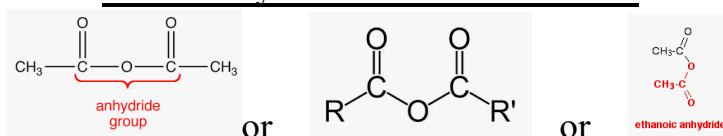
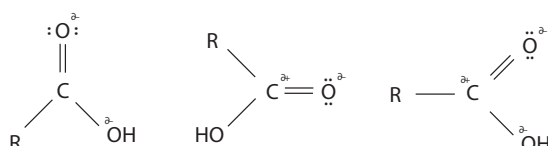


Year 2, Organic Chemistry, Chapter 22: Amines ($\text{NR}_1\text{R}_2\text{R}_3$), Nitriles ($\text{R}-\text{C}\equiv\text{N}$), Amides ($\text{R}-\text{C}=\text{O}(\text{NH}_2)$), Acyl Chlorides ($\text{R}-\text{C}=\text{O}(\text{Cl})$), and Acid Anhydrides.

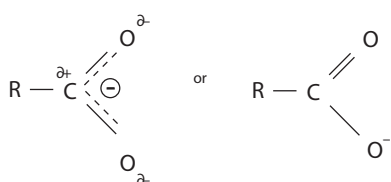
Acid Anhydrides can be shown as



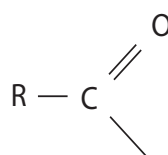
- Please make sure that you know by heart how to get into and how to get out of all of these substances (i.e. you can reel off the reagents and the reaction conditions even in your sleep).
- Nearly all of the species in this Chapter are derivatives of Carboxylic Acids, so let me start the Chapter with a visual description of some of the required substances.
- The following are three visual representations of a Carboxylic Acid.



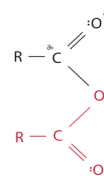
This is the Carboxylate derivative



This is the Acyl derivative



This is the Acid Anhydride



Here “Acyl” is being used adjectivally

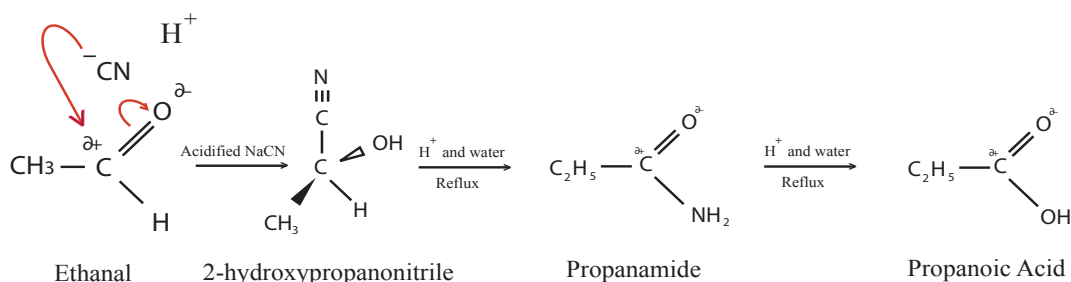
- Here are some of the other compounds that we will consider in this Chapter. Nitriles can be either acid or base catalysed. Do not worry about the reaction or the reagents just as yet. I just want you to start by being able to recognise the different substances in this Chapter.

Aldehyde
 $\text{R}-\text{C}=\text{O}(\text{H})$

Nitrile
 $\text{R}-\text{C}\equiv\text{N}$

Amide
 $\text{R}-\text{C}=\text{O}(\text{NH}_2)$

Carboxylic Acid
 $\text{R}-\text{C}=\text{O}(\text{OH})$



and overleaf are some of the reaction info trees that you need to memorise

The examiners, post-2015, are expecting you to have memorised reagents and reaction conditions. They **DO** expect you to have a working knowledge of the reactions of Amines / Nitriles / Amides / Acyl Chlorides / and Acid Anhydrides. As you will see (later in this Chapter), nowadays they are giving you **COMPLICATED** looking stuff merely to draw out from you **SIMPLE** principles, therefore please make sure that you understand THE BASIC PRINCIPLES that I have outlined in this Chapter. Memorise the REAGENTS and the REACTIONS involved.

This is my info tree on **Carboxylic Acids** (which you have seen in earlier Chapters).

Routes into a Carboxylic Acid

THE MAIN ROUTES

1° Alcohol plus Potassium Dichromate and conc. Sulphuric Acid (Heat)

Nitrile plus HCl plus water

Reflux an **Amide** with H^+ and Water

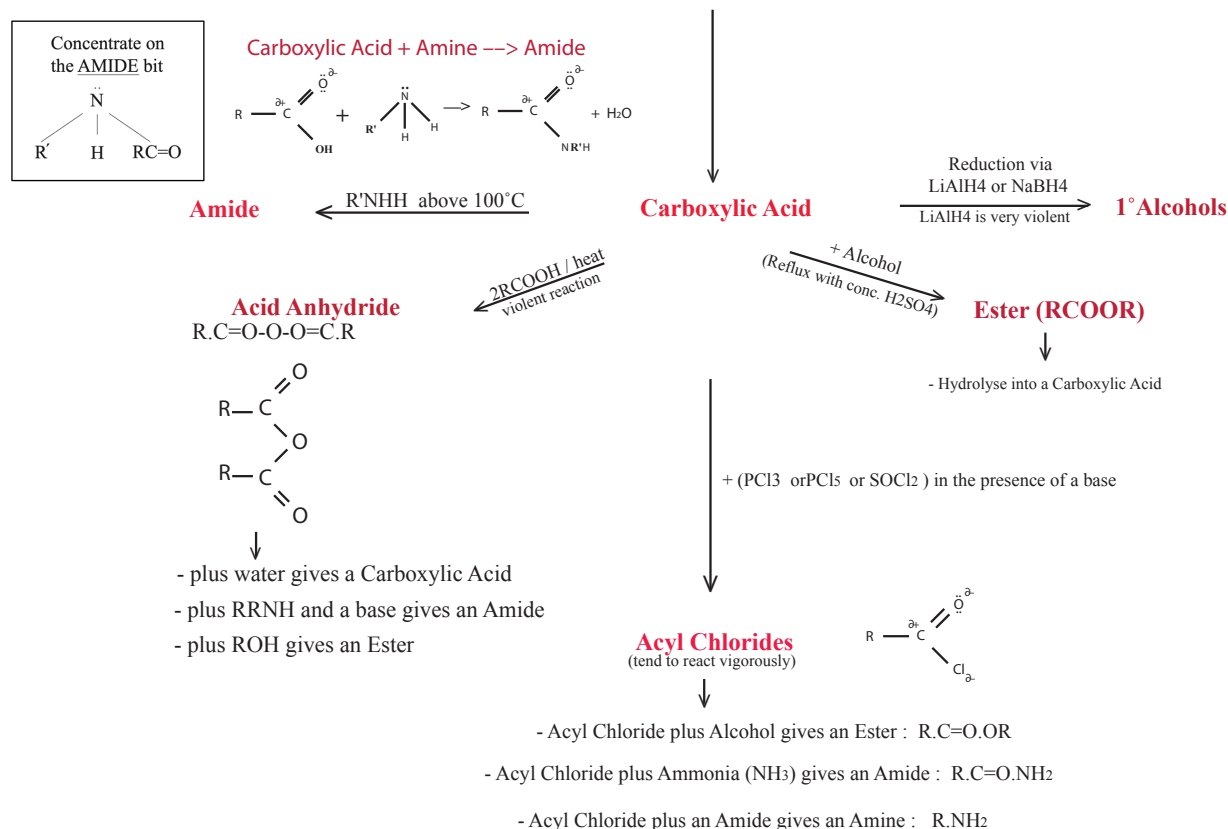
Acyl Chloride plus Water

Acid Anhydride plus Water

THE MINOR ROUTES

Tollen's/Fehling's/Benedict's also oxidise **Aldehydes** into Carboxylic Acids

The Triodomethane reaction with a **methyl Carbonyl compound** will produce a Carboxylic Acid and CHI_3

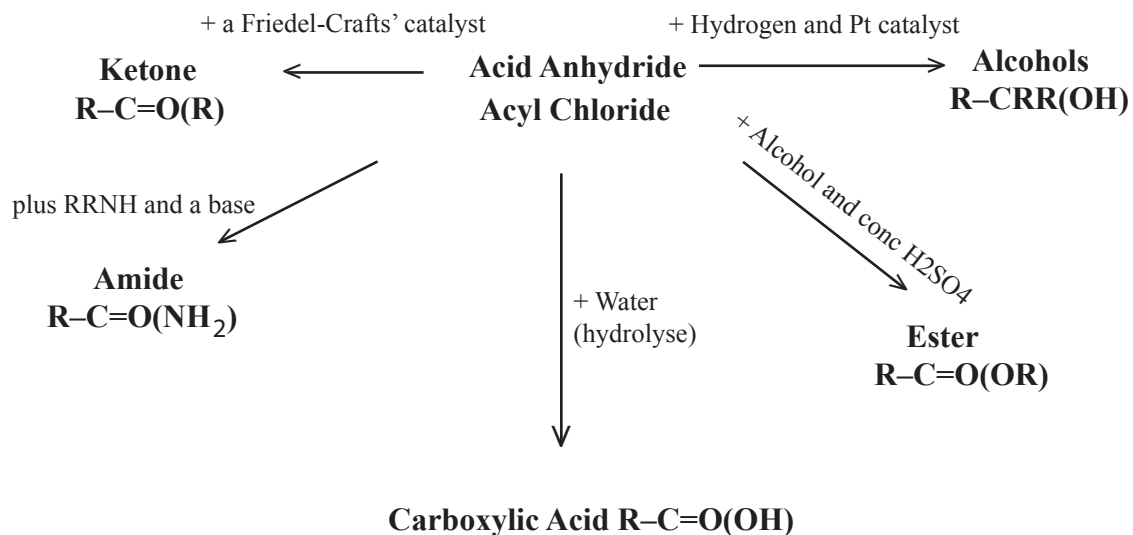


Please remember that whilst a Carboxylic Acid will react with an Alcohol in the presence of a strong acid to form an Ester and Water, so also an Ester can be hydrolysed back into a Carboxylic Acid and an Alcohol in the presence of a strong acid. The reaction is thus a reversible one. The conversion to an Ester is thus better performed in the presence of a strong base (rather than a strong acid), and then HCl added to create the Carboxylic Acid. The base reaction is not a reversible one.

