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Introduction: Nitric Oxide Chemistry

Nitric oxide is among the simplest of molecules, and its structure and reaction chemistry has been the subject of study by chemists for many years. Despite the apparent wealth of knowledge on NO, the recent two decades have revealed a new and unexpected role for NO as a key physiological regulator. This new role for NO has reinvigorated research into the fundamental chemistry of this simple molecule, much to the delight of chemists, and led *Science* magazine to designate NO as Molecule of the Year in 1992 (Koshland, D. E., Jr. *Science* **1992**, *258*, 1861). Investigative efforts to decipher the biological role of NO led many researchers to revisit the characteristic chemistry of metal−NO compounds. The inorganic chemistry of NO has a long and rich history; the general subject area of metal−NO compounds was covered comprehensively in a monograph published in 1992 (Richter-Addo, G. B.; Legzdins, P. *Metal Nitrosyls*; Oxford University Press: New York, 1992). Many important review articles on nitric oxide chemistry exist, and these previously published works provide a context within which the new role of NO as a physiologically important molecule can be understood. A select compilation of this seminal work is given at the end of this Introduction. The goal of this thematic issue is to illustrate the diverse aspects of NO chemistry in a modern context in which the role of NO as a physiological signal and metabolic intermediate is paramount. We have attempted to cover timely and important areas of NO chemistry, from physical and computational studies to the biological role in living systems, and we are grateful to the contributing authors for their comprehensive and up-to-date reviews on a broad range of subjects.

The first review is by Coppens, Novozhilova, and Kovalevsky, and it deals with the discovery of photoinduced *linkage isomers of transition-metal nitrosyl complexes*. The authors describe the characterization of these NO linkage isomers by spectroscopic, solid-state X-ray crystallographic, and computational methods. Extensions to the observation of NO linkage isomers in iron nitrosyl porphyrins is discussed, as is its relevance to heme−NO chemistry. The authors also summarize the observation of linkage isomers of other ligands such as dinitrogen, nitrogen dioxide, and sulfur dioxide.

Andrews and Citra examine the fundamental *reactions between NO and transition-metal atoms* using matrix isolation techniques. They review the literature dealing with the vibrational spectroscopy and electronic structures of simple transition-metal nitrosyls and their nitride-oxide products. Mason, Larkworthy, and Moore detail the theory and applications of *nitrogen NMR spectroscopy* for the characterization of metal nitrosyls, and they provide justification for the increased use of this technique for the study of the structures and reactions of metal−NO compounds.

Hayton, Legzdins, and Sharp describe the inorganic *chemistry of metal−NO complexes* and review the coordination and organometallic chemistry of metal nitrosyls including the various classes of chemical reactions displayed by the NO ligands in these complexes. Ford and Lorkovic present a discussion of the *kinetics and mechanisms of the reactions of NO* with transition-metal complexes. They also examine the kinetics and mechanisms of the reactions of metal−NO compounds in aqueous and nonaqueous solvents and relate them to the heme-based reactivity of the bound NO group. Richter-Addo and co-workers review *the inorganic chemistry of organic nitroso compounds*. They examine the different kinds of reactions that *N*-nitroso, *C*-nitroso, *O*-nitroso, and *S*-nitroso compounds undergo with metal complexes and heme and relate these transformations to the overall observed biological chemistry of NO.

Much of the understanding of metal−NO interactions has come from detailed examination of the solid-state X-ray crystal structures of various metal−NO and related complexes. Wyllie and Scheidt discuss the *solid-state structures of metalloporphyrin nitrosyl, nitrite, and nitrate derivatives* and provide a comparison between the structures of model heme complexes and relevant protein structures. Wang and co-workers review the extensive literature on the *chemistry of various classes of NO donors* and link these species with their biomedical applications. Hrabie and Keefer focus on the *chemistry of the diazeniumdiolates* and their use as NO donors.

Butler and Megson discuss the role that *non-heme iron* plays in the biological chemistry of NO, and they examine classes of compounds such as the iron−sulfur clusters, nitroprusside, and other non-heme iron complexes. Møller and Skibsted review the syntheses, structures, and chemical reactions of *myoglobin−NO derivatives*. They detail the various

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methods of MbNO preparation and their relationship to the meat-curing process. They also examine the thermodynamics of NO binding to Mb and describe ligand-exchange reactions and oxidations of the NO ligands in MbNO species.

The role of the enzyme *nitric oxide synthase (NOS)* in efficiently converting arginine to NO in biological systems is presented in two reviews. The first review by Roman, Martásek, and Masters deals with the *modulation of NOS activity*. The second review by Rosen and co-workers deals with the action of NOS on arginine to eventually produce NO: Several *chemical models for NO generation* from arginine are presented and discussed as are models for the generation of other free radicals by NOS.

Karlin and co-workers outline the relationship of metal−NO compounds to the general chemistry of *biological denitrification*. They review the NO_x-related chemistry of inorganic model complexes as models for nitrite reductase and nitric oxide reductase, and they compare and contrast these observations with the NO_x-related chemistry displayed by the metalloenzymes involved in denitrification.

Finally, Nagano and Yoshimura review the status of *imaging techniques* as applied to the detection and monitoring of biological NO. In this review, the authors compare and contrast various NO-detection methods used in the bioanalysis of NO but focus principally on the imaging techniques that utilize EPR spectroscopy and fluorometry. They also describe the recent successes in the in vivo detection of NO.

It is our hope that this thematic issue will provide an up-to-date and comprehensive account of these major areas in NO chemistry. We believe that this issue can also be used as a valuable resource for a specialized course in NO chemistry and biochemistry. Once again, we thank the contributing authors for their reviews and also acknowledge the many researchers whose work on the fundamental inorganic chemistry of NO provided the framework for the rapid advances made in the field of NO chemistry over the past decade.

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