

Application of Stimuli-Responsive and “Non-innocent” Ligands in Base Metal Catalysis

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1.1 Introduction

The development of efficient and selective catalysts is an important goal of modern research in chemistry – the science of matter and its transformations. Our society needs new catalysts to become more sustainable, and a desire for selectivity and efficiency in the preparation of medicines and materials has boosted our interest in developing new methods based on homogeneous catalysis, particularly on the development of new ligands that can be fine-tuned to specific needs. The properties of a metal complex as a whole are the result of the interaction between the metal center and its surrounding ligands. In traditional approaches, the steric and electronic properties of the spectator ligand are used to control the performance of the catalyst, but most of the reactivity takes place at the metal. Recent new approaches deviate from this concept and make use of ligands that play a 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 act in a synergistic manner to facilitate a chemical process. In this light, complexes based on the so-called “non-innocent” ligands offer interesting prospects and have attracted quite some attention.

The term “non-innocent” is broadly used, and diverse authors give different interpretations to the term. It was originally introduced by Jørgensen [3] to indicate that assigning metal oxidation states can be ambiguous when complexes contain redox-active ligands. As such, ligands that get reduced or oxidized in a redox process of a transition metal complex are often referred to as “redox non-innocent.” [4, 5] With modern spectroscopic techniques, combined with computational studies, assigning metal and ligand oxidations states has become less ambiguous, and hence, many authors started to use the term “redox-active ligands” instead. Gradually, many authors also started to use the term “non-innocent” for ligands that are more than just an ancillary ligand, frequently involving ligands that have reactive moieties that can act in cooperative (catalytic) chemical transformations, act as temporary electron reservoirs, or respond to external triggers to modify the properties or reactivity of a complex.

A common objective of many of these investigations is to achieve better control over the catalytic reactivity of first-row transition metal complexes, with the ultimate goal to replace the scarce, expensive noble metals currently used in a variety of catalytic processes by cheap and abundant first-row transition metals. Instead of providing a comprehensive overview of redox non-innocent [6, 7] and cooperative ligands [1, 8, 9], this chapter is intended to provide a conceptual introduction into the topic of achieving control over the catalytic reactivity of non-noble metals using non-innocent ligands on the basis of recent examples.

Noble metals are frequently used in several catalytic synthetic methodologies and many industrial processes [10]. Their catalytic reactivity is most frequently based on their well-established “two-electron reactivity,” involving typical elementary steps such as reductive elimination and oxidative addition. These elementary steps easily occur for late (mostly second and third rows) transition metals having two stable oxidation states differing by two electrons. However, most noble metals are scarce and are therefore expensive (and sometimes toxic [11]). Therefore, it is necessary to reinvestigate the use of cheaper, abundant, and benign metals to arrive at cost-effective alternatives. This is not an easy task, as base metals (Fe, Co, Cu, Ni, etc.) often favor one-electron redox processes, and typical elementary steps commonly observed in noble metal catalysis are only scarcely observed for base metals. As such, the unique properties of non-innocent ligands are advantageous to gain better control over the reactivity of base metals. In some cases, this leads to reactivity comparable to that of noble metal complexes (but more cost-effective and benign), whereas in other cases, the combination of a base metal with a “non-innocent” ligand can actually give access to unique new types of reactivity.

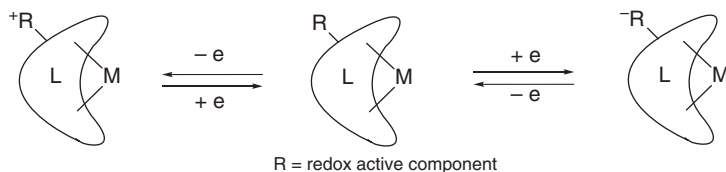
This chapter has four parts. In Section 1.2, the concept of responsive ligands is discussed, giving examples of a series of ligands that can be tuned using external stimuli such as light, pH, or ligand-based redox reactions. These can trigger a change in the properties of the ligand, thereby modifying the reactivity of the metal. Section 1.3 deals with redox-active ligands that behave as electron reservoirs. In the examples provided, this feature enables oxidative addition and reductive elimination steps for first-row transition metal complexes that, without the aid of redox-active ligands, are less inclined to undergo these catalytically relevant elementary steps. Section 1.4 focuses on recent examples of cooperative catalysis, in which non-noble metal reactivity is combined with ligand-based reactivity in key substrate activation steps. The last part (Section 1.5) deals with examples in which the coordinated substrate itself acts as a redox-active moiety in key elementary steps of a catalytic reaction. More specifically, these coordinated substrates get oxidized or reduced by the metal by a single electron, thus creating “substrate radicals,” which play an important role in catalytic radical-type transformations.

1.2 Stimuli-Responsive Ligands

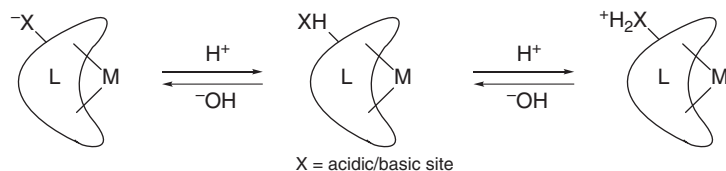
Common ancillary (innocent) ligands in homogeneous catalysis typically control the activity and selectivity of the catalyst by affecting the steric and electronic

properties around the reactive metal center. As such, changing the reactivity of the active metal center usually requires the synthesis of new ligands, which is often associated with elaborate synthetic procedures [6]. However, the electronic and steric properties of ligands can sometimes be influenced in an easier manner by using external stimuli, involving, for example, ligand protonation/deprotonation, ligand oxidation/reduction, or (reversible) light-induced ligand transformations (Scheme 1.1) [12].

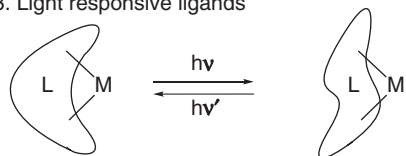
1. Redox responsive ligands



2. pH responsive ligands



3. Light responsive ligands



Scheme 1.1 Switching catalytic properties of a catalyst using external stimuli.

When using such responsive ligands, the metal oxidation state is typically unaffected, but its reactivity is nonetheless influenced by the new electronic and steric properties of the ligand. Furthermore, the solubility of the metal complex can sometimes be significantly influenced by such external stimuli. In most current literature, these ligands are nevertheless considered to be “innocent” ligands as they are not directly involved in substrate bond making/breaking processes nor lead to ambiguities in assigning the metal oxidation state. Stimuli-responsive ligands are particularly useful to influence the catalyst *during* a catalytic reaction and are therefore mainly applied to develop switchable catalytic systems.

1.2.1 Redox-Responsive Ligands

Oxidation or reduction of a complex containing one or more redox-active ligands can lead to oxidation or reduction of the ligand rather than the metal. As such, the ligand can switch between one or multiple oxidized and reduced states, by which the electronic properties of the ligand (and thereby the metal) change.

These redox processes can be triggered either chemically or electrochemically [13]. Often metallocenes such as ferrocene or cobaltocene are used because of their reversible oxidation and reduction cycles [14]. In other cases, the redox-active part of the ligand of interest is actually a metallocene moiety [15]. Upon oxidation of a ferrocenyl to a ferrocenylium group attached to the ligand, the electron density of the donor ligand decreases and thereby also that of the metal bound to this ligand, as can be observed in a shift of the CO stretch frequency to higher wavenumbers for carbonyl complexes [16]. Recently, a review appeared reporting a variety of chemical oxidants and reductants that allow the design of new catalysts with switchable ligands at a specific desired potential [17]. Examples of the use of redox-active ligands in catalysis frequently involve redox processes that partly occur at the redox-active ligand and partly at the catalytic metal center (see Section 1.3). Examples of redox-responsive ligands in catalysis wherein ligand-based redox processes affect the metal center and its catalytic properties indirectly are rare, especially for base metals. The main application of such reported examples is in the field of switchable catalysis. Furthermore, the solubility of the ligand can change significantly because of charge buildup, thus enabling separation of the catalyst from the reaction mixture after a catalytic reaction [18].

By oxidation or reduction of the ligand, the overall charge of the complex changes, which affects the catalytic activity of the central metal, and in some cases, this can be used to switch a catalyst ON and OFF. Most of the recently reported examples of such switchable catalysts involve systems based on noble metals [18–20], but a few examples of base metals are known as described below. One of the first redox-responsive base metal catalysts reported involves a titanium-based salen-type ligand substituted with two ferrocene (Fc) moieties (Figure 1.1a) [21]. The catalyst was used in the ring-opening polymerization of

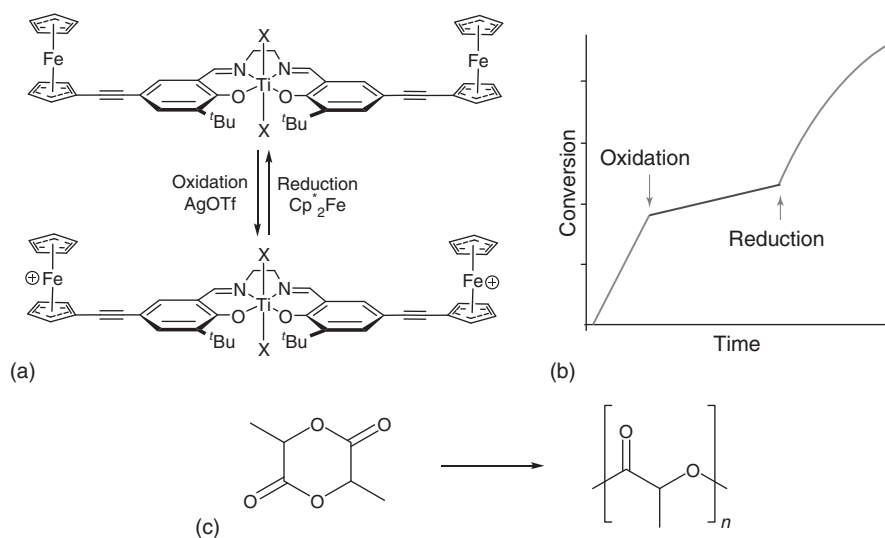


Figure 1.1 Titanium-based redox-switchable catalyst (a) and the effect of switching on the catalysis (b) on the polymerization reaction (c).

lactides, during which the neutral catalyst showed a 30-fold enhanced rate with respect to the oxidized complex. Oxidation of the ferrocenyl moieties of the catalyst does not completely shut down the catalytic activity, but by addition of small amounts of oxidant or reductant, the catalyst can nonetheless be switched between a more active (ON) and less active (OFF) state *during catalysis* (Figure 1.1b).

More recently, new titanium and zirconium catalysts were developed based on sulfan ($Y = \text{NMe}$) and thiofian ($Y = \text{S}$) ligands (Figure 1.2a) containing a ferrocene moiety closer to the metal center [22]. The reduced and oxidized catalysts showed opposing rates for the ring-opening polymerization of L-lactide and ϵ -caprolactone, respectively (Figure 1.2b). By switching between the two states during the polymerization reaction, the catalyst can be used to generate block copolymers with a high degree of regularity. In particular, this last example elegantly shows the power of switchable catalysts for application in polymerization reactions. Given the potential of such systems, we expect that many more examples of redox-switchable catalysts used for a variety of other catalytic reactions are likely to be disclosed in the next couple of years.

