FURTHER ORGANIC CHEMISTRY

18

G1   ELECTROPHILIC ADDITION REACTIONS

G.1.1   Describe and explain the electrophilic addition mechanisms of the reactions of alkenes with halogens and hydrogen halides.

G.1.2   Predict and explain the formation of the major product in terms of the relative stabilities of carbocations.

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The typical reactions that alkenes undergo are addition reactions in which the double bond is converted to a single bond and two new bonds are formed. These reactions occur in two stages and are initiated by species known as **electrophiles**. These are species that will attack a molecule at a region of high electron density, such as a double or triple bond by accepting an electron pair. First the electrophile attacks the double bond, which you may recall comprises a **σ-bond** and a **π-bond**. This results in the destruction of the π–bond and the electrons from that bond form a new σ-bond to the electrophile, which itself undergoes heterolytic fission. This results in the formation of an intermediate **carbocation** (a species in which the carbon carries a positive charge and has only three electron pairs around it). If a neutral molecule, such as a halogen, is the electrophile, the approach of the molecule

to the double bond causes a movement of electrons in the halogen–halogen bond and hence an induced dipole is produced. Using ethene and bromine as the example, the mechanism of the first stage of the addition is
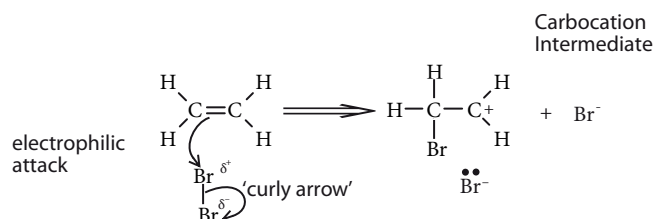

Figure 1801   The first step of electrophilic addition

Then in the second step (or stage), this carbocation will react with an anion present to complete the addition process:
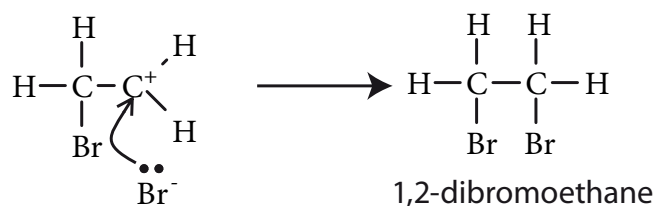

Figure 1802   The second step of electrophilic addition

Note the use of 'curly arrows' in the equations above. These curly arrows should start at the bond or lone pair initially containing the electrons and should end at the atom the bond is formed to, or where the electron pair creates a **lone pair**. Evidence in favour of an ionic mechanism comes from the fact that if the reaction is carried out in the presence of NaCl(aq), where Cl⁻ anions are present,

the carbocation intermediate reacts not only with Br$^-$ but also with Cl$^-$ to also produce $CH_2Br–CH_2Cl$, 1-bromo-2-chloroethane.

The example above involves a symmetrical electrophile, for example, where the two bromine atoms are identical. The reaction can also occur with polar non–symmetrical electrophiles, such as H–Br or I-Cl. In this case, the more positively charged of the two atoms (the one with the lower electronegativity) will be the one that attacks the alkene. This is important where the alkene is also non–symmetrical (such as propene, $CH_2=CHCH_3$) as the addition reaction can then result in two different products. In these cases, the initial electrophilic attack can produce two different carbocations. So for example, the addition of HX to propene can form the secondary carbocation $CH_3–C^+H–CH_3$ or the primary carbocation $CH_3–CH_2–C^+H_2$. These carbocations will have different stabilities and the more stable will always predominate and lead to the major product.

It is found that the lower the electrical charge carried by a particular atom, then the more stable the species is. In the case of carbocations, the **inductive effect** (that is the ability of the covalent bond to polarise and reduce the charge) of the atoms bonded on to the carbon carrying the positive charge must be considered. Empirically it appears that alkyl groups attached to this atom reduce the charge that it carries more than hydrogen atoms do. This means that tertiary carbocations (with three carbon atoms attached to the charged one) are more stable than secondary carbocations (two carbon atoms) which in turn are more stable than primary carbocations (one carbon):
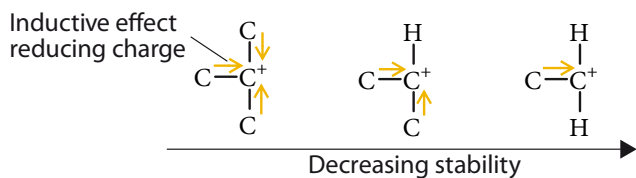

Figure 1803   The relative stability of carbocations

Combining a knowledge of the polarity of the attacking electrophile with that of the stability of the intermediate carbocations allows the prediction of the major product from an addition reaction between an asymmetrical electrophile and an asymmetrical alkene. Consider the reaction of iodine monochloride with propene as an example. Iodine is less electronegative than chlorine and so it will have a partial positive charge as a result of the polarity of the Cl-I bond. This means that the iodine atom is the one that attacks the double bond. There are also two possible carbocations that could form, a more

stable secondary carbocation and a less stable primary carbocation. The major product from the reaction is therefore the one that results from the secondary carbocation as shown in Figure 1804.
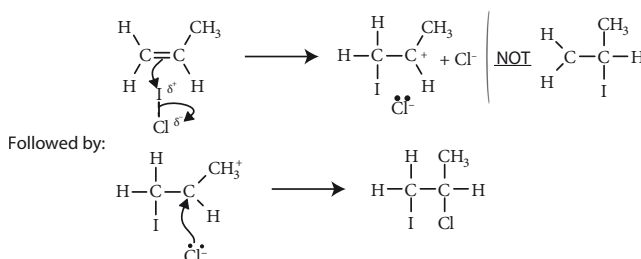

Figure 1804   The addition of iodine monochloride to propene

Therefore the major product of this reaction is $CH_3–CHI–CH_2Cl$ rather than $CH_3–CHCl–CH_2I$.

Empirical observation led to the formulation of **Markovnikov's Rule**:

"When a molecule H–X adds to a multiple carbon–carbon bond, the hydrogen atom will always attach itself to the carbon atom that already has most hydrogens attached to it".

Some people like to memorise this as "the rich get richer". The reason for this is that in electrophiles involving hydrogen, the hydrogen is almost always the atom that carries the partial positive charge owing to its relatively low electronegativity. In addition the carbocation with the least number of hydrogens on the charged carbon is the more stable, so that this hydrogen attaches itself to the carbon that already has most hydrogens. Consider the addition of hydrogen bromide to methylpropene, there are two possible products as shown in Figure 1805.
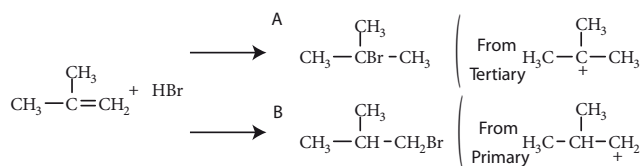

Figure 1805   The reaction of hydrogen bromide and methylpropene

The reaction, in accordance with Markovnikov's Rule, gives a product that is almost entirely 'A' with very little 'B'. This is in keeping with the explanation in terms of the stability of the intermediate carbocations shown.

1. Which one of the following is the major product when propene reacts with hydrogen bromide?

   A CH_3-CH_2-CH_2-Br
   B CH_3-CHBr-CH_3
   C   Br-CH_2-CH_2-CH_2-Br
   D CH_3-CHBr-CH_2-Br

2. Which one of the methylbutane carbocations below would you expect to be the more stable?

   A CH_3-(CH_3)CH-CH_2-CH_2^+
   B CH_3-(CH_3)CH-CH^+-CH_3
   C CH_3-$(CH_3)C^+$-CH_2-CH_3
   D $^+CH_2$-(CH_3)CH-CH_2-CH_3

3. Draw the mechanism for the reaction of iodine monochloride (I-Cl) with 2-methylbut-1-ene. State which of the two possible products will predominate and explain why this is the case.

