DOI: 10.1002/anie.201006778

Ligands that Store and Release Electrons during Catalysis**

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cobalt · cross-coupling · homogeneous catalysis ·
ligand cooperativity · N,O ligands

Dedicated to Professor Karl Wieghardt

Numerous (organometallic) transition-metal-catalyzed transformations involve elementary steps wherein two electrons are formally transferred from or to the metal (i.e., oxidative addition and reductive elimination). Such two-electron processes are widespread in the coordination sphere of noble transition metals (Pd, Rh, Pt, etc.), which explains their dominant role in homogeneous catalysis. In contrast, most of the cheaper (first-row) transition metals undergo one-electron transformations, which can be tremendously valuable in mediating radical-type reactions, but also limits their applicability in organic reactions that require two-electron oxidative addition or reductive elimination steps. The 2010 Nobel Prize for Chemistry indeed acknowledges the catalytic value of noble transition metals (Pd in C–C bond formation), but recent developments show that ligands serving as electron reservoirs offer valuable opportunities to expand the development of organometallic catalysis with first-row transition metals.

An oxidation-state change of the metal during a reaction commonly implies a change in the number of metal d electrons. However, for complexes that bear redox-active ligands, formal oxidation states changes do not always alter the true d-electron configuration of the transition metal. The actual redox process may well occur at a ligand site rather than the metal, hence leaving the metal d-electron count unchanged. The term "ligand redox non-innocence" is generally used to underline such oxidation-state ambiguities.[1] Redox non-innocence of ligands has long been considered a spectroscopic curiosity, but over the past years the concept proved to be of crucial importance for understanding the reactivity of (synthetic models of) several metalloenzymes[2] and various synthetic open-shell organometallic compounds.[3] Generation of ligand radicals can lead to interesting ligand-centered reactivity, with the mechanism of galactose oxidase serving as an inspiration for synthetic chemists.[4] In particular, in the field of organometallic chemistry, redox-active ligands offer ample opportunities for fast and/or new transformations.

Although still dominated by stoichiometric examples, this concept is slowly but surely entering the area of catalysis and ligand redox non-innocence is clearly becoming a useful synthetic tool to enhance reactivity and steer selectivity.[5] The field is currently developing along two important and emerging research lines: 1) The use of redox non-innocence to generate reactive ligand radicals and thereby impose ligand-centred (radical) reactivity in catalysis (Figure 1, left),[6] and 2) the use of nonreactive redox-active ligands as electron reservoirs ("electron borrowing" principle) to facilitate two-electron reactivity (noble-metal character) for metals that have an intrinsic tendency to react by one-electron pathways (Figure 1, right).[7,8]

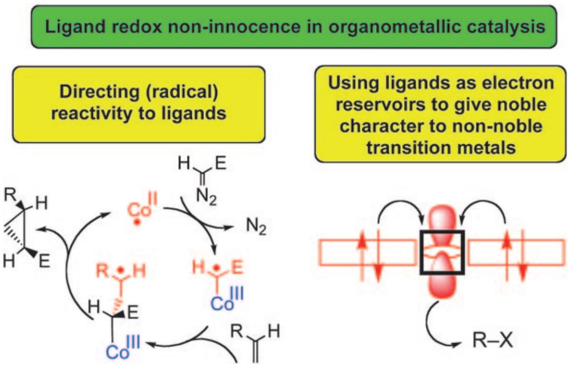

Figure 1. Complementary approaches toward use of redox-active ligands to steer and control catalytic reactions.

Chirik and co-workers recently suggested that the electron-storage capacity of the redox non-innocent pyridine-2,6-diimine (PDI)[9] can be used for selective C–C coupling steps in catalytic [2+2] cycloisomerization reactions of α,ω-dienes with iron.[7] The oxidative addition and reductive elimination processes associated with the C–C bond-forming processes are believed to involve oxidation and reduction of the ligand rather than the metal (which stays as Fe^{II} throughout the entire catalytic cycle), and thereby the redox-active PDI ligand imposes some noble character to the iron. This concept

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[**] Financial support from the University of Amsterdam (UvA), the Netherlands Organisation for Scientific Research—Chemical Sciences (NWO-CW), and the European Research Council (ERC) is acknowledged.

is highly compelling and suggests that it could well be possible to replace noble metals currently used in several organometallic catalytic reactions by cheaper and more abundant first-row transition metals (perhaps even main-group metals). Noteworthy in this respect is also the work of Abu-Omar[8a] and Heyduk,[8b,c] who showed that oxidative addition of Cl_2, Br_2, and O_2 to d^0 Zr^{IV} is possible due to the presence of reducing equivalents stored on the redox-active ligands. However, with these highly oxidizing reagents one can never fully exclude an outer-sphere ligand oxidation process (followed by halogenide or (su)peroxide coordination to the metal). Hence these examples (irrespective of their appeal) do not unequivocally demonstrate the idea that redox-active ligands can indeed provide the electrons required to allow selective metal-centered two-electron oxidative addition reactions, while this concept is of crucial importance for many of the useful synthetic transformations that are catalyzed by expensive noble transition metals (typically involving metal–C and C–C bond formation).

