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A fluorescent probe for the determination of Ce^{4+} in aqueous media

Liang Huang [a], Yong Liu [b], Cai Ma [a], Pinxian Xi [a,*], Wei Kou [b], Zhengzhi Zeng [a,*]

[a] Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, State Key Laboratory of Applied Organic Chemistry and College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, PR China
[b] Medical College of Northwest University for Nationalities, Lanzhou 730030, PR China

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ABSTRACT

A rhodamine-based probe bearing an N,N-dimethylaniline unit was developed as a fluorescent chemodosimeter for Ce^{4+} in aqueous media. Importantly, the sensor can selectively respond to Ce^{4+} over other commonly coexistent metal ions (such as La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Er^{3+}, Tb^{3+}, Ho^{3+}, Tm^{3+}, Yb^{3+}, Lu^{3+}, Y^{3+}) in aqueous media with a rapid response time. The system, which utilizes an irreversible Ce^{4+}-promoted oxidation reaction, responds instantaneously at room temperature with linear proportionality to the amount of Ce^{4+}.

1. Introduction

Recently, the design and synthesis of fluorescent sensors for metal ions has attracted considerable attention. A large amount of work has been undertaken on the development on the development of fluorescent probes for alkali/alkaline earth/transition metal ions due to their importance in many biological and environmental processes [1]. In this regard, reports on the sensing and detection of different lanthanide ions are relatively scarce despite of their well-known involvement in biological/therapeutic/imaging processes and catalytic reactions [2,3]. Cerium ion has an ionic radius similar to that of a calcium ion and which generally has a higher affinity for Ca^{2+} binding sites present in biological molecules because of its higher charge. Moreover, Ce^{4+} represents the most notable oxidant among lanthanide ions which could react with various biomolecules including proteins, fatty acids, RNA and DNA. While Ce^{4+} has strong antibacterial properties, excess amounts of Ce^{4+} can also cause serious damage to biological systems [4]. To the best of our knowledge, no work on fluorescent probe for Ce^{4+} has previously been reported. Therefore, the development of highly selective and sensitive turn-on fluorescent probes for monitoring Ce^{4+} still remains a significant challenge.

It is known that CAN (Ceric ammonium nitrate) promotes an irreversible oxidative cyclization of the originally N-acylhydrazones into 1,3,4-oxadiazoles in mild conditions [5], (Scheme 1) and rhodamines undergo a great fluorescence enhancement via their structure change from spirocyclic (nonfluorescent and colorless) to ring-open (fluorescent and pink) states induced by specific chemical environments at room temperature [6]. We envisioned that this irreversible N-acylhydrazone reaction could be incorporated into the rhodamine hydrazone system and become involved in the conversion from the nonfluorescent spirocyclic form to the fluorescent ring-opened one.

2. Experiment procedure

^1H and ^{13}C NMR spectra were taken on a Varian mercury-400 spectrometer with TMS as an internal standard and $CDCl_3$, DMSO as solvent. Absorption spectra were determined on a Varian UV-Cary100 spectrophotometer. Fluorescence spectra measurements were performed on a Hitachi F-4500 spectrofluorimeter. All pH measurements were made with a pH-10C digital pH meter. HRMS were determined on a Bruker Daltonics APEXII 47e FT-ICR spectrometer.

All the materials for synthesis were purchased from commercial suppliers and used without further purification. Methanol for spectra detection was HPLC reagent without fluorescent impurities.

Stock solutions of the metal ions (2.5×10^{-3} mol L^{-1}) were prepared in deionized water. A stock solution of **L1**

* Corresponding authors. Tel./fax: +86 931 8912582.
E-mail addresses: xipx@lzu.edu.cn (P. Xi), zengzhzh@yahoo.com.cn (Z. Zeng).

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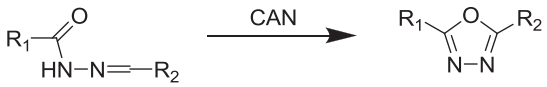


Scheme 1. Oxidative cyclization of N-acylhydrazones by CAN.

