

## Notes

### Construction of molecular logic gates through a redox and protonation triggered OFF-ON fluorescent probe

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Received 18 March 2018; revised and accepted 20 July 2018

A BODIPY based fluorescent probe **1** for protons and oxidants has been reported. Probe **1** shows weak fluorescence due to the PET process and exhibits OFF-ON fluorescent emission response towards protons (HCl) and oxidants (Cu(ClO<sub>4</sub>)<sub>2</sub>) in CH<sub>3</sub>CN-H<sub>2</sub>O and CH<sub>3</sub>CN solution. The suppressed PET process is responsible for the change in fluorescent emission. Further, the OFF-ON fluorescent probe **1** can mimic the Boolean logic operation and work as a molecular OR logic gate with protons and oxidants as stimulus inputs and fluorescent emission at 520 nm as output. The combinations of Cu(ClO<sub>4</sub>)<sub>2</sub> and sodium L-ascorbate can be used to produce a molecular system displaying INHIBIT logic, due to indirect fluorescence quenching.

**Keywords:** BODIPY, Molecular logic gates, Molecular machines, Switchable materials, Redox fluorescent probes, Fluorescent probes, OFF-ON probes, Protonation

The design of molecular and supramolecular switches that change their fluorescence properties upon interaction with chemical inputs is not only an academically rewarding exercise but has also contributed decisively to the enormous success of chemosensing in analytical chemistry, applications in environmental sciences, life sciences, and clinical diagnostics<sup>1</sup>. The development of signal-controlling redox functionalities in molecular systems has attracted substantial research efforts directed to the design of information storage and processing systems and the development of new electronic materials<sup>2</sup>. In addition, designing fluorescent redox switchable materials is essential to provide a non-destructive readout capability. Moreover, such materials may also find use as probes for redox processes and in studies on electron and energy transfer mechanisms<sup>3</sup>. On the other hand, the measurement of pH by means of fluorescent probes is a simple but instructive example for the conceptual approach to fluorescence switching, sensing and imaging pH inside live cells<sup>4</sup>.

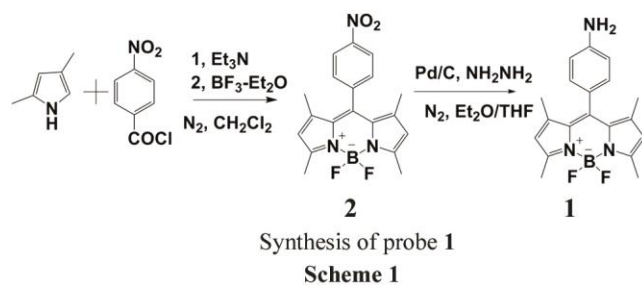
With the increasing demands of future information technology for miniaturization and function density, molecular logic gates that are capable of performing Boolean logic operation in response to physical, chemical, and biological inputs are becoming an inspiring trend in the forefront of research<sup>5</sup>. As fluorescence is a non-destructive readout signal with high detection sensitivity and simplicity, molecular logic gates with fluorescence as the output signal have attracted great attention<sup>6</sup>. Among various fluorescent dyes, the BODIPY scaffold has been found to be a most promising candidate for fluorescent sensing and labeling due to its excellent photophysical properties, such as sharp absorption and fluorescence peaks, high stability, and high fluorescence quantum yield<sup>7</sup>. Recently, several redox molecular dyads containing BODIPYs fluorophore including ferrocene-, flavin-, catechol-, quinine- and TTF-appended electrofluorochromic molecules were reported<sup>8</sup>.

Pan *et al.*<sup>9</sup> have explored a BODIPY-aniline based fluorescent sensor for detection of pH and CO<sub>2</sub> gas. In the present study, the amino-BODIPY (**1**) with amino group as redox moiety, which acts as a bi-functional fluorescent probe for both oxidant and proton, is reported. In this work, the fluorescent emission of **1** was weak due to the PET (photo-induced electron transfer) process, and the fluorescence was turned on by the redox and protonation process. This redox and protonation triggered OFF-ON fluorescent probe based on amino-BODIPY system could be used to mimic molecular logic gate.

