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Crystal Structure of Lysine 5,6-aminomutase Reveals a Unique Locking Mechanism Preventing Radical Damage in the Absence of Substrate. C. L. Drennan, F. Berkovitch, E. Behshad, K. H. Tang, E. A. Enns, P.A. Frey, Dept. of Chemistry, Massachusetts Inst. of Technology, Cambridge, MA 02139; Dept. of Biochemistry, Univ. of Wisconsin, Madison, WI 53726.

Lysine 5,6-aminomutase is an adenosylcobalamin and pyridoxal-5'-phosphate-dependent enzyme that catalyzes a 1,2 rearrangement of the terminal amino group of DL-lysine and of L- β -lysine. We have solved an X-ray structure of a substrate-free form of Lysine-5,6-aminomutase from *Clostridium sticklandii*. In this structure, a Rossmann-like domain covalently binds pyridoxal-5'-phosphate via lysine 144 and positions it into the putative active site of a neighboring TIM barrel domain, while simultaneously positioning the other cofactor, adenosylcobalamin, $\sim 25\text{\AA}$ from the active site. In this new mode of pyridoxal-5'-phosphate binding, the cofactor acts as an anchor, tethering the separate polypeptide chain of the Rossmann-like domain to the TIM barrel domain. Upon substrate binding and transaldimination of the lysine144 linkage, the Rossmann domain would be free to rotate and bring adenosylcobalamin, pyridoxal-5'-phosphate, and substrate into proximity. Thus, the structure embodies a novel locking mechanism to keep the adenosylcobalamin out of the active site and prevent radical generation in the absence of substrate.