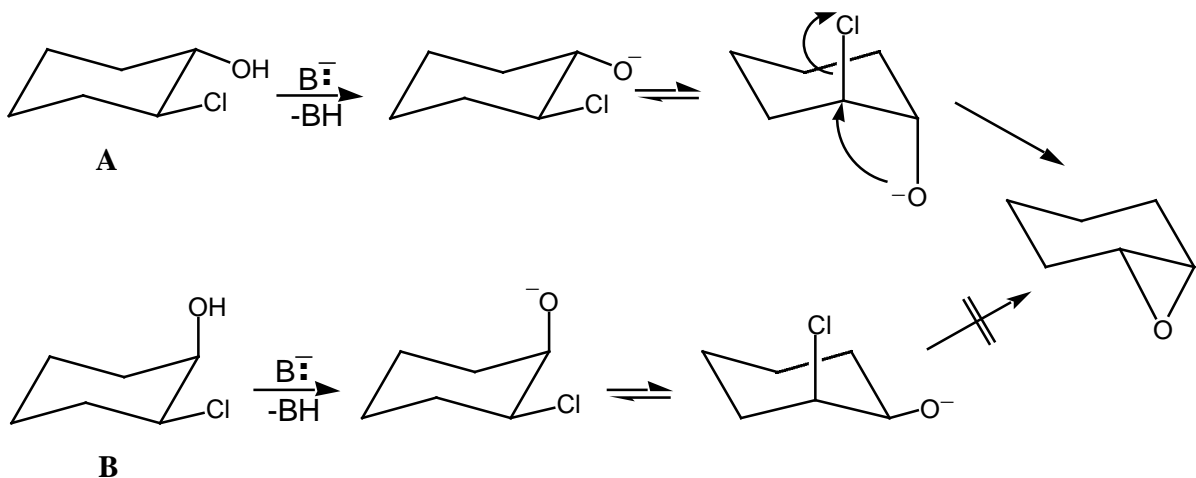
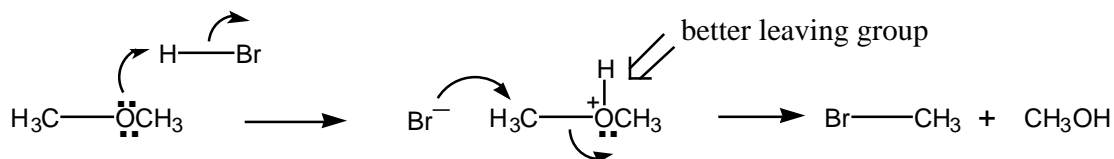


Answers to Problem Set #6  
CH241-2001F

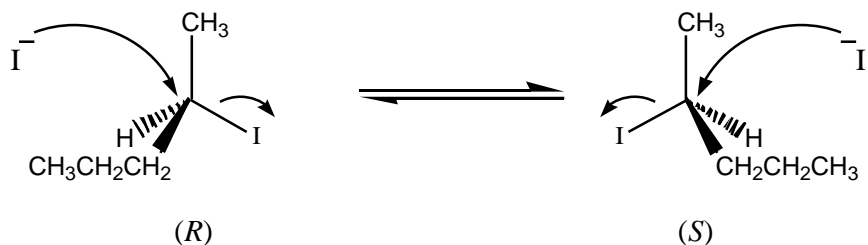
- [1] (a) Deprotonation of **A** by a base results in an anion that can adopt a conformation suitable for an intramolecular, "S<sub>N</sub>2 like" displacement of Cl from the back. The corresponding anion from **B** is not oriented favorably to displace Cl from behind.



