18 Extension Topic - Organic Chemistry
Carboxylic Acids & Derivatives

GUIDING QUESTIONS

Carboxylic Acids

- How are carboxylic acids synthesised?
- What types of reactions do carboxylic acids undergo and why?

Acid Derivatives

- How are acyl chlorides and esters synthesised?
- What types of reactions do acyl chlorides and esters undergo and why?
- How do the ease of hydrolysis of acyl chlorides compare with that of alkyl and aryl chlorides?

How do we compare the acidity of organic compounds in aqueous medium?

LEARNING OUTCOMES

Students should be able to:

11.7 (a) describe the formation of carboxylic acids from alcohols, aldehydes and nitriles
11.7 (b) describe the reactions of carboxylic acids in the formation of:
  (i) salts
  (ii) esters on condensation with alcohols, using ethyl ethanoate as an example
  (iii) acyl chlorides, using ethanoyl chloride as an example
  (iv) primary alcohols, via reduction with lithium aluminium hydride, using ethanol as an example.
11.7 (c) explain the acidity of carboxylic acids and of chlorine-substituted ethanoic acids in terms of their structures
11.7 (d) describe the hydrolysis of acyl chlorides
11.7 (e) describe the condensation reactions of acyl chlorides with alcohols, phenols and primary amines
11.7 (f) explain the relative ease of hydrolysis of acyl chlorides, alkyl chlorides and aryl chlorides
11.7 (g) describe the formation of esters from the condensation reaction of acyl chlorides, using phenyl benzoate as an example
11.7 (h) describe the acid and base hydrolysis of esters

REFERENCES

1. Peter Cann & Peter Hughes, *Chemistry*, 2015, Hodder Education, Chapter 18
2. Graham C. Hill & John S. Holman, *Chemistry in Context*, Nelson, Chapter 29

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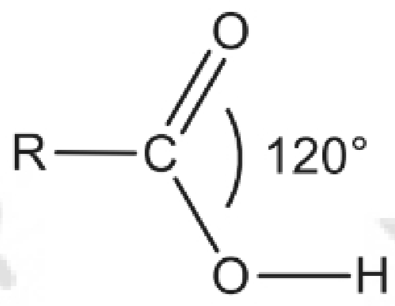
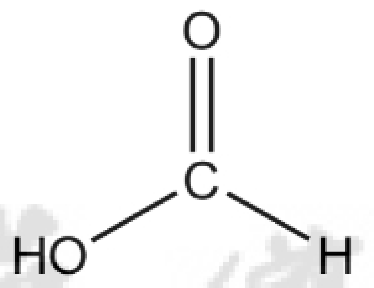
1 INTRODUCTION TO CARBOXYLIC ACIDS

All carboxylic acids contain the carboxyl group (–CO_2H), as shown below:



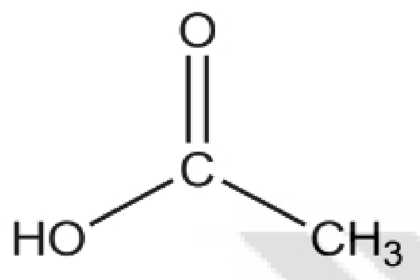
The molecule is trigonal planar about the carboxyl carbon, which is *sp*^{2} hybridised, with bond angles approximately 120°.

Examples of carboxylic acids:



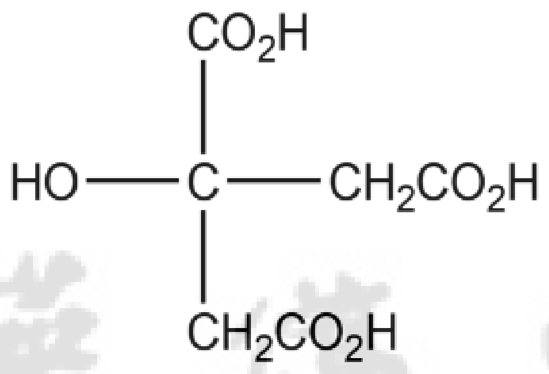
formic acid (methanoic acid)

Simplest carboxylic acid. First isolated in the 17th century by distillation of dead ants.



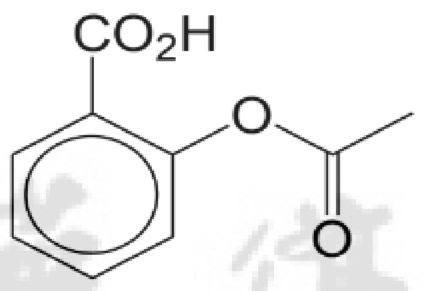
acetic acid (ethanoic acid)

Important chemical reagent and industrial chemical.



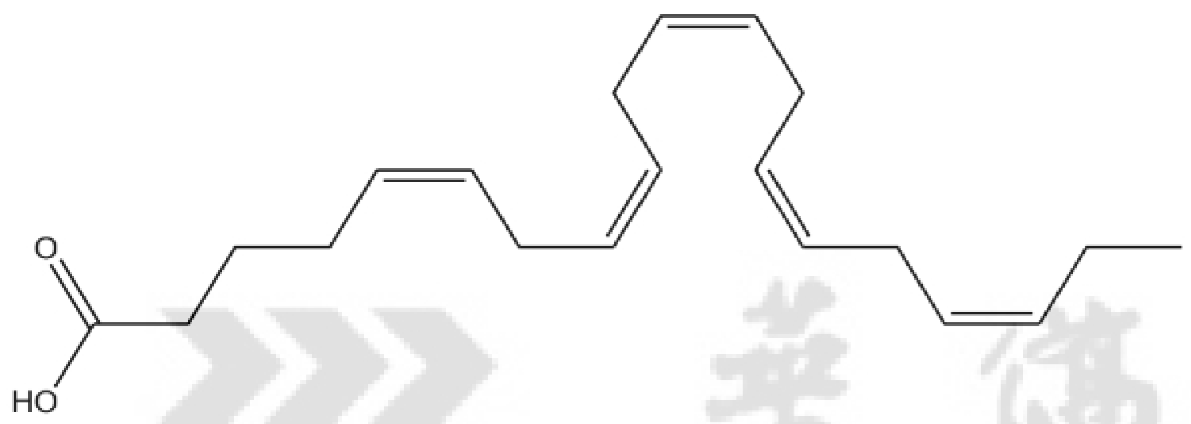
citric acid

A tribasic acid. Found in citrus fruits. Often used as a flavouring in soft drinks.



aspirin

A commonly used pain-killer, which is also an anti-inflammatory medicine.



eicosapentaenoic acid

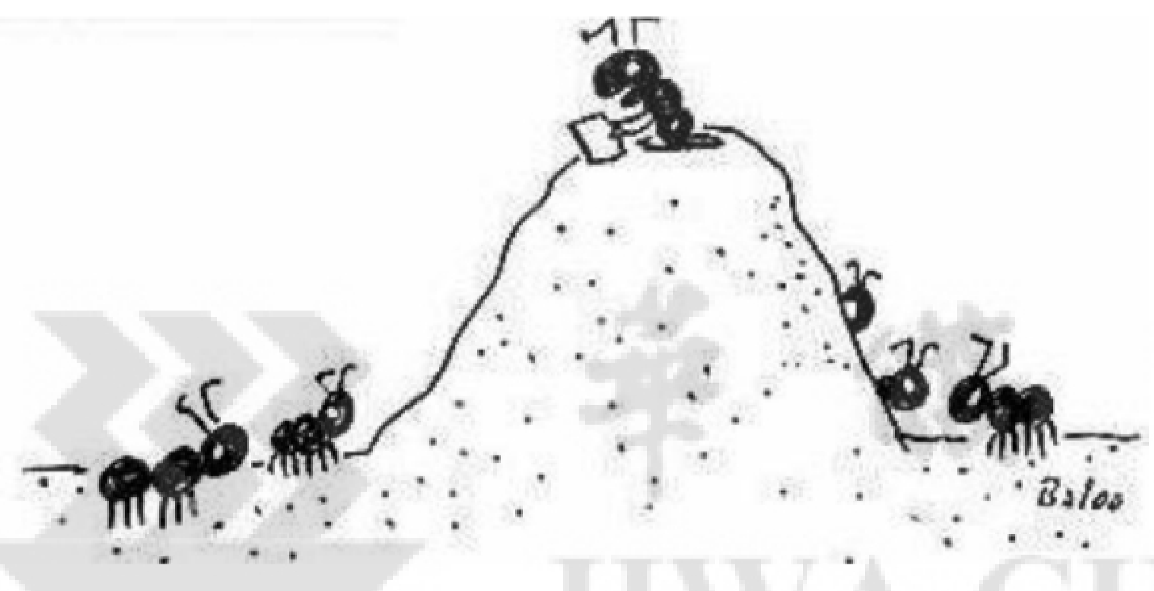
An omega-3 fatty acid.
Found in fish such as salmon and cod.

Did you know?

Ant hills had long been known to emit acidic vapour when the English naturalist John Ray attempted his somewhat brutal distillation of ants, but it is thanks to him that the source was discovered. Methanoic acid, also known by its trivial name, formic acid, is the weapon of choice for the members of the family formicidae, along with hundreds more species of wasp, bee and termite in the invertebrate order Hymenoptera. Sprayed or stung (along with a variety of other substances) the acid is a powerful and painful deterrent for would-be aggressors, and an effective biocide. A paste of baking soda (sodium bicarbonate) and very cold water can be applied to neutralise the acid and sooth the pain.

John Ray (1628-1705)

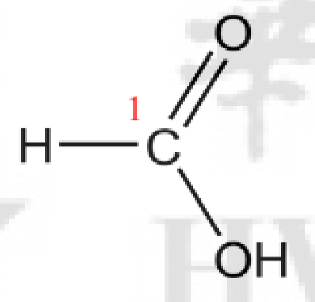
Picture source: http://www.ucmp.berkeley.edu/history/ray.html



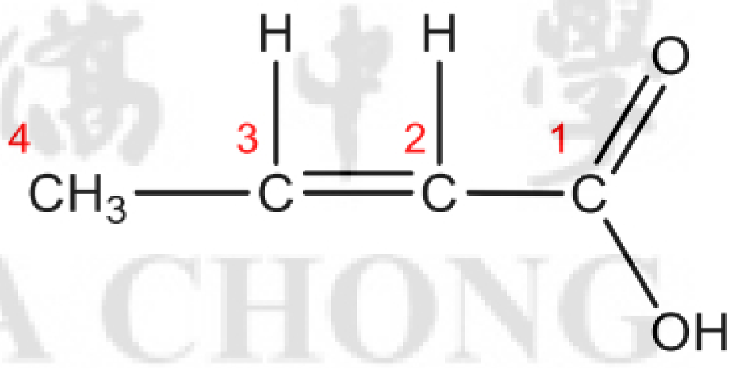
Picture source: www.CartoonStock.com

1.1 Nomenclature

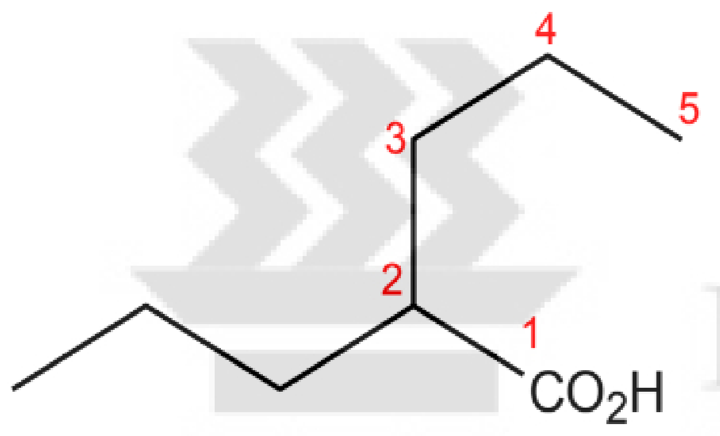
Straight chain carboxylic acids are named by replacing the terminal '-e' of the corresponding alkane with "-oic acid". For branched carboxylic acids, find the longest chain containing the $-CO_2H$ group, and change the terminal '-e' of the parent alkane to the suffix '-oic acid'. The carboxyl carbon is numbered C^1.



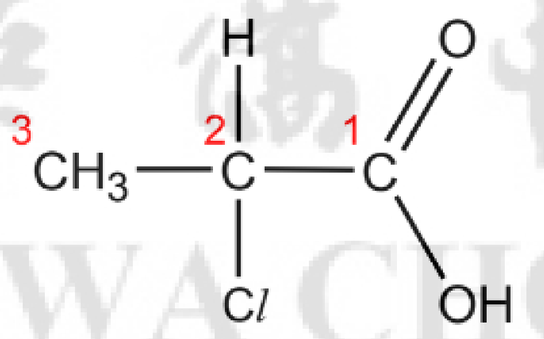
methanoic acid



cis-but-2-enoic acid



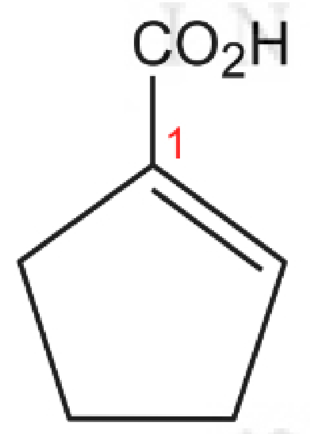
2-propylpentanoic acid



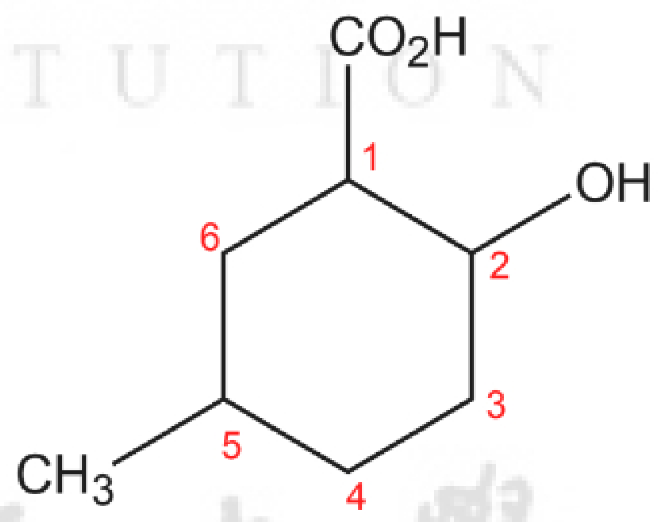
2-chloropropanoic acid

Compounds that contain the $-CO_2H$ group bonded to a ring are named using the suffix 'carboxylic acid'. If the carboxyl group is directly attached to an aromatic ring, the suffix used is 'benzoic acid'. The carbon in the ring that is attached to the $-CO_2H$ group is numbered C^1.

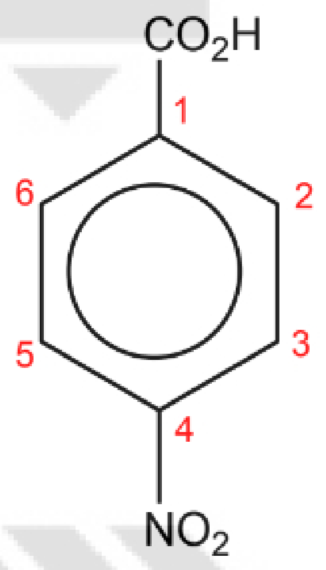
For aromatic acids which have 2 $-CO_2H$ groups attached directly to the benzene ring, it is named as dicarboxylic acids.



