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8-Hydroxyquinoline-Substituted Boron−Dipyrromethene Compounds: Synthesis, Structure, and OFF−ON−OFF Type of pH-Sensing Properties

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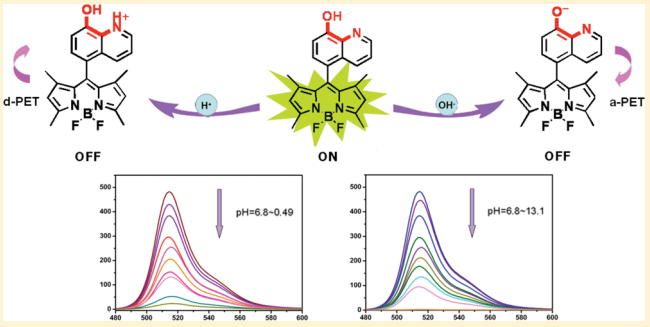
Supporting Information

ABSTRACT: A series of four novel 8-hydroxyquinoline-substituted boron−dipyrromethene derivatives, namely 4,4-difluoro-8-(5-(8-hydroxyquinoline))-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (**1**), 4,4-difluoro-8-(5-(8-hydroxyquinoline))-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (**2**), 4,4-difluoro-8-(5-azastyryl-(8-hydroxyquinoline))-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (**3**), and 4,4-difluoro-8-(5-azastyryl-(8-hydroxyquinoline))-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (**4**), have been synthesized and characterized by a series of spectroscopic methods. The molecular structures of **1** and **2** have been determined by single-crystal X-ray diffraction analyses. The two methyl substituents attached at C-1 and C-7 positions of boron−dipyrromethene (Bodipy) in compound **2** was revealed to prevent the free rotation of the 8-hydroxyquinoline (8-HQ) moiety, resulting in an almost vertical 8-HQ-Bodipy configuration of this compound. This is obviously different from those for **1** with the dihedral angle between 8-hydroxyquinoline and Bodipy moieties of 65.44 and 66.79° due to the lack of methyl substituents in the latter compound. The intense fluorescence from the Bodipy subunit of these compounds was revealed to gradually get diminished along with either decreasing or increasing the pH value under acidic and basic conditions, respectively, in particular for **1**, **2**, and **4** because of the photoinduced intramolecular electron transfer from excited Bodipy moiety to 8-HQ unit and just an opposite process. This renders these compounds the first OFF−ON−OFF type of pH-dependent fluorescent sensors. Nevertheless, both the intrinsic fluorescence of these compounds and their fluorescent quenching properties along with the change in the pH value have been found to depend on the steric configuration as well as the linking group between 8-hydroxyquinoline and Bodipy moieties, revealing the effect of molecular structure on their fluorescence properties.



INTRODUCTION

There has been a growing interest in the development of versatile fluorescent chemosensors in recent years because of their potential applications in chemical and biological target systems[1] associated with their easy signal transduction nature.[2] The reasonable construction for a highly efficient fluorescent sensor is to conjugate a suitable fluorescent signaling unit with an efficient receptor for targets to be detected. Among numerous fluorophores, 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (Bodipy) has been revealed to be the most attractive as a fluorescent signaling unit in constructing fluorescent sensors toward heavy-metal ions,[3] pH,[4] solvent polarity,[5] and small molecules[6] because of its favorable characteristics such as pronounced photostability, high extinction coefficient, narrow emission band, high fluorescence quantum yield, and the extra feature of excitation/emission wavelengths in the visible region.[7]

On the other hand, the 8-hydroxyquinoline moiety has been usually employed as a functional receptor for metal ions owing to its unique pyridyl N and −OH structural characteristics.[8,9] Nevertheless, since the end groups of pyridyl N and −OH in the 8-hydroxyquinoline moiety are able to act as a weak acid and a weak base under acidic and basic conditions, respectively, associated with the equilibrium between the protonated quinolinium $NH^{+}\sim-OH$ form and deprotonated quinolinate $N\sim-O^{-}$ form,[10] this moiety appears to be able to act as the pH indicator for both acidic and basic systems. However, despite the large number of investigations on the fluorescent sensors with the 8-HQ moiety as receptor for metal ions,[11] there still exists no exploration on the fluorescent sensors with 8-HQ moiety as pH indicator to the best of our knowledge.

For the purpose of preparing versatile fluorescent sensors for the acidic and/or basic systems, novel fluorescent compounds

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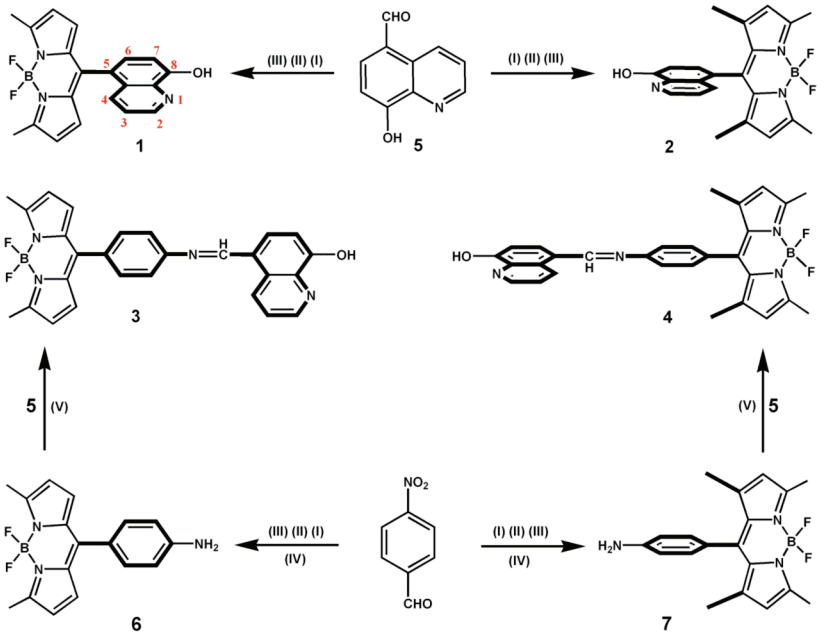
Scheme 1. Synthesis of 8-Hydroxyquinoline-Bodipy-Conjugated Derivatives 1−4[a]



