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Redox Non-Innocent Ligands: Versatile New Tools to Control Catalytic Reactions

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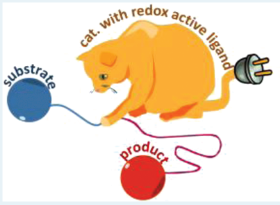

ABSTRACT: In this (tutorial overview) perspective we highlight the use of "redox non-innocent" ligands in catalysis. Two main types of reactivity in which the redox non-innocent ligand is involved can be specified: (A) The redox active ligand participates in the catalytic cycle only by accepting/donating electrons, and (B) the ligand actively participates in the formation/breaking of substrate covalent bonds. On the basis of these two types of behavior, four main application strategies of redox-active ligands in catalysis can be distinguished: The first strategy (**I**) involves oxidation/reduction of the ligand to tune the electronic properties (i.e., Lewis acidity/basicity) of the metal. In the second approach (**II**) the ligand is used as an electron reservoir. This allows multiple-electron transformations for metal complexes that are reluctant to such transformations otherwise (e.g., because the metal would need to accommodate an uncommon, high-energy oxidation state). This includes examples of (first row) transition metals that have a tendency to react via one-electron pathways, and even "oxidative addition" reactions for d^0 transition metal complexes become possible with redox active ligands as electron reservoirs. The electron-reservoir function of the ligand tolerates the metal to maintain its most common or most stable oxidation state by delivering or accepting the electron density associated with the multielectron transformation (most typically two-electron transformations such as oxidative addition/reductive elimination). The third strategy (**III**) involves the generation of reactive ligand-radicals that actively participate in the making and breaking of chemical bonds during catalysis. Cooperative substrate activation by the redox non-innocent ligand and the metal allows reactions that are difficult to achieve otherwise. The last strategy (**IV**) involves (radical-type) activation of the substrates or modification of the substrate reactivity in cases where the substrate itself acts as a redox non-innocent ligand. These four approaches are illustrated by recent literature data.

KEYWORDS: *catalysis, redox non-innocent ligand, radical, electron reservoir, Lewis acidity, electron transfer, selectivity tuning, redox active ligands*

I. INTRODUCTION

The development of highly efficient and selective catalysts is one of the major goals of research in chemistry—the science of matter and its transformations. To ensure a sustainable society, new catalysts need to be developed, and a desire for more selective and efficient methods for the preparation of organic materials has led to sustained interest in methods based on homogeneous catalysis, particularly in the development of new ligands which can be tuned to specific needs. The properties of a metal complex as a whole are the result of the interaction of the metal center and its surrounding ligands. In traditional approaches, the steric and electronic properties of the ligands are used to control the performance of the catalyst, but the ligands play a spectator role—the reactivity takes place at the metal center. Recent new approaches deviate from this concept, and make use of more reactive (actor) ligands, that can play a much more prominent role in the elementary bond activation steps in a catalytic cycle.[1,2] The central idea is that the metal and the ligand can cooperate in a synergistic manner, and their interplay facilitates the chemical process. In this light, complexes based on so-called "redox non-innocent" ligands offer interesting prospects to uncover new catalytic reactions.

Redox transformations of coordination compounds have since long drawn considerable attention in the chemical community, which is to a large extent because of (catalytic) reduction and oxidation reactions mediated by transition metal complexes. The most common ("classical") behavior of a transition complex in a redox process involves oxidation or reduction of the metal, leaving the ligand unaffected. In some cases, however, ligands can also participate in the redox process. In such cases, the ligand is referred to as being "redox non-innocent" or "redox active".[3,4] Such species have attracted substantial attention over the past decade, since they offer a unique opportunity to modify the reactivity of transition metal complexes. Four main strategies can be distinguished in this context: (i) Modification of the Lewis acidity of the metal by reduction/oxidation of the ligand, which strongly influences the substrate affinity as well as the energy profile of subsequent follow-up reactions. (ii) An "electron-reservoir" function of the redox active ligand, which allows the metal to store electrons on the ligand in elementary steps generating excessive electron density, and accept electron density from the ligands in elementary steps generating deficiencies, in all cases avoiding uncommon oxidation states of the metal. (iii) The third

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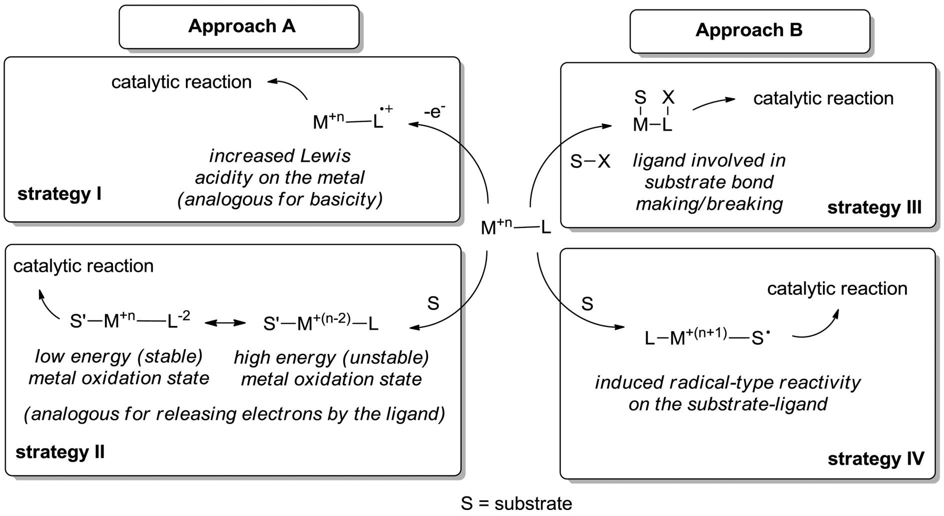


Figure 1. General representation of four main strategies of using redox non-innocent ligands in catalysis.

