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Bis(2-pyridyl)-Substituted Boratriazaindacene as an NIR-Emitting Chemosensor for Hg(II)

Ali Coskun, M. Deniz Yilmaz, and Engin U. Akkaya*

Department of Chemistry, Middle East Technical University, Ankara, Turkey TR-06531

akkayaeu@metu.edu.tr

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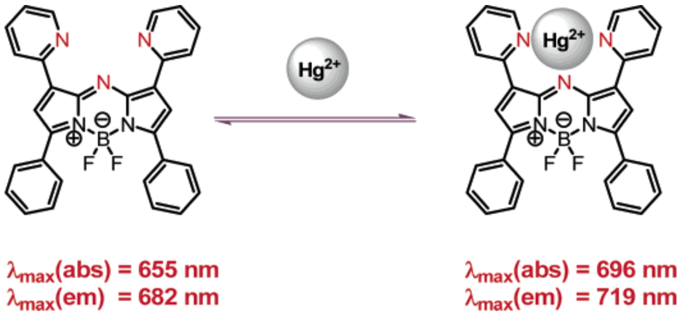
ABSTRACT



Aryl-substituted boratriazaindacenes (Aza-Bodipy's) are a new class of dyes with long wavelength absorption and emissions. We now report the first application of these dyes in metal ion sensing. 2-Pyridyl substituents at positions 1 and 7 create a well-defined pocket for metal ion binding. The chemosensor described here is selective for Hg(II) ions, and both absorption and emission spectra display large changes that would allow ratiometric sensing.

Development of novel ratiometric fluorescent chemosensors is a challenging area of supramolecular photochemistry.[1] Such fluorescent reporters of ions or neutral molecules are especially valuable if they can communicate analyte concentrations in the red end of the visible spectrum. This is not only due to the rarity of naturally occurring fluorophores emitting beyond 650 nm, but also due to much reduced scattering at longer wavelengths compared to most common blue or green emitting fluorophores. Thus, especially for use in heavily pigmented and highly scattering biological media, red or near-infrared (near IR) emitting fluorophores are desperately[2] needed.

Boradiazaindacenes (BODIPY or BDP dyes) are dipyrrin−difloroboron chelates which display remarkable properties as fluorophores.[3] However, until recently, the only way to push the absorption and the emission wavelengths to the red end of the visible spectrum was to switch to ring fused pyrroles (indoles, benzoindoles, etc.).[4] Unfortunately, this strategy reduces the chances of straightforward access to water soluble derivatives. Within the past few years, as a result of works in a number of laboratories (Rurack and Daub,[5] Ziessel,[6] Akkaya,[7] Boens and Dehaen,[8] Nagano[9]) a new facet of boradiazaindacenes, namely, a remarkably rich chemistry presented itself. Thus, there are new methodologies

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(1) (a) De Silva, A. P.; Fox, D. B.; Moody, T. S.; Weir, S. M. *Trends Biotech.* **2001**, *19*, 29−34. (b) Callan, J. F.; de Silva, A. P.; Magri, D. C. *Tetrahedron* **2005**, *61*, 8551−8588.

(2) (a) Czarnik, A. W. *Chem. Biol.* **1995**, *2*, 423−428.

(3) (a) Treibs, A.; Kreuzer, F.-H. *Justus Liebigs Ann. Chem.* **1968**, *718*, 208−223. (b) Haugland, R. P. *The Handbook. A Guide to Fluorescent Probes and Labeling Technologies*, 10th ed.; Molecular Probes, Inc.: Eugene, 2005.

(4) Chen, J.; Burghart, A.; Derecskei-Kovacs, A.; Burgess, K. *J. Org. Chem.* **2000**, *65*, 2900−2906. (b) Burghart, A.; Thoresen, L. H.; Chen, J.; Burgess, K.; Bergstrom, F.; Johansson, L. B. A. *Chem. Commun.* **2000**, 2203−2204.

(5) Rurack, K.; Kollmannsberger, M.; Daub, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 385−387.

