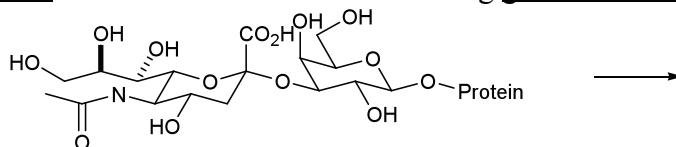
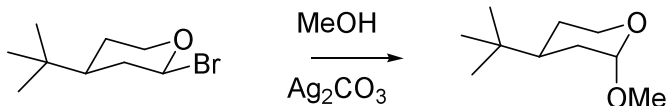


Medicinal Chemistry Assignment 6

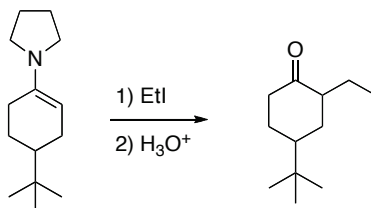
1. During the maturation of the influenza virus, neuraminic acid is hydrolyzed into two constituent sugars. Provide a detailed mechanism for this reaction using general acid catalysis.



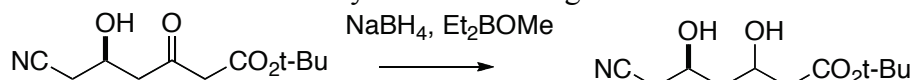
2. During the above transformation, the conformation of one of the sugars changes. Explain why this happens.
3. Explain the following observation by drawing a detailed mechanism:



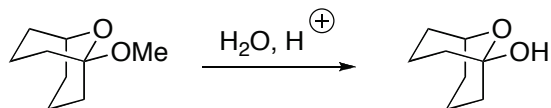
4. Predict the relative stereochemistry of the product of the following reaction and explain the origin of selectivity.



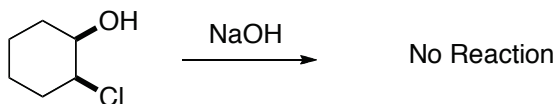
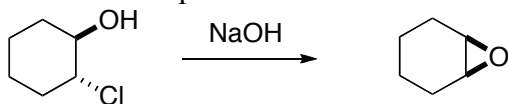
5. The reduction of 2-hydroxy ketones can be performed with very high stereoselectivity. The key to these reactions is the formation of a complex or chelate with a Lewis acid. Using this knowledge, predict and account for the stereochemistry of the following reaction.



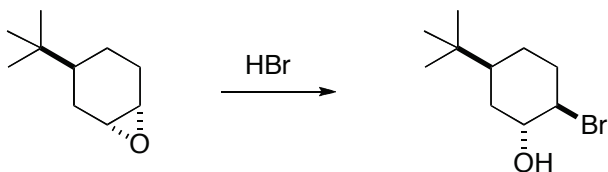
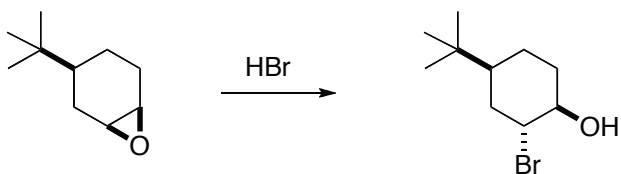
6. The following reaction proceeds very slowly, requiring several days to complete. Give a mechanism to account for the observation that this process proceeds extremely slowly. (Hint: build a model and consider all reaction paths)



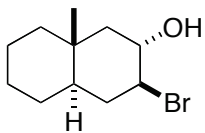
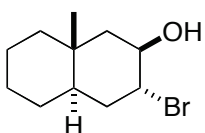
7. A chemist is trying to prepare a series of epoxides and performs the following reactions. The first transformation proceeds rapidly, but the second substrate is unreactive even after several days. Provide an explanation.



