Student Name: Quoc-Huy Pham

Student Number: 8623625

Partner's Name and Student #:
John Reilly (7664342)

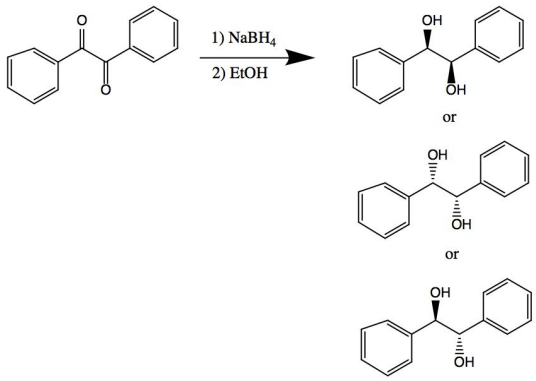
Demonstrator's Name: Craig Yu

Lab Day (T/W/Th/F): W
Lab Week (even/odd): even
Lab time: 10:00

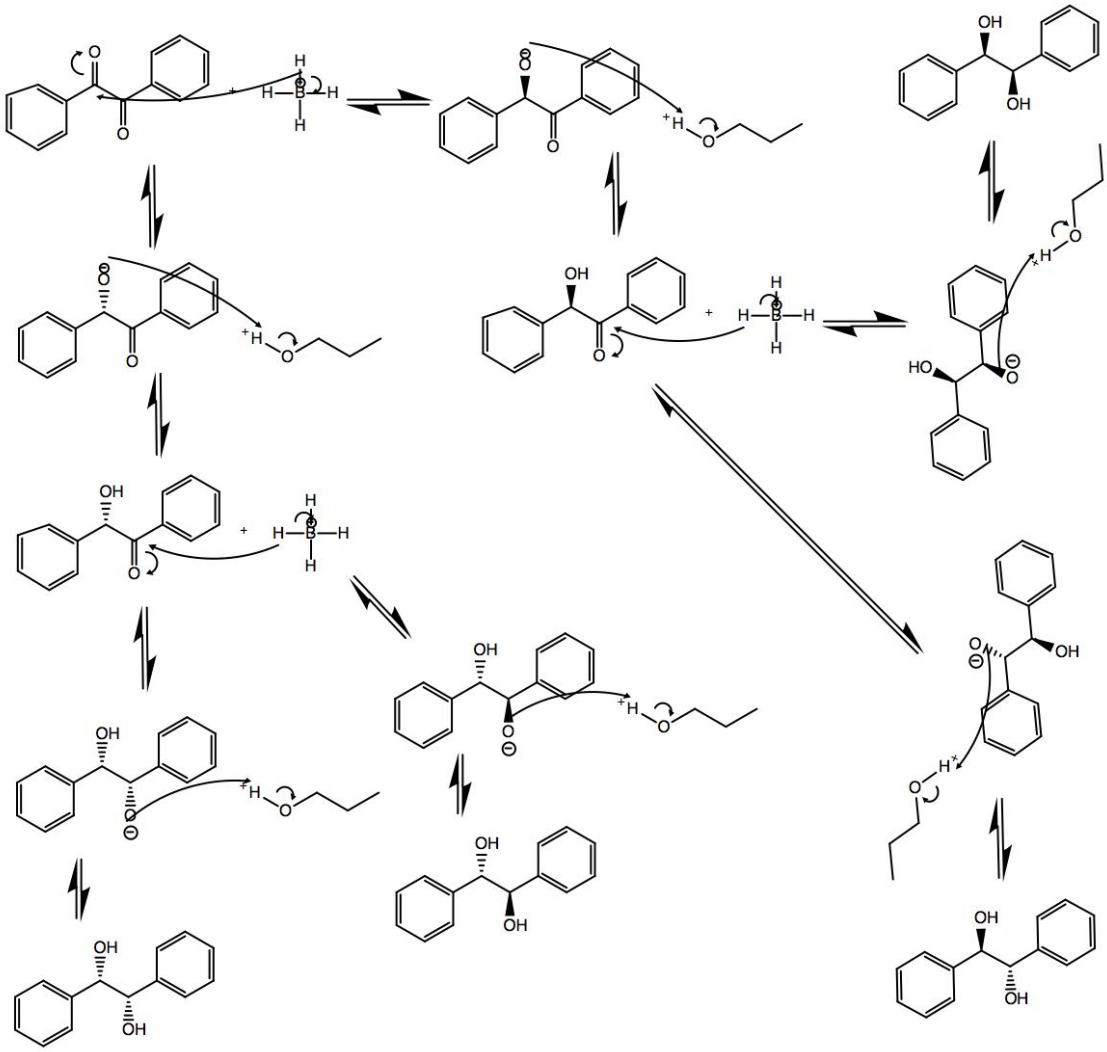
Experiment 4.
Stereochemical Analysis of the Reduction of Benzil

Initials: H.P.

