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Fluorescence signaling of BF_3 species by transformation of an ESIPT dye to its difluoroboron adduct

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New selective and sensitive probes were developed for signaling chemically and industrially important, but toxic, BF_3 species. These probes utilize the transformation of 2-(2-hydroxyphenyl)benzothiazole derivatives into their boron difluoride adducts. Benzothiazole-based probes demonstrated significant off-on fluorescence enhancement ($I/I_0 > 2000$) in the presence of BF_3 species in acetonitrile. The BF_3 signaling was nearly instantaneous and completed within less than 1 min. Furthermore, interference from possible BF_3 decomposition contaminants, such as boric acid, HF, and BF_4^-, was not observed. A dye-immobilized polymer, prepared by RAFT copolymerization of dye-derived acrylamide monomer with methyl methacrylate, was successfully used for the signaling of BF_3 species with a detection limit of 8.7×10^{-8} M. These probes could be useful for the sensitive and selective fluorescent detection of important but toxic BF_3 species in chemical and industrial applications.

1. INTRODUCTION

Boron halides are widely used in laboratory and industrial applications as catalysts and reagents for numerous organic reactions and as starting materials for many organoboron and inorganic boron compounds [1–5]. In particular, boron trifluoride, BF_3, has been widely used as a Lewis acid catalyst and in vapor deposition processes in the semiconductor industry [6–8]. BF_3 is also used in polymer synthesis, because it efficiently polymerizes unsaturated compounds such as butylenes, styrene, and vinyl esters, and easily cleaves cyclic molecules, such as tetrahydrofuran [9]. Furthermore, it is used industrially as an initiator in cationic polymerization, to yield highly reactive exo-olefin terminated polyisobutylene [10], and as a dopant for the preparation of highly conducting polyaniline [11]. However, BF_3 is toxic, primarily as a pulmonary irritant [12]. In laboratory tests on animals, exposure to BF_3 induced serious effects ranging from increased pneumonitis to death. The threshold limit value is 1 ppm [13–15], and inhalation toxicity studies on rats have shown that exposure to BF_3 at 17 mg/m^3 resulted in renal toxicity [16].

Despite the widespread application of these hazardous species, few reliable BF_3 determination methods have been reported. Earlier, a procedure for the sampling and analysis of gaseous boron trifluoride has been developed [17,18]. In addition, analyses of the hydrolysis products (boron, halide, and free halogen) of boron trihalides, BX_3, have been reported [19]. Recently, detection of chemically and biologically important species through selective and efficient optical signaling and imaging systems became an active area of research [20–27]. However, we found only two reports regarding optical BF_3 sensors: these reports describe the uses of hybrid mesostructured thin films functionalized with grafted dibenzoylmethane and rhodamine–naphthalimide conjugate based ratiometric fluorescence probe [28,29]. Very recently, reaction-based colorimetric signaling for closely related species BBr_3 has been reported, using the dibromoborylation of *N*,*N*-dimethylaniline, with a rather high detection sensitivity [30].

BF_3 forms stable complexes with oxygen, nitrogen, and sulfur compounds, including alcohols, acids, ethers, amines, and sulfides. These complexes constitute most of the commercially available BF_3 species. Furthermore, many dyes can be transformed into more useful fluorescent dye systems using boron-complexed anionic N,N or N,O ligands, such as 2-(hydroxyphenyl)benzazoles [31] and aniline-imines (BORANILs) [32]. Systems containing a tetrahedral boron(III) center are particularly effective and have attracted the attention of many synthetic chemists [33]. These systems frequently display unusual spectroscopic behavior, including greatly enhanced emissions. Some of the most important examples are 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)-based dyes. These difluoroboron adducts have been widely used because of

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their exceptional optical properties, such as strong UV absorption, narrow absorption and emission bands, high fluorescence quantum yields, and photostability [34–38]. Moreover, boron difluoride complexes derived from β-diketonates have been developed for photonics applications, such as OLEDs, solid dye lasers, chemical sensors, and two-photon biological labels [39].

