

27b - Discovery of a Pathway for Azide Biosynthesis By a Promiscuous *N*-Nitrosylase



Thursday, November 9, 2023



8:00 AM - 8:18 AM

*Celebration 1 (Convention Level, Hyatt Regency Orlando)*

Abstract

The azide moiety is an electron-rich functionality with extensive applications in the fields of synthetic chemistry, material science, pharmaceuticals, and bioorthogonal chemistry. Organic azides share a commonplace in industrial ventures as synthetic precursors for triazole/tetrazole-containing compounds and decorate the antiretroviral drug, Zidovudine, used to treat HIV/AIDS. The importance of the azido group in the chemical biology space is further underscored with the bioorthogonal alkyne-azide cycloaddition click reaction that has allowed selective imaging and studies of azide/alkyne labelled biomolecules, such as glycans, lipids, proteins, and nucleic acids. However, the prevalence of the azido group in synthetic molecules and its significance in chemical biology is contrasted by the lack of biosynthetic tools for azide construction. In this present work, we uncover a promiscuous N-N bond forming enzyme and employ a bioretrosynthetic approach to enzymatically synthesize various organic azides. Through structural-based characterization and site-directed mutagenesis, we further propose a plausible enzymatic pathway for azidation that sets the stage for future biocatalytic applications and biosynthetic pathway engineering.

Presenting Author

**Antonio Del Rio Flores**

University of California, Berkeley

Author



Wenjun Zhang
UC Berkeley

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