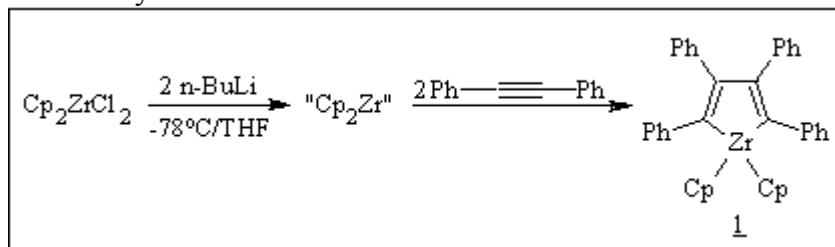


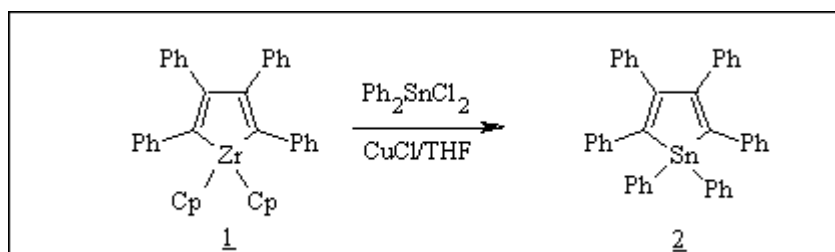
Unit 5/6M: Introduction to Organic Synthesis V & VI
Preparation of Hexaphenylstannole (Last updated 08/26/04)

I Introduction to Organometallic Compounds

Formation of zirconacycle intermediate:



Transmetalation reaction and formation of hexaphenylstannole:



The two-step reaction sequence shown above describes the formation of an intermediate organometallic heterocycle, a zirconacycle (**1**), followed by a transmetalation reaction, yielding hexaphenylstannole (**2**). The zirconacycle (**1**) is a moisture-sensitive compound that readily decomposes when exposed to atmospheric moisture, whereas hexaphenylstannole (**2**) is moisture and air stable. Both compounds are examples of organometallic compounds, compounds that have metal-carbon bonds. The study of organometallic chemistry is particularly fruitful since many of these compounds are known to catalyze important industrial reactions. For example, the commercial production of stereoregular polypropylene is catalyzed by several organometallic compounds. After a brief examination of the bonding in zirconocene dichloride, I'll provide a discussion of the experimental techniques necessary to complete this two-step reaction.

Metalloenes: Some Simple Organometallic Compounds

Zirconocene dichloride (Cp_2ZrCl_2) is an example of a "bent sandwich" compound (Figure 1. c and d). The first isolated organometallic sandwich compound was ferrocene, Cp_2Fe (Figure 1. a and b). Ferrocene is an air-stable orange solid. These molecules are probably strikingly different from the organic compounds you have seen before. In these compounds a metal atom is equally bound to all atoms of the cyclic organic moiety containing the delocalized π system. Cp is not an element, it is the cyclopentadienyl anion (C_5H_5^- or Cp in shorthand). It is a planar, resonance stabilized, five-membered ring containing 6 π electrons. These electrons are responsible for bonding to the metal atom in a Lewis acid-base interaction. (The metal cation is the Lewis acid, an electron acceptor,

and the cyclopentadienyl anion is the Lewis base, the electron donor.) To indicate that all five of the cyclopentadienyl carbon atoms are bonding to the metal atom a special nomenclature is used: The Greek letter η (eta) followed by a superscript with the number, 5 in this case, is placed in front of the formula for cyclopentadienyl anion. Therefore the complete description of the bonding in ferrocene would be $(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe}$. Since the cyclopentadienyl anion is found bound to metal atoms so frequently,

