Synthesis and Fluorescent Properties of 2-(1*H*-Benzimidazol-2-yl)-phenol Derivatives

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A high yield one pot synthesis of 2-(2-hydroxyaryl)-1*H*-benzimidazole derivatives by 2-hydroxy aromatic aldehydes with aromatic 1,2-diamines in the presence of manganese(III) acetate at room temperature was developed. Nine fluorescencers 2-(2-hydroxyaryl)-1*H*-benzimidazoles with substituent(s) X (X = H, CH_3, CH_3O, Cl) and two fluorescencers 2-(2-hydroxyaryl)-1*H*-naphth[2,3-*d*]imidazoles with substituent of H or Cl were prepared in 38 - 87% yield and the ultraviolet absorption and fluorescent spectra of the eleven compounds synthesized were measured in methanol. The fluorescent characteristics of the 2-(2-hydroxyaryl)benzimidazole derivatives prepared were investigated on the basis of excited-state intramolecular proton transfer mechanism, Stokes' shift, quantum yield, and the relationship between fluorescent intensity and the substituents were derived.

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Introduction.

The synthesis and development of fluorescence sensors for biological applications have been an important field of chemistry and pharmaceutics, recently, many novel series of fluorescent probes have been designed and synthesized [1-8]. 2-(2-Hydroxy-phenyl)benzimidazole (HPBI) and its derivatives were a series of important fluorescent compounds, these compounds have generated a lot of interest [9-11] because of their intense emission property *via* excited-state intramolecular proton transfer (ESIPT). The HPBI derivatives were useful as a new series of fluorescent probes [12-14], high-energy radiation detector, plastic scintillators [15-18] and polymer ultraviolet stabilizers [10], as well as for their implications in biology and potential applications as molecular switches in logic or memory circuits [19]. Recently we there have been very interest in the development and synthesis of HPBI and its derivatives. The HPBI is usually prepared from salicylic acid and 1,2-phenylenediamine in polyphospholic acid at high temperature (150-250 °C) in 14-30% yield [17,20-21]. Our laboratory has reported the photolysis method of [*N,N'*-*o*-phenylenebis(salicylideneaminato)]diaqua manganese(III) at room temperature for effective formation of HPBI in 40% yield [22]. Manganese triacetate is rapidly evolving as a new and exceptionally versatile reagent in organic synthesis, recently, it has been widely employed in the synthesis of many kinds of heterocyclic compounds [23-27]. Herein, we wish to report an one-pot synthesis of HPBI and its derivatives in higher yield by the oxidative condensation of 2-hydroxybenzaldehyde or substituted 2-hydroxy-benzaldehydes with corresponding aromatic 1,2-diamines using manganese triacetate as a relatively benign oxidizing reagent under milder reaction conditions and the fluorescent properties of some prepared HPBI derivatives.

Results and Discussion.

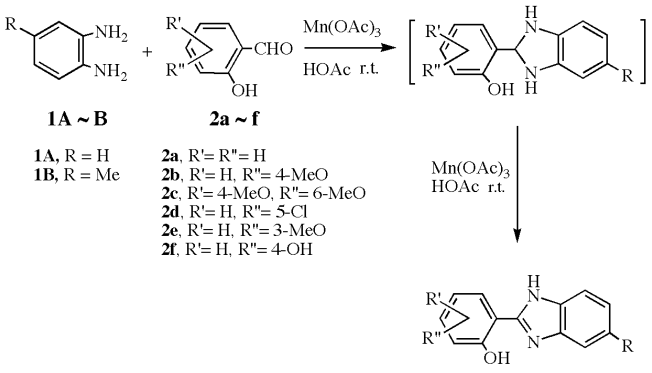
I. Synthesis.

Reactions of 2-Hydroxy Aromatic Aldehydes with Aromatic 1,2-Diamines in the Presence of Manganese(III) Acetate.

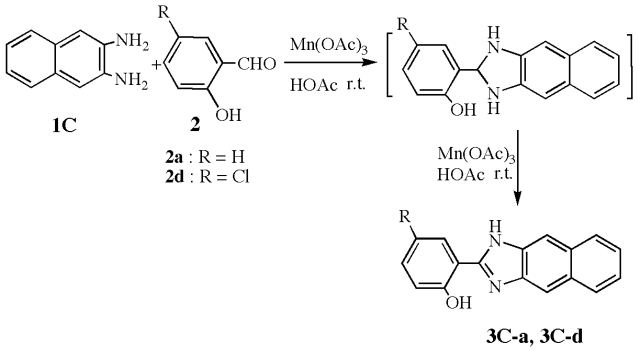
When the reaction of benzene-1,2-diamine (**1A**) with 2-hydroxybenzaldehyde (**2a**) in the presence of manganese(III) acetate was carried out by stirring for 12 hours in acetic acid at room temperature until the dark brown colored solution of manganese (III) acetate turned transparent, the corresponding product 2-(1*H*-benzoimidazol-2-yl)-phenol (**3A-a**) was obtained in 85 % yield (Scheme 1 and Table 1). Similarly, the reaction of **1A** separately with 2-hydroxy-4-methoxybenzaldehyde (**2b**), 2-hydroxy-4,6-dimethoxybenzaldehyde (**2c**), 5-chloro-2-hydroxybenz-

