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4,4′-Substituted biphenyl coronands. Preparation of a new selective fluorescent sensor for mercury salts

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Abstract—Six new 4,4′-substituted biphenyl coronands have been prepared. The ligands containing dimethylamino groups in the biphenyl moiety have been used in transition metal cations' complexation and one of them (**3**) has demonstrated to be a selective fluorescent sensor for mercury. Stoichiometries of the formed complexes and complexation constants have been determined by titration experiments. In addition, the extractant ability of some ligands has also been studied. Finally, the electrochemical properties of some of these ligands are also described.

1. Introduction

Molecular systems that combine binding ability and photochemical or photophysical properties are of great interest for designing chemosensors.[1] Recently it has been established that conformational restriction is a viable mechanism for transducing ion binding into enhanced fluorescence emission in organic fluorophores.[2] Among the systems studied it is possible to find biphenyl and bipyridyl derivatives that experiment fluorescence enhancement after complexation. It is well established that more rigid fluorophores are more fluorescent[3] even though this restriction is due to complex formation.[4] On the other hand, it is also known that substituents in the biphenyl systems have strong influence on its fluorescent properties.[5] For all these reasons, we have been interested in using the 4,4′-bis(*N*,*N*-dimethylamino)-biphenyl (TMB, tetramethylbenzidine) subunit in the design and synthesis of red-ox and fluorescent sensors.[6] In particular our interest has been directed toward the preparation of crown ether and azacrown ether derivatives covalently attached to the 2,2′ position of TMB[7] and their use as fluorescent and red-ox chemosensors. Among all the possible target cations our interest has been mainly directed toward Cd^{2+}, Hg^{2+} and Pb^{2+} because they are highly toxic environmental pollutants and they are generated from both natural and industrial sources. In addition Zn^{2+} has been also studied due to its electronic configuration that makes it similar to Cd^{2+} and Hg^{2+}.

The studied ligands are shown in Chart 1 and in addition to the TMB moiety they contend an *ortho*-disubstituted benzene system. The presence of this additional aromatic ring has the goal of increasing the rigidity of the cavity to improve cation selectivity. In addition, several heteroatoms and functional groups are present in these ligands to study the influence of the donor atom nature.

On the other hand, solvent extraction belongs to one of the most important processes in water treatment and the use of complexing agents plays an important role in such processes. In solvent extraction of metallic ions it is possible to use a variety of ligands as extracting agents and among

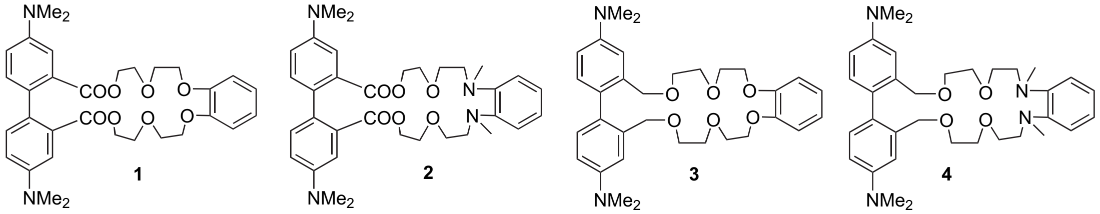

Chart 1.

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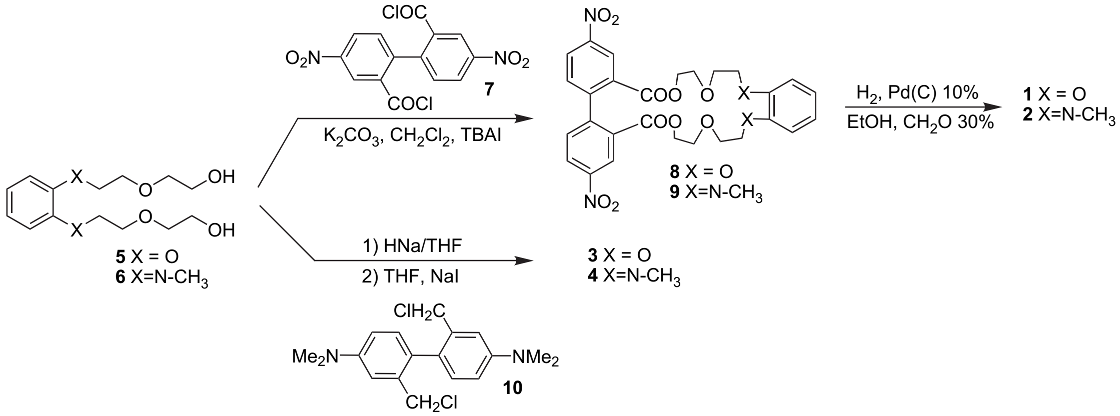


Scheme 1.

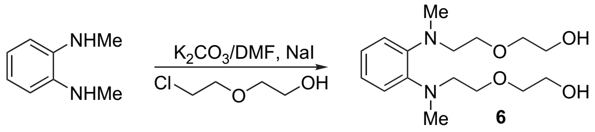
these complexing agents, macrocyclic polyethers have been widely used and the strong influence of the ligand topology on the extraction efficiency has been well established.[8] For this reason, we have been also interested in evaluating the ability of the prepared ligands in cation extraction.