#### Experimental

All reagents for synthesis obtained commercially were used without further purification. <sup>1</sup>H NMR spectra were recorded in DMSO-*d*<sub>6</sub> solution on the Bruker 400 MHz instrument, and spectral data reported in ppm relative to tetramethylsilane (TMS) as internal standard. UV-vis spectra were recorded on a Perkin Elmer Lambda 35 UV/vis spectrophotometer, while fluorescent spectra were recorded on a Perkin Elmer LS55 fluorescence spectrophotometer.

The amino-BODIPY **1** was prepared through the condensation reaction of 4-nitrobenzoyl chloride with 2, 4-dimethylpyrrole according to a published procedure<sup>9,10</sup>. Reduction of precursor with Pd/C-NH<sub>2</sub>NH<sub>2</sub> gave the target compound **1** (Scheme 1). The purity and structure



of **1** was confirmed by the  $^1\text{H}$  NMR data (Supplementary data, Fig. S1), which was consistent with the reported data [ $^1\text{H}$  NMR (400 Hz,  $\text{DMSO-}d_6$ ),  $\delta$ : 6.90–6.93 (d, 2H, ArH), 6.68–6.71 (d, 2H, ArH), 6.15 (s, 2H, Pyrrole H), 5.45 (s, 2H,  $\text{NH}_2$ ), 2.42 (s, 6H,  $\text{CH}_3$ ), 1.49 (s, 6H,  $\text{CH}_3$ )].

## Results and discussion

Fluorescent ON-OFF pH probes generally require a pH-sensitive moiety whereby protonation/deprotonation modifies the quantum yield of a linked fluorophore either through PET (photoinduced electron transfer) quenching phenomena or ICT (internal charge transfer). Among the various pH-sensitive moieties, the amino group is one of the popular basic moiety used for protonation to moderate the fluorescence.

Probe **1** showed a weak fluorescence ( $\Phi = 0.03$ ) at 520 nm in  $\text{CH}_3\text{CN-H}_2\text{O}$  (v:v, 1:1) solution due to an efficient PET process from the lone pairs of electrons on amino group to the excited BODIPY fluorophore. The fluorescent properties of probe **1** upon protonation by HCl solution were investigated in  $\text{CH}_3\text{CN-H}_2\text{O}$  solution. As shown in Fig. 1, the fluorescence of **1** increased remarkably with the acidity of the solution. The color of the solution changed from yellow to bright green and the solution gave off visible green fluorescence emission. Thus, probe **1** could act as an efficient off-on fluorescent indicator for acidic environment. The protonated amino group of probe **1** suppressed the PET process accounting for the turn-on fluorescence response of probe **1**.

The electrochemical properties of **1** were studied by cyclic voltammetry (CV) in acetonitrile containing 0.10 M tetrabutylammonium perchlorate (TBAP) using a glassy carbon electrode with a reversible redox oxidation waves at +0.65 V (Supplementary data, Fig. S2), which corresponded to that of the cation of compound **1**. The results showed that compound **1** would be suitable for oxidation-reduction chemical switch. Therefore, the chemical oxidation of probe **1** was carried out.

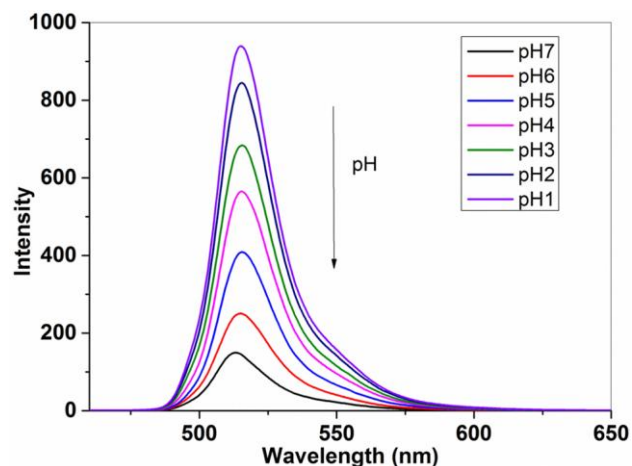


Fig. 1 — Fluorescence emission spectra of probe **1** (5  $\mu\text{M}$ ) in  $\text{CH}_3\text{CN-H}_2\text{O}$  solution in the presence of HCl. An enhanced fluorescence signal was observed on protonation of amino group.

