

Synthesis and Characterization of Cobalt(III) Complexes with Nitrogen-Containing Heterocyclic Ligands as Possible Anti-Cancer Pro-Drugs



*Mario Garcia, *Kaila F. Hart, *Natalie Joe, *Matthew Nopah, §Thomas Padilla, and *Aimee M. Morris

Department of Chemistry, *Fort Lewis College, Durango, Colorado and §San Juan College, Farmington, New Mexico

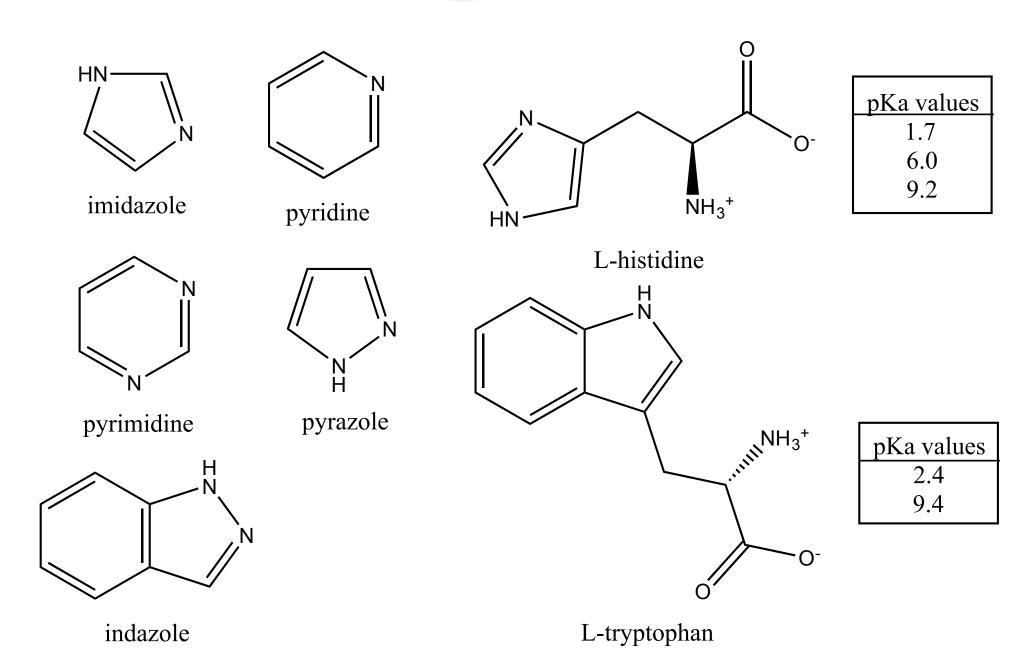
Purpose

Research into better cancer treatments has been a progressively growing field. Metal containing coordination compounds offer unique chemistry that could prove useful. A ruthenium(III) compound with two indazole and four chlorine ligands, KP1019, is currently in phase III clinical trials as a pro-drug for the treatment of cancer. Our research delved into creating similar compounds to KP1019 but with cobalt centers instead of ruthenium, and with various nitrogen-containing heterocyclic ligands.

Starting with cobalt(II) chloride and ligands including: imidazole, pyrimidine, indazole, pyridine, pyrazole, L-histidine or L-tryptophan, we attempted to oxidized the metal center and attach the desired ligands. Each ligand presented its own unique aspects and binding properties. A 4:1 metal to ligand ratio was most commonly used, however this ratio was altered based on the denticity of the specific ligand and our desired binding sites.

$$\begin{array}{c} \text{coCl}_2 \bullet 6\text{H}_2\text{O} \ + \ 4 \text{ Ligand} \\ \text{or} \\ \text{Cl}_2 \text{ (g)} \\ \text{or} \\ \text{30\% H}_2\text{O}_2 \\ \end{array}$$

