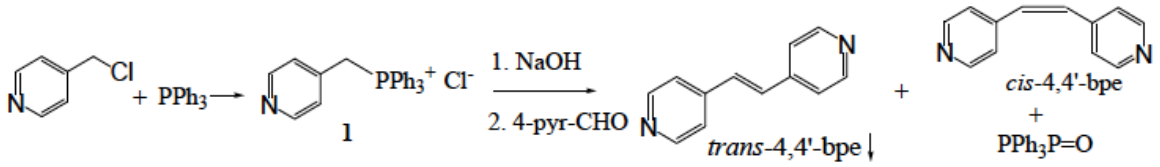
The Wittig Reaction: Preparation of *trans*-4,4'-bpe

Background:

The Wittig reaction provides an invaluable method for the conversion of an aldehyde or ketone to an olefin. This method involves the nucleophilic addition of a phosphorous stabilized anion (the ylide) to the carbonyl compound with subsequent elimination providing an alkene. Triphenylphosphine oxide, which contains a strong P=O bond, is produced as a side product in the Wittig reaction.



In this experiment, you will prepare *trans*-1,2-bis(4-pyridyl)ethylene (*trans*-4,4'-bpe) by the Wittig reaction. The product *trans*-4,4'-bpe will serve as the reactant in your Green Chemistry Experiment so <u>be sure to keep your product in a safe place</u> until the lab period. First, you will prepare triphenyl(4-pyridylmethyl)phosphonium chloride (**1**) that will form the ylide. Because the ylide is very reactive it is generated in the presence of the 4-pyridine carboxyaldehyde (4-pyr-CHO) by treatment of the phosphonium salt with a strong base (NaOH) to generate the alkene. Although the reaction produces a mixture of *cis*- and *trans*- isomers of 4,4'-bpe, only *trans*-4,4'-bpe will precipitate under the reactions conditions.

Procedure:

A. Preparation of triphenyl(4-pyridinylmethyl)phosphonium chloride (1)

Preheat an oil bath at 80 °C. Weigh 2.25 g of 4-pyridylmethyl chloride and 3.6 g of triphenylphosphine into a 50 ml Erlenmeyer flask. Add a stir bar and 15 ml of DMF to the flask, plug the flask with glass wool and stir the reaction mixture at 80 °C for 45 minutes. While the reaction is proceeding, prepare an ice bath for crystallization. After 45 minutes of stirring, cool down reaction mixture to room temperature then place the mixture in an ice bath and allow the product to sit undisturbed. A precipitate should begin to form within 15-20 min. If precipitation does not occur after 30 minutes, scratch the bottom of flask and add small chunks of ice to initiate crystallization. While waiting for the precipitation to complete, prepare a vacuum filtration apparatus. After 30 minutes you should have a significant amount (i.e. full flask) of a white-to-pale orange precipitate in the form of the salt **1**. Filter the precipitation by vacuum filtration. Obtain a melting point of your salt. A ^{1}H NMR spectrum of the salt will be provided and will need to be interpreted.

B. Preparation of *trans*-1,2-bis(4-pyridinyl)ethene (*trans*-4,4'-bpe)

Prepare a solution of 38% aqueous NaOH. *(Check with your TA to see if this is necessary; this solution may have been prepared for you in the stockroom.)* Weigh 25 g of NaOH and add the solid to 40 mL of cold distilled water in a 100 mL beaker while stirring with a glass rod or spatula to avoid forming a glassy chunk of solid that is difficult to dissolve. When all of the NaOH is dissolved, cool the solution by placing the beaker in an ice bath.

Weigh 4.0 g of the triphenyl(4-pyridinylmethyl)phosphonium chloride **1** that you prepared in Part A in a 125 mL Erlenmeyer flask and suspend the solid in 10 mL of dichloromethane. Plug the neck with glass wool. Stir the suspension for 5 minutes. Add 1.2 mL of 4-pyridine carboxyaldehyde to the suspension while stirring. Slowly add the **COLD** NaOH solution to the flask. Clamp the flask securely, re-plug the flask with the glass wool and allow the flask to stir for 30 minutes.

