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Nitrile Oxidation at a Ruthenium Complex leading to Intermolecular Imido Group Transfer

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Abstract

The oxidation of an acetonitrile ligand coordinated to ruthenium is explored in deuterated dimethylsulfoxide by ^1H NMR spectroscopy. When oxidized with an iodosoarene oxygen atom transfer (OAT) reagent, kinetic studies demonstrate that the nitrile ligand does not dissociate before reacting. Instead, OAT to the central nitrile carbon is implicated (nitrile oxidation), and is further supported by the product of the reaction, *N*-acyl-dimethylsulfoximine. The *N*-acyl-dimethylsulfoximine likely formed by an imido group transfer reaction from ruthenium to the NMR solvent, and the product was synthesized independently to verify its identity in the reaction. This reaction represents the first time that a nitrile oxidation reaction has resulted in intermolecular imido group transfer to a substrate, presumably through a reactive ruthenium(IV)imido intermediate. This suggests that nitrile oxidation is a plausible route into reactive metal-imido intermediates for amination and aziridination reactions.

Graphical Abstract

TEXT OF COMMUNICATION

Nitrile oxidation is an underexplored organometallic reaction where an oxygen atom is transferred to the central carbon of a coordinated nitrile ligand, generating functional groups that can be formalized as metal-imidos, metal-iminyls, or metal-nitrenes.¹ Given the rich histories of these compounds as intermediates in amination and aziridination catalysis,² nitrile oxidation represents a potential way to generate reactive imido functional groups from inexpensive starting materials like acetonitrile and oxygen atom transfer reagents like

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Supporting Information Available: Experimental details, Figure S1, ^1H and ^{13}C NMR spectra, UV-visible spectra, and kinetics studies are available free of charge at pubs.acs.org.

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hydrogen peroxide, pyridine-*N*-oxide, or iodosobenzene. Although new cyclic classes of imido precursors like dioxazolones and isoxazolones have been developed in recent years to complement traditional azide and iminoiodinane precursors,³ utilizing acetonitrile as both a reaction solvent and an imido precursor would be advantageous, both for the sake of cost and for the sake of simplicity.

The nitrile oxidation reaction was first observed in 1998, when pyridine-*N*-oxide was used as an oxygen atom transfer (OAT) reagent in an attempt to oxidize a tungsten-nitrile compound to a tungsten-oxo product.⁴ Instead of dissociation of the nitrile ligand and OAT to the metal at the vacant coordination site, OAT to the κ^2 -coordinated nitrile was observed instead to synthesize a tungsten-imido compound (Scheme 1). The nitrile oxidation reaction proceeded smoothly with acetonitrile, propionitrile, and benzonitrile in the coordination sphere, and the structures were confirmed by single crystal X-ray spectroscopy. The corresponding metal-imido compounds, however, were stable, and did not transfer the imido moiety to phosphine substrates, even when heated.

Since this first report of nitrile oxidation, only a few others have been published, and they are summarized here. They include an unexpected aerobic nitrile oxidation of a tungsten-acetonitrile compound during column chromatography to form a tungsten-imido,⁵ nitrile oxidation of a dinuclear molybdenum-acetonitrile compound with nitrate or nitrite to form an amidato bridging ligand,⁶ and an iodosoarene oxidation of an electron-deficient 3,5-bis(trifluoromethyl)benzonitrile ligand coordinated to iridium that led to insertion into the iridium-carbon bond of a cyclometalated 2-phenylpyridine ligand.⁷ In all cases, intermolecular imido group transfer to a substrate was not observed: the tungsten-imido compound and the amidato-bridged dinuclear molybdenum compound were both stable, and the amide-functionalized 2-phenylpyridine ligand could not be cleaved from iridium or generated catalytically.

