# CHEM 191
## Module 4
## Structures and reactions of biological molecules

## Lecture 1
## Introduction to Biological Molecules and Functional Groups

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## Module 4 Lecture 1
## Learning objectives

- Be able to distinguish and name functional groups covered in this lecture
- Describe and compare the properties of these functional groups

  (*developed in more depth throughout the module*)

  - know the oxidation products of different classes of alcohols.
  - understand the difference in reactivity of amines and amides.
- Appreciate the importance of molecular shape for biological activity

**Textbook** 'Chemistry: The Central Science' **15th edition**
*Referral to specific pages given throughout lecture slides*

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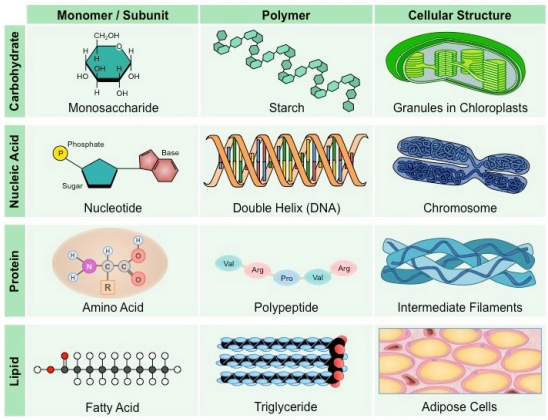
## What are 'biological molecules' ?

- Chemical compounds found in living organisms
- Are 'organic', which in chemistry means containing **carbon**
- In addition to carbon, may contain **hydrogen**, **oxygen**, **nitrogen**, **phosphorus**, **sulfur**, and additional minor elements.




https://www.curioustem.org/stem-articles/classes-of-organic-molecules

There are four major classes of biological molecules:

- Carbohydrates
- Nucleic acids
- Proteins
- Lipids

These often large molecules are necessary for life. Each is an important component of a cell and performs a wide array of functions.

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## Functional groups and shape of biological molecules

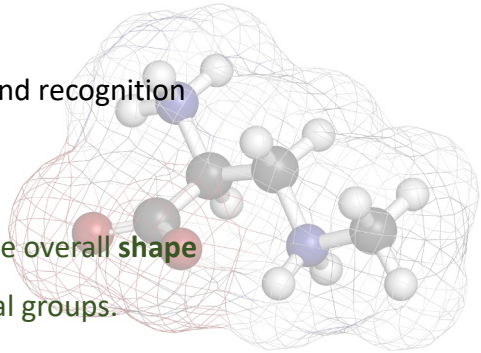
The chemistry of biological molecules is dominated by two key factors:

**Functional group chemistry**

- The properties and reactivity of a large biological molecule can be attributed to the chemistry of the functional group(s) it contains
- *This lecture recaps/introduces the functional groups important in biological molecules*

**Molecular shape**

- Is very important in terms of biological function and recognition
- *Developed further throughout module 4*



These factors are *linked* – **functional groups** can influence overall **shape** and **shape** can influence the reactivity of functional groups.

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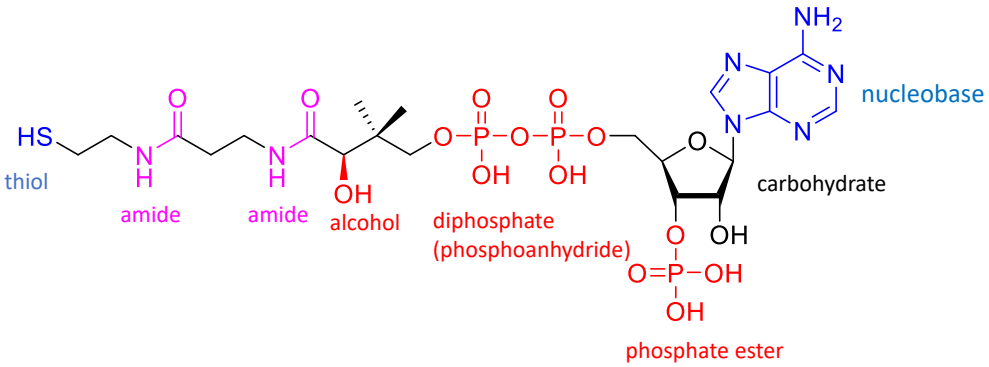
## Functional groups and shape of biological molecules - example

### Coenzyme A (CoA)

Coenzymes help enzymes catalyse reactions, for example the biosynthesis of fatty acids

