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# Laboratory Manual for

Chemistry 339

# Advanced Organic Synthesis Laboratory

By

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## I. Introduction

#### A. Microscale Kit

Drawings of some of the microscale equipment are shown on the following page.

### **B.** The Laboratory Notebook

You are required to have a bound 8"x10" hard cover laboratory notebook. In this notebook is to be kept an account of your laboratory experience in a formal write-up of each experiment. All entries in your notebook must be made in ink (not pencil). Record your name on the outside front cover and also on the inside cover together with your address and telephone number in order to help recover your notebook in case of loss. Number the pages of the notebook. Leave a couple of pages blank in the front to serve as a table of contents.

#### Experiments are to be written up in the following manner:

Before the laboratory period: Write in the title of the experiment on a fresh page, together with the date. Write out the equations for any reactions that are taking place. Calculate and list all pertinent molecular weights of chemicals used. List the weights of materials to be used in the experiment. Answer prelab questions that are found at the end of each experiment.

During the laboratory period: Have your notebook with you in the laboratory while you are working. As you perform the experiment write down everything that you do that is pertinent to the experiment. Write down the weights of materials that you actually use; write the procedure in detail as you perform the experiment. It is important that you write down what you do and what happens in your experiment. Do not write down what is supposed to happen unless it really happens. It is to be a record of your laboratory experience, not someone else's. Write down the results as they occur, write them directly in your notebook, not on some scrap of paper. Calculate yields and other pertinent data and enter this directly in your notebook. Show what the calculations were, so that you can check the results later if necessary. Do all this during the laboratory period, not later on at home.

After or during the laboratory period: Prepare graphs, if needed; do more complex calculations; add anything pertinent that is not already included. Write out any conclusions or explanations that may be necessary.

Remember the notebook is a daily record of your experiences. Prepare the write-ups carefully as this will be a substantial part of your laboratory grade.

#### C. Reports.

At the end of each experiment is a report form. At the completion of an experiment fill out the report form, tear it out, cut off the holes on the left edge, and turn this in together with spectra, GLC's etc. All data reported on the report form must also be in your notebook. The report form is due at the completion of each experiment. Reports that are turned in at some other time will not be accepted unless advanced permission is granted.



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Microscale Glassware

Drawings by Ace Glass Incorporated

### D. Attendance

Regular attendance in the laboratory is required. If for some reason you cannot be present, usually because of illness, be sure to inform your TA or your instructor, in person or by telephone, as soon as possible.

#### E. Basic Laboratory Procedures

### 1. A Typical Reaction Set-up

Reactions are normally carried out in the conical vials with stirring by means of the magnetic spin vane and a magnetic stirrer. Often the reaction mixtures are heated to the boiling point of the solvent and so in order to prevent the vapors from escaping into the laboratory, either an air cooled or a water-cooled condenser is used to condense the vapors to liquid and to allow the liquid to drop back (reflux) into the vial. An air condenser is used when the temperature of the refluxing liquid is fairly high. In the case of low-boiling liquids, the water-cooled condenser is used. Which one to use comes with experience, but if you find that the air condenser does not condense all the vapors and they start coming out the top, then one should switch to the water-cooled condenser. An air condenser is not recommended for liquids boiling below 100°C.

Often it is necessary to run reactions in such a way that water vapor from the air does not come in contact with the reaction mixture. In this case the drying tube is connected to the top of the condenser or to any other compatible fitting. The drying tube is filled with a drying agent such as anhydrous calcium chloride, prevented from falling out by two cotton plugs, one at the constriction and another at the open end. Any air that passes through the drying tube is dried by the calcium chloride.

Sometimes it is necessary to add a reagent to a reaction mixture while the mixture is refluxing or distilling. In this event the Claisen head is a useful item. The Claisen head is first connected to the vial. Then a condenser, Hickman still, or drying tube is connected to one of the top fittings of the Claisen head (usually the right hand one in the drawing) and a screw cap and septum is connected to the other fitting. The reagent can then be added to the reaction mixture through the septum by means of a hypodermic syringe and needle.

