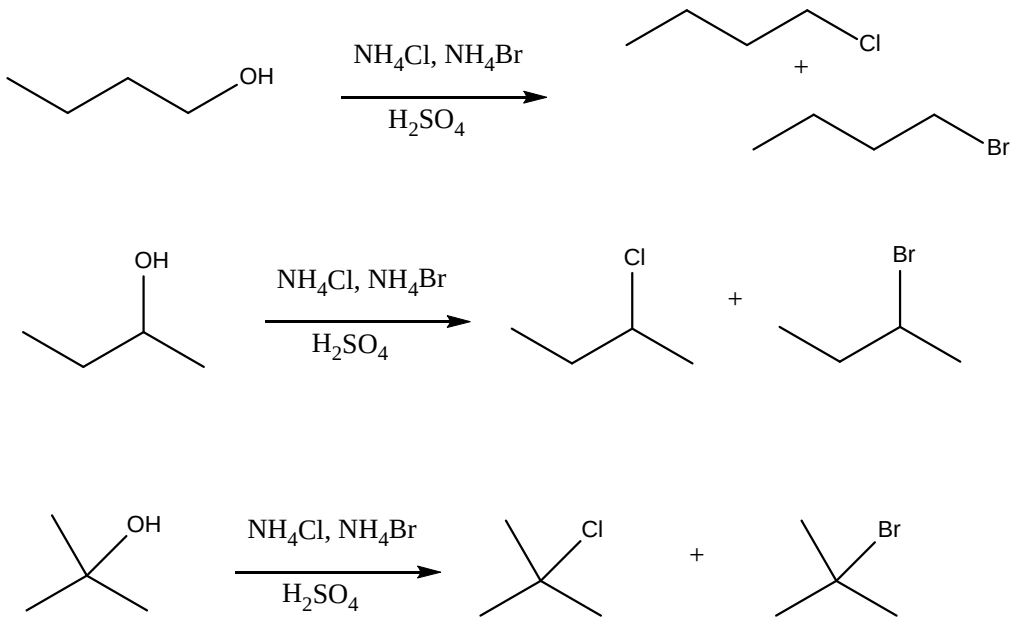
Experiment #3 – Mechanistic Study of the Halogenation of Primary, Secondary and Tertiary Alcohols

Reference. Experiment adapted from *Introduction to Organic Laboratory Techniques; A Microscale Approach*, 3rd edition by Pavia, Lampman, Kriz, and Engel; Brooks/Cole - Thomson Learning: Pacific Grove, CA, 1999.

Relevant textbook readings. Smith, Chapters 7 and 9, Mohrig, Techniques 11, 12, 16 and 19.

Overview. You will investigate the influence of structure on the substitution of a primary (1-butanol), a secondary (2-butanol) and a tertiary (2-methyl-2-propanol) alcohol. An equimolar mixture of ammonium chloride and ammonium bromide in sulfuric acid will be reacted with each alcohol to produce a mixture of the corresponding alkyl bromide and alkyl chloride. The ratio of these will be determined for each reaction and this information will be used to evaluate which substitution mechanism is operating for each substrate. Each group will run the reaction using either 1-butanol or 2-butanol, and each group will run the reaction with 2-methyl-2-propanol



PART ONE: Reaction of 1-butanol or 2-butanol

Running the Reaction. Add 10 ml of the warm nucleophile mixture to a 25 ml round-bottom flask and attach a condenser and drying tube which contains moistened glass wool. (The glass wool is used to trap any HCl or HBr fumes). Through the condenser add 0.75 ml of 1-butanol or 2-butanol then heat this to reflux using a sand bath. Maintain this gentle reflux (75 minutes for

1-butanol and 60- minutes for 2-butanol) to complete the reaction. During this long reflux you can run 2-methyl-2-propanol reaction

Work Up. After reflux cool the reaction first in the air and then by immersing the flask (with the condenser still attached) in a beaker of cold tap water. Remove the condenser and add 0.75 ml of pentane and gently swirl the mixture. Allow the layers to fully separate; then using a pipet remove most of the lower aqueous layer and transfer it to a waste beaker. Transfer the remainder of the reaction mixture to a centrifuge tube or conical vial. Allow the layers to fully separate and remove the remaining aqueous layer. Wash the remaining organic layer first with 1.0 ml of water and then with 1-2 ml of saturated sodium bicarbonate solution. Transfer the organic layer to a reaction tube and dry it with anhydrous sodium sulfate. Transfer the dry solution to a capped vial for analysis.

