

# Chirality and the Origins of Life: A Case Study in Organic Chemistry

by

Michael C. Young and Richard J. Hooley  
Department of Chemistry  
University of California, Riverside

## Before Class

1. Read the case scenario provided below.
2. In addition, read the following in advance of class:
  - a. Noorduin, et al. "Emergence of a Single Solid Chiral State from a Nearly Racemic Amino Acid Derivative." *J. Am. Chem. Soc.* 2008, 130, 1158–1159.
  - b. Chapter 5 and section 26.1 ("Stereochemistry," pages 143–173 and "Amino Acid Structures," pages 1045–1049) of your assigned organic chemistry textbook (McMurry, 8<sup>th</sup> edition).
  - c. The definition of "Ostwald ripening" (from *Wikipedia*; attached to the end of this worksheet).
3. Answer the pre-case question and be prepared to submit your response to your discussion group when you arrive to class.
4. Read and familiarize yourself with the case study questions; these will be discussed and answered in groups during the discussion sessions.

## In Class

1. You will be divided into collaborative groups for the pre-case discussion in which you identify the major issues of the case, and determine what types of questions need to be answered in order to resolve the case.
2. You will work in your collaborative groups and arrive at answers to the case study questions.

## After Class

Complete the post-case study individual report. The due date for this final report will be announced in class.



Case copyright held by the **National Center for Case Study Teaching in Science**, University at Buffalo, State University of New York. Originally published November 6, 2014. Please see our **usage guidelines**, which outline our policy concerning permissible reproduction of this work. Title block detail from Michelangelo's "Creation of Adam."

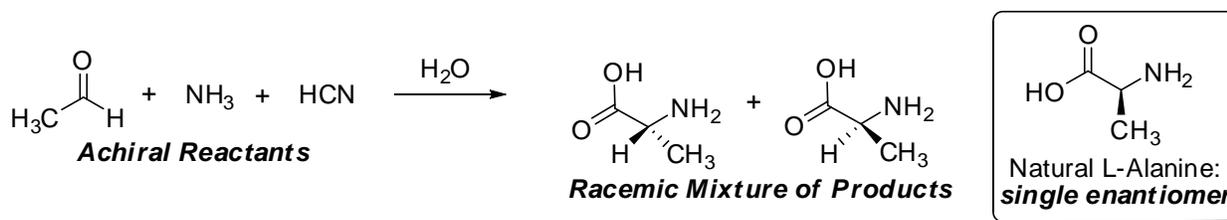
## The Case Scenario

Carsten and Charles were having a philosophical discussion on the origins of life in the universe. Carsten had been reading some literature on the topic. This stated that the fact that amino acids are chiral, but naturally exist in only one form, means that evolution cannot be responsible for the initial formation of proteins and other building blocks of life. Charles disagreed with this, saying that the proportion of each form can alter over time—four billion years should be sufficient time for anything to occur. After a spirited debate, they decided to do some reading, and came across a paper in the *Journal of the American Chemical Society* by Noorduin, et al., that discussed their topic in more detail.

### Background

Natural amino acids form the basis for the structure of all proteins and enzymes in living organisms. The key to this is that each amino acid contains one stereocenter in its structure. All natural amino acids exist as a single enantiomer (the L isomer); this enantiomeric purity allows proteins (amino acid polymers) to form stable three dimensional structures.

When determining how life on this planet began, the question of how *enantiomerically pure* amino acids were created from *achiral* building blocks is still a significant puzzle. A plausible “prebiotic” synthesis of amino acids that can be performed in a laboratory setting called the Strecker reaction is shown below. While this addresses the issue of how amino acids could have originally been formed, it does not address the chirality issue—achiral reactants always give a racemic mixture of products.



There are many questions to ask about how life began: from a chemist’s point of view, the most interesting is “how could amino acids have been converted from achiral starting materials to 100% of a single (L) enantiomer, allowing the creation of proteins and other building blocks of life as we know them?” In this case study, you will address that issue.

This question can be split into two parts: (a) how was the enantiomeric purity enhanced to 100% over time from a *small* excess, and (b) how did that small excess occur in the first place? The first question is addressed by your assigned reading (Noorduin, et al.). The second is much trickier...

