

Biomimicry: Investigating the Active Site Model of Lactate Racemase

Stephanie Podguski, Maisy Ross

Advisor: Dr. Brandon Tate

Department of Chemistry, SUNY Geneseo, Geneseo New York 14454



Abstract:

Because of humans' heavy impact on nature with industrialization and resource extraction, biomimetics, also known as biomimicry, is a study that has emerged. Biomimetics utilizes observations from nature to comprehend the principles of underlying mechanisms and apply concepts that may benefit science, medicine, engineering and the like. An area of biochemistry we are applying this to is the lactate racemase enzyme. This metalloenzyme is found in many prokaryotic organisms and catalyzes the interconversion between the two optical isomers of lactic acid. The structure of this enzyme consists of a square-planar nickel (II) ion coordinated by a histidine residue and a pincer ligand. We are synthesizing a model of this enzyme using biomimetic chemistry to further expand our knowledge on the mechanism and reactivity of lactate racemase. We hope that the findings from this model will lead to a greater understanding of the unique organometallic cofactor of lactate racemase. This will help improve designs for biomimetic catalysts that can be used in many different areas of everyday life, especially but not exclusively, renewable fuels.

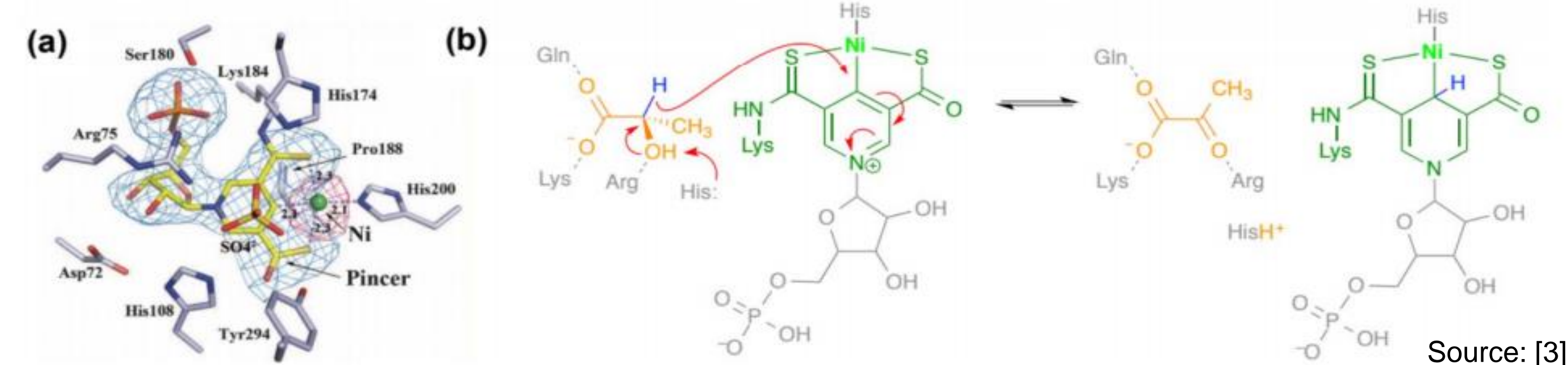
Background:

Across the globe, our reliance on fossil fuels in everyday life can be damaging to the Earth and is unsustainable. The possibility to find a renewable energy source within the field of Chemistry is promising and would be greatly beneficial to our society. Energy sources such as wind power and solar energy, although useful, are inconsistent. To make better use of this energy, chemists are in search of a chemical fuel cell, which can release the energy when it is needed.

We look to hydrogen gas, as it can be renewably produced by electrolysis of water. It is a clean energy source, but has a very low energy density when compared to other conventional fuels. The goal of our project is to develop a catalyst, using the lactate racemase model, that with carbon dioxide, is capable of performing the conversion from hydrogen to a liquid, or liquifiable fuel. This liquid hydrogen has a higher energy density than that of hydrogen gas.

