

Catalytic Mechanism of Quinolone Biosynthesis in Dioxygenase AsqJ

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The Fe(II)/ α -ketoglutarate-dependent dioxygenase AsqJ from *Aspergillus nidulans* is an outstanding, multifunctional enzyme. It stereoselectively catalyzes both a ferryl-induced desaturation reaction and epoxidation of quinolone alkaloids, important natural products with antibacterial and antitumor activities. We investigate here the mechanistic concepts of this unique dioxygenase using a combination of quantum chemical QM and QM/MM calculations, X-ray crystallography, and HPLC/MS analysis. Our reaction barriers for the various stages of the reaction cycle are thermodynamically and kinetically feasible, and the calculations show that intrinsic strain of the substrate is important for catalysis. We further engineer AsqJ *in silico* and *in vitro* enabling catalysis of different quinolone substrates.