

# Modulation of Boradiazaindacene Emission by Cation-Mediated Oxidative PET

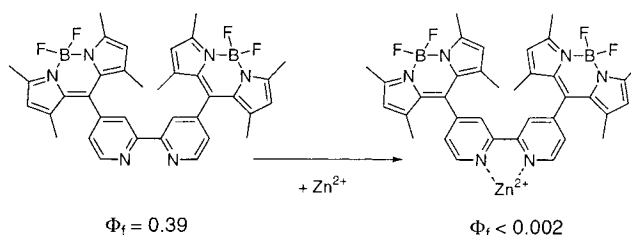
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## ABSTRACT



Bright green boradiazaindacene fluorescence is quenched by an oxidative photoinduced electron transfer (PET) from the excited state fluorophore to the bipyridyl unit complexed to metal cations. The closed shell diamagnetic cation Zn(II) is one of the most effective quenchers of fluorescence in this system, demonstrating that the quenching is not simply related to the facilitated intersystem crossing. The molecule also acts as a NOR logic gate with two chemical inputs, TFA and Zn(II).

For the rational design of novel fluorescent probes, there is a long list of parameters to be optimized and it is not likely to find one sensor/probe to suit all conceivable applications, even just for a single analyte. With that in mind, the flurry of activity<sup>1</sup> surrounding fluorescent chemosensors can be better understood. One phenomenon that served the chemosensor community very well is photoinduced electron transfer (PET).<sup>2</sup> In principle, PET can take place in two directions: from a donor to the excited-state fluorophore (reductive PET), or from an excited-state fluorophore to a receptor (oxidative PET). Both events are accompanied by a quench-

ing of the fluorophore emission. There are many examples of the first type, in many instances the fluorescence is “turned off” in the absence of the analyte (e.g., cation). When the analyte is added, PET is inhibited and a large enhancement of fluorescence is observed (“off–on” switch). Oxidative PET is well-known<sup>3</sup> but rarely utilized in sensing applications. It has been observed in certain bipyridyl fluorophores where the fluorophore–bipyridyl conjugation is broken by saturated carbons or by orthogonality.<sup>4</sup> The binding of the cation quenches the fluorescence of the receptor–fluorophore. Quenching is most likely caused by the favorable energetics of the electron transfer to the LUMO of the bipyridyl–metal complex, since the metal binding to the bipyridyl moiety lowers both HOMO and LUMO energy levels of the ligand, compared to the metal-free state. Complexation-induced planarization of the bipyridyl moiety plays a part as well. Boradiazaindacene dyes (aka, BODIPY, BDP, BDPY, or dipyrromethene dyes) are well-known compounds that pos-

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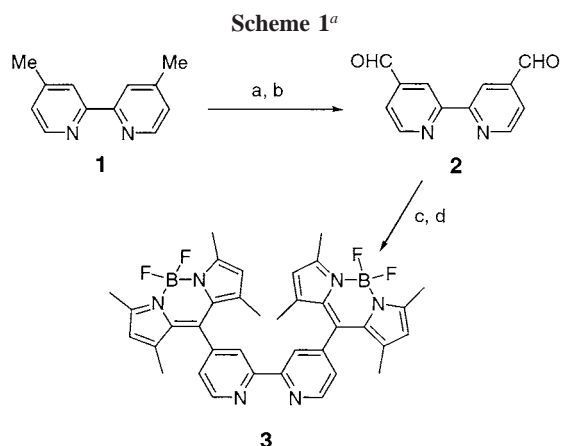
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possess highly desirable qualities as fluorophores such as high quantum yield and extinction coefficient, solubility, being amenable to structural modification, etc. There are interesting examples of boradiazaindacene-based fluorescent chemosensors<sup>5</sup> in recent literature.

