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DOI
10.1002/anie.201410048
10.1002/ange.201410048

Publication date
2015

Document Version
Final published version

Published in
Angewandte Chemie, International Edition

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Citation for published version (APA):

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Download date: 29 Oct 2023
Redox-Active Ligands

Redox-Active Ligand-Induced Homolytic Bond Activation**

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Dedicated to Professor Thomas B. Rauchfuss on the occasion of his 65th birthday

Abstract: Coordination of the novel redox-active phosphine-appended aminophenol pincer ligand (PNO) to Pd^{II} generates a paramagnetic complex with a persistent ligand-centered radical. The complex undergoes fully reversible single-electron oxidation and reduction. Homolytic bond activation of diphenyl disulfide by the single-electron reduced species leads to a ligand-based mixed-valent dinuclear palladium complex with a single bridging thiolate ligand. Mechanistic investigations support an unprecedented intramolecular ligand-to-disulfide single-electron transfer process to induce homolytic S–S cleavage, thereby releasing a thiol (sulfanyl) radical. This could be a new strategy for small-molecule bond activation.

Redox-active ligands are frequently encountered in important natural processes mediated by metalloenzymes. In inorganic chemistry, these systems have long been considered to be primarily a spectroscopic curiosity, with major focus on understanding the electronic structure and bonding within homoleptic systems. Recently, heteroleptic complexes have been shown to offer unique reactivity in stoichiometric activation reactions and in catalysis, since the redox-active nature of these ligands allows their use as an electron reservoir during (catalytic) turnover. The majority of redox-active frameworks are based on nitrogen or oxygen donors, with aminophenol-based N,O ligands as archetypal redox-active systems that can span three oxidation states. In contrast and at odds with the relevance of phosphorus ligands in homogeneous catalysis, few phosphine-containing redox-active ligands exist. Thomas and co-workers recently described an (o-anilino)phenylphosphine ligand that is susceptible to oxidation in the coordination sphere of Cu^{II}, but radical P–P coupling precluded the use of this scaffold as a reversible redox-active ligand. Installation as a redox-innocent entity adjacent to a redox-active framework is less likely to affect the coordinative properties at phosphorus, but relatively few of these ligands have been developed.

Bond homolysis is a very useful reaction to probe for accessible ligand-based reactivity. Established ligand-mediated bond activation (and formation) reactions classify overall as two-electron processes. Metal-mediated one-electron homolysis is much rarer, while reductive homolytic bond fission originating from ligand-based overall single-electron transfer is, to the best of our knowledge, unknown. Methodologies that facilitate odd-electron transfer processes will allow the controlled generation of reactive substrate radicals for synthetic chemistry.

Common: two-electron homolysis of e.g. disulfides

\[
\begin{align*}
M^0 & \rightarrow RS \cdot SR \\
& \rightarrow RS^+ \; M^{+2} \\
& \rightarrow RS \\
M & = \text{noble metal}
\end{align*}
\]

Unknown: ligand-induced reductive one-electron bond homolysis

\[
\begin{align*}
\text{Ph} \quad \text{Pd}^{II} & \rightarrow RS \cdot SR \\
& \rightarrow \text{Ph} \: \text{Pd}^{II} \cdot \text{SR}
\end{align*}
\]

Figure 1. a) Typical reactivity concerning bond homolysis by noble metal complexes. b) Unprecedented reductive single-electron transfer from a redox-active ligand to a disulfide substrate, generating a thiolate and a thiol radical.

Recently, we reported a tridentate redox-active NNO ligand that accommodates radical-type C–H activation reactivity on a Pd^{II} platform. In order to arrive at a redox-active phosphine ligand, we sought to merge the redox-active aminophenol framework with a flanking diphenylphosphine group. Addition of this (sterically encumbered) donor should impact the redox properties of the N,O moiety upon coordination to a transition metal, relative to the previous NNO scaffold. We herein describe the facile synthesis and electronic structure of a phosphorus ligand that is ‘redox active’ when coordinated to Pd^{II}. This system, which displays a markedly lower reduction potential than the Pd complex with our previously reported NNO system, is able to facilitate radical-type homolytic bond activation of disulfides, with formation of a well-defined ligand-based mixed-valent dinuclear complex.

