6 Tartaric acid

Purpose

In this chapter you will learn the stereochemistry of chain compounds with two or more asymmetric carbon atoms. Topics that will be discussed are the number of stereoisomers, their Newman or Fischer projections and the *R*, *S* nomenclature for such compounds. Sugars will be studied in detail since they are the most important among compounds which have two or more asymmetric carbon atoms.

New terms and concepts

erythro form
threo form
meso form
D, L series of sugars
pseudoasymmety
R configuration
S configuration

Goals of this chapter

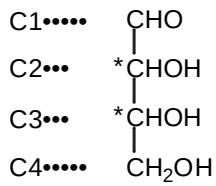
After you master this chapter successfully, you will be able to do the following:

1 to know that the number of stereoisomers for a compound with n asymmetric carbon atoms is in general 2^n, but that the value may vary depending on the symmetry of the molecule. Such a phenomenon as the *meso* form or pseudo-asymmetry is related to the number of isomers.
2 to understand that the stereoisomers of a compound with two asymmetric carbon atoms are classified into *erythro* and *threo* forms. When the molecule is symmetrical, the isomers are classified into optically active and inactive (*meso*) forms.
3 to classify a group of sugars with three to six carbon atoms into D- and L-series.
4 to assign stereochemistry (*R*, *S*) to each asymmetric carbon atom.
5 to understand the convention in writing the Fischer projections for compounds with two or more asymmetric carbon atoms, and the relation between conformation and configuration of these molecules.

6.1 Erythrose and threose

The simplest sugar glyceraldehydes is an aldotriose (with three carbon atoms), which is a very good example of compounds with one asymmetric carbon atom. An aldotetrose (with four carbon atoms) is also a good example of compounds with two asymmetric carbon atoms.

Sugars, which have one more HCOH unit in the middle of the molecule than glyceraldehydes, are aldotetroses **1**. These have two asymmetric carbon atoms C2 and C3.



1

For each asymmetric carbon atom, there are two possible configurations, *R* or *S*, regardless of the configuration of the other asymmetric carbon atom. This is valid whatever the number of

asymmetric carbon atoms.

Q6.1

How many stereoisomers are there for the aldopentose **1**? Generally speaking, how many stereoisomers are there for a compound with n asymmetric carbon atoms?□

A Fischer projection for compounds with two or more asymmetric carbon atoms is drawn in the following way.

1) Carbon atoms are arranged vertically. As previously mentioned, the most highly oxidized carbon atom occupies the top position (C1).
2) Horizontal ligands are above the plane of the paper and vertical ligands are below the plane of the paper.
3) As a matter of fact, the carbon chain does not form a straight line. So not all carbon atoms can be on the plane of the paper at the same time. When you consider the configuration of a given carbon atom, you have to suppose the carbon in question is on the plane of the paper although other carbon atoms may be out of the plane.

Q6.2

Draw all Fischer projections and corresponding flying-wedge pictures for **1**. Place the CHO group at the top of the the carbon chain.□

A 6.1

Four, and in general 2^n. **1** has two asymmetric carbon atoms and each has two possibilities. Then, all possible combinations are as follows; (*R*, *R*), (*R*, *S*), (*S*, *R*), (*S*, *S*). The labels are listed in the order C2, C3.

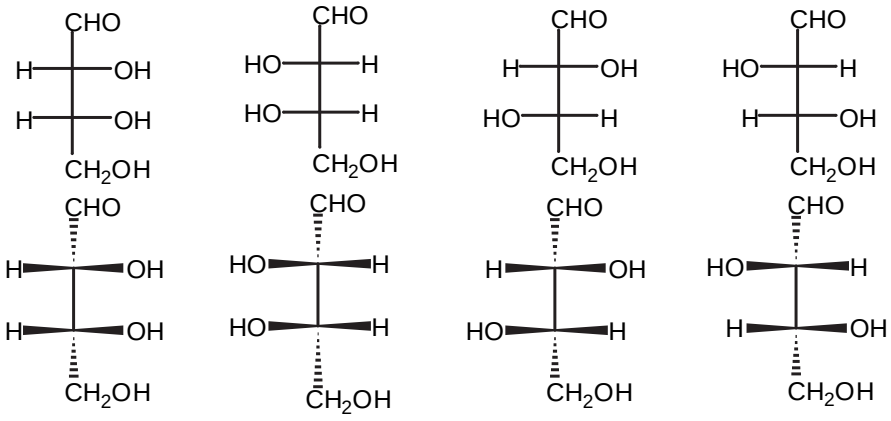
Generally, the possible number of stereoisomers is 2^n. Note that this is the maximum. Sometimes the actual number is less than that.□

