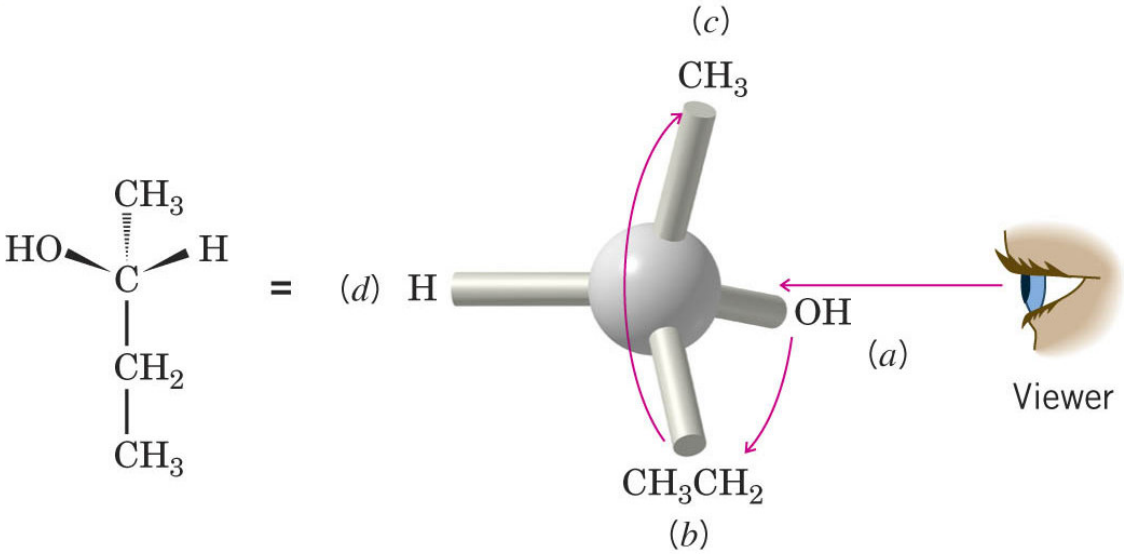
5.3 Configuration and the *R–S* Convention

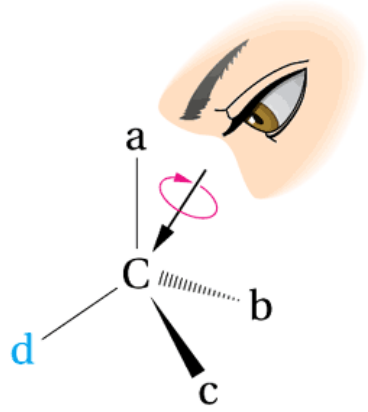
- *Enantiomers* are another type of configurational isomers; they are said to have opposite configurations.
- When referring to a particular enantiomer, its configuration should be specified.
- A convention for doing this is known as the R–S convention
  - Also called the Cahn–Ingold–Prelog system
  - The four groups attached to the stereogenic carbon are assigned priorities from highest (a) to lowest (d)
  - Priorities are assigned by specific rules.

How it works?

The four groups attached to the stereogenic center are placed in a priority order (by a system we will describe next), $a \rightarrow b \rightarrow c \rightarrow d$. The stereogenic center is then observed *from the side opposite the lowest priority group, d.* If the remaining three groups ($a \rightarrow b \rightarrow c$) form a clockwise array, the configuration is designated *R* (from the Latin *rectus*, right).** If they form a *counterclockwise* array, the configuration is designated as *S* (from the Latin *sinister*, left).

