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Reaction-based fluorometric analysis of *N*-bromosuccinimide by oxidative deprotection of dithiane†

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In this study, a fluorescent probe is developed for the first time for *N*-bromosuccinimide (NBS), a synthetically and analytically important compound. Pyrene–dithiane-based probe **1** showed prominently selective and sensitive signaling behavior toward NBS owing to the oxidative cleavage of the dithiane protecting group of 1-pyrenecarboxaldehyde. The NBS-selective signaling of the probe was possible under competitive conditions in the presence of common metal ions and anions as a background. The detection limit of the probe for NBS was found to be 5.6×10^{-8} M (10.0 ppb). The signaling product was sufficiently stable under the oxidative stress of NBS in contrast to another tested compound, 6-methoxy-2-naphthaldehyde-based dithiane derivative **2**, which showed a gradually decaying response because of the reaction of the signaling product with the residual NBS. In the practical application of the probe, a smartphone was used as a stand-alone device, and the fluorometric assays of the commercial NBS reagents could be conducted rapidly and in a convenient manner.

1. Introduction

N-Halosuccinimides are widely used as a basic synthetic and analytical reagent in chemistry because they are easier and safer to handle than chlorine, bromine, and iodine. In particular, *N*-bromosuccinimide (NBS) has been extensively utilized as a source of bromine in various electrophilic additions and radical reactions, acting as an efficient brominating and mild oxidizing agent.[1] It has also been used in synthetic organic chemistry for the oxidation of *N*-benzylamides to aldehydes or ketones,[2] amidation of benzylic C–H bonds,[3] and as a catalyst for the oxathioacetalization, thioacetalization, and transthioacetalization of carbonyl compounds.[4] The chlorine and iodine analogs of NBS, *N*-chlorosuccinimide (NCS)[5] and *N*-iodosuccinimide (NIS),[6] respectively, have similar properties and are employed for various synthetic applications.

In analytical chemistry, NBS and NCS have been broadly used as oxidants for the flow injection chemiluminescence determination[7] of a number of pertinent species such as sulfide,[8] hydrazine,[9] pyrogallol,[10] urea,[11] humic acid,[12] and proteins.[13] NBS has also been utilized as an oxidant for the spectrophotometric determination of drugs, including omeprazole,[14] aripiprazole,[15] and catecholamine derivatives in pharmaceutical formulations.[16] Because of their widespread use for various chemical and analytical applications, it is very important to develop accurate assays of *N*-halosuccinimides. However, a convenient analytical method for the determination of these important chemicals is not so well established.

Analysis of *N*-halosuccinimides has been conducted mainly by traditional analytical methods such as titration and the ion-selective electrode method. For instance, the iodometric determination by the reaction of *N*-halosuccinimides with iodide and subsequent titration with thiosulfate[17] and arsenite[18] has been reported. In the ion-selective electrode method, *N*-halo compounds are reduced with sulfite ions and the generated chloride, bromide, and iodide ions are determined.[19,20] The electrochemical determination of NBS by amperometric membrane electrode,[21] chronovoltammetry,[22] and potentiometry[23] has also been reported. However, optical analysis employing colorimetric or fluorescence responses is more advantageous than these traditional analytical methods because of its sensitivity, selectivity, easy experimental procedure, and simple data analysis. Nonetheless, we were unable to find any literature on optical methods for the assay of *N*-halosuccinimides.

Dithiane and dithiolane have been extensively utilized as protecting groups for ketones and aldehydes. They are readily cleaved by a number of hydrolytic methods, for instance, Hg(II) induced,[24] halogenative, and oxidative hydrolysis.[25] Furthermore, oxidants such as chlorite (ClO_2^-),[26] 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[27] and *o*-iodoxybenzoic

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acid (IBX)[28] have been effectively employed for the oxidative deprotection of dithiane or dithiolane. It is worth noting that *N*-halosuccinimides[29] (NCS[30,31] and NBS[32,33]) have also been used for mild deprotection of dithianes to the corresponding aldehydes and ketones.

In this work, we designed the selective and sensitive off-on type fluorescent signaling probe for the determination of NBS. The signaling response was realized through smooth oxidative deprotection of dithiane-protected 1-pyrenecarboxaldehyde. Suppressed fluorescence owing to the presence of dithiane moiety was remarkably enhanced through conversion to the parent aldehyde. The interference from the Hg^{2+} ions in NBS signaling was effectively eliminated using a masking agent, ethylenediaminetetraacetic acid (EDTA).