2. Results and discussion

2.1. Synthesis

Ligands **1** and **2** were easily prepared as described in Scheme 1 starting, respectively, from 2,2′-bis(chlorocarbonyl)-4,4′-dinitrobiphenyl (**7**)[9] and the corresponding phenyl derivative compounds **8** and **9** could be isolated. Reductive amination of the nitro groups gave rise to the corresponding dimethylamino ligands **1** and **2**, respectively, almost with quantitative yields. On the other hand, direct reaction between 4,4′-bis(dimethylamino)-2,2′-bis(chloromethyl)biphenyl (**10**)[7] and the corresponding chains gave rise to **3** and **4**.

To carry out the syntheses described above, compound **5** was prepared from catechol as is described in the literature.[10] The synthesis of **6** was accomplished from *o-N,N*′-dimethylphenylenediamine[11] by alkylation with 2-[2-chloroethoxy]-ethanol (Scheme 2).



Scheme 2.

2.2. Complexation studies

Due to the presence of the TMB moiety in the prepared ligands, they present fluorescent properties. The influence of the cyclic systems directly bound to the 2,2′ positions of the TMB gives rise to the expected changes in the emission bands.[12] Thus, **1** and **2** present the emission band at λ_{max}=487 and 481 nm, respectively, whereas both **3** and **4** show values of 372 nm.

Complexation experiments were carried out in CH_3CN with solutions of Zn^{2+}, Cd^{2+}, Pb^{2+}, Ni^{2+}, Hg^{2+} as triflate salts. The results obtained with ligands **1**, **2** and **4** and all the studied cations were very similar, since a quenching of the fluorescence was observed after the salt addition (results obtained for ligand **4** are reflected in Fig. 1, as an example; for the other ligands, refer to Supplementary data). This behaviour could be due not only to the presence of the transition metal cation in the solution,[13] but also to the modifications in the dihedral angle between both aromatic rings or the conformational restriction induced by the complexation event.[14]

By contrast ligand **3** showed a more interesting behaviour when complexation experiments were carried out with the studied salts. Thus, even though all the cations are complexed by the ligand the fluorescent properties in each case were different. Three types of fluorescent behaviours were observed with this ligand (Fig. 2 for Zn^{2+}, Cd^{2+} and Hg^{2+} and Supplementary data for Ni^{2+} and Pb^{2+}) the most interesting result being those obtained with Hg^{2+}. In the presence of this cation a new band at λ=464 nm that could be attributed to the formation of intermolecular excimers[15,12] appears. Oppositely, Cd^{2+} and Ni^{2+} did not give rise to any modification of the fluorescence and the intensity of the new band was very small in the presence of Zn^{2+} and Pb^{2+}.

The different behaviour observed in the presence of Hg^{2+} makes compound **3** able to act as a selective fluorescent sensor for this cation. As Zn^{2+}, Cd^{2+} and Hg^{2+} have the same electronic configuration, selectivity experiments were

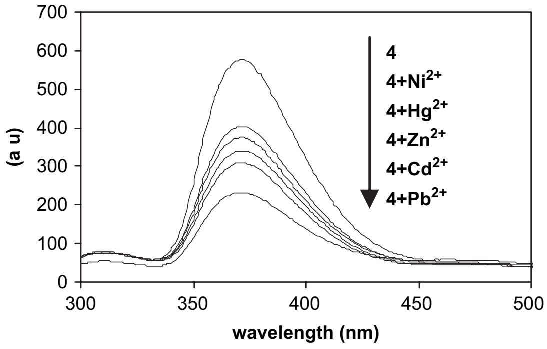


Figure 1. Fluorescent response of ligand **4** in CH_3CN in the presence of 1 equiv of Ni^{2+}, Hg^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} as triflate salts.

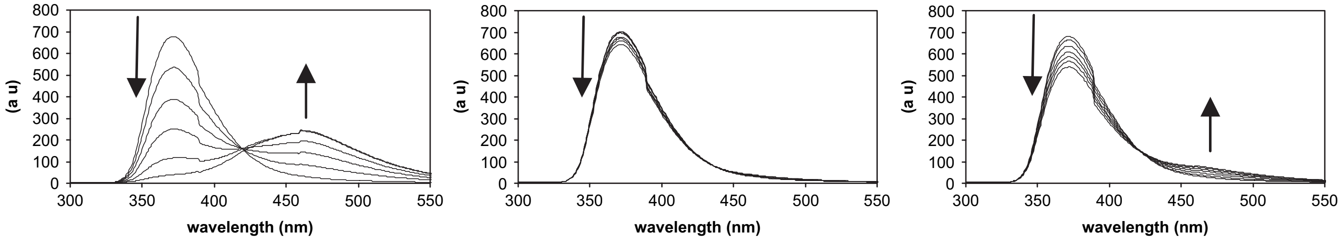


Figure 2. (From left to right) Complexation experiments with ligand **3** in CH_3CN with Hg^{2+}, Cd^{2+} and Zn^{2+}, all of them as triflate salts.

carried out with an equimolecular mixture of these three cations. The results obtained with the mixture were the same observed in the presence of pure Hg^{2+} samples (Fig. 3).

