SYNTHETIC PROCEDURE

**Preparation of ketal-ester (2)**
1) Weigh out approximately 10.00 g of the ethyl and methyl ester of 2-cyclohexanone carboxylate (1). Place this in a round bottom flask (a single neck 100 mL or the 250 mL two-neck will work if you put a septa over the side arm) along with 50 mL of toluene, a 1.4 molar excess of ethylene glycol, 0.5 g of p-toluenesulfonic acid and a couple of boiling stones. Set up a reflux using a Dean-Stark water trap and allow it to reflux for 12 hours.

Work up: There should be two phases in the water trap when the reaction is completed. Turn off the heat and allow the reaction to come to room temperature. Pour the reaction mixture into a separatory funnel and wash with water, twice with 10% NaHCO$_3$ and then brine. Dry the mixture of MgSO$_4$. Filter it into a round bottom flask and remove the solvent with the Rotovapor. Set up a simple distillation under an aspirator vacuum and collect the product. It should boil at about 130° depending on how good the vacuum is. Get the weight of the product, calculate the yield and obtain all the appropriate spectral data to confirm the identity of the compound.

**Preparation of ketal-alcohol (3)**
2) Take the 500 mL three neck flask and put a ground glass stopper in one of the joints. Weigh out approximately 5.0 grams of Mg° and place them in the flask along with a stir bar. Put a condenser on the center neck of the flask and the addition funnel on the third neck. Run N$_2$ through the system. Carefully (and quickly) add 100 mL of ether to the addition funnel and add it to the Mg°. Add a molar equivalent of CH$_3$I and 100 mL of ether to the addition funnel. Add this solution to the round bottom over a period of 1/2 hour and then reflux the solution for an additional hour. Take a 1/2 molar equivalent of the ketal-ester (2) and 100 mL of ether and place it in the addition funnel. Add this to the solution (without heating) over a period of 1/2 hour and allow it to stir for another 1/2 hour.

Work up: To the cooled solution add 100 mL of 3.5 M acetic acid. (Add it slowly!) Separate the two layers in a separatory funnel. Save the ether layer and extract the aqueous layers twice with 50 mL of ether. Combine all the ether layers and wash 10%
NaHCO$_3$ (twice) followed by brine and then dry over MgSO$_4$. Filter and remove the ether with the rotovapor. Distill as you did for the synthesis of (2). Calculate the yield and obtain all the appropriate spectral data. The boiling point will be around 150°.

**Preparation of ketal-alkene (4)**

3) Take the ketal-alcohol (3) (somewhere between 5-10 g) and dissolve it in toluene (50 ml solvent per 5 g of 3). Add 0.50 g of p-toluene sulfonic acid and set up a reflux as you did for the preparation of (2). Allow it to reflux for 12 hours.

Work up:
After cooling, pour the sample into a separatory funnel and wash with 10% NaHCO$_3$ and brine. Dry the sample over MgSO$_4$ and remove the solvent with the rotovapor.

Pack one of the 50 mL syringes with about 30 mL of dry silica gel and allow about 50 mL of hexane to run through the column using mild suction. Add about 1/3 of the sample to the top of the syringe column and elute with another 50 mL of hexane. Take 75 mL of 5% ethyl acetate in hexane and run that through the column. Save the eluent and remove the solvent with the rotovapor. The remaining material should be the ketal-alkene (4). Save a small sample and acquire all appropriate spectral data.

**Preparation of ketal-epoxide (5)**

4) Dissolve approximately 2 gram of the ketal-alkene (4) in 10 mL of CH$_2$Cl$_2$ (you can do this in a small Erlenmeyer flask). Dissolve a 1.5 molar equivalent of mCPBA (note that it is about 50%) in 75 mL of CH$_2$Cl$_2$ in a 125 mL Erlenmeyer. Add about 0.5 g of solid NaHCO$_3$ and stir with the flask in an ice bath. Add the ketal-alkene solution and allow the reaction to stir for 1 hour at 0°C.

Work up:
Pour the reaction mixture into a separatory funnel and wash with 10% Na$_2$S$_2$O$_3$, 5% NaOH and brine. Dry the sample over MgSO$_4$ and remove the solvent with the rotovapor. Pack another silica gel column as you did before but use 10% ethyl acetate in hexane instead of 5%.

**Preparation of the furan (6)**

Before you begin this experiment you need to know that the furan will decompose in a couple of days. You can probably make the furan and purify it and run the oxidation the next day. Any more delay will probably require a second purification and a loss of product.

5) Place 25 mL of 2 N HCl in an Erlenmeyer flask with vigorous stirring. Add a pentane solution of the ketal-epoxide (5) (30 mL pentane / 1 g furan). Allow the sample to stir for about an hour. The reaction progress can be monitored using TLC.

Work up:
Once you know that all of the ketal-epoxide has been consumed, pour the mixture into a separatory funnel and drain off the HCl. Pour the pentane layer into another flask and extract the HCl solution 3 times with equal volumes of pentane. Combine all the pentane layers and wash with 10% NaHCO$_3$ (Be careful!), and brine. Dry the pentane over K$_2$CO$_3$, filter and remove the solvent with the rotovapor. Pack a column with silica (about 10 mL should be enough). Run some pentane through the column. Place the sample on the column and elute with a couple of volumes of pentane. The compound is
not real stable and you might see the column turn purple. (This is the color of the degradation products.)

You can store this sample in the freezer or remove the solvent with the rotovapor and proceed to the final step!

**Oxidation of the furan (6) to ?**

6) First go to the library and find a procedure to purify mCPBA. (Schwartz et al., *J. Org. Chem.* 1964, 29 1976.) You will also need to assay the purity of the sample. Mrs. Paar will set up the reagents you will need.

You will want to use 100-200 mg of furan for the oxidation. Try three different conditions and do all the reactions in the hood. Dissolve the furan in 5 mL of ethanol free chloroform. To one sample add 2 equivalents of oxidizing agent. To the second sample add 1 equivalent of oxidizing agent. To the third sample add about 5 ul of concentrated HCl and then add 1 equivalent of oxidizing agent. Follow the reactions using GC or TLC. You can work up all the reactions as you did for the preparation of (5). Remove the solvent and place the samples on a vacuum pump for a few minutes and obtain a $^1$H NMR spectrum of the reaction products in CDCl$_3$. Bring the spectra to me to determine the next step.