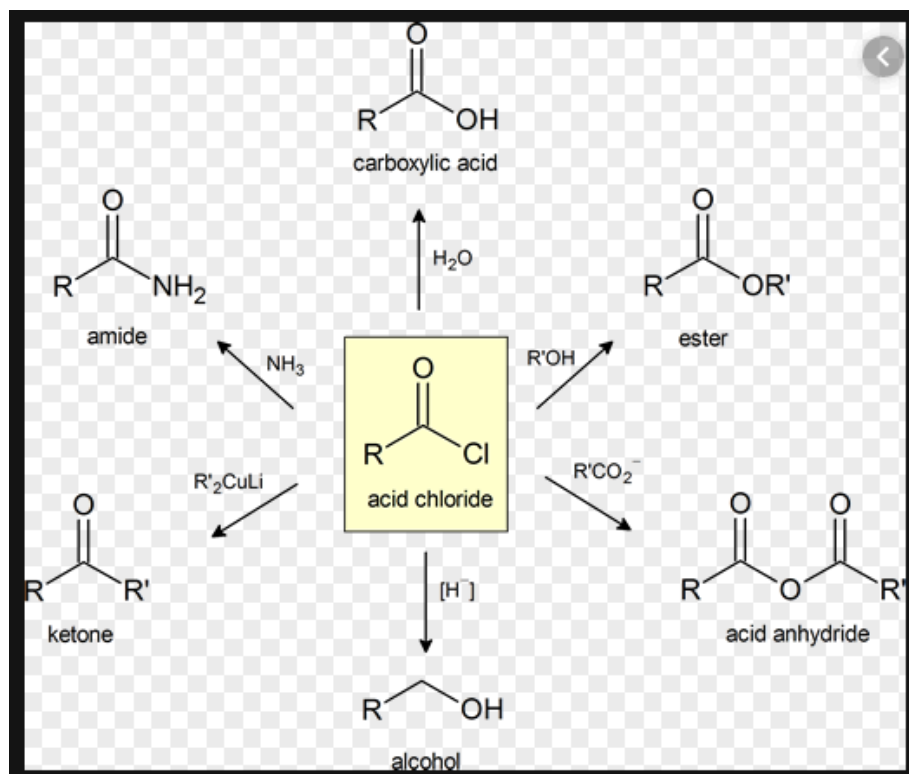
NB The reactions of a Carboxylic acid as just an ordinary acid, albeit a weak one, have been ignored.

This is my info tree on Acid Anhydrides and Acyl Chlorides and **they both react very violently and are very dangerous substances** (even in the best run labs).

Reactions of Acid Anhydrides and Acyl Chlorides



and this is Chemistry LibreTexts' version of the reactions of Acyl Chlorides

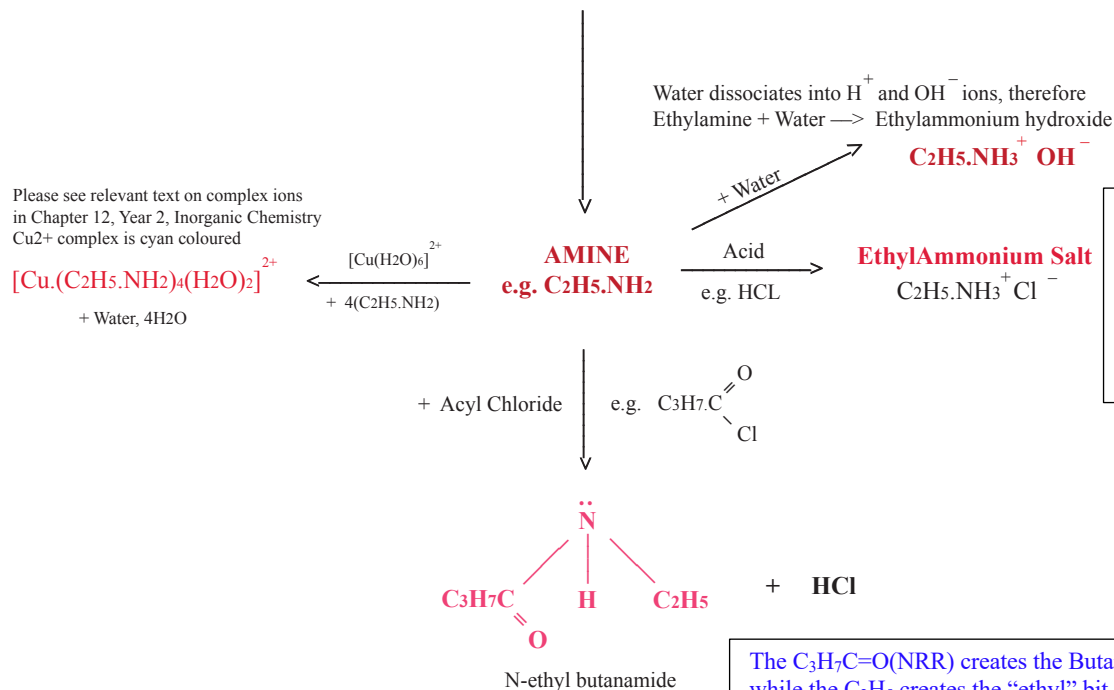


Here is an Amine Info tree. A couple of years ago Edexcel asked a question that required a knowledge of every reaction that Amines undergo.

AMINE INFO TREE

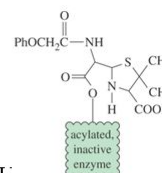
Halogenoalkane and Ammonia in a chemical bomb (Chapter 7, First Year Organics)

Reduction of a Nitrile (e.g. using LiAlH_4 / or Hydrogen and Platinum)

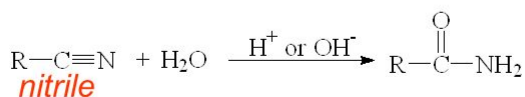
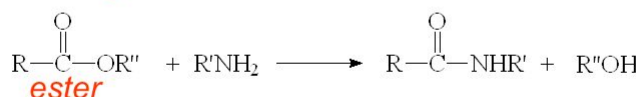
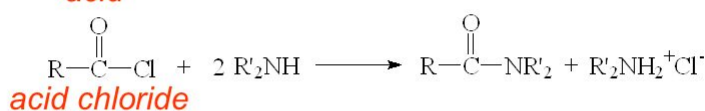
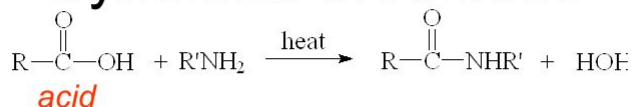


- I start talking about Amides on page 12, but for the moment this is a collection of routes into Amides (Source: L G Wade, 6th Edition) using (in the first four cases) an Amine

Synthesis of Amides



Acid + Amine gives Amide \rightarrow

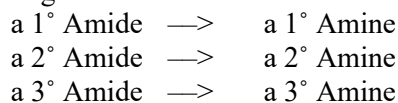


Chapter 21

23

=>

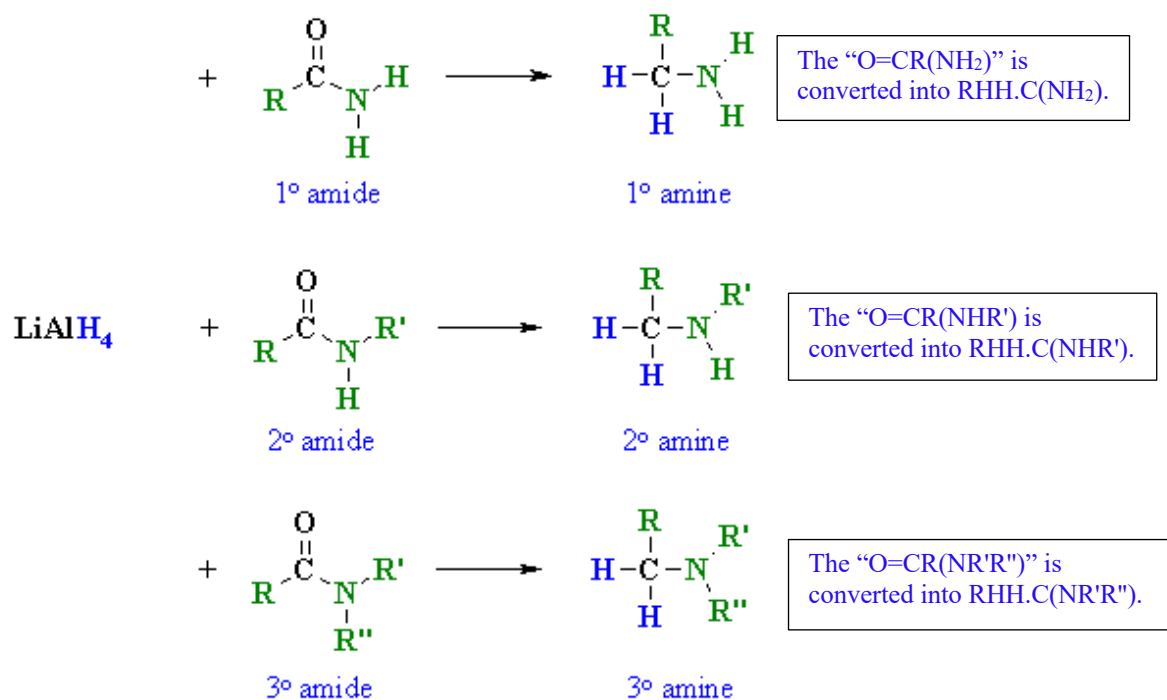
- I have mentioned the work of Dr Ian Hunt of Calgary University elsewhere in the book, and here is another of his pieces of work. In essence what Dr Hunt is telling you is that if you reduce an Amide with LiAlH_4 you will get an Amine.



Summary

- Amides, RCONR'_2 , can be reduced to the amine, $\text{RCH}_2\text{NR}'_2$ by conversion of the C=O to $-(\text{CH}_2)-$
- Amides can be reduced by LiAlH_4 but **NOT** by the less reactive NaBH_4
- Typical reagents : LiAlH_4 / ether solvent, followed by aqueous work-up. (A “work-up” is the series of sequential actions required to achieve a certain end-product.)
- Note that this reaction is different to that of other C=O compounds which reduce to *alcohols* (for example [esters](#)). Here, you are going from an Amide to an Amine.
- The nature of the amine obtained depends on the substituents present on the original amide.
- Look at the N substituents in the following examples (those bonds don't change !)

