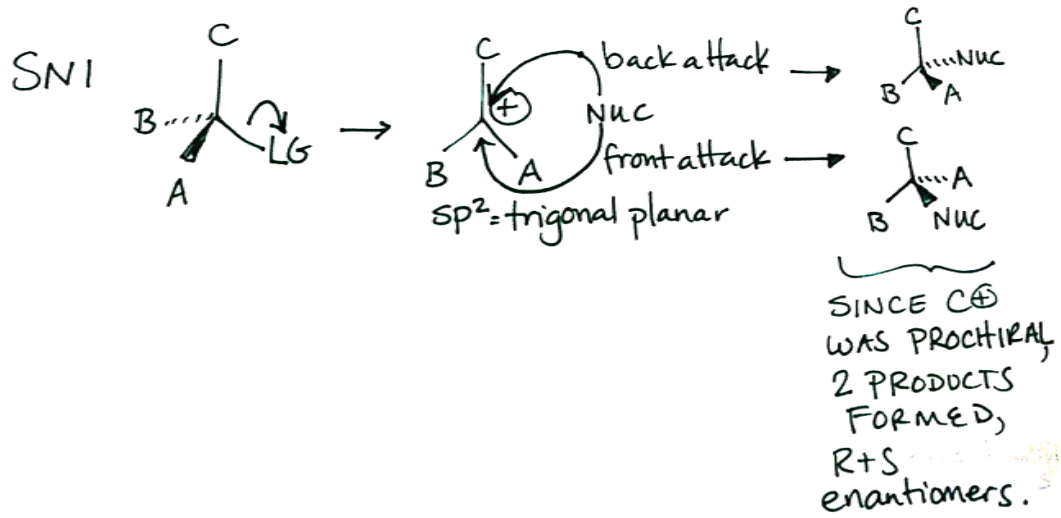
12AL Experiment 11 (3 days): Nucleophilic Substitution Reactions

Instructor note: Day 1 (half of the class); Day 2 (other half); Day 3 (everyone to finish up any separation & purification steps etc). Initial reflux reaction must be performed under hood and there is limited space; also, limited macro distillation equipment. As always, experiments are individual.

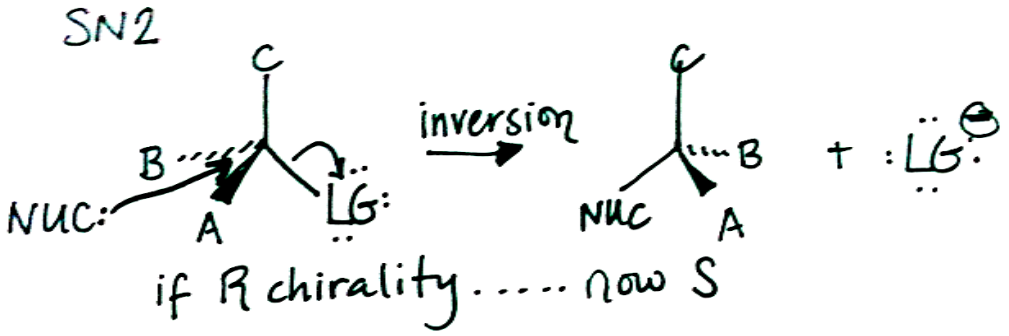
Safety: Proper lab goggles/glasses must be worn (even over prescription glasses). As always, ask where organic waste containers are located in the lab.

Background: Nucleophilic Substitution Reactions are important reactions that allow one to remove one functional group and replace it with another. For example, an alkyl halide can easily be converted to an alcohol by reaction with sodium hydroxide or water. An alcohol can be converted back to an alkyl halide by reaction with acid halides, HX. In general, any functional group can be removed from the reactant and replaced as long as the incoming nucleophile is a stronger base than the leaving group OR if a leaving group can leave first creating a very stable carbocation intermediate. (It is very important that you review the strengths of acids and bases and the factors that affect their strength from the beginning chapters of your lecture textbook – this has been a prevalent theme all semester long!)

There are two types of nucleophilic substitution reactions: SN1 and SN2. Unimolecular SN reactions (SN1) are two-step reactions characteristic of secondary and tertiary reactants. The first step is the rate-determining step as the leaving group breaks off creating a high energy carbocation intermediate. Thus, SN1 reactions are said to be unimolecular because the RDS only involves one molecule, the reactant that is to be substituted. SN1 reactions do NOT depend on the strength of the incoming nucleophile, which attacks the carbocation quickly in the second step of the reaction. Polar protic solvents, like water, acids, & alcohols, support SN1 reactions due to the stabilizing attraction between the carbocation and the electron rich atoms in the polar protic compound. Please note that solvents may also play the role of the attacking nucleophile. It is also important to pay attention to the groups that are attached to the carbocation – remember, if you have 3 unique groups attached to your carbocation, it is said to be prochiral – that is, the carbon will become chiral if the attacking nucleophile is also unique. Remember, carbocations are sp2 hybridized assuming a trigonal planar shape – flat surfaces can be attacked from two opposite sides, causing two enantiomers to form. Be careful when drawing mechanisms and pay attention to these details.



