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SYNTHESIS, SPECTRAL AND THEORETICAL CHARACTERIZATION OF 5,6-DICHLORO/DIMETHYL-2-(2′,3′/2′,4′/2′,5′/3′,4′/3′,5′-DIMETHOXYPHENYL)-1*H*-BENZIMIDAZOLES

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Abstract. 5,6-Dichloro/dimethyl-2-(2′,3′/2′,4′/2′,5′/3′,4′/3′,5′-dimethoxyphenyl)-1*H*-benzimidazoles were synthesized and characterized by using analytical data, FT-IR, FT-Raman, NMR, ESI-MS and fluorescence spectroscopy. The optimized molecular geometry, zero point energy, dipole moment, ESE, band gap and charge distributions were calculated by Gaussian 09 using Density Functional Theory (DFT, RB3LYP) with 6-31++G(d,p) basis set. According to the calculations, the molecules have structures with various torsion angles between the benzimidazole and benzene rings from 9.7º to 47.8º. The calculated energy values with ZPE correction and DFT show that the methyl derivatives are more stable than the chloro forms. 3′,4′-Dimethoxy derivatives have higher decomposition points in comparison with the other compounds in series. The chlorine atoms of 5,6-dichloro-2-(2′,3′/2′,4′/2′,5′/3′,4′/3′,5′-dimethoxyphenyl)-1*H*-benzimidazoles are positively charged whereas the C5 and C6 carbon atoms are negatively charged due to the attached chlorine atoms, in virtue of the electron withdrawing characteristic of the imidazole part of the benzimidazole ring. Also, some calculated prominent bond lengths and bond angles were discussed.

Keywords: dimethoxyphenylbenzimidazoles, spectral characterization, density functional theory, charge distribution, geometry optimization.

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Introduction

Various benzimidazole derivatives display a wide range of biological activity. For instance, vitamin B12 has 5,6-dimethylbenzimidazole moiety as coordinated to the Co(II) ion [1,2]. On the other hand, various drugs and pharmaceutical compositions contain benzimidazole derivatives. Perhaps the most important one is an antisecretory agent, omeprazole [5-methoxy-2-(4-methoxy-3,5-dimethylpyridin-2-yl-methylsulphinyl)-1*H*-benzimidazole] [3]. The other important benzimidazol derivatives that are used as drugs are: thiabendazole [4,5], albendazole, mebendazole, flubendazole [6,7] astemizole [8] and fenbendazole [9]. The high therapeutic properties of the related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents [10–12]. They displayed many biological activities, such as: antiviral [13] and antitumoral [14]; antifungal and antimycotic [15]; antihistaminic and antiallergic [16]; antimicrobial [17–20] and antihelminthic activity [21]; all are unique characteristics known for benzimidazole derivatives [10]. These compounds are also extensively used in industrial processes as corrosion inhibitors for metal and alloy surfaces [22,23]. These different applications have attracted many experimentalists and theorists to investigate the spectroscopic and structural properties of benzimidazole [24–26] and some its derivatives [27].

In this study, 5,6-dichloro/dimethyl-2-(2′,3′/2′,4′/2′,5′/3′,4′/3′,5′-dimethoxyphenyl)-1*H*-benzimidazoles (**1**–**10**, Figure 1) were synthesized and characterized by analytical and spectroscopic methods, such as: FT-IR, FT-Raman, ^{1}H- and ^{13}C-NMR, fluorescence spectra and ESI-MS. In addition, the optimized structure and charge distribution of the molecules are investigated using the Gaussian09 program applying Density Functional Theory (DFT) method.

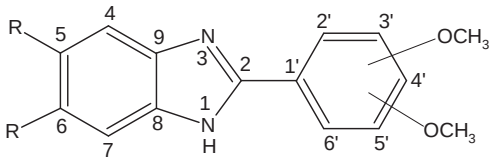


Figure 1. Schematic view of the compounds in the study.

1) R = Cl; 2′,3′-dimethoxy
2) R = Cl; 2′,4′-dimethoxy
3) R = Cl; 2′,5′-dimethoxy
4) R = Cl; 3′,4′-dimethoxy
5) R = Cl; 3′,5′-dimethoxy
6) R= CH_3; 2′,3′-dimethoxy
7) R= CH_3; 2′,4′-dimethoxy
8) R= CH_3; 2′,5′-dimethoxy
9) R= CH_3; 3′,4′-dimethoxy
10) R= CH_3; 3′,5′-dimethoxy

Compounds **1**, **2**, **5**, **6**, **7** and **10** are reported for the first time in this study. Mukhopadhyay and Tapaswi reported some methoxy/dimethoxyphenylbenzimidazoles including **3**, **4**, **8** and **9** [28]. Our research was focused on the investigation of the effect of electropositive (methyl) and electronegative (chloro) substituents on the characteristics of a series of compounds.

Results and discussion

Some physicochemical and spectral data of compounds are presented in Experimental section. We present only the Raman and fluorescence data for the known molecules (**3**, **4**, **8** and **9**) for which these data are absent in the literature. The other spectral and physicochemical data are omitted. It was observed that compounds decomposed before they started to melt. 3′,4′-Dimethoxy derivatives (**4** and **9**) have higher decomposition points as compared to the others. Compound **5**, 5,6-dichloro-2-(3′,5′-dimethoxyphenyl)-1*H*-benzimidazole, has the lowest decomposition point (125°C). It was also observed that the colour of the dichloro derivatives (**1**–**5**) is darker than the dimethyl derivatives (**6**–**10**) probably because of the intramolecular charge transfer transitions.

FT-IR and FT-Raman spectra

FT-IR and FT-Raman spectral data of compounds are given in Experimental section. FT-IR and FT-Raman spectra of compound **8** were also presented in Figure 2 as an example for comparison of the IR and Raman spectra. The characteristic ν(N–H) vibration frequencies of compounds exhibit a medium broad band at ca. 3200 cm^{-1} in the IR spectra. The ν(C=C) frequencies for the ring residue are expected to appear at around 1600 cm^{-1} with their own characteristics for the compounds in the IR spectra. Similarly, the (C=N) asymmetric stretching frequencies are expected to appear at *ca*. 1590 cm^{-1}.

