Chem 118B Organic Health Sciences III:

Lab G – Dehydration of 2-Methylcyclohexanol

Purpose

The purpose of this experiment is to perform a dehydration reaction of 2-methylcyclohexanol. The product will then be distilled, and analyzed by gas chromatography, IR, ^{13}C NMR, and DEPT spectroscopy.

Learning Objectives

Setup and run a dehydration reaction.

Distillation for purification.

Analysis of NMR and IR to determine chemical structure and product selectivity.

Analysis of gas chromatography to determine product ratios.

Equipment

- Vials
- 10.0 mL Side-arm distillation flask
- Hotplate
- Boiling Chips
- Thermometer
- Distillation setup
- 15 mL Test tube
- 400 mL Bekaer (ice bath)
- Pasteur pipet

Chemicals

- 2-Methylcyclohexanol
- 85% Phosphoric acid
- 1% $KMnO_4$ solution
- Saturated sodium chloride solution
- Anhydrous sodium sulfate

Review Material –

Vollhardt, P.; Schore, N. E.; *Organic Chemistry: Structure and Function*, Chapter 9.2–3

New Material –

Vollhardt, P.; Schore, N. E.; *Organic Chemistry: Structure and Function*, Chapter 11.7, 10.6

References –

Taft, R.L.; Champian, W.C; *J. Chem. Ed.*, **1967**, *44*, 620

Theory and Background

Introduction

As was seen in Lab C, alcohols in the presence of strong acid can become oxonium ion leaving groups. With the use of a strong, non-nucleophilic base such as phosphoric acid or sulfuric acid the leaving group produces elimination reactions.

Primary alcohols will undergo dehydration by bimolecular elimination mechanisms (E2), and secondary and tertiary alcohols will undergo unimolecular elimination mechanisms (E1). The steps of acid-catalyzed dehydration of an alcohol are generally reversible, so the product formed is a mixture of alkenes with the major product(s) being the more thermodynamically stable alkene(s). The relative ratio of products is exemplary of the relative energies of the various alkenes based on the starting material's carbon skeleton.

The products of acid-catalyzed dehydration typically show regioselectivity similar to Saytzev (base) elimination of haloalkanes, but lack stereoselectivity unless there is a significant thermodynamic difference between stereoisomers. Additionally, the E1 mechanism has a carbocation intermediate so is subject to rearrangements. So, the major product(s) of a dehydration reaction may show significantly different regioselectivity than Saytzev elimination of haloalkanes if there is a significantly more stable regioisomer available by rearrangement.

Cyclohexanol

2-Methylcyclohexanol is commercially available as a mixture of cis and trans isomers. Because the reaction proceeds by an E1 mechanism, there is no stereoselectivity and both cis and trans isomers will react similarly, and give the same products. The relative position of the secondary alcohol to the methyl means that the acid-catalyzed dehydration will give two different regioisomers: 1-methylcyclohexene and 3-methylcyclohexene (Figure G.1. Since two possible isomers can form, the separation and identification of the two products is vital. This experiment will use comparisons between ^{13}C NMR, DEPT and gas chromatography to determine the relative product ratios.

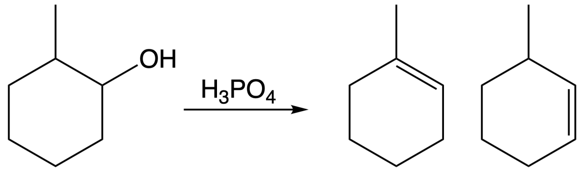


Figure G.1: Dehydration of 2-methyl-1-cyclohexanol.

Distillation (mixed volatiles)

The crude product in this reaction is collected as it forms by distillation. This is a simple (single step) distillation of a lower boiling compound from a higher boiling but still volatile compound. The distillation of a mixture of volatile compounds is more complex than that of a mixture of a volatile and non-volatile compound (see Lab C) as all components in the mixture will have a vapor pressure and be able to evaporate. Since all compounds are volatile it seems on the surface that boiling a mixture and collecting the vapor will simply result in recollection of a mixture, however in practice it is possible to separate compounds by differences in boiling point.

When a mixture is heated the average energy of the particles increases, when the energy of a particle is greater than the attractive energy of the intermolecular forces the molecule can separate from the condensed phase and become vapor (evaporate). When the vapor pressure of the substance reaches outside (typically atmospheric) pressure the average particle has enough energy to evaporate and the substance boils. Once boiling has begun any additional energy added goes directly to the phase transition of particles rather than increasing the kinetic energy (temperature) until the whole sample becomes vapor.

