CHEM 322: THE GRIGNARD REACTION: SYNTHESIS OF AN ALCOHOL

INTRODUCTION

This experiment illustrates how one can change a carbon atom from electron-poor to electron-rich, and then use that carbon to attack a different electron-poor carbon to create a new C-C bond. It also introduces anhydrous technique, the technique of slow addition of a reactant to keep its concentration low, chemical tests for oxidizability and for discrimination among classes of alcohols, and the purification technique of fractional distillation.

The reaction is carried out in three steps.

1. An alkyl halide is treated with Mg metal in dry ether to generate an electron-rich “Grignard reagent”. The C bearing the halogen is electron-poor (halogens are more electronegative than C). That C changes to electron-rich once connected to Mg (which is less electronegative than C). This change is sometimes called “Umpolung” – German for “change in polarity”.

2. The Grignard reagent is mixed with a compound that has an electron-deficient carbonyl carbon. In this case, acetone is used. The electron-rich C attacks the electron-poor C forming a new C-C bond. Simultaneously, the carbonyl oxygen atom takes up one pair of electrons, creating the anion of an alcohol.

3. The alcohol is recovered by adding acidic water to the completed reaction mixture (the magnesium salts become soluble under these conditions, simplifying recovery). The mechanism for the process is shown below, using 1-bromobutane and acetone as reactants:

Grignard reactions fail unless conditions are strictly anhydrous. If even a trace of water or other source of slightly acidic protons is present, the reaction of the alkyl halide with the Mg will not even begin. Thus, all reagents must be painstakingly dried before starting the reaction, as must all glassware. The reagents will have been dried for you. If staff are not able to dry glassware, you must do it yourself the morning before the lab session. Drying arrangements will be settled Monday in class.

Glassware to dry in the oven:
1. 50 ml graduated cylinder
1. 50 mL Erlenmeyer flask
1. separatory funnel (remove stopcock beforehand)
1. skinny condenser
1. boiling flask, 250 ml
1. Claisen adapter
1. beaker, 50 or 100 ml (for measuring reagents)

EXPERIMENTAL SECTION: SYNTHESIS

As you prepare your notebook, calculate the mass and volume of 1-bromobutane that is 0.1 mole.

In order to conserve expensive anhydrous ether, pairs of students will work together. Clamp a 250 mL flask, add 2.5 g of clean magnesium turnings and a mid-size stirring bar, and attach a Claisen adapter. Attach tubing to a condenser and mount it on the curved side arm of the adapter. Leave the condenser open to the atmosphere. Center a magnetic stirrer/hot plate under the flask (touch boiling flask directly onto stir plate). Mount the separatory funnel (is the valve closed?) on the straight neck of the Claisen adapter (with stopper to keep moisture out).

In the Erlenmeyer flask, weigh or measure 0.1 mole of 1-bromobutane. Add about 30 mL of ANHYDROUS (check the label!) diethyl ether, and swirl until no more Schlieren lines are visible. Pour the mixture into the separatory funnel (stopper with paper towel). Turn on condenser water (note: do not turn on heat; the reaction will boil without external heat), then drain about 5 mL of the mixture from the separatory funnel into the flask and begin stirring. Obtain another 10 mL of anhydrous ether in the original E-flask and keep it near the apparatus.
(covered). As soon as the reaction starts (signaled by boiling), immediately pour the 10 ml of ether into the open end of the condenser to moderate the reaction. The purpose of adding ether is to keep the Grignard reagent dilute. If its concentration gets too high it can couple with unreacted bromobutane, an undesirable side reaction that makes octane. (Draw a likely mechanism for this in your notebook as part of Figure 1. Put the published b.p. of octane in your notebook “reagents table”)

After the boiling decreases, begin dropwise** addition of the 1-bromobutane solution from the separatory funnel at such a rate that the ether refluxes gently without external heating (about 2 drops per second). Continue stirring to assure good contact between the reagents. Make sure that all the magnesium is under the liquid surface. As soon as all contents of the separatory funnel have run into the boiling flask, close the valve on the separatory funnel and stopper it (to keep it dry). When most of the magnesium is gone the rate of refluxing will diminish because the bromobutane will be almost completely reacted. Gently heat the mixture at this point for about 5 minutes. The reaction is over when the rate of boiling is very slow after you remove the heat source.  **Why is this important?

When the reaction is finished, put a cool stir plate and an ice bath under the flask and continue stirring. Low temperature helps to obtain good yields of the alcohol in the next step. While it is cooling, weigh 6.5 g (0.11 mole, 8.2 ml) of dry acetone into the original Erlenmeyer flask, add 15 ml of anhydrous ether, and mix well. Add this solution to the separatory funnel. Allow the solution to drip slowly into the cold, stirred Grignard reagent. Keep the flask in the cooling bath and replenish ice as needed. The reaction is very exothermic and the drops may hiss as they contact the reagent. A white precipitate will form (it is the magnesium salt of the alcohol). When addition is complete, allow the mixture to stir for a few minutes. During this time, put 100 mL of ice chips in a beaker, add 4 mL of conc. sulfuric acid, and mix well.