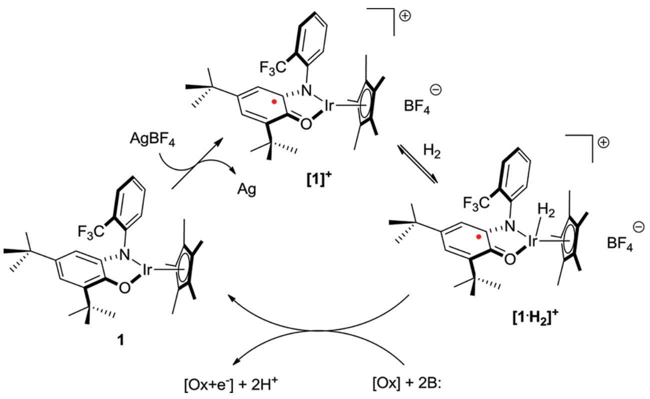
strategy involves the generation of reactive ligand-radicals that actively participate in the making and breaking of chemical bonds during catalysis. Cooperative substrate activation by the redox non-innocent ligand and the metal allows reactions that are difficult to achieve otherwise. (iv) The last strategy involves (radical-type) activation of the substrates or modification of the substrate reactivity in cases where the substrate itself acts as a redox non-innocent ligand. Speaking more generally, redox non-innocent ligands can either participate in the catalytic cycle by (A) accepting/releasing electrons (strategies **I** and **II**) or by (B) forming/breaking chemical bonds of the substrate (strategies **III** and **IV**) (Figure 1).

The general redox non-innocent behavior of ligands has been (part of) the topic of a recent Forum Issue in Inorganic Chemistry,[5] a special Issue in the European Journal of Inorganic Chemistry[6], and some other reviews.[7−10] Stoichiometric reactions at redox non-innocent ligands have been recently reviewed,[3] and a few scattered aspects of the cooperative role of redox non-innocent ligands in catalysis have also been summarized in some recent reviews.[7,11−15] Here we will present a tutorial overview of the above-mentioned four application strategies in catalytic processes. The idea of this perspective is not to present a full comprehensive review on the topic of redox noninnocence; we rather present some recent and illustrative examples that show the power of the above four concepts in catalysis.

II. REDOX NON-INNOCENT LIGANDS USED TO MODIFY THE LEWIS ACID−BASE PROPERTIES OF THE METAL

A change of the electronic properties of the ligand can have a strong influence on the reactivity and catalytic behavior of the complex. Such modifications are typically achieved by introducing electron-withdrawing or donating substituents at the ligand, which often requires laborious synthesis, repeating (and sometimes revising) the whole synthetic protocol. A more straightforward approach involves oxidation or reduction of redox non-innocent ligands, by which the Lewis acidic properties of the metal can be tuned in one step without large changes in the steric environment of the complex. This concept was recently applied by Rauchfuss et al. in the oxidation of dihydrogen (Scheme 1).[16,17]

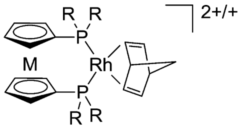
Scheme 1. Ligand Oxidation Leading to Increased Lewis Acidity of the Metal



Here, complex **1** is oxidized by silver tetrafluoroborate forming compound [**1**]$^+$. The cationic complex [**1**]$^+$ contains a one-electron oxidized ligand-radical, which makes the metal a stronger Lewis acid than in the nonoxidized form **1**. Therefore [**1**]$^+$ reacts with dihydrogen to produce the adduct [**1·H$_2$**]$^+$, which undergoes deprotonation by noncoordinating base 2,6-(t-Bu)$_2$C$_5$H$_3$N (2,6-di-tBu-pyridine; TBP). Further oxidation by [**1**]$^+$ or Ag$^+$, followed by yet another deprotonation step completes the catalytic redox process leading effectively to oxidation of H_2 by Ag$^+$ (Scheme 1). The electrons of H_2 actually reduce the oxidized form of the redox non-innocent ligand back to its neutral form, and hence the ligand also serves as an electron-reservoir in this system. In the catalytic experiment, **1** (1 equiv) was found to be able to oxidize 3 equiv of H_2 in the presence of $AgBF_4$ (6 equiv) and TBP (6 equiv) within 1.5 h.

Other catalytic reactions may require an electron-rich metal to facilitate the rate determining (slowest) step of the catalytic cycle. Oxidative addition of H_2 is frequently rate determining in olefin hydrogenation reactions. Thus, the rate of alkene hydrogenation catalyzed by Rh^{I}-diphosphinoferrocene complexes of the type **2a** (Scheme 2) is known to increase by increasing the basicity of the phosphine moieties, which can be achieved by introducing alkyl substituents (R = ^{t}Bu) instead of phenyl substituents (R = Ph) on the phosphorus atom. This can be easily rationalized by an enhanced electron density on

Scheme 2. Rh-Complexes, Used in Hydrogenation Reactions



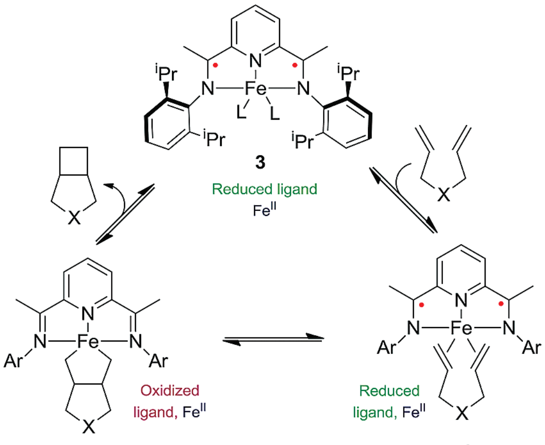
2a, M = Fe, R = Ph, *t*Bu, charge = +1
2b, M = Co, R = Ph, charge = +1,+2

rhodium, which facilitates the oxidative addition step.[18] A similar rate-enhancing effect on the hydrogenation of cyclohexene can also be achieved by changing the charge of the redox-active cobaltocene-based ligand moiety in the isostructural complexes **2b**.[19] While both mono- and dicationic complexes **2b** are active in hydrogenation, the reduced form (**2b**, charge = +1) leads to a 16-times faster reaction as compared to the oxidized, dicationic form of the complex (**2b**, charge = +2). Some other examples employing related concepts were reviewed by Allgeier and Mirkin.[20]

