Substituent Effects on Fluorescent Properties of Imidazo[1,2-*a*]pyridine-Based Compounds

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In order to search for novel fluorescent organic compounds, 20 derivatives of imidazo[1,2-*a*]pyridine (**1**) were synthesized, and their fluorescent properties were studied. Though the parent compound **1** (λ_{fl} = 370.5 nm, Φ = 0.57 in ethanol) was in the liquid state at ambient temperature, 2-phenylimidazo[1,2-*a*]pyridine (**5**), 2-(2-naphthyl)imidazo-[1,2-*a*]pyridine (**16**), 7-methylimidazo[1,2-*a*]pyridine (**3**), 7-methyl-2-phenylimidazo[1,2-*a*]pyridine (**12**), and 7-methyl-2-(2-naphthyl)imidazo[1,2-*a*]pyridine (**17**) were found to give thermally stable solid compounds (mp 55—190 °C) without much affecting the fluorescent properties of the parent compound (λ_{fl} = 374—381 nm, Φ = 0.50—0.78 in ethanol). Among the 4′-substituted 2-phenyl derivatives, it was found that the introduction of the strong electron-donating amino and dimethylamino groups (2-(4-aminophenyl)imidazo[1,2-*a*]pyridine (**7**) and 2-[4-(dimethylamino)phenyl]imidazo-[1,2-*a*]pyridine (**8**), respectively) caused marked red shift of their fluorescence (λ_{fl} = 445 and 446 nm, respectively, in ethanol), thus providing the way for tuning the fluorescence color of the IP derivatives. The observed red shift of the fluorescence of **7** and **8** was ascribed to the contribution of the excited intramolecular charge transfer state.

Fluorescent organic compounds have been the subject of intense research for photo-functional materials, and have found wider application in various fields such as photo-therapy, laser chemistry, high performance sensors, fluorescent probes, or electro-luminescence devices.[1] The compounds for these applications are required not only to show efficient fluorescence but to have a variety of additional functionalities such as molecular recognition, high stability, and physiological activity. Since there are limitations in modification of the existent fluorophores, new series of fluorescent compounds are actively studied to develop novel functionalized fluorescent compounds.

We previously reported a new series of fluorophores, pyrido[1′,2′ : 1,2]imidazo[4,5-*b*]quinoxaline derivatives,[2] which have a characteristic ring structure with a bridgehead nitrogen, and show high thermal stability and useful biological activities. The parent compound, pyrido[1′,2′ : 1,2] imidazo[4,5-*b*]quinoxaline, shows a strong green fluorescence, and its color is tunable by the introduction of various substituents on the pyridoimidazoquinoxaline ring.

Imidazo[1,2-*a*]pyridine (**1**) composes a part of pyrido [1′,2′ : 1,2]imidazo[4,5-*b*]quinoxaline structure, and **1** itself has been reported[3] to have an efficient π–π^* type fluorescence around 500 nm. Though there have been some fluorescence studies[4] on the limited number of its derivatives, there has been neither systematic study on the fluorescence properties of the **1** derivatives nor reports on their application as functional compounds. The reasons for poor attention may be that **1** is a liquid at ambient temperature, and the fluorescence of **1** derivatives reported so far had been limited to the UV region.

To design **1** derivatives as good fluorescent precursors for photo-functional compounds, the following conditions should be considered; (1) retaining or improving the good fluorescent properties of the parent **1**; (2) having sufficient thermal stability; and (3) bearing active site(s) for introducing additional functional group(s). Fluorescent properties of dyes are sensitive to the structural modification of their parent molecule, and thus it is essential to study the relationship between the molecular structure and fluorescent properties in order to design novel functionality for the fluorophore. In this report, twenty derivatives of **1** were synthesized either by the introduction of a variety of substituents or by the expansion of the ring system, and the absorption and fluorescence spectra of each compound were collected.

Results and Discussion

Synthesis. It is preferable that various derivatives can be obtained by the same synthetic procedure. Several reaction pathways have been reported for construction of the imidazopyridine ring; (a) imidazole-ring formation by coupling of 2-aminopyridyl and α-halocarbonyl compounds (Tschitschibabin method),[5] (b) reaction of 2-chloropyridine with triazole, and subsequent elimination of nitrogens,[6] (c) intramolecular photo-cyclization of styrylimidazole,[7] (d) reaction of a α-bromoacyl derivative with sulfonohydrazide and subsequently with pyridine,[8] and (e) pyridine ring formation starting from imidazole compounds.[9] The Tschitschibabin method has been frequently used since a variety of starting compounds are available either commer-

cially or synthetically, and it does not require severe reaction conditions.

Structures of the **1** derivatives synthesized in this study are illustrated in Fig. 1 All derivatives, except for **21**, were synthesized by the Tschitschibabin method (Scheme 1(a)).

Methylimidazopyridines **2**—**4** were obtained by coupling of the corresponding methyl-substituted 2-aminopyridines and bromoacetaldehyde diethyl acetal (20—98%). The products were viscous liquids except for **3**, the melting point of which was 55—57 °C. Compounds **5**—**11** are the 2-phenylimidazopyridines having different substituents at the *p*-position. Reaction of 2-bromo-1-(4-substituted phenyl)-ethanone and 2-aminopyridine yielded 2-phenylimidazo-[1,2-*a*]pyridine (**5**) and its derivatives **6**, **10**, **11**, and reduction of the nitro group of **11**, followed by methylation gave **7** and **8**, respectively (Scheme 2). All compounds were obtained as solids (mp 135—270 °C) in good to fair yields (60—94%). Compounds **12**—**15** having substituent(s) on the pyridine part of phenylimidazopyridine had higher melting points (163—268 °C) compared to that of **5**, but their yields were not high enough (< 60%). 2-(2-Naphthyl)imidazo[1,2-*a*]pyridine (**16**) was prepared from 2-bromo-1-(2-naphthyl)ethanone and 2-aminopyridine (80%).

