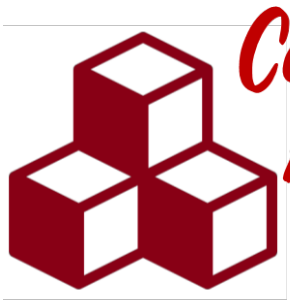
Montogue

Quiz CH210

Organic Chemistry



Carbohydrates, Amino Acids and Lipids

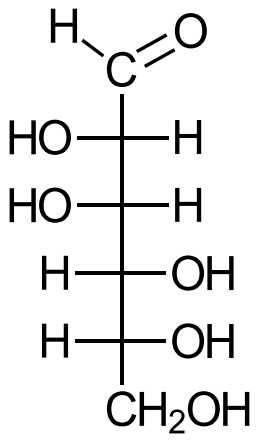
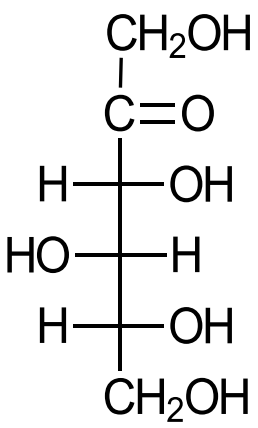
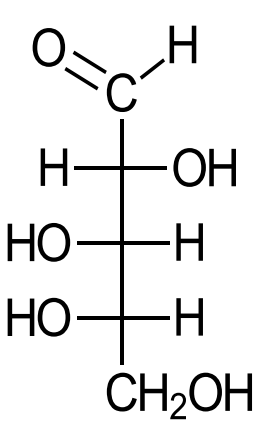
Lucas Monteiro Nogueira

PROBLEMS

Part I: Carbohydrates

Problem 1

Classify each of the following carbohydrates as an aldose or ketose and insert the appropriate term to indicate the number of carbons present (e.g., an *aldopentose*). Next, determine whether each of these carbohydrates is a *D* sugar or a *L* sugar and assign a configuration for each chiral center.

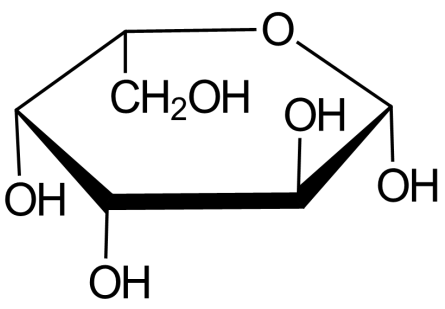
1.1	1.2	1.3
		

Problem 2

Problem 2.1: Draw a Haworth projection for each of the following compounds. Fischer projections of simple carbohydrates can be found in the Additional Information section.

2.1.1. *α-D*-Mannopyranose
2.1.2. *β-D*-Mannopyranose
2.1.3. *α-D*-Allopyranose
2.1.4. *β-D*-Galactopyranose
2.1.5. *α-L*-Glucopyranose

Problem 2.2: Draw a Fischer projection of the following carbohydrate.



▶ Problem 3

Problem 3.1: Draw the most stable chair conformation of the following carbohydrates.

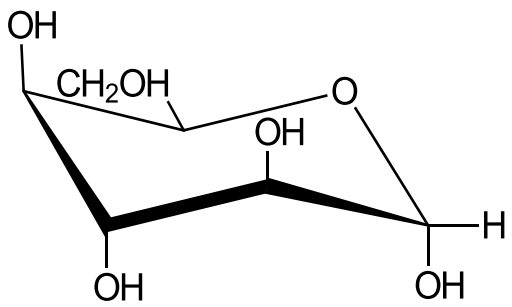
3.1.1. α-*D*-Mannopyranose

3.1.2. α-*D*-Allopyranose

3.1.3. β-*D*-Galactopyranose

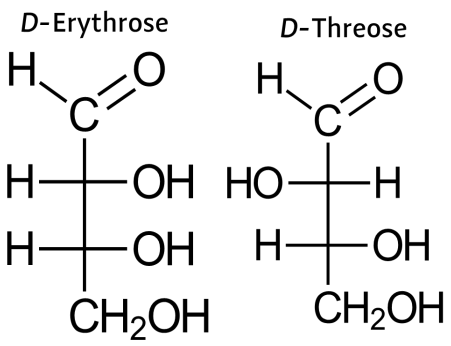
3.1.4. α-*L*-Glucopyranose

Problem 3.2: Draw a Fischer projection for the following carbohydrate.



▶ Problem 4

Consider the structures of the following two *D*-aldotetroses. Each of these compounds exists as a furanose ring, which is formed when the OH at C4 attacks the aldehyde group. Draw the furanose rings for the following carbohydrates.



4.1. α-*D*-Erythrofuranose

4.2. β-*D*-Threofuranose

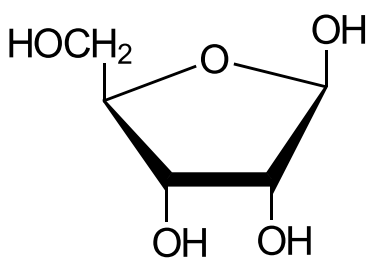
▶ Problem 5 (McMurry, 2008)

5.1. Reduction of *D*-glucose leads to an optically active alditol (*D*-glucitol), whereas reduction of *D*-galactose leads to an optically inactive alditol. Explain.

5.2. Reduction of *L*-gulose with $NaBH_4$ leads to the same alditol (*D*-glucitol) as reduction of *D*-glucose. Explain.

▶ Problem 6 (McMurry, 2008)

Draw the products you would obtain by reaction of β-*D*-ribofuranose, shown below, with:



6.1. $(CH_3CO)_2O$, pyridine

6.2. CH_3I, Ag_2O

▶ Problem 7 (McMurry, 2008)

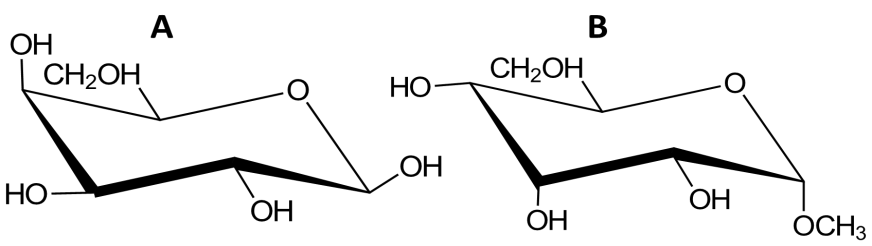
All aldoses exhibit mutarotation. For example, α-*D*-galactopyranose has specific rotation $[\alpha]_D = +150.7^\circ$ and β-*D*-galactopyranose has specific rotation $[\alpha]_D = +52.8^\circ$. If either anomer is dissolved in water and allowed to reach equilibrium, the specific rotation of the solution is $+80.2^\circ$. What are the percentages of each anomer at equilibrium?

▶ Problem 8

Regarding carbohydrate science, evaluate the following statements as true or false. The Additional Information section may prove useful.

1.( ) All aldoses are reducing sugars, but no known ketose is a reducing sugar.

2.( ) The stable chair conformation of two sugars in their pyranose forms, A and B, are shown below. We can surmise that molecule A is a reducing sugar, while molecule B is *not* a reducing sugar.



3.( ) Oxidation of an aldose by a powerful oxidizing agent such as HNO_3 yields dicarboxylic acids. Aldose-derived dicarboxylic acids are known as aldaric acids.

4.( ) Kiliani-Fischer lengthening of *D*-arabinose should yield a mixture of *D*-allose and *D*-altrose.

5.( ) *D*-Threose can undergo Kiliani-Fischer lengthening to yield a mixture of *D*-xylose and *D*-lyxose.

6.( ) Two of the four aldopentoses, namely *D*-ribose and *D*-xylose, yield *D*-erythrose upon undergoing Wohl degradation.

Part II: Amino Acids

▶ Problem 9

Regarding amino acid science, evaluate the following statements as true or false. The Additional Information section may prove useful.

1.( ) The α carbon of all 20 common amino acids is a chirality center.

2.( ) Of the 20 common amino acids, 19 are primary amines. Only proline is a secondary amine.

3.( ) In addition to the nitrogen associated with the amine group, some common amino acids have extra N atoms. This is the case of asparagine and glutamine, which have amide groups.

4.( ) Two of the 20 common amino acids have sulfur atoms. Methionine has a thiol group, while cysteine has a thioether (sulfide) group.

5.( ) Three of the 20 common amino acids have aromatic rings.

6.( ) Of the 19 *L* amino acids, 18 have the *S* configuration at the α carbon. Cysteine is the only common amino acid that has an *R* configuration.

▶ Problem 10

Draw the form of the amino acid that is expected to predominate at the stated pH. Refer to the Additional Information section for amino acid structures and pK_a values.

10.1. Alanine at a pH of 10.
10.2. Proline at a pH of 10
10.3. Tyrosine at a pH of 9
10.4. Asparigine at physiological pH (≈7.4)
10.5. Histidine at physiological pH
10.6. Glutamic acid at a pH of 2

▶ Problem 11

Problem 11.1: Calculate the p*I* of the following amino acids.

11.1.1. Glycine
11.1.2. Aspartic acid
11.1.3. Lysine
11.1.4. Tyrosine

Problem 11.2: (*Klein, 2017*) A mixture containing phenylalanine, tryptophan, and leucine was subjected to electrophoresis. Determine which of the amino acids moved the farthest distance assuming that the experiment was performed at the pH indicated.

11.2.1. pH = 6.0	**11.2.2.** pH = 5.0

▶ Problem 12

Problem 12.1: What alkyl halides would you use to prepare the following α-amino acids by the amidomalonate method?

12.1.1. Leucine

12.1.2. Tyrosine

12.1.3. Methionine

12.1.4. Histidine

Problem 12.2: (*Klein, 2017*) Consider the following observations.

12.2.1. Under similar conditions, alanine and valine were each prepared with an amidomalonate synthesis, but alanine was obtained in higher yields than valine. Explain.

12.2.2. The amidomalonate synthesis can be used to prepare amino acids from alkyl halides. When the amidomalonate synthesis is used to make glycine, no alkyl halide is required. Explain.

▶ Problem 13

Draw the products that are expected when each of the following amino acids is treated with ninhydrin.

13.1. *L*-Leucine

13.2. *L*-Threonine

13.3. *L*-Glutamine

13.4. *L*-Proline

Part III: Lipids

▶ Problem 14

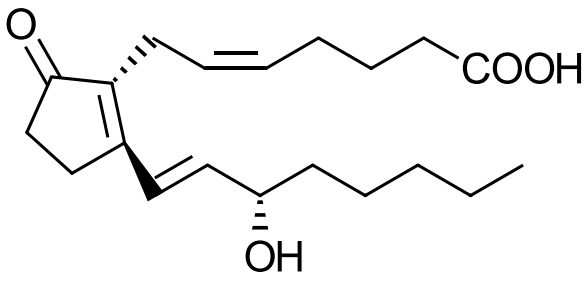
Regarding lipid science, evaluate the following statements as true or false. The Additional Information section may prove useful.

1.( ) Arachidic acid has a greater melting point than stearic acid, which in turn has a greater melting point than palmitic acid.

2.( ) A triglyceride constructed from one equivalent of glycerol and three equivalents of stearic acid is likely more soluble in water than a diglyceride constructed from one equivalent of glycerol and two equivalents of stearic acid.

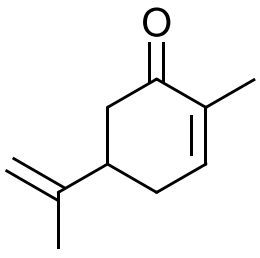
3.( ) Phosphoglycerides that contain ethanolamine are called *cephalins*, while those that contain choline are called *lecithins*.

4.( ) The hypothetical prostaglandin illustrated below is labeled PGB_3.



5.( ) We can surmise that water is more appropriate for extracting terpenes from plant tissues than hexane.

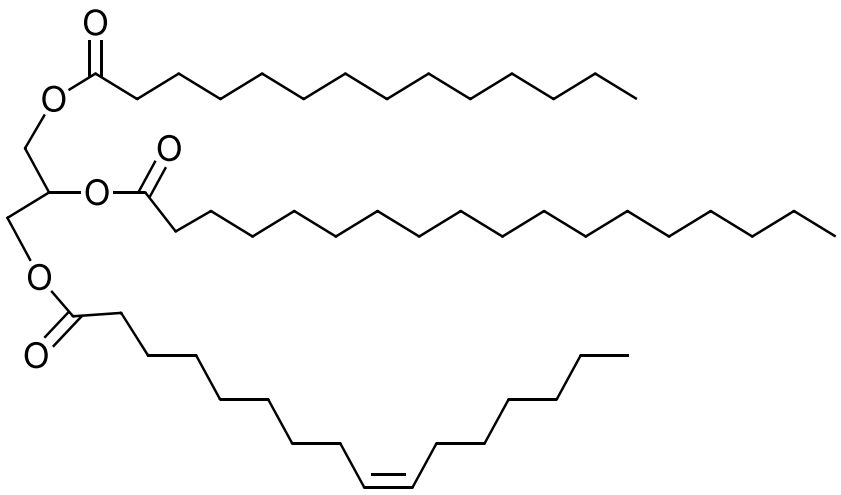
6.( ) The following molecule, carvone, is a terpene.



▶ Problem 15

15.1. An achiral triglyceride was hydrolyzed to yield one equivalent of myristic acid and two equivalents of lauric acid. Draw the structure of the triglyceride.

15.2. Identify the products that are expected when the triglyceride drawn in the next page is hydrolyzed with aqueous sodium hydroxide. With reference to the Additional Information section, answer: from which fatty acids is this triglyceride derived?



▶ Problem 16 (Carey, 2008)

Describe an efficient synthesis of each of the following compounds from octadecanoic (stearic) acid using any necessary organic or inorganic reagents.