III. REDOX NON-INNOCENT LIGANDS AS ELECTRON-RESERVOIRS

Perhaps the most straightforward application of redox non-innocent ligands in catalysis is their ability to function as electron-reservoirs.[21,22] Many important transformations in homogeneous catalysis are based on elementary steps in which multiple (most typically two) electrons are being transferred between the metal and the (activated) substrate (e.g., reductive elimination, oxidation addition). Such transformations are common for expensive noble metals (Pd, Pt, Rh, etc.), but more difficult to achieve with cheaper and more abundant first-row transition metals (Fe, Co, etc.). However, if additional electrons can be temporarily stored on (or released from) a redox active ligand, the complex as a whole can mediate multielectron transformations without necessitating the metal to adopt an uncommon oxidation state. In other words, redox non-innocent ligands allow first-row transition metals to mimic some of the catalytic properties of more noble metals.[5,7−9]

Scheme 3. Redox Non-Innocent 2,6-Diiminepyridine Ligand Action as an Electron-Reservoir in Fe-catalyzed [2 + 2]-Cycloaddition Ring-Closure Reactions



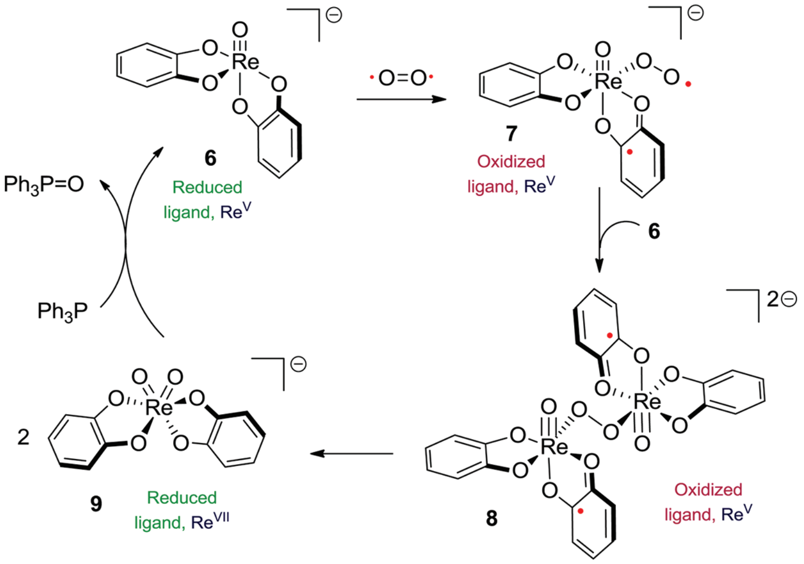
X = CH_2, NAlk, $C(CO_2Et)_2$

Chirik and co-workers made significant progress in the application of this concept in (formal) Fe^{II}-catalyzed [2 + 2]-cycloaddition reactions. In one example (Scheme 3),[23,24] bis-dinitrogen iron complex **3** (L = N_2) reacts with a diene substrate to form the π-complex **4**. Both **3** and **4** contain a dianionic tridendate N_3-ligand that is formally the 2e-reduced form of the applied redox-active 2,6-diiminepyridine ligand.[25,26] According to the authors complex **4** is in equilibrium with compound **5**. This transformation is formally a two-electron oxidative addition process. The electrons required for this transformation do not stem from the metal, but from the dianionic, two-electron reduced 2,6-diiminepyridine ligand, thus allowing iron to maintain the energetically favorable Fe^{II} oxidation state (avoiding the less favorable Fe^{IV} oxidation state). Subsequently, intermediate **5** undergoes a formal two-electron reductive elimination reaction to liberate the product. This process is again ligand based, leading to regeneration of complex **3** containing the two-electron reduced form of the 2,6-diiminepyridine ligand. Hence, again the electron-storage capacity of the ligand allows the metal to maintain its stable Fe^{II} oxidation state, which hence does not need to adopt the high-energy (unstable) Fe^0 oxidation state. The yield of the reaction depends on the nature of X (see Scheme 3), reaching 95% for X = N-^{t}Bu with TOF > 250 h^{-1}. Related Fe^{II} complexes are capable of catalyzing enyne cyclizations,[27] intermolecular [2 + 2] cycloadditions of alkenes to butadienes,[28] and olefin polymerization.[29,30] The role of the redox non-innocent 2,6-diiminepyridine ligand in the latter processes is, however, less clear and still debatable.

Interestingly, the electron-reservoir properties of redox active ligands has also proven to be useful to impose a one-electron transformation on late transition metals. Rhenium complexes are known to be powerful oxo-transfer reagents.[31,32] However, closed-shell rhenium complexes do not react easily with (triplet) dioxygen to generate oxo-ligands. This is possibly related to the "spin-forbidden" nature of this transformation, but this is a somewhat controversial explanation. In any case, reactions of metal complexes with O_2 (even with closed-shell species) generally tend to proceed via a preceding one-electron redox step to form an end-on superoxo M−O−O• intermediate.[33−35] Subsequent homolysis of the oxygen−oxygen bond then gives access to oxo species. Closed-shell d^2 Re^V complexes have a general tendency to react via two-electron processes rather than one-electron redox reactions, and hence complex **6** (Scheme 4) has a low probability to form an $[(L^{2-})_2(O)Re^{VI}{-}O{-}O\bullet]^-$ intermediate. However, the redox non-innocent ligands bound to the metal allow rhenium to maintain its +5 oxidation state and give access to the intermediate $[(L^{2-})(L^{\bullet-})(O)Re^V{-}O{-}O\bullet]^-$ species **7**, containing a one-electron oxidized catechol ligand (semiquinone). In this way, formation of the bis-oxo d^0 Re^{VI} complex **9** (via intermediate **8**) becomes accessible via a formally "spin-forbidden" reaction with molecular oxygen (Scheme 4). The transformation **6** → **9** requires half an equivalent of oxygen for each complex **6**, which shows that both oxygen atoms are incorporated in the product **9**.[36]

