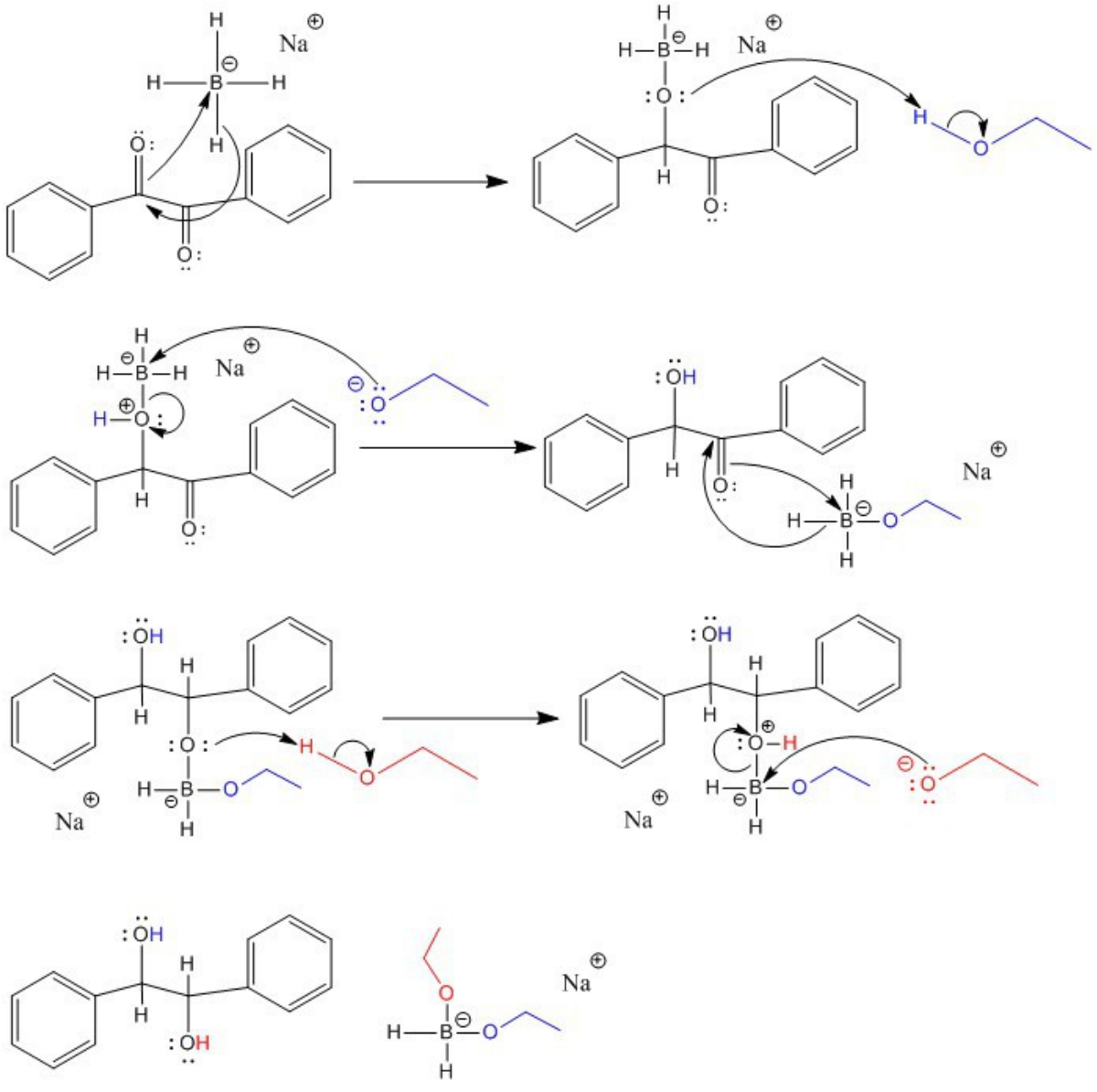
Lab # 4
Stereochemical Analysis of the Reduction of Benzyl

