6.4: DIASTEREOMERS - MORE THAN ONE CHIRAL CENTER

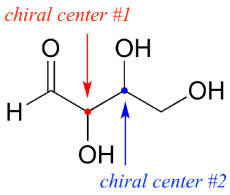
Learning Objective

- recognize and classify diastereomers

Diastereomers are stereoisomers with two or more chiral centers that are not enantiomers. Diastereomers have different physical properties (melting points, boiling points, and densities). Depending on the reaction mechanism, diastereomers can produce different stereochemical products.

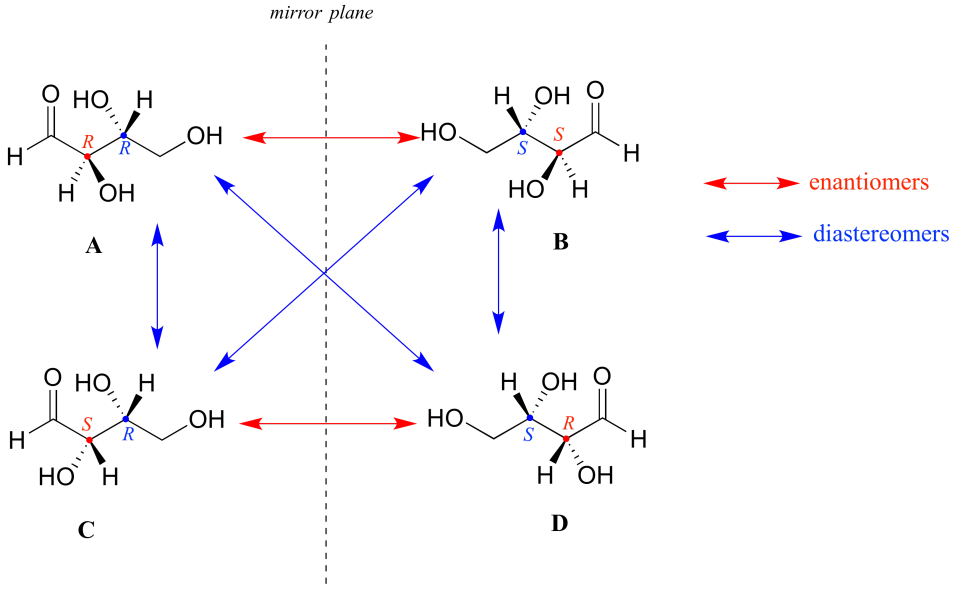
INTRODUCTION

So far, we have been analyzing compounds with a single chiral center. Next, we turn our attention to those which have multiple chiral centers. We'll start with some stereoisomeric four-carbon sugars with two chiral centers.



To avoid confusion, we will simply refer to the different stereoisomers by capital letters.

Look first at compound A below. Both chiral centers in have the *R* configuration (you should confirm this for yourself!). The mirror image of Compound A is compound B, which has the *S* configuration at both chiral centers. If we were to pick up compound A, flip it over and put it next to compound B, we would see that they are *not* superimposable (again, confirm this for yourself with your models!). A and B are nonsuperimposable mirror images: in other words, enantiomers.



Now, look at compound C, in which the configuration is *S* at chiral center 1 and *R* at chiral center 2. Compounds A and C are stereoisomers: they have the same molecular formula and the same bond connectivity, but a different arrangement of atoms in space (recall that this is the definition of the term 'stereoisomer). However, they are *not* mirror images of each other (confirm this with your models!), and so they are *not* enantiomers. By definition, they are **diastereomers** of each other.

Notice that compounds C and B also have a diastereomeric relationship, by the same definition.

So, compounds A and B are a pair of enantiomers, and compound C is a diastereomer of both of them. Does compound C have its own enantiomer? Compound D is the mirror image of compound C, and the two are not superimposable. Therefore, C and D are a pair of enantiomers. Compound D is also a diastereomer of compounds A and B.

This can also seem very confusing at first, but there some simple shortcuts to analyzing stereoisomers:

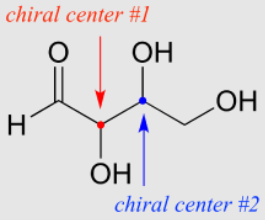
Stereoisomer shortcuts

If ***all*** of the chiral centers are of opposite R/S configuration between two stereoisomers, they are enantiomers.

If ***at least one, but not all*** of the chiral centers are opposite between two stereoisomers, they are diastereomers.

