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SYNTHESIS AND SPECTROSCOPIC PROPERTIES OF 2,5-BIS(BENZOAZOL-2-YL)PYRAZINES

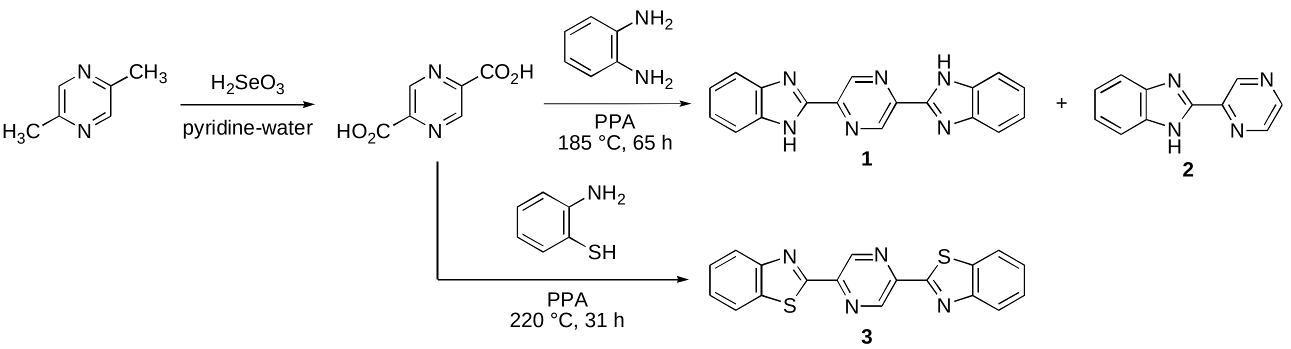
Ryota Saito,[1,2]* Shinnosuke Machida,[1] Saori Suzuki,[2] and Akira Katoh[1]

[1]Department of Materials and Life Science, Seikei University, 3-3-1 Kichijoji-kitamachi, Musashino, Tokyo 180-8633, Japan [2]Department of Chemistry, Faculty of Science, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274-8510, Japan e-mail: saito@chem.sci.toho-u.ac.jp

Abstract – A class of π-conjugated 2,5-bis(benzoazol-2-yl)pyrazine dyes have been synthesized in which 2,5-bis(benzimidazol-2-yl)pyrazine (**1**) exhibits strong fluorescence in solution. The enhanced fluorescence of **1** with a base leads to future applications such as anion sensing feasible upon chemical modification.

Fluorescent organic molecules continue to arouse strong interest because of their fascinating applications such as electroluminescent materials,[1] molecular probes for clinical uses,[2] and molecular sensors for chemical and biochemical analytes.[3] Although there has already been a wide choice of fluorescent molecules for particular applications, development of organic molecules exhibiting brilliant fluorescence have still be important because new types of fluorophores have still been desired in the field of bioimaging, organic electroluminescence, and chromatography.[1–3] Our research group has been interested in the chemistry and fluorescent properties of nitrogen-containing heterocyclic molecules, especially pyrazines, for many years.[4] We have previously studied new luminescent chromophores based on the pyrazine nucleus, which posses two aromatic substituent on the central pyrazine ring and exhibit intense fluorescence.[4c] In continuing efforts to develop brilliant fluorescent compounds based on aryl-substituted pyrazine chromophores, our interest has focused on introducing benzimidazol and benzothiazole groups to the pyrazine nucleus, as these benzoazoles are widely found in strong luminescent materials such as 5’,5’-bis(benzimidazol-2-yl)bipyridine,[5] 2,6-bis(benzimidazol-2-yl)pyridine,[6] and naturally occurring firefly luciferin.[7] Herein, we report synthesis and fluorescent properties of π-conjugated (benzoazol-2-yl)pyrazines (**1**–**3**), which are obtained easily, and one of them, **1**, exhibits very strong fluorescence in solution to be reported in this paper for the first time.

