Introduction/Background

Image: ***François Auguste Victor Grignard (1871-1935)***[1]

François Auguste Victor Grignard, was a French chemist who discovered one of the world's first synthetic organometallic reactions.

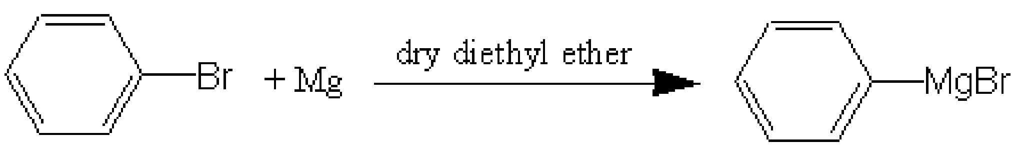
Grignard began studying mathematics at Lyon, France but then transferred to chemistry, In 1910, He become a professor of chemistry at the University of Nancy in France. During World War I, he worked in the new field of chemical warfare. He helped with the manufacture of phosgene and the detection of mustard gas.[2]

He is most celebrated, however, for devising a new method for creating an organic synthesis reactions that makes carbon-carbon bonds. The Grignard reaction is an important synthetic reaction. Essentially, a wide variety of compounds can be made by careful selection of the starting materials for this reaction. François Grignard and fellow Frenchman Paul Sabatier were awarded the Nobel Prize in Chemistry in 1912.[2]

* * *

"A useful way to introduce carbon-carbon bonds in molecules is to use organometallic reagents in what is known as a Grignard (pronounced "grin-yard") reaction. These reagents contain a carbon metal bond that is very polar. The carbon atom is the more electronegative element and we can think the Grignard reagent as a carbon nucleophile. This carbon nucleophile can be used in S_N2 reactions or in addition reactions."[3]

Grignard reagents are made by adding a halogenoalkane to small bits of magnesium in a flask containing ethoxyethane (commonly called diethyl ether or just "ether"). The flask is fitted with a reflux condenser, and the mixture is warmed over a water bath for 20 - 30 minutes.[4]

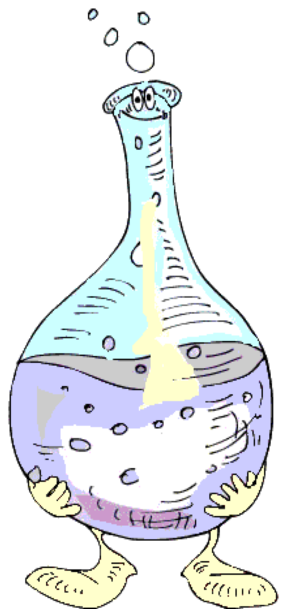


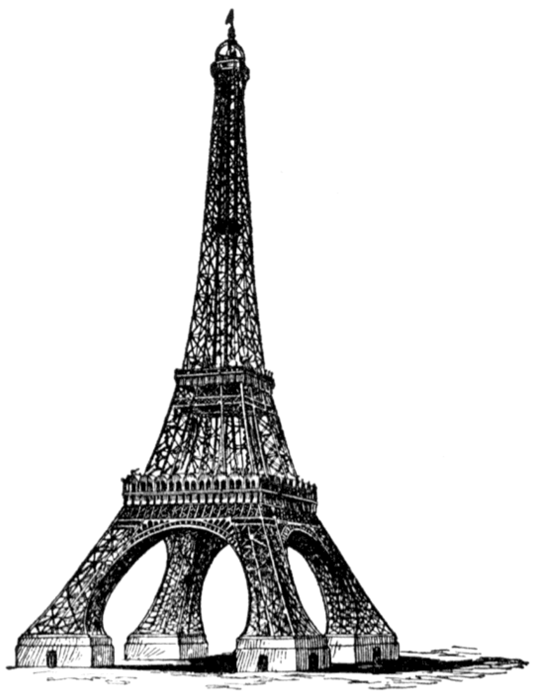
In this project, we will perform a Grignard reaction using a pre-made Grignard reagent. Grignard reagents can easily be made from haloalkanes and haloaromatics, but the

[1] http://upload.wikimedia.org/wikipedia/commons/c/c4/Viktor-grignard.jpg
[2] Wikipedia, *Victor Grignard*, http://en.wikipedia.org/wiki/Fran%C3%A7ois_Auguste_Victor_Grignard
[3] Berg, Michael A. G.; Poiner, Roy D. *Journal of Chemical Education.* **2007**, 84, 483
[4] Jim Clark, *An Inroduction to Grignard Reagents*, http://www.chemguide.co.uk/organicprops/haloalkanes/grignard.html (2003).

