiral (ky-ral), a word derived from the Greek word cheir, which means “hand.” A chiral object has a nonsuperimposable mirror image. In other words, its mirror image is not the same as an image of the object itself. A hand is chiral because when you look at your right hand in a mirror, you see a left hand, not a right hand

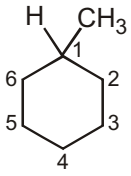
In contrast, a chair is not chiral; the reflection of the chair in the mirror looks the same as the chair itself. Objects that are not chiral are said to be achiral. An achiral object has a superimposable mirror image



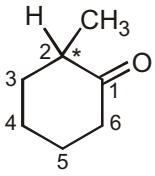
A chiral molecule has a nonsuperimposable mirror image.
An achiral molecule has a superimposable mirror image.

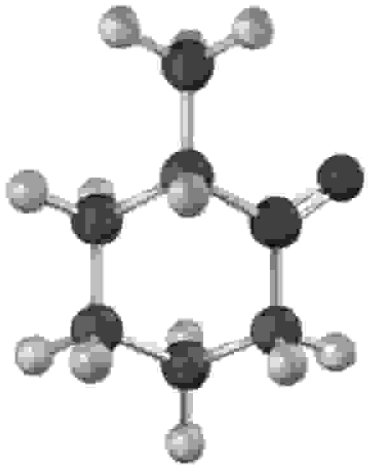
Symmetry plane





Methylcyclohexane (achiral)





2-Methylcyclohexanone (chiral)

► **Achiral structures are superimposable on their mirror images**

Solved Example

- Which of the following objects are chiral?
  (a) Soda can (b) Screwdriver (c) Screw (d) Shoe

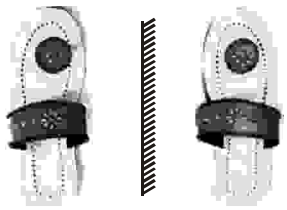
Sol. (c, d)

Solved Example

- Ignoring specific markings, which of the following objects are chiral ?
  (I) a shoe (II) a book
  (III) a pencil (IV) a pair of shoes (consider the pair as one object)
  (V) a pair of scissors
  (A) I only (B) I & V (C) I, IV, V (D) III, IV, V

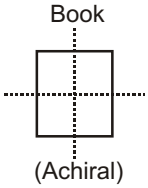
Sol. (B)

(I)



A shoe (chiral)

(II)

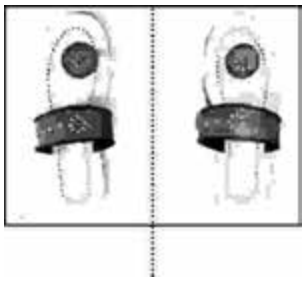


(Achiral)

(III)

A pencil
(Achiral)

Pair of shoe

(IV) 

Internal POS
(Achiral)

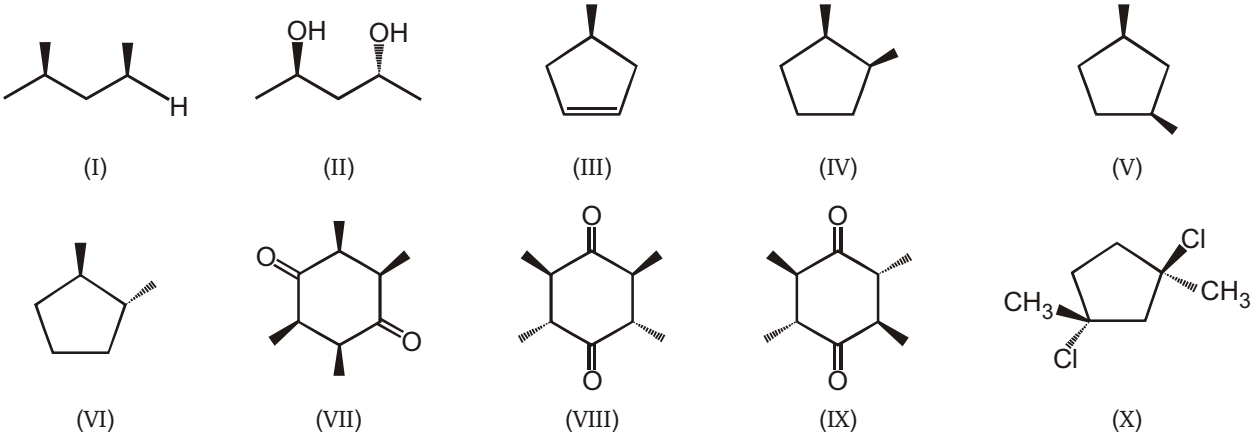
(V) 

(chiral)
(asymmetric)

(a pair of scissors)

Solved Example

- How many compounds shown below are chiral?



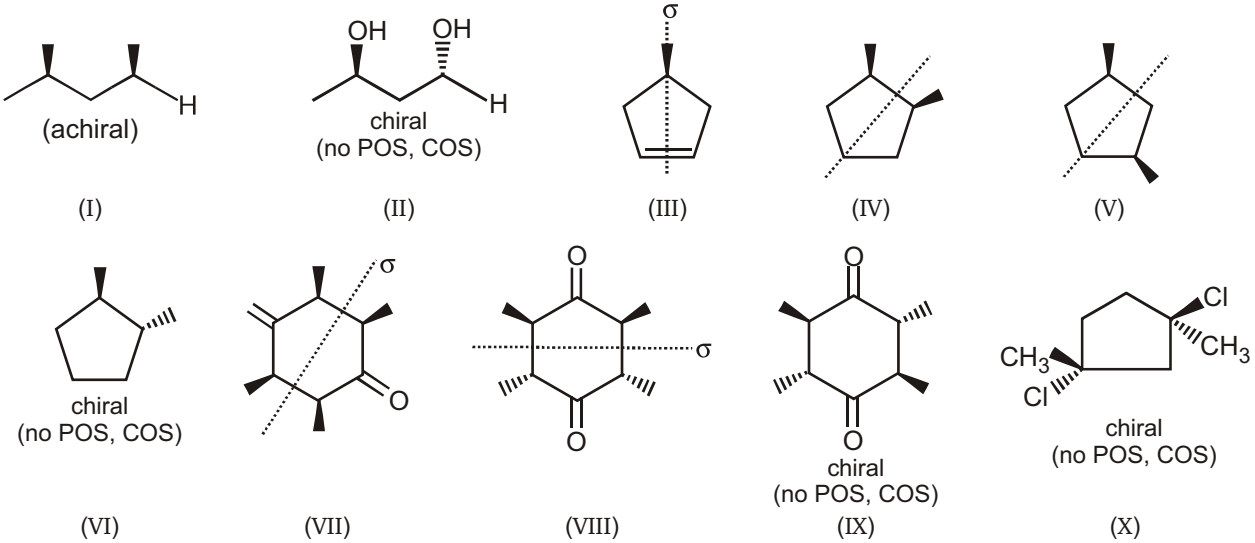
(I) (II) (III) (IV) (V)

(VI) (VII) (VIII) (IX) (X)

(A) 4 (B) 5 (C) 6 (D) 8

Ans. (A)

Sol. Compound which are chiral are (II), (VI), (IX), (X)

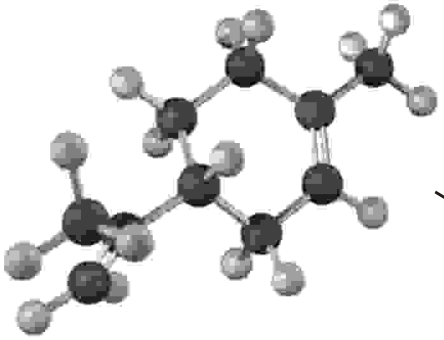


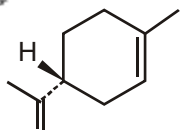
(I) (II) (III) (IV) (V)

(VI) (VII) (VIII) (IX) (X)

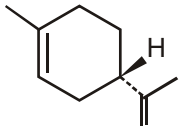
Chirality in Nature and Chiral Environments

Although the different enantiomers of a chiral molecule have the same physical properties, they usually have different biological properties. For example, the (+) enantiomer of limonene has the odor of oranges and lemons, but the (–) enantiomer has the odor of pine trees.

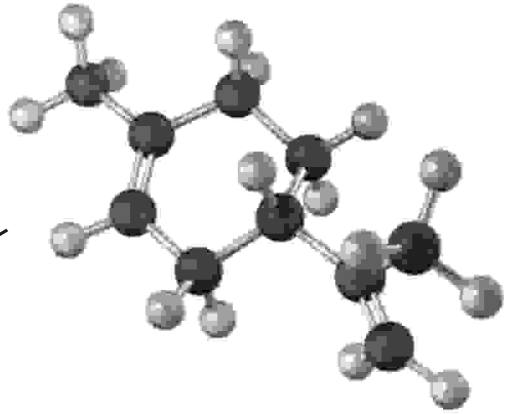




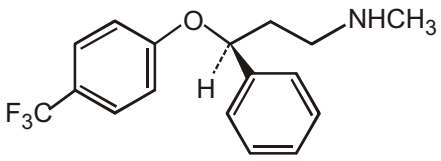
(+)-Limonene
(in citrus fruits)



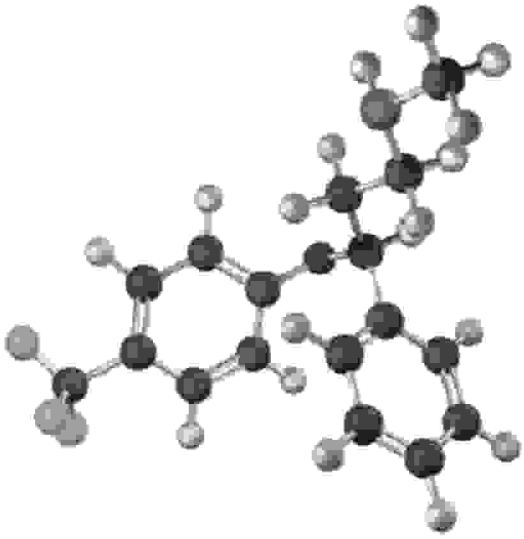
(–)-Limonene
(in pine trees)



More dramatic examples of how a change in chirality can affect the biological properties of a molecule are found in many drugs, such as fluoxetine, a heavily prescribed medication sold under the trade name Prozac. Racemic fluoxetine is an extraordinarily effective antidepressant but has no activity against migraine. The pure S enantiomer, however, works remarkably well in preventing migraine. Other examples of how chirality affects biological properties are given in A Deeper Look at the end of this chapter.



(S)-Fluoxetine
(prevents migraine)



☑ SPECIAL TOPIC

MESO COMPOUNDS

This is a topic that notoriously confuses students, so let's start off with analogy.

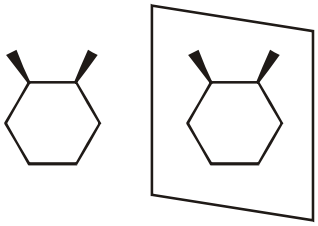
Now imagine that the parents, out of nowhere, have a one more child who is born without a twin—just a regular one-baby birth. When you look at this family, you would see a lot of sets of twins, and then one child who has no twin (and has tw'o moles—one on each side of his face). You might ask that child, where is your twin? Where is your mirror image? He would answer :

''I don't have a twin. I am the mirror image of myself. That's why the family has an odd number of children, instead of an even number.''

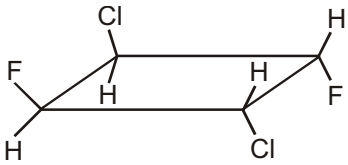
The analogy goes like this: when you have a lot of stereocenters in a compound, there will be many stereoisomers (brothers and sisters). But, they will be paired up into sets of enantiomers (twins). Any one molecule will have many, many diastereomers (brothers and sisters), but it will have only one internal enantiomer (its mirror image twin). For example, consider the following compound :

A meso compound has stereocenters, but the compound also has symmetry that allows it to be the mirror image of itself. Consider cis- l ,2-dimethylcyclohexane as an example. This molecule has a plane of symmetry cutting the molecule in half. Everything on the left side of the plane is mirrored by everything on the right side:

If a molecule has an internal plane of symmetry, then it is a meso compound. If you try to draw the enantiomer (using either one of the two methods we saw), you will find that you are drawing the same thing again. This molecule does not have a twin. It is its own mirror image :



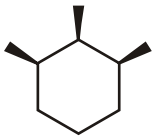
It can also happen when the compound has a center of inversion. For example,



compound will be superimposable on its mirror image, and the compound is meso.

Solved Example

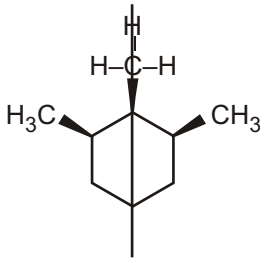
- Is the following a meso compound?



Ans. We need to try to draw the mirror image and see if it is just the same compound redrawn. If we use the second method for drawing enantiomers (placing the mirror on the side), then we will be able to see that the compound we would draw is the same thing :

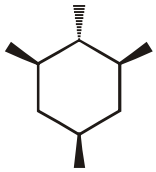
Therefore, it is a meso compound.

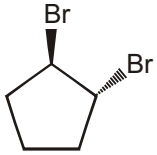
A simpler way to draw the conclusion would be to recognize that the molecule has an internal plane of symmetry that chops through the center of one of the methyl groups:

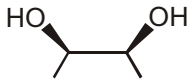


Solved Example

- Identify which of the following compounds is a meso compound.

(a) 

(b) 

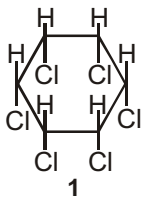
(c) 

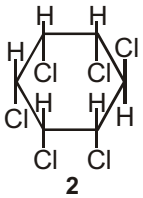
Sol. (a, c)

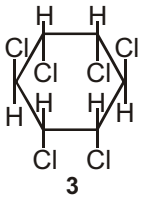
Solved Example

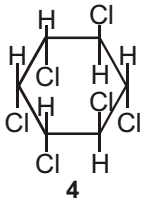
- Find the number of meso, enantiomer, diastereomer structures in gamexene ($C_6H_6Cl_6$)

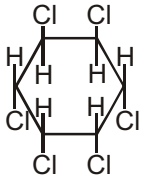
Sol.

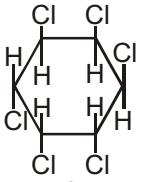

1
all cis
meso

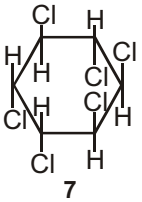

2
1-trans
meso

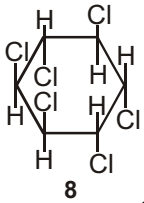

3
1,4-trans
meso


4
1,3-trans
meso

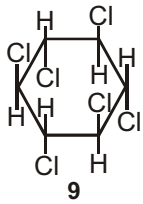

5
1,2-trans
meso


6
1,2,3-trans
meso


7


8

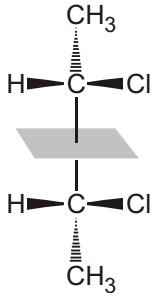
1,2,4-trans
Enantiomers

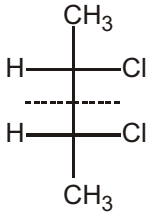

9
1,3,5-trans
meso

Ans. 7 meso, 2 enantiomer, 8 diastereomers

Final Definition of Meso Compound

A meso comound is one whose molecules are superimposable on their mirror images even though they contain chiral centers. A meso compound is optically inactive due to internal compensation (*i.e.,* cancellation) because half part of molecule rotate the PPL clockwise and other half part anticlockwise. The rotation caused by half part of molecule is cancelled by an equal and opposite rotation caused by another half part of molecule that is the mirror image of the first.

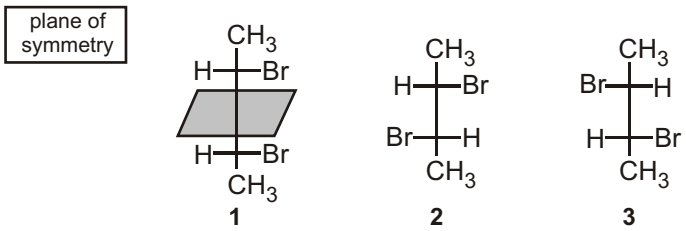




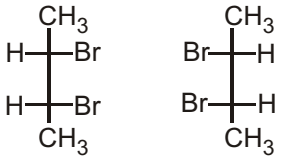
The molecule has a plane of symmetry, and cannot be chiral. (Caution : If we do not see a plane of symmetry, however, this does not necessarily mean that the molecule is chiral).

In the examples we have just seen, each compound with two chirality centers has four stereoisomers. However, some compounds with two chirality centers have only three stereoisomers. This is why we emphasized in that the maximum number of stereoisomers a compound with *n* chirality centers can have is 2^n, instead of stating that a compound with n chirality centers has 2^n stereoisomers.

An example of a compound with two chirality centers that has only three stereoisomers is 2,3-dibromobutane.



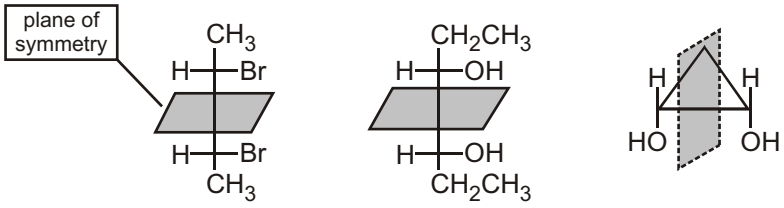
The ''missing'' stereoisomers is the mirror image of stereoisomer **1**. Stereoisomer **1** has a plane of symmetry, which means that it does not have a nonidentical mirror image. If we draw the mirror image of stereoisomer **1**, we find that it and stereoisomer **1** are identical. To convince yourself that the two structures are identical, rotate by 180° the mirror image of stereoisomer **1** that you just drew and you will see that it is identical to stereoisomer **1**. (Remember, you can move Fischer projections only by rotating them 180º in the plane of the paper.)



superimposable mirror images

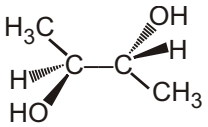
A meso compound is an achiral compound that has two or more chirality centers.

Stereoisomer **1** is called a meso compound. Even though a meso compound has chirality centers, it is an achiral molecule because it has a plane of symmetry. Mesos is the Greek word for ''middle.'' Because of the plane of symmetry, a meso compound does not rotate the plane of polarized light. It is optically inactive. A meso compound can be recognized by the fact that it has two or more chirality centers and a plane of symmetry. If a compound has a plane of symmetry, it will not be optically active even thugh it has chirality centers.

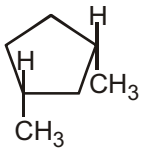


meso compounds

If a compound with two chirality centers has the same four groups bonded to each of the chirality centers, one of its stereoisomers will be a meso compound.



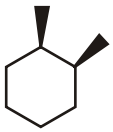
a meso compound

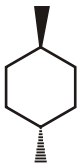


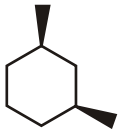
a meso compound

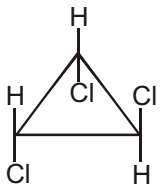
Solved Example

- Which of the following is a meso molecule

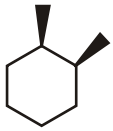
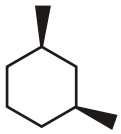
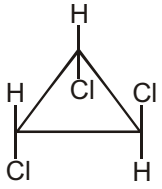
(A) 

(B) 

(C) 

(D) 

Ans. (A,C,D)

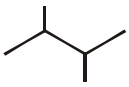
Compound	Chiral Carbon	POS
(A) 	2	✔
(B) 	0	✔
(C) 	2	✔
(D) 	–	✔

Solved Example

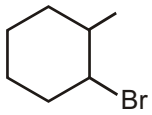
- How many compound has a stereoisomer that is a meso compound : suppose this value is *x*. So the value of *x* 7 is :

2-bromo-3-chlorobutane (A)

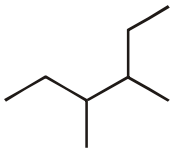
2,2-dibromopropane (B)

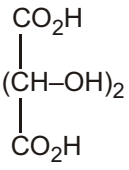

(C)

2, 3-dichlorobutane (D)



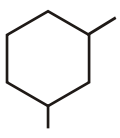
(E)

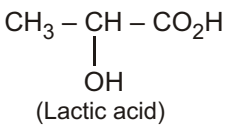

(F)



(Tartaric acid)
(G)

1, 2-dimethyl cyclohexane (H)

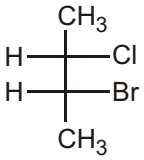
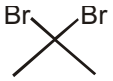
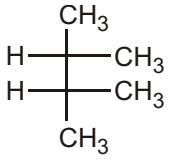
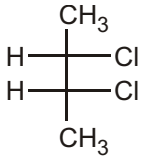
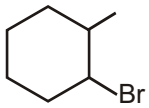
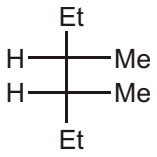
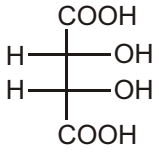
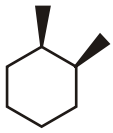
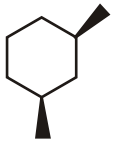
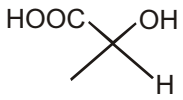

(I)



(Lactic acid)
(J)

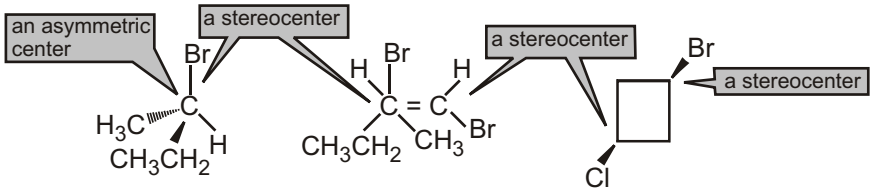
Ans. 12

Sol.

