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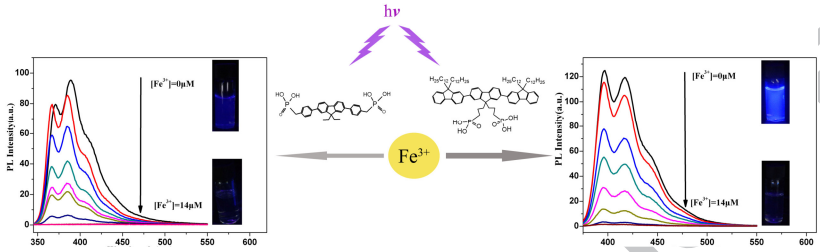

*Corresponding author. Tel.: +86 25 52090621; fax: +86 25 83792637.
E-mail address: sun@seu.edu.cn (Y. Sun).

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[a] School of Chemistry and Chemical Engineering, Southeast University, Nanjing, 211189, P. R China.
[b] Department of Chemical Engineering, Zhenjiang College, Zhenjiang, Jiangsu 212003, P. R China

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ABSTRACT

A series of novel fluorene derivatives containing -PO(OH)$_2$ (**1, 2**), -HS (**3**) and -N$^+$(CH$_3$)$_3$ (**4**) were synthesized and only phosphonic -functionalized fluorene derivatives can detect Fe^{3+} with high selectivity over other metal ions. The fluorescence quenching of **1** and **2** with titration Fe^{3+} in water-DMF solution fits the Perrin model of static quenching. Spectral analysis showed that Fe^{3+} bound with fluorene -based chemosensor through the O-atoms at the phosphonic group to form nonfluorescent complexes. The binding ratio was estimated by the Job plot and the trace levels of iron in samples were successfully monitored.
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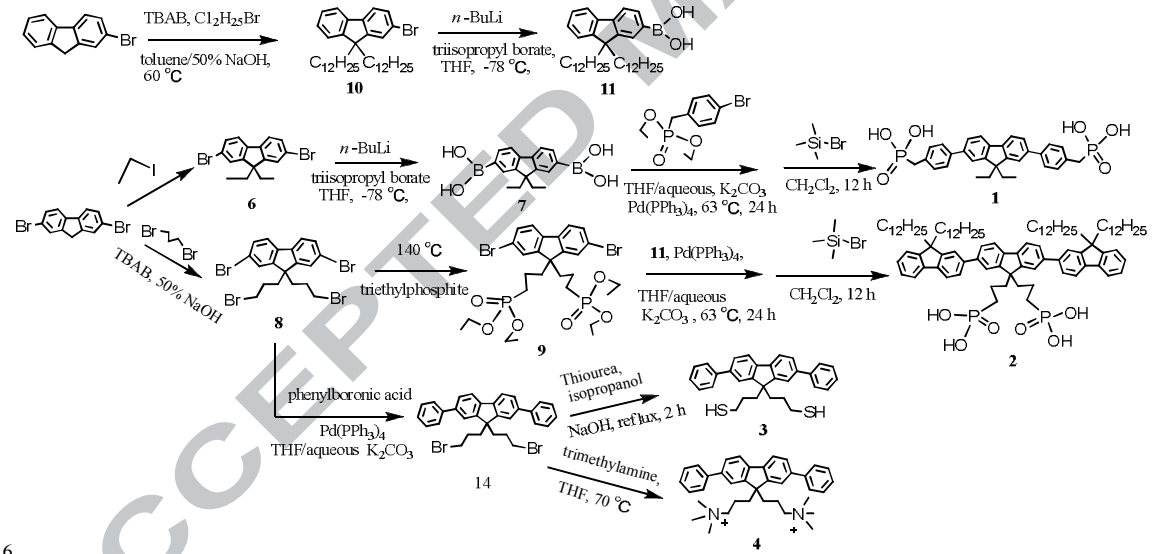

Scheme 1. Synthesis of chemosensor **1, 2, 3** and **4**.

