The synthesis and characterization of model complexes for the metalloenzyme Quercetin Dioxygenase

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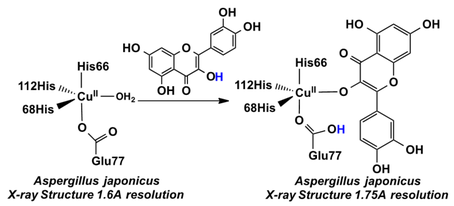
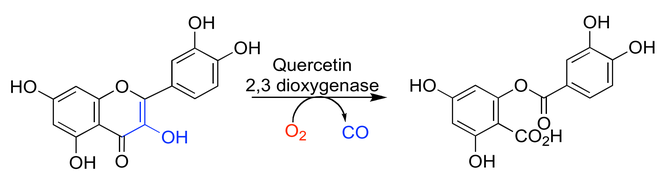
Introduction

Metalloenzymes are proteins that catalyze a specific reaction and contain metals that are tightly bound at the active site.
Dioxygenases, a subclass of metalloenzymes, transfer both oxygen atoms of O_2 into substrate. They have the ability to cleave and degrade aromatic compounds and play an important role in many biological functions.[1] **Aromatic compounds** are one of the most prevalent and persistent pollutants in the environment.
Quercetin 2,3 Dioxygenase (QDO), is unique in that it is the only known dioxygenase that is copper dependent. The copper center is bound to three histidines, one glutamate, and the antioxidant quercetin.[2] *Bacillus subtilis* is one of the known bacterial forms of QDO. The active site differs from the copper-containing fungal form, *Aspergillus japonicus*, as first-row transition metals, such as Fe(II), Co(II), Zn(II), and Mn(II), can be coordinated.



Aspergillus japonicus
X-ray Structure 1.6A resolution

Aspergillus japonicus
X-ray Structure 1.75A resolution



Research Goals

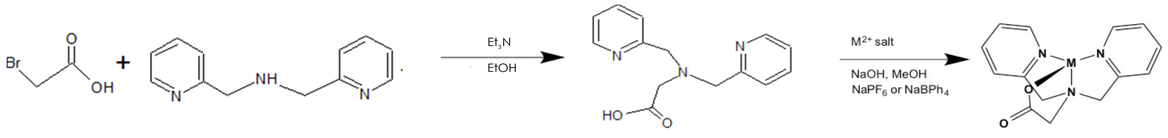
The proposed biomimetic compounds are predicted to react with O-heterocyclic compounds in a similar reaction mechanism as QDO

- Synthesize and characterize structural model complexes of the unique QDO active site.
- Study model complexes to further understand how the enzyme cleaves the O-heterocyclic ring of quercetin.

Synthesis

Synthesis of Ligand and Metal Complexes

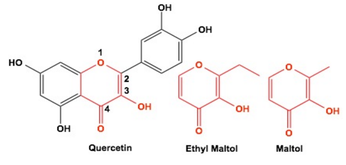
N,N-bis(2-pyridlymethyl)glycine)(BPG)[3] and M^{2+}(BPG):

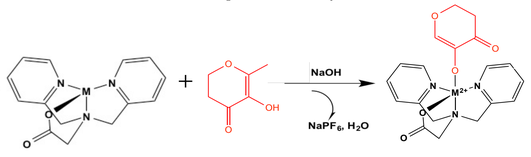


Reactivity

Reactivity of Ligand and Metal Complexes

Given the structural similarities with quercetin, we explored the reaction of our QDO model complexes with O_2 as the oxidant and substrate substructure, **maltol**. Both of these substructures contain the enol moiety which is thought to play an important role in binding to the metal center, but are **smaller and less bulky** than quercetin.


Quercetin Ethyl Maltol Maltol



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2. Fusetti, F.; Schröter, K. H.; Steiner, R. A.; Van Noort, P. I.; Pijning, T.; Rozeboom, H. J.; Kalk, K. H.; Egmond, M. R.; Dijkstra, B. W. *Struct. Lond. Engl.* **2002**, *10*, 259–268.
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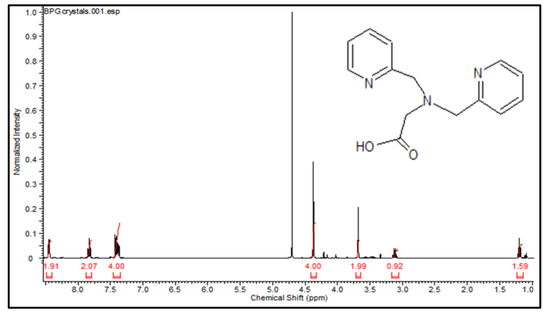
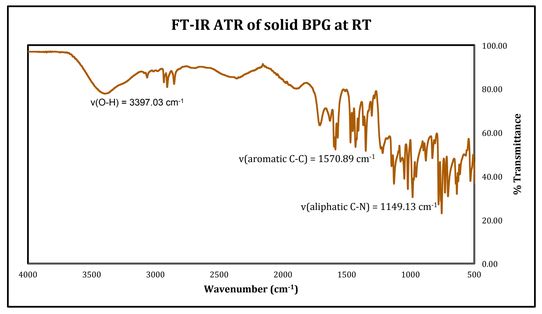
Characterization

