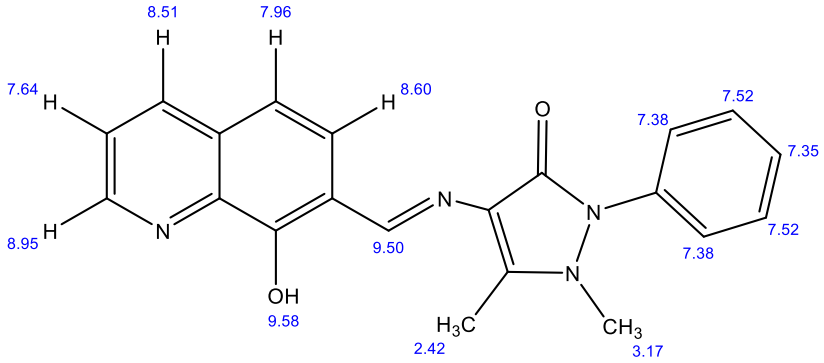
The Synthesis of 8-Hydroxyquinoline-7-Carbaldehyde Schiff-Base as a Fluorescence Chemosensor for Al^{3+}

By: Glenn Harding



4-(8’-hydroxyquinolin-7’-yl)methyleneimino-1-phenyl-2,3-dimethyl-5-pyzole (HQ7A-sensor)

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12/18/2019

Abstract

For this project, we attempted to synthesize and study the activity of the 4-(8'-hydroxyquinolin-7'-yl)methyleneimino-1-phenyl-2,3-dimethyl-5-pyzole (HQ7A sensor) with several metal ion, including Al^{3+} using UV visible spectroscopy and fluorescent studies. First, 8-Hydroxyquinoline has to undergo a Reimer-Tiemann reaction by being refluxed for 12 hours with chloroform and sodium hydroxide in ethanol. Then distill of excess chloroform and ethanol, acidified with hydrochloric acid, extracted with chloroform, and separated through column chromatography. Then, having the 8-Hydroxyquinoline-7-Carbaldehyde (HQ7A) isolated, refluxing it with a 1:1 mol ratio of 4-aminoantipyrine in ethanol for 8 hours. After the 8 hour reflux, a yellow precipitate falls out of solution and has to be separated by vacuum filtration. After forming the sensor, the isosbestic points are found by testing absorbance, the intensity of fluorescence is measured against different ions, and the intensity of the fluorescence is measured with the addition of aluminum.

Introduction

Aluminum is the third most abundant element in the Earth's crust and is linked to causing many health problems in humans such as Parkinson's Disease and Alzheimer's Disease. Aluminum also endangers freshwater fish and influences agricultural production in acidic soils. The problem with the formation of the aldehydes especially the 7 aldehyde, is the overall formation of the aldehydes is inefficient. Starting with 14.5519 grams of the starting material, only a few hundred milligrams of both aldehydes were formed. The sensor being made using HQ7A is important because it is much more effective in detecting Al^{3+} than the 8-Hydroxyquinoline-5-Carbaldhyde (HQ5A) sensor.

