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Rapid fluorophosphate nerve agent detection with lanthanides

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Abstract

We explore the detection of vapors of diisopropylfluorophosphate, a model compound for nerve agents such as Sarin, by means of photoluminescence quenching of filter paper impregnated with sensitized complexes of lanthanides, involving thenoyltrifluoroacetone and 1,10-phenanthroline as sensitizing ligands. We find that the presence of the fluorophosphate vapor is detectable in as little as 2 s, by simple visual observation under illumination with a hand-held low intensity ultraviolet lamp.

Keywords: Fluorophosphate nerve agents; Diisopropylfluorophosphate; Photoluminescence; Europium; Terbium; Sensitizing ligands

1. Introduction

Organofluorophosphates such as Sarin, Cyclosarin and Soman are potent nerve agents that can be deployed easily because of their high vapor pressures. Sarin, for instance, was employed in the 1995 terrorist attack on the Tokyo subway system. The rapid and sensitive detection of this class of nerve agent is thus of interest, especially in a field scenario. We have examined such detection by using the model compound diisopropylfluorophosphate, which, while not as lethal as the above nerve agents, is itself not entirely harmless. Like the above nerve agents, diisopropylfluorophoshate functions as an acetylcholinesterase inhibitor. This inhibition leads to paralysis and death. The structures of diisopropylfluorophosphate and the above nerve agents are shown in Fig. 1.

Ideally, we would like to have a non-luminescent sensor chemical which, on exposure to the fluorophosphate vapor, becomes photoluminescent to reveal the presence of the nerve agent with high sensitivity. We have in the past pursued this type of photoluminescence strategy in connection with the detection of latent fingerprints and traces of explosives [1–3]. In the present instance, the opposite scenario is exploited, namely the quenching of the luminescence of the sensor chemical upon exposure to the nerve agent. Our detection of this quenching is by the naked eye (with the room lights turned off), utilizing as the luminescence excitation source nothing more than a low intensity ordinary hand-held ultraviolet lamp. The chemical sensor is simply a piece of filter paper impregnated with a suitable lanthanide complex [1–3]. Specifically, the complexes we mostly focus on here involve Eu^{3+} with four thenoyltrifluoroacetone (TTFA, bidentate) ligands, and the Tb^{3+} mixed-ligand complex with TTFA and 1,10 phenanthroline (*ortho*-phenanthroline, OP, bidentate) ligands. We have also examined two other ligands, namely ethylenediaminetetraacetic acid (EDTA) and diethylenetriaminepentaacetic acid (DTPA), but they are somewhat less interesting. Their discussion is thus deferred to later in this article. Fig. 2 shows the binding of the OP and TTFA ligands to the trivalent lanthanide. Europium and terbium are the strongest lanthanide luminescers. One water of hydration bound to the lanthanide ion completes the full 9-fold lanthanide coordination. The TTFA ligand serves to sensitize the red europium luminescence (under near-UV illumination). TTFA is spectrally mismatched with terbium. Thus, the OP ligand has to serve the luminescence-sensitization function (under deep-UV illumination) to produce the characteristic green terbium luminescence. OP also sensitizes Eu luminescence, but not as well as TTFA. Without the presence of these sensitizing ligands, no lanthanide luminescence is observed

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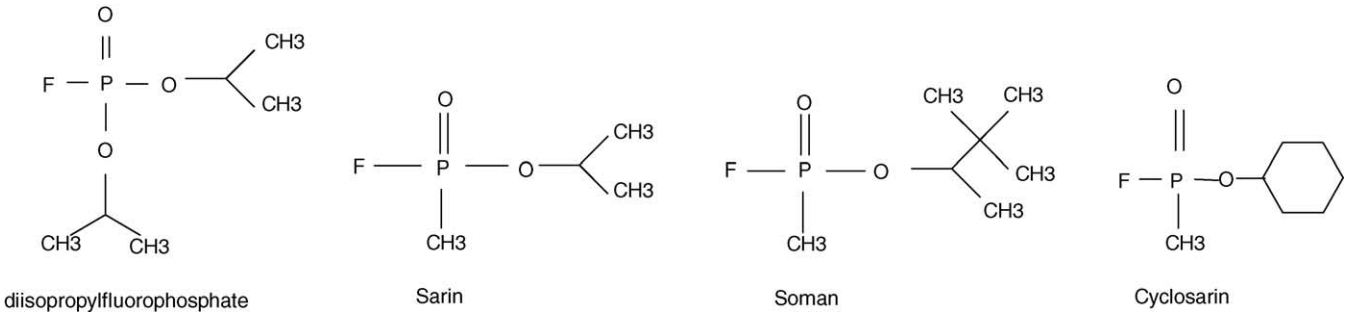

Fig. 1. Structures of diisopropylfluorophosphate and fluorophosphate nerve agents.