16.1. Octadecane
16.2. 1-Phenyloctadecane
16.3. 3-Ethylicosane
16.4. Icosanoic acid
16.5. 1-Octadecanamine
16.6. 1-Heptadecanamine
16.7. 1-Nonadecanamine

▶ Problem 17 (McMurry, 2008)

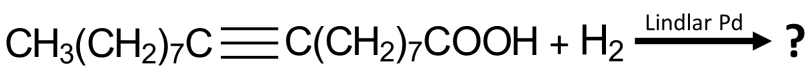
Describe an efficient synthesis of each of the following compounds from 9-octadecenoic (oleic) acid using any necessary organic or inorganic reagents.

17.1. Methyl oleate
17.2. Methyl stearate (methyl octadecanoic acid)
17.3. Nonanal
17.4. Nonanedioic acid
17.5. 9-Octadecynoic acid (stearolic acid)
17.6. 18-Pentatriacontanone, $CH_3(CH_2)_{16}CO(CH_2)_{16}CH_3$

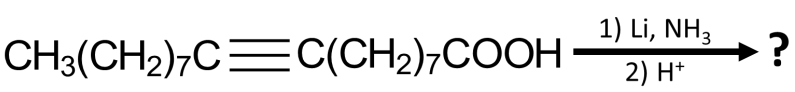
▶ Problem 18 (Carey, 2008)

Identify the products of the following reactions.

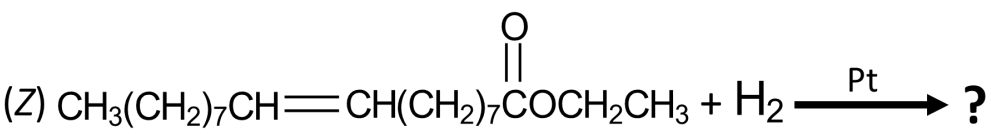
18.1.



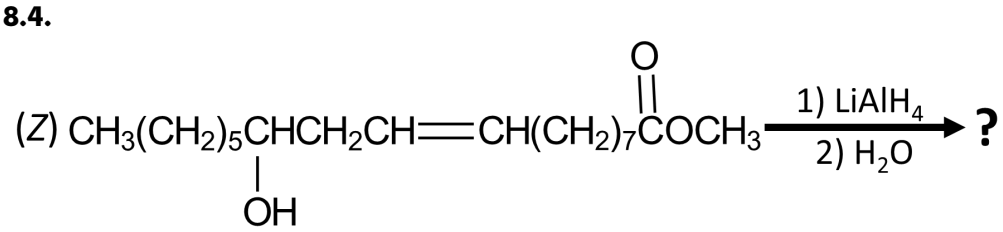
18.2.



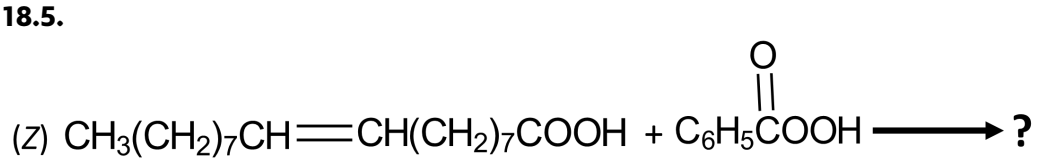
18.3.



18.4.

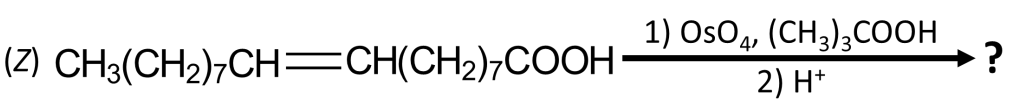


18.5.



18.6. Product of Problem 18.5 + H_3O^+

18.7.



ADDITIONAL INFORMATION

Figure 1 *D*-aldoses with three to six carbon atoms.

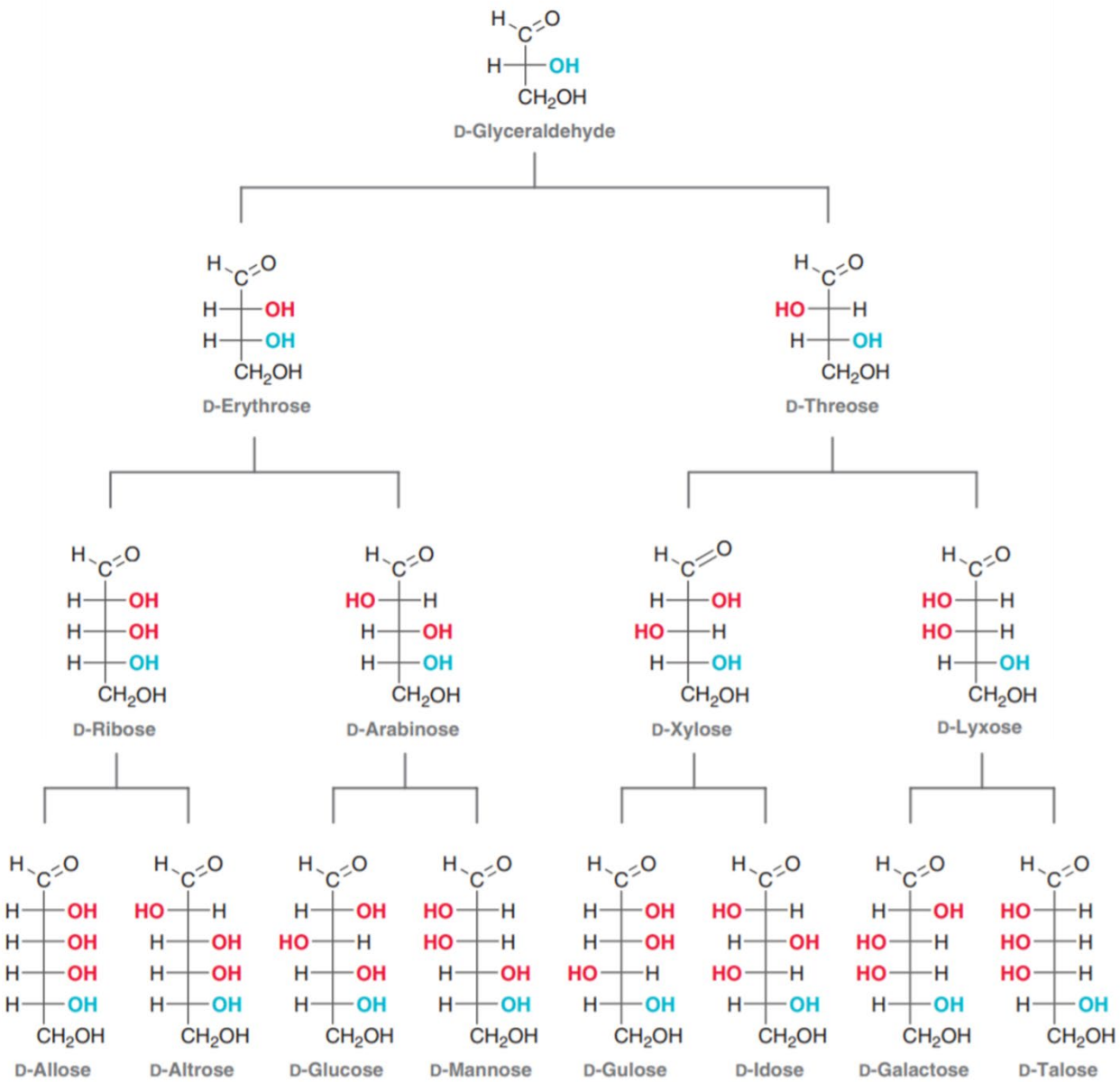


Figure 2 Common fatty acids.

Name	Carbons	Structure
Saturated acids		
lauric acid	12	COOH
myristic acid	14	COOH
palmitic acid	16	COOH
stearic acid	18	COOH
arachidic acid	20	COOH
Unsaturated acids		
oleic acid	18	COOH
linoleic acid	18	COOH
linolenic acid	18	COOH
eleostearic acid	18	COOH
arachidonic acid	20	COOH

Figure 3 Common amino acids.

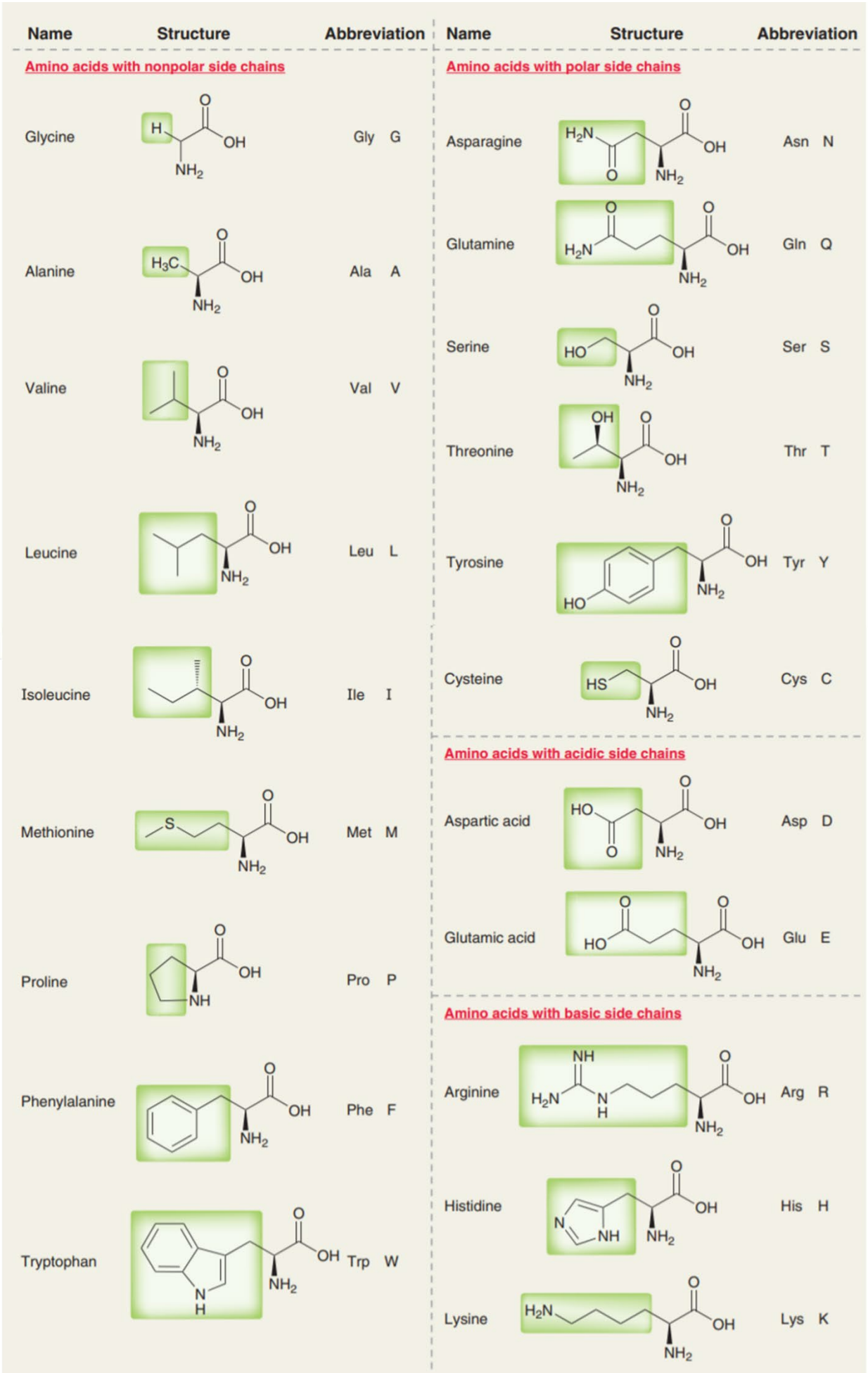


Table 1 pK_a values for common amino acids.

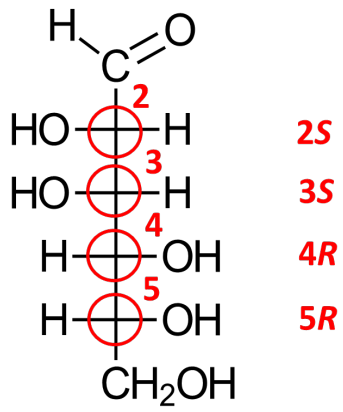
AMINO ACID	α-COOH	α-NH_3^+	SIDE CHAIN
Alanine	2.34	9.69	—
Arginine	2.17	9.04	12.48
Asparagine	2.02	8.80	—
Aspartic acid	1.88	9.60	3.65
Cysteine	1.96	10.28	8.18
Glutamic acid	2.19	9.67	4.25
Glutamine	2.17	9.13	—
Glycine	2.34	9.60	—
Histidine	1.82	9.17	6.00
Isoleucine	2.36	9.60	—
Leucine	2.36	9.60	—
Lysine	2.18	8.95	10.53
Methionine	2.28	9.21	—
Phenylalanine	1.83	9.13	—
Proline	1.99	10.60	—
Serine	2.21	9.15	—
Threonine	2.09	9.10	—
Tryptophan	2.83	9.39	—
Tyrosine	2.20	9.11	10.07
Valine	2.32	9.62	—

SOLUTIONS

P.1 ➡ *Solution*

1.1: This carbohydrate is an aldehyde and has six carbons, so it is an *aldohexose*. The chiral center farthest from the carbonyl group has a hydroxyl to the right in the Fischer projection, so it is a *D* carbohydrate.

To classify the configuration of each chiral center, consider the following rule: a chiral center is *R* when the hydroxyl is to the right of the carbon in a Fischer projection, and *S* when the hydroxyl is to the left. Accordingly, we posit the following configurations for each chiral center, numbering carbons such that 1 is attributed to the uppermost carbon.

