LAB 4:

Stereochemical Analysis of the Reduction of Benzil

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CHM1321 - Z05

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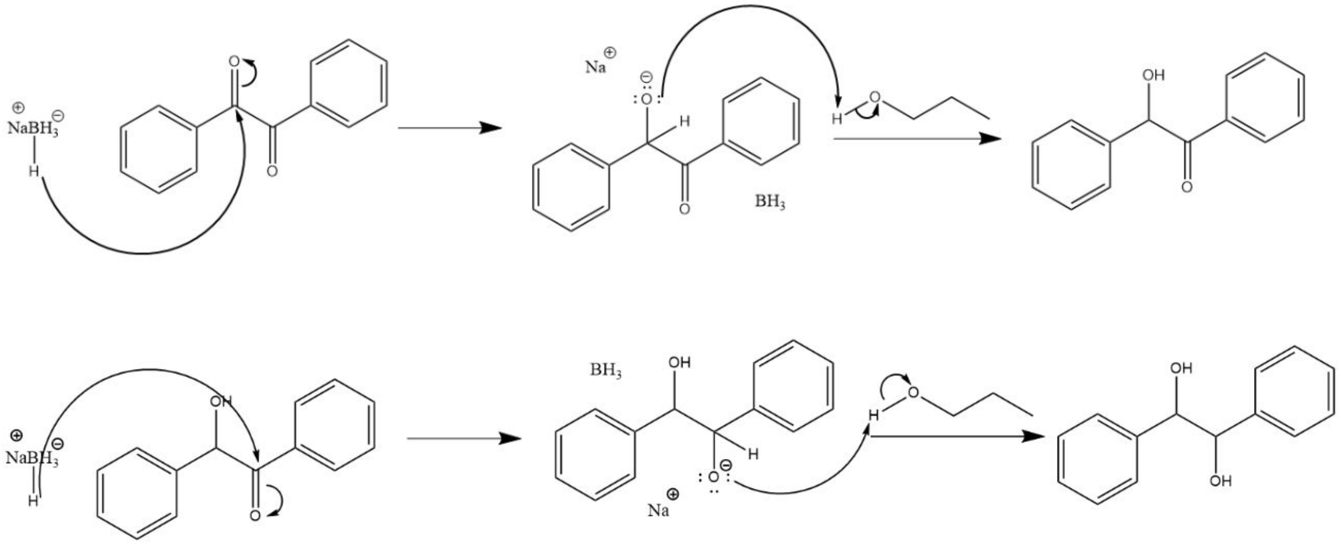
Procedure

See lab manual Experiment 4:The Stereochemical Analysis of the Reduction of Benzil(pg 1-6)

Mechanism

Figure 1.0. Flowchart depicting the steps of the mechanism for the reduction of benzil to benzoin



Qualitative Observations

- ➢ Benzil was a yellow coloured powder. Upon dissolving the benzil in the clear ethanol and dichloromethane solutions, the whole solution became a bright yellow colour.
- ➢ This solution was stirred in an ice bath with no change in colour.
- ➢ Eventually, sodium borohydride was added to the solution. After all the sodium borohydride had been added to the solution and some time had passed, the solution became a bit paler in colour than it was originally.
- ➢ The erlenmeyer flask was then removed from the ice bath and stirred. Since multiple TLCs had to be performed the solution was left at room temperature and stirred for a long period of time. During this time the clear solution became more translucent (almost opaque) and the yellow colour had further diminished. The solution looked almost like watered down milk with a yellow tinge.
- ➢ When 10 ml of the hot water was added to the mixture the mixture became clear and the yellow colour could be seen a bit more, although it was still pale. It is at this stage that the mixture was also heated on a hot plate and an intense bubbling was seen.
- ➢ When 20 ml of the hot water was added to the reaction mixture the solution became colourless. The mixture was gently boiled and stirred.
- ➢ Next, the mixture was removed from the hot plate and allowed to cool slowly. Over time crystals began to form on the sides of the flask. These crystals were white in colour.
- ➢ After the flask had cooled to room temperature the crystals were collected using gravity and suction filtration. The crystals were flaky and white.

Quantitative Observations and Results
Part A

Table 1.0. Reagents involved in the reduction of benzil

Reagent	Amount (g or ml)	Molecular Weight (g/mole)*	Moles (mmol)	Density (g/ml)
Benzil	1.00 g	210.232	4.76	-
NaBH4	0.30 g	37.832	7.93	-
EtOH	5 ml	46.069	-	-
Dichloromethane	5 ml	84.927	-	-

*Molecular weights for reagents from (National Center for Biotechnology Information. PubChem Compound Database; CID=8651, CID=4311764, CID=702, CID=6344)