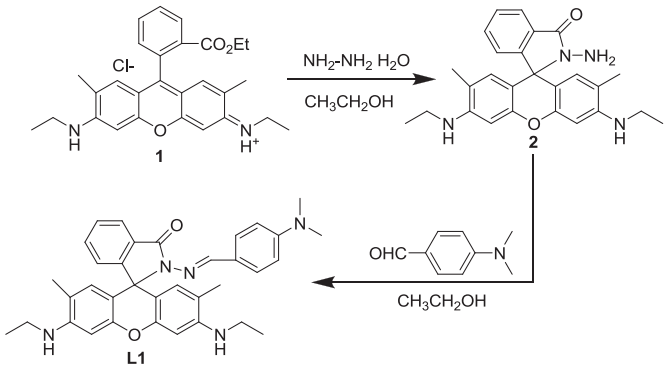
(1×10^{-3} mol L^{-1}) was prepared in DMF: CH_3CN (1:1 v/v). The solution of **L1** was then diluted to 2×10^{-5} mol L^{-1} with water/CH_3CN (1:1 v/v). In titration experiments, each time a 2×10^{-3} L solution of **L1** (2×10^{-5} mol L^{-1}) was filled in a quartz optical cell of 1 cm optical path length, and the Ce^{4+} stock solution was added into the quartz optical cell gradually by using a micro-pippet. Spectral data were recorded at 2 min after the addition. In selectivity experiments, the test samples were prepared by placing appropriate amounts of metal ion stock into 2 mL solution of **L1** (2×10^{-5} mol L^{-1}). For fluorescence measurements, excitation was provided at 500 nm, and emission was collected from 510 to 650 nm.

2.1. Synthesis of compound *L1* and *RG*

Compound **2** was synthesized by an improved method according to the literature [1g].

Compound **L1**. Rhodamine 6G hydrazide (0.214 g 0.5 mmol) and 4-(dimethylamino)benzaldehyde (0.075 g, 0.5 mmol) were mixed in boiling ethanol (60 mL) with 3 drops of acetic acid (Scheme 2). After heating under reflux for 16 h, the reaction mixture was cooled and half of the volume of the solvent was removed under reduced pressure. The yellow precipitate was collected by filtration, washed with ethanol/ether (1:1) and dried over P_2O_5 under vacuum. Yield: 67%. ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 8.27 (s, 1H), 7.98–8.02 (t, 1H), 7.38–7.45 (t, 4H), 7.01–7.05 (p, 1H), 6.52–6.57 (d, 2H, $J = 8.6$), 6.36–6.38 (d, 4H, $J = 4.2$), 3.14–3.24 (p, 4H, $J = 7.2$), 2.91 (s, 6H), 1.84 (s, 6H), 1.27–1.34 (t, 6H, $J = 7$ Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm): 164.78, 152.35, 151.43, 151.10, 147.53, 147.39, 132.96, 129.01, 128.93, 127.69, 123.46, 123.16, 123.06, 117.89, 111.42, 106.55, 96.71, 65.65, 40.17, 38.32, 16.64, 14.73. ESI-MS m/z = 560.3 $[M + H]^+$, calc. for $C_{35}H_{37}N_5O_2$ = 559.29. Elemental Analysis. Found (calculated) for $C_{35}H_{37}N_5O_2$ (%): C, 74.75 (75.11); H, 6.58 (6.66); N, 12.38 (12.51).

Compound **RG**. To a solution of **L1** (34 mg, 0.06 mmol) in CH_3CN (30 mL)/DMF (2 mL) was added CAN (187 mg, 0.36 mmol). Then the reaction mixture was stirred at room temperature for 3 h. After the solvent was evaporated under reduced pressure, the crude product was column chromatographed on silica-gel (CH_2Cl_2/MeOH = 5:1, v/v) to give the 18 mg of rhodamine 19 (72%) as a red solid. ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 7.95–7.97 (d, 1H, $J = 7.6$ Hz), 7.66–7.77 (m, 2H), 7.17–7.19 (d, 1H, $J = 7.6$ Hz), 6.21–6.32 (ss, 4H), 3.12–3.19 (m, 4H), 1.89 (s, 6H), 1.18–1.22 (t, 6H, $J = 7.2$ Hz), ^{13}C NMR (DMSO-d6, 100 MHz) δ (ppm): 169.05, 152.76, 150.95, 148.55, 135.25, 129.70, 127.77, 126.78, 124.43, 124.03, 118.46, 104.76, 95.18, 37.40, 17.03, 14.08.



Scheme 2. Synthesis of compound **L1**.

3. Results and discussions

Herein, we report a new rhodamine derivative (**L1**) bearing an N,N-dimethylaniline unit, which has been demonstrated to be a chemodosimeter for Ce^{4+}. The rhodamine derivative **L1** was prepared in high yield from Rhodamine 6G by using a two-step procedure. The structure of **L1** was confirmed by ^{1}H NMR, ^{13}C NMR, MS data and X-ray analysis (Figs. S6 and S7). The single crystal of **L1** was grown in dichloromethane and acetonitrile solutions, and a unique spirolactam structure ring formation was observed (Fig. 1).