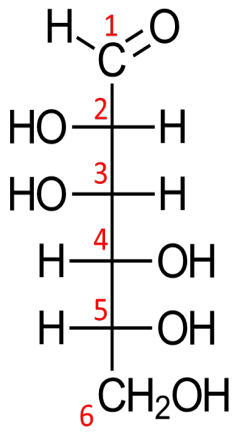


1.2 and 1.3: The classifications of the two other molecules are provided below.

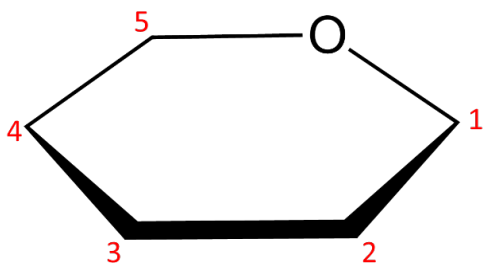
Problem	Classification	*L* or *D*?	Chiral center stereochemistry
1.2	Ketohexose	*D*	3*R*, 4*S*, 5*R*
1.3	Aldopentose	*L*	2*R*, 3*S*, 4*R*

P.2 ➡ *Solution*

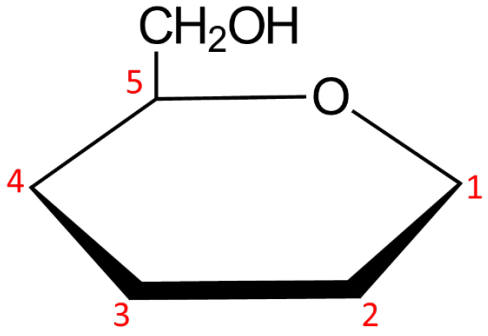
2.1.1: The Fischer projection of *D*-mannose is given in the next page. Carbons are numbered 1 to 6, starting at the carbonyl group.



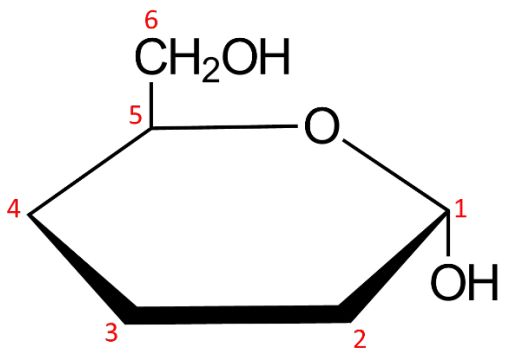
Let's work out how to draw a Haworth projection with the information conveyed by a Fischer projection. We begin by drawing a hexagonal ring with the oxygen atom usually in the back right corner. Positions C1 to C5 are numbered clockwise, starting with the carbon to the right of the oxygen atom.



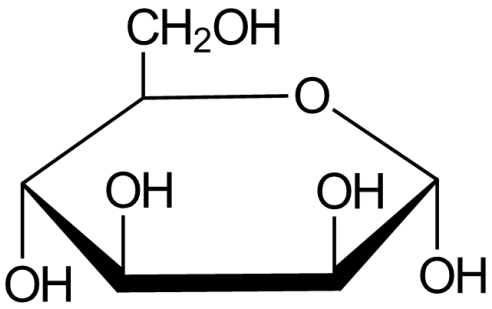
A pyranose ring contains only five carbon atoms, but mannose has six. This difference can be easily reconciled if we note that carbon 6 (i.e., the one farthest from the carbonyl group in a Fischer projection) is written as a CH_2OH group and attached to the C5 position. The *D* in the name of the carbohydrate indicates that the CH_2OH group must be in the up position in the pyranose ring.



One position of the pyranose carbon has been established. We can now turn to the remaining positions. The configuration at C1, the anomeric carbon, is given in the name of the pyranose ring form. The term *alpha* means that the OH group at the C1 position must be down (*trans* to the CH_2OH group).

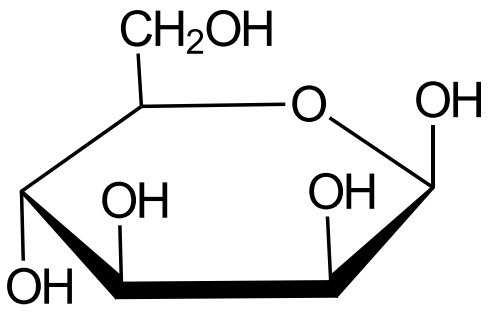


The remaining chiral centers (C2, C3, and C4) are drawn using the following rule: any OH groups on the right side of the Fischer projection of the open-chain form will be pointing down in the Haworth projection of the cyclic form, while any OH groups on the left side of the Fischer projection will be pointing up in the Haworth projection. This rule leads to the following structure.

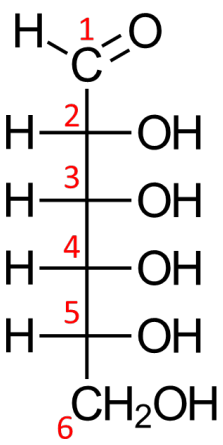


The Haworth projection of α-*D*-mannopyranose has been established.

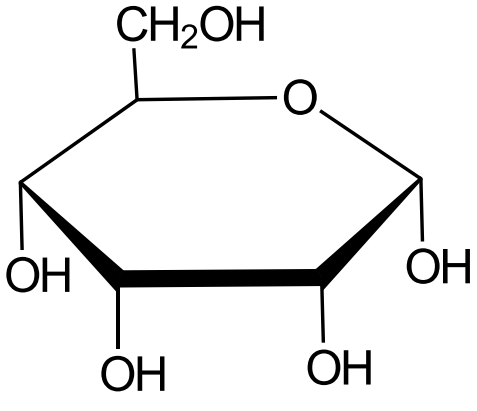
2.1.2: The structure of *D*-mannose was given in the previous problem, and the Haworth projection of α-*D*-mannopyranose was developed therein. The only difference between the Haworth projection of α-*D*-mannopyranose and that of β-*D*-mannopyranose is the position of the hydroxyl attached to the anomeric (C1) carbon, which should be pointing up in the latter.



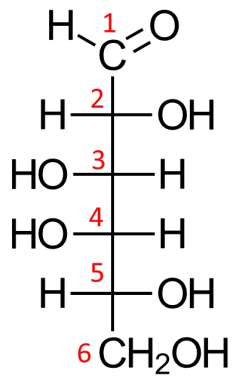
2.1.3: The Fischer projection of *D*-allose is given below.



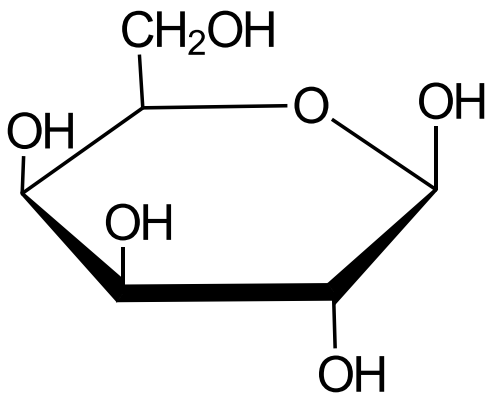
Converting this Fischer projection to a Haworth projection is no different from the approach outlined in Problem 2.1.1. We begin by positioning the CH_2OH group upward in the C5 position (because the sugar in question is a *D* molecule). Next, we place an OH group downward in the C1 position (because the sugar in question is an α anomer). Lastly, we locate the hydroxyl groups of carbons C2, C3, and C4, which are all to the right in the Fischer projection and hence should be pointing down in the corresponding Haworth projection.



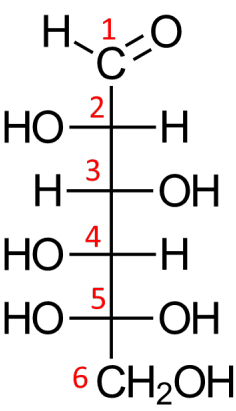
2.1.4: The Fischer projection of *D*-galactose is given in the next page.



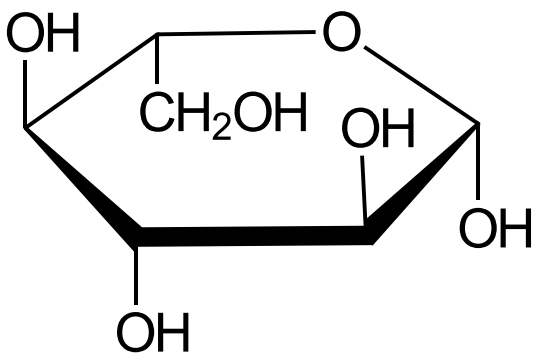
Converting this Fischer projection to a Haworth projection is no different from the approach outlined in Problem 2.1.1. We begin by positioning the CH_2OH group upward in the C5 position (because the sugar in question is a *D* molecule). Next, we place an OH group upward in the C1 position (because the sugar in question is an β anomer). Lastly, we locate the hydroxyl groups of carbons C2, C3, and C4.



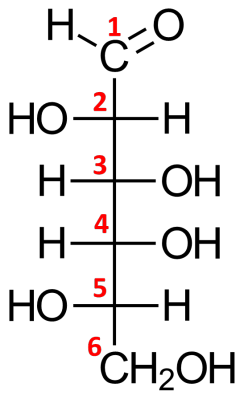
2.1.5: The Fischer projection of *L*-glucose is shown below.



Converting this Fischer projection to a Haworth projection is no different from the approach outlined in Problem 2.1.1. We begin by positioning the CH_2OH group downward in the C5 position (because the sugar in question is a *L* molecule). Next, we place an OH group upward in the C1 position (because the sugar in question is an β anomer). Lastly, we locate the hydroxyl groups of carbons C2, C3, and C4.

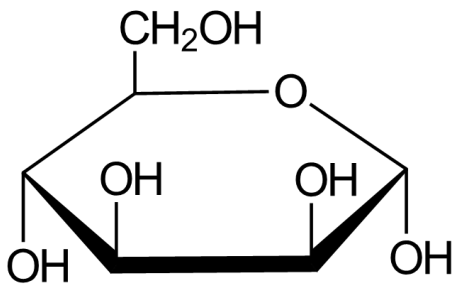


2.2: The CH_2OH group is pointing down; accordingly, this is a *L* carbohydrate and the C5 carbon has the hydroxyl pointing to the left in the Fischer projection. Carbon C2 is pointing up, and hence should appear with the hydroxyl to the left in the Fischer projection. Carbons C3 and C4 are pointing down, and hence should appear with the hydroxyl to the right in the Fischer projection. The open-chain molecule we are looking for is shown below. This sugar is *L*-altrose.

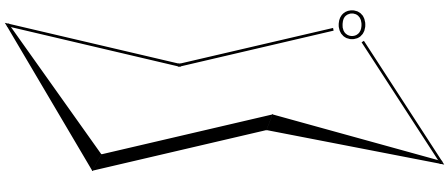


P.3 ➡ ***Solution***

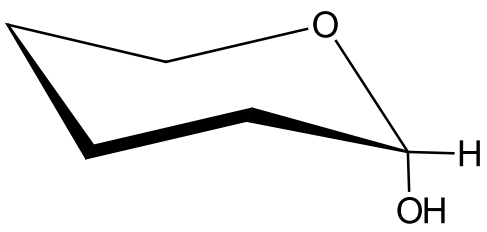
3.1.1: The Haworth projection of *α-D*-mannopyranose is shown below.



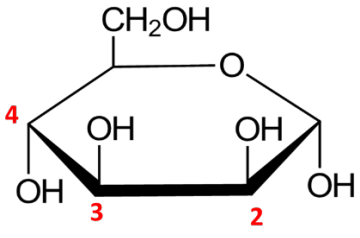
We begin by placing the oxygen on the upper, rear-right corner. Needless to say, other configurations are possible.

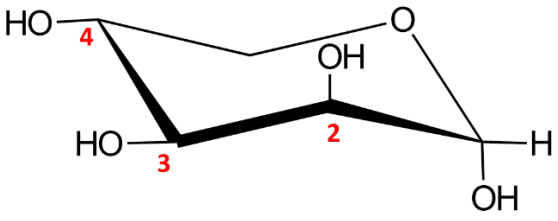


The alpha in the name of the molecule indicates that the hydroxyl attached to the anomeric carbon should be drawn pointing down. Were the sugar in question a beta molecule, the anomeric carbon would have its hydroxyl pointing up.

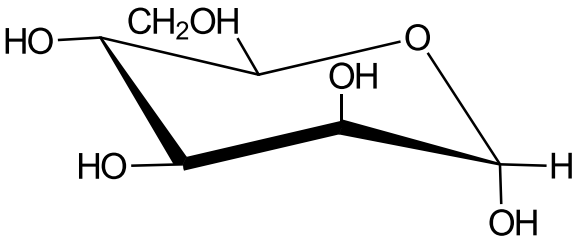


Then, we distribute the three remaining hydroxyls.

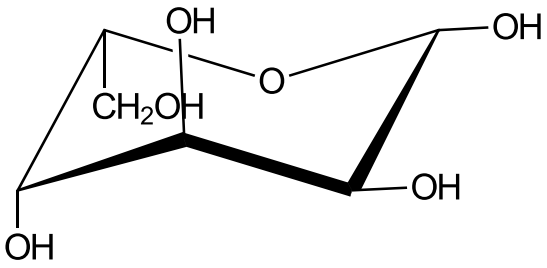




Lastly, we place the CH_2OH group, which is pointing up in the Haworth projection.

