

# Chemistry 5b

## *Advanced Techniques of Synthesis and Analysis*

### Coordination and Organometallic Compounds

*Fall 2016*

**Professor:** Theodor Agapie (x3617, 314 Noyes, [agapie@caltech.edu](mailto:agapie@caltech.edu))

**Teaching Assistants:** Nate Hirscher (x3682, 304 Noyes, [nhirsche@caltech.edu](mailto:nhirsche@caltech.edu))

Bradley Gorsline ([bgorslin@caltech.edu](mailto:bgorslin@caltech.edu))

Dirk Schild ([djschild@caltech.edu](mailto:djschild@caltech.edu))

**Lecture:** October 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup>

Monday & Wednesday 12 pm (118 Schlinger)

**Lab Periods:** Monday 8-4, Thursday 1-4, Friday 8-4 (105 Mead)

## INTRODUCTION

In Chemistry 5b you will learn many of the basic techniques and skills as well as some of the philosophy and art required in the practice of synthetic chemistry. The course has been designed to introduce you to many important reactions that have fundamental significance in synthetic and reaction chemistry. In order to develop your manipulative skills, you will handle many different types of compounds. In Chemistry 5b you will handle compounds that are reactive towards either the dioxygen or the water in air. Thus, their preparation and handling will require special techniques to exclude air. An additional emphasis is placed on learning about the operation of instruments important to the synthetic chemist and interpretation of the information obtained from them. There will usually be a one hour lecture per week.

<b>Chemistry 5b Projects</b>	<b>Points</b>
I. An Introduction to Schlenk and Cannula Techniques: Reactions of $[(C_5H_5)Fe(CO)_2]_2$	300
II. Vacuum Line Techniques - Synthesis and Study of a Cobalt Dinitrogen Complex	300
III. Asymmetric Synthesis - Use of a Chiral Manganese Catalyst for the Asymmetric Epoxidation of Styrene	300

The laboratory will be open ONLY during scheduled times (see Page 1). Project I will be performed individually. Due to the limited amount of special equipment required, you will perform Project II *in pairs*. Project III is designed to be collaborative. You will use the data obtained in the first part to propose new catalysts that you will synthesize and test in the second part. Given the nature of Project III (requiring ordering of chemicals as proposed by you), this should be the first one to work on.

It is *essential* that you plan ahead. If you adopt the habit of coming to the laboratory without a detailed understanding of the chemistry you are to pursue and the apparatus needed, you will end up feeling rushed, and you will not gain the maximum benefit from the course. You also might not finish the course.

## GRADING

The grading in this course will be on a points-earned basis. You will be evaluated both on the quality of your work as well as the amount accomplished. You must pay special attention to pre-laboratory preparation, reaction yield maximization, careful purity checks, and laboratory write-ups.

### *Laboratory Component*

The following general guidelines will be used in grading the laboratory work.

1. 30% for completion of the experiment and obtaining a product.
2. 30% for TA's evaluation of purity and yield of product and quality of experimental data.
3. 40% for TA's evaluation of general laboratory technique in performance of experiment, including proper regard for laboratory safety, preparation for the laboratory, and lab notebook.

#### *Written Component*

Three written reports will be required throughout the term: (1) 2 short papers which communicate the main conclusions, not to exceed one page including figures, and (2) one full *JACS* style paper including title, abstract, introduction, results and discussion, conclusion, experimental, and references. You may choose which type of written report you will submit for each project. The short papers must be submitted within two weeks of finishing the laboratory component, and the full paper must be submitted by the last day of classes in the term (all written reports must be submitted by this date). For the first experiment (Project III), you are required to turn in a short draft of the report a week after the first part of the experiment is finished; this should include your proposed catalysts and the chemicals to be ordered for the second part. For the full paper, you will have the option of turning in a mostly complete document one week before the final due date to receive feedback from the TA. *You are highly encouraged to take advantage of this opportunity.* The short papers will count for 10% of the project, whereas the full paper will count for 50% of the project. The remainder for each project will be the lab component.

#### *Overall Grade*

The following *approximate* grading scale will be used to determine your overall grade:

<b>Grade</b>	<b>Points</b>
A	≥ 800
B	≥ 700
C	≥ 600
D	≥ 350
F	< 350

For those taking this course pass-fail, a passing grade will be a C or better.

### **NOTEBOOKS**

Probably the most important single aspect of successful laboratory work is careful preparation prior to the beginning of the actual laboratory period. Two hours are scheduled per week for laboratory preparation; make certain that you use them. It is expected that during this period you will carefully read

the text, notes, references, and experimental procedures for your work in the laboratory section for that week. It will also be required that calculation of the amounts of materials to be used and tables of the known physical constants of the starting materials and products which you expect to work with during a given laboratory session be entered in your notebook during the preparation period. Finally it is strongly suggested that an approximate schedule of the work you hope to do in the weekly laboratory session should be entered in your notes, together with a list of any questions you may have for your teaching assistants (TA's). Plan your experiments in advance so as to make the best possible use of your laboratory time.

**Please Note:** You must have your TA check and approve your apparatus before actually starting your preparations. The TA will initial your notebook at that time.

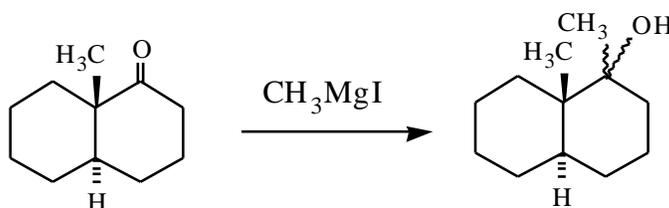
A laboratory notebook is a diary of your work. It is not an autobiography written after the completion of an experiment. It serves its purpose best if all pertinent observations are entered immediately and in such a way that the information is comprehensible not only to you but to anyone who may wish to learn of your work and its results.

Although the detailed organization of the notebook will be left to the student in consultation with his/her TA's, the following must be present:

1. *Table of Contents.* This should occupy the first few pages of your book. It should be kept current and should indicate the number of the page on which a given note is entered. As the pages are filled, bear in mind that a given note can be continued to a later page and that paper is cheap.
2. *Title.* Can be the same as listed in the lab manual.
3. *Table of Compounds.* For each material to be employed, the molecular weight, known physical properties and spectral properties of direct interest to you, notes on hazards associated with these chemicals, ... these should be entered for each reaction in a given laboratory experiment, together with any other pertinent matters, such as number of moles, questions for the TA's arising from your preparation for the laboratory, notes on the instrumentation, schedule, calculations, etc. Plan your experiments in advance.
4. *Experimental Section.* This should contain the data on which the work was done, an exact description of the experiment (containing tare weights, quantities, observations, calculations of yields, designations of any labeling codes used for spectra and glassware containing impure products and by-products, etc., and any other data which would be necessary for *another* person to duplicate your work).

- Results.* This section should contain the physical constants for your pure products, yields, any necessary calculations, and answers to more general questions. Spectra can be stored in the notebook, but a permanent record of the spectra should also be kept in writing. For infrared spectra, record the position and relative intensities of the bands: e.g.  $\nu_{\max}$  (10%  $\text{CCl}_4$ ): 3030 (s), 2965 (m), 1645 (w), 1075 (sh)  $\text{cm}^{-1}$ . Similarly for UV spectra:  $\lambda_{\max}$  (EtOH) 267 nm,  $\epsilon = 10,400$ ; and for NMR spectra  $\delta$  ( $\text{CDCl}_3$ ): 1.15 (3H, doublet,  $J=7$  Hz), 2.1-2.6 (4H, broad multiple, maxima at 2.26 and 2.47), 10.2 (1H quartet,  $J=7$  Hz, solvent dependent) ppm. All of the critical data for materials prepared should be summarized in a table at the end of the Results section.
- Bibliography.* References to physical constants obtained from the literature and to other aspects of the chemistry involved in a given experiment should be entered in this section.
- Notes.* With the exception of section 3 above, students are encouraged to write *all* of their notes during the laboratory period. Including observations during reactions and interpretations of data.

### SAMPLE EXPERIMENTAL WRITE-UP



Substance	Amount Used	Molecular Weight	Moles
Ketone	6.01 g	166.26	0.0362
$\text{CH}_3\text{I}$ (density = 2.2279 g/mL)	22.5 mL or 51.3 g	142	0.3610
Mg	8.75 g	24.3	0.3600

#### Experimental:

Into a oven-dried, 1-L 3-necked flask equipped with a reflux condenser, 250 mL addition funnel, drying tube, and magnetic stirring bar were placed 8.75 g (0.36 mole) of magnesium turnings and 75 mL of anhydrous ether. A solution of 22.5 mL (0.36 mole) of freshly distilled methyl iodide in 200 mL of anhydrous ether was added *via* the addition funnel to the stirred suspension of magnesium turnings at a rate sufficient to maintain a steady refluxing of the reaction mixture. After the addition was complete, the methyl magnesium iodide was allowed to stir for 10 min. at  $0^\circ\text{C}$ . A solution of 6.01 g (0.036 mol) of the

ketone in 75 mL of anhydrous ether was added dropwise via the addition funnel over a period of 40 min to the reaction mixture at 0°C. After stirring for 2 hr at 25°C, the reaction mixture was poured into a 1-L separatory funnel containing 250 mL of saturated ammonium chloride. The organic layer was separated, and the aqueous phase extracted with five 200 mL portions of ether. The ethereal extracts were combined and washed with 200 mL of 1% ammonium chloride and 200 mL of brine. The ethereal extract was dried ( $\text{MgSO}_4$ ), concentrated, and distilled giving 6.16 g (93%) of alcohol bp 85°C (1 mm); IR ( $\text{CHCl}_3$ ) 3605  $\text{cm}^{-1}$  (-OH);  $^1\text{H NMR } \delta$  ( $\text{CDCl}_3$ ): 0.86 (s, 1.15,  $\text{CH}_3$ ), 0.95 (s, 1.85,  $-\text{CH}_3$ ) 1.10 (s, 3, angular  $\text{CH}_3$ ); VPC analysis (SE-30, 200°C) indicated the product consisted of two components.

## LABORATORY RULES AND REGULATIONS

1. Safety glasses, goggles or face shields, and shoes (no sandals) must be worn at *all* times. Note that normal prescription lenses are insufficient. Violations will not be tolerated.
2. Each student must be prepared to show written evidence in his/her notebook of prior preparation for the laboratory.
3. Work is not permitted in the laboratory except during the regularly assigned periods when teaching assistants are present.
4. Attendance in the assigned section of the course is compulsory and attendance records will be kept. In cases where it appears *necessary* to attend another section, permission must be obtained before starting work.
5. The working space, desk drawers, cabinets, and instruments must be kept neat and clean at all times. The permission of a TA *must* be obtained before equipment is left assembled between laboratory periods.
6. The performance of unauthorized experiments is absolutely not allowed.
7. Common sense and consideration for fellow workers must be exercised rigorously and constantly.

These rules will be enforced under the Honor System. The penalty for noncompliance with rules 1 and 2 will be ejection from the laboratory for a minimum of one hour. Violation of rule 6 may, at the discretion of the instructor, call for expulsion from the course.

## SAFETY

Work in the synthetic chemistry laboratory involves the use of inflammable solvents, some corrosive and toxic chemicals, and apparatus which, if used improperly, can cause minor to severe injury. *Safety glasses and shoes must be worn at all times while in the laboratory.*

### I. Solvents

A. Never heat inflammable solvents, even small amounts, with or near a flame. As for refluxing or distillation, never place solvents in an open beaker. Pouring solvents in the vicinity of a flame is extremely hazardous. Use an oil bath, steam bath, water bath, heating mantle, or hot plate as a heat source whenever possible.

B. Ethyl ether and petroleum ether (bp 30-60°C) are especially dangerous. Never heat them on a hot plate; always use a water or steam bath, and collect the distillate in an ice-cooled flask. In the case of ethyl ether, the receiver should be a filtering or distilling flask connected to the condenser with a cork and with a piece of rubber tubing leading from the side tube on the flask to the floor. This allows the heavy ether vapors to spread

along the floor instead of the desk top where they may be ignited by burners. Carbon disulfide is extremely hazardous. It has been known to ignite from hot steam pipes or electrical sparks, as from the thermostat on a hot plate, or the motor on a stirrer.

C. If an inflammable solvent is spilled, have all workers at the desk turn off their burners and clean it up immediately using a cloth. First Notify the TA. Wring the solvent from the cloth into the solvent waste can and then rinse the cloth in the sink with much water. *Use gloves.*

D. If acetone is used to aid in drying glassware, use it sparingly and not near a flame.

E. Inflammable solvents which you may have contact with are: ether, ligroin (petroleum ether), cyclohexane, toluene, xylene, alcohols, ethyl acetate, carbon disulfide, acetone, dioxane, etc. If in doubt about the inflammability of a solvent, assume that it is hazardous.

F. Benzene and chlorinated solvents are toxic. In some cases the toxic effect is cumulative. Avoid contact with the skin and inhalation of solvent vapors.

G. Many organic solvents freely permeate latex gloves commonly used in laboratories, and are therefore inadequate protection of the skin from solvent vapors. Thicker neoprene or butyl rubber gloves are recommended.

## II. Chemicals

A. Especially corrosive substances which give off noxious fumes (e.g., bromine, acetyl chloride, benzyl chloride, phosphorus trichloride, acetic anhydride, fuming nitric and sulfuric acids, chlorosulfonic acid, benzene sulfonyl chloride, etc.) should be handled in the hoods. Use proper gloves. Do not spill these chemicals on yourself or on the desk tops. They will cause very painful burns. Bromine is especially bad. Do not put any of these in organic waste cans.

B. Over the last several years a number of organic compounds have been confirmed as carcinogens and the list is steadily growing. *It is best to assume that all chemicals are toxic, and possibly carcinogenic.*

C. Sodium and potassium metals react explosively with water. They are rapidly corroded by the atmosphere and should be stored in kerosene or oil. These metals should not be allowed to come into contact with the skin. They may be handled with dry filter paper or tweezers. Unused pieces of metal may be destroyed by dropping into 95% ethyl alcohol, or they may be returned to the bottle. Avoid all contact between chlorinated solvents and sodium or potassium.

D. Concentrated acids and alkalis are corrosive to the desk tops, clothing, and skin. If there is a spill, first notify the TA. Dilute with a large volume of water. If an acid, neutralize with solid sodium bicarbonate; and if a base, with 3% acetic acid. Sulfuric acid is troublesome, since drops adhering to the tops of bottles tend to absorb moisture and run down the outside of the bottle.

E. Mercury and its vapor are poisonous. Avoid spilling, and notify the TA if any has been spilled. The Institute has special facilities for cleaning up mercury spills.

### III. Apparatus

A. Approved safety glasses, goggles, or a face shield must be worn at all times when in the lab. Normal prescription lenses are insufficient due to the possibility of explosion.

B. When inserting tubing or thermometers into bored stoppers, it is wise to take some simple precautions. The tubing and stopper should be held by a towel so that if the tubing breaks, the towel will reduce the impact of the jagged edge. If the tubing does not enter the hole in the stopper easily, the hole may be made larger with a file (if a cork) or lubricated with water, alcohol, or glycerin. Hold the tubing close to the stopper. In removing tubing from stoppers follow the same technique. *Very serious cuts have resulted from carelessness in inserting tubes in stoppers.*

C. Closed systems are liable to explode if heated. Never carry out an atmospheric pressure distillation in a closed system.

D. Do not support apparatus on books, boxes, pencils, etc. Use large, strong wooden blocks, rings, or lab jacks. Assemblies with a high center of gravity (as when a reagent is added through the top of a condenser) should be assembled and operated with much care.

E. Use glass stirring rods with care for breaking up solids. They are liable to break.

F. Do not evacuate Erlenmeyer flasks larger than 50 mL (except filtering flasks). They may collapse.

G. Oil baths and melting point baths can cause severe burns if spilled. Make sure they are well supported. *Be especially careful not to get water into oil baths.* We will use electric heating mantles in preference to oil baths when possible.

H. Dewar flasks and vacuum desiccators, because they are evacuated, implode easily when tipped over or dropped. Make sure the ones you use are wound on the outside with friction tape or are contained in protective shields so they will not shower glass around the laboratory if broken.

### IV. Accidents

A. *Fire.* Personal safety is most important. If a person's clothing catches on fire, he/she needs help. Prevent him/her from running. If he/she is close enough, put him/her under the safety shower because it is more effective than a blanket. If not make him/her lie down and smother the flames by rolling, wrapping with lab coats, blankets, towels, etc. *Never turn a carbon dioxide extinguisher on a person.*

1. If a fire breaks out, turn off all burners and remove solvents if time allows. There are carbon dioxide extinguishers in the laboratory and the positions and operation of these should be known. Point the extinguisher at the base of the flames. Very small fires can be put out with a damp towel by smothering. Only after the safety of all is assured should the matter of extinguishing the fire be considered.

2. Because a few seconds delay can result in very serious injury, every person in the laboratory should plan in advance what he/she will do in case of such an emergency.

B. *Chemicals.* If corrosive chemicals are spilled on the clothing, immediate showering (with clothing on) is the best remedy. Safety showers are located by each door. If chemicals are spilled on the skin, wash them off with large volumes of water. Bromine should be washed off with water and the skin then massaged with ethanol or glycerin. Do not apply a burn ointment. If the chemical is spilled in the eye, it should immediately be washed out thoroughly with water using the eyewash sprayer in the sinks. If acid was involved, a weak solution of sodium bicarbonate in an eye cup should then be used. If a base, boric acid is effective.

1. If corrosive chemicals are spilled on the desk, dilute them with a large volume of water and then neutralize with sodium bicarbonate if an acid, or dilute acetic acid if a base.

## **INSTRUMENTS**

Each student will be assumed to know how to operate the infrared and NMR spectrometers. If you need a refresher, instructions on each of these machines will be provided by the TA's during the regularly scheduled laboratory periods.

Students will be checked out in small groups or on an individual basis on any other pieces of equipment which might be required for particular experiments.

It is essential that all of the equipment be used carefully and that communal and individual areas and equipment be maintained in a clean and tidy condition.

**RESERVE BOOK LIST**

## I. Spectroscopy References

- A. Applications of Absorption Spectroscopy of Organic Compounds. J.R. Dyer. Good basic explanation of principles of UV, IR and NMR, with limited tables on the absorptions of various chromophores in IR and UV and proton chemical shifts for NMR.
- B. Spectrometric Identification of Organic Compounds. Silverstein and Bassler. Very limited explanation of theory but best reference for tables of spectroscopic values for Mass Spec, UV, IR NMR of organic molecules and units within larger molecules. Many good examples and complete spectral analysis of compounds towards end of volume.
- C. Infrared Absorption Spectroscopy. K. Nakanishi. Devoted to IR spectroscopy at the practical level. Organized according to functional groups. Widely used by those involved with spectral analysis. Representative examples given.

## II. Information on Physical Constants and Toxicity Data of Organic Compounds

- A. Handbook of Chemistry and Physics. CRC. Best tabulated values of physical constants of organic, inorganic, and organometallic compounds. Includes such information as: solubility, melting point, specific gravity, specific rotation, etc. Good section on rules for naming organic compounds.
- B. The Merck Index. An encyclopedia of organic compounds. Good for finding structural information for compounds if only their common name is available. Good data on toxicity, physical properties and literature references for preparation and purification.

## III. Laboratory Techniques

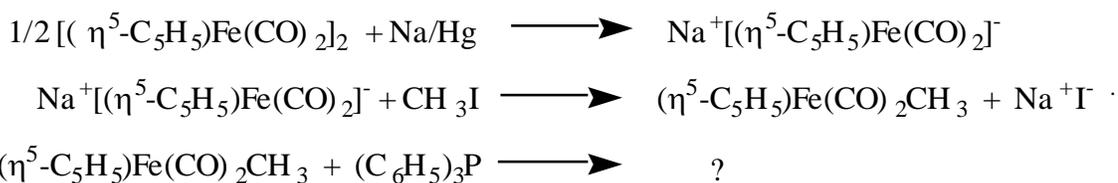
- A. Research Techniques in Organic Chemistry. Bates and Schaefer. An excellent book to compliment your laboratory text. A general treatment of running reactions is presented. A section on product isolation, extraction, distillation etc. complements Ault, but with a somewhat different perspective. There are sections on chromatography as well.
- B. Organic Structure Determination. Pasto and Johnson. Organized in a similar fashion as Ault. Part I in the text deals with physical methods of separation, purification and characterization. In this section you will find reasonable discussions on gas and thin-layer chromatography.
- C. The Manipulation of Air Sensitive Compounds. Shriver. Presents details of vacuum line and inert atmosphere chamber techniques, along with other means of dealing with air sensitive materials.
- D. Experimental Organometallic Chemistry: A Practicum in Synthesis and Characterization. Wayda and Darensbourg. Developed from a symposium sponsored by the Division of Inorganic Chemistry of the ACS. Contains practical information for handling air sensitive materials, tips for making measurements, etc. Note: Chapter 4 details the vacuum line techniques used in Project 2; it is included as Appendix I.