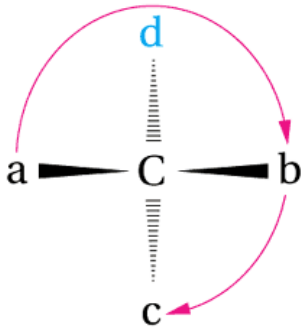


(*R*)-2-Butanol

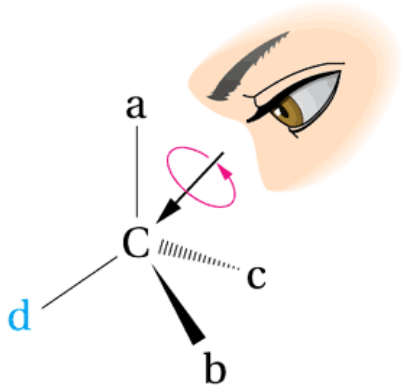


a → b → c clockwise
R

or

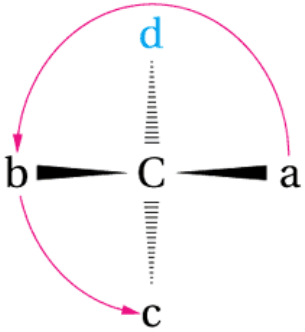


a → b → c clockwise
R



a → b → c counterclockwise
S

or



a → b → c counterclockwise
S

Rules of Priority

Rule 1.

The atoms directly attached to the stereogenic center are ranked according to *atomic number:* the higher the atomic number, the higher the priority.

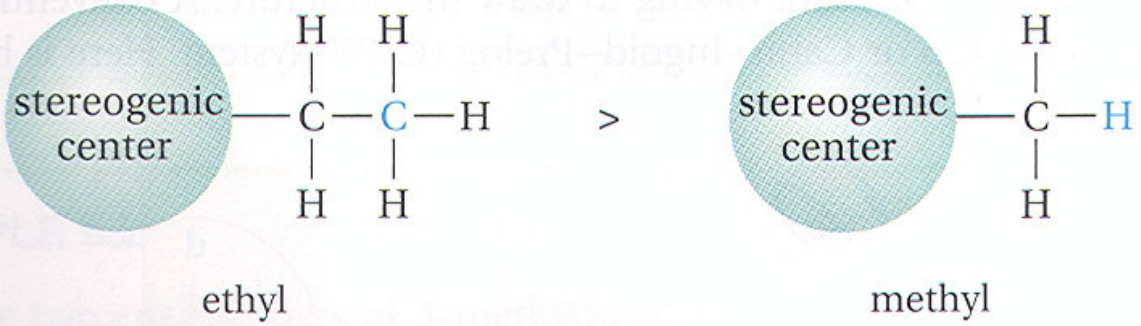
$$\underset{\text{high priority}}{Cl} > O > C > \underset{\text{low priority}}{H}$$

If one of the four groups is H, it always has the lowest priority, and one views the stereogenic center looking down the C—H bond from C to H.

Rules

Rule 2.

If a decision cannot be reached with rule 1 (that is, if two or more of the directly attached atoms are the same), work outward from the stereogenic center until a decision is reached. For example, the ethyl group has a higher priority than the methyl group, because at the first point of difference, working outward from the stereogenic center, we come to a *carbon* (higher priority) in the ethyl group and a *hydrogen* (lower priority) in the methyl group.



EXAMPLE 5.3

Assign a priority order to the following groups: —H, —Br, —CH_2CH_3, and —CH_2OCH_3.

SOLUTION —Br > —CH_2OCH_3 > —CH_2CH_3 > —H

The atomic numbers of the directly attached atoms are ordered Br > C > H. To prioritize the two carbon groups, we must go out until a point of difference is reached.

—CH_2OCH_3 > —CH_2CH_3 (O > C)

PROBLEM 5.8 Assign a priority order to each of the following sets of groups:

a. —CH_3, —$CH(CH_3)_2$, —H, —NH_2
b. —OH, —F, —CH_3, —CH_2OH
c. —OCH_3, —$NHCH_3$, —CH_2NH_2, —OH
d. —CH_2CH_3, —$CH_2CH_2CH_3$, —$C(CH_3)_3$, —$CH(CH_3)_2$

5.8 In each case, proceed from high to low priority.

a. $-NH_2 > -CH(CH_3)_2 > -CH_3 > -H$

b. $-F > -OH > CH_2OH > -CH_3$

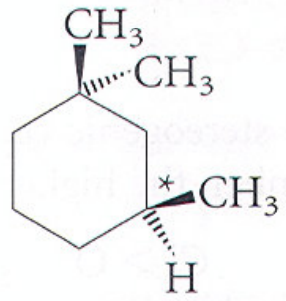
c. $-OCH_3 > -OH > -NHCH_3 > CH_2NH_2$

The oxygen in the methoxy group ($-OCH_3$) is bonded to carbon, whereas the hydroxyl oxygen ($-OH$) is bonded only to hydrogen.

d. $-C(CH_3)_3 > -CH(CH_3)_2 > -CH_2CH_2CH_3 > -CH_2CH_3$

Stereogenic enters in cyclic compounds

For stereogenic centers in cyclic compounds, the same rule for assigning priorities is followed. For example, in 1,1,3-trimethylcyclohexane, the four groups attached to carbon-3 in order of priority are $—CH_2C(CH_3)_2CH_2 > —CH_2CH_2 > —CH_3 > —H$.