The C–Cl stretching vibration was observed in the range of 656 – 670 cm^{-1} for **1** – **5** as medium band in the FT-IR spectra [29]. The characteristic ν(C–H) modes of ring residues are observed in the range of 3038 – 3093 cm^{-1}, particularly in the Raman spectra of compounds (Figure 2). The aliphatic ν(C–H) bands appeared as weak or medium in the range of 2800 – 2970 cm^{-1} both in the IR and Raman spectra. The strong bands above 1600 cm^{-1} and the medium bands around 1590 cm^{-1} in the Raman spectra are considered to belong to C=N and C=C bonds, respectively. The corresponding to these frequencies bands in the IR spectra are weak in most of compounds. The FT-Raman spectra of compounds **1**–**5** are smooth; however, those of **6**–**10** are not smooth, probably due to disturbing fluorescence effect.

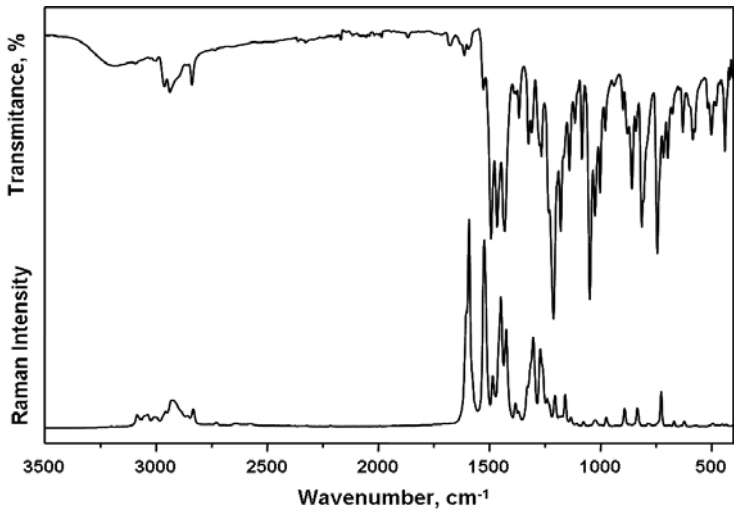


Figure 2. FT-IR and FT-Raman spectra of compound 8.

NMR spectra

The ^{1}H- and ^{13}C-NMR (Attached Proton Test, APT) spectral data of compounds are given in Experimental section. In addition, ^{1}H-NMR spectrum of **2** is presented in Figure 3. Mukhopadhyay and Tapaswi reported the ^{1}H- and ^{13}C-NMR spectral data of compounds **3**, **4**, **8** and **9** [28]. Our NMR data of these compounds are mostly in line with those of the present study.

The NH protons appear in the 11.66 – 12.86 ppm range as a broad singlet in most of compounds in DMSO-d_6. Chemical shifts of NH peaks of compounds **4** and **5** could not be detected. Reason of this probably is the tautomeric equilibrium of the hydrogen atom in the imidazole ring between the two nitrogen atoms [30,31]. This fluxional behaviour causes acidic character of NH proton. Consequently, NH protons of **4** and **5** that have higher acidic character than in the other compounds disappear; NH protons of the other compounds appear as broad singlet.

It is observed that the protons H4 and H7 have very close chemical shifts. These protons are almost identical and they are affected by the methyl or chloro substituents at the neighbouring carbon atoms (C5 and C6). They appear as a singlet (in **1**, **5**, **7** and **8**) or a broad singlet (in **2**, **3**, **4** and **9**) as expected, in the range of 7.78 – 7.85 ppm and 7.32 – 7.47 ppm for the chloro and methyl derivatives, respectively. In compounds **6** and **10** they give separate singlets. The methoxy and methyl protons give singlet in the range of 3.79 – 4.02 and 2.30 – 2.39 ppm, respectively.

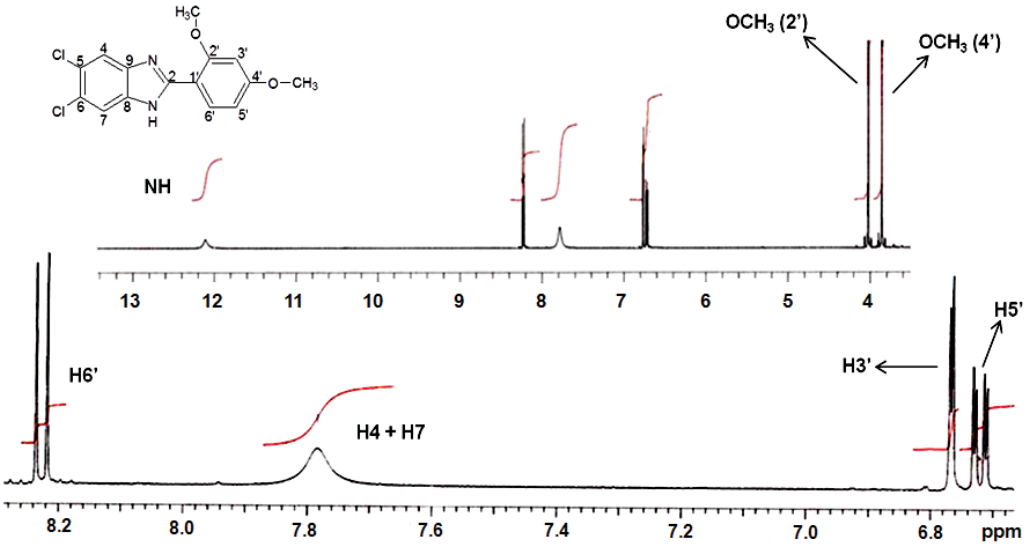


Figure 3. Fragment of ^{1}H-NMR spectrum for compound 2 and expanded view of the aromatic region

In the APT spectra of compounds, the signal at the highest ppm values should belong to N–C=N (C2) carbon atom *e.g.* for compound **2** it is found at 163.31 ppm. The methoxy and methyl carbon atoms appear in the ranges of 56.10 – 61.61 and 19.24 – 20.81 ppm, respectively. The signals around 150 ppm are assigned to C8, C9, C**'** and the carbon atoms attached to the methoxy group (for example C2' and C3'carbon atoms in **1**).