# Project I

*Reaction Chemistry of  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$  ("Fp<sub>2</sub>")*

## 1.0 Introduction

The late 1960's and early 1970's saw an explosive growth in the field of organometallic chemistry. This has been attributed to (1) the ready availability of both IR and particularly of high resolution NMR spectrometers (much like those found in Mead lab), along with (2) the advancement of techniques for the routine manipulation of air sensitive materials. In this experiment you will use these tools to investigate the reaction chemistry of a classic organometallic complex:  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$ , commonly abbreviated  $\text{Fp}_2$ . You will carry out three reactions and isolate two products:



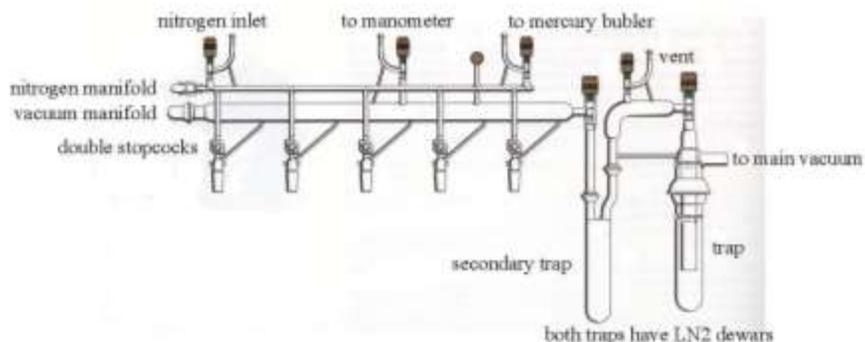
The first reaction involves reduction of the title compound with sodium amalgam to yield  $\text{Fp}^-$  anion. Nucleophilic attack by this anion on methyl iodide will afford the iron-methyl complex  $\text{Fp-CH}_3$ . Next, what appears to be a straightforward ligand displacement reaction is performed. You will not be told the structure of your final product; rather, you will be asked to assign it a structure on the basis of spectral data which you will obtain. Successful completion of this experiment will require that you understand something about the structure and bonding in metal carbonyl complexes, including the spectral characteristics of various carbonyl bonding motifs.

You will also be introduced to the broad category of experimental procedures generally termed "Schlenk Techniques", named for the Schlenk who investigated the complex structures and equilibria for common Grignard reagents in solution. These techniques have been modified and refined to deal with transition metal compounds that are sensitive to the components of normal air (dioxygen and water are typically the most problematic) and are thus also referred to as "Inert Atmosphere Techniques". Moderate-to-quite-air-sensitive compounds are routinely manipulated by these procedures in modern laboratories. Extremely air sensitive or very volatile compounds, however, are not amenable to Schlenk techniques and are handled using "Vacuum Line Techniques", which will be introduced in the second project.

This project is divided into three sections. Section I describes the inert atmosphere techniques which will be employed to carry out the syntheses. Section II provides an overview of bonding in metal carbonyl complexes and Section III outlines the experimental procedures.

## 1.1 Schlenk Techniques

The basic piece of equipment used in this project is the double manifold, or **Schlenk line**:



Inert gas (argon or nitrogen) is provided through the top manifold. The inert gas enters from a tank via the indicated stopcock and any over pressure exits through a mercury bubbler (not shown). The vacuum manifolds in Mead are all connected to one main manifold, which is isolated from the oil pump by a liquid nitrogen trap (solvents degrade pump oil). Each individual manifold also has a trap; this trap is easily removed and, in fact, should be removed and emptied regularly. The vacuum in the individual manifolds is roughly indicated by the manometer. The main vacuum line is equipped with an electronic vacuum gauge. **There are certain hazards associated with this apparatus.** First of all, any time there is pressure or vacuum in use there is a possibility of glassware failing due to fatigue. Using the mercury bubbler as an outlet for the over pressure of nitrogen greatly reduces the chance of explosion, but the risk of implosion is not as readily controllable. Even glassware that is in apparently good condition can fail under vacuum as small as that provided by a water aspirator -- the probabilities increase somewhat on a vacuum manifold, especially when the apparatus is subjected to thermal shocks. **KEEP THE SHIELDS IN FRONT OF ANY GLASSWARE UNDER VACUUM!!** Liquid dinitrogen in an open dewar presents no hazards beyond frost bite, however, liquid dinitrogen condenses dioxygen at atmospheric pressure. Should a trap cooled with liquid dinitrogen be left exposed to the air, dioxygen will condense. Liquid dioxygen is a deep blue color -- if you ever see a deep blue color in a trap, get a TA immediately and follow his/her instructions. **LIQUID OXYGEN IN THE PRESENCE OF ORGANIC SOLVENTS PRESENTS AN EXTREME EXPLOSION HAZARD.** We will always assume there are organic solvents in the trap. The third inherent hazard working with a vacuum line is mercury. You will notice that the mercury bubblers and manometers are vented to a hood to reduce exposure to mercury vapor. Treating the bubbler and manometer gently will keep this hazard to a minimum. If you do manage to get mercury somewhere in the vacuum line, or outside the line, get help cleaning it up. Making mistakes in the lab is forgivable, not owning up to them is not.

**Vacuum Glassware** (Schlenkware) is made with a side arm for evacuation of the apparatus and for the entering inert gas used to flush the apparatus. The stopcocks on the side-arms often have what are called "numbered keys", or stopcocks that have been ground together to a perfect fit; these have had a number etched into each piece and are to be kept together. These keys provide better protection from the atmosphere than standard taper joints. Numbered key-glassware should never be put in the bins for cleaning as the keys tend to stray. This is one time when you have to wash your own.

**Vacuum Grease** should be used when assembling an apparatus for use on the double manifold. In general, heavier greases should be used on small areas, and lighter greases on larger areas. You will use Apiezon "H" grease, an almost black, heavy grease to lubricate the standard taper joints used for all your reactions. The somewhat lighter "N" grease is used for the vac line itself (it stands up to repeated turning of stopcocks much better) and the very light "M" grease is used for O-rings and large areas such as desiccators. Vacuum grease is available at each double manifold in five cc disposable syringes. Penny head stoppers should be greased by applying a minimum of grease to the upper portion of the stopper only. The stopper is then pushed straight into the joint, allowing the air to escape out the ends. DO NOT TWIST. Stopcocks are greased similarly, leaving the holes ungreased, of course. Grease should be removed using ligroin (petroleum ether), kimwipes, pipe cleaners and a pair of forceps.

A **septum** (plural "septa") is a stopper with a thin section in the middle to allow transfer of liquids in and out of the vessel with needles. Septa should always be folded down and wired when in use. *Never pump down on a septum capped flask-- always use ground glass stoppers.* Septa do not hold vacuum very well, even when they have not been pierced, and are best used only with a positive pressure of dinitrogen.

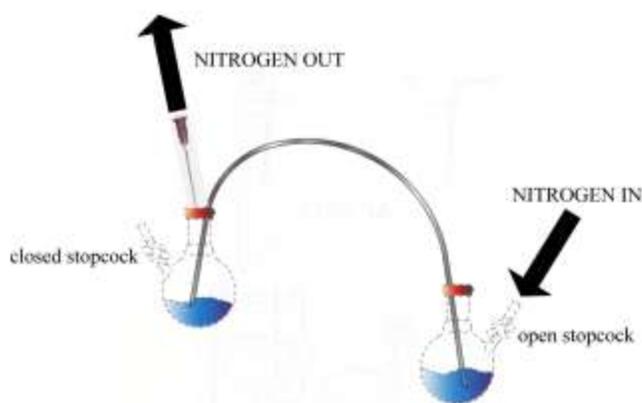
**Exchanging a ground glass stopper for a septum or vice versa**, requires a moderately strong flow of dinitrogen. To remove a ground glass stopper, first clean off all excess grease, then wrap a kimwipe around a pair of forceps, wet with ligroin, remove the stopper and carefully and quickly remove all grease from the joint. Insert the septum, fold over and wire. Exchange in the other direction is much simpler -- remove the wire from the septum, grease the stopper, remove the septum and insert the stopper.

**Pump/fill cycles** are used to establish an inert atmosphere in a vessel. The vessel is sealed, but attached to the line via pressure tubing. The vessel is evacuated by opening the double stopcock so that the vacuum manifold and the hose are connected, then filled with argon by moving the stopcock until the argon manifold and the hose are connected. The argon flow should be monitored via the mercury bubbler during this procedure. For best results, pump/fill cycles should be repeated three times.

A **cannula** is a long double ended needle. It is used to transfer liquids from one vessel to another. Cannula should be kept in the oven, and purged with dinitrogen while still warm. The other end of the

cannula is inserted into the receiving flask, and the stopcock closed so that the only flow of dinitrogen is through the cannula. A needle is placed in the receiving septum to vent, and the cannula is pushed into the liquid to be transferred. *Do not transfer liquids through a cannula with vacuum -- the interface of the septum and needle will leak air.*

A **cannula filter** is a long needle with a piece of filter paper tightly wired onto a lipped glass attachment at one end. These can also be made with plain cannula. Ask a TA how to make one -- it is better shown than described. One note -- always use new septa for a cannula filtration. Old septa are prone to leak and slow down the procedure.



**Syringes** are used to transfer liquids without exposing them to air, but unlike a cannula, a flow of dinitrogen is not required. An inert atmosphere should be established in a syringe by repeatedly drawing dinitrogen into the syringe and expelling it. *Do not pull hard on a syringe to create a vacuum -- the syringe will leak.* Allow the positive pressure of the dinitrogen flow to push the barrel out. By the same token, beware that the barrel is not forced all the way out of the syringe and broken. If the compounds in question are water sensitive, the syringe should be dried in the oven and cooled in a desiccator.

A few **general comments** on working in an inert atmosphere. Many practices that are useful and efficient in air-stable synthesis are essential here. *Clamp everything well, wire every stopcock, stopper, and piece of tubing.* A momentary exposure to atmosphere can severely decrease your yield. Secondly, *planning ahead is essential.* Get everything ready, then move quickly -- moving quickly is often the key to minimizing contamination-- but stay calm. Getting flustered will not help your chemistry.

## 1.2 Bonding in Metal Carbonyl Complexes

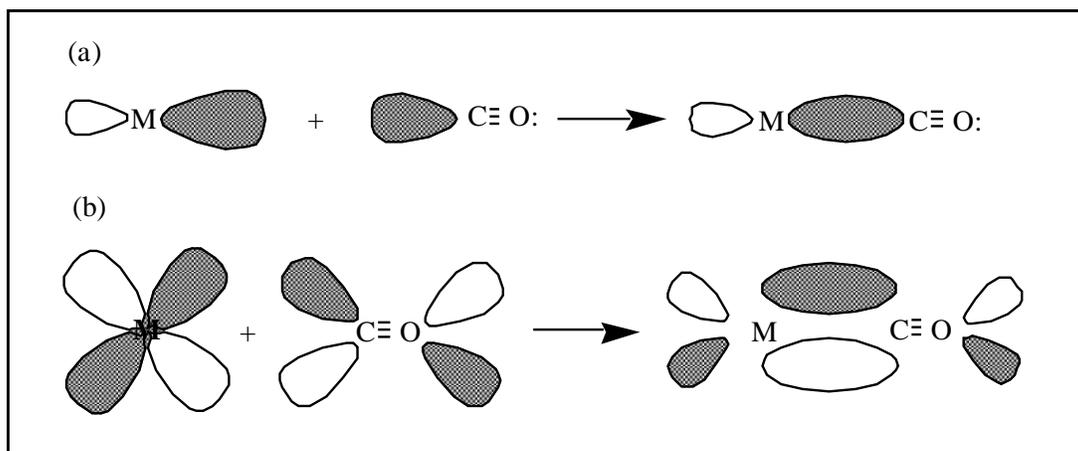
Among the stable, isolated organotransition metal compounds which have been studied, metal carbonyls are well represented. In this stage of the project you will characterize the carbonyl complex  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$ .

The simplest metal carbonyls are of the type  $M(CO)_n$ . The known mononuclear, binary metal carbonyls are listed in Table 1. In addition, there are several anionic metal carbonyl ions which are isoelectronic with many of the neutral carbonyls (e.g.  $[V(CO)_6]^-$  is isoelectronic and isostructural with  $Cr(CO)_6$ , and  $[Fe(CO)_4]^{2-}$  is isoelectronic and isostructural with  $Ni(CO)_4$ ).

The description of the bonding in these compounds may be formulated as a resonance hybrid:



or, more graphically, in terms of a molecular orbitals picture:

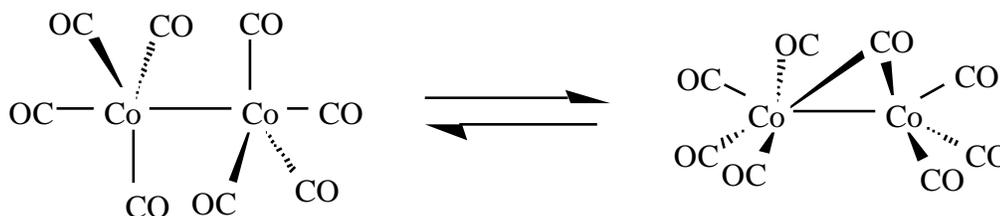


In the MO formulation there is first a dative overlap, (a), of the carbon  $\sigma$  orbital (lone pair) with an empty metal orbital of  $\sigma$  symmetry, and a second overlap, (b), of a filled metal d orbital with an empty  $\pi^*$  antibonding orbital of carbon monoxide. The resulting bonding situation is *synergistic*, since the drift of metal electron density in CO orbitals tends to make CO negative and thus to increase its basicity via the  $\sigma$  orbital of carbon; while at the same time the drift of electrons to the metal through the  $\sigma$  bonds tends to make CO positive and hence increases its  $\pi$ -acceptor strength. The resulting total bond energy is therefore greater than the sum of the  $\sigma$  and  $\pi$  contributions.

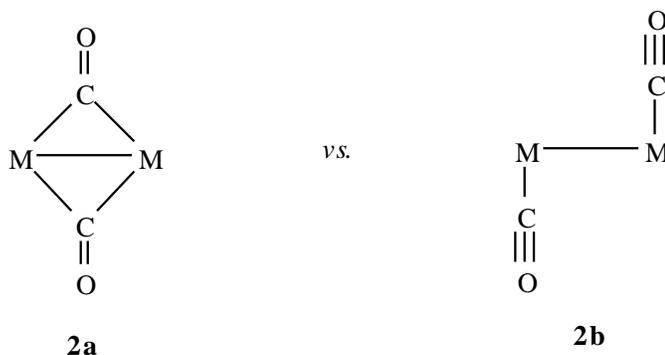
**Table 1. Mononuclear, Binary Metal Carbonyls**

Compound	Color and Form	Structure
$V(CO)_6$	black crystals	octahedral
$Cr(CO)_6$ , $Mo(CO)_6$ , $W(CO)_6$	colorless, volatile crystals	octahedral
$Fe(CO)_5$	yellow liquid, mp $-20^\circ C$ , bp $103^\circ C$	trigonal bipyramidal
$Ru(CO)_5$	colorless, unstable liquid, mp $-22^\circ C$	trigonal bipyramidal
$Os(CO)_5$	colorless, unstable liquid, mp $-15^\circ C$	trigonal bipyramidal
$Ni(CO)_4$	colorless, toxic liquid, mp $-25^\circ C$ , bp $45^\circ C$	tetrahedral

Carbon monoxide may also serve to bridge two (or three) metal centers in binuclear (or polynuclear) carbonyl complexes (*e.g.*,  $\text{Co}_2(\text{CO})_8$ ):



Bridging CO's often occur in pairs, and any pair of bridging groups can be regarded as an alternative to a non-bridged arrangement with two terminal groups:



The bonding in the bridged structure may be compared with that in ketones (*e.g.*, acetone), however the keto bridge is apparently not itself sufficient to keep the metal atoms close together, since bridging carbonyls are almost always found in conjunction with a metal-metal bond. The relative stability of **2a** *vs.* **2b** appears to depend primarily on the size of the metal atoms (Table 2). Thus the "bite" of the bridging carbonyl seems to best match the M-M bond distance for the first row Group VIII metals.

**Table 2. Binuclear and Polynuclear Binary Metal Carbonyls**

<i>Binuclear</i>	Number of Bridging CO groups	<i>Polynuclear</i>	Number of Bridging CO groups
$\text{Mn}_2(\text{CO})_{10}$	0	$\text{Ru}_3(\text{CO})_{12}$	0
$\text{Fe}_2(\text{CO})_9$	3	$\text{Os}_3(\text{CO})_{12}$	0
$\text{Os}_2(\text{CO})_9$	1	$\text{Co}_4(\text{CO})_{12}$	3
$\text{Co}_2(\text{CO})_8$	0x2	$\text{Rh}_4(\text{CO})_{12}$	0
$\text{Rh}_2(\text{CO})_8$	0?	$\text{Ir}_4(\text{CO})_{12}$	0

### 1.3 Chemistry of $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$

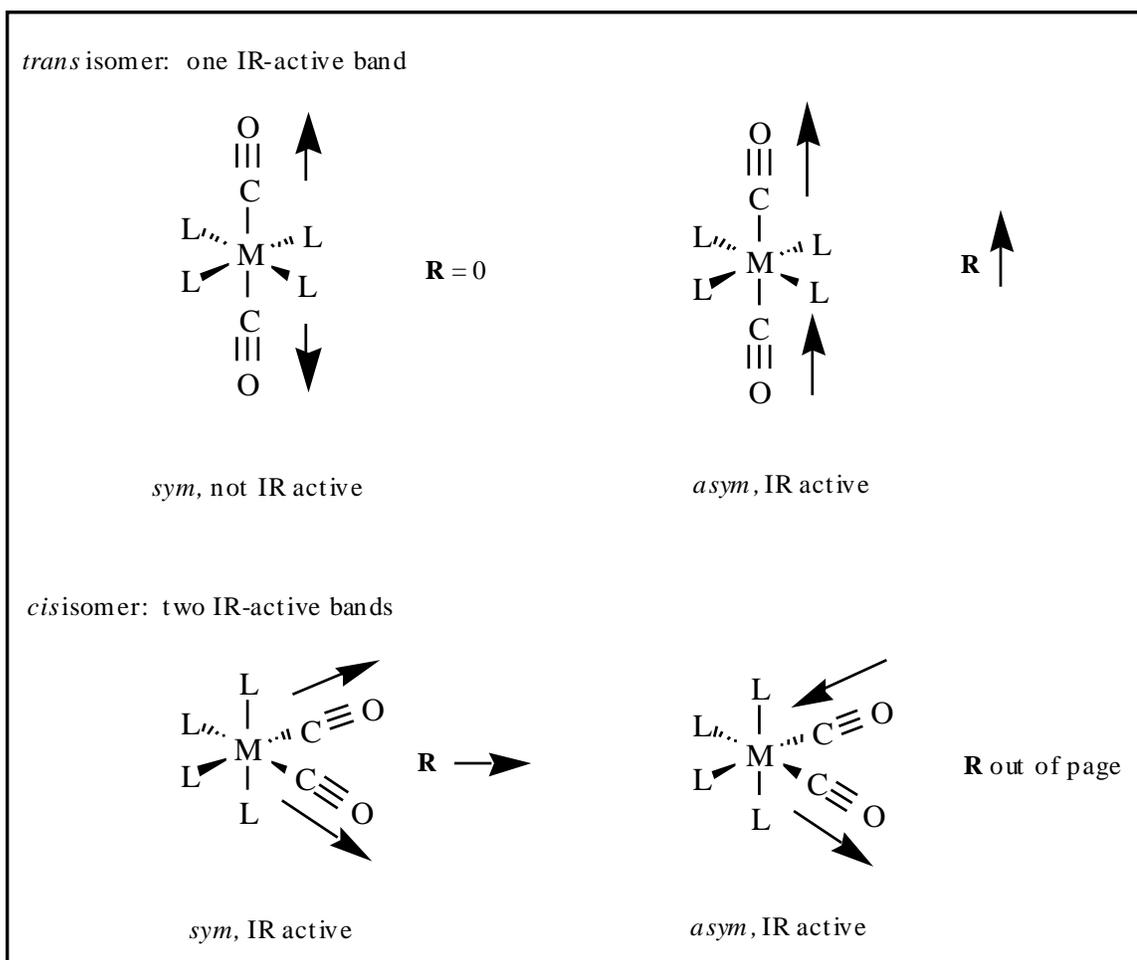
#### 1.3.1 Characterization of $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$

*Time: 1h*

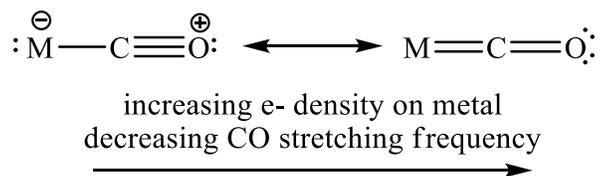
Infrared spectrum:

Infrared spectroscopy of metal carbonyls has proved to be a valuable and convenient source of information concerning both structure and bonding. The high intensity of the bands attributable to the carbon-oxygen stretching mode in a metal carbonyl makes the IR technique particularly convenient. It is often possible to infer the symmetry of the arrangement of the CO groups from the number of CO stretching bands observed in the IR spectrum. The procedure consists of first determining from symmetry requirements how many CO bands ought to appear in the IR spectrum for each possible structure. The experimental observations are then compared with predictions, and those structures which disagree are discarded. In favorable cases only one structure remains. This procedure is reasonably reliable. However, due regard must be given to the possibilities that bands may be weak or superimposed.

