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**Title:** STUDIES OF NON-HEME IRON ENZYME CATALYZED C-C and C-N BOND FORMING REACTIONS

**Abstract:** Members belonging to non-heme iron and 2-oxoglutarate (Fe/2OG) dependent enzymes are characterized by a cupin-fold structural feature and the use of a potent iron-oxo species to initiate the reaction. Fe/2OG enzymes are known to catalyze a wide variety of oxidative transformations including hydroxylation, halogenation, etc. To date, an overwhelming number of genes (> 160,000) present in sequenced genomes are annotated as Fe/2OG enzymes. On the other hand, only a few hundred are characterized. It remains a challenging task to predict the function of an Fe/2OG enzyme. We applied Sequence Similarity Networks and Genome Neighborhood Tool to search for enzymes that can catalyze synthetically challenging reactions, i.e. C-C and C-N bond formations. Moreover, we carried out biochemical and biophysical studies of these enzymes to reveal the plausible reaction mechanisms and factors used to dictate the reaction outcomes. While an Fe(IV)-oxo is deployed as a common intermediate to initiate the hydrogen atom (H•) abstraction, reaction outcome are diverged to aziridination, cyclopropanation and isonitrile formaUon. Following H• abstraction, a preinstalled group, e.g. a tertiary carbon center, a nitronate and an hetero-atom, furnishes stereo- and regio-selective C-N and C-C bond formations. Using this approach to identify enzymes with targeted function and to prepare non-proteinogenic amino acids are currently ongoing.