

# Phenanthroimidazole derivatives as fluorimetric chemosensors in aqueous medium

R. Cristina M. Ferreira, Susana P. G. Costa and M. Manuela M. Raposo\*

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

*mfox@quimica.uminho.pt*

**Abstract:** The new 2,4,5-tri-substituted imidazole derivatives **2a-c** were obtained in good yields through a Radziszewski reaction. The new compounds were characterized by the usual spectroscopic techniques and a detailed photophysical study was undertaken. The evaluation of the compounds as fluorimetric chemosensors was carried out by performing spectrofluorimetric titrations in acetonitrile and acetonitrile/water in the presence of relevant organic and inorganic anions, and of alkaline, alkaline-earth and transition metal cations.

**Keywords:** Chemosensors; Fluorimetric sensors; Radziszewski reaction; Fluorescence; Phenanthroimidazole.

## 1. Introduction

In recent years the research on sensors with good sensitivity and selectivity in aqueous medium has been of great interest.<sup>1</sup> Chemosensors soluble in aqueous media are very interesting, because of their prospective application in biomedical and environmental pollution tests.<sup>2</sup>

Fluorescent sensor molecules for the detection of metal ions have attracted considerable interest which has led to the development of highly specific probes with a broad range of applications in environmental chemistry, biochemistry, and cell biology.<sup>3</sup> The analyses based on fluorescence sensors are easy to handle and less expensive. For many fluorescent chemosensors the change in emission intensity by interaction with the analyte is measured, but a shift of the emission wavelength is also a convenient means to monitor the sensing process.<sup>4</sup>

2,4,5-Triaryl-imidazoles are versatile compounds with application in medicine, due to their biological activity, and materials sciences, for their interesting optical properties. These properties can be tuned by careful selection of substituents at positions 2, 4 and 5: replacement of the aryl group by an heterocyclic group results in larger  $\pi$ -conjugated systems with improved optical properties for application in nonlinear optics, OLEDs, DNA intercalators, and chemosensors.<sup>5</sup>

Considering our current research interests in this theme,<sup>4,5</sup> we now report the synthesis of new phenanthroimidazoles, substituted at position 2 with (hetero)aryl groups of different electronic character, in order to evaluate their photophysical properties and chemosensory ability. The new derivatives were characterized by the usual techniques and a detailed photophysical study was undertaken. The evaluation of the compounds as fluorimetric chemosensors was carried out by performing titrations in acetonitrile and acetonitrile/water in the presence of relevant organic and inorganic anions, and of alkaline, alkaline-earth and transition metal cations.

## 2. Experimental

### 2.1. General procedure for the synthesis of phenanthroimidazole 2a-c

The heterocyclic aldehyde **1** (0.073 g, 1 mmol), 9,10-phenanthredione (0.085 g, 1 mmol) and NH<sub>4</sub>OAc (0.632 g, 20 mmol) were dissolved in glacial acetic acid (5 mL), followed by stirring and heating at reflux for 8 h. The mixture was then cooled to room temperature and ethyl acetate was added (15 mL) and washed with water (3 x 10 mL). After drying the organic layer with anhydrous MgSO<sub>4</sub>, the solution was filtered and the

solvent was evaporated to dryness. The resulting solid was dissolved in acetone and precipitation with petroleum ether afforded the pure compound.

### 2.1.1 2-Phenyl-1*H*-phenanthro[9,10-*d*]imidazole (**2a**).<sup>6</sup>

Compound **2a** was obtained as off white solid (115 mg, 54%). Mp. 316.6-317.3 °C. UV-vis (acetonitrile):  $\lambda_{\max}$  nm (log  $\epsilon$ ) 312 (4.70). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  = 7.49 – 7.51 (m, 1H, H-4'), 7.58 – 7.66 (m, 2H, H-3' and H-5'), 7.66 – 7.77 (m, 2H, H-7 and H-2), 8.30 (d, *J* = 7.2 Hz, 2H, H-6 and H-3), 8.55 (dd, *J* = 8 and 0.8 Hz, 2H, H-8 and H-1), 8.58 (dd, *J* = 8 and 1.2 Hz, 2H, H2' and H6'), 8.83 – 8.88 (m, 2H, H5 and H4), 13.44 (s, 1H, NH) ppm. <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  = 121.86, 121.97, 122.40, 123.71, 124.07, 125.12, 125.33, 126.12, 126.97, 127.04, 127.13, 127.51, 127.65, 127.67, 128.91, 129.91, 130.36, 136.96, 149.08 ppm.