The solution of **L1** in aqueous media is colorless and weakly fluorescent, indicating that the spirolactam form of **L1** exists predominantly. Spectrophotometric titrations for **L1** with varying pH revealed that **L1** retained the spirocyclic form within the pH range of 5.0–12.0. As we expected, addition of CAN to the solution of **L1** in CH_3CN/water (1:1, v/v) at pH 5–10 caused an immediate and significant enhancement of fluorescence intensity in the 510–650 nm range (Fig. S2). This observation indicates that the CAN-induced oxidation of **L1** could take place in a wide pH range at room temperature.

To explore the mechanism, the mixtures of **L1** with CAN in CH_3CN/water (1:1, v/v) were detected by the ESI mass spectrum analysis. The peak at m/z 558.5 corresponding to $[\mathbf{RG1}+\mathbf{1}]^+$ was observed in the ESI mass spectrum of **L1** with 20 equiv CAN in the CH_3CN/water (1:1, v/v) solution. The peak at m/z 415.4 assigned to $[\mathbf{RG}+\mathbf{1}]^+$ was also observed under the same condition. After addition of 40 equiv CAN, **L1** almost completely converted to **RG** (Figs. S10 and S11). We then attempted to isolate the reaction product of the probe **L1** and Ce^{4+} ions. Unfortunately only product **RG** could be isolated from chromatograph on silica-gel (Figs. S8 and S9). From the molecular structure, NMR and mass spectral results of **L1** with CAN, it is concluded that the addition of the CAN induced an oxidative cyclization to form product **RG1**, and then further promoted oxidation of the compound to the brilliant pink and highly fluorescent Rhodamine 6G (**RG**) in the CH_3CN/water (1:1, v/v) solution (Scheme 3b). This result was also supported by Evans et al., (Scheme 3a) [7].

The UV–vis absorption spectrum of **L1** (10 μM) in CH_3CN/water (1:1, v/v) exhibited only a very weak band above 500 nm, which are attributed to the trace ring-opened form of molecules of **L1**. The

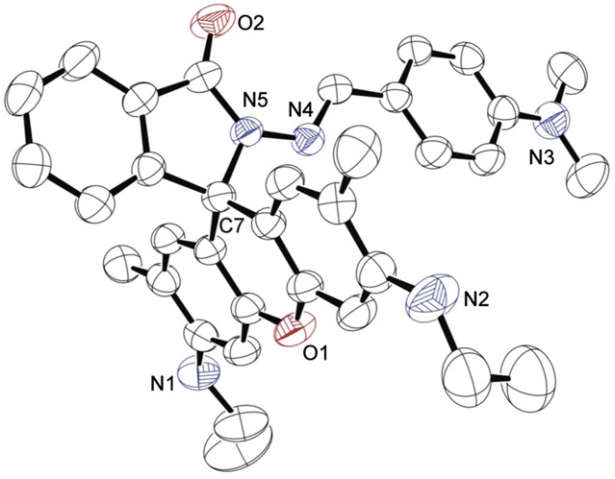
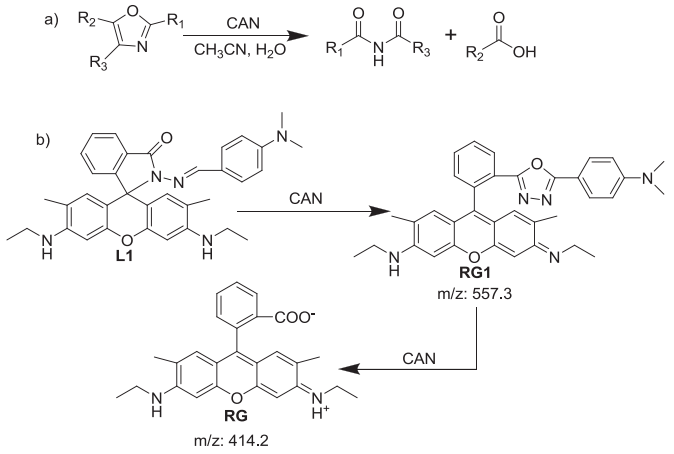


Fig. 1. ORTEP diagram of the compound **L1** (50% probability level for the thermal ellipsoids).



