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Progress toward colorimetric and fluorescent detection of carbonyl sulfide[†]

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We report here that a fluorescent benzobisimidazolium salt (**TBBI**) can be used for the fluorescent and colorimetric detection of carbonyl sulfide (COS) over related heterocumulenes including CO₂ and CS₂ in wet MeCN. The reaction between **TBBI** and COS in the presence of fluoride yields a highly fluorescent ($\lambda_{\text{em}} = 354$ nm) and colored product ($\lambda_{\text{max}} = 321, 621$ nm), that is readily observed by the naked eye. We view these results as a first step toward developing activity-based probes for COS detection.

Carbonyl sulfide (COS) is an important organosulfur species in the global sulfur cycle¹ that is generated during the burning of biomass,^{2,3} combustion of biofuels,⁴ and in different production processes in the pulp and paper industries.⁵ In addition, geochemical production of COS arises from volcanic activity, emission from hot springs, and deep sea thermal vents.⁶ Although the chemical properties and reactivity of COS have long been established,⁷ the biological implications of COS have only recently begun to emerge.⁸ As an example, treatment of α -amino acids with COS under prebiotic reaction conditions results in the formation of dipeptides, demonstrating the potential role of COS in origin of life chemical ligation.⁹ Aligned with our interests in studying biological reactive sulfur species,¹⁰ our group has recently advanced the use of COS-releasing compounds for the controlled release of hydrogen sulfide (H₂S) due to the rapid catalyzed hydrolysis of COS by carbonic anhydrase, a ubiquitous metalloenzyme.¹¹ Although enzymatic pathways for endogenous COS production in mammals remain undiscovered, COS has been detected in porcine cardiovascular tissues¹² and exhaled breath from cystic fibrosis patients¹³ by using gas chromatography mass spectrometry. More recently, in our investigation of esterase-sensitive COS-based H₂S donors in human lung epithelial (BEAS2B) cells, we

observed COS-dependent inhibition of mitochondrial bioenergetics. This finding suggests that COS may possess biological activities and properties akin to H₂S.¹⁴ As the potential roles of COS in biological systems and investigations into COS releasing compounds expand, a currently unmet need to further such investigations is the development of minimally invasive and sensitive methods for COS detection. Based on the significant impacts of colorimetric and fluorescent activity-based probes for the detection of reactive sulfur species, such as cysteine, reduced glutathione, and H₂S, we envisioned that analogous platforms could be developed for COS detection.^{15,16} To the best of our knowledge, no activity-based probes for COS detection or differentiation from the related heterocumulenes CO₂ or CS₂ have been reported.

Based on the electrophilicity and structural similarities between carbon dioxide (CO₂), carbon disulfide (CS₂), and COS,⁷ we anticipated that a nucleophilic platform could be used to develop chemical tools for COS detection. For example, N-heterocyclic carbenes can insert into heterocumulenes, which has been demonstrated separately for CO₂,¹⁷ CS₂,¹⁸ and COS.¹⁹ Bridging the gap to heterocumulene detection, the vast majority of work has aimed at the spectroscopic²⁰ or electrochemical detection²¹ of CO₂. Of these reported methods, we were drawn to the prior use of a fluorescent, colorimetric benzobisimidazolium probe (**TBBI**) for CO₂ detection.²² In this system, treatment of **TBBI** with tetra-*n*-butylammonium fluoride (TBAF) produces a “carbene-like” intermediate²³ that readily reacts with CO₂ through carbene insertion into CO₂ and subsequent hydrolysis to form bicarbonate (Fig. 1a). This reactivity was also investigated for CS₂ by ¹³C NMR spectroscopy and shown to result in the generation of an imidazolium-dithiocarboxylate betaine through carbene insertion into CS₂ (Fig. 1b). Building from structural similarities between these compounds, we hypothesized the treatment of **TBBI** with COS in the presence of fluoride would provide a unique spectroscopic response for COS that would be distinguishable from that of CO₂ and CS₂. Based on this motivation, we report here the first demonstration of selective COS detection by UV-Vis and fluorescence spectroscopy.

