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π-Extended Dipyrrins Capable of Highly Fluorogenic Complexation with Metal Ions

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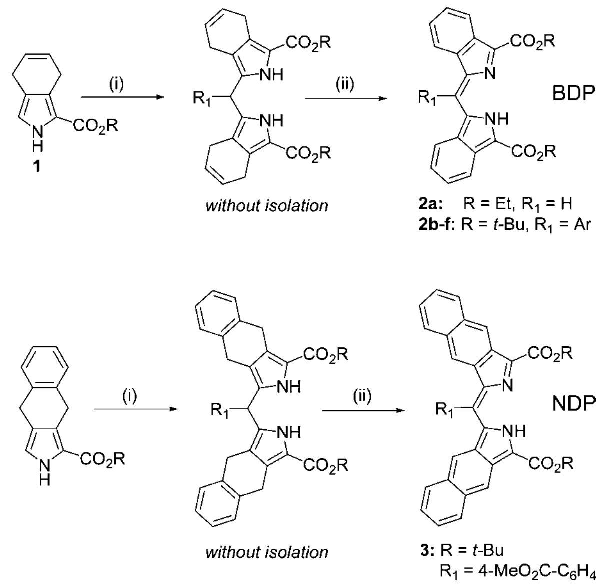
Abstract: The synthesis and properties of a new family of π-extended dipyrrins capable of forming brightly fluorescent complexes with metal ions are reported. The metal complexes possess tunable spectral bands and exhibit different emission properties depending on the mode of metal coordination.

Boron dipyrrins (BODIPYs) form a popular group of fluorophores because of their high emission quantum yields, excellent photostability, and versatile chemistry.[1] While boron complexes of dipyrrins are by far the most recognized, dipyrrins have also long been known to form stable adducts with metal ions.[2−4] Metallodipyrrins are typically isolated as homoleptic bis complexes (ML_2, L = dipyrrin) and mainly find use as building blocks for construction of various supramolecular assemblies.[5] Curiously, unlike BODIPYs, homoleptic metallodipyrrins practically do not fluoresce, although there are several important exceptions.[6] For example, Holten, Lindsey, and co-workers[6a] showed that by increasing the size of the *meso*-aryl group in Zn bisaryldipyrrins, the nonradiative decay could be diminished, affording a considerable gain in emission. On the other hand, some recently reported heteroleptic Al^{3+} and Sn^{2+} monodipyrrinates (MLX_n) exhibit bright fluorescence,[7,8] suggesting that the emissivity of metallodipyrrins could in part be related to the mode of metal coordination. Overall, the interplay between the structure and photophysics of metallodipyrrins is not well understood, and metallodipyrrins are generally considered to be poorly emissive species.[1a]

Here we report a new family of aromatically π-extended dipyrrin molecules capable of forming bright fluorescent complexes with metal ions and exhibiting a unique fluorescence modulation effect mediated by exciton coupling.[9] A recently described approach to π-extended porphyrins based on 4,7-dihydroisoindole and its derivatives (Scheme 1)[10] paved a new way to π-extended oligopyrroles, including 2,2′-alkoxycarbonyldibenzo[2,3]dipyrrins (BDPs) and -dinaphtho[2,3]dipyrrins (NDPs). A simple one-pot procedure leading to BDPs relies on the condensation of 2-substituted 4,7-dihydroisoindole **1** with aldehydes[10c] followed by the oxidation of dipyrromethanes with dichlorodicyanoquinone (DDQ). Similarly, dinaphthodipyrrins can be synthesized from the corresponding pyrrole esters reported previously (Scheme 1).[10a]

All of the synthesized dipyrrins exhibit broad absorption bands ($\varepsilon = 4-7 \times 10^4\ M^{-1}\ cm^{-1}$) ranging from 550−570 nm for BDPs (**2a**−**f**) to 660−700 nm for NDP **3**. Taken as free bases, BDPs and NDPs fluoresce very weakly ($\phi_{fl} = 0.01-0.02$ at 22 °C); however, upon addition of metal salts [e.g., $Zn(OAc)_2$, $Ca(OAc)_2$, YCl_3, $LaCl_3$, $GdCl_3$], their solutions instantly become fluorescent. For example, upon addition of $Zn(OAc)_2$, purple solutions of BDPs in *N*,*N*-dimethylformamide (DMF) immediately changed color to deep-blue with the appearance of bright-red fluorescence (Figure 1b). In contrast, metalation of regular dipyrrins typically requires heating and/or the presence of bases and leads to nonemissive products.