Iron is an essential element present in the biosystem and both its deficiency and overload can induce various disorders.[1,2] According to the U.S. Environmental Protection Agency (EPA), the maximum content of iron in drinking water is ~5.357 μM. For that reason, the detection of trace irons becomes very important in the chemical research. Therefore, highly sensitive and selective Fe^{3+} fluorescent sensors are greatly desirable. A fluorescent sensor is generally constituted by a fluorophore (signaling moiety), which is covalently linked, through an appropriate spacer, to a ionophore (recognition moiety).[3,4] The recognition of the target species by the recognition moiety as a result of a selective fluorophore-ionophore interaction between the two is converted into an enhancement or quenching of the fluorophore emission. In recent years, several fluorescent sensors have been developed for the detection of transition and heavy metal ions, such as naphthalene fluorophore containing -PO(OH)$_2$ for detecting Cu^{2+},[5] thiourea-appended naphthalimides for detecting Zn^{2+} and Hg^{2+},[6] aromatic imino diacetate for detecting Cd^{2+} and F$^-$.[7,8] Meanwhile, various sensors for Fe^{3+} have been reported.[9-12] However, to the best of our knowledge , the static quenching mechanism for fluorene-based chemosensor with Fe^{3+} is still unexplored. Moreover, using the Perrin model as external standard calibration curve to monitor trace levels of iron ions is rarely reported.

We have recently reported two phosphonic acid-functionalized fluorene derivatives 9,9-Bis (3'- phosphonic acid propyl)-2,7-diphenylfluorene and 2,7-diphenylfluorene -9-

*Corresponding author. Tel.: +86 25 52090621; fax: +86 25 83792637.
E-mail address: sun@seu.edu.cn (Y. Sun).

ylphosphonic acid.[13] In order to further extend this work, other new fluorescent materials with various functional groups (compounds **1**, **2**, **3**, **4**) have been constructed. Compared to our previously reported molecules, the sensitivity of compound **1** and **2** for iron ions has been enhanced through changing the position of phosphonic acid and the conjugated length of fluorophore, respectively. The fluorescence of compound 3 and 4 has been hardly quenched with titration iron ions by replacing the phosphonic acid to -HS and $-N^{+}(CH_3)_3$, respectively. Meanwhile, we investigated their ability to function as a fluorescent sensor for Fe^{3+} in semi-aqueous solution and discussed the quenching mechanism by the fluorescence lifetime measurement. We also successfully monitored trace levels of iron (III) with them in samples.

The synthesis routes of the monomer and fluorescent materials **1**, **2**, **3**, **4** are presented in Scheme 1. The boronic acid derivative was coupled with two equiv of monomer **5** under palladium-catalyzed Suzuki conditions to afford compound **12**, subsequently the reaction of **12** with bromotrimethylsilane and methanol afforded fluorescent material 1 in a yield of 30% without further purification. The monomer **9** was also subjected to Suzuki coupling with **11** (made by metal-halogen exchange and nucleophilic substitution of **10**) to produce fluorescent material **2**. Formation of **3** and **4** from **14** was achieved by using Thiourea and trimethylamine respectively. Structures of compounds **1**, **2**, **3** and **4** were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and HRMS (data is shown in the Supporting information Figs. S1–S13).

The influence of iron (III) on the fluorescence response of **1**, **2**, **3** and **4** in water-DMF (5/5, v/v) solution was studied at pH=6-7. The emission intensity of **1** and **2** at 386 and 397 nm monotonically decreases with titration Fe^{3+} and finally the fluorescence disappears when the concentration of Fe^{3+} achieves 16 μM (Fig. 1a and 1b). Such high quenching phenomenon is probably due to photoinduced electron transfer (PET) or energy transfer.[14,15] For **3** and **4**, the fluorescence is hardly quenched with titration Fe^{3+} (Fig. S14). These phenomenons suggest that the phosphonic acid-functionalized fluorene derivatives are sensitive to iron (III), whereas the trialkylamino-functionalized and mercapto-functionalized fluorene derivatives are insensitive. Therefore, it indicates that the metal binding sites for fluorene derivatives are the phosphonic acids.[16, 17]