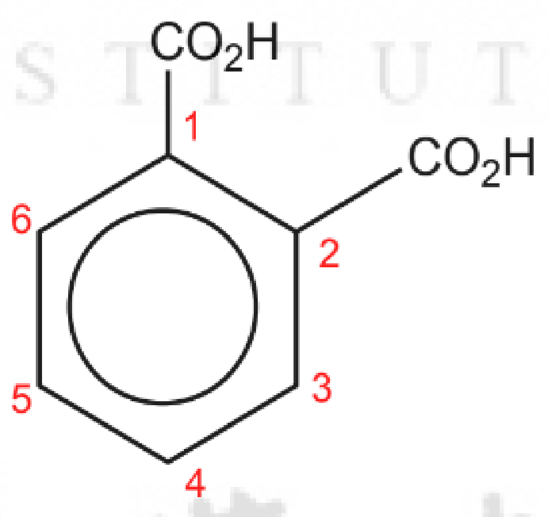
cyclopent-1-ene carboxylic acid



2-hydroxy-5-methylcyclohexane carboxylic acid



4-nitrobenzoic acid



benzene-1,2-dicarboxylic acid

Self-Practice Question 1.1

Draw the structural formula for each of the following compounds:

1. 2-hydroxy-3-methylbutanoic acid

2. cyclohept-4-ene-1,3-dicarboxylic acid

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2 PHYSICAL PROPERTIES OF CARBOXYLIC ACIDS

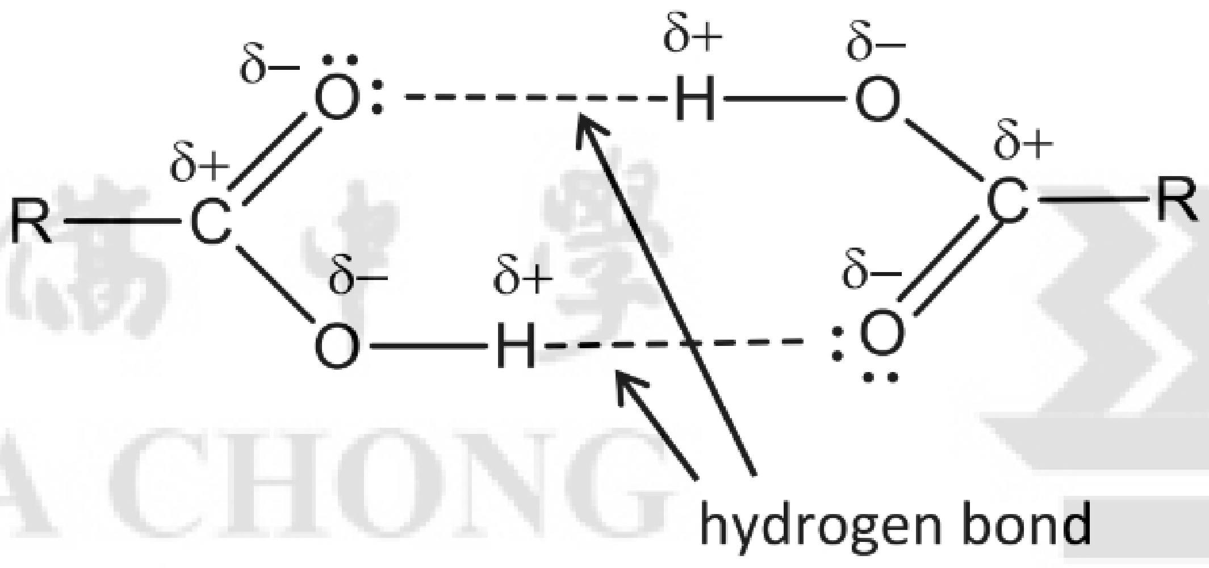
2.1 Boiling points

Alcohol		M_r	b.p. /°C	Carboxylic acid		M_r	b.p. /°C
Ethanol	CH_3CH_2OH	46	78	Methanoic acid	HCO_2H	46	101
Propan-1-ol	$CH_3CH_2CH_2OH$	60	97	Ethanoic acid	CH_3CO_2H	60	118
Butan-1-ol	$CH_3CH_2CH_2CH_2OH$	74	118	Propanoic acid	$CH_3CH_2CO_2H$	74	141

Carboxylic acids have higher boiling points than corresponding alcohols with similar size of electron cloud (size of electron cloud may be compared based on M_r) because:

1. Hydrogen bonding between carboxylic acid molecules is stronger than that between alcohol molecules. This is due to the presence of the electron-withdrawing C=O group causing the δ+ on the H atom to be intensified and the O–H bond to be more polarised in the carboxylic acid.

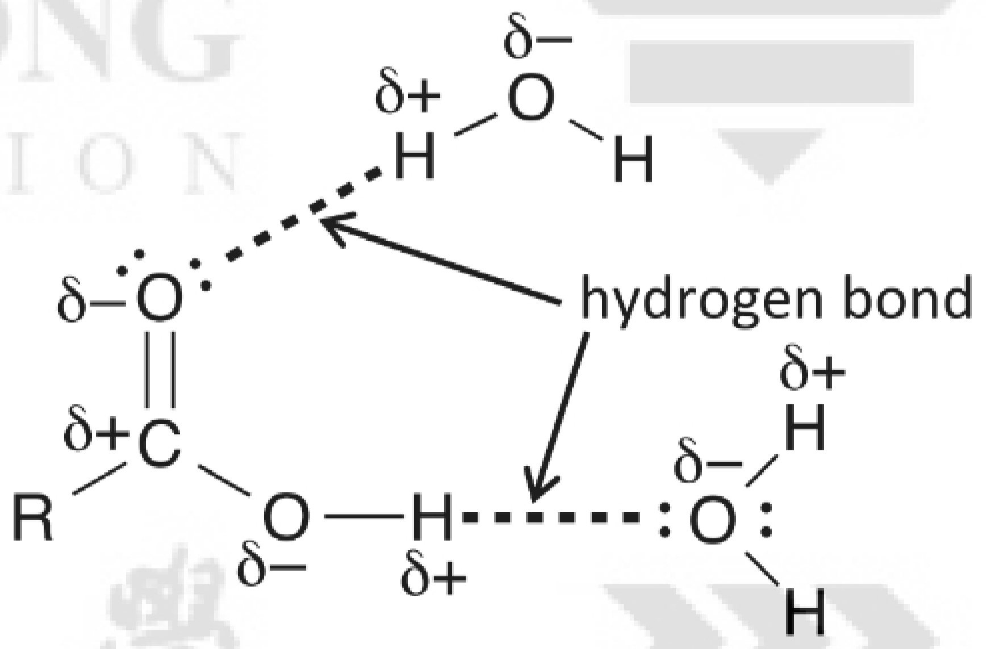
2. Carboxylic acids can dimerise (in the pure liquid) through hydrogen bonding (diagram below), effectively doubling the number of electrons (or size of electron cloud) in the dimer. This results in stronger dispersion forces between dimers.



2.2 Solubility

In non-hydrogen-bonding solvents such as benzene, carboxylic acids can form the hydrogen-bonded dimers. Carboxylic acids, especially those with longer hydrocarbon chains, are generally soluble in such non-polar solvents as dispersion forces can be formed between the solvent molecules and the hydrocarbon chain of the dimers.

In water, the carboxylic acid does not dimerise. The carboxylic acid molecules (the –CO_2H group) can form hydrogen bonding with the water molecules.



For carboxylic acids with longer hydrocarbon chains, solubility in water decreases as the hydrocarbon chain gets longer. The longer the non-polar hydrocarbon chain, the stronger the dispersion forces between carboxylic acid molecules. Energy released from hydrogen bonding between –CO_2H group and water molecules is less than the energy needed to overcome these dispersion forces, as well as the existing hydrogen bonding between water molecules.

Similarly, benzoic acid (a white crystalline solid at room temperature) is only slightly soluble in cold water but dissolves readily in hot water.

Self-Practice Question 2.1

Which of the following statements best explains why the boiling point of propanoic acid (141 °C) is higher than that of 2-fluorobutane (25 °C)?

A The relative molecular mass of propanoic acid is higher than that of 2-fluorobutane.

B The covalent bonds in propanoic acid are stronger than those in 2-fluorobutane.

C There are hydrogen bonds between propanoic acid molecules, but not between 2-fluorobutane molecules.

D Propanoic acid molecule has a larger surface area than 2-fluorobutane.

3 PREPARATION OF CARBOXYLIC ACIDS

LO 11.7 (a): describe the formation of carboxylic acids from alcohols, aldehydes and nitriles

Carboxylic acids can be prepared from:

- Oxidative cleavage of alkenes (Topic 11 Alkenes)
- Side chain oxidation of alkylbenzenes (Topic 12 Arenes)
- Acid and alkaline hydrolysis of nitriles (Topic 13 Halogen Derivatives)
- Oxidation of primary alcohols (Topic 16 Hydroxy Compounds)
- Oxidation of aldehydes (Topic 17 Carbonyl Compounds)
- Hydrolysis of acyl chlorides (covered later in Section 6.2.1)
- Acid and alkaline hydrolysis of esters/amides (esters covered later in Section 7.4, amides in Topic 19 Nitrogen Compounds)

Self-Practice Question 3.1

1. Suggest the product formed from the oxidation of 2-methyl-1-butanol, using hot acidified potassium manganate(VII).

2. The same carboxylic acid is obtained either by the hydrolysis of a nitrile **P**, or by the oxidation of an alcohol **Q**. Which of the following pairs could **P** and **Q** be?

	P	**Q**
A	CH_3CH_2CN	CH_3CH_2OH
B	$(CH_3)_2CHCN$	$(CH_3)_3COH$
C	$C_6H_5CH(CH_3)CN$	$C_6H_5CH_2CH(OH)CH_3$
D	$C_6H_5CH_2CN$	$C_6H_5CH_2CH_2OH$
E	C_6H_5CN	C_6H_5OH

3. Give the synthetic routes to show the conversion of the halogenoalkane to propanoic acid:

(i) CH_3CH_2Br

(ii) $CH_3CH_2CH_2Br$

(iii) $CH_3CH_2CHBrCH_2CH_2CH_3$

4 REACTIONS OF CARBOXYLIC ACIDS

LO 11.7 (b): describe the reactions of carboxylic acids in the formation of:

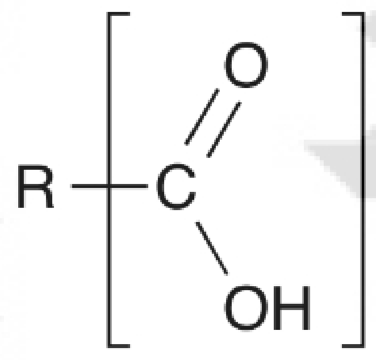
(i) salts

(ii) esters on condensation with alcohols, using ethyl ethanoate as an example

(iii) acyl chlorides, using ethanoyl chloride as an example

(iv) primary alcohols, via reduction with lithium aluminium hydride, using ethanol as an example.

The characteristic chemical behaviour of carboxylic acids is determined by the carboxyl group.



There are 3 main kinds of reactions that carboxylic acids undergo:

(i) **Acid-metal/Acid-base reactions** (O–H bond is broken to form salts)

(ii) **Nucleophilic (acyl) substitution** (replacement of the –OH group)

(iii) **Reduction** of the CO_2H group

The C=O and O–H bonds are so close in proximity that carboxylic acids do not behave exactly like alcohols, aldehydes or ketones. For example,

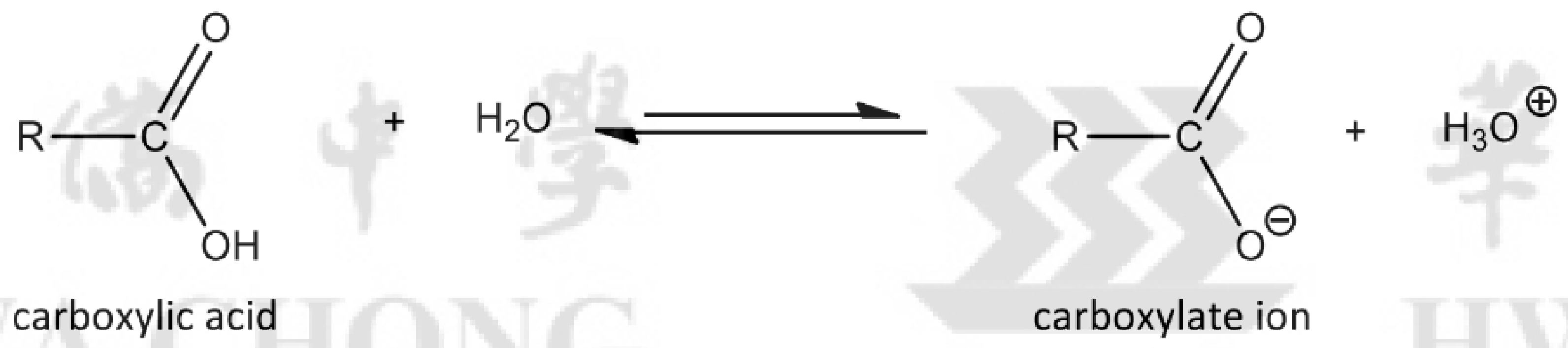
(i) carboxylic acids are stronger acids than alcohols (discussed further in Section 4.1.1)

(ii) carboxylic acids do not undergo nucleophilic addition like aldehydes and ketones and do not give a positive test with 2,4-dinitrophenylhydrazine and aqueous alkaline iodine. This is because the delocalisation of electrons from the O–H group into the C=O group makes the carboxyl carbon less electron deficient and less readily attacked by nucleophiles.

4.1 Acidity of Carboxylic Acids

LO 11.7 (c): explain the acidity of carboxylic acids and of chlorine-substituted ethanoic acids in terms of their structures

Carboxylic acids are weak Bronsted acids. The O–H bond breaks to give H^+ and the conjugate base, RCO_2^- (carboxylate ion).



As seen in Topic 16 Hydroxy Compounds, the strength of acids depends on the stability of the conjugate base formed.

The conjugate base is negatively charged. The more dispersed the negative charge, the less likely the conjugate base will accept a proton (to re-form the acid), the more stable it is.

The more stable the conjugate base, the greater the extent of acid dissociation, the larger the K_a (the smaller the pK_a) and the stronger the acid.

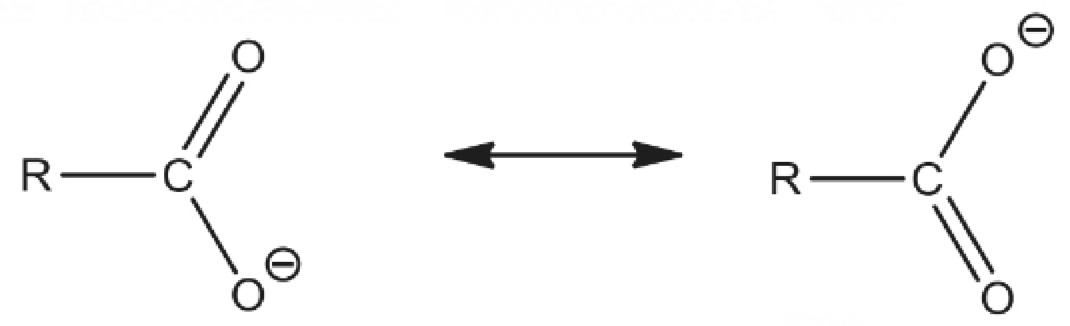
4.1.1 Relative acidities of carboxylic acids, phenols and aliphatic alcohols

	Ethanol	Water	Phenol	Ethanoic acid
pK_a	15.9	15.7	9.95	4.75

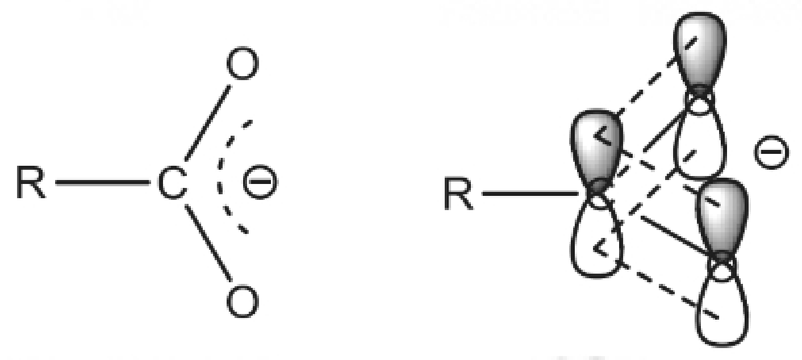
Table 1. pK_a values to compare the acidities of ethanol, water, phenol and ethanoic acid.