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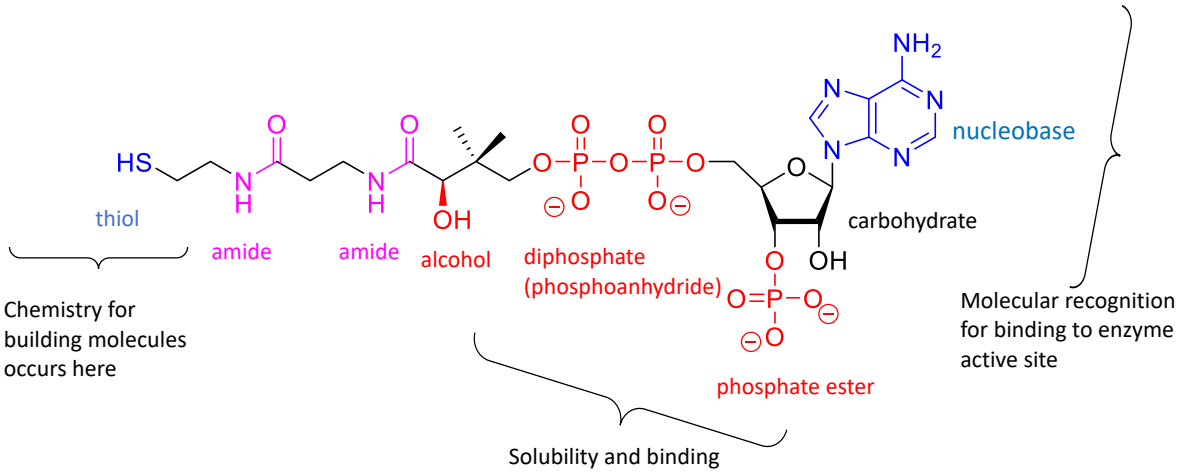
## Functional groups and shape of biological molecules - example

### Coenzyme A (CoA)

Coenzymes help enzymes catalyse reactions, for example the biosynthesis of fatty acids

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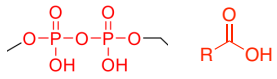
## Alcohols

**NOT an alcohol**



- R-OH, 'hydroxyl' where R = $sp^3$ hybridised carbon
- Low molecular weight alcohols are soluble in water due to hydrogen bonding

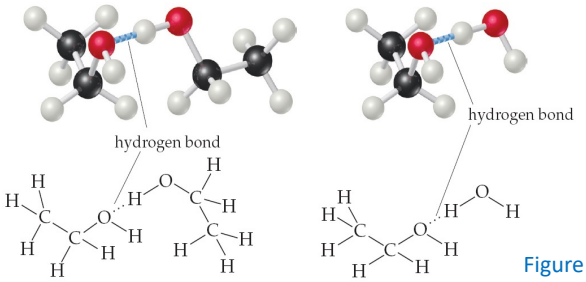



Figure 27.3

- Undergo nucleophilic substitution reactions (module 3)
- Can be oxidised
- Form esters with carboxylic acids (lecture 5)

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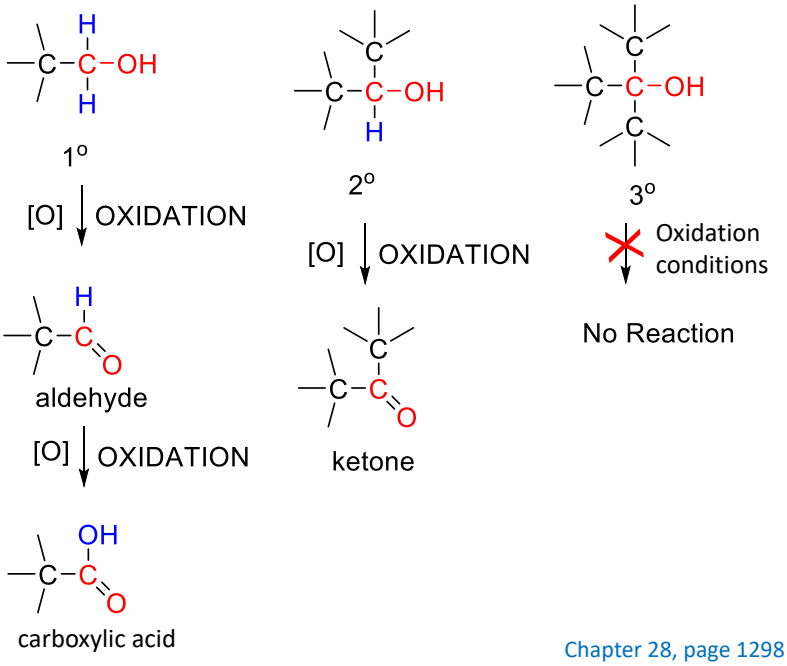
## Oxidation of alcohols

3 classes of alcohols behave differently with oxidising agents.