process is laborious and highly sensitive to atmospheric moisture. Today, pre-made Grignard reagents dissolved in inert solvents, like ether, can be purchased from chemical supply companies. These Grignard reagents can be used directly and quickly in reactions.[3]

The reaction of Grignard reagents with aldehydes will give secondary alcohols and with ketones will give tertiary alcohols. You will explore the synthesis of a tertiary alcohol using a methylcyclohexanone. Several analytical techniques such as TLC, melting point, IR, and NMR will be used to demonstrate that you have synthesized and purified the desired compound.[3]

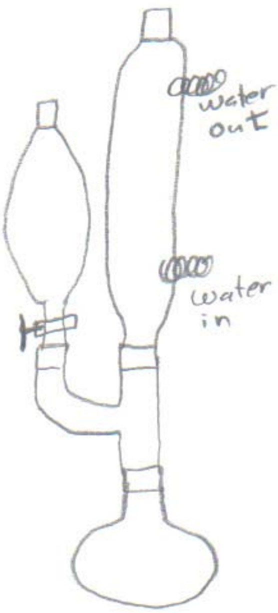




http://etc.usf.edu/clipart/3700/3758/eiffel-tower_1_lg.gif

Procedure

1. Set up equipment as shown in the picture below using a **DRY** 100mL round bottom flask, condenser (water out is top outlet; water in is bottom outlet), additional funnel, and stirring plate. At least two clamps please. Place a stirring magnet in the flask.



2. Measure 0.01 mole of a methylcyclohexanone, and add to 30mL of anhydrous ether in beaker. Add the ketone and ether solution to the closed separatory funnel. ****Ether: hazard class 3, extremely flammable and should be kept away from heat sources, extremely volatile and should be used in a well ventilated area.***

3. Bring your 100 mL round bottom with a stopper to the dispensing hood. Use a syringe to draw out 4.5mL of the Grignard reagent, phenyl magnesium bromide from the stock bottle. Inject the Grignard reagent directly into the round bottom flask and place the stopper on the ground-glass opening. At your hood, refasten the flask to the set-up. ****Phenyl Magnesium Bromide: highly flammable, reacts violently with water, causes burns***

4. Plug the top openings of the condenser and additional funnel with plugs of cottonballs.

5. **Slow step.** Slowly add the ketone solution over the course of 30 minutes into the round-bottom flask. Also at this time turn on the stirring plate to mix solution to the mixture already in the flask. ****When adding ketone solution, adjust the rate so that ether does not boil too vigorously, which may cause burns.***

6. Pour the reaction mixture into a small beaker. Using a 10% solution of sulfuric acid, dropwise, acidify the product. Determine the pH using pH paper. ****Sulfuric Acid: corrosive! Very irritating to respiratory and digestive systems, skin, and eyes, wear gloves and goggles***

7. Extract the acidic aqueous suspension using three 10 mL portions of ether (use Methyl *tert*-Butyl Ether now). a) Add 10 mL of MTBE to the separatory funnel containing the aqueous solution. b) Shake to extract. c) Let settle. d) Drain out the bottom (aqueous) layer into a flask. e) Drain out the ether layer into a separate beaker. f) Add the aqueous solution back into the separatory funnel. g) Repeat twice more. ****When extracting, remember to open the spout to relieve pressure. Do this away from your body and others.***

8. Use the separatory funnel to eliminate any acid remaining in the combined ether extracts. Pour 15 mL of saturated sodium bicarbonate into a separatory funnel containing

combined ether extract. Place the top on the funnel. Shake contents under the hood away from self. Extract the bottom layer. This is the aqueous layer. You will need to keep the ether layer for the next steps.

9. Dry the ether layer using an anhydrous drying agent ($MgSO_4$ or Na_2SO_4). Filter out the drying agent with gravity filtration. Collect the ether in a preweighed beaker. Evaporate the ether in the hood with a stream of forced air or on a hot water bath (use a boiling stick).

10. Obtain the mass of your crude product.

11. Hand in a vial with your product: Include your name, date, and name of your product on the label.

Analysis

Options (do at least one of the following analyses):

1) You may do a TLC of your product (dissolved in a suitable solvent). Since the product is not commercially available, you may compare your product to the starting ketone, and biphenyl (a possible side product).

2) You may perform a UV scan of your product (dissolved in a suitable solvent). Since the product is not commercially available, you may compare your product to the starting ketone, and biphenyl (a possible side product).

3) You may perform an IR scan of your product.

