

Nucleophilic Addition: The Grignard reagent

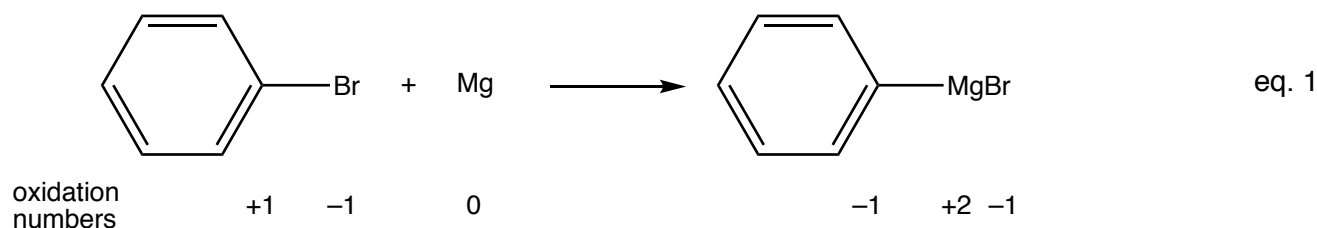
Objective

To develop organic laboratory techniques, to synthesize a Grignard reagent, and react that reagent with a ketone to generate a tertiary alcohol. To develop additional techniques for analyzing molecules using IR spectroscopy.

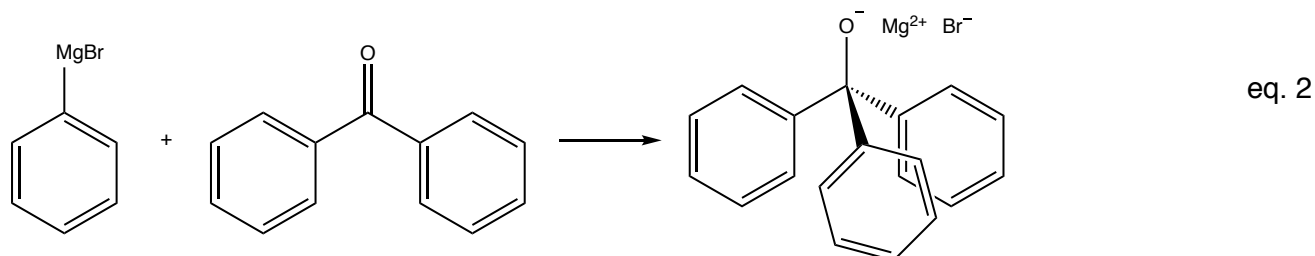
Background

Nucleophilic substitutions at secondary and tertiary sites are difficult; often elimination reactions occur instead. Thus, substitution reactions aren't a particularly good method for synthesizing secondary and tertiary alcohols. On the other hand, reacting Grignard reagents, carbon-based nucleophiles, with carbonyls is an effective way of making secondary and tertiary alcohols. Additionally, since alcohols can be reduced to alkanes or converted to other functional groups, the reaction of a Grignard reagent with a carbonyl is an excellent way to form carbon-carbon bonds.

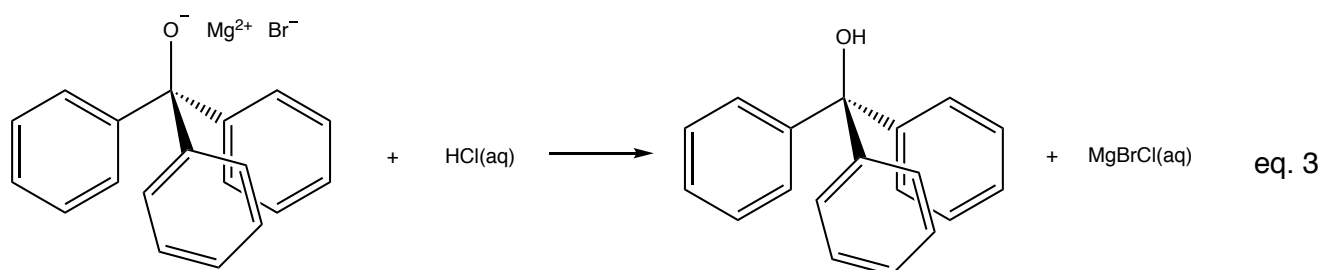
Let's first consider the formation of the Grignard reagent. The reaction between magnesium metal and an alkyl halide results in the formation of a metal to carbon bond. The organometallic reaction occurring is called an oxidative addition; the alkyl halide is added to the metal and, in the process, the metal is oxidized. Of course, if the metal is oxidized, something must be reduced. That "something" is the carbon atom. Notice in equation 1, that the oxidation number of the carbon atom changes from +1 to -1. Additionally, when one considers the electronegativities of the elements bonded to the carbon, it is clear that the C atom in the product is more electron rich than the C atom in the reactant.



Now that we have formed a carbon-based nucleophile, we could react it with a variety of carbon-based electrophiles to form a carbon-carbon bond. Since we wish to make a tertiary alcohol, we will react our Grignard reagent with a ketone, more specifically benzophenone. The carbon of a carbonyl is electrophilic, and even though the carbon is a secondary carbon atom, because it is planar, it is an excellent site for a nucleophilic attack. It is important to note that, since there is no leaving group (see equation 2), the reaction that is occurring is not a nucleophilic substitution. The reaction is a nucleophilic addition.



Notice that in equation 2, the product of the nucleophilic addition is an alkoxide. Converting an alkoxide to an alcohol is simple. Alkoxides are strong bases, and a neutralization reaction occurs when an acid is added to an alkoxide. The products of the neutralization reaction are an alcohol and a salt.