From the pK_a values above, carboxylic acids are stronger acids than phenols or aliphatic alcohols.

The negative charge on the carboxylate ion is delocalised **equally over two highly electronegative oxygen atoms**. The negative charge is **dispersed** and the carboxylate anion is greatly **stabilised**.

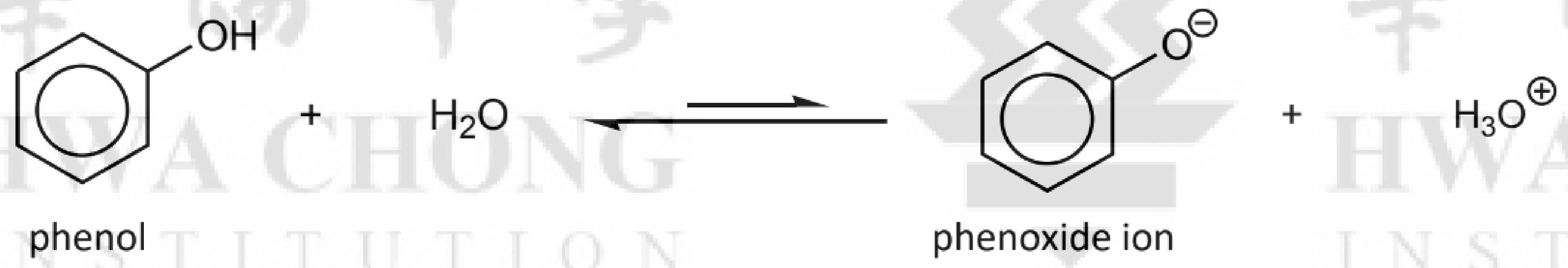


two equivalent resonance forms



resonance stabilised carboxylate ion

Recall that the negative charge on the phenoxide ion is also delocalised i.e. over the benzene ring which explains why phenol is more acidic than alcohols and water. However, the delocalisation in the phenoxide ion is less than that in the carboxylate ion, as the carbon atoms in the benzene ring do not bear the negative charge as well as the two electronegative O atoms in the carboxylate ion. Hence the carboxylate ions are more stabilised than the phenoxide ion and phenols are weaker acids than carboxylic acids.



The electron-donating alkyl group (–R) **intensifies** the negative charge on the alkoxide anion and the alkoxide anion is **destabilised.**

$$\underset{\text{alcohol}}{ROH} + H_2O \rightleftharpoons \underset{\text{alkoxide ion}}{R{-}O^{\ominus}} + H_3O^{\oplus}$$

The difference in acidity of carboxylic acids, phenols and alcohols affects their behaviour with sodium metal, sodium hydroxide and sodium carbonate (or sodium bicarbonate):

	Na	**NaOH(aq)** **a strong base**	**Na_2CO_3(aq) / $NaHCO_3$(aq)** **weak bases**
Aliphatic alcohols (ROH)	✓	×	×
Phenols	✓	✓	×
Carboxylic acids (RCO_2H)	✓	✓	✓

(✓: react ×: doesn't react)

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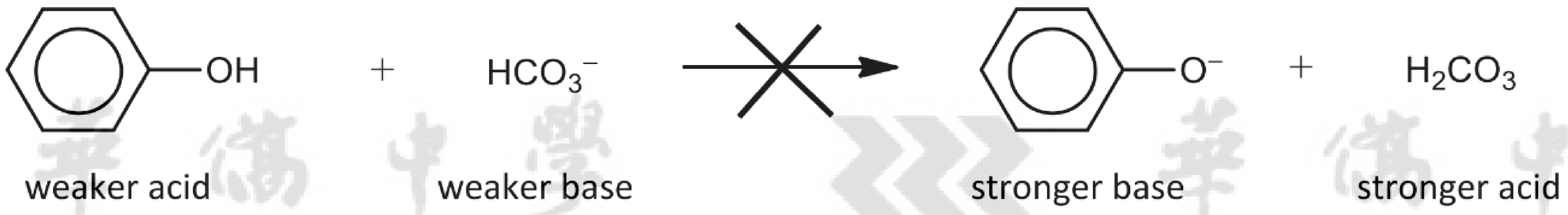
Recall from Topic 15 Acid-Base Equilibria that the stronger acid is able to protonate the conjugate base of the weaker acid. Carboxylic acids (e.g. ethanoic acid, pK_a = 4.75) are stronger acids than carbonic acid (pK_a = 6.4) so they can donate a proton to the carbonate or bicarbonate ion.

$$\underset{\text{stronger acid}}{CH_3CO_2H} + \underset{\text{stronger base}}{HCO_3^-} \longrightarrow \underset{\text{weaker base}}{CH_3CO_2^-} + \underset{\text{weaker acid}}{H_2CO_3}$$

Hence whenever we add carbonate or bicarbonate to carboxylic acid, an acid-base reaction occurs. Effervescence of CO_2 is observed as the H_2CO_3 produced decomposes readily into CO_2 and H_2O.

$$H_2CO_3 \rightleftharpoons CO_2 + H_2O$$

Phenol (pK_a = 9.95) is a weaker acid than carbonic acid, hence phenol is unable to donate a proton to the carbonate or bicarbonate ion.



Similarly, alcohols (e.g. ethanol, pK_a = 15.9) do not react with sodium hydroxide, as being weaker acids than water (pK_a = 15.7), they are unable to donate a proton to the hydroxide ion.

$$\underset{\text{weaker acid}}{CH_3CH_2OH} + \underset{\text{weaker base}}{OH^-} \not\longrightarrow \underset{\text{stronger base}}{CH_3CH_2O^-} + \underset{\text{stronger acid}}{H_2O}$$

Self-Practice Question 4.1

(a) Arrange the following molecules in order of decreasing acid strength (as Bronsted acid).

C_6H_5OH, H_2CO_3, CH_3CO_2H, HCl, CH_3CH_2OH

(b) State if each of the following reactions will occur. If yes, complete the equation.

(i) $C_6H_5O^- + H_2CO_3 \rightarrow$

(ii) $CH_3CO_2^- + H_2CO_3 \rightarrow$

(iii) $CH_3CO_2^- + HCl \rightarrow$

(iii) $CH_3CH_2O^- + CH_3CO_2H \rightarrow$

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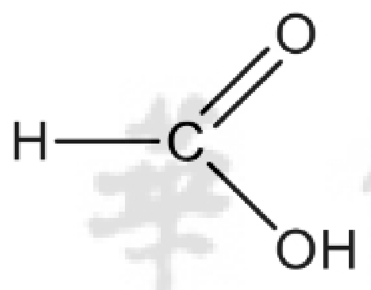
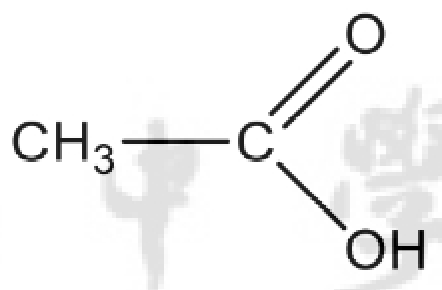
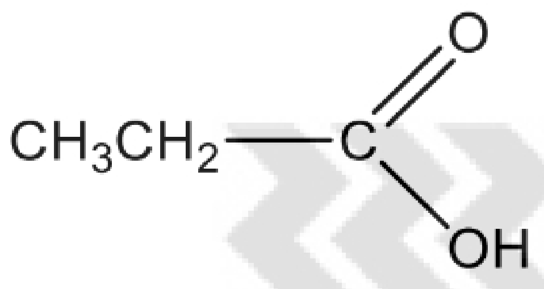
4.1.2 Effect of Substituents on Acidity of Carboxylic Acids

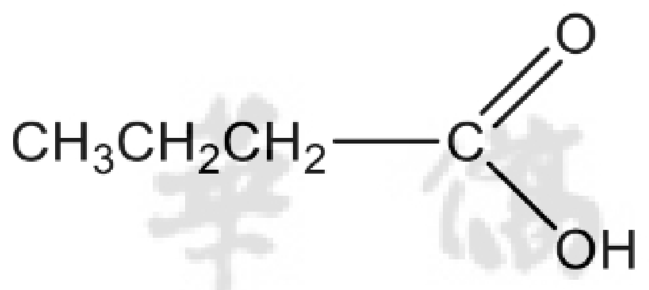
Electron-donating groups

Electron-donating groups (e.g. alkyl groups) intensify the negative charge on the carboxylate anion, destabilise the anion and decrease the acidity of the carboxylic acid.


pK_a = 3.77


pK_a = 4.75

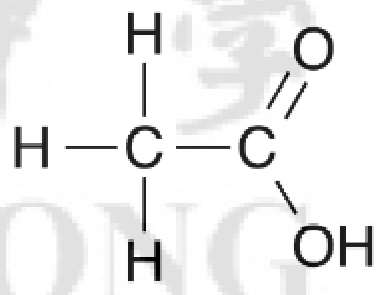

pK_a = 4.88

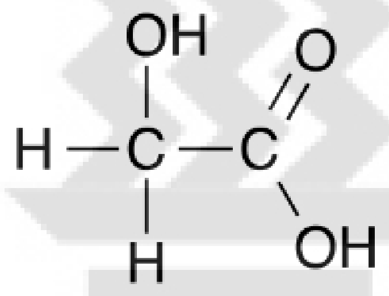

pK_a = 4.82

(The similar pK_a values of ethanoic acid, propanoic acid and butanoic acid suggest that the length of the alkyl chain does not have a significant impact on acidity.)

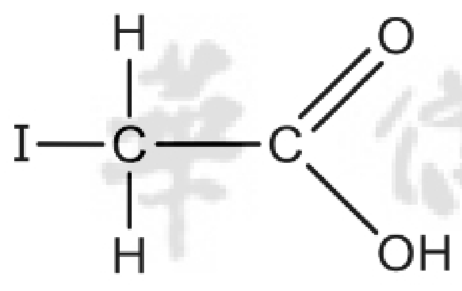
Electron-withdrawing groups

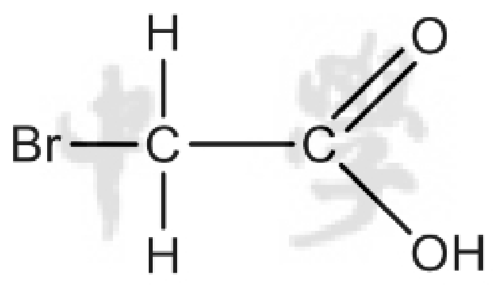
Electron-withdrawing groups (e.g. halogens, NO_2, OH, NH_2) disperse the negative charge on the carboxylate anion, stabilise the anion and increase the acidity of the carboxylic acid.

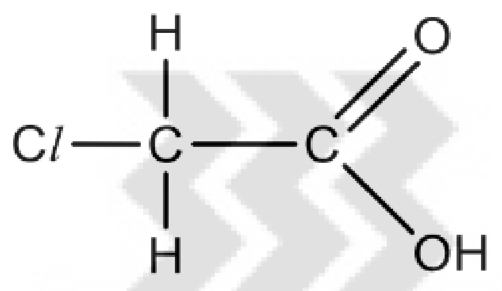

pK_a = 4.75

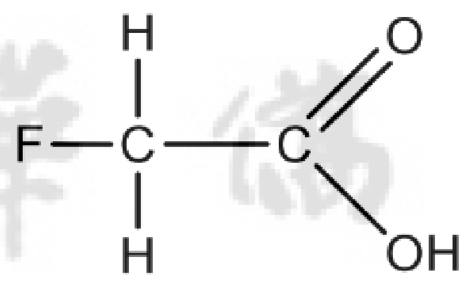

pK_a = 3.83

The halogen (e.g. C*l*), –OH or $–NH_2$ group exert an electron-withdrawing inductive effect (O and N are electronegative atoms). The more electronegative the halogen atom, the greater the electron-withdrawing effect, the stronger the acid.


pK_a = 3.15

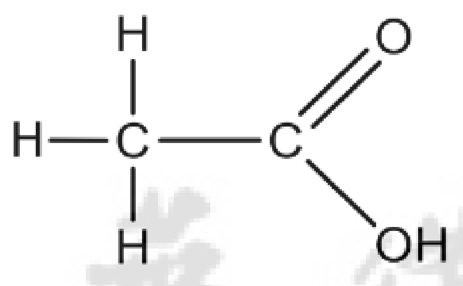

pK_a = 2.89

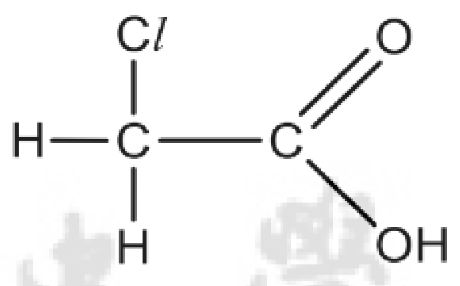

pK_a = 2.87

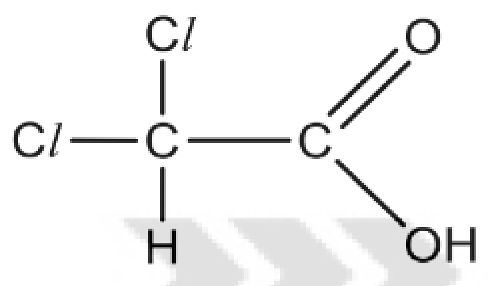

pK_a = 2.60

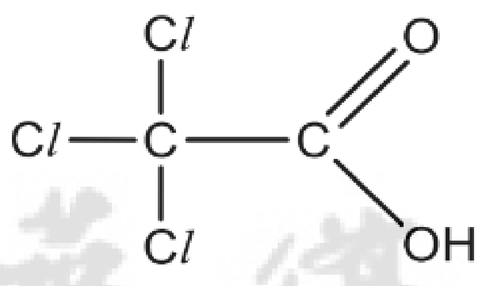
Number of electron-withdrawing groups

Increasing the number of electron-withdrawing groups increases acidity.


pK_a = 4.75

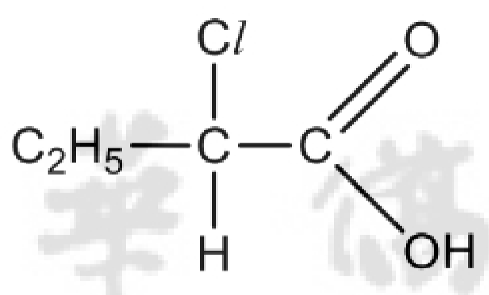

pK_a = 2.87

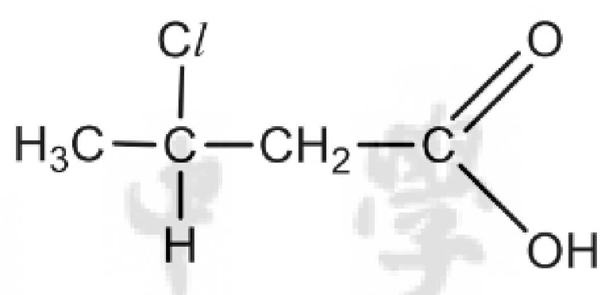

pK_a = 1.48

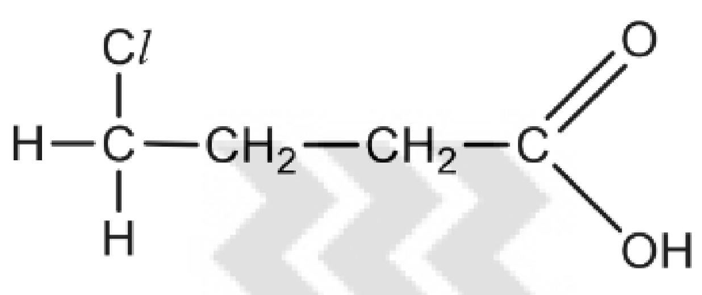

pK_a = 0.64

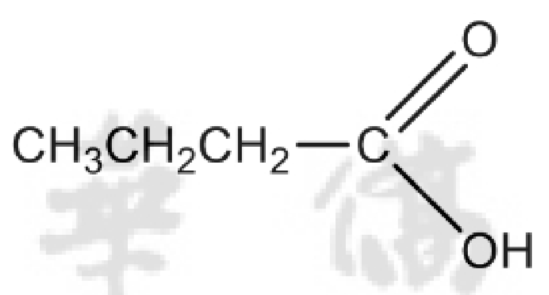
Proximity of electron-withdrawing groups to the $–CO_2H$ group

The nearer the electron-withdrawing group is to the carboxyl group, the greater the inductive effect, and the stronger the acid. As inductive effect decreases with increasing distance, it becomes insignificant when the electron-withdrawing effect is acting through more than 4 atoms.