Scheme 1[a]



[a] Reagents and conditions: (i) R_1CHO, *p*-toluenesulfonic acid, Bu_4NCl, CH_2Cl_2, r.t., 12−24 h; (ii) DDQ (3 equiv), THF, r.t., 10−30 min. Yields: **2a**, 93%; **2b** ($R_1 = 3,5\text{-}t\text{-}Bu_2C_6H_3$), 88%; **2c** ($R_1 = 4\text{-}BrC_6H_4$), 92%; **2d** ($R_1 = 4\text{-}MeO_2CC_6H_4$), 87%; **2e** ($R_1 = 3,5\text{-}(MeO)_2C_6H_3$), 84%; **2f** ($R_1$ = 2-thienyl), 82%; **3**, 78%.

The optical transitions of the new π-extended dipyrrinates span the entire red spectral range (Figure 1a), resembling in shape the bands of BODIPY, dibenzo-BODIPY,[12] and dibenzoaza-BODIPY.[13] The emission quantum yields reach as high as 0.7 in the case of ZnBDPs (Table 1). The fluorescence quantum yields of the NDP complexes are somewhat lower, reflecting a ∼100 nm red shift in the NDP transition and subsequent enhancement of the nonradiative decay.[14] The unusually high emissivity of BDP and NDP complexes is probably related to the structures of the π-extended dipyrrin ligands themselves, which are different than those of other dipyrrins reported to date. By comparison, in similarly π-extended porphyrins, the $S_1 \rightarrow S_0$ radiative rate was found to be higher than in the corresponding nonaromatically extended analogues.[15] From the practical point of view, the red absorption bands of BDPs and NDPs and their strongly fluorogenic complexation make these dipyrrins promising as probes for biological sensing of metal ions (e.g., Zn^{2+}).

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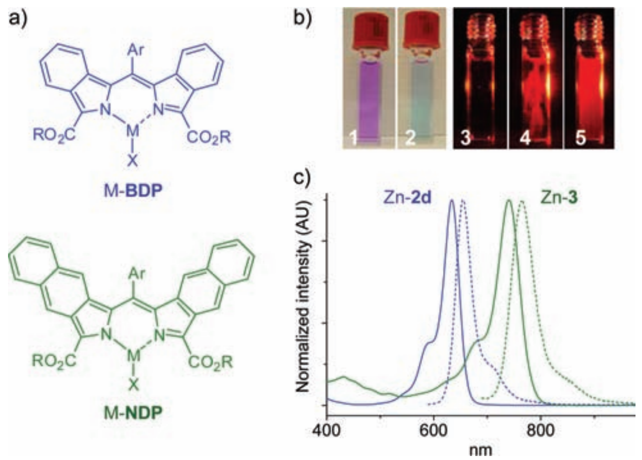

Figure 1. (a) Structures of heteroleptic metal complexes of BDPs and NDPs. (b) Color changes upon addition of $Zn(OAc)_2$ to a solution of **2a** in DMF (1 and 2), upon illumination of the solution with a red light-emitting diode ($\lambda_{max} = 635$ nm) from the side (3), after addition of a few crystals of $Zn(OAc)_2$ (4), and after the solution was shaken (5). (c) Absorption and emission spectra of Zn complexes of BDP **2d** (blue) and NDP **3** (green). The complexes were prepared in situ by adding $Zn(OAc)_2$ to solutions of free-base dipyrrins ($\sim 5 \times 10^{-6}$ M) in DMF (X = OAc).

Table 1. Optical Properties of Zn and Ca Complexes of π-Extended Dipyrrins in DMF[a]

complex	abs λ_{max} (nm)	em λ_{max} (nm)	ϕ_{fl}[b]	complex	abs λ_{max} (nm)	em λ_{max} (nm)	ϕ_{fl}[b]
Zn−**2a**	637	650	0.70	Ca−**2a**	639	650	0.64
Zn−**2d**	631	639	0.65	Ca−**2d**	638	645	0.58
Zn−**3**	740	761	0.08	Ca−**3**	737	762	0.05

[a] Complexes were generated in situ upon addition of metal acetates (∼10-fold excess) to solutions of dipyrrins. [b] Relative to rhodamine 6G in EtOH ($\phi_{fl} = 0.94$).[11]

A remarkable feature of the observed complexation is the complete on−off switching of fluorescence depending on the mode of metal coordination. For example, when BDP **2d** was reacted with $Zn(OAc)_2$ in acetone, an intensely fluorescent solution formed instantly (Figure 1b); however, after a few hours, the fluorescence disappeared, and dark-blue crystals precipitated. These crystals were poorly soluble in acetone but very soluble in toluene, CH_2Cl_2, and pyridine. The solutions revealed different absorption spectra (Figure 2a) and practically no fluorescence. The crystals were unambiguously identified as the homoleptic ML_2 complex (p S21, Supporting Information). Upon reaction of this complex with excess Zn salt in pyridine, the spectrum again adopted the BODIPY-like shape, and the fluorescence was fully regained (Figure 2a). The conversion could be followed by NMR spectroscopy (Figure 2b and Figure S11, Supporting Information) and absorption and fluorescence spectroscopy (Figure S10).

