Recognition of transition metals by benzimidazoles with an optical response

Cátia I. C. Esteves, M. Manuela M. Raposo and Susana P. G. Costa*

Centro de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal

spc@quimica.uminho.pt

Abstract:

The photophysical properties of a set of benzimidazoles bearing thiophene, pyrrole and furan at position 2 were evaluated by UV-vis absorption and fluorescence spectroscopy in acetonitrile. Interaction studies with biologically and analytically important transition metal cations, such as Cd^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+} and Pb^{2+}, were carried out through spectrophotometric and spectrofluorimetric titrations. It was found that benzomidazoles **1a-c** show higher sensitivity and ability to interact with Fe^{3+} and Hg^{2+} in acetonitrile, and could be considered as potential fluorimetric chemosensors for these cations.

Keywords*:* Benzimidazole; Chemosensors; UV-vis; Fluorescence.

1. Introduction

Heterocyclic systems containing in its structure potential chelating atoms and groups have the ability to act both in the recognition of ions and in the signalling of the recognition event because, variation of their absorption/fluorescence properties may occur upon complexation. Benzimidazole and its derivatives have been studied in ion recognition systems that display colour changes or fluorescence quenching or enhancement upon binding.[1] Acidity of the NH can be modulated by the presence of heterocycles, such as thiophene, pyrrole and furan, electronically connected to the imidazole group, as a way to enhance intramolecular electronic delocalization. Thiophene, pyrrole and furan are also known for their interesting photophysical properties, which enable their use as fluorescent sensors and markers, among other application.[2] Fluorescent sensors are preferred because they can be used as *in vivo* probes, mapping the spatial and temporal distribution of the biological analytes, and have other advantages including multiple modes of detection (such as fluorescence quenching, enhancing, life time), extremely high sensitivity, relatively low cost and easy availability.[3]

Detecting metallic cations is of great interest as mercury, lead, and cadmium are some examples of metals that are toxic for living organisms, and easy detection in the environment is desirable. Hg^{2+} or its methylated derivative can be taken up in the food chain of aquatic organisms doing huge harm to humans and nature. Also, many metallic cations are involved in biochemical reactions and their correct balance within cells or living systems in mandatory for health. Iron is the most abundant transition metal in cellular systems, more specifically, Fe^{3+} is an essential element in the growth and development of living systems as well as in many biochemical processes at the cellular level.[4] Metallic cations can be complexed through N, O and S donor atoms in aromatic heterocycles.

Following our previous work on fluorimetric and colorimetric heterocyclic chemosensors,[1c,2,4] we now report the interaction studies of a set of benzimidazoles bearing at position 2 different five-membered heterocycles (thiophene, pyrrole and furan) with biologically important cations, through spectrophotometric and spectrofluorimetric titrations.

2. Experimental

2.1. Spectrophotometric and spectrofluorimetric titrations of benzimidazoles 1a-c

Solutions of benzimidazoles **1a**-**c** (ca. 1.0×10^{-5} to 1.0×10^{-6} M) and of the ions under study (ca. 1.0×10^{-1} to 1.0×10^{-3} M) were prepared in UV-grade acetonitrile (in the form of

hydrated perchlorate salt for Cu^{2+}, Fe^{3+}, Fe^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+}). Titration of the compounds with the several metal cations was performed by the sequential addition of equivalents of cation to the benzimidazole solution, in a 10 mm path length quartz cuvette. Absorption and emission spectra were acquired in a Shimadzu UV/2501PC spectrophotometer and a HORIBA Jobin Yvon FluoroMax-4 spectrofluorometer, respectively. Emission spectra were measured by excitation at the wavelength of maximum absorption for each compound.

3. Results and discussion

3.1. Photophysical study of benzimidazoles 1a-c

The structure of the studied benzimidazoles **1a**-**c** is shown in Figure 1.

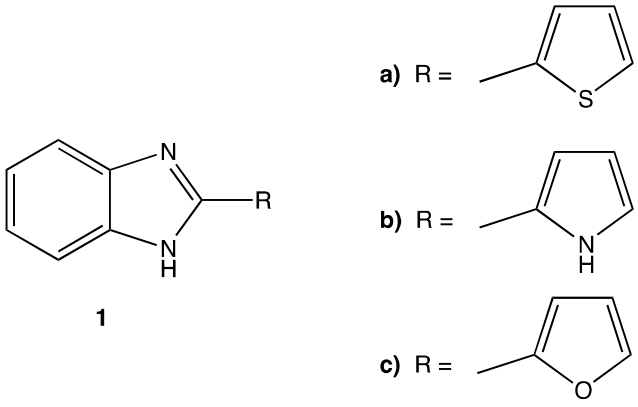

Figure 1. Structure of benzimidazoles **1a**-**c**.

