

**SYNTHESIS OF HYDROGENASE MIMICS FOR USE AS CATALYSTS IN
THE HYDROGEN EVOLUTION REACTION**

An Undergraduate Research Scholars Thesis

by

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ABSTRACT

Synthesis of Hydrogenase Mimics for Use as Catalysts in the Hydrogen Evolution Reaction

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The conducted research explored the synthesis of hydrogenase mimics containing first-row transition metals, similar to those in marine bacterium, for the purpose of catalyzing the hydrogen evolution reaction (HER). The HER involves the reduction of two hydrogen protons by two electrons to produce hydrogen gas, which is an attractive alternative to fossil fuels. It is hypothesized that by mimicking the structure of hydrogenases the HER may be catalyzed with turnover frequencies comparable to known hydrogenases and commercial catalysts like platinum. The proposed hydrogenase mimics would utilize diamine dithiol ligands, because amine groups have been shown effective in relaying protons. The nickel-based metallic reagent was synthesized, to be used with diamine dithiol ligands to synthesize the proposed hydrogenase mimic. Characterization of the intermediate compounds was conducted *via* ^1H NMR and mass spectrometry. By comparing the catalytic activity of the proposed hydrogenase mimics when used in the HER to state-of-the-art catalysts, like platinum, a more sustainable HER catalyst may be established. While the proposed hydrogenase mimic synthesis was unsuccessful, alterations to the methods and additional time could yield the desired results.

DEDICATION

I would like to dedicate this work to my parents for always supporting and encouraging my academic endeavors, and my Pappy for fostering my love of science from a young age.

ACKNOWLEDGEMENTS

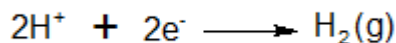
I would like to thank my faculty advisor, Dr. Olbelina A. Ulloa and the Foundational Sciences Department at Texas A&M University at Galveston for their support of my research at every step of the process. Thank you to Dr. Karl Kaiser for allowing me access to his laboratory to conduct this research. I would also like to thank TAMUG Texas Comprehensive Research Fund (TCRF), the Aggies Commit to Excellence Scholarship program, and the Texas A&M LAUNCH Undergraduate Research Scholars Program for providing me with the funding necessary to conduct and present my research. Thank you to Texas Sea Grant as well because this publication is supported in part by an Institutional Grant (NA18OAR4170088) to the Texas Sea Grant College Program from the National Sea Grant Office, National Oceanic and Atmospheric Administration, U.S. Department of Commerce.

NOMENCLATURE

HER	Hydrogen Evolution Reaction
TOF	Turnover Frequency
DI	Deionized
M	Molar
^1H NMR	Proton Nuclear Magnetic Resonance
$\text{Na}_2\text{S}_2\text{O}_3$	Sodium thiosulfate
$\text{Na}_2\text{Cr}_2\text{O}_7$	Sodium dichromate
NaOH	Sodium hydroxide
KCl	Potassium chloride
K_2CO_3	Potassium carbonate
$\text{Cr}(\text{OH})_6$	Chromium hydroxide
HCl (aq)	Hydrochloric acid
NH_4OH	Ammonium hydroxide
NiCl_2	Nickel (II) chloride
dppe	1,2-Bis(diphenylphosphino)ethane

SECTION I

INTRODUCTION



Scheme 1. The hydrogen evolution reaction

The hydrogen evolution reaction (HER) is a process by which two protons are reduced by two electrons in order to produce hydrogen gas, as seen in Scheme 1.¹ The purpose of this research is to synthesize high efficiency hydrogenase mimics that effectively catalyze the HER. Hydrogenases are enzyme catalysts that produce hydrogen as a byproduct of photosynthesis.² They occur in nature as microorganisms that can produce hydrogen gas quickly to be used in processes like methanogenesis.³ One type of marine bacterium that utilizes hydrogenases is *Alteromonas macleodii* “deep ecotype.”⁴ Some hydrogenases catalyze the reduction of sulfate to hydrogen sulfide, which gives wetlands their characteristic smell.³ Most of the recent studies conducted into hydrogenases have revealed their presence in deep-sea hydrothermal vents where hydrogen fuels carbon fixation.⁵ Hydrogenases are an attractive catalyst for the HER because they produce hydrogen gas on demand, and hydrogen is a promising alternative to fossil fuels.⁶