The name of each stereoisomer is given. Note that two names are used to differentiate the stereochemistry of ligands. **Erythrose** has the same two ligands on the same side of the Fischer projection while **threose** has them on opposite sides. The two names are used extensively for all compounds with two asymmetric carbon atoms. Isomers having the same stereochemistry as that of erythrose is given prefix "*erythro*-", and isomers having the same stereochemistry as that of threose is given prefix "*threo*-"

Q6.3

Device a diagram that visualizes the relation (enantio or diastereo) among stereoisomers **2**~**5**.□

A6.2



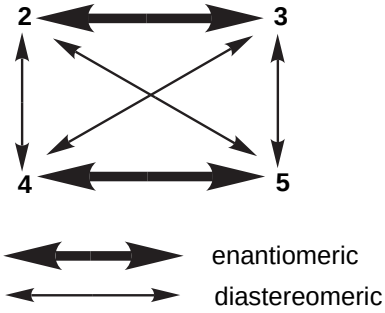
2 **3** **4** **5**

Q6.4

Determine the *R*, *S* configuration of compounds **2**~**5**.

A6.3

It is clear from the Fischer projection that **2** and **3**, and **4** and **5** form an enantiomeric pair. The rest of combinations are all diastereomeric.



or

	2	3	4	5
2		E	D	D
3	E		D	D
4	D	D		E
5	D	D	E	

E enantiomeric
D diastereomeric

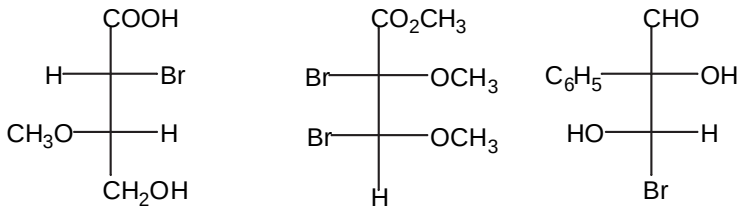
S6.1 *Erythro* form, *threo* form

for compounds with two asymmetric carbon atoms;
erythro form: the same ligands (both horizontal) at the same side of Fischer projection
threo form: the same ligands (both horizontal) at the opposite side of Fischer projection

erythro form *threo* form

Q6.5

Are these compounds *erythro* or *threo*?



6 **7** **8**

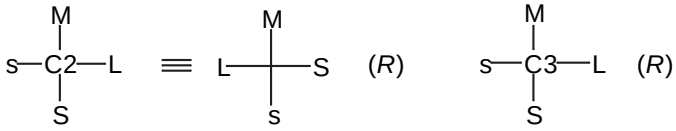
A6.4

2 (2*R*, 3*R*), **3** (2*S*, 3*S*), **4** (2*R*, 3*S*), **5** (2*S*, 3*R*). Since the aldehyde carbon is C1, the asymmetric carbon atoms in question are C2 and C3. The priority of four ligands for each C2 and C3 will be as follows. For compounds with more than two asymmetric carbon atoms, some ligands are not a single atom or a functional group, but a half of the whole molecule. There should be no problem since the rule itself is the same.

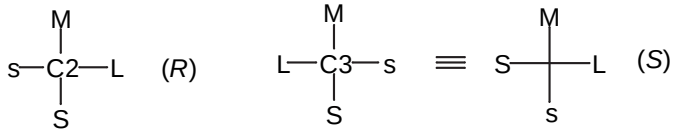
Since OH and H are L and s, the problem is the priority of two vertical ligands.