### Question

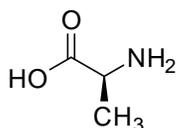
1. Define the following terms: *racemic mixture*, *enantiomer*, *achiral*, *enantiomeric excess*, and *diastereomer* (see McMurry, Chapter 5).

## Part 1 – Amino Acids, Chirality, and Racemization

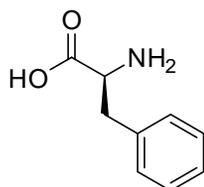
In this first section, you will answer questions about the chiral nature of amino acids and how they are susceptible to interconversion between enantiomers (“racemization”).

### Questions

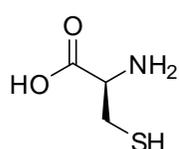
- a. Four natural amino acids are shown below. Determine the chiral centers in each amino acid and assign those centers *R* or *S*, according to the Cahn-Ingold-Prelog rules.



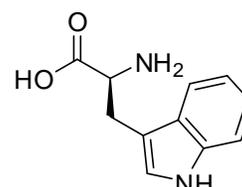
L-Alanine



L-Phenylalanine

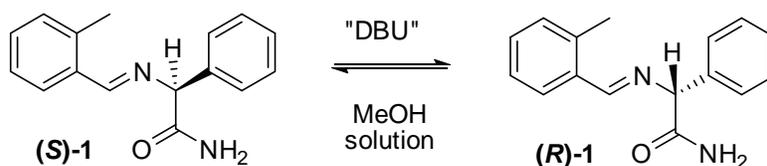


L-Cysteine

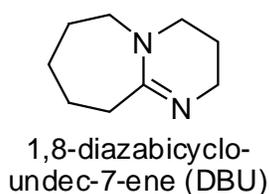


L-Tryptophan

- b. In Noorduyn, et al., amino acid surrogate **1** (a molecule that mimics the reactive behavior of natural amino acids) was used to illustrate enantiomeric enhancement upon crystallization. The first experiment was to illustrate racemization in solution upon treatment with added base, as shown below. Determine the position of the stereocenter in **1**, and use the Cahn-Ingold-Prelog rules to confirm the *R/S* stereochemistry.



- c. DBU (1,8-diazabicycloundec-7-ene) is an organic amine base that can reversibly deprotonate **1**. There are two lone pairs in DBU. Which is most basic? Draw the two protonated species, and see which one is *most* stabilized by resonance.



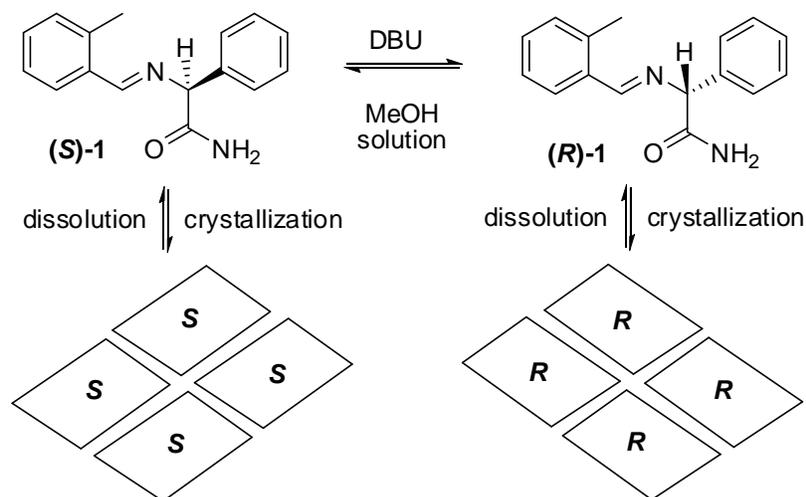
- a. Drawing DBU as B: (i.e., “base”), draw the mechanism for racemization of **1** upon treatment with base. Pay attention to the geometry of the charged intermediate.
- b. Why did Noorduyn, et al, use the amino acid surrogate **1** instead of a natural amino acid? (*Hint*: What happens when you treat L-alanine with a base?)