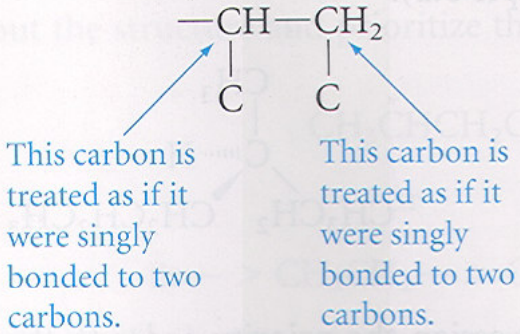


1,1,3-trimethylcyclohexane

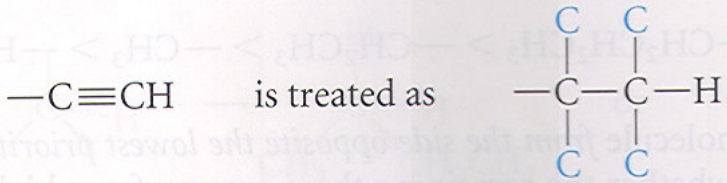
A third, somewhat more complicated, rule is required to handle double or triple bonds and aromatic rings (which are written in the Kekulé fashion).

Rule 3.

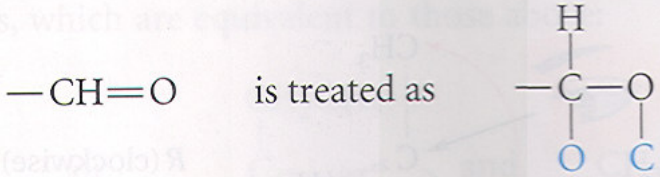
Multiple bonds are treated as if they were an equal number of single bonds. For example, the vinyl group —CH=CH_2 is counted as



Similarly,



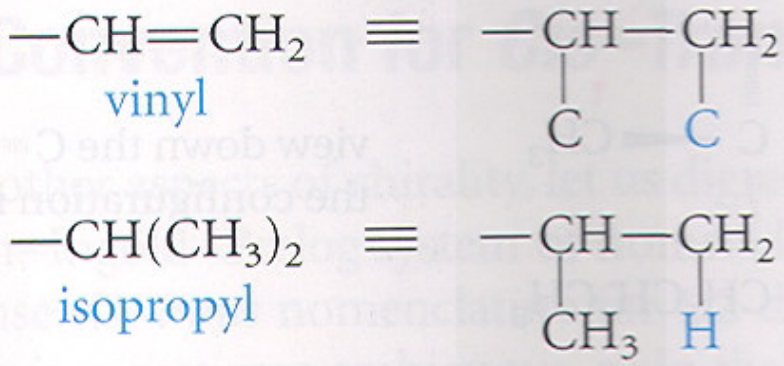
and



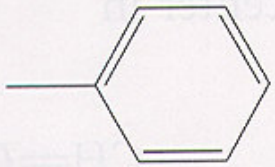
EXAMPLE 5.4

Which group has the higher priority, isopropyl or vinyl?

SOLUTION The vinyl group has the higher priority. We go out until we reach a difference, shown in color.



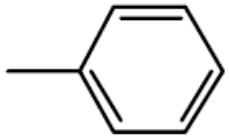
PROBLEM 5.9 Assign a priority order to

a. $-C\equiv CH$ and $-CH=CH_2$ b. $-CH=CH_2$ and 

c. $-CH=O$, $-CH=CH_2$, $-CH_2CH_3$, and $-CH_2OH$

5.9 a. $-C\equiv CH > -CH=CH_2$

The acetylenic carbon ($-C\equiv$) is treated as though it is bonded to three carbons, while the olefinic carbon ($-CH=$) is treated as though it is bonded to two carbons and a hydrogen (see Sec. 5.3).

b.  $> -CH=CH_2$

The phenyl carbon is treated as though it is bonded to three carbons.

c. $-CH=O > -CH_2OH > -CH=CH_2 > -CH_2CH_3$

The aldehyde carbon is treated as though it is bonded to two oxygens.