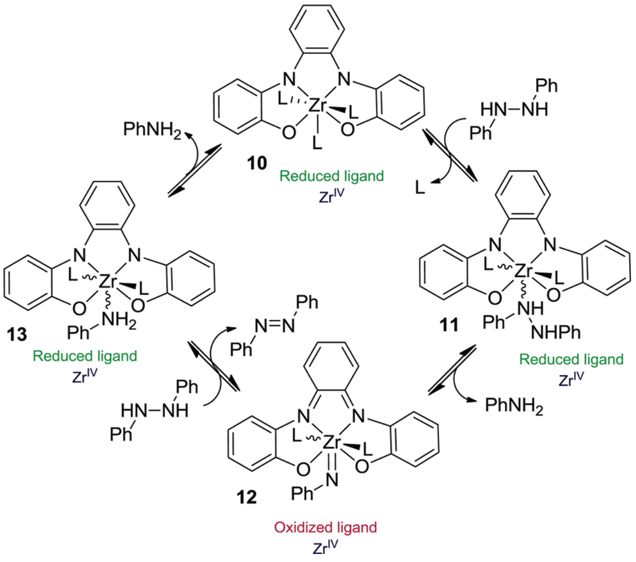
The oxo-transfer capabilities of complex **9** were demonstrated by oxidation of Ph_3P to $Ph_3P{=}O$.[36] PPh_3 binds strongly to complex **6** (to form **6•PPh_3**), which prevents true one-pot catalytic turnover in oxidation of Ph_3P to $Ph_3P{=}O$. Catalytic turnover, however, becomes possible with less coordinating substrates. Thus, complex **6** catalyzes aerobic oxidation of benzyl alcohol to benzaldehyde.[37] A drawback of this catalytic system is the too easy oxidation of the hydroquinolate ligand, forming free quinone. A possible solution for this problem may consist in using electron-withdrawing groups on the ligand,

Scheme 4. Electron-Reservoir Properties of Redox Active Ligands Assisting in Dioxygen Fixation



which makes the ligand less prone to oxidation. Indeed, employing the bis(tetrabromo-catecholate) analogue of complex **6** increases the catalytic activity, and in oxidation of benzyl alcohol (neat) the catalyst enables about 7 catalytic turnover cycles. The interesting feature of the sequence of reactions shown in Scheme 4 is that the redox non-innocent ligands do not only act as electron-reservoirs, but also seem to play an important role in lowering the exchange interactions through delocalization of the unpaired electron generated in the first step of the reaction, thus facilitating spin-crossover in the formally "spin-forbidden" reaction between triplet oxygen and the closed-shell (singlet) d^2 rhenium(V) complex **6**.

Scheme 5. "Oxidative Addition" Reactions at d^0 Zr^{IV} Complexes by Virtue of the Electron Releasing Properties of Redox-Active Ligands

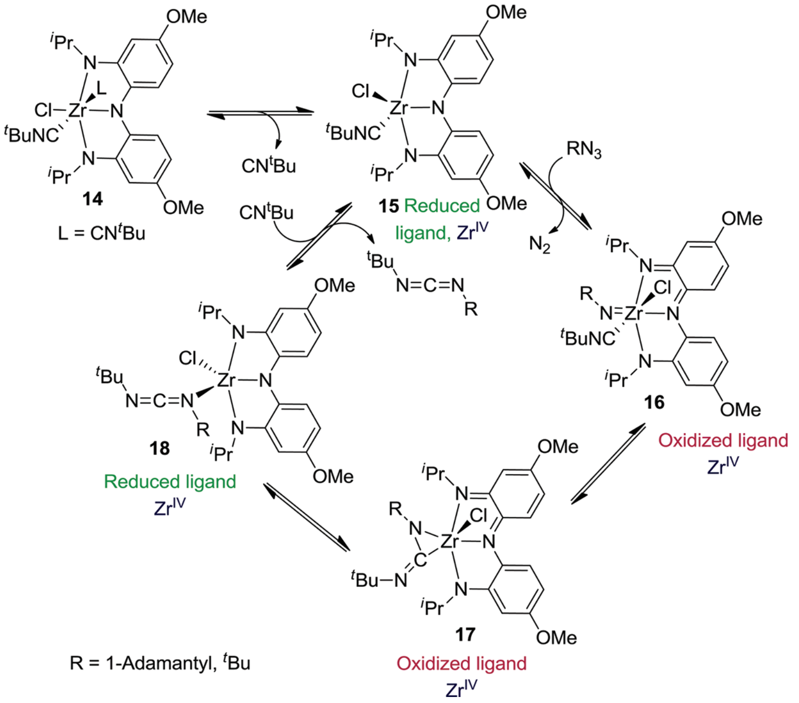


Storing electron density on redox-active ligands and releasing the electrons when needed in a chemical transformation is a concept that can also involve electron-pairs instead of single unpaired electrons. Again this concept can be used to prevent the metal from adopting uncommon oxidation states, and even allow redox transformations that are simply impossible otherwise. This is for example the case in the transformations reported by Heyduk et al. shown in Scheme 5, which illustrate that oxidative addition reactions become possible for d^0 Zr^{IV} complexes containing redox active ligands capable of releasing electron density.[38] The *ortho*-diamido Zr(IV) complex **10** catalyzes the dispropotionation of diphenyl hydrazine to aniline and azobenzene ($2PhNH{-}NHPh \rightarrow 2PhNH_2 + PhN{=}NPh$).[39] The first step of the catalytic cycle involves coordination of the diphenyl hydrazine moiety to zirconium (Scheme 5), which leads to complex **11**. To accomplish the next step—elimination of aniline, which is an "oxidative addition" process—two electrons are required. These are obviously not available from the d^0 zirconium(IV) metal site. Hence, this step is only possible by virtue of the electron-releasing properties of the redox active ligand. In other words, the ligand must donate two electrons (via the metal, thus allowing the observed net oxidative addition at the metal site), and hence the ligand gets oxidized in the process to form the *ortho*-diimine species **12**. The next step involves reaction of complex **12** with a second molecule of diphenyl hydrazine, thus forming azobenzene and the aniline adduct **13**. In this process, the oxidized form of the ligand (*ortho*-diimine form) accepts the two electrons that are released in this step of the catalytic cycle, and the ligand thereby gets reduced back to the *ortho*-diamide form in species **13**. In this way, zirconium can maintain its most stable +IV oxidation state throughout the entire catalytic reaction. Elimination of aniline closes the catalytic cycle. Full conversion of diphenyl hydrazine into aniline and azobenzene (2:1 ratio) can be achieved with 10 mol % catalyst loading within 1 day. With a lower catalysts loading of 1 mol % the reaction requires 6 days (yielding the same product ratio).