- Primary (1°) oxidised to aldehydes then to carboxylic acids
- Secondary (2°) oxidised to ketones
- Tertiary alcohols (3°) not readily oxidised




Chapter 28, page 1298

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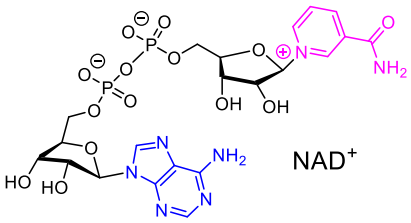
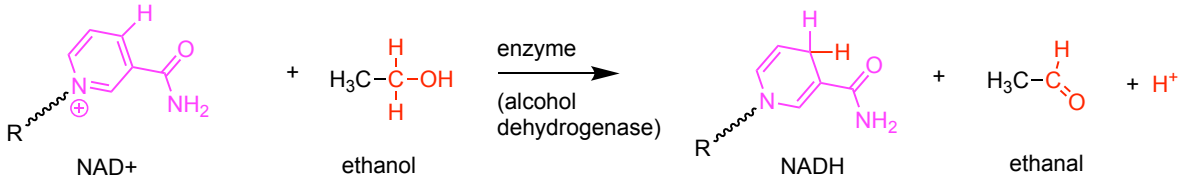
## Oxidation and reduction in living systems

- Living systems don't use laboratory chemicals to do oxidations
- Usually done using enzymes, e.g. ethanol is enzymatically oxidised to ethanal in the liver, the oxidant is a coenzyme called $NAD^+$




The reaction is represented as:




NADH is also used as a coenzyme by other enzymes to achieve reverse process (i.e. reduction reactions)

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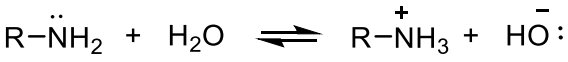
## Amines and amides

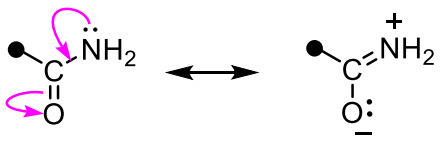
The distinction between amines and amides is important.

Amines are significantly basic and nucleophilic:



Amides are not appreciably basic or nucleophilic

- An amide has a C=O next to the nitrogen.
- The C=O bond is polar and withdraws the nitrogen lone pair of electrons away from the nitrogen, shown here in a resonance diagram -



Amides can act as **electrophiles** and react with nucleophiles such as water under harsh conditions but are not very reactive and are quite resistant to hydrolysis

*more details about this later in the module….*

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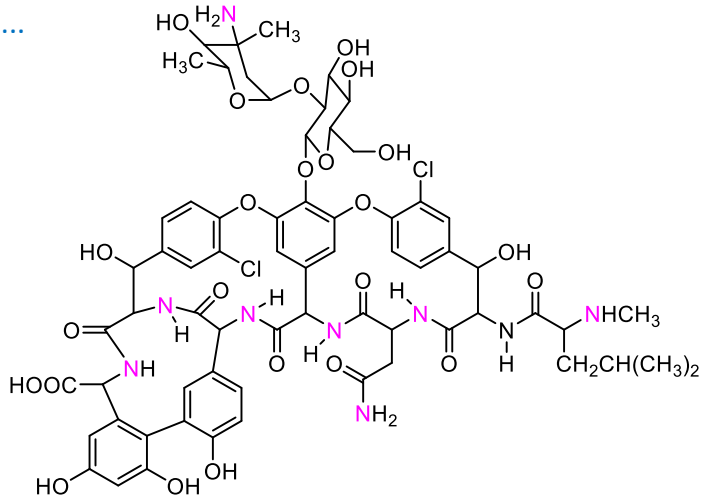
## Vancomycin

- An antibiotic isolated from soil organism *Streptomyces orientalis*
- Very effective against penicillin resistant bacteria
- Contains both amides and amines…..

Has 9 nitrogen atoms.