4. Methylpropene can react with hydrogen bromide to produce two isomeric bromoalkanes.

   a) Draw the structural formulae of the two possible products and state which you would expect to predominate.
   b) These bromoalkanes can be hydrolysed to give two different alcohols:

      i   What reagent and conditions are required for this?
      ii   Give the names of the two alcohols and state whether they are primary, secondary or tertiary alcohols.

5. The hydration of propene to produce propan–2–ol is reversible. Discuss, in terms of Le Chatelier's principle, how the reaction conditions can be varied to favour the forward or reverse reaction. Why is the major product propan–2–ol rather than propan–1–ol?

G2 NUCLEOPHILIC ADDITION REACTIONS

G.2.1 Describe, using equations, the addition of hydrogen cyanide to aldehydes and ketones.

G.2.2 Describe and explain the mechanism for the addition of hydrogen cyanide to aldehydes and ketones.

G.2.3 Describe, using equations, the hydrolysis of cyanohydrins to form carboxylic acids.
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The **carbonyl group**, found in **aldehydes** and **ketones**, is quite polar with the carbon atom being the positive end of the dipole. This carbon atom is therefore electron deficient and hence susceptible to **nucleophilic attack** and through this **addition** to the carbon–oxygen double bond occurs. A **nucleophile** is a molecule or ion that has a lone pair of electrons that it can use to form a new bond to a centre of positive charge. A good example of this type of reaction is the addition of hydrogen cyanide to the carbonyl group, as shown in Figure 1806.
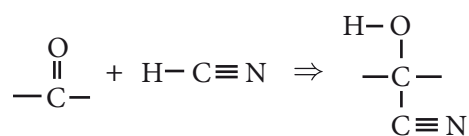
Figure 1806   The addition of hydrogen cyanide to the carbonyl group

This reaction requires a base catalyst to convert the hydrogen cyanide into the more nucleophilic cyanide ion and the carbon of the cyanide ion then acts as a nucleophile, attacking the carbonyl carbon to produce an intermediate anion. This reacts with the water present to form the hydroxynitrile product (also known as a cyanohydrin) containing an alcohol with a nitrile group on it, regenerating the base catalyst:

$$HCN + OH^- \rightleftharpoons CN^- + H_2O$$

Figure 1807   The mechanism of the nucleophilic attack of hydrogen cyanide to a carbonyl group

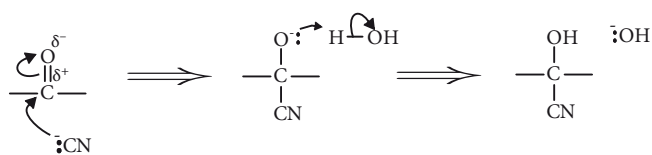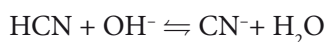This hydroxynitrile can be hydrolysed by refluxing with either dilute acid (or dilute alkali) to produce an ammonium salt (or ammonia) and a carboxylic acid (or its anion). The acid produced contains one more carbon atom than the original aldehyde or ketone and so this reaction is a means of lengthening the carbon chain, see Figure 1808.
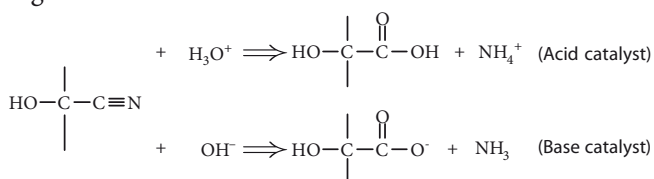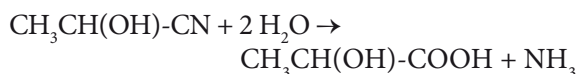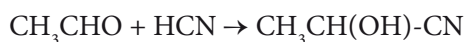

Figure 1808   The lengthening of a carbon chain via the addition of hydrogen cyanide to an aldehyde

The hydrolysis of the addition product from the reaction of hydrogen cyanide with ethanal, is therefore 2-hydroxypropanoic acid (lactic acid which is formed when milk goes sour).

$$CH_3CHO + HCN \rightarrow CH_3CH(OH)\text{-}CN$$

$$CH_3CH(OH)\text{-}CN + 2\,H_2O \rightarrow$$
$$CH_3CH(OH)\text{-}COOH + NH_3$$

G4   ADDITION–ELIMINATION REACTIONS

G.4.1   Describe, using equations, the reactions of 2,4-dinitrophenylhydrazine with aldehydes and ketones.

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With some nucleophiles that have a hydrogen atom attached to the same atom that acts as the **nucleophile**, the initial addition product from the reaction with the **carbonyl** group can eliminate water (hence they are sometimes called 'condensation reactions') to reform

the double bond resulting in an **addition–elimination** reaction. Carbonyl compounds can react in this way with molecules containing the -NH$_2$ group, as shown in Figure 1809:
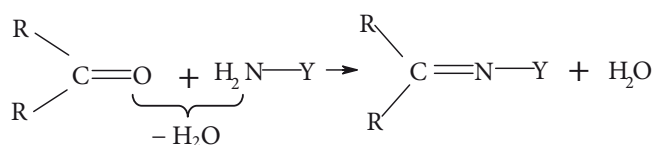
Figure 1809   A typical nucleophilic addition-elimination reaction

The most commonly encountered reaction of this type is that which occurs between carbonyl compounds and 2,4–dinitrophenylhydrazine (2,4-DNP). In this a lone pair on the terminal nitrogen acts as the nucleophile and an addition reaction occurs, by a mechanism similar to that in Figure 1807, followed by the gain and loss of hydrogen ions, to form the intermediate. This then eliminates a hydrogen ion and a hydroxide ion (that is water overall) to give the final product, as shown in Figure 1810.
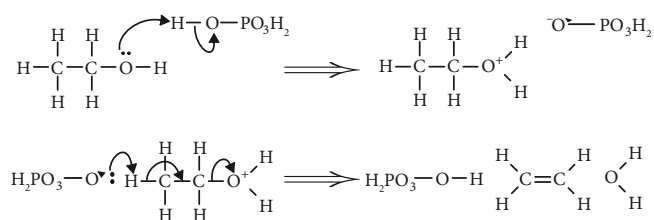
Figure 1810   The addition-elimination reaction of 2.4-dinitrophenylhydrazine with the carbonyl group

This final product is an orange–yellow crystalline solid. Its formation is used as a test for aldehydes and ketones. The sharp melting point of these crystalline derivatives was formerly used to identify the aldehyde or ketone that they were formed from. Some examples are given in Figure 1811:

Carbonyl compound	melting point of 2,4-dinitrophenylhydrazone / °C
methanal	167
ethanal	164
propanal	156
propanone	128
butanal	123
butanone	115

Figure 1811   The melting points of some 2.4-dinitrophenylhydrazones

Exercise   G4

1. When propanal is reacted with hydrogen cyanide and the initial product hydrolysed, the final product will be:

    A $CH_3\text{- }CH_2\text{-}COOH$
    B $CH_3\text{-}CH(OH)\text{-}COOH$
    C $CH_3\text{-}CH_2\text{-}CH_2\text{-}COOH$
    D $CH_3\text{-}CH_2\text{-}CH(OH)\text{-}COOH$

2. In the reaction between a carbonyl compound and hydrogen cyanide a base is usually added to convert the hydrogen cyanide into the cyanide ion. This is done because the cyanide ion is:

    A   a stronger reducing agent.
    B   a stronger oxidising agent.
    C   a stronger acid.
    D   a stronger nucleophile.

3. The product of the reaction between butanone and 2,4-dinitrophenylhydrazine is likely to be:

    A   a purple liquid.
    B   a red solid.
    C   a yellow solid.
    D   a green liquid.

4. 2-hydroxypropanoic acid may be prepared from ethanal by a two stage process via an intermediate compound (X).

    a)   Draw the stuctural formulae of these two compounds.
    b)   Draw the structure of the probable intermediate (X).
    c)   Give the reagents and conditions required to convert ethanal into X.
    d)   Outline the mechanism of this reaction.
    e)   Give the reagents and conditions required to convert X into hydroxypropanoic acid.
    f)   Hydroxypropanoic acid can exist as a pair of enantiomers. Explain why this occurs and draw diagrams to illustrate how the enantiomers differ.
    g)   What is meant by 'optical activity' and how is this related to enantiomers?
    h)   In view of this why is the hydroxypropanoic acid produced in the above process optically inactive? Explain in terms of your answer to (d) why this occurs.

