Stereochemistry I

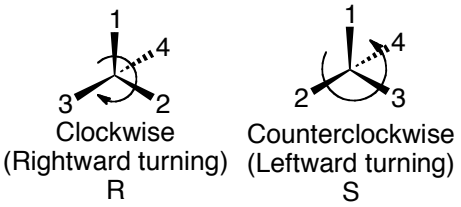
R and *S* in Alkanes

- A chiral carbon has four different groups attached to it, the differences may be several bonds away, but so long as they are different in any way the groups are considered different.
    - Stereocenters are chiral carbons and vice versa

- Chiral molecules are asymmetric molecules
    - They do not have an internal mirror plane
    - They nearly always have at least one stereocenter
        - Chiral molecules may lack a mirror plane *and* have no chiral centers, they exist but are beyond the scope of this course (i.e. helicene)
    - They are optically active and rotate plane-polarized light
        - Left (counterclockwise) rotation is (-) and levorotory
        - Right (clockwise) rotation is (+) and dextrorotory

- Individual chiral centers are classified as either R or S.
    - R/S designation is completely unrelated to the direction of rotation of plane polarized light.

- Assigning R vs. S stereocenters – The Absolute Configuration:
    - Working outward from the chiral carbon assign priority to each attached group. (Cahn-Ingold-Prelog Priority Rules)
        - 1st priority is assigned by atomic number, heavier atoms get priority
            - In order 1st Br then Cl then C and lastly H 4th
        - if isotopes are encountered the heavier isotope gets priority
            - ^{14}C then ^{13}C then ^{12}C
        - If two of the same atom are encountered priority is assigned by the *first difference* in bonded atoms
        - Multiple bonds count as multiple single bonds to the same atom
    - Once priority is assigned rotate the lowest priority to the back
        - If 1 → 2 → 3 proceeds clockwise the center is R (right turning)
        - If 1 → 2 → 3 proceeds counterclockwise the center is S (left/sinister turning)

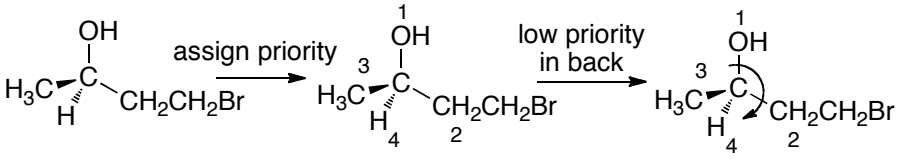


Clockwise (Rightward turning) R

Counterclockwise (Leftward turning) S

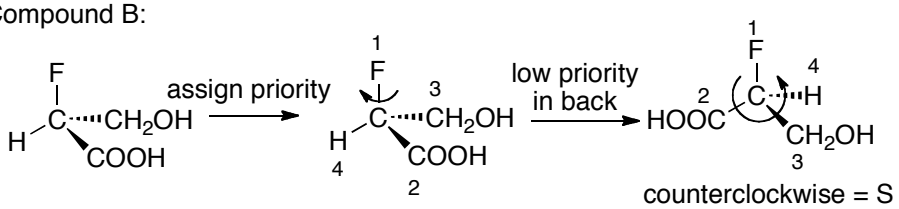
Examples:

Compound A:



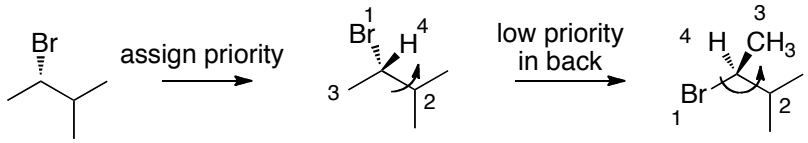
(2R)-4-bromo-2-butanol

Compound B:



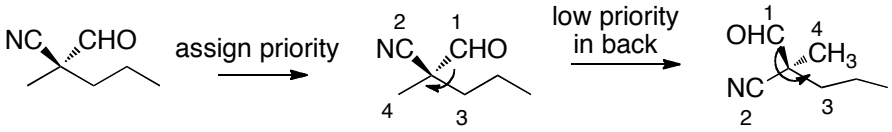
(2S)-2-fluoro-3-hydroxypropanoic acid

Compound C:



