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A Level Chemistry B (Salters)

H433/02 Scientific literacy in chemistry

Advance Notice

Practice Paper – Set 1

Time Allowed: 2 hours 15 minutes

To be read on receipt.
To prepare candidates for the Practice paper.

NOTES FOR GUIDANCE (CANDIDATES)

1. This leaflet contains an article which is needed in preparation for a question in the externally assessed examination H433/02 Scientific literacy in chemistry.

2. You will need to read the article carefully and also have covered the learning outcomes for A Level in Chemistry B (Salters). The examination paper will contain questions on the article. You will be expected to apply your knowledge and understanding of the work covered in A Level in Chemistry B (Salters) to answer this question. There are 20–25 marks available on the question paper for this question.

3. You can seek advice from your teacher about the content of the article and you can discuss it with others in your class. You may also investigate the topic yourself using any resources available to you.

4. You will not be able to bring your copy of the article, or other materials, into the examination. The examination paper will contain a fresh copy of the article.

5. You will not have time to read this article for the first time in the examination if you are to complete the examination paper within the specified time. However, you should refer to the article when answering the questions.

INSTRUCTIONS TO EXAMS OFFICER/INVIGILATOR

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This document consists of **8** pages. Any blank pages are indicated.

Dettol

Adapted from an article in the 'Chemistry in your Cupboard' series published by the Royal Society of Chemistry.

Antiseptics and disinfectants

Before the mid-1800s, major surgery was often a death sentence. Amputations of damaged limbs were carried out as a last resort but patients frequently died from post-operative infections.

This changed in the 1860s when Joseph Lister developed antiseptic surgery using carbolic acid to sterilise wounds and instruments. Lister was aware of the germ theory of infections developed by Louis Pasteur and others, and knew that carbolic acid (which we now call phenol) was able to kill germs, **Fig. 1**.

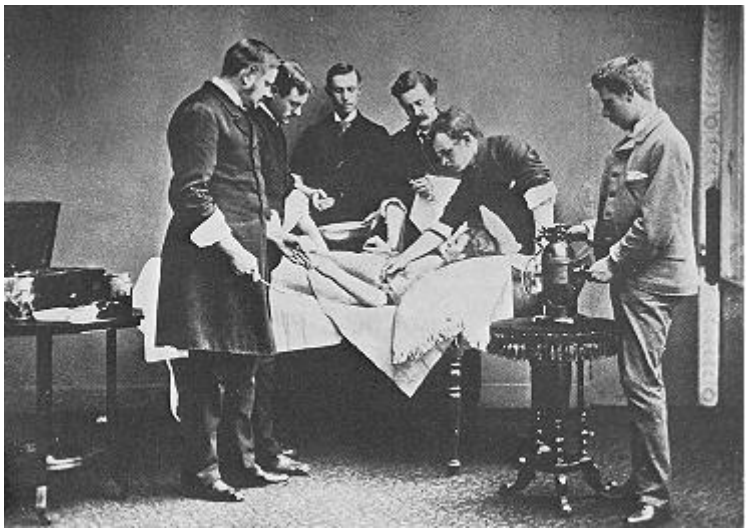

Fig. 1: An operation in the 1870s.
Doctors are using a carbolic acid spray as an antiseptic.

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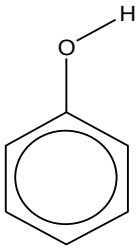

Fig. 2: Structure of phenol

Nowadays, disinfectants are just as important for germ-killing in hospitals, homes and elsewhere. Many products are still based on phenol derivatives as the active ingredient. This article looks at Dettol, made by Reckitt Benckiser.

Structure activity relationships

Phenol is effective at killing germs but is otherwise a far from ideal antiseptic as it causes nasty skin burns. One technique used by pharmaceutical chemists when faced with this sort of situation is to synthesise a number of compounds related to the substance that is known to be effective. This is in the hope that one or more of these compounds will be as active, or better, than the original but with fewer side effects (such as skin burning). Even better is the possibility of establishing a structure-activity relationship. This is a pattern which links some structural feature of the molecule with its pharmacological efficiency (i.e. how effective it is as a medicine) in a systematic way.

This enables the chemist to predict which derivatives might be more effective and therefore guide the synthesis of new compounds. **Fig. 3** shows some derivatives of phenol along with their germ-killing power relative to phenol. All of the compounds (except phenol itself) are substituted phenols. That is the new group or groups attached to the benzene ring replace one or more of the hydrogens.