aldehyde (**2d**), 2-hydroxy-3-methoxybenzaldehyde (**2e**), 2,4-dihydroxy-benzaldehyde (**2f**) for a period of time gave corresponding phenol ring substituted 2-(1*H*-benzimidazol-2-yl)-phenols **3A-b**-**3A-f** in 38-87 % yield (Scheme 1 and Table 1). The reaction of 4-methylbenzene-1,2-diamine (**1B**) with **2a** and substituted 2-hydroxy-benzaldehydes **2b**, **2d** gave the corresponding HPBI derivatives **3B-a, 3B-b** and **3B-d** in 68-86 % yield (Scheme 1 and Table 1). Also the reaction of naphthalene-2,3-diamine (**1C**) with **2a** and **2d** gave the corresponding analogous compounds of HPBI **3C-a** and **3C-d** in 69 and 60 % yield (Scheme 2 and Table 1).

Scheme 1



Scheme 2



The reaction pathways for the formation of 2-(2-hydroxyaryl)benzimidazoles **3** could be explained as the following [27-28]. The reaction of **1** with **2** gives a Schiff base. Then the nucleophilic addition of the second amino group to the imide in the presence of manganese(III) acetate to give a cyclic intermediate, which is subsequently dehydrogenated further by manganese (III) acetate to deliver benzimidazoles **3** (Scheme 1 and Scheme 2).

Table 1

Synthesis of 2-(2-Hydroxyphenyl)benzimidazole and its Derivatives **3A-a**~**3C-d**, Aromatic 1,2-Diamines with 2 -Hydroxy Aromatic Aldehydes in the Presence of Manganese(III) Acetate[a]

Entry	1,2-Diamine	2-Hydroxyaldehyde	Time hour	Product (yield/%)[b]
1	**1A**	**2a**	12	**3A-a** (85)
2	**1A**	**2b**	24	**3A-b** (62)
3	**1A**	**2c**	36	**3A-c** (38)
4	**1A**	**2d**	6	**3A-d** (87)
5	**1A**	**2e**	24	**3A-e** (53)
6	**1A**	**2f**	36	**3A-f** (46)
7	**1B**	**2a**	12	**3B-a** (85)
8	**1B**	**2b**	24	**3B-b** (68)
9	**1B**	**2d**	6	**3B-d** (86)
10	**1C**	**2a**	36	**3C-a** (69)
11	**1C**	**2d**	24	**3C-d** (60)

[a] The reactions were carried out in acetic acid at a molar ratio 1:1:2 for **1**:**2**:manganese(III) acetate at room temperature for a period of time. [b] Isolated yield (based on the amount of **2** used).

II. Spectroscopic Properties.

A. Ultraviolet and Fluorescent Spectra.

All 1*H*-benzimidazole and 1*H*-naphthoimidazole derivatives reported in this paper have fluorescent properties, however, the fluorescent intensity is largely different among the derivatives. In order to evaluate the fluorescent properties, the absorption and emission spectra of these 2-(2-hydroxyaryl)-benzimidazoles **3** were measured in methanol, the data are listed in Table 2.

Table 2

Photophysical Characteristics of the 2-(2-Hydroxyaryl)-benzimidazole Derivatives **3** in Methanol at 25 °C

Compd	λ abs [a] (nm)	ε [b] ($Lmol^{-1}cm^{-1}$)	λ em [c] (nm)	Stokes'Shift (cm^{-1})	Quantum Yield [d] (Φ)
3A-a	316	21600	460	9906	0.694
3A-b	317	31600	433	8451	0.362
3A-c	327	37000	430	7326	0.251
3A-d	326	22800	467	9261	0.547
3A-e	302	25200	361	6112	0.157
3A-f	317	33000	431	8344	0.400
3B-a	319	25300	458	9514	0.541
3B-b	320	35200	433	8156	0.454
3B-d	328	23900	469	9166	0.645
3C-a	348	29300	485	8118	0.271
3C-d	353	29100	489	7880	0.316

[a] Maximum absorption wavelength in methanol (solvent for fluorescence analysis). [b] Absorption coefficient, e (at the wavelength corresponding to the maximum of the absorption band) in methanol. [c] Maximum emission wavelength excited at the maximum absorption wavelength. [d] Quantum yield values relative to Quinine sulfate in 0.1 N H_2SO_4 (from measurements using 350 nm excitation wavelength, Φ = 0.577).