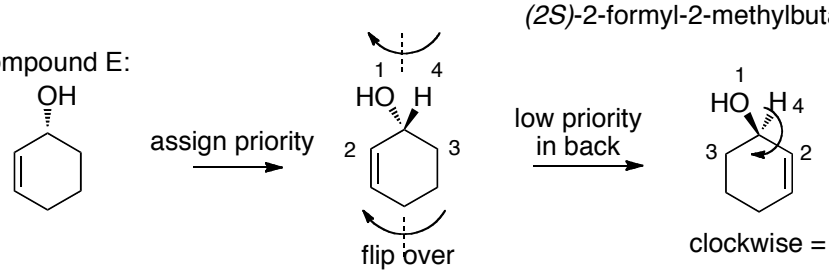
(2S)-2-bromo-3-methylbutane

Compound D:



(2S)-2-formyl-2-methylbutanenitrile

Compound E:



(1R,2Z)-cyclohex-2-en-1-ol

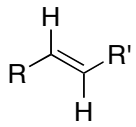
Stereochemistry II

E and *Z* in Alkenes

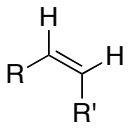
- Alkenes can have multiple geometric isomers (non-superimposable, non-mirror images)

- If there are exactly two substituents and two hydrogens attached an alkene the isomer may be labeled as *cis*- or *trans*-.

a *trans* alkene
H opposite



vs.

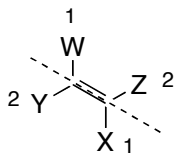


a *cis* alkene
H on same side

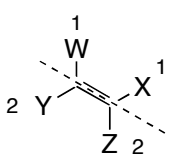
- If there are two or more substituents attached to an alkene the isomer may be labeled as *E*- or *Z*-
  - All *cis*- are *Z*-, but not all *Z*- are *cis*-; all *trans*- are *E*-, but not all *E*- are *trans*-. Cis- and *trans*- are accepted when appropriate, but *E* and *Z* always work.

- Assigning Relative Configuration: *E* vs. *Z*
  - For each sp^2 carbon in the alkene identify the two substituents and prioritize them 1 and 2 using the Cahn-Ingold-Prelog Rules.
    - 1^{st} priority is assigned by atomic number, heavier atoms get priority
      - In order 1^{st} Br then Cl then C and lastly H 4^{th}
    - if isotopes are encountered the heavier isotope gets priority
      - ^{14}C then ^{13}C then ^{12}C
    - If two of the same atom are encountered priority is assigned by the *first difference* in bonded atoms
    - Multiple bonds count as multiple single bonds to the same atom
  - If both high priority groups are on the same side of the alkene the molecule is *Z*. (similar to a *cis*)
    - This can be remembered by *Z* is on the Zame Zide.
  - If the high priority groups are on opposite sides of the alkene the molecule is *E*. (similar to *trans*)
  - If the there is no difference between the groups then the molecule is symmetrical and thus *E*/*Z* is unnecessary**.** (e.g. monosubstituted alkenes)

an *E* alkene
1st priority opposite



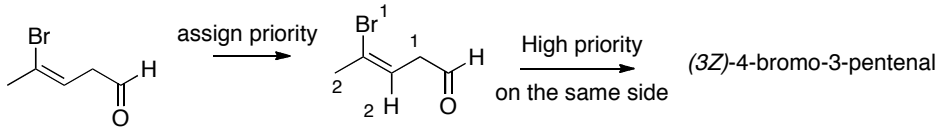
vs.



a *Z* alkene
1st priority on the same side

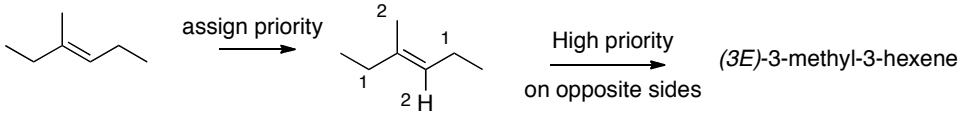
Examples:

Compound A:



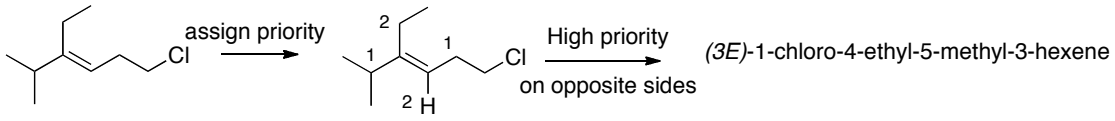
(3Z)-4-bromo-3-pentenal

Compound B:



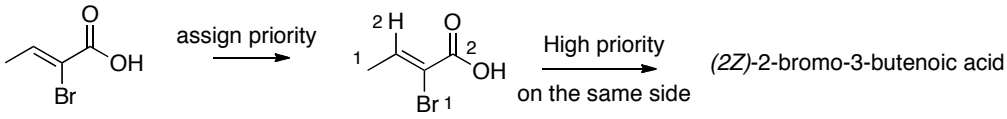
(3E)-3-methyl-3-hexene

Compound C:



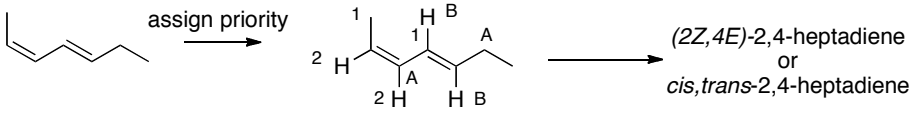
(3E)-1-chloro-4-ethyl-5-methyl-3-hexene

Compound D:



(2Z)-2-bromo-3-butenoic acid

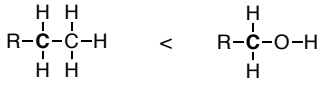
Compound E:



(2Z,4E)-2,4-heptadiene
or
cis,trans-2,4-heptadiene

Cahn-Ingold-Prelog Examples:

Example 1: Larger Atomic Number gets Priority

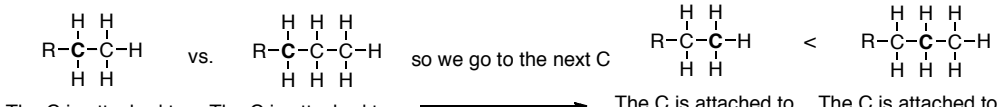


The C is attached to C, H, H < The C is attached to O, H, H

C < O

Oxygen is larger than carbon so the alcohol gets priority, functional groups usually get priority as they tend to have larger atoms.

Example 2: Longer Chains Get Priority

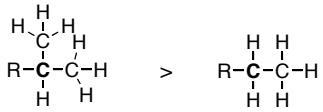


The C is attached to C, H, H vs. The C is attached to C, H, H — so we go to the next C → The C is attached to H, H, H < The C is attached to C, H, H

H < C

Longer chains will get priority as any atom will win over H.

Example 3: Branched Chains get Priority

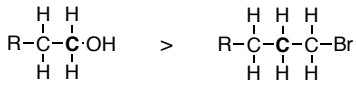


The C is attached to C, C, H > The C is attached to C, H, H

C > H

The first C attached to each is the same, but the second C is larger than H. Branched chains will usually get priority.

Example 4: First Difference gets Priority

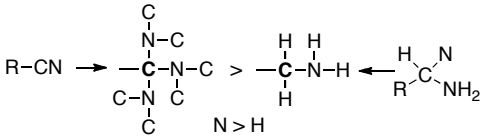


The C is attached to O, H, H > The C is attached to C, H, H

O > C

The Br is too far away, it is not the first difference. Closer differences take priority not the ultimately largest atom.

Example 5: Multiple Bonds Count Multiple Times

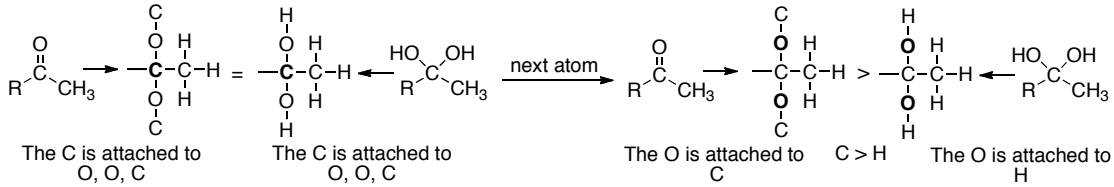


The C is attached to N, N, N > The C is attached to N, H, H

N > H

The triple bond counts as 3 bonds to N so N is larger than H.

Example 6: Mulitple Bonds Count Extra for Both Atoms



The C is attached to O, O, C = The C is attached to O, O, C — next atom → The O is attached to C > The O is attached to H

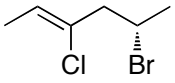
C > H

The carbonyl counts as two C-O bonds from the carbons perspective so we need to go on to the next atom. The O is attached to H in the diol and *back* through the second bond to the C in the carbonyl.

