

29.4 ISOMERISM: OPTICAL

Learning outcomes

Candidates should be able to:

1. understand that enantiomers have identical physical and chemical properties apart from their ability to rotate plane polarised light and their potential biological activity
2. understand and use the terms optically active and racemic mixture
3. describe the effect on plane polarised light of the two optical isomers of a single substance
4. explain the relevance of chirality to the synthetic preparation of drug molecules including:
 - (a) the potential different biological activity of the two enantiomers
 - (b) the need to separate a racemic mixture into two pure enantiomers
 - (c) the use of chiral catalysts to produce a single pure optical isomer(Candidates should appreciate that compounds can contain more than one chiral centre, but knowledge of meso compounds and nomenclature such as diastereoisomers is **not** required.)

Introduction

'Stereo' means 'space', and stereoisomers are molecules that have the same number of atoms and bonds, so they are connected in the same way, but the spatial arrangement of the atoms is different.

Stereoisomers are molecules that have the same **structural formula** but have the atoms arranged differently in space.

There are two types of stereoisomerism

Geometrical (cis/trans)

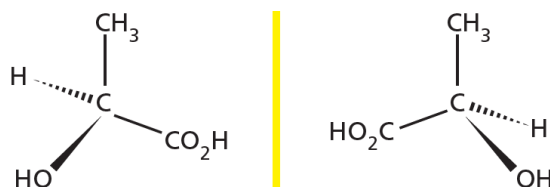
Optical

Optical isomerism

A carbon atom that has **four different atoms** or **groups of atoms** attached to it is called **achiral carbon** or a **chiral centre**.

Compounds with a chiral centre (**chiral molecules**) exist as two **optical isomers**, which are also known as **enantiomers**.

The enantiomers are **non-superimposable mirror images** of each other.

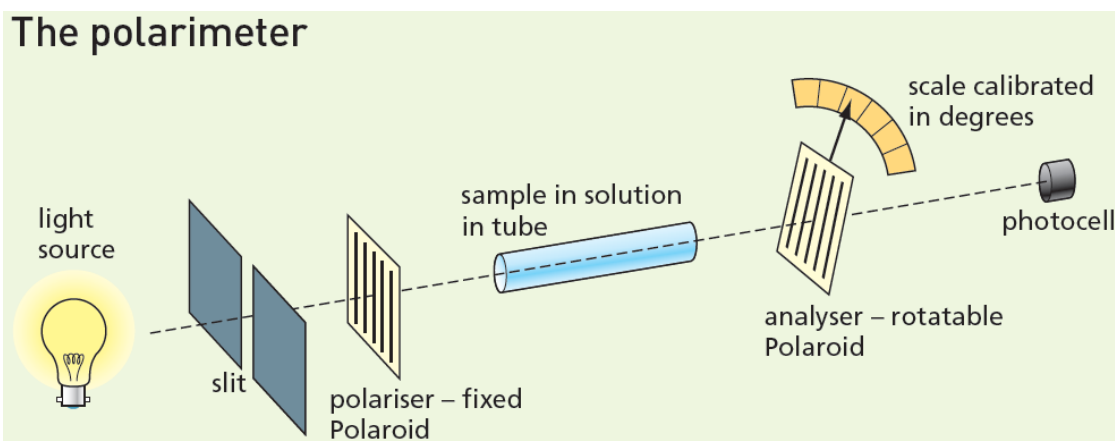


Their physical and chemical properties are **identical**, but they differ in their ability to rotate **plane-polarised light**.

Hence, these isomers are called 'optical' isomers

One of the optical isomers will rotate the plane of polarised light in the **clockwise** direction

Whereas the other isomer will rotate it in the **anti-clockwise** direction



The angles through which the (+) and (-) enantiomers rotate the plane of polarisation are equal, but they are in opposite directions. A 50 : 50 mixture of the two isomers, therefore, has no effect on the passage of plane-polarised light. The clockwise rotation caused by the (+) isomer is exactly cancelled by the anticlockwise rotation caused by the (-) isomer.

This equal mixture of the two enantiomers is called a **racemic mixture** or **racemate**.

relevance of chirality to the synthetic preparation of drug molecules

- the different biological activity of the two enantiomers
- the need to separate a racemic mixture into two pure enantiomers
- the use of chiral catalysts to produce a single pure optical isomer

1. Define enantiomers.

.....
.....
..... [1]

2. 2-aminobutane, $\text{CH}_3\text{CH}(\text{NH}_2)\text{CH}_2\text{CH}_3$, exists as a mixture of two enantiomers.
Define enantiomers.