Table 2, which lists the photophysical characteristics of the compounds studied, clearly demonstrates the dependence of fluorescent properties on the structure of hydroxyaryl groups and benzimidazole ring (or naphthoimidazole ring). All eleven compounds **3** display an intense fluorescence emission with a quantum yield ranging 0.157 to

0.694 for total fluorescence and show large Stokes' shifts from 6112 to 9906 cm^{-1}, a typical characteristic shift for emission of the corresponding excited-state intramolecular proton transfer (ESIPT) fluors [9-11]. These products display special photophysical properties which render them potentially suitable as fluorescent probes. It was found from the data in Table 2 that when it is a product which bearing the electron-attracting chlorine atom at the C-5 position in 2-hydroxyphenyl, such as **3A-d**, **3B-d** and **3C-d**, their maximum absorption wavelength and maximum emission wavelength are shifted approximately 5-10 nm toward longer wavelength relative to values of the **3A-a**, **3B-a** and **3C-a**, but their Stokes' shift relatively decrease, the differences in Stokes' shift of **3A-d**, **3B-d** and **3C-d** with **3A-a**, **3B-a** and **3C-a** are respectively 645, 348, 238 (cm^{-1}). On the other hand, when a methoxy group which is an electron-donating group is attached to the benzene ring of 2-hydroxyphenyl group of the 2-(2-hydroxyaryl) benzimidazoles **3** at the C-4 or C-6 position, such as **3A-b**, **3A-c** or **3B-b**, their maximum absorption wavelength and absorption coefficient (ε) were increased, but the maximum emission wavelength, Stokes' shift and quantum yield were decreased relative to those of the **3A-a** or **3B-a**. When a methoxy group is attached to the benzene ring of 2-hydroxyphenyl group at the C-3 position that is an *ortho* - position of the hydroxy group, such as the compound **3A-e**, its maximum absorption wavelength and corresponding maximum emission wavelength is respectively 302 nm and 361 nm, a blue-shift was shown, and both the Stokes' shift (6112 cm^{-1}) and the quantum yield (0.157) were decreased relative to those of **3A-a**. When a methyl group which is an electron-donating group is added to the benzene ring at the C-5 (or C-6) position, that is a benzene ring of benzimidazole structure in the compounds **3**, such as compounds **3B-a**, **3B-b** or **3B-d**, their absorption coefficient (**ε**) were increased (the **Δε** are respectively 3700, 3600 and 1100 $Lmol^{-1}cm^{-1}$), but Stokes' shift values were decreased relative to the values of the **3A-a**, **3A-b** and **3A-d**. When a same 2-hydroxyaryl structure is connected respectively to the benzimidazole ring and naphthoimidazole ring at the 2 position, such as compounds **3C-a** and **3C-d**, a larger change of their fluorescence properties is observed as show in Table 2. For example, their maximum absorption wavelength, absorption coefficient (**ε**) and the maximum emission wavelength respectively were increased approximately 30 nm, 6300-7700 $Lmol^{-1}cm^{-1}$ and 25 nm, but, Stokes' shift and quantum yield respectively were decreased relative to these values of the **3A-a** and **3A-d**.

B. Dependence of Normal and Tautomer Emission on the Structure of *o*-Hydroxyaryl Groups in Methanol at 25 °C.

In recent years, the dual emission characteristics, normal and tautomer, of the HPBI in many cases at room temperature has been studied and reported [11]. It is known that the HPBI can have two intramolecular hydrogen bonded rotamers **I, II** and one tautomer **III** in the ground state as shown in Scheme 3. **I** is more stable than **II** and **III**, the tautomer **III** has a higher energy than both **I** and **II** in the ground state [11a]. Quantum chemical calculations indicate that the barrier for the interconversion between **I** and **II** increases in the excited electronic state, and hence **I** and **II** are not freely interconvertible in the excited singlet state. It has been also demonstrated that only **II** on excitation undergoes ESIPT to form a tautomer **III**, which gives rise to an emission (tautomer emission) with large Stokes' shift. Rotamer **I** does not undergo ESIPT and is responsible for the short wavelength normal emission (Figure 1). The driving force of ESIPT is the nitrogen atoms of the five-membered ring of HPBI becoming richer in π- electrons than the oxygen atom of the hydroxyl group in the S_1 state [11b].