	C2			C3		
ligand	CHO		$CH(OH)CH_2OH$	CH_2OH		CH(OH)CHO
1st atom	C	=	C	C	=	C
2nd atom	OOH	>	OCH	OHH	<	OCH

For **2**,



For **4**,



3 and **4** are the enantiomers of **2** and **4**, respectively.□

Q6.6

A and B correspond to either the *erythro* or the *threo* forms of an optically active compound $C_6H_5C^*HBrC^*HBrCOOH$. Complete the table below. When you find that the given data are not sufficient to determine a certain value, mark "?" at an appropriate place.

	(+)-A	(-)-A	(±)-A	(+)-B	(-)-B	(±)-B
specific rotation (°)	68		**?**			
melting point (°C)			201			90

□

A6.5

6: *threo* form (note that hydrogens are the marker), **7**: *erythro* form, **8**: *erythro* form.□

Note that *erythro* and *threo* forms have different specific rotation.

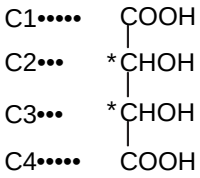
A6.6

	(+)-A	(-)-A	(±)-A	(+)-B	(-)-B	(±)-B
specific rotation (°)	68	-68	**?**	**?**	**?**	0
melting point (°C)	**?**	**?**	201	**?**	**?**	90

□

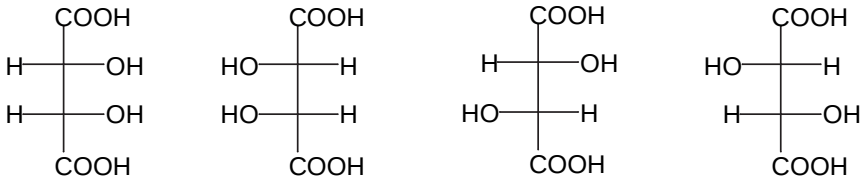
6.2 Tartaric acid; *meso* form

Tartaric acid **9** is formally the oxidized product of aldotetrose **1**. The two termini of 1, -CHO and $-CH_2OH$, are both -COOH in **9**.



9

9 has, like **1**, two asymmetric carbon atoms C2 and C3, and we prone to assume there are $2^2 = 4$ stereoisomers. To confirm whether this prediction is correct, you will draw stereoisomers **10**~**13** by analogy with **2**~**5**.



10 **11** **12** **13**

There is some difference between the stereochemistry of tartaric acid **9** and that of aldotetrose **1** in that **9** has an identical set of ligands (OH, COOH, half of the molecule, H) at C2 and C3. Will this affect the stereochemistry of **9**?

Q6.7

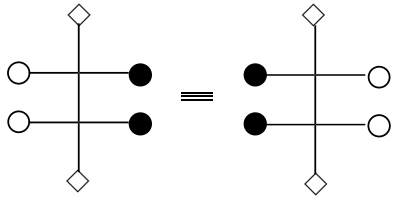
Determine the configuration of C2 and C3 of **10** and **11** in terms of the *R*, *S* nomenclature.□

Though **10** and **11** seem to have different stereochemistry, you will find by careful examination of a molecular model that in fact **10** and **11** are the same molecule.

Another important point is that there is a center of symmetry in the center of **10** (and **11**). This means that the upper half and the lower half of the molecule are identical. Hence **10** and **11** are "intramolecular" racemic compounds and optically inactive. Optically inactive compounds with asymmetric carbon atom(s) are called the ***meso* form**.

S6.2 *Meso* form

optically inactive stereoisomer because of the presence of symmetry in the molecule. *Meso* forms have the following Fischer projection.



This means that tartaric acid has only three stereoisomer, **12** and **13**, the enantiomeric pair, and the optically inactive (*meso*) **10** (= **11**). You must remember that the number of stereoisomers will be less than 2^n when there is symmetry in the molecule.