The photophysical properties of benzimidazoles **1a**-**c** were evaluated by UV-vis absorption and fluorescence spectroscopy and spectra of degassed 10^{-6}-10^{-5} M solutions in acetonitrile were obtained. The UV-Vis absorption and fluorescence data for benzimidazoles **1a**-**c** (maximum absorption wavelengths, λ_{abs}; molar extinction coefficient, ε; maximum emission wavelength, λ_{em}; relative fluorescence quantum yield, Φ_F; Stokes' shift, $\Delta\lambda$) are presented in Table 1. Relative fluorescence quantum yields were calculated using 9,10-diphenylanthracene as fluorescence standard (Φ_F = 0.95 in ethanol).[5]

Table 1. UV-vis absorption and fluorescence data for benzimidazoles **1a-c** in acetonitrile.

Compound	UV/Vis		Fluorescence		
	λ_{abs} (nm)	log ε	λ_{em} (nm)	Stokes' shift (cm^{-1})	Φ_F
1a	317	4.16	382	5368	0.40
1b	307	4.42	344	3504	0.48
1c	304	4.02	340	3483	0.51

Benzimidazoles **1a-c** showed an intense lowest energy charge-transfer band in the range 304-317 nm and fluorescence maxima between 340-382 nm, corresponding to 36-65 nm Stokes' shift's. Furylbenzimidazole **1c** was the most fluorescent (Φ_F 0.51) whereas thienylbenzimidazole **1a** displayed the largest Stokes' shift (5368 cm^{-1}). In Figure 2 is shown the normalised absorption and fluorescence spectra of benzimidazoles **1a-c**.

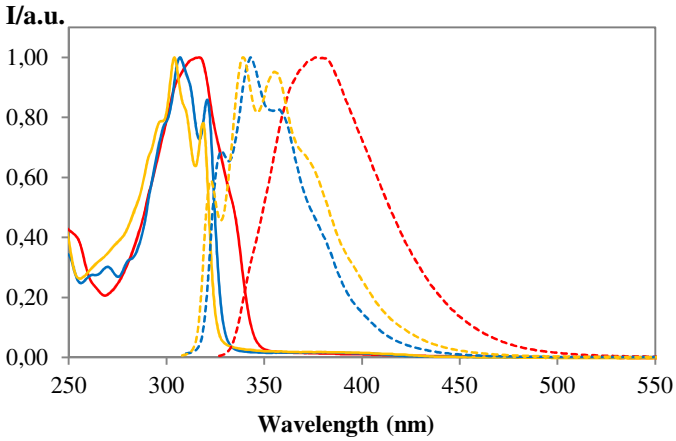

Figure 2. Normalised UV-visible absorption and emission spectra of benzimidazole derivatives **1a** (thiophene), **1b** (pyrrole) and **1c** (furan) in 10^{-5} M solutions in acetonitrile (absorption, full line; emission, dotted line).

3.2. Spectrophotometric and spectrofluorimetric titrations of 1a-c with metal cations

The modification of benzimidazole through the introduction of different heterocycles at its position 2 was expected to provide additional binding sites for a variety of metal cations

through the heterocycle N, O and S donor atoms, as well as improved photophysical properties for the chemosensing studies. Considering the biological, environmental and analytical relevance of selected metal cations such as Cd^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Hg^{2+} and Pb^{2+}, the interaction of benzimidazoles **1a-c** with these cations was evaluated through UV-vis and fluorescence spectroscopies in spectrophotometric and spectrofluorimetric titrations in acetonitrile.

Spectrophotometric titrations revealed that no changes were seen in the absorption spectra of benzimidazoles **1a-c** after addition of up to 200 equiv of the different cations, but significant changes occurred to the fluorescence spectra.

For benzimidazole **1a** in the spectrofluorimetric titrations with Fe^{3+} and Hg^{2+} there was a slight increase of the fluorescence intensity with a few equiv of these cations (a chelation enhancement of fluorescence, CHEF effect), which was followed by a decrease of the fluorescence intensity (a chelation enhancement of quenching, CHEQ effect). In Figure 3 it can be seen that benzimidazole **1a** was more sensitive to Fe^{3+} when compared to Hg^{2+}: a total fluorescence quenching occurred after addition of 250 equivalents of Fe^{3+}, whereas 280 equiv of Hg^{2+} were necessary for a 70% of quenching.

