

# Expt 4: Synthesis of Adipic Acid via Oxidative Cleavage of Cyclohexene

## INTRODUCTION

In CHEM 331, you learned several different ways in which alkenes can be oxidized. For example, epoxidation, dihydroxylation and ozonolysis or oxidative cleavage using potassium permanganate ( $\text{KMnO}_4$ ) of alkenes can all be achieved with the proper choice of reagents. All of these transformations involve electrophilic additions to the electron-rich pi bond of the alkene, which serves as a nucleophile. However, only in the case of ozonolysis is the carbon-carbon sigma bond also cleaved. The type of carbonyl compounds would then be dependent upon the substitution of the alkene and the type of oxidant used. If the cleavage product is a ketone, the oxidation process is generally complete but if the cleavage product is an aldehyde, it may be further oxidized to form a carboxylic acid functional group.

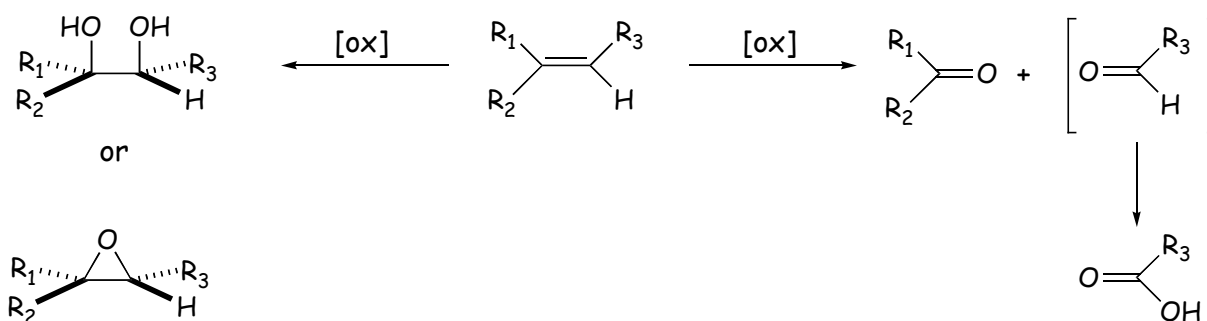


Figure 1: Oxidations of Alkenes

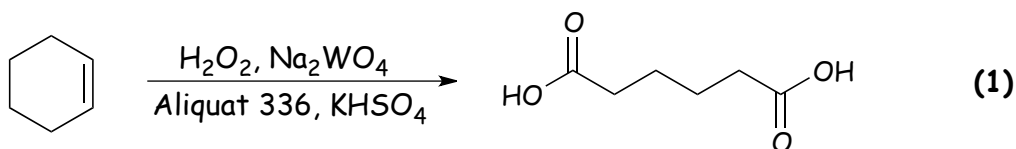
The oxidative cleavage of alkenes is generally believed to proceed through an initial oxidation of the pi bond to form a 1,2 diol (a "glycol"). Continued oxidation of the 1,2-diol then results in cleavage of the carbon-carbon sigma bond. Although ozonolysis is a reliable and highly useful synthetic transformation, working with ozone ( $\text{O}_3$ ) is inconvenient and potentially hazardous. Since ozone is a highly reactive gas, it must be generated as needed from molecular oxygen ( $\text{O}_2$ ) using a specialized apparatus. Moreover, the ozonide and molozone intermediate that are formed over the course of the reaction contain relatively weak oxygen-oxygen bonds and can be explosive if not handled properly.

Conveniently, there are other methods for accomplishing the oxidative cleavage of alkenes without the use of ozone. One traditional alternative uses a hot, aqueous solution of acidic potassium permanganate ( $\text{KMnO}_4$ ), which is a powerful oxidant.

However,  $\text{KMnO}_4$  does not dissolve in organic solvents and can react explosively with certain classes of organic compounds. Additionally, this method produces a large quantity of heavy-metal waste in the form of manganese dioxide ( $\text{MnO}_2$ ). Industrial preparation of adipic acid uses nitric acid, a strong oxidizing acid that presents many chemical safety hazards and environmental risks. Nitric acid can react violently with some organic compounds, causing serious accidents in the lab. Additionally, the use of nitric acid in the preparation of adipic acid results in the emission of nitrous oxide ( $\text{N}_2\text{O}$ ), a suspected green house gas, which may lead to global warming.

