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COMMUNICATION

A 'chemically-gated' photoresponsive compound as a visible detector for organophosphorus nerve agents†

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We describe a versatile and convenient visible detection method for organophosphorus compounds based on a colorless 'pro-photoresponsive' organic molecule that undergoes photochemical ring-closing to produce a colored isomer only after it reacts with vapors of the phosphorylating agent.

Today there is still an urgent need for cheap and easy ways to detect lethal airborne agents such as those used in chemical warfare and as pesticides. Among the most noteworthy targets are the odorless, colorless and volatile neurotoxic organophosphates such as sarin, cyclosarin, soman and tabun (Chart 1).[1] The huge lethality of these highly potent and rapidly acting compounds is due to their irreversible inhibition of the cholinesterase enzymes, which give rise to subsequent accumulation of the neurotransmitter acetylcholine in the brain and its periphery resulting in hypersecretion, bronchoconstriction, miosis, muscular twitching, mental confusion, convulsive seizures, flaccid paralysis, respiratory distress and eventual death.

Most of the reported examples of detectors for organophosphates use complicated biochemical assays (fluorometric[2] or amperometric[3]), changes in the optical properties[4] (color,[5] fluorescence,[6] diffraction) of small molecules, polymers[7] or gels,[8] conduction and resistivity in electronic devices,[9] or physical changes in piezoelectric devices[10] to monitor the levels of airborne organophosphate toxins. In many cases, the readout method relies on specific equipment or protocols limiting their widespread use in public spaces. We suggest that a more convenient detection method would take advantage of the ambient conditions (light or heat) to trigger an optical signal that is visually obvious to anyone present regardless of their technical background or expertise. Although fluorescence is a more sensitive optical read-out technique, the convenience of a readily observable change in color of a bulk material cannot be downplayed. Such a material could be processed into films or applied to almost any surface as a coating without the need for electronic and/or optical controls. In this communication, we demonstrate how a molecular photoswitch provides an observable readout when it undergoes 'chemically-gated' photochromism.

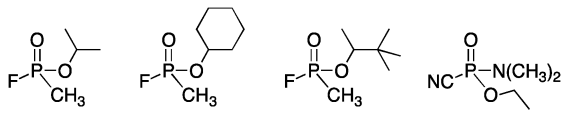

Chart 1 Some of the most common organophosphorus nerve agents.

In molecular systems that exhibit 'chemically-gated' photochromism, a change in color in response to a photochemical stimulus occurs only after the molecule has undergone a chemical reaction with another compound.[11] Because the reactivity of organophosphate nerve agents involves conversion of an active hydroxyl group of an enzyme to a phosphate ester,[12] a detection system that possesses competitive functionality seems the most appropriate. The colorless dithienylethene shown in Scheme 1 (**1o**) is an excellent candidate for this role. Using similar compounds,[13] Irie has shown that intramolecular proton transfer of the phenolic hydrogen efficiently quenches the excited states of the molecules and prevents ring-closing to form its colored isomer (**1c**). In the absence of the intramolecular hydrogen bond between the –OH and the oxygen atom of the imide carbonyl group, these systems undergo photochemically induced ring-closing as is typical for this photoresponsive class of compounds.[14] The authors originally demonstrate this fact by acetylating the phenol of their 'pro-photochromic' compound with acetic anhydride. In our studies, we show that this compound works equally well in solution and in an immobilized state when exposed to vapors of an organophosphate to generate colorless compound **2o**, which undergoes ring-closing (**2o** → **2c**) when exposed to UV light and produces an easily observable change in color. Visible light resets the system by triggering the reverse reaction and regenerating the ring-open isomer.

The appeal of using this specific photochromic backbone lies at many levels. The reverse ring-opening reactions tend to be only photochemical driven so the colored readout signal will always be visible to those in the vicinity. The backbone can be decorated with functional groups to fine-tune the type of light needed to trigger the ring-closing reaction as well as the color produced when the cyclization reaction occurs.[14]

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† Electronic supplementary information (ESI) available: Detailed descriptions of experimental methods, synthetic procedures, characterization of new compounds and additional absorption spectra. See DOI: 10.1039/c1cc13685b.

