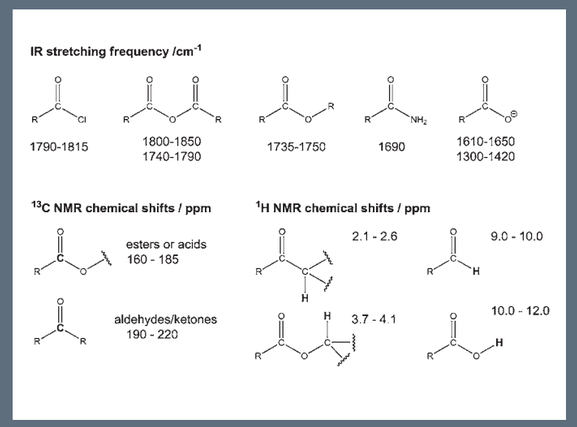
UNIVERSITY OF LEICESTER

DEPARTMENT OF CHEMISTRY

REVISION AID

# Carbonyl chemistry



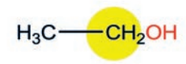


**University of Leicester**
Department of Chemistry
University Road
Leicester, LE1 7RH, UK
**t: +44 (0)116 252 2100**
**e: chemadmin@le.ac.uk**
**w: www.le.ac.uk/chemistry**

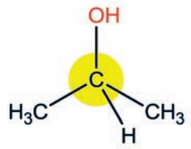
/Leicesterchem
uniofleicester
@Leicesterchem


## Preparation of carbonyl compounds by oxidation of alcohols

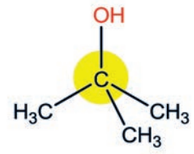
Alcohols can be classified into one of three groups according to how many other groups are bonded to the carbon that has the –OH group (NOTE: H does not count as a group).



ethanol, $CH_3CH_2OH$
**Primary** (1°) alcohol



propan-2-ol, $CH_3CH(OH)CH_3$
**Secondary** (2°) alcohol

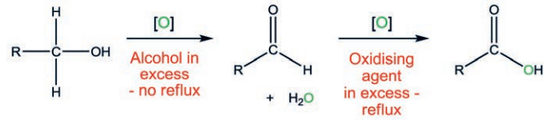


2-methyl propan-2-ol, $(CH_3)_3C(OH)$
**Tertiary** (3°) alcohol

Alcohols can be oxidised using a suitable oxidising agent (e.g. acidified potassium dichromate, $K_2Cr_2O_7$). The product from the reaction depends on the type of alcohol;

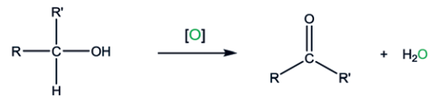
**Primary alcohols** are oxidised to aldehydes. Aldehydes can be further oxidised to carboxylic acids;

Primary alcohols → Aldehydes → Carboxylic acids




**Secondary alcohols** are oxidised to ketones.

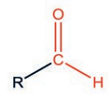
Secondary alcohols → Ketones



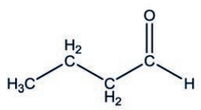

*They cannot be oxidised further as they do not have an available C-H bond on the carbon attached to the oxygen (important in the oxidation mechanism)*

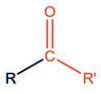
**Tertiary alcohols** cannot be oxidised for the same reason.

## Types of carbonyl compound

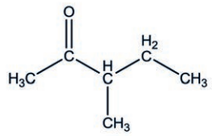


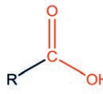
aldehyde e.g. butanal



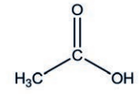


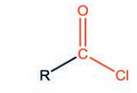
ketone e.g. 3-methyl pentan-2-one



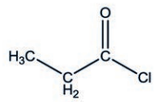


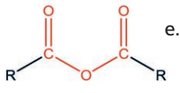
carboxylic acid e.g. ethanoic acid



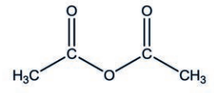


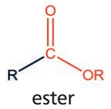
acid chloride e.g. propanoyl chloride



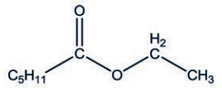


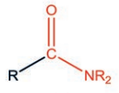
acid anhydride e.g.



