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Sequential Photooxidation of a Pt(II) (Diimine)cysteamine Complex: Intermolecular Oxygen Atom Transfer versus Sulfinate Formation

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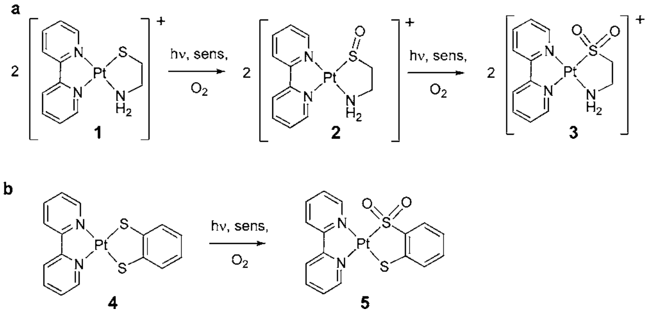
Supporting Information

ABSTRACT: The thiolato complex [platinum(II)(bipyridine)(*N*,*S*-aminoethanethiolate)]$^+$Ch$^-$ (**1**) undergoes sequential reactions with singlet oxygen to initially form the corresponding sulfenato complex [platinum(II)(bipyridine)(*N*,*S*(=O)-aminoethansulfenate)]$^+$ (**2**) followed by a much slower reaction to the corresponding sulfinato complex. In contrast with many platinum dithiolato complexes, **1** does not produce any singlet oxygen, but its rate constant for singlet oxygen removal (k_T) is quite large (3.2×10^7 M^{-1} s^{-1}) and chemical reaction accounts for ca. 25% of the value of k_T. The behavior of **1** is strikingly different from that of the complex platinum(II) (bipyridine)(1,2-benzenditholate) (**4**). The latter complex reacts with $^1O_2$ (either from an external sensitizer or via a self-sensitized pathway) to form a sulfinato complex. These two very different reactivity pathways imply different mechanistic pathways: The reaction of **1** with $^1O_2$ must involve O−O bond cleavage and intermolecular oxygen atom transfer, while the reactive intermediate in complex **4** collapses intramolecularly to the sulfinato moiety.

The chemistry of platinum (diimine)(thiolato) complexes has been extensively studied during the past 3 decades. When dithiolato ligands are employed, such complexes exhibit strong luminescence due to a charge-transfer complex formed from donation from dithiolate to diimine ligands.[1,2] Many of these complexes are also sensitizers for the production of singlet oxygen, although the actual quantum yields for these processes are not known.[2−4] Some of these platinum dithiolato complexes undergo self-sensitized oxidation reactions, with products ranging from mono- and disulfinates[4] to dithiolenes.[3] Interestingly, products with singly oxidized sulfur sites, i.e., platinum sulfenates, have not been reported for these complexes. The factors that determine which product is formed and the nature of the intermediates involved are poorly understood. Platinum diimine complexes bearing one or several alkylthiolato complexes are also of interest as small model complexes for platinum-bound cysteine. Such complexes are formed during the interaction of *cis*-platinum drugs with the sulfur-rich sites of metallothionein, leading to inactivation of this enzyme and the well-known nephrotoxicity of these drugs.[5] The chemistry and photophysics of platinum diimine complexes with just one alkylthiolato ligand (as a model for one metal-bound cysteine site) have received much less attention than those of the dithiolate complexes. We now report a detailed study of the photooxidation of a platinum (diimine)(monothiolato) complex, namely, [platinum(II) (bipyridine)(*N*,*S*-aminoethanethiolate)]$^+$Cl$^-$ (**1**).[6] In striking contrast with the dithiolate complexes, which form sulfinato products upon photooxidation, complex **1** undergoes *sequential* oxidation reactions with singlet oxygen, initially forming only the sulfenato adduct, followed by the slow formation of a sulfinato complex (Scheme 1).