Hydrogen fuel cells, which are powered by hydrogen gas, produce electricity with efficiencies as high as 60%, and without the production of the greenhouse gas carbon dioxide.¹ For comparison, gasoline powered engines operate at 25% efficiency.¹ Hydrogen gas is currently accessed by many industries through the reforming of natural gas.¹ This method is cost-effective since natural gas is readily available, but it creates competition for the global methane supply while producing greenhouse gas byproducts such as unconverted methane and carbon dioxide.⁷ A more

appealing way to produce hydrogen is through the HER, seen in Scheme 1.¹ Since this process does not involve carbon, the byproducts do not include the greenhouse gas carbon dioxide.¹ Furthermore, by using the HER, hydrogen gas would be supplied on demand from a proton source like water, eliminating the need for storage.^{1,6} However, this method requires the development of catalysts to lower the energy barriers of production.¹

Catalysts have been used for over 100 years, and are required in more than 75% of industrial processes for chemical production.⁸ Currently, catalytic processes favor the use of metallic complexes containing precious earth metals like platinum, which has a high exchange current density, leading to an increase in the reported electrocatalytic activity of the HER.⁹ However, platinum is expensive and increases operational costs, so research is being done to find alternative catalysts that function at higher efficiencies and are comprised of less expensive earth-abundant metals such as nickel, iron, and cobalt.¹⁰

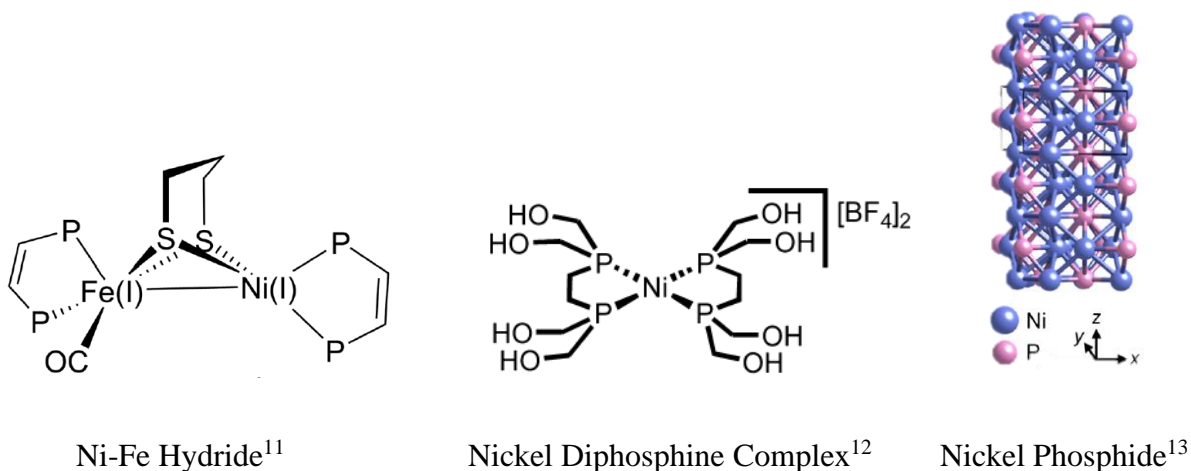


Figure 1. Examples of metal complexes that catalyze the HER¹¹⁻¹³

These first-row transition metals have shown promise as central atoms in HER hydrogenases like Ni-Fe hydrides which catalyze proton reduction and hydrogen oxidation (Figure

1).¹¹ Also, a nickel diphosphine complex was synthesized for use in HERs, resulting in the determination that the monometallic nickel complex functioned at high rates and was stable under acidic conditions (Figure 1).¹² Furthermore, a nanostructured nickel phosphide was also tested as an electrocatalyst for HERs and revealed one of the highest reported activities among any non-noble metal electrocatalyst as well as high stability in acidic conditions (Figure 1).¹³ Earth-abundant metals have also been used in metal organic sheet (MOS) catalysts, which contain repeating chains of monometallic complexes and yield similar results of high catalytic activity as well as stability.¹⁴