Here we report novel reaction-based BF_3-selective fluorescent signaling probes. These probes are based on the BF_2 adduct formation of an excited-state intramolecular proton transfer (ESIPT) dye of benzothiazole. It has previously been reported that some 2-(2-hydroxyphenyl) benzazoles are readily transformed into their BF_2 adducts via complexation with BF_3 and that these adducts have high quantum efficiencies [40]. The rigid structures of these adducts are comprised of BF_2-complexed benzazole and phenol moieties, which block the vibrational and rotational nonradiative deactivation channels. This leads to greatly enhanced fluorescence quantum yields, compared those of their parent fluorophores [41]. Designed probes demonstrated remarkable BF_3-selective and sensitive off-on fluorescence signaling behavior. Furthermore, these probes were successfully applied to the signaling of BF_3 species in commercial products, such as diethyl ether, acetonitrile, methanol, and acetic acid complexes, using reversible addition-fragmentation chain transfer (RAFT) polymerized dye.

2. EXPERIMENTAL SECTION

2.1. General

2-(2-Hydroxyphenyl)benzothiazole (**1HBT**), 2-(2-hydroxyphenyl)benzoxazole (**1HBO**), 2-(2-hydroxyphenyl)-1*H*-benzimidazole (**1HBI**), and boron trifluoride complexes were purchased from Sigma-Aldrich Co. Polyphosphoric acid was obtained from Alfa Aesar. All other solvents and reagents were purchased from commercial suppliers. ^1H (600 MHz) and ^{13}C (150 MHz) NMR spectra were obtained using a Varian VNS NMR spectrometer with residual solvent signals as standards. UV–vis spectra were obtained with a Scinco S-3100 spectrophotometer equipped with a Peltier temperature controller. Fluorescence spectra were measured with a PTI QuantaMaster steady-state spectrofluorometer. Mass spectra were obtained using a Micromass Autospec mass spectrometer. Gel permeation chromatography was conducted with an Agilent 1100 S system. Column chromatography was performed using silica gel (Merck, 240 mesh). All spectroscopic measurements were carried out using spectroscopic grade solvents.

2.2. Preparation of BF_2 adduct of **1HBT**

The BF_2 adduct of **1HBT** was prepared as per a previously reported procedure [42]. A mixture of **1HBT** (682 mg, 3.0 mmol) and *N*,*N*-diisopropylethylamine (1.05 mL, 6.0 mmol) in dichloromethane (8 mL) was stirred for 10 min at room temperature. Then, $BF_3{\cdot}Et_2O$ (1.48 mL, 12.0 mmol) was added dropwise and the mixture was stirred for 30 min. The resulting precipitate was filtered and washed three times with dichloromethane. The product was purified by column chromatography (CH_2Cl_2:CH_3OH = 29:1, *v*/*v*) to yield **1HBT-BF$_2$** as a white powder. Yield: (650 mg, 79%). ^1H NMR (600 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.92 (dd, *J* = 8.1, 0.5 Hz, 1H), 7.68 (td, *J* = 7.9, 7.5, 1.3 Hz, 2H), 7.62–7.54 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.03 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) *δ* 169.1, 156.3, 143.6, 137.1, 129.1, 128.8, 127.3, 126.9, 122.0, 120.6, 120.5, 120.4, 113.1. LRMS: (DIP$^+$); *m/z* calcd for $C_{13}H_8BF_2NOS^+$ [M]$^+$: 275.0, found 274.8.