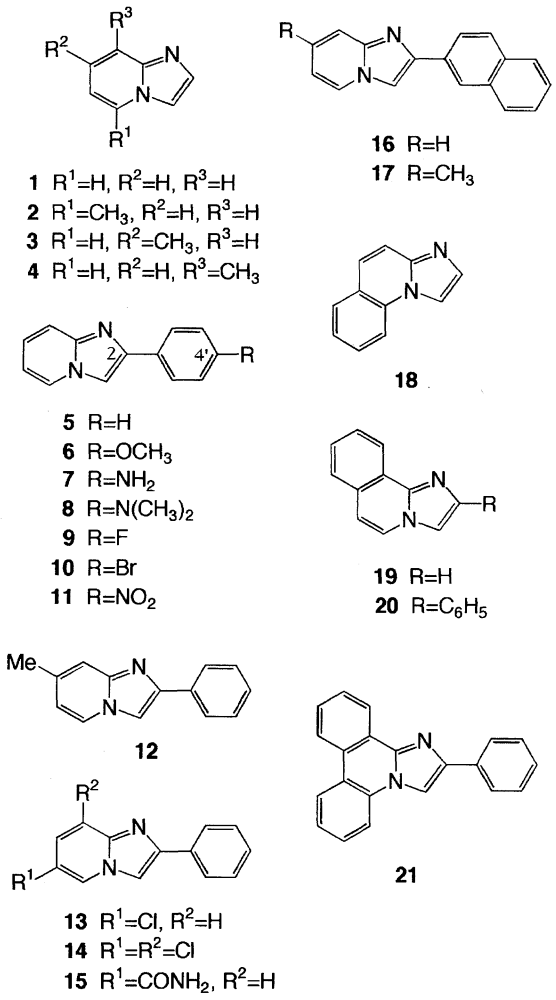
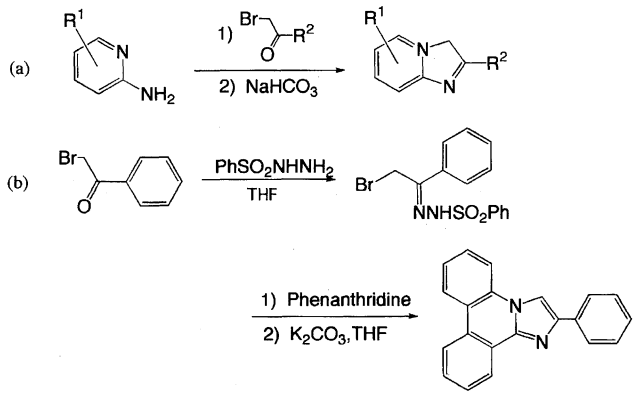


Fig. 1. Structure of imidazo[1,2-*a*]pyridine derivatives.



Scheme 1. Synthesis of imidazo[1,2-*a*]pyridine derivatives **1**—**20** (a) and **21** (b).

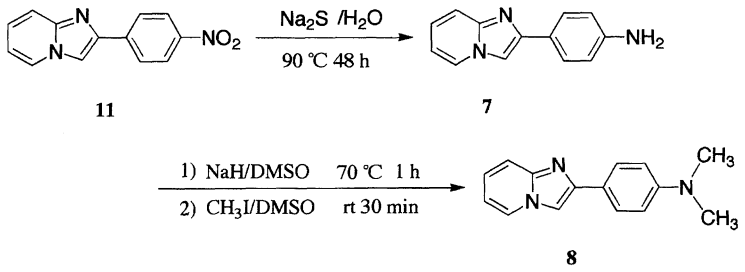
Imidazo[1,2-*a*]quinoline (**18**), imidazo[2,1-*a*]isoquinoline (**19**), and 2-phenylimidazo[2,1-*a*]isoquinoline (**20**), in which a benzene ring was fused to their imidazopyridine ring, were synthesized by coupling of the corresponding ketone with 2-aminoquinoline or 1-aminoisoquinoline. Imidazoisoquinolines **19** and **20** were obtained as solids, but imidazoquinoline **18** was in a liquid state. 2-Phenylimidazo[1,2-*f*]phenanthridine (**21**) was synthesized by the route shown in Scheme 1(b), due to difficulty in obtaining 6-aminophenanthridine as the starting material. 2-Bromo-1-phenylethanone phenylsulfonylhydrazone, which was the product from 2-bromo-1-phenylethanone and benzenesulfonohydrazide, was coupled with phenanthridine to give **21**.

Absorption and Fluorescence Spectra. The absorption and fluorescence spectra of each compound were obtained in ethanol solution at 20 °C. Imidazo[1,2-*a*]pyridine (**1**) showed an absorption band at around 280 nm, and an efficient fluorescence was observed at a round 370 nm (Φ = 0.57; Fig. 2).[10] The absorption and fluorescence maxima of **1**—**21** were collected in Table 1.

Figure 2 also shows the absorption and fluorescence spectra of the selected imidazopyridine derivatives. For each compound, the shape of the excitation spectrum agreed with the corresponding absorption spectrum, and the fluorescence intensity increased linearly with its concentration from 10^{-6} to 10^{-4} mol dm^{-3}. Therefore, the emission of the imidazopyridine derivatives were proved to be unimolecular fluorescence from the lowest excited state (S_1).

Methyl substitution at the pyridine part (compounds **2**, **3**, and **4**) only slightly affected both on the absorption and fluorescence band of **1** and on the fluorescence quantum yield.

2-Phenylimidazo[1,2-*a*]pyridine (**5**) showed a bathochromic shift of the absorption band about 25 nm, but the fluorescence of **5** appeared in the same area as **1**. Regardless of the substituents at the 4′-position of **5**, the absorption spectra of **6**—**11** were comparable to that of **5**. However, their fluorescent properties were markedly different. Compounds **6**—**8** having electron-donating groups showed an efficient fluorescence (Φ = 0.54—0.58). While the introduction of a methoxy group caused only a small red shift of the fluores-



Scheme 2. Synthesis of imidazo[1,2-*a*]pyridine derivatives **7** and **8**.

Table 1. Absorption and Fluorescence Maxima of Imidazo[1,2-*a*]pyridine and Its Derivatives in Ethanol at 20 °C

Compound	Mp/°C	λ_{abs}/nm[c] (log ϵ)	λ_{fl}/nm	Φ
1	97—98 (3 mmHg)[a]	278 (3.84), 297 (3.79)	371	0.57
2	117—119 (4 mmHg)[a]	280 (3.82), 290 (3.69)	362	0.58
3	55—57	268.5 (3.81), 278 (3.86), 298 (3.69)	380	0.59
4	88—90 (3.5 mmHg)[a]	279.5 (3.85), 292.5 (3.76)	365	0.61
5	134[b]	313 (3.86), 322 (3.89)	374	0.50
6	136[b]	325.5 (4.07)	381	0.55
7	219[b]	332.5 (4.03)	445	0.54
8	204[b]	277.5 (4.41), 337.5 (4.29)	446	0.58
9	169	314 (3.88), 322 (3.90)	370	0.40
10	215—217	314 (4.44), 324 (4.44)	375	0.27
11	269[b]	346 (4.15)	—	0
12	163[b]	315 (3.91), 321 (3.91)	378	0.56
13	204—207	330 (3.91)	382	0.13
14	158—160	332 (3.96)	385	0.06
15	266—268	328.5 (3.86)	419	0.20
16	160[b]	320.5 (4.185), 343s	375	0.63
17	190[b]	321 (4.17)	381	0.78
18	151—152 (3 mmHg)[a]	258.5 (3.78), 313 (3.89)	385	0.53
19	92—93	280 (3.87), 293 (3.70)	380	0.12
20	142—143	270 (4.73), 300s	384	0.32
21	167—168	265 (4.74), 315.5s	394	0.17

a) Boiling point. b) Measured with DSC. c) Symbol s indicates a shoulder peak.

