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Acid-Responsive Fluorescent Compounds Based on Nitro-Group-Substituted L-Shaped Pentacycles, Pyrrolo[1,2-*a*][1,8]naphthylidines

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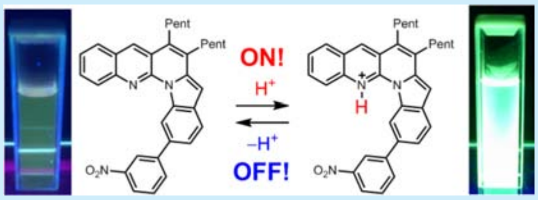
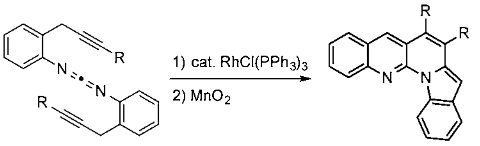
Supporting Information

ABSTRACT: Acid-responsive fluorescent compounds were prepared by introducing a nitrophenyl group to L-shaped pentacycles with a pyrrolo[1,2-*a*][1,8]naphthylidine backbone. These compounds show almost no fluorescence under neutral conditions, but emit green to orange fluorescence upon addition of trifluoroacetic acid. Acid titration experiments and NMR spectroscopy, plus DFT calculations, show that formation of a pyridinium cation species is responsible for the appearance of fluorescence.



Small π-conjugated molecules have attracted much attention in the research fields of both fundamental and applications chemistry. While linear polycyclic ring-fused aromatic compounds such as pentacene derivatives have been investigated extensively,[1] L-shaped polycyclic ring-fused aromatic compounds containing the 6−6−6−5−6 ring system as a corner unit have been studied to a lesser extent.[2] Recently, we reported the synthesis of L-shaped penta- to heptacyclic compounds (e.g., **2**) having a pyrrolo[1,2-*a*][1,8]naphthylidine backbone via fully intramolecular [2 + 2 + 2] cycloaddition of bis(propargyl phenyl)carbodiimides **1** and naphthyl analogues followed by oxidative aromatization (eq 1). In particular, the L-shaped molecules contain spatially separated frontier molecular orbitals (FMOs) and they are highly fluorescent, even in polar solvents such as methanol (Figure 1).[3]



1

2a: R = Pent
2b: R = Me

(1)

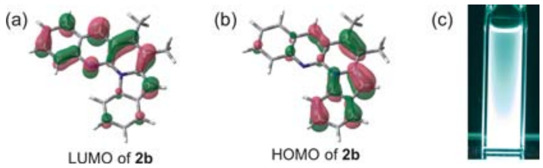


Figure 1. (a) HOMO, (b) LUMO, and (c) photograph under irradiation with UV light (λ = 365 nm) in CH_2Cl_2 of **2b**.

The nitro group is widely recognized as a strong quencher of fluorescent dyes. Indeed, even if the nitro group is not directly conjugated to the fluorophore but is located at a proximal position, such compounds are usually nonfluorescent. Nitro groups are strongly electron withdrawing and thus greatly lower the lowest unoccupied molecular orbital (LUMO) energy level of aromatic compounds. Therefore, in the nitroaryl-substituted fluorophore, the intramolecular photoinduced electron transfer (PeT) process from the excited fluorophore to the electron-deficient nitro aryl moiety (donor-excited PeT; d-PeT) dominates, which results in quenching of the fluorescence.[4] Indeed, nitro-substituted fluorescent compounds are still rare even now.[5] On the other hand, Nagano et al. demonstrated that an appropriate manipulation of the relative free energy change of the PeT process (ΔG_{eT}) may realize a fluorescent nitro-substituted compound.[4] In this context, we envisioned that introduction of a nitroaryl group to an analyte-responsive fluorophore would create a simple and diverse fluorescence switching system. Thus, we have designed nitrophenyl-group-substituted, acid-responsive fluorescent compounds[6] based on our L-shaped pyrrolo[1,2-*a*][1,8]naphthylidine compounds. We anticipated that the introduction of nitrophenyl group(s) would quench the fluorophore of the pentacycles and that protonation of the pyridine site would turn on the fluorescence as a consequence of drastically lowering the LUMOs of the fluorophore.[7] Herein, we report their synthesis and the characterization of their photophysical properties.

