Organic Chemistry

$C_8H_{10}N_4O_2$

1,3,7-trimethylpurine-2,6-dione

-

Caffeine

Chapters 8 to 12, 15 to 18

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PART I

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Functional Groups

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1 Overview

Functional groups are the main determinant of the chemical properties of a molecule. Molecules with the same functional group are of the same *family* and similar *chemical properties.*
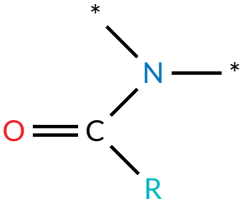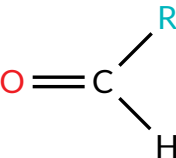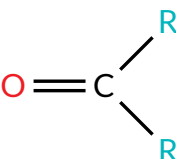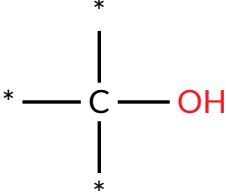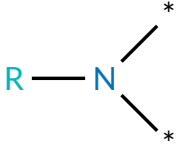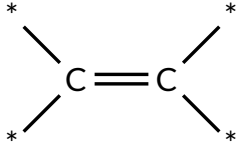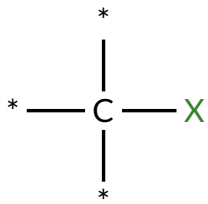
Functional groups can be any size — the ketone functional group is just an oxygen double-bonded to a carbon atom with two R groups on either side, while the carboxylic acid functional group has a more complex structure.

2 Basic Functional Groups

Note that this table is ordered based on the *priority* of the functional group, in terms of where it appears in an IUPAC-named chemical compound.

R, as used below, represents a substituent alkyl or aryl group, the former being an arbitrary carbon chain, and the latter being some aromatic ring derivative.

Name	Prefix Form	Suffix Form	Structure
Carboxylic Acid	carboxy–*	*–oic acid	
Ester	–	*–oate	
Acyl Halide	halocarbonyl–*	*–oyl halide	

Amide	carbamoyl–*	*–amide	
Nitrile	cyano–*	*–nitrile	$N \equiv C — R$
Aldehyde	formyl–*	*–al	
Ketone	oxo–*	*–one	
Alcohol	hydroxy–*	*–ol	
Amine	amino–*	*–amine	
Alkene	alkenyl–*	*–ene	
Alkyl Halide	halogen–*	–	

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PART II

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Isomers

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1   Overview

Isomers are molecules that share the same structural formula, yet exist in different forms. The two main forms of isomerism are structural isomerism and stereoisomerism. In both cases, the molecular formula of the compounds is the same, while the chemical and physical properties may differ greatly.

2   Structural Isomerism

2.1   Chain Isomerism

In chain isomerism, molecules have the same functional groups, except they are placed in different positions along the carbon chain. Chain isomers typically have similar chemical properties, but different physical properties (since the shape of the carbon chain can determine the strength of id-id interactions).
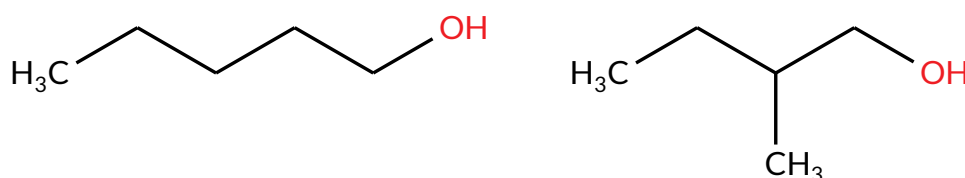
Pentanol and 3-methylbutan-1-ol are chain isomers.

2.2   Positional Isomerism

Positional isomers have the same arrangement of their carbon chains, and the same functional groups. However, said functional groups are placed at different positions.
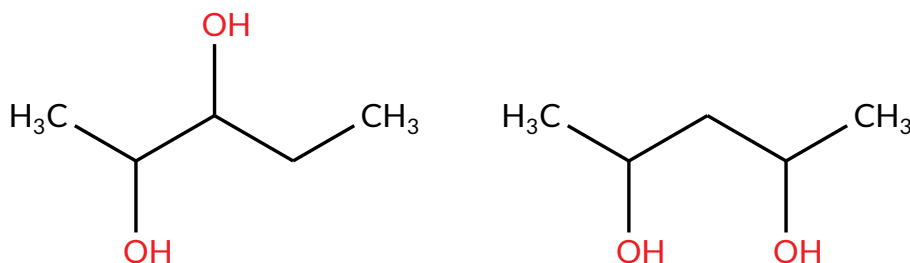
Butan-2,3-ol and butan-2,4-ol are positional isomers.

2.3   Functional Group Isomerism

This is somewhat a misnomer since it is exactly the opposite of what it seems to intuit. Functional group isomers share only their molecular formulas; the carbon chain, the functional groups, etc. are all different.
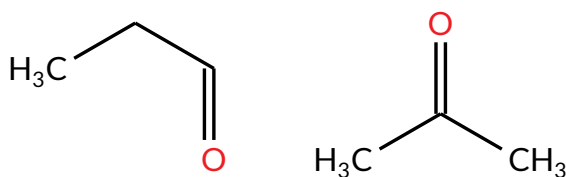
Propanal and acetone are functional group isomers.

3   Stereoisomerism

Stereoisomers of molecules have the same structure and functional groups, but those groups are arranged in a spatially differing way. The main forms of stereoisomerism are cis/trans (or E/Z) isomerism, and optical isomerism.

Note that for certain cis/trans (E/Z) isomers, the trans (or E) variant can 'pack' better, resulting in a higher melting point. This doesn't affect the boiling point since the molecules are too far apart in the gaseous phase for it to matter.

Additionally, the presence of *intramolecular* (within the same molecule) hydrogen bonds can also be a factor since it reduces the strength of *intermolecular* hydrogen bonds. Other than these, the chemical and physical properties of stereoisomers are mostly the same.

3.1 Cis/Trans Isomerism

Only alkenes can exhibit cis-trans isomerism, due to the C=C bond that restricts rotation along its axis. This is because of the π-bonds that only bond at 180° intervals. At these positions, it forms the cis and trans isomers.
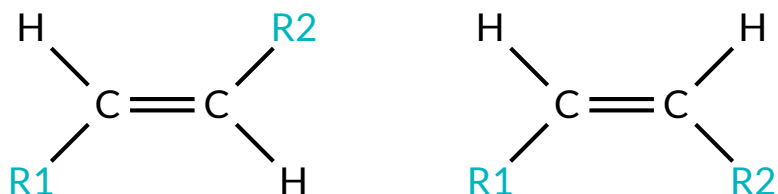
The molecule on the left is the *trans* isomer while the one on the right is the *cis* isomer. *trans* is from Latin, meaning *other side*, while *cis* obviously means *same side*. In the former, the larger groups are on opposite sides of the alkene double bond, while in the latter, the larger groups are on the same side. Note that these *groups* do not necessarily have to be functional groups — they can be as large or as simple as one wishes.

When naming cis/trans isomers, the qualifier *cis* or *trans* is placed before the stem name, like so:

- cis-but-2-ene
- trans-but-2-ene

Note that cis/trans isomerism is not applicable to molecules where identical groups are attached to the any one carbon atom, since there is a line of symmetry going along the plane of the double bond.
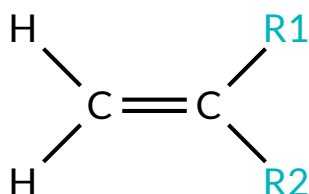
3.2 E/Z Isomerism

E/Z is generally the more comprehensive, general form of cis/trans. Consider the alkene below, with two variants due to the lack of a plane of symmetry:
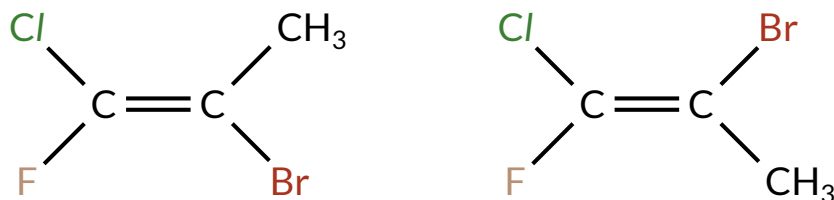
It has 4 distinct substituents, and thus a cis/trans designation cannot be used. Behold, E/Z isomerism. At its core, it is simply another method of handling alkene isomers that works for more general forms of molecules.

It follows a scheme of priorities (Cahn-Ingold-Prelog, or CIP), which are determined as such:

i. The group with the largest atomic mass *directly attached* to the alkene's carbon has the highest priority.

ii. In the event of a tie, look at the atoms directly attached to *that* offending atom. Use the previous rule, favouring higher priority atoms, to tiebreak. Double bonds are counted twice.

iii. Recursively evaluate the previous rule with attached atoms, to continue the tiebreaking process.

The above scheme should be used to find the two highest-priority groups attached to the alkene, after which, if the two groups are attached on the same side of the alkene, then the molecule is the *Z* isomer, and it is known as the *E* isomer if the reverse is true.

E and Z come from the German *entgegen* and *zusammen*, *opposite* and *together* respectively.

3.3 Optical Isomerism

Due to the 3-dimensional tetrahedral nature of a carbon atom, if there are 4 *distinct* substituents, two non-superimposable mirror images can exist, resulting from a lack of any plane of symmetry. Such carbons are called *chiral carbons*, and are the *chiral centres* of the molecule. A molecule can have multiple chiral centres.

Consider butan-2-ol below. Carbon 2, with the OH group, has 4 different groups attached to it. As such, it is a chiral carbon.
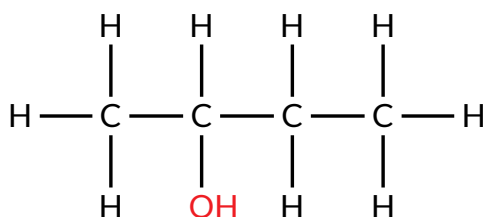
Indeed, it can take the form of 2 non-superimposable mirror images, that are differentiated by the adjacency of 2 of the 4 groups bonded to the chiral carbon. As can be seen, these two mirror images cannot be rearranged into the other, and are distinct — these are called *enantiomers*.
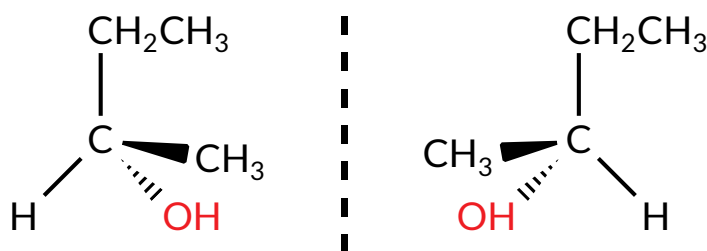
The solid wedge indicates a bond coming out of the plane of the paper, while the dashed wedge indicates a bond going into the plane.

Optical isomers have identical physical properties, except for their treatment of plane-polarised light (this is where the light wave is only oscillating along one plane). One of the isomers will rotate this light clockwise, while the other will rotate it counterclockwise. The magnitude of both rotations are the same.

If equal amounts of each enantiomer are present in a solution, it is called a *racemic mixture*, and the net rotation of plane polarised light will be 0, for obvious reasons.

Enantiomers usually have identical chemical properties, except for certain interactions that require a certain spatial orientation to work, such as proteins, that can only work with one of the optical isomers.

Reaction Mechanisms

1   Bond Breaking

1.1   Homolytic Fission

Homolytic fission involves the splitting of a single bond, with an equal (*homo*) distribution of the two electrons of the aforementioned bond. This results in the formation of radicals, since now both atoms from the bond will have unpaired electrons.

The movement of these single electrons is represented with single-hooked arrows. The arrow starts from the bond line, and points towards the target atom receiving the electron.
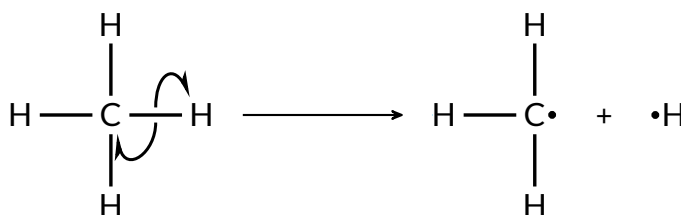
The homolytic fission of CH_4, forming $\cdot CH_3$ and $\cdot H$ radicals.

1.2   Heterolytic Fission

As the name implies, heterolytic fission is the opposite; it distributes both electrons of the bond to a single atom, which usually results in the formation of ions. The transfer here is represented using a full (double-hooked) arrow.
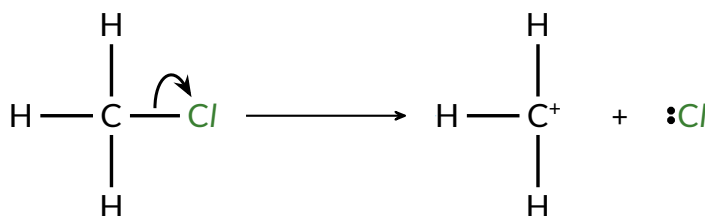
The heterolytic fission of CH_3Cl, resulting in CH_3^+ and Cl^- ions

2 Bond Forming

2.1 Single Electrons

Bond forming is essentially the reverse of bond breaking, and hence the same notations apply — single-hooked arrows for the movement of single electrons, and double-hooked arrows for the movement of an electron pair.

In this case, two single electrons from each atom contribute to the new bond.
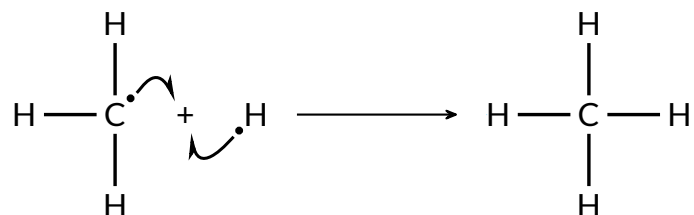
The formation of a bond between $\cdot CH_3$ and $\cdot H$ radicals to form CH_4.

2.2 Electron Pairs

Electron pairs usually come from negatively charged radicals or lone pars, although this is not a rule. Both electrons come from a single source to form a bond, but this is *not* a dative bond — it is simply a normal bond.
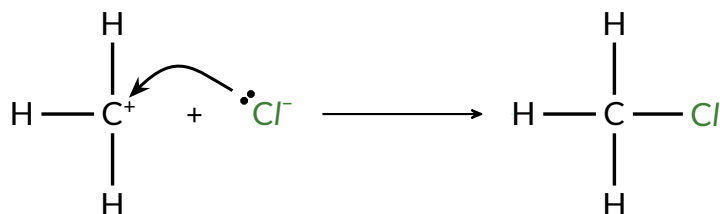
The formation of a bond between $\cdot CH_3$ and Cl^- radicals, to form CH_3Cl.

3 Electrophiles and Nucleophiles

3.1 Electrophiles

Electrophiles are electron-deficient species that accept an electron pair from a nucleophile donor. Most electrophiles either have a positive charge, or contain an atom that is polarised and thus has a partial positive charge.

Examples of electrophiles include CH_3^+, Br^+, NO_2^+, polarised Br_2, and HBr.

3.2 Nucleophiles

Nucleophiles are electron-rich species that donate electron pairs to electrophiles. This process typically results in the formation of a new covalent bond. Nucleophiles usually contain atoms that are either negatively charged, or, more frequently, contain lone electron pairs that are not bonded.

Molecules with a π-bond, such as ethene or benzene, can also act as nucleophiles, due to the high electron density of the π-system.

Examples of nucleophiles include H_2O, NH_3, and OH^-.

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PART IV

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Induction and Resonance

1   Inductive Effect

The inductive effect occurs through covalent bonds, where there is a significant difference in the electronegativity of participating atoms. Electrons are either withdrawn or donated through a -bond, due to the polarity of the molecule.

1.1   Withdrawal

Below, C*l* is more electronegative than the carbon it is bonded to. As such, it *inductively withdraws* electrons through the -bond.
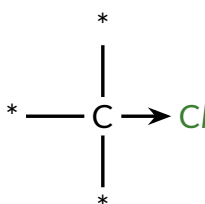
Note that the arrow represents a withdrawal of electrons, *not* a dative bond.

1.2   Donation

Alkyl groups, or groups with the general formula C_nH_{2n+1}, *inductively donate* electrons. This behaviour is due to hyperconjugation, which lowers the total energy of the system, through an interaction between electrons in a -bond of the alkyl group, with a partially-filled or empty p-orbital in the adjacent atom.
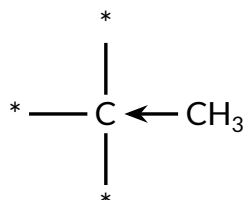
Again, the arrow *does not* represent a dative bond.

2   Resonance Effect

The resonance effect is the withdrawal or donation of electrons through the side-on overlap of *unhybridised* p-orbitals. Thus, the resonance effect can only occur when the central atom is sp^1 or sp^2 hybridised, since only those configurations have unhybridised p-orbitals.

2.1   Withdrawal

In the case below, electrons flow from the double-bonds to the substituent, via the resonance effect. In general, substituents that exhibit an electron-withdrawing resonance effect usually take the form of $-Y=Z$, where Z is more electronegative than Y. Examples include carbonyls and nitriles.
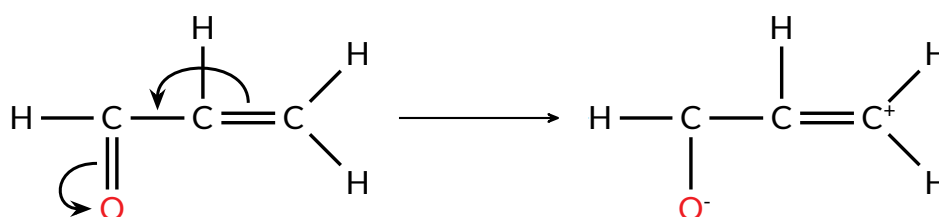
Electrons move from the electron-rich double-bonds, which have unhybridised p-orbitals, to an adjacent atom.

2.2 Donation

On the other hand, groups can donate electrons through resonance, flowing from the substituent to a single-bond, forming a double-bond. Substituents such as halogens (F, Cl, etc.), hydroxyls ($-OH$), and amines ($-NH_2$) are examples. They usually contain a lone pair of electrons that are free for donation.
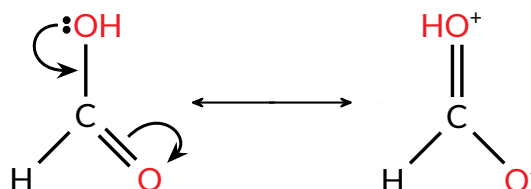
This example shows both resonant withdrawal and donation.

2.3 Overall Effect

Since it is possible for a substituent group to simultaneously withdraw and donate electrons through different mechanisms, it can be difficult to determine whether the overall effect serves to withdraw or donate electrons.

Behold, the second ugly table.

Substituent Group	Strength	Overall Effect
Alkyl/aryl groups (eg. $-CH_3$)	Weak	Donating
$-OH$, $-NH_2$, $-OCH_3$	Strong	Donating
$-Cl$, $-Br$	Weak	Withdrawing
$-CHO$, $-NO_2$, $-CN$, $-CO_2H$	Strong	Withdrawing

2.3.1 Caveats

Note that this table only applies to benzene rings, which will be covered *later*. This is because the resonance effect (overlapping of p-orbitals with π-electron clouds) is only commonly applicable to arenes, or where the atom is sp^2 hybridised.

In all other cases, where the substituent is bonded to an sp^3 hybridised atom, the electron-donating or withdrawing behaviour is determined mostly by the electronegativity, since there is no unhybridised p-orbital to overlap with. Hence, alkyl groups are basically the only electron-donating species in this case.

Alkanes

1 Open Chain

Open chain alkanes have the general formula of C_nH_{2n+2}. They are called 'open-chain' because the two endsof the chain are separate, in contrast with cycloalkanes. Open chain alkanes can either be straight-chained or branch-chained. The terminology should be pretty much self explanatory.
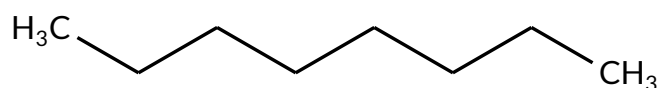
Octane is an example of a straight-chain alkane.
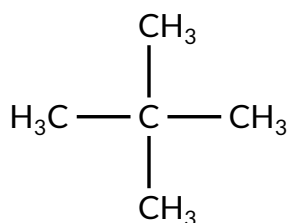
2,2-dimethylpropane is an example of a branched alkane.

2 Cycloalkanes

Cycloalkanes are alkanes where the carbon atoms at either end of the chain are bonded together, forming a closed loop and taking the shape of regular polygons.
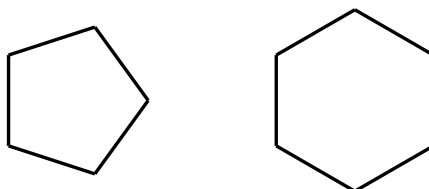
Cyclopentane (left) and cyclohexane (right)

3   Physical Properties

3.1   Melting and Boiling Points

The melting and boiling points of alkanes follow a simple pattern. Due to the fact that they rely solely on induced dipole interactions for intermolecular bonding, both melting and boiling points increase with the length of the carbon chain, and by extension M_r. Note that small chains (eg. CH_4) have very low boiling points.

However, because branched alkanes have a smaller surface area for a given number of carbon atoms than straight-chained alkanes, their melting and boiling points will be lower, due to a smaller area for polarisation.

3.2   Density

Most liquid alkanes, up to a certain point, are less dense than water. Additionally, since they are insoluble, they form an immiscible layer above water.

As the number of carbon atoms increases, the strength of the intermolecular interactions will increase as well — this forces each molecule ever so slightly closer together, marginally increasing density.

3.3   Solubility

As described before, alkanes rely only on induced-dipole interactions for intermolecular bonding; they are insoluble in polar solvents such as water. However, they are highly soluble in non-polar solvents like CCl_4. In fact, since solubility is dependent on the strength of solvent-solute bonds, larger alkanes will be more soluble in non-polar solvents.

4 Classification of Carbons

This applies to many things — carbons, halogenoalkanes, and alcohols. Essentially, the classification of an atom with substituent groups refers to the number of such groups attached to the carbon, and the number of hydrogens (ie. unfilled slots so to speak) attached to it.

As example, there are 4 possible classifications of carbons in an alkane: *primary*, *secondary*, *tertiary*, and *quaternary*.

Primary (1°)	Secondary (2°)	Tertiary (3°)	Quaternary (4°)
H—C—R1 with H above and H below	R2—C—R1 with R2 above (H—C) and H below	R2—C—R1 with R2 above (R3—C) and H below	R2—C—R1 with R2 above (R3—C) and R4 below

The table (ew) above gives a visual representation. *R* represents an alkyl group substituent. This principle also applies when classifying alkyl radicals.

5   Alkane Reactions

5.1   Free Radical Substitution

5.1.1 Mechanism of Reaction

In the steps below, the free radical substitution of methane (CH_4) by chlorine (Cl_2) will be used. This applies for any alkane, and a sufficiently reactive halogen.

Conditions: UV Light, Br_2 / Cl_2 gas
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.

Stage I.   Initiation

The $Cl-Cl$ bond is *homolytically* broken to form 2 Cl radicals. The energy required to break this bond is provided by the UV light.

$$Cl - Cl \longrightarrow 2\,Cl\bullet$$
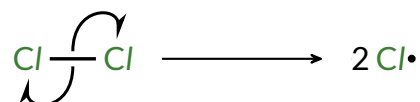
Stage II.   Propagation

The highly reactive Cl radicals then react with the CH_4 molecules, bonding with one of the hydrogen atoms to form HCl and a carbocation radical, CH_3.

$$Cl\bullet \ + \ CH_4 \longrightarrow \bullet CH_3 \ + \ HCl$$
$$Cl_2 \ + \ \bullet CH_3 \longrightarrow CH_3Cl \ + \ Cl\bullet$$
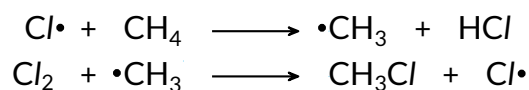
This newly-minted CH_3 radical can react with a Cl_2 molecule to form CH_3Cl and another Cl radical, thus recreating the consumed radical. As long as the supply of Cl_2 gas has not been exhausted, this reaction can continue, and no additional UV light is required to sustain it.

Stage III. Termination

In the termination stage, two radicals combine to form stable products, effectively terminating the chain reaction.

$$Cl\bullet \ + \ Cl\bullet \ \longrightarrow \ Cl_2$$
$$\bullet CH_3 \ + \ \bullet CH_3 \ \longrightarrow \ CH_3CH_3$$
$$Cl\bullet \ + \ \bullet CH_3 \ \longrightarrow \ CH_3Cl$$
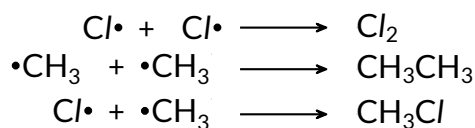
Once all the radicals have been consumed in this manner, the reaction will stop, unless more UV light is provided (along with more Cl_2 gas).

5.1.2 Multi-substitution

Free radical substitution of alkanes is usually not the preferred way to produce halogenated alkanes, due to the random nature of the process and the possibility of multi-substitution, where more than one halogen atom has been substituted onto the alkane.

If there are still Cl radicals remaining, in the reaction chamber, CH_3Cl formed during the termination stage can still react with it, forming a CH_2Cl radical, which can continue to react.

$$CH_3Cl \ + \ Cl\bullet \ \longrightarrow \ \bullet CH_2Cl$$
$$CH_2Cl\bullet \ + \ Cl_2 \ \longrightarrow \ \bullet CH_2Cl_2 \ + \ Cl\bullet$$
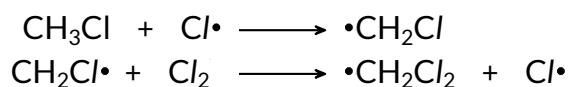
Indeed, this can continue *ad-infinitum*, so until all the hydrogen atoms on the alkane have been substituted. In the case of methane, this results in the formation of CH_3Cl, CH_2Cl_2, $CHCl_3$ and CCl_4.

In fact, the will also be a small amount of alkanes with more than 1 carbon in the chain; this is due to the possibility of two molecules of $\bullet CH_2Cl$ reacting, which then has its hydrogens further substituted.

5.1.3 Isomerism of Products

Because every hydrogen atom can be substituted by the halogen atom, alkanes with 3 or more carbon atoms in the chain can form isomers. The probability of the formation of each isomer depends on both the number of possible hydrogen atoms that can be substituted to result in it, as well as the stability of the carbon radical intermediate.
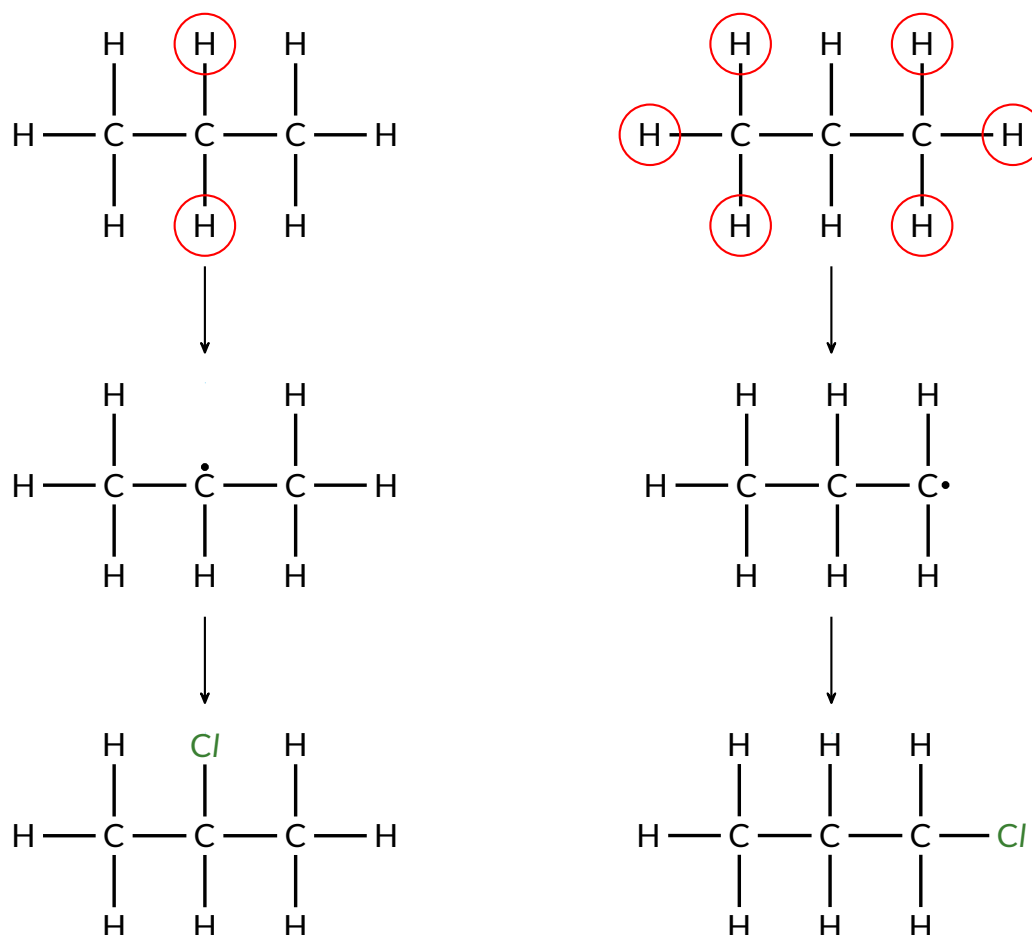
In the example above, propane can be substituted by Cl to form 2 different isomers, 2- chloro-propane and 1-chloropropane. Only 2 hydrogens can be substituted to form the former, while 6 hydrogens can be substituted to form the latter. Thus, the *expected* ratio of products from the free radical substitution of propane with chlorine is 2 : 6 in favour of 1-chloromethane.

However, the stability of the carbon radical intermediate also plays a part in the ratio of products. For 1-chloropropane, it involves forming a carbon radical on carbon 1, which only has 1 electron-donating alkyl group (through the induction effect) to stabilise the positive charge. On the other hand, for 2-chloropropane, the positive charge is on carbon 2, which has 2 electron-donating alkyl groups to stabilise it. Thus, it is more likely to form, and hence 2-chloropropane is more likely to form. Therefore, the actual ratio of products is around 4 : 6, not 2 : 6.

5.1.4 Halogen Reactivity

The reactivity of the free radical substitution naturally depends on the species of halogen that is reacting. As is typical of halogens, the reactivity increases in this order: $I_2 < Br_2 < Cl_2 < F_2$. In fact, the substitution by fluorine is too reactive — even in the dark and at room temperature. On the other hand, the substitution of iodine is not feasible ($\Delta G > 0$).

In the propagation steps of the reaction, several bonds are formed and broken. Using X as a halogen atom:

$\Delta H_1 = BE(C–H) - BE(H–X)$ $\quad CH_3–H + X\bullet \quad \longrightarrow \quad \bullet CH_3 + H–X$
$\Delta H_2 = BE(X–X) - BE(C–X)$ $\quad \bullet CH_3 + X–X \quad \longrightarrow \quad CH_3–X + X\bullet$
$\Delta H_r = \Delta H_1 + \Delta H_2$ $\quad\quad CH_4 + X_2 \quad\quad \longrightarrow \quad CH_3X + HX$
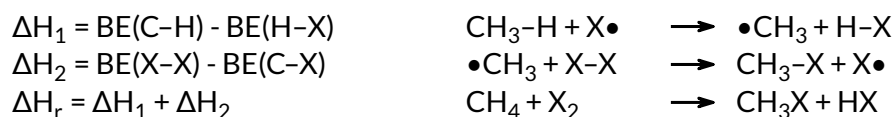
The values of the bond energies for H–X, X–X, and C–X are below:

	$H{-}X\,/\,kJ\,mol^{-1}$	$H{-}X\,/\,kJ\,mol^{-1}$	$H{-}X\,/\,kJ\,mol^{-1}$	$\Delta H_r\,/\,kJ\,mol^{-1}$
F_2	562	484	158	−478
Cl_2	431	340	244	−117
Br_2	366	280	193	−43
I_2	299	240	151	+22

As can be seen, the reaction with F_2 is highly exothermic; even the F–F bond energy is relatively small, hence the reaction is highly spontaneous — even at room temperature and without UV light, since the initiation stage requires little energy to progress.

On the other hand, the ΔH of the reaction with I_2 is positive, hence the reaction is not as spontaneous, and it is not as likely to take place.

5.2   Combustion

Alkanes are a type of combustible fuel, and there exists a general formula describing the required amounts of O_2 to combust a given hydrocarbon.

$$C_xH_y \;+\; x + \frac{y}{4}O_2 \longrightarrow xCO_2 \;+\; \frac{y}{2}H_2O$$
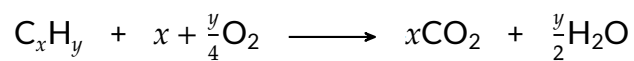
Note that while this combustion process is highly exothermic, it still has a high activation energy, and requires an energy input like a spark to begin the reaction.

PART VI

Alkenes

1 Open Chain

Alkenes are simply unsaturated hydrocarbons, with one or more double bonds. They have the general form of C_nH_{2n}.
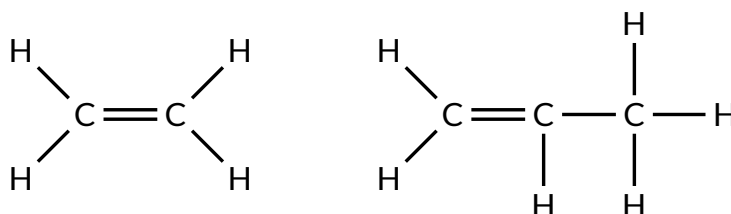
Ethene (C_2H_4) and propene (C_3H_6) are examples of alkenes.

2 Cycloalkenes

Cycloalkenes are simply cycloalkanes where one or more of the $C-C$ bonds have been replaced with a $C=C$ double bond.
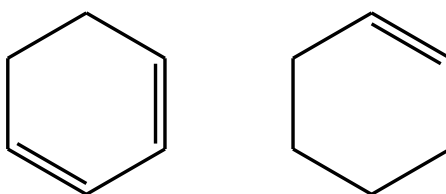
Cyclohex-1,3-ene and cyclohexene are examples of cycloalkenes.

3 Physical Properties

The physical properties of alkenes, including melting and boiling points, density and solubility follow the same trends as alkanes. Larger molecules have higher melting and boiling points, and higher densities, and alkenes are generally only soluble in non-polar solvents.

4 Stability of Carbocations

Before reactions and mechanisms of alkenes can be discussed, it is important to note the rules governing the formation of products, and the behaviour of molecules during the reaction.

All physical systems have a tendency to move to the lowest energy state — this state is characterised by the formation of the most stable molecules. As such, ions and radicals are inherently unstable.

4.1 Structure

One of the important intermediate products are carbocations, which are alkyl groups with an sp^2 hybridised central carbon atom, and carries a positive charge on that atom.
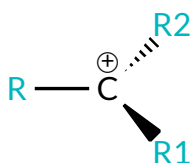
The 3 substituent groups are arranged in a trigonal planar fashion, with the p-orbitals above and below this plane. As such, nucleophiles can attack the carbocation from either the top or bottom.

4.2 Stability

Charged ions are inherently more unstable than their neutral molecule counterparts; any species that stabilises the charge on the carbon ion would in turn increase the stability of the entire molecule. The primary reason for this is that molecules that are created from a more stable intermediate product have a higher chance to form. Thus, the probability of formation of a given product of a reaction can be estimated by looking at the stability of the intermediate compound leading to its creation.

For carbocations, the carbon atom has a positive charge, thus electron-donating substituents such as alkyl groups ($-CH_3$), would stabilise the ion, as the donated electrons partially disperse the positive charge on the central atom.

Conversely, electron-withdrawing species such as halogens (F, C*l* etc.) would further destabilise the carbocation, and as such products that involve the formation of these intermediates would have constitute much lower proportion of the final products.

5 Creation of Alkenes

There are two methods of creating alkenes that are covered here, both of which involve elimination reactions, where a small molecule is *eliminated* along an alkane, and a double bond formed in its place.

For brevity, only the conditions and overall reaction will be covered.

5.1 Elimination of Hydrogen Halide

The main section that elaborates on this reaction can be found *here*, in the chapter on halogenoalkanes.

Conditions: Ethanolic KOH or NaOH, heat.
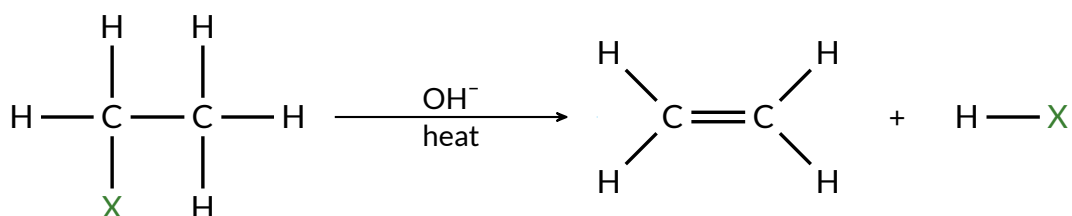
5.2 Dehydration (Elimination of Water)

Detail on this reaction, including the handling of isomers via Zaitsev's rule, can be found *here*, in the chapter on alcohols.

Conditions: Excess concentrated H_2SO_4, 170 °C, *OR*
Al_2O_3, heat.
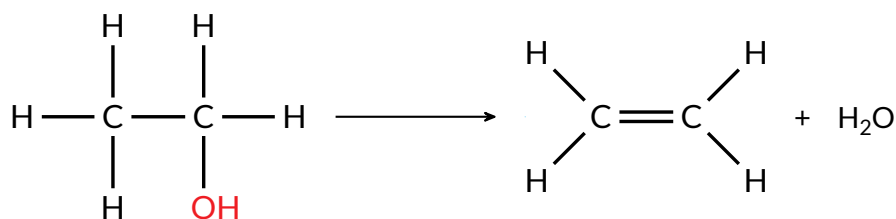
6 Alkene Reactions

6.1 Electrophilic Addition

The primary reaction mechanism of alkenes is electrophilic addition. Due to the high electron density of the π-bonds, electrophiles are readily attracted — thus alkenes are far more reactive than alkanes.