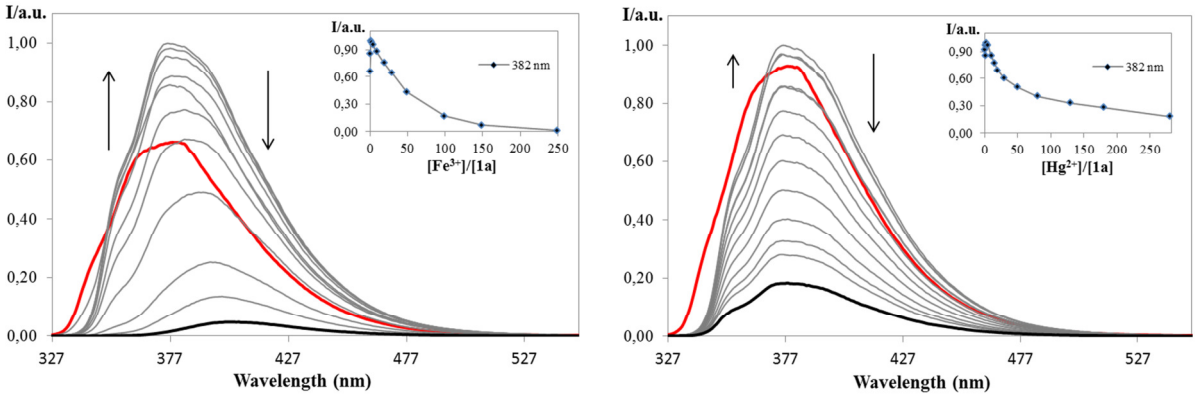

Figure 3. Fluorimetric titrations of 2-(thiophen-2-yl)-1*H*-benzimidazole **1a** with Fe^{3+} and Hg^{2+} in acetonitrile [λ_{exc} **1a** = 317 nm]. Inset: normalised emission at 382 nm as a function of added cation equivalents.

Higher sensitivity towards Fe^{3+} was also seen for benzimidazole **1b** with only 1 equiv of cation causing a total quenching. As for the other cations, the fluorimetric titrations revealed

that addition of 70 equiv of Cd^{2+} caused an 85% quenching of fluorescence, 0.8 equiv. of Cu^{2+} caused a 95% quenching, and with Fe^{2+}, Hg^{2+} and Pb^{2+} addition of 1 equiv caused a 90% quenching of fluorescence, respectively (Figure 4).