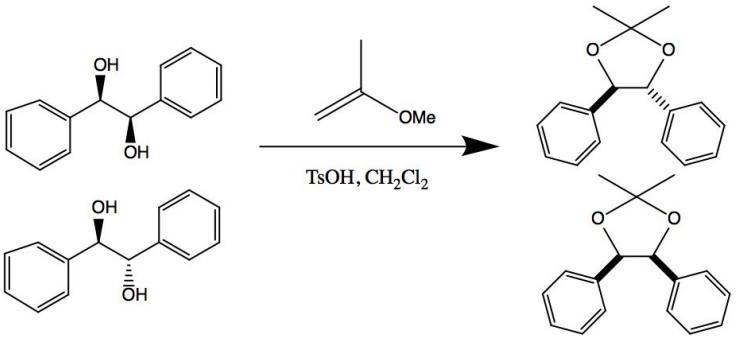
Introduction:
For the reduction of benzil, in which:



The mechanism goes as follows:



For the production of derivatives, the chemical equation follows as such:



Part A: The Reduction of benzil into Hydrobenzoin

Table of Reagents

Compound	Mol. Wt (g/mol)	Amount	Density (g/mL)	mmol
Benzil	210.23	1.00 g		4.76
Ethanol	46.09	10 mL	0.790[1]	
$NaBH_4$	37.83	0.30 g		7.93
Water	11.02	30 mL	0.9718 (at 80°C)[2]	

Procedure:

- 1.00 g of benzil was obtained using folded weighing paper and placed into a 50 mL Erlenmeyer flask
- A magnetic stir bar was gently slid into the flask
- 10 mL of ethanol was measured and added into the flask
- An ice bath was placed on top of a magnetic stir plate that is set to the maximum setting

[1] "Ethanol | CH3CH2OH - PubChem." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Web. 13 Mar. 2017.
[2] Harr, L., Gallagher, J.S.,. and Kell, G.S. *NBS/NRC Steam Tables*, Hemisphere Publishing Corp., 1984

- The flask was placed into the ice bath and stirred for 5 minutes. The mixture became a pale yellow
- 0.1 g of $NaBH_4$ was obtained and added into the flask
- The flask was placed into the ice bath and stirred for 2 minutes
- 0.1 g of $NaBH_4$ was obtained and added again into the flask
- The flask was placed into the ice bath and stirred for 2 minutes
- 0.1 g of $NaBH_4$ was obtained and added again into the flask
- The flask was placed into the ice bath and stirred for 10 minutes. The mixture completely lost its yellow colour
- The flask was replaced from the ice bath and placed on the stir plate with the ice bath removed for 10 minutes
- 50 mL of distilled water was obtained and heated to 80°C using a hot plate.
- A TLC of the reaction mixture was created with the acetonide (*cis- and trans-*), a co-spot and the reaction mixture as the lane in order to determine if the reaction was complete. 1:9 EtOAc:Hexane was obtained and used as an eluent
- 10 mL of hot water was added to the flask
- The mixture was transferred to an alternate flask and placed on a hot plate for 5 minutes. There was intense bubbling.
- 20 mL of hot water was added to the flask and stirred for 10 minutes. The mixture remained a partially translucent and lacked any yellow colour.
- A tube was attached to the nozzle of the water sink and to a suction flask
- A Buchner funnel was attached to the top of the suction flask with filter paper placed on it
- The mixture was poured onto the funnel. Distilled water was added to ensure all the solids were on the funnel. The filtered liquid still contained some of the crystals
- The crystals was collected, dried and weighed. A scoopula was used to scrape off some of the crystals. 0.71 g were collected.
- The filtered liquid was transferred to a clean 250 mL beaker
- The filtered liquid was poured onto the funnel
- The crystals was collected, dried and weighed. A scoopula was used to scrape off some of the crystals. 0.20 g were collected.
- A total mass of 0.91 g was obtained. Melting point (meso form) (Literature) = 136°C[3]

[3] "MESO-HYDROBENZOIN." *MESO-HYDROBENZOIN | C14H14O2 | ChemSpider*. Web. 13 Mar. 2017.