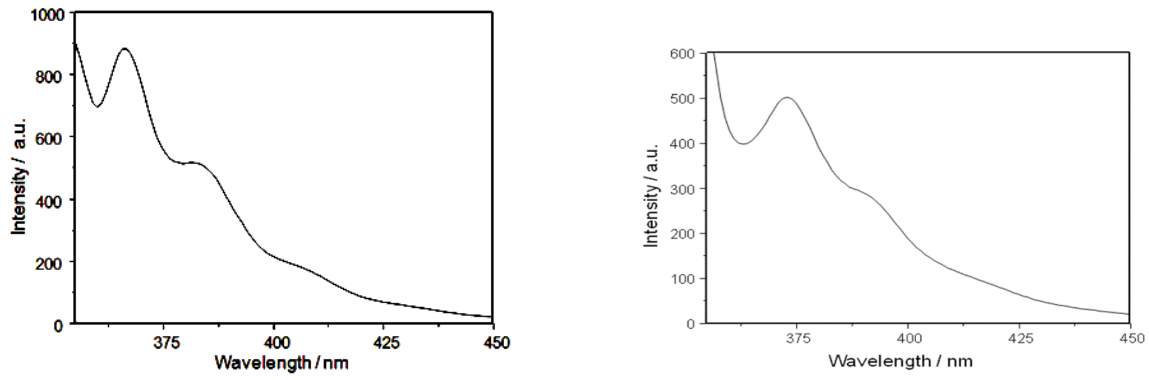
ESI-MS spectra

The ESI-MS data of molecular ions of compounds with the relative abundance and the calculated isotopic patterns [32] for **1** and **6** (one compound from both groups) are given in Experimental section.

Compound **1** {5,6-dichloro-2-(2′,3′-dimethoxyphenyl)-1*H*-benzimidazole, $C_{15}H_{12}Cl_2N_2O_2$} has two chlorine atoms whereas compound **6** {2-(2′,3′-dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole, $C_{17}H_{18}N_2O_2$} has no chlorine. Five distinct isotopic patterns were observed in the ESI-MS spectra of **1** since chlorine has two isotopes: ^{35}Cl (75.8 %): ^{37}Cl (24.2 %) (3:1). Three distinct isotopic patterns appeared in the ESI-MS spectra of **6**. The experimental ESI-MS data of compounds are compatible with the calculated ones.

Fluorescence spectra

Excitation and emission spectra of compounds were obtained in ethanol at room temperature (excitation wavelength: 354 nm; concentration: ~10^{-4} M). The fluorescence spectra of **2** and **8** are shown in Figure 4.



Compound 2 **Compound 8**

Figure 4. Fluorescence spectra for compounds 2 and 8.

Compounds exhibit dual or triple fluorescence in ethanol. Most of compounds display dual fluorescence in ethanol with a medium band and a shoulder. Compounds **2**, **3** and **5** exhibit triple fluorescence emissions in ethanol. These bands probably result from: 1- the normal Stokes shift originating from a locally excited π^* electronic state; 2- intramolecular charge transfer and; 3-monocation protonated at the benzimidazole nitrogen atom N3 as a result of the interaction with the solvent (H-bonding). The fluorescence spectra of **1** and **6** are similar to each other. Compounds **2**–**5** are blue-shifted with respect to **1**. Compound **7** is blue-shifted in comparison to **6** whereas the fluorescence spectra of the other methyl derivatives are similar to that of **6**.

Theoretical aspects: geometry optimization

The calculated HOMO (highest occupied molecular orbital), LUMO (lowest unoccupied molecular orbital) levels, band gap, energy (based on DFT and ZPE methods), dipole moment, electronic spatial extend (ESE) and dihedral angle values for compounds are given in Table 1. The geometry optimization studies of the compounds reveal that all molecules belong to C_1 symmetry point group. The optimized structures of compounds are shown in Figure 5. According to the optimized structures, **1**, **2**, **3**, **6**, **7** and **8** (2,3-, 2,4- and 2,5-dimethoxy derivatives) have torsion angles (dihedral angle; *i.e.* N1-C2-C1'-C6') between the benzimidazole and benzene rings in the 41.9 – 47.8° range; while compounds **4**, **5**, **9** and **10** (3,4- and 3,5-dimethoxy derivatives) are less twisted (torsion angles in the range of 9.7 – 16.7°). Another major dihedral angles involving N3-C2-C1'-C6' (134.3 – 138.3° for **1**, **2**, **3**, **6**, **7** and 163.3 – 170.3° for **4**, **5**, **9** and **10**) and N1-C2-C1'-C2' (135.6 – 140.9° for **1**, **2**, **3**, **6**,**7** and 163.3 – 170.2° for **4**, **5**, **9** and **10**) support this conclusion.

Some considerable bond lengths are the following: N3–C2: 1.315 – 1.319 Å; NH1–C2: 1.387 – 1.390 Å; C2–C1': 1.468 – 1.474 Å; Cl–C: around 1.750 Å; $H_3C–C_{arom}$: around 1.510 Å. It is significant that the NH1–C2 bond length is longer than N3–C2 as expected. Some important bond angles values are as follows (as ranges): N3-C2-NH: 112.07 – 112.34°; N3-C2-C1': 124.95 – 127.69° (this angle is lower in 3,4- and 3,5-dimethoxy derivatives and higher in the other derivatives); NH-C2-C1': 120.23 – 122.97° (higher in 3,4- and 3,5-dimethoxy derivatives, lower in the others); C2-C1'-C2': 118.45 – 122.45° (lower in 3,4- and 3,5-dimethoxy derivatives, higher in the others); C2-C1'-C6': 118.92 – 122.65° (higher in 3,4- and 3,5-dimethoxy derivatives, lower in the others); C8-N3-C2: around 105.40° and C9-NH-C2: around 107.25°. From this, it can be concluded that the positions of the methoxy groups affect the N3-C2-C1', NH-C2-C1', C2-C1'-C2' and C2-C1'-C6' bond angles in considerable values.

The calculated band-gaps of the compounds are in the range of 4.304 – 4.698 eV (Table 1). The band gap of the 2,4-, 2,5- and 3,4-dimethoxy derivatives involving the chloro groups (**2**–**4**) are slightly lower than those of the corresponding dimethyl derivatives (**7**–**9**).

Table 1

Some theoretical values for compounds 1–10.

