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Metal–Dioxygen Complexes: A Perspective

In the usual course of events, new molecules have been found first in the inorganic and organic fields, and the knowledge accumulated has then been used to unravel the molecular structure of biological substances. The reverse occurred with metal–dioxygen complexes. Hemoglobin was crystallized in the 1840s, and its dioxygen stoichiometry and equilibria were thoroughly elucidated by the beginning of this century. Correct corresponding information for the non-heme dioxygen carriers, hemerythrin and hemocyanin, was more elusive but definitively established about 40 years ago. Shortly thereafter, the molecular structures of myoglobin and hemoglobin were determined from X-ray diffraction, while molecular structural details have been revealed more recently for hemerythrin and hemocyanin. The general structural features of all three types of dioxygen-carrying proteins, including their dioxygen binding sites, have now been largely determined.

These discoveries provided an irresistible challenge to inorganic and organic chemists, who have searched for synthetic structural and functional analogues of these biological dioxygen carriers. This search, plus the intrinsic chemical interest in understanding metal–dioxygen interactions, has led to the creation of a host of novel substances containing transition metals that bind to and/or react with dioxygen. While some of these substances may find use as materials or as industrial catalysts, the collection of articles in this thematic issue clearly reflects the compulsion to understand the active sites of biological dioxygen carriers and, more recently, the closely related biological dioxygen activators. Thus, the articles include metal complexes of dioxygen, superoxides, and peroxides, and while focusing on characterization of stable complexes, also inevitably include dioxygen activation by metal complexes. Earlier compilations by L. Vaska (*Acc. Chem. Res.* **1976**, *9*, 175) and by M. H. Gubelmann and A. F. Williams (*Struct. Bonding* (*Berlin*) **1983**, *55*, 2) and *Oxygen Complexes and Oxygen Activation by Transition Metal Complexes* (Martell, A. E., Sawyer, D. T., Eds.; Plenum Press: New York, 1988) provide a useful background and historical perspective to the following 12 articles in this thematic issue.

Peroxo complexes of chromium, molybdenum, and tungsten are among the earliest known and best characterized; these are collected and discussed by Dickman and Pope. Busch and Alcock discuss dioxygen binding and autooxidation in non-heme macrocyclic "lacunar" complexes of iron, cobalt, and nickel. Butler, Clague, and Meister discuss vanadium–peroxo complexes, which have recently been shown to have biological as well as synthetic usefulness. Bytheway and Hall discuss theoretical calculations used to understand the electronic nature of metal–dioxygen interactions in both heme and non-heme systems. Momenteau and Reed present a comprehensive and insightful summary of synthetic heme dioxygen carriers, which provided the first successful modeling of a biological dioxygen carrier. Springer, Sligar, Olson, and Phillips discuss the factors affecting recognition of small molecules by the active site of myoglobin, including application of one of the most powerful new tools available to the protein chemists, namely, site-directed mutagenesis. The most recent structural information about hemerythrin and hemocyanin is summarized by Stenkamp and by Magnus, Ton-That, and Carpenter, respectively, the crystallographers who are largely responsible for recent progress on the structures of these proteins. Kitajima and Moro-oka provide a thorough summary of copper–dioxygen complexes, an area in which great progress has been made in the past few years, including a rendition of an accurate structural model for the dicopper–dioxygen adduct in hemocyanin. A similarly comprehensive summary is provided by Feig and Lippard for reactions of non-heme iron(II) complexes with dioxygen, including proteins which activate as well as bind dioxygen. Pecoraro, Baldwin, and Gelasco survey the recent flurry of activity in the reactions of manganese complexes and clusters with dioxygen, superoxide, and peroxide. Solomon, Tuczek, Root, and Brown discuss in detail the interplay between spectroscopy and theory which has led to a clearer understanding of the bonding in dinuclear iron–, copper, and cobalt–dioxygen complexes and in non-heme proteins.

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These articles illustrate that a detailed understanding of and the ability to control dioxygen binding and dioxygen activation by metal complexes remains in general an elusive goal, even though much spectroscopic and structural information has been gathered about metal–dioxygen complexes. Dioxygen activation by metal complexes and clusters is likely to be one of the most active areas of future research. However, given the similarities in metalloproteins which reversibly bind dioxygen to those that activate dioxygen, we expect that an understanding of one will not be achieved without the other in either biological or synthetic systems. We hope that the collection of articles in this issue provides both a reference frame and stimulus to scientists in the study of metal–dioxygen interactions.

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