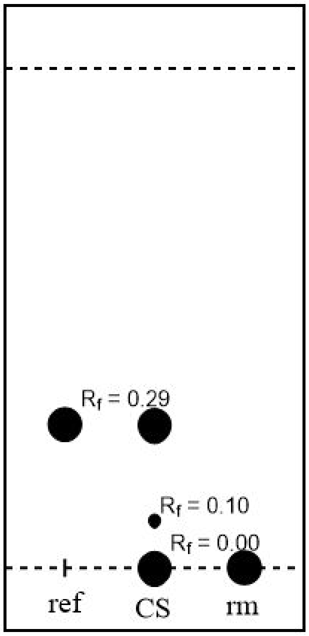
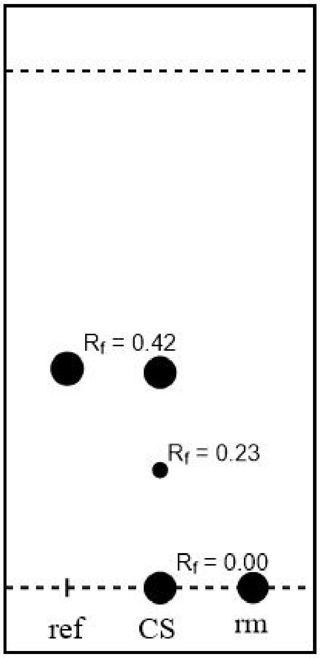
TLC's	**Figure 2.1.** TLC of Reaction mixture using benzil as reference at the start of the reaction
Legend: L = lowest Spot (Vertically) H = Highest Spot (Vertically) M = Most Middle Spot (Vertically) d_s = displacement between former and new solvent line d_X= displacement between starting solvent line and molecule ● = 1 Spot visible under UV light	 Solvent System: EtOAc:hex 1:9 *displacements*: d_s= 4.8 cm d_{ref} = 1.4 cm $d_{CS(H)}$ = 1.4 cm $d_{CS(M)}$ = 0.5 cm $d_{CS(L)}$ = 0.0 cm d_{rm}= 0.0 cm Ref = reference CS = Co-Spot rm = reaction mixture

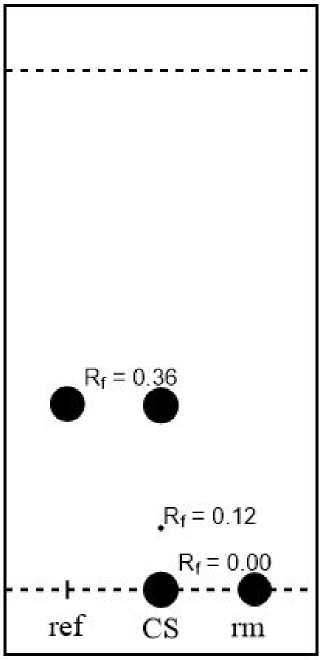
Figure 2.2. TLC of Reaction mixture using benzil as reference in the middle of the reaction	**Figure 2.3.** TLC of Reaction mixture using benzil as reference at the end of the reaction



Solvent System:
EtOAc:hex
1:9

displacements:
d_s= 4.3 cm
d_{ref} = 1.8 cm
$d_{CS(H)}$ = 1.8 cm
$d_{CS(M)}$ = 1.0 cm
$d_{CS(L)}$ = 0.0 cm
d_{rm}= 0.0 cm

Ref = reference
CS = Co-Spot
rm = reaction mixture

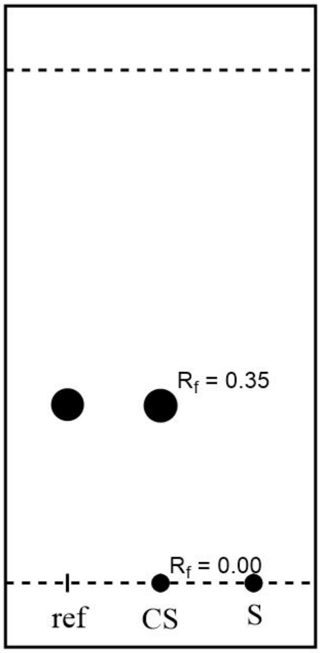


Solvent System:
EtOAc:hex
1:9

displacements:
d_s= 4.1 cm
d_{ref} = 1.5 cm
$d_{CS(H)}$ = 1.5 cm
$d_{CS(M)}$ = 0.5 cm
$d_{CS(L)}$ = 0.0 cm
d_{rm}= 0.0 cm

Ref = reference
CS = Co-Spot
rm = reaction mixture

Figure 3.1. TLC of the final product (benzoin) using benzil as reference - Trial 1

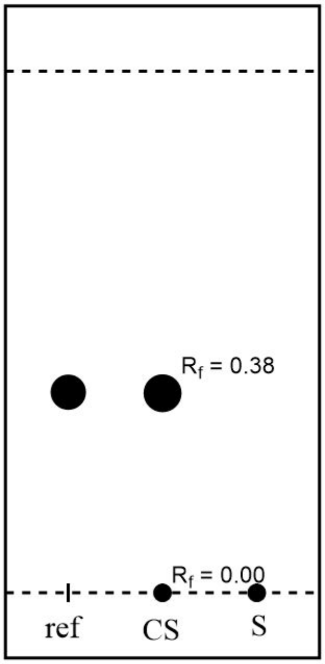


Solvent System:
EtOAc:hex
1:9

displacements:
d_s= 4.6 cm
d_{ref} = 1.6 cm
$d_{CS(H)}$ = 1.6 cm
$d_{CS(L)}$ = 0.0 cm
d_{rm}= 0.0 cm

Ref = reference
CS = Co-Spot
S = sample of final product

Figure 3.2. TLC of the final product (benzoin) using benzil as reference - Trial 2



