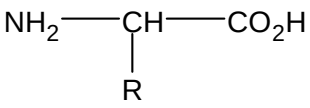
Amino Acids, Proteins and DNA

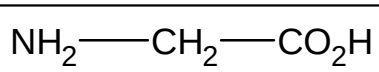
General structure of an α amino acid



The R group can be a variety of different things depending on what amino acid it is.

The alpha in '**α'** amino acid means both NH_2 and COOH groups are joined to the same C.

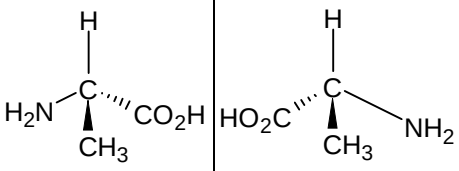
The simplest amino acid is glycine, where the R is an H



Optical Activity

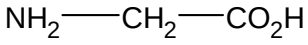
All amino acids, except glycine, are chiral because there are four different groups around the C

They rotate plane polarised light.

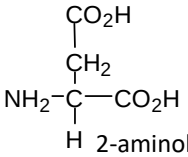


Naming amino acids

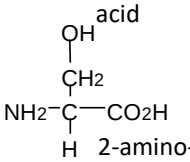
You do not need to know any common names for the 20 essential amino acids. You should, however, be able to name given amino acids using IUPAC organic naming



(2-)aminoethanoic acid

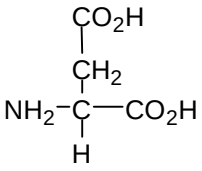


2-aminobutanedioic acid

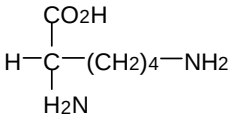


2-amino-3-hydroxypropanoic acid

Some amino acids have an extra carboxylic acid or an amine group on the R group. These are classed as acidic or basic (respectively) amino acids



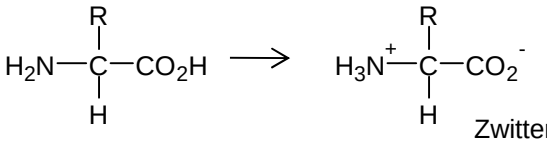
Aspartic acid



Lycine (basic)
2,6-diaminohexanoic acid

Zwitterions

The no charge form of an amino acid never occurs. The amino acid exists as a dipolar zwitterion.



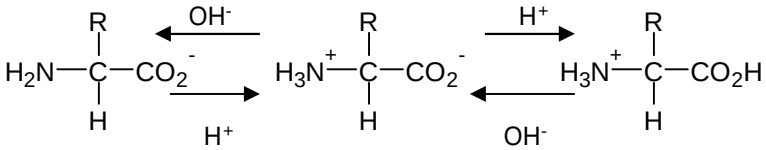
Zwitterion

Amino acids are often **solids**

The **ionic interaction** between zwitterions explains the relatively high melting points of amino acids as opposed to the weaker hydrogen bonding that would occur in the no charge form.

Acidity and Basicity

The amine group is basic and the carboxylic acid group is acidic.



Species in alkaline solution High pH

Species in neutral solution

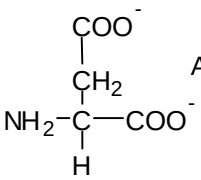
Species in acidic solution Low pH

Amino acids act as weak buffers and will only gradually change pH if small amounts of acid or alkali are added to the amino acids.

$^{+}NH_3\text{-}CH_2\text{-}CO_2^{-} + HCl \rightarrow Cl^{-}\ NH_3^{+}\text{-}CH_2\text{-}CO_2H$

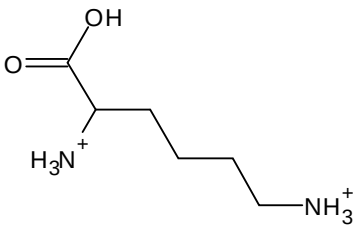
$^{+}NH_3\text{-}CH_2\text{-}CO_2^{-} + NaOH \rightarrow\ NH_2\text{-}CH_2\text{-}CO_2^{-}Na^{+} + H_2O$

The extra carboxylic acid or amine groups on the R group will also react and change form in alkaline and acid conditions.



