Terminal Ni\textsuperscript{III}-oxygen adducts for the activation of strong C–H bonds

Paolo Pirovano,\textsuperscript{a} Erik R. Farquhar,\textsuperscript{b} Marcel Swart,\textsuperscript{c} Aidan R. McDonald*\textsuperscript{d}

\textsuperscript{a}School of Chemistry and CRANN/AMBER Nanoscience Institute, Trinity College Dublin, The University of Dublin, College Green, Dublin 2, Ireland
\textsuperscript{b}Case Western Reserve University Center for Synchrotron Biosciences, National Synchrotron Light Source, Brookhaven National Laboratory II, Upton, NY 11973, USA
\textsuperscript{c}ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain and Institut de Química Computacional i Catàlisi; Universitat de Girona, Facultat de Ciències, Campus Montlivi, 17003 Girona, Spain

**ABSTRACT:** Two metastable Ni\textsuperscript{III} complexes, [Ni\textsuperscript{III}(OAc)(L)] and [Ni\textsuperscript{III}(ONO\textsubscript{2})(L)] (L = N,N\textprime{}(2,6-dimethylphenyl)-2,6-pyrindinedicarboxamidate, OAc = acetate), were prepared, adding to the previously prepared [Ni\textsuperscript{II}(OCO\textsubscript{2}H)](L), with the purpose of probing the properties of terminal late-transition metal oxidants. These high-valent oxidants were prepared by the one-electron oxidation of their Ni\textsuperscript{II} precursors ([Ni\textsuperscript{II}(OAc)(L)] and [Ni\textsuperscript{II}(ONO\textsubscript{2})(L)]) with tris(4-bromophenyl)ammoniumyl hexachloroantimonate. Fascinatingly, the reaction between any [Ni\textsuperscript{II}(X)(L)] and NaOCl/acetic acid (AcOH) or cerium ammonium nitrate ((NH\textsubscript{4})\textsubscript{2}[Ce\textsuperscript{IV}(NO\textsubscript{3})\textsubscript{6}], CAN), yielded [Ni\textsuperscript{III}(OAc)(L)] and [Ni\textsuperscript{III}(ONO\textsubscript{2})(L)], respectively. An array of spectroscopic characterizations (electronic absorption, electron paramagnetic resonance, X-ray absorption spectroscopies), electrochemical methods, and computational predictions (density functional theory) have been used to determine the structural, electronic, and magnetic properties of these highly reactive metastable oxidants. The Ni\textsuperscript{III}-oxo adducts proved competent in the oxidation of phenols (weak O–H bonds) and a series of hydrocarbon substrates (some with strong C–H bonds). Kinetic investigation of the reactions with di-tert-butylphenols showed a 15-fold enhanced reaction rate for [Ni\textsuperscript{III}(ONO\textsubscript{2})(L)] compared to [Ni\textsuperscript{II}(OCO\textsubscript{2}H)(L)] and [Ni\textsuperscript{II}(OAc)(L)], demonstrating the effect of electron-deficiency of the O-ligand on oxidizing power. The oxidation of a series of hydrocarbons by [Ni\textsuperscript{III}(OAc)(L)] was further examined. A linear correlation between the rate constant and the BDE of the C–H bonds in the substrates was indicative of a hydrogen atom transfer mechanism. The reaction rate with DHA (k\textsubscript{cat} = 8.1 M\textsuperscript{−1}s\textsuperscript{−1}) compared favorably with the most reactive high-valent metal-oxido-adducts, and showcases the exceptional reactivity of late transition metal-oxygen adducts.

**Introduction**

The oxidative functionalization of C–H bonds in inert hydrocarbons represents a powerful transformation. Great economic and environmental value would derive from the possibility of converting readily available feedstock chemicals (*i.e.* natural gas and petroleum) into higher value oxidized products, while avoiding the currently employed endothermic and energy-intensive processes, such as cracking and dehydrogenation.\textsuperscript{1} To this end, catalysts based on cheap and abundant first-row transition metals are particularly attractive.

Numerous Fe- and Cu-containing metalloenzymes (oxygenases) perform such hydrocarbon oxidations under ambient conditions, selectively producing hydroxylated, halogenated, or desaturated hydrocarbons.\textsuperscript{2} It has been determined that in many of these natural and non-natural catalyst systems, activation of the C–H bond in the substrate occurs through hydrogen atom transfer (HAT) brought about by a metal in a high-oxidation state with a terminal oxygen ligand.\textsuperscript{3} Examples of enzymatic and synthetic high-valent terminal Mn- and Fe-oxy species are abundant,\textsuperscript{4} however there remain very few examples of terminal late transition metal-oxygen adducts.

While no examples of terminal Ni- and Cu-oxo complexes have yet been reported, progress has been made in preparing late transition metal oxygen adducts. Tolman and co-workers have explored a unique Cu\textsuperscript{III}–OH complex, which could oxidatively activate strong C–H bonds, at rates that rivalled or surpassed Fe-, Mn-, and Ru-oxo complexes (Table 2).\textsuperscript{5} For nickel, in contrast, the scarcity of well-characterized terminal high-valent Ni–O oxidants has posed a problem. We recently reported a Ni\textsuperscript{II–III}–OCO\textsubscript{2}H complex (1b, Scheme 1), prepared from 1a,\textsuperscript{6} which we deemed capable of HAT; unfortunately, in the conditions of the study, the reactions were limited to substrates containing weak O–H and C–H bonds.\textsuperscript{7} Dinuclear, bridged Ni\textsuperscript{II–III}–(O): complexes have also been widely studied, and examples of intramolecular HAT have been observed.\textsuperscript{8} Ray observed the formation of multiple metastable putative Ni\textsuperscript{II–IV}–OCX species, from the reaction of a Ni\textsuperscript{II} complex and 3-chloroperoxybenzoic acid (m-CPBA), and the resulting mixture was capable of oxidizing hydrocarbons with weak C–H bonds (1,4-cyclohexadiene).\textsuperscript{9} To date, the most powerful high-valent nickel oxidant, reported by Company, was a putative formally Ni\textsuperscript{IV} species, obtained from the reaction of a macrocyclic Ni\textsuperscript{III} complex with m-CPBA.\textsuperscript{10} Overall, the Roy/Company species lacked sufficient stability to allow exhaustive characterization. Other terminal Ni\textsuperscript{II–III}–O complexes displayed no particular oxidizing power towards C–H bonds.\textsuperscript{11}