Scheme 1 depicts the synthesis of aryl-group-substituted L-shaped compounds **5**−**7**. Initially, **2a** was brominated with *N*-

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Scheme 1. Synthesis of Aryl-Substituted L-Shaped Compounds

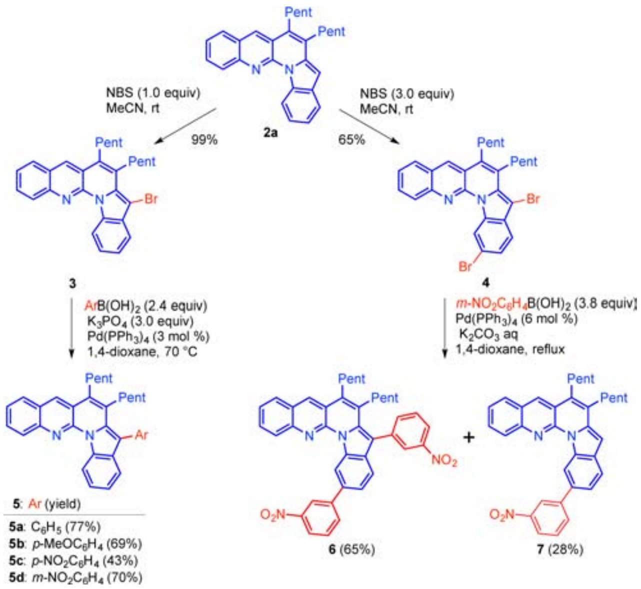

Table 1. Photophysical Properties of L-Shaped Compounds[a]

compd	λ_{max} (nm)	λ_{em}[b] (nm)	Stokes shift (cm^{-1})	Φ_F[b]	τ_s[c] (ns)
2a	404,[d] 425, 451[d]	479, 512	1296	0.71	6.72
5a	412,[d] 433, 460[d]	496, 524	1578	0.72	6.35
5b	412,[d] 435, 461[d]	514	2237	0.89	6.36
5c	409,[d] 432, 456[d]	501, 512	1970	–[e]	–
5d	409,[d] 428, 455[d]	503	2097	–[e]	–
6	417,[d] 440, 465[d]	506	1743	–[e]	–
7	415,[d] 437, 464[d]	514	2096	–[e]	–

[a] In CH_2Cl_2. [b] Excitation at λ_{max}. [c] Fluorescence lifetime excited at 405 nm. [d] Shoulder peak. [e] $\Phi_F < 0.01$.

bromosuccinimide (NBS) to perform cross-coupling reactions. When **2a** was treated with an equimolar amount of NBS in acetonitrile at room temperature, the reaction occurred highly selectively on the 5-position to furnish **3** in 99% yield. When **2a** was treated with 3 equiv of NBS under the same conditions, 2,5-dibrominated compound **4** was formed in 65% yield. With the bromide **3** and dibromide **4** in hand, we carried out the Suzuki–Miyaura coupling reaction to install aryl groups. The reactions of **3** with phenyl, *p*-methoxyphenyl, and *m*-nitrophenyl boronic acid delivered the corresponding aryl-substituted compounds **5a**, **5b**, and **5d** in moderate yields, while the reaction with *p*-nitrophenyl boronic acid afforded the product **5c** in a relatively low yield of 43%. The coupling reaction of 2,5-dibromide **4** provided the expected biscoupling product **6** in moderate yield along with monocoupling product **7**.

Table 1 summarizes some photophysical properties of the L-shaped compounds (**2a** and **5**–**7**) under neutral conditions, and their fluorescence spectra are depicted in Figure S17. The spectral data show that installation of an aryl group onto the 5-position results in only a ca. 10 nm red shift, suggesting ineffective conjugation between the aryl group and the backbone. With regard to fluorescence properties, both phenyl- and *p*-methoxyphenyl-substituted compounds **5a** and **5b** strongly emit with high quantum yields and exhibit a similar fluorescence lifetime (6.4 ns) to **2a** (6.7 ns). Meanwhile, all nitrophenyl-substituted compounds (**5c**, **5d**, **6**, and **7**) exhibit very weak emission, demonstrating the high fluorescence quenching ability of the nitrophenyl group.