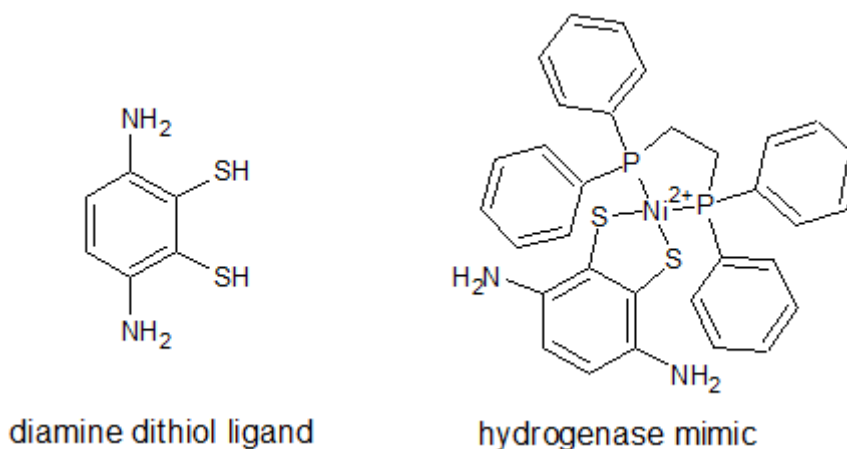


Figure 2. The diamine dithiol ligand and proposed hydrogenase mimic

The conducted research focuses on the synthesis of a diamine dithiol ligand¹⁵ and a proposed hydrogenase mimic. The synthesis of the hydrogenase mimic has not been completed yet. Mimicking natural hydrogenases is proposed because of the functionality of those compounds. This type of ligand, seen in Figure 2, contains pendant amine groups which have been used as proton relay during the H-H bond formation of the HER when oriented near the metal center.¹⁶ The proposed diamine dithiol ligand will be combined with a metallic complex, NiCl₂ddpe to

produce hydrogenase mimic. Turnover frequency (TOF) is the average number of chemical reactions that occur at the active site per unit of time.¹⁶ Furthermore, overpotential is the voltage difference observed between the theoretically determined reduction potential of the half reaction and the experimental value of the redox event.¹⁶

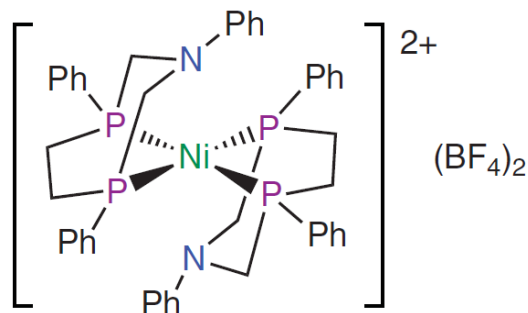


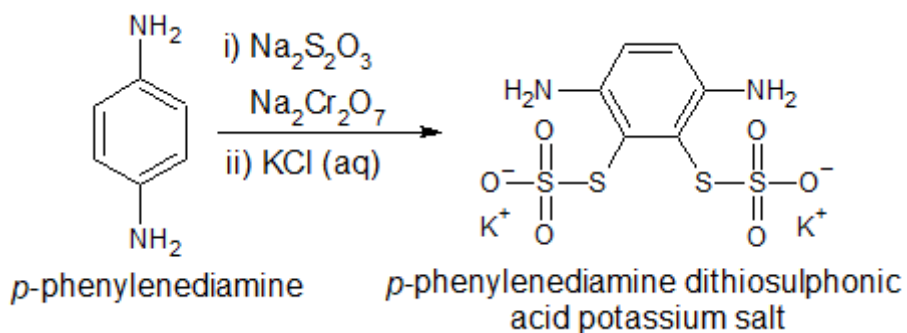
Figure 3. An example of a nickel catalyst with a high TOF¹⁶

The TOF results of a synthesized nickel phosphide catalyst (Figure 3) for the production of hydrogen gas were as high as 1040s^{-1} with an overpotential of about 290 mV.¹⁶ Characterization of the complexes will be done *via* ^1H NMR and mass spectrometry. Upon successful synthesis and characterization, the hydrogenase mimics will be tested for their efficiency in HERs *via* electrochemical analysis in the presence of acids. Upon completion of the synthesis and characterization of the proposed nickel complex as a hydrogenase mimic, a family of proposed hydrogenase mimics, containing cobalt or iron and a diamine dithiol ligand, will be evaluated. If a hydrogenase mimic comprised of a first-row transition metal is synthesized for use as catalysts in HERs, then the complex will be a feasible alternative to the catalysts currently being used by the industry.