Solvent System:
EtOAc:hex
1:9

displacements:
d_s= 4.8 cm
d_{ref} = 1.8 cm
$d_{CS(H)}$ = 1.8 cm
$d_{CS(L)}$ = 0.0 cm
d_{rm}= 0.0 cm

Ref = reference
CS = Co-Spot
S = sample of final product

Table 2.0. Results regarding the final product of the reduction reaction, benzoin

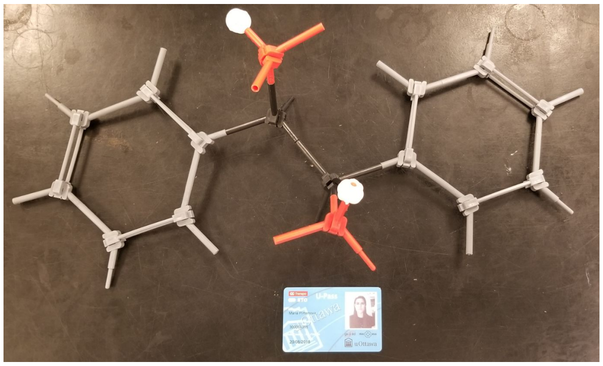
Product	**Amount (g or ml)**	**Molecular Weight (g/mole)***	**Moles (mM)**	**% Yield**
Benzoin	0.80 g	212.248	3.77	79.2

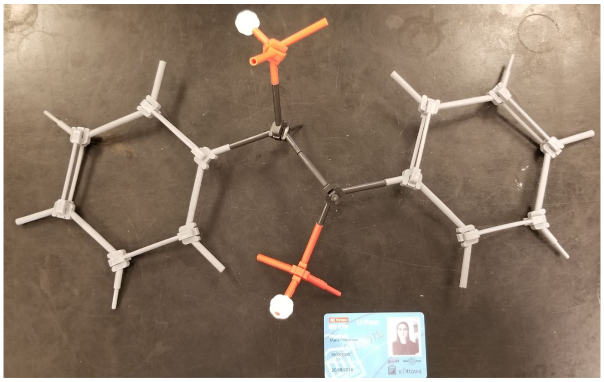
* Molecular weight benzoin (National Center for Biotechnology Information. PubChem Compound Database; CID=8400)

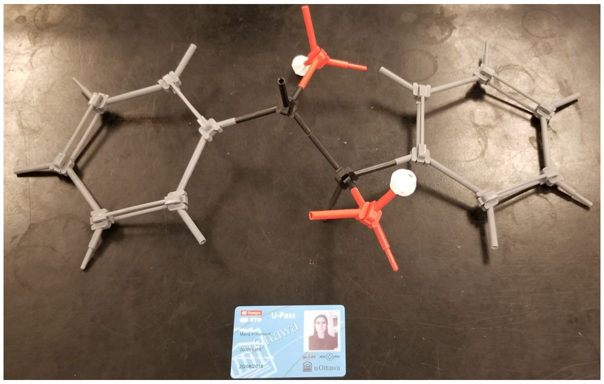
Part B

Maria Pimenova (300065365)