(6) (a) Goze, C.; Ulrich, G.; Mallon, L. J.; Allen, B. D.; Harriman, A.; Ziessel, R. *J. Am. Chem. Soc.* **2006**, *128*, 10231−10239. (b) Ziessel, R.; Goze, C.; Ulrich, G.; Cesario, M.; Retailleau, P.; Harriman, A.; Rostron, J. P. *Chem. Eur. J.* **2005**, *11*, 7366−7378. (c) Ulrich, G.; Goze, C.; Guardigli, M.; Roda, A.; Ziessel, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 3694−3698. (d) Goze, C.; Ulrich, G.; Ziessel, R. *Org. Lett.* **2006**, *8*, 4444−4448.

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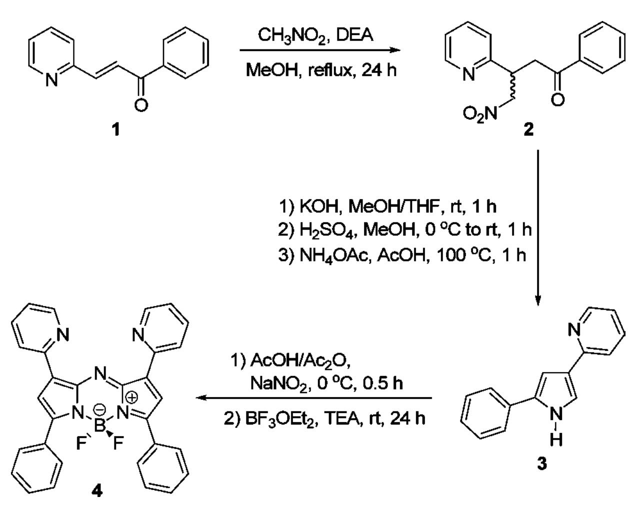

Figure 1. Synthesis of the near-IR emitting chemosensor **4**.

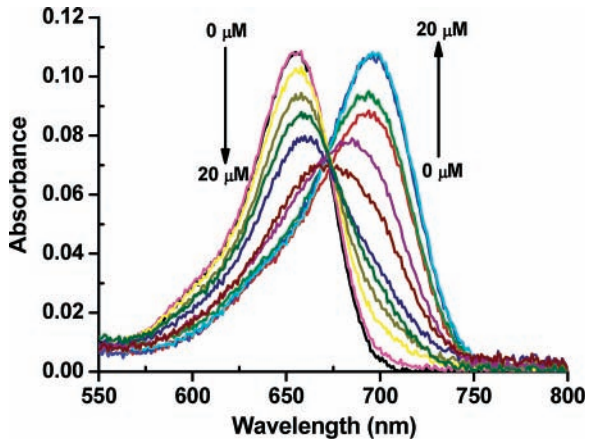

Figure 2. Absorbance response of the boratriazaindacene **4** to increasing concentrations of Hg(II) in the form of perchlorate salt. Measurements were done in acetonitrile at 1.3 μM dye concentration. Metal ion concentrations were varied in the following order: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20 μM.

for extending the conjugation, or placing a dialkylamino substituent on the boradiazaindacene system, both of which lead to longer wavelength emitting dyes. Another possibility, demonstrated elegantly by O'Shea[10] and later by Carreira,[11] is to synthesize an 8-aza-substituted boradiazaindacene, which is, of course, better named as boratriazaindacene. Tetraphenyl-substituted boratriazaindacenes show significantly red-shifted absorption and emission spectra. This property of boratriazaindacenes has been exploited[10] within the context of photodynamic therapy along with extended conjugation distyryl-boradiazaindacenes.[7d] Boratriazaindacenes offer a tremendous potential as chemosensors communicating in the NIR region of the spectrum, but until now, only examples for acid switching of PET[12] and ICT[13] processes have been reported. As a part of our ongoing effort in the design and synthesis of novel chemosensors, we targeted a boratriazaindacene carrying two 2-pyridyl groups at the 1 and 7 positions. Our modeling studies showed that this would create a well-defined binding pocket for transition metal sensing. The synthesis (Figure 1) starts with the known compound **1**. In analogy to the literature procedures, we carried out a nitromethane conjugate addition to pyridine-2-carboxaldehyde leading to the compound **2**, which was then converted into 2-phenyl-4-pyridylpyrrole (**3**). Partial nitrosylation, followed by a treatment with BF_3-etherate, resulted in the formation of the target fluorophore in the form of a green powder following silica gel column chromatography. Absorption spectrum of the compound **4** was acquired in acetonitrile and shows a peak at 655 nm. The emission peak in optically dilute solutions is at 682 nm in the same solvent. In a survey of different metal ions, it was apparent that mercuric ions produced the largest spectral changes in both the absorption and emission spectra. The concentration dependent changes in the absorption spectrum are shown in Figure 2. On mercuric ion addition, a clean isosbestic point of 672 nm was observed, and Hg(II)−**4** complex has a red-shifted absorbance peak at 690 nm. The extinction coefficient at the absorption maximum is 77 000 M^{-1} cm^{-1}. The emission spectrum (Figure 3) also shows a red-shift on Hg(II) binding. The free chemosensor has a λ_{max}(emission) of 682 nm which moves to 719 nm on Hg(II) binding. The dissociation constant was determined to be 5.4×10^{-6} M, with a 1:1 binding stoichiometry as revealed in a Job plot analysis. The quantum yields in acetonitrile are 0.19 for the compound **4** and 0.17 for the **4**-Hg(II) complex in reference to tetra-*tert*-butylphthalocyanine.[14] The boratriazaindacene derivative **4** shows spectacular metal ion selectivity. This is