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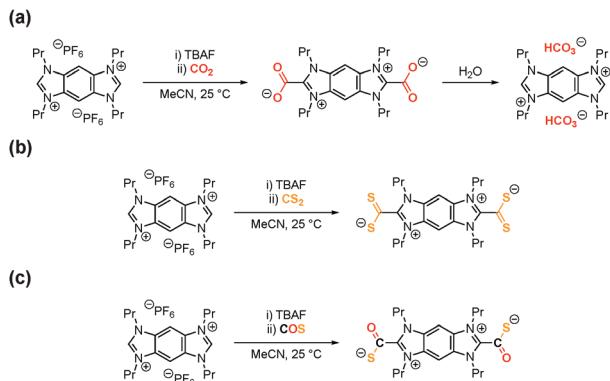


Fig. 1 (a) Reaction of CO_2 and **TBBI** in the presence of fluoride. (b) Reaction between CS_2 and **TBBI** in the presence of fluoride. (c) Proposed reaction between COS and **TBBI** in the presence of fluoride.

One challenge when working with COS is that commercial sources often contain H_2S as a common impurity. To overcome this challenge, we prepared COS through the acidic hydrolysis of KSCN using modifications of known methods (Fig. 2a).²⁴ Based on the growing interest in various aspects of COS chemistry, including delivery, organometallic chemistry, and chemical biology, we have included this method here and in the ESI.† A key requirement when preparing COS is purification of the product, which can be accomplished by sparging through aqueous KOH, aniline in anhydrous ethanol, ice water, and neat H_2SO_4 . The purified COS can be collected and stored in a gas storage flask or added directly into a solution or NMR tube for use as a reactant or reagent (Fig. 2b). COS has a characteristic ^{13}C NMR chemical shift at $\delta = 154.34$ ppm (CD_3CN) and IR stretch at 2927 and 2909 cm^{-1} , which match prior reports.²⁵

To investigate the proposed strategy of carbene insertion for COS detection, we prepared **TBBI**²² and monitored its reactivity toward COS in the presence of TBAF by UV-Vis spectroscopy (Fig. 3a). The parent **TBBI** compound (15 μM in MeCN containing 1% (v/v) H_2O) has an absorption band centered at 290 nm, which shifts to 344 nm upon addition of TBAF (6.0 equiv.). This

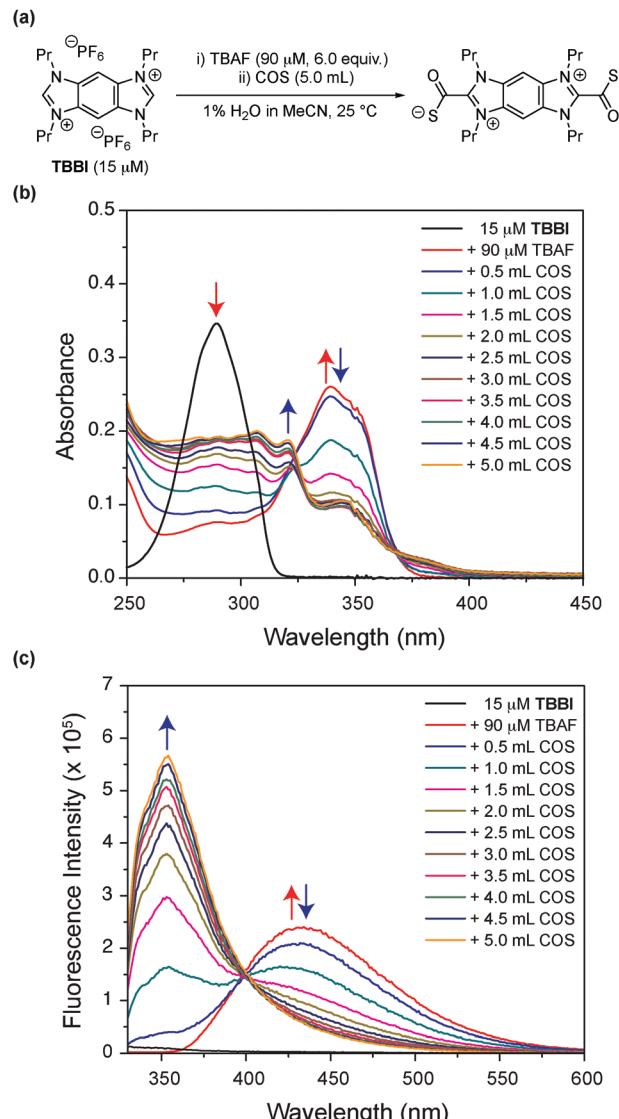


Fig. 3 (a) Reaction of **TBBI** with COS. (b) UV-Vis spectra and (c) fluorescence spectra for **TBBI** (15 μM), TBAF (90 μM), and COS (5.0 mL).