SECTION II

METHODS

Part One: Ligand Synthesis

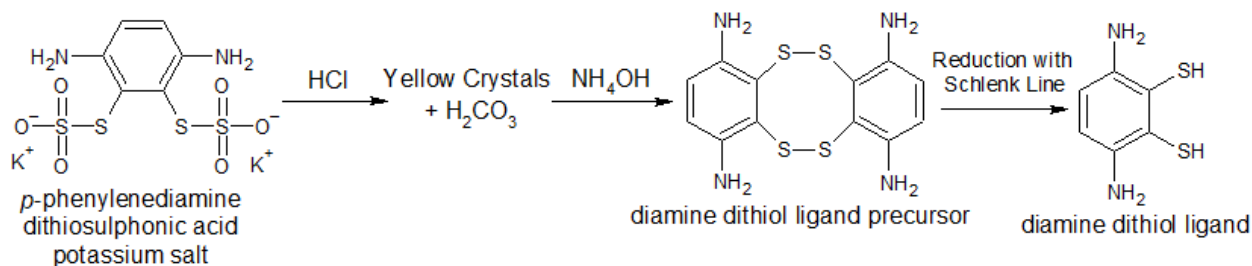


Scheme 2. Synthesis of *p*-phenylene diamine to the diamine dithiosulphonic acid potassium salt.

The synthesis of the diamine dithiol ligand starts with the production of *p*-phenylene diamine dithiosulphonic acid potassium salt as reported by Green and Perkin, scaled down to an expected yield of 10 g (Scheme 2).¹⁵ First, a solution of 109 g (0.70 mol) of sodium thiosulfate ($\text{Na}_2\text{S}_2\text{O}_3$) in 165 mL of deionized (DI) water, was created and set aside. Next a solution containing 29 g (0.11 mol) of sodium dichromate ($\text{Na}_2\text{Cr}_2\text{O}_7$) in 55 mL of DI water was prepared. This solution was neutralized with a saturated sodium hydroxide (NaOH) solution. A third solution containing 12 g (0.11 mol) of *p*-phenylenediamine in 55 mL of DI water was prepared and placed in an ice bath. The $\text{Na}_2\text{S}_2\text{O}_3$ and $\text{Na}_2\text{Cr}_2\text{O}_7$ solutions were combined and the pH of the resulting solution was checked to ensure that it is nearly neutralized. Enough ice to double the volume of the *p*-phenylenediamine solution was added, followed by 55 mL of glacial acetic acid. Immediately, the $\text{Na}_2\text{S}_2\text{O}_3$ / $\text{Na}_2\text{Cr}_2\text{O}_7$ solution was added to the cold *p*-phenylenediamine solution.

The pH of the resulting solution was neutralized with NaOH(aq). Next, 109 g (1.46 mol) of potassium chloride (KCl) was added. The solution was stirred at room temperature for two days.

After the two-day stirring period, the solution was filtered through Celite to isolate the precipitate that had formed. The precipitate was washed with 50 mL of a 2:1 solution by volume of water to methanol, and was extracted with enough boiling water until the water ran clear, approximately 70 mL. To the resulting hot filtrate, 3.0 g (0.55 mol) of potassium carbonate (K₂CO₃) was added and stirred for an hour, still hot, to cause chromium hydroxide (Cr(OH)₆) to precipitate out. After the precipitate formed, 3.3 g (0.27 mol) of decolorizing charcoal was added to the mixture. After stirring for an hour, the resulting mixture was filtered and the filtrate was treated KCl. After cooling overnight, crystals of the *p*-phenylenediamine dithiosulphonic potassium salt precipitated. The crystals were washed with cold water and then dried in the frit under vacuum for an hour. The crystals were weighed and characterized by mass spectrometry.

