Biocompatible Chemistry: Interfacing Non-Enzymatic Reactions With Microbial Metabolism

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Chemical modifications of small molecule metabolites occur continuously in every organism and play a fundamental role in essentially all biological processes, from the construction of the building blocks for genetic information storage and cellular enzymatic machinery to the continual processing of nutrients that sustains life. Although these reactions have been thoroughly investigated from an observational standpoint, there have been relatively few attempts to alter biological chemistry using tools and approaches from synthetic organic chemistry. My lab is currently developing biocompatible reactions: non-enzymatic chemical transformations that can be used to manipulate the structures of small molecules in the presence of living organisms, altering both metabolite architectures and biological functions. We have shown that biocompatible catalysts can utilize microbial metabolites directly for synthetic chemistry. We have discovered a palladium catalyst that can utilize microbially generated hydrogen gas in alkene hydrogenations. We have also identified an iron catalyst that can perform cyclopropanation reactions using microbially synthesized styrene. In both cases we could apply these reactions for preparative scale chemical synthesis. Simultaneously, we have also demonstrated the feasibility of using non-enzymatic chemistry to control bacterial growth. We have shown that biocompatible ruthenium and iron catalysts can promote chemical reactions that rescue the growth of auxotrophic microorganisms, supplying key nutrients required to support life and rendering growth of the organism dependent on the success of a non-biological transformation. The success of our work lays the foundation for further applications of biocompatible chemistry in synthetic chemistry, synthetic biology, and medicine.