Understanding the Oxidative Chemistry of Particulate Methane Monooxygenase Models

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Background

Particulate methane monooxygenase (pMMO) is a membrane protein found in methanotrophic bacteria that catalyzes the two-electron reduction of dioxygen to form an unknown reactive intermediate that performs the partial oxidation of methane to methanol.

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\text{CH}_4 + 2\text{H}^+ + 2e^- + \text{pMMO} \rightarrow \text{CH}_3\text{OH} + \text{O}_2 + \text{H}_2\text{O}
\]

This reaction has generated significant interest for its potential for both carbon sequestration and for use of methane as an alternative energy source. Methane is one of the main forms of atmospheric carbon and greenhouse gas, as well as the major component of natural gas. Industrial processes for the oxidation of methane to methanol require high temperatures and pressures and suffer from low yields, making them dangerous and expensive. This difficult oxidative chemistry is performed by pMMO under ambient conditions at one of two unique copper sites.

Complex 2 exhibited EPR spectroscopic parameters very similar to those observed for the CuB site of pMMO, generating curiosity regarding its reactivity.

Oxidation of CHD and DHA as external substrates was explored for complexes 1-3.

Reactivity of pMMO Models

All of the four complexes above feature both aliphatic and aromatic nitrogen donor atoms, reminiscent of the coordination environment of the CuB site of pMMO. The variations to the ligand framework across complexes 1-4 are meant to vary the steric and electronic properties of the complex to study which factors affect the complex’s reactivity. Reactivity studies were halted for 4 due to solubility issues.

Complexes 1-3 were capable of C-H bond activation and substrate oxidation in the case of CHD and DHA, but not for substrates with higher bond dissociation energies. The variations to the ligand framework did not seem to affect reactivity. Further investigation will be required to determine what factors dictate the observed reactivity.

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Upper left: crystal structure of pMMO; upper right: crystal structure of one protomer of pMMO indicating both of its copper binding sites; lower left: structure of the CuB site of pMMO; lower right: structure of the CuC site of pMMO.

The structure of the CuB site was originally modelled as a dinuclear site and remained ambiguous until 2019, when it was demonstrated to be mononuclear. This has left the site of substrate oxidation an open question, with some reports proposing the CuB site and others the CuC site as the site of substrate binding and oxidation. Synthetic model studies may provide some insight.