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Preface: Forum on Redox-Active Ligands

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The oxidation state of a transition metal or any element is a central and often defining theme in inorganic chemistry. Students are trained to apply this concept to balance redox reactions or to systematize the chemistry of transition-metal compounds.[1] Straightforward procedures and ligand classification methods have been developed that appear in most textbooks.[2,3] Do the values obtained from these exercises have any physical significance? For classical Werner-type compounds such as *cis*-[$Co(NH_3)_4Cl_2$] or organometallic species such as ferrocene, the oxidation-state assignment and subsequent determination of a d^n electron configuration resulting from these methods provide convenient and portable explanations for the substitutional lability of the cobalt(II) compound or the stability of the organometallic ferrous species.

As coordination and related chemistry advances, chemists have tried to extend the utility of the oxidation formalism to predict spectroscopic and magnetic properties and to further understand reactivity. While this approach is often correct, there are instances where these rote procedures provide answers that are deceiving. Such cases were recognized in the early days of coordination chemistry, and in 1966, Jørgensen classified ligands as "innocent" and "noninnocent" in an attempt to avoid confusion. The distinction between these two classifications depended on whether the ligand allowed "the oxidation states of the central atoms to be defined".[4] As discussed by Kaim in this Forum, the term "noninnocent" ligand implies and has been taken to mean an uncertainty in oxidation state assignment.

What do we mean by uncertainty in assigning oxidation state? The answer depends on the specific compound. In many cases, the term "noninnocent" has become synonymous with situations where the formal oxidation state, the one determined by a prescribed set of rules, differs from an oxidation state that is determined by experiment. For example, consider what is known as compound I, an active oxidant in the cytochrome P-450 family of enzymes. It is an iron heme compound with oxo and thiolate ligands. The formal oxidation state of the compound is iron(V). If we were to consider the preparation of a synthetic model compound that performs the same functions, should this be the oxidation state and, more importantly, the d-electron count of the target molecule? A recent report from Green and co-workers described the spectroscopic and kinetic characterization of an oxo iron heme compound that hydroxylates the unactivated C−H bonds of lauric acid.[5] All of the data on this species support an Fe^{IV} d^4 compound with a one-electron-oxidized heme thiolate supporting ligand rather than the formal iron(V) alternative. The possibility for a "noninnocent" heme thiolate has been recognized and generally accepted for some time, but the ability to experimentally determine the correct d^n configuration and, hence, the true iron oxidation state definitively established the electronic structure.

One of the limitations of the oxidation-state formalism is the inability to account for many types of ligand-centered radicals. In returning to Jørgensen's definition, we can then ask, is the oxidation state in compound I ambiguous and, therefore, is the heme thiolate ligand noninnocent? As noted by Wieghardt,[6] the presence of ligand-centered radicals, in contrast to those in their typical closed-shell form, is what can differentiate a *formal* oxidation state of a compound from its *physical* or *spectroscopic* one. This is because the d-electron configuration of a metal complex is, in principle, an experimentally measurable quantity that we can determine the physical oxidation states of metal complexes. It is important to realize, however, that the physical oxidation state of the iron in compound I is by no means ambiguous. On the basis of the experimental data, it is certainly an Fe^{IV} d^4 species.

An important distinction arises when considering how compound I is formed. Two-electron oxidation of an Fe^{III} d^5 species gives rise to an Fe^{IV} d^4 oxo, which is an active oxidant. A second oxidation occurs at the heme thiolate ligands, demonstrating that the redox events occur at *both* the ligand and metal. A newer term, "redox-active ligand", has been coined to capture such possibilities. Oftentimes, the two descriptions "redox-active" and "noninnocent" ligands are used interchangeably in the literature. However, care must be used when using the latter because clearly defined physical oxidation states have often been established for a case where ambivalence has been implied.

Are there cases where the oxidation state of a metal complex is ambiguous despite the availability of spectroscopic data? As recognized by the Dewar−Chatt−Duncanson model[7] for olefin complexes such as $(\eta^5\text{-}C_5Me_5)_2Ti(\eta^2\text{-}CH_2{=}CH_2)$,[8] the oxidation state of metal can be either titanium(II) or titanium(IV). This is the case with most π-acid ligands found in highly covalent organometallic compounds. Are these ligands also "noninnocent"? It is precisely this situation that is well-described by Jørgensen's 1966 definition. As a consequence, many π-accepting ligands such as CO, alkynes, alkenes, and diimines are best described as "noninnocent". In fact, using such a definition, a simple ligand such as hydride could, in principle, be noninnocent. Although formalism dictates that we assign it as "H^-", spectroscopic oxidation states may reveal cases where it is more aptly described as "H^+" or "$H^\cdot$" and certainly reactivity of this type is well documented.