Experimentation

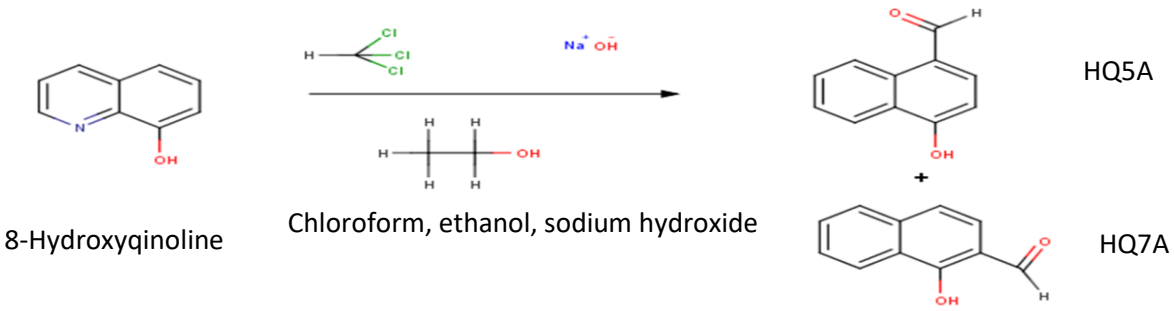
Chemicals

- 8-Hydroxyquinoline
- Chloroform
- Sodium Hydroxide
- Hydrochloric acid
- Dichloromethane
- Methanol
- Ethanol
- 4-aminoantipyrine
- Hexane
- Ethyl acetate
- Petroleum ether

Equipment/Materials

- 3 neck 250 ml round bottom flask
- Condenser
- Oil bath
- Silica gel
- Round bottom flasks
- Rotary evaporator
- Columns
- NMR
- $CDCl_3$
- Pasteur pipets
- Separatory funnel
- Vacuum filtration apparatus
- Soxhlet extraction apparatus

Step 1 Part 1: Formation of Aldehyde



Synthesis of 8-Hydrozyquinoline-7-Carbaldehyde (HQ7A)

1. Measure 14.5 grams (0.1 mol) of 8-hydroxyquinoline (8-HQ) in 250 ml round bottom flask and dissolved in 60 ml of ethanol.
2. Add 35 grams of sodium hydroxide in 60 mL of water
3. Heat to dissolve the precipitate
4. Reflux while adding 32 ml chloroform dropwise for 1 hour
5. Reflux for 12 hours at 100 degrees Celsius
6. Distill off excess chloroform and ethanol dilute residue with 200mL of water and pour into 500ml beaker acidify solution with 1M hydrochloric acid to pH 4
7. Filter and dry precipitate, continuously extract with chloroform then distill off excess chloroform
8. Purify crude product by column chromatography with mixture of petroleum ether ethyl acetate (v/v 40:1) to afford yellow-pink HQ5A
9. Elute with a gradient of petroleum ether ethyl acetate (v/v 20:1) to get white solid HQ7A

The procedures above were followed how the paper listed them up until acidifying with hydrochloric acid and purifying the crude product by column chromatography. the solution was over acidified to a pH 3 due to misreading of pH paper. When the crude was spotted on a TLC plate with petroleum ether and ethyl acetate, it did not give good separation. A solvent system of dichloromethane and methanol was used to separate the products. First only dichloromethane was ran through until fluorescence could not be seen when the fractions were spotted on a TLC plate. Afterwards, the solvent system was changed to 97% dichloromethane and 3% methanol. Using the later system, fractions 51-57 turned green. Those fractions were also compared on a TLC plate to see if the compound is HQ7A. Those fractions were collected, dried, and had the NMR taken. The NMR showed that the compound collected was HQ7A. From the compound that us subject to this column, 100 mg of HQ5A was separated and 30 mg of HQ7A was separated. With HQ7A formed, we moved on to the next step.

A: Vayani's compound (HQ7A/HQ5A)

B: Justin's compound (HQ5A)

C: starting material (8HQ)