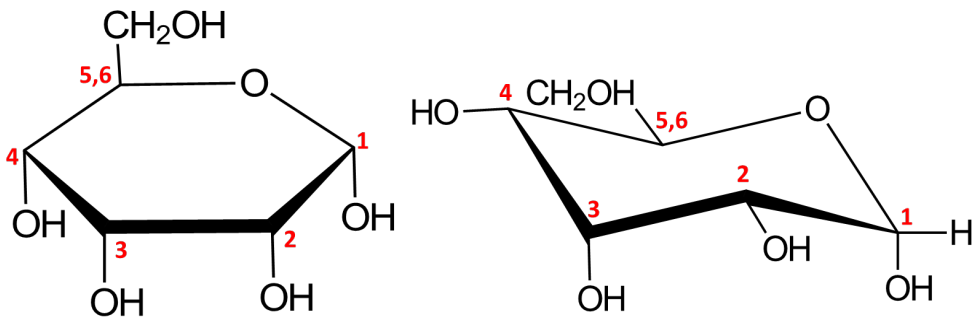


The first chair conformation has been drawn. Now, recall that the other chair conformation is made by performing a *ring flip*, in which all axial positions become equatorial positions and all equatorial positions become axial positions. This conformation is drawn below.



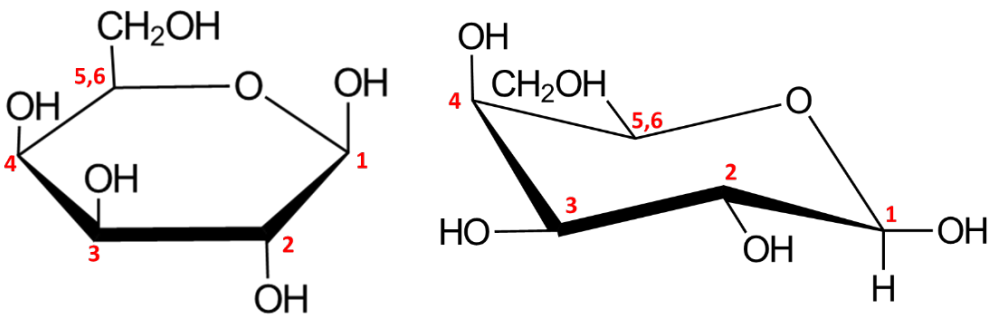
The most stable chair conformation is the one in which the largest groups occupy equatorial positions. In the present case, the first conformation we drew has two hydroxyls and the CH_2OH group – which is the bulkiest substituent – in equatorial positions. Accordingly, the first chair conformation is more stable than the second.

3.1.2: The conversion from Haworth projection to chair conformation is outlined below.



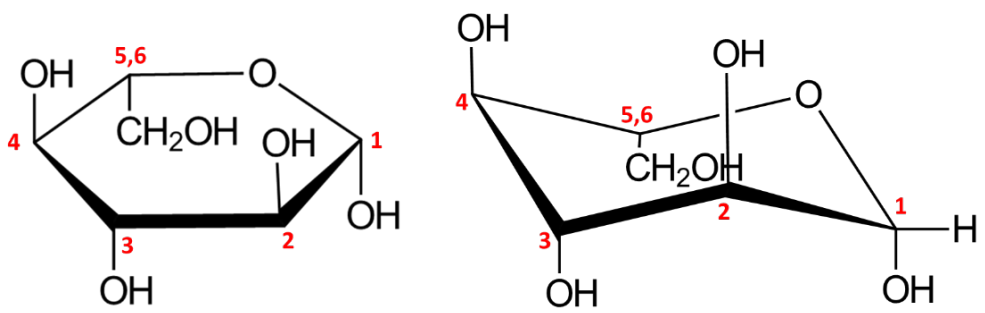
Try performing a ring flip and drawing the other chair conformation yourself. The chair conformation we drew has the CH_2OH group in an equatorial position and is therefore more stable than the alternative conformation.

3.1.3: The conversion from Haworth projection to chair conformation is outlined below.



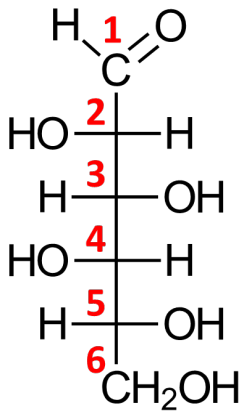
Try performing a ring flip and drawing the other chair conformation yourself. The chair conformation we drew has the CH_2OH group in an equatorial position and is therefore more stable than the alternative conformation.

3.1.4: The conversion from Haworth projection to chair conformation is outlined below.



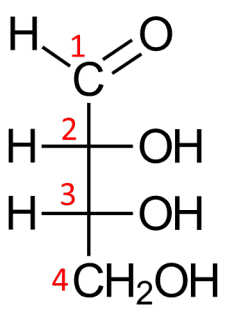
In contrast to previous problems, in this chair conformation the CH_2OH group and all hydroxyls are not on equatorial positions, leading us to conclude that this is *not* the most stable chair conformation. Try drawing the stable chair conformation yourself.

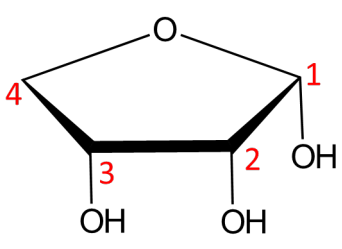
3.2: The anomeric position becomes an aldehyde in the open-chain form. The OH group at C5 must be pointing to the right, because this is a *D* sugar (CH_2OH is "up" in the chair conformation). Carbon C2 must be pointing to the left in the Fischer projection, because it is pointing "up" in the chair conformation. Carbon C3, in turn, must be pointing to the right in the Fischer projection, because it is pointing "down" in the chair conformation. Carbon C4 must be pointing to the left in the Fischer projection. The open chain form of the carbohydrate is shown below. The carbohydrate in question is *D*-idose.



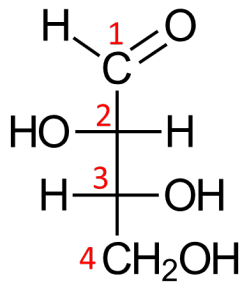
P.4 ➡ *Solution*

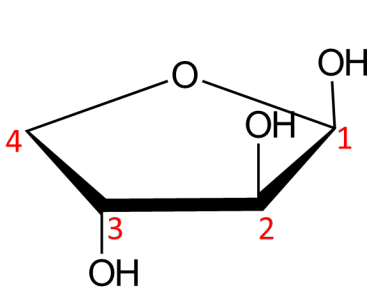
4.1: The anomeric OH group is drawn pointing down (because it is the α anomer). The remaining two OH groups (at C2 and C3) are both on the right side of the Fischer projection of *D*-erythrose, so both OH groups are drawn pointing down in the Haworth projection.





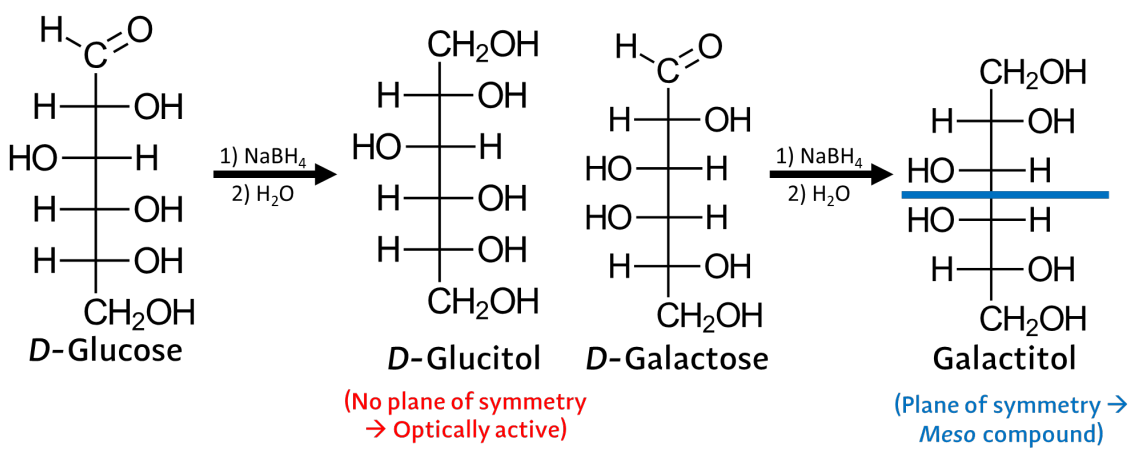
4.2: The anomeric OH group is drawn pointing up (because it is the β anomer). Carbon C2 in the Fischer projection has the hydroxyl on the left side, and hence should be drawn pointing up in the Haworth projection. Carbon C3 has the hydroxyl on the right side, which means that it should be drawn pointing down in the Haworth projection.



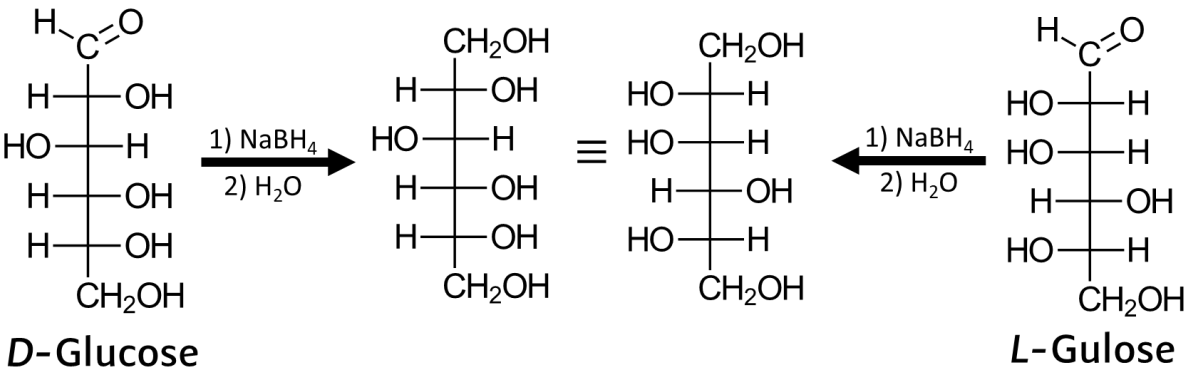


P.5 ➡ *Solution*

5.1: Reaction of *D*-galactose with a reducing agent such as $NaBH_4$ yields *D*-glucitol, an optically active alditol. A similar reaction, when applied to *D*-galactose, yields an alditol that has a plane of symmetry and is a *meso* compound.

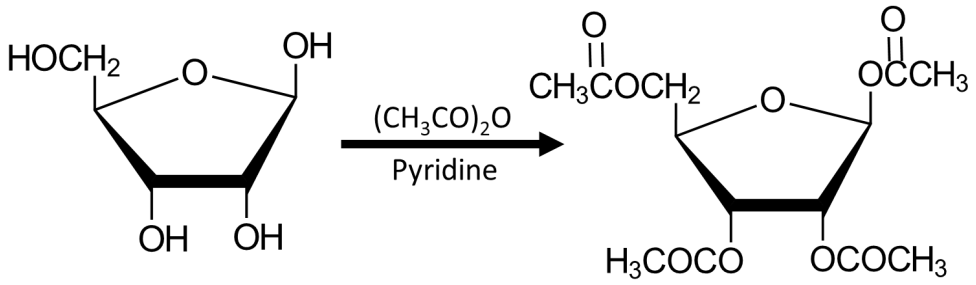


5.2: Reaction of an aldose with $NaBH_4$ produces a polyol (alditol). Because an alditol has the same functional group at both ends, two different aldoses can yield the same alditol. Here, *L*-gulose and *D*-glucose form the same alditol; to see this, rotate the Fischer projection of *L*-gulitol 180 degrees and you should get *D*-glucitol.

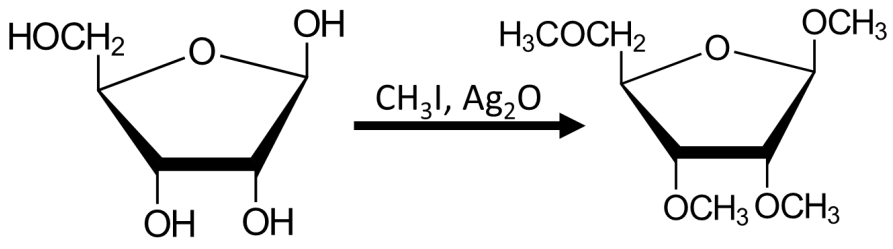


P.6 ➡ *Solution*

6.1: Treatment of sugars with acid anhydrides and acid chlorides in the presence of a base leads to esterification.



6.2: Carbohydrates are converted into ethers by treatment with an alkyl halide in the presence of base. Strong bases tend to degrade sugar molecules, but mild bases such as Ag_2O work well and give high yields of ethers.



P.7 ➡ *Solution*

Let x be the percentage of *D*-galactose present as the α anomer and y be the percentage of *D*-galactose present as the β anomer. Thus, we may write

$$150.7^{\circ}\,x + 52.8^{\circ}\,y = 80.2^{\circ}$$

Since $x + y = 1$, or $x = 1 - y$, we have

$$150.7^{\circ}(1-y) + 52.8^{\circ}\,y = 80.2^{\circ}$$

$$\therefore 150.7 - 150.7y + 52.8y = 80.2$$

$$\therefore -97.9y = -70.5$$

$$\therefore y = 0.72$$

That is, 72% of the solution is constituted of the β anomer. In turn, 100 – 72= 28% of the solution is constituted of the α anomer.

P.8 ➡ *Solution*

1. False. A sugar is said to be *reducing* if it lends itself to typical tests such as Tollens' reagent, Fehling's reagent, and Benedict's reagent. All aldoses are reducing sugars because they contain an aldehyde group, but some ketoses are reducing, too. Fructose, for example, reduces Tollens' reagent, even though it contains no aldehyde group. Reduction occurs because fructose is readily isomerized to an aldose in basic solution by a series of keto-enol tautomeric shifts.

2. True. For a carbohydrate to be a reducing sugar, the anomeric carbon must be linked to a hydroxyl. In chair conformation A, this carbon is indeed linked to a hydroxyl; thus, carbohydrate A is a reducing sugar. In chair conformation B, the anomeric carbon is linked to a methoxy (OCH_3) group; accordingly, carbohydrate B is not a reducing sugar.