Part B: The Determination of Stereoisomers of Hydrobenzoin

Table of Reagents

Compound	Mol. Wt (g/mol)	Amount	Density (g/mL)	mmol
Hydrobenzoin	214.26	600 g		2.8
Dichloromethane	84.93	25 mL	1.33[4]	
Sodium sulfate	142.04	500 g		3.52
p-toluenesulfonic acid	172.2	50 mg		0.29
2-methoxypropene	72.11	10 mL		

Procedure:

- 600 mg of diol product was added into a 50 mL round-bottom flask
- 25 mL of dichloromethane and 500 mg of sodium sulfate was added to the flask and stirred
- 1.0 mL of 2-methoxypropene and 50 mg of p-toluenesulfonic acid was added to the mixture and stirred for 30 minutes
- Two TLC plates were prepared with the reaction mixture as the reference, *syn* acetonide spotted on one of the plates, and *anti* acetonide on the other plate
- The plates were eluted in 1:9 EtOAc:Hexane and developed

[4] "DICHLOROMETHANE | CH2Cl2 - PubChem." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Web. 13 Mar. 2017.

Data:

Table 1: Experimental data of TLC of trans-acetonide compared with reaction mixture

Measurement (cm)	Displacement before addition of hot water	Displacement after addition of hot water
Solvent front (R_s)	5.8	5
Displacement of Reference	4.2	3.2
Displacement of Co-spot	0.35	0.45/3.2
Displacement of Reaction Mixture	0.35	0.4

Figure 1. TLC plate of reaction mixture compared with references before addition of hot water

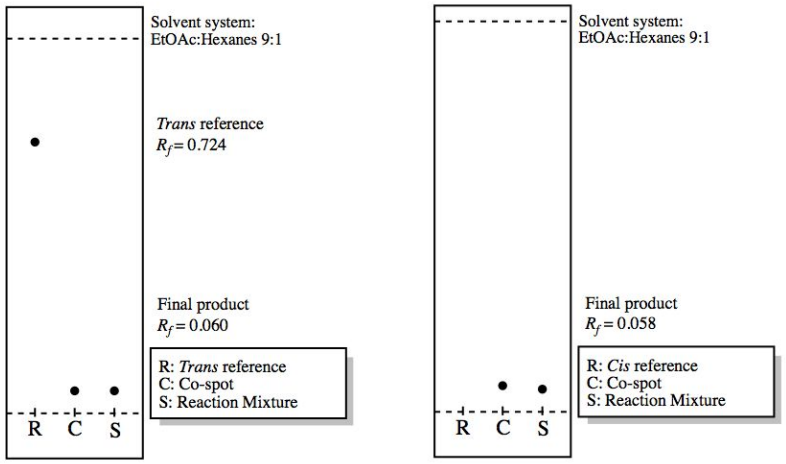


Table 2: Experimental data of TLC of cis-acetonide compared with reaction mixture

Measurement (cm)	Displacement before addition of hot water	Displacement after addition of hot water
Solvent front (R_s)	6	4
Displacement of Reference	N/A	3.2
Displacement of Co-spot	0.4	0.75/3.1
Displacement of Reaction Mixture	0.3	0.9

Figure 2. TLC plate of reaction mixture compared with references after addition of hot water

