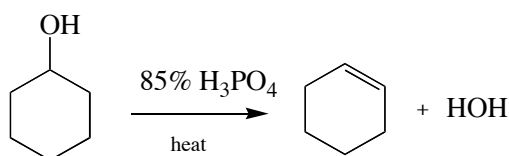


Synthesis of Cyclohexene The Dehydration of Cyclohexanol.

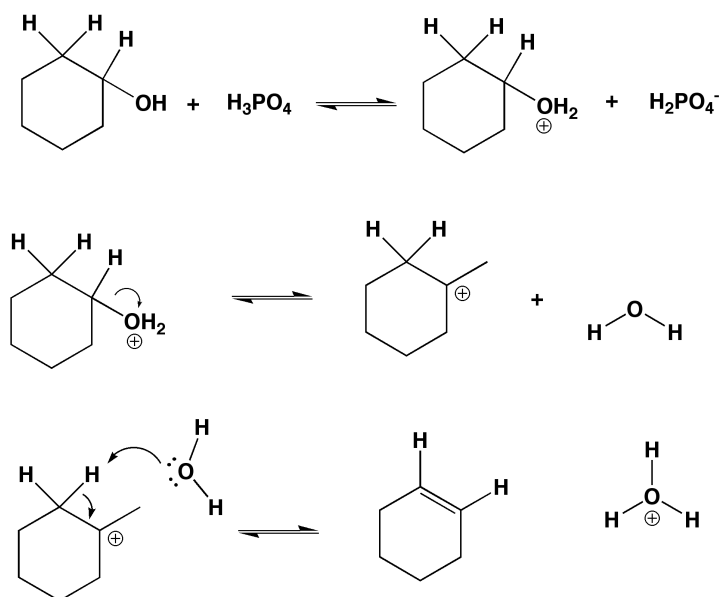
The general approach towards carrying out an organic reaction:

- (1) Write out the balanced reaction, using structural formulas.
- (2) Construct a table of relevant information for reactants and products – e.g., MPs, BPs, MWs, densities, hazardous properties.
- (3) Calculate the correct molar ratios of reactants. Convert moles to grams and milliliters.
- (4) Mix correct amounts of reactants, solvents, catalysts in correct order to give specific concentrations. Possibly heat or cool or irradiate with UV light, allow to react for necessary amount of time, possibly follow reaction progress using chromatography (e.g., TLC, GC) or spectroscopy (e.g., IR, NMR).
- (5) After reaction is complete, the reaction mixture is usually a complex mixture of desired product(s), byproducts, unreacted starting materials, solvents, and catalyst. Product may be light, heat, or air (O₂) sensitive.
- (6) Separation and purification steps (so-called reaction work-up). Some combination of extractions, distillations, recrystallizations, chromatography, etc are used for the work-up.
- (7) Identify product(s) using spectroscopy (IR, NMR, etc), chromatography (GC, TLC, etc), physical properties (MP, BP, etc), and occasionally chemical tests.

Cyclohexene. In the presence of a strong acid, an alcohol can be dehydrated to form an alkene. The acid used in this experiment is 85% phosphoric acid and the alcohol is cyclohexanol. The phosphoric acid is a catalyst and as such increases the rate of reaction but does not affect the overall stoichiometry. It can be seen from the balanced reaction that 1 mole of alcohol produces 1 mole of alkene. The theoretical yield of alkene in moles is therefore equal to the number of moles of alcohol used.