During a reaction, the comparatively weaker π-bond is preferentially broken over the stronger -bond; only a C−C bond remains, and atoms are *added* to the carbons, since they are now able to form an additional bond each. Hence, electrophilic *addition*.

The detailed mechanisms for each type of electrophilic addition, which are *required knowledge*, can be found in ***the appendix***.

6.1.1 Electrophilic Addition of Hydrogen Halides

In this reaction, the hydrogen and halogen atom are added across the double bond of the alkene. The hydrogen halide should be in a gaseous state for this reaction.

Conditions: Gaseous HX (usually HC*l* or HBr).
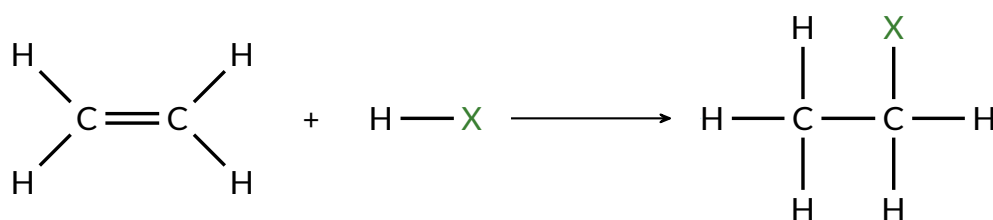
6.1.2 Markovnikov's Rule

This rule governs the major product that is formed when asymmetrical compounds are electrophilically added to alkenes, such as hydrogen halides. It does not apply to symmetrical reactants like Cl_2 or Br_2.

The rule states basically states that when a hydrogen compound with the general form H−X is added to an alkene that is asymmetrical about the double-bond, the hydrogen atom will be added to the carbon with *more* existing hydrogen atoms. Note that *X* can be a halogen, a hydroxide (ie. H−X is H_2O) or some other electronegative species.

A detailed illustration of the rule can be found in ***the appendix***.

6.1.3 Electrophilic Addition of Halogens

The electrophilic addition of halogens to alkanes does not involve Markovnikov's rule, since it is symmetrical. As the non-polar halogen molecule approaches the electron-rich π-bond, it is polarised, forming δ^+ and δ^- partial charges.

Note that the halogens used are usually either Br_2 or Cl_2, since F_2 is too reactive, and I_2 is too *unreactive.* The reaction mechanism involves the formation of a *cyclic halonium ion* (bromonium or chloronium) — the double bond breaks, and each carbon forms a single bond with one positive halide ion (both carbons bond to the same atom).

Conditions: No UV Light, gaseous X_2.
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
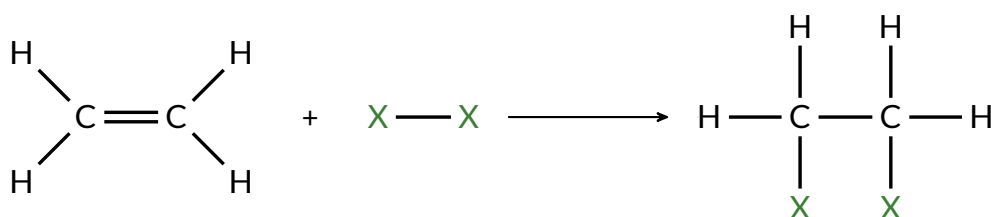
6.1.4 Electrophilic Addition of Aqueous Br_2

The mechanics of this reaction are basically the same as that of the electrophilic addition of Br_2. The conditions and observations are fairly similar as well, except for the colour change — aqueous Br_2 is *yellow*, not reddish-brown.

Also, since the Br atoms are not both added across the double bond in a symmetrical manner, Markovnikov's Rule applies — the OH group will preferentially attack the carbon that has more stabilising alkyl groups.

Conditions: No UV Light, aqueous Br_2.
Observations: *Yellow* $Br_{2\,(aq)}$ decolourises.
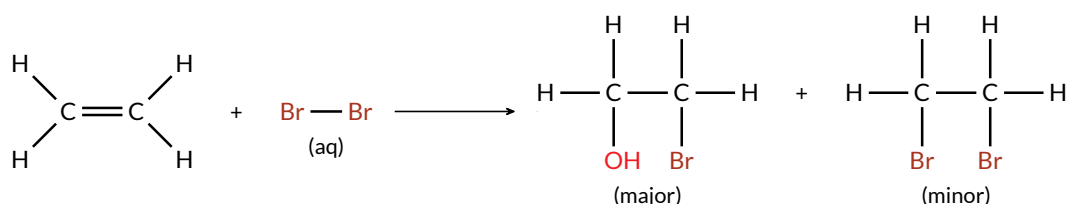
Both products are formed, except 1,2-dibromoethane is in much lower proportions.

6.1.5 Electrophilic Addition of Steam (Hydration)

Under certain (usually industrial) conditions, alkenes can react with steam to form alcohols. Since this reaction involves the formation of a carbocation intermediate, the proportion of products will be governed by Markovnikov's Rule.

Conditions: 300 °C, at 70 atm, H_3PO_4 catalyst, *OR*
Concentrated H_2SO_4, H_2O, warming.
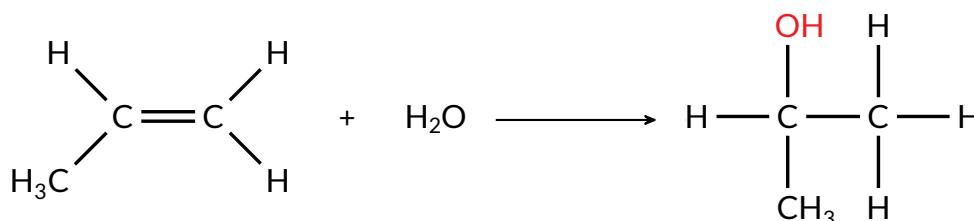
6.2 Reduction (Hydrogenation)

Hydrogen gas can be used to saturate alkenes, through the use of an insoluble metal catalyst such as nickel, palladium or platinum, as well as sufficiently high temperatures and pressures.

It was commonly used in the food industry to produce margarine from unsaturated plant oils. However, the resulting dense fats were found to be hazardous to human health, and subsequent usage was discontinued.

Note that although hydrogen atoms are added across the double bond, this is *not* an electrophilic addition reaction; it is actually a reduction-addition reaction.

Conditions: $H_{2\,(g)}$, high temperature and pressure, Ni, Pd or Pt catalyst.
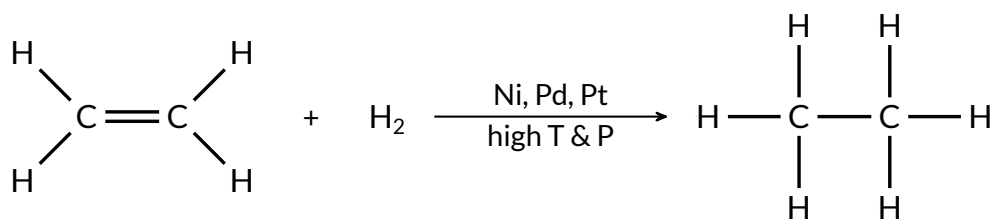
6.3   Mild Oxidation

Alkenes can be mildly oxidised with potassium manganate (VII), KMnO4, forming *diols*. This requires a cold environment, and either an acidic or alkaline medium (for MnO_4^- to function).

On a side note, balancing redox reactions involving organic molecules simply involves adding H_2O to balance the H or O (for oxidation and reduction respectively), and adding an appropriate number of [O] or [H] to balance the remaining oxygen or water.

6.3.1 Acidic Medium

A dilute acid is used to provide the acidic medium, in the form of H^+ ions. Typically, this is H_2SO_4. The oxidising agent, MnO_4^-, is reduced, forming Mn_2^+.

Conditions: Cold $KMnO_4$, acid (H_2SO_4).
Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+}.
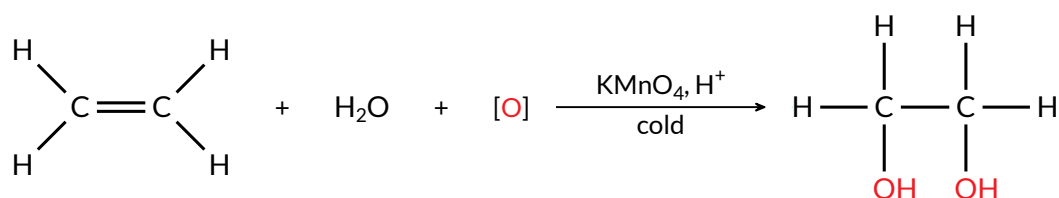
6.3.2 Alkaline Medium

An aqueous base, such as NaOH, is used to provide the OH^- ions. The oxidising agent MnO_4^- is reduced to MnO_2.

Conditions: Cold $KMnO_4$, aqueous base (NaOH).
Observations: *Purple* $KMnO_4$ decolourises, forming a *brown* precipitate of MnO_2.
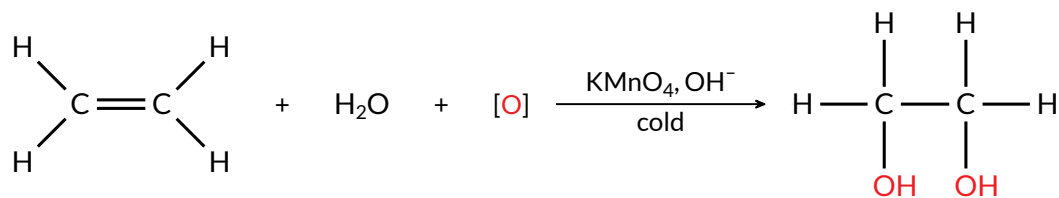
6.4   Strong Oxidation (Oxidative Cleavage)
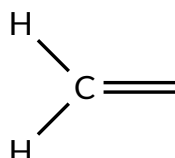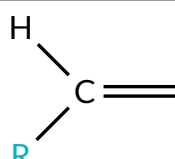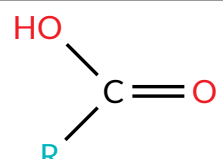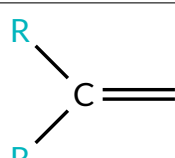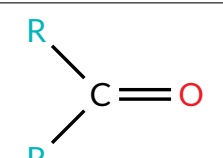
When the $KMnO_4$ solution containing an alkene is heated, *strong oxidation* will take place. The double bond is *cleaved* instead of added to, and each side of the double bond forms its own fragment. In the case of cycloalkenes however, the end product might still only be one molecule.

Furthermore, only a strong oxidising agent like MnO_4^- can be used. The difference between mild and strong oxidation also depends *only* on the temperature of the reacting solution. Only heated solutions will result in oxidative cleavage.

Conditions: $KMnO_4$, dilute H_2SO_4, heat.
Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+}.

Depending on the number of substituents (or inversely, the number of hydrogen atoms) attached to the carbon with the double bond, there are 3 possible products. Again, a table is the best way to present this, unfortunately.

Substituents	Structure	Product
0		$CO_2 + H_2O$
1		
2		

6.4.1 Further Oxidation of Ethanedioic Acid

The sole special case that must be noted is that if the oxidative cleavage results in the formation of ethanedioic acid ($C_2H_2O_4$), it is further oxidised to form $2\,CO_2$ and H_2O.

Ethandioic acid, or oxalic acid.
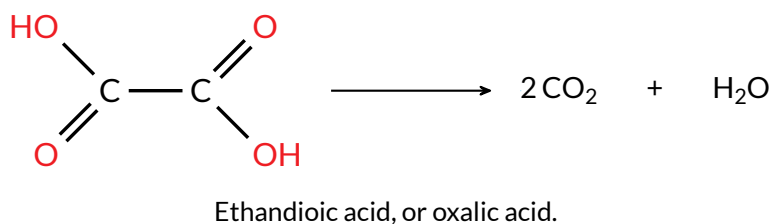
6.4.2 Uses of Oxidative Cleavage

Oxidative cleavage can be used to determine the position of the double bond in carbon chains and cycloalkenes, given the products (fragments) of the cleavage reaction.

Most importantly, if CO_2 is one of the products (gas evolved), then there are 2 possibilities — either the original molecule has a terminal C=C double bond, or the cleavage involved the formation of ethanedioic acid that further decomposed to form CO_2.

PART VII

Arenes

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1 Benzene

Benzene is simplest possible aromatic compound, or arene. The first known and isolated arene compounds had pleasant smells, such as benzaldehyde. Unfortunately, even though most known arenes now smell terrible and are carcinogenic, the name stuck.
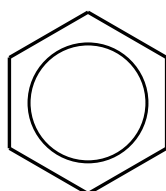
The structural representation of benzene.

The most common form of arene is the benzene ring, or phenyl functional group. Note that aromatic rings with other configurations and structures can also form, such as with nitrogen.

Its basic structure consists of 6 carbon atoms, arranged in a hexagonal fashion. However, unlike cyclohexane, benzene is a flat, planar molecule. All 6 carbon atoms are sp^2 hybridised, forming the following structure:
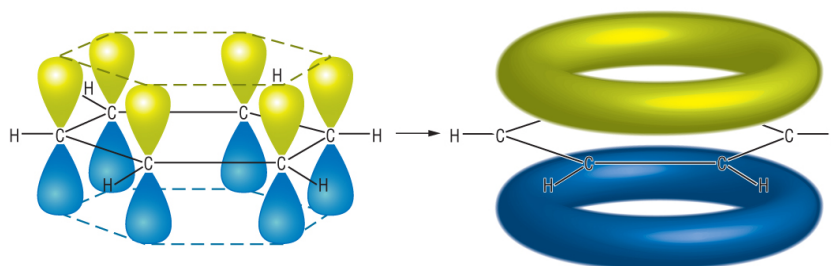
The trigonal structure of the sp^2 hybrid orbitals dictates this structure, since the angle between each orbital is 120°, which is the internal angle of a regular hexagon. Note that there is one H atom bonded to each carbon, making the molecular formula of benzene C_6H_6.

The carbon atoms are bonded to each other through π-bonds with their unhybridised p-orbitals, while the bonds with the hydrogen atoms (or other substituents if substituted) are done with the sp^2 orbitals.

Furthermore, the 6 π-bond electrons are delocalised, and move freely within the ring. This increases the stability of the benzene ring, which increases the amount of energy needed to modify it by fiddling with bonds.

1.1 Physical Properties

Since benzene is a regular hexagon, each C=C bond is the same length. However, it shorter than a C−C bond, but longer than a C≡C bond.

Benzene is a volatile, flammable and carcinogenic. Don't drink it. Don't eat it. Don't touch it. It also happens to be colourless, with a distinct 'aromatic' odour.

As a non-polar molecule, it has relatively low melting and boiling points (5.5 °C and 80.1 °C), as well as low solubility in water. Of course, it is soluble in non-polar solvents, and in fact can be used as a solvent in its own right.

2 Substituted Benzenes

The primary reaction mechanism of benzenes is electrophilic substitution, which involves the electrophiles attacking the electron-rich π-system of the benzene ring. As mentioned in Chapter 4 on Induction and Resonance, certain groups and atoms have the ability to withdraw or donate electrons, which affects the characteristics of the benzene ring.

2.1 Effect of Reactivity

If a benzene has electron-donating substituents, (such as CH_3) it will be more reactive, since it would increase the electron density of the π-system, making it a more appealing target for electrophiles. Thus, the ring is said to be *activated*. Conversely, electron-withdrawing substituents (such as $-NO_2$ or $-CO_2H$) *deactivate* the benzene, which decreases the reactivity of the benzene ring by making it less susceptible to electrophilic attacks.

Importantly, it *must be noted* that for the nitration of benzene, when the benzene ring is *activated*, the required temperature for reaction is only *30 °C*, whereas for *deactivated* rings, the required temperature is *above 50 °C*.

2.2 Effect on Positions of Further Substituents

Since the main way substituents affect the benzene ring is through the distortion of its π-system electrons, naturally this distortion can affect the positions of additional substituents on the ring.

For instance, an electrophilic substitution, of an electrophile R on methylbenzene can produce 3 possible products:

2-directed	4-directed	3-directed
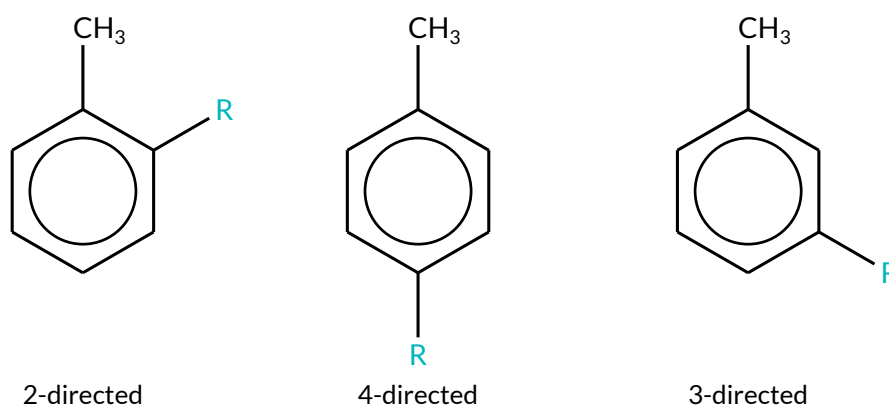
In this case, the CH_3 is considered to be attached to carbon 1.

The exact reasoning for this directing behaviour is complex, and has to deal with the resonance structures of the intermediate benzene, and the distribution of electrons within the π-system. Furthermore, there are only two types of substituents: *2,4-directing* and *3-directing*. Also note that this is similar in concept to major and minor products; both will be produced, except one in much larger quantities.

The directing effects of various groups are summarised below.

Substituent	Electron Effect	Directing Effect
Alkyl/aryl groups (eg. $-CH_3$)	Weakly Activating	2,4-directing
$-OH, -NH_2, -OCH_3$	Strongly Activating	2,4-directing
$-Cl, -Br$	Weakly Deactivating	2,4-directing
$-CHO, -NO_2, -CN, -CO_2H$	Strongly Deactivating	3-directing

For a quick-and-easy way to remember which groups are withdrawing and which are donating, electronegative atoms (O, N, halogens, etc.) are electron withdrawing (deactivating) when they are indirectly attached to the benzene ring, but are generally electron donating (activating) when directly attached to the benzene ring.

This can be explained by the fact that, when directly attached, there is the possibility of a p-orbital overlap with the π-electron cloud of the benzene, thus allowing for the electron density to be added to the benzene ring.

Conversely, when indirectly attached, the effect of electronegativity generally *pulls* the electron density through the -bonds. For example, even though N can have its p-orbital overlap with the π-electron cloud, $-NO_2$ substituents are still strongly deactivating, as the two highly electronegative O atoms can still act to retract electron density away from the benzene ring, *through* the N atom.

2.3   Directing Mechanism

The exact mechanism behind the directing effects of substituents can be explored through the resonance structure of the substituted ring. Technically, the 2, 3, and 4 positions are called *ortho*, *meta*, and *para* respectively. It's just a naming thing.

2.3.1 Electron-withdrawing Groups

Taking nitrobenzene as an example, the attached NO_2 group is electron-withdrawing. As such, based on the resonance structure of the π-system below, there will be three points with a partial positive charge (δ^+). Since the substitution requires the attack of an *electrophile*, these positions are *less favourable*. Hence, the electrophile will tend to target the meta (or 3-directed) position, and the NO_2 group is said to be meta-directing, or 3-directing.
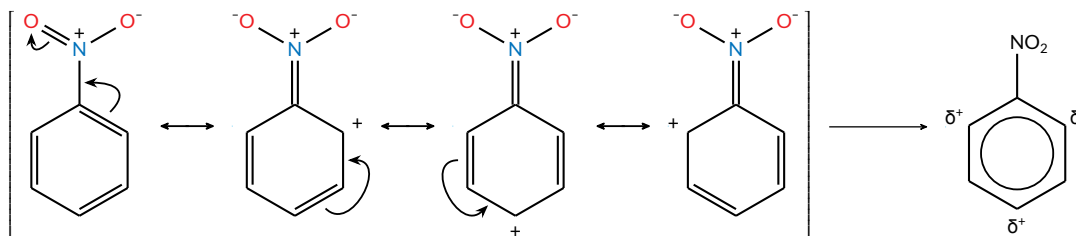
The δ^+ positions represent areas of low electron density.

2.3.2 Electron-donating Groups

On the other hand, for an electron-donating group such as NH_2, the reverse is true; there will be 3 areas of *high electron density* (actually the same 3 positions), which *attracts* electrophiles, and as such favours substituting further groups on the ortho/para positions, or 2,4 positions. Thus, NH_2 is said to be ortho/para-directing, or 2,4-directing.
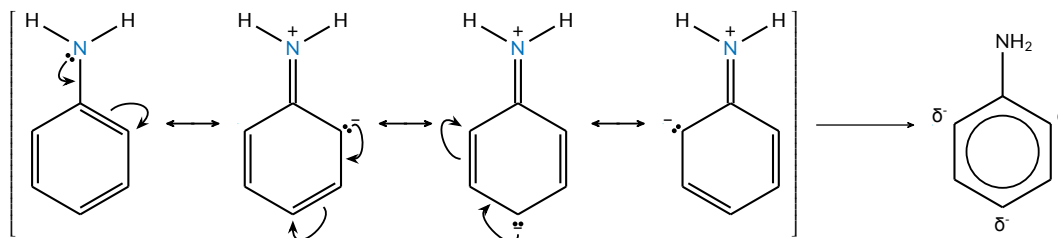
The δ^- positions represent areas of high electron density.

2.3.3 Halogen Substituents

Halogens are a special case, since they can donate electrons through resonance, but can also withdraw electrons through the induction effect due to their substantial electronegativity difference, compared to carbon.

The overall effect is that halogens are *ortho/para* (2,4) directors, and they are weakly electron-withdrawing.

3 Arene Reactions

Benzene undergoes substitution reactions rather than addition reactions, since adding atoms to the ring would destroy the delocalised π-system of the ring, which is energetically unfavourable. Instead, the H atoms on the ring are substituted.

The main mechanism for this is electrophilic substitution, the details of which can be found in *the appendix*.

3.1 Nitration of Benzene

The nitration of benzene involves the substitution of one of the H atoms on the benzene with a nitro ($-NO_2$) group. It has a number of specific requirements:

Conditions: Concentrated HNO_3, concentrated H_2SO_4 catalyst.
                        Constant temperature of $50\,°C$.

Observations: *Pale yellow* oily liquid, nitrobenzene.
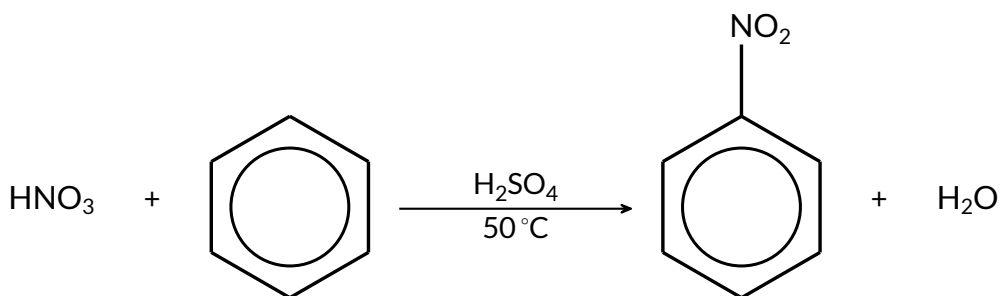
3.2 Halogenation of Benzene

Halogenation of benzene requires rather specific conditions, such as anhydrous $FeBr_3$ or $FeCl_2$ (for a reaction with bromine and chlorine respectively), and a warm environment.

Aluminium-based analogues of these catalysts ($AlBr_3$, $AlCl_3$) can also be used, as can pure filings of the metal, in which case the catalyst will be generated *in-situ* ($2 Fe_{(s)} + 3 Br_{2 (l)} \rightarrow 2 FeBr_3$).

The in-depth explanation about the need for an anhydrous catalyst can be found *here*.

Conditions: Warm, anhydrous $FeBr_3$, $AlBr_3$, or Fe / Al filings (for bromine),
Anhydrous $FeCl_3$, $AlCl_3$, or Fe / Al filings (for chlorine)

Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
Formation of white fumes of HX gas.
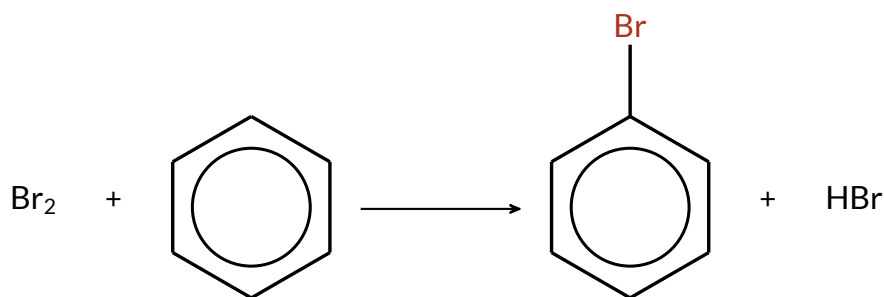
3.3 Alkylbenzene Reactions

3.3.1 Halogenation

The reagents and conditions for the halogenation of alkylbenzenes is similar to that of normal, unsubstituted benzenes. This time, however, there are two major products, and one minor product, due to the 2,4-directing nature of alkyl groups.

The conditions here are basically the same as that for normal benzene.

Conditions: Warm, anhydrous $FeBr_3$, $AlBr_3$, or Fe / Al filings (for bromine),
Anhydrous $FeCl_3$, $AlCl_3$, or Fe / Al filings (for chlorine)

Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
Formation of white fumes of HX gas.
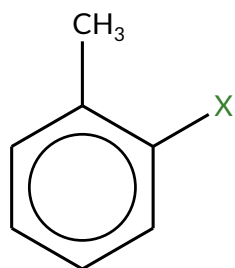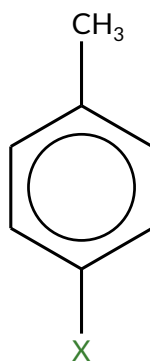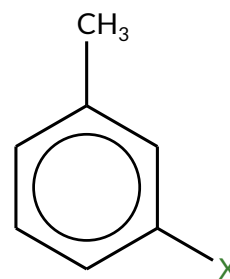
2-directed, *ortho* (major)   4-directed, *para* (major)   3-directed, *meta* (minor)

3.3.2 Nitration

Similarly, the nitration of alkylbenzenes also gives two major products, and one minor product. Note that the required temperature is lower, due to the activating effect of the CH_3 substituent.

Conditions: Concentrated HNO_3, concentrated H_2SO_4 catalyst.
Constant temperature of 30 °C.

Observations: *Pale yellow* oily liquid, nitrobenzene.
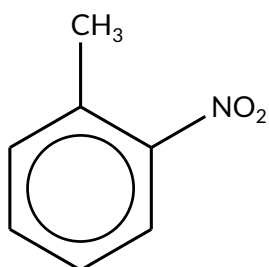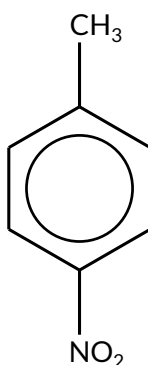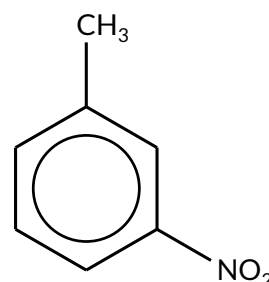
| 2-directed, *ortho* (major) | 4-directed, *para* (major) | 3-directed, *meta* (minor) |

3.3.3 Free Radical Substitution

In the absence of Lewis-acid catalysts, halogens will not react with the benzene ring. In this case, the halogens will react with the side-chain of the alkylbenzene, with UV light.

Conditions: UV Light, Br_2 / Cl_2 gas
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
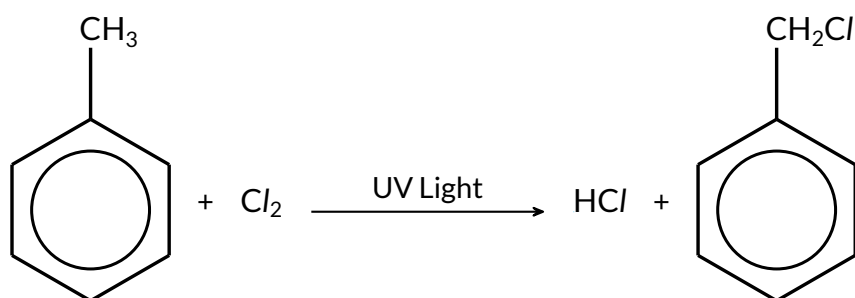
Naturally, the alkyl side-chain can also undergo multiple substitutions.

3.3.4 Side-chain Oxidation

When reacted with the strong oxidising agent, $KMnO_4$, and heated, the alkyl chain attached to the benzene will be oxidised. Regardless of the length of the chain, benzoic acid is always formed.

Note that the carbon attached to the benzene ring *must* have *at least 1* hydrogen atom (ie. it cannot be a teritary carbon) for this oxidation to occur.

Conditions: Heat, $KMnO_4$, dilute acid or alkali.

Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+} (*acid*), or
forms *brown* precipitate of MnO_2 (*alkali*).
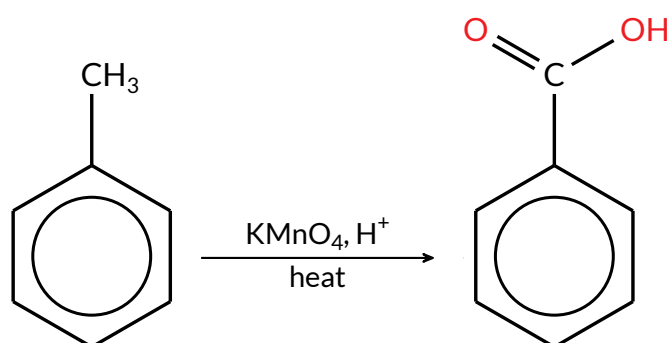
In this case, an acidic medium is used, hence H^+.

Alternatively, an alkali medium can be used, for instance with NaOH (aq). Instead of forming benzoic acid however, the benzoate ion is formed, which would form an ionic bond with Na.
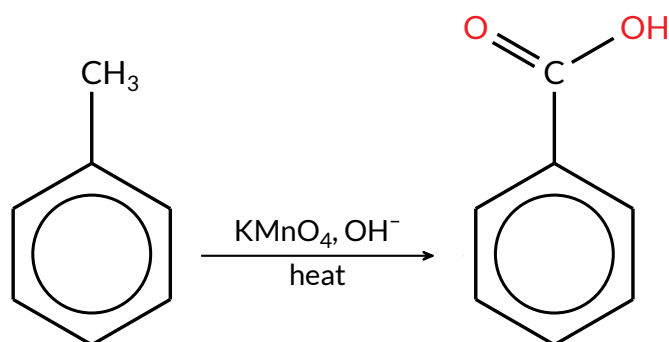
If the alkyl chain is 2-long, (ie. ethylbenzene), then CO_2 will be formed from the oxidation of the second carbon, in addition to benzoic acid.
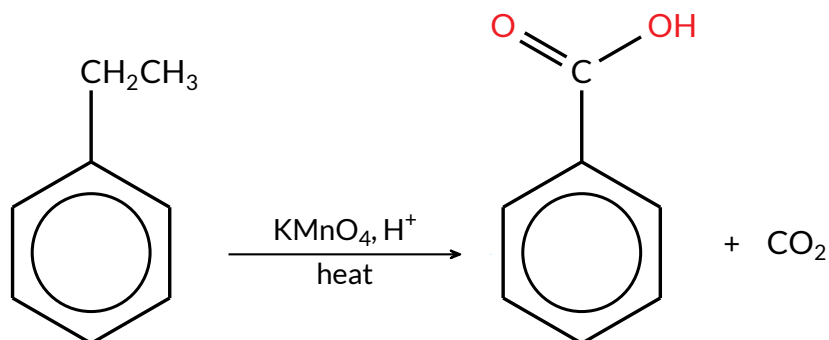
If the chain is 3 or longer, then the rest of the chain (apart from the first) will be oxidised to form a carboxylic acid.

<div align="right">
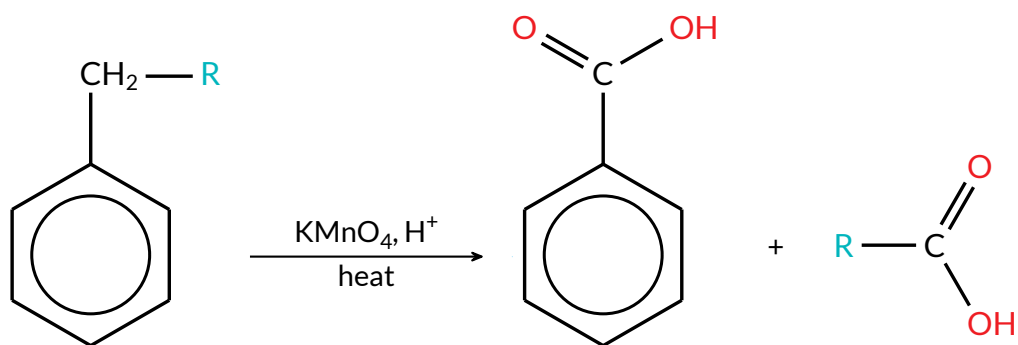
PART VIII

</div>

Halogen Derivatives

1   Halogenoalkanes (Alkyl Halides)

Halogenoalkanes are simply alkanes, with one or more halogen atoms taking the place of a hydrogen atom. They are classified in a similar way to alkanes and alcohols, and methane-based molecules are classified as primary halogenoalkanes.
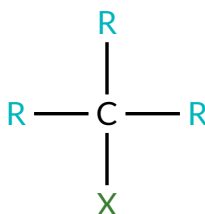
The general structure of an alkyl halide.

1.1   Physical Properties

Melting and Boiling Points

Compared to their alkane counterparts, halogenoalkanes have a higher boiling point for the same carbon chain length. The primary method of intermolecular bonding is still via instantaneous dipole-induced dipole interactions, which is strengthened by the larger electron cloud due to the halogen.

However, permanent-dipole interactions are still present, and contribute slightly to the increase in melting and boiling points. This is of more significance for chloroalkanes, since Cl is more negative than both Br and I, hence creating a larger dipole moment.

When comparing between different halogens with otherwise identical carbon chains, the melting and boiling points increases as the halogen atom's size increases — the instantaneous dipole-induced dipole interaction plays a larger role in determining that.

Solubility

The solubility of alkyl halides are pretty much the same as for regular alkanes.

2 Halogenoarenes

Halogenoarenes are simply molecules where the halogen atom is *directly attached* to the benzene ring.
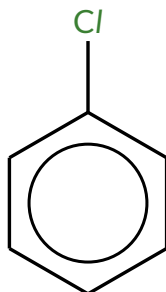
Chlorobenzene is a halogenoarene.

3 Creation of Halogenated Molecules

3.1 Free Radical Substitution

As covered above, alkanes can undergo free radical substitution, replacing one or more of their hydrogen atoms with halogen atoms.

Conditions: UV Light, Br_2 / Cl_2 gas
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.

$$R \!-\! CH_3 \ + \ X_2 \longrightarrow HX \ + \ R \!-\! CH_2X$$
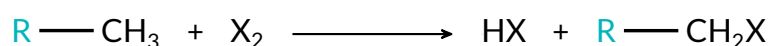
However, this is usually a *bad* way to prepare halogenoalkanes, due to the mix of products that will be formed, including isomers and multisubstituted molecules. It is difficult (or nigh impossible) to control the extent or position of substitution, but to decreases the chances of multisubstitution, the alkane should be used in excess, as a last resort.

3.2   Electrophilic Addition to Alkenes

3.2.1 Addition of X_2

Halogen molecules (X_2) can be added to alkenes to form halogenoalkanes, as covered above. Naturally, this results in having two halogen atoms in the molecule, or a *dihalide*.

Conditions: No UV Light, gaseous X_2.
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
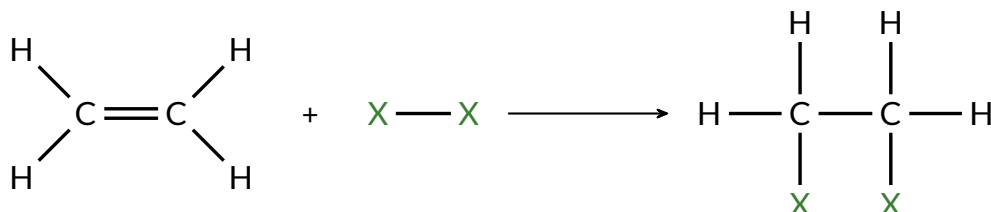
3.2.2 Addition of HX

Gaseous HX can also be added, resulting in a monohalogenated molecule.

Conditions: Gaseous HX (usually HC*l* or HBr).
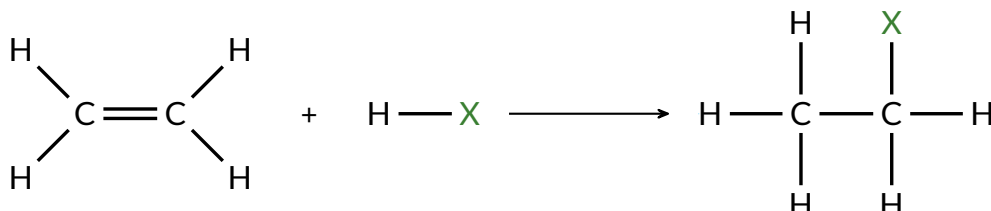
3.3 Nucleophilic Substitution of OH groups (Chlorine)

3.3.1 Phosphorous Pentachloride (PCl_5)

Conditions: Solid PCl_5, room temperature.
Observations: Formation of white fumes of HCl gas.

$$R-OH \ + \ PCl_5 \ \longrightarrow \ R-Cl \ + \ POCl_3 \ + \ HCl$$

3.3.2 Phosphorous Trichloride (PCl_3)

Conditions: Solid PCl_3, room temperature.

$$3\,R-OH \ + \ PCl_3 \ \longrightarrow \ 3\,R-Cl \ + \ H_3PO_3$$
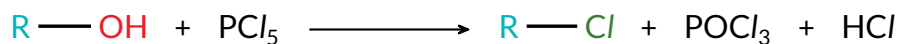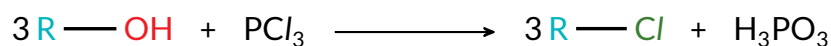
3.3.3 Thionyl Chloride ($SOCl_2$)

This reaction is slightly preferred over the others, since both by-products (SO_2 and HCl) are gaseous, and would bubble out of the solution, leaving mainly the halogenoalkane in the reaction mixture.