In all of these examples, “R/R'/R””, **must have** a C atom in it (because that is what makes the 1° / 2° / and 3° amines in this example).

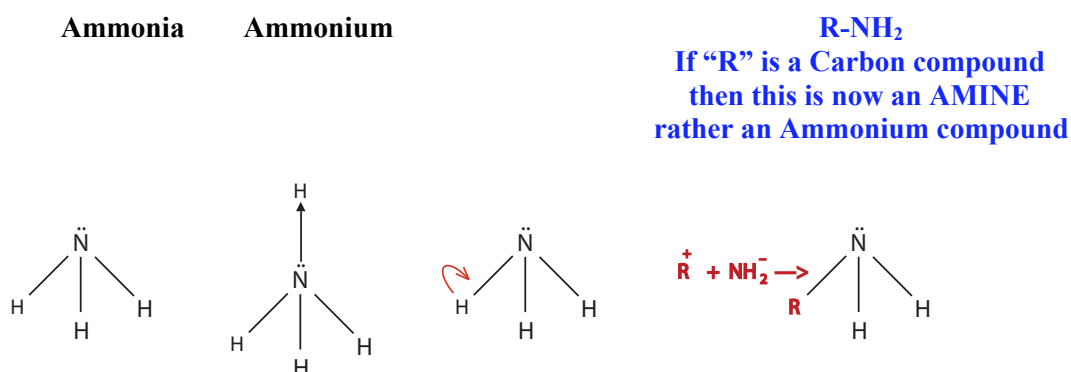


- R , R' or R'' may be either alkyl or aryl substituents.
- In the potential mechanism shown below, note that it is an **O** system that leaves.
- This is consistent with **O** systems being *better* [leaving groups](#) than the less electronegative **N** systems.

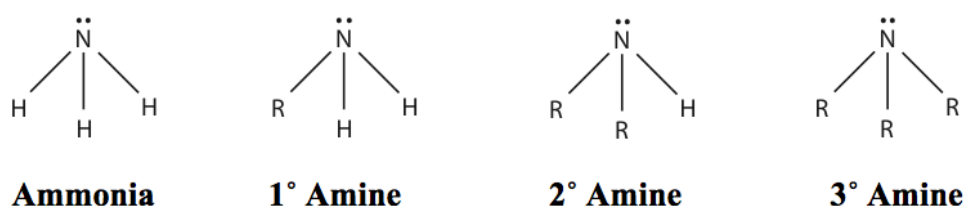
Source: Dr Ian Hunt of Calgary University.

A) Amines ($\text{NR}_1\text{R}_2\text{R}_3$ where at least one “R” must be a Carbon compound)

- The two most important features of Amines are that they are (i) nucleophiles and (ii) that they are bases.¹
- When an Ammonia molecule *gains* a fourth proton it becomes Ammonium (NH_4^+), but if it *loses* a proton then the remaining “ NH_2^- ” species gains a negative charge ($\text{NH}_3 \rightarrow \text{H}^+ + \text{NH}_2^-$), and when this anion adds on to an Alkyl or Aryl species² then an Amine is formed:
 $\text{NH}_2^- + \text{R}^+ \rightarrow \text{Amine}$



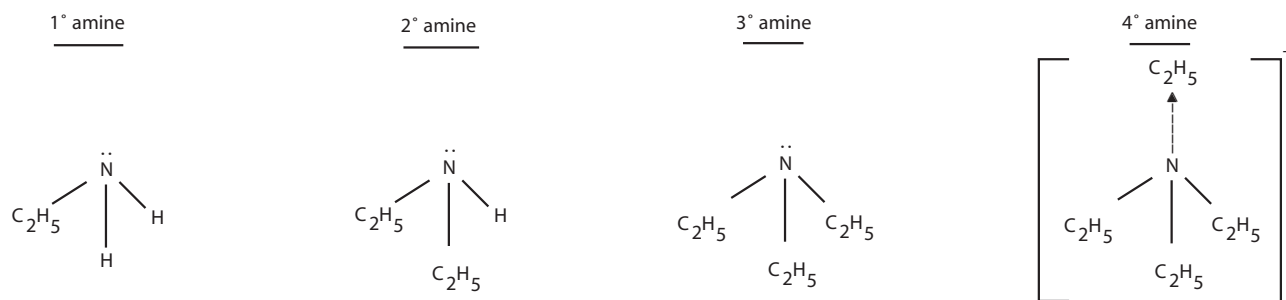
- The simplest Organic Amine would be Methylamine ($\text{CH}_3\text{-NH}_2$). “R” = CH_3^+ on the right above, but the CH_3 could have been any Alkyl ($\text{C}_n\text{H}_{2n+1}$) or Aryl species. An Amine could be extraordinarily large and complicated depending on “R”, and of course there could 1/2/or 3 “R” species and possibly even 4 (if a dative bond were formed through the lone pair of electrons on the N atom).
- In our first year together I mentioned that sometimes, when talking about an Amine, I find that it is much more helpful to concentrate on the “ NH_2 ” bit of the compound rather than on the “R” bit of the compound, and in the context of teaching you about 1° / 2° / 3° / and 4° Amines I showed you what they looked like where “R” can be either Alkyl or Aryl – but it should not be an “H” species, otherwise “NRRR” (with the lone pair on the N atom would equal “NHHH” or “ NH_3 ” i.e. just ordinary Ammonia).
- If “R” is an Alkyl or Aryl species, then



- Please note that the species overleaf are all **AMINES** (and not **AMIDES**). In the diagram, I have used “ $\text{-C}_2\text{H}_5$ ” for my “R”, but I could have used any legitimate species such as $\text{-C}_n\text{H}_{2n+1}$ / a ring Alkyl group / or an Arene species / and so on.

¹ Some nucleophiles are bases (i.e. lone pair donors).

² There are also Inorganic Amine species.



- The reason that I show you the above diagram this year is twofold viz. so that I can show you that
 - repeated replacement/substitution of an “R” species will create the species above, but also to show you that
 - the “:NHHH” / “:NHHR” / “:NHRR” / “:NRRR” species can each use their lone pairs of electrons to bond with something else, and the lone pair of electrons **makes the species into a nucleophile and a base**. (In the 4° Amine on the right above, that is precisely what has happened.)

The naming of Amines

- There are several different systems for naming Amines, and Professor William Reusch of Michigan State University (Chemistry LibreTexts) gives as his example

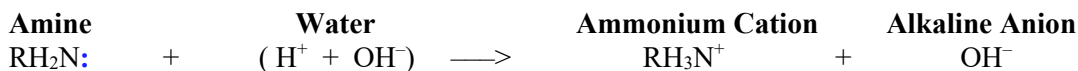
a 1° amine	a 1° amine	a 2° amine	a 3° amine
IUPAC name 1-aminobutane	IUPAC name 2-amino-2-methylpropane	IUPAC name 1-methylaminopropane	IUPAC name dimethylaminoethane
CA name butanamine	CA name 2-methyl-2-propanamine	CA name N-methylpropanamine	CA name N,N-dimethylethanamine
Common name n-butylamine	Common name tert-butylamine	Common name methylpropylamine	Common name ethyldimethylamine

where “CA” stands for the “Chemical Abstract Service”, and it is fairly common to use “n” or “N” as in “n-butylamine” to indicate that the “R” species is attached to the N atom. The phrase “tert” is also commonly used to indicate a tertiary **carbon** species – and if you look at the second molecule from the left above, you will see that the carbon species is indeed a 3° alkyl species (where the C atom that is attached to the “-NH₂” species is attached to three other C atoms).

- It is worth looking at each name above to see the logic of the naming system used, but do not worry about the names of Amines because in ‘A’ Level examinations the examiners are obliged to draw the molecule for you. **You cannot be expected to guess the nature of the naming system that they are using.**
- In one aspect, the most important feature of an Amine is the lone pair of electrons on the N atom. As I have already pointed out, this makes Amines nucleophilic and basic³. (The negatively charged lone pair of electrons makes them seek out the positively charged protons in the nuclei of other molecules, **therefore Amines are nucleophiles.**)

³ Under the Lewis definition, a species that is capable of donating a lone pair of electrons is called a base.

- When an Amine comes into contact with Water, it will form a dative bond with the H^+ ions in the Water. If I use “:” to draw attention to the lone pair of electrons on an N atom, then



- Last year I told you that if you heated a Halogenoalkane and Ammonia in a “chemical bomb” (i.e. a very thick-walled sealable titanium steel container capable of withstanding very high pressures) then you would get an Amine. I did not tell you about the ability of an Amine to act as a “ligand”, but I will do so in the relevant Chapters in Inorganic Chemistry.
- OK, that is complicated First Year ‘A’ Level stuff, so let us now get on to the Second Year stuff.

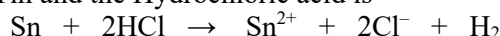
Conversion of Benzene to Phenylamine (also known as Aniline): $\text{C}_6\text{H}_6 \longrightarrow \text{C}_6\text{H}_5\text{NH}_2$
 [NB Both Phenylamine and Nitrobenzene are toxic and are skin irritants.]

- If Ammonia were to dissociate a proton then it would form



- NH_2^- has a negative charge therefore it would be repelled by the areas of high electron density of the delocalised π ring above and below the plane of the six C atoms in a Benzene ring (C_6H_6). NH_2^- is a nucleophile and it will thus **not** react with Benzene. Therefore, in order to produce Phenylamine (also known as Aniline, $\text{C}_6\text{H}_5\text{NH}_2$), one must first create Nitrobenzene, $\text{C}_6\text{H}_5\text{NO}_2$ **and then reduce the Nitrobenzene by reacting it with Tin and Hydrochloric Acid**. This produces $\text{C}_6\text{H}_5\text{NH}_3^+$ and the H^+ is then removed by reacting it with an OH^- ion (from NaOH or KOH) and $\text{C}_6\text{H}_5\text{NH}_2$ is thus formed. (This was described in detail in Chapter 16 of Year 2 Organic Chemistry.)

