

The Thiolysis of Cyclohexene-oxide by Thiophenol in Water

in the Presence of Different Lewis Acids

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Abstract

The synthesis of β -hydroxysulfides from cyclohexene-oxide and thiophenol using InCl_3 and other catalysts at different pHs have demonstrated promising results and yields some reaching to 100% of the desired product. After the recreation of these results it is desired to test the viability of RuCl_3 as a catalyst in the synthesis of β -hydroxysulfide from cyclohexene-oxide and thiophenol.

Introduction

The opening of 1,2-epoxides with thiol nucleophiles is a common way to synthesize β -hydroxyl sulfides for preparation of allylic alcohols(2), cyclic sulfides (3), thioketones (4) and certain intermediates involved in the synthesis of natural products (5) and compounds of biological and pharmacological interest(6)[1]. Previously there were mainly two ways of carrying out the thiolysis of 1,2-epoxides which include thiolysis under basic conditions or thiols in the presence of a variety of activating agents. While these two pathways are feasible they both have their drawbacks, in specific mostly producing a poor yield after a long period of time. It was these facts and the interest in organic synthesis performed exclusively in water that drew Fringuelli to investigate the Lewis acid- catalyzed thiolysis of epoxides in an aqueous medium (1). This synthetic pathway based on their previous work with azidolysis, bromolysis, and iodolysis in water (1). Water as a reaction medium has a number of advantages such as, “it responds to the demand for hydrogen bonding of the substrates, its high heat capacity is a helpful property for processes scaling- up, and the pH is easily changed and controlled as well as the concentration of aqua ion when the process is catalyzed by a Lewis acid. (1-[7])” This led to the investigation of the thiolysis of 1,2-epoxides catalyzed by Lewis acids in water as the only

solvent and the dependence of the reaction on the pH conducted by Francesco Fringuelli and his colleagues (1). The chemical equation for the reaction can be seen below in Figure A.