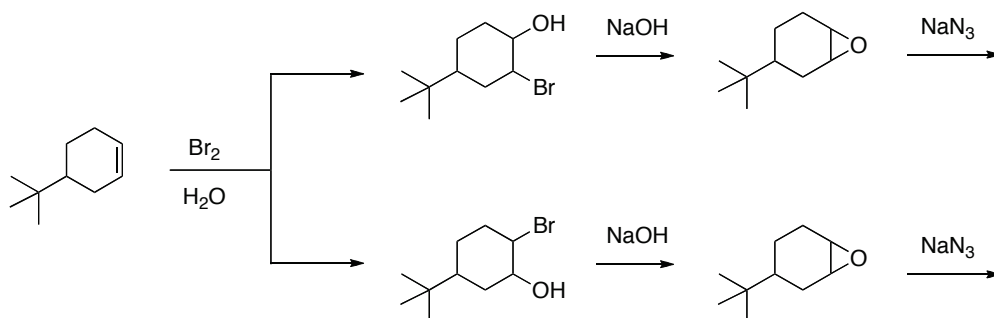
8. Account for the different regioselectivities in the following transformations:



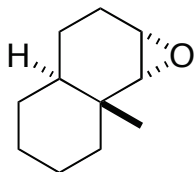
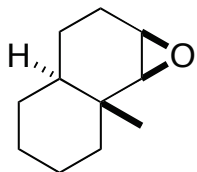
9. Which of these two compounds will form an epoxide upon treatment with base?



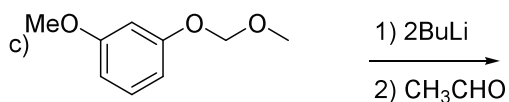
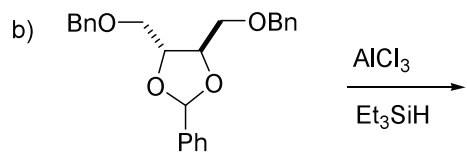
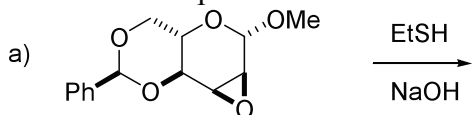
10. Provide the relative stereochemistry for all products and predict the regio- and stereochemistry of the final product. Provide justifications for each predicted product by considering both reaction pathways.



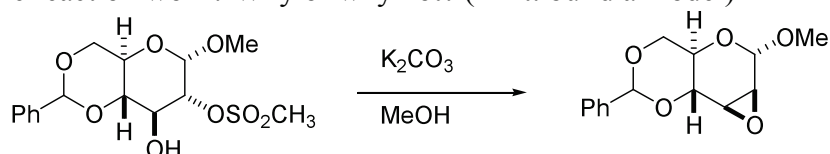
11. Predict the products that will be formed upon treating the following epoxides with azide ion.



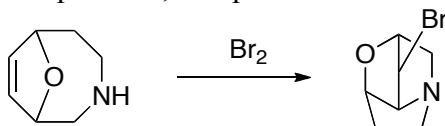
12. Predict the product of the following transformations.



13. A student plans to carry out the following synthetic step during the preparation of a glycosidase inhibitor. Will the reaction work? Why or why not? (Hint: build a model)



14. During a total synthesis of a *lolium* alkaloid, the following reaction was performed. Predict the stereochemistry of the product and write a mechanism to account for its formation. The process involves an initial reaction that is non-selective, but ultimately gives an almost 95% yield of a single isomer product. Describe how this is possible, and provide the name of the principle involved.



15. To date over 18 drugs have been developed to treat AIDS. Yet, each of these drugs when used alone in the clinic results in failure. Explain why this is so. Suggest a means by which AIDS drugs can be administered to give successful antiviral action.
16. A typical AIDS infection has three distinct stages.
- What are these infection stages called?
 - Describe each stage briefly in terms of symptoms, viral load and CD4 levels.
 - The HIV virus has spread extremely rapidly throughout the world, and despite the fact that it is extremely deadly (and kills its host), has shown no signs of becoming less virulent. Considering the stages of HIV infection, why do you think the virus has been so successful? Is there a strong evolutionary pressure for the virus to become less virulent?
17. The development of HAART for AIDS has led to a significant improvement in the quality of life for AIDS sufferers (at least in developed countries). However it is not a cure and resistant forms of the virus continue to appear. Provide an explanation for the emergence of resistance, even in the face of triple combination therapy.