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(7) (a) Dost, Z.; Atilgan, S.; Akkaya, E. U. *Tetrahedron* **2006**, *62*, 8484−8488. (b) Coskun, A.; Deniz, E.; Akkaya, E. U. *Org. Lett.* **2005**, *7*, 5187−5189. (c) Saki, N.; Dinc, T.; Akkaya, E. U. *Tetrahedron* **2006**, *62*, 2721−2725. (d) Atilgan, S.; Ekmekci, Z.; Dogan, A. L.; Guc, D.; Akkaya, E. U. *Chem. Commun.* **2006**, 4398−4400. (e) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2005**, *127*, 10464−10465. (f) Coskun, A.; Akkaya, E. U. *J. Am. Chem. Soc.* **2006**, *128*, 14474−14475. (g) Coskun, A.; Turfan, B. T.; Akkaya, E. U. *Tetrahedron Lett.* **2003**, *44*, 5649−5651.

(8) (a) Baruah, M.; Qin, W.; Vallee, R. A. L.; Beljonne, D.; Rohand, T.; Dehaen, W.; Boens, N. *Org. Lett.* **2005**, *7*, 4377−4380. (b) Rohand, T.; Baruah, M.; Qin, W.; Boens, N.; Dehaen, W. *Chem. Commun.* **2006**, 266−268. (c) Rohand, T.; Qin, W.; Boens, N.; Dehaen, W. *Eur. J. Org. Chem.* **2006**, 4658−4663.

(9) Gabe, Y.; Ueno, T.; Urano, Y.; Kojima, H.; Nagano, T. *Anal. Bioanal. Chem.* **2006**, *386*, 621−626.

(10) (a) Killoran, J.; Allen, L.; Gallagher, J. F.; Gallagher, W. M.; O'Shea, D. F. *Chem. Commun.* **2002**, 1862−1863. (b) Gorman, A.; Killoran, J.; O'Shea, C.; Kenna, T.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2004**, *126*, 10619−10631. (c) McDonnell, S. O.; Hall, M. J.; Allen, L. T.; Byrne, A.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2005**, *127*, 16360−16361.

(11) (a) Zhao, W.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1677−1679. (b) Zhao, W.; Carreira, E. M. *Chem. Eur. J.* **2006**, *12*, 7254−7263.

(12) Hall, M. J.; Allen, L. A.; O'Shea, D. F. *Org. Biomol. Chem.* **2006**, *4*, 776−780.

(13) McDonnell, S. O.; O'Shea, D. F. *Org. Lett.* **2006**, *8*, 3493−3496.

(14) (a) Teuchner, K.; Pfarrherr, A.; Stiel, H.; Freyer, W.; Leupold, D. *Photochem. Photobiol.* **1993**, *57*, 465−471. (b) Freyer, W.; Dahne, S.; Minh, L. Q.; Teuchner, K. *Z. Chem.* **1986**, *26*, 334−336. (c) Stiel, H.; Teuchner, K.; Paul, A.; Freyer, W.; Leupold, D. *J. Photochem. Photobiol. A* **1994**, *80*, 289−298.

