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Redox-active Aza-crown Ethers Derived from Biphenyl. Electrochemical and Solution Studies of Complexation

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Abstract: Two new ligands **4** and **5**, containing in their structures aza-crown ethers moieties in addition to tetramethylbenzidine units, have been prepared. Their ability to complex transition metal cations has been studied by NMR and electrochemical techniques. Ligand **5** gives rise to two diastereoisomeric complexes with $Cd(NO_3)_2$.

INTRODUCTION

A combination of coronands with suitable redox-active groups has proven to be a good method for the development of receptors for the electrochemical sensing of substrates.[1] The strategy includes the selection of suitable binding site, well known for displaying large affinity for the target guest, and its subsequent functionalisation with redox-active groups.[2] We have recently reported the use of the 4,4'-bis(dimethylamino)biphenyl group framework as redox-active group.[3] This group was covalently attached to crown ethers for the electrochemical sensing of alkali and alkaline-earth cations. An interesting selective cathodic shift was found for Mg^{2+} with some tetramethylbenzidine-containing receptors. Even though there are some ligands already described that show electrochemical sensing on the basis of conformational changes[2a], the 4,4'-bis(dimethylamino) biphenyl group shows two characteristics which are not usually found in other redox-active groups such as ferrocene; (i) the oxidation can induce coplanarity in the aromatic rings (ii) there are dimethyl amino groups which can also display co-ordination towards substrates. We have now extended our previous work on biphenyl derivatives and have synthesised new aza-oxa macrocycles containing the bis(dimethylamino)biphenyl group and have studied their complexing and electrochemical behaviour in the presence of Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+} in aqueous and non aqueous environments.

RESULTS AND DISCUSSION

Synthesis and NMR studies

Preparation of aza-crown ethers **4** and **5** was accomplished by the method outlined in scheme 1.

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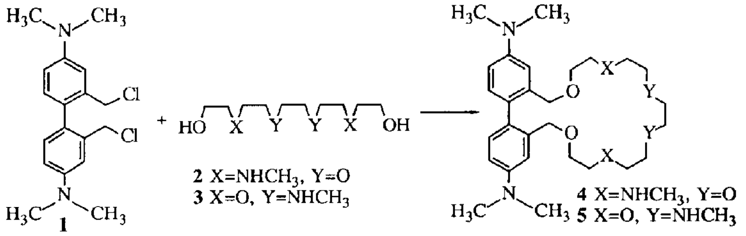
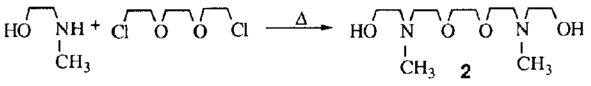
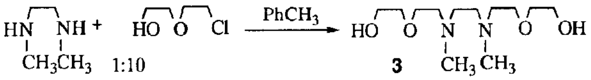
Treatment of 2,2'-bis(chloromethyl)-4,4'-dimethylaminobiphenyl (**1**)[3b] with the appropriate diol under high dilution conditions provided the cyclic ligands **4** and **5**. Compound **2** was prepared by reaction between 2-(methylamino)ethanol and 1,2-bis(2-chloroethoxy)ethane.[4] On the other hand, compound **3** was obtained from N,N-dimethylethylenediamine and 2-(2-chloroethoxy)ethanol.[5] When this last reaction was carried out using a 1:2 molar ratio the monoalkylated amine was also isolated as a byproduct. A 1:10 molar ratio was used in order to increase the yield of the dialkylated compound. In this way the desired compound was isolated in 92% yield (Schemes 2 and 3).



Scheme 1



Scheme 2



Scheme 3

Qualitative NMR studies of the complexation of $Hg(CN)_2$, $Cd(NO_3)_2$ and $Pb(NO_3)_2$ with ligands **4** and **5** were carried out in different solvents (chloroform, acetone and methanol). In these experiments ^1H NMR spectra were recorded in the presence of different amounts of the studied salt. First it was possible to establish that the metal is complexed by the aza-oxa moiety but not by the aromatic amines. Thus, signals corresponding to the diastereotopic benzylic hydrogens that appeared as two separated doublets in the free ligand **4** (δ=4.31, δ=4.20) became a singlet (δ=4.25) in the complex **4**·$Hg(CN)_2$. In addition, an upfield shift was observed not only for the methylene groups in the crown but also for the methyl groups attached to the N-donor atom. In fact, this effect on the methyl group is stronger in the lead or cadmiun complexes (δ=2.75 and δ=2.72 respectively) than in the mercury one (δ=2.18). These results could be a consequence of the greater ionic character of lead and cadmiun salts.