Compound	Chiral centre	POS	Meso
(A) 	2	✗	✗
(B) 	0	✔	✗
(C) 	0	✔	✗
(D) 	2	✔	✔
(E) 	2	✗	✗
(F) 	2	✔	✔
(G) 	2	✔	✔
(H) 	2	✔	✔
(I) 	2	✔	✔
(J) 	1	✗	✗

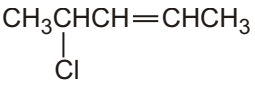
DIFFERENCE BETWEEN CHIRAL CENTER AND STEREOCENTER

An asymmetric center is also called a stereocenter (or a stereogenic center), but they do not mean quite the same thing. A stereocenter is an atom at which the interchange of two groups produces a stereoisomer. Thus, stereocenters include both (1) asymmetric centers, where the interchange of two groups produces an enantiomer, and (2) the sp^2 carbons of an alkene or the sp^3 carbons of a cyclic compound, where the interchange of two groups converts a cis isomer to a trans isomer or vice versa. This means that although all asymmetric centers are stereocenters , not all stereocenters are asymmetric centers.



Solved Example

- (a) How many asymmetric centers does the following compound have?
  (b) How many stereocenters does it have?

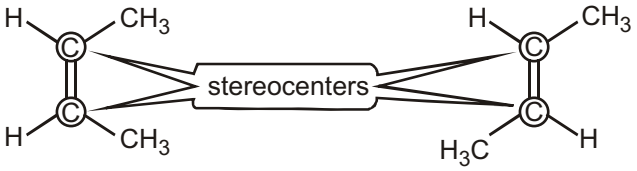


Ans. (a) (1) (b) (3)

Solved Example

- One source defines a meso compound as “an achiral compound with stereocenters.” Why is this a poor definition?

Sol. A stereocenter is an atom at which the interchange of two groups gives a stereoisomer. Stereocenters include both chirality centers and double-bonded carbons giving rise to cis-trans isomers. For example, the isomers of but-2-ene are achiral and they contain stereocenters (circled), so they would meet this definition. They have no chiral diastereomers, however, so they are not correctly called meso.



☑ SPECIAL TOPIC

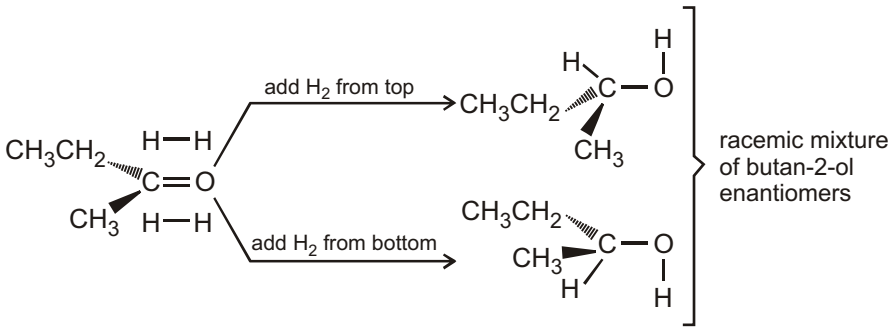
RACEMIC MIXTURE

► **A racemic mixture is a mixture of two enantiomers in equal proportions. This principle is very important. Never forget that, if the starting materials of a reaction are achiral, and the products are chiral, they will be formed as a racemic mixture of two enantiomers.**

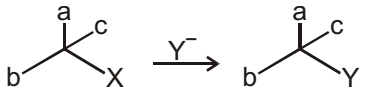
Racemic Mixture :

A mixture of equal amounts of a pair of enantiomers is called a racemic mixture, a racemic modification, or a racemate. Racemic mixtures do not rotate plane polarized light. They are optically inactive because for every molecule in a racemic mixture that rotates the plane of polarization in one direction, there is a mirror-image

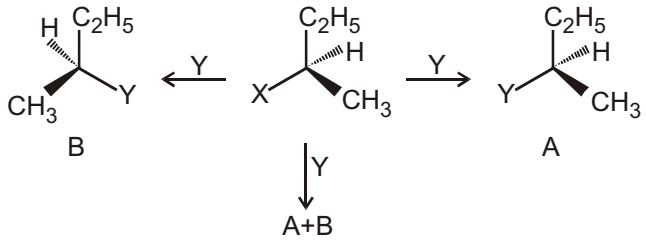
molecule that rotates the plane in the opposite direction. As a result, the light emerges from a racemic mixture with its plane of polarization unchanged.



(i) Retention: Retention of configuration is the preservation of integrity of the spatial arrangement of bonds to an asymmetric centre during a chemical reaction or transformation. It is also the configurational correlation when a chemical species XCabc is converted into the chemical species YCabc having the same relative configuration.



(ii) Inversion, retention and racemisation: There are three outcomes for a reaction at an asymmetric carbon atom. Consider the replacement of a group *X* by *Y* in the following reaction:



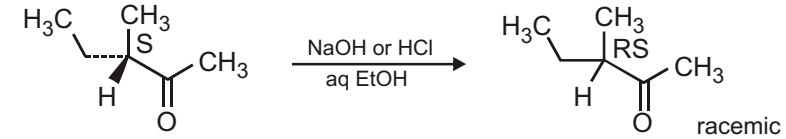
If (A) is the only compound obtained, the process is called retention of configuration.

If (B) is the only compound obtained, the process is called inversion of configuration.

If a 50:50 mixture of the above two is obtained then the process is called recemisation and theproduct is optically inactive, as one isomer will rotate light in the direction opposite to another.

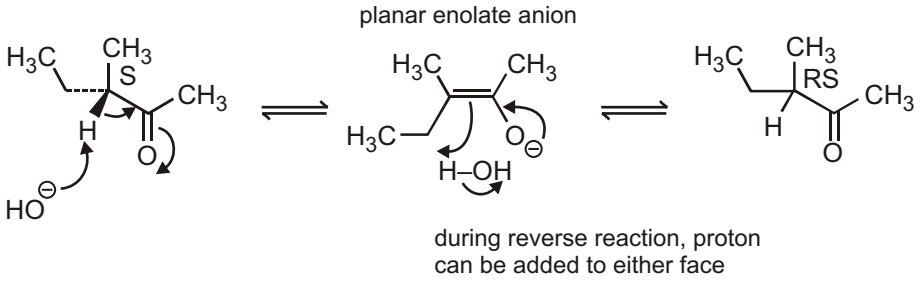
Racemization

The process of hydrogen exchange shown above has implications if the a-carbon is chiral and has a hydrogen attached. Removal of the proton will generate a planar enol or enolate anion, and regeneration of the keto form may then involve supply of protons from either face of the double bond, so changing a particular enantiomer into its racemic form. Reacquiring a proton in the same stereochemical manner that it was lost will generate the original substrate, but if it is acquired from the other face of the double bond it will give the enantiomer, *i.e.,* together making a racemate. Note that removal and replacement of protons at the other a-carbon, *i.e.,* the methyl, will occur, but has no stereochemical consequences.

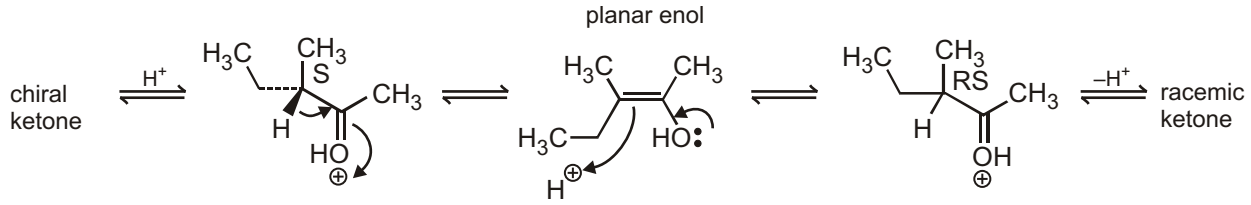


chiral centre must be to carbonyl and contain an H substituent

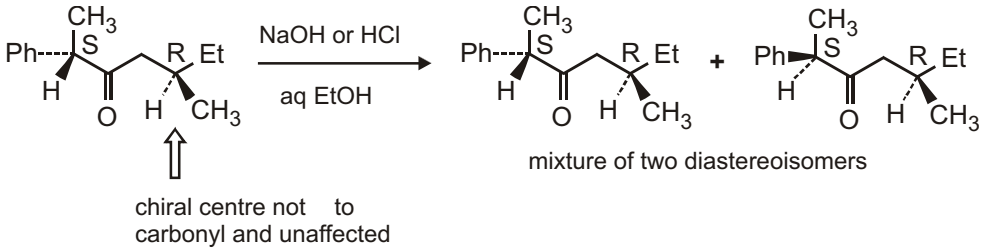
in base:



in acid:



The chiral centre must be to the carbonyl and must contain a hydrogen substituent. If there is more than one chiral centre in the molecule with only one centre to the carbonyl, then the other centres will not be affected by enolization, so the product will be a mixture of **diastereoisomers** of the original compound rather than the racemate.



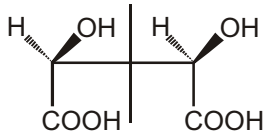
Solved Example

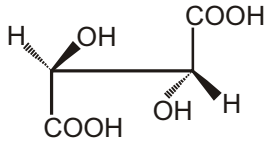
- Which of the following symmetry(s) are present in any conformer of meso tarteric acid ?

(A) POS (Plane of symmetry) (B) COS (Centre of symmetry)

(C) AAOS (Alternate axis of symmetry) (*D) All

Sol.


(POS = S_1)


(COS = S_2)

Solved Example

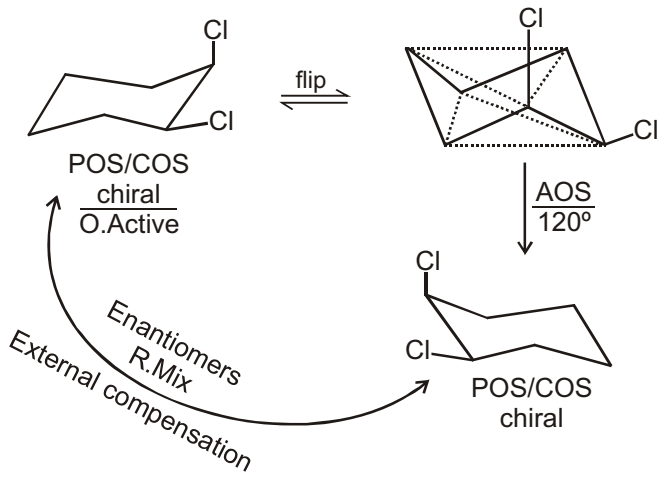
- Cis-1,2-dichloro cyclohexane is optically inactive due to

(A) Plane of symmetry (B) Internal compensation

(C) External compensation (D) All

Ans. (C)

Sol.



Be economical

When we draw organic structures we try to be as realistic as we can be without putting in superfluous detail. Look at these three pictures.

1

2

3

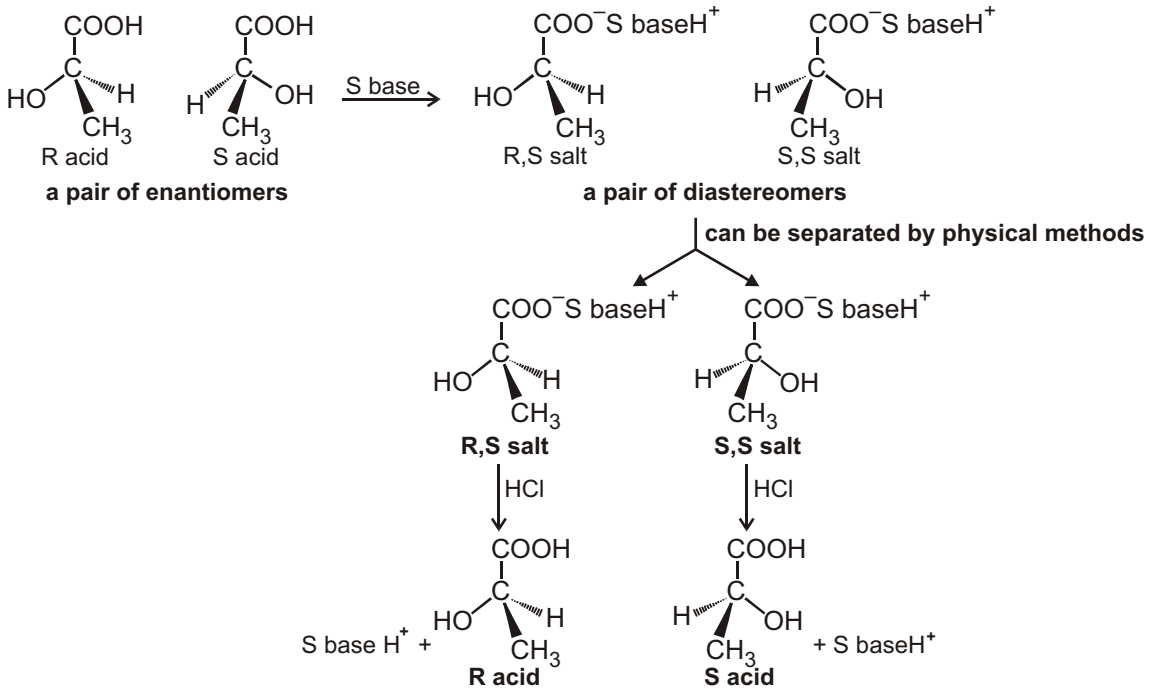
(1) is immediately recognizable as Leonardo da Vinci's Mona Lisa. You may not recognize (2)—it's also Leonardo da Vinci's Mona Lisa—this time viewed from above. The frame is very ornate, but the picture tells us as much about the painting as our rejected linear and 90° angle diagrams did about our fatty acid. They're both correct—in their way—but sadly useless. What we need when we draw molecules is the equivalent of (3). It gets across the idea of the original, and includes all the detail necessary for us to recognize what it's a picture of, and leaves out the rest. And it was quick to draw—this picture was drawn in less than 10 minutes: we haven't got time to produce great works of art!

☑ SPECIAL TOPIC

SEPARATION OF ENANTIOMERS

Enantiomers cannot be separated by the usual separation techniques such as fractional distillation or crystallization because their identcal boiling points and solubilities cause them to distill or crystallize simultaneously. Louis Pasteur was the first to separate a pair of enantiomers successfully.

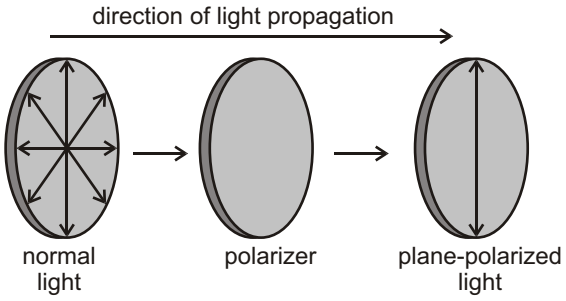
''Separation of enantiomers is called the **resolution of a racemic mixture**.



☑ SPECIAL TOPIC

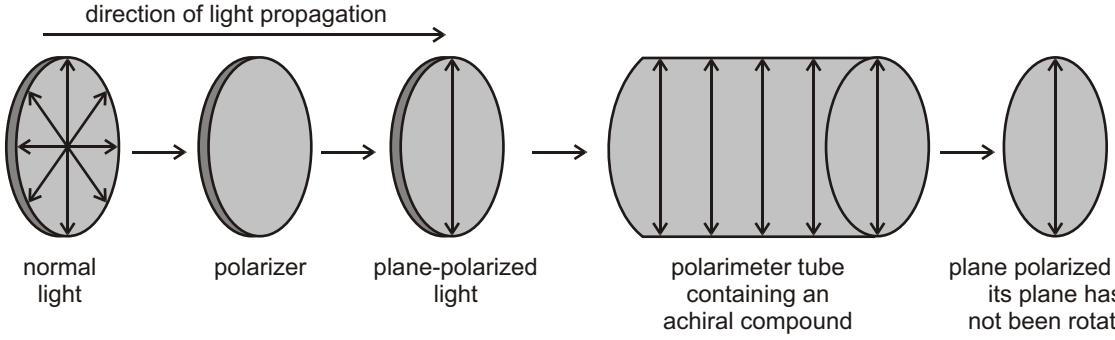
OPTICAL ROTATION

Normal light consists of electromagnetic waves that oscillate in all planes passing through the direction the light travels. Plane-polarized light oscillates only in a single plane passing through the direction the light travles. Plane-polarized light is produced by passing normal light through a polarizer such as a polarized lens or a Nicol prism.

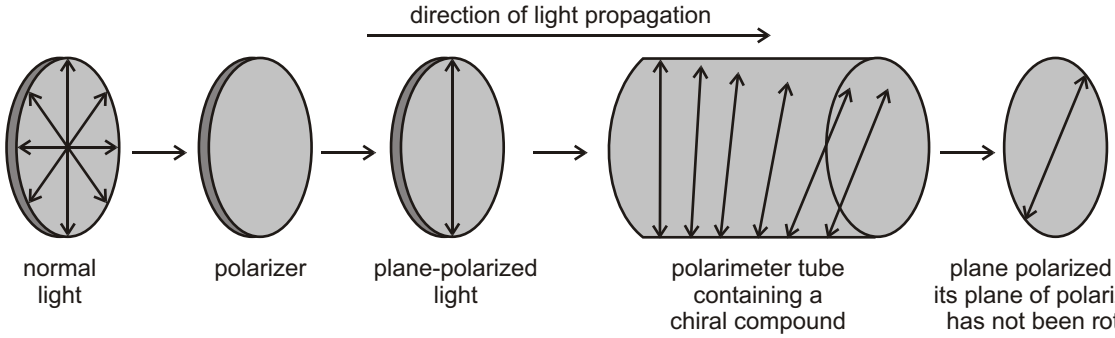


Some compounds rotated the plane of polarization in a clockwise direction and some in a counterclockwise direction, while others did not rotate the plane of polarization at all. Ability to rotate the plane of polairzation was attributable to some asymmetry that existed in the molecule.

When plane-polarized light passes through a solution of achiral molecules, the light emerges from the solution with its plane of polarization unchanged because there is no asymmetry in the molecules. An achiral compound does not rotate the plane of polarization. It is optically inactive.



If one enantiomer rotates the plane of polarization in a clock-wise direction, its mirror image will rotate the plane of polarization exactly the same amount in a counterclockwise direction.



A compound that rotates the plane of polarization is said to be **optically active**. in other words, chiral compounds are optically active and achiral compounds are **optically inactive**.

If an optically active compound rotates the plane of polarization in a clockwise direction, it is called **dextrorotatory**, indicated by (+). If an optically active compound rotates the plane of polarization in a counterclockwise direction, it is called **Laevorotatory**, indicated by (–). Dextro and levo are Latin prefixes for "to the right" and "to the left," respectively.

Do not confuse (+) and (–) with *R* and *S*. The (+) and (–) symbols indicate the direction in which an optically active compound rotates plane-polarized light, where as *R* and *S* indicate the arrangement of the groups about chirality center. Some compounds with the *R* configuration are (+) and some are (–).

The amount that an optically active compound rotates the plane of polarization can be measured with an instrument called a polarimeter.

☞ **Specific rotation**

Since optical rotation of the kind we are interested in is caused by individual molecules of the active compound, the amount of rotation depends upon how many molecules the light encounters in passing through the tube.

Specific rotation is the number of degrees of rotation observed if a 1-dm (10-cm) tube is used, and the compound being examined is present to the extent of 1 g/mL. This is usually calculated from observations with tubes of other lengths and at different concentrations by means of the equation

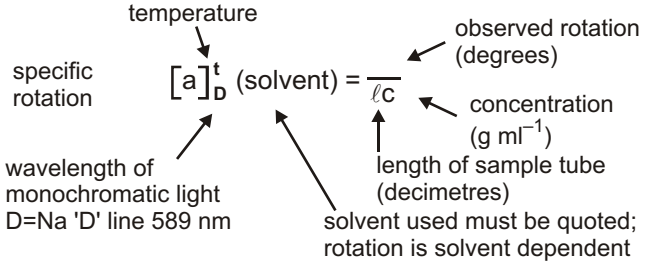
$$[\ ]_D^T \quad \frac{}{l \quad d}$$

$$\text{specific rotation} \quad \frac{\text{observed rotation (degrees)}}{\text{length (dm)} \quad \text{g / mL}}$$

where *d* represents density for a pure liquid or concentration for a solution and $[\ ]_D^T$ is specific rotation at constant temperature and D-Line of sodium.

Optically active compounds are those compounds which are not superimposable on their mirror images. One method to identify optically active compounds is to make separate models of the molecule and its mirror image, and check the superimposition of the molecule on its mirror image.