1.2.2 pH-Responsive Ligands

Ligands that can be easily protonated or deprotonated by applying relatively mild pH changes are commonly used to affect the solubility of catalysts. With this method, homogeneous catalysts can be easily recycled, thus saving cost and avoiding metal contamination in the products. Reversible protonation of amine groups to obtain water-soluble complexes has been applied to noble-metal-catalyzed reactions such as olefin metathesis [23] and cross-coupling reactions [24]. The selectivity of rhodium metathesis catalysts can be further altered upon protonation of the ligand [25]. By using similar

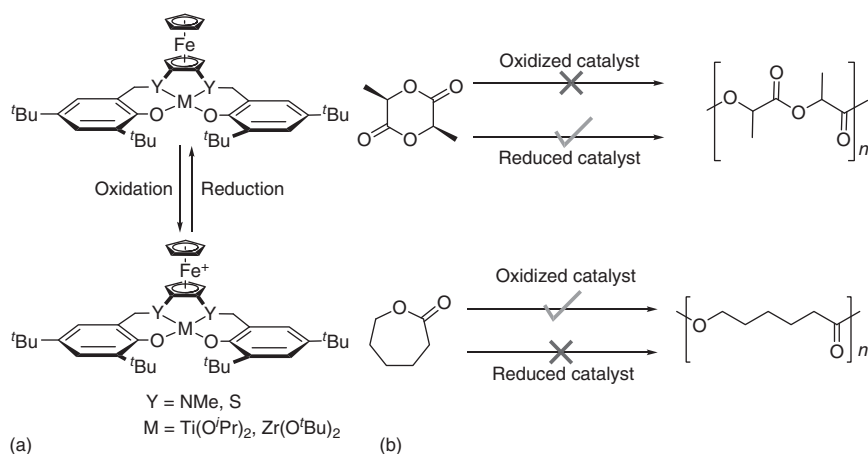


Figure 1.2 Ferrocene containing redox-switchable catalysts (a) and inverted reactivity for the resulting oxidized and reduced complexes (b). Source: Wang et al. 2014 [22]. Reproduced with permission of ACS.

ammonium-tagged NHC ligands, a copper-catalyzed click reaction in water was developed by Li and coworkers [26]. The products could simply be extracted in order to recycle the catalyst several times with a small loss of overall yield, but the catalyst was not switchable. In 2012, the same group reported a similar copper complex for the carbonylation of boronic acids, benzoxazoles, and terminal alkynes [27]. In this case, the catalyst precipitates upon protonation and could be separated by centrifugation (Figure 1.3). The catalyst can be recycled up to four times with only moderate loss in activity. Related copper-catalyzed reactions based on NHC complexes with pendant bases have also been reported [28], but the effects of deprotonation on the catalysis or recyclability of the complex were not discussed in detail for these systems.

The second type of proton-switchable ligands is composed of bipyridine and phenanthroline ligands equipped with moieties that can be (de)protonated. Many late transition metal catalysts based on iridium [29–31], rhodium [32], and rhenium [33] have been reported to use this class of ligands. Recent base metal examples include a switchable copper catalyst for the Ullmann reaction of aryl bromides. The catalyst can be deprotonated in basic water to obtain a highly active catalyst, which could be recycled by acidification (Figure 1.4) [34].

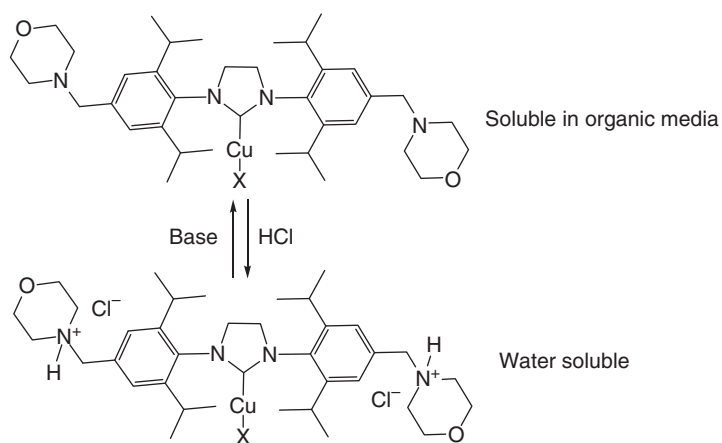


Figure 1.3 Proton-switchable copper catalyst.

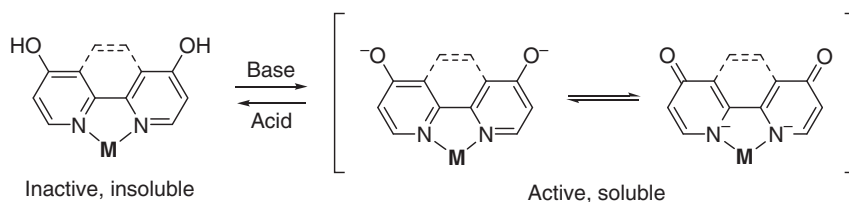


Figure 1.4 Reversible deprotonation of a 4,7-dihydroxy-1,10-phenanthroline (including dotted lines) or 4,4'-dihydroxy-2,2'-bipyridine (excluding dotted lines)-based complex.

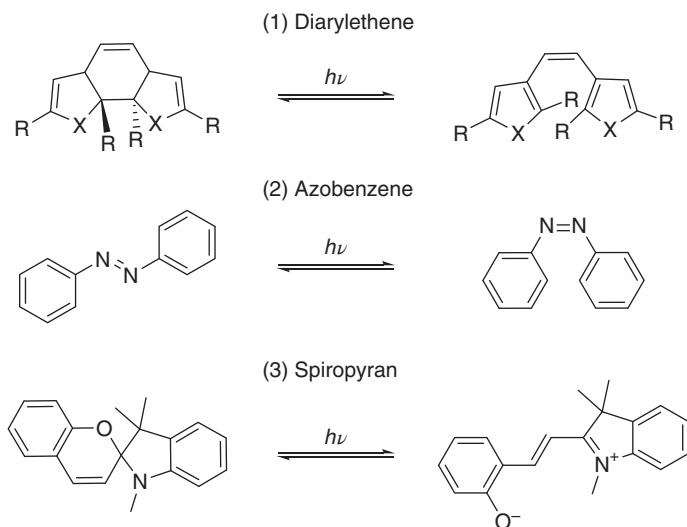


Figure 1.5 Light-active scaffolds that undergo structural changes upon irradiation.

Another example of a proton-switchable catalyst involves a cobalt complex based on bipyridine for the hydrogenation of carbon dioxide to formate [35]. The alcohol substituents were introduced either at the 4,4'- or the 6,6'-positions. The obtained complexes show a large dependence on the concentration of base as the deprotonated complex is active and more stable under the reaction conditions. Recyclability data were not reported for these systems, but the complexes do, however, show a significantly higher activity after deprotonation of the ligand.

1.2.3 Light-Responsive Ligands

Light, being rather non-invasive, is perhaps the most interesting external trigger to switch a bistable catalyst. Upon irradiation with light, many molecules such as diarylethenes, azobenzenes, or spiropyrans can undergo structural rearrangement (Figure 1.5). Incorporation of these switchable moieties in a catalyst could result in easy control of its catalytic activity [36, 37], and use of different wavelengths typically allows two-way switching of these scaffolds.

An elegant example of this type of responsive catalyst was reported by the group of Branda for a copper-catalyzed cyclopropanation reaction (Figure 1.6) [38].

Upon reversible isomerization of the open ligand (Figure 1.6, right complex) to the cyclized complex (Figure 1.6, left complex), almost all stereoselectivity was lost. Although switching the ligand was more difficult after copper coordination, it was still feasible after addition of a small amount of a coordinating solvent to the reaction mixture.

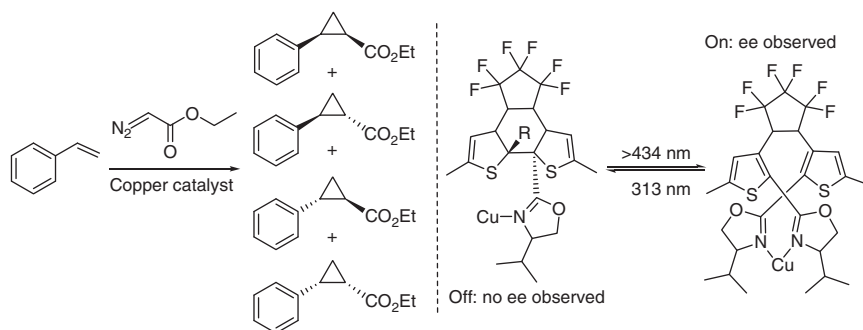
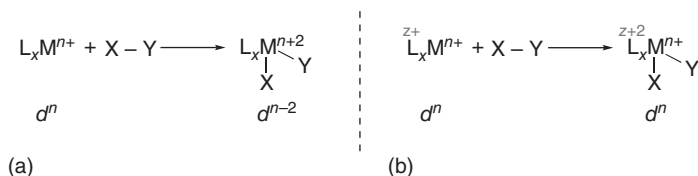


Figure 1.6 Light-induced enantioselective cyclopropanation.

1.3 Redox-Active Ligands as Electron Reservoirs

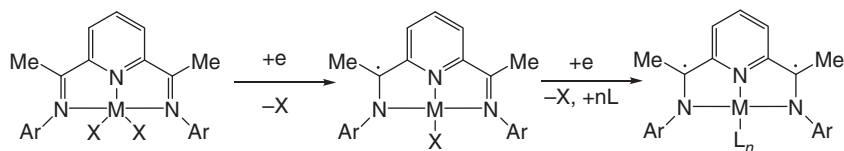
The most straightforward application of redox-active ligands is as electron reservoir, to facilitate redox processes for base metals that would otherwise be difficult or impossible. As such, redox-active ligands can participate in key redox processes of a catalytic cycle, such as oxidative addition or reductive elimination steps (Scheme 1.2). The ligand can temporarily store or release additional electrons allowing the metal complex to perform multielectron steps, avoiding formation of high-energy oxidation states of the metal if the energy levels of redox-active ligands are more accessible [39]. In this way, even purely ligand-centered redox processes become possible leaving the metal in the same oxidation state throughout an entire catalytic cycle. As such, by making use of redox-active ligands, the reactivity of first-row transition metals can be tuned toward catalytic properties more typically observed for noble metals [40].



Scheme 1.2 (a) Classic oxidative addition and (b) oxidative addition in metal complexes with redox-active ligands.

1.3.1 Bis(imino)pyridine (BIP)

The bis(imino)pyridine (BIP) ligand (Scheme 1.3) has perhaps been most frequently used as an electron reservoir. This class of ligands consists of pyridine derivatives with imine functionalities at the 2,6-positions and stabilizes metals in low (formal)-oxidation states. The three nitrogen centers of the ligand bind to a metal in a tridentate manner, forming pincer complexes (Scheme 1.3, left). The obtained non-innocent ligand can have more than one oxidation state, as the ligand and π^* -orbitals can accept several electrons. The ligand can easily be synthesized



Scheme 1.3 Bis(imino)pyridine complex (left), mono-reduced (middle), and bis-reduced complexes (right).

by Schiff base condensation of commercially available 2,6-diacetylpyridine with 2 equiv. of an aniline derivative. Most commonly, variations in the ligand are made by changing the anilines in the condensation reaction. The highly conjugated ligand framework of bis(imino)pyridine stabilizes unusual formal oxidation states of the metal. A neutral complex is able to accept up to three electrons, leading to ambiguity about the oxidation states of the metal center [41–45].

A variety of coordination complexes with different transition metals have been prepared. Extensive studies by Chirik and coworkers [46–48], Wieghardt [42, 46–48], Budzelaar and coworkers [42, 43], de Bruin [41, 42], deBeer [48], and others have established unusual electronic structures of first-row transition metal complexes containing the BIP ligand. In many cases, the studies revealed the presence of unpaired electrons at the ligand, coupled antiferromagnetically to unpaired electrons at the metal. For example, the four-coordinated compound, (BIP)Fe(N₂) is best described as an intermediate spin ferrous derivative ($S_{\text{Fe}} = 1$) antiferromagnetically coupled to a bis(imino)pyridine triplet dianion (Scheme 1.3, right) [46–48]. BIP complexes of first-row transition metals have been used for various multiple electron transfer processes. The obtained complexes occasionally even outperform noble metal complexes.