Conditions: Warm, liquid $SOCl_2$.

Observations: Formation of colourless, pungent SO_2 gas, white fumes of HCl gas.

$$R-OH \ + \ SOCl_2 \ \longrightarrow \ R-Cl \ + \ SO_2 \ + \ HCl$$

3.3.4 Hydrogen Chloride (HC*l*)

Here, a distinction must be made between *primary*, *secondary*, and *tertiary* alcohols; tertiary alcohols will react fine with simply concentrated HC*l*.

Conditions: Concentrated HC*l* (aq) / gaseous HC*l*, *OR*
Solid NaC*l*, concentrated H_2SO_4, heat.

$$R \!-\! OH \;+\; HCl \longrightarrow R \!-\! Cl \;+\; H_2O$$
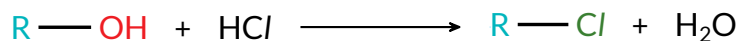
HC*l* can be prepared *in-situ* with NaC*l* and H_2SO_4.

For primary and secondary alcohols, anhydrous $ZnCl_2$ catalyst must be used, and the reaction mixture must be heated. Apart from that, the reaction is similar.

Conditions: Concentrated HC*l* (aq) / gaseous HC*l*.
Anhydrous $ZnCl_2$ catalyst, heat.

$$R \!-\! OH \;+\; HCl \longrightarrow R \!-\! Cl \;+\; H_2O$$
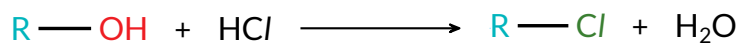
3.4 Nucleophilic Substitution of OH groups (Bromine)

3.4.1 Hydrogen Bromide (HBr)

Gaseous hydrogen bromide (HBr) can be reacted with alcohols to give bromoalkanes.

Conditions: Gaseous HBr.

$$R - OH \ + \ HBr \ \longrightarrow \ R - Br \ + \ H_2O$$
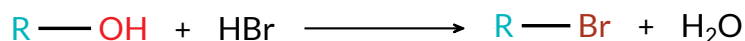
HBr can be prepared by reacting concentrated H_2SO_4 with solid NaBr.

Conditions: Solid NaBr, concentrated H_2SO_4, heat.

$$NaBr \ + \ H_2SO_4 \ \longrightarrow \ HBr \ + \ NaHSO_4$$
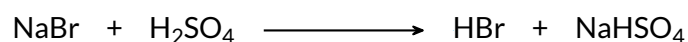
3.4.2 Phosphorous Tribromide (PBr$_3$)

PBr$_3$ is typically prepared *in-situ* by heating red phosphorous with liquid bromine. It then proceeds to react with the alcohol, in a manner similar to that of PCl_3.

Conditions: Liquid PBr$_3$, *OR*
                      Liquid Br$_2$, red phosphorous, heat.

$$2\,P \ + \ 3\,Br_2 \ \longrightarrow \ 2\,PBr_3$$
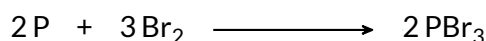
In-situ formation of PBr$_3$.

$$3\,R - OH \ + \ PBr_3 \ \longrightarrow \ 3\,R - Br \ + \ H_3PO_3$$
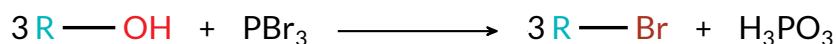
3.5   Nucleophilic Substitution of OH groups (Iodine)

3.5.1 Phosphorous Triiodide (PI$_3$)

This reaction is identical to the reaction involving PBr$_3$, above.

Conditions: Liquid PI$_3$, *OR*
                       Solid I$_2$, red phosphorous, heat.

$$2\,P \;+\; 3\,I_2 \longrightarrow 2\,PI_3$$
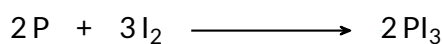
In-situ formation of PI$_3$.

$$3\,R—OH \;+\; PI_3 \longrightarrow 3\,R—I \;+\; H_3PO_3$$
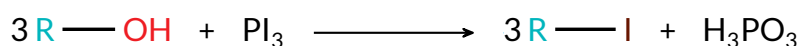
3.6   Electrophilic Substitution of Arenes

Halogens can be substituted onto a benzene ring through the use of a catalyst, in an electrophilic substitution reaction.

Conditions: Warm, anhydrous FeBr$_3$, A*l*Br$_3$, or Fe / A*l* filings (for bromine),
                       Anhydrous FeC*l*$_3$, A*l*C*l*$_3$, or Fe / A*l* filings (for chlorine)

Observations: *Reddish-brown* Br$_2$ / *yellowish-green* C*l*$_2$ decolourises.
                       Formation of white fumes of HX gas.
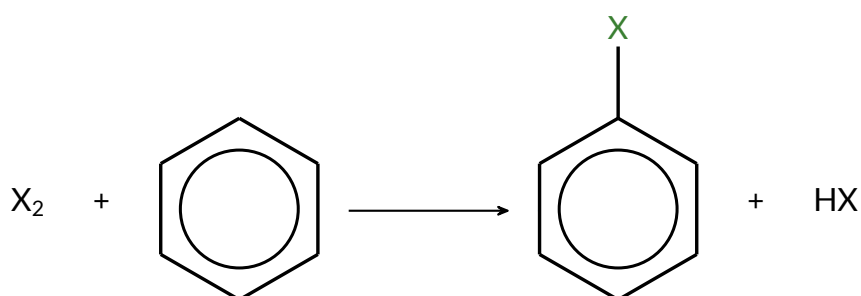
4 Halogenoalkane Reactions

4.1 Nucleophilic Substitution

Due to the high relatively electronegativity of the halogen atom attached to the carbon atom, the carbon atom is *electron-deficient*, which makes it more susceptible to attacks from nucleophiles (*electron-rich*), and as such halogenoalkanes are fairly reactive.

The full mechanism of this reaction can be found in *the appendix*.

4.1.1 Formation of Alcohols

The OH^- ion acts as a nucleophile, substituting the attached halogen atom.

Conditions: Aqueous NaOH or KOH, heat.

$$R - X \ + \ OH^- \longrightarrow R - OH \ + \ X^-$$
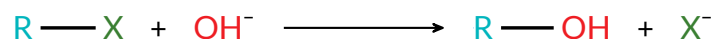
4.1.2 Formation of Amines

This reaction forms a primary amine. Ethanolic NH_3 is simply a solution of NH_3 in ethanol. Also, the reaction mixture must be heated in a sealed tube, to prevent the NH_3 from escaping.

Conditions: Ethanolic concentrated NH_3, heat in sealed tube.

$$R - X \ + \ NH_3 \longrightarrow R - NH_2 \ + \ HX$$
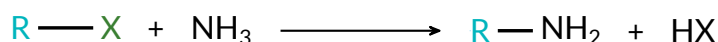
However, this amine turns out to be a *stronger* nucleophile than NH_3, due to the electron-donating alkyl groups, which opens the possibility for multiply-substituted amines, forming secondary amines, tertiary amines, and even quaternary ammonium salts.

$$RX \ + \ RNH_2 \longrightarrow R_2NH \ + \ HX$$
$$RX \ + \ R_2NH \longrightarrow R_3N \ + \ HX$$
$$RX \ + \ R_3N \longrightarrow R_4N^+X^-$$
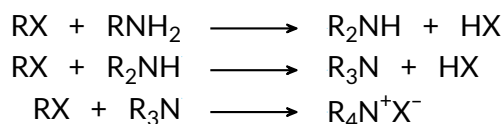
Thus, to prevent this from happening, NH_3 should be used in excess, in essence 'crowding-out' the amines formed from reacting further.

4.1.3 Formation of Nitriles

In this reaction, the lone pair is donated not by the nitrogen atom, but by the *carbon* atom. This reaction is important, as it serves to increase the length of the carbon chain, forming a cyanohydrin — a *step-up* reaction — which is useful in the synthesis of organic molecules.

Conditions: Ethanolic KCN, heat.

$$R - X \ + \ CN^- \longrightarrow R - CN \ + \ X^-$$
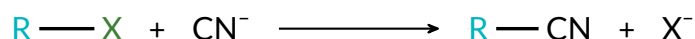
Indeed, the nitrile that is formed can be hydrolysed to form carboxylic acids.

Conditions: Dilute H_2SO_4 or HC*l*, heat, *OR*
Dilute NaOH, heat.

$$R - C \equiv N \ \xrightarrow[\text{heat with reflux}]{\text{dil. } H_2SO_4} \ R - C \underset{OH}{\overset{O}{\diagup}}$$
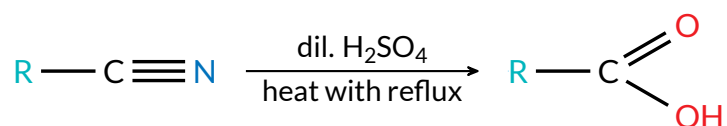
If NaOH is used instead of H_2SO_4, a carboxylate salt is formed instead.

$$R - C \equiv N \ \xrightarrow[\text{heat with reflux}]{\text{dil. NaOH}} \ R - C \underset{O^-Na^+}{\overset{O}{\diagup}}$$
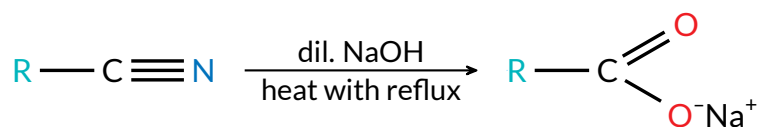
Furthermore, it can also be reduced to form amines, either through the very strong reducing agent LiA*l*H$_4$ (dissolved in dry, diethyl ether due to its high reactivity with water), the slightly weaker NaBrH$_4$ dissolved in methanol, or the traditional, copious application of H_2 gas with a metal catalyst at high temperatures and pressures.

Conditions: LiA*l*H$_4$ in dry ether (diethyl ether), *OR*
H_2 (g), Ni catalyst, high temperature and pressure.

$$R - C \equiv N \ \xrightarrow[\text{[H]}]{\text{reduction}} \ R - \underset{H}{\overset{H}{\underset{|}{\overset{|}{C}}}} - N \underset{H}{\overset{H}{<}}$$
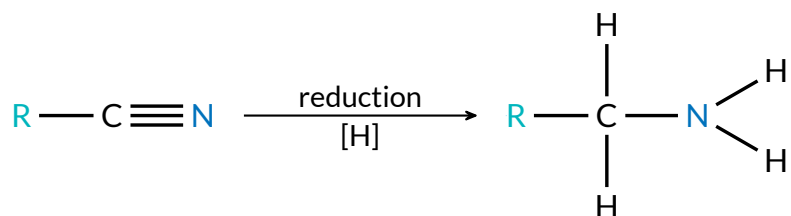
4.2 Elimination

OH^- behaves as a Brønsted-Lowry base, accepting, or in this case removing, an H^+ ion from the halogenoalkane. At the same time that this $C-H$ bond breaks, the $C-X$ bond in the adjacent carbon atom breaks, thus forming HX, and an alkene.

Conditions: Ethanolic KOH or NaOH, heat.
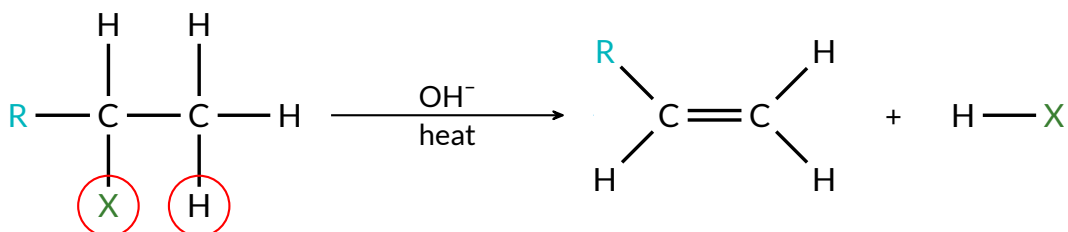
The alkane can be of any length, the important bit happens here. The circled atoms are the ones forming the HX molecule.

Naturally, isomerism, either optical or cis/trans (E/Z), may occur, and a mix of products can be formed.

One might notice that these reaction conditions are similar to that for the nucleophilic substitution of alcohols. Indeed, both reactions will occur at the same time, forming both alcohols and alkenes.

To favour one reaction over the other, there are a number of factors that can be controlled

- Type of halogenoalkane (primary, secondary or tertiary)
- Temperature of reaction mixture
- Concentration of KOH or NaOH
- Solvent used (ethanol or water)

Primary alkyl halides tend to mainly favour nucleophilic substitution, while tertiary alkyl halides tend to favour the elimination reaction — secondary alkyl halides favour either reaction.

Furthermore, the higher the temperature of the mixture, the more likely it is that the elimination reaction will take place. A higher concentration of NaOH or KOH will also increase the likelihood of the elimination reaction occurring. Finally, using ethanol as a solvent for the hydroxide, versus water, will also favour elimination.

5 Halogenoarene Reactions

Since the halogen atom is directly bonded to the benzene ring, its p-orbitals overlap in a parallel manner to the π-system of the benzene ring, and thus get delocalised.

This makes the bond stronger than a typical $C-X$ bond, and also reduces the effect of the electronegativity of the halogen atom. Thus, it is less susceptible to nucleophile attacks, and is fairly unreactive. The high electron density also tends to repel the electron-rich nucleophiles.

5.1 Electrophilic Substitution

Of course, being attached to a benzene ring, halogenoarenes can undergo electrophilic substitution — this is really a reaction of the benzene ring, not specific to the halogen.

However, it must be noted that since halogens are deactivating, the conditions for some reactions become slightly harsher; nitration would require temperatures *above* 50 °C. Also, it is *ortho/para*, or 2,4-directing.

The two kinds electrophilic substitution reactions that the benzene ring can undergo can be found in the *relevant chapter*.

6 Distinguishing Tests

6.1 Comparing Colour of Precipitate

The primary means of determining the identity of the attached halogen is by looking at the colour of the precipitate formed, when reacted with $AgNO_3$ — silver halides are insoluble.

1. Aqueous NaOH or KOH is added with heat, to substitute the halogen with an OH^- group, forming the X^- ion.
2. Excess, dilute HNO_3 is added to neutralise unreacted OH^-.
3. Aqueous $AgNO_3$ is added, to form the AgX precipitate.

Conditions: Aqueous NaOH or KOH, dilute HNO_3, aqueous $AgNO_3$.

Observations: Chlorine   White precipitate of Ag*Cl*.
Bromine   Cream precipitate of AgBr.
Iodine   Yellow precipitate of AgI.

6.2 Comparing Rate of Formation of Precipitate

The steps are identical to that above, but instead of comparing the colour, the rate of formation is measured instead. Since the rate-determining step in nucleophilic substitution involves breaking the $C-X$ bond, the weaker this bond, the faster the precipitate will form.

Hence, iodoalkanes will form the precipitate the fastest, followed by bromoalkanes, and finally chloroalkanes.

7 Chlorofluorocarbons (CFCs)

CFCs were commonly used as refrigerants and aerosol propellants, due to their inert, odourless, and non-toxic properties. Indeed, Teflon is a fluoroalkane, and is typically used to coat non-stick surfaces.

However, under the Montreal Protocol, the use of CFCs were banned due to their harmful effect on the ozone layer. Naturally, there is the following equilibrium in the ozone layer:

$$O + O_2 \rightleftharpoons O_3$$
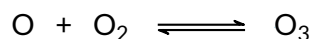
Also, in the presence of UV light in the stratosphere, the previously inert chlorofluorocarbons undergo photodecomposition.

$$CF_3Cl \xrightleftharpoons{uv} Cl\bullet + \bullet CF_3$$
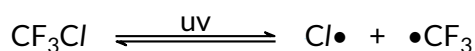
When the ozone equilibrium is exposed to these chlorine radicals, they are disrupted, since the radicals can act as a homogeneous catalyst, reforming afterwards.

$$Cl\bullet + O_3 \longrightarrow ClO\bullet + O_2$$
$$ClO\bullet + O \longrightarrow Cl\bullet + O_2$$
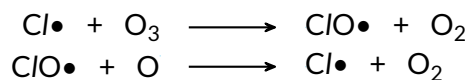
Thus, the ozone molecules are destroyed, and depletes the free oxygen atoms required in the formation of ozone.

PART IX

Alcohols

1 Aliphatic Alcohols

Aliphatic alcohols generally have the formula $R-OH$ — the OH group dictates the reactions of the alcohol. In a way they are basically carbon chains with one or more OH groups replacing a hydrogen atom. Indeed, they are classified similarly to halogenoalkanes in this respect:

Primary (1°)	Secondary (2°)	Tertiary (3°)
$\begin{array}{c} H \\ \vert \\ R-C-OH \\ \vert \\ H \end{array}$	$\begin{array}{c} R \\ \vert \\ R-C-OH \\ \vert \\ H \end{array}$	$\begin{array}{c} R \\ \vert \\ R-C-OH \\ \vert \\ R \end{array}$

Methanol, CH_3OH, is classified as a primary alcohol.

1.1 Physical Properties

Melting and Boiling Points

Compared to an alkane of a similar length, alcohols generally have much higher melting and boiling points. This is due to the formation of intermolecular hydrogen bonds (note that hydrogen bonds are a special kind of permanent dipole interaction), due to the difference in electronegativity in the O and H atoms. However, like other aliphatic carbon chains in general, instantaneous dipole-induced dipole (id-id) interactions are still present.

Solubility

Alcohols are also much more soluble in water and other polar solvents than alkanes, due again to their ability to form hydrogen bonds, this time resulting in favourable solvent-solute interactions that enable dissolution. They also retain their solubility in non-polar solvents due to the carbon backbone.

2 Phenols

Phenols are benzene rings with one or more OH groups directly bonded to the ring itself. They have markedly different properties from normal alcohols, and are covered in the *following chapter*.
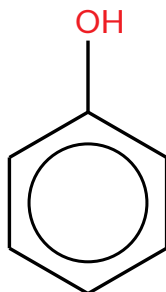
Phenol in all its glory.

3 Creation of Alcohols

Alcohols are versatile and crucial in organic synthesis, in that they can be transformed to and from a wide variety of other compounds and functional groups.

3.1 Electrophilic Addition (Hydration) of Alkenes

As previously mentioned, alkenes can undergo electrophilic addition with steam or water, forming a mono-alcohol.

Conditions: $300\,°C$, at 70 atm, H_3PO_4 catalyst, *OR*
Concentrated H_2SO_4, H_2O, warming.
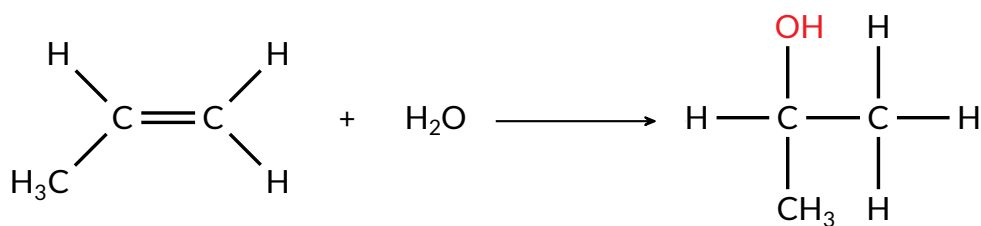
3.2 Nucleophilic Substitution of Halogenoalkanes

Alkyl halides can undergo nucleophilic substitution to create alcohols as well — the OH^- ion acts as the nucleophile here, attacking the partial-positively charged C atom attached to the halogen.

Conditions: Aqueous NaOH or KOH, heat.

$$R - X \ + \ OH^- \longrightarrow R - OH \ + \ X^-$$
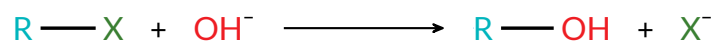
3.3 Reduction of Aldehydes and Ketones

Carbonyl compounds (covered *later*) can be reduced, forming either primary or secondary alcohols. Tertiary alcohols cannot be created through this method.

All 3 common reducing agents can be used.

Conditions: $LiAlH_4$ in dry ether (diethyl ether), *OR*
                         $NaBH_4$ in methanol, *OR*
                         $H_{2\ (g)}$, Ni catalyst, high temperature and pressure.
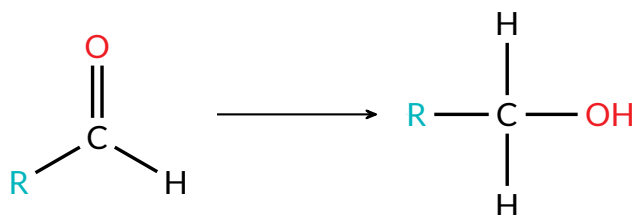
Aldehydes (above) are reduced to primary alcohols, while ketones (below) are reduced to secondary alcohols.
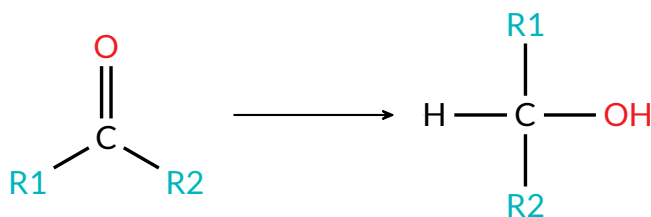
3.4 Reduction of Carboxylic Acids

Carboxylic acids, also covered *later*, can also be reduced, forming primary alcohols. This reduction requires a strong reducing agent, so only $LiAlH_4$ can be used. See the *appendix* for a list of reducing agents and their applicable uses.

Conditions: $LiAlH_4$ in dry ether (diethyl ether).
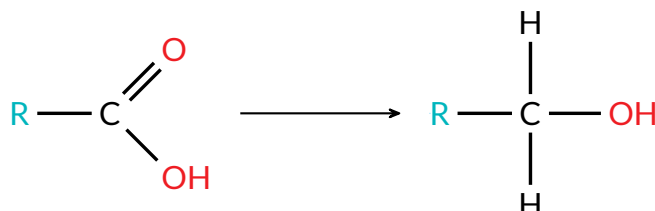
3.5 Hydrolysis of Esters

Finally, esters can be hydrolysed to form an alcohol as one of its products. Note that this hydrolysis is preferably conducted in an alkaline medium, since the reaction is slow and reversible in an acidic medium, but fast and irreversible under alkaline conditions. All that is required is a dilute acid to protonate the carboxylate salt after.

Conditions: Dilute H_2SO_4, heat under reflux, *OR*
Dilute NaOH, heat under reflux.
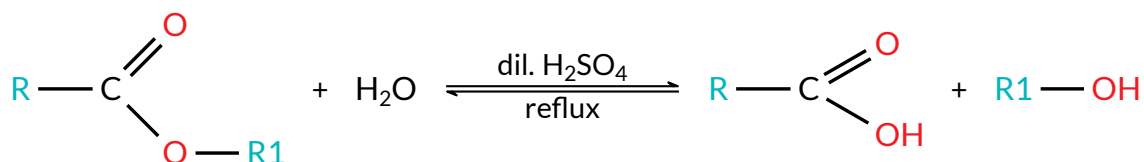
A carboxylic acid is also formed, but for our purposes the alcohol is the main product.
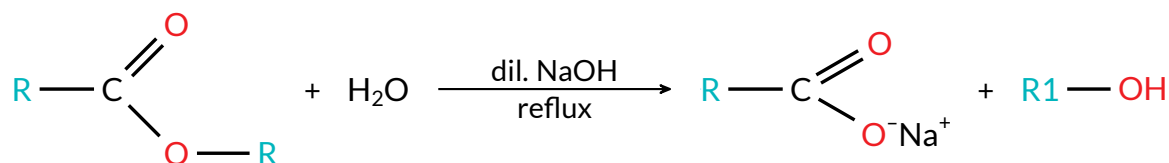
4 Alcohol Reactions

4.1 Acidity of Alcohols

Firstly, alcohols do have some weak acidic properties, as the OH group is able to allow H^+ to dissociate, albeit only slightly. This effect is so weak that alcohols react with neither bases (eg. NaOH) nor turn blue litmus paper red.

The H^+ ion dissociates to a smaller extent than water, due to the presence of electron-donating alkyl groups that are not present in water (water only has H atoms bonded to the oxygen). These alkyl groups *intensify* the negative charge on the alkoxide ion, destabilising it. Thus, the H^+ ion is unlikely to dissociate, as things like to remain stable.

4.1.1 Effect of Substituents

Substituents along the alcohol's carbon chain can have an effect on its acidity. Of course, groups closer to the OH itself (better yet, attached to the same carbon atom) have a greater effect. Note that the length of the alkyl group (or the carbon chain) of the alcohol does not have a significant impact on its acidity.

Electron withdrawing groups will *disperse* the negative charge on the alkoxide anion, thus resulting in a higher likelihood for the H^+ ion to dissociate, meaning a higher acidity (and thus higher K_a). Conversely, electron-donating groups (basically alkyl groups) *intensify* the negative charge, destabilising the anion and decreasing acidity.

Note that the classification of electron-donating/withdrawing groups is different from that of arenes, as the carbon attached to the alcohol is sp^3 hybridised. Refer to **this explanation** for an elaboration.

4.2   Reactions as an Acid

4.2.1 Reaction with Metals

In a manner similar to acids, alcohols can react with *reactive* metals to form ionic salts. However, these reactions will be slower than that of mineral acids or even carboxylic acids.

The $O-H$ bond is broken, and the H atom is replaced with the metal cation.

Conditions: Solid metal (eg. Na, K, etc.), room temperature.
Observations: Slow effervescence of H_2 gas.

$$2\,R\!-\!OH \ + \ 2\,Na_{(s)} \ \longrightarrow \ 2\,R\!-\!O^-Na^+ \ + \ H_{2\,(g)}$$
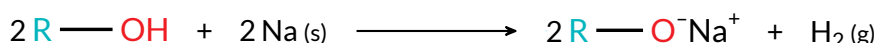
4.2.2 Reaction with Bases and Carbonates

Alcohols are far too weak of an acid to react react with carbonates (CO_3^{2-}) to form CO_2, and also do not react with bases (eg. NaOH) either.

4.3   Esterification (Nucleophilic Acyl Substitution)

4.3.1 With Carboxylic Acids

While this is more a property of carboxylic acids than alcohols, alcohols are still a main reagent, and so it is included here. These are condensation reactions, since H_2O or HCl is removed and the carbon chains joined.

There are two main methods of creating esters, one of which is vastly more effective than the other. But first, the ineffective method. Carboxylic acids and alcohols can react together in a slow and reversible reaction, with the use of heat and a catalytic dehydrating agent — a few drops of concentrated H_2SO_4 is often used.

An additional limitation of this method is that phenols cannot be used to esterify, as it is too weak a nucleophile to perform the necessary substitution of the OH on the carboxylic acid.

To note, the $C-O$ bond in the carboxylic acid is broken, while only the $O-H$ bond in the alcohol is broken.

Conditions: Carboxylic acid and alcohol,
                             Several drops of concentrated H_2SO_4, heated under reflux.
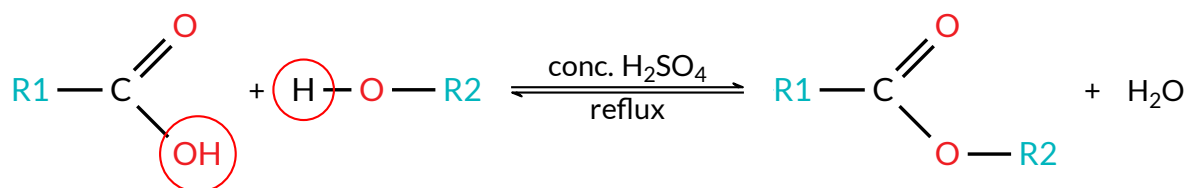
Note that it is the circled groups that form the water that is removed — this is important.

4.3.2 With Acyl Chlorides

Alternatively, acyl chlorides (which are themselves derivatives of carboxylic acids) can be used instead. This reaction is far superior, allowing for the esterification with phenols (which carboxylic acids cannot do).

It is also conducted at room temperature and is an irreversible reaction requiring no catalysts, due to the high reactivity of the acyl chloride.

Conditions: Acyl chloride and alcohol,
                         Room temperature.
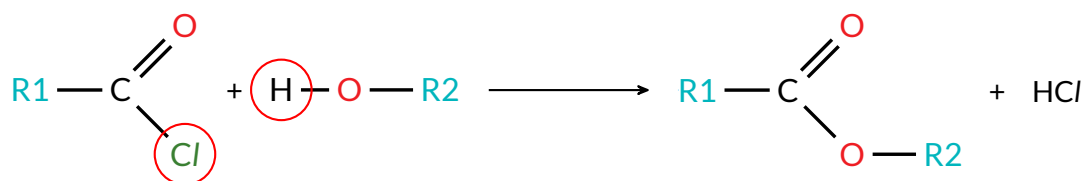
Again, note that it is the circled groups that form the water that is removed — this is important.

4.4 Nucleophilic Substitution with Halogens

Alcohols can undergo nucleophilic substitution, where the OH group is substituted by a halogen atom. However, this has been covered in a previous chapter, under the *formation of halogenoalkanes*, and will not be reproduced here for brevity.

(click the bolded bit, this PDF has links!)

4.5 Dehydration (Elimination of Water)

Alcohols can undergo dehydration, where an OH group combines with the H atom on a *neighbouring* carbon, forming water and an alkene, under the right conditions.

Conditions: Excess concentrated H_2SO_4, 170 °C, *OR*
                     Al_2O_3, heat.
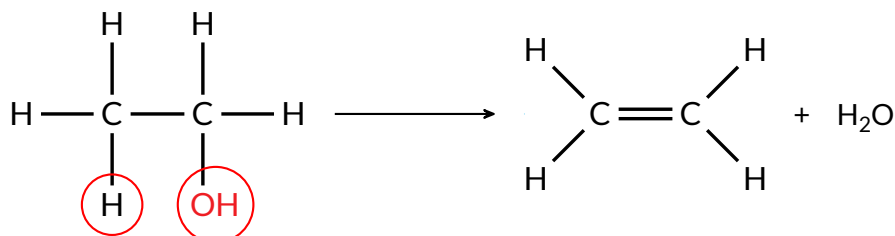
Note that it is the circled groups that form the water that is removed.

Naturally, this reaction cannot take place when there is no hydrogen atom on any adjacent carbon atom.

4.5.1 Zaitsev's Rule

It is obvious that in certain cases, there will be ambiguity regarding which hydrogen atom is removed together with the OH group. This is resolved with the Rule of Zaitsev, which states that the major product will be the alkene with more alkyl substituents on the double-bonded carbons.

For example:
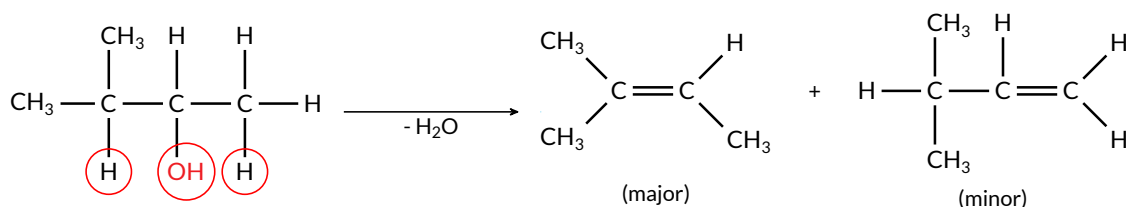
4.5.2 Elimination of Water in Gem-diols

Gem-diols, or carbons with two OH groups attached at once, will generally spontaneously eliminate H_2O to form a ketone or aldehyde. The reason for this reaction is generally understood to be the much higher stability of the resulting carbonyl.

Strongly electron-withdrawing substituents can result in the preference of the gem-diol, since the resulting carbonyl would be destabilised due to the very large partial-positive charge on the central carbon (with 2 or 3 electron-withdrawing groups).

In general however, water is eliminated.
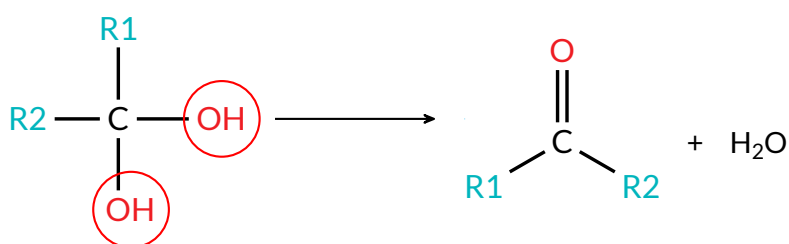
4.6   Combustion

Alcohols such as ethanol can be burned as fuel, reacting with oxygen in the air to form CO_2 and H_2O.

$$CH_3CH_2OH_{(l)} + 3O_{2(g)} \longrightarrow 2CO_{2(g)} + 3H_2O_{(l)}$$
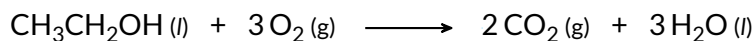
4.7   Oxidation of Primary Alcohols

Here again, a distinction must be made between primary, secondary and tertiary alcohols. For primary alcohols, there are two stages of oxidation — first to an aldehyde, then further oxidation to a carboxylic acid.

4.7.1 Controlled Oxidation to Aldehydes

The *controlled* part of this reaction lies in the immediate distillation of the aldehyde that is formed, using a fractionating column. Since aldehydes lack hydrogen bonding, they have a lower boiling point than their parent alcohol, and can be distilled away before they are further oxidised.

Note that, in this case, the *only* suitable oxidising agent is $Cr_2O_7^{2-}$, as the alternative, MnO_4^-, is too strong and will immediately oxidise the alcohol to a carboxylic acid. (note: this may be desired under some circumstances)

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4,
                heat with immediate distillation.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed).
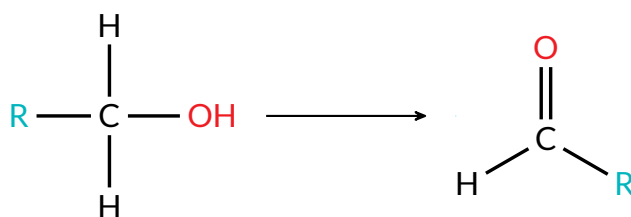
4.7.2 Complete Oxidation to Carboxylic Acids

When the aldehyde is not distilled immediately and instead left to interact with the remaining oxidising agent, it will be further oxidised to a carboxylic acid. Alternatively, the strong oxidising agent $KMnO_4$ can be used to immediately create a carboxylic acid.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR* *Purple* MnO_4^- decolourises (Mn^{2+} formed).
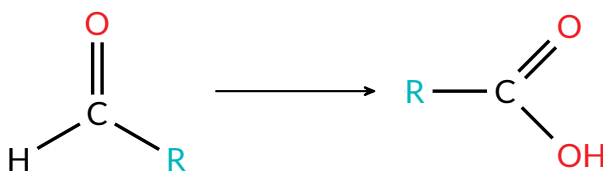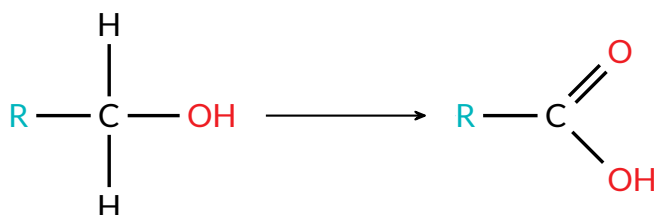
It is also possible to start with aldehydes, and oxidise them to carboxylic acids.

Note that, with $KMnO_4$, two special carboxylic acids can be *even further oxidised* to give CO_2 and H_2O; they are ethanedioic acid and methanoic acid.
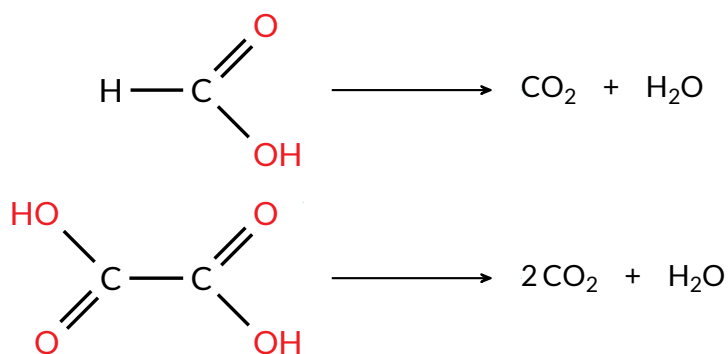
4.8 Oxidation of Secondary Alcohols

Unlike primary alcohols, secondary alcohols only have a single stage of oxidation, and thus either $K_2Cr_2O_7$ or $KMnO_4$ can be used. Secondary alcohols are oxidised to ketones, which cannot be further oxidised.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)
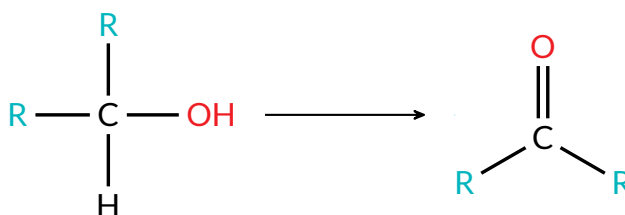
4.9 Oxidation of Tertiary Alcohols

This is really a pointless section, because tertiary alcohols cannot be oxidised under normal conditions. They do not have a hydrogen atom on the central carbon, thus preventing the addition of oxygen atoms.

4.10 Tri-iodomethane (Iodoform) Formation

This reaction is useful both in determining the structure of a given compound, and in reducing the length of the carbon chain by forming a carboxylate ion.

It can only occur in the presence of a specific arrangement of groups, which allows for the finger-printing of a compound. Note that this is actually a redox reaction, as the alcohol is oxidised and the iodine is reduced to I^-.