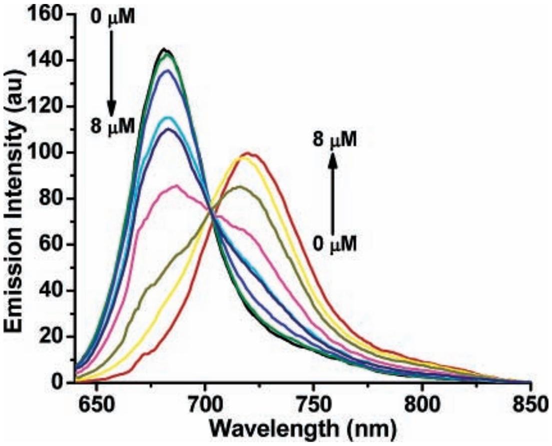

Figure 3. Emission response of the boratriazaindacene **4** to increasing concentrations of Hg(II) ions in the form of perchlorate salt. Measurements were done in acetonitrile at 1.3 μM dye concentration. Metal ion concentrations were varied in the following order: 0, 1, 2, 3, 4, 5, 6, 7, 8 μM. Excitation was at 660 nm, with slit widths of 5 nm.

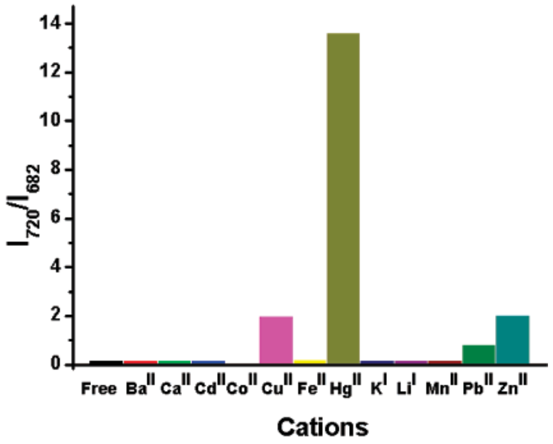

Figure 4. Selectivity of ratiometric sensing: Each cation is added at a concentration of 20 μM to an acetonitrile solution of the dye **4** (1.3 μM). The counterions are perchlorate. Excitation was at 660 nm, with slit widths of 5 nm.

in part due to rigid nature of the ligand and the selectivity imposed by the type of the donor atoms. Plotting emission intensity ratios (I_{720}/I_{682}) (Figure 4), it becomes clear that among the metal ions studied, Ba(II), Ca(II), Cd(II), Co(II), Cu(II), Fe(II), Hg(II), K(I), Li(I), Mn(II), Pb(II), Zn(II), cupric, and zinc cations show some minor ratio changes, whereas on Hg(II) addition at the same concentration (20 μM), the emission ratio changes more than 90-fold. Bathochromic shift on metal ion binding also deserves attention, it has been shown earlier that when there are electron-withdrawing groups which are part of the fluorophore π-system and involved in cation binding, charge separated excited-state is more stabilized than the ground state, and thus S_0-S_1 energy gap is reduced. In compound **4**, the 2-pyridyl substituents interact with the mercuric ions exactly in this way, thus creating the observed bathochromic shift in the emission spectrum.

There are numerous examples of boradiazaindacene (BODIPY)-based chemosensors,[6−8,15] but this is the first demonstration of boratriazaindacenes acting as chemosensors for metal cations. It appears that appropriate derivatization of these novel fluorophores would lead to satisfactory chemosensors for other molecular or ionic species of interest. As a bonus, such boratriazaindaces would have very long wavelength emissions in the otherwise silent region of the electromagnetic spectrum. Further work along these lines is expected to yield other promising chemosensors.

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Supporting Information Available: Syntheses, experimental details, ^{1}H, ^{13}C NMR spectra, and additional spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) (a) Bricks, J. L.; Kovalchuk, A.; Trieflinger, C.; Nofz, M.; Buschel, M.; Tolmachev, A. I.; Daub, J.; Rurack, K. *J. Am. Chem. Soc.* **2005**, *127*, 13522−13529. (b) Zeng, L.; Miller, E. W.; Pralle, A.; Isacoff, E. Y.; Chang, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 10−11.