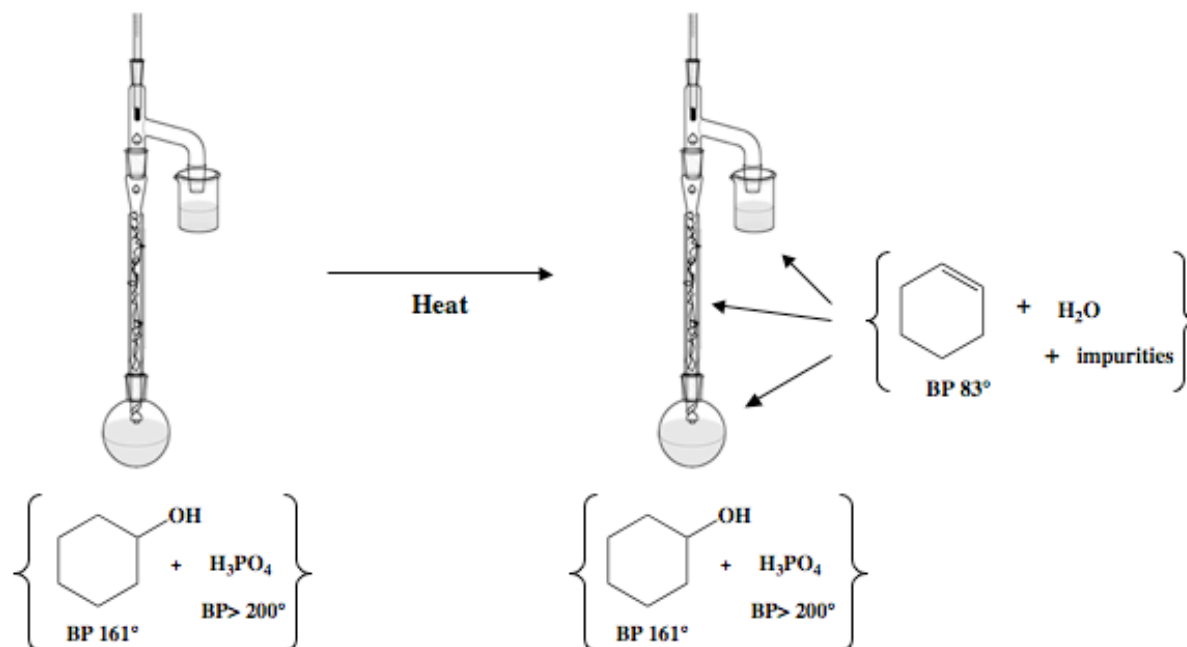


Mechanism.



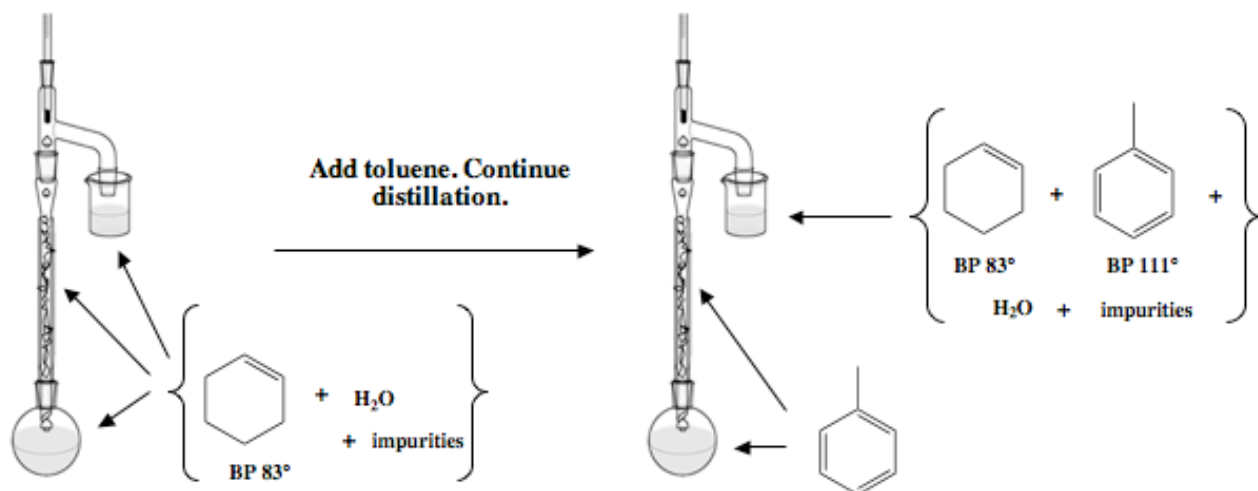
The first step in the mechanism is protonation of the alcohol group by the acid (slightly exothermic). The second step is the loss of water to form the carbocation (highly endothermic). The final step is removal of a *beta* hydrogen by base (water) to form the alkene (exothermic). The overall reaction is slightly endothermic.

General Approach. The reaction is carried out in a fractional distillation apparatus. As the alcohol and acid are heated, alkene and water are produced and co-distill into a collection vial. As in any distillation, unless precautions are taken, some of the product will be lost as hold-up in the apparatus. Hold-up would result in a reduced yield of product. To overcome this problem and to ensure that a maximum amount of product is distilled, a higher boiling "chaser" solvent is added to the distillation flask and the distillation is continued until the temperature rises well over the BP of cyclohexene. At this point it can be assumed that all product has distilled into the collection vial, along with some chaser.



Cyclohexanol plus Phosphoric Acid are heated

As the reaction proceeds, cyclohexanol is being converted to cyclohexene and water (plus some impurities). The low-boiling cyclohexene and water boil at the high temperatures and distill up the column and into the collection vial. As with all distillations though some is left behind in the flask and in the column.