Representative models of benzoin product

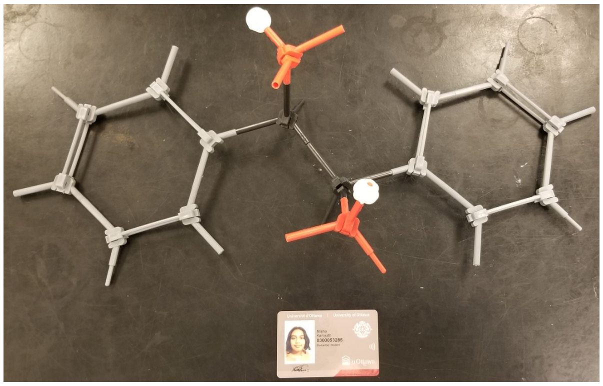


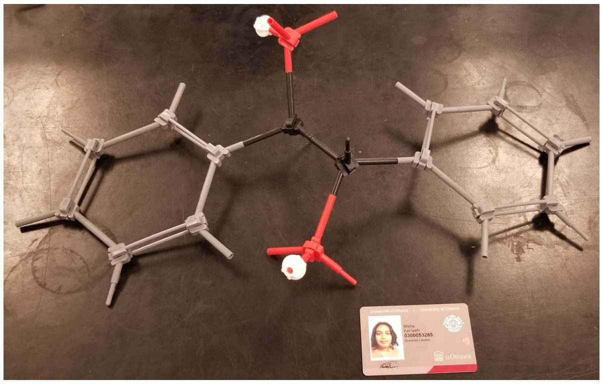


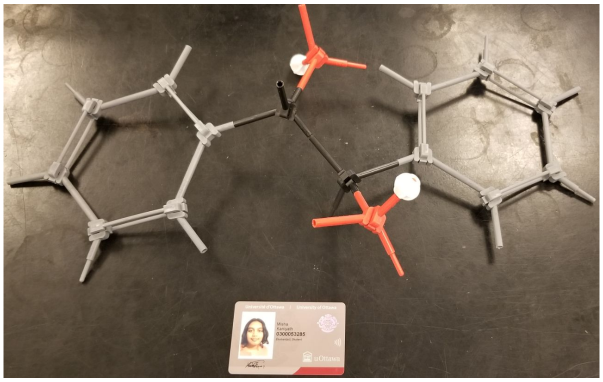


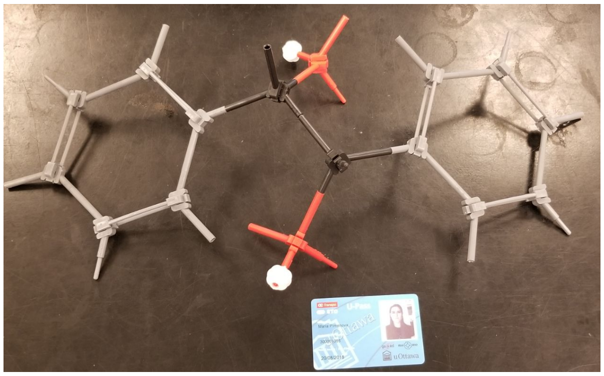
Misha Kaniyath (300053285)

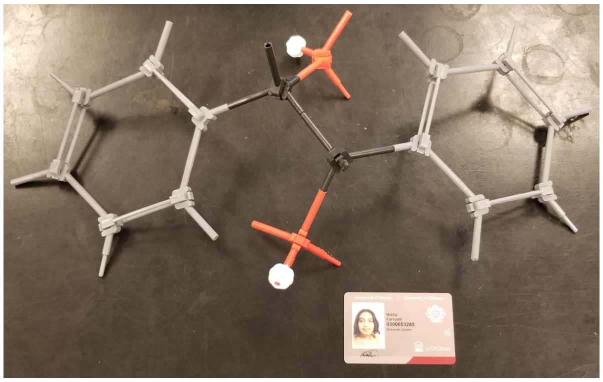
Representative models of benzoin product











Calculations

Sample Rf Calculation from Part A, Figure 3.1.

Given:	*Calculation:*
d_s= 4.6 cm d_{ref} = 1.6 cm $d_{CS(H)}$ = 1.6 cm $d_{CS(L)}$ = 0.0 cm d_{rm}= 0.0 cm	**$Rf = d_x/d_s$** $Rf_{ref,\ CS(H)}$ = 1.6 cm /4.6 cm = 0.35 $Rf_{rm,\ CS(L)}$ = 0.0 cm /4.6 cm = 0.00

Calculation of the percent yield of benzoin product

Because stoichiometrically all of the benzil becomes benzoin product the ratio of products to reactants is 1:1. Therefore, the amount of benzoin that should have been obtained theoretically in millimoles is 4.76 mmol

$$\%\ \text{Yield} = \frac{\text{actual yield (in mmol)}}{\text{theoretical yield (in mmol)}} \times 100$$

$$\%\ \text{Yield} = \frac{\text{\# of mol of product}}{\text{\# of mol of starting material}} \times 100$$

$$\%\ \text{Yield} = \frac{3.77\ \text{mmol}}{4.76\ \text{mmol}} \times 100$$

% Yield = 79.2%

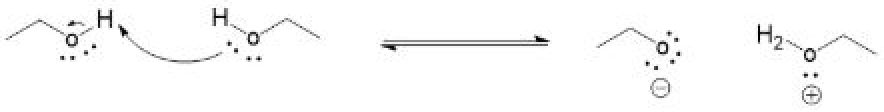
Discussion

Part A

The purpose of this lab was to reduce benzil to produce pure benzoin product, and then calculate the percent yield of the product. Essentially, when reducing benzil to benzoin, the carbonyl groups of the benzil is reduced as it will be acted on by a nucleophile which will be added to its pi bond and increase the number of electrons on the carbonyl. During the lab, firstly, dichloromethane was utilized as a non-reactive material. It was used in order to increase the solubility of the benzil solid in order to dissolve it. Ethanol was another solvent that was used, but as a reactive material. Ethanol is a protic solvent and is required for the reduction reaction mechanism.

Sodium Borohydride (NaBH4) was also utilized as the reducing agent of the reaction (figure 4.1). It is able to do so due to its nucleophilic properties in the form of 4 hydride ions (H-) which it is able to give away to electrophiles. It is the transfer of a hydride from a sodium borohydride molecule to each of the carbonyl groups of benzil that allows for the formation of the alkoxide (this is result of the breaking of the pi-bond in the carbonyl group and the transfer of those electrons to the oxygen).

Figure 4.0. Reaction of 2 ethanol molecules



Additionally, 2 molecules of ethanol participate in the reaction to enable the transfer of hydrides. 2 molecules of ethanol react to form a negatively charged nucleophilic alkoxide (see Fig. 4.0.). It is this molecule that donates electrons to the borohydride molecule. This causes the borohydride to become more nucleophilic and so, it is prompted to donate a hydride nucleophile to the carbonyl group to make the alkoxide, as described previously (“Experiment 4 : Stereochemical Analysis of the Reduction of Benzil,” 2014).

Figure 4.1. Reaction of Borohydride and Carbonyl and the formation of Borate Ester

This results in the formation of Borate Ester (ROBH$_3^-$) (See Fig 4.1.). Since, the oxygen on the alkoxide has an excess of electrons it forms a bond with a hydrogen (H) molecule from an ethanol molecule, thus the reduction of the carbonyl group is complete and the product that we end up with has the reduced carbonyl groups which are alcohols, thus giving benzoin. This whole process was performed within the reaction while it was being stirred in an ice bath.

