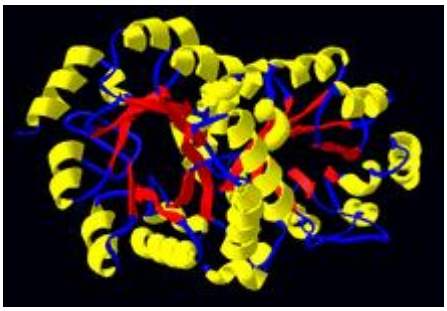
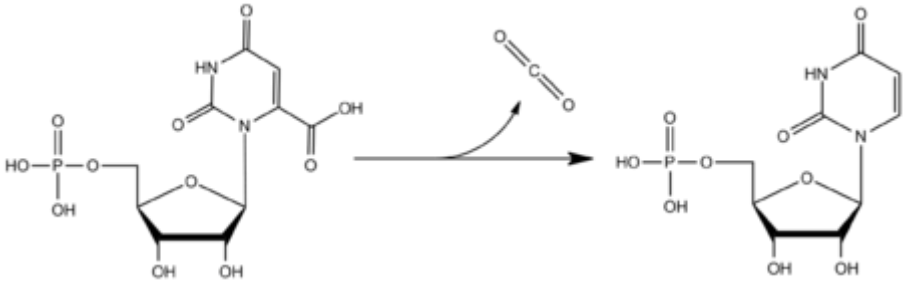
Orotidine 5'-phosphate decarboxylase



E. coli OMP decarboxylase.

Orotidine 5'-phosphate decarboxylase (OMP decarboxylase) or **orotidylate decarboxylase** is an enzyme involved in pyrimidine biosynthesis. It catalyzes the decarboxylation of orotidine monophosphate (OMP) to form uridine monophosphate (UMP). The function of this enzyme is essential to the de novo biosynthesis of the pyrimidine nucleotides uridine triphosphate, cytidine triphosphate, and thymidine triphosphate.



Schematic of reaction catalyzed by OMP decarboxylase

- **OMP decarboxylase is known for being an extraordinarily efficient catalyst capable of accelerating the uncatalyzed reaction rate by a factor of 10^{17}. To put this in perspective, a reaction that would take *78 million years* in the absence of enzyme takes *18 milliseconds* when it is enzyme catalyzed.**

This extreme enzymatic efficiency is especially interesting because OMP decarboxylases uses no cofactor and contains no metal sites or prosthetic groups. The catalysis relies on a handful of charged amino acid residues positioned within the active site of the enzyme.

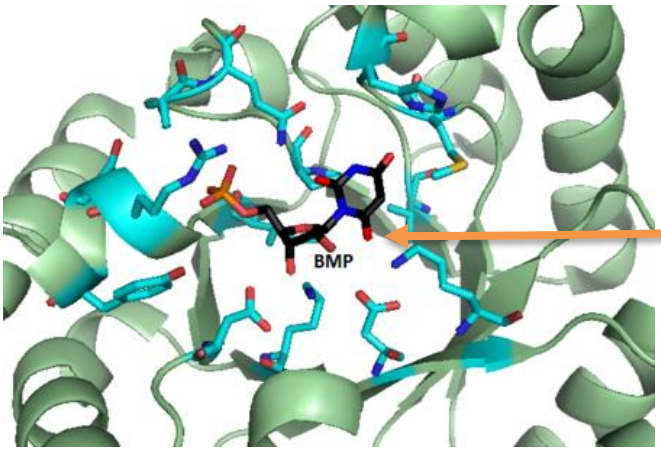
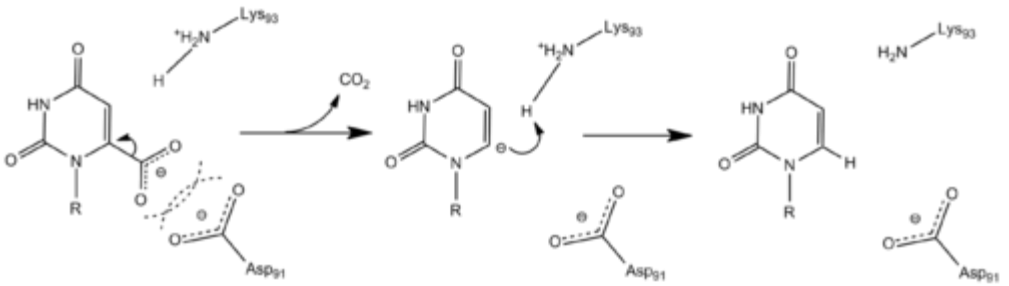


Image representing the structure of the active site of OMP decarboxylase when bound to the inhibitor BMP. Note the Lys and Asp residues surrounding the 6-hydroxyl of the substrate.

The exact mechanism by which OMP decarboxylase catalyzes its reaction has been a subject of rigorous scientific investigation. The driving force for the loss of the carboxyl linked to the C6 of the pyrimidine ring comes from the close proximity of an aspartate residue carboxyl group in the enzyme's active site, which destabilizes the ground state relative to the transition state of the uncatalyzed reaction. There have been multiple hypotheses about what form the transition state takes before protonation of the C6 carbon occurs to yield the final product. Many studies investigated the binding of a potent inhibitor of OMP decarboxylase, 6-hydroxy uridine monophosphate (BMP, a barbituric acid derivative), within the active site, to identify which essential amino acid residues are directly involved with stabilization of the transition state.

Current consensus suggests that the mechanism proceeds through a stabilized carbanion at the C6 after loss of carbon dioxide. This mechanism was suggested from studies investigating kinetic isotope effects in conjunction with competitive inhibition and active site mutagenesis. In this mechanism the short-lived carbanion species is stabilized by a nearby lysine residue, before it is quenched by a proton.



The carbanion is likely stabilized by the nearby protonated lysine residue. The Lys93 and Asp91 residue numbering corresponds to the sequence for OMP decarboxylase from Saccaromyces cerevisiae.