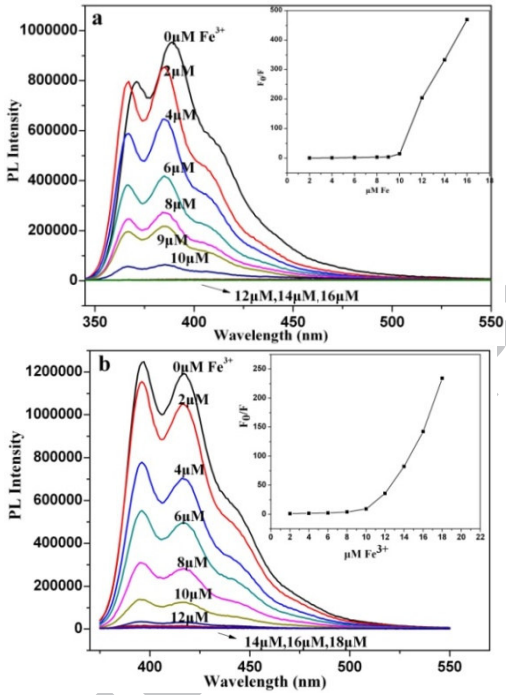

Figure 1. Fluorescence spectrum changes of compound **1** (c=10 μM) (a) and compound **2** (c=10 μM) (b) in water-DMF (5/5, v/v) at increasing concentrations of Fe^{3+} solution with 330 nm excitation. Insert: Variation of F_0/F of emission as a function of Fe^{3+}. (where F_0 and F refer to the emission luminance intensity for compounds in the absence and presence of Fe^{3+}).

As seen in figure 2a, under lower concentration, the observed fluorescence quenching, F_0/F, of these compounds is not linear with quencher (Fe^{3+}) concentration and thus fails to obey the Stern-Volmer model of dynamic quenching. However, the $ln\ F_0/F$ values are linear with quencher concentration, in agreement with the Perrin model of static quenching (Fig. 2b). The Perrin linear equations of **1** and **2** are showed in Table S1. The fluorescence quenching efficiency values (k_{SV}) of them, in the Perrin equation are $K \approx 1.992\times10^{5}\ M^{-1}$ and $2.594\times10^{5}\ M^{-1}$ respectively. It suggests that all the added quencher (Fe^{3+}) is bound to the ligands. This agreement with the Perrin model further supports that fluorescence quenching for systems of this type occurs intramolecularly. [18,19]

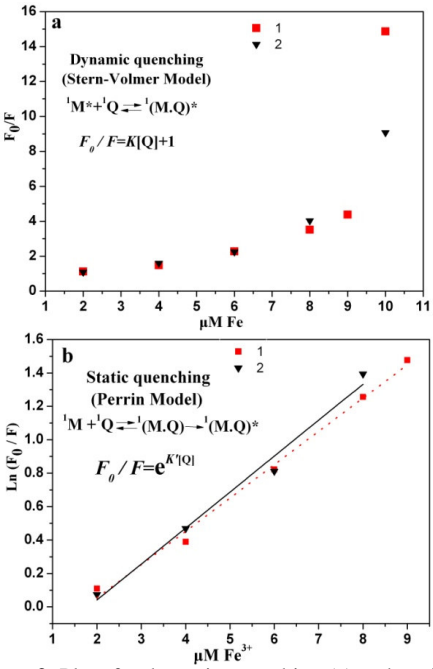

Figure 2. Plots for dynamic quenching (a) and static quenching (b) of the compound **1** and **2** by Fe^{3+}. The conditions were as described in the legend of Figure 1.

In order to investigate the possible static quenching of Fe^{3+} for chemosensor **1** and **2**, their fluorescence lifetime was recorded in water-DMF (5/5, v/v) solutions containing 0μM and 6μM Fe^{3+}. The fluorescence decay time profiles of these chemosensors with (blue line) or without (red line) 6μM Fe^{3+} were shown in Figure 3 together with the instrumental response function (IRF, gray line). The corresponding curves (black line) were fitted according to equation[20] $I_{fl}(t)=\left[\sum_{i=1}^{n} B_i \cdot \exp\left(-\frac{t}{\tau_i}\right)\right] \otimes IRF(t)+A$. The contribution of background fluorescence and stray light is included in the additive parameter *A*. The time constant τ_i as well as the amplitude-weighted average decay time $<\tau>=\sum_{i=1}^{n\leq 3} W_i \cdot \tau_i$ is given in Table S2. Static quenching refers to the formation of a ground-state complex between a fluorophore and a quencher. It means that the fluorescence decay intensity of the fluorophore decreases without altering the excited state lifetime. So static quenching is observed because that the fluorophore–quencher interaction does not change the decay time $<\tau>$. Therefore, the fluorescence lifetime measurement is the most common method to identify the quenching mechanism.[21, 22] As shown in Figure 3, the decay of them is all monoexponential. The florescence intensity of **1** and **2** is all quenched with addition of 6 μM Fe^{3+} (insert of Fig. 3a, 3b), while their fluorescence lifetime does not change. It indicates that the quenching is not initiated by dynamic quenching, but probably by static quenching resulting from the formation of **1-Fe** and **2-Fe** complexes.

