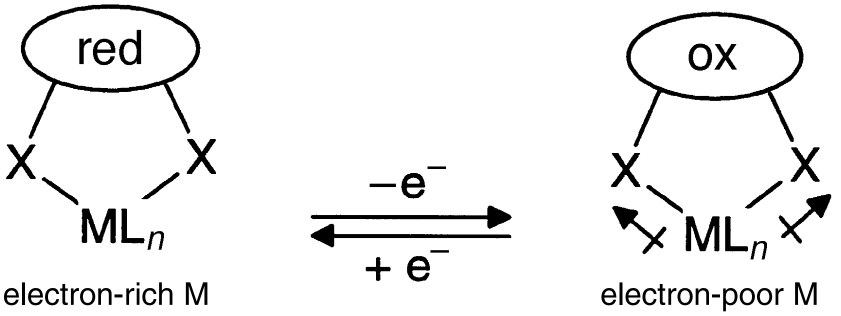
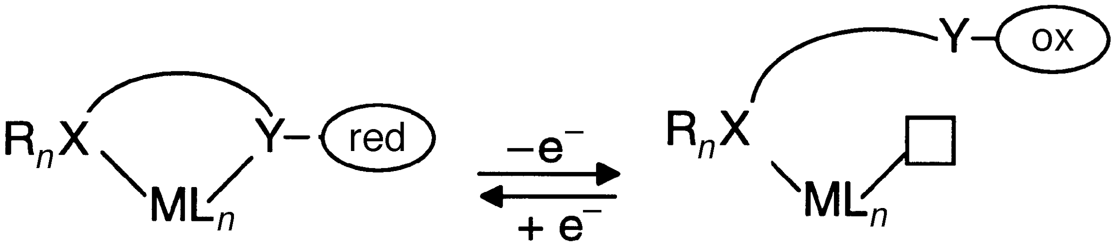
Use of redox-active ligands to control the reactivity of metal complexes

- substitutionally inert redox-switchable ligands



X = strongly binding ligand
Y = weakly binding ligand
R = substituent of tunable electronic nature
□ = ligand or solvent

- redox-switchable hemilabile ligands



- reactive fragment redox-switchable ligands

Three ways to control the stoichiometric and catalytic activity of transition metal complexes by oxidation or reduction of a ligand. More about the design of such ligands is reviewed by A. M. Allgeier and C. A. Mirkin on the following pages.

Ligand Design for Electrochemically Controlling Stoichiometric and Catalytic Reactivity of Transition Metals

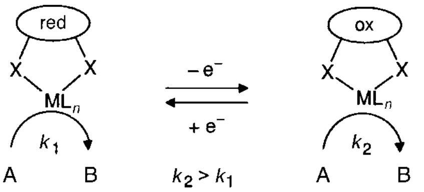
Alan M. Allgeier and Chad A. Mirkin*

Chemists have several tools at their disposal for studying and subsequently controlling reactivity. Recently, redox-active ligands were utilized in novel ways to control the reactivity of transition metal complexes. Several redox-active ligands undergo stable and reversible changes in oxidation state, which allows one to tune the electron richness of the ligand and the bound metal. In this contribution we present an overview of redox-active ligands, which have been categorized into three classes based on their mode of reactivity control. In addition, specific examples are presented which demonstrate the utility of redox-active ligands for controlling metal–ligand binding constants and both stoichiometric and catalytic reactions involving transition metals. In some cases, these oxidation state dependent changes in reactivity can be quite significant, and alter reaction rates by several orders of magnitude and ligand binding constants by many orders of magnitude. Further development of redox-active ligands will be anchored upon a firm understanding of the factors that influence the charge-dependent behavior of transition metal complexes of these ligands. Perspectives on the future direction of research in this area are presented, in particular with respect to the interest in new redox-active groups and potential applications in redox-switchable catalysis and materials for the separation of molecules.

Keywords: cyclic voltammetry • homogeneous catalysis • ligand effects • redox chemistry • substituent effects

1. Introduction

An electrode is one of the most powerful, yet most underutilized, reagents available to the synthetic chemist. It offers an almost unlimited source of or sink for electrons of mechanically tunable (through a potentiostat) free energy. These electrons can be used to effect oxidation or reduction of substrates directly at an electrode surface (e.g. reduction of H^+ to H_2)[1] or, alternatively, they can be used to reversibly interconvert a compound between two useful states of reactivity (Scheme 1). These compounds, which are often referred to as redox switches, have found extensive application in chemistry. The sensitivities of their formal potentials to their electronic and chemical environments have been exploited in the development of sensors for ions[2] and small molecules.[3] A key component of these complexes is a redox-active ligand that can be interconverted between two or more useful oxidation states through a series of applied potentials.



Scheme 1. Redox-active ligands can be used to reversibly alter the reactivity of transition metals. red = reduced form of the ligand, ox = oxidized form of the ligand, A = substrate, B = product.

2. Perspective on Redox-Active Ligands

2.1. Overview of Redox-Active Ligands

Of significant interest to inorganic chemists has been the incorporation of redox-active groups into a variety of metal-binding ligands. Cryptand and crown sequestering agents which incorporate ferrocenyl,[2c, 4] cobaltocenyl,[2d, 5] anthraquinone,[6] and other redox-active groups have been synthesized.[7] These molecules have been used for the electrochemical recognition of alkali and alkaline earth metal cations,[2a,c,d, 4a–c, 7, 8] late transition metals, and some coinage metals.[2d, 4b, 9] They also offer electrochemical control over metal binding constants and have been used in a variety of electrochemically driven metal ion transport systems.[6, 10] In addition, redox switches have been designed for electrochemically detecting a variety of anionic and neutral guest

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species.[2a,d, 11] These areas have been reviewed thoroughly and will not be treated further here.[2a,c,d, 4d]

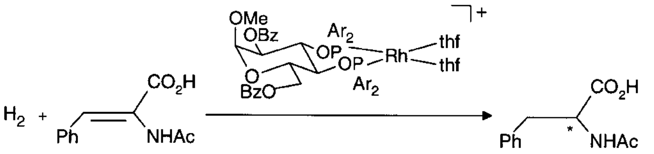
In addition to ligands that can be used to control the thermodynamic binding affinities of transition metals, several redox-active ligands that alter the reactivity of a bound transition metal as a function of ligand oxidation state have been designed and synthesized. This latter group of ligands, which provides electrochemical control over several stoichiometric and catalytic reactions of transition metals, constitutes the topic of this review (Scheme 1). By making use of the different stabilities of oxidation states associated with certain redox-active groups, researchers have designed ligands that when complexed to transition metals yield compounds with electrochemically switchable states of reactivity. Catalysts formed from these ligands may be inactive or sluggish in one oxidation state, but active following oxidation or reduction. Alternatively, they may show selectivities for specific transformations that depend upon the oxidation state of the complex.

Hembre and McQueen recently reported the use of a redox-active ligand as an electron shuttle in a catalytic process.[12] While the presence of the redox-active moiety is essential to the completion of the catalytic reaction, the moiety itself is not used to tune the reactivity of the bound transition metal. Such electrocatalysts are beyond the scope of the present review and will not be discussed further.

2.2. Alternative Methods for Controlling the Reactivity of Transition Metals

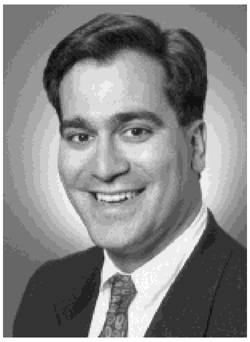
2.2.1. *Ligand Substituent Effects*

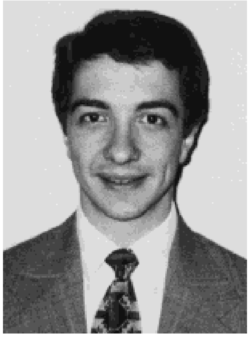
In general, the use of redox-active groups and electrochemistry offers some distinct advantages over complementary synthetic-based approaches to altering the reactivity of transition metals. With a redox-active group, one can control the electron richness of a ligand through mechanically driven electrochemical oxidation or reduction processes without the need for further conventional synthetic steps. Such adjustments in the electronic nature of the ligand can provide corresponding changes in the reactivity of the bound metal. Indeed, there are many examples that demonstrate how subtle changes in the electron-donating properties of a ligand can markedly affect the reactivity of transition metals.[13] For instance, in the enantioselective hydrogenation of acetamidoacrylates, chiral rhodium–diphosphonite catalysts bearing electron-donating substituents incorporated into the aryl (Ar) groups offer higher enantioselectivity than the corresponding catalysts with electron-withdrawing groups [Eq. (a)].[13h] One drawback to the above experiment and others like it is the extensive synthetic work necessary to make ligands with varying degrees of electron richness. In contrast, one redox-active ligand can be shuttled between multiple states of charge and, therefore, multiple states of electron richness by electrochemically driven redox processes without extra conventional synthetic steps. Numerous studies have established a dependence of both stoichiometric[13a] and catalytic reactivity[13b–i] on substituent electronic effects; this bodes well for the use of redox-active ligands in the rational design of complexes with stoichiometric and catalytic chemistries that can be electrochemically controlled.



