CHAPTER 19

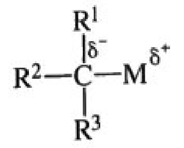
Organometallic Chemistry

It should by now be no surprise to you that carbon atoms are not the least bit "happy" about bearing a charge. This reluctance to form ions is seen in the high energies of carbocations, for example, which are not formed at all at primary carbon atoms and are possible for tertiary carbon atoms only if a highly polar solvent is present to assist in stabilizing the ion (Chap. 14). The same aversion to accommodate a charge attends the formation of unstabilized carbanions, that is, anions that are not delocalized through electronegative substitutents like carbonyl groups (Chap. 18). Nonetheless, it's possible to generate chemical species that behave as though they are unstabilized carbanions. Their creation and reactions are the subject of this chapter.

19.1 INTRODUCTION

Organometallic compounds are substances that contain carbon-metal bonds, and they may be generally represented by the structure **1**, in which the metal, **M**, may be Li, Na, Mg, Cu, Zn, Hg, Pd, or other transition elements. Organomagnesium compounds **1**, M = MgBr, which are commonly called **Grignard reagents**, were the first organometallic substances to be extensively studied, and they are still among the most important. (See the Historical Highlight *Grignard and the Beginnings of Modern Organometallic Chemistry*, which is available online.) The polarization of the bond between the carbon atom and the electropositive metal in these reagents renders the carbon atom electron-rich, or Lewis basic, and the carbon atom bears a partial negative charge, δ^-, as shown. With this polarization in mind, you should not consider the metallated carbon atom as a true anion, because it retains some covalent bonding to its metallic partner, although the extent of this bonding remains a point of discussion among chemists.

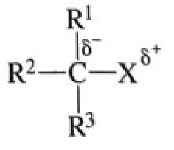
One of the characteristic properties of organometallic reagents **1** is that the carbon atom serves as a **nucleophile** in chemical reactions. In contrast, when a carbon atom is bonded to more electronegative elements such as the halogen atom in the alkyl halide **2** (X = Cl, Br, or I) or oxygen atom in the carbonyl compound **3**, it is electron-deficient or Lewis acidic and possesses a partial positive charge. Such carbon atoms then serve as **electrophiles** in chemical reactions.



$R^2{-}C(R^1)(R^3){-}M$, C^{δ^-}, M^{δ^+}

1

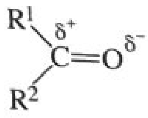
An organometallic reagent



$R^2{-}C(R^1)(R^3){-}X$, C^{δ^-}, X^{δ^+}

2

An alkyl halide

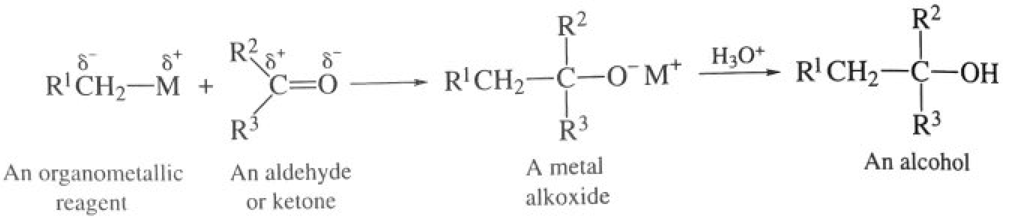


3

A carbonyl-containing compound

Because of their nucleophilic character, organometallic compounds are widely utilized as reagents in reactions that produce new carbon-carbon bonds. For example, two typical reactions of organometallic reagents **1** with carbon electrophiles such as alkyl halides **2** and carbonyl compounds **3** are illustrated by the general transformations shown in Equations 19.1 and 19.2. In each of these reactions, the nucleophilic carbon atom of one reactant becomes attached to the electrophilic carbon atom of the other reactant with the resulting formation of a new carbon-carbon bond. Thus, like many bond-forming processes, these reactions may be viewed in the simple context of *combinations of Lewis bases with Lewis acids.*

$$\underset{\text{An organometallic reagent}}{R^1\overset{\delta^-}{C}H_2{-}\overset{\delta^+}{M}} + \underset{\text{An alkyl halide}}{\overset{\delta^-}{X}{-}\overset{\delta^+}{C}H_2R^2} \longrightarrow \underset{\text{An alkane}}{R^1CH_2{-}CH_2R^2} + MX \qquad (19.1)$$



$$\underset{\text{An organometallic reagent}}{R^1\overset{\delta^-}{C}H_2{-}\overset{\delta^+}{M}} + \underset{\text{An aldehyde or ketone}}{(R^2)(R^3)\overset{\delta^+}{C}{=}\overset{\delta^-}{O}} \longrightarrow \underset{\text{A metal alkoxide}}{R^1CH_2{-}\underset{R^3}{\overset{R^2}{C}}{-}O^-M^+} \xrightarrow{H_3O^+} \underset{\text{An alcohol}}{R^1CH_2{-}\underset{R^3}{\overset{R^2}{C}}{-}OH} \qquad (19.2)$$

The following discussions focus on the preparation and reactions of two important classes of organometallic compounds, Grignard reagents **1** (M = MgX) and organozinc reagents 1 (M = ZnX). Of course, many of the principles that are presented may be applied to the chemistry of other organometallic reagents. The first series of experiments encompass the preparation of Grignard reagents from aryl and alkyl bromides, followed by their representative reactions with (1) an ester to produce a tertiary alcohol, (2) carbon dioxide to produce a carboxylic acid, and (3) an aldehyde to produce a secondary alcohol. The other set of experiments involves the preparation of an organozinc reagent and its reaction with a ketone to prepare a tertiary alcohol.