1.3.1.1 Ethylene Polymerization with BIP

In 1998, Brookhart and coworkers [49] and Gibson and coworkers [50] introduced BIP complexes of mid-to-late first-row transition metals for ethylene polymerization [51]. This was a major breakthrough in the field of olefin polymerization catalysis, as most catalysts explored until then were based on early d^0 transition metals. The abundance of high-valent Ti^{IV}, Zr^{IV}, and Hf^{IV} complexes in polymerization reactions is readily understood from the fact that β -hydrogen elimination is a suppressed chain transfer/chain termination process for these metals, as it requires not only a vacant site but also the presence of (at least two) d -electrons. Some palladium catalysts equipped with bulky ligands shielding the axial positions are known to produce polymers by slowing down chain transfer. This is because direct olefin dissociation (after β -hydrogen elimination) is a thermodynamically uphill process for these systems, and the bulky ligand prevents/suppresses olefin substitution and chain transfer to monomer. However, β -hydrogen elimination is still rapid, leading to chain-walking and production of highly branched polymers. As such, it is quite remarkable that (ⁱPrBIP)FeX₂ complexes (Figure 1.7A) show a high activity to produce linear, high-density polyethylene in the presence of MMAO (a modified methylaluminumoxane activator). The activity is even higher than many of the typical metallocene-based

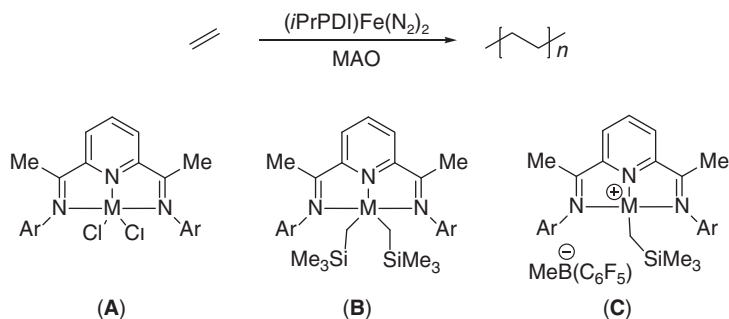


Figure 1.7 Bis(imino)pyridyl complexes used in the polymerization of ethylene.

catalysts [52–54]. The bulky aryl substituents are crucial for the production of high-molecular-weight polymers, presumably because they slow down the rate of chain transfer to the monomer (like Pd). Following these seminal works, Chirik and coworkers developed a new family of related mono- and dialkyl complexes (Figure 1.7B) [55]. The corresponding cationic complex (Figure 1.7C) was obtained by addition of $[\text{PhMe}_2\text{NH}][\text{BPh}_4]$. The cationic complex proved to be even more active and produced polymers with higher molecular weight (MW) and smaller polydispersity than with MMAO-activated catalysts. These results are consistent with chain termination by β -H elimination, which is, however, much slower than olefin insertion into the Fe—C bond of the growing chain.

Interestingly, Gambarotta and Budzelaar re-examined the alkylation process and found that ligand alkylation as well as ligand reduction occurred under the catalytic conditions, at least during the activation process of the bis-halide precursor to the active catalysts with (M)MAO [56, 57]. The newly obtained complexes also proved highly active in olefin polymerization with (M)MAO activators. Hence, the nature of the “real” active species was unclear for a long time. Despite these confusing findings, Chirik was able to show that the “active Brookhart catalyst” involved in the polymerization reaction is a cationic $[(\text{BIP})\text{Fe}^{\text{II}}\text{-alkyl}]$ with an unmodified and non-reduced BIP ligand [50]. As such, it seems that the redox activity of the BIP ligand scaffold is not directly involved in the chain growth process (which is not a redox process anyway). It has been suggested in some reports that an Fe^{III} complex can also be an effective catalyst. From DFT-calculated energy barriers, the Fe^{III} catalyst was found to be more effective during the propagation steps ($10.8 \text{ kcal mol}^{-1}$ for Fe^{III} vs. $14.2 \text{ kcal mol}^{-1}$ for Fe^{II}) [58]. However, the termination/propagation ratio and the experimental polymer MW favor an Fe^{II} catalyst as the active species.

1.3.1.2 Cycloaddition Reactions

Although the redox activity of the BIP ligand does not seem to play a direct role in chain propagation by the Brookhart/Gibson catalysts described above (although it does seem to play a role in the catalyst activation steps), the Chirik group recently reported a number of catalytic reactions in which metal–ligand redox cooperation does seem to play a direct role in some of the key steps of the

catalytic mechanism. This seems to be particularly relevant in a series of [2+2] cycloaddition reactions reported by the Chirik group (see below). Although the redox activity of the BIP ligand is difficult to study under the catalytic conditions, mechanistic model studies clearly revealed the importance of the redox-active BIP ligand. To determine where the electrons end up after oxidative addition, a C—C bond cleavage of biphenylene was explored. The reaction is relatively easy because of the thermodynamic driving force of ring-opening of the trained four-membered ring and formation of two strong metal–aryl bonds in the metal-cyclic product. The electronic structure of the iron metallocycle **D** (Figure 1.8) was studied by a combination of X-ray diffraction, SQUID magnetometry, NMR spectroscopy, X-ray absorption and emission spectroscopies, and DFT. The combined experimental and computational data established an Fe^{III} product with a bis(imino)pyridine radical anion. The net two-electron process occurs with one electron oxidation at the supporting ligand and one electron oxidation at the iron center [59].

Chirik and coworkers applied similar concepts in intramolecular [2+2] cycloaddition reactions (Scheme 1.4, top) [60]. According to the proposed mechanism, initial reaction of the (PDI)FeN₂ complex **E** with the diene substrate forms the corresponding π -complex **F**. Here, both complexes have the BIP ligand in the two-electron reduced form. Complex (**F**) is proposed to undergo a subsequent two-electron oxidative addition process to generate complex **G**. Similar to the above model studies, the electrons required for this transformation are proposed to derive from the reduced ligand, in this case both electrons. Therefore, the iron center can maintain the energetically favorable Fe^{II} oxidation state (instead of the less favorable Fe^{IV} oxidation state). Subsequently, intermediate **G** participates in a two-electron ligand-based reductive elimination reaction to release the product and regenerate the catalyst (**E**). Here, the electron storage capacity of the ligand allows the metal to maintain its stable Fe^{II} oxidation state instead of a high energy Fe⁰ oxidation state. These complexes have also been applied successfully in related enyne cyclizations [61].

The same catalysts are also active in the intermolecular reaction between ethylene and various 1,3-butadienes to form the corresponding derivatives (Scheme 1.4, bottom) [62]. In these reactions, a β -H elimination step follows the initial cycloaddition step. An equimolar mixture of ethylene and butadiene in the presence of 5 mol% iron catalyst at 23 °C afforded the expected vinyl cyclobutane in a good yield. When a methyl group was introduced into the diene, a 1,4-addition of ethylene to the 1,3-diene occurred, as described previously by Ritter and coworkers [63]. The sterically more hindered isoprene

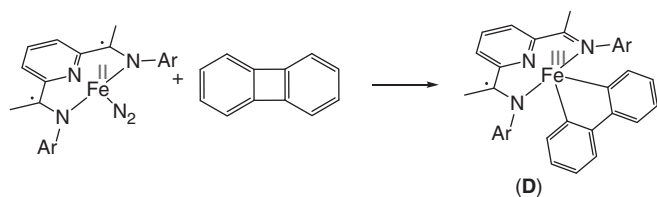
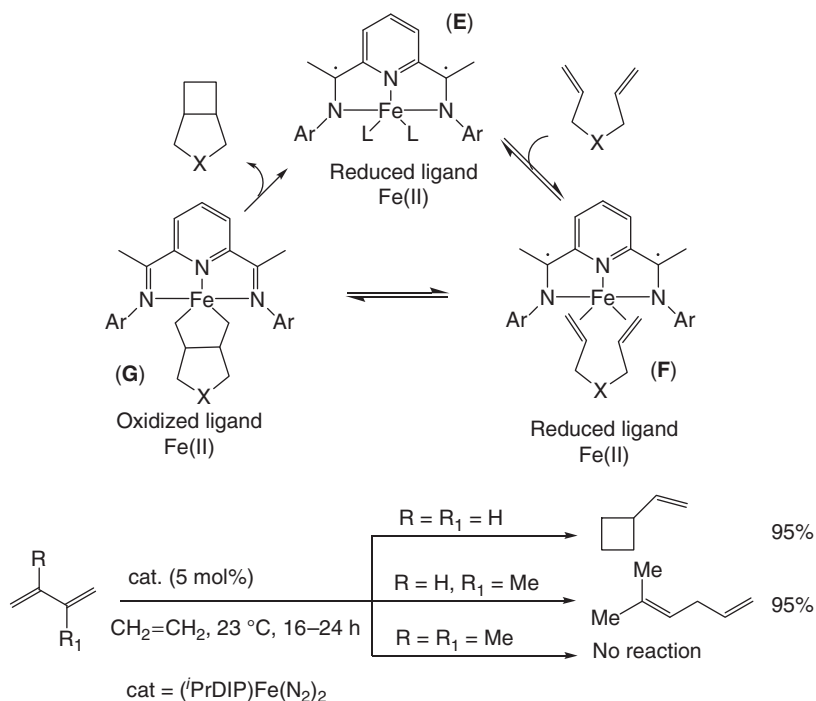


Figure 1.8 Ligand-mediated oxidative addition.



Scheme 1.4 Ligand-mediated cycloaddition reactions.

is a weaker ligand, disfavoring ligand-induced reductive elimination over β -H elimination.

1.3.1.3 Hydrogenation and Hydro-addition Reactions

Addition of H—X (X = H, Si, B, etc.) to alkenes has long relied on precious metal catalysts supported by strong field ligands to enable highly predictable two-electron redox chemistry that constitutes key bond-breaking and bond-forming steps during catalytic turnover. Recent advancements in the field, making efficient use of redox-active ligands, have, however, made it possible to also use base metals for these transformations. Electron transfer from and to the ligand framework in the oxidative addition of H—X bonds and reductive elimination of C—H bonds seems to play an important role in these base metal-catalyzed reactions. Substituted (BIP)Fe(N₂)₂ catalysts exhibit high turnover frequencies at both low catalyst loadings and hydrogen pressures for the hydrogenation of α,β -unsaturated alkenes. Exploration of structure–reactivity relationships established smaller aryl substituents (**I** over **H**) and more electron-donating ligands (**J** over **H**, **I**) resulted in an improved performance [64] (Figure 1.9). Synthesis of enantiopure, C₁ symmetric complex **K** has led to the development of highly enantioselective hydrogenation reactions of substituted styrene derivatives [65].

The observation of improved hydrogenation activity upon introduction of more electron-donating chelates inspired the synthesis of NHC pincer complexes

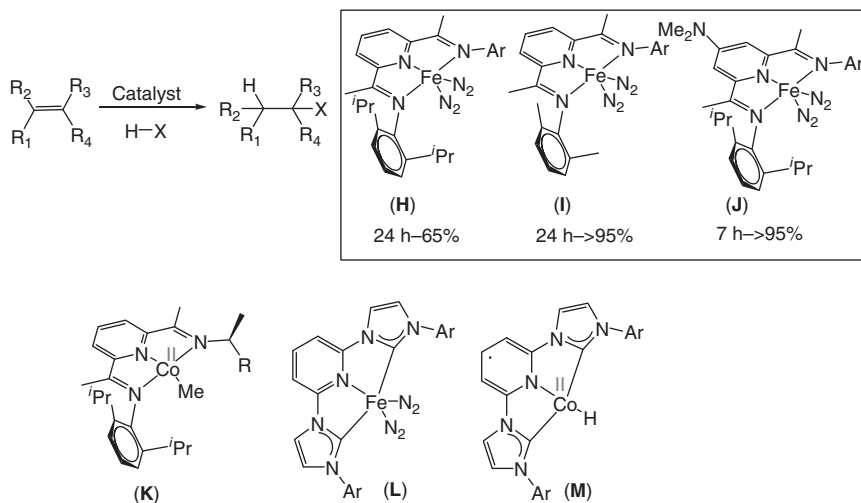


Figure 1.9 Family of BIP-related complexes (H–M) for the hydrogenation of alkenes.

L and **M** [66, 67], which also show high activity for unactivated di-, tri-, and tetra-substituted alkenes [68]. However, in contrast to the BIP ligand complexes, detailed spectroscopic studies indicate that the carbon–nitrogen–carbon (CNC) pincer acts as a classical ancillary ligand without involvement of ligand redox activity [69]. As such, one can conclude that application of strong field ligands, forcing low spin configurations, is a valuable alternative strategy to enable two-electron oxidative addition/reductive elimination reactions at iron and cobalt.