(a)

Chad A. Mirkin was born in Phoenix, AZ (USA) in 1963. After earning his B.S. in Chemistry at Dickinson College in Carlisle, PA in 1986 and a Ph.D. in Chemistry from the Pennsylvania State University in 1989, he worked as an NSF Postdoctoral Fellow at the Massachusetts Institute of Technology. In 1991 he became an Assistant Professor of Chemistry at Northwestern University; he is currently Charles E. and Emma H. Morrison Professor of Chemistry. He has an interdisciplinary research program aimed at the design, synthesis, and study of surface-confined electroactive materials. For his efforts in this area, he has won numerous awards including the 1998 E. Bright Wilson Award, the 1997 BFGoodrich Collegiate Inventors Award, a Camille Dreyfus Teacher-Scholar Award, an A. P. Sloan Foundation Fellowship, a Beckman Young Investigator Award, an ONR Young Investigator Award, a DuPont Young Professor Award, and an NSF Young Investigator Award.

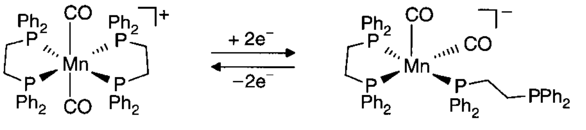

C. A. Mirkin


A. M. Allgeier

Alan M. Allgeier was born in Erie, PA (USA) in 1971. He earned his B.S. in Chemistry at Case Western Reserve University in Cleveland, OH, where he performed research under Prof. Anthony J. Pearson. Subsequently, he studied inorganic chemistry at Northwestern University, and in 1997 received his Ph.D. with Prof. Chad A. Mirkin for his work on ferrocene-based redox-switchable ligands. He is currently a Research Chemist for DuPont and works in the field of catalysis.

2.2.2. Controlling the Reactivity of Transition Metals with Redox Processes at the Central Metal

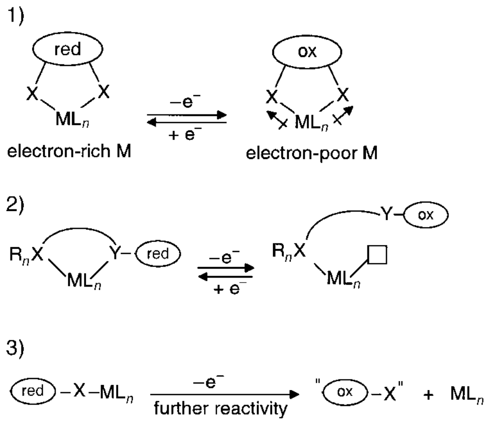
In addition to ligand-based approaches for controlling the reactivity of transition metals, there are very effective metal-based approaches. By changing the d-electron count of a transition metal through a metal-based oxidation or reduction reaction, one can control the electronic and steric properties of the metal's coordination sphere. For example, when the six-coordinate manganese complex **1** is electrochemically reduced by a two-electron process, an electron count of 18 is maintained in that a phosphane ligand is dissociated to form **2** [Eq. (b)].[14] This can be an effective way of electrochemically opening and closing a coordination site at a metal center. When this approach is applied to metal–arene complexes, interesting changes in arene hapticity are observed,[15] which often lead to reactivity inaccessible to the complexes before reduction.[16] In one example, electochemical reduction of a manganese–η^6-benzene complex leads to a cyclodimerization of the complexed arene.[16] Furthermore, complexes susceptible to this type of electrochemical reaction display a variety of behaviors associated with their redox reactions, including changes in the mode of ligand binding (e.g. linkage isomerism),[15, 17] redox-induced ligand exchange reactions,[18] geometrical isomerism,[19] and redox-induced binding or expulsion of a ligand.[14, 20] This approach has even been used in elaborate gas-separation schemes involving a Cu^I/Cu^{II} redox couple.[21] As opposed to ligand-based approaches to changing the reactivity of transition metals, these redox reactions based at the central metal *drastically* alter both the electronic (oxidation state) and steric environments of the bound metal and, therefore, the type of chemistry that the metal center might mediate. A ligand-based approach, however, allows for more subtle but substantial changes in the electronic properties of the transition metal without a formal change in the oxidation state of the metal. For studies which probe the impact of redox processes on catalytic performance, it is especially important that the complex remains in the catalytically relevant formal oxidation state.



1 **2** (b)

2.3. Categorization of Redox-Active Ligands for Transition Metals

Although we have provided representative examples of the above chemistry, our goal is to survey the redox-active ligands designed for controlling the reactivity of transition metals. Such ligands may be categorized into three classes according to their method of altering the reactivity and coordinating properties of transition metals: 1) substitutionally inert, redox-active ligands, 2) redox-switchable hemilabile ligands (RHLs), and 3) redox-active ligands that are reactive (leaving) fragments in a transition metal complex (Scheme 2).



Scheme 2. Classification of redox-switchable ligands. 1) Substitutionally inert, redox-active ligands; X = strongly binding ligand. 2) Redox-switchable hemilabile ligands (RHLs); Y = weakly binding ligand, R = substituent of tunable electronic nature, □ = ligand or solvent. 3) Redox-active ligands that are released upon oxidation.

For ligands in class 1, the redox-active group is incorporated into a ligand which forms a strong, substitutionally inert interaction with a chosen transition metal. Changes in the oxidation state of the ligand affect the reactivity of the metal by altering its electronic nature without changing its formal oxidation state.[22] The RHLs (class 2), which were pioneered and have been extensively studied by our group,[23] are multidentate ligands with at least one substitutionally inert center (R_nX) and one substitutionally labile center (Y). A redox-switchable group is covalently attached to the substitutionally labile portion of the ligand, and, therefore, changes in the oxidation state of the redox-active group allow one to modulate the strength of the adjacent metal–ligand bond, in some cases leading to dissociation of the labile portion of the ligand.[23, 24] The substitutionally inert linkage serves to anchor the ligand to the metal center and provides tunability (through choice of the R group) with regard to the electronic properties of the metal center. This ligand type allows one to control a coordination site or set of coordination sites at a transition metal to which the ligand is bound, without changing the formal oxidation state of the metal center (Scheme 2). In contrast with ligands of class 1, which primarily offer electrochemical control of the electronic properties of the transition metals to which they are bound (without significant concomitant changes in steric properties), RHLs offer electrochemical control of both the steric and electronic environments of transition metals. If one is designing a catalytic system with electrochemically switchable selectivities for desired transformations, this could be quite useful. Finally, some metal complexes have redox-active ligands (class 3) which may be completely expelled as reactive fragments from the coordination sphere of the transition metal upon electrochemical oxidation or reduction, or change their mode or strength of binding (Scheme 2).[25] Although these ligands have thus far been primarily monodentate, they could in principle be easily extended to polydentate systems.

In addition to the aforementioned ligand types, several redox-active ligands and their metal complexes have been examined and characterized electrochemically; however, they have not been studied with regard to their ability to change the reactivity of transition metals as a function of the oxidation state of the ligand.[19b–d, 26] Sometimes redox-active groups based on ferrocene or cobaltocene are incorporated into ligands for their structural properties, but not studied with regard to their electrochemical behavior.[4d, 9b, 26e–g, 27] Indeed, ferrocene-based ligands have been used in the design of several very effective and useful homogeneous catalysts.[4d] These systems will not be commented on further in this review.

3. Substitutionally Inert, Redox-Active Ligands

3.1. General Description

Changes in the oxidation state of a substitutionally inert, redox-active ligand affects the electronic nature of a bound metal by through-bond electron donation or withdrawal as well as through-space dipole interactions. This can be shown by examining the UV/Vis or IR spectroscopic properties of complexes bearing redox-active ligands and, especially, the changes in these properties upon oxidation or reduction of the ligand.[22a,b, 28]

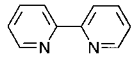
3.2. Dependence of the Carbonyl Stretching Frequency on the Oxidation State of the Ligand

3.2.1. Theoretical Basis

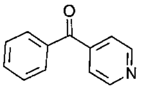
With respect to the dependence of the carbonyl stretching frequency on the oxidation state of the ligand, attention has been devoted primarily to metal–carbonyl complexes. The vibrational energies of carbonyl ligands are sensitive to the electronic nature of the metal to which they are bound, since electron density can be displaced from the metal into carbonyl π^* orbitals. This π backbonding results in a decrease in the C–O bond strength and, consequently, a decrease in the CO stretching frequency. Therefore, if a redox-active ligand undergoes a change in oxidation state that results in a change in the electronic character of the bound transition metal, this can be determined by an analysis of the ν_{CO} region of the IR spectrum. A large series of transition metal complexes (**3**–**17**) have been studied in this manner[22a,b, 28b–g,i,j] (Table 1); included are redox-active ligands which are more stable in their oxidized states (reducible ligands) and others which are more stable in their reduced state (oxidizable ligands). Reducible ligands lead to lower CO stretching frequencies, because

Table 1. Metal–carbonyl complexes with redox-active ligands.