☞ **Optical activity** is the ability of a compound to rotate the plane of polarized light. This property arises from an interaction of the electromagnetic radiation of polarized light with the unsymmetric electric fields generated by the electrons in a chiral molecule. The rotation observed will clearly depend on the number of molecules exerting their effect, *i.e.*, it depends upon the concentration. Observed rotations are thus converted into specific rotations that are a characteristic of the compound according to the formula below.



☞ **Enantiomers** have equal and opposite rotations. The (+) – or **dextrorotatory** enantiomer is the one that rotates the plane of polarization clockwise (as determined when facing the beam), and the (–)- or **laevorotatory** enantiomer is the one that rotates the plane anticlockwise. In older publications, *d* and *l* were used as abbreviations for dextrorotatory and laevorotatory respectively, but these are not now employed, thus avoiding any possible confusion with D and L.

☞ **Ibuprofen** is an interesting case, in that the (S)-(+)-form is an active analgesic, but the (R)-(–)-enantiomer is inactive. However, in the body there is some metabolic conversion of the inactive (R)-isomer into the active (S)-isomer, so that the potential activity from the racemate is considerably more than 50%. Box 10.11 shows a mechanism to account for this isomerism.

There are two approaches to producing drugs as a single enantiomer. If a synthetic route produces a racemic mixture, then it is possible to separate the two enantiomers by a process known as resolution (see Section 3.4.8). This is often a tedious process and, of course, half of the product is then not required. The alternative approach, and the one now favoured, is to design a synthesis that produces only the required enantiomer, *i.e.*, a chiral synthesis.

Solved Example

- A solution prepared by mixing 10 mL of a 0.10 M solution of the *R* enatiomer of a compound and 30 mL of a 0.10 of a 0.10 M solution of the *S* enantiomer was found to have an observed specific rotation of + 4.8. What is the specific rotation of each of the enantiomers? (**Hint :** mL × M = millimole, abbreviated as mmol)

Sol. One mmol (10 mL × 0.10 M) of the *R* enantiomer is mixed with 3 mmol (30 mL × 0.10 M) of the S enantiomer ; 1 mmol of the *R* enantiomer plus 1 mmol of the *S* enantiomer will form 2 mmol of a racemic mixture, so there will be 2 mmol of *S* enantiomer left over. Because 2 out of 4 mmol is excess *S* enantiomer, the solution has a 50% enantiomeric excess. Knowing the enantiomeric excess and the observed specific rotation allows us to calculate the specific rotation

$$\text{enantiomeric excess} \quad \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}} \quad 100\%$$

$$50\% \quad \frac{4.8}{x} \quad 100\%$$

$$\frac{50}{100} \quad \frac{4.8}{x}$$

$$\frac{1}{2} \quad \frac{4.8}{x}$$

$$x \quad 2(\ 4.8)$$

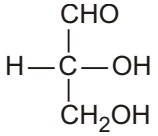
$$x \quad 9.6$$

The *S* enantiomer has a specific rotation of + 9.6, so the *R* enantiomer has a specific rotation of – 9.6.

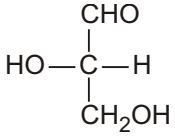
☑ SPECIAL TOPIC

D, L-CONFIGURATION

Another example is :

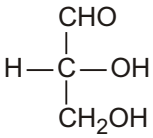


(+) Glyceraldehyde

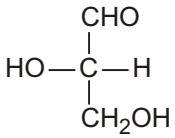


(–) Glyceraldehyde

In a molecule, the configuration is the attachment of various groups in space. Here, we will describe a method of specifying the relative spatial position of the four groups attached to a chiral carbon. An optically active compound may have a *D*– or *L*– configuration. In any configuration, in which at the chiral carbon, the –OH or any such group is on the right and H atom is on the left-hand side and the more oxidised carbon atom at the top and the less oxidised carbon at the bottom (but the chiral carbon should be next to less oxidised carbon which is written at the bottom) is assigned a *D* configuration. The configuration involving H and OH at reverse positions is assigned *L* configuration. For example, consider glyceraldehyde; the two configurations are

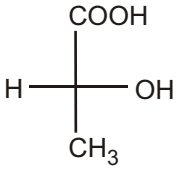


D(+) Glyceraldehyde

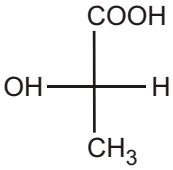


L(–) Glyceraldehyde

It is not always that the *D* configuration is (+) rotatory. In lactic acid, the *D* configuration is (–) laevo-rotatory and the terms *D* and *d* are different from each other.

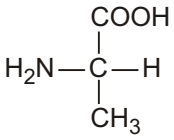


D(–) Lactic Acid



L(+) Lactic Acid

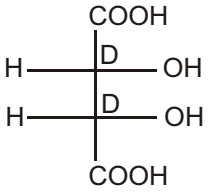
or

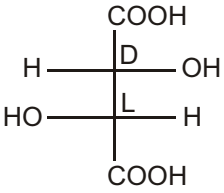


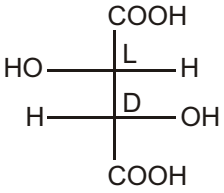
L-Serine
(Amino acid)

Any assymetric compound prepared or derived form *D*-glyceraldehyde will have *D*-configuration. Similar is the case with *L*-glyceraldehyde.

If the molecule has more than one asymmetric atom, there can be different configurations at different chiral carbon.



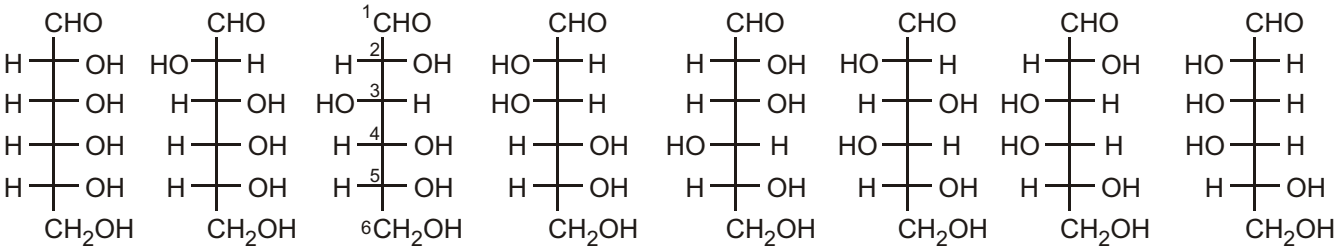




This, however, is an older method of designating the configuration of enantiomers.

Fischer projections of glucose and stereoisomers

The sugar glucose has four chiral centres; therefore, 2^4 16 different stereoisomers of this structure may be considered. These are shown below as Fischer projections.

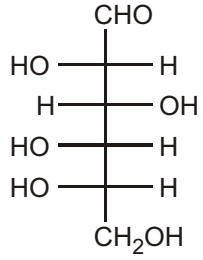


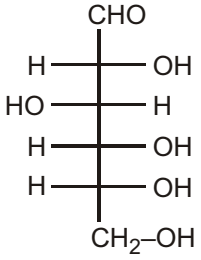
D-(+)-allose **D-(+)-altrose** **D-(+)-glucose** **D-(+)-mannose** **D-(–)-gulose** **D-(+)-idose** **D-(+)-galactose** **D-(+)-talose (C-4 epimer of D-glucose)**

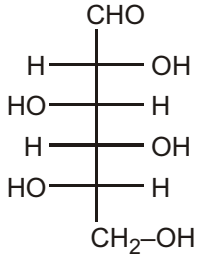
❑ **NOTE :** Mirror images of the above 8 *D*-isomers are *L*-isomers.

Solved Example

- Which of the following is the structure of L-Glucose?

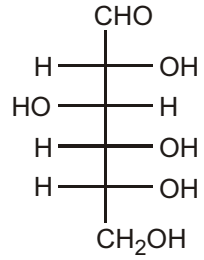
(A)


(B)


(C)


(D) None of these

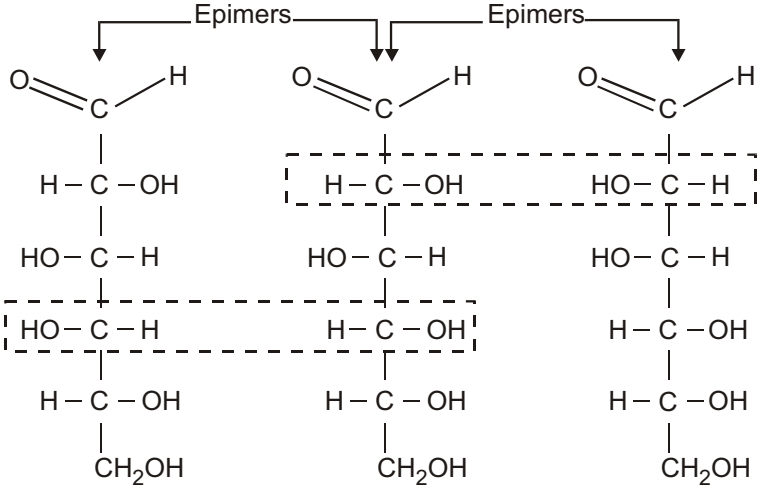
Sol. (A) *L*-Glucose is enantiomer of *D*-Glucose.

D-Glucose is


☑ SPECIAL TOPIC

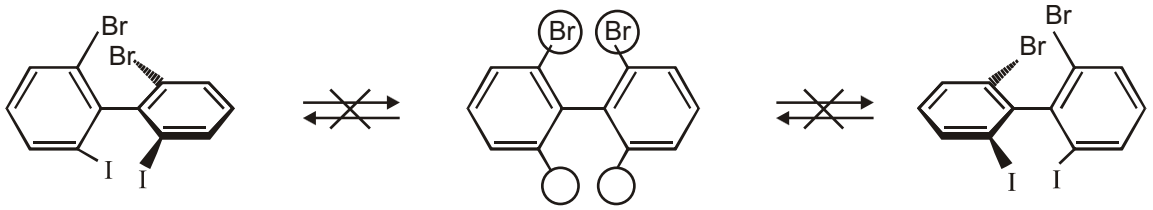
EPIMERS

Epimers A pair of diastereomers that differ only in the configuration about of a single carbon atom are said to be epimers. *D*(+)-glucose is epimeric with *D*(+)-mannose and *D*(+)-galactose as shown below.



STEREOCHEMISTRY OF BIPHENYL

Three conformations of a sterically crowded derivative of biphenyl. The center drawing shows the molecule in its most symmetric conformation. This conformation is planar, and it has a mirror plane of symmetry. If the molecule could achieve this conformation, or even pass through it for an instant, it would not be optically active. This planar conformation is very high in energy, however, because the iodine and bromine atoms are too large to be forced so close together. The molecule is conformationally locked. It can exist only in one of the two staggered conformations shown on the left and right.

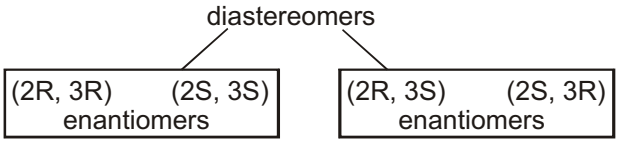


staggered conformation (chiral) | eclipsed conformation (symmetric, achiral) | staggered conformation (chiral)

HOW TO FIND TOTAL STEREOISOMER

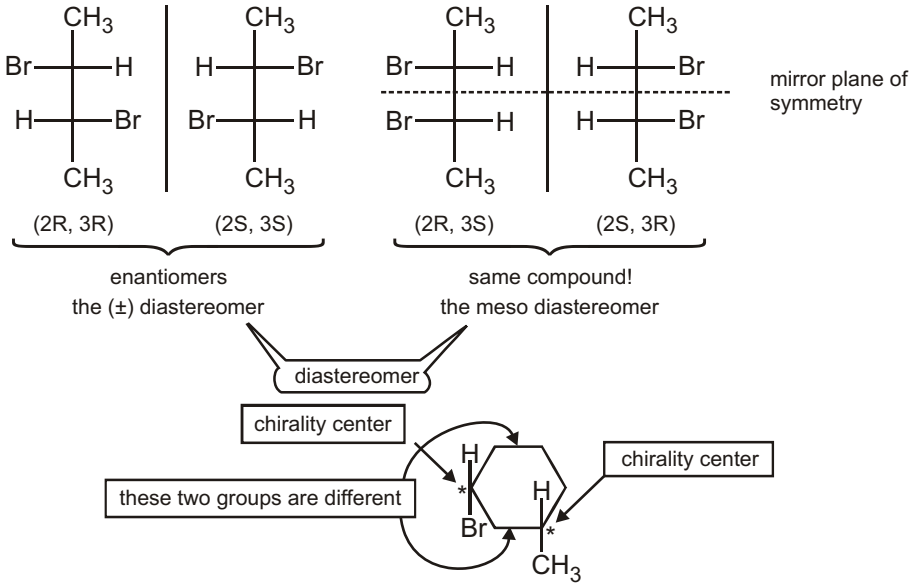
Stereochemistry of Molecules with Two or More Asymmetric Carbons

In the preceding section, we saw there are four stereoisomers (two pairs of enantiomers) of 2-bromo-3-chlorobutane. These four isomers are simply all the permutations of (*R*) and (*S*) configurations at the two asymmetric carbon atoms, C2 and C3:



A compound with *n* asymmetric carbon atoms might have as many as has 2^n stereoisomers. This formula is called the **2^n rule**, where *n* is the number of chirality centers (usually asymmetric carbon atoms). The 2^n rule suggests we should look for a maximum 2^n of stereoisomers. We may not always find 2^n isomers, especially when two of the asymmetric carbon atoms have identical substituents.

2,3-Dibromobutane has fewer than 2^n stereoisomers. It has two asymmetric carbons (C2 and C3), so the 2^n rule predicts a maximum of four stereoisomers. The four permutations of (*R*) and (*S*) configurations at C2 and C3 are shown next. Make molecular models of these structures to compare them.



Because the compound has two chirality centers, it has four stereoisomers. The cis isomer exists as a pair of enantiomers, and the trans isomer exists as a pair of enantiomers.

cis-1-bromo-3-methylexane and trans-1-bromo-3-methylexane

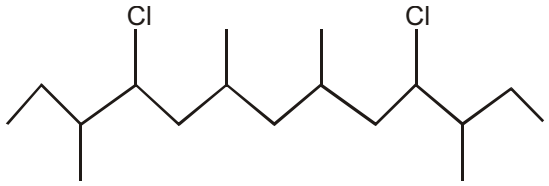
Calculation of total number of optical isomerism

(a) For unsymmetrical compound, total O.I. 2^n (where 'n' is number of chiral center)

(b) For symmetrical compound, total O.I.

No. of Chiral centre n	Optically active	Meso	Total optical isomerism
Even no. (n)	$2^{n\ 1}$	$2^{n/2\ 1}$	$2^{n\ 1}\ \ 2^{n/2\ 1}$
Odd no. (n)	$2^{n\ 1}\ \ 2^{n\ 1/2}$	$2^{n\ 1/2}$	$2^{n\ 1}$

Solved Example



How many stereoisomers (enantiomers and diastereomers).

are there of this molecule. Note the possible symmetry of the stereoisomers is a function of the absolute configurations.

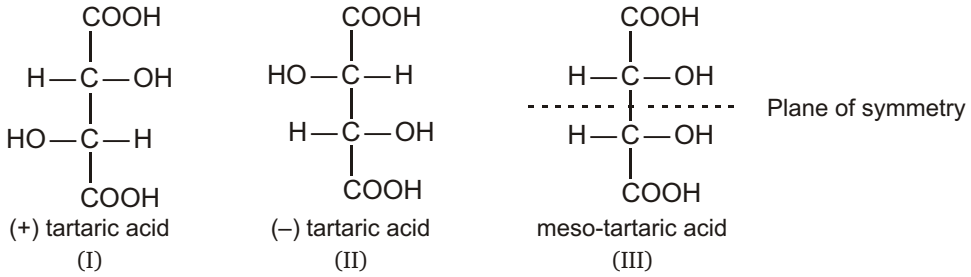
Ans. Total optical isomer $2^{n\ 1}\ \ 2^{n/2\ 1}$

$2^{6\ 1}\ \ 2^{6/2\ 1}$

32 (Optical active) 4 (Meso)

36

Consider the case of tartaric acid. It has two asymmetric carbon atoms. It has the following possible isomers:

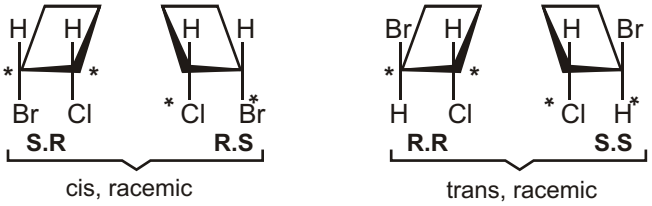


Solved Example

Give the names, structural formulas and stereochemical designations of the isomers of (a) bromochlorocyclobutane, (b) dichlorocyclobutane, (c) bromochlorocyclopentane, (d) diiodocyclopentane, (e) dimethylcyclohexane. Indicate chiral C's.

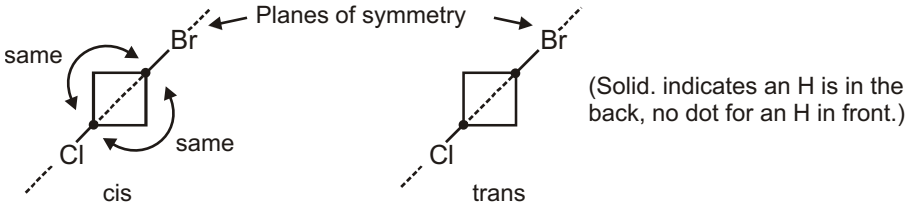
(a) There is only one structure for 1-bromo-l-chlorocyclobutane :

With l-bromo-2-chlorocyclobutane there are cis and trans isomers and both substituted C's are chiral. Both geometric isomers form racemic mixtures.



1-Bromo-2-chlorocyclobutane

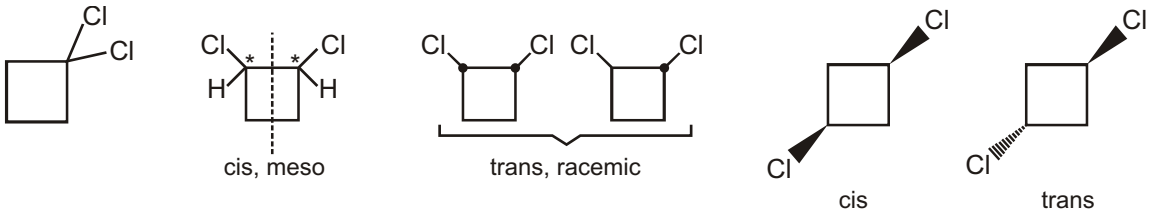
(a) In 1-bromo-3-chlorocyclobutane there are cis and trans isomers, but no enantiomers; C^1 and C^3 are not chiral, because a plane perpendicular to the ring bisects them and their four substituents. The sequence of atoms is identical going around the ring clockwise or counterclockwise from C^1 to C^3.



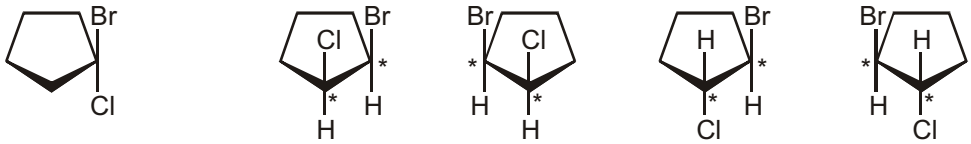
1-Bromo-3-chlorocyclobutane

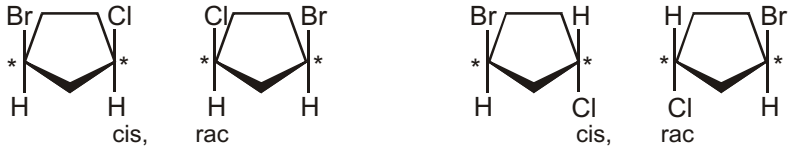
In these structural formulas, the other atoms on C^1 and C^3 are directly in back of those shown and are bisected by the indicated plane.

(b) Same as (a) except that the cis-1,2-dichlorocyclobutane has a plane of symmetry (dashed line below) and is meso.



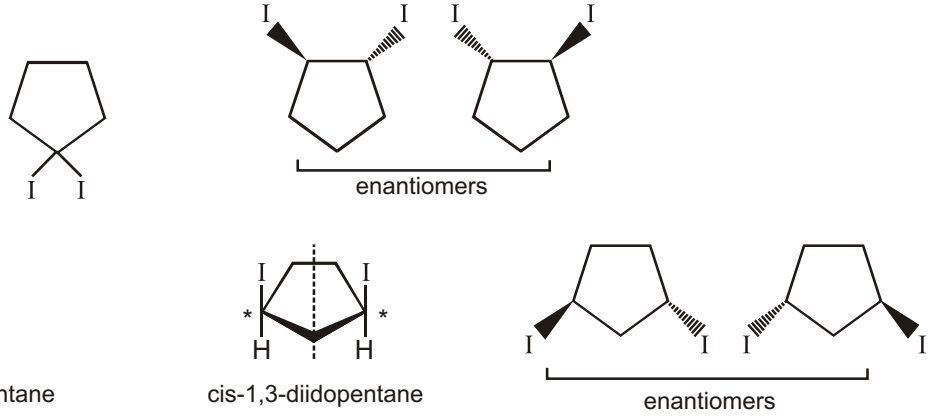
(c) There are nine isomers because both 1,2- and 1,3-isomers have cis and trans geometric isomers, and these have enantiomers.