2. Experimental

2.1 General

1-Pyrenecarboxaldehyde, 6-methoxy-2-naphthaldehyde, 1,3-propanedithiol, and iodine were purchased from Merck KGaA. *N*-Bromosuccinimide (NBS), *N*-chlorosuccinimide (NCS), and *N*-iodosuccinimide (NIS) were also purchased from Merck KGaA, and used after standardization by iodometric titration.[17] All other chemicals and solvents were obtained from commercial sources. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectra were measured on a Varian VNS NMR spectrometer using residual solvent signals as a reference. UV–vis and fluorescence spectra were measured with a Scinco S-3100 spectrophotometer and FluoroMate FS-2 fluorescence spectrophotometer, respectively. Mass spectra were obtained using a Micromass Autospec mass spectrometer. Melting points of probes **1** and **2** were recorded on a Stuart SMP 30 advanced digital melting point apparatus.

2.2 Preparation of dithiane derivatives 1 and 2

Dithiane derivatives of 1-pyrenecarboxaldehyde and 6-methoxy-2-naphthaldehyde were prepared by following the somewhat modified reported literature method.[34] Briefly, 1-pyrenecarboxaldehyde (230 mg, 1.0 mmol) or 6-methoxy-2-naphthaldehyde (186 mg, 1.0 mmol) was dissolved in 10 mL of dichloromethane and 1,3-propanedithiol (0.11 mL, 1.1 mmol) was added. Next, iodine (25 mg, 0.1 mmol) was added as a catalyst, and the reaction mixture was stirred at room temperature for 2 h. Subsequently, the reaction was quenched by adding sodium thiosulfate (0.1 N, 5 mL) and sodium hydroxide (0.1 N, 5 mL) solutions. The reaction mixture was then washed three times with distilled water, and the organic phase was dried over anhydrous $MgSO_4$. Dithiane products were obtained by recrystallization from a mixture of dichloromethane and methanol.

Probe 1.[34] Yellowish powder (240 mg, 75%). Mp: 209.0 ± 0.3 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.56 (d, J = 9.3 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.21–8.16 (m, 4H), 8.07–8.00 (m, 3H), 6.23 (s, 1H), 3.32–3.27 (m, 2H), 3.07–3.03 (m, 2H), 2.32–2.28 (m, 1H), 2.16–2.05 (m, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 132.2, 131.4, 131.3, 130.7, 127.9, 127.76, 127.75, 127.3, 126.03, 125.95, 125.5, 125.3, 125.2, 125.0, 124.8, 122.7, 49.0, 32.9, 25.4. MS (EI) m/z calcd for $C_{20}H_{16}S_2$ $[M]^+$ 320.1; found, 319.7.

Probe 2.[35] White powder (199 mg, 72%). Mp: 190.7 ± 0.3 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.88 (d, J = 1.7 Hz, 1H), 7.72 (t, J = 8.3 Hz, 2H), 7.54 (dd, J = 8.5, 1.9 Hz, 1H), 7.15 (dd, J = 8.9, 2.5 Hz, 1H), 7.11 (d, J = 2.6 Hz, 1H), 5.31 (s, 1H), 3.90 (s, 3H), 3.12–3.07 (m, 2H), 2.96–2.92 (m, 2H), 2.21–2.16 (m, 1H), 2.00–1.93 (m, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 158.0, 134.5, 134.2, 129.5, 128.8, 127.3, 126.6, 126.2, 119.1, 105.7, 55.3, 51.5, 32.2, 25.2. MS (EI) m/z calcd for $C_{15}H_{16}OS_2$ $[M]^+$ 276.1; found, 276.1.

2.3 Preparation of stock solutions

Stock solutions of probes **1** and **2** (5.0×10^{-4} M) and NBS (1.0×10^{-2} M) were prepared in spectroscopic grade acetonitrile, and those of the tested metal ions and anions were prepared in deionized water (1.0×10^{-2} M) using the perchlorate and sodium salts of the metal ions and anions, respectively. A solution of EDTA (10.0 mM) in deionized water was also prepared.