- The reaction between the Tin and the Hydrochloric acid is

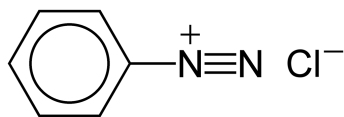


and the **reducing agent for the reduction of Nitrobenzene is the Sn^{2+}** , which is oxidised to Sn^{4+} i.e. Tin(IV) hydroxide, $\text{Sn}(\text{OH})_4$. Water is added to this and the Phenylamine is distilled off. However, this simple description hides the complexities of the process that is involved, and if you would like to read a detailed account of the process of converting $\text{C}_6\text{H}_5\text{NO}_2$ into $\text{C}_6\text{H}_5\text{NH}_2$, then you should go to http://rod.beavon.org.uk/phenylamine_prep.htm where Mr Beavon has outlined the full complexities involved (including the precautions necessary to avoid an explosion in a lab).

- In earlier Chapters (e.g. Chapter 16) I have also talked at considerable length about the conversion of
 - Benzene into Nitrobenzene ($\text{C}_6\text{H}_5\text{NO}_2$) using conc. HNO_3 (and conc. H_2SO_4 as the catalyst), *but all the while keeping the temperature at 55°C* ⁴, and then Nitrobenzene into Phenylamine ($\text{C}_6\text{H}_5\text{NH}_2$) using Tin and Hydrochloric Acid, and
 - I have also talked about the formation of Azo and Diazo compounds using NaNO_2 and HCl (cf. footnote⁵) to convert Phenylamine into “BDAC” (Benzenediazoniumchloride), and then BDAC into Azo compounds (cf. overleaf).

⁴ Nitrobenzene is made by reacting Benzene with HNO_3 and $2\text{H}_2\text{SO}_4$ **at 55°C (and certainly below 60°C to avoid the creation of Dinitrobenzene)**.

⁵ If you cannot remember the details of the conversion from Benzene to Nitrobenzene to Phenylamine to BDAC and then to an azo dye or to Phenol, then please revise it. You are **HIGHLY LIKELY** to get a question on it in the exams.



- BDAC *can* be obtained by reacting Phenylamine with “Nitrous acid” (HNO₂) – but nitrous acid is very unstable and decomposes very quickly, therefore the Nitrous Acid has to be made and used on-the-spot (*in situ*) by reacting NaNO₂(aq) with 2HCl(aq) and we would thus get

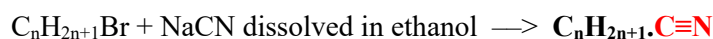
at 5°C but definitely at < 10°C



(NB “At 5°C” to avoid the decomposition of the Nitrous Acid that is formed *in situ*.)

B) Nitriles (“R.C≡N”)

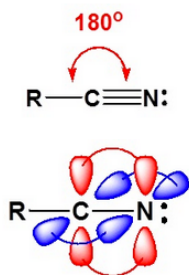
- Last year I described how a Halogenoalkane could be reacted with an “OH⁻” species to produce either an Alcohol or an Alkene. Refluxing a *primary* Halogenoalkane with Water will result in a preponderance of an **Alcohol**; but, refluxing a *tertiary* Halogenoalkane at a high temperature with a concentrated “OH⁻” species from Sodium or Potassium Hydroxide dissolved in Ethanol, will result in a preponderance of an **Alkene**. Please go back and read Chapter 7 on Halogenoalkanes now, first of all because that will remind you of what I am talking about – but much more importantly, because at the end of this year you will be examined on **everything** that you will have learnt in the last two years of your ‘A’ Level Chemistry studies.
- Here I am going to tell you that if you reflux a Halogenoalkane with “CN⁻” (i.e. from NaCN or KCN) and with **no Water**, i.e. with just ethanolic NaCN or KCN, then the resulting product will be a Nitrile



and I have already told you in Chapter 19 on Aldehydes, that this route will increase the size of your Carbon chain by one C atom.

NB An Iodoform reaction will **remove** one C atom from a C chain, while the reaction with a “CN⁻” species **adds** one C atom to a C chain.

- If a C atom in an organic molecule forms a **triple bond** with an N atom, then this constitutes a **Nitrile**.
- The triple bond in a Nitrile species consists of one σ bond and two π bonds. Let me show you a couple of (last year’s sort of) diagrams, because that will serve to remind you of how the triple bond is created in the molecule. There is a sigma bond that connects the nuclei of the C and the N atoms, and then there is a π bond above and below (*but in real life there is no “above and “below” in space*), and there is also a π bond to the left and to the right of the species. As you can see overleaf, the species is surrounded by a large amount of electron density, and if/when an H⁺ species breaks away from HCN, then the CN⁻ species is going to be very **nucleophilic**. It will absolutely love protons.

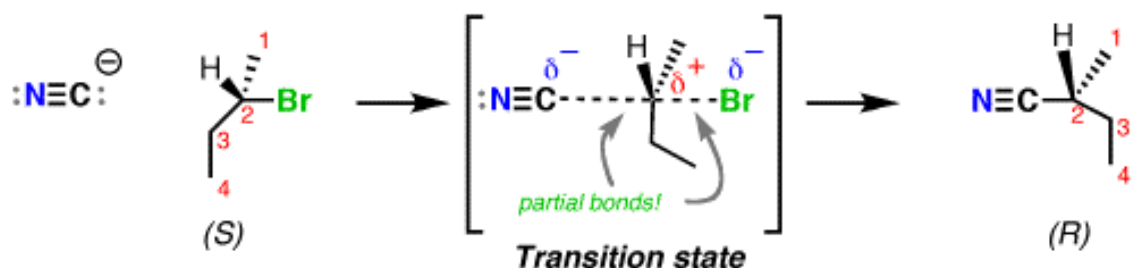


Source: Professors Farmer/Kennepohl/and Reusch⁶

- In Organic Chemistry, any organic molecule that has a “ $\text{C}\equiv\text{N}$ ” species can be called a Nitrile, and this can be written as “ $\text{R}-\text{C}\equiv\text{N}$ ” where the “R” can be any legitimate organic species such as an “-H” / or an “-Alkyl” / or an “-Aryl” species i.e. Benzene or any of its derivatives or its sister compounds (and the adjective “Aryl” is derived from the word “aromatic”).
- If a halogenoalkane were refluxed with ethanol and NaCN or KCN (and NO water at all), then a **Nitrile ($\text{R}-\text{C}\equiv\text{N}$)** would be produced via an $\text{S}_{\text{N}}2$ reaction mechanism. The following is a diagram of an $\text{S}_{\text{N}}2$ mechanism (but I am not good at showing the umbrella being blown inside out that occurs in such a mechanism), therefore this is how Dr James Ashenhurst of “Master Organic Chemistry” describes the attack (from, so-to-speak ‘the rear’) that is involved in an $\text{S}_{\text{N}}2$ reaction. For a substitution reaction to occur, there must be two or more species involved in the middle step of the reaction. The “1” and “2” in the names $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ therefore do not refer to the number of molecules involved in the reaction but refer instead to the number of species in the middle step of the reaction.

The "backside attack" hypothesis fits all experimental data

In the "backside attack", the nucleophile attacks the substrate from the backside in a single step, resulting in inversion of configuration.



- Explains bimolecular rate law (depends on conc. of nucleophile and substrate)
- Explains inversion of stereochemistry
- Explains sensitivity to steric hindrance (bulky groups slow down backside attack)

This is called the **$\text{S}_{\text{N}}2$** mechanism (**S**ubstitution, **N**ucleophilic, **b**imolecular)

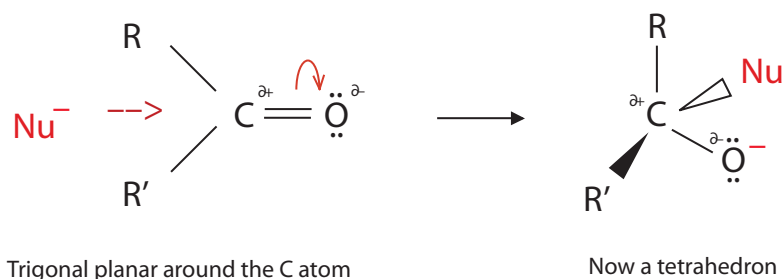
Source: Dr James Ashenhurst, “Master Organic Chemistry”

⁶ They have a huge amount more to say about Nitriles at https://chem.libretexts.org/LibreTexts/Athabasca_University/Chemistry_360%3A_Organic_Chemistry_II/Chapter_20%3A_Carboxylic_Acids_and_Nitriles/20.07_Chemistry_of_Nitriles

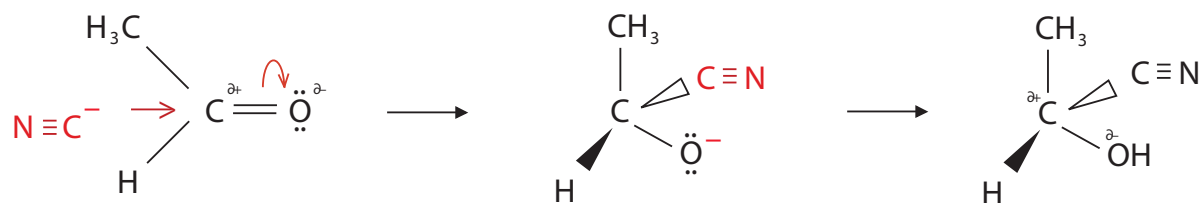
The Nucleophilic ADDITION reaction of a Carbonyl Species ($R_1-C=O(R_2)$) with Hydrogen Cyanide ($H-C\equiv N$) to form a Nitrile ($R-C\equiv N$)

(This reaction takes place with most Carbonyl compounds but it ADDS one C atom to a C chain.)

- Technically the movement of electrons should be shown by curly arrows, but I have drawn it below with a straight arrow. You can see the Nu^- , and here it is a “ $C\equiv N$ ” species (with the negative charge on the C atom) attacking the $C^{\delta+}$ atom, and a **nucleophilic addition reaction** is about to take place in which the double bond will break heterolytically (and the C atom will then be attached to four species instead of three).



