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Synthesis of highly fluorescent diketopyrrolopyrrole derivative and two-step response of fluorescence to acid

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ABSTRACT

A highly fluorescent diketopyrrolopyrrole derivative with amino groups was synthesized from Pigment Red 254 by a Pd-catalyzed amination reaction. The amino-substituted diketopyrrolopyrrole exhibits a two-step response of fluorescence depending on acidity. This optical property can be applied to a colorimetric detection of acids in the gas phase.

1,4-Diketo-3,6-diphenylpyrrolo[3,4-*c*]pyrrole (DPP) and its derivatives are widely used to color plastic, surface coatings, and color filters owing to their brilliant color and high stability.[1] Most DPP derivatives have poor solubility in organic solvents owing to their strong intermolecular hydrogen bonding and π–π stacking. The alkylation of nitrogen atoms in lactam moieties prohibits the formation of hydrogen bonds and provides high solubility as well as strong luminescence. Because of the high potential of soluble DPP, new functional materials for light-emitting diodes,[2] dye lasers,[3] and organic solar cells[4] have been developed in recent years. Since the optical properties of DPP strongly depend on the electron density of the substituent on their aromatic ring, DPP with a variety of substituents has been synthesized by the reaction of succinate ester and benzonitrile derivatives.[1] However, in the case of DPP with electron-donating groups such as an amino group, the synthetic method gives only a low yield of the product.[2c,3] This situation prompted us to investigate the post-functionalization of DPP[5] at the aryl halide moieties by an organometallic catalysis instead of the conventional method.[6] Quite recently, Yang and co-workers created a two-photon excitation fluorescent material synthesized via the post-functionalization of Br-substituted DPP with diphenylamine using an organometallic catalyst.[7] We independently investigated the post-functionalization of commercially available Cl-substituted DPP, so-called Pigment Red 254, by a Pd-catalyzed amination reaction to create a new functional material. Since Pigment Red 254 is a useful and inexpensive starting material, our approach provides a convenient synthetic procedure. We herein report the high-yield synthesis of an amino-substituted DPP that exhibits strong luminescence and a two-step response to an acid.

DPP with benzyl groups **1** was synthesized with a 70% yield from a reaction of benzyl bromide and Pigment Red 254 in the presence of K_2CO_3 in DMF as shown in Scheme 1 (see Supplementary data).[8] Compound **1** exhibits good solubility in organic solvents such as $CHCl_3$, CH_2Cl_2, toluene, and DMSO. The introduction of amino groups on the aromatic ring was performed by a Pd-catalyzed amination reaction of aryl chlorides and amines, which was recently developed by Buchwald, Hartwig, and their co-workers.[9] The synthesis of compound **2** by the reaction of compound **1** with morpholine in the presence of $Pd(OAc)_2$ with 2-(2′,6′-dimethoxybiphenyl)-dicyclohexylphosphine (SPhos)[9c] was examined. Product **2** was easily purified by column chromatography on silica gel and was isolated with an 88% yield.

Single crystals of **2** suitable for an X-ray diffraction study were obtained by the slow diffusion of ether into its solution in DMF. The crystal structure of **2** is shown in Figure 1.[10] Compound **2** crystallizes in the monoclinic space group *C*2/c with an inversion center at the midpoint of C2 and C2*. In the crystal lattice, intermolecular π–π stacking of the phenyl ring is observed with a 3.4 Å separation (Fig. S-1). Since DPP is an aromatic compound with an electron-accepting property, cyclic voltammograms of **1** and **2** exhibit a reversible electrochemical reduction (Fig. S-2). Owing to the electron-donating property of the morpholine substituents, the reduction of **2** occurs at a more negative reduction potential ($E_{1/2}$ = −1.87 V vs Fc^+/Fc) than that of **1** (−1.62 V). In addition, **2** exhibits a two-electron redox couple at 0.27 V, which is probably due to the oxidation of the morpholinyl moieties. In contrast, **1** does not exhibit a reversible oxidation couple.

Figure 2 shows the absorption and fluorescence spectra of **1** and **2** in $CHCl_3$. The introduction of morpholine substituents causes bathochromic shifts of the absorption and fluorescence spectra with respect to the parent compound **1**. As with other soluble DPP derivatives,[2–4] **2** has a strong absorbance (ε = 42,300) in the visible region (λ_{max} = 522 nm). The fluorescence spectrum exhibits a maximum fluorescence band at 578 nm with a shoulder at approximately 616 nm upon excitation at a wavelength of 522 nm. The solution of **2** exhibits a high quantum yield (Φ_f = 0.91).