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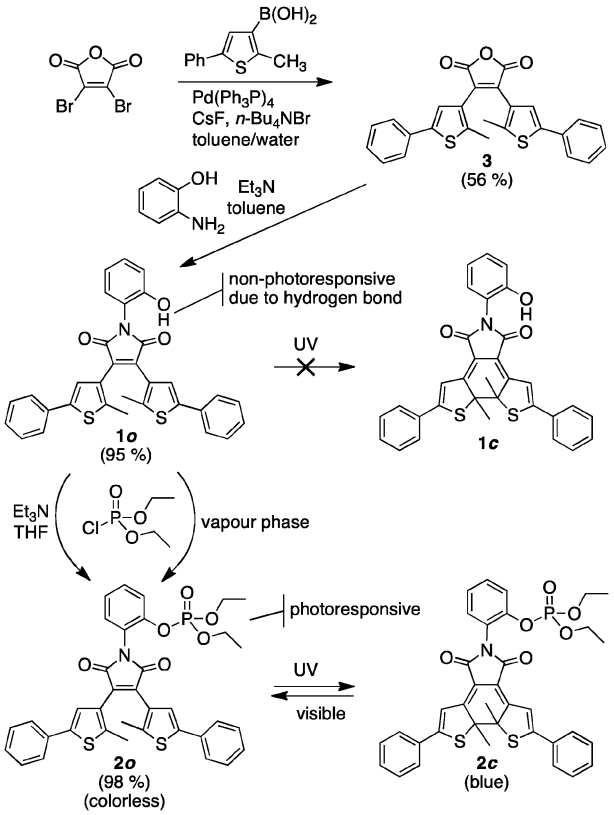

Scheme 1 Synthesis and photochemical behavior of compounds **1** and **2**.

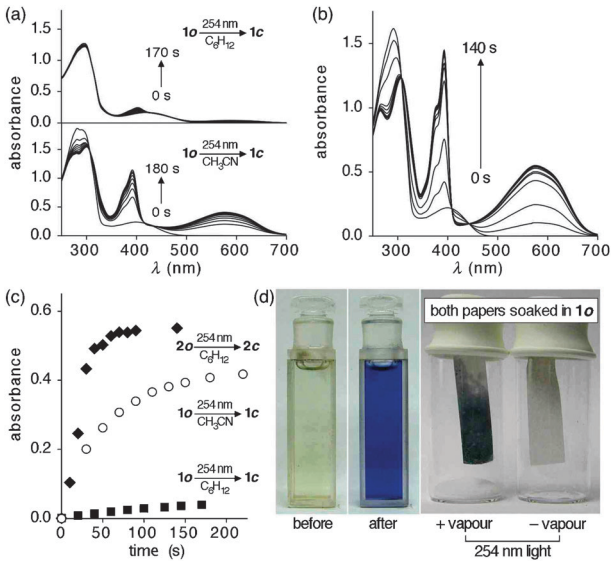

Fig. 1 Changes in the UV-vis absorption spectrum of (a) a cyclohexane (top) and a CH_3CN (bottom) solution of **1o** (1.5–2.5 × 10^{-4} M), and (b) a cyclohexane solution of **2o** (1.5 × 10^{-4} M) as it is exposed to 254 nm light. (c) Changes in the absorption at 575 nm of cyclohexane and acetonitrile solutions of **1o**, and a cyclohexane solution of **2o** as they are exposed to 254 nm light. All concentrations are 1.5 × 10^{-4} M. (d) Visual changes in the color of the cyclohexane solution of **2o** as it is exposed to 254 nm light, and a piece of paper treated with a solution of **1o** and air-dried in a sealed vial containing a few drops of diethyl chlorophosphate while being exposed to 365 nm light (left). The vial on the right shows an identical piece of treated paper in a vial without added diethyl chlorophosphate but with exposure to UV light.

This allows the tailoring of the detection system so it can be activated using the particular environmental light source present, whether it's the sun, LEDs or even the fluorescent lighting typically found in interior spaces. Our detection system also relies only on a one-step reaction, which gives it some advantages over the elegant examples that use two-step processes.[6b,d] Another appealing feature is that the toxic organophosphate is sequestered by the system until it is reset using visible light to trigger the back reaction (**2c** → **2o**) and hydrolysis (**2o** → **1o**).

The ring-open isomer of the phenolic dithienylethene (**1o**) was synthesized by following the procedures published for the preparation of a similar compound.†[13] The synthesis is shown in Scheme 1 and involves the double Suzuki coupling of two known starting materials, 3,4-dibromo-furan-2,5-dione[15] and (2-methyl-5-phenylthiophen-3-yl)boronic acid,[16] to produce an anhydride (**3**) bearing the required hexatriene. This anhydride is converted to the maleimide **1o** in good yield by reacting it with *o*-hydroxyaniline. The phosphorylated version of the phenolic compound (**2o**) was prepared by treating **1o** with diethyl chlorophosphate. This phosphorylating agent was used in all studies described in this communication as it represents a less toxic mimic of sarin.