### 2.1.2. 2-(Thiophen-2-yl)-1*H*-phenanthro[9,10-*d*]imidazole (**2b**).

Compound **2b** was obtained as beige solid (175 mg, 82%). UV-vis (acetonitrile):  $\lambda_{\max}$  nm (log  $\epsilon$ ) 335 (4.50). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  = 7.26 – 7.28 (m, 1H, H-4'), 7.59 – 7.76 (m, 5H, H-5', H-2, H-7, H-3 and H-6), 7.92 (dd, *J* = 3.6 and 1.2 Hz, 1H, H-3'), 8.44 – 8.52 (m, 2H, H-1 and H-8), 8.81 – 8.87 (m, 2H, H-4 and H-5), 13.53 (s, 1H, NH) ppm. IR (KBr disc):  $\nu$  = 3236, 3073, 1948, 1683, 1614, 1564, 1487, 1456, 1411, 1363, 1294, 1239, 1193, 1166, 1123, 1077, 1041, 854, 714, 699 cm<sup>-1</sup>. <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  = 121.78, 121.88, 123.72, 124.12, 125.16, 125.37, 125.78, 127.08, 127.16, 127.79, 128.21, 133.90, 136.73, 144.89 ppm.

### 2.1.3. 2-(Furan-2-yl)-1*H*-phenanthro[9,10-*d*]imidazole (**2c**)

Compound **2c** was obtained as light brown solid (205 mg, 87%). UV-vis (acetonitrile):  $\lambda_{\max}$  nm (log  $\epsilon$ ) 312 (4.50). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 300 MHz):  $\delta$  = 6.76 (dd, *J* = 3.2 and 1.6 Hz, 1H, H-4'), 7.23 (dd, *J* = 3.2 and 0.8 Hz, 1H, H-3'), 7.60 – 7.64 (m, 2H, H-2 and H-7), 7.69 – 7.71 (m, 2H, H-3 and H-6), 7.96 (dd, *J* = 1.6 and 0.8 Hz, 1H, H-5'), 8.53 (dd, *J* = 7.6 and 0.8 Hz, 2H, H-1 and H-8), 8.81 – 8.86 (m, 2H, H-4 and H-5), 13.67 (s, 1H, NH) ppm. IR (KBr disc):  $\nu$  = 3438, 3222, 3072, 1950, 1773, 1692, 1614, 1538, 1514, 1453, 1409, 1368, 1276, 1233, 1170, 1113, 1040, 1018, 754, 724 cm<sup>-1</sup>. <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  = 109.30, 112.32, 121.86, 121.97, 122.30, 123.71, 124.04, 125.21, 125.38, 126.82, 126.94, 127.11, 127.58, 127.71, 136.85, 141.63, 143.98, 145.80 ppm.

## 2.2. Spectrophotometric and spectrofluorimetric titrations of compounds **2a-c**

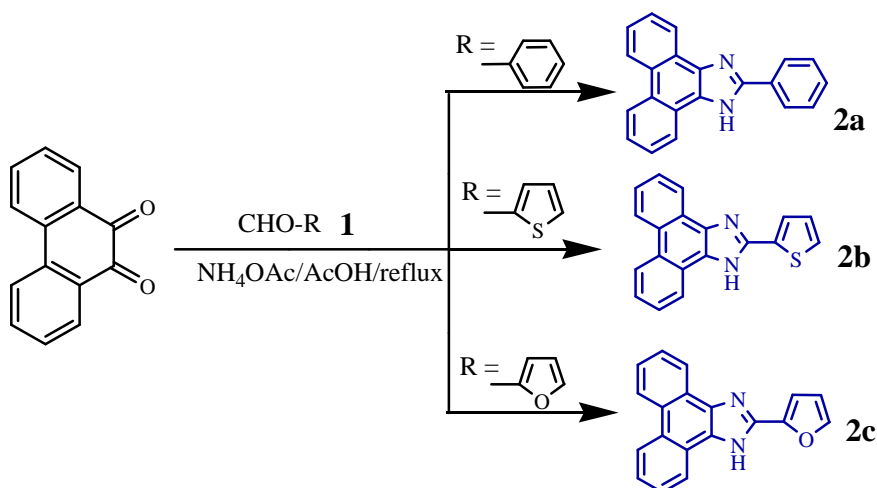
Solutions of phenanthroimidazole derivatives **2a-c** (ca.  $1.0 \times 10^{-5}$  M) and of the ions under study (ca.  $1.0 \times 10^{-2}$  M) were prepared in ACN and ACN/H<sub>2</sub>O (95:5) in the presence of relevant organic and inorganic anions (AcO<sup>-</sup>, F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, CN<sup>-</sup>, NO<sub>3</sub><sup>-</sup>, BzO<sup>-</sup>, H<sub>2</sub>PO<sub>4</sub><sup>-</sup>, HSO<sub>4</sub><sup>-</sup>), and of alkaline, alkaline-earth and transition metal cations (Cu<sup>2+</sup>, Cd<sup>2+</sup>, Pd<sup>2+</sup>, Ni<sup>2+</sup>, Hg<sup>2+</sup>, Zn<sup>2+</sup>, Fe<sup>2+</sup>, Fe<sup>3+</sup> and Cr<sup>3+</sup>).