2,5-Bis(benzimidazol-2-yl)pyrazine (**1**)[8] was prepared by reacting 2,5-pyrazinedicarboxylic acid, prepared by oxidation of 2,5-dimethylpyrazine,[9] with two equimolar of phenylenediamine in polyphosphoric acid (PPA) as shown in Scheme 1. Fluorescent (benzimidazol-2-yl)pyrazine (**2**)[10] was also obtained as a by-product, indicating decarboxylation occurred during the reaction under such a high temperature condition. This side reaction substantially reduced the yield of the desired compound. 2,5-Bis(benzothiazol-2-yl)pyrazine (**3**)[11] was prepared in the same manner with 2-aminobenzenethiol (**5**) as shown in Scheme 1. In this case, multiple by-products were detected by TLC analysis and were hard to be isolated. Only **3** was isolated by repeated column chromatography on silica gel.



Scheme 1

The absorption spectra of obtained **1**–**3** were measured in dimethyl sulfoxide (DMSO) at room temperature under aerated condition. The results are presented in Figure 1 and Table 1. The absorption bands of **1** were observed at 395 (shoulder), 378 and 325 nm (shoulder). By comparison of the absorption spectrum of **2**, it is found that the longer peaks attribute to the absorption of the whole molecule **1**, while the shorter peak corresponds to the partial electron transition of the (benzimidazol-2-yl)pyrazine moiety. Similar result was obtained when the absorption of **3** was measured as shown in Figure 1.

Fluorescence spectra of **1**–**3** in DMSO at room temperature under aerated condition are shown in Figure 2, and the data are listed in Table 1, accompanied by fluorescence quantum yields determined relative to quinine sulfate in 0.1 mol L^{-1} sulfuric acid (Φ = 0.55, excited at 366 nm). The dye **1** exhibited blue emission band at λ_{FL} = 444 nm, which is longer than that of **2** at λ_{FL} = 378 nm as expected from the

Table 1. Absorption and Fluorescence Data of Benzoazolylpyrazines **1**–**3**

Compound	solvent	λ_{abs} /nm (ε /$dm^3M^{-1}cm^{-1}$)	λ_{FL} /nm	fluorescence quantum yield, Φ
1	DMSO	395 (sh 34000), 378 (37800), 325 (sh 18800)	444	0.90
	DMSO containing NaOMe	412 (36800), 336 (15400)	477	1.0
2	DMSO	327 (19000)	378	0.29
3	DMSO	394 (sh 245009), 375 (29900)	447	0.009

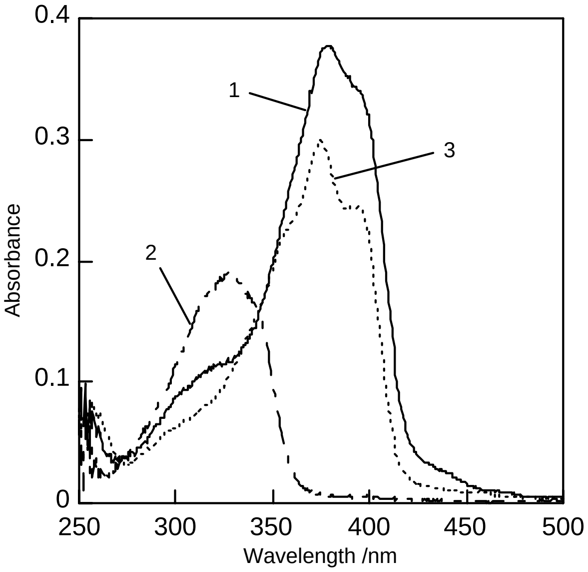


Figure 1. Absorption spectra of **1** (solid line), **2** (dash-dotted line), and **3** (broken line) in DMSO; *c* = 1.0×10^{-5} M