The ice bath was essential to ensure that other side reactions could not occur as at higher temperatures there is more energy available for other undesirable reactions to occur. At the end of this reaction; however, we are still left with some borate ester. Borate ester is an undesirable byproduct as it is jelly-like and could be difficult to remove from the desired product (benzoin). So, in order to more easily purify the desired product water is often added to the mixture so that borate ester can be hydrolyzed to form boric acid or tetrahydroxyborate which is easily dissolved in water allowing for the desired product to be separated easily ("Experiment 4 : Stereochemical Analysis of the Reduction of Benzil," 2014). In the figure 4.3, the reaction shows that H_2 gas was also being formed. This is the reason as to the intense bubbling seen during the first addition of water. The borohydride ions would have also reacted with the water to produce borane (BH3) and H2. The borane would then go on to react with any ethanol to produce borate ester which can then be turned to Boris acid of tetrahydroxyborate as described previously.

Figure 4.2. Hydrolysis of Borate Ester to Boric Acid or Tetrahydroxyborate

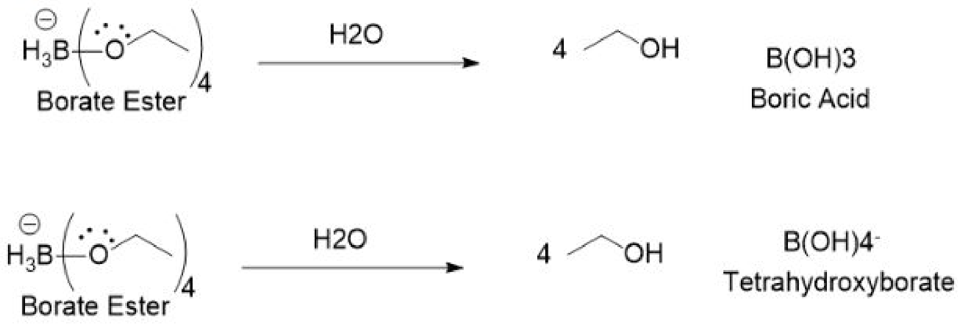
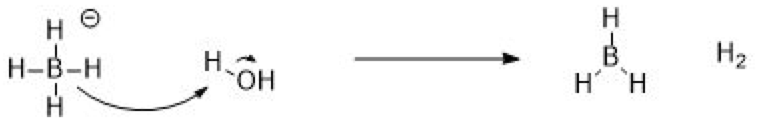


Figure 4.3. Borohydride reacts with water to form Borane and H2 gas



Hot water was used so that the benzoin would dissolve in it at higher temperatures so that all of the reaction mixture could be well mixed and any impurities like borate ester would not be trapped along with the crystals. At cooler temperatures, the benzoin would not dissolve in the water and precipitate out as crystals. Therefore, once the mixture cooled the crystals precipitated out of the solution. These were then filtered and dried and weighed. A percent yield of 79.2% was calculated (see calculations).

TLCs

The first 3 TLCs (Figures 2.1, 2.2, 2.3) were tests to see if the reduction reaction was completed. 3 plates were developed in a solvent system of EtOAc:hex 1:9. They showed whether the reaction product had different rf values than that of the reference (starting reagent benzil) meaning the reaction was complete. There was a small spot in the middle co spot lane due to contamination.

Figure 5.1 Benzil molecule

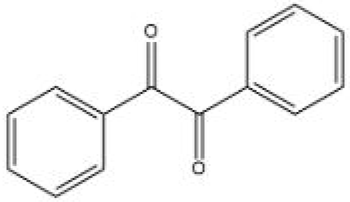
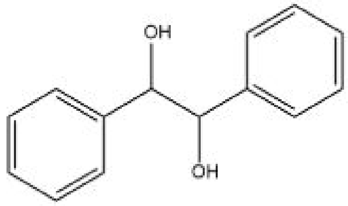


