Carboxylic Acid-Directed C—H Oxidations and Desaturations using a Non-heme Iron Catalyst and H_2O_2

Marinus A. Bigi and M. Christina White

Non-heme iron enzymes are a class of oxygen-activating metalloenzymes that catalyze a variety of remarkable C—H oxidations, including hydroxylation, desaturation, and halogenation. The non-heme iron model complex Fe(PDP) **1** has been reported to catalyze predictably site-selective C—H oxidations of 2° and 3° C—H bonds when using H_2O_2 as terminal oxidant. Interestingly, preliminary evidence suggested that carboxylic acids could function as directing groups. Herein, we demonstrate, through a survey of steric, electronic, and stereoelectronic effects, that carboxylic acids render the C—H oxidation intramolecular by acting as ligands for Fe(PDP). Furthermore, oxidation of carboxylic acid-containing substrates leads to the unexpected observation of 'double oxidation' products featuring two adjacent sites of formal C—H oxidation. Mechanistic analysis suggests that these products arise from oxidation of *in situ* generated olefins, and that these olefins, in turn, arise from a short-lived carbon-centered radical. Based on our analysis, non-heme iron complexes are demonstrated for the first time to exhibit mixed oxygenase/desaturase activity on unactivated, aliphatic C—H bonds.