Titration experiments with the different cations using fluorescence showed that the stoichiometries of the formed complexes were always 1:1 (see Supplementary data). Complexation constants for these complexes were determined as described in Section 4 and they are reflected in Table 1.

The values of the complexation constants suggest that substitution of the ester groups for the corresponding ether groups gives rise to very small changes in Ni^{2+} and Zn^{2+} complexation and slightly larger in Cd^{2+} complexation. On the other hand, complexation of Hg^{2+} and Pb^{2+} was stronger with **3** ($\log K = 6.8 \pm 0.4$ and 6.2 ± 0.2, respectively) than with **1** ($\log K = 5.6 \pm 0.2$ and 5.3 ± 0.1, respectively) but shows the opposite tendency when **2** ($\log K = 6.3 \pm 0.4$ and 6.2 ± 0.2, respectively) and **4** ($\log K = 4.9 \pm 0.2$ and 5.9 ± 0.1, respectively) were compared. When complexation constants with ligands **3** and **4** were compared it was observed that substitution of oxygen by nitrogen atoms gives rise to stronger complexes with Ni^{2+} and Cd^{2+} and keeping similar strength with Zn^{2+}. The opposite behaviour was observed with Pb^{2+} and even more with Hg^{2+}. This behaviour agrees with both the preference of Hg^{2+} for being complexated by crown ether containing six oxygen atoms[16] and the usual coordination properties in divalent lead complexes.[17]

2.3. Extraction experiments

Extraction experiments were carried out with ligands **2**, **4**, **8** and **9** that were chosen to study the influence of different functional groups in extraction ability. Thus, comparison between ligands **2** and **4** results allows knowing the influence that ester or ether groups have in extraction properties. The preliminary extraction experiments were carried out with alkaline cations as their picrate salts. Extraction constants for these ligands determined by using the Cram's method are shown in Table 2.[18]

As can be seen in Figure 4 substitution of ester by ether groups gives rise to a big increase of the extraction properties. This behaviour could be related to two factors: (a) the higher flexibility and size showed by the cavity and (b) the much more donor character of the ether oxygen atom. Comparison between ligands **2** and **9** demonstrates that the type of substitution in the biphenyl moiety has a very small influence on extraction of Li^+ and Na^+. However, larger effects were observed with Cs^+ and even more with K^+. Thus the extraction constants for these cations were around 20 and 10 times higher, respectively, when ligand **9** was used. One explanation to this fact can be found in the higher

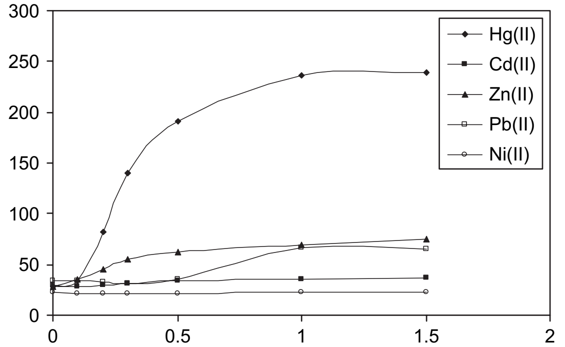


Figure 3. Effect of 1 equiv of metal ions on the emission at 470 nm for solutions of **3** (3.0×10^{-5} M) in acetonitrile.

Table 1. Complexation constants ($\log K$) for ligands **1**–**4** in acetonitrile determined by fluorescence titrations

	Ni^{2+}	Zn^{2+}	Cd^{2+}	Hg^{2+}	Pb^{2+}
1	5.1±0.5	5.9±0.3	5.8±0.2	5.6±0.2	5.3±0.1
2	6.1±0.4	5.8±0.3	5.4±0.3	6.3±0.4	6.2±0.2
3	5.7±0.5	5.9±0.2	5.7±0.2	6.8±0.4	6.2±0.2
4	6.9±0.3	5.6±0.2	7.0±0.5	4.9±0.2	5.9±0.1

Table 2. $-\log K_e$ (water/chloroform) determined by using Cram's method

	2	**4**	**8**	**9**
Li^+	2.46	4.77	4.76	2.83
Na^+	2.38	4.75	4.66	2.75
K^+	2.77	5.19	4.52	4.05
Cs^+	2.13	3.79	4.13	3.22

All the salts were picrates.

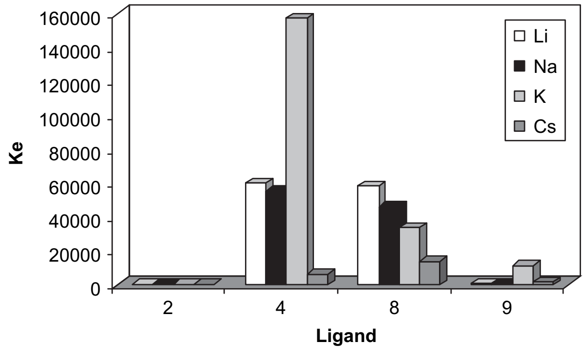


Figure 4. Comparison of alkaline cation extraction (water/chloroform) with ligands **2**, **4**, **8** and **9**.

lipophilic character of the nitro group, which is an important point for the extraction properties.