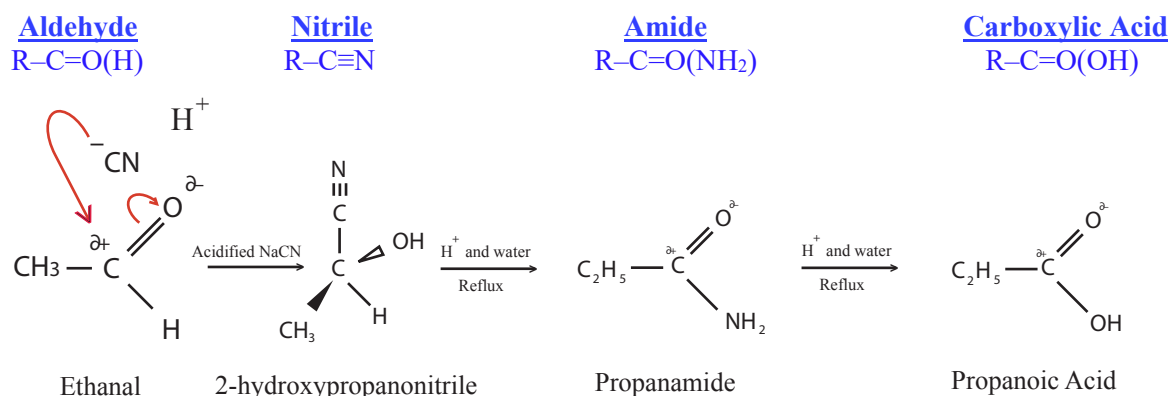
- The negative charge that was on the attacking nucleophile is now on the $O^{\delta-}$ atom, and the positively charged companion of the CN^- nucleophile is still hovering somewhere in the vicinity.
- If HCN is used, then an Alcohol will result because H^+ and O^- will give the “ $-OH$ ” of an Alcohol.
- The “ $C\equiv N$ ” species can be provided by either HCN, or by *acidified* Sodium or Potassium Cyanide (NaCN).
- Please remember that when the H atom in HCN breaks away as a proton from a molecule of HCN ($HCN \rightarrow H^+ + CN^-$), it leaves its electron on the C atom to which it was attached thus leaving the “ $C\equiv N$ ” species with a lone pair of electrons, and thus **the negative charge is actually located on the Carbon atom, and the species should really be written as “ NC^- ” and not “ CN^- ”** (but it is rarely written in this manner).
- In the middle species of the diagram below, the π bond in the “ $>C=O$ ” has broken heterolytically and the negative charge is therefore now on the O atom. In the diagram on the right, the proton from the HCN forms a bond with the O^- species to form an Hydroxy/or Hydroxide species.
- This is a Nucleophilic Addition reaction: $RR'>C=O + HCN \rightarrow RR'>C\equiv N(OH)$, cf. footnote⁷. If you are asked to draw the nucleophilic addition reaction of a “ CN^- ” species to a Carbonyl species $RR'>C=O + HCN \rightarrow RR'>C\equiv N(OH)$, then please draw the following three steps.



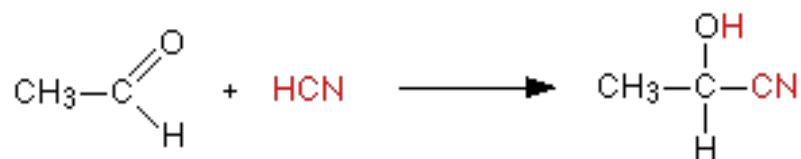
NC^- and ethanal **now there are 3 C atoms in the chain** counting must start from the CN species

⁷ Please remember that the brackets indicate that the species inside the brackets are bonded to the C atom to the left of the brackets.

- Please note that the Carbonyl compound started life with TWO Carbon atoms – it was Ethanal. The longest Carbon chain now has THREE Carbon atoms in it, therefore it is a “Propanonitrile” or “Propanenitrile”⁸. The C atom to which the N atom is bonded must now be regarded as the first C atom in the chain of three C atoms. The second atom in the chain has an “–OH” species attached to it, therefore the name must state where the “–OH” species is located (i.e. 2-hydroxy). The displayed formula can be written as CH₃.CH(OH).C≡N and the name of the molecule is 2-hydroxy propanonitrile or 2-hydroxypropanenitrile.
- This reaction is extremely slow because HCN is a very weak acid (with a pK_a of 9.3 compared to the pK_a of 4-5 for many stronger *organic* acids⁹). **HCN is toxic, therefore to achieve a pH of 4-5 it is better to use NaCN that has been acidified.** The acid speeds up the reaction, and the effect of the acidification is to make the C atom more δ⁺ and thus *more susceptible* to an attack from a nucleophile. The reaction is complicated and I do not intend to go into it in any detail. If you want to read more about this reaction, then you should read Jim Clark’s memo on <https://www.chemguide.co.uk/mechanisms/nucadd/hcntt.html>.
- In the diagram on page 11 you will be able to deduce that the C atom in stages 2 and 3 is the central atom in a tetrahedron (viz. where a Pharaoh would have been buried in his/her pyramid), and that this C atom has four different species attached to it. **The molecule is therefore chiral and it will have optical isomers.** The products that are formed in this reaction are therefore “**racemic**” i.e. they are a mixture of the different optical isomers. This knowledge has been tested in recent exams!
- I do not believe that you will be asked to do so in the exam, but if you are presented with the reaction from Ethanal to Ethanoic Acid, then this is what you might see (and please note the increase in the number of Carbon atoms during the reaction).



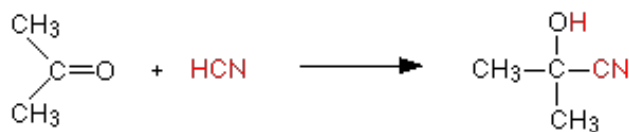
- This is a useful progression in Organic Synthesis.
- Jim Clark of “chemguide” shows the conversion from Ethanal, an **Aldehyde**, to 2-hydroxy-2-propanenitrile thus



⁸ “Propano-“ is the adjectival form of the noun “propane”.

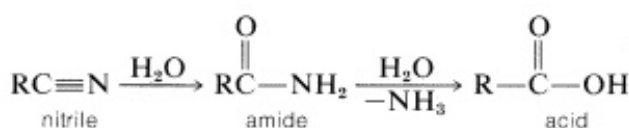
⁹ The smaller the pK_a, the **stronger** the acid. **(NB Please remember that pK_a ≠ pH.)**

and with Propanone (a **Ketone**) to 2-hydroxy-2-methylpropanenitrile

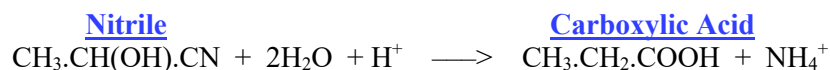


propanonitrile = propanenitrile

From a Nitrile to a Carboxylic Acid



- For organic synthesis purposes, a Nitrile is a good way into a Carboxylic Acid. (NB Please remember that in going from the Aldehyde to the Nitrile, one C atom is added to the Carbon chain.)
- I do not intend to go into this reaction in any more detail than I have already done because many intermediate species are involved. All that I will say is that where I showed the conversion on page 8 as “Reflux with H⁺ and Water”, in fact the hydrolysis can be achieved **either** through
 - acid hydrolysis** of a Nitrile into a Carboxylic Acid viz.



(NB CH₃CH₂COOH or C₂H₅COOH is a Weak Acid, which means that it holds on to its proton and does not dissociate the proton easily therefore it is disinclined to react)

ii) or through **alkaline hydrolysis** (e.g. using NaOH) viz.



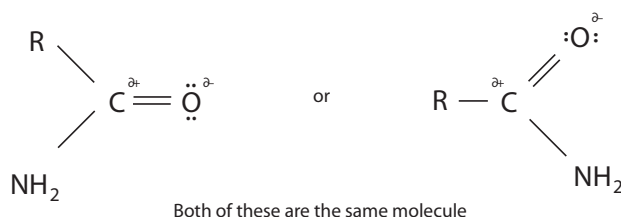
and HCl must then be added to the latter reaction in order to convert the C₂H₅.COO⁻ salt into the Carboxylic Acid.

C) Amides: “R-C=O(NH₂)”

- Let us start by reminding ourselves that basically¹⁰ an “-NH₂” species is one where an “H⁺” (a proton) has broken away heterolytically from an Ammonia molecule leaving behind a negatively charged “-NH₂” anionic species. If the species has a negative charge on it, then it must love positively charged protons and be a **nucleophile**, therefore if it reacts with something, the reaction will be a **nucleophilic** reaction.

¹⁰ By the way, I have just created a little Chemistry ‘pun’ in using the word “basic”. If you cannot spot it, then just read on. I have been writing away since 4 o’clock this morning (it is now 11.38 am) and I just needed a tiny humour break from the relentless pursuit of the conveyance of knowledge.

- An **Amide** is in effect a Carboxylic Acid where the Hydroxy species “–OH” has been replaced by an “–NH₂” species, and if you look at the diagrams that I have drawn for you below, you will quickly see that the “–NH₂” species has replaced the “–OH” species in a Carboxylic Acid.



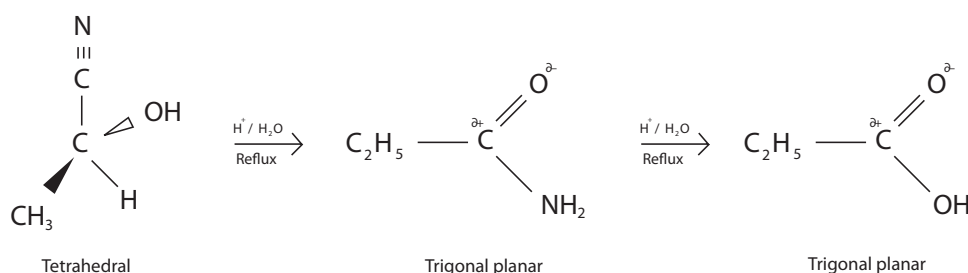
The reactions of Amides: “R.C=O(NH₂)”

- Of all the Carbonyl compounds, the Amides are not particularly reactive whilst the Acyl Chlorides are the **most** reactive.
- For ‘A’ Level purposes, all that you need to know is that an Amide will convert into an Acid. On page 11 I drew the following for you.

