The Chemical Evolution of a Nitrogenase Model, XXIII. The Nature of the Active Site and the Role of Homocitric Acid in MoFe-Nitrogenase

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The iron-molybdenum cofactor (FeMo-co) of bacterial nitrogenase is a heterometallic cluster of composition MoFe₇S₉ that is attached to the apoprotein by a coordinative Mo-N bond to the imidazole group of his442, and by a Fe-S bond to cys275. The molybdenum atom of FeMo-co in the enzyme in addition is coordinated to one molecule of homocitrate (hc), which is required for maximal N₂ reducing activity. The molybdenum atom in the enzyme-bound FeMo-co thus is hexacoordinated and cannot react with substrates unless free coordination sites are made available. It is proposed that the reactions of the substrates of nitrogenase occur at a molybdenum active site consisting of a mononuclear molybdenum homocitrate complex attached to his442 of the apoprotein that in the functional enzyme is generated from FeMo-co by a reversible, redox-linked dissociation of the Fe₇S₉-cys cluster. Studies with catalytic model systems consisting of complexes of molybdenum with imidazole and hydroxo-carboxylate ligands support this proposal and provide a rationale for the specific activating effect of homocitrate in nitrogenase.