There is an important distinction between these two types of noninnocent ligands. Attempting this type of disambiguation challenges our notion of the chemical bond itself, a concept that has by and large avoided reevaluation since the time of Pauling's pioneering definition.[9] In 1949, Coulson and Fischer provided a complete four-state picture of the two-center, two-electron bond

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of H_2,[10] which has since been experimentally verified using the δ bond in quadruply bonded rhenium compounds as a paradigm.[11] This backdrop provides the foundation for a covalent model of the metal—ligand bond, which is at the core of ligand-field theory. For the case of a closed-shell, π-acidic ligand in a metal complex, the typical molecular orbital treatment produces an approximation where two electrons that are spin-paired occupy a single molecular orbital. This is accurately described by single-determinant wave functions, which are commonly used in modern computational methods. In cases where the orbital overlap between the metal and ligand weakens, as in the case of a stretched dihydrogen or a singlet diradical, the opposite spins become spatially separated and the electronic coupling weakens. This case, where the singlet ground state is maintained, is exemplary of a radical-type, noninnocent ligand. This bonding situation is no longer accurately described by a single-determinant wave function and relies on more sophisticated multiconfigurational quantum mechanical treatments.[12]

In certain molecules, the possibility exists for both types of noninnocent ligands and experimentally distinguishing which bonding picture best describes the electronic structure can be challenging. As recounted by Eisenberg and Gray in this *Inorganic Chemistry* Forum, the synthesis of four-coordinate, planar nickel compounds with dithiolene and later related quinone and amido phenolate based ligands was such a case. While the nickel(II) oxidation state for these compounds was widely accepted,[13] controversy arose as to whether the compounds were best described using a π-acid model[14] or ligand radicals.[13] In the more traditional π-acid case, one of the bidentate ligands is treated in its two-electron-reduced, closed-shell form, while the other is neutral. A hybrid between these two structures accounts for the experimental indistinguishability between the two ligands. The alternative posited that each chelate was, in fact, equivalent by virtue of one-electron reduction, forming ligand-centered radicals. Antiferromagnetic coupling mediated by the nickel accounted for the observed diamagnetic ground state. The ambiguity between the two models confounded chemists for quite some time because there are often not straightforward experiments to distinguish the possibilities. Only recently has a modern computational study been performed on the diiminobenzosemiquinonate version of these compounds that supports the ligand radical description with a singlet—triplet gap of approximately 3100 cm^{-1}.[15] Perhaps if the singlet—triplet gap were lower, the two states could be detected by SQUID magnetometry.

What began as a controversy over the best electronic structural description of a nickel(II) coordination compound has blossomed into a vibrant, if not sometimes controversial, field of inorganic chemistry. No longer is this area of inorganic chemistry merely concerned with trying to determine oxidation-state assignments, but rather it has grown into an interesting design concept for molecules whereby redox events can occur at ligands in concert with or independent from the metal center. This allows chemists to now exploit redox-active ligands and apply these molecules to some of the most challenging problems facing our discipline today. Whether it is new catalysts for organic transformations, functional model compounds of metalloenzymes, bistable materials, or efficient molecules for energy conversion, the applications of transition-metal compounds with noninnocent ligands abound. It is therefore not surprising that there has been a renewed interest in compounds of this type. Because of this explosive increase in attention, an *Inorganic Chemistry* Forum devoted to the topic seemed timely and appropriate. Herein is a collection of manuscripts that capture both the diversity and liveliness of this area of coordination chemistry.

The increase in the popularity of redox-active metal—ligand complexes can also be traced to the improved ability of methods for electronic structure determination. The ability to obtain high-quality X-ray crystallographic data in a matter of hours has allowed routine characterization of ligand bond distortions, which are often diagnostic of redox activity. Advances in spectroscopic techniques including NMR, electron paramagnetic resonance, and Mössbauer as well as the introduction of high-energy X-ray techniques have also aided in the experimental identification of ligand-centered radicals. Perhaps the most significant advance has occurred in computational chemistry. The introduction of the broken-symmetry formalism,[16] whereby the static electron correlation of the singlet diradical state is simulated with a spin-symmetry broken single-determinant wave function, has allowed the *prediction* of metrical and spectroscopic parameters that are diagnostic of many redox-active ligands. The accuracy of these methods has reached such a high level of success that oftentimes when a discrepancy exists, the experimenter is forced to double check the measurements!