As an example of this procedure, consider a metal complex of the type  $ML_4(CO)_2$  (**see drawings on next page**), where L is some ligand other than CO such as Cl,  $NH_3$ , or  $P(C_6H_5)_3$ . Since only those CO stretching vibrations which induce a net dipole in the molecule (R) will absorb infrared radiation, we may predict the number of bands expected for the *cis*- and *trans* isomers. A simple measurement of the number of CO stretching frequencies allows a decision concerning whether the complex is the *cis* or *trans* isomer (or a mixture of both).

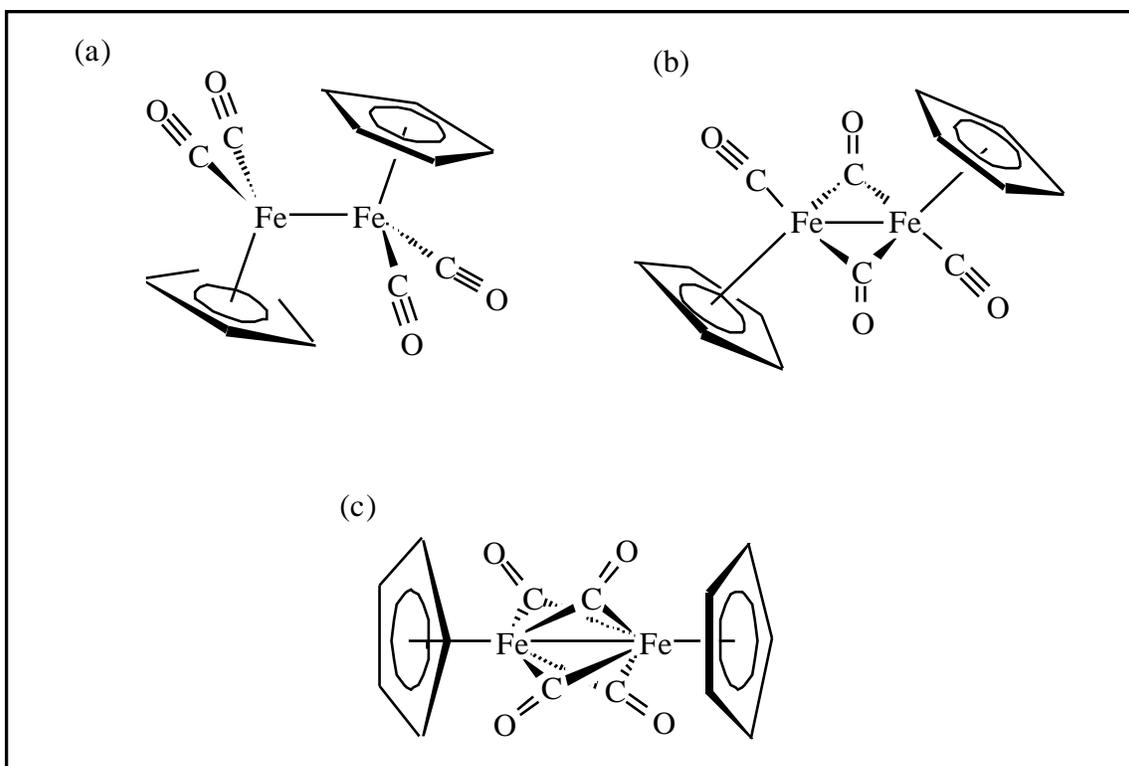


In addition, the *position* of the CO stretching frequency provides information about the bonding modes and the extent of "back-bonding" in a metal carbonyl. Terminal carbonyls of neutral or cationic complexes exhibit bands in the region 2125-1850  $\text{cm}^{-1}$ . For example, the infrared spectrum of  $\text{Fe}_2(\text{CO})_9$  exhibits CO stretching frequencies at  $\sim 2090$ ,  $\sim 2020$ , and  $\sim 1830$   $\text{cm}^{-1}$ . From this information alone it may be inferred that the structure must contain both terminal and bridging carbonyls. In using the positions of the CO bands to indicate the presence of bridging CO groups it is important to keep certain conditions in mind: the frequencies of *terminal* CO groups can be quite low if (a) there are a number of other ligands present in the complex that are good donors but poor  $\pi$ -acceptors or (b) the complex bears a net negative charge. Both of these effects tend to increase the extent of back donation from metal to carbonyl (i.e., increase the metal-carbon bond order) thus decreasing the carbon-oxygen bond order and CO stretching frequency:



A series of isoelectronic species illustrating this trend (with their IR-active CO stretching frequency) is:  $\text{Ni}(\text{CO})_4$  ( $\sim 2060 \text{ cm}^{-1}$ );  $[\text{Co}(\text{CO})_4]^-$  ( $\sim 1890 \text{ cm}^{-1}$ );  $[\text{Fe}(\text{CO})_4]^{2-}$  ( $\sim 1790 \text{ cm}^{-1}$ ).

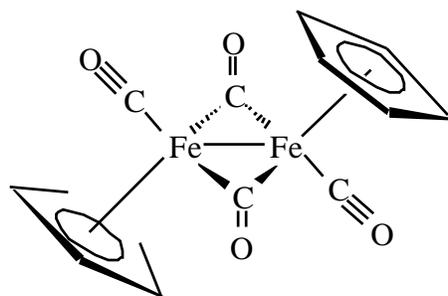
Prepare a KBr pellet of  $\text{Fp}_2$  and record the IR spectrum. For comparison measure the infrared spectrum of  $\text{Fe}(\text{CO})_5$  as a thin film on NaCl or KBr plates. On the basis of the IR data decide which of the following structures is most consistent with your data?



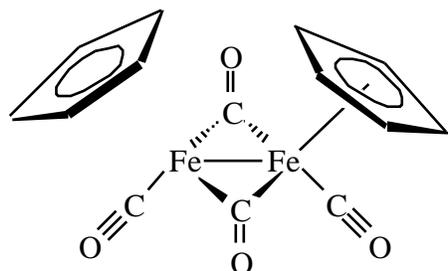
NMR spectrum:

Record the NMR spectrum of a saturated solution of  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$  in  $\text{CDCl}_3$  (1% TMS). The sample can be prepared in air but you must work quickly. The reported spectrum is a singlet at 4.75 ppm downfield of TMS. A single NMR resonance for all ten protons in the complex is consistent with the three possibilities; however, structure (b) has additional possibilities:

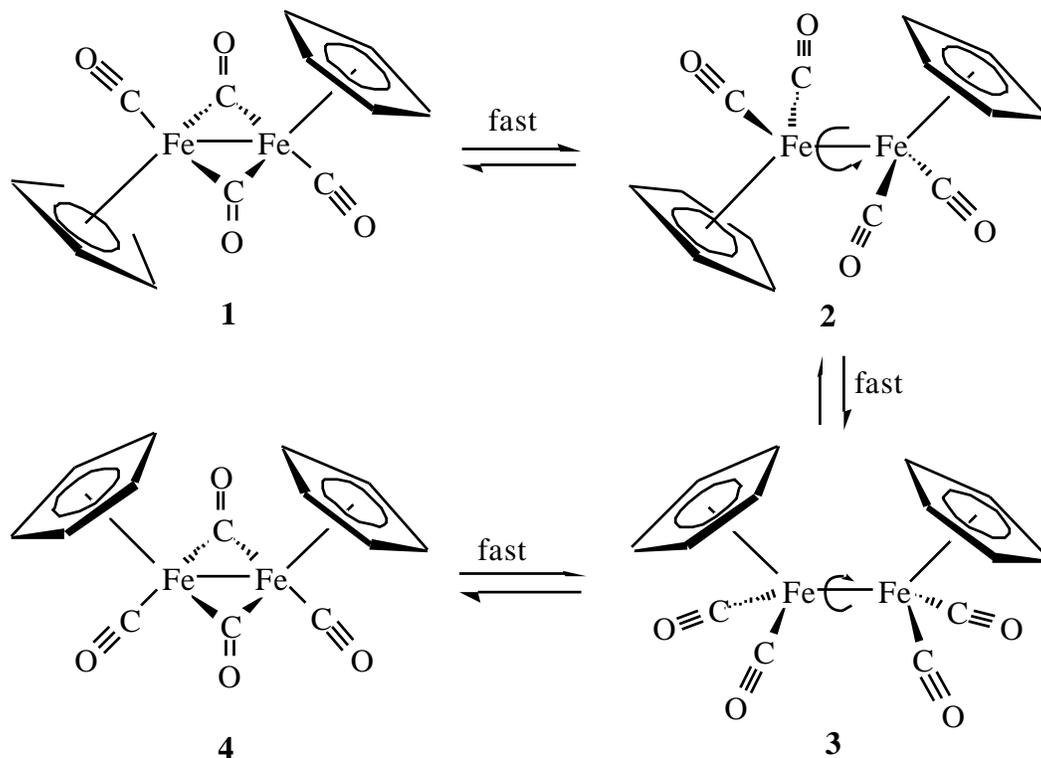
- (i) The structure of the complex is:

*trans* isomer

(ii) The structure of the complex is:

*cis* isomer

(iii) both *cis* and *trans* isomers are present in solution and are interconverting faster than the time required for the NMR experiment (the "NMR time scale").



Upon stepwise cooling, the NMR signal broadens, collapses, and finally gives rise to two singlets on either side of the original signal. Propose structures for the singlet at room temperature and the two singlets that arise upon cooling.

Melting Point:

Prepare a melting point capillary of  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$  (in air) and measure the decomposition temperature and range.

*1.3.2 Synthesis of  $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2\text{CH}_3$* *Time: 9 h*

You will perform several cannula transfers during this phase of the experiment. Dinitrogen pressure through an oil bubbler is generally insufficient for such maneuvers; all manipulations in this section are therefore to be performed on the Schlenk line, where the pressure is controlled by mercury bubblers. Before you begin, ensure that the line is properly configured, that the traps are full of liquid dinitrogen and under vacuum, and that the argon tank is not empty.

Procedure:

Place 3.0 g of the binuclear complex  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$  in a 250-mL sidearmed Schlenk flask equipped with a stirbar. Close with a rubber septum and attach an argon exit needle. With the stopcock closed, attach the flask to the Schlenk line *via* the sidearm and secure the flask with a clamp. Flush out the air by passing a steady flow of dinitrogen through the flask *via* the sidearm for ten minutes.

In a 24/40 round-bottom flask, place 60 mL tetrahydrofuran and cap with another rubber septum. Attach a long hypodermic needle for an argon inlet and use a cannula for the argon exit. Bubble argon through the solvent for ten minutes to remove most of the dioxygen. Transfer the purged tetrahydrofuran *via* the cannula to the purged flask containing  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2]_2$ . Leave it under a gentle argon flow.

Measure out 15 mL of the 0.5% sodium/mercury amalgam provided in the dry box, into another 250-mL round-bottom Schlenk flask. (Remember that mercury is very heavy--be careful not to break the flask!) Attach this flask to the Schlenk line using three cycles of vacuum and argon backfill for the tubing, then transfer the tetrahydrofuran solution *via* cannula into the flask containing the amalgam. Remove the argon exit needle, remove the cannula, and gently swirl the mixture by hand for fifteen minutes; this must be done carefully to avoid breaking the flask with the heavy amalgam. During this time the deep maroon color of the mixture changes to dark orange-brown.

You will now transfer the reaction mixture away from the residual amalgam and treat it with methyl iodide. Charge a clean 250-mL sidearm flask with 20 mL tetrahydrofuran and a magnetic stir-bar. Close with a rubber septum containing a metal needle fitted with a filter paper on the flat end (use for cannula transfer), the other end of which is fitted through another septum which also has an argon exit needle. Clamp the flask over a magnetic stirrer so that it is positioned within reach of the flask containing

the amalgam reaction mixture. Flush this flask with argon for ten minutes, add methyl iodide (3 mL-- Caution! Methyl iodide is a potent mutagen!) *via* syringe, and stir.

With argon flowing through the sidearm, remove the septum from the flask containing the amalgam reaction mixture and immediately replace it with the septum containing the free end of the wide-bore filter cannula. Keep the argon flow moderately high for a few minutes to sweep out the small amount of air that will enter the assembly. Both flasks are now connected *via* the cannula, in preparation for another transfer procedure.

Configure the system so that argon now flows from the flask containing amalgam, through the flask containing methyl iodide and out through an exit needle. Finally, carefully lower the end of the cannula below the level of the THF solution in the amalgam-containing flask so that the solution is added slowly to the methyl iodide solution. Reduce the argon flow, and take sufficient care to avoid transferring any of the settled amalgam. When transfer is complete, leave the methylation reaction stirring under a gentle flow of argon and dispose of the amalgam in the container provided.

After the reaction is complete (typically as discerned by the formation of insoluble NaI), the solvent and excess methyl iodide are removed *in vacuo*. Under argon flush, exchange the septum for a ground-glass stopper. Close the sidearm and evacuate the hose above the stopcock. With the solution stirring, carefully open the stopcock. The solvent will be transferred to the liquid dinitrogen trap. Be careful to avoid bumping! Also be aware that your product will sublime into the trap if left under vacuum for too long!

When the solution has been reduced to a very thick, semi-solid mass, close the stopcock and remove the assembly from the line. In the inert atmosphere box, use a spatula to scrape the solid out of the flask and into a vacuum sublimator. Attach the sublimator to the Schlenk line. Pump out the rubber tubing, open the stopcock and evacuate the sublimator. Place it in a beaker of warm (50-60°C) water to effect sublimation. To prevent loss of a significant amount of product into the trap, keep the stopcock closed most of the time, opening only for short periods every five to ten minutes to maintain a good vacuum in the sublimator. After about 45 minutes, discontinue the sublimation and scrape the pure orange, waxy product off of the probe. Break up the remaining residue with a spatula, replace the probe and continue the sublimation. This may be performed *quickly* in the air. Continue this procedure until no more product forms on the probe and the residue appears dry. The yield should be in the range 1-1.5 g. Isolated  $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2\text{CH}_3$  ( $\text{FpCH}_3$ ) is only slowly oxidized in air and is additionally somewhat light sensitive. To avoid any decomposition, it should be stored in a vial covered with aluminum foil in the inert atmosphere box.

Obtain the IR and  $^1\text{H-NMR}$  spectra of  $\text{FpCH}_3$  and compare them with those of  $\text{Fp}_2$ . Assign the bands in the NMR spectrum and account for the general features of the infrared spectrum.

*1.3.3 Reaction of  $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2\text{CH}_3$  with  $\text{PPh}_3$*

*Time: 6-9 h*

Procedure:

In the inert atmosphere box place triphenylphosphine (1.0 g) and  $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2\text{CH}_3$  (0.75 g) in a 25 mL test tube and stopper the tube with a rubber septum. Remove from the box and in a hood pass a gentle stream of dinitrogen through the tube using a hypodermic needle inlet and exit. Immerse the lower portion of the tube for one hour in an oil bath maintained at 110-120°C. Allow the tube to cool and wash the reaction mixture twice by decantation in air with 20-mL portions of low-boiling petroleum ether (bp 30 - 40°C). These washings remove unreacted starting materials but dissolve little of the desired product.

Further workup of this product will involve cannula filtrations; this is a convenient time to transfer your work to the Schlenk line. Add 20 mL of high-boiling petroleum ether (bp 100 - 140°C), replace the septum, and flush out the tube and solvent with argon for ten minutes. Warm the tube in a water bath at 80-90°C on a hot plate. With occasional shaking the bulk of the product should dissolve after about ten minutes.

Prepare a filter cannula by wiring on a small filter paper circle to the flat end of a metal needle and inserting it through two septa. Attach the septum at the open end of the cannula to a clean test tube and insert an argon inlet needle into the septum. Pass argon through the system for two minutes.

Quickly replace the septum of the test tube containing the warm petroleum ether solution of your product, with the septum which is equipped with the filter end of the cannula. Replace the argon inlet needle of the empty tube with an exit needle and transfer the inlet needle to the tube containing the solution. Carefully lower the filter paper until it is below the surface of the liquid. The warm, clear solution will pass through the cannula into the other test tube. When filtration is complete, cool the solution in ice-water until orange crystals form, about 20 minutes.

With a clean filter cannula, repeat the procedure to transfer the supernatant away from your product; if your crystals are large enough, you may not need to use a piece of filter paper. Discard the mother liquor. Scrape any crystals on the filter paper back into the test tube. Wash them in air twice with 5 mL of low-boiling petroleum ether, removing the solvent by decantation.

Finally, dry your product. Cover the mouth of the test tube with foil and pierce the resulting drum with a few holes. Place the test tube in a drying vessel, essentially a Schlenk tube large enough to hold your test tube, and evacuate for 10 minutes.

Measure the IR spectrum of the orange crystals in Nujol. Determine the  $^1\text{H-NMR}$  spectrum of the compound. The analytical and molecular weight data of the crystals (within 5%) are as follows: C: 68.7%, H: 4.9%, Fe: 12.8%; MW: 455. Based on these data, propose a structure for the orange crystals.

# **Project II**

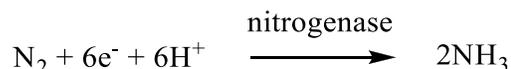
## ***Vacuum Line Techniques***

### ***Synthesis and Study of a Cobalt Dinitrogen Complex***

## 2.0 Introduction

Some of the important goals of, and indeed impetus for modern inorganic and organometallic chemistry concern the activation of common, small molecules such as  $\text{H}_2$ ,  $\text{N}_2$ ,  $\text{C}_2\text{H}_4$  and  $\text{CO}_2$  by transition metal complexes. Apart from possessing considerable chemical variety and complexity (and therefore attractive from a general scientific point of view), the field has relevance to future economic and environmental issues.

A prime example concerns the fixation of atmospheric dinitrogen ("dinitrogen"). The active components in chemical fertilizers, essential to keeping world food production in step with the rising level of demand, are so-called "fixed" forms of dinitrogen ( $\text{NH}_3$ ,  $\text{NH}_4^+$ ,  $\text{NO}_3^-$ , *etc.*). Nature has devised an enzymatic procedure for fixing dinitrogen, which utilizes ATP hydrolysis for energy and works at  $25^\circ\text{C}$  and 0.8 atm of  $\text{N}_2$ .



Currently, the best way to synthetically fix dinitrogen is *via* the Haber-Bosch process, a brute force, high temperature and pressure reaction over a promoted iron catalyst:



Clearly, a more efficient catalyst, operative at lower temperatures where the exothermic equilibrium lies more toward ammonia at reasonable pressures, might have a significant impact on world food production. As yet, such a catalyst, either hetero- or homogeneous, has not been developed.

In order to understand some of the criteria for  $\text{N}_2$  activation, it is necessary to study the coordination chemistry of molecular nitrogen ("dinitrogen"). In 1967, A. Sacco and M. Rossi reported the reaction of  $\text{N}_2$  with  $\text{CoH}_3(\text{PPh}_3)_3$  (Ph = phenyl) to form  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$  and  $\text{H}_2$ . This cobalt complex, along with a ruthenium dinitrogen complex,  $[(\text{NH}_3)_5\text{RuN}_2]^{2+}$ , were the earliest examples of transition metal compounds having a dinitrogen coordinated as a ligand. Since then, a number of dinitrogen complexes involving other metals (Ti, Zr, Mo, W, Re to name a few) have been prepared and their reactivity examined. Most are rather unstable, and the  $\text{N}_2$  ligand is readily displaced. Only a very few have been successfully converted to reduced dinitrogen products (ammonia or hydrazine).