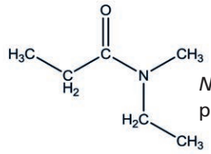


ester e.g. ethyl hexanoate





amide e.g. *N*-ethyl-*N*-methyl propanamide

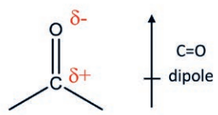


## The carbonyl group

The carbonyl group, a C=O, is probably the most important functional group in organic chemistry. It can be found in a large number of commercially and biologically important molecules.

The C=O is polarised because oxygen is more electronegative than carbon.

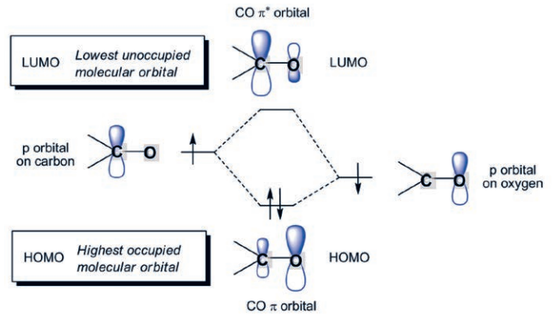
| Electronegativity *(Pauling scale)* | |
|---|---|
| O | 3.5 |
| C | 2.5 |



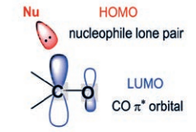

This makes the carbon atom susceptible to nucleophilic attack and forms the basis of many organic reactions.

## Molecular orbitals on a carbonyl group

The carbonyl double bond consists of two parts; one σ bond and one π bond. The π bond results from the overlap of the p orbitals on the C and O atoms.




When a nucleophile approaches the carbonyl group, electrons from the HOMO (the nucleophile lone pair) move into the LUMO of the electrophile (the π* CO orbital). Owing to the larger coefficient of the π* orbital at carbon, this is where the nucleophile attacks (a better HOMO-LUMO interaction).




*The optimal angle of attack to maximise orbital overlap and minimise repulsion with the π orbital is 107°;*
***the Bürgi-Dunitz trajectory***

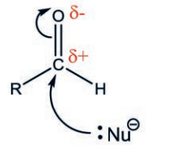
## Nucleophilic addition reactions

Owing to the dipole induced in the carbonyl C=O by the oxygen atom, aldehydes and ketones are susceptible to nucleophilic attack at the carbon atom.

Overall, a nucleophile is added to the C=O and so the reaction is called a **nucleophilic addition** reaction.

The reaction occurs in two steps;

1. Nucleophilic attack on the carbonyl group
2. Protonation of the anion that results

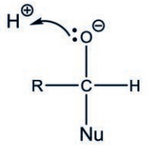



**Examples**

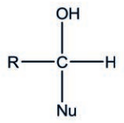
$:Nu^{\ominus}$ = $^{-}CN$, *Reagent HCN*

$:Nu^{\ominus}$ = $H^{-}$, *Reagent $NaBH_4$*

*Nucleophilic addition*




*Protonation*



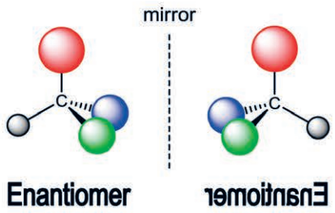

**Examples**

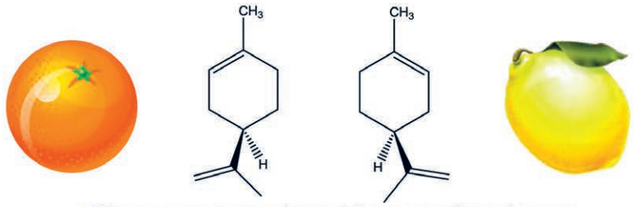
Nu = CN, *Product = an hydroxy nitrile*

Nu = H, *Product = an alcohol*

## Optical isomerism

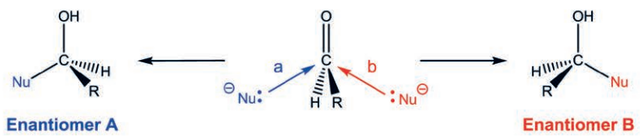
Molecules that have four different substituents attached to a single carbon atom have a non-superimposable mirror image. Such molecules are called **chiral** with each mirror image called an **enantiomer** or **optical isomer** of the mirror image.