The process of boiling is the same for a mixture, however the mixture boils when the *combined* vapor pressure of the volatile components reaches outside pressure, not the pressure of the individual components. Compounds with higher boiling points require more energy (higher temperatures) to evaporate, so the vapor over the mixture is enriched in the substance with the lower boiling point. This means that collecting the vapor (the distillate) will result in a mixture with a larger fraction of *lower* boiling material and collecting the liquid left behind (the distilland) will result in a mixture with a larger fraction of the higher boiling material.

In theory, careful control of temperature will allow us to get a complete separation of the two materials. However, in practice, it takes several iterations of evaporating, enriching, condensing, and re-evaporating to get complete separation. In this experiment, we use a simple single step distillation, but fractional distillation setups will allow for better separations and separation of molecules with more similar boiling points.

Gas-Chromatography

Chromatography is the general name for a variety of methods that purify mixtures by using physical properties to partition substances between mobile and stationary phases. Substances that predominately spend time in the mobile phase are moved along the chromatography apparatus (the column) and substances that predominately spend time associated with the stationary phase move more slowly. This separates the substances and each will exit the column (elute) at a different time. The retention time (how long a substance takes to exit the column) for different substances will be different, and this allows complex mixtures or similar compounds to be separated. Different stationary and mobile phases will separate substances by different properties and in different orders. The separated compounds can be then detected by UV-Vis spectroscopy, refractive index, or other methods, and further analyzed by mass spectrometry.

Gas chromatography (GC) uses an inert gas such as helium as the mobile phase and a non-polar wax surface as the stationary phase. The substance to be separated is injected onto the column and the column is heated. As each substance begins to evaporate it is carried by the mobile phase, as it condenses it sits on the stationary phase until it evaporates again. Thus compounds are separated by boiling point and by interaction with the stationary surface. GC works similarly to distillation, but with long columns (15–30 m columns are typical and columns as long as 105 m are manufactured). The additional length increases the efficiency of the separation (many iterations of exchange between mobile/stationary phases) and can be equivalent to more than 10,000 simple distillations. Comparison of the area of the elution peaks in a gas chromatogram allows for very accurate estimates of different product ratios. The area of the peaks can be estimated as triangles (area $= 1/2 \times$ base $\times$ height) if the peaks are symmetrical or if peaks are complex by physically cutting out and weighing the chart paper on an analytical balance.

Gas chromatography is often paired with mass spectroscopy to analyze the m/z and fragmentation patterns of each purified substance as it elutes from the column. Mass spectroscopy is very sensitive and only a few nanograms of material are needed to provide a spectrum. The mass spectrum can then be compared to known compounds to identify the substance. GC-MS analysis is commonly used for analysis of complex mixtures such quality control in industry, environmental monitoring, food safety, and pharmaceutical production.

Procedure

This experiment will be done INDIVIDUALLY.

Safety Precautions

1. Phosphoric acid is highly corrosive. Wear gloves and avoid contact with skin/clothing.
2. 2-methylcyclohexanol, 1-methylcyclohexene and 3-methylcyclohexene are all highly flammable—use caution near hot plate.

Preparation

1. Obtain a sample of 2-methylcyclohexanol and measure the mass of the vial, cap and sample.

2. Pour the sample into a 10.0 ml side-arm distillation flask and measure the mass of the empty vial to determine the mass of 2-methylcyclohexanol added by difference.

3. Add 0.5 mL of 85% phosphoric acid to the 10.0 mL side-arm distillation flask and mix the contents by gently swirling the flask.

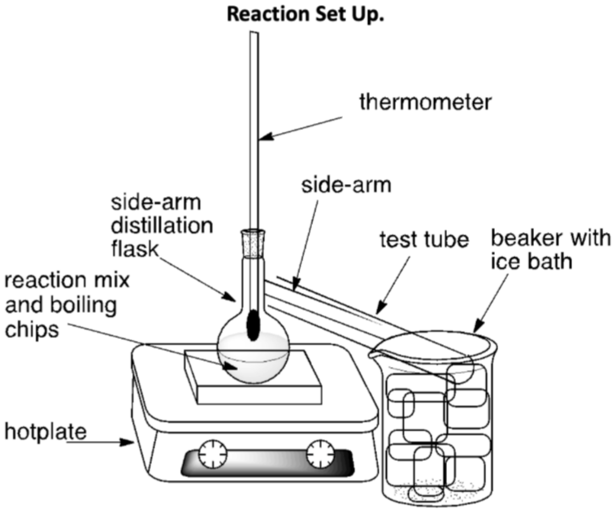


Figure G.2: Setup for the dehydration reaction

4. Add several boiling chips.

5. Clamp the side-arm flask above a heating plate. Make sure the round bottom portion is fitted into an appropriate sized opening on an aluminum heating block as shown in Figure G.2.