Figure A-chemical equation of reaction

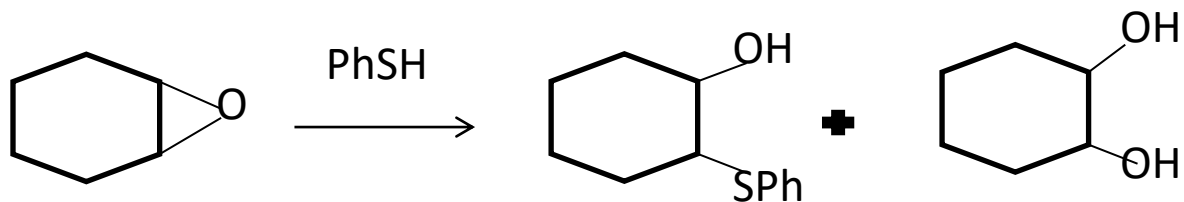
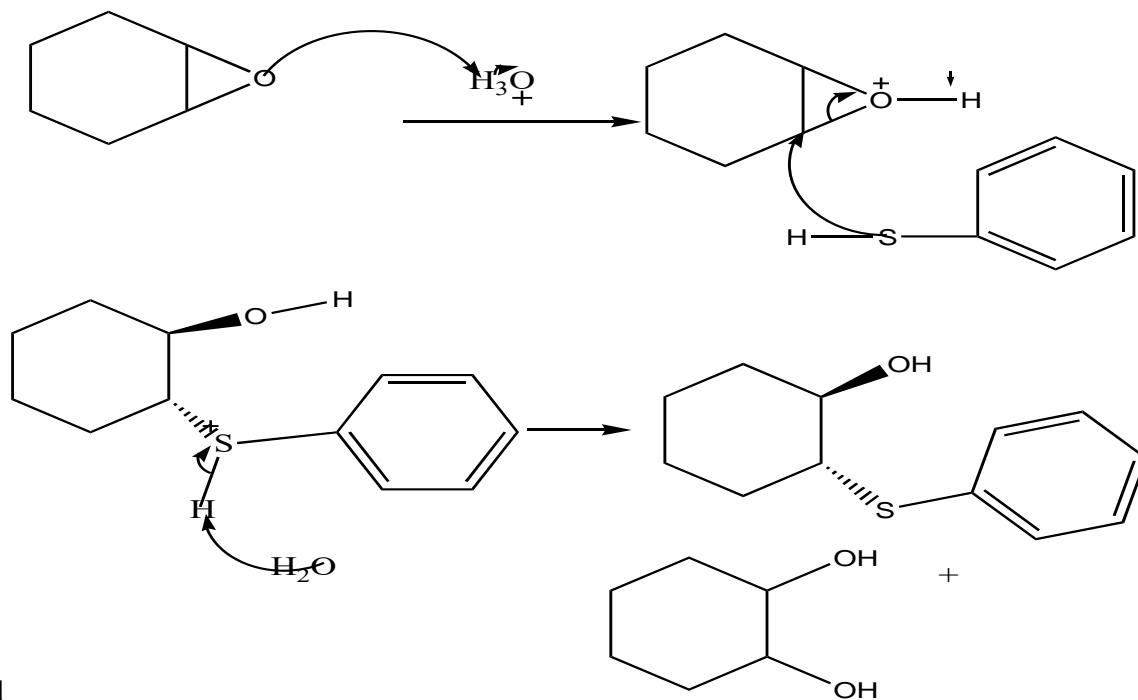
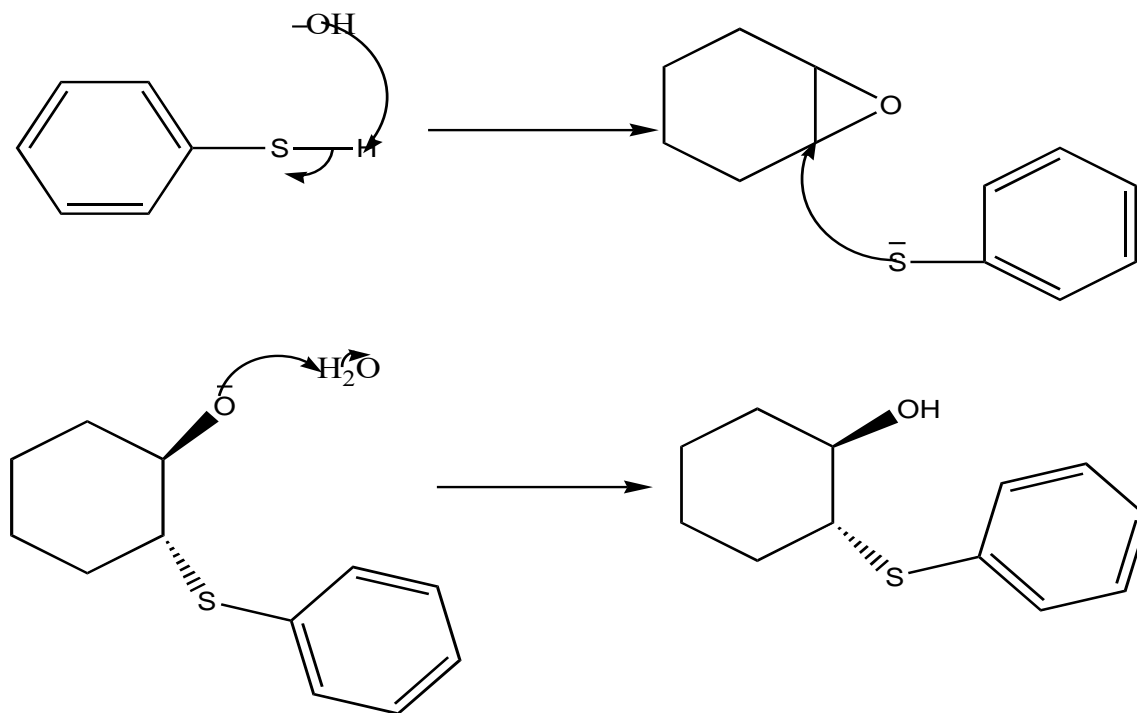