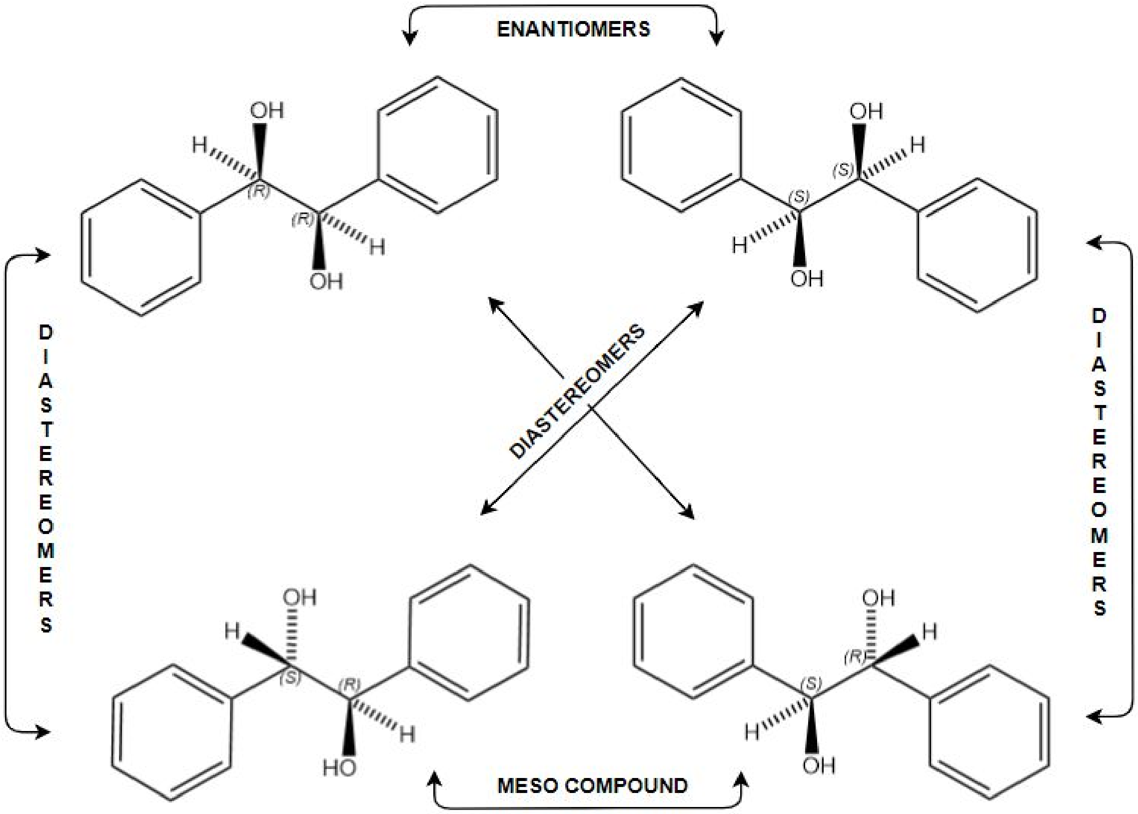
Figure 5.2 Benzoin molecule



The final TLCs (figures 3.1, 3.2) were done to test if the final product was something new and the reaction went through successfully. Figure 3.1 and 3.2 show that the final product benzoin had a very low rf value (0) and was much more polar than the reference. This makes sense due to benzoin being a significantly more polar molecule than benzil. Figures 5.1 and 5.2 show the molecules of benzil and benzoin. Benzoin has 4 hydrogen acceptors while benzil has only 2 therefore it makes sense the final product showed to have a lower rf since it bonded to the silica lining of the TLC plate better than benzil.

Part B

Fig 6.0. The Stereoisomers of Benzoin



These are all of the possible benzoin products that could result from the reduction of benzil. The bottom two mirror images are meso compounds as they are the same and therefore, superposable. It is possible to have a meso compound because the molecule is symmetrical. This molecule has 2 stereocenters, but because of the meso compounds there is one less stereoisomer for a total of 3. The enantiomers are non-superimposable mirror images and the diastereomers are non-superposable, but not mirror images.

Sources of Error

A major source of error for this lab would be that a lot of the final product was left behind in the erlenmeyer flask when pouring it out into a funnel for gravitational filtration. This would affect the actual amount of precipitate collected as the actual amount would have been greater than the one displayed here. This would increase the percent yield of benzoin.

Since, there was a time constraint the final mixture could not be cooled completely to room temperature before filtration. This would mean that not all of the crystals would have precipitated completely before the filtration, thus reducing the final amount of product collected which would, in turn, reduce the percent yield.

A source of error that could not be controlled very well was that during gravitational and suction filtration a lot of the crystals “escaped” the filter paper and found their way down to the erlenmeyer flask. This could have been the result of the crystals slipping under the filter paper. Unfortunately, this would have led to a loss in the actual yield of the final product and consequently to the percent yield.

The crystals could have also been left to dry a bit longer as the moisture could have contributed to its weight during measuring. This would have given a larger than actual weight for the final product collected and consequently would increase the % yield.

Since the preparation of the TLCs took a fairly long time the reaction mixture sat at room temperature for a while. This means that there is a possibility that some side reactions occurred during this time. This could change the composition of the crystal. Some undesirable impurities might have been present in the mixture without our knowledge. This would change the percent yield of the benzoin

Sometimes, during recrystallization when the final mixture is taken off the hot plate to cool, the mixture is filtered when hot to remove impurities like dust that did not dissolve within the solution. Since, this was not done during the lab, this could mean that some of the dist or other particles could have contributed to the mass of the final product and consequently given a bigger % yield than what is actual.

Conclusion

Part A: the percent yield of the final product, benzoin, was determined to be 79.2%.
Part B: 2 stereocenters have been identified on benzoin and a full stereochemical analysis showed that there were a total of 3 stereoisomers due to one pair being meso compounds.

Questions

1.
The statement is true. If a compound's boiling point is less than the boiling point of the solvent the compound is at risk of melting instead of dissolving. If the organic compound melts the phenomenon "oiling out" will be seen, similar to what extraction looked like in experiment 3.
.

2.

- ➢ Assuming there is a 100 mL sample:
- ➢ At 108° C → 39.1 g of compound/100 mL solution
- ➢ At 25° C → 35.6 g of compound/100 mL solution
- ➢ The difference between the amount at 108° C and at 25° C is 3.5 g (39.1g-35.6g). ∴ there would be 3.5 g of crystals.

