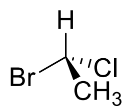
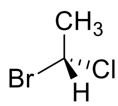
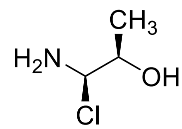
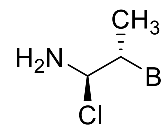
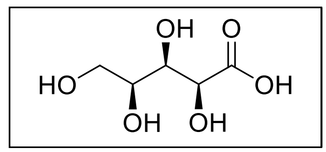
1. What is the difference between constitutional isomers and stereoisomers?

2. Both enantiomers and diastereomers are stereoisomers. a) How do they differ? b) Comment on their physical properties.

3. For each of the following chiral molecules, a) assign *R* and *S* configuration for all chiral centres. b) Convert the structure to a Fischer projection.

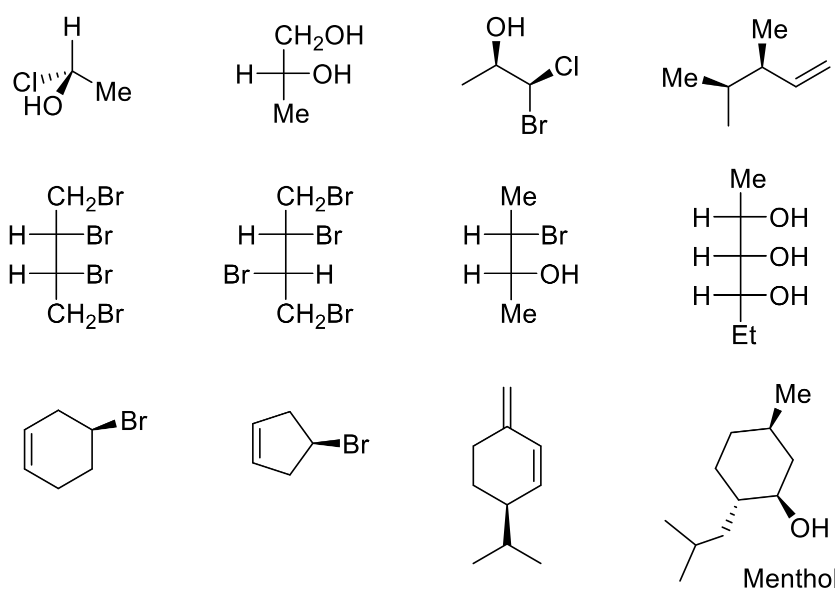
(a)  (b)  (c)  (d) 

4. Convert the following molecule into a Fischer projection, placing the $–CO_2H$ group at the top.



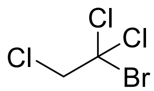
5. For each structure below,

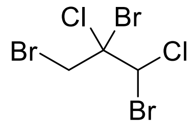
a) Indicate how many chiral centre(s) is (or are) present by putting * next to it (or them).
b) Determine the chiral configuration (*R* or *S*) at each chiral centre.
c) Determine if the molecule has any internal plane of symmetry. Indicate if the molecule is meso compound or not.
d) Determine if the molecule is chiral or achiral.

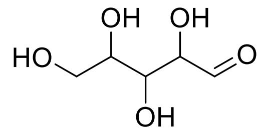


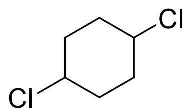
Menthol

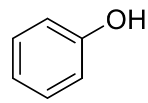
6. For each of the following molecule, a) indicate if the molecule is chiral or achiral. b) Use asterisks (*) to show all chiral centres. c) Identify the meso compounds.

(a) 

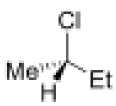
(b) 

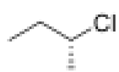
(c) 

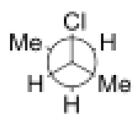
(d) 

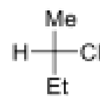
(e) 

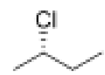
7. Determine whether each of the following structure is the representation of (*R*)-2-chlorobutane or (*S*)-2-chlorobutane.