Scheme 3. CAN-Induced Oxidation of Fluorescent Probe **L1**.

characteristic peak for C_7-atom at $\delta = 65.65$ ppm in the ^{13}C NMR spectrum of **L1** also confirms this conclusion (Fig. S7). Upon the addition of up to 40 equiv of CAN, a new strong absorption band centered at 528 nm was formed and led to the color change from colorless to pink. This indicated that the opened-ring form of **L1** became the main species in the examined solution. Other rare earth ions, such as La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Er^{3+}, Tb^{3+}, Ho^{3+}, Tm^{3+}, Yb^{3+}, Lu^{3+}, Y^{3+}, did not show any significant color and spectral change under identical conditions (Fig. 2). The emission spectra were also recorded under the same conditions. On addition and gradual increase of [CAN] to the nonfluorescent CH_3CN/water (1:1, v/v) solution of **L1**, a significant enhancement in fluorescence intensity at 554 nm was observed following excitation at 500 nm, and the emission quantum yield (Φ) was found to be 0.25 (Fig. 3). From the Ce^{4+} concentration-dependent fluorescence changes, the

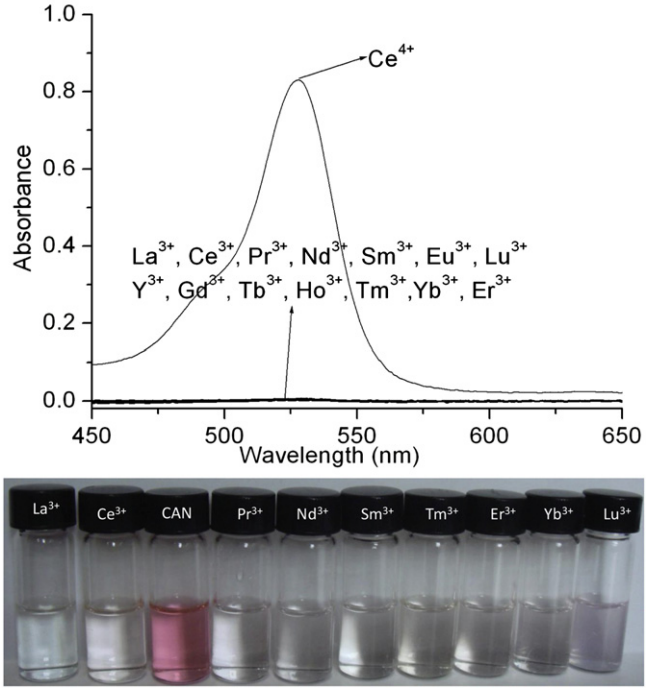


Fig. 2. Changes in the absorption spectra of **L1** (10 μM) in the presence of different metal ions (400 μM) in CH_3CN/water (1:1, v/v). Bottom: Photos of color changes of **L1** (10 μM) upon addition of 400 μM different metal ions in CH_3CN/water (1:1, v/v) solution.