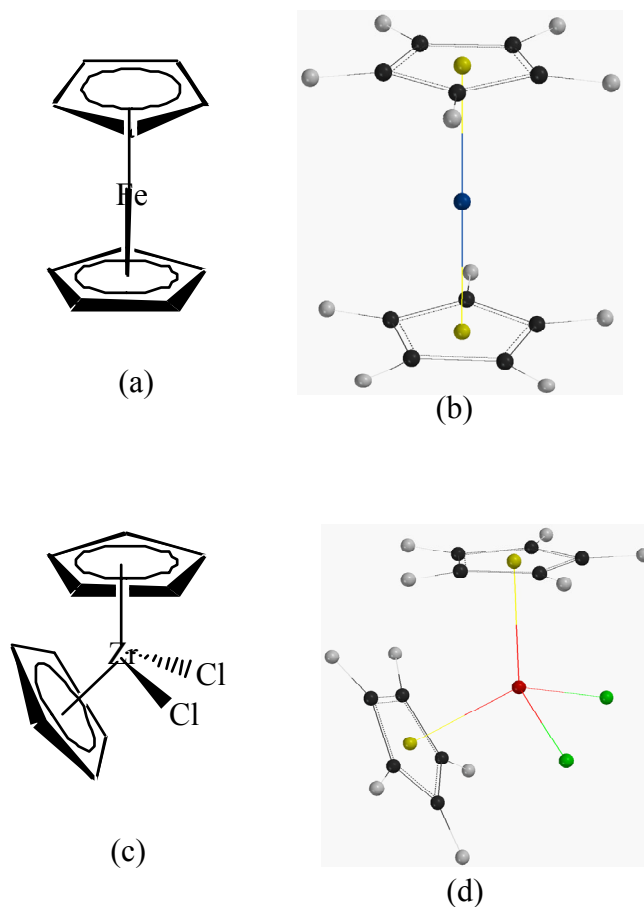


Figure 1: The sandwich compound ferrocene (Cp_2Fe) has an iron(II) ion between two stacked cyclopentadienyl anions. A ChemDraw depiction of the compound (a) and a Spartan Ball and Stick rendition (b) illustrate the origin of the sandwich name. Zirconocene dichloride is an example of a "bent sandwich" compound, here drawn with ChemDraw (c) and Spartan (d).

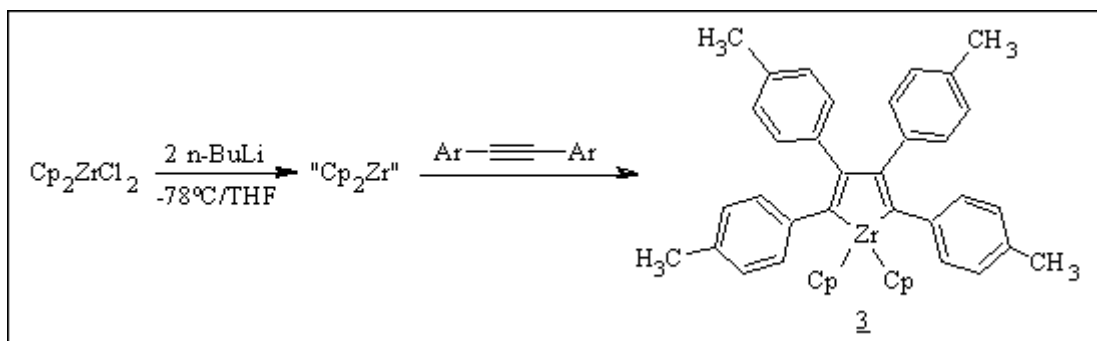
the abbreviation "Cp" will be used to represent the $\eta^5\text{-C}_5\text{H}_5$ ligand. As you can see in the figure, the Cp rings of ferrocene are stacked on top of each other sandwiching the iron ion in the middle. In zirconocene dichloride, since the central zirconium ion has two Cp ligands and two chloride ligands, the Cp ligands are bent away from the chloride ligands yielding a "bent sandwich" compound. (The geometry around the zirconium ion is distorted tetrahedral.)

Zirconocene dichloride is an air-stable white crystalline compound. The bonding between the zirconium(IV) cation and the cyclopentadienyl rings is quite robust, but the Zr-Cl bonds are less strong. In the presence of water, zirconocene dichloride readily loses chloride ions and forms oxygen bridges between the Cp_2Zr units. For that reason we'll store our zirconocene dichloride in the dry boxes to prevent exposure to atmospheric moisture. (Keep the moisture sensitivity of zirconocene dichloride in mind when you work with it.)