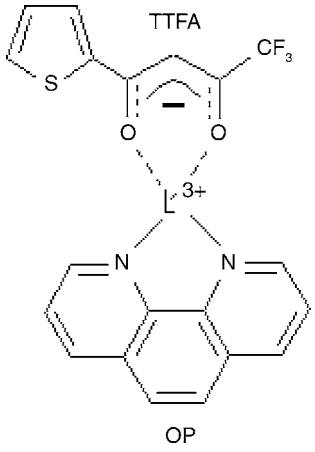

Fig. 2. Binding of sensitizing ligands to lanthanides (L^{3+}).

under the UV lamp. That europium and terbium are 9-fold coordinated is easily seen by contemplation of europium or terbium chlorides, which come as the hexahydrate salts, typical of such lanthanide salts generally. Lanthanide acetates and nitrates are quite generally hydrated as well, but the number of waters of hydration is variable, presumably owing to steric effects.

2. Sensor preparation and examination

The lanthanide complexes are easily prepared. One simply mixes in methanol solvent the lanthanide chloride hexahydrate with the TTFA and/or OP. All reagents discussed in this article were purchased from Aldrich and were used as received. We use a molar ratio of 1:5, i.e., with excess ligand, to ensure the fullest coordination with that ligand, when preparing lanthanide single-ligand complexes, and a molar ratio 1:3:3 when preparing the mixed-ligand complexes. The complex formation is essentially instantaneous. We have in our work employed a 10^{-2} M complex concentration, but it is not critical. Filter paper (Whatman 1) is then briefly immersed in the solution and left to dry. The diisopropylfluorophosphate is a liquid. The dried impregnated filter paper is simply placed over the opening of the fluorophosphate-containing bottle to be exposed to the supernatant vapor. The filter paper is then removed and immediately visually inspected under the UV lamp (Model UVGL-58, Mineralite®, UVP, Upland, CA), which has more than ample intensity. In the exposed locale, the intense luminescence from the impregnated paper is quenched, i.e., a dark spot of the dimensions of the bottle opening is seen under the UV lamp (with no optical filter needed for the observation). Radical luminescence quenching is instantly observed when the filter paper is exposed to the fluorophosphate in liquid form.

3. Lanthanide luminescence quenching

3.1. OP and TTFA ligands

We note from the outset that water is a notorious quencher of lanthanide luminescence [4]. While one water of hydration in a lanthanide complex is still tolerable, proximity of additional waters of hydration results in severe lanthanide luminescence quenching, which we have taken advantage of in the past in connection with the above-mentioned explosives detection [2,3], by quenching lanthanide luminescence of unreacted complex. Here, we take advantage of it in terms of quenching of reacted complex because the reaction facilitates subsequent hydration.

When the impregnated filter paper was exposed to the fluorophosphate vapor, the luminescence quenching was seen on exposure time-spans of as little as 4 s, as depicted in Figs. 3 and 4 (taken with a digital camera, Kodak DC 120) for Eu–TTFA and 2 s for the mixed-ligand Tb–OP/TTFA, as seen in Fig. 5. Subsequent experimentation revealed that the drying time of the filter paper prior to exposure to the fluorophosphate vapor plays an important role. If the drying time is too short, then there is still much water in the filter paper. Under this condition, either no luminescence quenching takes place, or it is much reduced. We will take this issue up again shortly. For now, we note that with well dried filter paper, for 15 min or longer, under ambient conditions (Lubbock generally has low ambient humidity), we found the Eu–TTFA sensitivity to be the same (2 s) as the Tb–OP/TTFA sensitivity. It is to be noted here that the digital photographs with the (technologically somewhat antiquated) camera on hand do not render images (shown in the figures without any image processing

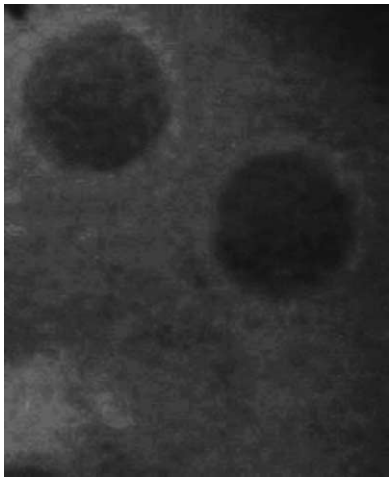

Fig. 3. Luminescence quenching of Eu–TTFA. Top left—8 s fluorophosphate vapor exposure; middle right—15 s; bottom center—4 s.