Practice Examples:

Assign *R, S, E,* or *Z* to each molecule.
Assign the correct IUPAC name to molecules whose functional groups you've learned.

A



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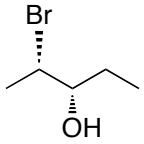
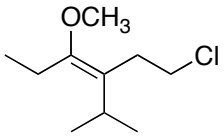


C



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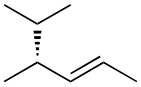

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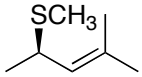

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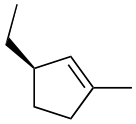

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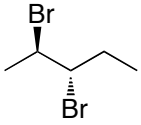

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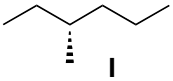

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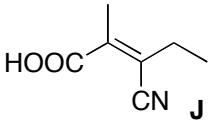

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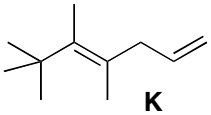

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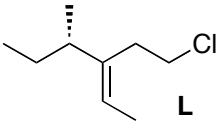

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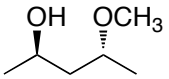

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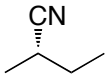

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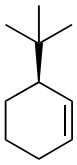

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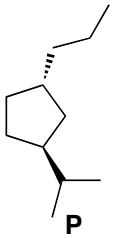

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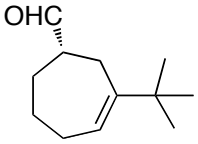

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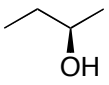

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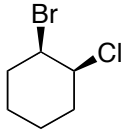

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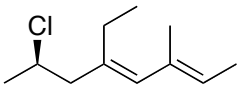

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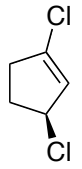

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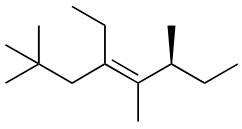

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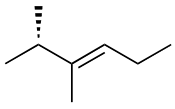

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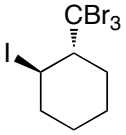

X

Practice Examples Key:

A) *(Z)*-cyclohexene or
cis-cyclohexene
B) *(2Z,5S)*-5-bromo-3-chloro-2-heptene
C) *(2S,3S)*-2-bromo-3-pentanol
D) *(E)*-1-chloro-3-isopropyl-4-methoxy-3-hexene or
(E)-1-chloro-3-(1-methylethyl)-4-methoxy-3-hexene)
E) *(2E,4R)*-4,5-dimethyl-2-hexene
F) *(R)*-2-methyl-4-methylthio-2-pentene
G) *(1Z,3R)*-3-ethyl-1-methylcyclopentene
H) *(2R,3S)*-2,3-dibromopentane
I) *(R)*-3-methylhexane
J) *(Z)*-3-cyano-2-methyl-2-pentenoic acid
K) *(E)*-4,5,6,6-tetramethyl-1,4-heptadiene
L) *(2E,4S)*-3-(2-chloroethyl)-4-methyl-2-hexene
M) *(2R,4R)*-4-methoxy-2-pentanol
N) *(S)*-2-methylbutanenitrile
O) *(1Z,3R)*-3-*tert*-butylcyclohexene or
(1Z,3R)-3-(1,1-dimethylethyl)cyclohexene
P) *(1S,3S)*-1-isopropyl-3-propylcyclopentane or
(1S,3S)-1-(1-methylethyl)-3-propylcyclopentane
Q) *(1S,3E)*-3-*tert*-butyl-3-cycloheptenecarbaldehyde or
(1S,3E)-3-(1,1-dimethylethyl)-3-cycloheptenecarbaldehyde
R) *(R)*-2-butanol
S) *(1R,2S)*-1-bromo-2-chlorocyclohexane
T) *(2E,4E,7R)*-7-chloro-5-ethyl-3-methyl-2,4-octadiene
U) *(1E,3S)*-1,3-dichlorocyclopentene
V) *(4E,6S)*-4-ethyl-2,2,5,6-tetramethyl-4-octene
W) *(E)*-2,3-dimethyl-3-hexene
X) *(1R,2S)*-1-iodo-2-(1,1,1-tribromomethyl)cyclohexane