3. True. For a carbohydrate to be a reducing sugar, the anomeric carbon should be linked to a hydroxyl. In chair conformation A, this carbon is indeed linked to a hydroxyl; thus, carbohydrate A is a reducing sugar. In chair conformation B, the anomeric carbon is linked to a methoxy (OCH_3) group; accordingly, carbohydrate B is not a reducing sugar.

4. False. In Kiliani-Fischer synthesis of a sugar, the aldose chain is lengthened by one carbon; the C1 aldehyde group of the starting sugar becomes C2 of the chain-lengthened sugar, and a new C1 carbon is added. An aldopentose such as *D*-arabinose is converted to two hexoses, differing only in their stereochemistry at C2. Referring to the Figure 1 in the Additional Information section, we see that lengthening of *D*-arabinose should yield *D*-glucose and *D*-mannose. *D*-Allose and *D*-altrose are products of lengthening of *D*-ribose.

5. True. As explained in the answer to the previous statement, Kiliani-Fischer synthesis increases the carbon count of a sugar by one unit. With reference to Figure 1, we see that the lengthening descendants of *D*-threose indeed are *D*-xylose and *D*-lyxose.

6. False. Wohl degradation is the reverse equivalent of Kiliani-Fischer lengthening, yielding a sugar with one less carbon than the starting molecule. With reference to Figure 1 in the Additional Information section, we see that *D*-ribose and *D*-arabinose become *D*-erythrose when their chains are shortened; Wohl degradation of *D*-xylose actually yields *D*-threose.

P.9 ➡ *Solution*

These statements can be easily evaluated with recourse to Figure 3 in the Additional Information section.

1. False. The α carbon of glycine is linked to two hydrogens and does not constitute a chirality center.

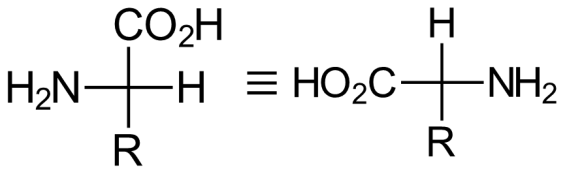
2. True. Proline is a secondary amine and the only amino acid whose nitrogen and α carbon atoms are part of a ring.

3. True. Recall that an amide function is essentially a carbonyl group attached to an amino group. Asparagine and glutamine indeed have amide groups.

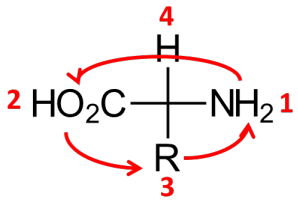
4. False. The definitions have been swapped; in actuality, methionine has a a thioether group and cysteine has a thiol group.

5. False. There are four common amino acids endowed with aromatic rings, namely phenylalanine, tyrosine, tryptophan and histidine.

6. True. A Fischer projection of the α-carbon of an *L*-amino acid is pictured below.

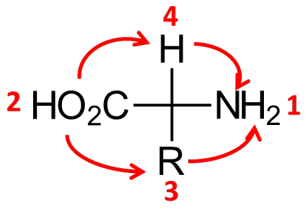


For most *L* amino acids, the group priority distribution indicates that they have an *S* configuration, as shown.



Group	Priority
$-NH_2$	1
$-CO_2H$	2
$-R$	3
$-H$	4

For cysteine, however, the group priority distribution imply that they have an *R* configuration, as shown.

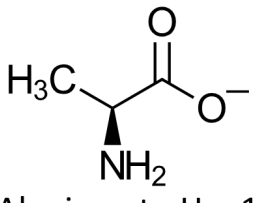


Group	Priority
$-NH_2$	1
$-CH_2SH$	2
$-CO_2H$	3
$-H$	4

P.10 ➡ *Solution*

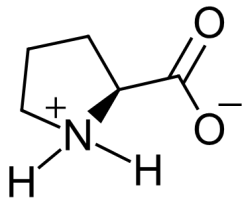
In each case, we first identify the pK_a of the carboxylic acid group and determine which form predominates. The protonated form (COOH) will predominate if pH < pK_a, while the carboxylate ion will predominate if pH > pK_a. Next, we identify the pK_a of the α-amino group and determine which form predominates. The protonated form (RNH_3^+) will predominate if pH < pK_a, while the uncharged form (RNH_2) will predominate if pH > pK_a. If necessary, a similar analysis is applied to the side chain.

10.1: The pK_a of the α-COOH group of alanine is 2.34; since pH = 10 > 2.34, the α-carboxylic acid group of alanine should mainly occur in the carboxylate ion form. The pK_a of the α-NH_3^+ group of alanine is 9.69; since pH = 10 > 9.69, the α-amino group of alanine should mainly occur in the uncharged form.



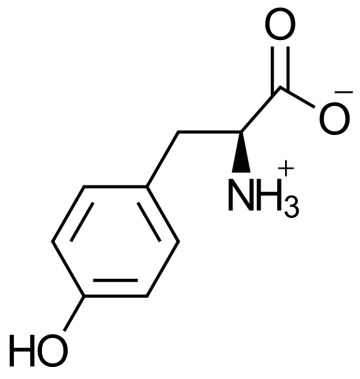
Alanine at pH = 10

10.2: The pK_a of the α-COOH group of alanine is 1.99; since pH = 10 > 1.99, the α-carboxylic acid group of proline should mainly occur in the carboxylate ion form. The pK_a of the α-NH_3^+ group of proline is 10.6; since pH = 10 < 10.6, the α-amino group of proline should mainly occur in the protonated form.



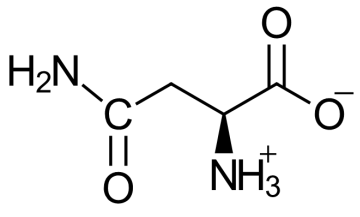
Proline at pH = 10

10.3: The pK_a of the α-COOH group of tyrosine is 2.20; since pH = 9 > 2.20, the α-carboxylic acid group of tyrosine should mainly occur in the carboxylate ion form. The pK_a of the α-NH_3^+ group of tyrosine is 9.11; since pH = 9 < 9.11, the α-amino group of tyrosine should mainly occur in the protonated form. We also have to consider the phenol group in the side chain of tyrosine. The side chain pK_a is 10.07; since pH = 9 < 10.07, we surmise that tyrosine's phenol group will occur mainly in the protonated form.



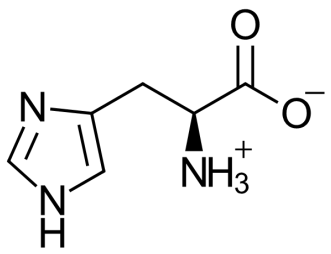
Tyrosine at pH = 9

10.4: The pK_a of the α-COOH group of asparigine is 2.02; since pH = 7.4 > 2.02, the α-carboxylic acid group of asparigine should mainly occur in the carboxylate ion form. The pK_a of the α-NH_3^+ group of asparigine is 8.8; since pH = 7.4 < 8.8, the α-amino group of asparigine should mainly occur in the protonated form.



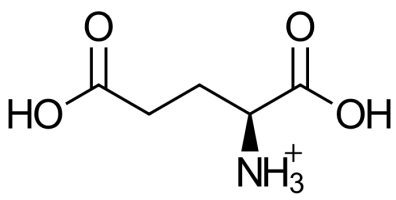
Asparigine at
physiological pH

10.5: The pK_a of the α-COOH group of histidine is 1.82; since pH = 7.4 > 1.82, the α-carboxylic acid group of histidine should mainly occur in the carboxylate ion form. The pK_a of the α-NH_3^+ group of histidine is 9.17; since pH = 7.4 < 9.17, the α-amino group of histidine should mainly occur in the protonated form. We also have to consider the basic nitrogen in the side chain of histidine. The side chain pK_a is 6.0; since pH = 7.4 > 6.0, we surmise that histidine's additional basic nitrogen should mainly occur in the uncharged form.



Histidine at
physiological pH

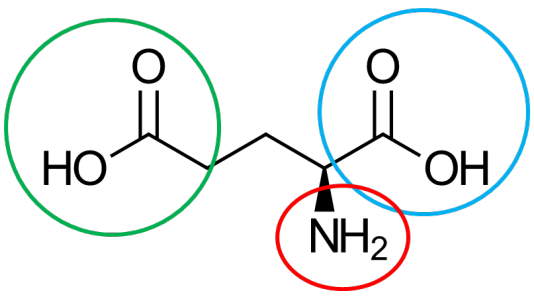
10.6: The pK_a of the α-COOH group of glutamic acid is 2.19; since pH = 2 < 2.19, the α-carboxylic acid group of GA should mainly occur in the protonated form. The pK_a of the α-NH_3^+ group of GA is 9.67; since pH = 2 < 9.67, the α-amino group of GA should mainly occur in the protonated form. We also have to consider the second carboxylic acid group in the side chain of GA. This carboxylic acid has a pK_a of 4.25; since pH = 2 < 4.25, we surmise that GA's additional carboxylic acid should mainly occur in the protonated form.



Glutamic acid
at pH = 2

P.11 ➡ ***Solution***

For amino acids with no carboxyacid or amino groups in their side chains, the p*I* is simply the average of the two pK_a values. For amino acids with acidic or basic side chains, the p*I* is the average of the two pK_a values that correspond with the similar groups. For example, the p*I* of glutamic acid is determined by the two acid groups. pK_a values can be found on Table 1.



α-Carboxylic acid pK_a = 2.19
α-Amino pK_a = 9.67
Side chain carboxylic acid pK_a = 4.25

$$pI = \frac{2.19 + 4.25}{2} = 3.22$$

11.1.1: For glycine, the pK_a of the acid group is 2.34 and the pK_a of the amino group is 9.60. Thus, the p*I* is

$$pI = \frac{2.34 + 9.60}{2} = \boxed{5.97}$$

11.1.2: For aspartic acid, the pK_a of the acid group is 1.88 and the pK_a of the amino group is 9.60. In addition, the carboxyacid group in the side chain has a pK_a of 3.65. Thus, the p*I* is

$$pI = \frac{1.88 + 3.65}{2} = \boxed{2.77}$$

11.1.3: For lysine, the pK_a of the acid group is 2.18 and the pK_a of the amino group is 8.95. In addition, the amino group in the side chain has a pK_a of 10.53. Thus, the p*I* is

$$pI = \frac{8.95 + 10.53}{2} = \boxed{9.74}$$

11.1.4: For tyrosine, the pK_a of the acid group is 2.20 and the pK_a of the amino group is 9.11. In addition, the phenol group in the side chain has a pK_a of 10.07; this acidic hydroxyl is not considered in the computation of the isoelectric point. Thus, the p*I* is

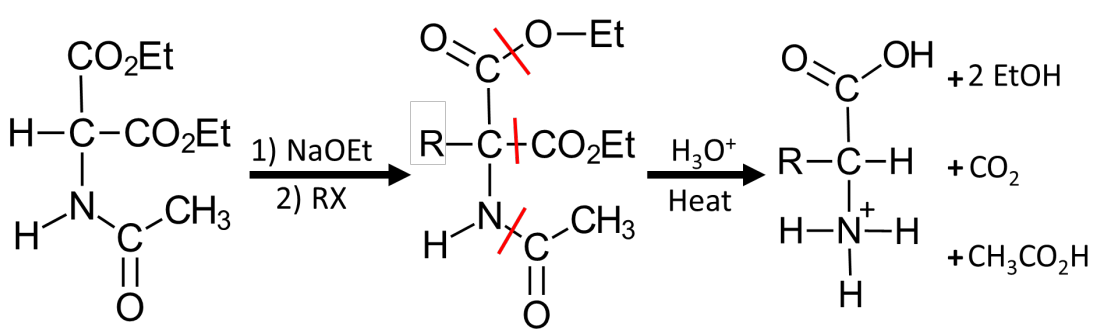
$$pI = \frac{2.20 + 9.11}{2} = \boxed{5.66}$$

11.2.1: In an electrophoresis procedure, the greater the difference between p*I* and the solution pH, the faster and farther the amino acid will migrate in the direction of the cathode (if the p*I* of the amino acid is greater than the pH of the solution) or the anode (if the p*I* of the amino acid is lower than the pH of the solution). With reference to Table 1, we calculate p*I* = 5.48 for phenylalanine, p*I* = 6.11 for tryptophan, and p*I* = 6.00 for leucine. Notice that the difference between the pH of the solution, which is 6.0, and the p*I* is greatest for phenylalanine. Thus, Phe is the amino acid that will move the farthest distance.

11.2.2: In this case, the difference between p*I* and the pH of the solution is greatest for tryptophan. Thus, Trp is the amino acid that will travel the farthest distance in this electrophoresis procedure.

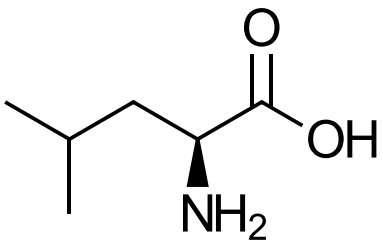
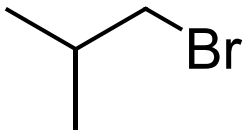
P.12 ➡ *Solution*

The amidomalonate synthetic route begins with conversion of diethyl acetamidomalonate into enolate ion by treatment with base, followed by an S_N2 alkylation with a primary alkyl halide. Hydrolysis of both the amide protecting group and the esters occurs when the alkylated product is warmed with aqueous acid, and decarboxylation then takes place to yield an α-amino acid.

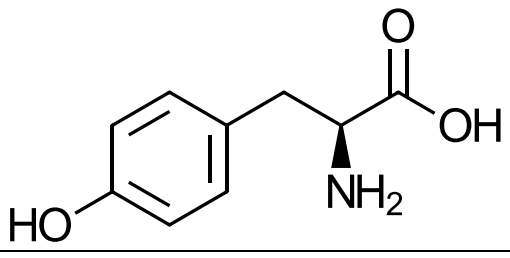
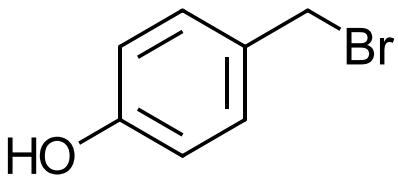


In the amidomalonate synthesis, shown above, an alkyl halide RX is converted to RCH(NH_3^+)CO_2H. Choose an alkyl halide such that *R* completes the structure of the target amino acid.