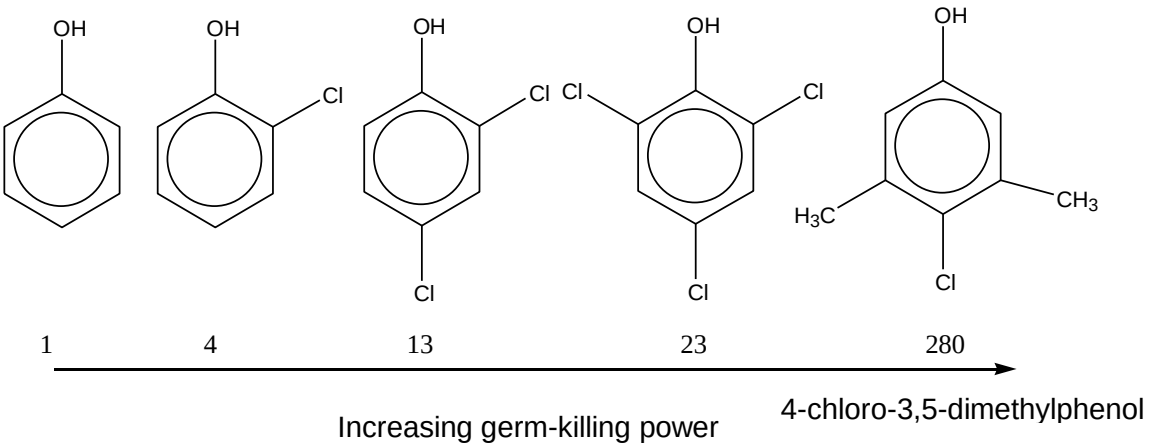

Fig. 3: The relative germ-killing power of some substituted phenols

The structure-activity relationships that have been established for derivatives of phenol are:

- the −OH group is required for activity;
- activity increases with a halogen in the 4- position (ie opposite the −OH group in the ring);
- activity increases with alkyl substituents of increased chain length;
- increased substitution makes the compound less water-soluble; and
- increased substitution decreases toxicity to humans when taken by mouth.

Phenol is already an effective germicide, so a greater killing power is not really needed. What the greater efficiency of 4-chloro-3,5-dimethylphenol means is that much smaller concentration can be used and therefore fewer side-effects will be expected.

Dettol

The active germ-killing ingredient in Dettol is in fact 4-chloro-3,5-dimethylphenol, also known by its non-systematic name *para*-chloro-*meta*-xylenol or PCMX, **Fig. 4**. The prefix *para* is a non-systematic way of indicating the 4- position on the benzene ring, i.e. opposite the −OH group. *Meta* indicates the 3- and 5- positions.

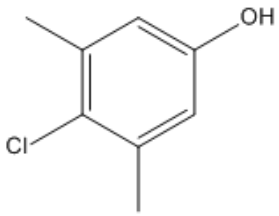

Fig. 4: Structure of *para*-chloro-*meta*-xylenol or PCMX

A number of disinfectant and antiseptic products are available under the Dettol brand including disinfectants for surfaces, antiseptics for use on the body, wipes and sprays. Here we will concentrate on the 'core' product - the liquid antiseptic, **Fig. 5**.

Fig. 5: Dettol liquid antiseptic, contains chloroxylenol

Biocides, disinfectants and antiseptics

All the terms above refer to germ (i.e. microbe)-killing. Biocide is a general term which covers active ingredients that kill microbes. Disinfectants kill microbes (bacteria, fungi and viruses) and are used on surfaces (such as worktops, sinks etc) but not living things (such as skin) as they may harm them. Antiseptics also kill microorganisms but may be used on the body surface (skin) although not in the body (e.g. by mouth).

How does PCMX kill bacteria?

The detailed biochemistry of the action of PCMX and other phenol-based antibacterial agents is beyond the scope of this article. However, very simply, they are understood to work by the −OH group of the molecule binding to proteins present on the cell membrane of bacteria, disrupting the cell membrane and allowing the contents of the cell to leak out.

This allows more PCMX to enter the cell, binding further with proteins and enzymes, and effectively shutting down the cell's functions. At high concentrations of PCMX, the proteins and nucleic acids in the cell are coagulated and cease to function, leading to rapid cell death.

The acidity of phenols

Phenol, C_6H_5OH, is weakly acidic - it was once called carbolic acid (not to be confused with carbo*xylic* acids, which contain the group −COOH). The acidic hydrogen (the one that is lost as H^+ when phenol behaves as an acid) is the hydrogen of the −O-H group. This is because oxygen is much more electronegative than hydrogen (3.5 on the Pauling scale compared with 2.1) so the O-H bond is polarised $O^{\delta-}$-$H^{\delta+}$, making it relatively easy for this hydrogen to be lost as a proton (H^+ ion), **Fig. 6**.

The negative ion formed is called the phenoxide ion and is often represented in text as PhO^-, Ph, being used to represent a benzene ring, which is sometimes called the phenyl group. Because it is ionic, the phenoxide ion is more soluble in water than phenol itself.