Scheme 1. (a) Sequential Reaction of Complex 1 with Singlet Oxygen and (b) Direct Conversion of the Platinum Dithiolato Complex 4 to the Sulfinato Complex 5



Unlike the platinum(II) (bipyridine)(dithiolato) complexes,[2−4] **1** does not sensitize the production of singlet oxygen. However, upon reaction with $^1O_2$ produced by an external photosensitizer (in water or methanol/water, sens = methylene blue, tungsten−halogen lamp, cutoff filter at 493 nm to prevent excitation of **1**), complex **1** is cleanly converted to the corresponding sulfenato complex **2**. We have followed the reaction by IR, UV/vis, ^{1}H and ^{195}Pt NMR, and liquid chromatography/mass spectroscopy (LC−MS). No platinum(IV) intermediates or products other than **2** were observed until conversion of **1** to **2** was complete.[7] When the reaction was carried out in D_2O, no deuterium incorporation at the methylene site of **1** adjacent to the sulfur atom was observed by MS. Spectroscopic data of the complexes are summarized in Table S1 in the SI. The sulfenato complex **2** can also be obtained upon reaction of **1** with 1 equiv of hydrogen peroxide. The assignment

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of **2** as a platinum(II) sulfenato complex was confirmed by an X-ray molecular structure (Figure 1).

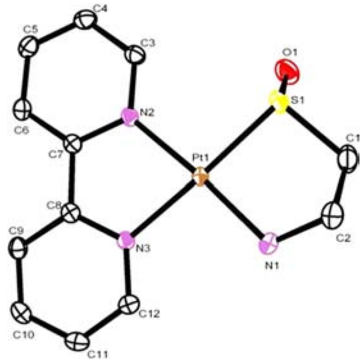


Figure 1. X-ray molecular structure of **2**. Solvent molecules, hydrogen atoms, and the Cl^- counterion have been omitted for clarity.

The bond distance of the S═O bond of complex **2** (1.52 Å) is within the expected range of metal sulfenato complexes (1.5−1.6 Å).[8] It is longer than that of the sulfinato complex **5** (1.45 Å),[4] consistent with the fact that the S═O bond of a sulfenate is more polar than that of a sulfinate.[8] Continuous exposure of the sulfenato complex **2** to singlet oxygen leads to slow conversion to the corresponding sulfinato complex **3**. This complex was also characterized by IR, UV/vis, and ^1H and ^{195}Pt NMR. While we were unable to obtain an X-ray molecular structure of **3**, its identity as a sulfur-bound sulfinate was confirmed by the characteristic IR stretches for the $Pt-S(=O)_2$ moiety at 1210 and 1070 cm^{-1}.[5] An ^{18}O-labeling experiment showed a change of these peaks to 1162 and 1024 cm^{-1}, consistent with their assignment as sulfur-bound sulfinato bands.[9]

Kinetic analysis of the photooxidation of complexes **1** and **2** is consistent with formation of the sulfenate **2** as the only initial product. The total rate constant (k_T) of singlet oxygen removal by **1** is about 1 order of magnitude higher than that of complex **2**, i.e., 3.2×10^7 M^{-1} s^{-1} for **1** and 2.5×10^6 M^{-1} s^{-1} for the sulfenato complex **2** (Table 1 and Figure S3 in the SI). It appears that singlet oxygen removal is largely due to interaction of the metal thiolato or metal sulfenato moiety, as the sulfinato complex **3**, where the metal−sulfur bond is completely oxidized, has a $^1O_2$ removal rate constant that is quite small, i.e., $k_T = 9.8 \times 10^5$ M^{-1} s^{-1}.