5. Phenylethanone (acetophenone) is the molecule (⬡-CO-CH_3). Write the formula for the organic product formed when:

    a)   It reacts with hydrogen cyanide.
    b)   When this product is hydrolysed.
    c)   It reacts with 2,4-dinitrophenylhydrazine.

    The melting point of this final product is 238°C. What use was made historically of this melting point and that of related compounds?

G3   ELIMINATION REACTIONS

G.3.1   Describe, using equations, the dehydration reactions of alcohols with phosphoric acid to form alkenes.

G.3.2   Describe and explain the mechanism for the elimination of water from alcohols.
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An **elimination reaction** is the opposite of an addition reaction. In it a multiple bond is formed between two neighbouring atoms and a small molecule is formed from the groups that were originally attached to these atoms.

When alcohols are heated to a temperature of ~170°C with an excess of concentrated phosphoric or sulfuric acid, they undergo dehydration to form an alkene. For example, ethanol loses water to form ethene:

$$C_2H_5OH \longrightarrow C_2H_4 \ + \ H_2O$$

In this reaction, the acid protonates the hydroxyl group, so that water, a much better leaving group than the hydroxide ion, is lost in the second elimination step, in which the conjugate base of the acid accepts a hydrogen ion from the carbon next to the one attached to the –OH group, as shown in Figure 1812.
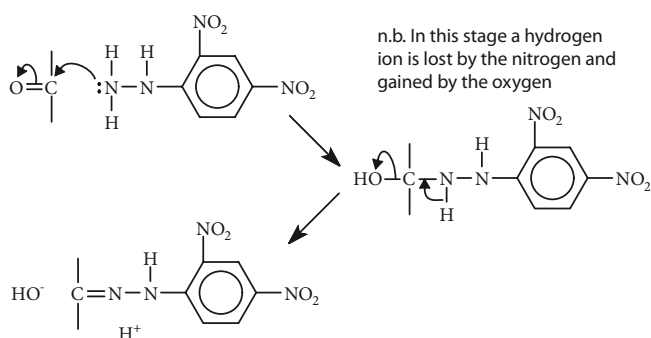
OPTION

Figure 1812   Mechanism of the acid catalysed elimination reaction of an alcohol

Note that if the hydroxyl group is in the middle, rather than at the end of the hydrocarbon chain, then the elimination can occur in more than one direction. Hence a mixture of products may result. So that whilst in the dehydration of ethanol or cyclohexanol only one product is possible, the dehydration of 2-methylbutan-2-ol yields a mixture of 2-methylbut-1-ene and 2-methylbut-2-ene, as shown in Figure 1813:
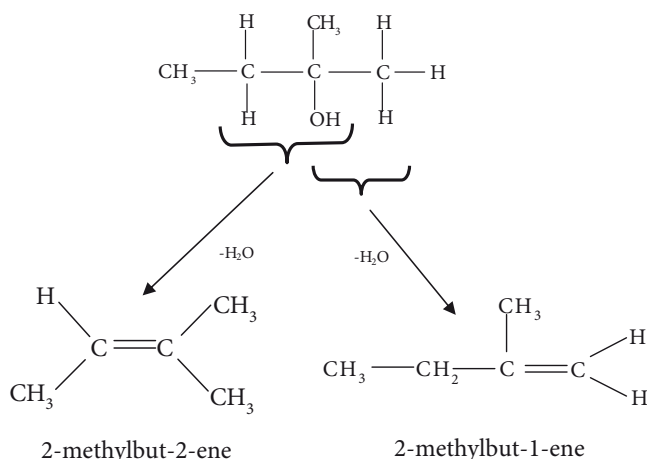

Figure 1813   Mixed products from the dehydration of 2-methylbutan-2-ol

It is interesting to note that, as shown in Figure 1814, the dehydration reaction at a slightly lower temperature in the presence of excess ethanol yields ethoxyethane through a nucleophilic substitution reaction:
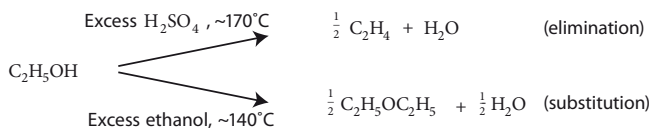

Figure 1814   Competing dehydration reactions of ethanol

Exercise   G3

1.   Which one of the following will give more than one product when it undergoes dehydration to form an alkene?

A   Propan-1-ol.
B   Propan-2-ol.
C   Butan-1-ol.
D   Butan-2-ol.

2.   When alcohols dehydrate the reaction goes via

A   a carbocation.
B   a carbanion.
C   a free radical.
D   an alkane.

3.   Give the mechanism for the dehydration of cylohexanol. State the conditions required to bring about this reaction and explain why only one product is possible.

G5   ARENES

G.5.1   Describe and explain the structure of benzene using physical and chemical evidence.

G.5.2   Describe and explain the relative rates of hydrolysis of benzene compounds halogenated in the ring and in the side-chain.

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Benzene a, hydrocarbon with the formula C_6H_6, is a typical **arene** (indeed the term is used to describe hydrocarbons involving a ring structure or fused ring structure? similar to that of benzene. The fact that there are three different structural isomers with the formula $C_6H_4X_2$ indicates that benzene probably contains a six membered ring and for a long time it was thought to be a cyclic molecule equivalent to 'cyclohexatriene'. There are however many pieces of evidence that lead to the conclusion that this is not in fact the correct structure for benzene. Briefly these are:

1.   'Cyclohexatriene' would not be symmetrical owing to the fact that double bonds are shorter than single bonds (C–C = 0.154 nm, C=C = 0.134 nm), yet X–ray crystallography shows that benzene has

sixfold rotational symmetry and its bonds are all of an equal intermediate length (0.139 nm).

2.   Benzene most commonly undergoes substitution reactions, rather than the addition reactions that characterise alkenes. For example it does not decolourise bromine water, a common test for carbon–carbon double bonds.

3.   Benzene is found to be more thermodynamically stable than would be predicted for 'cyclohexatriene'. For example the enthalpy changes for both the hydrogenation and the combustion of benzene are significantly less exothermic than would be predicted for cyclohexatriene.

Cyclohexene reacts with hydrogen to form cyclohexane and this reaction releases 119 kJ mol^{-1} of heat energy. If benzene was cyclohexatriene and contained three double bonds then it would be reasonable to expect it to release three times this amount of energy (that is 357 kJ mol^{-1}). In fact only 207 kJ mol^{-1} of heat energy is released so that the delocalisation of the double bonds results in benzene being stabilised by about 150 kJ mol^{-1}. This is illustrated in Figure 1815.
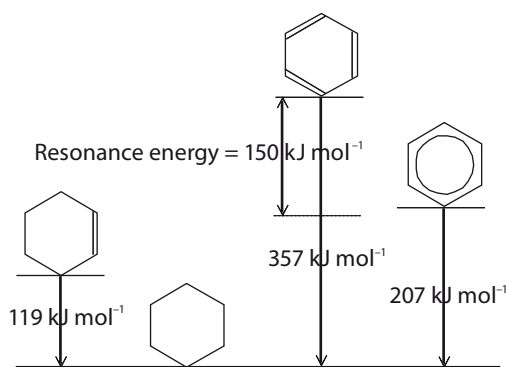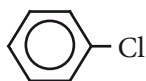

Figure 1815   The thermochemistry of the hydrogenation of benzene

Whilst most **halogenoalkanes** readily undergo nucleophilic substitution reactions, halogenated benzene derivatives, in which the halogen is attached directly to the benzene ring:

are very resistant to nucleophilic substitution, requiring heating to over 300ºC under high pressure. This is the result of three factors:

•   The charge on the carbon atom that is attached to

the halogen is much reduced by distortion of the delocalised π–bond.

•   Attack on the carbon atom from the side opposite to the carbon–halogen bond is blocked by the presence of the benzene ring.