Aspartic acid in high pH

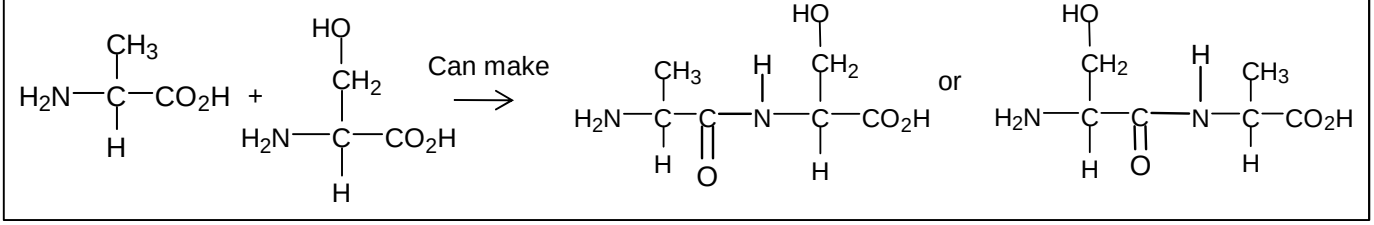
Skeletal formula of lycine in low pH



Dipeptides

Dipeptides are simple combination molecules of two amino acids with one amide (peptide) link.

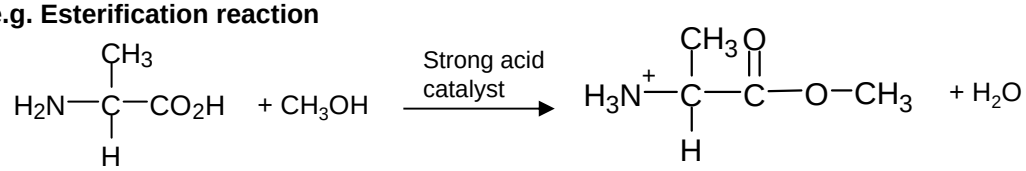
For any two different amino acids there are two possible combinations of the amino acids in the dipeptide.

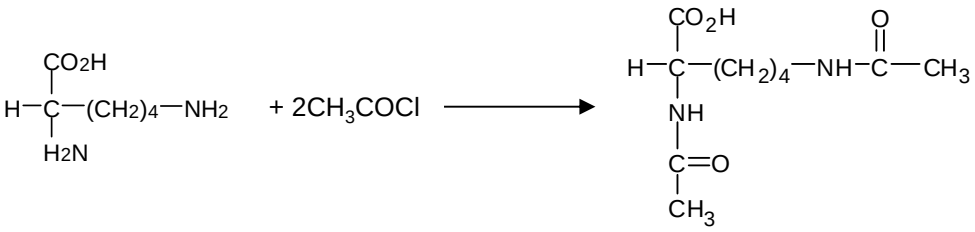


Other reactions of amino acids

The carboxylic acid group and amine group in amino acids can undergo the usual reactions of these functional groups met in earlier topics. Sometimes questions refer to these.

e.g. Esterification reaction



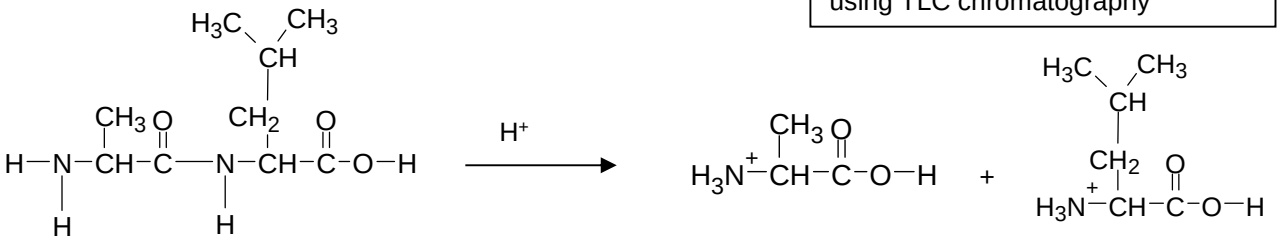


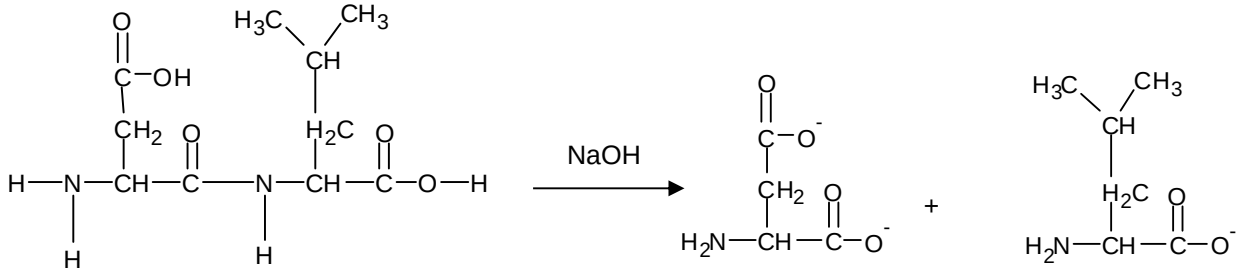
If the R group contains an amine or carboxylic acid then these will do the same reactions as the **α** amine and carboxylic groups