2.3. Preparation of 2-(2-hydroxy-4-aminophenyl)benzothiazole 2

Amine derivative **2** was synthesized according to a slightly modified literature procedure [43]. A solution of 4-aminosalicylic acid (1.53 g, 10 mmol) and 2-aminothiophenol (1.25 g, 10 mmol) in polyphosphoric acid (10 mL) was stirred at 180 °C for 4 h. After the mixture had cooled to room temperature it was adjusted to pH 7.0 using 10% sodium hydroxide solution. The resulting precipitate was filtered and washed with distilled water until the washed solution became colorless. The precipitate was purified by column chromatography (CH_2Cl_2:CH_3OH = 9:1, *v*/*v*) to yield **2** as a dark green powder. Yield: (1.86 g, 77%). ^1H NMR (600 MHz, DMSO-d_6) δ 11.73 (s, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 8.6 Hz, 1H), 6.17 (s, 1H), 5.94 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) *δ* 168.2, 159.0, 154.0, 152.1, 132.7, 130.3, 126.7, 124.5, 122.1, 121.2, 107.5, 106.6, 99.7. LRMS: (DIP$^+$); *m/z* calcd for $C_{13}H_{11}N_2OS^+$ [M + H]$^+$: 243.1, found 243.0.

2.4. Preparation of 2-(2-hydroxy-4-acrylamidophenyl)benzothiazole monomer 3

Acrylamide monomer **3** was prepared following a slightly modified literature procedure [44]. Acryloyl chloride (180 mg, 2.0 mmol) was added to a solution of amine **2** (243 mg, 1.0 mmol) in DMF (5 mL). The reaction mixture was stirred for 6 h at room temperature, and then poured into distilled water (10 mL). The precipitate was filtered and dried in a vacuum oven. The product was purified by column chromatography (CH_2Cl_2:CH_3OH = 19:1, *v*/*v*) to yield a dark green powder. Yield: (265 mg, 90%). ^1H NMR (600 MHz, DMSO-d_6) δ 11.65 (s, 1H), 10.37 (s, 1H), 8.12 (t, *J* = 8.2 Hz, 2H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.68 (s, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.21 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.46 (dd, *J* = 16.9, 10.1 Hz, 1H), 6.30 (d, *J* = 17.3 Hz, 1H), 5.81 (d, *J* = 10.4 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) *δ* 165.4, 163.9, 157.3, 151.9, 143.1, 134.4, 132.1, 129.5, 128.0, 126.8, 125.2, 122.3, 122.2, 114.4, 111.5, 107.0. LRMS: (DIP$^+$); *m/z* calcd for $C_{16}H_{12}N_2O_2S^+$ [M]$^+$: 296.1, found 296.2.

2.5. Preparation of polymeric probe **4**

Poly(methyl methacrylate)-based polymeric probe **4** was prepared by RAFT copolymerization of methyl methacrylate (MMA) and acrylamide-functionalized dye monomer **3**. MMA (1.5 mL, 14 mmol) and AIBN (2 mg, 0.011 mmol) were dissolved in benzene (0.5 mL). RAFT reagent (2-cyano-2-propyl benzodithioate, 12.3 mg, 0.056 mmol) and ESIPT dye monomer **3** (41 mg, 0.14 mmol) were added to the solution. The resulting mixture was de-gassed by argon flushing. The solution was polymerized by heating it in a water bath (60 °C) for 15 h. To remove the unpolymerized methyl methacrylate and acrylamide dye **3**, the product was reprecipitated using methanol three times. M_n: 1.46×10^4, polydispersity index (PDI): 1.22 (by GPC analysis). ^1H NMR (600 MHz, $CDCl_3$) δ 12.59 (s), 8.3–7.85 (m), 7.7–7.2 (m), 3.92–3.25 (m), 3.58 (s), 2.24–.60 (m), 1.79 (s), 1.51–1.33 (m), 1.20 (m), 1.01 (s), 0.82 (s). ^{13}C NMR (150 MHz, $CDCl_3$) *δ* 178.1, 178.0, 177.7, 176.9, 54.4, 54.2, 51.8, 51.8, 51.7, 51.7, 45.5, 44.9, 44.9, 44.5, 18.7, 16.5.

2.6. Standardization of commercial BF_3 species by acid-base titration [45]

Solutions of commercially obtained BF_3 species were prepared by dissolving them in distilled water (25 mL) with 20 mL of aqueous calcium chloride solution (20%, *w*/*w*). The samples were heated to 80 °C for 30 min. After cooling the solution, the resulting mixtures were titrated with standard 0.1 M sodium hydroxide solution using