Figure B-reaction mechanism in presence of



acid

Figure C- reaction mechanism in the presence of base



Experiment

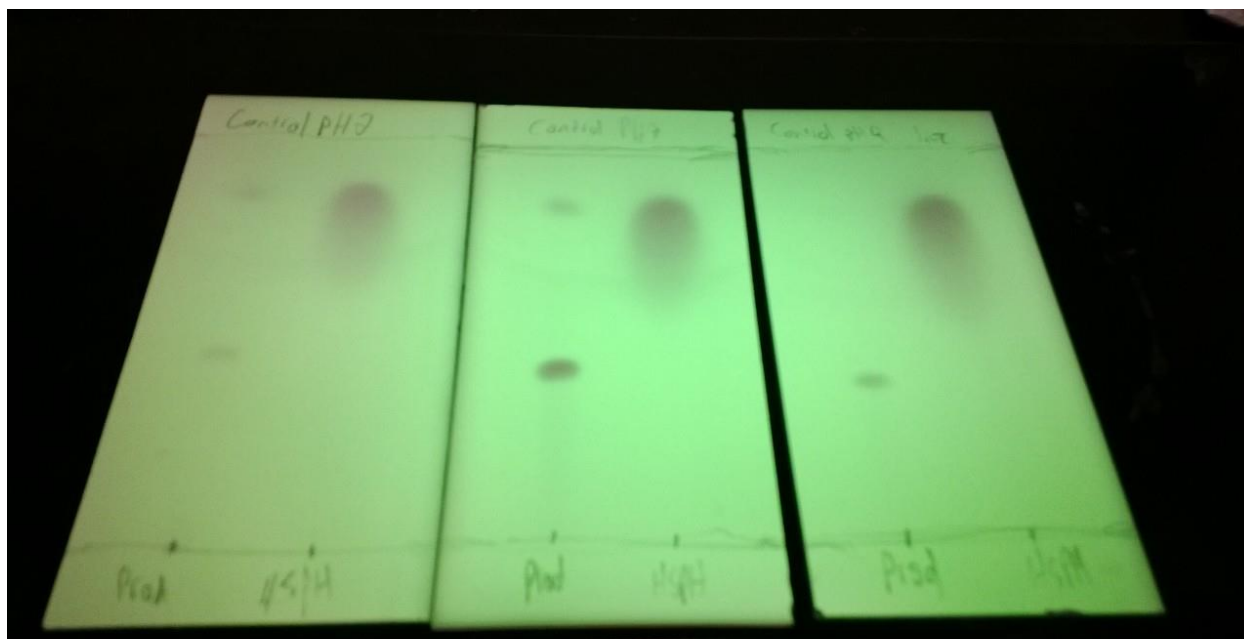
In the original study, they carry out a number of different reactions in the presence of different lewis acid catalysts however due to the limited time available the reactions that were studied were the control reaction with no catalyst, with an InCl_3 catalyst, and the new catalyst of RuCl_3 . The RuCl_3 is believed to be capable of acting as a lewis acid catalyst like the InCl_3 but it might also form a coordination complex and might create a new product all together. Procedure of the synthesis of B-hydroxysulfide in the reference paper was as follows, “in a flask thermostatted at 30 C, equipped with a magnetic stirrer and pH-stat apparatus, thiophenol (0.15 mL, 1.5 mmol) was dissolved in water (2.0 mL). The resulting pH was 4.5. By adding some drops of a concentrated aqueous solution of H_2SO_4 or NaOH the pH was adjusted at the desired

value. The epoxide (1.0 mmol) was added under stirring and the pH was kept constant at the fixed value by adding a 10% aqueous H₂SO₄ solution. After the times reported in Tables some drops of concentrated NaOH solution were added and the mixture was extracted with Et₂O (3–2 mL). The combined organic layers were dried and evaporated under reduced pressure to give the β -hydroxy sulfide which was purified by column chromatography. (1)” However due to the resources available and other various reasons the procedure needed to be altered. First rather than worry about heating the reaction to 30 degrees Celsius the reaction was left at room temperature and the time allowed for the reaction to take place was doubled. Next the original experiment calls for the reaction to take place at pHs of 2,4,7,and 9 but because the reaction times at a pH of 4 were so long it was believed that the pH could not be monitored for that long and it would cause poor results. Lastly after the reaction takes place the procedure says to add some drops of NaOH to the reaction mixture and believing that this could possibly create an alkoxide and ruin the reaction this step was taken out.