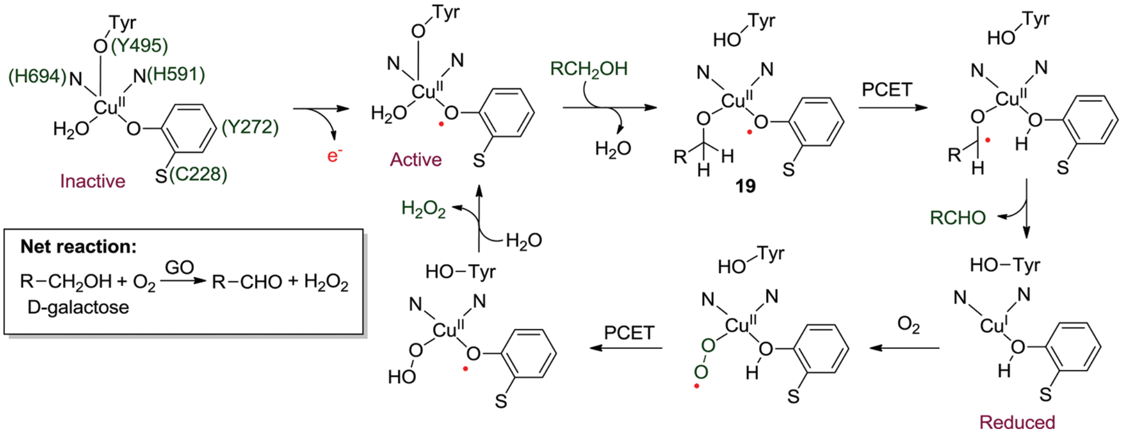
Related approaches were recently employed in mediating (stoichiometric) "oxidative addition" and "reductive elimination" reactions at cobalt centers bearing redox-active ligands.[8,40,41] These reactions also proceed without a change in the d-electron configuration of the metal.

The related zirconium complex **14** catalyzes nitrene transfer reactions from organic azides to *tert*-butyl isocyanide to form nonsymmetrical carbodiimides (Scheme 6).[42] The reaction starts by ligand dissociation to form the intermediate **15**, thus allowing coordination of the azide at the thus generated vacant

Scheme 6. Redox Active Ligand Participation in Catalytic Formation of Carbodiimides from Isocyanides and Organic Azides



Scheme 7. Cooperative Substrate Activation by the Metal and the Redox Active Tyrosine Radical in Radical-Type Catalytic Turnover Mediated by GOase



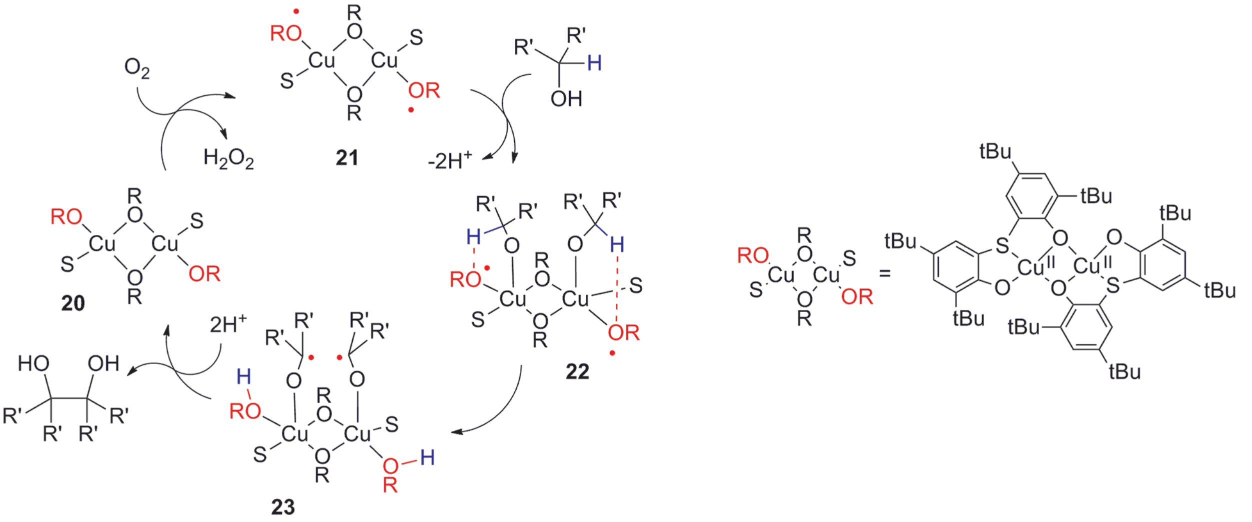
site. Dinitrogen is eliminated (stepwise or simultaneously) forming the imido intermediate **16**. Kinetic studies revealed that nitrogen elimination is rate-limiting. Similar to the above example in Scheme 5, the ligand gets oxidized in the process to produce **16**, as the d^0 Zr^{IV} has no electrons available for this oxidative process itself. The next step is an intramolecular nucleophilic attack of the imido nitrogen onto the isocyanide triple bond, thus leading to compound **17**. Subsequent "reductive elimination" to form the carbodiimide complex **18** and dissociation of the product closes the catalytic cycle. The "reductive elimination" from **17** to **18** is again based on the redox non-innocence of the ligand, and does not lead to a change of the metal d-electron count. Reaction of ^{t}BuNC with adamantyl and *tert*-butyl azides proceeds with complete conversion into carbodiimide in 2 h, using 10 mol % of the catalyst.[43]

The properties of redox non-innocent imine-ligands in somewhat related processes have been discussed in some recent publications,[44,45] and also the phenyl moiety of *ansa*-cylopentadienyl-arene complexes of tantalum[46] and titanium[47−49] has been suggested to play a redox non-innocent role in controlling the selectivity of catalytic process of ethylene trimerization. However, electron-transfer from the metal to the phenyl moiety of these latter systems seems to be incomplete, and is perhaps better described as π-back-donation rather than a redox process.