Probe **1** also showed a weak fluorescence ( $\Phi = 0.05$ ) at 520 nm in  $\text{CH}_3\text{CN}$  due to the PET process. Oxidative titrations of **1** with  $\text{Cu}(\text{ClO}_4)_2$  in  $\text{CH}_3\text{CN}$  at 298 K were carried out by fluorescent spectroscopy. Time course study revealed that the reaction between probe **1** and  $\text{Cu}(\text{ClO}_4)_2$  was completed in about 40–50 min in  $\text{CH}_3\text{CN}$  solution. Probe **1** exhibited strong OFF-ON fluorescence responses towards  $\text{Cu}(\text{ClO}_4)_2$  and the solution gave off strong green fluorescence emission with the color of the solution changing from yellow to red.

To evaluate the sensitivity of probe **1** based assay, varying amounts of  $\text{Cu}(\text{ClO}_4)_2$  were spiked into the solution of probe **1**. The solutions were incubated at room temperature for 1 h and then analyzed by fluorometry. Figure 2a shows that the fluorescence emission centered at 520 nm increased as a function of  $\text{Cu}(\text{ClO}_4)_2$  concentrations in  $\text{CH}_3\text{CN}$  solution with concentrations between 0.5 and 3 equiv. The fluorescence almost reached the maximum intensity after addition of one equivalent of this oxidant metal cation.

The back-reduction was achieved by adding sodium L-ascorbate. Figure 2b shows that upon the addition of sodium L-ascorbate from 0.5 to 2 equiv. to the oxidized solution, the fluorescence gradually decreases. However, on adding only sodium L-ascorbate to the solution of probe **1**, no fluorescence changes were observed, clearly indicating that,  $\text{Cu}(\text{ClO}_4)_2$  and sodium L-ascorbate together can be used to control the OFF-ON-OFF switching of the fluorescent probe **1**.

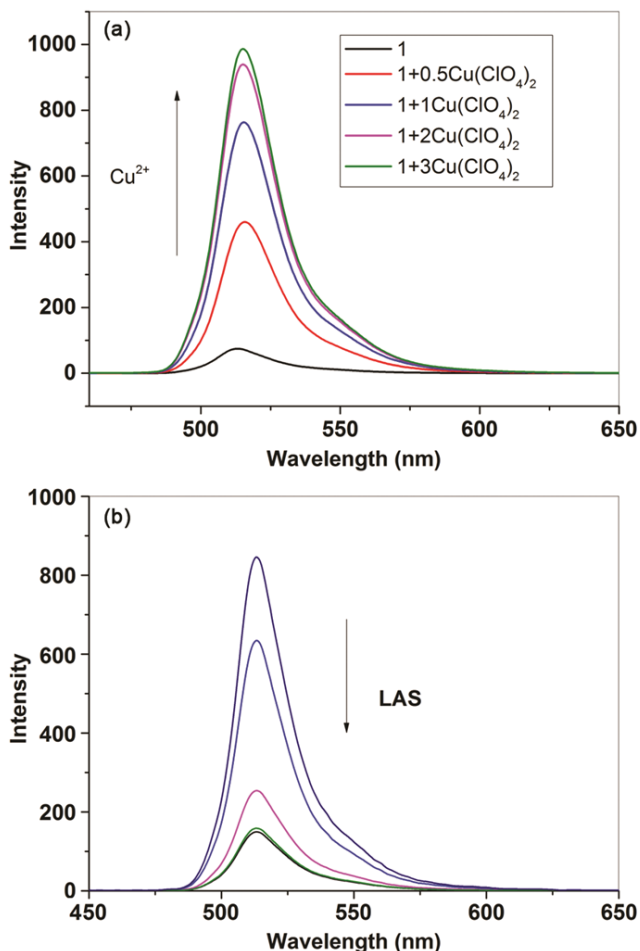


Fig. 2 — Fluorescence emission change of probe **1** in CH<sub>3</sub>CN solution. [(a) fluorescence enhancement upon titration of Cu(ClO<sub>4</sub>)<sub>2</sub> (0–3 equiv.); (b) Fluorescence quenching when further chemically reduced by sodium L-ascorbate, in presence of 2 equiv. Cu(ClO<sub>4</sub>)<sub>2</sub>].