•   The p–electrons on the halogen interact with the π–bond of the benzene ring to produce a carbon-halogen bond that has a partial double bond character and is stronger than the usual bond.

If the halogen is not directly attached to the benzene ring (such as in $C_6H_5–CH_2–Cl$), then the reactivity is similar to halogenoalkanes. Early insecticides, such as DDT, contained chlorine atoms directly bonded on to a benzene ring and their resistance to substitution reactions is part of the reason why they are so persistent in the environment.

Exercise   G5

1.   Which one of the following would you expect to undergo most rapid hydrolysis?

A   Cl-⬡-CH$_3$

B   Br-⬡-CH$_3$

C   ⬡-CH$_2$-Cl

D   ⬡-CH$_2$-Br

2.   Which one of the following implies that benzene does not contain carbon-carbon double bonds?

A   It is a cyclic molecule.
B   It is planar.
C   It has a regular hexagonal shape.
D   It is a liquid at room temperature and pressure.

3.   How many isomers, involving a benzene ring, are there of $C_6H_4Cl_2$?

  A   2
  B   3
  C   4
  D   5

4.   Does delocalisation in the benzene ring increase or decrease thermodynamic stability? Explain the evidence for this involving the hydrogenation reactions of cyclohexene (C_6H_{10}) and benzene (C_6H_6).

5.   A research chemist considers the possible conversion of 4-chloro(chloromethyl)benzene (Cl-◯-CH_2Cl) to 4-hydroxy(chloromethyl) benzene (HO-◯-CH_2Cl) and to 4-chlorophenylmethanol (Cl-◯-CH_2OH). State which is likely to be successsful and explain in detail why this conversion is much more feasible than the other.

G6   ORGANOMETALLIC CHEMISTRY

> G.6.1   Outline the formation of Grignard reagents.
>
> G.6.2   Describe, using equations, the reactions of Grignard reagents with water, carbon dioxide, aldehydes and ketones.
>
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Usually metals form ionic bonds, though a number of exceptions to this have already been met (anhydrous $AlCl_3$ and ions such as $Cr_2O_7^{2-}$). In organometallic compounds metal atoms are bonded to carbon by polar covalent bonds. Some of the first compounds of this type to be discovered were the **Grignard reagents** in which magnesium is covalently bonded to a hydrocarbon chain. They are usually formed by the reaction between magnesium metal and a halogenoalkane:

$$Mg + R\text{-}X \rightarrow R\text{-}Mg\text{-}X$$
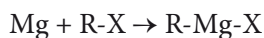
Grignard reagents react very readily with moisture and so their formation requires very anhydrous conditions. Hence the solvent usually used for this reaction is ethoxyethane that has been dried by having sodium wire in it. The reaction is also often initiated by a trace of iodine. In the

above reaction, X can be Cl, Br or I; fluorides do not react because of the strength of the C–F bond.

Grignard reagents are not isolated, but are used as prepared. Because of the polarity of the Mg-C bond, in many of their reactions Grignard reagents react as if they contained a **carbanion** (a carbon with a negative charge, R^-). As mentioned they react with water to yield the corresponding alkane:

$$R\text{-}MgX + H_2O \rightarrow R\text{-}H + Mg(OH)X$$
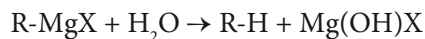
The most important reactions of Grignard reagents however are those in which they form new carbon-carbon bonds, so extending the length of the hydrocarbon chain. For example they react with **carbon dioxide** to form an intermediate, which is readily hydrolysed by dilute acid to a carboxylic acid containing one more carbon than the Grignard reagent:

$$R\text{-}MgX + CO_2 \rightarrow [R\text{-}CO_2MgX]\ (+ H^+_{(aq)})$$
$$\rightarrow R\text{-}COOH_{(aq)} + Mg^{2+}_{(aq)} + X^-_{(aq)}$$

Grignard reagents also undergo similar addition reactions with the **carbonyl** group:

$$R\text{-}MgX + C{=}O \rightarrow [R\text{-}COMgX] + (H^+_{(aq)}) \rightarrow$$
$$R\text{-}COH_{(aq)} + Mg^{2+}_{(aq)} + X^-_{(aq)}$$

Hence with methanal the product is a primary alcohol. With an aldehyde it is a secondary alcohol and with a ketone it is a tertiary alcohol. The equations below, which do not show the intermediate, give specific examples of reactions of this type:

$$C_2H_5\text{-}MgX + H_2C{=}O\ (+ H^+) \rightarrow$$
$$C_2H_5\text{-}CH_2\text{-}OH + Mg^{2+} + X^-$$

$$C_2H_5\text{-}MgX + CH_3\text{-}CHO\ (+ H^+) \rightarrow$$
$$C_2H_5\text{-}CH(CH_3)\text{-}OH + Mg^{2+} + X^-$$

$$C_2H_5\text{-}MgX + CH_3\text{-}CO\text{-}CH_3\ (+ H^+) \rightarrow$$
$$C_2H_5\text{-}C(CH_3)_2\text{-}OH + Mg^{2+} + X^-$$

Exercise G6

1. The carbon atom bonded to the magnesium in a Grignard reagent acts as a strong:

   A   electrophile.
   B   nucleophile.
   C   acid.
   D   oxidising agent.

2. Which one of the following is most important for the successful preparation of a Grignard reagent?

   A   A high temperature.
   B   A high pressure.
   C   Anhydrous conditions.
   D   Anaerobic conditions.

3. Which one of the following reacts with a Grignard reagent to produce a product containing the same hydrocarbon skeleton as the halogenoalkane from which it was formed?

   A H_2O
   B CH_2O
   C CH_3CHO
   D CH_3COCH_3

4. Describe how you would go about preparing a Grignard reagent from magnesium turnings and 1-bromobutane.

5. Outline a reaction, involving ethylmagnesium bromide, that you could use to prepare a sample of 3-methylpentan-3-ol ($(C_2H_5)_3COH$).

G7, G11 REACTION PATHWAYS (SL AND HL)

G.7.1 & G 11.1   Deduce reaction pathways given the starting materials and the product.
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Figure 1816   A summary reactions for SL students

As previously encountered, it is important to be able to devise synthetic pathways by which one compound can be converted into another even if a direct conversion is not possible. This can be done by considering what possible products the reactant could be converted to and what reactions can produce the desired product, in order to find an appropriate intermediate compound. If a lengthening of the hydrocarbon chain is required, then this may be achieved through the formation of a nitrile or via a Grignard reagent. The conditions required to bring about these reactions are also important, and in some cases the mechanism should also be known. The groups of compounds for which such knowledge is expected of Standard Level students studying the Further Organic Chemistry Option is given in Figure 1816 and those for students studying it at Higher Level is given in Figure 1817. Further details of these reactions can be found from the relevant sections of the text.

OPTION

Figure 1817   A summary reactions for HL students

M= mechanism required

Exercise

*(Note that questions with an asterisk * are for HL students only.)*

1.   Give reagents and conditions for a scheme to convert ethanal (CH_3CHO) to 2-hydroxypropanoic acid ($CH_3CH(OH)COOH$).

2.   What reagents and conditions would you require to produce methylpropan-2-ol from propanone?

3.   How could you produce a sample of benzene from chlorobenzene? Give appropriate reagents and conditions.

4.*   If you required a sample of 4-nitromethylbenzene (O_2N-⬡-CH_3)and you had only benzene as the organic starting material, describe, giving reagents and conditions for each step. How you might achieve this. What would be the probable major impurity in the product?

5.*   Give appropriate reagents and conditions for the conversion of benzene into chloromethylbenzene (⬡-CH_2-Cl).

G8   ACID–BASE REACTIONS

> **G.8.1**   Describe and explain the acidic properties of phenol and substituted phenols in terms of bonding.
>
> **G.8.2**   Describe and explain the acidic properties of substituted carboxylic acids in terms of bonding.
>
> **G.8.3**   Compare and explain the relative basicities of ammonia and amines.
>
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The **acidity** of a compound to a large extent depends on the stability of the anion formed when it dissociates. This in turn is mainly dependent on the degree to which the charge on the anion formed can be distributed amongst other atoms in the molecule.

