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Detecting a peroxide-based explosive *via* molecular gelation†

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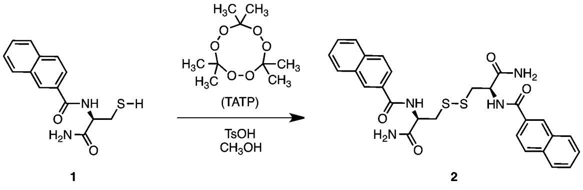
A convenient and portable triacetone triperoxide (TATP) sensor was developed utilizing a thiol-to-disulfide oxidation to trigger a solution-to-gel phase transition. Using this method, TATP can be detected visually without any instrumentation.

The continued safety of civilian and military personnel requires methods for on-site explosives detection. Existing methods range from those based on high-end instrumentation, which provide both accuracy and sensitivity, to those without instrumentation, which are portable but less accurate and less sensitive.[1] The ideal method depends on the location, method of sampling, and sense of urgency.

Triacetone triperoxide (TATP) is a peroxide-based explosive that is easily accessible due to its facile synthesis from readily available reagents (acetone, hydrogen peroxide, and acid). As a consequence, several recent terrorist plots have used TATP.[2] Portable TATP sensors have been developed and a few are commercialized.[3] Several of these methods rely on spectrometers to detect changes in absorption or emission spectra of dyes, and most methods involve time-intensive sample pre-treatment to convert TATP into more reactive components. Suslick and co-workers recently reported a colorimetric array-based sensor for detecting TATP vapors that utilizes an in-line acid catalyst for decomposition and a flatbed scanner for analysis.[4] The system has both a fast response time and the ability to discriminate TATP from other common oxidants. Several methods based on visual detection have also been reported. For example, Finney and Malashikhin detected TATP based on an increase in fluorescence of a dye (with UV illumination) that is observable with the naked eye.[5] We describe herein an alternative instrument-free approach, in which the presence of TATP triggers a solution-to-gel phase transition.

Gel-based sensors provide an unambiguous visual change in the material's physical properties and, in contrast to colorimetric and fluorescent sensors, there is no interference from opaque or colored samples. The detection process typically involves an analyte-triggered chemical reaction, which converts a nongelator into a gelator, followed by gel formation. Response times can vary from seconds to minutes depending on the analyte concentration as well as the rate of the chemical reaction. To date, we have developed gelation-based sensors for nitric oxide,[6a] Hg^{2+} ions,[6b] and several proteases.[6c]

A gelation-based sensor requires three components: (1) a non-gelling reactant, (2) a gelling product, and (3) an analyte-mediated chemical reaction to convert the reactant into product. We initially selected L-cysteine derivative **1** (a nongelator) as the reactant because of the known peroxide-induced thiol-to-disulfide reaction as well as the reported gelation ability of disulfide **2** (eqn (1)).[7] These disulfide-based gelators were first reported in 1892[8] and were more recently studied by Menger[7] and Bradley.[9,10] Disulfide **2** has one of the lowest critical gel concentrations (cgc) known for small molecules (0.25 mM in 25/75 DMSO/H_2O), and it forms gels in a variety of organic solvents. A low cgc is important for sensing because in many cases the analyte is a stoichiometric reagent in the chemical transformation. As a result, sensors based on gelators with lower cgcs will detect lower analyte concentrations.



(1)

Thiol **1** and disulfide **2** were synthesized from commercially available L-cysteine methyl ester (ESI†). No reaction was observed when thiol **1** was treated directly with TATP. To generate a stronger oxidant, *p*-toluenesulfonic acid (TsOH) was used to presumably generate H_2O_2 (and acetone) *in situ* from the degradation of TATP.[11] When TATP is added to a mixture of **1** and TsOH in MeOH, a stable gel is formed within 30 min (Fig. 1). It is important to note that no gel was observed without TATP, indicating a negligible background rate of oxidation (ESI†).[12] Based on these promising initial results, the system was further optimized to develop a gelation-based sensor with an even lower detection limit and faster response time.

Fig. 1 A gel forms within 30 min of adding TATP (2.5 mg) to a vial containing thiol **1** (36 mM) and TsOH (1.3 M) in MeOH.

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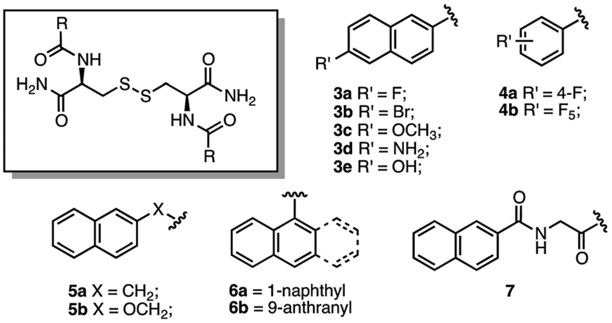
One approach to lowering the detection limit is to modify the structure of disulfide **2** to identify an alternative gelator with a lower cgc in MeOH (ESI†). (Note that the cgc of **2** is 4.6 mM in MeOH.) Because of the largely unpredictable relationship between structure and gelation ability,[13] several approaches were investigated. For example, previous studies of peptide- and disulfide-based gelators have shown improvements in cgc with halogen substitution and attributed these results to increased hydrophobicity.[9,14] In this case, however, halogenated disulfides **3a** and **4a** exhibited higher cgcs (6.5 mM and 25 mM, respectively) than disulfide **2** while both **3b** and **4b** were nongelators. Disulfides with electron-donating substituents at the same position were synthesized to compare to the halogenated derivatives but none of these compounds (**3c–3e**) formed gels under these conditions. Because π-stacking was suggested to be important in the self-assembly of these disulfide-based gelators,[7] compounds **5a–5b** and **6a–6b** were synthesized and screened for gelation. Extending the linker length in **5a** led to a nongelator, as did changing the point of attachment (**6a**) and extending the aromatic unit (**6b**). In contrast, using the larger linker (**5b**) led to a gelator, albeit with a higher cgc (8.5 mM). Because intermolecular H-bonding is also suggested to drive the self-assembly of these disulfides,[7] a glycine residue was inserted between the naphthyl and amide residues (**7**). This amino acid-based compound did not form a gel under these conditions. Overall, these results highlight the challenges involved in the design and discovery of new gelators.[13] In total, three new gelators were discovered through these efforts.[15] Among all the compounds synthesized, the original disulfide (**2**) remained the best gelator for the TATP sensor because it had the lowest cgc in MeOH. Thus, further optimizations were performed using disulfide **2**.