Formation of Zirconacycle Intermediate

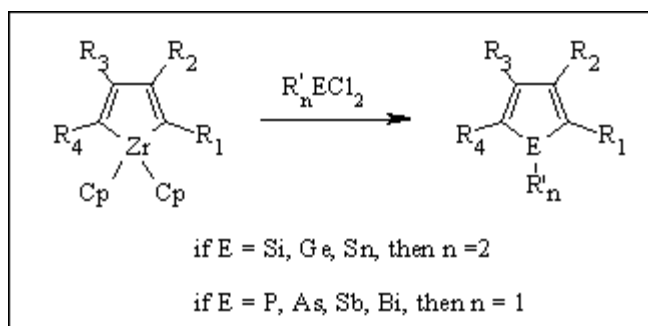
When zirconocene dichloride is reduced with suitable reducing agent, a highly reactive zirconocene equivalent is formed, " Cp_2Zr ." In the reduction of zirconocene dichloride the Zr(IV) is formally reduced by the addition of 2 electrons forming Zr(II) in " Cp_2Zr ." The formation of this reactive species is achieved at -78°C with two equivalents of n-butyllithium (BuLi) in anhydrous THF. If two equivalents of an alkyne are added, a zirconacyclopentadiene will be formed. For this model reaction, the alkyne that we introduce will be diphenylacetylene resulting in the zirconacycle (**1**) shown in the first two reactions. The IUPAC name for the zirconacycle product is 1,1-bis(cyclopentadienyl)-2,3,4,5-tetraphenylzirconacyclopenta-2,4-diene. This moisture-sensitive compound is bright red. When it is exposed to moisture it rapidly degrades and turns brown.

Note that if the diphenylalkyne had methyl substituents attached to each phenyl ring, the resulting zirconacycle would have the same methyl group substitution. For example the reaction of Cp_2ZrCl_2 with 2 equivalents of BuLi at -78°C , followed by the addition of 2 equivalents of ditoluylacetylene would yield the following zirconacycle (**3**).



Transmetalation from Zirconium(IV) to Sn(IV)

The culminating step in this multi-step reaction sequence is a transmetalation reaction yielding an air- and moisture-stable metallacyclopentadiene, hexaphenylstannole. This reaction is a specific example of the much more general synthetic reaction of transferring a carbon fragment from a 5-membered zirconacycle to a main group halide, described by the following general chemical equation,



The main group element (E) in the dihalide (R'_nECl_2) could be a Group 14 (C, Si, Ge, Sn, or maybe even Pb) or a Group 15 (N, P, As, Sb, or Bi) element. As a model reaction we have chosen diphenyltin dichloride (Ph_2SnCl_2) for several reasons. The foremost reason is that the product, hexaphenylstannole, is an air- and moisture-stable crystalline solid. The really intriguing quality of this compound is that it is luminescent, and because of this property, it could be used as a fluorescent probe. In order to synthesize a good probe, you may want to make a stannole with reactive functional groups on the phenyl rings that you could use to covalently bind to proteins, enzymes, or whichever biological molecule you are interested in. When you repeat this multi-step reaction sequence with your unique compounds, your target will be just such a derivatized-metallole.

The mechanism for this transmetalation can be rationalized as a nucleophile-electrophile interaction. The two sp^2 -hybridized carbon atoms attached to the zirconocene moiety in the zirconacyclopentadiene have components of both a covalent bond and an ionic bond. Another way to think of the bonding is to think of the carbon atoms as Lewis bases (having an available electron pair) and the zirconium atom as a Lewis acid (an electron pair acceptor). Whichever construct you use, the zirconium atom is electropositive compared to the two carbon atoms attached to it. This charge separation is the basis of the zirconacyclopentadiene's reactivity toward a transmetalation reaction. We have only to introduce a better electrophilic site in order to promote the transfer of the carbon fragment of the zirconacyclopentadiene to the main group element. When researchers tried to run the transmetalation reaction between zirconacyclopentadienes and organostannanes (R_2SnX_2), only very small amounts of the stannoles were formed. However, after much trial and no results, it was found that when either a stoichiometric or a catalytic amount of cuprous chloride was added, stannoles were formed in 70% - 90% yields. The explanation that has been proposed for the enhanced reactivity of the zirconacyclopentadiene in the presence of cuprous chloride is based on the Lewis-acidic nature of the cuprous ion (Cu^{1+}). The proposed mechanism involves an insertion of the copper ion into one of the zirconium-carbon bonds. The carbon atom in the new copper-carbon complex is now "activated," and subsequently reacts with the main group halide, displacing a chloride ion. The process is then repeated with the other zirconium-carbon bond.