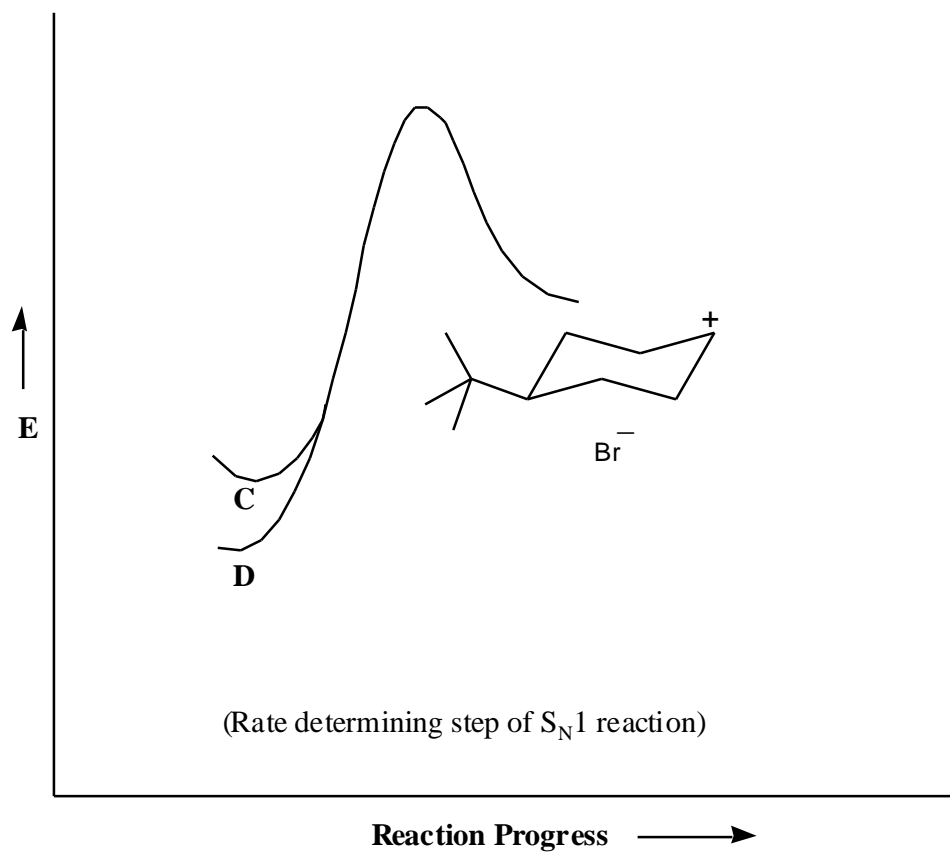
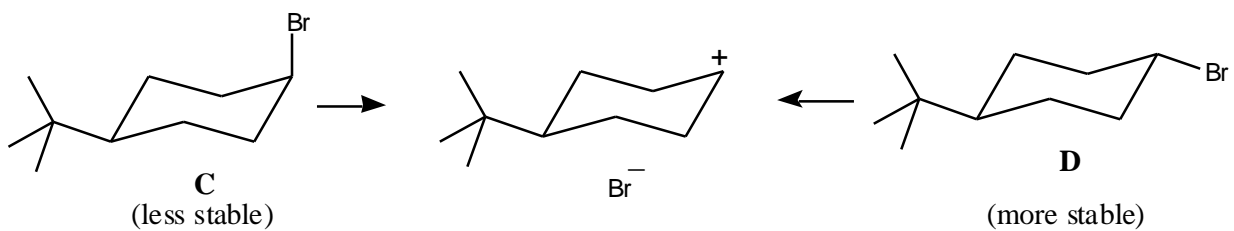
- (b) The methoxide ion is a poor leaving group and cannot be displaced by the bromide ion. (Methoxide is a stronger base than bromide.) In HBr, however, protonation results in an excellent leaving group, namely methanol, which can be then displaced by bromide.



- (c) The substrate undergoes an S<sub>N</sub>2 reaction with iodide. As the leaving group is also iodide, eventually an equilibrium is established at which point there are equal amounts of both enantiomers present. The material is now racemic and hence the loss in optical activity.



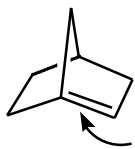
- (d) In an S<sub>N</sub>1 reaction, ionization of the substrate is the rate determining step. The crucial point to recognize here is that both **C** and **D** give the same set of ions. **C** reacts faster, however, because it is less stable than **D** and therefore starts out at a higher energy.



(e) Compound **F**, unlike **E**, has a hydrogen with the correct geometry for an E2 elimination.

