

# 基于硼-二吡咯亚甲基二聚体的红光三价铁离子探针的合成与性质

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**摘要:** 在硼-二吡咯亚甲基(BODIPY)的  $\beta$ - $\beta$ (2/6)位偶联得到一种新型的红光二聚体 BODIPY 荧光探针 **1**, 该探针可以发生高效的能量转移, 假-斯托克斯位移可以达到 222 nm。探针 **1** 能够专一性地识别三价铁离子, 不受其它常见金属离子的干扰, 可以作为检测三价铁离子的高选择性的探针。

**关键词:** 硼-二吡咯亚甲基染料; 荧光探针; 红光; 能量转移; 三价铁离子

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## Synthesis and Properties of Red fluorescent Probe for Fe<sup>3+</sup> Based on Boron-Dipyrromethene Dimer

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**Abstract:** A red fluorescence boron-dipyrromethene (BODIPY, BODIPY core=4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) dimer **1**, which is linked through  $\beta$ - $\beta$  (2/6) position from a coupling reaction, exhibits efficient energy transfer with 222 nm pseudo Stokes' shift. The BODIPY dimer **1** shows high selectivity and sensitivity towards Fe (III) when the ion co-exists with common interfering metal ions and it may be used as an indicator for Fe<sup>3+</sup>.

**Key words:** Boron-dipyrromethene (BODIPY) dyes; fluorescent sensor; red visible; energy transfer; Fe<sup>3+</sup>

Boron-dipyrromethene (BODIPY, BODIPY core=4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) dyes have attracted increasing interests in the last decade for its remarkable photophysical properties, such as high extinction coefficient, high fluorescence quantum yields. Its structure can be easily modified to synthesis versatile dyes for practical applications<sup>[1]</sup>, such as fluorescence indicators for cations, anions, small molecules, reactive oxygen species and so on<sup>[2]</sup>. However, the Stokes' shift of BODIPY is 5~20 nm and the

emission wavelength around 500~560 nm limits its application in living cell imaging. To red shift the main BODIPY absorption band, several approaches have been explored, such as the substitution of aromatic or heteroaromatic groups at the 3-, 5- and/or 1-, 7-positions on the pyrrole moieties<sup>[3]</sup>, aromatic ring fusion<sup>[4]</sup>, replacing the *meso*-carbon atom with an azoatom<sup>[5]</sup>. Recently, Bard et al.<sup>[6]</sup> have reported an alternative way to red shift the main BODIPY absorption band by synthesizing the BODIPY dimers

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and trimers.

Ferric ion plays diverse and crucial roles in several biological processes. Particularly, ferric ion is an important element in enzymes, proteins, etc. The abnormal quantity of ferric ions may cause lots of disease and damage human health<sup>[7]</sup>, including hepatitis, cancer, etc. Owing to simplicity and high sensitivity, fluorescence is a powerful method to probe ions. Lots of highly selective and sensitive rhodamine-based chemosensors have been exploited for the detection of  $\text{Fe}^{3+}$  ion<sup>[8]</sup>. However, only a few BODIPY-based probes for  $\text{Fe}^{3+}$  have been reported<sup>[9]</sup>. Recently we have reported a BODIPY derivative with 5-(quinolin-2-yl)thiophen-2-yl (TQ) substituted at *meso*-phenyl position that exhibits specific response to  $\text{Fe}^{3+}$ <sup>[9b]</sup>. Herein, we extend this research by oxidative coupling BODIPY at the  $\beta$ - $\beta$  (2/6) positions so that its absorbance and fluorescence bands are red shifted to the red region. The  $\text{Fe}^{3+}$ -detection properties have been investigated by fluorescence titration spectroscopy.

## 1 Experimental

### 1.1 Reagents and instruments

Unless otherwise noted, all reagents or solvents were analytical reagents obtained from commercial suppliers and used without further purification. All air and moisture sensitive reactions were carried out under an argon atmosphere. Dry  $\text{CH}_2\text{Cl}_2$  was obtained by refluxing and distilling over  $\text{CaH}_2$  under nitrogen. Triethylamine was obtained by simple distillation.