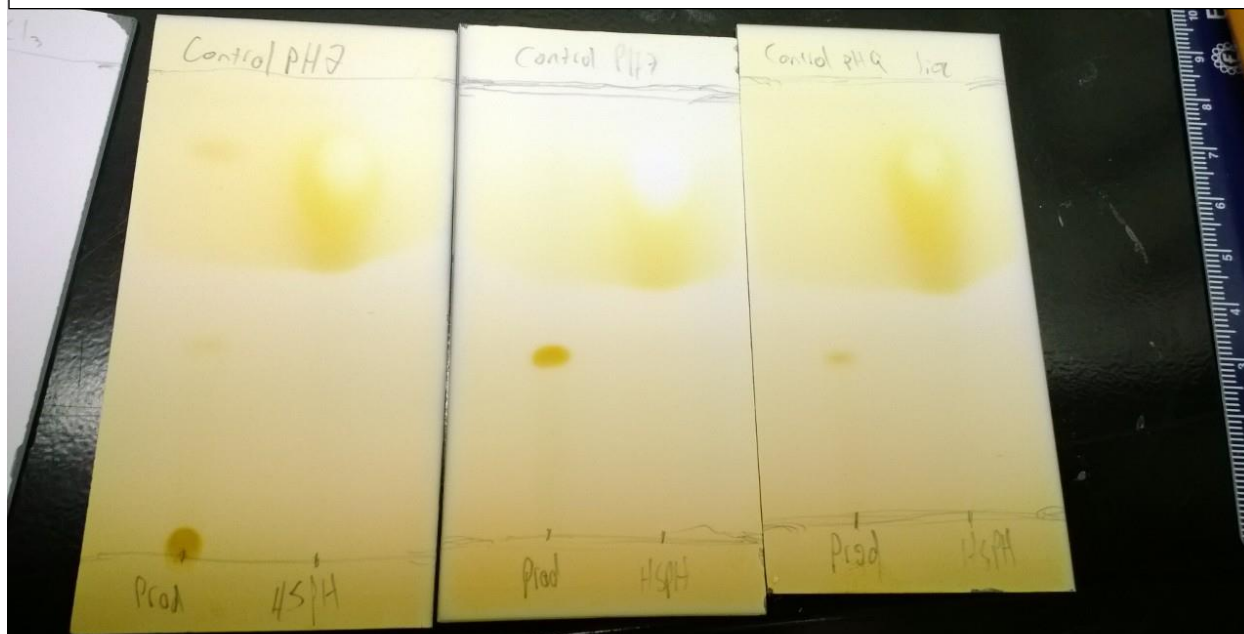
Results and Discussion

The control reactions that were carried out with no catalyst present matched the original paper results. When the crude products were spotted with regular thiol on a TLC plate there was a distinct separation of a new product that did not travel as far as another spot. The top spot is believed to be unreacted thiol because it matches with the stock thiol spotted on the TLC. Also the product distribution of the β -hydroxysulfide and the diol side product matched the reference values because when placed in an iodine chamber to check for diol at a pH of 2 there was diol present and at the pHs of 7 and 9 there was no diol present on the TLC plate. This can be rationalized by the mechanism where in base the proton on the thiol can be taken to make the thiol a stronger nucleophile and promoting the attack of the thiol over the attack of the water,

Where the thiol cannot be deprotonated in the acidic pH causing the formation of the diol, this is shown in the mechanisms in figures B and C.