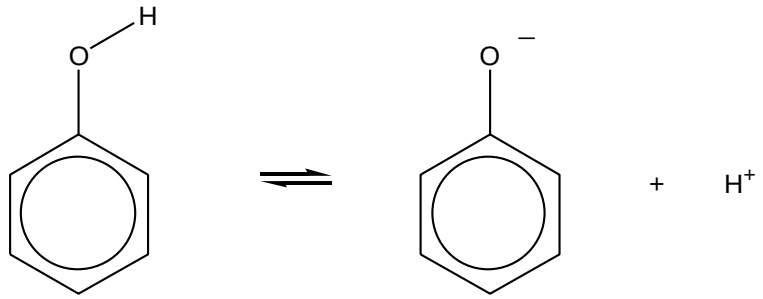

Fig. 6: Phenol, is also weakly basic – the oxygen atom has two lone pairs, one of which can accept a H^+ ion to form the ion $PhOH_2^+$

The pK_a value is a measure of the strength of an acid (how easily a H^+ ion is lost).
$pK_a = -\log_{10}K_a$

(This is analogous with $pH = -\log_{10}[H^+]$)

The pK_a value is a measure of the strength of an acid (how easily a H^+ ion is lost).
The larger the pK_a value, the weaker the acid.

- PCMX pK_a = 9.7; $K_a = 1.99 \times 10^{-10}$ mol dm^{-3}
- phenol pK_a = 9.9; $K_a = 1.28 \times 10^{-10}$ mol dm^{-3}
- ethanol pK_a = 15.9; $K_a = 7.9 \times 10^{-15}$ mol dm^{-3}

The acidity of phenols

Why is phenol so much more acidic than ethanol? In other words, why is the H of the OH group of ethanol so much less likely to be lost than that of the OH group of phenol?

$$C_2H_5OH \rightleftharpoons C_2H_5O^- + H^+$$

The answer lies in the relative stabilities of the negative ions left after a H^+ ion has been lost. In the ethoxide ion, the charge remains localised on the oxygen atom. In the phenoxide ion, PhO^-, the negative charge is spread over the benzene ring due to overlap of a p-orbital on the oxygen atom with the delocalised π-system of the benzene ring,

Making the active ingredient soluble

PCMX is, as expected, not very soluble in water; only 330 mg dm^{-3}.

This is because only the –O-H group can form hydrogen bonds with water.

Because they are acidic, phenols and substituted phenols are more soluble in alkaline solutions. However, strongly alkaline solutions are caustic and damage the skin so a slightly alkaline solution, pH 10, is used. In fact, PCMX shows slightly less activity at pH 10 than in a neutral solution.

Dettol actually contains nearly 150 times as much as its solubility in pure water. How is this achieved?

PCMX is soluble in relatively non-polar solvents - one such is pine oil which is used in the formulation of Dettol. This oil is derived, not surprisingly, from needles, twigs and cones of pine trees. Pine oil is a mixture composed largely of *alpha*-terpineol, which is moderately polar because of its single −OH group, **Fig. 7**.

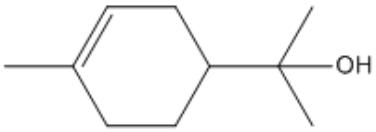

Fig. 7: Structure of *alpha*-terpineol

The answer to increasing the solubility of PCMX is to use a soap.

Soaps and detergents have ‘tadpole-shaped’ molecules in that they have a non-polar ‘tail’ and a polar or ionic ‘head’. The ‘tail’ can form intermolecular bonds with non-polar molecules whilst the ‘head’ can form hydrogen bonds with water. This is an example of the ‘like dissolves like’ rule.

The soap used in Dettol is made from castor oil which contains ricinoleic acid (systematic name 12-hydroxy-(*cis*)-9-octadecenoic acid), **Fig. 8**.

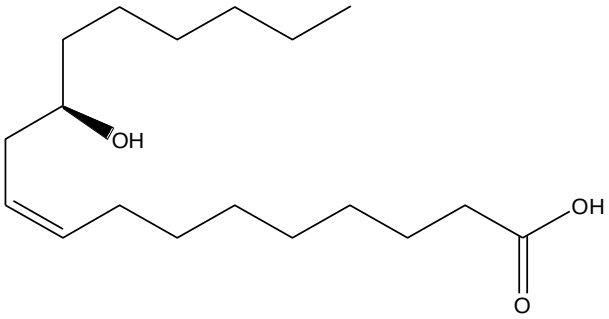

Fig. 8: Structure of ricinoleic acid

Making the active ingredient soluble

The ricinoleic acid is reacted with sodium hydroxide to form the ionic salt sodium ricinoleate. This salt has an ionic head and a largely non-polar tail – the classic shape of a detergent or surfactant molecule, see **Fig. 9**.