2.4 Investigation of NBS signaling behavior

The NBS signaling experiment of probe **1** was conducted under the optimized conditions in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). Sample solutions were prepared by adding stock solutions of the buffer (150 μL, 0.20 M), probe **1** (30 μL, 5.0×10^{-4} M), EDTA (30 μL, 1.0×10^{-2} M), and NBS or metal ions or anions (15 μL, 1.0×10^{-2} M) to each vial. The sample solution was diluted using deionized water and acetonitrile to give a final volume of 3.0 mL with a composition of 1 : 1 (v/v) mixture of water and acetonitrile. The final concentrations of the probe, analyte (NBS or metal ions, or anions), EDTA, and buffer in the solution were 5.0×10^{-6} M, 5.0×10^{-5} M, 1.0×10^{-4} M, and 1.0×10^{-2} M, respectively. Error bars were estimated as the standard error of the mean of three independent experiments.

2.5 Determination of the detection limit

Following the IUPAC recommendation, the detection limit of NBS assay was estimated by the expression $3s_{bl}/m$, where s_{bl} is the standard deviation of the responses without the analyte (number of measurements = 10) and m is the slope of the calibration plot.[36]

2.6 Smartphone-based NBS determination by probe 1

A handmade paper cube box with a square hole in the upper side was prepared for preventing interference of environmental light. The prepared samples were placed in a 96-well plate, and the fluorescence emission of the samples was obtained by excitation using a 365 nm UV LED bar (JENO, HDL 1807). The digital images of the samples were taken using a smartphone (Galaxy S7, Samsung Electronics) without any special settings. The red, green, and blue channel levels of the obtained fluorescence images were determined using a smartphone application (RGB Grabber, Shunamicode). Using an Excel program embedded in a smartphone, a calibration curve was obtained

by plotting the changes in the blue channel value, which showed the most variation among the three, as a function of [NBS].

2.7 NMR and mass evidence of NBS signaling

Probe **1** (64 mg, 0.2 mmol) and NBS (78 mg, 0.44 mmol) were dissolved in 10 mL of 50% acetate-buffered aqueous acetonitrile solution. After stirring for 1 h, the reaction product was extracted using dichloromethane. The crude product was purified by column chromatography (silica gel, dichloromethane) to obtain a powdery product (28 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.77 (s, 1H), 9.41 (d, J = 9.6 Hz, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.33–8.21 (m, 5H), 8.12–8.06 (m, 2H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 192.9, 135.4, 131.2, 130.9, 130.8, 130.65, 130.56, 130.3, 127.3, 127.1, 126.9, 126.7, 126.5, 124.5, 124.4, 123.9, 122.9. MS (EI) m/z calcd for $C_{17}H_{10}O$ $[M]^+$ 229.7; found, 230.1.

3. Results and discussion

Dithiane-based NBS-signaling probes **1** and **2** were prepared by the reaction of 1-pyrenecarboxaldehyde and 6-methoxy-2-naphthaldehyde with 1,3-propanedithiol (I_2-catalyzed, probe **1**: 75% yield, probe **2**: 72% yield) following the literature procedure (Scheme 1).[34] While conducting screening experiments to find the optimized conditions for NBS selectivity of the probe over commonly encountered chemical species such as metal ions and anions, we observed a substantial response from Hg^{2+} ions (Fig. 1, without EDTA). It is already known that thioacetals or thioketals are prone to cleavage by Hg^{2+} ions.[37–39] Since our aim was to develop an NBS-selective probe, we attempted to suppress this unwanted Hg^{2+} interference using a suitable metal chelating additive. It was found that among the tested masking agents, EDTA effectively suppressed the interference from Hg^{2+} ions without affecting the NBS signaling (log K_f for Hg(II)–EDTA complex = 21.7)[40] (Fig. 1, with EDTA). Based on this finding, all the experiments were carried out in an acetate buffered aqueous acetonitrile solution containing EDTA as a masking agent to circumvent the Hg^{2+} interference. Probe **1** was also tested as a fluorescent signaling probe for other closely related *N*-halosuccinimides. As shown in Fig. S1 (ESI†), probe **1** exhibited similar turn-on type fluorescence signaling behaviors for NCS and NIS, too. Subsequent experiments focused on the characterization of the signaling behavior of probe **1** for the representative *N*-halosuccinimide NBS, which is the most widely used in synthetic and analytical applications.