[a] Key: (I) pyrrole, TFA, CH_2Cl_2, rt; (II) DDQ, CH_2Cl_2, rt; (III) DIEA, $BF_3 \cdot OEt_2$, rt; (IV) $NH_2NH_2-H_2O$, 10% Pd−C, MeOH, CH_2Cl_2, reflux; (V) acetic acid, MeOH, reflux.

simultaneously possessing the excellent Bodipy signaling unit and the efficient 8-HQ receptor should be developed. However, introduction of a Bodipy signaling unit at the C-2 position of 8-hydroxyquinoline, adjacent to the binding site of the pyridyl N atom, was revealed to be still selective only to metal ions such as Hg^{2+} or Cu^{2+}.[12] Nevertheless, further investigation revealed that substitution at the C-2 and/or C-4 positions in the 8-HQ moiety mainly tunes the coordinating property of the pyridyl N group, while substitution at the C-5 and/or C-7 positions induces change in the binding ability of the −OH group.[13] As a consequence, designing and preparing novel fluorescent sensors in which the Bodipy unit is attached at the C-5 position are of interest. In the present paper, four novel 8-hydroxyquinoline-substituted boron−dipyrromethene derivatives, namely 4,4-difluoro-8-(5-(8-hydroxyquinoline))-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (**1**), 4,4-difluoro-8-(5-(8-hydroxyquinoline))-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (**2**), 4,4-difluoro-8-(5-azastyryl(8-hydroxyquinoline))-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (**3**), and 4,4-difluoro-8-(5-azastyryl-(8-hydroxyquinoline))-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (**4**), Scheme 1, were designed and synthesized. As expected, the intense fluorescence of compounds **1**, **2**, and **4** has been revealed to change depending on the pH value; the fluorescence gradually diminished with either *decreasing* or *increasing* pH value of their solution in a mixed solvent of H_2O and acetonitrile (1:9) because of the protonated quinolinium $NH^+\sim-OH$ form and deprotonated quinolinate $N\sim-O^-$ form of the 8-HQ moiety under acidic and basic conditions, respectively. This in turn leads to a photoinduced electron transfer from the excited Bodipy moiety to the 8-HQ unit under acidic conditions and just a reverse-electron transfer process under basic conditions responsible for the gradual fluorescent quenching in the acidic and basic systems. As a consequence, these compounds seem to represent the first example of a novel OFF−ON−OFF type of fluorescent pH sensors, which will be helpful for developing novel versatile fluorescent pH sensors with potential applications in chemical and biological fields.

RESULT AND DISCUSSION

Design and Synthesis. Considering the potential effect of the Bodipy unit attached at the C-5 position of 8-HQ moiety on the −OH group, two different Bodipy signaling units are directly connected onto the C-5 position of 8-HQ moiety in compounds **1** and **2**, respectively. With the aim of investigating the effect of the linking group between the fluorophor and receptor on the sensitive capacity of the target compounds, an aza-styryl group with a C═N moiety was introduced between an 8-HQ receptor and the Bodipy signaling unit in compounds **3** and **4**, Scheme 1. These four 8-hydroxyquinoline-substituted boron−dipyrromethene compounds were synthesized according to the literature procedure.[7] Satisfactory elemental analysis results have been obtained for the whole series of four newly prepared compounds **1**−**4** after repeated column chromatography and/or recrystallization. These four compounds have also been characterized by MALDI-TOF mass and ^1H as well as ^{13}C NMR spectroscopy (Figures S1−S4, Supporting Information). The molecular structures of **1** and **2** were clearly revealed by single-crystal X-ray analyses.

Crystal Structures of 1 and 2. Single crystals of compounds **1** and **2** suitable for X-ray diffraction analysis were obtained by slow diffusion of hexane into a $CHCl_3$ solution of these compounds, and the basic features are listed in Table S1 (Supporting Information). Compound **1** crystallizes in the orthorhombic system containing two molecules with slightly different configurations per unit cell, Figure 1A,B. In contrast, compound **2** crystallizes in the triclinic system with only one molecule per unit cell, Figure 1C. In both compounds, the C_9BN_2 (Bodipy) framework consisting of one central six-membered and two adjacent five-membered rings is essentially flat, with the maximum deviation from the least-squares mean plane being 0.023 and 0.035 Å in **1** and 0.099 Å

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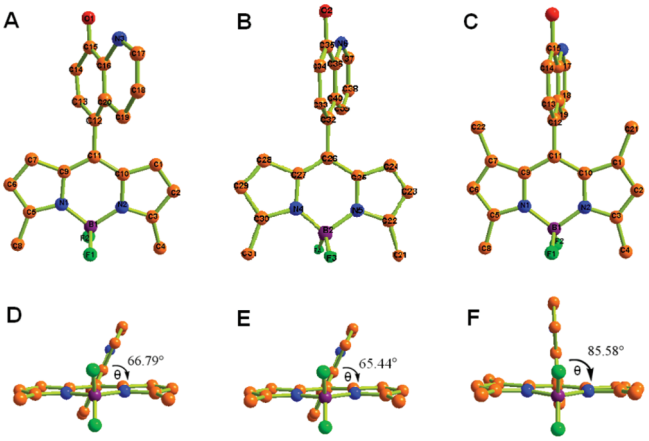

