A convenient colorimetric and ratiometric fluorescent probe for detection of cyanide based on BODIPY derivative in aqueous media

Yanhua Yu [a, *], Tingting Shu [a], Changzhi Dong [a, b]

[a] *Institute for Interdisciplinary Research, Jianghan University, Wuhan 430056, China*
[b] *University Paris Diderot, Sorbonne Paris Cité, ITODYS, UMR CNRS 7086, 15 rue J-A de Baïf, 75205 Paris Cedex 13, France*

ARTICLE INFO

ABSTRACT

A convenient colorimetric and ratiometric fluorescent probe based on BODIPY derivative for cyanide detection has been synthesized, whose structural contains a dicyanovinyl group used as a sensing unit. Among the tested analytes, such as CN^-, F^-, Cl^-, Br^-, I^-, ClO_4^-, AcO^-, NO_3^-, $H_2PO_4^-$ HSO_4^-, S_2^- and N_3^-, only CN^- could react with dicyanovinyl moiety by nucleophilic addition, which disrupted the π-conjugation of the probe and hindered the intramolecular charge transfer (ICT), leading a blue shift of absorption and fluorescence spectrum and a concomitant color change from yellow to light pink. The detection limit of this probe was calculated to be 0.98 μM, which is lower than the maximum concentration in drinking water (1.9 μM) permitted by the World Health Organization (WHO). Moreover, the probe showed excellent selectivity and anti-interference ability towards CN^- over other anions. The reaction mechanism was fully supported by ^1H NMR and MS spectrum.

1. Introduction

Over the past decades, the research of design and synthesis of convenient probes for anions detection has been gained considerable attention because their key roles in chemical, biological and environmental systems [1–3]. It is generally known that among anions, cyanide is the most toxic anion and is lethal for humans due to its ability of inhibiting cellular respiration lead to inadequate oxygen supply in the body by binding Fe^{3+} which present in cytochrome oxidase at very low concentrations. About 0.5–3.5 mg per kilogram of body weight is deadly to human beings [4,5] The maximum permissible concentration of cyanide in drinking is water 1.9 μM set by the World Health Organization (WHO) [6]. However, cyanide is still widely used in various chemical and industrial processes, such as gold extraction, plastic manufacturing, electroplating, tanning, synthesis of fibres and resins [7,8]. Its widespread application often unavoidably leads to the release of toxic chemicals, which cause the contamination of different water resource and harm to public health [9]. As a consequence, many chemists have devoted themselves to develop efficient method for cyanide detection.

Until now, mang solutions have been proposed for detecting cyanide, for example, titrimetric [10], chromatographic [11,12], electrometric [13,14] and fluorescent sensors [15–30]. Among these techniques, fluorescent sensors have attracted much more attention because of their various advantages over the other methods, such as simplicity, excellent sensitivity, high selectivity, "naked-eye" detection and inexpensive character. Although a lot of colorimetric and fluorescent sensors for cyanide have been reported, most of them were based on fluorescence quenching [31,32] or enhancement [33–35] which means that the detection signal is the fluorescence intensity at a single wavelength, this could be obviously affected by much factors, such as the probes concentration, the efficiency of instrument and environmental conditions. By comparison, the ratiometric fluorescent probes could surmount the shortcomings of the single wavelength based sensors, due to the ratio of two different wavelengths can provide a built-in correction without considering the effects of instruments, environmental and concentration of receptor. However, to the best of our knowledge, not too much ratiometric fluorescent probes for the detection of cyanide have been reported in the literature [36–39]. Moreover, a majority of fluorescent probes for the detection of cyanide can only occur in an organic solvent which are not suitable for water sample detection. Therefore, it is significant to develop fluorescent sensors for cyanide which can display both color and fluorescence changes in an aqueous solution in a ratiometric manner.

Keeping this in mind, in this work, we have developed a convenient colorimetric and ratiometric fluorescent probe **1** based

---

* Corresponding author.
 E-mail address: hpyyh@aliyun.com (Y. Yu).

on dipyrromethene boron difluoride (BODIPY) (Scheme 1) for cyanide detection in tetrahydrofuran–water mixture with a low detection limit.

We chose BODIPY dyes as fluorescent probe due to their outstanding properties such as narrow emission bandwidth, large molar absorption coefficients, high photophysical stability, high fluorescence quantum yield and tunable fluorescence characteristic [40–42]. Our probe design relies on the nucleophilic attack of cyanide anion to a dicyanovinyl group, which installed onto the 5′ position of BODIPY platform through a simple Knoevenagel condensation on the β-formyl BODIPY 2 [43]. We envisioned that there is an intramolecular charge transfer (ICT) process in probe 1. The interaction between probe 1 and cyanide could disrupt the π-conjugation and block the ICT process to produce a colorimetric and ratiometric spectroscopic response. As expected, we observed a blue shift in the absorption and emission band of probe 1 upon reaction with cyanide in tetrahydrofuran–water mixture. As a consequence, probe 1 could be utilized as a selective colorimetric and ratiometric fluorescent probe for the detection of cyanide.