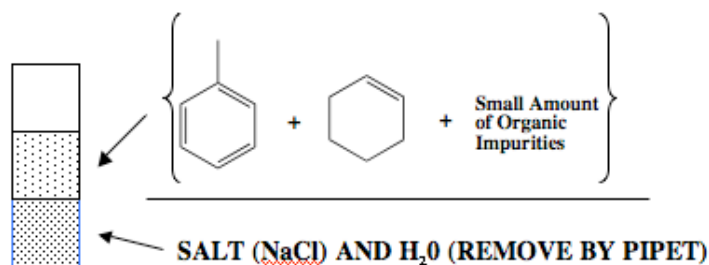
If we stop the distillation here, a significant amount of product would be left behind and lost.

To maximize yield, stop the distillation, add chaser (toluene) and continue the distillation. The higher-boiling toluene pushes over (chases) the product into the collection vial.

Once the toluene distills up the column and reaches the thermometer, most of the cyclohexene and water has been pushed over into the collection vial along with some toluene. The distilling flask contains phosphoric acid, toluene, and higher-boiling impurities. The column contains mostly toluene.

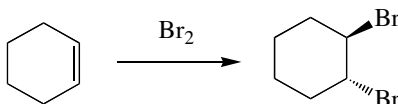
What has been accomplished by adding chaser? Almost all of the desired product, cyclohexene, has been collected in the vial. The downside is that another impurity (toluene) has been added to the product.

The collection vial now contains cyclohexene, water, toluene, and small amounts of other impurities. Because any water present will interfere with the distillation (water will co-distill and will not separate), prior to a final distillation, to obtain pure product, all water must be removed. This is done in two steps. First, the sample is mixed well with an aqueous saturated sodium chloride solution (sat'd salt) and the lower aqueous layer is removed and discarded. This is a pre-drying step that removes most of the water.

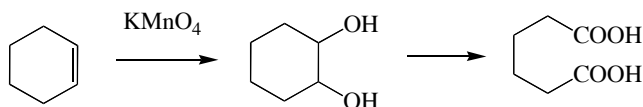


Next, anhydrous calcium chloride pellets are added. Anhydrous CaCl_2 is an inorganic drying agent that binds strongly with water and thus removes any traces of water from the solution. After about five minutes, the solution is separated from the pellets and transferred to the clean and dry fractional distillation apparatus. The dried solution is then fractionally distilled to produce purified cyclohexene. To achieve optimal separation, the distillation must be done at a slow steady rate. To ensure that the fraction collected as product is relatively pure cyclohexene, this fraction is collected over a narrow range at the boiling point of cyclohexene. The purity of the cyclohexene is determined by gas chromatographic (GC) analysis and a % yield calculated.

Chemical Tests. The presence of the alkene functional group can be indicated by carrying out simple reactions in which a color change can be observed. One such reaction is with bromine in dichloromethane. The bromine reagent is a reddish-orange color. When it is dripped slowly into a sample of alkene, the bromine reacts with the alkene to form a nearly colorless dibromide. Because the bromine is consumed, the mixture loses the reddish-orange color. If a sample decolorizes bromine under these conditions it can be inferred that an alkene functional group is likely present.



A second color test is the reaction with potassium permanganate. An alkene reacts with potassium permanganate to form a colorless diol. Under acid conditions the diol reacts further to form a mixture of colorless carboxylic acids or in the case of a cyclic alkene, a dicarboxylic acid. As the permanganate is consumed, the mixture loses its deep purple color. At the same time manganese dioxide, a brown precipitate, forms. If a sample decolorizes permanganate and forms a brown precipitate it can be inferred that an alkene functional group is present.



Procedure. (rev 6/10)

During Weeks 2 and 3 of lab, you will do two experiments - Cyclohexene and Melting Points (MPs). Because of a limited number of melting point devices and gas chromatographs, one half of the class will do Cyclohexene during the 2nd week and the other half will do MPs. During Week 3, you will switch and do the experiment that you did not do during Week 2. The experiment that you will do during Week 2 will be posted on the web. **Be sure to prepare for the correct experiment.** Melting Points are described in a separate handout.

The " Things to Watch Out For In Distillations" listed for the distillation experiment are common to this distillation as well - review them carefully. As always, use care when inserting the thermometer into the thermometer adaptor. Hold the thermometer close to the adaptor and push and twist gently away from you. Breakage could result in a serious injury. Check for frayed connectors and cracked flasks. Cyclohexene has a disagreeable odor, characteristic of volatile alkenes. Allow the apparatus to cool before disassembling it **in the fume hood**, and dispose of the wastes in the hood in the ORGANIC LIQUID WASTE CONTAINER. Rinse the apparatus in the waste hood with a SMALL AMOUNT of acetone and dispose of that in the ORGANIC LIQUID WASTE CONTAINER.

CAUTION: cyclohexene is very flammable. Handle phosphoric acid with care. It is corrosive to tissue. If your skin comes into contact with phosphoric acid, wash the contaminated area immediately with water, then soap and water. Clean up spills immediately using the sodium bicarbonate in the hood.