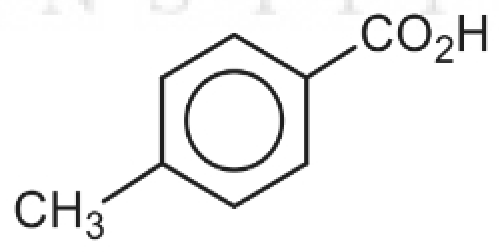

pK_a = 2.86


pK_a = 4.05

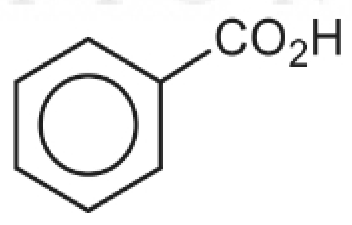

pK_a = 4.52


pK_a = 4.82

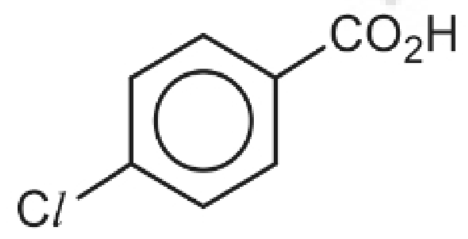
The effects of electron-donating and electron-withdrawing groups are also observed for substituted benzoic acids.



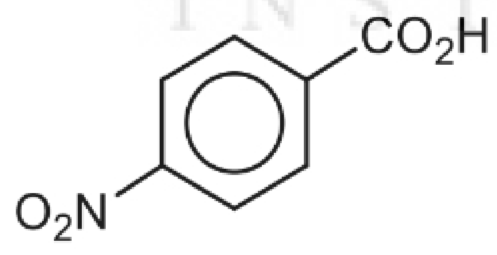
pK_a = 4.34



pK_a = 4.19



pK_a = 4.00



pK_a = 3.41

Lecture Exercise 4.1

Arrange these compounds in order of increasing pK_a values.

ethanoic acid, chloroethanoic acid, ethanol, phenol, water

4.1.3 Acid-metal (Redox)/Acid-base reactions

Like inorganic acids, carboxylic acids react with metals, bases, carbonates and bicarbonates to form salts.

With metals	$CH_3CO_2H + Na \longrightarrow CH_3CO_2^-Na^+ + ½\ H_2$
With bases	$CH_3CO_2H + NaOH \longrightarrow CH_3CO_2^-Na^+ + H_2O$
With carbonates	$2\ CH_3CO_2H + Na_2CO_3 \longrightarrow 2\ CH_3CO_2^-Na^+ + CO_2 + H_2O$
With bicarbonates	$CH_3CO_2H + NaHCO_3 \longrightarrow CH_3CO_2^-Na^+ + CO_2 + H_2O$

The effervescence of CO_2 with carbonates or bicarbonates can be used as a *distinguishing test* for the presence of carboxylic acids. CO_2 forms a white ppt when bubbled through limewater.

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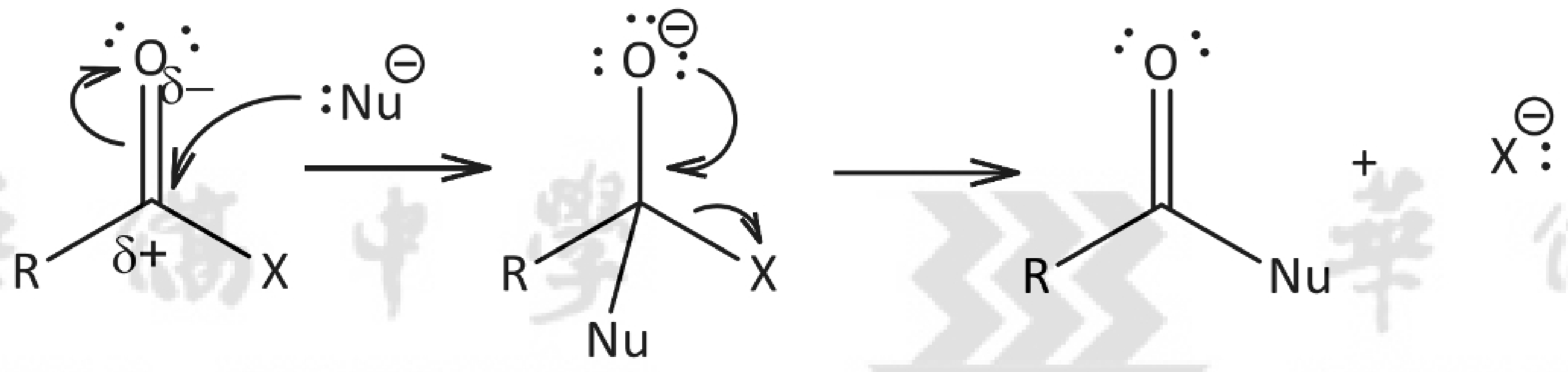
4.2 Nucleophilic (acyl) substitution

Carboxylic acid and its derivatives can undergo nucleophilic (acyl) substitution reactions at the C=O carbon. This type of reaction occurs because:

- the C=O carbon has a partial positive charge due to the electronegative O
- the C=O carbon has a planar geometry and is relatively unhindered, which makes it susceptible towards nucleophilic attack.

For your information only (not in H2 syllabus)

Nucleophilic (acyl) substitution reactions of carboxylic acids, esters, amides and acyl chlorides involves first the nucleophilic addition of nucleophile across the C=O, to form a tetrahedral intermediate, followed by elimination of a small molecule of H_2O, ROH, NH_3 or HC*l* respectively:



R = alkyl, aryl, H
X = OH, OR, NH_2, C*l*, etc

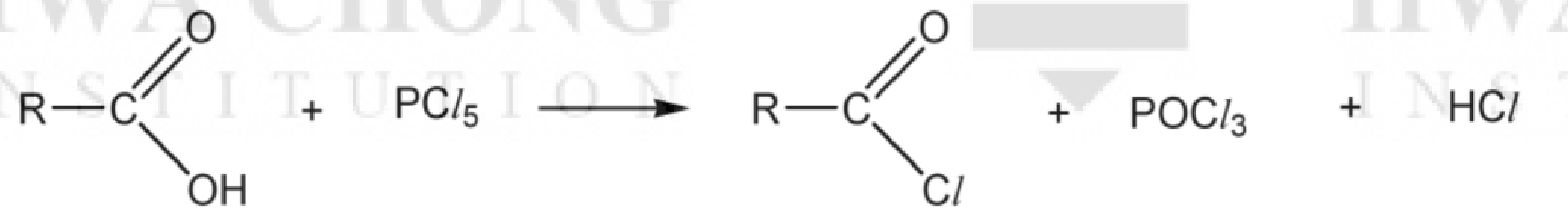
4.2.1 Condensation to form esters

Carboxylic acids can react with alcohols, but not phenols, in a condensation reaction to form esters, when heated in the presence of concentrated sulfuric acid (refer to Topic 16 Hydroxy Compounds).

In this reaction, the C–O bond of the $–CO_2H$ group is broken, as evidenced by isotopic labelling (recall this technique under Reaction Mechanisms in Topic 6 Reaction Kinetics).

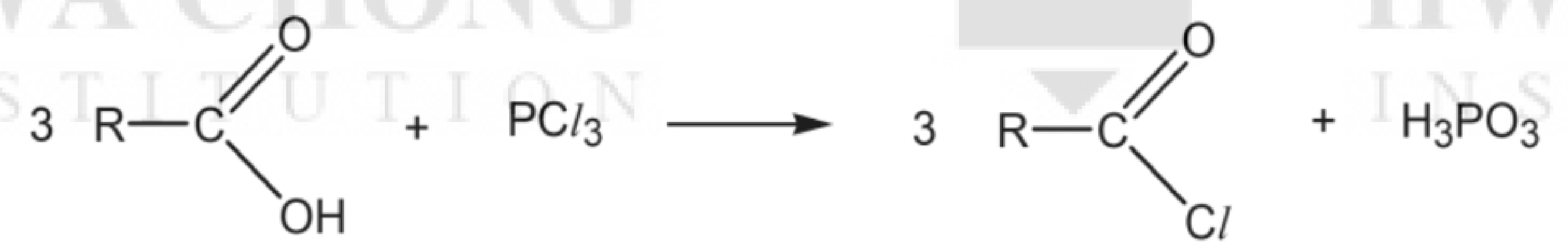
4.2.2 Formation of acyl chlorides

Like alcohols, the –OH group in carboxylic acids can be replaced with a –C*l* group to form acyl chlorides, using the same chlorinating reagents: PCl_5, PCl_3 and $SOCl_2$.



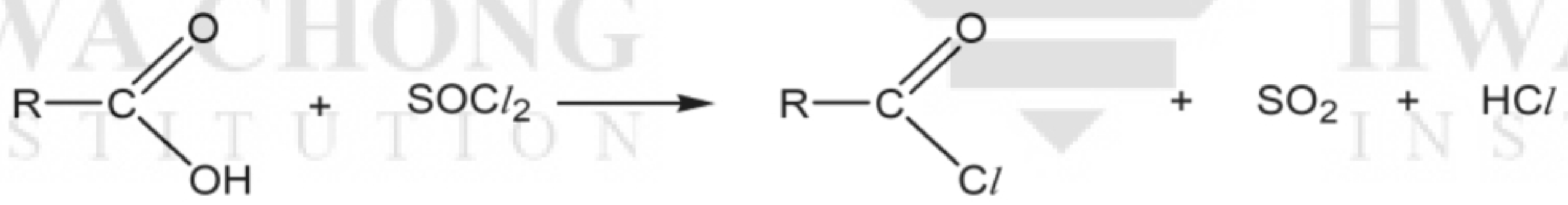
Reagents and conditions: PCl_5, room temperature

Observations: White fumes of HC*l* produced.



Reagents and conditions: PCl_3 , room temperature

Comments: PBr_3 or P/I_2 heat may be used to obtain respective acyl halides.



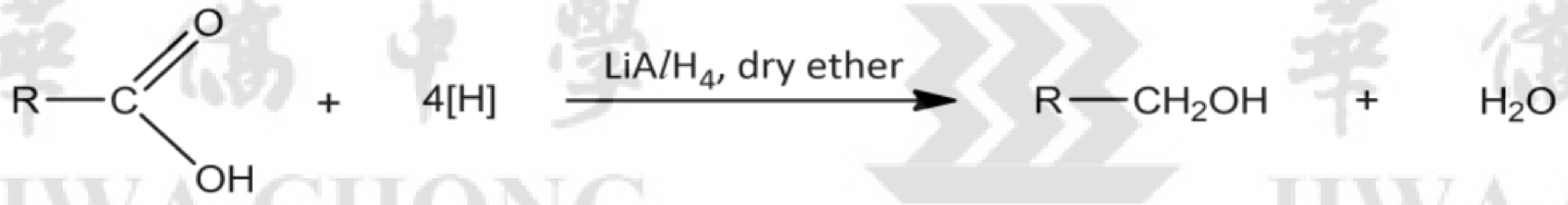
Reagents and conditions: $SOCl_2$, warm

Comments: Most convenient industrial method as by-products are gases and easily removed. Unreacted $SOCl_2$ is also easily distilled off (b.p. 79°C).

Carboxylic acids are often converted into acyl chlorides, which are highly reactive and could in turn be easily converted to other compounds.

4.3 Reduction to Primary Alcohols

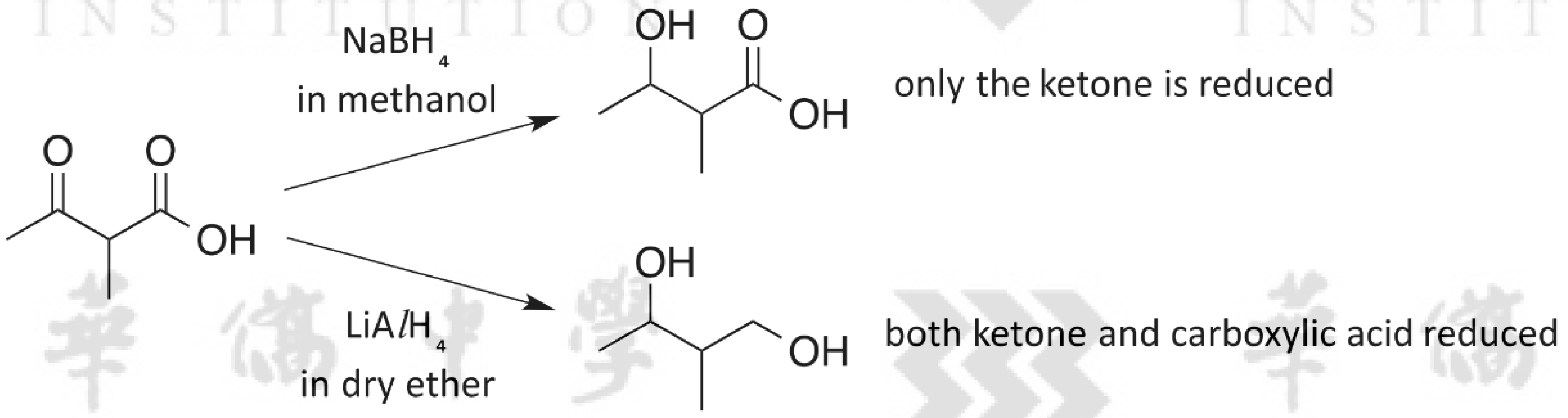
Carboxylic acids are reduced to primary alcohols using lithium aluminium hydride.