Nitrile oxidation is rarely observed because nitrile ligands are weak ligands that predominately dissociate in solution, resulting in OAT to the metal. The handful of times that nitrile oxidation has been observed, it has not resulted in intermolecular imido group transfer to a substrate, but has instead generated stable metal compounds. If nitrile oxidation was instead followed by imido transfer to a substrate, it would be a first in the field and provide a proof-of-concept that nitrile oxidation could be coupled to valuable amination and aziridination reactions. In this communication, nitrile oxidation is reported at a ruthenium-acetonitrile complex and is followed by intermolecular imido group transfer to the reaction solvent, deuterated dimethylsulfoxide.

OAT to Ruthenium.

The goal of this project was to choose a metal that is an active imido transfer catalyst that could also facilitate a nitrile oxidation reaction. Ruthenium has been used as a catalyst for aziridination and amination reactions,^{8,9} and it also catalyzes nitrile hydration in basic conditions by activating the central nitrile carbon to nucleophilic attack by water.¹⁰ For this study, the known polypyridyl-ruthenium compound [Ru(terpy)(bipy)MeCN][NO₃]₂ was synthesized (**1**, terpy = 2,2':6',2''-terpyridine, bipy = 2,2'-bipyridine, MeCN = acetonitrile), with a coordinated acetonitrile ligand and with strong σ -donating polypyridyl

ligands that support oxidation of the metal center.^{11–13} The +2 charge on the metal might also be expected to slow dissociation of the coordinated acetonitrile ligand and make the central nitrile carbon more electrophilic. The oxygen atom transfer (OAT) reagent 2-*tert*-butylsulfonyliodosobenzene (**2**) was selected as the oxidant because the iodosoarene moiety is nucleophilic, and the *tert*-butylsulfonyl group of **2** prevents intermolecular interactions between the iodosoarene functional groups, making the OAT reagent soluble.^{14–19}

The ruthenium compound **1** and the OAT reagent **2** were reacted in deuterated dimethylsulfoxide (DMSO-*d*₆), and the reaction was monitored by ¹H NMR spectroscopy (Figure 1). Approximately one-half of an equivalent of unbound acetonitrile (2.09 ppm) was present in the sample of **1**, which provided clues to the fate of the coordinated nitrile ligand in the reaction. As the reaction progressed, the coordinated acetonitrile peak at 2.33 ppm disappeared, while a new resonance at 1.93 ppm increased. Intriguingly, the concentration of the unbound acetonitrile resonance was essentially unchanged during the course of the reaction (starting at 0.0094 *M* and ending at 0.0091 *M*, using an internal standard). This suggested that the coordinated acetonitrile ligand was part of a chemical reaction and did not simply dissociate. It was also noted that a new metal species grew in with the reacted acetonitrile peak at 1.93 ppm.

When the products of the reaction could not be isolated due to the small scale of the NMR reaction, it was postulated that the new ruthenium species was a ruthenium(II), six *d*-electron species because it was diamagnetic. A ruthenium(IV)imido with four *d*-electrons would be expected to be paramagnetic. UV-visible absorption spectroscopy of the completed reaction revealed an MLCT band at 415 nm, which was consistent with an earlier report of a sulfur-coordinated [Ru(terpy)(bipy)DMSO]²⁺ adduct with an MLCT band at 412 nm (the MLCT band of the acetonitrile adduct, **1**, was found to be 454 nm in the same report).²⁰ The DMSO-*d*₆ adduct, [Ru(terpy)(bipy)DMSO-*d*₆][NO₃]₂ (**3**), was synthesized *in-situ* by refluxing [Ru(terpy)(bipy)Cl]Cl with two equivalents of silver nitrate in DMSO-*d*₆ (Scheme 2). Chloride abstraction, followed by coordination of the DMSO-*d*₆ solvent, yielded an authentic sample of **3**. The ¹H NMR spectrum of the *in-situ* sample of **3** was identical to the ¹H NMR spectrum of the ruthenium product in the reaction between **1** and **2** (Supporting Information, Figure S1), confirming the identity of the ruthenium product as the DMSO-*d*₆ adduct **3**.