Substituted (BIP)Fe(N₂)₂ complexes have also been successfully applied for hydroboration and isomerization of alkenes with pinacolboranes [70]. An analogous cobalt catalyst has been found to be even more reactive and was applied for hindered alkenes and alkynes as well [71–74]. The mechanism involves selective insertion of an alkynyl boronate ester into a Co–H bond (the oxidative addition product), which was also proven spectroscopically.

Redox non-innocent bis(imino)pyridine complexes of iron have also been successfully applied for hydrosilylation of alkenes. Both PhSiH₃ and Ph₂SiH₂ were found to be effective in silylation and give anti-Markovnikov addition products within minutes [75]. The mechanism is the same as described for hydrogenation and hydroboration. The carbon–silicon bond formation reaction was also studied by the Ritter group using bidentate imino-pyridine complex **N** (Figure 1.10) [76]. The X-ray crystal structure indicates that the C–N bond lengths in the imino functionalities (1.343 ± 0.015 Å) are clearly intermediate between a C–N double bond (c. 1.28 Å) and a single bond (c. 1.46 Å). Similarly, the C–C bond length in the pyridine group is 1.382 ± 0.015 Å, which is the intermediate between a single bond (1.47 Å) and a double bond (1.35 Å). These parameters are clearly indicating a radical anion state of the ligand. The hydrosilylation of carbonyls has also been investigated using manganese complexes **O**, **P** [77]. However, the

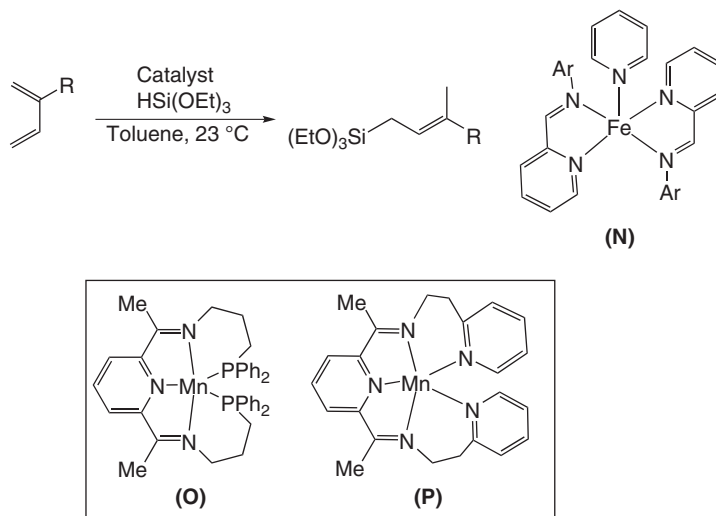


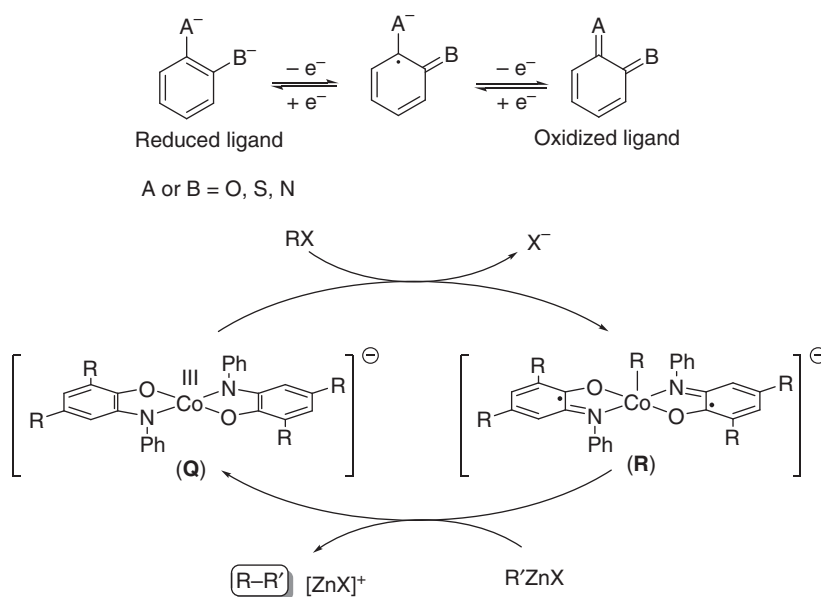
Figure 1.10 N,P Catalysts for hydrosilylation of alkenes.

redox involvement of the non-innocent macrocyclic BIP analog was not detailed or investigated in all these cases.

1.3.2 Other Ligands as Electron Reservoirs

Dithion, catechol, *o*-aminophenol, and *o*-phenylenediamine-type bidentate ligands have also been reported to show non-innocent behavior in combination with base metals (Scheme 1.5, left). The coordination behavior of these ligands in their different oxidation states has been studied in great detail [78, 79]. The ligands have three oxidation states (for 1,2-diol, it is catecholato in the fully reduced form, semiquinonato in the one-electron oxidized form, and quinone in the fully oxidized form). The phenyl backbone of these ligands is often substituted to tune the electronic properties, prevent unwanted radical–radical coupling reactions, and stabilize different oxidation states. Very recently, Pinter, de Proft, and coworkers reported a DFT study, which revealed that the reduced ligands strengthen the metal–ligand bonds, resulting in stabilized $M-L^{-1/2}$ configurations [80]. This strongly contributes to the overall thermodynamic driving force for ligand-centered electron transfer.

A key development in the field of C–C coupling involving redox-active ligands coordinated to a Co center came from the work of Soper and coworkers [81]. The unusual square planar nucleophilic triplet ground state of the Co^{III} bis-iminophenolate (Scheme 1.5, **Q**) is able to accommodate the formal oxidative addition of an alkyl fragment to yield a five-coordinate square pyramidal Co^{III} species (Scheme 1.5, **R**) with anti-ferromagnetically coupled ligand diradicals. Subsequently, the complex can transfer a formal R^+ group to either aryl or alkyl zinc bromides to yield the corresponding C–C coupled products. This sets the stage for further development of catalytic cross-coupling methodologies involving first-row metals, exploiting the role of redox-active ligands.



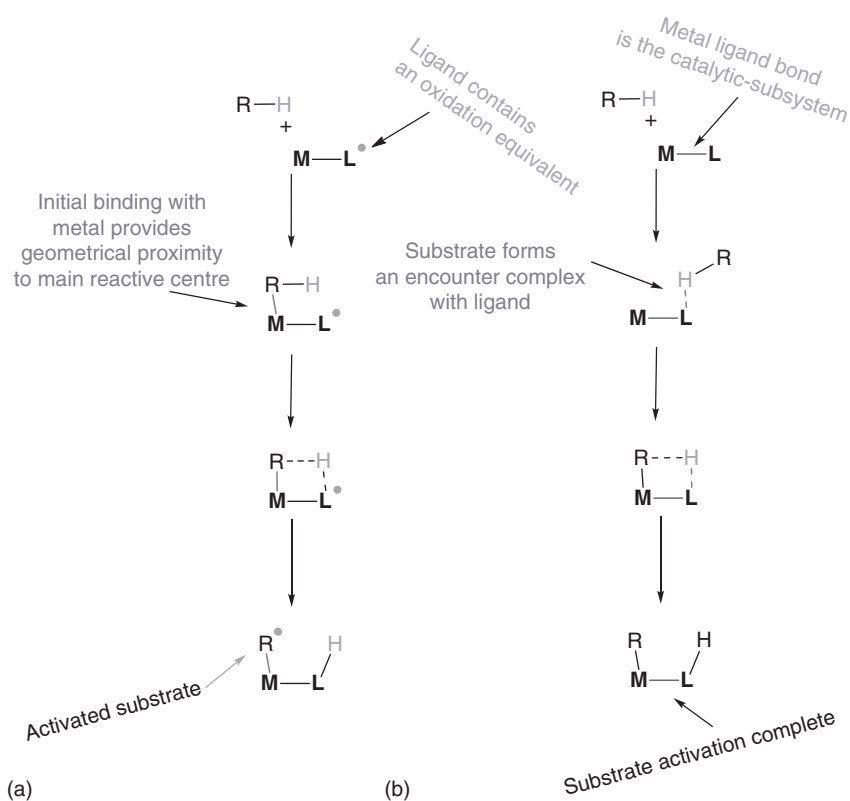
Scheme 1.5 Catechol-derived redox non-innocent ligands reported in literature (left) and corresponding cobalt reactivity (right).

Other types of coupling reactions have also been reported with base metals such as canonical Ni⁰-catalyzed Kumada coupling between an aryl bromide and an aryl Grignard reagent [82] and homodimerization of benzyl halide [83]. The coupling reaction proceeds via a similar mechanism as the corresponding noble-metal-catalyzed reaction. The ligand-assisted oxidative addition product has been successfully isolated and characterized by Chaudhuri, Fensterbank, and coworkers [84, 85].

1.4 Cooperative Ligands

In cooperative catalysis, the metal and the ligand act together to activate the substrate. This is a useful approach to enhance and control the reactivity of (first-row) transition metals in catalytic reactions. The first and most well-known examples are catalysts containing ligands that function as internal bases or acids, as pioneered by Noyori, Beller and Milstein for noble metal catalysis [86, 87]. However, catalysts containing other reactive ligand moieties such as ligand radicals are gradually being explored as well (Scheme 1.6).

In the cooperative mode of action, the substrate may initially bind to the metal [88–91] or directly interact with the reactive part of the ligand [92]. These initial interactions are key to bringing the substrate geometrically close and physically accessible to the main reactive center. Scheme 1.6 illustrates the general substrate activation in cooperative non-innocent ligand catalysis. The substrate activation usually involves abstraction of a hydrogen atom or a proton from the substrate.



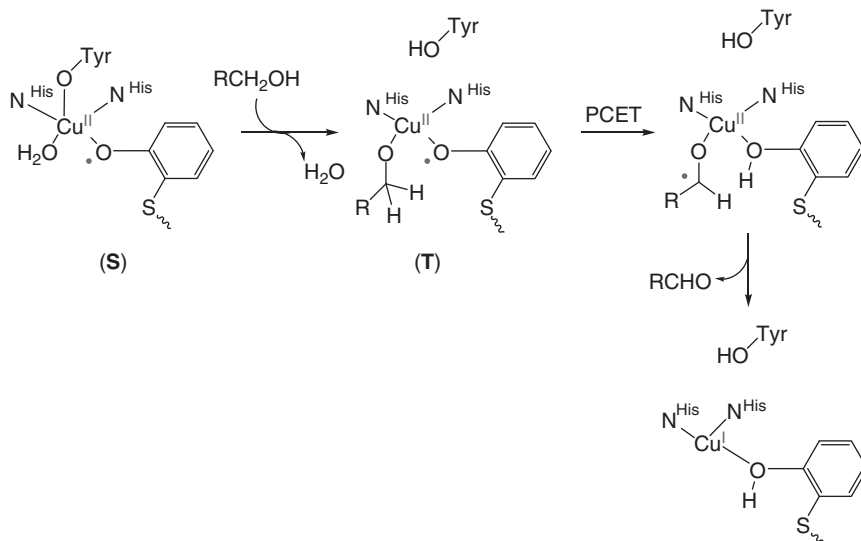
Scheme 1.6 Substrate activation by a cooperative ligand: (a) substrate activation involving ligand radicals and (b) substrate activation by the ligand acting as an internal base.