D: my crude

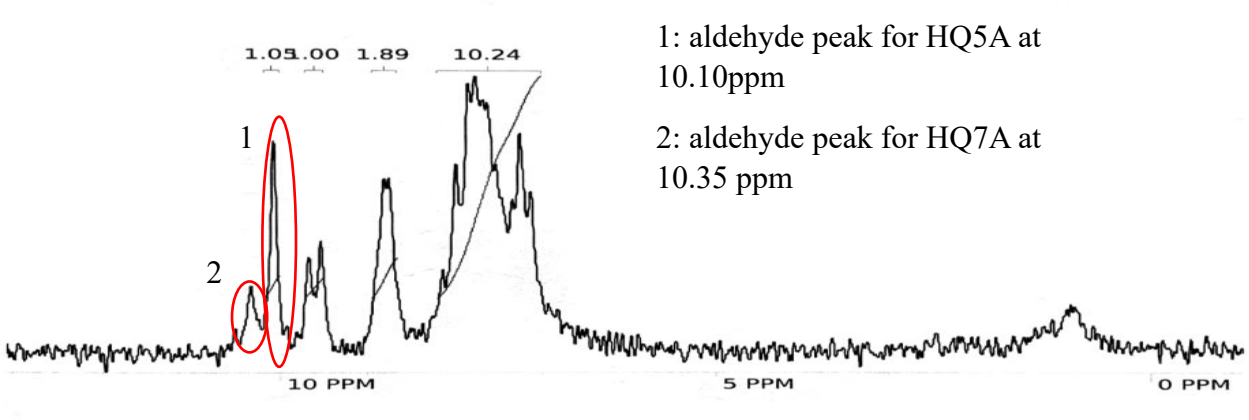
Under UV light

Solvent system:

97% dichloromethane

3% methanol

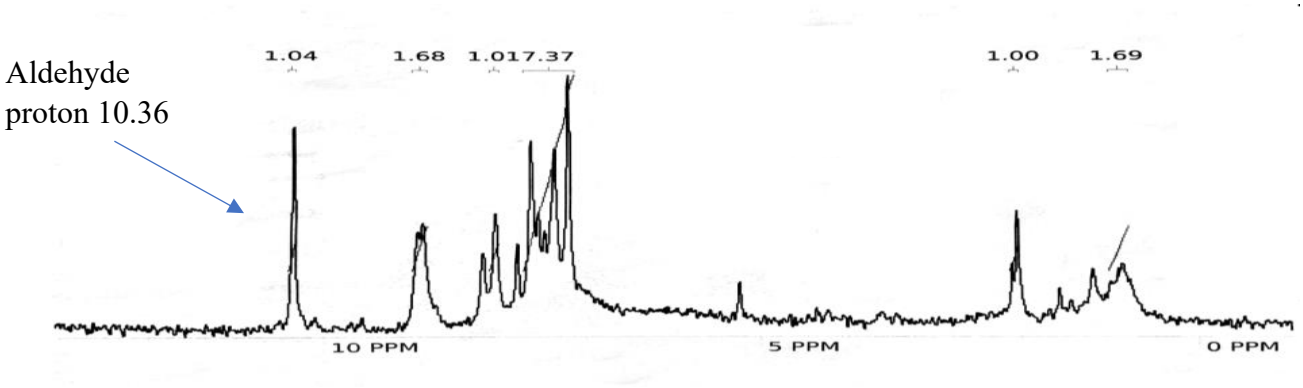
TLC plate shows evidence of having both aldehydes when compared to two previously made samples. One with both aldehydes but unknown at the time and one with the nontargeted aldehyde (HQ5).



1: aldehyde peak for HQ5A at 10.10ppm

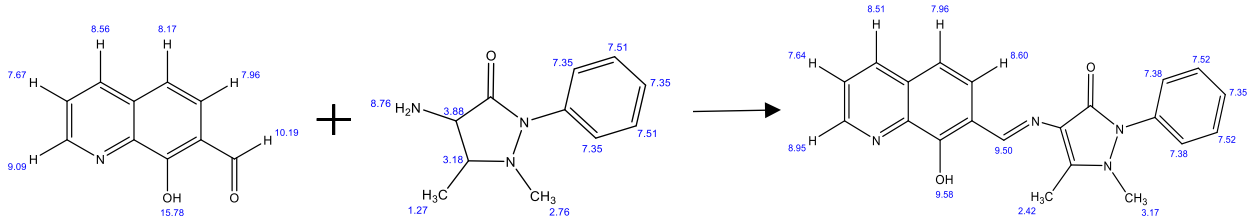
2: aldehyde peak for HQ7A at 10.35 ppm

NMR of the crude shows aldehyde peaks for both HQ7A (10.35ppm) and HQ5A (10.10ppm).



NMR of the collected green color fractions showing only HQ7A.