In this experiment we shall synthesize and partially characterize  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$  using modern high vacuum line techniques. The characterization of this complex and others derived from it will introduce the student to the quantitative gas handling capabilities of the high vacuum line and Toepler pump, and teach additional laboratory skills needed for the handling of air sensitive compounds.

This project is divided into two sections. Section I discusses the general theory and methods of manipulating gases, solutions and solids on the high vacuum line. Section II describes the chemistry involved, outlines the actual experiment and suggests optional work for interested students.

## 2.1 High Vacuum Line Manipulations

### Theory:

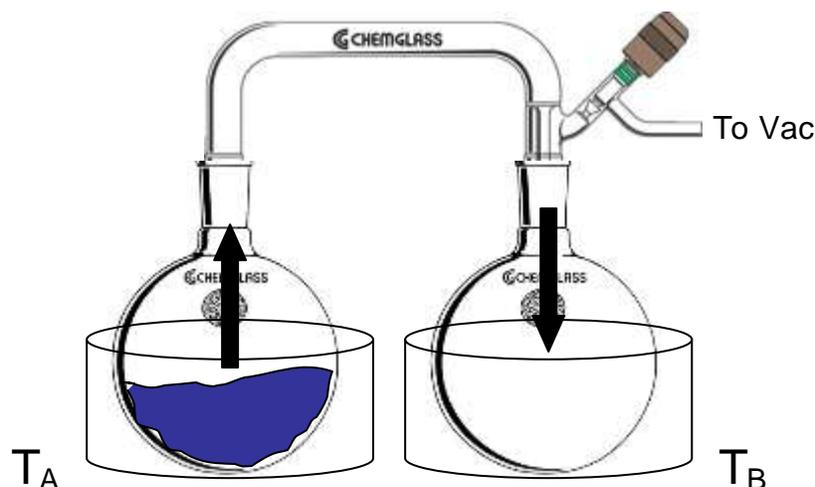
The most commonly used method of handling air and/or moisture sensitive compounds is the double-manifold Schlenk technique. Here, solutions and solids are placed in glassware (Schlenk tubes, *etc.*) equipped with stopcocks, which are connected via rubber hoses to the vacuum/inert gas manifold. Air is excluded by repeated evacuation and filling with gas ( $N_2$  or, preferably, Ar). Solvents (degassed) and solutions are transferred from flask to flask via steel cannula inserted through rubber septa, and the various pieces of glassware are mated and interchanged under inert gas counterflow. In this manner, a wide range of synthetic techniques may be performed, enabling a chemist to work on reasonable scales and with often highly air sensitive compounds.

There are two main limitations of this method. First, small amounts of extremely air sensitive compounds may be unavoidably exposed to air during the various puncturing of septa and counterflow operations. Even the best rubber tubing retains small amounts of  $O_2$  and  $H_2O$ , that eventually contaminates the system. Second, quantitative manipulation of volatiles and gases is almost impossible.

High vacuum line procedures have been developed to deal with these problems. The key difference between the two methods is in the manner volatiles are transferred. Rather than forcing solution through tubing or syringe, the technique of **Vacuum Transfer** is employed.

### Vacuum Transfer:

It is known that liquids exert a temperature dependent vapor pressure. If two flasks, A (filled) and B (empty) are connected to a common manifold (see Figure 1) and surrounding bath temperature  $T_A=T_B$ , liquid will evaporate until the manifold is filled with a vapor pressure appropriate for that liquid at  $T_A=T_B$ . If the temperature is adjusted such that  $T_A>T_B$ , the system is no longer at equilibrium and the vapor pressure in flask B will reduce by condensation. The system is again at equilibrium when all liquid is in flask B and  $p_{vap}$  is at the proper value for  $T_A=T_B$ . In practice, one usually chooses  $T_B$  such that the equilibrium vapor pressure is essentially zero, making the transfer quantitative.



**Figure 1.** Typical set-up for vacuum transfer.

The *rate* of transfer is dependent on three things:

(A) *Conductance of Manifold*

Gas may be likened to current: the smaller the diameter of glass tubing, the greater the resistance to gas flow, and thus the slower the liquid transfer. In practice, one wants to minimize the number of stopcocks (by far the major source of resistance) and the path length the gas must travel.

(B) *Vacuum Quality*

If one were to attempt a liquid transfer in the presence of, say, one atmosphere dinitrogen, the rate of transfer would be extremely slow. Diffusion problems (related to mean free path) are minimized by evacuating the manifold system to the point, where the vapor pressure of the liquid to be transferred is much greater than any residual gas pressure. Transfer of toluene ( $p_{vap} \approx 30$  torr at 25°C), for example, can be completely shut down by as little as a few millitorr of gas.

(C) *Liquid Volatility*

The vapor pressure of a liquid is a measure of the concentration of molecules maintained in the manifold. If, by analogy to traditional kinetics, a given vacuum manifold is assigned a rate constant  $k_{vac}$ , then

$$\text{Transfer Rate} \cong k_{vac} p_{vap}$$

Thus, a liquid with a vapor pressure of 60 torr at RT would transfer about twice as fast as one with  $P_{AP}$  of 30 torr. This expression is only approximate since, for one thing, the evaporation of liquid tends to lower the bulk temperature faster than a water bath can supply heat. As a rule of thumb, a liquid must have a vapor pressure of at least 5 torr (bp approx. 140°C) to "move" on a vacuum line at an appreciable rate.

Keeping these general ideas in mind will help the student plan out a vac-line synthesis in an intelligent manner. Apart from the pervading concept of vacuum transfer, all other high vacuum manipulations are pretty much the same as those used in Schlenk-type synthesis, and are briefly discussed in the following sections.

#### General Description of High Vacuum Line:

The Chem 5b high vacuum line at first glance may appear to be a jumbled mass of glass, clamps and valves, but the underlying scheme is quite simple. A written description of the procedures on a vacuum line are of only limited value. The best way to learn is to work as an apprentice with the TA. Thus, the goal here is to sketch out the general principles, and let the TA supply the details when you are ready to carry out the experiment in lab. Detailed descriptions of the workings of a vacuum system and the common procedures can be found in Reserve Book III, D, Chapter 4; the abstract for this chapter is included in Appendix I.

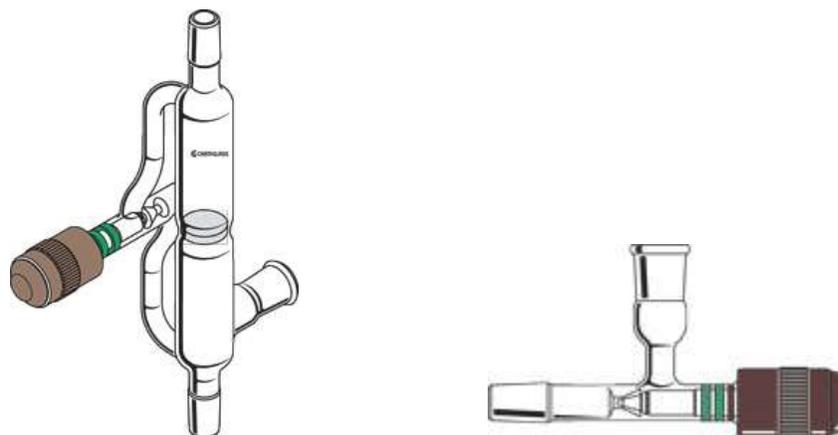
The vacuum status of each working manifold may be either *static* or *dynamic*; *i.e.*, closed or open to the main vacuum. Since most normal operations may be performed in a static vacuum condition, it is possible to do chemistry on several parts of the line simultaneously. Successful and efficient use of the entire line is dependent on what is known as "sharing vacuum". This requires both courtesy and foresight, and is outlined here:

1. Whenever a manifold is to be evacuated, always check *every* stopcock to the main line to make sure no one else is on dynamic vacuum. Air pulled into the main manifold rapidly diffuses throughout all manifolds open to it, leading to possible contamination.
2. Never pull off volatiles without an  $LN_2$  trap between the working and main manifolds. Solvents eventually will plug the main traps and destroy vacuum.
3. Never leave traps unattended. Always be present to refill boiled off  $LN_2$ . If you must leave for an extended time, drop the trap.

#### Manipulations

##### (A) *Swivel Frit*

The majority of vacuum line synthesis is performed using a "swivel frit" setup (see Figure 2).



**Figure 2.** The 90° valve allows the swivel frit to be attached to the vacuum line.

A standard 14/20 round bottom flask is charged with reactants and magnetic stirbar, and is attached via springs or rubber bands to a swivel frit fitted with a "90°" needle valve and receiver flask. Use a modest amount of Apiezon H grease (see discussion of greases in next section) on all three joints. Frit assembly is attached to a manifold port (**CAUTION:** frit is designed to swivel about needle valve joint, so loop a rubber band around upper flask and a part of the line to prevent this from happening prematurely!) at a station suggested by the TA, along with desired solvent pots (think ahead to which will be needed). The appropriate solvent trap is attached to the manifold with O-ring clamps, and the whole working section is evacuated. A dewar is placed on the trap and filled with LN<sub>2</sub> prior to any solvent transfer.

**Note:** A word here about using the vacuum: the system is equipped with a mercury diffusion pump capable of  $<10^{-4}$  torr. The whole purpose of having a good pump is to exclude as much air as possible from reactions, so when a manifold, frit, flask, tubing or whatever is to be evacuated, always observe the deflection of the thermocouple vacuum gauge when valves are opened. Wait until the gauge shows *complete* evacuation: if it doesn't return to its initial reading, don't continue. Tell the TA.

When the manifold and frit assembly are evacuated, the trap is isolated by closing stopcocks to the main and working manifolds. An insulated Pyrex dish containing an acetone/dry ice slush (-78 °C) is placed around the reaction flask. A water bath and magnetic stirrer are placed under the solvent pot, and while stirring, the needle valve is carefully opened.

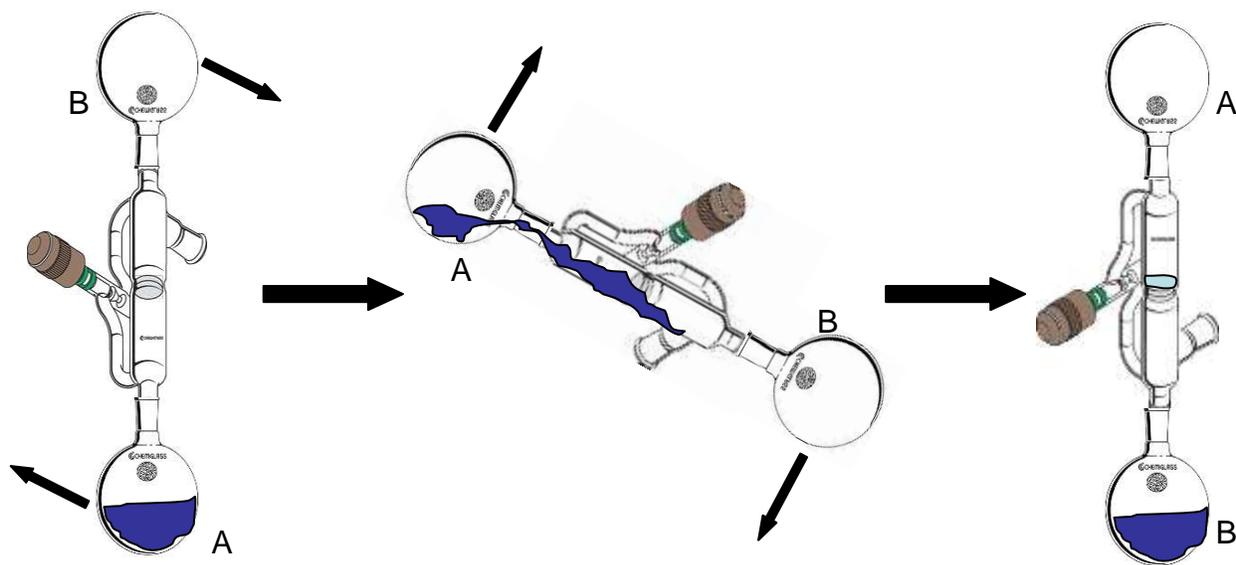
**Important:** Solvent pots are maintained by the TA, and are rigorously dried (sodium benzophenone ketyl or LAH) and gas free. Never open the needle valves until *all* gas is excluded from the system.

Volatile solvents, such as diethyl ether or petroleum ether transfer quite quickly, so be careful not to open the needle valve too fast, lest the resultant solvent "wind" blow your solid reactants all over the manifold. Toluene transfers slowly, so one may open the valve all the way in most cases. When enough solvent has been transferred, close the solvent pot valve first, and when manometer indicates complete transfer (*i.e.*, mercury stops rising), close the frit needle valve.

#### Filtering:

After reactions have been carried out, one generally must filter off insolubles and/or collect crystallized products. To do this, the sidearm bypass valve is closed, springs to the needle valve removed and the frit assembly is swiveled, keeping the sidearm on the top side (see Figure 3).

The supernatant may now be "pushed" through by heating the top section, or "pulled" through by cooling the bottom flask in a dry ice slush bath. Ask the TA which method is appropriate.



**Figure 3.** An illustration of the proper way to filter using a swivel frit.

#### Washing:

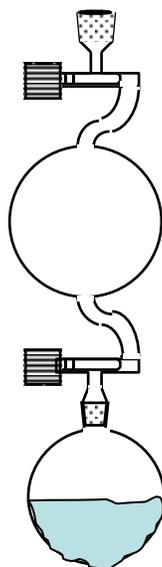
If the solid collected on the frit must be washed, one may make elegant use of the vacuum transfer principle. To do this, filtrate is cooled to  $-78\text{ }^{\circ}\text{C}$ , and any gases removed by evacuating. The filtrate is then warmed with water bath, and the sidearm valve opened.

Now, while stirring the filtrate solution, carefully swab the top flask and upper portions of the assembly with acetone/dry ice slush. Solvent condenses on the walls and runs onto the frit. Filter as before and repeat as necessary.

With these techniques, most types of synthesis may be performed. A limitation of high vacuum line work is that only volatiles may be "moved" about the line. In order to transfer solutions, one must revert to Schlenk techniques or syringe. When such occasions arise (as they will in the present experiment, in fact), they may be accommodated in the framework of vacuum line work quite easily.

### (B) *Quantitative Gas Measurement*

The main advantage of high vacuum line work is the ability to handle gases quantitatively. To perform a reaction with a desired amount of gas, one normally employs the setup shown below:



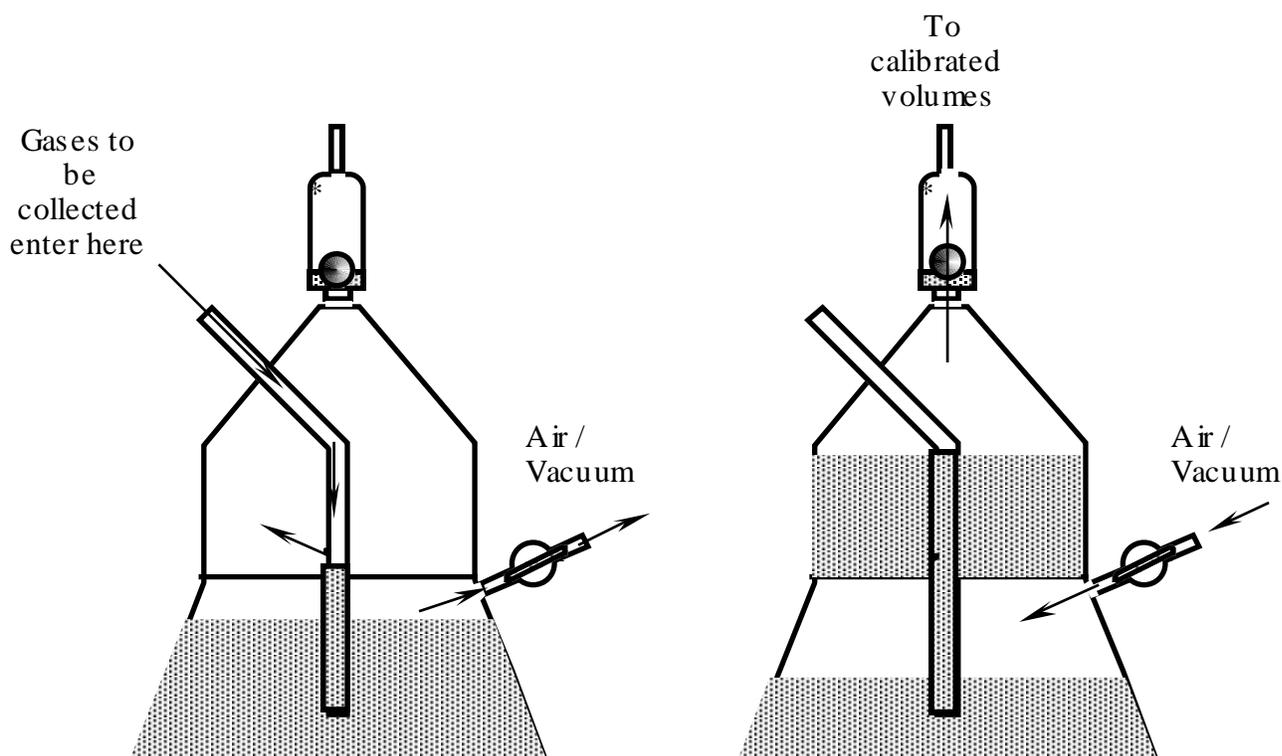
Here, a 14/20 round-bottom flask containing reactants and stirbar is fitted with a calibrated volume gas bulb and attached to a vacuum manifold. Solvent is condensed in as per usual, and the lower valve on the gas bulb is closed. The manifold is evacuated, and the desired pressure of gas is admitted into the manifold. The upper valve is now closed, and the lower gas bulb valve is opened to the reactions. A convenient formula relating amount, volume, and pressure is readily derived from the ideal gas law:

$$n(\text{mmol}) = \frac{P(\text{torr}) \times V(\text{mL})}{R(\text{torr} \cdot \text{mL} \cdot \text{mmol}^{-1} \cdot \text{K}^{-1}) \times T(\text{K})}$$

$$= \frac{P(\text{torr}) \times V(\text{mL})}{18,500} \quad \text{at } 23^\circ\text{C}$$

### Evolved Gas Measurement: Toepler Pump Operation

One of the most useful and effective ways to gather quantitative stoichiometric information about reactions involving gases is through the use of a Toepler pump. A Toepler pump, at its simplest, is merely a piston of mercury employed to move a gas to be measured quantitatively into a series of calibrated volumes, where the pressure is read (see below).



Here, mercury is cycled up and down by admitting air or evacuating the lower chamber, and is controlled by a series of electrical contacts, delays, and an air bleed-in needle valve. Any gas in the expansion chamber is pushed up through a mercury-sealed steel ball valve. When the mercury lowers, gas is trapped in the calibrated section. A vacuum exists above the mercury as it falls to its low point, until a small hole in the glass tubing carrying the gas to be collected is exposed. Gas expands into the upper volume of the pump, and after ~7 seconds the mercury rises, sealing off the part and beginning another cycle.

An additional feature on the Chem 5b Toepler pump is the CuO-filled furnace tube, connected between the calibrated gas volume section and Toepler trap presection. The design is such that a gas may be collected first, then cycled through the CuO tube indefinitely before being collected for measurement.

again. When heated to 330 °C, CuO cleanly "burns" H<sub>2</sub> to H<sub>2</sub>O, and CO to CO<sub>2</sub>. These products are trapped out of the burn cycle in an LN<sub>2</sub> U-trap. As an example of its utility, one can collect a mixture of N<sub>2</sub>, CO and H<sub>2</sub>, burn it, collect residual N<sub>2</sub>, replace the LN<sub>2</sub> trap with a -78 °C slush and collect the CO<sub>2</sub>, and thus determine the exact ratio of gases in the initial mixture.

The detailed operating procedures of the Toepler pump will be supplied by the TA in charge. This hopefully will insure that no mishaps occur: a mistake handling ~60 lbs mercury could be *very* messy and expensive.

**Note on Greases:** The greases used on high vacuum lines have low volatility ( $10^{-6} - 10^{-8}$  torr), come in several grades (T, L, M, N, H, etc.). Each type is designed for a particular use. Use them sparingly, and only as directed.