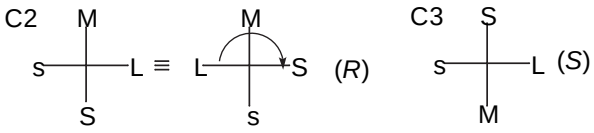
(+)-Tartaric acid is widely distributed in nature, particularly in fruits as an acid, and in calcium or magnesium salts. Since tartaric acid is obtained as a by-product in wine production, it has been known from olden times. Hence it is quite understandable that considerable development of organic stereochemistry was made by Pasteur's study on tartaric acid. When Pasteur initiated his study, (+)-tartaric acid and racemic acid (in modern terminology, (±)-tartaric acid: the word racemate came from the name of this compound) were known, but the stereochemical relation between the two compounds was not known at that time. Pasteur could successfully resolve (±)-tartaric acid by physical methods (in fact with his own hands, a magnifier and a tweezers), establishing the relation among stereoisomers.

Q6.8

Show the relation among stereoisomers of tartaric acid **10**~**13** (*cf.* Q6.3).□

A6.7

The priority of ligands are; OH > COOH > CH(OH)COOH > H. The configurations are;
10: (2*R*, 3*S*), **11**: (2*S*, 3*R*), **12**: (2*R*, 3*R*), **13**: (2*S*, 3*S*).
As an example the configuration of C2 and C3 for **10** is shown.

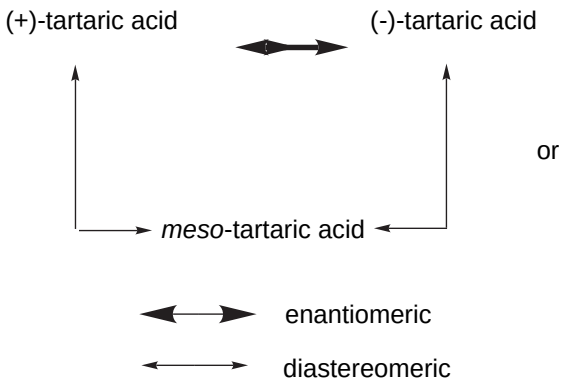


Q6.9

Complete the Table below. When you find that the given data are not sufficient to determine the required value, mark "?" at an appropriate place.

	(+)-tartaric acid	(-)-tartaric acid	(±)-tartaric acid	*meso*-tartaric acid
specific rotation (°)	+12			
melting point (°C)	170		206	140
solubility (g/100g)		139		125

A6.8



or

	10	11	12	13
10		I	D	D
11	I		D	D
12	D	D		E
13	D	D	E	

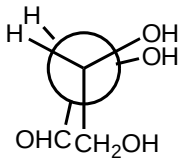
E: enantiomeric
D diastereomeric
I: identcal

A6.9

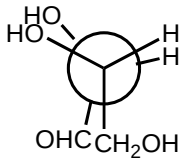
	(+)-tartaric acid	(-)-tartaric acid	(±)-tartaric acid	*meso*-tartaric acid
specific rotation (°)	+12	-12	0	0
melting point (°C)	170	170	206	140
solubility (g/100g)	139	139	**?**	125

6.3 Configuration and conformation

Try to convert the Fischer projection of (-)-erythrose **2** and (+)-erythrose **3** into corresponding Newman projections. If we strictly copy the Fischer projections, the Newman projections **14** and **15** obtained are necessarily in the eclipsed conformation. Molecules are not likely in the eclipsed form, but exist in the more stable staggered conformation. You have to change **14** and **15** into staggered conformations. It must be noted, however, that more than one staggered conformation is possible.



14



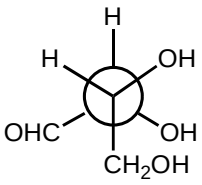
15

Q6.10

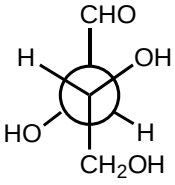
Draw all possible staggered conformers of **14**.□

There may be several factors that determine the most favorable conformation of the molecule. One is certainly the steric repulsion between ligands. It is likely that the molecule will be most stable when the largest ligand bonded to C2 and the largest ligand bonded to C3 are antiperiplanar (*trans*). It is possible that an attractive interaction might occur between the two ligands regardless of their sizes. For the sake of simplicity, this possibility will not be considered here.