The observed spectral changes most likely originate from the solvent-dependent equilibrium between heteroleptic (MLX) and homoleptic (ML_2) species. At first, the fluorescent MLX complex forms rapidly, but its subsequent reaction with excess ligand (L) and/or disproportionation leads to the formation of ML_2, which precipitates out of the solution, thereby shifting the equilibrium. In coordinating solvents (e.g., pyridine), where the solubilities of inorganic Zn salts, MLX, and ML_2 are high, the equilibrium can be shifted back to MLX by increasing the concentration of Zn^{2+}. Notably, such equilibria are not common for metallodipyrrins, which typically exist as stable homoleptic adducts, notwithstanding that some heteroleptic complexes have been reported in the literature.[16−18] The higher lability of our dipyrrinates could be a result of the steric and/or electronic effects of 2,2′-alkoxycarbonyl groups,[19] which may weaken the coordination bonds and facilitate exchange reactions.

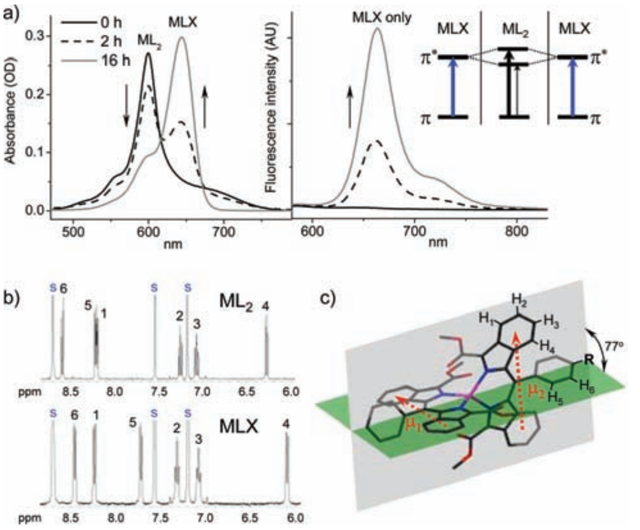

Figure 2. (a) Changes in the absorption and emission spectra ($\lambda_{ex} = 560$ nm) of Zn−**2d** (ML_2) upon addition of excess $Zn(OAc)_2$: ML_2 in pyridine before addition of $Zn(OAc)_2$ (black) and 2 h (red) and 16 h (blue) after addition. Inset: exciton splitting effect; the line thickness reflects the transition probability. (b) Aromatic regions of the ^1H NMR spectra of the ML_2 and MLX forms of Zn−**2d** in pyridine-d_5 [solvent resonances are marked in blue; assignments are based on ^1H COSY experiments (Figures S2 and S4) and refer to the structure on the right]. (c) Optimized structure of the homoleptic Zn−**2e** complex [B3LYP/6-31G(d); pendant groups have been omitted for clarity]. Dotted arrows show the orientations of the transition dipole moments (μ_1 and μ_2) of the individual dipyrrin units.

Direct evidence that heteroleptic BDP complexes are highly fluorescent was obtained by synthesizing a Zn dipyrrin-β-diketonate by way of a ligand-exchange reaction. Treatment of **2a** with a stoichiometric amount of $Zn(acac)_2$ in acetone gave the desired Zn(acac)−**2a**, which readily precipitated from the reaction mixture. As expected, Zn(acac)−**2a** showed absorption features similar to those of BODIPY and bright-red fluorescence ($\phi_{fl} = 0.7$ in THF) (Figure S14).

