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π-Extended dipyrrins capable of highly fluorogenic complexation with metal ions

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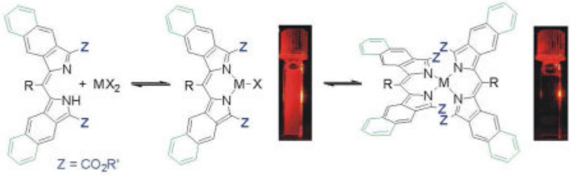
Abstract



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 posses tunable spectral bands and exhibit different emission properties depending on the mode of metal coordination.

Boron dipyrrins (BODIPY) form a popular group of fluorophores due to 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.[2,3,4] Metallodipyrrins are typically isolated as homoleptic *bis*-complexes (ML_2, L=dipyrrin), which mainly find use as building blocks for construction of various supramolecular assemblies.[5] Curiously, unlike BODIPY, homoleptic metallodipyrrins practically do not fluoresce, although there are several important exemptions.[6] For example, Holten, Lindsey et al showed that by increasing the size of the *meso*-aryl group in Zn *bis*-aryldipyrrins, the non-radiative decay could be diminished, affording considerable gain in emission.[6a] On the other hand, some recently reported heteroleptic Al^{3+} and Sn^{2+} *mono*-dipyrrinates (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 generally metallodipyrrins are considered 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′-alkoxycarbonyl-dibenzo- (BDP) and dinaphtho[2,3]dipyrrins (NDP). A simple one-pot procedure leading to BDP's relies on the

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

condensation of 2-substituted 4,7-dihydroisoindole **1** with aldehydes,10c followed by the oxidation of dipyrromethanes with DDQ. Similarly, dinaphthodipyrrins can be synthesized from the corresponding pyrrole-esters reported previously (Scheme 1).10a

All the synthesized dipyrrins exhibit broad absorption bands ($\varepsilon \sim 4–7 \times 10^4$ $M^{-1}cm^{-1}$) ranging from 550–570 nm for BDP's (**2a**–**f**) to 660–700 nm for NDP (**3**). Taken as free-bases, BDP's and NDP's fluoresce very weakly (φ_{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 BDP's in DMF immediately change color to deep blue with appearance of bright red fluorescence (Fig. 1b). In contrast, metallation of regular dipyrrins typically requires heating and/or presence of bases and leads to non-emissive products.

The optical transitions of the new π-extended dipyrrinates span the entire red spectral range (Fig. 1a), resembling in shape the bands of BODIPY, dibenzo-BODIPY12 and dibenzo-aza-BODIPY.13 The emission quantum yields reach as high as 0.7 in the case of ZnBDP's (Table 1). The fluorescence quantum yields of NDP complexes are somewhat lower, reflecting a ~100 nm red-shift in the NDP transition and subsequent enhancement of the non-radiative decay.14 The high emissivity of BDP and NDP complexes is probably related to the structures of π-extended dipyrrin ligands themselves, which are different that 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 non-aromatically extended analogues.15 From the practical point of view, red absorption bands of BDP's and NDP's and their strongly fluorogenic complexation make these dipyrrins promising as probes for biological sensing of metal ions (e.g. Zn^{2+}).

A remarkable feature of the observed complexation is complete on-off switching of fluorescence depending on the mode of metal coordination. For example, when BDP **2d** reacted with $Zn(OAc)_2$ in acetone, an intensely fluorescent solution formed instantly (Fig. 1b); but after a few hours the fluorescence disappeared and dark blue crystals precipitated. These crystals were poorly soluble in acetone, but well soluble in toluene, CH_2Cl_2 or pyridine. The solutions revealed different absorption spectra (Fig. 2a) and practically no fluorescence. The crystals were unambiguously identified as the homoleptic ML_2 complex (S21). Upon reaction of this complex with excess of Zn salt (in pyridine), the spectrum again adopted the BODIPY-like shape, and the fluorescence was fully regained (Fig. 2a). The conversion could be followed by NMR (Fig. 2b, S17), absorption and fluorescence (S17).

The observed spectral changes most likely originate from the solvent-dependent equilibrium between heteroleptic (MLX) and homoleptic (ML_2) species. At first, 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, where the solubilities of inorganic Zn salts, MLX and ML_2 are high (e.g. in pyridine), 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.16,17,18 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.

The 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 the 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 (φ_{fl}=0.7 in THF) (S35).