Reagents and conditions: $LiAlH_4$, dry ether, room temperature

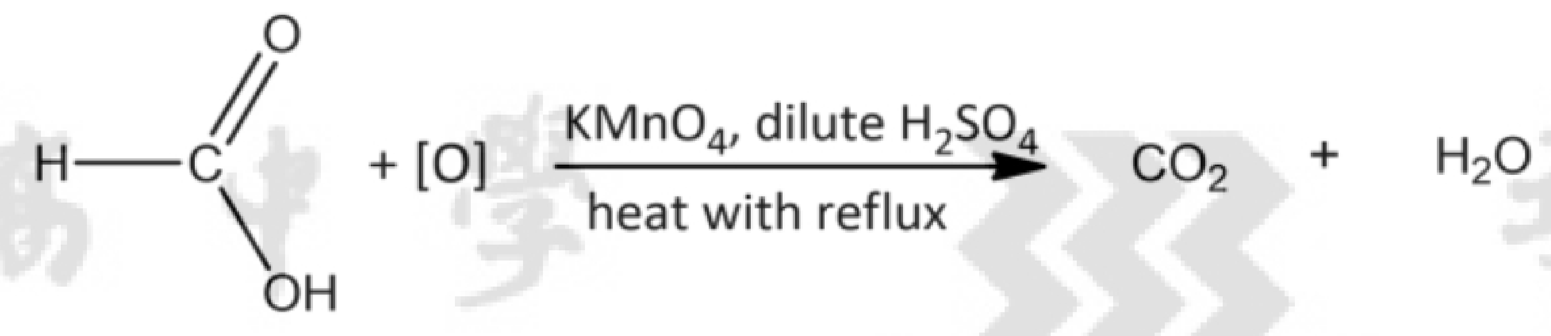
The $LiAlH_4$ must be used in anhydrous conditions! Note that carboxylic acids can only be reduced back to primary alcohols and not aldehydes.

Weaker reducing agents, such as $NaBH_4$ or H_2 with catalyst, will **not** work. Refer to Topic 17 Carbonyl Compounds for the comparison between the different reducing agents. With careful consideration of the reducing agents to be used, selective reduction can be done. For example,

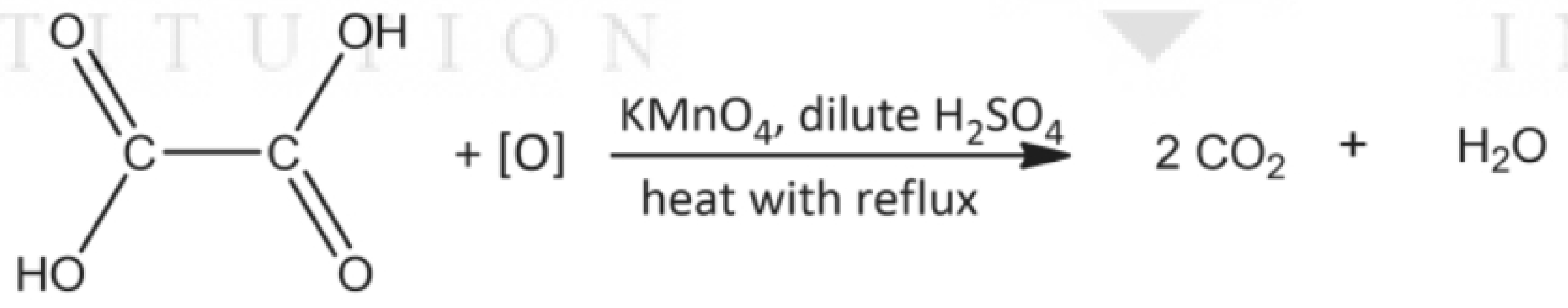


4.4 Special case: Oxidation of Methanoic acid and Ethanedioic acid

Only **TWO** carboxylic acids undergo further oxidation – **methanoic acid** and **ethanedioic acid**. All other acids cannot be oxidised by $KMnO_4$.



methanoic acid



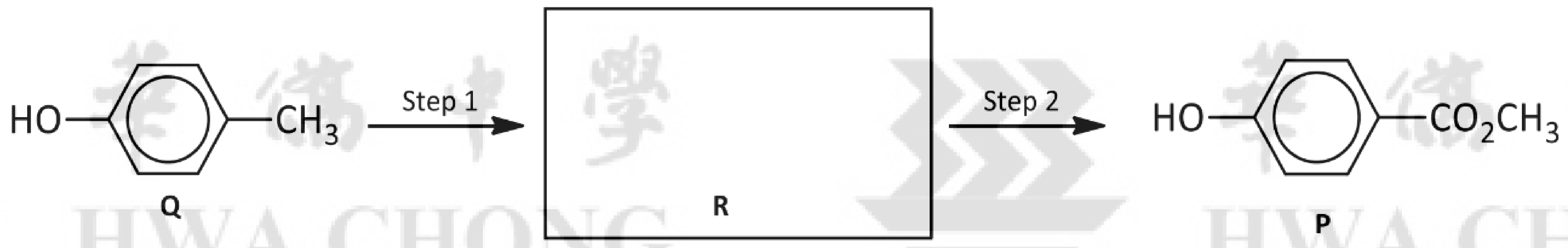
ethanedioic acid

Reagents and conditions: $KMnO_4$, dilute H_2SO_4, heat under reflux

Observations: Purple solution (MnO_4^-) decolourises (Mn^{2+}).
Effervescence of CO_2 observed.

Lecture Exercise 4.3

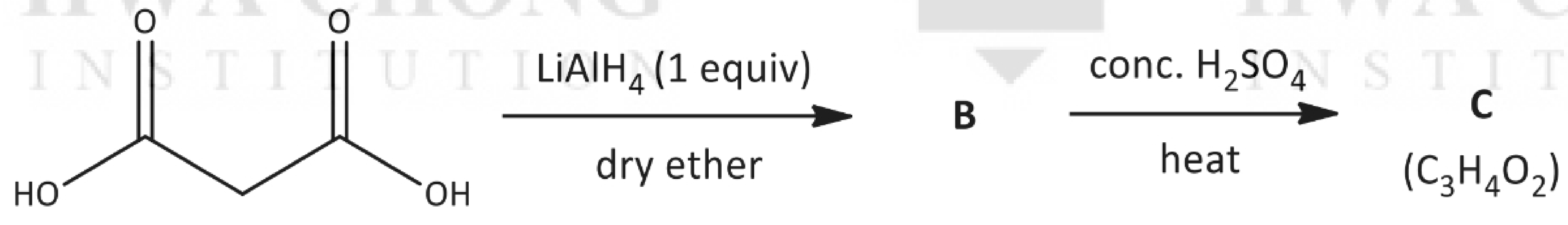
Substance **P** is now commonly used in antiseptic creams. **P** could be synthesised in the lab from compound **Q** by a method which involves an intermediate **R**.



(i) Draw the structure of the intermediate **R**.
(ii) Suggest reagents and conditions for Steps 1 and 2.

Lecture Exercise 4.4

The reaction scheme below shows how compound **C** can be made from malonic acid. **C** is made from **B** via intra-molecular esterification.



malonic acid

Suggest the structures for compound **B** and **C**.

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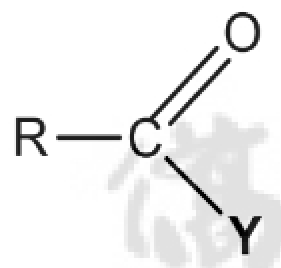
5 CARBOXYLIC ACID DERIVATIVES

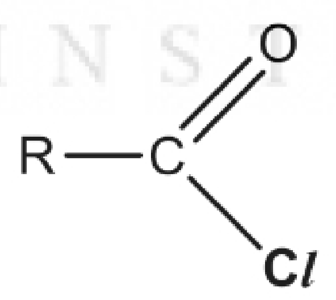
5.1 Introduction

Carboxylic acid derivatives are compounds in which the –OH group in the acid is replaced by –**Y**.

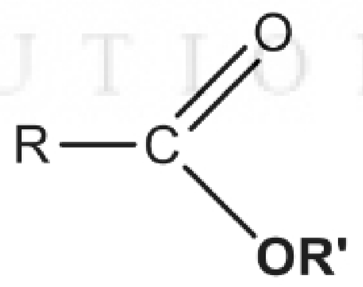


where **Y** = –X (F, C*l*, Br, I), –OR’, –NH_2

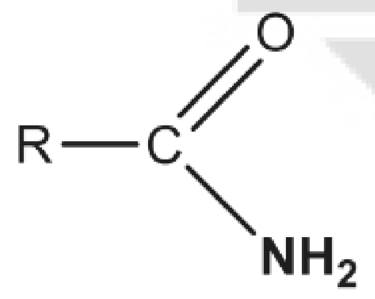
Some examples of acid derivatives are as follows:



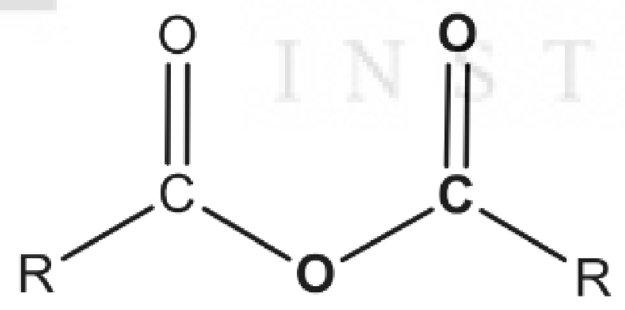
acyl chloride
(acid chloride)



ester



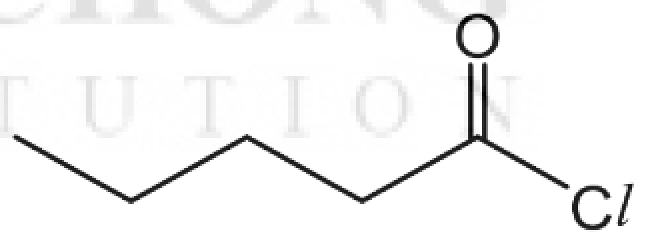
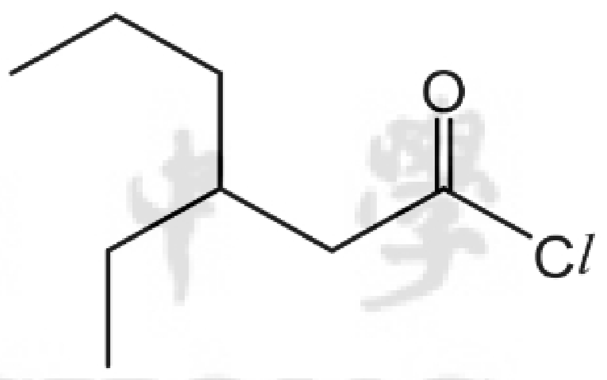
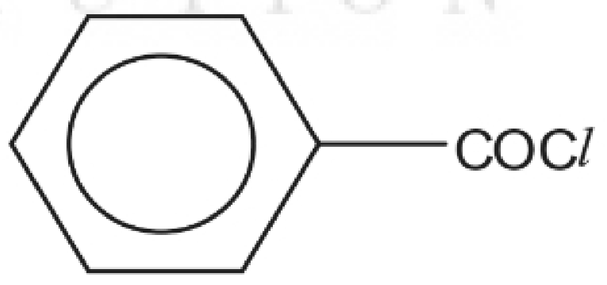
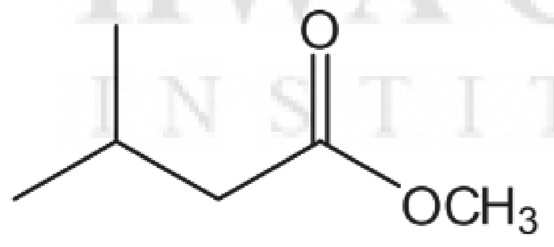
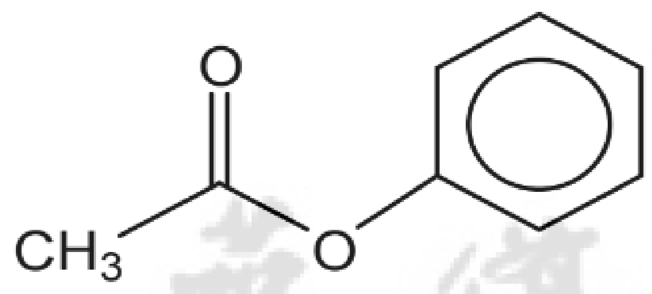
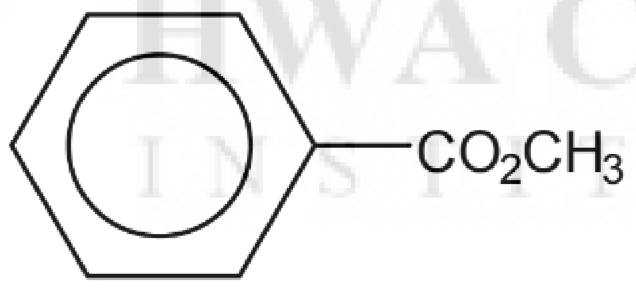
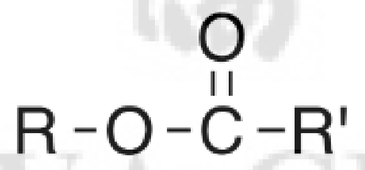
amide



acid anhydride
(not in H2 syllabus)

In the following sections, we will focus on acyl chlorides and esters.
Amides will be covered in Topic 19 Nitrogen Compounds.

5.2 Nomenclature

Functional Group	Acyl chloride (RCOC*l*)	Ester (RCO_2R')
Nomenclature	Replace the *‘-oic acid’* of the parent carboxylic acid with *‘-oyl chloride’*.	First, name the R group attached to the oxygen, followed by the parent carboxylic acid, replacing the *‘-oic acid’* with *‘oate’*.
Examples	 pentanoyl chloride  3-ethylhexanoyl chloride  benzoyl chloride	 methyl 3-methylbutanoate  phenyl ethanoate  methyl benzoate Note that condensed structural formula of esters can also be written as R–OCO–R’ which just refers to:  $R-O-\overset{\overset{\large O}{\|}}{C}-R'$

5.3 Physical properties of Carboxylic Acid Derivatives

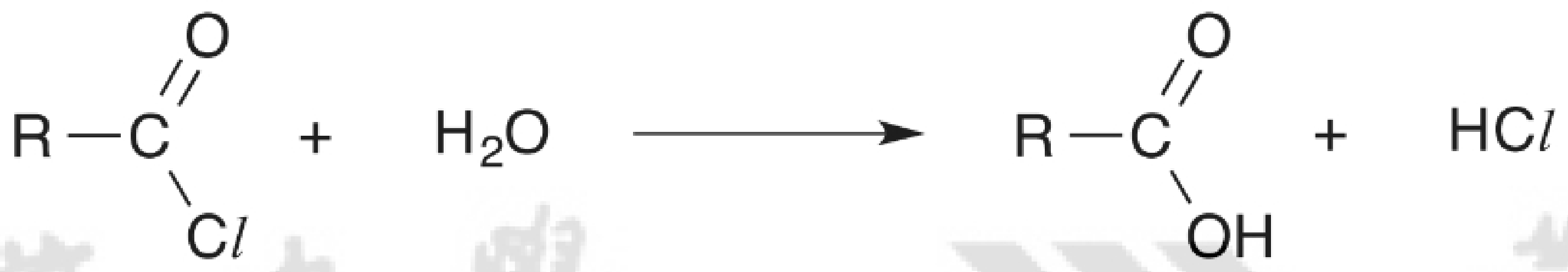
5.3.1 Boiling Points

Name	Formula	M_r	Boiling point/ °C
ethanoic acid	CH_3CO_2H	60	118
ethanoyl chloride	CH_3COCl	78.5	51
methyl ethanoate	$CH_3CO_2CH_3$	74	58

Esters and acyl chlorides have lower boiling points than their corresponding carboxylic acids. Their intermolecular **permanent dipole-permanent dipole attractions** are weaker than the hydrogen bonding for carboxylic acids, and require less energy to break. (Esters and acyl chlorides are unable to form intermolecular hydrogen bonding as they lack a hydrogen atom *directly* attached to a highly electronegative oxygen atom.)

