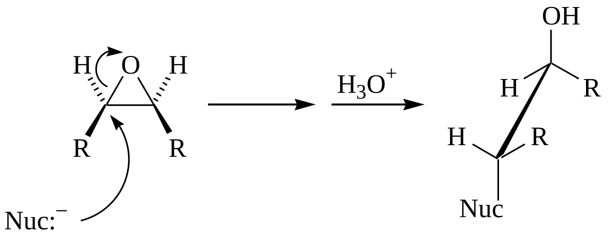
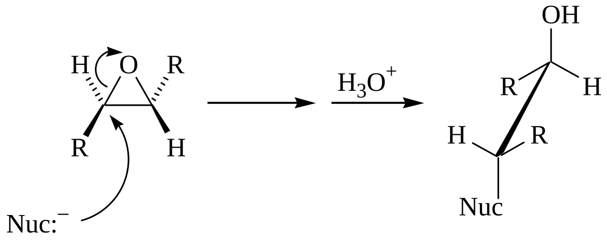
Title: **Epoxidation of trans-Cinnamyl Alcohol**[1]

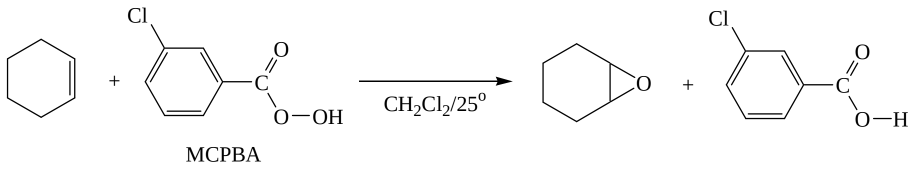
Introduction:

Epoxidation of alkenes leads to a useful three-membered-ring ether (an epoxide) that is reactive toward nucleophiles. Nucleophilic attack on epoxides gives a ring-opened product that possesses two functional groups located on adjacent carbon atoms. Often this ring-opening is stereo-specific, leading to products where the stereochemistry at the adjacent carbons of the ring-opened product can be predicted reliably.



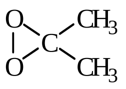


The traditional reaction conditions for epoxidation involve *m*-chloroperoxybenzoic acid (MPCBA) in an inert solvent.



MPCBA is the oxygen-transfer agent, leading to the epoxide along with *m*-chlorobenzoic acid as the byproduct. MCPBA is a solid that is relatively easy to handle and weigh out. Dichloromethane is the solvent of choice because it dissolves both MCPBA and most alkenes.

In this experiment we will use a greener alternative for transfer of an oxygen atom to the alkene *trans*-cinnamyl alcohol. The oxygen transfer agent, generated *in situ*, is a molecule called dimethyldioxirane, which is formed from transfer of oxygen to acetone from OXONE® (a complex mixture containing the equivalent of potassium peroxomonosulfate, $KHSO_5$). The reaction actually takes place in two phases (an organic phase and H_2O), as shown in the scheme on the next page.



dimethyldioxirane

To understand what is going on in this scheme, start with the reaction shown in water. Acetone dissolved in water reacts with $KHSO_5$ to produce dimethyldioxirane. The dimethyldioxirane migrates into the organic phase and reacts with *trans*-cinnamyl alcohol, producing the epoxide and regenerating acetone.

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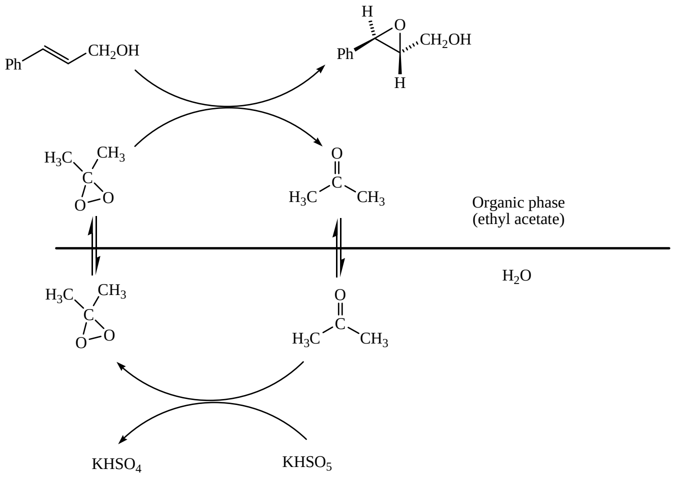
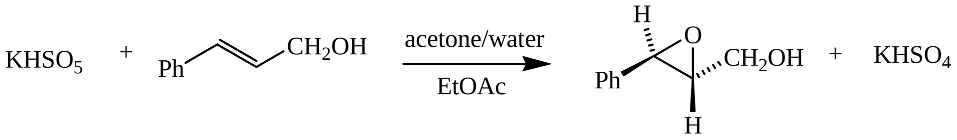
[1] Adapted from a report by N. Hashimoto and A. Kanda, *Organic Process Research and Development*, **2002**, *4*, 405.



