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Dyes bearing thiazolylazo groups as chromogenic chemosensors for metal cations

Tatina Ábalos,[a,b,c] María Moragues,[a,b,c] Santiago Royo,[a,b,c] Diego Jiménez,[b] Ramón Martínez-Máñez,*[a,b,c] Juan Soto,[a,b] Félix Sancenón[a,b,c] and Joan Cano[d,e]

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A family of dyes (**L^1**-**L^6**) containing a thiazolylazo group as signalling subunit and several macrocyclic cavities, with different ring sizes and type and number of heteroatoms, as binding sites, have been synthesised and characterized. Acetonitrile solutions of **L^1**-**L^6** show broad and structureless absorption bands in the 554-577 nm range with typical molar absorption coefficients ranging from 20000 to 32000 M^{-1} cm^{-1}. A detailed protonation study was carried out with compounds **L^1**, **L^2** and **L^5** in acetonitrile solutions. Addition of one equivalent of protons to **L^1** and **L^2** resulted in the development of a new band at 425 and 370 nm, respectively that was ascribed to protonation in the aniline nitrogen. In contrast, protonation of **L^5** resulted in bathocrhomic shift of 25 nm of the absorption band that was conceivable with protonation of one of the nitrogen atoms of the azo moiety. These results were in agreement with ^{1}H NMR data. Theoretical studies on the model ligand **L^1** and on different possible protonation species were also performed using density functional theory (DFT) quantum mechanical calculations. Colour modulations in acetonitrile solutions of **L^1**-**L^6** in the presence of the metal cations Fe^{3+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+} have been studied. A selective chromogenic response of **L^4** in the presence of Pb^{2+} and **L^5** in the presence of Hg^{2+} was observed. To get a better insight into the chromophoric nature in the presence of metal cations, the interaction of Hg^{2+} with the model compound **L^1** in two different coordination modes was studied theoretically by using density functional theory (DFT) quantum mechanical calculations.

Introduction

Since the discovery of crown ethers by Pedersen in the early sixties a huge amount of work dealing with the synthesis of selective receptors for positively charged species has been carried out.[1] In these first stages the interaction between abiotic receptors and the target cationic species was studied by means of potentiometric and NMR measurements. An important improvement in the field was introduced by Vögtle in 1978 with the synthesis of the first chromogenic receptors for cations.[2] Usually those receptors are composed by two subunits namely the binding site and the signalling unit that are coupled through a covalent bond.[3] The binding sites are designed to achieve a great complementarity with the target metal cation and, usually, have a crown ether nature.[4] Macrocyclic cavities with different size and shapes have been synthesized and employed as binding sites.[5] Selectivity to certain metal cations can be achieved varying the size and the number and type of the heteroatoms on the macrocyclic cavity. At this respect, hard cations coordinate well with hard donor atoms such as oxygen whereas selectivity toward soft cations can be achieved by the use of soft donor atoms in the binding site. Additionally, and in order to obtain a visual response upon cation binding, one of the heteroatoms of the macrocyclic cavity should be included in the electronic structure of the dye.

Among organic dyes used as signalling subunits in the development of chromogenic receptors,[6] azo dyes have been widely used due to their simple synthesis and their well-known spectroscopic properties.[7] Reaction between *N*,*N*-disubstituted anilines and diazonium salts of a great variety of aniline derivatives leads to the obtention of azo dyes with characteristic charge-transfer absorption bands in the 430-480 nm interval and colours ranging from light-yellow to red-orange. By changing aniline derivatives by 2-aminothiazole and 2-aminobenzothiazole a series of thiazolylazo dyes with absorption bands shifted to 480-650 nm interval can be obtained (with colours ranging from orange to deep blue). Some thiazolylazo dyes have been reported to form coloured chelates with a great variety of transition metal cations (Fe^{3+}, Hg^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Co^{2+}, Mn^{2+}, Pd^{2+} and Cd^{2+}) through interaction with nitrogen atoms from the thiazol and azo moieties and with oxygen atoms usually presented in benzene rings.[8] Several thiazolylazo dyes have been used for the

[a] *Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Unidad Mixta Universidad Politécnica de Valencia-Universidad de Valencia, Spain.*
[b] *Departamento de Química, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022, Valencia, Spain. E-mail: rmaez@qim.upv.es*
[c] *CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN).*
[d] *Instituto de Ciencia Molecular (ICMol), C/ Catedrático José Beltrán nº 2, 46980 Paterna (Valencia), Spain.*
[e] *Fundació General de la Universitat de València (FGUV).*

remediation of the environmentally pollutant Hg^{2+} and Co^{2+} cations.[9] Also the use of these azo dyes have been reported in capillary electrophoresis separations of Co^{2+}, Ni^{2+}, Zn^{2+} and Fe^{2+} and as masking agents in several analytical determinations.[10] Nevertheless thiazolylazo dyes have barely been used as signalling subunits in the development of cation receptors based on supramolecular chemistry concepts.

Following our interest in the design of electrochemical and chromo-fluorogenic probes for target guests,[11] herein we report the synthesis, coordination and chromogenic properties in the presence of metal cations of six receptors containing a thiazolylazo group as signalling subunit and several macrocyclic cavities, with different sizes and number and types of heteroatoms, as binding sites. Of the six receptors presented here, four are described for the first time (**L**^{2}, **L**^{4}-**L**^{6}), **L**^{1} was used as model because the lack of macrocyclic subunit and **L**^{3} was synthesized by Dix and Vögtle in 1978 who studied its coordination behaviour toward alkaline and alkaline-earth cations.[12] In order to get a complete understanding of the chromogenic behaviour of this family of thiazolylazo dyes, different possible protonations on **L**^{1} and different coordination modes with Hg^{2+} have also been studied theoretically using density functional theory (DFT) quantum mechanical calculations.

Experimental section

General remarks: All commercially available reagents were used without further purification. Air/water-sensitive reactions were performed in flame-dried glassware under argon. Acetonitrile was dried with CaH_2 and distilled prior to use.

Physical measurements: Metal cations (Cd^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} as perchlorate or triflate salts) were used to obtain acetonitrile solutions of concentration ca. 5.0 x 10^{-3} mol dm^{-3}. Protonation studies were carried out with acetonitrile solutions of perchloric acid. Photophysical studies of the behaviour of acetonitrile solutions of all the ligands in the presence of metal cations cited above and protons were carried out. The UV-visible behaviour was studied with a Perkin Elmer Lambda 35 spectrometer. The concentration of ligands used in the UV-visible measurements was ca. 5.0 x 10^{-5} mol dm^{-3} in acetonitrile. UV-visible spectra were recorded in the presence of equimolar quantities of all the ligands and the corresponding metal cations.

The ^{1}H and ^{13}C NMR spectra were recorded with a Varian Gemini spectrometer. Chemical shifts are reported in ppm downfield from TMS signal. Spetra taken in $CDCl_3$ were referenced to residual $CHCl_3$. Also ^{1}H-NMR studies in the presence of increasing quantities of protons were carried out. For these protonation studies the correspondent receptor (concentration of ca. 1.0 x 10^{-2} mol dm^{-3}) were dissolved in deuterated acetonitrile and then titrated with perchloric acid.

