Experiment 12: Wittig Reaction of trans-Cinnamaldehyde

Number of labs - two

Reactions performed – Wittig

Chemicals used: trans-cinnamaldehyde, benzyltriphenylphosphonium chloride, dichloromethane, 50% w/v NaOH

Supplies needed:

Techniques: Recrystallization

Prelab

The Wittig reaction was discovered in 1954 by Georg Wittig, for which he was awarded the Nobel Prize in Chemistry in 1979. It is one of the most direct methods for the synthesis of alkenes with the fewest isomeric products. The reaction utilizes a carbonyl compound as an electrophile, which is attacked by a phosphorus ylide (“Wittig reagent”) as the nucleophile. While many other routes to alkenes can proceed via elimination reactions (E1 or E2 reactions from alcohols or alkyl halides, for example), in elimination reactions the carbon skeleton is already pre-assembled. In the Wittig reaction, however, two smaller carbon units are conjoined to make the alkene double bond. Thus molecules of increasing size and complexity can be quickly assembled. In addition, there is no ambiguity regarding the site of the double bond. This is in contrast to elimination reactions, which give Zaitsev mixtures of more and less substituted structural isomers, as well as (where possible) the corresponding stereoisomers. The Wittig reaction is nicely complementary to the aldol condensation, in which carbonyl compounds are attacked not by a phosphorus ylide but by an enolate. Aldol condensations always result in “enones”, alkenes with a carbonyl attached. Wittig reactions are more general in that the product carbonyl does not need to have an attached carbonyl.

The general mechanism of the Wittig reaction is shown below. The phosphonium salt is deprotonated by base. The positively charged phosphorus atom is a strong electron-withdrawing group, which activates the neighboring carbon atom as a weak acid. For many phosphonium ions, a very strong base (butyllithium, sodium amide or hydrides) is required in order to do the deprotonation. The use of such strong base requires moisture-free conditions and inert atmospheres. In this experiment, the hydrogens being removed are activated in the benzyl position, and very concentrated sodium hydroxide is strong enough to carry out the deprotonation. This is because the carbanion 3 that is produced is stabilized not only by the positive phosphorus, but also by conjugation with the benzene ring.

Once the carbanion/ylide is formed, it is strongly nucleophilic, and attacks carbonyls just like other strong nucleophiles, producing an alkoxide. The alkoxide rapidly closes onto the phosphorus
to form the 4-membered oxaphosphetane ring, which is not thermodynamically stable at higher temperatures. The 4-membered ring, rapidly fragments by what is called a reverse [2+2] electrocyclic process to give the desired alkene and triphenylphosphine oxide as a side product.

Using the example in the mechanism, one can clearly see that although the Wittig is a powerful synthetic reaction, it gives a rather large molecule as a by-product, triphenylphosphine oxide. This material can, in theory (rarely in practice), be reduced back to the phosphine. P-O bonds are very strong, and the strong reducing agents necessary are often more expensive than just purchasing more triphenylphosphine.

Finally, although Zaitsev mixtures of alkenes are avoided, stereoisomers (cis/trans, E/Z) are still formed as mixtures. These are usually formed as the result of which possible oxaphosphetane intermediate is more stable. Often, trans- or E-isomers are preferred. The starting cinnamaldehyde in this experiment is trans or E in configuration. The two possible products for your Wittig reaction are E,E or E,Z. This can be discerned by a difference in melting point. (E,E)-1,4-diphenyl-1,3-butadiene has a melting point of 153 °C, while the (E,Z)-isomer has a melting point of 88 °C.

Lab 1
Part 1: Wittig Reaction
- In a clean, dry 25-mL round-bottomed flask, combine 3.0 mmol (calculate the mass needed, density = 1.05 g/mL) of trans-cinnamaldehyde and 5 mL of dichloromethane.
- Add 1.17 g of benzyltriphenylphosphonium chloride along with a magnetic stir bar.
- With vigorous stirring, using a short stem syringe-pump pipette, add 2.0 mL of 50% NaOH drop wise over 30 seconds to 1 minute. Observe any changes in the reaction.
- Attach a condenser to the flask; flowing water through it is not necessary.
- Stir the mixture at room temperature for 30 minutes.

Part 2: Separation
- Transfer the mixture to a separatory funnel, followed by 20 mL of dichloromethane and 15 mL of water to wash the remnants of the mixture into the funnel.
- Drain the lower dichloromethane layer into a small beaker and set aside.
- Drain the contents of the separatory funnel into a waste beaker.
- Return the dichloromethane layer to the separatory funnel and wash with 20 mL of water.
- Drain the dichloromethane layer into a clean, dry beaker and dry over Na₂SO₄.
- Decant the solution phase into another clean, dry beaker and allow the solvent to evaporate in your drawer until the next lab period.
Lab 2:
Part 3: Purification

- Add 5 mL of 60% ethanol with a few drops of HCl (any molarity) added to the oily material remaining in the beaker. A solid should form, that with further trituration (breaking up and mixing with a stirring rod) should become more solid and colorless (white) over time.
- Collect the solid by vacuum filtration. *This procedure above removes the bulk of the triphenylphosphine oxide by-product of the Wittig reaction. It can be used to recover the material if it were to be recycled (by reduction of the phosphine oxide to phosphine).*
- To do the final purification, the solid can be recrystallized from 95% ethanol. Perform this recrystallization, and collect the material again by vacuum filtration (you will have to clean your Buchner funnel and use fresh paper).
- Dry the solid under the heat lamps for 10 minutes. Obtain a melting point and FT-ATR spectrum. Determine which isomer of 1,4-diphenyl-1,3-butadiene you obtained.