Compared to the remarkable change in emission, the UV-vis absorption spectrum of complex **2** in CH<sub>3</sub>CN was not substantially affected by the addition of the oxidant, Cu(ClO<sub>4</sub>)<sub>2</sub> (Fig. 3).

The fluorescence of probe **1** could be restored by oxidizing the amino to cation, which prevents the electron transfer between the amino group and BODIPY fluorophore. As shown in Fig. 4, the excited fluorophore allows for a competition between PET and emission pathways. In the neutral state, electron transfer from the electron-rich donor quenches the excited state fluorophore resulting in a weak fluorescent emission. The electron-donor module becomes electron deficient after oxidation of the electron donor. In this case, the PET process from the electron donor to the fluorophore was prohibited and resulted in strong fluorescent emission<sup>3a</sup>.

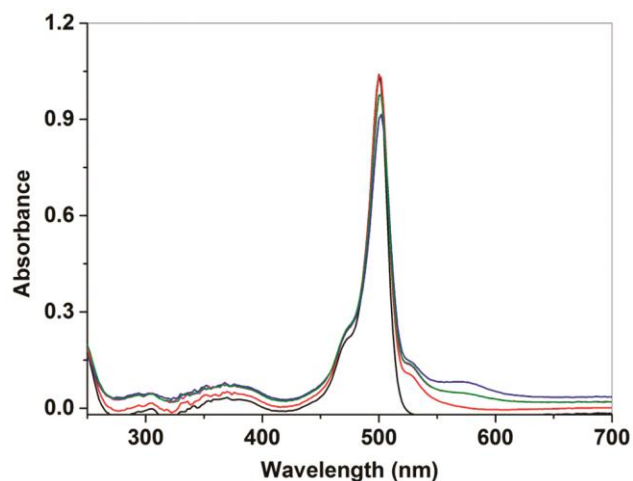


Fig. 3 — UV-vis spectra of probe **1** in CH<sub>3</sub>CN solution in the presence of various concentrations of Cu(ClO<sub>4</sub>)<sub>2</sub>.

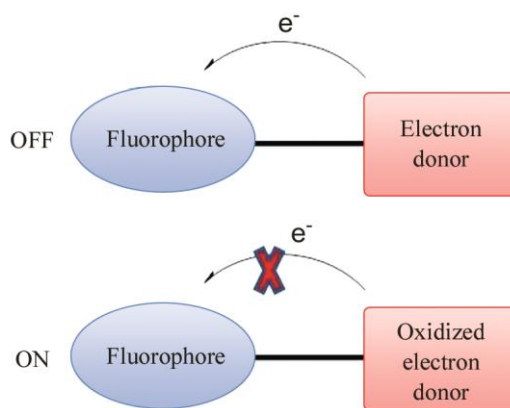
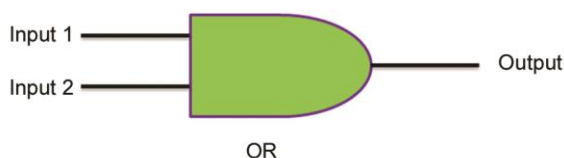


Fig. 4 — Schematic representation of a PET redox-fluorescent switch consisting of probe **1** with ‘fluorophore-spacer-electron donor’ arrangement.

In recent times, mimicking the function of silicon chips and building electronic devices based on optoelectronic responses of organic/ inorganic molecules in the presence of external stimuli have attracted great attention. The molecular scaffolds that display sensitive optical behavior (output) and transform macroscopic properties according to logic operations in the presence of chemical inputs are in high demand to develop tunable miniaturized logic gates<sup>11</sup>. Logic gates are the fundamental components of electronic and digital circuit. These logic gates perform logical operations in which they produce logical output signals with one or more logical input signals. These signals are represented in two binary conditions namely, low (0) and high (1) states, making them fundamental units of silicon-based computer components. Thus, the molecular logic gates could be used to make essential computer components, by



Truth table of an OR logic gate for Probe 1

| Input 1 (acid) | Input 2 (oxidant) | Output (520 nm) |
|----------------|-------------------|-----------------|
| 0              | 0                 | 0               |
| 1              | 0                 | 1               |
| 0              | 1                 | 1               |
| 1              | 1                 | 1               |

Fig. 5 — Schematic representation of an OR gate built from probe 1.

