

Selective Hg(II) Sensing with Improved Stokes Shift by Coupling the Internal Charge Transfer Process to Excitation Energy Transfer

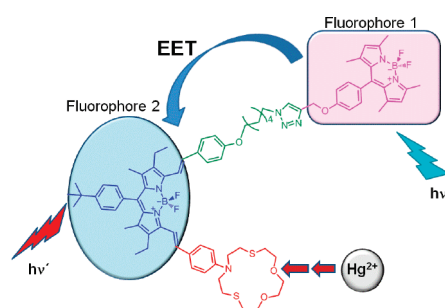
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ABSTRACT



Versatile chemistry of the Bodipy chromophore allows modular assembly of an excitation energy donor, acceptor, and a cation selective ligand in just a couple of steps. The new approach should be applicable in other designs which target molecular sensors with large Stokes shifts and red to near IR emission.

Ion sensing and signaling continues to be a vibrant field of study.¹ The signal transduction phenomenon, which is at the core of signal generation, is a binding event which changes the spectral signature of a particular chromophore or fluorophore. In designing a molecular sensor, typically an ion-selective ligand is incorporated into the structure. The ion binding is then expected to alter either ground state or excited

state properties to yield a quantifiable signal. This signal in many cases will be in the form of a shift in the absorbance spectra or changes in the emission characteristics (intensity, lifetime, or position of the emission maximum). While some of the selective ion sensors are actually serendipitous discoveries of selective interactions of a particular receptor with the analyte in question, it is indeed possible to rationally design molecular sensors. To that end, ion-induced changes in internal charge transfer (ICT)² or photoinduced electron transfer (PET)³ appear to be very useful. However, other

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(1) (a) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515. (b) Xu, Z.; Yoon, J.; Spring, D. R. *Chem. Soc. Rev.* **2010**, *39*, 1996. (c) Kim, J. S.; Quang, D. T. *Chem. Rev.* **2007**, *107*, 3780. (d) Wu, J.-S.; Hwang, I.-C.; Kim, K. S.; Kim, J. S. *Org. Lett.* **2007**, *9*, 907. (e) Lee, M. H.; Wu, J. -S.; Lee, J. W.; Jung, J. H.; Kim, J. S. *Org. Lett.* **2006**, *8*, 371.

(2) (a) Bourson, J.; Valeur, B. *J. Phys. Chem.* **1989**, *93*, 3871. (b) Oguz, U.; Akkaya, E. U. *Tetrahedron Lett.* **1998**, *39*, 5857.