(*Note: these shortcuts to not take into account the possibility of additional stereoisomers due to alkene groups: we will come to that later)*

Here's another way of looking at the four stereoisomers, where one chiral center is associated with red and the other blue. Pairs of enantiomers are stacked together.



possible configurations:

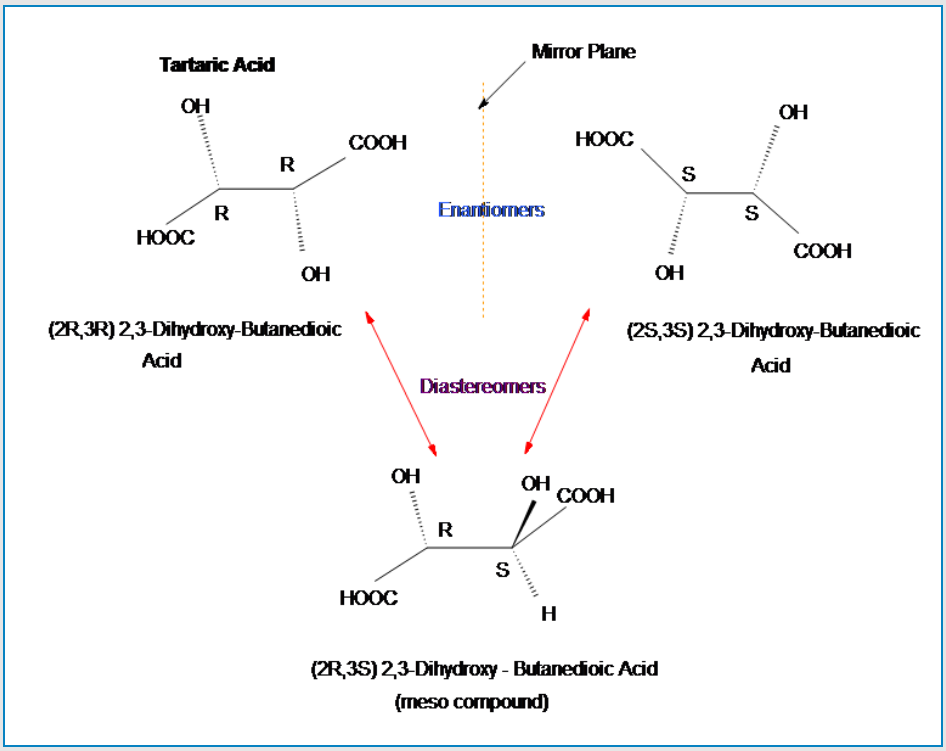
RR *RS*
SS *SR*

We know, using the shortcut above, that the enantiomer of RR must be SS - both chiral centers are different. We also know that RS and SR are diastereomers of RR, because in each case one - but not both - chiral centers are different.

DIASTEREOMERS VS. ENANTIOMERS IN WINE CHEMISTRY

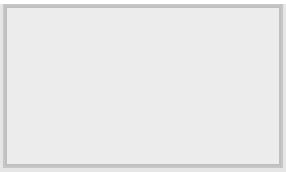
Tartaric acid, $C_4H_6O_6$, is an organic compound that can be found in grape, bananas, and in wine. The structures of tartaric acid itself is really interesting. Naturally, it is in the form of (R,R) stereocenters. Artificially, it can be in the meso form (R,S), which is achiral. R,R tartaric acid is enantiomer to is mirror image which is S,S tartaric acid and diasteromers to meso-tartaric acid (Figure 5.6.2).

(R,R) and (S,S) tartaric acid have similar physical properties and reactivity. However, meso-tartaric acid have different physical properties and reactivity. For example, melting point of (R,R) & (S,S) tartaric is about 170 degree Celsius, and melting point of meso-tartaric acid is about 145 degree Celsius.



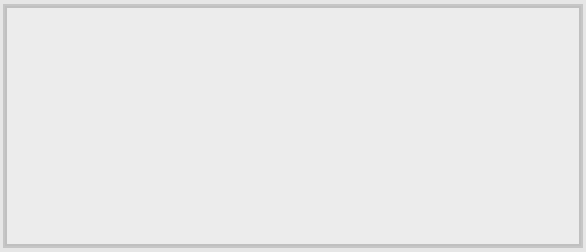
DIASTEREOMERS VS. ENANTIOMERS IN SUGAR CHEMISTRY

D-erythrose is a common four-carbon sugar.



A note on sugar nomenclature: biochemists use a special system to refer to the stereochemistry of sugar molecules, employing names of historical origin in addition to the designators '*D*' and '*L*'. You will learn about this system if you take a biochemistry class. We will use the *D/L* designations here to refer to different sugars, but we won't worry about learning the system.

As you can see, *D*-erythrose is a chiral molecule: C_2 and C_3 are stereocenters, both of which have the *R* configuration. In addition, you should make a model to convince yourself that it is impossible to find a plane of symmetry through the molecule, regardless of the conformation. Does D-erythrose have an enantiomer? Of course it does – if it is a chiral molecule, it must. The enantiomer of erythrose is its mirror image, and is named L-erythrose (once again, you should use models to convince yourself that these mirror images of erythrose are not superimposable).

