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Colorimetric and fluorogenic signaling of fluoride ions by thiophosphinated dichlorofluorescein

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ABSTRACT

Highly selective chemosignaling behavior of thiophosphinated dichlorofluorescein towards fluoride ions was investigated. Prominent chromogenic and fluorescence turn-on type signaling was realized by employing fluoride-selective cleavage of the latent thiophosphinated probe in mixed aqueous media. The signaling process was confirmed by the UV–vis, fluorescence measurements as well as ^{1}H and ^{31}P NMR spectroscopy. Possible interferences from Hg^{2+} and Cu^{2+} ions were readily suppressed by using diethylenetriaminepentaacetic acid as a masking agent. With the aid of the masking agent, the probe also showed potentially useful sensing ability for the determination of fluoride ions in practical samples of tap water and simulated wastewater. The detection limit of the probe in the determination of fluoride ions was 9.8 nM.

1. Introduction

The sensitive and selective sensing of anionic species that play crucial roles in a broad range of biological, medical, and chemical processes is currently a topical scientific issue [1]. Among the numerous anions, the fluoride ion is widely used in a number of applications such as dental care [2], treatment of osteoporosis [3,4], fluoridation of water supplies [5], and even in chemical and nuclear warfare agents [6,7]. Fluoride ions are also relevant in industrial applications, in particular, in the steel and aluminum industries, and widely employed as a well-established reagent in organic synthesis [8].

Fluoride ions are routinely analyzed by absorption spectrometry, ion chromatography, and potentiometry using fluoride-selective electrodes [9]. However, optical sensing is a more attractive technique offering simplicity and easy visual detection by exploiting color or fluorescence changes. A number of unique fluoride sensors and probes exhibiting attractive optical signaling have been reported [10–12]. Fluoride-selective sensors are mainly based on hydrogen bonding interactions between fluoride and phenolic OH groups, and the NH groups of urea, thiourea, amides and pyrrole NH units [10]. The apparent drawback of the sensing strategies utilizing hydrogen bonding is the largely hampered signaling in protic solvents, and the general inability to function in aqueous environments. Although there has been extensive progress in the development of signaling techniques for this important species, the design of selective signaling systems that are adequately operative in aqueous environment is still a challenge [13,14].

The chemodosimetric approach has been particularly successful for the determination of fluoride ions in aqueous environments [15,16]. Fluoride-triggered cleavage of the Si–O bond has been effectively designed by exploiting the well-known high affinity of silicon for fluoride ions [17]. Representative probes successfully using this strategy are based on the silyl ether of phenolic dyes such as resorufin, boron-dipyrromethene, hydroxycoumarin, and hydroxynaphthalene benzothiazole [18–20]. The nucleophilic addition reaction of fluoride ions to the electron-deficient fluorophore of squaraine and fluoride-induced intramolecular cyclization to form a highly fluorescent coumarin have been reported [21,22]. On the other hand, a series of organoboron compounds exploiting the strong interaction between the boron atom and fluoride ions have also attracted interest [23].

Dimethylphosphinyl and dimethylphosphinothionyl groups have been used as side chain phenolic OH protecting groups for tyrosine in peptide synthesis [24,25]. In this case, the dimethylphosphinyl group, which is the most labile of the phosphinyl groups, is known to be readily removed by fluoride ions (Scheme 1).

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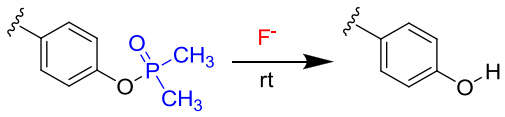

Scheme 1. Deprotection of dimethylphosphinyl group by fluoride ions.

Herein, a novel fluoride-selective probe based on the selective cleavage of thiophosphinated dichlorofluorescein is described. We recently reported the Hg^{2+}-selective signaling behavior of dimethylthiophosphinated *N*,*N*-diethylrhodol [26]. This compound was also found to be subject to fluoride-assisted hydrolysis under mild conditions. However, the fluoride-induced cleavage of the *N*,*N*-diethylrhodol derivative was too slow for a practically useful fluoride probe. After a systematic search, we found that the dichlorofluorescein analogue exhibits practically useful signaling behavior. In addition, the Hg^{2+} response of the probe was successfully removed by using a chelating agent diethylenetriaminepentaacetic acid (DTPA). Furthermore, the signaling was not significantly affected by the presence of up to 30% water, which enables the probe to detect fluoride ions in mixed aqueous media.

2. Experimental section

2.1. General

2′,7′-Dichlorofluorescein was purchased from Aldrich Chemical Co. Dimethylthiophosphinoyl chloride and 2′,7′-dichlorofluorescein sodium salt were obtained from TCI. All other chemicals and solvents were used without further purification. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were acquired on a Varian VNS spectrometer and referenced to the residual solvent signal. ^{31}P NMR spectra were recorded at 243 MHz and the chemical shifts are reported referenced to 85% phosphoric acid. UV–vis spectra were acquired using a Jasco V-550 spectrophotometer equipped with a Peltier temperature controller. Fluorescence spectra were measured by means of a PTI QuantaMaster steady state spectrofluorometer and a Scinco FluoroMate FS-2. Fourier transform infrared (FT-IR) spectra were recorded on a Thermo-Scientific Nicolet 6700 IR spectrometer. All melting points were determined on a Barnstead Electrothermal 9100 melting apparatus. Mass spectra were obtained using a Thermo Scientific Q-Exactive mass spectrometer. UV–vis and fluorescence measurements were performed using spectroscopy grade DMSO purchased from Aldrich Chemical Co. Column chromatography was carried out with silica gel (240 mesh).