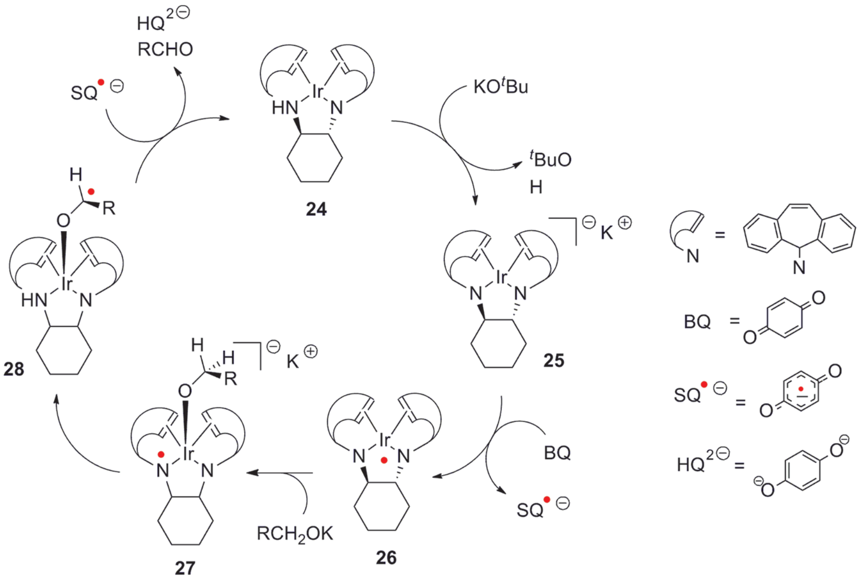
IV. COOPERATIVE LIGAND-CENTERED REACTIVITY BASED ON REDOX NON-INNOCENT LIGANDS

In the two previous approaches (**I** and **II**), redox non-innocent ligands play an indirect "spectator" role in catalysis by modifying the electronic properties of the metal or by acting as an electron reservoir, but the intrinsic reactivity is still metal-based. In other cases, however, the redox non-innocent ligand proved to play a much more prominent role in the bond-activation processes during the catalytic reaction. "Actor"

Scheme 8. Catalytic Cycle of Cu^{II}-Catalyzed Dimerization of Secondary Alcohols



Scheme 9. Catalytic Cycle of Ir-Catalyzed Oxidation of Primary Alcohols



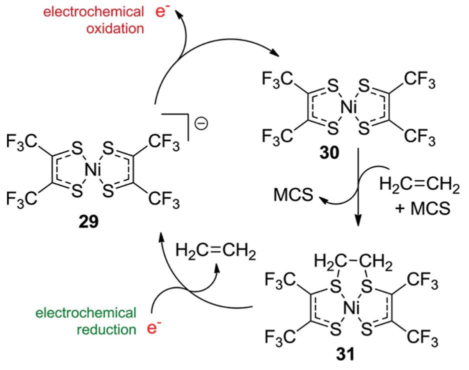
behavior of redox non-innocent ligands is important, for example, in the catalytic mechanism of several enzymes (exemplified in particular by oxidases) that proceed via radical-type reactions. Galactose Oxidase (GOase) is probably one of the most well-studied enzymes in this perspective. GOase catalyzes the oxidation of D-galactose into D-galacto-hexodialdose and hydrogen peroxide in the presence of oxygen (Scheme 7).[50,51] The active site of the enzyme contains a copper(II) center, surrounded by two histidine and two tyrosine residues (Scheme 7). The catalytic cycle starts with one-electron oxidation of the tyrosine-272 moiety, to form the "active" form of the enzyme. The thus formed oxygen-centered radical **19** promotes oxidation of the CH_2OH-group of the galactose substrate through a proton-coupled electron-transfer (PCET) path to produce the "reduced" form of the enzyme (Cu^I). The latter then reacts with dioxygen, again following a PCET path, to produce hydrogen peroxide, which closes the catalytic cycle. The redox-active ligand in this mechanism plays a prominent role in the bond-activation processes leading to oxidation of the alcohol substrate, and is certainly not just a spectator ligand. This is a clear example of cooperative substrate activation by both the metal and the radical-type redox-active ligand. The substrate binds to the metal, which places it close to the reactive ligand radical, and the actual bond-breaking process takes place between the non-innocent ligand and the substrate.

A number of related bioinspired catalytic processes have been reported. Wieghardt and Chaudhuri reported Cu^{II}-thiophenol complex **20** (Scheme 8),[52] which does not only catalyze oxidation of primary alcohols to aldehydes in the presence of air, but (in contrast to GOase) also promotes the formation of diols from secondary alcohols (Scheme 8). The catalytic cycle involves oxidation of the Cu complex **20** by oxygen, which leads to biradical species **21** (analogous to intermediate **19** in the GOase oxidation cycle). Coordination of two (deprotonated) alcohol substrates to intermediate **21** produces intermediate **22**. The formation of **22** is directly followed by α-hydrogen atom transfer from the secondary alcoholates (β-positions with respect to the metal) to the oxygen-centered radicals of the aminophenol ligands (rate-limiting step). Radical dimerization and elimination of the diol closes the catalytic cycle.[53]

A related bioinspired approach to alcohol oxidation was recently disclosed by Grützmacher et al.[54] This system is based on iridium instead of copper, and employs nitrogen-centered (aminyl) radical ligands instead of oxygen-centered ligand radicals. Deprotonation of complex **24** (Scheme 9) with KO^{t}Bu forms the anionic intermediate **25**, which undergoes one-electron oxidation by benzoquinone (BQ) to form the radical intermediate **26**. The latter reacts with the alcoholate substrate to produce intermediate **27**, very similar to intermediate **19** in the GOase catalytic cycle. The dibenzotropylamino substituent plays the same role as a tyrosine moiety in GOase, and enables facile hydrogen atom transfer from the alcoholate substrate to the nitrogen-centered ligand. Subsequent oxidation of **28** by semiquinonate ($SQ^{\bullet -}$) produces the aldehyde and regenerates the catalyst.