Titration of compounds **2a-c** was performed by the sequential addition of the ion to the phenanthroimidazole solution, in a 10 mm path length quartz cuvette and absorption emission spectra (by excitation at the wavelength of maximum absorption for each compound) were measured, as indicated in Table 1.

## 3. Results and discussion

### 3.1. Synthesis and characterization

Phenanthroimidazoles **2a-c** were synthesized in moderate to good yields (54-87 %), by Radziszewski reaction between aldehydes **1** and phenanthrenequinone (Scheme). The new compounds were completely characterized by the usual spectroscopic techniques (Table 1).






**Scheme.** Synthesis of phenanthroimidazoles **2a-c**.

The absorption and emission spectra of phenanthroimidazoles **2a-c** were measured in acetonitrile (Table 1). Compounds **2a-c**, differing in the substituent at position 2 of the imidazole ring, displayed shifts according to the electronic character of the substituent, e.g., imidazole **2b** bearing a thiophene displayed a bathochromic shift for the maximum

wavelength of absorption (12 nm) and emission (6 nm) when compared to **2a** (Table 1). The relative fluorescence quantum yields were determined by using  $10^{-6}$  M solutions of DPA in ethanol as standard ( $\Phi_F = 0.95$ ).<sup>7</sup> For the  $\Phi_F$  determination, the fluorescence standard was excited at the wavelengths of maximum absorption found for each of the compounds to be tested and in all fluorimetric measurements the absorbance of the solution did not exceed 0.1.

**Table 1.** Yields, UV-visible absorption and fluorescence data for imidazoles **2a-c** in acetonitrile solution.

Imidazole	R	Yield (%)	UV/Vis		Fluorescence		
			$\lambda_{\max}$ (nm)	log $\epsilon$	$\lambda_{\text{em}}$ (nm)	$\Phi_F$	Stokes' shift (nm)
<b>2a</b>		54	307	4.6	384	0.38	77
<b>2b</b>		82	319	4.5	390	0.55	71
<b>2c</b>		87	305	4.5	395	0.31	90

Phenanthroimidazoles **2** exhibited high fluorescence quantum yields in ACN ( $\Phi_F = 0.31$  and 0.55), the highest being for **2b** (Table 1). Stokes' shifts directly relate to energy differences between the ground and excited states and all compounds showed large Stokes' shifts (from 71 nm to 90 nm) and these values are an interesting feature for biological fluorescent probes that allows an improved separation of light inherent to the matrix and the light dispersed by the sample.




Considering these photophysical properties, derivatives **2a-c** would be interesting candidates as chemosensors due to the high fluorescence quantum yields, important for maximization of the response in the analysis of very dilute samples.