Compound	*LUMO (eV)*	*HOMO (eV)*	*Band gap (eV)*	*Dipole moment (D)*	*ESE[a] (a.u.)*	*Dihedral angle (°)*	*Energy (Hartrees)*	
							TE[b]	*ZPE[c]*
1	-1.564	-6.262	4.698	6.92	10581.9	46.0	-1759.20	153.12
2	-1.389	-5.881	4.492	7.55	11285.7	41.9	-1759.20	153.30
3	-1.573	-5.900	4.327	7.68	10820.1	43.6	-1759.21	153.23
4	-1.681	-5.985	4.304	7.89	12285.2	10.7	-1759.20	153.08
5	-1.735	-6.153	4.418	8.24	12019.0	9.7	-1759.21	153.16
6	-1.080	-5.759	4.679	3.04	8582.7	46.0	-918.66	199.85
7	-0.909	-5.487	4.578	3.85	9215.6	44.5	-918.61	199.78
8	-1.119	-5.521	4.402	2.78	8456.7	47.8	-918.66	199.84
9	-1.195	-5.531	4.336	4.79	10023.8	10.6	-918.66	199.79
10	-1.284	-5.681	4.397	4.08	9498.7	16.7	-918.67	199.87

[a]*ESE- Electronic Spatial Extent;*

[b]*TE-Total energy from DFT calculations;*

[c]*ZPE- Zero point energy from DFT calculations.*

The electronic spatial extent (*ESE*) is defined as the area covering the volume around the molecule beyond and is a measure of the sensitivity of the molecule to the electric field [33]. The *ESE* values of the compounds increase in the following order: **8**<**6**<**7**<**10**<**9**<**3**<**1**<**2**<**5**<**4**. Since the studied molecules are clustered in two groups, it is seen that the rich in electrons dichloro derivatives have higher *ESE* values in comparison with dimethyl derivatives. Among all compounds, 5,6-dichloro-2-(3′,4′-dimethoxyphenyl)-1*H*-benzimidazole **4** has the highest *ESE* value and 2-(2′,5′-dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole **8** has the lowest value. The highest *ESE* value in the 5,6-dimethyl derivatives belongs to **9** (3′,4′-dimethoxy). It is observed that 3′,4′-dimethoxy derivatives (**4** and **9**) have highest molecular volume values at their groups.

Theoretical stability order of **1**–**10** was based on the zero point energies (*ZPE*). The geometry of each compound was optimized by *DFT* methods. The energies of the each optimized geometry are shown in Table 1. According to *ZPE*

calculations, the order of stability is **10**>**6**>**8**>**9**>**7**>**2**>**3**>**5**>**1**>**4**. The *ZPE* and *DFT* calculations show that the more stable forms exist within methyl species in vacuum.

As expected, the calculated dipole moment values of the dichloro derivatives (**1**–**5**) are higher than those of the dimethyl derivatives. The compound that has the highest dipole moment value is 5,6-dichloro-2-(3′,5′-dimethoxyphenyl)-1*H*-benzimidazole (**5**) with the value of 8.24 D. 2-(2′,5′-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (**8**) has the lowest dipole moment among the studied compounds (2.78 D).

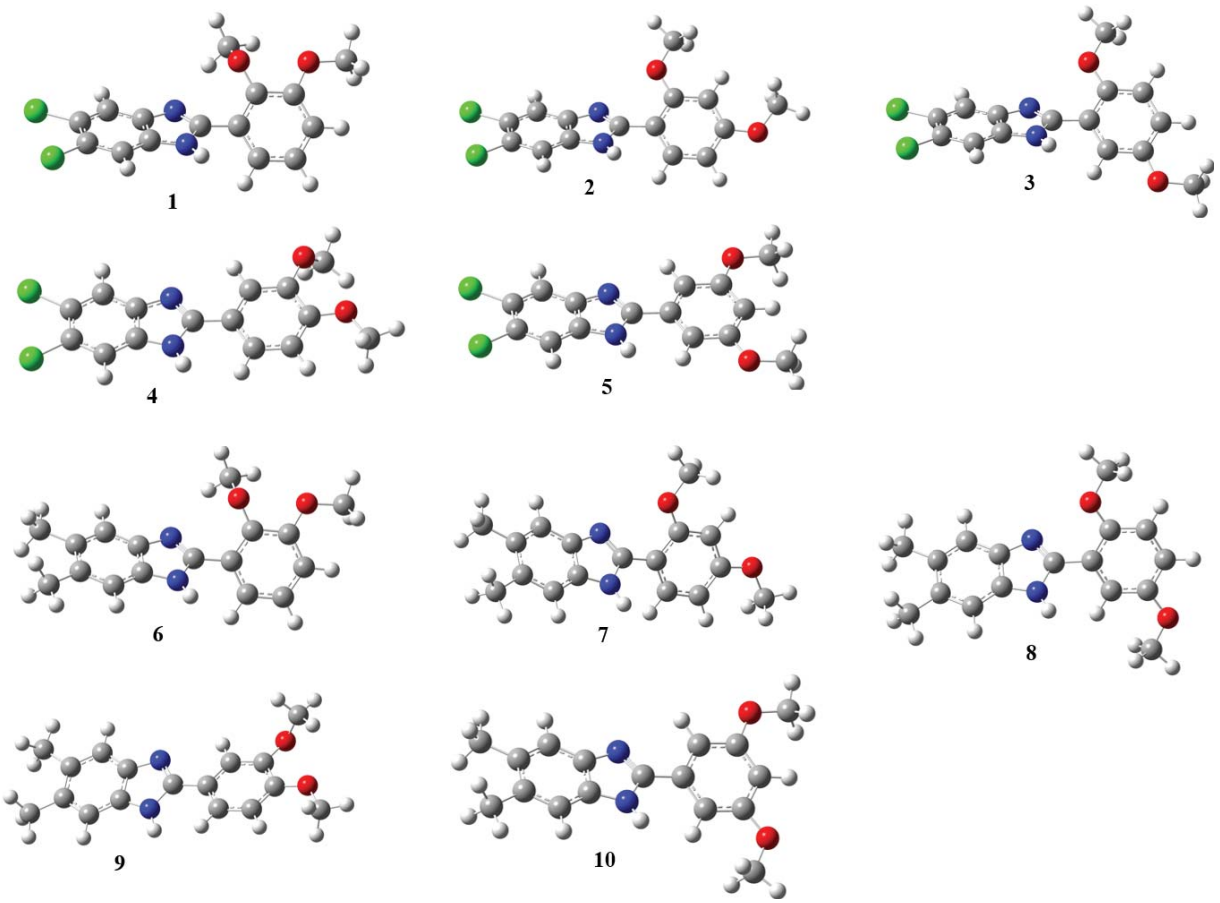


Figure 5. The optimized structures of compounds.