This Forum contains a blend of historical overviews, individualized accounts, and primary literature that present new data. As mentioned above, Eisenberg and Gray provide a history of the controversy and challenges in the early days of the electronic structure determination of metal dithiolene complexes. One salient feature of their account is how many of the early bonding models proposed for these compounds have withstood the scrutiny of modern computational and spectroscopic methods. Other pioneers, Kaim and Pierpont, also provide overviews of their defining contributions to the field. Kaim's manuscript presents a pedagogical survey of the various types of redox-active ligands encountered in coordination chemistry. Multinuclear complexes and various excited states are also examined. Pierpont's contribution presents an overview of the coordination chemistry and redox noninnocence in the first-row transition-metal chemistry of 1,2-diolate ligands, the oxygenated analogues of the diothiolenes. Several instructive examples of the redox series of compounds are presented along with diagnostic spectral features used to identify various aspects of the electronic structure. All of these articles are useful for learning how chemists identify and often struggle with diagnosing the presence of ligand-centered radicals.

Wieghardt is another scientist who has defined the field of ligand-centered radicals. One salient feature of his work is the development of the tools and parameters, both experimental and computational, used for identifying ligand-centered radicals. His contribution to this Forum continues in this vein and presents a comprehensive density functional theory (DFT) study analyzing the electronic structure of 2,2′-bipyridines, one of the most widely used classes of ligands in coordination chemistry. The computational results, validated with existing experimental data, provide the guiding metrics for identifying the oxidation level of a coordinated bipyridine. In its neutral form, bipyridine ($[bpy]^0$) is a very weak π acceptor, while its dianionic variant ($[bpy]^{2-}$) may act as a strong π donor. Most relevant to redox noninnocent ligands, the radical anion ($[bpy]^{\bullet -}$) is neither a π donor nor acceptor but is well-suited to form singlet diradicals by antiferromagnetic coupling with unpaired spins of an open-shell transition-metal ion. Given the ubiquity of these chelates in solar energy conversion, such fundamental insight will prove valuable in understanding the electronic structure of these important molecules.

Although some ligands, such as catecholates, have reached privileged status among redox-active ligands, new spectroscopic methods continue to evolve to establish their effect on the electronic structure of metal complexes. The Forum article by Crans and co-workers reports solid-state ^{51}V NMR spectroscopy as a tool for elucidating the redox activity of catecholates in oxovanadium compounds. Isotropic chemical shift anisotropy parameters were found to be a more sensitive probe of the orbital occupancy and electron distribution. A correlation between substitution of the catecholate ligand, the highest occupied molecular orbital (HOMO)–lowest unoccupied molecular orbital (LUMO) gap of the complex, and ultimately the ^{51}V chemical shift was established. Ideally, techniques such as these will continue to develop into routine tools in the chemistry of noninnocent ligands.

The true pioneer of the redox-active ligands has been Nature. Metalloproteins have evolved to incorporate terrestrially abundant metal ions such as iron and copper, which preferentially react via one-electron redox couples.[17] Because many important biological transformations are multielectron processes, redox-active supporting ligands have been incorporated into enzymatic active sites not only to promote the desired two- or four-electron chemistry but also to inhibit potentially deleterious radical reactions. The Forum contains two articles that highlight the role of redox-active ligands in bioinorganic-inspired coordination chemistry. Burgmayer and co-workers report the synthesis of tris(pyrazolyl)boratemolybdenum dithiolene complexes by treatment of the corresponding anionic molybdenum tetrasulfide reagent with a substituted alkyne. The electronic structures of this class of compounds are of interest to understand the structure within the catalytically active site of molybdenum enzymes that engage in two-electron chemistry and formal oxygen-atom transfer. The second bioinspired contribution is from Stack and co-workers and describes the chemistry of copper quinone complexes, which are relevant to the enzyme tyrosinase, responsible for hydroxylation of phenolate. Spectroscopic and X-ray diffraction studies are coupled with DFT calculations to correlate the geometries of various copper(II) semiquinone complexes with their magnetic and optical properties. Ideally, such an understanding will guide the design efforts for improved hydroxylation reactions.

An emerging application of redox-active ligands is imparting reactivity to otherwise inert metal–ligand multiple bonds. While similar to the approaches used for mimicking the chemistry of metalloproteins, recent studies have been extended to metals not typically found in biological systems. In the Forum, Heyduk and co-workers present an overview of their program designed to enable reactivity of early-transition-metal imido complexes by the introduction of redox-active [NON] and [NNN]-based pincer ligands. Typically, breaking early-transition-metal nitrogen bonds of imides and amides is challenging; however, the introduction of noninnocent ligands has produced rare examples of nitrene group transfer from tantalum imido complexes. This remarkable and rare reactivity is ascribed to the redox-active ligands serving as an electron reservoir. This is analogous to the role of a cofactor in biology and demonstrates that the redox potential of both the ligand and the metal must be considered and finely tuned for the development of new nitrene transfer catalysts with improved reaction scope. A second contribution with this theme is from Soper and co-workers, who describe the use of redox-active ligands to impart one-electron-type reactivity to rhenium oxo compounds. This creative use of redox-active amido phenolate ligands opens the possibility of a ligand-based one-electron reservoir that enables radical additions to the metal–oxygen bond. The work establishes design criteria for new oxidants that utilize low-barrier radical steps for selective multielectron chemistry.