19.2 GRIGNARD REAGENTS: PREPARATION

Reactions of Organic Halides with Magnesium Metal

Grignard reagents, R–MgX or Ar–MgX, are typically prepared by the reaction of an alkyl halide, R–X, or an aryl halide, Ar–X, with magnesium metal in an *anhydrous* ethereal solvent (Eq. 19.3); the organometallic reagent dissolves as it is formed. You may note that carbon is transformed from an *electrophilic center* in the starting material R–X or Ar–X into a *nucleophilic center* in the product R–MgX or Ar–MgX in this process.

$$\underset{\text{An alkyl halide}}{\overset{\delta^+}{R}{-}\overset{\delta^-}{X}} \text{ or } \underset{\text{An aryl halide}}{\overset{\delta^+}{Ar}{-}\overset{\delta^-}{X}} + Mg^\circ \xrightarrow[\text{or THF (solvent)}]{\text{dry diethyl ether}} \underset{\text{An alkyl magnesium halide}}{\overset{\delta^-}{R}{-}\overset{\delta^+}{Mg}X} \text{ or } \underset{\text{An aryl magnesium halide}}{\overset{\delta^-}{Ar}{-}\overset{\delta^+}{Mg}X} \qquad (19.3)$$

Although it is customary to represent the Grignard reagent by the formula R–MgX or Ar–MgX, the structure of the organometallic species in solution is rather more complex. For example, with alkyl magnesium halides, there is an equilibrium between RMgX, R_2Mg, and MgX_2 that depends on the solvent, the halide ion, and the nature of the alkyl group. Moreover, the various organometallic species form aggregates in solution.

Grignard reagents are readily prepared from alkyl and aryl chlorides, bromides, and iodides but are rarely synthesized from organofluorides. The ease of formation of Grignard reagents from alkyl halides follows the order R–I > R–Br > R–Cl. Aryl halides are less reactive than their alkyl counterparts, and aryl bromides and chlorides are comparable in reactivity.

In the experiments in this chapter, you will prepare one or both of the Grignard reagents derived from bromobenzene (**4**) and 1-bromobutane (**6**) in an ethereal solvent, according to Equations 19.4 and 19.5. The preparation of these reagents theoretically requires equivalent amounts of the organic halide and magnesium, but a slight excess of magnesium is normally used.

(19.4)

4
Bromobenzene

5
Phenylmagnesium bromide

$$CH_3CH_2CH_2CH_2\text{—}Br + Mg \xrightarrow{\text{diethyl ether}} CH_3CH_2CH_2CH_2\text{—}MgBr \qquad (19.5)$$

6
1-Bromobutane

7
1-Butylmagnesium bromide

Using an ethereal solvent is critical for the efficient preparation of the Grignard reagent because the basic oxygen atom of the ether complexes with the electropositive magnesium atom to help stabilize the organometallic species. The ethereal solvents most commonly used in this reaction are diethyl ether, $(C_2H_5)_2O$, and tetrahydrofuran, THF, $(CH_2)_4O$. Diethyl ether is often the solvent of choice because it is less expensive, may be purchased in anhydrous form, and is easily removed from the reaction mixture owing to its low boiling point (bp 36 °C, 760 torr). Tetrahydrofuran is a stronger Lewis base than diethyl ether and it also has better solvating ability; it may be used when the Grignard reagent does not form readily in diethyl ether.

You should be careful to use freshly opened containers of *anhydrous* diethyl ether or THF, because opening the container exposes its contents to atmospheric oxygen, which promotes the formation of **hydroperoxides**. For example, diethyl ether can be converted to the hydroperoxide, $CH_3CH(OOH)OCH_2CH_3$. Such peroxides are *explosive*, and large volumes of *anhydrous* diethyl ether or THF suspected to contain peroxides should *not* be evaporated to dryness. Moreover, emptied containers should be *thoroughly* rinsed with water to remove any peroxides before being discarded. Peroxides in *anhydrous* diethyl ether or THF may be conveniently destroyed by distillation from alkali metals such as sodium or potassium metal or from lithium aluminum hydride, $LiAlH_4$. The presence of peroxides in diethyl ether and THF may be detected by placing a drop of the solvent on a piece of *moistened* starch/iodide test paper. If the paper turns dark violet, owing to formation of a starch-iodine complex, then the ether contains peroxides.

