

LIMONENE PRACTICAL

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1 Introduction

Essential oils, derived from natural sources are found in many common household products including, fruit juices, spices, natural flavourings, beverages, fragrances and cleaning products. Many of these essential oils belong to the terpene family. They may be cyclic, acyclic, unsaturated or saturated. Regardless of their structural diversity, they all share common traits, they contain multiples of 5 carbon atoms, generally joined through a head-to-tail arrangement (Figure 1).

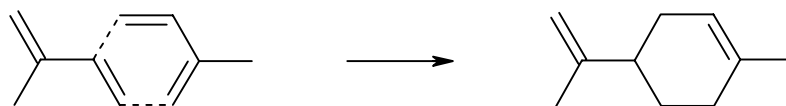


Figure 1: Head to tail bonding of isoprene units to form limonene

Terpenes such as limonene may be found in abundance in oils sacs located in the outer, coloured or flavedo portion of rinds of many common citrus fruits. D-Limonene is the major constituent of citrus peel oils (90-95%). Through the citrus industry 50,000 tonnes of limonene are produced annually. Several products and intermediates can be synthesised from limonene, but perhaps the most important is *p*-cymene, which has application in the fragrance, polymer, pharmaceutical industries and as a solvent.

1.1 Limonene as a solvent

Limonene has been used successfully in the food and cosmetic industry for years, and is generally considered safe. In recent years limonene based products have been used in some pathology laboratories as a replacement for xylene, a known toxic substance. Upon further examination of d-limonene as a solvent replacement for xylene it was found that it was readily absorbed, metabolised and cleared by the human body. It also performs adequately as a wax solvent and clearing agent, and has a reduced fire risk compared to xylene.

1.2 Using *p*-cymene to make PET

Poly(ethylene terephthalate), shown in Figure 2, can be prepared by the direct esterification of terephthalic acid and ethylene glycol or by transesterification of dimethyl terephthalate with ethylene glycol. In both cases the starting materials are currently petroleum derivatives.

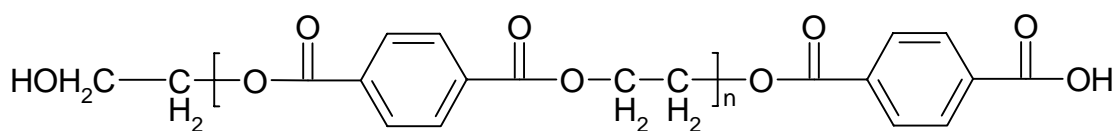
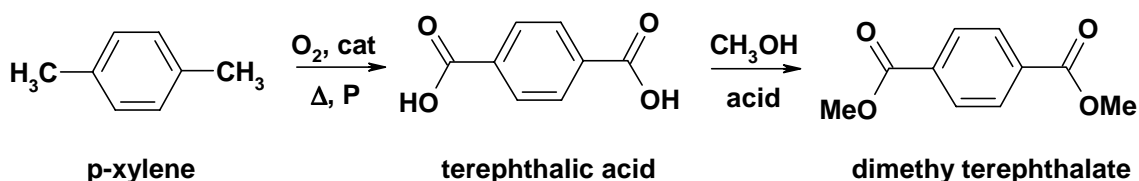


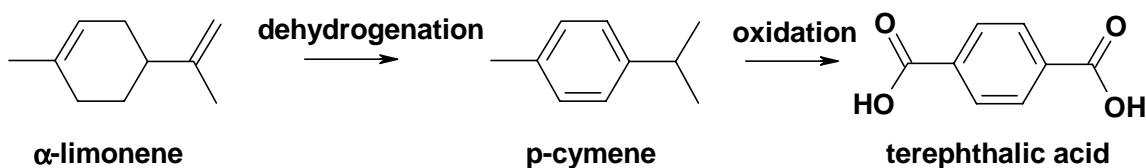
Figure 2: Structure of PET

The diester of terephthalic acid is made by the reaction as shown below in Scheme 1. The acid or diester and ethylene glycol are combined to make the monomer for polymerisation, before the polymerisation to make PET is carried out.



Scheme 1: Production of terephthalic acid and dimethyl terephthalate from *p*-xylene

However, it is also possible to produce terephthalic acid by the oxidation of *p*-cymene, which in turn can be produced from the dehydrogenation of α -limonene, as shown below in Scheme 2.



