REACTION: Witting Reaction

In this experiment, a traditional Witting reaction will be carried out to synthesize an alkene product. You will generate the phosphine ylide in situ by deprotonating the phosphonium chloride salt. You will use a variety of aldehydes and evaluate the reactivity of each product. The stereochemistry of the alkene products will be examined by TLC and proton NMR.

Aldehydes:

- benzaldehyde
- 4-methylbenzaldehyde
- p-anisaldehyde
- p-chlorobenzaldehyde
- cinnamaldehyde

READING ASSIGNMENT:

- This handout for background and procedure!
- Supplementary info can be found in Janice Gorzynski Smith (2nd Ed) Chapter 21.10

PRE-LAB ASSIGNMENT:

- Rewrite the procedure in your own words!
- Table of reagents including the amounts you will need of each aldehyde (look up the molecular weights of each and based on those calculate the amount required for each)

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1 Adapted from a procedure provided by Dr. Layne Morsch, Ph. D., University of Illinois Springfield
**BACKGROUND:**

The German chemist Georg Wittig developed the **Wittig reaction** in 1954, but it took 25 years before he received full recognition for originating one of the most synthetically useful reactions in organic chemistry. In 1979, Wittig shared the Nobel prize in chemistry with Hebert C. Brown of the United States. The Wittig reaction is often used for the preparation of alkenes from carbonyl compounds, especially for the synthesis of exocyclic alkenes that are difficult to prepare from other methods.

The Wittig reaction is used to construct larger molecules with carbon-carbon double bonds. The reaction involves the attack of a nucleophilic carbon atom, stabilized by a neighboring electron-withdrawing group, on the carbonyl carbon atom of an aldehyde or ketone. In the Wittig reaction, the nucleophile is a phosphorus ylide, which is stabilized by resonance involving a triphenylphosphonium group. An **ylide** is a species that contains two oppositely charged atoms bonded to each other, and both atoms have octets. After the attack on the aldehyde a stable betaine intermediate is formed (both phosphorus and oxygen now have complete octets) and then collapses to yield the desired alkene product and phosphine oxide. The driving force for this reaction is the irreversible formation of phosphine oxide which has the strong P=O bond. The Mechanism of the reaction is shown below:

The stereochemistry of the Wittig reaction can be divided into two types depending on the structure of the Wittig reagents (or ylides): **Stabilized Wittig reagents** have a group, such as a carbonyl group, that can share the carbanion’s negative charge, and **Unstabilized Wittig reagents** do not have such a group. Stabilized Wittig reagents from primarily $E$ isomer, and unstabilized Wittig reagent form primarily $Z$ isomers. *Which type is the reagent you will be using this week?*
This particular procedure for the Witting reaction is considered to be green chemistry as it is using more environmentally safe reagents and excludes the use of an organic solvent.

**CAUTION**

**Benzyltriphenylphosphonium chloride** is harmful if inhaled, ingested, or absorbed through the skin. Wear gloves, and keep all chemicals/reactions in the hood at all times.

**Sodium hydroxide** is extremely corrosive! Wear gloves and avoid contact with skin, eyes, and clothing.

**All aldehydes** are skin irritants. Wear gloves and avoid contact with skin, eyes, and clothing.

**EXPERIMENTAL:**

Measure out 390 mg of the phosphonium chloride salt and the appropriate amount of aldehyde (1.1 equivalents with respect to the the phosphonium chloride) and place it in a 10 mL Erlenmeyer flask. Measure 2 mL of 6M NaOH and add it to the flask. Stir the mixture for 30 minutes at room temperature. The product is a non-polar organic molecule and will be insoluble in the aqueous solution and therefore precipitate out during the course of the reaction.

Use vacuum filtration to collect the product from the reaction mixture, rinse with ~ 10 mL of distilled water. Recrystallize the product using 95% ethanol.

Analyze your product using TLC (10% EtOAc in Hexanes). The E and Z isomers of the alkenes should show up as different spots on your TC plate (*Which one do you expect to show up higher on the plate? Why?*). Prepare an NMR sample by dissolving ~100 mg of your product in 1.0 mL CDCl₃. Follow your TA’s instruction on how to obtain an NMR spectrum.

**LAB WRITE-UP:**

Write a complete lab report as described in the *Report Guidelines for Students* handout. Include all your results and provide a discussion for the stereoselectivity of the reaction you ran (E vs Z alkene).