Prepare a flow diagram including all steps in the reaction, work-up, and identification. Prepare a table of reagents, products, and byproducts. (Sample of each on Chem 269 website – handouts page.)

Preparation of Cyclohexene. As always, if the sand bath is being used in an experiment, turn it on right away to a setting of just under 40. This way it will reach operating temperature by the time it is needed. In this experiment the phosphoric acid need not be measured very accurately. However, the

amount of cyclohexanol determines the theoretical amount of product so it must be measured accurately. Place the round-bottomed (rb) flask into a 30 mL beaker to hold it upright, set this onto the balance and press zero (this will set the weight of the container to zero – this is called taring the flask), and measure in about 2.0 g (± 0.05 g, but weigh it exactly, e.g., 1.964 g or 2.033 g) of cyclohexanol by dropping it in with a pipet. Using a buret in the hood, add about 0.5 mL of 85% phosphoric acid to the rb flask. Note that the rb flask becomes warm - addition of acid to alcohol is exothermic. Set up a fractional distillation apparatus in the same way as in the distillation experiment (remember the boiling chips). Be sure to use the **distillation** column (in some rare cases a slightly longer narrower glass tube that looks a lot like the distillation column may have inadvertently gotten mixed in to some of the lockers. Be sure to **not** use this tube - this tube, a chromatography column used in another course, does not connect tightly.) Use the black plastic connector to connect the flask to the distilling head. This is more resistant to the reactants than is the white connector. Insulate the column by loosely wrapping it with a piece of aluminum foil. Be sure to use an ice-cooled receiver. Otherwise product will evaporate and the odor will be disagreeable.

Heat the mixture sufficiently to distill product over into the collection vial (remember to make a small depression in the sand bath so that the flask may be lowered into it for effective heating). Unlike in a normal distillation this first distillation can and should be done fairly rapidly, not at the usual rate of one drop per 20-30 seconds, but instead at a rate of about one drop per second or two. (If liquid is not collecting in the vial within about 20 minutes, something is wrong – there may not be enough heat, the column may be packed too tightly, you may have measured the quantities incorrectly, or there may be a leak. Check with your TA.) Note the temperature range over which distillate is collected. Continue distilling until distillation slows dramatically and most of the liquid has distilled (there will be about 0.5 mL of liquid remaining in the flask). Lift the apparatus out of the hot sand and allow it to cool for a couple of minutes. At this point, most of the product mixture has been collected in the collection vial. There should be two phases (layers) of liquid in the vial. Water, being one of the products, is insoluble in cyclohexene so forms a second layer. The density of water is greater than that of cyclohexene so the water layer would be expected to form the lower layer. This may not be obvious for two reasons: on this small scale of reaction there is such a small amount of water formed it may simply cause the liquid to appear cloudy at first and not form a second layer immediately; also, water tends to adhere to glass so instead of actually forming a second lower layer it may just appear as small droplets sticking to the side of the vial.

If one were to stop at this point, a significant amount of product would be left behind in the distilling apparatus (recall “HOLDUP”) and the yield of product would suffer. A method to ensure that all desired product distills is to add a higher-boiling liquid (called a chaser) to the distilling flask and to then continue the distillation. To add chaser, slide the sand bath to one side so that the chaser, if spilled, will not fall into the hot sand. Measure about 2 mL of toluene into a 10 mL graduated cylinder, carefully remove the thermometer and adaptor, and pipet the toluene onto the top of the copper-packed column. The toluene will drip down into the rb flask. Replace the thermometer and continue the distillation. When the temperature reaches 90°, continue distilling until about 25 drops (about 1 mL, very approximate) of toluene has been collected then lift the apparatus up from the hot sand to stop the distillation. Remove and cap the vial. For safe keeping place it into a small beaker. Allow the apparatus to cool before trying to clean it.

Pipet the contents of the vial into a reaction tube. To minimize loss of product rinse the vial with a small amount (< 10 drops) of fresh toluene and pipet this into the reaction tube. Rinsing in this way is a general technique used to minimize loss of product and should be used whenever a material is being transferred from one container to another (call this a transfer rinse). At this point, water, toluene, and