applied) as good as what one sees on visual inspection, color- or contrast-wise. In the discussion below, we primarily focus on europium, noting that the terbium results are analogous. It is interesting to examine the side of the filter paper opposite to that exposed to the fluorophosphate vapor. For impregnated filter paper that was dried only for roughly 10–15 min prior to use, hence filter paper that still contains considerable interstitial water (methanol is hygroscopic) nothing was seen on that opposite side. However, for impregnated filter paper that had dried for about 1 h prior to use, the opposite-side examination revealed an easily observed increase in lanthanide luminescence, i.e., an indication that water had been removed from there, to reduce europium luminescence quenching (by water of hydration). The attack of the fluorophosphate is thus hygroscopic. This is not surprising in that we believe that it

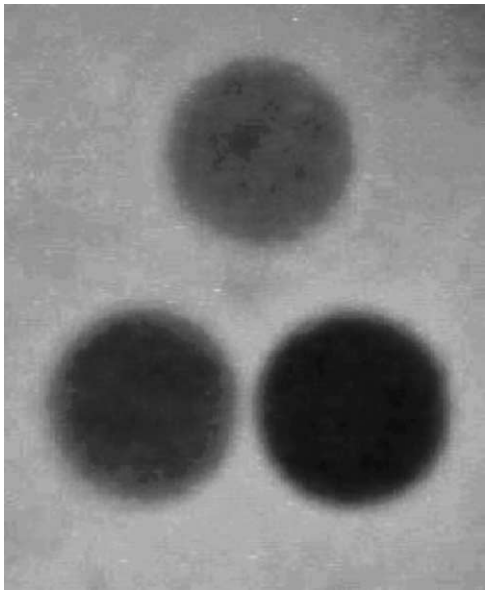

Fig. 4. Luminescence quenching of Eu–TTFA. Top—0.5 min fluorophosphate vapor exposure; bottom left—1 min; bottom right—2 min.

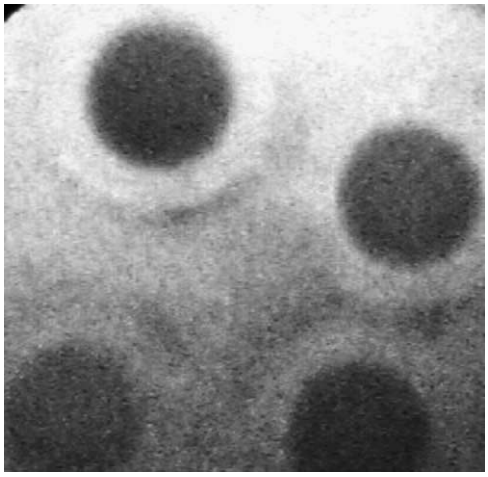

Fig. 5. Luminescence quenching of Tb–TTFA/OP. Center—2 s fluorophosphate vapor exposure; bottom left—5 s; bottom right—10 s; top right—20 s; top left—40 s.

involves the hydrolysis of the phosphorus–fluorine bond to liberate F^-. The fluoride anion then attacks the lanthanide complex to displace thenoytrifluoroacetone ligands. At the same time, it permits added hydration of the complex to quench luminescence. This is a quick chemical step, taking place in seconds. Support for this reaction mechanism is provided by the observation that such fluorescence quenching was observed as well when the impregnated filter paper was placed over the opening of an HF-containing bottle for a few seconds, to be exposed to HF fumes. For longer exposure (about 2 min) of the filter paper to the flourophosphate vapor, the reaction permeated the filter paper thickness, such that the europium luminescence on the opposite side of the exposed paper also became quenched. The europium luminescence quenching on the side of the exposed filter paper continued to become more pronounced over time spans on the order of 1 h after exposure. We interpret this as due to diffusion of water molecules toward the reacted europium complex. The europium luminescence quenching subsequently began to fade slowly (evaporation of water or its binding to the filter paper), over a time-span of roughly 12–24 h, with eventual regeneration of the original pre-exposure luminescence intensity. Here, especially in filter paper dried for a long time before use, the reconstituted luminescence was actually slightly increased over the original one. We interpret this as follows. When the phosphorus–fluorine bond is cleaved by hydrolysis, a derivative of phosphoric acid ($–POO^-$) is formed, and it can (slowly) occupy the ninth europium binding site (normally occupied by water) to reduce luminescence quenching. We do not know whether the previously disrupted bonding of sensitizing ligands is reconstituted. After all, luminescence sensitization is only a matter of proximity of sensitizer to acceptor, with R^{-6} dependence (where R is the distance between the interacting entities), rather than an issue of chemical bonding, unless the bonding has spectroscopic consequences. The long-term effect was observed over days. The results with