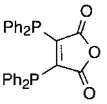
Complex[a]	Ref.	Ligand-based redox process	$\Delta\nu_{CO}$ [cm^{-1}]
3: *fac*-$[ClRe(CO)_3(bpy)]$	[28c]	1-e$^-$ reduction	−25 to −34
4: *fac*-$[ClRe(CO)_3(4\text{-bzpy})_2]$	[28c]	1-e$^-$ reduction	−14 to −20
		2-e$^-$ reduction	−26 to −37
5: *fac*-$[BrRe(CO)_3(bma)]$	[28f]	1-e$^-$ reduction	−15 to −32
6: *fac*-$[Re(CO)_4(dppc)]^{2+}$	[22a]	1-e$^-$ reduction	−11 to −17
7: *fac*-$[Re(CO)_3(dppc)(NCCH_3)]^{2+}$	[22a]	1-e$^-$ reduction	−13 to −21
8: *fac*-$[ClRe(CO)_3(dppf)]$	[28d]	1-e$^-$ oxidation	12 to 20
9: *fac*-$[ClRe(CO)_3(FcPPh_2)_2]$	[28d]	1-e$^-$ oxidation	5 to 9
		2-e$^-$ oxidation	8 to 16
10: *fac*-$[ClRe(CO)_3(FcPy)_2]$	[28d]	2-e$^-$ oxidation	4 to 7
11: *fac*-$[Re(CO)_3\{poly\text{-}(btbt)\}(NCCH_3)]^+$	[28e]	controlled-potential oxidation[b]	4 to 6
12: $[Re(CO)_5Fc]$	[28d]	1-e$^-$ oxidation	12 to 33
13: $[LM(CO)_5]$ M = Cr, Mo, W; L = Fc_xPPh_{3-x} ($x = 1$–3)	[28g]	sequential 1-e$^-$ oxidations	each ≈ 5
14: $[M(CO)_4(dppbc)]$ M = Cr (**14a**), Mo (**14b**), W (**14c**)	[28b]	1-e$^-$ oxidation	≤ 30
15: $[(\eta^6\text{-PhFc})Cr(CO)_3]$	[22b]	1-e$^-$ oxidation	10 to 20
16: $[(FcC)Co_3(CO)_8PPh_3]$	[28i]	1-e$^-$ oxidation	13 to 19
17: $[(FcCO)Os_3H(CO)_{10}]$	[28j]	1-e$^-$ oxidation	6 to 8

[a]


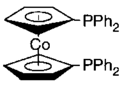
η^2-2,2-bipyridine (bpy)



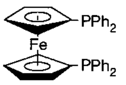
4-benzoylpyridine (4-bzpy)



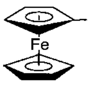
η^2-2,3-bis(diphenylphosphanyl)maleic anhydride (bma)



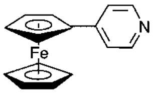
η^2-1,1′-bis(diphenylphosphanyl)cobalticene (dppc)



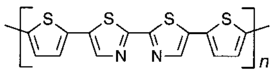
η^2-1,1′-bis(diphenylphosphanyl)ferrocene (dppf)



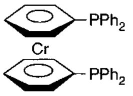
ferrocenyl (Fc)



4-ferrocenylpyridine (FcPy)

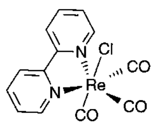


poly-[5,5′-bis(2-thienyl)-2,2′-bithiazole] (poly-(btbt))



η^2-1,1′-bis(diphenylphosphanyl(η^6-benzene))-chromium (dppbc)

[b] Oxidized at 1.5 V versus Ag wire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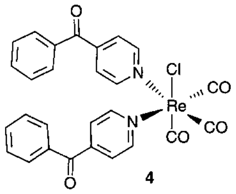
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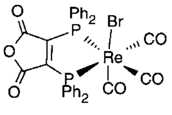
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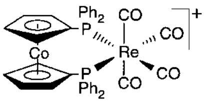
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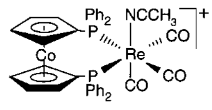
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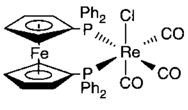
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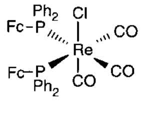
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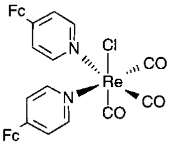
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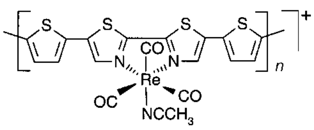
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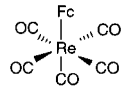
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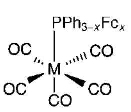
M = Cr, Mo, W

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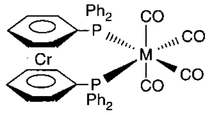
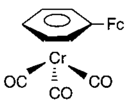

M = Cr (**14a**), Mo (**14b**), W (**14c**)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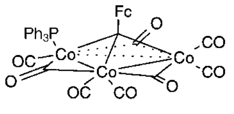
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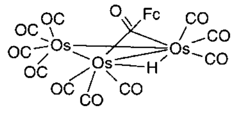
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reduction increases the electron density at the metal, which results in increased π backbonding into the CO ligands. Conversely, oxidizable redox-active ligands deplete a metal center of electron density upon oxidation and thus lead to increased CO stretching frequencies. These ligands have been complexed to a variety of transition metal fragments including mononuclear rhenium–carbonyl complexes,[22a, 28c,d,f,i] Group 6 metal–carbonyl complexes,[28b,g] and several metal–carbonyl clusters.[28i,j]

3.2.2. Factors Controlling the Magnitude of $\Delta\nu_{CO}$

Examination of a series of structurally related complexes, such as the rhenium–carbonyl complexes[22a, 28c,d,f] **3**–**12** shown in Table 1, reveals some of the factors that control the magnitude of changes in ν_{CO} ($\Delta\nu_{CO}$) upon oxidation or reduction of a pendant redox-active ligand. Alterations in the relative orientation of the redox-active center and the central metal as well as in the distance separating them can lead to significant changes in $\Delta\nu_{CO}$. For example, **8** contains a chelating diphosphanylferrocene ligand, and **9** two monodentate Fc-functionalized phosphane ligands (Fc = ferrocenyl).[28d] Despite very similar coordination spheres for the two complexes, one-electron oxidation of **8** leads to approximately twice the increase in $\Delta\nu_{CO}$ over that of **9**. One clear difference between **8** and **9** is the proximity of the redox-active Fe center to the complexed Re atom. With a shorter Fe–Re distance (4.506(1) Å for **8** versus 5.157(2) and 5.519(2) Å for **9**)[28d] and two phosphane groups bound to the Re atom, the 1,1′-bis(diphenylphosphanyl)ferrocene (dppf) ligand of **8** withdraws more electron density from the Re center than the monodentate $FcPPh_2$ ligands of **9** when both complexes are transformed from their totally reduced state (see Table 1) to their singly oxidized states.[28d] Also affecting the charge-dependent carbonyl stretching frequencies are the electronic natures of the redox-active ligand and the bound metal as well as the degree of electronic communication between the two. Although complexes **9** and **10** both contain monodentate ferrocene-based ligands, the identity of the bridging group between the ferrocenyl group and the Re atom is different, and the distance separating the Fe and Re centers is greater in **10** than in **9**.[28d] Oxidation of **10** results in a product with a smaller $\Delta\nu_{CO}$ than the oxidation of **9**, which reflects that there is less electronic communication between the ferrocenyl group and the Re center in **10**.[28d] Like **9** and **10**, complexes **3**–**5** and **8** also contain redox-active ligand(s) and the $[XRe(CO)_3]$ fragment.[28c,d,f] The redox-active ligands have different electronic natures, however, and bring about a range of $\Delta\nu_{CO}$ values upon their oxidation or reduction. The above-mentioned factors are also observable in the comparison between **3** and **4**, which contain reducible pyridine-based ligands.[28c] Upon one-electron reduction, complex **3** with a bidentate bipyridine (bpy) ligand undergoes a larger average change in its CO stretching frequencies than **4**.[28c] Furthermore, the largest changes in CO stretching frequency occur for complexes with redox-active groups directly bound to a metal as in **3**[28c] and **12**.[28d] Examination of the complexes in Table 1 and the corresponding spectroscopic data shows how the charge-dependent behavior of such complexes can be tuned. Changes in the oxidation state in geometrically constrained (i.e., the redox center is fixed close in space to the metal center), bidentate, redox-active ligands perturb the electronic properties of the bound transition metals (i.e., $>\Delta\nu_{CO}$) more than changes in oxidation state for monodentate ligands that can move the redox-active group farther away from the metal center of interest. Additionally, by controlling the distance and the degree of electronic communication between a redox-active center and a metal, one can tune the magnitude of changes in physical properties (e.g. $\Delta\nu_{CO}$) and chemical reactivity (Section 3.3) that result from ligand-based redox processes.

3.2.3. Qualitative Evaluation of Substituent Effects for Ferrocenyl and Ferrocenylium Ligands

An interesting issue involving the use of ligands with redox-active substituents is the difference between substituent effects for the reduced and oxidized forms of the ligand. For example, what effect does switching from a ferrocenyl to a ferrocenylium group have upon the substituent effect? Although σ constants calculated from Taft equations have been determined for ferrocenyl and other metallocenyl substituents,[29] we are not aware of any such determination for ferrocenylium.

