

A Race to Racemize

Elementary Problem 5 - 10 points

Deadline: August 31st at 8:30 PM IST

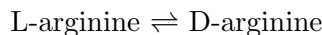
At ambient temperatures, amino acid racemization is a slow reaction. As such, it can be used for dating biological objects and, moreover, for studying their thermal history. Let us consider L-isoleucine (L-Ile) or (2S,3S)-2-amino-3-methylpentanoic acid as an example. It isomerizes and forms (2R,3S)-2-amino-3-methylpentanoic acid, also known as D-allo-isoleucine.

Note: The term ‘racemization’ may be used here in a rather broad manner.

1. Racemization rates for different free (i.e., in aqueous solution; not in polymerised form) amino acids differ substantially. An interesting experiment shows:
 - (i) The racemization rate of free serine is significantly more than that of free valine.
 - (ii) Substitution on the carboxylate moiety enhances the racemization rates of both free serine and free valine.

What conclusion can you draw about the racemization process from these crucial observations? (Strictly within 200 words)

2. Amino acids with a single chiral centre undergo racemization, e.g. L-arginine racemizes:



(The forward rate constant is k_1 and the backward rate constant is k_2)

The time evolution of concentrations is governed by:

$$\left[\begin{array}{c} 1 + \frac{[D]}{[L]} \\ \ln \frac{[D]}{[L]} \\ 1 - \frac{[D]}{[L]} \end{array} \right] = 2kt + c$$

Here [D] and [L] are concentrations of D- and L-arginine at time t , k is the corresponding rate constant, and the term c is set according to the initial concentrations. Emperor Proteinus passed away during his journey to Aminoland in 1000 AD. To facilitate the repatriation of the remains, his body was boiled in water (373 K) immediately after his death for a certain time. Let us try to estimate the boiling time with the help of chemical kinetics.

We know that the rate constant k_1 of arginine racemization within a protein at 373 K and pH = 7 has the value of $5.10 \times 10^3 \text{ h}^{-1}$. In order to analyse the isomeric composition of arginine in

the Emperor's bones, we need to start with transferring arginine into solution. His bones were hydrolyzed in a highly acidic environment for 4 hours at 383 K. The ratio of the optical isomers was $[D]:[L] = 0.090$. His wife Peptidia's body was not boiled after her death. Her bones were hydrolyzed using the same procedure and in this case the ratio was $[D]:[L] = 0.059$. (Note that the racemization also takes place during the hydrolysis, with the rate constant k_h , different from k_1). **How long was Emperor Proteinus boiled in water in 1000 AD?**

[**Note:** The racemization of arginine is an extremely slow process at temperatures typically encountered in graves. As both bodies are only some 1000 years old, we can neglect the natural racemization during this time.]

3. In fact, the reverse reaction cannot be neglected. Rate constant for the backward reaction is k_2 . Let us define the deviation of concentration from its equilibrium value $[L]_{eq} : x = [L] - [L]_{eq}$. It is possible to derive that x evolves with time according to the following equation:

$$x = x_0 e^{-k_1 t} e^{-k_2 t}$$

Where x_0 is the deviation from equilibrium at $t = 0$ h. The rate constant for the forward reaction is $k_{1374K} = 9.02 * 10^{-5} h^{-1}$.

Let us boil 1.00 mol dm^{-1} L-isoleucine solution for 1943 hours at 374 K. The rate constant for the forward reaction is $k_{1374K} = 9.02 * 10^{-5} h^{-1}$, K_{conv} for L-isoleucine conversion has the value of 1.38 (at 374 K). In the following calculation, abbreviate the concentration of L-isoleucine as $[L]$ and that of D-allo-isoleucine as $[D]$.

Evaluate (with three significant figures): $[L]_{eq}$ and diastomeric excess d_e after boiling.

4. At the start of the reaction, we can neglect the reverse reaction. The epimerization then follows the first-order kinetics:



The value of the rate constant for above reaction at 374 K is $k_{1374K} = 9.02 * 10^{-5} h^{-1}$ and at 421 K is $k_{1421K} = 1.18 * 10^{-2} h^{-1}$. In the following calculation, abbreviate the concentration of L-isoleucine as $[L]$ and of D-allo-isoleucine as $[D]$. We can define a quantity d_e (diastereomeric excess):

$$d_e = \left| \frac{[D] - [L]}{[D] + [L]} \right| * 100$$

We propose to boil L-isoleucine for 1943 hours at 374 K. **What is the value of d_e (with three significant figures) for L-isoleucine before boiling and after boiling?**