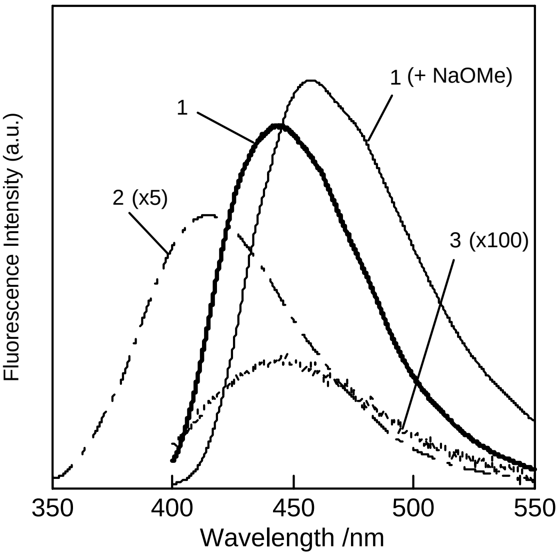


Figure 2. Fluorescence spectra (corrected) of **1** (thick solid line), **2** (dash-dotted line) and **3** (broken line) in DMSO and **1** in DMSO containing 5% (v/v) of 1 M NaOMe in methanol (thin solid line); *c* = 2.0×10^{-7} M

expanded π-conjugation.

The striking result is that the dye **1** exhibits strong blue fluorescence with high fluorescence quantum yield (Φ_1 = 0.90). The emission profile of **3** was similar to that of **1**, except the fluorescence quantum yield, Φ_3 = 0.009, is much lower than that of **1**.[12]

In order to get information about the physicochemical property of **1**, the optimized structure and the energy levels of HOMO and LUMO were estimated by the AM1 method.[13] For comparison, those properties of **2** and **3** were also calculated, and the results are listed in Table 2. For each compound, the pyrazine nitrogen and the imine nitrogen of the benzoazole unit prefer to be in the *s-trans* configuration each other rather than in the *s-cis* probably due to the electronic repulsion between the lone pairs on the sp^2 nitrogen atoms, according to the calculation. The conformations of **1** and **2** were estimated to be almost planar, while that of **3** was found to slightly twist (Table 1). The deviation from the planar in **3** is possibly attributable to the avoidance of the dipole-dipole repulsion caused by the lone pairs on the

Table 2. AM1-calculated dihedral angle between pyrazine ring and benzoazole, heat of formation (in kcal•mol^{-1}), dipole moment in the ground state (μ in Debye), HOMO and LUMO energy levels (in eV), and differential energy (ΔE in eV) between the HOMO and LUMO of 2,5-bis(benzimidazol-2-yl)-pyrazine (**1**), 2-(benzimidazol-2-yl)pyrazine (**2**), and 2,5-bis(benzothiazol-2-yl)pyrazine (**3**)

Compound	Dihedral angle	Heat of formation /kcal•mol^{-1}	μ /D	HOMO /eV	LUMO /eV	ΔE /eV
1	0.3°	185.8	0.06	-8.720	-1.455	7.265
2	0.3°	115.1	2.95	-8.867	-0.997	7.870
3	28.5, 30.4°	146.9	0.11	-9.172	-1.754	7.418

pyrazine nitrogen and on the sulfur. To confirm these estimations X-ray crystal analysis of these compounds should be performed, but it has not been completed because single crystals of these compounds suitable for the analysis have been hardly obtained. The HOMO-LUMO gap (ΔE) for **1** was smaller than that for **2** as expected, showing good agreement with the difference in the experimentally observed 0-0 bands for **1** and **2**. Figure 3 depicts frontier molecular orbitals for **1**–**3**. For each compound, the HOMO coefficients are mainly distributed over the benzoazole moiety and the LUMO coefficients are localized on the pyrazine ring. From these results, the lowest-energy (0-0) transition for all dyes can be assignable as charge-transfer transition from benzoazole moiety to the π^* orbital of the pyrazine ring. At this point, the charge transfer would occur from one side for **2**, giving large transition moment, while the transition would occur from each side of the pyrazine for **1**, giving almost symmetric moment. Figure 4 exhibits the optimized structure of **1** and **3** in the excited states calculated by the AM1 method, and both of them are estimated to take planar conformation in the excited states. These simulations suggest that the dye **1** does not change its conformation upon excitation, while the rotation of the aryl groups may occur in **3** in the excited state. Thus, it is conceivable that the planer π-conjugated structure and the symmetrical transition moment of **1** cause the efficient fluorescence emission like other strong fluorescent π-conjugated dyes.[14] Although the reason that accounts for the weak fluorescence of **3** is still unclear at present, the nonradiative deactivation such as free rotations and/or the S_1-T_1 intersystem crossing could cause the decreased fluorescence efficiency of **3**.