## 2. Use of the Hickman Still, Distillation

In normal use, the Hickman Still is connected to a vial and its purpose is to serve as a distillate collector. A liquid is placed in the vial together with a spin vane or a boiling chip. On heating, the liquid distills and is collected in the cup of the Hickman Still. As the liquid collects in the cup, it is removed from the top with a micropipet. In the case of low boiling materials, a water cooled condenser may be attached to the top of the Hickman Still to improve condensation. The Hickman Still works well for the distillation of small amounts of material, from 0.3 to 2 mL. It is particularly useful for purifying liquid starting materials for reactions.

## 3. Use of the Craig Tube, Crystallization

Crystallizations on a small scale can be conveniently carried out in the Craig tube. A small amount of the solid is placed in the Craig tube along with about 1 or 2 mL of solvent. The tube is heated with stirring to dissolve the solid. Stirring is conveniently carried out by spinning a spatula in the tube while heating. If the solid does not dissolve completely, more solvent should be added and heating continued until solution is complete. The solution is then allowed to cool slowly to room temperature, or sometimes to 0°C in a bath of ice water. If crystallization does not occur spontaneously, crystallization can often be induced by scratching the walls of the tube or by "seeding" with a few crystallist of the pure compound.

When crystallization is complete, the Teflon (or glass) top to the Craig tube is inserted, a section of thin wire about 6 inches long is wrapped around the stem, and the assembly is placed upside down in a 12 mL centrifuge tube. The wire should extend above the lip so that the tube may be pulled out easily. This assembly is then placed in the centrifuge, an equal weight is placed in the opposite tube holder, and the centrifuge is run for about a minute. (The equal weight may be another assembly, or it may be a centrifuge tube containing the proper amount of water.) The assembly is removed from the centrifuge, the Craig tube is removed from the centrifuge tube by means of the wire, the tube is opened, and the crystalline contents are removed. The crystals should appear almost dry. If not you probably did not run the centrifuge long enough. Check on this visually as soon as you remove the assembly from the centrifuge. If there is still liquid in the Craig tube, then you should continue to centrifuge until all the liquid has been centrifuged out and the crystals appear dry. Empty the crystals out onto a small tared weighing dish, allow them to air dry, and weigh.

#### 4. The Centrifuge

The centrifuge is useful in various ways in addition to the one involving filtration in the Craig tube. It is very important to always balance the centrifuge with a weight placed opposite to the holder in which the sample is placed. Often this is just another centrifuge tube containing a sufficient amount of water to achieve balance. Use the analytical balance to adjust the weight. If the centrifuge is not balanced properly, there is great strain on the bearings and the centrifuge might actually walk itself off the counter.

#### 5. The Balance

The balance weighs to the nearest milligram (0.001 g). When recording weights, always report three figures after the decimal. For example, 2.312 g. If the last digit is a zero, always report it as zero 2.310 g. If the weight is less than one gram, always put a zero before the decimal. For example 0.310 g. Always include the units. In microscale the basic weight unit is the milligram (mg) and the basic mole unit is the millimole (mmol).

#### 6. The Micropipet

Micropipets are useful in transferring liquids from one container to another. In this way they are used like any ordinary medicine dropper. However, the micropipets are fairly accurately made and the drop size is consistent from one pipet to another. The long pipet makes possible the removing of material from a deep bottle, from the Hickman Still, or from any other container. The short pipets serve the same purpose but are somewhat less fragile because the drawn-out section is shorter. The short ones are useful in making micro drying columns or chromatography columns. A filter pipet is a micropipet that has had a very small wad of cotton stuffed in the tip. The cotton filters solutions both going in and coming out.