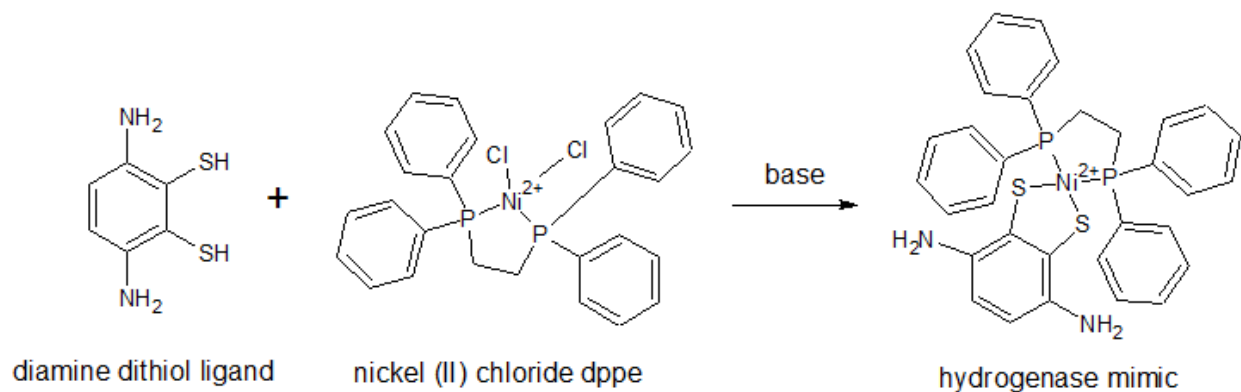


Scheme 3. Synthesis of diamine dithiol ligand from *p*-phenylenediamine dithiosulphonic acid potassium salt

Crystals of *p*-phenylenediamine dithiosulphonic acid potassium salt were dissolved in hot water and treated dropwise with 5 mL of aqueous hydrochloric acid (Scheme 3).¹⁵ This was stirred and then placed in the refrigerator to cool, so that a yellow needle-like precipitate could

recrystallize. No distinct crystals were formed as expected from the literature¹⁵, but the solution was yellow in color, so it was concentrated on the rotary film evaporator and set in the refrigerator overnight for recrystallization. The resulting yellow crystals were suspended in 5 mL of 3M ammonium hydroxide (NH₄OH) (Scheme 3).¹⁵ According to the literature, this basification should result in red crystals, indicating the desired diamine dithiol ligand precursor was created.¹⁵ However, the result of basification was a red solution that had no distinct crystals. Mass spectrometry later revealed that the dimerization process did not work and this solution still contained the *p*-phenylenediamine dithiosulphonic acid potassium salt. When successfully isolated, these red diamine dithiol ligand precursor crystals can be weighed and a few should be set aside in a vial for mass spectrometry characterization. Upon successful synthesis of the diamine dithiol ligand precursor, the diamine dithiol ligand may be synthesized using Schlenk techniques.