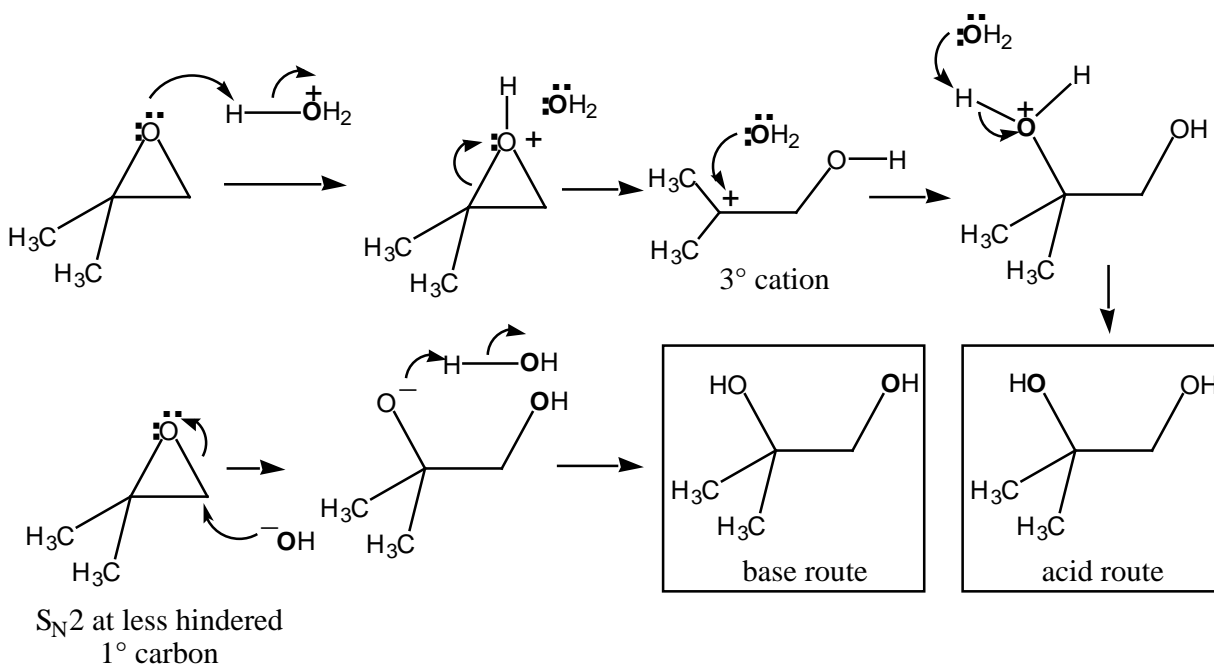


(f) The  $S_N2$  reaction is difficult because the substrate is a tertiary halide and the cage prevents the nucleophile from a "back-side" approach. It is also difficult to generate a planar, carbocationic center at the bridgehead (due to strain introduced in the cage), so  $S_N1$  and  $E1$  reactions are unfavorable. In fact, an elimination reaction of either kind,  $E1$  or  $E2$ , which would require a double bond to the bridgehead, is unfavorable because of poor orbital overlap (see below and p 115-117 in text).



This double bond is fictitious as the two orbitals making up the bond do not overlap.

- [2] Under acidic conditions the epoxide is protonated and the ring opens to give a stable tertiary cation. The cation is subsequently captured by water and deprotonated to give the final product by way of an  $S_N1$  mechanism. In the presence of a strong nucleophile such as hydroxide, however, the reaction proceeds by way of an  $S_N2$  mechanism at the less hindered, primary carbon.



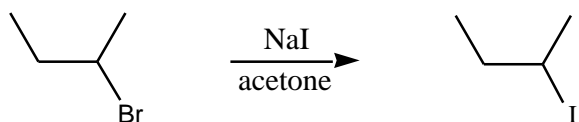
- [3] (a) The substrates are tertiary halides and therefore, under the given conditions,  $S_N1$  reactions are more likely than  $S_N2$ . Thus, the second reaction, which has a more stable carbocation intermediate than the first (why?), will be faster. Note that elimination reactions are not as important as we are dealing with relatively strong nucleophiles and weak bases.



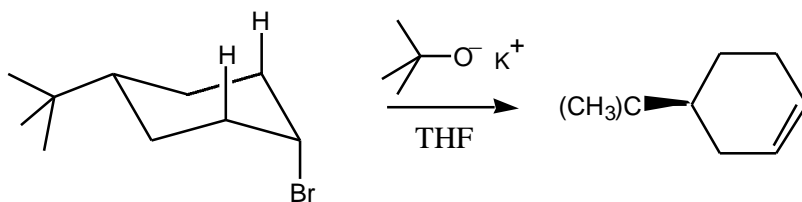
(b) These are primary halides that prefer to react by  $S_N2$  mechanisms. In this case, the transition state, which has developing charges, is stabilized by the more polar solvent. Hence the first reaction is faster.