Experimental and theoretical studies on metal-based oxidants have highlighted several factors that affect the HAT reactivity of these species.\textsuperscript{5,12} An important development in the field is the observation that the rate of the reaction is correlated with its thermodynamic driving force.\textsuperscript{13} The existence of a linear relationship between the reaction energy and the activation energy, within a family of simple reactions, was recognized from early kinetic and theoretical studies (Bell-Evans-Polanyi principle).\textsuperscript{14} Mayer has applied a Marcus-theory based approach to describe the HAT reactivity for metal complexes, from which he re-derived the aforementioned relation.\textsuperscript{12c,14} In a HAT reaction between a
metal-oxygen adduct and a C–H bond, the ΔG° is equal to the difference between the bond dissociation free energy (BDFE) of the C–H bond that is broken in the substrate and that of the O–H bond that is formed. An important consequence of the linear free energy relationship is that a higher-energy intermediate will display higher reaction rates, as well as provide the driving force for the activation of stronger C–H bonds. High-valent compounds of the later transition metals are destabilized by their higher electronegativity, lower stability of the high oxidation states, and destabilizing interactions between occupied d-orbitals and π-donating O ligands; hence, we expect late transition metal oxidants could be powerful reagents.\textsuperscript{1b,1c}

To this end, we have explored a series of well-defined, well-characterized, highly reactive high-valent nickel-oxygen complexes. Herein, we report the preparation of two new Ni\textsuperscript{III}-OX complexes, [Ni\textsuperscript{III}(OAc)(L)] (2b) and [Ni\textsuperscript{III}(ONO\textsubscript{2})(L)] (3b), from their Ni\textsuperscript{II}-OX precursors 2a and 3a, respectively (Scheme 1, L = N,N’-(2,6-dimethylphenyl)-2,6-pyrindinedicarboxamidate). We present an investigation into relationships between the properties of the O-donor ligands in 1-3b and their oxidative reactivity. Moreover, we demonstrate that [Ni\textsuperscript{II}(OAc)(L)] (2b) can oxidize a wide range of hydrocarbon substrates, and is capable of activating very strong C–H bonds, making it one of the most potent high-valent metal-based oxidants reported to date.

**Scheme 1. Synthesis of Ni\textsuperscript{I} complexes 2a, 3a, and 4.**

\[
\text{NiCl}_2, \text{CH}_3\text{OH}, 65 \, ^\circ \text{C}; 2) \text{NaOCH}_3; 3) \text{CH}_2\text{CN} \text{Et}_4\text{NNOAc}, \text{CH}_3\text{CN}, \text{Et}_2\text{O}, \text{room temperature}; \text{for } 3a: \text{Et}_4\text{NNNO}_2, \text{CH}_2\text{OH}, \text{Et}_2\text{O}, \text{room temperature}. \text{The synthesis of 1a was previously reported.}\textsuperscript{a}

**Results and discussion**

**Synthesis of [Ni\textsuperscript{II}(X)(L)] complexes:** Et\textsubscript{4}N[Ni\textsuperscript{II}(OAc)(L)] (2a) and Et\textsubscript{4}N[Ni\textsuperscript{II}(ONO\textsubscript{2})(L)] (3a) were obtained via a two-step synthesis (Scheme 1). The neutral complex [Ni\textsuperscript{II}(NCCH\textsubscript{3})(L)] (4) was first synthesized by reacting LH\textsubscript{2} with NiCl\textsubscript{2} (1 equiv.) in the presence of NaOCH\textsubscript{3} (2.1 equiv.), in CH\textsubscript{3}OH. Subsequent CH\textsubscript{2}CN ligand introduction and filtration of insoluble by-products allowed for isolation of pure 4. The product was obtained in 75% yield. The CH\textsubscript{2}CN ligand in 4 could be displaced by the addition of either tetraethylammonium acetate (Et\textsubscript{4}NNOAc, 1.1 equiv.) to a CH\textsubscript{3}CN solution of 4, or tetraethylammonium nitrate (Et\textsubscript{4}NNNO\textsubscript{2}, 1.1 equiv.) to a CH\textsubscript{3}OH solution of 4, to yield 2a and 3a, respectively. 1H and 13C NMR, attenuated total reflectance Fourier transform infra-red (ATR-FTIR), and high resolution electrospray ionization mass spectrometry (ESI-MS) confirmed the structure, composition, and elemental assignments of the complexes.