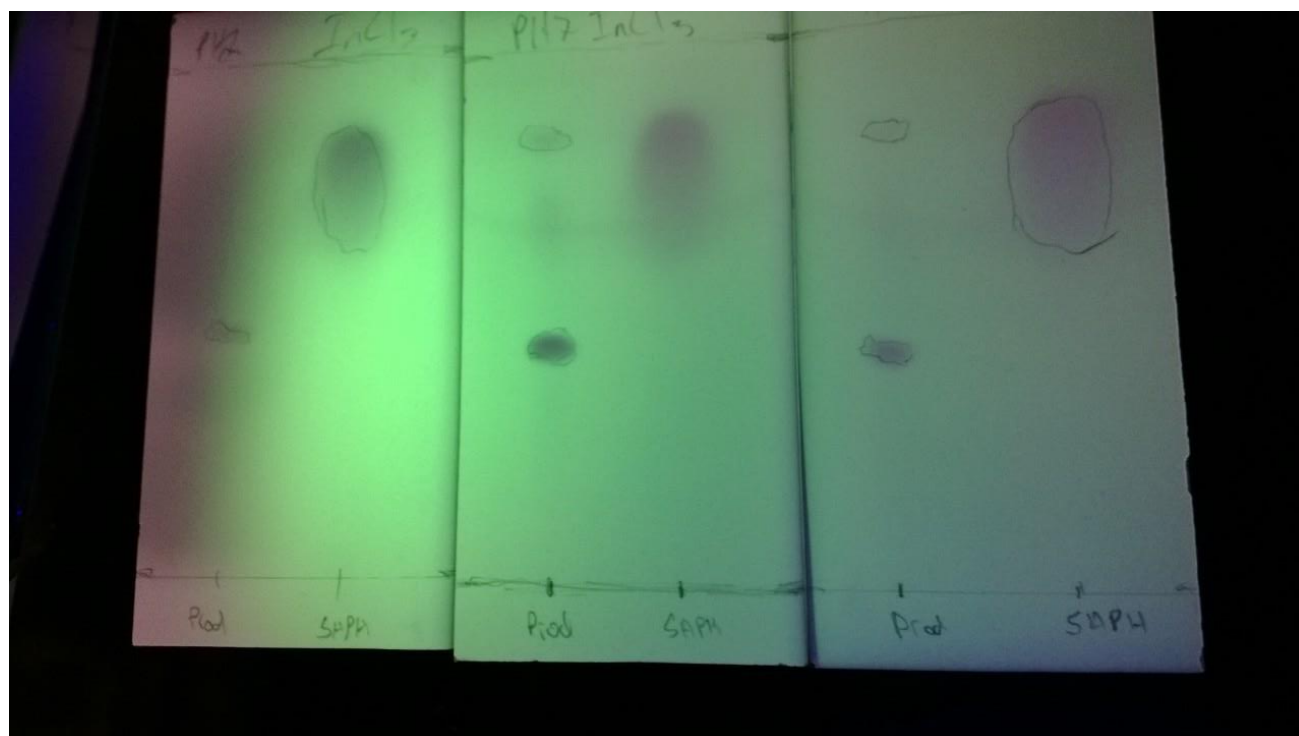


TLC of control crude products pH 2,7,9 from left to right. Thiophenol is spotted on the right and the crude products are on the left. Thiolysis product is visible on all TLC plates along with unreacted thiophenol