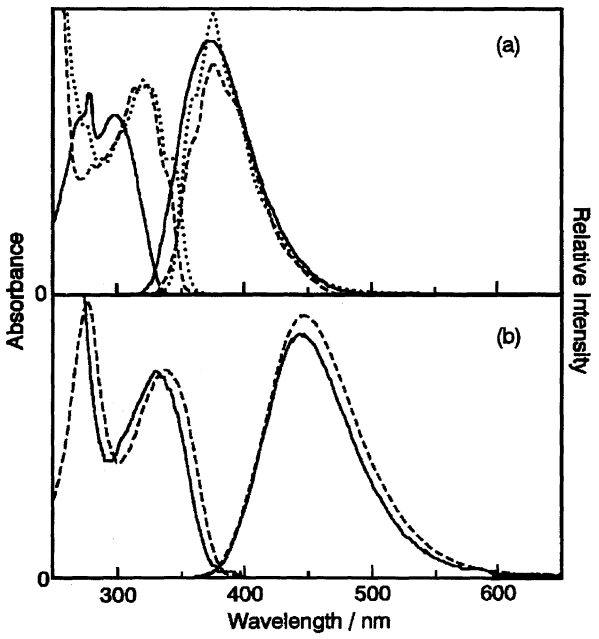


Fig. 2. Absorption and fluorescence spectra of imidazo-[1,2-*a*]pyridine derivatives. (a) **1** (—), **5** (- - -), and **16** (···); (b) **7** (—) and **8** (- - -).

cence, 2-(4-aminophenyl) or 2-[4-(dimethylamino)phenyl] substitution (compounds **7** or **8**, respectively) produced a marked red shift (ca. 80 nm), and a bright blue fluorescence (ca. 450 nm) was observed. In contrast, 4′-substitution with electron-withdrawing groups such as fluoro, bromo, and nitro groups did not have any favorable effect on the fluorescence and resulted in low fluorescence quantum yields (**10** and **11**).

Compounds **12**—**15** have substituent(s) on the pyridine part of phenylimidazopyridine. Chloro and carbamoyl substitution (compounds **13**—**15**) generally reduced the fluorescence efficiency. The introduction of the methyl group at 7-position gave **12**, which showed the high melting point (163 °C) and the same fluorescent property as **5**.

The introduction of a 2-(2-naphthyl) group (compound **16**) instead of a 2-phenyl group little affected the fluorescence band, however, it increased the fluorescence quantum yield (Φ = 0.63) and the melting point (160—163 °C). Furthermore, methylation of **16** at 7-position gave much more efficient fluorescence and a much higher melting point (**17**).

The condensation of benzene to the pyridine part of **1** caused a small shift in both the absorption and fluorescence bands compared to those of **1**. Compound **18**, having the fused benzene at 5- and 6-positions of **1**, showed an efficient

fluorescence (Φ = 0.53). In contrast, compound **19**, condensing the benzene at 7- and 8-positions, showed only a weak fluorescence (Φ = 0.12). The introduction of a phenyl group at the 2-position (compound **20**) improved the quantum yield to some extent (Φ = 0.32). The condensation of two benzenes into the imidazopyridine ring (compound **21**) gave only a weak fluorescence (Φ = 0.17).

Modification of Imidazopyridine Ring. Methyl, 2-phenyl, and 2-(2-naphthyl) substitutions (compounds **2**—**5**, **16**) did not make the efficient fluorescence of the parent **1** deteriorate, but they did not cause a notable shift of the fluorescence that appeared in the near UV region either. The introduction of the substituents generally increased the melting points. Though methyl imidazopyridines **2** and **4** were still in a liquid state, 7-methylation (compound **3**) gave the solid **1** derivative. 2-Phenyl and 2-(2-naphthyl) groups (compounds **5** and **16**, respectively), the larger substituents, increased melting points much higher (134—135 °C and 160 °C, respectively). It is to be remarked that further modification of **5** and **16** with a 7-methyl group both raised the melting point by an additional 30 degrees, but still had little effect on the fluorescent property. Therefore, combinations of 7-methyl and 2-phenyl (or 2-naphthyl) substitutions are effective for controlling their melting point without impairment of the fluorescent property of the parent compound. It is noteworthy that the fluorescence quantum yield of **16** and **17** were much larger than that of **1**.

Except for methylation, however, modification of the pyridine part of **1** generally had unfavorable results on the fluorescent property. Compounds **13**—**15** showed less than 0.20 of quantum yield, though their melting point was very high. Expansion of the **1** ring system by condensation of benzene did not yield satisfactory results at all. The derivatives showed either an efficient fluorescence with low melting point (**18**) or a weak fluorescence with a higher melting point (**19**—**21**).

4′-Substitution of Phenylimidazopyridine. The fluorescence maximum of phenylimidazopyridine observed in the near UV region was not shiftted much by 2-(4-methoxyphenyl), 2-(4-fluorophenyl), and 2-(4-bromophenyl) substitution (compounds **6**, **9**, and **10**, respectively). The low quantum yield of **10** might be due to the 'heavy atom effect' of the bromo group. The complete disappearance of the fluorescence upon 4′-nitro substitution (compound **11**) was consistent with a well-known fact that the nitro group often strongly increases the non-radiative deactivating process from the excited state.

In contrast, the introduction of the amino and dimethylamino groups at the 4′-position shifted the fluorescence to the visible region (bright blue) without decreasing the quantum yield. Therefore, the substitution at the 4′-position of phenylimidazopyridine is a useful method for tuning the fluorescence color. Since the amino group is substitution-labile, the 4′-amino group can serve as the site for introducing or connecting to other functional unit(s) in order to develop novel photofunctional compounds.

To understand further the effects of 4′-substitution, the absorption and fluorescence spectra of **5**—**9** were also measured in cyclohexane, dipropyl ether, and dichloromethane (Table 2), and were analyzed using the Lippert-Mataga equation Eq. 1,[11]

$$\Delta\nu = \nu_{abs} - \nu_{fluo} = \frac{2(\Delta\mu)^2}{hca^3}\Delta f + \text{Const.},$$
$$\Delta f = \frac{\epsilon - 1}{2\epsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}, \quad (1)$$

where $\Delta\nu$ is the difference between the fluorescence and absorption maxima, Δf is the Lippert's solvent polarity parameter, ϵ and n are the relative permittivity and the optical refractive index of solvents, respectively, and a is an effective radius of the Onsager cavity[12] of a compound.