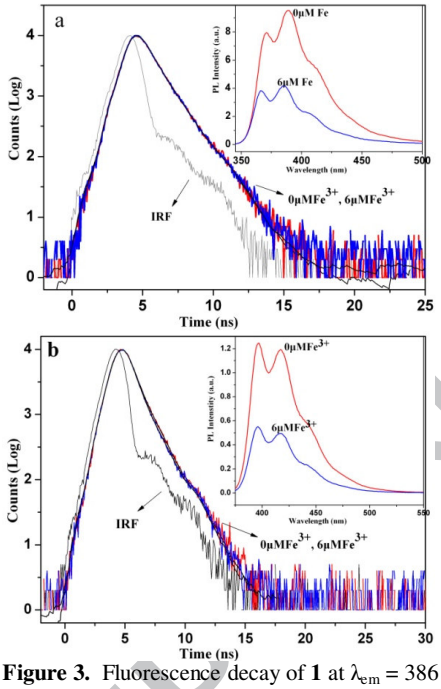

Figure 3. Fluorescence decay of **1** at λ_{em} = 386 nm (a) and **2** at λ_{em} = 397 nm (b), obtained by irradiating (λ_{exc} = 330 nm) in water-DMF (5/5, v/v) solutions of different Fe^{3+} concentrations: 0 μM (red line) and 6 μM (blue line). Additionally, the corresponding fitted curves (black line) and the instrumental response function (IRF, gray line) are shown. The decay time τ is summarized in Table S2. Insets: Photoluminescence spectra recorded with 0 μM and 6 μM Fe^{3+} (λ_{ex}=330 nm).

In order to confirm the fact that the quenching effect of chemosensor **1** and **2** is attributed to the formation of complexes between iron (III) and phosphonic groups, the complexes were prepared by stirring the $FeCl_3$ in C_2H_5OH with chemosensor **1** or **2** for 10 mins, and then characterized by UV and FTIR. Figure S15 shows the UV spectra of compound **1**, complex **1-Fe**, **2** and complex **2-Fe** in water-DMF solutions. The absorption onset of **1** was blue-shifted by 40 nm after coordinating with iron (Fig. S15 a), and the absorption onset of **2** was blue-shifted by 12 nm (Fig. S15 b). The changes in the absorption spectra indicated that the new complexes were formed by the strong association interaction between the analytes (Fe^{3+}) and the receptors (phosphonic groups). The FTIR spectra of them were shown in figure 4. The FT-IR spectrum of **1** exhibited stretching peaks originating from (P=O) and (P–OH) at 1110 cm^{-1} and 995 cm^{-1}. The absorption signals at 1110 cm^{-1} and 990 cm^{-1} showed stretching frequency of (P=O) and (P–OH) of **2**. However, the characteristic absorption peaks of P=O, P–OH all disappeared and overlapped to form a new broad band (P–OFe stretching band) at 1034 cm^{-1} for complex **1–Fe** and **2–Fe**. It provided insight into the coordination mode of ligand to iron. These results were similar to those published by Chung et al,[9] who studied Fe^{3+}-binding with pyrene-based chemosensor .

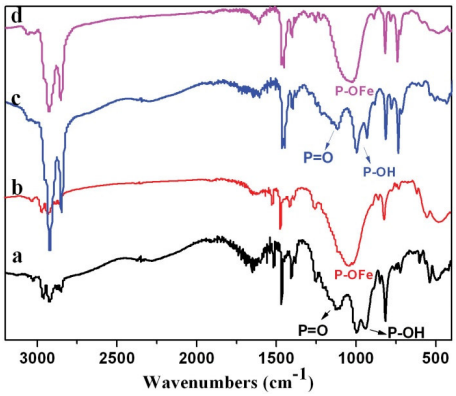

Figure. 4 FT-IR spectra of compound **1** (a), complex **1–Fe** (b), compound **2** (c) and complex **2–Fe** (d).