The novel aminophenolphosphine ligand PNO\(^{12}\) (\(^{31}P\) NMR \(\delta = -20.25\)) was prepared as an air-sensitive...
white solid in 58% overall yield through a two-step procedure from commercially available \( O \)-idoaniline and 3,5-di-tert-butylcatechol.\[^{[18]}\] Reaction with \([PdCl_2(MeCN)_2]\) gave complex 1 as an orange solid in 67% yield (\(^{31}P\) NMR \( \delta = 43.98 \)). Addition of triethylamine resulted in a rapid color change to green, and subsequent exposure to air afforded the dark-red paramagnetic species 2 in 78% yield (Scheme 1). Magnetic susceptibility measurements (Evans’ method) showed an effective magnetic moment (\( \mu_{\text{eff}} \)) of 1.81 \( \mu_B \), thus indicating an \( S = \frac{1}{2} \) ground state. Hence, this species is best formulated as \([PdCl(PNO-IsoQ)]\), and this assignment was confirmed by single-crystal X-ray diffraction (Figure 2; ISQ = iminosemiquinonato).

**Scheme 1.** Synthetic route to complexes 1 and 2.

**Figure 2.** a) Displacement ellipsoid plot (50% probability level) of complex 2 at 110(2) K. b) Relevant experimental (XRD) and computed (DFT) metric parameters support the PNO-IsoQ state in 2. Selected bond angles \( \beta \): N-Pd-Cl 174.90(5); P-Pd-1-O1 167.43(4); P-Pd-O1-Cl 94.038(17); N-Pd-O1 81.16(6). Complex 2 shows a slightly distorted square-planar geometry with an acute \( \alpha \),N1-Pd1-O1 angle of 81.16(6)\(^\circ\). Palladium–ligand bond lengths and angles in 2 compare well with PdCl complexes bearing redox-innocent monoanionic PNO pincers.\[^{[19]}\] The metric parameters found for the amidophenolate fragment support the ISQ oxidation state of the ligand\[^{[20]}\] and these data are reproduced by DFT (b3-lyp/def2-TZVP) metric parameters support the PNO-IsoQ state in Figure 2. Displacement ellipsoid plot (50 % probability level) of complex 2 at 110(2) K. Relevant experimental (XRD) and computed (DFT) metric parameters support the ISQ oxidation state of the ligand and these data are reproduced by DFT (b3-lyp/def2-TZVP) metric parameters support the PNO-IsoQ state in Figure 2. a) Experimental and simulated EPR spectrum of 2 (toluene, RT) \( g \approx 9.366829 \) GHz, \( T = 298 \) K, Mod Ampl. = 1 Gauss, power \( = 20 \) mW. Simulated (DFT) \( g \) value and hyperfine couplings \( A(\text{MHz}) \): \( g = 2.0052 \) (2.0062); \( A_{\text{iso}} \) = 10.70 (+ 3.61); \( A_{\text{iso}} \) = 13.55 (-16.04); \( A_{\text{iso}} \) = 16.45 (+ 11.0); \( A_{\text{iso}} \) = 4.90 (-5.06); \( A_{\text{iso}} \) (NR) = 0.78; \( A_{\text{iso}} \) = 4.95 (-5.24); \( A_{\text{iso}} \) (NR) = 2.60; \( A_{\text{iso}} \) = 7.18 (-5.66); \( A_{\text{iso}} \) (NR) = 2.15 NR = not resolved; DFT parameters: ORCA (b3-lyp, def2-TZVP). b) DFT (b3-lyp/def2-TZVP) calculated spin-density plot for 2.