The magnesium metal used for the preparation of the Grignard reagent is normally in the form of turnings—thin shavings that have a high surface area relative to chunks of the metal. This type of magnesium is generally suitable for the preparation of most Grignard reagents. However, if the turnings have been repeatedly exposed to atmospheric oxygen, their surface may be covered by a coating of magnesium oxide, which decreases their reactivity. Magnesium ribbon rather than turnings may also be used *after* the oxide coating on it has been scraped off with the edge of a spatula.

Initiating the reaction between the organic halide and magnesium may be difficult, especially with unreactive halides. In these cases, the reaction may often be initiated by adding a small crystal of iodine, I_2, to the reaction mixture. The iodine facilitates the reaction either by activating the metal through removal of some of its oxide coating or by converting a small amount of the R–X halide to the corresponding iodide, which is more reactive toward magnesium. Alternatively, the mixture can be placed in the bath of an ultrasonicator to initiate the reaction.

The formation of a Grignard reagent is an **exothermic** process. Since side reactions may occur if the reaction is allowed to proceed uncontrolled, it is important to regulate the rate at which the reaction proceeds. Grignard reactions often require an **induction period**, so it is *important* to be sure that the reaction of the alkyl or aryl halide with the magnesium has initiated *before* adding large quantities of the halide. Once the reaction is in progress, the halide should be added *dropwise and slowly* to the stirred suspension of the magnesium metal in the ethereal solvent; the halide may be added either neat or as a solution in the ethereal solvent. Adding the halide slowly keeps its concentration low, thus enabling better control of the rate of the reaction and the evolution of heat. The heat that is generated usually brings the solvent to its reflux temperature, so the heat of the reaction is ultimately transferred to the cooling water in the condenser. Should it appear that the reaction is getting out of control, as evidenced by vapors escaping from the top of the condenser, the reaction mixture must be immediately cooled with an ice-water bath. Indeed, as a general rule, it is prudent always to have such a cooling bath prepared when performing an exothermic reaction.

Side Reactions

Side reactions may be encountered when forming Grignard reagents. For example, as the **conjugate bases** of the exceedingly weak organic acids R–H (R = aryl and alkyl), Grignard reagents are *very* strong bases that react rapidly with water according to Equation 19.6. This reaction results in the destruction of the Grignard reagent and the formation of the corresponding hydrocarbon, RH, and a basic magnesium salt. Grignard reagents also cannot be prepared when carboxyl (CO_2H), hydroxyl (OH), or amino (NH_2) groups are present in the alkyl or aryl halide; the acidic hydrogens of these functional groups will simply protonate the highly basic carbon atom of the Grignard reagent, thus destroying it as it forms.

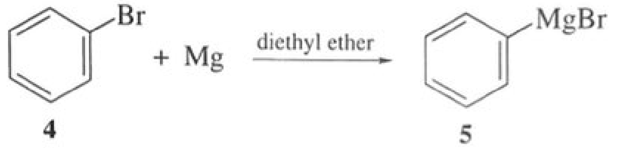
$$\text{R—MgX} + \text{H}_2\text{O} \longrightarrow \text{R—H} + \text{HO—Mg—X} \qquad (19.6)$$

The reaction of Grignard reagents with water (Eq. 19.6) dictates that all reagents, solvents, and apparatus used for their preparation must be *thoroughly* dry. Consequently, *anhydrous* ethereal solvents that typically contain less than 0.01% water must be used. *Anhydrous* diethyl ether rapidly absorbs atmospheric moisture, so opening a container of it a number of times over a period of several days renders the diethyl ether unsuitable for use in preparing a Grignard reagent. Only freshly opened cans should be used, and the cans should always be tightly sealed *immediately* after the necessary volume of ether has been removed. These operations will also minimize the formation of dangerous hydroperoxides.

Other side reactions that may occur during formation of a Grignard reagent are shown in Equations 19.7–19.9, but these can be minimized by taking certain precautions. For example, reaction of the Grignard reagent with oxygen and carbon dioxide (Eqs. 19.7 and 19.8) is typically avoided in the research laboratory by

Grignard reagents are readily prepared from alkyl and aryl chlorides, bromides, and iodides but are rarely synthesized from organofluorides. The ease of formation of Grignard reagents from alkyl halides follows the order R–I > R–Br > R–Cl. Aryl halides are less reactive than their alkyl counterparts, and aryl bromides and chlorides are comparable in reactivity.

In the experiments in this chapter, you will prepare one or both of the Grignard reagents derived from bromobenzene (**4**) and 1-bromobutane (**6**) in an ethereal solvent, according to Equations 19.4 and 19.5. The preparation of these reagents theoretically requires equivalent amounts of the organic halide and magnesium, but a slight excess of magnesium is normally used.



