WITTIG REACTION USING A STABILIZED YLIDE: THE SYNTHESIS OF (E)-ETHYL CINNAMATE

(This experiment was developed and tested at Colby College with the help of Traci Speed '03.)

Background

The Wittig reaction, named after Georg Wittig, is employed to convert the carbonyl group of aldehydes and ketones into an alkene group. This reaction is of great importance in organic chemistry and led to a Nobel Prize for Wittig in 1979 that was shared with H.C. Brown who worked on organoborane chemistry. In a typical Wittig sequence (Scheme 1), triphenylphosphine (1) reacts with an alkyl halide (2) to form a phosphonium halide (3). The subsequent addition of a strong base eliminates the hydrogen halide to produce an alkylidenephosphorane, otherwise known as an ylide (4) due to the opposing charges on adjacent atoms.

Scheme 1

\[
\text{Ph}_3\text{P} + \text{R}_1\text{H}_2\text{C} = \text{X} \rightarrow \text{Ph}_3\text{P}^\circ - \text{CH}_2\text{R}_1 \xrightarrow{\text{base}} \text{Ph}_3\text{P} = \text{CHR}_1
\]

(1) \hspace{2cm} (2) \hspace{2cm} (3) \hspace{2cm} (4) \hspace{2cm} (5) \hspace{2cm} (6) \hspace{2cm} (7)

The anionic carbon of the ylide acts as a nucleophile, see Scheme 2, and adds to the carbonyl carbon in 5 resulting in the production of triphenylphosphine oxide (6) and an alkene (7). The reaction conditions can be manipulated to favor the production of either the E or the Z isomer by varying a number of parameters such as temperature, solvent, stabilizing salts, excess base, etc.

Scheme 2

\[
\text{Ph}_3\text{P} = \text{CHR}_1 + \text{O} = \text{CHR}_2 \rightarrow \text{Ph}_3\text{PO} + \text{R}_1\text{CH} = \text{CHR}_2
\]

(4) \hspace{2cm} (5) \hspace{2cm} (6) \hspace{2cm} (7)

Ylides such as (4) in which R\text{\textsuperscript{1}} = electron withdrawing groups are particularly stable and are commercially available. In this experiment, you will use one such stabilized ylide, (carbethoxymethylene)triphenylphosphorane (4, R\text{\textsuperscript{1}} = \text{CO}_2\text{Et}), to prepare (E)-ethyl cinnamate from benzaldehyde.

Procedure

In a clean and dry 50-mL round-bottomed flask equipped with a magnetic stir bar, weigh 0.5g benzaldehyde. Add 20 mL of dichloromethane to the flask. Loosely stopper the flask, place it in an ice bath, and stir for at least ten minutes. After this time, slowly add 1.97g
(carbethoxymethylene)triphenylphosphorane and continue to stir in the ice bath for an additional ten minutes. Then allow the solution to warm up to room temperature while continuing to stir.

Retrieve the stir bar from the flask and, using a rotary evaporator, remove the solvent from the reaction mixture. Add 10 mL of hexanes to the residue in the flask and gently stir with the glass rod. The product ester is soluble in hexanes but the triphenylphosphine oxide is not. Vacuum filter the solution using another 10 mL of hexanes to rinse the flask. Transfer the filtrate to another dry, clean, and tared round-bottomed flask. Remove hexanes using a rotary evaporator, weigh the flask again, and determine the percent yield of product. Finally, characterize the product using $^1$H NMR, GC/MS and IR. **Caution:** Triphenylphosphine oxide is detrimental to the column in the GC/MS instrument. So filter your solution through a disposable pipette, packed with tissue and a little silica gel, *prior* to injection.

**HAZARDS AND DISPOSAL**

Hexanes are flammable and both the ylid and benzaldehyde are potential irritants. The residue from the filtration step must be disposed in the specially marked solid waste container kept under the hood.

**PRELAB**

(a) Read the section 16.17 in your text.
(b) Draw a complete reaction scheme for this experiment using correct chemical structures.
(c) How can you tell the difference between (E)- and (Z)- ethyl cinnamate using $^1$H NMR spectroscopy?
(d) Identify the limiting reagent in this reaction. Be sure to show your calculations.

**WHAT SHOULD BE IN YOUR LABORATORY REPORT**

*Do not exceed a total of two pages for text.*

(a) Introduction (one brief paragraph)
(b) Using ChemBiodraw, show the mechanism for the reaction
(c) Results and discussion, including an analysis your data
(d) Conclusion (one paragraph)
(e) Attach all data, label clearly as attachments.