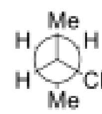




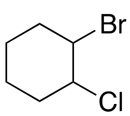


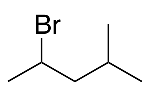


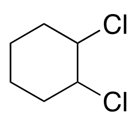


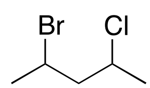


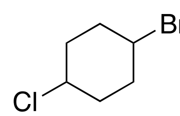
8. Draw all possible stereoisomers for each of the following compounds and complete the names of each stereoisomer by including *R* and *S* configurations along with the carbon number in parenthesis. *(Note that the indication of carbon number is not necessary when the molecule contains one chiral centre.)*

a) 

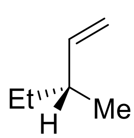
b) 

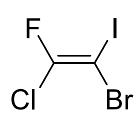
c) 

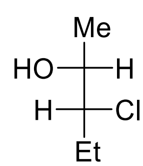
d) 

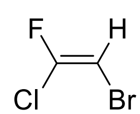
e) 

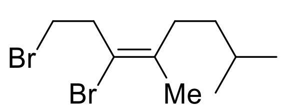
9. Which of the following compounds are chiral or achiral? For molecules that are chiral, provide the name including *R* and *S* designations. For molecules that contain carbon-carbon double bond, indicate whether stereochemistry around the double bond has *trans*- *(E)* or *cis*- *(Z)* configuration.

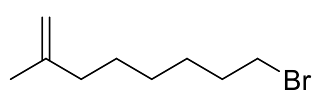


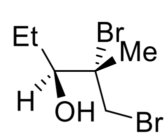


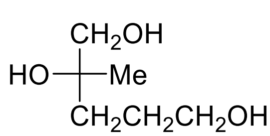


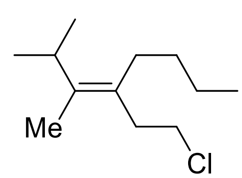




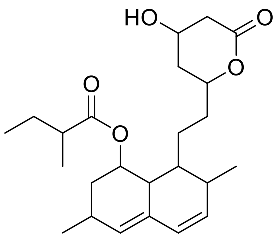


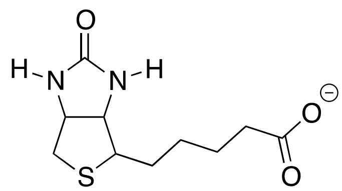


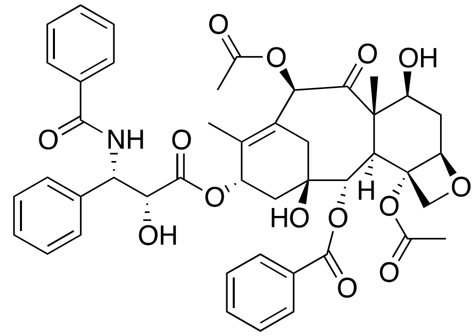




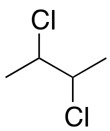
10. Determine the number of chiral centres in each of the following molecules.

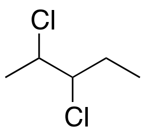
a) 

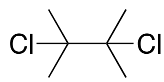
b) 

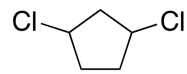
c) 

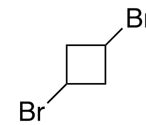
11. For each of the following compounds, draw all possible stereoisomers in 3D bond-line and Fischer projection. Which compound(s) has (or have) an achiral stereoisomer?

a) 

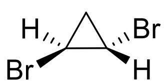
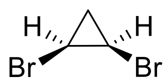
b) 

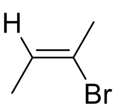
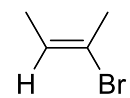
c) 

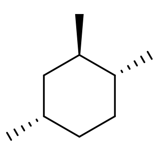
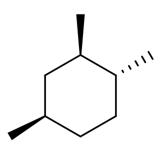
d) 

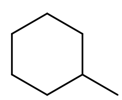
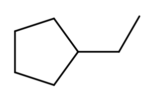
e) 

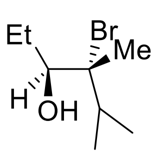
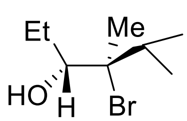
12. Indicate whether each of the following pairs of compounds are related as identical compounds, enantiomers, diastereomers, or constitutional isomers:

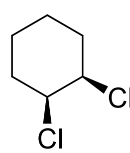
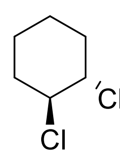
 and 

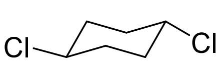
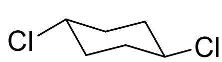
 and 

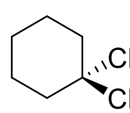
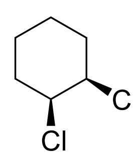
 and 

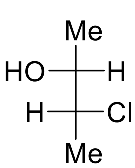
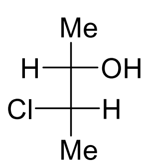
 and 

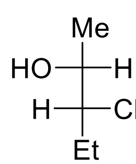
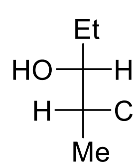
 and 

 and 

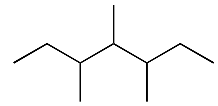
 and 

 and 

 and 

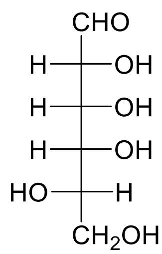
 and 

13. Draw two chiral stereoisomers of 3,4,5-trimethylheptane, whose structure is provided, in 3D bond-line and Fischer Projection.

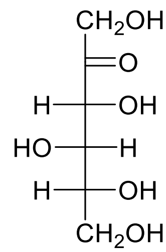


14. a) Assign *R* and *S* configuration at each chiral centre for the molecules given below. b) Draw a Fischer projection formula for its enantiomer.

(a)

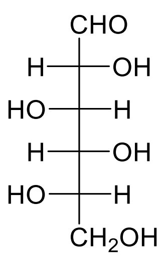


(b)



15. Characterize the members of each of the following pairs of structures as either same molecules, enantiomers or diastereomers.

(a)



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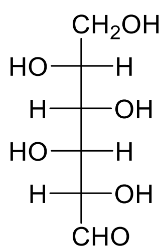

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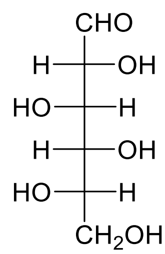

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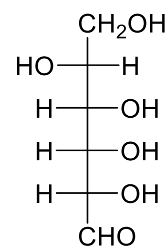
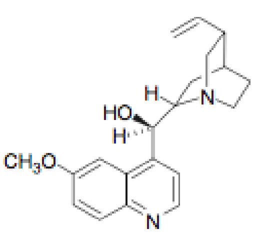


16. (S)-Lactic acid has a specific rotation of +3.8°. (a) If the ee of a solution of lactic acid is 60%, what is [α] for this solution? (b) How much of the dextrorotatory and levorotatory isomers does the solution contain?

17. The [α] of a pure quinine, an antimalarial drug, is -165°.



quinine
(antimalarial drug)

a. Calculate the *ee* of a solution with the following [α] values: –50, –83, and –120.
b. For each *ee*, calculate the percent of each enantiomer present.
c. What is [α] for the enantiomer of quinine?
d. If a solution contains 80% quinine and 20% of its enantiomer, what is the *ee* of the solution?
e. What is [α] for the solution described in part (d)?

Solutions

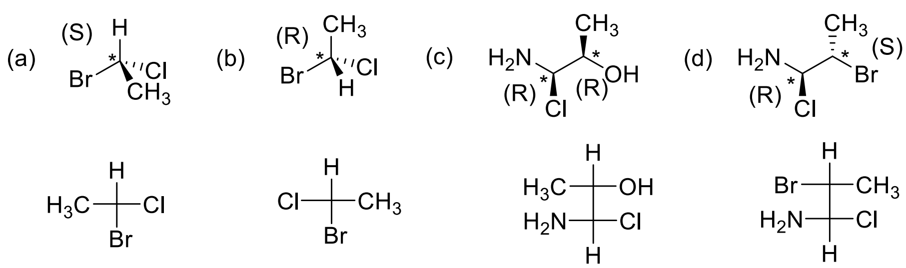
1. **Constitutional Isomers** – Compounds that have the same molecular formula but have different structures due to different bond connectivity. Ex.) For molecular formula C_2H_6O, CH_3-O-CH_3 (dimethyl ether) and CH_3CH_2OH (Ethanol)

   Stereoisomers – Compounds with the same molecular formula as well as the same bond connectivity (therefore the same structure). Only difference is in their 3-D spatial bond arrangements.