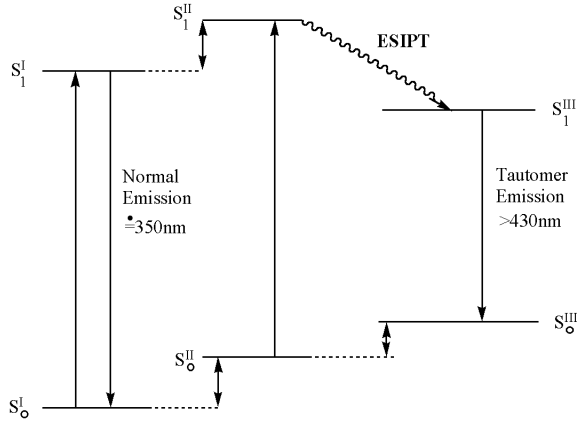
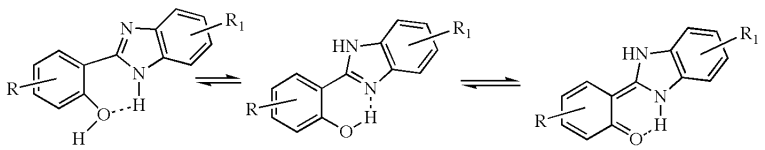


Figure 1. The excitation and emission processes of the rotamer **I**, **II** and the tautomer **III** of the **HPBI** and its derivatives

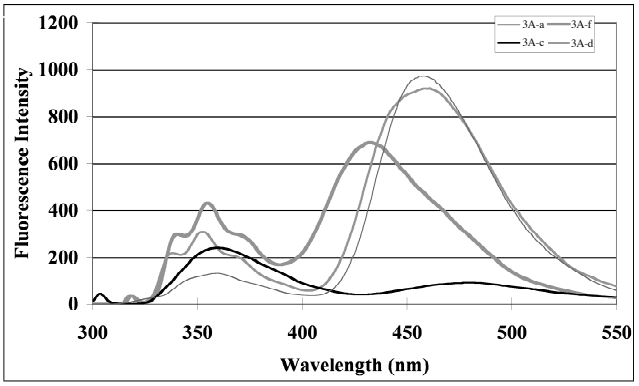
Scheme 3



I **II** **III**

R = H, OH, OCH_3,Cl R_1= H, CH_3

In relation to this dual emission property of HPBI, it has been reported that the relative intensities of the two kinds of emission largely change with the temperature and solvents [11]. Herein we wish to report a dependence of normal and tautomer emissions on the structure of *o*-hydroxyaryl groups for HPBI and its derivatives in methanol at 25 °C, because the relative intensities also depend on the substituents as is exemplified in Figure 2. We have evaluated respectively quantum yield of the normal emission (Φ_N) and quantum yield of the tautomer emission (Φ_T) for the all HPBI and its derivatives synthesized, and have calculated a ratio (Φ_N/Φ_T) of the corresponding compounds, the data are listed in Table 3.



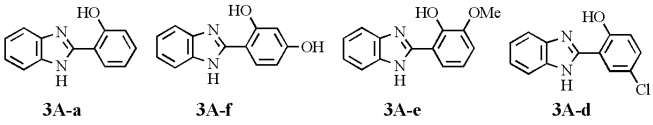


Figure 2. The fluorescent spectra of compounds **3A-a**, **3A-f, 3A-e** and **3A-d** in methanol at 25 °C. The spectra near 355 nm correspond to normal emission and the spectra near at 430 – 480 nm to tautomer emission.

Table 3

The Quantum Yield of the Normal Emission (Φ_N) and Quantum Yield of the Tautomer Emission (Φ_T) for the all HPBI and its Derivatives Synthesized [a]

sample	normal emission Quantum Yield Φ_N	tautomer emission Quantum Yield Φ_T	Φ_N / Φ_T
3A-a	0.106	0.588	0.180
3A-b	0.070	0.292	0.240
3A-c	0.020	0.231	0.087
3A-d	0.035	0.512	0.068
3A-e	0.097	0.060	1.617
3A-f	0.097	0.303	0.320
3B-a	0.076	0.465	0.163
3B-b	0.069	0.385	0.179
3B-d	0.048	0.597	0.080
3C-a	0.020	0.251	0.080
3C-d	0.013	0.303	0.043

[a] Quantum yield of the normal emission and the tautomer emission are evaluated in methanol at 25 °C , the quantum yield values is that relative to Quinine sulfate in 0.1 *N* H_2SO_4 (from measurements using 350 nm excitation wavelength, $\Phi = 0.577$)