II Experimental Procedures

Performing a Reaction under an Inert Atmosphere

Because both the n-butyllithium and the zirconacycle intermediate (**1**) are extremely moisture-sensitive, this reaction must be performed in dry glassware and an inert atmosphere to prevent water vapor in the air from coming into contact with the reaction mixture. The essential apparatus is a vessel (round-bottomed flask or vial) that has a rubber (or Teflon) septum firmly sealing the vessel. A standard procedure is to introduce any moisture-sensitive solid reagents and a magnetic spin bar into the vessel in the glove box. Before removing the reaction vessel from the glove box, the septum is attached to the vessel (sometimes it is wise to wire the septum down to the neck of the vessel). When the vessel is removed from the glove box, it is immediately connected to your nitrogen line with a needle piercing the septum. With a positive flow of nitrogen into the reaction vessel, pressure will build up in the vessel unless you provide a vent for the nitrogen gas. The bubbler is used for this purpose. Insert the needle of the bubbler into the septum right after inserting the nitrogen line. (If your nitrogen line has a T-joint with a septum on one of the T's, you can insert the bubbler needle into the T's septum instead of the reaction vessel.) You'll be able to monitor the flow rate of the nitrogen gas exiting the reaction vessel by observing the bubbles of nitrogen gas escaping for the bubbler. Adjust the nitrogen flow so that one bubble exits the bubbler every several seconds. Now you have a positive pressure of nitrogen gas in your reaction vessel and you can introduce anhydrous solvent(s) and any liquid reagents by syringe or cannula.

Glassware Preparation:

You will need to bring three reaction vessels each equipped with magnetic spin bars and septa into one of the glove boxes. You should also plan on bringing 3 spatulas for each of the reagents. **Be sure to flame dry the reaction vessels** before introducing them into the antechamber of the glove box. One vessel will be charged with zirconocene dichloride (Cp_2ZrCl_2), the second with diphenylacetylene (PhCCPh), and the third vessel will contain both the diphenyltin dichloride (Ph_2SnCl_2) and the cuprous chloride (CuCl). For the initial reaction, mass 0.5 mmol of zirconocene dichloride into the first vessel, 1.0 mmol of diphenylacetylene into the second vessel, and 0.5 mmol of both diphenyltin dichloride and cuprous chloride into the third vessel. All vessels must be sealed with septa before removing them from the glove box.

Formation of reduced Zirconocene (" Cp_2Zr "):

The active zirconocene species can be generated by reducing zirconocene dichloride in tetrahydrofuran (THF) at -78°C . (Magnesium may be used as the reducing agent, but n-butyllithium is normally used.) Once a solution of zirconocene dichloride in THF is cooled, using a dry ice/acetone slurry (-78°C), two equivalents of n-butyllithium are added and the resulting yellow solution is stirred at -78°C for up to one hour (though some procedures only call for 10 minutes at -78°C).

When you remove your zirconocene dichloride reaction vessel from the glove box, secure it to a stand with a magnetic stirrer and either a beaker or a styrofoam coffee cup that will hold the cold bath. Purge your nitrogen line by turning it on and check to make sure there is a flow of gas exiting from the needle. Quickly insert your nitrogen line

needle into the septum of the zirconocene dichloride reaction vessel and the pressure release needle of the oil bubbler. Adjust the flow rate to one bubble every several seconds. With a purged syringe (or cannula), transfer enough **anhydrous THF** to dissolve the zirconocene dichloride to the reaction vessel. (Ten milliliters should be more than sufficient.) Stir the mixture until all the zirconocene dichloride dissolves.