Step 2 Part 1: Imine Formation



8-Hydroxyquinoline-7-Carbaldhyde

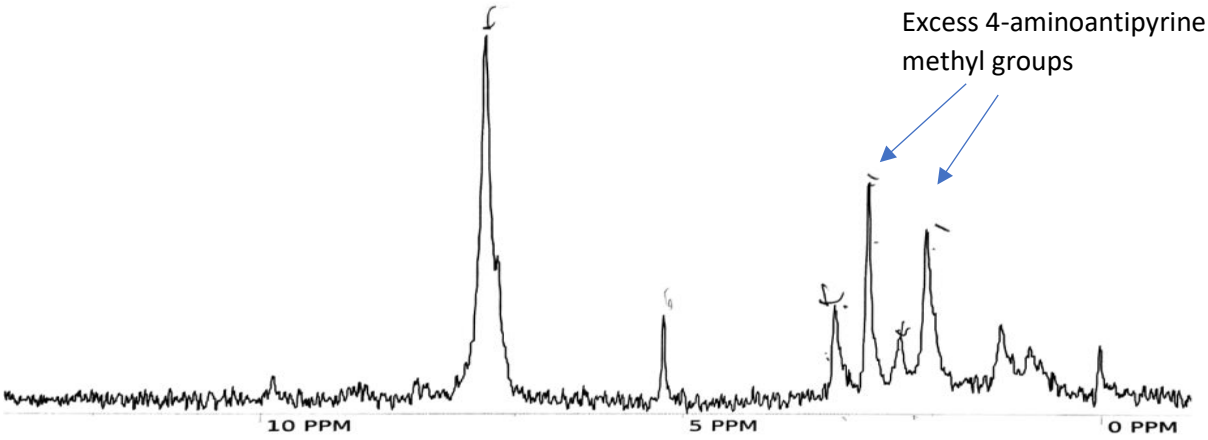
4-aminoantipyrine

4-(8'-Hydroxyquinolin-7'-yl)Methyleneimino-1-phenyl-2,3-dimethyl-5-pyzzole

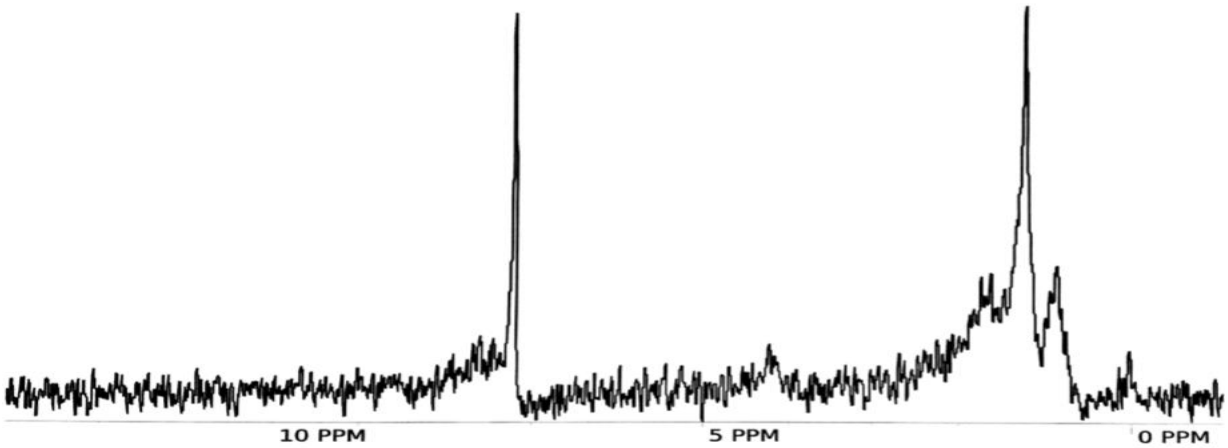
Synthesis of 4-(8'-hydroxyquinolin-7'-yl)methyleneimino-1-phenyl-2,3-dimethyl-5-pyzole (HQ7A-sensor)

1. Dissolve 346 mg of HQ7A in 15 mL of hot ethanol
2. Add a solution of 406 mg 4-aminoantipyrine in 5 mL of ethanol
3. Reflux for 8 hours under stirring conditions (yellow precipitate should form)
4. Filter and dry precipitate