In **alcohols**, if the molecule loses a hydrogen ion, the charge on the resultant anion is concentrated onto a single oxygen atom. In the case of **phenols**, some of the charge may be distributed on to the benzene ring through interaction of a lone pair of electrons on the oxygen with the delocalised π–electrons. The reduction in charge that this produces is much less than that from the complete delocalisation between two oxygen atoms found in carboxylic acids, so that phenol is only very weakly acidic. Like carboxylic acids, phenols will form salts with strong bases such as sodium hydroxide, but unlike carboxylic acids, simple phenols will not produce carbon dioxide when they react with carbonates because they are weaker acids than 'carbonic acid'. This is summarised in Figure 1818.
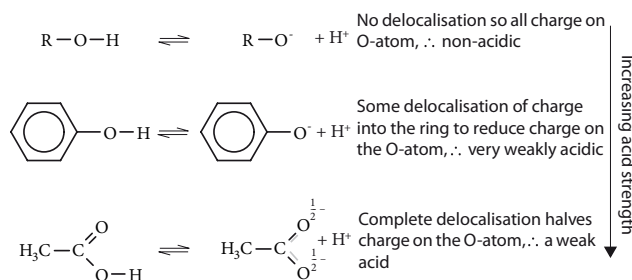

Figure 1818   The relationship between redistribution of charge and acid strength

In the case of a substituted phenol, a group that donates electrons (such as $-CH_3$) will increase the charge density

in the ring and hence on the oxygen, making the anion less stable and the acid weaker. Conversely groups that withdraw electrons (such as –Cl and –NO$_2$) will further reduce the electron density and hence make the acid stronger, as shown below. In the case of 2,4,6-trinitrophenol the effect of the three nitro groups is so large as to make it quite a strong acid. This is as summarised in Figure 1819.
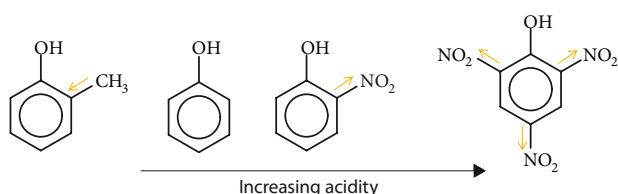

Figure 1819   The effect of substituents on the acidity of substituted phenols

The same is true for carboxylic acids. Substituents that donate electrons (e.g. –CH$_3$) make the acid weaker, whereas electron withdrawing substituents (e.g. –Cl) make the acid stronger; see Figure 1820.
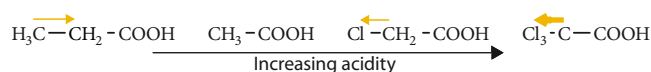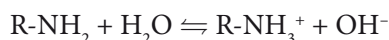

Figure 1820   The effect of substituents on the acidity of carboxylic acids

Amines are closely related to ammonia and many of their reactions are analogous to those of ammonia. Like ammonia they have an unpleasant 'fishy' smell. When dissolved in water, like ammonia, they act as weak bases and form an alkaline solution:

$$R\text{-}NH_2 + H_2O \rightleftharpoons R\text{-}NH_3^+ + OH^-$$

Acids drive this equilibrium to the right and convert the amine into a salt:

$$R\text{-}NH_2 + HCl \rightarrow R\text{-}NH_3^+\ Cl^-$$
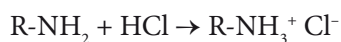
For example ethylamine and hydrochloric acid form ethylammonium chloride. These salts are white crystalline solids. When they are warmed with an alkali such as aqueous sodium hydroxide, the equilibrium is driven to the left and the free amine regenerated:

$$R\text{-}NH_3^+ + OH^- \rightarrow R\text{-}NH_2 + H_2O$$
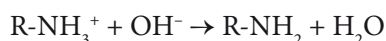
The principle of reducing the electrical charge on the atom to stabilise the ion also applies to the cations formed when these species act as weak bases. In this case however a positive charge needs minimising, so that electron donating groups, such as alkyl groups, help to stabilise

the cation. This means that alkyl amines are stronger bases than ammonia and the base strength increases from methylamine (primary amine), through dimethylamine (secondary amine) to trimethylamine (tertiary amine), which is quite a strong base.

In **amides** (–CO–NH$_2$) the lone pair of electrons on the nitrogen is involved in a delocalised π-bond with the electrons in the carbon–oxygen double bond. This means that this pair of electrons is not available to form a bond to a hydrogen ion. Hence amides are non-basic. The relative base strengths of compounds containing the –NH$_2$ group are summarised in Figure 1821.
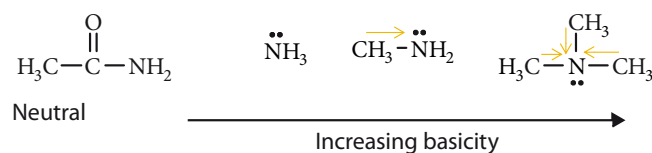

Figure 1821   Factors affecting the basicity of the –NH$_2$ group

Exercise

1. Which one of the following will have the highest pH when in aqueous solution?

    A $CH_3\text{-}CH_2\text{-}COOH$
    B $Cl\text{-}CH_2\text{-}COOH$
    C NH_3
    D $CH_3\text{-}NH_2$

2. Phenols are stronger acids than alcohols because:

    A   They are solids rather than liquids.
    B   They form stronger hydrogen bonds to water.
    C   They have a stronger C-O bond.
    D   The charge on the conjugate base is partly delocalised.

3. Which one of the following gives the correct order of increasing base strength?

    A $CH_3CONH_2 < NH_3 < CH_3NH_2 < (CH_3)_3N$
    B $CH_3CONH_2 < (CH_3)_3N < CH_3NH_2 < NH_3$
    C $(CH_3)_3N < CH_3NH_2 < NH_3 < CH_3CONH_2$
    D $NH_3 < CH_3NH_2 < (CH_3)_3N < CH_3CONH_2$

4. Explain why ethanol is neutral, phenol a very weak acid, ethanoic acid a weak acid, and trichloroethanoic acid a quite strong acid.

5. Explain why adding a methyl group makes a carboxylic acid a weaker acid (HCOOH is a stronger acid than CH_3COOH), but an amine a stronger base (CH_3NH_2 is a weaker base than $(CH_3)_2NH_2$).

G9 ADDITION–ELIMINATION REACTIONS

G.9.1 Describe, using equations, the reactions of acid anhydrides with nucleophiles to form carboxylic acids, esters, amides and substituted amides.

G.9.2 Describe, using equations, the reactions of acyl chlorides with nucleophiles to form carboxylic acids, esters, amides and substituted amides.

G.9.3 Explain the reactions of acyl chlorides with nucleophiles in terms of an addition–elimination mechanism.

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As was seen above the **carbonyl group** in aldehydes and ketones can undergo a nucleophilic addition-elimination reaction, with for example 2,4-dinitrophenylhydrazine. The carbonyl group in compounds related to carboxylic acids, such as **acid anhydrides** (R-CO-O-CO-R) and **acyl chlorides** (R-CO-Cl) is even more polar than that in aldehydes and ketones as a result of the electron withdrawing power of the additional chlorine or oxygen bonded to it. As a result, these compounds are much more reactive. The carbonyl group in them can also undergo addition-elimination reactions but in this case, because the compound has a good 'leaving group' (i.e. R-CO-O⁻ and Cl⁻ respectively), the C=O bond in the carbonyl group is reformed in the final product so that the leaving group appears to have been substituted by the nucleophile. Using water as the nucleophile, which gives a carboxylic acid as the final product, the reactions can be represented in Figure 1822.
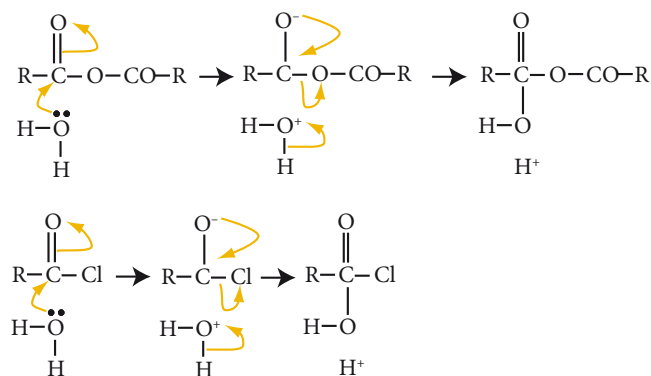