The profound differences in the optical spectra of *mono*- and *bis*- complexes and complete on/off switching of fluorescence suggest 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 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, oriented in the individual dipyrrins between the isoindolic residues (μ_1 and μ_2, Fig. 2c),17a can interact, resulting in a pair of non-degenerate states, shifted up and down relative to the transition of the parent ML complex (Fig. 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, non-planar 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 (Fig. 2a) appear to fit well the exciton coupling model. The peaks at 599 and 669 nm, obtained by fitting the absorption spectrum of ML_2 with a pair of Lorentzians (S35), are shifted by 1118 cm^{-1} up and 629 cm^{-1} down relative to the principal band of the parent MLX complex (λ_{max}=642 nm). The asymmetry is likely to be caused by the difference in the vibrational couplings and/or different 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 predicted by the theory (2.0).9 Fast non-radiative 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 the 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 broad emission (λ_{max}=785 nm) with negligible quantum yield φ_{fl}<0.01 and average lifetime of about 1.6 ns (S36).

Strong coupling of the transition dipoles suggests that the mutual orientation of the dipyrrin units in ML_2 deviates from the strictly orthogonal (D_{2h} symmetry). The X-ray crystal structure (CCDC # 749261) of ML_2 Zn-**2e** (Fig. 3) fully corroborates this assumption. The angle between the mean-square planes of the dipyrrins in Zn-**2e** is only 64.5°, which is lower than 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 quite significant ruffling of the dipyrrin ligands, which resembles distortions of some non-planar porphyrins.24

Notably, the computed structure (DFT/B3LYP/6-31G(d)) of homoleptic Zn-**2e** (Fig. 2c) was also found non-orthogonal, 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 due to the propensity of the ligand π-systems to align in co-planar fashion.22 Non-orthogonal 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 ($d_{Zn\text{-}O}$=2.8–2.9Å *vs* $d_{Zn\text{-}N}$=2.0Å), 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 entire red/near infrared 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 theory9 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, biomedical imaging and sensing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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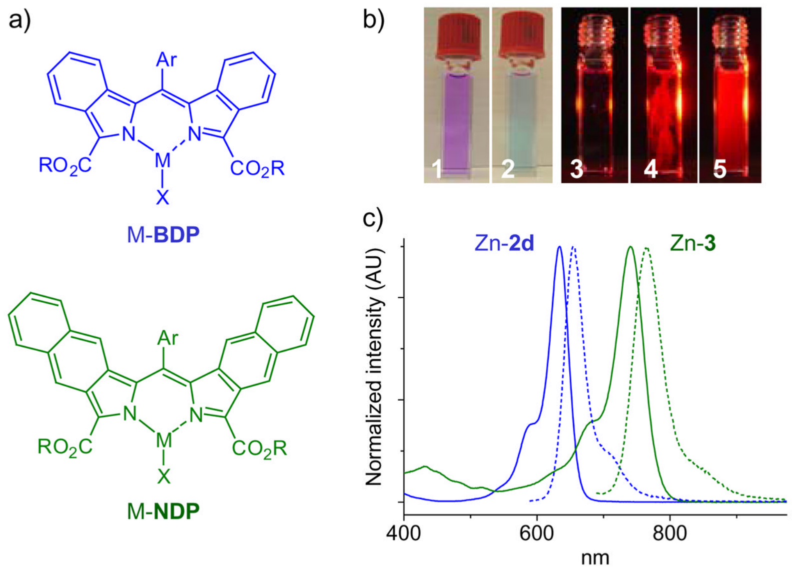


Figure 1.

(a) Structures of heteroleptic metal complexes of BDP's and NDP's. (b) Color changes upon addition of $Zn(OAc)_2$ to a solution of **2a** in DMF (1,2). The solution was illuminated with red LED (λ_{max}=635 nm) from the side (3), a few crystals of $Zn(OAc)_2$ were added (4), the solution was shaken (5). (c) Absorption and emission spectra of Zn complexes of BDP **2d** (blue) and NDP **3** (green). Complexes were prepared *in situ* by adding $Zn(OAc)_2$ to solutions of free-base dipyrrins (~5×10^{-6} M) in DMF (X=OAc).