[1]

3. Explain what is meant by the term chiral centre.

.....
..... [1]

4. Describe what is meant by a racemic mixture.

.....
..... [1]

5. Cortisone is an optically active molecule.
Explain what is meant by optically active.

.....
.....
..... [1]

6. The structure of compound **P** is shown in Fig. 7.1.

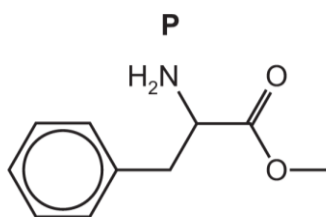


Fig. 7.1

(i) **P** is optically active.

Use an asterisk (*) to identify all chiral carbon atoms on the structure of **P** in Fig. 7.1.

[1]

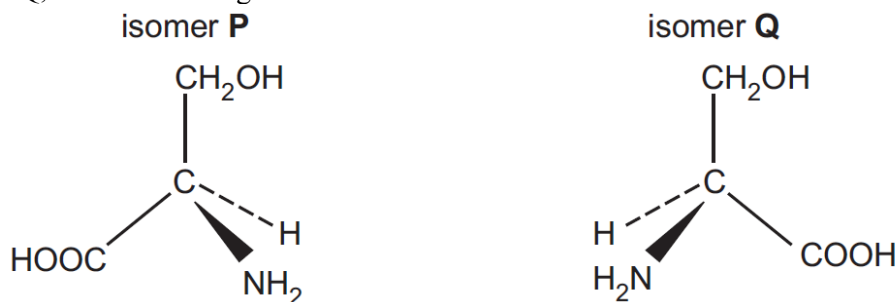
(ii) Plane polarised light is passed through a pure sample of one enantiomer of **P**. This is then repeated with a pure sample of the other enantiomer of **P**.

Describe the results of these two experiments, stating the similarities and differences of the results.

.....

 [2]

7. The amino acid serine, $\text{HOCH}_2\text{CH}(\text{NH}_2)\text{COOH}$, exists in two optically active forms. These optical isomers, isomer **P** and isomer **Q**, are shown in Fig. 8.1.



Isomer **P** and isomer **Q** have identical physical and chemical properties, except for two specific properties. One of these two properties is their differing effect on plane-polarised light.

State the other property by which they differ.

.....
 [1]

- (b) A solution of pure isomer **P** of a particular concentration rotates plane-polarised light by 5.0° in a clockwise direction.

Describe how a solution of pure isomer **Q** of the same concentration affects plane-polarised light.

.....
 [1]

- (c) State another term, in addition to stereoisomers, optical isomers and non-superimposable mirror images, which can be used to describe this pair of chiral compounds, isomer **P** and isomer **Q**.

..... [1]

- (d) Give the term used to describe a mixture containing equal amounts of isomer **P** and isomer **Q**.

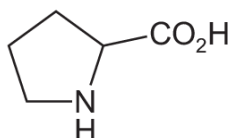
..... [1]

- (e) Describe one way in which a single pure optical isomer of serine can be produced, instead of making a mixture of isomer **P** and isomer **Q**.

..... [1]

8. Identify with an asterisk (*) the chiral centre in proline.

[1]



9. The synthesis produces two enantiomers of tulobuterol.
 (ii) Suggest one disadvantage of producing two enantiomers in this synthesis.

.....
 [1]

- (iii) Suggest a method of adapting the synthesis to produce a single enantiomer.

..... [1]

10. A group of drugs known as statins are used to lower cholesterol in the blood. A commonly used statin is atorvastatin.