## EXPERIMENTAL OVERVIEW

In this experiment, you will the oxidative cleavage of cyclohexene to produce as the only product 1,6-hexanedioic acid (adipic acid), shown in Equation 1 below. This reaction uses sodium tungstate ( $\text{Na}_2\text{WO}_4$ ) as a catalyst and hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) as a cheap and readily available oxidant. Importantly, this procedure embodies the principles of "green" chemistry since the only by-product is water.



Besides the "green" by product, the use of an aqueous solvent system, catalytic amounts of reagents, the starting material is cyclohexene. You may recall that one of the experiments in CHEM 331 was the synthesis of cyclohexene *via* the acid-catalyzed dehydration of cyclohexanol. In keeping with the theme of sustainable chemistry, we retained your samples of cyclohexanol and this is the material you will be using in this experiment.

Adipic acid is an important industrial chemical, and approximately 2.5 billion kilograms of this compound are produced each year for the use in the production of the polymer "Nylon 6,6" and is comprised of alternating units of adipic acid and 1,6-diaminohexane. Nylon 6,6 is used in the production of carpet fibers, upholstery, tire reinforcements, auto parts, apparel and other products.

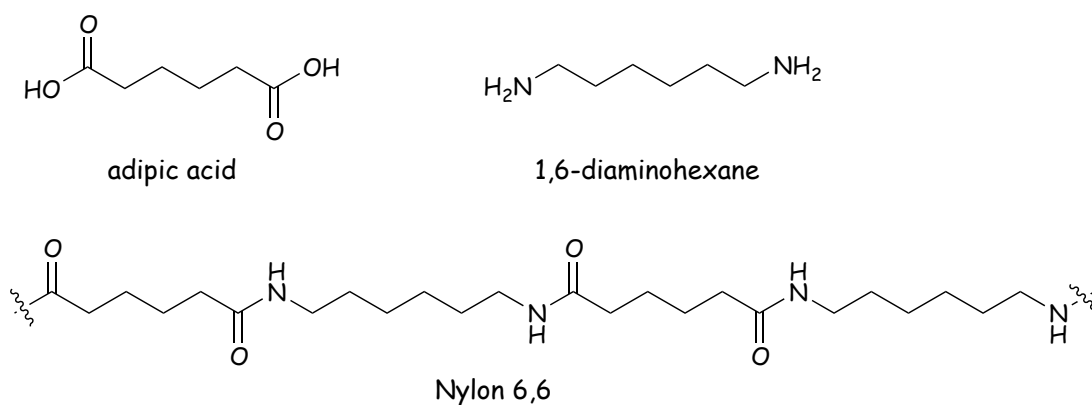
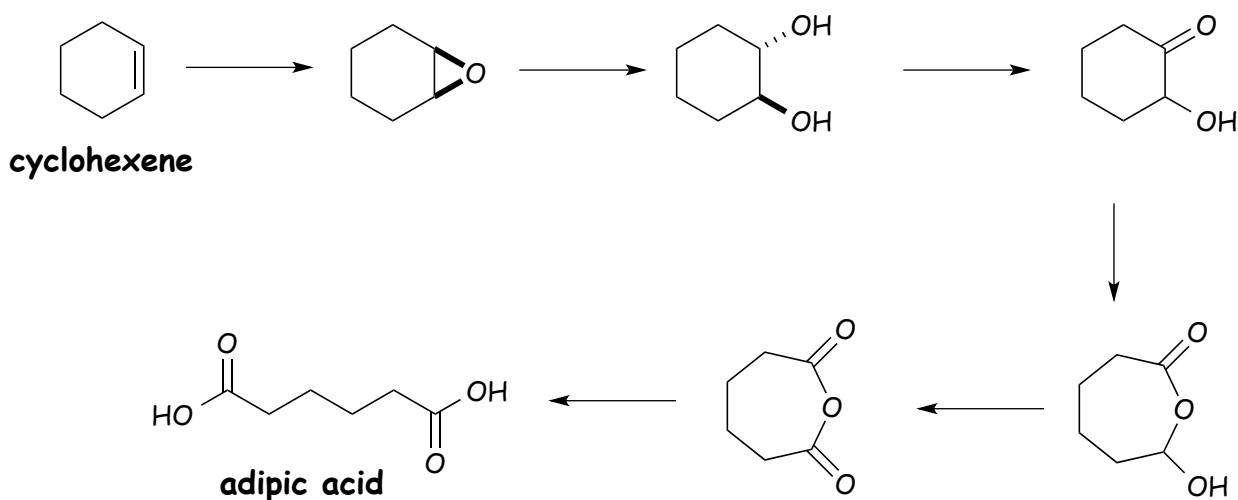
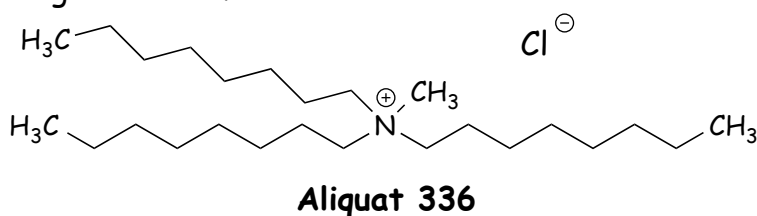


