

# Wittig Reaction Using a Stabilized Phosphorus Ylid: An Efficient and Stereoselective Synthesis of Ethyl *trans*-Cinnamate

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The conversion of aldehydes and ketones into olefins, by means of the Wittig reaction (1), is an important synthetic procedure that is usually covered in most introductory organic chemistry courses. In a typical Wittig reaction (Scheme I), a phosphonium salt, 1, is treated with a base to generate the ylid, 2, which is subsequently reacted with a ketone or aldehyde to produce the alkene, 3. As the reaction is often performed under anhydrous conditions with strong bases, implementing the procedure in the undergraduate instructional laboratory could involve substantial resources and pose significant hazards. It is not surprising, therefore, that our present repertoire of Wittig reactions for teaching purposes is limited to a few creative experiments, most of which use aqueous sodium hydroxide as the base (2–7). There is also a report of an experiment using an “instant ylid” (8), a solid mixture of phosphonium salt and sodium amide, and an advanced procedure using dimsyl anion (9).

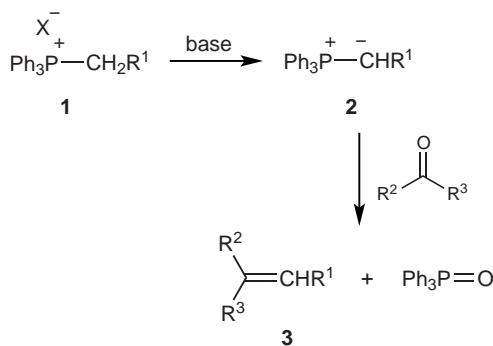
Phosphorus ylids such as 2, in which R<sup>1</sup> is an electron withdrawing group, are particularly stable and are commercially available. While the use of such ylids is widely reported in the chemical literature, there is no indication that these reagents have been used in the laboratory in a teaching context. In this article we describe an instructive experiment for the synthesis of ethyl *trans*-cinnamate, 6 (Scheme II), a pleasant smelling ester used in perfumery and flavoring, by the reaction of benzaldehyde, 4, with the stable ylid (carbethoxymethylene)triphenylphosphorane, 5. This reaction has also been reported in the literature (10).

The experiment is well suited to the teaching laboratory and offers several important advantages. The synthesis, workup, and characterization of 6 may be accomplished in a single laboratory session with commonly available laboratory equipment and glassware. The reagents are also relatively in-

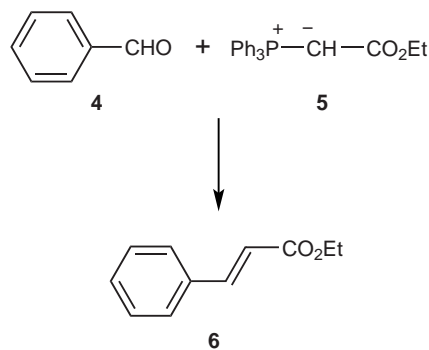
expensive, which might be an important consideration in courses with large enrollments. Furthermore, the product is obtained in high yield and excellent purity, and no special precautions are necessary to dry glassware, solvents, and reagents. The reaction is highly stereoselective in that the product is formed predominantly as the *trans* isomer, and the students can use <sup>1</sup>H NMR spectroscopy to ascertain the stereochemistry about the double bond. At the instructor's discretion, molecular modeling of the two isomers may be also included as an informative exercise to complement the wet chemistry.

## Experimental Procedure

Benzaldehyde (0.50 g, 4.7 mmol)<sup>1</sup> was weighed into a clean and dry 50-mL round-bottomed flask equipped with a magnetic stir bar, and dichloromethane (20 mL) was added. The flask was loosely stoppered, placed in an ice bath, and stirred for at least 10 minutes. After this time, (carbethoxymethylene)triphenylphosphorane<sup>2</sup> (2.0 g, 5.7 mmol) was slowly added to the flask. Stirring was continued in the ice bath for an additional ten minutes after which time the solution was allowed to warm up to room temperature. The stir bar was removed from the flask and the reaction mixture was freed of solvent using a rotary evaporator.<sup>3</sup> Subsequently, 20 mL of hexanes was added to the residue in the flask and the suspension was gently stirred with a glass rod. The mixture was filtered by vacuum using a Büchner funnel, and another 20 mL of hexanes was used to rinse the flask. The filtrate was transferred to a dry, clean, preweighed round-bottomed flask and the solvent was removed using a rotary evaporator. The pale yellow product was obtained in essentially quantitative yield<sup>4</sup> and was of adequate purity for analysis by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, and GC–MS.



