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Signaling of chloramine: a fluorescent probe for trichloroisocyanuric acid based on deoximation of a coumarin oxime

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ABSTRACT

A new chloramine signaling probe, based on a coumarin oxime, was developed. The coumarin oxime **1** exhibited efficient off–on type fluorescent signaling behavior toward trichloroisocyanuric acid (TCCA) in an aqueous acetonitrile solution. The signaling is due to the TCCA-assisted transformation of the oxime function to its carbonyl analogue. The presence of common metal ions and anions did not interfere with the TCCA signaling of this probe. Probe **1** was found to be useful for the sensitive determination of the concentration of the practical oxidant TCCA in an aqueous environment, with a detection limit of 7.58×10^{-7} M.

Chloramines are inorganic or organic nitrogen compounds, which contain one or more chlorine atoms attached to the nitrogen atoms. They are inexpensive, stable in aqueous solution, and environmentally benign oxidants that are broadly used both in daily life and for industrial applications.[1] Because they are easier to handle than chlorine gas or metal hypochlorites, they are widely used in the purification of drinking water and as sanitizing agents in swimming pools.[2] Chloramines are also commonly used in synthetic reactions.[3,4] The usefulness of chloramines arises from the fact that they behave as a source of both a halonium ion and various nitrogen-containing species.[5] As a result, these reagents can react with a wide range of functional groups, leading to a number of molecular transformations such as chlorination of alkenes and aromatics, oxidation of ethers and alcohols, epoxidation of alkenes, and nitrosation of amines.[6] In organic syntheses, hypochlorites could also be substituted with *N*-chloramines, especially when anhydrous conditions are necessary. Among the organic chloramines, in particular, trichloroisocyanuric acid (TCCA) and sodium *N*-chloro-*p*-toluenesulfonamide (chloramine-T) have become increasingly important.

Chloramines have commonly been analyzed by titrimetry using iodide, amperometry, and flow-injection analysis.[7] Specific analytical methods such as HPLC, GC, and mass spectrometry have also been used for these oxidants.[8] The colorimetric method using *N*,*N*-diethyl-*p*-phenylenediamine (DPD) is one of the more commonly used techniques for the analysis of chlorine in water.[9] However, we could not find any literature on the use of fluorescent signaling approach for analyzing chloramines.

Reaction-based probes have attracted much research interest recently due to their specificity and cumulative signaling advantages.[10] In particular, there are noticeable achievements in the signaling or visualizing of biologically important reactive oxygen or nitrogen species, such as hydrogen peroxide, peroxynitrite, and hypochlorous acid.[11] However, optical probes for practical oxidants such as peracids and chloramines are not reported often in spite of their importance in a variety of industrial applications. We have developed a series of reaction-based optical probes for the determination of these practical oxidants, using desulfurization of thioamides for peracetic acid and oxone, thiocoumarin for mCPBA, as well as oxidative hydrolysis of phenolic acetate for perborates.[12]

Protection of carbonyl functions by converting them to oximes is one of the most useful tactics in organic synthesis.[13] In this case, deprotection of oximes to form carbonyls could be effected by a variety of oxidation and reduction reactions.[14] Recently, a broad range of *N*-halosulfonamides has been reported for the regeneration of carbonyl compounds from oximes (Scheme 1).[15] We devised a new reaction-based probe for the convenient determination of practical oxidant chloramines by using the oxime-carbonyl transformation. The oxime derivative of ethoxycoumarin exhibited a pronouncedly sensitive fluorogenic signaling behavior toward the industrially important chloramine TCCA in aqueous acetonitrile solution.

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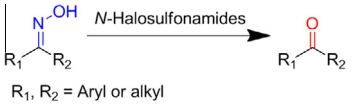
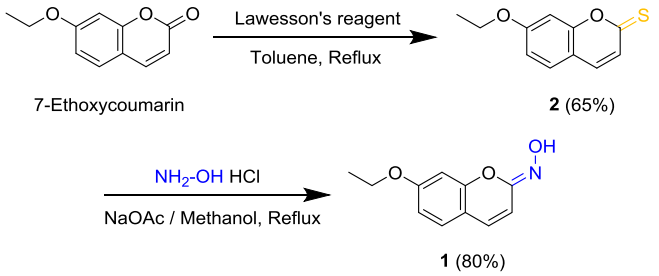


Scheme 1. Deprotection of oximes with *N*-halosulfonamides.

Probe **1** for chloramine signaling was prepared by a two-step reaction from 7-ethoxycoumarin (Scheme 2). Thionation of 7-ethoxycoumarin with Lawesson's reagent yielded thiocoumarin **2** (toluene, 65%).[12c] Reaction of thiocoumarin **2** with hydroxylamine produced the desired 7-ethoxycoumarin oxime **1** (NH_2OH, EtOH, 80%).[16] We tried to prepare more chromogenic coumarin derivatives having dialkylamino (coumarin 334) or benzothiazole substituents (coumarin 6), but the stability of the parent dyes under the oxidative stress of the chloramine under consideration here was inadequate.

