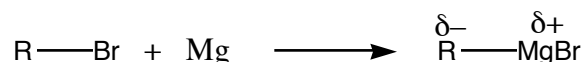


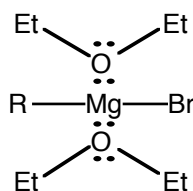
Experiment 12: Grignard Synthesis of Triphenylmethanol

Reactions that form carbon-carbon bonds are among the most useful to the synthetic organic chemist. In 1912, Victor Grignard received the Nobel prize in chemistry for his discovery of a new series of reactions that result in the formation of a carbon-carbon bond. A Grignard synthesis first involves the preparation of an organomagnesium reagent via the reaction of an alkyl bromide with magnesium metal:



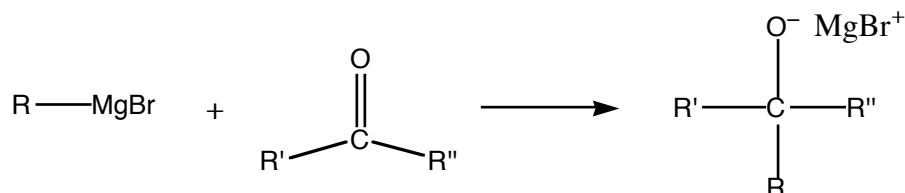
The resulting “Grignard reagent” acts as both a good nucleophile and a strong base. Its nucleophilic character allows it to react with the electrophilic carbon in a carbonyl group, thus forming the carbon-carbon bond. Its basic property means that it will react with acidic compounds, such as carboxylic acids, phenols, thiols and even alcohols and water; therefore, reaction conditions must be free from acids and strictly anhydrous. Grignard reagents will also react with oxygen to form hydroperoxides, thus they are highly unstable when exposed to the atmosphere and are generally not isolated from solution.

For a variety of reasons, anhydrous diethyl ether is the solvent of choice for carrying out a Grignard synthesis. Vapors from the highly volatile solvent help to prevent oxygen from reaching the reaction solution. In addition, evidence suggests that the ether molecules actually coordinate with and help stabilize the Grignard reagent:

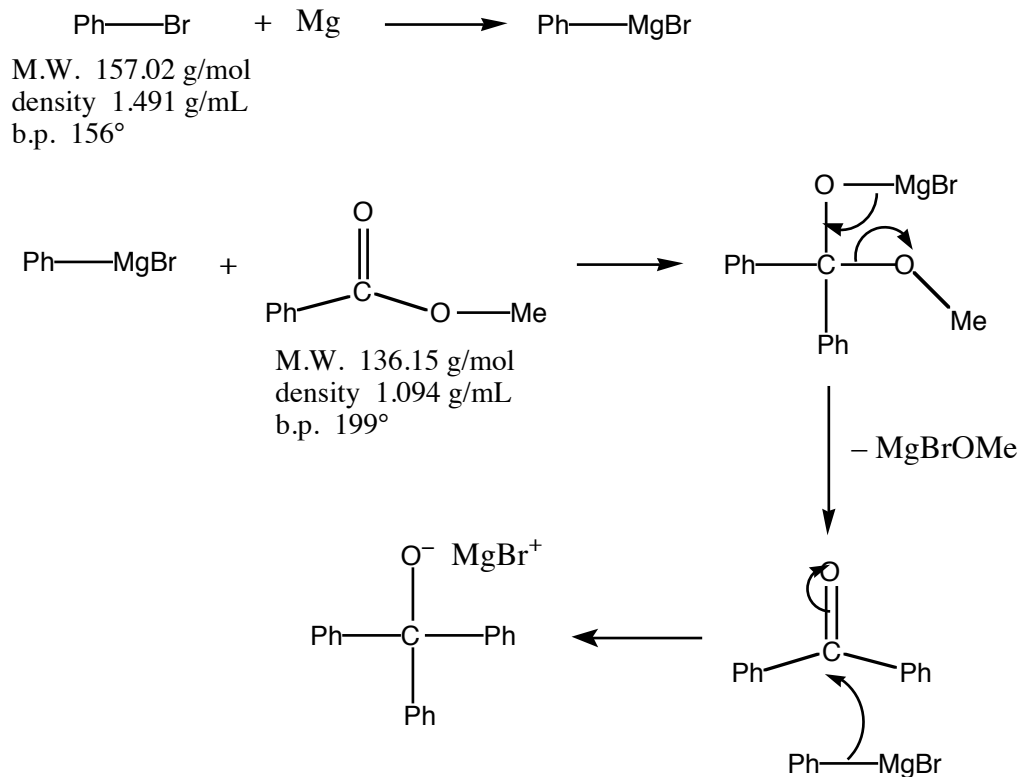


The magnesium metal used in the synthesis contains a layer of oxide on the surface that prevents it from reacting with the alkyl bromide. The pieces of metal must be gently scratched while in the ether solution to expose fresh surface area so that the reaction can commence. Formation of the Grignard reagent is highly exothermic. Once the reaction begins, it will continue to reflux in the absence of an external heat source. The reaction mixture is protected from atmospheric moisture by adding a drying tube, which contains calcium chloride, to the reflux apparatus. Read sections 7.2 Addition of Reagents during a Reaction and 7.3 Anhydrous Reaction Conditions in *LTOC* on pp 89-93.

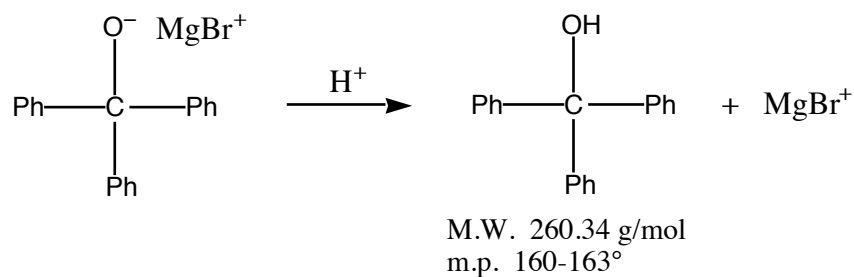
Once the Grignard reagent has formed, the carbonyl containing compound is added to the solution. A magnesium alkoxide is produced from the ensuing reaction:



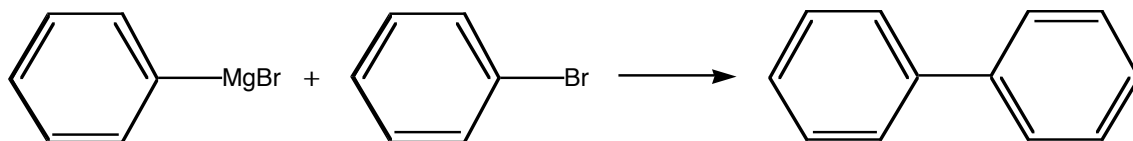
In the experiment that you will perform, bromobenzene is the alkyl bromide used to make the Grignard reagent, and the carbonyl containing compound is methyl benzoate, an ester. In this case, the magnesium alkoxide breaks apart releasing a ketone, which can react further with more Grignard reagent:



The final step of the synthesis is the hydrolysis of the magnesium alkoxide by a mineral acid. This reaction produces the alcohol, triphenylmethanol in this case, and water soluble magnesium salts:



A side-reaction can occur between phenylmagnesium bromide and bromobenzene, which produces biphenyl:



This impurity is much more soluble in ligroin than is triphenylmethanol; thus, it can be removed from the product via a recrystallization procedure.

Outline the steps of the following procedure:

You will set up your apparatus according to the diagram on [Figure Page, Expt. 12](#) (you may bring the page to lab with you). You will mark the separatory funnel with two lines—one at the volume level for 9 mL and the other at 24 mL.

The importance of using absolutely dry glassware for this reaction cannot be over-emphasized. Place the glassware that you cleaned last week in a 110° oven for 10 minutes or more before assembling the apparatus. A calcium chloride drying tube inserted into the top of the condenser will help to keep moisture out of the apparatus. As the glassware cools, dry air is pulled in through the calcium chloride. Allow the set-up to cool to room temperature before proceeding.

Warning! Diethyl ether is extremely flammable. Use only in a fume hood and keep away from flames and heat sources, such as hot plates.

Prepare an ice bath that will be used to cool the reaction if it becomes too vigorous. Attach a ring clamp to a bar in your fume hood. Weigh 2 g of magnesium turnings on weighing paper, then place them in the 100 mL round-bottom flask. Pour bromobenzene into the separatory funnel first, filling it up to the first mark (9 mL). Next, pour anhydrous diethyl ether directly from the **can** (not the bottle) into the separatory funnel up to the second mark (24 mL) and swirl to mix. Immediately stopper the funnel and re-place it on the Claisen adapter as shown in the figure.