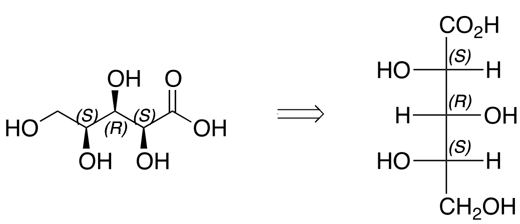
2. a) Enantiomers are the stereoisomers that are mirror-images and non-superimposable. (i.e. *R/S* configurations of one enantiomer are exactly opposite of the other enantiomer at each chiral centre). Any stereoisomers that do not satisfy the criteria of being enantiomers are diastereomers. Diastereomers have *R/S* configurations that are identical at one or more chiral centres.

   b) Physical properties of enantiomers are identical; whereas, diastereomers have different physical properties. Hence, diastereomers can be separated from one another by physical separation methods such as distillation or melting point (recrystallization). Speaking of m.p as an example, enantiomers have identical m.p.; whereas, two diastereomers have different m.p

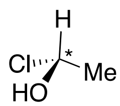
3.



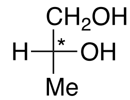
4.



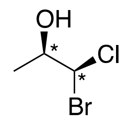
5.



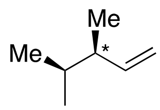
(R)-1-chloroethanol
No plane of symmetry
The molecule is chiral



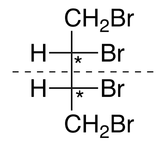
(*R*)-propane-1,2-diol
No plane of symmetry
The molecule is chiral



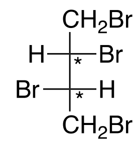
(1*S*,2*R*)-1-bromo-1-chloropropan-2-ol
No plane of symmetry
The molecule is chiral



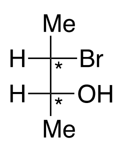
(*R*)-3,4-dimethylpent-1-ene
No plane of symmetry
The molecule is chiral



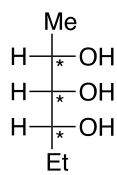
(2*R*,3*S*)-1,2,3,4-tetrabromobutane
Plane of symmetry exists
The molecule is meso compound
The molecule is achiral



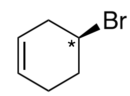
(2*S*,3*S*)-1,2,3,4-tetrabromobutane
No plane of symmetry
The molecule is chiral



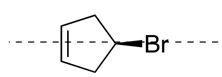
(2*R*,3*S*)-3-bromobutan-2-ol
No plane of symmetry
The molecule is chiral



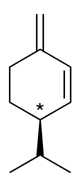
(2*S*,3*S*,4*R*)-hexane-2,3,4-triol
No plane of symmetry
The molecule is chiral



(*S*)-4-bromocyclohex-1-ene
No plane of symmetry
The molecule is chiral

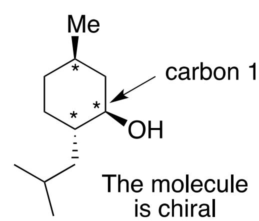


4-bromocyclopent-1-ene
Plane of symmetry exists
No chiral centres present
The molecule is achiral



No plane of symmetry
The molecule is chiral

(*R*)-3-isopropyl-6-methylenecyclohex-1-ene

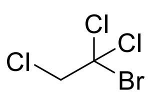


The molecule is chiral

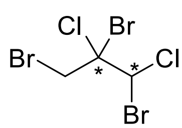
(1*R*,2*S*,5*R*)-2-isobutyl-5-methylcyclohexanol
No plane of symmetry

6.

