Selected Chapter 2 problem answers

1. (a) \( \text{OCl} \quad \text{OCH}_3\text{OH} \)
   Higher priorities on the same side \( \Rightarrow Z \)

(b) \( \text{implies} \quad \text{Thus trans} \)

(c) \( \text{Thus } (1R, s\text{-trans}, 3E) \)

(d) \( \text{Thus } Z \) (or syn)

(e) \( \text{Here the } -\text{ON group is exo} \)

(f) \( \text{This is the Mecke notation for racemic} \)
   \( \text{Thus, this is rac-trans} \)

(g) \( \text{Also a Mecke notation, this means enantiopure but only the relative configuration is known.} \)
   \( \text{Thus, (1R*, 3R*, SR*) or rel-(1R, 3R, SR)} \)
(1) If "up" is in a Haworth projection, then the β anomomer

(This is β-D-allopyranose, which is epimeric with glucose at C3)

(2) Structures A and B are positional isomers because the methoxy group is on C2 in A but is on C1 in B. Structures A and E are enantiomers (assign each stereogenic center as R or S to determine this, or convert Newman projection C into a Fischer projection for easy comparison with A). Structures A and D are functional group isomers because A is a methyl ether while D is an alcohol. Structures A and E are diastereomers (can be determined by a variety of ways).

(3) (a) 11

\[ \text{Cl} \quad \text{CO}_2\text{H} \quad \text{C} \quad \text{N} \]

(R)-2-chloro-3-oxopropionic acid

(acid highest priority so aldehyde carbonyl indicated by "oxo")

(b) 4

\[ \text{H} \quad \text{C} \quad \text{H} = \text{C} \text{H}_2 \quad \text{O} \quad \text{H} \]

In a Fischer projection if the low priority group is on a horizontal position, the configuration is the opposite of what it appears (i.e., in the horizontal, that group is coming towards us)

(R)-3-bromo-3-phenylpropene

(c) 8

\[ \text{H} \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3 \]

(3R,4S)-3-bromo-4-chloro-3-methylhexane
(d) \[ \text{Structure} \]

\[ \text{Structure} \]

\[ (2S,3S)-2\text{-methyl-}2,3\text{-butanediol} \]

(e) \[ \text{Structure} \]

\[ (2R,3S)-4\text{-chloro-}2,3\text{-dihydroxybutanal} \]

(f) \[ \text{Structure} \]

\[ (5)-1,3\text{-dichloro-}1,2\text{-propanediene} \]

(g) \[ \text{Structure} \]

"The structure in the book is poorly drawn!"

This is a trans isomer of 1,2-dichlorocyclohexane.
It must be either \((S,S)\) or \((R,R)\). It cannot be \((R,S)\)
but that is the meso cis isomer. The C-3 line is \(S\)
so this must be: \((2S,2S)-1,2\text{-dichlorocyclohexane}\.

(h) \[ \text{Structure} \]

\[ \text{Assign first} \]

\[ \text{Assign first} \]

\[ \text{Assign first} \]

\[ \text{Assign first} \]

\[ \text{Assign first} \]

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\[ \text{Assign first} \]

\[ \text{Assign first} \]

\[ \text{Assign first} \]
(i) - Similar to (g), this must be either (S,S) or (P,R). Assigning the ring carbon to the right gives R.

thus, (1R, 2R)-1,2-dimethylcyclopropane

(j) Thus, (R)-1,2-cyclononadiene

(k) Thus, (R)-1-(bromomethylidene)-1-methylcyclohexane

(l) Thus, (R)-6,6'-dime thy)-2,2'-diphenylacidi
(4) The helicene 112 goes in the clockwise direction as it goes away from the viewer, hence it is P (which corresponds to the S configuration).

(5) Dendrimer 113 has 12 chirality centers (and no E/Z isomerism of double bonds), hence $2^{12} = 4096$ possible stereoisomers.

(6) a.  

b.  

c.  

(7) a. heterotopic, stereoheterotopic, and enantiotopic.

b. heterotopic, stereoheterotopic, and diastereotopic.
(a) Chiral if it is $D_3$ point group.
(b) Chiral if it is $C_2$ point group.
(c) Chiral if it is $C_2$ point group.
(Using a model kit is most beneficial for each of the above.)

(there are many ways each of these can be drawn)

(a)

(b)
(a) 

(b) 

(c) 

(d) 

(e) 

(f) 

(g) 

(h) 

(i) 

(j) 

(k) 

(l) 

(R)-(+) -1,2-epoxybutane 

(R)-(−) -3-hexanol

- The chirality center bonds were not directly affected. 

⇒ Retention
(b) This is a Hoffmann degradation of a 2° amide to a 2° amine. No bonds directed attached to the chirality center are affected, thus retention.

(c) The 1st rxn is a substitution rxn at the O and does not change the configuration at the chirality center. The 2nd rxn is a classic $S_{N}2$ w/ inversion of configuration at the C but it stays S while the tritium (T) is not the same priority as the OTS leaving group!

(d) Even though there has been a change from S to R (bk 01 different priority than H), it overall is retention of configuration
The reagents for the transformation are butyllithium followed by an acidic workup w/ an alcohol.