Figure 1. Molecular structures of **1** in top-view (A and B) and side-view (D and E), and molecular structures of **2** in top-view (C) and in side-view (F), with all hydrogen atoms omitted for clarity.

in **2**, respectively. More interestingly, all of the C−C and C−N bond lengths within the C_9BN_2 backbone locate in the range of 1.363−1.426 and 1.336−1.401 Å, respectively, without any clear distinction between single and double bonds, indicating the strongly delocalized π-system nature of the C_9BN_2 (Bodipy) framework in both **1** and **2**. However, this π-electron delocalization is interrupted between the two B−N bonds (1.535−1.555 Å), which is in agreement with the results reported for other Bodipys.[14] As shown in Figure 1D,E, the dihedral angles between the mean plane of 8-HQ unit and the C_9BN_2 moiety of the two 8-HQ-bodipy molecules with slightly different configurations in the same unit cell of compound **1** are 66.79 and 65.44°, respectively, suggesting the inefficient electronic coupling between 8-HQ and C_9BN_2 (Bodipy) units in this compound. However, owing to the introduction of two methyl groups onto the C-1 and C-7 atoms in the Bodipy moiety, this dihedral angle increases to 85.58° in compound **2**, Figure 1F, indicating the almost nonelectronic coupling nature between the 8-HQ moiety and C_9BN_2 unit in **2**.[15] This difference in molecular configuration because of different steric arrangements between **1** and **2** leads to different electron transfer efficiencies between the 8-HQ unit and C_9BN_2 (Bodipy) moieties in these two compounds, which in turn are responsible for their different optical properties as detailed below.

Spectroscopic Properties of 1−4. The electronic absorption and steady-state fluorescence spectra of compounds **1**−**4** were measured in a variety of solvents with different polarities including toluene, CH_2Cl_2, THF, CH_3CN, and MeOH, and the data are summarized in Table 1. The electronic absorption maxima of these compounds are centered at 501−517 nm, ascribed to the S_0-S_1 transition of Bodipy moieties, along with high molar absorption coefficients. The fluorescence emission spectra display a slightly Stokes-shifted (ca. 13 nm), mirror-symmetrical band relative to the absorption of Bodipy unit, Figure S5 (Supporting Information), with the maximum emission wavelengths in the range of 510−528 nm. Moreover, along with the decrease in the solvent polarity from MeOH, CH_3CN, THF, and CH_2Cl_2 to toluene, the maxima of both electronic absorption and fluorescence emission bands for compounds **1**−**4** take a slight shift to the lower energy direction, ca. 5 nm, Figure S6 (Supporting Information), indicating the very small change in the dipole moment between the ground and excited state of Bodipy moiety in these four compounds.[16]

Table 1. Spectral Parameters of the 8-Hydroxyquinoline-Bodipy-Conjugated Derivatives 1−4 in Different Solvents

BDP	solvent	λ_{Abs} (max/nm)	log(ε_{max})	λ_{em} (max/nm)	$\Delta\nu_{max}$ (nm)	Φ_f
1	MeOH	511	3.99	523	12	0.0028
	CH_3CN	511	4.02	523	12	0.1138
	THF	514	4.03	527	12	0.1733
	CH_2Cl_2	515	4.02	527	13	0.2869
	toluene	516	4.04	528	12	0.2506
2	MeOH	502	4.35	515	13	0.0147
	CH_3CN	501	4.25	514	13	0.2090
	THF	504	4.36	518	15	0.3226
	CH_2Cl_2	505	4.37	518	13	0.3809
	toluene	507	4.39	521	14	0.3090
3	MeOH	509	3.96	522	13	0.0004
	CH_3CN	510	3.97	524	14	0.0054
	THF	511	4.05	526	15	0.0128
	CH_2Cl_2	512	4.03	527	15	0.0212
	toluene	512	4.09	528	16	0.0866
4	MeOH	497	4.22	511	12	0.0017
	CH_3CN	498	4.20	512	14	0.0870
	THF	501	4.23	515	14	0.0892
	CH_2Cl_2	502	4.23	515	14	0.1306
	toluene	503	4.26	516	13	0.1964

However, in comparison with **1**, the maxima of both absorption and emission bands of compound **2** in the series of solvents including acetonitrile take an obvious blue-shift, ca. 10 nm, Figure 2 and Table 1. Nevertheless, the fluorescence quantum yield of compound **1** is also significantly lower than that for **2**, probably because of the nearly orthogonal configuration of the latter compound which limits the effective interaction between Bodipy and 8-HQ units and results in less excited energy loss from the excited Bodipy moiety via nonirradiative decay. This is also true for compound **3** relative to **4**. These results clearly reveal the effect of molecular configuration on the electronic absorption and emission spectroscopic properties of 8-HQ-Bodipy-conjugated derivatives. It is worth noting that introduction of an aza-styryl group with a C=N moiety between the 8-HQ unit and Bodipy moiety in compound **4** seems to induce little shift, ca. 3 nm, in both the absorption and emission bands relative to those of **2**, Figure 2, suggesting the lower influence of the aza-styryl group between the 8-HQ unit and Bodipy moiety on the maxima of absorption and emission bands of this compound. However, the fluorescence quantum yield of **4** is a bit lower than that for **2** because of the introduction of an aza-styryl group with the electron-donating −C=N− bond between the 8-HQ and Bodipy moieties in **4**, which results in additional partial fluorescent quenching of Bodipy chromophore. This is also true for **3** and **1**. Moreover, the effects of the molecular configuration and the linking group between the 8-HQ moiety and Bodipy chromophore on the spectroscopic properties are further clearly validated by the obviously small fluorescence quantum yield and more red-shifted in both absorption and emission bands for compound **3** in comparison with those for **2**, Figure 2 and Table 1.