Synthetic procedures: The synthesis of macrocyclic subunits 10-phenyl-10-aza-1,4,7-trioxacyclododecane (**3**), 13-phenyl-13-aza-1,4,7,10-tetraoxacyclopentadecane (**4**), 16-phenyl-16-aza-1,4,7,10,13-pentaoxacycloheptadecane (**5**), 10-phenyl-10-aza-1,4-dioxa-7,13-dithiacyclopentadecane (**6**) and 4-phenyl-4-aza-1,7-dioxa-10,13-dithiacyclopentadecane (**7**) were previously published.[13] The synthesis of receptors **L**^{1} and **L**^{3} was also previously published.[14,12]

*General procedure for the synthesis of thiazolylazo derivatives (**L**^{1}-**L**^{6}):* 2-amino-5-nitrothiazole (**1**) was diazotated with $NaNO_2$ and HCl and subsequently reacted with *N*,*N*-dimethylaniline (**2**) or the corresponding phenyl-macrocycle (**3**-**7**) dissolved in water solutions containing acetic acid to give the correspondent receptors **L**^{1}-**L**^{6} as blue solids.

*Synthesis of **L**^{1}*: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 1320 mg, 9.1 mmol) was dissolved in 50 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (628 mg, 9.1 mmol) dissolved in water (15 mL) was added. After 10 minutes *N*,*N*-dimethylaniline (**2**, 1000 mg, 8.26 mmol) dissolved in 50 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent. The final receptor **L**^{1} (1373 mg, 4.96 mmol) was isolated as a dark blue solid. Yield: 60%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.20 (6H, s, N-(C$\underline{H}_3$)$_2$), 6.77 (2H, d, C$_6\underline{H}_4$), 7.91 (2H, d, C$_6\underline{H}_4$), 8.58 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 40.3, 112.7, 143.1, 143.8, 147.0, 154.2, 181.4. HRMS calc. for $C_{11}H_{11}N_5O_2S$, 207.0633, found 207.0689.

*Synthesis of **L**^{2}*: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 100 mg, 0.69 mmol) was dissolved in 5 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (47.6 mg, 0.69 mmol) dissolved in water (1.5 mL) was added. After 10 minutes 10-phenyl-10-aza-1,4,7-trioxacyclododecane (**3**, 158 mg, 0.63 mmol) dissolved in 5 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent. The final receptor **L**^{2} (102.5 mg, 0.25 mmol) was isolated as a dark blue solid. Yield: 40%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.65 (8H, s, O-C$\underline{H}_2$-O), 3.76 (4H, t, N-C$\underline{H}_2$-O), 3.80 (4H, t, O-C$\underline{H}_2$-O), 6.78 (2H, d, C$_6\underline{H}_4$), 7.91 (2H, d, C$_6\underline{H}_4$), 8.58 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 53.5, 70.0, 70.4, 71.3, 112.7, 143.1, 143.8, 147.0, 154.2, 181.4. HRMS calc. for $C_{17}H_{21}N_5O_5S$, 407.1263, found 407.1275.

*Synthesis of **L**^{3}*: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 100 mg, 0.69 mmol) was dissolved in 5 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (47.6 mg, 0.69 mmol) dissolved in water (1.5 mL) was added. After 10 minutes 13-phenyl-13-aza-1,4,7,10-tetraoxacyclopentadecane (**4**, 186 mg, 0.63 mmol) dissolved in 5 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent.

The final receptor **L**^{3} (117 mg, 0.26 mmol) was isolated as a dark blue solid. Yield: 41%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.65 (4H, s, O-C$\underline{H}_2$-O), 3.68 (12H, m, O-C$\underline{H}_2$-O and N-C$\underline{H}_2$-O), 3.83 (4H, t, O-C$\underline{H}_2$-O), 6.79 (2H, d, C$_6\underline{H}_4$), 7.89 (2H, d, C$_6\underline{H}_4$), 8.56 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 53.1, 68.3, 70.1, 70.5, 71.3, 112.9, 142.8, 143.6, 147.2, 154.1, 181.7. HRMS calc. for $C_{19}H_{25}N_5O_6S$, 451.1526, found 451.1511.

Synthesis of ***L***^{4}: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 100 mg, 0.69 mmol) was dissolved in 5 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (47.6 mg, 0.69 mmol) dissolved in water (1.5 mL) was added. After 10 minutes 16-phenyl-16-aza-1,4,7,10,13-pentaoxacycloheptadecane (**5**, 213.6 mg, 0.63 mmol) dissolved in 5 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent. The final receptor **L**^{4} (139 mg, 0.28 mmol) was isolated as a dark blue solid. Yield: 45%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.71-3.85 (24H, m, O-C$\underline{H}_2$-O and N-C$\underline{H}_2$-O), 6.80 (2H, d, C$_6\underline{H}_4$), 7.93 (2H, d, C$_6\underline{H}_4$), 8.60 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 51.2, 68.4, 70.7, 70.9, 113.0, 143.5, 144.2, 147.6, 153.9, 183.5. HRMS calc. for $C_{21}H_{29}N_5O_7S$, 495.1788, found 495.1769.

Synthesis of ***L***^{5}: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 100 mg, 0.69 mmol) was dissolved in 5 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (47.6 mg, 0.69 mmol) dissolved in water (1.5 mL) was added. After 10 minutes 10-phenyl-10-aza-1,4-dioxa-7,13-dithiacyclopentadecane (**6**, 206 mg, 0.63 mmol) dissolved in 5 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent. The final receptor **L**^{5} (145 mg, 0.3 mmol) was isolated as a dark blue solid. Yield: 48%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 2.76 (4H, t, S-C$\underline{H}_2$-S), 2.93 (4H, t, S-C$\underline{H}_2$-S), 3.63 (4H, s, O-C$\underline{H}_2$-O), 3.80 (8H, m, S-C$\underline{H}_2$-N, O-C$\underline{H}_2$-O), 6.78 (2H, d, C$_6\underline{H}_4$), 7.92 (2H, d, C$_6\underline{H}_4$), 8.60 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 29.6, 31.7, 52.4, 70.8, 74.4, 112.4, 143.5, 144.5, 147.6, 154.7, 182.1. HRMS calc. for $C_{19}H_{25}N_5O_4S_3$, 483.1069, found 483.1075.