To evaluate the effects of acid on the photophysical properties of nonfluorescent nitrophenyl-substituted compounds **5c**, **5d**, **6**, and **7**, their electronic absorption spectra and fluorescence spectra excited at two different wavelengths, corresponding to the maximum absorption bands of neutral (428–441 nm) and acidic compounds (500–510 nm), were measured using a trifluoroacetic acid (TFA) titration.[8] The results are summarized in Table 2. In **5c**, **5d**, and **6**, with increasing amounts of TFA, a color change from green to orange is observed: the original absorption bands at around 430 and 460 nm diminished and a new distinct band formed at longer wavelengths of <500 nm (e.g., **5d**, Figure 2a). In this process, a well-defined isosbestic point was observed at around 460 nm, suggesting the production of one major protonated product. Importantly, addition of TFA turns on fluorescence, producing new distinct bands at ca. 590 and 630 (sh) nm when excited at 510 nm (e.g., **5d**, Figure 2b). In particular, **6**, which contains two nitrophenyl groups, exhibited fluorescence upon addition of TFA (Figures S20 and S21). Meanwhile, in the absorption spectrum of **7** upon addition of TFA, although a well-defined isosbestic point was observed at 475 nm, distinct absorption maxima were not observed (Figure 2c). When **7** was excited at 440 nm after addition of TFA (Figure 2d), **7** showed the highest quantum yield of 0.34 among the protonated L-shaped compounds that we measured. The fluorescence lifetime measurements revealed that protonated **7** features relatively a long lifetime for organic fluorophores. On the other hand, the fluorescence of protonated **5c**, **5d**, and **6** decays biexponentially: Its contributions depend on the excitation wavelength, suggesting dual fluorescence.[9] We confirmed that emission induced by TFA is quenched by addition of base and this process is reversible: neutralization with triethylamine (Figures S22 and S23) or with aqueous sodium hydrogen

Table 2. Photophysical Properties of Protonated L-Shaped Compounds[a]

		excited at 428–441 nm						excited at 500–510 nm					
compd	λ_{max} (nm)	λ_{em}[b] (nm)	Φ_F[b]	τ_s1[c] (ns)	A_1[d]	τ_s2[c] (ns)	A_2[e]	λ_{em}[f] (nm)	Φ_F[f]	τ_s1[g] (ns)	A_1[d]	τ_s2[g] (ns)	A_2[e]
5c+H	472,[h] 500, 545[h]	526, 579	0.06	1.71	0.07	19.63	0.93	591, 629[h]	0.07	1.77	0.77	14.47	0.23
5d+H	473,[h] 501, 540[h]	511, 531, 582	0.06	1.05	0.54	16.75	0.46	589, 625[h]	0.07	1.09	0.56	20.19	0.44
6+H	479,[h] 510, 551[h]	510,[h] 534	0.05	1.88	0.02	17.86	0.98	539,[h] 601	0.06	0.73	0.52	18.70	0.48
7+H	465,[h] 507, 549[h]	496, 515	0.34	0.33	0.01	15.03	0.99	—	—[i]	—	—	—	—

[a] Equivalents of TFA: **5c**+H, 2.3 × 10^5; **5d**+H, 2.3 × 10^5; **6**+H, 5.6 × 10^4; **7**+H, 1.2 × 10^5. [b] Excitation at 432, 428, 441, 440 nm for **5c**+H, **5d**+H, **6**+H, **7**+H, respectively. [c] Fluorescence lifetime excited at 405 nm. [d] Contribution of τ_s1. [e] Contribution of τ_s2. [f] Excitation at 500, 501, 510, 507 nm for **5c**+H, **5d**+H, **6**+H, **7**+H, respectively. [g] Fluorescence lifetime excited at 470 nm. [h] Shoulder peak. [i] $\Phi_F < 0.01$.

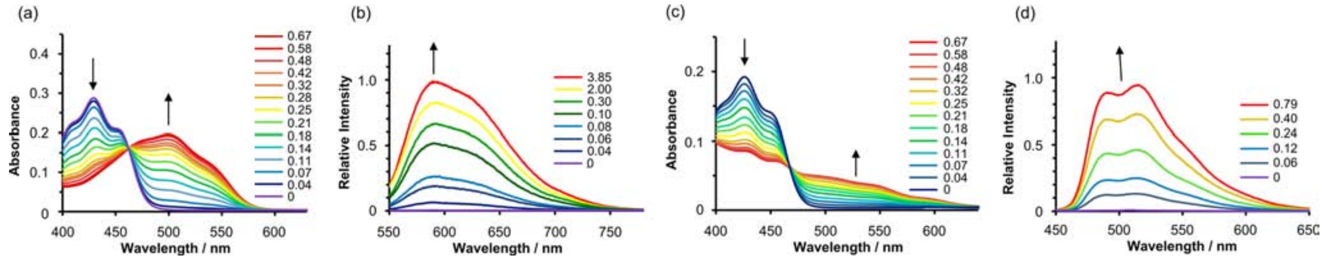

Figure 2. (a) UV−vis and (b) fluorescence spectra of **5d** and (c) UV−vis and (d) fluorescence spectra of **7** in dichloromethane ((a) 20 μM, (b) 2 μM, (c) 20 μM, (d) 0.4 μM) on addition of different amounts of TFA (vol %).