Identify the two amine groups



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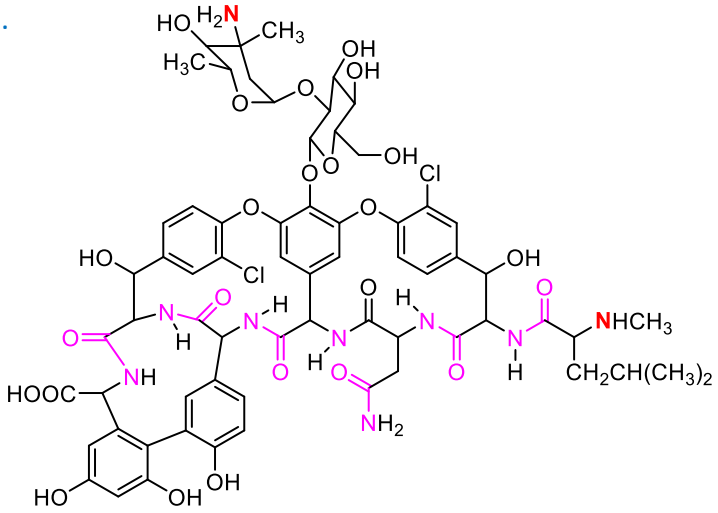
## Vancomycin

- An antibiotic isolated from soil organism *Streptomyces orientalis*
- Very effective against penicillin resistant bacteria
- Contains both amides and amines…..

Red N are amines
Pink groups are amides

*Can you also identify the alcohols?*



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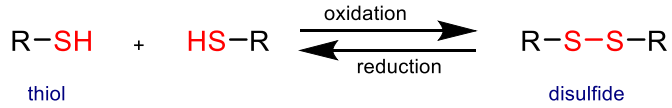
## Thiols and disulfides

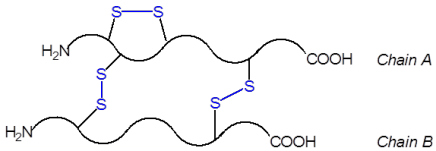
- Important reaction in protein chemistry – oxidation of a thiol leads to a disulfide
- Formation of disulfides can 'link' peptide chain together, "disulfide bridge" , important for peptide/protein shape




This can be achieved with quite mild oxidants – *e.g.* $O_2$.

The reverse reaction can also be achieved using mild reducing agents

Disulfides in insulin

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## Phosphorus containing functional groups

$H_3PO_4$ forms a series of phosphate esters where the OH groups are successively replaced by OR groups from alcohols


**phosphoric acid** | **phosphate monoester** | **phosphate diester (or phosphodiester)** | **phosphate triester**

Phosphoric acid, phosphate monoesters and phosphate diesters are **strong acids** and are generally **ionised at physiological pH**. Thus, they are usually represented in ionic form.

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## Example of a phosphate – DNA and RNA

Phosphate groups can:

- Help to solubilise compounds in water
- Are quite resistant to hydrolysis by water

  (-ve charge repels incoming nucleophiles)

- Backbone is connected by phosphodiesters

*We will discuss DNA and RNA in lecture 9*

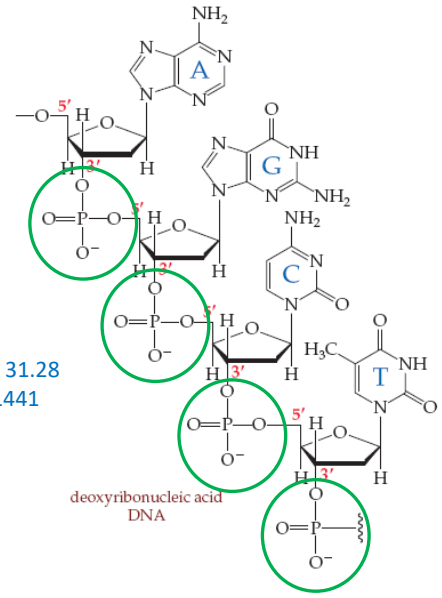


Figure 31.28
Page 1441

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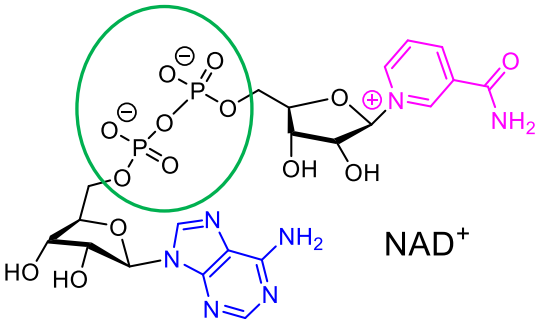
## Example of a diphosphate – $NAD^+$

Phosphate units may combine, with the loss of water, to form di- or triphosphates

$NAD^+$ has a diphosphate unit:

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## Biological recognition

The interaction between small molecules and large biomolecules (e.g. enzymes) is important in living systems

