1 Diradical intermediate within the context of tryptophan tryptophylquinone biosynthesis.

Yukl ET, Liu F, Krzystek J, Shin S, Jensen LMR, Davidson VL, Wilmot CM, Liu A.
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Recommendations:

Donald Hamelberg [+Follow] . F1000 Chemical Biology > Biocatalysis
Georgia State University, Atlanta, GA, USA.
Score:
25 Apr 2013 | New Finding
DOI: 10.3410/f.717996656.793474050

This paper exemplifies the use of X-ray crystallography to capture the progression of an enzymatic reaction over several months. The reactant, intermediate, and product states in the biosynthesis of tryptophan tryptophylquinone cofactor on methylamine dehydrogenase are resolved in the active site of the enzyme, MauG. In addition to providing an atomic level description of the mechanism and suggesting an order of the reaction steps, this work provides a wealth of high-resolution structural data that can be used to validate theoretical models and potentially guide complementary mechanistic computational studies.

Acknowledgments

Disclosures
Donald Hamelberg and Aimin Liu, the senior author of the recommended article, are both faculty members of the Department of Chemistry at Georgia State University (in separate labs). Donald Hamelberg was not involved with the current study in any way, which was selected for recommendation based entirely on its scientific merit.

No comments yet.

Comments:

Abstract:

Despite the importance of tryptophan (Trp) radicals in biology, very few radicals have been trapped and characterized in a physiologically meaningful context. Here we demonstrate that the diheme enzyme MauG uses Trp radical chemistry to catalyze formation of a Trp-derived tryptophan tryptophylquinone cofactor on its substrate protein, premethylamine dehydrogenase. The unusual six-electron oxidation that results in tryptophan tryptophylquinone formation occurs in three discrete two-electron catalytic steps. Here the exact order of these oxidation steps in the processive six-electron biosynthetic reaction is determined, and reaction intermediates are structurally characterized. The intermediates observed in crystal structures are also verified in solution using mass spectrometry. Furthermore, an unprecedented Trp-derived diradical species on premethylamine dehydrogenase, which is an intermediate in the first two-electron step, is characterized using high-frequency and -field electron paramagnetic resonance spectroscopy and UV-visible absorbance spectroscopy. This work defines a unique mechanism for radical-mediated catalysis of a protein substrate, and has broad implications in the areas of applied biocatalysis and understanding of oxidative protein modification during oxidative stress.

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