Scheme 2: Proposed reaction of α -limonene to terephthalic acid

Other naturally occurring terpenes have also been studied as potential precursors of *p*-cymene formation, including 3-carene, α -pinene and mixtures of terpenes (see Figure 3, below).¹

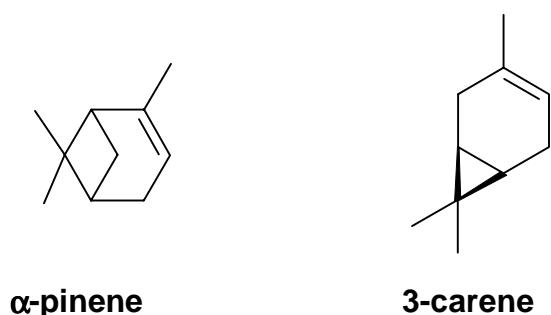
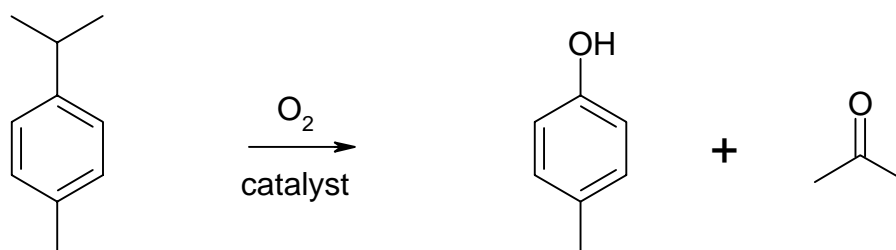


Figure 3: Chemical structures of α -pinene and 3-carene

1.3 *p*-Cymene to *p*-cresol

A second industrially important chemical that can be synthesised from *p*-cymene (and consequently from limonene) is *p*-cresol. Currently, amongst other methods *p*-cresol is manufactured via the Hock process (Scheme 3), the same process that is used worldwide to produce phenol. Starting from *p*-cymene (isopropyltoluene) the process involved a peroxy intermediate, producing *p*-cresol and acetone.



Scheme 3: Conversion of *p*-cymene to *p*-cresol via the Hock process

2 Objective

First and foremost this practical is aimed at giving you the opportunity to work on the transformation of a renewable feedstock into a bulk chemical. However, in addition to this several principles of green chemistry are covered during these experiments:

- It is better to prevent waste than to treat or clean up waste after it is formed.
- The use of auxiliary substances should be made unnecessary wherever possible and innocuous where used.
- A raw material or feedstock should be renewable rather than depleting wherever technically and economically possible.
- Catalytic reagents are superior to stoichiometric reagents.
- Substances and the form of a substance used in a chemical process should be chosen so as to minimise the potential for chemical accidents, including releases, explosions and fires.

As well as the intrinsic 'greenness' of some of the reactions, the practical is also designed so that you will gain skills in practical methods that perhaps you have not experienced before. Heterogeneous catalysis and heteropoly acids are materials you may not have come across in your undergraduate experimental course.

3 The practical

There are several dehydrogenation methods to convert limonene to *p*-cymene. Three of these methods are covered in this practical.

- 1) Dehydrogenation by N-lithioethylenediamine
- 2) Palladium fixed on charcoal liquid phase dehydrogenation
- 3) Heteropoly acid oxidative dehydrogenation

The group choosing to examine the palladium system (2) will also have the opportunity to study the extraction of limonene from orange peel using a literature method.

The practical procedures are written in the form of experimental procedures from literature papers in order for you to gain experience at following such methods. We have NOT attempted to “green” these literature methods and you should carefully note where improvements could be made.

3.1 General safety information

From a general safety perspective, all experiments in this practical should be carried out in a fume cupboard unless specifically told otherwise. Also lab coats and laboratory safety glasses should be worn in labs at all times. Gloves should be worn whenever handling chemicals.

Even though limonene is considered a natural product it is not without hazard, in fact bottles of limonene from Aldrich have “potentially damaging to the environment” warning labels on them. Be sure to examine all chemicals before using them for specific safety hazard data, if unsure ask.

If the catalyst is a powder beware of spilling it anywhere, keep the jar closed when not weighing it out. This holds for all chemicals.