pH-Dependent Fluorescence Spectra of Compounds 1−4. Before the pH-dependent photophysical properties of compounds **1**−**4** can be expounded, it is necessary to give a very

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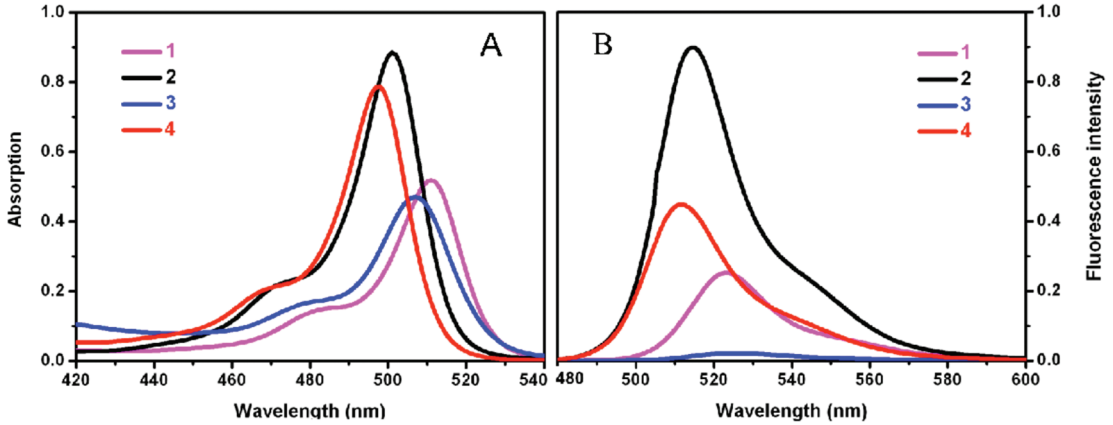

Figure 2. Electronic absorption (A) and fluorescence spectra (B) of compounds **1**−**4** at a concentration of 5×10^{-5} M in CH_3CN with excitation wavelength of 450 nm.

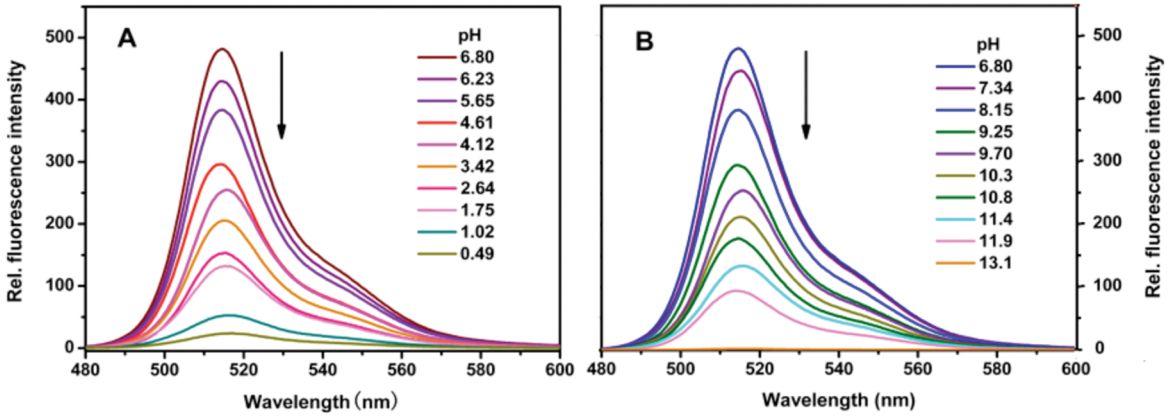

Figure 3. Dependence of the fluorescence emission spectra of compound **2** under acidic (A) and basic conditions (B), respectively, on the change of the pH value at the concentration of 1.25×10^{-5} M in a mixed solvent of H_2O and CH_3CN (1:9) with an excitation wavelength of 450 nm.

brief description of the fluorescence properties of pH-dependent fluorescent sensors in which Bodipy moiety is utilized as fluorescent signaling unit. The fluorescent intensity of reported pH sensors was found to change depending only on the change of pH value in a monotonous way, which gets increased or decreased along with the change (either increase or decrease) in the pH value in a monotonous way due to the only one photoinduced electron transfer mechanism between receptor and Bodipy signaling unit, resulting in the OFF−ON or ON−OFF type of fluorescent pH sensors.[17] There is still no report on the pH sensor whose fluorescent intensity changes in acidic and basic systems along with decreases and increases in the pH value, respectively, based on the opposite photoinduced electron transfer processes between a receptor and Bodipy signaling unit.