Although the impact of changing a substituent between its reduced and oxidized states will vary from system to system, examination of the literature provides some insight into the substituent effect of the ferrocenyl versus ferrocenylium group. A series of structurally similar $[(\eta^6\text{-}C_6H_5X)Cr(CO)_3]$ complexes has been examined with regard to the effect of various aryl substituents (X) upon the CO stretching frequencies of the complexes.[30] This series can be compared to the oxidized and reduced forms of **15** ($X = Fc$ or Fc^+) to determine the placement of ferrocenyl versus ferrocenylium within this series. Upon one-electron Fe-centered oxidation of **15**, the carbonyl stretching frequencies shift from $\nu_{CO} = 1964$ and $1887\ cm^{-1}$ to 1974 and $1907\ cm^{-1}$.[22b] This suggests that in this class of compounds the ferrocenyl group is more electron-donating than Me or $SiMe_3$ ($X = Me$: $\nu_{CO} = 1969$ and $1889\ cm^{-1}$; $X = SiMe_3$: $\nu_{CO} = 1968$ and $1890\ cm^{-1}$), whereas a ferrocenylium group is more withdrawing than H but less so than COOMe ($X = H$: $\nu_{CO} = 1974$ and $1894\ cm^{-1}$; $X = COOMe$: $\nu_{CO} = 1985$ and $1911\ cm^{-1}$).[30] Knowledge of such electronic substituent effects should allow the experimentalist to predictably design transition metal complexes with switchable states of electron richness. However, this analysis will be highly dependent on the class of compound. For example, in the aforementioned series of compounds, the methoxy group is not a particularly strong π donor owing to the interaction of the arene with the Cr center (a similar effect has been observed for Rh^I–arene complexes),[31] and we have already seen that the positioning of a redox-active group in a complex can substantially affect its electronic perturbation on a complex.

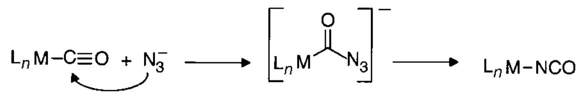
3.2.4. Application of Conducting Polymers

In connection with the influence of varying the electronic nature of a redox-active group, it is interesting to note that conducting polymers can be complexed to transition metals and serve as substitutionally inert, redox-active ligands. An example is polymer **11**, whose controlled-potential oxidation yields $\Delta\nu_{CO} = 4-6\ cm^{-1}$ (Table 1).[28e] Unlike other redox-active species which switch between integral amounts of charge, conducting polymers, in principle, allow access to a continuous range of intermediate states of charge because of their high electronic delocalization. Such effects may allow for tunable reactivity of a bound metal center, as opposed to switchable reactivity provided by other redox-active ligands. This depends upon the degree of electronic localization induced by the interaction between the metal centers and the conducting polymers. This issue has not yet been adequately addressed, in part because of the heterogeneous nature of conducting polymer–metal complexes and the difficulties associated with preparing and adequetely characterizing such complex materials.

3.3. Controlling Reactivity with Substitutionally Inert, Redox-Active Ligands

3.3.1. Nucleophilic Attack at Metal–Carbonyl Complexes

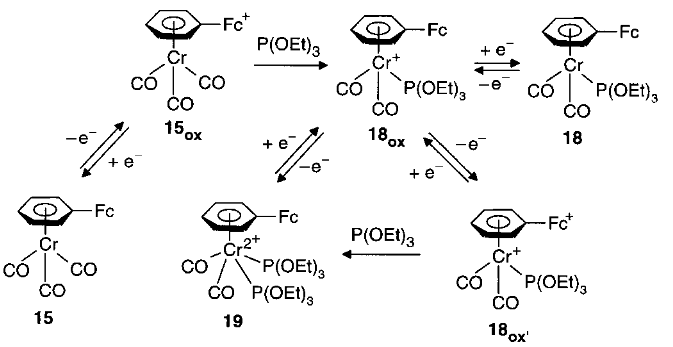
The above-mentioned studies indicate that the electron richness of metal–carbonyl complexes can be tuned by ligand-based redox processes. Since these effects are manifested in changes in ν_{CO}, they suggest that the rate of reactions involving these ligands also may be adjusted by ancillary ligand-based redox processes. Ideally suited for such a study are nucleophilic reactions at CO groups in transition metal–carbonyl complexes.[32] These reactions are selective, often proceeding to only one metal-containing product, and are generally irreversible.[32] Such reactions, for example azide or amine-*N*-oxide attack at a carbonyl group, have been thoroughly studied and are known to be first-order in both metal–carbonyl complex and nucleophile; the rate-determining step is nucleophilic attack on the CO group (Scheme 3).[32] Since carbonyl stretching frequencies are known to be dependent on the oxidation state of a pendant redox-active ligand, the electrophilicity of the carbonyl group should show a similar trend. Indeed, the rates of the reaction of **7** (Table 1) with three different amine-*N*-oxides also depend upon the state of charge of the (1,1′-bis(diphenylphosphanyl)cobalticene (dppc) ligand. For the reaction of trimethylamine-*N*-oxide, *N*-methylmorpholine-*N*-oxide, and dimethylaniline-*N*-oxide with **7**, the ratio k_{ox}/k_{red} is on average 200.[22a] Under a model of some simplified kinetic conditions, it was shown that the difference in reactivity between $\mathbf{7}_{ox}$ and $\mathbf{7}_{red}$ corresponds to $\Delta\Delta H^{\neq} = 3.1-3.2\ kcal\,mol^{-1}$.[22a] Furthermore, the reaction of **6** (Table 1) with $[nBu_4N][N_3]$ in acetonitrile is highly dependent on the state of charge of the cobaltocenyl moiety.[22a] In acetonitrile without added salt $\mathbf{6}_{ox}$ reacts 5400 times faster than $\mathbf{6}_{red}$;[22a] in 0.1 M $[nBu_4N][PF_6]$ in acetontrile the rate is enhanced only by a factor of 2200.[22a] The differences in k_{ox}/k_{red} ratios for nucleophilic attack by neutral amine-*N*-oxides are larger than expected based on $\Delta\nu_{CO} = -11$ to $-17\ cm^{-1}$, and suggest the possible involvement of electrostatic effects in further enhancing the rate of nucleophilic attack by N_3^-. Furthermore, the reaction rates are eight and three times slower for $\mathbf{6}_{ox}$ and $\mathbf{6}_{red}$, respectively, when the reactions are conducted in 0.1 M $[nBu_4N][PF_6]$ in acetonitrile.[22a] The results indicate that $\mathbf{6}_{ox}$ is more sensitive to electrostatic effects and are consistent with $\mathbf{6}_{ox}$ having a greater attraction to the anionic nucleophile than $\mathbf{6}_{red}$. Further investigation verified the difference in the role of electrostatic effects between $\mathbf{6}_{ox}$ and $\mathbf{6}_{red}$. The nonelectrostatic contributions to the rate enhancements were studied, and the nonelectrostatic rate constant ratio between $\mathbf{6}_{ox}$ and $\mathbf{6}_{red}$ was determined to be $k_{ox}/k_{red}(\text{nonelectrostatic}) = 1100$.[22a]



Scheme 3. Nucleophilic attack of an azide on a metal–carbonyl moiety; the first step is the rate-determining step.

3.3.2. Ligand Displacement and Addition

Substitutionally inert, redox-active ligands also can be used to control ligand displacement and ligand addition reactions (Scheme 4).[22b] Compound **15** displays rich yet complicated electrochemical behavior under a variety of conditions.[22b,e,f] In coordinating solvents, such as CH_3CN or DMF, one-electron oxidation of **15** occurs at the ferrocenyl group and is followed by intramolecular electron transfer from the Cr to

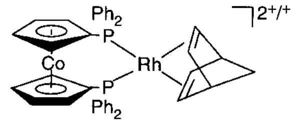


Scheme 4. A chromium complex with a redox-active ligand exhibits electrochemically modulated, reversible uptake and release of triethylphosphite.

the Fe center and rapid degradation of the complex.[22d] In dichloromethane, however, the oxidation process is reversible at reasonable scan rates (0.5 $\mathrm{V\,sec^{-1}}$) and activates the complex toward CO substitution by $P(OEt)_3$ to provide **18**$_{ox}$ (Scheme 4).[22b] Interestingly, this substitution changes the formal potential of the Cr center such that an intramolecular electron transfer occurs between the Cr and the Fe center, effectively "closing" the redox switch (Scheme 4).[22b] The Cr center can subsequently be electrochemically reduced. The mechanism was supported by an examination of the behavior of the model compound $[(\eta^6\text{-}C_6H_6)Cr(CO)_3]$ and a comparison with authentic samples of the predicted product.[22b] The reactivity of **18** is also dependent on the oxidation state of the ligand (Scheme 4). Upon oxidation of **18**$_{ox}$ an electron is removed from the ferrocenyl moiety to provide **18**$_{ox'}$, which in the presence of $P(OEt)_3$ undergoes ligand addition (Scheme 4).[22b] Once again, phosphite addition to the Cr center increases the electron richness of the metal such that an intramolecular electron transfer occurs between the Cr center and the ferrocenylium group; this "closes" the redox switch and reestablishes an electron count of 18 for each metal center.[22b] One-electron reduction of **19** leads to phosphite expulsion and closes a cycle, which may be viewed as a reversible chemical uptake and release scheme.[22b] Significantly, even in the presence of $P(OEt)_3$, $[(\eta^6\text{-}C_6H_6)Cr(CO)_2\text{-}P(OEt)_3]$ is degraded upon two-electron oxidation: This verifies the necessary involvement of the ferrocenyl group of **18** in the reversible uptake and release of phosphite.[22b]

Another interesting example of the use of a substitutionally inert, redox-active ligand to affect transition metal reactivity involves the ferrocenyl sulfide complex $[Rh\{\eta^2\text{-}(\eta^5\text{-}C_5H_5)Fe\text{-}(\eta^5\text{-}C_5H_4SCH_2CH_2PPh_2)\}_2]^+$.[22c] In the reduced state, this complex does not react with acetonitrile; however, after ferrocenyl-based oxidation, it cleanly reacts with two equavalents of acetonitrile to form the diamagnetic octahedral Rh^{III} complex *cis-cis-trans*-$[Rh(CH_3CN)_2\{\eta^2\text{-}(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4SCH_2CH_2PPh_2)\}_2]^+$. This appears to be the only example of a complex formed from a substitutionally inert, redox-active ligand which exhibits such oxidation state dependent ligand-uptake characteristics. Apparently oxidation of the ferrocenyl groups increases the Lewis acidity of the Rh center, which effects coordination of the acetonitrile ligand. This in turn results in a redistribution of electrons within the complex from Rh to the oxidized Fe centers. Therefore, conventional analogues of this ligand which have aryl substituents that vary in electron-withdrawing ability (e.g. NO_2, F) do not duplicate this effect. Indeed, in this system the ferrocenylium groups not only act as electron-withdrawing substituents but also provide an intramolecular means for effecting the Rh^I to Rh^{III} conversion with concomitant expansion of the complex's coordination sphere by acetonitrile ligand uptake.