Similar differences were observed between the ^1H NMR spectrum of **5** and that of its mercury complex. However, more interesting results were observed when the complex of **5** with $Cd(NO_3)_2$ was studied. In this case the spectrum demonstrated the presence of two species both of them being different from the free ligand. The two complexes were also observed in the ^{13}C NMR spectrum where most of the signals were duplicated. The elemental analysis of a sample showed a 1:1 stoichiometry for the complex. For this reason the duplicity of the signals in the NMR spectra was attributed to the presence of two diastereoisomers. The presence of these two diastereoisomeric complexes could be explained taking into account the following considerations: 1) In ligand **5** three chirality elements are present (one chiral axis and two stereocenters) but only one pair of enantiomers was observed due to the fast inversion of the nitrogen atoms. 2) Among the possible diastereoisomeric forms in the free ligand only those with a relative configuration RS on the nitrogen atoms could be involved in complexation. The forms with RR or SS configurations of the nitrogen atoms are unable to direct one lone pair from each nitrogen toward the center of the complexing cavity (Figure 1). 3) The RSR and RRS diastereoisomers are meso forms. In conclusion, the two diastereoisomeric complexes correspond to the RRS and RSR configuration of the ligand. At higher temperatures the ^1H NMR spectra showed that some signals became broader and others collapsed. These results suggested that both diastereoisomeric complexes interchanged quickly at temperatures higher than 50°C. Similar observations had been described by Sutherland et al. for related compounds[6]

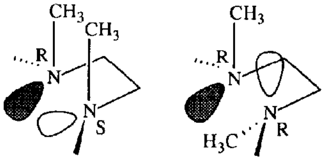


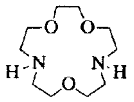
Figure 1. Configurations of the nitrogen atoms in ligand **5** suitable (R,S) and unsuitable (R,R) for complexing

Even though ligand **4** has identical chiral elements to **5**, its behaviour was completely different and only one species was observed in the NMR spectra of the cadmiun and lead complexes. This suggests that the relative position of the nitrogen atoms in the crown, far away from one another in ligand **4**, has a strong influence on the configuration interchange.

On the other hand, when the complex of **5** with $Hg(CN)_2$ was studied, only one diastereoisomer was observed. The different behaviour observed with both salts may be due to the greater covalent character of the mercury compound. One of the CN groups must pass through the cavity in order to allow the metal center to be coordinated, and this fact could make one configuration much more appropriate than the other for the whole complexation process.

Potentiometric Study.

The protonation behaviour of receptors **4** and **5** was studied in dioxane:water 70:30 v/v (0.1 mol dm^{-3} potassium nitrate, 25°C). Table 1 shows the stepwise protonation constants. Receptors **4** and **5** show two types of well defined nitrogen atoms; the ones in the macrocyclic core are expected to be more basic than the dimethylamino ones. Therefore the two first protonation constants are related to the protonation of the two nitrogen atoms in the macrocyclic cavity, whereas the last one is attributed to the protonation of the tetramethylbenzidine group. The expected second protonation process of the 4,4'-bis(dimethylamino)biphenyl moiety appears to be too acid to be determined potentiometrically. Additionally, when the two first protonation constants for these receptors are compared, the effect that the distance between the amino groups in the cavity has on the protonation process can be observed. The second protonation of receptor **5** takes place in one amine that is already close to an ammonium group and therefore due to electrostatic reasons, it behaves as a stronger acid than the amino group which protonates second in **4**. In this compound the previously formed ammonium cation is quite distant from the second protonation site. The two protonation constants of **4** and **5** can be compared to those of **6** and **7**, for which the logarithms of the constants for the processes $L + H^+ = HL^+$ and $HL^+ + H^+ = H_2L^{2+}$ are 8.76, 8.04 and 8.43, 5.77 for **6** and **7** respectively in water.