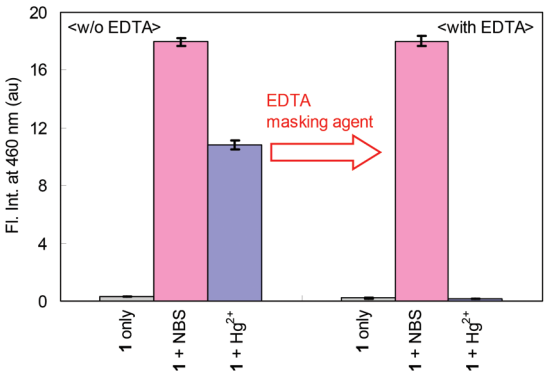
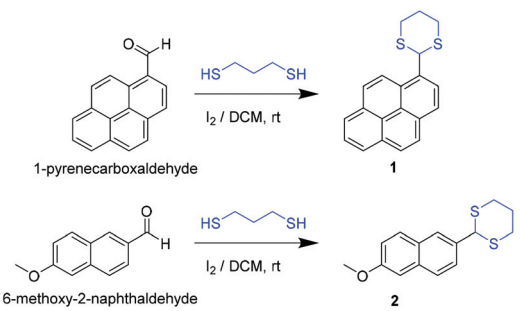


Fig. 1 Suppression of Hg^{2+} interference of probe **1** with EDTA as a masking agent. Fluorescence intensity changes were measured at 460 nm in the presence and absence of EDTA. [**1**] = 5.0 × 10^{-6} M, [NBS] = [Hg^{2+}] = 5.0 × 10^{-5} M, [EDTA] = none or 1.0 × 10^{-4} M in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). λ_{ex} = 340 nm. The error bars were obtained by three independent experiments.

UV–vis spectrum of probe **1** showed characteristic vibronic bands of the pyrene moiety at 316, 330, and 345 nm in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v) (Fig. S2, ESI†). Treatment of probe **1** with NBS resulted in a significant change in the absorption spectrum. New broad bands at 367 and 398 nm appeared while the pyrene vibronic bands of the probe were mostly diminished. The considerable spectral change was attributed to the oxidative deprotection of the dithiane moiety of the probe by NBS (*vide infra*). The newly emerged bands matched well with the absorptions of 1-pyrenecarboxaldehyde.

The fluorescence signaling behaviors of probe **1** toward NBS were more pronounced than the absorption responses. Under the same conditions using EDTA as a masking agent, probe **1** revealed a remarkable fluorescence enhancement on the addition of NBS. The off-on type signaling contrast, as estimated from the fluorescence intensity ratio in the presence and absence of analyte (I/I_0) at 460 nm, was 88.7 (Fig. 2). The selectivity of the probe toward NBS over possibly coexisting species in its routine applications, such as alkali, alkaline earth, and some transition metal ions as well as anions, was then evaluated. Most of the surveyed metal ions revealed no responses under the measurement conditions. For the assessment of the NBS selectivity of the probe, the fluorescence intensity ratio at 460 and 376 nm (I_{460}/I_{376}) was calculated in consideration of the large spectral changes induced by NBS. However, the signaling contrast became considerably diminished because the two pertinent signals at 460 and 376 nm both changed in the same increasing mode (Fig. S3, ESI†). Most of the tested anions also induced no noticeable responses of the probe. The fluorescence intensity ratio (I/I_0)



Scheme 1 Preparation of dithiane-based NBS signaling probes **1** and **2**.

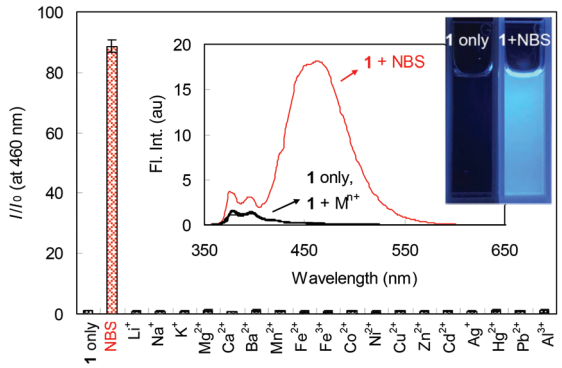
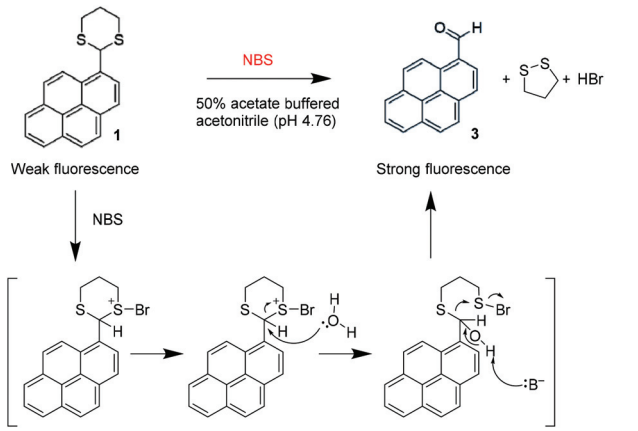