1.4.1 Cooperative Reactivity with Ligand Radicals

1.4.1.1 Galactose Oxidase (GOase) and its Models

Perhaps the most studied example of cooperative reactivity involving the reactivity of a ligand radical is the alcohol oxidation reaction catalyzed by the enzyme galactose oxidase (GOase). The first step in galactose oxidation by this enzyme is activation via one-electron oxidation of the sulfur-modified tyrosine-272 moiety to form an oxygen-centered (tyrosyl) radical (Scheme 1.7, **S**). The CH_2OH group on the galactose binds over the $\text{Cu}-\text{O}-\text{Tyr-495}$ bond to form the Cu(II) alkoxide complex **T** with the release of TyrOH (Scheme 1.7). Subsequent proton-coupled electronic transfer (PCET) shifts the radical to the galactose-alkoxide moiety, which, in turn, reduces the Cu(II) center of the enzyme to Cu(I) with the formation of the oxidized product. The reduced enzyme then reacts with dioxygen via a PCET pathway to form H_2O_2 , hence completing the catalytic cycle.

In this mechanism, the metal and the ligand cooperate to facilitate the reaction. The initial enzyme activation produces a chemically active oxygen-centered radical. However, this radical alone is incapable of performing the selective reaction. Binding of the substrate to the metal center is also essential to bring

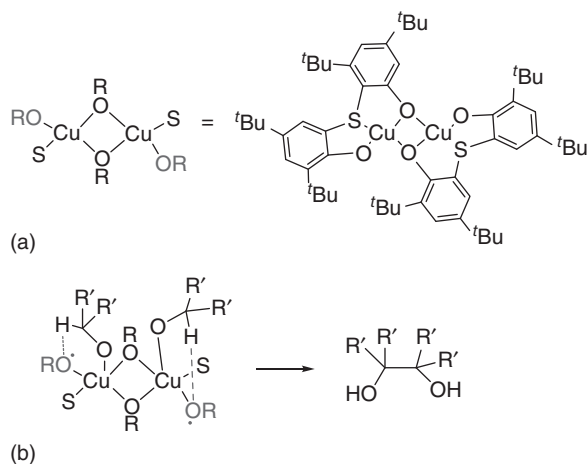


Scheme 1.7 Key steps in substrate activation and catalysis by the enzyme galactose oxidase.

the substrate and the ligand-centered radical close together. This geometrical arrangement enables the actual bond activation process. Subsequent electron transfer from the activated substrate to the metal is also important, hence the need of the redox-active Cu metal in the enzyme.

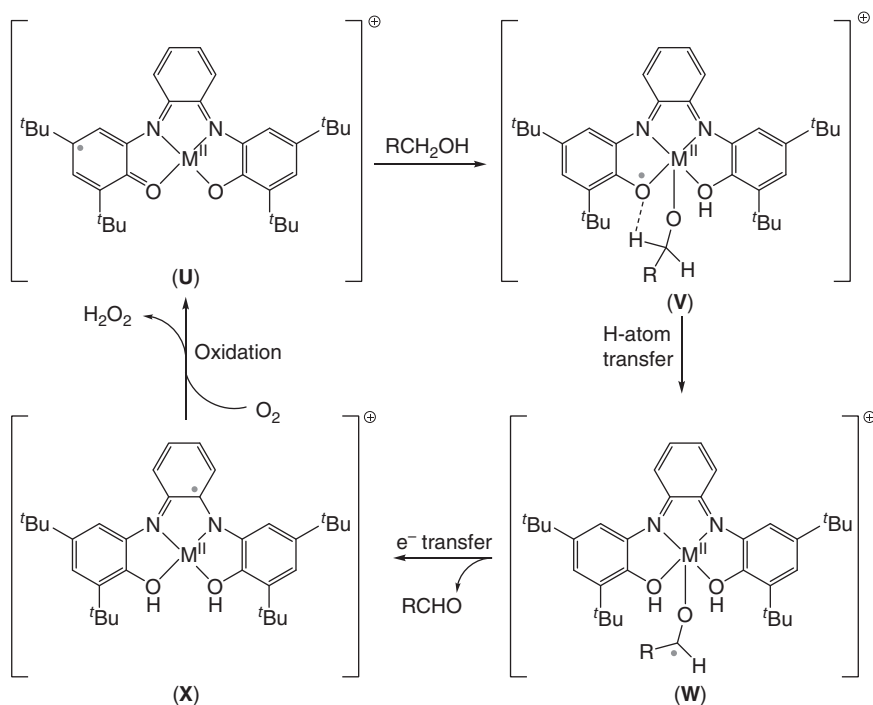
Analogous to the GOase system, Wieghardt and coworkers [90] reported a bioinspired Cu^{II}–thiophenol catalytic system (Figure 1.11). The initial catalyst activation step occurs by cooperative activation of the catalyst and the ligand to form a diradical system. In contrast to the GOase enzyme, this system has biradical characteristics. Therefore, it can carry out oxidation of two primary alcohols in a single catalytic turnover, enabling alcoholate-derived radical C–C coupling reactions with the formation of secondary diols.

Figure 1.11 (a) Cu(II)–thiophenol-based catalyst described by Wieghardt and Chaudhary. (b) Activation of two alcohol molecules.



1.4.1.2 Alcohol Oxidation by Salen Complexes

The Zn–Salen catalyst (Scheme 1.8) reported by Wiegardt and coworkers [91] is another good example of catalysis carried out by a ligand radical. Remarkably, this system works even with the redox inert Zn^{2+} metal ion (having a completely filled d -shell). The highly conjugated ligand framework presents the possibility to store an oxidizing equivalent on the ligand, which can be used to drive alcohol oxidation catalysis. The substrate first gets deprotonated over the metal–oxygen bond and the resulting alkoxide binds to the metal to form complex **V** (Scheme 1.8). Zn^{2+} is needed to bring the substrates together, but the bond-breaking processes are entirely based on ligand in this case.



Scheme 1.8 Catalytic cycle for alcohol oxidation by salen complexes.

In the same manner as the GOase enzyme, the metal substrate binding affords a favorable geometry, where the substrate can interact with the oxygen-centered radical to form an alcoholate complex (**W**) via a PCET mechanism. The cycle is completed by elimination of the aldehyde product and reoxidation of the reduced catalyst complex (**X**) by a dioxygen molecule to evolve H_2O_2 . The same mechanism is also proposed for the corresponding copper complex, despite Cu being redox active.

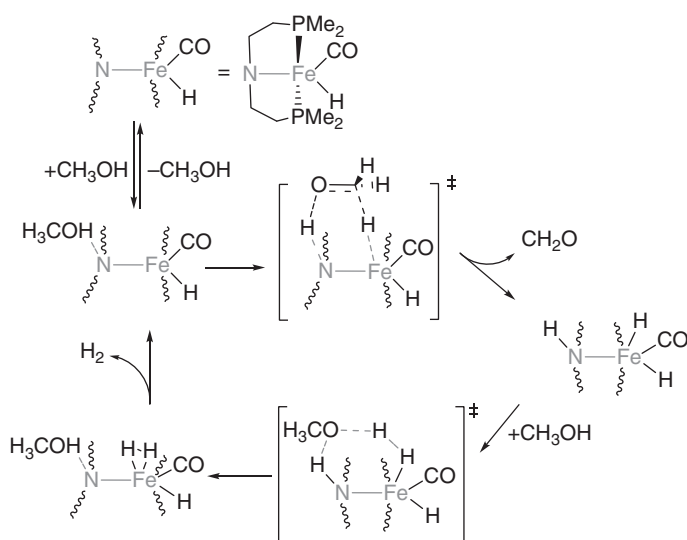
1.4.2 Base Metal Cooperative Catalysis with Ligands Acting as an Internal Base

Several well-described catalysts containing ligands that function as an internal base or acid were pioneered by Noyori, Beller and Milstein, initially using

primarily noble metals [86, 87]. Application of these types of ligands to use base metals in catalysis is widely setting the stage though, and in several cases, the use of cooperative ligands to shift part of the reactivity from the metal to the ligand is taken to advantage. Some illustrative recent examples are discussed below.

1.4.2.1 Fe–Pincer Complexes

The Fe–pincer system reported by Holthausen and coworkers [92] catalyzes oxidation of methanol, methanediol, and formic acid to CO_2 with the release of H_2 . The Fe–N bond is the active catalytic subsystem in this case over which the whole catalytic cycle is carried out cooperatively. In contrast to the above examples of GOase and Cu–thiophenol systems (Section 1.4.1), the substrate first interacts with the ligand (Scheme 1.9). This brings the substrate in proximity to the metal to drive the cooperative double oxidation of the substrate over the Fe–N bond. The catalyst releases formaldehyde, which is thought to convert to methanediol for further dehydrogenation to CO_2 . Dihydrogen is believed to be released from the FeH–NH moiety, aided by approach of another alcohol substrate molecule (Scheme 1.9).



Scheme 1.9 Cooperative activation and oxidation of methanol over an iron–pincer complex.

The catalyst is also believed to catalyze the proposed hydrolysis of formaldehyde to methanediol, as is required for further dehydrogenation (Figure 1.12). The carbonyl carbon in formaldehyde is susceptible to attack by a nucleophile. However, splitting a single water molecule over the $\text{C}=\text{O}$ bond is energetically unfavorable. This process can be accelerated by another water molecule, which leads to a more relaxed transition state (TS) geometry (Figure 1.12a). The second water molecule assists in the polarization of the water molecule to generate the nucleophile–electrophile (OH^- – H^+) pair. The Fe–N bond in the catalyst further stabilizes this process by allowing for spontaneous splitting of a water molecule (Figure 1.12b). This generates the nucleophile–electrophile pair in a relatively

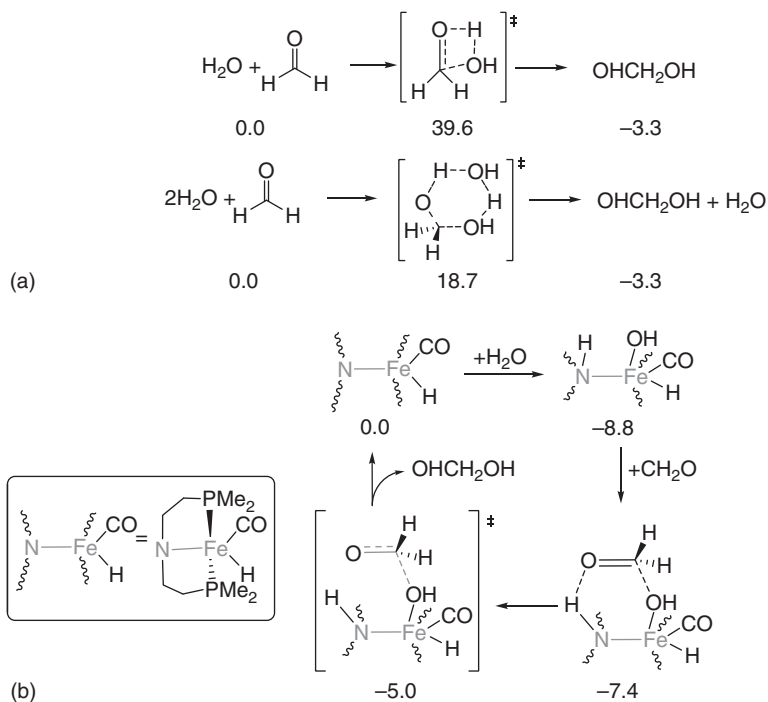


Figure 1.12 Cooperative activation of formaldehyde by an iron–pincer complex.

easy manner. The formaldehyde molecule can now easily be attacked by the hydroxide ligand at the metal to produce methanediol in a formaldehyde/water mixture. Once formed, methanediol is believed to undergo similar “alcohol” activation steps as described in Scheme 1.9.