Ensure temperature probes are definitely submerged in the oil bath, if they are not there is potential for the oil bath to overheat.

Make sure all flasks and condensers are securely and safely clamped. Especially if you are going to leave the experiment for any period of time. Also, be aware of what other experiments are going on around you.

3.2 Dehydrogenation of limonene using N-lithioethylenediamine

Chemicals used

Ethylenediamine
Lithium wire
Limonene
Anhydrous magnesium sulfate
Diethyl ether

Hazards specific to experiment

Ethylenedamine is strongly basic and corrosive.
Lithium wire oxidises easily in presence of oxygen and water and can be a fire hazard.
Hydrogen gas is evolved which is flammable and potentially explosive.
Be very careful on adding cold water to flask to destroy lithium. Make sure the flask is in an ice-bath.
The reaction must be carried out in a fumehood.

A 2-necked flask containing a magnetic follower should be fitted with a gas inlet and a straight reflux condenser with an oil-sealed outlet. The apparatus should then be flushed with nitrogen 10 minutes before the addition of ethylenediamine (0.35 mol, 21.04 g). The amine should be heated to 100 °C, with constant stirring at 600 rpm. Small pieces of lithium wire (0.15 mol, 1.04 g) should be added down the straight condenser.* The rate of addition of the lithium should be controlled by the evolution of hydrogen, and by the persistence of the dark blue colour formed; in total the metal should be added over at least 1 hour. After the addition the solution may revert to a tan colour. Allow the solution to mix at temperature for 1 hour after the final addition. Limonene is then added to the mixture slowly down the condenser, controlling the rate of hydrogen evolution. After the final addition of the limonene the reaction mixture is stirred at temperature for 1 hour. The flask is then cooled in ice, and water added slowly until most of the solid which first forms is dissolved. The reaction can be quite vigorous so beware. Filter the aqueous solution into a separating funnel and extract with 4 x 20ml portions of diethyl ether. Dry the organic phase using magnesium sulfate (or another common drying

* The wire should be washed with hexane and dried using a tissue before addition to the amine. Lengths between 1 – 2 cm should be added.

agent). Use a rotary evaporator to remove the diethyl ether. Analyse your product by gas chromatography (see method in section 4).

3.3 Solvent extraction²

Chemicals used

Orange peel
Pentane
Anhydrous sodium sulfate

Hazards specific to experiment

Pressure build-up in separating funnel.
Flammability of pentane.

NOTE: This experiment to be carried out by the group that is ALSO carrying out experiment 3.4 (quite a short experiment). By measuring the amount of limonene present in orange peel you will gain an insight into the sheer size of the fruit juice industry (50,000 tonnes of limonene per year).

Grate the citrus fruit rind using the finest texture of a common cheese grater. Care must be taken during the grating of the fruit. It is essential to grate only the flavedo, the coloured portion of the peel, and avoiding abrading the albedo, or white portion of the inner peel. It is also essential to avoid abrading the pulp to avoid excessive water contamination. Place approximately, 2.5 g of the finely grated peel into a suitable separating funnel. The rind should then be extracted three times with 7 ml portions of pentane for 10 min intervals, being certain to frequently vent the funnel (pentane was used for the extraction as opposed to the higher boiling hexane because pentane could be more readily removed by evaporation without risking oxidation of the terpene extracts). The combined extracts are then dried over anhydrous sodium sulfate (approximately 1 g) for 15 min. Filter the resulting solution to ensure complete removal of the sodium sulfate. Transfer the extract to a tared 50 ml beaker, and remove the solvent over a low heat ca. 35 °C, using a very gentle stream of nitrogen to avoid evaporation of the volatile components of the citrus essential oils. After evaporation of the pentane, weigh the essential oils and calculate a percent recovery. A GC of the oil should also be obtained (see method in section 4).

3.4 Conversion of limonene to *p*-cymene using a palladium catalyst on charcoal[†]

Chemicals used

Limonene
Pd on charcoal (5% w/w)
Nitrogen gas

Hazards specific to experiment

Care must be taken when passing gas through reaction rigs, do not over pressurise.

Be careful only to add the correct amount of Pd on charcoal.

The reaction must be carried out in a fume hood.

The reaction can be very vigorous, so ensure during reaction that the fumehood cover is pulled right down.