Hydrolysis of di-peptides/proteins

If proteins are heated with dilute acid or alkali they can be hydrolysed and split back into their constituent amino acids.

The composition of the protein molecule may then be deduced by using TLC chromatography





Chromatography of Amino Acids

A mixture of amino acids can be separated by chromatography and identified from the amount they have moved.

Method: **Thin-layer chromatography**

a) **Wearing gloves**, draw a **pencil line** 1 cm above the bottom of a TLC plate and mark spots for each sample, equally spaced along line.
b) Use a capillary tube to add a **tiny drop** of each solution to a different spot and allow the plate to air dry.
c) Add solvent to a chamber or large beaker with a lid so that is no more than **1cm in depth**
d) Place the TLC plate into the chamber, **making sure that the level of the solvent is below the pencil line**. Replace the **lid to get a tight** seal.
e) When the level of the solvent **reaches about 1 cm from the top of the plate**, remove the plate and mark the solvent level with a pencil. Allow the plate to **dry in the fume cupboard.**
f) Spray paper with **ninhydrin** and put in oven
Draw around them lightly in pencil.
g) Calculate the Rf values of the observed spots.

Wear plastic gloves to prevent contamination from the hands to the plate

pencil line –will not dissolve in the solvent

tiny drop – too big a drop will cause different spots to merge

Depth of solvent– if the solvent is too deep it will dissolve the sample spots from the plate

lid– to prevent evaporation of toxic solvent

Will get more accurate results if the solvent is allowed to rise to near the top of the plate but the Rf value can be calculated if the solvent front does not reach the top of the plate

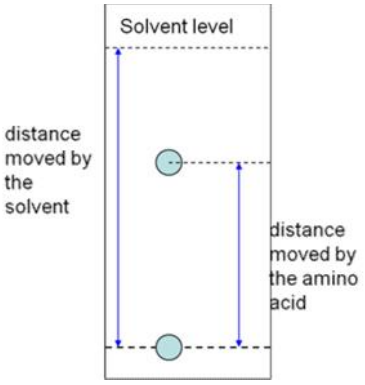
dry in **a fume** cupboard as the solvent is toxic

If ninhydrin is sprayed on an amino acid and then heated for 10 minutes then red to blue spots appear.
This is done because amino acids are transparent and cannot be seen.

R_f value = $\frac{\text{distance moved by amino acid}}{\text{distance moved by the solvent}}$

Measure how far each spot travels relative to the solvent front and calculate the *R*f value.
Each amino acid has its own R_f value
Compare *R*f values to those for known substances.

Some substances won't separate because similar compounds have similar *R*f values. So some spots may contain more than one compound

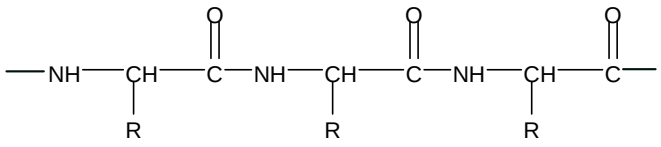


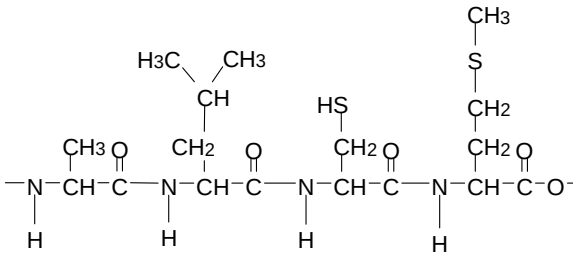
Proteins

Primary Structure of Proteins

Proteins are polymers made from combinations of amino acids.
The amino acids are linked by peptide links, which are the amide functional group.

The primary structure of proteins is the sequence of the 20 different naturally occurring amino acids joined together by condensation reactions with peptide links.