Moved on to the second step with less than one tenth of HQ7A than used in the literature. 30 mg of HQ7A was dissolved in 5 mL of ethanol and 35.2 mg of 4-aminoantipyrine in 5 mL of ethanol. Solutions were mixed and refluxed for 8 hours. Not a lot of precipitate formed so instead of filtering it, the ethanol was distilled off. The NMR was taken and showed that the HQ7A-sensor was formed but had two extra peaks from excess 4-aminoantipyrine. To remove the impurities and to try to get the solid yellow sensor, it was ran through a silica column with 95% dichloromethane and 5% methanol. The fluorescent fractions were collected, dried, and had the NMR taken. The NMR showed that the sensor degraded in the column.



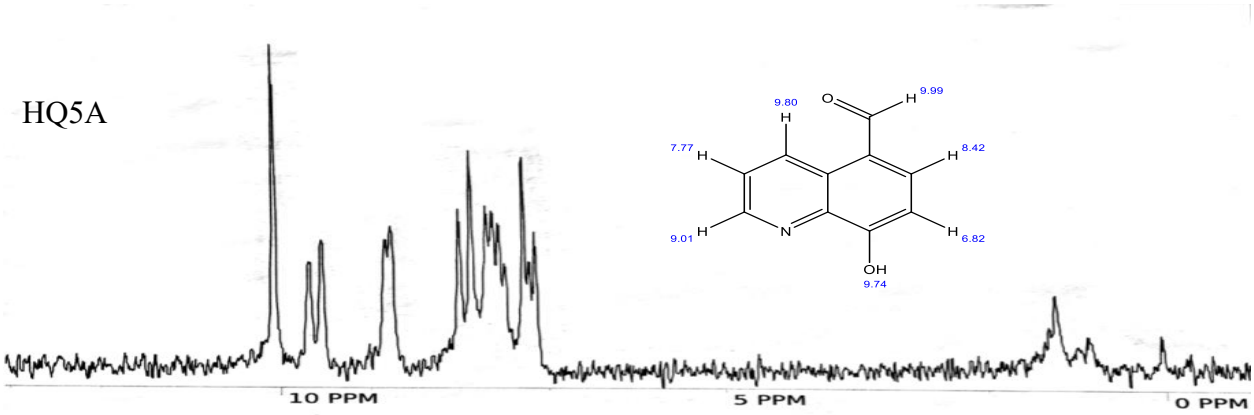
HQ7A-sensor before column.



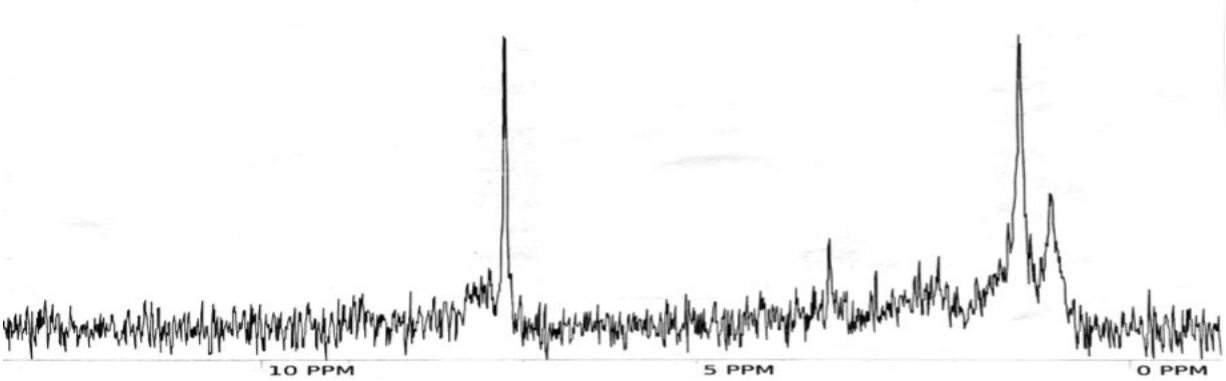
HQ7A-sensor after the column.