In addition to dithiolenes, semiquinones, and amido phenolates, bis(imino)pyridines have emerged as an important class of redox-active ligands. These ligands, originally developed in the 1960s as modular terpyridine mimics, have received renewed interest because of their success in olefin polymerization catalysis.[18] Budzelaar and Gambarotta's Forum article presents an overview of the bonding and, hence, redox activity of bis(imino)pyridine compounds of iron, cobalt, and nickel. A review of the electronic structure of iron– and cobalt–dinitrogen compounds is presented along with an overview of ligand-induced radical chemistry and its importance in C–C coupling reactions. In addition, this contribution also presents the synthesis and structural characterization of a new and interesting bis(imino)pyridine nickel–dinitrogen complex that once again highlights the redox activity of this class of ligands. Our contribution is in the spirit of classic redox-active ligand chemistry, whereby a series of bis(imino)pyridine iron carbonyl compounds that differ by three redox states are synthesized and characterized. Structural, spectroscopic, and computational studies are presented to examine whether the redox events are metal- or ligand-based and demonstrate the cooperativity between both entities.

α-Diimine ligands are related to the bis(imino)pyridines in that they exhibit a rich noninnocent chemistry and have numerous applications in catalysis. The article by Bart and co-workers describes the utility of these ligands in actinide chemistry with the goal of enabling new multielectron transformations at uranium, an element often reticent to participate in two-electron reactions such as oxidative addition and reductive elimination. Four-coordinate, bis(chelate) uranium compounds were synthesized and structurally and spectroscopically characterized as uranium(IV) derivatives with enediamide chelates. Alkylation of one example with iodomethane resulted in C–C bond formation in the backbone of the ligand with concomitant formation of a U–I bond, demonstrating the potential advantages in reactivity by storing electrons in the chelate. More broadly, these studies indicate a new and relatively unexplored horizon for redox-active ligands with the actinides.

The Forum also contains accounts that expand the types of ligands normally considered as redox-active. The contribution from de Bruin and co-workers reviews the chemistry of a relatively new addition to the field: carbenes. While there has been a long-standing interest in the electronic structure of metal carbene complexes because of their role in olefin metathesis and cyclopropanation catalysis, radical versions of these ligands have not been widely recognized or exploited. The expansion of the established paradigms of Fischer- and Schrock-type carbenes to include carbene radicals may also broaden the scope of reactivity associated with these compounds as well as provide new mechanistic understandings of known transformations. Also in the area of new ligand designs, Hicks and co-workers report the coordination chemistry of indigo diimine ("Nindigo") ligands with a family of palladium compounds. One interesting feature of these compounds is their ability to serve as sterically and electronically tunable binucleating ligands. The presence of two fused β-diketonate-ligands is a unique architecture that, when coupled with the redox activity of the ligand class, opens an array of possibilities for exciting compounds that offer metal−metal communication.

One question that often arises in redox-active ligand chemistry is whether the radical character of the ligand can be used to promote reaction chemistry at the ligand. The uranium compounds of Bart are one such example, and the article from Grapperhouse and co-workers recounts work from his laboratory on a different type of reaction, namely, the reversible cycloaddition of alkenes to metal complexes containing metal thiyl radicals. Studies have principally focused on hexacoordinate rhenium and ruthenium compounds with phosphinobenzenethiolate ligands. Alkene addition occurs selectively across cis sulfur ligands, which have an in-phase linear combination of p orbitals that have the appropriate symmetry to interact with the HOMO of the incoming olefin. From these studies, general features to enable the addition of unsaturated organic molecules to ligand radicals have been established and may expand the scope of ligand-based rather than metal-based cycloadditions.

Over the past 5 decades, the field of redox-active ligands has emerged from an electronic structure curiosity to a vibrant and diverse field of inorganic chemistry. The current Forum captures a portion of this excitement. This collection of manuscripts shows that noninnocent ligands are not just oddities for oxidation-state assignment but rather an intriguing design element for the synthesis of both main-group and transition-metal compounds. Fully exploiting the potential of noninnocent ligands in catalysis, group-transfer chemistry, energy storage and conversion, and biological applications remains in its infancy. Witnessing the continued growth of the field and the spectacular and surprising chemistry that will likely ensue will certainly be a truly guilty pleasure.

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