Fig. 2 NBS-selective signaling of probe **1** expressed by the fluorescence intensity ratio (I/I_0) at 460 nm. Inset shows the changes in fluorescence spectrum of the probe in the presence of NBS or metal ions. [**1**] = 5.0×10^{-6} M, [NBS] = [M^{n+}] = 5.0×10^{-5} M, [EDTA] = 1.0×10^{-4} M in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). λ_{ex} = 340 nm.



Scheme 2 Proposed mechanism for fluorescent NBS signaling by dithiane protected 1-pyrenecarboxaldehyde **1**.

of the probe at 460 nm was nearly constant, changing between 0.96 for fluoride and 1.04 for iodide ions (Fig. S4, ESI†).

Accurate determination of an analyte is frequently hampered by the presence of interfering species that exhibit cross-responses. Therefore, NBS signaling of probe **1** was measured in the presence of probable competing species in the analytes as a background. The fluorescence intensity changes of the probe induced by NBS measured at 460 nm in the presence of coexisting metal ions did not fluctuate more than 5% for the surveyed metal ions (Fig. 3). Results of competitive signaling experiment in the presence of anions also revealed the feasibility of the NBS-selective signaling, except for iodide,[18] HSO_3^-,[41] and sulfide ions[8] (Fig. S5, ESI†). With these redox-active ions, the NBS signal was significantly reduced because of the consumption of the NBS analyte in the relevant redox reactions. However, this situation did not pose a problem because the analysis of a target species involves the determination of the residual analytes after all the interactions and

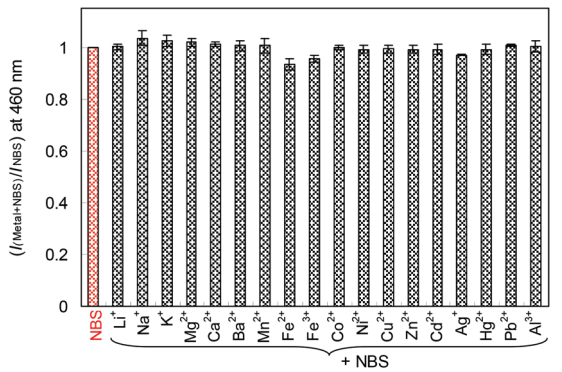


Fig. 3 NBS signaling of probe **1** in the presence of background metal ions as expressed by the fluorescence intensity ratio ($I_{(Metal+NBS)}/I_{NBS}$) at 460 nm. [**1**] = 5.0×10^{-6} M, [NBS] = [M^{n+}] = 5.0×10^{-5} M, [EDTA] = 1.0×10^{-4} M in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). λ_{ex} = 340 nm.

reactions with the matrix constituents have occurred. The other tested anions showed no noticeable interferences. In addition, representative aromatic halides (chlorobenzene, bromobenzene, and iodobenzene) also did not induce any measurable interferences (Fig. S6, ESI†). These results clearly showed that probe **1** could be applied for the determination of NBS in the presence of common metal ions, anions, or organic halides as a background in routine chemical and analytical applications.

NBS signaling of probe **1** was realized by the selective deprotection of the 1,3-dithiane functionality of the probe to yield its parent compound aldehyde **3** (Scheme 2). It was postulated that the reaction mechanism involved an attack of dithiane on the electrophilic bromine (Br^+) from NBS to form a bromosulfonium intermediate, which subsequently reacted with a water molecule to afford 1-pyrenecarboxaldehyde. This mechanism has been previously proposed for the NBS-assisted deprotection of dithianes to obtain aryl carboxaldehydes and ketones.[42] The suggested deprotection was confirmed by NMR and mass spectra. For this evidence, the NBS signaling product of the probe was purified by column chromatography (silica gel, dichloromethane). ^{1}H NMR spectrum of the purified signaling product was found to be identical to that of a reference compound 1-pyrenecarboxaldehyde **3** (Fig. 4). Among the various spectral changes, the disappearance of the singlet resonance of the dithiane methine proton at 6.23 ppm (marked by a blue asterisk) and appearance of a characteristic aldehydic proton resonance at 10.68 ppm (marked by a red asterisk) were diagnostic. The electron ionization mass spectrum also confirmed the suggested transformation as a peak was observed for aldehyde **3** at m/z = 229.7 (calcd for $C_{17}H_{10}O$, 230.07) (Fig. S7, ESI†).