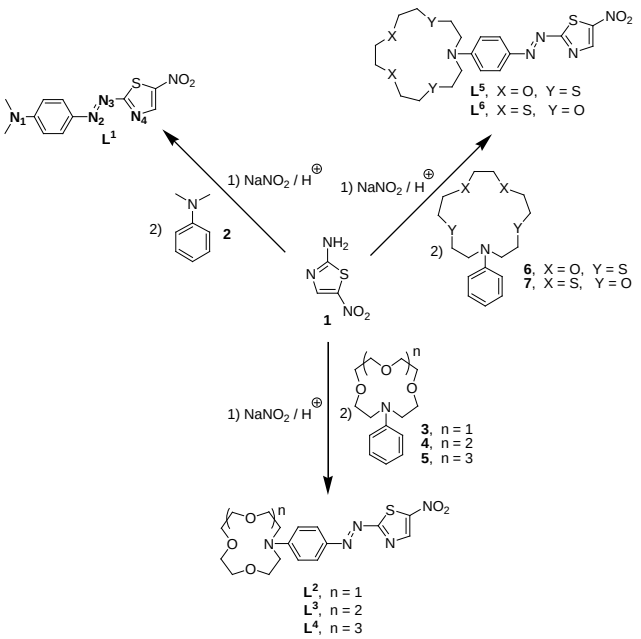
Synthesis of ***L***^{6}: In a round bottomed flask 2-amino-5-nitrothiazole (**1**, 100 mg, 0.69 mmol) was dissolved in 5 mL of an acetic acid-water 5:1 (v/v) mixture. The crude was cooled with an ice bath and then $NaNO_2$ (47.6 mg, 0.69 mmol) dissolved in water (1.5 mL) was added. After 10 minutes 4-phenyl-4-aza-1,7-dioxa-10,13-dithiacyclopentadecane (**7**, 206 mg, 0.63 mmol) dissolved in 5 mL of HCl-water 5:1 (v/v) was added dropwise to the crude reaction. Then the crude was allowed to react 30 minutes in an ice bath and 60 minutes at room temperature. The crude reaction was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$ solution. The crude reaction was purified with column chromatography employing aluminium oxide as stationary phase and CH_2Cl_2-CH_3CN 9:1 (v/v) as eluent. The final receptor **L**^{6} (121 mg, 0.25 mmol) was isolated as a dark blue solid. Yield: 40%, ^{1}H NMR (300 MHz, DMSO-D6): 2.80 (4H, t, S-C$\underline{H}_2$-S), 2.91 (4H, t, S-C$\underline{H}_2$-S), 3.73 (4H, s, O-C$\underline{H}_2$-O), 3.87 (8H, m, S-C$\underline{H}_2$-N, O-C$\underline{H}_2$-O), 6.77 (2H, d, C$_6\underline{H}_4$), 7.93 (2H, d, C$_6\underline{H}_4$), 8.59 (1H, s, thiazole). ^{13}C **{**^{1}H**}** NMR (75 MHz, $CDCl_3$): δ = 31.8, 33.0, 51.6, 70.5, 72.7, 112.4, 142.7, 143.8, 147.3, 154.7, 182.3. HRMS calc. for $C_{19}H_{25}N_5O_4S_3$, 483.1069, found 483.1057.

Computational Details. Calculations were performed through the Gaussian09 package using the B3LYP functional and the quadratic convergence approach.[15] Double-ζ all electron basis sets proposed by Ahlrichs *et al.* were used for all atoms except for the mercury atom where valence double-ζ proposed by Dunning and Huzinaga and Los Alamos electron core pseudopotential were used.[16] Molecular geometries were optimized for the used molecules. To optimize the computational time, the organic skeleton involves in the studied charge transfer band – formed by aniline, azo and thiazole groups– was frozen in metallic complexes. Energies and oscillator strengths of the electronic transitions were obtained from calculations based on the time dependent (TD) formalism.[17] In such cases, a polarizable continuum model with the parameters corresponding to the acetonitrile was used to simulate the electronic effects of the solvent.[18]

Results and discussion

Receptors **L**^{1}-**L**^{6} were synthesized (see Scheme 1) by diazotation reaction between the diazonium salt of 2-amino-5-nitrothiazole and *N*,*N*-dimethylaniline (to obtain **L**^{1}) or the corresponding 4-(*N*-crown)phenyl derivatives (to obtain **L**^{2}-**L**^{6}). The ligands **L**^{2}-**L**^{6} carry different macrocycles variying both the ring size and the type and number of heteroatoms. The 4-(*N*-crown)phenyl macrocycles, containing oxygen and nitrogen atoms, were synthesized by the Richman-Atkins procedure in which *N*,*N*-phenyldiethanolamine was deprotonated with sodium hydride followed by reaction, under high dilution conditions, with methanesulfonyl ester derivatives of the corresponding polyethylene glycol.[19] The macrocycles containing sulphur atoms, used to obtain receptors **L**^{5} and **L**^{6}, were synthesised by a modified procedure in which 3,6-dioxaoctane-1,8-dithiol and 3,6-dithiaoctane-1,8-diol were deprotonated with potassium carbonate and sodium hydride respectively following by reaction with the methanesulfonyl ester of *N*,*N*-phenyldiethanolamine. The synthesis of the receptors **L**^{1} and **L**^{3} was previously published. **L**^{1} has been used by several groups and its UV-visible behaviour extensively studied[14] whereas **L**^{3} was synthesized by Dix and Vögtle who studied how the coordination of alkaline and alkaline-earth cations modified the electronic levels of the dye.[12] The ^{1}H-NMR spectrum of receptors **L**^{2}-**L**^{6} shows protons of the macrocyclic unit in the 2.6 to 3.8 ppm range with two clearly defined zones for methylene protons adjacent to sulphur atoms (2.6-2.9 ppm) and methylene protons adjacent to nitrogen or oxygen atoms (3.5-3.8 ppm). The thiazolylazo moieties in **L**^{1}-**L**^{6} show two doublets centred at ca. 6.8 and 7.9 ppm and a singlet at ca. 8.6 nm corresponding to the 1,4-disubstituted benzene and

2,5-disubstituted thiazole ring respectively.



Scheme 1. Synthesis and chemical structure of receptors $\mathbf{L^1}$-$\mathbf{L^6}$.

UV-visible and ^{1}H-NMR behaviour upon coordination with protons: As stated above, receptors $\mathbf{L^1}$-$\mathbf{L^6}$ contain and aniline-type donor moiety attached through an azo linker with an acceptor 5-nitrothiazole heterocycle exhibiting π electron delocalization over the entire chromophoric system. As a consequence, $\mathbf{L^1}$-$\mathbf{L^6}$ receptors showed an intramolecular charge transfer band (vide infra), typical for such donor-acceptor-substituted dyes. These lowest-energy absorption bands are broad and structureless and centred at ca. 575 nm in acetonitrile. Typical molar absorption coefficients range from 20000 to 32000 M^{-1} cm^{-1} (see table 1). The subtle differences in the optical properties of the different dyes are imposed by the variations in the substituents on the aniline group. In fact, it has been reported that the presence of other heteroatoms in the crown unit attached to the aniline moiety can have an effect in the electronic properties of the chromophore via an influence in the electron donor capacity of the aniline moiety.[20]

Table 1. Absorption maxima and molar absorption coefficients of $\mathbf{L^1}$-$\mathbf{L^6}$.