Tb–OP/TTFA were similar to the Eu–TTFA results. No fluorescence quenching was observed with Tb–OP and Eu–OP. Eu–OP/TTFA fluorescence quenching was observed only for exposure to the fluorophosphate vapor for times longer than about 20–40 s. The TTFA ligand thus appears to be attached to Eu more tightly than to Tb, for reasons as yet not clear to us. OP is known to be a strong ligand. It also acts as a neutral ligand, whereas TTFA acts as a negatively charged ligand. Thus, we can understand that it resists attack by the fluoride anion.

3.2. EDTA and DTPA ligands

These are not lanthanide luminescence-sensitizing ligands. However, they do bind to lanthanides, and have been explored in the past as conjugating ligands to attach lanthanides to target molecules, as in the detection of fingerprints [1]. Thus, we have examined them in the present context in mixed-ligand complexes (as potential alternatives to TTFA) to serve as targets for attack by the fluoride anion. As usual, the powders of the lanthanide chloride hexahydrate, TTFA or OP, and EDTA or DTPA were mixed in methanol in 1:3:3 molar ratio to achieve, as before, a 10^{-2} M complex concentration. In the OP mixed-ligand complexes, EDTA performed somewhat better (by about a factor 2 in terms of exposure to the fluorophosphate vapor) than DTPA, but the sensitivity limit was in the 20 s range only. It must be noted, though, that neither EDTA nor DTPA are well soluble in methanol. Our solutions had considerable precipitate of these ligands left over. Unlike all other solutions, which were clear, the lanthanide-TTFA/EDTA and DTPA solutions were mildly colored, pale brownish, suggesting that proper complex formation was compromised. No lanthanide luminescence quenching at all was observed (exposure times 40 s or less).

4. Selectivity and false positives

Given that the pertinent chemistry involves the hydrolysis of the F–P bond followed by displacement of TTFA ligands by the fluoride anion, we do not expect any distinction between the various fluorophosphate nerve agents. We do not consider such selectivity to be essential in a field scenario. Since the observed luminescence quenching involves water, we placed impregnated filter paper over a bottle containing water to expose the sensor to water vapor in much the same way as it is exposed to the fluorophosphate vapor. The exposure time to water vapor was 10 min. No fluorescence quenching was observed. When we examined a more radical exposure to water, by placing drops of water on the impregnated filter paper, the result of Fig. 6 was obtained. The dark ring at the periphery of the drop corresponds to free TTFA ligand (we are using it in stoichiometric excess), pushed to the periphery in the manner of paper chromatography. The TTFA ligand strongly absorbs in the near-UV but is not fluorescent. Near the center of the spot, the lanthanide luminescence persists. We cannot think of any fluoro compounds one would normally find in ambient air, other than, perhaps,

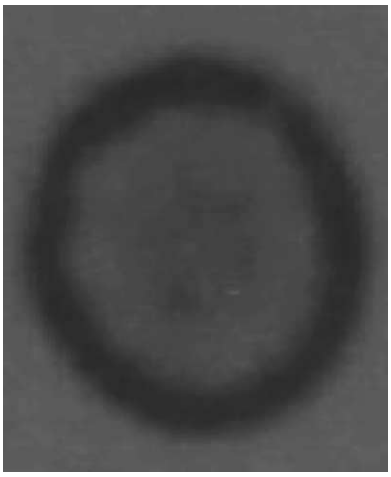

Fig. 6. Luminescence of Eu–TTFA impregnated filter paper upon spotting with a water drop.

fluorocarbons from leaky refrigerators or air conditioners. Thus, we exposed our sensor to the vapors of trichlorotrifluoroethane (freon), which is now banned as environmentally unfriendly, as well as to HF 7100 (manufactured by 3M). This latter fluorocarbon is volatile, much like freon, and is useful as a replacement of freon in forensic applications such as fingerprint detection. Ten-minute exposures to these vapors produced no fluorescence quenching.