Conditions: I_2 (aq), NaOH (aq), warmed.
Observations: *Yellow* precipitate of CHI_3 is formed.
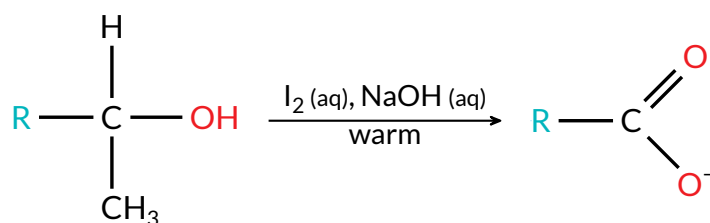
The group to the right of the R group is the necessary structure for a positive reaction.

Note that ethanol, where the R group is simply a hydrogen atom, is the only primary alcohol to have a reaction, since there will be no CH_3 group on any other primary alcohol.

Phenols

1 Structure

Phenols are basically benzene rings with an OH group substituted on the ring. However, their chemical behaviour is quite different from that of regular aliphatic alcohols — hence this separation of topic.
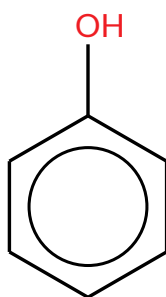
The structure of phenol.

1.1 Physical Properties

Melting and Boiling Points

Most phenols are solids at room temperature, due to the existence of hydrogen bonds facilitated by the OH group. As such, their melting points are much higher than simple benzene rings.

Solubility

Phenols are moderately soluble in water as compared to benzenes, due to their ability to form favourable solvent-solute interactions, which is again due to the hydrogen bonding provided by the OH group. This is despite the large hydrophobic benzene ring.

2   Phenol Reactions

2.1   Acidity of Phenols

Phenols are far more acidic than alcohols, due to the ability for the π-electron cloud of the benzene ring to delocalise the negative charge on the oxygen atom after H^+ dissociates. Thus, the conjugate base of phenol is much more stable than that of alcohols, and so the H^+ ion will be more likely to dissociate, increasing acidity.

2.1.1   Effect of Substituents

Similar to regular alcohols, electron-withdrawing substituents attached to the benzene ring can delocalise the negative charge of the phenoxide, increasing its stability and hence acidity.

Conversely, electron-donating groups (mainly through resonance) attached to the benzene ring have the opposite effect, intensifying the negative charge and further destabilising the phenoxide ion. Thus, acidity is reduced in this case.

2.2 Reactions as an Acid

While phenols can react with bases and metals, they are still too weak of an acid to react with carbonates.

2.2.1 Reaction with Metals

In a manner similar to acids and alcohols, phenols can react with *reactive* metals to form ionic salts.

The $O-H$ bond is broken, and the H atom is replaced with the metal cation.

Conditions: Solid metal (eg. Na, K, etc.), room temperature.
Observations: Slow effervescence of H_2 gas.

$$Na_{(s)} \quad + \quad \text{(phenol, OH)} \quad \longrightarrow \quad \text{(sodium phenoxide, } O^-Na^+\text{)} \quad + \quad \tfrac{1}{2}\,H_{2\,(g)}$$
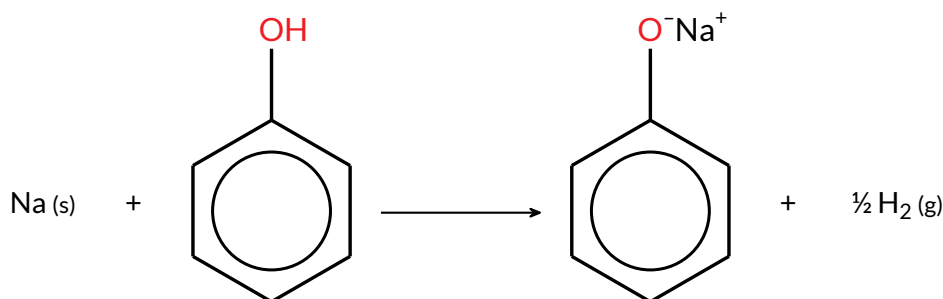
2.2.2 Reaction with Bases

Unlike alcohols, phenols are strong enough to react with bases, also forming ionic salts in a similar manner.

Conditions: Aqueous base (eg. NaOH, KOH, etc.), room temperature.
Observations: Phenol dissolves.

$$NaOH_{(aq)} \quad + \quad \text{(phenol, OH)} \quad \longrightarrow \quad \text{(sodium phenoxide, } O^-Na^+\text{)} \quad + \quad H_2O_{(g)}$$
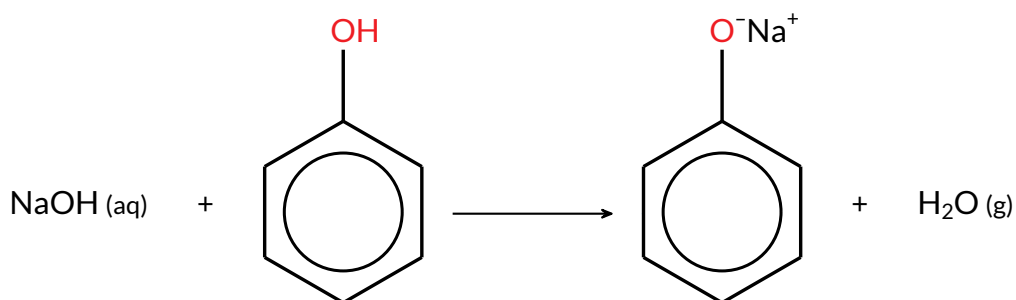
2.3 Oxidation

Another trick — the carbon atom attached to the OH group has no hydrogen atom, and so phenols *cannot* be oxidised.

2.4 Electrophilic Substitution

Phenols can undergo electrophilic substitution on the other, non OH-substituted positions. This is more a characteristic of the underlying benzene ring than it is of the OH group, however.

Still, the OH group is electron-donating via the resonance effect (due to the overlap of the p-orbital of the O atom with the π-electron cloud of the benzene ring), and as such is an *activating* substituent. Thus, the electron density in the ring is increased, and it undergoes electrophilic substitution reactions with greater ease.

Note that the OH group is *ortho/para*, or 2,4-directing.

2.4.1 Halogenation

Due to the activating nature of the OH group, it facilitate electrophilic substitution of hydrogens on the benzene ring without the use of a catalyst (eg. anhydrous $FeBr_3$ like for normal benzene), and at room temperature as well.

Conditions: Br_2 (aq) / Cl_2 (aq), room temperature.

Observations: *Yellow* Br_2 (aq) / *pale yellow* Cl_2 (aq) decolourises, white precipitate is formed.
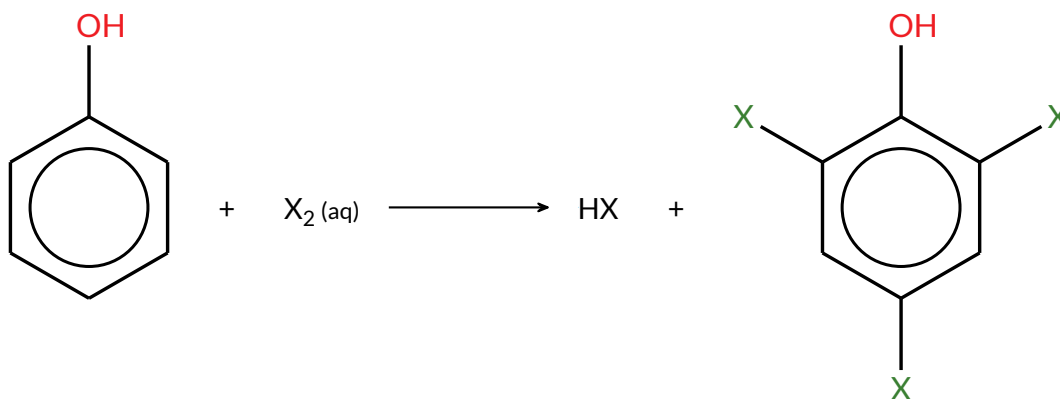
Alternatively, to prevent tri-substitution, methods can be employed to reduce the electrophilic reactivity of bromine, including using a non-polar inert solvent to prevent instantaneous dipole moments (or induced dipole moments in fact), and reducing the temperature.

Conditions: Br_2 (l) / Cl_2 (g) in inert, non-polar solvent (eg. CCl_4), room temperature.
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
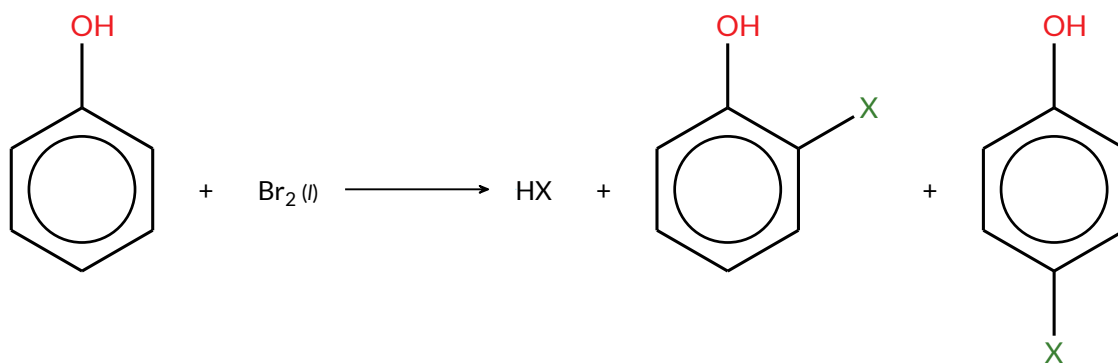
2.4.2 Nitration

Similar to benzene, phenols can also be nitrated, but this time without requiring concentrated H_2SO_4 as a catalyst. The degree of substitution can be controlled using the concentration of HNO_3 used.

Concentrated HNO_3 can be used to achieve tri-substitution, 'moderately concentrated' for di-substitution, and dilute HNO_3 for mono-substitution.

Conditions: Dilute HNO_3 (aq), room temperature.
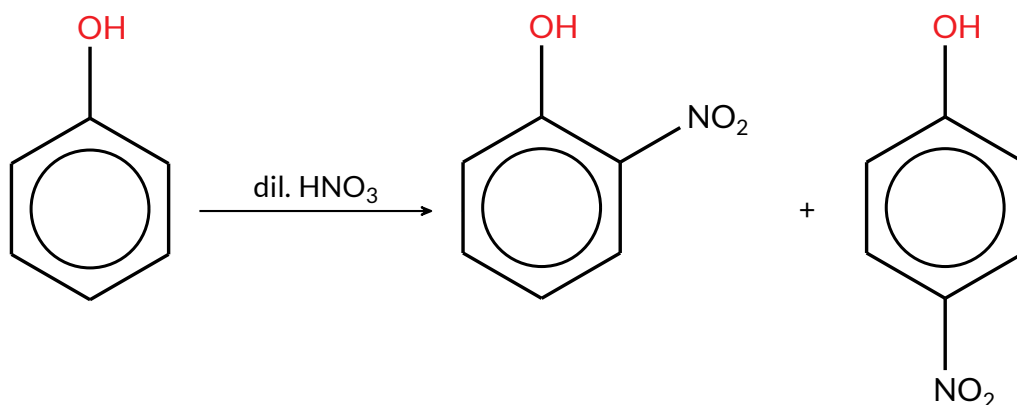
Conditions: Concentrated HNO_3 (aq), room temperature.
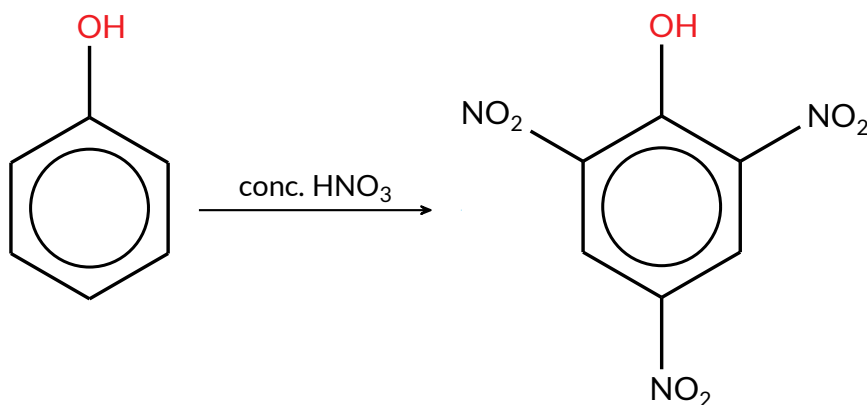
2.5 Formation of Complex with $FeCl_3$

Phenol can form a complex with neutral $FeCl_3$ (aq), forming a violet complex. This reaction is mainly used as a distinguishing test for the presence of phenol, due to the very obvious colour.

However, the violet only applies to unsubstituted phenol — the colour might change slightly if the phenol is indeed substituted.

Conditions: Neutral $FeCl_3$ (aq), room temperature.
Observations: *Violet* complex formed.

2.6 Esterification (Nucleophilic Acyl Substitution)

Similar to how alcohols can undergo esterification with carboxylic acids, phenols too can esterify, but only with acyl chlorides. This is because carboxylic acids are too unreactive, and phenols are too poor of a nucleophile to react with any significant yield.
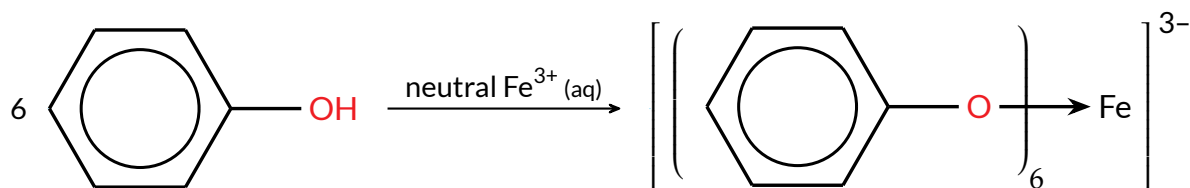
The poor nucleophile character is caused by the delocalisation of the lone pair on the O atom into the π-system. Thus, it is possible to increase the effectiveness of this reaction by deprotonating the phenol, exposing a negatively charged oxygen atom. Note that this is still insufficient to enable a reaction with carboxylic acids.

Conditions: Acyl chloride, NaOH (aq), room temperature.
Observations: Formation of white fumes of HCl gas.
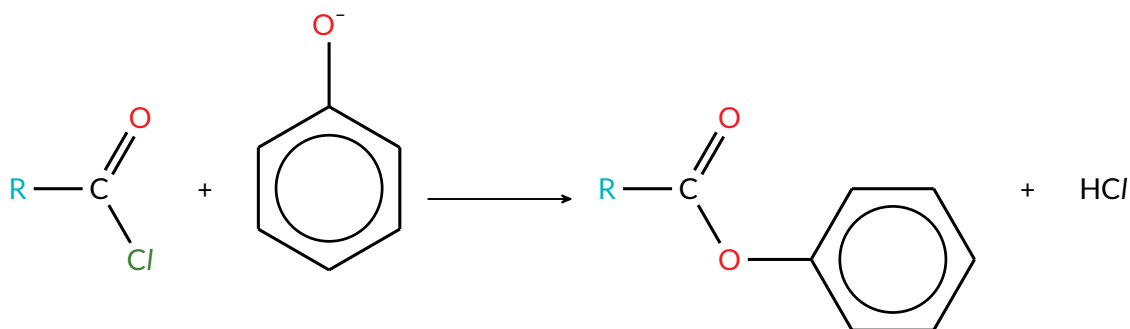
PART XI

Aldehydes and Ketones

1 Structure

Aldehydes and ketones have a very similar structure, both revolving around the carbonyl-bearing central carbon atom, with an oxygen atom double-bonded to it.

1.1 Ketones

Ketones are the more general form of carbonyls. There exists a central carbon atom, with one oxygen atom double-bonded to it, and two alkyl groups on either side. For ketones specifically, R in this case *cannot* be a hydrogen atom.
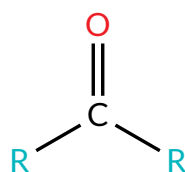
The structure of a ketone.

1.2 Aldehydes

Aldehydes are ketones where one or both of the R groups on the central carbon are instead replaced with hydrogen atoms. Methanal, where both are hydrogen atoms, is the simplest aldehyde and the only case (duh) where there are two hydrogens.
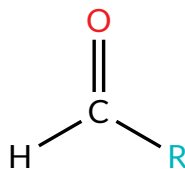
The structure of an aldehyde

1.3 Hybridisation

The central carbon in both aldehydes and ketones is sp^2 hybridised, resulting in a planar construction with a bond angle of 120°. As such, the unhybridised p-orbital of the carbon atom is able to overlap with the p-orbital the neighbouring oxygen atom, forming a π-bond.

Furthermore, the high electronegativity of the oxygen atom results in it having a partial negative charge, $δ^-$, while the carbon atom has a partial positive charge, $δ^+$. It is this polarisation and permanent dipole that lends aldehydes and ketones their chemical and physical properties.

2 Physical Properties

Melting and Boiling Points

Both aldehydes and ketones can form intermolecular permanent dipole interactions, thus resulting in stronger electrostatic forces of attraction, and thus higher melting and boiling points than their alkane counterparts.

However, the lack of an H atom attached to the O atom means that there is no possibility for intermolecular hydrogen bonds to be formed. Thus, aldehydes and ketones have lower melting and boiling points than their alcohol and carboxylic acid counterparts.

Solubility

Furthermore, due to the existence of both a polar and non-polar region, carbonyls are soluble in both polar solvents, like water, and non-polar solvents, like CCl_4. Their solubility in the former is due to their ability to form favourable solvent-solute interactions in the form of hydrogen bonds, between the partial negatively-charged O atom and the partial positively-charged hydrogen atom in H_2O.

Beyond 5 carbons however, the bulkiness of the alkyl chain prevents further solubility of both aldehydes and ketones.

3 Creation of Aldehydes and Ketones

3.1 Oxidation of Alcohols

3.1.1 Oxidation of Primary Alcohols

The details on the mechanics of this reaction can be found here, including the use of $K_2Cr_2O_7$ instead of $KMnO_4$.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, heat with immediate distillation.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed).
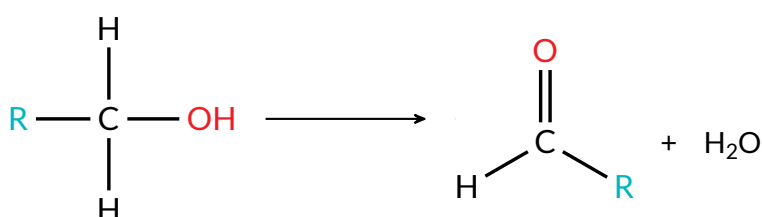
3.2 Oxidation of Secondary Alcohols

Secondary alcohols can be oxidised to ketones directly, using either $K_2Cr_2O_7$ or $KMnO_4$.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)

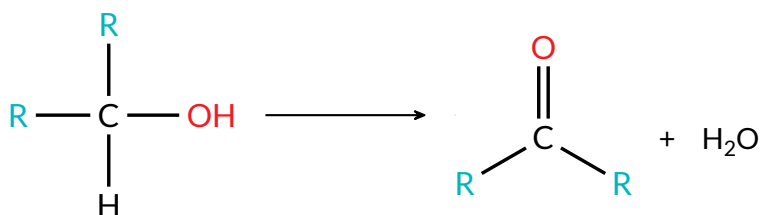## 3.3 Oxidative Cleavage of Alkenes

Certain alkenes can undergo strong oxidation, cleaving the double bond. The details are elaborated on *here*, but only one kind of alkene can form a ketone, where the carbon atom has two alkyl groups substituted, and no hydrogens.

Conditions: $KMnO_4$, dilute H_2SO_4, heat.
Observations: *Purple* $KMnO_4$ decolourises, forming colourless Mn^{2+}.
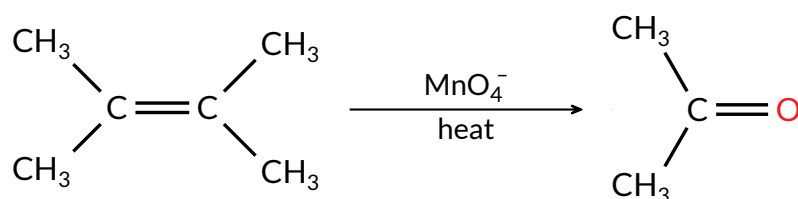
Note that alkenes with one hydrogen substituent and one alkyl substituent *will not* form aldehydes, since the hydrogen atom will be oxidised, and instead give a carboxylic acid.

4 Aldehyde and Ketone Reactions

4.1 Nucleophilic Addition

Like all other mechanisms, the reaction mechanism for this can be found in *the appendix*. Note that the trigonal-planar nature of the carbonyl makes it open to attack from both sides, which can result in stereoisomers and chirality.
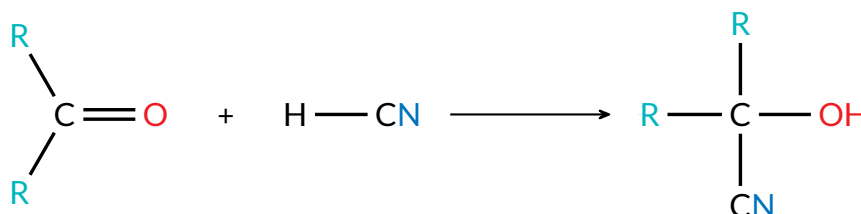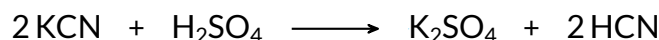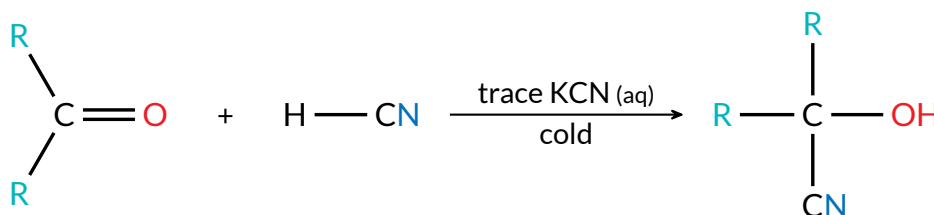

This is the basic scheme for nucleophilic addition.

4.1.1 Formation of Nitriles (Cyanohydrins)

The nucleophilic addition of CN to a carbonyl is perhaps one of the more common forms of nucleophilic addition. Since HCN is a toxic gas, it is typically generated *in-situ* by reacting KCN with dilute H_2SO_4.

$$2\,KCN \; + \; H_2SO_4 \longrightarrow K_2SO_4 \; + \; 2\,HCN$$

Conditions: Cold HCN, trace KCN (aq).

Even though the stated reactant of the reaction above is indeed HCN, simply using pure HCN will result in a dismal rate of reaction — HCN is a weak acid, and as such only partially dissociates in water to give CN^- ions, which is the actual electrophile.

Thus, a trace amount of KCN is added, which, as a salt, will completely dissociate in water to give CN^- ions, increasing the rate of reaction. Since CN^- is regenerated at the end of the reaction, the KCN added actually acts as a catalyst.

The resulting nitrile can be used to create carboxylic acids through hydrolysis, as well as amines through reduction. The details can be found *here*.

4.2 Condensation

Primary amines, which have a nucleophilic nitrogen atom with two attached hydrogen atoms, can undergo an elimination reaction with both aldehydes and ketones, with the removal of H_2O.
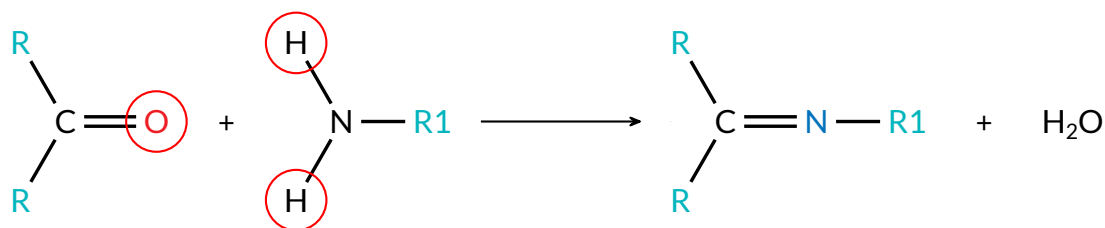
The circled atoms form the water that is eventually eliminated.

4.2.1 Distinguishing test with 2,4-DNPH

One of the more useful reactions involving this mechanism is the distinguishing test with 2,4-dinitrophenylhydrazine, which is a relatively large molecule with a distinct orange precipitate. This allows for the verification of the presence of an aldehyde or a ketone — both aliphatic and aromatic carbonyls will have a positive result.

The molecule is somewhat complex, but reading it right-to-left is sufficient to deduce its structure — hydrazine is the parent structure, and it has a substituent of 2,4-dinitrophenyl.

Conditions: 2,4-DNPH, room temperature.
Observations: *Orange* precipitate forms with a carbonyl.
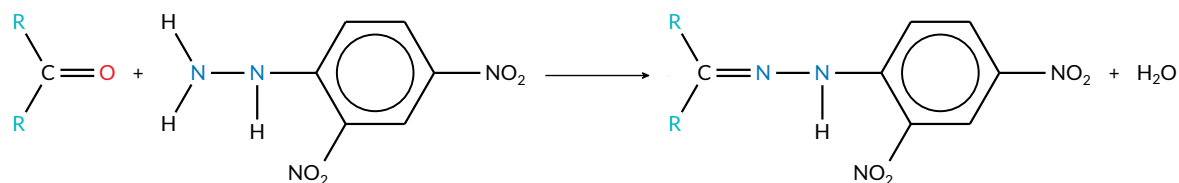
4.3   Reduction

In what is basically the reverse of the oxidation of alcohols, aldehydes can be reduced into primary alcohols, and ketones can be reduced into secondary alcohols.
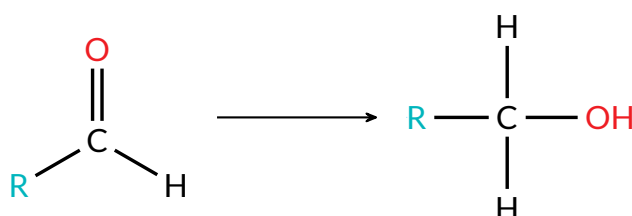
Clearly, tertiary alcohols cannot be formed like this.

4.3.1 Reduction of Aldehydes

Aldehydes are reduced to primary alcohols. Any of the three reducing agents can be used.

Conditions: $LiAlH_4$ in dry ether (diethyl ether), *OR*
                       $NaBH_4$ in methanol, *OR*
                       $H_{2\ (g)}$, Ni catalyst, high temperature and pressure.

4.3.2 Reduction of Ketones

Ketones are reduced to secondary alcohols. Any of the three reducing agents can be used.
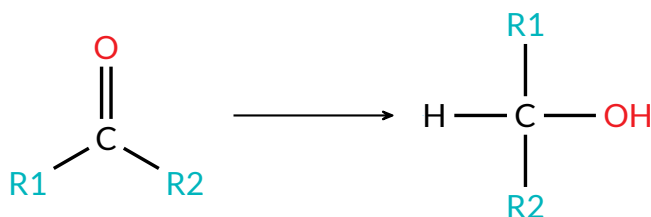
Conditions: $LiAlH_4$ in dry ether (diethyl ether), *OR*
                       $NaBH_4$ in methanol, *OR*
                       $H_{2\ (g)}$, Ni catalyst, high temperature and pressure.
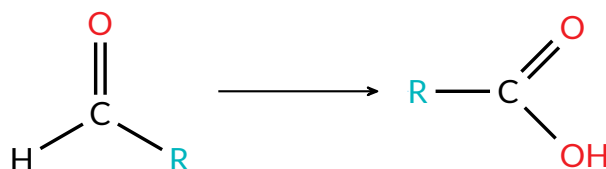

4.4   Oxidation

4.4.1 Oxidation of Aldehydes to Carboxylic Acids

As briefly covered in the chapter on *alcohols*, aldehydes can be further oxidised into carboxylic acids.

Also, two special carboxylic acids can be further oxidised, and they are covered above.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)

This reaction can also be used to distinguish aldehydes from ketones, as ketones will *not* undergo further oxidation due to their lack of a hydrogen atom on the central carbon.
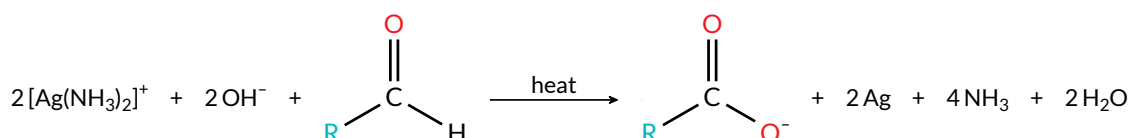
4.4.2 Tollens' Reagent

Tollens' Reagent, or the *silver mirror test*, can also be used to distinguish aldehydes and ketones. Only aldehydes, both aliphatic and aromatic, can react reduce the silver complex to silver metal, while ketones cannot — this is due to the fact that ketones cannot be oxidised.

A positive test results in the depositing of silver metal on the surface of the reaction vessel, hence the silver mirror.

Conditions: Tollens' Reagent, heat.
Observations: *Silver* metal coats the reaction vessel.

$$2\,[Ag(NH_3)_2]^+ \;+\; 2\,OH^- \;+\; \text{(RCHO)} \xrightarrow{\text{heat}} \text{(RCOO}^-) \;+\; 2\,Ag \;+\; 4\,NH_3 \;+\; 2\,H_2O$$
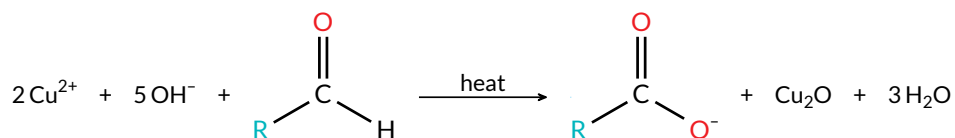
4.4.3 Fehling's Solution

Fehling's Solution, like Tollens' Reagent, relies on the oxidation of the aldehyde, and hence the reduction of itself. In this case, Cu^{2+} is reduced to Cu^+ in the form of Cu_2O, which gives a distinct, brick-red precipitate.

Fehling's Solution is used to distinguish between aliphatic and aromatic aldehydes. Again, since ketones cannot be oxidised, they do not give a positive test for Fehling's Solution.

Conditions: Fehling's Solution, heat.
Observations: *Brick-red*, or *reddish-brown* precipitate is formed.

$$2\,Cu^{2+} \ + \ 5\,OH^- \ + \ \underset{R}{\overset{O}{\underset{}{\|}}}C{\underset{}{H}} \xrightarrow{\text{heat}} \underset{R}{\overset{O}{\|}}C{\underset{}{O^-}} \ + \ Cu_2O \ + \ 3\,H_2O$$

The aldehyde here cannot be aromatic (aka the R group is a benzene ring). Only normal alkyl-based aldehydes will work.

4.4.4 Tri-iodomethane (Iodoform) Formation

Similar to alcohols, ketones and aldehydes can be oxidised by aqueous iodine to give the distinct yellow precipitate, which is useful as a fingerprinting, structural test.

Due to the requirements of having a CH_3 group, ethanal is the only aldehyde that gives a positive result for this test, since the R group will be a hydrogen atom. Otherwise, only terminal ketones will test positive.

Conditions: I_2 (aq), NaOH (aq), warmed.
Observations: *Yellow* precipitate of CHI_3 is formed.
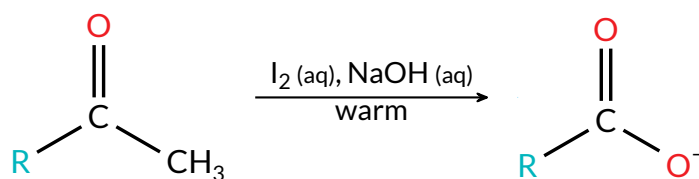
Carboxylic Acids

1   Structure

The structure of carboxylic acids is kind of an extension of a ketone or aldehyde — it features an oxygen atom double-bonded to a carbon atom, with an R group and an OH group attached as well.

The general structure of a carboxylic acid.

The central carbon is sp^2 hybridised, so the bond angle between all three groups is 120°.

2   Physical Properties

Melting and Boiling Points

Compared to both alkanes, carboxylic acids naturally have higher melting and boiling points. This is mostly due to the large permanent dipole moment, caused by the existence of two electron-withdrawing groups (the C=O and C−OH), creating a large partial-positive charge (δ^+) on the carbon atom. Thus, hydrogen bonds can form; these bonds are stronger than that in alcohols, because the dipole moment is greater.

Their melting and boiling points are also higher than that of aldehydes and ketones, since carbonyls lack the O−H partial charge disparity to form hydrogen bonds, and rely solely on permanent dipole interactions.

Note that hydrogen bonds between carboxylic acid molecules typically form between the H on the OH group, and the O atom double-bonded to the central carbon.

Furthermore, in both the liquid and gaseous state, two carboxylic acid molecules can *dimerise*, forming double-bonds between each other and effectively increasing molecular mass, which also increases id-id interaction strength.
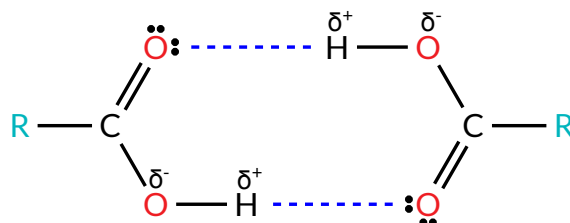
An illustration of two carboxylic acids dimerising.

Solubility

Carboxylic acids are fairly soluble in non-polar solvents, as they exist as the dimerised form shown above. This means that carboxylic acids are not acidic in a non-polar solvent, as they do not dissociate.

In water, the molecules do not dimerise; instead, they form hydrogen bonds with the water, dissociating into $R-CO_2^-$ and H^+ ions. This tends to increase the solubility due to the formation of favourable solvent-solute interactions.

However, with carbon chains longer than 5 atoms, solubility decreases due to the bulky alkyl chain.
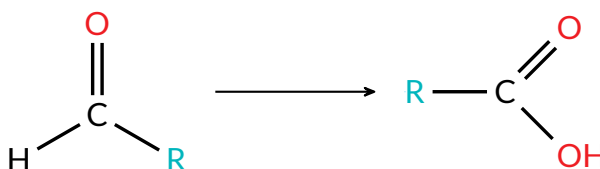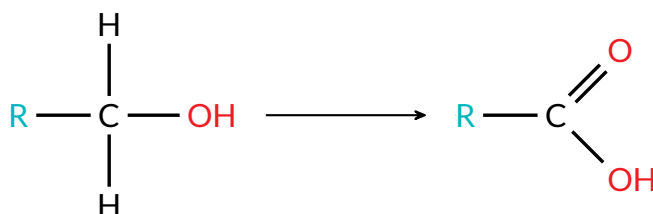
3   Creation of Carboxylic Acids

Carboxylic acids can be created in various ways, but one of the most common ways is through oxidation. Essentially, carboxylic acids are at the 'highest' oxidation state, followed by aldehydes and ketones, then alcohols.

3.1   Oxidation of Primary Alcohols

When the aldehydes can be oxidised to carboxylic acids. Alternatively, the strong oxidising agent $KMnO_4$ can be used to immediately create a carboxylic acid from a primary alcohol.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)

It is also possible to start with aldehydes, and oxidise them to carboxylic acids.

3.2 Side-chain Oxidation of Alkylbenzenes

As noted in the chapter on arenes, benzene rings with an alkyl chain can undergo side-chain oxidation to form benzoic acid.

Again, note that the carbon attached to the benzene ring *cannot* be tertiary, ie. it must have at least one hydrogen atom.

Conditions: Heat, $KMnO_4$, dilute acid or alkali.

Observations: *Purple* $KMnO_4$ decolourises (*acid*), or
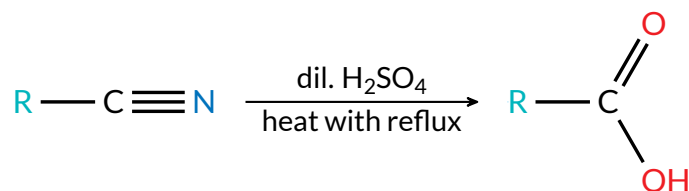forms *brown* precipitate of MnO_2 (*alkali*).
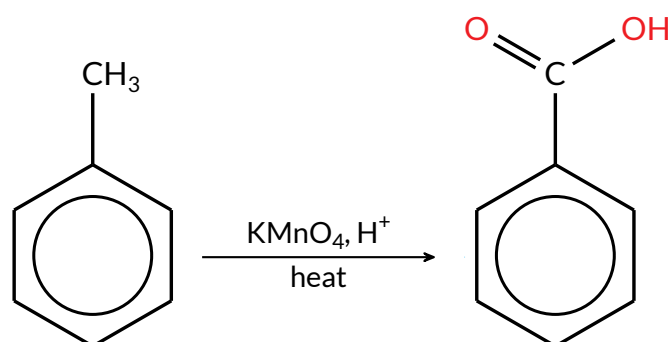
3.3 Hydrolysis of Nitriles

As covered in previous chapters, nitriles, $-C\equiv N$, can be hydrolysed to give carboxylic acids.

3.3.1 Acid Hydrolysis

The more straightforward method is acid hydrolysis — in this case, a carboxylic acid is immediately produced.

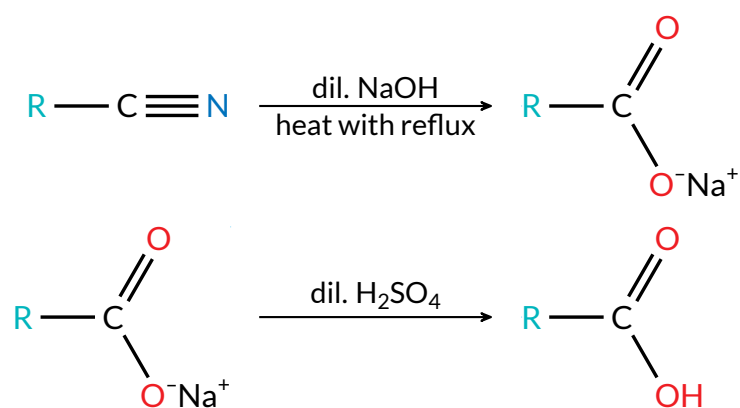**Conditions:** Dilute H_2SO_4 or HCl, heat under reflux.