Step 1 Part 2: Collecting Aldehydes

Since all of the HQ7A was used to make the failed sensor, more had to be isolated. A new way to purify the crude compound was needed since we were running out of dichloromethane. To separate the compounds from the crude, it was extracted with hexane and ethyl acetate by being tritrated and by Soxhlet extraction. From the first extraction, HQ5A and HQ7A were separated in a column the same way as the first crude extraction column. We were able to get 90 mg of HQ5A. We also got HQ7A but was unable to measure how much was isolated because we tried purifying it with charcoal and heat, the NMR said the compound decomposed.

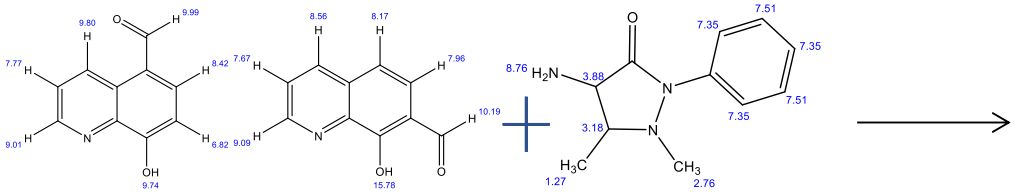


HQ5A that was extracted in the second column.



HQ7A after treatment with charcoal.

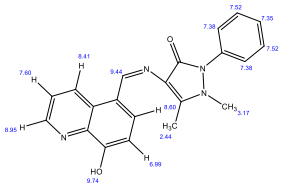
Step 2 Part 2: Imine Formation



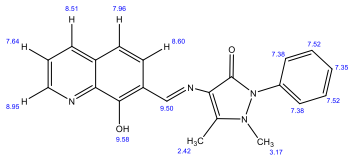
8-Hydroxyquinoline-5-Carbaldhyde

8-Hydroxyquinoline-7-Carbaldhyde

4-aminoantipyrine



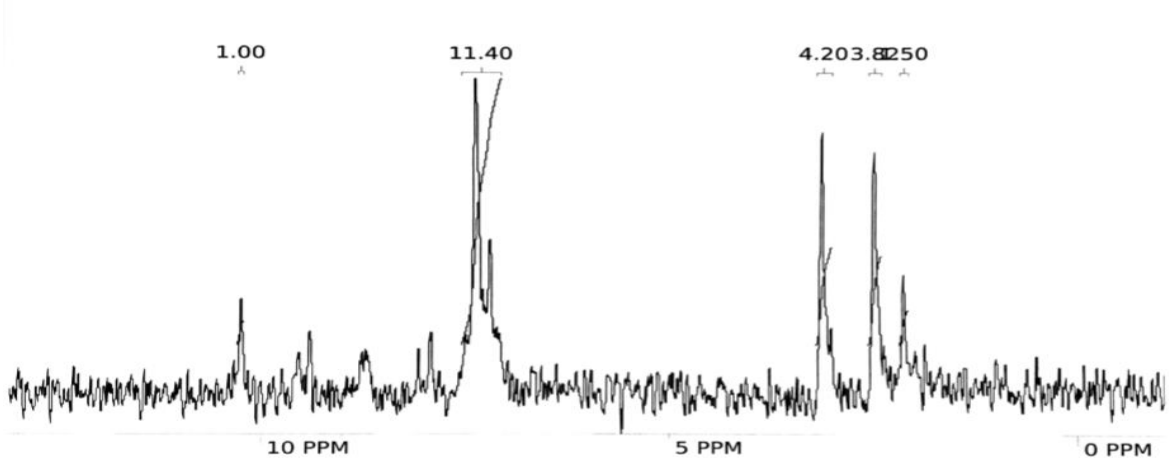
4-(8'-hydroxyquinolin-5'-yl)methyleneimino-1-phenyl-2,3-dimethyl-5-pyzole (HQ5A-sensor)