The profound differences in the optical spectra of the mono and bis complexes and the complete on−off switching of the fluorescence suggest the presence of a strong exciton coupling effect in ML_2.[9] Exciton coupling has been observed in various chromophore dimers, including dimers of BODIPY.[20] The ML_2 molecule may be viewed a "dimer" of two independent dipyrrin units held close to one another by the metal ion. In such a dimer, the two transition dipoles, which are oriented in the individual dipyrrins between the isoindolic residues (μ_1 and μ_2 in Figure 2c),[17a] can interact, resulting in a pair of nondegenerate states, one shifted up and the other down relative to the transition of the parent ML complex (Figure 2a inset). The magnitude of the coupling and the intensities of the corresponding bands depend on the strengths of the transition dipoles and on their mutual orientation. In particular, a nonplanar orientation (in different planes at an angle to each other) may produce a splitting in which the blue-shifted transition is allowed while the red-shifted one is forbidden.[9]

The experimental spectra of MLX and ML_2 (Figure 2a) appear to fit the exciton coupling model well. The peaks at 599 and 669 nm, obtained by fitting the absorption spectrum of ML_2 with a pair of Lorentzians (Figure S13), are shifted by 1118 cm^{-1} up and 629 cm^{-1} down relative to the principal band of the parent MLX complex ($\lambda_{max} = 642$ nm). The asymmetry is likely to be caused by the difference in the vibrational couplings and/or different

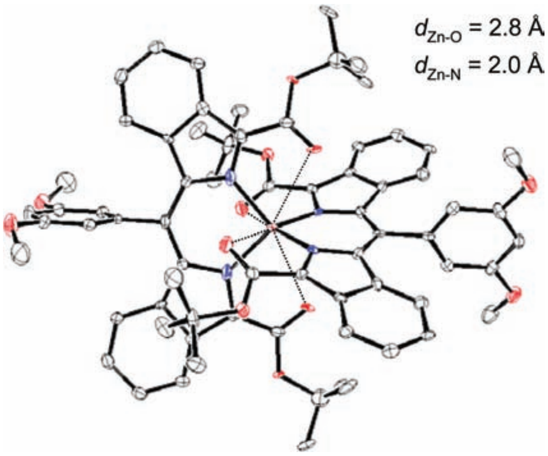

Figure 3. X-ray crystal structure (ORTEP) of the homoleptic Zn−**2e** complex. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level.

solvation of the mono and bis complexes. The ratio of the oscillator strengths (ML_2 vs MLX) was found to be 1.92, which is very close to the value predicted by the theory (2.0).[9] Fast nonradiative relaxation from the upper to the lower exciton state and slow emission from the latter, consistent with the low oscillator strength of the corresponding excitation, make intersystem crossing and internal conversion the most likely causes for the loss of fluorescence in ML_2. In toluene at 22 °C, ML_2 exhibits a broad emission (λ_{max} = 785 nm) with a negligible quantum yield ($\phi_{fl} < 0.01$) and an average lifetime of ∼1.6 ns (Figure S15).

The strong coupling of the transition dipoles suggests that the mutual orientation of the dipyrrin units in ML_2 deviates from strictly orthogonal (D_{2h} symmetry). The X-ray crystal structure (CCDC no. 749261) of ML_2 complex Zn−**2e** (Figure 3) fully corroborates this assumption. The angle between the mean-square planes of the dipyrrins in Zn−**2e** is only 64.5°, which is smaller than that found in the majority of known Zn−dipyrrin complexes.[21] Similarly flattened structures have been observed in Zn azadipyrrins (63−39°)[22] and Zn α-methoxydipyrrin (54.7°).[23] Also noteworthy is the quite significant ruffling of the dipyrrin ligands, which resembles distortions of some nonplanar porphyrins.[24]

Notably, the computed structure [DFT/B3LYP/6-31G(d)] of homoleptic Zn−**2e** (Figure 2c) was also found to be nonorthogonal, although the angle between the mean-square planes was somewhat larger (77°). This suggests that the distortion from the orthogonal geometry is not induced by the crystal packing forces but is an intrinsic property of the ML_2 molecule, which is flattened because of the propensity of the ligand π systems to align in coplanar fashion.[22] The nonorthogonal geometry may also facilitate interactions between the metal and the proximate carbonyl oxygens, which have been identified in some other homoleptic dipyrrin complexes.[19b] Although the Zn−O distances in Zn−**2e** are quite large (d_{Zn-O} = 2.8−2.9 Å vs d_{Zn-N} = 2.0 Å), the carbonyl groups still could be implicated in the overall ligand−metal bond stabilization.[19]

In conclusion, the developed method of synthesis of fluorogenic π-extended dipyrrins allows tuning of their optical bands across the red/near-IR optical spectrum. Metal complexes of π-extended metallodipyrrins are strongly fluorescent, and their fluorescence can be switched on and off by changing the mode of metal coordination. The molecular exciton theory[9] provides a new insight into the photophysics of metallodipyrrins, suggesting rational pathways to fluorogenic dipyrrin-based chelators. These results open up possibilities for engaging metallodipyrrins in a variety of applications, including construction of luminescent networks, electrooptical materials, and biomedical imaging and sensing.

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Supporting Information Available: Synthetic procedures, spectroscopic data, fluorescence lifetime data, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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