Single crystals of 2a, 3a, and 4, that were suitable for X-ray diffraction (XRD) measurements were obtained (Figure 1). All the complexes showed the Ni\textsuperscript{II} ion to be in a square planar coordination environment. The geometric parameters of the [Ni\textsuperscript{II}(L)] unit were similar to those of previously reported [Ni\textsuperscript{II}(L)] complexes (Table S1).\textsuperscript{a} The ‘OAc and ‘ONO\textsubscript{2} anions, in 2a and 3a, respectively, bind in a monodentate fashion (Figure 1), similarly to the bicarbonate ligand in 1a,\textsuperscript{a} and lie perpendicular to the [Ni(L)] plane. The XRD experiments confirmed the structure of compounds 2a, 3a, and 4, showing a nearly invariant square planar nickel coordination environment, with bond distances that are largely unaffected by the electron-donating ability of the ancillary ligands.

**Figure 1.** ORTEP plots (at 50% probability level) of the x-ray crystallographically-determined structures of 2a, 3a, and 4; hydrogen atoms for all and counterions for 2a and 3a have been omitted for clarity.

**Preparation and characterization of [Ni\textsuperscript{III}(OX)(L)] complexes:** We previously reported the generation of [Ni\textsuperscript{III}(OAc)(L)] (1b), by the one electron oxidation of 1a.\textsuperscript{b} In an analogous fashion, complexes 2a and 3a were oxidized to yield [Ni\textsuperscript{III}(OAc)(L)] and [Ni\textsuperscript{III}(ONO\textsubscript{2})(L)], respectively (Scheme 2). This was achieved by dissolving 2a and 3a in acetone (0.3 mM) and cooling these solutions to –40 °C. Addition of one equivalent of the one-electron oxidant tris(4-bromophenyl)ammonium hexachloroantimonate (magic blue, dissolved in CH\textsubscript{3}CN), caused an immediate reaction as evidenced by electronic absorption spectroscopy (Figure 2). For both 2a and 3a the immediate appearance of two intense visible and NIR absorption bands in the electronic absorption spectrum, assigned to 2b and 3b respectively, demonstrated their one-electron oxidation.

**Scheme 2. Synthetic routes to the Ni\textsuperscript{II} complexes 1-3b.**

(a) magic blue (1 equiv., acetone); (b) NaOCl/AcOH/H\textsubscript{2}O (15 equiv., acetone); (c) (NH\textsubscript{4})\textsubscript{2}Ce(NO\textsubscript{3})\textsubscript{6} (CAN, 5 equiv., acetone). Grey crossover reactions show that NaOCl/AcOH always yields 2b, and CAN always yields 3b.

**Figure 2.** UV-visible spectra of [Ni\textsuperscript{III}(OX)(L)] complexes 1b (black trace), 2b (blue trace), and 3b (red trace), in acetone solutions. Molar absorptivities were calculated using the Beer-Lambert equation from the measured absorbances and EPR-determined concentrations of the products.
Table 1. Salient spectroscopic features and properties of \([\text{Ni}^{II}(\text{L})]\) and \([\text{Ni}^{III}(\text{OX})(\text{L})]\).

| \(\lambda_{\text{max}}\) (nm) \(\left(\epsilon / M \text{ cm}^{-1}\right)\) | \(\begin{array}{c} \text{VC=O/} \\
\text{CN/N-O} \end{array}\) \(\left(\text{cm}^{-1}\right)\) | \(g_{\perp}, g_{\parallel}\) \((g_{0})\) | \(E_{1/2}\) for \(\text{Fc}/\text{Fc}^+\) \((\text{V})\) | \(\text{Ni-O (Å)}\) | \(\text{Ni K-pre-edge and -edge (eV)}\) | \(k\) \(2,6\)-DTBP \((M^{-1} \text{s}^{-1})\) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>470 (1200)</td>
<td>1618, 1585</td>
<td>0.48</td>
<td>1.878 (^{17}), 1.878 (^{15}), 1.871 (^{17})</td>
<td>8345</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>470 (1200)</td>
<td>1620, 1608, 1585</td>
<td>0.35</td>
<td>1.878 (^{17}), 1.864 (^{15}), 1.870 (^{17})</td>
<td>8333.1, 8345</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>455 (1200)</td>
<td>1623, 1609, 1587, 1290</td>
<td>0.56</td>
<td>1.888 (^{17}), 1.890 (^{15}), 1.888 (^{17})</td>
<td>8327.1, 8345</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>520 (6000), 780 (3600)</td>
<td>2.25, 2.02 (2.17)</td>
<td>1.84 (^{17}), 1.944/2.146 (^{15}) or 1.874 (^{17})</td>
<td>8345</td>
<td>0.104</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>510 (7000), 760 (3300)</td>
<td>2.24, 2.02 (2.17)</td>
<td>1.92 (^{17}), 1.929/2.118 (^{15}) or 1.864 (^{17})</td>
<td>8333.6, 8345</td>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>560 (6700), 890 (4600)</td>
<td>2.25, 2.01 (2.17)</td>
<td>1.93/2.08, 1.944/2.108 (^{15}) or 1.888 (^{17})</td>
<td>8333.8, 8345</td>
<td>1.96</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>435 (1400), 550 (110)</td>
<td>2337, 2311, 1630, 1585</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(a) from EXAFS fitting; (b) from DFT; (c) from XRD; (d) second order rate constant for the reaction with 2,6-di-tert-butylphenol at -40 °C; (e) \(d_z\) spin-density; (f) \(d_z\) spin density.

Such features in the visible region have been identified as typical of \(\text{Ni}^{III}\) complexes of 2,6-pyridinedicarboxamide ligands. Specifically, 2b displayed features at \(\lambda_{\text{max}} = 510\) and 760 nm, while 3b displayed absorption maxima at \(\lambda_{\text{max}} = 560\) and 890 nm (Figure 2). The presence of these features compares favorably to the electronic absorption spectrum of 1b (\(\lambda_{\text{max}} = 520\) and 780 nm, Figure 2), with only minor differences between the OCOH-ligated 1b and OAc-ligated 2b. In the case of the more electron-poor ONO\(_2\)-ligated 3b, red-shifted absorption features (compared to 1b and 2b) were observed, presumably as a result of the ONO\(_2\) ligand being markedly less basic.