Characterization of the Product. As indicated by your instructor, this solution will be analyzed using either Gas-Chromatography or ^{1}H NMR or both.

PART TWO: Reaction of 2-methyl-2-propanol

Running the Reaction. Add 6.0 ml of the nucleophile solution to a 15 ml centrifuge tube. Cool this tube using cold water (stop when crystals first begin to appear). Add 1.0 ml of 2-methyl-2-propanol, cap the tube and shake it vigorously for 5 min with occasional venting (wear gloves!).

Work Up. Allow the mixture to separate into two layers then remove the lower aqueous layer. (Do not leave any water – take a small amount of the top layer if necessary). Transfer the remaining organic layer to a reaction tube than contains 0.05 g of solid sodium bicarbonate. After bubbling has stopped, transfer the organic product to a screw capped vial. Note –to minimize evaporation the entire work-up process should be done as quickly as possible.

Characterization. This reaction product will be analyzed using either refractive index or ^{1}H NMR or both.

LAB REPORT

^{1}H NMR Interpretation. Assign peaks in the ^{1}H NMR spectra using literature values for the expected products. For the reaction of 2-methyl-2-propanol, the spectrum will be very simple because each product displays only one singlet and the relative integrations of these two singlets correspond directly to the product ratio. For the other two alcohols, the spectra will be much messier and the goal isn't so much to assign every peak (because some overlap), but to find a peak for each product that can be integrated so as to reveal the relative yield of that product. The protons on the carbon with the X attached (the "α protons") give well separated multiplets that can be used for this purpose. Convert the peak integrations to relative % product yields.

GC Interpretation. (See Mohrig Ch 19.) Two peaks (in addition to the pentane solvent peak, which elutes right at the start of the run) are expected for each reaction. The bromoalkane products have higher boiling points than the chloroalkanes, so the peak with the longer retention time can be assumed to be due to the RBr product. The peak areas (integrations) are assumed to be proportional to the relative amounts of each compound and are used to calculate relative % product yields.

Refractive index interpretation. (See Mohrig Ch 16.3-16.4.) For the 2-methyl-2-propanol reaction, no solvent is added during the work up procedures, so the obtained product mixture can be assumed to consist solely of the two products, t-BuCl and t-BuBr. (Does the ^{1}H NMR of your product support this assumption?) In such a case the refractive index of the mixture can be assumed to be a weighted average of the refractive indexes of the individual compounds that are mixed together: $\eta_{obs} = (\chi_A \times \eta_A) + (\chi_B \times \eta_B)$. In this equation χ_A and χ_B are the respective mole fractions for components A and B and must add to 1.0. η_{obs} is the observed refractive index of the mixture and η_A and η_B are the known refractive indexes of the individual compounds. Given the observed and literature refractive indexes, you can solve for the mole fractions of each compound, which in this experiment equates to the percentage yields of the two products.

Results Tables. Your results should include a table or tables that include all key raw data and calculated values. The final calculated percentages of chloro and bromo alkanes from each of the three reactions for each analytical method used should be included. The key data for each method used should also be included along with relevant literature values. For the refractive index measurement the measured refractive index, temperature and corrected refractive index should be given. For the ^{1}H NMR the chemical shift, splitting and integration of each peak should be included. For gas chromatography the retention times and peak areas should be included.

Results and Discussion. The main point of the experiment is to determine which nucleophilic alkyl substitution mechanism is occurring for each of the three reactions. Your discussion should use the data to draw conclusions as to the most likely mechanism for each alcohol. Make sure the conclusions are clearly backed up by the data you have collected and informed by the knowledge you are gaining from lecture.