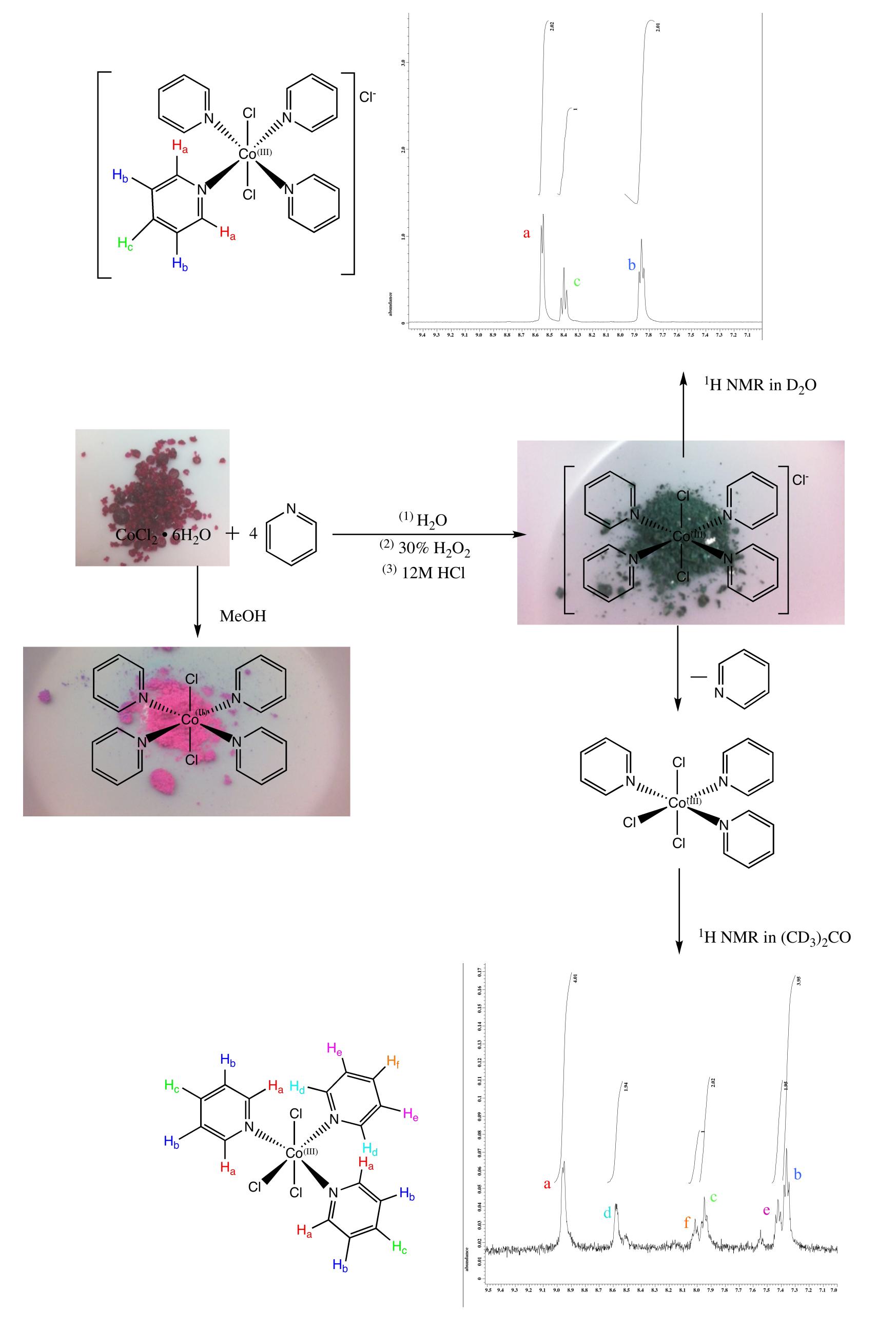
Ligands



Methods of Oxidation

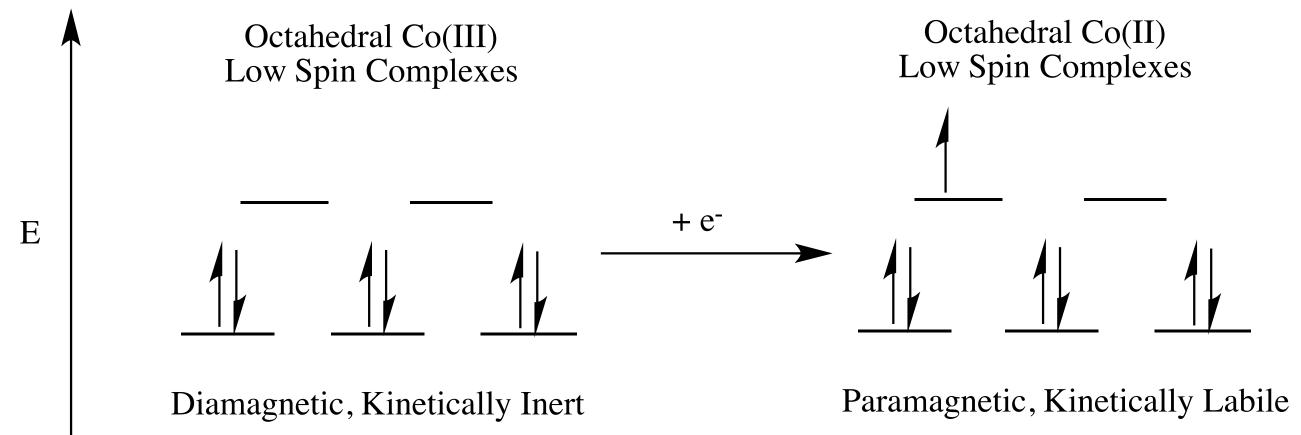
Scheme 1- Reduction half potentials of oxidizing agents utilized along with the oxidation half potential for cobalt. $\frac{1}{2}O_2(g) + 2H^+ + 2e^- \Rightarrow H_2O \qquad E^\circ = 1.229 V$	
$2^{-2(g)} + 2H + 2e^{-} \rightleftharpoons 2H_2O$ $H_2O_2 + 2H^+ + 2e^- \rightleftharpoons 2H_2O$	$E^{\circ} = 1.763 V$
$Cl_2(g) + 2e^- \rightleftharpoons 2Cl^-$	$E^{\circ} = 1.360 V$
$Co^{2+} \rightleftharpoons Co^{3+} + 1e^{-}$	$E^{\circ} = -1.92 V$

Experiments



Magmetic Properties

Octahedrally coordinated cobalt complexes have interesting magnetic properties that allow them to be potential pro-drugs. As shown below, a low spin Co(III) complex has all paired electrons and is inert, while a low spin Co(II) complex has an unpaired electron causing it to be reactive. The idea is to make Co(III) complexes that would only be reduced to their Co(II) counterparts in the hypoxic environment of cancer cells. This would allow for selective destruction of only the diseased cells.



Conclusion

We have successfully synthesized some octahedrally coordinated Co(III) complexes that contain heterocyclic ligands. Research continues in the lab to improve these syntheses and further characterize the synthesized compounds.

Acknowledgements

We would like to thank the NSF FOCUSS grant and NIH MARC grant for the financial support that was given to this research project.