1.4.2.2 Ligands Containing a Pendant Base

Activation of dihydrogen by base metals is still a challenging reaction in homogeneous catalysis. Catalytic systems that can bind and cleave molecular hydrogen are of particular interest in this regard. Inspired by the Fe–hydrogenase enzyme, DuBois and coworkers [93] proposed a mononuclear nickel complex that contains cyclic diphosphine ligands (Figure 1.13). Nitrogen bases were also incorporated in the ligand backbone. Because of the close proximity of the base around the metal, these are typically known as pendant bases. The system reported by Dubois and coworkers is able to reversibly bind and cleave dihydrogen by cooperative activation of the metal center and the pendant base. The molecular hydrogen molecule initially forms a sigma complex with the metal, which acidifies the molecule for cooperative proton abstraction by the nitrogen base, so to catalyze cleavage of the dihydrogen bond. Further improvements in the nickel-based catalytic system were also reported by varying the substituents on the ligand [94]. Chen and Yang [95] recently demonstrated the potential for applications of pendant bases with an iron center to catalyze the production of methanol from CO_2 and H_2 mixtures. In principle, the dihydrogen oxidation

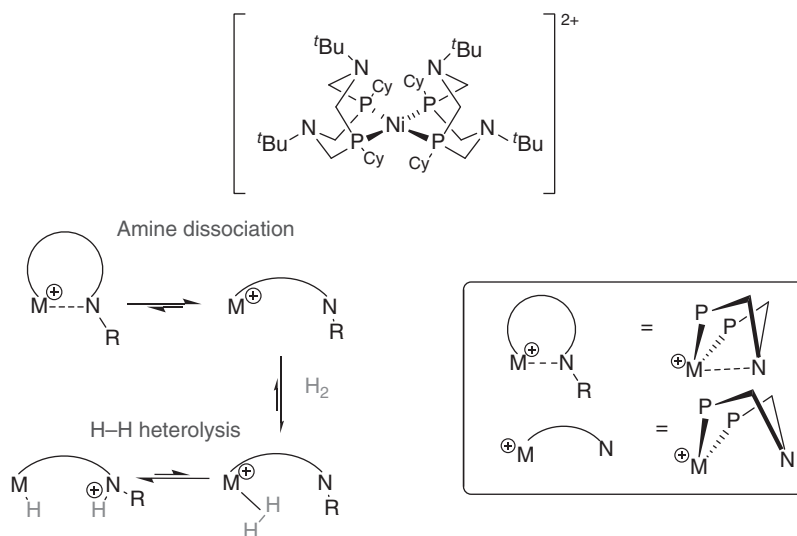


Figure 1.13 Dihydrogen cleavage catalyzed by a metal-pendant nitrogen-based system (DuBois system).

involves the same steps as described for the DuBois system in Figure 1.13. Further details on the DuBois system are described in Chapter 18.

Over the years, pendant catalysts for hydrogen oxidation have also been reported for other iron [96–99] and manganese [100] complexes. The catalytic activity in these systems is largely determined by the geometry of the ligand and the N-metal distance. In general, the metal center is responsible for electronic control of the catalysis and the pendant base controls the protonation step [99]. This cooperative activation thereby enables substrate activation, which is inaccessible without the functionalized ligand.

1.5 Substrate Radicals in Catalysis

Quite recently, several examples of catalytic reactions were disclosed in which formation and detection of discrete metal-bound substrate radicals was reported. These substrate-derived ligand radicals play a key role in a variety of synthetically useful C–C, C–N, and C–O bond formation reactions. These reactions proceed almost without exception via one-electron substrate activation and subsequent controlled radical steps (Figure 1.14). The carbene–radical and nitrene–radical examples discussed in this section provide perhaps the most clear-cut examples of the usefulness of ligand/substrate “non-innocence” involvement in catalysis.

Transition metal carbenes ($\text{M}=\text{CR}_2$) and nitrenes ($\text{M}=\text{NR}$) are the most clear-cut examples for which one-electron activation of the substrate has been well documented in the chemistry of non-noble metals [7, 101]. They are usually formed by addition of a high-energy carbene or nitrene precursor,

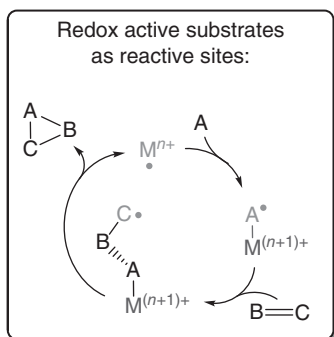


Figure 1.14 One-electron substrate activation and subsequent controlled radical steps.

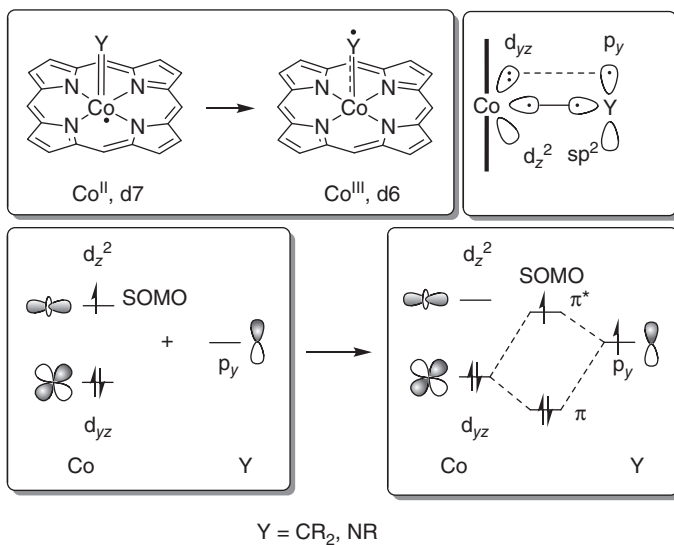


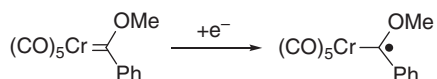
Figure 1.15 Electron transfer from metal to substrate (transformation of a metalloradical into a substrate radical).

such as diazo compounds (to generate carbenes) or iminoiodanes/azides (to generate nitrenes). By choosing a specific combination of a first-row transition metal and spectator ligands, one-electron transfer can occur from the metal to the metal-bound carbene or nitrene moiety, thus forming a carbon- or nitrogen-centered radical. The initial metalloradical is transferred to an organic radical, bound to the metal, and the formed species are typically called "carbene radicals" or "nitrene radicals." This specific situation occurs only when the energy level of the p_y orbital of the carbene or nitrene is lower than the d_z^2 orbital of the metal (Figure 1.15).

1.5.1 Carbene Radicals

Carbene radicals are perhaps one of the most useful "non-innocent" substrates to react via well-defined and controlled radical-type reactions in the coordination

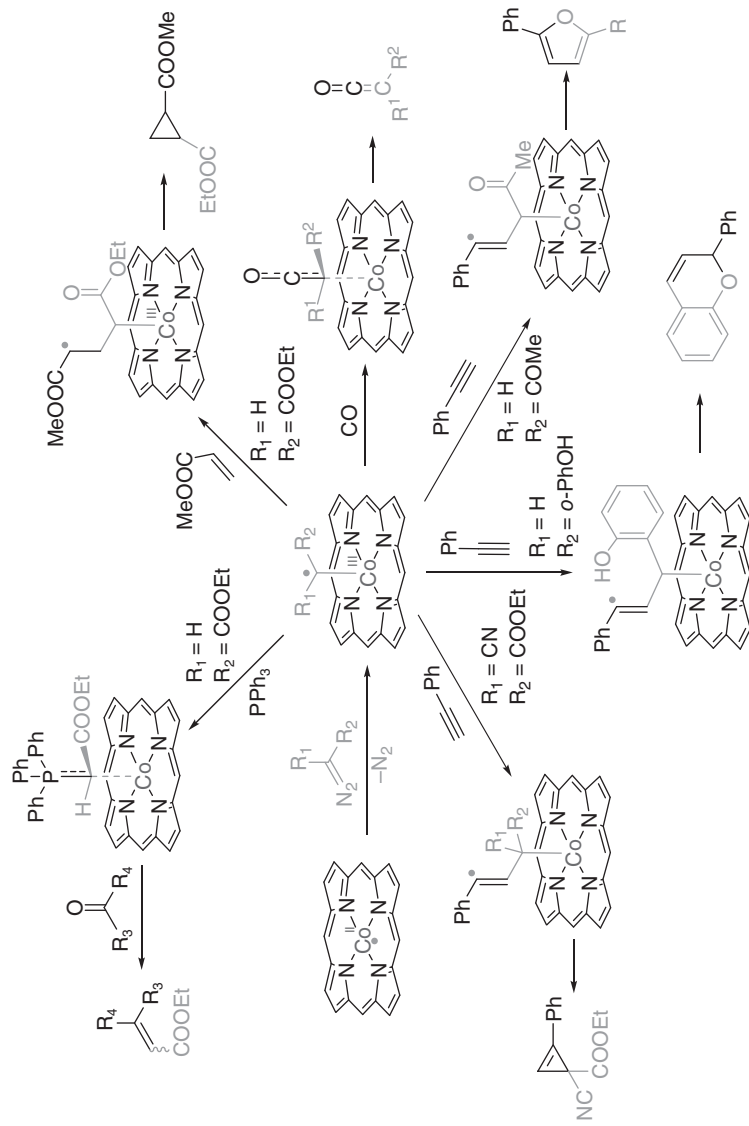
sphere of base metals. The first carbene radicals bound to non-noble transition metals were reported by the group of Casey in the 1970s [102, 103]. The radical was obtained by one-electron reduction of Fischer-type carbenes using external reducing agents (Scheme 1.10). Fischer-type carbene complexes behave as electrophilic species with their LUMO centered on the carbene carbon atom, and hence, the reduction occurs at the carbene carbon rather than the metal. Several examples have been reported involving early transition metal complexes of group 6 (Cr, Mo, and W), which, in most cases, were reduced by sodium/potassium alloy. Formation of persistent carbon-centered radical anions at $-50\text{ }^{\circ}\text{C}$ has been confirmed using electron paramagnetic resonance (EPR) spectroscopic measurements. However, none of these early examples were used in catalysis, and they were long considered to be just chemical curiosities.



Scheme 1.10 First example of a carbene radical complex by Casey and coworkers.

More recently, however, a series of base metal-catalyzed reactions were developed, in which carbene radicals are generated directly upon reaction of a carbene precursor with a metalloradical catalyst. In other words, the carbene radical formation involves a direct $1e^-$ reduction of the carbene by the same metal complex that facilitates its formation [104, 105]. As a direct result of the redox process being intramolecular, the carbene radical is formed without the need of an external reducing agent, in a catalytic manner. It was determined that low spin Group 9 transition metal complexes with metals in the +II oxidation state such as Co^{II} are suitable. The groups of Zhang and De Bruin have detected formation of carbene radicals upon metalloradical activation of diazo compounds (or their tosylhydrazone precursors) by cobalt(II) porphyrin ($[\text{Co}(\text{por})]$) complexes, using complementary techniques such as DFT and EPR [106]. Conclusive evidence of the existence of carbene radicals bound to metal complexes has been brought forward. Subsequently, several catalytic reactions have been developed in which C—C, C—O, and C—H bonds are formed by the involvement of carbene radicals (Scheme 1.11).

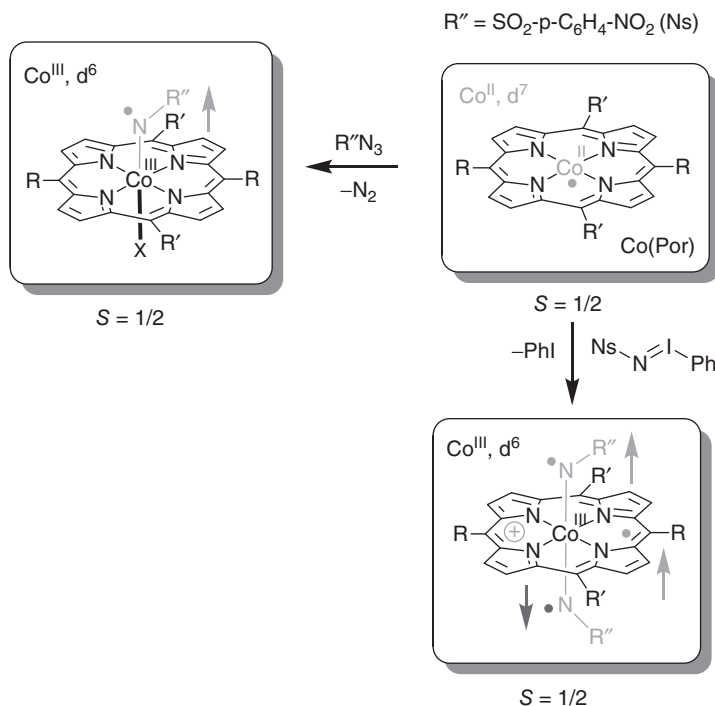
These examples include cyclopropanation [107, 108] C—H activation [109], cyclo-propanation [110], as well as ketene [111], alkene [112], 2*H*-chromene [113], furane [114], and indene [115] formation (Scheme 1.11). They all have in common the use of a substituted cobalt(II) porphyrin as the catalyst and a diazo or tosylhydrazone as a high-energy substrate to generate the carbene radical intermediate. After formation of the intermediate radical species, trapping it with different substrates such as alkenes, alkynes, carbon monoxide, or ketones yields an entire series of substituted organic molecules (Scheme 1.11). The reactivity difference between the carbene radical and that of a Fischer carbene is attributed to the more nucleophilic character of the radical. The radical can easily react with, for example, electron-deficient alkenes during cyclopropanation, making this method complementary to the more classical approaches toward cyclopropanation [116–118].