The 4′-amino and 4′-dimethylamino-phenylimidazopyridines (**7** and **8**) showed notable solvatochromism. Except for **7**, the value of $\Delta\nu$ showed linear dependence on Δf (Fig. 3) and the slope of the compound **8**, having stronger electron donating substituent, was much steeper than other compounds. Assuming the effective radius of the Onsager cavity as 5.0 Å, the difference of the dipole moment between the excited and ground states, $\Delta\mu$, of **8** is estimated to be 12.7 D. This value is comparable to those having donor–acceptor units in their molecular structure and showing substantial charge transfer from the donor unit to the acceptor unit in their excited state.[13] Therefore, the emitting level of **8** had a highly polar nature, and the contribution of intramolecular charge transfer is indicated.

The electronic state of **5**—**9** were calculated using the semi-empirical molecular orbital (MO) method including the configuration interaction. The simulated absorption spectra were in good agreement with the observed spectra, and the lowest excitation bands of the compounds were assigned to be a π–π^* type transition from the highest occupied MO

Table 2. Absorption and Fluorescence Maxima of **5**—**9** in Cyclohexane, Dipropyl Ether, and Dichloromethane

	Cyclohexane		Dipropyl ether		Dichloromethane	
Compound	λ_{abs}/nm (log ϵ)	λ_{fl}/nm (Φ)	λ_{abs}/nm[a] (log ϵ)	λ_{fl}/nm (Φ)	λ_{abs}/nm (log ϵ)	λ_{fl}/nm (Φ)
5	332 (3.81), 350 (3.64)	371 (0.44)	331 (3.80), 345 (3.56)	374 (0.43)	327 (3.89)	374 (0.55)
6	335 (3.60), 353 (3.43)	374 (0.47)	333 (3.99), 351s	377 (0.62)	328 (3.99)	381 (0.62)
7	340 (3.70), 358 (3.52)	381 (0.46)	340 (3.94)	395 (0.51)	332 (4.12)	398 (0.64)
8	346 (3.72), 363 (3.56)	389 (0.31)	341 (3.97)	399 (0.53)	341 (4.23)	432 (0.51)
9	331 (3.83), 348 (3.64)	369 (0.60)	328 (3.97), 345 (3.75)	371 (0.51)	326 (3.89)	374 (0.49)

a) Symbol s indicates a shoulder peak.

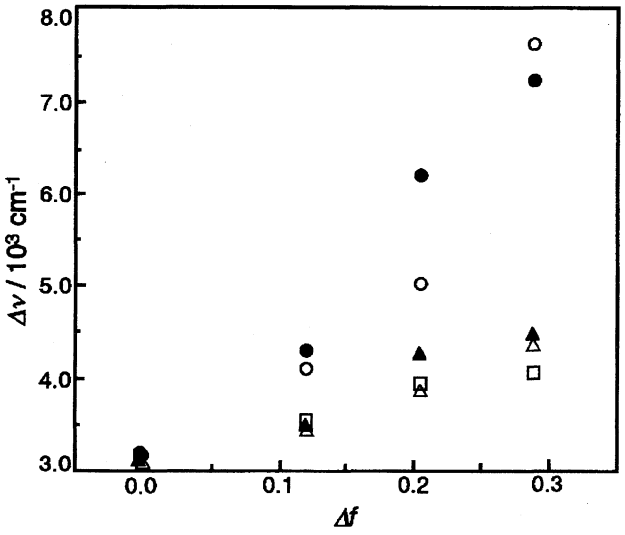


Fig. 3. Plot of $\Delta\nu$ vs. Δf on **5** (△), **6** (▲), **7** (○), **8** (●), and **9** (□).

(HOMO) to the lowest unoccupied MO (LUMO). Since the emitting state is the lowest energy excited state (S_1), it is likely that the electronic state of the emitting level is not much different from the Franck–Condon excited state. The LUMO of **5**, **6**, and **9** were mostly localized on the pyrido unit, while the HOMO resided on the imidazo part of the compounds (Fig. 4). In the case of **7** and **8**, however, the HOMO were extended further to the 2-phenyl unit, and therefore, the transition from the HOMO to the LUMO should induce a polar excited state. This explains the highly polar nature of the excited state of **8** shown from the steep slope of the Lippert–Mataga equation.

Conclusions

In conclusion, 20 derivatives of imidazo[1,2-*a*]pyridine (**1**) were synthesized and their fluorescent properties were examined. 2-Phenyl (including 2-(2-naphthyl)) and/or 7-methyl substitution is found to be a useful approach for preparation of the solid **1** derivatives without deterioration of the high quantum yield of the parent **1**. The introduction of a strong electron-donating amino or dimethylamino group at the 4′-position of phenylimidazopyridine can shift the fluorescence to the visible region in polar solvents, which is explained by the contribution of the excited intramolecular charge transfer state. The fluorescence color could be more finely tuned by careful adjustment of the electron donation strength of the 4′-substituent.

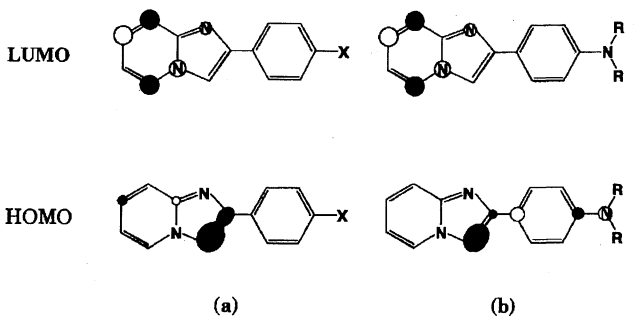


Fig. 4. Simulated electronic state of HOMO and LUMO. (a) Compounds **5** (X = H), **6** (X = OCH_3) and **9** (X = F); (b) compounds **7** (R = H) and **8** (R = CH_3).

Experimental and Measurement

The solvents used for spectroscopic measurements were the fluorometric grade obtained from Kanto Chemical. The melting points were measured with a Yazawa Kagaku micro melting-point apparatus and reported without any correction. The melting points were also measured with a Shimadzu DSC-50 under an argon atmosphere. Elemental analyses were done on a Yanaco MT-2 CHN-corder. A Perkin–Elmer FTIR 1640 spectrophotometer was used to record the IR spectra as KBr pellets or solution film. The mass spectra were recorded on a JEOL JMS-DX303 spectrometer (70 eV) and the ^{1}H NMR spectra (TMS as internal standard) on a JEOL JNM-GX270, or JNM-LA300 spectrometer. The electronic absorption spectra of the **1** derivatives in ethanol were recorded on a JASCO Ubest-50 spectrophotometer and their emission spectra on a JASCO FP-770 or a Shimadzu RF-5300PC spectrometer with a built-in spectral correction unit in air-saturated solution at 20 °C. The fluorescence quantum yield of **1** was calculated in reference to that of 2-aminopyridine in ethanol as a standard (excitation at 285 nm; $\Phi = 0.37$).

