

## 2. Epoxidation of Cholesterol

**M. Jones:** Oxiranes, 10.4a, Figure 10.27, pgs 452-455  
Asymmetric (Sharpless) Epoxidation, 10.4b, pgs 859-866  
Steroid Biosynthesis, 12.14, pgs 604-608  
Chromatography, 4.9, p 177, 10.2, pgs 749-752

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**and P.F. Schatz:** Technique 17, 17.1 – 17.7, pgs 178 – 189

This procedure has been adapted from the microscale procedure described in the third edition of *Macroscale and Microscale Organic Experiments* by Kenneth L. Williamson (Houghton Mifflin, Boston, 1999).

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### Introduction

In this experiment, you will perform an epoxidation of an alkene using a peroxyacid. You will also be introduced to a new technique, chromatography, which will be used in later experiments.

### Background

The epoxidation reaction is the formation of an oxirane (epoxide) from an alkene. There are different reagents which can be used to accomplish this transformation. Different reagent systems, including the Sharpless epoxidation of allylic alcohols using tartaric acid, have been used to affect this reaction stereospecifically. One of the more common reagents is a peroxyacid. A specific reagent used for this purpose is 3-chloroperoxybenzoic acid, more commonly known as *meta*-chloroperoxybenzoic acid (MCPBA). The mechanism is depicted in Figure 1.

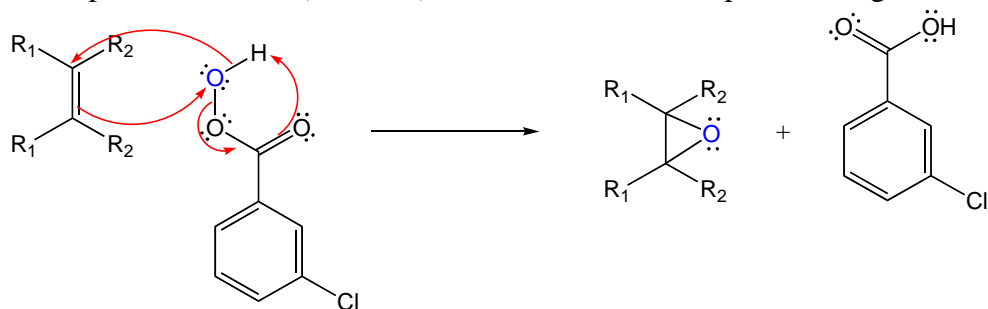


Figure 3. The mechanism for epoxidation of a generic alkene with *m*-CPBA.

The mechanism is concerted; therefore the epoxide retains the regiochemistry of the starting alkene.

In this laboratory experiment, you will be synthesizing an epoxide starting from cholesterol, which is an interesting molecule. All of the ring junctions are *trans* to one another and the groups are on the same side of the molecule.

