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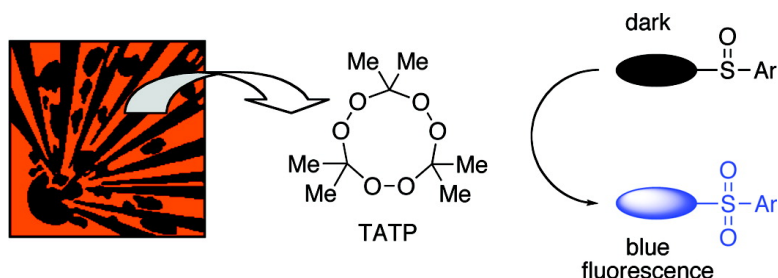
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Fluorescent Signaling Based on Sulfoxide Profluorophores: Application to the Visual Detection of the Explosive TATP

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Triacetone triperoxide (TATP, **1**, Chart 1) is an organic peroxide known since the 19th century,[1] and its explosive properties are well characterized.[2] Although it is too unstable for practical use, it has emerged as an improvised explosive of choice for terrorists because of its ease of preparation. While TATP can be detected using standard analytical methods such as mass spectrometry,[3] it is invisible to the common specialized techniques developed to detect nitrogen-containing explosives.[2,4] Because of the danger of handling or transporting TATP, a visual "naked eye" test for rapid first-pass analysis is desirable. A colorimetric visual test based on a peroxidase-catalyzed reaction of H_2O_2 released from TATP has been reported.[5] No visual fluorescence-based method has been reported,[6] although such a method could benefit from the greater sensitivity associated with fluorescence. We describe here aromatic sulfoxide reagents for visible fluorescence detection of nmol-quantities of TATP and show that these have potential for broader application.[7]

The peroxide character of TATP suggested developing a system in which fluorophore emission was modulated by the oxidation of an adjacent heteroatom.[8] While phosphine profluorophores were initially explored,[9] these proved unsuitable, and our attention turned to the oxidation of sulfur-containing substrates.[10] Peroxide oxidations of sulfides to sulfoxides and sulfoxides to sulfones have been studied extensively, as has the photochemistry of these species.[11] However, to our knowledge, there have been no systematic studies relating the oxidation state of sulfur and the fluorescence properties of a proximate fluorophore.

A series of pyrene derivatives (**2**–**4**, **a**–**c**, Table 1) were selected for initial evaluation on the basis of ease of synthetic access and the (partially) visible emission of pyrene. Notably, in each series, the sulfone exhibits the strongest fluorescence and the sulfoxide the weakest. Particularly in the case of benzylic sulfoxides **3b** and **4b**, precedent suggests an α-cleavage/radical recombination pathway as the dominant nonradiative deactivation pathway for the excited state,[11d] rather than photoinduced electron transfer (PET) quenching.[12–14] The suppression of this deactivation pathway in the corresponding sulfones correlates with the increased C–S bond strength of sulfones relative to sulfoxides, inferred from comparison of dimethyl sulfoxide and sulfone.[15]

The emission from sulfides **2a**–**4a** is varied, although even in the cases of weakly emissive **3a** and **4a** the sulfides are more emissive than the corresponding sulfoxides. Preliminary experiments indicate that α-cleavage occurs in **3a** and **4a** as well, although less efficiently than in the sulfoxides.[14] However, additional fluorescence quenching from PET cannot be excluded.

Ultimately, the fact that sulfones **2c**–**4c** are much more fluorescent than the corresponding sulfoxides provides an opportunity for oxidation-based visual TATP detection (Figure 1). An estimate of maximum response is provided by the ca. 50-fold increase in visible emission for **4c** relative to **4b**, which can easily be discerned by the naked eye (Figure 1, inset).
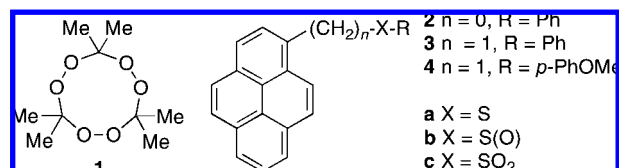
Chart 1. TATP and (Pro)fluorescent Probes

2	n = 0, R = Ph
3	n = 1, R = Ph
4	n = 1, R = p-PhOMe
a	X = S
b	X = S(O)
c	X = SO₂

Table 1. Fluorescence Properties of Pyrene Derivatives **2**–**4**, **a**–**c**[14]

compound	ε $(10^3\ cm^{-1}\ M^{-1})^a$	ϕ^b
2a	2.50	0.34
2b	3.50	0.02
2c	3.07	0.76
3a	4.37	0.01
3b	3.37	≤0.01
3c	5.08	0.47
4a	3.98	≤0.01
4b	3.88	<0.01
4c	5.20	0.41

^{a} For longest-wavelength λ_{max}. ^{b} Relative to pyrene ($\phi = 0.32$).[16]
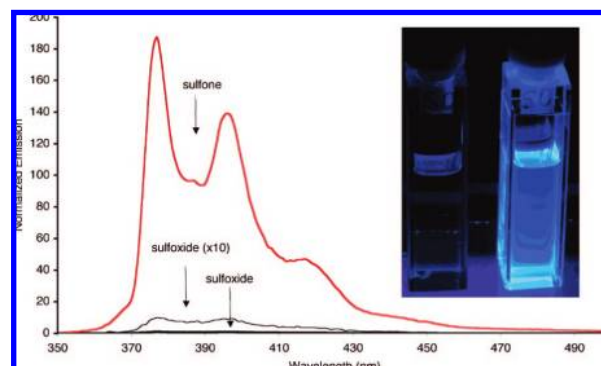

Figure 1. Emission of **4b** and **4c** in CH_2Cl_2, normalized to **4b** at 420 nm; emission from 10^{-4} M solutions of **4b** and **4c** (inset).