We observed that cerium ammonium nitrate \((\text{Ce}^{III}(\text{NO}_3)_3]\), CAN) affected the oxidation of 3a (0.3 mM acetone solution, -40 °C, 5 equiv. of CAN in CH\(_2\)OH) to give 3b as evidenced by electronic absorption spectroscopy and EPR (Figures S19-20). Fascinatingly, addition of excess CAN (5 equiv.) to either 1a or 2a, also caused the appearance of the characteristic absorption bands of 3b (\(\lambda_{\text{max}} = 560\) and 890 nm, Figures S21-22, see supporting information for experimental details), presumably as a result of the large excess of O\(_{\text{NO}_2}\) anions in CAN. In a similar way, we could generate species 2b by oxidizing 2a with hypochlorous acid (formed from an aqueous NaOCl/AcOH mixture, see supporting information for experimental details), as evidenced by electronic absorption and EPR spectroscopies (Figure S23-24). Furthermore, addition of NaOCl/AcOH to 1a or 3a resulted in the formation of features similar to those of 2b (Figure S25-26). In summary, oxidation of the \(\text{Ni}^{II}\) precursors 1-3a by magic blue is a method of general validity, while CAN and NaOCl/AcOH could only cleanly generate O\(_{\text{NO}_2}\)-ligated 3b and OAc-ligated 2b, respectively. We were surprised to observe the formation of anion-ligated complexes for CAN and NaOCl/AcOH, and find this observation quite intriguing given the wide employment of these oxidants to generate terminal metal-oxo species.

1-3b were thermally unstable: at -40°C, half-lives (\(t_{1/2}\)) of 90 minutes for 1b and 200 minutes for 3b were measured; in contrast, 2b showed no appreciable decay over the course of several hours at -40 °C. When 2b was prepared using NaOCl/AcOH it displayed a half-life of 750 s at 25 °C. Neither 1b nor 3b were stable at 25 °C.

Electronic paramagnetic resonance (EPR) spectroscopy analysis of 2-3b showed the presence of a single \(S = \frac{1}{2}\) species for each complex (Figure 3). The spectra displayed axial symmetry with \(g_{\perp} > g_{\parallel}\). The average \(g\) values (\(g_{0}\), Table 1) were consistent with the unpaired electron residing predominantly on the \(\text{Ni}^{III}\) ion. For 1-3b, the \(g\) values (Table S15-17) are essentially equivalent, and together with the shape of the signal (\(g_{\perp} > g_{\parallel}\)) are consistent with a low-spin, \(d_{\text{f}}\) \(\text{Ni}^{III}\) ion in square planar or elongated octahedral coordination environment. The similarities in \(g\)-value are consistent with the XAS-determined metal-ligand bond distances being almost equal for 1-3b, and suggests little to no difference in electronic symmetry at the metal site.

![EPR Spectra](image)

Figure 3. EPR spectra of 1b (black trace), 2b (blue trace), and 3b (red trace), collected from frozen acetone solutions at 77 K, microwave power = 31.6 mW. Simulated spectra can be found in supporting information (Figures S15-17).

Density functional theory (DFT) Mulliken spin density calculations were performed and suggested that the unpaired spin in 1-3b predominantly resides in a metal-based molecular orbital (\(d_{\text{f}}\) or \(d_{\text{f}}\) like molecular orbitals, Table S10). Often when \(g_{\perp} >> g_{\parallel}\) it has been
indicative of a d_s singly occupied molecular orbital. However, we cannot definitively conclude where the unpaired spin density resides, as detailed below. The yields of the S = 1/2 entities were determined to be ~95% (±15), through comparison with a spin standard ((2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), 0.4 mM), based on the concentration of the NiIII starting solutions. This corresponds to a nearly quantitative conversion of the NiIII precursors to NiII-oxygen adducts.

ESI-MS analysis was conducted by injecting thawed acetone solutions of 2b and 3b, immediately after thawing. In the solution of 2b, a peak at m/z = 495 was identified that corresponds to a mass of [2b + Li+]⁺ (Figure S18). For 3b, a mass peak at m/z = 510 was detected (Figure S18), which corresponds to [3b + H3O+]⁺. The isotopic patterns for the observed ions were typical of Ni-containing ions, demonstrating the ions are likely to be the expected NiIII products (simulated spectra in Figure S18). It should be noted that in the ESI-MS analysis of solutions of the NiII precursors 2-3a, only negatively-charged ions could be detected, meaning ESI-MS of the NiII precursor results in the anionic [NiII(OX)(L)]⁻ fragment flying. ESI-MS analysis of the NiII products 2-3b displayed the positively charged ions discussed above. This means that the ESI-MS analysis of 2-3b pertains only to the NiII oxidation state and not the precursor NiII species. The low-temperature ESI-MS analysis thus provides proof for the elemental composition of 2-3b.