As expected, compound **1o** is not significantly photoresponsive as long as it is irradiated in non-polar solvents. For example, exposing cyclohexane solutions of **1o** (1.5 × 10^{-4} M) to UV light (254 nm)§ produces only minor changes in their UV-vis absorption spectra even after almost 3 minutes of irradiation (Fig. 1a top), which is usually more than enough time to drive the photochemical ring-closing of typical dithienylethene derivatives. This is not the case for the phosphorylated version **2o**. Cyclohexane (or hexanes) solutions of this compound undergo immediate changes in their UV-vis absorption spectra when exposed to UV light as shown in Fig. 1b. As is typical when dithienylethenes undergo photochemical ring-closing, the high energy absorption bands at 290 nm decrease in intensity along with the appearance of a new set of broad bands in the visible region of the spectrum centered at 578 nm. This spectroscopic change explains the distinguishable color change of the solution from pale yellow to blue. Exposing the colored solutions to visible light (at wavelengths greater than 510 nm, for example) drives the reverse, ring-opening reactions and regenerates both the original color and the absorption spectra (Fig. S4, ESI†). These observations support the claim that intramolecular proton transfer of the phenolic hydrogen is the cause for the suppression of photochromism in compounds such as **1o**.[13] The claim is supported by the analogous spectroscopic and color changes that phenol **1o** undergoes when it is irradiated in solvents that compete for hydrogen bonding as illustrated in Fig. 1a, bottom, which shows the changes of a CH_3CN solution of **1o** when it is exposed to UV light.

Fig. 1c shows the comparative rates of growth of the absorbances corresponding to the ring-closed isomers of phenol **1o** and phosphate **2o** when solutions of them (cyclohexane and CH_3CN) are exposed to UV light. The increased rate of photochemical ring-closing for the phosphate (**2o** → **2c**) in cyclohexane over the parent phenol (**1o** → **1c**) in the more

competitive solvent CH_3CN is likely due to the fact that (1) this solvent does not completely eliminate the intramolecular hydrogen bonding between the phenol hydrogen and the carbonyl oxygen, and/or (2) this solvent allows a greater contribution of intramolecular charge transfer from a twisted conformation of the chromophore, which has been shown to suppress the photocyclization reaction.[17]

The demonstration of compound **1**'s ability to act as a visual detector of phosphorylating agents is shown in the last panel of Fig. 1. Two samples were prepared treating each with one drop of a solution containing **1o** (2 mg) dissolved in cyclohexane (0.2 mL). After air-drying the two pieces of paper, they were placed in separate vials. The vial shown on the left side of the image in Fig. 1 also contained a piece of filter paper soaked with 5 drops of diethyl chlorophosphate (placed at the bottom of the vial). Each vial was sealed and exposed to 365 nm light.¶ Only the paper in the vial containing the phosphorylating agent turned blue-green (after merely a few seconds) showing that the vapors of diethyl chlorophosphate reacted with **1o** to produce **2o**, which immediately ring-closed to the colored **2c**. The molecular system described in this manuscript is very sensitive to ambient light and even the fluorescent lighting conditions in the laboratory were enough to convert the vials from their light to dark states.

In this communication we have highlighted how a relatively simple detection system for organophosphorus compounds can be constructed using the visible change in color when a photoresponsive dithienylethene undergoes 'gated' photochromism. The color changes are easily apparent to the naked eye and can be tuned by judicious modifications to the molecular backbone. Future generation of these types of detection systems will focus on color tuning by mixing more than one photochromic system, and on enhancing the rate of the coloration reaction by introducing oximes as has been demonstrated by Rebek's recent report[18] to ensure degradation of any toxic and reactive phosphate ester, although this will limit the reversibility. The ability for analogous systems to respond to different environmental light conditions will also be demonstrated.

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Notes and references

§ All solution-state studies of the photochemical ring-closing reactions of compounds **1o** and **2o** were carried out using the light source from a lamp used for visualizing TLC plates at 254 nm or 365 nm (Spectroline E-series, 470 W cm^{-2}).

¶ Although this longer wavelength light does not induce as rapid of a photochromic response as does the higher energy light (254 nm) used for the cuvette studies, 365 nm light was used to minimize the amount of UV light filtered by the glass from the vial.

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