To explore the cation binding response of the bipyridyl ligand carrying two orthogonal boradiazaindacene units, we initiated the synthesis of the ligand **3** (Scheme 1). Orthogo-

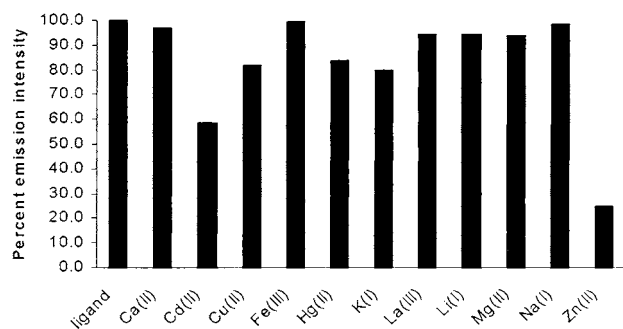


<sup>a</sup> Reaction conditions: (a)  $(\text{Me}_2\text{N})_2\text{CH}(\text{O}^t\text{Bu})$ , DMF, 140 °C, 82%; (b)  $\text{NaIO}_4$ , THF– $\text{H}_2\text{O}$ , rt, 76%; (c) 2,4-dimethylpyrrole, catalytic TFA, DCM, *p*-chloranil, rt; (d)  $\text{Et}_3\text{N}$ ,  $\text{BF}_3\text{--OEt}_2$ , 25% (c and d).

nality of the fluorescent units is ensured by the presence of methyl substituents on the 4-position of the pyrrole rings (or 1- and 7-positions in the boradiazaindacene systems). Thus, 4,4'-dimethylbipyridyl is converted to the bisaldehyde **2** according to a literature<sup>6</sup> procedure with a 62% overall yield. Boradiazaindacene units were appended in a one-pot reaction: 2,4-dimethylpyrrole was added to the dichloromethane solution of the bisaldehyde **2** under nitrogen in the presence of a catalytic amount of trifluoroacetic acid (TFA). Oxidation by *p*-chloranil, followed by neutralization and  $\text{BF}_3\text{--OEt}_2$  addition, resulted in a solution with an intense green fluorescence. Analytically pure target compound was obtained in 25% yield by column purification (silica gel, 5/95 MeOH/ $\text{CHCl}_3$ ). Solutions of the ligand **3** in organic solvents are highly fluorescent. In acetonitrile, the absorption spectrum shows a typical narrow boradiazaindacene peak at 498 nm. The extinction coefficient was  $120\,000\text{ L mol}^{-1}\text{ cm}^{-1}$ . Emission spectrum peaks occurred at 516 nm in the same solvent, and the quantum yield was determined to be 0.39 in reference to fluorescein that has a reported quantum yield of 0.925 in 1 M aqueous NaOH. A comparative study of the effects of added metal cations was performed (Figure 1). Zn(II) cation,

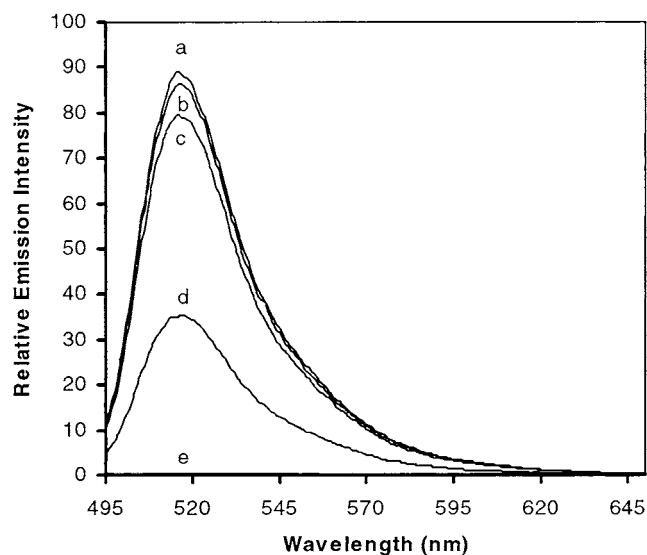
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**Figure 1.** Fluorescence emission intensity of boradiazaindacene **3** (ligand,  $0.62\ \mu\text{M}$ ) in acetonitrile, which contains 10 equiv of various cations, as a percentage of the emission intensity of the free ligand. Free ligand emission data were recorded at 516 nm; excitation was at 485 nm.