To study the pH-dependent optical properties of compounds **1**−**4** with unique pyridyl N and −OH structural characteristics, the pH titration experiments were carried out in a mixed solvent of H_2O and CH_3CN (v/v = 1:9) with a very small amount of TFA for protonation of pyridyl N group and NaOH (0.1 M) used for deprotonation of the −OH group, respectively. As shown in Figure S7 (Supporting Information), the electronic absorption spectrum of compound **2** remains almost unchanged along with changing (either decreasing or increasing) the pH value of the system. In good contrast, the intense fluorescence from the Bodipy subunit of **2** under acidic conditions gradually gets diminished (despite the maximum wavelength of this emission remaining almost unchanged) along with a *decrease* in the pH value from 6.8 to 0.49, Figure 3A. Most interestingly, along with an *increase* in the pH value from 6.8 to 13.1, the intense fluorescence of the same compound under basic conditions also gradually gets diminished in a similar manner as observed under acidic conditions, Figure 3B. These results reveal the typical characteristics of a pH-fluorescent probe through a photoinduced electron transfer (PET) quenching process between receptor and fluorescent signaling unit for this compound.[18] In other words, a photoinduced electron transfer quenching process between the 8-HQ receptor and Bodipy fluorescent signaling unit is responsible for the particular fluorescent properties in compound **2** along with either *decreasing* the pH from 6.8 to 0.49 or *increasing* the pH from 6.8 to 13.1. The unique pH-dependent fluorescent property of **2** indicates the potential application of this compound as a pH indicator under both acidic and basic conditions. This, to the best of our knowledge, represents the first example of a novel OFF−ON−OFF type of fluorescent pH sensor.

Similar to **2**, compounds **1** and **4** also display the similar fluorescence characteristics in slightly changed ranges of pH

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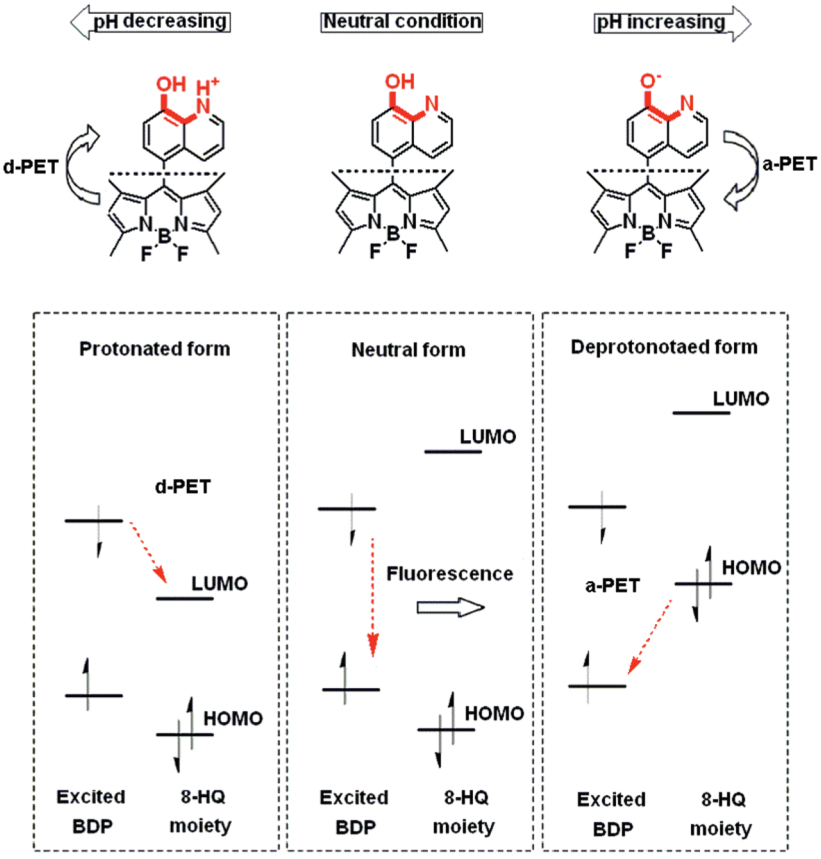

Figure 4. Proposed photoinduced electron transfer mechanism between Bodipy moiety and 8-HQ unit of compound **2** in protonated quinolinium, neutral, and deprotonated quinolinate states, respectively.

under both acidic and basic conditions, Figures S8 and S9 (Supporting Information) and, therefore, can also act as an OFF−ON−OFF type of pH fluorescent sensors. However, their sensitive properties toward the change of pH values appear to be not as good as that for analogue **2** (Figure 3) because of the relatively lower intrinsic fluorescent emission intensities for **1** and **4** in comparison with that for **2** as mentioned above due to the difference in molecular structure of these compounds. In particular, the intrinsic fluorescence of the compound **3** is too weak to be suitable for pH sensors. These results clearly reveal the effects of the molecular configuration and the linking group between 8-HQ moiety and Bodipy chromophore on the pH-dependent fluorescent properties of these compounds, which will be helpful for the design and synthesis of novel efficient fluorescent probes.

pH-Dependent PET Mechanism. For the purpose of understanding the interesting pH-dependent fluorescence characteristics of these compounds, the following PET quenching mechanism determined by the orbital energy levels of the excited states of Bodipy moiety and 8-HQ unit is proposed with compound **2** as an example, Figure 4. In principle, Bodipy can serve as both electron donor and acceptor upon photoexcitation. In other words, the photoinduced electron can transfer from the excited Bodipy moiety to the lowest unoccupied molecular orbital (LUMO) of the 8-HQ (donor-excited PET; d-PET) or just reversely from the highest occupied molecular orbital (HOMO) of 8-HQ to the excited Bodipy moiety (acceptor-excited PET; a-PET).[19] As far as the 8-HQ moiety is concerned