When the reaction with acetone is finished, pour the product including stir bar into a 600 mL beaker sitting in an ice bath under your hood. While stirring vigorously (by hand if necessary), slowly add the sulfuric acid solution. Heat will be generated, so pour slowly and mix well to avoid boiling the ether. When addition is complete, remove the stir bar and pour everything into a 500 mL separatory funnel.

To maximize recovery of product, run some of the aqueous bottom layer into the original reaction flask. Swirl until all the white precipitate has dissolved, then pour the rinse back into the separatory funnel (avoid magnesium chips, if possible). Finally rinse the reaction flask with about 10 mL of ordinary ether (can be wet) and add this to the separatory funnel. Add about 10 mL of ether to the 600 mL beaker used in the previous step, swirl vigorously, and add this to the separatory funnel.

Shake the separatory funnel vigorously, venting early and frequently (a fair amount of hydrogen gas is generated from reaction of residual magnesium and acid). Allow the layers to separate and save both in separate vessels (which layer is ether and which is aqueous?). Try to keep magnesium particles out of the stopcock (makes it hard to close) and out of the saved ether layer. If there is any magnesium in the drained funnel, rinse it out. Put the saved aqueous (lower) layer back into the separatory funnel and extract with one 20 mL portion of ether. Combine the new ether (top) layer with the previous (saved) ether layer.

Pour the combined ether solution back into the separatory funnel. Shake vigorously with several 20 mL portions of 5% sodium bicarbonate solution (to neutralize any remaining acid, which might catalyze dehydration of the highly susceptible 3° alcohol) until no more carbon dioxide is generated. Neutralize combined aqueous layers if necessary and discard down the drain. Pour the ether layer into an Erlenmeyer flask small enough to be almost completely filled (125 mL?). Make sure there is no visible water. Add enough anhydrous calcium chloride to cover the bottom of the flask. Seal with a rubber stopper and parafilm, and allow to dry until the next lab period.

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**EXPERIMENTAL SECTION: PURIFICATION**

**Assemble the apparatus:** Choose the smallest boiling flask that will contain your dried ether solution - have your choice approved by the instructor. Wind a folded paper towel at least 6 times around the neck of this flask as insulation, then clamp it over a heating mantle. Make sure the mantle is snug against the flask. Add a boiling chip and your dried product to the flask. Check out an Aldrich® Snyder fractionating column and metal clip. Verify that the Snyder distilling column has a Teflon sleeve on its bottom joint, connect it to the boiling flask, then add a
distillation head at the top and finish assembly as usual. **Be sure your thermometer bulb is low enough!** (Have someone check it for you.) Finally, insulate carefully around the boiling flask and around the entire distillation head. Use a 250 mL round flask to capture the ether.

**Fractionate the dried solution:** Heat with the Variac set at ~40-45% of max scale. The ether will boil out first – adjust heating to produce a drip rate of about 3-6 drops/sec. During distillation, weigh two mid-size test tubes to receive products. They can be supported in an Erlenmeyer flask standing on wire gauze on a ring. Eventually the drip rate will decrease. Increase your Variac setting to 70% of max scale. Boiling will continue in the flask, but the thermometer will not register any high temperature until all the residual ether has boiled out and the entire fractionating column has heated up. When the temperature starts to climb fast and passes 90 °C, change to your first weighed test tube. Adjust the Variac so that the drip rate is about one every 2 seconds (rather slow - helps to separate compounds with close boiling points). Watch for Schlieren lines in the collected liquid. When you start to see those, change to the second weighed tube and continue collection until the drip rate slows dramatically. Turn off the heat and lower the heating mantle. **Determine the weight of each fraction, and test both as described below.** Look up the boiling points of the two most likely contaminants and compare your results with those values.

**CHEMICAL TESTS**

Chemically characterize your fractions using the following tests. Compare behaviors of products and **controls.** Samples of pertinent compounds will be set out so that you can see the outcomes with known compounds.

**Note:** no chemical test by itself reveals either the purity or the identity of a tested chemical. It only tells whether certain classes of functional groups are present or absent. A positive result indicates that any among the groups which react with the reagent is present at a detectable level. It says nothing about presence or absence of other groups that do not react. For each test, you must decide which among the reactive groups is chemically possible given the history of your experiment.

Note on descriptors: “clear” is frequently misused. This word means “transparent” and is the opposite of “cloudy” or “opaque”. A liquid can be darkly colored and yet be clear, because one can still see through it. If something has no color, the proper descriptor is “colorless”.