It is worth noting that the fluorescence of **1** exhibited bathochromic shift (thin solid line in Figure 1) and the fluorescence quantum yield was enhanced ($\Phi_{\mathbf{1}+\mathrm{base}} \sim 1$) when **1** was dissolved in DMSO containing sodium methoxide (0.05 M). The NH units are known to interact strongly with anion.[15] Under this condition, the NH moiety of the 2-benzimidazolyl group could interact with methoxide anion to increase

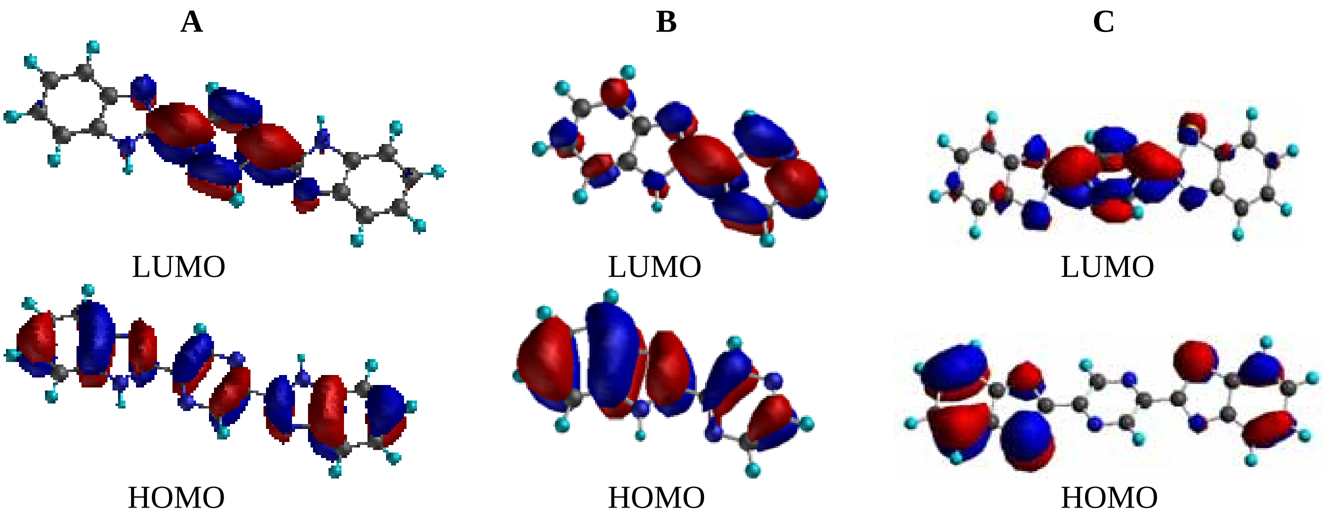


Figure 3. Frontier molecular orbitals (HOMO and LUMO) for **1** (**A**), **2** (**B**) and **3** (**C**) calculated by the AM1-COSMO method.