NBS signaling of probe **1** was very fast, and the fluorescence response was saturated immediately after the preparation of the measurement solution (Fig. 5). On the other hand, the probe itself was stable and induced no quantifiable responses under the measurement conditions. Meanwhile, the fluorescence signaling of naphthalene-based probe **2** toward NBS

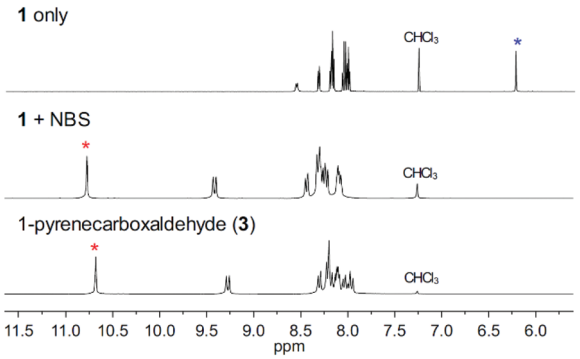


Fig. 4 Partial ^{1}H NMR spectra of probe **1**, **1** + NBS, and a reference compound 1-pyrenecarboxaldehyde (**3**) in $CDCl_3$. Resonances marked by blue and red asterisks were owing to the dithiane methine proton and the aldehydic proton, respectively.

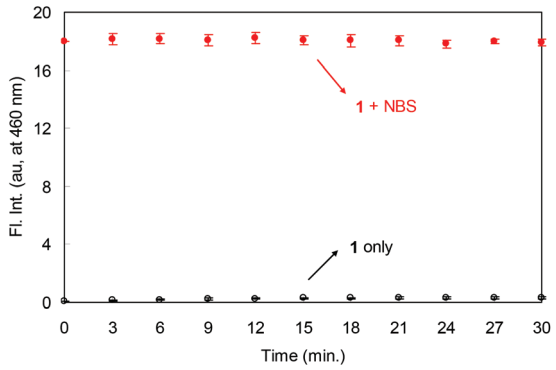


Fig. 5 Time-course plot of NBS signaling by probe **1** expressed by the fluorescence intensity change at 460 nm. [**1**] = 5.0 × 10^{-6} M, [NBS] = 5.0 × 10^{-5} M, [EDTA] = 1.0 × 10^{-4} M in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). λ_{ex} = 340 nm.

was also observed immediately after the preparation of the measurement solution; however, the developed signal was not maintained over time (Fig. S8, ESI†). We were able to confirm that the gradual decay of the signal was because of the instability of 6-methoxy-2-naphthaldehyde, the expected NBS signaling product of **2**, in the presence of the remaining reactive NBS.

The effect of pH on the signaling response was studied and revealed that the NBS signal of probe **1** was not influenced by the solution pH over the entire surveyed pH range of 4.8–10.5 (Fig. S9, ESI†). Meanwhile, the observed pH profile of the fluorescence change of probe **1** for NBS was found to be nearly identical to that of the reference compound **3**, which was the expected signaling product. Under the experimental conditions of pH ranging from 4.8 to 10.5, probe **1** itself experienced no detectable spectral variations. Quantitative behavior of NBS analysis by the probe was assessed by fluorescence titration (Fig. 6). The plot of the fluorescence response at 460 nm as a function of NBS concentration showed a linear relationship for up to 1.0 × 10^{-5} M of NBS. From this plot, the detection limit of probe **1** for NBS determination was estimated as 5.6 × 10^{-8} M (10.0 ppb) by IUPAC guidelines ($3s_{bl}/m$) (Fig. S10, ESI†).[36]