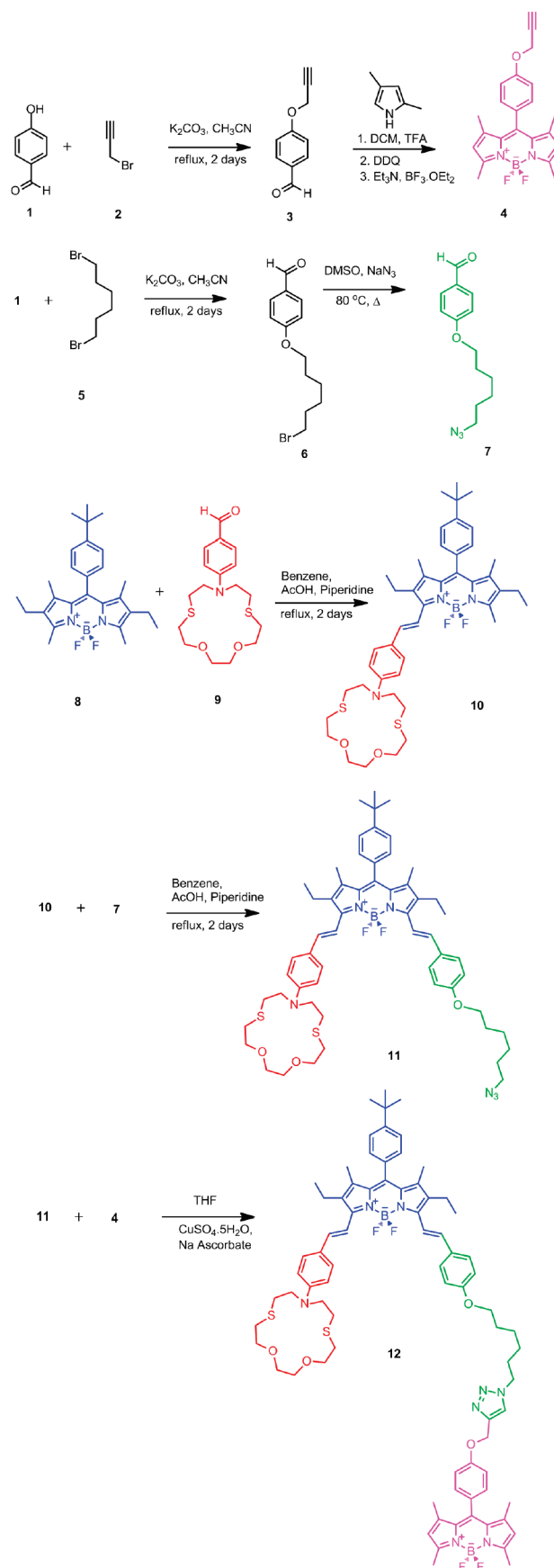
(3) (a) de Silva, A. P.; McClenaghan, N. D. *J. Am. Chem. Soc.* **2000**, *122*, 3965. (b) de Silva, A. P.; Gunaratne, H. Q. N.; Sandanayake, K. R. A. S. *Tetrahedron Lett.* **1990**, *31*, 5193. (c) Ozmen, B.; Akkaya, E. U. *Tetrahedron Lett.* **2000**, *41*, 9185.

fluorophore characteristics such as Stokes shift or brightness (usually defined as the product of quantum yield and the molar extinction coefficient) are more difficult to modulate. We recently proposed⁴ a systematic solution addressing this particular problem via coupling of excitation energy transfer to standard signal transduction processes. In this way, as long as the energy transfer is efficient, large pseudo-Stokes shifts are essentially guaranteed. As a bonus, if the excitation energy transfer (EET) efficiency itself can be modulated by ion binding, changes in intensity ratios take place at a wider range, thus increasing the dynamic range of the molecular sensor.^{4b} In our previous work,³ we demonstrated the utility of this approach by the synthesis of fluorophores linked through phenylethynyl groups. In this work, our intention was to move the operation wavelengths more into the red/near IR region and make use of unique Bodipy chemistry⁵ together with Huisgen type “Click” chemistry⁶ to emphasize the modularity of our approach.

The synthesis (Scheme 1) of the target molecule starts with the placement of a terminal alkyne moiety at the *meso* position of a Bodipy dye **4**. Azido-tethered aromatic aldehyde **7** was also prepared by a series of straightforward reactions. The core Bodipy unit **8** was functionalized through Knoevenagel reaction to yield **10**. A second condensation then places the azido linkage on the other side of the Bodipy core (**11**). Finally, the two chromophores are “clicked” together.

The target compound **12** is freely soluble in most organic solvents, and the absorption spectrum in THF in the absence and presence of various metal ions is highly informative (Figure 1). In the absence of any metal ions, there are two clearly identifiable peaks in the visible region, one around 500 nm (energy donor, shorter wavelength absorbing Bodipy) and one for the core distyryl-Bodipy centered at 690 nm. The addition of the conditions of the study, displaying metal ions at a remarkable 10 μ M concentration, results in essentially no change, except for the Hg(II) ions. The ligand under under-