(19.4)

4
Bromobenzene

5
Phenylmagnesium bromide

$$CH_3CH_2CH_2CH_2{-}Br + Mg \xrightarrow{\text{diethyl ether}} CH_3CH_2CH_2CH_2{-}MgBr \quad (19.5)$$

6
1-Bromobutane

7
1-Butylmagnesium bromide

Using an ethereal solvent is critical for the efficient preparation of the Grignard reagent because the basic oxygen atom of the ether complexes with the electropositive magnesium atom to help stabilize the organometallic species. The ethereal solvents most commonly used in this reaction are diethyl ether, $(C_2H_5)_2O$, and tetrahydrofuran, THF, $(CH_2)_4O$. Diethyl ether is often the solvent of choice because it is less expensive, may be purchased in anhydrous form, and is easily removed from the reaction mixture owing to its low boiling point (bp 36 °C, 760 torr). Tetrahydrofuran is a stronger Lewis base than diethyl ether and it also has better solvating ability; it may be used when the Grignard reagent does not form readily in diethyl ether.

You should be careful to use freshly opened containers of *anhydrous* diethyl ether or THF, because opening the container exposes its contents to atmospheric oxygen, which promotes the formation of **hydroperoxides**. For example, diethyl ether can be converted to the hydroperoxide, $CH_3CH(OOH)OCH_2CH_3$. Such peroxides are *explosive*, and large volumes of *anhydrous* diethyl ether or THF suspected to contain peroxides should *not* be evaporated to dryness. Moreover, emptied containers should be *thoroughly* rinsed with water to remove any peroxides before being discarded. Peroxides in *anhydrous* diethyl ether or THF may be conveniently destroyed by distillation from alkali metals such as sodium or potassium metal or from lithium aluminum hydride, $LiAlH_4$. The presence of peroxides in diethyl ether and THF may be detected by placing a drop of the solvent on a piece of *moistened* starch/iodide test paper. If the paper turns dark violet, owing to formation of a starch-iodine complex, then the ether contains peroxides.

The magnesium metal used for the preparation of the Grignard reagent is normally in the form of turnings—thin shavings that have a high surface area relative to chunks of the metal. This type of magnesium is generally suitable for the preparation of most Grignard reagents. However, if the turnings have been repeatedly exposed to atmospheric oxygen, their surface may be covered by a coating of magnesium oxide, which decreases their reactivity. Magnesium ribbon rather than turnings may also be used *after* the oxide coating on it has been scraped off with the edge of a spatula.

Initiating the reaction between the organic halide and magnesium may be difficult, especially with unreactive halides. In these cases, the reaction may often be initiated by adding a small crystal of iodine, I_2, to the reaction mixture. The iodine facilitates the reaction either by activating the metal through removal of some of its oxide coating or by converting a small amount of the R–X halide to the corresponding iodide, which is more reactive toward magnesium. Alternatively, the mixture can be placed in the bath of an ultrasonicator to initiate the reaction.

The formation of a Grignard reagent is an **exothermic** process. Since side reactions may occur if the reaction is allowed to proceed uncontrolled, it is important to regulate the rate at which the reaction proceeds. Grignard reactions often require an **induction period**, so it is *important* to be sure that the reaction of the alkyl or aryl halide with the magnesium has initiated *before* adding large quantities of the halide. Once the reaction is in progress, the halide should be added *dropwise and slowly* to the stirred suspension of the magnesium metal in the ethereal solvent; the halide may be added either neat or as a solution in the ethereal solvent. Adding the halide slowly keeps its concentration low, thus enabling better control of the rate of the reaction and the evolution of heat. The heat that is generated usually brings the solvent to its reflux temperature, so the heat of the reaction is ultimately transferred to the cooling water in the condenser. Should it appear that the reaction is getting out of control, as evidenced by vapors escaping from the top of the condenser, the reaction mixture must be immediately cooled with an ice-water bath. Indeed, as a general rule, it is prudent always to have such a cooling bath prepared when performing an exothermic reaction.

Side Reactions

Side reactions may be encountered when forming Grignard reagents. For example, as the **conjugate bases** of the exceedingly weak organic acids R–H (R = aryl and alkyl), Grignard reagents are *very* strong bases that react rapidly with water according to Equation 19.6. This reaction results in the destruction of the Grignard reagent and the formation of the corresponding hydrocarbon, RH, and a basic magnesium salt. Grignard reagents also cannot be prepared when carboxyl (CO_2H), hydroxyl (OH), or amino (NH_2) groups are present in the alkyl or aryl halide; the acidic hydrogens of these functional groups will simply protonate the highly basic carbon atom of the Grignard reagent, thus destroying it as it forms.

$$\mathrm{R{-}MgX} + \mathrm{H_2O} \longrightarrow \mathrm{R{-}H} + \mathrm{HO{-}Mg{-}X} \tag{19.6}$$

The reaction of Grignard reagents with water (Eq. 19.6) dictates that all reagents, solvents, and apparatus used for their preparation must be *thoroughly* dry. Consequently, *anhydrous* ethereal solvents that typically contain less than 0.01% water must be used. *Anhydrous* diethyl ether rapidly absorbs atmospheric moisture, so opening a container of it a number of times over a period of several days renders the diethyl ether unsuitable for use in preparing a Grignard reagent. Only freshly opened cans should be used, and the cans should always be tightly sealed *immediately* after the necessary volume of ether has been removed. These operations will also minimize the formation of dangerous hydroperoxides.