Table 1. Rate Constants for Singlet Oxygen Removal by Complexes 1−4 and Singlet Oxygen Quantum Yields

	rate constant of $^1O_2$ removal (k_T) × 10^7 M^{-1} s^{-1}	$^1O_2$ quantum yield[c] (Φ^Δ)
Pt^{II}(bpy)(*N,S*-aminoethanethiolate) (**1**)[a]	3.2 ± 0.3	0.00
Pt^{II}(bpy)(*N,S*(═O)-aminoethanesulfenate) (**2**)[a]	0.25 ± 0.03	0.00
Pt^{II}(bpy),(*NS*(═O)2-aminoethanesulfinate) (**3**)[a]	0.098 ± 0.008	0.00
Pt^{II}(bpy)(1,2-benzenditholate) (**4**)[b]	4.8 ± 0.4	0.50 ± 0.05

[a] In D_2O, with an average of 3−5 runs, the error is 1 standard deviation [b] In CD_2Cl_2, with an average of 3−5 runs, the error is 1 standard deviation [c] Determined at λ_{exc} = 532 nm from near-IR $^1O_2$ emission.

Chemical reaction with singlet oxygen constitutes a significant fraction of the k_T value for complex **1**: We carried out competition experiments [in CD_3OD/D_2O (2:1)] with the known singlet oxygen acceptor, 3-[10-(2-carboxyethyl)-anthracen-9-yl]propionic acid [k_T = 1.8×10^7 M^{-1} s^{-1} in CD_3OD/D_2O (2:1); we used this mixture because the solubility of the anthracene derivative in neat water is very poor], and the thiolato complex **1**.[10] The rate constant for chemical reaction (k_r) between **1** and singlet oxygen is 1.0×10^7 M^{-1} s^{-1}. We remeasured the total rate of singlet oxygen removal k_T in the 2:1 CD_3OD/D_2O mixture and found it to be 4.1×10^7 M^{-1} s^{-1}, very similar to the value in D_2O. Thus, chemical reaction accounts for ca. 25% of the total rate of singlet oxygen removal of complex **1** in methanol/water (2:1) and about 4 times the total rate of singlet oxygen removal (k_T) by the sulfenato complex **2**. These kinetic data are consistent with the surprising observation that no sulfinato product **3** is observed prior to complete conversion of the starting complex **1** to the sulfenato product **2**.

The reaction of **1** with singlet oxygen is rather different from the self-sensitized photooxidations of platinum dithiolate complexes studied by Schanze and co-workers[3] and especially the reaction of singlet oxygen with the complex platinum(II)(bipyridine)(1,2-benzenditholate) (**4**) reported by Gray et al.[4] Complex **4** undergoes self-sensitized photooxidation, leading to the formation of only mono- and disulfinato products, while complex **1** reacts with $^1O_2$ to produce the sulfenato complex **2**. Even though the dithiolato complex **4** has a second thiolato group that could act as an intramolecular trap for a peroxidic intermediate formed from the attack of $^1O_2$ on the thiolate ligand, no sulfenate or disulfenate formation was observed by Connick and Gray during the photooxidation of **4**.[4] This implies intramolecular collapse of the peroxidic intermediate during the photooxidation of **4** must be preferred over oxygen atom transfer, whereas during the photooxidation of **1**, intermolecular oxygen atom transfer from a peroxidic intermediate must be the sole reaction channel. The difference in reactivity is not due to protic versus aprotic conditions (reactions for complex **4** have been carried out in CH_2Cl_2 and CH_3CN) because the addition of water to an acetonitrile solution of **4** did not change the outcome of the reaction.