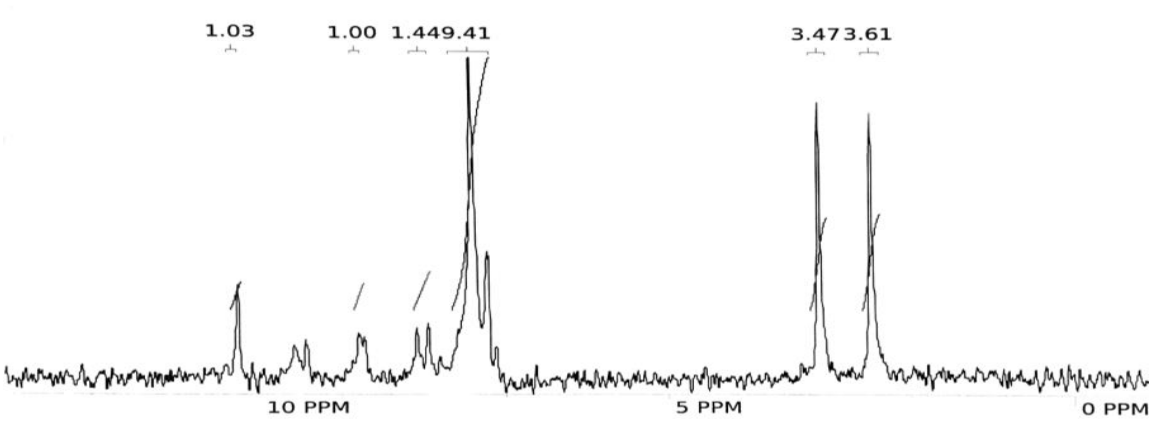
4-(8'-hydroxyquinolin-7'-yl)methyleneimino-1-phenyl-2,3-dimethyl-5-pyzole (HQ7A-sensor)

Our next strategy is to move on to synthesize mixture of sensors from the mixture of aldehydes (8-Hyrdoxyquinoline-7-Carbaldhyde and 8-Hydroxyquinoline-5-Carbaldhyde) made by Mohammed Vayani in fall 2014. hoping that after the second step the two sensors must have two different Rf values so we can isolate the two different sensors directly from chromatographic separation. Used 100 mg of my 8-Hydroxyquinolin-5-Carbaldehyde and 250 mg of Vayani's mixture and dissolved into 15 mL of ethanol and heated to fully dissolve. Then used 117.36 mg and 293.7 mg of 4-aminoantipyrine in 5 ml of ethanol. Refluxed both mixtures in separate round bottom flasks in an oil bath for 8 hours. A yellow precipitate formed in each reaction. The precipitate was filtered from the solution and washed with hot ethanol to remove any unreacted compounds. NMR was taken of both compounds and only showed HQ5A from both reactions.

Precipitate after the 8 hour reflux of pure HQ5A (on the left) and HQ5A and HQ7A mixture (on the right).

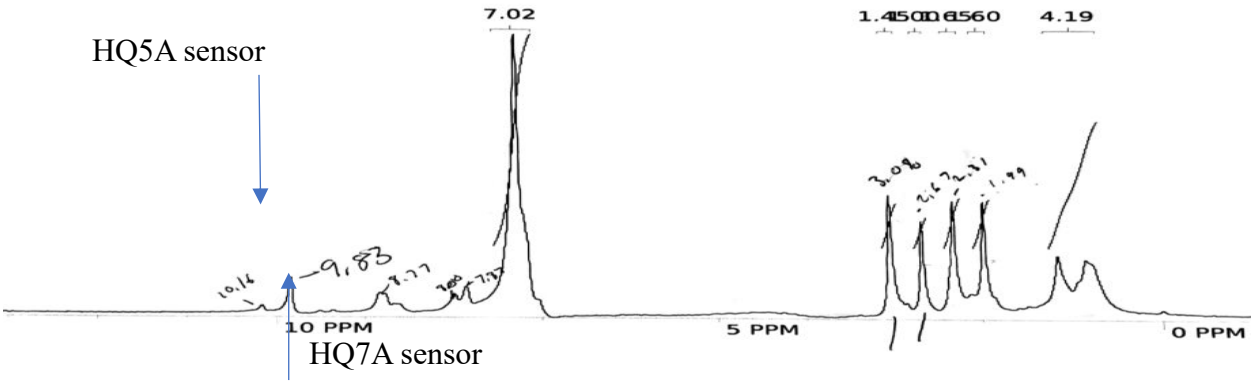


NMR from pure HQ5A sensor.