Other side reactions that may occur during formation of a Grignard reagent are shown in Equations 19.7–19.9, but these can be minimized by taking certain precautions. For example, reaction of the Grignard reagent with oxygen and carbon dioxide (Eqs. 19.7 and 19.8) is typically avoided in the research laboratory by performing the reaction under an inert atmosphere such as nitrogen (N_2) or argon. However, this precaution is not essential in the undergraduate laboratory, because when diethyl ether is used as the solvent, its very high vapor pressure effectively excludes most of the air from the reaction vessel.

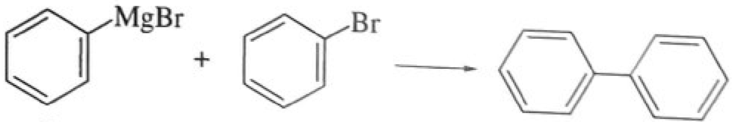
The coupling reaction (Eq. 19.9) is an example of a Wurtz-type reaction. Although this can be a useful process for preparing symmetrical hydrocarbons, R–R, it is normally desirable to minimize this side reaction by using dilute solutions, thereby avoiding high localized concentrations of the halide. This is accomplished by efficient stirring and by slowly adding the halide to the suspension of magnesium in the ethereal solvent.

$$\mathrm{RMgX} + \mathrm{O_2} \longrightarrow \mathrm{R{-}O{-}O^-\ {}^+MgX} \tag{19.7}$$

$$\mathrm{RMgX} + \mathrm{CO_2} \longrightarrow \mathrm{RCO_2^-\ {}^+MgX} \tag{19.8}$$

$$\mathrm{RMgX} + \mathrm{RX} \longrightarrow \mathrm{R{-}R} + \mathrm{MgX_2} \tag{19.9}$$

In the experiments that follow, phenylmagnesium bromide (**5**) and 1-butylmagnesium bromide (**7**) are prepared according to Equations 19.4 and 19.5, respectively. The most important side reaction in these experiments involves the Wurtz-type coupling of the Grignard reagent with the organic halide. For example, during the preparation of phenylmagnesium bromide, small quantities of biphenyl (**8**) are formed according to Equation 19.10; however, the presence of **8** does not interfere with the subsequent reactions of phenylmagnesium bromide. Although coupling also occurs during the preparation of 1-butylmagnesium bromide, the *n*-octane that is produced is volatile and easily removed.



5 Phenylmagnesium bromide

4 Bromobenzene

8 Biphenyl

(19.8)

EXPERIMENTAL PROCEDURES

Preparation of Grignard Reagents

Purpose To perform techniques required to prepare Grignard reagents from aryl and alkyl halides.

SAFETY ALERT

1. **Wear safety glasses or goggles and suitable protective gloves while performing the experiment.**
2. **Diethyl ether is *extremely* flammable and volatile, and its vapors can easily travel several feet along the bench top or the floor and then be ignited.**

Consequently, *be certain there are no open flames anywhere in the laboratory* whenever you are working with ether. Use a *flameless* heating source whenever heating is required.

3. **The *anhydrous* diethyl ether used in this experiment is contained in metal cans, and the screw or plastic cap should *always* be in place when the can is not in use to prevent evaporation, absorption of atmospheric moisture and oxygen, and accidental fires.**
4. ***Open containers of diethyl ether must not be kept at your laboratory bench or stored in your laboratory drawer*. Estimate the total volume of ether you will need and measure it in the hood into a container that is *loosely* stoppered.**
5. **You should use ovens to dry your glassware if possible. However, if drying ovens are not available and it is necessary to dry the glass apparatus with a flame or a heat gun, be *certain* that no one in the laboratory is working with diethyl ether. *Consult with your instructor before using any open flame.* Avoid excessive heating in the vicinity of the ring seals in the condenser and near the stopcock in the addition funnel, particularly if the stopcock is made of plastic or Teflon.**
6. **Lubricate all ground-glass joints in the apparatus carefully and mate them tightly to prevent the escape of diethyl ether during the reaction.**
7. **On the small scale of these experiments, the exothermic formation and reaction of Grignard reagents rarely causes a problem. Nevertheless, it is still good laboratory practice for you to have an ice-water bath ready if the reaction proceeds too rapidly, as evidenced by an *excessively* rapid rate of reflux and the emission of vapors from the top of the condenser.**

MINISCALE PROCEDURE

Prep & PhMgBr

Preparation Refer to the online resources to answer Pre-Lab Exercises, access videos, and read the MSDSs for the chemicals used or produced in this procedure. Review Sections 2.9, 2.10, 2.11, 2.22, 2.27, and 2.28.

Apparatus A 50-mL round-bottom flask, 5-mL syringe, separatory funnel with a ground-glass joint, condenser, Claisen adapter, drying tube, ice-water bath, apparatus for magnetic stirring, and *flameless* heating.