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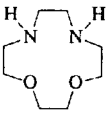

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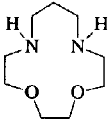

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Table 1. Stepwise protonation constants (log K) of **4** and **5** determined in dioxane:water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25°C)

Reaction	4 (log K)	5 (log K)
$L+H^+=HL^+$	8.31 (2)	8.37 (4)
$HL^++H^+=H_2L^{2+}$	7.16 (2)	3.56 (4)
$H_2L^{2+}+H^+=H_3L^{3+}$	3.79 (2)	3.13 (4)

Solution studies directed to the determination of stability constants for the formation of complexes of **4** and **5** with the metal ions Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+} for **4** and Cu^{2+}, Zn^{2+}, $Cd^{2+}$and Pb^{2+} for **5** have been also carried out in dioxane:water (70:30 v/v (0.1 mol dm^{-3} potassium nitrate, 25°C) (see Table 2 for **4** and Table 3 for **5**). Hg^{2+} was not studied with ligand **5** because of insolubility reasons.

Table 2. Stability constants (log K) for the formation of Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+} complexes of **4** in dioxane:water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25°C)

Reaction	Ni^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}
$M^{2+}+2H^++L=M(H_2L)^{4+}$	19.42(2)	18.86(2)	18.94(4)	19.84(9)	----
$M^{2+}+H^++L=M(HL)^{3+}$	12.12(3)	10.56(7)	11.63(6)	13.36(9)	16.00(3)
$M^{2+}+L=ML^{2+}$	---	4.07 (7)	3.15(7)	6.82(9)	7.97(5)
$M^{2+}+L+H_2O=ML(OH)^++H^+$	-4.15(2)	-2.90(2)	-5.34(4)	-1.40(9)	-1,34(5)
$M^{2+}+L+2H_2O=ML(OH)_2+2H^+$	-13.34(2)	-11.24(2)	-16.02(8)	-11.34(9)	-12.00(7)

Table 3. Stability constants (log K) for the formation of Cu^{2+}, Zn^{2+}, $Cd^{2+}$and Pb^{2+} complexes of **5** in dioxane:water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25°C)

Reaction	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
$M^{2+}+2H^++L=M(H_2L)^{4+}$	16.34(6)	16.81(10)	16.97(8)	16.80(5)
$M^{2+}+H^++L=M(HL)^{3+}$	12.52(4)	12.45(10)	12.50(6)	12.49(6)
$M^{2+}+L=ML^{2+}$	6.54(7)	----	4.73(3)	6.03(3)
$M^{2+}+L+H_2O=ML(OH)^++H^+$	0.12(4)	-1.63(8)	-4.63(5)	-2.13(4)
$M^{2+}+L+2H_2O=ML(OH)_2+2H^+$	-11.92(7)	-10.61(8)	-15.84(12)	-12.24(10)

Both receptors **4** and **5** form stable complexes with all the metal ions studied. Figure 2 shows the distribution diagram of the **4**-H^+-Cd^{2+} system. The logarithm of the stability constants found for the formation of the ML^{2+} complexes ($M^{2+}+L=ML^{2+}$) increases in the order $Cd^{2+}<Zn^{2+}<Pb^{2+}<Hg^{2+}$ for **4** and in the order $Cd^{2+}<Pb^{2+}<Cu^{2+}$ for **5**. Mercury has the largest stability constant over other transition metal ions. Similar coordination behaviour has also been observed in other aza-oxa crown derivatives.[7,8]

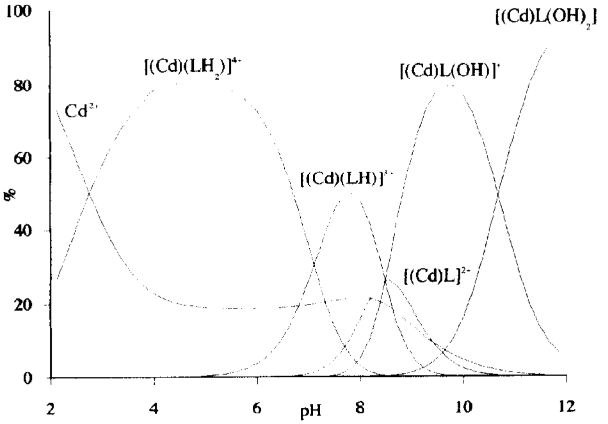

Fig. 2. Distribution diagram of the **4**·Cd^{2+} system.