The reaction is catalytic in acetone, so the overall reaction equation is simply:



The final product of this epoxidation is an *epoxyalcohol*, a useful intermediate in organic synthesis. Note that the product has two chirality centers. The procedure you will use yields racemic product, but chiral catalysts have been invented that allow enantiomeric excesses greater than 95% in the “asymmetric” epoxidation of allylic alcohols.[2]

Green aspects:

This procedure offers many advantages over traditional methods of epoxidation. OXONE is about half as expensive as MCPBA, and it is converted in the reaction to $KHSO_4$. $KHSO_4$, while relatively acidic, can be easily neutralized with dilute NaOH solution to give non-toxic Na_2SO_4. The reaction conditions require the use of relatively non-toxic organic solvents plus water. Acetone is recycled in the reaction, so all of the extra oxygen in oxone is incorporated into *trans*-cinnamyl alcohol. The workup involves the use of saturated NaCl solution (brine) and no other reagents. Ethyl acetate can be recycled in the workup process.

PRE-LAB QUESTIONS:

1. Use *Green Chemistry Assistant* to determine the theoretical atom economy of this transformation and set up the necessary reactant/product tables.

2. Say you didn’t know how long to let the reaction go. What are two independent techniques you could use to test to see if there is any allylic alcohol remaining in the reaction and any epoxyalcohol being produced? What are the advantages of each?

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[2] See Robert M. Hanson, S.Y. Ko, and K. Barry. Sharpless, "Catalytic Asymmetric Epoxidation" *U.S. Patent* 4,900,847, **1990**

Procedure:

Dissolve 3.55 g of $NaHCO_3$ in 40 mL of H_2O with magnetic stirring in a 250-mL Erlenmeyer flask. Add to the solution 11.2 mL of acetone, 40 mL of ethyl acetate, and 1.14 g of *trans*-cinnamyl alcohol. Look for the presence of two phases. [Which is which?]

Also prepare a solution of 5.20 g of OXONE (equivalent to 8.46 mmol of $KHSO_5$) in 36 mL of H_2O in a 50-mL Erlenmeyer flask.

OXONE is an irritant and strong oxidizer

Stir the two-phase mixture vigorously at room temperature while the OXONE solution is added dropwise over a period of 40 minutes. Stir the mixture for an additional 60 minutes at room temperature. [How could you tell that the reaction is done if you wanted to?]

Maintaining the reaction temperature close to room temperature is important.

It is also critical that stirring is brisk. This allows the two layers to mix well. If the phases do not mix, no reaction can occur.

Transfer the mixture to a 250-mL separatory funnel and drain off the lower aqueous layer. Wash the remaining organic layer with 25 mL of saturated NaCl solution, dry the organic layer over $MgSO_4$, and concentrate the extract by rotary evaporation.

Your instructor will demonstrate proper operation of a separatory funnel.

Determine the yield of your crude product, and analyze it using IR and NMR spectroscopy. Look for the following bands in the IR (cm^{-1}): 3450 (O-H stretch); 2990 (epoxide ring C-H stretch); 770, 890, and 1250 (epoxide C-O); and 700 and 760 (monosubstituted benzene ring). In the NMR spectrum, look for evidence that the reaction is complete by seeing if there is any trace of alkene H in the region 6.2-6.9 ppm.

LABORATORY NOTEBOOK REPORT:

Analyze the IR and NMR spectra as much as possible. Obtain a copy of the NMR of *trans*-cinnamyl alcohol (via the web or using the Aldrich catalog of NMR spectra found in the Science Library), and compare that spectrum with the NMR of your product. In the NMR of your product, pay close attention to the region of the spectrum from 2.5 to 5 ppm. This region should contain two epoxide ring protons and those from the CH_2 group next to the OH group. Explain why the two H atoms of the CH_2 group have different chemical shifts.