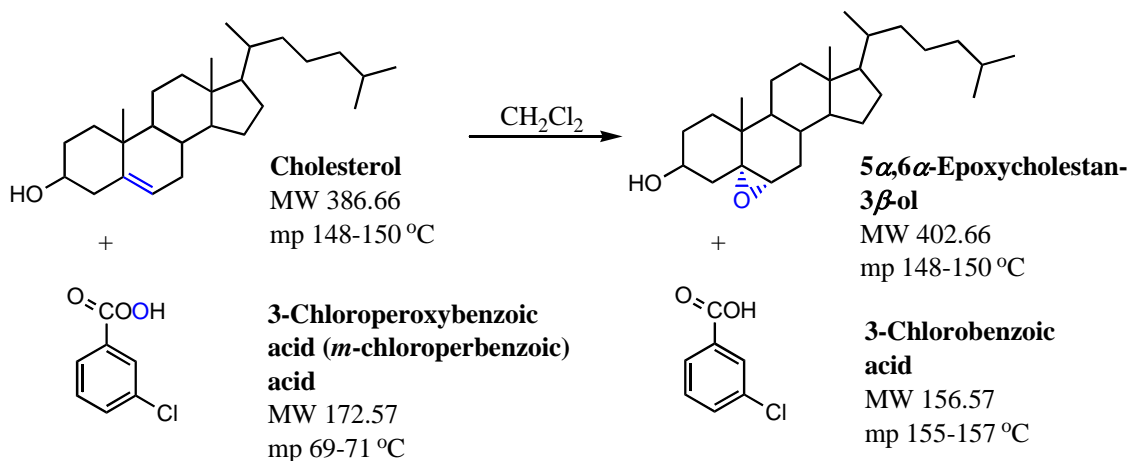


Figure 3. The overall reaction of this experiment.

Cholesterol has had a lot of recent notoriety especially with respect with human health. A lot has been discussed about testing for “good” and “bad” cholesterol, whether we can decrease it, and what is the basis for some people to have “high” or “low” cholesterol. These topics are not going to be discussed in this laboratory but should be on our minds.

A new technique, which will be introduced in this laboratory, is chromatography. It is used as a separation and/or purification method, especially if one has more than one product, and the normal extraction and/or recrystallization processes do not work. It is a technique of practice and patience.

It was first introduced to it in Chapter 4 when enantiomers were discussed, and this topic will be further discussed in Chapter 15. In a nutshell, you have two different phases, a stationary (one that does not move and provides a scaffold) and mobile (one that moves, in your case a solvent) phase. The polarity of the compound and solvent as well as the compounds’ molecular weights play into this separation process.

## Experiment

Remember to add either a boiling stick or chips when heating a reaction.

### New technique skill.

The product will be separated from the starting materials and the by-products using column chromatography. You will be preparing an alumina column using a micro-column. It is a good idea to prepare the column while the mixture is reacting for the 30 minutes. Add the *tert*-butyl methyl ether when you are close to adding the reaction mixture to the column.

### Reaction.

Place 200 mg of cholesterol and 1 mL of methylene chloride (dichloromethane, CH<sub>2</sub>Cl<sub>2</sub>) into a small reaction tube and warm (if needed) to dissolve. Place 140 mg of 3-chloroperoxybenzoic acid (*m*-chloroperbenzoic acid) and 2 mL of methylene chloride into another small reaction tube and warm to dissolve. Let both tubes cool to room temperature, and then add the benzoic acid solution to the cholesterol solution dropwise via pipette. Cap the reaction tube and heat for 30 minutes using a sand bath.

### Making the Column.

Obtain a micro-column that is fitted with a fritted disc (frit), column tip, and small funnel. Clean the column with a small amount of acetone. If your column does not have a frit, you may pack it with a small cotton plug at the tip. Assemble to column, tip and funnel. Weigh 3 g of alumina and pour into the column. Gently tap the sides of the column to pack the alumina.

### Workup.

The product will be separated from the starting material and any by-products using column chromatography. Once the reaction mixture is cooled, it is ready to be added to a column of alumina in *tert*-butyl methyl ether. Add 5 mL of *tert*-butyl methyl ether to the column using a pipette. The tip of the pipette should be placed against the side of the column, and the ether should be allowed to run down the inside of the column to prevent disturbing the alumina. After the ether has been loaded (and before the level of the ether is below the top of the column—about ½ cm), load the product in the same manner followed by an additional 25 mL of ether. Do not allow the column to go dry! The product is eluted into a tared 50-mL Erlenmeyer flask until 30 mL have been collected. The solution is concentrated to dryness in the hood. **(If the mass of product is less than 150 mg, then elute the column with another 10 mL of *tert*-butyl methyl ether.)** Recrystallize the resulting solid in acetone/water.

### Testing the Product.

Perform a Beilstein test to determine if your product contains chlorine. This test is performed by heating a copper wire in the flame of a Bunsen burner until no additional coloration of the flame is noticed. Next, the copper wire is cooled by dipping it into a beaker of deionized water. Then, dip the copper wire into your sample and heat in the flame again. Record any color change you observe.