5. Sensitivity considerations

The chemical, physical and physiological properties of nerve agents are widely reported [5,6]. For our purposes the vapor pressures, volatilities, and lethal doses are of principal interest. For Sarin and Soman, the vapor pressures (at 25 °C) are 2.9 and 0.4 mmHg, respectively. The corresponding figure reported by the manufacturer (Aldrich) for diisopropylfluorophosphate is 0.6. For Sarin and Soman, the corresponding volatilities (mg/m^3) are 22,000 and 3900, respectively. No volatility figures are available for the diisopropylfluorophosphate. However, given the vapor pressures, we presume that the volatility is intermediate between Sarin and Soman. The lethal exposure (mg min/m^3) to Sarin or Soman vapor by inhalation is on the order of 100 and for skin exposure on the order of 10,000. The nerve agents are more lethal still in liquid form. If our results with diisopropylfluorophosphate extrapolate to the nerve agents, this would correspond, respectively, to vapor exposures of very roughly 1 s and 1 min of our sensor in its present form. Our sensor experiences instant and total luminescence quenching when exposed to liquid diisopropylfluorophosphate.

6. Other field methods for nerve agent detection

Numerous instrumental methods exist for nerve agent detection, involving GC/mass spec., ion mobility, flame

spectrometry, etc. Portable, field-worthy, devices based on these methodologies are on the market, but they are expensive. We are aware only of three chemical sensing methodologies that resemble what is described here. One of them involves paper impregnated with reagents that yield colored products on reaction with nerve agents [7]. We gather that the sensors target the nerve agent in liquid (aerosol) form. We have no information on their speed or sensitivity. A bioassay-type method involving fluorescence is under study [8]. It is based directly on the mechanism of toxicity of the nerve agent and uses a cholinesterase. The liberated fluoride anion reacts with a non-fluorescent coumarin derivative to render it fluorescent. The method is designed for detection of nerve agents prior to release. We presume this to mean that the method targets the nerve agent in liquid form. The assay is reported to take 1–2 min. A method that involves lanthanide chelates with sensitizing ligands and also the analyte attached during sensor preparation has recently been reported [9]. Once that complex is immobilized in a polymer matrix, the polymer is treated such that the analyte is removed, leaving behind in the polymer a cavity of the dimensions of the analyte. This polymer + cavity system then forms the chemical sensor, which thus has chemical specificity. When it is subsequently exposed to the analyte, the cavity is re-occupied. This changes the ligand electric field at the site of the lanthanide ion to produce subtle, but measurable, spectral luminescence changes in wavelenths and quantum efficiencies. The sensing is thus spectroscopy-intensive (and not trivial). We glean from Ref. [9] that the sensor, which targets liquids, is not fast in response. Its mode of operation is quite different from that of our sensor, whose operation involves displacement of sensitizing ligands followed by hydration to produce strong luminescence quenching, the observation of which is not spectroscopy-intensive.

7. Discussion

We believe that the absence on short exposure of lanthanide luminescence quenching in insufficiently dried filter paper is simply a matter of solvation of fluoride anions, which then no longer readily attack ligands. After all, there are numerous chloride anions present in the very preparation of the lanthanide complexes, and they do not play a role in inhibiting the massive lanthanide luminescence production by the sensitizing OP and TTFA ligands.

When TTFA alone was spotted on filter paper, no fluorescence to speak of was found under short-wave or long-wave UV exposure. In contrast, the corresponding OP spotting initially produced a dark spot, which as the paper dried over roughly 2 min, began to reveal (under short-wave UV) the characteristic intense pale blue OP fluorescence, indicating that the presence of copious quantities of methanol/water quenches the OP fluorescence over this short time period. Given that we prepare the lanthanide complexes with excess ligand (to ensure fullest coordination), it is no surprise that we see a color distortion in fluorophosphate exposed areas of dried filter paper, corresponding to the superposition of the lanthanide and OP luminescences. We have not made use of this color distortion in the above-quoted sensitivity times. Rather, these times correspond to bona fide quenching of the lanthanide luminescence only. We note as well that the UV excitation is efficiently transferred from the sensitizer to the lanthanide, and that this transfer quenches the sensitizer ligand luminescence itself in an essentially permanent way.

The short-term quenching of the Eu or Tb luminescence, which takes place in seconds, represents the practical sensing value. We foresee the prospect of incorporation of the concept into “smart materials”. We foresee the prospect of remote addressing of the sensor by laser. We foresee the prospect of time-resolved visualization in instances in which there is background fluorescence to be suppressed, the time-resolved methodology having been described already [1,3]. Our results suggest that the Eu–TTFA complex is optimal, especially because it lends itself to near-UV excitation, which has considerable advantage over deep-UV excitation.

Acknowledgment

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