6. Mount a thermometer so the bulb is below the side-arm of the flask.

7. Align a 15 mL test tube with the sidearm so that the side arm reaches as far as possible into the test tube. Cool the test tube in an ice bath made with a 400 mL beaker. If the opening of the side arm is too close to the open end of the test tube and away from the ice the sample may not condense efficiently.

8. Carefully inspect the set up and compare to the TA demonstration set up before starting reaction.

9. Heat the flask gently. The sample will begin to reflux and allow time for the temperature to equilibrate before the sample begins to collect. Distillation should begin at about 105 °C. Do not let the vapor temperature exceed 110 °C. If your sample is not heating/distilling try lowering the hood sash as the air flow past can cool the flask.

10. Stop heating after about 10–15 minutes or when only 0.5 mL of material remains in the side-arm flask. (What is the remaining material?)

11. The residue in the side-arm flask is still highly acidic and viscous. Add 1–2 mL of water and swirl carefully to dilute the residue before pouring into the phosphoric acid waste bottle.

12. Remaining rinsings can be disposed of down the sink.

13. Wash and return the side-arm distillation flask to the rack. DO NOT put it in your locker.

Purification

The distillate will contain product alkene(s) and likely some phosphoric acid and water that also distilled. We can purify the product by extraction.

14. Add about 1.0 mL of saturated sodium chloride solution to the test tube containing your product. Mix the two by repeatedly squirting the solution in a Pasteur pipet.

15. Allow the two layers to settle and remove the lower (aqueous) layer using your Pasteur pipet.

16. Add a small amount of anhydrous sodium sulfate to absorb any remaining water from the organic product.

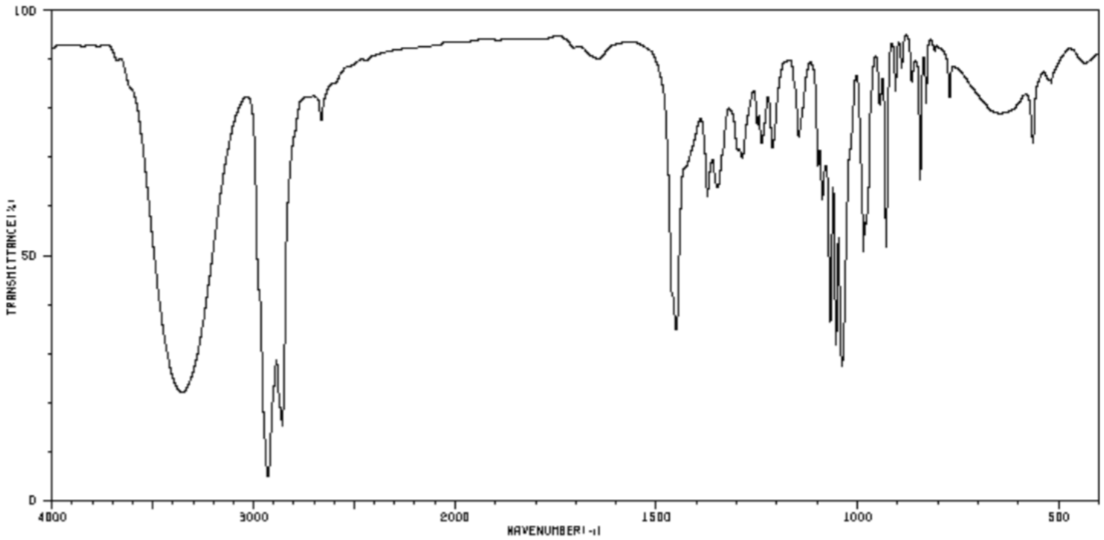
17. Allow to stand and dry for about 10 minutes.