	$\mathbf{L^1}$	$\mathbf{L^2}$	$\mathbf{L^3}$	$\mathbf{L^4}$	$\mathbf{L^5}$	$\mathbf{L^6}$
λ_{max} (nm)	577	574	575	574	575	554
ε (M^{-1} cm^{-1})	21400	29000	24400	23000	31600	20000

Ligands $\mathbf{L^1}$-$\mathbf{L^6}$ can act as polibases due to the presence in their structure of several nitrogen atoms that could, in principle, be protonated. However, a more closely look into the reported basicity of these nitrogen atoms indicates that most likely the protonation of the thiazole nitrogen is hindered because this is a poorly basic group showing protonation constants in the range -1.50 to 0.60.[21] In contrast, the reported protonation constants of azo dyes bearing the thiazole rings are in the range 1.80-2.80 in water and in organic solvents,[22] whereas protonation constants for aniline is 4.65 (in water).[23] These results suggest that protonation will take most likely in the aniline and/or azo groups. An additional issue related with the protonation of these compounds is the effect that the secondary heteroatoms on the macrocycle can have in relation to the protonation behaviour. In a recent report we have observed that different size and type of atoms in aniline crowns can modulate the basicity of the aniline nitrogen.[24] Additionally, protonation studies might clarify the coordination preferences of this family of receptors toward transition metal cations (vide infra).

A detailed protonation study was carried out with compounds $\mathbf{L^1}$, $\mathbf{L^2}$ and $\mathbf{L^5}$ in acetonitrile solutions. The addition of protons (up to 1 equivalent) to solutions of $\mathbf{L^1}$ leaded to a reduction in intensity of the band at 577 nm and the development of a new band at 425 nm. When higher acid concentrations were employed an additional bathochromic shift (ca. 10 nm) of the band centred at 577 nm occurred. These observed shifts and the fact that no clear isosbestic points were observed in the course of the titration pointed toward the presence of two protonation equilibrium for receptor $\mathbf{L^1}$. The initial hypsochromic shift was assigned to a preferential protonation in the aniline nitrogen, that decreases its donor strength, whereas the second bathochromic shift is conceivable with protonation of one of the nitrogen atoms of the azo moiety. From the titration curves values of logarithms of 4.77 ± 0.04 and 3.01 ± 0.03 were obtained for these protonation processes.[25]

In order to confirm the protonation sites, ^{1}H-NMR titrations experiments with $\mathbf{L^1}$ in deuterated acetonitrile were carried out. The most significant and remarkable change detected upon addition of one equivalent of protons was observed for the methyl signal that was shifted from 3.20 ppm to 4.56 ppm. This downfield strongly suggests a quaternization of the aniline nitrogen atom due to protonation. In the presence of an excess of protons the aromatic doublets at 7.89 ppm and 7.02 ppm from the 1,4-disubstituted benzene ring shifted to 7.71 ppm and 6.97 ppm and the singlet of the proton located in the nitrothiazole ring was shifted from 8.83 to 8.67 ppm. These upfield shifts could be ascribed to a second protonation process in one of the nitrogen atom of the azo moiety. The fact that bigger amounts of protons were required in order to protonante the azo group is indicative of its lower basicity when compared with the aniline nitrogen.

Receptor $\mathbf{L^2}$ contains a macrocyclic subunit having three oxygen and one nitrogen atoms. Upon addition of increasing amounts of protons to acetonitrile solutions of $\mathbf{L^2}$, the charge transfer band at 574 nm suffered a hypochromic shift in a progressive fashion and, at the same time, a new absorption band at 370 nm appeared. This significant hypsochromic shift of 206 nm was ascribed to protonation of the aniline nitrogen atom that is embedded in the crown subunit. Additionally, the presence of a clear isosbestic point at 430 nm strongly suggested that protonation only takes place at the aniline nitrogen in $\mathbf{L^2}$. This preferential protonation at the aniline moiety is due to favourable hydrogen bonding interactions between the protonated nitrogen atom and the oxygen atoms of the crown cavity and it has been already reported in other dyes also containing this macrocycle.[20] This stabilization of the protonated species by hydrogen bonding is reflected in the distinctly higher logarithm of the constant found for the protonation process that amounts to 6.88 ± 0.05 for

receptor $\mathbf{L^2}$ (obtained from least square treatment of the titration profiles). ^{1}H-NMR experiences with $\mathbf{L^2}$ in the presence of increasing quantities of protons were also carried out and confirmed the UV-vis results.

In contrast, receptor $\mathbf{L^5}$ shows a completely different behaviour. In this case the charge transfer band centred at 575 nm suffered a hyper- and bathochromic shift of 25 nm upon addition of protons. This shift is conceivable with protonation of the azo unit. Additionally the presence of two isosbestic points at 565 and 510 nm indicated that only one protonation occurs. In $\mathbf{L^5}$ the two bulky S atoms in the neighbourhood of the aniline nitrogen effectively shield the N atom from protonation and therefore only the nitrogen atom of the azo moiety was able to interact with protons. From the titration curves, and by least square treatment of the profiles, a value of the logarithm of the protonation constant of 3.03 ± 0.01 was obtained for the protonation of $\mathbf{L^5}$. The protonation site in receptor $\mathbf{L^5}$ was also confirmed by ^{1}H-NMR titration experiments in deuterated acetonitrile. Upon addition of an excess of protons the signals of the macrocyclic subunit located in the 2.50-3.70 interval remained unaltered, whereas the aromatic signals suffered remarkable shifts. For instance an upfield shift from 8.81 to 8.70 ppm was observed for the proton of the nitrothiazole ring.

Figure 1. Frontier MOs for $\mathbf{L^1}$ compound as obtained from the DFT quantum chemical calculations.

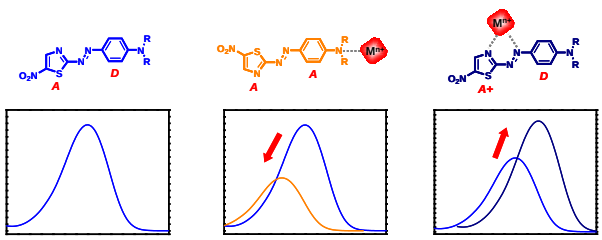
To get a better insight into the chromophoric nature of the title dyes, the model compound $\mathbf{L^1}$ was studied theoretically by using density functional theory (DFT) calculations using the Gaussian 09 package (see experimental section for details). Energies and oscillator strengths of the electronic transitions were obtained from calculations based on the time dependent (TD) formalism. In the most stable *trans* conformation of the azo group, TD calculations predicted for $\mathbf{L^1}$ the existence of an electronic absorption at 562 nm corresponding to the more intense electronic excitation observed. This result is in a good agreement with the experimental data (577 nm). This electronic transition involves an electron transfer from the HOMO to the LUMO orbitals (see Figure 1), which entails a π intraligand charge transfer (ILCT) that moves electronic density from the phenylamino group to the thiazole fragment (see Figure 1).