Characterization of Ligands

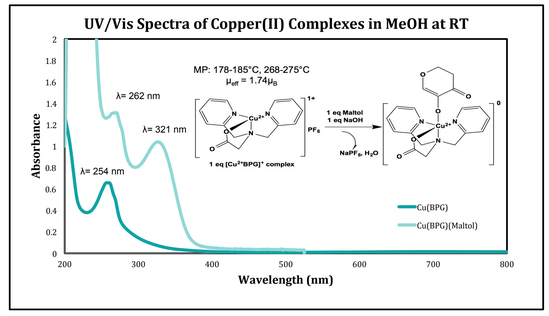
^{1}H NMR and IR Spectra of BPG

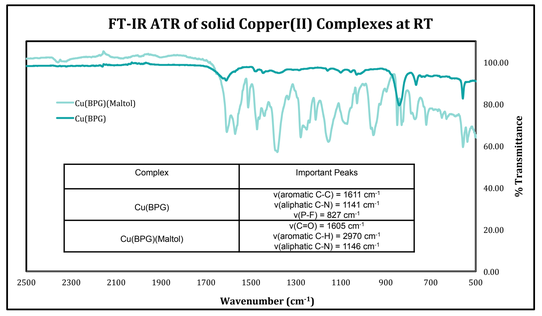




Characterization of Metal Complexes

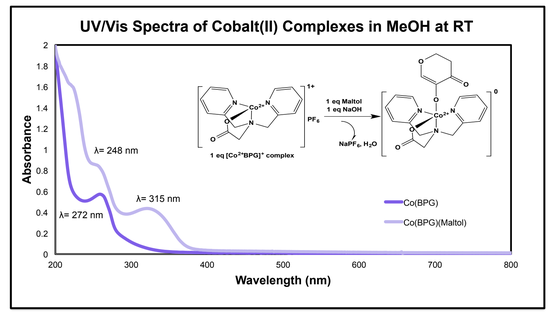
UV-Visible and IR Spectra of Copper Complexes

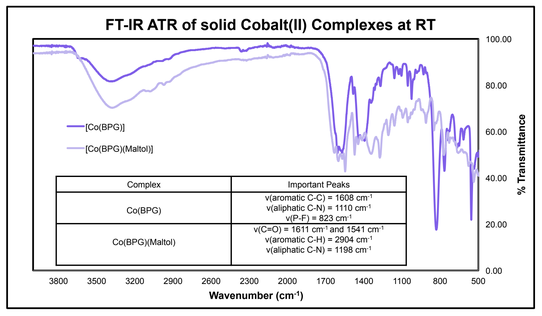




Complex	Important Peaks
Cu(BPG)	ν(aromatic C-C) = 1611 cm^{-1} ν(aliphatic C-N) = 1141 cm^{-1} ν(P-F) = 827 cm^{-1}
Cu(BPG)(Maltol)	ν(C=O) = 1605 cm^{-1} ν(aromatic C-H) = 2970 cm^{-1} ν(aliphatic C-N) = 1146 cm^{-1}

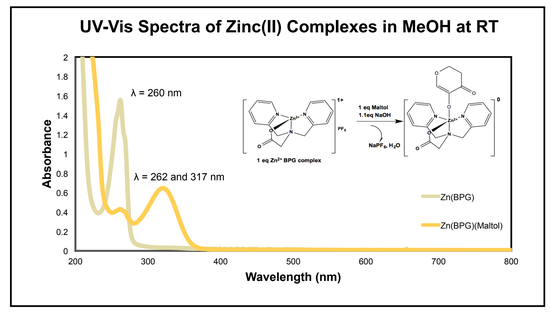
UV-Visible and IR Spectra of Cobalt Complexes

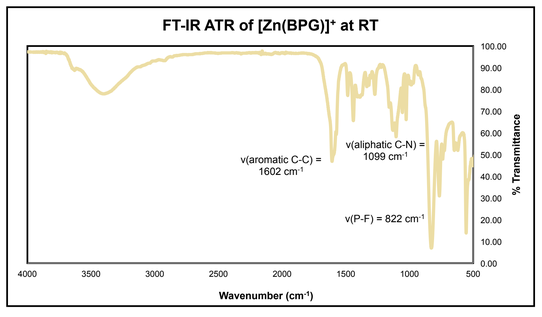




Complex	Important Peaks
Co(BPG)	ν(aromatic C-C) = 1608 cm^{-1} ν(aliphatic C-N) = 1110 cm^{-1} ν(P-F) = 823 cm^{-1}
Co(BPG)(Maltol)	ν(C=O) = 1611 cm^{-1} and 1541 cm^{-1} ν(aromatic C-H) = 2904 cm^{-1} ν(aliphatic C-N) = 1198 cm^{-1}

UV- Visible and IR Spectra of Zinc Complexes





Future Work

- Further characterization of metal complexes
- Carry out more reactions with metals and substrates
- Obtain crystals of our model complexes for crystallographic studies
- Synthesize new ligands that have a similar structure to the active site of QDO to further expand to other catalytic systems

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