A Preliminary Introduction to the Nature of Phenylalanine and Some Basic Reactions Related to It

Xiaoyue Shi
St John's College Cardiff, Cardiff, CF3 5YX, U.K.

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Abstract: The primary object of this study is to survey the nature of phenylalanine, and to study some basic reactions or other information related to it. This is a working which is based on theoretical research. Detailed information has been acquired about dehydration and condensation reaction, ionisation in water, important metabolisms, or a disease called phenylketonuria and so on. The work has contributed to our present understanding of this aromatic amino acid, and is a good reference for beginners in Chemistry who are interested in this topic.

1 INTRODUCTION

In recent years, with the deepening of biochemical research, more and more properties of amino acids have been recognized by people. Phenylalanine($C_9H_{11}NO_2$), with the bonding structure shown in Figure 1, as an aromatic amino acid and one of the essential amino acids that human bodies need, is also being developed in more and more fields, such as biosynthesis, microbio fermentation, treatment of relevant diseases.

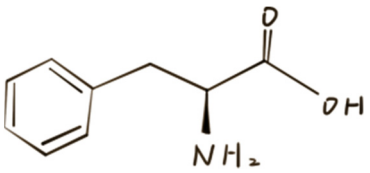

Figure 1: The Bonding Structure of Phenylalanine.

Unlike those professional researches, this article will provide an introduction to phenylalanine by giving a dossier of important information and facts. In the work, we introduce phenylalanine from four main aspects: the mode of obtaining, the contrast of solubility, basic reactions related and the metabolism in the human body. This work is a good source of useful information for those who are just beginning to do research in relavant field.

2 HOW IS PHENYLALANINE OBTAINED?

2.1 In Nature

Figure 2 shows the biosynthesis of phenylalanine. Aromatic amino acid, which includes phenylalanine, tyrosine, and tryptophan, can only be produced by plants and microbes. There is a common path in their synthesis, and shikimic acid is a common precursor to the synthesis of these aromatic acid. In this case we can call the common pathway shikimic acid pathway, that is, shikimic acid as the starting material until the formation of chorismic acid. The aromatic amino acid production pathway branches at chorismic acid. There are two pathways after this branch point: one to generate phenylalanine and tyrosine, and the other to form tryptophan. Chorismic acid is transformed to prephenic acid by chorismate mutase, which is then dehydrated and decarboxylated to form phenylpyruvic acid for phenylalanine production (Xiao, 2014).

From phenylpyruvic acid to L-phenylalanine, the molecules react under transamination. The mechanisms are shown in Figure 3.

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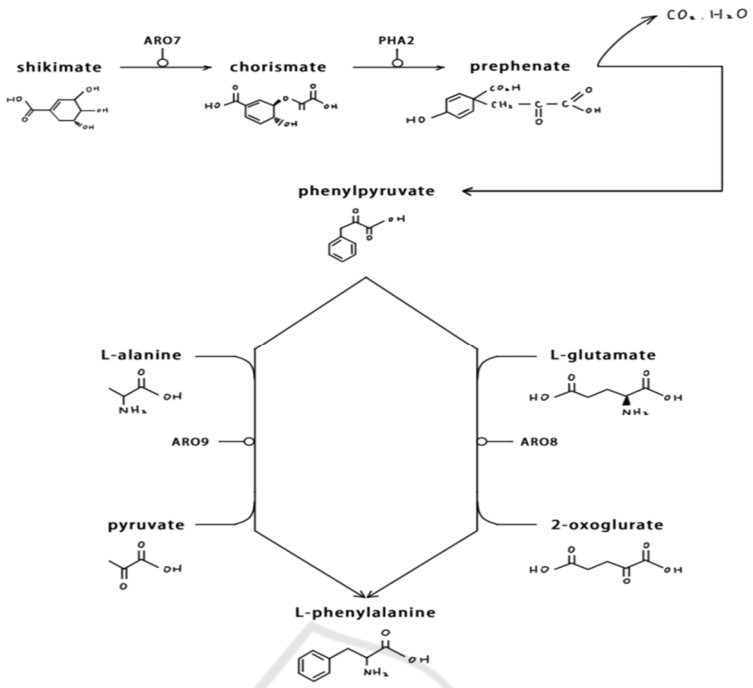