As we have seen before in the spectroscopic studies involving protons, from the point of view of chemical addressability, ligand $\mathbf{L^1}$ posses four potential protonation sites; i.e. the aniline nitrogen, the two nitrogens from the azo moiety and the thiazole ring. Additionally, in order to get a better understanding of the protonation behaviour, different possible protonations on $\mathbf{L^1}$ were studied theoretically using DFT calculations and the energies of the electronic transitions obtained from the TD formalism were compared with the position of the absorption bands found experimentally. Table 2 shows the theoretical energies (λ, in nm) for the ILCT transition associated to $\mathbf{L^1}$ ligand and the corresponding protonated molecules. In the table species $\mathbf{L^1}$, $\mathbf{L^1_1}$, $\mathbf{L^1_2}$, $\mathbf{L^1_3}$ and $\mathbf{L^1_4}$ correspond to species protonated in nitrogen atoms 1, 2, 3 and 4, respectively (see Scheme 1).

Table 2. Theoretical energies (λ, in nm) for the ILCT electronic transition for $\mathbf{L^1}$ ligand, the corresponding protonated molecules and two mercury(II) complexes (see text).

	$\mathbf{L^1}$	$\mathbf{L_1^1}$	$\mathbf{L_2^1}$	$\mathbf{L_3^1}$	$\mathbf{L_4^1}$	**Hg(L^1)-1**	**Hg(L^1)-2**
λ_{max} (nm)	567	409	572	477	510	613	407

Comparing the computational results with the experimental spectrum, the absorption bands at 425 and 370 for the protonated derivatives of receptors $\mathbf{L^1}$ and $\mathbf{L^2}$, respectively, are in agreement with protonation at the aniline for which a theoretical value of 409 nm for the electronic transition of lower energy was predicted for $\mathbf{L^1}$. Other predicted protonations at N3 and N4 suggested lower hypsocrhomic shifts that were not in agreement with the observed behavior. Additionally, from the theoretical studies, protonation at N2 is the only protonated species that is predicted to induce a bathochromic shift of the absorption band with respect to the unprotonated species (from 567 to 572 nm). This behavior is in agreement with that observed experimentally



for $\mathbf{L^5}$ which suffered a bathochromic shift of 25 nm strongly suggesting that the protonation in the azo group occurs in the nitrogen that is bonded to the aniline moiety.

Scheme 2. Coordination modes and colorimetric behaviour of receptors $\mathbf{L^1}$-$\mathbf{L^6}$ in the presence of metal cations.

UV-visible behaviour upon coordination with metal cations: The behaviour observed in the presence of different metal cations (vide infra) for acetonitrile solutions of $\mathbf{L^1}$-$\mathbf{L^6}$ can be rationalised in a similar fashion to that described above for protonation processes (vide ante). The ILCT transition at ca. 575 nm will be shifted to ca. 600 nm when the cation coordinated to the azo group, strengthening its acceptor character. On the contrary, coordination at the aniline nitrogen would result in a hypsochromic shift. Studies of metal coordination were carried out with ligands $\mathbf{L^1}$-$\mathbf{L^6}$ in acetonitrile, and three different behaviours were observed; i.e. selective coordination at the aniline, selective coordination at the azo moiety and no coordination. The possible coordination modes and the expected colorimetric behaviour are summarized in Scheme 2.

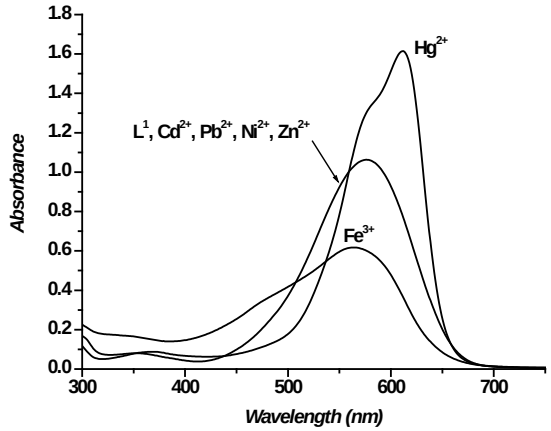


Figure 2. UV-visible behaviour of receptor $\mathbf{L^1}$ in acetonitrile (C = 5.0 x 10^{-5} mol dm^{-3}) in the presence of 1 equivalent of certain metal cations.

Upon addition of equimolar quantities of Cd^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} cations to acetonitrile solutions of $\mathbf{L^1}$ negligible changes in the UV-visible spectrum profile were observed (see Figure 2) indicating that very weak or no interaction of those cations with receptor $\mathbf{L^1}$ occurs. In contrast, the addition of equimolar quantities of Hg^{2+} induced the charge-transfer band at 560 nm to be shifted to 612 nm and the appearance of a broad shoulder at 580 nm suggesting a coordination of this metal cation with the azo-thiazole moiety. On the other hand the presence of Fe^{3+} induced a blue shift of the absorption band of $\mathbf{L^1}$ from 575 to 563 nm and the apparition of a new band at 485 nm. This behaviour suggested an interaction of this cation with the nitrogen of the aniline group. Those observed shifts were reflected in the colour of the $\mathbf{L^1}$ solutions that modulated from dark violet to blue and red-magenta for Hg^{2+} and Fe^{3+} respectively. Upon addition of increasing quantities of Hg^{2+} cation to acetonitrile solutions of $\mathbf{L^1}$ clear isosbestic points were found suggesting the formation of 1:1 complexes. Monitoring the changes at 610 nm upon Hg^{2+} addition, and through nonlinear least-square treatment of the titration profile, a logarithm of the stability constant of 5.51 ± 0.01 for the formation of the $[Hg(\mathbf{L^1})]^{2+}$ complex was obtained (see Table 3). Analogous titration studies with Fe^{3+} (monitoring the changes in the band at 612 nm) were carried out. In this case the complex stability constant log K for the formation of the complex $[Fe(\mathbf{L^1})]^{3+}$ was determined to 4.68 ± 0.02.

Table 3. Logarithms of the stability constants of receptors $\mathbf{L^1}$-$\mathbf{L^6}$ with Hg^{2+} and Pb^{2+} cations.

	$\mathbf{L^1}$	$\mathbf{L^2}$	$\mathbf{L^3}$	$\mathbf{L^4}$	$\mathbf{L^5}$	$\mathbf{L^6}$
Hg^{2+}	5.51 ± 0.02	4.79 ± 0.02	5.20 ± 0.2	5.33 ± 0.02	7.63 ± 0.09	4.93 ± 0.02
Pb^{2+}	-	-	-	6.17 ± 0.05	-	-

The response presented by solutions of $\mathbf{L^2}$ upon addition of equimolar quantities of metal cations was quite similar to that observed for $\mathbf{L^1}$; i.e. the Hg^{2+} metal cation coordinated the acceptor moiety and induced the apparition of two bands at 623 and 590 nm, whereas Fe^{3+} induced a hypocromic and blue shift from 574 to 568 nm and the development of a shoulder at 490 nm. The presence of other cations (i.e. Ni^{2+}, Zn^{2+} and Cd^{2+}) induced negligible changes in the visible spectrum of $\mathbf{L^2}$. The presence of isosbestic points in the titration studies of $\mathbf{L^2}$ with Hg^{2+} suggest the formation of well-defined 1:1 complexes with log K = 4.79 ± 0.02 (see Table 3). Fe^{3+} gave more complicated titration patterns indicative of the formation of different coordination complexes.