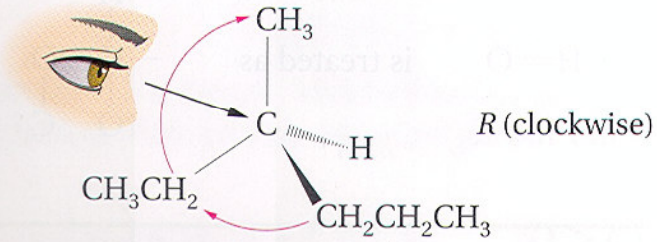
EXAMPLE 5.5

Assign the configuration (*R* or *S*) to the following enantiomer of 3-methylhexane (see Example 5.2)

SOLUTION First assign the priority order to the four different groups attached to the stereogenic center.

$$-CH_2CH_2CH_3 > -CH_2CH_3 > -CH_3 > -H$$

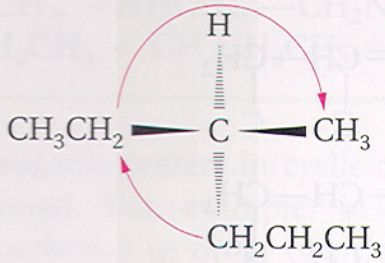
Now view the molecule *from the side opposite the lowest priority group* (—H) and determine whether the remaining three groups, from high to low priority, form a clockwise (*R*) or counterclockwise (*S*) array.



R (clockwise)

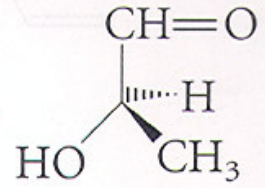
We write the name (*R*)-3-methylhexane.

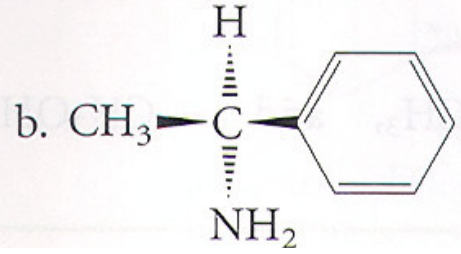
If we view the other representation of this molecule shown in Example 5.2, we come to the same conclusion.



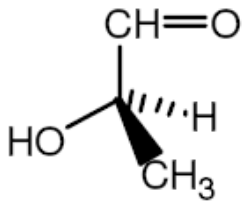
view down the C ····· H bond; the configuration is *R*

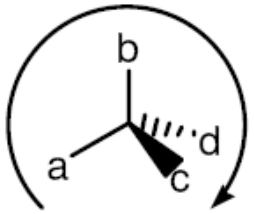
PROBLEM 5.10 Determine the configuration (*R* or *S*) at the stereogenic center in

a. 

b. 

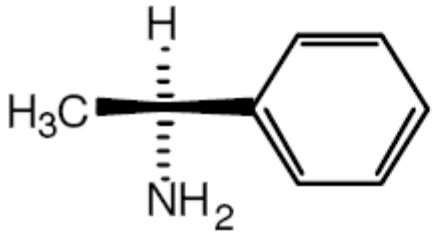
5.10 a. Priority order: OH > CH=O > CH_3 > H. Configuration is *R*.

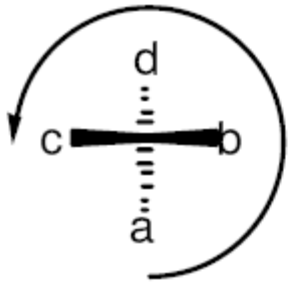




clockwise or *R*

b. Priority order: NH_2 > $-C_6H_5$ > CH_3 > H. The configuration is *S*.



