NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Chirality, Amino Acid Racemization, and the Authenticity of the Buyid Silks

by

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Part I – Reviewing the Basics

Mary and Parker are classmates in a biochemistry course where they have learned the structures of the 20 natural amino acids and their representations using Fischer projections. Since all but one of the natural amino acids have a chiral center, it is possible for each to exist in two forms (enantiomers or nonsuperimposable mirror images) but, according to their professor, only one form (the L enantiomer) occurs naturally. The mysterious thing, though, is that the other form (the D enantiomer) has been found in meteorites and in ancient artifacts like fabric and teeth. The first is admittedly strange: are extraterrestrials the nonsuperimposable mirror images of us? But the second is even more unexpected. Ancient artifacts and teeth were made by humans from materials on this planet. Where did the D form come from? This question was answered for them when their professor told them to read a journal article (Moini & Rollman, 2017) that described an investigation to determine the authenticity of thirteen Buyid silks from the Textile Museum at George Washington University. The Buyid dynasty ruled over Iraq and central and southern Iran from 934–1062 CE, and the Buyid silks were quite a find when they were dug up in the mid-1920s, but questions about their authenticity surfaced almost immediately (Craddock, 2009). Mary and Parker never dreamed that amino acids would be tied to one of the most famous silk forgeries in history.

Questions

1. What is the hybridization of a tetrahedral carbon?

2. What are the other types of hybridization of carbon and what are their molecular geometries?

3. Which of the structures in Figure 1 below contain a chiral center? Place an asterisk at each chiral center.

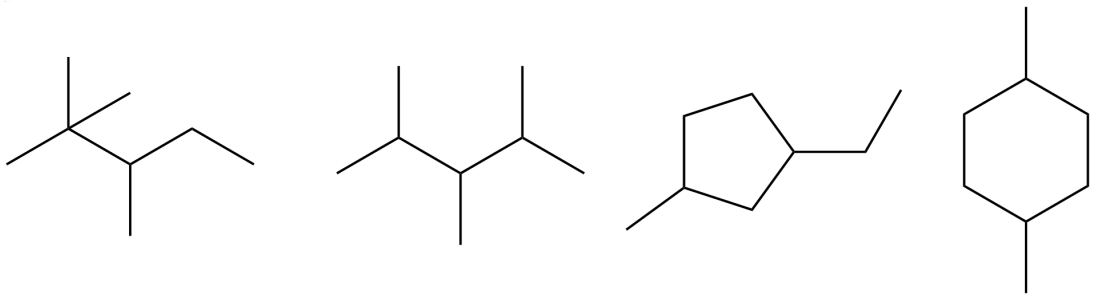

Figure 1. Structures.

4. The enantiomers of 1-bromo-1-chloroethane are shown in Figure 2. Which is the R enantiomer, and which is the S enantiomer?

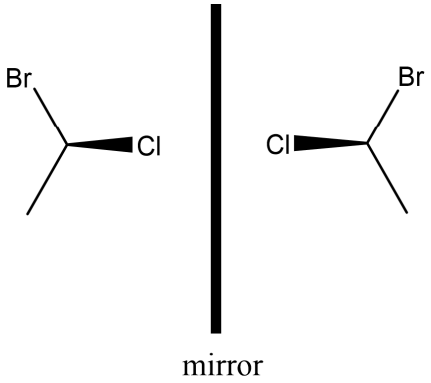

Figure 2. Enantiomers of 1-bromo-1-chloroethane.

5. For each Fischer projection in Figure 3, specify D or L.

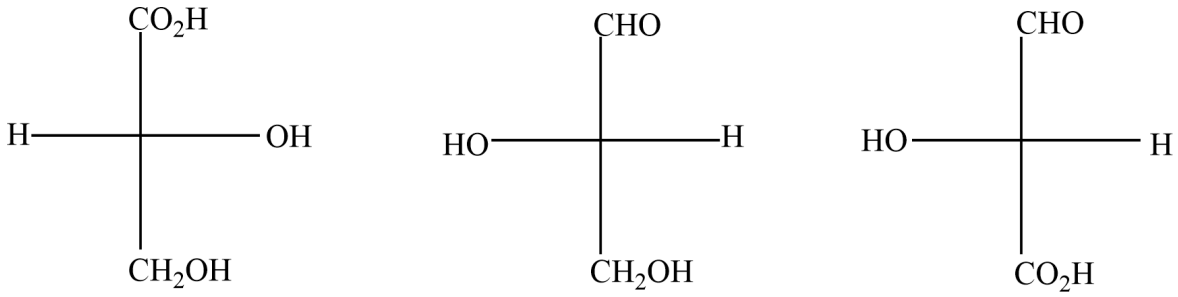

Figure 3. Fischer projections.

6. Thinking about the implied 3D information, specify the absolute configuration (R or S) of each of the molecules in Question 5.