Disposal

- Dispose of pH paper, TLC slides, capillary tubes, filter paper, gloves, and drying agent: in "hazardous solids" container under hood
- Dsipose of leftover liquid from extractions, TLC solvents, filtrate: in "hazardous liquids" container under hood
- Dispose of Paper towels: in general waste basket unless soaked in chemicals, then in "hazardous solids" container under hood

Physical Constants. Complete table of physical constants and safety data:

Name	Formula	M.W. g/mole	m.p. ºC	b.p. ºC	Density g/mL
Ether	$C_4H_{10}O$	74.1224	-116.3	34.6	0.7134
2-methyl-1-cyclohexanone	$C_7H_{12}O$	112.17	-14	162 - 163	0.924
3-methyl-1-cyclohexanone	$C_7H_{12}O$	112.17	-73	169 - 170	0.91 - 0.92
4-methyl-1-cyclohexanone	$C_7H_{12}O$	112.17	-41	169 - 171	0.914
Phenyl Magnesium bromide	C_6H_5BrMg	181.3145			1.14
Concentrated H_2SO_4	H_2SO_4	98.0734	3	280	1.84
Saturated sodium bicarbonate	$CHNaO_3$	84.00687	270	851	2.159
methyl-t-butylether MTBE	$C_5H_{12}O$	88.15	-109	55.2	0.7404
hexane	C_6H_{14}	86.1766	-95	69	0.6548
phenylmethylcyclohexanol					

Name	Solubility	Safety Information
Ether	Immiscible with water Miscible with alcohols and non-polar solvents	Irritation-Eyes, Nose, Throat, Skin
methylcyclohexanone	Insoluble in water Soluble in alcohols Soluble in nonpolar solvents	Warning: Flammable Warning: Irritating to mucous membranes
Phenyl Magnesium bromide	Reacts violently in water	Flammable
H_2SO_4 Concentrated Solution is 18M	Fully miscible (exothermic) in water	Cause severe skin burns. Causes severe eye burns.
Saturated sodium bicarbonate	Soluble in water	Eye contact may cause mild irritation, redness, and pain.
methyl-t-butylether MTBE	Immiscible with water Miscible with alcohols and non-polar solvents	Is an irritant. Take precautions to not allow contact with any part of your body. Flammable!
hexane	Immiscible with water Miscible with alcohols and non-polar solvents	Is an irritant. Take precautions to not allow contact with any part of your body. Flammable!
methylcyclohexanone	Insoluble in water Soluble in alcohols Soluble in nonpolar solvents	Warning: Flammable Warning: Irritating to mucous membranes

- **Pre-Lab**

Title & Purpose
Flowchart:
Calculations:
Calculate the theoretical yield for your expected product.

Write a balanced equation (with chemical structures) for the Grignard addition of phenyl magnesium bromide to 2-methyl-1-cyclohexanone.

What 2 precautions should you take when working with water sensitive reagents such as phenyl magnesium bromide?

Safety Question: http://www.pcl.ox.ac.uk/MSDS/DI/diethyl_ether.html
The MSDS (Material Safety Data Sheet) for diethyl ether states that Flash point: -40º C, Explosion limits: 1.7% - 48%, and Autoignition temperature: 170º C. Define (what are they), contrast (how are they different) and compare (how are they similar) these three physical properties.

Experimental Observations and Data
Hand in a copy of your experimental observations and data before you leave lab.

Lab Report
Results
____% yield of product (mass of recovered product x 100/theoretical yield).
Show your calculations please.
____Interpret TLC (if applicable)
____ Interpret the UV spectrum (if applicable)
____ Interpret the IR spectrum (if applicable)
____ Interpret the GC-FID chromatogram of your sample.
____ Interpret the IR spectrum of your product. http://domin.dom.edu/faculty/jbfriesen/Chem254lab.htm
____ Interpret the ^{1}H NMR spectrum of your product. http://domin.dom.edu/faculty/jbfriesen/Chem254lab.htm
____ Interpret the ^{13}C NMR spectrum of your product. http://domin.dom.edu/faculty/jbfriesen/Chem254lab.htm

Discussion and Conclusion
___What are two ways you could have increased your percent yield?
___What other two analytic tools could you have used in determining your final product?
___ Phenyl magnesium bromide is sometimes reacted with dry ice. What is the product obtained?
___A student discovered a significant amount of 2-phenyl-2-propanol in his product. How did that get there?
___When phenyl magnesium bromide is reacted with acetophenone a non-alcohol is usually found in the final product. What is the structure for this compound?

Green Question
Look up information regarding the Barbier Reaction. Explain the ways it is similar/dissimilar to the Grignard Reaction. How does the Barbier Reaction fit into the concept of green chemistry? Include your references please.