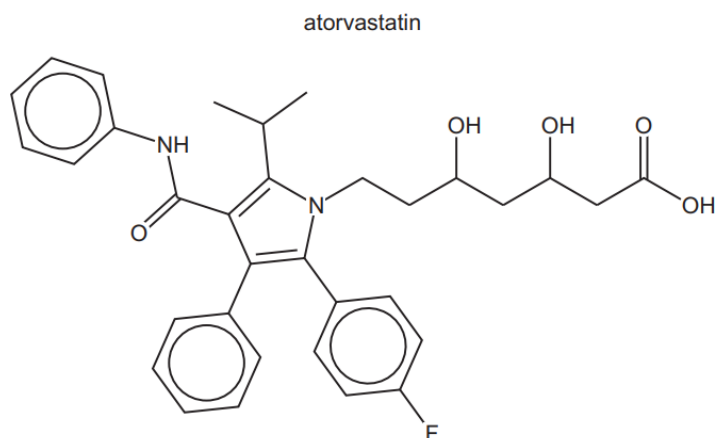


Fig. 5.1

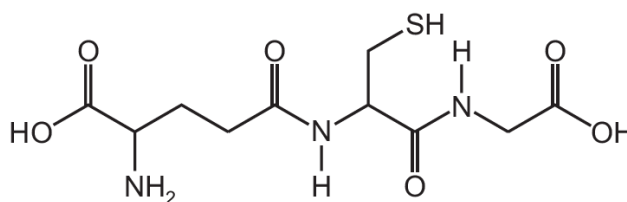
- (i) Atorvastatin contains chiral carbon atoms.
 Circle all chiral carbon atoms in Fig. 5.1.

[1]

- (ii) The synthetic preparation of atorvastatin requires the production of a single optical isomer.
 Suggest why.

.....
 [1]

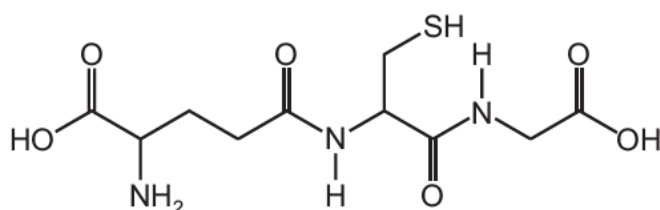
11. Glutathione is a naturally occurring compound found in plants.
 glutathione



On the diagram of glutathione, label each chiral centre with an asterisk (*).

[1]

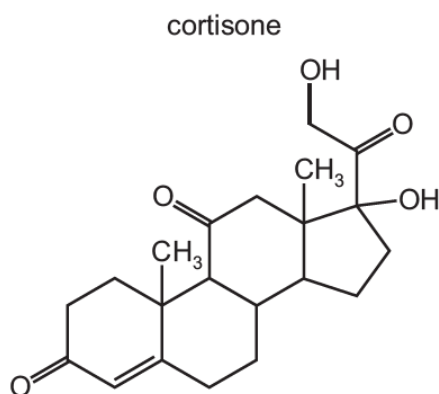
12. Glutathione is a naturally occurring compound found in plants.
 glutathione



On the diagram of glutathione, label each chiral centre with an asterisk (*).

[1]

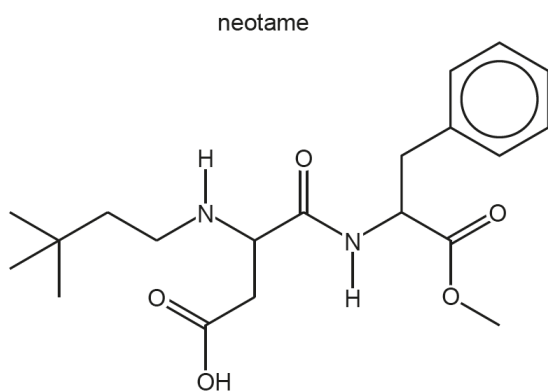
13. Cortisone, $C_{21}H_{28}O_5$, is a naturally occurring chemical that contains chiral carbon atoms.



Deduce the number of chiral carbon atoms in one molecule of cortisone.

..... [1]

14. Neotame is an artificial sweetener added to some foods.



State the number of chiral carbon atoms in a molecule of neotame.

..... [1]

15. State the number of chiral centres in a molecule of **F** and in a molecule of **J**.

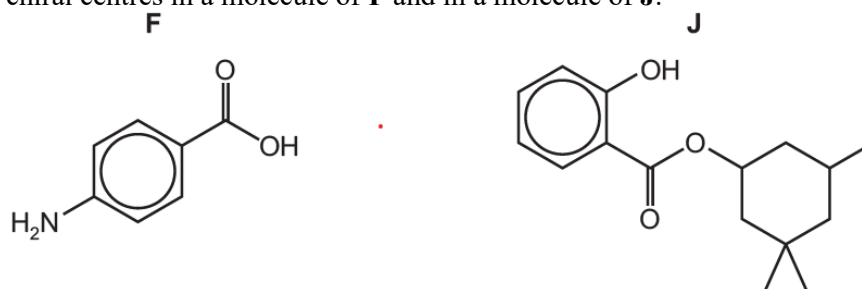


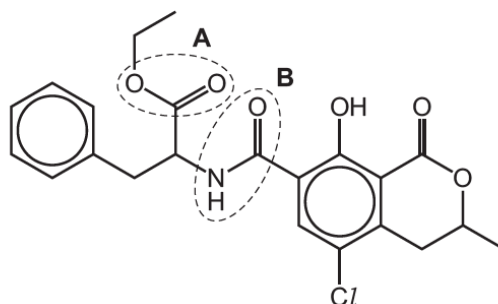
Fig. 4.1

number of chiral centres in: **F** = **J** =

[1]

16. Compound **F** has been found in small quantities in some cereals and dried fruit.

F



State the number of chiral carbon atoms in one molecule of **F**.