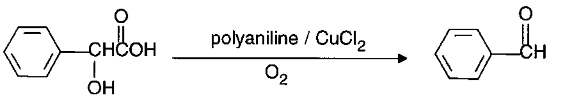
3.3.3. *Catalytic Reactivity*



20

In addition to stoichiometric reactions, catalytic reactions have been controlled with substitutionally inert, redox-active ligands. The traditional rhodium–diphosphane–norbornadiene catalyst **20** was synthesized with the chelating ligand dppc.[22d] The catalyst is active for the hydrogenation of cyclohexene to cyclohexane, and substantial rate enhancements (approximately 16-fold) are found for the reduced over the oxidized catalyst.[22d] This result was rationalized in terms of the reduced ligand having more basic phosphane groups. From isostructural complexes, hydrogenation rates are known to increase with increased phosphane basicity.[33] Catalyst **20** also has been employed in the hydrosilation of acetone. A trend in reactivity opposite to that for the hydrogenation reactions was observed; the catalyst derived from **20**$_{ox}$ has a greater hydrosilation turnover frequency than the catalyst derived from **20**$_{red}$.[22d] This phenomenological result was not further rationalized. These are important pioneering experiments because they demonstrate the concept and viability of redox-switchable catalysis through changes in the oxidation state of the ligand.

In complementary work, the reactivity of a heterogeneous catalyst comprised of polyaniline and $CuCl_2$ was tuned by adjusting the doping level of protonic acid, which is a chemical means of controlling the degree of oxidation of the polymer.[34] The complex catalytic system was used in the decarboxylative dehydrogenation of mandelic acid [Eq. (c)].



(c)

A comparison of two different protonic acid doping levels revealed that the less doped catalyst provided a faster rate of reaction.[34] Although the catalyst was inherently difficult to characterize, it was nonetheless clear that altering the doping level, and thus state of oxidation of the metal–polymer complex, provided a means of controlling the reactivity of the catalytic system.

4. Redox-Switchable Hemilabile Ligands (RHLs)

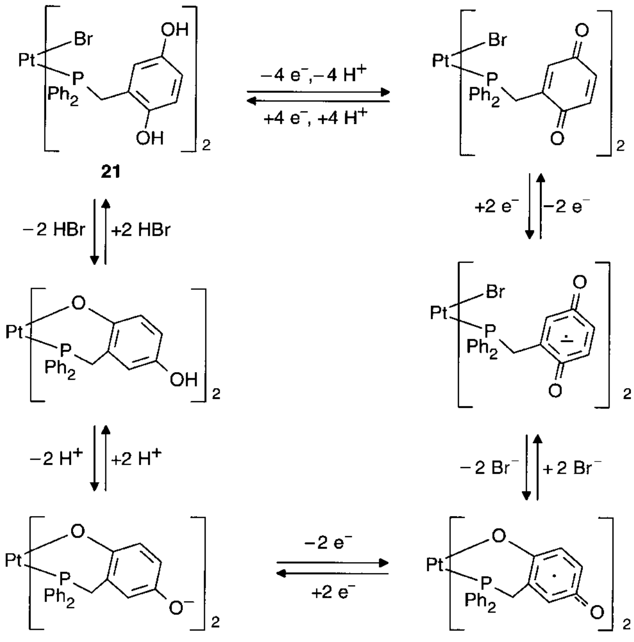
4.1. General Description

The RHLs (Scheme 2, class 2) have been designed and synthesized for complexation to a variety of metals.[23, 24]

Often phosphane ligands are used to form the substitutionally inert linkage to late transition metals; in these cases the alkyl- or arylphosphane substituents may be used to tailor the electronic nature of the metal center to which the RHL is bound. Weakly binding centers studied thus far include ethers,[23c] η^6-arenes,[23b] sulfides,[23c] η^1-thiophenes,[35] and η^1-quinones.[24] The redox groups employed have been the ferrocenyl moiety, quinones, and polythiophenyl derivatives. Changes in the state of charge of the redox group alter the strength of the bond between the metal and the labile group of the ligand; in some cases, this leads to dissociation of this group in favor of a stronger binding ligand or solvent molecule. Two initial entries into this area involved very different redox-active ligands.[23b, 24] Both studies took advantage of phosphanes as inert binding groups for late transition metals, but the redox-active group in one is a quinone, involving a proton-coupled redox process,[24] and the other utilizes ferrocene.[23b]

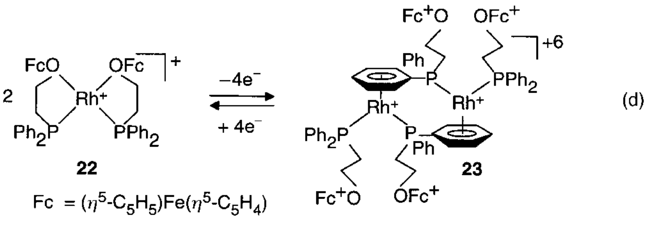
4.2. Controlling the Metal Coordination Sphere with RHLs

A Pt^{II} complex, and a similar Pd^{II} complex, bearing two phosphane ligands each with a pendant *p*-hydroquinonyl group exhibits both H^+- and electrochemically induced changes in its coordination sphere (Scheme 5).[24] When **21** is treated with sodium carbonate in methanol, the hydroquinone group is deprotonated, and the anionic oxygen atoms coordinate to the Pt center and displace Br^-.[24] The reaction is reversible, and **21** reforms upon treatment of the O,P-chelated complex with HBr. Similar changes in coordination sphere proceed under electrochemical conditions.[24] The cyclic voltammograms of **21** and its oxidized form (which contain quinonyl groups) exhibit irreversible waves at slow scan rates, which were attributed to reversible oxygen coordination accompanying displacement of Br^-, as outlined in Scheme 5.[24] These changes also can be effected with chemical oxidants and reductants in a medium with a controlled concentration of H^+.[24] A drawback to this approach, however, is the requirement of varying H^+ concentration to shuttle between the different chemical species of Scheme 5. This condition necessitates not only electrochemical changes but also chemical changes of the reaction medium (varying concentration of H^+).



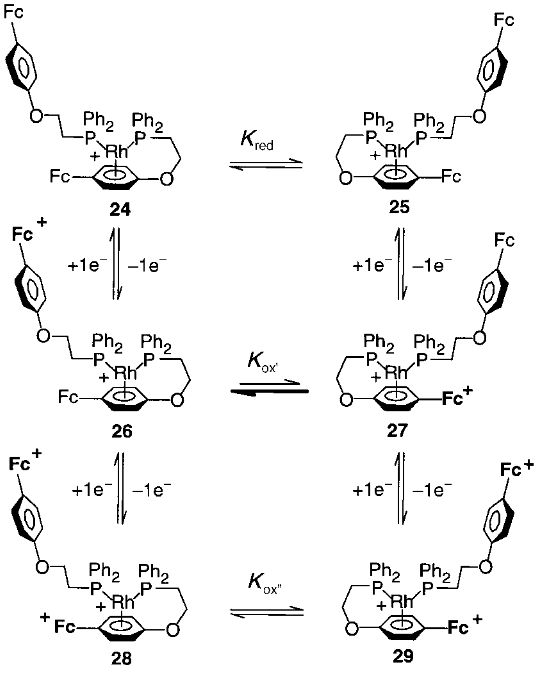
Scheme 5. A quinone-based RHL exhibits proton-coupled, electrochemically modulated binding to Pt^{II}.

A RHL system which avoids proton-coupled electrochemistry is based upon chelating ferrocenyl ether phosphane ligands bound to Rh^I [Eq. (d)].[23a] The Rh–O(ether) bond is weak, and oxidation of the adjacent ferrocenyl group further weakens this bond to the extent of dissociation to form the η^6-arene-bridged dimer **23** [Eq. (d)].[23a] Cyclic voltammetry of **22** is consistent with the proposed transformation and exhibits scan rate dependent behavior, which allows for detection of intermediate species. Furthermore, this mode of arene-ligand binding was substantiated by a crystal structure determination of an intermediate in the proposed mechanism for the reaction depicted in Equation (d).[23a] The oxidation state dependent behavior of **22** is proof for the RHL concept; the electrochemical interconversion of the square-planar complex **22** and the arene-bridged dimer **23** (with "piano-stool" geometry around each Rh center) shows how one can use RHLs to control the electronic and steric environment of transition metals. Furthermore, it provides a foundation for the synthesis and application of other complexes displaying similar and potentially useful behavior.