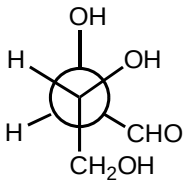
A6.10



16



17



18

□

Q6.11

Of **16**~**18**, which conformer do you think is the most stable?□

Q6.12

Draw the Newman projection of the most stable conformer of (+)-, (-)- and *meso*-tartaric acid.□

A6.11

17. It is difficult to decide the order for the sizes of ligand unequivocally. You can say, however, that in **16** and **18** the larger ligands CHO and CH_2OH are gauche rather than antiperiplanar.□

It was assumed that the two carboxy groups would be antiperiplanar in the most stable conformation. It is interesting to note that the two hydroxy groups of **10** are antiperiplanar though these seem to be on the same side in the Fischer projection.

S6.3 Configuration and conformation

The Fischer projections of compounds with more than two asymmetric carbon atoms do not necessarily represent the most stable conformation.

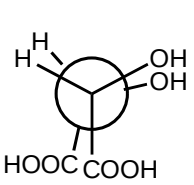
In fact the molecules are considered to assume a staggered conformation in which the repulsion among the ligands is minimal.

Note that the rotation about the single bond does not affect the configuration at all.

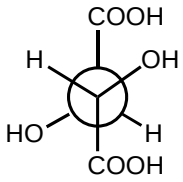
Q6.13

Suppose the barrier for rotation about a single bond is very high, and butane will keep one of its three staggered confirmations without rotation. Explain the stereochemical relation among the three conformers.□

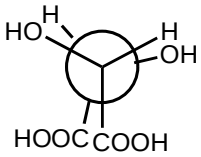
A6.12



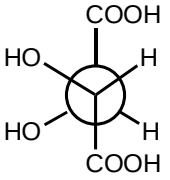
10



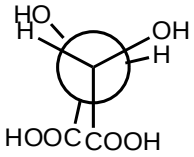
19



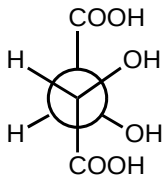
12



20



13



21

□

A6.13

The two gauche forms (Ch. 2, **6** and **19**) are a pair of enantiomers. If the rotation about the single bond is restricted, optical activity will arise. *Gauche* and *anti* forms are diastereomers.□

6.4 Compounds with three or more asymmetric carbon atoms

What we have learned about aldotetrose and tartaric acid can be extended to compounds with five carbon atoms (three asymmetric carbon atoms) or to even more complex compounds. When the given compounds have three asymmetric carbon atoms, each asymmetric carbon atom can be either *R* or *S* configuration, and the number of isomers is $2^3 = 8$ as a maximum. If the molecule has symmetry, this number will be reduced as is the case with tartaric acid.

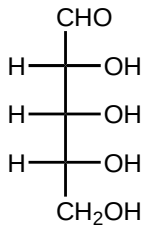
Q6.14

Draw Fischer projections of all possible configurations of aldopentose OHCC*H(OH)C*H(OH) C*H(OH)CH_2OH. If you find enantiomeric pairs, draw these side by side. □

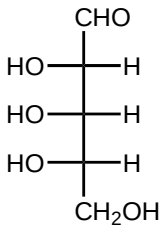
Q6.15

Determine the configuration (*R* or *S*) of all asymmetric carbon atoms of **22**~**29**.□

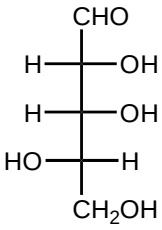
A6.14


(-)-ribose

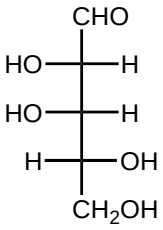
22


(+)-ribose

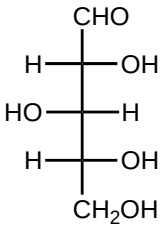
23


(+)-lyxose

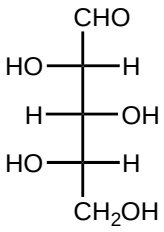
24


(-)-lyxose

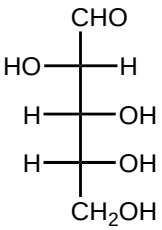
25


(+)-xylose

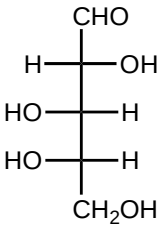
26


(-)-xylose

27


(-)-arabinose

28


(+)-arabinose

29

For reference, names are provided.