- The lithium halogen exchange rxn proceeds w/ retention of configuration, and so does the second step (a simple proton transfer rxn). Thus, overall the sequence is retention.

-since priorities of substituents at C2 have not changed, inversion has occurred at C2.

-since no changes of the bonds directly attached to C3 have changed, retention at C-3.

Although the sign of the rotation has changed, the configuration in both are still D → retention.
- Each of the four CH₂ hydrogens are in a unique environment and hence should have a different \textit{H} NMR chemical shift.

- The problem is tricky because the chirality about the axis of the allene and that two chirality centers are created when the "X test" is applied to any of these 4 hydrogens.

- Since the allene is \textit{S}, the four structures resulting from the "X tests" are as follows:

\[
\begin{align*}
(S, R, R) \\
(S, R, S) \\
(S, S, R) \\
(S, S, S)
\end{align*}
\]

\[
\begin{align*}
\text{these are all diastereomeric} \\
\text{relationships!}
\end{align*}
\]

- C-3 in \textit{109} (as well as \textit{110}) is chirotopic because the molecule is chiral. Thus all atoms and spaces are chirotopic. C-3 is non-stereogenic in \textit{109} (and \textit{110}) since interchanging two groups to that atom (\textit{H} and \textit{OH}, for example) does not generate a new stereoisomer; the interchange generates the same stereoisomer (with the Fischer projection turned upside down).
The reference for this run is: LeGoff, et al, JACS, 1958, 80, p. 622. The synthetic transformations taking place here are a malonic ester synthetic method (yielding an α-alkylated acetic acid), followed by reduction of the acid to a 2° alcohol, then conversion of a bromide, following by reducing to an alkane.

\[
\begin{align*}
\text{Br} & \quad \text{H} & \quad \text{NaCH(CO}_2\text{Et})_2 & \quad \text{CH}_3 & \quad \text{CH}_3 \\
\text{C}_6\text{H}_5\text{Br} & \quad \text{H} & \quad \text{CH}_3\text{CH}_2\text{OH} & \quad \text{CH}_3\text{CH}_2\text{OH} & \quad \text{KOH, H}_2\text{O} \\
(R)-(--) & \quad (S)-(--) & \quad \text{(retention)} & \quad (S)-(--) \\
(\text{Sn2}) & \quad (\text{inversion}) & \quad (\text{retention}) & \quad (\text{all parts retention}) \\
\end{align*}
\]

The first step goes by inversion since \( \text{Sn2} \). The next 3 transformations are all w/ retention of configuration (no bonds connected to the chirality center are changed). Overall, thus, the run converts \((R)-(\cdot)-2\)-bromo-octane to \((R)-(\cdot)-3\)-methyl-2-hexane with net inversion of configuration (so again this problem emphasizes the \( R/S \) and \( t/s \) designations do not, mof by themselves, indicate the stereochemical changes!).

(15) a) With no isotopic labels present, the parent reaction is stereoselective but not stereospecific. This is because stereoisomeric reactants are not possible w/o labelling.
The reaction takes place with inversion of configuration and without removal of the pro-(R) carboxyl group.

Some review needed for this problem: a basic Baeyer-Villiger reaction oxidizes a ketone to an ester:

\[ \text{R-C} - \text{R'} \xrightarrow{\text{B-V. oxid.}} \text{R-C} \text{O} - \text{R'} \]

And a LiAlH₄ reduction of an ester leads to two alcohols:

\[ \text{R-C} \text{O} - \text{R'} \xrightarrow{1) \text{LiAlH}_4} \xrightarrow{2) \text{H}^+} \text{RCH}_3\text{OH} + \text{R'OH} \]
Here are the reactants and products as described in the problem:

The answer book has a solid review of this problem. It is reproduced on the next page.
In order to determine the threeo and erythro designations, it is helpful to redraw selected portions of the molecule as Fischer projections. One example is shown above.

Note that the stereochemical designations do not change because the hexaepi structure is the mirror image of the original structure along the affected portions of the molecule. The hexaepi structure is not the enantiomer of the original structure, however, because the configuration of the chiral center in the lactone group is not changed.

The optical purity of the sample is \( \frac{16.19}{23.13} = 0.70 \) or 70%.

If we say the major enant = \( x \) and minor enant = \( y \), then:

\[ x + y = 100 \]

Thus, \( (70+y) + y = 100 \)

and \( x - y = 70 \)

so, \( x = 70 + y \)

so, \( x = 70 + y \)

\[ 2y = 30 \]

\[ y = 15 \]

So, the major enantiomer is 85% and the (R)-enantiomer is 15%.
(19) Simply invert the configuration at C-2:

![Chemical structure diagram]

2-epi-195A


Here's the compound:

![Chemical structure diagram]

Due to the chirality center at C-2, the methylene hydrogens at C-1 are diastereotopic and they should appear as separate signals in a $^1H$ NMR spectrum unless something "unusual" is happening. One possibility is that at high temps the reversible dissociation of the C-Mg bond occurs faster than the NMR timescale, leading to their environments being averaged.