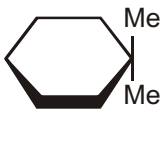


1-Bromo-3-chlorocyclopentane

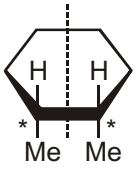
(d) The diiodocyclopentanes are similar to the bromochloro derivative, except that both the cis-1,2- and the cis-1,3-diiodo derivatives are meso. They both have planes of symmetry.



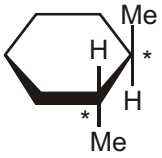
(e) There are nine isomeric dimethylcyclohexanes.

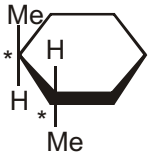


1,1-Dimethyl

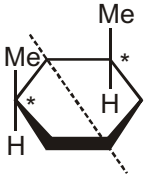


cis, meso-1,2-Dimethyl

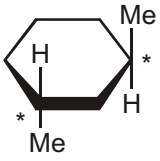


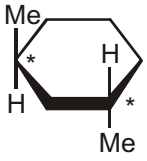


trans, rac-1,2-Dimethyl

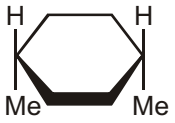


cis, meso-

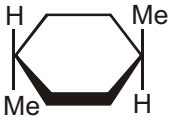




trans, rac-1,3-Dimethyl



cis



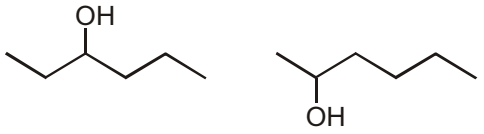
trans-1,4-Dimethyl

(no chiral centers)

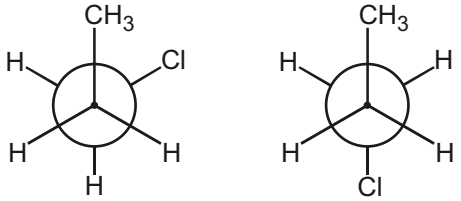
Solved Example

- Find relation between given pair?

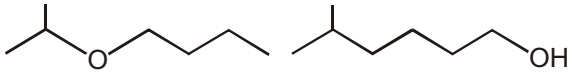
(1)



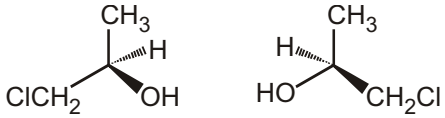
(2)



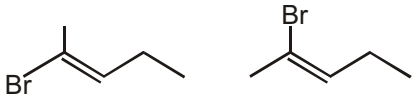
(3)



(4)



(5)



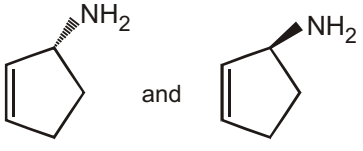
(6)

Ans. (1) constitutional isomer (positional isomer)
(2) Conformers
(3) Constitutional isomer (Functional isomer)
(4) Enantiomer
(5) Geometrical or Diastereomers
(6) Conformer (By ring flip)

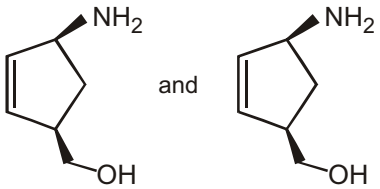
Solved Example

- Find relation between given pair?

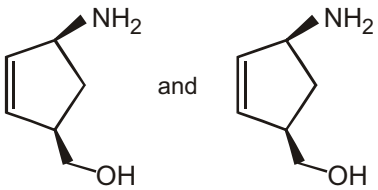
(a)



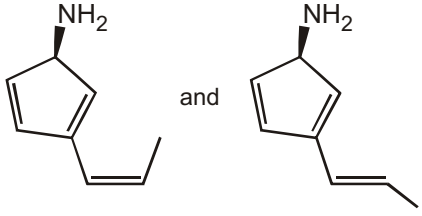
(b)

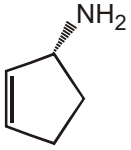
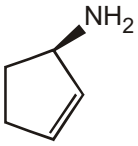


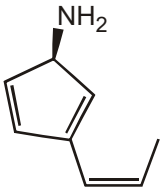
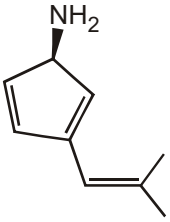
(c)



(d)



(e)  and 

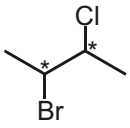
(f)  and 

Ans. (a) Enantiomers (b) Indenticle
(c) Positional isomer (d) Geometrical isomers
(e) Identical (f) Homologas compounds

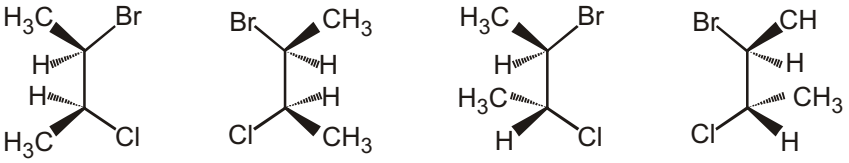
Solved Example

- Find total stereoisomers and relationship between them in 2-bromo-3-chlorobutane.

Ans. 2 stereocenters



4 stereoisomers



A B C D

(i) A and B are enantiomers.
(ii) C and D aare enantiomers.
(iii) A and C, or A and D, or B and C, or B and D are diastereomers.
(iv) Diastereomers are stereoisomers which are not mirror images of other.

Solved Example

- How many pair of diastereomer are possible for given compound

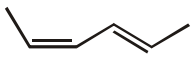
CH_3-CH $CH-CH$ $CH-CH_3$

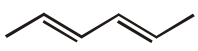
(A) 0 (B) 2 (C) 3 (D) 4

Ans. (C)

Draw the all possible configuration of given compound

(A)  cis, cis

(B)  cis, trans

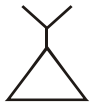
(C)  trans, trans

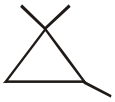
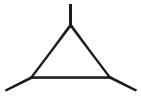
pair of diastereomars ((A) (B), (A) (C) and (B) (C))

Solved Example

- The total number of structural isomers possible for compound with the molecular formula C_6H_{12} having cyclopropane ring only.

Ans. 6

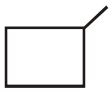
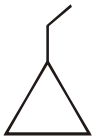
(a)  (b)  (c)  (d) 

(e)  (f) 

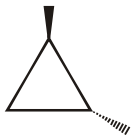
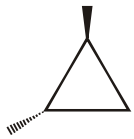
Solved Example

- The total number of cyclic structural as well as stereo isomers possible for compound with the molecular formula C_5H_{10} is :

Ans. 7

Sol. (a)  (b)  (c)  (d) 

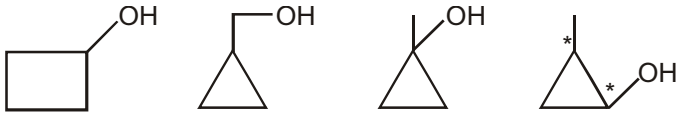
(e) 
Meso

(f)  (g) 

Solved Example

- The total number of cyclic structural as well as stereo isomers possible for compound with the molecular formula C_4H_8O (only alcohol) will be.

Ans. 7

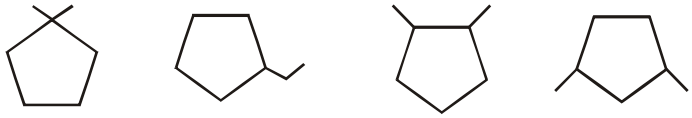


1 + 1 + 1 + 4 = 7 total

Solved Example

- The total number of five membered cyclic structural as well as stereoisomers possible for compound with the molecular formula C_7H_{14} is :

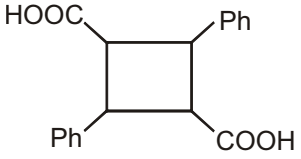
Ans. 8



1 1 3 3

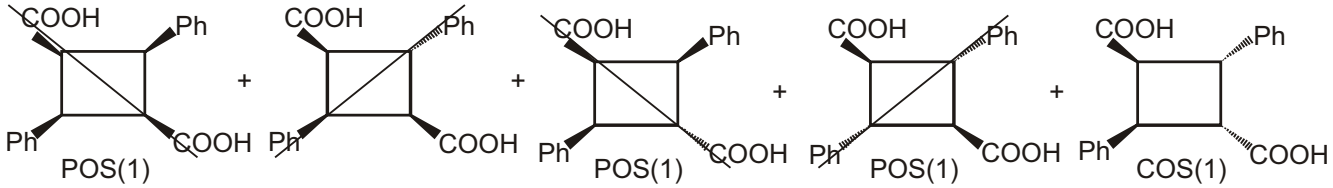
Solved Example

- Find the number of optical isomers of sires compound



(A) 3 (B) 2 (C) 6 (*D) Zero

Sol.

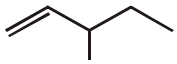
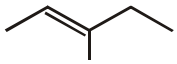
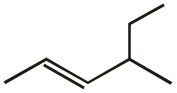
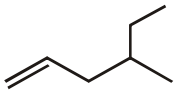


All are optically inactive

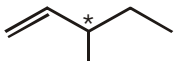
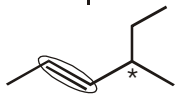
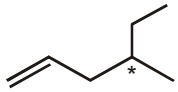
So number of optical isomers = Zero

Solved Example

- Identify Alkene showing both geometrical as well as optical isomerism.

(A)  (B)  (*C)  (D) 

Sol.

	Geometrical Isomerism	Optical Isomerism
(A) 	✗	✔
(B) 	✔	✗
(C) 	✔	✔
(D) 	✗	✔

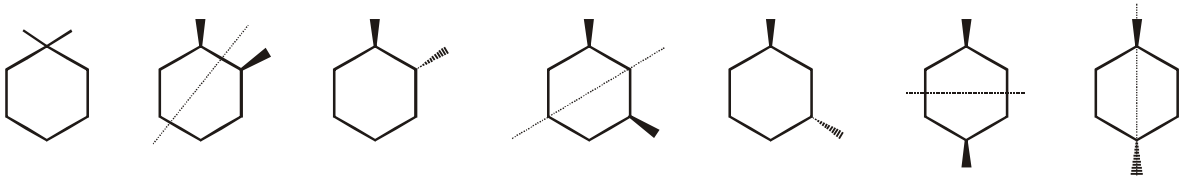
(* : Chiral centre)

Solved Example

- *X* Total possible isomers of dimethylcyclohexane which are chiral. Find the value of *X*?

Ans. 4

Sol.

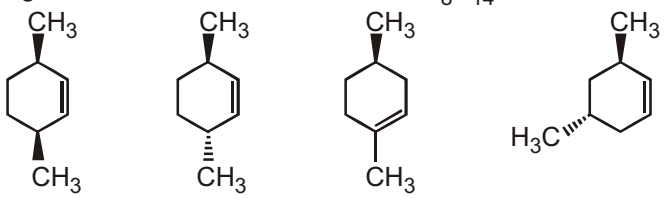


(achiral) (+M.I) (achiral) (+M.I) (achiral) (achiral)

There are 4 isomers which are chiral.

Solved Example

- Consider the following structures of molecular formula C_8H_{14}



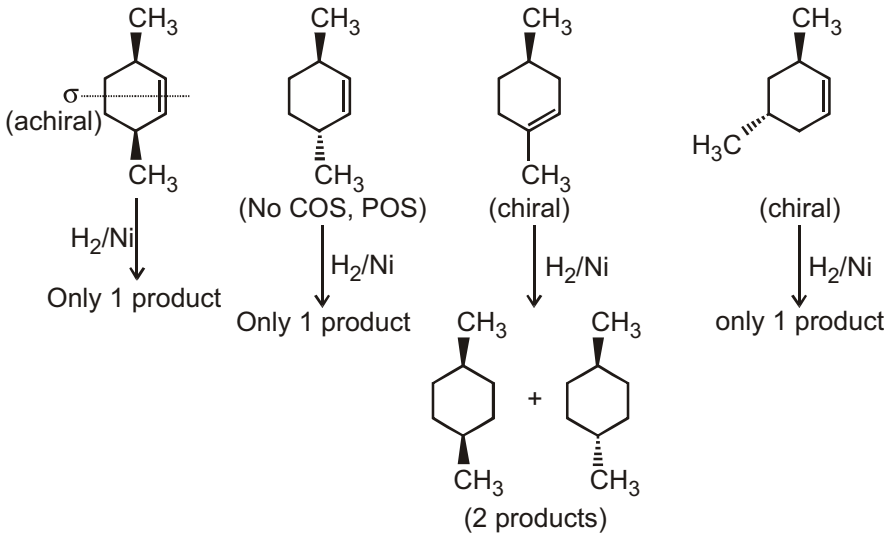
X Number of compounds which are optically active

Y Sum of total number of products obtained when each compound undergoes catalytic hydrogenation.

Find the sum of *X* *Y* ?

Ans. 8

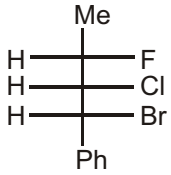
Sol.



X 3;*Y* 5 *X* *Y* 8

Solved Example

- How many pair of diastereomer are possible for Given compound



Ans. 6

Sol. Total stereoisomers will be 8. Given compound form 7 pairs with other sterioisomers in which expect 1 enantiomers all other 6 pairs will be distereomeric pairs.

Solved Example

- Total number of isomer has formula C_5H_8 with $2sp^3$ carbon, $2sp^2$ carbon, 1*sp* carbon.

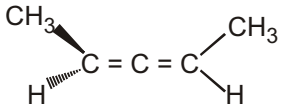
Ans. 4

Sol. **1.** *sp* carbon *i.e.,* 1C connected with 2 -bonds

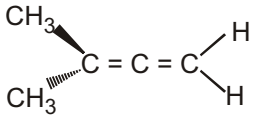
2. sp^2 carbon *i.e.,* 2C connected with 1 bond each

3. sp^3 carbon *i.e.,* 2C connected with only bonds.

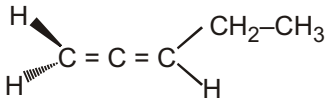
Possible structures are –



\+ enantiomer = 2



= 1

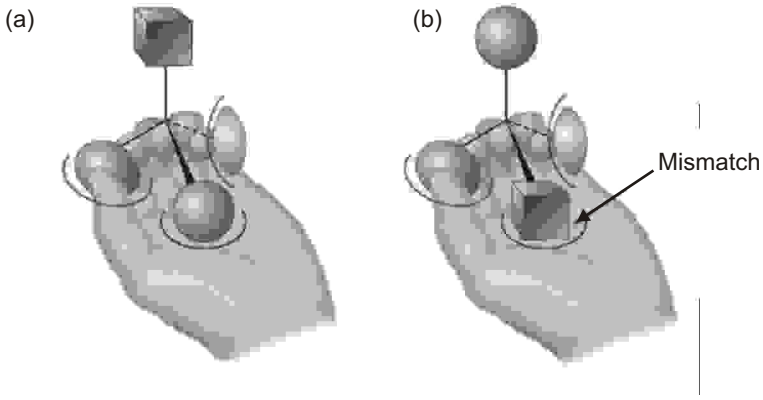


= 1

total = 4

WHY DO DIFFERENT ENANTIOMERS HAVE DIFFERENT BIOLOGICAL PROPERTIES?

Why do different enantiomers have different biological properties? To have a biological effect, a substance typically must fit into an appropriate receptor that has an exactly complementary shape. But because biological receptors are chiral, only one enantiomer of a chiral substrate can fit in, just as only a right hand can fit into right-handed glove. The mirror-image enantiomer will be a misfit, like a left hand in a right-handed glove. A representation of the interaction between a chiral molecule and a chiral biological receptor is shown in Figure : one enantiomer fits the receptor perfectly, but the other does not.



Imagine that a left hand interacts with a chiral object, much as chiral object, much as chiral molecule (a) One enantiomer fits a biological receptor interacts with a chiral molecule. One enantiomer fits into the hand perfectly, thumb, palm and finger, with the substituent exposed (b) The other enantiomer, however, can't fit into the hand. When the thumb and finger interact appropriately, the palm holds a substituent rather than a one, with the substituent exposed.

The hand-in-glove fit of a chiral substrate into a chiral receptor is relatively straightforward, but it's less obvious how a prochiral substrate can undergo a selective reaction. Take the reaction of ethanol with NAD catalyzed by yeast alcohol dehydrogenase. As we saw at the end of Section, the reaction occurs with exclusive removal of the pro-R hydrogen from ethanol and with addition only to the Re face of the NAD carbon.

We can understand this result by imagining that the chiral enzyme receptor again has three binding sites, as was previously the case in. When substituents of a prochiral substrate are held appropriately, however, only one of the two substituents—say, the pro-S one—is also held while the other, pro-R, substituent is exposed for reaction.

We describe the situation by saying that the receptor provides a chiral environment for the substrate. In the absence of a chiral environment, the two substituents are chemically identical, but in the presence of the chiral environment, they are chemically distinctive. The situation is similar to what happens when you pick up a coffee mug. By itself, the mug has a plane of symmetry and is achiral. When you pick up the mug, however, your hand provides a chiral environment so that one side becomes much more accessible and easier to drink from than the other.

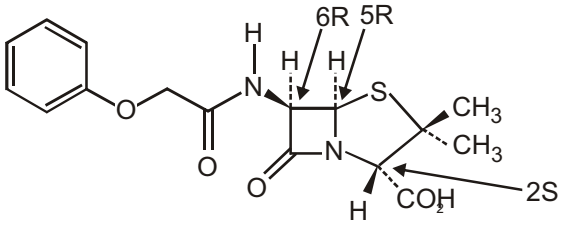
(a) When a prochiral molecule is held in a chiral environment, the two seemingly identical substituents are distinguishable. (b) similarly, when an achiral coffee mug is held in the chiral environment of your hand, it's much easier to drink from one side than the other because the two sides of the mug are now distinguishable.

(b)

CHIRAL DRUGS

The hundreds of different pharmaceutical agents approved for use by the U.S. Food and Drug Administration come from many sources. Many drugs are isolated directly from plants or bacteria, and others are made by chemical modification of naturally occurring compounds. An estimated 33%, however, are made entirely in the laboratory and have no relatives in nature.

Those drugs that come from natural sources, either directly or after chemical modification, are usually chiral and are generally found only as a single enantiomer rather than as a racemate. Penicillin V, for example, an antibiotic isolated from the Penicillium mold, has the 2S,5R,6R configuration. Its enantiomer, which does not occur naturally but can be made in the laboratory, has no antibiotic activity.



Penicillin V(2S, 5R, 6R configuration)

EXERCISE

MATCH THE COLUMN

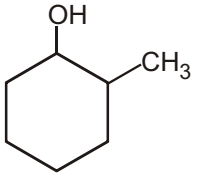
1. Match List-I with List-II and select the correct answer using the codes given below

List-I	**List-II**
(P) Distereomers	(1) Internal compansation
(Q) Meso compound	(2) External compansation
(R) Conformers	(3) Different reaction under chiral medium
(S) Racemic mixture	(4) Results by the free rotation about C–C bond
(T) Enantiomers	(5) Cis-Trans isomerism

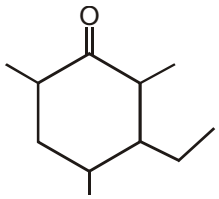
Codes :

	P	**Q**	**R**	**S**	**T**
(A)	5	2	4	1	3
(B)	3	1	4	2	5
(C)	3	2	5	5	4
(D)	5	1	4	2	3

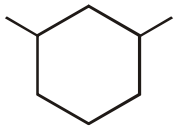
2. **Column I (Compound)** **Column II (Number of streocenter)**

(A) 

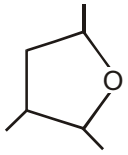
(P) 4

(B) 

(Q) 1

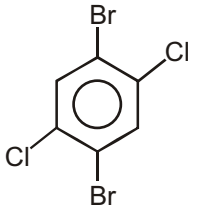
(C) 

(R) 3

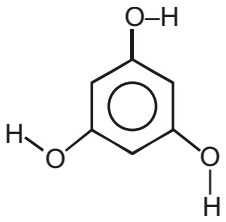
(D) 

(S) Shows G.I.

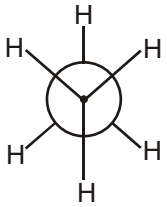
3. Column I **Column II**

(A) 

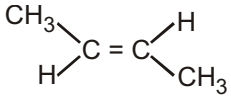
(P) C_2-axis of symmetry is present

(B) 

(Q) C_3-axis of symmetry is present

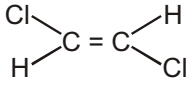
(C) 

(R) Ci (Center of symmetry) is present

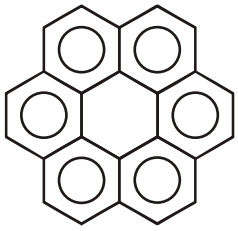
(D) 

(S) Plane of symmetry is present

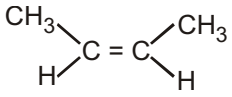
4. Column-I **Column-II**

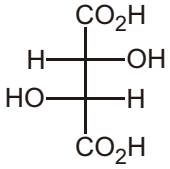
(A) 

(P) C_2 – axis of symmetry is present

(B) 

(Q) C_3–axis of symmetry is present

(C) 

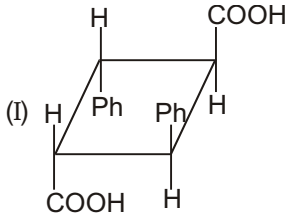
(D) 

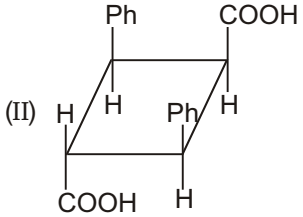
(R) Plane of symmetry is present

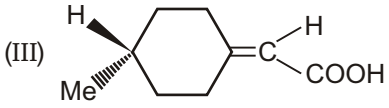
(S) Center of symmetry is present

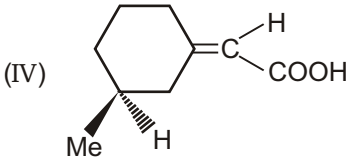
(T) S_4 alternative axis of symmetry

5.