While the reaction is proceeding, assemble a 250 mL separatory funnel and a ring stand and prepare 35 mL (1 x 15mL and 2 x 10 mL) of dichloromethane and 100 ml of distilled water,. When the reaction is complete, transfer the solution to the separatory funnel, wash out the flask with 100 mL of distilled water and then with 15 mL of dichloromethane. Gently invert the funnel and do NOT shake to avoid an emulsion. After inverting the funnel 3 to 4 times, place the funnel on a ring stand and remove the cap. Wait for layers to separate. If you have an emulsion, gently swirl the contents with a glass rod. You may have a third middle layer. Drain only the bottom layer (dichloromethane layer) from your separatory funnel. Add fresh 10 mL of dichloromethane and gently invert the funnel. Again, drain off only bottom layer. Repeat one more time with the third portion of fresh 10 mL of dichloromethane. Collect and combine all of your organic layers. Drain and dispose the water and oily brown layer.

Place the organic layers that you collected back into the separatory funnel and add 30 mL of 10% HCl. Shake the funnel until the organic layer is colorless. Note that you can shake the funnel more vigorously than before since dichloromethane will not form an emulsion with the acid solution. Your product is now present in the <u>water layer</u>. Place your separatory funnel on a ring stand, remove the cap, and allow the funnel to sit for 5 min to allow two layers to separate. It is important not to have any content of the organic layer present in the upper water layer. Thus, drain <u>all</u> of the bottom organic layer and collect the water layer in a clean 125 mL flask.

The final step is to neutralize the acidic water solution that you collected using a 20% NaOH solution (approximately 10–15 mL). Add the NaOH solution <u>dropwise</u> to the acidic water solution with gentle stirring, occasionally checking the pH using litmus paper. <u>Do not allow the pH to get higher than 7.</u> You will know when you are close to the neutral point when you begin to see a precipitate forming and redisolving. Once the precipitate forms, do NOT add more NaOH. Check if the pH is 7. Assemble a vacuum filtration apparatus and be sure to record the mass of the filter paper. Collect the precipitate by vacuum filtration and record the mass of the product. Save the supernatent in a labeled bottle in your drawer for the next day.

C. Purification of *trans*-1,2-bis(4-pyridinyl)ethene (*trans*-4,4'-bpe)

In this part of the experiment, you will work in pairs. Place 500 mg of your product from **Part B** into a 125 ml Erlenmeyer flask. Your samples can be combined. Add 50 ml of 20% NaOH and stir the solution for approximately 5 minutes. Transfer the resulting solution and any residual solid to a separatory funnel. Wash the 125 ml flask with 20 ml of $CHCl_3$ and transfer the $CHCl_3$ to the separatory funnel. Invert the funnel and drain off the bottom organic layer. Repeat the extraction twice using two 20 ml portions of $CHCl_3$. Combine all organic layers and dry with $MgSO_4$. Filter off the $MgSO_4$ and pour the solution into a pre-weighed round-bottom flask. Remove the organic solvent using a rotary evaporator until the isolated solid is completely dry.

Obtain a melting point of your *trans*-4,4'-bpe. Prepare a sample for ^1H NMR analysis.

Results and Discussion

Calculate the percent yield for the preparation of triphenyl(4-pyridinylmethyl)phosphonium chloride **1**. What is the limiting reagent in the reaction? Calculate the percent yield of your final product. Include your NMR spectra in the Appendix of your report. Discuss both the overall yield and purity of your product *trans*-4,4'-bpe based on ^1H NMR data and melting point. Why do we treat the crude product obtained from your Wittig reaction with 10% HCl? Clearly explain your answer.

References:

The Wittig Reaction:

Louden, G.M. "Organic Chemistry", 2nd ed.; Benjamin/Cummings: Menlo Park, CA, 1988, pp 800-803.

Name: _____ Section: _____

ID #: _____ Date: _____

Preparation of triphenyl(4-pyridinylmethyl)phosphonium chloride:

4-pyridylmethyl chloride(g): _____

triphenylphosphine(g): _____

amount of triphenyl(4-pyridinylmethyl)phosphonium chloride (g): _____

% yield: _____

mp of triphenyl(4-pyridinylmethyl)phosphonium chloride (°C): _____

Preparation of *trans*-4,4'-bpe:

amount of *trans*-4,4'-bpe (g): _____

% overall yield of 4,4'-bpe: _____

mp of *trans*-4,4'-bpe (°C): _____