Scheme 1. Synthesis of the Target Compound



(4) (a) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2005**, *127*, 10464. (b) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2006**, *128*, 14474. (c) Guliyev, R.; Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2009**, *131*, 9007. (5) (a) Rohand, T.; Baruah, M.; Qin, W.; Boens, N.; Dehaen, W. *Chem. Commun.* **2006**, 266. (b) Ulrich, G.; Goze, C.; Guardigli, M.; Roda, A.; Ziessel, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 3694. (c) Dost, Z.; Atilgan, S.; Akkaya, E. U. *Tetrahedron* **2006**, *62*, 8484. (d) Buyukcakil, O.; Bozdemir, O. A.; Kolemen, S.; Erbas, S.; Akkaya, E. U. *Org. Lett.* **2009**, *11*, 4644. (6) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (b) Yilmaz, M. D.; Bozdemir, O. A.; Akkaya, E. U. *Org. Lett.* **2006**, *8*, 2871. (7) (a) Atilgan, S.; Ekmekci, Z.; Dogan, A. L.; Guç, D.; Akkaya, E. U. *Chem. Commun.* **2006**, 4398. (b) Deniz, E.; Isbasar, G. C.; Bozdemir, Ö. A.; Yildirim, L. T.; Siemiarczuk, A.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 3401. (c) Erten-Ela, S.; Yilmaz, M. D.; Içli, B.; Dede, Y.; Içli, S.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 3299. (d) Erbas, S.; Gorgulu, A.; Kocakusakogullari, M.; Akkaya, E. U. *Chem. Commun.* **2009**, 33, 4956. (e) Bozdemir, O. A.; Sozmen, F.; Buyukcakil, O.; Guliyev, R.; Cakmak, Y.; Akkaya, E. U. *Org. Lett.* **2010**, *12*, 1400. (f) Atilgan, S.; Ozdemir, T.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 4065. (g) Ozlem, S.; Akkaya, E. U. *J. Am. Chem. Soc.* **2009**, *131*, 48. (h) Kutuk, I.; Ozdemir, T.; Atilgan, S. *Tetrahedron Lett.* **2010**, *51*, 892. (i) Bozdemir, O. A.; Guliyev, R.; Buyukcakil, O.; Selçuk, S.; Kolemen, S.; Gulseren, G.; Nalbantoglu, T.; Boyaci, H.; Akkaya, E. U. *J. Am. Chem. Soc.* **2010**, *132*, 8029.

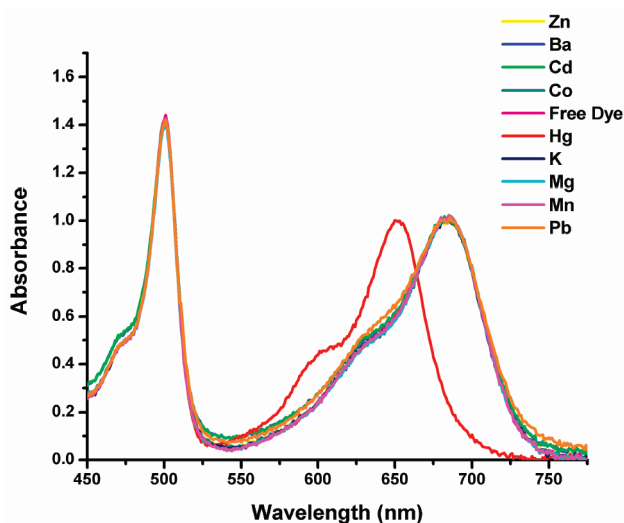


Figure 1. Absorbance spectra of the chemosensor compound **12** ($1.5 \mu\text{M}$) in THF in the absence and presence of various metal ions. Added metal ion concentrations were 1.0×10^{-5} M.

standable considering the charge transfer nature of the selectivity. Thus, in the presence of mercuric ions, the longer wavelength absorption peak shifts hypsochromically to 650 nm. This is a perfect example of a dialkylamino substituent being subdued by the binding of a Hg(II) ion. Fluorescence spectra are equally useful (Figure 2), and the free chemosensor shows

