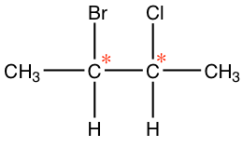
# 5.6: Compounds with More Than One Chirality Centers

## 5.6.1 Diastereomers

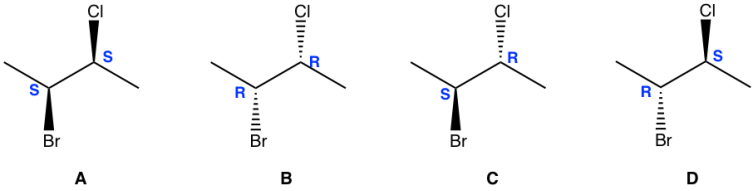
It is very common that there are more than one chirality centers in an organic compound. For the example of 2-bromo-3-chlorobutane below, there are 2 chirality centers, C2 and C3. With each chirality center has two possible configurations, **R** and **S**, the total number of possible stereoisomers for this compound is four, with configurations on C2 and C3 as **RR**, **SS**, **RS** and **SR** respectively.



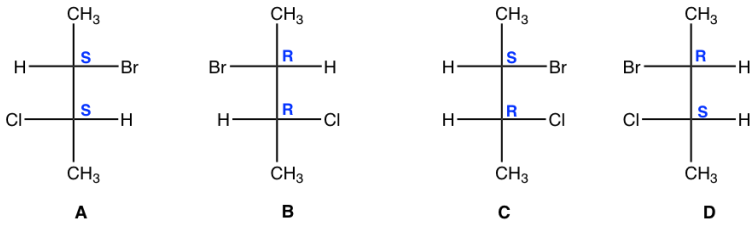

**2-bromo-3-chlorobutane**

As a general rule, for a compound has *n* chirality centers, the **maximum** number of stereoisomers for that compound is $2^n$.

The four stereoisomers of 2-bromo-3-chlorobutane consist of two pairs of enantiomers. Stereoisomers **A** and **B** are a pair of non-superimposable mirror images, so they are enantiomers. So are the isomers **C** and **D**. Then what is the relationship between isomer **A** and **C**?

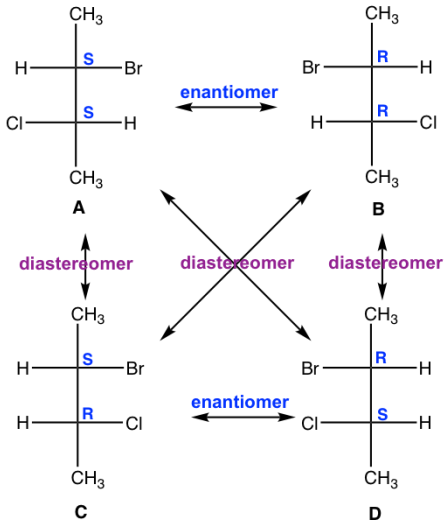



**Four stereoisomers of 2-bromo-3-chlorobutane in perspective formula**



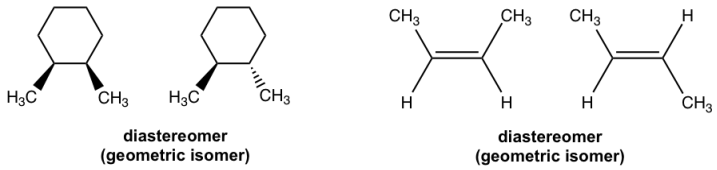

**Four stereoisomers of 2-bromo-3-chlorobutane in Fisher projection**

**A** and **C** are not identical, not enantiomers, and they are stereoisomers (have the same bonding but differ in the spatial arrangement of groups). Such type of stereoisomers are defined as **diastereomers**. **Diastereomers** are stereoisomers that are not enantiomers. For the four stereoisomers here, there are four pairs of diastereomers: **A** and **C**, **A** and **D**, **B** and **C**,**B** and **D**. The relationship between the four stereoisomers can be summarized as:




**Relationships between the four stereoisomers of 2-bromo-3-chlorobutane**

With the introduction of diastereomer concept, the way to categorize isomers can be revised, and the summary in **Fig. 5.1a** can be replaced by the updated version in **Fig. 5.6a**. The stereoisomer then has two sub-types, enantiomers and diastereomers, because **any stereoisomers that are not enantiomers can always be called diastereomers**. Based on such definition, the geometric isomers we learned earlier also belong to the diastereomer category.