Setting Up Weigh 0.5 g of magnesium turnings that have been freshly crushed with a spatula into the round-bottom flask, and add a stirbar. Place this flask and its contents, the separatory funnel, condenser, Claisen adapter, and drying tube in an oven at 110 °C for at least 30 min. If the separatory funnel has a plastic or Teflon stopcock and stopper, do *not* put the stopcock, its plastic retaining nut, and the stopper in the oven, as they may melt or soften. Using gloves or tongs, remove the glassware from the oven and let it cool, preferably in a desiccator. After the glassware is cool enough to handle, lubricate all the joints and quickly assemble the apparatus shown in Figure 2.66b. Attach the drying tube to the top of the condenser and place the stopper and stopcock in the separatory funnel. Allow the apparatus to cool to room temperature.

Optional Measures If an oven is not available, it will be necessary to dry the apparatus with a microburner or a heat gun. Assemble the apparatus as described above. *Be sure that no one in the laboratory is working with diethyl ether,* and then dry the assembled apparatus. Do not overheat any plastic parts of the apparatus. Allow the apparatus to cool to room temperature.

Verify that there are no *flames* in the laboratory before continuing. Prepare a solution of *either* 2.4 mL of bromobenzene or 2.5 mL of 1-bromobutane in 5 mL of *anhydrous* diethyl ether in a small, *dry* Erlenmeyer flask. Swirl the solution to achieve homogeneity. Add 5 mL of *anhydrous* diethyl ether to the round-bottom flask *through* the separatory funnel; *close the stopcock.* Be sure that water is running through the condenser. Transfer the ethereal solution of halide to the separatory funnel.

Reaction Add a 1/2 ~~0.5-mL portion~~ of the ethereal solution from the separatory funnel onto the magnesium turnings and stir the resulting mixture. If small bubbles form at the surface of the magnesium turnings or if the mixture becomes slightly cloudy or chalky, the reaction has started. The flask should become *slightly* warm. If the reaction has started, *disregard* the optional instructions in the next paragraph.

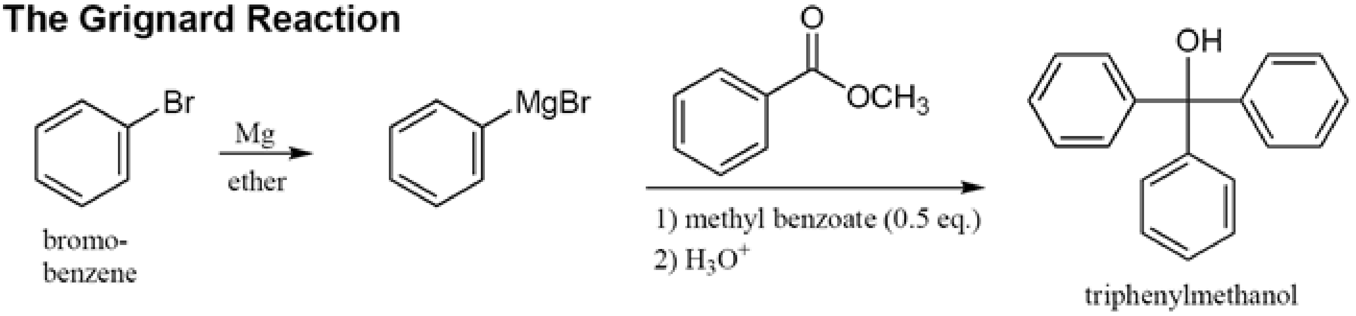
then p728

Optional Measures If the reaction does not start spontaneously, warm the mixture gently for several minutes and observe whether the mixture becomes slightly cloudy or chalky. If it does not, then obtain one or two additional magnesium turnings and crush them *thoroughly* with a heavy spatula or the end of a clamp. Remove the separatory funnel just long enough to add these broken pieces of magnesium to the flask and quickly replace the funnel. The clean, unoxidized surfaces of magnesium that are exposed should aid in initiating the reaction. If the reaction still has not started after an additional 3–5 min of warming, consult your instructor. The best remedy at this point is to add a small crystal of iodine to the mixture. Alternatively, a small amount of the preformed Grignard reagent may be added if it is available.

Once the reaction has started, *gently* heat the reaction mixture so that the solvent refluxes smoothly. Add another 5-mL portion of *anhydrous* diethyl ether to the reaction mixture through the top of the *condenser* and continue heating and stirring until the solvent is again refluxing. Add the remainder of the ethereal solution of the halide dropwise to the stirred reaction mixture at a rate that is just fast enough to maintain a gentle reflux. If the reaction becomes too vigorous, reduce the rate of addition and discontinue heating the flask, if necessary. If the spontaneous boiling of the mixture slows, increase the rate of addition slightly. If the rate of reflux still does not increase, heat the mixture as necessary to maintain gentle reflux during the remainder of addition. *It is important that reflux be maintained throughout the addition of the ethereal solution.* The addition should take about 5–10 min. Upon completing the addition, continue heating the mixture under gentle reflux for 15 min. If necessary, add *anhydrous* diethyl ether to the reaction flask so that there is no less than about 15 mL of solution. At the end of the reaction, the solution normally has a tan to brown, chalky appearance, and most of the magnesium will have disappeared, although residual bits of metal usually remain. Discontinue heating and allow the mixture to cool to room temperature.