Figure 2: Nylon 6,6

Structurally, sodium tungstate is similar to  $\text{KMnO}_4$ , and it serves as the active oxidant in the oxidative cleavage of cyclohexene. However the reduced tungsten by-product is re-oxidized by the hydrogen peroxide, allowing the  $\text{Na}_2\text{WO}_4$  to serve as a catalyst. This means that only a substoichiometric quantity of  $\text{Na}_2\text{WO}_4$  is necessary for the reaction to reach completion, avoiding a large amount of heavy-metal waste. The overall mechanism for oxidative cleavage under these conditions is complex and hasn't been fully elucidated, but it is thought to proceed through the following intermediates:



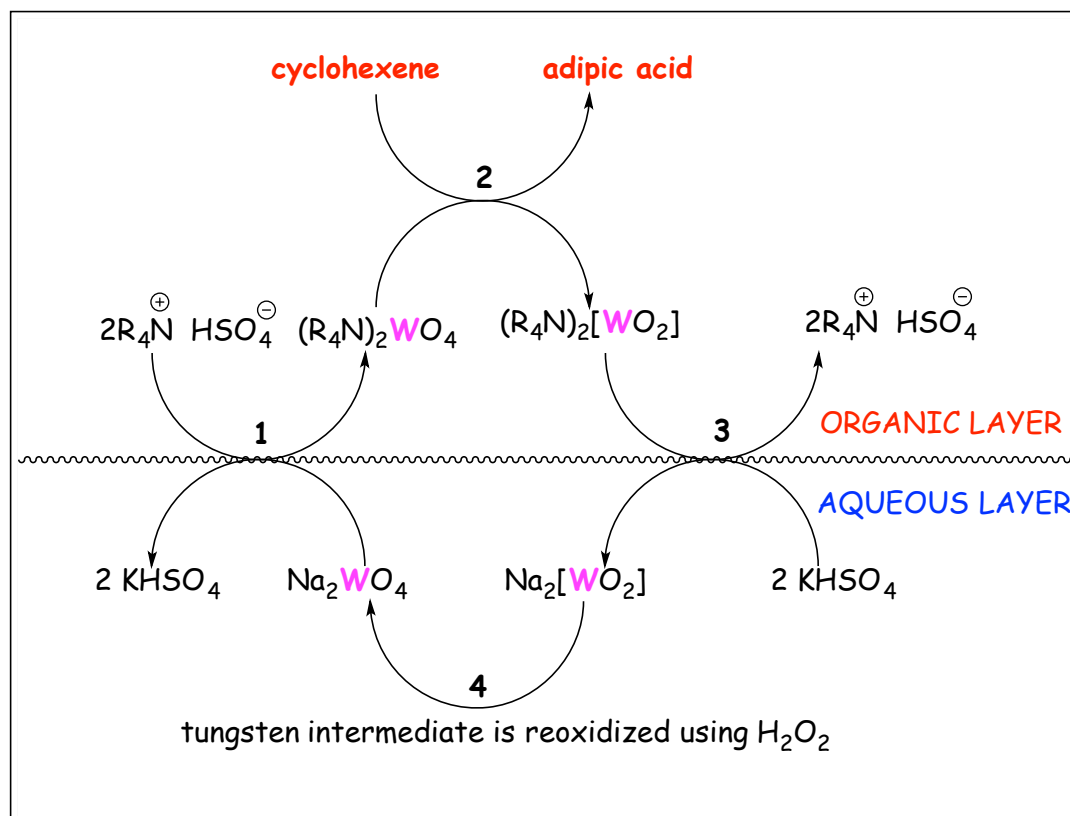
Another notable feature of this reaction is the use of the phase-transfer catalyst (PTC) generated *in situ* from potassium hydrogen sulfate ( $\text{KHSO}_4$ ) and Aliquat 336, which has the following structure.