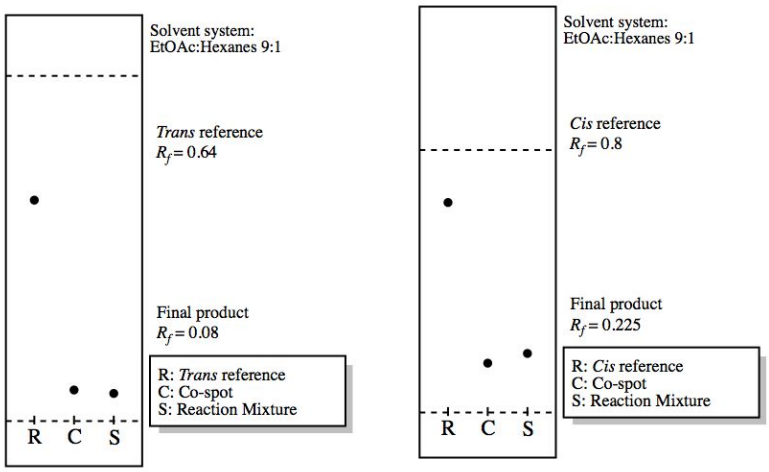


Table 3: Experimental data of TLC of final product

Measurement	Displacement (cm)
Solvent front (R_s)	5.5
Displacement of benzil	4.1
Displacement of Co-spot	1
Displacement of Reaction Mixture	1.1

Figure 3. TLC plate of final product compared with benzil reference

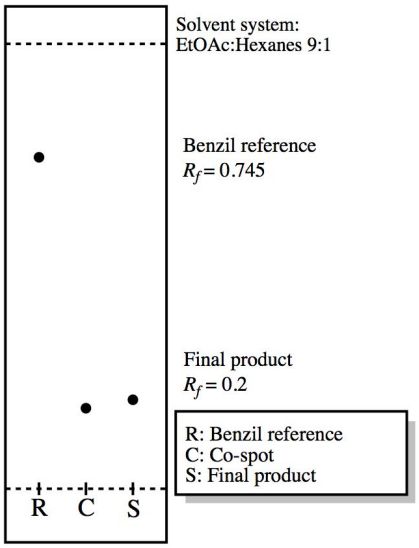


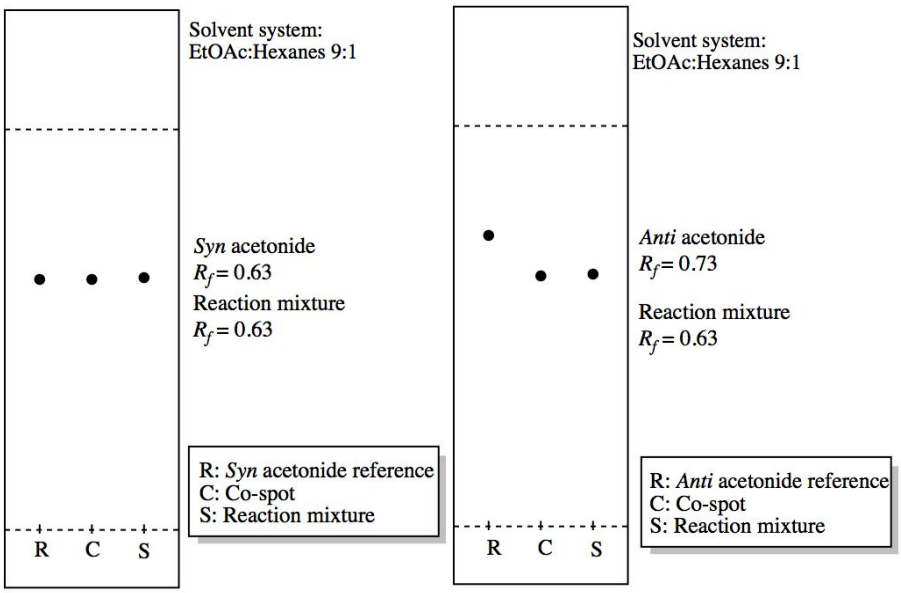
Table 4: Experimental data of TLC of syn acetonide compared with reaction mixture of Part B

Measurement	Displacement (cm)
Solvent front (R_s)	4.8
Displacement of Original Sample	3
Displacement of Co-spot	3
Displacement of Reaction Mixture	3

Table 5: Experimental data of TLC of anti acetonide compared with reaction mixture of Part B

Measurement	Displacement (cm)
Solvent front (R_s)	4.8
Displacement of Original Sample	3.5
Displacement of Co-spot	3
Displacement of Reaction Mixture	3

Figure 3. TLC plates of anti and syn acetonide compared with reaction mixture of Part B



Calculation:

Retention Factor:

TLC 1

Retention factor of reference

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{4.2\ cm}{5.8\ cm} = 0.724$$

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.060$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.060$$

TLC 2

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.066$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.058$$

TLC 3

Retention factor of reference

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{3.2\ cm}{5.0\ cm} = 0.64$$

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.09$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.08$$