**diastereomer (geometric isomer)** **diastereomer (geometric isomer)**

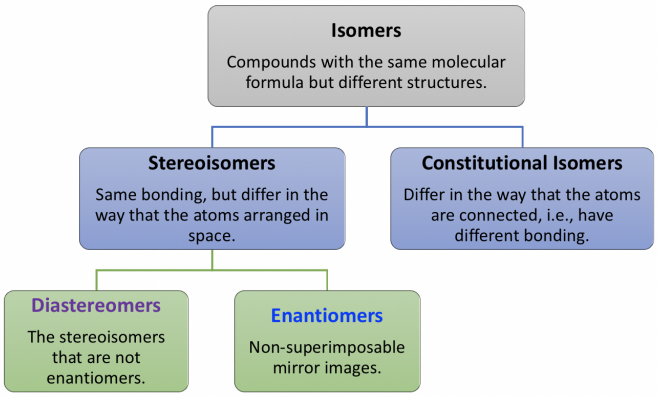


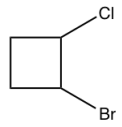

Figure 5.6a Updated Summarization of isomers

As mentioned earlier, enantiomers are very alike to each other, and they share same physical properties except optical activity (opposite sign for specific rotation). Enantiomers also generally have same chemical properties, except the reaction with other chiral reagents (not topics in this course).

However, diastereomers are not that closely related. Diastereomers have different physical properties, for example, different b.p, color, density, polarity, solubility etc. They also have different chemical properties.

Next, we will go through the examples of cyclic compounds, to see how the new concept of diastereomer relates to the knowledge about cyclic compounds we learned before.

**Examples** Draw the structures of all the stereoisomers for 1-bromo-2-chlorocyclobutane, and indicate the relationship between any two stereoisomers.



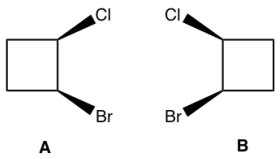

**1-bromo-2-chlorocyclobutane**

## Approach:

There are two chirality centers for 1-bromo-2-chlorocyclobutane molecule. So the maximum number of stereoisomer is four. To work on the stereoisomers for cyclic compound, we can start with cis/trans isomer, and then check does the enantiomer apply to each case.

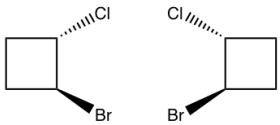
## Solution:

***cis*-1-bromo-2-chlorocyclobutane:**




**A** **B**

***trans*-1-bromo-2-chlorocyclobutane:**




**C** **D**

There are two ***cis***-isomers, **A** and **B**, and they are enantiomers of each other; similarly, there are also two ***trans***-isomers **C** and **D** that are enantiomers of each other as well.

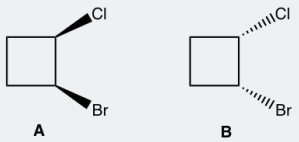
The relationship between *any* of the ***cis***-isomer to *any* of the ***trans***-isomer is **diastereomers (A** and **C, A** and **D, B** and **C, B** and **D)**. Since they are geometric isomers, and remember that the geometric isomers can also be called diastereomers.

## All geometric isomers are diastereomers (it is always correct to call a pair of geometric isomers as diastereomers), however not all the diastereomers are geometric isomers!

### Examples:

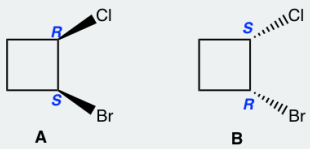
What is the relationship between the following pair of compounds, enantiomers, identical, diastereomers, constitutional isomers, non-isomers?

1.




**A** **B**

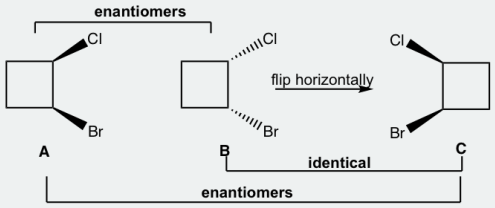
**Method I**: The basic way is to determine the configuration of each chirality center. As shown below that the configuration for both chirality centres are right opposite between the structure **A** and **B**. So they are enantiomers.




**A** **B**

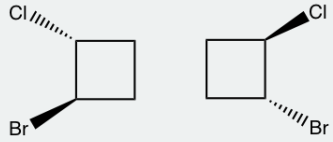
**Method II**: For the cyclic structures, sometimes rotate or flip a given structure in a certain way helps us to tell the relationship (using the molecular model helps the rotate or flip part). For this example, flipping structure **B** horizontally leads to structure

**C**, **B** and **C** are identical. Then it is easy to tell that **A** and **C** are just non-superimposable mirror images to each other, so **A** and **C** are enantiomers, then **A** and **B** are enantiomers as well.




If this method looks confusing to you, then you can stick to **Method I**.

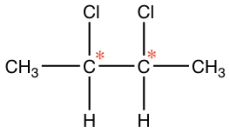
2.