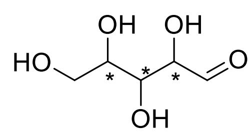
(a)



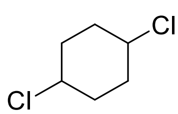
(b)



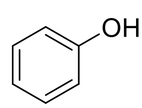
(c)



(d)

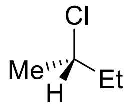


(e)

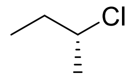


(a) No chiral centres present; therefore, achiral molecule.
(b) Chiral molecule, and there are TWO chiral centres.
(c) Chiral molecule, and there are THREE chiral centres.
(d) No chiral centres present, therefore, achiral molecule
(e) Achiral molecule. All of carbons in benzene ring are sp^2-hybridized, and they cannot be chiral centres.

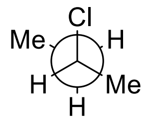
7.



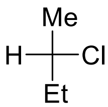
(*S*)-2-chlorobutane



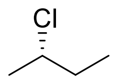
(*R*)-2-chlorobutane



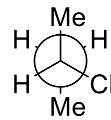
(*R*)-2-chlorobutane



(*S*)-2-chlorobutane

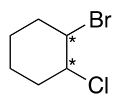


(*S*)-2-chlorobutane



(*S*)-2-chlorobutane

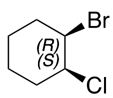
8.



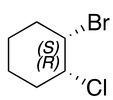
2 chiral centres ⟹ The total of four stereoisomers

Stereoisomer 1 has R and R
Stereoisomer 2 has R and S
Stereoisomer 3 has S and R
Stereoisomer 4 has S and S

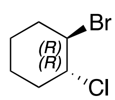
a)



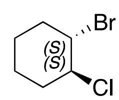
(1*R*,2*S*)-1-bromo-2-chlorocyclohexane



(1*S*,2*R*)-1-bromo-2-chlorocyclohexane

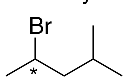


(1*R*,2*R*)-1-bromo-2-chlorocyclohexane



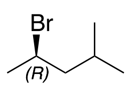
(1*S*,2*S*)-1-bromo-2-chlorocyclohexane

None of the stereoisomers have the plane of symmetry

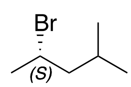


1 chiral centre ⟹ The total of two stereoisomers

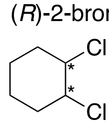
b)



(*R*)-2-bromo-4-methylpentane



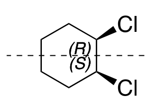
(*S*)-2-bromo-4-methylpentane



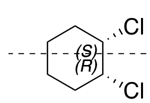
2 chiral centres ⟹ The total of four stereoisomers

Stereoisomer 1 has R and R
Stereoisomer 2 has R and S
Stereoisomer 3 has S and R
Stereoisomer 4 has S and S

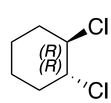
c)



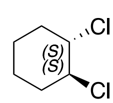
(1*R*,2*S*)-1,2-dichlorocyclohexane



(1*R*,2*S*)-1,2-dichlorocyclohexane



(1*R*,2*R*)-1,2-dichlorocyclohexan e



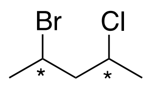
(1*S*,2*S*)-1,2-dichlorocyclohexane

None of the stereoisomers have the plane of symmetry

There is a plane of symmetry; hence, meso compound

Identcal stereoisomer

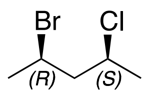
***** There are the total of three stereoisomers for 1,2-dichlorocyclohexane**



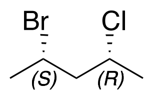
2 chiral centres ⟹ The total of four stereoisomers

None of the stereoisomers have the plane of symmetry

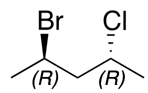
d)



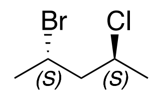
(2*R*,4*S*)-2-bromo-4-chloropentane



(2*S*,4*R*)-2-bromo-4-chloropentane



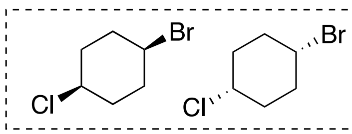
(2*R*,4*R*)-2-bromo-4-chloropentane



(2*S*,4*S*)-2-bromo-4-chloropentane

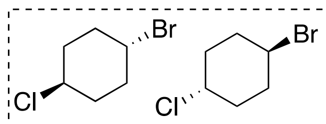
2 stereoismers

e)



Identical

Cis-1-bromo-4-chlorocyclohexane

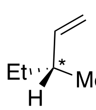


Identical

Trans-1-bromo-4-chlorocyclohexane

None of stereoisomers are chiral because there are no chiral centres present

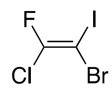
9.