Interestingly receptors $\mathbf{L^3}$ and, especially, $\mathbf{L^4}$ behave differently in the sense that the inclusion of large crowns induces a change in selectivity trend when compared with $\mathbf{L^1}$. $\mathbf{L^3}$ and $\mathbf{L^4}$ contain one and two more oxygen atom and one and two more ethylene bridges than the macrocycle in $\mathbf{L^2}$. For $\mathbf{L^3}$ the most significant feature was a hypochromic effect observed in the presence of Pb^{2+} that could be ascribed to a weak interaction with the nitrogen atom of the macrocyclic moiety. A similar reduction in the intensity of the absorption band was found for $\mathbf{L^3}$ in the presence of Fe^{3+}. The lack of isosbestic points and the existence of complex titration patterns found for Fe^{3+} and Pb^{2+} precluded the determination of the stability constants. Addition of Hg^{2+} to solutions of $\mathbf{L^3}$ resulted in similar behaviour to that found for $\mathbf{L^1}$ and $\mathbf{L^2}$; i.e. the shift of the 575 nm absorption band of the ligand to 622 nm and the appearance of a new band at 589 nm. From titration studies a logarithm of the stability constant of 5.20 ± 0.2 for the formation of the $[Hg(\mathbf{L^3})]^{2+}$ complex was obtained. As in the above cases the red shift observed upon Hg^{2+} addition is ascribed to preferential coordination with the thiazolylazo acceptor moiety.

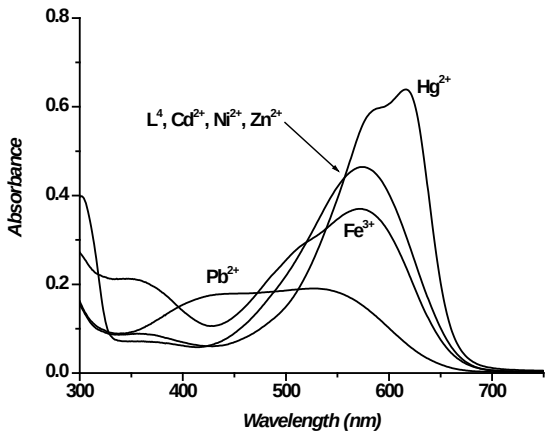


Figure 3. UV-visible behaviour of receptor $\mathbf{L^4}$ in acetonitrile (C = 2.0 x 10^{-5} mol dm^{-3}) in the presence of 1 equivalent of certain metal cations.

The hesitant selectivity trend towards Pb^{2+} found for $\mathbf{L^3}$ is fully developed when using $\mathbf{L^4}$. This ligand contains the largest macrocyclic cavity that is able to accommodate a large cation such as Pb^{2+} (anionic radius 1.19 Å).[26] In fact, addition of equimolar quantities of Pb^{2+} to acetonitrile solutions of $\mathbf{L^4}$ induced the apparition of blue shifted bands at 526 and 430 nm together with an important reduction in the absorbance intensity (see Figure 3). This strongly suggests strong coordination with the lone pair of the nitrogen atom imbebed in the macrocyle. Least square treatment of the titration profiles allows us to determine a logarithm of the stability constant of 6.17 ± 0.05 for the formation of the $[Pb(\mathbf{L^4})]^{2+}$ complex. It has to be noted that Pb^{2+} cation do not interact with $\mathbf{L^1}$ and $\mathbf{L^2}$ receptors. Apart of this

distinct response towards Pb^{2+} cation, the presence of Hg^{2+} induced a similar behaviour to that found for receptors **L**^{1}, **L**^{2} and **L**^{3}. From titration experiments a logarithm of the stability constant of 5.33 ± 0.02 for the formation of the $[Hg(\mathbf{L}^{4})]^{2+}$ complex was determined.

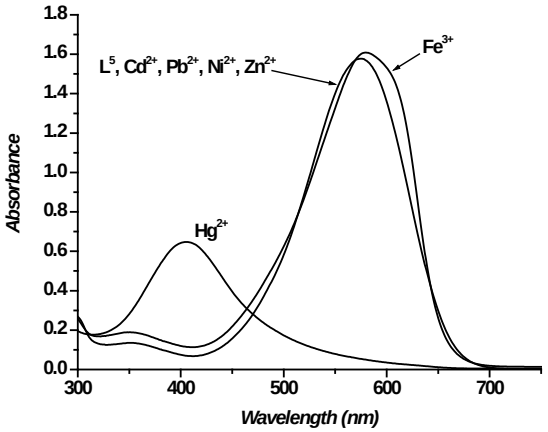


Figure 4. UV-visible behaviour of receptor **L**^{5} in acetonitrile (C = 5.0 x 10^{-5} mol dm^{-3}) in the presence of 1 equivalent of certain metal cations.

Remarkably, **L**^{5} behaves very differently to **L**^{1}-**L**^{4} and shows a selective response to Hg^{2+} due to the presence of sulphur atoms in the crown. In fact several examples of chromogenic and fluorogenic receptors functionalized with macrocycles containing two or more than two S atoms in its structure that selectively recognize Hg^{2+} cation have been described.[27] In particular the macocycle **6** has been reported by us and others to selectively coordinates Hg^{2+} over other transition-metal cations.[28] The presence in this macrocycle of two sulphur atoms close to the aniline nitrogen atom has the ability to strongly shield the site against complexation with non-thiophilic cations. Acetonitrile solutions of **L**^{5} show a charge-transfer band at 575 nm. Addition of equimolar amounts of Hg^{2+} induced a pronounced blue shift of the band to 406 nm with a colour change from blue to pale yellow (see Figure 4). This blue shift together with a high hypochromic effect is indicative of Hg^{2+} coordination within the macrocyclic subunit. This strong coordination with the crown was reflected in the high stability constant (log K = 7.63 ± 0.09) for the formation of $[Hg(\mathbf{L}^{5})]^{2+}$ complex calculated from titration profiles. This behaviour is clearly different to those shown by receptors **L**^{1}-**L**^{4}. The presence of the two S atoms in the macrocycle also induces a different behaviour in receptor **L**^{5} in the presence of the Fe^{3+} in the sense that, in this case, preferential coordination with the thiazolylazo moiety occurs. This was reflected in a slight red shift of the absorption band that was observed upon addition of Fe^{3+} to solutions of **L**^{5}. Titration profiles of receptor **L**^{5} with Fe^{3+} showed clear isosbestic points and least square treatment of the titration profiles indicated the formation of 1:1 complexes and a logarithm of the stability constant of 4.27 ± 0.08 for the formation of complex $[Fe(\mathbf{L}^{5})]^{3+}$ was calculated. As it can be seen in Figure 4 receptor **L**^{5} acts as a selective chromogenic chemosensor for Hg^{2+} cation.

