Systematic Investigation of C-H Oxidation Systems

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Scientists have been trying to mimic the reactivity and selectivity of nature's heme and non- heme enzymes for decades. Structural mimics of Cytochrome P450 enzymes like Fe-and Mn-porphyrin catalysts have demonstrated the ability to form high- valent metal oxidants, however both the reactivity and selectivity of these catalysts have been very poor. Classic mimics such as Barton's "Gif" and "GoAgg" systems were hypothesized to be mechanistically analogous to non-heme iron enzymes, however there is overwhelming evidence that these systems involve hydroxyl radicals or "Fenton" chemistry. Interestingly, our PDP–based platform (which is not structurally related to heme or non-heme enzymes) is the sole system that shows comparable reactivity and selectivity to said enzymes. Herein, we report a systematic approach aimed to target subtle and underappreciated mechanistic differences between these important systems. To this point, investigation of stereoretention for epoxidation of (Z)-olefins and hydroxylation of enantiopure tertiary C-H bonds have demonstrated differences in rate of rebound, sensitivity to molecular oxygen, and byproduct formation. In general, aerobic sensitivity and stereoretention have been inversely correlated, with our own PDP chemistry demonstrating the highest degree of stereoretention and lowest degree of aerobic sensitivity. In contrast, the other systems have demonstrated significant (Groves' porphyrin mimics) or complete (Barton's Gif/GoAgg chemistry) erosion of stereochemistry, with significant sensitivity to molecular oxygen.