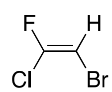
chiral

(*R*)-3-methylpent-1-ene

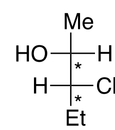
* cannot assign E/Z on the double bond



achiral (no chiral centre present)
E (trans) configuration

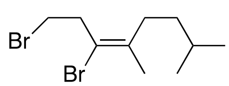


achiral (no chiral centre present)
Z (cis) configuration

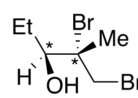


chiral

(2*R*,3*R*)-3-chloropentan-2-ol

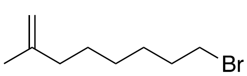


achiral (no chiral centre present)
E (trans) configuration



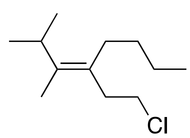
chiral

(2*S*,3*S*)-1,2-dibromo-2-methylpentan-3-ol

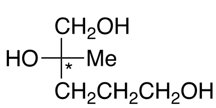


achiral (no chiral centre present)

* cannot assign E/Z on the double bond



achiral (no chiral centre present)
E (trans) configuration

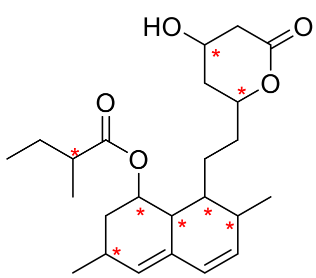


chiral

(*S*)-2-methylpentane-1,2,5-triol

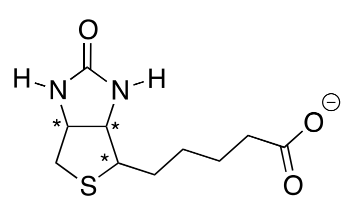
10.

a)



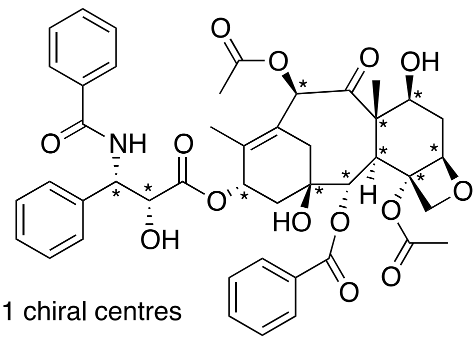
There are 8 chiral centres!

b)



Three Chiral Centres

c)

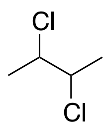


11 chiral centres

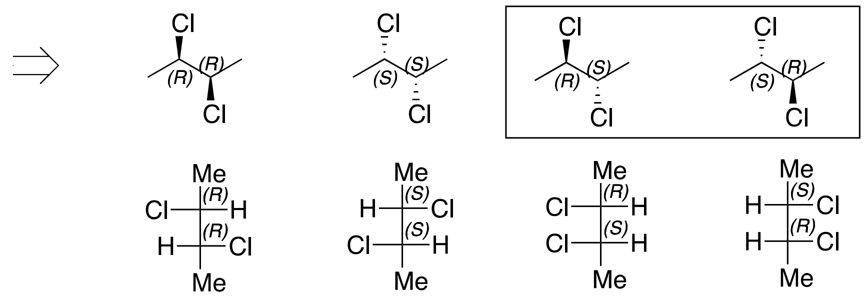
11. **Cyclic compounds do not need to be re-drawn** in Fischer projection.
Note* : Me = $-CH_3$ and Et = $-CH_2CH_3$

Same compound due to the presence of
Plane of symmetry
Meso compounds
Achiral stereoisomer

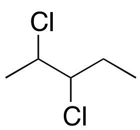
a)