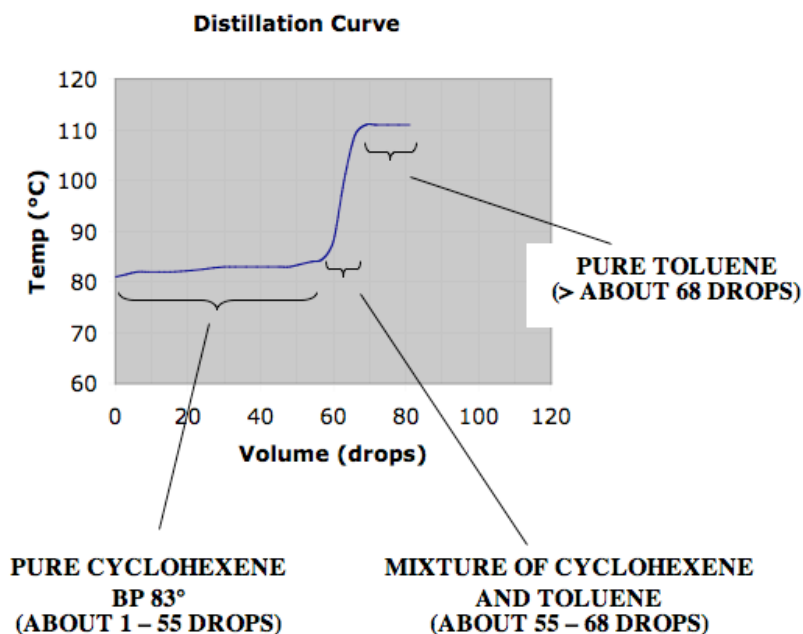
small amounts of other impurities are mixed in with the cyclohexene product. Water will interfere with the final distillation so it must be removed completely. To do this, add saturated aqueous sodium chloride solution to the reaction tube, the volume being about equal to the volume of liquid already in the tube. Mix the two layers thoroughly by drawing some of the lower up into the pipet and expelling it back through the solution repeatedly for a couple of minutes. This procedure is called washing or extracting and will be used in several future experiments. The technique will be demonstrated by your TA. Washing with saturated sodium chloride solution is a pre-drying step that removes most of the water from the organic phase. Remove the lower aqueous (NaCl) layer with a pipet and temporarily place it into another container, being very careful to remove all of the lower layer but none of the upper organic layer. Using a clean dry pipet transfer the organic layer to a clean dry vial (do a transfer rinse using a few drops of toluene). There should be no droplets of water present at this point. If there are carefully remove all visible droplets of water. Add several spheres of calcium chloride drying agent to the vial, cap the vial, and swirl the contents well to be sure that all of the liquid comes into contact with the drying agent. Notice that the spheres clump together. This indicates that the drying agent is doing its job and has absorbed water. To be sure that enough drying agent has been added, add an additional few spheres of calcium chloride, swirl, observe, and continue this until the newly added spheres no longer clump together. The danger of adding too much drying agent is that it also absorbs the product and can lead to loss. (If all the visible droplets of water were not completely removed first, instead of clumping together, the first few spheres of drying agent will break apart and form a cloudy looking mass (layer) at the bottom of the vial. In such a case carefully pipet the contents to another clean dry vial, leaving behind the cloudy layer. Do a transfer rinse with a few drops of toluene then add drying agent in small amounts as before until a few of the spheres no longer clump together.) Set the capped vial into a small beaker for safe keeping and allow the solution to dry for at least five minutes. During this time the fractional distillation apparatus should be cleaned and dried.

Water has been carefully removed from the organic product mixture, so it is important to not reintroduce any water to the mixture. To obtain pure product, the final distillation must be done carefully using clean, dry equipment. Rinse the apparatus first with water, then a little ethanol and then a little acetone to speed up the drying process. Blow air gently through and over the apparatus in the hood to evaporate the solvents. The column is most effectively dried by drawing air through it using the vacuum connection. It is essential to remove all water and organic solvents before the final distillation. **It is however not necessary to FILL the glassware with cleaning solvent. This would be extremely wasteful. Add a small amount of solvent, swirl it around and while pouring it into the waste container, turn the apparatus so that solvent comes into contact with the entire apparatus. Repeat this once more, again with just a small amount of solvent. (Remember to always try to be environmentally responsible by minimizing waste.)**

A final fractional distillation must now be done carefully to separate the chaser and any small amounts of other impurities from the product. Pipet the organic product mixture into the 5 mL rb flask, leaving the calcium chloride behind (do another transfer rinse) and distill the mixture carefully through the fractionating column. This fractional distillation is essentially the same as that of cyclohexane and toluene that you did in experiment one. This time however you will collect the cyclohexene as a pure fraction in a clean, dry, tared vial. You need not count drops of distillate.