Once the identity of the ruthenium product was discovered, the identity of the reacted acetonitrile ligand was explored. It was hypothesized that if nitrile oxidation occurred to generate a transient ruthenium(IV)acyl-imido, imido transfer to the DMSO-*d*₆ NMR solvent could occur, yielding an *N*-acyl-dimethylsulfoximine. The postulated product would show only one peak in the ¹H NMR spectrum because the methyl groups adjacent to sulfur would be deuterated. To test this hypothesis, a non-deuterated *N*-acyl-dimethylsulfoximine (**4**) was synthesized according to literature procedures,^{21–23} and its ¹H NMR spectrum was compared to the ¹H NMR spectrum of the reaction between **1** and **2** (Scheme 3). Importantly, the ¹H NMR spectrum of **4** in DMSO-*d*₆ included a three-proton singlet at 1.93 ppm, which matched the ¹H NMR spectrum of the completed reaction between **1** and **2**. In addition, the ¹³C NMR spectrum of the completed reaction of **1** and **2** included resonances for the reacted acetonitrile ligand at 178.6 ppm and 26.4 ppm that exactly matched

resonances in the ^{13}C NMR spectrum of independently synthesized **4**. This provided preliminary evidence that the acetonitrile ligand of **1** had reacted to form an *N*-acyl-dimethylsulfoximine.

To unambiguously confirm the identity of the product, a completed reaction of **1** and **2** was spiked with one equivalent of independently prepared **4** and the change monitored by ^1H NMR spectroscopy (Figure 2). The product peak at 1.93 ppm remained sharp but the concentration doubled (internal standard), confirming that the organic product of the reaction was indeed *N*-acyl-dimethylsulfoximine **4**, with deuterated methyl groups adjacent to the sulfur atom. A similar imidation reaction of sulfides and sulfoxides using a Ru(tetraphenylporphyrin)(CO) catalyst has been reported, but a dioxazolone was used as an imido transfer reagent to access reactive ruthenium species.²³

These results are significant because acetonitrile reacted with an OAT reagent, and imido group transfer to a substrate was observed. Next, the kinetics of the reaction were examined to ascertain if nitrile oxidation was the mechanism operating to access the reactive ruthenium species. If nitrile oxidation was occurring, it would be the first example of nitrile oxidation followed by intermolecular imido group transfer to a substrate.

Rate Law and Mechanism.

The order of the reactants **1** and **2** were determined under pseudo first-order conditions using ^1H NMR spectroscopy. Notably, the iodosoarene **2** fully dissolved at the start of the reaction, simplifying kinetic analysis. Ruthenium compound **1** (0.020 *M*) was reacted with excess **2** (0.110 *M*) in DMSO-*d*₆, and a linear plot was obtained when the $\ln[\mathbf{1}]$ was plotted as a function of time, giving a line of best fit with an R^2 value of 0.9929 after the reaction was 89% complete. Similarly, the reaction of the OAT reagent **2** (0.012 *M*) with excess **1** (0.040 *M*) gave a linear plot when the $\ln[\mathbf{2}]$ was plotted against time (R^2 value of 0.9913 after the reaction was 85% complete). These results clearly indicated that the reactants **1** and **2** were both first order, and the rate law is shown in Equation 1.

$$\text{Rate} = k[\mathbf{1}]^1[\mathbf{2}]^1 \quad (1)$$

After determining the rate equation, the mechanism of the reaction was explored. To ascertain if acetonitrile was coordinated to ruthenium when the metal was oxidized by **2**, the rate of the reaction was monitored with increasing amounts of acetonitrile added to the reaction mixture. For nitrile oxidation, the oxidant **2** would directly transfer an oxygen atom to the coordinated nitrile ligand of **1**, as represented by Equation 2. The reaction rate of this mechanism would not be slowed by adding unbound acetonitrile to the reaction mixture.