Phase transfer catalysts enhance the rate of a reaction between chemical species *in different phases* (i.e. aqueous and organic). A small amount of the catalyst extracts one reagent, typically an anion, from the aqueous phase across the interface into the other phase so that the reaction can then proceed. In order to do so, the PTC must possess qualities that make it both hydrophilic as well as hydrophobic.

Sodium tungstate is soluble in water but the cyclohexene is not. When cyclohexene and an aqueous solution of sodium tungstate with hydrogen peroxide are mixed, two layers will result and no reaction can occur. Being a "green chemistry" experiment, the use of a different solvent (besides water) is less appealing. In order to allow the reaction to occur, in the presence of two phases, a phase transfer catalyst will be added to the solution. PTCs are soluble in both aqueous solutions (because they are charged species) and organic solvents (because they contain large non-polar portions in their structures). Ammonium salts bearing hydrophobic alkyl groups, while still ionic, are frequently soluble in less polar organic systems. Through ion pairing, these salts can bring negatively charged species into the less polar system, allowing the reaction to occur. Since the ammonium salt can repeat this process again and again, it is generally used in catalytic amounts, hence the name "phase transfer catalyst".

General Scheme for Oxidation using  $\text{KHSO}_4$  and a PTC:



In this experiment a commercial phase transfer catalyst, formed from potassium hydrogen sulfate,  $\text{KHSO}_4$ , and Aliquat 336  $[(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2)_3(\text{CH}_3)\text{N}^+\text{Cl}^-]$  will be used. Ion exchange will allow the PTC to take the oxidizing tungstate oxidizer from the aqueous layer into the organic layer (Reaction 1 in Figure 3). This oxidizer is then able to oxidize the cyclohexene to adipic acid (Reaction 2), during which time the tungstate is reduced to a lower oxidation state. The PTC releases the reduced tungsten intermediate back into the aqueous layer (Reaction 3). Hydrogen peroxide is present in the aqueous layer to reoxidize the tungsten intermediate back to the tungstate oxidation state (Reaction 4) and the cycle begins again.

Since both the Aliquat 336 and the sodium tungstate function catalytically, only the hydrogen peroxide is needed as a stoichiometric reagent, and we will be using it in large excess. In addition, it is possible to reuse the aqueous layer containing the tungstate catalyst, further increasing the green nature of this experiment.

## NOTES FOR THIS EXPERIMENT:

**Note 1:** All reagents must be added in the order specified for this reaction to work!

**Note 2:** The 50% aqueous hydrogen peroxide is 50% by weight in water.

### FOR YOUR SAFETY:

1. **Wear Gloves** when handling 50% hydrogen peroxide solution. If any hydrogen peroxide comes in contact with your skin, rinse immediately with cold running water.
2. Wear gloves when handling the phase transfer catalyst, as it is an irritant and can transport contaminants through the skin.
3. Cyclohexene is flammable and has a strong odor; try to keep all vials and containers capped.