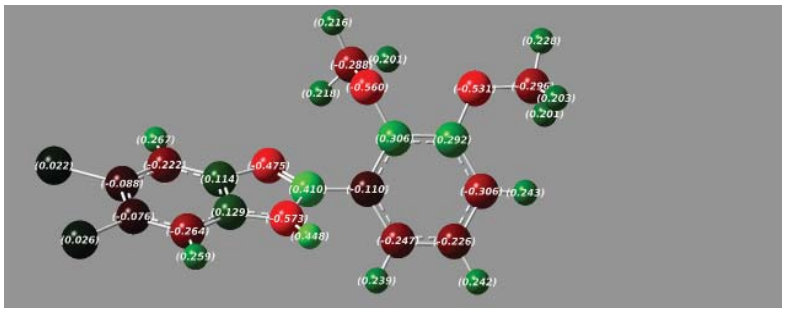
Atomic charges (charge distribution)

The charge distributions of compounds were calculated and are listed in Table 2. A full natural bond orbitals (NBO) analysis is obtained in Gaussian using the POP=NBO keyword. Natural Population Analysis (NPA) phase of NBO is used to show atomic partial charges which are obtained through summation over natural atomic orbitals (NAOs). The atomic charges calculated from NPAs are tabulated in Table 2. A distinguished feature of the results is that carbon atoms in methyl groups have partial negative charges. The exemplary charge distributions for **1** and **6** are depicted in Figure 6.

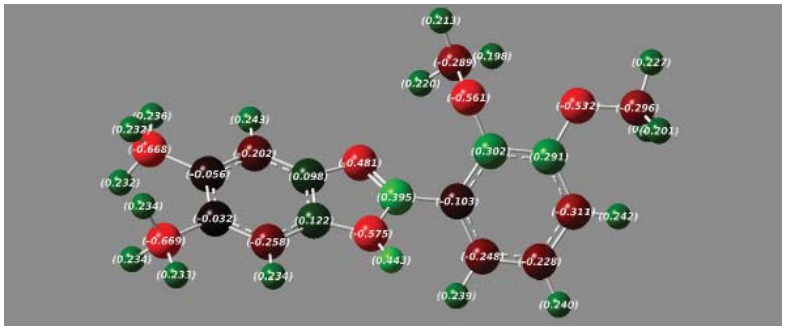
It is known that partial charges on atoms in a molecule arise from differences in electron affinity. Charge is transferred from one atom to the next through the covalent bond joining them. Groups of tightly bonded atoms are often electrically neutral with the partial charge on one atom balanced by the negative partial charge on the other atom [34]. Electronic charge density distribution in molecular systems has been described in terms of the topological properties [35].

It is very interesting that the chlorine atoms in compounds **1**–**5** are slightly positively charged, whereas C5 and C6 carbon atoms are negatively charged, due to the attached chlorine atoms. This unusual finding is interpreted in the light of the presence of the benzimidazole moiety. It has a conjugated system and two nitrogen atoms with high negative charges that withdraws electron from the chlorine atoms (Figure 6, Table 2).

The charge distribution shows that the more positive charge is concentrated on C2. In all compounds, C6' atom is negatively charged and the partial positive charge resides at C8 and C9. The carbon atoms bonded to the methoxy groups are positively charged, as expected. Atomic charge of the NH nitrogen (N1) is more negative than that of the C=N nitrogen atom (N3).



compound 1



compound 6

Figure 6. Atomic charges of compounds 1 and 6 with numerical values.

Table 2

Atomic charges values (e).

	Compounds									
Atoms	***1***	***2***	***3***	***4***	***5***	***6***	***7***[a]	***8***	***9***	***10***
N1[b]	-0.573	-0.576	-0.574	-0.572	-0.569	-0.575	-0.468	-0.579	-0.573	-0.574
C2	0.410	0.409	0.402	0.402	0.417	0.395	0.558	0.389	0.387	0.389
N2	-0.475	-0.464	-0.456	-0.482	-0.477	-0.481	-0.256	-0.461	-0.485	-0.478
C4	-0.222	-0.223	-0.221	-0.224	-0.208	-0.202	-0.559	-0.214	-0.203	-0.214
C5	-0.088	-0.089	-0.089	-0.088	-0.094	-0.056	0.786	-0.051	-0.056	-0.048
C6	-0.076	-0.078	-0.076	-0.083	-0.076	-0.032	0.471	-0.033	-0.039	-0.035
C7	-0.264	-0.266	-0.265	-0.252	-0.266	-0.258	-0.490	-0.260	-0.247	-0.260
C8	0.129	0.128	0.129	0.123	0.132	0.122	0.309	0.121	0.117	0.124
C9	0.114	0.112	0.111	0.116	0.107	0.098	-0.368	0.102	0.100	0.105
C1’	-0.110	-0.179	-0.105	-0.106	-0.082	-0.103	0.365	-0.101	-0.098	-0.066
C2’	0.306	0.392	0.328	-0.214	-0.261	0.302	0.574	0.326	-0.217	-0.235
C3’	0.292	-0.408	-0.298	0.273	0.351	0.291	-0.563	-0.297	0.271	0.334
C4’	-0.306	0.357	-0.291	0.295	-0.396	-0.311	-0.222	-0.246	0.289	-0.364
C5’	-0.226	-0.314	0.292	0.311	0.338	-0.228	0.785	0.291	-0.311	0.348
C6’	-0.247	-0.168	-0.244	-0.216	-0.287	-0.248	-1.475	-0.294	-0.220	-0.349
$Cl(CH_3)_{(5)}$[c]	0.022	0.019	0.021	0.023	0.023	-0.668	-0.642	-0.668	-0.668	-0.668
$Cl(CH_3)_{(6)}$[d]	0.026	0.022	0.024	0.025	0.026	-0.669	-0.636	-0.669	-0.669	-0.669
$\underline{O}CH_3$[e]	-0.560	-0.516	-0.521	-0.563	-0.531	-0.561	-0.285	-0.522	-0.565	-0.533
$\underline{O}CH_3$[e]	-0.531	-0.531	-0.540	-0.532	-0.537	-0.532	-0.334	-0.540	-0.535	-0.539
$O\underline{C}H_3$	-0.288	-0.298	-0.296	-0.289	-0.298	-0.289	-0.146	-0.296	-0.288	-0.288
$O\underline{C}H_3$	-0.296	-0.298	-0.296	-0.297	-0.297	-0.296	-0.174	-0.296	-0.296	-0.296

[a]*Mulliken charges- Atomic charges of **7** could not be obtained by NBO method;*

[b]*NH;*

[c,d]*-CH_3 for **6**–**10**;*

[e]*-OCH_3 groups were given as order 2,3; 2,4; 2,5; 3,4 and 3,5-positions.*

The dimethoxy carbon atoms are partially negatively charged and the methoxy oxygen atom is negatively charged in all of compounds, as shown in the charge distribution figures of **1** and **6** (Figure 6). Unexpectedly, in dimethyl derivatives (**6**–**10**) the methyl carbon atoms also have considerable negative charge (around -0.67 *e*).