Use the Grignard reagent as soon as possible after preparing it. Phenylmagnesium bromide is used in Parts A and B of Section 19.4, and 1-butylmagnesium bromide is used in Part C of that section.

Re



A ▪ *Preparation of Triphenylmethanol*

Purpose To demonstrate the preparation of a tertiary alcohol by the reaction of a Grignard reagent with an ester.

SAFETY ALERT

Review the Safety Alert for Preparation of Grignard Reagents (Sec. 19.2).

MINISCALE PROCEDURE

$PhMgBr + PhCO_2Me$

Preparation Refer to the online resources to answer Pre-Lab Exercises, access videos, and read the MSDSs for the chemicals used or produced in this procedure. Review Sections 2.10, 2.11, 2.13, 2.17, 2.21, 2.22, and 2.29.

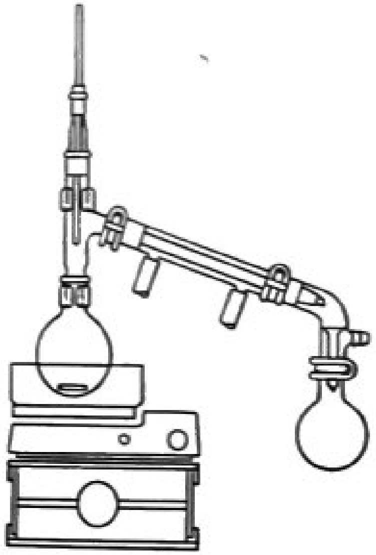
Apparatus Glass apparatus from the miniscale experimental procedure of Section 19.2, separatory funnel, ice-water bath, apparatus for magnetic stirring, simple distillation, vacuum filtration, and *flameless* heating.

Setting Up While the reaction mixture for the preparation of phenylmagnesium bromide (Sec. 19.2) is cooling to room temperature, dissolve 1.2 mL of methyl benzoate in about 5 mL of *anhydrous* diethyl ether, and place this solution in the separatory funnel with the *stopcock closed*. Cool the reaction flask containing the phenylmagnesium bromide in the ice-water bath.

Reaction Begin the *slow, dropwise* addition of the solution of methyl benzoate to the *stirred* solution of phenylmagnesium bromide. This reaction is *exothermic*, so you should control the rate of reaction by adjusting the rate of addition *and* by occasionally cooling the reaction flask as needed with the ice-water bath. The ring of condensate should be allowed to rise no more than one-third of the way up the reflux condenser. A white solid may form during the reaction, but this is normal. After the addition is complete and the exothermic reaction subsides, you may complete the reaction in one of two ways. Consult with your instructor to determine whether you should (1) heat the reaction mixture at reflux for 30 min or (2) stopper the flask after cooling the contents to room temperature and place it in the *hood* until the next laboratory period (no reflux required).★

Work-Up, Isolation, and Purification Place about 10 mL of cold 6 *M* sulfuric acid and about 5–10 g of crushed ice in a beaker. If the reaction mixture solidified upon cooling, add a small quantity of solvent-grade diethyl ether to the reaction flask. Pour the reaction mixture gradually with stirring into the ice-acid mixture. Rinse the round-bottom flask with 2–3 mL of solvent-grade diethyl ether and add this wash to the beaker. Continue stirring until the heterogeneous mixture is completely free of undissolved solids. It may be necessary to add a small portion of solvent-grade diethyl ether to dissolve all the organic material; the total volume of ether should be about 15–20 mL. Verify that the aqueous layer is acidic; if it is not, add cold 6 *M* sulfuric acid dropwise until the layer is acidic. If necessary, sequentially add 2- to 3-mL portions of solvent-grade diethyl ether and then water to dissolve all of the solids.

Transfer the entire mixture to a separatory funnel. Shake the funnel vigorously with venting to relieve pressure; separate the aqueous layer.* Wash the organic layer sequentially with about 5 mL of 3 *M* sulfuric acid, two 5-mL portions of saturated aqueous sodium bicarbonate (*vent!*), and finally with one 5-mL portion of saturated sodium chloride solution. Dry the organic layer using several spatula-tips full of *anhydrous* sodium sulfate. Swirl the flask occasionally for a period of 10–15 min to facilitate drying; add further small portions of *anhydrous* sodium sulfate if the solution remains cloudy.*



Filter or decant the solution into a 50-mL round-bottom flask and equip the flask for simple distillation. Remove the diethyl ether by simple distillation. Alternatively, use rotary evaporation or other techniques to concentrate the solution. The final traces of solvent may be removed by attaching the flask to a vacuum source and gently swirling the contents as the vacuum is applied. After the crude solid residue has dried, determine its melting range, which may be wide.*

Purify the triphenylmethanol by dissolving it in a *minimum* amount of boiling cyclohexane (ca. 10 mL/g product). Perform this operation at the hood or use a funnel that is attached to a vacuum source and inverted over the flask (Fig. 2.71b). Once all the material is in solution, evaporate the solvent *slowly* until small crystals of triphenylmethanol start to form. Allow the crystallization to continue at room temperature and then in an ice-water bath until no more crystals form. Isolate the product by vacuum filtration and air-dry it.