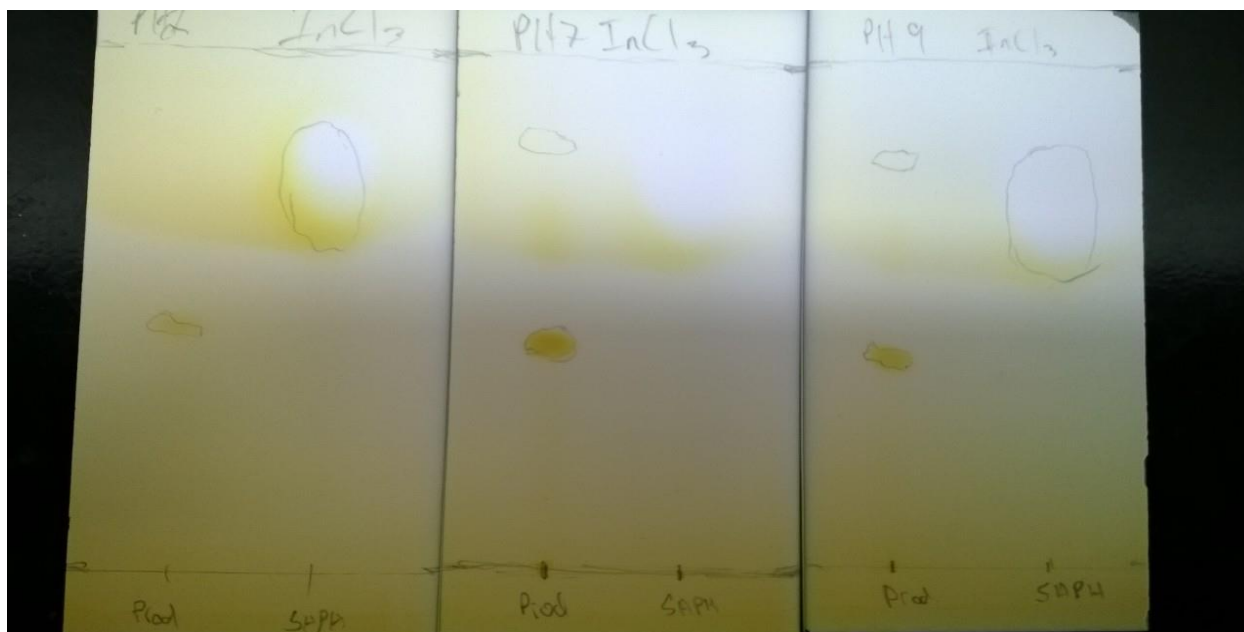


Control TLC plates after being placed in iodine chamber, pH of 2,7,9 from left to right. Product spotted on the left and stock thiophenol on the right. Diol present at pH 2 on the left.

In the reactions with the InCl_3 catalyst again the results match that of the original study. At a pH of 2, 7 and 9 when spotted on a TLC plate there was a clear separation of a new product and unreacted thiol and when placed in an in the iodine chamber there was no diol present. It is explained in the original paper that the InCl_3 coordinates both the thiol and the cyclohexene-oxide in such a way that it is more favorable for the thiol to act as the nucleophile then the water.



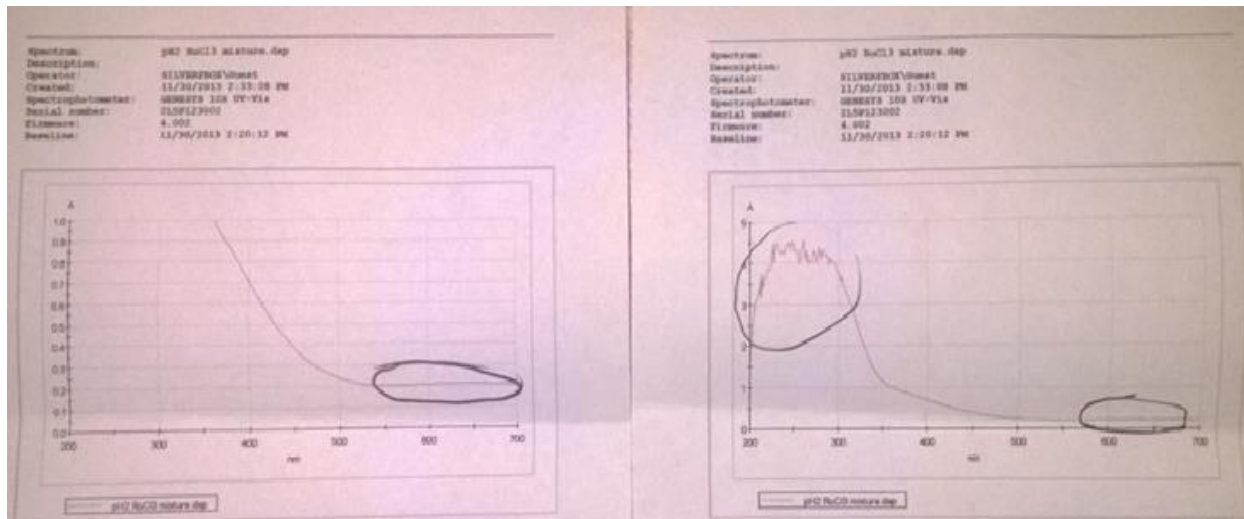
TLC of InCl_3 catalyzed crude products, pH 2,7, and 9 from left to right. Product spotted on the left and stock thiophenol on the right.