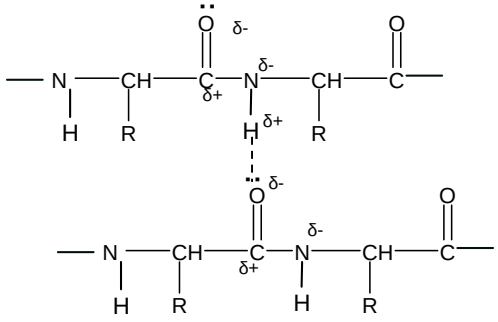


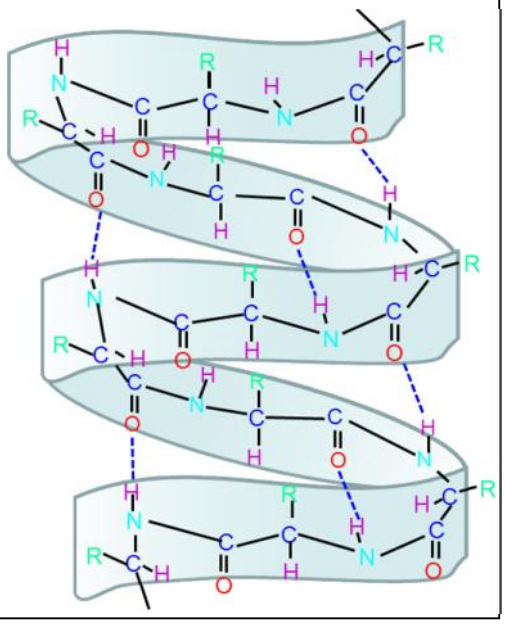
Secondary Structure of a Protein.

Secondary Structure: α-helix

The 3D arrangement of amino acids with the polypeptide chain in a corkscrew shape is held in place by Hydrogen bonds between the H of $-N^{\delta-}-H^{\delta+}$ group and the –O of $C^{\delta+}=O^{\delta-}$ of the fourth amino acid along the chain

The R-groups on the amino acids are all pointed to the outside of the helix



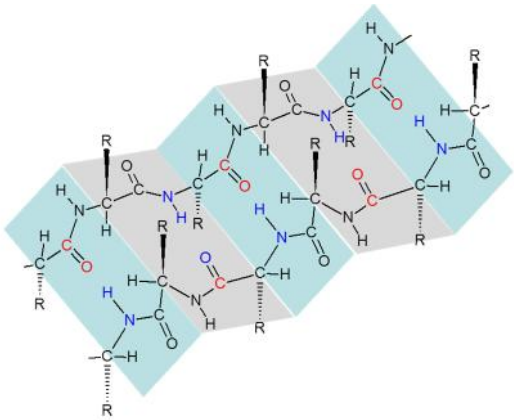


Secondary Structure: β-Pleated Sheet Structure of Proteins

The secondary structure can also take the form of a β–pleated sheets

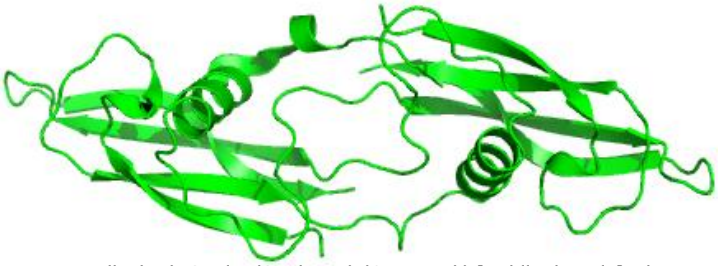
The protein chain folds into parallel strands side by side

The protein chain is held into a the pleated shape by Hydrogen bonds between the H of –N-H group and the –O of C=O of the amino acid much further along the chain in the parallel region .



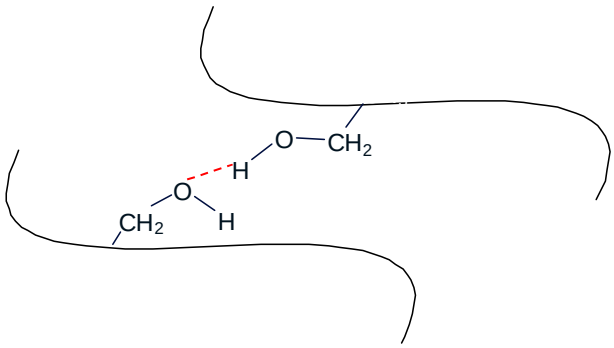
Tertiary Structures of Proteins

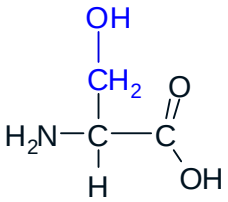
The tertiary structure is the folding of the secondary structure into more complex shapes. It is held in place by interactions between the R- side groups in more distant amino acids . These can be a variety of interactions including hydrogen bonding, sulfur-sulfur bonds and ionic interactions.