1. Jones Reagent (acidic Cr$^{6+}$ [CrO$_3$ or dichromate], a strong oxidizing agent – tests for the presence of oxidizable groups [1° or 2° alcohols or aldehydes])
   **Principle:** reducing agent + Cr$^{6+}$ (orange) → oxidized product + Cr$^{3+}$ (green)
   **Procedure:** Add 1 drop of Jones Reagent to about 0.5 mL of acetone and mix. Add two drops of substance to be tested and swirl vigorously for about 2 minutes. The reagent oxidizes aldehydes and 1° and 2° alcohols. It may slowly oxidize alkenes. It cannot oxidize 3° alcohols, but under acidic conditions these may slowly form alkenes which can then be slowly oxidized. A positive test is a rapid change in color from orange to cloudy green or brown. Take into account rate and extent of reaction before you draw conclusions. Positive controls: any primary and secondary alcohols. Negative control: any tertiary alcohol. (Record the names of the compounds you use as controls. Keep in mind that in this test, a positive result could be caused by any of several classes of compound, not necessarily the same class as the positive control you used.)

2. Lucas Test (12 M HCl/ZnCl$_2$ – acidic SN1 conditions – tests for ease of converting alcohol to alkyl halide [3° or 2° alcohols])
   **Principle:** ROH (soluble in reagent) → RCl (a liquid that is NOT soluble in the Lucas Reagent)
   **Procedure:** Mix 20 drops of Lucas reagent and 4 drops of your product vigorously for a few seconds, then let stand. Evidence of reaction is appearance of "foggy" cloudiness. Primary alcohols fail to react, secondary alcohols react in 5-30 minutes, and tertiary alcohols react immediately. (Record names of compounds used as controls. Ignore color in this test.)

3. Bromine test (tests for the presence of unsaturated bonds [alkenes or alkynes])
   **Principle:** Br$_2$ (brown) + alkene → dibromoalkane (colorless)
   **Procedure:** Add 1 M bromine in carbon tetrachloride dropwise to 0.5 mL of ether until color is brown or yellow and persistent when swirled, then add one drop of your product. Immediate loss of color indicates presence of unsaturated bonds. Choose appropriate positive and negative controls. (Record names.)
IR SPECTROSCOPY

Run IR spectra of both collected fractions (A and B). On each spectrum, label relevant peaks that you list in your IR peak assignments table and report in your discussion (including the responsible specific bond stretch or bend). Properly cite the published source(s) used for assigning molecular motions to peaks.

CLEAN UP: Fractions A and B and pot residue go into the "nonhalogenated mixed organics" bottle. Ether from the distillation goes into “ether to be reclaimed/distilled” bottle. Bromine test reagents and remaining 1-bromobutane go into “halogenated mixed organics.” Jones and Lucas test reagents can be washed down the drain (inside one of the main hoods) with lots of water.

LABORATORY REPORT: Must follow report guidelines for a major lab report**. Its discussion should open with a recapitulation of the objectives of the experiment and then offer thorough (yet concise) discussion of:
- how your results indicate that you met the objectives. This part should include
  • measured boiling point(s) and yield of the fraction you believe to be the desired product.
  • annotated IR spectra [one of each collected fraction, and web spectra of authentic 2-methyl-2-hexanol, acetone, and any other expected side products].
  • comments on what you learn by comparing these spectra, considering relative intensities of chosen peaks within a given spectrum. (It is risky to compare peak heights between spectra because heights depend on the thickness of the layer of compound.)
    For example, suppose you see a peak that suggests that your product was contaminated with acetone. Consider the intensity of that peak relative to the intensity of the O-H stretch in that same spectrum. Then decide if acetone contamination is serious or not.
  • a summary of what the chemical tests revealed about the presence of chemically reasonable side products. (Caution: do you expect a 1° or 2° alcohol in any fraction? Why?)
  • based on all of the above, speculation on what chemicals might be present in each fraction, roughly in what relative amounts, and how they might have formed.
    (To do this, evaluate boiling temperatures, chemical test results, and IR results as a whole, then decide. Here you should explain why octane and possibly certain alkenes [name them] might be expected as chemically plausible contaminants, and whether your data allow you to exclude any of these compounds.)
- stages of the experiment in which you suspect you lost product (and why).

**Additional useful resources available to you include:
  • Laboratory syllabus section “Sample Major Lab Report”
  • “How to Write a Strong Lab Report” on course webpage
  • Instructors, TAs, and other students (provided your work is your own and cited where appropriate)

In an appendix answer the following question:

Say you used 0.1 mole of limiting reagent in this experiment. Compute the theoretical yield of 2-methyl-2-hexanol. Suppose that your first fraction weighed 1.12 g and that its IR showed no O-H stretch. Assume that this fraction is pure octane. Suppose further that the mass of your second (alcohol) fraction was 4.00 g. Could the mass of the first fraction account for all the missing yield of alcohol? Why or why not? Support your answer with detailed calculations. Be careful - you need to consider stoichiometry of octane formation and how much product this would “rob” you of.

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This report must be submitted electronically (filename: YourLastname2015Grignard) as an email attachment to ksours@linfield.edu. The graded electronic copy will be archived in a portfolio of your lab work.

Hand-drawn material need not be included in the electronic copy but must accompany lab notebook pages that you submit at the start of your lab period. Two other reports (those for Single and Double Unknown Analyses) will be treated the same way.