Table 3 clearly demonstrates the dependence of fluorescent quantum yield on the structure of hydroxyaryl groups. When an electron-donating group (OH or OCH_3) is attached to the benzene ring of 2-hydroxyphenyl group of the 2-(2-hydroxyaryl) benzimidazoles **3**, such as **3A-f**, **3A-b** and **3A-e** or **3B-b**, the eleactron density of lone pair of the OH of 2-hydroxyphenyl group is increased relative to that of **3A-a** or **3B-a**, the population of the rotamer **I** increases. Hence the normal emission of the corresponding compounds **3** is relatively enhanced, the ratio values (Φ_N/Φ_T) become large compared with that of **3A-a** (0.180) such as the Φ_N/Φ_T of **3A-f**, **3A-b** and **3A-e** are respectively 0.320, 0.240 and 1.617. The Φ_N/Φ_T of **3B-b** is 0.179, which is also larger than that of **3B-a** (0.163). Here the donor electron effect of OH is stronger than that of OCH_3, hence the Φ_N/Φ_T of **3A-f** becomes even larger than that of the **3A-b** or **3B-b**. Since the OCH_3 of the **3A-e** is attached to *ortho* - position relative to the hydroxy group, the donor conjugation effect (+M effect) is stronger than that of **3A-b** in which the OCH_3 is attached to *meta* - position relative to the hydroxy group, consequently the Φ_N/Φ_T of **3A-e** becomes larger by about 9 times compared with that of the **3A-a**. In the case of **3A-e**, the normal emission dominates over the tautomer emission as shown in Figure 2. The Φ_N/Φ_T of **3A-c** is very low (0.087), which is an exception, because two kinds of the intramolcular hydrogen bonds (N–H···OCH_3 and O–H···N) exist simultaneously in **3A-c** [29]. On the other hand, when an electron-withdrawing group such as Cl is attached to the *para* - position relative to the OH of the 2-hydroxyphenyl group, such as **3A-d**, **3B-d** and **3C-d**, the electron density of the oxygen atom of OH is decreased relative to that of the **3A-a**, **3B-a** or **3C-a**, and the acidity of the OH is increased. Hence the intramolecular hydrogen bond of the form of the O–H···N is enhanced in the corresponding compounds **3**, the population of the rotamer **II**, which is responsible for the tautomer emission, becomes more predominant. Thus, the Φ_N/Φ_T of the compounds **3A-d**, **3B-d** and **3C-d** is less than that of **3A-a**, **3B-a** and **3C-a** (the data see Table 3). Evidently, the normal emission is inhibited in **3A-d**, **3B-d** and **3C-d**. In this case, it gives predominantly a high intensity emission with a high Stokes' shift due to ESIPT transform, useful for fluorescent molecular sensors.

EXPERIMENTAL

Measurements.

All ^1H and ^{13}C nmr spectra were taken with a GSX-400 nmr (400MHz for ^1H and 100 MHz for ^{13}C) spectrometer with tetramethylsilane being used as the internal standard. Chemical shifts are shown in δ values (ppm) and the coupling constants are expressed in J values (Hz). Mass spectra were taken with a JMS-DX300 mass spectrometer at an ionizing voltage of 70 eV. All of the melting points were determined with a yanagimoto micromelting-

point apparatus MP-J3. Elemental analyses were performed by the Instrumental Analysis Center, Ibaraki University, Mito, Japan. The ultraviolet absorption spectra were recorded at 25 °C using a UV-1600 UV-Visible spectrometer (Shimadzu, Kyoto, Japan). The fluorescence measurements were made on a F-4500 model spectrophotometer (Hitachi, Tokyo, Japan). The slit width was 2.5 nm for both excitation and emission. The photomultiplier voltage was 700 V. All compounds were dissolved in DMSO to obtain 10 mM stock solutions, the absorption and emission spectra were recorded in methanol, the methanol is a solvent for fluorescence analysis (Dojindo Laboratory, Kumamoto, Japan), the concentration of DMSO as co-solvent in methanol is 0.1% (v/v). Quantum yields were determined using quinine sulfate in 0.1 *N* H_2SO_4 (from measurements using 350 nm excitation wavelength, Φ = 0.577). The working equation was:

$$\Phi_{spl.} = (\Phi_{std.})(Area_{spl})(Absorbance_{std})(n^2_{spl}) / (Area_{std.})(Absorbance_{spl})(n^2_{std.})$$

The n is an index of refraction of solvent used.

Materials.

Manganese(III) acetate hydrate, *o*-phenylenediamine, 2,4-dihydroxybenzaldehyde and salicylaldehyde were commercially available and used as they were received (Wako). 3,4-Diaminotoluene, 5-chlorosalicylaldehyde, and 4,6-dimethoxysalicylaldehyde were purchased from Aldrich Chemical Co. Inc.. 2,3-Diaminonaphthalene and 2-hydroxy-4-methoxybenzaldehyde were purchased from Tokyo-kasei Co. Ltd. and used as received.