TLC 4

Retention factor of reference

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{3.2\ cm}{4.0\ cm} = 0.8$$

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.1875$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.225$$

TLC 5

Retention factor of Final product

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{4.1\ cm}{5.5\ cm} = 0.745$$

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.181$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.2$$

TLC 6

Retention factor of *syn* acetonide

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{3.0\ cm}{4.8\ cm} = 0.625$$

Retention factor of Co-spot

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.625$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.625$$

TLC 7

Retention factor of *anti* acetonide

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = \frac{3.5\ cm}{4.8\ cm} = 0.729$$

Retention factor of Co-spot

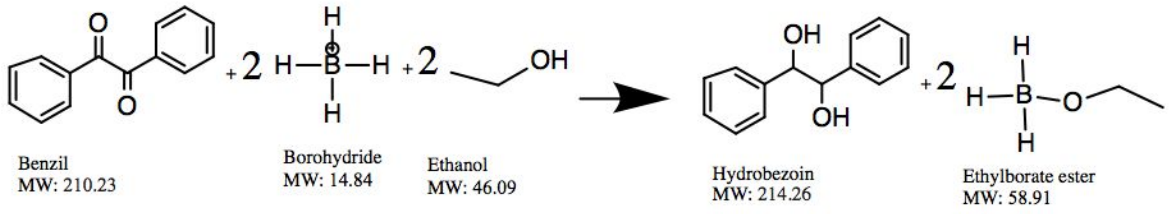
$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.625$$

Retention factor of Reaction Mixture

$$R_f = \frac{Displacement\ of\ Substance}{Displacement\ of\ solvent\ front} = 0.625$$

Percent Yield:

Mass obtained: 0.91 g of hydrobenzoin



Since the ethanol is in excess, either the benzil or the sodium borohydride is the limiting reagent. 4.76 mmol of benzil require 15.86 mmol of borohydride, while 7.93 mmol of sodium borohydride require 2.38 mmol of benzil. Thus, the limiting reagent is the sodium borohydride.

As a result, 2.83 mmol of benzil will produce 2.83 mmol (or 0.00283 moles) of hydrobenzoin.

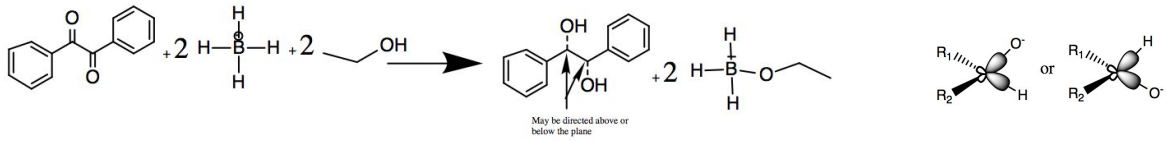
Theoretical yield (mass) = moles of hydrobenzoin × molar mass of hydrobenzoin
= 0.00283 moles of hydrobenzoin × 214.26 g/mol = 0.61 g of hydrobenzoin

$$\text{Percent Yield} = \frac{Experimental\ Yield}{Theoretical\ Yield} \times 100\%$$
$$= \frac{0.91\ g\ of\ hydrobenzoin}{0.61\ g\ of\ hydrobenzoin} \times 100\% = 149\%$$

Discussion:

During the reaction of Part A, the borohydride serves as an electrophile and attacks the ketone carbons of benzil either above or below the plane. This reduced the group which, along with the proton addition due to ethanol, produces alcohol groups. Since the alcohol group relies exclusively on sigma

bonds, those carbons are sp^3 hybridized. As a result, there are products that are stereoisomers to each other.



As a result of an error involving misidentification, the reference lane is that of acetonide instead of benzil. However, the TLC plates may indicate that the reaction is complete as the co-spot and the sample lane displayed only one spot and hence, the sample likely contains only one type of chemical. This is supplemented by the colour (or lack there of) in the final product, where the original mixture of benzil was yellow in colour, indicating that the presence of benzil molecules causes the mixture to reflect yellow light. After the reduction of the benzil by borohydride, the mixture eventually lost all its colour, indicating an absence of benzil molecules and that the reaction is complete. Though this contradicts how, according to the calculations, there are more moles of benzil than borohydride.