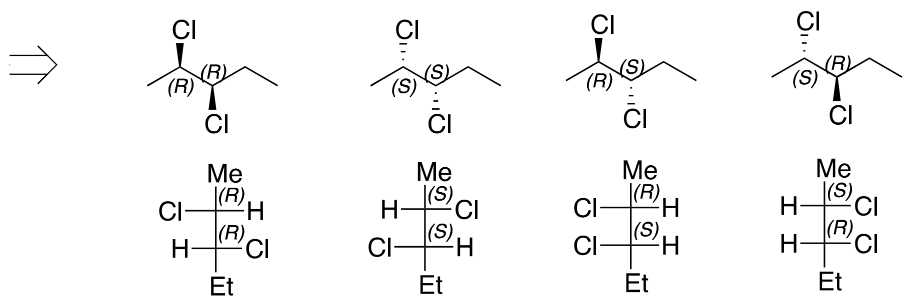
2,3-dichlorobutane
3 stereoisomers



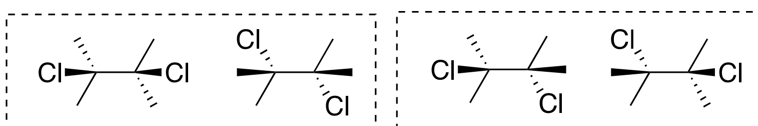
b)



2,3-dichloropentane
4 stereoisomers



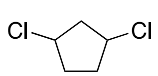
c)



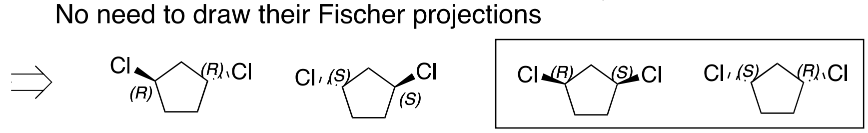
Identical Identical

None of the stereoisomers have chiral centres;
No need to draw their Fischer projections

d)



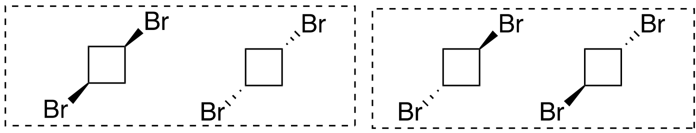
1,3-dichlorocyclopentane
3 stereoisomers



Same compound due to the presence of
Plane of symmetry
Meso compounds
Achiral stereoisomer

No need to draw ring compounds in Fischer projections

2 stereoisomers

e) 

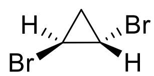
Identical
Cis-1,3-dibromocyclobutane

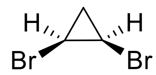
Identical
trans-1,3-dibromocyclobutane

None of stereoisomers are chiral because there are no chiral centres present

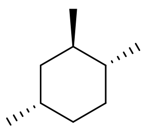
Answers continue on the following page.

12.



and


Diastereomers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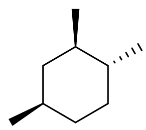
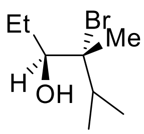
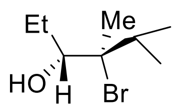
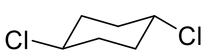

Diastereomers



and


Diastereomers



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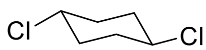
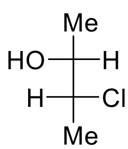


Identical



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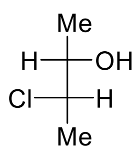
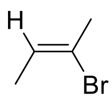


Enantiomers



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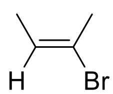
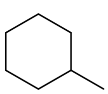


Diastereomers

E/Z Isomers are always diastereomers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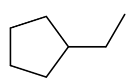
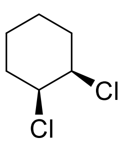

Constitutional Isomers



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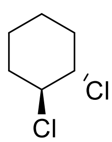
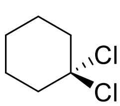


Diastereomers



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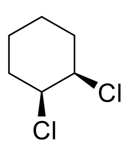
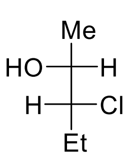