Molecular-orbital calculations were done by MOPAC AM1/1 (CAChe system on an Apple Macintosh PowerPC 9500, Sony/Tektronix Co.). The geometry of the molecules were optimized by MM2/AM1 and the absorption spectrum was simulated by ZINDO (CI = 9).

Synthesis. Practical grade bromoacetoaldehyde diethyl acetal, 2-bromo-1-phenylethanones, and 2-aminopyridines were obtained commercially (Tokyo Kasei, or Wako Junyaku), and were used without further purification. Analytical-grade acetonitrile and ethanol were used as solvents without further purification.

Imidazo[1,2-*a*]pyridine (**1**) and its methyl derivatives **2**—**4** were synthesized as follows; a solution of bromoacetaldehyde diethyl acetal (5.4 g, 25 mmol) in 25 cm^3 of 1,4-dioxane–water (3 : 2) was refluxed for 30 min. Then sodium carbonate (55 mmol) was added and corresponding methyl substituted 2-aminopyridine (25 mmol) at room temperature, and then this was refluxed for 22 h. After cooling, concentrated hydrochloric acid was added and insoluble solid was filtered off. The filtrate was basified with sodium hydroxide, and extracted with chloroform. Evaporation of chloroform gave crude product.

Imidazo[1,2-*a*]pyridine (1):[14] Purified by distillation under reduced pressure. (19%); bp 97—98 °C (3 mmHg, 1 mmHg = 133.322 Pa); IR 1634 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$, 270 MHz) δ_H = 6.73 (t, 1H, 6-H), 7.12 (t, 1H, 7-H), 7.55—7.68 (m, 3H, 2,3,8-H), 8.04 (d, 1H, 5-H).

5-Methylimidazo[1.2-*a*]pyridine (2):[14] The product was separated by a silica-gel column (chloroform–methanol (5 : 1)) and distilled in vacuo (98%); bp 117—119 °C (4 mmHg); IR 1639 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$, 270 MHz) δ_H = 2.58 (s, 3H, CH_3), 6.62 (d, 1H, 6-H), 7.13 (t, 1H, 7-H), 7.47 (s, 1H, 2-H), 7.53 (d, 1H, 2-H), 7.69 (d, 1H, 8-H).

7-Methylimidazo[1,2-*a*]pyridine (3):[14] The crude product was recrystallized from toluene–hexane solution (32%); mp 55—57 °C; IR 1647 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$, 270 MHz) δ_H = 2.40 (s, 3H, CH_3), 6.62 (d, 1H, 6-H), 7.37 (s, 1H, 8-H), 7.51 (s, 1H, 3-H), 7.56 (s, 1H, 2-H), 8.02 (d, 1H, 5-H).

8-Methylimidazo[1,2-*a*]pyridine (4):[14,15] The product was

separated by silica-gel column (chloroform–methanol (5 : 1)) and distilled in vacuo (20%); bp 88—90 °C (3.5 mmHg); IR 1629 cm^{-1} (C=N); ^1H NMR ($CDCl_3$, 270 MHz) δ_H = 2.63 (s, 3H, CH_3), 6.68 (t, 1H, 6-H), 6.94 (d, 1H, 7-H), 7.57 (s, 1H, 3-H), 7.63 (s, 1H, 2-H), 7.99 (d, 1H, 5-H).

2-Phenylimidazo[1,2-*a*]pyridine (**5**) and its derivatives **6** and **9—11** were obtained as follows; 2-Aminopyridine (1.89 g, 20 mmol) and corresponding 2-bromo-1-(4-substituted phenyl)-ethanone (20 mmol) in 30 cm^3 of 1,4-dioxane–water (2 : 1) solution was refluxed for 30 min, to which was added sodium carbonate (30 mmol) at room temperature, and then refluxed for 22 h. After cooling, concentrated hydrochloric acid was added and insoluble solid was filtered off. The filtrate was basified with sodium hydroxide, and extracted with chloroform. Evaporation of chloroform afforded the crude product.

2-Phenylimidazo[1,2-*a*]pyridine (5): Recrystallized from benzene (94%); mp 134 °C; IR 1634 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 6.90 (t, 1H, 4′-H), 7.25 (t, 1H, 7-H), 7.32 (t, 1H, 6-H), 7.44 (t, 2H, 3′, 5′-H), 7.58 (d, 1H, 8-H), 7.97 (d, 2H, 2′, 6′-H), 8.40 (s, 1H, 3-H), 8.53 (d, 1H, 5-H). EA Found: C, 80.22; H, 5.12; N, 14.39%. MS Found: *m/z* 194 (M^+). Calcd for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.43%. MS *m/z* 194 (M^+).

2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine (6): Recrystallized from benzene (52%); mp 136 °C (DSC); IR 1248 cm^{-1} (C–O–Ph); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 3.80 (s, 3H, OCH_3), 6.87 (t, 1H, 7-H), 7.01 (d, 2H, 3′-H), 7.22 (t, 1H, 6-H), 7.56 (d, 1H, 8-H), 7.89 (d, 2H, 2′-H), 8.29 (s, 1H, 3-H), 8.50 (d, 1H, 5-H). EA Found: C, 74.73; H, 5.25; N, 12.46%. MS Found: *m/z* 224 (M^+). Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49%. MS *m/z* 224 (M^+).

2-(4-Bromophenyl)imidazo[1,2-*a*]pyridine (10): Recrystallized from ethanol (67%); mp 215—217 °C; IR 506 cm^{-1} (C–Br); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 6.91 (t, 1H, 7-H), 7.27 (t, 1H, 6-H), 7.54—7.66 (m, 3H, 3′, 8-H), 7.92 (d, 2H, 2′-H), 8.43 (s, 1H, 3-H), 8.52 (d, 1H, 5-H). EA Found: C, 57.31; H, 3.09; N, 10.18%. MS Found: *m/z* 272 (M^+), 274 (M^++2). Calcd for $C_{13}H_9N_2Br$: C, 57.16; H, 3.32; N, 10.26%. MS *m/z* 272 (M^+), 274 (M^++2).