## REAGENT TABLE:

Reagents	MW (g/mol)	MP (°C)	BP (°C)	Density	Concentration
sodium tungstate dihydrate	329.86				
Aliquat 336	404.17			0.884	
hydrogen peroxide	34.02			1.2	50% by wt.
potassium hydrogen sulfate	136.17	214		2.322	
cyclohexene	82.15	-104	83	0.811	
Product	MW (g/mol)	MP (°C)	BP (°C)		
adipic acid	146.14	152-154	265/100mm		

## EXPERIMENTAL PROCEDURE:

1. Place 125 mg of sodium tungstate dihydrate in a clean, dry 5-mL conical vial containing a magnetic spin vane. Record the actual mass that you are using in your notebook.
2. Add 0.15 mL Aliquat 336 to the 5 mL conical vial. **[Note: This reagent is a very thick liquid. Pull back the plunger to about the 0.8 mL mark and let the Aliquat slowly move into the syringe barrel then push the plunger in slowly. Air bubbles should generally be pushed out in front of the liquid so do not panic if you see a lot of air bubbles in the syringe.]** Record the volume that you are using.
3. Add 2.0 mL of 50% hydrogen peroxide to the 5 mL conical vial. **[It is advised that you wear gloves throughout this experiment.]** Record the volume that you used.
4. At this time, add 92.5 mg (0.0925 g) potassium hydrogen sulfate and commence stirring (setting of 5, without heat) in the aluminum block. Record the actual mass that you are using.
5. To transfer the cyclohexene into the reaction vial, obtain a clean dry syringe, with needle, from your kit. Draw up 0.62 mL of cyclohexene into your syringe and place the shield on the needle. Weigh to obtain the combined mass of the cyclohexene and the syringe and record this mass in your notebook. Remove the shield, transfer the cyclohexene to the conical vial, place the needle shield on the needle again then reweigh the empty syringe. Record this mass in your notebook. **[If using a student sample with no septum, expect to have difficulties trying to remove any air bubbles. The sample vial cannot be fully inverted to allow the syringe to blow any air bubbles out in many cases.]**
6. Attach a water-cooled condenser to the top of the conical vial (Apparatus A.4B), turn on water and begin stirring at maximum speed (setting of 10). Turn on the heat to a setting of 4.5. Maximum stirring is required for maximum interaction of the two phases, where the reaction must occur.
7. When the reaction mixture begins to boil, allow to heat at reflux for 15 minutes. After this time, add approximately 0.5 mL of water **through the top of the condenser**, in order to wash down the inside of the condenser. Continue refluxing for another 15 minutes.

8. After a total of 30 minutes at reflux, remove the conical vial from the hot plate and allow the solution to cool *slightly* and separate into layers. **While still warm**, carefully and quickly remove only the aqueous layer, transferring it to a 30-mL beaker using a disposable pipette. Do NOT remove any of the oily-looking catalyst with the aqueous layer. The catalyst will inhibit formation of the product crystals. Leave behind any aqueous layer that cannot be removed without the oily catalyst.
9. Place the beaker containing the aqueous layer into an ice bath to induce crystallization of the product. Gently stir with a glass rod to facilitate crystal formation.
10. Collect the product by vacuum filtration on a Hirsch funnel and wash the crystals using 1 mL of ice water each time. Carefully place the Hirsch funnel containing the adipic acid into a beaker and leave it in your locker so the solid can dry until the next lab period.
11. Obtain the mass of the product (weigh a clean empty small sample vial with cap empty, transfer your product to the vial and reweigh the vial containing the product). Obtain a melting point and an infrared (IR) spectrum on your product and submit the vial with your product, properly labeled.

