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# A highly sensitive and selective fluorescent probe for trivalent aluminum ion based on rhodamine derivative in living cells

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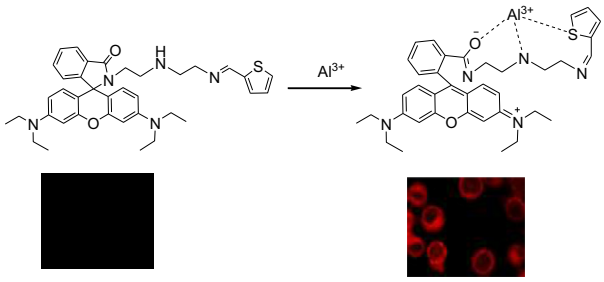
## HIGHLIGHTS

- A rhodamine derivative is used as a colormetric and fluorescent chemosensor for $Al^{3+}$.
- The chemosensor exhibits a highly sensitive response with a 70-fold enhancement.
- The chemosensor exhibits a high selectivity for $Al^{3+}$ over other metal ions.
- The chemosensor has been used in water samples and living cells successfully.

## GRAPHICAL ABSTRACT

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## ABSTRACT

A rhodamine spirolactam derivative (**1**) is developed as a colormetric and fluorescent probe for trivalent aluminum ions ($Al^{3+}$). It exhibits a highly sensitive "turn-on" fluorescent response toward $Al^{3+}$ with a 70-fold fluorescence intensity enhancement under 2 equiv. of $Al^{3+}$ added. The probe can be applied to the quantification of $Al^{3+}$ with a linear range covering from $5.0 \times 10^{-7}$ to $2.0 \times 10^{-5}$ M and a detection limit of $4.0 \times 10^{-8}$ M. Most importantly, the fluorescence changes of the probe are remarkably specific for $Al^{3+}$ in the presence of other metal ions, which meet the selective requirements for practical application. Moreover, the experiment results show that the response behavior of **1** towards $Al^{3+}$ is pH independent in neutral condition (pH 6.0–8.0) and the response of the probe is fast (response time less than 3 min). In addition, the proposed probe has been used to detect $Al^{3+}$ in water samples and image $Al^{3+}$ in living cells with satisfying results.



## 1. Introduction

Aluminum is the most abundant (8.3% by weight) metallic element and the third most abundant of all elements in the earth's crust [1,2]. The leaching of aluminum from soil by acid rain increases the free $Al^{3+}$ in the environment and surface water, which is deadly to growing plants [3,4]. And its toxicity causes microcytic hypochromic anemia, Al-related bone disease (ARBD), encephalopathy and neuronal disorder that will lead to dementia, myopathy and Alzheimer's disease [5,6]. Due to the potential impact of aluminum ions ($Al^{3+}$) on the environment and human health, the effective detection of $Al^{3+}$ ions is needed.

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Fluorescent probes have attracted considerable interest due to their high sensitivity, selectivity, rapid response rate and simple manipulation [7–9]. So far, some fluorescent probes have been developed for detection of $Al^{3+}$ [10–27]. However, most of them suffer from some limits, such as short emission wavelength [10–13], poor selectivity [10–26], being unsuitable for the applications of biological systems [11–19,27] (Table 1). So the probes for $Al^{3+}$ with excellent performance are still urgently needed.

Rhodamine dyes have recently attracted much attention in fluorescence sensing and bioimaging due to their excellent photophysical properties, such as high fluorescence quantum yield, visible absorption and fluorescence emission [28,29]. As we know, the rhodamine with spirolactam structure is colorless and non-fluorescent, whereas ring-opening of the spirolactam induced by the analyte gives rise to pink color and a strong fluorescence emission. Actually, it is an ideal mode to construct probes. Up to now, a number of rhodamine spirolactam-based probes have been designed for metal cations including $Cu^{2+}$ [30–32], $Hg^{2+}$ [33–35], $Zn^{2+}$ [36,37], $Pb^{2+}$ [38], $Fe^{3+}$ [39], $Cr^{3+}$ [40] and conventional anions such as $CN^-$ [41], $F^-$ [42], $P_2O_7^{4-}$ [19] and $CH_3COO^-$ [43]. However, the probes for $Al^{3+}$ are rare [18,19,23–27]. Moreover, few probes have been proposed for intracellular imaging of $Al^{3+}$.

In this paper, we design and synthesize a new rhodamine-based fluorescent probe **1** for colormetric and fluorescent determination of $Al^{3+}$. Probe **1** is colorless and exhibits weak fluorescence. Binding $Al^{3+}$ to probe **1** induced ring-opening of rhodamine, which resulted in color change from colorless to pink and red strong emission. In particular, probe **1** provides excellent selectivity toward $Al^{3+}$ over other metal ions. Furthermore, probe **1** has been successfully applied in the detection and quantification of $Al^{3+}$ in water samples and used to image $Al^{3+}$ in living cells.

## 2. Experimental

### 2.1. Reagents

Twice-distilled water was used throughout all experiments. Diethylenetriamine, rhodamine B and 2-thiophenecarboxaldehyde were purchased from Sigma–Aldrich. All other chemicals were of analytical reagent grade, purchased from Shanghai Chemical Reagent Corporation (Shanghai, China), and used without further purification. Thin layer chromatography (TLC) was carried out using silica gel 60 F254, and column chromatography was conducted over silica gel (200–300 mesh), both of which were obtained from the Qingdao Ocean Chemicals (Qingdao, China).

### 2.2. Syntheses

A convenient synthetic route for compound **1** from commercially available compounds was provided and depicted in Fig. 1.

