Experiment 4 – Stereochemical Analysis of the Reduction of Benzyl

CHM1321 Section C8

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March 15, 2018

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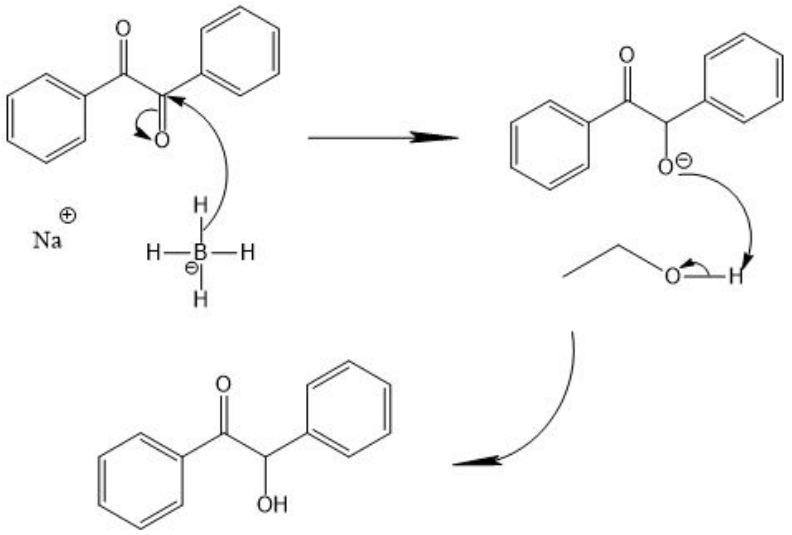
Introduction:

Part 1

The first part of our reaction involves the reduction of benzil using sodium borohydride. A reduction reaction is a half reaction that involves the gain of electrons, typically resulting from a oxygen hydrogen bond. The other half reaction is oxidation which involves losing electrons. In this experiments we are reducing a ketone (benzil), with a hydride (sodium borohydride) to produce a diol. The reason we do this is because ketones are most readily reduced with hydrided agents. The sodium borohydride reacts with the benzil via nucleophilic addition, this creates a intermediate base which reacts with the ethanol through a simple acid base reaction. This reaction is repeated twice, once for each of the oxygens on benzil, this creates hydrobenzoin, a diol.

$$C_{14}H_{10}O_2 + 2\,NaBH_4 + 2\,C_2H_5OH \longrightarrow C_{14}H_{14}O_2 + 2\,NaBH3 + 2\,C_2H_5O$$



Part 2

In the next step in our reaction we use the diol we just created as a reagent in the acetylation reaction. We react our diol with acetone, this is because since the diol has 2 OH groups you only need a 1 to 1 mole ratio to create a acetal, p-toluenesulfonic acid is used as a catalyst.

$$C_{14}H_{14}O_2 + C_2H_5OH \text{ ---} C_{16}H_{21}O_2(catalyst) \longrightarrow C_{16}H_{18}O_2 + H_2O$$

Procedure:

1. Measure 1 g of benzil using a piece of weighing paper folded along both diagonals. Place the compound in a 50 mL Erlenmeyer flask.
2. Place a magnetic stir bar in the flask. Add 5 mL of ethanol and 5 mL of dichloromethane to the flask and clamp over a magnetic stir plate.
3. Place an empty ice bath underneath the flask. Add ice and water to the ice bath and stir for 5 minutes.
4. Add 0.3 g of sodium borohydride in three equal portions to the reaction flask, with two minutes between each addition. Continue stirring for 10 minutes. The mixture should turn clear.
5. Remove the ice bath and allow the solution it to warm to room temperature for 10 minutes, stirring occasionally.
6. While the solution is warming to room temperature, heat 50 mL of water in an Erlenmeyer flask to 80 °C on a hot plate.
7. Once the solution is at room temperature take a TLC of the reaction mixture with the reference as benzil dissolved in dichloromethane, the co-spot and the reaction mixture. 1:9 EtOAc:Hexane should be used as the eluent.
8. Pour 10 mL of hot water into the reaction mixture. Transfer the mixture into a clean Erlenmeyer flask and place it on a hot plate, stirring occasionally. The solution should turn a pale yellow. After 5 minutes the the intense bubbling should stop.
9. Add 20 mL of hot water to the reaction mixture. Stir while heating for another 10 minutes.
10. Remove the flask from the heat and allow it to cool to room temperature. Then collect the crystals that form through suction filtration. Allow the solution to dry for 5 minutes
11. Determine the mass of the product.
12. Perform a TLC of the final product using 1:9 EtOAc:Hexane as the eluent. The crystals can be dissolved with a few drops of methylene chloride.