Furthermore, the images of these chemosensors were obtained under ultraviolet radiation. The chemosensor **1** and **2** emit blue light (Fig. 5a, 5c), whereas complete fluorescence quenching takes place for the **1–Fe** and **2–Fe** (Fig. 5b, 5d).

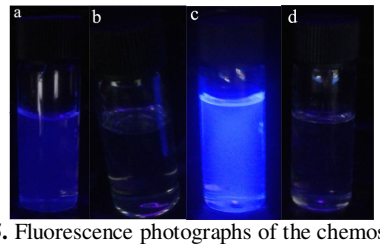

Figure 5. Fluorescence photographs of the chemosensor **1** (10 μM) (a), complex **1–Fe** (10 μM) (b), chemosensor **2** (10 μM) (c) and complex **2–Fe** (10 μM) (d) in water/DMF (5/5, v/v) solutions under a 365 nm UV lamp.

To elicit the interactions between Fe^{3+} and chemosensor **1**, **2** respectively, the binding stoichiometry was determined by Job plot.[23, 24] The Job's function F_{Job} is calculated according to the equation F_{Job}= *(1-X)* F_0-*F*. The plot of the luminescence versus the mole fraction of the added Fe^{3+} (Fig. 6) shows two parts that can be fitted by straight lines. The lines intersect at *X* equals to 0.5. These results reveal the formation of a 1:1 complex formulated as **1**- Fe^{3+} and **2**- Fe^{3+}, respectively. So the possible coordination mode is shown in Scheme S1. According to the Benesi-Hilderbrand equation $1/(F_0-F) = 1/\{K_a * (F_0- F_{min}) * [Fe^{3+}]\} + 1/(F_0- F_{min})$, (where F_{min} the minimum fluorescence intensity at 386 nm in the presence of Fe^{3+}),[25,26] the binding constant (K_a) is calculated to be 5.67×10^4 M^{-1} and 9.28×10^3 M^{-1} respectively (Fig. S16).

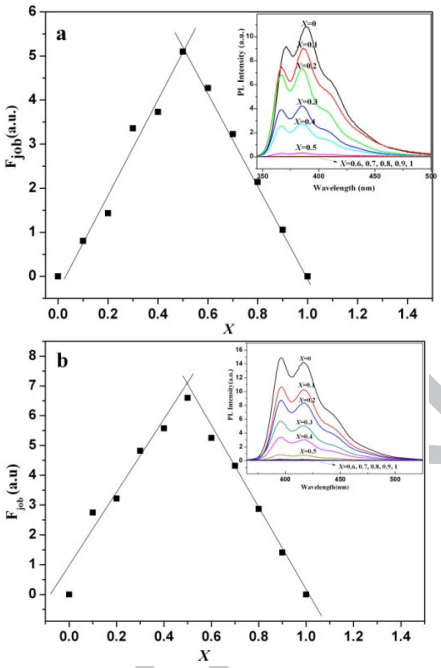

Figure 6. Job's plot for determining the binding stoichiometry in DMF/H_2O (v/v = 1/1) solution, showing a 1:1 stoichiometry between **1** and Fe^{3+} (a), **2** and Fe^{3+} (b). The variation of the Job's function (F_{Job}) at 386 nm (a) or at 397 nm (b) was measured as a function of the molar ratio X ([Fe^{3+}]/ ([Fe^{3+}] + [chemosensor])), respectively. Insets: Photoluminescence spectra recorded with various mole fraction of Fe^{3+} (X) at a constant total concentration of 10 μM (λ_{ex}=330 nm).

