Indirect evidence for a Ni\textsuperscript{III}-oxyl oxidant in the reaction of a Ni\textsuperscript{II} complex with peracid

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The reaction of a Ni\textsuperscript{III} complex and \textit{meta}-chloroperoxybenzoic acid (m-CPBA) resulted in the formation of a long-lived Ni\textsuperscript{III}–chlorobenzoate complex that is a capable hydrocarbon oxidant. Analysis of the post-reaction decay products showed the formation of oxidised derivatives of the supporting ligand (a benzoxazine), and heterolytic O–O bond scission in m-CPBA. This evidence indicates formation of a more potent transient Ni\textsuperscript{III}-oxyl species, which was further supported by DFT calculations.

The study of high-valent transition metal oxidants has attracted recent interest, largely because of their postulated role as highly reactive intermediates in several industrially and biologically relevant oxidation processes.\textsuperscript{1} Nickel-oxo (Ni=O) and -oxyl (Ni–O\textsuperscript{−}) species have been invoked as the putative oxidants in nickel-catalysed oxidation reactions. Ni=O complexes have been predicted to be the most reactive in a series of metals towards the oxidation of CH\textsubscript{2},\textsuperscript{2} although experimental insight into such species is limited.

Early mechanistic studies on Ni-catalysed epoxidation reactions proposed Ni\textsuperscript{IV}–O as an oxidising reagent, on the basis of analysis of product distribution and side reactions.\textsuperscript{3} More recently, Itoh and Palaniandavar have demonstrated Ni-catalysed alkane oxidations, and suggested a Ni\textsuperscript{II}–O\textsuperscript{−} or Ni\textsuperscript{III}–O\textsuperscript{−} oxidant.\textsuperscript{4} Several bis-μ-oxo-Ni\textsuperscript{II} have been reported,\textsuperscript{5} but terminal Ni–O\textsuperscript{−} or Ni=O are still largely unknown. The reactions of Ni\textsuperscript{III} complexes with peracids have yielded highly reactive but poorly-defined species, postulated to be Ni=O(X)\textsuperscript{−} or Ni–O\textsuperscript{−}.\textsuperscript{6} Itoh and co-workers recently demonstrated the formation of a highly unusual Ni\textsuperscript{II}–aminoxyl radical from the reaction between a Ni\textsuperscript{II} complex and peracid.\textsuperscript{7} We recently reported well-characterised examples of Ni\textsuperscript{III}-oxygen adducts, that were proficient hydrogen atom transfer (HAT) reagents.\textsuperscript{8} Further exploration of the active oxidants formed in the catalytic reactions would yield precious insights into their mechanisms of oxidation. Herein, we explore the reaction of a Ni\textsuperscript{II} complex (1, Scheme 1) towards \textit{meta}-chloroperoxybenzoic acid (m-CPBA), and provide evidence for the formation of a transient high valent Ni\textsuperscript{III}–O\textsuperscript{−} oxidant, and trap a thermodynamically more stable Ni\textsuperscript{III}–carboxylate product.

**Scheme 1.** Preparation of 3 by ligand exchange with 1.

Upon addition of m-CPBA (2 equiv.) to a solution of 1 at 25 °C (0.5 mM, 2 mL, acetone or CH\textsubscript{3}CN), a colour change from orange to dark purple occurred. The maximum yield of the purple species, on the basis of the intensity of the newly formed electronic absorption bands (λ\textsubscript{max} = 560 nm, 760 nm (shoulder), Figure 2), was obtained after 350 s. The purple species subsequently decayed with a half-life of 2100 s at 25 °C. We previously reported that [Ni\textsuperscript{III}(OX)(L\textsuperscript{*})] (OX = OCO\textsubscript{2}H, O\textsubscript{2}C\textsubscript{2}H\textsubscript{5}, O\textsubscript{2}CN\textsubscript{2}) complexes, displayed absorption features in the range λ\textsubscript{max} = 500-900 nm.\textsuperscript{9} The spectrum of the product of
the $m$-CPBA + 1 reaction is reminiscent of these compounds, suggesting a $[\text{Ni}^{III}(\text{OX})(L)]$ species had formed.

![Figure 2](image)

**Figure 2.** Electronic absorption spectra of 1 (0.5 mM, acetone, 25 °C, blue trace) and the same solution after addition of $m$-CPBA (2 equiv., 25 °C, purple trace); 3 (0.5 mM, acetone, -80 °C, orange trace) and of the oxidation product 2 resulting from the addition of 1 equiv. magic blue (red trace) to 3.