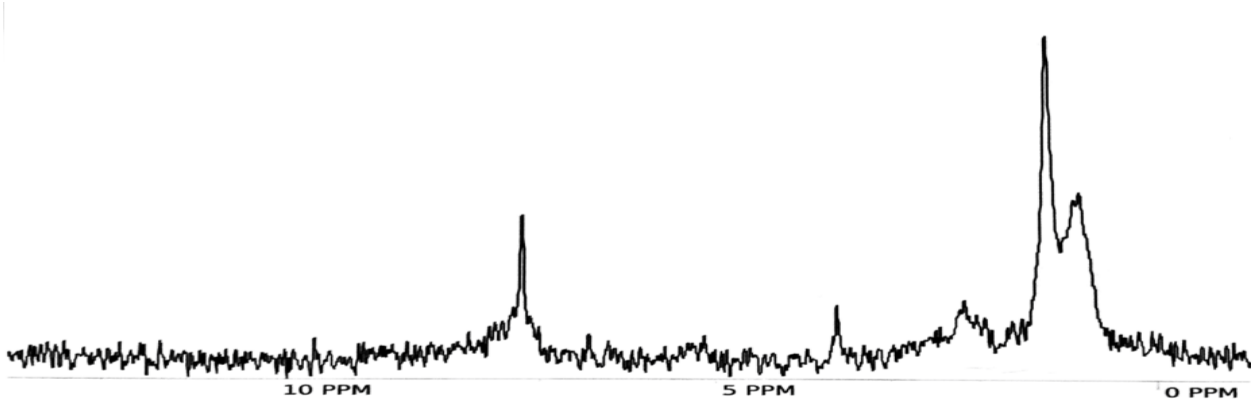


NMR from HQ5A and HQ7A mixture sensor.

The filtrate of both reactions were also saved to see if any sensor fell into the solution. The filtrate for the HQ5A and HQ7A mixture sensor was dried and had the NMR taken. The NMR showed strong possibility of having some of the HQ7A sensor in the solution. To try to separate it, it was placed in a column and ran with petroleum ether and ethyl acetate (ethyl acetate increased in volume from 2% to 5% to 10% to 15% to 25%). Fractions 21-47 were collected because showed fluorescence when spotted on a TLC plate. The NMR was taken and showed that any sensor that was collected degraded in the column.



Filtrate HQ5A and HQ7A mixture solution.



Sensor solution after running through a column.

Conclusion:

We were able to isolate the 8-Hydroxyquinoline-7-Carbaldehye compound but unable to form the sensor complex. Possible reasons are that the HQ7A that was isolated is impure since it was a green color instead of a white color as said in the literature. The other reason is because an insignificant amount of HQ7A was used to form the sensor complex. To continue this project, the synthesis of the aldehyde needs to be improved so more aldehyde compound is formed since so much starting material is used and not much product is formed. Another thing that needs to be improved is the how to purify the HQ7A by removing the green color. Overall, a lot of progress has been made since this project was first started in fall 2014 because we were finally able to isolate HQ7A. Future work should be able to go more smoothly and be able to study the activity of the sensor with several metal ions, including Al^{3+} using UV visible spectroscopy and fluorescent studies with all of the work done synthesizing and isolating the target compound (HQ7A).

Acknowledgements

Dr. Ghosh, Dr. Lavey, Dr. Rowley

Dr. Howell, Dr. Ansonoff, Dr. Scherr

John Engell, David Rasen, Geetha Apparaju

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