(I) 

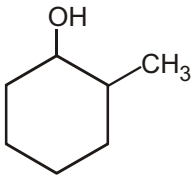
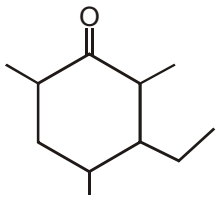
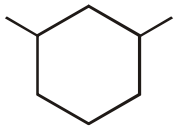
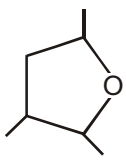
(II) 

(III) 

(IV) 

Column I	**Column II**
(A) Plane of symmetry	(P) I
(B) Centre of symmetry	(Q) II
(C) Show geometrical isomerism	(R) III
(D) Show optical isomerism	(S) IV

6.

ColumnI (Compound)	**Column II (Number of streocenter)**
(A) 	(P) 4
(B) 	(Q) 1
(C) 	(R) 3
(D) 	(S) Shows G.I.

FIND THE RELATIONSHIP

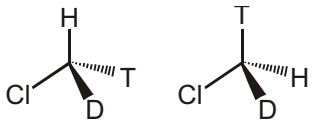
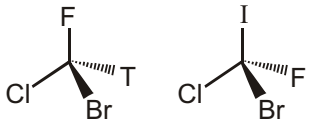
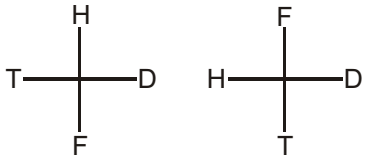
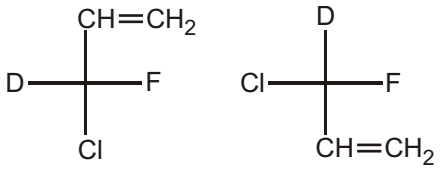
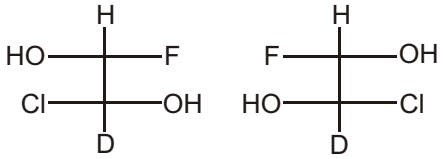
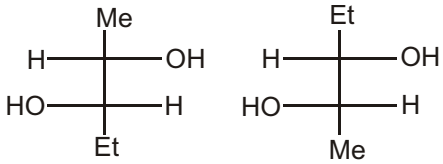
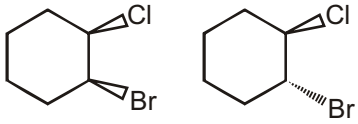
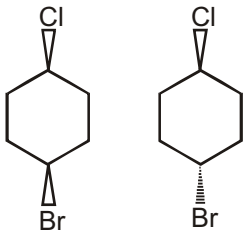
Relatoinship between compounds

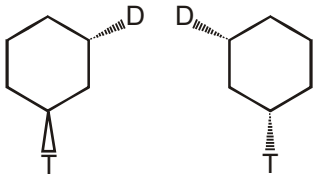
Non-superimposable mirror images compounds Enantiomer

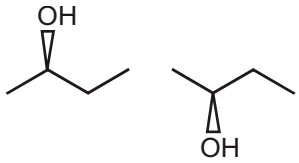
Non-superimposable non-mirror images compounds Diastereomers

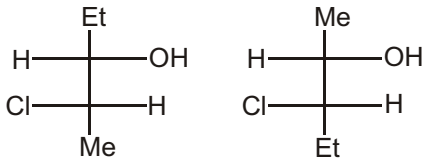
Problem: Indicate whether each of the following pairs of compounds are identical or are enantiomers, diastereomers, or constitutional isomers:

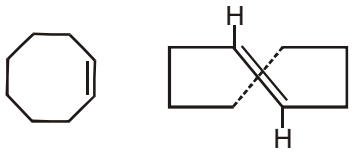
1. Find relationship between given pairs as enantiomer, diastereomer or other :

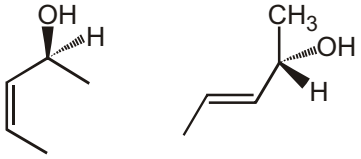
S.No.	Identify the relation	Enantiomer	Diastereomer	Other
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				

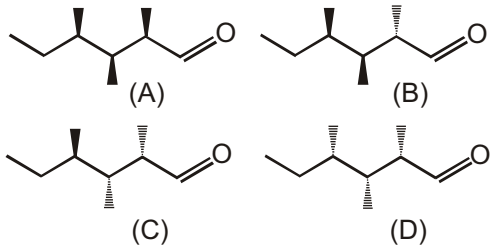
9. 

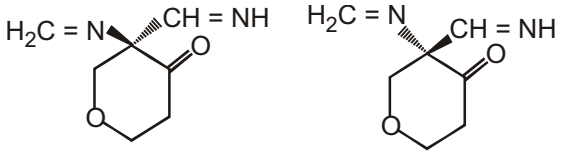
10. 

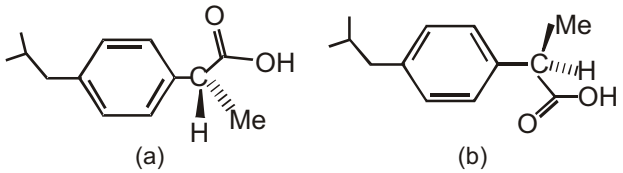
11. 

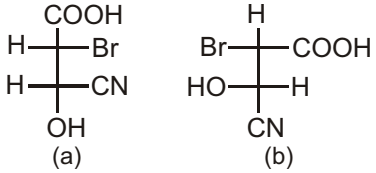
12. 

13. 

14. 

15. 

16. 

17. 

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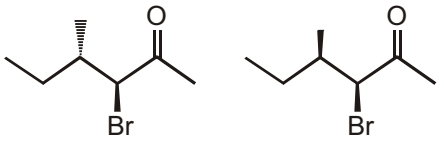
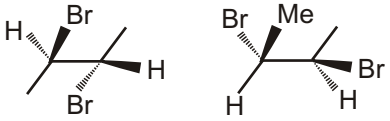


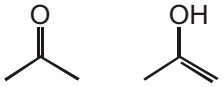
(a) (b)

19.



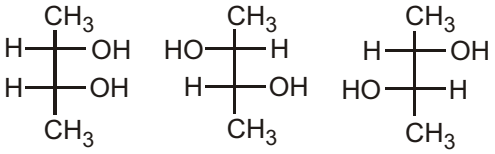
(a) (b)

20.



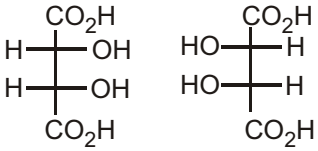
(a) (b)

21.



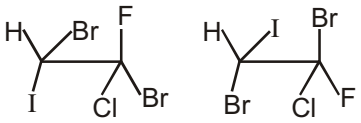
(a) (b) (c)

22.



(a) (b)

23.



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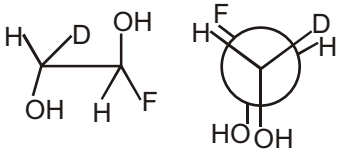
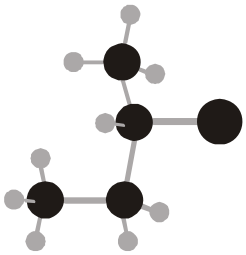
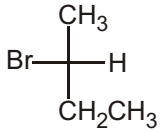


25.



and



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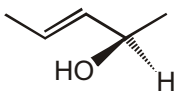
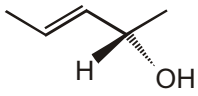
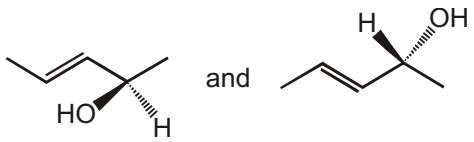
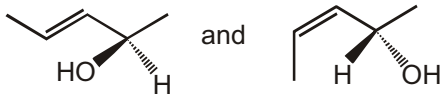
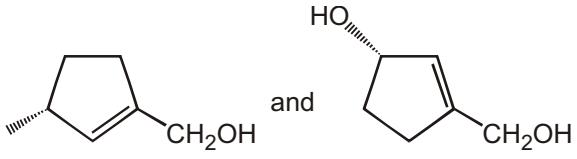


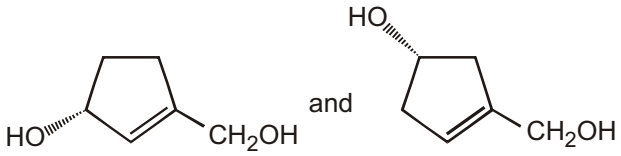
and

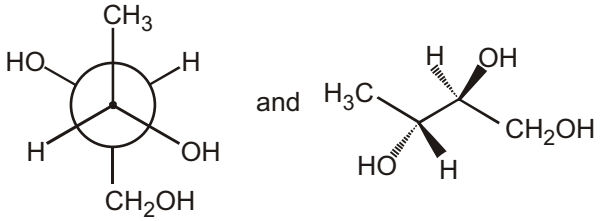


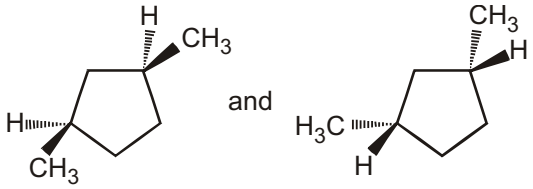
27. 

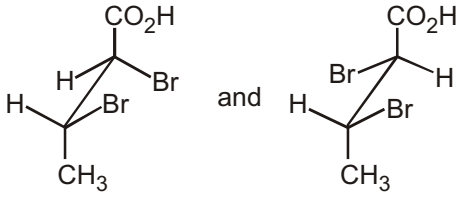
28. 

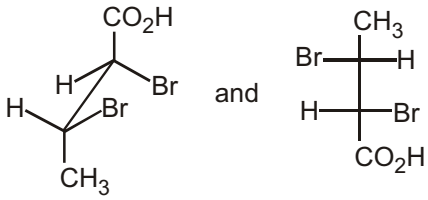
29. 

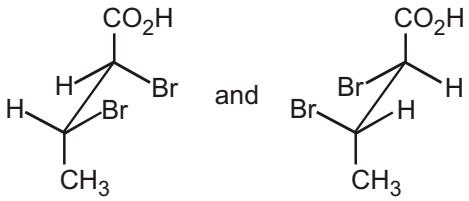
30. 

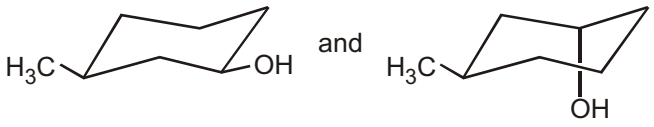
31. 

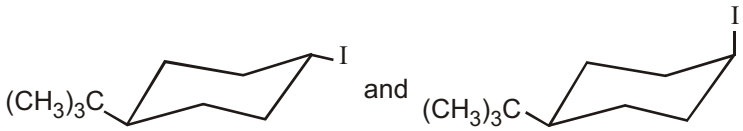
32. 

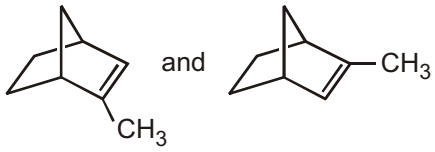
33. 

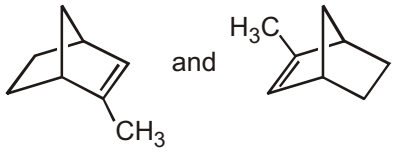
34. 

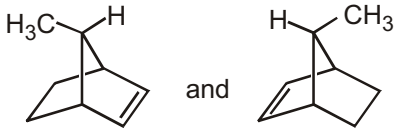
35. 

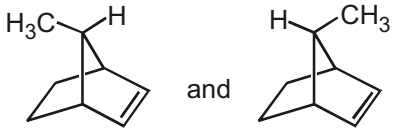
36. 

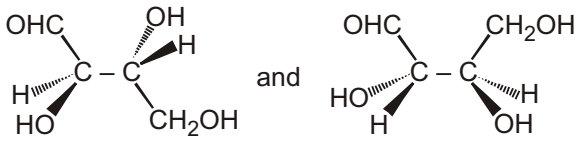
37. 

38. 

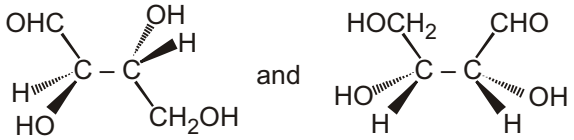
39. 

40. 

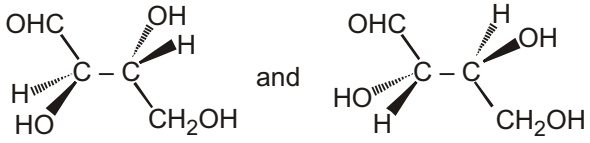
41. 

42. 

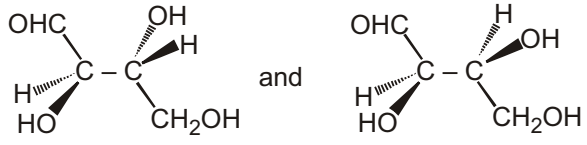
D-erythrose

43. 

D-erythrose

44. 

D-erythrose

45. 

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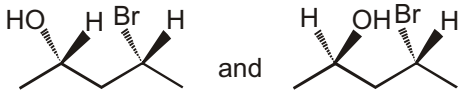
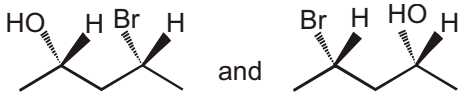
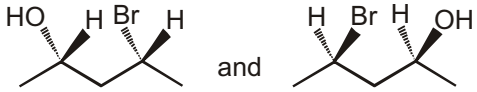
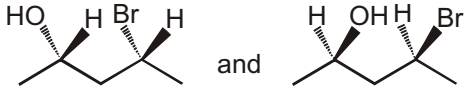
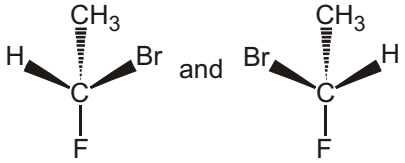
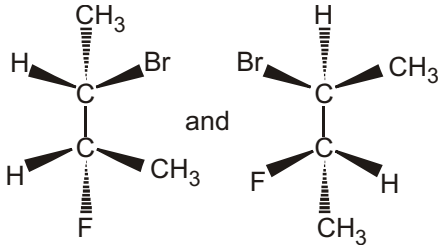
46. 

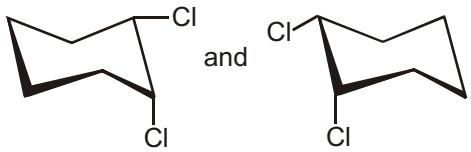
47. 

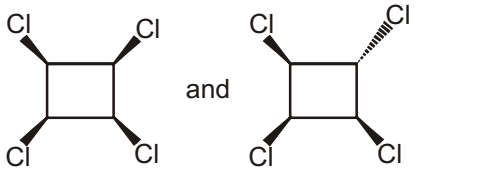
48. 

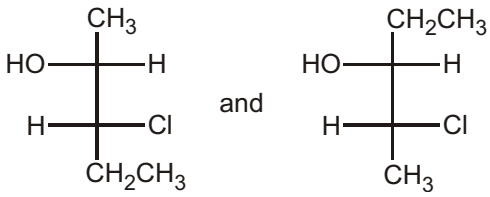
49. 

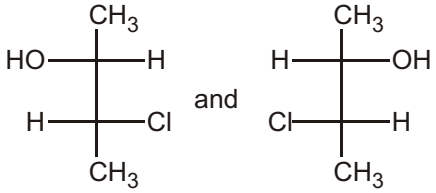
50. 

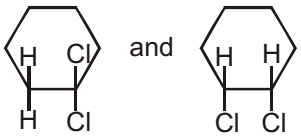
51. 

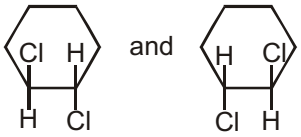
52. 

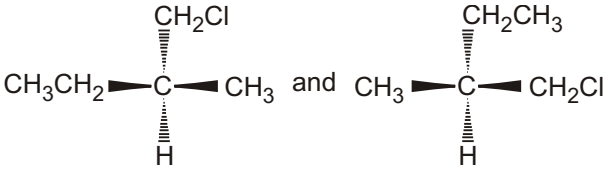
53. 

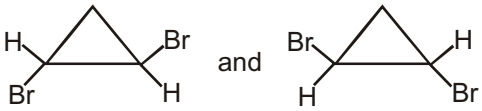
54. 

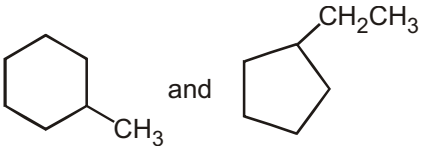
55. 

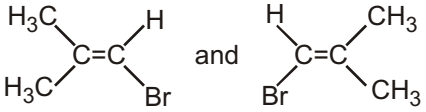
56. 

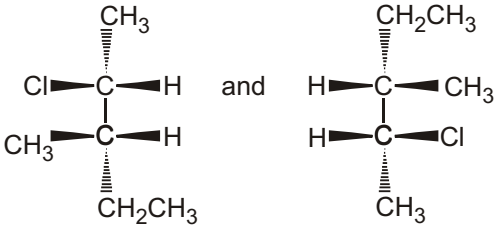
57. 

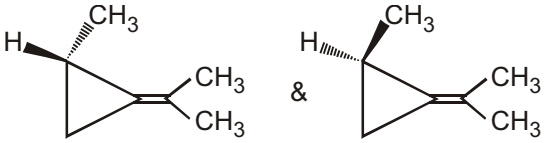
58. 

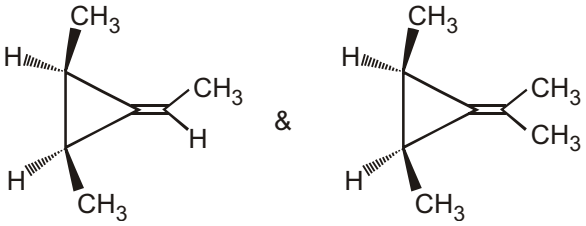
59. 

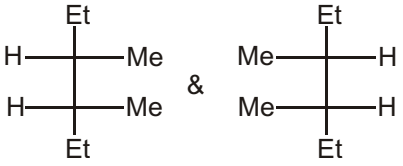
60. 

61. 

62. 

63. 

64. 

65. 