18. Use a Pasteur pipet to transfer your product to a tared vial and determine the mass of the product.

19. Label the vial with 118B – Methylcyclohexene Product, and your name and turn into your TA.

Data

IR of mixed 2-methylcyclohexanol



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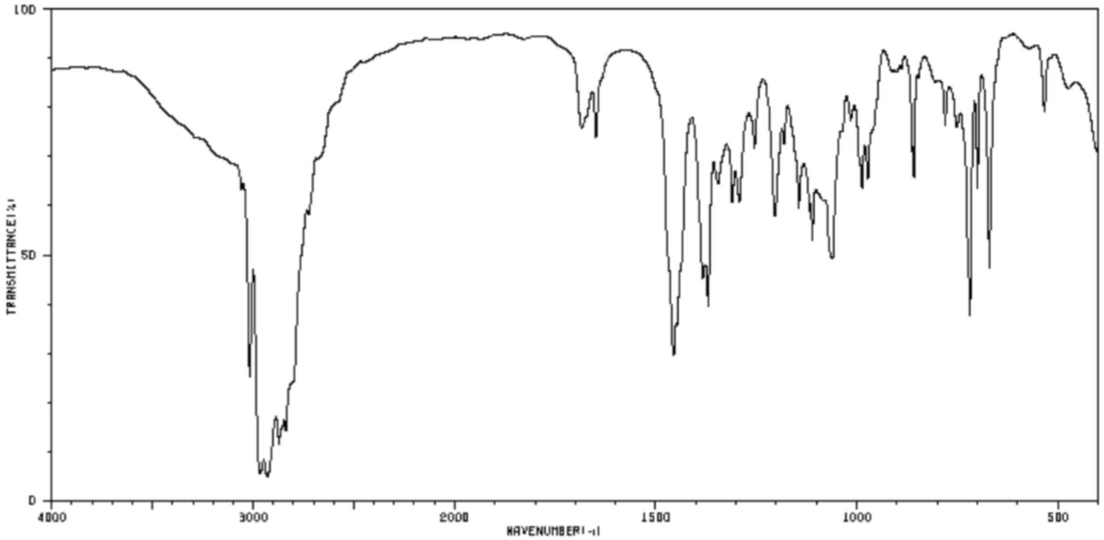
IR of Dehydration Product