Figure 2: The Biosynthesis of Phenylalanine

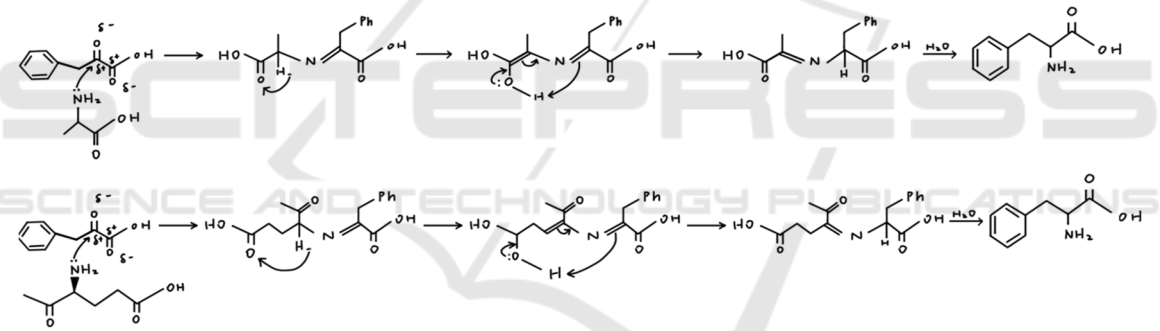

Figure 3: The Mechanisms for Synthesis of Phenylalanine (Hu, 1985).

2.2 None-Nature

Chemical synthesis, enzymatic technique, microbial fermentation, and asymmetric hydrogenation are the four primary approaches of non-natural phenylalanine synthesis.

As for chemical synthesis, somebody has already done it successfully as early as 1882. However, the route was too long and expensive.

For enzymatic method, there are two ways: Transaminase is used to make phenylalanine from phenylpyruvic acid, or phenylalanine ammonia-lyase is used to make phenylalanine from cinnamic acid. There are several advantages such as higher product concentration, fewer steps, and stronger production capacity. However, the cost of raw materials is excessive.

For microbial fermentation, there are two types: Precursor fermentation and direct fermentation. The former uses some intermediates in the pathway of amino acid biosynthesis as raw materials for fermentation to produce amino acids. Unfortunately, the cost is too high. In the latter, amino acids are produced directly from inorganic carbon and nitrogen sources, which is cheap and easy to obtain. Furthermore, because the reaction may be performed at normal temperature and pressure, this is one of the most common methods for producing amino acids (Lu, 2011; Pan, 1996).

For asymmetric hydrogenation, it adds a molecule of hydrogen across the double bond between α and β carbon of the amino acid. This is a method that people use extensively. This work was also recognised with the Nobel Prize in Chemistry (Li, 2002).

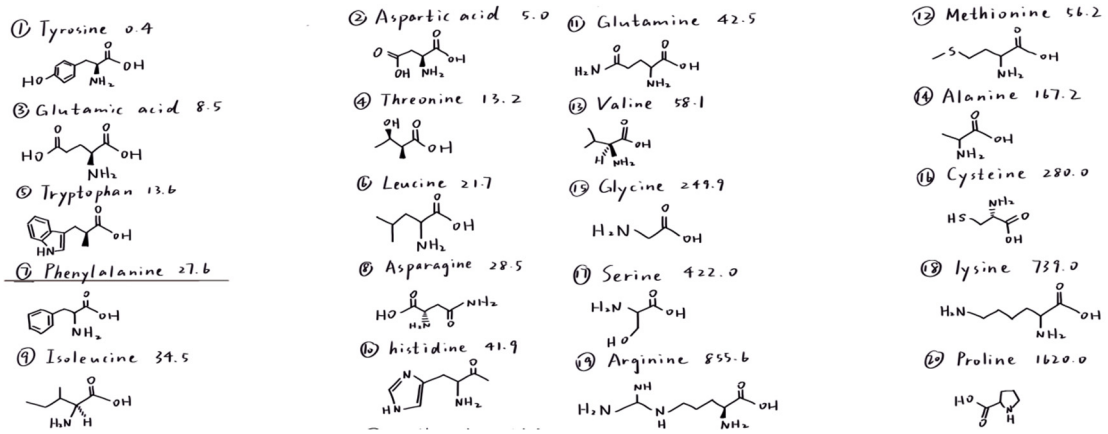

Figure 4: Solubility of 20 Amino Acids.

