Terpyridine–Lanthanide Complexes Respond to Fluorophosphate Containing Nerve Gas G-Agent Surrogates

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The detection of chemical warfare agents has become increasing important since the 1995 subway attack in Japan which killed 12 people and injured more than 5000.[1–3] Due to the availability of inexpensive starting materials and simple manufacturing processes, the development of nerve gas agents does not require highly trained expertise, expensive equipment, or strongly regulated materials such as plutonium. These factors combine to make nerve agents a weapon of choice for poorer nations[4,5] and as a result, there remains a high demand for affordable detection methods.[6]

A variety of approaches[2,5,7–13] to detect nerve agents has been reported including those based on colorimetric,[2,14] fluorimetric,[15–17] gas chromatography[18] fiber optics[19,20] and enzymatic assays.[21] A common limitation of these approaches is their general lack of selectivity, sensitivity, and operational complexity which makes differentiating among similar chemical structures problematic in real time. To make the problem more complex, G-type and V-type agents are organophosphates (OPs); the same chemical class as many widely used pesticides so that detection of these agents typically must compete with a background level of OPs. From a practical sense, colorimetric detection is generally considered best since it just requires a color change to be monitored. However, sensitivity is always an issue and from this point of view fluorescence based sensors with their very high sensitivities can be ideal.[15,17]

Metal complexes are well known for their chemical versatility[22,23] and we have been investigating metal–ligand functionalized polymers for several years.[24–29] As part of these studies, we explored the emission properties of macromolecules containing terpyridine (terpy) complexed to a variety of lanthanide ions including Dy^{III}, Tb^{III}, and Eu^{III} (see Figure 1). These materials are luminescent yet at the same time the binding constant between terpy and lanthanide is known to be small compared with terpy–transition metals due to the small bite angle of terpy and the large atomic radii of the lanthanide. This led us to consider the suitability of these complexes (like **1a**) for the detection of G-agents by combining the inherent weak binding to terpy with the reactive nature of these G-type agents.

Here we report that terpy–lanthanide complexes based on **1** indeed respond to the presence of G-type agents by quenching their fluorescence. The ability to selectively distinguish the G-type surrogate, diethylchlorophosphate (SAS-Cl), from a number of other organophosphates, including pinacoly methyl phosphonic acid, typically called SOS, is demonstrated. Three different lanthanide ions, Dy^{III}, Tb^{III}, and Eu^{III} were studied along with three derivatives of terpy. Forgiving the minor differences in their Stern–Volmer constants, they all showed instantaneous response times and detection levels near 75 ppb, which is below the minimum 1.7 ppm immediately dangerous to life level of sarin and soman set by the Centers for Disease Control and Prevention (CDC).[12] Another surrogate, diisopropylfluorophosphate (SAS-F) that captures the close structural as well as chemical similarity of sarin gas was also studied and the detection limit increased further to 6 ppb as the reactivity of this fluorophosphate is higher than chlorophosphate.

The ability of SAS-Cl to quench the emission of terpy–lanthanide complex prompted us to test SOS since the oxophilic nature of lanthanide was expected with this surrogate as well. Surprisingly, no quenching was observed suggesting it is the reactivity of the chlorophosphate not the oxophilicity that is important here. This led us to wonder if these metal-complexes might be insensitive to a variety of other OPs. As shown in Figure 2, **1b** is quiet sensitive to SAS-Cl, but insensitive to TBP, DPP, TPP, TEA, TEP and PA (see Figure 2 for names and abbreviations). Figure 2 shows the emission response of **1a**-Eu^{III} at 620 nm in the presence of these OPs including SAS-Cl. From this graph it is clear that SAS-Cl significantly quenches the red emission (620 nm)