By Elizabeth Speltz (SpeltzEB) (Own work) [Public domain], via Wikimedia Commons

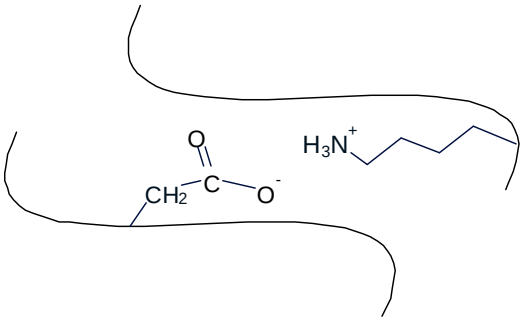
Hydrogen bonds





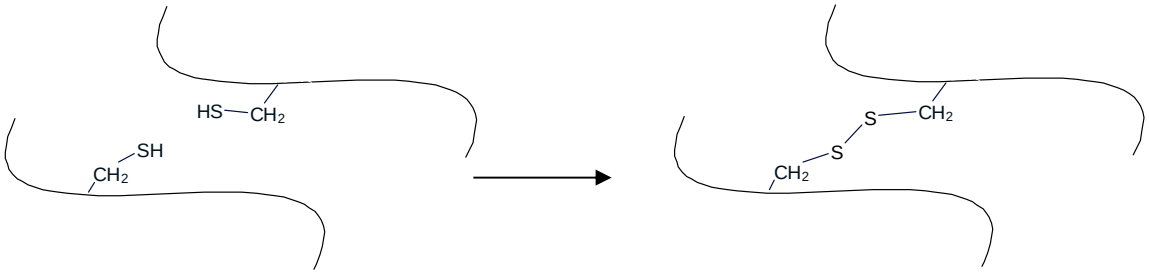
Hydrogen bonds could form between two serine side chains in different parts of the folded chain. (Other amino acids chains can also hydrogen bond)

ionic interactions

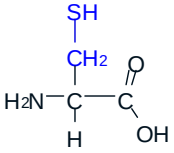


Ionic interactions could form between acidic amino acids such as aspartic acid and basic amino acids such as lysine. There is a transfer of a hydrogen ion from the -COOH to the -NH_2 group to form zwitterions just as in simple amino acids.

Sulfur bridges



If two cysteine side chains end up near each other due to folding in the protein chain, they can react to form a ***sulfur bridge***, which is a covalent bond.



cysteine (cys)

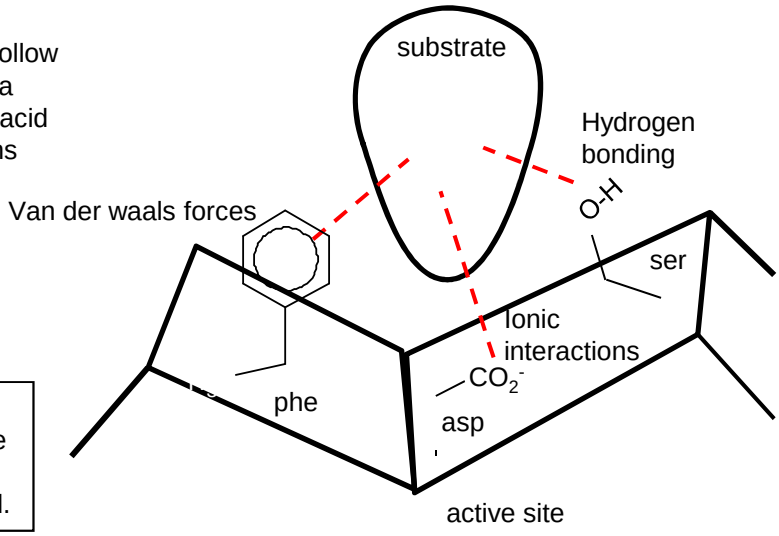
You don't need to learn the details of these interactions on this page but understand the principles of how the tertiary structure is held in place.

Enzymes

Enzymes are proteins.