Finally, comparison between ligands **8** and **9** indicates that substitution of nitrogen atoms by oxygen atoms give rise to higher extraction, which can be related to the hard character of the alkaline cations that make stronger interactions with the harder oxygen atoms than the softer nitrogen atoms. In addition, ligand **4** extracts preferably K^+ that agrees with the relation cavity size/cation radium. By contrast, both ligands **8** and **9** show a small K^+ extraction that could be related to the smaller cavity of this ligand due to the presence of the two ester groups. As it is shown in Figure 4, extraction of Li^+ by ligands **4** and **8** is very similar. The small size of this cation allows it to form strong complexes using only four oxygen atoms. For this reason it fits as well in ligand **4** as in ligand **8**.

2.4. Electrochemical experiments

The electrochemical response of compound **4** in MeCN solution has been studied, as well as the electrochemistry of such macrocyclic receptor in the presence of an excess of different metal ions, namely, Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Ni^{2+} and Zn^{2+}. The electrochemical response at glassy carbon and platinum electrodes is dominated by two successive one-electron-transfer processes involving the oxidation of the diaminobiphenyl moiety above +1.0 V versus AgCl/Ag. The obtained results were compared with those previously reported for ligand **11**[7] (Chart 2) and the corresponding potential data are shown in Table 3.

As shown in Figure 5, corresponding to a 10^{-3} mM solution of **11** in 0.10 M Bu_4NPF_6/MeCN, the CV response of that receptor at platinum electrode consists of three overlapped anodic peaks at +0.74 (Ia), +0.92 (IIa), and +1.09 V (IIIa) coupled with their cathodic counterparts at +0.72 (Ic), +0.84 (IIc). The voltammetric profile varies slowly with the potential scan rate and remains essentially identical for experiments performed at glassy carbon electrodes, thus denoting that no adsorption processes occur. The voltammetric behaviour at platinum and glassy electrodes in DMSO solutions was almost identical to that described in MeCN. All three pairs Ia/Ic, IIa/IIc and IIIa/IIIc, can be described as essentially reversible one-electron-transfer processes as judged by the variation of anodic-to-cathodic peak potential separation with the potential scan rate, $E_{pa}-E_{pc}$. The value of this parameter tends to 60 mV at low sweep rates, as expected for a one-electron reversible process. The response of this bis(dimethylamino)biphenyl-containing receptor is consistent with that reported for the oxidation of aromatic compounds.[19] Thus, the parent neutral ligand, L, is reversibly oxidized to the corresponding radical cation $L^{\bullet+}$ and a dication, L^{2+}, in two successive one-electron-transfer steps. Consistently, the value of the peak current function (peak current/(sweep rate)$^{1/2}$) determined for the receptors studied here was almost identical to that reported for different biphenyl-type receptors at the same concentration. These correspond to the Ia/Ic and IIa/IIc couples. The presence of an additional couple IIIa/IIIc is rationalized taking into account that the overall oxidation process is accompanied by a significant stereochemical modification: there is a transition from the dihedral neutral molecule, to the planar dication. Accordingly, the first electron-transfer step yields a nonplanar cation radical ($L^{\bullet+}$) that undergoes to some extent a relatively slow pre-organization process.[20] Under similar conditions, ligand **4** shows the Ia/Ic (0.62 V) and IIa/IIc (0.91 V) couples but not the pair IIIa/IIIc. The absence of these peaks suggests that the oxidation process of ligand exclusively occurs through the nonplanar dication. In addition, a new couple (IVa/IVc) around 1.5 V due to the oxidation of the *o*-phenylenediamine appears (Fig. 5b).

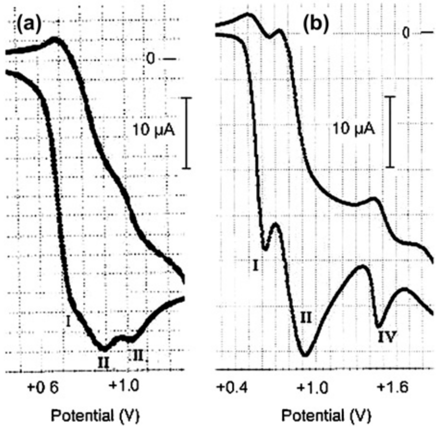


Figure 5. CVs of (a) a 2.0 mM **11** solution in 0.10 M Bu_4NPF_6/MeCN. (b) A 2.0 mM **4** solution in 0.10 M Bu_4NPF_6/MeCN. Potential scan rate 100 mV/s.

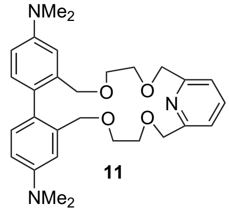


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Chart 2.