The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectroscopic measurements were performed at 500 MHz (DRX-500), and 125 MHz (DRX-500), respectively on a Bruker 500 MHz spectrometer. Mass spectra were obtained with a

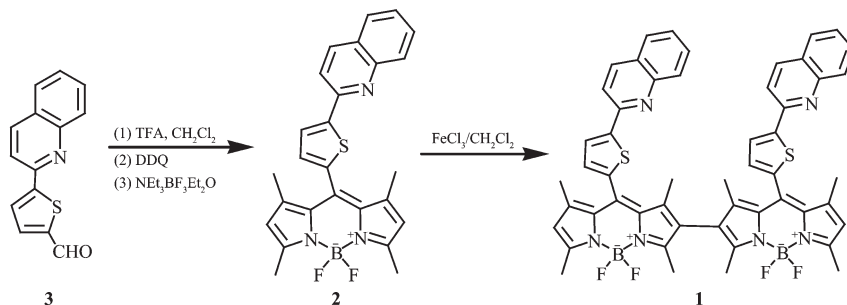
Bruker Daltonics Autoflex II<sup>TM</sup> MALDI TOF MS spectrometer. Fluorescence spectral measurements were carried out by using a Hitachi F-4600 fluorescence spectrophotometer. Electronic absorption spectra were recorded with a Shimadzu UV-2550 spectrophotometer.

### 1.2 Procedures for metal ion sensing

Stock solutions of all sorts of metal ions ( $0.1 \text{ mol} \cdot \text{L}^{-1}$ ), such as  $\text{Zn}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Hg}^{2+}$ , were prepared in deionized water. A stock solution of **1** ( $10 \text{ } \mu\text{mol} \cdot \text{L}^{-1}$ ) was prepared in DMSO. In titration experiments, each time a 3 mL solution of **1** ( $10 \text{ } \mu\text{mol} \cdot \text{L}^{-1}$ ) was filled in a quartz optical cell of 1 cm optical path length, and the  $\text{Fe}^{3+}$  stock solution was added into the quartz optical cell gradually by using a micro-pipet. In selectivity experiments, the test samples were prepared by adding appropriate amounts of metal ion stock solution into 3 mL solution of **1** ( $10 \text{ } \mu\text{mol} \cdot \text{L}^{-1}$ ). During fluorescence measurements of **1**, the excitation wavelength was 334 nm (for exciting the 2-(thiophen-2-yl)quinoline moiety) or 495 nm (for exciting BODIPY fluorophore) with the excitation slit of 5 nm and the emission slit of 10 nm. The emission spectra area of the measured compound **1** was obtained between 350~650 nm.

### 1.3 Synthesis of BODIPY dimer **1**

The synthesis of BODIPY dimer **1** is outlined in Scheme 1. The starting material **3** was prepared according to a published procedure (yield 45%)<sup>[9b]</sup>. The BODIPY monomer **2** was prepared through the trifluoroacetic acid catalyzed condensation reaction of 5-(quinolin-2-yl)thiophene-2-carbaldehyde with 2,4-dimethyl-pyrrole in 60% yield<sup>[9b]</sup>. The target BODIPY dimer **1** was produced by the self coupling reaction of



Scheme 1 Synthetic procedure for the preparation of BODIPY dimer **1**

**2** according to the following procedure: **2** (0.22 mmol, 100 mg) and  $\text{FeCl}_3$  (0.55 mmol, 152 mg) were mixed in 30 mL  $\text{CH}_2\text{Cl}_2$ . The mixture was stirred for 30 min at ambient temperature. Then the reaction was quenched with  $\text{CH}_3\text{OH}$  and washed with water, dried over anhydrous sodium sulfate, and concentrated at reduced pressure. The crude products were purified by silica-gel column chromatography using  $\text{CH}_2\text{Cl}_2$  as the eluent to afford the red powder **1**. Yield: 9.9%,  $^1\text{H}$  NMR( $\text{CDCl}_3$ , 500 MHz): 8.17 (d,  $J=15$  Hz, 2H), 8.06 (d,  $J=15$  Hz, 2H), 7.84~7.71 (m, 8H), 7.53 (t,  $J=10$  Hz, 2H), 7.06 (m, 2H), 6.04 (d,  $J=10$  Hz, 2H), 5.69 (s, 1H), 4.08 (s, 2H), 2.57 (s, 9H), 1.76 (d, 12H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz): 157.3, 156.8, 156.3, 156.1, 151.5, 148.1, 147.8, 144.3, 143.4, 143.2, 140.1, 137.9, 137.5, 136.8, 134.3, 133.4, 132.7, 132.2, 131.9, 130.1, 129.3, 129.1, 128.9, 127.5, 127.4, 126.7, 126.4, 125.7, 122.0, 121.5, 119.9, 117.2, 29.7, 23.3, 14.7, 14.1, 11.7. MALDI-TOF MS:  $m/z$ : 912.7 ( $\text{M}^+$ )

## 2 Results and discussion

B3LYP geometry optimizations is carried out with 6-31G (d) basis sets to determine the configuration of **1**. The structure of **1** is similar to the previously reported alkyl substituted BODIPYs. Both 2-(thiophen-2-yl)quinoline moiety and the indacene plane of **1** are nearly planar, also the torsion angle between the two planes are  $83.86^\circ$ . The two BODIPY monomeric units of dimers **1** are not orthogonal with the torsion angle being  $67.7^\circ$ .