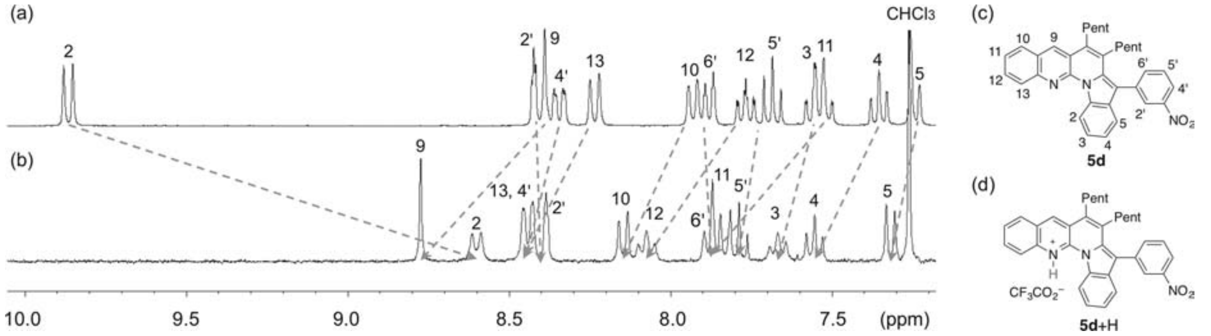

Figure 3. ^{1}H NMR of **5d** in $CF_3CO_2D/CDCl_3$: (a) 0 vol % and (b) 3 vol % of CF_3CO_2D. (c) Numbering of compound **5d**. (d) Structure of **5d**+H.

carbonate turned off the fluorescence without degradation of **5d** and **7**.

To identify the structure of the protonated compound, quantitative ^{1}H NMR titration experiments were carried out on **5d** in $CDCl_3$. As shown in Figure 3 and Table S1, upon addition of CF_3CO_2D (0 to 3.0 vol %), H-2 showed the largest upfield shift (9.86 to 8.60 ppm) and H-9 displayed the largest downfield shift (8.39 to 8.78 ppm). In contrast, signals of the nitrophenyl group hardly shifted. These observations strongly support the predominant formation of structure **5d**+H (Figure 3d) by protonation at the 14-nitrogen atom upon treatment with TFA, which turns on fluorescence.

To elucidate the electronic structure of nitrophenyl-substituted L-shaped compounds **5d**, **6**, and **7**, density functional theory (DFT) calculations at the B3LYP/6-31G** level were performed on the neutral and 14-N-protonated (pyridinium) forms (Figures 4 and S25). For all compounds in both neutral and acidic forms, the HOMOs and LUMOs are specially separated and the HOMOs reside primarily on the indole-containing sides of the skeleton. As expected, the LUMOs are localized on the *m*-nitrophenyl group in the neutral compounds, implying an efficient intramolecular PeT process from the excited fluorophore to the nitrophenyl group. In contrast, in their protonated forms, the LUMOs reside primarily on the pyridine-containing sides of the skeleton, which is relevant to highly fluorescent **2** (Figure 1). Thus, we conclude that the change in position of the LUMOs is responsible for the turn-on of the fluorescence of **5c**, **5d**, **6**, and **7**.

In conclusion, we have succeeded in functionalizing the 2- and 5-positions of L-shaped pentacycles **2** via bromination and Suzuki−Miyaura coupling. Thus, synthesized nitrophenyl-substituted L-shaped pentacyclic compounds behave as a fluorescent switch by acid: they are nonfluorescent in neutral conditions, but become emissive by addition of acid. The resulting fluorescence is quenchable by neutralization with base, and this process is reversible. This constitutes a rare example of a fluorescent dye containing a nitro group, which will contribute to new designs of fluorescent dyes.

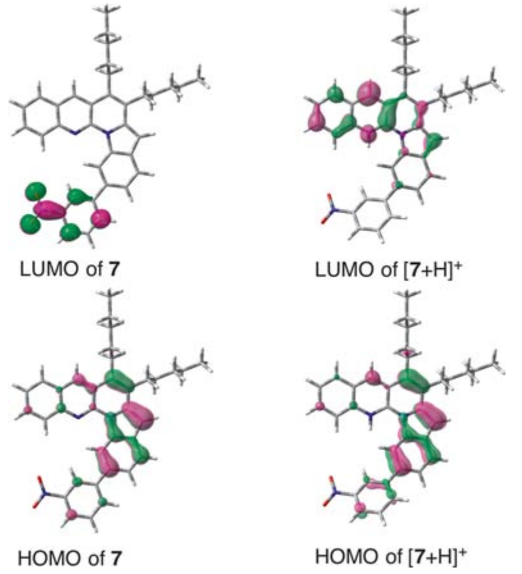

Figure 4. HOMOs and LUMOs of **7** and its 14-N protonated cation $[7+H]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, characterization data, copies of ^{1}H and ^{13}C NMR spectra of all new compounds, photophysical properties, and theoretical calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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