During the experiment, heat is added to the reaction mixture. A possible purpose of this addition of heat is to accelerate the rate of reaction into hydrobenzoin so that the reaction may be further completed. Another possible purpose to the addition of heat to the mixture is to boil off the ethanol solvent but not the water, considering that the water added to the mixture and the mixture itself on the hot plate was at an approximate temperature of 80°C, which exceeds the boiling point of ethanol (78°C). By boiling off all the ethanol in the mixture, then the probability of the reaction product re-dissolving into the mixture is greatly reduced, which allows for maximization of the crystal products collected. Though, the issue of impurities may arise if both the desired product and impurities are insoluble to water at low temperatures.

The formation of crystals in the mixture is the result of the cooling of the mixture from a high temperature, which provides kinetic energy for the molecules of solvent to produce volume for the molecules of solutes to occupy in disassociation, to a lower temperature. As the solution cools, the available volume for desired solute dissociation is reduced, causing the solute to associate with each other into crystals. The impurities, however, will remain dissolved in the solvent so when the mixture is filtered, the desired product can be collected on the filter paper while the impurities are carried along with the solvent. The rate of cooling has an effect on the purity of the extracted product, where with a slow rate, the impurities may re-dissolve into the solution while a faster rate of cooling prevents the re-dissolution of impurities and as a result, can trap some solvents in the crystals. This phenomenon of trapping some solvent is likely to have contributed to the very high percent yield, where the total experimental mass encompasses the desired product, impurities and some solvent. Another plausible factor to the very high experimental yield is the additional suction filtration of filtered liquid, which was originally employed for the purpose of purification and extracting as much product as possible. This additional filtration provided an additional 0.20 g of crystals. However, the original experimental mass collected still exceeds the theoretical mass by 0.11 g. The observation that the mixture remained translucent and colourless after it was heated could have been an indicator of deviation. This could be mitigated by increasing the water output of the water source, thereby increasing

the force pushing on the water and producing a vacuum with greater pressure acting towards it. This allows for a greater amount of force pushing down on the crystals.

From the retention factors derived from the TLC plates of Part B, the reaction product is *syn* acetonide as the reference and reaction product both have a retention factor of 0.625, meaning that the hydrobenzoin is *anti* with either a (*R,S*) or (*S,R*) configuration.

Question:

1. Given that the solubilities of the substances are 1 g/ 100 mL of solvent at 20 °C and 16 g/ 100 mL of solvent at 100 °C and the masses of A and B are 3.5 g and 10 g respectively:
   $\frac{16\ g}{100\ mL} = \frac{10\ g}{x\ mL}$, x = 62.5 mL
   $\frac{1\ g}{100\ mL} = \frac{x\ g\ of\ A}{62.5\ mL}$, x = 0.625g
   $\frac{1\ g}{100\ mL} = \frac{x\ g}{62.5\ mL}$, x = 0.625 g
   From that, 2.875 g of A and 9.375 g of B are collected, resulting in crystals that are comprised of 23.47% A and 76.53% B, a percent yield of 82.14% for A and 93.75% for B, and a mother liquor comprised of 0.625 g of A and 0.625 g of B

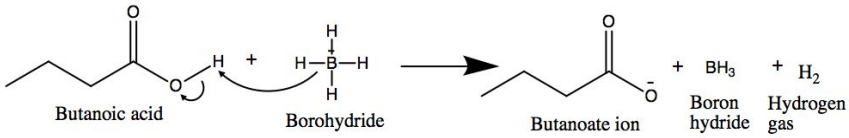
2. The crystal is comprised of 2.875 g of A and 9.375 g of B.
   $\frac{16\ g}{100\ mL} = \frac{9.375\ g}{x\ mL}$, x = 58.59 mL
   $\frac{1\ g}{100\ mL} = \frac{x\ g}{58.59\ mL}$, x = 0.586 g
   $\frac{1\ g}{100\ mL} = \frac{x\ g}{58.59\ mL}$, x = 0.586 g

   From that, 2.289 g of A and 8.789 g of B are collected, resulting in crystals that are comprised of 20.66% A and 79.33% B, a percent yield of 79.61% for A and 93.75% for B.