Scheme 1.11 Examples of metalloradical Co(por)-catalyzed reactions with carbene radicals as intermediates.

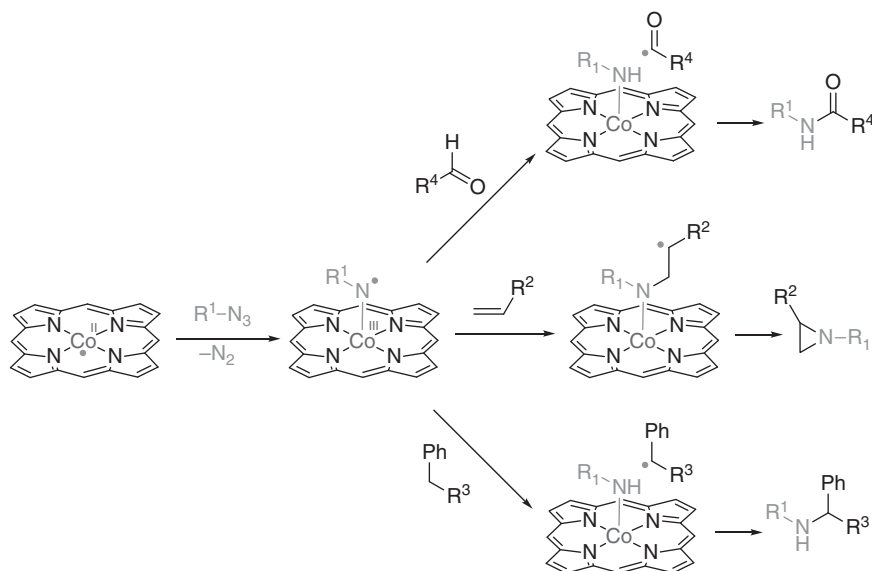
1.5.2 Nitrene Radicals

Similar to the formation of carbene radicals, using azides or iminoiodanes as substrates instead of diazo compounds results in nitrene formation [119]. In the presence of $[\text{Co}^{\text{II}}(\text{por})]$ complexes, reduction by one electron of the nitrene is favored, thus generating a nitrogen-based organic radical. Depending on the source of the nitrene transfer reagent, either a mono-nitrene radical or bis-nitrene radicals can be formed, giving rise to interesting reactivity in catalysis (Scheme 1.12). Compared to their carbene counterparts, nitrene radicals are more persistent in solution, thus allowing for detection at room temperature using a variety of spectroscopic techniques [120].



Scheme 1.12 Formation of bis-nitrene (left) and mono-nitrene (right) radicals.

Several examples of catalytic reactions in which nitrene radicals have been proposed and detected as intermediates are shown in Scheme 1.13. Addition to double bonds gives rise to aziridines [121], and activation of benzylic [122] or aldehydic [123] C—H bonds produces secondary amines or amides, respectively. Nitrene radical intermediates are more prone to C—H activations than their carbene equivalents, which are more susceptible to additions. Cobalt complexes are not the only species that can give rise to metalloradical catalysis involving nitrene radicals. Betley and coworkers proposed an Fe^{II} complex that can react with organic azides forming formally one-electron reduced nitrenes and catalytically activating benzylic C—H bonds to form secondary amines [124].



Scheme 1.13 Examples of metalloradical Co(Por)-catalyzed reactions with nitrene radicals as intermediates.

1.6 Summary and Conclusions

Material scarcity and environmental issues emerge an increasing demand on the development of new, cheap, and selective catalysts for sustainable synthesis in a variety of processes. As such, replacing noble metals by cheaper base metals in homogeneous catalysis is tremendously desirable. "Non-innocent" ligands offer several opportunities to achieve this goal. At its core, homogeneous catalysis is based on the properties of a metal complex and its surrounding ligands. Therefore, choosing the right combination of the metal and its surrounding ligands is key to the development of new catalysts. The use of "non-innocent" ligands goes beyond that of classical ancillary ligands, and a "non-innocent" ligand is typically directly involved in one of the key elementary steps of a catalytic reaction. In a broad description, "non-innocent" ligands act synergistically with the metal to enhance the selectivity and activity of the catalyst. In some cases, they facilitate reactions at base metals that are normally reserved to noble metals. In other cases, they enable entirely new reaction pathways.

Besides the classical ancillary ligands, four classes of "non-innocent" ligands can be distinguished in the field of base metal catalysis: (i) Stimuli-responsive ligands are mainly used in the development of switchable catalysts, in which external stimuli such as pH, light, or ligand-based redox reactions modify the properties of the ligand, and thereby the catalyst. (ii) Redox-active ligands are ligands that act as electron reservoirs, which are useful to facilitate two-electron elementary steps such as oxidative addition and reductive elimination at first-row transition metals, which more typically prefer one-electron transformations. (iii) Cooperative ligands participate actively in substrate bond-breaking and

bond-making processes, most typically in a synergistic manner with metal participation. Hydrogen atom or proton abstraction from the substrate by the ligand is most typically observed for this class of ligands. (iv) The last class of “non-innocent” ligands are coordinated substrates that behave as redox-active ligands. One-electron transfer from the first-row transition metal to the coordinated substrate leads to formation of discrete “substrate radicals,” which actively participate in a variety of catalytic radical-type transformations, giving access to a wide variety of ring-closing and C—H bond functionalization reactions.

Further developments in the field, taking advantage of the intrinsic reactivity of the ligand acting in synergy with the metal, will likely lead to many exciting new discoveries in the near future. This is expected not only to enable the replacement of noble metals in several important processes in homogeneous catalysis but also to uncover new reactivity with various synthetic possibilities. Controlled catalytic radical-type reactions, especially those in which all open-shell elementary steps occur in the coordination sphere of the metal without the formation of “free radicals,” provide exciting possibilities for future development of base metal catalysis taking advantage of the “non-innocent” nature of ligands and substrates.

References

- 1 Grützmacher, H. (2008). *Angew. Chem. Int. Ed.* 47: 1814–1818.
- 2 van der Vlugt, J.I. and Reek, J.N.H. (2009). *Angew. Chem. Int. Ed.* 48: 8832–8846.
- 3 Jørgensen, C.K. (1966). *Coord. Chem. Rev.* 1: 164–178.
- 4 Kaim, W. and Schwederski, B. (2010). *Coord. Chem. Rev.* 254: 1580–1588.
- 5 Kaim, W. (1987). *Coord. Chem. Rev.* 76: 187–235.
- 6 Lyaskovskyy, V. and de Bruin, B. (2012). *ACS Catal.* 2: 270–279.
- 7 Luca, O.R. and Crabtree, R.H. (2013). *Chem. Soc. Rev.* 42: 1440–1459.
- 8 Trincado, M. and Grützmacher, H. (2015). Cooperating ligands in catalysis. In: *Cooperative Catalysis: Designing Efficient Catalysts for Synthesis* (ed. R. Peters). Weinheim: Wiley-VCH Verlag GmbH & Co. KGaA. doi: 10.1002/9783527681020.ch3.
- 9 van de Vlugt, J.I. (2012). *Eur. J. Inorg. Chem.* 3: 363–375.
- 10 Crabtree, R.H. (2009). *The Organometallic Chemistry of the Transition Metals*, 5e. Hoboken, NJ: John Wiley & Sons.
- 11 Egorova, K.S. and Ananikov, V.P. (2016). *Angew. Chem. Int. Ed.* 40: 12150–12162.
- 12 Crabtree, R.H. (2011). *New J. Chem.* 35: 18–23.
- 13 Allgeier, A.M. and Mirkin, C.A. (1998). *Angew. Chem. Int. Ed.* 37: 894–908.
- 14 Kotz, J.C. and Nivert, C.L. (1973). *J. Organomet. Chem.* 52: 387–406.
- 15 Lorkovic, I.M., Duff, R.R. Jr., and Wrighton, M.S. (1995). *J. Am. Chem. Soc.* 117: 3617–3618.
- 16 Yeung, L.K., Kim, J.E., Chung, Y.K. et al. (1996). *Organometallics* 15: 3891–3897.
- 17 Luca, O.R., Gustafson, J.L., Maddox, S.M. et al. (2015). *Org. Chem. Front.* 2: 823–848.

- 18 Süßner, M. and Plenio, H. (2005). *Angew. Chem. Int. Ed.* 44: 6885–6888.
- 19 Savka, R., Foro, S., Gallei, M. et al. (2013). *Chem. Eur. J.* 19: 10655–10662.
- 20 Arumugam, K., Varnado, C.D., Sproules, S. et al. (2013). *Chem. Eur. J.* 19: 10866–10875.
- 21 Gregson, C.K.A., Gibson, V.C., Long, N.J. et al. (2006). *J. Am. Chem. Soc.* 128: 7410–7411.
- 22 Wang, X., Thevenon, A., Brosmer, J.L. et al. (2014). *J. Am. Chem. Soc.* 136: 11264–11267.
- 23 Balof, S.L., P'Pool, S.J., Berger, N.J. et al. (2008). *Dalton Trans.* 42: 5791–5799.
- 24 Li, L., Wang, J., Zhou, C. et al. (2011). *Green Chem.* 13: 2071–2077.
- 25 Peeck, L.H., Leuthäusser, S., and Plenio, H. (2010). *Organometallics* 29: 4339–4345.
- 26 Wang, W., Wu, J., Xia, C., and Li, F. (2011). *Green Chem.* 13: 3440–3445.
- 27 Wang, W., Zhang, G., Lang, R. et al. (2013). *Green Chem.* 15: 635–640.
- 28 Gaulier, C., Hospital, A., Legeret, B. et al. (2012). *Chem. Commun.* 48: 4005–4007.
- 29 Onishi, N., Xu, S., Manaka, Y. et al. (2015). *Inorg. Chem.* 54: 5114–5123.
- 30 Himeda, Y., Onozawa-Komatsuzaki, N., Miyazawa, S. et al. (2008). *Chem. Eur. J.* 14: 11076–11081.
- 31 Suna, Y., Ertem, M.Z., Wang, W.H. et al. (2014). *Organometallics* 33: 6519–6530.
- 32 Himeda, Y., Miyazawa, S., and Hirose, T. (2011). *ChemSusChem* 4: 487–493.
- 33 Manbeck, G.F., Muckerman, J.T., Szalda, D.J. et al. (2015). *J. Phys. Chem. B* 119: 7457–7466.
- 34 Lv, R., Wang, Y., Zhou, C. et al. (2013). *ChemCatChem* 5: 2978–2982.
- 35 Badiei, Y.M., Wang, W.H., Hull, J.F. et al. (2013). *Inorg. Chem.* 52: 12576–12586.
- 36 Akita, M. (2011). *Organometallics* 30: 43–51.
- 37 Neilson, B.M. and Bielawski, C.W. (2013). *ACS Catal.* 3: 1874–1885.
- 38 Sud, D., Norsten, T.B., and Branda, N.R. (2005). *Angew. Chem. Int. Ed.* 44: 2019–2021.
- 39 Chirik, P.J. and Wieghardt, K. (2010). *Science* 327: 794–795.
- 40 Chirik, P.J. (2011). *Inorg. Chem.* 50: 9737–9914.
- 41 de Bruin, B., Bill, E., Bothe, E. et al. (2000). *Inorg. Chem.* 39: 2936–2947.
- 42 Budzelaar, P.H.M., de Bruin, B., Gal, A.W. et al. (2001). *Inorg. Chem.* 40: 4649–4655.
- 43 Enright, D., Gambarotta, S., Yap, G.P.A., and Budzelaar, P.H.M. (2002). *Angew. Chem. Int. Ed.* 41: 3873–3876.
- 44 Gibson, V.C. and Spitzmesser, S.K. (2003). *Chem. Rev.* 103: 283–315.
- 45 Gibson, V.C. and Solan, G.A. (2011). *Top. Organomet. Chem.* 1–52.
- 46 Bart, S.C., Chlopek, K., Bill, E. et al. (2006). *J. Am. Chem. Soc.* 128: 13901–13912.
- 47 Bart, S.C., Lobkovsky, E., Bill, E. et al. (2007). *Inorg. Chem.* 46: 7055–7063.
- 48 Stieber, S.C.E., Milsmann, C., Hoyt, J.M. et al. (2012). *Inorg. Chem.* 51: 3770–3785.