Reaction of Aromatic 1,2-Diamines **1a-c** with 2-Hydroxy Aromatic Aldehydes **2** in the Presence of Manganese(III) Acetate.

The general procedure for the reaction of aromatic 1,2-diamines **1A~C** with 2-hydroxy aromatic aldehydes **2** in the presence of manganese(III) acetate was as follows. Manganese(III) acetate (2 mmol) was added to a stirred solution of diamine (1 mmol) and 2-hydroxyaldehyde (1 mmol) in the acetic acid (30 ml) in a flask equipped with a dry-air inlet tube. The mixture was stirred at room temperature for the period of time shown in Table 1. The reaction was monitored by TLC. The reaction was quenched by adding water (60 ml) and the mixture was then extracted with ether and ethyl acetate and the combined extract was washed with a saturated solution of sodium hydrogen carbonate, and dried over sodium sulfate. After removing the ether and ethyl acetate, the resulting products were separated by silica gel column (Wakogel C - 200) while eluted with a mixture of hexane-ethyl acetate (2:1 v/v). The products were further purified for analytical samples by recrystallization from appropriate solvents. The yields are listed in Table 1. Specific details are given below.

Products.

2-(1*H*-Benzoimidazol-2-yl)-phenol (**3A-a**).

This compound was obtained as colorless microcrystals, 178mg (85%), mp 240-242 °C (from ethanol) (lit 241-242 °C)[15]; ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide):δ = 13.22 (br s, 2H, OH and NH), 8.10 (dd, 1H, arom H, J = 1.6, 7.2 Hz), 7.76 (d, 1H, arom H, J =5.6 Hz), 7.65 (d, 1H, arom H, J =5.6 Hz), 7.44-7.32 (m, 3H, arom H), 7.10-7.04 (m, 2H, arom H); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 157.9, 151.6, 140.7, 133.0, 131.7, 126.2, 126.0, 123.2, 122.3, 119.0, 117.1, 112.5, 111.4; EI-MS: m/z (relative intensity) = 210 (100, M^+), 182 (20), 91 (18), 78 (14).

2-(1*H*-Benzoimidazol-2-yl)-5-methoxy-phenol (**3A-b**).

This compound was obtained as colorless microcrystals, 149 mg (62%), mp 233-234 °C (from ethanol); ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide):δ = 13.35 (br s, 1H, OH), 13.00 (s, 1H, NH), 7.95 (d, 1H, arom H, J = 8.4 Hz), 7.62 (dd, 2H, arom H, J = 3.2, 9.2 Hz), 7.25 (dd, 2H, arom H, J = 3.2, 9.2 Hz), 6.62 (dd, 1H, arom H, J = 2.4, 8.4 Hz), 6.58 (d, 1H, arom H, J = 2.4 Hz), 3.80 (s, 3H, CH_3O); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide) δ = 162.2, 159.7, 151.6, 139.9, 132.8, 127.5, 127.3, 122.6, 122.4, 106.5, 105.3, 101.4, 101.3, 55.4; EI-MS: m/z (relative intensity) = 240 (100, M^+), 197 (24), 169 (7), 143 (5), 120 (6), 106 (7), 65 (7).

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.68; H, 5.11; N, 11.43.

2-(1*H*-Benzoimidazol-2-yl)-3,5-dimethoxy-phenol (**3A-c**).

This compound was obtained as colorless needles, 103 mg (38%), mp 177-178 °C (from ethanol); ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ = 14.68 (br s, 1H, NH), 12.09 (br s, 1H, OH), 7.64 (dd, 2H, arom H, J = 3.2, 9.2Hz), 7.23 (dd, 2H, arom H, J = 3.2, 9.2 Hz), 6.35 (s, 2H, arom H), 4.01 (s, 3H, CH_3O), 3.80 (s, 3H, CH_3O); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 162.3, 161.6, 158.8, 150.2, 139.0, 132.4, 122.3, 122.2, 116.8, 111.9, 95.3, 94.3, 90.2, 55.6, 55.1; EI-MS: m/z (relative intensity) = 270 (100, M^+), 240 (16), 193 (20), 143 (12), 136 (20), 121 (17), 78 (6), 65 (5), 58 (10).

Anal. Calcd. for $C_{15}H_{14}N_2O_3$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.38; H, 5.31; N, 10.13.

2-(1*H*-Benzoimidazol-2-yl)-4-chloro-phenol (**3A-d**).