3.3.2 Alkaline Hydrolysis

The alternative is to conduct the hydrolysis in an alkaline medium using NaOH, which gives a carboxylate salt. This salt can be acidified using a dilute acid (I mean, why not start with an acid?)

to yield the carboxylic acid.

**Conditions:**   Dilute NaOH, heat under reflux.

The carboxylate salt can be acidified.

3.4 Oxidative Cleavage of Alkenes

Alkenes can undergo strong oxidation, cleaving the double bond. The details are elaborated on *here*, but only one kind of alkene can form a carboxylic, where the carbon atom has one alkyl group and one hydrogen atom.

Conditions: $KMnO_4$, dilute H_2SO_4, heat.
Observations: *Purple* $KMnO_4$ decolourises, forming colourless Mn^{2+}.
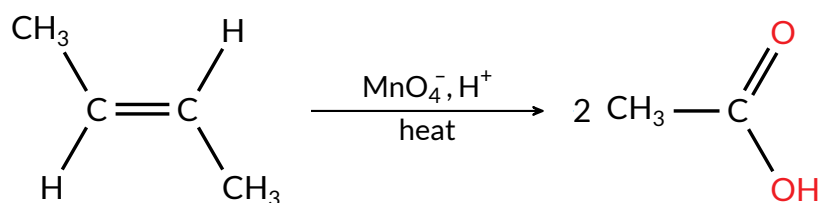
3.5 Hydrolysis of Esters

Finally, esters can be hydrolysed to form a carboxylic acid as one of its products. Note that this hydrolysis is preferably conducted in an alkaline medium, since the reaction is slow and reversible in an acidic medium, but fast and irreversible under alkaline conditions. All that is required is a dilute acid to protonate the carboxylate salt after.

Conditions: Dilute H_2SO_4, heat under reflux, *OR*
Dilute NaOH, heat under reflux.
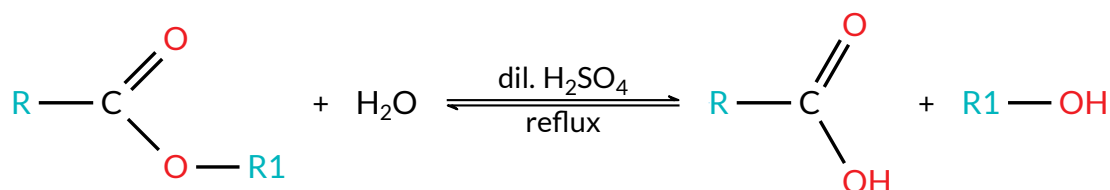
An alcohol is also formed, but for our purposes the carboxylic acid is the main product.
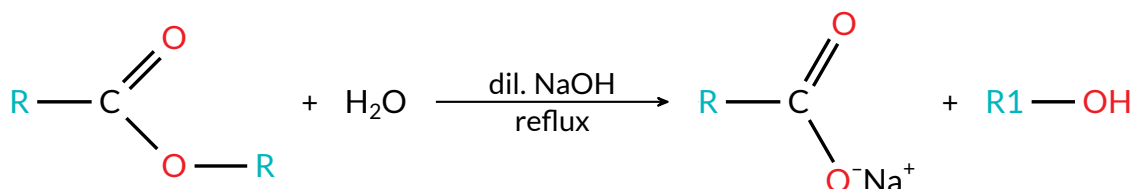
3.6 Hydrolysis of Acyl Chlorides

Acyl chlorides, which are a derivative of carboxylic acids where the OH group is replaced by a *Cl* atom, can be hydrolysed to form a carboxylic acid, and H*Cl*.

Conditions: H_2O, room temperature.
Observations: Formation of white fumes of H*Cl* gas.
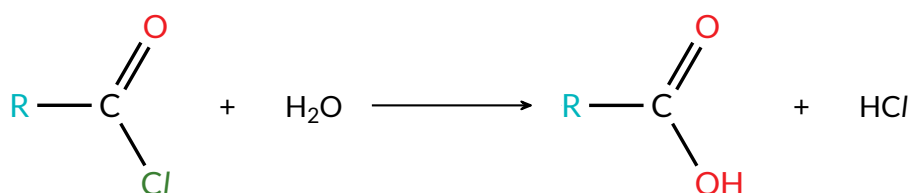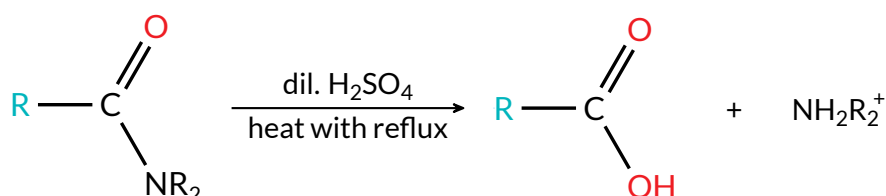
3.7 Hydrolysis of Amides

Amides can be hydrolysed with either acids or bases to give a carboxylic acid, and an amine. If the original amide is unsubstituted, then the result will be NH_3, or, in an acidic medium, NH_4^+. The products illustrated below can have R be an alkyl substituent or a hydrogen atom.

Note that the formation of NH_4^+ is due to the fact that NH_3 is a base, and will react with H^+ ions in the acidic medium.

3.7.1 Acid Hydrolysis

The hydrolysis of an amide in an acidic medium yields the carboxylic acid directly.

Conditions: Dilute H_2SO_4 or HCl, heat under reflux.

$$R-C(=O)NR_2 \xrightarrow[\text{heat with reflux}]{\text{dil. } H_2SO_4} R-C(=O)OH \quad + \quad NH_2R_2^+$$

3.7.2 Alkaline Hydrolysis

The alternative is to conduct the hydrolysis in an alkaline medium using NaOH, which gives a carboxylate salt. This salt can be acidified using a dilute acid to yield the carboxylic acid.

Conditions: Dilute NaOH, heat under reflux.

$$R-C(=O)NR_2 \xrightarrow[\text{heat with reflux}]{\text{dil. } H_2SO_4} R-C(=O)O^-Na^+ \quad + \quad NHR_2$$
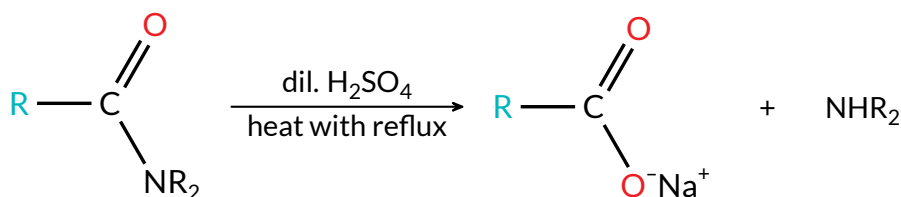
The carboxylate salt can be acidified later.

4 Carboxylic Acid Reactions

4.1 Acidity of Carboxylic Acids

Carboxylic acids are far more acidic than either alcohols or phenols, since the conjugate base (carboxylate anion) is greatly stabilised due to the delocalisation of the negative charge across the two electronegative oxygen atoms.
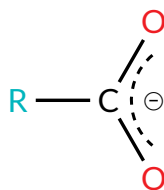
An illustration of this delocalisation.

This delocalisation immensely increases the stability of the anion, thus carboxylic acid is a much stronger acid, with a pK_a of 4.75, in contrast with that of ethanol and phenol, which are 15.9 and 9.95 respectively.

4.1.1 Effect of Substituents

In a similar vein to alcohols and phenols, substituents along the carbon chain can act to disperse or intensify the negative charge on the anion, modifying its stability and hence the acidity of the group. Naturally, groups closer to the central carbon have a greater effect than groups further away.

Electronegative groups and atoms, such as Cl or $-NO_2$, pull electron density away from the carboxyl carbon, dispersing the negative charge and stabilising the anion, hence increasing acidity.

Conversely, electron-donating groups, most notably alkyl chains, have the opposite effect, intensifying the negative charge and thus destabilising the anion and decreasing acidity. Note that the length of the alkyl chain does not have any significant impact on the acidity.

4.2 Reactions as an Acid

For all intents and purposes, carboxylic acid functions like a weak mineral acid, and can do all the things they can do; neutralise bases, react with metals, and liberate CO_2 gas from carbonates (CO_3^{2-}) and hydrogencarbonates (HCO_3^-).

The reactions will not be discussed in detail here, since they're basically normal acid-base reactions.

4.3 Nucleophilic Acyl Substitution
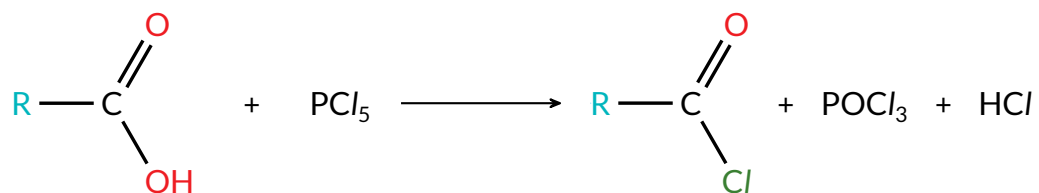
4.3.1 Formation of Acyl Chlorides

The carboxyl carbon undergoes a nucleophilic substitution, replacing the OH group with a Cl group, forming an acyl chloride.

Similar to alcohols, either PCl_5, PCl_3, or $SOCl_2$ can be used. However, HCl will not work to substitute the OH group on a carboxylic acid, unlike an alcohol.
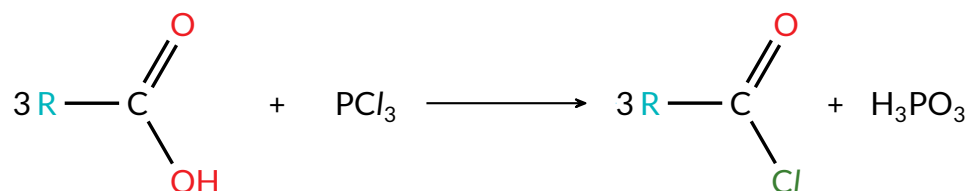
Phosphorous Pentachloride (PCl_5)

Conditions: Solid PCl_5, room temperature.
Observations: Formation of white fumes of HCl gas.

Phosphorous Trichloride (PCl_3)

**Conditions:**   Solid PCl_3, room temperature.

Thionyl Chloride (SOСl_2)

This reaction is slightly preferred over the others, since both by-products (SO$_2$ and HCl) are gaseous, and would bubble out of the solution, leaving mainly the halogenoalkane in the reaction mixture.

Conditions: Warm, liquid SOСl_2.

**Observations:**   Formation of colourless, pungent SO$_2$ gas, white fumes of HCl gas.
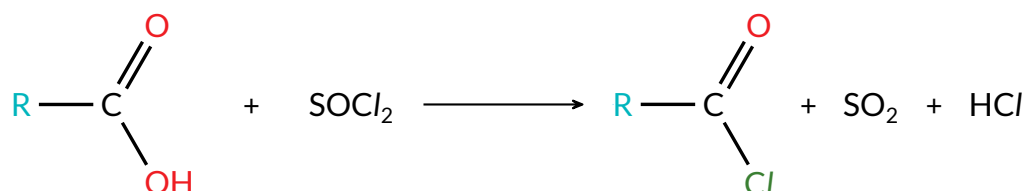
4.3.2 Esterification

As discussed *previously*, carboxylic acids can undergo esterification with alcohols, using concentrated H$_2$SO$_4$ as a catalyst and dehydrating agent.

Note that this is *not* the preferred method of creating esters, due to the need for heating and catalysis, and the fact that phenols cannot be used.

Conditions: Carboxylic acid and alcohol, Several drops of concentrated H$_2$SO$_4$, heated under reflux.
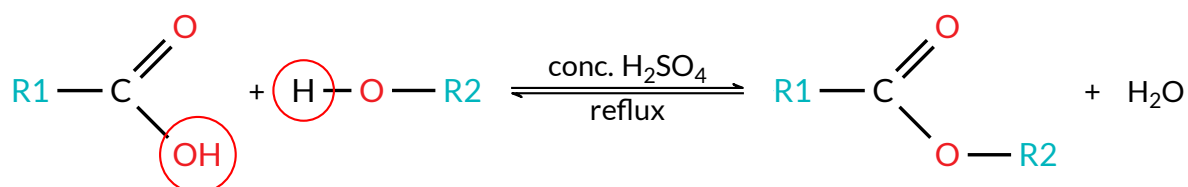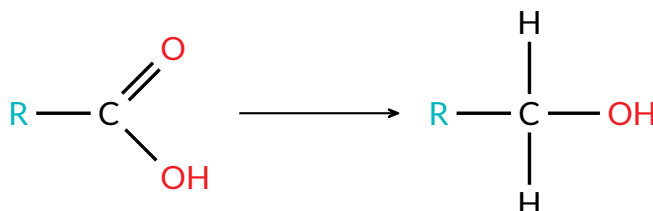

Note that it is the circled groups that form the water.

4.4 Reduction

Carboxylic acids can also be reduced to create alcohols. This reduction requires a strong reducing agent, so only $LiAlH_4$ can be used. See the *appendix* for a list of reducing agents and their applicable uses.

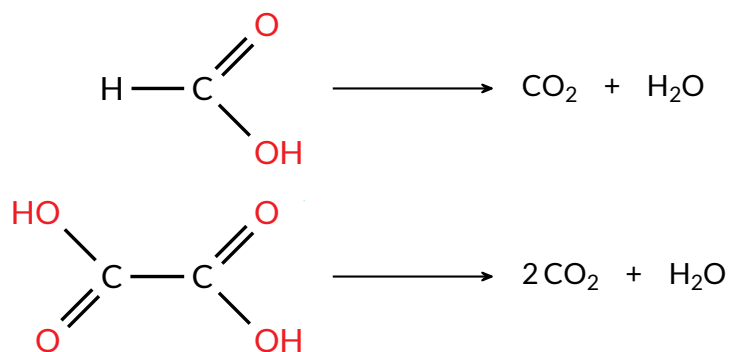**Conditions:** $LiAlH_4$ in dry ether (diethyl ether).

4.5 Oxidation

With the strong oxidising agent $KMnO_4$, two special carboxylic acids can be *even further oxidised* to give CO_2 and H_2O; they are ethanedioic acid and methanoic acid.

Conditions: $KMnO_4$ with dilute H_2SO_4,
heat under reflux.

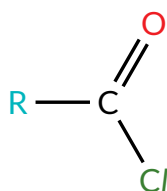**Observations:**   *Purple* MnO_4^- decolourises (Mn^{2+} formed).

Acyl Chlorides

1 Structure

Acyl chlorides, being a derivative of carboxylic acids, naturally share a similar structure. Indeed, they are basically identical save the replacement of the OH group with a *Cl* atom.

An acyl chloride.

2 Physical Properties

Melting and Boiling Points

Acyl chlorides have much lower melting and boiling points compared to their carboxylic acid brethren, given that there is no hydrogen atom directly attached to an electronegative atom. Thus, intermolecular hydrogen bonds cannot be formed, and acyl chlorides rely only on permanent dipole interactions, leading to lower melting and boiling points.

They also do not dimerise, owing to this lack of hydrogen bonding.

Solubility

The solubility of acyl chlorides in non-polar solvents depends on the length of the carbon chain, and hence its ability to form instantaneous dipole-induced dipole interactions with the solvent, and is not greatly dependent on the acyl group.

However, acyl chlorides cannot be said to *dissolve* in water — it reacts violently in a hydrolysis reaction, destroying the acyl chloride. Thus, it cannot exist in an aqueous state.

3 Creation of Acyl Chlorides

Acyl chlorides are most commonly created through the nucleophilic acyl substitution of a carboxylic acid, as covered previously. Either PCl_5, PCl_3, or $SOCl_2$ can be used.
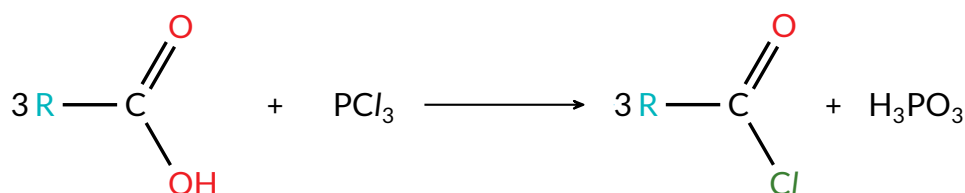
Phosphorous Pentachloride (PCl$_5$)

Conditions: Solid PCl_5, room temperature.
Observations: Formation of white fumes of HCl gas.
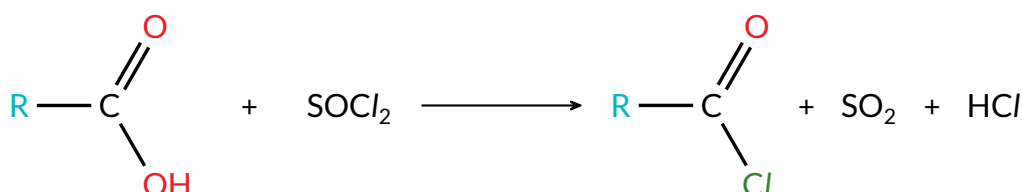

Phosphorous Trichloride (PCl$_3$)

Conditions: Solid PCl_3, room temperature.

Thionyl Chloride (SOCl$_2$)

This reaction is slightly preferred over the others, since both by-products (SO_2 and HCl) are gaseous, and would bubble out of the solution, leaving mainly the halogenoalkane in the reaction mixture.

Conditions: Warm, liquid $SOCl_2$.

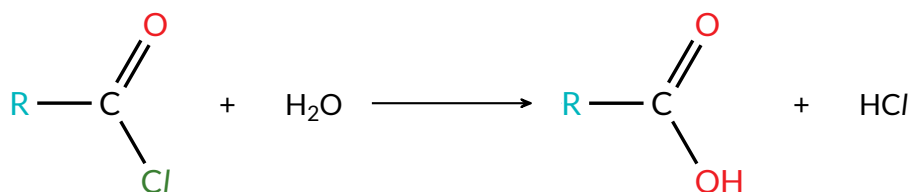**Observations:** Formation of colourless, pungent SO_2 gas, white fumes of HCl gas.

4   Acyl Chloride Reactions

4.1   Hydrolysis

Acyl chlorides can be hydrolysed, undergoing a rather violent reaction to form HCl and a carboxylic acid.

Conditions: H_2O, room temperature.
**Observations:**   Formation of white fumes of HCl gas.

4.2   Nucleophilic Acyl Substitution

Acyl chlorides themselves can undergo a substitution, replacing the Cl atom with another group.

4.2.1   Esterification

Acyl chlorides are the preferred path to esters, due to their high reactivity and yield, plus the ability to form phenyl esters.

Conditions: Acyl chloride, NaOH (aq), room temperature.
Observations: Formation of white fumes of HCl gas.
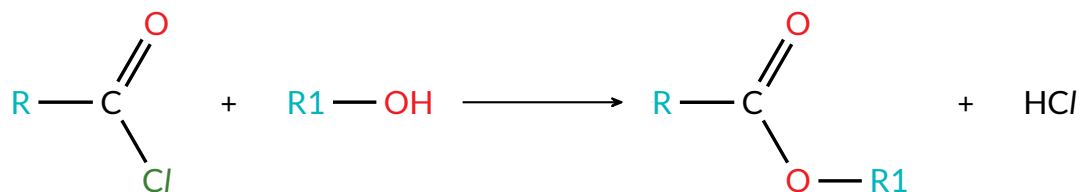
4.2.2 Formation of Amides

Amides, which are covered *later*, are an acyl derivative where the OH group is replaced with an NH_2 group — the hydrogen atoms on the nitrogen may also be substituted for R groups, creating substituted amides.

Acyl chlorides react readily with ammonia and amines to form primary amides and substituted amides respectively. Note that an excess of the amine (or ammonia) is used to compensate for the acid-base reaction between the HC*l* produced and the amine.

Finally, tertiary amines (where all the hydrogen atoms have been substituted) cannot be used, since they do not have a substitutable hydrogen atom.

Conditions: Acyl chloride, amine of choice in excess, room temperature.
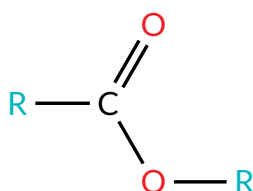**Observations:**   Formation of white fumes of HC*l* gas.
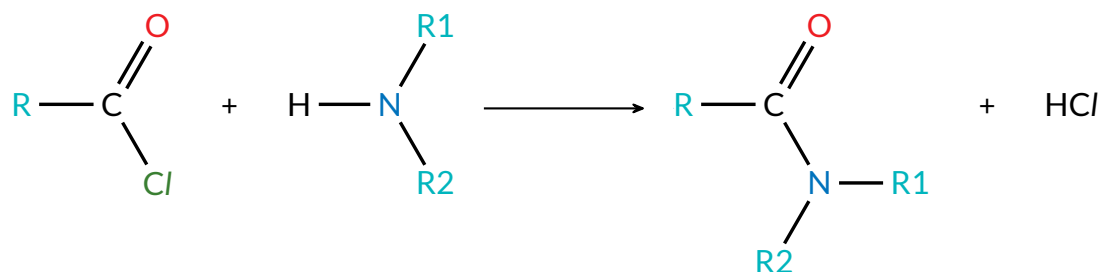
Esters

1 Structure

Esters are also an acyl derivative, where the OH group of a carboxylic acid is instead replaced with an oxygen atom bonded to an R group.

The structure of an ester.

2 Physical Properties

Melting and Boiling Points

Esters, like acyl chlorides, have far lower melting and boiling points than their equivalent carboxylic acid, due to the lack of intermolecular hydrogen bonding. Thus, they rely only on permanent dipole interactions, leading to low melting and boiling points.

Solubility

Esters are mostly insoluble in water once the carbon chain reaches any appreciable length, due again to the lack of hydrogen bonding. Thus, only permanent dipole interactions can be formed between water and the ester.
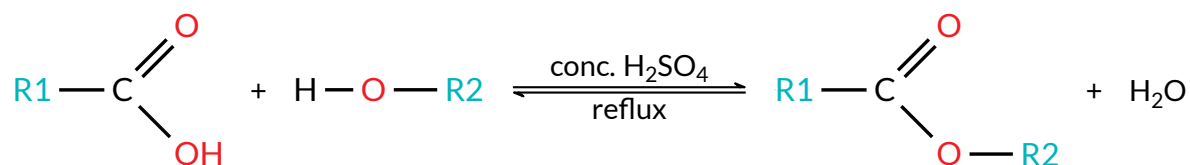
Of course, the carbon chain makes esters highly soluble in non-polar solvents.

3 Creation of Esters

There are two main methods of creating esters, one of which is superior to the other. Both have been discussed in detail before.
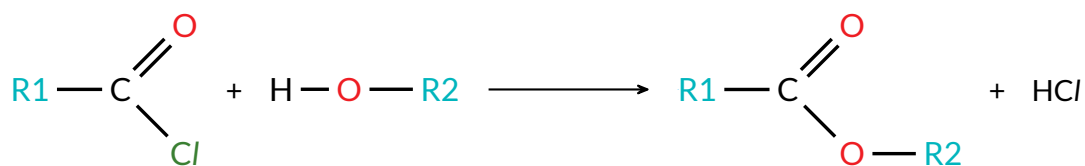
3.1 From Carboxylic Acids

Conditions: Carboxylic acid and alcohol,
Several drops of concentrated H_2SO_4, heated under reflux.

$$R1-C\underset{OH}{\overset{O}{\Big<}} \quad + \quad H-O-R2 \quad \underset{\text{reflux}}{\overset{\text{conc. } H_2SO_4}{\rightleftharpoons}} \quad R1-C\underset{O-R2}{\overset{O}{\Big<}} \quad + \quad H_2O$$

3.2 From Acyl Chlorides

Again, note that only acyl chlorides can react with phenols (or more effectively with phenoxide) to form an ester.

Conditions: Acyl chloride and alcohol,
Room temperature.

$$R1-C\underset{Cl}{\overset{O}{\Big<}} \quad + \quad H-O-R2 \quad \longrightarrow \quad R1-C\underset{O-R2}{\overset{O}{\Big<}} \quad + \quad HCl$$

4 Ester Reactions

4.1 Hydrolysis

Like most hydrolysis reactions, esters can be hydrolysed in either an acidic or alkaline medium. However, acid hydrolysis is the same equilibrium reaction as esterification with a carboxylic acid, only this time an excess of water is used to move the position of equilibrium — thus the reaction is slow and the yield is low.

4.1.1 Acid Hydrolysis

**Conditions:** Dilute H_2SO_4, heat under reflux.
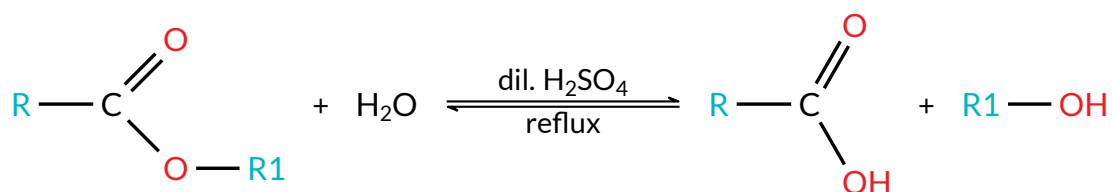
4.1.2 Alkaline Hydrolysis (Saponification)

Alternatively, using an alkaline medium results in a fast and irreversible reaction, creating a carboxylate salt. Dilute acid can be used to protonate the salt afterwards.

This reaction is also known as saponification, and is preferred for its higher yield and faster reaction.

Conditions: Dilute NaOH, heat under reflux.
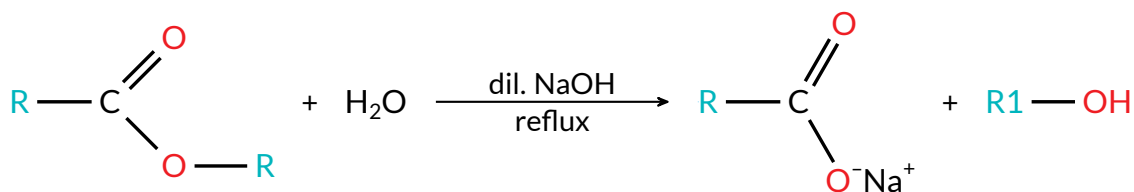
Amides

1 Structure

Amides are also a carboxylic acid derivative, this time where the OH group has been replaced with an NH_2 group that may or may not be substituted.

Naturally, amides can also be classified into primary, secondary and tertiary amides.

| Primary (1°) | Secondary (2°) | Tertiary (3°) |
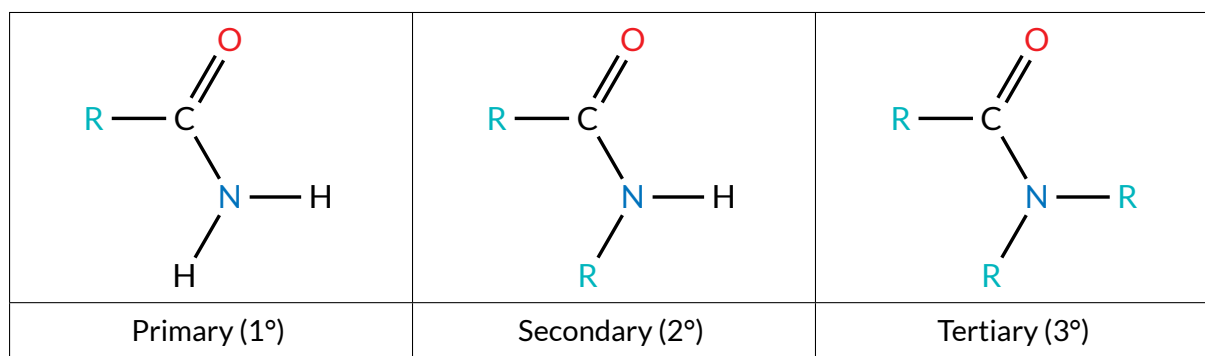
2 Physical Properties

Melting and Boiling Points

Amides are generally crystalline solids at room temperature, owing to their ability to form hydrogen bonds. The electronegative nitrogen atom has two hydrogen atoms (in unsubstituted amides), allowing two hydrogen bonds per molecule. Thus, they have higher melting and boiling points than carboxylic acids.

Solubility

Amides are generally quite soluble in water, again due to the ability to form hydrogen bonds with the water molecules. However, the presence of long alkyl chains can hinder the formation of these bonds, leading to decreased solubility at higher carbon lengths.

3 Creation of Amides

3.1 From Acyl Chlorides

Amides are generally created by reacting an acyl chloride with ammonia or an amide, replacing the Cl group. The amine is used in excess to compensate for the reaction with HCl produced during the reaction.

Furthermore, carboxylic acids cannot be used to create amides, since they will react in an acid-base reaction with the amine instead. Tertiary amines also cannot be used since they do not have a hydrogen atom to replace.

Conditions:　　　Acyl chloride, amine of choice in excess, room temperature.
Observations:　　Formation of white fumes of HCl gas.
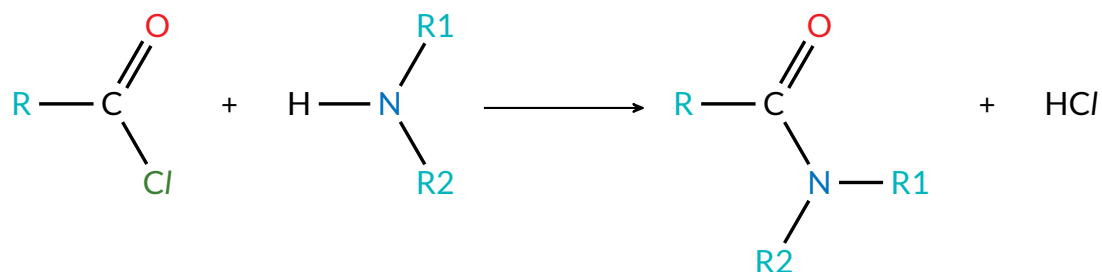
4 Amide Reactions

4.1 General Reactivity

Amides are generally unreactive compared to amides and carboxylic acids. This is due to the delocalisation of the lone pair on nitrogen across the carboxyl group; the carbon is sp^2 hybridised, allowing for p-orbital overlaps between the nitrogen, carbon and oxygen atoms.

There is reduced electron density on the nitrogen atom, and thus amides are neutral in solution since the lone pair is unavailable to accept a proton to act as a Brønsted base.
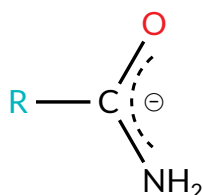
The delocalisation of the lone pair across the entire carboxyl group.

4.2 Hydrolysis

Amides can be hydrolysed with either acids or bases to give a carboxylic acid, and an amine. If the original amide is unsubstituted, then the result will be NH_3, or, in an acidic medium, NH_4^+. The products illustrated below can have R be an alkyl substituent or a hydrogen atom.

Note that the formation of NH_4^+ is due to the fact that NH_3 is a base, and will react with H^+ ions in the acidic medium.

4.2.1 Acid Hydrolysis

The hydrolysis of an amide in an acidic medium yields the carboxylic acid directly.

Conditions: Dilute H_2SO_4 or HCl, heat under reflux.

4.2.2 Alkaline Hydrolysis

The alternative is to conduct the hydrolysis in an alkaline medium using NaOH, which gives a carboxylate salt. This salt can be acidified using a dilute acid to yield the carboxylic acid.

Conditions: Dilute NaOH, heat under reflux.

$$R - C \overset{O}{\underset{NR_2}{\big\|}} \quad \xrightarrow[\text{heat with reflux}]{\text{dil. } H_2SO_4} \quad R - C \overset{O}{\underset{O^- Na^+}{\big\|}} \quad + \quad NHR_2$$
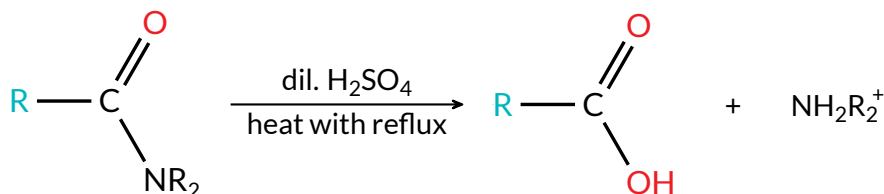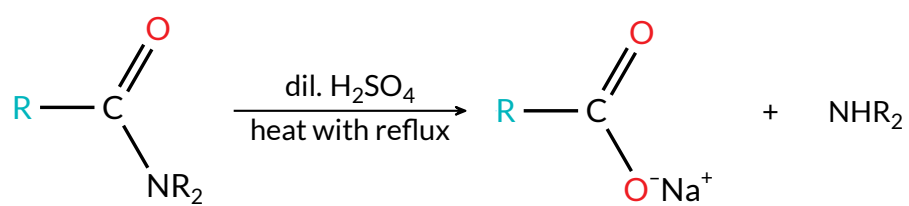
The carboxylate salt can be acidified later.

Amines

1 Structure

1.1 Aliphatic Amines

Aliphatic amines share a similar structure with ammonia — three substituents around a central nitrogen atom.

Primary (1°)	Secondary (2°)	Tertiary (3°)	Quaternary Ammonium Ion

1.2 Phenylamines

Phenylamines also exist, where the nitrogen is directly bonded to a benzene ring. These too can be classified as primary, secondary, tertiary or quaternary.

Primary (1°)	Secondary (2°)	Tertiary (3°)	Quaternary Ammonium Ion

2   Physical Properties

Melting and Boiling Points

Primary and secondary amines (and phenylamines) can form intermolecular hydrogen bonds, leading to increased melting and boiling points. However, they still have lower melting and boiling points compared to alcohols, due to the less polar nature of the $N-H$ bond compared to the $O-H$ bond.

Tertiary amines do not have a hydrogen atom bonded to the central nitrogen, and as such cannot form hydrogen bonds, relying only on pd-pd and id-id interactions, thus having lower melting and boiling points compared to primary or secondary amines of a similar molar mass.

Solubility

Aliphatic amines with relatively short carbon chains are able to form favourable solvent-solute interactions with water through hydrogen bonding, and as such are quite soluble in water.

Naturally, the longer the carbon chain, the less soluble the amine becomes — phenylamine is thus insoluble in water. Of course the solubility of amines in non-polar solvents depends mostly on the size of the alkyl groups attached.

3 Creation of Amines

3.1 Nucleophilic Substitution of Alkyl Halides

As covered *previously*, the halogen atom can be substituted by NH_3 in a nucleophilic reaction, giving a primary amine. Primary and secondary amines can also be used to give substituted amines.

Excess NH_3 is used to lower the possibility of multi-substitution.

Conditions: Ethanolic concentrated NH_3 in excess, heat in sealed tube.

$$R—X \; + \; NH_3 \longrightarrow R—NH_2 \; + \; HX$$
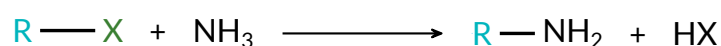
3.2 Reduction of Nitriles

Nitriles can be reduced to give primary amines.

Conditions: $LiAlH_4$ in dry ether (diethyl ether), *OR*
                       $H_{2\,(g)}$, Ni catalyst, high temperature and pressure.
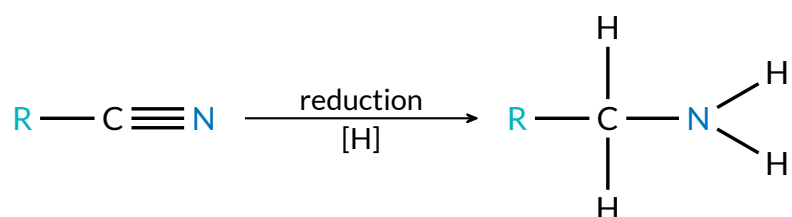
3.3 Reduction of Nitrobenzene

This reaction forms a phenylamine, and can be had through the reduction of nitrobenzene. While the reaction produces an amine salt, excess NaOH $_{(aq)}$ can be used to deprotonate the salt.

Conditions:　　　Tin (Sn) catalyst, excess concentrated HCl,
heat with reflux. Excess NaOH $_{(aq)}$ later.
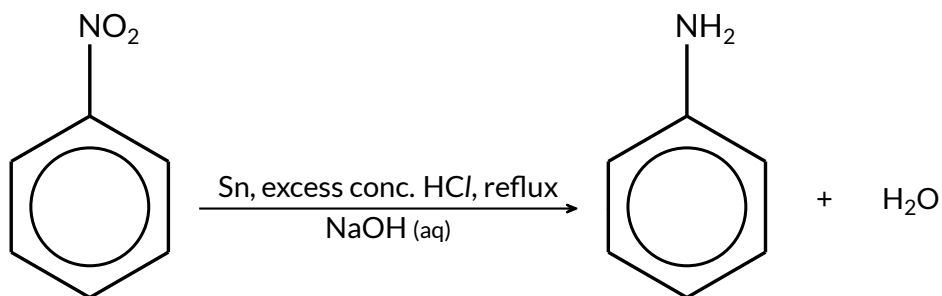
4   Amine Reactions

4.1   Basicity of Amines

Due to the lone pair of electrons on the central N atom in amines, they can act as a weak Brønsted base to accept a proton via a dative bond.

Note that the electron-donating nature of the alkyl groups also increases its nucleophilic character.

4.1.1   Aliphatic Amines

Aliphatic amines can act as a base, and the electron-donating alkyl groups can intensify the electron density on the central nitrogen, increasing the ability for it to attract a proton. Furthermore, once the conjugate acid is formed, the positive charge is stabilised by the donation of electrons.

4.1.2   Phenylamines

Compared to aliphatic amines, phenylamines are far weaker bases. The lone pair on the nitrogen atom is delocalised into the π-system of the benzene ring, reducing the amine's ability to attract a proton.

4.1.3   Effect of Substituents

In what is basically the opposite effect of acids, electron-donating groups for both aliphatic amines and phenylamines will increase their basicity, both by increasing the electron density to attract H^+ ions and by stabilising the conjugate acid.