..... [1]

17. Perindopril is a drug used to treat heart disease.

perindopril

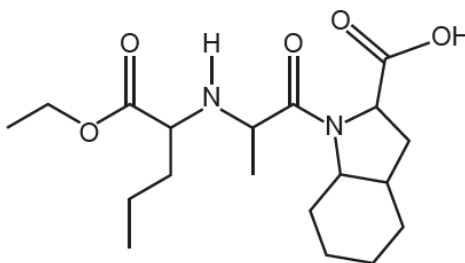


Fig. 6.1

- (i) State the number of chiral carbon atoms present in one molecule of perindopril.

..... [1]

- (ii) Suggest **one** benefit and **one** disadvantage of producing a drug such as perindopril as a single pure optical isomer.

benefit

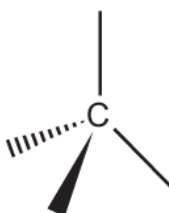
.....

disadvantage

..... [2]

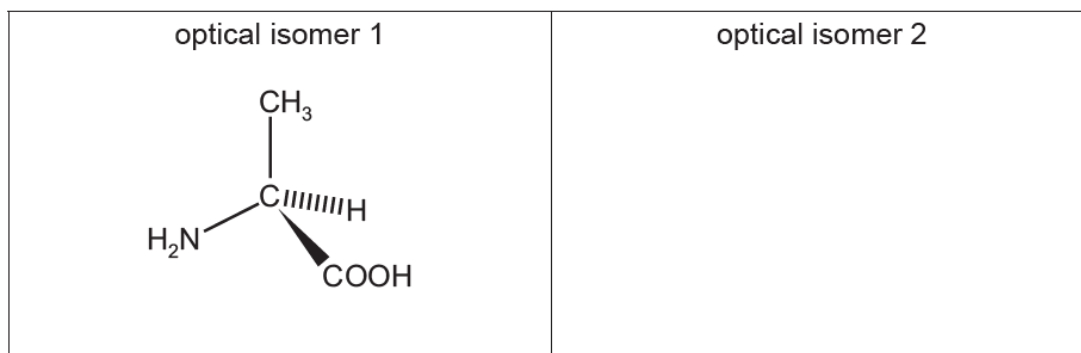
18. Apart from glycine, all naturally occurring amino acids have a chiral centre and exhibit stereoisomerism.
Draw the two stereoisomers of alanine, $\text{CH}_3\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$.

[1]



19. Alanine exists as a pair of optical isomers. The structure of one optical isomer is shown in Fig.
Draw the three-dimensional structure of the other optical isomer of alanine.

[1]



20. Compound **H** has the structural formula $\text{CH}_2=\text{CHCH}(\text{NH}_2)\text{COOH}$.
Compound **H** exhibits stereoisomerism.
Draw three-dimensional structures for the two stereoisomers of **H**.
Name this type of stereoisomerism.

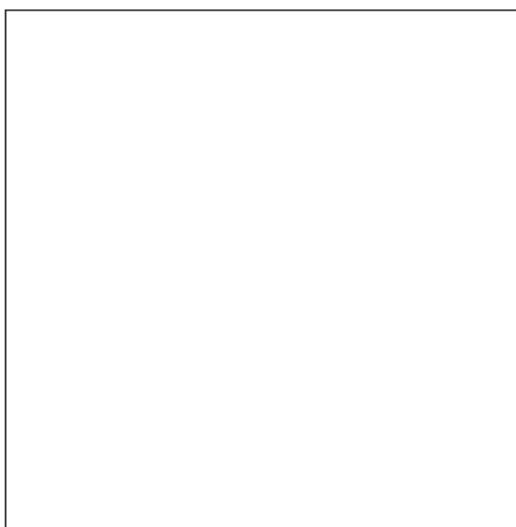
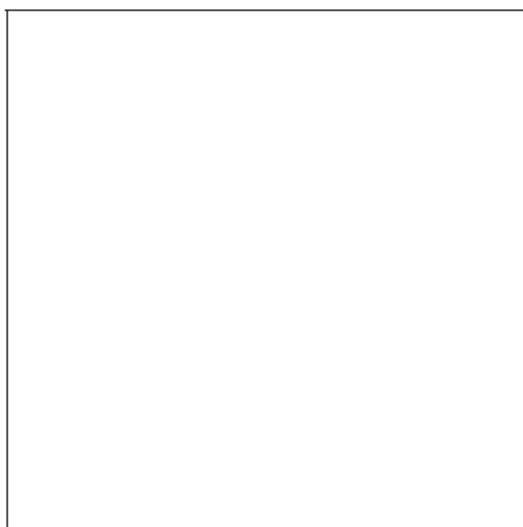