The active site of an enzyme is usually a hollow in the globular protein structure into which a substrate molecule can bond to the amino acid side chains through a variety of interactions including

- Hydrogen bonding
- Van der waals forces
- Permanent dipole forces
- Ionic interactions



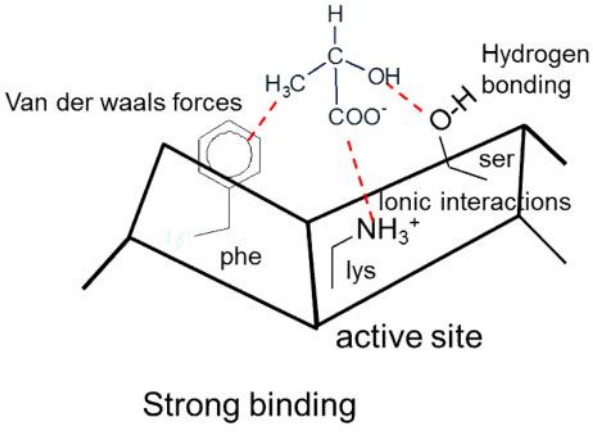
When the enzyme bonds to the active site it is called and enzyme-substrate complex.

The interactions need to be strong enough to hold the substrate for long enough for the enzyme catalysed reaction to occur, but weak enough for the product to be released.

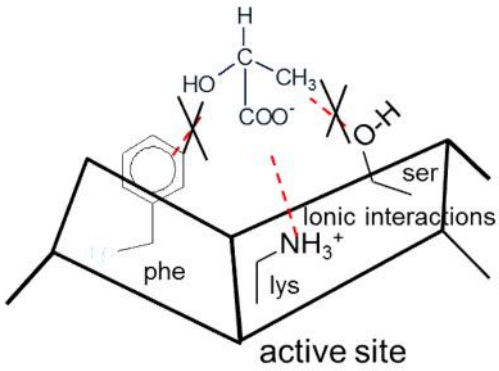
Only substrate molecules with the right shape and correct positions of functional groups will fit and bind to the active site- called the **lock and key hypothesis**

Stereospecific active site

If the substrate is chiral then its likely that only one enantiomer will fit in the enzyme and so only one isomer will be catalysed



Strong binding



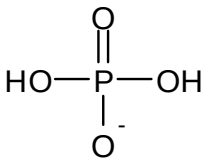
weak binding

Drugs as Enzyme Inhibitors

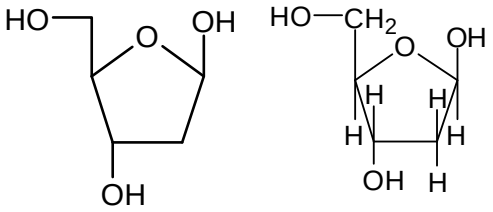
Many drugs act as an enzyme inhibitor by blocking the active site.
The inhibitor will often bind to the active site strongly so stopping the substrate attaching to the enzyme.
(Some Inhibitors can also attach elsewhere on the enzyme but in doing so can change the shape of the active site which also stops its effectiveness)
Computers can be used to help design such drugs

DNA

Key molecules in DNA

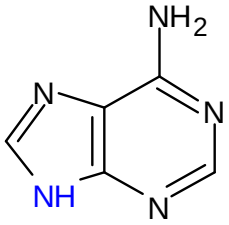


phosphate ion

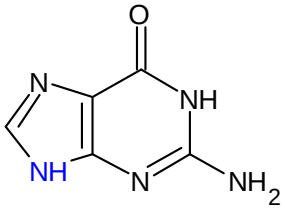


2-deoxyribose (a pentose sugar)

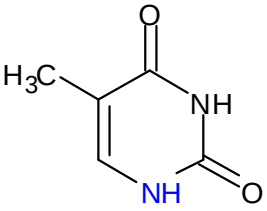
The 4 bases



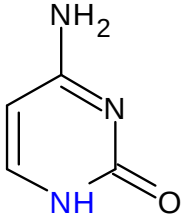
Adenine (A)



Guanine (G)



Thymine (T)