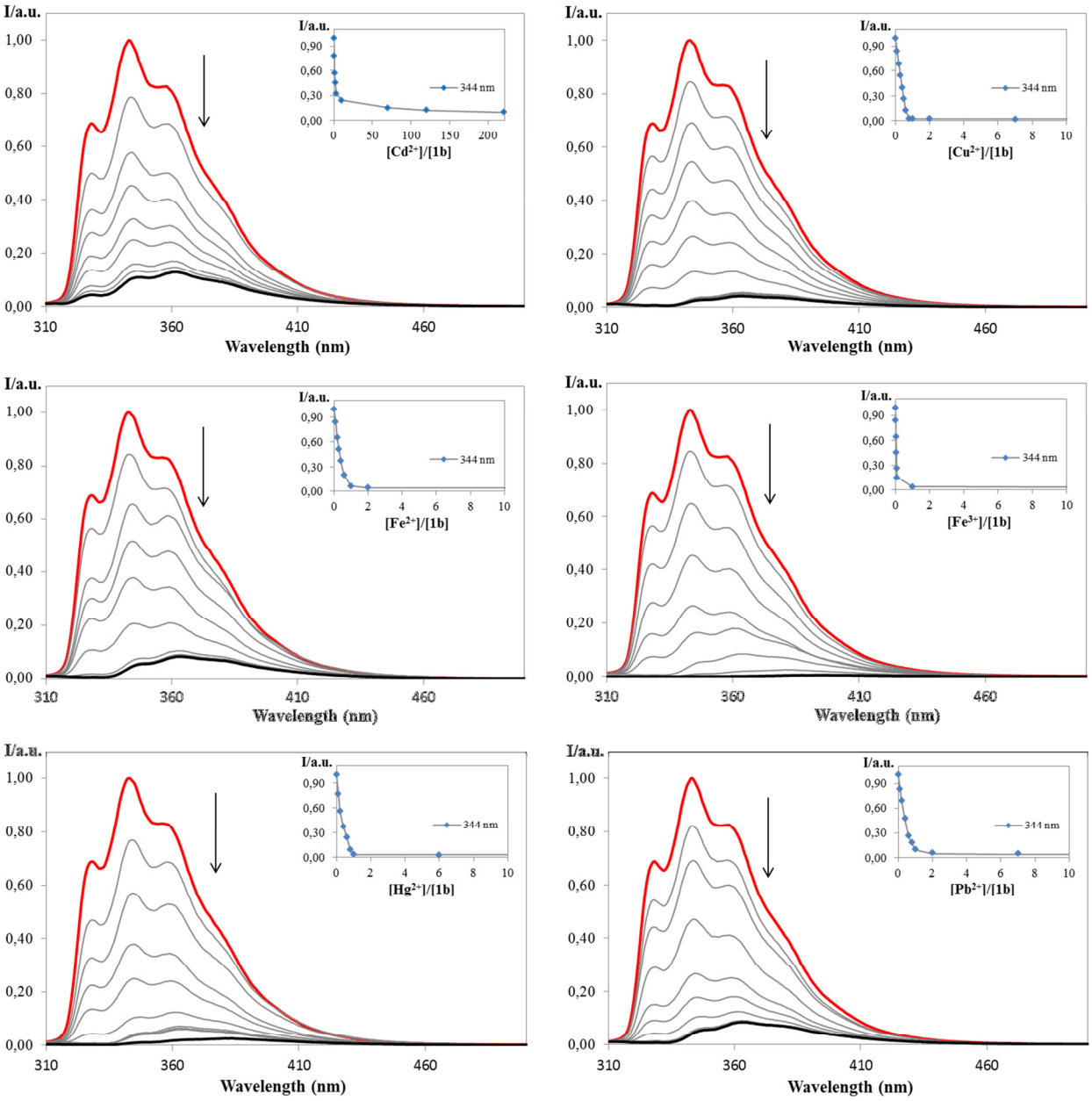

Figure 4. Fluorimetric titrations of 2-(1*H*-pyrrol-2-yl)-1*H*-benzimidazole **1b** with Cd^{2+}, Cu^{2+}, Fe^{3+}, Fe^{3+}, Hg^{2+} and Pb^{2+} in acetonitrile [λ_{exc} **1b** = 307 nm]. Inset: normalised emission at 344 nm as a function of added cation equivalents.

The spectrofluorimetric titrations of benzimidazole **1c** with Fe^{3+} and Hg^{2+} showed a total fluorescence quenching with 200 equiv of Fe^{3+} and a 95% quenching with the addition of 76 equiv of Hg^{2+} , for the band at 355 nm (Figure 5). Upon addition of 5 equiv of Cu^{2+}, the band at 340 nm suffered a 50% fluorescence quenching, and a new band at 371 nm had a slight 35% increase in fluorescence, reaching a plateau (Figure 5).