Conclusions

It is known that various benzimidazole derivatives are an important class of compounds due to the demonstrated biological activity. In this study, ten benzimidazole derivatives including dimethoxy or dimethyl groups, 5,6-dichloro/dimethyl-2-(2′,3′/2′,4′/2′,5′/3′,4′/3′,5′-dimethoxyphenyl)-1*H*-benzimidazoles (**1**–**10**) were synthesized in high yields. They were characterized using FT-IR, FT-Raman, NMR, ESI-MS, and fluorescence spectroscopy. It was found that compounds **2**, **3** and **5** show triple fluorescence whereas the other compounds present dual fluorescence. In addition, the optimized molecular geometry, bond lengths, bond angles, energy, dipole moment, ESE, band gap and charge distributions of compounds were calculated by using Gaussian 09 using DFT method (RB3LYP) with 6-31++G(d,p) basis set. The dihedral angles between the benzimidazole and benzene rings vary from 9.7º to 47.8º. The calculated energy values based on ZPE and DFT show that the order of stability is **10**>**6**>**8**>**9**>**7**>**2**>**3**>**5**>**1**>**4**. According to this order the methyl derivatives (**6**–**10**) are more stable than the chloro forms. 3′,4′-Dimethoxy derivatives (**4** and **9**) have higher melting points in comparison with the other compounds in series. The chloro derivatives have higher dipole moment as compared to the methyl derivatives, due to the electronegativity of chlorine atoms. 5,6-Dichloro-2-(3′,5′-dimethoxyphenyl)-1*H*-benzimidazole (**5**) has the highest dipole moment value of 8.24 D and 2-(2′,5′-dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (**8**) has the lowest dipole moment (2.78 D). According to the calculated atomic charges, the chlorine atoms in the compounds **1**–**5** are positively charged whereas C5 and C6 carbon atoms are negatively charged, due to the attached chlorine atoms. This was explained by the presence of the benzimidazole moiety exerting the electron withdrawing effect.

Experimental

General experimental procedure

All chemicals and solvents were of reagent grade and were used without further purification. Elemental analysis (C, H, N) data were obtained with a ThermoFinnigan Flash EA 1112 analyser. Decomposition points were determined using an Electro thermal melting-point apparatus. ^{1}H- and ^{13}C-NMR (APT) spectra were run on a Varian Unity Inova 500 NMR spectrometer. The residual DMSO-d_6 signal was also used as an internal reference. Fluorescence spectra were performed on a Shimadzu RF-5301 PC Spectrofluorophotometer. The Electron Spray Ionization-Mass Spectrometry (ESI-MS) analyses were carried out in positive ion modes using a ThermoFinnigan LCQ Advantage MAX LC/MS/MS. FT-IR spectra were recorded on a Bruker Optics Vertex 70 spectrometer using Attenuated Total Reflection (ATR) techniques between 400 and 4000 cm^{-1}. The FT-Raman spectra were also recorded on the same instrument with a R100/R RAMII Raman module equipped with Nd:YAG laser source operating at 1064 nm line with 200 mW power and a spectral resolution of ±2 cm^{-1}.

Synthesis of compounds

Compounds **1–10** were prepared according to the procedures found in the literature [36,37].

5,6-Dichloro-2-(2′,3′-dimethoxyphenyl)-1*H*-benzimidazole (1). For synthesis of **1**, 2,3-dimethoxybenzaldehyde (332 mg, 2 mmol) reacted with an equivalent amount of $NaHSO_3$ (208 mg, 2 mmol) at room temperature in ethanol (10 mL) for 4–5 hours. The resultant mixture was treated with 4,5-dichlorobenzene-1,2-diamine (354 mg, 2 mmol) in dimethylformamide (5 mL) and gently refluxed for 2-3 hours. The reaction mixture was then poured into iced water (100 mL). A precipitate of compound (**1**) was formed; it was filtered and crystallized from ethanol (600 mg, 93%). Brown solid. m.p.: 195 °C (decomp.). Anal. calcd. for $C_{15}H_{12}Cl_2N_2O_2$ (M_r=323.17), *w*/%, are: C, 55.75; H, 3.74; N, 8.67. Found: C, 53.50; H, 4.64; N, 8.86. ^{1}H NMR (DMSO-d_6) δ/ppm: 12.59 (br s, 1H, NH), 7.85 (s, 2H, H4+H7), 7.82 (dd, J = 9.3, 8.3 Hz, 1H, H5'), 7.22 (m, 2H, H4'+H6'), 3.89 (s, 3H, $OCH_{3(2')}$), 3.86 (s, 3H, $OCH_{3(3')}$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 153.54, 151.84, 147.75, 125.06, 123.12 (quaternary carbons), 125.24, 121.89, 121.86, 115.71, 61.61, 56.77 (H-bonded carbons). IR (ATR, $\bar{\nu}$/cm^{-1}): 3178 m,br, 2938 m, 2835 m, 1581 m, 1525 m, 1481 s, 1436 m, 1264 s, 1231 s, 1059 m, 966 s, 871 m, 742 s, 663 m, 531 m, 436 m. Raman ($\bar{\nu}$/cm^{-1}): 3071 w, 2935 w, 2836 w, 1600 s, 1521 s, 1442 m, 1411 m, 1322 w, 1284 w, 1228 m, 1118 w, 972 w, 875 w, 781 w, 733 w, 664 w. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 373 m,br, 392 sh. MS *m*/*z*: 323.4 (100%, $[M]^+$), 325.4 (66.9%, $[M+2]^+$), 324.4 (15.4%, $[M+1]^+$), 326.4 (10.6%, $[M+3]^+$), 327.3 (10.3%, $[M+4]^+$); Calculated [32]: 322.03 (100%), 323.03 (16.2%), 324.02 (63.9%), 325.03 (10.4%), 326.02 (10.2%), 327.02 (1.7%).