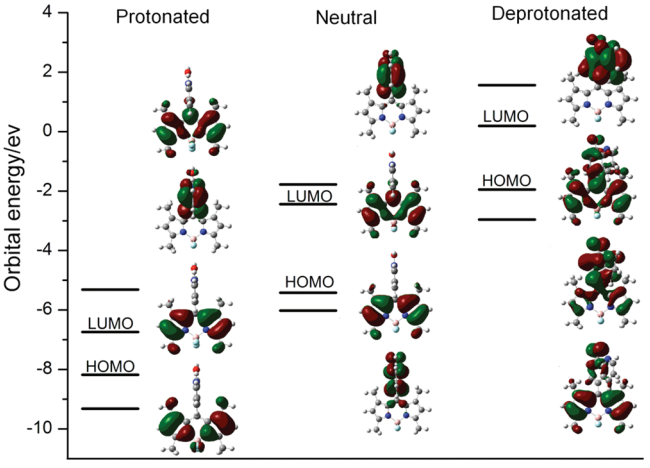

Figure 5. Energy levels and surfaces of frontier MOs of compound **2** in protonated, neutral, and deprotonated states, respectively.

as the receptor in **2**, its HOMO is located on the phenoxide side and LUMO on the pyridyl side.[13] When the N atom is protonated in the form of NH^+, the LUMO energy of electron-deficient 8-HQ unit becomes lower than that of the excited Bodipy moiety, Figure 4, leading to a d-PET quenching process. In contrast, when the OH group of 8-HQ is deprotonated into O^-, the HOMO energy of 8-HQ moiety gets increased and becomes higher than that of excited Bodipy fluorophore, Figure 4,

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which induces the electron transfer from 8-HQ moiety to Bodipy unit, giving rise to an reductive a-PET. These two opposite photoinduced electron transfer processes are in turn responsible for the special fluorescence characteristics of compound **2** along with the change in the pH value under acidic and basic conditions, resulting in a novel OFF−ON−OFF type of pH fluorescent switch to acidic and basic conditions, respectively.

The above-mentioned two opposite PET mechanisms are clearly validated by density functional theory (DFT) calculation with the B3LYP/6-31G(d) method (see the Supporting Information for computational details and the coordinates for calculated structures, Tables S2−4) based on the optimized molecular structure of compound **2**. The calculated frontier molecular orbital (MO) energies and surfaces are shown in Figure 5. As can be found, both the HOMO and LUMO of **2** in the neutral state are located almost completely on the Bodipy moiety, while the HOMO-1 and LUMO+1 are located mainly on the 8-HQ unit. As a result, the electronic transition between HOMO and LUMO for **2** is limited only on the Bodipy moiety, leading to an intensive intrinsic fluorescence from the bodipy moiety of this compound. When the N atom of 8-HQ in compound **2** is protonated in the form of NH^+, the LUMO energy of 8-HQ moiety, −6.74 eV, becomes lower than that for the Bodipy unit in the molecule of compound **2**, −5.31 eV, which in turn results in the electronic transfer from Bodipy moiety to 8-HQ moiety for compound **2** under acidic conditions, Figure 5. When the OH group of the 8-HQ moiety of **2** is deprotonated into O^- in the basic system, change occurs in the molecular structure of this compound as exemplified by the dihedral angle between Bodipy unit and 8-HQ moiety from ca. 90° in neutral state to ca. 60° in negative state. Along with this structural change, the HOMO energy of the 8-HQ moiety in the molecule of **2** gets increased to be close to those of the HOMO and LUMO of Bodipy moiety. As a consequence, the linear combination of these three MOs with similar energy levels generates three new frontier MOs for this compound in the negative state, namely LUMO (0.19 eV), HOMO (−1.95 eV), and HOMO-1 (−2.96 eV), all of which obviously have electronic distribution over both Bodipy and 8-HQ moieties, Figure 5. However, it must be pointed out that the HOMO-1 and LUMO for compound **2** in the negative state are mainly contributed from the Bodipy moiety, while the HOMO mainly from the 8-HQ moiety on the basis of the theoretical calculation result. As a result, the electron should transfer from the 8-HQ unit to the Bodipy moiety in **2** in the negative state, just in the opposite direction to that for the same compound in the positive state. These results rationalize the photoinduced electron transfer (PET) quenching mechanism proposed for compound **2** as detailed in last section.

CONCLUSION

In summary, a series of four novel 8-hydroxyquinoline-substituted boron-dipyrromethene derivatives have been designed and synthesized. Comparative studies reveal their special pH-dependent fluorescent properties under acidic and basic conditions. The intense intrinsic fluorescence of these compounds, in particular compounds **1**, **2**, and **4**, gradually gets diminished along with *decreasing* and *increasing* pH values, respectively, because of the protonated quinolinium $NH^+\sim-OH$ form and deprotonated quinolinate $N\sim-O^-$ form of the 8-HQ moiety under acidic and basic conditions, which leads to a photoinduced electron transfer from the excited Bodipy moiety to 8-HQ unit and the just opposite process responsible for the gradual fluorescent quenching in the acidic and basic systems. This renders these compounds the special OFF−ON−OFF type of pH-dependent fluorescent sensors. Nevertheless, single-crystal X-ray diffraction analysis together with the DFT theoretical calculations reveals the effect of molecular structure, actually the dihedral as well as the linking group between the 8-HQ receptor unit and Bodipy fluorescent signaling moiety, on the intrinsic fluorescent property and in turn the pH-sensing property of these compounds. The present result appears to represent the first example of pH fluorescent sensor, with 8-HQ as receptor and Bodipy as signaling unit, in particular with the OFF−ON−OFF type nature, which should be helpful for designing and preparing novel versatile fluorescent sensors with potential applications in chemical and biological fields.