  Percent yield = 3.5g/39.1g *100% = 9.0%
- ➢ Therefore the maximum yield would be 9.0%. (Rather low due the very miniscule difference in solubility of the compound.)

3.
The problem was that the methanol was at room temperature and cooling it in the ice bath would most likely result in a difference in temperature of around 10-15° C which isn't enough. To have a better yield it would be wise to heat the methanol initially to make solubility larger and it would also be possible to use less methanol since it would be more a efficient solvent at a higher temperature increasing the yield.

4.
1- butanol was not obtained because butanoic acid is not a strong enough base or reducing agent to produce an alcohol from a carboxyl group. Butanoic acid has an OH group whose proton quickly reacts with the negative hydrogen in sodium borohydride forming H_2 gas along with BH_3 and sodium butanoate.

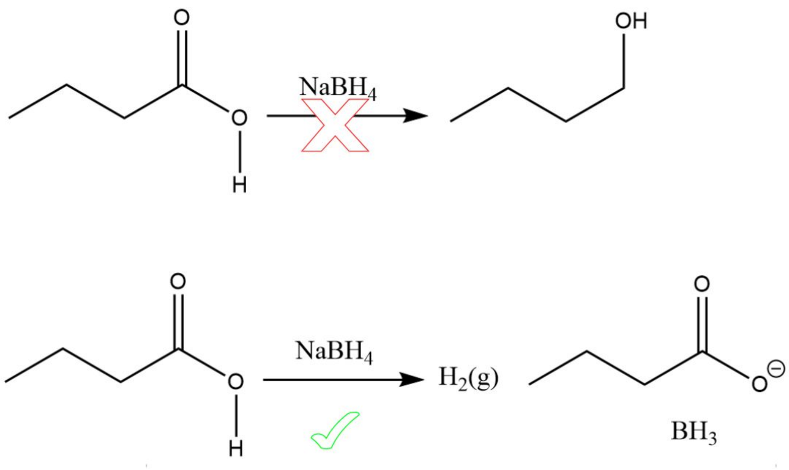


Figure. 7.0 Reaction of butanoic acid with sodium borohydride. Incorrect vs correct products formed

5.

Figure. 8.1. Overall reaction of 2,4-dimethylcyclopentanone and dibal

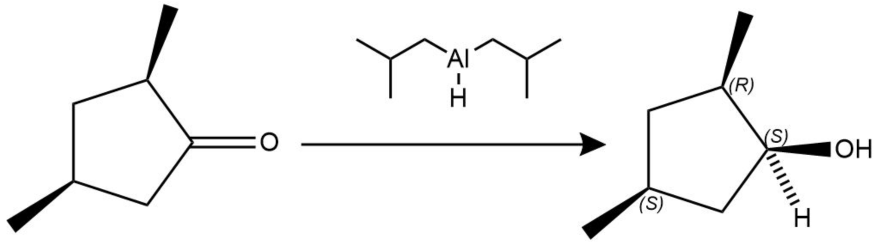
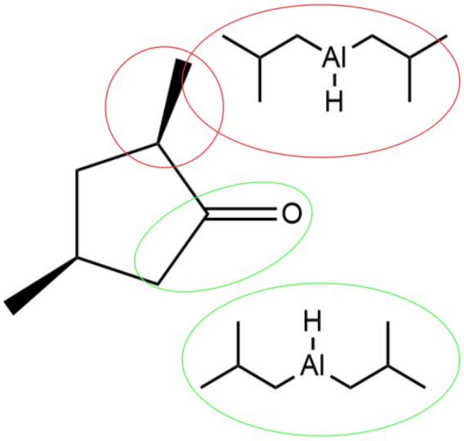


Figure 8.2. Approach of dibal molecule to 2,4-dimethylcyclopentanone



In red it is shown that the methyl group would get in the way of a dibal molecule and therefore bonding would not be favourable there. From the opposite side however, nothing stands in the way of the proton on dibal to break the pi bond on oxygen.

Unlike $NaBH_4$, reductions performed with DIBAL require equimolar amounts of DIBAL and substrate. This is due to the fact that a dibal only has 1 hydrogen donor on the Al therefore it can only reduce 1 ketone. $NaBH_4$ however would be able to reduce 4 ketones. Therefore with dibal a 1:1 mole ratio is required.

References

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National Center for Biotechnology Information. PubChem Compound Database; CID=6344, https://pubchem.ncbi.nlm.nih.gov/compound/6344 (accessed Mar. 6, 2019).

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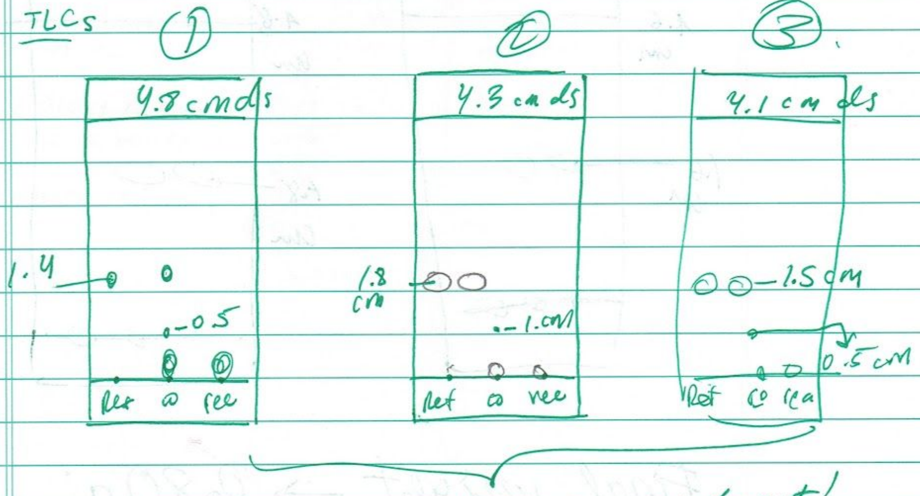
LAB 4: STEREOCHEMICAL ANALYSIS OF REDUCTION OF BENZIL