Probe **1** exhibited an absorption band at 325 nm in 90% aqueous acetonitrile solution, phosphate buffered at pH 8.0, which is similar to that of 7-ethoxycoumarin (λ_{max} = 323 nm). On the other hand, probe **1** showed weak fluorescence due to the quenching effect of the oxime group under the same conditions.[17] We surveyed the preliminary fluorescent signaling behavior of probe **1** toward a series of practical oxidants, such as hydrogen peroxide, *tert*-butyl hydrogen peroxide (TBHP), perborate, peracetic acid (PAA), and the chloramine TCCA (Fig. 1 and Fig. S1, Supplementary data). Among the tested oxidants, only TCCA and HOCl showed prominent signaling under the measurement conditions. The fluorescence enhancements I/I_0 observed at 392 nm were 105-fold for TCCA and 102-fold for HOCl. The colorimetric or fluorescent signaling of HOCl, due to the deoximation of oxime derivatives of various substances (such as BODIPY and phenanthroimidazole dye) to their carbonyl groups, have already been reported.[18] Peracetic acid also showed a considerable response (I/I_0 = 11.8). Other commonly used oxidants, such as hydrogen peroxide, TBHP, perborate, percarbonate, and superoxide, showed negligible signaling: the ratio I/I_0 varied between 0.79 for TBHP and 1.69 for perborate. The significant response toward HOCl in the selective TCCA signaling by **1** might not be a practical problem, because TCCA is generally used as a single component oxidant in many applications. We tried to obtain a signaling condition that could differentiate TCCA from HOCl, but failed. That can be ascribed to the fact that the TCCA in aqueous solution in situ generates HOCl as an active oxidant.[19] Meanwhile, the UV–vis absorption behavior of compound **1** was not useful for the determination of TCCA, because TCCA did not induce any diagnostic changes in the spectral properties of **1** (Fig. S2, Supplementary data).

The signaling is due to the oxidative transformation of the oxime moiety of **1** to a coumarin carbonyl function (Scheme 3).[20] The ^{1}H NMR spectrum of the purified reaction product, obtained by treatment of **1** with TCCA, was identical to those of ethoxycoumarin (Fig. 2). In the ^{1}H NMR spectrum, the resonances for



Scheme 2. Preparation of probe **1** for chloramine signaling.

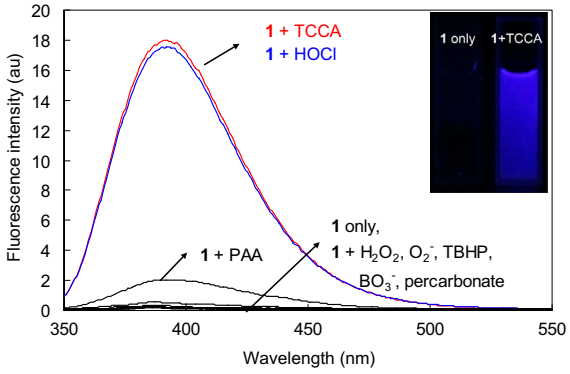
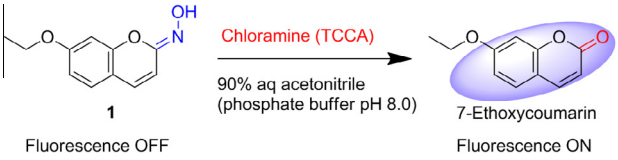


Figure 1. Fluorescence spectra of **1** in the presence of practical oxidants. Inset: fluorescence image of **1** in the absence and presence of TCCA. The spectra were recorded in a mixture of CH_3CN and phosphate buffer solution (pH 8.0, 10 mM), (1:9, v/v). [**1**] = 5.0×10^{-6} M, [oxidant] = 5.0×10^{-5} M. λ_{ex} = 325 nm. PAA: peracetic acid, TBHP: *tert*-butyl hydrogen peroxide.



Scheme 3. Signaling of chloramine by probe **1**.

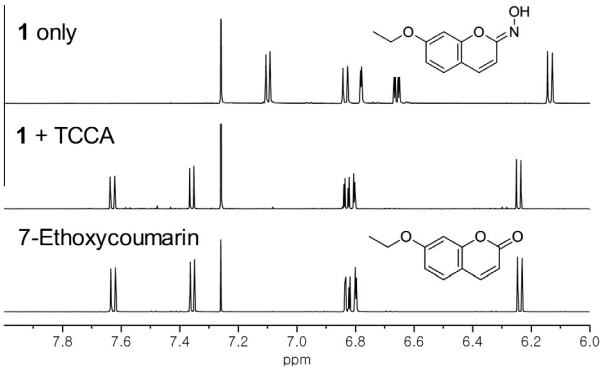


Figure 2. Partial ^{1}H NMR spectra of **1** in the absence and presence of TCCA, and 7-ethoxycoumarin. [**1**] = [7-ethoxycoumarin] = 15 mM and [TCCA] = 6 mM in $CDCl_3$. Middle spectrum (**1** + TCCA) was obtained after purification by column chromatography.

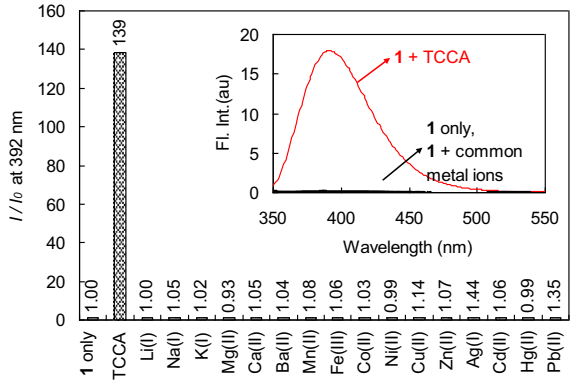


Figure 3. Fluorescence intensity ratio I/I_0 at 392 nm of **1** + TCCA and **1** in the presence of various metal ions. [**1**] = 5.0×10^{-6} M, [TCCA] = [M^{n+}] = 5.0×10^{-5} M. In a mixture of CH_3CN and phosphate buffer solution (pH 8.0, 10 mM), (1:9, v/v). λ_{ex} = 325 nm.