EXPERIMENTAL SECTION

Chemicals. Column chromatography was carried out on silica gel (Merck, Kieselgel 60, 70−230 mesh) with the indicated eluents. All other reagents and solvents were used as received. Dichloromethane was freshly distilled from CaH_2 under nitrogen. The compound of dipyrromethane was prepared according to the published procedures. The compound of 4,4-difluoro-8-(4-aminophenyl)-1,3,5,7-tetramethyl-4-bora-3a,4a- diaza-*s*-indacene (**7**) was prepared according to the literature procedure.[20]

General Instruments. ^1H and ^{13}C NMR spectra (^1H, 400 MHz, and ^{13}C, 100 MHz) were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ with shifts referenced to $SiMe_4$ (0.00 ppm). MALDI-TOF mass spectra were taken on a Bruker BIFLEX III ultra-highresolution Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer with α-cyano-4-hydroxycinnamic acid as matrix. Elemental analyses were performed on an Elementar Vavio El III. Electronic absorption spectra were recorded on a U-4100 spectrophotometer. Steady-state fluorescence spectroscopic studies were performed on an F 4500 (Hitachi). The slit width was 2.5 nm for emission. The photon multiplier voltage was 700 V. The relative fluorescence quantum yields of Bodipy derivatives were obtained by comparing the area under the corrected emission spectrum of the test sample with that of a solution of 4,4-difluoro-8-(4-methylphenyl)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene in CH_2Cl_2 with excitation wavelength of 450 nm, which has a quantum efficiency of 0.60 according to the literature.[20] The pH measurements were carried out with a PHS-25 pH analyzer. Crystal data for **1** and **2** were collected on a Bruker SMART CCD diffractometer with a Mo Kα sealed tube (λ = 0.71073 Å) at 293 K, and details of the structure refinement are given in Table S1 (Supporting Information). CCDC-793813 and -793814 containing the supplementary crystallographic data for this paper can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

pH-Dependent Fluorescence Experiments. To determine pH-dependent fluorescence properties of these compounds, the solutions of **1**−**4** in a mixed solvent of H_2O/CH_3CN (1:9) (1.25×10^{-5} M) were prepared. TFA and 0.1 M NaOH in a mixed solvent of H_2O/CH_3CN (1:9), respectively, were employed to tune the pH values for the purpose of investigating their pH-dependent fluorescence properties. All of the measurements were conducted at 20 °C.

Synthesis of 8-Hydroxyquinoline-5-carboxaldehyde (5). This known compound was synthesized by modifying the reported procedure with improved reaction yield.[21] Sodium hydroxide (10 g) in water (8 mL) was added into the solution of 8-hydroxyquinoline (5 g) in ethanol (20 mL) at 40 °C. After the mixture was heated to 65 °C, cetyltrimethylammonium bromide (0.013 g) was added to this reaction

mixture, and chloroform (5 mL) was subsequently dropped within 20 min. The resulting black mixture was refluxed for another 8 h, and then the volatiles were evaporated under reduced pressure. The semisolid residue was poured into cold water (150 mL) and the pH was adjusted to ca. 5 with acetic acid. The brown precipitate obtained was filtered off and dried in air, which was further dissolved in a relatively large amount of chloroform and then filtered again. The filtrate was evaporated under reduced pressure, and the residue was applied on a silica gel chromatography with CH_3Cl/MeOH (10:1) as eluent. The target compound was obtained as pale-yellow powder, 867 mg (19.3%).

Synthesis of 4,4-Difluoro-8-(5-(8-hydroxyquinoline)-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (1). To the mixture of 8-hydroxyquinoline-5-carboxaldehyde compound **5** (174 mg, 1 mmol) and 2-methylpyrrole (160 mg, 2.00 mmol) dissolved in CH_2Cl_2 (120 mL) was added one drop of TFA. The resulting mixture was then stirred at room temperature under N_2 atmosphere. When thin-layer chromatography (TLC) monitoring (silica, CH_2Cl_2) indicated the complete consumption of the aldehyde, a solution of DDQ (227 mg, 1 mmol) in CH_2Cl_2 (20 mL) was added, and the reaction mixture was further stirred for another 30 min. After the addition of *N*,*N*-diisopropylethylamine (DIEA) (2 mL) into the mixture, the resulting black-red mixture was stirred for 5 min. Then $BF_3 \cdot OEt_2$ (2.0 mL) was added into the reaction mixture, and stirring was continued for another 30 min. After the reaction mixture was washed with water, the organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was chromatographed on a silica gel column using $CHCl_3/CH_3OH$ (50:1) as eluent. Repeated chromatography followed by recrystallization from ethyl acetate and hexane gave the target compound **1** as black-green crystals: 88 mg (24%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.81 (t, J = 4 Hz, 1H), 8.23 (m, J = 10 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.41 (m, J = 12.8 Hz, 1H), 7.23 (overlapped with strong residual $CHCl_3$ signal at δ 7.24, 1H), 6.46 (d, J = 4 Hz, 2H), 6.20 (d, J = 4.4 Hz, 2H), 2.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 153.6, 148.4, 139.3, 137.7, 135.7, 134.7, 133.8, 130.2, 130.1, 129.7, 128.2, 122.3, 121.7, 119.6, 109.1, 14.9; MS (MALDI-TOF) an isotopic cluster peaking at m/z 363.2 [calcd for M^+ 363.14]. Anal. Calcd for $C_{20}H_{16}BF_2N_3O$: C, 66.14; H, 4.44; N, 11.57. Found: C, 66.29; H, 4.31; N, 11.29.