**Compound 2**: Rhodamine B (8.00 g, 16.8 mmol) and diethylenetriamine (40.0 mL, 368 mmol) were dissolved in ethanol (100 mL). The reaction mixture was stirred and refluxed for 24 h. After the solvent was evaporated under reduced pressure, the crude product was purified by silica gel column chromatography using $CH_2Cl_2/C_2H_5OH$ (10:1, v/v) as eluent to afford a pink solid product. Yield: 0.609 g (6.40%). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (d, $J$ = 8.0 Hz, 1H), 7.42 (m, 2H), 7.08 (m, 1H), 6.42 (d, $J$ = 8.0 Hz, 2H), 6.36 (s, 2H), 6.26 (d, $J$ = 8.0 Hz, 2H), 3.35-3.18 (m, 10H), 2.71 (d, $J$ = 8.0 Hz, 2H), 2.55 (t, $J$ = 8.0 Hz, 2H), 2.20 (t, J = 8.0 Hz, 2H), 1.16 (t, $J$ = 8.0 Hz, 12H). MS (TOF) m/z calcd. for $C_{32}H_{42}N_5O_2$ (M + H) 528.334, found 528.336.

**Compound 1**: Compound **2** (0.530 g, 1.00 mmol) and 2-Thiophenecarboxaldehyde (0.130 g, 1.20 mmol) were dissolved in ethanol (50.0 mL). The reaction mixture was stirred and refluxed for 12 h. After the solvent was evaporated under reduced pressure, the crude product was purified by silica gel column chromatography using $CH_2Cl_2/C_2H_5OH$ (15:1, v/v) as eluent to afford a yellow solid product. Yield: 0.250 g (40.2%). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.94 (d, $J$ = 8.0 Hz, 1H), 7.49 (s, 2H), 7.36 (m, $J$ = 8.0 Hz, 1H), 7.26 (s, 2H), 7.10 (d, $J$ = 8.0 Hz, 2H), 6.46 (d, $J$ = 8.7 Hz, 2H), 6.42 (s, 2H), 6.28 (d, $J$ = 8.5 Hz, 2H), 3.77 (t, $J$ = 9.8 Hz, 2H), 3.38-3.23 (m, 12H), 1.29 (s, 2H), 1.15 (t, $J$ = 6.5 Hz, 12H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.3, 160.4, 153.5, 153.3, 148.9, 132.6, 132.1, 131.1, 128.9, 128.2, 128.1, 127.6, 123.9, 122.7, 108.2, 105.1, 97.6, 77.5, 77.2, 76.9, 65.0, 52.3, 52.0, 47.2, 44.4, 39.2, 29.7, 12.6. MS (TOF) m/z 622.4. MS (TOF) m/z calcd. for $C_{37}H_{43}N_5O_2S$ (M + H) 622.322, found 622.321. Anal. calcd. for $C_{37}H_{43}N_5O_2S$: C, 71.47; H, 6.97; N, 11.26; O, 5.15. Found: C, 71.82; H, 6.89; N, 11.33; O, 5.04.

### 2.3. Apparatus

UV–vis absorption spectra were recorded with a Perkin Elmer Lambda 25 spectrophotometer. All fluorescence measurements

**Table 1**
The comparison of this probe with some other fluorescent probes for $Al^{3+}$.

| Probe | $\lambda_{em}$ (nm) | Operating range (μM) | Detection limit (μM) | Response time (min) | Interferents | Application |
|---|---|---|---|---|---|---|
| Ref. [10] | 400 | 1–25 | 1.06 | <3 | $Cr^{3+}$, $Co^{2+}$, $Ga^{3+}$, $In^{3+}$ | Cell image |
| Ref. [11] | 443 | —[a] | 0.1 | – | $In^{3+}$, $Cu^{2+}$ | – |
| Ref. [12] | 475 | – | 0.2 | – | $Fe^{3+}$, $Cr^{3+}$ | – |
| Ref. [13] | 460 | 1– 10 | – | – | $Pb^{2+}$, $Zn^{2+}$ | – |
| Ref. [14] | 603 | – | 0.5 | – | $Pb^{2+}$ | – |
| Ref. [15] | 557 | – | 0.5 | – | $In^{3+}$ | – |
| Ref. [16] | 665 | – | 0.12 | – | $In^{3+}$ | – |
| Ref. [17] | 531 | – | 10 | – | $Cu^{2+}$ | – |
| Ref. [18] | 552 | – | 0.86 | – | $Ga^{3+}$ | – |
| Ref. [19] | 585 | 4.0–40 | 4.0 | – | $Cr^{3+}$, $Fe^{3+}$, $Hg^{2+}$ | – |
| Ref. [20] | 510 | 0–13 | – | – | $Ga^{3+}$ | Cell image |
| Ref. [21] | 675 | 0–16 | 0.0324 | – | $Fe^{3+}$, $Cr^{3+}$ | Cell image |
| Ref. [22] | 529 | 0–1 | 0.1 | – | $Ga^{3+}$ | Cell image |
| Ref. [23] | 586 | 10–100 | 0.02 | 30 | $Hg^{2+}$ | Cell image |
| Ref. [24] | 577 | – | – | 30 | $Cr^{3+}$, $Fe^{3+}$ | – |
| Ref. [25] | 585 | 0.05–0.8 | 0.005 | 30 | $Hg^{2+}$ | Cell image |
| Ref. [26] | 530, 580 | 0.5–10 | 0.10 | <2 | $Mn^{2+}$ | Cell image |
| Ref. [27] | 584 | 0–18 | 0.0286 | – | no | – |
| This probe | 575 | 0.5–20 | 0.040 | <3 | no | Water sample, cell image |

[a] The data is not given in the literature.