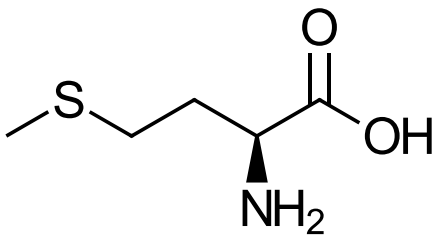
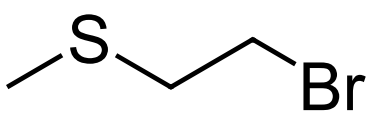
12.1.1:

Leucine	*Starting alkyl halide*
	 1-Bromo-2-methylpropane

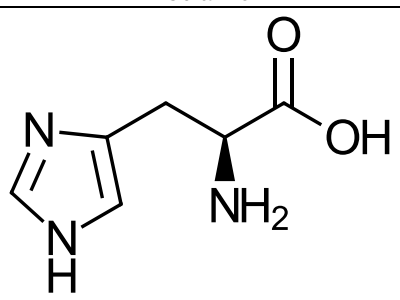
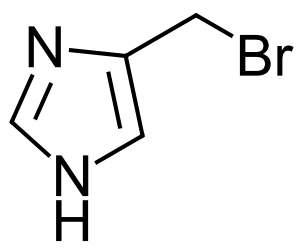
12.1.2:

Tyrosine	*Starting alkyl halide*
	 *p*-(Bromomethyl)phenol

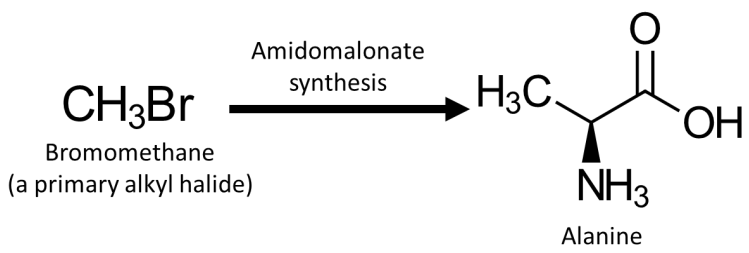
12.1.3:

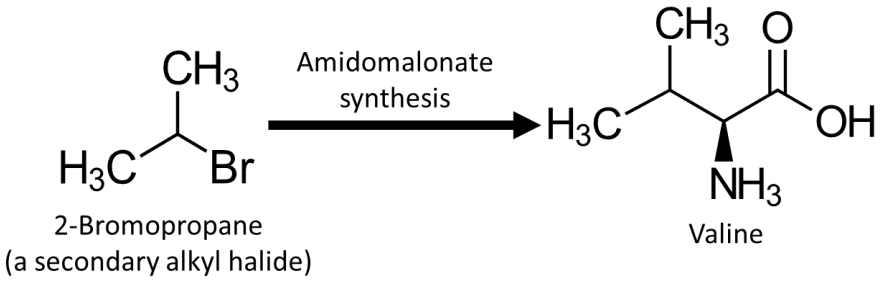
Methionine	*Starting alkyl halide*
	 1-Bromo-2-(methylthio)ethane

12.1.4:

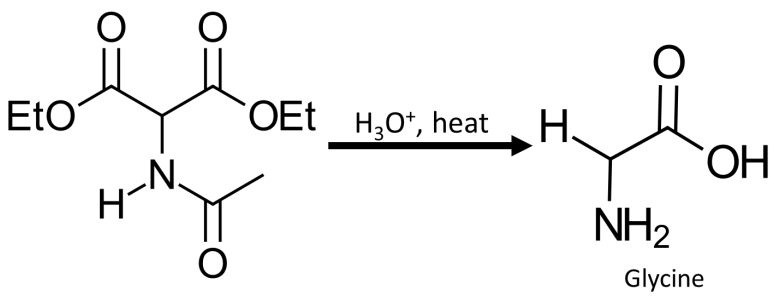
Histidine	*Starting alkyl halide*
	 4-(Bromomethyl)-1*H*-imidazole

12.2.1: Alanine can be prepared via the amidomalonate synthesis with higher yields than valine because the former requires an S_N2 reaction with a primary alkyl halide, while the latter requires an S_N2 reaction with a secondary (more hindered) alkyl halide.



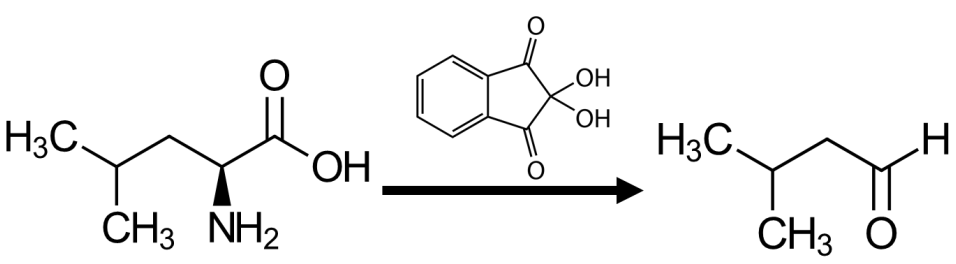


12.2.2: The side chain (*R* in the explanation to the solution) of glycine is simply a hydrogen atom. Therefore, no alkyl group needs to be installed at the α position when synthesizing this compound by amidomalonate synthesis.

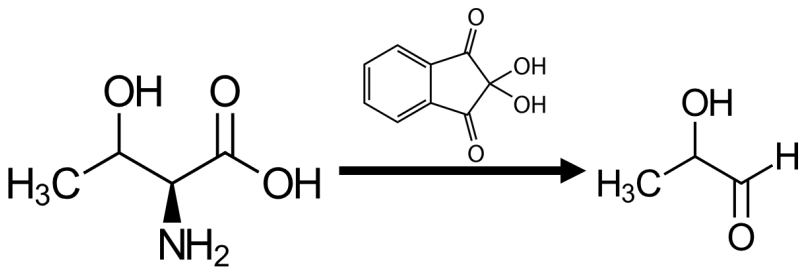


P.13 ➡ *Solution*

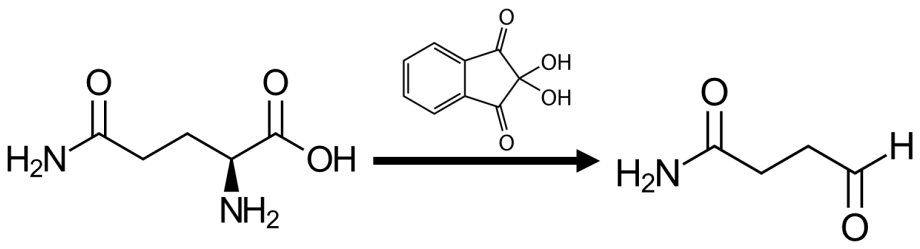
13.1: When an amino acid is treated with ninhydrin, the carboxylic acid group and the amino group connected to the α carbon are suppressed, and α position becomes an aldehyde group. The product of treatment of *L*-leucine with ninhydrin is 3-methylbutyraldehyde.



13.2: The product, in this case, is lactaldehyde.



13.3: The product, in this case, is 3-formylpropionamide.



13.4: Ninhydrin does not react with proline because the amino group is not primary.

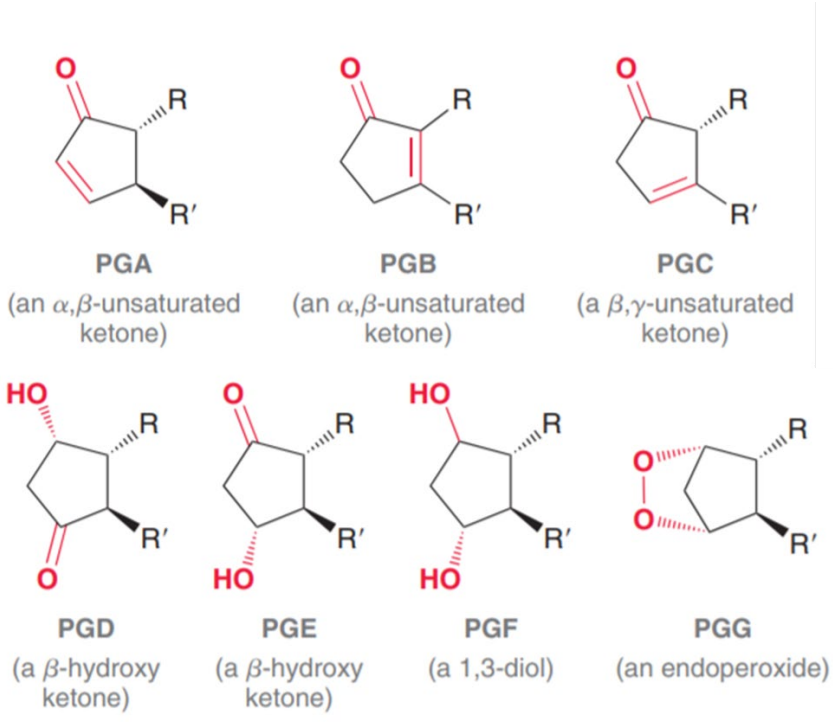
P.14 ➡ *Solution*

1. True. Two structural traits of fatty acids can be used to compare melting points: molecular weight and presence of *cis* double bonds. The greater the number of carbons (and hence the molecular weight) that constitute a fatty acid, the greater the melting point. Further, the greater the number of *cis* double bonds in a fatty acid, the lower the melting point. None of the three fatty acids at hand – arachidic acid, stearic acid and palmitic acid – have double bonds, hence we can compare their melting points on the basis of number of carbons only. Referring to Figure 2, we see that arachidic acid has 20 carbons and should have a greater MP than stearic acid, which has 18; stearic acid, in turn, most likely melts at a greater temperature than palmitic acid, which has 16 carbons.

2. False. A stearic acid-based triglyceride has one more long, nonpolar hydrocarbon residue than an equivalent diglyceride, and hence should be *less* soluble in water, which is a polar solvent.

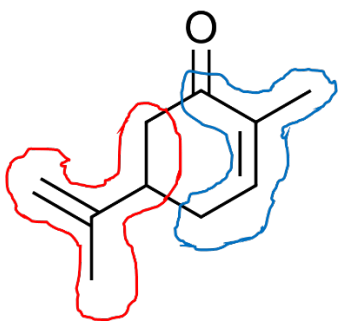
3. True. Cephalins - phosphoglycerides derived from ethanolamine – and lecithins – phosphoglycerides derived from choline – are particularly abundant in the cells of plants and animals.

4. False. A prostaglandin is designated PGX_Y, where X is a letter from A to G that specifies the structure of the 5-carbon ring, as shown below, and Y is the number of double bonds in the side chains. The prostaglandin at hand has a ring with B structure and two double bonds in its side chains; accordingly, it should be designated PGB_2.



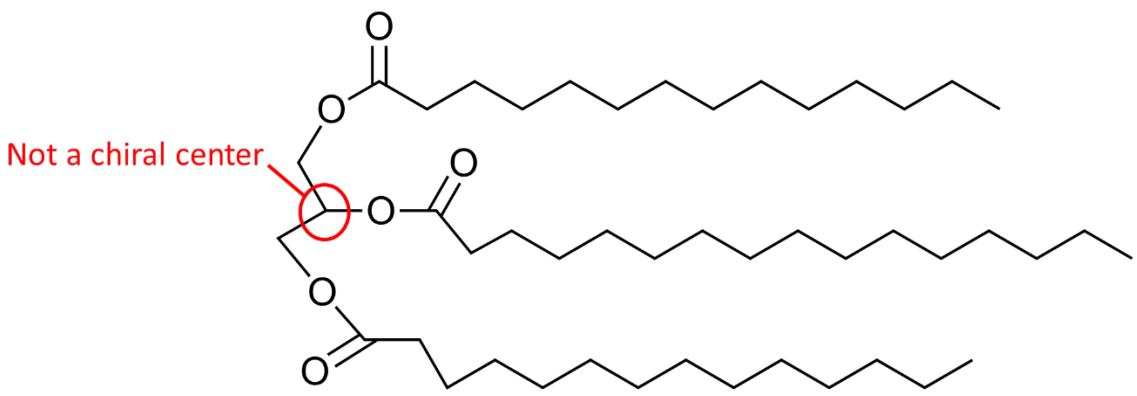
5. False. Water would not be appropriate because it is a polar solvent, and terpenes are nonpolar compounds. Hexane is a nonpolar solvent and would be a better choice.

6. True. According to the isoprene rule, all terpenes can be thought of as being assembled from *isoprene* units, each of which contain five carbon atoms. One natural consequence of this rule is that a terpene should have a number of carbons equal to a multiple of five. Carvone has 10 carbon atoms. Further, the structure of carvone can be divided into two isoprene-like components. Thus, carvone is indeed a terpene.