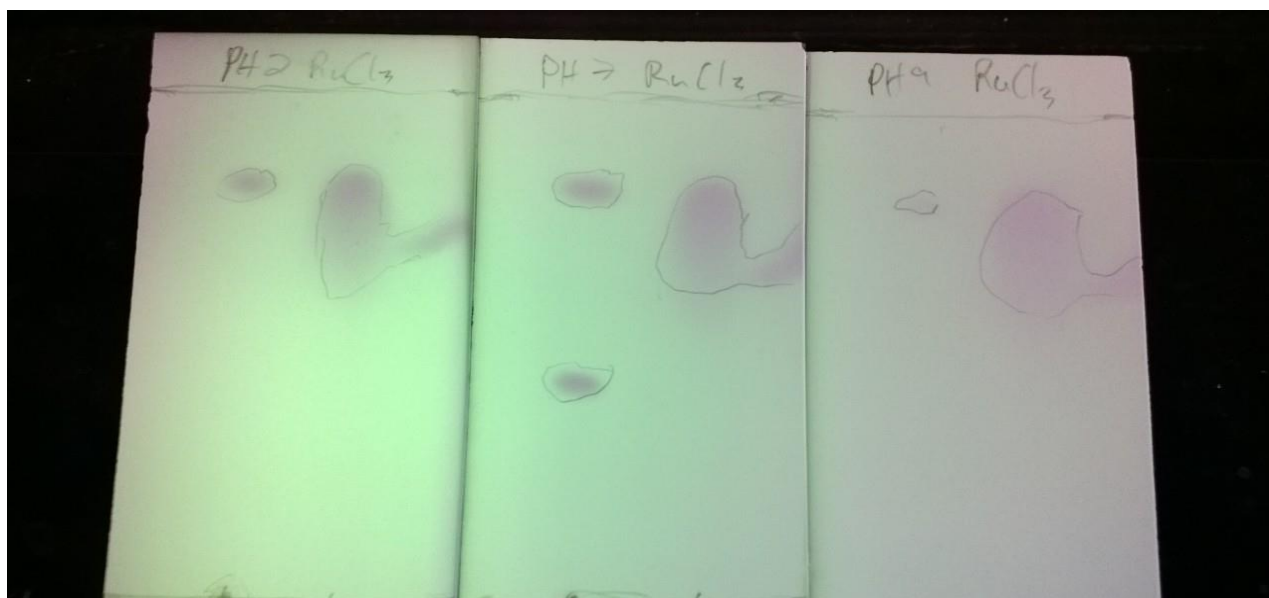
TLC plates of InCl_3 catalyzed crude products pH 2,7,9 from left to right. Product spotted on the left and stock thiophenol on the right. No diol by product present.

The RuCl_3 catalyzed reactions yielded interesting results at a pH of 7 yielded the same results acting as a lewis acid catalyst showing a thiolysis product on the TLC plate and showing no diol after being placed in an iodine chamber. At a pH of 9 there was no thiolysis product and no diol visible on the TLC plate and it is believed no reaction has taken place. At a pH of 2 when the crude product was spotted on a TLC plate the unreacted thiol was visible however there was no thiolysis product visible on the plate. Then after being placed in an iodine chamber there was no diol present in the product either. However unlike the crude product at a pH of 9 there was a distinct color change from the original dark brownish black to a dark green. Because of this color change a UV spec. of the crude product was taken and is shown below and the peaks around 200-300nm are most likely due to the unreacted thiophenol and the broad band around 600-700nm is characteristic of Ruthenium three complexes. This supports our hypothesis that the RuCl_3 had the capacity to form a coordination complex however more testing is necessary.

