TC2 - Amino Acids in Synthesis

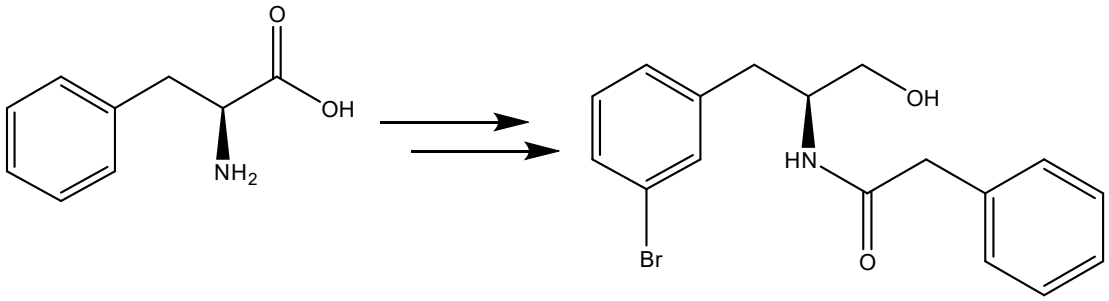
ARRANGING AMINO ACIDS IN THE PRIMARY STRUCTURE

Amino acids are considered as '**building blocks of life**'. This is primarily because they are so important in biosynthesis, without them, we wouldn't be able to form proteins, and we wouldn't exist today. One of the key features of the amino acids is that they all have the same general structure, but they have a variety of different side chains, with different properties.

Because there are 20 naturally occurring ones, they can arrange themselves in many different permutations. In fact, if you have a polypeptide chain consisting of the 20 different amino acids, then the number of different ways that you can arrange them is 20! = 2,432,902,008,176,640,000. And that is just for 20 amino acids! Protein usually have many more amino acids in them, the largest known protein, titin, has been shown to have 34,350 of these naturally occurring amino acids in total! In fact, when you look at the many different ways that these 20 amino acids can arrange in a protein of 34,350, the number very quickly approaches infinity! And bear in mind, that that's not even considering the many ways that protein can fold, and bond in 3D.

AMINO ACIDS IN SYNTHESIS – THE CHIRAL POOL

Amino acids are commonly found in nature. This means that they are relatively easy to obtain and therefore are very useful starting materials. They all have the same basic structure, containing a carboxylic acid, and an amine group which both make them incredibly useful in synthesis. A carboxylic acid can be converted into an alcohol, ester, amide, acyl chloride, or a carboxylate salt. And from each of these there is a plethora of further conversions which can be made. In a similar way, it's possible to convert amines into amides, imines, salts, and even alkenes.



Conversion of the functional groups in L-phenylalanine.

Because there are such a variety of amino acids, with such a variety of side chains, they can be used to produce a wide range of different products. The side chains on amino acids vary greatly, from glycine which has only an H atom, to phenylalanine which has a large benzene ring, and arginine, which has a relatively long chain and three nitrogen atoms in its side chain. These amino acids can be used as scaffolds to develop larger and more complicated drugs. So, if you want to develop a drug which has an alcohol group, an amide group, and a benzene ring, then you can start by using phenylalanine, and after some conversions then you can get to your desired product. This is often a much simpler way than trying to build the molecule from scratch, as a lot of the hard work has already been done for you!

Produced by Adam Stubbs at Newcastle University as part of a summer outreach project.

This can be used as a scaffold to build drugs, and is often much easier to do than to build a drug from simpler molecules. Crucially, this uses the stereochemistry of the precursor. This particular molecule could be made from L-phenylalanine in three stages, reducing the carboxylic group, converting the amine to an amide, and then adding the Br group. All of this is achieved by making use of the natural stereochemistry and functional groups present in amino acids.

CHIRALITY

One key property of amino acids is their chirality – the fact that they can exist as two different enantiomers. Chirality is incredibly important to consider in chemical synthesis. For example, if you are making a medicinal drug, then each enantiomer of the drug may have different potencies and effects on the body. One may be safe, whilst one may be dangerous. Some drugs can be produced from achiral precursors, by building up each part of the drug sequentially. One of the problems of this is that the drugs will not be chirally pure, in other words, if you start from achiral precursors, then you may end up with a mixture of each enantiomer in the final product. This isn't ideal, because the two enantiomers may have to be purified and separated, which can be an expensive process. Instead, it can be much easier to use a precursor which is chiral, such as amino acids. This way, if you are making the D-enantiomer of a drug, then you can begin with the D-enantiomer of an amino acid. Then you can be sure that the drug has the right chirality built in from the start, and save a lot of time and money!