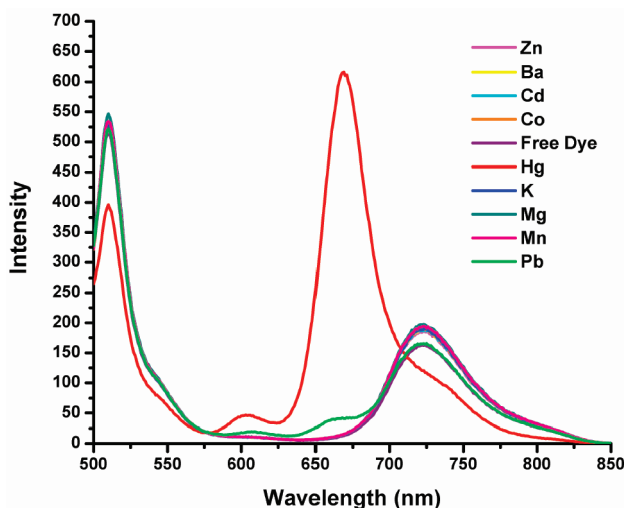


Figure 2. Emission spectra of compound **12** in THF ($1.5 \mu\text{M}$) in THF in the absence and presence of various metal ions. Added metal ion concentrations were 1.0×10^{-5} M. Excitation wavelength is 480 nm.

two emission peaks at 518 and 725 nm. Other metal ions are essentially ineffective, but the addition of Hg(II) ions results in a blue shift in the emission together with a large increase in intensity. The decrease in the emission intensity of shorter wavelength emitting Bodipy is also noteworthy, as it indicates

increased energy transfer efficiency due to larger spectral overlap between the donor and acceptor chromophore once the mercuric ion is tightly bound to the dithiaazacrown ligand. The excitation spectrum of compound **12** compared to that of the model compound **4** at equal concentrations shows the efficiency of energy transfer within the target molecule (Figure 3). When

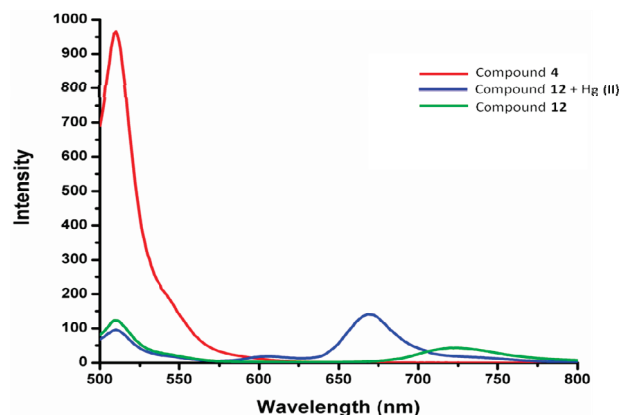


Figure 3. Excitation spectra of a model compound (**4**) and compound **12** at equal concentrations, with and without $10 \mu\text{M}$ Hg(II). For compound **4**, the emission data were collected at 518 nm, and for compound **12**, the data were collected at the isoemissive point 710 nm. The data were acquired in THF.

excited at 495 nm, emission can be collected from the longer wavelength emitting chromophore. The emission intensity from the energy donor chromophore is significantly quenched.

We then proceeded with the titration of chemosensor compound **12** with Hg(II) ions. As expected, the shorter wavelength peak is not altered, but the longer wavelength peak is clearly shifted hypsochromically, resulting in a clean isosbestic point at 662 nm (Figure 4).

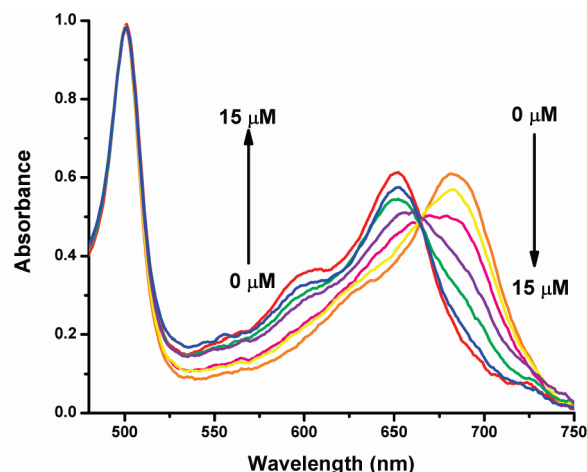


Figure 4. Hg(II) titration of the chemosensor compound **12**. Hg(II) concentration is varied between 0 and $15 \mu\text{M}$ in THF. The concentration of **12** was $1.5 \mu\text{M}$.