Figure 1822 The mechanism of the nucleophilic addition-elimination reaction of acid anhydrides and acyl chlorides with water

The reactions of acid anhydrides and acyl chlorides are very similar, with acyl chlorides being slightly the more reactive of the two. They react with a wide variety of nucleophiles which, in effect, replace the halogen or alkanoate group. These reactions are summarised in Figure 1823.
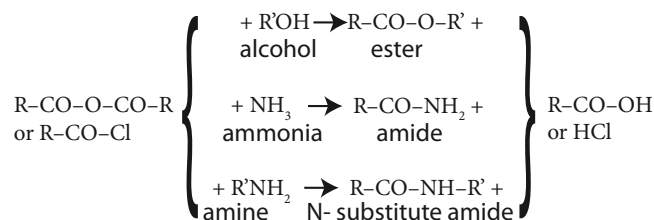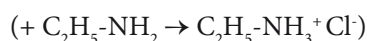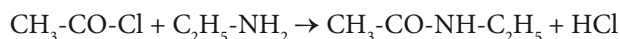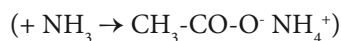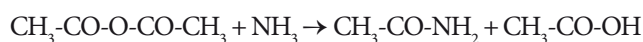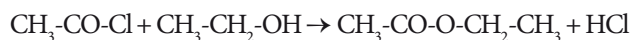

Figure 1823 A summary of the nucleophilic addition-elimination reactions of acid anhydrides and acyl chlorides

Specific examples are given below, and more complex examples are of commercial importance in the manufacture of the pain killers aspirin and paracetamol.

CH_3-CO-O-CO-CH_3 + H_2O → CH_3-CO-OH + CH_3-CO-OH

CH_3-CO-Cl + CH_3-CH_2-OH → CH_3-CO-O-CH_2-CH_3 + HCl

CH_3-CO-O-CO-CH_3 + NH_3 → CH_3-CO-NH_2 + CH_3-CO-OH

(+ NH_3 → CH_3-CO-O⁻ NH_4^+)

CH_3-CO-Cl + C_2H_5-NH_2 → CH_3-CO-NH-C_2H_5 + HCl

(+ C_2H_5-NH_2 → C_2H_5-NH_3^+ Cl⁻)
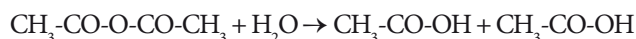
Exercise   G9

1. When ethanoyl chloride reacts with an alcohol the organic product is:

   A   an ester.
   B   an aldehyde.
   C   a ketone.
   D   a carboxylic acid.

2. Which one of the following substances would you react with ethanoic anhydride to produce CH_3-CO-NH-CH_3?

   A NH_3
   B CH_3-NH_2
   C CH_3-CO-NH_2
   D CH_3-NH-CH_3

3. When 0.1 moles of ethanoic anhydride and ethanoyl chloride are added to two separate beakers each containing 1 dm³ of water, which one will give the solution with the lowest pH?

   A   Neither as both are insoluble.
   B   Neither as they both give the same product.
   C   Ethanoic anhydride.
   D   Ethanoyl chloride.

4. When ethanoyl chloride is added to pure propan-2-ol a vigorous reaction takes place.

   a) Write a balanced equation for the reaction. Give the name of the product and state to what homologous series of compounds it belongs.
   b) Show the accepted mechanism by which this reaction takes place.
   c) Why is pure propan-2-ol used rather than an aqueous solution of the reagent?
   d) If no ethanoyl chloride were available, what other reagent could be substituted to give the required product? Would you expect the reaction with this second reagent to be more or less vigorous (under the same experimental conditions)?

5. Ethanoic anhydride reacts with ammonia.

   a) Write a balanced equation for the reaction. Give the name of the product and state to what homologous series of compounds it belongs.
   b) Show the accepted mechanism by which this reaction takes place.
   c) How many moles of ammonia would be required for each mole of ethanoic anhydride to give an approximately neutral mixture?
   d) Draw the formula of the product if ethylamine were used instead of ammonia. Name this new product.

G10 ELECTROPHILIC SUBSTITUTION REACTIONS

G.10.1 Describe, using equations, the nitration, chlorination, alkylation and acylation of benzene.

G.10.2 Describe and explain the mechanisms for the nitration, chlorination, alkylation and acylation of benzene.

G.10.3 Describe, using equations, the nitration, chlorination, alkylation and acylation of methylbenzene.

G.10.4 Describe and explain the directing effects and relative rates of reaction of different substituents on a benzene ring.

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The **benzene ring**, like the double bond, has a high electron density owing to the presence of π-electrons and this means that it too is susceptible to electrophilic attack to form a carbocation intermediate. In this case however, if it underwent a normal addition reaction, the product would not have a **delocalised π-bond** and so would lose the added stability that results from this. For this reason the intermediate carbocation loses a hydrogen ion to give a **substitution** product, which retains the delocalised π-electron system. The opposite is true for alkenes, where the **addition** product is the more stable.

OPTION

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The nitration of benzene is an example of such a reaction. Benzene is warmed with a mixture of concentrated nitric and sulfuric acids. In this mixture there is an equilibrium resulting in the formation of the nitronium ion (NO_2^+):

$$HNO_3 + 2\ H_2SO_4 \rightleftharpoons NO_2^+ + 2\ HSO_4^- + H_3O^+$$

This then acts as the electrophile, attacking the benzene ring to produce an intermediate carbocation in which the delocalised π-electron system is disrupted, as shown in Figure 1824.
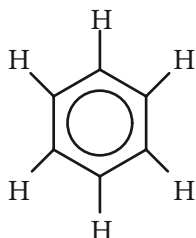

Figure 1824   The electrophilic attack of the nitronium ion on the benzene ring

If an anion were now added on to the carbocation to complete the addition reaction, then the additional stability associate with the delocalised π-bond would be permanently lost. Alternatively the carbocation can eliminate a hydrogen ion, restoring the delocalised π-electron system as shown in Figure 1825. This latter alternative is much more favourable energetically and results in an overall **electrophilic substitution** reaction.
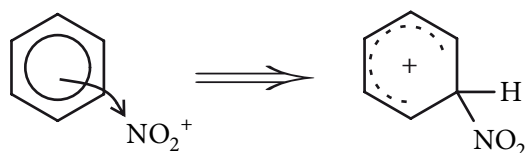

Figure 1825   The elimination of a hydrogen ion from the intermediate carbocation to form nitrobenzene

Benzene and related compounds, such as methylbenzene, undergo electrophilic substitution reactions with a range of other electrophiles, some of which are given in Figure 1826.
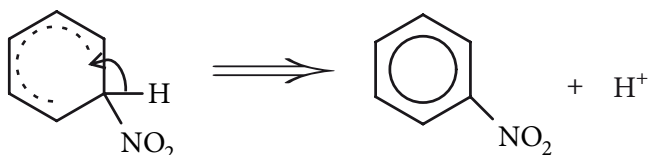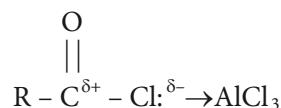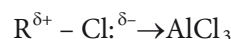

Figure 1826   Some electrophilic substitution reactions of benzene

These reactions occur by similar mechanisms to the nitration reaction above. As they all employ similar catalysts these are collectively known as **Friedel Crafts reactions**. In each case the electrophile results from the positive end of the polar species produced by the bonding of the reactant to the trivalent electron deficient metal chloride (MCl_3) catalyst (sometimes referred to as a halogen carrier) which acts as a Lewis acid.