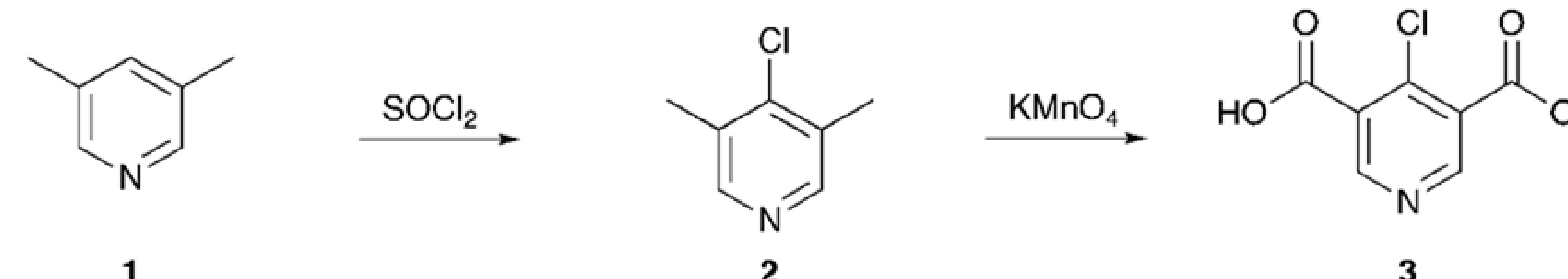
The mechanism of the lactate racemase enzyme is not well known, but it is hypothesized that the carbon to hydrogen bond activation in the form of a hydride transfer is the mechanism in action.

(a) Active site of lactate racemase. (b) Hypothesized mechanism.



Materials/Methods:

Synthesized key precursors of related enzyme models by refluxing 3,5-lutidine (Compound 1) with thionyl chloride at 65 degrees. Having produced 4-chloro-3,5-lutidine (Compound 2) we then oxidized this compound using potassium permanganate in aqueous solution, resulting in the formation of 4-chloropyridine-3,5-dicarboxylic acid (Compound 3). The products were then isolated by vacuum filtration and characterized by nuclear magnetic resonance (NMR) spectroscopy.



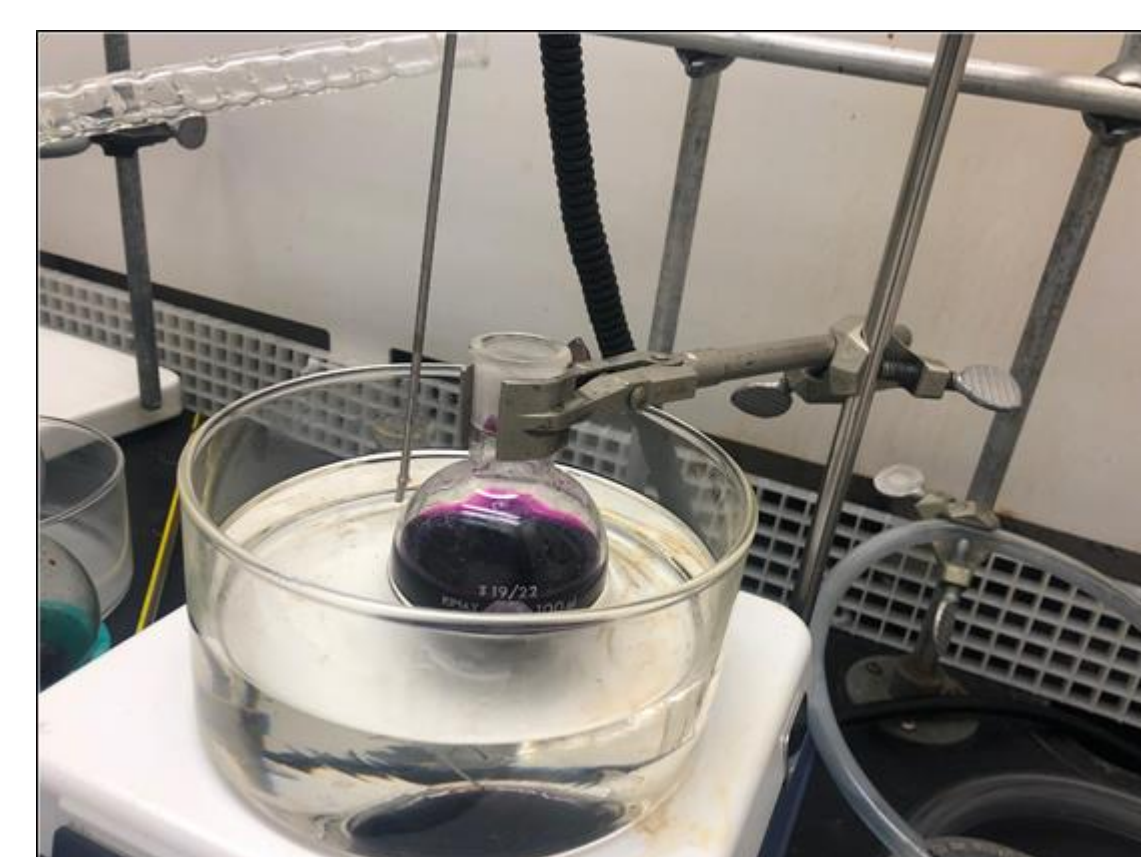
Results & Conclusions:



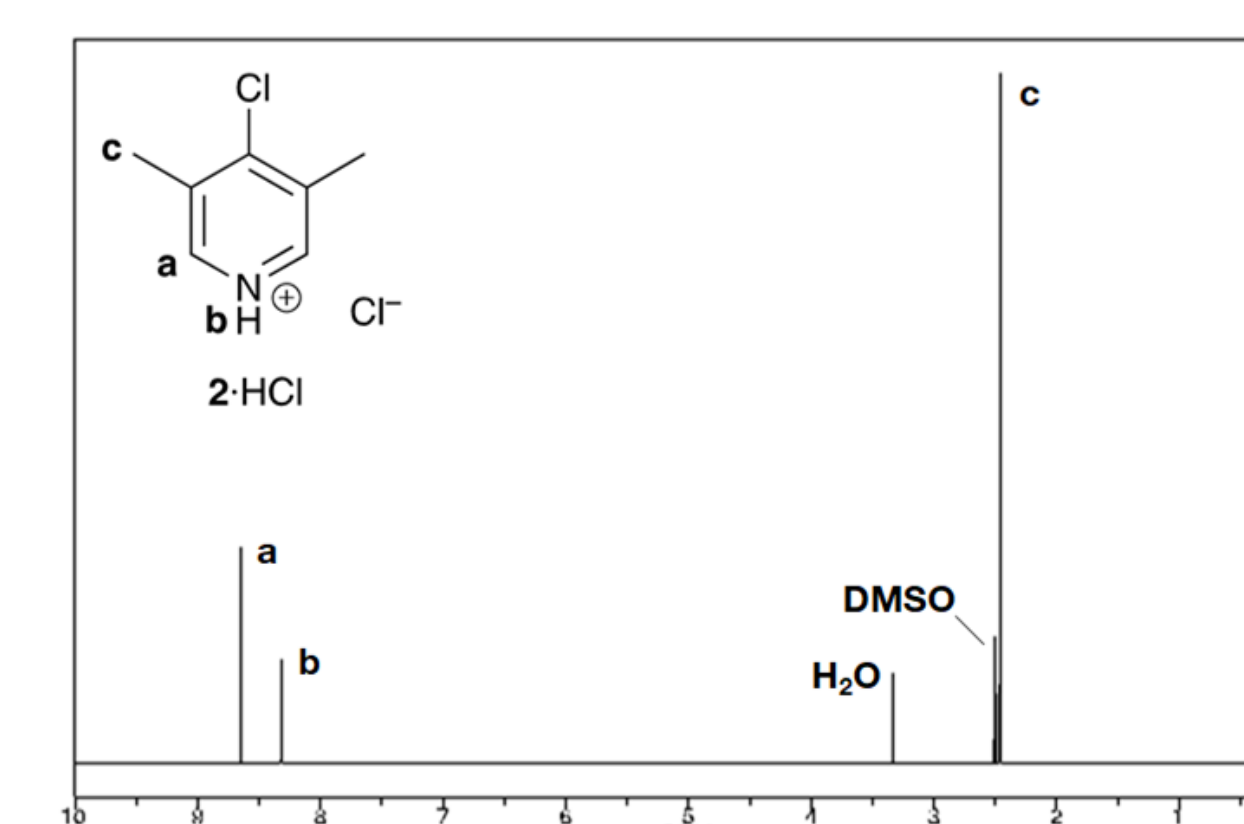
After the refluxing of Compound 1 with thionyl chloride, compound 2 was produced. The products were filtered, and compound 2 was contained in an organic solvent.