Another remarkable example was reported by Wang and Stiefel.[55] Here, redox non-innocent ligands were not employed in catalysis, but in a catalysis-related process—the purification of ethene gas streams. The approach is based on a different affinity of the olefin to the oxidized and reduced forms of a dithiolene complex. Anionic Ni complex **29** can be oxidized electrochemically to form the neutral complex **30** (Scheme 10).

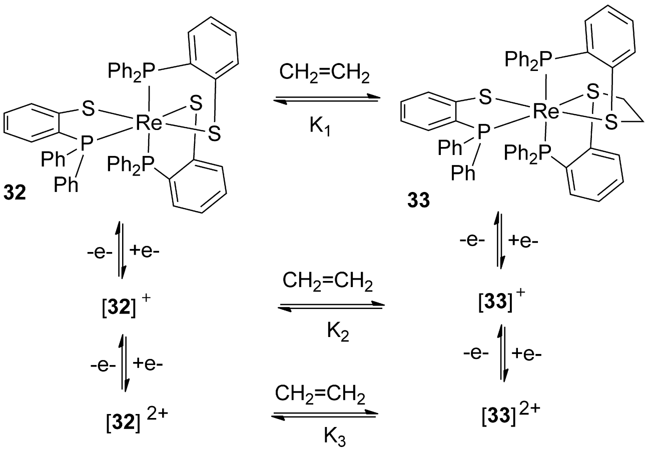
Scheme 10. Redox Non-Innocent Ligands Applied in Ethene Purification



The latter selectively forms a relatively strong adduct (**31**) with ethylene, while nonolefinic contaminations of the multicomponent stream (MCS) do not react with the complex. Interestingly, ethylene reacts with the sulfur-based ligand, and does not form a π-complex with the metal (which is typically observed for most other complexes). The olefin can be released subsequently from complex **31** by electrochemical reduction. Intermediate thiyl-radical ligands are likely to be involved in the process of ethylene capture.

Thiophosphane-rhenium complex **32** can also reversibly capture alkenes at its ligand sulfur-atoms upon electrochemical oxidation (Scheme 11).[56,57] Analogously to the above Ni-complex **29**, the oxidized forms of **32** (i.e., $\mathbf{32}^+$ and $\mathbf{32}^{2+}$) bind ethylene stronger than corresponding reduced species ($K_3 > K_2 > K_1$). Thus, in the nonoxidized form the equilibrium $\mathbf{32} \rightleftharpoons \mathbf{33}$ largely favors **32** with almost negligible concentrations of **33** even at rather high ethylene concentrations. For the dicationic species (2-electron oxidized form), the equilibrium $\mathbf{32}^{2+} \rightleftharpoons \mathbf{33}^{2+}$ is shifted entirely toward $\mathbf{33}^{2+}$ with no spectroscopic (UV−vis) indications for the presence of $\mathbf{32}^{2+}$ anymore. In case of the monocationic species (1-electron oxidized form), both $\mathbf{32}^+$ and $\mathbf{33}^+$ are detectable, and their equilibrium concentration strongly depends on the applied ethylene pressure.

Scheme 11. Ethylene Capture at the Redox Non-Innocent Thiyl-Radical Ligands of a Rhenium Complex

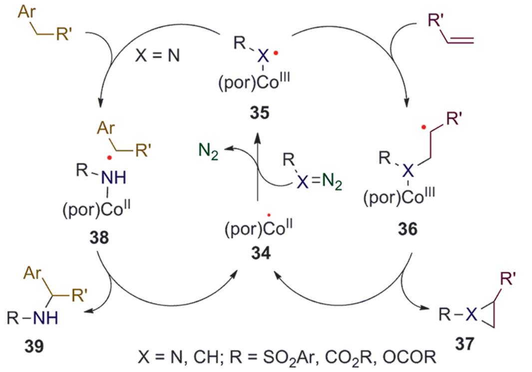


V. COOPERATIVE SUBSTRATE-CENTERED RADICAL-TYPE REACTIVITY BASED ON REDOX NON-INNOCENT SUBSTRATES

A strategy that is somewhat related to the previous concept (**III**) is to use directly the redox non-innocent properties of a substrate itself. The idea is that electron transfer to or from a redox active substrate imposes intrinsic radical-type behavior of this same substrate, which often leads to typical radical-type reactivity useful in subsequent elementary steps in a catalytic cycle. This concept has been applied in a number of organometallic transformations (both stoichiometric and in catalytic reactions), as described in some recent reviews.[11,58] The concept is, however, more general, and effectively leads to substrate-centered radical species that often have a completely different reactivity and selectivity compared to analogous closed-shell intermediates.

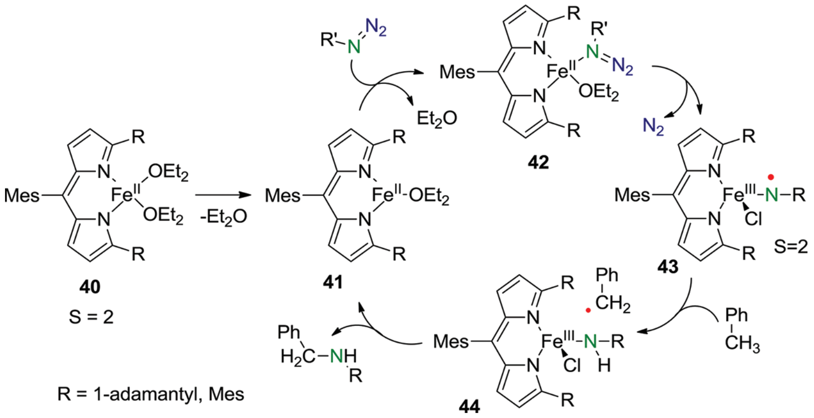
The concept is nicely illustrated by the recently disclosed catalytic mechanism of Co^{II} porphyrin catalyzed carbene and nitrene transfer reactions (Scheme 12). In these transformations, the Co^{II}-porphyrin-type catalysts (**34**) react with an organic azide or a diazo-compound with concomitant N_2-elimination to form ligand-centered radical species of the type