### 3.2 Spectrophotometric and spectrofluorimetric titrations of phenanthroimidazoles **2a-c** with metallic ions

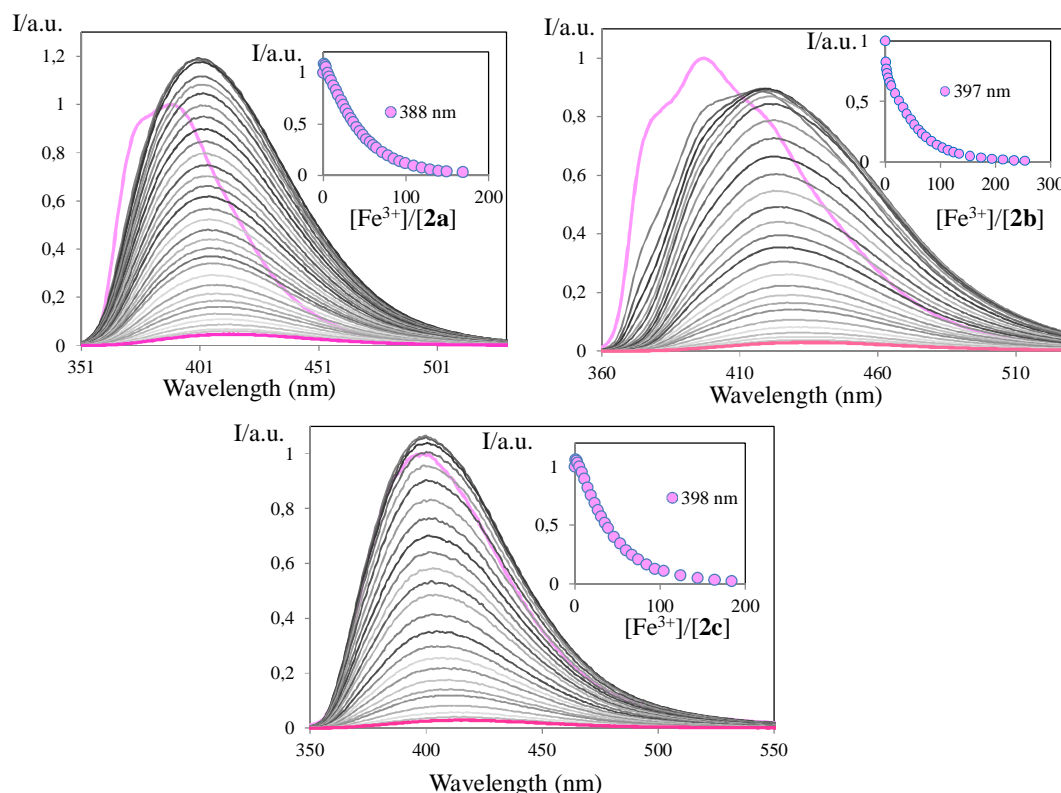
Phenanthroimidazoles **2a-c** ( $10^{-5}$  M) were evaluated as chemosensors in the presence of several relevant ions ( $\text{AcO}^-$ ,  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{CN}^-$ ,  $\text{NO}_3^-$ ,  $\text{BzO}^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{HSO}_4^-$ ,  $\text{Cu}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Pd}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Fe}^{3+}$  and  $\text{Cr}^{3+}$ ). Spectrophotometric and spectrofluorimetric titrations were carried out in ACN and ACN/ $\text{H}_2\text{O}$  solutions, in order to evaluate their chemosensory ability. Spectrophotometric titrations did not reveal any interaction with any of the ions tested as no colour change was observed. Spectrofluorimetric titrations

in a preliminary study with 50 equiv of each ion revealed that compounds **2a-c** displayed higher selectivity in aqueous mixtures (ACN/H<sub>2</sub>O (95:5)) than in ACN (Table 2).

**Table 2.** Results obtained in spectrofluorimetric titrations in ACN and ACN/H<sub>2</sub>O (95:5) in the presence of several ion solutions for phenanthroimidazoles **2**.