2-(4′-Fluorophenyl)imidazo[1,2-*a*]pyridine (9): 1-(4-Fluorophenyl)ethanone (5.53 g, 40 mmol) and copper(II) bromide (17.87 g, 80 mmol) in chloroform (150 cm^3) was refluxed for 3 h. After cooling, the solution was washed with water and dried over anhydrous sodium sulfate. The evaporation of chloroform gave 2-bromo-1-(4-fluorophenyl)ethanone (8.13g, 94%; liquid; M^+ *m/z* 217), which was used in the next reaction without further purification. 2-Bromo-1-(4-fluorophenyl)ethanone (2.64 g, 28 mmol), 2-aminopyridine (3.80 g, 28 mmol), and sodium carbonate (4.70 g, 56 mmol) in acetonitrile (280 cm^3) was refluxed for 24 h. After cooling, insoluble solid was filtered off. Evaporation of the filtrate afforded the crude product, which was recrystallized from chloroform with activated charcoal (37%); mp 169 °C; IR 1217 cm^{-1} (C–F); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 6.91 (t, 1H, 6-H), 7.28 (t, 1H, 7-H), 7.23—7.31 (m, 2H, 3′-H), 7.58 (d, 1H, 8-H), 8.01 (q, 2H, 2′-H), 8.39 (s, 1H, 3-H), 8.53 (d, 1H, 5-H). EA Found: C, 73.75; H, 4.02; N, 13.66%. MS Found: *m/z* 212.0751 (M^+). Calcd for $C_{13}H_9N_2F$: C, 73.57; H, 4.27; N, 13.20%. MS *m/z* 212.0750 (M^+).

2-(4-Nitrophenyl)imidazo[1,2-*a*]pyridine (11): A solution of 2-aminopyridine (3.80 g, 40 mmol), 2-bromo-1-(4-nitrophenyl) ethanone (9.76 g, 40 mmol), and sodium carbonate (6.72 g, 30 mmol) in acetonitrile (150 cm^3) was refluxed for 6 h. The yellow precipitates was collected and washed with acetonitrile–water (1 : 1) mixture (86%); mp 269 °C (DSC); IR 1512, 1336 cm^{-1} (NO_2); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 6.96 (t, 1H, 6-H), 7.31 (t, 1H, 7-H), 7.63 (d, 3H,8-H), 8.24 (d, 2H, 2′-H), 8.31 (d, 2H, 3′-H), 8.58 (d, 1H, 5-H), 8.66 (s, 1H, 3-H). EA Found: C, 65.19; H, 3.59; N, 17.38%. MS Found: *m/z* 239 (M^+). Calcd for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79; N, 17.56%. MS *m/z* 239 (M^+).

2-(4-Aminophenyl)imidazo[1,2-*a*]pyridine (7): Nitro compound **11** (1.43 g, 6 mmol) and sodium sulfide nonahydrate (4.80 g, 20 mmol) in water (100 cm^3) was maintained at 90 °C for 48 h. After cooling, the insoluble solid was filtered and evaporated to dryness. The crude product was recrystallized from dichloromethane with activated charcoal (78%); mp 219—221 °C; IR 3394, 3311 cm^{-1} (NH_2); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 5.27 (s, 2H, NH_2), 6.64 (d, 2H, 3′-H), 6.82 (t, 1H, 6-H), 7.18 (t, 1H, 7-H), 7.51 (d, 1H, 8-H), 7.65 (d, 2H, 2′-H), 8.12 (s, 1H, 3-H), 8.45 (d, 1H, 5-H). EA Found: C, 74.47; H, 5.33; N, 19.68%. HRMS Found: *m/z* 209.0958 (M^+). Calcd for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08%. MS *m/z* 209.0953 (M^+).

2-[4-(Dimethylamino)phenyl]imidazo[1,2-*a*]pyridine (8): A solution of sodium hydride (0.29 g, 12 mmol) in DMSO (20 cm^3) was stirred under nitrogen at 70 °C for 1 h, then added dropwise to a mixture of **9** (0.84 g, 4 mmol) and iodomethane (1.70 g, 12 mmol) in DMSO (20 cm^3) at room temperature under nitrogen. After this was stirred for 30 min, an insoluble solid was filtered off, and the filtrate was evaporated. The residue was washed with acetone, then dissolved in 2-aminoethanol and heated at 100 °C for 5 min. Removal of the solvent gave the crude product, which was washed with water, and recrystallized from cyclohexane with activated charcoal (35%); mp 204 °C (DSC); IR 2920—2804 cm^{-1} (CH_3); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 2.94 (s, 6H, CH_3), 6.78 (d, 2H, 3′-H), 6.84 (t, 1H, 6-H), 7.18 (t, 1H, 7-H), 7.51 (d, 1H, 8-H), 7.78 (d, 2H, 2′-H), 8.19 (s, 1H, 3-H), 8.47 (d, 1H, 5-H). EA Found: C, 75.61; H, 6.38; N, 17.23%. HRMS Found: *m/z* 237.1266 (M^+). Calcd for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71%. MS: *m/z* 237.1266 (M^+).

Compounds **12—15** were synthesized from the corresponding 2-aminopyridine derivatives, 2-bromo-1-phenylethanone, and sodium carbonate (1 : 1 : 2), which were dissolved in ethanol and refluxed for 20 h. After removal of the solvent, hydrochloric acid (1 mol dm^{-3}) was added and insoluble solid was filtered off. Then the filtrate was basified with sodium hydroxide to precipitate the crude product, and it was recrystallized from benzene.

7-Methyl-2-phenylimidazo[1,2-*a*]pyridine (12): Recrystallized from ethanol with activated charcoal (68%); mp 163 °C (DSC); IR 1644 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 2.35 (s, 3H, CH_3), 6.74 (d, 1H, 6-H), 7.30 (t, 1H, 4′-H), 7.35 (s, 1H, 8-H), 7.43 (t, 2H, 3′-H), 7.94 (d, 2H, 2′-H), 8.30 (s, 1H, 3-H), 8.40 (d, 1H, 5-H). EA Found: C, 81.03; H, 5.56; N, 13.34%. MS Found: *m/z* 208.1001 (M^+). Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45%. MS *m/z* 208.1000 (M^+).

6-Chloro-2-phenylimidazo[1,2-*a*]pyridine (13): Recrystallized from benzene (40%); mp 204—207 °C; IR 3032 cm^{-1} (C–H); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 7.30—7.40 (m, 2H, 4′, 8-H), 7.54 (t, 2H, 3′,5′-H), 7.65 (d, 1H, 7-H), 7.98 (d, 2H, 2′,6′-H), 8.40 (s, 1H, 3-H), 8.83 (s, 1H, 5-H). EA Found: C, 68.22; H, 3.85; N, 12.30%. MS Found: *m/z* 228 (M^+), 230 (M^++2). Calcd for $C_{13}H_9N_2Cl$: C, 68.28; H, 3.97; N, 12.25%. MS: *m/z* 228 (M^+), 230 (M^++2).