2. Results and discussion

2.1. Synthesis of probe 1

Synthesis of probe 1 was illustrated in Scheme 1, BODIPY 2 was reacted with malononitrile by the treatment of piperidine and a catalytic amount of HOAc under argon in the solution of toluene to give probe 1 in 63% yield.

2.2. Absorption and fluorescence titration of probe 1 with CN$^-$

To investigate the sensing ability of probe 1 for cyanide, the absorption and fluorescence titration of probe 1 with CN$^-$ were performed in the mixture of THF/H$_2$O (v/v, 9:1). As shown in Fig. 1, probe 1 shows a major absorption band at 515 nm. With the addition of increasing amounts of CN$^-$ to the solution of probe 1 (5 μM), the maximum absorption band at 515 nm decreased gradually and a novel band at 497 nm appeared simultaneously. The A$_{515 nm}$/A$_{497 nm}$ ratio varied as a function of the cyanide concentration and reached at a balance by addition of 36 μM CN$^-$. Furthermore, there is a good a linear relationship between the A$_{515 nm}$/A$_{497 nm}$ ratio and the concentration of cyanide ranged from 0 to 10 μM (Fig. 2). The linear equation is $y = -0.158x + 0.023$, where y is the ratio of A$_{515 nm}$/A$_{497 nm}$ and x is the concentration of CN$^-$. The coefficient of determination R^2 is 0.9598 and the error bar is in the rational range, which indicated that probe 1 could obtain accurate quantification for cyanide detection.

Moreover, the fluorescence titration of probe 1 (5 μM) towards cyanide was also investigated in the same condition. As shown in Fig. 3, the excitation of probe 1 at 515 nm gave a maximum emission band at 534 nm. Upon addition of cyanide gradually, a blue shift from 534 nm to 514 nm was observed, concomitant with 40% fluorescence intensity decreasing of its initial level. Similar to the absorption response of probe 1 to cyanide, when the concentration of cyanide up to 36 μM, the I$_{534}$
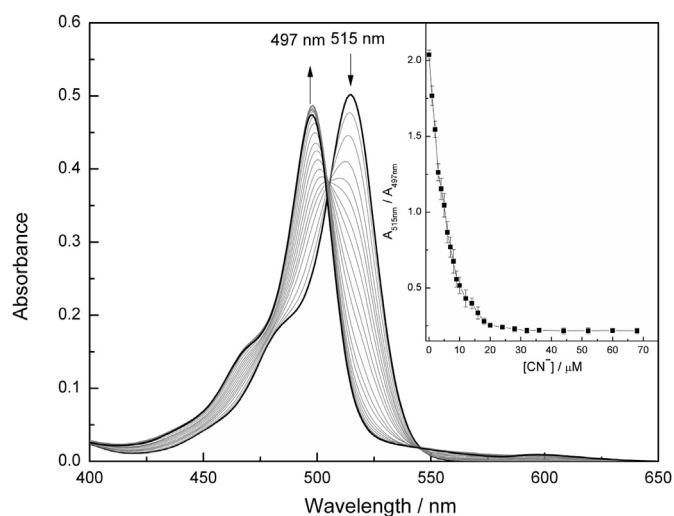

Fig. 1. Absorption of probe 1 (5 μM) in the mixture of THF and water (v/v, 9/1) in the presence of varying concentration of CN$^-$ (0–68 μM), inset shows the plot of A$_{515 nm}$/A$_{497 nm}$ vs. the concentration of CN$^-$.
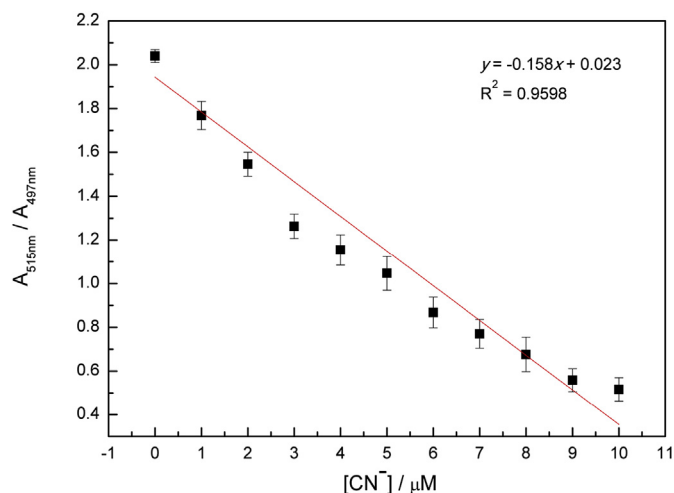

Fig. 2. Linear relationship between A$_{515 nm}$/A$_{497 nm}$ and the cyanide concentration (0–10 μM).

nm/I$_{514 nm}$ ratio reached a plateau. It also shows a good linear relationship between I$_{534 nm}$/I$_{514 nm}$ and the low concentration of cyanide (0–10 μM). The coefficient of determination R^2 is 0.9934 which means the quantification for cyanide detection could also be obtained by the ratio of fluorescent intensity between 534 nm and 514 nm (Fig. 4). The detection limit for CN$^-$ was calculated to be 0.98 μM (SI), which is lower than the maximum permissable concentration in drinking water (1.9 μM) set by the World Health Organization (WHO).