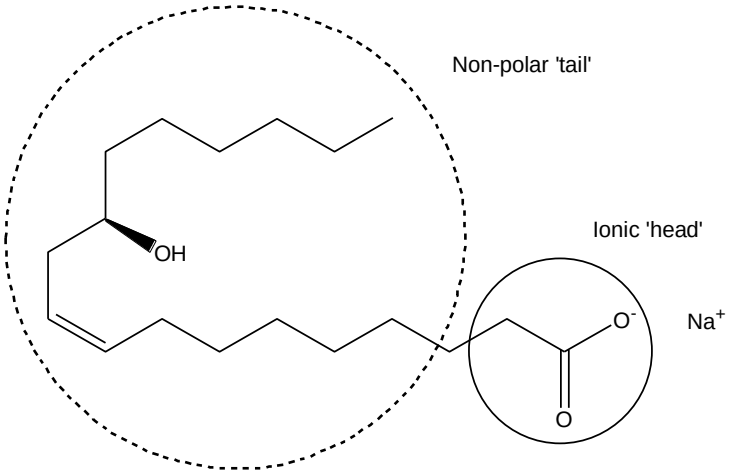

Fig. 9: Structure of sodium ricinoleate

In the bottle, Dettol consists of an almost clear liquid in which the PCMX is held in solution by the sodium ricinoleate.

On dilution in water, however, a cloudy liquid forms. This consists of droplets of pine oil containing dissolved PCMX. These are held dispersed in water by a layer of soap molecules arranged with their tails in the pine oil and their heads in the water, **Fig. 10**. These droplets are big enough to scatter light, hence the cloudiness of the suspension which is called an emulsion.

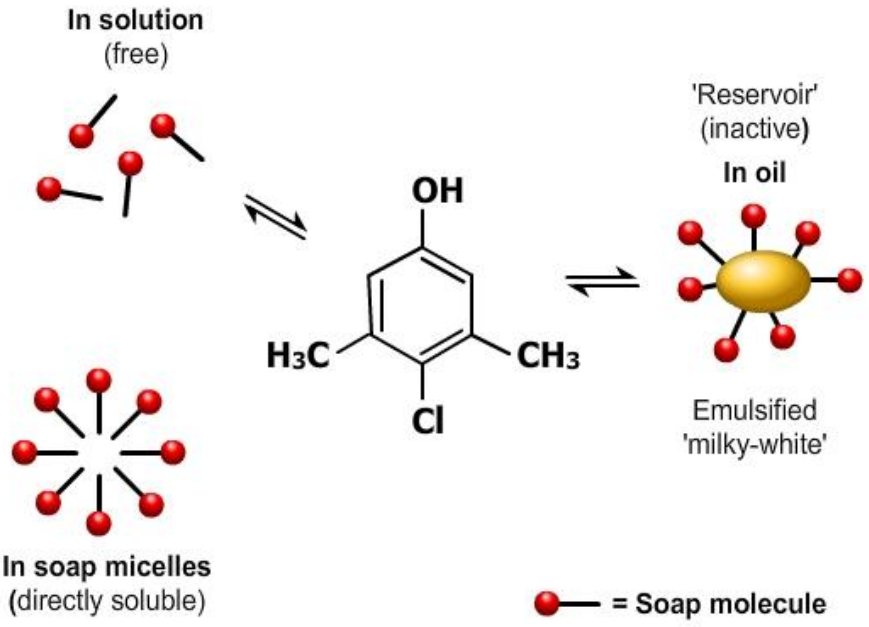

Fig. 10: PCMX in aqueous solution exists in a number of forms

The PCMX in the droplets of pine oil is not available to kill bacteria - it is the free aqueous PCMX that does this. However, an equilibrium exists between the emulsified PCMX in the droplets and free PCMX dissolved in the water. As PCMX is used up in killing bacteria, more is released from the droplets to keep the aqueous PCMX concentration essentially constant. So the droplets act as a reservoir of PCMX.

There is a further reservoir of PCMX in so-called micelles. These are groups of soap molecules clustered together with their non-polar tails entwined. Non-polar PCMX molecules can exist inside these micelles and be released in a similar way to those in the droplets. Also in solution are free soap molecules which in fact aid the penetration of PCMX into the bacterial cell walls. In addition, pine oil itself has a mild antibacterial action.

Pine oil also has a pleasant smell of pine and over the years, this has become associated in the mind of the public with antiseptic and disinfectant action, so much so that most disinfectant products are formulated with a pine smell.

Although improvements have been made over the years, the basic formulation of Dettol and similar products has remained the same since the 1930s.