6,8-Dichloro-2-phenylimidazo[1,2-*a*]pyridine (14): Recrystallized from benzene (6%); mp 158—160 °C (DSC); IR 1604 cm^{-1} (C=C, C=N); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 7.37 (t, 1H, 4′-H), 7.48 (t, 2H, 3′,5′-H), 7.66 (s, 1H, 7-H), 8.00 (d, 2H, 2′, 6′-H), 8.49 (s, 1H, 3-H), 8.85 (s, 1H, 5-H). EA Found: C, 59.13; H,

2.97; N, 10.67%. MS Found: *m/z* 262 (M^+), 264 (M^++2). Calcd for $C_{13}H_8N_2Cl_2$: C, 59.34; H, 3.06; N, 10.65%. MS *m/z* 262 (M^+), 264 (M^++2).

2-Phenylimidazo[1,2-*a*]pyridine-6-carboxamide (15): Recrystallized from benzene (58%); mp 266—268 °C; IR 1659 cm^{-1} (C=O); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 7.35 (t, 1H, 4′-H), 7.47 (t, 2H, 3′,5′-H), 7.62 (d, 1H, 8-H), 7.70 (d, 1H, 8-H), 8.00 (d, 2H, 2′,6′-H), 8.52 (s, 1H, 3-H), 9.10 (s, 1H, 5-H). EA Found: C, 70.95; H, 4.40; N, 17.45%. MS Found: *m/z* 237 (M^+). Calcd for $C_{14}H_{11}N_3O$: C, 70.90; H, 4.70; N, 17.70%. MS: *m/z* 237 (M^+).

2-(2-Naphthyl)imidazo[1,2-*a*]pyridine (16): 1-(2-Naphthyl)ethanone (1.70 g, 10 mmol) was refluxed with copper(II) bromide (4.47 g, 20 mmol) in chloroform (150 cm^3) for 3 h. After cooling, the solution was washed with water and dried over anhydrous sodium sulfate. The evaporation of chloroform gave a viscous oil. When hexane was added, the solid was precipitated. The crude product was recrystallized from hexane with activated charcoal to yield colorless crystals (2-bromo-1-(2-naphthyl)ethanone) (50%); mp 82 °C (DSC); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 4.59 (s, 2H, CH_2), 7.58 (t, 1H, 6-H), 7.64 (t, 1H, 7-H), 7.88—7.94 (m, 2H, 4,5-H), 7.98 (d, 1H, 8-H), 8.03 (d, 1H, 3-H), 8.51 (s, 1H, 1-H). MS Found: *m/z* 248 (M^+), 250 (M^++2). MS Calcd for $C_{12}H_9BrO$: *m/z* 248 (M^+), 250 (M^++2). 2-Bromo-1-(2-naphthyl)ethanone was used to the next reaction without further purification.

A solution of 2-bromo-1-(2-naphthyl)ethanone (1.25 g, 5 mmol), 2-aminopyridine (0.47 g, 5 mmol)), and sodium carbonate (6.72 g, 30 mmol) in ethanol (50 cm^3) was refluxed for 24 h. After cooling, hydrochloric acid (1 mol dm^{-3}) was added to the solution and insoluble solid was filtered off. The filtrate was basified with sodium hydroxide, then the precipitate was collected and washed with water. Recrystallized from cyclohexane with activated charcoal (64%); mp 160 °C (DSC); IR 1633 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 6.92 (t, 1H, 6-H), 7.28 (t, 1H, 7-H), 7.48—7.57 (m, 2H, 7′,8′-H), 7.63 (d, 1H, 8-H), 7.90 (d, 1H, 4′-H), 8.00 (t, 1H, 6′,9′-H), 8.12 (s, 1H,3′-H), 8.54, 8.56, 8.58 (s+d, 3H, 1′,3,5-H). EA Found: C, 85.03; H, 4.97; N, 11.56%. HRMS Found: *m/z* 244.0997 (M^+). Calcd for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47%. MS *m/z* 244.1000 (M^+).

7-Methyl-2-(2-naphthyl)imidazo[1,2-*a*]pyridine (17): 2-Bromo-1-(2-naphthyl)ehtanone (1.25 g, 5 mmol), 2-amino-4-methylpyridine (0.54 g, 5 mmol)), and sodium carbonate (0.84 g, 10 mmol) were treated as described in the synthesis of **16** (62%); mp 190 °C (DSC); IR 1643 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 2.38 (s, 3H, CH_3), 6.77 (d, 1H, 6-H), 7.39 (s, 1H, 8-H), 7.47—7.56 (m, 2H, 7′,8′-H), 7.90—8.01 (m, 3H, 4′,6′,9′-H), 8.08 (d, 1H, 3′-H), 8.44 (s, 1H, 3-H), 8.45 (d, 1H, 5-H), 8.52 (s, 1H, 1′-H). EA Found: C, 83.38; H, 5.45; N, 11.01%. MS Found: *m/z* 258 (M^+). Calcd for $C_{18}H_{14}N_2$: C, 83.69; H, 5.46; N, 10.84%. MS: *m/z* 258 (M^+).

Imidazo[1,2-*a*]quinoline (18): Bromoacetaldehyde diethyl acetal (1.0 g, 5 mmol) in 7 cm^3 of 1,4-dioxane–water (4 : 3) solution was refluxed for 30 min. To this was added sodium carbonate (0.8 g, 10 mmol) and 2-aminoquinoline (0.5 g, 3.5 mmol) at room temperature, and then it was refluxed for 22 h. After cooling, concentrated hydrochloric acid was added and insoluble solid was filtered off. The filtrate was basified with sodium hydroxide, and extracted with chloroform. Evaporation of the solvent, and distillation under reduced pressure gave **18**. Recrystallized from benzene (91%); bp 151—152 °C (3 mmHg); IR 1615 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 6.44—6.69 (m, 5H), 6.92 (d, 1H), 7.29 (d, 1H), 7.59 (s, 1H). HRMS Found: *m/z* 168.0689 (M^+). Calcd for $C_{11}H_8N_2$: MS *m/z* 168.0688 (M^+).

Imidazo[2,1-*a*]isoquinoline (19): Bromoacetaldehyde diethyl acetal (1.0 g, 5 mmol) and 1-aminoisoquinoline (0.5 g, 3.5 mmol) were treated as described in the synthesis of **18**. After extraction with chloroform, evaporation of the solvent gave the crude product as a solid and recrystallized it from benzene to yield colorless crystals (86%); mp 92—93 °C; IR (neat) 1636 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 270 MHz) δ_H = 7.05 (d, 1H), 7.56 (t, 1H), 7.58 (d, 2H), 7.64 (t, 1H), 7.71(d, 1H), 7.91 (d, 1H), 8.63 (d, 1H). EA Found: C, 78.28; H, 4.65; N, 16.83%. HRMS Found: *m/z* 168.0674 (M^+). Calcd for $C_{11}H_8N_2$: C, 78.55; H, 4.79; N, 16.65%. MS *m/z* 168.0688 (M^+).

