Photooxidation of Co-thiolato complexes in protic and aprotic solvents†

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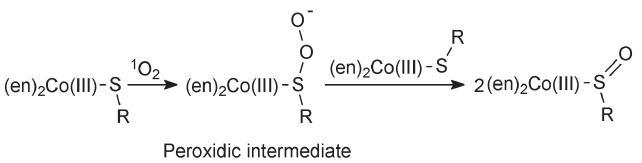
Protic solvents decrease the susceptibility of the thiolate ligand in Co(III) thiolato complexes toward attack by singlet oxygen, but greatly increase the conversion of the peroxidic intermediate to the sulfenato product.

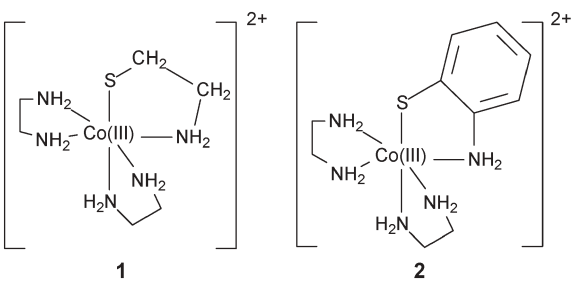
During the past several years, there have been numerous reports of reactions of triplet and singlet dioxygen with a variety of metal thiolate complexes leading to formation of isolable sulfenato and sulfinato complexes.[1–3] Peroxidic intermediates—mostly likely zwitterionic persulfoxides—in these reactions have not been directly observed, as such intermediates may often be better oxidants than triplet or even singlet oxygen itself. Given the abundance of metal-bound cysteine in metalloenzymes (for example in nitrile hydratase, which also contains cysteines that have been oxidized to the sulfenate and sulfinate moieties[2,3]), it is important to elucidate both the susceptibility of the thiolato moiety towards attack by dioxygen and the stability of the peroxidic intermediates under different (*i.e.* protic *vs.* aprotic) conditions. We had previously reported that a cobalt *N*,*S*-cysteinato-bound complex, namely (cysteinato-*N*,*S*)bis(ethylenediamine)cobalt(III), reacts efficiently with singlet oxygen in water, but due to the limited solubility of this compound, we were unable to study its chemistry with singlet oxygen in aprotic solvent systems.[4] We therefore chose to investigate two different Co-thiolato complexes which are soluble in both protic and aprotic solvents. We now report that protic solvents dramatically lower the rate of initial attack by singlet dioxygen on the thiolato moiety, but conversely increase the rate of product formation from the peroxidic intermediate.

The Co(III) complexes (2-mercaptoethylamine-*N*,*S*)bis(ethylenediamine)cobalt(III) tetrafluoroborate (**1**) $[Co(en)_2(N,S\text{-Aet})]^{2+}(BF_4^-)_2$ and (2-mercapto aniline-*N*,*S*)bis(ethylenediamine)-cobalt(III) tetrafluoroborate (**2**) $[Co(en)_2(N,S\text{-Mer})]^{2+}(BF_4^-)_2$ react with singlet dioxygen to form the corresponding sulfenato complexes $[Co(en)_2(N,S(O)\text{-Aet})]^{2+}(BF_4^-)_2$ (**3**) and $[Co(en)_2(N,S(O)\text{–Mer})]^{2+}(BF_4^-)_2$ (**4**).[5] Singlet oxygen was produced *via* continuous irradiation with a Oriel tungsten–halogen 200 W lamp, using Methylene Blue or Rose Bengal as sensitizers. A cut-off filter at 492 nm was employed to prevent excitation of the Co complexes. The reactions can be carried out in simple test tubes or directly in NMR tubes. Products were monitored by UV/vis and ^{1}H NMR spectroscopy, as well as comparison with authentic samples obtained *via* oxidation with hydrogen peroxide.[5] Control experiments demonstrate that the reaction is not a self-sensitzed photooxygenation, as no reaction takes place upon irradiation under an oxygen atmosphere without the presence of the sensitizer. During the initial stages of the reaction (up to 80% conversion), there is little formation of the corresponding sulfinato complexes. Prolonged irradiation leads to very slow formation of small amounts of the corresponding sulfinato complexes, probably *via* photooxidation of the sulfenato products **3** and **4**.