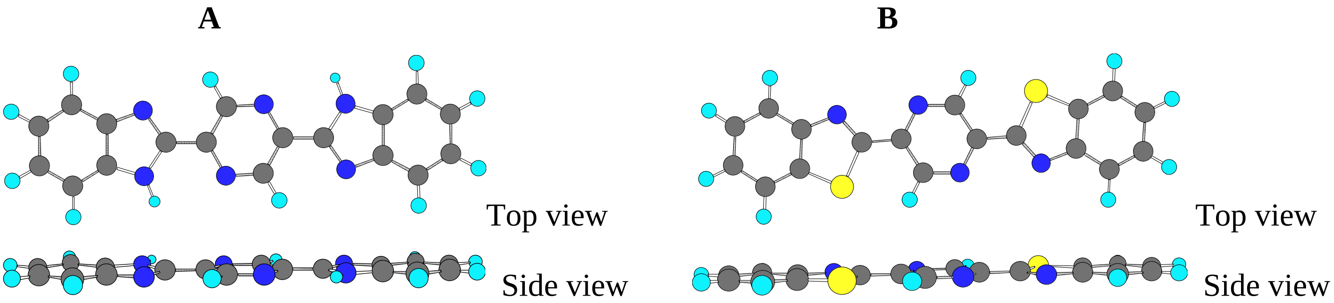


Figure 4. Computer-simulated optimized geometries of **1** (A) and **3** (B) in the first excited states estimated by the AM1 method

the electron donating character of the 2-benzimidazolyl moiety, possibly being connected with the high fluorescent efficiency.

In conclusion, we have succeeded in developing the intensely blue-fluorescent pyrazine dye **1**, whose quantum efficiency was found to as high as 0.90. The anomalously high fluorescence quantum yield of **1** accompanied by the spectral shift in the presence of the anion may provide this fluorescent dye potentially superior to conventional fluorometric anion sensors. Since derivatization of **1** can be attained by replacing the starting phenylenediamine with its derivatives and introducing substituents on the NH, we may say that we have established structural groundwork to aid in the further design of new fluorophores applicable in various areas. Further studies, including derivatization of **1**, are underway in our research group.

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8. 19%; mp > 370 ºC; ^{1}H-NMR (trifluoroacetic acid-*d*, 400 MHz) δ/ppm 7.66-7.68 (4H, m, C5’, C5”, C6’, C6”-H), 7.81-7. (4H, m, C4’, C4”, C7’, C7”-H), 9.75 (2H, s, C3, C6–H); IR (KBr) $\nu_{\mathrm{max}}/\mathrm{cm}^{-1}$ 3353 (νN-H), 3065 (νC-H, Ar), 1590, 1557, 1435, 1320 (νC=N, C=C; ring stretching), 746 (γC-H); HRMS (EI) Calcd for $C_{18}H_{12}N_6$: 312.1123. Found: 312.1141.
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10. 13%; mp 244.4 ºC; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.32-7.39 (2H, m, C5, C6-H), 7.53-7.56 (1H, m, C4-H), 7.87-7.90 (1H, m, C7-H), 8.60 (1H, dd, *J* = 1.6 and *J* = 2.5 Hz, C’5-H), 8.66 (1H, *J* = 2.5 Hz, Py-C6-H), 9.67 (1H, d, *J* = 1.6 Hz, Py-C3-H), 10.3 (1H, br. s, N-H); IR (KBr) $\nu_{\mathrm{max}}/\mathrm{cm}^{-1}$ 3441 (νN-H), 3085 (νC-H), 1592, 1464, (νC=N, C=C; ring stretching), 740 (γC-H); Anal. Calcd for $C_{11}H_8N_4$: C,67.34; H,4.11; N,28.55. Found: C,67.33; H,4.25; N,28.65.
11. 8%; mp > 370 ºC; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.45-7.60 (2H, m, C5, C6-H), 8.03 (1H, d, *J* = 7.8 Hz, C4-H), 8.19 (1H, d, *J* = 7.8 Hz, C7-H), 9.63 (1H, s, C’-H); IR (KBr) $\nu_{\mathrm{max}}/\mathrm{cm}^{-1}$ 3051 (νC-H), 1522, 1312 (νC=N, C=C; ring stretching), 764 (γC-H); Anal. Calcd for $C_{18}H_{10}N_4S_2$: C, 62.41; H, 2.91; N, 16.17. Found: C, 62.60; H, 3.01; N, 15.92.
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