This compound was obtained as colorless needles, 212 mg (87%), mp 301-303 °C (from ethanol) (lit 302-304 °C)[15]; ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ = 13.26 (br s, 2H, OH and NH), 8.15 (d, 1H, arom H, J = 2.8 Hz), 7.80 (d, 1H, arom H, J = 8.4Hz), 7.69 (d, 1H, arom H, J = 8.4 Hz), 7.47 (dd, 1H, arom H, J =2.8, 8.8 Hz), 7.37 (br s, 2H, arom H), 7.14 (d, 1H, arom H, J = 8.8 Hz); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 156.5, 150.1, 133.2, 133.1, 125.5, 125.4, 123.1, 123.0, 122.6, 122.5, 119.0, 118.9, 113.9;EI-MS: m/z (relative intensity) = 246 (33, M^+ +2), 244 (100, M^+), 216 (8), 181 (16), 149 (7), 90 (11), 57 (10).

2-(1*H*-Benzoimidazol-2-yl)-6-methoxy-phenol (**3A-e**).

This compound was obtained as colorless microcrystals, 127 mg (53%), mp 270-271 °C dec. (from ethanol); ^{1}H nmr (400MHz, deuteriodimethyl sulfoxide): δ = 13.25 (br s, 1H, OH), 13.17 (br s, 1H, NH), 7.72 (d, 1H, arom H, J = 8.4 Hz), 7.63 (dd, 1H, arom H, J = 1.6, 8.0 Hz), 7.59 (d, 1H, arom H, J = 8.4 Hz), 7.30 (br s, 2H, arom H), 7.15 (dd, 1H, arom H, J = 1.6, 8.0 Hz), 7.02 (t, 1H, arom H, J = 8.0 Hz), 3.84 (s, 3H, CH_3O); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 151.7, 148.4, 148.1, 139.0, 132.9, 123.5, 122.8, 122.7, 118.6, 117.5, 117.4, 113.8, 112.3, 55.7; EI-MS: m/z (relative intensity) = 240 (30, M^+), 197 (13), 169 (6), 123 (17), 97 (42), 57 (100).

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.65; H, 5.09; N, 11.48.

2-(1*H*-Benzoimidazol-2-yl)-benzene-1,3-diol (**3A-f**).

This compound was obtained as colorless microcrystals, 104 mg (46%), mp 279-282 °C dec. (from ethanol) (lit 280-284 °C)[30]; ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ =

13.17 (br s, 1H, OH), 12.88 (br s, 1H, NH), 9.96 (br s, 1H, OH), 7.82 (d, 1H, arom H, J = 8.8 Hz), 7.61 (br s, 1H, arom H), 7.53 (br s, 1H, arom H), 7.21 (d, 2H, arom H), 6.43 (dd, 1H, arom H, J = 2.4, 8.8 Hz), 6.38 (d, 1H, arom H, J = 2.4 Hz); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 160.7, 159.7, 152.2, 135.9, 129.8, 127.4, 127.3, 122.3, 107.5, 107.4, 104.3, 103.0, 102.9; EI-MS: m/z (relative intensity) = 226 (100, M^+), 169 (23), 149 (31), 99 (14), 69 (23), 55 (37).

2-(5(6)-Methyl-1*H*-benzoimidazol-2-yl)-phenol (**3B-a**).

This compound was obtained as colorless microcrystals, 195 mg (85%), mp 256-257 °C (from ethanol); ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ = 13.17 (br s, 1H, OH), 13.03 (br s, 1H, NH), 8.00 (dd, 1H, arom H, J = 1.6, 7.6 Hz), 7.57-7.32 (m, 3H, arom H), 7.11-6.96 (m, 3H, arom H), 2.43 (s, 3H, CH_3); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 157.8, 151.2, 132.5, 131.5, 131.4, 126.0, 125.9, 124.2, 119.0, 117.0, 112.6, 111.4, 111.3, 21.3; EI-MS: m/z (relative intensity) = 224 (100, M^+), 196 (14), 149 (8), 98 (9), 77 (9), 57 (6).

Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 74.78; H, 5.53; N, 12.25.

5-Methoxy-2-(5(6)-methyl-1*H*-benzoimidazol-2-yl)-phenol (**3B-b**).

This compound was obtained as colorless microcrystals, 173 mg (68%), mp 220-221 °C (from ethanol); ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ = 13.35 (br s, 1H, OH), 12.87 (br s, 1H, NH), 7.90 (d, 1H, arom H, J = 8.8 Hz), 7.46 (br s, 1H, arom H), 7.37 (br s, 1H, arom H), 7.04 (d, 1H, arom H, J = 8.0 Hz), 6.59 (dd, 1H, arom H, J_1 = 2.8, 8.8 Hz), 6.55 (d, 1H, arom H, J = 2.0 Hz), 3.79 (s, 3H, CH_3O), 2.42 (s, 3H, CH_3); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 161.9, 159.7, 151.6, 132.0, 127.0, 126.9, 123.8, 111.4,106.3, 106.2, 105.7, 101.4, 101.3, 55.3, 21.3; EI-MS: m/z (relative intensity) = 254 (12, M^+), 193 (92), 164 (18), 136 (100), 107 (65), 585 (55).