Part Two: Proposed Synthesis of Hydrogenase Mimic



Scheme 4. Proposed synthesis of the hydrogenase mimic

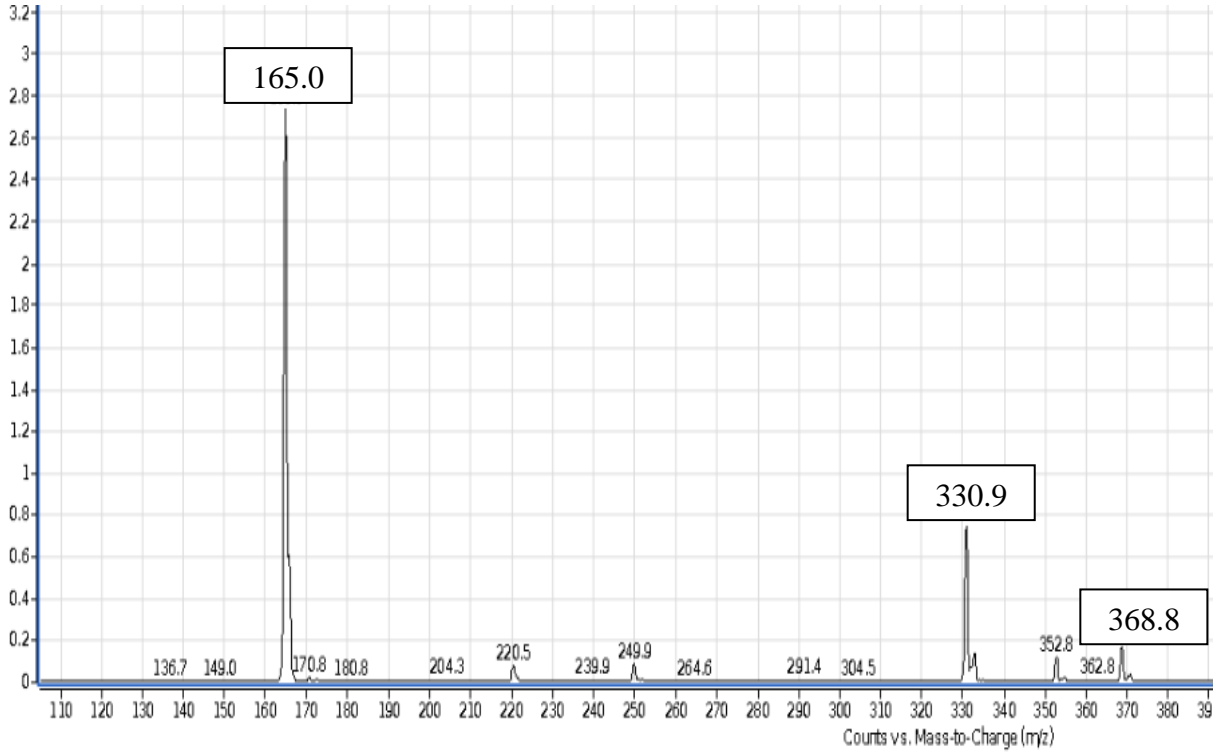
Synthesis of nickel (II) chloride dppe (NiCl₂dppe) reagent was completed based on the literature procedures¹⁷ and characterized *via* ¹H NMR. Following the completion of the diamine dithiol ligand and NiCl₂dppe, a proposed hydrogenase mimic may be synthesized and tested for

catalytic activity (Scheme 4). Since the dimerization procedure did not yield the diamine dithiol ligand crystals as expected, the reaction in Scheme 4 could not be carried out.

SECTION III

RESULTS

A.



B.

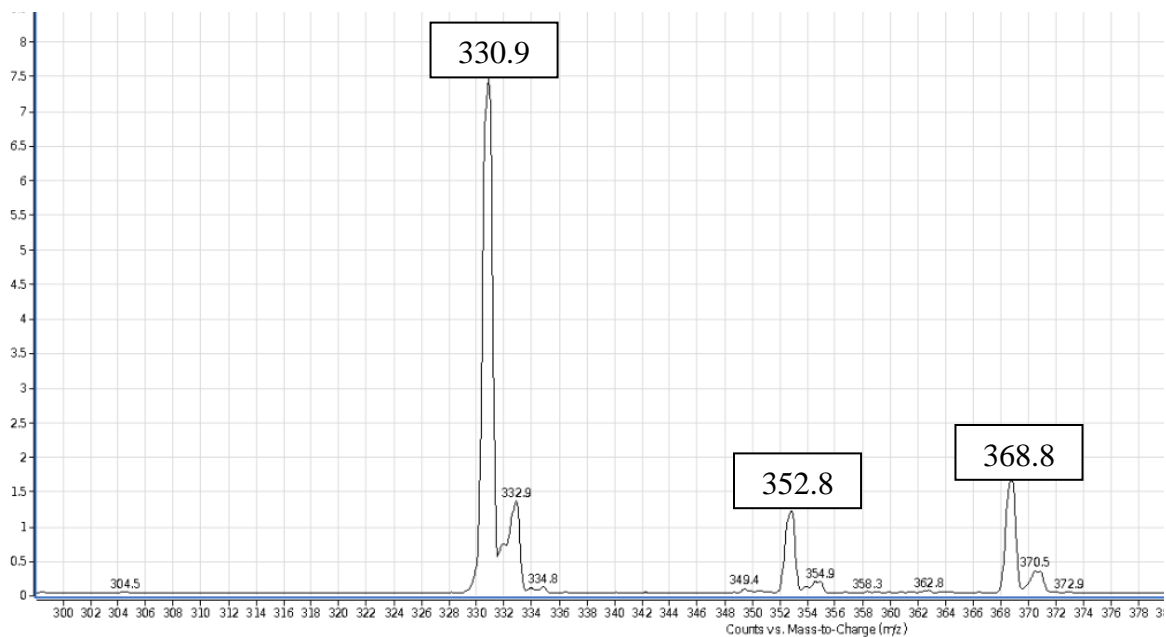


Figure 4. Mass spectrometry results for the *p*-phenylenediamine dithiosulphonic acid potassium salt crystals with the mass to charge ratio on the x-axis. **A** is the full mass spectrometry data set, whereas **B** is a zoomed in picture of the smaller peaks on the right.