Conversely, electron-withdrawing groups will reduce electron density and decrease the basicity of the amine.

4.2 Reactions as a Base

Amines can react with both organic acids (phenols and carboxylic acids) as well as mineral acids (eg. H_2SO_4). Due to the formation of ion-dipole interactions, the salts formed are generally soluble in water.

Conditions: Organic or mineral acid, room temperature.

$$R-NH_2 \ + \ HCl \ \longrightarrow \ R-NH_3^+ Cl^-$$
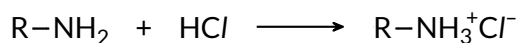
4.3 Nucleophilic Substitution of Alkyl Halides

Similar to how ammonia can be used in a nucleophilic substitution on alkyl halides to produce amines, amines themselves are actually stronger nucleophiles and can, themselves, substitute the halogen atom to form secondary and tertiary amines.

Since more substituted amines are stronger nucleophiles than less substituted ones due to more electron-donating alkyl groups, an excess of the original amine is used to prevent further substitution. This is the same reason why excess NH_3 is used.

Conditions: Ethanolic alkyl halide, heated in sealed tube.
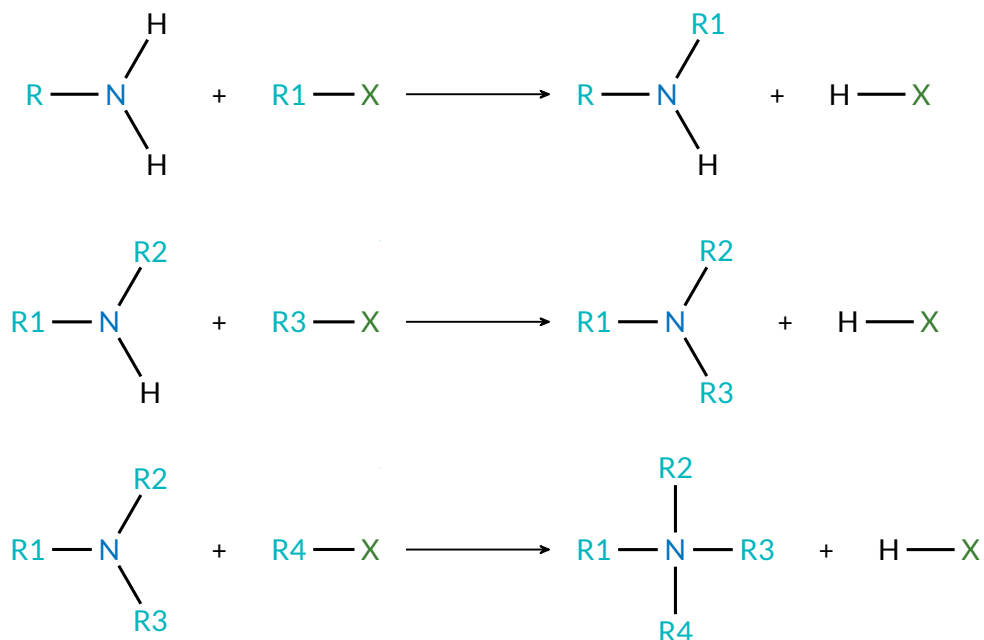
4.4 Nucleophilic Acyl Substitution of Acyl Chlorides

As covered in *acyl chlorides*, amines can undergo nucleophilic substitution with the chlorine atom in an acyl chloride to form amides.

Only primary and secondary amines can react in this manner due to them having unsubstituted hydrogen atoms.

Conditions:　　　　Acyl chloride, amine of choice in excess, room temperature.
Observations:　　　Formation of white fumes of HCl gas.
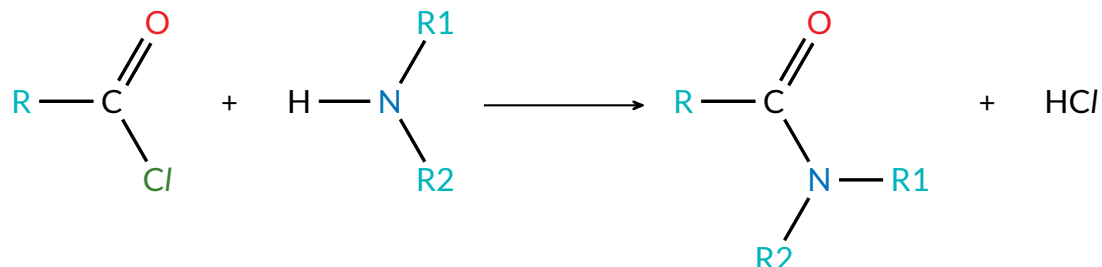
4.5　Electrophilic Addition of Aqueous Br_2

In a similar manner to phenols, the lone pair on the nitrogen atom is delocalised into the benzene ring, and thus increases its electron density. This makes it more susceptible to electrophile attacks, such as those by Br^-, and thus bromine can be electrophilically added to phenylamines without a Lewis acid catalyst.

Conditions:　　　　$Br_{2\,(aq)}$, room temperature.

Observations:　　　*Yellow* $Br_{2\,(aq)}$ decolourises,
　　　　　　　　　　　White precipitate of 2,4,6-tribromophenylamine formed.
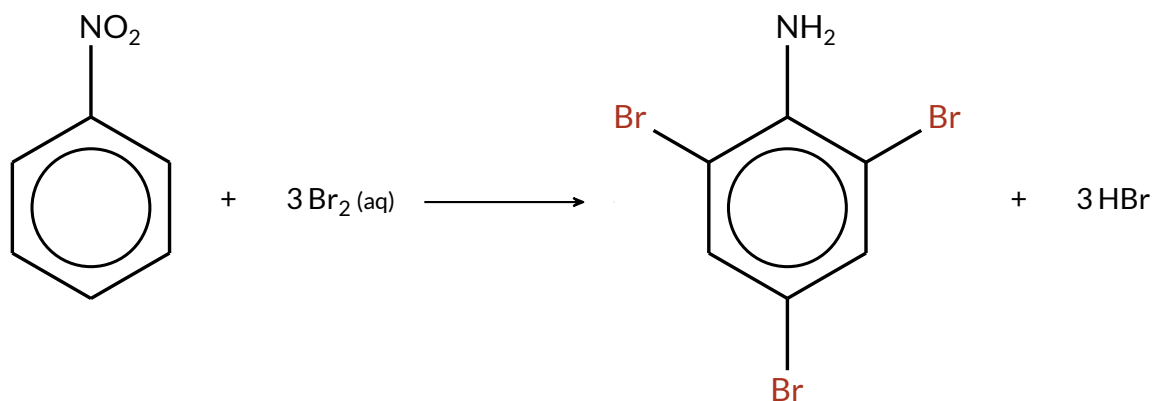
Appendices

Herein lie things that *must* be known, but for brevity are excluded from the main text.

Reaction Mechanisms

1 Electrophilic Addition

Electrophilic Addition the main reaction mechanism for alkenes, and involves an electrophile attacking the electron-rich π-bond of the alkene.

1.1 Markovnikov's Rule

This rule governs the major product when asymmetrical compounds are electrophilically added to alkenes, such as hydrogen halides. It does not apply to symmetrical reactants like Cl_2 or Br_2.

The rule states basically states that when a hydrogen compound with the general form $H-X$ is added to an alkene that is asymmetrical about the double-bond, the hydrogen atom will be added to the carbon with *more* existing hydrogen atoms. Note that *X* can be a halogen, a hydroxide (ie. $H-X$ is H_2O) or some other electronegative species.

The mirror of the rule, used more with the cyclic halonium ion, is that the nucleophile will be added to the more substituted carbon atom.

1.1.1 Addition of H–X to Unsymmetrical Alkenes

The behaviour that Markovnikov's rule predicts can be derived from the fact that adding the non-hydrogen species to the least substituted carbon would result in a less stable intermediate being formed. This can be illustrated using the electrophilic addition of HBr to prop-1-ene (C_3H_6).

If the Markovnikov's rule is *not* followed, the following will take place:
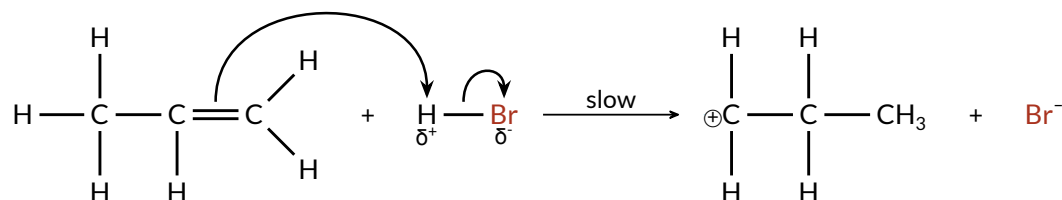
The hydrogen was added to the centre carbon, in violation of Markovnikov's rule.

The positively-charged carbon on the intermediate only has 1 electron-donating alkyl group to stabilise its charge --- compare this to the example below where Markovnikov's Rule is followed:
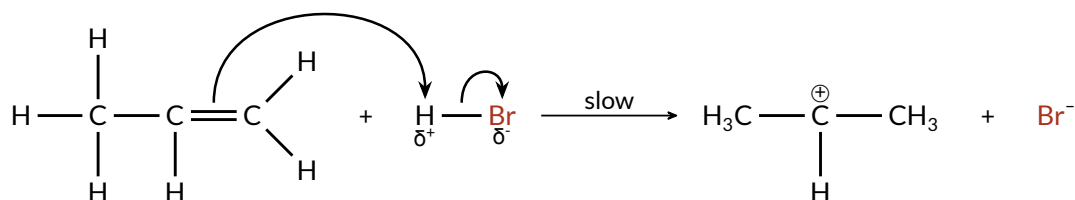
The hydrogen was added to the terminal carbon, following Markovnikov's rule.

In this case, the carbon atom containing the positive charge has 2 electron-donating alkyl groups attached to it, making this intermediate molecule more stable than the one above it.

As such, it is more likely to form, and hence 2-bromopropane will be the *major product*, and 1-bromopropane will be the *minor product*.

1.2 Electrophilic Addition of HX

In this reaction, the hydrogen and halogen atom are added across the double bond of the alkene. The hydrogen halide should be in a gaseous state for this reaction.

Conditions: Gaseous HX (usually HC*l* or HBr).

Step 1
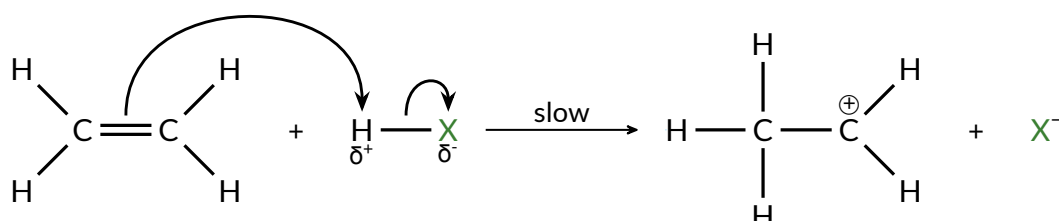
This is the rate-determining step, which involves breaking the π-bond. The polar HX molecule has to approach the electron cloud of the π-bond in the correct orientation (hydrogen-facing), where the π-bond electrons attack the electron deficient, H$^{\delta+}$ atom.

The H−X bond then undergoes heterolytic fission, producing a carbocation intermediate and a halide ion.

Step 2
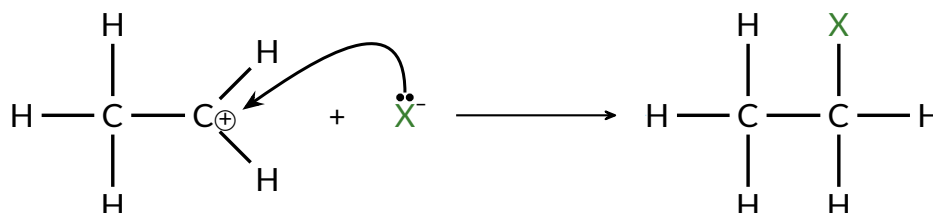
The electron pair arrow points to the plus charge on the carbon, *not* the carbon atom itself.

This is the fast step; the bromide anion acts as a nucleophile, attacking the positively-charged carbocation.

Overall Reaction
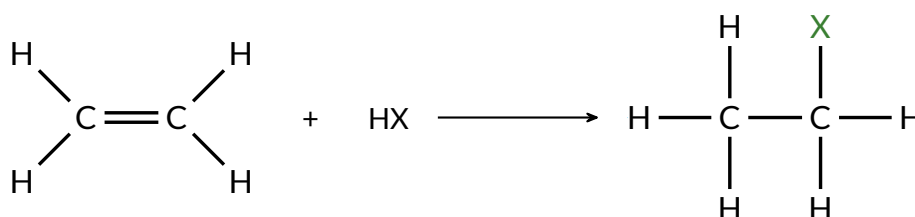
1.3 Electrophilic Addition of X_2

The electrophilic addition of halogens to alkanes does not involve Markovnikov's rule, since it is symmetrical. As the non-polar halogen molecule approaches the high-electron-density π-bond, it is polarised, forming δ⁺ and δ⁻ partial charges. The reaction mechanism involves the formation of a *cyclic halonium ion* --- the double bond breaks, and each carbon forms a single bond with one positive halide ion.

Conditions: No UV Light, gaseous X_2.
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.

Step 1

This initial step is the slow, rate-determining one. The resulting cyclic halonium ion is highly unstable, due to the geometric constraints of having a three-membered ring.
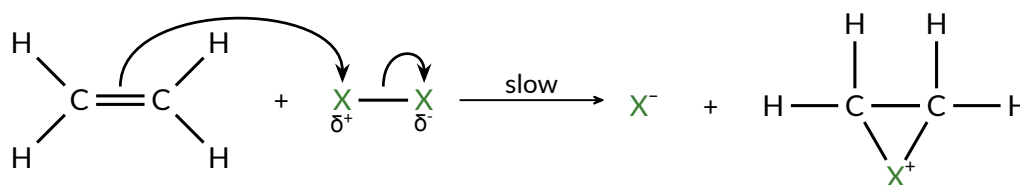
Step 2

In the second, fast step, the negatively-charged bromide ion from the first step attacks the overall positively-charged cyclic bromonium ion. The bromide ion attacks one of the carbons attached to the positive bromide ion, breaking that bond.
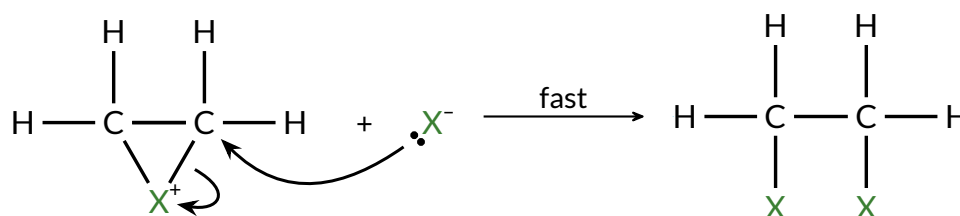
Overall Reaction
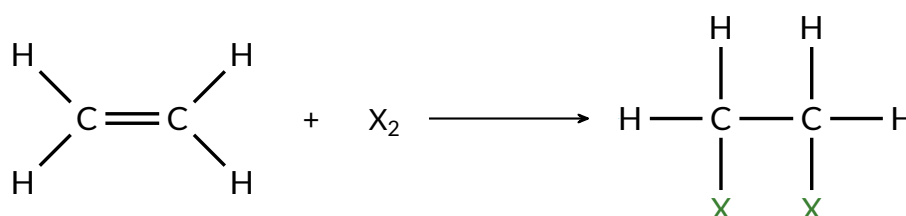
1.4 Electrophilic Addition of Aqueous X_2

The mechanics of this reaction are basically the same as that of the electrophilic addition of Br_2, and the conditions and observations are fairly similar as well.

Also, since the Br atoms are not both added across the double bond in a symmetrical manner, Markovnikov's Rule applies --- the OH group will preferentially attack the carbon that has more stabilising alkyl groups.

Conditions: No UV Light, aqueous Br_2.
Observations: *Yellow* $Br_{2\,(aq)}$ decolourises.

Step 1
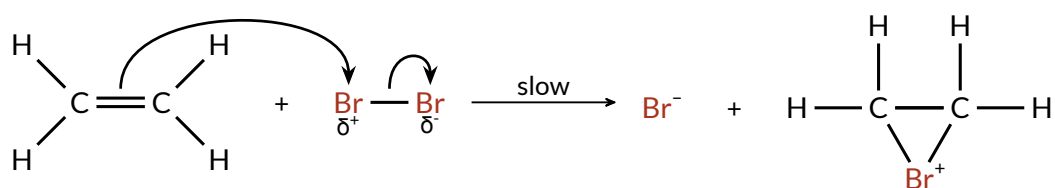
The cyclic bromonium ion is formed.

Step 2

Once the cyclic bromonium ion is formed however, it is susceptible to attack from any and all nucleophiles --- including water, which has lone pairs and is a stronger nucleophile Br^-. Since it is in much higher concentrations than Br^-, the primary product will now have an OH group.
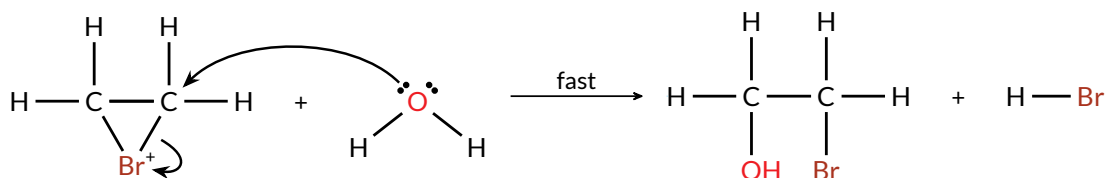
Following Markovnikov's Rule, the OH^- group will attach to the more substituted carbon.

Overall Reaction
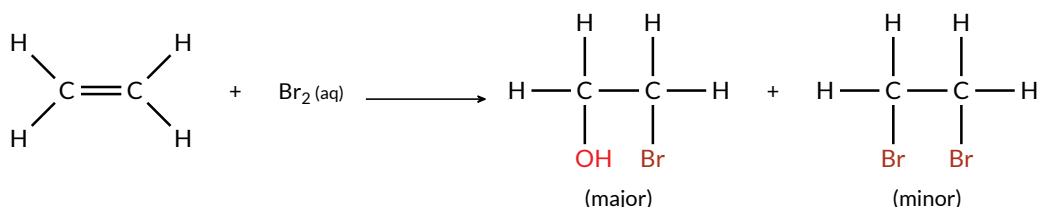
1.5 Electrophilic Addition of Steam (Hydration)

Under certain (usually industrial) conditions, alkenes can react with steam to form alcohols. Since this reaction involves the formation of a carbocation intermediate, the proportion of products will

be governed by Markovnikov's Rule.

Conditions: $300\,°C$, at 70 atm, H_3PO_4 catalyst, *OR*
Concentrated H_2SO_4, H_2O, warming.

Step 0

The first step is to form H_3O^+ (aq). Simply put, it is aqueous H^+.
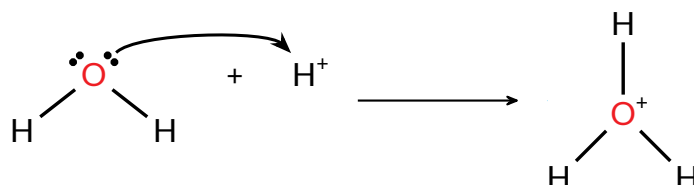
Step 1

The electron-rich double-bond (C=C) is then attacked by one of the H atoms on the H_3O^+, acting as an electrophile.
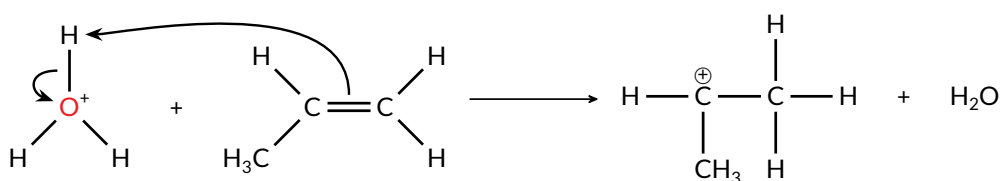
Since the alkene is not symmetrical, there are two product possibilities; hence, the positive charge will be on the carbon atom with more electron donating alkyl groups, in this case carbon 2.

Step 2

One of the lone pairs on the oxygen atom of a water molecule acts as an nucleophile, attacking the newly-formed carbocation. This results in a protonated alcohol, which is basically an alcohol with an extra H atom on the OH group.
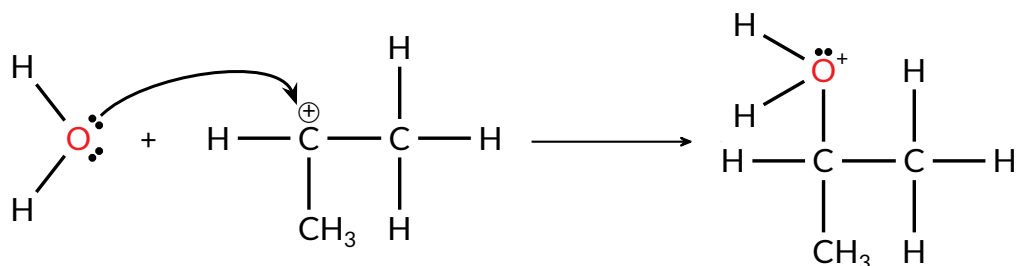
Step 3

The acid catalyst is regenerated as a lone pair on another water molecule's O atom attacks the extra H of the OH group. This forms the alcohol proper, and the H_3O^+ ion.
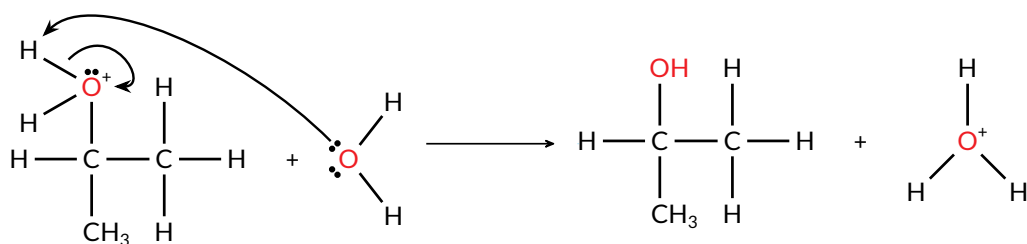
Overall Reaction
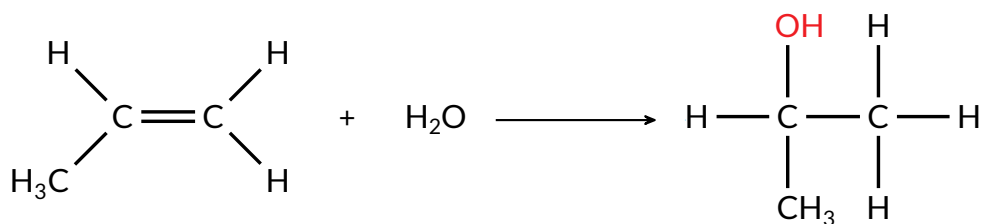
2 Electrophilic Substitution

In general, benzene rings undergo electrophilic substitution, since more bonds cannot be formed.

The delocalised π-system of benzene has a very high electron density, and thus is a prime target for electrophiles, which will substitute the H atoms on the ring. Thus, the most common form of reaction involving benzenes is electrophilic substitution, barring special conditions and requirements.

Step 1

In the first, rate-determining step, the aromaticity of the benzene ring is partially and temporarily broken, disrupted by the attacking electrophile.
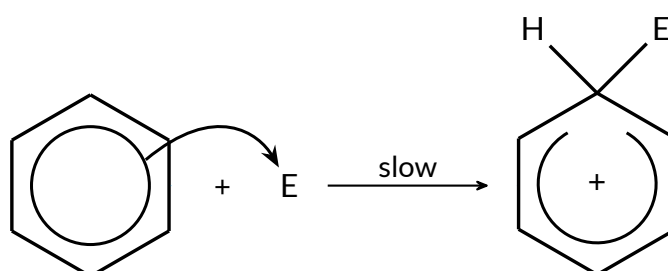
Note that the '+' is drawn in the centre of the ring, not on any one carbon.

Two electrons out of six from the delocalised π-system are used to form the bond between the electrophile, E, and the carbon. Thus, there is a positive charge on the carbon; due to the delocalised nature of the π-system however, this positive charge is delocalised across *all 6 carbons*, making it much more stable than a simple carbocation.

However, the activation energy for this step is still large, and only strong electrophiles are able to attack the benzene ring without catalysts.

Step 2

Next, a nucleophile ($\overset{..}{:}Nu^-$ in this example) attacks the hydrogen attached to the hydrogen on the carbon atom, restoring the aromaticity of the benzene ring. The new substituent is now in place, and the two electrons in the C−H bond are returned to the π-system.
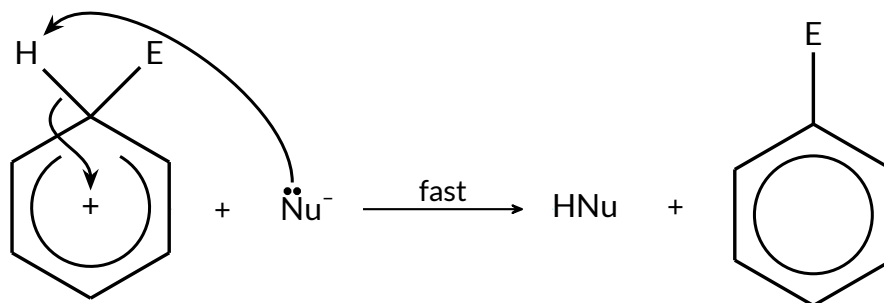
Note that the arenium ion (which is the partially delocalised benzene) has 5 sp^2 carbons, and one sp^3 carbon. This results in a disruption of the planar structure of benzene --- it is restored once the substitution is completed.

2.1 Nitration of Benzene

The nitration of benzene involves the substitution of one of the H atoms on the benzene with a nitro ($-NO_2$) group. It has a number of specific requirements:

Conditions: Concentrated HNO_3, concentrated H_2SO_4 catalyst.
Constant temperature of $50\,°C$.

Observations: *Pale yellow* oily liquid, nitrobenzene.

A New Electrophile

Since H_2SO_4 is a stronger acid than HNO_3, it donates a proton to HNO_3, forming H_2O, HSO_4^-, and NO_2^+, the electrophile. Next, another molecule of H_2SO_4 then forms H^+ (aq), or H_3O^+. The overall equation is as such:

$$2\,H_2SO_4 \;+\; HNO_3 \longrightarrow NO_2^+ \;+\; H_3O^+ \;+\; 2\,HSO_4^-$$
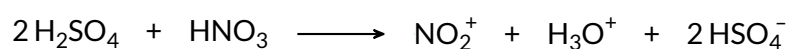
The catalyst H_2SO_4 is restored in a later step.

The π-Electrons Strike Back

Now that the electrophile NO_2^+ has been formed, it is attacked by the π-system. As with all electrophilic substitutions, this involves the breaking of the aromatic system, and is the slow step. The mechanism follows the general mechanism outlined above.
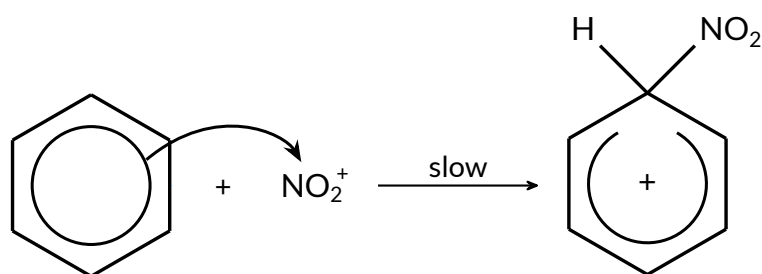
Return of the Aromaticity

The HSO_4^- intermediate acts as a nucleophile and attacks the H atom bonded to the benzene intermediate. This restores both the π-system of the benzene ring, as well as the catalyst, H_2SO_4.
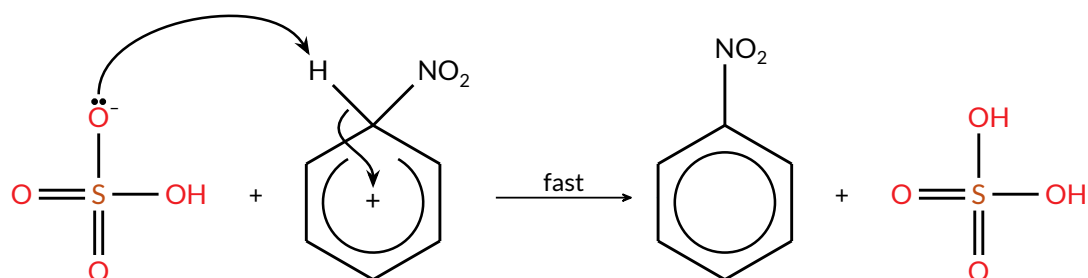
The Product Awakens
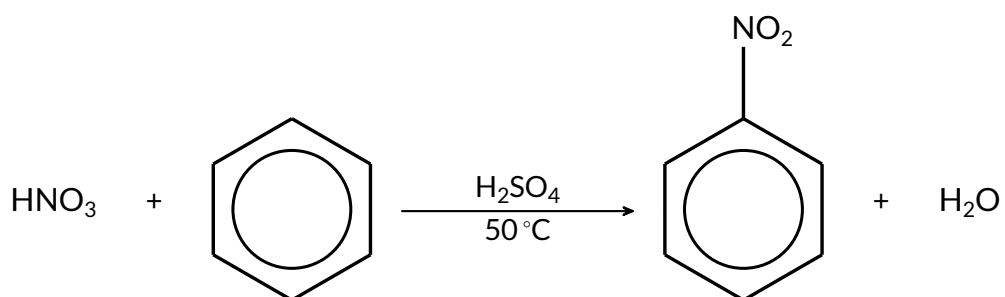
2.2 Halogenation of Benzene

Halogenation of benzene requires rather specific conditions, such as anhydrous $FeBr_3$ or $FeCl_2$ (for a reaction with bromine and chlorine respectively), and a warm environment.

Aluminium-based analogues of these catalysts ($AlBr_3$, $AlCl_3$) can also be used, as can pure filings of the metal, in which case the catalyst will be generated *in-situ* ($2\,Fe_{(s)} + 3\,Br_{2\,(l)}$ -> $2\,FeBr_3$).

Conditions: Warm, anhydrous $FeBr_3$, $AlBr_3$, or Fe / Al filings (for bromine),
Anhydrous $FeCl_3$, $AlCl_3$, or Fe / Al filings (for chlorine)

Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
Formation of white fumes of HX gas.

2.2.1 Catalysts

Lewis acid catalysts must be used, since the $Br-Br$ and $Cl-Cl$ molecules are only instantaneously polar (instantaneous dipole moments). As such, they are nowhere near strong enough to attack the benzene system on their own.

Indeed, this can be used to distinguish between alkenes and benzenes, since the former does not require a catalyst for addition of halogens.

Furthermore, the entire reaction must be conducted in the absence of water; the reaction mechanism for the lewis-acid catalyst involves accepting a lone pair, the lone pair on water can, and will, in sufficient concentrations, destroy the catalyst.

2.2.2 Reaction Mechanism

Generation of Electrophile

The reaction below uses Iron (III) chlorine ($FeCl_3$) as an example, adding Cl to benzene, and this reaction mechanism applies to aluminium-based catalysts as well.

$$FeBr_3 \ + \ Br_2 \ \longrightarrow \ Br^+ \ + \ FeBr_4^-$$
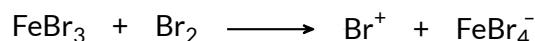
The catalyst is $FeBr_4^-$, and the *electrophile* is Br^+

Formation of Benzene Intermediate

Again, this mechanism is similar in nature to electrophilic substitution in general. Now, the electrophile (Br^+) attacks the π-system, forming the arenium ion.
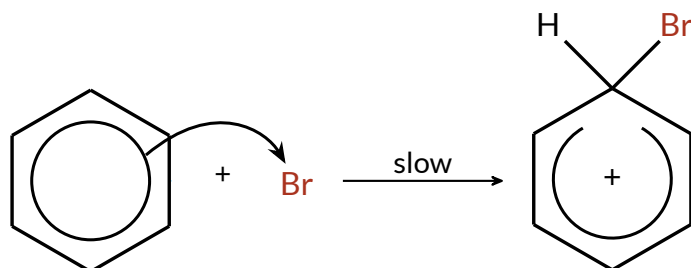
Restoration of π-system and Aromaticity

In the final step, the $FeBr_4^-$ acts as a nucleophile, attacking the H atom attached to the benzene intermediate. This regenerates the catalyst $FeBr_3$, and also forms HBr.
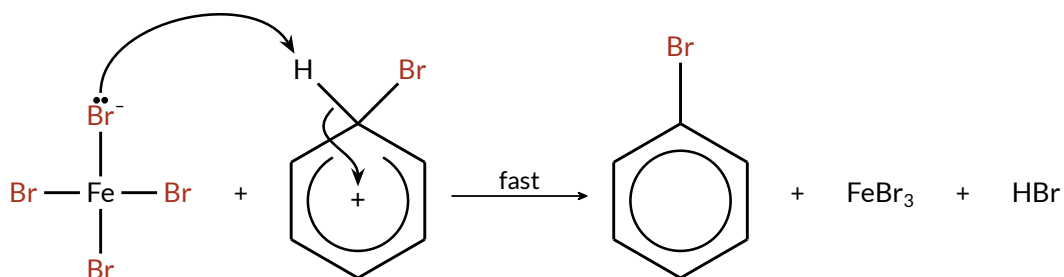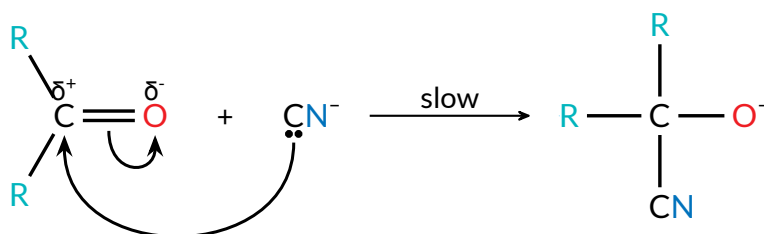

Overall Reaction
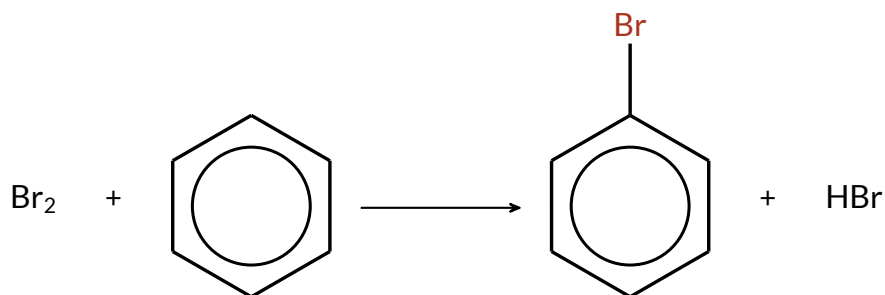
3   Nucleophilic Addition

Due to the electronegativity of the oxygen atom, the electron density is drawn towards it. Thus, the carbon atom is able to be attacked by electrophiles due to its partial positive charge.

Note that aldehydes will be more reactive than ketones in nucleophilic addition, since they only have one electron-donating alkyl group on the central carbon, whereas ketones have two alkyl groups that are able to inductively donate electrons to stabilise the positive charge, slightly reducing reactivity.

The mechanism is a two-step mechanism with the slow step as the first step. Here, the nucleophilic addition of CN to a carbonyl will be illustrated.

Step 1

Here, the central carbon is attacked by the nucleophile. This also serves to repel the electrons in the π-bond towards the electronegative O atom, forming a stable alkoxide anion.

Step 2

Now, the alkoxide ion attacks an undissociated HCN molecule, protonating itself and regenerating the CN^- nucleophile.

127
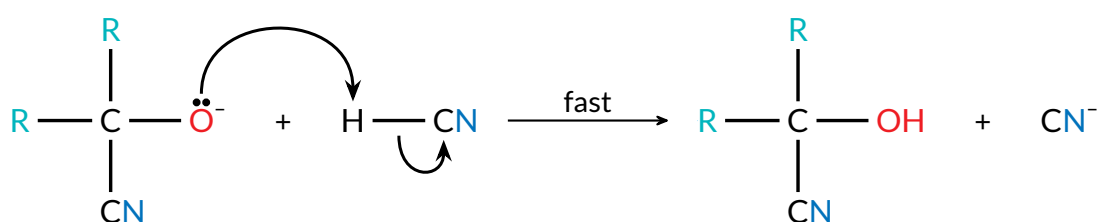
Overall Reaction
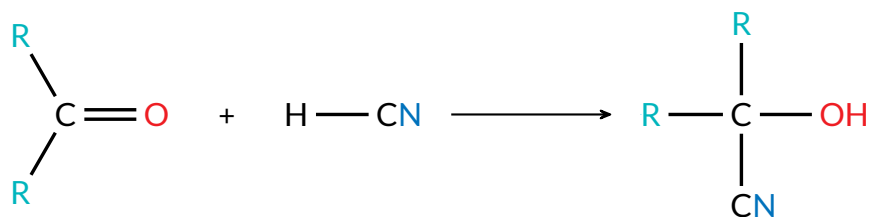
3.1 Stereoisomerism of Product

Since the carbonyl is trigonal planar, the nucleophile can attack from either the top or bottom side, with equal probability. Hence, if the product formed is chiral, the resulting solution will be a *racemic mixture*.
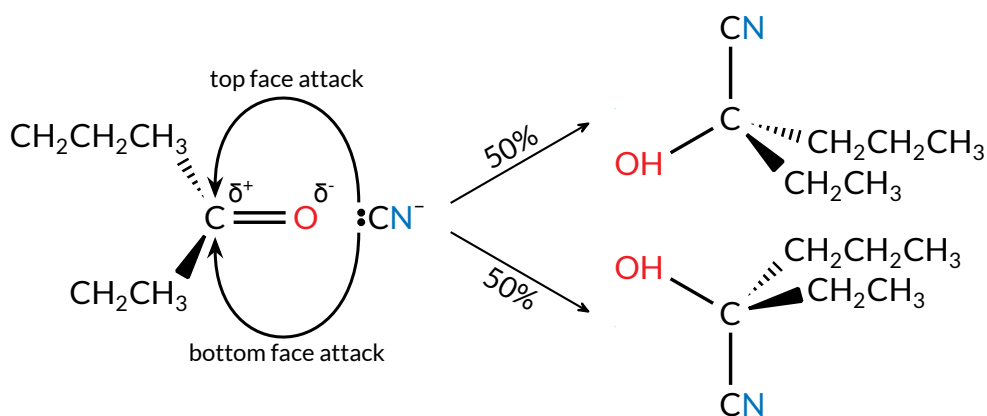
4 Nucleophilic Substitution

Due to the high relatively electronegativity of the halogen atom attached to the carbon atom, the carbon atom is *electron-deficient*, which makes it more susceptible to attacks from nucleophiles (*electron-rich*), and as such halogenoalkanes are fairly reactive.