A recent breakthrough in the field was reported by Soper and co-workers,[10a] who provided an elegant example of metal–C bond formation by metal-centered oxidative additions without a change of the metal d-electron configuration, by virtue of electron transfer from redox-active ligands to the metal. The applied system is an unusual paramagnetic square-planar Co^{III} complex $[Co^{III}(ap^{2-})_2]^-$, which contains two redox-active amidophenolate ligands (ap^{2-}). These ligands are easily oxidized in a one-electron process to form stable iminosemiquinone radical ligands (isq^-), and thus behave as robust, nonreactive “redox non-innocent ligands” (Figure 2).

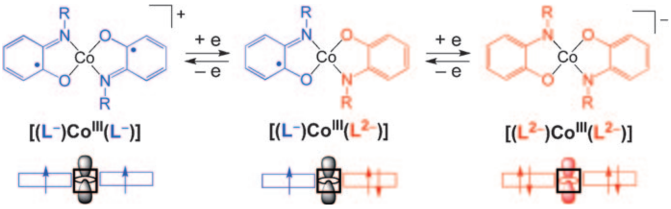

Figure 2. Redox non-innocent ap^{2-}/isq^- ligands.

The Co^{III} system adopts an unusual intermediate spin $d_{xy}^2 d_{z^2}^2 d_{xy}^1 d_{yx}^1$ electron configuration ($S=1$),[10b] wherein the doubly occupied d_{z^2} orbital must be the highest occupied molecular orbital (HOMO) of the complex, thus explaining the nucleophilic character of the metal (Figure 3). Reaction of the anionic complex with electrophilic alkyl halogenides R–X leads to formation of Co–C bonds by oxidative addition, which shows the characteristics of S_N2-type reactions (i.e., reactivity order $I > Br > Cl$ and strong influence of steric factors in R). The observed nucleophilic reactivity is atypical for d^6 Co^{III} ions, and is normally reserved for low-valent, low-spin d^8 M^I species (M = Co, Rh, Ir).

Oxidative addition at the Co^{III} center would formally lead to a Co^V species, but the actual process occurs without a change of the true oxidation state of the metal. The two electrons required to make the Co–C bond are actually obtained from the two redox-active ap^{2-} ligands, which are each oxidized by one electron to form a neutral diamagnetic Co^{III} complex with two antiferromagnetically coupled isq^- ligand radicals (Figure 3). The possible role of the spin-flip associated with the formation of the diamagnetic product is not clear, and it would be interesting to address this question in a further (computational) study, which should also provide a better understanding of the unusual electronic structure of the $[Co^{III}(R^-)(isq^-)_2]$ species. The anionic starting complex and some of the neutral oxidative addition products ($R = CH_2Cl$ and Et) were characterized by X-ray diffraction. The bond-length changes within the ligand framework clearly confirm that the actual redox processes occur at the ligands, and hence provide solid proof for the involvement of redox-active ligands as electron reservoirs to achieve two-electron reactions with cheap, readily available transition metals. Even more noteworthy is that the same system allows for C–C bond-forming reductive elimination reactions, again without a change of the metal oxidation state. Treatment of the $[Co^{III}(R^-)(isq^-)_2]$ species with organozinc reagents led to reductive C–C bond formation with regeneration of the anionic $[Co^{III}(ap^{2-})_2]^-$ complex. Together, these reactions comprise a complete, well-defined stoichiometric cycle for Co^{III}-mediated Negishi-type cross-coupling reactions. The exact mechanism of the reductive elimination step is presently not clear. Ligand-centered redox processes in C–C bond-forming reductive eliminations without a change in the metal oxidation state were also proposed by Haneline and Heyduk.[8d]

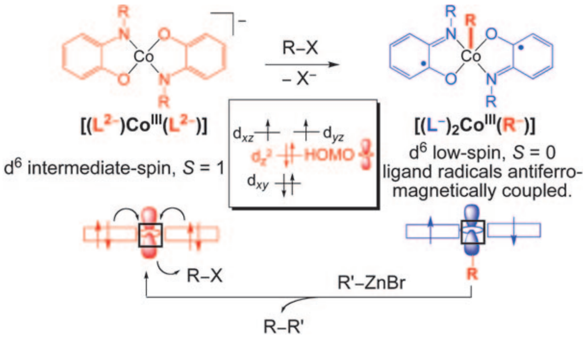

Figure 3. Ligand-centered redox processes in oxidative addition and reductive elimination without a change of the metal oxidation state.

The remarkable discoveries of Soper and co-workers can clearly expand the development of cheap catalysts based on abundant first-row transition metals. The elegance of this approach relies on the use of redox-active ligands to circumvent some of the limitations of first-row transition metals. Optimization of the stoichiometric reaction conditions may soon lead to true one-pot catalytic cross-couplings with cobalt. Whether this novel concept will turn out to be more generally applicable in organometallic catalysis is a research question to be answered in the near future.

Received: October 28, 2010

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[1] An illustrative example is the high-valent iron–oxo species in Cytochrome P450, which is formally an Fe^{V} species, but in reality the Fe^{IV}–ligand radical species $[Fe^{IV}(O)(por^{\bullet -})]$ (por^{2-} = protoporphyrinato-IX): B. Meunier, S. P. de Visser, S. Shaik, *Chem. Rev.* **2004**, *104*, 3947 – 3980.

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