$$^{\delta+}Cl - Cl^{\delta-} \rightarrow MCl_3$$
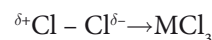
As this complex attacks the benzene ring the Cl–Cl bond breaks heterolytically to form the carbocation and the MCl_4^- anion breaks free, so that in fact the attacking chlorine atom behaves as if it were a Cl^+ ion. In the second step of the reaction this acts as a base and accepts the H^+ lost to form hydrogen chloride and regenerates the MCl_3 catalyst. In bromination, finely divided iron is simply added to the dry reaction mixture where it reacts with the bromine to produce the iron(III) bromide catalyst. In the case of the reactions with chloroalkanes and acyl chlorides, the aluminium chloride catalyst acts as a Lewis acid and binds to the chlorine, causing the carbon-chlorine bond to be even more strongly polarised. This results in the carbon in each case behaving as if it were a carbocation:

$$R^{\delta+} - Cl{:}^{\delta-} \rightarrow AlCl_3$$

$$\overset{\displaystyle O}{\underset{\displaystyle R - C^{\delta+} - Cl{:}^{\delta-} \rightarrow AlCl_3}{\|}}$$

The presence of a substituent group on the benzene ring can significantly affect its reactivity with respect to electrophilic substitution reactions. Generally speaking groups which increase the electron density of the π-electron system, either through an **inductive effect** (for example $-CH_3$) or by donating a pair of electrons to the delocalised π-electron system (known as a **mesomeric effect**, occurring for example with –OH), are activating groups and increase the reactivity of the ring whereas those that withdraw electrons (for example $-NO_2$) are deactivating groups and decrease the reactivity. Substituents usually affect the reactivity of the 2,4,6 positions more than that of the 3,5 positions (though the halogens are an exception to this) hence the reaction of methylbenzene with the common electrophiles yields a mixture of the 2- and 4- substitution products as shown in Figure 1827.
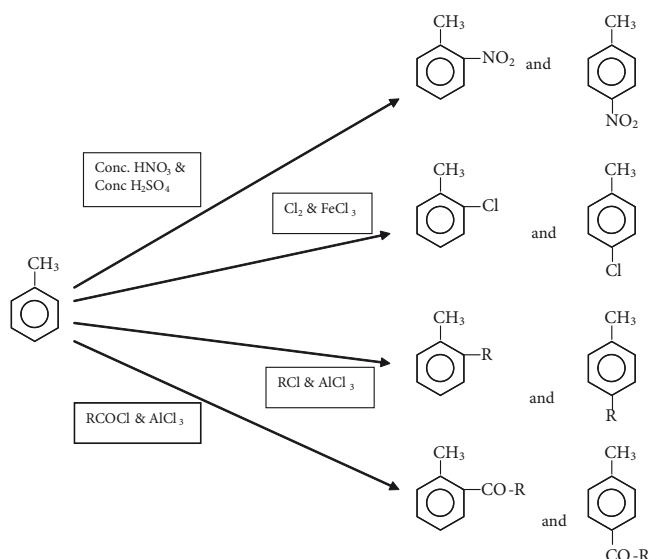
Figure 1827   Some electrophilic substitution reactions of methylbenzene

The effect of the major substituents on the reactivity and position of further substitution is summarised in Figure 1828.
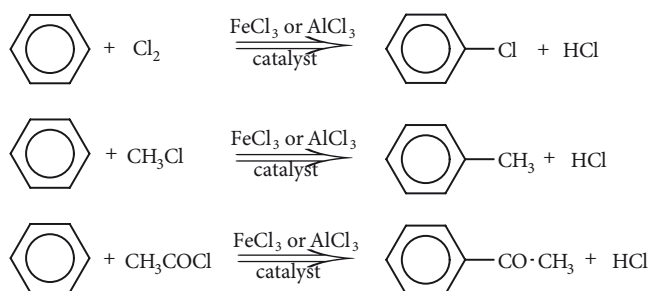

Figure 1828   The effect of substituents on the reactivity and positional preference for electrophilic substitution reactions of the benzene ring

The directional effects can be explained in terms of the charge distribution of the intermediates. The decreased reactivity due to the presence of $-NO_2$ can be explained in terms of its electron-withdrawing nature and lack of a non-bonded electron pair. The slightly increased reactivity due to the presence of $-CH_3$ can be explained in terms of its electron-releasing nature. The greatly increased reactivity due to the presence of $-OH$ can be explained in terms of its partial donation of a non-bonded electron pair. This increase in activity is so great that, for example phenol (C_6H_5OH), will react rapidly with aqueous chlorine at room temperature and pressure to produce 2,4,6–trichlorophenol (the antiseptic, TCP) even without a Friedel Crafts catalyst. See Figure 1829.
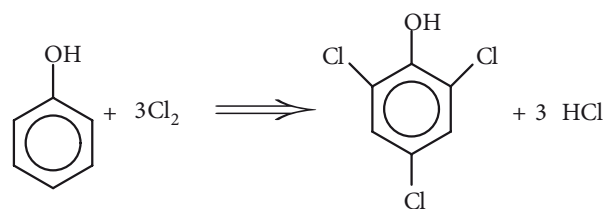
Figure 1829   The reaction of phenol with chlorine

It should be noted that with methylbenzene, two possible chlorination reactions are possible. In the presence of ultraviolet light a free radical substitution of the side chain occurs, whereas in the dark with a Friedel Crafts catalyst (normally $FeCl_3$ or $AlCl_3$) the substitution occurs on the ring, as summarised in Figure 1830.
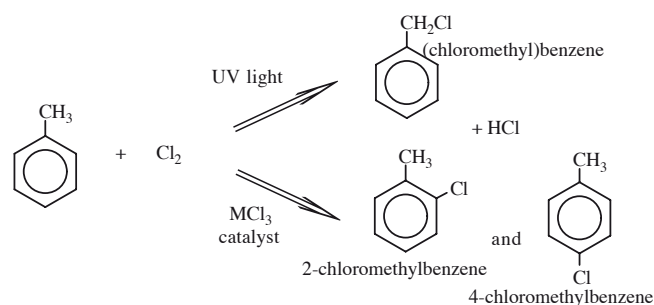
Figure 1830   The effect of reaction conditions on the chlorination reactions of methylbenzene

The next page show a summary of the major reaction pathways.