Limonene (20 ml, 0.125 mol) is placed in a 3-necked 100 ml round bottomed flask fitted with a condenser with an oil trap. One neck is fitted with a suba-seal through which nitrogen gas was passed (through a syringe needle). The final neck is fitted with a glass stopper, through which samples are taken. The limonene is heated, with magnetic stirring to 100 °C and 2 ml of limonene should be withdrawn by glass pipette. Pd on charcoal (0.1 g of 5% wt) is carefully added to the flask through the side arm via a glass funnel, residue remaining on the glass funnel is washed into the flask using the 2 ml of limonene previously withdrawn. Reaction is carried out under a nitrogen atmosphere at 100 °C for 3 hours. At the end of reaction the reaction mixture should be allowed to cool before being filtered and weighed. A sample of the filtrate should be analysed by GC (see method in section 4).

[†] Coupled in with liquid phase dehydrogenation (quite a short experiment) is also the extraction of limonene (experiment 3.3).

3.5 Oxidative dehydrogenation of limonene using a $\text{H}_5[\text{PMo}_{10}\text{O}_{40}]^3$

Chemicals used

$\text{H}_3[\text{PMo}_{12}\text{O}_{40}].\text{aq}$
1,2-Dichloroethane (DCE)
Tetraglyme
Nitrogen

Hazards specific to experiment

Care must be taken when passing gas through reaction rigs, do not over pressurise.

$\text{H}_3[\text{PMo}_{12}\text{O}_{40}].\text{aq}$ is an acid and consequently should be handled with due care and attention.

The $\text{H}_3[\text{PMo}_{12}\text{O}_{40}].\text{aq}$ (0.24 mmol, 200mg) is dissolved in 20 cm³ of 1,2-dichloroethane (DCE) by addition of tetraglyme (2.5 mmol, 550 μl) in a small 50 ml beaker with magnetic stirring. The catalyst is filtered into the reaction vessel (a two necked 100 ml round bottomed flask) through the side arm. The d-limonene substrate (20 mmol, 2.72 g) is added through the side arm, which should then be stoppered. The condenser remains unstoppered so the reaction is exposed to the air whilst being heated to 70 °C, with constant magnetic stirring. The reaction should be complete within 4 hours. After this time the reaction flask is allowed to cool to room temperature before the products are decanted into a 100 ml separating funnel. The catalyst is extracted with 3 x 20 ml portions of distilled water. The organic phase is then decanted into a conical flask containing magnesium sulfate (or another appropriate drying agent) and allowed to dry for at least 15 minutes. The product mixture is then filtered into a clean flask. GC analysis is then carried out on the product (see method in section 4).

4 Analysis of product by Gas Chromatography

4.1 Introduction

Chromatography is a separation process based on the differential affinities of mixtures in the form of a thin film liquid or gas phase and a stationary phase; the stationary phase is normally in the form of a packed column or a thin layer adhering to a suitable backing material.⁴

Providing that the components are sufficiently volatile, gas-liquid chromatography (GLC or GC) is perhaps the most powerful tool for the rapid and convenient analysis of the composition of mixtures of organic compounds. For routine analytical work the stationary phase is packed into a glass column approximately 2-3 m in length and 2-4 mm internal diameter, which is in the form a circular spiral, and located in a temperature controlled oven. The mobile gas phase (normally nitrogen) enters the column at one end, which also incorporates a heated injection port for sample introduction. The components pass down through the column at a rate proportional to their affinity for the column (the higher the affinity, the longer the residence time on the column, hence the later the component exits the column).

The components pass through a detector system when they exit the column, which is linked to a pen or a printer producing the chromatograph (see Figure 4 below).