Synthesis of 4,4-Difluoro-8-(5-(8-hydroxyquinoline)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (2). By employing the above-described procedure with 2,4-dimethylpyrrole (190 mg, 2.00 mmol) instead of 2-methylpyrrole as starting material, 4,4-difluoro-8-(5-(8-hydroxyquinoline)-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene **2** was obtained as purple-red powder: 82 mg (21%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (t, J = 4 Hz, 1H), 8.10 (m, J = 9.6 Hz, 1H), 7.42 (m, J = 26.4 Hz, 2H), 7.28 (d, J = 8 Hz, 1H), 5.93 (s, 2H), 2.56 (s, 6H), 1.10 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 153.2, 148.6, 142.9, 138.3, 138.2, 133.7, 132.4, 127.9, 127.1, 122.8, 122.6, 121.4, 110.1, 14.6, 14.1; MS (MALDI-TOF) an isotopic cluster peaking at m/z 391.10 [calcd for M^+ 391.17]. Anal. Calcd for $C_{22}H_{20}BF_2N_3O$: C, 67.54; H, 5.15; N, 10.74. Found: C, 67.27; H, 5.46; N, 10.56.

Synthesis of 4,4-Difluoro-8-(4-aminophenyl)-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (6). By utilizing the above-described procedure used to prepare compound **1** with 4-nitrobenzaldehyde (604 mg, 4.00 mmol) instead of 8-hydroxyquinoline-5-carboxaldehyde as starting material, 4,4-difluoro-8- (4-nitrophenyl)-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene was prepared. After the reaction of 4,4-difluoro-8-(4-nitrophenyl)-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (172 mg, 0.5 mmol) with $NH_2NH_2-H_2O$ (0.7 mL, 80%) in refluxing ethanol (30 mL) with Pd/C (10 mg) as catalyst under N_2 atmosphere for 6 h, the resulting mixture was cooled to room temperature, and the catalyst and the solvent were removed by filtration and evaporation under reduced pressure, respectively. The residue was then chromatographed on a silica gel column with CH_2Cl_2 as eluent, affording compound **6** as a red powder 121 mg (78%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (d, J = 8.2 Hz, 2H), 6.80 (d, J = 2.4 Hz, 2H), 6.74 (d, J = 8.2 Hz, 2H), 6.26 (d, J = 4 Hz, 2H), 3.98 (s, 2H), 2.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 148.7, 143.4, 134.4, 132.3, 130.1, 124.1, 118.9, 114.2, 14.8; MS (MALDI-TOF) an isotopic cluster peaking at m/z 310.94 [calcd for M^+ 311.14]. Anal. Calcd for $C_{17}H_{16}BF_2N_3$: C, 65.62; H, 5.18; N, 13.51. Found: C, 65.53; H, 5.24; N, 13.48.

Synthesis of 4,4-difluoro-8-(5-azastyryl(8-hydroxyquinoline))-3,5-dimethyl-4-bora-3a,4a-diaza-*s*-indacene (3). To a solution containing compound **5** (17 mg, 0.1 mmol) and **6** (32 mg, 0.1 mmol) in EtOH (5 mL) and CH_2Cl_2 (1 mL) was added one drop of glacial acetic acid. The resulting reaction mixture was refluxed for 5 h under N_2 and then cooled to room temperature. The red precipitate was filtrated and washed by EtOH. Recrystallization from $CHCl_3$ and MeOH yielded a pure sample of **3** as a black-red powder: 37 mg, 80% as orange-red powder; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.96 (d, J = 8.8 Hz, 1H), 8.86 (d, J = 28 Hz, 2H), 7.91 (d, J = 7.6 Hz, 1H), 7.64 (t, J = 8 Hz, 1H), 7.56 (d, J = 8 Hz, 2H), 7.33 (d, J = 8 Hz, 2H), 7.24 (overlapped with strong residual $CHCl_3$ signal at δ 7.24, 1H), 6.78 (s, 2H), 6.28 (s, 2H), 2.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 157.4, 155.6, 154.2, 148.3, 142.3, 138.4, 135.8, 135.2, 134.5, 131.6, 131.4, 130.3, 127.0, 123.6, 122.7, 120.7, 119.3, 114.3, 109.3, 14.9; MS (MALDI-TOF) an isotopic cluster peaking at m/z 466.16 [calcd for M^+ 466.18]. Anal. Calcd for $C_{27}H_{21}BF_2N_4O$: C, 69.55; H, 4.54; N, 12.02. Found: C, 69.36; H, 4.60; N, 11.89.

Synthesis of 4,4-Difluoro-8-(5-azastyryl(8-hydroxyquinoline))-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (4). By using the above-described procedure with **7** instead of **6** as starting material, compound **4** was obtained in the yield of 41 mg (84%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.98 (d, J = 8.8 Hz, 1H), 8.86 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8 Hz, 1H), 7.64 (t, J = 8.8 Hz, 1H), 7.39 (m, J = 30.4 Hz, 4H), 7.24 (overlapped with residual $CHCl_3$ signal at δ 7.24, 1H), 5.99 (s, 2H), 2.56 (s, 6H), 1.49 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 155.5, 153.2, 148.2, 143.1, 141.6, 138.3, 135.6, 135.2, 132.3, 131.6, 129.0, 126.9, 123.5, 122.7, 121.6, 121.2, 109.3, 14.7, 14.6; MS (MALDI-TOF) an isotopic cluster peaking at m/z 494.28 [calcd for M^+ 494.21]. Anal. Calcd for $C_{29}H_{25}BF_2N_4O$: C, 70.46; H, 5.10; N, 11.33. Found: C, 70.14; H, 5.33; N, 11.08.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR and ^{13}C NMR spectra of compounds **1**−**4** in $CDCl_3$; the electronic absorption and fluorescent spectra and the spectral parameters of compounds **1**−**4** in different solvents; pH-dependent optical properties of compounds **1**, **2**, and **4**; the crystal data and structure refinements of compounds **1** and **2**; computational details for DFT calculation of compound **2** and tables of coordinates for calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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