Neither 2b nor 3b were sufficiently thermally stable to grow crystals suitable for X-ray crystallography. Therefore, we performed Ni K-edge X-ray absorption spectroscopy (XAS) on frozen solutions of both complexes. The Ni K-edge energy obtained for both 2b and 3b (8345 eV, Table 1) was within the range expected for NiII ions and was almost the exact same as that obtained for 1b (8345 eV). A comparison of the Ni K-edge X-ray absorption near-edge spectra (XANES)(Figures 4 and 544) showed little difference between precursor complexes 1-3a, suggesting that the anionic oxy-donor ligand does not dramatically affect the Ni K-edge energy (Figures 4, S45-S46, Table 1). As with a comparison of the XANES of 1a and 1b, there was little-to-no shift in the Ni K-edge upon comparison of 2-3a with 2-3b, respectively (Table 1, Figure S46). However, the XANES spectra of NiII complexes 2-3a display a markedly different profile/shape to those of 2-3b (Figure S46), indicating a reaction had occurred upon oxidation of 1-3a to yield 1-3b. Analogous observations that identify no edge energy changes when comparing NiIIII species, within comparable coordination environments, have previously been observed. In this instance, contributions to the edge from 1s-to-3p absorption features distort the edge shape (8340 eV), making determination of nickel oxidation state from edge energy alone challenging. We further note that the weak 1s-to-3p pre-edge transitions show modest 0.5-1 eV blue shifts (Table 1, Figure S46) upon conversion of 2a to 2b (8333.1 eV to 8333.6 eV) and 3a to 3b (8332.7 eV to 8333.8 eV), providing further evidence for an altered ligand field in 2-3b consistent with an increase in Ni oxidation state.

Extended X-ray absorption fine structure (EXAFS) analysis of 2b and 3b showed that both contained a first coordination sphere with 4-5 O/N scatterers (Table 1, Tables S5-S8). For 1-3b, there was a small but statistically significant expansion of the average scatterer distance from the absorber in NiIIII 1-3b (the distance gets longer going from 1b to 3b). This would suggest the ‘ONO ligand in 3b was more weakly bound, and a weaker field donor. For 3b the best fits were obtained through splitting the first shell, yielding scattering atoms at 1.93 and a rather long 2.08 Å, respectively. The latter shell presumably reflects a ‘ONO ligand bound in a bidentate fashion in 3b. Fitting the data with a very short Ni-O bond (ca. 1.65 Å) resulted in very poor fits, eliminating the possibility of 1-3b being terminal NiIIII=O.

To further understand the structural properties of 2b and 3b, we performed DFT calculations using an array of methods (Tables S9-10, Figures S48-S50). Firstly, the DFT-predicted Ni-O bond lengths for 1-3a correlated well with the X-ray crystallographically determined bond lengths, and those measured using XAS. For the NiIIII complexes 1-3b, DFT methods suggested negligible difference in relative energy (ca. 1 kcal/mol for species where the unpaired electron resides in a metal-based d_v- or d_d-like molecular orbital (Table S10). Fascinatingly, dramatic differences in the ligand-binding mode are predicted whether the unpaired electron resides in a d_v- or d_d-like orbital, where the ligands are coordinated either in monodentate (d_v) or bidentate (d_d) fashion (Figures S48-S50). The metal-ligand bond-length predictions are also predicted to be affected by the nature of the binding mode (Table 1). Critically, the XAS-determined Ni-O bond length for 3b correlates well with that predicted for 3b with the unpaired electron residing in a d_v-like molecular orbital. The XAS thus suggests that in 3b the ‘ONO ligand may be bidentate, whereas for 1b and 2b the ancillary ligands are likely monodentate. DFT predicts negligible energy differences between 1-3b with the respective binding modes, while EPR suggests that for 1-3b the d_s is occupied, and thus all three should have bidentate donors. Overall, the DFT calculations correlate well with the XAS-determined bond lengths, although the binding mode for the ancillary O-donor ligands remains unclear. Importantly, the ‘ONO ligand in 3b appears to be the weakest-field donor, causing 3b to be the most electrophilic oxidant.

Reactivity Studies: In order to ascertain the effect of varying the oxygen-adduct (i.e. OCOH for 1b, OAc for 2b, ONO for 3b), we performed the reaction between 2,6-di-tert-butylphenol (2,6-DTBP, in excess) and 2b and 3b at -40 °C. We previously demonstrated that 1b reacted with 2,6-DTBP at -40 °C. In order to ensure a fair/effective comparison, we used magic blue as the oxidant in the preparation of 2b and 3b (as was the case for 1b), and the same reaction temperature (-40°C) and solvent medium (acetone) was used for all three reactivity studies. The reactions between 2b and 3b and 2,6-DTBP were monitored by electronic absorption spectroscopy: upon addition of an excess of substrate (>10 equiv. 2,6-DTBP) to 0.3 mM solutions of 2b and 3b in acetone, decay of the absorbance features attributed to 2b and 3b was observed. After the reactions, the radical homo-coupling product 3,3',5,5'-teta-tet-tert-butyl-[1',1'-bis(cyclohexane)]-2,2',5,5'-tetraene-4,4'-dione, together with small amounts of its hydroquinoid form 3,3',5,5'-teta-tet-tert-butyl-[1',1'-biphenyl]-4,4'-diol (Scheme S1), were detected by ESI-MS. The decay was monitored over the course of the reaction, and pseudo first order rate constants (k obs) were obtained by exponential fitting of the decay plot. Second-order rate constants (k) were determined by plotting k obs (determined at varying substrate concentrations) against substrate concentration and calculating the

Figure 4. Normalized XANES spectra of complexes 2a, 2b, 3a, and 3b. The inset shows an expansion of the pre-edge region.
slope of the resulting linear plot (Figure 5). The reactions of 2b and 3b with 2,6-DTBP proceeded with $k_2$ of 0.125 and 1.96 M·s⁻¹, respectively (Table S3). The $k_2$ determined for 2b was thus comparable with that measured for 1b ($k_2 = 0.104$ M·s⁻¹), while that determined for 3b was approximately 15 times greater. The ‘ONO$_2$ ligand thus appears to enhance the oxidative reactivity of 3b by an order of magnitude compared to the terminal ‘OCO$_2$H and ‘OAc ligands in 1b and 2b.