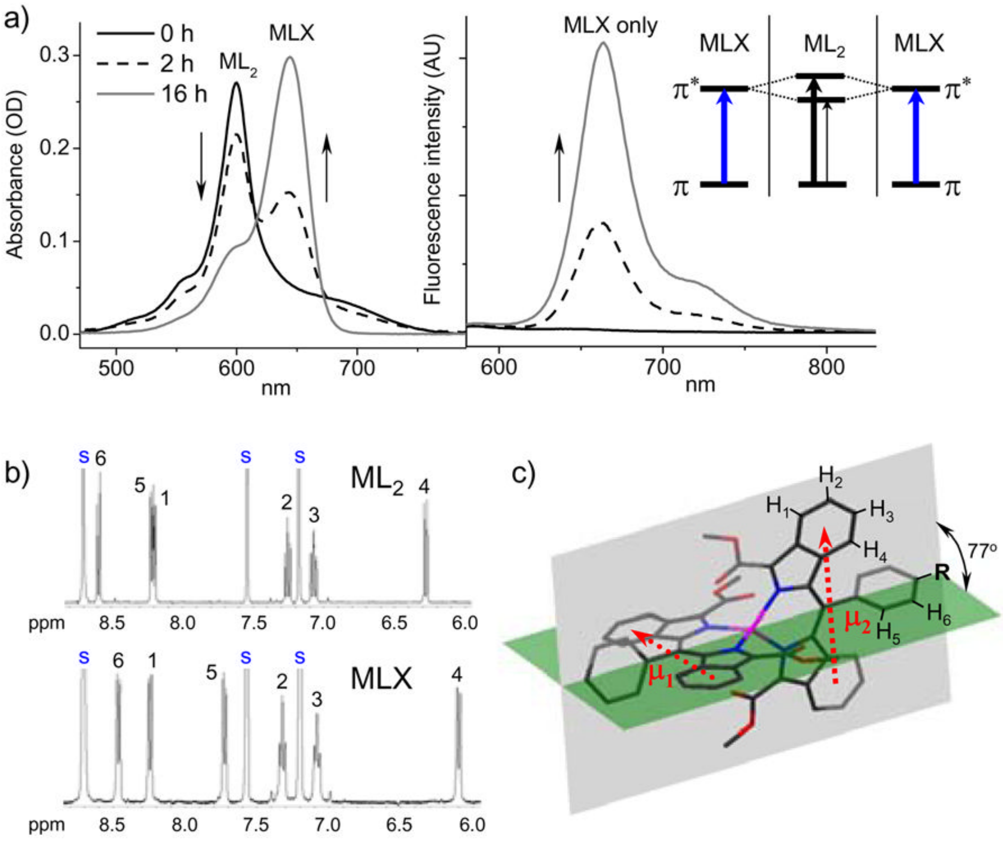


Figure 2.

(a) Changes in the absorption and emission spectra (λ_{ex}=560 nm) of Zn-**2d** (ML_2) upon addition of $Zn(OAc)_2$ (excess). ML_2 in pyridine before addition of $Zn(OAc)_2$ (black), 2 h (red) and 16 h (blue) after addition. Inset: exciton splitting effect; line thickness reflects the transition probability. (b) Aromatic regions of the ^{1}H NMR spectra of ML_2 and MLX forms of Zn-**2d** in pyridine-d_5 (solvent resonances are marked in blue, assignments are based on ^{1}H COSY experiments (S7) and refer to the structure on the right). (c) Optimized structure of homoleptic Zn-**2e** complex (B3LYP/6-31G(d), pendant groups are omitted for clarity). Dotted arrows show orientation of the transition dipole moments (μ_1 and μ_2) of the individual dipyrrin units.