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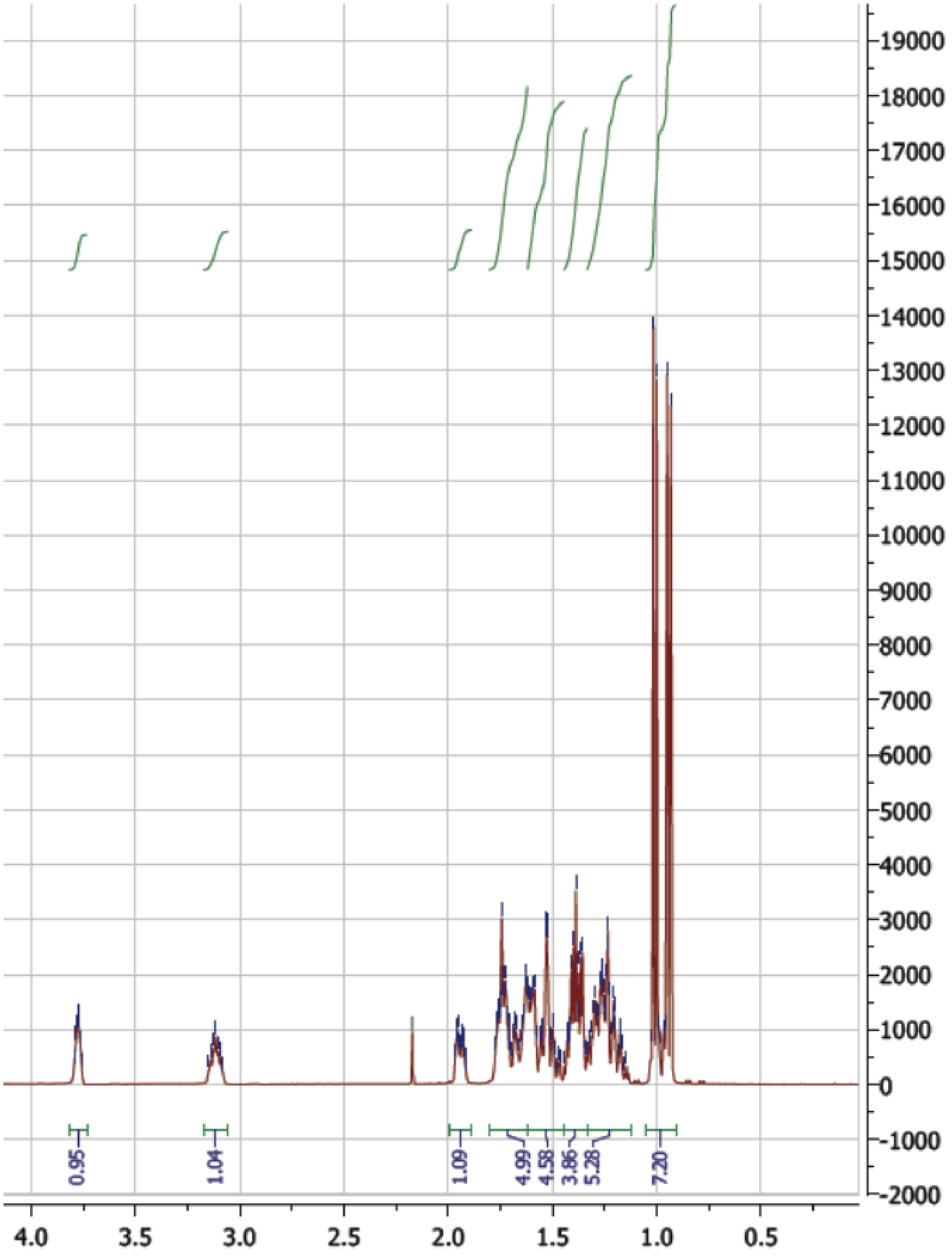
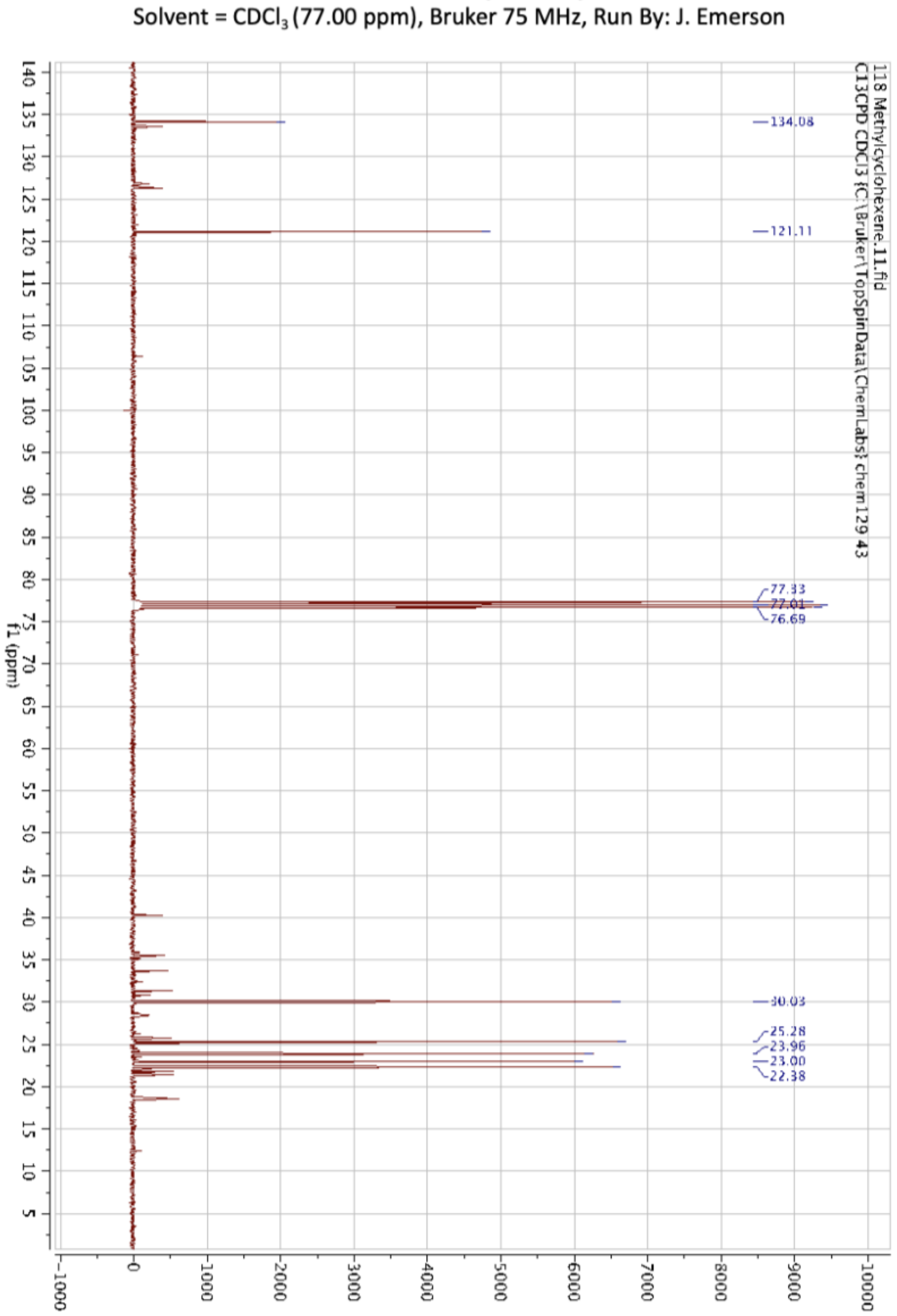
^{1}H NMR of mixed 2-methylcyclohexanol starting material