2.3. The selective response of probe 1 to CN$^-$

The sensing properties of probe 1 for anions (CN$^-$, F$^-$, Cl$^-$, Br$^-$, I$^-$, ClO$_4^-$, AcO$^-$, NO$_3^-$, H$_2$PO$_4^-$, HSO$_4^-$, S^{2-} and N$_3^-$) were investigated by UV/vis and fluorescence measurements. As shown in Fig. 5, among the tested anions, only addition of CN$^-$ led to the absorption band at 515 completely disappearance and a novel band at 497 nm appearance, a blue shift (18 nm) was observed. Addition of other anions did not show any significant changes,
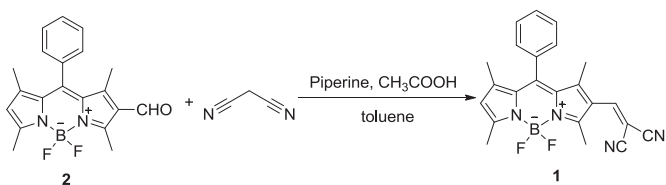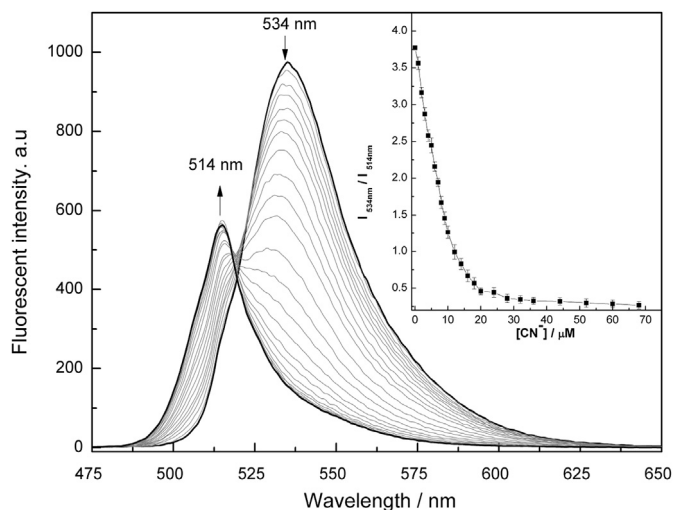

Scheme 1. Synthesis of probe 1.

Fig. 3. Fluorescence emission of probe **1** (5 μM) in the mixture of THF and water (v/v, 9/1) in the presence of varying concentration of CN^- (0−68 μM), inset shows the plot of $I_{543\ nm}/I_{514\ nm}$ vs. the concentration of CN^-.

which indicated that only CN^- could react with the dicyanovinyl group of probe **1** reducing the π-conjugation and blocking the ICT process. These results were further confirmed by ^{1}H NMR and MS analyses As a consequence, a distinct color change from yellow to pink was clearly observed by addition of CN^- (Fig. 6). So probe **1** can be used as a colorimetric sensor for the detection of cyanide in the manner of "naked-eye". Moreover, the fluorescence responses of probe **1** (5 μM) to the anions mentioned above were also investigated. As shown in Fig. 7, probe **1** has a maximum emission band at 534 nm upon excitation at 515 nm. The addition of CN^- resulted in a disappearance of the emission band at 543 nm and appearance of a new band at 514 nm. Meanwhile, the fluorescence quantum yield (Φ_F) decreased from 0.65 to 0.11(SI). While other anions did not give an obvious fluorescence change. All the results showed that probe **1** has high selectivity for cyanide.

2.4. Competition studies

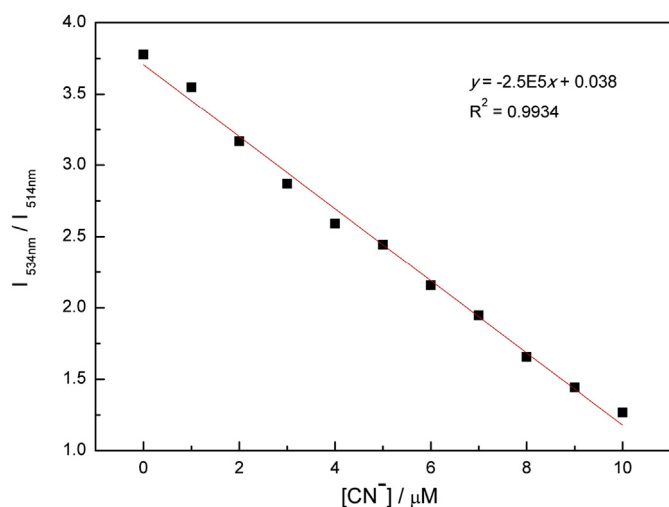To investigate the ability of probe **1** for cyanide detection in the