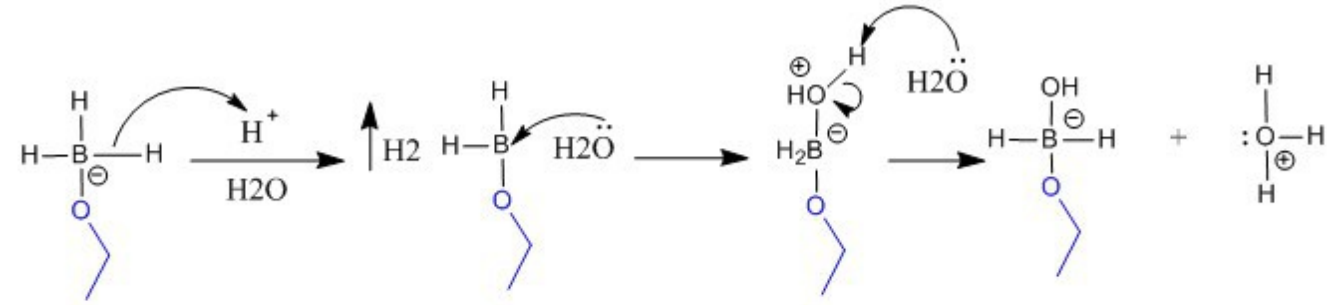
February 2015

Introduction:
Oxidation-reduction reactions, commonly known as redox reactions, are an important class of chemical reactions encountered in everyday processes. They play a key role in cellular respiration and photosynthesis by producing energy in the form of ATP and provide the main materials for life-sustaining processes. The basic definition of an oxidation reaction implies that a compound loses electrons while a reduction reaction gains electrons. In organic chemistry, redox reactions are defined in other terms, related to the gain or loss of hydrogen atoms in a molecule.

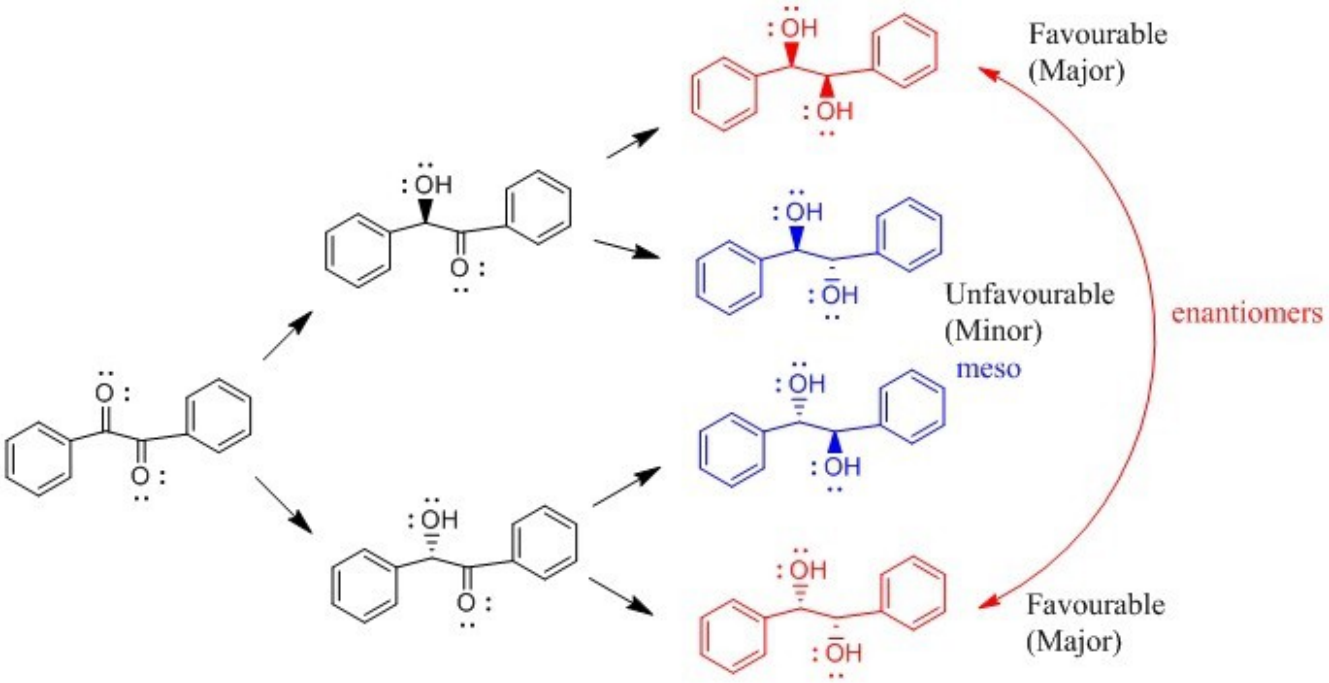
Reagents that carry out oxidations or reductions are often called "agents". A reducing agent will reduce a molecule while an oxidizing agent will oxidize a molecule. A commonly used reducing agent is Sodium Borohydride ($NaBH_4$) because it is very effective in the reduction of aldehydes and ketones to alcohols. However by itself, it will generally not reduce esters, carboxylic acids, or amides. In this lab, Benzyl is reduced by Sodium Borohydride to form Hydrodenzoin and alkoxyborohydride which is shown by the following mechanism:



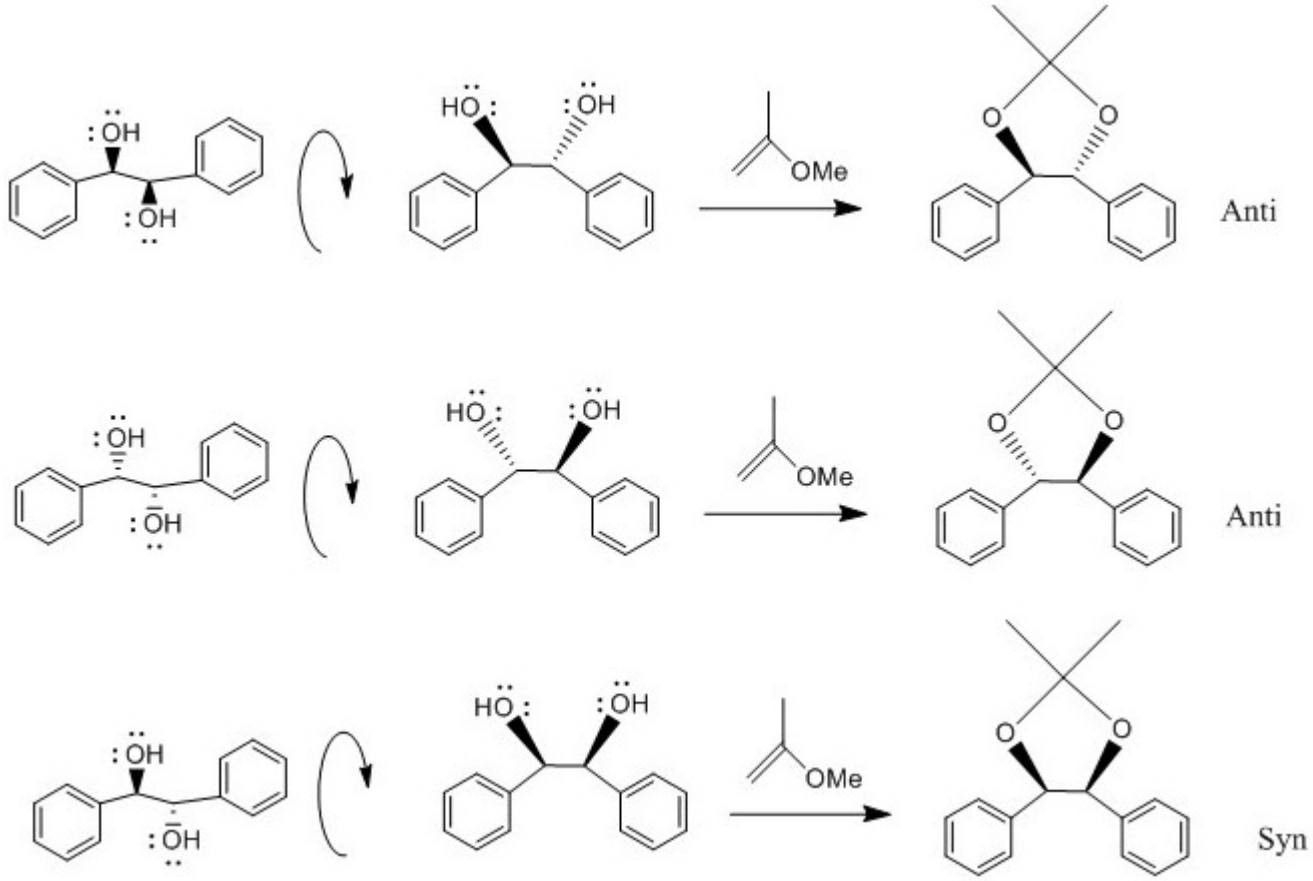
Once all of the carbonyl molecules have been replaced by the Benzyl, an acid or base work-up is performed. The workup is a process that is done to stop a reaction and to facilitate the purification of the desired product. This is done by catalyzing the hydrolysis of the alkoxyborohydride into water soluble Boric acid and is shown by the following mechanism:



Stereoselectivity is the property of a chemical reaction in which a single reactant forms an unequal mixture of stereoisomers during the non-stereospecific creation of a new stereocenter or during the non-stereospecific transformation of a pre-existing one. The selectivity arises from differences in steric effects and electronic effects in the mechanistic pathways leading to the different products. In this lab, As Benzil is reduced to Benzoin and then to Hydrobenzoin, certain stereoisomers are favored over others resulting in the formation of an unequal mixture of these stereoisomers illustrated below.



The transition states of the reductions of hydrobenzoin into the diastereomeric bezoins are themselves diastereomers and have different energies. This means that the rates of conversion of hydrobenzoin into syn and anti diastereomers are different. Reacting the diol products produced in this experiment with 2-methoxypropene and acid generates acetonides. The cis and trans isomers of these derivatives have different R_f values on TLC which makes it possible to identify the stereoisomers shown below.



Recrystallization is an important method of purifying organic compounds and is the best way to obtain ultra-pure samples of organic materials. the process consists of dissolving the impure material in hot solvent, filtering the solution to remove impurities, and allowing the desired compound to crystallize by cooling.

Procedure:
Refer to lab manual **(CHM 1321 Organic Chemistry Laboratory, Dr. Rashmi Venkateswaran, 2013, Lab. 4, p. 40-41).**

Table of Reagents:

	Compound	Molar Weight($gmol^{-1}$)	Quantity	mmol	Equivalents	Density(gmL^{-1})
A)	Benzil	210.23	1.01g	4.80	17	-
	Sodium borohydride	37.83	0.22g	5.81	20	-
	Hydrobenzoin	214.26	0.72g	3.36	12	-
	Ethanol	46.07	10.5mL	180	620	0.789
B)	2-methoxypropene	72.11	1.1mL	11.5	40	0.753
	Dichloromethane	84.93	25.0mL	391	1400	1.33
	p-toluenesulfonic acid	172.202	0.05g	0.29	1.0	-

Observations:
- Benzil is a yellow powder
- Ethanol is a clear aromatic liquid
- When benzil and ethanol mixed, a yellow solution formed
- Sodium borohydride is a white powder
- When NaBH3 was added to the reaction solution, the yellow color began to dissipate but still present
- When hot water was added to the reaction solution, bubbles formed
- As the solution cooled, it began forming crystals
- when emptying the flask containing the crystals into the filter and when removing the purified crystals from the filter, some crystals were stuck to the sides and were unable to be weighed
- when p-toluenesulfonic acid was added to the flask, the reaction mixture turned to a black color

Sample Calculations: ***finding the mmol for 2-methoxypropene***

Density = $0.753 gmL^{-1}$ grams = $(1.1mL)(0.753 gmL^{-1})$
MW = $72.11 gmol^{-1}$ = 0.828g
Quantity = 1.1mL mmol = $\frac{0.828g}{72.11 gmol^{-1}} \times \frac{1000mmol}{1mol}$ = 11.5mmol
mmol = ?

finding the equivalents value for 2-methoxypropene

The smallest mmol value was 0.29 therefore, it's equivalents value equals 1.0
mmol of 2-methoxypropene = 11.5 equivalents = $\frac{11.5mmol}{0.29mmol}$
mmol of p-toluenesulfonic acid = 0.29
equivalents of 2-methoxypropene = ? equivalents = 40

calculating R_f value for the sample spot on the first TLC place

Distance from origin to solvent front = 5.1cm $R_f = \frac{2.2cm}{5.1cm}$
distance from origin to solute spot = 2.2cm
R_f = ? R_f = 0.43

Calculating the %yield of Hydrobenzoin

Benzil is the limiting reagent
mmol of Benzil = 4.80mmol %yield = $\frac{3.36mmol}{4.80mmol} \times 100$
mmol of Hydrobenzoin = 3.36mmol
%yield = ? %yield = 70%

Questions:

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

x = 21.9mL **x = 62.5mL**

A $\frac{1g}{100mL} = \frac{x}{62.5mL}$ B $\frac{1g}{100mL} = \frac{x}{62.5mL}$

x = 0.625g A in solution x = 0.625g B in solution

3.5g of A - 0.625g of A in solution = 2.875g of solid A
10g of B - 0.625g of B in solution = 9.375g of solid B
total solid isolated = 2.875g + 9.375g = 12.25g of solid

