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Fluorescent dyad for cooperative recognition of copper cation and halogen anion

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ABSTRACT

TMS-ethynyl triazolyl benzothiadiazole (BTD) derivatives have been successfully synthesized by mono deprotection of di-TMS-ethynyl BTD followed by click chemistry. The fluorescence intensity of TMS-ethynyl triazolyl BTD–DCM dyad **8**, as well as triazolyl BTD **3,** and the DCM derivative **7** could be selectively quenched by Cu^{2+}, but almost not affected by different tested anions. Interestingly, the fluorescence emission of DCM-based fluorophores **7** and **8** was highly sensitive to a combination of Cu^{2+}, F^-, or Br^- in a sequence dependent manner. With the dyad **8**, the detection limit as low as 0.13 ppb could be attained for F^- in MeCN. The Cu^{2+}-promoted aerobic oxidative dimerization of DCM moiety to tetrahydrofuran derivatives has also been demonstrated for the first time.

The development of fluorescent chemosensors and chemodosimeters for sensing environmentally or biologically important metal ions and anions has gained considerable attention in recent years.[1] For example, fluorescent sensors for Cu^{2+} have been extensively investigated as it is a significant metal pollutant due to its wide industrial use, and it is also implicated in various biological activities as enzyme cofactors, in neurogenerative diseases and oxidative stress.[2] Most Cu^{2+} chemosensors (chelation-based probes[1b]) are based on PET (photoinduced electron transfer)/EET (electron energy transfer) mechanisms. Chemodosimeters (reaction-based probes[1b]) for Cu^{2+} by oxidation of aromatic amine[3] or phenol derivatives,[4] and hydrolysis[5] have been recently reported. On the other hand, F^- triggered Si–O bond cleavage has been used for the design of fluoride specific chemodosimeters.[6] However, the design of chemosensors for the detection of both cation and anion is more challenging.[4b]

Dicyanomethylene-4*H*-pyran (DCM) derivatives, thanks to their excellent optical-electronic properties (red light emission, high fluorescent yield, and good photostability), have been investigated for OLED emitters, logic gates, optical chemosensors and bioimaging.[7] Benzothiadiazole (BTD) derivatives have also been used in the development of organic light-emitting materials or fluoroionophores for Ni^{2+} and Cu^{2+}.[8] DCM derivatives have absorption near 450–500 nm and emission around 600–650 nm; while the emission band of BTD derivatives appears near 500 nm when excited around 370 nm. Such a spectroscopic property is favorable to energy transfer between these two fluorophores. As a continuing interest in the development of fluorescent molecules,[9] we envisioned to conjugate these two fluorophores with the click chemistry to prepare the dyad **8** with the trimethylsilyl (TMS) group on the BTD moiety so as to study their sensing properties toward various cations and anions. Such a system may exhibit the phenomenon of fluorescence resonance energy transfer from BTD to DCM. The triazolyl BTD **3** was synthesized for comparison.

4,7-Di-trimethylsilylethynyl benzothiadiazole **1**[10] can be mono desilylated with a catalytic amount of KOH in MeOH to **2** (Scheme 1). Copper-catalyzed Huisgen [3+2] cycloaddition[11] of the crude **2** with ethyl 3-azidopropanoate led to compound **3**[12] in 62% yield for two steps. The azido functionalized DCM **7** was prepared by condensation of *tert*-butyl DCM **6**[13] with the azido aldehyde **5** which was obtained by mesylation of the hydroxy aldehyde **4** followed by substitution with NaN_3 in DMF at 90 °C. The (*E*)-isomer was obtained in 75% yield. Click reaction of **7**[14] with the monotrimethylsilyl ethynyl BTD **2** led to the target compound **8**[15] in 46% for two steps.

As expected, compounds **3** and **7** displayed the usual photophysical properties of BTD ($\lambda_{emission}$ = 498 nm when excited at 370 nm, Fig. 1 and S1) and DCM ($\lambda_{emission}$ = 615 nm when excited at max. absorption of 457 nm, Fig. 2 and S2), while the dyad **8** displays an emission band of DCM fluorophore (605 nm, Fig. 3) when excited at 370 nm (absorption of BTD, Fig. S3), as a consequence of the energy transfer from BTD to DCM moiety (Fig. S4). The fluorescence quantum yield (Φ_F) for **3** and **7** was determined to be 0.79 and 0.30 with reference to quinine sulfate in MeCN, with a molar

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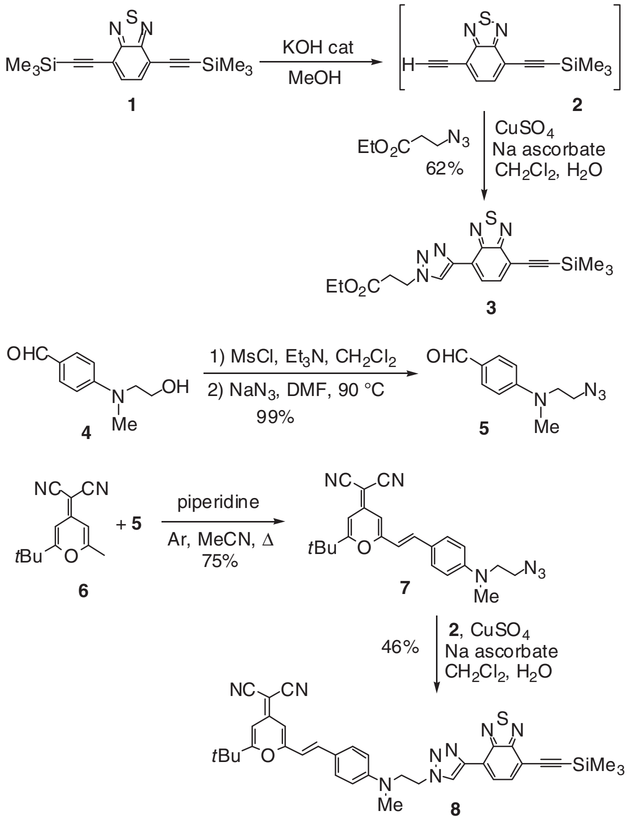