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## 7. Extraction

Extraction is a process whereby a compound is extracted from one solvent by another solvent that is immiscible with the first. For example, water and benzene are immiscible as they will not mix with each other. Consider the case of a compound dissolved in water and you want to transfer the compound from the water solution to an organic solvent, such as methylene chloride. The water solution is placed in a vial with about an equal volume of methylene chloride, the vial is capped with a septum cap, and the mixture is shaken. In order to relieve pressure built up by the two solvents, the cap must be loosened periodically to let the gases escape. Do this frequently. The shaking is stopped and the vial is allowed to stand for a few minutes until the two liquids have separated into two distinct phases. Open the vial and by means of a micropipet transfer the lower layer, in this case methylene chloride, to another vial. This operation must be done carefully in order not to transfer any of the top layer. Some of the compound that was formerly in the water is now in the methylene chloride solution. However, there may still be some of the compound remaining in the water, and so a second extraction is performed. Normally three extractions will transfer about 95% of the compound. In the case of very water soluble compounds more extractions may be necessary. From a knowledge of the structure of the compound in question, it is often possible to decide whether or not three extractions will be sufficient.

### 8. The Automatic Delivery Pipet

The automatic delivery pipet is a device for measuring volumes very accurately. Do not use this pipet unless extreme accuracy is needed, such as measuring the reagents for a reaction. The pipets must be handled carefully as they are expensive. First place a plastic tip of the correct size onto the pipet. All liquids are contained in this tip. Liquids are never drawn up into the pipet itself. Using the calibrated screw cap on the top set the volume desired. Then test out the operation by pressing the top cap until the plunger hits the first stop. Release it. Does the pipet work easily? Depress the plunger again, to the first stop and then continue pressing until the plunger hits the second stop. Release. Does the pipet work easily? You are now ready to measure and transfer a liquid. Depress the plunger to the first stop only. Dip the tip into the liquid and release the plunger slowly and watch the tip fill with the liquid. Carefully move the pipet to the container and depress the plunger to the first stop and then on to the second stop. That last stop is used to blow that last drop of liquid out of the tip. When making the transfer, have the container very close to the bottle of reagent so that there will not be a great chance of any of the liquid dripping out before you can empty the pipet properly. Sometimes for solvents with very high vapor pressures such as ether and methylene chloride, the vapor will rapidly expel liquid before you have a chance to transfer it. In this case just work the plunger up and down a few times with the tip in the liquid. This will tend to equalize the pressure and help to keep the liquid in the pipet while the transfer is being made.

#### 9. Evaporation of Solvents

Evaporation of solvents is commonly carried out by directing a stream of nitrogen onto the surface of the liquid while warming gently. A nitrogen line has been installed in the laboratories with an outlet at each hood space. The connections will be found on the wood panels below the hoods. Two valves control the nitrogen at each station. The first in the line is an on/off valve and the second is a needle valve. Connect a section of rubber tubing to the needle valve and to the other end of the tubing attach a micropipet. Clamp the micropipet in a downward position in the hood. Turn on the nitrogen by first pulling out the on/off valve so that it is directed out away from the hood and then opening the needle valve. Adjust the needle valve to give a gentle flow of gas. Test it with your hand. The idea is not to have such a strong stream that the solution is blown out of the flask. Carefully place the solution to be evaporated under the pipet making sure that the gas stream is not too fast. Using mild heating from the hot plate, swirl the solution gently and continue until the evaporation has been completed. Turn off the nitrogen. At the end of the laboratory period **always** leave the nitrogen line in the off position using the on/off valve.

#### 10. Sublimation.

Sublimations are generally carried out under vacuum. Place about 50 mg of the solid to be sublimed in a dry 5 mL conical vial. Attach the sublimer by means of the screw cap and place the assembly in the hole of the aluminum heating block on a hot plate. Attach the side arm to a vacuum pump and start the vacuum. Using a Pasteur pipet, place ice water in the cold finger, being careful not to spill any over the sides. If water runs over it, may be sucked into the flask, a situation which will cause you to have to take it all apart, dry the flask out and reassemble.