There are two primary mechanisms of nucleophilic substitution --- single-step and two-step reactions. Generally, primary halogenoalkanes (molecules with 1 or 0 alkyl groups attached to the halogen-containing carbon) react via a one-step mechanism, while tertiary halogenoalkanes react via a two-step mechanism. Secondary halogenoalkanes can react via either mechanism, depending on the specific molecule.

The primary differentiating factor is the size of the substituents on the central carbon --- larger groups will hinder S_N2 substitution, forcing an S_N1 reaction.

Either way, the overall reaction is as such:
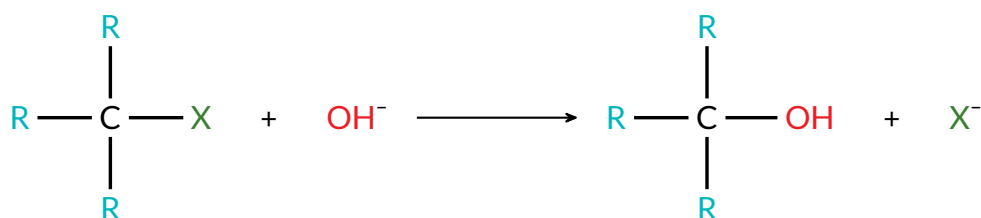
4.1 Nucleophilic Substitution (S_N2, single-step)

The nucleophilic substitution of CH_3CH_2Br by OH^- is a one-step reaction. Take note that S_N2 is a *one*-step reaction --- it is S_N2 because *two* molecules are involved in the slow (only) step.

<div align="center">transition state</div>
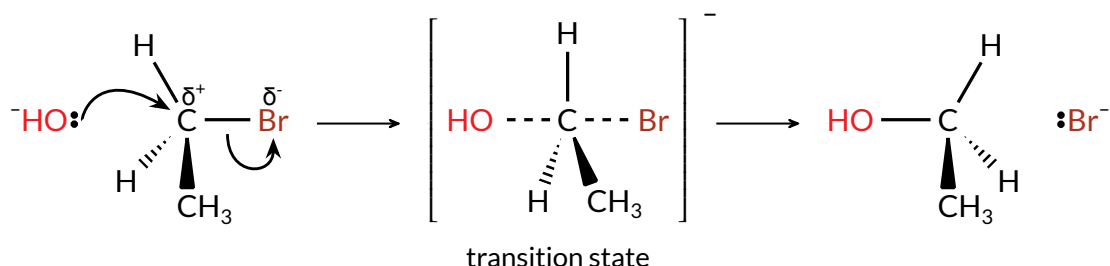
Due to the difference in electronegativity between the C and Br atoms, the C−Br bond is polar. Thus, nucleophiles will be attracted towards the partially-positive carbon atom. They attack from the side opposite the leaving atom (Br in this case) due to spatial constraints.

As the nucleophile attacks, it donates a lone pair to the carbon atom to stabilise it, forming a bond. At the same time, this weakens the C−Br bond, and it begins to break. At this stage, the *transition state* is formed, which is an unstable, activated complex where bond-breaking and bond-forming occur simultaneously --- this is a *one-step* mechanism.

4.1.1 Stereoisomerism of Product

Note that the chirality of the molecule will be *inverted*, if it is chiral. Imagine the attacking nucleophile 'pushing' the other groups away from itself.
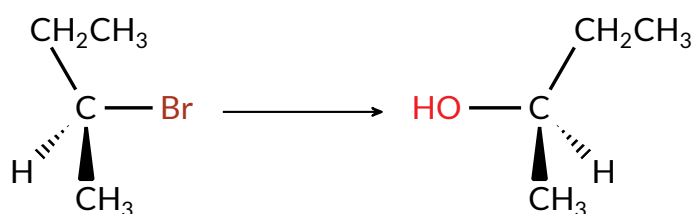
4.1.2 Reaction Pathway

Since this is a single-step reaction, there is one activation energy step, and the energy profile diagram looks like this:
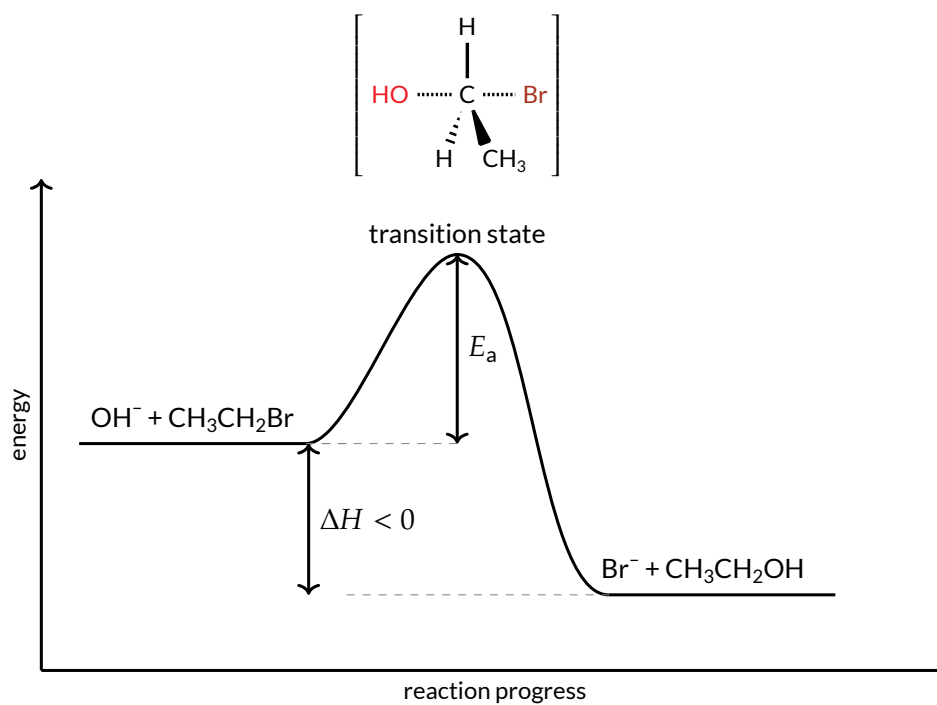
4.2 Nucleophilic Substitution (S_N1, two-step)

The S_N1 reaction is a *two-step* reaction, because larger groups attached to the central carbon often hinder the direct attack of nucleophiles, and thus require the formation of a carbocation. Only one molecule is involved in the slow (first) step, hence it is a unimolecular reaction.

Again, the reaction hinges on the polar $C-Br$ bond, due to the differences in electronegativity.

Step 1
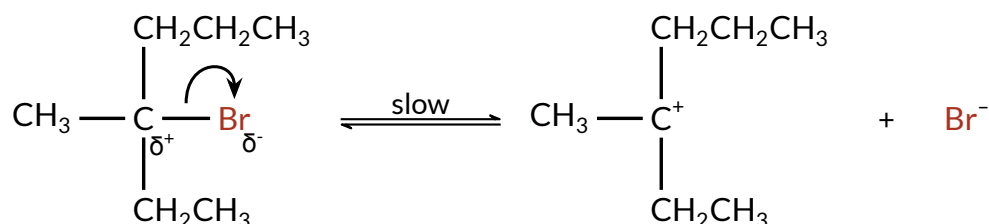
The $C-Br$ bond undergoes heterolytic fission, giving a carbocation intermediate, and a bromide ion. The reaction is more feasible due to the 3 electron-donating alkyl groups that stabilise the positive charge on the carbocation intermediate, which would not be possible in a primary alcohol.

Step 2
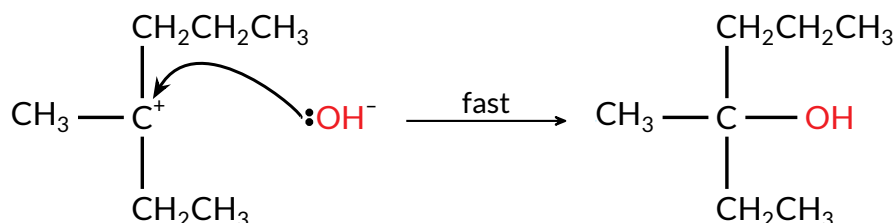
The carbocation intermediate is now attacked by the OH^- ion, forming the product.

4.2.1 Stereoisomerism of Product

Since the carbocation is trigonal planar (wrt. the central carbon), the nucleophile can attack from both sides of the carbocation, with equal probability. Hence, if the product formed is chiral, the resulting solution will be a *racemic mixture*.
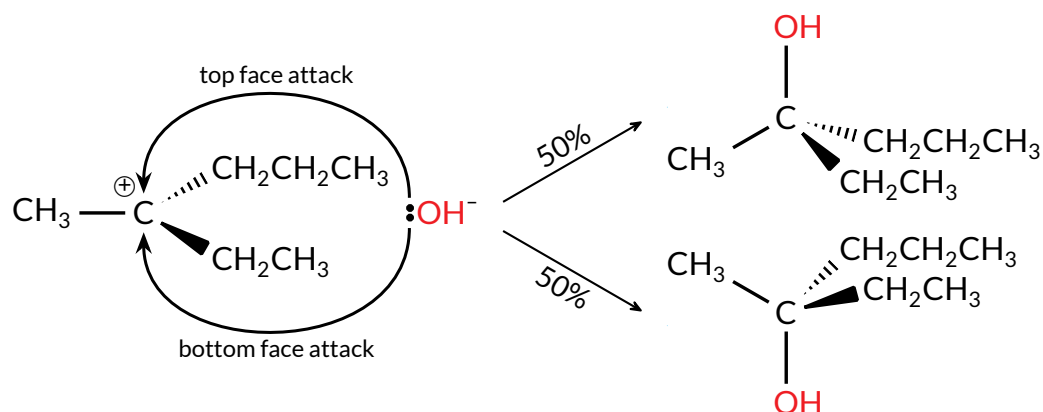
4.2.2 Reaction Pathway

Since this is a two-step reaction, there are two activation energies that must be overcome, and isolatable intermediates (the carbocation and bromide ion).
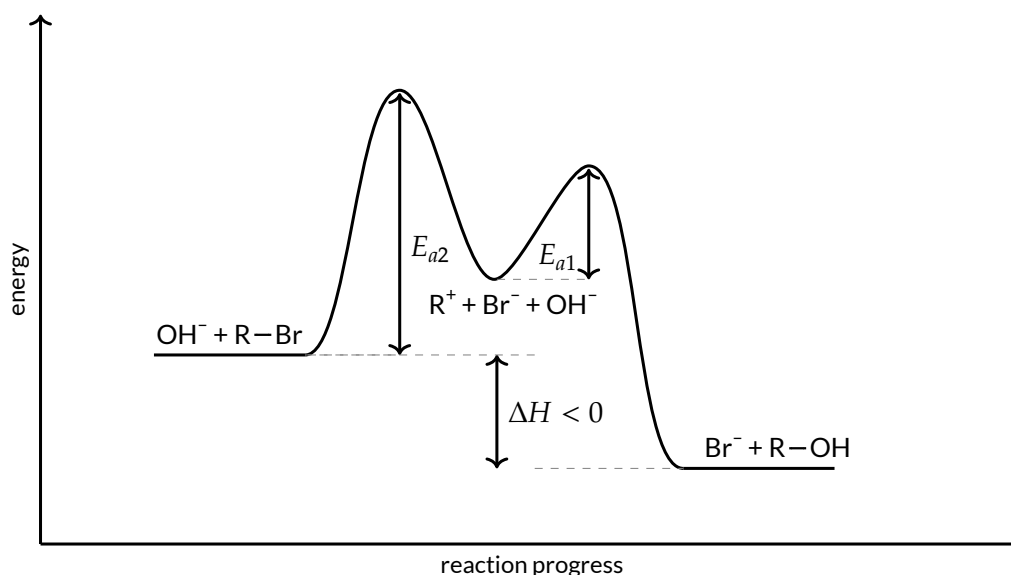
APPENDIX B

Grand List of Reactions

1   Alkanes

1.1   Free Radical Substitution

Multisubstitution and isomerism of products is possible.

Conditions: UV Light, Br_2 / Cl_2 gas
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
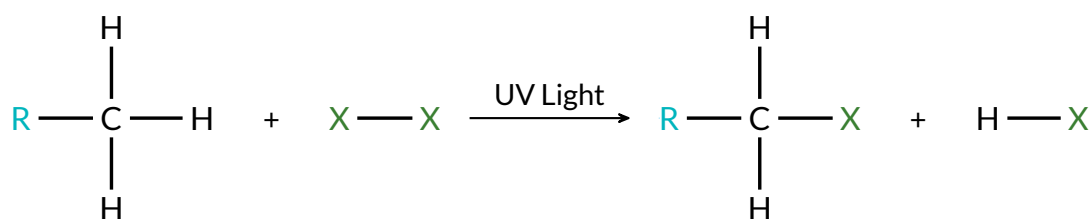
1.2   Combustion

This generally applies to hydrocarbons.

$$C_xH_y \;+\; x + \tfrac{y}{4}\,O_2 \longrightarrow x\,CO_2 \;+\; \tfrac{y}{2}\,H_2O$$
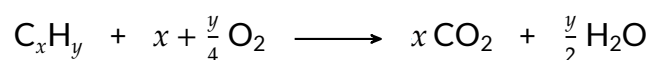
2   Alkenes

2.1   Electrophilic Addition of X_2

Conditions: No UV Light, gaseous X_2.
Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
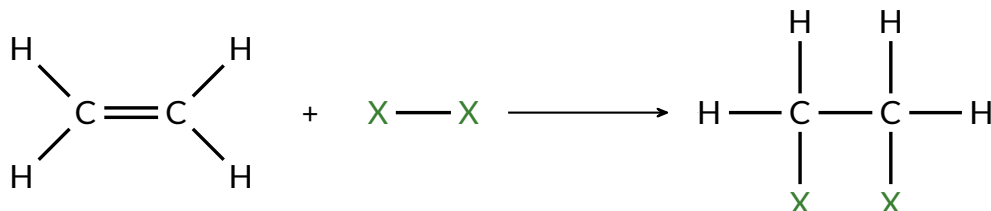
2.2   Electrophilic Addition of HX

Note that Markovnikov's Rule applies.

Conditions: Gaseous HX (usually HC*l* or HB*r*).
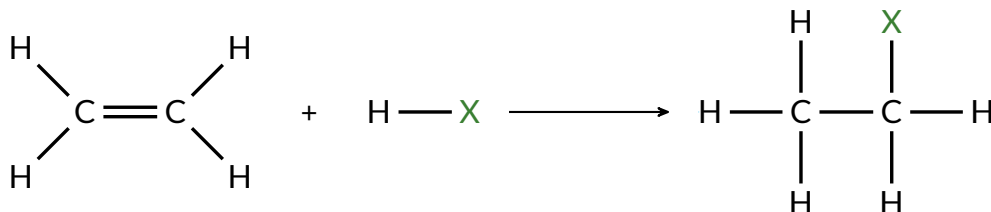
2.3   Electrophilic Addition of Aqueous Br_2

Note that Markovnikov's Rule applies.

Conditions: No UV Light, aqueous Br_2.
Observations: *Yellow* Br_2 (aq) decolourises.
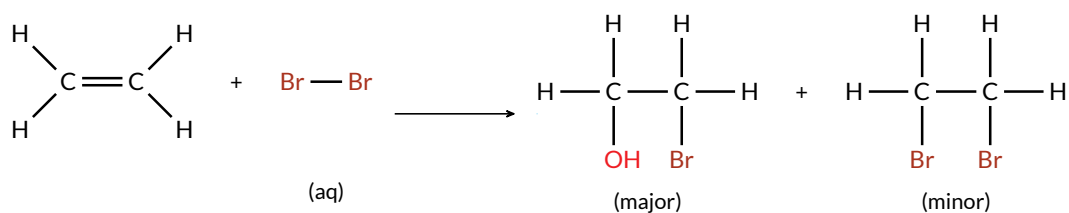
2.4 Electrophilic Addition of Steam (Hydration)

Conditions: 300 °C, at 70 atm, H_3PO_4 catalyst, *OR*
                   Concentrated H_2SO_4, H_2O, warming.
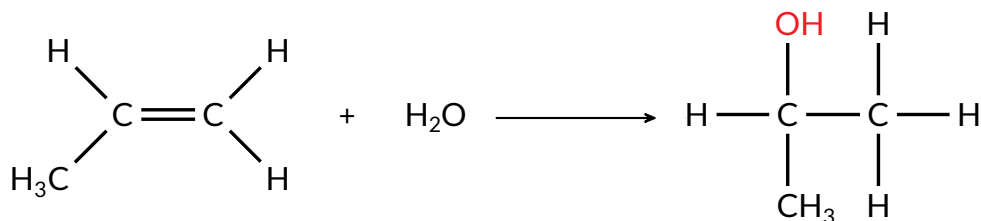
2.5 Reduction (Hydrogenation)

Conditions: High temperature and pressure, Ni, Pd or Pt catalyst.
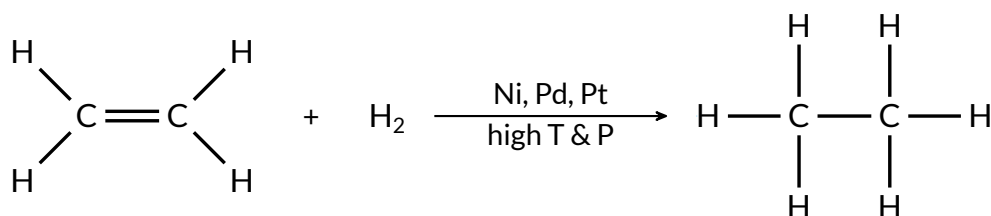
2.6 Mild Oxidation

2.6.1 Acidic Medium

Conditions: Cold $KMnO_4$, acid (H_2SO_4).
Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+}.
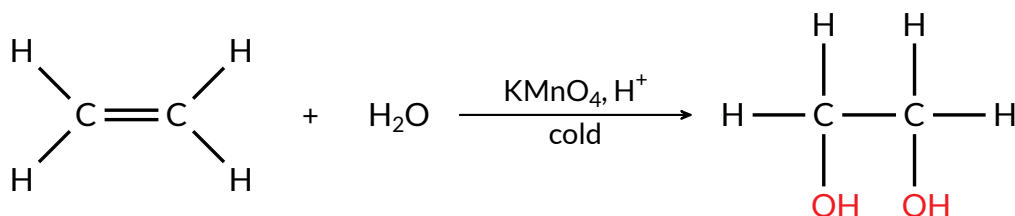
2.6.2 Alkaline Medium

Conditions: Cold $KMnO_4$, aqueous base (NaOH).
Observations: *Purple* $KMnO_4$ decolourises, forming a *brown* precipitate of MnO_2.
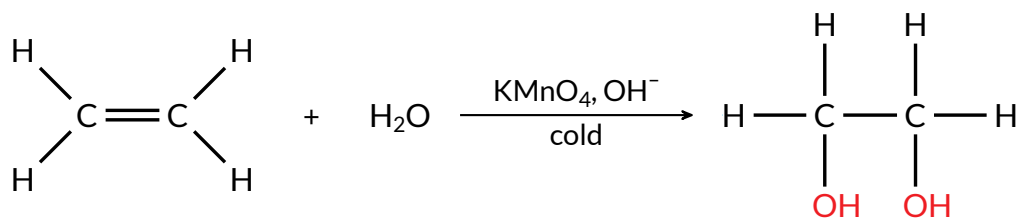
2.7 Strong Oxidation (Oxidative Cleavage)

Conditions: $KMnO_4$, dilute H_2SO_4, heat.
Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+}.

Substituents	Structure	Product
0		$CO_2 + H_2O$
1		
2		

3   Arenes

3.1   Electrophilic Substitution of NO_2 (Nitration)

The NO_2 substituent is 3-directing.

Conditions: Concentrated HNO_3, concentrated H_2SO_4 catalyst.
Constant temperature of 50 °C.

Observations: *Pale yellow* oily liquid, nitrobenzene.

$$HNO_3 \quad + \quad \text{C}_6\text{H}_6 \quad \xrightarrow[\text{50 °C}]{H_2SO_4} \quad \text{C}_6\text{H}_5\text{NO}_2 \quad + \quad H_2O$$
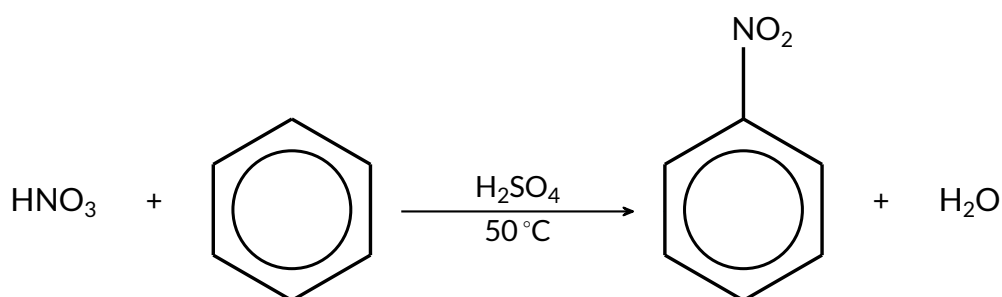
3.2   Electrophilic Substitution of Halogens

The halogen substituent is 2,4-directing.

Conditions: Warm, anhydrous $FeBr_3$, $AlBr_3$, or Fe / Al filings (for bromine),
Anhydrous $FeCl_3$, $AlCl_3$, or Fe / Al filings (for chlorine)

Observations: *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.
Formation of white fumes of HX gas.

$$Br_2 \quad + \quad \text{C}_6\text{H}_6 \quad \longrightarrow \quad \text{C}_6\text{H}_5\text{Br} \quad + \quad HBr$$
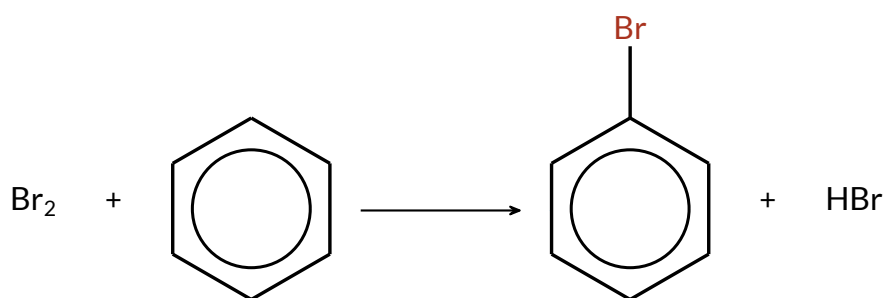
3.3 Side-chain Oxidation of Alkylbenzenes

Conditions: Heat, $KMnO_4$, dilute acid or alkali.

Observations: *Purple* $KMnO_4$ decolourises, forming Mn^{2+} (*acid*), or forms *brown* precipitate of MnO_2 (*alkali*).
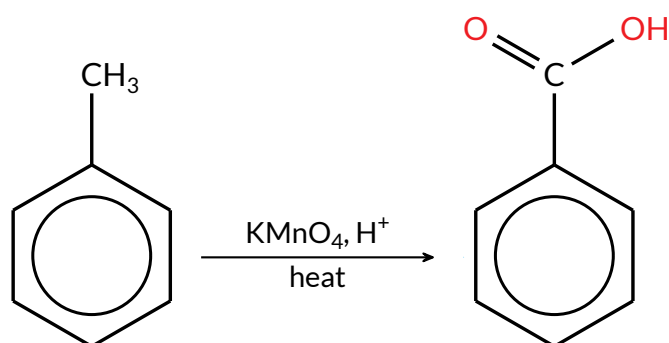
If the alkyl chain is 2-long, (ie. ethylbenzene), then CO_2 will be formed from the oxidation of the second carbon, in addition to benzoic acid.
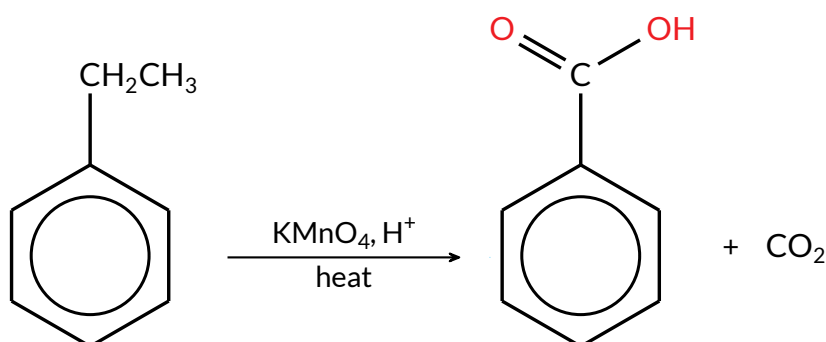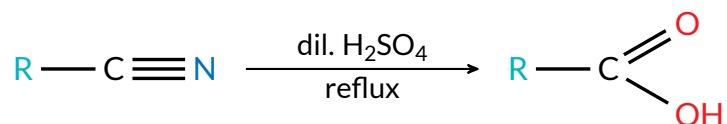

If the chain is 3 or longer, then the rest of the chain (apart from the first) will be oxidised to form a carboxylic acid.
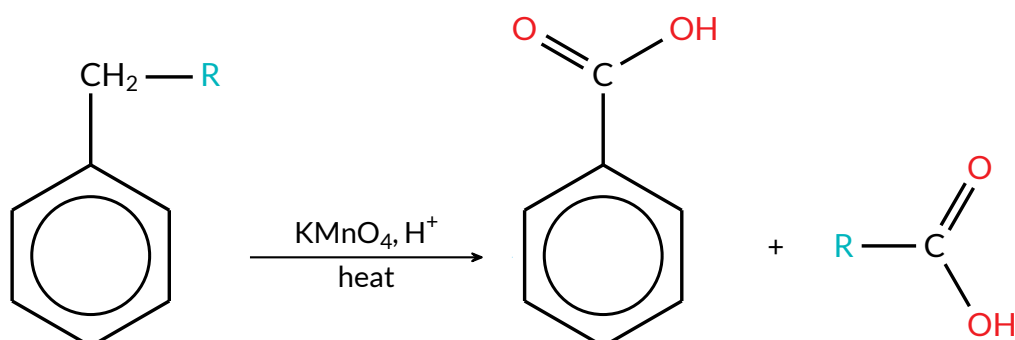
4   Nitriles

4.1   Acid Hydrolysis

Conditions: Dilute H_2SO_4 or HC*l*, heat.

R—C≡N $\xrightarrow[\text{reflux}]{\text{dil. } H_2SO_4}$ R—C(=O)OH

4.2   Alkaline Hydrolysis

Conditions: Dilute NaOH, heat.

R—C≡N $\xrightarrow[\text{reflux}]{\text{dil. NaOH}}$ R—C(=O)O⁻Na⁺
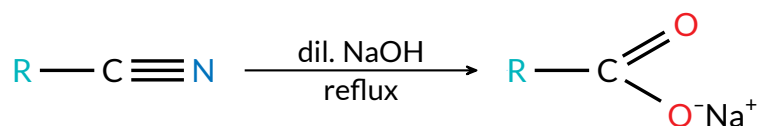
4.3   Reduction to Amines

Conditions: LiA*l*H$_4$ in dry ether (diethyl ether), *OR*
$H_{2\,(g)}$, Ni catalyst, high temperature and pressure.

R—C≡N $\xrightarrow[\text{[H]}]{\text{reduction}}$ R—CH$_2$—NH$_2$
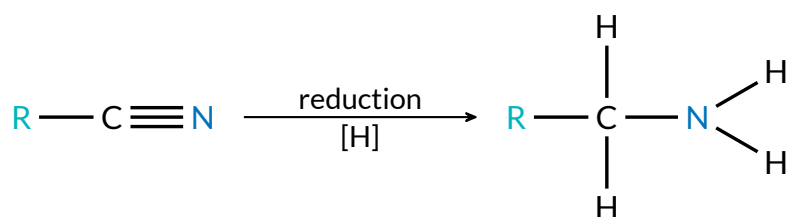
5 Alkyl Halides

5.1 Nucleophilic Substitution of OH

Conditions: Aqueous NaOH or KOH, heat.

$$R - X \ + \ OH^- \ \longrightarrow \ R - OH \ + \ X^-$$
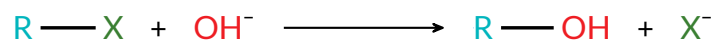
5.2 Nucleophilic Substitution of NH$_2$

Note that multisubstitution is possible, hence the use of excess NH$_3$.

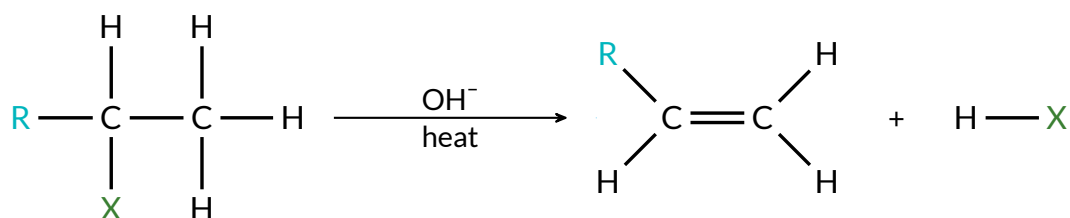**Conditions:**   Ethanolic concentrated NH$_3$, heat in sealed tube.

$$R - X \ + \ NH_3 \ \longrightarrow \ R - NH_2 \ + \ HX$$
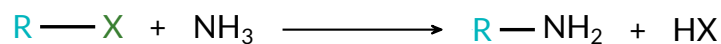
5.3 Nucleophilic Substitution of CN

Conditions: Ethanolic KCN, heat with reflux.

$$R - X \ + \ CN^- \ \longrightarrow \ R - CN \ + \ X^-$$
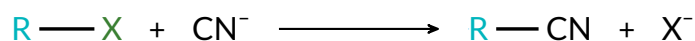
5.4 Elimination of HX

Conditions: Ethanolic KOH or NaOH, heat.

6   Alcohols

6.1   Nucleophilic Acyl Substitution (Esterification)

6.1.1 With Carboxylic Acids

Conditions: Carboxylic acid and alcohol,
Several drops of concentrated H_2SO_4, heated under reflux.

$$R1-C(=O)OH \ + \ H-O-R2 \ \underset{reflux}{\overset{conc. \ H_2SO_4}{\rightleftharpoons}} \ R1-C(=O)O-R2 \ + \ H_2O$$
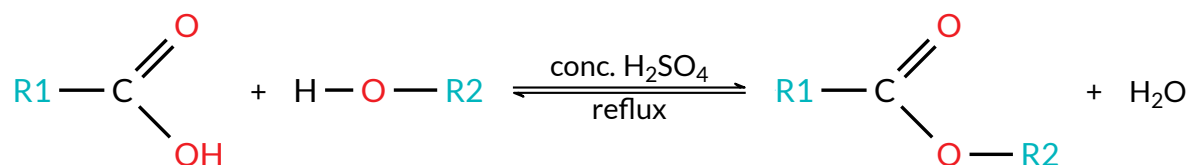
6.1.2 With Acyl Chlorides

Conditions: Acyl chloride and alcohol,
Room temperature.

$$R1-C(=O)Cl \ + \ H-O-R2 \ \longrightarrow \ R1-C(=O)O-R2 \ + \ HCl$$

6.2   Nucleophilic Substitution of Halogens

6.2.1   Chlorine (Cl_2 Substitution)

Phosphorus Pentachloride (PCl$_5$)

Conditions: Solid PCl$_5$, room temperature.
Observations: Formation of white fumes of HCl gas.

$$R - OH \ + \ PCl_5 \ \longrightarrow \ R - Cl \ + \ POCl_3 \ + \ HCl$$
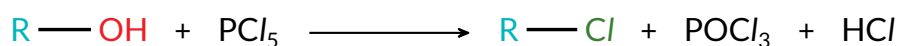
Phosphorus Trichloride (PCl$_3$)
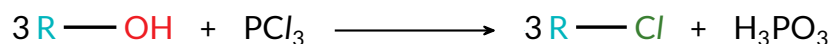
Conditions: Solid PCl$_3$, room temperature.

$$3\,R - OH \ + \ PCl_3 \ \longrightarrow \ 3\,R - Cl \ + \ H_3PO_3$$

Thionyl Chloride (SOCl$_2$)

Conditions: Warm, liquid SOCl$_2$.

Observations: Formation of colourless, pungent SO$_2$ gas,
white fumes of HCl gas.

$$R - OH \ + \ SOCl_2 \ \longrightarrow \ R - Cl \ + \ SO_2 \ + \ HCl$$
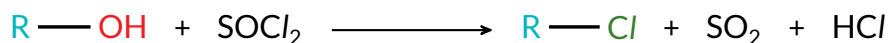
HCl with Tertiary Alcohols

Conditions: Concentrated HCl $_{(aq)}$ / gaseous HCl, *OR*
Solid NaCl, concentrated H$_2$SO$_4$, heat.

$$R - OH \ + \ HCl \ \longrightarrow \ R - Cl \ + \ H_2O$$
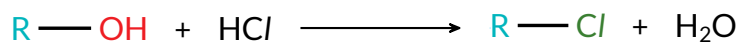
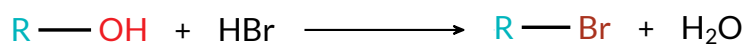HCl can be prepared *in-situ* with NaCl and H$_2$SO$_4$.

HC*l* with Primary and Secondary Alcohols

Conditions: Concentrated HC*l* (aq) / gaseous HC*l*.
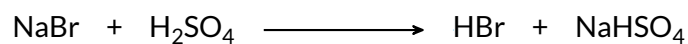Anhydrous ZnC*l*$_2$ catalyst, heat.

$$R \text{—} OH \ + \ HCl \ \longrightarrow \ R \text{—} Cl \ + \ H_2O$$
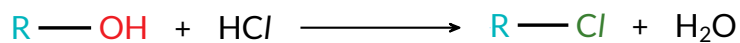
6.2.2 Bromine (Br$_2$ Substitution)

Hydrogen Bromide (HBr)

Conditions: Gaseous HBr.

$$R \text{—} OH \ + \ HBr \ \longrightarrow \ R \text{—} Br \ + \ H_2O$$

Conditions: Solid NaBr, concentrated H$_2$SO$_4$, heat.

$$NaBr \ + \ H_2SO_4 \ \longrightarrow \ HBr \ + \ NaHSO_4$$

Creation of HBr.

Phosphorous Tribromide (PBr$_3$)

Conditions: Liquid PBr$_3$, *OR*
Liquid Br$_2$, red phosphorous, heat.

$$3\,R \text{—} OH \ + \ PBr_3 \ \longrightarrow \ 3\,R \text{—} Br \ + \ H_3PO_3$$

$$2\,P \ + \ 3\,Br_2 \ \longrightarrow \ 2\,PBr_3$$
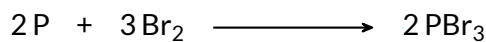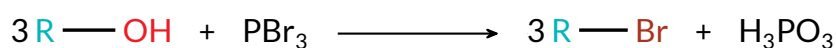
In-situ formation of PBr$_3$.

6.2.3 Iodine (I_2 Substitution)

Phosphorous Triiodide (PI_3)

Conditions: Liquid PI_3, *OR*
Solid I_2, red phosphorous, heat.

$$3\ R-OH\ +\ PI_3\ \longrightarrow\ 3\ R-I\ +\ H_3PO_3$$
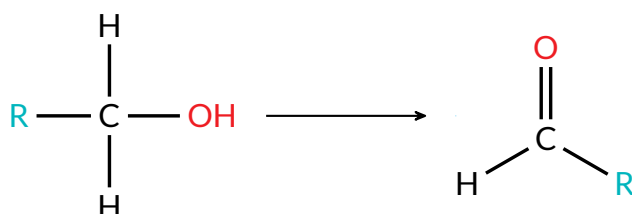
$$2\ P\ +\ 3\ I_2\ \longrightarrow\ 2\ PI_3$$
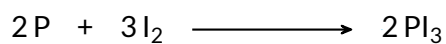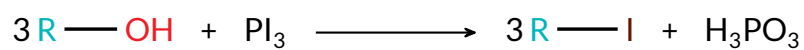
In-situ formation of PI_3.

6.3 Oxidation

6.3.1 Controlled Oxidation of Primary Alcohols

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4,
heat with immediate distillation.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed).

6.3.2 Complete Oxidation of Primary Alcohols

Oxidising aldehydes gives the same result.

