Cluster Preface: Biocatalysis

Todd K. Hyster*

Department of Chemistry, Princeton University, Frick Chemical Laboratory Princeton, NJ 08544
jthyster@princeton.edu

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Todd Hyster is a native of Minnesota and obtained his BS in chemistry from the University of Minnesota – Twin Cities in 2008. He received his PhD from Colorado State University in 2013, working in the labs of Tomislav Rovis. He then went on to be a NIH postdoctoral fellow in the labs of Frances Arnold at Caltech. Since the fall of 2015, he has been an assistant professor in the chemistry department at Princeton University.

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Abstract Enzymes are valuable catalysts in chemical synthesis because they offer levels of efficiency and product selectivity that surpass what can be achieved using traditional catalytic strategies. This Cluster highlights advances in this important field, highlighting different ways in which biocatalysis can be used in organic chemistry.

Key words biocatalysis, catalysis, enzyme, asymmetric catalysis, carbene transfer, cycloaddition, cascade reactions, photochemistry

The use of enzymes as catalysts for chemical synthesis has witnessed remarkable growth in the last decade. As academic and industrial researchers continue to utilize these catalysts in new and fascinating ways, biocatalysts are becoming essential tools for modern synthetic organic chemists.[1] In this issue, we highlight some important work in this field, with contributions from groups that view this area from unique perspectives.

From upstate New York, Fasan and co-workers demonstrate that evolved myoglobin variants can catalyze carbene insertions into aliphatic N–H bonds.[2] The enzyme is able to control the chemoselectivity of the transformation, affording only product from a single N–H bond insertion. This work highlights the ability of metalloproteins to function as catalysts for non-natural reactions and underscores the opportunities for enzymes to address selectivity challenges that would be hard to overcome using small molecule catalysts.

Narayan and co-workers review examples where biocatalytic transformations are run in sequence with traditional organic reactions.[3] This includes examples from their group where nonheme iron dioxygenases are used to prepare *ortho*-quinone methides *in situ* that can react with alkenes and nucleophiles to provide substituted phenols and ethers.

Berkowitz and co-workers share their work conducting Hammett linear free energy relationship studies on a substrate promiscuous ketoreductase discovered by their lab.[4] They find that the rate-determining step is dependent on the electronics of the substrate, with hydride transfer from NADPH being rate determining with β-keto esters and aldehydes, and acetal dehydration determining the rate with trifluoromethyl ketones.

Finally, Hyster highlights his groups recent developments in photoenzymatic catalysis with substrate promiscuous oxidoreductases.[5] This work demonstrates that visible light irradiation is a viable mechanism for achieving new enzyme functions.

This Cluster serves as our first foray into this very exciting and impactful area of synthetic chemistry. As biocatalysis continues to grow in the coming years, we anticipate it will cement itself as a vital tool for modern chemical synthesis. This is an area where groups from across the world are making important advances and we are excited to see where it goes in the years to come.

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