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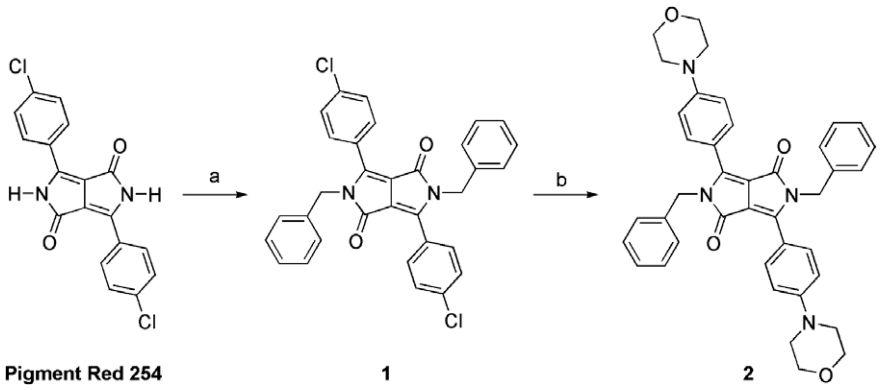

Scheme 1. Synthesis of **2**: Reagents and conditions: (a) benzyl bromide, K_2CO_3, DMF, 120 °C, 70% yield; (b) $Pd(OAc)_2$/SPhos, *t*-BuONa, toluene, 100 °C, 88% yield.

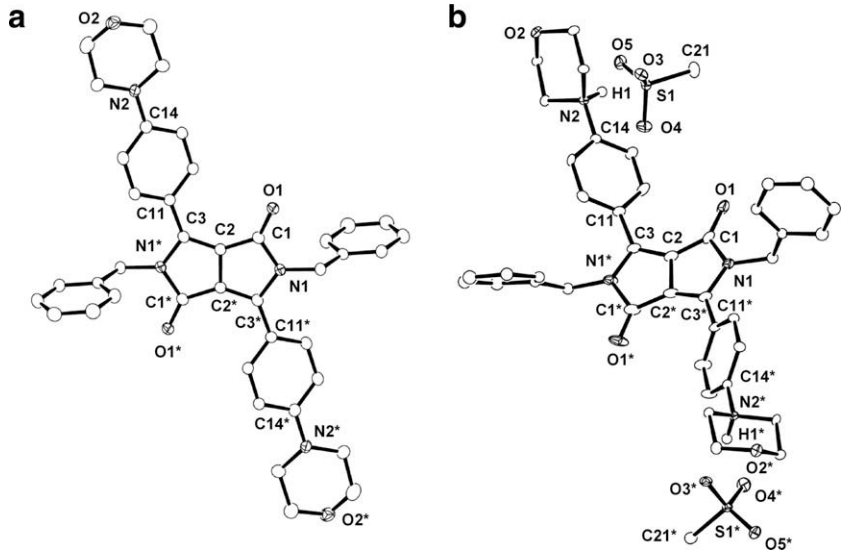

Figure 1. ORTEP drawings of (a) **2** and (b) **2**·**2H**$^+$ with methanesulfonate at 50% ellipsoidal level. Benzyl groups in **2**·**2H**$^+$ show one of the disordered positions. Atoms with asterisks are crystallographically equivalent to those having the same number without asterisk.

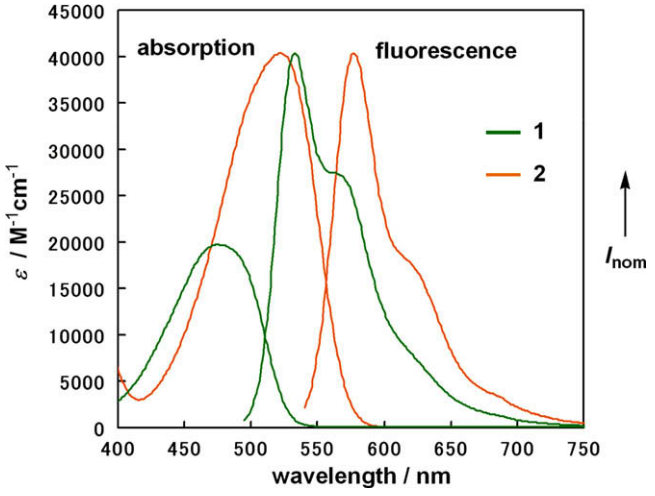

Figure 2. Absorption and fluorescence spectra of **1** (green line, λ_{ex} = 475 nm) and **2** (orange line, λ_{ex} = 522 nm) in $CHCl_3$ (2×10^{-5} M).

