

## Cold Iron: Trapping an Intermediate in Hydroxyethylphosphonate Dioxygenase Catalysis

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Hydroxyethylphosphonate dioxygenase (HEPD) is a non-heme iron enzyme that catalyzes the O<sub>2</sub>-dependent carbon-carbon scission of 2-hydroxyethylphosphonate (2-HEP) to hydroxymethylphosphonate (HMP) and formate in phosphinothricin (PT) biosynthesis. Nature often uses O<sub>2</sub> to cleave C-C bonds that are activated by a proximal group (such as vicinal diols or alkenes); by contrast, the *sp*<sup>3</sup>-*sp*<sup>3</sup> C-C bond in 2-HEP is relatively inert. Though the initial studies of this unusual reaction led to the hypothesis that one of two mechanistic pathways was operative, subsequent experiments led to the conclusion that neither route was active.

Since then, myriad approaches have been used to interrogate the mechanism of HEPD catalysis. Chief among these techniques has been the use of deuterated substrates that have enabled the trapping and direct characterization of a reactive Fe(IV) intermediate in the catalytic cycle. This unanticipated iron-oxo species has been supported by a number of different lines of evidence and has spurred a new mechanistic hypothesis for HEPD.