The rotary evaporator was used to evaporate this organic solvent and leave us with Compound 2, whose NMR is shown below, which confirms our synthesis.



Compound 2 was then oxidized using potassium permanganate in an aqueous solution, shown on the left.

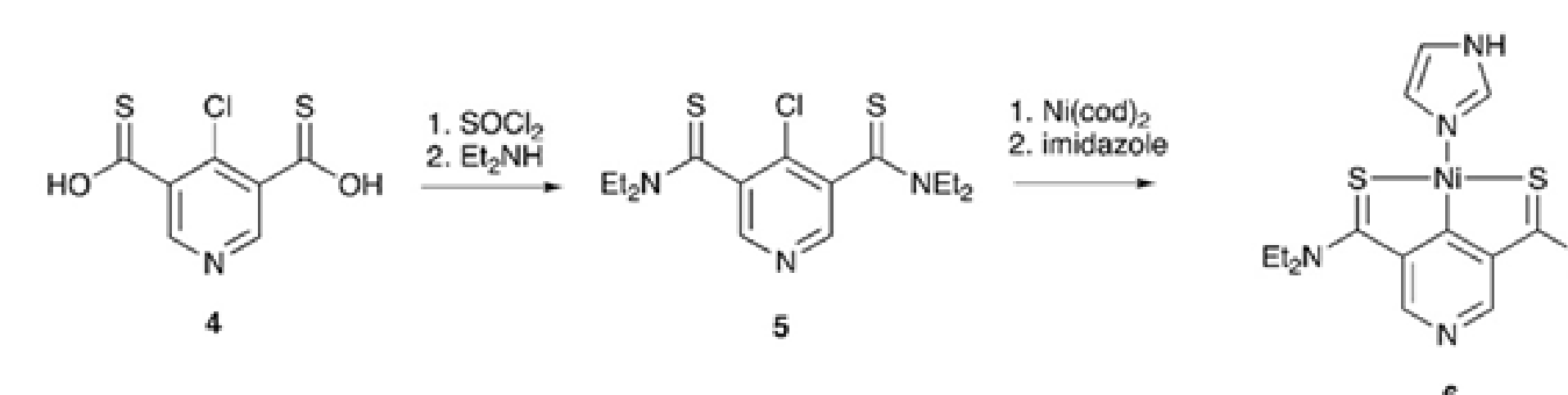


Future Directions:

The immediate goal of this project is to continue on with the schematic shown to the left by utilizing compounds similar to Lawesson's reagent. This will allow us to create at least one structural model of the lactase racemase cofactor as proposed by a previous student.

After generating the structural model, our next aim is to grow high quality crystals using X-ray diffraction in order to continue investigating the reactivity as a hydride carrier.

We anticipate this project will shed light on the role of the unique organometallic cofactor of lactate racemase and may inform the design of biomimetic catalysts for related reactions, particularly reactions relevant to hydrogen storage and renewable fuels.



References:

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