To investigate the protonation of the two morpholinyl moieties, titration experiments were performed on **2** by UV/Vis and fluorescence spectroscopy. In UV/Vis spectroscopy, the absorption bands at 373 and 522 nm decrease upon the addition of trifluoroacetic acid (TFA) with isosbestic points at 395 and 436 nm (Fig. 3a).[11] After the addition of more than 1250 equiv, new isosbestic points were observed at 420 and 456 nm (Fig. 3b). Since compound **1** exhibits no response to TFA, these results indicate two-step protonation at the morpholinyl moieties of **2**. Figure 3c and d shows profiles of the fluorescence spectra upon the titration of **2** with TFA with excitation at the wavelengths of the isosbestic points observed in the absorption spectra (436 or 456 nm). The fluorescence of **2** in $CHCl_3$ decreases upon the addition of TFA until the amount of TFA reaches 1000 equiv. Interestingly, the addition of more than 1250 equiv of TFA generates new fluorescence at 540 nm. Figure 4 shows the experimentally obtained evolution of the molar ratio of the monoprotonated species **2**·**H**$^+$ and the diprotonated species **2**·**2H**$^+$ based on the titration by UV/Vis spectroscopy (see Supplementary data). The process of protonation was also investigated by ^{1}H NMR spectroscopy. The resonance of an aromatic proton at the ortho position to the morpholinyl group exhibits a downfield shift upon the addition of TFA to **2** in $CDCl_3$ (4×10^{-3} M) (Fig. S-3). Since the NMR measurements were carried out at a higher concentration than UV/Vis spectroscopy, the NMR spectra exhibit the formation of **2**·**H**$^+$ and **2**·**2H**$^+$ upon addition of small amount of TFA which are 30 and 600 equiv, respectively. The chemical structure of **2**·**2H**$^+$ was confirmed by an X-ray diffraction study (Fig. 1b).[12] The crystal was obtained by the slow evaporation of $CHCl_3$ solution of **2** with 10-fold the amount of methanesulfonic

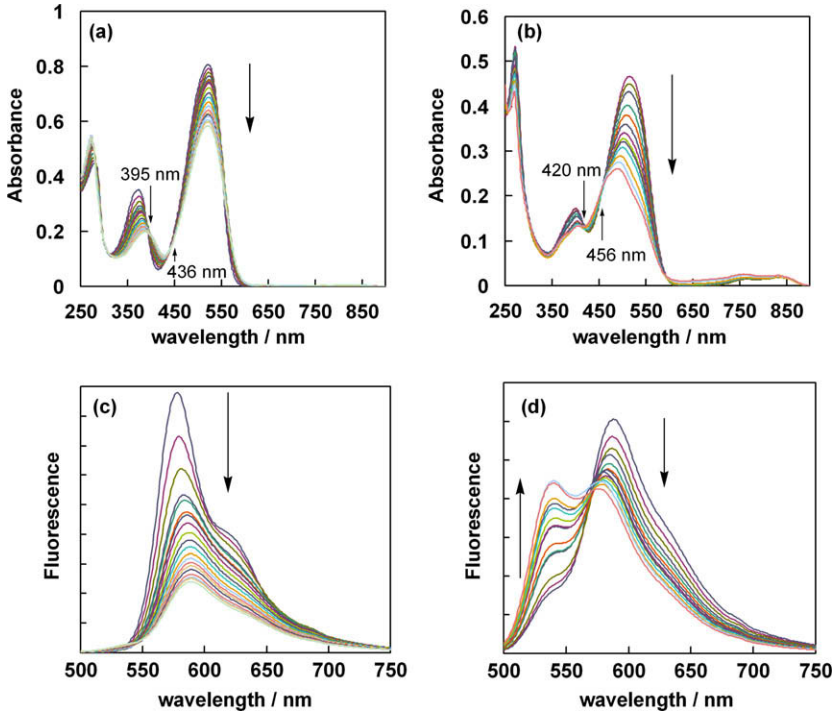

Figure 3. UV/Vis spectra of **2** in $CHCl_3$ (2×10^{-5} M) (a) 0–1000 equiv of TFA and (b) 1250–5000 equiv of TFA. Fluorescence spectra (c) 0–1000 equiv of TFA (λ_{ex} = 436 nm) and (d) 1250–5000 equiv of TFA (λ_{ex} = 456 nm).

