

# Active Site Mimics of Nickel Superoxide Dismutase

*Victoria Grace Snider,*  
*Department of Chemistry*

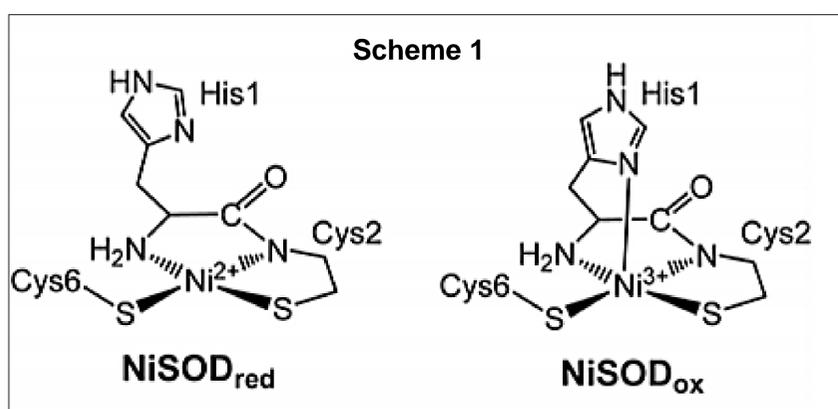
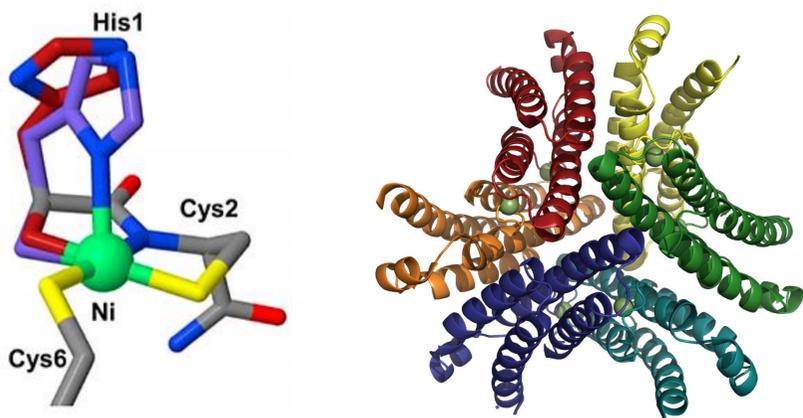
## Background & Significance

To combat oxidative stress, all aerobic organisms have a form of Superoxide Dismutase. Nickel Superoxide Dismutase (NiSOD) is a metalloenzyme that regulates superoxide ( $O_2^{\cdot-}$ ) levels in aerobic organisms by facilitating the disproportionation of superoxide to oxygen ( $O_2$ ) and hydrogen peroxide ( $H_2O_2$ ).



Superoxide is a member of reactive oxygen species (ROS), which can cause significant damage to the surrounding cells if not eliminated<sup>1</sup>. ROS have been linked with such diseases as diabetes, Parkinson's, and Alzheimer's as well as the cell death which occurs after a heart attack or stroke<sup>1</sup>.

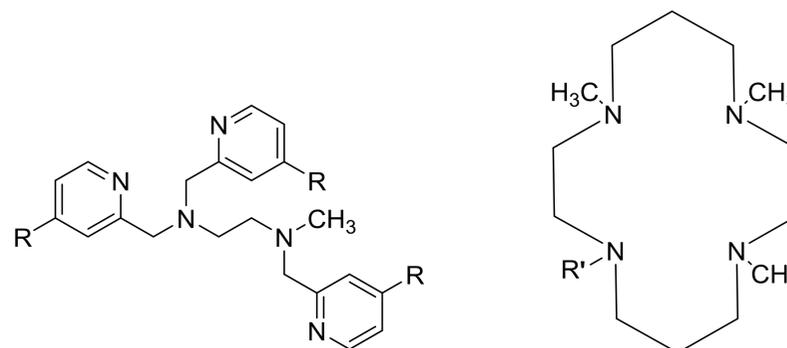
## Structure of the Active Site in NiSOD



In the reduced form, Ni(II)SOD, the Ni ion is coordinated by a primary amine-N, one anionic carboxamido N, and two thiolato-S donors to form a square-planar coordination motif. In the oxidized form, the metal center gets oxidized to Ni(III), and undergoes a geometry change to square-pyramidal through axial ligation by a neighboring histidine (see scheme 1)<sup>2</sup>.

## Design of Biomimetic Ligand

In my research, my aim is to synthesize ligands of biomimetic Ni complexes that will act as models of the NiSOD active center. Unlike native NiSOD, which contains a sulfur-rich coordination sphere, our ligands only contain nitrogen coordination. This is in response to the observation that an S-rich environment can cause damaging oxidation to the ligand. We are currently synthesizing two ligands N,N,N'-Tris(2-pyridylmethyl)-N'-methylethylenediamine (TPMEN) and 1,4,8-Trimethyl-1,4,8,11-tetraacyclotetradecane (trimethylcyclam, TMC),



TPMEN

TMC

R = H, Me, OMe

R' = H, Py, Me

## Discussion & Future Direction

Currently, I am in the process of modifying the TPMEN ligand with the above R groups in order to probe the effect on the ligand of functional groups with differing electron densities. The TMC ligand will be further modified at the non-methylated nitrogen with a pyridine. The pyridine will axially coordinate to the nickel ion to investigate the role of the histidine from the native NiSOD.

## Acknowledgements

Many thanks to Dr. Ansuree Mukherjee for her mentorship and guidance. Thanks also to Dr. Vogler for his help with NMR. This work was funded by UAH College of Science research grant.

## References

1. Broering et al. *Biochemistry* **2013**, 52, 4-18
2. Gale et al. *Inorg. Chem.* **2011**, 50 (19), 9216-9218