![Figure 5. Plots of $k_{\text{obs}}$ versus [2,6-DTBP] determined for the reaction between 1b (black), 2b (blue), and 3b (red) and 2,6-DTBP at -40°C in acetone.](Image)

We also determined $k_2$ for the reaction of 3b with 2,4-di-tert-butylphenol (2,4-DTBP, $k_2 = 158$ M·s⁻¹), which was 80 times larger than that of 2,6-DTBP (Figure S28). Importantly, different reaction kinetics between these two sterically disparate substrates by the same oxidant has been considered to imply a HAT mechanism. Furthermore, a kinetic isotope effect for the reaction of 1b with 2,6-DTBP of 2.1 was previously measured. The rate constants and KIE values are an important indication that 1,3b perform HAT, rather than another form of proton-coupled electron transfer (PCET) on phenols.

Mayer and co-workers have been at the forefront in defining the HAT reactivity properties of metal-based oxidants. They have demonstrated that thermodynamic driving forces (ΔG of the HAT reaction) determine the reactivity properties of metal-based oxidants. In the HAT reactions between 1,3b and 2,6-DTBP, ΔG would explicitly be correlated with the BDEE of the newly formed O–H bond in the [Ni$_{\text{III}}$(O(H)X)(L)] products (defined as 3a(H)). The BDEE of H$_2$ can be defined as the sum of the free energies of two steps (plus a constant), [Ni$_{\text{III}}$(OX)] + e $\rightarrow$ [Ni$_{\text{III}}$(OX)(L)]$^-$ (1-3a) and [Ni$_{\text{II}}$(OX)(L)]$^-$ (1-3a) + H$^+$ $\rightarrow$ [Ni$_{\text{II}}$(O(H)X)(L)]$^-$ (1-3a(H)), which are represented by $E^p_{\text{Ni(OH)}}$ of 1-3a and the pK$_{\text{A(OH)}}$ of 1-3a(H), respectively. We have endeavored to calculate the BDEE of 1-3a(H) by obtaining $E^p_{\text{Ni(OH)}}$ of 1-3a and a pK$_{\text{A(OH)}}$ of 1-3a(H).

Cyclic voltammograms for solutions of 1-3a in acetone (Bu$_3$NPF$_6$ (0.1 M, Bu$_3$N = tetrabutylammonium), scan rate of 0.05 V/s) displayed quasi-reversible ($\Delta E_{\text{poe}}$: 1a: 0.11 V, 2a: 0.07 V, 3a: 0.13 V) redox waves at $E_{1/2}$ = 0.48, 0.35, and 0.56 V vs. Fe$^3$/Fe$^2$ respectively (Figure 6, Fe$^2$ = ferrocene). The measured $E^p_{\text{Ni(OH)}}$ for 1-3a showed the expected correlation with the electronic properties of the terminal ligands, i.e. the more basic ligands yielded complexes with smaller $E^p_{\text{Ni(OH)}}$ (‘OAc < ‘OCO$_2$H < ‘ONO$_2$). A comparison of the pK$_{\text{A(OH)}}$ of the conjugate acids of the ligands showed that the ‘OCO$_2$H and ‘OAc ligands have similar values (aqueous scale pK$_{\text{A}}$ of AcOH = 4.7, H$_2$CO$_3$ = 3.5). In contrast the ‘ONO$_2$ ligand is much more electron-poor (aqueous scale pK$_{\text{A}}$ of HNO$_2$ = 1.2). The most electrophilic Ni$_{\text{II}}$-oxygen adduct is therefore likely to be 3b, based on the $E^p_{\text{Ni(OH)}}$ for 3a.

![Figure 6. Steady state cyclic voltammograms of 1a (black), 2a (blue), and 3a (red); conditions: 0.3 mM (acetone), 0.1 M Bu$_3$NPF$_6$, scan rate 0.05 V s$^-$, room temperature.](Image)

**Determination of the pK$_{\text{A}}$ of the O–H in 1-3a(H).** As of yet, we have been unable to synthesize the conjugate acid complexes 1-3a(H) (i.e. [Ni$_{\text{II}}$(HCO$_3$)(L)]$_2$), [Ni$_{\text{II}}$(HOAc)(L)], [Ni$_{\text{II}}$(HNO$_2$)(L)]). Upon reaction between AcOH or HNO$_2$ (1 equiv., room temperature) and complex 4, the complex decomposed to yield N$_2$N'-bis(2,6-dimethylphenyl)-2,6-pyridinedicarboxamide, as evidenced by 'H NMR spectroscopy (Figures S29-30). Similarly, electronic absorption and 'H NMR analyses of the reaction between 2a and either Et$_3$O,HBF$_4$ or AcOH showed protonation and decomposition of the complex (Figures S31-33). We are thus unable to experimentally determine the pK$_{\text{A}}$ values of 1-3a(H) and in turn cannot calculate the BDEE of 1-3a(H).

**Discussion on the relative HAT reactivities of 1-3b towards phenols.** In considering the reaction between 1-3b and phenols, the following factors were considered:

(a) On the ancillary ligands of 1-3b (‘OAc, ‘OCO$_2$H, ‘ONO$_2$) there are multiple O-atoms that can be the acceptor/binding site of the incoming H-atom during the reaction between 1-3b and 2,6-DTBP. It is also possible that rather than the ancillary O-atom donor, it is the carboxamido- N- or O-atom that accepts the proton. Given the stark differences in reactivity of 3b compared to 1/2b, we surmise the H-atom to be delivered to the ancillary ligand. While our reactivity studies indicated a (concerted) HAT reaction, that does not necessarily mean the proton and electron are delivered to the same location (Scheme 3). Arguments can be made for at least two mechanistic postulates (thus HAT or separated concerted proton and electron transfer), where the incoming proton either arrives at the proximal or distal O-atoms of the metal bound ‘OCO$_2$H, ‘OAc, and ‘ONO$_2$ ligands in 1-3b.