Part B

1. Place 600 mg of your diol product in a 50 mL round bottom flask and add 25 mL of acetone. Once the compound has dissolved, add 500 mg of anhydrous sodium sulfate and a stirring bar to the flask.
2. Add 50 mg of p-toluenesulfonic acid. Stir the mixture at room temperature for 15 minutes.
3. Take a TLC of the reaction mixture using the diol product as the reference. 1:9 EtOAc:Hexane should be used as the eluent.
4. Prepare two more TLC plates. The reaction mixture should be spotted for each plate. Once plate should use the anti acetonide for the reference and the other should use syn acetonide. Elute both plates using 1:9 EtOAc:Hexanes as the eluent.

Observations:

We started the experiment with 1.01 g of benzil, which was a pale yellow color, after it was reacted with the sodium borohydride in the ice bath it was still a pale yellow color. However when we left it to warm up the solution slowly turned colorless. When we added the hot water the solution did not react at first, but after a couple minutes it started bubbling intensely for more than 5 minutes, it did not change color. Then we added more hot water, and the reaction started bubbling again, before calming down after a couple minutes. After 10 minutes most of the water evaporated and the solution was white and foggy.

Table:

Table 1: Table of reagents for the reduction with NaBH4

Compound	Mol. Wt (g/mol)	Amount	Density (g/mL)	mmol
Benzil	210.232	1.01 g	N/A	4.8
Sodium borohydride	37.83	0.3 g	N/A	7.9
Ethanol	46.07	5 mL	0.789	85.6
Dichloromethane	84.93	5 mL	N/A	N/A

Table 2: Table of reagents for acetalization

Compound	Mol. Wt (g/mol)	Amou nt	Density (g/mL)	mmol
Hydrobenzoin	214.264	600 mg	N/A	2.8
Acetone	58.08	25 mL	0.791	34000
P-toluenesulfonic acid	172.2	50 mg	N/A	N/A

Table 3: Table of products for the reduction with NaBH4

Compound	Mol. Wt (g/mol)	Amou nt	Density (g/mL)	mmol
Hydrobenzoin	214.264	600 mg	N/A	2.8
Acetone	58.08	25 mL	0.791	34000
P-toluenesulfonic acid	172.2	50 mg	N/A	N/A

Results:

Figure 1: Benzil TLC plate

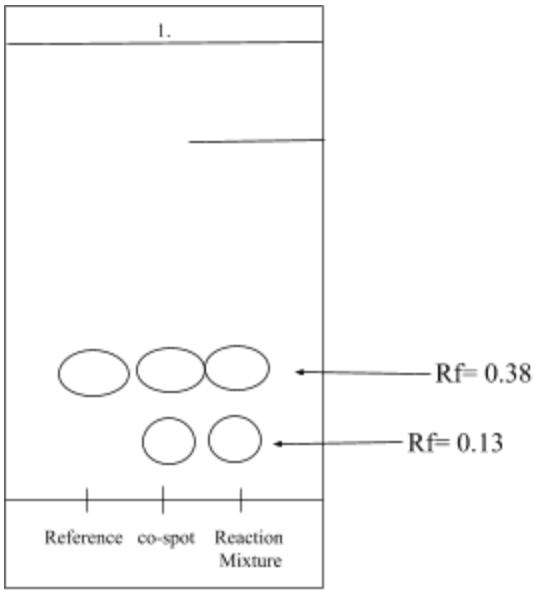


Figure 2: Crystal TLC plate

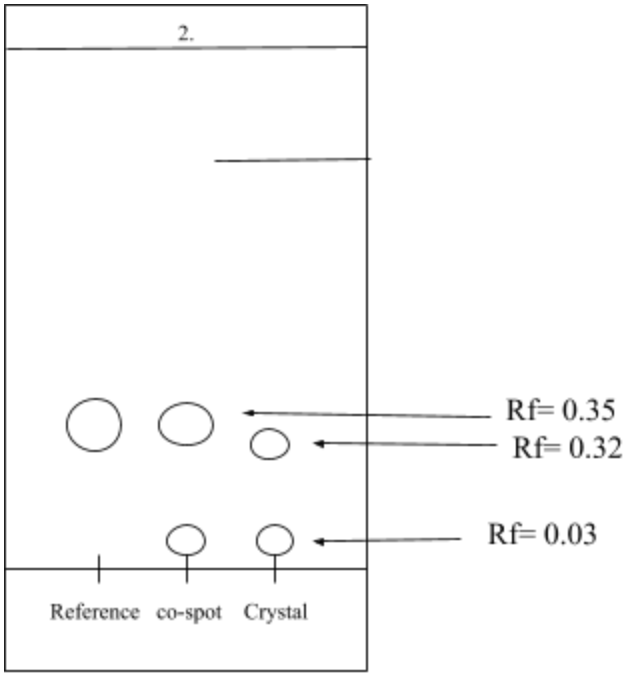


Figure 3: Diol product TLC plate

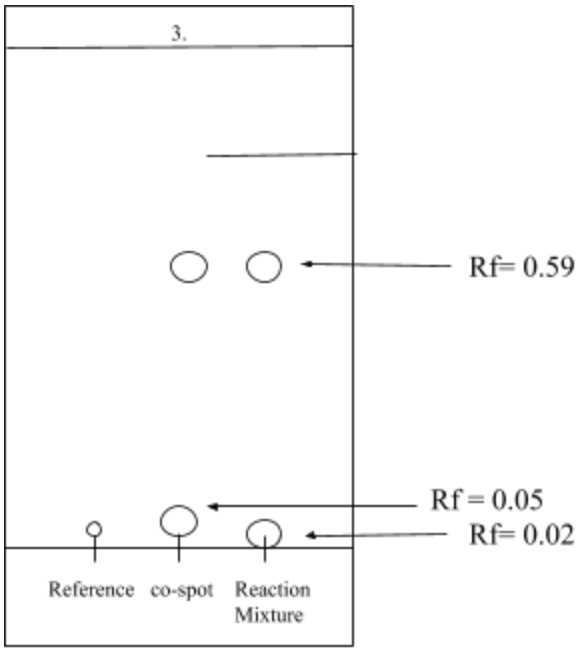


Figure 4: Anti acetonide TLC plate

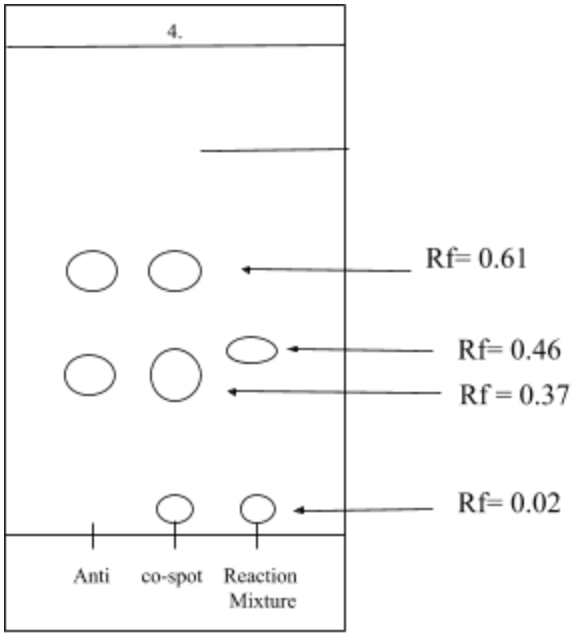
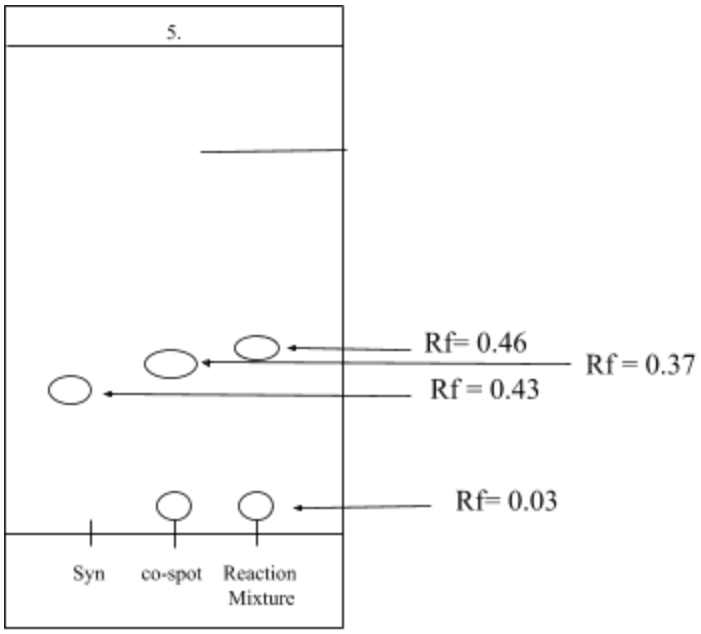


