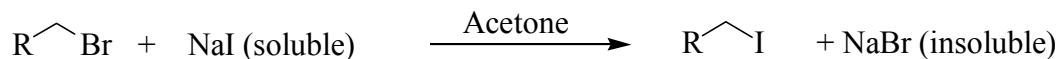


Organic Chemistry - CHEM 231A

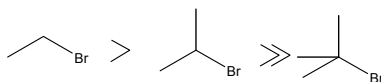
Problem Set #3

Due November 26, 2001

- 1a. Iodide ion is a good nucleophile and sodium iodide is quite soluble in acetone. On the other hand, sodium chloride and sodium bromide have low solubilities in acetone. As a result, the reaction of alkyl bromides and alkyl chlorides with NaI/acetone can serve as a *simple* test reaction as indicated below.

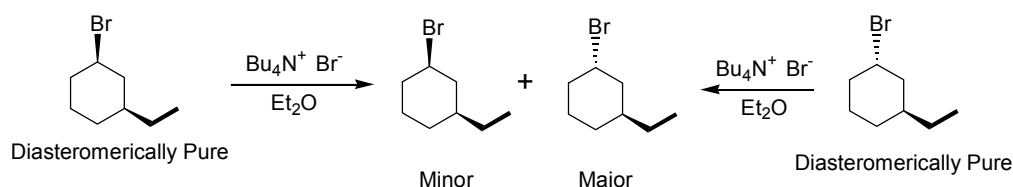


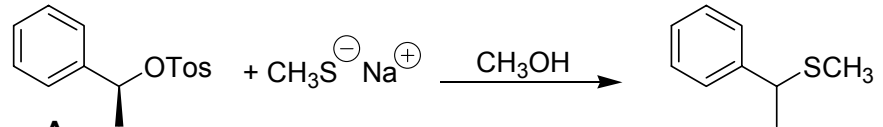
The reactivity order of the following alkyl bromides with NaI/acetone is:



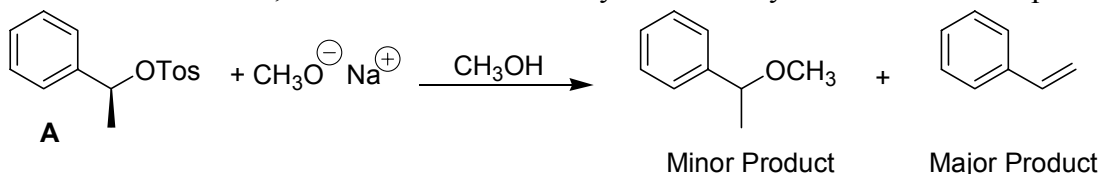
Write a mechanism for this reaction. Explain how your mechanism accounts for the observed reactivity order. (It will help to build molecular models.)

- 1b. The optical rotation of a solution of (+)-2-bromobutane in diethyl ether does not change with time. However, when tetrabutylammonium bromide is dissolved in this solution, the rotation decreases slowly with time to zero. The NMR spectrum of the solution, however, does not change. Clearly explain what is happening. Why does the rotation decrease to zero? Why doesn't it become negative?
- 1c. Explain the following observation: Reaction of either diastereomeric pair of 1-bromo-3-ethylcyclohexane in the presence of tetrabutyl ammonium bromide yields the same diastereomeric ratio, with the trans diastereomer predominating.



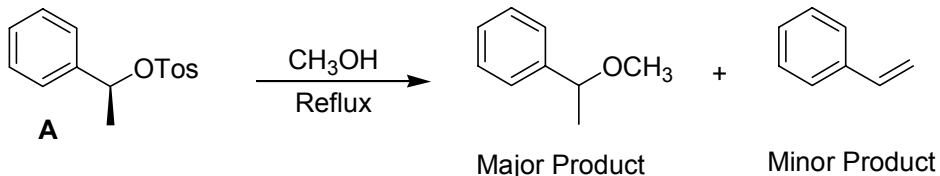
- 1d. Discuss how these three experiments above are related to our general understanding of the mechanism of bimolecular nucleophilic substitution reactions.
- 2a. When the optically active tosylate (A) shown below was reacted with CH₃SNa in CH₃OH, the reaction was observed to be second order and the substitution product shown was formed almost exclusively. Show the mechanism for this reaction and predict the stereochemistry of the product.
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- The diagram shows the reaction of tosylate (A) with methanethiolate (CH₃S⁻ Na⁺) in methanol (CH₃OH). The starting material (A) is 1-phenylethyl tosylate with the tosylate group on a wedge. The product is 1-phenylethyl methyl sulfide with the methyl group on a dash.
- 2b. If the solvent in part (a) was changed from methanol to dimethylformamide (DMF) the same product was formed but at a much faster rate. Explain.

- 2c. When **A** was reacted with NaOCH₃ in CH₃OH, the reaction was still kinetically second order. However, the major product was the alkene shown below. Account for the shift from predominant substitution for the reaction in part (a) to predominant elimination for the reaction with CH₃ONa/CH₃OH. Also, show the stereochemistry of the methyl ether substitution product.



- 2d. How would you change reagents or reaction conditions so that **A** would give almost exclusively the alkene (C₆H₅CH=CH₂)?

- 2e. When **A** is refluxed in methanol (no added CH₃ONa), both substitution and elimination products are formed as in part (c). However, substitution predominates and the stereochemical result is different than that observed for part (c). Predict the stereochemistry of the substitution product and explain why these results are observed from the reaction of **A** in methanol.



3. Consider the following reaction conditions and NMR spectra:

The starting material, compound A, C₇H₁₅BrO, has the following NMR spectrum:

Doublet	1.2 ppm	int 5.6 cm	Quintet	1.23 ppm	int 3.8 cm
Quartet	1.51 ppm	int 3.7 cm	Doublet	1.79 ppm	int 5.7 cm
Quartet	1.87 ppm	int 3.6 cm	Sextet	3.83 ppm	int 1.8 cm
Sextet	4.13 ppm	int 1.9 cm			

When A is reacted with NaH in Et₂O at 0 °C, one product, compound B, C₇H₁₄O, is formed with the following NMR spectrum:

Doublet	1.21 ppm	int 4.2 cm	Quintet	1.25 ppm	int 1.3 cm
Quartet	1.49 ppm	int 3.0 cm	Sextet	3.85 ppm	int 1.2 cm

- 3a. What is the structure of compound A?
 3b. What is the structure of compound B?
 3c. Write a mechanism that accounts for the formation of compound B.
 3d. In a different reaction, when compound A is heated in dimethyl formamide, not only is compound B formed, but a new product, compound C, C₇H₁₄O, is formed with the following NMR spectrum:

Doublet	1.22 ppm	int 4.4 cm	Quartet	1.53 ppm	int 3.1 cm
Doublet	1.61 ppm	int 4.5 cm	Quartet	2.05 ppm	int 3.0 cm
Sextet	3.79 ppm	int 1.5 cm	Quintet	5.35 ppm	int 1.4 cm
Quartet	5.39 ppm	int 1.5 cm			

3d. (cont) What is the structure of compound C?

3f. Write a mechanism that accounts for the formation of compound B & C.

4. Perform a retrosynthetic analysis AND a step-by-step synthesis of each of the following compounds. When doing the retrosynthetic analysis, work backwards one step at a time. Writing mechanisms are NOT required.