5.3.2 Solubility

Esters are much less soluble in water compared to carboxylic acids and alcohols. Many esters are immiscible with water. Acyl chlorides, on the other hand, hydrolyse in water:



5.3.3 Odour

Acyl chlorides are colourless liquids with a sharp, irritating odour (partly due to the rapid hydrolysis to HC*l* and carboxylic acids).
Esters are colourless liquids with a pleasant and sweet or fruity smell. Esters are often used in the preparation of perfumes and artificial flavourings.

Self-Practice Question 5.1
Suggest a reason why the boiling point of ethanoyl chloride is higher than that of 2-chloropropane.

Self-Practice Question 5.2

Which of the following statements best explains why the solubility of ethyl ethanoate $CH_3CO_2CH_2CH_3$ in water is lower than that of propanoic acid?

A Ethyl ethanoate molecules cannot form hydrogen-bonded dimers like propanoic acid molecules.

B Ethyl ethanoate molecules have a larger non-polar alkyl chain compared to propanoic acid molecules.

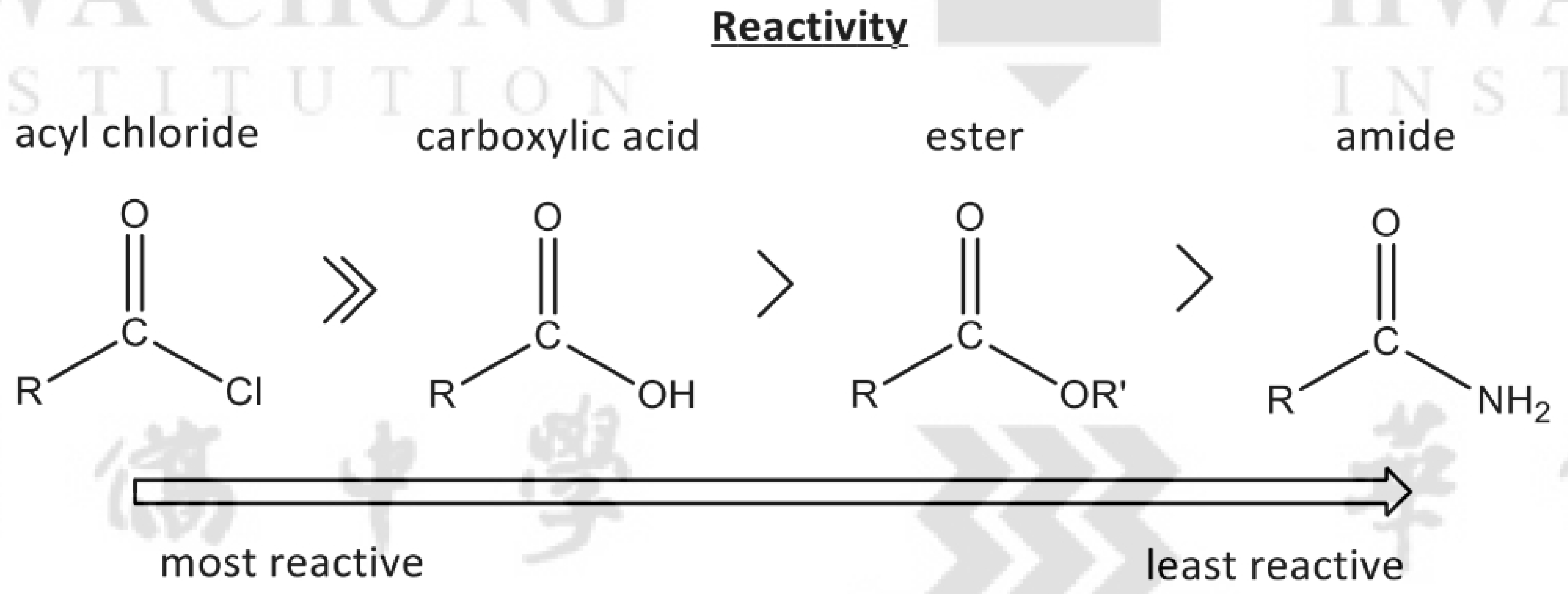
C Ethyl ethanoate molecules form weaker hydrogen bonds with water compared to propanoic acid molecules.

D Ethyl ethanoate molecule has a greater number of electrons than the propanoic acid molecule.

5.4 CHEMICAL REACTIVITY OF CARBOXYLIC ACID DERIVATIVES

Relative reactivity of carboxylic acids and their derivatives

Carboxylic acids and their derivatives differ greatly in reactivity towards nucleophilic substitution.



Reasons for the above trend:

1. **Inductive Effect**
   - A halogen substituent withdraws electrons through inductive effect from the C=O group, thus increases the partial positive charge on the carbon atom. This makes acyl halides more readily attacked by nucleophiles.
   - An amino group (—NH_2) or alkoxy group (—OR') donates electrons to the carbonyl carbon through resonance effect. This decreases the partial positive charge on the carbon atom. Hence, amides and esters are less readily attacked by nucleophiles.

2. **Leaving Group**
   - In general, the weaker the base, the better the leaving group. Halide anions are better leaving groups compared to the hydroxide ion as halides are weaker bases while the hydroxide ion is a stronger base (refer to discussion of leaving groups under nucleophilic substitution of alcohols in Topic 16 Hydroxy Compounds).

Because of these reactivity differences, it is usually possible to convert a more reactive acid derivative into a less reactive one.

6 ACYL CHLORIDES

6.1 Preparation of Acyl Chlorides

Acyl chlorides can be prepared from the following:

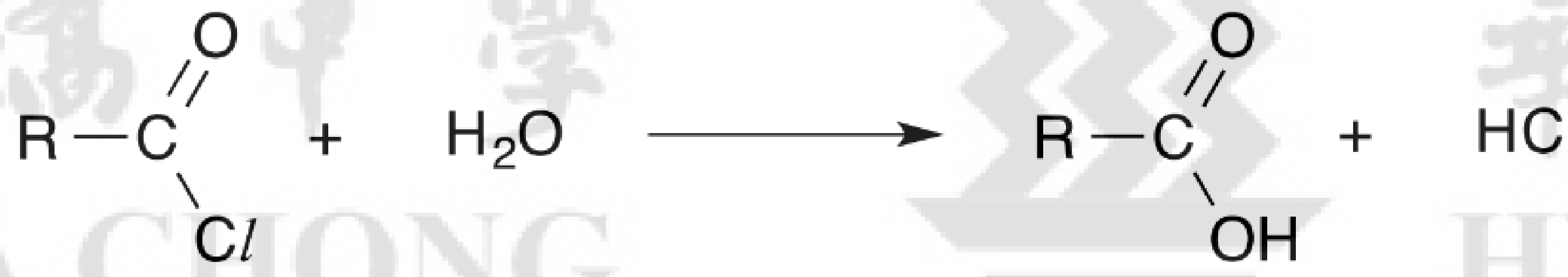
- Nucleophilic substitution of carboxylic acids (Section 4.2.2)

6.2 Reactions of Acyl Chlorides

6.2.1 Hydrolysis to form carboxylic acids (nucleophilic (acyl) substitution with water)

LO 11.7 (d): describe the hydrolysis of acyl chlorides

Acyl chlorides react with water violently at room temperature to give a carboxylic acid and white fumes of HC*l*. In fact, aliphatic acyl chlorides usually fume in moist air due to the formation of hydrogen chloride.



Reagents and conditions: water, room temperature

Comments: Rapid reaction forming white fumes of HC*l*

Lecture Exercise 6.1

Suggest a simple chemical test to distinguish CH_3CO_2H from CH_3COCl.

6.2.2 Condensation to form esters (nucleophilic (acyl) substitution with alcohols/phenols)

LO 11.7 (e)part: describe the condensation reactions of acyl chlorides with alcohols, phenols

LO 11.7 (g)part: describe the formation of esters from the condensation reaction of acyl chlorides

Acyl chlorides react with both <u>alcohols and phenols</u> to form esters via a condensation reaction. Refer to Topic 16 Hydroxy Compounds for the details of the reaction.

Lecture Exercise 6.2

What are the starting materials for the preparation of phenyl benzoate in the laboratory?

A C_6H_5OH, $C_6H_5CO_2H$, H_2SO_4

B C_6H_5Cl, $C_6H_5CO_2H$

C C_6H_5Cl, $C_6H_5CO_2H$, NaOH

D C_6H_5OH, C_6H_5COCl

E C_6H_5OH, C_6H_5COCl, NaOH

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Self-Practice Question 6.1

The small hive beetle, which invades colonies of the honeybee, identifies these colonies by detecting the bees' own alarm signal, the pheromone 3-methylbutyl ethanoate. How may this ester be made in the laboratory?

A $(CH_3)_2CHCH_2CO_2H + CH_3CH_2OH \xrightarrow[\text{heat}]{\text{conc. } H_2SO_4} \text{ester} + H_2O$

B $(CH_3)_2CHCH_2CO_2H + CH_3OH \xrightarrow[\text{heat}]{\text{conc. } H_2SO_4} \text{ester} + H_2O$

C $(CH_3)_2CHCH_2CH_2OH + CH_3COCl \longrightarrow \text{ester} + HCl$

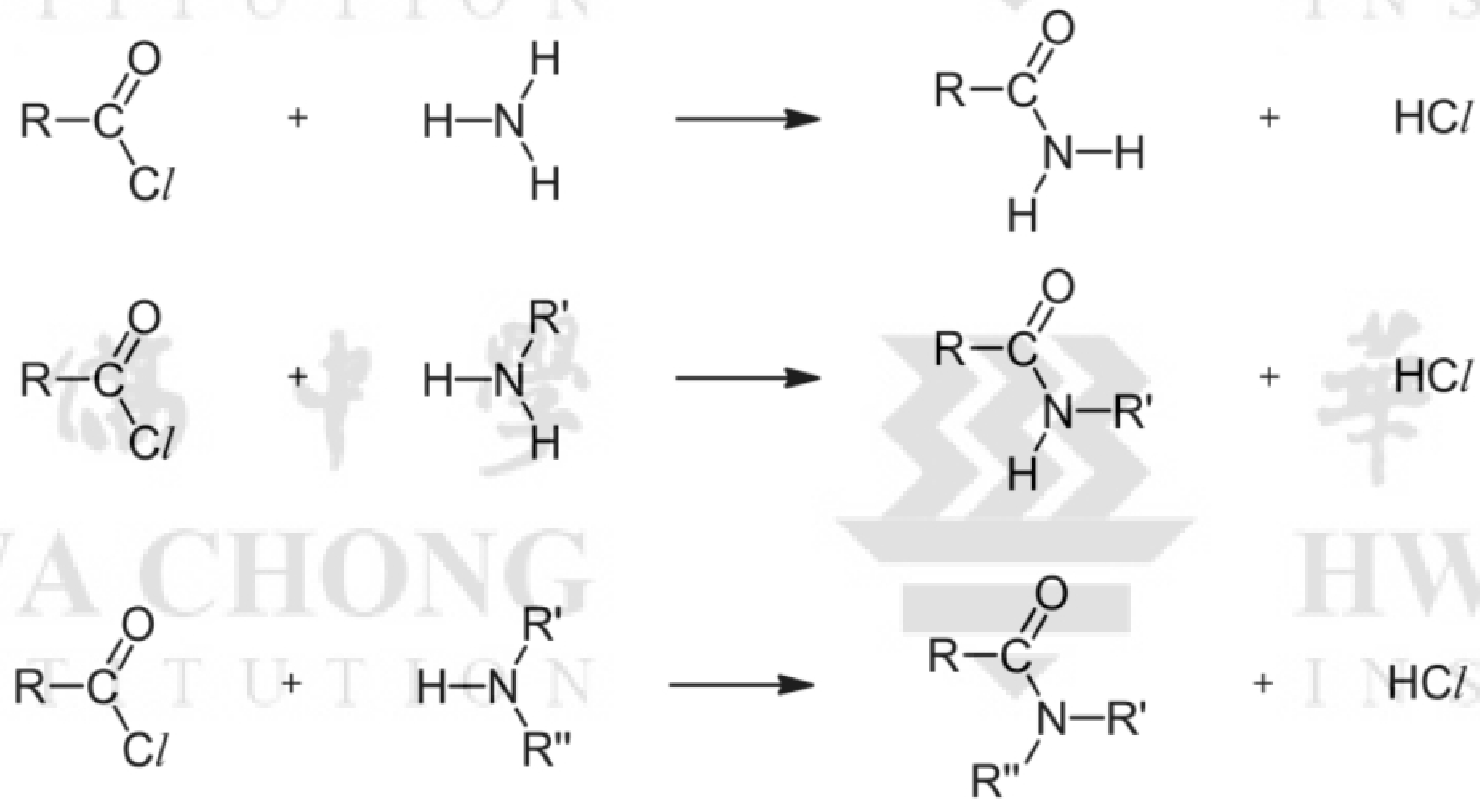
D $CH_3CH_2CH(CH_3)CH_2OH + CH_3COCl \longrightarrow \text{ester} + HCl$

[N2010/I/28]

6.2.3 Condensation to form amides (nucleophilic (acyl) substitution with ammonia/amines)

LO 11.7 (e)part: describe the condensation reactions of acyl chlorides with primary amines

Acyl chlorides react readily with ammonia to form amides, and with primary and secondary amines to form N-substituted amides. Tertiary amines do not form amides as they do not contain a replaceable H atom on the N.



Reagents and conditions: ammonia or primary amines or secondary amines (in excess), room temperature

Ammonia or amines are added in **excess** to ensure complete reaction as some ammonia or amines reacts with the acidic HC*l* to form an ammonium salt via acid-base reaction, i.e., $NH_3 + HCl \rightarrow NH_4Cl$

Carboxylic acids **cannot** be used in place of the acyl chlorides. This is because they react with amines/ammonia in an acid-base reaction instead. E.g. $CH_3CO_2H + NH_3 \rightarrow CH_3CO_2^-NH_4^+$

Self-PracticeQuestion 6.2

Which of these compounds **cannot** be made in one step from ethanoyl chloride?