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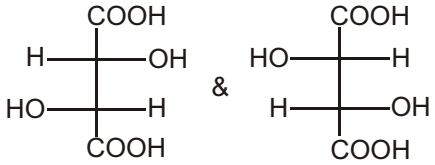

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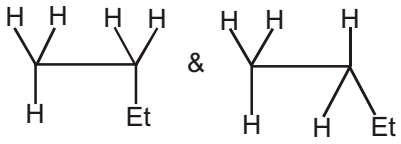

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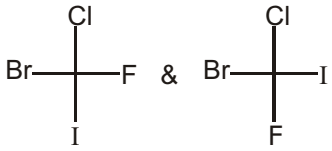

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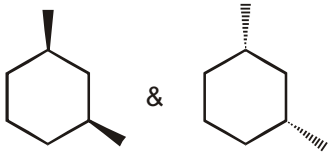

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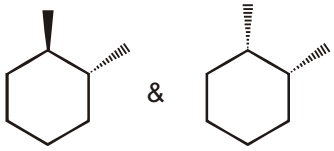

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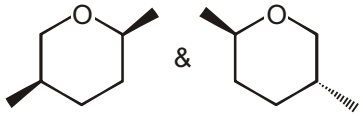

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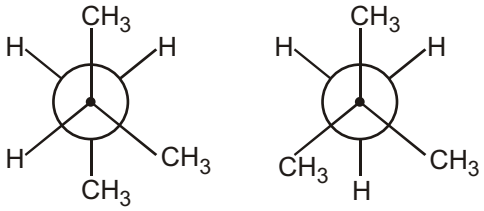

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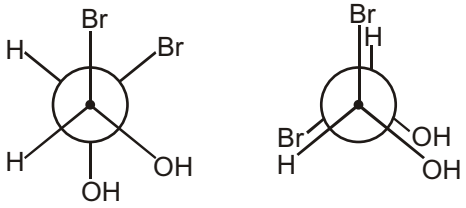

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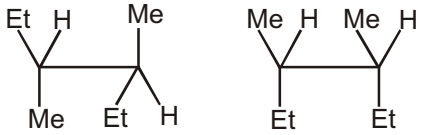

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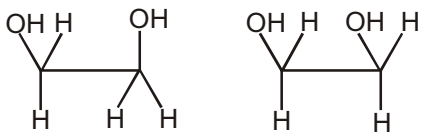

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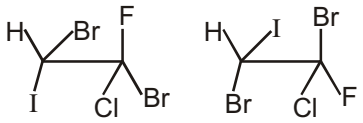

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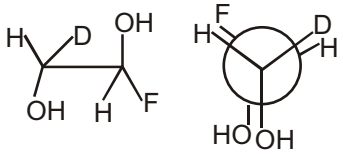

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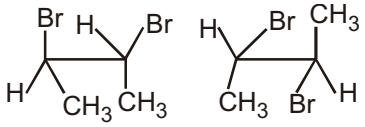

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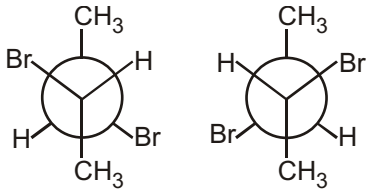

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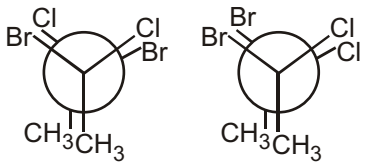

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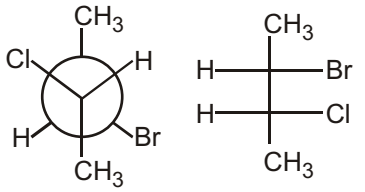

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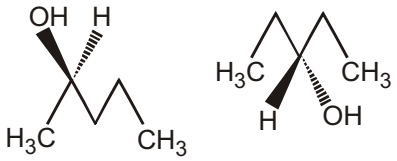

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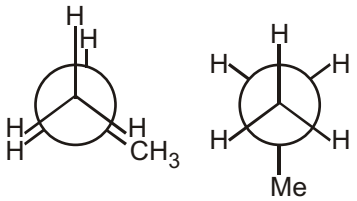

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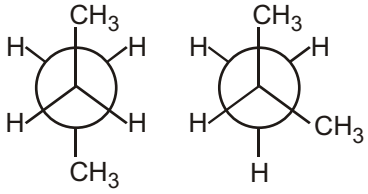
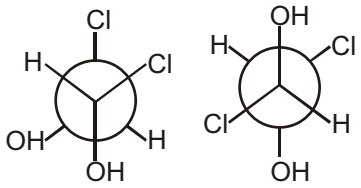
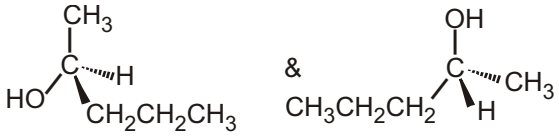
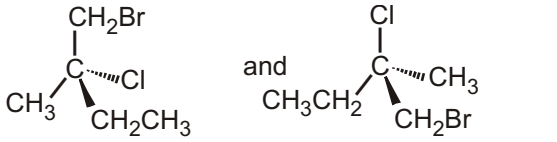
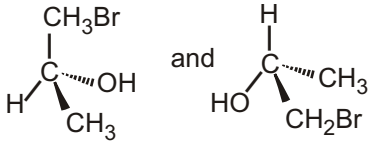
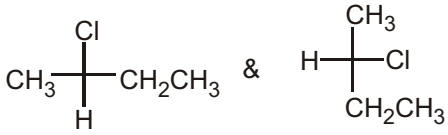


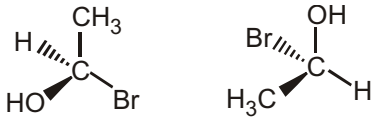
85. 

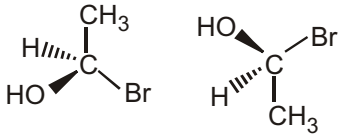
86. 

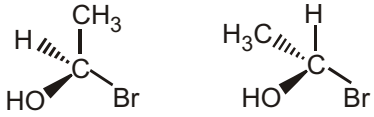
87. 

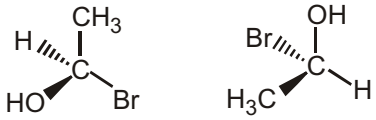
88. 

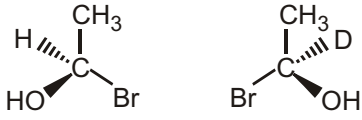
89. 

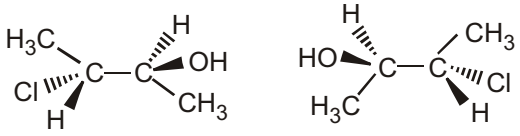
90. 

91. 

92. 

93. 

94. 

95. 

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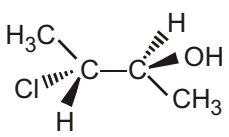

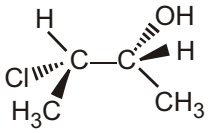

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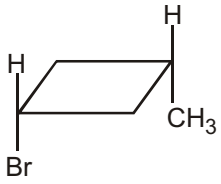

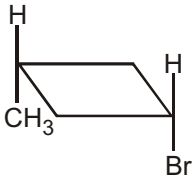

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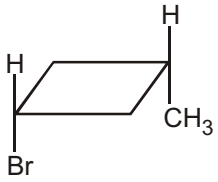

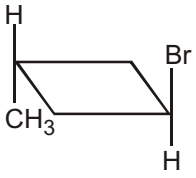

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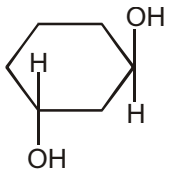
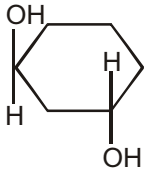
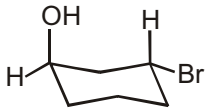
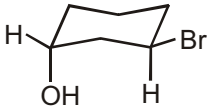


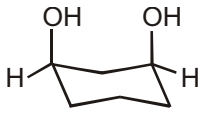


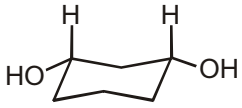
100.



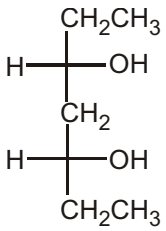


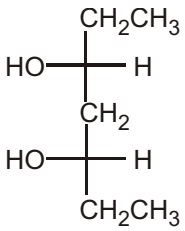
101.



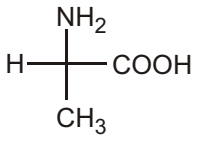


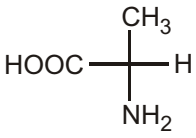
102.



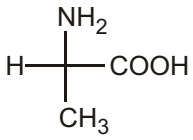


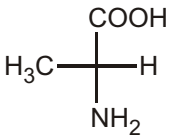
103.





104.





UNSOLVED EXAMPLES

1. Which of the following compounds has an asymmetric center?

(a) $CH_3CH_2CHCH_3$ (Cl)

(b) $CH_3CH_2CHCH_3$ (CH_3)

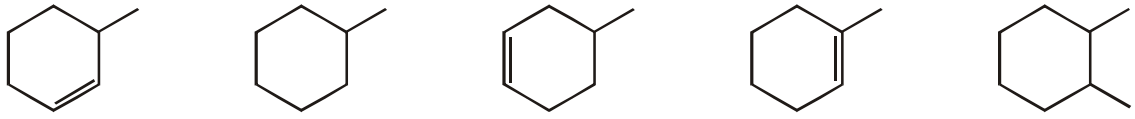
(c) $CH_3CH_2C(CH_3)CH_2CH_2CH_3$ (Br)

(d) CH_3CH_2OH

(e) $CH_3CH_2CHCH_2CH_3$ (Br)

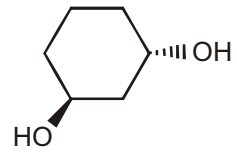
(f) $CH2\ CHCHCH_3$ (NH_2)

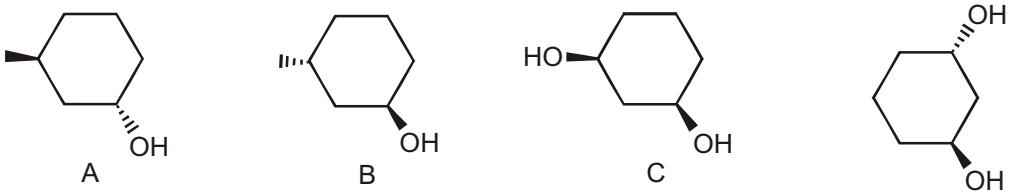
2. Which of the following compounds has one or more asymmetric centers?



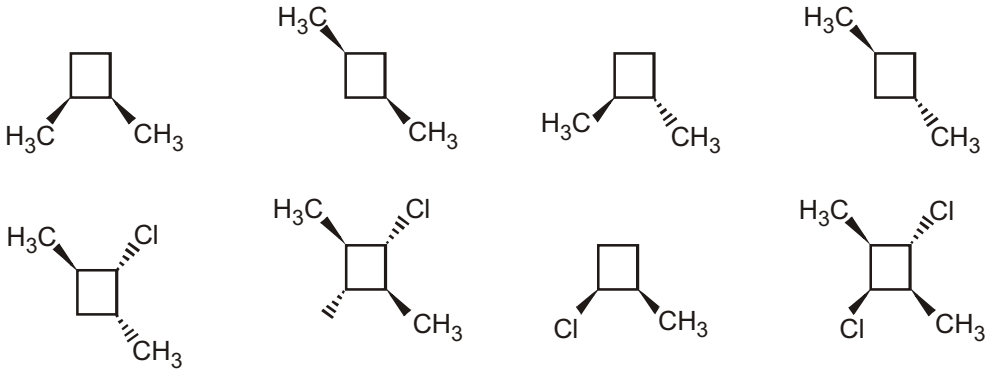
A B C D E

3. Indicate whether each of the structures in the second row is an enantiomer of, is a diastereomer of, or is identical to the structure in the top row.

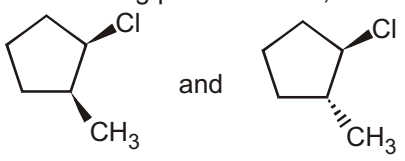


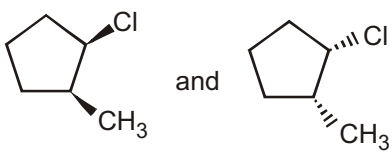


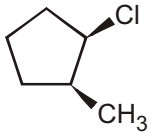
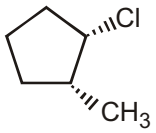
4. Which of the following are optically active?

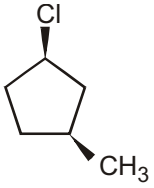
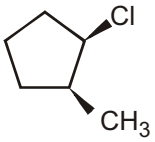


5. Are the following pairs identical, enantiomers, diastereomers, or constitutional isomers?

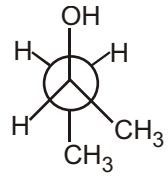
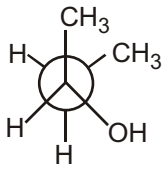
(a) 

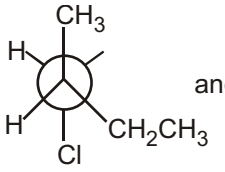
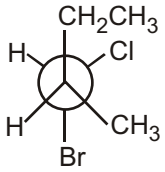
(b) 

(c)  and 

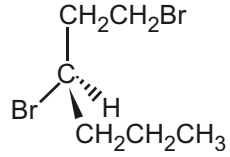
(d)  and 

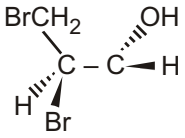
6. Are the following pairs identical, enantiomers, diastereomers, or constitutional isomers?

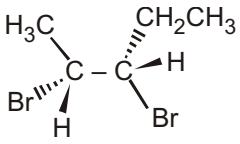
(a)  and 

(b)  and 

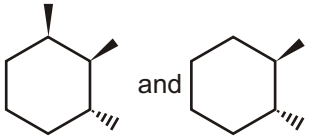
7. What is the configuration of the asymmetric centers in the following structures?

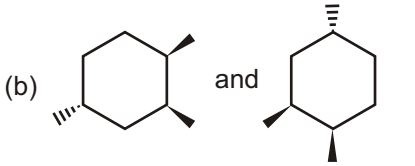
(a) 

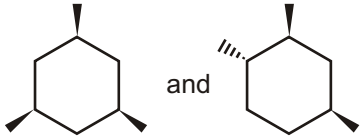
(b) 

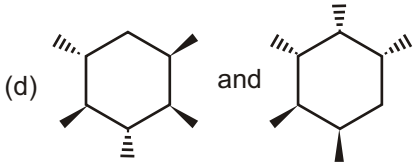
(c) 

8. Are the following pairs identical, enantiomers, diastereomers, or constitutional isomers?

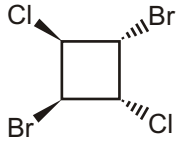
(a) 

(b) 

(c) 

(d) 

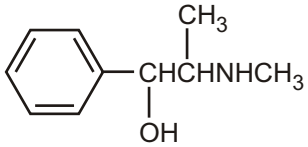
9. Is the following compound optically active?



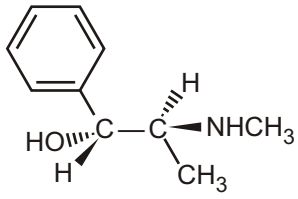
10. For any centuries, the Chinese have used extracts from a group of herbs known as ephedra to treat asthma. A compound named ephedrine has been isolated from these herbs and found to be a potent dilator of air passages in the lungs.

(a) How many stereoisomers does ephedrine have ?

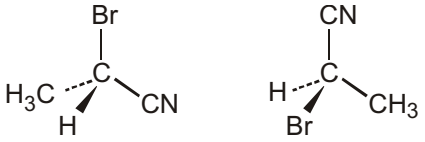
(b) The stereoisomer shown here is the one that is pharmacologically active. What is the configuration of each of the asymmetric centers ?

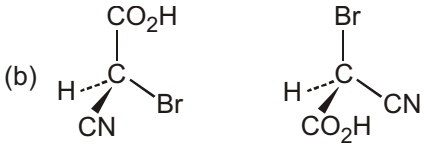


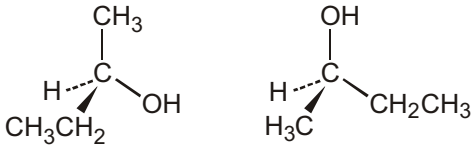
ephedrine

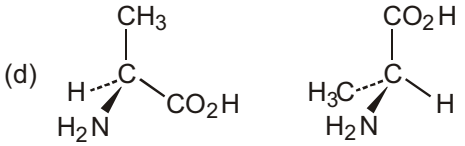


11. Which of the following pairs of structures represent the same enantiomer, and which represent different enantiomers?

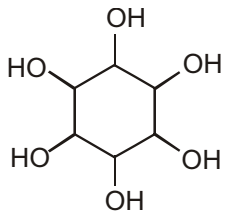
(a) 

(b) 

(c) 

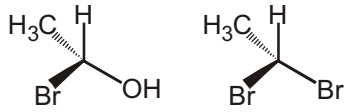
(d) 

12. Just for fun, you might like to try and work out just how many diastereoisomers inositol has and how many of them are meso compounds.

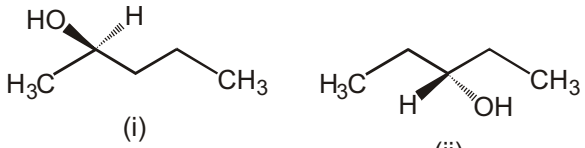


inositol

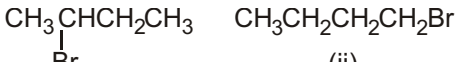
13. Identify chiral and achiral molecules in each of the following pair of compounds. (Wedge and Dash representations).

(I) 

(i) (ii)

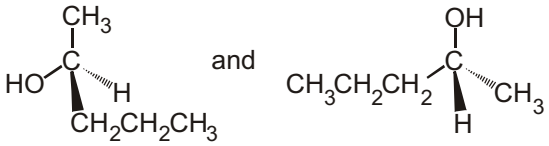
(II) 

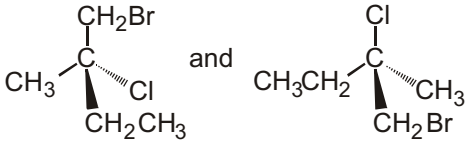
(i) (ii)

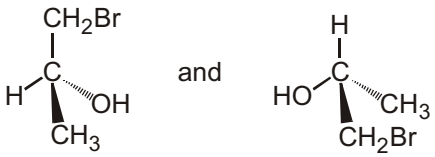
(III) 

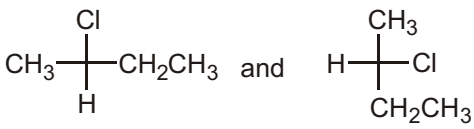
(i) (ii)

14. Do the following structures represent identical molecules or a pair of enantiomers ?

(a) 

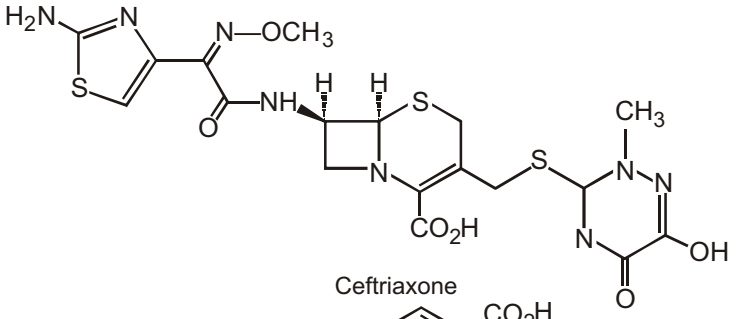
(b) 

(c) 

(d) 

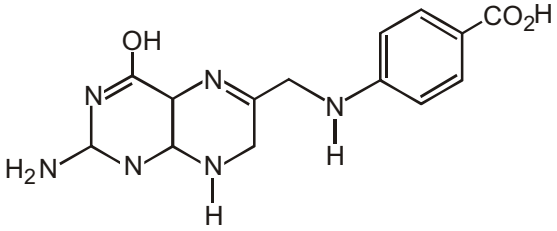
15. For each of the following compounds, identify any centers of chirality, and calculate the number of possible optical isomers :

(a)



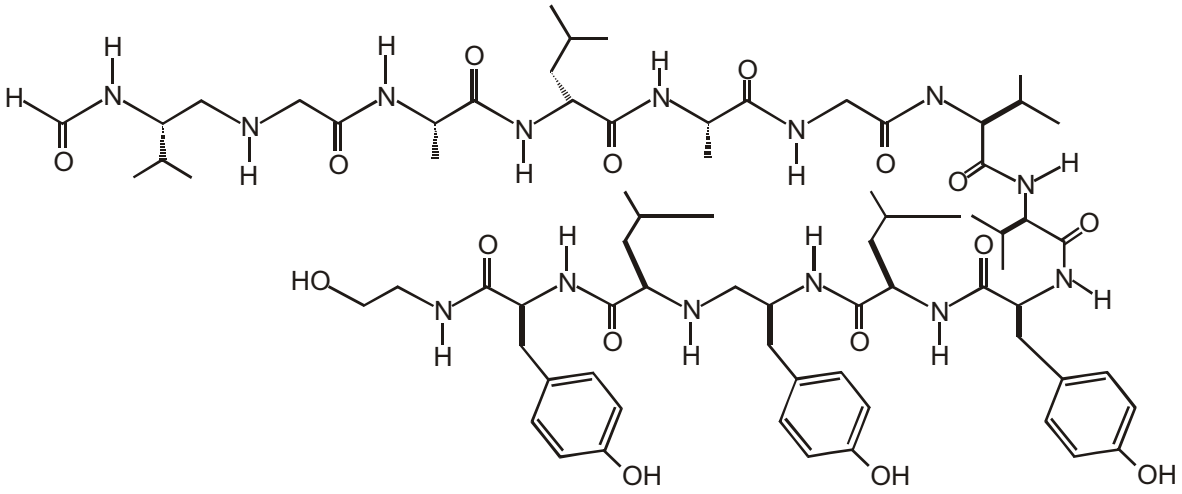
Ceftriaxone

(b)



Dihydrofolic acid

(c)



Gramicidin A

16. If molecule is pyramidal, **X** stereoisomers are possible for :

Cabde

find the value of **X.**

17. Total number of plane of symmetry in all conformations of 1, 2-dibromo of ethane

18. Total number of isomers of molecular formula of C6H12 having cyclobutane ring are.

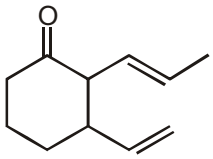
19. (i) Total stereoisomers of 2, 3-di-chlorobutane are (a).

(ii) $CH_3-CH=CH-CH=CH-\underset{Cl}{\overset{H}{C}}-CH_3$

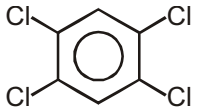
Total number of stereocentre in given compound are (b).

Value of a + b will be.