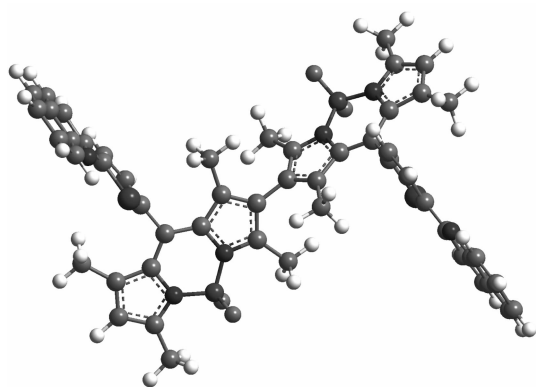


Fig.1 Geometry optimization of **1** at the B3LYP/6-31G(d) level<sup>[10]</sup>

### 2.1 Spectroscopic properties of **1** and **2**

The UV/Vis absorption and fluorescence spectra of **1** and **2** in  $\text{CH}_2\text{Cl}_2$  are shown in Fig.2. The absorption maxima of **2** is centered at approximately 514 nm, while the absorption of **1** is red shifted to 536 nm due to the formation of dimeric structure through the (2/6) positions coupling. The shoulder at 505 nm of **1** is attributed to the molecular C-C frame vibration, which is typical of BODIPY dyes. The weaker absorption band in the 300~400 nm region of **1** is attributed to the transition from 2-(thiophen-2-yl)quinoline moiety<sup>[2c]</sup>. Exciting 2-(thiophen-2-yl)quinoline moiety in compound **1** at 334 nm, both the emission band for 2-(thiophen-2-yl)quinoline (TQ) moiety at 386 nm and the emission typical for BODIPY fluorophore at 556 nm are observed. These results indicate that energy transfer partially occurs at compound **1** from TQ moiety to the BODIPY acceptor.

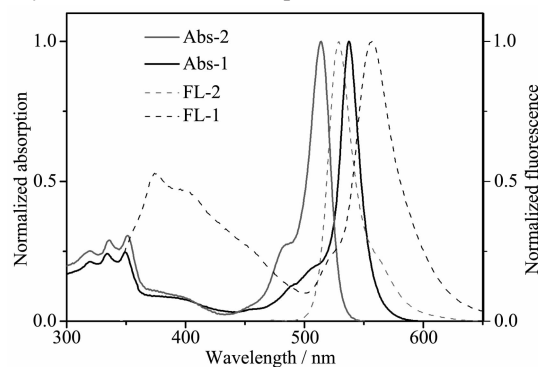


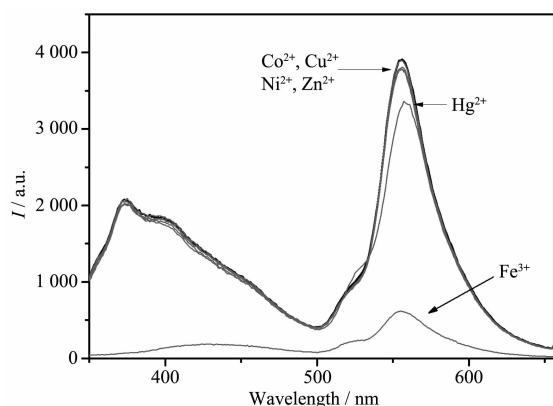
Fig.2 Absorption (solid line) and fluorescence (dash line) spectra of **1** ( $10 \mu\text{mol} \cdot \text{L}^{-1}$ ) and **2** ( $10 \mu\text{mol} \cdot \text{L}^{-1}$ ) in  $\text{CH}_2\text{Cl}_2$  solvent ( $\lambda_{\text{ex}}=334$  nm)

### 2.2 Detective property of **1**

Exciting at 334 nm, the fluorescence intensity of **1** at 386 nm and 556 nm are significantly quenched upon the addition of  $\text{Fe}^{3+}$ , since specific chelating property of the 2-(thiophen-2-yl)quinoline and the  $\text{Fe}^{3+}$  ion<sup>[9b]</sup>. The fluorescence spectrum of **1** is almost not influenced by the addition of 100 equiv. of other metal ions such as  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ , and a little decreased by the addition of 100 equiv. of  $\text{Hg}^{2+}$ , suggesting that compound **1** has high selectivity toward  $\text{Fe}^{3+}$  (Fig.3).

