The Wittig
Reaction: Synthesis of Alkenes

1 Benzyltriphenyl-phophonium chloride — mw = 389 g/mol
2 9-Anthraldehyde — mw = 206 g/mol
3 The "Wittig Reagent" an "ylide"
**4** 9-(2-Phenylethenyl)anthracene — mw = 280, mp = 100-150°

Intro   The "Wittig Reaction" is one of the premier methods for the synthesis of alkenes. It uses a carbonyl compound as an electrophile, which is attacked by a "phosphorus ylide" (the "Wittig reagent".)   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. (In contrast to elimination reactions, which often give mixtures of "more substituted" and "less substituted" structural isomers.) 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 alkene product **4** that you make today is the one that was used a few weeks ago as the colorizer for the chemiluminscence experiment (it gave the green solution.)

General Wittig Reaction: Synthesis of Alkenes
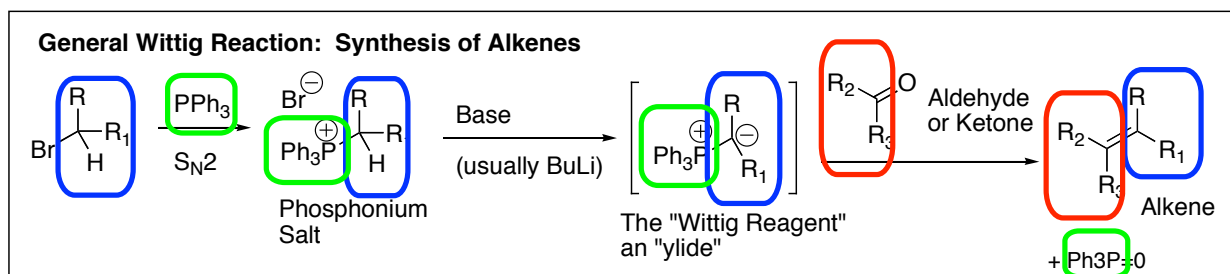
Mechanism

The general mechanism of the Wittig reaction is shown above. The phosphonium ion 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 (commonly butyl lithium) is required in order to do the deprotonation. The use of such strong base requires moisture-free conditions such as were required for doing the Grignard reaction. In today's experiment, however, very concentrated sodium hydroxide is

Wittig Mechanism
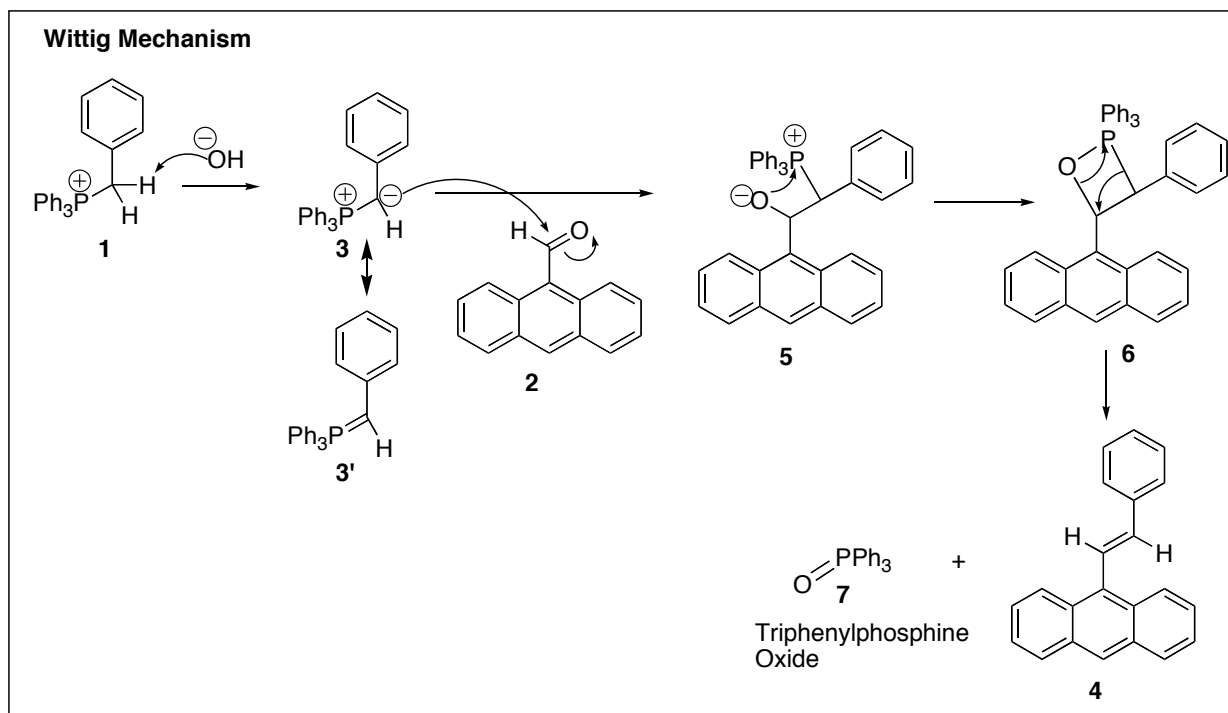
strong enough to do the deprotonation. This is because the carbanion **3** that is produced is stabilized not only by the positive phosphorus, but also by conjugation with the benzene ring. Notice that carbanion **3** has a resonance structure, **3'**, in which it is unnecessary to draw any formal charges. Either resonance structure is reasonable; **3'** has the advantage that it involves no formal charge, and has a double bond to carbon in exactly the same place where the final alkene C=C double bond ends. But **3'** has the disadvantage that it doesn't illustrate why the carbon should be so nucleophilic. In addition, it involves a phosphorus with five bonds. Resonance structure **3** is useful in that it shows why the carbon should be so nucleophilic, and also is consistent with the popular octet rule.

