

EXP. 38-A

PREPARATION OF TRIPHENYL METHANOL BY GRIGNARD REACTION

USE OF CARBON NUCLEOPHILES IN ORGANIC SYNTHESIS

LEARNING OBJECTIVES: To understand the theory of Grignard reactions, introduce or review nucleophilic attacks on sp^2 carbon, learn the preparation and use of carbon nucleophiles in organic synthesis, and learn how to set up an anhydrous reaction.

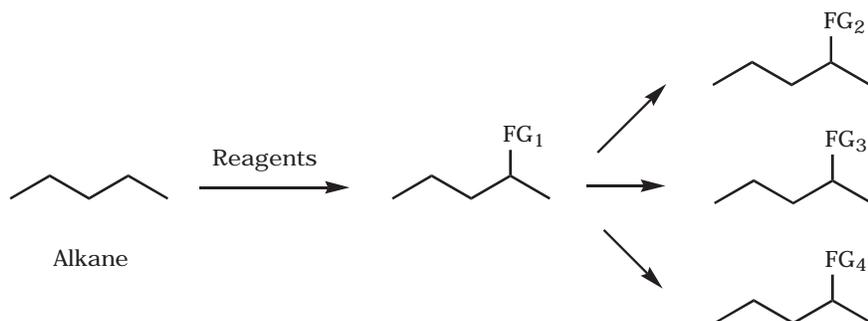
QUIZ PREPARATION: Recitation notes and readings assigned in the syllabus.

GRIGNARD REACTIONS: THEORY AND BACKGROUND

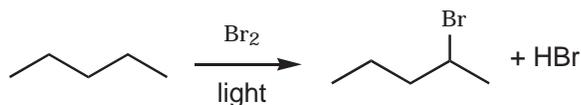
NATURAL SOURCES OF ORGANIC CHEMICALS: All forms of life, dead or alive, such as animals, plants, and fossils.

OIL (fossil fuels): Made up primarily of **hydrocarbons**, notably **alkanes**, **alkenes**, and **aromatics** (benzene-based compounds).

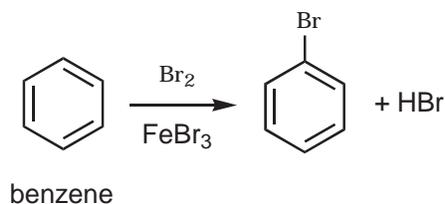
ALKANE FUNCTIONALIZATION: The intent is to introduce a **reactive group** (FG₁) in the otherwise unreactive alkane chain. Once a reactive group is in place, other functional groups (FG_n) can be introduced.



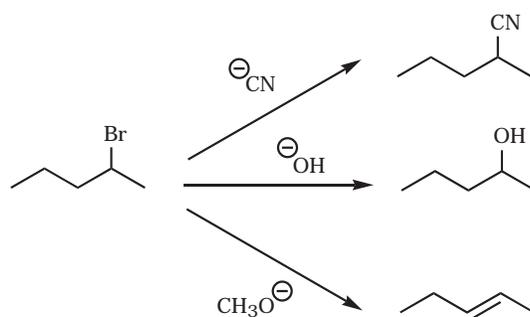
The choices for FG₁ are very limited, especially in a laboratory setting. One of the few **synthetically useful** reactions that alkanes undergo is **free radical halogenation**, i.e. insertion of a halogen (normally chlorine or bromine) onto the carbon chain:



Aromatic hydrocarbons (benzene based) can undergo a modified version of this reaction:



Alkyl halides can be transformed into a variety of other functional groups by S_N2 reactions and eliminations:



Alkyl halides can be converted into **CARBON NUCLEOPHILES**. Carbon nucleophiles enable **chain expansion** by formation of **carbon-carbon bonds**. Carbon nucleophiles contain a negatively charged carbon with an unshared electron pair. In most cases that happens **when carbon is bonded to a metal**.

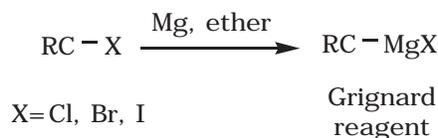


Such compounds are called **organometallics**.