In a distillation such as this, the idea is to separate lower-boiling and higher-boiling impurities from the desired product. To do this, do not collect distillate as product until the thermometer reaches the BP of the product (\pm about 3° C) (in this case the product is cyclohexene). That is, first have an "impurities" vial attached to the apparatus to collect low-boiling impurities (if any). When the temperature of distillate closely approaches the BP of product, replace the "impurities" receiving vial with a clean, dry,

tared "product" vial. Collect distillate as product while the temperature remains at the BP of product (\pm about 3°C). Once the temperature rises steeply above the BP plateau of the product, replace the vial with the "impurities" vial once again to collect any higher-boiling distillate, then stop the distillation by lifting the apparatus away from the heat. Cap the product vial to prevent evaporation and weigh it. Note that the temperature may fluctuate by a few degrees during collection of the product - this is okay. As an example look at the following figure. In this example, "pure" cyclohexene would be collected in vial 1 from 0-55 drops (BP 83). Once the temperature rises steeply after about 55 drops, pure cyclohexene is no longer distilling. Material between 55 and 68 drops (BP 83-111) is a mixture of cyclohexene and toluene. After about 68 drops, pure toluene would distill. Because in our experiment we simply want to obtain pure cyclohexene, the distillation can be stopped as soon as the temperature begins to rise sharply after about 55 drops in this example. You need not construct a graph such as this but you should keep in mind that this is what is happening as you distill.



At this point the product should be clear, not cloudy (clear does not mean colorless). Cloudiness indicates the presence of water, which must be removed completely before GC analysis. If the product is cloudy, add more drying agent, swirl and let stand for a few minutes, then transfer the product to a clean dry vial. In some cases the product may need to be redistilled (check with TA if still cloudy).

Sign up for the GC analysis then continue working on the experiment or cleaning your equipment until you are called to carry out the GC analysis – do not waste time waiting in line. Demonstrate the presence of the alkene functional group by testing your product with bromine and permanganate as described below.

In the write-up, based on the actual purity of product as shown by GC, calculate the % yield (refer to the discussion of % yield given below.)

WASTE DISPOSAL: Dispose of all liquid wastes in the ORGANIC LIQUID WASTE container in the hood. SAVE THE COPPER WIRE, COPPER SPONGE, AND ALUMINUM FOIL FOR FUTURE USE.

Chemical Tests to Distinguish Alkenes from Alkanes.

Often, simple chemical reactions can be used to detect the presence of a functional group. Here, you will carry out two such reactions. Run the test reactions on your product and cyclohexane side-by-side to observe the results of a negative test. If you have an insufficient amount of product, scale down quantities by a factor of two for example.

(1) Bromine in Dichloromethane. Caution; bromine is extremely hazardous to breathe and causes severe burns if it touches the skin. A dilute bromine solution is used in this test so the hazard potential is much less than if pure bromine were used. The solvent, dichloromethane, is also toxic and must be kept in the hood. If you accidentally allow the bromine solution to touch your skin, immediately rinse the contaminated area with a dilute aqueous sodium thiosulfate solution, which will be stored near the bromine in the hood, then wash with soap and water. Carry out all operations with bromine in the fume hood.

The bromine solution is reddish-orange. Bromine reacts with an alkene to form a colorless dibromide. Thus, if a bromine solution is added dropwise to an alkene, the solution will decolorize until all of the alkene has reacted. Alkanes on the other hand do not react with bromine in this way, so the very first drop of bromine solution will cause a reddish-orange color to persist. (Alkanes do react with bromine by a free radical mechanism initiated by light, but this reaction is much slower.)

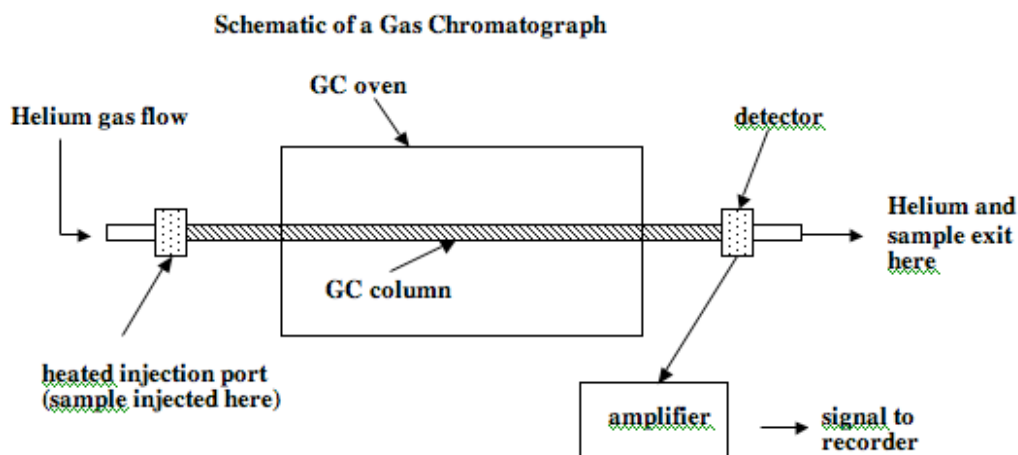
The test: in the hood, add about 0.5 mL of your cyclohexene product to a small test tube and about 0.5 mL of cyclohexane to another small test tube. To each, add dropwise, with swirling, 3 - 4 drops of a 3% solution of bromine in dichloromethane. Record any observed color changes after addition of each drop. Dispose of all wastes from this test in the Organic Liquid Waste container.