Procedure¹

Warning: ether is very volatile and extremely flammable. Ether must be kept away from ignition sources. Ether containers must be capped when not in use, and open containers of ether must be kept in the hood. 6M hydrochloric acid is corrosive and it will cause burns on contact.

Synthesis of Phenyl Magnesium Bromide

For this experiment, all equipment must be oven dried.² Fill a 25-mL Erlenmeyer flask with approximately 20 mL of anhydrous ethyl ether. Cap the flask. Add 0.15 g of shiny magnesium turnings and a stir bar to a 25-mL round-bottom flask. Cap the round-bottom flask with a Claisen head. Seal one opening in the Claisen head with a septum and the other opening with a drying tube packed with calcium chloride.

Place 0.70 mL of bromobenzene into a tared 5-mL conical vial. Cap the vial, determine the mass of the bromobenzene in the vial, and add 4 mL of ether to the vial. After the bromobenzene dissolves transfer 0.8 mL of the resulting solution to the flask that contains the magnesium. Warm the flask gently, by placing it a few inches over a hot plate set to 60

¹ Adapted from Pavia, Lampman, Kiz, and Engel, "Triphenylmethanol", *Introduction to Organic Laboratory Techniques: A Microscale Approach*. Saunders College Publishing, 1999.

² Alternatively, equipment can be rinsed with acetone and allowed to air-dry for two days.

°C. Gently stir the contents of the flask. Small bubbles should be seen forming on the magnesium. If the reaction does not start you can crush the magnesium with a dry glass stirring rod. If the reaction still doesn't start after crushing the magnesium several times, you can add a small iodine crystal to the reaction. Once the reaction has started and a brownish gray suspension has begun to form, slowly add the remaining bromobenzene–ether solution over fifteen minutes. It is important that the reaction stays warm. The exothermic reaction should keep the reaction going; however, if the reaction stops, warm the flask over the hot plate. After adding all of the bromobenzene–ether solution to the flask, add 2.0 mL of anhydrous ethyl ether to the vial. Transfer the ether from the vial to the flask. The formation of the Grignard reaction should take approximately 30 minutes.

Reaction of Phenyl Magnesium Bromide with Benzophenone

In a 5-mL vial, prepare a solution of 1.09 g benzophenone in 2 mL of anhydrous ethyl ether and cap the vial. Once the Grignard reagent has cooled to room temperature add the benzophenone solution to the Grignard reagent quickly, but not so quickly that the exothermic reaction causes the ether to boil. Make certain that the flask has cooled to room temperature. Add 1 mL of anhydrous ethyl ether to the benzophenone vial. A solid will form in the flask that contains the Grignard reagent and the benzophenone. Once the stirring has become ineffective, transfer the 1 mL of ether from the benzophenone vial to the reaction flask, and stir the contents of the flask with a dry spatula. Cap the flask. The reaction should be complete within fifteen minutes from the initial formation of the product. (*Stop here at the end of day one.*)

Isolation of Triphenylmethanol

To the reaction flask that contains the product from day one, add 6.0 mL of 6 M hydrochloric acid dropwise. Use a spatula to break up the solid and cap and shake the vial to help dissolve the solid. Because the left over magnesium will react with the acid to form hydrogen, and the neutralization reaction will release heat, the flask must be vented to release the pressure. Make certain that the flask contains at least 10 mL of ethyl ether. The contents of the flask should separate into two layers. Make certain that no solids remain in the flask before separating the organic from the aqueous layers. Add ethyl ether or hydrochloric acid in small amounts until no solids remain.

Transfer the contents of the reaction flask to a separatory funnel. Drain the aqueous layer to a beaker. Transfer the ether layer to a dry Erlenmeyer flask. Return the aqueous layer to the separatory funnel and add 5 mL of ethyl ether to the aqueous layer. Drain the aqueous layer to a beaker and discard it. Combine the two ethyl ether layers and dry with anhydrous sodium sulfate.

Transfer the dry ethyl ether to an Erlenmeyer flask and evaporate the ether using a 50 °C water bath and a gentle stream of compressed air. Add 3 mL of petroleum ether to the oily solid that remains after the ethyl ether has evaporated. Warm the resulting suspension in a 50 °C water bath for a few minutes, cool to room temperature, and isolate the product by vacuum filtration using a Hirsch funnel. Dry the product on the Hirsch funnel and obtain a mass for the crude product.

Recrystallization

Recrystallize the crude product from hot isopropanol. After drying the product using the vacuum filtration apparatus, remember to determine the mass of the product.

Analysis of the triphenylmethanol

Determine the melting point of the product.

While an IR spectrum of the product can be obtained by creating a KBr pellet, it can also be obtained using the Attenuated Total Reflectance (ATR) method. When using the ATR, follow the on-screen instructions. When directed to do so, place a small amount of the triphenylmethanol product on the crystal in the center of the anvil on the spectrometer.

A KBr pellet is prepared by combining 2 mg of the product with 60 mg of KBr. The KBr and triphenylmethanol are ground together with a marble mortar and pestle and the resulting powder is transferred to a KBr press. Turning the bolts on the KBr applies pressure to the KBr inside, and the KBr is fused into a transparent pellet.

Report

In a typed report, list the amounts of the reactants – magnesium, bromobenzene, and benzophenone – (mass and moles), your yield (actual, in grams and moles, and percent, if there was a problem during the recrystallization, report the yield of the crude product), and the melting point of your product. Remember, percent yields are based on the theoretical yield of the reaction. Comparing your crude product to your recrystallized product will not provide the “percent yield” for the reaction. Compare the IR spectra of the starting materials to the IR Spectrum of your product. Comment on which peak(s) from the starting materials have been lost and whether any prominent new peaks are observed. Attach your IR spectra to your report. Do not write a formal “experimental”.