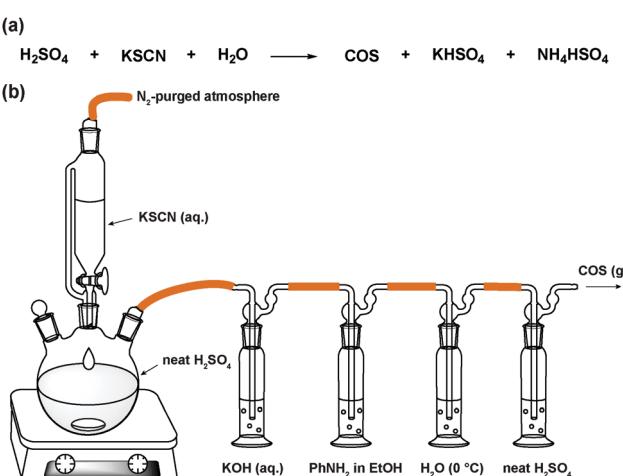


Fig. 2 (a) Acid-mediated hydrolysis of KSCN to generate COS. (b) Schematic of laboratory-scale COS synthesis and purification.

change in absorbance is consistent with the previous report of hydrogen bond formation between the C1-H in **TBBI** and F^- .²² Subsequent addition of COS in 0.5 mL increments resulted in a decrease in the 344 nm absorbance and concomitant increase of a new absorbance at 321 nm. We note that this observed reaction with COS did not occur if anhydrous MeCN was used, which highlights that residual H_2O is required. The new absorbance at 321 nm is unique to COS and is not observed upon reaction of **TBBI** with CO_2 or CS_2 in the presence of TBAF.

Building from this observation, we next investigated the reaction by fluorescence spectroscopy. The parent **TBBI** compound (15 μM , MeCN containing 1% (v/v) H_2O) showed negligible fluorescence when excited at 321 nm, but addition of TBAF (6.0 equiv.) resulted in the appearance of a broad emission centered at 434 nm, which we attribute to formation of the hydrogen bonded **TBBI** intermediate. Subsequent addition of COS in 0.5 mL increments led to a clean ratiometric response,

with a decrease at the 434 nm emission and concomitant increase at 354 nm (Fig. 3c). The product formed upon COS addition is persistent, unlike in the case for CO_2 in which rapid hydrolysis to bicarbonate is observed. A plot of COS concentrations against the ratio of fluorescence intensities at 354 and 434 nm is linear ($R^2 = 0.986$), which suggests that this detection method could be used to quantify COS concentrations (see ESI,† Fig. S3). Taken together, these results demonstrate that **TBBI** can be used to spectroscopically distinguish between CO_2 , CS_2 , and COS in the presence of the fluoride.

To confirm the formation of the proposed thiocarboxylate product, we accessed this compound by treatment of **TBBI** with KHMDS (2.2 equiv.) and subsequent addition of COS (g). The addition of COS (g) to a solution of doubly deprotonated **TBBI** in THF-d_8 yielded a yellow-orange solution and the appearance of a new resonance in the ^{13}C NMR spectrum at 190.34 ppm corresponding to thiocarboxylate formation (Fig. 4a and b). This observed chemical shift is within the range of previously synthesized imidazolium-2-thiocarboxylates.¹⁹ We further characterized this compound by IR spectroscopy and observed C-S and C=O stretching frequencies at 990 and 1524 cm^{-1} , respectively (see ESI,† Fig. S6). We next measured the fluorescence spectrum of this product in MeCN ($\lambda_{\text{ex}} = 321 \text{ nm}$, $\lambda_{\text{em}} = 330\text{--}600 \text{ nm}$) and observed

a nearly identical match to the spectroscopic properties observed under experimental conditions (Fig. 4c). When taken together, the combined ^{13}C NMR data and fluorescence spectroscopy data both support the formation of the proposed thiocarboxylate upon treatment of **TBBI** with F^- and COS (g).

The stability and unique spectroscopic properties of product formed upon COS addition prompted us to investigate whether this **TBBI** system could be used for naked-eye optical detection of COS. The recognition of CS_2 by 10 mM **TBBI** in the presence of fluoride was previously reported to generate a color change from clear to yellow red and form an imidazolium-dithiocarboxylate betaine.²² To further investigate this reactivity, we charged a series of cuvettes with 10 mM **TBBI** and 60 mM TBAF in MeCN containing 1% (v/v) H_2O to generate the hydrogen bonded intermediate; this was followed by addition of CO_2 , CS_2 , or COS (Fig. 5). Consistent with previous results, the cuvette containing CO_2 yielded a white precipitate corresponding to the bicarbonate salt of **TBBI**, whereas the cuvette containing CS_2 yielded a pale orange solution. The reaction between **TBBI** and COS yielded a teal green color and transitioned to a dark forest green upon standing for an extended period of time. This color is due to the combination of the major broad absorbance at 321 nm, which tails into the visible region of the spectrum, and a significantly weaker absorbance at 621 nm that appears upon COS addition (see ESI,† Fig. S7). These results demonstrate the unique ability of **TBBI** to serve as a versatile platform for distinct recognition of CO_2 , COS, and CS_2 by naked eye detection.