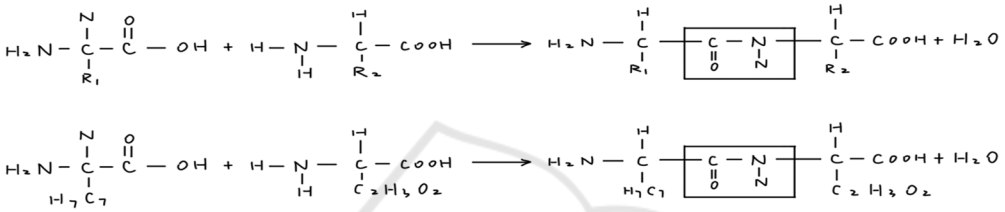

Figure 5: The Dehydration and Condensation Reaction of Two Amino Acid Molecules.

3 COMPARISON OF SOLUBILITY OF 20 AMINO ACIDS

Figure 4 shows the solubility of these amino acids, which is one measure of their characteristics. Even though there are only 20 of them, because they have such a wide range of properties, when starting to combine them, an infinite number of possibilities can be made which leads to quite a considerable number of differences in properties. Nature is guiding evolution by property from an evolutionary standpoint. Whatever the thing is, it needs to do something more efficiently and more effectively so that it can survive. And the fact that it has so many options feeds into this evolutionary development, which is beneficial to nature. For instance, nature finds a way to resist to medicine over time. The organism is trying to overcome whatever fighting. Often, it is just a single amino acid reaction.

4 SOME BASIC REACTIONS

4.1 The Dehydration and Condensation Reaction of Two Amino Acid Molecules

This is a reaction that join two amino acid molecules together. The general formula of reaction and the reaction of phenylalanine are shown in Figure 5.

The condensation reaction between two amino acid molecules is known as amino acid dehydration and condensation. Amino and carboxyl groups also generate a water molecule together.

The bonds that bind two amino acid molecules are called peptide bonds. A compound which is formed by the dehydration and condensation of two amino acid molecules is called a dipeptide, which contains a peptide bond. This process can be performed hundreds of thousands of times to produce a molecule that is extremely large. A polypeptide is a substance that is generated by the dehydration and condensation of several amino acid molecules and contains multiple peptide linkages. A peptide chain is a type of polypeptide that has a chain structure. A protein molecule with a specific spatial structure can be formed by twisting and folding peptide chains. A cell contains hundreds of thousands of amino acids of various kinds. The order of amino acids varies greatly

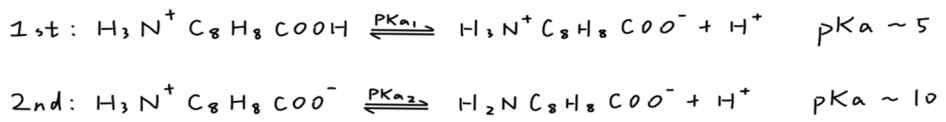

Figure 6: Reactions for Ionization of Phenylalanine in Water.

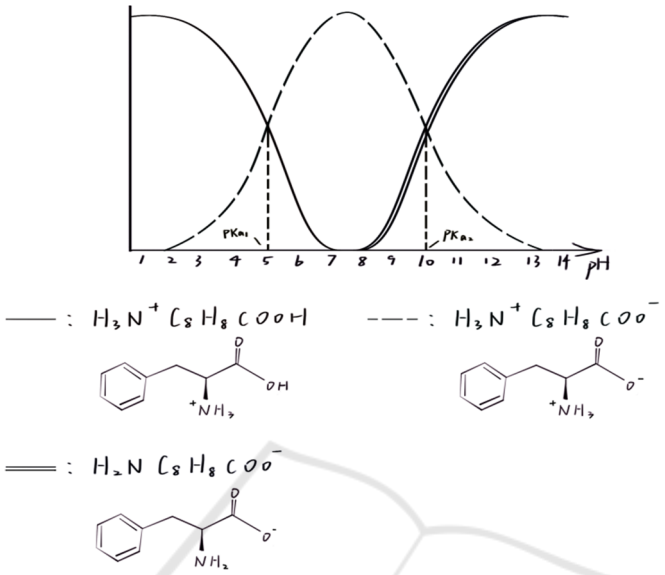

Figure 7: The Concentration of Different Ions in the Process of Phenylalanine Ionization (Fu, 2010).

when forming a peptide chain, and the way of twisting, folding, and forming the spatial structure also differs in thousands of ways. As a result, protein molecules have a wide range of structures (Chen, 2015).