Table 3. Peak potential data in V versus AgCl/Ag for ligands **4** and **11** in MeCN solution (0.10 M Bu_4NPF_6)

Ligand	Anodic peaks			Cathodic peaks		
	Ia	IIa	IIIa	Ic	IIc	IIIc
4	+0.62	+0.91	—	+0.51	+0.74	—
4+K^+	+0.58	+0.82	—	+0.49	+0.67	—
4+Zn^{2+}	+0.85		+1.02	+0.75		+0.96
4+Cd^{2+}	+0.88		+1.04	+0.85		0.99
11	+0.74	+0.92	+1.09	+0.72	+0.84	—
11+Zn^{2+}	+0.81		—	+0.72		—
11+Cd^{2+}	+0.86		—	+0.77		—

From CVs at 100 mV/s at platinum electrode.

The most remarkable facts for compounds **11** and **4** were their different behaviours in the presence of Zn^{2+} and Cd^{2+}. For ligand **11**, the preferred way for the oxidation was through the nonplanar radical cation and thus, peak III disappeared totally and overlapping of peaks II and I was observed. The small size of this ligand precludes the rotation toward the planar radical cation. By contrast, the larger size of ligand **4** allows the transition metal cations to be located close to the softer nitrogen atoms of the *o*-phenylenediamine moiety and now the oxidation through the planar geometry is

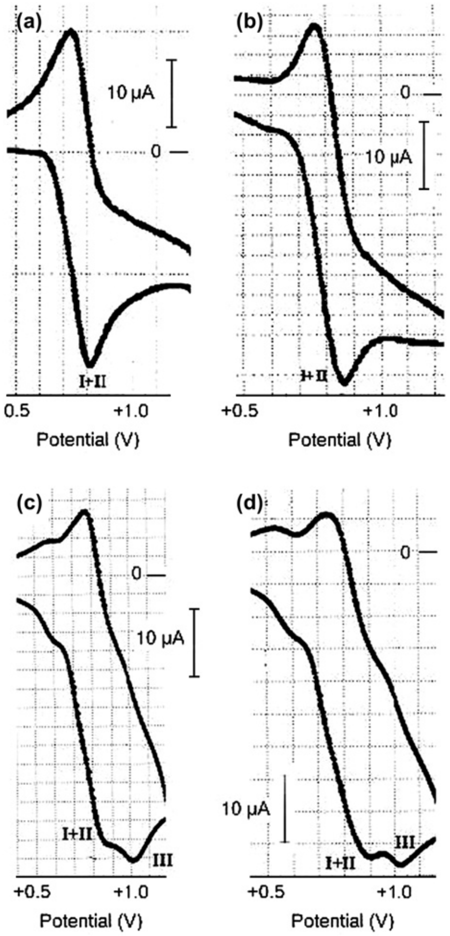

Figure 6. CVs of (a) a 2.0 mM **11**+4 times excess of Zn^{2+} solution in 0.10 M Bu_4NPF_6/MeCN. (b) A 2.0 mM **11**+4 times excess of Cd^{2+} solution in 0.10 M Bu_4NPF_6/MeCN. (c) A 2.0 mM **4**+4 times excess of Zn^{2+} solution in 0.10 M Bu_4NPF_6/MeCN. (d) A 2.0 mM **4**+4 times excess of Cd^{2+} solution in 0.10 M Bu_4NPF_6/MeCN. Potential scan rate 100 mV/s.

possible (Fig. 6). When the cation is large enough to be coordinated by the six donor atoms (for example, K^+, radio 1.33 Å) the dihedral/planar interconversion of the radical cation is precluded and only peaks I and II appear in the cyclovoltamogramme (Fig. 7).

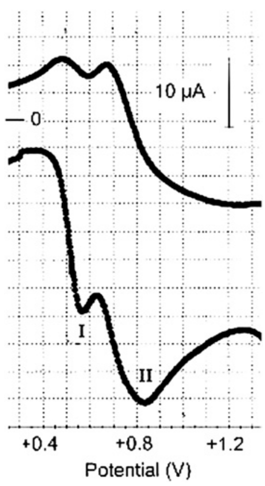

Figure 7. CVs of a 2.0 mM **4**+K^+ solution in 0.10 M Bu_4NPF_6/MeCN. Potential scan rate 100 mV/s.

3. Conclusions

Several new coronands derived from 4,4′-disubstituted biphenyl have been synthesized. Extraction experiments with alkaline cations demonstrated that these ligands showed the expected behaviour. Thus, ligand **4** was the best extractant for potassium salts. In relation to the electrochemical properties of the studied ligands, it is possible to conclude that the oxidation mechanism is strongly dependent on the cation and the cavity size. Thus, with small cations or with soft cations that are close to the nitrogen atoms the planar radical cation can be observed. By contrast with larger cations like K^+ the formation of this type of cation radical is precluded and consistently with that coordination, the couple IIIa/IIIc disappears.