The change in the position of the S atoms in the macrocycle between **L**^{5} and **L**^{6} induced a remarkable change in the coordination behaviour of the later. In this case upon addition of one equivalent of Hg^{2+} the charge-transfer band at 560 nm was shifted to 570 nm and a broad shoulder appeared at 650 nm. Also a band at 375 nm was observed. The presence of these bands at longer and lower wavelengths seems to be indicative of the simultaneous formation of metal-aniline and metal-thiazolylazo complexes, although, from the intensities of the bands, the formation of the thiazolylazo complexes appeared to be predominant. The remote position of the sulphur atoms, with respect to the nitrogen in the macrocycle, induced, upon coordination of Hg^{2+} cation with the macrocyclic subunit in **L**^{6}, poor interactions with the lone pair and a poor spectral response. Neither of the other cations tested induced significant changes in the visible spectrum of **L**^{6}.

To get a better insight into the chromophoric nature in the presence of metal cations, the interaction of Hg^{2+} with compound **L**^{1} in two different coordination modes was studied theoretically by using density functional theory (DFT) quantum mechanical calculations. As carried out before for protonations, the energies of the electronic transitions for the different complexes were obtained from calculations based on the time dependent (TD) formalism. As we have seen, the metals studied and the protons have a similar electronic effect when bind a given ligand. Both, metal and protons, accept electronic density that results in changes in the the energies of HOMO and LUMO orbitals, therefore having direct consequences on the energy of the ICLT band. In the interaction of the model compound **L**^{1} with Hg^{2+} two coordination complexes were studied; in one model the Hg^{+2} cation was coordinated by the N2 and N4 atoms of **L**^{1}, whereas in the second model the Hg^{+2} cation coordinated the aniline N1. In the theoretical calculations the remaining positions of the coordination sphere of Hg^{+2} (tetrahedral geometry) were occupied by solvent (acetonitrile) molecules. TD calculations for the chelation by coordination in N2 and N4 predict a moderate and an intense ILCT electronic transitions at 613 nm and 576 nm that are very close to those experimentally observed (610 nm and 578 nm) for complexes of Hg^{2+} with ligands from **L**^{1}, **L**^{2}, **L**^{3}, **L**^{4} and **L**^{6}. Moreover, TD calculations for the complex with the Hg^{2+} coordination at the aniline anticipated the appearance of a band at 407 nm. This result is in very good agreement with that found for the interaction of Hg^{2+} with **L**^{5} that resulted in and electronic transition at 406 nm.

Conclusions

In summary, we have prepared and characterized a family of dyes (**L**^{1}-**L**^{6}) containing a thiazolylazo group as signalling subunit and several macrocyclic cavities, with different ring sizes and type and number of heteroatoms, as binding sites. Acetonitrile solutions of receptors **L**^{1}-**L**^{6} showed absorption bands in the 554-577 nm range with typical molar absorption coefficients ranging from 20000 to 32000 M^{-1} cm^{-1}. In these spectroscopic studies involving protons, from the point of view of chemical addressability, ligands **L**^{1}-**L**^{6} posses four potential protonation sites; i.e. the aniline nitrogen, the two nitrogens from the azo moiety and the thiazole ring. From experimental data ^{1}H NMR and theoretical studies carried out using density functional theory (DFT) quantum mechanical calculations on the model ligand **L**^{1}, it was found that hypsochromic shifts were related to protonation at the aniline nitrogen, whereas bathochromic shifts dealt with

coordination at the nitrogen of the azo moiety that is closer to the aniline group. A similar behaviour (hypsochromic and bathochromic shifts) were observed in acetonitrile solutions of $\mathbf{L^1}$-$\mathbf{L^6}$ in the presence of the metal cations Fe^{3+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+}. Additionally a remarkable selective chromogenic response for $\mathbf{L^4}$ in the presence of Pb^{2+} and for $\mathbf{L^5}$ in the presence of Hg^{2+} was observed. Finally the experimental chromogenic data found for $\mathbf{L^1}$-$\mathbf{L^6}$ in the presence of Hg^{2+} cation was studied more in detail by using DFT calculations. Two different coordination modes were selected; coordination of the Hg^{2+} cation with the aniline that induced a hypsochromic shift and coordination of Hg^{2+} by two nitrogen atoms from the thiazolylazo group that resulted in a bathochromic shift. The calculations were in very good agreement with the experimental results.

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Notes and references

1 (a) L. Fabbrizzi, A. Poggi, *Chem. Soc. Rev.*, 1995, 197; (b) R. A. Bissell, A. P. de Silva, H. Q. N. Gunaratne, P. L. M. Lynch, G. E. M. Maguire, K. R. A. S. Sandanayake, *Chem. Soc. Rev.*, 1992, 187.

2 J. P. Dix, F. Vögtle, *Angew. Chem. Int. Ed. Engl.*, 1978, **17**, 857.

3 (a) R. Martínez-Máñez, F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419 (b) P. D. Beer, P. A. Gale, *Angew. Chem. Int. Ed.*, 2001, **40**, 486.

4 (a) B. Valeur, I. Leray, *Coord. Chem. Rev.*, 2000, **205**, 3; A. W. Czarnik, *Acc. Chem. Res.*, 1994, **27**, 302; K. Rurack, U. Resch-Genger, *Chem. Soc. Rev.*, 2002, **31**, 116.

5 (a) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515; (b) K. Rurack, *Spectrochim. Acta, Part A*, 2001, **57**, 2161.

6 (a) H. G. Löhr, F. Vögtle, *Acc. Chem. Res.*, 1985, **18**, 65; M. Takagi, K. Ueno, *Top. Curr. Chem.*, 1984, **121**, 39.

7 See for example: (a) J. V. Ros-Lis, R. Martínez-Máñez, F. Sancenón, J. Soto, K. Rurack, H. Weiβhoff, *Eur. J. Org. Chem.*, 2007, 2449; (b) Y. –J. Chen, W. –S. Chung, *Eur. J. Org. Chem.*, 2009, 4770; (c) H. G. Lee, J. –E. Lee, K. S. Choi, *Inorg. Chem. Commun.*, 2006, **9**, 582; (d) P. Mahato, A. Ghosh, S. Saha, S. Mishra, S. K. Mishra, A. Das, *Inorg. Chem.*, 2010, **49**, 11485.

8 (a) H. R. Hovind, *Analyst*, 1975, **100**, 769; (b) V. A. Lemos, E. S. Santos, M. S. Santos, R. T. Yamaki, *Microchim. Acta*, 2007, **158**, 189.

9 (a) M. M. Saeed, S. Z. Bajwa, M. S. Ansari, R. Ahmed, *Radiochim. Acta*, 2005, **93**, 177; (b) A. M. Starvin, P. T. Rao, *J. Hazard. Mater.*, 2004, **113**, 75.