(b) According to cyclic voltammetry 3a displayed a higher $E^p_{\text{Ni(OH)}}$ than 1-2a, while XAS indicated that 3b displayed the longest Ni–O bond length. These observations indicate that the ‘ONO$_2$ ligand in 3b is a relatively weak-field donor, and causes the Ni$_{\text{II}}$-oxygen adduct 3b to be relatively more electrophilic.

(c) We were unable to determine the BDEE of 1-3a(H), preventing an accurate comparison of the relative BDEE of 1-3a(H) to relative reactivity. Critically, we cannot say with certainty that reaction of 1-3a with H$^+$-donors would result in the same O-atom being protonated as reaction of 1-3b with H-atom donors.

(d) HNO$_2$ is considerably more acidic than H$_2$CO$_3$ and AcOH. Based on this, we postulate that when comparing metal-bound HNO$_2$ to metal-bound H$_2$CO$_3$ and AcOH in 1-3a(H), that the pK$_{\text{A}}$ of the HNO$_2$ in 3a(H) will be lower than for 1-2a(H).
(e) For free AcOH and HNO₂, the BDE₃₁₋₂ are 112 kcal/mol and 101.7 kcal/mol, respectively. To the best of our knowledge BDE/BDE₃₁₋₂ of H₂CO₃ are yet to be predicted/determined. Based on the higher BDE₃₁₋₂ value for AcOH, one would anticipate the acetoxyl radical to display higher rate constants for HAT than the nitro-oxyl radical. This contrasts with our observation that ONO₂-ligated 3b displayed a higher kᵢ than OAc-ligated 2b, suggesting that the BDE₃₁₋₂ in 3a(H) is greater than that in 1a(H) or 2a(H).

Scheme 3. Possible PCET mechanisms for the reaction of NiIII-oxo adducts (NiIII-acetate here) with alcohols (ROH).

In summary, 3a displayed a higher ΔE¹(ν(C-H)) than 1-2a, and 3b is postulated to be the most electrophilic oxidant, while 3a(H) is postulated to contain a more acidic proton than 1-2a(H). 3b displayed a higher kᵢ for the oxidation of phenols, suggesting that the BDE₃₁₋₂ in 3a(H) is greater than that in 1-2a(H). Based on these observations, we surmise that in the reaction between 1-3b and phenols, electron transfer has a greater contribution to HAT reaction rate than proton transfer. This is because the postulated relatively low pKᵢ value in 3a(H) does not cause a relatively low reaction rate, whereas the relatively high ΔE¹(ν(C-H)) for 3a appears to correlate with a higher oxidation rate for 3b. We believe this is an interesting outcome, because it suggests the reactivity of highly-valent oxidants may be tuned by simply tuning the electronic properties of the ancillary oxygen-atom donor ligand.

Hydrocarbon oxidation: At low temperatures (-40 °C), only 1-benzyl-1,4-dihydronicotinamide (BNAH, BDE = 68 kcal mol⁻¹) and 10-methyl-9,10-dihydronicotinamide (BDE = 74 kcal mol⁻¹) were capable of bringing about the decay of 2b and 3b (i.e. were oxidized by 2b and 3b). At room temperature we explored the reactivity of 2b towards hydrocarbon substrates with gradually increasing C–H bond strengths (BDE = 78-90 kcal/mol) including xanthene, 9,10-dihydroanthracene (DHA), fluorene, benzyl alcohol, ethylbenzene and toluene. 2b was found to reductively hydrogenated all of the listed substrates at 25 °C, along timescales that allowed kinetic analysis of the reactions. We determined kᵢ for the reaction of each of these substrates with 2b using methods analogous to those described above for phenols (Table S4, Figures S35-43).

A plot of the logarithms of the kᵢ for the reaction of 2b with each substrate against the substrate BDE₃₁₋₂ showed a linear correlation (Figure 7). This is what was expected for a HAT mechanism, in which BDEs determine the ΔHᵢ of the reaction. Conversely, the correlations between kᵢ and either pKᵢ or reduction potentials ΔE¹(ν(C-H)) of the substrates are poor: the C–H bond of fluorene is more acidic than that of any of the other substrates, and xanthene is far more easily oxidized than the rest. The observed linear relationship between reaction rate and BDE₃₁₋₂ is thus a strong indication of a HAT rate-determining step. Deriving Gibbs energies of activation from the measured kᵢ values, a ΔGᵢ/Δ(BDE) slope of -0.31 can be determined (Figure S44). This value compares favorably with the ΔGᵢ/Δ(ΔGᵢ) value of -0.5 predicted by Marcus theory and experimental values in the range of -0.15 – -0.7 for other comparable complexes (Table 2).

Figure 7. Plot of log(kᵢ), for the reactions of 2b with hydrocarbon substrates, measured at 25 °C, against the BDE₃₁₋₂ of the substrates. BDEs from references. The reaction rate of DHA was corrected by a factor of 2 to account for the second HAT event from anthracenyl radical.