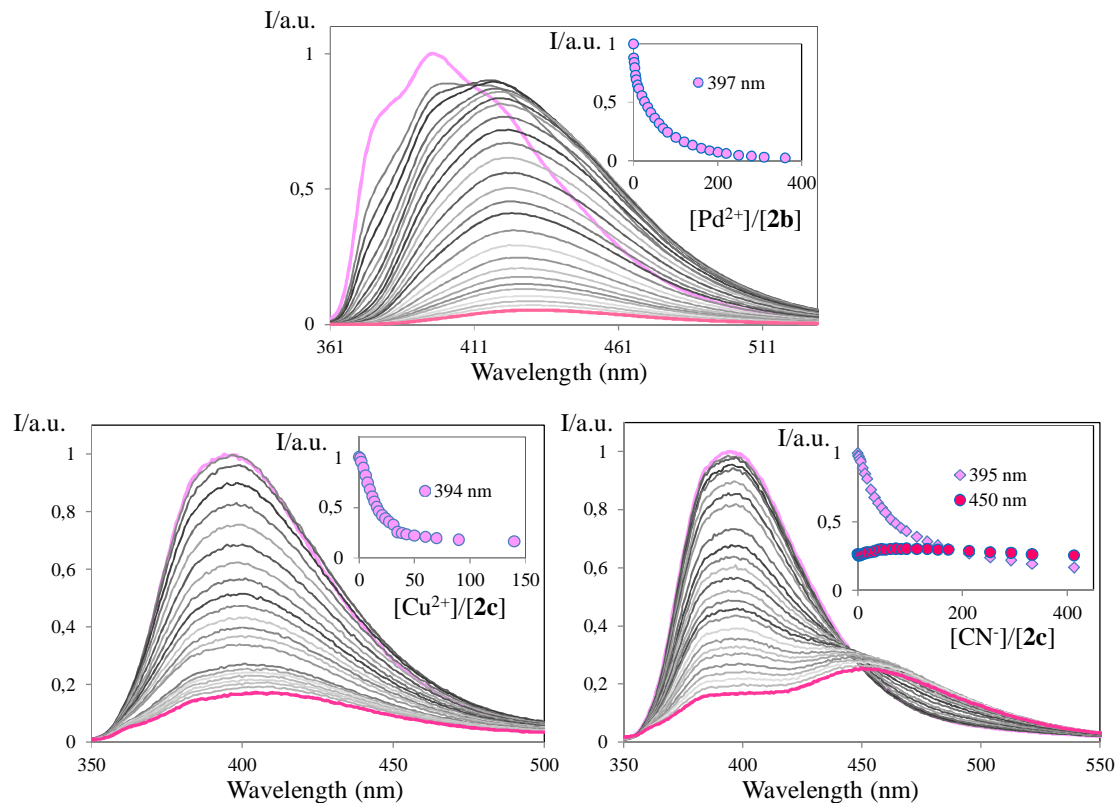
Imidazole	R	ACN						ACN/H <sub>2</sub> O (95:05)			
		F <sup>-</sup>	CN <sup>-</sup>	AcO <sup>-</sup>	Fe <sup>3+</sup>	Cu <sup>2+</sup>	Pd <sup>2+</sup>	CN <sup>-</sup>	Fe <sup>3+</sup>	Cu <sup>2+</sup>	Pd <sup>2+</sup>
<b>2a</b>		✓		✓	✓				✓		
<b>2b</b>		✓	✓	✓	✓		✓			✓	
<b>2c</b>		✓	✓	✓	✓	✓	✓	✓	✓		

In the spectrofluorimetric titrations with Fe<sup>3+</sup>, a strong decrease of the fluorescence intensity (a chelation enhancement of quenching, CHEQ effect) was observed for the all derivatives, with an almost complete fluorescence quenching (**2a**, 169 equiv; **2b**, 245 equiv; **2c**, 184 equiv) (Figure 2).



**Figure 2:** Spectrofluorimetric titrations of phenanthroimidazoles **2a-c** with addition of increasing amounts of Fe<sup>3+</sup> in ACN/H<sub>2</sub>O (95:5). The inset represents the normalized emission ([**2a-c**] = 1x10<sup>-5</sup> M, T = 298 K).

Spectrofluorimetric titrations of derivatives **2b** with Pd<sup>2+</sup> and **2c** with Cu<sup>2+</sup> showed a strong decrease of the fluorescence intensity with an almost complete fluorescence quenching (Figure 3).



**Figure 3:** Spectrofluorimetric titrations of compounds **2b-c** with addition of increasing amounts of Pd<sup>2+</sup>, Cu<sup>2+</sup> and CN<sup>-</sup> in ACN/H<sub>2</sub>O. The inset represents the normalized emission ( $[2b-c] = 1 \times 10^{-5}$  M, T = 298 K).

Spectrofluorimetric titration of compound **2c** in presence of CN<sup>-</sup> ion revealed that the plateau was achieved after addition of 413 equiv of anion. In the titration, the intensity of the emission band was reduced (CHEQ effect), accompanied by a red shift, and a new band was formed, with an isoemissive point at 450 nm, indicating the presence of two emissive species in the solution.

#### 4. Conclusions

The synthesis of new phenanthroimidazoles **2a-c** was achieved in moderate to good yields by simple experimental procedures. The photophysical properties were evaluated

by fluorescence spectroscopy and revealed that the imidazole derivatives are highly emissive.