The absorption spectra thus present multiple opportunities of ratiometric sensing of ions, in this case, mercuric ions.

When the titration process is followed fluorometrically (Figure 5), the results clearly validate our design principles. A

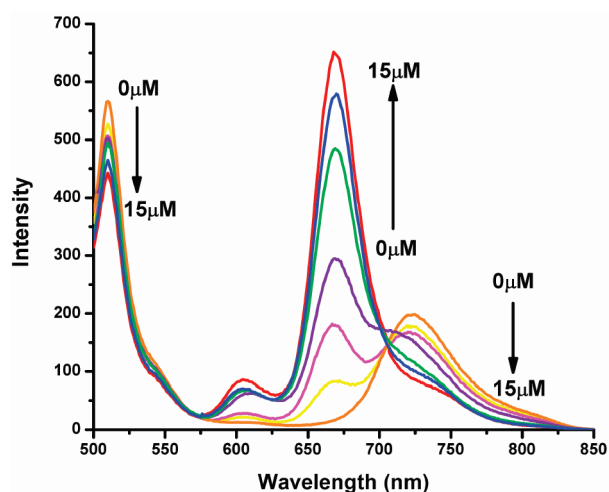


Figure 5. Hg(II) titration of the chemosensor **12** in THF. Ion concentration was varied between 0 and 15 μM . The chemosensor concentration was held at 1.5 μM . The binding stoichiometry is 1:1, and the dissociation constant was determined to be 3.1×10^{-6} M (Supporting Information).

shorter wavelength peak diminishes somewhat when the concentration of Hg(II) increases due to increased spectral overlap, hence more efficient energy transfer. Titration shows a clean equilibration between the two states, metal-free and metal-bound, with a single identifiable isoemissive point. Time-resolved fluorescence spectroscopy provides more quantitative data on the EET process. For compound **12** in THF, without Hg(II), the emission lifetime is 3.0 ns, but when Hg(II) is added in micromolar quantities, the lifetime is reduced to 1.8 ns. Corresponding energy transfer efficiencies are 11% and 45%, respectively (Supporting Information, Table S1).

The selectivity of the chemosensor was further studied in competition experiments with other metal ions (Figure 6).

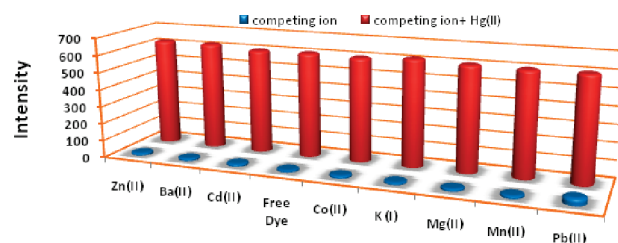


Figure 6. Free dye **12** (chemosensor) concentration was set at 1.5 μM . The concentration of the competing cation was 100 mM, and the concentration of Hg^{2+} was 10 mM. Excitation was at 500 nm with a slit width of 5.0 nm.

Thus, an excess of the competing ion was added (100 μM) in addition to 10.0 μM Hg(II). The data show that the presence of large excesses of competing ions has practically no effect on the emission intensity at 660 nm.

In conclusion, the principal outcomes of energy transfer coupled to internal charge transfer were obtained in a simple modular design. These are a large pseudo-Stokes shift (approximately 300–250 nm) and multiple ratiometric measurement opportunities. The applicability of ratiometry can be clearly demonstrated by recording the emission wavelength ratios at 760–723 nm (I_{760}/I_{723}) as a function of Hg(II) concentration (Supporting Information). Naturally, selectivity is conserved here as well.

Further work on this subject is ongoing to address water solubility. Since all the concepts applied here are expected to be transferable to any selected solvent, water-soluble probes using EET–ICT coupling are expected to emerge. Our work along this line is in progress.

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Supporting Information Available: Experimental procedures, structural proofs, and spectral data for all new compounds are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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