**Scheme 2.** Synthetic route to complexes 3 and 4.

Oxidative addition of a disulfide to low-valent Pd is usually a two-electron process.\[^{[21]}\] Given the demonstrated reversible one-electron chemistry of species 3 at a mild potential, we sought to investigate its reactivity toward disulfides. Addition of TlPF\(_6\) to a suspension of 3 in benzene produced the soluble paramagnetic species 5. Magnetic susceptibility measurements of 5 at 298 K using Evans’ method gave an effective magnetic moment (\( \mu_{\text{eff}} \)) of 1.90 \( \mu_B \), thus indicating an \( S = \frac{1}{2} \) ground state. This observation implies one-electron oxidation of PNO-IsoQ to PNO-IsoQ\(^{2+}\). CSI-MS studies in benzene indicate the presence of a dinuclear species in solution at \( m/z \) 1279.28 \([M]^+\), formulated as \([Pd_2(\mu-...]]\)

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\[^{[18]}\] Cyclic voltammetry of 2 in CH\(_2Cl_2\) solution shows fully reversible one-electron oxidation and reduction events at +0.07 V and -0.75 V vs. Feccoli, respectively. Reversible ligand-based redox chemistry was also observed by UV/Vis spectrophotometry in an optically transparent thin-layer electrolysis (OTLLE) cell (see the Supporting Information for details of the redox chemistry). Chemical reduction of 2 with \([CoCp_2]^-\) in CH\(_2Cl_2\) furnished air-sensitive diamagnetic complex 3, formulated as \([CoCp_2][PdCl(PNO-AP)]\) (\(^{31}P\) NMR \( \delta = 36.56; \) AP = amidophenolato). To assess the steric constraint imposed on the Pd center by the flanking phosphine donor, complex 3 was exposed to exogenous phosphines. No reaction was observed with PPh\(_3\), but coordination of PMe\(_3\) rapidly produced complex 4 (\(^{31}P\) NMR \( \delta = 41.52 \) (d) and -10.61 (d); \( J_{P-P} \) 40.2 Hz), formulated as \([Pd(PMe_3)(PNO-AP)]\) (Scheme 2).

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**Figure 3.** a) Experimental and simulated EPR spectrum of 2 (toluene, RT) \( g \approx 9.366829 \) GHz, \( T = 298 \) K, Mod Ampl. = 1 Gauss, power \( = 20 \) mW. Simulated (DFT) \( g \) value and hyperfine couplings \( A(\text{MHz}) \): \( g = 2.0052 \) (2.0062); \( A_{\text{iso}} \) = 10.70 (+ 3.61); \( A_{\text{iso}} \) = 13.55 (-16.04); \( A_{\text{iso}} \) = 16.45 (+ 11.0); \( A_{\text{iso}} \) = 4.90 (-5.06); \( A_{\text{iso}} \) (NR) = 0.78; \( A_{\text{iso}} \) = 4.95 (-5.24); \( A_{\text{iso}} \) (NR) = 2.60; \( A_{\text{iso}} \) = 7.18 (-5.66); \( A_{\text{iso}} \) (NR) = 2.15 NR = not resolved; DFT parameters: ORCA (b3-lyp, def2-TZVP). b) DFT (b3-lyp/def2-TZVP) calculated spin-density plot for 2.

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**Scheme 2.** Synthetic route to complexes 3 and 4.
SPh)(PNO)₃]. UV/Vis spectroscopy shows characteristic absorption bands for both PNO³⁺ and PNO³⁻ ligand fragments. X-band EPR spectroscopy of compound 5 in toluene at 298 K showed an isotropic signal with no resolved hyperfine couplings. The g∥ value of 2.0041 supports the presence of a PNO³⁻ ligand radical. This assignment was corroborated by X-ray diffraction (Figure 4).

![Figure 4](image_url)

The molecular structure contains one thiophenolate unit bridging two Pd⁴⁺(PNO) centers. This bridging monothiolate motif, although not unique, is rather uncommon, particularly with Pd. Strikingly, the observed metric parameters indicate different oxidation states for the two PNO ligands present, that is, the amidophenolato (N11-O11) and the iminosemiquinonato (N12-O12) forms. VT-EPR spectroscopic data indicate facile electron exchange between the PNO³⁺ and the PNO³⁻ moieties of 5 in solution (see the Supporting Information). We are not aware of similar examples of monobridged dinuclear complexes that show ligand-based mixed valency. For homodinuclear reaction centers, the mixed valency is typically metal-centered or shared between the metal and (bridging) ligand. Systems with separated mixed-valent ligand-based redox centers could be of interest for studying intramolecular electron-transfer processes and potentially also for ligand-assisted redox catalysis. Selective formation of such species through controllable synthetic procedures from stable monomeric precursors might allow the study of these electronic configurations.