Scheme 1 Photooxidation of Co-thiolato complexes.

We have measured rates of singlet dioxygen disappearance (k_t) by complexes **1** and **2** in several protic and aprotic solvents (due to the very short lifetime of singlet oxygen in non-deuterated solvents, we employed deuterated solvents through these experiments). These time-resolved singlet oxygen luminescence quenching experiments were conducted by exciting a solution containing the sensitizer and varying amounts of substrate (quencher, complex **1** or **2**) with a short (a few ns) laser pulse and monitoring the singlet oxygen decay at right angle. The value of the rate constant k_t thus obtained is the sum of all processes by which singlet dioxygen is removed, and therefore corresponds to the susceptibility of the cobalt thiolato complex towards initial attack by $^1O_2$. For complexes **1** and **2**, the value of k_t is highly solvent dependent: The rate of attack by singlet oxygen in DMF is about twice as high as in methanol and four times higher than in water (Fig. 1). This is in dramatic contrast with the well-studied photooxidation of organic sulfides where there is very little variation of k_t for different solvents. In order to evaluate the rate of product formation (k_r), competition experiments were carried out between the thiolate complexes and two anthracene derivatives, namely 9,10-dimethylanthracene in DMF and methanol, and



Scheme 2 Structures of complexes employed in this study.

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† Electronic supplementary information (ESI) available: details of the time-resolved measurements of k_t and competition experiments. See DOI: 10.1039/b514601a

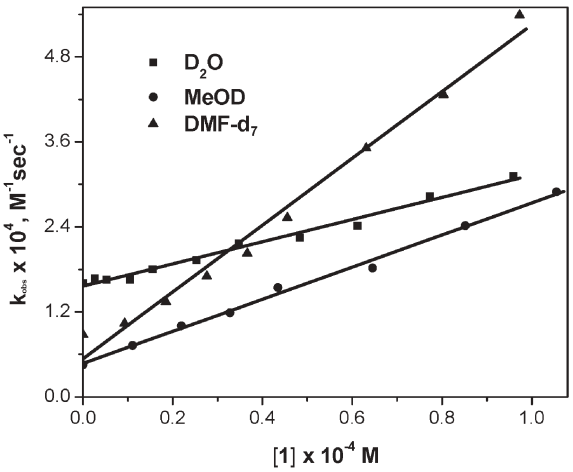

Fig. 1 Rates of singlet oxygen removal (k_t) of (*N*,*S*)bis(ethylenediamine)cobalt(III) tetrafluoroborate (**1**) in D_2O, CD_3OD and DMF-d_7. The intercepts are not identical, since the singlet oxygen lifetimes are different in each solvent.

3-(10-(2-carboxyethyl)anthracen-9-yl)propionate in water. These two anthracene derivatives react with singlet dioxygen only *via* chemical reaction to give the corresponding 9,10-endoperoxides. Products were analyzed by monitoring by ^{1}H NMR (for the anthracene derivatives) and by UV/vis spectroscopy (for the Co complexes). The competition experiments are carried out under continuous irradiation such that the two substrates compete for one reactive intermediate (*i.e.* singlet oxygen) that is produced under steady-state conditions. All results were fitted into the equation by Higgins *et al.*[6]

$$\frac{\log\left\{\left[\left[\mathrm{Co(en)_2(S\text{-}R)}\right]^{2+}\right]^{f}/\left[\left[\mathrm{Co(en)_2(S\text{-}R)}\right]^{2+}\right]^{0}\right\}}{\log\left\{[\mathrm{DMA}]^{f}/[\mathrm{DMA}]^{0}\right\}} = \frac{k_r\left(\left[\mathrm{Co(en)_2(S\text{-}R)}\right]^{2+}\right)}{k_r(\mathrm{DMA})}$$

The rate ratio thus obtained is independent of the singlet oxygen concentration in solution. A control experiment demonstrated that no oxidation of complexes **1** or **2** by the 9,10-dimethylanthracene endoperoxide product occurs. If all of the peroxidic intermediate formed during the initial reaction of the thiolate with singlet oxygen were converted to the sulfenato product, then the rate of product formation k_r would equal twice the total rate of singlet oxygen removal by the starting complex, *i.e.* $k_r = 2k_t$. Results for the values of the rates of singlet oxygen disappearance (k_t) and chemical reaction rate constants (k_r) are summarized in Table 1.