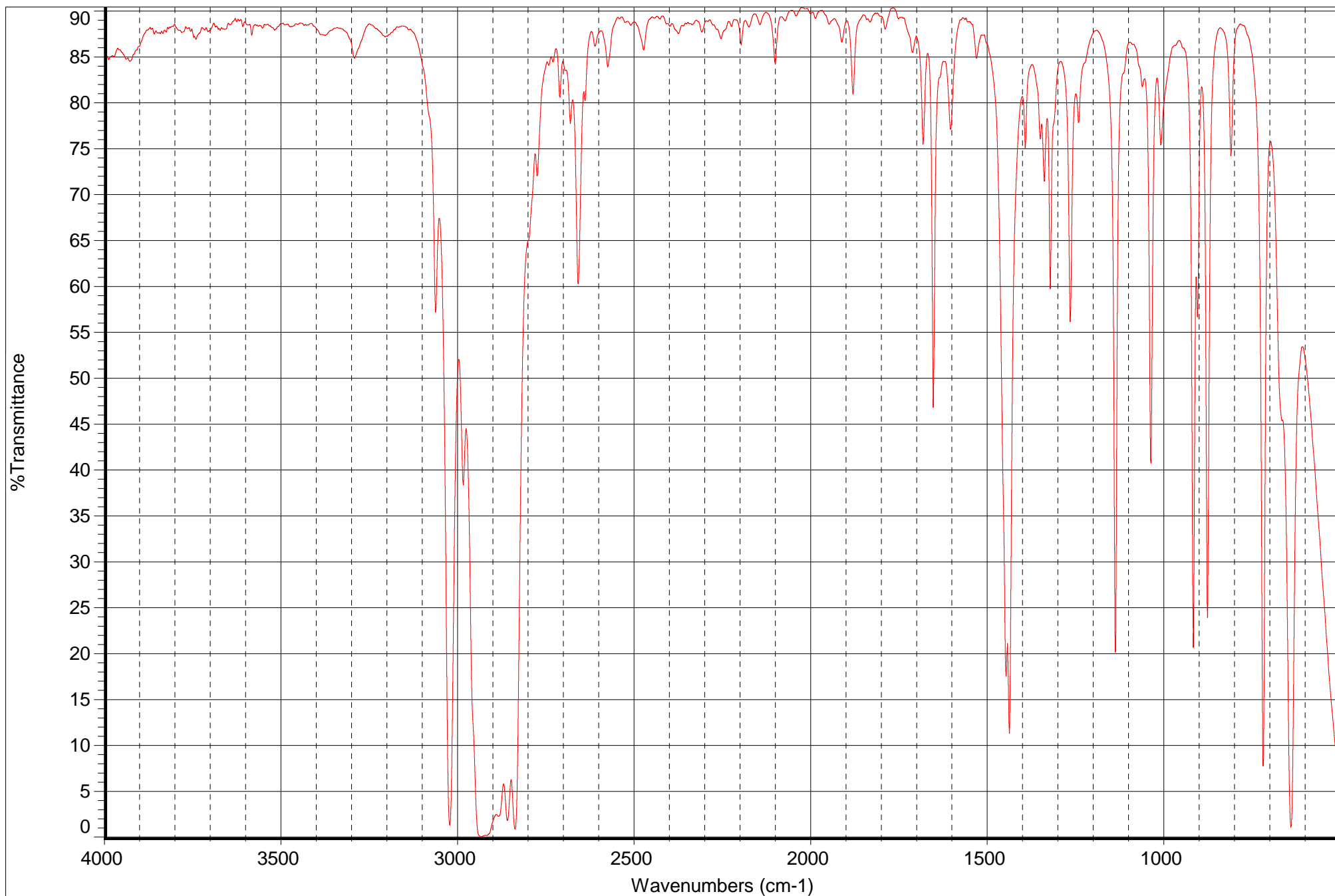
### **WASTE DISPOSAL AND CLEAN-UP:**

1. The aqueous filtrate (Step 10) may be discarded in the "tungsten waste" container.
2. The Aliquat waste from the conical vial should be placed in the "Aliquat/acetone waste bottle".
3. The conical vial should be cleaned with methanol (place in tungsten waste also), soapy water and then acetone, which should be disposed of in the "recyclable acetone waste" container. Repeat if needed. The water cooled condenser will also need to be meticulously cleaned as PTC usually gets caught up inside.

### **CALCULATIONS**

Since all reagents are either used catalytically ( $\text{Na}_2\text{WO}_4$ ,  $\text{KHSO}_4$ , Aliquat 336) or in excess ( $\text{H}_2\text{O}_2$ ), the cyclohexene **MUST** be the limiting reagent in this reaction.

1. Calculate the number of moles of cyclohexene you used, based on the syringe weights.
2. Based on the moles of cyclohexene, calculate the theoretical yield of adipic acid.
3. Calculate the percent yield of adipic acid for your reaction.



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cyclohexene

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