which is a small diamagnetic cation, is the most effective quencher (Figure 2), much more than the paramagnetic Cu-



**Figure 2.** Quenching of boradiazaindacene **3** ( $0.62\ \mu\text{M}$ ) fluorescence in acetonitrile by the addition of micromolar Zn(II). (a)  $0\ \mu\text{M}$ , (b)  $0.01\ \mu\text{M}$ , (c)  $0.1\ \mu\text{M}$ , (d)  $10\ \mu\text{M}$ , (e)  $100\ \mu\text{M}$  (baseline). Excitation was at 485 nm, and the excitation and emission slits were set at 5 nm.

(II) and the HTM quencher Hg(II). In fact, with just 0.1 mM Zn(II), the emission is completely quenched. The stoichiometry of the interaction is 1:1 for the ligand **3** and Zn(II). Dissociation constants were determined; there appears to be a correlation between the strength of interaction and the magnitude of quenching, especially among the closed shell group IB metal cations:  $K_d$  for the **3**–Zn(II) complex was determined to be  $9.0 \times 10^{-8}\text{ M}$ , whereas the dissociation constants for the **3**–Cd(II) and **3**–Hg(II) complexes were  $5.0 \times 10^{-5}$  and  $6.0 \times 10^{-4}\text{ M}$ , respectively.

An exciting extension of the fluorescent chemosensor studies has been the development of molecular equivalents of logic gates and implementation of these gates in molecular arithmetic.<sup>7</sup> A number of logic gates,<sup>8</sup> including AND,<sup>8a-c</sup> NAND,<sup>8d</sup> TRANSFER,<sup>8d</sup> OR,<sup>8e</sup> NOR,<sup>4</sup> INHIBIT,<sup>4,8f</sup> XOR,<sup>8g</sup> YES,<sup>8h</sup> and NOT,<sup>8i</sup> have been reported previously. Naturally, true “on–off” or “off–on” switching, i.e., switching between a nonfluorescent state and a highly fluorescent one, would be highly desirable, but moderate changes are more common. Encouraged by our observation that the bright green fluorescence of the ligand **3** is totally quenched by 100  $\mu\text{M}$  equivalents of Zn(II), we explored the possibility of NOR logic gate behavior. As expected, addition of a small amount of trifluoroacetic acid (TFA) to the acetonitrile solution to bring up the formal TFA concentration to 100  $\mu\text{M}$  causes a remarkable quenching, just like the Zn(II) cation, further confirming the proposed mechanism of the static quenching: protonation of the bipyridyl unit facilitates oxidative

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**Table 1.** Emission Response in Accordance with NOR Logic Gate Behavior<sup>a</sup>

input 1	input 2	output (normalized)
0	0	1 (1.000)
100 $\mu\text{M}$ Zn(II)	0	0 (0.002)
0	100 $\mu\text{M}$ TFA	0 (0.003)
100 $\mu\text{M}$ Zn(II)	100 $\mu\text{M}$ TFA	0 (0.002)

<sup>a</sup> Emission of boradiazaindacene **3** in acetonitrile. Emission values at the maximum (516 nm) of the emission peak were normalized to the emission intensity of the free ligand **3**. Excitation was at 485 nm, and slits were set at 5 nm.

PET just like the chelation to the metal ions. Not surprisingly, the addition of both chemical inputs yields a quenched signal as well. (Table 1) We have to note that the residual emission in +Zn(II) and +TFA solutions are at the instrumental noise level, representing a true off state (0). Thus, a remarkable digital action of a two-input NOR logic gate has been demonstrated. In addition, oxidative PET appears to be a viable alternative to the reductive PET in developing novel fluorescent chemosensors for ions and small molecules.

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