Nature performs challenging synthetic transformations using powerful enzymes. These enzymes are frequently found in the biosynthetic pathways of natural products, many of which have served as inspirations for generations of synthetic chemists over the last fifty years. With recent advances in our abilities to manipulate the biosynthetic pathways, many powerful enzymes have been revealed and characterized. In this talk, I will present a selection of recent work in the identification, characterization and engineering of several enzymes that catalyze difficult transformations and generate structural complexity in natural product isolated from fungi. Examples include multifunctional P450s, new C-C bond forming enzymes and the emerging family of pericyclases. Interesting biological activities associated with newly discovered fungal natural products will also be discussed.