Fig. 4. Linear relationship between $I_{543\ nm}/I_{514\ nm}$ and the cyanide concentration (0−10 μM).

complicated environment, a competition experiment was implemented. As shown in Fig. 8, addition of the interfering anions into the solution of probe **1** (5 μM), such as F^-, Cl^-, Br^-, I^-, ClO_4^-, AcO^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, S^{2-} and N_3^- (100 μM), did not lead to any significant fluorescence changes comparing to the blank sample. While a blue shift (20 nm) of fluorescence was observed in all of the interfering samples when CN^- (40 μM) was added into them. This demonstrated that probe **1** has the excellent selectivity for cyanide detection over the other anions.

2.5. The effect of pH

In general, the pH value of a sample can influence definitely the performance of a probe, since the physico-chemical properties of the probe depend on the ionic state of the probe due to its protonation or deprotonation. Therefore, the pH influence on probe **1** in the absence or presence of cyanide was investigated in the mixtures of THF and different buffer (v/v, 9/1) solutions. As depicted in Fig. 9, in the pH range from 2.0 to 12.0, almost negligible fluorescence intensity at 534 nm changes of probe **1** were observed, while the fluorescence of probe **1** with CN^- in the pH range from 2.0 to 12.0 could also keep the similar intensity at 514 nm, which indicated that probe **1** remained steady and could detect CN^- in a reasonable pH range.

2.6. Effect of reaction time

To test the ability of probe **1** for rapid cyanide detection, we examined the time courses of the fluorescence intensity of probe **1** (5 μM) in the presence of CN^- (40 μM) in the mixture of THF and water (v/v, 9/1) at room temperature. As shown in Fig. 10 the ratio of fluorescent intensity between 534 nm and 514 nm was reached equilibrium within 100 s. As a result, this approach is rapid, simple and sensitive for the detection of cyanide.

2.7. Sensing mechanism studies

In order to confirm that the changes in the absorption and fluorescence spectra of probe **1** induced by an irreversible nucleophilic addition reaction between cyanide and dicyanovinyl moiety, ^{1}H NMR titration experiment and MS spectral study were carried out. As depicted in Fig. 11, the shift of proton H_a and H_b are 6.3 and 8.1 ppm. Addition of 0.4 equiv. of CN^- caused protons H_a and H_b of probe **1** to shift upfield. While upon addition of 1.0 equiv. of CN^-, a complete disappearance of H_b at 8.1 ppm with an appearance of a
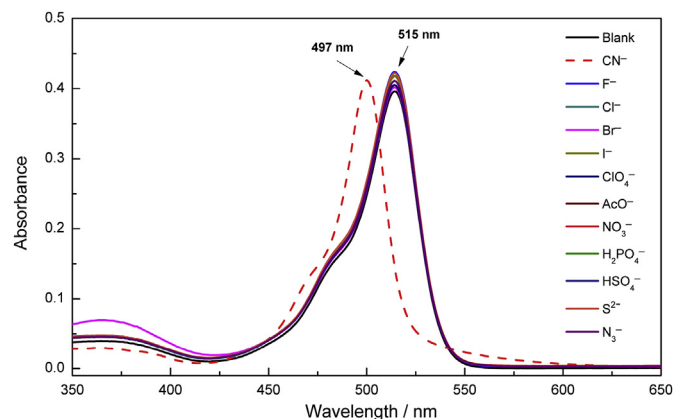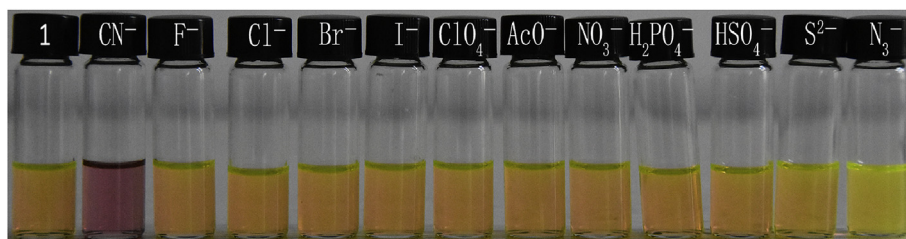

Fig. 5. The absorption spectra of probe **1** (5 μM) in the mixture of THF/H$_2$O (v/v, 9:1) after the addition of the different anions (40 μM) at 25 °C.