Bimolecular SN reactions (SN2) are one-step reactions characteristic of primary and secondary reactants. This concerted one-step involves the simultaneous departure of the leaving group and the attack of the incoming nucleophile. Thus, it is important for the reactant to be non-bulky. Also, because two molecules are involved at once, the incoming nucleophile must attack the electrophilic carbon from the backside as the leaving group leaves – therefore, a chiral carbon will invert its chirality assuming the incoming nucleophile is high priority. It is important to always check your chirality and make sure you are properly inverting structures when you draw your products. SN2 reactions are dependent on the strength of the incoming nucleophile – it must be a stronger base than the leaving group for a reaction to occur – if the leaving group is a stronger base, then a primary reactant will not undergo a reaction; a secondary reactant, however, still may proceed through an SN1 mechanism. The best type of solvent for SN2 reactions depends on the type of nucleophile that is attacking – negatively charged nucleophiles will be hindered by polar protic solvents preventing attack on primary reactants, and causing secondary reactants to undergo another mechanism – SN1. So it is important if running an SN2 reaction on a primary reactant to choose a polar aprotic solvent, like acetone or DMSO, when using a negatively charged nucleophile. Neutral nucleophiles, on the otherhand, are not as attracted to a polar protic solvent and can proceed without interruption.



Today you will be reacting different butanols with acid halides. The goal is to remove the alcohol and replace it with a halogen. Things to consider: are my alcohols primary, secondary, or tertiary? Who is the nucleophile? Who is the solvent? Is my nucleophile charged? If so, will the nucleophile be affected by the solvent? Will this affect the type of mechanism any secondary butanols undergo? Do I need to worry about chirality? These are important questions to consider anytime you are working with nucleophilic substitution reactions.

Objective: 1. To perform a series of nucleophilic substitution reactions. 2. To successfully synthesize an alkyl halide from an alcohol. 3. To use IR spectroscopy to prove purity of product. 4. To practice a series of SN reactions in the postlab in order to understand all the aspects of each SN reaction.

Procedure:

1. Set up a REFLUX apparatus IN THE HOOD. Use a hot plate for heating.

2. Measure out 6.6 mL of alcohol (Day 1 students: 1-butanol; Day 2 students: 2-butanol) and put in your reflux round-bottom flask.

3. Add ACID-RESISTANT boiling chips – we have two types in our lab: Glass Beads & a special Plastic Chip (do not use the calcium carbonate chips that you usually use).

4. Cool the flask in an ice-water bath in the hood. VERY SLOWLY add 10.0mL of 48% hydrobromic acid; swirl the flask.

5. VERY SLOWLY add 2.0 mL concentrated sulfuric acid (18M). Swirl the flask.

6. Remove flask from ice-water bath and carefully attach and clamp to reflux apparatus. Heat under reflux for **ONE HOUR** (start timing once mixture begins to boil).

7. Let cool to room temperature before removing from apparatus.

8. Set up a MACRO Simple-Distillation apparatus. Remember, never let go of a piece of glassware until it is securely clamped; lightly lubricate all glass joints with glycerol.

9. Co-distill your product and water using a graduated cylinder as the collection container. Your alkyl bromide product and water have almost identical boiling points so they co-distill together. Collect the first 6.0 mL of co-distillate leaving behind the higher boiling point species in the flask.

10. Pour the 6.0 mL of co-distillate into a clean large test-tube. Rinse the graduated cylinder with 10.0 mL of dI water and also pour into the test-tube. Cork the test-tube and gently shake.

11. Separate the organic and aqueous layers using a plastic pipette. What piece of information do you need to look up in order to determine if your 1-bromobutane/2-bromobutane is on the top or bottom?

12. Dry the organic layer by adding a tiny amount of anhydrous powder. Remember, just a tiny amount to soak up any remaining water droplets that you may have not been able to remove.

13. Run an IR on your product. Analyze your IR – ALL bonds and their wavenumbers should be labeled in the appropriate positions on the spectrum. Also, draw the structure of your product on the spectrum. Attach to your postlab.

12AL Prelab Experiment 11: Nucleophilic Substitution Reactions

Complete the following information. If needed, review and/or research nucleophilic substitution reactions in your lecture textbook.

1. SN2
    a. Name =

    b. How many molecules involved in slow step?

    c. How many steps involved in mechanism?

    d. List what occurs in the step(s)

    e. When do you have to worry about chirality?

    f. What type of reactants undergo SN2?

    g. Secondary reactants undergo SN1 & SN2. If the nucleophile is negatively charged, what solvent (polar protic or polar aprotic) will support SN2?

    h. Secondary reactants undergo SN1 & SN2. If the incoming nucleophile is a weaker base than the leaving group, what will occur?

2. SN1
    a. Name =
    b. How many molecules involved in slow step?
    c. How many steps involved in mechanism?
    d. List what occurs in the step(s)
    e. When do you have to worry about chirality?
    f. What type of reactants undergo SN1?
    g. Secondary reactants undergo SN1 & SN2. What solvent (polar protic or polar aprotic) will support SN1?

12AL Postlab Experiment 11: Nucleophilic Substitution Reactions

1. Have you attached your completely analyzed IR?

2. Given the following reactants, perform the following tasks:

   a. Label the alcohol type: primary, secondary, or tertiary

   b. Label whether the alcohol will undergo SN1 or SN2 AND briefly indicate why.

   c. Perform the appropriate mechanism; watch your stereochemistry where necessary. Label any chirality (R, S) of product(s).

3-pentanol + HCl

1-pentanol + HCl

(3S) 3-hexanol + HCl

(3R) 3-methyl-3-hexanol + HCl

3-ethyl-3-pentanol + HCl