4.3. Determination of Thermodynamic and Kinetic Perturbations Induced by Oxidation of RHLs

In addition to ether moieties, η^6-arenes have been incorporated into redox-switchable hemilabile ligands,[31] and these ligands have been used to quantitatively determine the thermodynamic perturbation that results in a Rh^I–RHL complex upon ligand-based redox processes.[23b] The oxidation-induced thermodynamic perturbation in **24** was determined through analysis of cyclic voltammetry data and their relationship to a series of intramolecular arene–arene exchange reactions (Scheme 6). The cyclic voltammogram of **24** exhibits two reversible waves within a potential window common for ferrocenyl-based oxidation. These waves, whose half-wave potentials $E_{1/2}$ are separated by 143 mV, are assigned to the two ferrocenyl groups of **24**; the ferrocenyl group attached to the Rh-bound arene is oxidized at a more



$$\Delta E_{1/2} = -(RT/nF)\ln(K_{ox'}/K_{red})$$
$$K_{red} = K_{ox''} = 1$$
$$K_{ox'} = 3.8 \times 10^{-3}$$

Scheme 6. A degenerate exchange reaction can be used to evaluate the thermodynamic perturbation that results from RHL oxidation.

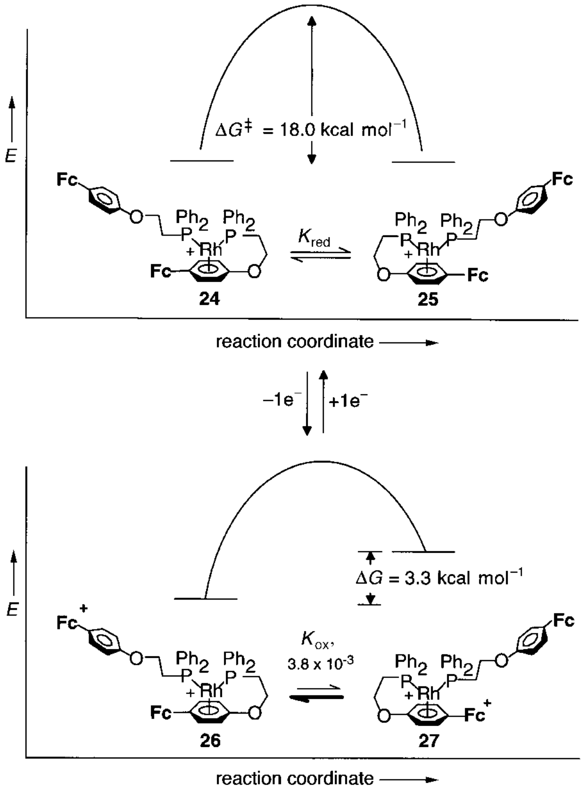


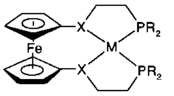
Figure 1. RHL oxidation in complex **24** results in a change in the equilibrium constant and in the Gibbs energy for an arene–arene exchange reaction.

positive potential than the free ferrocenylarene.[23b] A ladder diagram was used to describe and evaluate the exchange processes (Scheme 6).[23b] Assuming that $E_{1/2}$ for the oxidation of **27** is equal to that for the oxidation of **24** to **26** allows for the determination of $K_{ox'}$. An equation derived from the Nernst equation—($\Delta E_{1/2} = -(RT/nF)\ln(K_{ox'}/K_{red})$—can be used to calculate the ratio $K_{ox'}/K_{red}$. Since K_{red} (and $K_{ox''}$) describes a degenerate process, this analysis gives the absolute value of 3.8×10^{-3} for $K_{ox'}$. At 20°C, $\Delta G = 3.3$ kcal mol^{-1}, which presumably represents the destabilization of the complex due to weakening of the η^6-arene–Rh interaction (Figure 1).[23b] Significantly, this type of analysis can in general be applied to any RHL complex that undergoes a degenerate exchange process. In the absence of a degenerate process, one cannot obtain the absolute thermodynamic perturbation that results from ligand oxidation. Instead, the cyclic voltammetry for such a process merely yields a ratio of equilibrium constants for the reaction involving the oxidized and reduced species.[23b]

In addition to the thermodynamic perturbation associated with RHL oxidation, the kinetic perturbation also has been evaluated for this unusual process. The degenerate arene–arene exchange reaction of **24** was detected and studied by exchange spectroscopy (EXSY), and kinetic parameters were determined (at $T = 20$ °C: $k = 0.36$ s^{-1}, $\Delta G^{\neq} = 18.0$ kcal mol^{-1}, $\Delta H^{\neq} = 22.5$ kcal mol^{-1}, $\Delta S^{\neq} = 15.3$ cal mol^{-1} K^{-1}).[23b] The arene exchange reactions between **26** and **27** as well as **28** and **29** were also studied by EXSY.[36] The rate of the exchange reaction for the singly oxidized compound **26** is nearly identical to that of **24**, which is consistent with a dissociative mechanism (at $T = 20$ °C: $k = 0.35$ s^{-1}, $\Delta G^{\neq} = 17.9$ kcal mol^{-1}, $\Delta H^{\neq} = 23.0$ kcal mol^{-1}, $\Delta S^{\neq} = 17.3$ cal mol^{-1} K^{-1}). The doubly oxidized **28**, however, has a higher rate of exchange than **24** or **26** (at $T = 20$ °C: $k = 0.54$ s^{-1}, $\Delta G^{\neq} = 17.2$ kcal mol^{-1}, $\Delta H^{\neq} = 12.8$ kcal mol^{-1}, $\Delta S^{\neq} = -15.3$ cal mol^{-1} K^{-1}). The results can be understood as the weaker Rh–arene bond in **28** leading to a greater rate of dissociation and exchange.[36] As will be discussed in Section 4.6, the oxidation of **24** significantly impacts its catalytic reactivity.

While the above work allowed for the determination of the impact of RHL oxidation upon complex stability, other work has provided insight into some of the fundamental factors (e.g. electrostatic and inductive effects, ligand geometry) which contribute to effects that depend on the oxidation state of the RHL. This work shows how such factors can be synthetically adjusted to tune the behavior of RHL complexes. The contributions of two factors toward weakening of the metal–ligand bonds were considered: 1) inductive withdrawal of electron density from the metal–ligand bond toward the electron-deficient redox-active group and 2) electrostatic repulsion between the cationic redox-active group and the bound cationic metal center. Several characteristics of RHL complexes influence the relative importance of the two above-mentioned factors: 1) the electronic nature of the ligand (the redox-active group and the phosphane moiety) and the bound transition metal, 2) the valency of the central metal, and 3) the distance separating the redox-active group and the metal atom. The electrochemical behavior of a series of RHL complexes in which oxidizable RHLs are bound to cationic metal centers was investigated to address these fundamental factors (Table 2).[23c] Cyclic voltammetry was employed to record formal potentials, which are measures of the change in thermodynamic stability in the complex upon oxidation ($\Delta G = -nFE$). Additionally, ratios of ligand binding constants in the reduced and oxidized states were determined from cyclic voltammetry with minor assumptions.[23c] For example, oxidation of the ligand in **34** decreases its binding affinity for Rh ($K_{red}/K_{ox} = 4.43 \times 10^6$).[23c] These parameters were used to compare the compounds in Table 2.

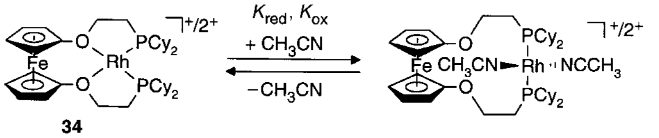
Table 2. Comparison of tetradentate RHLs and their metal complexes.



Complex	X	M	R	$E_{1/2}$ [mV][a]	K_{red}/K_{ox}
30	O	–	Ph	– 203	–
31	O	–	Cy	– 200	–
32	S	–	Ph	37	–
33	O	Rh^{I}	Ph	270[b]	$> 9.98 \times 10^7$
34	O	Rh^{I}	Cy	193	4.43×10^6
35	S	Rh^{I}	Ph	677[c]	1.27×10^{11}
36	O	Pd^{II}	Ph	420[b]	$> 1.58 \times 10^{10}$
37	O	Pd^{II}	Cy	388	9.88×10^9

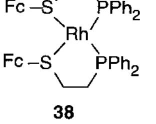
[a] Half-wave potential, except where noted. All values are quoted versus Fc/Fc$^+$. [b] Potential of anodic peak E_{pa}; appears to be irreversible at moderate scan rates ($< 1\,\mathrm{V\,s^{-1}}$). [c] $E_{1/2}$ recorded at $100\,\mathrm{V\,s^{-1}}$; at moderate scan rates the wave appears to be irreversible.