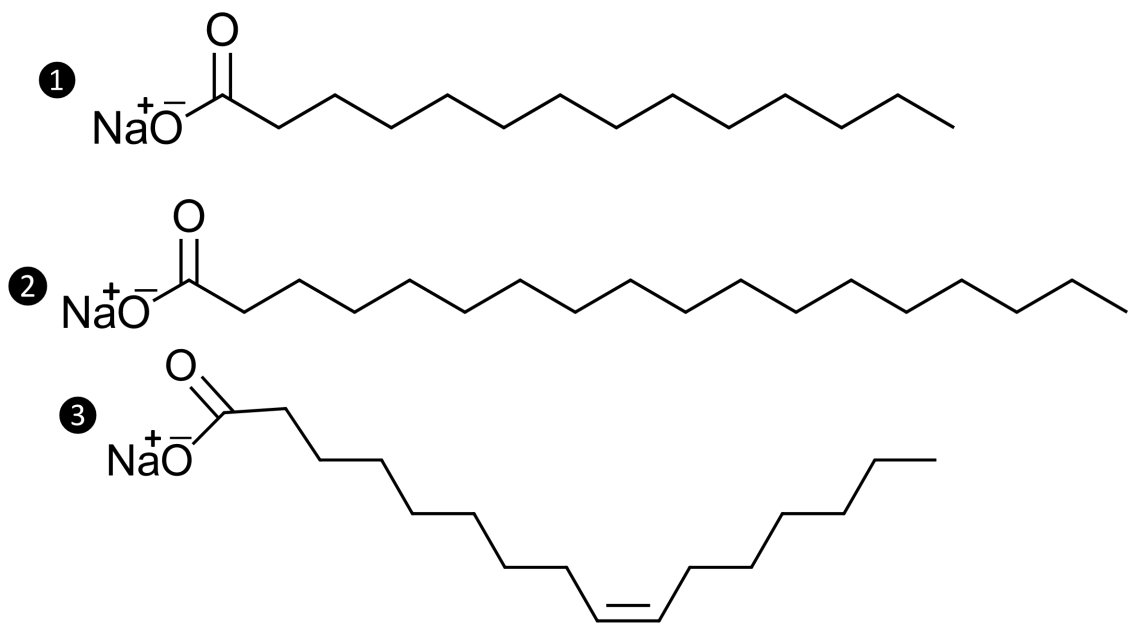


P.15 ➡ *Solution*

15.1: The products of hydrolysis indicate that the starting triglyceride has two lauric acid residues and one myristic acid residue. In order to be achiral, the palmitic acid residue must be connected to C2 of the glycerol backbone, as shown below. Otherwise, the highlighted position (C2 of the glycerol backbone) would be a chiral center.

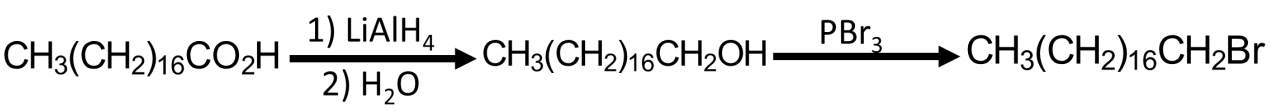


15.2: Treatment of the triglyceride at hand with aqueous sodium hydroxide should yield a mixture of three organic salts: sodium myristate (1), sodium stearate (2), and sodium oleate (3), in addition to some glycerol.

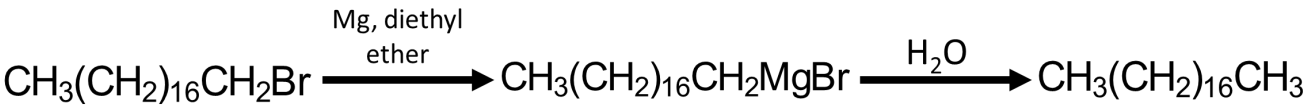


P.16 ➡ *Solution*

16.1: There are no direct methods for reduction of a carboxylic acid to an alkane. A number of indirect methods that may be used, however, involve first converting the carboxylic acid to an alkyl bromide via the corresponding alcohol.

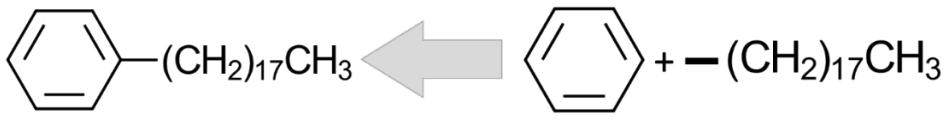


Once the alkyl bromide is in hand, it may be made into an alkane by conversion to a Grignard reagent followed by addition of water.

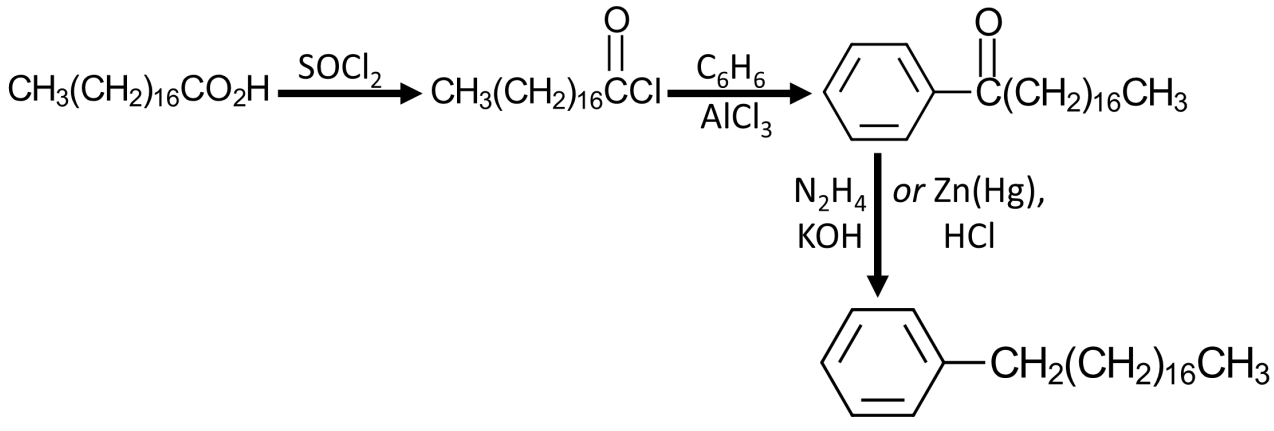


Carey notes that other routes are possible. For example, E2 elimination from 1-bromooctadecane followed by hydrogenation of the resulting alkene will also yield octadecane.

16.2: Retrosynthetic analysis reveals that the 18-carbon chain of the starting material must be attached to a benzene ring.

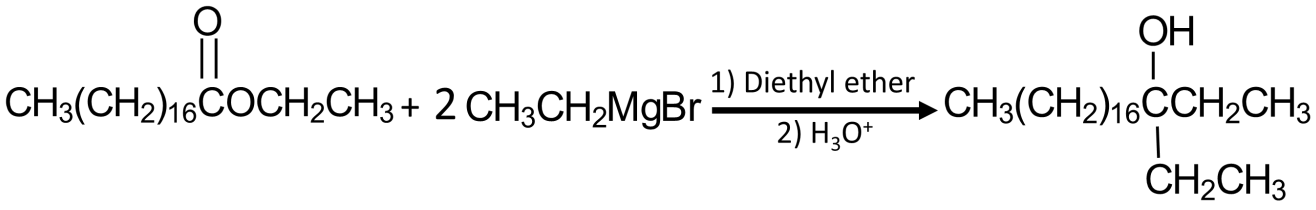


To achieve this product starting from octodecanoic acid, first convert it to an acid chloride and attach it to an aromatic ring via Friedel-Crafts acylation; then, apply a Wolff-Kishner or Clemmensen reduction of the ensuing ketone.

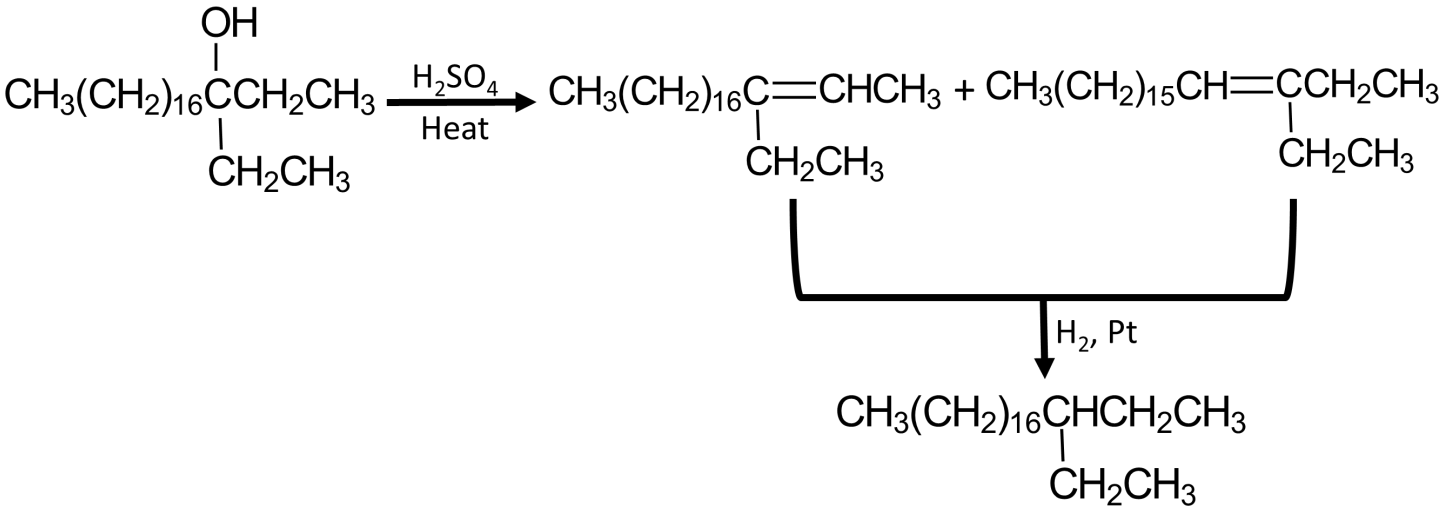


16.3: Retrosynthetic analysis reveals that two ethyl groups have been attached to a C_{18} unit.

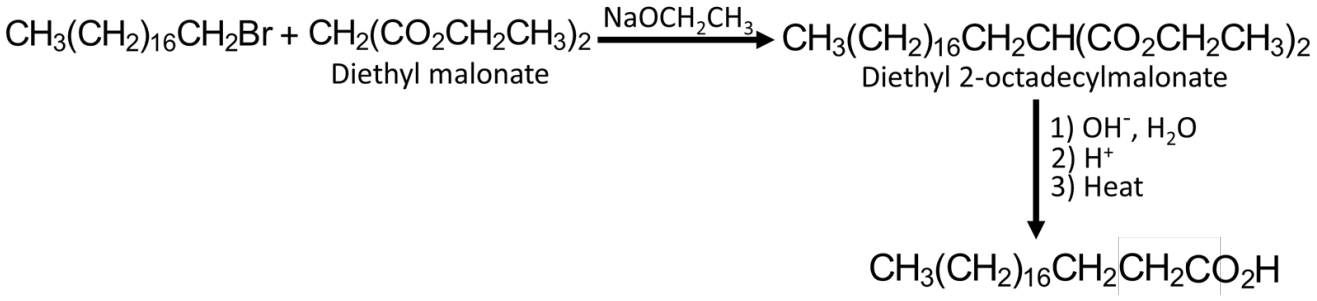
The necessary carbon-carbon bonds can be assembled by the reaction of an ester with a Grignard reagent. The ester can be obtained by reacting octadecanoic acid with ethanol.



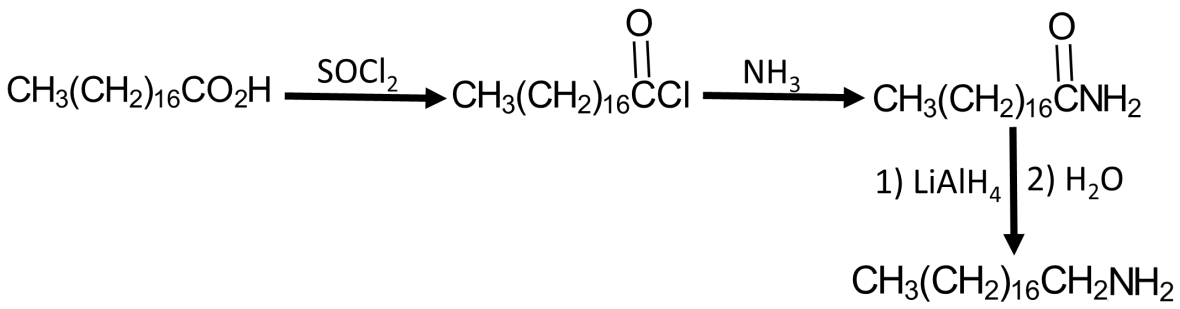
With the correct carbon skeleton in place, all that is needed is to convert the alcohol to an alkene and then apply catalytic hydrogenation.



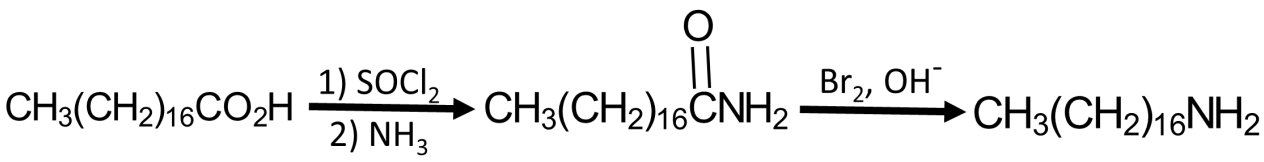
16.4: Icosanoic acid contains two more carbon atoms than octadecanoic acid. A reasonable approach is to employ malonic ester synthesis, as shown below. 1-Bromooctadecane can be obtained by reducing octadecanoic acid and then reacting the ensuing alcohol with PBr_3, as described in Problem 16.1.