Scheme I. Generalized Wittig reaction.



Scheme II. Wittig reaction to synthesize ethyl *trans*-cinnamate.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.69 (d,  $J = 16$  Hz, 1H), 7.52 (m, 2H), 7.36 (m, 3H), 6.44 (d,  $J = 16$  Hz, 1H), 4.26 (q,  $J = 7$  Hz, 2H), 1.34 (t,  $J = 7$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 166.9, 144.5 (carbon  $\beta$  to carbonyl), 134.4, 130.2, 128.9, 128.0, 118.3 (carbon  $\alpha$  to carbonyl), 60.4, 14.3.

IR (neat,  $\text{cm}^{-1}$ ): 3083, 3047, 2992, 1722, 1650.

MS ( $m/z$ ): 176, 131, 103, 77.

## Hazards

Caution should be exercised when using flammable solvents such as hexanes. Benzaldehyde and (carbethoxymethylene)triphenylphosphorane are potential irritants. Dichloromethane is a suspected carcinogen.

## Results and Discussion

The reaction is straightforward and proceeds in essentially quantitative yield. Isolation of the product is also simple and relies on the fact that triphenylphosphine oxide, a byproduct of the reaction, is insoluble in hexanes whereas the product ester, **6**, is soluble. This separation protocol demonstrates clearly how chemists take advantage of differential solubilities to purify compounds. There was also an excellent match between the  $^1\text{H}$  NMR, IR, and GC–MS data obtained by students and the literature data for **6**. In particular, students were able to use  $^1\text{H}$  NMR spectroscopy to verify that **6** has the trans configuration about the olefinic double bond. The coupling constant of 16 Hz displayed by the protons that are  $\alpha$  and  $\beta$  to the carbonyl group falls into the 12–18 Hz coupling constant range typical of the hydrogens of trans alkenes. A cis configuration would have displayed a coupling constant of 6–12 Hz.

Furthermore, we found it worthwhile to have our students model the E and Z isomers of **6** using the semiempirical PM3 method and compute charges on the  $\alpha$  and  $\beta$  carbon atoms. The calculation, which did not take much time, indicated that the E isomer was more stable than the Z isomer and, to the surprise of some students, there was less electron density at the  $\beta$  carbon than at the  $\alpha$  carbon. This exercise also provided an excellent opportunity to demonstrate the source of the significant differences in chemical shifts of the  $\alpha$  and  $\beta$  protons in **6** that appear at  $\delta$  6.44 and 7.69 ppm, respectively. Such a difference in chemical shift may be attributed to contributions from resonance structure, **6a** (Figure 1), that shows a positive charge on the  $\beta$  carbon and the influence of the phenyl substituent. These two effects perturb the magnetic environment around the  $\beta$  proton causing it to be somewhat more “deshielded,” and thus further downfield, relative to the  $\alpha$  proton.

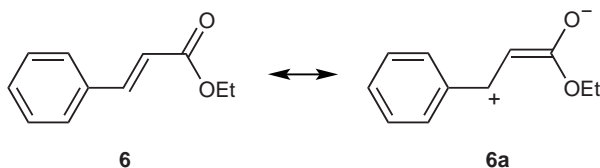


Figure 1. Resonance structures of ethyl *trans*-cinnamate.

## Conclusion

The Wittig reaction proved to be a valuable teaching resource in our experience and was also well received by students. In addition to illustrating the reaction itself, the experiment emphasizes important aspects of organic chemistry such as stereochemistry, instrumental analysis, and molecular modeling. It is anticipated that this exercise will augment and add variety to the limited pool of experiments currently available for teaching this important reaction.

## Acknowledgments

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## Supplemental Material

Instructions for the students, a list of chemicals and equipment, and the spectral and computational data are available in this issue of *JCE Online*.

## Notes

1. The experiment may also be run at half this scale with equally good results.
2. The ylid was obtained from Acros Organics. It should be refrigerated when not in use.
3. If a rotary evaporator is unavailable, simple distillation may be used to remove the solvent. The product obtained from simple distillation was discolored in some cases but gave comparable spectral data.
4. Occasionally, yields apparently in excess of one hundred percent were obtained owing to the presence of residual solvent or triphenylphosphine oxide. Increased cloudiness of the solution, during the evaporation of hexanes, gives an early indication of the incomplete removal of triphenylphosphine oxide. If it occurs, this problem is readily overcome by simply filtering the solution and continuing with the rotary evaporation.

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