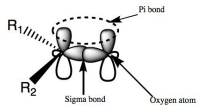
3. One factor in why the recovery of the crystals was so poor is the solubility of the crude product with respects to methanol, where it is possible that the crystals are soluble with the methanol that is being used to rinse the crystals. As a result, the rinsing causes some of the crystals to become dissolved and be transported across the filtration paper. In order to avoid this issue, she should use a rinsing liquid in which the crystals are not soluble in (presumably a non-polar solvent). The temperature of the solvent in which the crude product is dissolved is also a factor in the low yield, where at 25°C, the time in which the crude product may not be sufficient for crystallization, resulting in some of the product remain dissolved in the solvent. To solve this issue, she could either heat the solvent to a higher temperature like 60°C or use a solvent which has a slower cooling rate, thus allowing more time for crystallization.

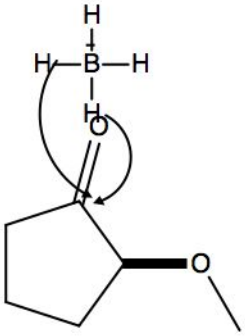
4. a) The reason why 1-butanol is not produced is that, as a result of the acidic nature of the carboxyl group of butanoic acid and how the boron hydride may act as a base, the reaction is a acid-base reaction. Since the reaction between an acid and a base has greater priority than an nucleophilic reaction, the former occurs during the reaction of butanoic acid and boron hydride.

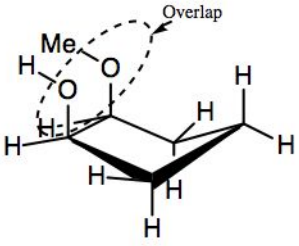
b) Instead of 1-butanol, boron hydride, hydrogen gas, and butanoate ions are formed. The bubbling of the mixture and the heat are likely the result of hydrogen gas.

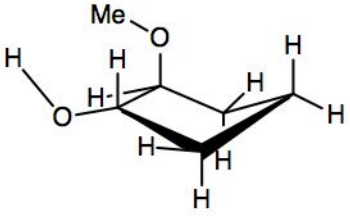


5. The initial molecule of 2-Methoxycyclopentan-1-one has two carbon-oxygen bonds, one that forms a ketone group and one that forms an ether group. The stereocenter is at the carbon of the ether bond, which is bold, indicating that it is above the plane of the entire molecule. As a result, it is an *(S)*-configuration. In the reaction, the borohydride (more specifically, the hydrogen atom) serves as the nucleophile. Between the two carbon-oxygen bonds, the ketone group is more susceptible to nucleophilic attack than the ether group since the ketone has a pi bond, which is weaker than the sigma bond of the ether bond. This results, after the addition of a proton from the methanol, in an alcohol group attached to a carbon with a sp^3 hybridization. The nucleophilic agent may attack the ketone carbon from above or below, resulting in an (*R*) and (*S*) configuration respectively. However, the (*R*) configuration of the alcohol carbon produces bonding orbital overlap while (*S*) configuration lacks such overlap. As a result, the (*S*) configuration is more stable and is more favoured.









Works Cited

"DICHLOROMETHANE | CH2Cl2 - PubChem." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Web. 13 Mar. 2017.

"Ethanol | CH3CH2OH - PubChem." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Web. 13 Mar. 2017.

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"MESO-HYDROBENZOIN." *MESO-HYDROBENZOIN | C14H14O2 | ChemSpider*. Web. 13 Mar. 2017.

m_{benzil} = 1.00 g
$V_{ethanol}$ = 10 mL (95%)

0.1 g of $NaBH_4$

Times stirred
- 5 minutes
- 2 —
- 2
- 2 —
- 10 —

Stir plate set to FAST

Liquid:
Yellow to pale yellow (practically white)

(T) Solvent front: 5.8 cm — R: 4.2 cm — C: 0.35 — S: .35
(C) Solvent front: ? cm — cm — C: 4 — S: 03
(T) Solvent front: 5 cm — R: 3.2 cm — C: 0.45 cm / 3.2 cm — S: 0.4 cm
(C) Solvent front: 4 cm — R: 3.2 cm — C: 3.1 cm, 0.75 — S: 0.9 cm
1:9 EtOAc:Hex — 5.5 cm — 4.1 cm — 1 cm — 1.1

m_{crude} = 0.70 g ± 0.21 g

Part B → Rinse flasks with acetone & dry

500 mg of sulfate
50 mg of p-acid

Solvent
S & A 5.8 4.8
S: 3 A 3.5
S: 3 A 3
S: 3 A 3.4

D: 4.7
↳ MA
↳ 2.3
↳ 2.4