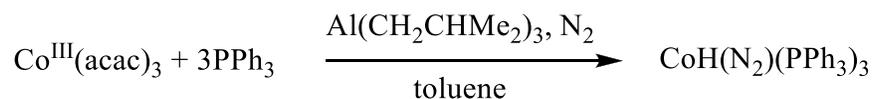
**H:** Use only on joints that may come in contact with solvents, such as RB flasks and frit joints. H grease is quite viscous, and is inappropriate for stopcocks.

**N:** Less viscous than H. Is used on stopcocks, usually. Since the TA takes care of regreasing vac-line stopcocks, the student need never use this grade.

**M:** Less viscous than N, also of lower quality and cheaper. This grease is used to connect glassware onto 24/40 vac-line ports.

## 2.2 Synthesis and Reactions of CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub> (Ph=Phenyl)

The synthesis of CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub> reported by A. Sacco (*Inorg. Chim. Acta.* **1968**, 2, 127) involved direct reaction of molecular nitrogen with the parent CoH<sub>3</sub>(PPh<sub>3</sub>)<sub>3</sub>. Unfortunately, their literature preparation of the trihydride has proved to be irreproducible. Because of this, the method of Yamamoto et. al (*J. Amer. Chem. Soc.* **1971**, 93, 371) shall be used instead:



The mechanism of this reaction is clearly very complex, but presumably involves formation of an unstable cobalt isobutyl species, which undergoes reduction, and then undergoes β-H elimination to give a cobalt hydride plus isobutene. N<sub>2</sub> adds to this complex in a later step, giving the final observed product.

### 2.2.1 Synthesis

Time: 6+ h

**Note:** This synthesis requires a *full* lab day. Do not attempt it unless you are able to begin in the morning. There is, however, a 3 hour reaction time wait, when you can attend to other things (lunch, classes, *etc.*). Calculate amounts of reagents needed before coming to lab.

Procedure:

A 250 mL round bottom flask is charged with 2 g  $\text{Co}^{\text{III}}(\text{acac})_3$ , three equivalents of triphenylphosphine and stirbar, and is attached to large frit assembly equipped with 250 mL receiver flask and stirbar (see Appendix I, Figure 4). This assembly is attached to vacuum manifold, along with toluene and diethyl ether pots, and evacuated. After evacuation is complete, reaction flask is cooled to  $-78^\circ\text{C}$ , and *ca.* 40 mL toluene is transferred onto the contents as described in the previous section. The solution is maintained at  $-78^\circ\text{C}$  with stirring, and 1 atm  $\text{N}_2$  is admitted. While toluene is transferring, a 20 mL disposable syringe is equipped with 20 gauge needle, and a piece of polyethylene tubing is cut to a length just long enough to reach through the needle valve bore and into the neck of the reaction flask (leave about an inch protruding from the needle valve). Nitrogen is adjusted until the bubbler is registering a vigorous flow, and the Teflon needle is carefully removed from the frit assembly. Polyethylene tubing is connected to syringe needle and snaked into the neck of the reaction flask, 10 mL  $\text{N}_2$  is pulled into the syringe, and the tubing disconnected. Syringe is vented to the atmosphere, and flushed three times by pulling  $\text{N}_2$  in from the needle valve bore and venting into the atmosphere. With a final 10 mL  $\text{N}_2$  charge, a bottle of isobutylaluminum (25% in toluene) is grasped with one hand, inverted, and needle is carefully inserted through system cap.  $\text{N}_2$  is injected, and, still holding the bottle inverted, syringe is charged with 10.4 mL solution (assume a density of 0.85 to calculate equivalents).

**Note:** It takes some strength to withdraw the plunger with one hand.  
Ask for assistance if necessary. Try not to ream out puncture too much:  
hold needle steady.

After the desired amount of solution is withdrawn, the bottle is tilted right-side up, a small amount of gas is pulled into the syringe to clear the needle, and needle is withdrawn. Quickly tip syringe upward so as not to leak, and cap the isobutylaluminum bottle. The syringe is connected to the polyethylene tubing, and the isobutylaluminum is carefully injected into the stirred solution at  $-78^\circ\text{C}$ . The tubing is withdrawn and Teflon valve is replaced. Nitrogen flow is stopped. The reaction mixture is allowed to warm slowly with constant vigorous stirring. When the reaction mixture reaches about  $0^\circ\text{C}$ , apply a vacuum to the apparatus quickly to remove most of the atmosphere above the reaction mixture,

then rapidly readmit fresh N<sub>2</sub>. Take care not to allow the reaction mixture to foam out of the reaction flask when evacuating. Repeat this procedure every 10 - 15 minutes for the first 1.5 hr. Note the change in color as the reaction proceeds.

After 3 hours (any less time and product will be contaminated with starting materials, any longer and decomposition will occur), solvent is removed *in vacuo* as rapidly as possible, until about 30 mL solution remains. The -78°C slush bath is reapplied, and *ca.* 30 mL diethyl ether is distilled in. The solution is warmed to RT; the product is filtered off, and washed 3 times with diethyl ether. All solvent is removed *in vacuo*, and frit assembly is brought into the glove box along with a labeled sample bottle and spatula. Average yield is 60%. Expect to weigh your product in another lab period; it is unlikely that you will get to it on the same day as the experiment.

Record the NMR and IR spectra of the product.

**Note:** Some solvent remains trapped in the product, even after an hour of pumping on the frit. Take special care to integrate residual solvent protons versus phosphine phenyl peaks, since this shall affect quantitative weighings for Toepler experiments later.

### 2.2.2 Reaction of CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub> with HCl

Time: 6 h



#### Procedure:

A 25 mL round bottom is charged with about 300 mg (weigh as accurately as possible in the glove box) CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub>, stirbar, and is fitted to a calibrated gas volume (see above discussion). The assembly is attached to the Toepler section of the vac-line, along with HCl gas lecture bottle and THF solvent pot. The manifold is evacuated and *ca.* 10 mL of THF is transferred into reaction flask. HCl is freed of traces of other gases (air, N<sub>2</sub>, H<sub>2</sub>) by freeze-pump-thaw cycles (TA will explain the technique), and 4 equivalents HCl is admitted to the gas bulb. The reaction flask is cooled to 0°C, and the HCl is introduced. The reaction is stirred for about one half hour, and residual gas is measured by Toepler pump. Calculate equivalents gas evolved. Burn collected gas and recollect. Calculate the equivalents of N<sub>2</sub> and H<sub>2</sub> evolved in the reaction of CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub> with HCl.

Optional: The acidolysis of CoH(N<sub>2</sub>)(PPh<sub>3</sub>)<sub>3</sub> is carried out at 0°C to avoid additional reaction. If there is time, take up residue in THF and introduce excess HCl at RT. Note the color change. Collect the residual gas, and calculate a stoichiometry. Can you explain?

2.2.3 *Optional Reactions of  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$* *Time: 6 h*

The student may choose one or two of the following experiments to perform.

(A) *Reaction with CO*

A 25 mL round bottom flask is charged with *ca.* 300 mg  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$  and fitted with a calibrated volume. The assembly is attached to a manifold, along with toluene solvent pot and CO lecture bottle.

The system is evacuated, and about 10 mL toluene is distilled into reaction flask. About 4 equivalents CO are measured into gas bulb, and introduced to the stirred solution. Observe any color changes. After one half hour, remove solvent and residual gas, and analyze the reaction residue by IR and NMR.

Optional: If the student is interested, the above procedure may be done with frit assembly, to attempt isolating product, or a Toepler experiment may be performed.

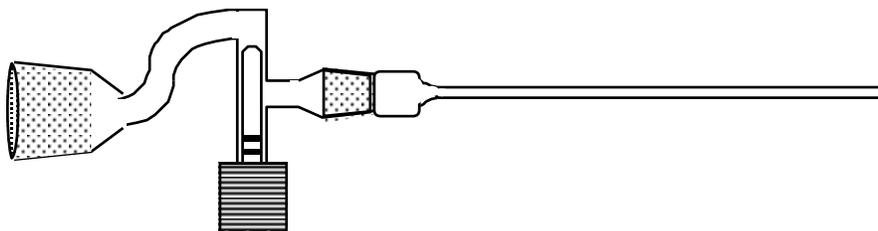
(B) *Reaction with  $\text{CO}_2$* 

Follow above procedure, and substitute  $\text{CO}_2$  for CO.

(C) *Reaction with  $\text{H}_2$* 

As was mentioned in the introduction, the first preparation of  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$  was from the cobalt trihydride,  $\text{CoH}_3(\text{PPh}_3)_3$ . The difficulty that confronts us is that the glove box maintains a dinitrogen atmosphere, which would react with any trihydride we attempted to bring in.

We can avoid this problem by performing a sealed NMR tube experiment: an NMR tube, attached by Pyrex glass to a 14/20 female joint, is charged with ~50 mg (about 3 microspatulas full) of  $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$  and *ca.* 0.4 mL  $\text{C}_6\text{H}_6$  (or, better,  $\text{C}_6\text{D}_6$ ) and is attached to a "180°" needle valve (see below)



The NMR assembly is attached to a manifold with access to  $\text{H}_2$  gas, and the system is evacuated. About half of the NMR tube is immersed in the  $\text{LN}_2$  dewar, and residual gas is pumped off. 700 torr  $\text{H}_2$  is admitted (it is important to have slightly less than an atmosphere of gas, or else the tube won't collapse

when sealed off by torch), and the tube is carefully worked by a torch (cool flame) until a good seal is obtained.

**Note:** Don't attempt this operation without a TA present, since using a torch around a manifold full of  $H_2$  is potentially disastrous.

After tube is thawed and the seal is inspected, record the NMR spectrum. Ask TA how the NMR tube is to be safely recycled.

(D) *Potluck*

There are many additional experiments that can be performed, most of which have never been done. If you think of one that may be interesting to try, discuss the possibility with the TA, and something may be worked out.

**A Word on Gases:** One of the most common and potentially deadly mistakes that can occur on a vacuum line is due to the failure to distinguish between condensable and non-condensable gases.

All gases fall under one of two categories.

Non-condensable: The lowest temperature normally worked with on vacuum lines is  $-195^\circ\text{C}$ , the bp of  $N_2$ . Only He and  $H_2$  remain gases at this temperature. Dinitrogen will, of course, condense if the pressure exceeds atmospheric pressure torr.

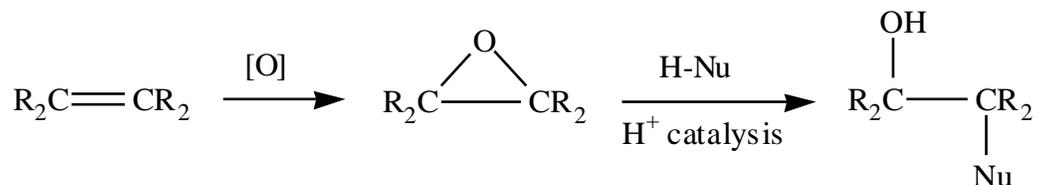
Condensable: The remainder of gases fall into this category: Ar,  $O_2$ , CO, ethylene, methane,  $CO_2$ , etc. Gases such as methane, Ar,  $O_2$  and CO have appreciable vapor pressures at  $-195^\circ\text{C}$ , such that they cannot be completely condensed. Any time the pressure increases beyond the equilibrium vapor pressure, they condense into an  $LN_2$  trap. The major danger is when an unwary person removes a trap filled with condensed gas. The most common manifestation of this is when a vacuum pump is shut off and the  $LN_2$  traps are not removed. Liquid dioxygen collects, and can be particularly nasty. If you suspect a problem of this nature, **keep the dewar surrounding the trap filled with  $LN_2$**  and immediately *summon* a TA. Other dangers arise when a trap is unintentionally filled with a large amount of, for example, liquid argon, when the argon manifold is left open to a  $LN_2$ -cooled trap. Removal of the dewar then results in a rapid increase in volume and pressure as the liquid gas rapidly boils. Obviously, a pressure explosion may occur, and if the system is closed when the dewar is removed, an explosion is a certainty!

## **Project III**

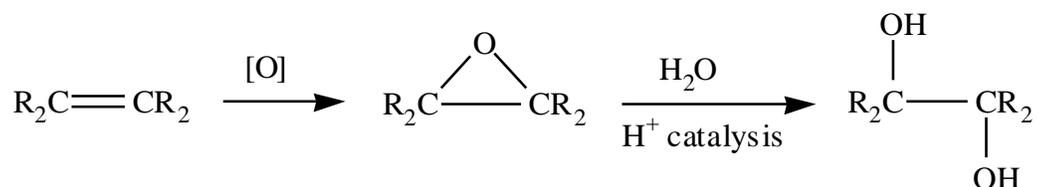
*Asymmetric Synthesis - Use of a Chiral Manganese Catalyst for the  
Asymmetric Epoxidation of Styrene*

### 3.0 Introduction

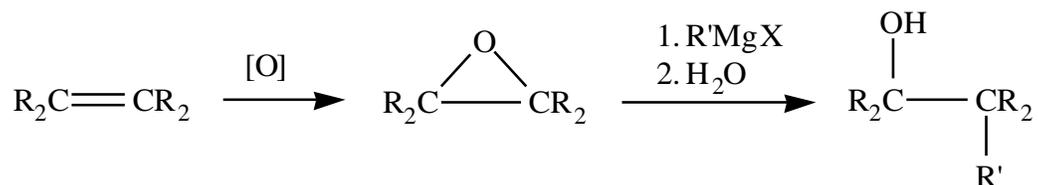
Chemists have discovered and developed many elegant and synthetically useful transformations of carbon-carbon double bonds. One important class of reactions involves oxidation to epoxides which serve as synthetic intermediates towards a wide variety of oxygen-bearing functionalities. Epoxides react with strong nucleophiles (e.g.  $\text{RS}^-$ ,  $\text{RSi}^-$ ) under basic conditions and even weak nucleophiles (e.g.  $\text{H}_2\text{O}$ ) will react under acidic conditions with opening of the epoxide ring.



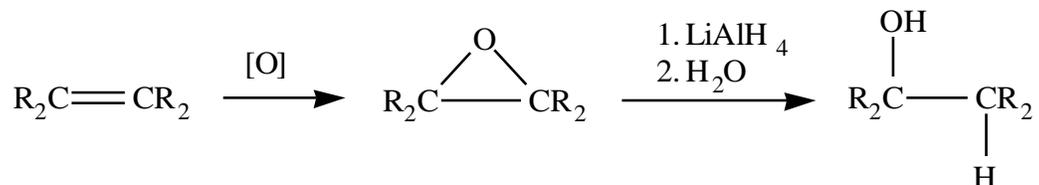
Hydrolysis in dilute mineral acid is a widely used method for the preparation of (*trans*-) 1,2-diols from alkenes.



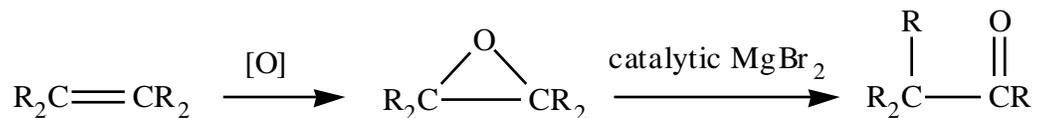
Reactions with carbon nucleophiles such as Grignard reagents and organocuprates lead to ring opening and carbon-carbon bond formation.



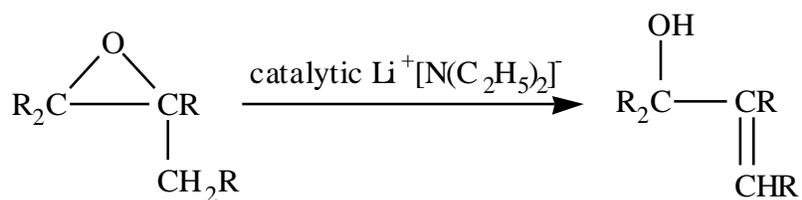
Reductions using aluminum-hydride reagents afford alcohols.



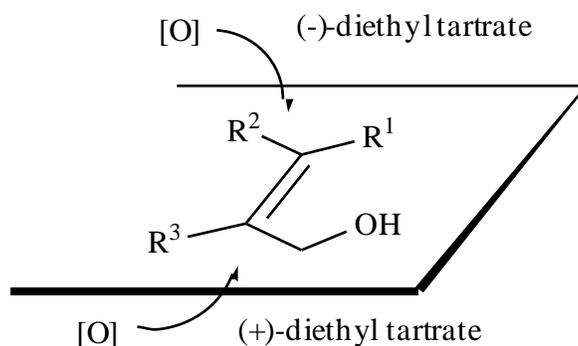
In addition, epoxides undergo Lewis acid-catalyzed rearrangements to carbonyls,



and base catalyzed rearrangements to allylic alcohols.

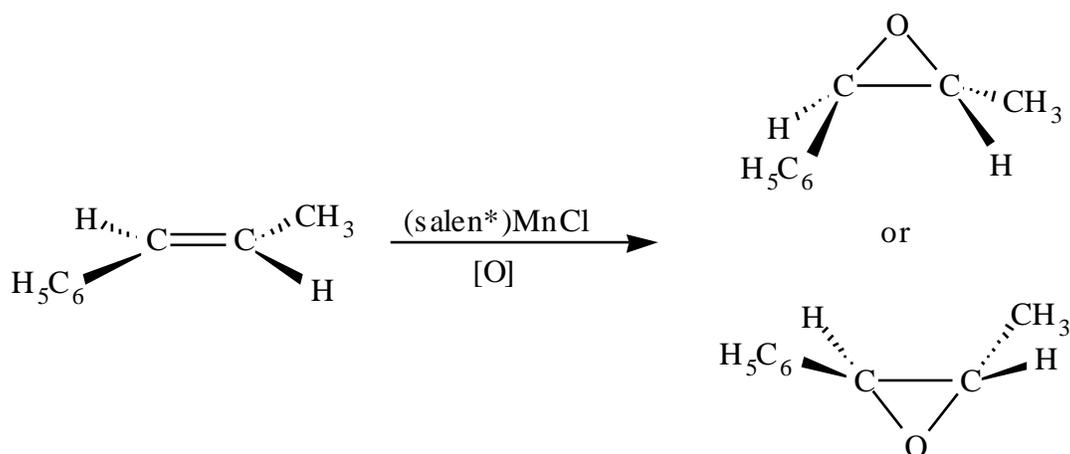


Traditionally, olefin epoxidations have been accomplished by a variety of peroxy-acids. Since the early 1980's, however, a number of very effective transition metal-based catalyst systems have been developed which have significantly extended the scope of these reactions by allowing *enantioselective* oxygen transfer to form asymmetric epoxides. The most prevalent of these systems has been the Sharpless oxidation of prochiral allylic alcohols (which uses *tert*-butyl hydroperoxide in the presence of titanium tetra(isopropoxide) and either (+)- or (-)- diethyl tartrate) to give asymmetric epoxides in high optical yields.