Fig. 6. Color changes of probe **1** (5 μM) in the mixture of THF/H$_2$O (v/v, 9:1) after the addition of the different anions (40 μM) at 25 °C. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

new peak (H$_{b'}$) at 4.3 ppm, and a slight upfield shift of H$_a$ from 6.3 to 6.0 ppm were observed. Moreover, the MS spectral study showed that the MS value of probe **1**+CN$^-$ is 426.76, which corresponded to the calculated value of addition product (ESI). These phenomenon clearly clarified that the cyanide anion is added to the dicyanovinyl group as expected and induced the disruption in the extended π-conjugation of BODIPY and hindered the intramolecular charge transfer. The resulting anionic species was responsible for the optical spectral changes for the probe **1**.
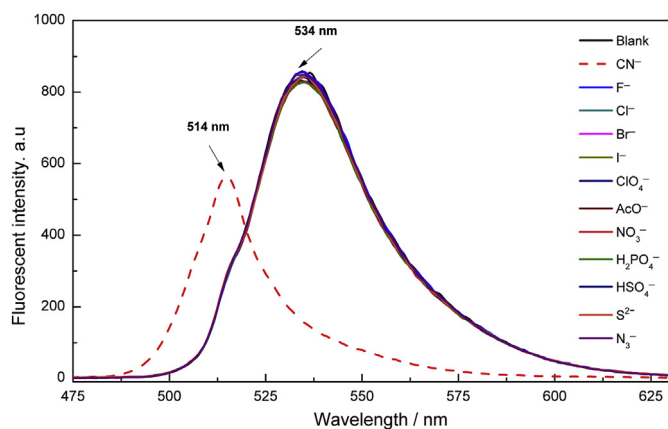
3. Experimental section

3.1. Reagents and chemicals

All reagents and solvents were purchased from Alfa Aesar (Shanghai, China) without further purification, Organic solvents were purchased from Aladdin (Shanghai, China). Distilled water was used in all experiments. All anions were prepared from their tetrabutylammonium (TBA$^+$) salts, expect for Na$_2$S and NaN$_3$.

Fig. 7. Fluorescence spectra of probe **1** (5 μM) in the mixture of THF and water (v/v, 9/1) in the presence of different anions (λ$_{ex}$ = 515 nm).
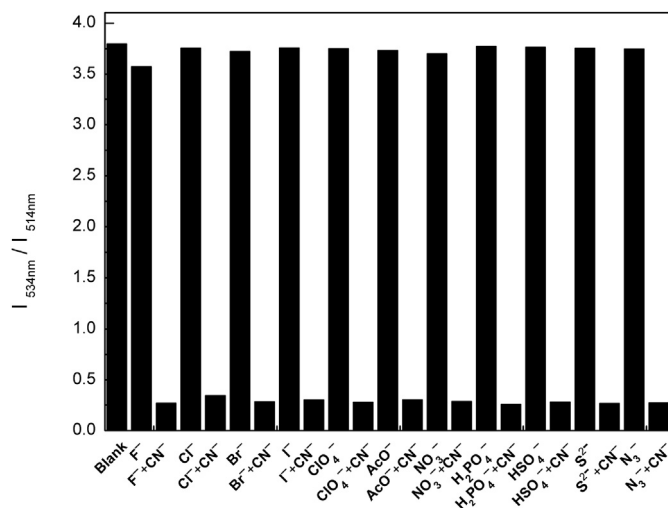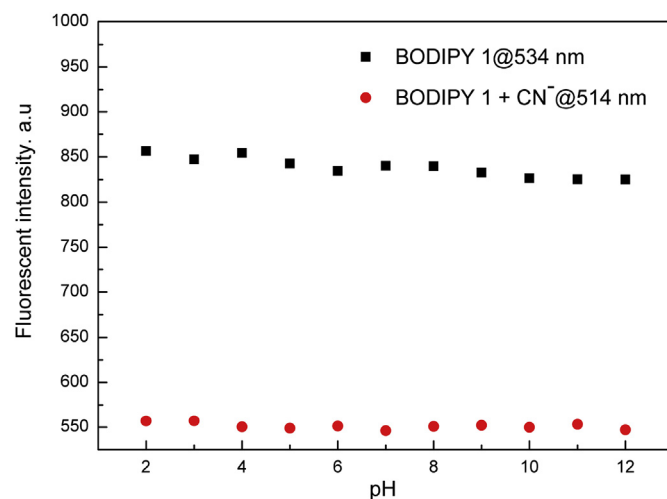

Fig. 9. pH dependence of fluorescent intensity of probe **1**, without and with CN$^-$, measured at 534 nm and 514 nm, respectively.

Fig. 8. Fluorescence intensity ratio (I$_{534\ nm}$/I$_{514\ nm}$) of probe **1** (5 μmol/L) in the mixture of THF and water (v/v, 9/1) in the presence of different anions (100 μmol/L) without/with CN$^-$ (40 μmol/L).