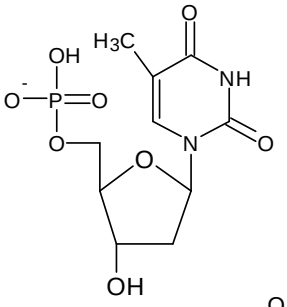


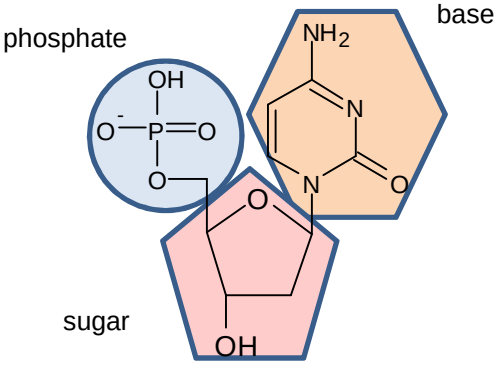
Cytosine (C)

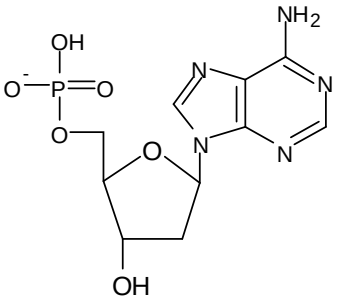
The structures of these substances are given in the Chemistry Data Booklet.

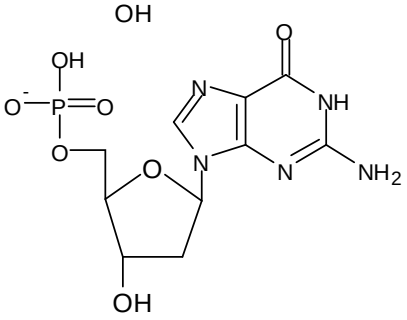
Nucleotides

A nucleotide is made up from a phosphate ion bonded to 2-deoxyribose which is in turn bonded to one of the four bases adenine, cytosine, guanine and thymine



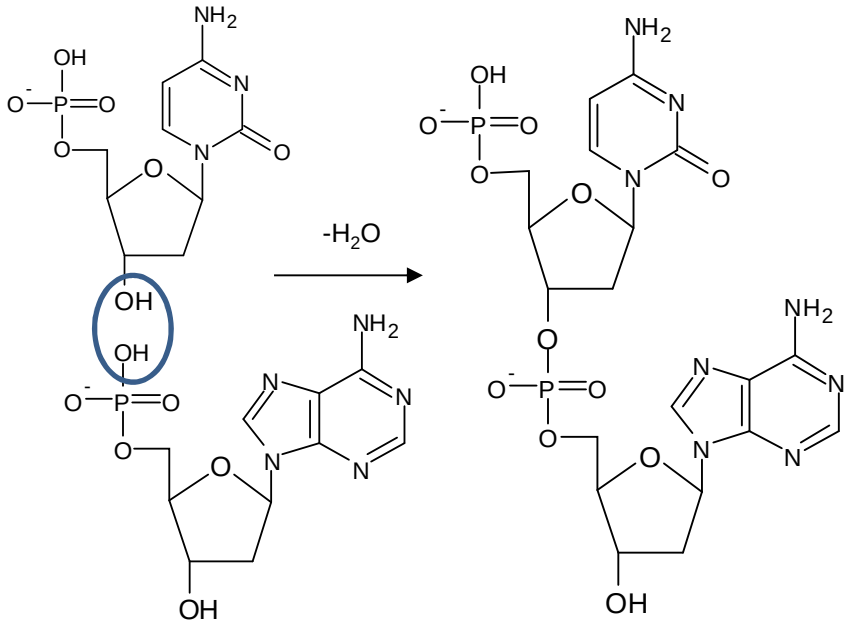






Although the structures will be given in the data sheet you need to learn which atoms on the base joins on to the sugar and how the sugar attaches to the phosphate ions

Sugar- phosphate chain

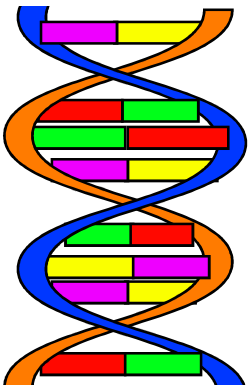


A single strand of DNA (deoxyribonucleic acid) is a polymer of nucleotides linked by covalent bonds between the phosphate group of one nucleotide and the 2-deoxyribose of another nucleotide.