In summary, we have demonstrated that the **TBBI** platform can be used for the colorimetric and fluorescent detection of COS. Importantly, these spectroscopic responses for COS are distinct from those generated by CO_2 or CS_2 . We view that these advances provide a first step toward developing activity-based chemical tools for COS detection and imaging, which we anticipate can

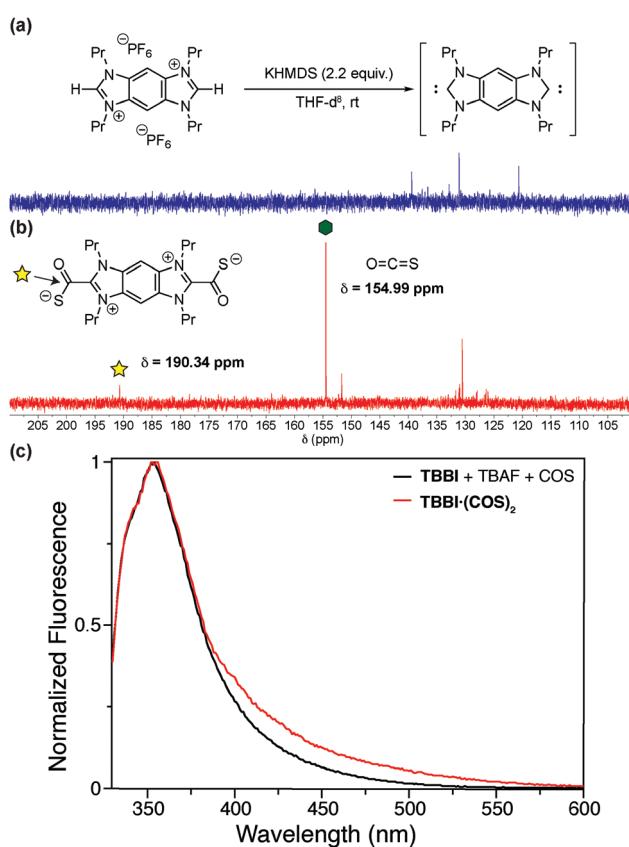


Fig. 4 (a) The $^{13}\text{C}(\text{H})$ NMR spectrum of **TBBI** (30 mM) treated with KHMDS (2.2 equiv.) in THF-d_8 . (b) The $^{13}\text{C}(\text{H})$ NMR spectrum following the addition of COS (g) to a solution of doubly deprotonated **TBBI**. (c) Normalized fluorescence spectra comparing emission from **TBBI** + TBAF + COS and the synthesized thiocarboxylate adduct (**TBBI-(COS)2**).

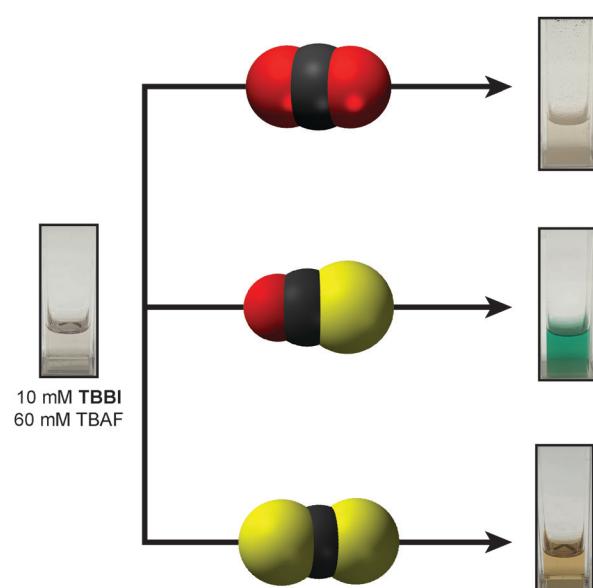


Fig. 5 Naked-eye detection and differentiation of CO_2 , CS_2 , and COS using **TBBI** (10 mM) in the presence of TBAF (60 mM).

be used to investigate the growing evidence for a biological role of COS in complex environments.

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Conflicts of interest

There are no conflicts to declare.

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