For instance the logarithms of the formation constants for the species $[M(L)]^{2+}$ for ligands **6** and **8** in water with metal ions are in the sequence $Ni^{2+}<Zn^{2+}<Pb^{2+}<Cd^{2+}<Cu^{2+}<Hg^{2+}$ for **6** (log K=3.6, 5.1, 5.8, 6.4, 7.1, 16.7 respectively) and in the sequence $Zn^{2+}<Cd^{2+}<Pb^{2+}<Ni^{2+}<Cu^{2+}<Hg^{2+}$ for **8** (log K= 4.89, 5.40, 5.70, 5.83, 8.39, 13.3 respectively). Even though a different solvent has been used, the cavity in **6** and **8** appears to be much more suitable for Hg^{2+} than the cavity in **4** and **5** is. This is reflected in the very high stability constant for mercury found in its interation with **6** and **8** ($L + Hg^{2+} = [Hg(L)]^{2+}$, log K=16.7 and 13.3 for **6** and **8** respectively) that is significantly reduced with the ligand **4** is taken into account ($L + Hg^{2+} = [Hg(L)]^{2+}$, log K=7.97).

For all metal ions, except for Hg^{2+} and **4**, two protonation processes of the $[M(L)]^{2+}$ species were found ($[M(L)]^{2+} + H^+ = [M(HL)]^{3+}$ and $[M(HL)]^{3+} + H^+ = [M(H_2L)]^{4+}$). The first protonation process would take place on a nitrogen atom in the macrocyclic cavity and is a consequence of the competition between protons and metal ion coordination by the amino group. The second is probably related with protonation of the tetramethylbenzidine framework.

Electrochemical Cation Recognition.

One of the most interesting features of receptors **4** and **5** is the presence near the coordination site of an electroactive tetramethylbenzidine group. Electrochemical experiments were performed to detect the influence that the coordination of different metal ions has on the electrochemical properties of receptors **4** and **5**. RDE techniques were carried out on 4-H^+-M^{2+} (M^{2+} = Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+}) and 5-H^+-M^{2+} (M^{2+}= Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+}) in dioxane:water (70:30, 0.1 mol dm^{-3} KNO_3) as a function of the pH. The electrochemical behaviour of **4** and **5** is pH-dependent (see Figure 3) with a reversible oxidation process at ca. 630 mV vs. sce (standar calomel electrode) at basic pH that is anodically shifted to ca. 720 mV when the pH decreases. Addition of these metal ions to the solution of **4** or **5** (metal-to-ligand ratio = 1) does not produce any significant change of the L-H^+ curve. Maximum cathodic shifts were found for the interaction of **4** and Pb^{2+} in the 6-8 pH range ($\Delta E_{1/2}$ ca. 25 mV), whereas maximum anodic shifts was detected for **4** and Ni^{2+} in the same pH range ($\Delta E_{1/2}$ ca. 20 mV). This suggests some kind of electrochemical recognition, although the electrochemical shift is too small to be of practical interest. This is puzzling bearing in mind that different metals displaying distinct coordination behaviour in solution would be expected to induce different electrochemical shifts. As we have recently pointed out this might be explained by bearing in mind that when the complex is formed the oxidation process produces two effects: an electrostatic repulsion between the radical cation and the positively charged metal ion in the macrocyclic cavity and a conformational change in the receptor due to the formation of a radical cation that imposes coplanarity between both aromatic rings in order to allow delocalisation. The first effect is not difficult to evaluate and generally produces a decrease of the complex formation constant and a consequent electrochemical anodic shift (anodic shifts have also been also reported and explained on the basis of the different charge of the complex and the free receptor at a certain pH). On the contrary the second effect is more complex and conformational changes in the complexation site upon oxidation can produce either an enhancement or a decrease of the coordination ability against a target cation at a given pH.