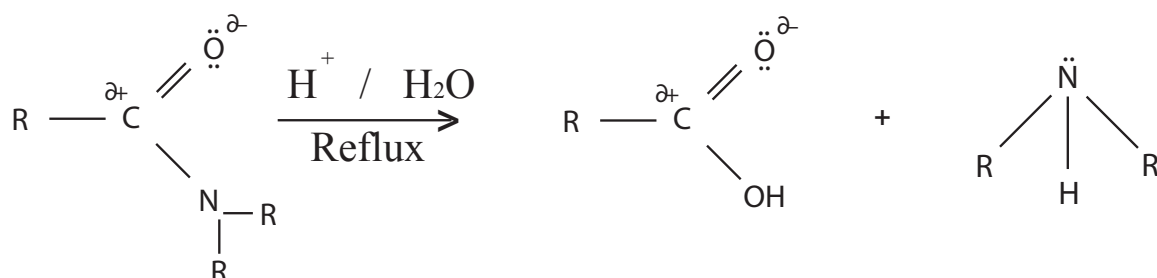
Nitrile (R–C≡N)

Amide (R–C=O(NR₁R₂))

Acid (R–C=O(OH))

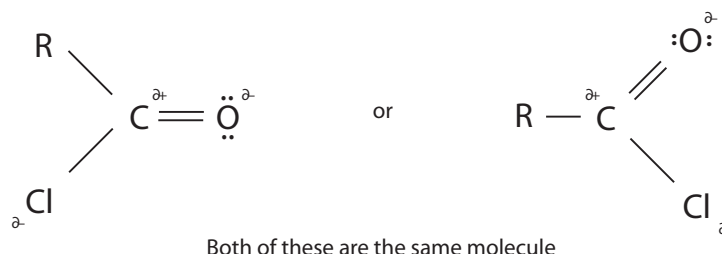


- The middle species of the three species above is Propanamide.
- If you heat an Amide “R.C=O(NR₁R₂)” with **either** a strong acid (e.g. H₂SO₄) or a strong base (e.g. NaOH), then the Amide will be **hydrolysed** into an Acid (“R.C=O(OH)”) and an Amine (“NHR₁R₂”) as follows. **This reaction is reversible.**



D) Acyl Chlorides: “R-C=O(Cl)”

- An **Acyl Chloride** is effectively a Carboxylic Acid where the Hydroxy species “-OH” has been replaced by a “-Cl” species. An Acyl Chloride is a **VERY REACTIVE** substance that tends to produce toxic HCl when it reacts, **and it should therefore be treated with extreme caution.**

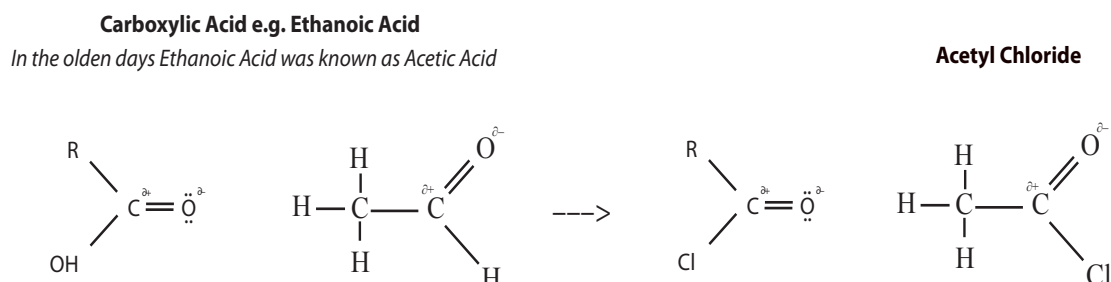


- When it comes to naming an Acyl Chloride, start with finding out how many C atoms there are in the molecule and then add “-oyl Chloride” to get the Acyl Chloride e.g. 4 C atoms would give Butanoyl Chloride, 5C atoms would give Pentanoyl Chloride, and so on.
- In contrast to the not particularly reactive Amides, Acyl Chlorides are **very** reactive species. In fact, California State University (Dominguez Hills), says that Acyl Chlorides are the most reactive of all the derivatives of Organic Acids.

Name	Structure	Found or Used In:
Carboxylic Acid	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OH} \end{array}$	Vinegar, Cream of Tartar
Ester	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OR}' \end{array}$	Fats, Cell Membranes
Amide	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NHR}' \end{array}$	Nylon, Proteins
Acyl Chloride	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{Cl} \end{array}$	Synthesis of Carboxyl Derivatives
Acid Anhydride	$\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{R}-\text{C}-\text{O}-\text{C}-\text{R} \end{array}$	Synthesis of Carboxyl Derivatives

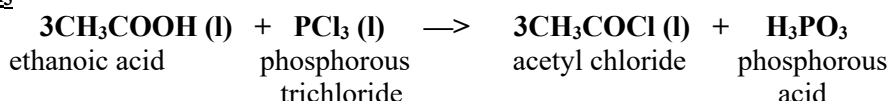
- The table above was taken from one of the early Chemistry lectures that CSUDH gives to what we in England would call “freshers”, and if you want to learn a tiny bit more than ‘A’ Level stuff about Chemistry, then you can do worse than read the lecture on <http://chemistry2.csudh.edu/rpendarvis/carboxder.html> . I have given you a more than sufficient grounding in ‘A’ Level Chemistry for you to be able to read and to understand every single word of the lecture.

- If you were to take a Carboxylic Acid and substitute a Chlorine atom for the Hydroxyl (“–OH”) species at the acid end of the Acid, then an Acyl Chloride would be obtained. I have drawn the molecules below in two different ways so as to familiarise you with the different ways of drawing such molecules. The Acyl Chloride in the diagram below is Acetyl Chloride.¹¹



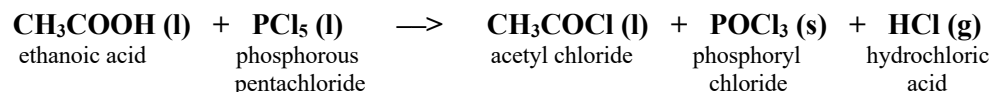
- Acyl (or Acid) Chlorides can be obtained by reacting the relevant Carboxylic Acid e.g. Ethanoic Acid, which used to be called Acetic Acid¹² with **PCl₃** / **PCl₅** / or **SOCl₂**. (There are other ways of making Acyl Chlorides, but these three will do for ‘A’ Level purposes.)

With PCl₃



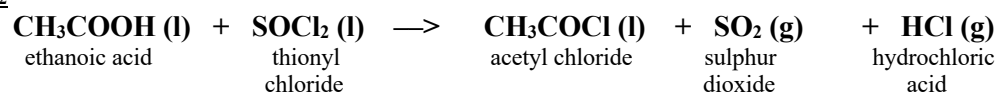
3 molecules of Ethanoic Acid *each* take one Cl atom from the molecule of PCl₃.

With PCl₅



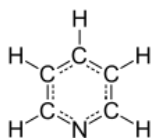
Just one molecule of Ethanoic Acid takes a Cl atom from the PCl₅.

With SOCl₂



Here also just one molecule of Ethanoic Acid takes a Cl atom from the SOCl₂.

- HCl is a pretty nasty/choking/**toxic** fuming by-product. **Do not go near it. However, a base such as Pyridine (C₅NH₅) can be used in the reaction to neutralise the HCl as it is formed.** C₅NH₅ is a Lewis Base because the N atom has a lone pair of electrons which it can donate.



Source: Wikipedia

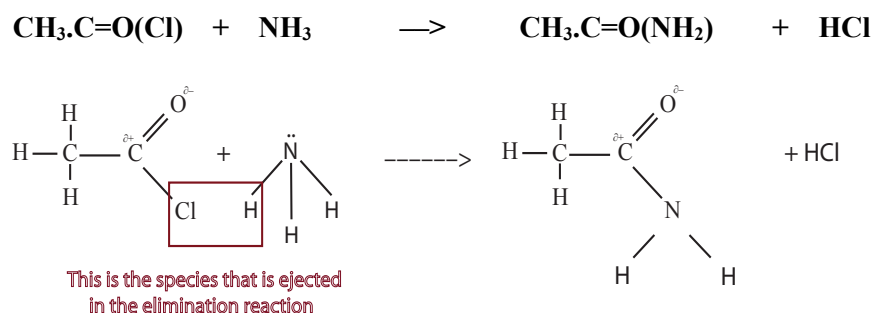
¹¹ Just as Ethanoic Acid used to be called Acetic Acid, so also Methanoic Acid used to be called Formic Acid.

¹² Pure liquid Acetic Acid is called “glacial” because Acetic Acid “freezes” at about 16°C.

- On page 3 and on page 22 I have drawn an info tree for Acyl Chlorides and Acid Anhydrides, and in it you will see that one of the group of reactions for Acyl Chlorides is that for Nitrogen containing substances.

Reactions of Acyl Chlorides and Nitrogen bearing compounds

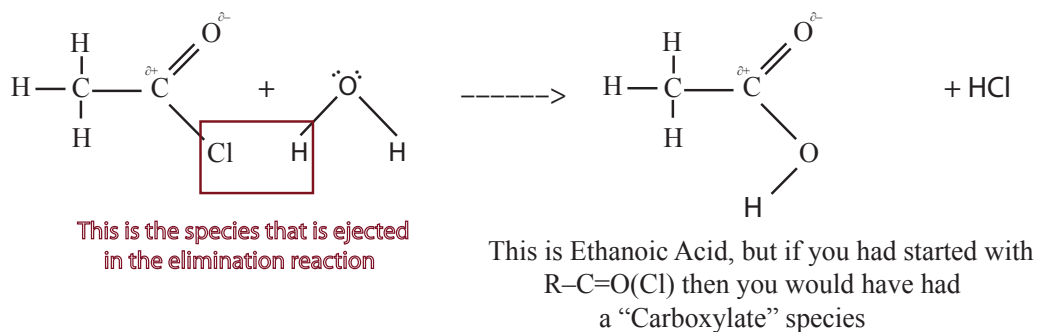
- Let us look at the simplest one of these (below) viz that for an Acyl Chloride (e.g. Ethanoyl Chloride) and Ammonia.



- I have used Ammonia here, but instead of the NH_3 above, I could have substituted NHR_1R_2 and then I could have made a variety of Amides.

Reactions of Acyl Chlorides and Oxygen containing compounds

- If you look at the diagram above and then substitute a molecule of Water for the molecule of Ammonia, then you would get the following.