In relation to the sensing properties of these ligands we can conclude that **3** showed to be a selective fluorescent sensor for Hg^{2+}. The new band observed in the fluorescent spectra of this ligand in the presence of mercury salts can be related to the formation of an excimer as it has been observed in other related compounds. Finally, it can be concluded that the presence of six oxygen atoms in the cavity gives rise to the stronger complexes with this mercury whereas ligand **4** where two oxygen atoms have been substituted by nitrogen give rise to its stronger complexes with Cd^{2+} and Ni^{2+}.

4. Experimental

4.1. General methods

All commercially available reagents were used without further purification. Water sensitive reactions were performed under argon. Column chromatography was carried out on silica gel Merck 60 (230–400 mesh) and on SDS activated neutral aluminium oxide (0.05–0.2 mm; activity degree 1). IR spectra were recorded on a Perkin–Elmer 1750 FT-IR and a Bruker Equinox 55 FT-IR. NMR spectra were recorded with Bruker Avance 300/500 and Varian Unity-300/400 spectrometers. Chemical shifts are reported in parts per million downfield from TMS. Spectra were referenced to residual undeuterated solvent. High resolution mass spectra were taken with a Fisons VG-AUTOSPEC and those using the electrospray ionizing technique were recorded on an HPLC-MS with ion trap Bruker 3000-Esquire Plus. UV spectra were run at 20 °C (thermostated) on a Shimadzu UV-2102 PC. Fluorescence spectra were carried out in a Varian Cary Eclipse Fluorimeter.

4.1.1. Synthesis of *N*,*N*′-dimethyl-*N*,*N*′-bis(ethoxyethanol)-*o*-phenylenediamine (6). *N*,*N*′-Dimethyl-*o*-phenylenediamine (2.795 g, 20.4 mmol) was added over a solution of 2-(2-chloroethoxy)ethanol (17.2 ml, 204 mmol), potassium carbonate (18 g, 130.5 mmol) and sodium iodide (5 mg) in dry toluene (160 ml). The mixture was refluxed using a Dean–Stark until the thin layer chromatography did not show starting material (72 h). After the reaction was finished, the mixture was allowed to cool at room temperature and filtered off. Solvent was evaporated under reduced pressure and the remaining oil was distilled (230 °C, 0.4 mmHg) to give **6** as a yellow oil (5.601 g, 88%). IR (KBr): 3350 (OH), 2859, 1588 (C=C), 1493, 1449, 1118 (C–O–C), 748 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ (ppm): 6.92 (4H, m, Ar–H), 3.64 (4H, t, J=5.9 Hz, CH_2–O), 3.59 (4H, t, J=5.9 Hz, CH_2–O), 3.48 (4H, t, J=5.9 Hz, CH_2–OH), 3.42 (4H, t, J=5.9 Hz, CH_2–NR_2), 2.8 (6H, s, N–CH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 145.0, 122.0, 119.2, 72.3, 68.5, 61.5, 52.4, 40.3. HRMS (EI): M^+ calcd for $C_{16}H_{24}N_2O_4$ 312.2050; found 312.2037.

4.1.2. Synthesis of 2,2′-(4,4′-dinitrobiphenyl)-10,11-benzo-2,19-dicarboxy-22-crown-6 (8). The reaction was carried out under dry conditions. Two solutions were prepared.

Solution A: 1,2-Bis(5-hydroxy-3-oxy-1-pentyloxy)benzene **5** (0.286 g, 1 mmol) in dry dichloromethane (18 ml).

Solution B: 4,4′-Dinitro-2,2′-bis(chlorocarbonyl)-biphenyl (**7**) (0.406 g, 1.1 mmol) in dry dichloromethane (18 ml).

Both solutions were added dropwise, simultaneously and at the same rate over a stirring, cold (0 °C) solution of anhydrous potassium carbonate (0.692 g, 5 mmol) and tetrabutylammonium iodide (4 mg) in dry dichloromethane (165 ml). The solution was stirred during 5 days at room temperature. Then, the suspension was filtered off, washed with ethyl acetate and the solvent was evaporated under vacuum. Purification by column chromatography (silica gel, CH_2Cl_2/MeOH 99:1) gave **8** as an orange oil (0.214 g, 37%). IR (KBr): 3418, 2928 (CH_2), 1731 (C=O), 1607 (C=C), 1504 (N=O), 1360 (N=O), 746 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.90 (2H, d, J=2.1 Hz, Ar–H), 8.43 (2H, dd, J_1=2.1 Hz, J_2=8.1 Hz, Ar–H), 7.42 (2H, d, J=8.1 Hz, Ar–H), 6.90–6.82 (4H, m, Ar–H), 4.36–4.20 (4H, m, CH_2–O), 4.11–4.06 (4H, m, CH_2–O), 3.76–3.58 (8H, m, CH_2–O). ^{13}C NMR ($CDCl_3$) δ (ppm): 149.3, 147.8, 131.4, 131.2, 126.8, 125.9, 123.5, 122.2, 120.4, 115.1, 70.1, 69.6, 69.1, 65.7. HRMS (EI): M^+ calcd for $C_{28}H_{26}N_2O_{12}$ 582.1486; found 582.1483.