OPTION

CH₃/H- ⬡ -NO₂ or NO₂

CH₃/H- ⬡ -Cl or Cl

Polyhalogenated isomers

Heat with X₂ & FeX₃

Heat with c. HNO₃ & c. H₂SO₄

CH₃/H- ⬡ -R or R

CH₃/H- ⬡ -CO-R or CO-R

Heat with R-Cl & AlCl₃

Heat with R-CO-Cl & AlCl₃

R/H-CH₂-CH₂-OH

R-CH₂-CO-Cl/O-CO-CH₂-R

R/H-CH₂-CH₂-CN
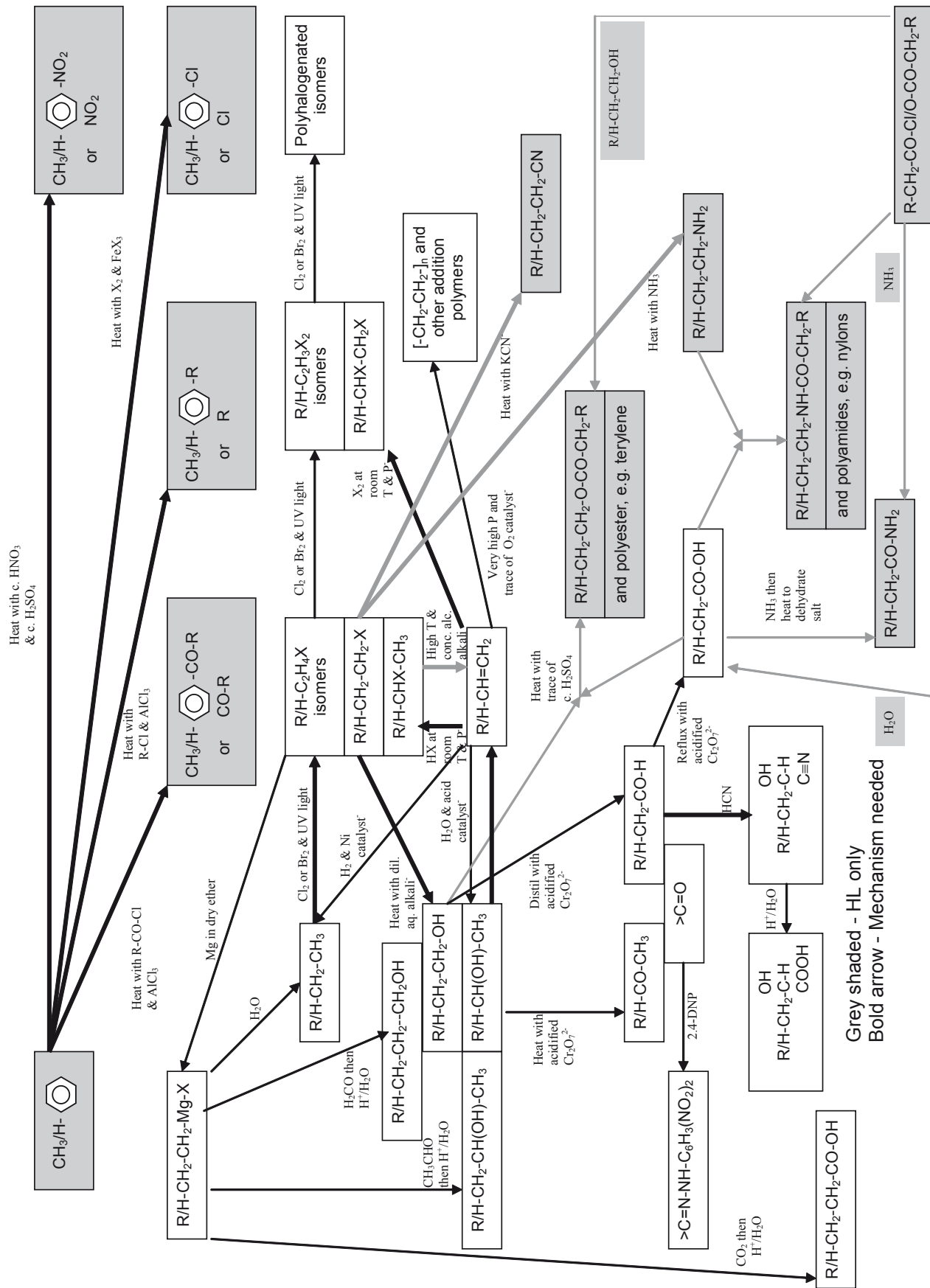
R/H-CH₂-CH₂-NH₂

Heat with NH₃

NH₃

R/H-CH₂-CH₂-NH-CO-CH₂-R and polyamides, e.g. nylons

R/H-CH₂-CO-NH₂

H₂O

Cl₂ or Br₂ & UV light

R/H-C₂H₃X₂ isomers / R/H-CHX-CH₂X

[-CH₂-CH₂-]ₙ and other addition polymers

Heat with KCN

R/H-CH₂-CH₂-O-CO-CH₂-R and polyester, e.g. terylene

X₂ at room T & P

Very high P and trace of O₂ catalyst

Cl₂ or Br₂ & UV light

R/H-C₂H₄X isomers / R/H-CH₂-CH₂-X / R/H-CHX-CH₃

High T & conc. alc. alkali

R/H-CH=CH₂

R/H-CH₂-CO-OH

NH₃ then heat to dehydrate salt

HX at room T & P

H₂O & acid catalyst

H₂ & Ni catalyst

Heat with dil. aq. alkali

Heat with trace of c. H₂SO₄

Cl₂ or Br₂ & UV light

R/H-CH₂-CH₃

H₂O

Mg in dry ether

H₂CO then H⁺/H₂O

R/H-CH₂-CH₂-CH₂OH

R/H-CH₂-CH₂-OH / R/H-CH(OH)-CH₃

Distil with acidified Cr₂O₇²⁻

R/H-CH₂-CO-H

Reflux with acidified Cr₂O₇²⁻

HCN

OH R/H-CH₂-C-H C≡N

>C=O / R/H-CO-CH₃

Heat with acidified Cr₂O₇²⁻

2,4-DNP

H⁺/H₂O

OH R/H-CH₂-C-H COOH

CH₃CHO then H⁺/H₂O

R/H-CH₂-CH(OH)-CH₃

R/H-CH₂-CH₂-Mg-X

CO₂ then H⁺/H₂O

>C=N-NH-C₆H₃(NO₂)₂

R/H-CH₂-CH₂-CO-OH

Grey shaded - HL only
Bold arrow - Mechanism needed

CH₃/H- ⬡

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Exercise

1. When methylbenzene is nitrated the product will contain significant quantities of

   A   2-nitro(methylbenzene) and 3-nitro(methylbenzene).
   B   3-nitro(methylbenzene) and 4-nitro(methylbenzene).
   C   2-nitro(methylbenzene) and 4-nitro(methylbenzene).
   D   2-nitro(methylbenzene), 3-nitro(methylbenzene) and 4-nitro(methylbenzene).

2. Which one of the following will be the most reactive when heated with ethanoyl chloride and anhydrous aluminium chloride?

   A   ◯-NO$_2$
   B   ◯-H
   C   ◯-CH$_3$
   D   ◯-OH

3. Methylbenzene can react with bromine under different conditions to form two different products.

   a) Write balanced equations for the two reactions stating the conditions required in each case.
   b) Give the name and structural formula of both products.
   c) State the type of mechanisms by which the two reactions occur.

4. Benzene is readily converted to nitrobenzene.

   a) To what class of reactions does this belong?
   b) State the reagents and conditions required to bring this about and write a balanced equation for the reaction.
   c) Write the mechanism by which this reaction occurs.

5. Benzene, methylbenzene and phenol will all undergo nitration reactions with nitric acid.

   a) How would you expect the reactivity of these three compounds with nitric acid to vary? How can this variation be explained?
   b) Write the mechanism for the nitration of benzene.
   c) Would you expect the replacement of a second hydrogen on the benzene ring to take place more readily or less readily than the first one? Explain.
   d) Give the structural formulas of the major products you would expect from the nitration of methylbenzene, phenol and nitrobenzene.

GENERAL EXERCISE FOR OPTION G

The questions below involve a knowledge of various sections of the option. Note that questions marked with an asterisk * are for HL students only.

1. For each of the following mechanisms, give the balanced equation for a specific example of a reaction that occurs by each mechanism, and then draw the mechanism for the reaction.

   Elimination
   Nucleophilic addition
   Addition–elimination
   * Electrophilic addition

2. Write the structural formula of the major product from each of the following reactions:

   a) Reacting butanal with ethylmagnesium bromide and hydrolysing the product.
   b) Warming propanal with 2,4–dinitrophenylhydrazine solution.
   c) Reacting butan–2–ol with methylmagnesium chloride.
   d)* Reacting ethanoyl chloride with ammonia.
   e)* Refluxing methylbenzene with a mixture of concentrated nitric and sulfuric acids.

3. What would be seen in each of the following reactions?

   a) Adding water to a solution of methylmagnesium iodide in ethoxyethane.
   b) Adding 2,4–dinitrophenylhydrazine solution to propanone.

    c)   Propan-2-ol is warmed with concentrated phosphoric acid.

4.   Explain why:

    a)   a solution of methylamine in water has a pH ~11.

    b)   a pungent smelling gas is evolved when a white, crystalline salt, CH_3NH_3Cl is warmed with aqueous sodium hydroxide.

    c)   ethanamide is a crystalline solid.

    d)   a solution of trimethylamine is even more alkaline than a solution of methylamine of the same concentration, whereas a solution of ethanamide is almost neutral.

5.   This is a question about phenylethanone (acetophenone) (◯-CO-CH₃).

    a)*   Write a balanced equation for the preparation of this compound from benzene, giving the required conditions.

    b)   How could you show that phenylethanone is a ketone?

    c)   Phenylethanone will react with ethylmagnesium bromide. Draw the structural formula of the final product that results from the hydrolysis of the intermediate. To what class of compounds does it belong?