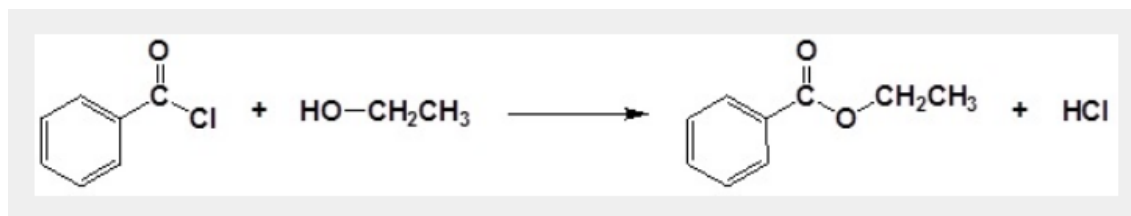


- Just as with Ammonia (where we could have used NHR_1R_2), so also instead of Water (which gave us an acid) we could have used an Alcohol (which would have given us an Ester)

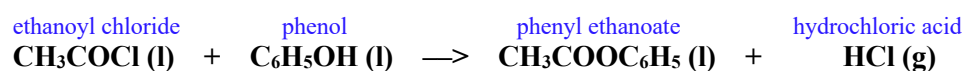


Source: Chemistry LibreTexts

or we could have used any suitable Arene such as Phenol and we would have got a Phenyl Carboxylate species – and if you look at the equation that I have just quoted from Chemistry LibreTexts I could substituted the Phenyl bit (or any other Benzene derived compound such as say Phenol) on either of the two “R” species (one shown in green and the other in red). The diagram below is also from Chemistry LibreTexts. As it happens what you have created below is an Ester because and Acyl Chloride (just as will a Carboxylic Acid) will react with an Alcohol to produce an Ester.



- If I had used Ethanoyl Chloride (which used to be called Acetyl Chloride) and “-C₆H₅” as the green “R” species at the bottom of page 17, then I would have used Phenol (C₆H₅OH) and the resulting reaction equation would have been

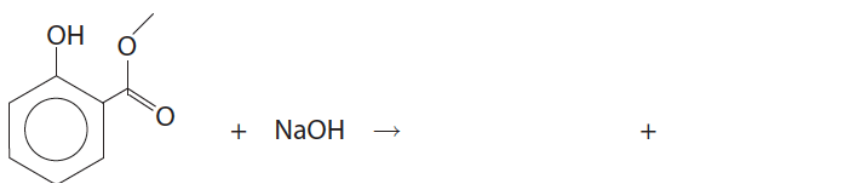


and if you look closely, you will see that I have produced an Ester. If I look at the “CH₃COO-” bit I can see that it is an “Ethanoate”, and if I look at the “-C₆H₅” then I will see that it is a “Phenyl” Ester.

- You now have the basic principles and starting points for most of the reactions of Acyl Chlorides. The principles and the examples that I have used here are fairly simple, and I doubt that you will be asked something more complicated in the exams. What the examiners justifiably might do, is to give you a diagram with more complicated stuff in it and ask you to use your knowledge of the basic principles to unravel what is going on. That is not unfair – but, in my opinion, what is unfair about the modern ‘A’ Level exams is that they do not give you enough time to do the things that they ask. For example, in the June 2016 Edexcel paper (Q15) the examiners requested the following where Question (a) (i) is just an acid base reaction giving Water plus a salt – it is after all just a 1 mark question)

- (a) (i) Complete the equation for the alkaline hydrolysis of the ester group in methyl salicylate, using sodium hydroxide.

(1)



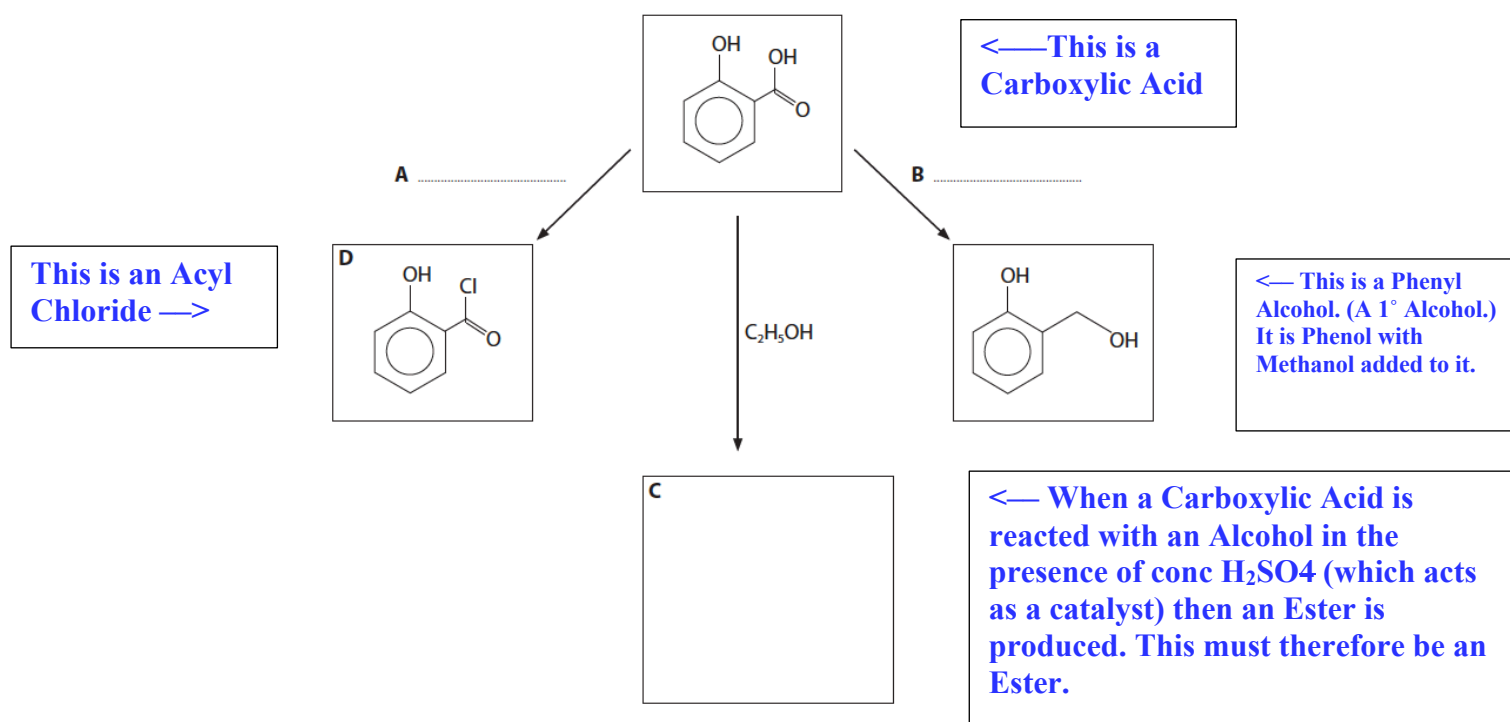
- Aspirin is Acetylsalicylic Acid, and there used to be lots of questions about Aspirin in the exams in the olden days, so there is nothing unfair about the question ‘*per se*’. The question (Q15) became relentlessly more and more challenging as it progressed. If you look at the diagram on the next page, you will see the Phenyl Acyl Chloride that we have been discussing in the last few pages.

- However, I have now given you all the basic principles that you need to answer whatever the examiners throw at you. It does not matter what they ask. **You CAN answer the question.** Don't panic! You know more than enough to answer the question. Use your brain and you will get through the exam (**ANY EXAM if you have done your preparation properly!**).
- However, the rule is to look at the number of marks allocated and then DO NOT spend more than that number of minutes on the question – otherwise you will not finish the exam paper!

(d) Salicylic acid can undergo various reactions as outlined below.

- (i) Give the **formula** of the reagents **A** and **B** and the **skeletal** formula of the product **C**.

(3)



My comments in blue are meant to show you that you know everything that you need to know in order to answer this Question.

- We have already learnt (on page 15 of this Chapter) that if you react a Carboxylic Acid with PCl_3 or PCl_5 or SOCl_2 then you will get the corresponding Acyl Chloride, **and that is what they wanted you to give them for reagent “A”**.
- You need to reduce a Carboxylic Acid to get to an Alcohol, therefore quote the standard reducing agent for this (LiAlH_4) – **and now you have given them reagent “B”**.
- If you react an Acid with an Alcohol then you get an Ester. (I taught you that in your First Year in the Sixth Form). All that you need to do is to give the appropriate Ester and **you will have identified compound “C”**.

- The remaining thing that I need to tell you on this topic is that, if an Acyl Chloride is reacted with the anionic salt of a Carboxylic Acid, then an **Acid Anhydride** will be formed.
- Please see the info tree on pages 3 and 22.

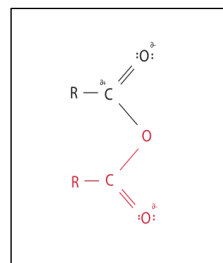
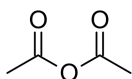
HOWEVER, to bang out these answers in seconds, YOU MUST KNOW YOUR STUFF!

- In the last few months before your ‘A’ Levels these are the rules that you must obey viz.

REVISE, REVISE, REVISE!
MEMORISE YOUR INFO TREES
MEMORISE YOUR INFO TREES!

- Every night before you fall asleep, go through every one of your info trees for every one of your ‘A’ Level subjects.

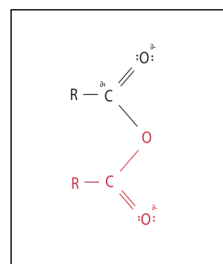
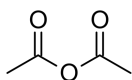
E) Acid Anhydrides/Acyl Anhydrides



- Wikipedia defines an “Anhydride” as **a chemical compound that reacts with water to form an acid**. Anhydrides of inorganic acids are usually **oxides of non-metallic elements**.
 - Carbon dioxide, CO₂, is the anhydride of **carbonic acid**, H₂CO₃.
 - Nitrogen pentoxide, N₂O₅, is the anhydride of **nitric acid**, HNO₃.
 - Phosphorus pentoxide, P₂O₅, is the anhydride of **phosphoric acid**, H₃PO₄.
 - Sulphur dioxide, SO₂, is the anhydride of **sulphurous acid**, H₂SO₃.
 - Sulphur trioxide, SO₃, is the anhydride of **sulphuric acid**, H₂SO₄.

and the anhydrides of organic acids contain the carbonyl group, “>C=O”.