Electrospray ionisation mass spectrometry (ESI-MS) analysis of the 1 + m-CPBA mixture revealed one peak, with an isotopic pattern typical of a Ni-containing species, at $m/z = 696$, consistent with a $[\text{Ni}(\text{OOCOC}_{6}H_{5}Cl)(L)]^{+}$ ion (m/z 696.2139, Figure S3); presumably this species results from the ionisation of a neutral $[\text{Ni}^{III}(\text{O}_{2}CC_{6}H_{5}Cl)(L)]$ species present in solution.

Electron paramagnetic resonance (EPR) analysis of the reaction mixture (Figure 3) displayed a signal suggestive of a mixture of two low-spin $S = \frac{1}{2}$ $d^9$ Ni$^{III}$ species, similar to previously reported Ni$^{III}$ complexes.\textsuperscript{9} We simulated the spectrum as an approximately 1:1 mixture of an axial signal ($g_{\perp} = 2.23$, $g_{\parallel} = 2.01$) and a markedly more rhombic one ($g_{\perp} = 2.42$, $g_{\parallel} = 2.26$, $g_{z} = 1.99$). Double integration of the signal and comparison with a radical standard (0.5 mM 2,2,6,6-tetramethylpiperidin-1-yl)oxyl, TEMPO) demonstrated a total yield of $S = \frac{1}{3}$ of about 50 ± 20%, on the basis of the starting concentration of 1. On the basis of the electronic absorption, mass, and EPR spectra, and in analogy with previously studied $[\text{Ni}^{III}(\text{OX})(L^*)]$ complexes, we postulated that one of the products was $[\text{Ni}^{IV}(\text{O}_{2}CC_{6}H_{5}Cl)(L)]$ (2).

We have previously demonstrated that $[\text{Ni}^{III}(\text{OX})(L^*)]$ could be prepared by the one electron oxidation of the corresponding $[\text{Ni}^{III}(\text{OX})(L^*)]$\textsuperscript{9}. In order to prepare the putative $[\text{Ni}^{III}(\text{O}_{2}CC_{6}H_{5}Cl)(L)]$, we synthesised Et$_3$N$[\text{Ni}^{III}(\text{O}_{2}CC_{6}H_{5}Cl)(L)]$, 3 (Scheme 1), by the reaction of 1 with crude Et$_3$N(OOCOC$_6$H$_5$Cl) (obtained by the metathesis of Et$_3$NCl and NaOOCOC$_6$H$_5$Cl in CH$_3$OH, see supp. info). Single crystal X-ray diffraction measurements confirmed the structure of 3 (Figure 1), and was supported by NMR, FT-IR, and ESI-MS (see supp. info).

The oxidation of 3 with tris(3-bromophenyl)ammoniumyl hexachloroantimonate (magic blue, 1 equiv., -80 °C, acetone) resulted in a purple solution, whose electronic absorption spectrum displayed bands at $\lambda_{\text{max}} = 580$ and 780 (shoulder) nm (Figure 2). Such features have been identified as typical for $[\text{Ni}^{III}(\text{OX})(L^*)]$ complexes,\textsuperscript{9} allowing us to identify this compound as $[\text{Ni}^{III}(\text{O}_{2}CC_{6}H_{5}Cl)(L)]$ (2). Critically, the obtained spectrum possessed a similar profile to that obtained from the 1 + m-CPBA mixture, with intense bands in the visible region (Figure 2, Figure S1). However, there was a shift in the $\lambda_{\text{max}}$ values (20 nm), which we attribute to the presence of at least two Ni$^{III}$ species in the 1 + m-CPBA reaction mixture. The EPR spectrum of 2 (Figures 3 and S2) corresponded to a single species ($g_{\perp} = 2.42$, $g_{\parallel} = 2.26$, $g_{z} = 1.99$). Such signals are typical of $[\text{Ni}^{III}(\text{OX})(L^*)]$ species.\textsuperscript{8} Importantly, 2 displayed EPR features identical to the rhombic component in the mixture obtained from the mixture of 1 and m-CPBA (Figure 3). ESI-MS analysis of pure 2 showed a peak at $m/z = 696$, corresponding to a $[2]^+$ ion, which was also observed in the 1 + m-CPBA mixture (Figure S4). The same product (2, $[\text{Ni}^{IV}(\text{OOCOC}_{6}H_{5}Cl)(L)]$) was thus acquired from the one-electron oxidation of 3, as from the reaction of 1 with excess m-CPBA.