Once the carbanion/ylide **3** is formed, it is strongly nucleophilic, and attacks carbonyls just like other strong nucleophiles (for example, Grignard reagents…), producing an alkoxide **5**. Alkoxide **5** rapidly closes onto the phosphorus to form the 4-membered ring **6**, which is not very stable. The "betaine" **6**, with its 4-membered ring, rapidly fragments to give the desired alkene **4** and triphenylphosphine oxide **7** as a side product.

Wittig Reactions and the Phosphine Oxide Side Product 7: This side product is non-trivial to remove. It's too "organic" to wash out into a water layer, and it's too heavy to boil away. In today's experiment, we will remove it based on its polarity and H-bonding ability, in contrast to the non-polar alkene **4**. This separation will be accomplished by recrystallization from a somewhat polar hydrogen-bonding alcohol solvent, but it needs to be done carefully to selectively remove phosphine oxide **7** without losing too much of alkene **4**.

The Diagnostic Color Changes of Wittig Reactions: One interesting aspect of Wittig reactions that is not well illustrated today is that normally the carbanion/ylides **3** are colored, often intensely so. (Many are a deep, blood red or sometimes grape-juice purple). The product alkene and phosphine oxides are normally not colored, as is normally true of the phosphonium salt and the carbonyl electrophile. Thus you can often monitor Wittig reactions by color: formation of color shows you've made the ylide; disappearance of the color shows that the ylide has reacted and gone on to final products. While you will see some meaningful color changes today, they won't be as intense or diagnostic, for a couple of reasons. 1) In today's case, the extended conjugation of both the starting anthraldehyde **2** and the product alkene **4** make both of them colored. So whereas

normally there is no color at the beginning or the end, only during the ylide middle, today the colors of both the starting aldehyde and the product alkene partially mask the color of the ylide. 2) In today's case, the conjugation of the ylide carbanion with the benzene weakens the color of the ylide. It's not nearly as intense or red as for a non-conjugated ylide. Still, you will be able to see some changes in color as the reaction proceeds.   One additional factor to consider is whether the phosphonium salt or the carbonyl is the limiting reactant. If the carbonyl is in surplus, all of the ylide (and it's color) should get consumed. But if the carbonyl is limiting, even after it is fully reacted there may be some residual ylide (and it's color) that survives.

        The Unusual Solvent Combination for Today: Most reactions are conducted in a homogeneous solution, where everything is dissolved and can move around such that reactants can collide. This is difficult to accomplish, however, when you have both strongly hydrophobic reactants (the aldehyde in today's experiment) and strongly hydrophilic reactants (sodium hydroxide). The phosphonium salt is also ionic, and thus also has problems dissolving in organic solvent. Rather than having a homogeneous solvent system that can get these extremely opposite chemicals all into the same solution, today's solvent system will be a mixture of water and dichloromethane. These two are not cosoluble, and will give two separate layers. Thus the ionic hydroxide and the phosphonium salt can go into the water, and the aldehyde and the product alkene can go into the dichloromethane. When the ylide forms, it has no overall charge, and thus can switch phase from the water to the organic phase. (This is called a "Phase Transfer" reaction.) **Note: Phase transfer can only take place at the interface between the two phases. In order to maximize contact between the two phases, it is very important that the mixture be well stirred to provide lots of small droplets and lots of surface area for organic/water contact.**