The coordination of dimer **1** with  $\text{Fe}^{3+}$  is investigated by spectrophotometric titration in DMSO, as

shown in Fig.4. When exciting at 334 nm, the fluorescence intensity of **1** at 386 nm and 556 nm



( $C_{\text{Co}^{2+}}, C_{\text{Cu}^{2+}}, C_{\text{Ni}^{2+}}, C_{\text{Zn}^{2+}}, C_{\text{Hg}^{2+}}$ ) in equivalent=1/2( $C_{\text{Co}^{2+}}, C_{\text{Cu}^{2+}}, C_{\text{Ni}^{2+}}, C_{\text{Zn}^{2+}}, C_{\text{Hg}^{2+}}$ ) in mol·L<sup>-1</sup>;  $C_{\text{Fe}^{3+}}$  in equivalent=1/3 ( $C_{\text{Fe}^{3+}}$ ) in mol·L<sup>-1</sup>

Fig.3 Fluorescence spectra of 10  $\mu\text{mol}\cdot\text{L}^{-1}$  **1** upon addition of different metal ions (100 equiv.  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Fe}^{3+}$ ) in DMSO solution

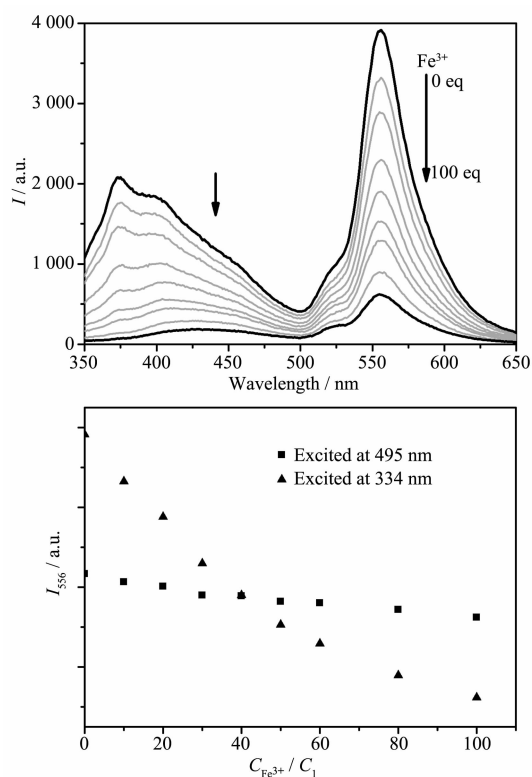


Fig.4 Top: changes in the fluorescence spectrum of **1** (10  $\mu\text{mol}\cdot\text{L}^{-1}$  in DMSO) as a function of  $\text{Fe}^{3+}$  concentration; Bottom: the changes of emission intensity of **1** (10  $\mu\text{mol}\cdot\text{L}^{-1}$  in DMSO) at 556 nm as a function of  $C_{\text{Fe}^{3+}}/C_1$  excited at 334 nm and 495 nm

gradually decreased upon addition of increasing amount of  $\text{Fe}^{3+}$  (0~100 equiv. of  $\text{Fe}^{3+}$ ). However, exciting at 495 nm, the fluorescence intensity of **1** at 556 nm is almost unaffected. The results further indicate that the coordination of the 2-(thiophen-2-yl)quinoline to  $\text{Fe}^{3+}$  inhibits the energy transfer from 2-(thiophen-2-yl)quinoline to the BODIPY, which is the main reason for the fluorescence quenching.

In summary, we have designed a red-visible BODIPY dimer containing 2-(thiophen-2-yl)quinoline substituent at *meso* position which shows specific binding with  $\text{Fe}^{3+}$  in DMSO solution. The high selectivity of **1** toward  $\text{Fe}^{3+}$  with significant fluorescence quenching may have applications as  $\text{Fe}^{3+}$  indicator in aqueous media.

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