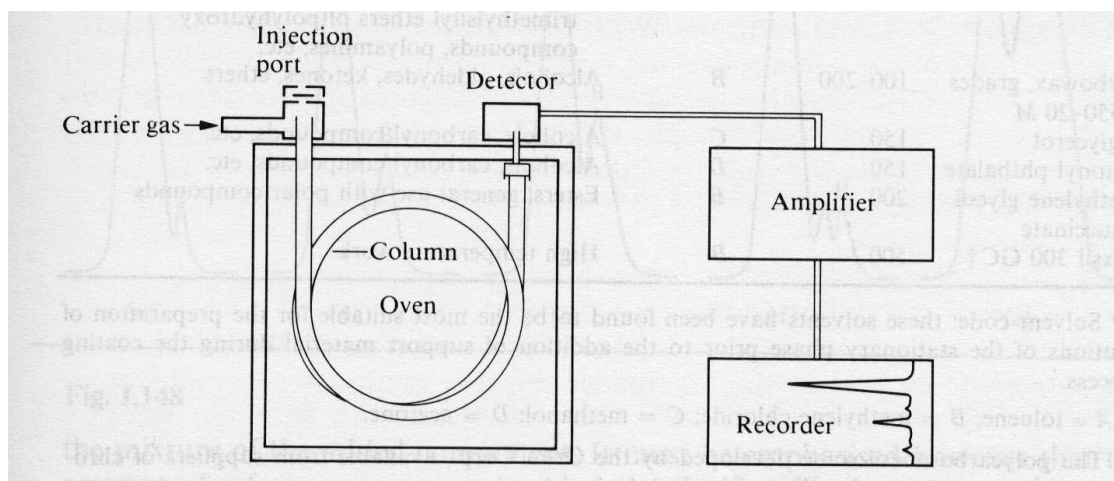


Figure 4: Schematic representation of a GLC

The form of the stationary phase (generally silica based) can be varied in terms of polarity and thermal stability, and can be specifically chosen to suit the range of components being studied.

4.2 Analysis of your reaction system

GC can be a qualitative and a quantitative analytical method. In this case we are using it as a quantitative method, we wish to know the concentration of *p*-cymene in our reaction mixture. In the case of the reactions studied during the experiment virtually all the limonene is reacted to form *p*-cymene and other by-products, so we can not use the ratio of the areas under the peaks between limonene and *p*-cymene, therefore we need to use an external standard. An external standard is a substance placed in the reaction mixture, which is chemically inert and has a retention time on the GC column unique compared to the reaction products. In this case we are using *n*-dodecane, a long chain alkane.

A calibration curve has already been plotted showing the relationship between the areas under the peaks for *n*-dodecane and *p*-cymene at several different concentrations. The response factor (R_f) is calculated from such calibration curves using equations (1) and (2).

$$\text{Mass}_{(\text{product})}/\text{Mass}_{(\text{std})} = R_f \times \text{Area}_{(\text{product})}/\text{Area}_{(\text{std})} \quad (1)$$

$$R_f = (\text{Mass}_{(\text{product})}/\text{Mass}_{(\text{std})}) \times (\text{Area}_{(\text{std})}/\text{Area}_{(\text{product})}) \quad (2)$$

In this case the response factor (R_f) has been calculated to be 0.896, which means that the detector signal for *n*-dodecane and *p*-cymene is almost the same. To calculate the mass of product in the reaction mixtures simply rearrange the equation (1) to give the mass of product, as you should know the other values.

To run a GC of a sample using an external standard:

- 1) Accurately weigh a drop of sample into a small sample jar.
- 2) Add to this an accurately weighed drop of external standard (*n*-dodecane).
- 3) Dilute mixture with suitable GC solvent (diethylether).
- 4) Run a GC using DB17 column under the following conditions:

Injector Temp:	200°C
Detector Temp.	200 °C
Initial Temp:	60 °C
Final Temp:	200 °C
Ramp rate:	8 °C/min
Injection:	1 µL

5 Discussion/questions

5.1 Structure of report

The report should be written as a typical practical report, which means the structure should be as below:

- Abstract
- Introduction – a brief introduction is fine
- Results – see section 5.2
- Discussion – see section 5.3
- Conclusions
- Bibliography – if any references are cited

5.2 Results

The following calculations/analysis should be included in the results section:

- % Yield calculation.
- Selectivity to *p*-cymene (compared to other products).
- Atom economy of method.
- E-factor calculation.
- Fate/treatment of reactants and waste.
- Pro's and con's of reaction method along with suggested improvements.

5.3 Discussion

Compare and contrast the results of all the methods, which will have to be obtained from the other student groups. In interpretation of these results consider (and answer) the following questions:

- Which method works best on a laboratory scale?
- Which method is cheapest per kg of *p*-cymene?
- Which method is the “Greenest” – explain how you have reached your conclusion?
- Which method do you foresee as being easiest to scale-up? Would it be safe to scale up your choice?
- How else might the reaction be carried out? How are dehydrogenation reactions carried out in industry?

6 Bibliography

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