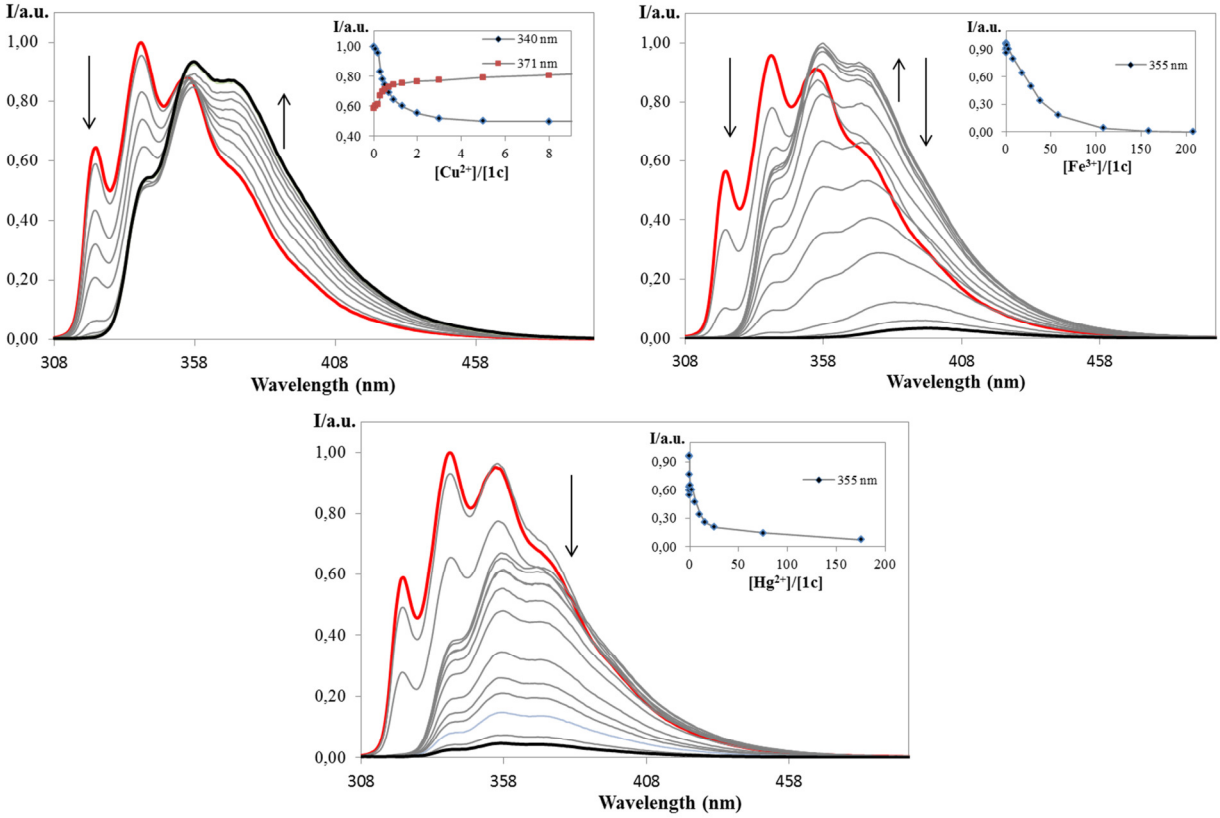

Figure 5. Fluorimetric titrations of 2-(furan-2-yl)-1*H*-benzimidazole **1c** with Cu^{2+}, Fe^{3+} and Hg^{2+} in acetonitrile [λ_{exc} **1c** = 304 nm]. Inset: normalised emission at the indicated wavelength as a function of added cation equivalents.

By comparison of the obtained spectrofluorimetric titration results for benzimidazoles **1a-c**, it can be concluded that pyrrolylbenzimidazole **1b** was the most sensitive to the presence of Cu^{2+}, Fe^{3+}, Fe^{3+}, Hg^{2+} and Pb^{2+} as it required the lower amount of the various cations (1-2 equiv) for a higher percentage of fluorescence quenching. Also, Cd^{2+} could only be detected by **1b** although it required a larger amount (70 equiv) for a 85% quenching.

Although benzimidazoles **1a-c** were not selective, in general they showed higher sensitivity for Fe^{3+} and Hg^{2+} and can be considered interesting candidates as fluorimetric chemosensors due to the high fluorescence quantum yield, which is important for maximization of response in the analysis of very dilute samples. As for Fe^{2+} and Fe^{3+}, benzimidazoles **1a** and **1c** were able to differentiate between the two forms since no quenching was seen with Fe^{2+} while interaction with Fe^{3+} resulted in a total quenching of fluorescence for **1a** and a partial quenching for **1c**.

The sensitivity of benzimidazoles **1a-c** can be compared qualitatively using as criteria for sensitivity the number of cation equivalents necessary to achieve the highest fluorescence quenching, until reaching a plateau (Table 2).

Table 2. Comparison of the number of equivalents necessary to increase (CHEF) or decrease (CHEQ) the fluorescence intensity in spectrofluorimetric titrations of benzimidazoles **1a-c** with different metallic cations.

	1a		**1b**		**1c**	
Cation	N. equiv	% CHEF/CHEQ (382 nm)	N. equiv	% CHEF/CHEQ (344 nm)	N. equiv	% CHEF/CHEQ (371/340 nm)
Cd^{2+}	70/200	10/0	200/70	0/85	200/200	0/30
Cu^{2+}	19/200	40/0	200/0.8	0/95	5/5	35/50
Fe^{2+}	19/200	30/0	200/1	0/90	200/200	0/40
Fe^{3+}	1/250	35/95	200/1	0/100	0.5/200	30/100
Hg^{2+}	3/280	10/70	200/6	0/90	200/76	0/95
Pb^{2+}	7/200	35/0	200/2	0/90	200/200	0/40

4. Conclusions

The set of benzimidazoles bearing thiophene, pyrrole and furan **1a-c** are highly emissive, with good fluorescence quantum yields (Φ_F = 0.40 for **1a**; Φ_F = 0.48 for **1b** and Φ_F = 0.51 for **1b**) in acetonitrile. Through spectrophotometric and spectrofluorimetric titration with several metal cations it was concluded that benzimidazoles **1** show higher sensitivity and ability to

interact with Fe^{3+} and Hg^{2+} in acetonitrile, and could be considered as potential fluorimetric chemosensors for these cations.

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