Scheme 1. Synthesis of fluorophores **3**, **7,** and dyad **8**.

extinction coefficient of 11,800 and 43,000 mol^{-1} L cm^{-1}, respectively. The molar extinction coefficient was found to be 40,700 mol^{-1} L cm^{-1} for compound **8**. To get an insight into the binding properties of compounds **3**, **7,** and **8**, we first investigated absorption and emission changes upon addition of 8 equiv of selected cations and anions in MeCN. Through deprotection of the TMS group, F^- induces a slight fluorescence quenching of compounds **3** and **8**, associated with a slight blue shift from 496 to 489 nm in the case of compound **3**. No influence on fluorescence emission was observed with other tested anions on **3**, **7,** and **8** (Figs. 1–3).

Among the metal cations tested, Cu^{2+}, Ni^{2+}, and to a lower extent Hg^{2+}, Co^{2+} and Fe^{2+} induced a significant decrease in fluorescence intensity in **3** (Fig. 1). For DCM derivative **7**, the presence of Cu^{2+} resulted in a complete quenching of fluorescence, while Fe^{2+} and Hg^{2+} induced a decrease of fluorescence intensity to ca. 75% and 60% of their initial value, respectively (Fig. 2). In the case of dyad **8**, addition of Cu^{2+} immediately resulted in a discoloration of the solution, associated with the apparition of the characteristic fluorescence of BTD around 490 nm (Fig. 3). Moreover, the max. absorption band of the DCM fluorophore at 457 nm disappeared upon addition of Cu^{2+} to compounds **7** and **8** (Figs. S2 and S3). Among other metal cations tested, the most notable effects were exhibited by Ni^{2+}, Fe^{2+}, and Hg^{2+}, resulting in a ca. 50–70% quenching of fluorescence.

Having established the selectivity of ion recognition by fluorophores **3**, **7,** and **8**, our interest then focused on studying the effect of combining cations and anions. Our choice turned to Cu^{2+} as a cation, since it affects both DCM and BTD moieties. F^- (which induces TMS-alkyne deprotection) and Br^- (inert) were selected as anions, on the basis of their ability to form stable complexes of

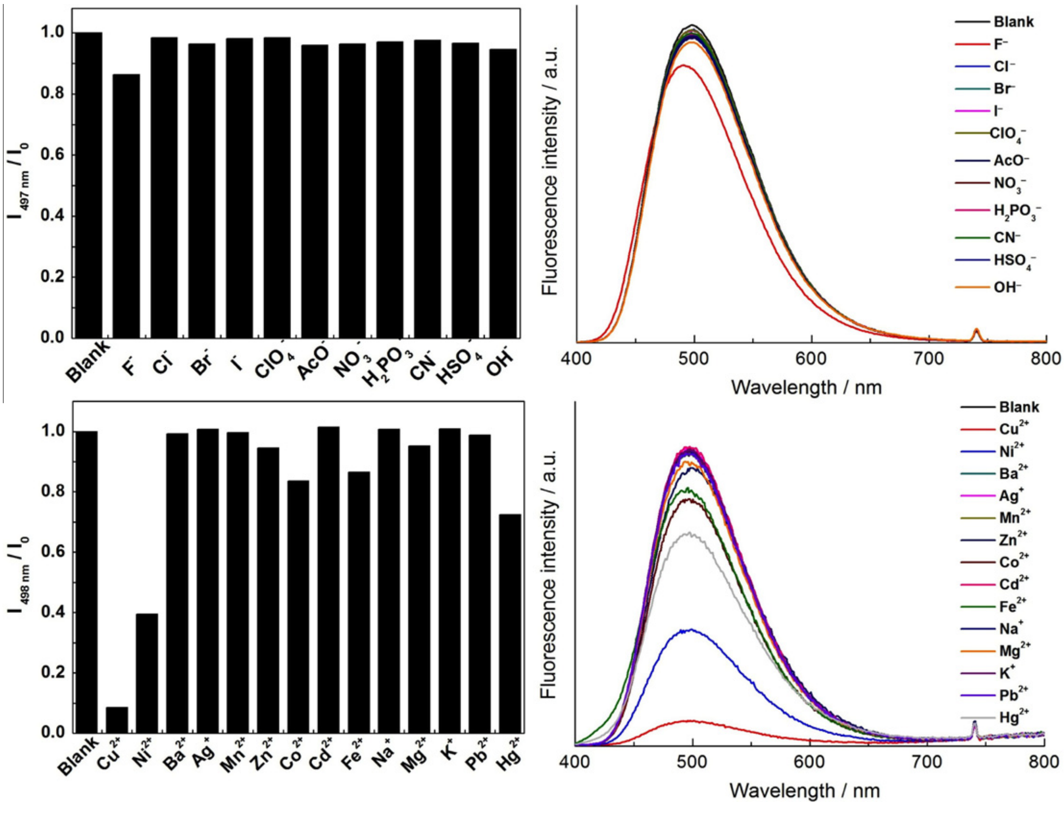

Figure 1. Fluorescence intensity ratio (left) and emission spectra (right) of **3** (10 μM in MeCN) after addition of 8 equiv ions (λ_{ex} = 370 nm).