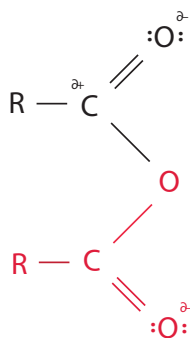
E) Acid Anhydrides/Acyl Anhydrides



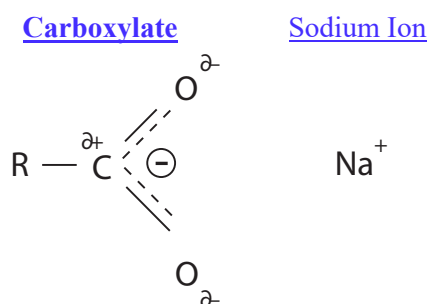
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 - Sulphur dioxide, SO₂, is the anhydride of **sulphurous acid**, H₂SO₃.
 - Sulphur trioxide, SO₃, is the anhydride of **sulphuric acid**, H₂SO₄.

whereas the anhydrides of organic acids contain the carbonyl group, “>C=O”.

- Jim Clark in his excellent website “chemguide” puts forward a nice little tip. He says look at the Acid Anhydride as though it were an ordinary Carbonyl compound (“R.C=O”) species which just happens to have another (inverted) “R.C=O” attached to it through an “O” atom, and regard the second “R.C=O” species (*the bit that I have drawn in black in the diagram below*) as the bit that will become the substituent in a reaction. His advice makes a lot of sense.



- Mr Clark says that one could think of the species shown in red as the “Cl” species in an Acyl Chloride, and the comparison is not a bad one given that an Acid Anhydride has reactions that are similar to those of Acyl Chlorides (cf. the info tree on pages 3 and 22).
- The bit in red above is what is known as a **Carboxylate species** “R.C=O(O⁻)”. It is the negatively charged anion of a Carboxylic Acid. If “R” = “-CH₃” and you were to add a metal cation e.g. Sodium, Na⁺ to the CH₃.COO⁻ (CH₃.C=O(O⁻)), then you would get **Sodium Acetate** “R-COO(Na)” (below).



NB The dotted line above indicates a delocalised π bond.

- Using Mr Clark’s methodology, one way of thinking about the reaction of Ethanoic Anhydride with Ethanol would be to take **red** bit (on page 20) off the Acid Anhydride, and then take an **H⁺** proton off an Ethanol molecule to leave “-O-C₂H₅”, and then put the two **red** species together and the two **blue** species together to get



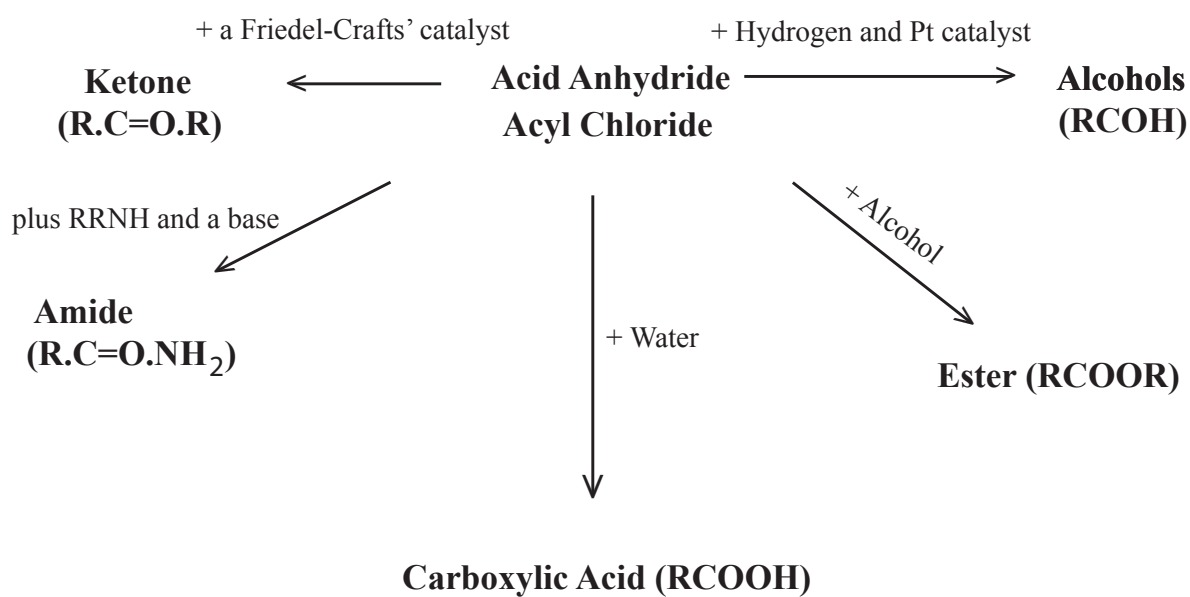
- If you look closely at Ethyl Acetate, then you will see that **it is just an Ester**.
- The way into an Acid Anhydride would be to distil an Acyl Chloride with R-C=O(ONa). I can recommend the first few minutes of the Khan Academy’s video on

<https://www.khanacademy.org/science/organic-chemistry/carboxylic-acids-derivatives/reactions-carboxylic-jay/v/preparation-of-acid-anhydrides>

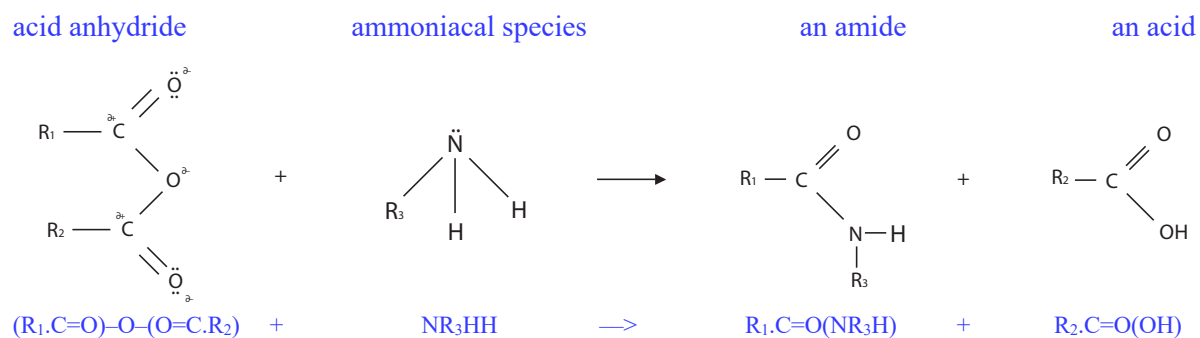
It is **very good**.

- There are many routes out of Acid Anhydrides and Acyl Chlorides, and some of them are shown overleaf.

Reactions of Acid Anhydrides and Acyl Chlorides



- The reaction from an Acid Anhydride to an Amide and an acid

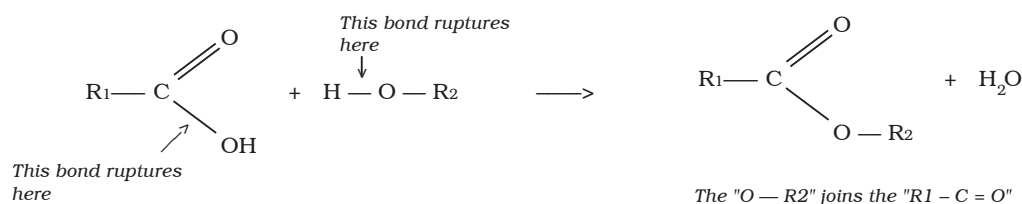


where “R₁” / “R₂” / and “R₃” could be differing species (but, equally, “R₃” could be an H atom).

F) Esters

- When we were talking about Alcohols last year (Chapter 6 of last year's section on Organic Chemistry), I told you that
- For the Esterification of an Alcohol, the Syllabus requires you to know that
 - “an **Alcohol** and a **Carboxylic Acid** must be **REFLUXED** in the presence of concentrated H_2SO_4 until Esterification takes place”, and then
 - you must draw the diagram (for example) of Ethanol and Butanoic Acid (cf. below).

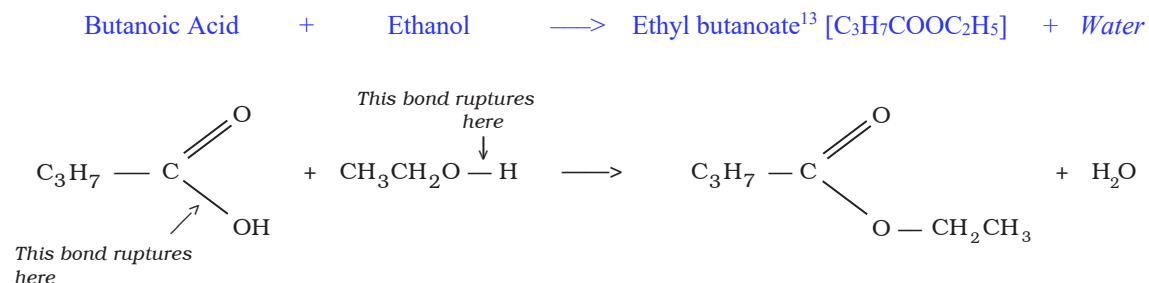
- Generically, $\text{R}_1\text{COOH} + \text{R}_2\text{OH} \xrightarrow[\text{Reflux}]{\text{conc H}_2\text{SO}_4} \text{R}_1\text{COOR}_2 + \text{H}_2\text{O}$
- Please note that R_2COOR_1 is not formed! R_2COOR_1 and R_1COOR_2 are NOT the same Ester** therefore please note carefully in the diagram the exact place at which each one of the two bonds breaks. *[You ARE expected to know exactly where the bonds break!]*



NB A double bond is stronger than a single bond, therefore the single bond in the acid is the one that ruptures.

NB In Organic Chemistry, it is not important to show the non-organic products of a reaction therefore it is *NOT necessary* to show the water formed in this reaction. However, I tend to show it because then I can check that my equations are stoichiometrically correct (i.e. the moles in the equation are in the right proportions).

- When the reaction is completed, the resulting solution can be distilled and the Ester thus separated from the unreacted reactants/catalyst. Thus,



- When an Acid Anhydride or an Acyl Chloride is reacted with an Alcohol, then this also gives an Ester.

¹³ Remember to ask yourself what the “-oate” molecule is (here it is a butanoate), and then ask what sort of butanoate it is (here it is an ethyl butanoate).