**Different enantiomers have different smells and tastes;**
(+) limonene is found in oranges; (–) limonene is found in lemons

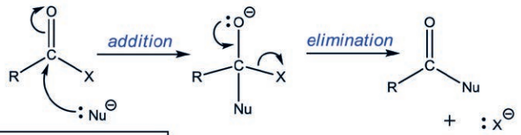
In nucleophilic addition reactions to an aldehyde or unsymmetrical ketone, there is an equal chance of the nucleophile adding to either face of the carbonyl group;




The product mixture therefore contains an equal amount of enantiomer A and enantiomer B.
The mixture is called a **racemic mixture** or a **racemate**.

## Nucleophilic addition-elimination reactions

In the **nucleophilic addition** to a carbonyl group, the negatively charged tetrahedral intermediate is not stable. Therefore, if the carbonyl containing compound also contains a good leaving group attached to the carbonyl carbon, this is **eliminated** and the carbonyl C=O double bond is reformed;



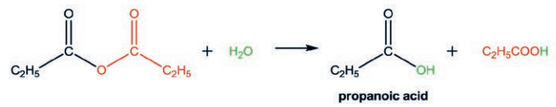

X = a good leaving group

**Nucleophilic addition-elimination** occurs when nucleophiles are reacted with acid chlorides (X = Cl) or acid anhydrides [X = OC(O)R].

For large scale production, industrial chemists prefer to use acid anhydrides instead of acid chlorides. This is because;

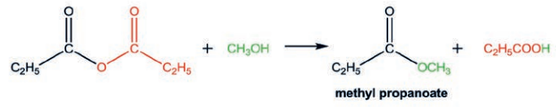
- Acid chlorides react readily with water in the atmosphere and so require strictly anhydrous conditions
- Acid chlorides produce corrosive hydrochloric acid as a byproduct.
- Acid anhydrides produce a much weaker carboxylic acid.

When the nucleophile is **water** → a **carboxylic acid**



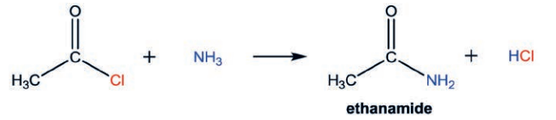

**propanoic acid**

When the nucleophile is an **alcohol** → an **ester**



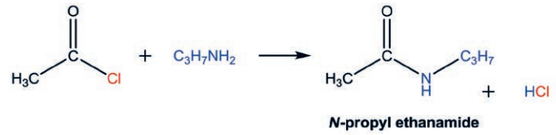

**methyl propanoate**

When the nucleophile is **ammonia** → an **amide**




**ethanamide**

When the nucleophile is an **amine** → an ***N*-substituted amide**




***N*-propyl ethanamide**

## Nucleophilic addition-elimination in the body...

At some stage, most people have suffered from a headache or similar pain and taken an aspirin. Have you ever thought about how it works?

Aspirin acts at the site of the pain to block the start of the nerve signal to the brain. It does this by inhibiting the formation of prostaglandins which are the chemicals responsible for the sensitisation of the nerve endings. **Prostaglandins** are made in the cells from **arachidonic acid** in a reaction catalysed by the enzyme **cyclooxygenase (COX);**

Enzymes are proteins and as such are made up of amino acids. Aspirin inhibits the COX enzyme by reacting with the OH group on the amino acid serine and transferring an acetyl group. As the serine is in the part of the enzyme that forms the active site, the reaction above has the effect of making the active site on the COX enzyme smaller. The arachidonic acid is no longer able to enter the cavity, so the prostaglandin does not form and the pain is relieved.