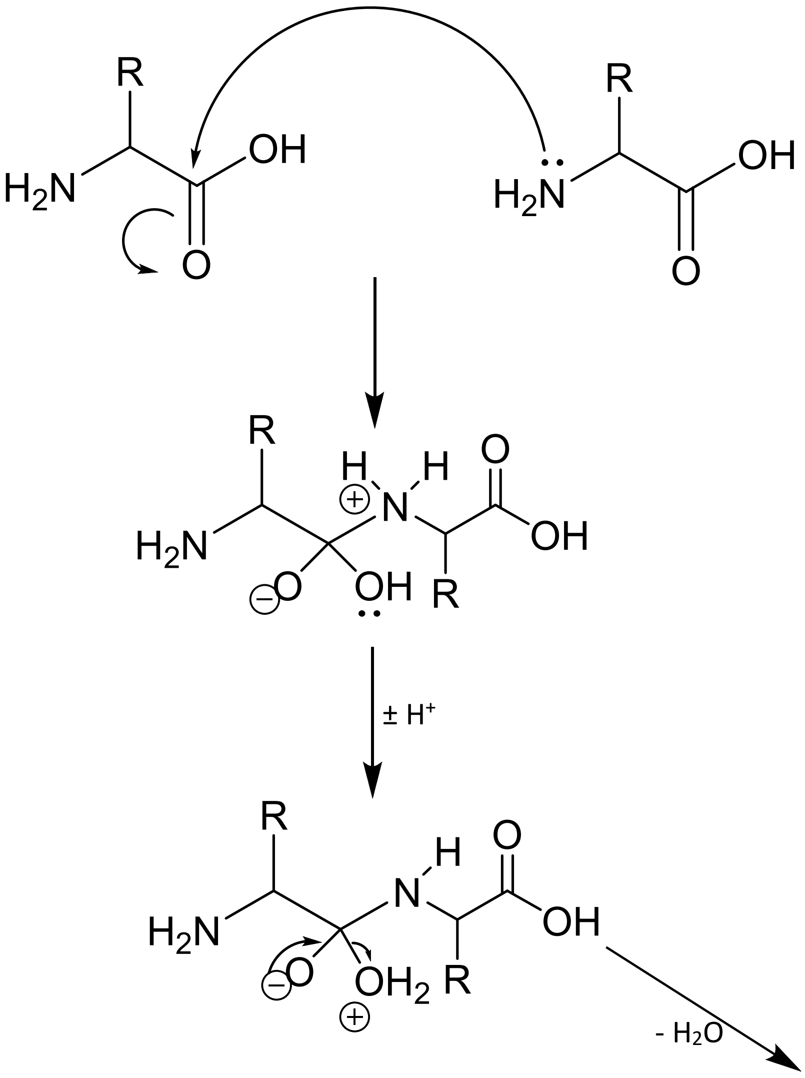
TA3 - Peptide Bonds

Amino acids join together via **condensation reactions** to form **peptide bonds**. Chains of amino acids are called **polypeptides**. The order of amino acids in these chains is **specific**, and this determines the **primary structure** of a protein.

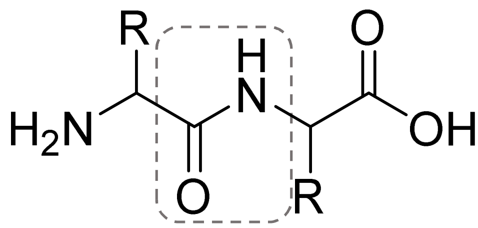
A condensation reaction is one where two molecules combine to produce a larger one, **eliminating** a small molecule, such as $\mathbf{H_2O}$ in the process.



These H-N-C=O bonds formed are called **amide bonds**. When they amino acids into peptides, they are also known as **peptide bonds**. Be careful, they are only peptide bonds if they are in a peptide!