2-Phenylimidazo[2,1-*a*]isoquinoline (20):[8] A solution of 2-bromo-1-phenylethanone (1.0 g, 5 mmol) in 15 cm^3 of 1,4-dioxane–water (4 : 3) was refluxed for 30 min. To this was added sodium carbonate (0.84 g, 10 mmol) and 1-aminoisoquinoline (0.5 g, 3.5 mmol) at room temperature, and then refluxed for 22 h. After cooling, concentrated hydrochloric acid was added to precipitate white solid, which was washed with aqueous sodium hydroxide and ether. Recrystallized from benzene–hexane solution gave colorless crystals (23%); mp 142—143 °C, lit, 8) mp 148—149 °C; IR 1662 cm^{-1} (C=N); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 7.30 (t, 1H, 4′-H), 7.44 (t, 2H, 3′,5′-H), 7.48 (d, 1H, 6-H), 7.53—7.69 (m, 3H, 7, 8,9-H), 7.91 (d, 1H, 10-H), 8.05 (d, 2H, 2′,6′-H), 8.32 (d, 1H, 5-H), 9.13 (s, 1H, 3-H). HRMS Found: *m/z* 244.0992 (M^+). Calcd for $C_{17}H_{12}N_2$: MS *m/z* 244.1000 (M^+).

6-Phenylimidazo[1,2-*f*]phenanthridine (21): 2-Bromoacetophenone (3.99 g, 20 mmol) was treated with benzenesulfonohydrazide (3.44 g, 20 mmol) in tetrahydrofuran (50 cm^3) for 15 min at 60 °C. After evaporation, 20 cm^3 of benzene was added, and subsequent concentration gave a white precipitate. It was washed with benzene to give 2-bromo-1-phenylethanone phenylsulfonylhydrazone (5.34 g, 76%; M^+ 352). The intermediate (0.88 g, 2.5 mmol) in tetrahydrofuran (15 cm^3) was added phenanthridine (0.45 g, 2.5 mmol) and potassium carbonate (1.04 g, 7.5 mmol), and stirred for 3 d at room temperature. Removal of insoluble solidby filtration followed by evaporation gave a reddish-brown oil. The crude compound was separated on silica gel (Wakogel C-200) with chloroform eluent. Recrystallized from benzene–hexane solution (8%); mp 167—168 °C; IR 1604, 1593 cm^{-1} (C=N, C=C); ^1H NMR (DMSO-d_6, 300 MHz) δ_H = 7.35 (t, 1H, 4′-H), 7.50 (t, 2H, 3′, 5′-H), 7.65, 7.82 (t, 1H, t-1H, 9,10-H), 7.72—7.79 (m, 2H, 5,6-H), 8.10 (d, 2H, 2′, 6′-H), 8.37, 8.74 (d, 1H, d-1H, 8,11-H), 8.61, 8.68 (d, 1H, d, 1H, 4,7-H), 9.16 (s, 1H, 3-H). EA Found: C, 84.96; H, 4.69; N, 9.54%. HRMS Found: *m/z* 294.1163 (M^+). Calcd for $C_{21}H_{14}N_2$: C, 85.69; H, 4.79; N, 9.52%. MS *m/z* 294.1157 (M^+).

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References

1) a) "Fluorescence Spectroscopy — New Methods and Applications," ed by O. S. Wolfbeis, Springer-Verlag, Berlin (1993); b) "Dye Laser Principles," ed by F. J. Duarte and L. W. Hillman, Academic Press, San Diego (1990); c) "Introduction to the Issue on Organic Electroluminescence," ed by S. R. Forrest and P. E. Burrows, IEEE, New York (1998).

2) a) H. Tomoda, S. Saito, and S. Shiraishi, *Chem. Lett.*, **1990**, 267; b) H. Tomoda, S. Saito, K. Araki, and S. Shiraishi, *Bull. Chem. Soc. Jpn.*, **71**, 1125 (1998).

3) a) J. R. Barrio, P. D. Sattsangi, B. A. Gruber, L. G. Dammann, and N. J. Leonard, *J. Am. Chem. Soc.*, **98**, 7408 (1976);

b) D. A. Lerner, P. M. Horowitz, and E. M. Evleth, *J. Phys. Chem.*, **81**, 12 (1977).

4) a) E. J. Lantham and S. P. Stanforth, *J. Heterocycl. Chem.*, **32**, 787 (1995); **33**, 991 (1996); b) J. Catalán, E. Mena, F. Fabero, and F. Amat-Guerri, *J. Chem. Phys.*, **96**, 2005 (1992).

5) a) E. S. Hand and W. W. Paudler, *J. Org. Chem.*, **43**, 2900 (1978); b) A. E. Tschitschibabin, *Ber. Dtsch. Chem. Ges.*, **57**, 2092 (1924).

6) A. J. Hubert and J. Reimlinger, *Chem. Ber.*, **103**, 3811 (1970).

7) a) G. Cooper and W. J. Irwin, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 75; b) A. Reiser, L. J. Leyshon, D. Saunders, M. V. Mijovic, A. Bright, and J. Bogie, *J. Am. Chem. Soc.*, **94**, 2414 (1972).

8) S. Ito, A. Kakehi, and T. Miwa, *Heterocycles*, **32**, 2373 (1991).

9) H. J. Knölker, R. Boese, and R. Hitzemann, *Chem. Ber.*, **123**, 327 (1990).

10) lit Ref. 4b: Reported fluorescence of 1 was $\lambda_{fl} = 374$ nm ($\Phi = 0.47$) in methanol.

11) a) N. Mataga, Y. Kaifu, and M. Koizumi, *Bull. Chem. Soc. Jpn.*, **29**, 465 (1956); b) E. Lippert, *Z. Naturforsch., Teil A*, **1955**, 541.

12) L. Onsager, *J. Am. Chem. Soc.*, **58**, 1486 (1936).

13) a) R. S. Mulliken, *J. Am. Chem. Soc.*, **72**, 600 (1950); b) W. Rettig, *Top. Curr. Chem.*, **169**, 253 (1994).

14) W. W. Paudler and H. L. Blewitt, *Tetrahedron*, **21**, 353 (1965).

15) E. S. Hand, W. W. Paudler, and S. Zachow, *J. Org. Chem.*, **42**, 3377 (1977).