10 (a) M. Wang, J. –M. Lin, F. Qu, X. Shan, Z. Chen, *J. Cromatograph. A*, 2004, **1029**, 249; (b) I. Takase, A. S. Luna, R. Calixto de Campos, *Talanta*, 2003, **61**, 597; (c) A. S. Amin, *Anal. Lett.*, 2001, **34**, 163.

11 (a) M. Moragues, R. Martínez-Máñez, F. Sancenón, *Chem. Soc. Rev.*, 2011, **40**, 2593; (b) R. Martínez-Máñez, F. Sancenón, M. Hecht, M. Biyical, K. Rurack, *Anal. Bioanal. Chem.*, 2011, **399**, 55; (c) R. Martínez-Máñez, J. Soto, J. M. Lloris, T. Pardo, *Trends Inorg. Chem.*, 1998, **5**, 183.

12 J. P. Dix, F. Vögtle, *Angew. Chem.*, 1978, **90**, 893.

13 D. Jiménez, R. Martínez-Máñez, F. Sancenón, J. V. Ros-Lis, J. Soto, A. Benito, E, García-Breijo, *Eur. J. Inorg. Chem.*, 2005, 2393.

14 (a) K. Higashino, T. Nakaya, E. Ishiguro, *J. Photochem. Photobiol. A*, 1994, **79**, 81; (b) H. Mustroph, J. Epperlein, *Zeitschrift Chem.*, 1983, **23**, 298.

15 (a) A. D. Becke, *Phys. Rev. A*, 1988, **38**, 3098; (b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785; (c) A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.

16 (a) A. Schaefer, A. Horn, R. Ahlrichs, *J. Chem. Phys.*, 1992, **97**, 2571; (b) P. J. Hay, W. R. Wadt, *J. Chem. Phys.*, 1985, **82**, 270; (c) *GAUSSIAN 09*; Gaussian, Inc.: Pittsburg, PA, 2009.

17 M. E. Casida, C. Jamorski, K. C. Casida, D. R. Salahub, *J. Chem. Phys.* 1998, **108**, 4439.

18 J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.*, 2005, **105**, 2999.

19 (a) J. E. Richman, T. J. Atkins, *J. Am. Chem. Soc.*, 1974, **96**, 2268; (b) T. J. Atkins, J. E. Richman, W. F. Oettle, *Org. Synth.*, 1978, **58**, 86; (c) K. E. Krakowiak, J. S. Bradshaw, D. J. Zamecka-Krakowiak, *Chem. Rev.*, 1989, **89**, 929.

20 J. V. Ros-Lis, R. Martínez-Máñez, F. Sancenón, J. Soto, M. Spieles, K. Rurack, *Chem. Eur. J.*, 2008, **14**, 10101.

21 (a) L. Forlani, P. De Maria, A. Fini, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1156; (b) P. Haake, L. P. Bausher, *J. Phys. Chem.*, 1968, **72**, 2213.

22 (a) E, Sawicki, *J. Org. Chem.*, 1957, **22**, 365; (b) O. Siiman, A. Lepp, *J. Phys. Chem.*, 1984, **88**, 2641; (c) H. Wada, O. Nakazawa, G. Nakagawa, *Talanta*, 1974, **21**, 97; (d) I. I. Pogoida, P. P. Kish, *Org. Reagenty Anal. Khim.*, 1976, **2**, 102.

23 R. M. Smith, A. E. Martell, Eds., *Critical Stability Cosntants*, Plenum, New York, Vol. 2, 1974.

24 B. García-Acosta, R. Martínez-Máñez, F. Sancenón, J. Soto, K. Rurack, M. Spieles, E. García-Breijo, L. Gil, *Inorg. Chem.*, 2007, **46**, 3123.

25 *HyperChem 6.03 Molecular Modeling System*, Hypercube Inc, Gainesville, Florida, USA, 2000.

26 See for example: (a) K. Tsubaki, D. Tanima, Y. Kuroda, K. Fuji, T. Kawabata, *Org. Lett.*, 2006, **8**, 5797; (b) H. J. Kim, S. H. Kim, J. H. Kim, L. N. Ahn, J. H. Lee, C. –H. Lee, J. S. Kim, *Tetrahedron Lett.*, 2009, **50**, 2782; (c) T. Ábalos, D. Jiménez, M. Moragues, S. Royo, R. Martínez-Máñez, F. Sancenón, J. Soto, A. M. Costero, M. Parra, S. Gil, *Dalton Trans.*, 2010, **39**, 3449; (d) M. Schmittel, H. –W. Lin, *Angew. Chem. Int. Ed.*, 2007, **46**, 893.

27 See for example: (a) E. M. Nolan, S. J. Lippard, *Chem. Rev.*, 2008, **108**, 3443; (b) X. Zhang, J. Huang, *Chem. Commun.*, 2010, **46**, 6042; (c) Q. Zhao, S. Liu, F. Li, T. Yi, C. Huang, *Dalton Trans.*, 2008, 3836; (d) H. G. Lee, J. –E. Lee, K. S. Choi, *Inorg. Chem. Commun.*, 2006, **9**, 582; (e) S. Tatay, P. Gaviña, E. Coronado, E. Palomares, *Org. Lett.*, 2006, **8**, 3857; (f) H. Lee, S. S. Lee, *Org. Lett.*, 2009, **11**, 1393; (g) S. Yoon, E. W. Miller, Q. He, P. H. Do, C. J. Chang, *Angew. Chem. Int. Ed.*, 2007, **46**, 6658; (h) K. Rurack, U. Resch-Genger, J. L. Bricks, M. Spieles, *Chem. Commun.*, 2000, 2103; (i) C. S. Lim, D. W. Kang, Y. S. Tian, J. H. Han, H. L. Hwang, B. R. Cho, *Chem. Commun.*, 2010, **46**, 2388.

28 (a) J. V. Ros-Lis, R. Martínez-Máñez, K. Rurack, F. Sancenón, J. Soto, M. Spieles, *Inorg. Chem.*, 2004, **43**, 5183; (b) A. B. Descalzo, R. Martínez-Máñez, R. Radeglia, K. Rurack, J. Soto, *J. Am. Chem. Soc.*, 2003, **125**, 3418; (c) M. Yuan, Y. Li, J. Li, C. Li, X. Liu, J. Lv, J. Xu, H. Liu, S. Wang, D. Zhu, *Org. Lett.*, 2007, **9**, 2313; (d) M. Zhu, M. Yuan, X. Liu, J. Xu, J. Lv, C. Huang, H. Liu, Y. Li, S. Wang, D. Zhu, *Org. Lett.*, 2008, **10**, 1481 (e) M. Tian, H. Ihmels, *Chem. Commun.*, 2009, 3175; (f) M. Tian, H. Ihmels, K. Benner, *Chem. Commun.*, 2010, **46**, 5719; (g) H. H. Wang, L. Xue, Y. –Y. Qian, H. Jiang, *Org. Lett.*, 2010, **12**, 292; (h) S. Atilgan, I. Kutuk, T, Ozdemir, *Tetrahedron Lett.*, 2010, **51**, 892.