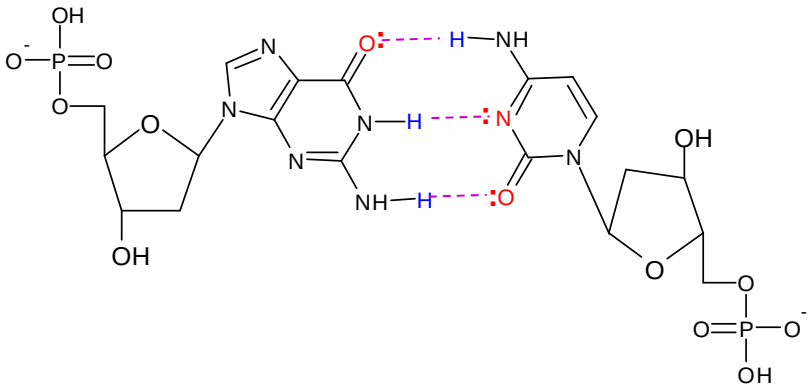
This results in a sugar-phosphate-sugar- phosphate polymer chain with bases attached to the sugars in the chain.

Carefully learn how these join together

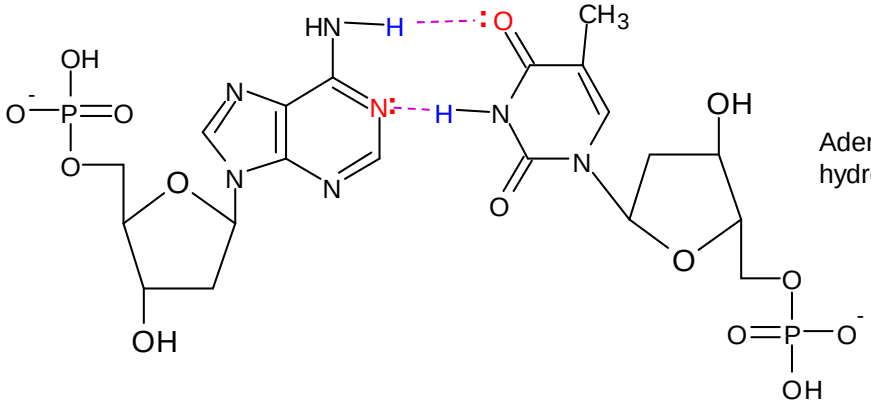
DNA exists as two complementary strands of the sugar phosphate polymer chain arranged in the form of a double helix.



Hydrogen bonding between base pairs leads to the two complementary strands of DNA.



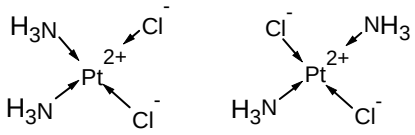
Guanine pairs with cytosine by 3 hydrogen bonds



Adenine pairs with thymine by 2 hydrogen bonds

Cisplatin

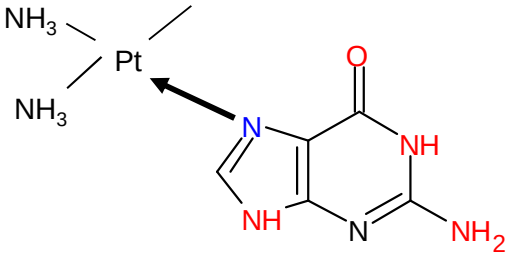
The Pt(II) complex cisplatin is used as an anticancer drug.



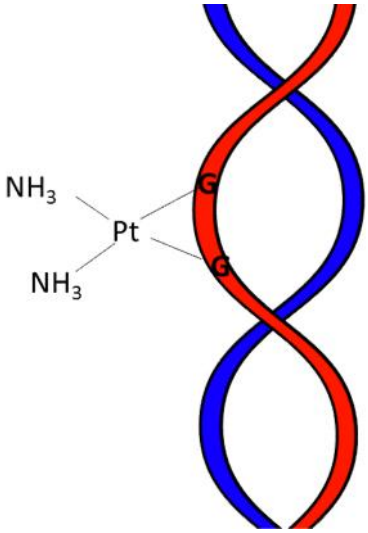
cisplatin transplatin

The cisplatin version only works as two chloride ions are displaced and the molecule joins on to the DNA. In doing this it stops the replication of cancerous cells.

Cisplatin prevents DNA replication in cancer cells by a ligand replacement reaction with DNA in which a dative covalent bond is formed between platinum and a nitrogen atom on guanine



The N and O atoms marked in red can't bond to cis-platin as they are involved in the bonding within the DNA



Cisplatin can also prevent the replication of healthy cells by bonding on to healthy DNA which may lead to unwanted side effects like hair loss.
Unwanted side effects can be minimised by giving cis-platin in small doses.
Society needs to assess the balance between the benefits and the adverse effects of drugs, such as the anticancer drug cisplatin.