Cool the zirconocene dichloride solution by adding some pellets of dry ice and isopropanol (2-propanol) to the cold bath. As the temperature in the reaction vessel cools, watch the oil bubbler. You may have to increase the flow of nitrogen to prevent oil from being sucked into the oil bubbler tygon tubing caused by the reduced pressure in the reaction vessel (remember the gas law relationships, as the temperature is decreased the pressure will decrease). If the zirconocene dichloride solution's surface is below the surface of the dry ice/isopropanol level, the reaction solution should cool to -78°C within about 10 minutes. Next, dropwise dispense 2 equivalents (1 mmol if you are using 0.5 mmol of Cp_2ZrCl_2) of butyllithium solution (1.6 M in hexanes) from either a plastic syringe or a buret. Allow the solution to stir at -78°C for between 10 minutes and 1 hour. Be sure to record how long you allow the butyllithium and zirconocene dichloride to react.

While you are setting up the zirconocene dichloride reaction, connect the diphenylacetylene reaction vessel to a nearby nitrogen line with a pressure release to another oil bubbler. When you add the **anhydrous THF** to the zirconocene dichloride reaction vessel, you can also add sufficient **anhydrous THF** to the diphenylacetylene reaction vessel to dissolve it (less than 10 mL will be needed).

Formation of Zirconacycle (**1**):

Before the cold bath is removed, a solution of two equivalents of diphenylacetylene (1 mmol) dissolved in THF is added to the reaction vessel. The cold bath is then removed, and the solution is allowed to warm to room temperature while it is stirred. In the warming process, the solution undergoes several color changes. The final color should be deep red. One of the experimental procedures recommends a 3 hour reaction time from the time the cold bath is removed until the reaction is complete. The zirconacycle product (**1** in the original equation) in solution is extremely moisture-sensitive and must be kept under a positive pressure of dry nitrogen gas. At this point the zirconacycle can be used in situ (without isolation), effectively transferring the tetraphenylbutadienyl moiety to another substrate, or it can be isolated and characterized. The IUPAC name for the zirconacycle product is 1,1-bis(cyclopentadienyl)-2,3,4,5-tetraphenylzirconacyclopenta-2,4-diene.

Formation of Hexaphenylstannole (**2**):

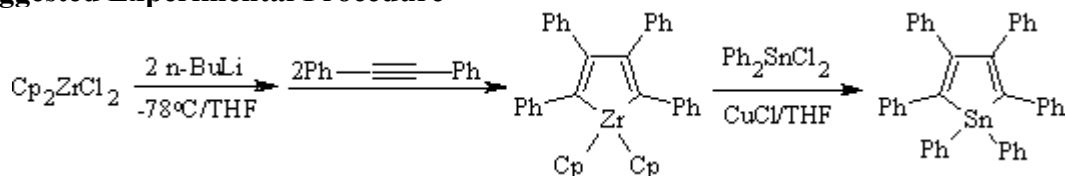
Add the suspension formed from a stoichiometric amount of diphenyltin dichloride (0.5 mmol) and a catalytic amount (10 mol %) of cuprous chloride (CuCl) in **anhydrous THF** to the reaction vessel containing the room temperature red zirconacycle solution. Make sure there is a positive pressure of nitrogen in the reaction vessel and visually monitor the reaction. When the red color of the zirconacycle disappears, you should TLC the reaction mixture. Look for the formation of the luminescent product, hexaphenylstannole. The reaction may take 24 hours to complete (though it may be complete in as little as 1 hour). If the red color of the zirconacycle intermediate remains

after 24 hours, consider gently refluxing the solution. (If you chose to reflux the reaction mixture, be sure to add a reflux condenser before you start heating.)