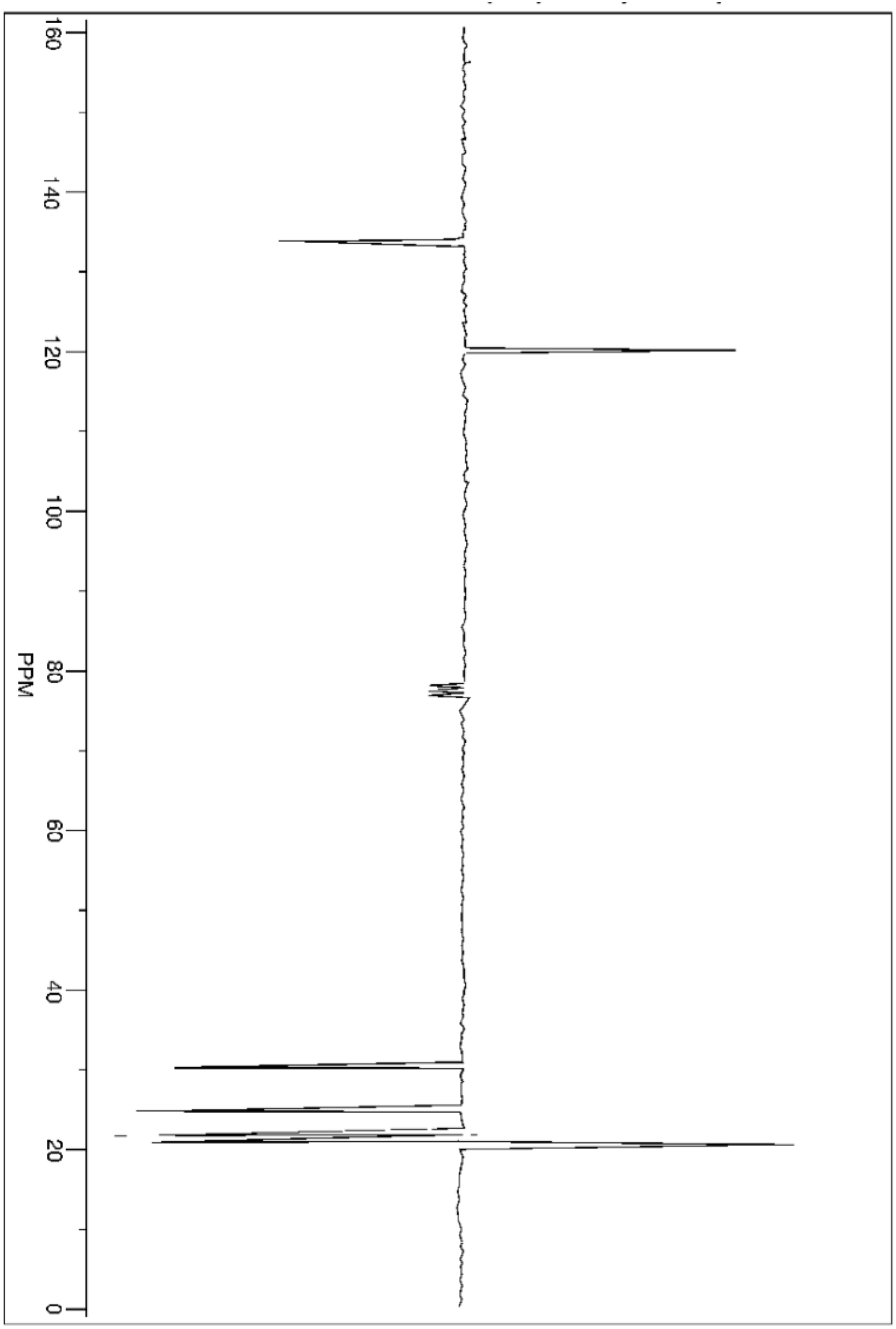
Solvent = $CDCl_3$ (7.26 ppm), Bruker 300 MHz, Run By: J. Emerson