The occurrence of outer-sphere electron transfer from 2 to PhSSPh is excluded on the basis of their relative redox potentials. The formation of species 5 (Scheme 3) is proposed to involve initial chloride dissociation and disulfide coordination. Dialkyl disulfides have a higher S–S bond dissociation energy than diaryl disulfides and are thus less prone to undergoing bond homolysis. Using di(tert-butyl)disulfide instead of PhSSPh allowed observation of the corresponding Pd–disulfide adduct by NMR spectroscopy. The ³¹P NMR chemical shift of δ = 39.82 is similar to that of neutral 4. The non-equivalent tert-butyl groups of the substrate are shifted upfield in the ¹H NMR spectrum, which otherwise resembles that of 4 (see the Supporting Information). Subsequent intramolecular ligand-to-substrate single-electron transfer results in homolytic S–S bond cleavage with formation of [PNO³⁺PdSPh] and release of a PhS radical. This thyl radical can either undergo self-recombination or react with a ‘vacant’ [PNO³⁺Pd] complex, thus forming PhSSPh or a second equivalent of [PNO³⁻PdSPh], respectively. The final step is the formation of the mixed-valent [(PNO³⁺Pd)(μ-SPh)Pd(PNO³⁻)] (5), through coordination of a sulfur lone pair in [PNO³⁻PdSPh] to free [PNO³⁺Pd]. Starting with a 4:1 ratio of 3/PhSSPh also leads to the clean production of complex 5, thus supporting this pathway. Detection of thyl radicals by EPR spectroscopy with DMPO (DMPO = 5,5-dimethyl-1-pyrroline N-oxide) as a spin-trapping agent was unsuccessful, probably owing to a high recombination rate relative to the generation rate of these thyl radicals, the short lifetime of DMPO·(SPh) adducts, and the competitive reaction of PhS with the solvent benzene. Using a mixture of PhSSPh and di(p-tolyldisulfide

![Scheme 3](image_url)

**Scheme 3.** Proposed mechanism for the formation of dinuclear [(PNO³⁺Pd)(μ-SPh)Pd(PNO³⁻)] (5) with mixed valency in the two PNO scaffolds.
led to co-formation of phenyl(p-tolyl)disulfide, as detected by GC–MS, thus supporting the intermediary of thyl radicals created by this ligand-to-substrate electron transfer process.

In conclusion, the first example of a phosphine ligand appended to a redox-active aminophenol framework is reported. This PNO[$^{18}$] pincer ligand can coordinate to Pd$^{II}$ as a neutral (1), radical monoanionic (2), or dianionic scaffold (3, 4), as supported by spectroscopic, X-ray crystallography, and computational data. Cyclic voltammetry and spectrroelectrochemistry demonstrate reversible single-electron redox events for complex 2. The bulky phosphine arm and rigid backbone enforce considerable steric crowding around the Pd center. One-electron reduction generates complex 3, which is a competent reagent for homolytic bond activation of disulfides through ligand-to-substrate single-electron transfer. The resulting dinuclear Pd species 5, featuring a monomolate bridgehead, contains a unique mixed-valence ligand set, with one PNO[$^{18}$] and one PNO[$^{18}$] unit. The introduction of a flanking phosphine group could allow the expansion of the concept of ligand-induced electron transfer and radical-type reactivity to “softer” low-valent noble metals.

Received: October 13, 2014
Revised: October 30, 2014
Published online: November 27, 2014

Keywords: bond activation · mixed valency · palladium · phosphine ligands · redox-active ligands

The simulated spectrum and calculated hyperfine couplings correlate well with the experimental data, with the exception of some hyperfine interactions (see the Supporting Information).


Reduction potential vs. SCE: PhSSPh/C0 1.6 V; tBuSS/tBu/C0 2.71 V. Bond dissociation energy (BDE) of PhSSPh ≈55.0 kcal mol⁻¹; dialkyldisulfides C25 65 kcal mol⁻¹; MeSSMe: 73.2 kcal mol⁻¹.