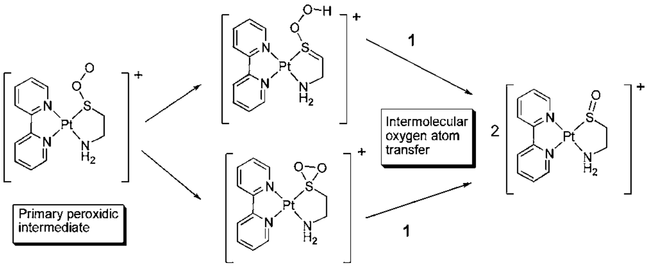
Given this striking and unexpected contrast between complexes **1** and **4**, we decided to reinvestigate some aspects of the photochemistry of complex **4**. Singlet oxygen luminescence measurements (external reference sensitizer, C_{60}; Φ^Δ = 1.0) confirmed that unlike complexes **1**−**3**, complex **4** is indeed a singlet oxygen sensitizer with a quantum yield of 0.50 (Table 1). Time-resolved singlet oxygen luminescence quenching experiments with $^1O_2$ generated by an external photosensitizer (methylene blue, excited at 532 nm) demonstrated that $^1O_2$ interacts with complex **4**, with a total rate constant of singlet oxygen removal of 4.8×10^7 M^{-1} s^{-1}, in reasonable agreement with the value of 1×10^8 M^{-1} s^{-1} obtained by Connick and Gray via transient absorption spectroscopy during the self-sensitized photooxidation of **4**.[4] Photooxidation of complex **4** using externally generated singlet oxygen without exciting **4** (sensitizer = methylene blue; cutoff filter at 645 nm) leads to the same sulfinate product (**5**) that was reported by Connick and Gray when complex **4** is irradiated under aerobic conditions without an external sensitizer, confirming that singlet oxygen indeed oxidizes **4** to the sulfinate (Scheme 1b). No sulfenate or disulfenate was obtained in the presence of externally generated singlet oxygen.

It is possible that the sulfinato product **5** is the result of an intramolecular isomerization of a disulfenato complex, which could be the initial product; a similar hypothesis was raised by

Darensbourg et al. for the formation of a nickel(II) sulfinato product during the oxidation of nickel(II) dithiolato complexes.[11] To investigate this possibility, we carried out the photooxidation of **4** at low temperature (−42 °C) in an NMR tube placed into a transparent Dewar flask. If a disulfenato product were initially formed, its isomerization should be sufficiently slow at −42 °C, so that it could be observed by low-temperature NMR. However, no intermediate during the photooxidation of **4** was detected even at −42 °C. While the lack of observation of a low-temperature intermediate does not conclusively rule out a transient disulfenato complex, the sulfinato product **5** may well be the primary product of the photooxidation of **4**.

A key step during the photooxidation of organic sulfides is the abstraction of a proton on the α-carbon atom by the primary peroxidic intermediate (most likely a persulfoxide), leading to a hydroperoxysulfonium ylide, which undergoes intramolecular oxygen-atom-transfer reaction, leading to sulfoxide products.[12] It is not known whether or not the reaction of singlet oxygen with metal thiolates proceeds via an analogous mechanism.[13] It is striking that complex **1** (which undergoes intramolecular oxygen atom transfer) does possess two hydrogen atoms on the α-carbon atom, while complex **4** does not. However, no H/D exchange was observed at the methylene site adjacent to the sulfur atom during the photooxidation of **1** in D_2O, in contrast with the photooxidation of organic sulfides, which does proceed via a hydroperoxysulfonium ylide and concomitant H/D exchange at the methylene group adjacent to the sulfur atom.[14] Thus, alternatively, the intermediate responsible for intermolecular oxygen atom transfer may possibly be a thiadioxirane-type moiety. Both of these possible secondary intermediates are depicted in Scheme 2.

Scheme 2. Possible Secondary Intermediates Formed during the Photooxidation of 1 and Intermolecular Oxygen Atom Transfer



Formation of the thiadioxiranes has been ruled out for the photooxidation of organic sulfides because the sulfur lone pair would have to rotate away from the second oxygen−sulfur bond formed from rearrangement of the initial persulfoxide.[12] On the other hand, for a metallothiolate, the in-plane 3p orbital of the sulfur interacts with the metal,[15] perhaps thereby making formation of the thiadioxiranes easier. If this were the case, interaction between the π system of the benzene ring of complex **4** and the thiolate ligand would inhibit the ring-closing step required to form a thiadioxirane. In conclusion, we have demonstrated that the photooxidation of a platinum monothiolato complex proceeds via sequential oxidation reactions. Unlike for platinum benzenedithiolato complexes, a peroxidic intermediate in this process is capable of rapid intermolecular oxygen atom transfer. The nature of the reactive intermediates in these reactions appears to be different from those involved in the photooxidation of organic sulfides.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and X-ray crystallographic data in CIF format for **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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