type of stereoisomerism

[2]

21. Alanine, $\text{H}_2\text{NCH}(\text{CH}_3)\text{CO}_2\text{H}$, and glutamic acid, $\text{H}_2\text{NCH}(\text{CH}_2\text{CH}_2\text{CO}_2\text{H})\text{CO}_2\text{H}$, are two naturally occurring amino acids.
 $\text{H}_2\text{NCH}(\text{CH}_3)\text{CO}_2\text{H}$ exists as two optical isomers.
Draw three-dimensional structures of these two optical isomers.

[2]

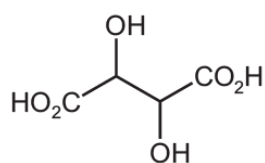


22. 2-aminopropanoic acid, $\text{CH}_3\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$, exists as two stereoisomers.
 Draw three-dimensional diagrams to show the two stereoisomers of 2-aminopropanoic acid.
 State the type of stereoisomerism shown.

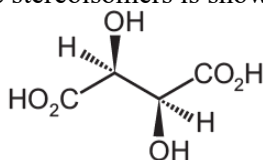
type of stereoisomerism

[2]

23. Fumaric acid reacts with cold, dilute, acidified manganate(VII) to form compound P.

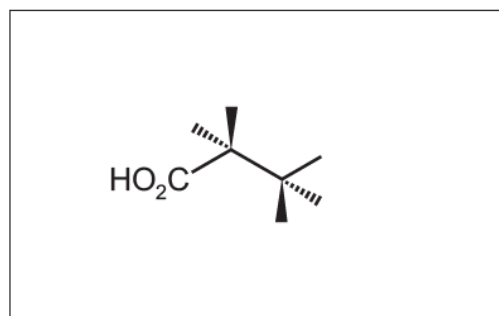
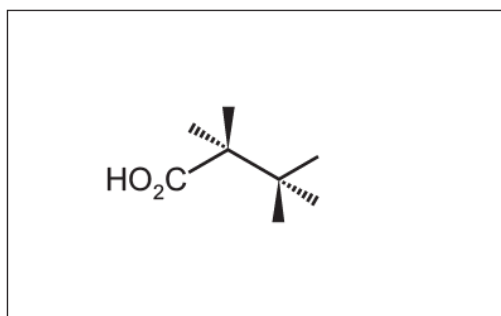


Only three stereoisomers of P exist. One of the stereoisomers is shown.



Complete the three-dimensional diagrams in the boxes to show the other two stereoisomers of P.

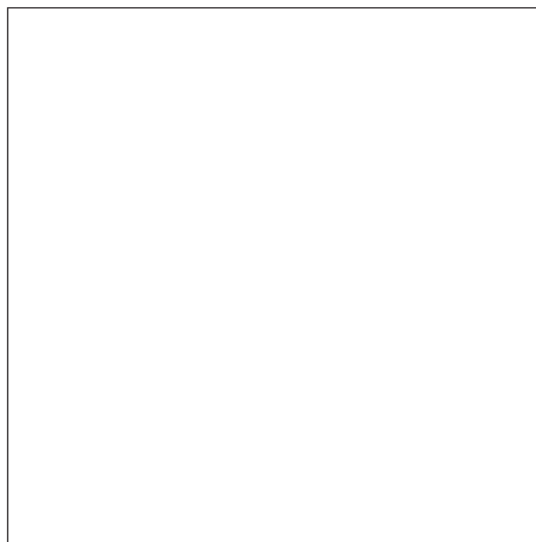
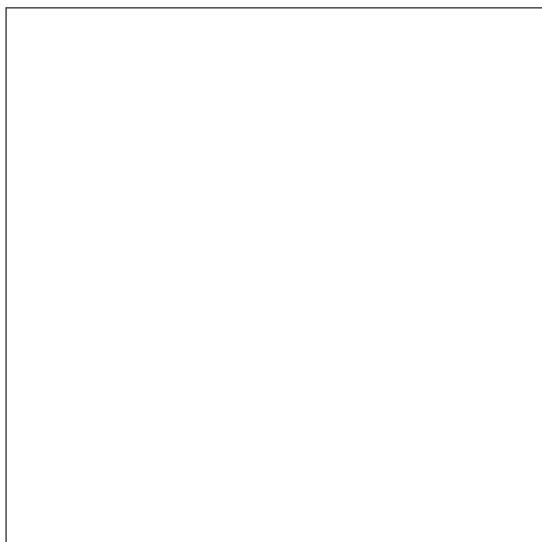
[2]