The formation of 2 corresponds to a net one-electron oxidation of 1. m-CPBA can react either as a two- or one-electron oxidant. Two-electron oxidation by m-CPBA results from heterolytic O–O bond scission, while a one-electron oxidation derives from homolytic O–O bond scission. It has been previously reported that these two occurrences can be distinguished on the basis of the m-CPBA-derived product.\textsuperscript{4,10} In the former a Ni$^{IV}$=O/Ni$^{III}$–O moity and meta-chlorobenzoic acid (m-CPBA) would form and in the latter a Ni$^{IV}$=O/Ni$^{III}$–O entity and a meta-chlorobenzeno carbonyl radical would form. The meta-chlorobenzeno carboxyl radical would decay further by decarboxylation and further radical-type reactions to yield chlorobenzene, 1,3-dichlorobenzene, or 3-chlorophenol.\textsuperscript{10} We analysed the 1 + m-CPBA reaction mixture by GC-MS, after

![Figure 3](image)

**Figure 3.** X-Band EPR spectra of the reaction mixture of 1 and m-CPBA (top, black line; dashed line = simulated spectrum) and of 3 and magic blue (purple, bottom); measured at 77 K in frozen acetone solution, 2 mW microwave power. Simulated spectra (middle) of the two individual components of the 1 + m-CPBA mixture are in red ($g_{\perp} = 2.23$, $g_{\parallel} = 2.01$) and blue ($g_{\perp} = 2.42$, $g_{\parallel} = 2.26$, $g_{z} = 1.99$).
acidic work-up, but didn’t identify any of chlorobenzene, 1,3-dichlorobenzene, or 3-chlorophenol. Moreover, separation by column chromatography of the post-reaction mixture showed recovery of m-CBA in high yield (>90%, see supp. Info.). These observations suggest that the reaction of 1 with m-CPBA resulted in heterolytic cleavage of the O–O bond, and the formation of a Ni\textsuperscript{III}=O/Ni\textsuperscript{II}–O species. 2 is not a Ni\textsuperscript{IV}=O/Ni\textsuperscript{II}–O complex, and therefore, we assume it derives from the transient Ni\textsuperscript{IV}=O/Ni\textsuperscript{II}–O species (Scheme S1).

Heterolytic O–O bond scission is further corroborated by DFT calculations (S12g/TZ2P//BP86-D\textsubscript{2}/TDZP including COSMO solvation and ZORA relativistic effects\textsuperscript{11}) which showed that after binding of m-CPBA, the O–O bond broke spontaneously resulting in a hydroxo-Ni\textsuperscript{II}–carboxylate adduct (Figure S21). Subsequent spontaneous loss of m-CBA, after proton transfer from this adduct, lead to the formation of a Ni\textsuperscript{IV}–O\textsuperscript{2−} species (Figure S22). The Ni\textsuperscript{III}–O\textsuperscript{2−} entity (S = 1) was found to be more stable than the Ni\textsuperscript{IV}O\textsuperscript{−} (S = 0) by ca. 9 kcal/mol\textsuperscript{−1}, and carries unpaired spin density on both the metal, nitrogens, and the oxygen atom (Figure 4).

In order to understand the 1 + m-CPBA reaction further we performed an acidic work-up of the reaction mixture, which caused demetallation, and isolated all organic products by column chromatography. Alongside non-derivatised ligand (LH\textsubscript{2}) one major ligand-oxidised product (4) was obtained (Figure 5), as well as traces of other degradation products (see supp. info., Scheme S2). Importantly, none of these ligand-derived organic molecules were formed in the reaction of LH\textsubscript{2} with m-CPBA (room temperature, acetone) or from the natural decay of the Ni\textsuperscript{III}–carboxylate 2 (prepared with magic blue in acetone, -45 °C to room temperature).

Crystals of 4 that were suitable for X-ray diffraction, obtained from ethanol/H\textsubscript{2}O, demonstrated 4 to be a benzoazine derivative of LH\textsubscript{2} (Figure 5). The yield of 4, after column chromatography, was 35% relative to the quantity of 1. We believe there are two plausible mechanisms for the formation of 4 in the reaction of 1 with m-CPBA (Scheme 2). In both cases, the putative Ni\textsuperscript{III}–O\textsuperscript{2−} presumably abstracts a hydrogen atom from a methine H–C(CH\textsubscript{3})\textsubscript{2}, yielding a methine radical and a Ni\textsuperscript{II}–OH. These products could undergo radical rebound to yield a hydroxylated species (mechanism A, Scheme 2). The hydroxylated ligand could then undergo cyclisation-condensation, to yield the benzoazine product. Alternatively, the methine radical would react directly with the carboxamide oxygen, in a radical coupling fashion, ultimately yielding the benzoazine (mechanism B, Scheme 2). Analogous benzo-1,3-oxazines have typically been prepared by the acid-promoted cyclisation-condensation of 2-acylamido-benzylalcohols, thus supporting mechanism A.\textsuperscript{12} Metal based oxidants such as MnO\textsubscript{2} or PbO\textsubscript{2} have been observed to effect this kind of transformation.\textsuperscript{13} To the extent of our knowledge, radical-type mechanisms (as in mechanism B, Scheme 2) have not been investigated.