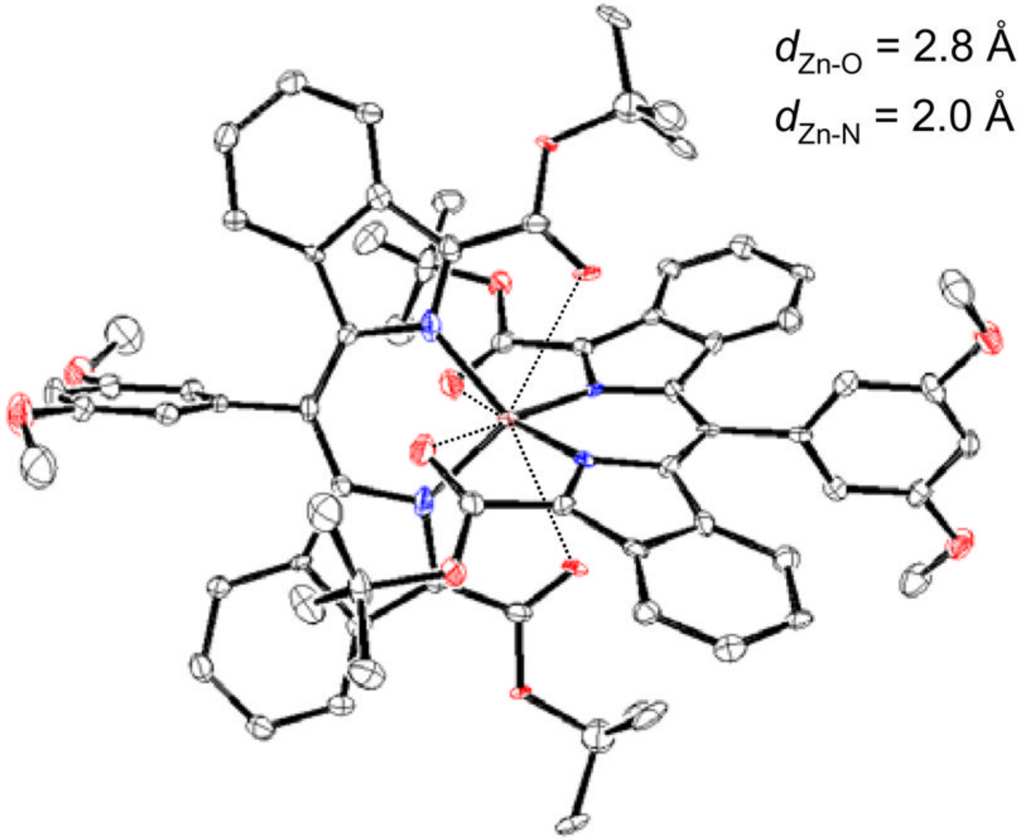
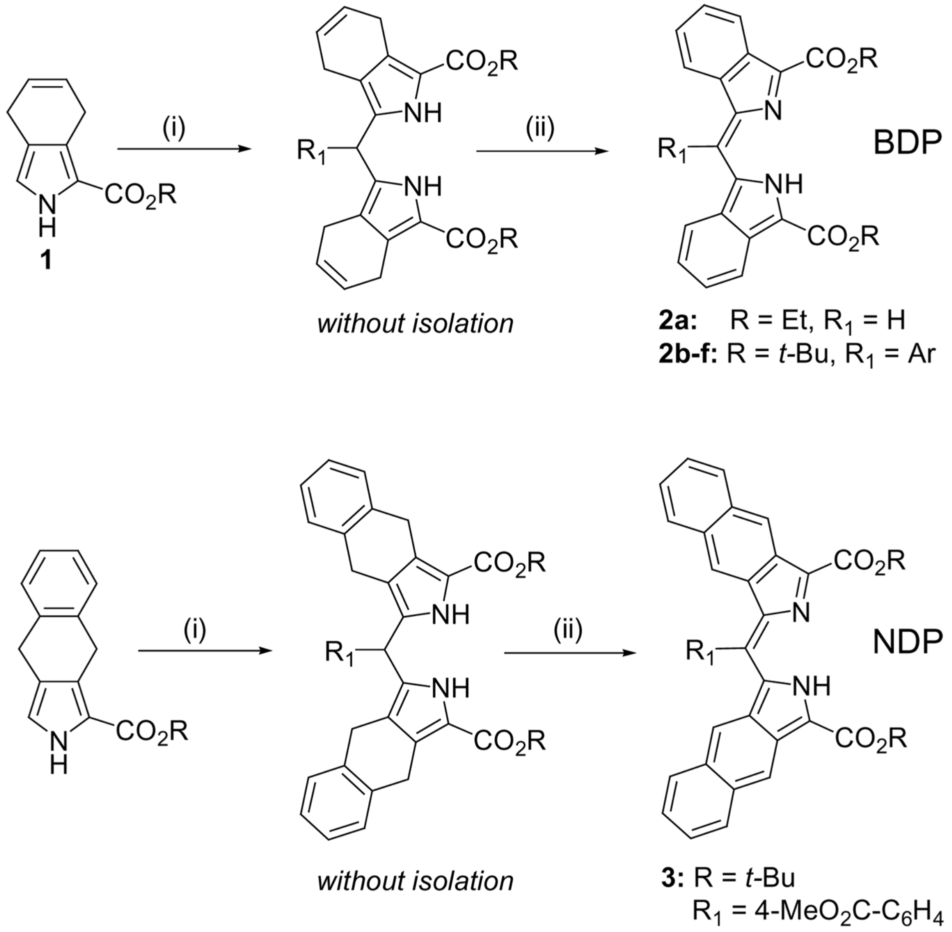


Figure 3.
X-ray crystal structure (ORTEP) of homoleptic Zn-**2e** complex. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level.



Scheme 1.

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

Table 1

Optical properties of Zn and Ca complexes of π-extended dipyrrins in DMF.[a]

Comp.	Abs λ_{max}, nm	Emiss λ_{max}, nm	φ_{fl}^{b}	Comp.	Abs λ_{max}, nm	Emiss 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 (ca 10-fold excess) to solutions of dipyrrins;

[b] relative to Rhodamine 6G in EtOH (φ_{fl}=0.94).11