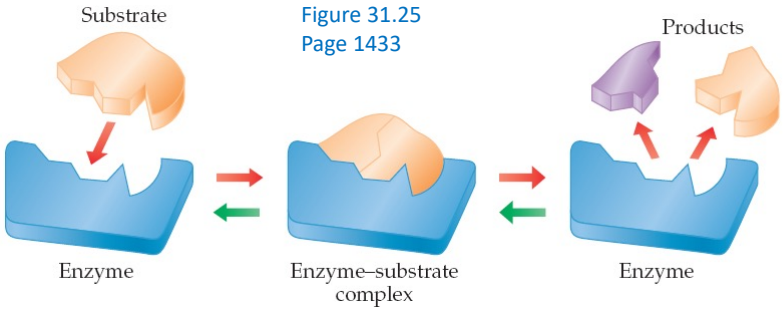


Figure 31.25
Page 1433

Small molecules often fit into larger biomolecule 'pockets' like a 'hand in a glove'

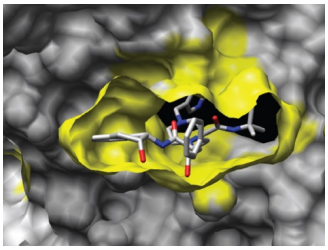

Figure 31.26
Page 1433

The shape and chirality of small molecules and large biomolecules are governed by

- Functional groups, polar and non-polar interactions, H-bonds, avoidance of steric clashes, rigid/planar backbones and framework

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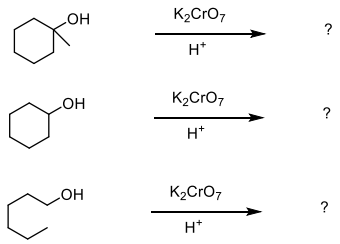
## * Homework *

Give structures for the products of the following reactions:

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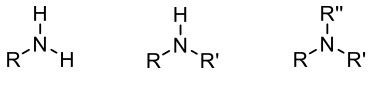
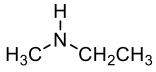
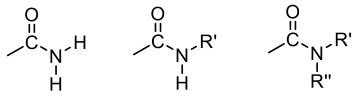
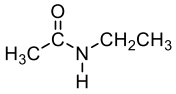
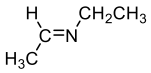
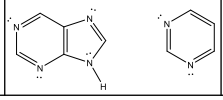
## Nitrogen containing functional groups

Common in biological chemistry:

| Functional group | General Structure | Example | In this module |
|---|---|---|---|
| amine |  1° 2° 3° |  a 2° amine | Lectures 6 – 8, amino acids, peptides |
| amide |  1° 2° 3° |  a 2° amide | Lectures 6 – 8, amino acids, peptides |
| imine |  |  | Lecture 2, vision |
| Aromatic amines | *Many different types – ring sizes and nitrogen positions. E.g. the nucleobases **purine** and **pyrimidine**.* |  | Lectures 8-9, DNA and RNA |

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## Sulfur containing functional groups

Common in biological chemistry:

| Functional group | General formula | Example |
|---|---|---|
| **Thiol** | R–**SH** | $H_3C$–**SH** Methane thiol (very smelly)  |
| **Sulfide** | R–**S**–R' | $H_3C$–**S**–$CH_3$ Dimethyl sulfide (smelly)  *Dead horse water lily* |
| **Disulfide** | R–**S**–**S**–R' | $H_3C$–**S**–**S**–$CH_3$ |

R = alkyl (hydrocarbon based group)

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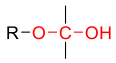
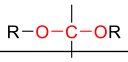
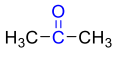
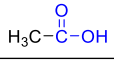
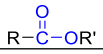
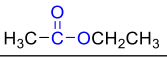
## Oxygen containing functional groups

| Functional Group | General formula | Example | Name | In this module |
|---|---|---|---|---|
| Alcohol |  | $CH_3OH$ | methanol | Common in biological molecules |
| Ether |  | $CH_3OCH_2CH_3$ | methyl ethyl ether | Rare in biological molecules |
| Hemiacetal |  | $CH_3OCH_2OH$ | | Lectures 3 and 4, carbohydrates |
| Acetal |  | $CH_3OCH_2OCH_3$ | | Lectures 3 and 4, carbohydrates |
| Aldehyde |  |  | Ethanal (acetaldehyde) | Lectures 2 -4, addition reactions, incl. carbohydrate chemistry |
| Ketone |  |  | Propanone (acetone) | Lectures 2-4, addition reactions, incl. carbohydrate chemistry |
| Carboxylic acid |  |  | Ethanoic acid (acetic acid) | Lectures 5-7, substitution reactions of derivatives, lipids, amino acids |
| Ester |  |  | Ethyl ethanoate | Lectures 5-7, lipids, amino acids |

**R = alkyl (hydrocarbon) group**

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