To decrease the response time, the TATP degradation and thiol oxidation reaction rates were independently optimized. Rate studies were first performed on the TsOH-mediated decomposition of TATP. As noted above, the main decomposition products have been suggested to be H_2O_2 and acetone.[11] To provide support for this proposal, the degradation reaction was performed in the presence of 2,4-dinitrophenyl hydrazine, which should react with any acetone present to form a hydrazone.[16] Approximately 30% of the expected acetone was trapped as the hydrazone (ESI†). Based on the mechanism of acetone formation, this result suggests that H_2O_2 is also generated during this reaction. Rate studies revealed a fractional order (0.7) dependence on [TsOH] for the TATP degradation (ESI†). Rate studies were then performed on the H_2O_2-mediated oxidation of thiol **1**, which revealed an approximate first-order dependence on [H_2O_2] (ESI†). Combined, these results suggest that increasing the rate of TATP degradation (by increasing the [TsOH]) will increase the oxidation and gelation rate. However, a background reaction involving esterification of the amide in **2** became significant at higher TsOH concentrations (ESI†). The optimized TsOH concentration was empirically determined to be 36 equivalents relative to thiol **1** (ESI†).[17]

To lower the detection limit, we investigated the impact of decreasing the reaction volume. A decrease in reaction volume will decrease the quantity of TATP required to form a gel based on the reaction stoichiometry. For example, while 20 mg of TATP is required to gel a 4 mL solution of **1** (36 mM in MeOH), only 2 mg of TATP is required to gel a 0.4 mL of the same solution. A further decrease in detection limit can be obtained by decreasing the diameter of the container because the yield stress of a gel is inversely proportional to the container diameter (with constant volume).[18] Therefore, when using the vial inversion test, smaller containers will require less gelator to form stable gels. This effect can be attributed to a relative increase in the surface area between the container and the gel. As evidence, the amount of **2** needed to gel 0.5 mL of MeOH decreased from 4.6 mM (1.3 mg) in a 13 mm inner diameter vial to 2.0 mM (0.5 mg) in 4.6 mm inner diameter vial.

Using all of these optimized conditions, a simple one-pot method was developed. Specifically, **1** (36 mM), TsOH (1.3 M), and TATP (1.5 mg) were pre-mixed and then transferred to a small tube, where gelation was observed within 8 min (Fig. 2).[12] Note that faster response times can be obtained with higher concentrations of TATP. For example, gelation occurs within 2 min when 12 mg of TATP is added (ESI†). Overall, this method is convenient and simple to use and interpret.

Similar to most portable TATP sensors, this gel-based sensor is also sensitive to other hydrogen-based peroxides and strong oxidants such as bleach, Cr^{3+}, Cr^{6+} and peracetic acid (ESI†). Fortunately, none of these oxidants have a similar white powder appearance to TATP and can therefore be distinguished. In addition, oxidants with similar white powder formulations, such as potassium iodide, potassium chlorate and benzoyl peroxide do not trigger gelation even under acidic conditions (ESI†).

In summary, a convenient and portable gel-based sensor for detecting mg quantities of solid TATP was developed. Given that hundreds of grams of TATP are used in improvised explosive devices, milligram-sized samples should be readily accessible. The sensor is based on a TATP-triggered gelation *via* a thiol-to-disulfide oxidation reaction. Although modifying the original structure

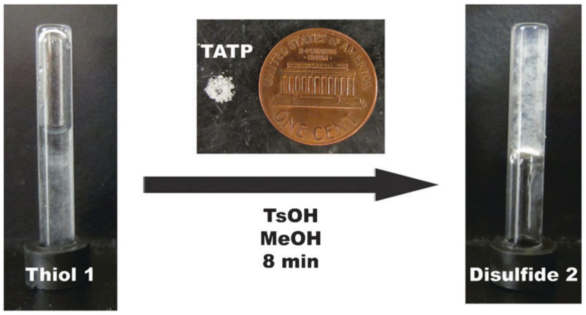


Fig. 2 Gel formation is observed within 8 min of mixing **1** (36 mM), TsOH (1.3 M), and TATP (1.5 mg) in MeOH.

did not produce a better gelator, optimizing the oxidation and gelation rates, as well as the reaction volume and container size, improved both the detection limit and response time. Overall, we believe that this sensor is complementary to the traditional colorimetric and fluorescent approaches used in TATP detection, with the added advantages of unambiguous signal read-out and no instrumentation needed.

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