Begin running water through the condenser. Unstopper the separatory funnel and add the ether and bromobenzene mixture to the reaction flask all at once by opening the stopcock. Close the stopcock and pour ether from the **can** into the separatory funnel up to the second mark (24 mL), but **do not** add it to the reaction flask yet. Watch for signs of reaction such as a *cloudy* solution and bubbles on the surface of the metal. If the reaction does not begin immediately, move the separatory funnel to the ring clamp, insert a *dry* stirring rod into the flask, and scratch the surface of the magnesium metal under the liquid. Be **very careful** not to punch a hole in the bottom of the flask! Place your hand around the base of the flask to keep it warm. If the reaction still has not begun after scratching the magnesium for several minutes, add one to two drops of 1,2-dibromoethane (**toxic!**). If the reaction fails to occur at this point, inform your lab instructor. It is important that the un-reacted reagents *not* be placed in the Byproducts Jar, where an explosive reaction could occur.

Once you are *sure* the reaction has commenced, open the stopcock and slowly add the 24 mL of ether. **Do NOT add the 24 mL of ether until the reaction is bubbling vigorously.** The additional ether helps to keep the reaction under control. Use the ice bath if the reaction is extremely vigorous, but do not overcool the mixture; the reaction will be stopped by too much cooling.

Once the reaction begins, it should continue to boil without external heat. When boiling has stopped, heat the flask with a *very low* steam bath to gently reflux the mixture for ten minutes. Continue with the next part immediately.

Pour diethyl ether from the **can** into the separatory funnel until the meniscus is about half-way between the two marks (approx. 15 mL). Measure 4.6 mL (5 g) of methyl benzoate in a graduated cylinder and add it to the ether in the sep funnel. Open the stopcock *slowly* to add this solution dropwise to the reaction mixture. When the addition is completed, swirl the flask until it is at room temperature. Remove the Claisen adapter and separatory funnel, place the condenser with drying tube directly on the round-bottom flask (be sure the connection is tight), and reflux the reaction over *low* steam for 30 minutes. Review section 7.1, pp 87-89, in *LTOC*, and view Video 7.1: Refluxing the Reaction at: <http://www.macmillanhighered.com/Catalog/studentresources/mohrig4e#> (click on “Videos”).

Pour 40 mL of 1 M sulfuric acid into a 250 mL Erlenmeyer flask, and then add about 25 g of ice. Pour the reaction mixture into this flask, then use *small amounts* of sulfuric acid and ether (from the **bottle**, not the can) to rinse out the round-bottom flask. Swirl the flask thoroughly until the hydrolysis reaction is completed (when bubbling has stopped and the solids have dissolved). Pour the mixture into a sep funnel (rinse the flask with small amounts of ether). More ether may be added if the volume of the organic layer is low. Shake the funnel and vent periodically. Drain and discard the lower, aqueous layer. Add another portion of 1 M sulfuric acid to the sep funnel to further wash the ether layer. Finally, wash the ether layer with saturated sodium chloride solution. Use an amount of wash liquid equal to approximately one-third of the volume of the ether layer for all washes in the sep funnel.

Pour the ether layer out of the top of the sep funnel into an Erlenmeyer flask, and dry it with about 5 g of granular anhydrous sodium sulfate. Swirl the flask from time to time for 5 minutes. Filter off the drying agent by gravity through filter paper held in a funnel, collecting the filtrate in an Erlenmeyer flask. Rinse the drying agent with a small amount of ether.

To the ether solution, add 25 mL of ligroin, and concentrate the mixture by heating it on a steam bath. Evaporate just until the mixture is cloudy, as crystals of triphenylmethanol begin to form. Remove the flask from the steam and allow the mixture to cool to room temperature, then place it on ice. Collect the product by vacuum filtration and wash it with three 5 mL portions of cold ligroin. Obtain the weight and melting point of your product next week.

Pour the ether/ligroin filtrate into the appropriate **Laboratory Byproducts** jar.

Students at Bucknell University wrote the following song to help them understand and remember the Grignard reaction.

Oh Grignard, the Beautiful
(sung to the tune of "America the Beautiful")

The carbonyl is polarized
The carbon end is plus
A nucleophile will thus attack
The carbon nucleus
A Grignard yields an alcohol
Of types there are but three
It forms a bond to correspond
From C to shining C.
A secondary's synthesis
Requires an aldehyde
For tertiary, a carbanion
And ketone may collide
And Grignards add formaldehyde
The product's primary
They stick like glue to CO₂
Join C to lonely C.

Taken from "Chemistry Classes are Transformed", by M.B. Brennan, *Chemical and Engineering News*, Sept. 29, 1997, p. 39.

Name _____ Date _____

T. A. _____ Lab period _____

Results and Calculations (to be handed in two days after the next lab period)

Calculate the percent yield of triphenylmethanol.

Melting range for triphenylmethanol _____

If your percent yield is low, provide some explanation for the loss of product.