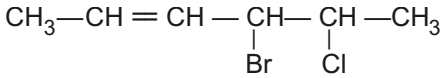
20. How many stereoisomers of given compound are possible when alkenyl substituent have a cis configuration



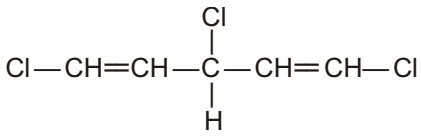
21. Total number of plane of symmetry present in given compound is



22. Find out the total number of stereocentre in the given compound.



23. Find out the total number of stereoisomers of the given following compound.



24. Find the total number of isomers of C_7H_{14} (only 5-member ring).

◎ Special Problems

1. Number of stereocenters in cis-2-butene are:

(A) 0 (B) 1 (C) 2 (D) 3

2. Number of Carbon needed by Ester to show optical isomerism are:

(A) 4 (B) 5 (C) 6 (D) 7

3. Number of stereocenters in D-glucose :

(A) 1 (B) 5 (C) 4 (D) 7

4. Number of chiral centers in alpha-D-Glucopyranose are:

(A) 4 (B) 5 (C) 6 (D) 7

5. Number of enantiomers of 2-butanol are:

(A) 0 (B) 1 (C) 2 (D) 3

6. Number of diastereomers of Gammaxene are:

(A) 6 (B) 8 (C) 16 (D) 24

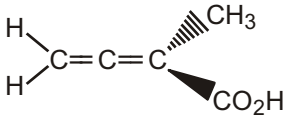
7. Number of diastereomers in 3-methyl-5-propylcyclohexene are:

(A) 2 (B) 4 (C) 6 (D) 3

8. Number of Carbon needed by a cycloalkane to show optical isomerism are:

(A) 4 (B) 5 (C) 6 (D) 7

9. Which of the following is true for the given compound?



(A) can show optical isomerism (B) can show geometrical isomerism

(C) no POS or COS present in the compound (D) None of these above is true

10. Number of chiral centers in beta-D-Glucofuranose are:

(A) 4 (B) 5 (C) 6 (D) 7

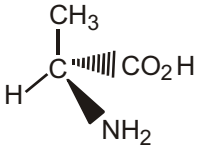
11. Number of diastereomers of 2-cyclohexyl pent-2-ene are:

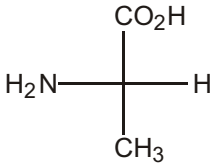
(A) 0 (B) 1 (C) 2 (D) 3

12. Number of diastereomer pairs of Tartaric acid are:

(A) 1 (B) 2 (C) 3 (D) 0

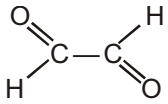
13. D,L configurations of given isomers respectively are:





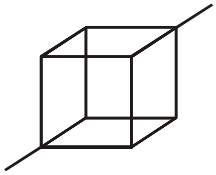
(A) D,D (B) L,L (C) D,L (D) L,D

14. Which of the following molecules have P.O.S. and n-fold perpendicular Axis of Symmetry?

(A) 

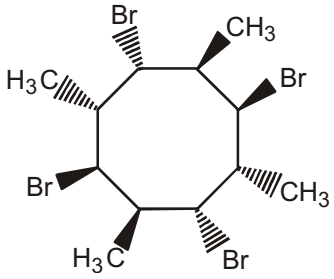
(B) 2-chlorobutane (C) s-cis-1,3-butadiene (D) Lactic acid

15. Number of P.O.S. in given compound is-



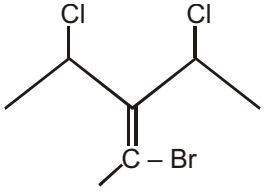
(A) 1 (B) 3 (C) 6 (D) 9

16. The given molecule has which Axis of Symmetry?



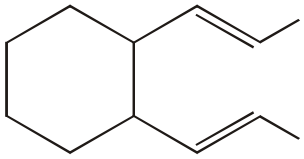
(A) S2 (B) S4 (C) POS (D) S6

17. Total number of stereoisomers of the given compound is:



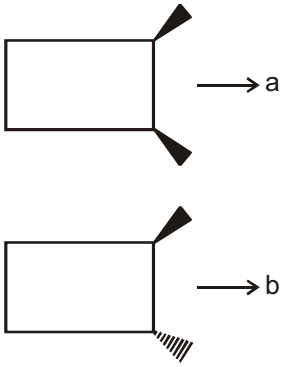
(A) 2 (B) 4 (C) 6 (D) 8

18. Total number of stereoisomers of the given compound is:



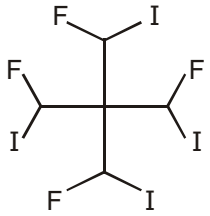
(A) 8 (B) 16 (C) 10 (D) 32

19. a and b are diastereomers of the given compouds. What are the values of a and b respectively:



(A) 1,1 (B) 1,2 (C) 2,1 (D) 2,2

20. Number of meso isomers of the given compound is:



(A) 5 (B) 2 (C) 0 (D) 1

21. Which of the following Axis of symmetry is present in Trans-2-butene?

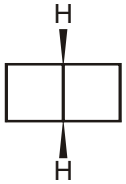
(A) 2 (B) 3 (C) 4 (D) 6

22. Which of the following is chiral?

(A) Flask (B) Chair

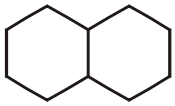
(C) Aishwarya Rai (D) Book

23. Number of stereoisomers for the given compound are:



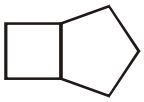
(A) 1 (B) 2 (C) 3 (D) 4

24. Number of stereoisomers for the given compound are:



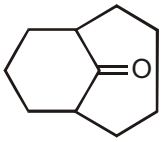
(A) 1 (B) 2 (C) 3 (D) 4

25. Number of stereoisomers for the given compound are:



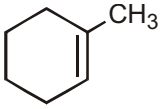
(A) 1 (B) 2 (C) 3 (D) 4

26. Number of stereoisomers for the given compound are:



(A) 1 (B) 2 (C) 3 (D) 4

27. Number of Carbon atoms that lie in same plane are:



(A) 3 (B) 4 (C) 5 (D) 7

28. Which of the following statements can be used to prove that carbon is tetrahedral?

(A) Methyl bromide does not have constitutional isomers.

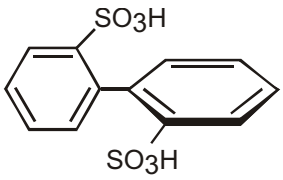
(B) Tetrachloromethane does not have a dipole moment.

(C) Dibromomethane does not have constitutional isomers.

(D) None of these.

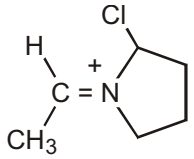
29. What happens when the given compound is heated?

(A) Racemic mixture (B) Diastereomers



(C) 100% pure enantiomer (D) No change

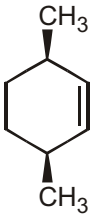
30. Number of stereocenters in the given compound are:



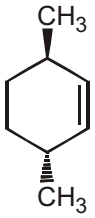
(A) 0 (B) 1 (C) 2 (D) 3

31. An optically active compound A with molecular formula C_8H_{14} undergoes catalytic hydrogenation to give an optically inactive product. Which of the following can be the structure of A?

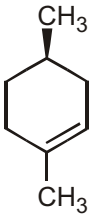
(A)



(B)



(C)



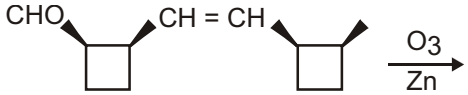
(D) B & C

32. Which of the following compounds can be resolved?

(A) cis-1,3-dimethylcyclohexane (B) 1,1-dimethylcyclohexane

(C) cis-1,4-dimethylcyclohexane (D) cis-1-ethyl-3-methylcyclohexane

33.

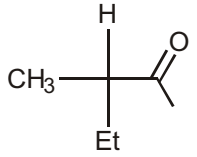


Number of chiral products are:

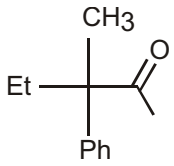
(A) 0 (B) 1 (C) 2 (D) 3

34. Which of the following is chiral and gives racemic mixture on treatment with trace of base?

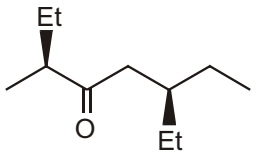
(A)



(B)



(C)

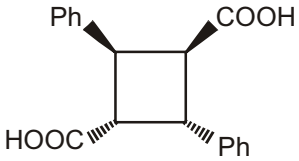


(D) All of these

35. The given compound has which Axis of Symmetry (S_n):

(A) S_2 (B) S_3 (C) S_4 (D) S_6

36. The given compound possesses which of the following:



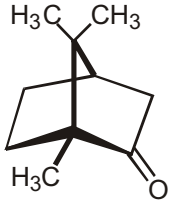
(A) Mirror symmetry (B) Center of inversion

(C) n-fold alternating axis of symmetry (D) All of these

37. Which of the following is the correct expression for maximum number of configurational isomers?
n = number of stereocenters m= number of stereogenic double bonds

(A) 2(n–m) (B) 2m + 2n (C) 2m + 2n/2 (D) 2(n+m)/2

38. The number of stereoisomers of Camphor which can exist are:

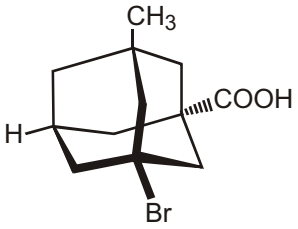


(A) 1 (B) 2 (C) 3 (D) 4

39. The number of stereoisomers of Twistane which can exist are:

(A) 2 (B) 3 (C) 4 (D) 8

40. The number of Stereocenters and stereoisomers of the given Adamantane derivative which can exist are:



(A) 2, 2 (B) 2, 4 (C) 4, 2 (D) 4, 4

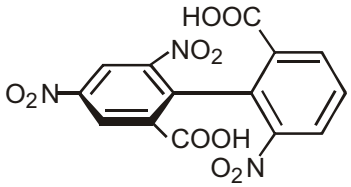
41. The number of stereoisomers of Penta-2,3-diene (consider only cumulated dienes) which can exist are:

(A) 2 (B) 3 (C) 4 (D) 6

42. The number of Stereocenters and stereoisomers of cyclooctene are:

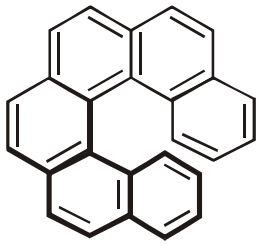
(A) 0, 1 (B) 1, 1 (C) 2, 3 (D) 2, 4

43. The number of stereoisomers of the given compound which can exist are:



(A) 0 (B) 1 (C) 2 (D) 4

44. The number of stereoisomers of the given compound which can exist are:



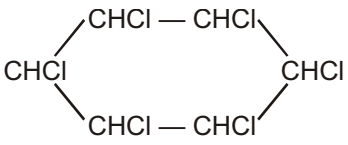
(A) 0 (B) 1 (C) 2 (D) 4

45. $CH_3-\underset{\underset{Br}{|}}{CH}-CH$ $\quad CH-\underset{\underset{Br}{|}}{CH}-CH_3$

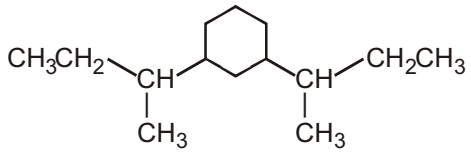
A mixture of all stereoisomers possible from this structure is subjected to fractional distillation. Then how many fractions will be obtained ?

(A) 5 (B) 6 (C) 3 (D) 4

46. Find number of meso-isomers of



(A) 6 (B) 9 (C) 8 (D) 7

47. How many meso-isomers are possible for 

(A) 1 (B) 2 (C) 3 (D) 4

48. Which one of the following statements is not true ?

(A) Diastereomers are a pair of stereoisomers that are not mirror images of one another.

(B) A pair of enantiomeric compounds has identical melting points.

(C) Diastereomers do not have equal specific rotations.

(D) Diastereomers are superimposable mirror images of one another.

49. The amount of the major enantiomer in a solution which is 80% optically pure is?

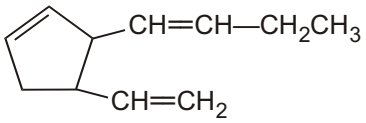
(A) 90% (B) 60% (C) 70% (D) 80%

50. Consider the following compound :

What is the number of stereoisomers possible for the above compound?

(A) 2 (B) 3 (C) 4 (D) 5

51. Stereoisomers possible for following compound is

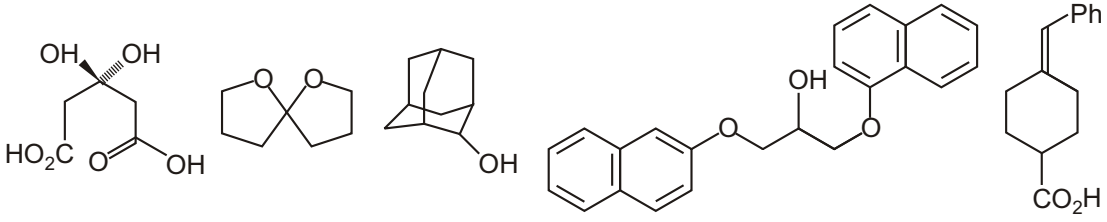


(A) 8 (B) 16 (C) 32 (D) 64

52. (+)-Tartaric acid has a specific rotation of +12.0°. Calculate the specific rotation of a mixture of 68% (+)-tartaric acid and 32% (–)- tartaric acid.

SUBJECTIVE TYPE QUESTIONS

1. Are these compounds chiral ? Draw diagrams to justify your answer.

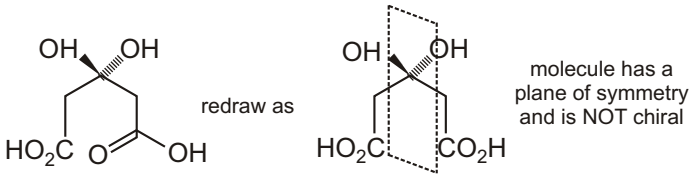


Purpose of the problem

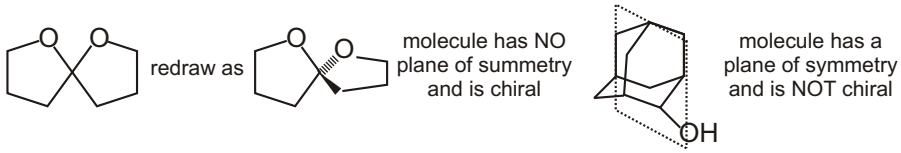
Reinforcement of the very important criterion for chirality. The previous problems were almost childish compared with this one; make sure you understand the answer.

Suggested solution

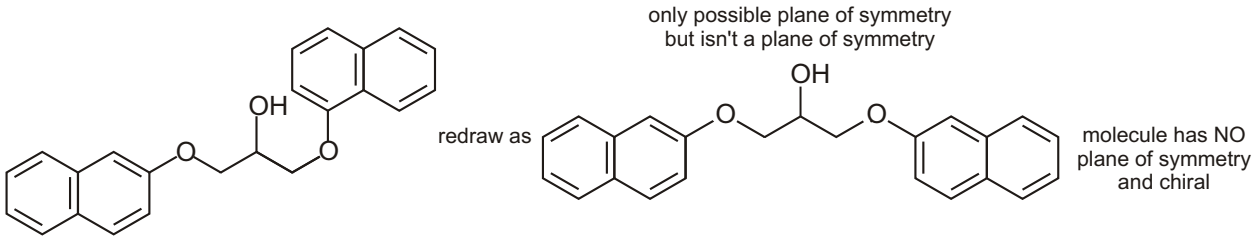
Only one thing matters – does the molecule have a plane of symmetry ? We need to redraw some of them to see if they do. On an account look for chiral centres of carbon atoms with four different groups or whatever-just look for a plane of symmetry (POS).



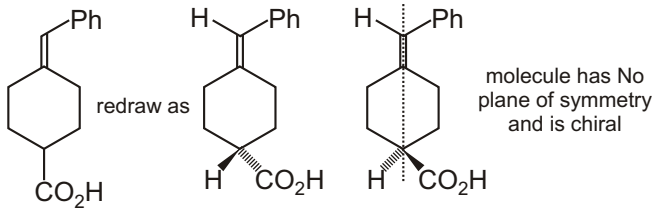
The second molecule is a 'spiro' compound having two rings joined at a tetrahedral carbon atom. These two rings are orthogonal so there is no plane of symmetry. The third molecule does have a plane of symmetry. It is much easier to see this if you make a model.



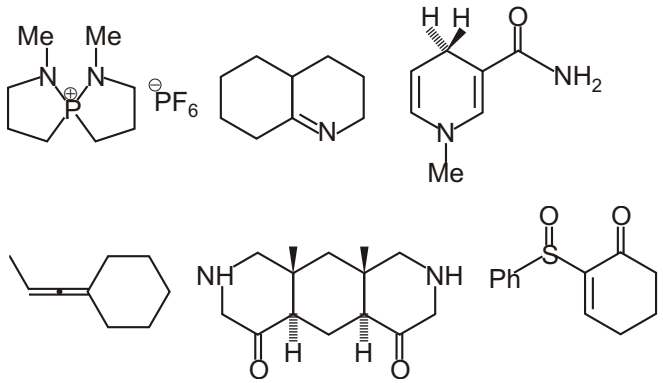
The fourth molecule is a bit of a trick. It needs to be redrawn to see if it has a plane of symmetry but when you did the redrawing your might not have noticed that the two naphithalene rings were joined at different positions. The molecule is chiral.



The last molecule is an interesting case. It is chiral but, if you got this one wrong, don't be too disappointed. Again, making a model will help but the vital thing is to realise that the CO_2H group is on a tetrahedral centre so the ring itself is not a plane of symmetry. The alkene puts the phenyl group to one side and a hydrogen atom to the other so the plane at right angles to the ring (dotted line) isn't a plane of symmetry either.



2. What makes molecule chiral ? Give three examples of different types of chirality. State with explanations whether the following compounds are chiral.



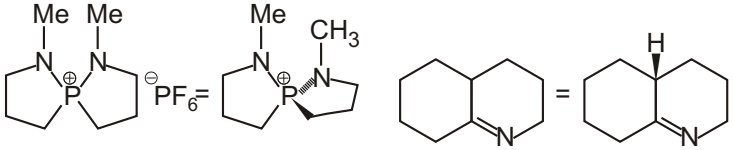
Purpose of the problem

Revision of the criterion for chirality with examples of the main classes of chiral molecules. Examstyle question.

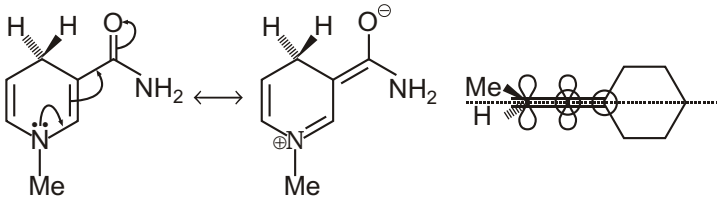
Suggested solution

Molecules are chiral if they have no plane of symmetry. This may arise form a tetrahedral atom with four different substituents or from a molecule that is forced to adopt shape that lacks a plane of symmetry. Examples include spiro compounds, axial chirality in allenes, chirality in allenes, chiral C, P, S, etc. You should give definite examples in this part of the answer, which are different from those given in the question, Ask someone to check if yours are all right.

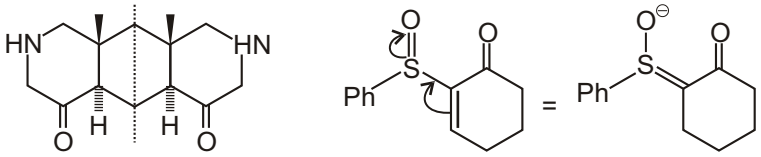
The phosphorus compound does not have a chiral phosphorus atom but the molecule is chiral because it is a spiro compound like the second molecule in the last question. The second molecule is nearly planar but the combination of a double bond and a tetrahedral centre at the other ring junction removes all possibility of a plane of symmetry. This too is chiral.



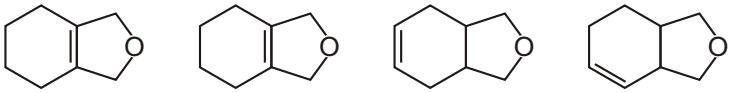
The third molecule tries to look chiral but it is almost planar because of conjugation, and the hydrogen atom above the plane reflects the hydrogen atom below it. The plane of the ring is a plane of symmetry and the molecule is not chiral. The fourth molecule is an allene with the two alkenes orthogonal to each other. It needs to be drawn more realistically to show the there is a plane of symmetry cutting the cyclohexane ring at right angles and passing through the methyl group on other end of the allene. Not chiral either.



The last two molecules are more straight forward. The tricyclic compound has a plane of symmetry vertically down the middle and is not chiral. The sulfoxide is a simple example of a stereogenic atom other than carbon. Sulfoxides are tetrahedral with the oxygen atom and the lone pair above and before the plane as drawn. This one is chiral.



3. Discuss the stereochemistry of these compounds. (Hint. This means saying how many diastereoisomers there are, drawing clear diagrams of each, and saying whether they are chiral or Not.)

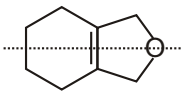


Motive of the Problem

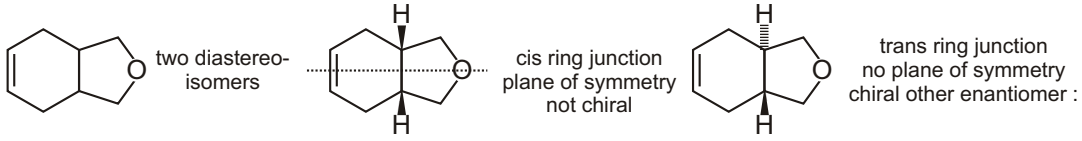
Making sure that you can handle this important approach to the stereochemistry of molecules.