Composition of the crystal

% A = $\frac{2.875g}{12.25g}$ x 100 = 23.5% % B = $\frac{9.375g}{12.25g}$ x 100 = 76.5%

Yield of the process

$\frac{12.25g}{3.5g + 10g}$ x 100 = 90.7% yield

Composition of the mother liquor

A $\frac{1g}{100mL} = \frac{x}{62.5mL}$ B $\frac{1g}{100mL} = \frac{x}{62.5mL}$

x = 0.625g A in solution x = 0.625g B in solution

Therefore, the mother liquor contains 0.625g of A and 0.625g of B.

2. A $\frac{1g}{100mL} = \frac{x}{100mL}$ B $\frac{1g}{100mL} = \frac{x}{100mL}$

x = 1g A in solution x = 1g B in solution

2.875g of A – 1.0g of A in solution = 1.875g of solid A
9.375g of B – 1.0g of B in solution = 8.375g of solid B
total solid isolated = 1.875g + 8.375g = 10.25g of solid

Composition of the crystal

% A = $\frac{1.875g}{10.25g}$ x 100 = 18.3% % B = $\frac{8.375g}{10.25g}$ x 100 = 81.7%

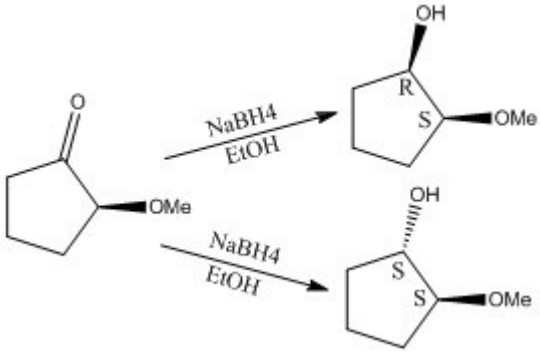
Yield of the process

$\frac{10.25g}{2.875g + 9.375g}$ x 100 = 83.7% yield

3. The reason to why the recovery was so low is that the solvent dissolves the crude product at room temperature. This makes it highly likely that much of the product remains in solution. It's best to find a solvent that dissolves at boiling point and recrystallizes at room temperature.

4. a) 1-butanol is not obtained because sodium borohydride is not a powerful enough reducing agent to reduce a carboxylic acid.
b) The products of the reaction are hydrogen gas and borate ester.

5.



The R,S configuration will be the major (favored) stereoisomer in this reaction because it is the most stable (lowest energy).

Discussion:
The purpose of this lab was to determine the mechanisms of reactions; what exactly occurs during a reaction, how to perform a recrystallization, and understanding the effects of stereoselectivity; certain stereoisomers will be sterically favored over others.

Sodium borohydride is added to a solution containing benzil and ethanol to completely reduce benzil to hydrobezoin. Borohydride is a very strong reducing agent so an ice bath is used to control the rate of the reduction and minimize the heat produced by the reaction. Borohydride is also added in thirds for this same reason. The first mechanism in the introduction shows exactly how this reaction occurs.

A TLC plate is used to see if all the benzyl in the solution has reacted to form hydrobenzoin. Since hydrobenzoin is more polar than benzil (hydroxyl groups are more molar than ketone groups), the sample spot should be lower on the plate than the reference spot. If there are two spots in the sample column, that would mean there is still some benzyl in the mixture that has not reduced and more borohydride is required.

Once all the Benzyl had been reduced, hot water is added to the reaction solution. This is also known as the work-up. It's purpose is to quench a reaction and to deactivate any unreacted reagents. In this case, hot water will catalyze the hydrolysis of any borohydride and alkoxyborohydride still in solution to water soluble Boric acid. Bubbles are formed because a byproduct of this reaction is hydrogen gas, shown in the second mechanism.

As the solution cools down, its solubility will begin to decrease. this will result in the recrystallization of hydrobenzoin. the crystals are filtered to lose any impurities and to dry the crystals. A TLC is conducted to test the polarity of the final product which should be the same as the first TLC.