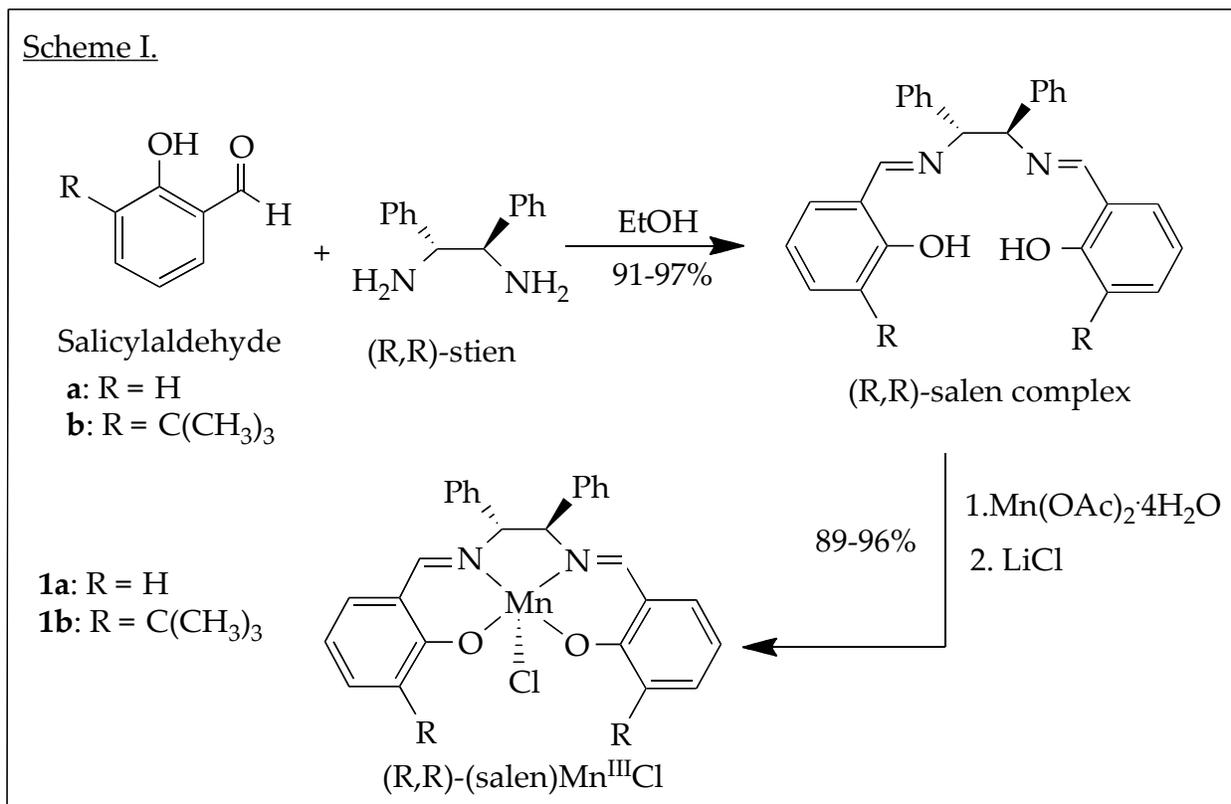


The high enantioselectivity of this reaction is attributed to precoordination of the alcohol function to the titanium center, which serves to orient the face of the incoming double bond. In 1990, the Harvard chemist, Eric Jacobsen published the first of several important papers on the enantioselective epoxidation of *unfunctionalized olefins* catalyzed by chiral manganese complexes. In this system the stereoselectivity relies solely on nonbonded interactions, thus lifting the requirement for a precoordinating pendant group. In fact, alkyl- and aryl-substituted olefins react with the highest enantioselectivity yet realized for nonenzymatic catalysts.

This experiment is based upon some early work by Jacobsen, who employed a chiral (salen) $\text{Mn}^{\text{III}}\text{Cl}$  catalyst to epoxidize *trans*- $\beta$ -methylstyrene.

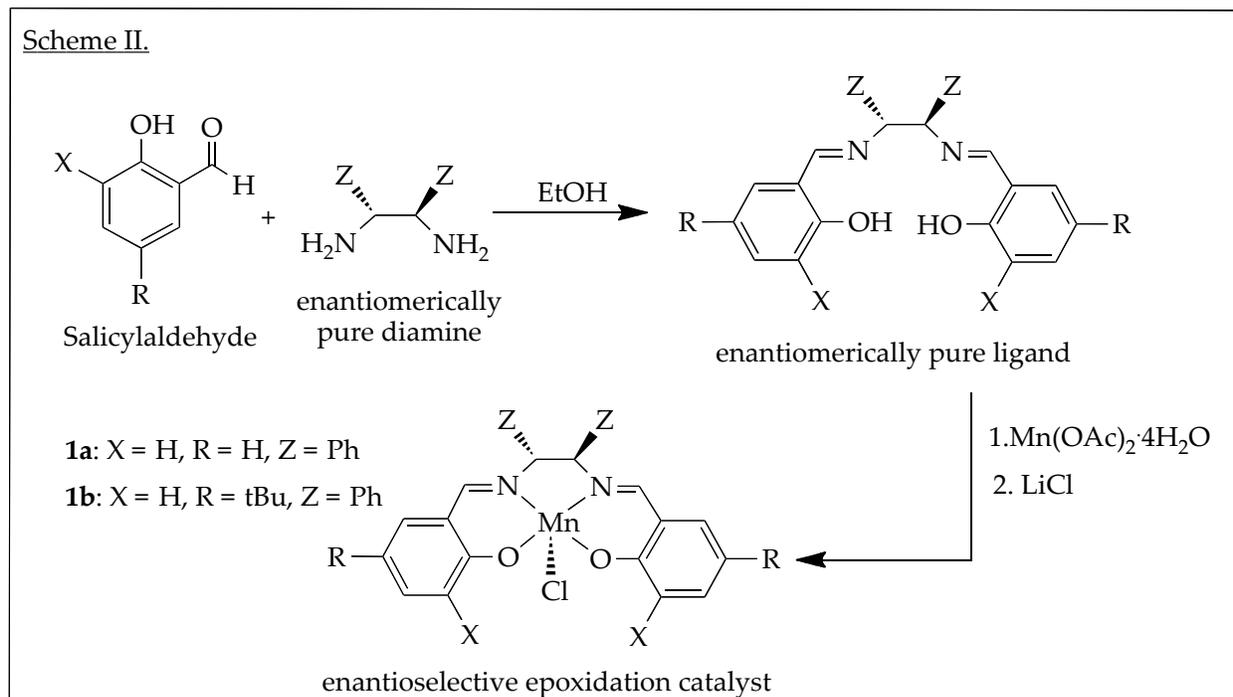


One of his original chiral salen ligands for the chiral manganese catalysts is prepared by treating the Schiff base of 5-methyl-3-*tert*-butylsalicylaldehyde with either (*R,R*)- or (*S,S*)-1,2-diamino-1,2-diphenylethane (sometimes abbreviated (*R,R*)- or (*S,S*)-stilbenediamine (stien) or (+)- or (-)-1,2-diphenylethylenediamine (DPEDA)). The second of these reagents has recently been made commercially available. The first is not readily available, and although it is required to realize high asymmetric induction in the epoxidation (see below), we will use commercial salicylaldehyde and 3-*tert*-butylsalicylaldehyde instead. The simplest catalyst, (*salen*\*)Mn<sup>III</sup>Cl, is then prepared in one step by reaction of the ligand with Mn<sup>II</sup>(OAc)<sub>2</sub>•4H<sub>2</sub>O in air (to oxidize Mn<sup>II</sup> to Mn<sup>III</sup>), followed by treatment of the solution with LiCl (Scheme I). The Mn<sup>III</sup>(*salen*) complexes are obtained in high yields, are thermally stable and can be stored as solids indefinitely without precautions to exclude light, air, or moisture. Although iodosylarenes have also been used, the epoxidation reactions are most conveniently carried out in undiluted, buffered commercial bleach solutions at pH 11.3. Enantioselectivities do not differ significantly in either case suggesting that both reactions have in common an oxo intermediate, *e.g.* (*salen*\*)ClMn<sup>V</sup>=O, as the active oxidizing agent (in contrast to Ni(*salen*) and Co(*salen*) catalyzed epoxidations in which free ClO• has been implicated).

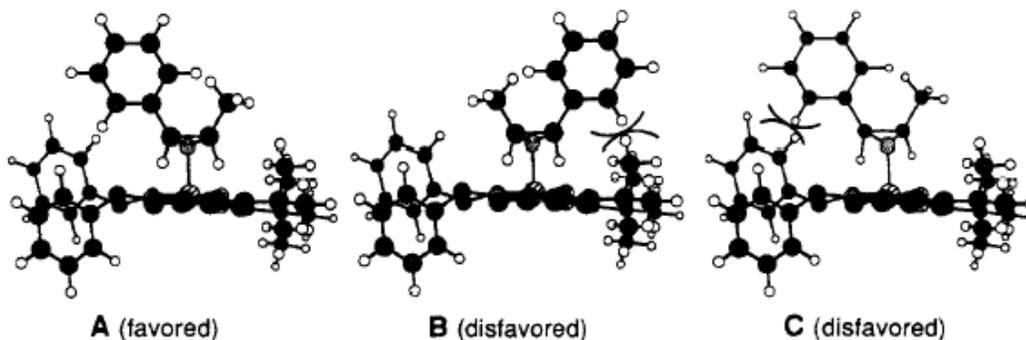


Some of the more effective epoxidation catalysts developed in Jacobsen's laboratories are shown in Scheme II. Note that the synthesis of each family of catalyst involves the coupling of a salicylaldehyde derivative to a diamine of known stereochemical configuration. Modifications to the steric and electronic environments at the metal center can be obtained by merely choosing an appropriately substituted salicylaldehyde during the ligand synthesis.

The observed epoxidation enantioselection for these catalysts can be explained by analyzing key steric interactions for side-on perpendicular approach of the olefin to the manganese oxo bonds of the implicated Mn<sup>V</sup> intermediates, as illustrated in structures **A-C** for the epoxidation of *cis*- $\beta$ -methylstyrene by the 3-*tert*-butylsalicylaldehyde salen derivative **1b** (Figure 1). The most favored approach is seen in structure **A** in which the olefin is approaching from above the page. In **B**, the side of approach is the same but the opposite enantioface of the olefin is presented resulting in unfavorable interaction of the more bulky (phenyl) substituent with the ligand *tert*-butyl groups.



In structure C approach is from behind the page as depicted resulting in unfavorable interactions imposed as a consequence of the asymmetry of the catalyst. Consistent with these arguments is that the highest ee's should be imparted to *cis*-olefins bearing one large and one small substituent.



**Figure 1.** The possible approaches of *cis*- $\beta$ -methylstyrene to the (salen)  $\text{Mn}^{\text{III}}\text{Cl}$  catalyst where the stein backbone is on the left and the *tert*-butyl groups are on the right.

For this project you will work in pairs to synthesize multiple variants of these chiral epoxidation catalysts to study the effects of catalyst structure on enantioselectivity in the reaction with two olefins. This project will be divided into two separate components: first, you will synthesize two different, pre-determined epoxidation catalysts and test their behavior in epoxidation reactions. Check with the TAs for the specific catalyst-substrate combination. Then, you will analyze the data from the first two

epoxidations of two substrates (data will be shared among all groups) and propose two new catalysts to be synthesized and studied with the goal of better understanding the effect of catalyst structure on reactivity. Each group will then synthesize and run epoxidation studies on one of the two newly proposed catalysts.

Each group will be assigned one of two different catalysts to synthesize (**1a** or **1b**, Scheme I). Within a group, one student will be responsible for the synthesis of both ligand and catalyst, while the other will carry out the subsequent epoxidation reaction and characterization of the product. You will share your results with all your labmates to compare the enantioselectivity of the two catalysts. A draft of your report including the analysis of your results from the first part of the project is due a week after finishing the first part. As part of this draft, each group will submit a short proposal describing a new epoxidation catalyst related to **1a** and **1b** to be studied in the second part of the project. For ease of comparison to the first two catalysts, you should only propose a single change per catalyst structure. You should peruse chemical supplier catalogs to identify commercially available precursors of interest, and discuss your proposal with the instructor and TAs. You will then proceed to synthesize your proposed catalyst and use in an epoxidation reaction. During this second part of the project, students will reverse their experimental work within each group compared to the first part, so that each student has a chance to work on each aspect of the experiment. You will share your results with the rest of the class. The final report for this experiment should include a discussion of data collected for all catalysts.

### 3.1 Experimental

The following catalyst preparation and epoxidation procedures are general and may be scaled to the amount of starting compounds supplied by the TA's. All solvents may be used without further purification. All reactions should be carried out in a fume hood.

#### 3.1.1 Synthesis of Ligands

*Time: 3 h*

##### Procedure:

Salicylaldehyde **a** or **b** (4.72 mmol, 2.0 equivalents, see Scheme I) is weighed directly into a 50 mL single neck RB flask. (*R,R*)-stien (500 mg, 2.36 mmol, 1.0 equivalent) is added followed by absolute ethanol (12 mL, to give a 0.2 M stien solution). The mixture is refluxed for 1 h (in air is O.K.) and allowed to cool to room temperature with continuous stirring. Water is then added dropwise to the stirred, cooled solution (occasionally product begins to crystallize prior to addition of water). The resulting yellow crystalline solid is collected by filtration and washed with a small portion of cold 95% ethanol. The yields of analytically pure salen ligand obtained in this manner are typically in the range of 91-97%. Acquire a <sup>1</sup>H-NMR of the product in deuterated chloroform.

### 3.1.2 Synthesis of Catalyst

Time: 3 h

#### Procedure:

The ligand is redissolved in hot absolute ethanol in a 100 mL RB flask to give a 0.1 molar solution. Solid  $\text{Mn}^{\text{II}}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  (2.0 equivalents) is added in one portion and the solution is refluxed for 1 h. Approximately 3 equivalents of solid LiCl are then added and the mixture is heated to reflux for an additional 0.5 h. The product is purified by evaporating the reaction mixture to dryness, redissolving the crude product in methylene chloride, and filtering to remove excess  $\text{Mn}^{\text{II}}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ . The solution is then concentrated on a hot plate while stirring. Cooling this mixture to  $0^\circ\text{C}$  affords the  $\text{Mn}^{\text{III}}(\text{salen})$  complex as dark brown needles isolated by filtration in ~75% yield. An additional crop of material can be obtained from the mother liquor. Acquire a  $^1\text{H-NMR}$  of this complex in  $\text{CDCl}_3$  and calculate the paramagnetic susceptibility  $\chi_p$  and number of unpaired electrons of this complex using Evans method.

### 3.1.3 Epoxidation

Time: 6 h

#### Procedure:

To 25.0 mL of undiluted household bleach in a 250 mL Erlenmeyer flask is added 10.0 mL of 0.05 M  $\text{Na}_2\text{HPO}_4$ . The pH of the resulting buffered solution (~0.55 M in NaOCl) is adjusted to pH = 11.3 by addition of a few drops of 2 M NaOH. To this solution is added a solution of catalyst (1.0 mmol) and *trans*- $\beta$ -methylstyrene or *cis*- $\beta$ -methylstyrene (1.18 g, 10 mmol) in 10 mL of  $\text{CH}_2\text{Cl}_2$ . The two-phase mixture is stirred at room temperature, and the progress of the reaction is monitored by TLC (20%  $\text{CH}_2\text{Cl}_2$ : 80% hexanes). After 3 hours, 100 mL of hexanes is added to the mixture, and the brown organic phase is separated, washed twice with 100 mL of saturated NaCl solution, and then dried ( $\text{Na}_2\text{SO}_4$ ). Filtration and solvent removal affords the crude epoxide.

#### Purification:

A flash chromatography column is wet packed with silica gel using 20%  $\text{CH}_2\text{Cl}_2$ : 80% hexanes (if you don't know how to run a column, talk to a TA). The crude epoxide is first eluted with 20%  $\text{CH}_2\text{Cl}_2$ : 80% hexanes (200 mL) followed by 30%  $\text{CH}_2\text{Cl}_2$ : 70% hexanes (200 mL) and finally with 40%  $\text{CH}_2\text{Cl}_2$ : 60% hexanes (*ca.* 300 mL). The fractions are collected in *ca.* 40 mL portions and evaluated by analytic TLC (20%  $\text{CH}_2\text{Cl}_2$ : 80% hexanes). The epoxide containing fractions are combined into a pre-weighed flask, and the solvent is removed by rotovap.

#### NMR Analysis:

The *ee* of the epoxide was determined by  $^1\text{H}$  NMR analysis in the presence of the NMR shift reagent *tris*-(3-heptafluorobutyl-*d*-camphorato)-europium(III),  $\text{Eu}(\text{hfc})_3$ . This is a paramagnetic complex that will shift the NMR signals of molecules that coordinate to it. Since  $\text{Eu}(\text{hfc})_3$  is chiral the signals of the two enantiomers of your epoxide will shift to a different degree. Run an NMR using 1-2 drops of your product in approximately 0.6 mL  $\text{CDCl}_3$ . Now add a few mg of  $\text{Eu}(\text{hfc})_3$  and rerun the spectrum. Notice how some of the signals have been shifted downfield. Continue adding  $\text{Eu}(\text{hfc})_3$  in small aliquots until the fastest moving signal has shifted by about 2 ppm. Be aware that  $\text{Eu}(\text{hfc})_3$  is expensive, so avoid using too much! You should now be able to resolve shoulders on the sides of your main peaks which correspond to the minor isomer. Expand the scale and carefully integrate the signals using the whole width of the paper. Using this information, approximate the % *ee* obtained in your epoxidation reaction.

Optional:

Carry out an epoxidation on another prochiral olefin which you think will be more or less suited to this catalytic system. Compare your results with those for *trans*- $\beta$ -methylstyrene and discuss the results in the context of the arguments above with regard to steric effects on enantioface selection. Are your results consistent with expectations based on these arguments?

### 3.2 References

1. Carruthers, W. *Some Modern Methods of Organic Synthesis*, 3<sup>rd</sup> Edition, Cambridge University Press, New York, NY, section 6.3: "Oxidation of Carbon-Carbon Double Bonds".
2. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Amer. Chem. Soc.* **1990**, *112*, 2801-2803, and references cited therein.
3. Larrow, J. L.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.*, **1994**, *59*, 1939-1942, and references cited therein.

# **Appendix I**

**Chapter 4 of Reserve Book III, D**

## **VACUUM LINE TECHNIQUES FOR HANDLING AIR-SENSITIVE ORGANOMETALLIC COMPOUNDS**

*Barbara J. Burger and John E. Bercaw*

Vacuum line techniques for handling air sensitive organometallic compounds are described. The vacuum line is discussed in six sections: (i) the pumps and main traps, (ii) the main manifold with pressure gauges, (iii) work stations, (iv) the cryogenic traps and Toepler pump, (v) the inert gas purifiers and inlet system, and (vi) the specialty gas inlet system. Use of a swivel frit assembly in the synthesis of air sensitive compounds is described along procedures for the addition of gases, volatile and nonvolatile liquids and solutions to reaction mixtures. High temperature and pressure reactions are discussed in terms of the use of sealed NMR tubes and heavy walled reaction vessels. The procedure for molecular weight determination using the Signer method is also included.

Our research group carries out preparative chemistry in fume hoods, on bench tops, in high pressure (Parr) reactors, in glove boxes, in Schlenk tubes, and with cannulas and septa, just as other groups concerned with the synthesis and characterization of air-sensitive organo-transition metal compounds. In this article we attempt to describe the less common methods, procedures and the equipment, *i.e.* those associated with a vacuum line, which have evolved over the past decades in the Bercaw group. Many of the techniques are taken from the literature and have been improved upon or modified for working with small amounts (50 mg - 35 g) of an organotransition metal compound. Others have evolved out of necessity, and, as far as we are aware, are not described elsewhere.

### **The Vacuum Line**

Most of the reaction chemistry that is done in our laboratory involves the use of vacuum lines (Figure 1). The use of a vacuum line offers two major advantages over more standard Schlenk techniques: hoses and rubber septa, which are more permeable to air and moisture, are completely excluded and quantitative manipulation of gases and volatile liquids can be performed conveniently. Although the construction of a vacuum line as complex as that shown involves a relatively large investment of time

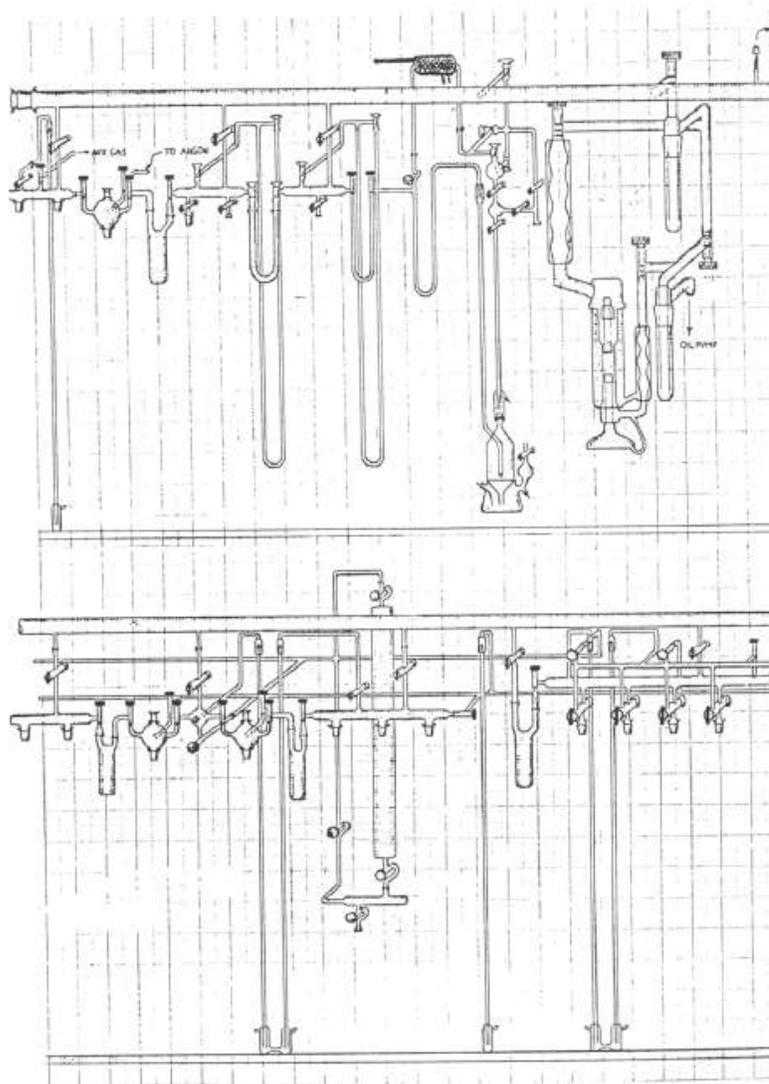


Figure 1. Diagram of a Bercaw group vacuum line (courtesy of Dr. Dean M. Roddick).

and money (*ca.* \$15,000 in parts and labor), it becomes a permanent piece of equipment which is shared by two or three group members and used extensively on a regular basis. Moreover, it is often faster to assemble a complicated apparatus on the vacuum line, rather than at a Schlenk line, since many of the required components are permanently in place.