Suggested solution

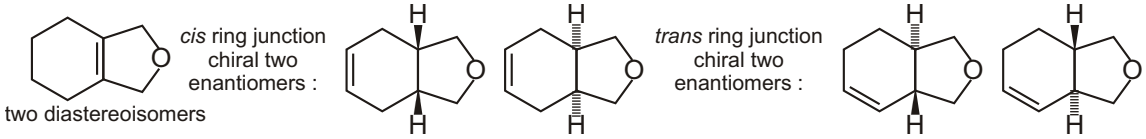
Just follow the hint given in the question! Diastereoisomers are different compounds so they must be distinguished first. Then it is easy to say if each diastereoisomer is chiral or not. The first two are simple.



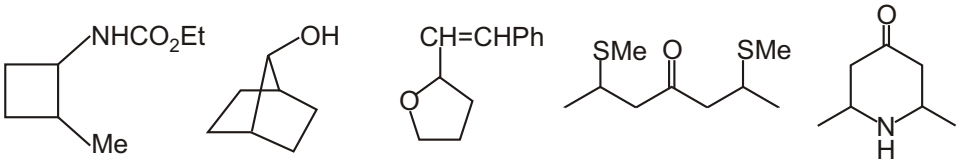
The third structure may exist as two diastereoisomers: one has a plane of symmetry (a meso compound) but the other is chiral (it has C_2 symmetry).



The last compound is most complicated as it has no symmetry. Again we can have a cis or trans ring junction but this time both diastereoisomers are chiral.



4. Discuss the stereochemistry of these compounds. The diagrams are deliberately poor ones that are ambiguous about stereochemistry – your answer should use good diagrams that shown the stereochemistry clearly.

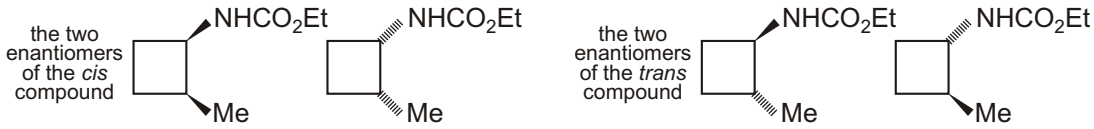


Purpose of the problem

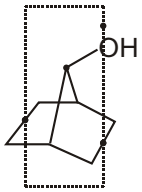
Practice at spotting stereochemistry and unravelling the different possible stereochemical relationships.

Suggested solution

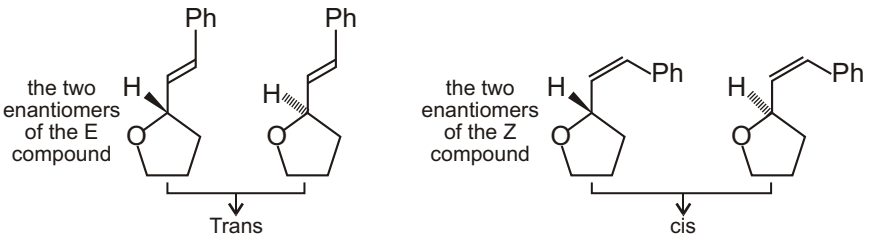
The first compound is simple : two diastereoisomers, cis and trans, both are chiral.



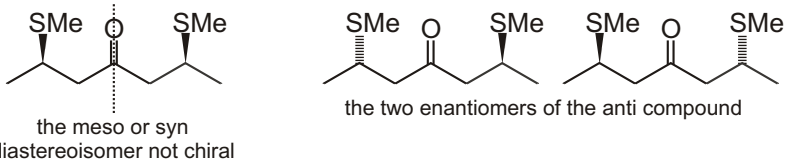
The second is simple too – the molecule has a plane of symmetry passing through the black dots and is not chiral. No diastereoisomers.



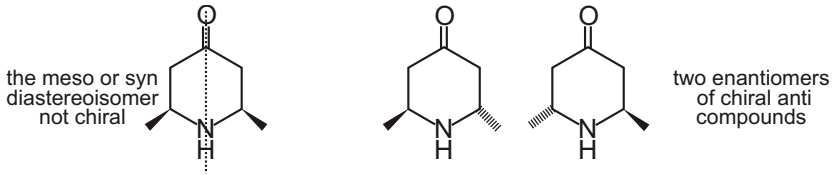
The third compound has two stereochemical units : an alkene that can be Z (*cis*) or E (*trans*) and the provides two different compounds, or diastereoisomers. There is also a chiral centre as each allene isomer has two enantiomers.



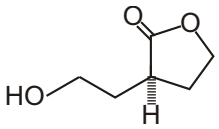
The fourth compound has some symmetry. There are two diastereoisomers with the MeS groups arranged *syn* or *anti* (as drawn). One has a plane of symmetry and is a *meso* compound while the other is chiral.



The fifth compound is similar : two diastereoisomers; one is chiral.



5. This compound racemizes in base. Why is that ?

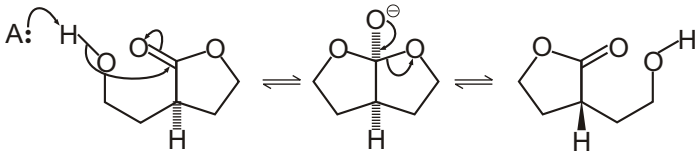


Purpose of the problem

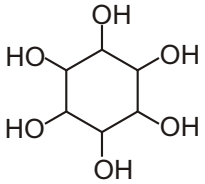
To draw your attention to the dangers in nearly symmetrical molecules and revision of ester exchange.

Suggested solution

Ester exchange in base goes through a symmetrical tetrahedral intermediate with a plane of symmetry. Loss of the right-hand leaving group gives one enantiomer of the ester and loss of the left-hand leaving group gives the other.



6. Just for fun, you might like to try and work out just how many diastereoisomers inositol has and how many of them are meso compounds,



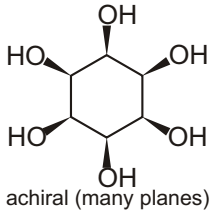
Purpose of the problem

Fun, it says! There is a more serious purpose in that the relationship between symmetry and stereochemistry is interesting and, in this human brain chemical, important to understand.

Suggested solution

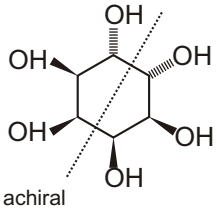
If we start with all the OH group on one side and gradually move them over, we should get the right answer. If you got too many diastereoisomers, check that some of yours aren't the same as other. There are either diasteroisomers altogether and, incredibly, all except one are achiral. Some have one, some two, and two of the most synmetrical have many planes of symmetry.

all OHs up



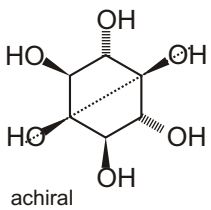
achiral (many planes)

four OHs up



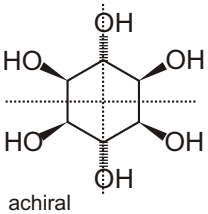
achiral

four OHs up



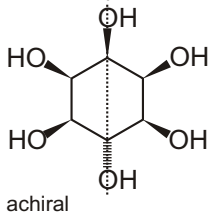
achiral

four OHs up



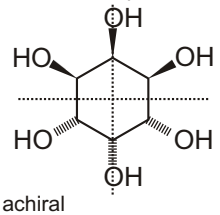
achiral

five OHs up



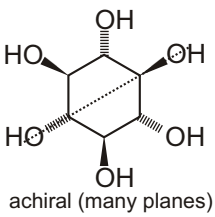
achiral

three OHs up



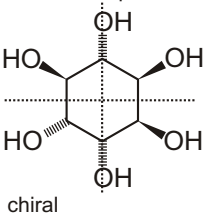
achiral

three OHs up



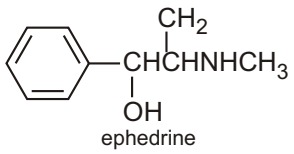
achiral (many planes)

three OHs up

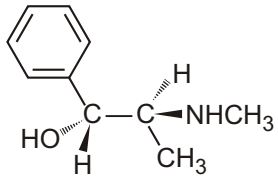


chiral

7. What is meant by operators in terms of elements of symmetry ? What is order of symmetry operation ? Show the symmetry operators of chair form of cyclohexane.
8. How many stereoisomers are possible for a molecule having the formula CA_4* where *A** represent an asymmetric centre. Are all of them optically active?
9. If the compound C_{abcd} is assumed to be square-planar, then how many stereoisomers are possible? What are the stereochemical relationships among them? If each of the square planer structure assumes pyramidal structure then how many stereoisomers are possible and what is their stereochemical relationship.
10. For many centuries, the chinese have used extracts from a group of herbs known as ephedra to treat asthma. A compound named ephedrine has been isolated from these herbs and found to be a potent dilator of air passage in the lungs.
    (a) How many stereoisomers does ephedrine have?
    (b) The stereoisomers shown here is the one that is pharmacologically active. What is the configuration of each of the asymmetric centres?



ephedrine

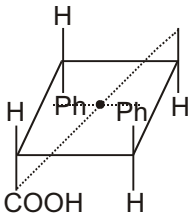


Answers

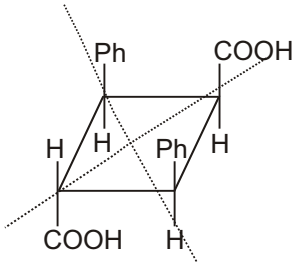
Match the Column

1. **D**
2. **A- S B-PS C-S D-RS**
3. A P, R, S ; B Q, S ; C P, Q, R, S ; D P, R, S
4. A – P,R,S ; B – P, Q, R, S ; C – P, R ; D – P

5. (A) Q; (B) P; (C) P,Q,S; (D) R,S]

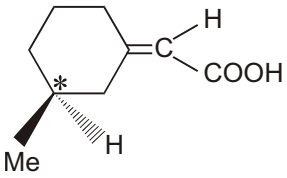
Sol. (I) 

Show G.I. no O.I. center of symmetry

(II) 

P.O.S. Show G.I. No. O.I.

(III) Chiral molecular No symmetry show O.I.

(IV) 

Chiral molecular No symmetry show O.I. Me is on the side of COOH show G.I.

6. A S ; B P, S ; C S ; D RS

FIND THE RELATIONSHIP

1. Enantiomer	**2.** Enantiomer	**3.** Identical	**4.** Identical
5. Enantiomer	**6.** Identical	**7.** Diastereomer	**8.** Diastereomer
9. Diastereomers	**10.** Enantiomer	**11.** Positional isomers	**12.** Diastereomers
13. Diastereomers	**14.** A, B diastereomers ; B, C diastereomers A, D Enantiomers ; A and C diastereomers		
15. Enantiomer	**16.** Identical	**17.** Identical	**18.** Diastereomer
19. Diastereomer	**20.** Constitutional isomer	**21.** Enantiomer (bc) ; Diastereomer (ab) & (ca)	
22. Identical	**23.** Enantiomer	**24.** Identical	**25.** Enantiomer
26. Enantiomer	**27.** Identical	**28.** Diastereomer	**29.** Enantiomer
30. Positional Isomer	**31.** Enantiomer	**32.** Identical	**33.** Diastereomer
34. Identical	**35.** Enantiomer	**36.** Diastereomer	**37.** Diastereomer
38. Enantiomer	**39.** Identical	**40.** Identical	**41.** Diastereomer
42. Diastereomer	**43.** Identical	**44.** Enantiomer	**45.** Diastereomer
46. Diastereomer	**47.** Enantiomer	**48.** Identical	**49.** Enantiomer
50. Enantiomers	**51.** Identical	**52.** Identical	**53.** Diastereomers
54. Consitutional isomers	**55.** Enantiomers	**56.** Consitutional isomers	
57. Enantiomers	**58.** Identical	**59.** Enantiomers	**60.** Consitutional isomers
61. Identical	**62.** Identical	**63.** Enantiomers	**64.** Different Compound
65. Identical	**66.** Enantiomers	**67.** Identical	**68.** Enantiomers
69. Identical	**70.** Diastereomers	**71.** Diastereomers	**72.** Consitutional isomers

73. Diastereomers **74.** Diastereomers **75.** Identical **76.** Enantiomer
77. Identical **78.** Identical **79.** Identical **80.** Diastereomer
81. Enantiomer **82.** Constitutional isomer **83.** Other
84. Constitution alisomer **85.** Diastereomer **86.** Enantiomer **87.** Enantiomer
88. Enantiomer **89.** Enantiomer **90.** enantiomers **91.** enantiomers.
92. enantiomers. **93.** Identical **94.** Different **95.** enantiomers.
96. enantiomers. **97.** Identicla **98.** diastereomers. **99.** enantiomers.
100. Identical **101.** Identical **102.** Identical **103.** Identical
104. enantiomers.

Unsolved Question

1. a, c, f **2.** A, C, E

3. A -Identical B- Enantiomer C- Diastereomers D- Identical **4.** iii, iv, vi

5. (a) Diastereomers (b) Enantiomers (c) Enantiomers (d) Constitutional isomers

6. (a) Enantiomers (b) Diastereomers

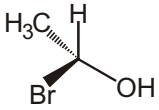
7. (a) R (b) 2R, 3S (c) 2R, 3S

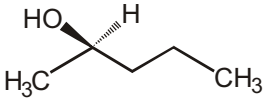
8. (a) Diastereomers (b) Constitutional isomers
(c) Constitutional isomers (d) Diastereomers

9. Nobecause it has C.O.S. **10.** (a) 2 (b) 1R, 2S

11. (a) Enantiomer (b) Identical (c) Identical (d) Identical

12. Total SI = 9 Meso =7

13. (i) 

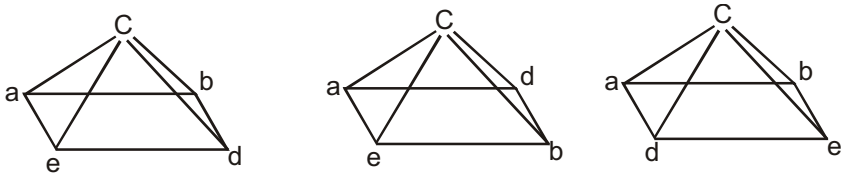
(ii) 

(iii) $CH_3\,CHCH_2CH_3$ (Br)

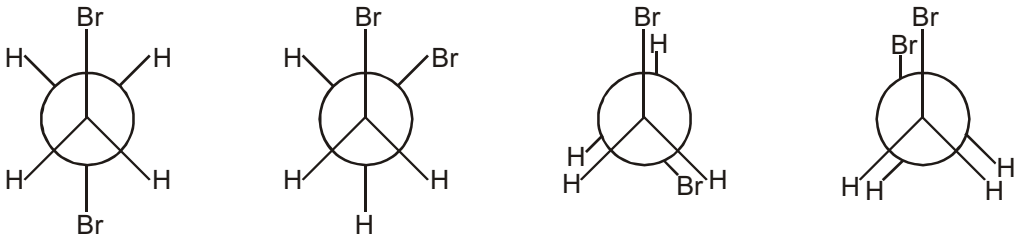
14. The first structure shown in part (a) has the S configuration and the second structure has the R configuration. Because they have opposite configurations, the structures represent a pair of enantiomers. All pairs are Eantiomers.

15. (a) chiral centers= 2 No. of O.I. = 22 (b) chiral centers= 3 No. of O.I. = 23
(c) chiral centers= 11 No. of O.I. = 211

16. 6 or 8

Sol. 

Each having one enantiomer, total 6-isomers.

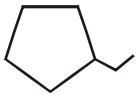
17. 

Ans. 3

18. 7 **19.** 8 **20.** 4 **21.** 3 **22.** 4 **23.** 4 **24.** 8

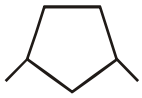
Sol.

1



1

3

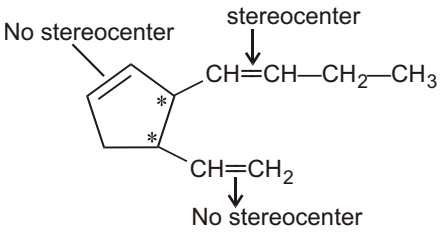


3

Special Problems

1.	(C)	**2.**	(B)	**3.**	(C)	**4.**	(B)	**5.**	(C)	**6.**	(B)	**7.**	(A)	**8.**	(B)
9.	(D)	**10.**	(B)	**11.**	(C)	**12.**	(B)	**13.**	(B)	**14.**	(A)	**15.**	(B)	**16.**	(B)
17.	(B)	**18.**	(C)	**19.**	(C)	**20.**	(D)	**21.**	(A)	**22.**	(C)	**23.**	(A)	**24.**	(B)
25.	(C)	**26.**	(C)	**27.**	(C)	**28.**	(C)	**29.**	(A)	**30.**	(D)	**31.**	(D)	**32.**	(D)
33.	(B)	**34.**	(D)	**35.**	(C)	**36.**	(B)	**37.**	(A)	**38.**	(B)	**39.**	(A)	**40.**	(C)
41.	(A)	**42.**	(C)	**43.**	(B)	**44.**	(C)	**45.**	(D)	**46.**	(D)	**47.**	(B)	**48.**	(D)
49.	(A)	**50.**	(C)	**51.**	(A)										

51.



Hence, total stereoisomer = 23 = 8]

52. Ans. 4.32°]

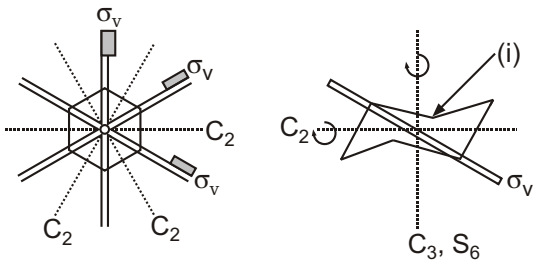
Racemic 32%, (+) 36%]

Subjective Type Questions

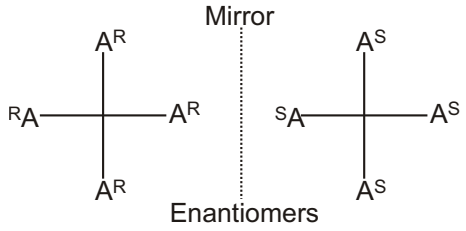
7. If a structure of a molecule can be transformed into an identical or indistinguishable structure by the physical movement based on an element of symmetry, without breaking O , deforming any part of the molecule, then that manipulation is called a symmetry operation.

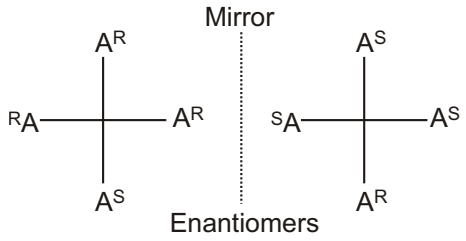
The order of a symmetry operation is the number of total operations that can be done to convert a structure to its equivalent/identical structure.

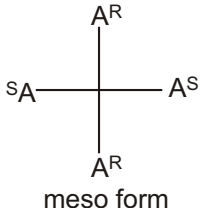
The chair form of cyclohexane belongs to the point group D_{3d}. Its elements of symmetry are $C_3, 3C_2, 3$, (diagonal) planes, i, S_6. Its operation of identity $E(C_1)$ is also a symmetry operation. Moreover two times C_3 operation is an identify operation (E). It can also be confirmed that five times operation of S_6 is also an operation of identify. Therefore, the order of symmetry operation of chair form of cyclohexane is 12. They are E, C_3^1, C_3^2, $3C_2$,$3S_V$,i, S_6^1, S_6^5. The structure of the chair form of cyclohexane is as follows.



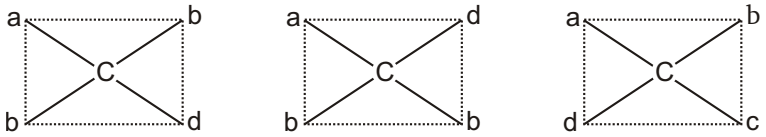
8. The molecule represented as CA_4* can have two pairs of enantiomers and one meso-compound, the asymmetric substituents can have both R and S configurations. The Fisher projection of stereoisomers in a perpendicular mirror plane can be shown as follows.



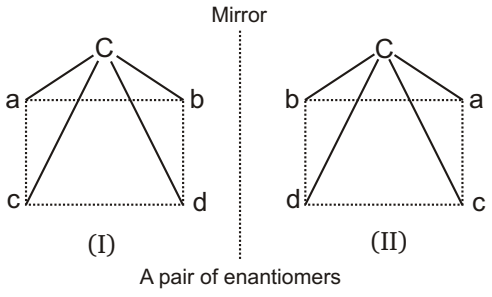




9. When the compound C_{abcd} assumed square-planar structure then three stereoisomers are possible. Since all of them have planar structure, none of them is chiral. Stereochemically they are diastereoisomers. Structures are shown here.



When each of these square-planar structures is converted to pyramidal structure with *C* at the apex then three pairs of enantiomers are formed, that is, six stereoisomers are formed. Only one pair of enantiomers (transformed to pyramid form from I) is shown here.



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