The priority is common to all compounds.

C2: OH > CHO > CH(OH)CH(OH)CH_2OH > H. C3: OH > CH(OH)CHO > CH(OH)CH_2OH > H.

C4: OH > CH(OH)CH(OH)CHO > CH_2OH > H□

A6.15

	22	**23**	**24**	**25**	**26**	**27**	**28**	**29**
C2	*R*	*S*	*R*	*S*	*R*	*S*	*S*	*R*
C3	*R*	*S*	*R*	*S*	*S*	*R*	*R*	*S*
C4	*R*	*S*	*S*	*R*	*R*	*S*	*R*	*S*

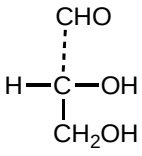
6.5 D, L nomenclature of sugars

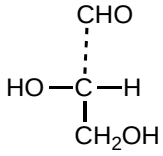
Sugars are generally classified into two families, D- and L-series. If the configuration of the asymmetric carbon atom farthest from the carbonyl carbon atom is similar to that of D-glyceraldehyde, the compound will belong to the D-series. If similar to that of the L-series, the compound will belong to the L-series. This method was successfully employed when the sugar chemistry was being developed and the absolute configuration was not yet determined.

S6.4 D, L-nomenclature (sugar)

D-series: the configuration of the asymmetric carbon atom furthest from the carbonyl carbon is identical with D-glyceraldehyde.

L-series: the configuration of the asymmetric carbon atom furthest from the carbonyl carbon is identical with L-glyceraldehyde


D-series


L-series

Q6.16

Classify eight stereoisomers of aldopentose **22**~**29** into D- and L-series.□

Q6.17

How many stereoisomers are there for trihydroxyglutaric acid HOOCCH(OH)CH(OH)CH(OH)COOH? Let us consider the problem step by step.

1) Two asymmetric carbon atoms C2 and C4 can be treated as was done with C2 and C3 of tartaric acid. How many stereoisomers are possible for C2 and C4?
2) Is C3 asymmetric or not?
3) Taking all these facts into consideration, predict the number of stereoisomers of trihydroxyglutaric acid.□

A6.16

D-series; **22**, **25**, **26**, **28**
L-series; **23**, **24**, **27**, **29**□

S6.5 Pseudoasymmetry

A carbon atom, which has two chiral ligands and two ligands with the same structure but different configuration, is called pseudo-asymmetry. As for the priority of the latter two ligands, the one with *R* configuration has higher priority.

Q6.18

Draw the Fischer projections of the stereoisomers of trihydroxyglutaric acid **30**~**33** with reference to the table in A6.17, and decide if it is optically active or *meso* for each isomer.□

A6.17

1) Since the same consideration is applicable given that C2 and C4 have the same sets of ligands, there are three isomers, (2*R*, 4*R*), (2*S*, 4*S*) and (2*R*, 4*S* = 3*S*, 4*R*; meso).
2) C3 has the following ligands; OH, C*H(OH)COOH, C*H(OH)COOH, H. The point is that two ligands out of four have an asymmetric center. If two CH(OH)COOH are both *R* or *S*, these two are identical and cannot be optically active. If one is *R* and the other *S*, the central atom (C3) of trihydroxyglutaric acid is now asymmetric. According to the sequence rule, the ligand with *R* configuration has higher priority than the one with *S* configuration.
3) When the configurations of C2 and C4 are (2*R*, 4*R*) and (2*S*, 4*S*), you need not worry about the configuration of C3 because it is not an asymmetric carbon atom. When the configurations of C2 and C4 are (2*R*, 4*S* = 3*S*, 4*R*; meso), you must decide whether C3 is *R* or *S*. The asymmetry of C3 type is called **pseudo-asymmetry**, and marked as *r* or *s* (small letter). To summarize;