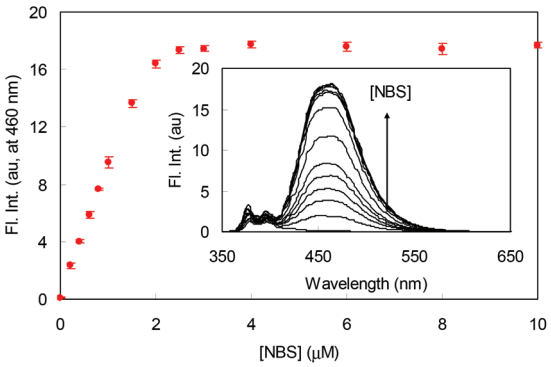


Fig. 6 Concentration-dependent fluorescence signaling of NBS by probe **1**. Inset: Changes in fluorescence spectra of the probe. [**1**] = 5.0 × 10^{-6} M, [NBS] = 0–5.0 × 10^{-5} M, [EDTA] = 1.0 × 10^{-4} M in a mixture of an acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v). λ_{ex} = 340 nm.

The developed system was then used for rapid and convenient analysis of NBS using a smartphone as a stand-alone device without the help of other laboratory instruments. First, varying concentrations of NBS in 50% acetate buffered solution were prepared. After the addition of probe **1** to each sample, the images of the fluorescent solutions were captured by a smartphone in a handmade dark box under illumination with a portable 365 nm LED bar. Next, the obtained images were analyzed with a smartphone-embedded application by plotting the red, green, and blue channel levels as a function of NBS concentration (Fig. S11, ESI†). Among these channels, the plot of the blue channel level with [NBS] afforded the most pronounced result and showed a good linear relationship up to 5.0 × 10^{-6} M of NBS (R^2 = 0.9960) (Fig. 7). From this plot, the detection limit of probe **1** for NBS determination by means of a smartphone was estimated as 2.4 × 10^{-7} M (42.7 ppb) following the IUPAC guidelines ($3s_{bl}/m$).[36]

Finally, as a practical application of the developed system, commercial NBS reagents were assayed. We tested one used laboratory stock and one freshly opened NBS reagents as ana-

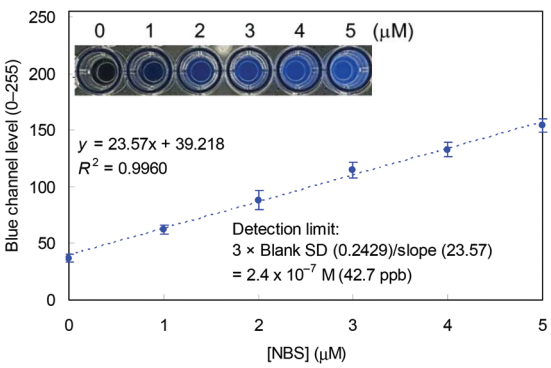


Fig. 7 Changes in the blue channel level of signaling images as a function of [NBS] obtained using a smartphone. [**1**] = 5.0 × 10^{-6} M, [NBS] = 0–5.0 × 10^{-6} M, [EDTA] = 1.0 × 10^{-4} M in a mixture of acetate buffer (pH 4.76, 20 mM) and acetonitrile (1 : 1, v/v).

Table 1 Assay of the commercial NBS reagents with probe **1** and iodometric titration

Sample	Determined by probe **1**	Iodometric titration[a]	Relative error (%)
Laboratory used NBS	97.1 ± 0.5%	96.7 ± 0.7%	0.4%
Freshly opened NBS	97.2 ± 0.3%	97.4 ± 0.4%	−0.2%

[a] Determined by the iodometric titration.[17] Reported values are given as mean ± standard deviation, $n = 3$.

lytes. The commercial NBS reagents were first standardized using the iodometric titration method.[17] As shown in Table 1, the amount of NBS determined using probe **1** agreed well with the results of iodometric titration (relative error = ±0.4%). These results implied that the developed probe could be successfully utilized as a fast and convenient assay for commercial NBS reagents.

4. Conclusions

A novel reaction-based probe was developed for the determination of NBS, a synthetically and analytically important compound. Signaling was realized by the oxidative deprotection of dithiane-protected 1-pyrenecarboxaldehyde with NBS. Using the probe, selective signaling toward NBS was possible in the presence of other commonly encountered metal ions and anions as well as organic halides. Furthermore, signaling was possible over a wide pH range of 4.8–10.5. The detection limit of the probe for NBS was found to be 5.6×10^{-8} M (10.0 ppb). Rapid and convenient NBS signaling was confirmed by a smartphone as a stand-alone device and assays of commercial reagents were conducted successfully using the developed probe.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

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Notes and references

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