## Part 2 – Chirality Enhancement via Crystallization

In this section, you will discuss the results of Noorduin, et al., and describe why the phenomenon is observed.

### Questions

- a. The concept of the paper is shown below. Upon addition of a *small excess* of one enantiomer of **1** or a different chiral species (such as phenylglycine), crystals of **1** with 100% enantiomeric excess can be obtained over time. The key to this theory and experiment is selective crystallization. Read the Ostwald ripening attachment (P-1) and explain why a large crystal is more thermodynamically favorable than a small one.



- b. The experiment also relies on the fact that individual enantiomers crystallize *together* in a single crystal (i.e., the crystals are either all-S or all-R, not a racemic crystal). Explain why this occurs; consider the solid state interaction of two molecules of the *same* handedness and *different* handedness. See McMurry, pages 161–163.
- c. If there is only a small excess of one enantiomer in solution, can selective crystallization *alone* (i.e., in the absence of base) cause chirality enhancement?
- d. Discuss why the combination of added base (DBU in this case) and *selective crystallization* allows the enhancement of chirality of the system. Consider equilibrium effects and Le Chatelier's principle in your answer.
- e. This is a proof-of-principle experiment (i.e., it mimics the natural process, but several changes were made to allow study in a laboratory setting). To maximize the speed of the enhancement, glass beads and magnetic stirring were employed. How does this speed up the process? Is this a plausible method of mimicking natural evolution? Why did the researchers not simply perform the experiment as it would occur in prebiotic systems?

### Part 3 – Critical Analysis

You have discussed the results of Noorduin, et al. This is a controlled experiment designed to show the proof of principle that a slight excess of one enantiomer can lead to complete conversion to a single enantiomer over time, under the correct conditions. Here, in this question set, you will discuss whether this applies to prebiotic systems and is a good model for the origin of life.

#### *Counterpoints:*

- a. Is base-catalyzed racemization the most favorable acid-base reaction for natural amino acids? Determine the most acidic H atom in **1** and in L-alanine. Are they the same?
- b. This theory relies on *crystallization*. Are there large solid deposits of amino acids in nature? Are amino acids more or less soluble in water than **1**? In question 2b you described why crystals of one enantiomer are more favorable than crystals of a racemic mixture. Is this always the case (see McMurry, pages 161–163)?
- c. Provide a critical analysis of this experiment. Discuss whether or not you believe the results of *this* experiment. Discuss whether this is a good “proof-of-principle” experiment, and whether it can apply to natural amino acids in a prebiotic environment.

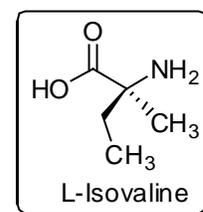
## Part 4 – Extraterrestrial Amino Acids

[http://en.wikipedia.org/wiki/Murchison\\_meteorite](http://en.wikipedia.org/wiki/Murchison_meteorite)

So far, you have discussed chirality amplification. This theory still requires a small excess of one enantiomer to begin the amplification process. In this question set you will discuss how that original excess appeared.

One (disputed) theory of the original genesis of “chiral molecules” on Earth comes from outer space. The Murchison meteorite, which fell to earth in Australia in 1969, was shown to contain traces of amino acids and other simple organic materials. These materials displayed a “slightly enhanced” enantiomeric ratio, i.e., more of one enantiomer than the other (Engel & Macko 1997; Cronin & Pozzarello 1997). The theory was posited that similarly chiral materials crashed to earth during the prebiotic period (Pizzarello & Groy 2011). (*Note:* There are a lot of scientifically dubious theories on this topic. We won't discuss how the enhanced chirality appeared on the meteor while in outer space; ask a physicist.)

- The presence of natural amino acids with enantiomeric excess from the meteorite is still a subject of debate. Discuss why this is—what are the experimental issues with stating that alanine found on the Murchison meteorite has an excess of one (L) enantiomer? How might “false positives” be observed in the analysis of these meteorite samples?
- An argument put forward to corroborate the meteorite theory is the presence of unnatural  $\alpha$ -alkyl amino acids such as isovaline, which was observed to exist in the meteorite with a slight enhancement of the L isomer. Discuss *why* the observation of *unnatural* amino acids such as these is less susceptible to false positives than the presence of alanine above.
- Assume that there was an excess of (L)-isovaline on the Murchison meteorite. Discuss the plausibility of (L)-isovaline conferring chirality on species such as **1**, based on your reading of Noorduyn, et al.