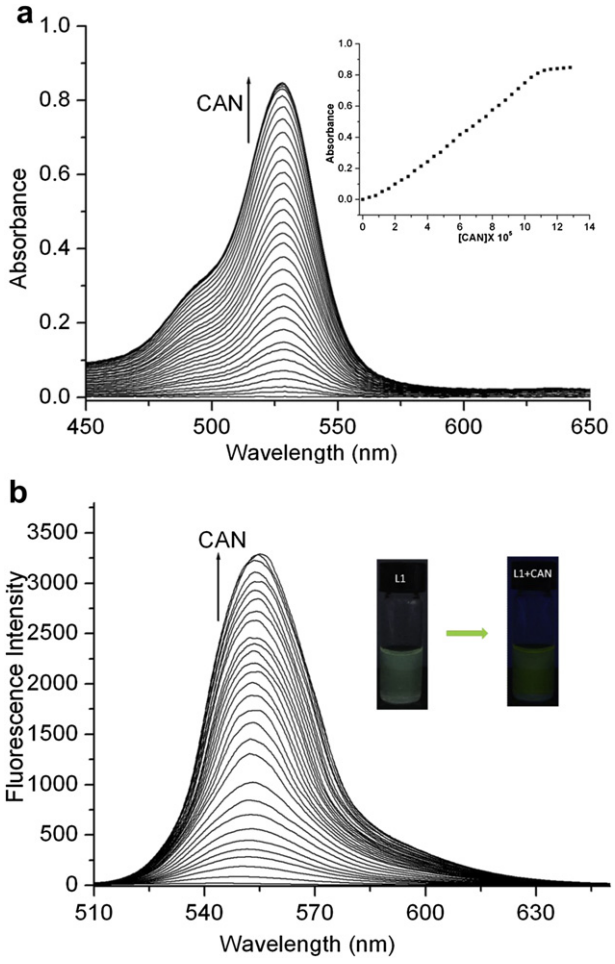


Fig. 3. (a) Absorption spectra of **L1** (10 μM) in CH_3CN/water (1:1, v/v) in the presence of different amounts of CAN (0–40 equiv). Inset: absorbance at 529 nm as a function of CAN concentration. (b) Fluorescence spectra of **L1** (10 μM) in CH_3CN/water (1:1, v/v) upon addition of CAN (0–40 equiv). ($\lambda_{ex} = 500$ nm).

detection limit of **L1** for the determination of Ce^{4+} was estimated to be 8×10^{-5} M in CH_3CN/water (1:1, v/v) solution.

To eliminate the influence of the acidic NH_4NO_3, fluorescence titration of **L1** (10 μM) with NH_4NO_3 was investigated in CH_3CN/water (1:1, v/v) solution. As shown in Fig. S5, the solution didn't display any fluorescence change upon addition of 40 equiv NH_4NO_3. Therefore, the fluorescence changes of **L1** with CAN are mainly attributed to Ce^{4+} ion.

An important feature of the chemodosimeter is its high selectivity toward the analyte over other competitive species. The fluorescence responses of **L1** (10 μM) to other rare earth ions were examined in CH_3CN/water (1:1, v/v) solution. Upon addition of 40 equiv metal ions (La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Er^{3+}, Tb^{3+}, Ho^{3+}, Tm^{3+}, Yb^{3+}, Lu^{3+}, Y^{3+}), no significant fluorescence intensity changes were observed (Fig. S3). Only the Ce^{4+} led to a prominent enhancement in fluorescence intensity, and the fluorescence intensity changes caused by the addition of Ce^{4+} were not influenced by the presence of other rare earth ions (Fig. 4). All of these results suggest the high selectivity of **L1** for Ce^{4+} over other competing cations in CH_3CN/water (1:1, v/v) solution.

As a sensor demonstration of a real-time determination was necessary. We next investigated the time evolution of the responses of **L1** (10 μM) in the presence of 40 equiv of Ce^{4+} in CH_3CN/water (1:1, v/v) solution. We found that the interaction of **L1**

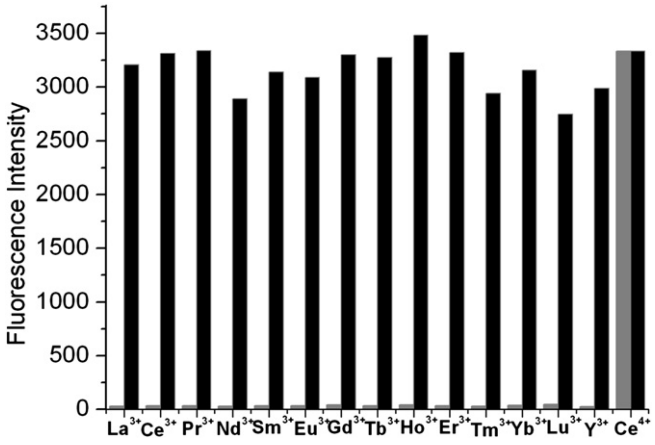


Fig. 4. Fluorescence intensities of 10 μm **L1** upon the addition of various metal ions in CH_3CN/water (1:1, v/v) solution. Gray bars represent the fluorescence response of **L1** to the metal ion of interest (400 μm). Black bars represent the addition of CAN (400 μm) to the foregoing solution. (λ_{ex} = 500 nm).

with Ce^{4+} was completed in less than 5 min. Therefore, chemodosimeter **L1** was a sensitive sensor and could be used in the real-time determination of Ce^{4+} in environmental analysis (Fig. S4).

4. Summary

In summary, a fluorescence sensing system for Ce^{4+} has been developed for the first time based on a metal-catalyzed oxidative reaction. The rhodamine-derived probe undergoes an oxidative cyclization and a concomitant oxidative ring opening upon reaction with the CAN, resulting in both colour and fluorescence evolution. In addition, the new fluorescent sensor showed an excellent selectivity for Ce^{4+} over other rare earth ions examined in CH_3CN/water (1:1, v/v) solution. This work provides a basis for the development of an efficient fluorescent sensing system for Ce^{4+} in the aqueous solution.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.dyepig.2011.07.001.

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