You can use either of the above methods, the answer is “identical”.

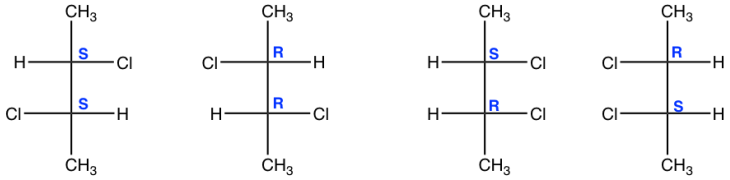
## 5.6.2 Meso compound

Next, we will see another example of a compound containing two chirality centers, 2,3-dichlorobutane, the compound that has the same substituents on C2 and C3 carbons.



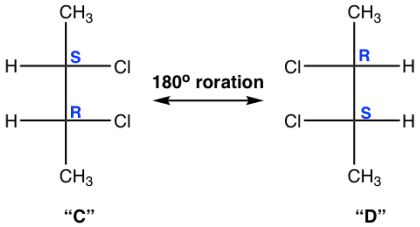

**2,3-dichlorobutane**

Theoretically, there are *maximum* four stereoisomers, the structures are shown by Fisher projections here.




Stereoisomer **A** and **B** are non-superimposable mirror images, so they are enantiomers.

We will take a detailed look at stereoisomer **C** and **D**. Yes, they are mirror images, but are they really non-superimposable? If isomer **C** is rotated 180° (180° rotation still get the same structure back for Fisher projection), then it could get superimposed on isomer **D**. So, isomer **C** and **D** are superimposable mirror images, that means they are the same, **identical**!




**superimposable mirror image;**
**identical;**
**meso compound**

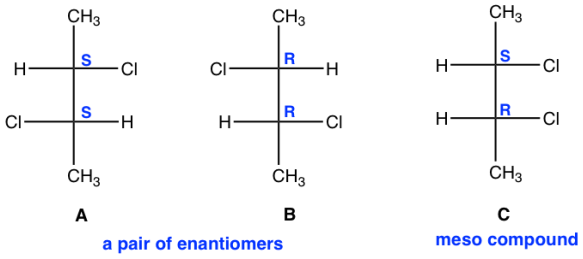
Then "**C**" and "**D**" are just different drawings for the same stereoisomer. The next questions is, is this stereoisomer chiral? We have confirmed that this isomer does get superimposed on its mirror image, that means it is **achiral**.

This is so weird! How come a compound that contain two chirality centers (C2 and C3) is achiral?

Yes, it does happen! A compound that is achiral but contain chirality centers is called **meso compound**. **A meso compounds is achiral and optical inactive** (does **NOT** rotate the plane of polarization of plan-polarized light), but it does have multiple chirality centers.

Because that one stereoisomer is meso compound, the total number of stereoisomers for 2,3-dichlorobutane is **three**.

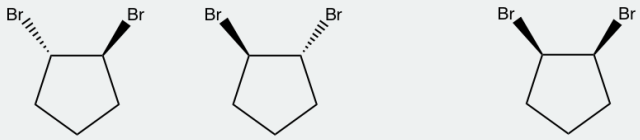
Attention, $2^n$ is the **maximum** number of stereoisomers. Some compounds may have ***less*** than the maximum, because of the existence of meso compounds.




**Three stereoisomers of 2,3-dichlorobutane**

**Examples: Draw all the stereoisomers of 1,2-dibromocyclopentane.**

**Solutions**: there are total three stereoisomers.




**two *trans*-isomers, a pair enantiomers** **one *cis*-isomer, meso compound**

Exercises 5.8

- Draw all stereoisomers for 1-ethyl-3-methylcyclohexane.
- Draw all stereoisomers for 1-ethyl-4-methylcyclohexane.
- Draw all stereoisomers for 1,2-dimethylcyclohexane.

Answers to Practice Questions Chapter 5

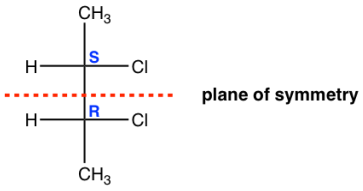
## 5.6.3 Chiral or achiral by looking for Plane of symmetry

The existence of chirality centers does not guarantee the chirality of a molecule, for example of the meso compound. Following the definition of chirality always involve the comparison between original structure and its mirror image, that needs extra work. Is there any easier way to tell whether a moleculeis chiral or achiral?

We can check the **plane of symmetry**. Plane of symmetry is a plane that cuts the molecule in half and that one half is the mirror image of the other.