^{13}**C NMR of crude dehydration product** Solvent = $CDCl_3$ (77.00 ppm), Bruker 75 MHz, Run By: J.

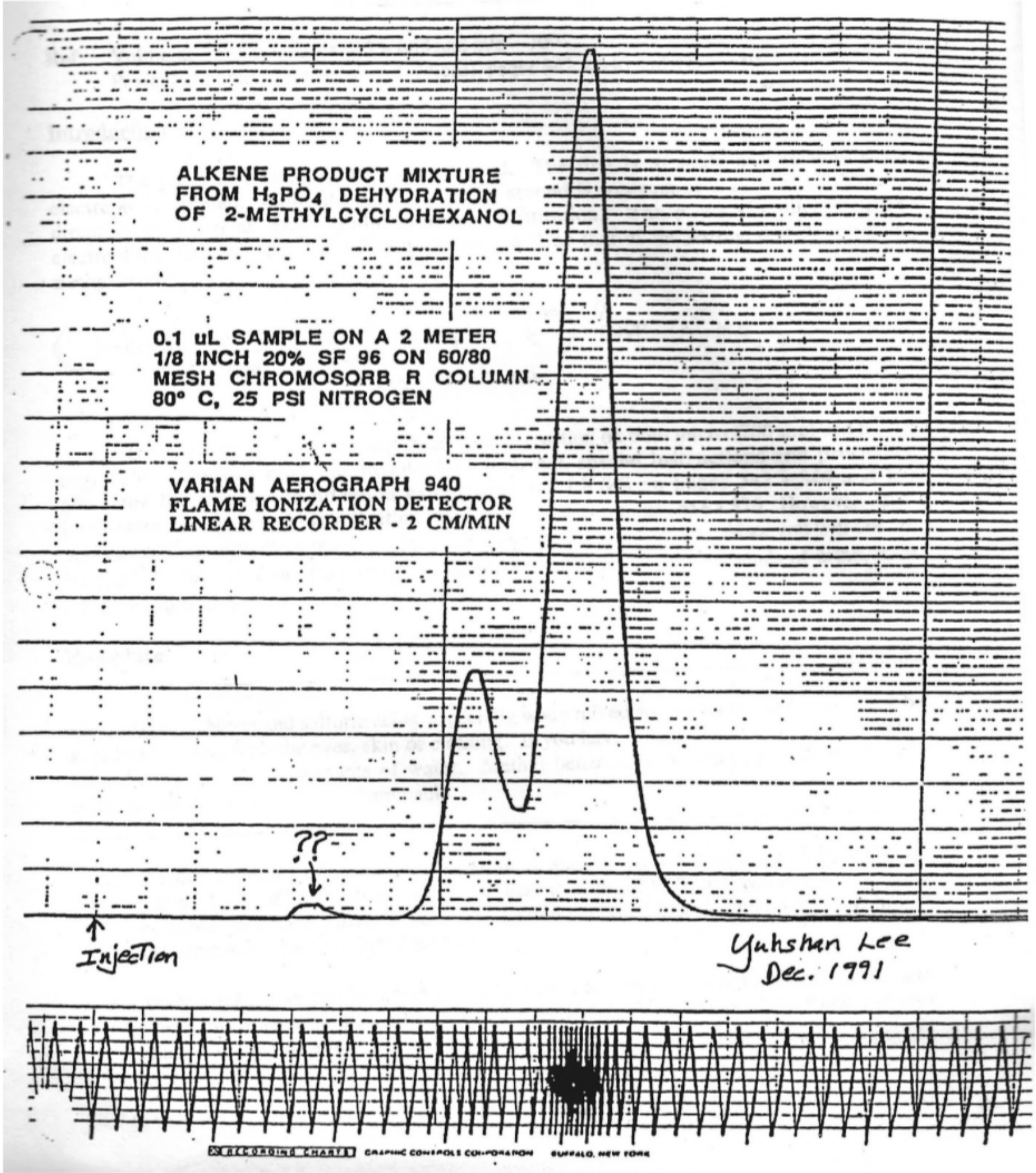


Simulated ^{13} Attached Proton Test (APT) of dehydration product

Solvent = $CDCl_3$ 75 MHz



GC Trace of Crude Product of 2-Methylcyclohexanol Dehydration
By Y. Lee



Name: ______________________________

Section: __________ Date: ______________

Report Sheet:

Lab G – Dehydration of 2-Methylcyclohexanol

Data Collection

Starting Materials

Complete Report Table G.1.

Report Table G.1: Physical Quantities Table

Reagent/Catalyst	**Quantity used (mL)**	**Quantity used (g)**	**Quantity used (mol)**
2-methylcyclohexanol			
85% (15 M) H_3PO_4			

Limiting Reagent: ____________________ g/mol

Product

Mass of Methylcyclohexenes (mixed): ____________________ g

Boiling Point, Methylcyclohexenes (mixed): ____________________ °C

Description: ____________________ g/mol

Data Analysis

Calculate the Theoretical Yield (show calculation):

Theoretical yield: ____________________ g

Theoretical yield: ____________________ mol

Calculate the Percent Yield (show calculation):

Actual yield: ____________________ g

Actual yield: ____________________ mol

Peercent yield: ____________________ %

Observations

Describe any special conditions, errors or deviations from the stated procedure on the back of this page. You may attach additional pages if needed.

Questions

1. Write the full mechanism for the dehydration of 2-methylcyclohexanol.

2. Consider the IR of the starting 2-methylcyclohexanol and the dehydration product. What differences do you see to indicate that a reaction has taken place?

3. 2-Methycyclohexanol is prepared commercially by catalytic hydrogenation of *o*-cresol (2-methylphenol) and consists of a mixture of *cis*- and *trans*- isomers.

   a. Describe how you can determine the ratio of *cis*- and *trans*-2-methylcyclohexanols from the ^{1}H NMR spectrum provided. (*Hint: What do the peaks at 3.05 ppm and 3.75 ppm represent and what does their integration show?*)

   b. Give the ratio of the two isomers. *cis*- : *trans*- ____________________

4. Using the ^{13}C NMR spectrum and DEPT of a typical sample of the 2-methylcyclohexanol dehydration product provided answer the following. (The triplet at 77.00 ppm in the ^{13}C NMR is due to solvent.) (*Hint: How might the DEPT of the two cycloalkenes differ?*)

a. What is the major alkene formed? (circle one:)

1-methylcyclohexene or 3-methylcyclohexene

b. Identify which peaks in the spectrum belong to which carbons in the product (assigning the absorptions). Some peaks may be indistinguishable.

(A) ppm: ______________ C = ____________________________
(B) ppm: ______________ C = ____________________________
(C) ppm: ______________ C = ____________________________
(D) ppm: ______________ C = ____________________________
(E) ppm: ______________ C = ____________________________
(F) ppm: ______________ C = ____________________________
(G) ppm: ______________ C = ____________________________

c. Clearly describe why these assignments confirm your conclusions about the major structure.

d. Give a reason why this product would be the major product considering the mechanism.

5. Using the GC trace for the alkene products provided and the method of triangulation described in the pre-lab reading to estimate peak areas. (*Note: The two peaks are overlapped. The peak marked ?? is an artifact and can be ignored.*)

a. Calculate the exact ratio of 1- and 3-methylcyclohexene products.

Area of major peak = ____
Area of minor peak = ____
Ratio major to minor = ____

b. Which substance elutes more quickly? Why might that compound have a shorter retention time?

6. The 3-methylcyclohexene formed is the Z isomer. Why is no E isomer formed?

7. Consider the boiling points of 2-methylcyclohexanol, 1-methylcyclohexene, 3-methylcyclohexene and phosphoric acid. What is happening when we heat the mixture to 110 °C? Why do we not see 2-methylcyclohexanol in the collection flask?

8. Discuss how this reaction follows (or doesn't follow) the principles of green chemistry outlined previously. In particular, discuss principles 3, 5, and 6, and how this reaction follows (or doesn't follow) each of these principles.

9. Predict the major organic products of the following reactions.