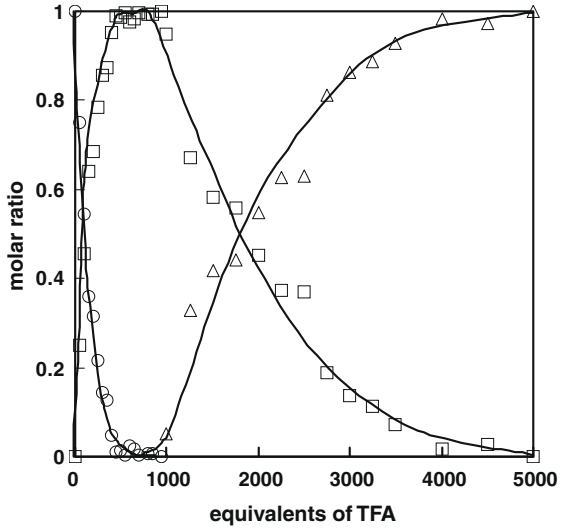

Figure 4. Calculated molar ratio for **2** (circle), monoprotonated **2**·$\mathbf{H}^+$ (square), and diprotonated species **2**·$\mathbf{2H}^+$ (triangle) as a function of equivalents of TFA.

acid instead of TFA. Similarly to **2**, compound **2**·$\mathbf{2H}^+$ crystallizes in the space group *C*2/c with an inversion center at the midpoint of C2 and C2*. The position of the hydrogen atom (H1) on the morpholinyl moiety can be determined by a difference Fourier map. Owing to the protonation, the bond distance of N2–C14 in **2**·$\mathbf{2H}^+$ (1.474 Å) is longer than that in the neutral molecule **2** (1.395 Å). **2**·$\mathbf{2H}^+$ exhibits a large dihedral angle between the pyrrolopyrrole plane and the phenyl ring (38°) in comparison with **2** (28°), which indicates less conjugation of the pyrrolopyrrole and the phenyl ring in **2**·$\mathbf{2H}^+$. The short conjugation is likely to be one of the origins of the hypsochromic shift of **2**·$\mathbf{2H}^+$ shown in Figure 3d.

Although there have been extensive studies of chemical detection systems using fluorescence in the literature,[13] this is a rare example of a two-step response of fluorescence to acid that is, the quenching and regeneration of fluorescence.[14] The quenching of the fluorescence might be caused by an intramolecular charge transfer owing to large dipole moment in the monoprotonated species (**2**·$\mathbf{H}^+$), which is not observed for **2** and **2**·$\mathbf{2H}^+$ owing to small dipole moment.[14a] Since monoprotonated **2**·$\mathbf{H}^+$ exhibits very weak fluorescence and diprotonated **2**·$\mathbf{2H}^+$ has a different color of fluorescence (540 nm) from that of the neutral **2** (578 nm), the fluorophore was applied in a colorimetric detection of acids in the gas phase.[14,15] Figure 5a shows the orange fluorescence of **2** cast on a thin silica gel sheet upon the irradiation of UV light (365 nm). The response of the cast silica gel sheet depends on the strength of the acid as follows. Upon exposure to formic acid vapor, the emission was quenched (Fig. 5b). When the same silica gel sheet was exposed to the vapor of a strong acid such as TFA or HCl, intense yellow fluorescence was observed within 1 s (Fig. 5c). The orange fluorescence was immediately recovered when the yellow

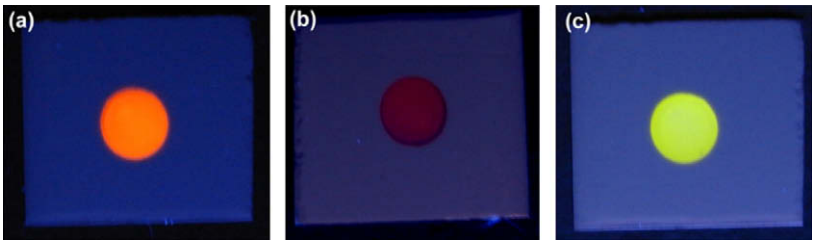

Figure 5. (a) Photographs of **2** casted on thin layer silica gel sheet upon irradiation of UV light (λ = 365 nm) (b) after exposure to formic acid (c) after exposure to TFA.

fluorescent sheet was exposed to ammonia vapor. These reversible phenomena were observed several times (Fig. S-7).

In summary, a Pd-catalyzed amination reaction allows the convenient functionalization of commercially available Pigment Red 254. The incorporation of amino substituents into DPP not only caused bathochromic shifts of the absorption and fluorescence spectra but also allowed the modulation of its photoluminescent properties upon exposure to acidic media. Using **2** as a fluorophore, we demonstrated the colorimetric detection of acid, which exhibits a response with the intensity and color of fluorescence depending on the acidity. Since organometallic coupling reactions including other C–C and C-heteroatom formation reactions can be used in the method of synthesis, various molecular designs of DPP derivatives are possible, providing new materials based on DPP in future.

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Supplementary data

Supplementary data (general experimental information, experimental detail, characterization data of **1** and **2**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.069.

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