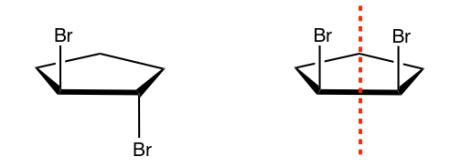
- **If a molecule does have a plan of symmetry, then the molecule is achiral.**
- **The molecule that does not have a plane of symmetry in any conformation is chiral.**

For the meso isomer of 2,3-dichlorobutane, the plane of symmetry is the plane that is labelled in the structure below.



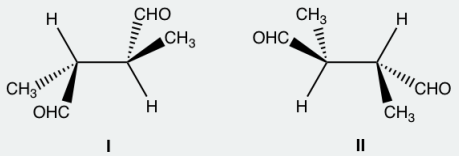

## Examples:Determine whether the following molecule is chiral or achiral.


## Solution:

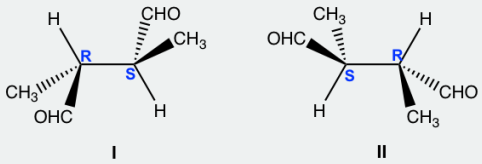



Checking the plane of symmetry provides a quick way to determine the chirality of a molecule. But sometimes you may need to look for the proper conformation to get the plane of symmetry. See following example.

## Examples: What is the relationship of the following pair of structures?

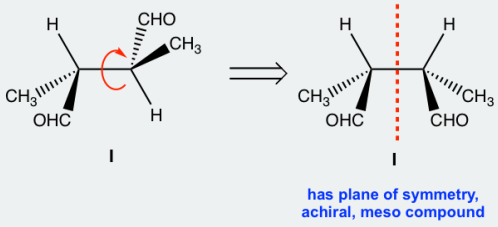



**Approach**: Determine the R/S configuration of each carbon.




For both structures, the chirality centres are bonded with the same groups, and structure **I** has **R** and **S**, structure **II** has **S** and **R**. Are they enantiomers?

A bit further investigation is necessary to get the conclusion. Let's rotate the groups around the 2nd chirality centre of structure **I** (you can use the molecular model to do the rotation, that is very helpful for visualizing the spatial arrangement of the groups):




Rotation of the groups around the chirality centre does not change the configuration, however it does change the conformation to eclipsed conformation. In the eclipsed conformation, it is easier to tell that the structure has a plane of symmetry, so it is a

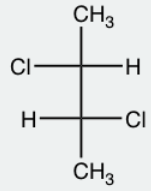
meso compound that is achiral. Achiral compound does not have enantiomer, so **structure II is also meso compound that is identical to structure I.**

**Solution:** Identical

(You can rotate, or do switches to compare between the two structures, but make sure to keep track on any action. If it is easy to get lost by rotating or switch, assign R/S configuration is a safer way.)

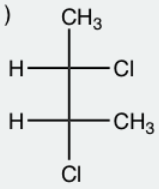
## Examples

If the specific rotation of this molecule is +50° (hypothetic value), determine the specific rotation of molecules in following questions:



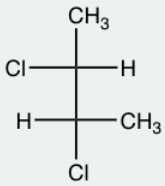

specific rotation is +50°

1)



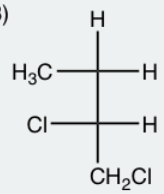

a) +50°
b) - 50°
c) 0°
d) not enough information to decide

2)




a) +50°
b) - 50°
c) 0°
d) not enough information to decide

3)

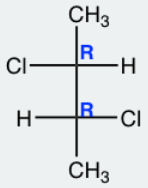



a) +50°
b) - 50°
c) 0°
d) not enough information to decide

**Thinking**: Determine the relationship between the molecule in each question with the given one, and apply the knowledge of specific rotation.

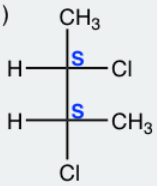
### Solutions:

If the specific rotation of this molecule is +50° (hypothetic value), determine the specific rotation of molecules in following questions:




specific rotation is +50°

1)




a) +50°

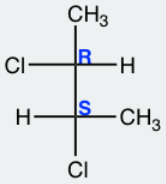
b) - 50°

c) 0°

d) not enough information to decide

this molecule is **enantiomer** to the given molecule, so the specific rotation has the same value, but opposite sign

2)




a) +50°

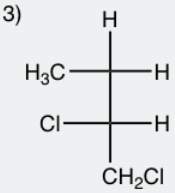
b) - 50°

c) 0°

d) not enough information to decide

this molecule is **diastereomer** to the given molecule, and it is a meso compound, so **ahiral**

3)




a) +50°

b) - 50°

c) 0°

d) not enough information to decide

this molecule is **constitutional isomer** to the given molecule, so the specific rotation has no connection to each other