Conditions: $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4,
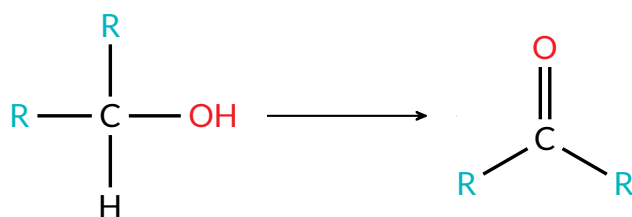heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed).
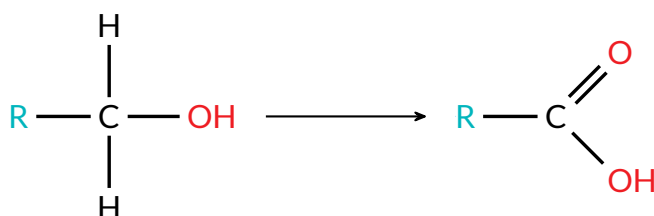
6.3.3 Oxidation of Secondary Alcohols

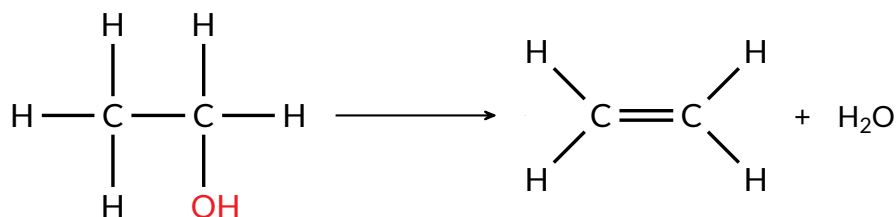**Conditions:** $K_2Cr_2O_7$ with dilute H_2SO_4, *OR* $KMnO_4$ with dilute H_2SO_4, heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)

6.4 Dehydration (Elimination of H_2O)
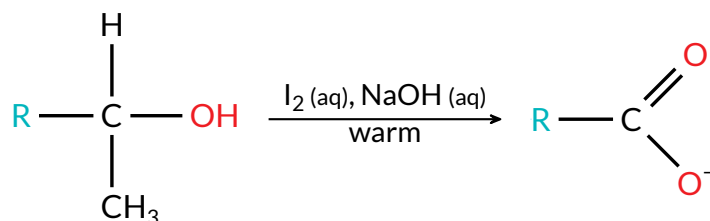
Note that Zaitsev's Rule applies.

Conditions: Excess concentrated H_2SO_4, $170\,°C$, *OR*
Al_2O_3, heat.

6.5 Tri-iodomethane Formation

Conditions: I_2 (aq), NaOH (aq), warmed.
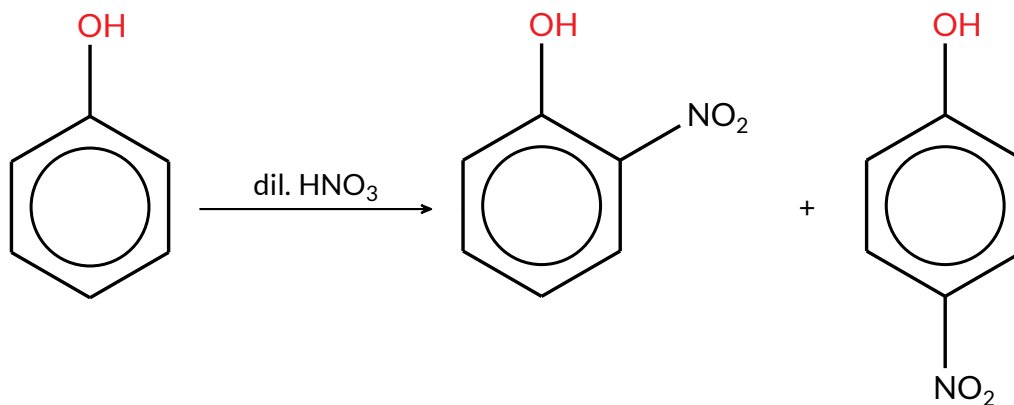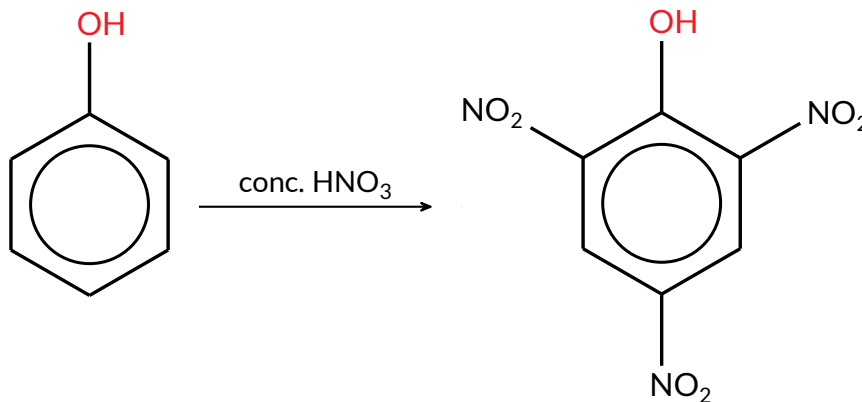**Observations:** *Yellow* precipitate of CHI_3 is formed.

7 Phenols

7.1 Electrophilic Substitution of NO_2 (Nitration)

Concentrated HNO_3 can be used to achieve tri-substitution, `moderately concentrated' for di-substitution, and dilute HNO_3 for mono-substitution.

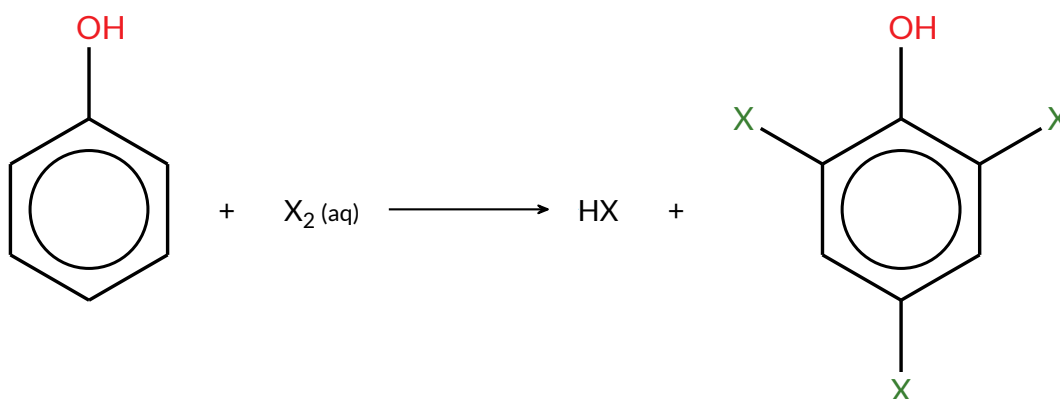**Conditions:** Dilute HNO_3 (aq), room temperature.

Conditions: Concentrated HNO_3 (aq), room temperature.

7.2 Electrophilic Substitution of Halogens

Conditions: Br_2 (aq) / Cl_2 (aq), room temperature.

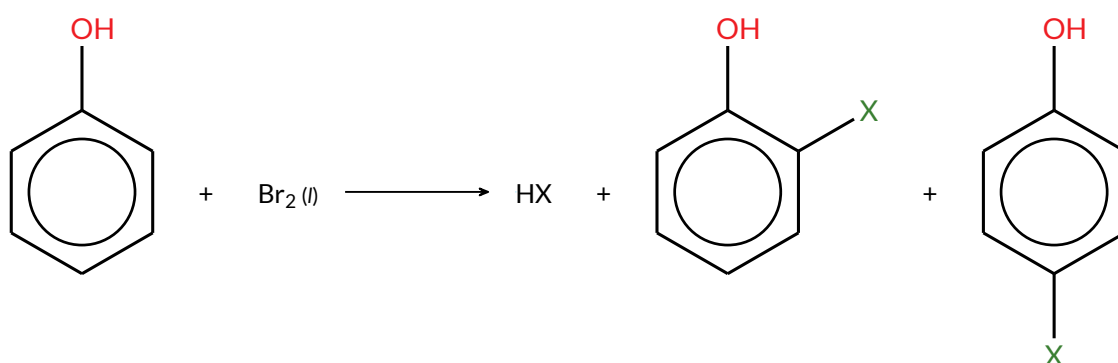**Observations:** *Yellow* Br_2 (aq) / *pale yellow* Cl_2 (aq) decolourises, white precipitate is formed.

Liquid Br_2 in a non-polar solvent at low temperatures can be used for mono-substitution.

Conditions: Br_2 (l) / Cl_2 (g) in inert, non-polar solvent (eg. CCl_4), room temperature.
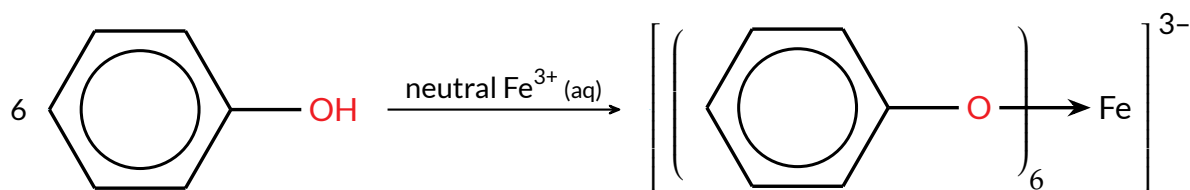**Observations:** *Reddish-brown* Br_2 / *yellowish-green* Cl_2 decolourises.

7.3   FeCl_3 Complex Formation

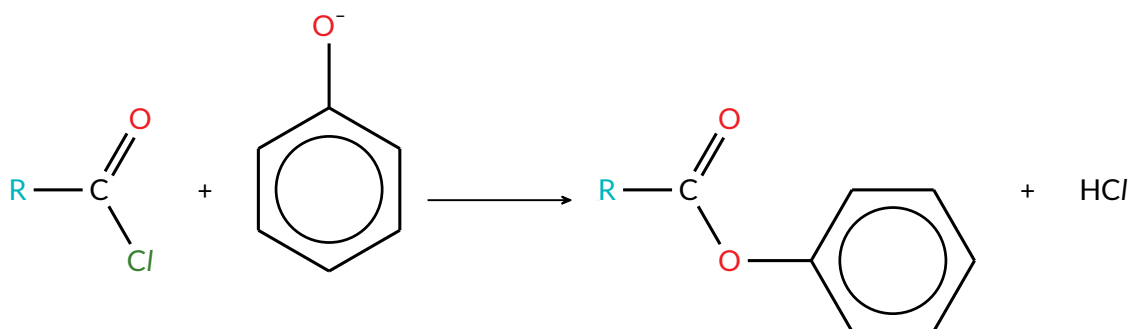**Conditions:**   Neutral FeCl_3 (aq), room temperature.
Observations: *Violet* complex formed.

7.4   Nucleophilic Acyl Substitution (Esterification)

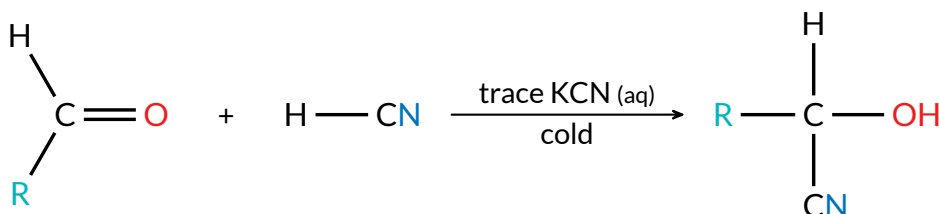**Conditions:**   Acyl chloride, NaOH (aq), room temperature.
Observations: Formation of white fumes of HCl gas.

8   Aldehydes

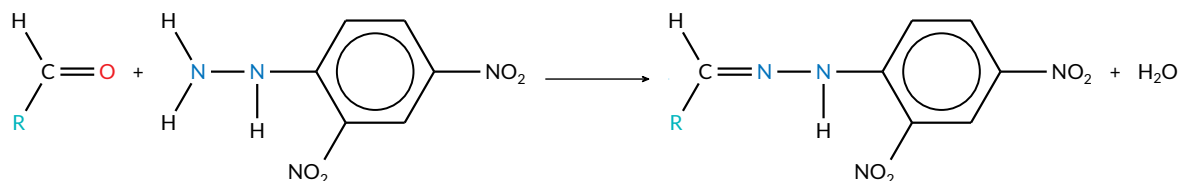## 8.1   Nucleophilic Addition of CN

Conditions: Cold HCN, trace KCN (aq).

8.2   Condensation with 2,4-DNPH
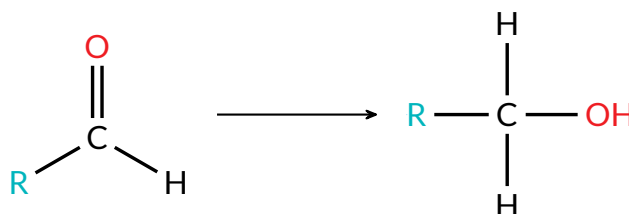
Conditions: 2,4-DNPH, room temperature.
Observations: *Orange* precipitate forms with a carbonyl.

8.3   Reduction

Aldehydes are reduced to primary alcohols.

Conditions: LiAlH$_4$ in dry ether (diethyl ether), *OR*
                      NaBH$_4$ in methanol, *OR*
                      H$_2$ (g), Ni catalyst, high temperature and pressure.

8.4   Oxidation to Carboxylic Acids

Conditions: K$_2$Cr$_2$O$_7$ with dilute H$_2$SO$_4$, *OR* KMnO$_4$ with dilute H$_2$SO$_4$,
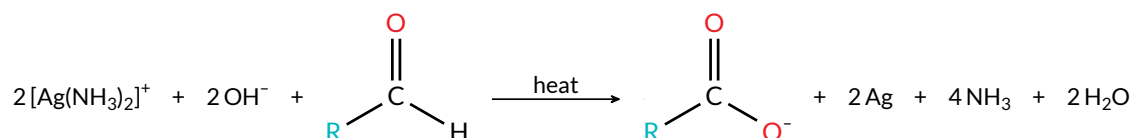   heat under reflux.

Observations: *Orange* $Cr_2O_7^{2-}$, turns *green* (Cr^{3+} formed), *OR*
Purple MnO_4^- decolourises (Mn^{2+} formed)
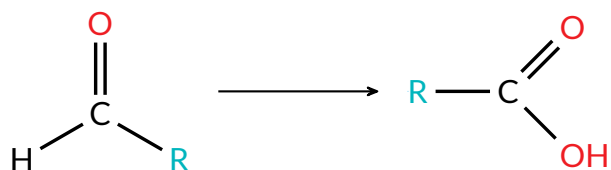
8.5 Oxidation by Tollens' Reagent

Conditions: Tollens' Reagent, heat.
Observations: *Silver* metal coats the reaction vessel.

$$2\,[Ag(NH_3)_2]^+ \;+\; 2\,OH^- \;+\; \text{(aldehyde)} \xrightarrow{\text{heat}} \text{(carboxylate)} \;+\; 2\,Ag \;+\; 4\,NH_3 \;+\; 2\,H_2O$$
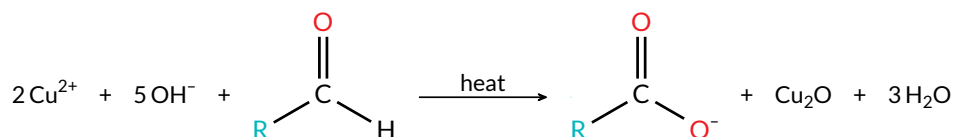
8.6 Oxidation by Fehling's Solution

Only aliphatic (non-benzene) aldehydes will be oxidised by Fehling's Solution.

Conditions: Fehling's Solution, heat.
Observations: *Brick-red*, or *reddish-brown* precipitate is formed.

$$2\,Cu^{2+} \;+\; 5\,OH^- \;+\; \text{(aldehyde)} \xrightarrow{\text{heat}} \text{(carboxylate)} \;+\; Cu_2O \;+\; 3\,H_2O$$
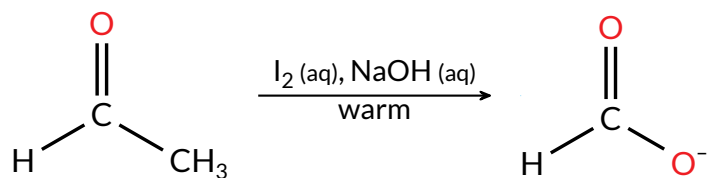
8.7 Tri-iodomethane Formation

Ethanal is the only aldehyde that can undergo this reaction.
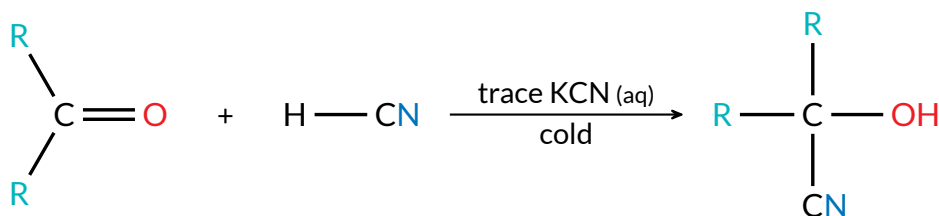
Conditions: I_2 (aq), NaOH (aq), warmed.
Observations: *Yellow* precipitate of CHI_3 is formed.

9   Ketones

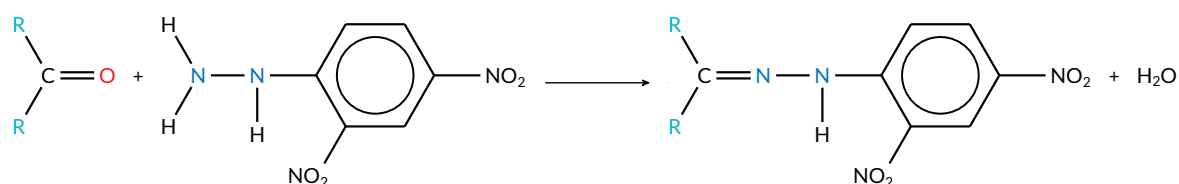## 9.1 Nucleophilic Addition of CN

Conditions: Cold HCN, trace KCN (aq).

9.2 Condensation with 2,4-DNPH

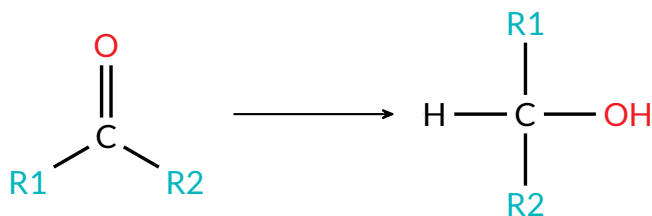**Conditions:**   2,4-DNPH, room temperature.
Observations: *Orange* precipitate forms with a carbonyl.

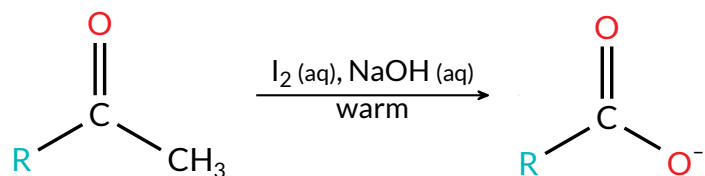## 9.3 Reduction

Ketones are reduced to secondary alcohols.

Conditions: LiAlH$_4$ in dry ether (diethyl ether), *OR*
                    NaBH$_4$ in methanol, *OR*
                    H$_{2 (g)}$, Ni catalyst, high temperature and pressure.

9.4 Tri-iodomethane Formation

Conditions: I$_{2 (aq)}$, NaOH (aq), warmed.
Observations: *Yellow* precipitate of CHI$_3$ is formed.

154

10 Carboxylic Acids
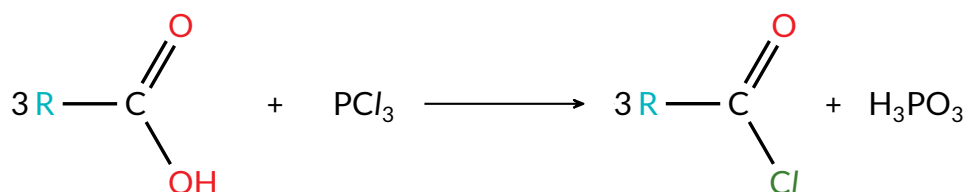
10.1 Nucleophilic Acyl Substitution (Acyl Chloride)

Phosphorous Pentachloride (PCl_5)

Conditions: Solid PCl_5, room temperature.
Observations: Formation of white fumes of HCl gas.
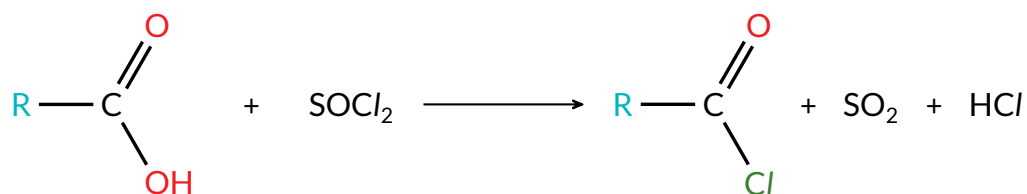

Phosphorous Trichloride (PCl_3)

Conditions: Solid PCl_3, room temperature.

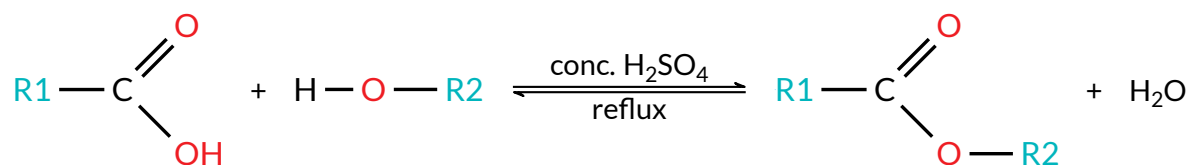### Thionyl Chloride (SOCl_2)

Conditions: Warm, liquid SOCl_2.

Observations: Formation of colourless, pungent SO$_2$ gas, white fumes of HCl gas.

10.2 Nucleophilic Acyl Substitution (Esterification)

Phenols cannot be used.
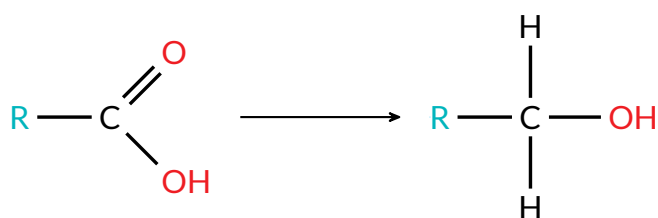
Conditions: Carboxylic acid and alcohol,
Several drops of concentrated H_2SO_4, heated under reflux.

10.3 Reduction

Carboxylic acids are oxidised to primary alcohols.

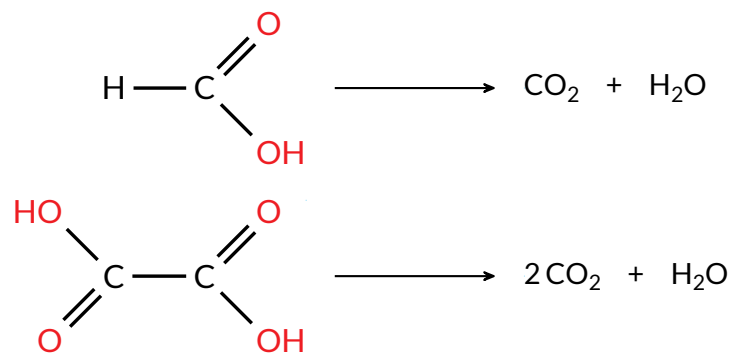**Conditions:** $LiAlH_4$ in dry ether (diethyl ether).

10.4 Oxidation

Two carboxylic acids can be further oxidised with $KMnO_4$.

Conditions: $KMnO_4$ with dilute H_2SO_4,
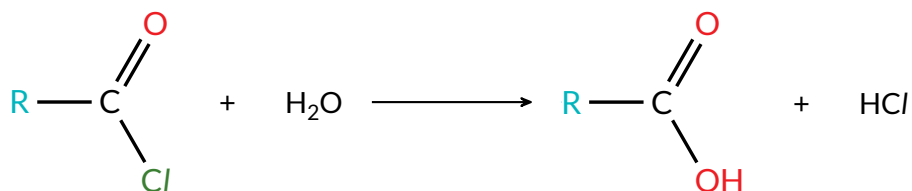heat under reflux.

Observations: *Purple* MnO_4^- decolourises (Mn^{2+} formed).
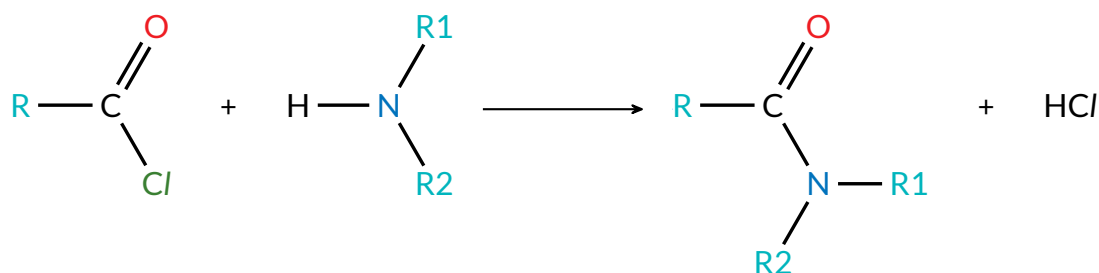

$$H-C(=O)(OH) \longrightarrow CO_2 + H_2O$$

$$HO-C(=O)-C(=O)(OH) \longrightarrow 2\,CO_2 + H_2O$$

11 Acyl Chlorides

11.1 Hydrolysis

Conditions: H_2O, room temperature.
Observations: Formation of white fumes of HC*l* gas.

$$R-C(=O)Cl \quad + \quad H_2O \quad \longrightarrow \quad R-C(=O)OH \quad + \quad HCl$$

11.2 Nucleophilic Acyl Substitution (Amide Formation)

Conditions: Acyl chloride, amine of choice in excess, room temperature.
Observations: Formation of white fumes of HC*l* gas.

$$R-C(=O)Cl \quad + \quad H-N(R1)(R2) \quad \longrightarrow \quad R-C(=O)-N(R1)(R2) \quad + \quad HCl$$

11.3 Nucleophilic Acyl Substitution (Esterification)

Phenols *can* be used.

Conditions: Acyl chloride, NaOH (aq), room temperature.
Observations: Formation of white fumes of HC*l* gas.

$$R-C(=O)Cl \quad + \quad R1-OH \quad \longrightarrow \quad R-C(=O)-O-R1 \quad + \quad HCl$$
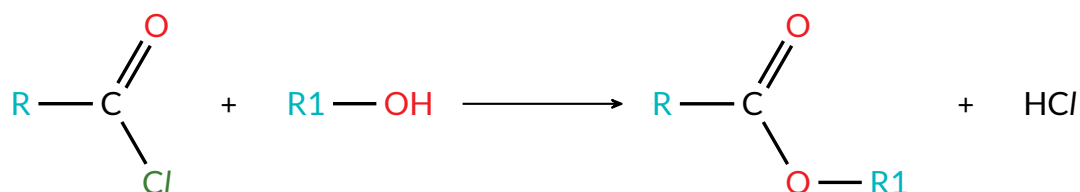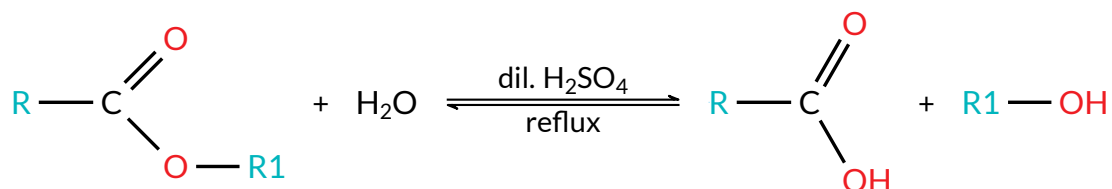
12 Esters

12.1 Acid Hydrolysis

This reaction is slow and reversible.

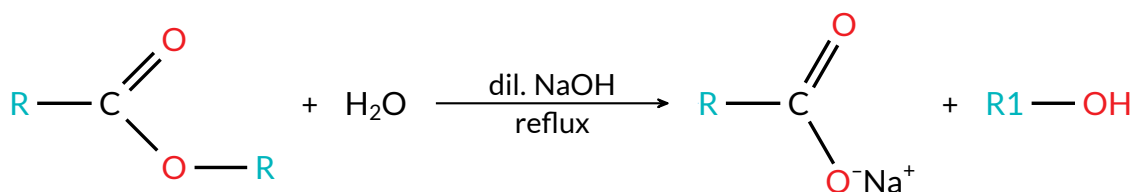**Conditions:** Dilute H_2SO_4, heat under reflux.

12.2 Alkaline Hydrolysis (Saponification)

This reaction is fast and irreversible.

Conditions: Dilute NaOH, heat under reflux.

13   Amides

13.1 Acid Hydrolysis

Conditions: Dilute H_2SO_4 or HCl, heat under reflux.
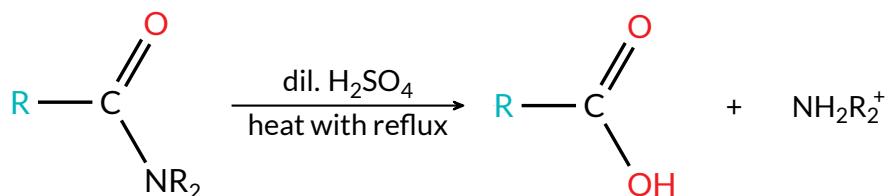
13.2 Alkaline Hydrolysis

Conditions: Dilute NaOH, heat under reflux.
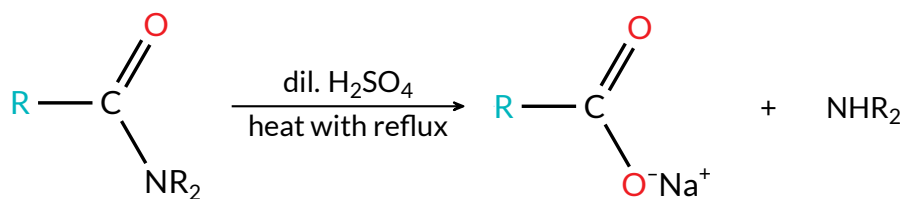
14 Amines

14.1 Nucleophilic Substitution of Alkyl Halides

Conditions: Ethanolic alkyl halide, heated in sealed tube.
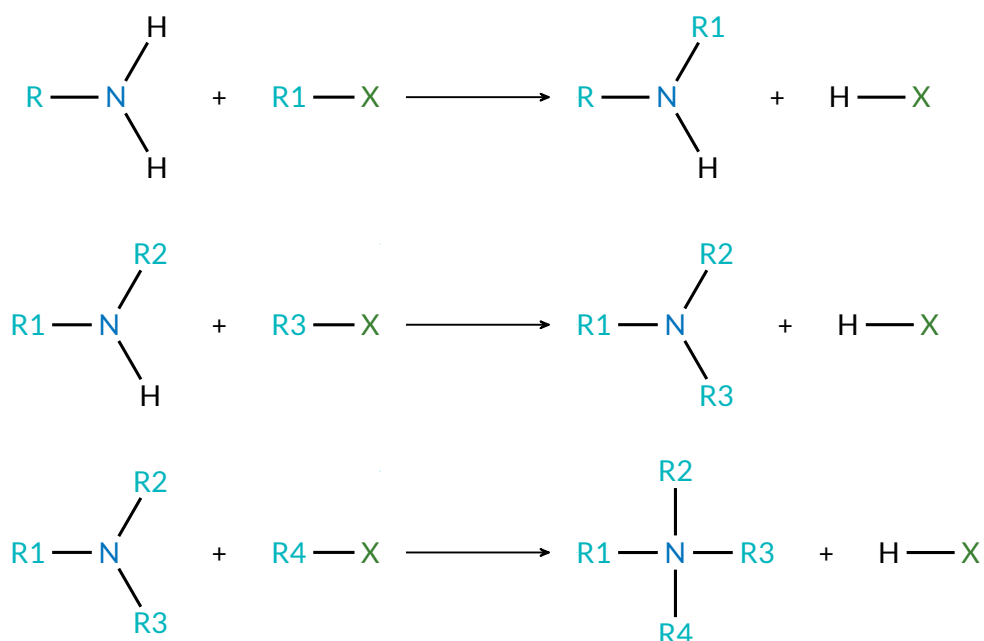
14.2 Nucleophilic Acyl Substitution of Acyl Chlorides

Conditions: Acyl chloride, amine of choice in excess, room temperature.
Observations: Formation of white fumes of HC*l* gas.
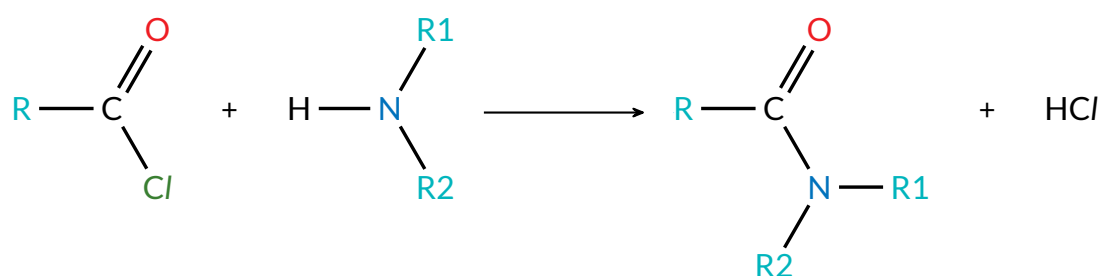
14.3 Electrophilic Addition of Bromine to Phenylamines

Conditions: Br_2 (aq), room temperature.

Observations: *Yellow* Br_2 (aq) decolourises,
                        White precipitate of 2,4,6-tribromophenylamine formed.

APPENDIX C

Summary Tables

1 Nature of Substituent Groups

The activating and deactivating nature of substituent groups in this table only applies when attached to aromatic rings.

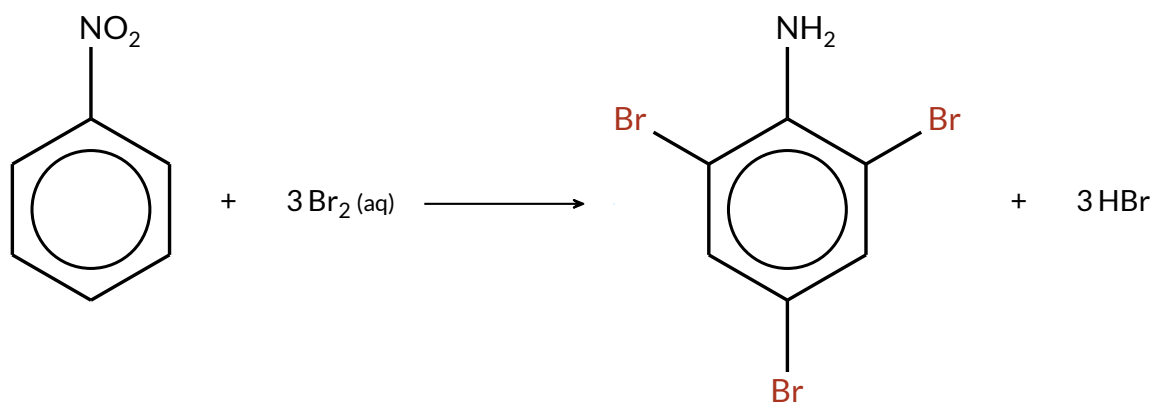| Substituent	Electron Effect	Directing Effect
Alkyl/aryl groups (eg. $-CH_3$)	Weakly Activating	2,4-directing
$-OH, -NH_2, -OCH_3$	Strongly Activating	2,4-directing
$-Cl, -Br$	Weakly Deactivating	2,4-directing
$-CHO, -NO_2, -CN, -CO_2H$	Strongly Deactivating	3-directing

For the electron-manipulating nature when attached to carbon chains, only the electronegativity of the atom should be considered --- F, O, N, and Cl, since there are no overlapping p-orbitals.

2 List and Uses of Reducing Agents

The strength of the 3 common reducing agents used, LiAl$_4$, NaBH$_4$ and good old H$_2$ (g) with Ni catalyst, can be defined in terms of their ability to reduce the various functional groups.

Group	LiAl$_4$	NaBH$_4$	H$_2$, Pt catalyst
Alkenes (C=C)	No	No	Yes
Aldehydes and Ketones (C=O)	Yes	Yes	Yes
Carboxylic Acids (CO$_2$H)	Yes	No	No
Nitriles (C≡N)	Yes	No	Yes

3   Acidic Reactions of Organic Acids

Alcohols, Phenols and Carboxylic Acids are weak organic acids (weak acids in the sense that they dissociate only partially), with reactivity in increasing order.

Acid Group	Reactive Metals (Na)	Bases (NaOH)	Carbonates (Na_2CO_3)
Alcohols (OH)	Yes	No	No
Phenols (OH)	Yes	Yes	No
Carboxylic Acids (CO_2H)	Yes	Yes	Yes

APPENDIX D

Distinguishing Tests

This appendix section is split into sections, organised by reagents, and lists each functional group followed by the results of a reaction.

1   Oxidising Agents

	$KMnO_4$, dil. H_2SO_4	$K_2Cr_2O_7$, dil. H_2SO_4
Alkenes (C=C)	*Purple* decolourises when heated	-
1° and 2° Alcohols (OH)	*Purple* decolourises	*Orange* to *green*
3° Alcohols (OH)	-	-
Phenols (OH)	-	-
Aldehydes (C=O)	*Purple* decolourises	*Orange* to *green*
Ketones (C=O)	-	-

2 Liquid or Aqueous Br$_2$

	Br$_2$ (aq) or Br$_2$ (l)
Alkenes (C=C)	*Yellow* Br$_2$ (aq) / *Reddish-brown* Br$_2$ (l) decolourises
Alcohols (OH)	-
Arenes (Benzene)	-
Phenols (OH)	*Yellow* Br$_2$ (aq) / *Reddish-brown* Br$_2$ (l) decolourises
Amines (NH$_2$)	-
Phenylamines (NH$_2$)	*Yellow* Br$_2$ (aq) / *Reddish-brown* Br$_2$ (l) decolourises

3 Neutral FeCl_3

	Neutral FeCl_3 (aq)
Alcohols (OH)	-
Phenols (OH)	*Violet* complex

4   2,4-DNPH, Tollens' and Fehling's Solution

	2,4-DNPH	Tollens' Reagent	Fehling's Solution
Aliphatic Aldehydes	*Orange* precipitate	*Silver* mirror formed	*Brick-red* precipitate
Aromatic Aldehydes	*Orange* precipitate	*Silver* mirror formed	-
Ketones	*Orange* precipitate	-	-