The two mechanisms can be differentiated by the source of the oxygen atom in the product: the putative Ni\textsuperscript{III}–O\textsuperscript{2−} oxidant in case A, or the carboxamide O-atom originally present in the ligand in case B. In order to resolve this question, we performed the reaction between 1 and m-CPBA in the presence of H\textsubscript{2}O\textsuperscript{18} (435 equiv.). By ESI-MS, we observed ~30% \textsuperscript{18}O incorporation in the benzoazine product 4 (Figure S5). This is a strong indication that the benzoazine is formed through the intermediate alcohol product, derived from hydroxylation by a putative Ni\textsuperscript{III}–O\textsuperscript{2−} species, because such a species is likely to exchange with H\textsubscript{2}O\textsuperscript{18} whereas the carboxamide oxygen is unlikely to undergo exchange with H\textsubscript{2}\textsuperscript{18}O.

This was supported by DFT analysis, which showed that although in the Ni\textsuperscript{III}–O\textsuperscript{2−} species the methine hydrogen H–C(CH\textsubscript{3})\textsubscript{2} was further away from the oxygen atom (2.95 Å) than the methyl hydrogens HCH\textsubscript{2}CH\textsubscript{3} (2.51 Å), the barrier for HAT was found to be significantly lower for the methine (8.7 kcal-mol\textsuperscript{−1}) than the methyl (13.8 kcal-mol\textsuperscript{−1}) hydrogen atoms (Figure 6). For the subsequent step (Scheme 2), where either hydroxide radical rebound (mechanism A) or carboxamide O-
atom radical coupling (mechanism B), DFT also supports the experimental observations. The barrier for the rebound pathway was found to be substantially lower (6.5 vs. 14.4 kcal·mol$^{-1}$, Figure 6), corroborating the results from the isotopic labelling experiments. This allowed us to conclude that a metal-based oxidant, distinct from the Ni$^{III}$-containing 2, is transiently formed when 1 was reacted with m-CPBA, and causes the oxidation of the supporting ligand.

The formation of degradation product 4 demonstrates that the putative Ni$^{III}$–O$^{-}$ intermediate can be reduced by the transfer of one of the ligand’s hydrogen atoms. In the reaction between 1 and m-CPBA, we postulate that the observed species 2 is formed by a similar process, in which an exogenous reductant, most likely the solvent, causes the conversion of Ni$^{III}$–O$^{-}$ to Ni$^{III}$–OH (Scheme S1). The latter subsequently reacts with m-CBA via ligand exchange, to form 2. While we cannot confirm the structure of the second EPR-active product (axial signal, Figure 3) in the reaction of 1 and m-CPBA, we postulate that it is a Ni$^{III}$ species supported by the oxidised ligand (thus a Ni$^{III}$ ion supported by 4).

We have previously demonstrated$^{3b}$ that [Ni$^{III}$(OX)(L$^*$)] complexes were not capable of oxidising cyclohexane (BDE$_{C-H}$ = 99 kcal/mol).$^{15}$ We believe the putative Ni$^{II}$–O$^{-}$ will be a more potent oxidant than the [Ni$^{III}$(OX)(L$^*$)] complexes. We reacted 1 and m-CPBA in the presence of excess cyclohexane (80% by volume). Cyclohexanol, the hydroxylated product of cyclohexane, was found in trace amounts by GC-MS. The putative transient Ni$^{III}$–O$^{-}$ is thus capable of oxidising non-activated, alkylic C–H bonds, and is a superior oxidant compared to well-characterised [Ni$^{III}$(OX)(L$^*$)] complexes.

In conclusion, the reaction of 1 with m-CPBA leads to the formation of a stable [Ni$^{III}$L(O$_2$C$_2$H$_4$C)] species, that previous studies have shown can oxide substrates with relatively weak C–H bonds (e.g. toluene). The analysis of organic decay products led us to surmise the existence of a more powerful, transient Ni$^{III}$–O$^{-}$ precursor to this Ni$^{III}$ species. The slow reaction of m-CPBA and instability of the Ni$^{III}$–O$^{-}$ prevented its spectroscopic observation. When compared to the previously investigated [Ni$^{II}$(OX)(L$^*$)], this formally Ni$^{IV}$ entity demonstrated a greater oxidative power, reacting with strong C–H bonds in cyclohexane and effecting the degradation of the supporting ligand. The Ni$^{III}$–O$^{-}$ mediated ligand oxidation resulted in the unexpected formation of benzoazine 4. Future efforts will focus on the stabilisation of the Ni$^{III}$–O$^{-}$ to facilitate its isolation.

Conflicts of interest: There are no conflicts of interest to declare.

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References


Graphical Abstract

The oxidation of a Ni\textsuperscript{II} complex with m-CPBA is shown to promote the formation of a transient Ni\textsuperscript{III}-O\textsuperscript{\cdot} species. Methine C-H bond activation in the supporting ligand led to a benzoxazine product.