The sensory ability was evaluated for several ions by spectrofluorimetric titrations in acetonitrile and acetonitrile/water. Phenanthroimidazoles **2a-c** were more selective in aqueous mixtures (ACN/H<sub>2</sub>O (95:05)) than in ACN.

### Acknowledgements

Thank are due to *Fundação para a Ciência e Tecnologia* (Portugal) and FEDER-COMPETE for financial support through Centro de Química (PEst-C/QUI/UI0686/2013 (FCOMP-01-0124-FEDER-037302)) and a PhD grant to R.C.M. Ferreira (SFRH/BD/86408/2012). The NMR spectrometer Bruker Avance III 400 is part of the National NMR Network and was purchased with funds from FCT and FEDER. We are also grateful to the Instituto da Educação of Universidade do Minho for providing the laboratory infrastructure necessary for the development of this work

### References

1. a) Velmurugan, K.; Mathankumar, S.; Santoshkumar, S.; Amudha, S.; Nandhakumar, R. *Spectrochim. Acta A*, **2015**, *139*, 119-123. b) Cao, W.; Zheng, X.-J.; Fang, D.-C.; Jin, L.-P. *Dalton Trans.*, **2015**, *44*, 5191-5196.
2. a) Patil, S.; Patil, R.; Fegade, U.; Bondhopadhyay, B.; Pete, U.; Suban, K. S.; Singh, N.; Basu, A.; Bendre, R.; Kuwar, A. *Photochem. Photobiol. Sci.*, **2015**, *14*, 439-443. b) Udhayakumari, D.; Velmathi, S.; Boobalan, M. S.; Venkatesan, P.; Wu, S.-P. *J. Lumin.*, **2015**, *158*, 484-492.
3. Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.
4. a) Batista, R. M. F.; Ferreira, R. C. M.; Raposo, M. M. M.; Costa, S. P. G. *Tetrahedron*, **2012**, *68*, 7322-7330. b) Batista, R. M. F.; Oliveira, E.; Costa, S. P. G.; Lodeiro, C.; Raposo, M. M. M. *Tetrahedron*, **2011**, *67*, 7106-7113.
5. a) Marín-Hernández, C.; Santos-Figueroa, L. E.; Moragues, M. E.; Raposo, M. M. M.; Batista, R. M. F.; Costa, S. P. G.; Pardo, T.; Martínez-Máñez, R.; Sancenón, F. *J. Org. Chem.* **2014**, *79*, 10752-10761. b) Batista, R. M. F.; Costa, S. P. G.; Raposo, M. M. M. *Sensors Act. B Chem.* **2014**, *191*, 791-799. c) Batista, R. M. F.; Oliveira, E.; Costa, S. P. G.; Lodeiro, C.; Raposo, M. M. M. *Supramol. Chem.* **2014**, *26*, 71-80. d) Pina J.; Seixas de Melo, J.; Batista, R. M. F.; Costa, S. P. G.; Raposo, M. M. M. *J. Org.*



*Chem.* **2013**, *78*, 11389-11395. e) Pedras B.; Batista, R. M. F.; Tormo, L.; Costa, S. P. G.; Raposo, M. M. M.; Orellana, G.; Capelo, J. L.; Lordeiro, C. *Inorg. Chim. Acta* **2012**, *381*, 95-103. f) Santos-Figueroa, L. E.; Moragues, M. E.; Raposo, M. M. M.; Batista, R. M. F.; Costa, S. P. G.; Sancenón, F.; Martínez-Máñez, R.; Ros-Lis, J. V.; Soto, J. *Org. Biomol. Chem.* **2012**, *10*, 7418-7428. g) Xu, Z.; Kim, S. K.; Yoon, J. *Chem. Soc. Rev.* **2010**, *39*, 1457-1466. h) Batista R. M. F.; Costa, S. P. G.; Belsley, M.; Raposo, M. M. M. *Dyes Pigments* **2009**, *80*, 329-336.

6. a) Jourshari, M. S.; Mamaghani. M.; Shirini, F.; Tabatabaeian, K.; Rassa, M.; Langari, H. *Chinese Chem. Lett.*, **2013**, *24*, 993-996. b) Steck, E. A.; Day, A. R. *J. Am. Chem. Soc.*, **1946**, *68*, 771-772.

7. Morris, J. V.; Mahaney, M. A.; Huberr, J. R. *J. Phys. Chem.* **1976**, *80*, 969.