

The role of substrate hydrogen bonding in the non-heme iron enzyme EgtB.

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Ergothioneine is an important cellular antioxidant that occurs in many bacteria, most fungi and also in human tissue.^{1,2} The central step in ergothioneine biosynthesis is catalyzed by the non-heme iron enzyme EgtB. This enzyme mediates oxygen dependent sulfur – carbon bond formation between cysteine or γ -glutamyl cysteine and trimethyl histidine. In the active site of EgtB the two substrates are linked through a hydrogen bond between their amino acid moieties.³ Due to geometric constraints this interaction must break in the course of the reaction. To elucidate the precise sequence of elementary steps during EgtB catalysis we examined the contributions of this hydrogen bond in substrate binding and transition state stabilization using substrate analogs and kinetic analysis.

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