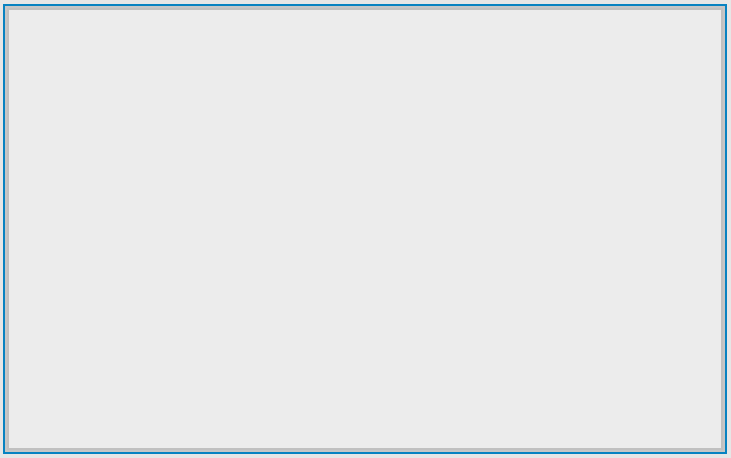


Notice that both chiral centers in L-erythrose both have the *S* configuration.

Note

In a pair of enantiomers, **all** of the chiral centers are of the opposite configuration.

What happens if we draw a stereoisomer of erythrose in which the configuration is *S* at C_2 and *R* at C_3? This stereoisomer, which is a sugar called D-threose, is *not* a mirror image of erythrose. D-threose is a **diastereomer** of both D-erythrose and L-erythrose.



The definition of diastereomers is simple: if two molecules are stereoisomers (same molecular formula, same connectivity, different arrangement of atoms in space) but are *not* enantiomers, then they are diastereomers by default. *In practical terms, this means that at least one - but not all - of the chiral centers are opposite in a pair of diastereomers.* By definition, two molecules that are diastereomers are *not* mirror images of each other.

L-threose, the enantiomer of D-threose, has the *R* configuration at C_2 and the *S* configuration at C_3. L-threose is a diastereomer of both erythrose enantiomers.

Erythronolide B, a precursor to the 'macrocyclic' antibiotic erythromycin, has 10 stereocenters. It's enantiomer is that molecule in which all 10 stereocenters are inverted.

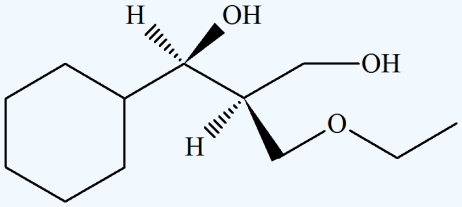
In total, there are 2^{10} = 1024 stereoisomers in the erythronolide B family: 1022 of these are diastereomers of the structure above, one is the enantiomer of the structure above, and the last ***is*** the structure above.

We know that enantiomers have identical physical properties and equal but opposite degrees of specific rotation. Diastereomers, in theory at least, have different physical properties – we stipulate 'in theory' because sometimes the physical properties of two or more diastereomers are so similar that it is very difficult to separate them. In addition, the specific rotations of diastereomers are unrelated – they could be the same sign or opposite signs, and similar in magnitude or very dissimilar.

Exercises

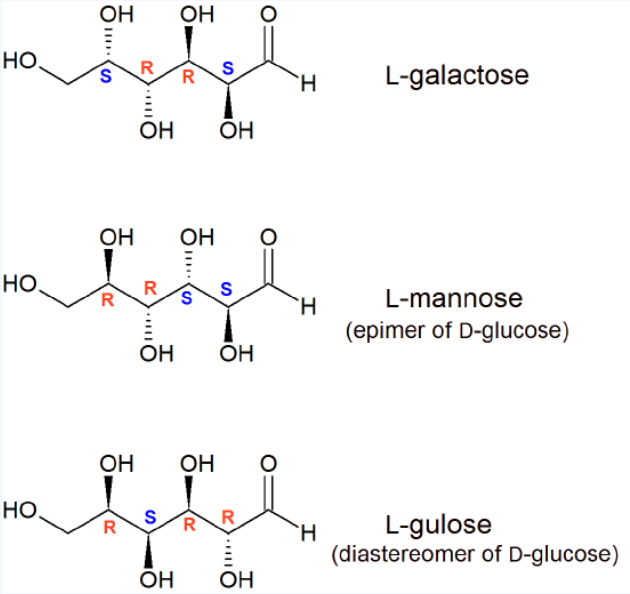
1. Draw the structures of L-galactose (the enantiomer of D-galactose) and two more diastereomers of D-glucose (one should be an epimer).

2. Determine the stereochemistry of the following molecule:

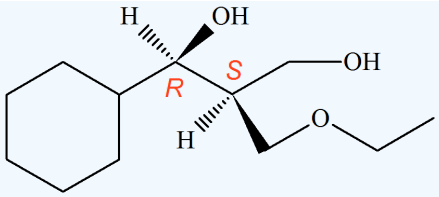


Answer

1.



2.



CONTRIBUTORS AND ATTRIBUTIONS

- Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)
- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, Athabasca University)

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