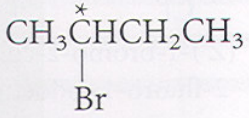


counterclockwise or *S*

EXAMPLE 5.6

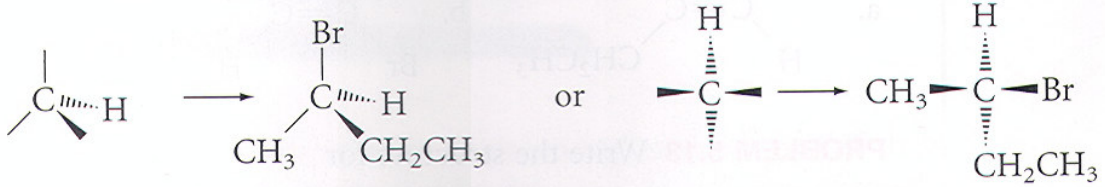
Draw the structure of (*R*)-2-bromobutane.

SOLUTION First, write out the structure and prioritize the groups attached to the stereogenic center.

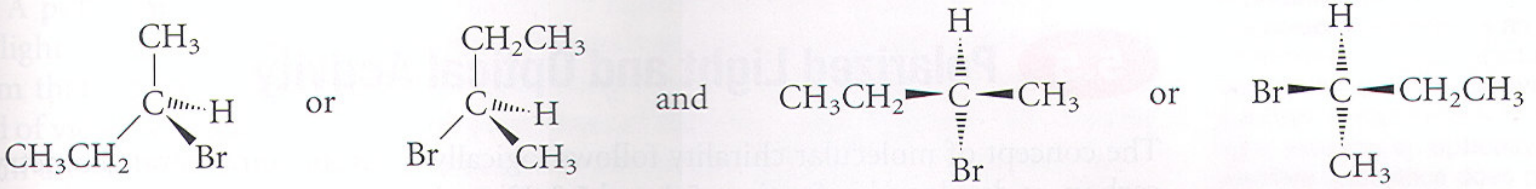


$$Br— > CH_3CH_2— > CH_3— > H—$$

Now make the drawing with the H (lowest priority group) "away" from you, and place the three remaining groups ($Br \rightarrow CH_3CH_2 \rightarrow CH_3$) in a clockwise (*R*) array.



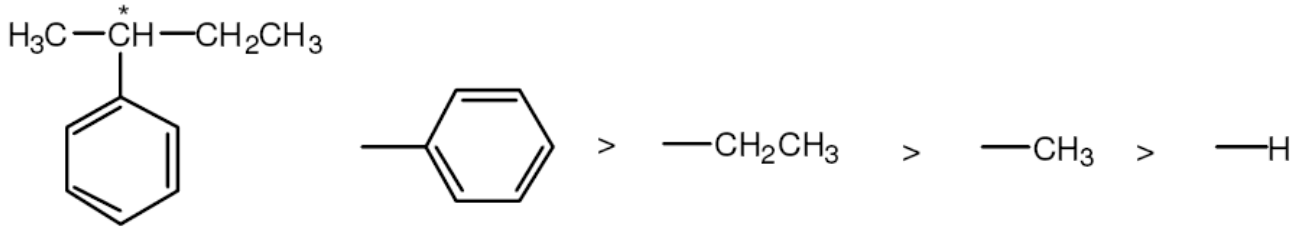
Of course, we could have started with the top-priority group at either of the other two bonds to give the following structures, which are equivalent to those above:



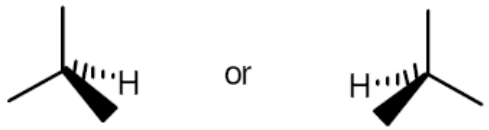
PROBLEM 5.11 Draw the structure of

a. (*S*)-2-phenylbutane. b. (*R*)-3-methyl-1-pentene. c. (*S*)-3-methylcyclopentene.