(2) Potassium Permanganate. Potassium permanganate is purple. It reacts with alkenes to produce a colorless diol and a finely-divided brown precipitate of manganese dioxide. Under acidic conditions the diol can further react to form a colorless dicarboxylic acid. Thus, when permanganate is added dropwise to an alkene, the purple color disappears and a brownish suspension forms until all of the alkene has reacted. Permanganate does not react with alkanes, so the first drop of permanganate added to an alkane immediately results in a purple solution.

The test: add about 0.3 mL of your product cyclohexene to a small test tube and about 0.3 mL of cyclohexane to another small tube. To each, add dropwise, with swirling, 2 - 3 drops of an aqueous solution containing 1% potassium permanganate and 10% sulfuric acid. Record any observed changes after addition of each drop. Dispose of wastes from this test in the Organic Liquid Waste container in the hood.

BEFORE YOU LEAVE THE LAB: turn off the sand bath, put away your equipment and lock your drawer, clean up your work areas, close the fume hood sash completely, and ask your TA for her or his signature. In general, please try to keep the lab in as good condition as you found it. If you see caps off of bottles, replace the caps. If you see spilled chemicals, clean them up or at least report it to your TA.

Gas Chromatography (GC).

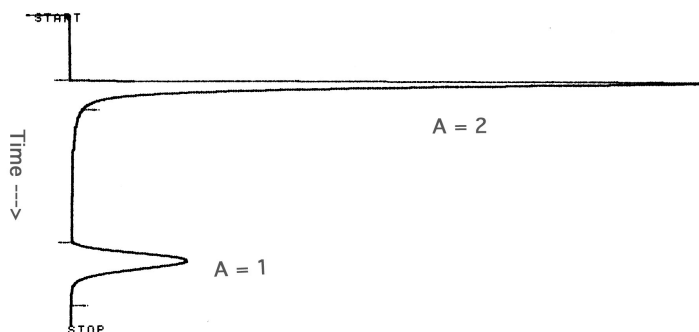


A very small sample ($\sim 0.1 \mu\text{l} = 0.0001 \text{ ml}$) is injected into the hot injector port.

The liquid vaporizes, helium pushes the plug of sample vapor through the thermostated column.

The lower-boiling liquid passes through more quickly than the higher-boiling liquid. As the vapor reaches the detector, a signal is sent to the amplifier and a recorder draws the chromatogram.

An example. The following GC trace is that of a mixture of a lower-boiling and higher-boiling liquid compound in a ratio of 2 : 1.



The injection point is at "start" at the top of the chromatogram. The peak labeled "A = 2" is due to the low-boiling liquid which reaches the detector first. The peak labeled "A = 1" is due to the high-boiling liquid which reaches the detector later.

The time between "start" and when the peak appears is known as the retention time.

The area of the peak, not the height, is proportional to the relative amounts of liquid 1 and liquid 2. (A on the chromatogram refers to area)

In our lab, the relative areas are reported by an electronic integrator.

This chromatogram would look similar to the chromatogram of a mixture of 2 parts cyclohexene to 1 part toluene.

Factors affecting separation in GC.

Column Material: chosen for compounds being separated.

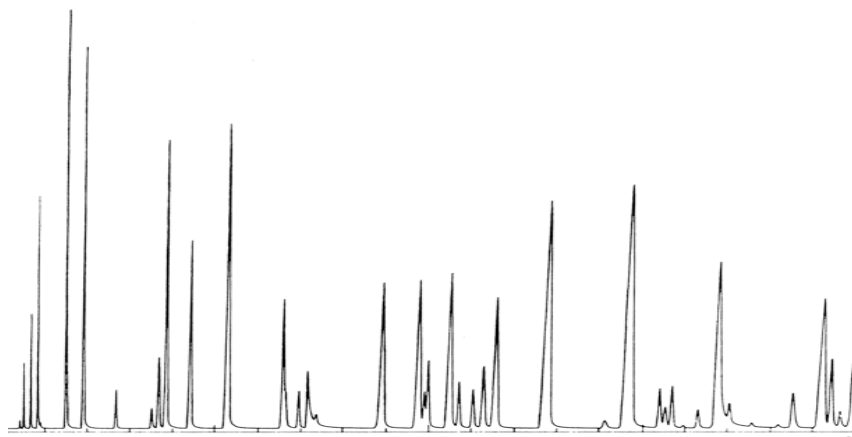
Column Length: the longer the column, the longer the compounds take to go through, resulting in a potentially better separation.