- 49 Small, B.L., Brookhart, M., and Bennett, A.M.A. (1998). *J. Am. Chem. Soc.* 120: 4049–4050.
- 50 Britovsek, G.J.P., Gibson, V.C., Kimberley, B.S. et al. (1998). *ChemCommun.* 849–850.
- 51 Gibson, V.C., Redshaw, C., and Solan, G.A. (2007). *Chem. Rev.* 107: 1745–1776.
- 52 Bennett, A.M.A. (1998). *EI Du Pont de Nemours and Co*, USA, PCT Int. Appl., WO 9827124.
- 53 Britovsek, G.J.P., Bruce, M., Gibson, V.C. et al. (1999). *J. Am. Chem. Soc.* 121: 8728–8740.
- 54 Britovsek, G.J.P., Mastroianni, S., Solan, G.A. et al. (2000). *Chem. Eur. J.* 6: 2221–2231.
- 55 Bouwkamp, M.W., Lobkovsky, E., and Chirik, P.J. (2005). *J. Am. Chem. Soc.* 127: 9660–9661.
- 56 Scott, J., Gambarotta, S., Korobkov, I., and Budzelaar, P.H.M. (2005). *J. Am. Chem. Soc.* 127: 13019–13029.
- 57 Poli, R. (2011). *Eur. J. Inorg. Chem.* 1513–1530.
- 58 Cruz, V.L., Ramos, J., Martinez-Salazar, J. et al. (2009). *Organometallics* 28: 5889–5895.
- 59 Darmon, J.M., Stieber, S.C.E., Sylvester, K.T. et al. (2012). *J. Am. Chem. Soc.* 134: 17125–17137.
- 60 Bouwkamp, M.W., Bowman, A.C., Lobkovsky, E., and Chirik, P.J. (2006). *J. Am. Chem. Soc.* 128: 13340–13341.
- 61 Sylvester, K.T. and Chirik, P.J. (2009). *J. Am. Chem. Soc.* 131: 8772–8774.
- 62 Russell, S.K., Lobkovsky, E., and Chirik, P.J. (2011). *J. Am. Chem. Soc.* 133: 8858–8861.
- 63 Moreau, B., Wu, J.Y., and Ritter, T. (2009). *Org. Lett.* 11: 337–339.
- 64 Russell, S.K., Darmon, J.M., Lobkovsky, E., and Chirik, P.J. (2010). *Inorg. Chem.* 49: 2782–2792.
- 65 Monfette, S., Turner, Z.R., Semproni, S.P., and Chirik, P.J. (2012). *J. Am. Chem. Soc.* 134: 4561–4564.
- 66 Danopoulos, A.A., Wright, J.A., Motherwell, W.B., and Ellwood, S. (2004). *Organometallics* 23: 4807–4810.
- 67 Yu, R.P., Darmon, J.M., Milsman, C. et al. (2013). *J. Am. Chem. Soc.* 135: 13168–13184.
- 68 Gibson, V.C., Tellmann, K.P., Humphries, M.J., and Wass, D.F. (2002). *Chem. Commun.* 2316–2317.
- 69 Darmon, J.M., Yu, R.P., Semproni, S.P. et al. (2014). *Organometallics* 33: 5423–5433.
- 70 Obligacion, J.V. and Chirik, P.J. (2013). *Org. Lett.* 15: 2680–2688.
- 71 Obligacion, J.V., Neely, J.M., Yazdani, A.N. et al. (2015). *J. Am. Chem. Soc.* 137: 5855–5858.
- 72 Obligacion, J.V. and Chirik, P.J. (2013). *J. Am. Chem. Soc.* 135: 19107–19110.
- 73 Obligacion, J.V., Semproni, S.P., and Chirik, P.J. (2014). *J. Am. Chem. Soc.* 136: 4133–4136.
- 74 Palmer, W.N., Diao, T., Pappas, L., and Chirik, P.J. (2015). *ACS Catal.* 5: 622–626.

- 75 Tondreau, A.M., Atienza, C.C.H., Weller, K.J. et al. *Science* 2012 (6068): 335, 576–570.
- 76 Wu, J.Y., Stanzl, B.N., and Ritter, T. (2010). *J. Am. Chem. Soc.* 132: 13214–13216.
- 77 Mukhopadhyay, T.K., Flores, M., Groy, T.L., and Trovitch, R.J. (2014). *J. Am. Chem. Soc.* 136: 882–885.
- 78 Pierpont, C.G. (2011). *Inorg. Chem.* 50: 9766–9772.
- 79 Poddelsky, A.I., Cherkasov, V.K., and Abakumov, G.A. (2009). *Coord. Chem. Rev.* 253: 291–324.
- 80 Skara, G., Pinter, B., Geerlings, P., and De Proft, F. (2015). *Chem. Sci.* 6: 4109–4117.
- 81 Smith, A.L., Hardcastle, K.I., and Soper, J.D. (2010). *J. Am. Chem. Soc.* 132: 14358–14360.
- 82 Tennyson, A.G., Lynch, V.M., and Bielawski, C.W. (2010). *J. Am. Chem. Soc.* 132: 9420–9429.
- 83 van der Meer, M., Rechkemmer, Y., Peremykin, I. et al. (2014). *Chem. Commun.* 50: 11104–11106.
- 84 Mukherjee, C., Weyhermüller, T., Bothe, E., and Chaudhuri, P. (2008). *Inorg. Chem.* 47: 2740–2746.
- 85 Jacquet, J., Salanouve, E., Orio, M. et al. (2014). *Chem. Commun.* 50: 10394–10397.
- 86 Werkmeister, S., Junge, K., and Beller, M. (2014). *Org. Process Res. Dev.* 18: 289–302.
- 87 Gunanathan, C. and Milstein, D. (2014). *Chem. Rev.* 114: 12024–12087.
- 88 Que, L. and Tolman, W.B. (2008). *Nature* 455: 333–340.
- 89 Whittaker, J.W. (2003). *Chem. Rev.* 103: 2347–2364.
- 90 Chaudhuri, P., Hess, M., Flörke, U., and Wieghardt, K. (1998). *Angew. Chem. Int. Ed.* 37: 2217–2220.
- 91 Chaudhari, P., Hess, M., Müller, J. et al. (1999). *J. Am. Chem. Soc.* 121: 9599–9610.
- 92 Bielinski, E., Förster, M., Zhang, Y. et al. (2015). *ACS Catal.* 5: 2404–2415.
- 93 Henry, R.M., Shoemaker, R.K., DuBois, D.L., and DuBois, M.L. (2006). *J. Am. Chem. Soc.* 128: 3002–3010.
- 94 Yang, J.Y., Chen, S., Dougherty, W.G. et al. (2010). *Chem. Commun.* 46: 8618–8620.
- 95 Chen, X. and Yang, X. (2016). *J. Phys. Chem. Lett.* 7: 1035–1041.
- 96 Liu, T., Chen, S., O'Hagan, M.J. et al. (2012). *J. Am. Chem. Soc.* 134: 6257–6272.
- 97 Liu, T., DuBois, D.L., and Bullock, R.M. (2013). *Nat. Chem.* 5: 228–233.
- 98 Darmon, J.M., Raugei, S., Liu, T. et al. (2014). *ACS Catal.* 4: 1246–1260.
- 99 Liu, T., Wang, X., Hoffmann, C. et al. (2014). *Angew. Chem. Int. Ed.* 53: 5300–5304.
- 100 Hulley, E.B., Helm, M.L., and Bullock, R.M. (2014). *Chem. Sci.* 5: 4729–4741.
- 101 Dzik, W.I., Zhang, X.P., and de Bruin, B. (2011). *Inorg. Chem.* 50: 9896–9903.
- 102 Krusic, P.J., Klabunde, U., Casey, C.P., and Block, T.F. (1976). *J. Am. Chem. Soc.* 98: 2015–2018.

- 103 Block, T.F., Fenske, R.F., and Casey, C.P. (1976). *J. Am. Chem. Soc.* 98: 441–443.
- 104 Fuchibe, K. and Iwasawa, N. (2003). *Chem. Eur. J.* 9: 905–914.
- 105 Dzik, W.I., Xu, X., Zhang, X.P. et al. (2010). *J. Am. Chem. Soc.* 132: 10891–10902.
- 106 Lu, H., Dzik, W.I., Xu, X. et al. (2011). *J. Am. Chem. Soc.* 133: 8518–8521.
- 107 Xu, X., Zhu, S.F., Cui, X. et al. (2013). *Angew. Chem. Int. Ed.* 52: 11857–11861.
- 108 Zhu, S.F., Xu, X., Perman, J.A., and Zhang, X.P. (2010). *J. Am. Chem. Soc.* 132: 12796–12799.
- 109 Cui, X., Xu, X., Jin, L.M. et al. (2015). *Chem. Sci.* 6: 1219–1224.
- 110 Cui, X., Xu, X., Lu, H.J. et al. (2011). *J. Am. Chem. Soc.* 133: 3304–3307.
- 111 Paul, N.D., Chirila, A., Lu, H.J. et al. (2013). *Chem. Eur. J.* 19: 12953–12958.
- 112 Lee, M.Y., Chen, Y., and Zhang, X.P. (2003). *Organometallics* 22: 4905–4909.
- 113 Paul, N.D., Mandal, S., Otte, M. et al. (2014). *J. Am. Chem. Soc.* 136: 1090–1096.
- 114 Cui, X., Xu, X., Wojtas, L. et al. (2012). *J. Am. Chem. Soc.* 134: 19981–19984.
- 115 Das, B.G., Chirila, A., Tromp, M. et al. (2016). *J. Am. Chem. Soc.* 138: 8968–8975.
- 116 Lebel, H., Marcoux, J.F., Molinaro, C., and Charette, A.B. (2003). *Chem. Rev.* 103: 977–1050.
- 117 Davies, H.M.L. and Beckwith, R.E.J. (2003). *Chem. Rev.* 103: 2861–2903.
- 118 Li, A.H., Dai, L.X., and Aggarwal, V.K. (1997). *Chem. Rev.* 97: 2341–2372.
- 119 Olivos Suarez, A.I., Lyaskovskyy, V., Reek, J.N.H. et al. (2013). *Angew. Chem. Int. Ed. Engl.* 52: 12510–12529.
- 120 Goswami, M., Lyaskovskyy, V., Domingos, S.R. et al. (2015). *J. Am. Chem. Soc.* 137: 5468–5479.
- 121 Suarez, A.I.O., Jiang, H.L., Zhang, X.P., and de Bruin, B. (2011). *Dalton Trans.* 40: 5697–5705.
- 122 Lyaskovskyy, V., Suarez, A.I.O., Lu, H.J. et al. (2011). *J. Am. Chem. Soc.* 133: 12264–12273.
- 123 Jin, L.M., Lu, H.J., Cui, Y. et al. (2014). *Chem. Sci.* 5: 2422–2427.
- 124 King, E.R., Hennessy, E.T., and Betley, T.A. (2011). *J. Am. Chem. Soc.* 133: 4917–4923.