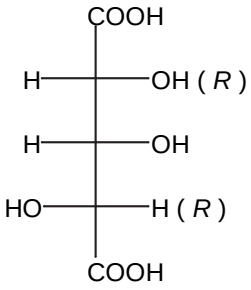
	C2	C3	C4
30	*R*	—	*R*
31	*S*	—	*S*
32	*R*	*r*	*S*
33	*R*	*s*	*S*

□

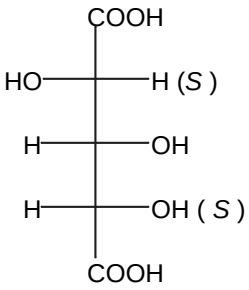
Q6.19

Show the stereochemical relation of **30**~**33** by such a diagram as that in A6.3 and A6.8.□

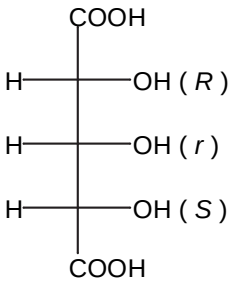
A6.18



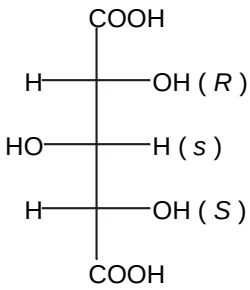
30 active



31 active



32 *meso*



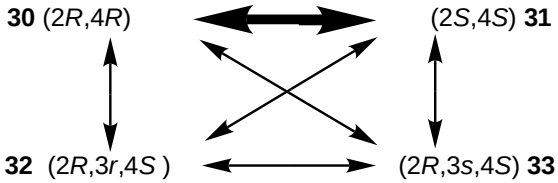
33 *meso*

Since C3 of **30** and **31** is not an asymmetric carbon atom, you may write the C3 part as HO-C3-H instead of writing it as H-C3-OH.□

Q6.20

Draw the Fischer projections of all possible stereoisomers of aldohexose OHCC*H(OH)C*H(OH)C*H(OH)C*H(OH)CH_2OH. Firstly draw all stereoisomers belonging to the D-series, and then draw the L-series.□

A6.19

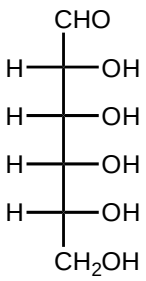


□

Q6.21

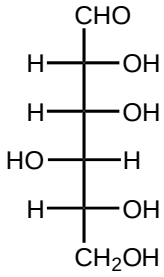
Find the number of stereoisomers of HOOCC*H(OH)C*H(OH)C*H(OH)C*H(OH)COOH, glucaric acid.□

A6.20



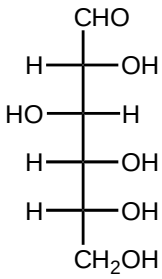
(+)-allose

34



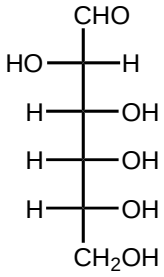
(-)-gulose

35



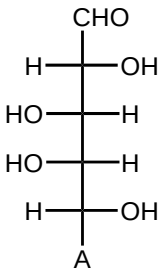
(+)-glucose

36



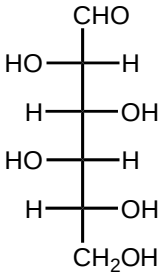
(+)-altrose

37



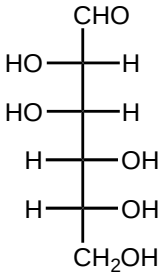
((+)-galactose

38



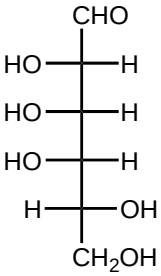
(-)-idose

39



(+)-mannose

40



(+)-talose

41

In fact the L-series can be obtained simply by exchanging the positions of H and OH each bonded to the same carbon atom.□

Q6.22

Draw the Fischer projection of the stereoisomers of glucaric acid.□

A6.21

First of all, all possibilities will be listed up. The maximum number is $2^4 = 16$. You have to examine the possibility of meso forms and pseudo-asymmetry. The compounds **46**, **47**, **54** and **55** are meso form. Each pair of **44** and **45**, **52** and **53**, **49** and **51**, **43** and **57** is identical. Thus, the number of stereoisomers is 10.