TLCs

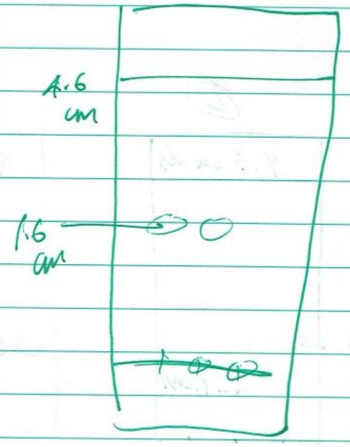


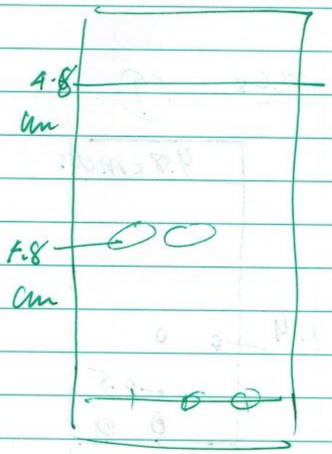
all have central spot!

OBSERVATIONS

-Multiple failed attemps > reaction incomplete.
benzyl → yellow powder
sodium borohydride → white small crystals.
lots of bubbling when stir bar is in.
Went from yellow (apple juice colour) to a pale yellow / opaque.

strange ~~[illegible]~~ odor when hot water added.





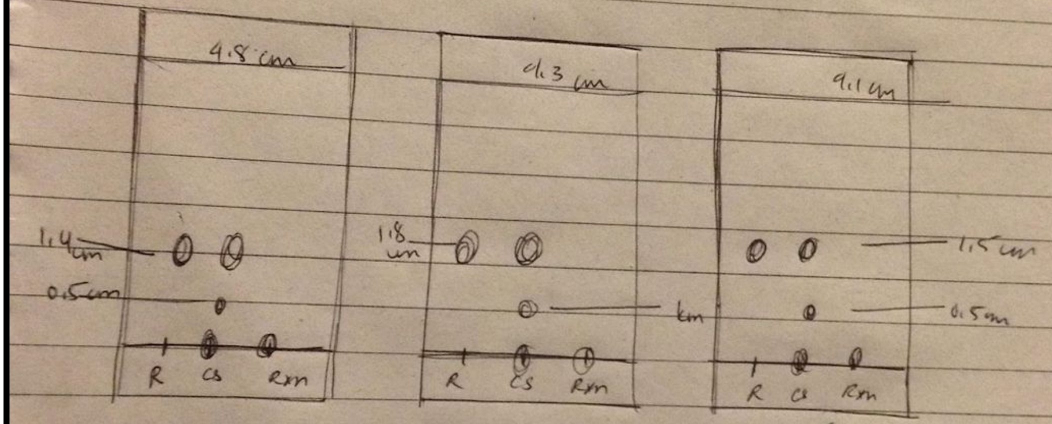
Final weight → 0.80 g of solid.

[redacted]

LAB-4 ⇒ Stereochemical Analysis of the Reduction of Benzene

Mass of Benzil =

TLC of the Rxn

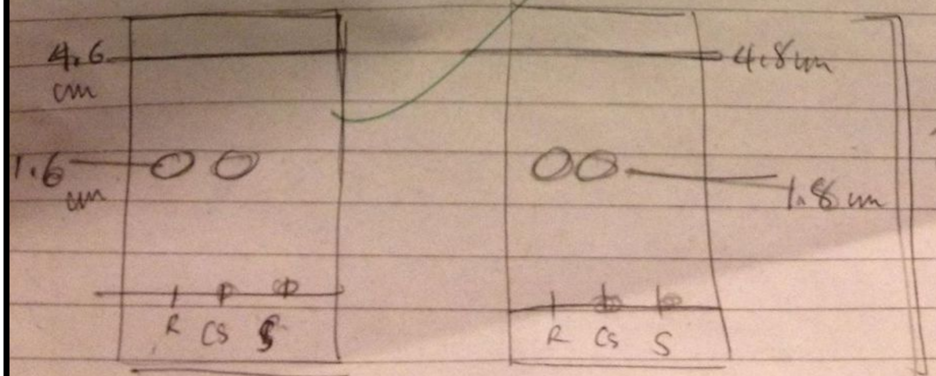


R = benzil in dichloromethane (ask TA)

1:9 EtOAc : Hexanes → ELUENT

TLC of Crystal

R → Benzile   CS → Co Spot   S → Product



These are the same

0.80 g of solid collected