4.1.3. Synthesis of 2,2′-TMB-10,11-benzo-22-crown-6 (1). An heterogeneous solution of **8** (0.384 g, 0.66 mmol), formaldehyde (0.3 ml, 30% in water) and Pd/C 10% (0.1 g) in anhydrous ethanol (50 ml) was stirred under hydrogen (30 lib/inch^2). The mixture was followed by thin layer chromatography until the reaction was finished (45 min), then the reaction was filtered off and the solid was washed with HCl 10%. The aqueous layer was basified accurately with potassium carbonate, extracted with ethyl acetate (3×25 ml) and washed with brine. Organic layers were joined, dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give compound **1** as a yellow-orange solid without further purification (0.323 g, 85%). Mp: 66–68 °C. IR (KBr): 3060, 2874, 1722 (C=O), 1608 (C=C), 1503, 1255 (C–O), 741 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.28 (2H, d, J=2.8 Hz, Ar–H), 7.09 (2H, d, J=9.0 Hz, Ar–H), 6.92–6.82 (6H, m, Ar–H), 4.24 (4H, t, J=5.1 Hz, CH_2–O), 4.09 (4H, m, CH_2–O), 3.75 (4H, m, CH_2–O), 3.61 (4H, m, CH_2–O), 2.96 (6H, s, $(CH_3)_2$–N). ^{13}C NMR ($CDCl_3$) δ (ppm): 168.9, 149.5, 142.4, 132.1, 131.1, 122.0, 122.0 115.6, 115.0, 113.9, 70.0, 69.7, 69.5, 64.5, 40.9. HRMS (EI): M^+ calcd for $C_{32}H_{38}N_2O_8$ 578.2628; found 578.2628.

4.1.4. Synthesis of 2,2′-(4,4′-dinitrobiphenyl)-*N*,*N*′-dimethyl-2,19-dicarboxy-9,12-diaza-10,11-benzo-22-crown-6 (9). Using the same procedure employed in the preparation of **8**, *N*,*N*′-dimethyl-*N*,*N*′-bis(ethoxyethanol)-*o*-phenylenediamine (**6**) (0.395 g, 1.27 mmol) and 4,4′-dinitro-2,2′-bis(chlorocarbonyl)-biphenyl **7** (0.467 g, 1.27 mmol) gave ligand **9** after chromatographic purification (neutral alumina, CH_2Cl_2/MeOH 97:3) as a pale brown oil (0.1338 g, 18%). IR (KBr): 3005, 2867, 1727 (C=O), 1608 (C=C), 1524 (N=O), 1348 (N=O), 1270, 1122, 748 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.96 (2H, d, J=2.4 Hz, Ar–H), 8.44 (2H, dd, J_1=2.4 Hz, J_2=8.4 Hz, Ar–H), 7.38 (2H, d, J=8.4 Hz, Ar–H), 6.92 (4H, m, Ar–H), 4.19 (4H, t, J=4.5 Hz, CH_2OOC), 3.54–3.29 (12H, m, CH_2–N+CH_2–O), 2.75 (6H, s, $(CH_3)_2N$). ^{13}C NMR ($CDCl_3$) δ (ppm): 164.7, 148.1, 147.8, 145.8, 131.1, 130.9, 126.6, 122.5, 119.8, 119.8, 69.0, 68.4, 65.5, 53.1, 40.3. HRMS (EI): M^+ calcd for $C_{30}H_{32}N_4O_{10}$ 608.2118; found 608.2155.

4.1.5. Synthesis of 2,2′-TMB-*N*,*N*′-dimethyl-2,19-dicarboxy-9,12-diaza-10,11-benzo-22-crown-6 (2). Following the same procedure employed in the synthesis of **1**, ligand **9** (0.2137 g, 0.35 mmol) by reductive methylation, gave compound **2** as a yellow oil without further purification (0.167 g, 80%). IR (KBr): 3002, 2868, 1714 (C=O), 1613 (C=C), 1495, 1125, 752 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.23 (2H, d, J=8.4 Hz, Ar–H), 6.92 (4H, m, Ar–H), 6.88 (2H, d, J=3 Hz, Ar–H), 6.64 (2H, dd, J=8.4 Hz, J=3 Hz, Ar–H), 4.68 (4H, dd, CH_2OOC), 4.17 (4H, dd, O–CH_2CH_2OOC), 3.67–3.34 (8H, CH_2–O+CH_2–N), 2.97 (12H, s, CH_3N), 2.95 (6H, s, CH_3N). ^{13}C NMR ($CDCl_3$) δ (ppm): 152.7, 144.8, 132.6, 132.2, 125.9, 123.1, 117.0, 117.0, 107.2, 106.3, 69.0, 66.2, 64.6, 64.3, 39.2, 35.8. HRMS (EI): M^+ calcd for $C_{34}H_{44}N_4O_6$ 604.3261; found 604.3232.