The influence of the electronic nature of the ligand is demonstrated by changing the weakly binding group from ether to sulfide, which significantly changes the electronic nature of the redox-active group. Ligand **30** undergoes reversible oxidation and reduction at a much lower potential than **32** (– 203 vs. 37 mV), a reflection of the donation of π electron density from the ether into the ferrocenyl moiety.[23c] In addition, the electronic nature of the phosphane groups plays a significant role in determining the behavior of RHL complexes. In addition to Fe-based oxidations and reductions, electron transfer processes characterized as Rh^{I}/Rh^{II} redox couples can be observed by cyclic voltammetry. Although these couples have been characterized as one-electron oxidations/reductions by rotating disk electrode experiments, EPR data that unambiguously confirms the formation of paramagnetic Rh^{II} centers have not been obtained owing to the transient nature of the oxidized forms of these complexes. Nevertheless, all oxidized forms of complexes with phenyl-substituted ligands are unstable, as evidenced by irreversible oxidations at moderate scan rates. However, the electron-rich complex **34** with a cyclohexyl-substituted ligand has a relatively more stable "Rh^{II}" oxidation state, and exhibits reversible Fe- and Rh-based oxidations.[23c] Studies on other model complexes support this conclusion.[23c] Furthermore, relative to phenyl substituents, cyclohexyl groups "soften" the bound metal, reducing electrostatic repulsion and inductive electron withdrawal between the central metal and the redox-active group. This yields a modest decrease in oxidation potential, as shown by a comparison of **33** to **34** and **36** to **37**. The valency of the central metal also impacts the charge-dependent behavior of RHL–metal complexes. The Pd^{II} complexes **36** and **37** exhibit much higher half-wave potentials $E_{1/2}$ than their Rh^{I} counterparts **33** and **34**, respectively (Table 2). With X-ray crystallography it was shown that these square-planar complexes all have nearly identical Fe–M nonbonding separations of about 4.0 Å. Since this parameter is fixed, the differences between the Pd^{II} complexes and the Rh^{I} complexes reflect enhanced electrostatic repulsion between the central metal and the oxidized redox group. Since differences in electron-withdrawing effects are also present, it was clear that Pd^{II} complexes exhibit greater changes in their ligand binding constants than Rh^{I} complexes. Indeed, **37** exhibits a greater K_{red}/K_{ox} value (9.98×10^9)[23c] than any other reported redox-active metal–ligand complex that is stable in two oxidation states. Complex **35** exhibits a larger K_{red}/K_{ox} ratio, but its oxidized form has a short lifetime and must be detected by ultrafast voltammetry. Changes of this magnitude suggest that substantial changes in complex reactivity should occur upon ligand-based oxidation. Complex **34** shows just such a change in its reaction with acetonitrile [Eq. (e)]. The Rh–O bonds weaken upon oxidation of the ferrocenyl group, and the complex's binding constant for acetonitrile increases by 2.27×10^7.[23c]



34 (e)

Although it is difficult to separate the contributions of electrostatic repulsion and inductive withdrawal in the oxidatively induced destabilization of RHL complexes, a comparison of electronically similar but structurally different complexes has addressed this issue for one class of RHLs. Complex **38** is a bis(phosphane)bis(sulfide)rhodium complex, just like **33** (Table 2); however, the former exhibits a much smaller K_{red}/K_{ox} value (3.87×10^3 vs. 1.27×10^{11}) for one-electron oxidation. The main difference between **35** and **38** is the geometric constraint imposed by the tetradentate ligand in **35**. As a result, the Rh–Fe separation in **35** is fixed and significantly shorter (4.055(7) Å) than that of **38** (≈ 5.2 Å).[23c] Owing to their shorter Rh–Fe separations, the contribution of electrostatic repulsion to the destabilization of tetradentate RHL complexes should be larger than in similar bidentate complexes. While the absolute contribution of electrostatic repulsion could not be directly extracted from the experiments in that study, results of cyclic voltammetry and the determined binding-constant ratios indicated that electrostatic repulsion significantly contributes to the destabilization of the RHL systems upon their oxidation.



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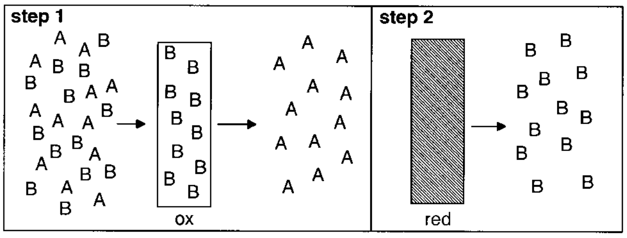
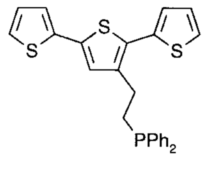
4.5. Polymeric RHLs: A Glimpse at The Future

With regard to the application of RHL – transition metal chemistry to separation technology and heterogeneous catalysis, current work is aimed at extending these systems to polymeric supports. The envisioned transition metal complexes will be designed to exhibit selective binding of a desirable component of a multicomponent mixture (Scheme 7). Furthermore, this binding will be switchable, such that the desired component binds to the metal in a particular oxidation state of the ligand. Separation of the resulting metal complex from the mixture followed by electrochemical switching of the ligand to the original oxidation state is expected to yield the purified component. Polymer-supported metal complexes will facilitate these separations of the metal – substrate complexes. Furthermore, they can be readily used to modify or construct functionalized membranes.[37] Two options exist for polymeric RHLs: conducting polymers and redox-active polymers. Conducting polymers are being incorporated into RHL – metal complexes in which the metal forms an intimate interaction with the polymer.[35] Oxidation of the polymer is expected to weaken this interaction by removing electron density from the polymer and thus the polymer – metal bond. As referred to in Section 3.2.4., conducting polymers (e.g. polythiophene, polypyrrole) offer potential advantages over other redox-active ligands because they can be oxidized to a range of intermediate oxidation states.[38a,b] In principle, this property, which results from the high electronic delocalization of the conducting polymer, can be taken advantage of in tuning, and not merely switching, the reactivity of RHL – transition metal complexes. Also of interest are redox-active polymers which bear electronically isolated redox-active groups (e.g. polyvinylferrocene). Although they do not allow for the "tunability" of highly conjugated conducting polymers, redox polymers do provide a heterogeneous support for RHL – metal complexes[39] and can be prepared with higher molecular weights than electrochemically deposited conducting polymers.



Scheme 7. RHL-modified membranes may be used in electrochemically controlled devices for the separation of small molecules.

Toward the development of polymeric RHLs, several systems have been synthesized and preliminarily studied. Conducting polymer RHLs have been developed based on ligands **39**[35b] and **40**.[35a] Substituted terthiophenes were chosen as the monomer building blocks because of their favorable polymerization potentials as well as their ability to coordinate to transition metals in either an η^1 or η^5 binding mode. For example, Ru complexes **41** and **42** were prepared from ligands **39** and **40**, respectively. Both complexes were electrochemically polymerized in anodic fashion to form stable films confined to the electrode surface. A typical electrochemical response for poly-**41** is a reversible wave with $E_{pa} = 505$ mV and $E_{pc} = 435$ mV (vs. Fc/Fc$^+$); a color change from red to blue accompanies the polymer oxidation. The film is rapidly degraded at higher potentials. This demonstrates the importance of carefully designing a polymeric RHL that is electrochemically compatible with the metal center of interest. The stability of the polymer and the retention of the metal – thiophene complex upon oxidation was confirmed by IR spectroscopy with a comparison of the carbonyl stretching frequencies for **41** and poly-**41**: Both exhibit a ν_{CO} of about 1990 cm^{-1}. Importantly, the η^1-thiophenyl ligands in **41** and poly-**41** can be displaced by more strongly coordinating ligands such as CO and acetonitrile, demonstrating the hemilability of both the monomeric and polymeric ligands. Oxidation of polymers formed from **41** and **42** should deplete the metal – thiophenyl bonds of electron density and weaken this interaction. Polymer oxidation should not only accelerate the uptake reactions involving CO and acetonitrile, but also affect the equilibrium constants associated with these reactions. Significantly, this weakening, in principle, can be varied by controlling the degree of oxidation of the highly delocalized conducting polymeric ligands. However, with these preliminary test systems it has been difficult to separate the electronic effects associated with polymer oxidation from other effects, such as porosity changes and substrate partitioning coefficients. Nevertheless, incorporation of phosphinite, cyclopentadienyl, and phosphane moieties as substitutionally inert groups will lead to a variety of metal complexes with interesting and electrochemically controllable catalytic activity. Note that **41** is chiral and can easily be obtained enantiomerically pure; therefore, it may be a good initial candidate for developing chiral transition metal based materials that are suitable for electrochemically controllable separation of enantiomer pairs.



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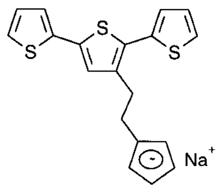

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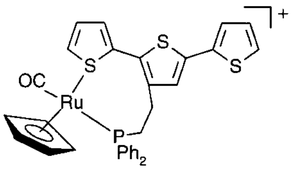

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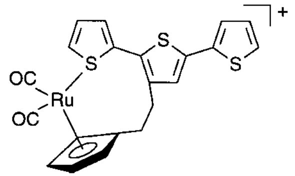
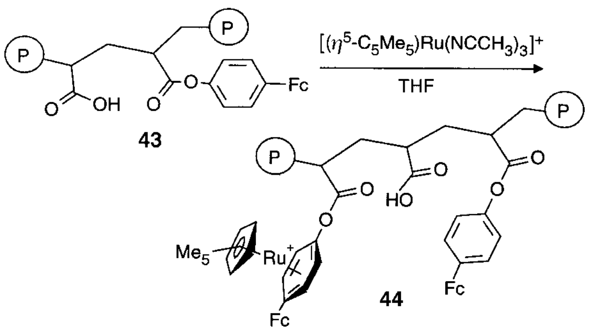


42

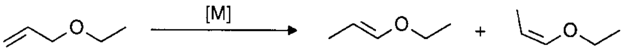
Under the class of redox polymers, a first-generation system was recently investigated. Inspired by complex **24** (Section 4.3), polymer **44** was prepared by modification of poly(acrylic acid), to incorporate ferrocenylarene sites (**43**), and subsequent complexation of the [(η^5-C$_5$Me$_5$)Ru]$^+$ fragment [Eq. (f)].[39] This new system is a model for the expansion of RHL–metal chemistry to redox polymers, and its exhibits an oxidation-induced change in binding constant for Ru of over two orders of magnitude. The feasibility of using **43** for electrochemically controlling transition metal binding constants has provided motivation for the development of future polymeric RHLs incorporating *p*-ferrocenylphenyl acrylate.