Iron sensing ability of chemosensors was investigated in water–DMF (5/5) (v/v) at different pH using HCl and Tris. It could be seen that the optimal pH was at the range from 5.0 to 7.0 (Fig. S17). The value of pH 7 was adjusted throughout the experiment. At the same time, the selectivity of compound **1** and **2** for Fe^{3+} over other metal ions (Fe^{2+}, Na^+, K^+, Mg^{2+},Ca^{2+}, Ni^{2+}, Mn^{2+}, Co^{2+}, Cu^{2+}, Cd^{2+}, Zn^{2+} and Ag^+) was investigated by the competition experiments (Fig. 7). While only Fe^{3+} induced dramatic decrease of fluorescence intensity, all competitive ions had no obvious interference with the detection of Fe^{3+} . These observations indicate that Fe^{3+} is the only metal ion that readily binds with fluorene-based chemosensors (**1** and **2**), causing static fluorescence quenching and forming complexes.[9, 27, 28] So they can serve as potential "On–Off" fluorescent sensors to selectively detect Fe^{3+} in water-DMF solution at pH 7.0.

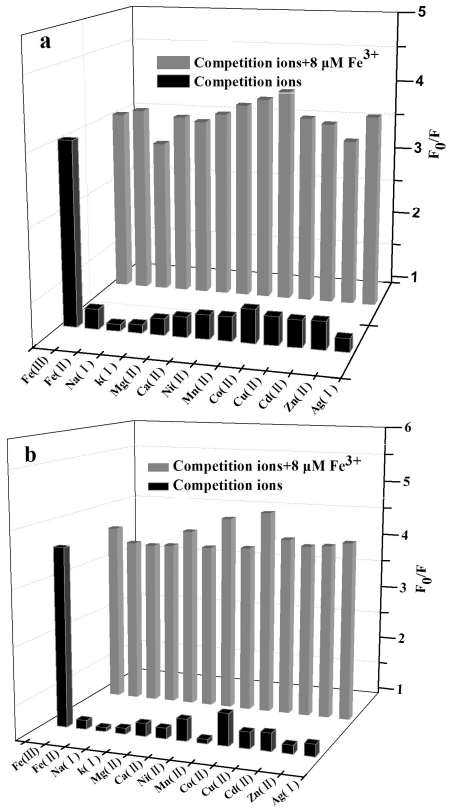

Figure 7. Relative fluorescence intensity (F_0/ F) change profile of **1** (10 μM) (a) and **2** (10 μM) (b) in water-DMF (5/5, v/v) in the presence of various metal ions(100 μM Na^+, 100 μM K^+ , 100 μM Mg^{2+} and the rest of cations in the same concentration as that of Fe^{3+}). The excitation wavelength is 330 nm. F_0 corresponds to emission without metal ions.

From figure 2b, the two working curves were linear in the range of 2～9 μM and 2～10 μM respectively (table S1). It is possible for this optical sensing system to determine the content of Fe^{3+} in samples with its external standard calibration curve. According to the General procedure (Supporting information), we got Fe^{3+} concentrations of samples M1, M2 and M3 from an External standard Calibration (Fig. 2b). Table 1 collected the original concentrations of M1, M2 and M3. As observed, the results were in good agreement with those obtained by Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES). It demonstrates that a new approach has been developed for the fluorimetric determination of iron (III) with **1** and **2** as the fluorescent reagent in water-DMF solution.

Table 1. Iron (III) Concentrations (μM) Found in Different Samples with the fluorescence spectra, by Resorting to an External standard Calibration, and by ICP-OES Measurements.

sample[a]	External standard Calibration(μM)		ICP-OES(μM)
	Compound 1	Compound 2	
M1	6.43	7. 95	7.84
M2	20.58	21.36	22.0
M3	47.43	49.95	48.13

[a]M1, M2, M3 are uncertain concentration of $FeCl_3$ solution sample.

In this letter, a series of novel fluorescent materials **1**, **2**, **3** and **4** have been synthesized by Suzuki-Miyaura reaction. Only compound **1** and **2** containing phosphonic groups exhibited high selectivity and sensitivity for Fe^{3+} detection. The analysis of fluorescence intensity showed that their fluorescence quenching was a static quenching process, which was also demonstrated by the unchanging fluorescence lifetime and the new formation of broad bands (P-OFe stretching bands). Meanwhile, the binding ratios of **1-Fe** and **2-Fe** complexes were both determined to be 1:1. Moreover, an external standard calibration curve of fluorescence quenching was applied successfully to the determination of iron (III) concentration in samples. Further experiments will be in progress to detect Fe^{3+} in biological systems using these sensors.

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Supplementary data

Supplementary data (synthetic and experimental details) associated with this article can be found, in the online version, at

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