Analysis of the post-reaction mixtures was conducted by GC-MS, and the identified oxidized products were consistent with HAT-initiated oxidation. Oxygenated products were formed from all substrates (xanthone from xanthene, anthraquinone from DHA, fluorenone from fluorene, benzoic acid from benzyl alcohol and toluene and acetophenone from ethylbenzene, Scheme S2). However, from the reaction of DHA with 2b, the main product was the aromatized anthracene, with only traces on anthraquinone being formed. In no case did we find products incorporating chlorine or acetate moieties, demonstrating that the NaOCl/AcOH oxidant is not responsible for the substrate oxidation.

To further investigate the mechanism of the reaction between 2b and hydrocarbon substrates, we employed the deuteronated substrates [D₄]xanthene and [D₄]DHA. The reactions with the deuteronated substrates proceeded more slowly than with the corresponding protonic substrates, giving kinetic isotope effects (KIE) values of 3.0 and 3.3 respectively (Figure S36). These values closely match the KIE value determined for the reaction between 1b and 2,6-DTBP (2.1). The presence of a primary kinetic isotope effect lends further evidence that C–H bond breaking occurs in the rate determining step. The relatively small size of the effect could be explained by the high temperature of the experiment. Should the difference in activation energies be exactly equal to the difference between the zero-point energies of C–H and C–D stretching vibrations, a KIE of 6.9 would be predicted at 25 °C. Lower values, as in the case of 1b and 2b, can arise from a not fully linear O···H·C reaction axis, or from a significant vibration involving the hydrogen atom in the transition state.

DHA is a commonly employed substrate in HAT studies, allowing us to compare the reactivity properties of 2b to those of previously reported high-valent metal-oxygen adducts. We have tabulated the determined kᵢ values for the reaction between DHA and selected complexes of Mn, Fe, Ru and Cu at 25 °C (Table 2). The kᵢ for 2b was about half of that of [FeV(μ-O)(NPy)]²⁺, and only one order of magnitude smaller than [RuV(μ-O)(bpy)²⁺(py)]²⁺ and [CuIV(μ-O)(pyN₄)²⁺], which rank among the most reactive oxidants reported to date. Permanganate (MnO₄⁻), as well as the MnIV-dioxo [MnIV(MeEBC)(O)₂]²⁻, are considerably slower. It should be noted that 2b is not an oxo complex. By comparison, an FeIII-alkoxide complex ([FeIII(OCH₃)(PYS)]²⁻) is a much weaker
oxidant compared to Fe(IV)=O. The high reaction rate of 2b, as well as that of Tolman’s Cu(III)-OH complex, lend weight to the postulated high oxidizing power of complexes based on the late-transition metals.

Table 2. Kinetic parameters for the HAT reactions of selected high valent metal-oxo and other metal-oxygen complexes with DHA.*

<table>
<thead>
<tr>
<th>Reaction</th>
<th>k^‡ (M⁻¹s⁻¹)</th>
<th>KIE</th>
<th>ΔA^G/(AE/ΔBDE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2b</td>
<td>8.11</td>
<td>3.0</td>
<td>0.31</td>
</tr>
<tr>
<td>[Mn(VO)₃]^{3−}</td>
<td>0.12</td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td>[Fe(IV)(Me₂EBC)(O)]_{3−}</td>
<td>~0.03</td>
<td>3.78⁷⁺</td>
<td>0.21</td>
</tr>
<tr>
<td>[Fe(IV)(O)(NPy)]_{2−}</td>
<td>18</td>
<td>10⁶⁻</td>
<td>0.15</td>
</tr>
<tr>
<td>[Fe(III)(OCH₃)(PSy)]_{2−}</td>
<td>0.0049</td>
<td>5.5</td>
<td>0.17</td>
</tr>
<tr>
<td>[Ru(IV)(bpy)₂(py)]_{2−}</td>
<td>125</td>
<td>50-100</td>
<td>0.47</td>
</tr>
<tr>
<td>[Cu(III)(OH)(pyN₂O₂)]_{5,12e}</td>
<td>~190</td>
<td>24⁸⁻</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Notes: The authors declare no competing financial interest.

ACKNOWLEDGMENT

This publication has emanated from research supported by the European Union (FP7-333948, ERC-2015-STRG-678202). Research in the McDonald lab is supported in part by a research grant from Science Foundation Ireland (SFI/12/RC/2278), and in the Swart lab by the Ministerio de Economía y Competitividad (MINECO, projects CTQ2014-59212-P and CTQ2015-70851-ERC), the DIUE of the Generalitat de Catalunya (project 2014SGR1202, and PhD grant 2015_Fi_B_00165), and the European Fund for Regional Development (FEDER, UNG110-4-801). XAS experiments were conducted at SSRL beamline 2-2 (SLAC National Accelerator Laboratory, USA), with support from the DOE Office of Science (DE-AC02-76SF00515 and DE-SC0012704) and NIH (P30-EB-099989). We are grateful to: COST Action CM1305 (ECOSTBio) for networking support; Dr. Brendan Twamley for performing X-ray crystallography measurements; Dr. Anthony Fitzpatrick and Dr. Grace Morgan for EPR technical support; Dr. Apparao Draksharapu and Prof. Wesley Browne for identifying NaOCl/ACOH as a useful oxidant.

REFERENCES


While the thermodynamic relationships are strictly meant to hold for free energies, it is often necessary to substitute BDFs for BDFEs, due to the limited availability of BDFE data in the literature.


The absence of acetate-containing products makes a rebound recombination mechanism unlikely, i.e. one in which HAT is followed by reaction of the resulting carbon-based radical with a ligand in the metal coordination sphere. More likely, water or dioxygen in the solution is the source of the oxygen groups in the oxygenated products. When the oxidation of xanthene was performed in the presence of 30 µL of H[18O], both [18O]xanthone and [18O]xanthone were identified in approximately 1:1 ratio by ESIMS.