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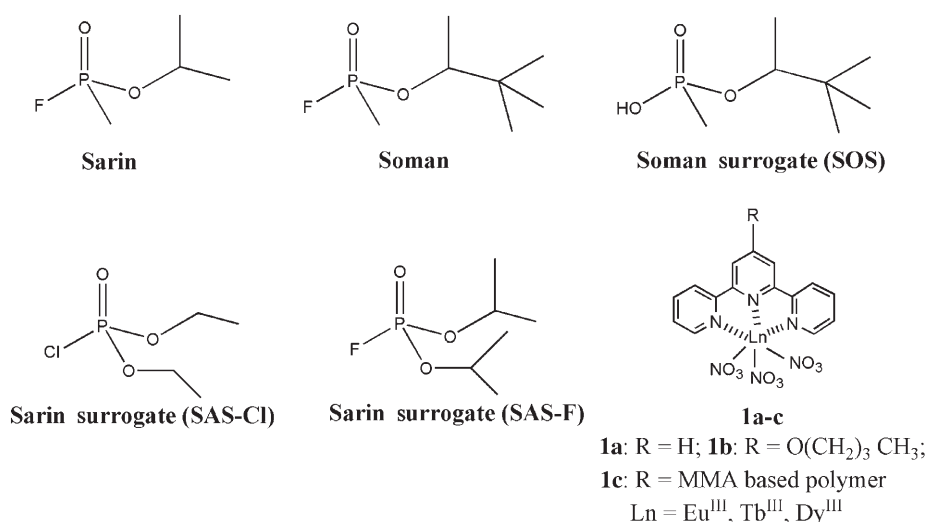
Figure 1. Chemical structure of sarin, and soman along with three surrogates, SAS-Cl, SAS-F and SOS, and **1a–c**. SAS-Cl and SAS-F, typically called the sarin surrogates, captures the chemical reactivity of the G-type agents while the other, typically referred to as the soman surrogate, SOS, does not. Molecules, **1a–c**, are terpy–lanthanide complexes used for fluorimetric detection. Three emissive lanthanide ions, Eu^{III}, Dy^{III}, and Tb^{III}, were studied.
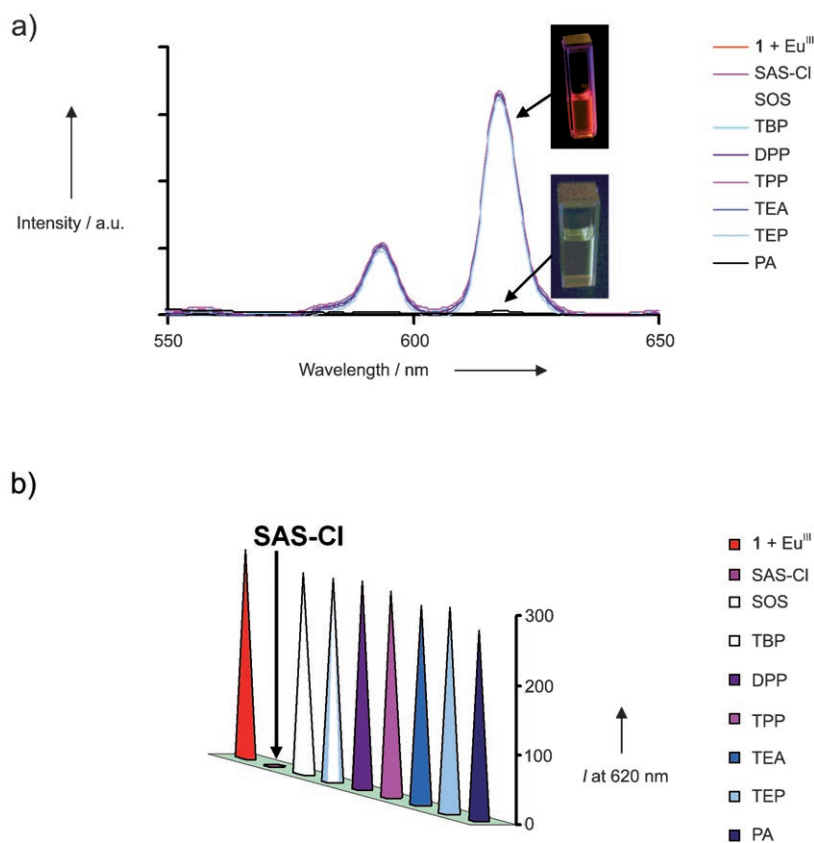

Figure 2. a) Emission spectra and b) a plot of emission intensity for **1a**-Eu^{III} at 620 nm upon addition of SAS-Cl and other OPs, pinacoly methyl phosphonic acid (SOS), tributylphosphate (TBP), diphenylphosphate (DPP), triphenyl phosphine (TPP), triethyl amine (TEA), triethylphosphate (TEP) and phosphoric acid (PA). The concentration of SAS-Cl and all other agents was held constant at 75 ppb. The spectra were collected in 1:1 $CHCl_3/CH_3OH$ with an excitation wavelength at 350 nm.

from **1a**-Eu^{III} while the other compounds show little or no change in the emission intensity.

Very similar results were obtained for **1**-Dy^{III} and **1**-Tb^{III} as well as terpy–lanthanide complexes based on **1b–c**. In addition, the introduction of a 200-fold excess of these OPs to solutions of **1** did not impact the emission or the ability of **1** to detect SAS-Cl. Similar results were also observed with SAS-F. In an effort to more fully compare the three lanthanide systems with SAS-Cl and SAS-F, Stern–Volmer (SV) plots were generated for each system from the emission curves. Figure 3a–c show the response for SAS-F (SAS-Cl data is in the Supporting Information). The SV constant (K_{SV}) was obtained as the slope of the line from a plot of concentration vs fluorescence intensity (I_o/I) as shown in Figure 3d. The K_{SV} values were found to be 6.0×10^6, 4.2×10^6, $2.1 \times 10^6\,M^{-1}$ for **1**-Eu^{III}, **1**-Tb^{III}, and **1**-Dy^{III}, respectively. The similarity of the three values suggests they are all equally quenched by SAS-F. The K_{SV} values for SAS-Cl quenching were found to be 7.8×10^5, 3.7×10^5, $2.4 \times 10^5\,M^{-1}$ for **1**-Eu^{III}, **1**-Tb^{III}, and **1**-Dy^{III}, respectively. The observed K_{SV} value of SAS-Cl is one order of magnitude less than SAS-F, a quantitative measure of the difference in reactivity. The fact that **1**-Eu^{III} has the most intense and highest wavelength band minimizes interference from the weak but present background signals between 450–500 nm.