From the data in Table 1, it is readily apparent that protic solvents have two opposite effects on the photooxidation of the thiolato complexes. They reduce the rate of initial attack by the singlet oxygen molecule. Conversely, protic solvents dramatically increase the fraction of product formation *vs.* singlet oxygen removal, *i.e.* the ratio of $k_r/2k_t$. The latter effect is very similar to what has been found for the well-studied reaction of organic sulfides with singlet oxygen.[7] For organic sulfides, the effect has been attributed to stabilization of the peroxidic intermediate (a persulfoxide) by hydrogen bonding, and, based on our data, it is likely that the same type of intermediate is formed during the photooxidation of the cobalt complexes. On the other hand, the decrease in the value of k_t under protic conditions for complexes **1** and **2** is dramatically different from what is observed for organic sulfides. The decrease in the rate of initial attack by singlet oxygen (k_t) in protic solvents could be due to a decrease in the nucleophilicity of the thiolate ligand due to hydrogen bonding or due to a solvent effect on direct physical quenching of $^1O_2$ by the Co metal center. To investigate whether such octahedral Co(ethylenediamine) complexes physically quench singlet oxygen, we measured the rate of singlet oxygen removal of complex *trans*-dichlorobis(ethylenediamine)cobalt(III) chloride (**5**) $Co(en)_2Cl_2$ in CD_3OD and DMF-d_7.[5] Complex **5** is stable for prolonged periods in CD_3OD–DMF-d_7 and it only removes singlet oxygen *via* physical quenching. The value of k_t for this complex is much smaller than the k_t values for complexes **1** and **2**. Furthermore, the k_t values of complex **5** are identical within limits of error in CD_3OD and DMF-d_7, indicating that the solvent effect on k_t for complexes **1** and **2** is based on the sulfur rather than the metal. Thus, hydrogen bonding to the highly electron rich sulfur atom of metal thiolates may be sufficiently large to decrease the nucleophilicity of the sulfur atom and reduce its susceptibility to initial attack by singlet oxygen.[8] Support for this hypothesis also comes from a recent observation by Carrano and co-workers who noted that intramolecular hydrogen bonding decreases the rate of nucleophilic attack of Zn thiolates on methyl iodide.[9] In summary, hydrogen bonding may play a contradictory role in the photooxidation of metal thiolates: It decreases the susceptibility of the thiolate toward attack by singlet oxygen, but it greatly increases the conversion of the peroxidic intermediate to form oxygenated products. Further experiments to test if the former effect is also operative when other electrophiles are reacted with the cobalt complexes **1** and **2** are in progress.

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Table 1 Rate constants of singlet oxygen disappearance (k_t) and chemical reaction rate constants (k_r) in protic and aprotic solvents

Compound	Solvent	$k_t^a \times 10^8$ M^{-1} s^{-1}	$k_r^a \times 10^8$ M^{-1} s^{-1}	$k_r/2k_t \times 100\%$
1	DMF-d_7	6.4 ± 0.8	0.01 ± 0.007	0.08%
1	CD_3OD	3.3 ± 0.9	1.2 ± 0.5	18%
1	D_2O	1.4 ± 0.2	0.84 ± 0.16	30%
2	DMF-d_7	6.7 ± 0.4	0.01 ± 0.002	0.07%
2	CD_3OD	2.5 ± 0.3	0.12 ± 0.03	2.6%
2	D_2O	1.3 ± 0.1	0.36 ± 0.15	14%
5	CD_3OD	0.43 ± 0.02	0.0	
5	DMF-d_7	0.41 ± 0.02	0.0	

[a] Average of four to six runs. Error is one standard deviation.

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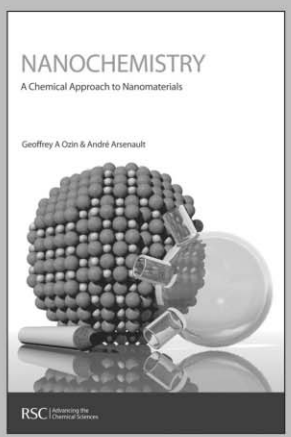

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