A $CH_3COC_2H_5$

B $CH_3CONHC_6H_5$

C CH_3CONH_2

D CH_3CO_2H

[N1997/III/28]

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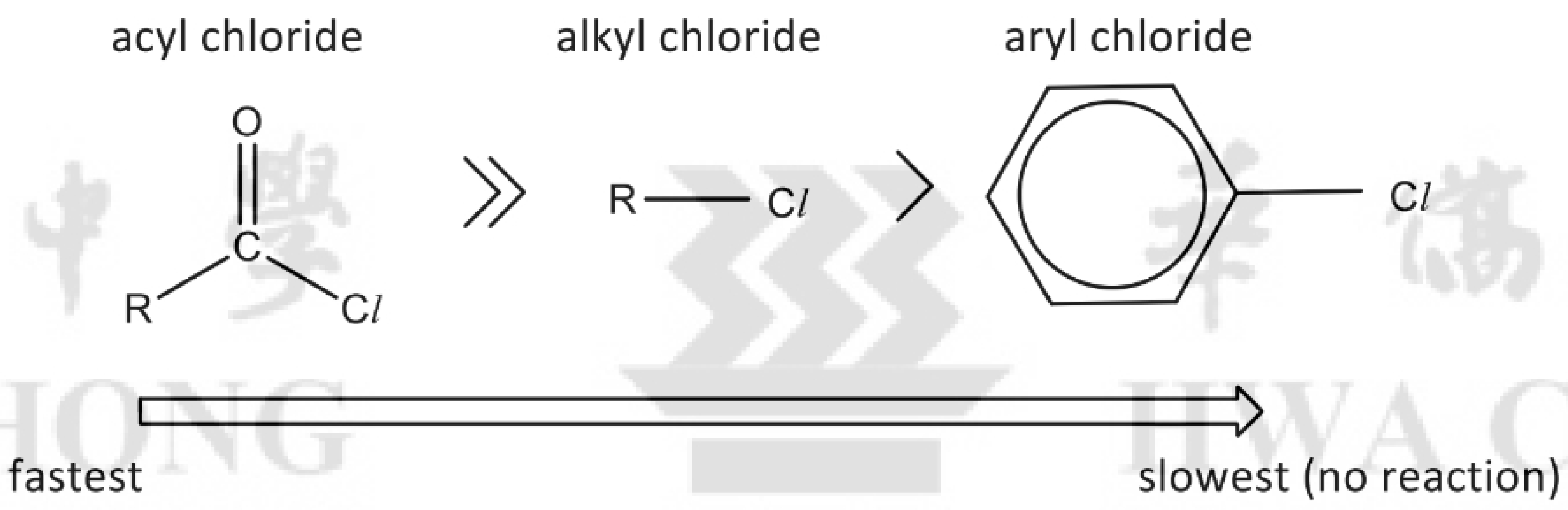
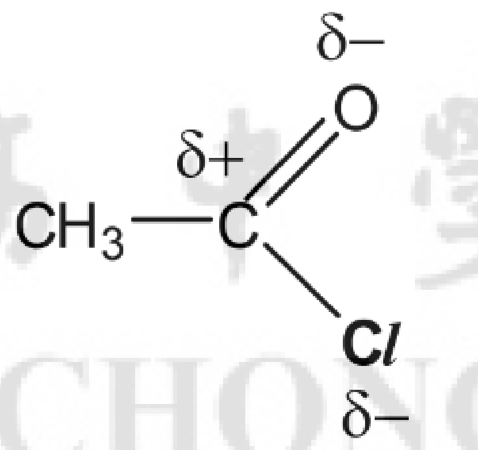
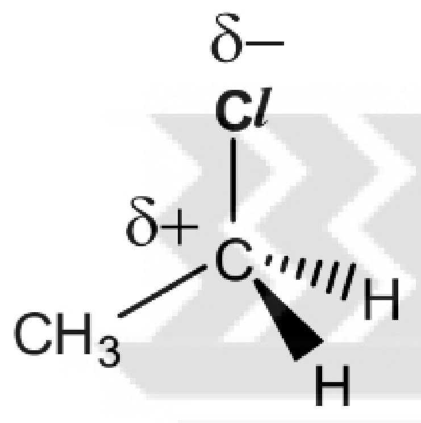
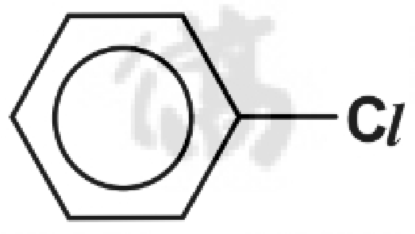
6.3 Relative rate of hydrolysis of acyl chlorides, alkyl chlorides and aryl chlorides

LO 11.7 (f): explain the relative ease of hydrolysis of acyl chlorides, alkyl chlorides and aryl chlorides

Type of chlorides		**Acyl chlorides**	**Alkyl chlorides**	**Aryl chlorides**
Rate of hydrolysis		 Note: The relative reactivity of alkyl chlorides and aryl chlorides was covered in Halogen Derivatives.		
Example		ethanoyl chloride 	chloroethane 	Chlorobenzene 
Hydrolysis conditions		H_2O room temperature	aqueous NaOH/ KOH heat under reflux	Not possible under ordinary lab conditions (only possible under very high temperature and pressure with aq. alkali)
Reasons	**Electronic factor**	C–C*l* cleaves easily without heating Highly electron deficient carbon on C–C*l* due to 2 electronegative atoms C*l* and O Attracts nucleophile more strongly	C–C*l* cleaves only with heating Less electron deficient carbon on C–C*l* due to polarisation by one electronegative C*l* atom only Attracts nucleophile less strongly	C–C*l* does not cleave easily Least electron deficient carbon on C–C*l* due to the delocalisation of the lone pair of electrons on C*l* into the benzene ring imparting partial double bond character to the C– C*l* bond in aryl chlorides, strengthening the bond. Attracts nucleophile minimally
	Steric factor	Planar acyl carbon makes it less hindered for the nucleophile to attack.	Tetrahedral geometry around chloro-substituted carbon is relatively more hindered.	Bulky aromatic ring hinders nucleophilic attack. Electron-rich benzene ring repels nucleophile.
Reaction with aq $AgNO_3$		White ppt of AgC*l* observed immediately.	No ppt formed in the cold. To obtain AgC*l* ppt, aqueous NaOH and heating are required (refer to Topic 13 Halogen Derivatives)	No ppt observed even after prolonged boiling with aqueous NaOH.

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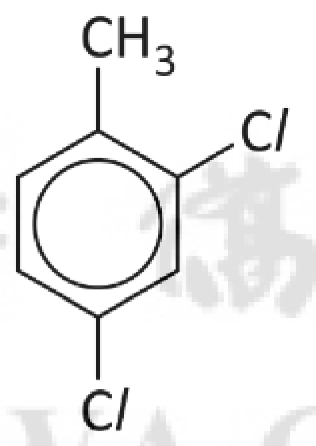
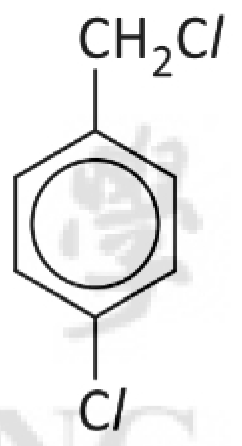
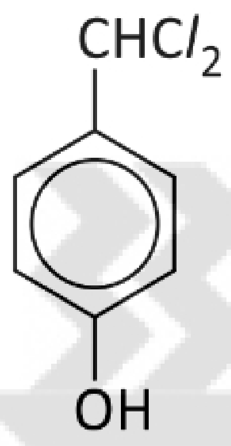
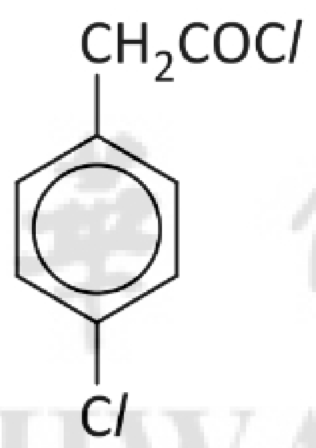
Lecture Exercise 6.3

1. Liquid **L** gives a white precipitate only when shaken for some time with aqueous silver nitrate. Which of the following structure(s) could be **L**?

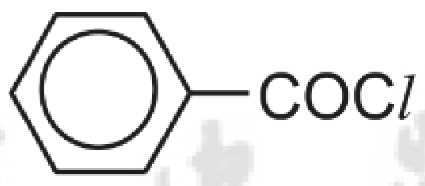
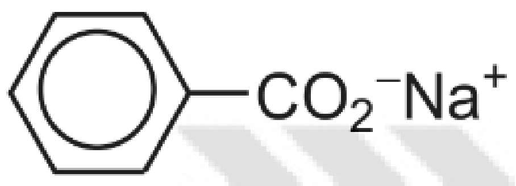
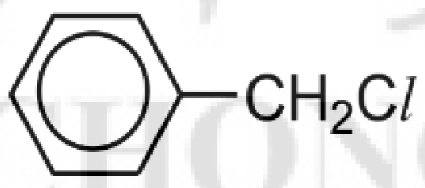
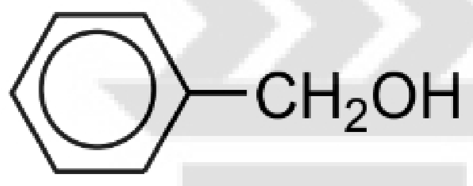
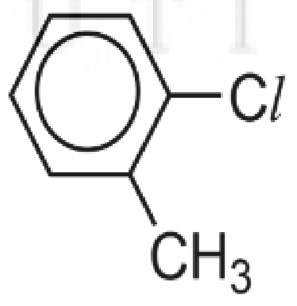
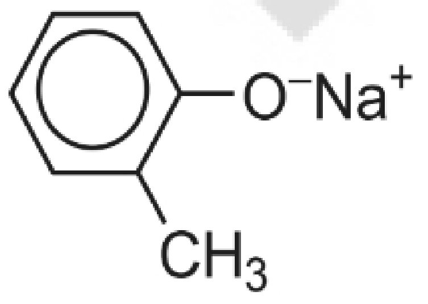








2. Which hydrolysis reaction, using NaOH(aq), will be the slowest?

	reactant	**product**
A	CH_3CH_2Cl	CH_3CH_2OH
B		
C		
D		

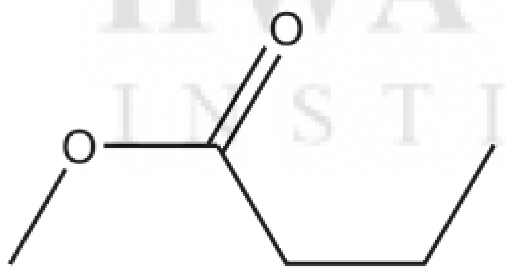
[N2003/I/23]

7 ESTERS

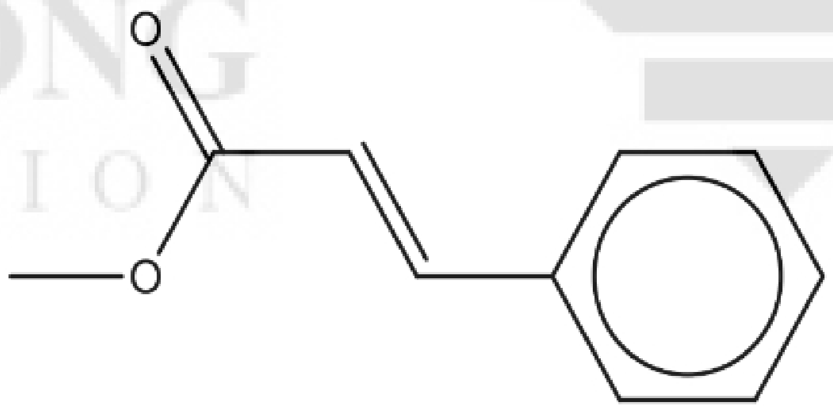
7.1 Introduction

Esters are generally sweet-smelling compounds and are widely used as flavourings and perfumes. Ester linkages also occur naturally in fats and lipids.

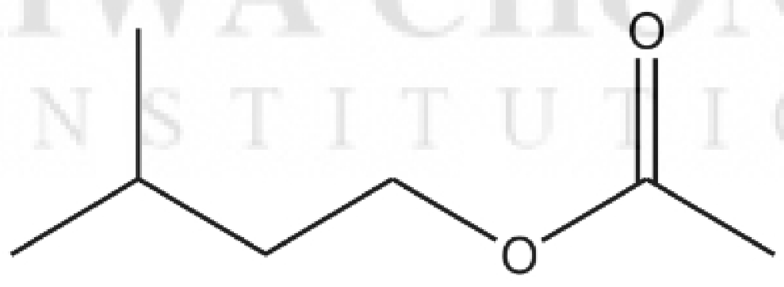
Small esters, together with other volatile organic compounds, often give off fragrances that are characteristic of fruits.



methyl butanoate
(apples)



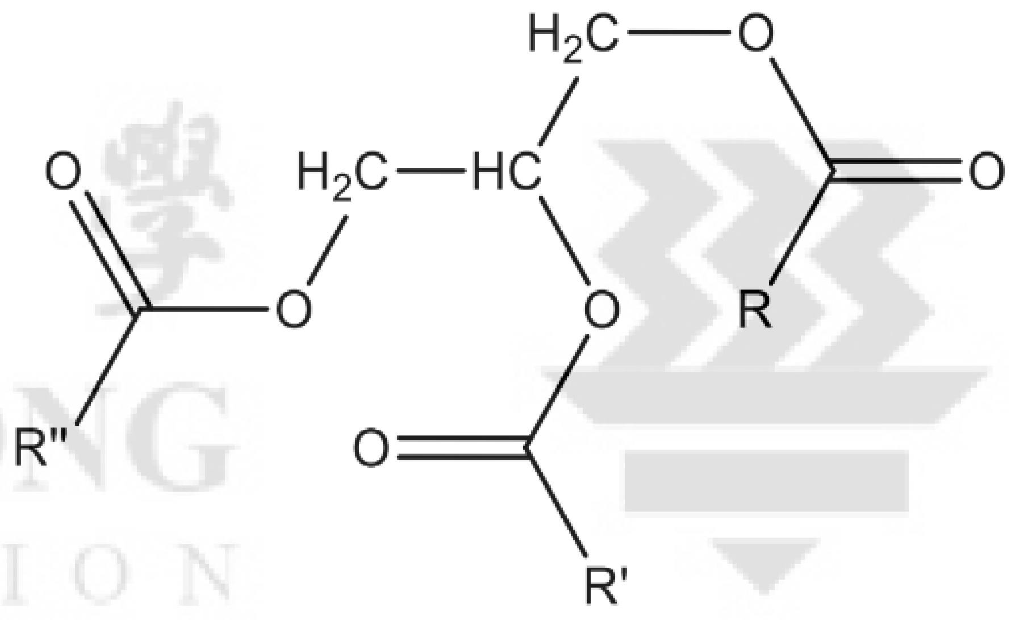
methyl trans-cinnamate
(strawberry)



isoamyl acetate
(banana)

Some esters are pheromones (chemicals that will influence the behavior of animals of the same species). For instance, isoamyl acetate is a pheromone that attracts other bees and is released by a honey bee's sting. This serves as a trigger for other bees to congregate and attack!

Fats are made up of triglycerides which are esters of fatty acids, as shown below (the R groups represent long hydrocarbon chains). Saponification is used in making soap from fats.



A trigylceride

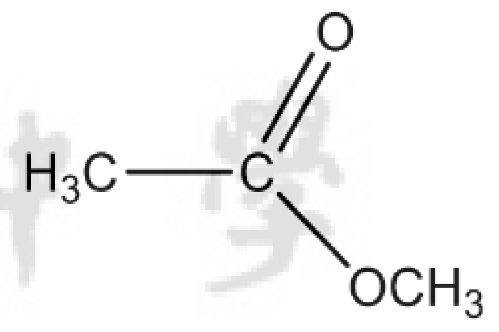
Saponification involves base (such as NaOH) hydrolysis of triglycerides to form the sodium salt of a carboxylate, which has a long chain hydrocarbon non-polar "tail" and a polar negatively charged "head". These carboxylate salts are effectively soap. Your hands feel slippery when they come into contact with alkalis because of the saponification of fats and oils on your hands. The esters in the oil (triglycerides) undergo saponification in the presence of hydroxide ions and soap is effectively produced!

Esters are prepared industrially mainly for use as essence, perfumes and artificial flavourings, e.g.:
(i) ethyl methanoate – rum flavouring
(ii) methyl butanoate – apple flavour
(iii) propyl pentanoate – pineapple flavour

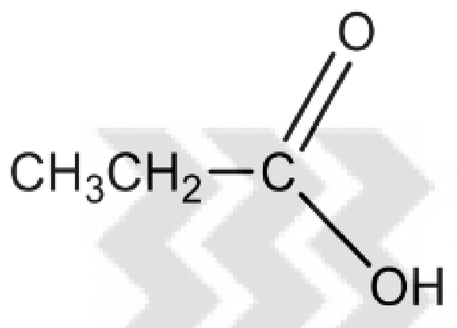
Esters are also widely used as organic solvents, e.g.:
(i) ethyl ethanoate – paints and varnishes
(ii) butyl ethanoate – extraction of penicillin
(iii) pentyl ethanoate – nitrocellulose

7.2 Isomerism

Saturated esters and carboxylic acids have the general formula $C_nH_{2n}O_2$ where n equals to the number of carbon atoms in the compound. Esters and carboxylic acids are constitutional isomers if they have the same number of carbon atoms in the compound.

