Experiment 14

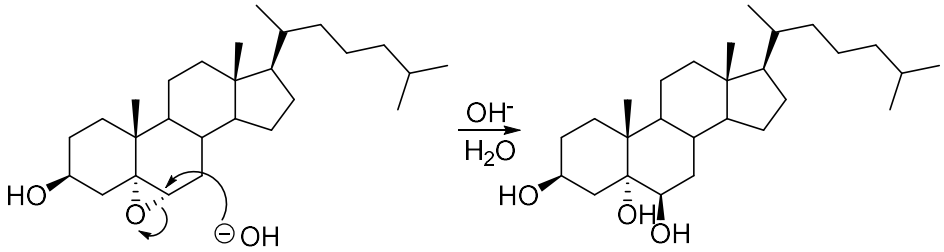
Epoxidation of Cholesterol: Stereoselective Reaction of a Steroid

Study Questions

1) Why is one face of the double bond attacked preferentially by the peroxyacid? **Answer:** The angular methyls block attack on the other face.

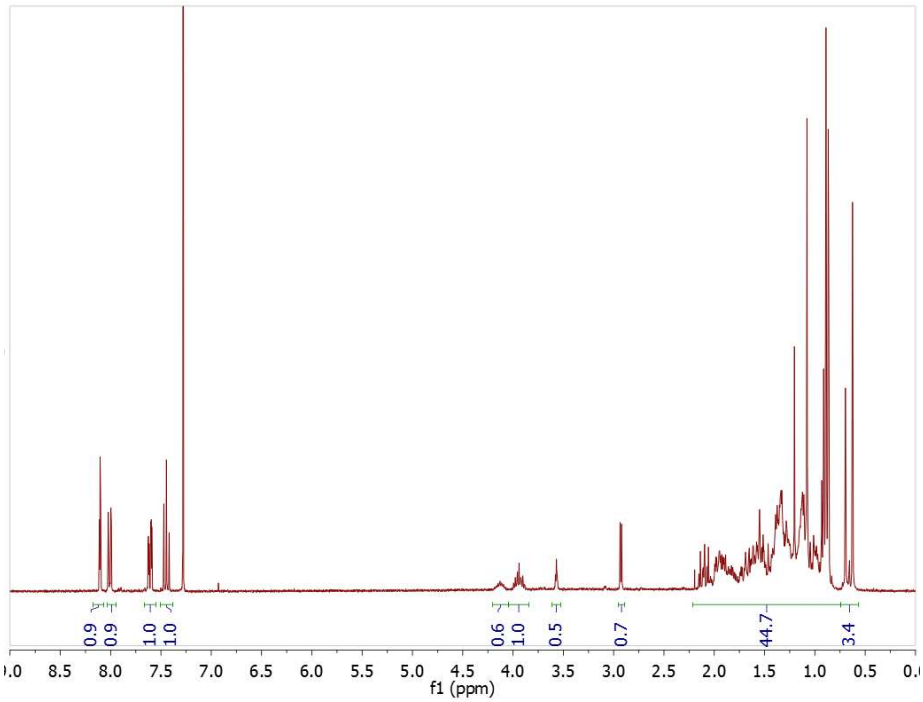
2) Why is the *m*-CPBA byproduct easily removed with a basic wash step? What happens to the active functional group under basic conditions that make it water soluble? **Answer:** The *m*-CPBA byproduct is a carboxylic acid, so it can easily be removed by chemically-active extraction. It will be deprotonated by mild base and pulled into the aqueous phase.

3) If you allowed your product to remain in the separatory funnel in contact with water and base for a long enough time, what side product would you expect to collect? (Hint: what reaction do epoxides undergo in basic conditions?) **Answer:** The epoxycholesterol would undergo a nucleophilic ring opening to make a diol. The attack would most likely happen on the less-substituted carbon.



Interestingly, this reaction is extremely slow for epoxycholesterol, possibly because the angular methyls are blocking attack on the top face of the molecule again. For more information, see "Surprising Unreactivity of Cholesterol-5,6-Epoxides Towards Nucleophiles" (Paillasse, M. R., Saffon, N., Gornitzka, H., Silvente-Poirot, S., Poirot, M., de Medina, P. *J Lipid Res.* **2012,** *4,* 718–725.)

4) A student ran this reaction and got the product NMR shown below. What is the likely cause of the peaks between 7.4 ppm and 8.2 ppm? What could the student do to remove the compound responsible for these peaks?



Answer: There are a lot of aromatic peaks showing up in this NMR between 7.4 and 8.2 ppm. These indicate that not all of the *m*-CPBA byproduct was removed during the extraction. The student should perform the extraction again, and run a TLC of the aqueous phase afterwards to check that the *m*-CPBA is all gone.