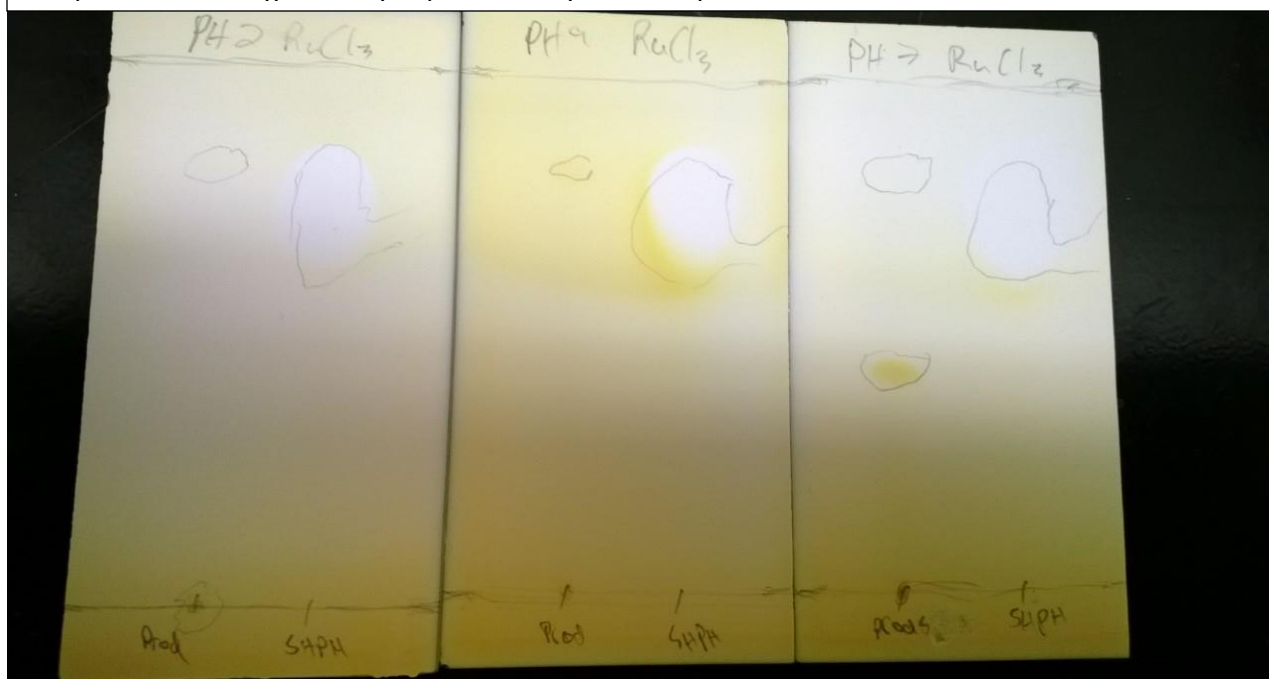
Unfortunately do to the restricted time period of which we had to work with the purification of this product could not be performed this semester.



This is a picture of the UV spectroscopy performed on the crude Ruthenium product and on the right is the full spectrum and on the left is an enlarged picture. The band on the right picture around 200nm is most likely the unreacted thiophenol and the broad band between 600-700nm is characteristic of ruthenium 3 complexes.



TLC of RuCl₃ catalyzed crude products pH 2,7,9 from left to right. Product spotted on the left and stock thiophenol on the right. Thiolysis product only visible at pH of 7.



TLC plates of RuCl₃ catalyzed crude products after placed in an iodine chamber pH 2,9,7 from left to right. Product spotted on the left and stock thiophenol on the right. No diol is present on any of the TLC plates.

Conclusion

In conclusion the recreation of the results from the paper "Thiolysis of Alkyl- and Aryl-1,2-epoxides in Water Catalyzed by InCl₃." were successful. The proper product distributions were achieved in their respective pHs and the InCl₃ catalyst proved to make 100% of the thiolysis product. The testing of the RuCl₃ catalyst showed that it does not seem to react at a pH of 9 also, it acts as a lewis acid catalyst in a pH of 7. The results also provide evidence of the color change of the product and the UV spectroscopy point toward the original hypothesis that in a pH of 2 a new coordination complex is formed with the RuCl₃ however more testing is required to be certain.

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