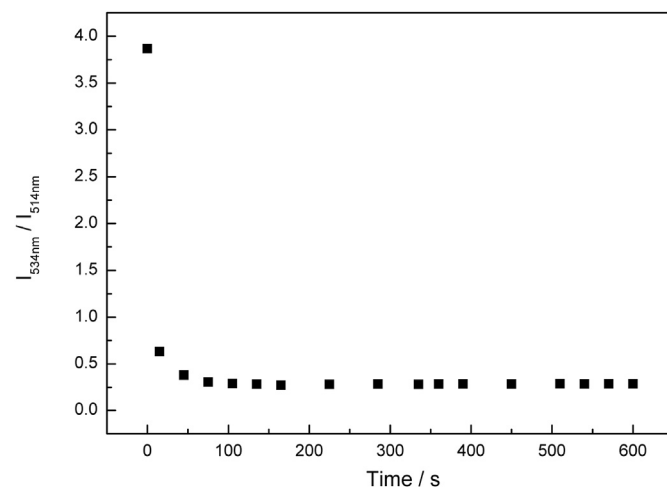**Fig. 10.** Time-dependent fluorescence intensity ratio (I$_{534\ nm}$/I$_{514\ nm}$) of probe **1** (5 μmol/L) in the mixture of THF and water (v/v, 9/1) in the presence CN$^-$ (40 μmol/L).
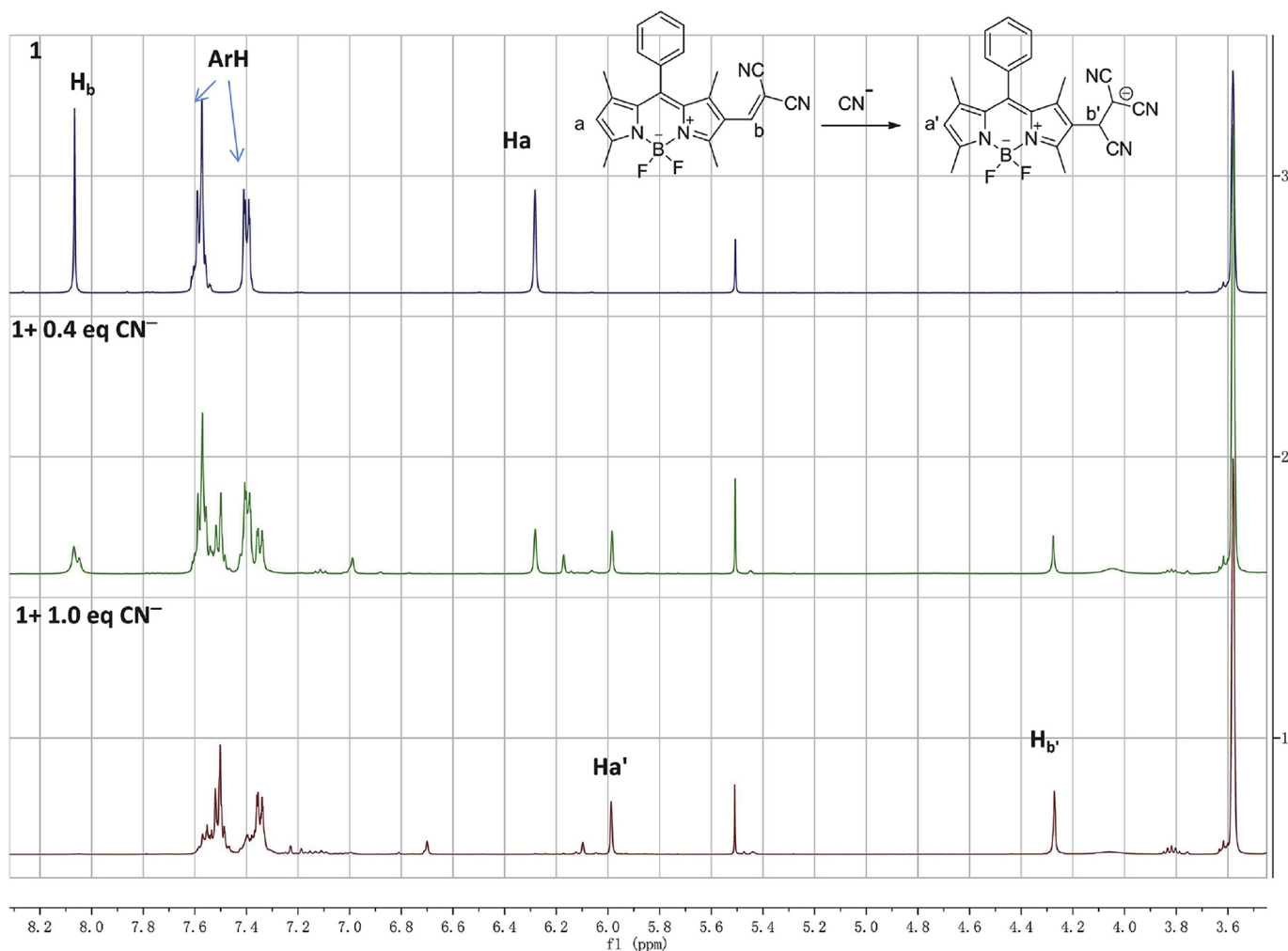
Fig. 11. The ^{1}H NMR spectra of probe **1** in THF-d$_8$ in the presence of 0.4 and 1.0 equivalent of CN$^-$.