If dissociation of acetonitrile was prerequisite to oxidation, this would lead to a rapid equilibrium with the five-coordinate ruthenium compound, $[\text{Ru}(\text{terpy})(\text{bipy})]^{+2}$ (Equation 3). The rate of this reversible reaction would slow down as acetonitrile is added.

The pseudo first-order conditions employed to determine the order of the ruthenium reactant **1** were replicated, and the reaction was run in the presence of 5 equivalents, 10 equivalents, and 15 equivalents of acetonitrile added to the reaction mixture. The observed rate constants from the first-order plots are shown in Table 1.

The observed rate constants showed no dependence on acetonitrile added, which is consistent with the mechanism of nitrile oxidation according to Equation 2. Furthermore, we attempted to measure the rate of acetonitrile dissociation from **1** in DMSO-*d*₆ with 15 equivalents of a strongly coordinating ligand, pyridine, present in solution (**2** was excluded from the reaction).¹³ The substitution reaction was too slow to conveniently gather kinetic data, as only 13% of **1** had reacted after 24 hours (entry 5 in Table 1). In sharp contrast, the reaction between **1** and **2** was 89% complete after 42 minutes. The rate of dissociation, therefore, was much slower than the reaction rate between **1** and **2**, ruling out dissociation of acetonitrile as the first step of the reaction and confirming the nitrile oxidation mechanism. Notably, this is the first nitrile oxidation reaction observed at ruthenium.

The proposed mechanism in the reaction between **1** and **2** is presented here. The data are consistent with nitrile oxidation (OAT to acetonitrile when it is coordinated to ruthenium) in the first step, plausibly generating a transient Ru(IV)imido intermediate (see abstract graphic). In the second step, imido group transfer occurs to the DMSO-*d*₆ solvent, yielding *N*-acyl-dimethylsulfoximine **4** and the solvent-coordinated **3**, [Ru(terpy)(bipy)DMSO-*d*₆][NO₃]₂. Notably, imido transfer from isolated Ru(IV)imido compounds to tertiary phosphines has been observed previously, but transfer was approximately 60 times faster from the Ru(V) oxidation state.²⁴ This suggests that easily-oxidized substrates like DMSO and phosphines can react with Ru(IV)imido species.

In conclusion, this reaction is significant because it is the first time nitrile oxidation at any metal has been followed by intermolecular imido transfer to a substrate. This suggests that nitrile oxidation is a plausible route into reactive metal-imido compounds for amination or aziridination reactions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(a) A ruthenium-acetonitrile complex (**1**) and a soluble iodosoarene oxygen atom transfer reagent (**2**) for the study of nitrile oxidation. (b) Expansion of the alkyl region of the ^1H NMR spectrum to show the reaction of the acetonitrile ligand.

Figure 2. Overlay of the ¹H NMR spectra of the reaction between **1** and **2**, before and after spiking with the independently prepared *N*-acyl-dimethylsulfoximine **4**.

Scheme 1.

First reported nitrile oxidation reaction, resulting in stable tungsten-imido products.

Scheme 2.

Independent synthesis of $[\text{Ru}(\text{terpy})(\text{bipy})\text{DMSO-}d_6][\text{NO}_3]_2$ (**3**).

Scheme 3.

Independent synthesis of *N*-acetyl-dimethylsulfoximine (**4**). ¹H NMR data of independently prepared **4** in DMSO-*d*₆: 3.31 (s, 6H), 1.93 (s, 3H).

Table 1.

First order rate constants for the reaction of **1** and **2**, with various ligands added to the reaction mixture.

Entry	Equivalents Nitrile	Observed Rate Constant
1	0 equiv	$5.4 \times 10^{-2} \text{ s}^{-1}$
2	5 equiv	$5.0 \times 10^{-2} \text{ s}^{-1}$
3	10 equiv	$5.2 \times 10^{-2} \text{ s}^{-1}$
4	15 equiv	$5.3 \times 10^{-2} \text{ s}^{-1}$
5	15 equiv Pyridine	24 h = 13% dissociation