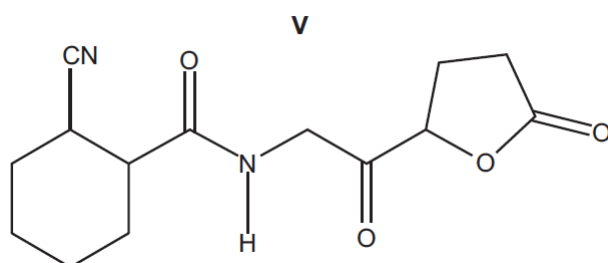
24. P, Q, R, S, T, U, and V are the seven structural isomers with molecular formula $\text{C}_5\text{H}_{10}\text{O}$ that have a carbonyl group.
- | | | |
|--|--|--|
| P $\text{CH}_3(\text{CH}_2)_3\text{CHO}$ | Q $\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CHO}$ | R $(\text{CH}_3)_2\text{CHCH}_2\text{CHO}$ |
| S $(\text{CH}_3)_3\text{CCHO}$ | T $\text{CH}_3\text{CH}_2\text{CH}_2\text{COCH}_3$ | U $\text{CH}_3\text{CH}_2\text{COCH}_2\text{CH}_3$ |
| V $(\text{CH}_3)_2\text{CHCOCH}_3$ | | |

(a) Only one of these seven compounds has stereoisomers.
 Draw three-dimensional diagrams of the two stereoisomers of this compound.

[2]



25. The structure of compound V is shown.



(i) Name all the functional groups in V.

.....

 [2]

(ii) Deduce the number of possible optical isomers for V.

..... [1]

(iii) Suggest one reason, other than better biological activity and lower dosage required, why it is beneficial to synthesise a single optical isomer of V for use as a drug.

.....

 [1]

(c) A sample of V is hydrolysed with an excess of hot aqueous alkali.

The products are isolated from the reaction mixture at pH 12.

Draw the structures of the two organic products of the complete alkaline hydrolysis of V in Fig. 8.1.

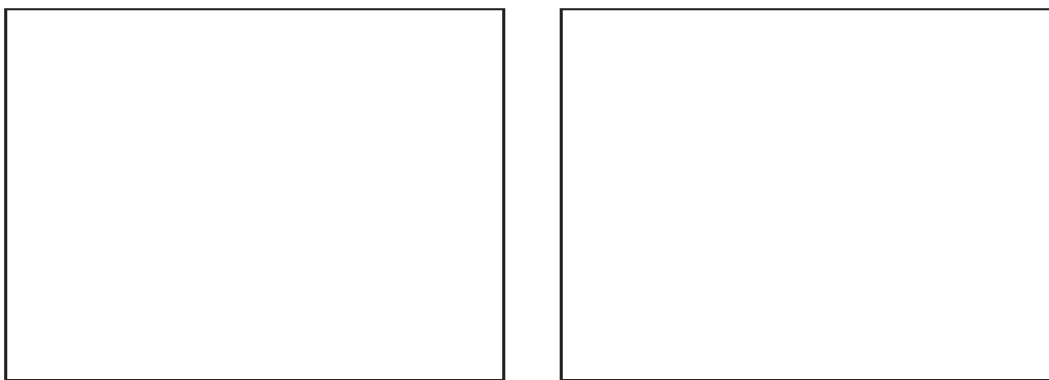


Fig. 8.1

*****This is not a complete note. It is just to guide you. It is recommended to study the prescribed textbooks along with this material. *****