The vacuum line consists of six main sections: (i) the pumps and main traps, (ii) the main manifold with pressure gauges, (iii) the work stations, (iv) the cryogenic traps and Toepler pump, (v) the inert gas purifiers and inlet system, and (vi) the specialty gas inlet system.

Each vacuum line is equipped with two pumps which operate in series. A mercury diffusion pump, together with a mechanical fore pump, provide a residual pressure of  $<10^{-4}$  torr, which is adequate for the syntheses that we undertake. Two traps cooled by large Dewars filled with liquid nitrogen are placed, one before and one after the diffusion pump to protect the pumps from condensables and the mechanical pump from mercury. The mechanical pump is exhausted to the hood. The residual pressure in the manifold is measured by the use of either a rotating McLeod gauge or a thermocouple gauge. The McLeod gauge provides the more accurate measurement of the residual pressure in the system, especially at pressures  $<10^{-3}$  torr.<sup>i</sup> Disadvantages with this gauge are that it needs to be regreased and cleaned regularly, and since it is slow, it is not as convenient when one is trying to locate a leak in the line. Although they periodically need to be recalibrated, the thermocouple gauges are relatively inexpensive and provide a continuous indication of residual pressures  $>10^{-3}$  torr.

The main manifold of the vacuum line is kept evacuated and isolated from the work stations on the line by stopcocks which are lightly greased with Apiezon N Grease. There are two types of work stations: a standard Schlenk line section, consisting of vacuum and inert gas manifolds connected by three way stopcocks to standard taper 24/40 inner joints, and a high vacuum work station for working with smaller quantities of material or for accessing the cryogenic traps and Toepler pump section. The two manifolds of the Schlenk line work station are equipped with mercury bubbler/manometers, which serve two general purposes: (i) to provide a rough measure<sup>ii</sup> of the amount of gas that is admitted to a manifold and (ii) to provide an exit when the pressure in the manifold is excessive. Gas is exited from the bubbler into tygon tubing affixed to a hood exhaust. A separate mechanical pump for the vacuum manifold of the Schlenk line work station is used for several of our lines, allowing two people to work simultaneously at the line without interfering with each other. The vacuum manifold is also connected (via a large stopcock) to the main manifold of the high vacuum line, so that access to high vacuum is still possible. Similarly, the inert gas manifold is connected (via a stopcock and manifold) to the specialty gas section of the main line. Large capacity, removable traps, affixed to the end of the vacuum manifold by means of O-ring joints, are used to collect the large volumes of solvent which are removed *in vacuo* from reaction mixtures. The standard taper 24/40 outlets may be fitted with butyl rubber tubing with an outer joint. Thus, the Schlenk line may be operated with its own rough pump in a conventional mode, or, when connected to the main vacuum and specialty gas system, more like the work station described below.

The high vacuum work station is the heart of the line. It consists of two main 24/40 standard taper inner joints connected via Teflon needle valves<sup>iii</sup> to (i) the high vacuum manifold, (ii) the inert gas manifold, (iii) the specialty gas manifold, (iv) each other, (v) manifolds leading to large volume, removable traps, (vi) outlets on these smaller manifolds for admitting gases from bulbs or lecture bottles

or solvents, reagents, *etc.* from flasks or calibrated volumes, and (vii) at the right to the cryogenic traps and Toepler pump system. The large number of connections provided to these ports presents a design problem, which we have solved by incorporating 100 mL flasks as connectors. Glass strain at the connections is thus relieved by spreading out the area of the glass seals. Moreover, the flasks serve as a splash guards and provide easy access for cleaning through their stoppered 14/20 standard taper outer joints at the top. The entire work station, as well as most of the other manifolds, Schlenk line, bubblers, *etc.* are interconnected and connected to the line *via* O-ring joints for easy removal when cleaning.

The cryogenic trap section of the line consists of one more large capacity, removable trap, and three U traps leading to the inlet of the Toepler pump. These traps can be used to separate volatile materials on the basis of differing vapor pressures, as is performed routinely for boranes, phosphines, *etc.* on lines similar in design to this section of the vacuum system. Normally, we use these traps to assure complete removal of solvent and other liquid nitrogen condensable compounds from noncondensables such as CO, H<sub>2</sub>, CH<sub>4</sub> and N<sub>2</sub>, which are quantitatively collected by the Toepler pump. Needle valves are used to allow only small pressures of gas to flow into the Toepler pump, in order to prevent damage from a "mercury hammer"<sup>iv</sup>. The pressure is indicated by manometers at one or two points along the manifolds connecting the traps. These manometers are also useful in measuring out known amounts of reagents or gases into calibrated bulbs, which may be attached to outlets along the manifolds. The Toepler section consists of the pump, several precalibrated volumes separated by 2-way, oblique bore stopcocks, an outlet for attaching a gas infrared cell, mass spectrometry sample bulbs, *etc.*, a stopcock to the main high vacuum manifold, and a recirculating manifold<sup>v</sup>, a section of which is packed with CuO that may be heated to 320°C (*vide infra*). The CuO section of the tube is wrapped, along with a glass tube to hold a 360°C thermometer, with heating tape which is connected to a Variac transformer, then encased in thermal insulating material. The inlet tube of the Toepler pump and the first, tubular calibrated volume of the pump are positioned parallel to each other so that a section of meter stick may be taped into place. Thus, when the Hg level is allowed to rise to a mark above the top valve assembly, the inlet tube functions as the Hg column of a manometer for reading the pressure in the calibrated volumes.<sup>vi</sup> The Toepler pump cycle is automated by using the mercury as a switch alternately connecting the common lead to the top lead (which activates the solenoid valve to open the lower chamber to a mechanical pump) and the lower lead (which activates the solenoid valve to open the lower chamber to a slow, filtered air lead. The Toepler pump control box is assembled at Caltech and is comprised of a 6.3 V transformer (e.g. Triad F 14X), a relay (e.g. PB KRP11AG), a thermal delay relay (e.g. 6N02), a 2 ohm 10 W resistor, five female AC plugs, chassis mount (for the mechanical pumps, diffusion pump heater, CuO tube heater, *etc.*), five tineon lamps, 125 V, 0.3 W, five SPST 10 A power switches, a fuse holder, an amphenol 5 pin

hex chassis mount female connector (to receive male connector with wires from alligator clips attached to leads on Toepler pump), a 6 foot power cord, 3 wire, number 16 or larger, and two 4 pin terminal strips all contained in an aluminum chassis with cover plate (3X5X10).<sup>vii</sup>

The two working inert gases, dinitrogen and argon, are taken from 1A cylinders through regulators, copper tubing and metal to glass seals and passed through purifiers before they enter the vacuum line. Two large capacity columns (Figure 2), one filled with MnO supported on vermiculite<sup>viii</sup>, the other with 4Å molecular sieves, remove dioxygen and water, respectively. Periodically (approximately annually) the oxidized MnO (of empirical formula  $Mn_3O_4$ ) needs to be reduced. Reduction is accomplished conveniently by passing dihydrogen (hood exhaust) through the column while heating to 300-350°C. The column filled with molecular sieves is normally regenerated at the same time by passing dinitrogen at approximately 250°C. The columns may be heated using commercially available heating tape, or by wrapping the inner column with nichrome wire. Strips of asbestos tape on the sides, one next to the glass column, the other over the nichrome wire are essential to hold the wire in place. The asbestos tape is wetted to adhere it to the column and wire. The resistance of the wire is chosen to maximize the power at 120 V and 5 A, the maximum settings for a standard Variac transformer. The glass outer jacket of the column reduces the cooling effects of drafts. Wrapping the outer jacket with aluminum foil<sup>ix</sup> during this process further increases the heating efficiency. The normal working inert gas, Ar, is transferred through glass tubing to the Ar manifold of the two working stations. A mercury bubbler is connected to this manifold and the Hg level and regulator set to maintain *ca.* +50 torr Ar pressure without continual bubbling. The dinitrogen is usually transferred through glass tubing to the specialty gas manifold described below. N<sub>2</sub> is the inert gas of choice when working with an apparatus cooled near liquid nitrogen temperature<sup>x</sup>.

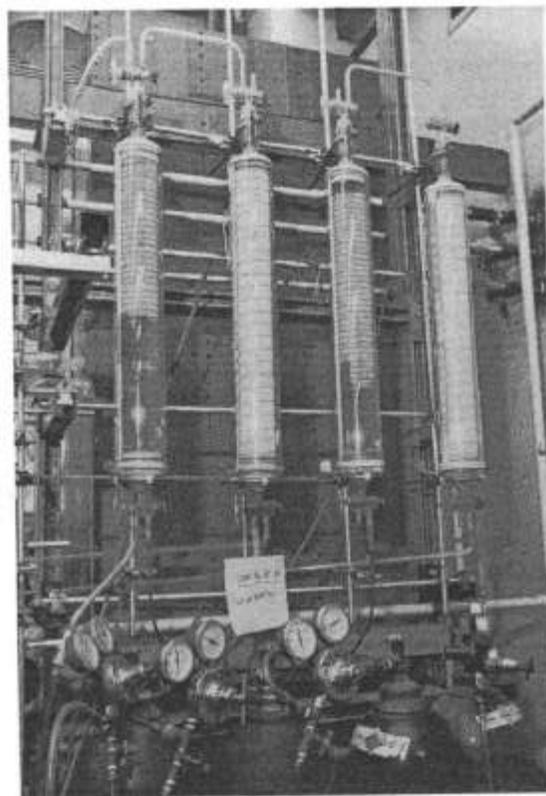


Figure 2. Inert Gas Purification Columns

A smaller, all-in-one column, filled with MnO/vermiculite (lower half) and molecular sieves (upper half) is used for purifying specialty gases such as dihydrogen, dideuterium, and carbon monoxide<sup>xi</sup>. This apparatus is attached to the vacuum line near the inert gas manifold, as shown in Figure 1. It is a good working practice to leave the column filled with the last specialty gas used, with a label indicating the column contents. Replacing the gas by evacuating the column packed with vermiculite and molecular sieves is quite time consuming.

### Solvent Pots and Their Use

When using a vacuum line, solvents are introduced by vacuum transferring from a solvent pot into the reaction flask. To prepare a solvent pot, the solvent is rigorously dried by refluxing over an appropriate drying agent in a solvent still. Drying agents such as "titanocene"<sup>xii</sup> or sodium and benzophenone (for preparation of Na/benzophenone-ketyl) and a stir bar are added to a large round bottomed flask (~ 500 mL). The flask is then attached to a 180° needle valve adapter, which consists of a

24/40 standard taper inner joint, straight needle valve and 24/40 standard taper outer joint as shown in Figure 3. With exclusion of air, solvent is transferred from the solvent still to the solvent pot (transfer is facilitated greatly by evacuating the solvent pot first<sup>xiii</sup>). The solvent pot is then degassed by attaching to the high vacuum line and, while stirring at room temperature, pumping on the solvent through a  $-196^{\circ}\text{C}$  trap for a couple of minutes. To transfer solvent from the pot into a reaction flask, the entire assembly interconnecting the two is completely evacuated. Cooling the reaction flask with either a dry ice/ethanol bath ( $-78^{\circ}\text{C}$ ) or with liquid nitrogen ( $-196^{\circ}\text{C}$ ) and slowly opening the needle valve of the solvent pot while stirring magnetically causes solvent to transfer into the flask. The rate of transfer will depend on: (i) the vapor pressure of the solvent, (ii) the residual pressure in the manifold and the temperature of the solvent pot. Keeping a room temperature<sup>xiv</sup> water bath under the solvent pot will facilitate the transfer.

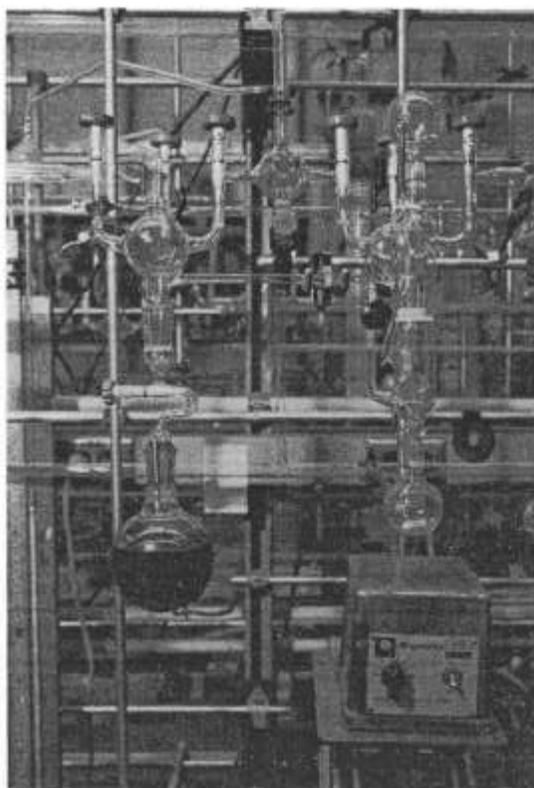


Figure 3. Vacuum Line Work Station

### Swivel Frit Assemblies and Their Use

Preparative synthesis on a vacuum line is carried out primarily using a swivel frit assembly. Although they may be constructed in virtually any size, a typical frit assembly has 14/20 standard taper joints and can accommodate up to approximately 10-15 grams of solid. A diagram of an apparatus of

moderate size is shown below in Figure 4. A quick opening Teflon valve or a stopcock is centered in the pressure-equalizing side arm, to isolate one side of the frit from the other. An adapter consisting of a 14/20 standard taper inner joint, right angle Teflon needle valve and 24/40 standard taper outer joint, is used to attach the assembly to a port of the working section of the vacuum line.

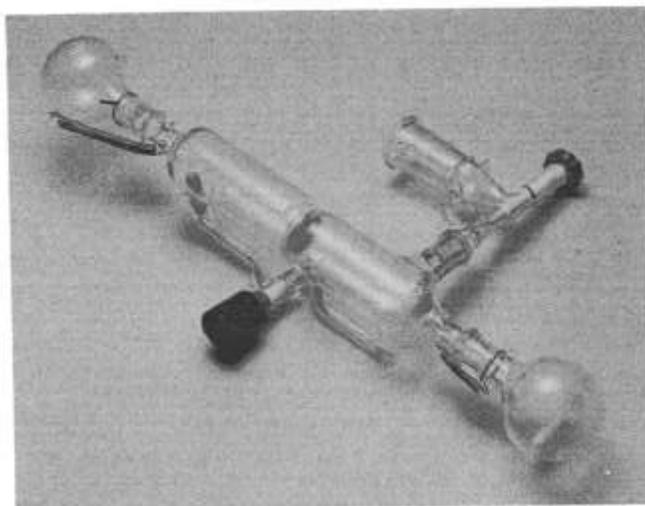


Figure 4. A Standard Frit Assembly

In a typical experiment, one of the round bottomed flasks is charged with solid reagents (these are loaded in the inert atmosphere glove box if they are air sensitive), and a magnetic stir bar is placed in both flasks. The joints of the frit and the needle valve are greased lightly with Apiezon H grease<sup>xv</sup> and are secured with springs or rubber bands. With the Teflon needle valve tightly closed, the assembly is removed from the glove box and attached to the vacuum line at one of the ports of a working station *via* 24/40 standard taper joint, lightly greased with M or H grease. The system is evacuated, first up to the Teflon needle valve of the adapter, then including the entire frit assembly. An appropriate solvent is then transferred into the reaction flask following the procedure described above.

#### **Adding Reagents to the Reaction Flask of the Swivel Frit Assembly**

**Condensable Gases.** To add a desired quantity of a condensable gas, a gas bulb of known volume is normally used. The working section, gas bulb and connection to the gas supply, manometer<sup>xvi</sup> and frit assembly are all evacuated. If the frit assembly contains solvents or volatile materials, the lower flask is cooled to  $-78^{\circ}\text{C}$  or  $-196^{\circ}\text{C}$  before evacuation. The frit assembly is then isolated from the ensuing procedures by closing the needle valve of the adapter. Gas is admitted to the desired pressure calculated

using the simplified expression of footnote 6. The stopcock of the calibrated bulb is closed and the gas remaining in the manometer and the rest of the working section is removed by evacuation by condensing it back into its storage bulb or evacuating the system through a removable trap<sup>xvii</sup>. The working section is then isolated from the vacuum manifold by closing the stopcock to the main manifold, and the gas in the bulb is condensed into the reaction flask by cooling to  $-196^{\circ}\text{C}$ . If the gaseous reagent has been purified by freeze-pump-thaw cycles prior to use and is stored in a  $-196^{\circ}\text{C}$  trap, the desired quantity of gas can be admitted into the manifold and calibrated gas bulb by removing the liquid nitrogen coolant and slowly warming to room temperature until the desired quantity has been admitted to the manifold. The need for a calibrated gas volume can be eliminated by determining the volume of the manifold and using it as the calibrated gas volume, although a manometer correction must then be applied to account for the increase in volume with increase in pressure.

***Volatile Liquids.*** Volatile liquids can be added to a reaction flask of a frit assembly by either of two methods, depending on the quantity of liquid being added and its vapor pressure at room temperature. The first method is analogous to that used for gaseous reagents, and thus is suited to small amounts of very volatile compounds. The liquid to be added is rigorously dried, degassed and stored (in vacuo) in a solvent container such as a round bottomed flask with adapter consisting of a standard taper inner joint,  $180^{\circ}$  Teflon needle valve and 24/40 standard taper outer joint. The liquid is then admitted into a calibrated gas bulb and condensed into the frit assembly as described above for a gaseous reagent. For larger amounts of liquids, a graduated volume<sup>xviii</sup> attached to an adapter consisting of a standard taper inner joint,  $180^{\circ}$  Teflon needle valve and 24/40 standard taper outer joint is useful (Figure 5). The desired amount of liquid is vacuum transferred into the graduated volume. Once this is accomplished and the manifold is evacuated (either by condensing any residual vapor back into the solvent container or into a  $-196^{\circ}$  trap), the liquid is then vacuum transferred into the reaction flask of the frit assembly.

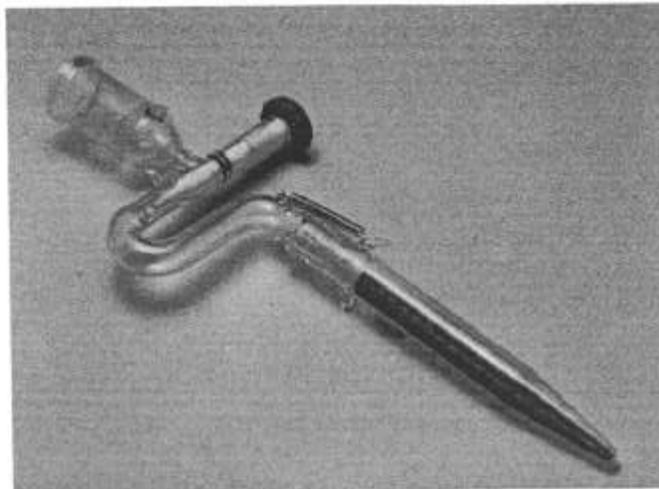


Figure 5. Graduated Volume for Adding Liquids

For storing liquids which are low boiling (just above room temperature) or which are not compatible with Apiezon greases, a solvent container such as that shown in Figure 6 is convenient to use. This container is similar in design to that described later in the section on thick-walled reaction vessels except that it is constructed from standard wall thickness glass tubing. The liquid to be stored is first purified by the appropriate means and then vacuum transferred into the container for storage under vacuum.