There are four notable peaks in Figure 4 at 165.0 m/z, 330.9 m/z, 352.8 m/z, and 368.8 m/z. It can be deduced that these refer to the presence of half the *p*-phenylenediamine dithiosulphonic acid potassium salt mass, *p*-phenylenediamine dithiosulphonic acid, *p*-phenylenediamine dithiosulphonic acid sodium salt, and *p*-phenylenediamine dithiosulphonic acid potassium salt.

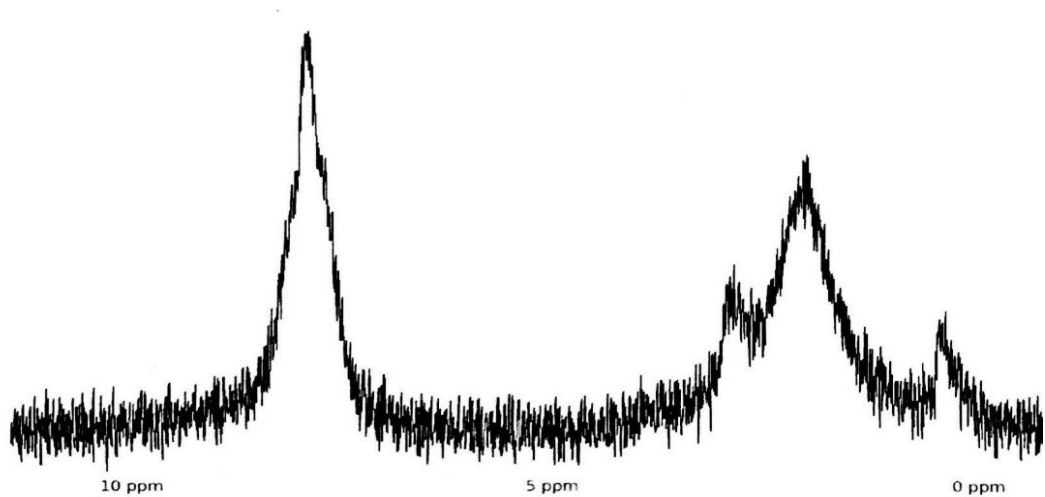


Figure 5. ^1H NMR NiCl_2dppe in deuterated chloroform

Analyzing Figure 5, the peak at 7.26 refers to the deuterated chloroform solvent. The short peaks refer to the presence of nickel (II) chloride dppe. The middle peak indicates that there is unreacted dppe left in the sample.

SECTION IV

CONCLUSION

The purpose of this research was to synthesize a new nickel-based complex that mimics the catalytic activity of hydrogenases in the HER.^{15, 17} The proposed compound mimics the structure of hydrogenase by incorporating a first row transition metal center¹¹ and amine groups to function as proton relays.^{16, 18} Since it is less expensive to produce than platinum-based catalysts, this type of hydrogenase mimic could be commercialized to expand the hydrogen economy and make hydrogen gas a household alternative to fossil fuels.¹ The results in Figure 3 show that the NiCl₂dppe was successfully synthesized based on the literature.¹⁷ Furthermore, the results in Figure 2 reveal that using the literature procedures, *p*-phenylenediamine dithiosulphonic acid potassium salt was synthesized properly.¹⁵ The dimerization step required to convert the *p*-phenylenediamine dithiosulphonic acid potassium salt into the diamine dithiol ligand precursor based on literature procedures was unsuccessful.¹⁵ Repetition of this synthesis was not possible due to the loss of laboratory access during the coronavirus pandemic. Once this project can be resumed, the diamine dithiol ligand and NiCl₂dppe would be combined under basic conditions to synthesize the proposed hydrogenase mimic. This would be followed by electrochemical tests to determine turnover rates and overpotential of the hydrogenase mimic.

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