Anal. Calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.78; H, 5.43; N, 11.25.

4-Chloro-2-(6-methyl-1*H*-benzoimidazol-2-yl)-phenol (**3B-d**).

This compound was obtained as colorless needles, 222 mg (86%), mp 299-300 °C (from ethanol); ^{1}H nmr (400 MHz, deuteriodimethyl sulfoxide): δ = 13.25 (br s, 1H, OH), 13.10 (br s, 1H, NH), 8.12 (d, 1H, arom H, J = 2.8 Hz), 7.58 (d, 1H, arom H, J = 8.0Hz), 7.50 (d, 1H, arom H, J = 8.0 Hz), 7.37 (dd, 1H, arom H, J = 2.8, 8.4 Hz), 7.10 (br s, 1H, arom H), 7.04 (d, 1H, arom H, J = 8.4 Hz), 2.45 (s, 3H, CH_3); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 156.4, 149.5, 133.2, 131.2, 131.1, 125.5, 125.4, 124.7, 122.6, 122.5, 118.9, 113.9, 113.8, 21.3; EI-MS: m/z (relative intensity) = 260 (33, M^+ +2), 258 (100, M^+), 193 (42), 164 (8), 136 (42), 107 (30), 77 (19), 58 (22).

Anal. Calcd. for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; N, 10.83. Found: C, 64.69; H, 4.41; N, 10.50.

2-(1*H*-Naphtho[2,3-d]imidazol-2-yl)-phenol (**3C-a**).

This compound was obtained as light yellow microcrystals, 180 mg (69%), mp 334-335 °C dec. (from ethanol) (lit 340-346 °C)[31]; ^{1}H nmr (400MHz, deuteriodimethyl sulfoxide): δ = 13.28 (br s, 1H, OH), 13.21 (br s, 1H, NH), 8.25 (br s, arom H, 1H), 8.14 (dd, 1H, arom H, J_1 = 1.6, 7.6 Hz), 8.05-8.00 (m, 3H, arom H), 7.46-7.41 (m, 3H, arom H), 7.09-7.04 (m, 2H, arom H); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 158.6, 155.7, 141.2, 133.5, 132.6, 130.4, 129.9, 127.9, 127.4, 126.8, 126.7, 124.1, 123.4, 119.1, 117.3, 112.1, 107.4; EI-MS: m/z (relative intensity) = 260 (53, M^+), 240 (100), 197 (21), 169 (6), 120 (5), 106 (6), 57 (12).

4-Chloro-2-(1*H*-naphtho[2,3-d]imidazol-2-yl)-phenol (**3C-d**).

This compound was obtained as light yellow microcrystals, 177 mg (60%), mp 360 °C dec. (from ethanol); ^{1}H nmr (400MHz, deuteriodimethyl sulfoxide): δ = 13.33 (br s, 2H, OH and NH), 8.27 (d, 1H, arom H, J = 2.8 Hz), 8.20 (br s, 2H, arom H), 8.05 (m, 2H, arom H), 7.48 (dd, 1H, arom H, J = 2.8, 8.8 Hz), 7.43 (m, 2H, arom H), 7.12 (d, 1H, arom H, J = 8.8 Hz); ^{13}C nmr (100 MHz, deuteriodimethyl sulfoxide): δ = 157.3, 154.3, 132.02, 132.0, 130.21, 130.20, 127.70, 127.66, 127.60, 126.12, 126.07, 123.88, 123.84, 122.7, 119.1, 119.0, 113.5; EI-MS: m/z (relative intensity) = 296 (34, M^+ +2), 294 (100, M^+), 260 (10), 231 (10), 149 (12), 140 (16), 115 (20), 57 (12).

Anal. Calcd. for $C_{17}H_{11}ClN_2O$: C, 69.28; H, 3.76; N, 9.50. Found: C, 68.98; H, 3.83; N, 9.25.

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[29] The protons of OH and NH of **3A-c** both show a broad singlet peak at 12.09 ppm (OH) and 14.68 ppm (NH), respectively in ^{1}H NMR spectrum, and the chemical shift of NH-proton is much more low-field than that of the other members of the family (*e.g.* 13.22 ppm (**3A-a**), 13.00 ppm (**3A-b**)), indicating that **3A-c** exists in the form of two kinds of intramolecular hydrogen bond (N–H…OCH_3 and O–H···N).

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