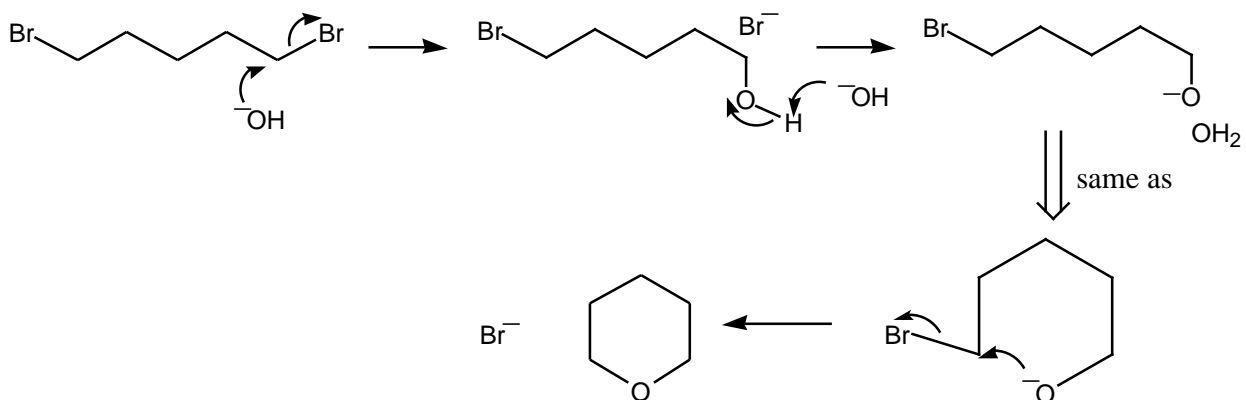
(c) Strong nucleophile, weak base, polar aprotic solvent, and secondary substrates all point to substitution by an  $S_N2$  mechanism. The key difference here is in the nature of the leaving groups. The second reaction is faster as bromide is a much better leaving group than methoxide. Also see answer to question 1b on the first page of this handout.



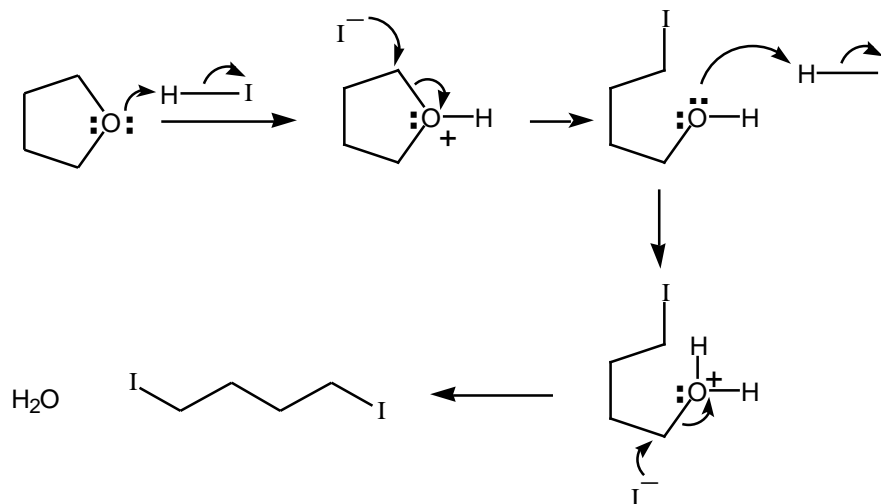
(d) The strong bulky base will afford an alkene from the secondary substrate by an E2 mechanism. The first reaction is faster as there are hydrogens with the correct antiperiplanar geometry required for the bimolecular elimination. Also see answer to problem 1e on the second page of this handout.



[4] (a) The crux of the mechanism involves two nucleophilic displacements; one intermolecular (in the first step) and the second intramolecular (in the final step).



(b) Protonation by HI gives a good leaving group that is displaced by iodide. Another round of a similar protonation-displacement sequence gives the final product.



(c) The alkenes result from E2 elimination reactions that require the leaving group to be antiperiplanar to the H (or D) that is being removed by base. Please pay particular attention to the stereochemistry of the resulting alkenes. When the deuterium is removed, the two methyl groups wind up trans to each other. Removal of the proton, however, puts the methyl groups on the same side of the double bond. Newman projections are especially helpful in figuring out the geometric subtleties of the reaction. These are shown below.