Column Temperature: higher temperature, shorter retention time. Lower temperature, longer retention time. A longer retention time may lead to a better separation.

Helium Flow Rate: higher flow rate, shorter retention time. Lower flow rate, longer retention time.

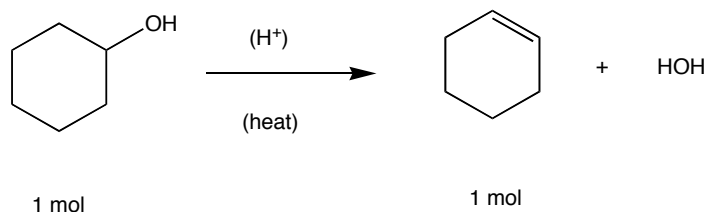
In practice, the column material and length is chosen to work with a particular mixture of compounds. Fine tuning of the separation is done by adjusting the temperature and flow rate. For example, if a poor separation is observed (overlapping peaks), the column temperature could be lowered, which would probably result in a better separation.

Another example of a GC analysis. The following is a GC of a fraction of crude oil (petroleum) approximately corresponding to a gasoline fraction, which contains the various isomers of the C₄ – C₇ hydrocarbons. Gasoline from different refineries and therefore different gas stations would have a slightly different amount of each compound. This would result in unique GCs which could be used for example as a “fingerprint” in arson investigations.



Calculating the Percent Yield.

Theoretical yield. First write out the balanced equation. For this reaction, this is very simple. One reactant produces one product (water is also a product but we are only interested in the cyclohexene here) in a 1:1 ratio. Note that the phosphoric acid is a catalyst and is not involved in the yield calculation.



One molecule of cyclohexanol should produce one molecule of cyclohexene. One mole (mol) of cyclohexanol should produce one mole of cyclohexene.

If 2.05 g of cyclohexanol is used (use the actual amount used in your experiment) convert this to moles by dividing by the molecular weight of cyclohexanol (MW = 100.2 g/mol).

$$2.05 \text{ g cyclohexanol} / 100.2 \text{ g/mol} = 0.0205 \text{ mol (or 20.5 mmol)}$$

Because 1 mol of cyclohexanol should produce 1 mol of cyclohexene, 0.0205 mol of cyclohexanol should produce 0.0205 mol of cyclohexene. Convert this number of moles of cyclohexene to grams of cyclohexene by multiplying by the MW of cyclohexene (82.1 g/mol).

$$0.0205 \text{ mol} \times 82.1 \text{ g/mol} = 1.68 \text{ g cyclohexene}$$

In other words, 2.05 g of cyclohexanol should produce 1.68 g of cyclohexene. This is the best-case yield also known as the theoretical yield.

Percent Yield. The theoretical yield is what would be obtained in an ideal world, if every molecule of cyclohexanol were converted to a molecule of cyclohexene. The percent yield is the percentage of the theoretical yield that you actually obtain after isolating product at the end of the procedure.

Let's say that after the final fractional distillation of the cyclohexene, 1.22 g was collected. The percent yield then would be

$$\text{percent yield} = (\text{actual} / \text{theoretical}) \times 100 = (1.22 \text{ g} / 1.68 \text{ g}) \times 100 = 73 \%$$

This assumes that the 1.22 g that was obtained was 100% pure. Let's say that when the gas chromatographic analysis was done the sample was found to be 89% cyclohexene and 11% toluene. This means that the 1.22 g of liquid isolated in the distillation was not pure cyclohexene. The actual amount of cyclohexene collected then was $1.22 \text{ g} \times 0.89 = 1.09 \text{ g}$ (small print: an assumption is being made: that the GC detector response is the same for cyclohexene and toluene. We will accept this assumption for our purposes. In fact it is a good assumption in this case).

The percent yield then would be $(1.09 \text{ g actual} / 1.68 \text{ g theoretical}) \times 100 = 65\%$.

Postlab Questions

- 1.) Draw the structure of the major product that would be obtained from the dehydration of 3,5-dimethylcyclohexanol.
- 2.) Mixing cyclohexanol with phosphoric acid is an exothermic process, whereas the overall reaction from cyclohexanol to cyclohexene is endothermic. Referring to the mechanism above, construct an

energy diagram showing the course of the reaction. Label the diagram with the starting alcohol, the protonated alcohol, the carbocation, and the product.

3.) In GC, what effect would raising the column temperature have on the retention time?

4.) Looking at the fractional distillation curve above, draw a gas chromatogram for a one drop sample taken at the 60 drop mark. Label each peak clearly with the compound associated with that peak, and the relative amounts and relative retention times of each component.

5.) Draw the structure of the product from the reaction of cyclohexene plus bromine. Show stereochemistry clearly.