(f)

4.6. Controlling Catalytic Reactivity with RHLs

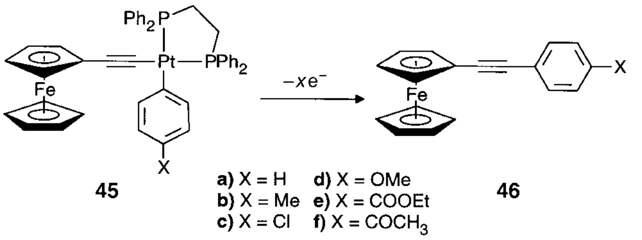
Although RHLs are still in the early stages of development, one ligand has been used to prepare a $\mathrm{Rh^I}$ catalyst with electrochemically switchable reactivity (**24**, see Figure 3). Recall that **24** exhibits an increase in the rate of intramolecular arene–arene exchange upon oxidation of both ferrocenyl groups (**28**; Section 4.3.) Complex **24** also behaves as an olefin-isomerization catalyst whose activity is dependent on the oxidation state of the RHL. For example, the isomerization of ethyl allyl ether to *cis*- and *trans*-1-propenyl ethyl ether proceeds smoothly with either **24** or **28**, but the rate of reaction is significantly higher with **28** (2–3 times higher) [Eq. (g)].[36] This difference in rate reflects the greater lability of the ferrocenyliumarene ligand in **28** compared to the ferrocenylarene ligand in **24** (see Section 4.3). Significantly, the rate of reaction with the singly oxidized species **26** (Scheme 6) is nearly identical to that with the reduced catalyst **24**;[36] this shows the importance of oxidizing the multidentate RHL ligand.[36] This experiment to demonstrate the ability of RHLs to yield electrochemical control over a catalyst's reactivity sets the stage for further development of RHL–metal catalysts for more sophisticated and perhaps more useful reactions. The thermodynamic perturbation associated with the oxidation of **24** is fairly modest in comparison with some of the other complexes discussed in this review (e.g. **33**–**37**). Therefore, with the optimum design of RHL–transition metal catalysts, it is likely that substantially large oxidation state dependent changes in both catalytic activity and selectivity will be realized with this approach and other ligands.



(g)

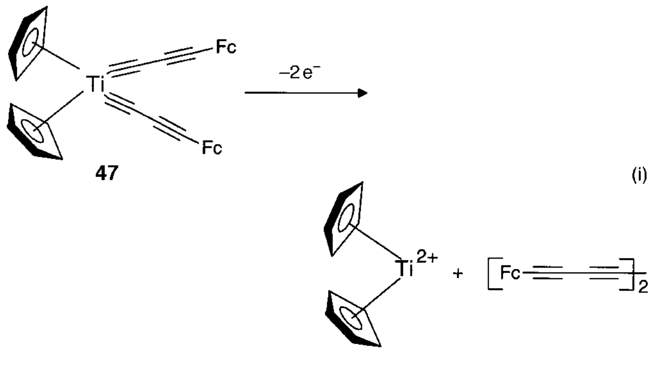
5. Redox-Active Ligands with Reactive (Leaving) Fragments

While the above-mentioned examples describe redox-active ligand–metal complexes whose chemistry may be altered in a reversible fashion, other workers have studied redox-active ligand–metal complexes that exhibit electrochemically induced irreversible changes in reactivity. In some cases ferrocene-containing alkynyl ligands take part in ligand-based oxidation-induced reductive eliminations [Eq. (h) and (i)].[25a,b] Prior to these studies it was shown that oxidation of a metal center can induce reductive elimination as a means of returning electron density to the electron-deficient metal fragment.[40] According to recent work, this reaction can also be promoted in **45** by ligand-based chemical or electrochemical oxidation [Eq. (h)].[25b] The mechanism of the reaction was studied with electronic spectroscopy, and the first intermediate observed upon treatment of **45e** with a chemical oxidant was the ferrocenium version of **45e**.[25b] Unexpectedly, kinetic studies with **45a–f** showed that electron-withdrawing aryl substituents decrease the rate of reaction.[25b] One might expect that such substituents would reduce the electron density at the $\mathrm{Pt^{II}}$ center and increase the rate of reductive elimination. These data suggested that the initial rapid oxidation is followed by intramolecular electron transfer from the $\mathrm{Pt^{II}}$ center to the ferrocenylium group.[25b] Consistent with the results, one would expect electron-donating substituents to favor this process. In the final step reductive elimination occurs to yield the arylalkyne coupling product **46**.[25b] The fate of the Pt fragment was not discussed.



(h)

Similar oxidatively induced reductive elimination was observed for **47** [Eq. (i)].[25a] From a mechanistic point of view, the reaction in Equation (i) must be different from that in Equation (h), because the electron-deficient d^0 Ti center is not likely to undergo the intramolecular oxidation observed for d^8 complexes (**45**). However, a comparison of the cyclic



voltammetry data of **47** to that of model compounds confirms that the oxidation of **47** results in removal of an electron from the ferrocenyl group.[25a] Rather than a metal →metal electron transfer as in **45**, initial oxidation of **47** is probably followed by electron transfer from the Ti–C bond to the ferrocenylium group to yield $[Cp_2Ti]^{2+}$ and two alkynyl radicals, which couple to yield the product.[25a]

6. Summary and Outlook

Redox-active ligands offer a novel tool for controlling the reactivity of transition metals with distinct advantages over other methods, such as variations in ligand substituents or redox reactions at the central metal. Redox groups with stable and reversible changes in oxidation state can be exploited for the development of transition metal complexes with switchable states of reactivity. The redox-active ligands which have appeared so far in the literature can be categorized into three classes: 1) substitutionally inert, redox-active ligands, 2) redox-switchable hemilabile ligands (RHLs), and 3) redox-active ligands which are reactive (leaving) fragments. Changes in the oxidation state of substitutionally inert ligands attenuate the electronic character of a bound metal, thereby yielding control over the carbonyl stretching frequency for a variety of metal–carbonyl complexes. Additionally, stoichiometric and catalytic reactivity may be controlled with substitutionally inert, redox-active ligands and RHLs. Indeed, oxidation of a redox-active ligand has led to rate enhancements by a factor as large as 5400 for nucleophilic attack at a metal–carbonyl complex.[22a]

A fundamental understanding of the factors that control the magnitude of changes in reactivity accompanying changes in the oxidation state of the ligand will allow for the rational design of future metal complexes with tunable states of reactivity. Toward this goal, degenerate exchange reactions were investigated to determine the thermodynamic and kinetic perturbations that result from oxidation of an RHL.[23b] Additionally, in a series of cationic phosphane ether RHL–metal complexes electrostatic repulsion was shown to be a significant factor in changing ligand binding constants. These binding constants can be tuned by choice of phosphane substituents, the bound central metal, and ligand geometry to provide very large oxidation-induced changes in binding constant (as high as 10^{11}).[23c]

The idea of electrochemically controlling the reactivity of transition metals with redox-active ligands is still in its infancy, and several challenges remain. A large percentage of the work reported here involves the use of metallocenes as redox groups; however, a wide array of other redox-active moieties are available to the synthetic chemist. Of special interest are reducible redox groups and those with three or more stable oxidation states, which would allow for a greater level of control over the reactivity of a transition metal complex. With such control, we envision the development of new and potentially useful catalysts with switchable reactivity or, alternatively, materials for new molecule-separation technologies. Redox-switchable catalysts may exhibit desirable changes in chemical selectivity as a function of oxidation state, or they may provide a means of interconverting a catalyst between a reactive active state and a more stable inactive state, thereby simplifying catalyst recovery. Regarding molecular separations, we believe the greatest potential exists in enantiomeric separations. Spurred by the high level of control which catalytic chemists have obtained in asymmetric catalysis, chiral transition metal complexes of redox-active ligands can be designed to exhibit electrochemically induced reversible uptake and release of molecular compounds. These systems could be used for the separation of enantiomer pairs that are critical to the pharmaceutical industry. Even if the metal centers used in Scheme 7 exhibit modest or even poor enantioselectivity, because the process can be repeated it can in principle provide high levels of purity of a desirable enantiomer. This could be a distinct advantage over asymmetric catalysis in which suitable product purities are often unattainable.

In short, this field has a great deal of promise. Significant strides have been made with regard to developing a fundamental understanding of how both the coordination environment and electronic character of a transition metal center can be controlled with the appropriate redox-active ligand and an applied potential. Although technologically useful systems have not yet been developed, in view of the current level of understanding it would not be surprising to see such systems emerge over the next decade.

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