2.2. Preparation of 1

2′,7′-Dichlorofluorescein (100 mg, 0.25 mmol) in dichloromethane (10 mL) was mixed with triethylamine (77 μL, 0.55 mmol) and dimethylthiophosphinoyl chloride (58 μL, 0.55 mmol). The mixture was stirred overnight at room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using dichloromethane to produce 91 mg (yield: 62%) of **1** as a white powder. m.p. 234–235 °C; IR (KBr, cm^{-1}) 2909 (w), 1768 (s, lactone C=O), 1601 (m), 1562 (m), 1475 (s), 1406 (s), 1260 (s), 1180 (s, lactone C–O), 916 (s), 751 (s, P=S); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.04 (dt, J = 7.7 and 0.9 Hz, 1H), 7.83 (td, J = 7.6 and 1.1 Hz, 2H), 7.77 (td, J = 7.6 and 1.1 Hz, 2H), 7.59 (d, J = 1.7 Hz, 2H), 7.44 (dt, J = 7.7 and 0.8 Hz, 1H), 6.98 (s, 2H), 2.14 (dd, J = 13.6 and 4.6 Hz, 12H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.44, 151.53, 149.44 (d, J = 1.7 Hz), 148.53 (d, J = 9.2 Hz), 136.56, 131.28, 129.06, 125.96, 125.92, 124.49, 122.40 (d, J = 4.7 Hz), 116.69 (d, J = 1.8 Hz), 112.46 (d, J = 4.6 Hz), 80.38, 24.42 (d, J = 71.0 Hz), 24.37 (d, J = 70.8 Hz); ^{31}P NMR (243 MHz, DMSO-d_6) δ 104.42; HRMS (ESI); *m*/*z* calcd for $C_{24}H_{21}Cl_2O_5P_2S_2$ $[M+H]^+$: 584.9683, found 584.9679.

2.3. Preparation of mono-thiophosphinated DCF

Dimethylthiophosphinoyl chloride (29 μL, 0.275 mmol) in dichloromethane (10 mL) was added slowly to a mixture of 2′,7′-dichlorofluorescein (100 mg, 0.25 mmol) and triethylamine (77 μL, 0.55 mmol) in 50 mL of dichloromethane. After stirring overnight at room temperature, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using dichloromethane and dichloromethane-methanol (49:1, v/v) to produce 89 mg (72% yield) of mono-thiophosphinated DCF as a pale yellow powder. m.p. >132 °C (dec.); IR (KBr, cm^{-1}) 3420 (m, br, phenolic O–H), 2922 (w), 1768 (s, lactone C=O), 1605 (m), 1570 (w), 1481 (s), 1407 (s), 1264 (s), 1187 (s, lactone C–O), 917 (s), 758 (m, P=S); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.14 (s, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.82 (t, J = 7.4 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 1.7 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 6.94 (s, 1H), 6.92 (s, 1H), 6.69 (s, 1H), 2.13 (dd, J = 13.7, 3.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.57, 155.76, 151.71, 150.22, 149.77 (d, J = 1.4 Hz), 148.36 (d, J = 9.3 Hz), 136.46, 131.13, 128.95, 128.70, 128.69, 126.14, 125.72, 124.43, 122.03 (d, J = 4.5 Hz), 117.11, 116.97 (d, J = 1.5 Hz), 110.55, 104.12, 81.14, 24.46 (d, J = 71.0 Hz), 24.40 (d, J = 70.8 Hz); HRMS (ESI); *m*/*z* calcd for $C_{22}H_{16}Cl_2O_5PS$ $[M+H]^+$: 492.9833 found 492.9820.

2.4. Time course plot of signaling

Time course for the signaling of fluoride ions by **1** was followed by monitoring the changes in fluorescence intensity of the solutions at 536 nm. The concentrations of the probe **1** and fluoride ions were 5.0 μM and 0.5 mM, respectively, in a mixture of DMSO and tris buffer solution (pH 8.0), (7:3, v/v).

2.5. pH effect on fluoride signaling

The effects of pH on the fluoride signaling of **1** were elucidated by measuring the response in a pH range between 4.0 and 9.0 using buffer solutions. The buffer solutions used were acetate buffer for 4.0 to 5.6, phosphate buffer for 6.2 to 7.0, and tris buffer for 8.0 to 9.0. Final concentrations of probe **1**, fluoride ions, and each buffer solution were 5.0 μM, 0.5 mM, and 10 mM, respectively, under the same measurement conditions.

2.6. Detection limit for the fluoride ions

Following IUPAC recommendations, the detection limit was obtained using the equation $3 \times s_{bl}/m$, where s_{bl} is the standard deviation of the blank signal (the number of measurements = 20) and m is the slope of the calibration curve [27].

2.7. Fluoride ion signaling for practical samples

Fluoride ion signaling for tap water and simulated wastewater as well as distilled water samples was carried out to confirm the practical ability of the probe **1**. The changes in the signaling of **1** for the 'distilled water', 'tap water', and 'simulated wastewater' were measured as a function of fluoride concentrations. Stock solutions of sodium fluoride (1.0×10^{-3} M) were prepared in distilled water, tap water, and simulated wastewater. Stock solution of **1** (5.0×10^{-4} M) was prepared in DMSO. The pH of DTPA solution (1.0×10^{-1} M) was adjusted to pH 8 with sodium hydroxide prior to mixing with tris