Compounds **2**–**5** were synthesized in a similar manner to the synthesis of **1**.

5,6-Dichloro-2-(2′,4′-dimethoxyphenyl)-1*H*-benzimidazole (2). 2,4-Dimethoxybenzaldehyde (517 mg, 2 mmol) was employed for synthesizing compound **2.** Yield: 258 mg, 80%. Reddish brown solid. m.p.: 222 °C (decomp.). Anal. calcd. for $C_{15}H_{12}Cl_2N_2O_2$ (M_r=323.17), *w*/%, are: C, 55.75; H, 3.74; N, 8.67. Found: C, 55.56; H, 4.01; N, 8.76. ^{1}H NMR (DMSO-d_6) δ/ppm: 12.11 (s, br, 1H, NH), 8.23 (d, J = 8.8 Hz, 1H, H6'), 7.78 (s, br, 2H, H4+H7), 6.77 (d, J = 2.4 Hz, 1H, H3'), 6.72 (dd, J = 8.8, 2.4 Hz, 1H, H5'), 4.02 (s, 3H, $OCH_{3(2')}$), 3.86 (s, 3H, $OCH_{3(4')}$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 163.31, 159.09, 152.49, 124.43, 110.71, 99.30 (quaternary carbons), 131.82, 107.25, 107.22, 99.35, 99.33, 56.72, 56.23 (H-bonded carbons). IR (ATR, $\bar{\nu}$/cm^{-1}): 3386 m, 3305 m, 3099 w, 2938 w, 2834 w, 1612 s, 1582 m, 1470 m, 1418 m, 1285 s, 1257 s, 1215 s, 1178 m, 1093 m, 1033 s, 937 w, 863 m,

820 s, 726 m, 669 m, 522 m, 486 m, 424 m. Raman ($\overline{\nu}$/cm^{-1}): 3078 w, 2936 w, 2831 w, 1609 s, 1573 m, 1530 s, 1445 m, 1413 m, 1287 w, 1249 m, 1224 w, 1133 w, 1092 w, 966 w, 726 w, 664w, 619 w. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 365 m, 382 sh, 408 sh.

5,6-Dichloro-2-(2´,5´-dimethoxyphenyl)-1*H*-benzimidazole (3). Raman ($\overline{\nu}$/cm^{-1}): 3080 w, 2936 w, 2831 w, 1590 m, 1520 s, 1479 m, 1442 m, 1413 m, 1359 w, 1262 m, 1218 m, 1174 w, 1083 w, 973 w, 887 m, 819 w, 737 w, 674 w, 620 w (cm^{-1}). Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 365 m, 381 m, 409 sh.

5,6-Dichloro-2-(3´,4´-dimethoxyphenyl)-1*H*-benzimidazole (4). Raman ($\overline{\nu}$/cm^{-1}): 3068 w, 3005 w, 2939 w, 2836 w, 1603 s, 1544 m, 1496 m, 1439 m, 1417 sh, 1269 m, 1228 w, 1095 w, 975 w, 888 w, 765 w, 664 w. Fluorescence (ethanol, c = 1·10^{-4} mol/L): (λ_{max}/nm): 365 m,br, 382 sh.

5,6-Dichloro-2-(3´,5´-dimethoxyphenyl)-1*H*-benzimidazole (5). 3,5-Dimethoxybenzaldehyde (332 mg, 2 mmol) was employed for synthesizing compound **5.** Yield: 485 mg, 75%. Light brown solid. m.p.: 126°C (decomp.); Anal. calcd. for $C_{15}H_{12}Cl_2N_2O_2$ (M_r=323.17), *w*/%, are: C, 55.75; H, 3.74; N, 8.67. Found: C, 55.58; H, 3.90; N, 8.75. ^{1}H NMR (DMSO-d_6) δ/ppm: 7.78 (s, 2H, H4+H7), 7.73 (d, J = 1.9 Hz, 1H, H6'), 7.72 (d, J = 1.9 Hz, 1H, H2'), 7.12 (s, 1H, H4'), 3.87 (s, 3H, $OCH_{3(5')}$), 3.83 (s, 3H, $OCH_{3(3')}$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 154.74, 151.59, 149.66, 124.87, 122.37 (quaternary carbons), 120.57, 120.53, 112.57, 110.67, 110.64, 56.37, 56.31 (H-bonded carbons). IR (ATR, $\overline{\nu}$/cm^{-1}): 3178 m,br, 3139 m,br, 2937 m, 2838 m, 1679 w, 1614 m, 1594 m, 1475 m, 1413 m, 1351 m, 1251 m, 1204 m, 1161 m, 1098 m, 1056 s, 963 m, 851 m, 723 m, 656 m, 501 m, 429 m. Raman ($\overline{\nu}$/cm^{-1}): 3068 w, 3017 w, 2936 w, 2839 w, 1606 s, 1534 s, 1442 m, 1414 m, 1281 m, 1250 m, 1095 w, 1052 w, 992 m, 885 w, 786 w, 658 w. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 365 m,br, 381 sh, 392 m,br.