The two diastereomeric products that are made do not separate well by TLC. In order to see the two isomers, it is necessary to convert the products into derivatives. To more easily identify the stereoisomers produced in the reduction of benzil, hydrobenzoin is converted to acetonide by reacting with 2-methoxypropene and acid. The cis and trans isomers of these derivatives have different R_f values on TLC making it possible to identify the stereoisomers that have been prepared. The solution is compared with syn and anti acetonide on two different TLC plates. Due to stereoselectivity, one stereoisomer will be the major product and will be favored over the other. TLC's will show which stereoismer was the major product by lining up its spot with one of the reference acetonide spots. The minor product will be too faint to read and therefore won't be recorded.

The first reduction of benzyl results in two stereoisomers of benzoin, each has a 50 percent chance of forming since each has the same energy state. The second reduction of benzoin into hydrobenzoin is stereoselective and will produce major and minor products. These products are cis and trans hydrobenzoins. This refers to the hydroxyl groups being on the same or opposite sides of each other. Trans-hydrobenzoins will have a lower energy state because their polar hydroxyl groups will be as far apart from each other as possible, resulting in a more stable molecule. This means that trans-hydrobenzoin is the major product because it takes less energy to form. Cis-hydrobenzoins will therefore be the minor product because the hydroxyl groups will be on the same side as each other so more energy is needed form this product.

Since it has now been determined that trans-hydrobenzoin is the major product, when the solution is converted to acetonide derivatives, anti-acetonide will be the major product. When comparing the product with the reference, anti-acetonide's spot will line up while the cis-acetonide spots will not. When calculating the percent yield of the crystals formed, it was determined to be 70% which is a relatively low percent. During this experiment, many errors can occur which could affect this result. Too much solvent can prevent all the hydrobenzoin from recrystallizing, when collecting the crystals for weighing, some were stuck to the inside of the filter funnel, filter paper, inside of the flask and could not be included in the weight reading. Both of these factors could result in a lower percent yield. Not allowing the crystals to completely dry can result in a higher percent yield since extra mass will be added to the weight reading.

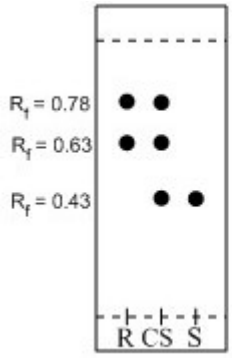
The final three TLC plates showed obscure results. For the TLC where the new solution of acetonides was compared with the reference diol product, 4 dots appeared in the sample column. Only one spot was suppose to appear which would have represented the major product, anti-acetonide. The minor product would have been too faint to see. When comparing the prepared solution with the reference solutions of cis and anti acetonide, the reference solutions revealed multiple spots as well. They were only suppose to reveal one spot since they were pure solutions. Multiple spots could mean that these solution were contaminated with other compounds. However, when analyzing the last two TLC plates, it was confirmed that two rows of spots lined up with each other on the anti-acetonide plate while no rows lined up on the cis-acetonide plate. It could then be confirmed that anti-acetonide was the major product.

Conclusion:
In conclusion, a 70 percent yield was obtained for the diol product and anti-acetonide was determined to be the major product.

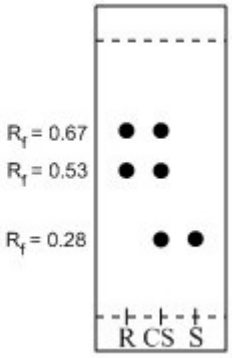
Part A:
Eluent: 2:8 EtOAc:Hexanes
Reference: Benzyl
Sample: Hydrobezoin

R: Reference spot
CS: Co-spot
S: Sample spot

Before recrystallization

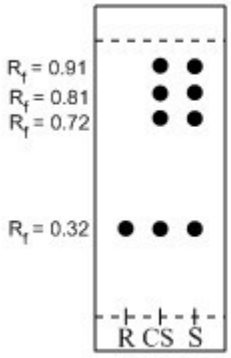


After recrystallization (purified)

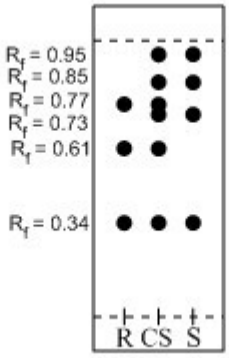


Part B:
Eluent: 2:8 EtOAc:Hexanes

Reference: Purified hydrobenzoin
Sample: Acetonide solution



Reference: Cis-acetonide
Sample: Acetonide solution



Reference: Anti-acetonide
Sample: Acetonide solution