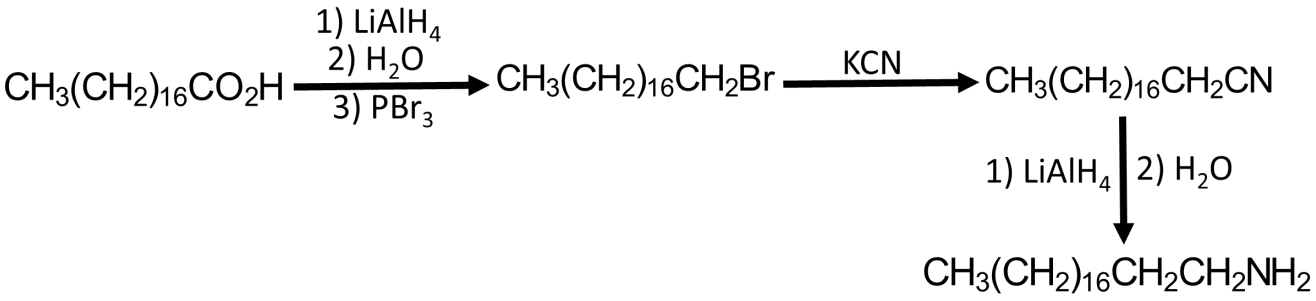
16.5: Treatment of the starting acid with $SOCl_2$ yields an acid chloride, and aminolysis converts the acid chloride to an octadecanamide. Finally, reduction of the amide gives 1-octadecanamine.



16.6: The carbon chain must be shortened by one atom. To achieve this transformation, we first prepare octanamide as we did in the previous problem. Then, a Hoffman rearrangement should lead to 1-heptadecanamine.

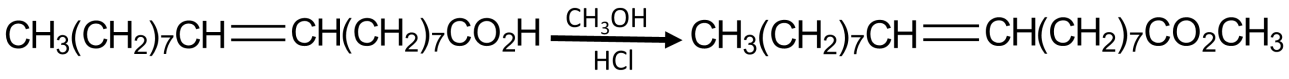


16.7: In this case, the carbon chain must be lengthened by one atom. To achieve this transformation, we begin by preparing an alkyl halide as we did in Problem 16.1. Then, nucleophilic substitution should trade the bromide group for a cyano group. Hydrolysis of the ensuing nitrile completes the synthesis.

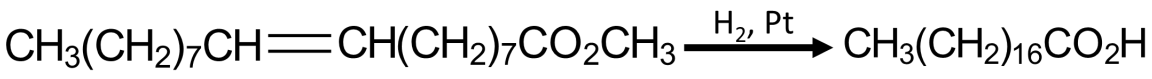


P.17 ➡ *Solution*

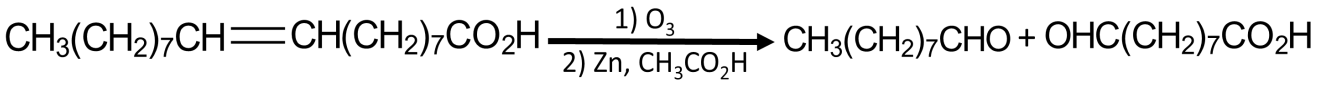
17.1: Esterification of methanol with oleic acid yields methyl oleate.



17.2: The first step is to convert oleic acid to methyl oleate, as we did in Problem 17.1. Then, catalytic hydrogenation of this ester yields methyl octadecanoic acid.

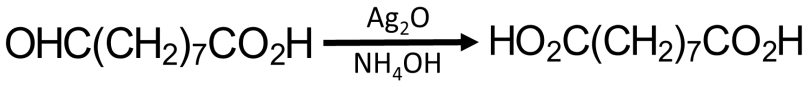


17.3: Nonanal is one of the organic products of ozonolysis of oleic acid; the other is 9-oxononanoic acid.

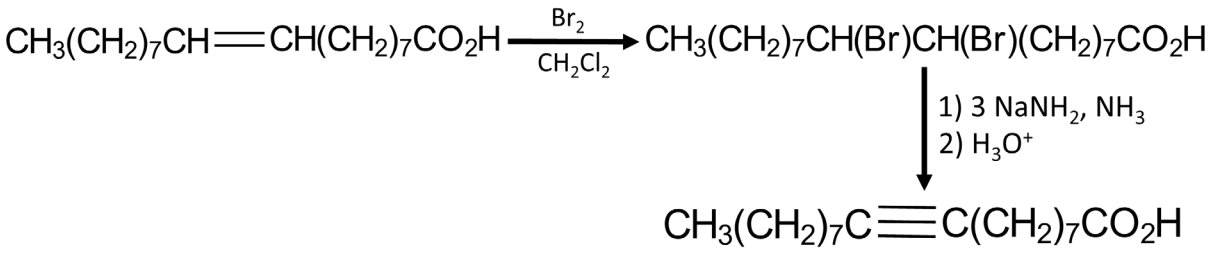


17.4: As shown in the previous problem, ozonolysis of oleic acid should yield 9-oxononanoic acid as one of its organic products. Tollens oxidation of

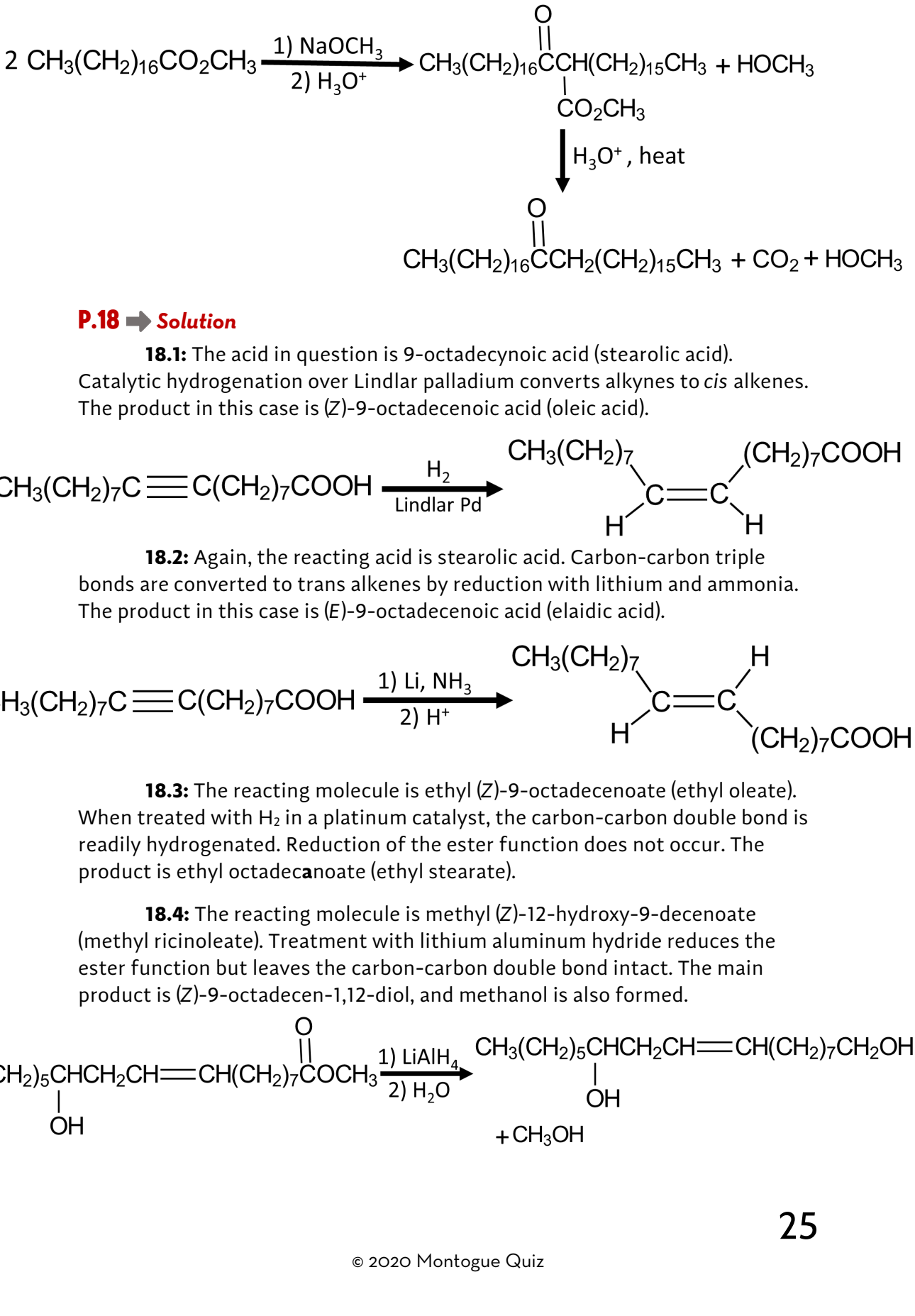
this product converts the formyl group to a carboxylic acid group, yielding nonanedioic acid.



17.5: We first brominate oleic acid. Then, treatment of the acid with sodium amide should eliminate the bromine atoms and form a triple C-C bond. Since there are two bromine atoms, in principle two equivalents of $NaNH_2$ are needed. However, one equivalent of base will be neutralized by the carboxylic acid group; accordingly, we provide three equivalents of base.



17.6: We begin by converting oleic acid to methyl oleate, as we did in Problem 17.1, and then to methyl stearate, as we did in Problem 17.2. Claisen condensation of methyl stearate should yield a β-keto ester. Decarboxylation of this product gives 18-pentatriacontanone.



P.18 ➡ *Solution*

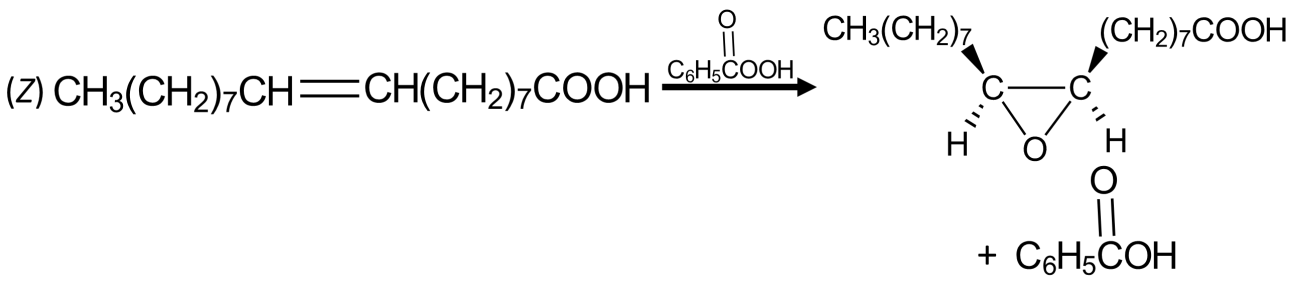
18.1: The acid in question is 9-octadecynoic acid (stearolic acid). Catalytic hydrogenation over Lindlar palladium converts alkynes to *cis* alkenes. The product in this case is (*Z*)-9-octadecenoic acid (oleic acid).

18.2: Again, the reacting acid is stearolic acid. Carbon-carbon triple bonds are converted to trans alkenes by reduction with lithium and ammonia. The product in this case is (*E*)-9-octadecenoic acid (elaidic acid).

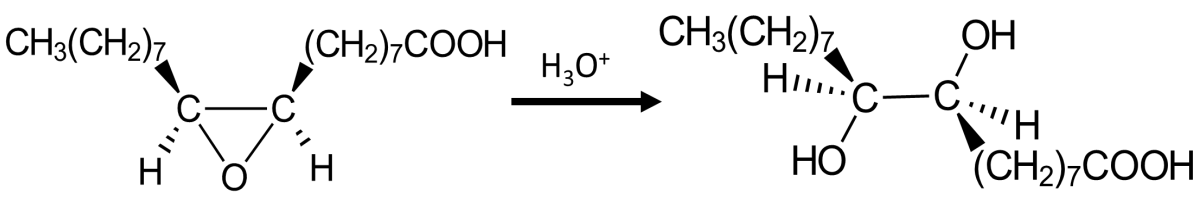
18.3: The reacting molecule is ethyl (*Z*)-9-octadecenoate (ethyl oleate). When treated with H_2 in a platinum catalyst, the carbon-carbon double bond is readily hydrogenated. Reduction of the ester function does not occur. The product is ethyl octadec**a**noate (ethyl stearate).

18.4: The reacting molecule is methyl (*Z*)-12-hydroxy-9-decenoate (methyl ricinoleate). Treatment with lithium aluminum hydride reduces the ester function but leaves the carbon-carbon double bond intact. The main product is (*Z*)-9-octadecen-1,12-diol, and methanol is also formed.

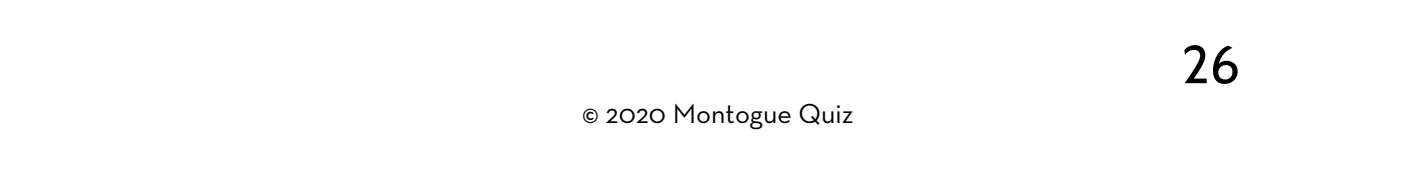
18.5: The starting lipid is oleic acid, which shall react with a peroxycarboxilic acid. Epoxidation of the double bond occurs when an alkene is treated with a peroxy acid. The reaction is stereospecific, that is, substituents that are *cis* to each other in the alkene remain *cis* in the epoxide. The main product is *cis*-9,10-epoxyoctadecanoic acid, and benzoic acid is also formed.



18.6: Acid-catalyzed hydrolysis of the epoxide yields a diol; its stereochemistry corresponds to net *anti* hydroxylation of the double bond of the original alkene. The product is 9,10-dihydroxyoctadecanoic acid. The product is chiral but is formed as a racemic mixture containing equal amounts of the 9*R*,10*R* and 9*S*,10*S* stereoisomers when the starting epoxide is racemic.



18.7: Hydroxylation of carbon-carbon double bonds with osmium tetroxide proceeds with *syn* addition of hydroxyl groups. The product is chiral but is formed as a racemic mixture containing equal amounts of the 9*R*,10*S* and 9*S*,10*R* stereoisomers.



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