Peptide bond formation is a **nucleophilic addition-elimination** reaction. Where the **nucleophilic** (electron-rich) lone pair on the amine group attacks the electron-poor carbonyl group in an **addition** step. This forms a tetrahedral intermediate which then collapses to **eliminate** water and give the dipeptide.

The peptide bond is marked here:



Produced by Lucy Jakubecz at Newcastle University as part of an MChem project.
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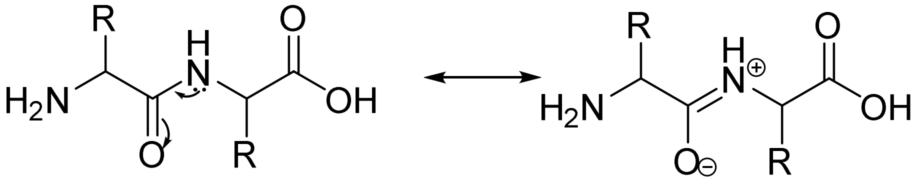
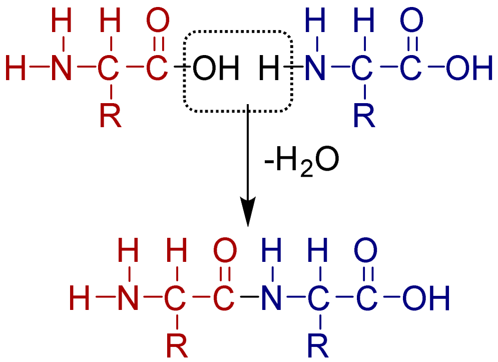
This amide bond which forms is **rigid and planar**, just like a double bond is. This is because the nitrogen lone pair is delocalised onto the carbonyl oxygen. This stabilises the peptide bond, and makes it rigid. This makes the peptide bond planar, because it takes a lot of energy to overcome this double-bond character, and it is therefore **inflexible**, unlike single bonds.



CONDENSATION VS. HYDROLYSIS



The general equation for peptide formation is this condensation reaction:

$H_2NCHRCOOH + HNHCHRCOOH \rightarrow$
$H_2NCHRCONHCHRCOOH + H_2O$

But what about the reverse reaction? Adding water to a peptide:

$H_2NCHRCONHCHRCOOH + H_2O \rightarrow H_2NCHRCOOH +$
$HNHCHRCOOH$

This is a **hydrolysis reaction** – adding water to split a bond. It is the opposite to a condensation reaction, and is chemically possible. But think about it, our bodies are full of protein in our muscles and elsewhere, and also full of water. So why does the protein in our muscle not break down into amino acids? Equally, our hair and nails are made from keratin, a type of protein. So why don't they break down whenever we shower or swim?

The answer depends on the **rates of each reaction**, and the **reaction conditions**. When two amino acids form a dipeptide, they create a strong peptide/amide bond. As we've already seen, this is **stabilised by delocalisation** of the amide lone pair. So even though it is possible to add water to a peptide and split it into its constituent amino acids, it's **not very favourable**, because amides are more stable than the amino acids. To do this, we would have to overcome this strong peptide bond, which is unfeasible under standard conditions. If the reaction is heated up to extreme temperatures, then it may provide enough energy to break this peptide bond, and start to break down proteins. Proteins can also be hydrolysed more easily at extreme pH levels, or using enzymes to catalyse the reactions, such as proteases.

EQUILIBRIA

This is a great example of an **equilibrium** reaction. At standard temperatures, the equilibrium lies massively to the right, and amino acids will condense to form peptides. Under standard conditions, the peptides don't break down. But if the temperature is raised high enough, then it gives the system energy to break the peptide bonds, and hydrolyse the polypeptides. This changes the position of the equilibrium, so that it is much easier to hydrolyse the peptides.

$H_2NCHRCOOH + H_2NCHRCOOH \leftrightarrow H_2NCHRCONHCHRCOOH + H_2O$

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