Scheme 12. Formation of Reactive Substrate-Based Radical Ligands in Catalytic Nitrene or Carbene Transfer Reactions Proceeding via Controlled Radical-Type Transformations



X = N, CH; R = SO_2Ar, CO_2R, OCOR

Scheme 13. Catalytic Cycle of the Nitrene Insertion into the C−H Bond of Toluene



35. The latter are in fact products of a redox reaction, in which single-electron transfer from the Co^{II} site to the redox non-innocent carbene and nitrene ligands (generated in the coordination sphere upon N_2-loss) occurs. Density functional theory (DFT) calculations in combination with kinetic studies showed that the formation of these carbene/nitrene radical ligands is the rate-limiting step in the catalytic cycle. The intermediates **35** can react further with alkenes (with a comparable barrier as the formation of **35**) to form complexes of the type **36** (Scheme 12, right), which in turn cyclize in a virtually barrierless manner under formation of aziridines (**37**, X = N)[59−63] or cyclopropanes (**37**, X = CH)[64−70] in high yields (e.g., 60−80% yield using 5 mol % of Co(TPP) as the catalyst). High enantioselectivities can be achieved in the cyclopropanation reactions with chiral cobalt-porphyrin complexes, despite the radical nature of the reaction mechanism.[60,67,71−73]

A further remarkable feature of these cyclopropanation systems is that they are not very sensitive toward carbene dimerization (a common problem with many other catalysts), and in addition the carbene species of the type **35** (X = C) can even cyclopropanate alkenes with electron-withdrawing substituents R′. The latter is not possible for closed-shell rhodium, ruthenium, or copper(I) catalysts (with common redox-*innocent* ligands). The electrophilic character of carbenes generated at Cu^I, Rh^{II}_2, and Ru^{II} catalysts (Fischer-type carbenes) prevents reactions with electron-deficient olefins and promotes carbene dimerization. The radical-type species **35**, however, have a more nucleophilic character. Consequently they have a decreased carbene dimerization activity, and they are capable of reacting with electron-deficient vinylic substrates. This nicely illustrates how redox non-innocent substrates can be used to our benefit, as they clearly allow us to steer and control chemo-selectivities of radical-type catalytic transformations, without compromising diastereo- and enantioselectivies imposed by the other (chiral) auxiliary ligands.

Alternatively, species of the type **35** (X = N) can insert into allylic[74,75] or benzylic C−H bonds, thus producing amines (Scheme 12, left).[76−82] In this case, because of a considerable radical character of the nitrene nitrogen atom, species **35** abstracts a hydrogen atom from the allylic or benzylic position of (for example) ethylbenzene or tetralin. This results in intermediates of the type **38**, which then collapse (in a virtually barrierless manner) to produce the target amines **39**. The yields of the amines vary depending on the nature of substituent R. The most successful results are obtained with 2,2,2-trichlorethoxycarbonyl (Troc) substituent, which gives 50−85% yield of the product using 5 mol % of the CoTPP catalyst in about 48 h at 40 °C.

Remarkably, the porphyrin ligand in species **35** (X = C, N) seems to behave redox-innocently, and no significant spin density is found on this moiety.

A similar reactivity has been reported for nonheme Fe^{II} complex **40** (S = 2), which also catalyzes the insertion of nitrenes into benzylic C−H bonds (TON ∼14).[83] A mechanism, similar to the one discussed above, was proposed (Scheme 13). Dissociation of one the solvent molecules from the starting metal complex **40** is followed by coordination of the organic azide to intermediate **41** producing adduct **42**, from which dinitrogen elimination leads to a one-electron reduced "nitrene" ligand in **43** (this radical-type ligand could alternatively be described as a one-electron oxidized "imido" ligand). Intermediate **43** is proposed to have high spin iron(III) center (d^5, $S = 5/2$), which is antiferromagnetically (AFM) coupled with the one-electron reduced "nitrene" radical ligand ($S = 1/2$), leading to a total $S = 2$ spin-state ($\mu_{\mathrm{eff}} = 5.3(1)$, R′ = p-^{t}Bu-C_6H_4): $(d_{x^2-y^2})^1(d_{z^2})^1(d_{xy})^1(d_{xz})^1(d_{xy})^1$-AFC-$(p_{\mathrm{nitrene}})^1$. Similar to compound **35**, unpaired electrons in complex **43** are mainly delocalized over the nitrene moiety and the metal, and no significant spin density was found on the dipyrrolomethane ligand (DFT). Species **43** abstracts a hydrogen-atom from toluene to produce intermediate **44**, which collapses to form the amine product to close the catalytic cycle.

VI. CONCLUSIONS

Redox non-innocent ligands provide a variety of new and versatile tools to control the activity and selectivity of transition metal complexes in catalysis. They can have a "spectator" role, meaning that they do not directly interact with the substrate, and in which case the catalytic activity is primarily metal-centered. In this case, the redox active ligands can, however, modify the Lewis acidity/basicity of the metal, or influence the catalytic process by acting as electron reservoirs (still without any covalent interactions with the substrate, and thus acting as a "spectator"). On the other hand, redox non-innocent ligands can also play a much more "active" ("actor") role, in which they actively participate in the catalytic processes by undergoing covalent bond making/breaking of the substrates. The use of redox non-innocent ligands as electron reservoirs during catalysis allows reactions in which the metal can maintain its most favored oxidation states throughout the entire catalytic cycle. This concept can be used to perform multiple-electron transformations (normally restricted to noble, late second- and third-row transition metals) with cheaper first-row transition metals (which commonly prefer one-electron redox steps), and even remarkable "oxidative addition" processes at d^0 transition metal complexes become possible during catalysis. In some cases the substrate itself acts a redox non-innocent ligand. This dramatically changes its reactivity, and has a remarkable influence on the activity and selectivity of the catalytic process. In some illustrative examples, carbene and nitrene substrate-based radical ligands have shown the ability to mediate selective radical-type transformations. The one-electron reduced open-shell forms of the carbene or nitrene ligands reveal completely different chemo-selectivities than their more common closed-shell analogues. Hence, redox non-innocent ligands have proven themselves as a versatile new tools to control catalytic reactions, and many exciting applications of these new tools can be expected in the near future.

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