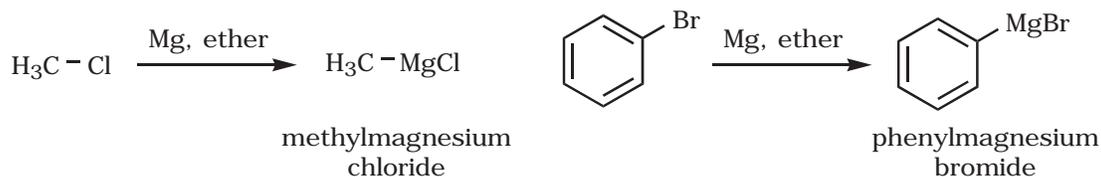
One of the most important and versatile classes of organometallics are those containing a carbon-magnesium bond. They are called **GRIGNARD REAGENTS**, after Victor Grignard, whose development of their chemistry won him a Nobel Prize. See his biography at

<http://www.nobel.se/chemistry/laureates/1912/grignard-bio.html>

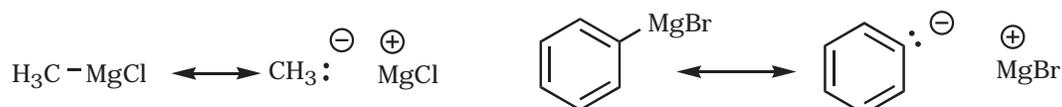
Grignard reagents are prepared by insertion of Mg metal into the carbon-halogen bond of alkyl and aryl halides:



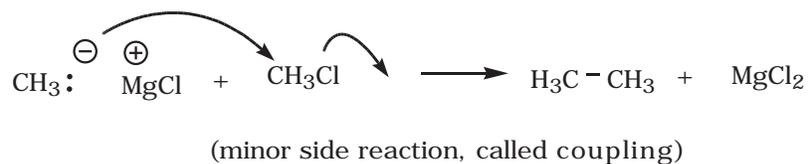
Examples:



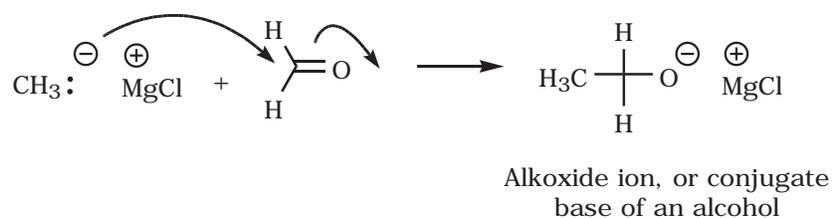
The corresponding **resonance structures** reveal the nucleophilic (and also basic) character of the carbon atom attached to Mg:



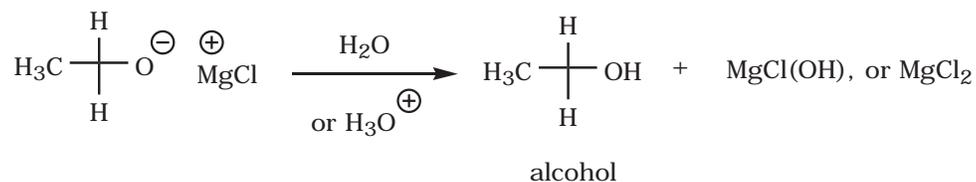
Their own synthesis makes it apparent that Grignard reagents are not very good nucleophiles for regular S_N2 reactions. If they were, they would attack the alkyl halide that's used in their synthesis:



Instead, their main use is in **nucleophilic addition reactions** of carbonyl compounds. That is, substances containing $\text{C}=\text{O}$ bonds. Such substances are usually aldehydes and ketones.



The alkoxide ion is not as stable as its conjugate acid, the alcohol. Therefore, this step is always followed by treatment with water or a strong acid to protonate the alkoxide and convert it into the more stable alcohol as the final product.



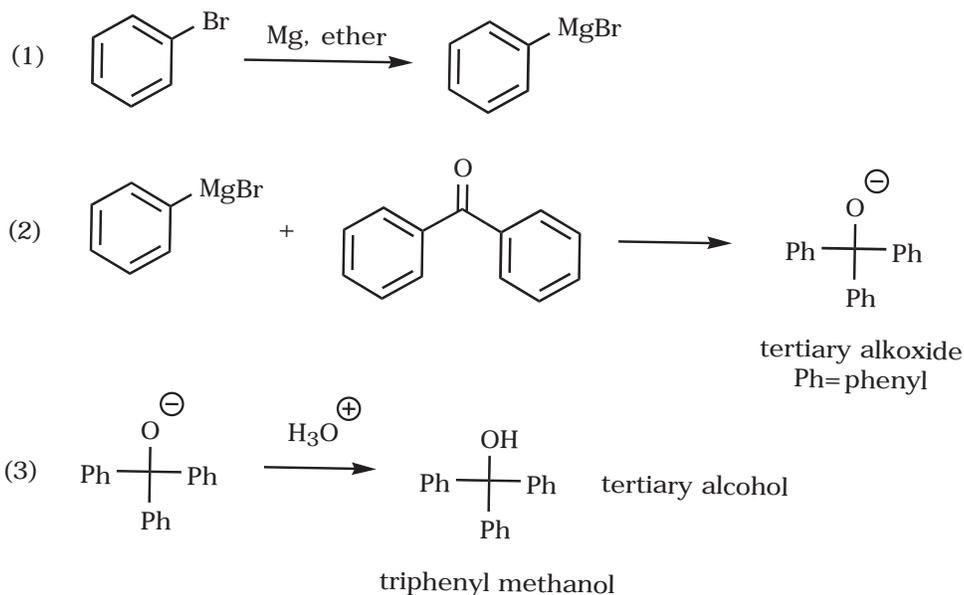
Most carbonyl compounds yield primary, secondary, or tertiary alcohols when reacted with Grignard reagents, depending on the specific case. The following table illustrates the synthetic range. For additional examples refer to your organic chemistry text.