3.2. Apparatus

^{1}H NMR, ^{13}C NMR spectra were collected on a Bruker Advance 400 MHz spectrometer in CDCl$_3$ and THF-d$_8$, tetramethylsilane (TMS) as internal standard. MS spectra were recorded on a Bruker amaZon SL instrument using standard conditions (ESI). UV–vis spectra were recorded on a Perkin Elmer Lambda 25 spectrometer. Fluorescence measurements were performed on a Perkin Elmer LS 55 spectrometer. All the measurement experiments were performed at room temperature.

3.3. General method

Stock solution of F$^-$, Cl$^-$, Br$^-$, I$^-$, ClO$_4^-$, AcO$^-$, NO$_3^-$, H$_2$PO$_4^-$, HSO$_4^-$ and CN$^-$ (10 mM) and probe 1 (1 mM) were prepared in THF. S$_2^-$ and N$_3^-$ were prepared in distilled water. Test solution were used by diluting stock solution using THF and water (9:1, v/v). All absorption and fluorescence spectra were recorded in a 1.0 cm quartz cell. The fluorescence quantum yield (Φ_F) was determined by the standard method by using Rhodamine 6G in EtOH as a reference. The refractive index of the solvent was taken into account in the measurements.

3.4. Synthesis of probe 1

To a solution of compound 2 (130 mg, 0.4 mmol) in toluene (25 mL) was added malononitrile (106 mg, 1.6 mmol), piperidine (50 μL, 0.5 mmol) and a catalytic amount of HOAc under argon. The mixture was stirred at refluxing conditions overnight and washed with water (2 × 50 mL). The organic layers were combined, dried over anhydrous MgSO$_4$, and evaporated in vacuo. The crude product was purified by column chromatography (CH$_2$Cl$_2$) to give compound 1 (98 mg) as a red solid in 63% yield. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.69 (s, 1H), 7.63–7.44 (m, 3H), 7.34–7.16 (m, 2H), 6.19 (s, 1H), 2.65 (s, 3H), 2.63 (s, 3H), 1.44 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.15, 153.43, 152.66, 148.27, 142.91, 139.19, 134.56, 133.81, 130.95, 129.78, 129.70, 127.66, 124.69, 122.98, 114.44, 113.22, 82.02, 15.23, 14.94, 14.37, 14.26; MS: calculated for [M-H]$^-$: 399.76, measured: 399.16.

4. Conclusions

In summary, a convenient colorimetric and ratiometric probe **1** for the selective and sensitive sensing of cyanide ions based on BODIPY dye was prepared. Among the tested anions, only cyanide could react with dicyanovinyl group within 100 s in the mixture of THF and water (v/v, 9/1) to cause the disruption of the extended π-conjugation of BODIPY and a blue shift of absorption and fluorescence spectrum, along with a color change from yellow-green to light pink. The sensing mechanism was investigated by ^{1}H NMR and MS spectroscopy. Moreover, there is a negligible influence of pH to

the detection of cyanide by probe **1**. All these results showed that this probe has attractive characteristics and was useful for detecting cyanide in environmental applications.

Acknowledgements

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ancr.2017.01.004.