## Final Report

Write a two- to three-page report on the case study, following the structure below

- Provide answers to the case study questions in Part 1 (a–e) at the start of your report.
- Critical Analysis Report: Using the answers to the case study questions in Parts 2–4, describe the major points of the case in essay format. Summarize the outcomes and concepts discussed in your lab session. *Incorporate* the answers to the case study questions into your report essay—do not write separate individual answers.
- Provide a short description of the outcomes of the experiment by Noorduin, et al. How does the experiment by Noorduin, et al., provide a “proof of principle” to the theory of chirality enhancement?
- Provide a critical analysis of the experiment. Does this experiment provide the answer to our question (i.e., how did amino acids become 100% “L” from achiral starting materials)? Describe the positive and negative contributions of this paper to the theory.
- In your conclusion, please address the final point from Part 4. Noorduin’s paper suggests a reason for the enhancement of chirality from a small excess (1–2%) to complete asymmetry (100%). It does not address how that initial excess appeared in the first place. You have been given one theory about how chiral molecules appeared on earth—do you believe it? Are there weaknesses in that theory? This section is intended to be open—ended—points will be given for your analysis, not just whether your answer is “correct.” (There is no proven answer to this question.)

### References

McMurry, J.E. 2012. *Organic Chemistry*, 8<sup>th</sup> edition, Cengage Learning.

Noorduin, et al. 2008. Emergence of a single solid chiral state from a nearly racemic amino acid derivative. *Journal of the American Chemical Society* 130: 1158–1159.

Wikipedia. Murchison meteorite. [http://en.wikipedia.org/wiki/Murchison\\_meteorite](http://en.wikipedia.org/wiki/Murchison_meteorite)

Wikipedia. Ostwald Ripening. [http://en.wikipedia.org/wiki/Ostwald\\_ripening](http://en.wikipedia.org/wiki/Ostwald_ripening)

### Further Reading

These references below are optional and only for students who want a deeper understanding of the material. They are not necessary for the case or final report.

Engel, M. H, and Macko, S. A. 1997. Isotopic evidence for extraterrestrial non-racemic amino acids in the Murchison meteorite. *Nature* 389: 265–268.

Cronin, J. R., and Pizzarello, S. 1997. Enantiomeric excesses in meteoritic amino acids. *Science* 275: 951–955.

Pizzarello, S.; Groy, T.L 2011. Molecular asymmetry in extraterrestrial organic chemistry: An analytical perspective. *Geochimica et Cosmochimica Acta* 75: 645–656.

## Assigned Reading

### *Ostwald Ripening*

*From Wikipedia ([http://en.wikipedia.org/wiki/Ostwald\\_ripening](http://en.wikipedia.org/wiki/Ostwald_ripening)), last accessed October 14, 2014:*

This thermodynamically-driven spontaneous process occurs because larger particles are more energetically favored than smaller particles. This stems from the fact that molecules on the surface of a particle are energetically less stable than the ones in the interior.

Consider a cubic crystal of atoms: all the atoms inside are bonded to 6 neighbors and are quite stable, but atoms on the surface are only bonded to 5 neighbors or fewer, which makes these surface atoms less stable. Large particles are more energetically favorable since, continuing with this example, more atoms are bonded to 6 neighbors and fewer atoms are at the unfavorable surface. As the system tries to lower its overall energy, molecules on the surface of a small particle (energetically unfavorable, with only 3 or 4 or 5 bonded neighbors) will tend to detach from the particle, as per the Kelvin equation, and diffuse into the solution. When all small particles do this, it increases the concentration of free molecules in solution. When the free molecules in solution are supersaturated, the free molecules have a tendency to condense on the surface of larger particles. Therefore, all smaller particles shrink, while larger particles grow, and overall the average size will increase. As time tends to infinity, the entire population of particles becomes one large spherical particle to minimize the total surface area.