4.1.6. Synthesis of 2,2′-TMB-10,11-benzo-22-crown-6 (3). In a two-neck round bottom flask, under argon, a stirred solution of 1,2-bis(5-hydroxy-3-oxy-1-pentyloxy)benzene (**5**) (0.286 g, 1 mmol) and NaH 60% mineral oil (0.120 g, 3 mmol) in THF (50 ml) was refluxed for 2 h. 2,2′-Bis(chloromethyl)-4,4′-bis(dimethylamine)biphenyl (**10**) (0.335 g, 1 mmol) and sodium iodide (5 mg) in THF (50 ml) was added dropwise over this solution. The mixture was heated for 48 h and quenched with water. THF was removed under vacuum, the aqueous layer was extracted with ethyl acetate (3×25 ml) and organic layers were washed with brine, dried with anhydrous sodium sulfate and evaporated under reduced pressure. Column chromatography (silica gel, EtOAc to EtOAc/MeOH 95:5) gave compound **3** as pale yellow oil (0.2036 g, 37%). IR (KBr): 3080, 2867 (CH_3, CH_2), 1681 (C=O), 1608 (C=C), 1126 (C–O–C), 744 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.93 (2H, d, J=8.5 Hz, Ar–H), 6.87 (6H, m, Ar–H), 6.67 (2H, dd, J_1=2.5 Hz, J_2=8.5 Hz, Ar–H), 4.35 (4H, s, CH_2–O), 4.11 (4H, t, J=3.9 Hz, CH_2–O), 3.83–3.49 (12H, m, CH_2–O), 2.96 (12H, s, $(CH_3)_2N$). ^{13}C NMR ($CDCl_3$) δ (ppm): 150.2, 149.5, 137.9, 131.4, 128.6, 121.9, 114.9, 112.7, 111.7, 71.8, 71.2, 70.3, 70.1, 69.8, 41.1. HRMS (EI): M^+ calcd for $C_{32}H_{42}N_2O_6$ 550.3043; found 550.3056.

4.1.7. Synthesis of 2,2′-TMB-*N*,*N*′-dimethyl-9,12-diaza-10,11-benzo-22-crown-6 (4). Proceeding as in the synthesis of **3**, *N*,*N*′-dimethyl-*N*,*N*′-bis(ethoxyethanol)-*o*-phenylenediamine (**6**) (0.312 g, 1 mmol) and 2,2′-bis(chloromethyl)-4,4′-bis(dimethylamine)biphenyl (**10**) (0.335 g, 1 mmol) gave compound **4** after chromatographic purification (neutral alumina, hexane/EtOAc 50:50 to EtOAc) as a brown oil

(0.276 g, 48%). IR (KBr): 3080, 2852, 2792, 1607.82, 1493 (C=C), 1448, 1347, 1118, 1090 and 804 (C–N) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.94–6.89 (8H, m, Ar–H), 6.67 (2H, dd, J_1=3.0 Hz, J_2=8.4 Hz, Ar–H), 4.33 (4H, s, CH_2–O), 3.58–3.42 (12H, m, CH_2–O), 3.3 (4H, t, J=6.6 Hz, CH_2–N), 2.96 (12H, s, $(CH_3)_2N$), 2.73 (6H, s, CH_3–N). ^{13}C NMR ($CDCl_3$) δ (ppm): 150.2, 145.9, 138.0, 131.3, 128.4, 122.4, 119.7, 112.3, 111.6, 71.7, 70.5, 70.0, 69.2, 53.3, 41.1, 40.4. HRMS (EI): M$^+$ calcd for $C_{34}H_{48}N_4O_4$ 576.3675; found 576.3679.

4.2. Fluorescence titrations with cations. General procedure

The spectrum of free ligand (3.0 ml, 10^{-5} M) in acetonitrile was recorded. Then, an aliquot of a solution 10^{-3} M in the metallic salt and 10^{-5} M in the ligand was added (0.1 equiv), the mixture was stirred for 30 s and the spectrum was recorded. This procedure was repeated several times until the concentration of the salt was larger than the ligand and no variation of the signals was observed. The plot of the variation of the absorbance/emission versus the ratio between the salt and the complex gave the titration curve and so the stoichiometry of the complex. The constant value was calculated making use of the program Specfit.[21]

4.3. Electrochemical experiments

Electrochemical measurements were performed at 298 K in a conventional three-electrode cell under argon atmosphere. Nominal ca. 2.0 mM concentrations of the ligand were used in dry MeCN and DMSO using tetrabutylammonium hexafluorophosphate (0.10 M) as a supporting electrolyte. A 4 times excess of metallic salts was used in each case (triflate salts for the transition metal cations and perchlorate for alkaline cations). Experiments were performed using a BAS CV 50 W equipment using a BAS MF2012 glassy carbon electrode (GCE) (geometrical area 0.071 cm^2), and a BAS MF2014 platinum electrode (geometrical area 0.018 cm^2) as a working electrode. A platinum wire auxiliary electrode and a AgCl (3 M NaCl)/Ag reference electrode separated from the test solution by a salt bridge only containing supporting electrolyte completed the electrode arrangement. The potential of such reference electrode was -35 mV versus the saturated calomel reference electrode (SCE).

4.4. Extraction experiments

These experiments were carried out as described in Ref. 9.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.09.084.

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