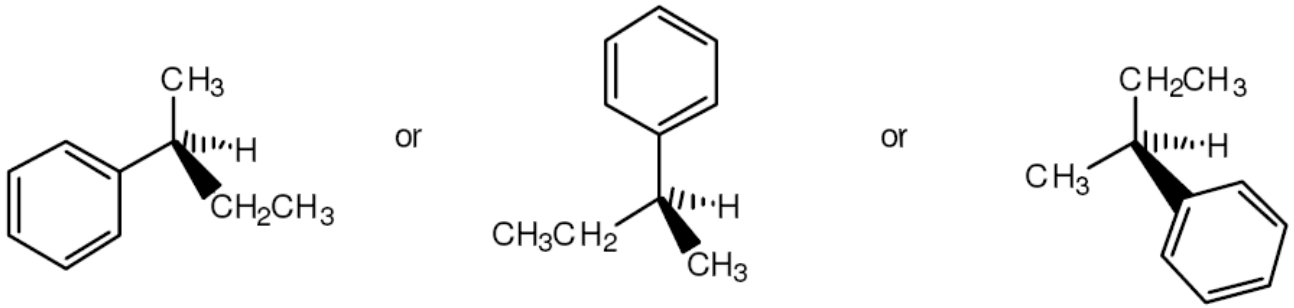
5.11 a. The priority of groups around the stereogenic center is as follows:



First, draw the lowest-priority group pointing away from you:

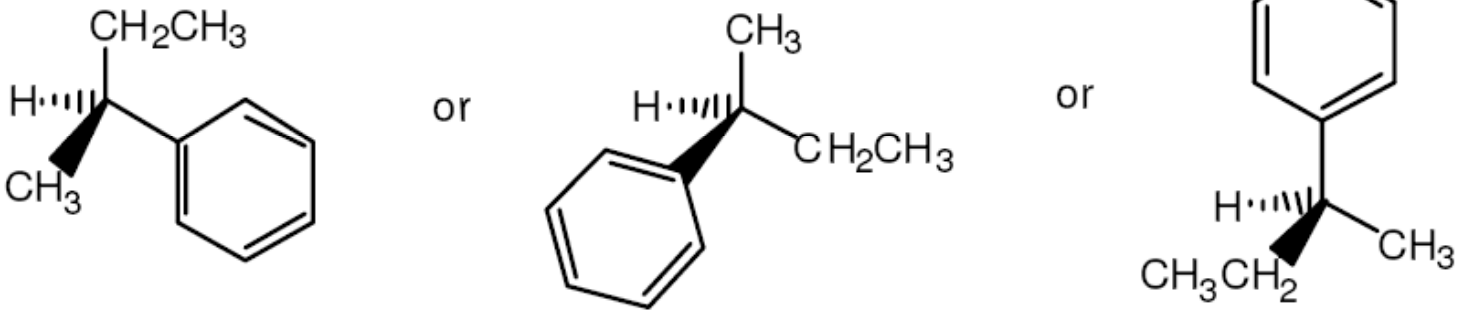


Then fill in the groups in priority order, counterclockwise (*S*),



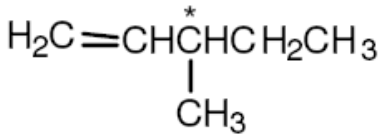
and

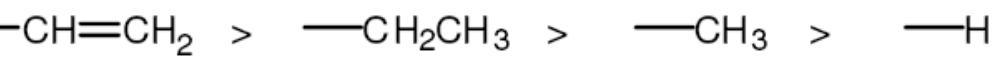
Similarly,

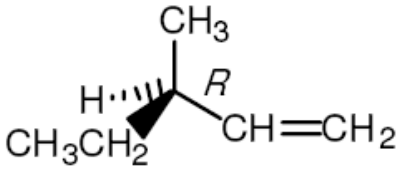


As you can see, there are many ways to write the correct answer. In subsequent problems, only one correct way will be shown. Work with models if you have difficulty.

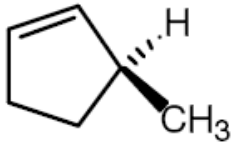
b. The priority around the stereogenic center is as follows:





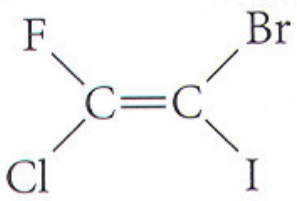


c. The same rules apply for cyclic and acyclic compounds.