References

[1] S. Kubik, Chem. Soc. Rev. 39 (3648) (2010) 14.
[2] P. Alreja, N. Kaur, RSC Adv. 6 (2016) 23169.
[3] M.H. Lee, J.S. Kim, J.L. Sessler, Chem. Soc. Rev. 44 (2015) 4185.
[4] B. Vennesland, E.E. Conn, C.J. Knowles, J. Westley, F. Wissing, Academic Press, London, 1981. Phytochemistry, 22,1983, 2640.
[5] D.W. Boening, C.M. Chew, Water Air Soil Pollut. 109 (1999) 67.
[6] C. Arivazhagan, R. Borthakur, R. Jagan, S. Ghosh, Dalton Trans. 45 (2016) 5014.
[7] R. Mudliar, S.S. Umare, D.S. Ramteke, S.R. Wate, J. Hazard. Mater. 164 (2009) 1474.
[8] N. Kuyucak, A. Akcil, Min. Eng. 50–51 (2013) 13.
[9] R.R. Dash, A. Gaur, C. Balomajumder, J. Hazard. Mater. 163 (2009) 1.
[10] T. Suzuki, A. Hioki, M. Kurahashi, Anal. Chim. Acta. 476 (2003) 159.
[11] T.T. Christisona, J.S. Rohrera, J. Chromatogr. A 1155 (2007) 31.
[12] A. Ishii, H. Seno, K.W. Suzuki, O. Suzuki, T. Kumazawa, Anal. Chem. 70 (1998) 4873.
[13] A.E. Lindsay, D. O'Hare, Anal. Chim. Acta. 558 (2006) 158.
[14] A. Safavi, N. Maleki, H.R. Shahbaazi, Anal. Chim. Acta. 503 (2004) 213.
[15] F. Wang, L. Wang, X.Q. Chen, J.Y. Yoon, Chem. Soc. Rev. 43 (2014) 4312.
[16] Z.C. Xu, X.Q. Chen, H.N. Kim, J.Y. Yoon, Chem. Soc. Rev. 39 (2010) 127.
[17] J.J. Li, X.L. Qi, W. Wei, Y.C. Liu, X. Xu, Q.H. Lin, W. Dong, Sens. Actuators B 220 (2015) 986.
[18] C. Cheng, H.Y. Chen, C.S. Wu, J.S. Meena, T. Simon, F.H. Ko, Sens. Actuators B 227 (2016) 283.
[19] Q.S. Zhang, J. Zhang, H.J. Zuo, C.Y. Wang, Y.J. Shen, Tetrahedron 72 (2016) 1244.
[20] S.D. Wang, X.L. Fei, J. Guo, Q.B. Yang, Y.X. Li, Y. Song, Talanta 148 (2016) 229.
[21] K.M. Xiong, F.J. Huo, C.X. Yin, Y.T. Yang, J.B. Chao, Y.B. Zhang, M. Xu, Sens. Actuators B 220 (2015) 822.
[22] X.B. Cheng, H. Li, F. Zheng, Q. Lin, Y.M. Zhang, H. Yao, T.B. Wei, Dyes Pigments 127 (2016) 59.
[23] Y. Shiraishi, M. Nakamura, N. Matsushita, T. Hirai, New J. Chem. 40 (2016) 195.
[24] J.B. Chao, Z.Q. Li, Y.B. Zhang, F.J. Huo, C.X. Yin, H.B. Tong, Y.H. Liu, Sens. Actuators B 228 (2016) 192.
[25] S.T. Wang, Y.W. Sie, C.F. Wan, A.T. Wu, J. Lumin. 173 (2016) 25.
[26] S.T. Wang, J.L. Chir, Y. Jhong, A.T. Wu, Dyes Pigments 167 (2015) 413.
[27] C. Arivazhagan, R. Borthakur, R. Jagan, S. Ghosh, Dalton Trans. 45 (2016) 5014.
[28] S. Suganya, S. Velmathi, Sens. Actuators B 221 (2015) 1104.
[29] J.J. Li, W. Wei, X.L. Qi, G.C. Zuo, J.K. Fang, W. Dong, Sens. Actuators B 228 (2016) 330.
[30] Y. Singh, T. Ghosh, Talanta 148 (2016) 257.
[31] S.B. Zhao, H.T. Liu, F. Wu, L.N. Zhu, Chem. Lett. 45 (2016) 570.
[32] T.B. Wei, H. Li, Q.Q. Wang, G.T. Yan, Y.R. Zhu, T.T. Lu, B.B. Shi, Q. Lin, Y.M. Zhang, Supramol. Chem. 28 (2016) 314.
[33] L. Yang, X. Li, Y. Qu, W.S. Qu, X. Zhang, Y.D. Hang, H. Ågren, J.L. Hua, Sens. Actuators B 203 (2014) 833.
[34] R. Sukato, N. Sangpetch, T. Palaga, S. Jantra, V. Vchirawongkwinc, C. Jongwohan, M. Sukwattanasinitt, S. Wacharasindhu, J. Hazard. Mater. 314 (2016) 277.
[35] T.B. Wei, W.T. Li, Q. Li, J.X. Su, W.J. Qu, Q. Lin, H. Yao, Y.M. Zhang, Tetrahedron Lett. 57 (2016) 2767.
[36] X.Y. Sun, Y. Wang, X.H. Deng, J.F. Zhang, Z. Zhang, RSC Adv. 6 (2016) 10266.
[37] W.C. Lin, J.W. Hu, K.Y. Chen, Anal. Chim. Acta 893 (2015) 91.
[38] A.K. Mahapatra, K. Maiti, R. Maji, S.K. Manna, S. Mondal, S.S. Ali, S. Manna, RSC Adv. 5 (2015) 24274.
[39] G.L. Fu, C.H. Zhao, Tetrahedron 69 (2013) 1700.
[40] A. Loudet, K. Burgess, Chem. Rev. 107 (2007) 4891.
[41] N. Boens, V. Leen, W. Dehaen, Chem. Soc. Rev. 41 (2012) 1130.
[42] J.S. Lee, H.K. Kim, S. Feng, M. Vendrell, Y.T. Chang, Chem. Commun. 47 (2011) 2339.
[43] L.J. Jiao, C.J. Yu, J.L. Li, Z.Y. Wang, M. Wu, E. Hao, J. Org. Chem. 74 (2009) 7525.