

Preface to Volume 6

Metal-Carbon Bonds in Enzymes and Cofactors

This is the 6th volume within the *MILS* series; together with the 44 volumes published in our former series *Metal Ions in Biological Systems* this sums up to in total 50 books. This event is celebrated with a comprehensive Author Index, given at the end of this book. It encompasses the names of all colleagues who contributed to these 44 *MIBS* and 6 *MILS* volumes. All these authors deserve our special thanks; without their excellent contributions the two series could not have been successful.

The present Volume 6 is devoted to naturally occurring metal-carbon bonds, a topic recently obtaining (again) significant momentum, largely – but not only – due to new insights gained with hydrogenases. The field started out about 50 years ago when coenzyme B_{12} was identified as organometallic derivative of vitamin B_{12} . This moved the cobalt-carbon bond into the center of interest and consequently, the first two chapters of this book are devoted to the organometallic chemistry of B_{12} coenzymes and to the biochemistry of cobalamin- and corrinoïd-dependent enzymes. B_{12} coenzymes are required in the metabolism of a broad range of organisms including humans; however, only microorganisms have the ability to biosynthesize B_{12} and other natural corrinoïds. This fact alone, together with new metabolic insights (e.g., riboswitches), guarantees a continued fascination – not only for the B_{12} community.

Related to Co-corrin, the Ni-porphinoid unit (F_{430}) is the prosthetic group of methyl-coenzyme M reductase. This enzyme, the topic of Chapter 3, catalyzes the methane-forming step in methanogenic archaea and most

probably also the methane-oxidizing step in methanotrophic archaea. Chapter 4 deals with acetyl-coenzyme A synthases/carbon monoxide dehydrogenases, *i.e.*, bifunctional nickel-containing enzymes, which catalyze the synthesis of acetyl-CoA and the reversible reduction of CO_2 to CO in anaerobic, mostly thermophilic, organisms, able to grow chemiautotrophically on simple inorganic compounds like CO_2 . Ni-C bonds with methyl, acetyl, carbonyl, and carboxylate groups are evidenced.

[NiFe]-, [FeFe]-, and [Fe]-hydrogenases are detailed in the next three chapters. These enzymes, present in many microorganisms, catalyze the oxidation of molecular hydrogen or the reduction of protons. All of them have a $\text{Fe}(\text{CO})_x$ unit in their active site. Iron-cyanide units occur in [NiFe]- and [FeFe]-hydrogenases. However, despite the indicated similarities they clearly have independent evolutionary origins. The participation of the commonly considered toxic ligands CO and CN^- in the active sites of hydrogenases is still a surprise to many; yet, exactly their occurrence incites a great interest in physical chemists as well as evolutionary biologists.

The dual role of heme as cofactor and substrate in the biosynthesis of carbon monoxide is the topic of Chapter 8. Carbon monoxide is a ubiquitous molecule in the atmosphere but it is also produced in mammalian, plastidic, and bacterial cells as a byproduct in the catalytic cycle of heme degradation as catalyzed by the enzyme heme oxygenase. Most fascinating is the fact that the biological role of CO spans the range from toxic to cytoprotective, depending on its concentration. CO generated by heme oxygenase is now known to function in several important physiological processes, including vasodilation, apoptosis, inflammation, and possibly neurotransmission.

The relevance of the copper-carbon bond in biological inorganic chemistry will probably not easily come to the mind of most biochemical and inorganic researchers. However, there is a vast amount of literature, cunningly presented in Chapter 9. CO as well as CN^- have proven very useful in obtaining insights into the active site structures and mechanisms of copper proteins. Naturally, in these instances both ligands are inhibitors and used as probes. However, there is also the recently described copper-carbon unit present in a carbon monoxide dehydrogenase, which contains a novel molybdenum-copper catalytic site, or the copper(I)-arene unit, which was evidenced in a bacterial copper chaperone. Apparently also a plant receptor site (ETR1) utilizes Cu(I) to sense the growth hormone ethylene.

Chapter 10 focuses on the interaction of CN^- with enzymes containing vanadium, manganese, non-heme iron, and zinc, and the inhibiting properties of this ligand, allowing its use as a probe. The reaction mechanism of the molybdenum hydroxylase xanthine oxidoreductase is revisited in Chapter 11; previously a molybdenum-carbon bond was postulated but now proof is presented against its formation. The terminating Chapter 12 reviews

briefly the most popular computational approaches employed in theoretical studies of bioorganometallic species by providing detailed examples.

Taken together, *MILS-6* summarizes our knowledge on *Metal-Carbon Bonds in Enzymes and Cofactors*; i.e., it emphasizes the role of metal-carbon bonds for life as well as research. However, there are many metal-carbon bonds which occur in the environment in compounds like alkyl-arsenicals or -mercurials and in lead- or tinorganyls, etc., most of them known as being toxic. Consequently, the next volume (*MILS-7*) will be devoted to *Organometallics in Environment and Toxicology*.

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