Figure 5: Syn acetonide TLC plate



Calculations:

Percentage yield:

$$\frac{0.91\ g}{1.01\ g} \times 100\% = 90.1\%$$

Discussion:

The purpose of this lab was to create a acetal from benzil. In the first part of the lab we created a hydrobenzoin product through suction filtration and recrystallization. The drastic change in temperature through the ice bath and addition of hot water was a example of recrystallization. This is a technique that is used to remove impurities, the suction filtration is also used to remove further impurities. The first TLC we took was to determine whether a reaction had taken place, we could tell this because the reaction mixture had different spots than the reference, this shows that a additional product had been created. The second TLC was to determine if the reaction was complete and our product was pure. Our crystals were not completely pure, we could tell this because our crystals had 2 spots. There were 3 possible hydrobenzoin products that we could have created a (1R, 2R) isomer, a (1S, 2S) isomer, and a meso compound. This is because the hydride can attack the benzil from the top or the bottom face. The third TLC was used to determine the major product, you can tell this because the reaction mixture had 2 spots, one

which was in line with the diol, which meant it was a major product. TLC 4 and 5 are used to determine which stereoisomers are present. The anti acetonide is the trans isomer and the syn acetonide is the cis isomer. In the fourth TLC the spots matched up with reaction mixture, this meant that the trans isomer was present, however in the fifth TLC the spots did not match up, this means that the cis isomer was less present.

A possible source of error was that the reaction wasn't reached to completion, this would affect the TLC's. Another source error is that on TLC 5 is because the top co-spot did not match up with the reference or the reaction mixture, TLC 3 also could have been a source of error because the reference spot was very small.

Questions:

1. You are given a mixture containing two compounds, A and B. Both compounds have a solubility of 1 g/ 100 mL of solvent at 20 °C and 16 g/ 100 mL of solvent at 100 °C. The sample is composed of 3.5 g of A and 10 g of B. At 100 °C the entire sample just dissolves in a minimum amount of solvent. The solution is cooled to 20 °C and crystals are collected. Calculate the composition of the crystals and the yield of the process. What is the composition of the mother liquor? (Hint: find the minimum amount of solvent needed to dissolve the component that is present in excess; that should be enough to also dissolve the other component).

The minimum volume of solvent needed to dissolve the compounds at 100 °C must be calculated.

$$\frac{16\ g\ A}{100\ mL} = \frac{3.5\ g\ B}{x\ mL} \qquad \frac{16\ g\ B}{100\ mL} = \frac{10\ g\ B}{x\ mL}$$

$$x = 21.875\ mL \qquad x = 62.5\ mL$$

$$Total = 21.875\ mL + 62.5\ mL$$

$$Total = 84.375\ mL$$

Then we cool the solution to 20 degrees which will cause crystals to form. In a 84.375ml solution at 20 degrees we have

$$\frac{1\ gA}{100\ mL} = \frac{x\ gA}{84.375\ mL} \qquad \frac{1\ gB}{100\ mL} = \frac{x\ gA}{84.375\ mL}$$

$$x = 0.8375\ g\ A \qquad x = 0.8375\ g\ B$$

This means that we will have the following amount of compound has been crystallized:

$$3.5 - 0.8375g = 2.6625\ gA \qquad 10 - 0.8375 = 9.1625\ gB$$

$$2.6625\ gA + 9.1625\ gB = 11.825\ g\ total$$

Therefore the composition of the crystal is:

22.5% *compound A* 77.5% *compound B*

The obtained percent yield is:

$$\frac{11.825\ g}{13.5\ g} \times 100\% = 87.6\ \%$$

The composition of the mother liquid is:

$$\frac{3.5\ g\ A}{13.5\ g\ Total} = 25.9\ \%\ compound\ A \qquad \frac{10\ g\ A}{13.5\ g\ Total} = 77.1\ \%\ compound\ B$$

2. If the crystals obtained in question (1) are recrystallized from 100 mL of solvent, what will be the yield and composition of the crystals obtained?

Crystals consist of 2.875g A and 9.375g B dissolved in 100 ml of solvent 100ml at 20ºC can dissolve 1g of A and 1g of B. Calculate the excess of A and B that will crystallize from the solution due to the drop in temperature

$2.875g\ A - 1g\ A = 1.875g\ solid\ A$ $9.375\ g\ B - 1g\ B = 8.375g\ solid\ B$

$Total\ solid\ formed = 1.875g\ A + 8.375g\ B = 10.25\ g\ total$

Composition of the crystals:

$A = \frac{1.875\ g\ A}{10.25\ g} \times 100\% = 18.29\%$ $B = \frac{8.375\ g\ A}{10.25\ g} \times 100\% = 81.17\ \%$

Percent Yield:

$$\frac{10.25\ g}{2.87\ gA + 9.375\ gB} \times 100\% = 83.67\%$$

3. A student dissolves 80 mg of a crude product in 4.5 mL (the minimum required) of methanol at 25 °C. She cools the solution in an ice bath and obtains crystals. The crystals are recovered by filtration and rinsed with 0.5 mL of ice-cold methanol. After drying, the weight of the crystals is 5 mg. Why was the recovery so poor? What could she do to improve the process?

The recovery was so poor is because methanol and the product are both polar so the product was too soluble in the methanol. This means that it's harder to precipitate the product from the methanol. To improve the process she could either use a combination of polar and non-polar solvents, or she could cool the solution for longer.

4. When butanoic acid reacts with sodium borohydride, 1-butanol is not obtained. However, bubbling is still observed and heat is produced.

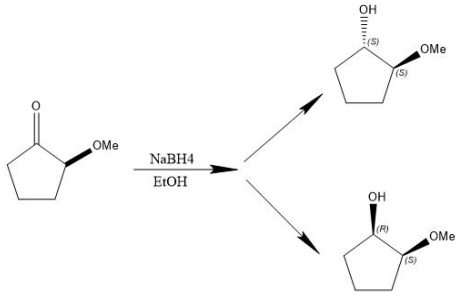
a. Why is 1-butanol not obtained?

1-butanol is not obtained from butanoic acid because butanol is a carboxylic acid and sodium borohydride is not a powerful enough reducing agent to perform the reduction. Sodium borohydride is is very effective for the reduction of aldehydes and ketones to alcohols, but by itself it won't normally reduce carboxylic acids, esters or amides.

b. What is the product of this reaction?

The product of this reaction is hydrogen gas. When the hydrogen atoms of the NaBH4 interact with the protons on the butanoic acid, the result is hydrogen gas, which can be seen as bubbles when the reaction occurs.

5. Predict the configurations of each stereocenter in the product of the following and provide a justification for your choice.



The configurations shown are based on the stereochemistry creating cis and trans products. The R and S configuration has a lower energy when compared to the S and S configuration so it will be more stable and, therefore, is the main stereoisomer in this reaction.

Conclusion:

The final product was weighed at 0.91 g, which gives a percent yield of 90.1%. The stereoisomers produced in the reaction were two trans isomers and a MESO compound.

Raw Data:

Exp 4

1.01 g Benzil

- Pale yellow

-once removed from ice bath it was pale yellow
- It faded to colorless

When added hot water and heated it bubbled intensly for more than 5 min

- Most of the water evaporated
- When 20 ml of water was added it bubbled again
- The soln was white and foggy.

Product + Watch glass 47.09 g
Watch glass 46.18

Product = 0.91

Schneider