Constitutional Isomers



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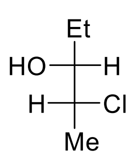
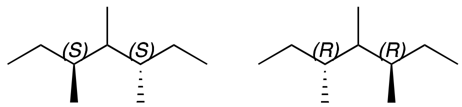


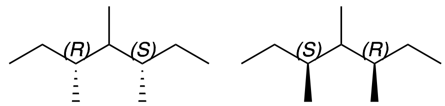
Constitutional Isomers

13. 2 chiral stereoisomers

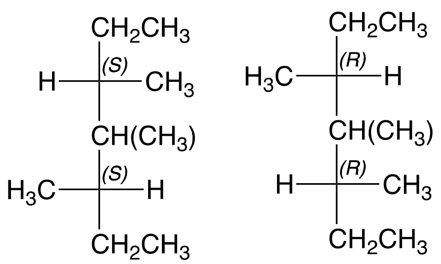


(3*S*,5*S*)-3,4,5-trimethylheptane (3*R*,5*R*)-3,4,5-trimethylheptane

These are related as enantiomers

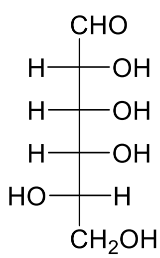


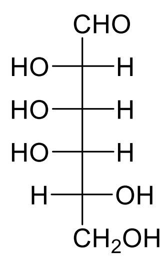
Achiral stereoisomers
(plane of symmetry found)



14.

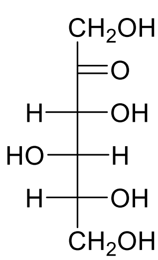
aldose

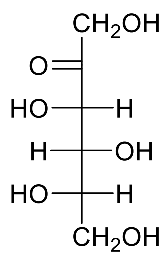
(a) 

has an enantiomer 

C-1	Not a chiral centre
C-2	R
C-3	R
C-4	R
C-5	S
C-6	Not a chiral centre

ketose

(b) 

has an enantiomer 

C-1	Not a chiral centre
C-2	Not a chiral centre
C-3	R
C-4	S
C-5	R
C-6	Not a chiral centre

15. (a) Two Fischer projection formula are enantiomers to each other (rotate the second Fischer projection by 180° to place the carbonyl carbon to the top)
(b) Two Fischer projection formula are diastereomers to each other. C-3 have the opposite configuration.

16.

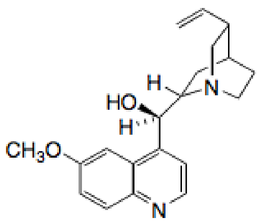
a. $\frac{[\alpha]\text{ mixture}}{+3.8} \times 100\% = 60\%\ ee$

$[\alpha]$ mixture = +2.3

b. % one enantiomer – % other enantiomer = *ee*
80% – 20% = 60% *ee*

80% dextrorotatory (+) enantiomer
20% levorotatory (–) enantiomer

17.



quinine

$$ee = \frac{[\alpha]\ \text{mixture}}{[\alpha]\ \text{pure enantiomer}} \times 100\%$$

quinine = **A**
quinine's enantiomer = **B**

a.

$$\frac{-50}{-165} \times 100\% = 30\%\ ee$$

$$\frac{-83}{-165} \times 100\% = 50\%\ ee$$

$$\frac{-120}{-165} \times 100\% = 73\%\ ee$$

b. 30% *ee* = 30% excess one compound (**A**)
remaining 70% = mixture of 2 compounds (35% each **A** and **B**)
Amount of **A** = 30 + 35 = **65%**
Amount of **B** = **35%**

50% *ee* = 50% excess one compound (**A**)
remaining 50% = mixture of 2 compounds (25% each **A** and **B**)
Amount of **A** = 50 + 25 = **75%**
Amount of **B** = **25%**

73% *ee* = 73% excess of one compound (**A**)
remaining 27% = mixture of 2 compounds (13.5% each **A** and **B**)
Amount of **A** = 73 + 13.5 = **86.5%**
Amount of **B** = **13.5%**

c. [ ] = +165
d. 80% – 20% = 60% *ee*

e. $$60\% = \frac{[\ ]\ \text{mixture}}{-165} \times 100\%$$

[ ] mixture = –99