TATP does not react directly with profluorophores **2b**–**4b**. However, in the presence of methyltrioxorhenium (MTO) they react rapidly with the H_2O_2 generated by UV irradiation of TATP,[17,18] undergoing oxidation to the corresponding sulfones. Beginning with photolysis of 500 nmol (ca. 0.1 mg) of TATP, a 5-fold increase in visible fluorescence can be attained within 15 min (illustrated with **4b**/**4c**, Figure 2).[19] With regard to detection limits, we have found that we can generate a visual response to as little as 100 nmol of TATP. Although a longer reaction time (90 min) is required for full development, the fluorescence can still be easily seen with the naked eye (Figure 2, inset).[14]

A concern for potential practical application is reaction with other oxidants.[2–4] In this respect, we note that **2b**–**4b**, with or without MTO, do not react appreciably with oxidants such as ′BuOOH,
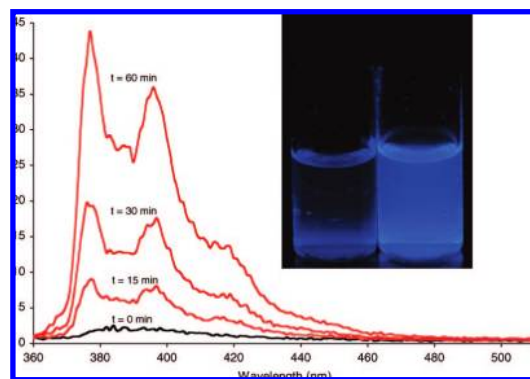
Figure 2. Emission during oxidation of **4b** (10^{-4} M in CH_2Cl_2) with 500 nmol photolyzed TATP in the presence of MTO, normalized to $t = 0$ at 420 nm; solutions before and after reaction with 100 nmol photolyzed TATP (inset).[14,19]

NaOCl, $LiClO_4$, $K_2Cr_2O_7$, or air. They do react spontaneously, in the absence of MTO, with $KMnO_4$, which is occasionally used in improvised explosives.[2a] A potential limitation of this approach is that **2b−4b** are not stable to prolonged UV irradiation (although they are stable to visible light). Given that radical fragmentation/recombination is integral to the signaling mechanism, it is not clear that this limitation can be entirely overcome. However, **2b** degrades more slowly than **3b** or **4b** while still showing significant fluorescence enhancement upon oxidation to **2c**, indicating that there is potential to suppress degradation through structural modification while retaining useful fluorescence response.[20]

In conclusion, we have reported the first visual fluorescent assay for TATP detection. It is operationally simple and capable of detecting nmol-quantities of TATP, requiring no sample preparation beyond brief photolysis, and is more sensitive than the reported visual colorimetric detection method.[21] With regard to broader impact, we believe that aryl sulfoxides have application in the detection of species beyond oxidants of interest. As an example, we find that titration of **2b** with metal ions such as Li^+ and Zn^{2+} leads to fluorescence enhancement.[14,22] More detailed study of this observation, as well as development of second-generation sulfoxide reagents with longer excitation/emission wavelengths and increased stability, are ongoing.

Supporting Information Available: Synthetic procedures and full spectroscopic characterization for new compounds; absorption and emission spectra for **2−4**, **a−c**; photolysis of **2−4**, **a−c**; details of TATP reaction; metal titrations of **2b**.This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) In support of an α-cleavage pathway in quenching fluorescence from **3b** and **4b**, we find that broad-spectrum UV irradiation leads to complete decomposition within 30 min, in analogy to the results described in ref 11d. The products formed are consistent with radical fragmentation/recombination; see Supporting Information.
(13) For leading studies on intramolecular electron transfer involving sulfides, see: (a) Görner, H.; Griesbeck, A. G.; Heinrich, T.; Kramer, W.; Oelgemöller, M. *Chem.−Eur. J.* **2001**, *7*, 1530–1538. (b) Griesbeck, A. G.; Schieffer, S. *Photochem. Photobiol. Sci.* **2003**, *2*, 113–117. To our knowledge, there is no precedent for electron transfer quenching of fluorescence by sulfoxides.
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(19) For the emission spectra in Figure 2, 50 μL of TATP solution (0.01 M in toluene, 0.5 μmol) was diluted with 50 μL EtOH and photolyzed for 15 min with a hand-held UV lamp. This solution, as well as 40 μL of MTO solution (0.08 M in EtOH, 32 μmol), were added to a solution of **4b** (2.50 mL, 10^{-4} M in CH_2Cl_2) in a quartz cuvette. Fluorescence spectra were recorded over a 90 minute period. A similar procedure was used for the inset picture, but with 10 μL of TATP solution.
(20) Similarly, we note that while **3b** and **4b** are prone to acid-catalyzed hydrolysis, **2b** is stable in the presence of acid.
(21) The reported colorimetric assay (ref 5) is applicable to mg-quantities of TATP. The method described here is thus more sensitive, and comparable in terms of ease-of-use, although slightly slower. The reported instrument-based fluorescence method (ref 6) for TATP detection is ca. 100-fold more sensitive than the method described here.
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