2-(2´,3´-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (6). Compound **6** was synthesized in a similar manner to that described for synthesis of compound **1**. 4,5-Dimethylbenzene-1,2-diamine (272 mg, 2 mmol) was used for the synthesis of compounds **6**–**10** instead of 4,5-dichlorobenzene-1,2-diamine. Yield: 503 mg, 89%. Light yellow solid. m.p.: 149°C (decomp.); Anal. calcd. for $C_{17}H_{18}N_2O_2$ (M_r=282.34), *w*/%, are: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.48; H, 6.61; N, 10.14. ^{1}H NMR (DMSO-d_6) δ/ppm: 11.97 (s, 1H, NH), 7.85 (dd, J = 6.8, 1.9 Hz, H6'), 7.47 (s, 1H, H4), 7.44 (s, 1H, H7), 7.26 (dd, J = 7.8, 1.9 Hz, H4'), 7.21 (dd, J = 7.8, 6.8 Hz, H5'), 3.95 (s, 3H, $OCH_{3(2')}$), 3.90 (s, 3H, $OCH_{3(3')}$), 2.39 (s, 3H, $CH_{3(5)}$), 2.38 (s, 3H, $CH_{3(6)}$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 153.55, 152.85, 148.38, 147.33, 134.43, 130.80, 124.42 (quaternary carbons), 124.99, 124.55, 123.66, 121.78, 114.62, 112.84, 61.40, 56.70, 20.77 (H-bonded carbons). IR (ATR, $\overline{\nu}$/cm^{-1}): 3594 m, 3157 m,br, 2937 m, 2837 w, 1659 m, 1583 m, 1525 m, 1482 m, 1438 m, 1264 s, 1227 m, 1136 m, 1061 m, 1002 s, 855 m, 797 m, 744 m, 711 m, 499 m, 440 m. Raman ($\overline{\nu}$/cm^{-1}): 3083 w, 3042 w, 2935 w, 2839 w, 1603 s, 1521 s, 1465 m, 1442 m, 1417 m, 1386 w, 1307 m, 1256 m, 1238 m, 1159 w, 1130 w, 982 w, 885 w, 784 w, 730 m. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 372 m,br, 392 sh. MS *m*/*z*: 283.2 (100%, [M+1]$^+$), 284.2 (12.7%, [M+2]$^+$), 285.3 (1.7%, [M+2]$^+$); Calculated [32]: 282.14 (100%), 283.14 (18.4%), 284.14 (1.6%).

2-(2´,4´-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (7). Compound **7** was synthesized in a similar manner to **2**. 4,5-Dimethylbenzene-1,2-diamine (272 mg, 2 mmol) was used instead of 4,5-dichlorobenzene-1,2-diamine. Yield: 520 mg, 92%. Beige solid. m.p.: 207 °C (decomp.); Anal. calcd. for $C_{17}H_{18}N_2O_2$ (M_r=282.34), *w*/%, are: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.10; H, 6.52; N, 10.19. ^{1}H NMR (DMSO-d_6) δ/ppm: 11.66 (br s, 1H, NH), 8.20 (d, J = 8.3 Hz, 1H, H6'), 7.33 (s, 2H, H4+H7), 6.72 (d, J = 2.4 Hz, 1H, H3'), 6.68 (dd, J = 8.8, 2.4 Hz, 1H, H5'), 3.99 (s, 3H, $OCH_{3(4')}$), 3.84 (s, 3H, $OCH_{3(2')}$), 2.30 (s, 6H, $2CH_3$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 162.38, 158.56, 149.02, 130.35, 112.07 (quaternary carbons), 131.33, 106.87, 106.85, 99.26, 99.24, 56.47, 56.13, 20.79, 20.76 (H-bonded carbons). IR (ATR, $\overline{\nu}$/cm^{-1}): 3224 m,br, 2963 m, 2937 m, 2833 m, 1611 m, 1581 m, 1447 m, 1423 s, 1279 s, 1208 s, 1170 m, 1078 m, 1040 m, 834 m, 686 m, 509 m, 463 m, 404 m. Raman ($\overline{\nu}$/cm^{-1}): 3093 w, 3043 w, 2939 w, 2831 w, 1609 s, 1577 w, 1534 s, 1448 m, 1427 m, 1383 w, 1335 w, 1307 m, 1259 m, 1159 w, 1121 w, 960 m, 730 m, 554 w. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 364 m,br, 380 m,br.

2-(2´,5´-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (8). Raman ($\overline{\nu}$/cm^{-1}):3088 w, 3040 w, 2927 w, 2836 w, 1610 sh, 1595 s, 1525 s, 1487 w, 1449 m, 1427 m, 1385 w, 1307 m, 1273 m, 1207 w, 1159 w, 1027 w, 977 w, 895 w, 837 w, 730 m. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 374 m,br, 392 sh.

2-(3´,4´-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (9). Raman ($\overline{\nu}$/cm^{-1}): 3078 w, 3047 w, 2920 m, 2836 w, 1631 w, 1606 s, 1549 m, 1499 m, 1461 m, 1417 m, 1363 w, 1317 m, 1291 m, 1235 w, 1164 w, 1133 w, 992 w, 768 w, 730 w. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 375 m,br, 392 m,br.

2-(3´,5´-Dimethoxyphenyl)-5,6-dimethyl-1*H*-benzimidazole (10). Compound **10** was synthesized in a similar manner to **5**. 4,5-Dimethylbenzene-1,2-diamine (272 mg, 2 mmol) was used instead of 4,5-dichlorobenzene-1,2-diamine. Yield: 440 mg, 78%. Dirty white solid. m.p.: 251 °C (decomp.); Anal. calcd. for $C_{17}H_{18}N_2O_2$ (M_r=282.34), *w*/%, are: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.25; H, 6.59; N, 10.06. ^{1}H NMR (DMSO-d_6) δ/ppm: 12.86 (br s, 1H, NH), 7.37 (s, 2H, H2'+H6'), 7.33 (s, 1H, H4), 7.32 (s, 1H, H7), 6.61 (s, 1H, H6'), 3.84 (s, 6H, $2OCH_3$), 2.33 (s, 6H, $2CH_3$); ^{13}C NMR (APT, 125 MHz, DMSO-d_6) δ/ppm: 161.48, 150.83, 143.05, 134.12, 132.96, 132.00, 130.66 (quaternary carbons), 161.47, 119.61, 111.97, 104.77, 102.40, 56.14, 56.10, 20.73, 19.24 (H-bonded carbons). IR (ATR, $\overline{\nu}$/cm^{-1}): 3018 w, 2966 w, 2832 w, 1607 m, 1593 s, 1464 m, 1417 m, 1304 m, 1253 m, 1202 m, 1159 s, 1049 s, 844 m, 854 m, 721 m, 677 m, 572 m, 436 m. Raman ($\overline{\nu}$/cm^{-1}): 3038 w, 2920 m, 2834 w, 1603 s, 1562 w, 1537 m, 1455 m, 1420 m, 1379 w, 1307 s, 1259 m, 1164 w, 1047 w, 991 m, 802 w, 730 m. Fluorescence spectra (EtOH, c = 1·10^{-4} mol/L) λ_{max}/nm: 375 m,br, 392 m,br.

Computational method

GAUSSIAN 09 software package was used for theoretical calculations [38]. The quantum chemical calculations were performed by applying DFT (RB3LYP) method with the standard 6-31++G(d,p) basis set. The default options for the self-consistent field convergence and threshold limits in the optimization were used.

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