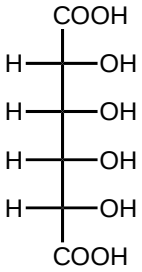
	C2	C3	C4	C5
42	*R*	*R*	*R*	*R*
43	*R*	*R*	*R*	*S*
44	*R*	*R*	*S*	*S*
45	*R*	*S*	*S*	*S*
46	*R*	*R*	*S*	*S*
47	*R*	*S*	*R*	*S*
48	*R*	*S*	*S*	*R*
49	*R*	*S*	*S*	*S*

	C2	C3	C4	C5
50	*S*	*S*	*S*	*S*
51	*S*	*S*	*S*	*R*
52	*S*	*S*	*R*	*S*
53	*S*	*R*	*S*	*S*
54	*S*	*S*	*R*	*R*
55	*S*	*R*	*S*	*R*
56	*S*	*R*	*R*	*S*
57	*S*	*R*	*R*	*R*

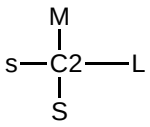
□

A6.22

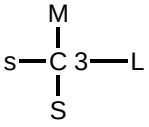
As an example the configuration of the isomer given below will be determined.



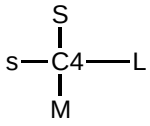
Priority; C2, C5: OH > COOH > CH(OH)R > H. C3, C4: OH > CH(OH)COOH > CH(OH)R > H.



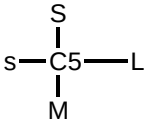
R-configuration



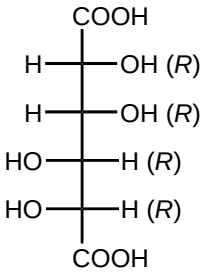
R-configuration



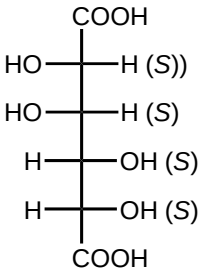
S-configuration



S-configuration



42



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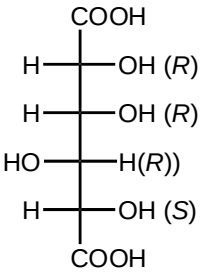

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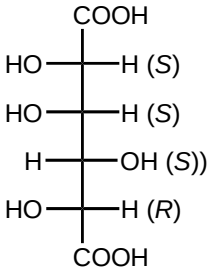

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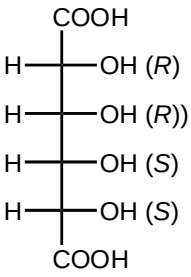
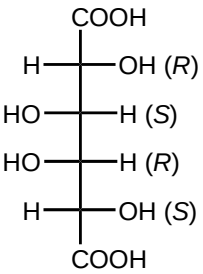


46



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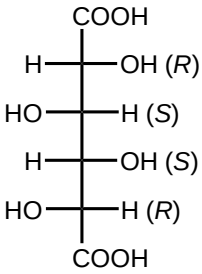

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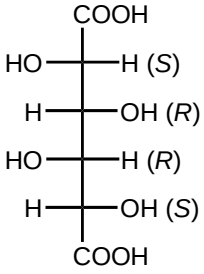

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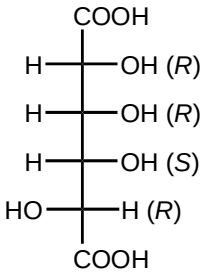

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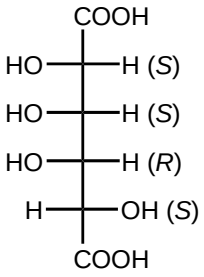

52

enantiomeric pairs: **42** and **50**, **43** and **51**, **48** and **56**, **44** and **52**.

meso form: **46** and **47**