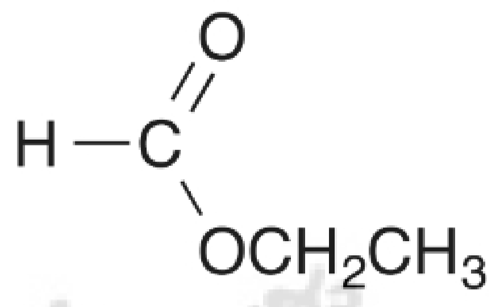


methyl ethanoate

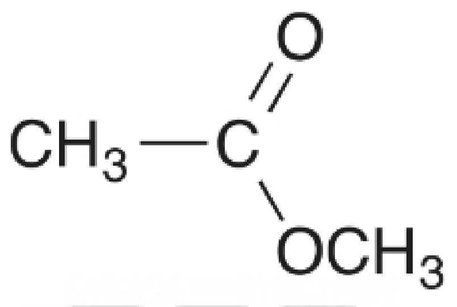


propanoic acid

For esters only, the carboxyl group may occur at different positions along the alkyl chain.



ethyl methanoate



methyl ethanoate

Self-Practice Question 7.1

Draw the structures of four isomeric esters with the formula $C_4H_8O_2$, and name them.

7.3 Preparation of Esters

LO 11.7 (g)part: describe the formation of esters from the condensation reaction of acyl chlorides

Esters can be prepared from:

- condensation reaction between carboxylic acid and an alcohol (Topic 16 Hydroxy Compounds)
- condensation reaction between acyl chloride and an alcohol (Section 6.2.2)

Self-Practice Question 7.2

Which procedure gives the best yield of ethyl ethanoate, $CH_3CO_2C_2H_5$, starting from ethanoic acid, CH_3CO_2H, and ethanol, C_2H_5OH?

A reacting CH_3CO_2H with $SOCl_2$, then adding C_2H_5OH

B reacting C_2H_5OH with $SOCl_2$, then adding CH_3CO_2H

C refluxing a mixture of CH_3CO_2H and C_2H_5OH with NaOH (aq)

D refluxing C_2H_5OH with concentrated H_2SO_4, then adding CH_3CO_2H

[J2000/III/25]

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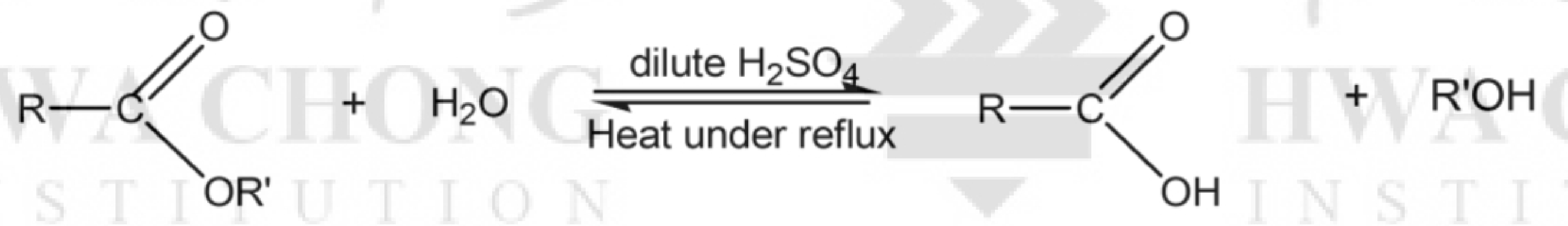
7.4 Reactions of Esters

LO 11.7 (h): describe the acid and base hydrolysis of esters

Esters can undergo acid or base hydrolysis to yield the alcohols and carboxylic acids. These reactions occur via the general nucleophilic (acyl) substitution mechanism shown in Section 4.2.

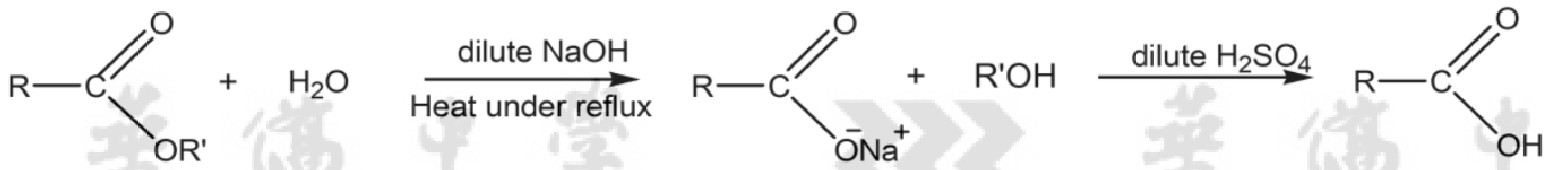
7.4.1 Acid hydrolysis



Reagents and conditions: dilute H_2SO_4, heat under reflux

The acid hydrolysis reaction is reversible. A large excess of water (dilute acid) is used to ensure equilibrium lies to the right. Notice that this is the reverse of the condensation reaction of alcohols and carboxylic acids to form esters.

7.4.2 Base hydrolysis (saponification)



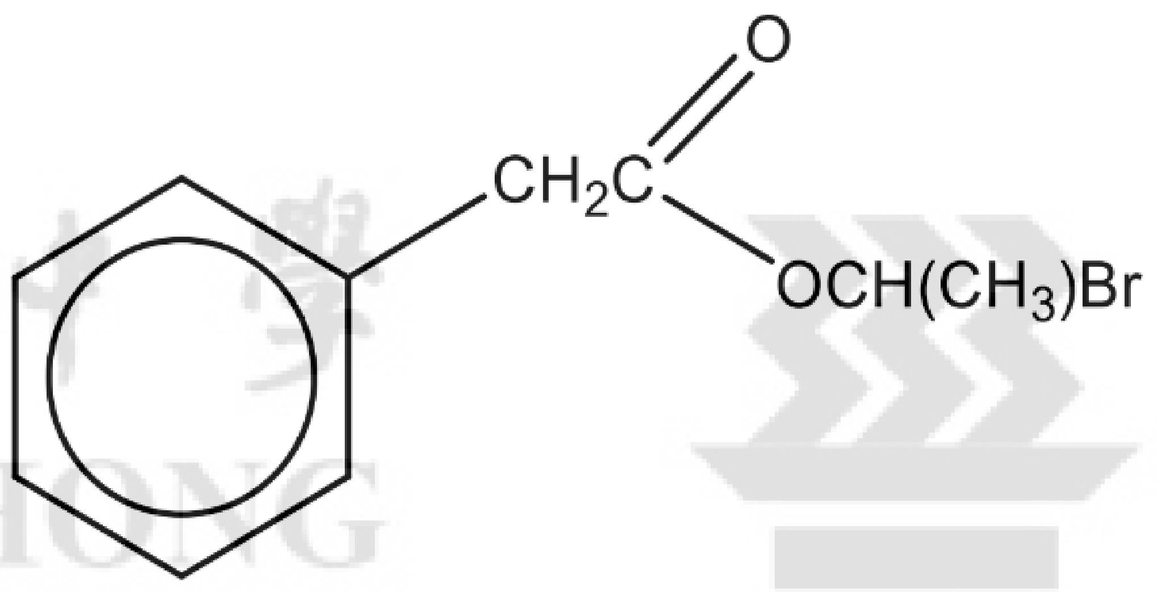
Reagents and conditions: dilute NaOH, heat under reflux
followed by acidification with dilute H_2SO_4 at room temperature and pressure

The base hydrolysis reaction is rapid and irreversible. The RCO_2^- ion formed has little tendency to undergo nucleophilic attack again by the alcohol, thus the reaction goes to completion.

To obtain the carboxylic acid from its salt, aqueous acid is added to the mixture at the end of the reaction to protonate the carboxylate anion.

Self-Practice Question 7.3

Draw the structures of the products formed when the following ester is subjected to

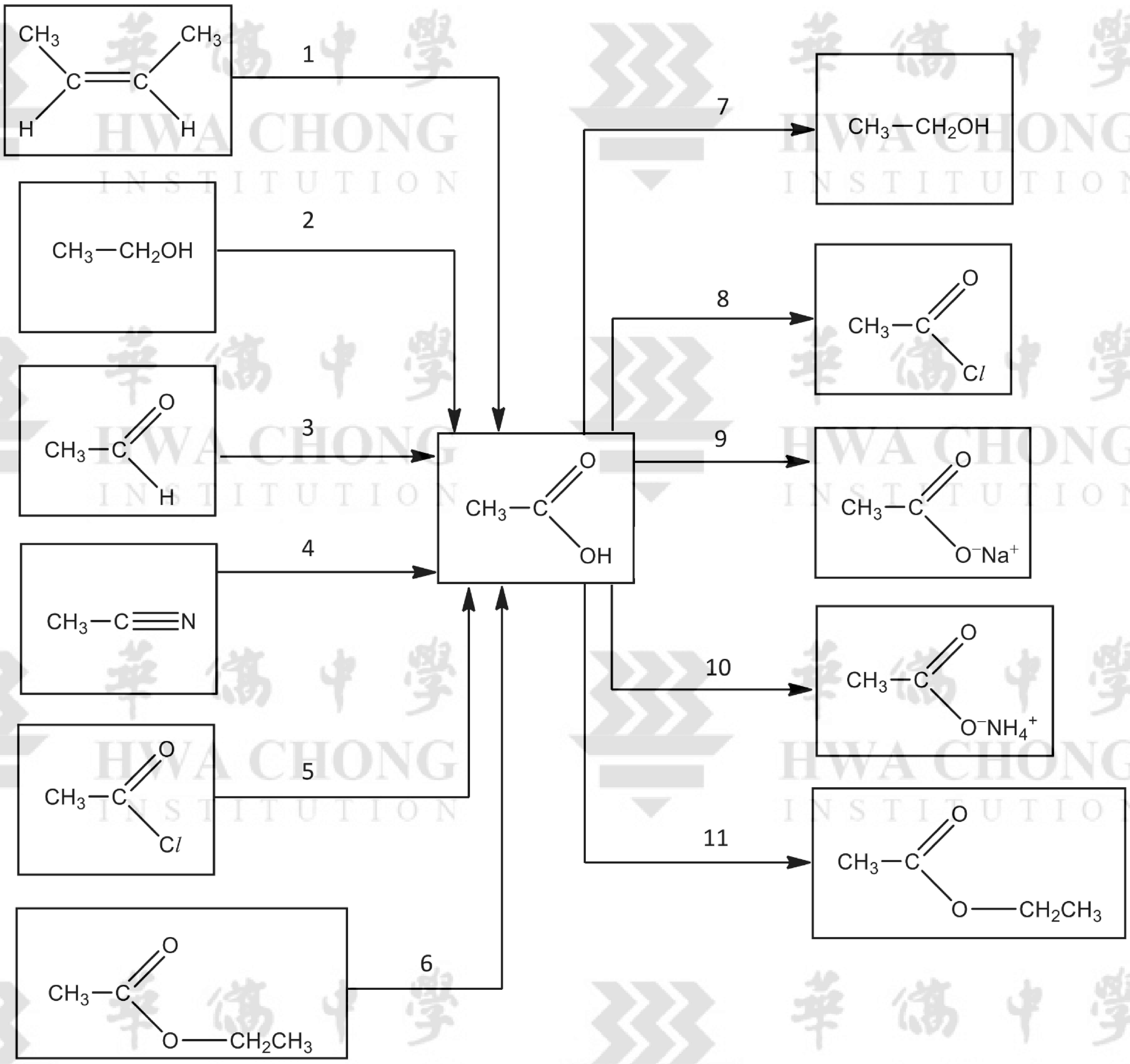


(i) acid hydrolysis,
(ii) base hydrolysis.

Summary of reactions of carboxylic acids and derivatives

State the reagents and conditions needed for the conversions on the arrows below:

Carboxylic acids



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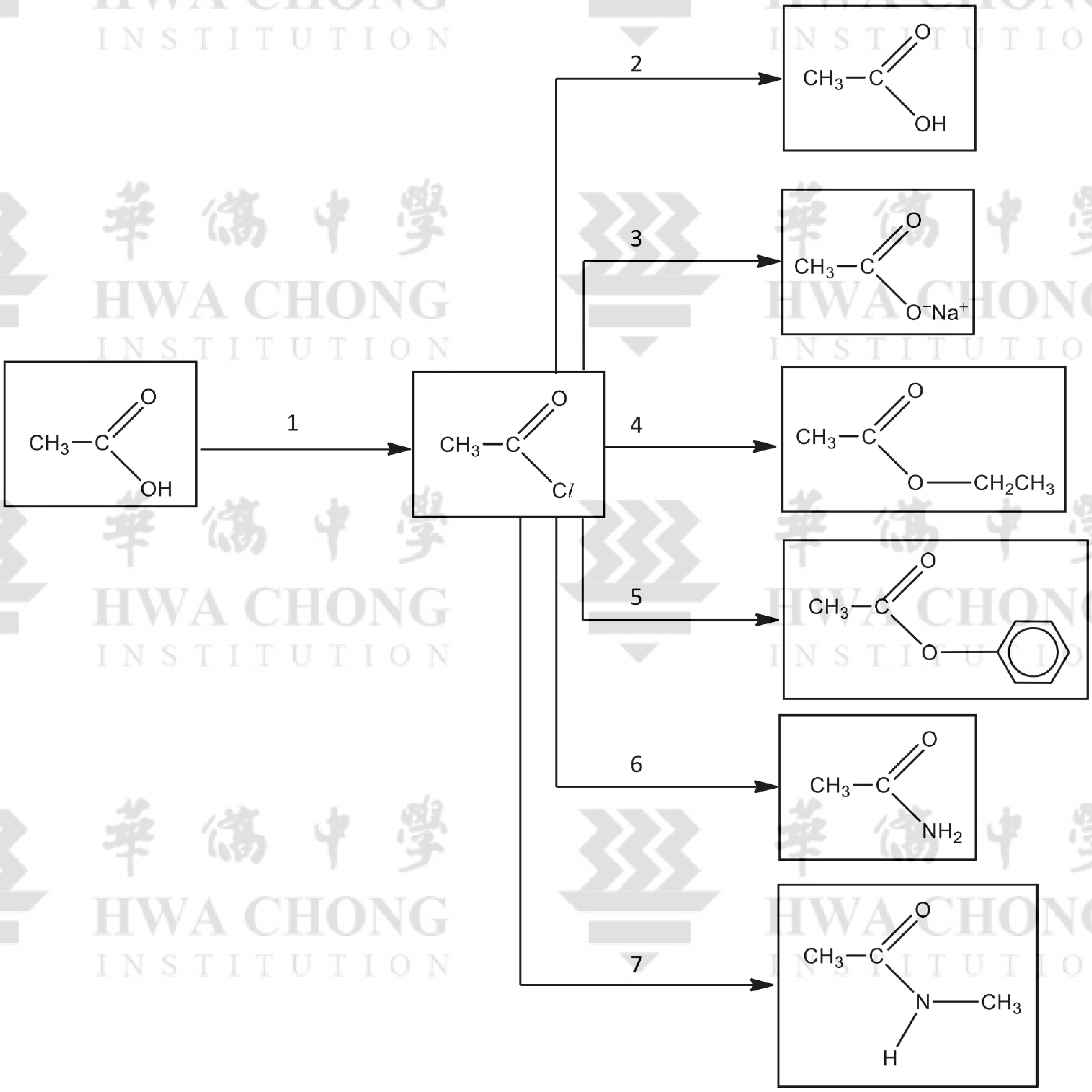
Acyl chlorides



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