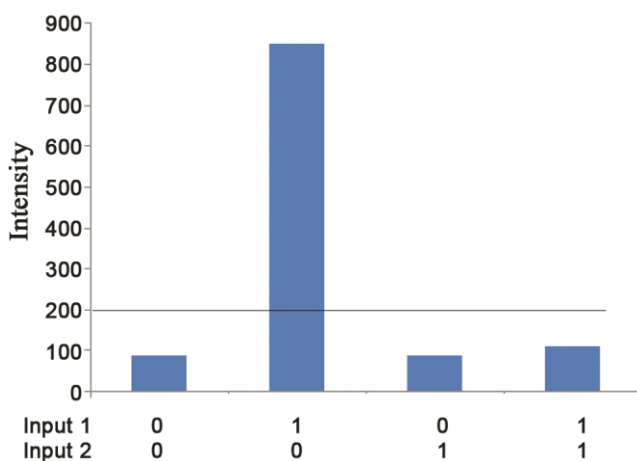


Fig. 6 — Schematic representation of an INHIBIT gate built from probe 1.

converting chemical input signals into measurable output signals.

From above results, we find that the fluorescence of probe 1 can be turned on by acid (protons) and oxidants<sup>9</sup>. These studies inspired us to utilize probe 1 to develop an OR logic gate for a molecular traffic signal with two inputs: acid and oxidant as input-1 and input-2, respectively. The output of the OR gate is normally switched on if either one or both inputs are turned ON.

To create logic circuits according to the truth tables, digital values have been assigned as binary numerals, “1” and “0” to illustrate high and low emission outputs as well as applied inputs (present 1; absent 0), respectively. In a truth table, output emissions which are 50% or above the maximum have been considered as high (1) and the emission intensity below 200 a.u. has been considered as low (0), respectively. Starting with the neutral state of probe 1, this molecule can perform as a molecular OR

logic gate as shown in Fig. 5. Probe 1 can be oxidized or protonated to fluorescent 1, which emits at 520 nm as an output, with acid and oxidant as input-1 and input-2 respectively. Thus, an OR logic gate was obtained when the output is read at 520 nm.

The fluorescence change of probe 1 induced by oxidation-reduction reaction could also be used to construct INHIBIT logic gates<sup>12</sup> with  $\text{Cu}(\text{ClO}_4)_2$  and sodium L-ascorbate as two inputs. Four situations are examined (Fig. 6), in which  $\text{Cu}(\text{ClO}_4)_2$  as input-1 is 5  $\mu\text{M}$  (high, 1) or 0  $\mu\text{M}$  (low, 0) and sodium L-ascorbate as input-2 is 5  $\mu\text{M}$  (high, 1) or 0  $\mu\text{M}$  (low, 0). The fluorescent emission at 520 nm acts as the output. As shown in Fig. 6, the emission at 520 nm (output) becomes high only when 1 equiv. of  $\text{Cu}(\text{ClO}_4)_2$  is added. In contrast, the emission is low for any other combination.

In summary, a PET based OFF-ON fluorescent probe 1 for protons and oxidants has been developed. Molecular OR and INHIBIT logic gates have been constructed by employing probe 1 as gate and protons, oxidant and reductant as chemical inputs, which is promising for the construction of next-generation molecular devices with better applicability.

### Supplementary data

Supplementary data associated with this article are available in the electronic form at [http://www.niscair.res.in/jinfo/ijca/IJCA\\_57A\(8-9\)1128-1132\\_SupplData.pdf](http://www.niscair.res.in/jinfo/ijca/IJCA_57A(8-9)1128-1132_SupplData.pdf).

### Acknowledgement

This work was supported by Sheng Tongsheng Innovation Fund (GSAU-ST51737) and FuXi Young Talents Introduction Projects of Gansu Agricultural University (GSAU-RCZX201704).

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