7. Consider the reaction below in Figure 4.

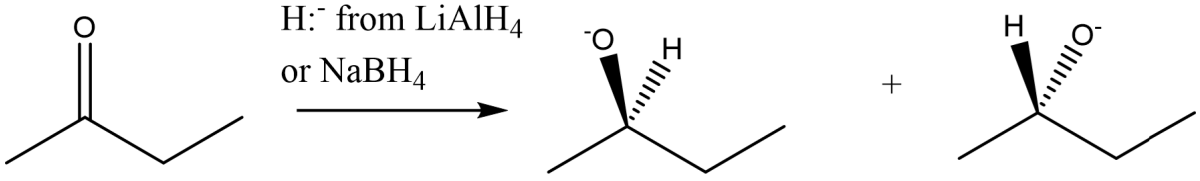

Figure 4. Reaction and products.

a) Is the first product the R or the S enantiomer?

b) What about the second product?

c) What is the expected ratio of the two products?

d) Would the reaction mixture be optically active?

Part II – Using Aspartic Acid Racemization to Date Ancient Artifacts

Questions

1. Explain why all amino acid residues in a protein are capable of epimerization. In your explanation include structures as appropriate.

2. Aspartic acid racemization (AAR) was used to date the Buyid silks because aspartic acid has the fastest racemization of all amino acids (Waite & Collins, 2000). Why is the rate of racemization important?

3. An explanation of why the racemization rate of aspartic acid is fastest involves a cyclic succinimidyl intermediate.
   a) Draw the structure of succinimide.

   b) A portion of a protein containing aspartic acid is shown in Figure 5 with each of the carbons numbered. Place the numbers on the corresponding carbons in the structure of succinimide you drew for Question 3(a) above.

   c) The pka of methane is about 60 while the pKa of acetone is about 19. Why is acetone so much more acidic than methane even though the hydrogen atoms in both are covalently bonded to carbon?

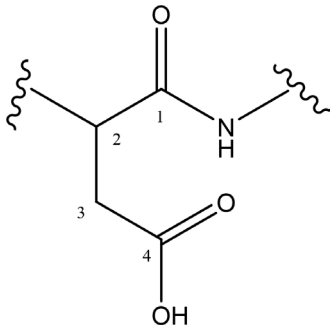

Figure 5. Portion of protein.

   d) All amino acids have a hydrogen alpha to the peptide bond carbonyl. To justify why the hydrogen in an aspartic acid residue is more acidic than the comparable hydrogen for other residues, resonance stabilization of the resulting enolate can be instructive. Draw the resonance structures for the enolates of acetic anhydride and methyl acetate.

e) Based on the resonance structures in Quesion 3(d) above, which enolate is expected to be more stable? Explain your choice.

f) Consider now the two molecules in Figure 6 below. N-methylsuccinimide contains an imide functional group while N-methyl-2-pyrrolidone contains an amide functional group. Draw the resonance structures for the enolates of each. Based on the number of resonance structures for the enolates, which do you predict to be more acidic? Explain your choice.

Figure 6. N-methylsuccinimide and N-methyl-2-pyrrolidone.

g) We now understand that a hydrogen alpha to an imide carbonyl is more acidic than a hydrogen alpha to an amide carbonyl. All amino acid residues in a peptide have a hydrogen alpha to an amide carbonyl. In the case of aspartic acid, however, its side chain carboxylic acid can condense with the nitrogen in the peptide bond to form an imide. A portion of a peptide containing aspartic acid is given below in Figure 7. Circle the nitrogen and the carbonyl that would condense to form a succinimidyl ring.

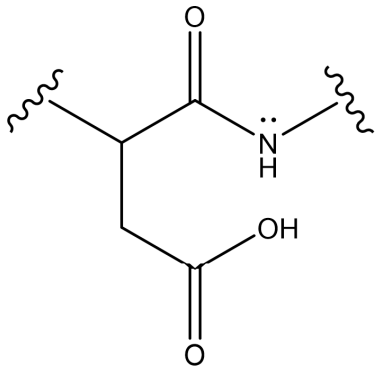

Figure 7. A portion of a peptide containing aspartic acid.

4. Propose an explanation for the observation that aspartic acid residues in proteins epimerize faster than other residues. (*Hint:* Radkiewicz et al., 1996.)

5. The epimerization of aspartic acid residues is catalyzed by acid or base. Moini and Rollman (2017) used base-catalyzed epimerization. What experimental conditions were used?

6. How do you expect the base (for example, NaOH (aq)) to catalyze the epimerization?

7. In Moini and Rollman (2017), thirteen Buyid silk specimens from the Textile Museums at George Washington University were analyzed. The amino acid racemization ratios of how many of these were consistent with authentic silk fabrics from the Buyid period of the Persian Empire?

References

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