GR + formaldehyde -----> primary alcohol

GR + other aldehydes -----> secondary alcohol

GR + ketone -----> tertiary alcohol

Experiment 31A involves the preparation and use of phenylmagnesium bromide to prepare a tertiary alcohol by reacting the Grignard reagent with benzophenone (a ketone):



EXP. 38 A

PRACTICAL CONSIDERATIONS PROCEDURAL CHANGES SAFETY TIPS

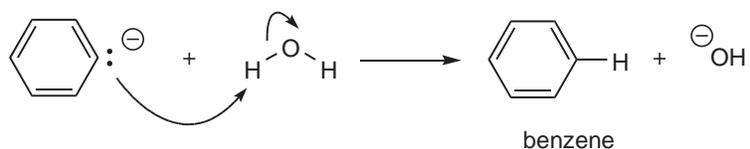
[Refer to pages 317 - 324 of your textbook \(4th ed.\)](#)

The experimental procedure is presented on p. 320. It is divided into major sections as follows:

Preparation of glassware. The most important thing to note here is that all glassware must be **DRY**. This means free of water. Water can destroy all or some of your Grignard reagent by acting as an acid. Remember that many good nucleophiles are also good bases. Since water is a strong acid, it can protonate the Grignard reagent to yield its conjugate acid, effectively derailing your reaction. If you have trouble getting your reaction to start, this could be one of the problems.



Grignard reagent resonance forms



The best way to prepare the glassware for the reaction is to wash it well with soap and water first. Then rinse it with acetone until all the water has been washed off. Finally, blow a soft stream of air on the glassware to dry it, or place it in the oven for at least 5 min. to evaporate the acetone.

Formation of the Grignard reagent. Please note that the solvent **ether is very volatile and releases noxious vapors at room temperature.** Prolonged exposure to these vapors can make you drowsy. If you feel dizzy from breathing ether vapors, notify your instructor immediately and step outside the building to get some fresh air.

If the conditions of the experiment are all in place, you should notice formation of a cloudiness and “boiling” (actually formation of bubbles from the reaction). If you don’t see such signs, heat the reaction pot **mildly** (to about 50 degrees, no more!), **DO NOT ATTEMPT TO CRUSH THE MAGNESIUM** as the textbook recommends on p. 296. This is a good way to break your flask and possibly hurt your hand. If heating fails to start the reaction, add a crystal of iodine (ask your instructor for help) and continue heating and stirring. Finally, if all fails, borrow a drop of Grignard solution from another student whose reaction started, and quickly add it to your reaction mixture.

Since ether boils at a very low temperature, you may lose some of it as the reaction proceeds under the action of heat. Keep adding ether to compensate for these losses. You will know when the reaction is complete because all or nearly all of the magnesium has dissolved. If a few bits of metal remain, do not wait for them to dissolve, as they might be impurities. Proceed with the next step.

Addition of benzophenone (p. 323). The only important thing to note here is that after this step you should stop the experiment, since you will not have time to finish it in one session. The following session you will perform the **hydrolysis** step (bottom of p. 323).

Hydrolysis. In this step you deliberately add a source of protons (dil. HCl) to protonate the conjugate base of the product (triphenylmethanol) and convert it to the actual alcohol. What follows is a series of extractions and purification procedures to obtain the final **solid**. This solvent is crystallized from hot isopropyl alcohol (also called isopropanol).

Spectroscopy. After calculating the percent yield, obtain an IR spectrum using the KBr pellet technique that your instructor will demonstrate. This technique is frequently used when the product is a solid.