Reactions of the Peroxo Intermediate of Soluble Methane Monooxygenase Hydroxylase with Ether Substrates

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There is growing interest in identifying multiple oxidizing species in metalloenzyme-catalyzed reactions, particularly the role of (hydro)peroxo- versus oxo-intermediates in substrate oxidations. Soluble methane monooxygenase (sMMO), which uses a carboxylate-bridged diiron center and dioxygen to catalyze the conversion of methane to methanol, provides a valuable system for studying the reactivity of multiple oxidants. Whereas previous studies revealed that a di(μ-oxo)diiron(IV) intermediate termed Q is responsible for the catalytic activity with methane, preliminary investigations demonstrated that the peroxodiiron(III) intermediate (H_{peroxo}), which precedes Q formation in the catalytic cycle, will epoxidize propylene. We have therefore undertaken a more extensive investigation of the reactivity of H_{peroxo} with hydrocarbon substrates. In particular, the kinetics of single-turnover reactions of H_{peroxo} and Q with ethyl vinyl ether and diethyl ether were monitored by single- and double-mixing stopped-flow optical spectroscopy. For both substrates, the rate constants for reaction with H_{peroxo} are significantly greater than for Q. An analytical model that explains the observed kinetics will be presented, and evidence that H_{peroxo} is a more electrophilic oxidant than Q will be described. The data suggest that H_{peroxo} reacts via two-electron transfer mechanisms and that Q reacts by single-electron transfer steps. Mechanisms for the reactions of both intermediates will be discussed. This work was supported by grants from the NIGMS and NCI.