Having demonstrated the sensitivity and selectivity of these terpy–lanthanide complexes for SAS-Cl and SAS-F, we considered their sensitivity to HCl and HF. HCl and HF are the by-products from hydrolysis of SAS-Cl and SAS-F, respectively, and as a result
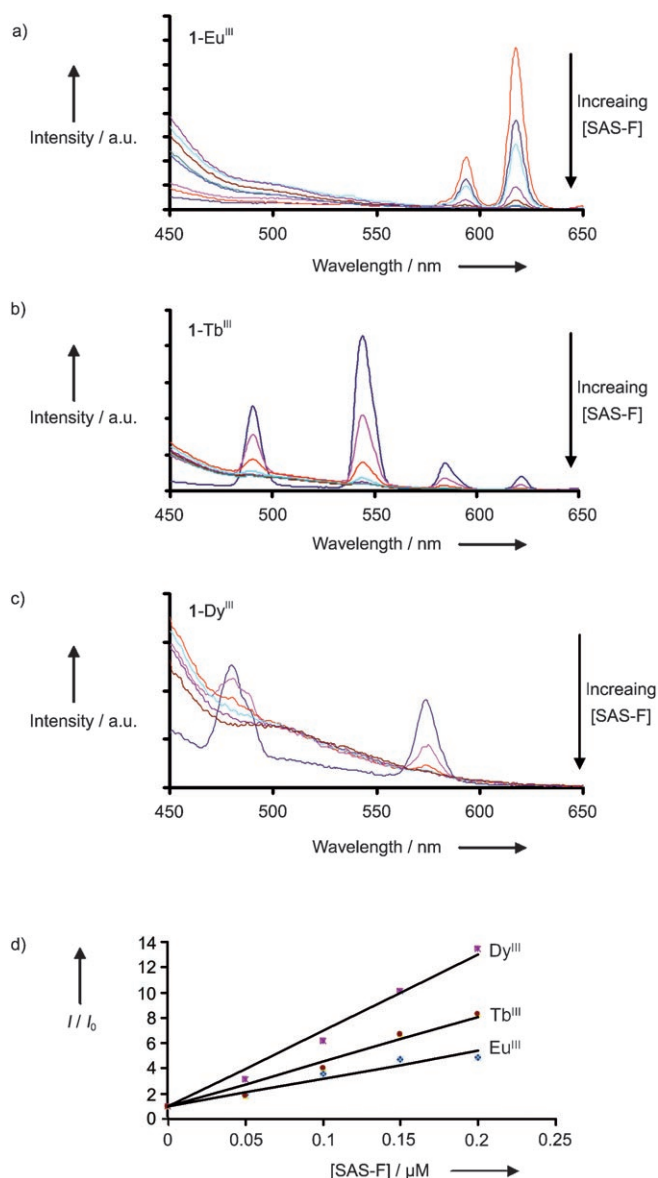
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Figure 3. Emission spectra of 3 mL of 10 mм of a) **1c**-Eu^{III}, b) **1c**-Tb^{III}, and c) **1c**-Dy^{III} as a function of increasing SAS-F concentration. Excitation wavelength (λ_{ex}) was 350 nm. d) Stern–Volmer plots of SAS concentration vs I_o/I.

care was taken in all of the experiments to ensure that residual acid was not responsible for the loss of emission.[3] Using K_{SV} as a comparison for quenching efficiency, it was determined that K_{SV} for HCl was $2.54 \times 10^2 \, \text{m}^{-1}$ which is three orders of magnitude less than that for SAS-Cl. This means that SAS-Cl is much more effective (1000 times more effective) at quenching the emission of these complexes than HCl. NMR studies at much higher concentrations confirmed phosphorylation of the terpy nitrogen (see Supporting Information) implying that the reactivity of SAS contributes to quenching of the complex. In another control experiment, where SAS-Cl was first added to **1a** followed by Eu^{III}, no emission was observed suggesting the absence of the "antenna effect" due to phosphorylation of the terpyridine nitro-

gens (see Supporting Information). Finally the K_{SV} for HF was measured to be $1.29 \times 10^4 \, \text{m}^{-1}$, two orders of magnitude lower than SAS-F proving that HF is an extremely inefficient quencher compared to SAS-F (see Supporting Information). In fact, less than one percent of the measured signal would be from HF quenching. These results more than confirm that both HF and HCl are not quenching the emission of these terpy–lanthanide complexes, when compared to SAS. The huge difference in the K_{SV} values between SAS and the acids confirms that the added reactivity of SAS is the main reason for the observed quenching and not due to the acids.

In conclusion, a new simple, yet sensitive and selective, metal-complex has been reported for G-type chemical warfare agents. The system exploits the emission and weak binding of terpy–lanthanide complexes which turn-off in the presence of SAS. The detection limit is 6 ppb, making the system practically useful. The sensitivity for SAS, yet not SOS or many other OPs, indicates that chemical reactivity is an important consideration and one approach to developing selectively sensitive chemical sensors for G-type agents.

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