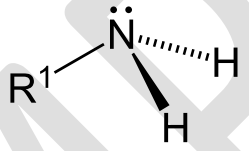
A Guide to Amination in Human Amino Acid Synthesis

This guide will first give an overview of amination and then describe in detail the process of amination in human amino acid synthesis.

What is Amination?

Amination is the name of the chemical process for the addition of an amine into an organic molecule, which forms a new carbon-nitrogen bond. An amine group is an R-NH_2 (*R-group*-Nitrogen-Hydrogen-Hydrogen) molecule that is added to another organic molecule. The R-group side chain is often a carbon-based group. An organic molecule is a molecule consisting of the carbon, hydrogen, oxygen, or nitrogen elements (C, H, O, and N respectively).



A primary amine molecule

How does Amination Occur Within the Body?

The body synthesizes (produces) amino acids (a building block of proteins). Amination is an important part of amino acid synthesis within the body. Amino acid synthesis is enzyme-catalyzed (facilitated by a special protein), and the amination reaction in amino acid synthesis is referred to as a *transamination* reaction. This amination reaction occurs in a cell.

What are Enzymes?

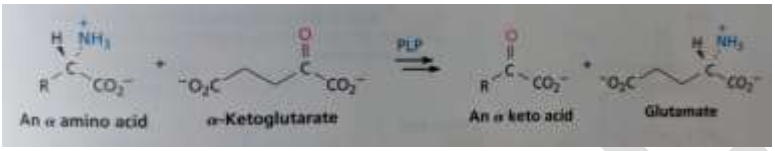
An enzyme is a special protein used in biochemical reactions to allow a reaction to take place. Often, molecules will not react spontaneously (on their own), and an enzyme is required to facilitate a reaction between two non- or weakly-reactive molecules. For the transamination reaction, these enzymes are in an enzyme class called *transaminases*.

What is Amino Acid Synthesis?

Our body acquires amino acids from the breakdown of proteins within the foods we eat. However, some of these amino acids are synthesized in the body. Amino acids can be broken down and rebuilt into different amino acids based on the body's needs.

What is a Transamination Reaction?

In the body, the amination in amino acid synthesis occurs as a *transamination* reaction. Transamination is a deamination (removal of an amine group) of one molecule and the amination of another molecule. The reaction is called a transamination because the amine is transferred from one molecule to another.



The reaction for glutamate synthesis

How Does Transamination Work in the Process of Amino Acid Synthesis?

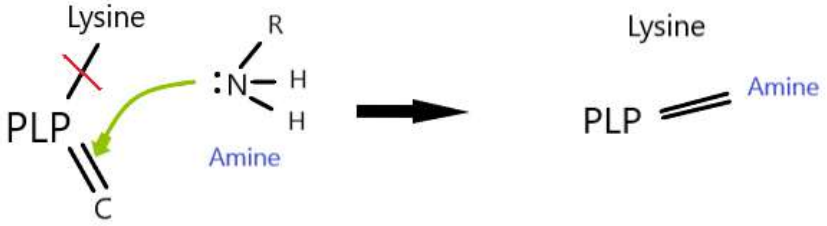
The process of transamination in amino acid synthesis occurs in two phases. The first phase involves the transfer of the amine of an amino acid to an intermediate enzyme. The second phase involves the addition of a different alpha keto acid to that amine, which is released as a new amino acid.

In short, the amine from a first amino acid transfers to a new amino acid with the enzyme as an intermediate.

The First Phase of Enzyme-Catalyzed Transamination

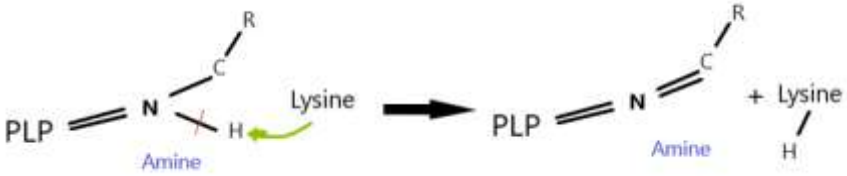
The first phase of transamination occurs in four main steps.

1. The amine group of an amino acid will be electrophilically attracted (attracted by atomic electrical forces) to the enzyme pyridoxal phosphate (PLP) and binds to PLP through a nucleophilic reaction. The nitrogen of the amine is attracted to the carbon double bond in the enzyme. Lysine on the enzyme is detached.



The first step of the transamination reaction

2. The amine now attached to PLP loses a hydrogen atom. The carbon of the R-group of the amine becomes double bonded to the nitrogen atom of the amine.

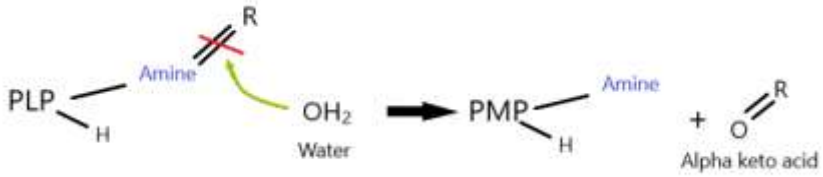


The second step of the transamination reaction

3. Free lysine in the cell donates a hydrogen to PLP, cleaving the double bond between PLP and the amine. The amine and PLP remain singly bonded.

The third step of the transamination reaction

4. In the aqueous environment of the cell, water is attracted to the amine and cleaves the new double bond between the carbon and the nitrogen (a reaction called hydrolysis). The R-group from the amine is released and bonded to water, which forms an alpha keto acid. The enzyme's new form is called Pyridoxamine Phosphate (PMP).



The fourth step of the transamination reaction

The first phase of the reaction is complete.

The Second Phase of Enzyme-Catalyzed Transamination

The exact reverse of the first phase occurs in the second phase of the reaction.

PMP + Alpha keto acid → PLP + Amino acid

1. An alpha keto acid (different from the first) will add to the amine on the enzyme, PMP. The addition forms a carbon-nitrogen double bond.

2. A hydrogen atom attaches to the newly added alpha keto acid's carbon atom, cleaving the double bond between the nitrogen and the carbon.

3. Free lysine in the cell will bind to PMP and cleave the added amine, which frees the amine. The cleavage frees the new amino acid from PMP. PMP is regenerated to PLP.

Bibliography

McMurry, John, and Begley, Tadgh. *The Organic Chemistry of Biological Pathways*. Roberts and Company, 2005, pp. 223-27.

Petsko, Gregory A, and Dagmar Ringe. *Protein Structure and Function*. Oxford University Press, 2009, p.4; 154.