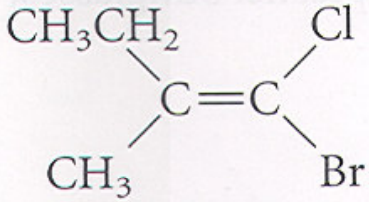


5.4 The *E-Z* Convention for *Cis–Trans* Isomers

Before we continue with other aspects of chirality, let us digress briefly to describe a useful extension of the Cahn–Ingold–Prelog system of nomenclature to *cis–trans* isomers. Although we can easily use *cis–trans* nomenclature for 1,2-dichloroethene or 2-butene (see Sec. 3.5), that system is sometimes ambiguous, as in the following examples:



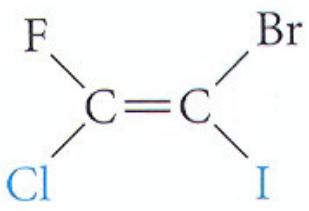
cis or *trans?*



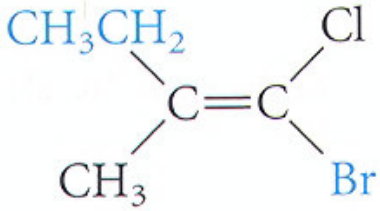
cis or *trans?*

The system we have just discussed for stereogenic centers has been extended to double-bond isomers. We use exactly the same priority rules. *The two groups attached to each carbon of the double bond are assigned priorities.* If the two higher priority groups are on *opposite* sides of the double bond, the prefix *E* (from the German *entgegen*, opposite) is used. If the two higher priority groups are on the *same* side of the

double bond, the prefix is *Z* (from the German *zusammen*, together). The higher priority groups for the above examples are shown here in color, and the correct names are given below the structures.

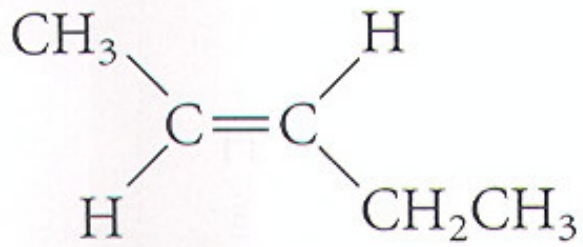


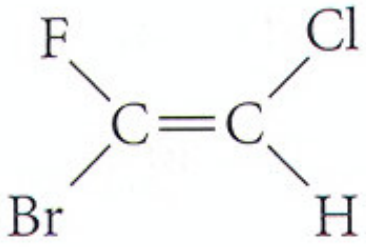
(*Z*)-1-bromo-2-chloro-2-fluoro-1-iodoethene



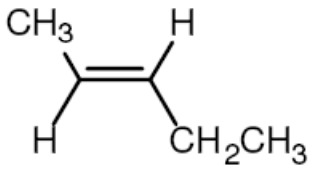
(*E*)-1-bromo-1-chloro-2-methyl-1-butene

PROBLEM 5.12 Name each compound by the *E*-*Z* system.

a. 

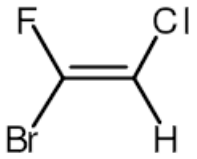
b. 

5.12 a. The priority order at each doubly bonded carbon is CH_3 > H and CH_3CH_2 > H. The configuration is *E*.



(*E*)-2-pentene

b. The priority order is Br > F and Cl > H. The configuration is *E*.

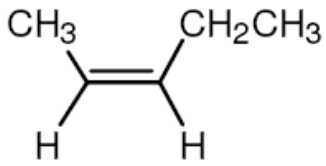


(*E*)-1-bromo-2-chloro-1-fluoroethane

PROBLEM 5.13 Write the structure for

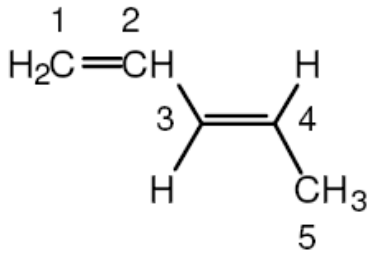
a. (*Z*)-2-pentene. b. (*E*)-1,3-pentadiene.

5.13 a. The two highest-priority groups, CH_3 and CH_3CH_2, are *zusammen*, or together.



(*Z*)-2-pentene

b. The priorities are $CH_2{=}C{-}$ > H and $CH_3{-}$ > H. The two highest-priority groups, $CH_2{=}CH{-}$ and $CH_3{-}$, are *entgegen* (opposite).



(E)-1,3-pentadiene