4.2 Ionization of Phenylalanine in Water

The presence of $R\text{-}NH_2$ and $R\text{-}COOH$ in amino acids makes them amphoteric. According to the quantity of amino and carboxyl groups linked, all amino acids can be categorised into three types: neutral amino acid, acidic amino acid, and basic amino acid.

For phenylalanine, it is a neutral amino acid. Figure 6 shows the two steps of ionization.

When pH < pKa_1, the main form in solution is $H_3N^+C_8H_8COOH$.

When pH = pKa_1, there is about 50% of $H_3N^+C_8H_8COOH$ and 50% of $H_3N^+C_8H_8COO^-$.

When pKa_1 < pH < pKa_2, the main form in solution is $H_3N{+}C_8H_8COO^-$.

When pH = pKa_2, there is about 50% of $H3N^+COO^-$ and 50% of $H_2NC_8H_8COO^-$.

When pH > pKa_2, the main form in solution is $H_2NC_8H_8COO^-$ (Qie, 2000).

This can be converted into a graph, as shown in Figure 7.

5 METABOLISM IN THE HUMAN BODY AND A RELATED DISEASE

5.1 Metabolism Route

Figure 8 shows the metabolism route of phenylalanine. Inside the human body, most of the phenylalanine are oxidized to tyrosine by the catalysis of phenylalanine hydroxylase, and together with tyrosine, they synthesize important neurotransmitters and hormones, and participate in the body's glucose and fat metabolism. The remaining phenylalanine is converted into phenylpyruvic acid.

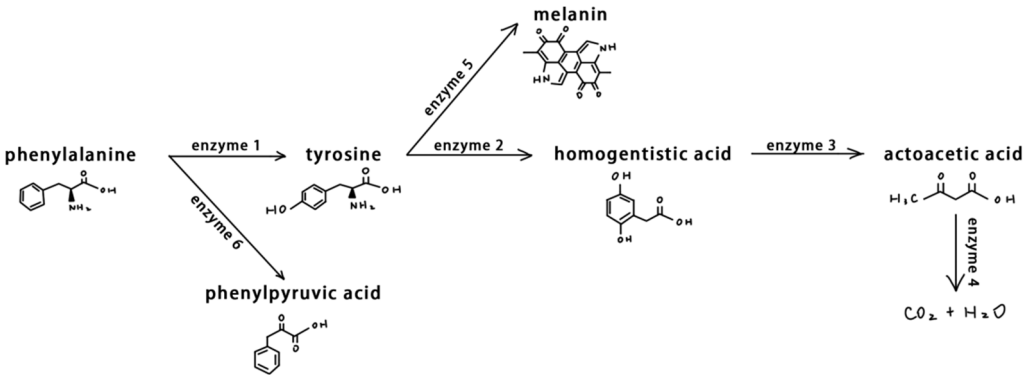

Figure 8: The Metabolism Route of Phenylalanine.

5.2 The Disease: Phenylketonuria

Mutations in any of the genes that encode the enzymes needed can lead to defects in the activity of those enzymes, which may lead to metabolic disorders in phenylalanine.

There are two types of phenylketonuria: deficiency of PKU or deficiency of BH_4. Phenylalanine cannot be turned into tyrosine in the former, resulting in brain cell destruction. However, the latter not only makes phenylalanine unable to be converted into tyrosine, it also blocks important neurotransmitters and therefore exacerbates the damage to the nervous system. When phenylketonuria patients are born, they normally have no abnormalities and are easy to be misdiagnosed (Zhang, 2022). Symptoms normally appear between the ages of 3 and 6 months, and they are most noticeable at the age of one year. Phenylketonuria patients should avoid phenylalanine-containing foods.

Phenylalanine ($C_9H_{11}NO_2$) can form phenylpyruvic acid ($C_9H_8O_3$) under transamination, which can be further converted into derivatives such as phenylacetic acid ($C_8H_8O_2$). At this point, the urine is full of various metabolites including big amount of phenylpyruvic acid. That is why the disease is called phenylketonuria (Xie, 2011).

6 CONCLUSION

In this investigation, the aim is to provide basic information and important facts of phenylalanine for beginners on this topic, which includes the way of obtaining in both nature and non-nature, the comparison of solubility of 20 amino acids, two typical reactions and its activity in the human body. It is unfortunate that the study did not include any in-depth knowledge, as they are too advanced for beginners. The insights gained from this study may be of assistance to future research into certain aspect of phenylalanine. This would be a fruitful area for further work.

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