Figure 6. Solvent Container

***Solutions and Non-Volatile Liquids.*** In many instances, it is desirable to add a solution (such as a commercially available solution of a Grignard or alkyl-lithium reagent) or a non-volatile liquid such as

dimethylphenylphosphine to a reaction flask. This addition to the reaction flask of the swivel frit assembly can be accomplished in the following manner: under an argon counterflow, the Teflon plug from the right angle Teflon needle valve of the adapter<sup>xix</sup> is removed. A syringe attached to a length of polyethylene tubing (approximately six inches in length) is inserted into the needle valve and degassed by drawing argon through the syringe several times. Filled with argon, the syringe is disconnected from the tubing. The syringe is inserted into the reagent container (usually stored under an inert atmosphere and capped with a sure-seal top or a septum) and the desired volume drawn out. The syringe is then reattached to the tubing and the solution syringed into the reaction mixture. The Teflon plug is then fit back into the adapter, leaving the reaction vessel open to the mercury bubbler/manometer. This same technique can be used for non-volatile liquids, which have been previously degassed and are stored under an inert atmosphere.

### **Filtering Using a Swivel Frit**

When working up a reaction mixture, an unwanted solid (salt, *etc.*) often needs to be removed from a solution of the desired product. Alternatively, the product of a reaction might be insoluble directly from the reaction mixture. In either case, a filtration is required. There are two general ways in which to do this; both rely on differences in pressures to drive the filtering process. The first method is especially convenient when filtering a hot solution. The entire frit assembly is filled with argon. Prior to filtration, the valve of the side arm is closed and the assembly is inverted. A slight vacuum is pulled on the bottom flask causing the solution to pass through the frit. When a cold solution is to be filtered, a different approach is taken. The entire frit assembly is cooled by "swabbing" the outside with a dry ice/ethanol slush<sup>xx</sup>. Inverting the frit assembly with the stopcock along the side arm closed and admitting a partial atmosphere of argon into the top half of the frit assembly will facilitate the process. A little forethought when assembling the frit, flasks and needle valve adapter (*i.e.* which side to put the needle valve adapter on) will save time later.

### **Washing a Solid on a Frit**

To wash a solid which has been collected on a frit, the flask containing the wash solvent (the filtrate in the receiving flask or fresh solvent from a solvent pot attached at a nearby port of the working section) is cooled with a dry ice/ethanol slush bath and then degassed. After closing the valve of the sidearm along the side of the frit assembly, the slush bath is replaced with a warm water bath and the top flask is cooled by "swabbing" with slush. Condensation of the wash solvent occurs on the upper half of the frit and upper flask the percolator action of the solvent effectively washes the solid. The resultant

solution is forced back into the bottom flask by replacing the warm water bath with a slush bath. The valve of the side arm should be closed during this process.

### Procedures for Carrying Out Reactions in an NMR Tube

We routinely use high field NMR spectrometry to screen reactions, to characterize compounds and to measure reaction kinetics. By working in a sealed NMR tube it is possible carry out reactions involving very air sensitive materials an volatile reagents, as well as those which require conditions of high temperature or moderate pressure (0 - *ca.* 3 atm). The procedure for assembling the reagents for a reaction in a sealed NMR tube is described below for the reaction of  $(C_5Me_5)_2ScCH_3$  with 2-butyne. In the inert atmosphere glove box, an NMR tube<sup>xxi</sup> fused to a small diameter standard wall Pyrex tube and then to a 14/20 standard taper outer joint is charged with a known amount of the solid starting material. The NMR tube is then attached to a calibrated gas volume such as the one shown in Figure 7. Deuterated solvent (approximately 0.5 mL) is added either in the glove box or by vacuum transferring from a NMR solvent pot on the vacuum line. The NMR tube is then evacuated while cooling at  $-78^\circ C$ , and the stopcock separating the NMR tube from the calibrated volume above is closed. 2-butyne (which has been dried over 4 Å molecular sieves) is freeze-pump-thawed on the vacuum line, and a specified pressure is admitted to the manifold and gas volume above the NMR tube. Residual 2-butyne is returned to the storage to its storage container by cooling. The known amount of 2-butyne in the gas volume is then condensed into the NMR tube ( $-196^\circ C$ ). The tube is now sealed with a cool flame of a glass blowing torch while maintaining cooling ( $-196^\circ C$ ) of the lower half of the tube. Sealed NMR tubes should be allowed to warm behind proper shielding in a fume hood, since condensed  $O_2$  or excess pressure can lead to an explosion. If the tube is to be heated in the NMR probe, pre-testing of the tube strength by heating briefly at least  $20^\circ C$  higher temperature than the probe is highly recommended. If volatiles are condensed into an NMR tube which exhibit greater than one atmosphere vapor pressure at the temperature of the probe, a preliminary calculation should be done to determine what the actual pressure inside the NMR tube will be during the experiment. For pressures approaching or greater than five atmospheres, use of medium walled or thick walled NMR tubes is recommended.

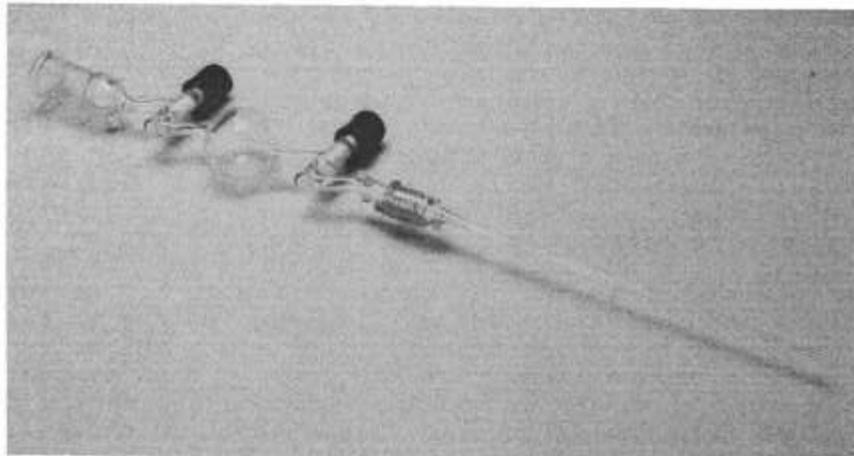


Figure 7. NMR Tube Attached to a Gas Volume

### **Thick Walled Reaction Vessels.**

Many of our reactions are carried out at high temperatures and/or moderate pressures (1-7 atm). A convenient way to do this type of reaction is to use a thick-walled reaction vessel, shown in Figure 8. Solid starting materials are added in the inert atmosphere glove box; solvents and gases are added on the vacuum line as described above. The glass vessel can then be heated in an oil bath for the appropriate length of time.

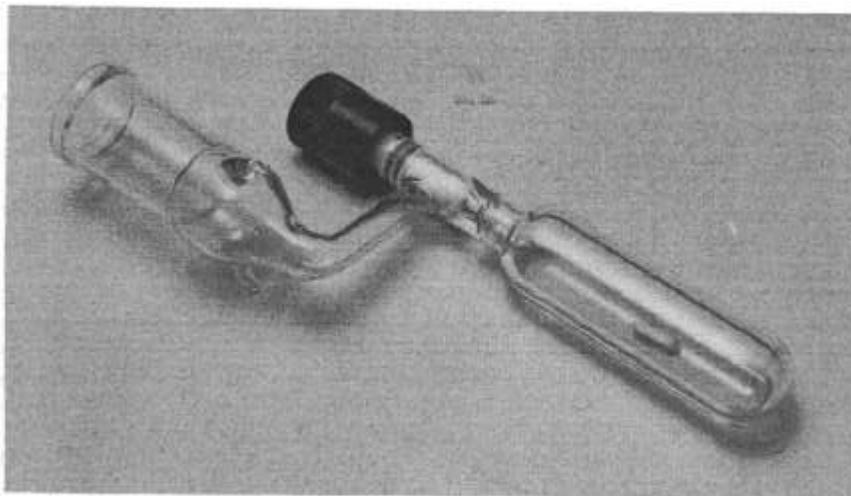


Figure 8. Thick Walled Reaction Vessel

Once the reaction is completed, excess pressure is released, for example by cooling the vessel and carefully venting it through a trap cooled at  $-196^{\circ}\text{C}$ . The solution is transferred to a swivel frit assembly for work up, using either an inert atmosphere glove box or a syringe attached to polyethylene tubing,

following the procedure described above for adding solutions to the swivel frit assembly. The second method is much quicker and is suited to solutions of thermally sensitive, moderately air sensitive compounds.

### Use of a Toepler Pump

To quantify the amount of a non condensable gas liberated during a reaction, a Toepler pump is employed. The basic operating principle of a Toepler Pump is the use of a mercury piston which is pushed up the upper cylinder by atmospheric pressure admitted to the lower chamber, and allowed to fall as the lower cylinder is evacuated. These procedures are alternated by the relay/control mechanism described earlier, and the gas collected on each cycle is trapped by a one way, float valve in the upper calibrated volumes. Our pumps use a simple stainless steel ball bearing seated into a spherically ground portion of the valve. Toepler pumps of several different designs are commercially available; ours are of a hybrid design and are constructed in the Caltech glass shop. If the volume of the upper cylinder is 500 mL and the volume being pumped (the cryogenic traps, manometers, manifolds etc. back to the reaction flask is 1500 mL, 75% of the residual gas of the sample being collected will be left behind on each cycle. Thus, many cycles will be needed to reduce the amount of residual gas to a negligible value ( $((0.75)^n \rightarrow 0$ , where  $n$  is the number of Toepler pump cycles). An indication of the amount of residual gas is provided by the size of the bubble formed when the mercury approaches the upper valve. The pressure in the calibrated volume should be measured occasionally (by allowing the Hg level to rise to the mark above the valve). When no difference is detected from reading to reading, gas collection may be stopped.

To separate (hot CuO) combustible gases<sup>xxi</sup> from non combustibles, the sample is first collected and the total amount of gas is measured. The stopcock leading back to the cryoscopic traps is closed, the stopcocks opening the pathway around the recirculating manifold section are opened. The Teflon needle valve leading back to the last trap is opened only slightly so that excessive pressures of gas are prevented from building up at the inlet of the Toepler pump. The gas mixture is now circulated by the Toepler pump through the heated CuO section (320°C), the trap cooled to -196°C and back into the calibrated section, etc. until all H<sub>2</sub> is oxidized to H<sub>2</sub>O and CO is oxidized to CO<sub>2</sub>, both of which are trapped out at -196°C. By closing the stopcock immediately above the last section of the calibrated volume, the residual, non combustible gas (N<sub>2</sub> and/or CH<sub>4</sub>) may be collected and its pressure determined. By periodically repeating these procedures it can be determined if more cycles through the CuO tube are required. The residual gas is measured and analyzed by infrared spectroscopy, gas chromatography or mass spectrometry by withdrawing a sample into a gas cell or gas sample bulb attached to the port at the top of the Toepler pump section of the vacuum line. The residual N<sub>2</sub>/CH<sub>4</sub> is pumped out of the

calibrated volumes. The trap at  $-196^{\circ}\text{C}$  is warmed to  $-78^{\circ}\text{C}$  by replacing the liquid nitrogen with a dry ice/ethanol in the dewar surrounding it, and the  $\text{CO}_2$  is now collected by the Toepler pump. The amount of  $\text{CO}_2$  is, of course, the same as the amount of  $\text{CO}$  in the original sample. The difference is the amount of  $\text{H}_2$ , now as  $\text{H}_2\text{O}$  in the  $-78^{\circ}\text{C}$  trap, in the original sample. Thus, by applying Dalton's Law of Partial Pressures, one can easily quantitatively determine the composition of  $\text{H}_2/\text{CH}_4$ ,  $\text{H}_2/\text{N}_2$ ,  $\text{CO}/\text{CH}_4$ ,  $\text{CO}/\text{N}_2$ ,  $\text{CO}/\text{H}_2$ ,  $\text{CO}/\text{H}_2/\text{CH}_4$ , and  $\text{CO}/\text{H}_2/\text{N}_2$  binary and tertiary mixtures, and if coupled with mass spectrometry to quantify the proportions of methane in  $\text{N}_2$ ,  $\text{CO}/\text{H}_2/\text{CH}_4/\text{N}_2$  quaternary gas mixtures.

### **Molecular Weight Determination for Non-Volatile Organometallic Compounds**

Of all the methods that are available for determining the molecular weight of an organometallic compound, the most straightforward is undoubtedly that developed by Signer<sup>xxiii</sup>. This method is based on the simple idea that the vapor pressure of an ideal solution is proportional to the concentration of the solute (Raoult's Law). The major advantages of this technique is that it does not require any sophisticated equipment, only about 0.05 g of the unknown compound are needed and it can be suited to extremely air sensitive compounds with the adaptations described below. The limitations of this method are that the sample must be stable in solution at room temperature for 3-7 days and the accuracy of this method is  $\pm 10\%$  at best. The molecular weight apparatus consists of two graduated capillary tubes (approximately 10 mL in volume, constructed from sections of a Mohr pipette) each sealed to a round bulb. The two bulbs are connected to a short glass tube with solvent seal connectors. In the middle of the glass tube, there is a stopcock through which the entire assembly can be evacuated. A diagram of the apparatus is shown in Figure 9. The procedure for determining the molecular weight of an unknown air sensitive compound is outlined below.

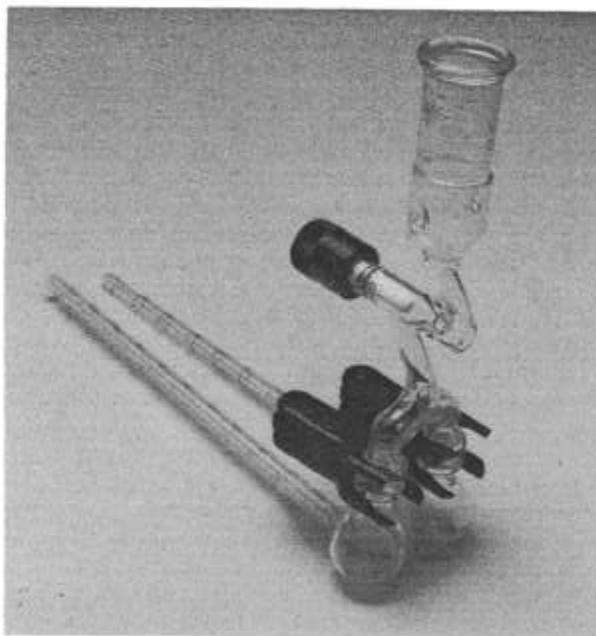


Figure 9. Molecular Weight Determination Apparatus

In the glove box, 0.010-0.015 g of the standard (azobenzene or ferrocene are good choices) is carefully weighed out ( $\pm .1$  mg) and placed in one bulb. Similarly, an amount of the unknown is accurately weighed out and placed in the other bulb. A solvent which is very inert toward the sample (benzene, cyclohexane, tetrahydrofuran) is added (ca. 0.5-0.8 mL) to each bulb and the apparatus is assembled. The bulbs are cooled to  $-78^{\circ}\text{C}$ , and the apparatus is evacuated on the vacuum line. The assembly is then allowed to come to room temperature and placed (with the solvent in the bulbs) in a location free from drafts, away from direct sunlight or room light (a cardboard box or large pot work nicely). The volume change should be periodically monitored by tilting the assembly so that the solutions flow into the volumetric portions of the apparatus. The volume of each solution will change by transfer of solvent vapor until the vapor pressures of the two solution equilibrate, usually requiring 3-7 days. The experimental molecular weight is determined by the following relationship:

$$MW_x = \frac{(mg_x)(MW_s)(ml_s)}{(mg_s)(ml_x)}$$

where  $mg_x$  = weight of unknown in mg  
 $mg_s$  = weight of standard in mg  
 $MW_x$  = molecular weight of unknown

$MW_S$  = molecular weight of standard

$mL_X$  = volume of standard solution

$mL_S$  = volume of unknown solution

**Acknowledgments.** The authors wish to thank members of the Bercaw group, past and present, who have contributed to the development of the procedures and equipment described in this chapter. JEB wishes to thank Professor Hans H. Brintzinger (presently at the University of Konstanz, West Germany) for inspiring many of the original concepts when the two of us were at the University of Michigan.

- 
- i. Because it operates with a Hg column, the McLeod gauge does not read the partial pressure of mercury (*ca.*  $10^{-3}$  torr) which continually fills those portions exposed to liquid Hg.
  - ii. The accurate measurement of pressure requires use of a manometer. The bubbler is less accurate since the level of the pool of mercury at the base varies slightly as the column height varies.
  - iii. Our group has invested heavily in Fischer Porter brand 4 mm needle valves. These provide fine control when they are opened, and are thus preferable for those sections of the system where control is needed, for example, for solvent removal and at the points of entry to the cryogenic trap and Toepler section. In recent years less expensive, but equally effective Teflon needle valves have become available.
  - iv. The base of the Toepler pump and the bases of the mercury bubblers should be placed in plastic cups and secured with plaster of Paris to a depth of 3 or 4 inches. Thus, mercury spillage is avoided is the glass base is broken.
  - v. The pathway of this recirculating section should have as little volume as possible out of the circuit, since gases must flow freely to prevent them from "hiding in corners" from the reactive CuO.
  - vi. A simplified ideal gas formula is used to calculate the mmols of gas in the volumes:  $n$  (mmols) =  $p$  (torr). $V$  (mL)/ $1.85 \times 10^4$  at 23.5°C.
  - vii. The circuit diagram is available on request.

- 
- viii. Brown, T. L.; Dickerhoof, D. W.; Bafus, D. A.; Morgan, G. L. *Rev. Sci. Instruments* **1962**, 33, 491-492.
- ix. Care should be taken not to allow the aluminum foil to contact the electrical leads!
- x. Since Ar has only *ca.* 100 torr of vapor pressure at liquid nitrogen temperature, a dangerous buildup of liquid Ar will occur if the pressure of Ar exceeds this value while a trap, flask, NMR tube, etc. is being cooled with liquid nitrogen. Similarly care must be taken to not allow the pressure to exceed one atmosphere when cooling a part of the line with N<sub>2</sub> as the inert gas
- xi. The purity of commercially available carbon monoxide (e.g. Matheson) is normally sufficient for our experiments.
- xii. Marvich, R. H.; Brintzinger, H. H. *J. Amer. Chem. Soc.*, **1971**, 93, 2046-2048.
- xiii. For solvent pots of greater than 500 mL in volume, it is recommended that they be taped or otherwise treated to prevent flying glass should the flask implode. This advisory note applies whenever large glassware is evacuated.
- xiv. Heating the solvent pot above room temperature will only slightly increase the rate of transfer, and has the undesirable effect of causing solvent condensation along the path of the transfer.
- xv. Thicker Apiezon H grease is used to compensate for the poorer fit of standard taper joints and to reduce the amount of solvent wash out. The joints are greased only along the top half of the ground glass section to minimize contamination from grease; however, we have never noted deleterious effects of Apiezon greases on our compounds.
- xvi. If the high vacuum working station is used the bubbler/manometer may be accurately used as a manometer since the pools of Hg are interconnected (see Figure 1).
- xvii. If a very reactive, noxious or poisonous reagent is used, the residual reagent should be trapped out into one of the removable traps, and the reagent should be carefully transferred to the fume hood where it is allowed to warm slowly.

- 
- xviii. A section of a Mohr pipette or graduated centrifuge tube sealed to a 14/20 standard taper outer joint have proven to be quite satisfactory.
- xix. Caution: the reaction flask may be cooled only to  $-78^{\circ}\text{C}$ ; cooling to liquid nitrogen temperature will lead to dangerous buildup of liquid Ar. If the reaction flask must be cooled to liquid nitrogen temperature,  $\text{N}_2$  should be used as the inert gas and great care must be exercised to avoid condensation of liquid nitrogen.
- xx. Care should be taken to avoid cooling the Teflon valves. The much different coefficients of thermal expansion for Teflon and glass results in leakage when the valve is cooled much below room temperature.
- xxi. We have found that Wilmad (507 pp) NMR tubes provide adequate resolution for routine high field NMR spectra.
- xxii. Care should be taken to avoid  $\text{O}_2$ , even in small amounts, as a component of these gas mixtures. An explosive mixture with  $\text{H}_2$ ,  $\text{CO}$  or  $\text{CH}_4$  could easily be produced and detonated by sparks at the electrodes of the relay or on contact with the hot  $\text{CuO}$ .
- xxiii. E.P. Clark, *Ind. Eng. Chem., Anal. Ed.* **1941**, 13, 820.