Analysis Weigh the triphenylmethanol and calculate the percent yield; determine its melting point. Obtain IR and ^{1}H NMR spectra of your starting materials and product, and compare them with those of authentic samples (Figs. 8.48, 15.19, 15.20, 15.33, 15.34, 19.2, and 19.3). If possible, analyze your product by GC-MS to determine if it is contaminated with benzophenone (**10**).

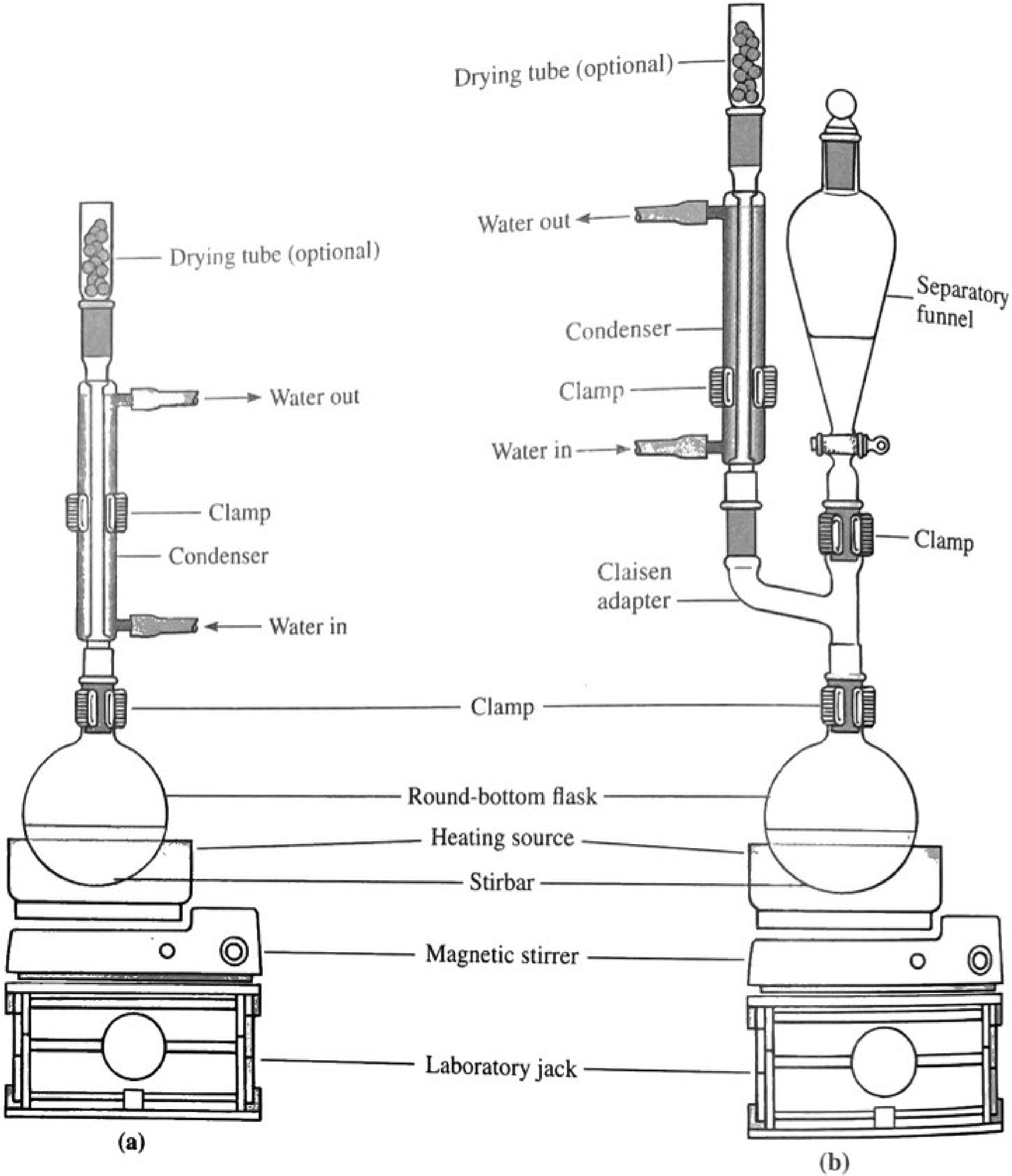


Figure 2.66
(a) Miniscale apparatus for heating a reaction mixture under reflux. (b) Miniscale apparatus for a reaction being heated under reflux and equipped for adding a liquid reagent or solution.