Isolation of Hexaphenylstannole:

When you have determined that the reaction is complete, remove the THF using the rotoevaporator. Dissolve the crude product in methylene chloride and filter out the byproduct salts and the unreacted cuprous chloride. Evaporate the methylene chloride in a tared vessel and obtain a crude yield. Reserve a small portion of this crude for TLC analysis. Prepare a silica column in hexanes of appropriate size to accommodate your crude product. Apply your product to the column and begin eluting the column with pure hexanes. Monitor the eluant by TLC. The diphenylacetylene starting material sure elute with pure hexanes. In order to elute the stannole, you will have to gradually increase the proportion of methylene chloride to hexanes in the eluent. Record the volumes of eluent(s) that you add to your column as well as the color and volume of the solutions that you recover from the column. Be sure to carefully label all your fractions. While collecting fractions, you can be performing TLC analyses of the previous fractions. (I usually try to spot 4 to 6 fractions on a single TLC plate.) Identify the fractions that contain the hexaphenylstannole, combine them together, remove the solvent with the rotoevaporator in a pre-weighed 25 mL round-bottomed flask. Record your crude weigh and calculate your yield.

Suggested Experimental Procedure



In this preparation, hexaphenylstannole, is synthesized without the isolation of the zirconacycle. In the *in situ* reaction described here, zirconocene dichloride, is reduced with n-butyllithium at -78°C , a solution of 2 equivalents of diphenylacetylene is added, the reaction mixture is allowed to warm to room temperature, and then the zirconacycle in solution is "quenched" by the addition of 1 equivalent of diphenyltin dichloride with 10 mol % equivalent of cuprous chloride. This procedure combines units 5 and 6 into one procedure.

Experiment

In the dry box prepare three reaction vessels all with rubber septa. **Label each vessel clearly.** Into the first, weigh 0.50 mmol of zirconocene dichloride and add a magnetic stir bar. Into the second, weigh 1.0 mmol of diphenylacetylene and into the third combine 0.50 mmol diphenyltin dichloride and 0.05 mmol of the green cuprous chloride (you may want to include a magnetic stir bar in this last vessel too, see the next paragraph). Make sure you label each vessel as to their contents and make sure you have sealed the vessels with the septa. Remove the three vessels from the dry box and connect the zirconocene dichloride vessel to your nitrogen and vent lines. Dissolve the zirconocene dichloride in a minimum of **anhydrous THF** (probably less than 5 mL) at room temperature before cooling the reaction vessel to -78°C with a dry ice/acetone bath. Add 1 equivalent of n-butyllithium and stir for (perhaps) 30 minutes. While the

zirconocene dichloride is being reduced, dissolve your diphenylacetylene in a minimum of **anhydrous THF** (probably less than 2 mL, since diphenylacetylene is quite soluble in THF). While the reaction mixture is still at -78°C , add your diphenylacetylene solution and then remove the ice bath and allow the reaction mixture to warm to room temperature. The reaction mixture should develop a deep red color.

The remaining vessel should contain the diphenyltin dichloride and the cuprous chloride catalyst. Add a minimum of **anhydrous THF** to dissolve the diphenyltin dichloride (again probably about 2 mL). The cuprous chloride will not dissolve appreciably. Now combine the $\text{Ph}_2\text{SnCl}_2/\text{CuCl}$ suspension with the red zirconacycle solution. You can do this by syringe or cannula (if you use a cannula, **BE SURE TO FLUSH IT WITH SOLVENT RIGHT AWAY SO IT DOESN'T GET CLOGGED**). Since the CuCl is only sparingly soluble in THF, you may want to add the zirconacycle solution to the $\text{Ph}_2\text{SnCl}_2/\text{CuCl}$ solution. **If you do this, make sure you have included a magnetic stir bar in the $\text{Ph}_2\text{SnCl}_2/\text{CuCl}$ vessel in the dry box.** Stir the reaction mixture at room temperature and record any observations. The reaction should be complete after a couple of hours. You can monitor the reaction by TLC as soon as the red color disappears.

When the reaction is completed, evaporate the THF (you can use the rotoevaporator for this) and extract the residue with methylene chloride. Filter or spin the methylene chloride solution to separate the supernatant from the insoluble copper salts. Removing the methylene chloride will yield a residue that is a combination of your crude product, zirconocene dichloride, and any unreacted starting materials. Make sure you record its weight. Use column chromatography to isolate the hexaphenylstannole product (See pages 119-123 of your laboratory text for a discussion of column chromatography.).