Wittig Reaction Procedure
1. May work with partner, or may work alone.
2. Place a small (smallest possible) stirring bar in a large test-tube.
3. Set the test-tube into a 125-mL Erlenmeyer so that you can stand it on a stir-plate. (Or clamp.)
4. Weigh out ~0.300 g of 9-anthraldehyde **2** and add this to the test tube. (Record exact mass)
5. Add three pipets of dichloromethane and stir. (Squeeze the bulb, draw up what you get, ~1mL)
    - Note: does the aldehyde dissolve?
    - What color is the solution?
6. Weigh out 0.480 g of benzyltriphenylphosphonium chloride **1** and place it into the test tube.
7. Add 1 pipet of water, using this to try to rinse down any phophonium salt that's stuck on the sides
    - Note: does the salt dissolve?
    - What color is the salt?
    - Is the solution warm to the touch at this point?
8. Stir the mixture vigorously, and then add 0.65 mL of 50% sodium hydroxide solution by syringe.
    - Note: Is the solution warm to the touch at this point?
    - What colors are the layers?
    - Which layer is on top, the aqueous or the organic layer?
9. Stir the solution vigorously for 10 minutes.
10. Workup: Dilute with 5 mL of dichloromethane and 12 mL of water, and pour the mixture into the separatory funnel. Add 20 more mL of water to the separatory funnel
11. Rinse the test tube with another 3 mL of dichloromethane and 12 mL of water and pour this also into the separatory funnel.   Shake it up vigorously, and then allow time to settle.
    - Which layer is on top, the aqueous or the organic layer?
12. Pour the organic layer into a 125-mL Erlenmeyer. (Adding a long-stemmed funnel may help.)

13. Add an additional 8-mL of dichloromethane to the separatory funnel, and shake vigorously again. (Any yellow color is product, so where yellow is, more CH_2Cl_2 rinse might be good….)
14. Pour the organic layer into the same 125-mL Erlenmeyer that has the other dichloromethane.
15. "Dry" the organic solution with sodium sulfate.
16. At this point or sooner, get a 400-mL beaker ~1/3 filled with hot water in it, and warm on hot plate. Maybe target ~55° water bath; with the hot-plate around 5, maybe?)
17. Filter the organic solution into a separate ground-glass-neck125-mL Erlenmeyer, using a long-stemmed funnel lightly-plugged with glass wool to filter off the sodium sulfate.
18. Rinse the original Erlenmeyer and the funnel (anything yellow) with additional dichloromethane.
19. Add a boiling stick to your organic solution, and then place the Erlenmeyer into the warm-water bath to boil off the dichloromethane. (Be thorough…. Once it's boiled down some, you can turn up the hot plate to a higher temperature to facilitate a faster boil-off. No point in wasting lots of time boiling the solvent off if we can do it faster. But, we don't it to go crazy and go boiling over the top, either.)
    - Note: How do you know when to quit? If you know what your theoretical yield is, it will help you realize approximately how much stuff you should expect to have left once the solvent is removed…
20. Once the solvent is pretty much gone, remove from hot bath, add a vacuum adaptor, turn on vacuum, and continue under vacuum for 2 minutes to remove any last traces of CH_2Cl_2.
21. Remove your Erlenmeyer from the hot water bath.
    - Does anything crystallize?
    - At this point you have at least two things present: the desired alkene **4** and the undesired phosphine oxide side product **7**. If you also have some CH_2Cl_2 solvent that hasn't quite all boiled away, that will reduce your eventual yield and prevent crystallization.
    - Place your material into an ice bath, and scratch it with a boiling stick. If it crystallizes, that confirms that you've done an adequate job of boiling off your dichloromethane. If it doesn't crystallize, you should probably boil some more off. (Jasperse has a quick way.)
    - If you don't get rid of your dichloromethane adequately, leftover dichloromethane will keep product dissolved at the end of the recrystallization process, and your yield will be compromised.
22. Purify your alkene by recrystallizing from 1-propanol solvent. (The water bath can now be boiling hot, so turn up your hot-plate setting to ~5.) The concept here is that the triphenylphosphine oxide is more soluble in the propanol than is the alkene product, because the phosphine oxide can use its oxygen to hydrogen-bond to the solvent, whereas the alkene has no hydrogen-bonding capability.
    - Do you remember the logic and procedure for a recrystallization? If not, try to review!
    - A good starting guess may be about 6 mL.
    - This recrystallization can be done right in the same 125-mL Erlenmeyer flask.
23. After Buchner funnel filtration, rinse with a very small amount (2-4 mL?) of ice-cold propanol. We don't want to add water and make the solvent much "worse" for fear that water will knock the triphenylphosphine oxide out of solution and contaminate the product.
24. Let things dry thoroughly before getting your yield and mp. (Vacuum for at least 10 minutes.) Once you have your mass, also calculate your % yield. (Don't expect a very high yield. The solvent good enough to host all of the triphenylphosphine oxide also hosted much product.)

    Lab Report: Standard synthesis style lab report. Be sure to include detailed observations on some of the things that happened. For product, include yield, mp, and % yield.
    Questions: None assigned.