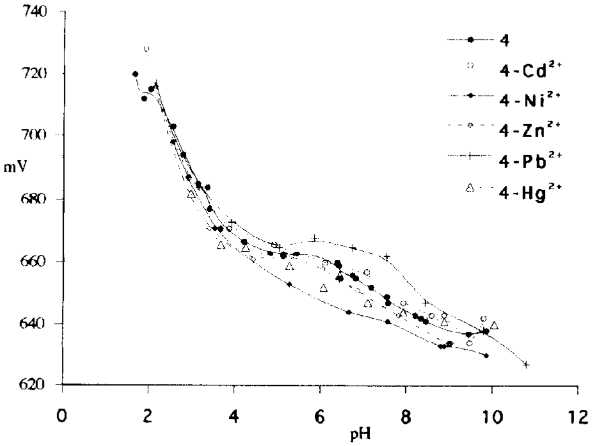

Fig. 3. Oxidation potential shift (± 5 mV) of the bis(dimethylamino)biphenyl fragment of **4** as a function of the pH with and without the presence of Cd^{2+}, Ni^{2+}, Zn^{2+}, Pb^{2+} and Hg^{2+}.

CONCLUSIONS

Receptors **4** and **5** containing a tetramethylbenzidine group as building block in aza-oxa macrocycles have been synthesised and characterised. Their coordination behaviour with transition metal ions has been investigated in aqueous environment and in aprotic solvents. The relative position of the nitrogen atoms also determines the existence of two diastereoisomeric complexes in the complexation of $Cd(NO_3)_2$ with ligand **5**. These two complexes are generated because the coordination with the metal cation hinden the inversion at the nitrogen centres. The fact that a similar behavior were not observed with ligand **4** is probably because in this compound both nitrogen atoms are quite distant from one another and their movements are not so restricted by coordination. In the aqueous environment ligands **4** and **5** are able to complex all the transition metal cations studied. The higher constants were observed in the complexation of mercury salts although these constants are not as high as when other aza-oxa macrocycles are considered. The oxidation potential of the tetramethylbenzidine group is pH-dependent. Only small shifts were observed upon addition of metal ions to a solution of **4** or **5**. Maximum cathodic and anodic displacements were found for Pb^{2+} and Ni^{2+} and **4** with $\Delta E_{1/2}$ of ca. 25 mV.

EXPERIMENTAL SECTION

General Methods

All commercially available reagents were used without further purification. Air-water sensitive reactions were performed in flame-dried glassware under argon. Tetrahydrofuran was distilled from Na-K amalgam prior to use. Column chromatographies were carried out on SDS 60 A-CC silica gel and on Scharlau activated neutral aluminium oxide (activity degree 1).

Melting points were measured on a Cambridge Instrument and a Reichter Termovar. NMR spectra were recorded on a Bruker AC-250, Varian Unity-300/400 spectrometers. Chemical shifts were reported in parts per million downfield from TMS. Spectra taken in $CDCl_3$ were referenced to either TMS or residual $CHCl_3$. When the spectra were recorded in acetone-d_6, the residual solvent was taken as reference. Mass spectra were taken on a VG-AUTOSPEC mass.

Electrohemical dara were obtained with a programmable function generator Tacussel IMT-1, connected to a Tacussel PJT 120-1 potentiostat. The working electrode was platinum with a saturated calomel reference electrode separated from the text solution by a salt bridge containing the solvent/supporting electrolyte. The auxiliary electrode was platimun wire. Potentiometric titrations were carried out in dioxane:water (70:30 v/v, 0.1 mol dm^{-3} KNO_3) using a reaction vessel water-thermostatted at 25.0 ± 0.1°C under nitrogen. Experimental potentiometric details have been previously published[3]. The computer program SUPERQUAD[9] was used to calculate the protonation and stability constants. The titration curves for each system (ca. 250 experimental points corresponding to at least three titration curves, pH = $-\log[H^+]$ range investigated 2.5-10, concentration of the ligand and metal ion was *ca.* 1.5×10^{-3} mol dm^{-3}) were treated either as a single set or as separated entities without significat variations in the values of the stability constants. Finally, the sets of data were merged together and treated simultaneously to give the stability constants.

Synthesis of N,N'-dimethyl-3,12-diaza-6,9-dioxatetradecane-1,14-diol. (2). A mixture of 2-(methylamino)ethanol (4.09 ml, 88.20 mmol) and 1,9-dichloro-3,6-dioxaoctane (0.77 ml, 4.90 mmol) was heated under reflux for 40 hours. After cooling, sodium hydroxide (0.392 g, 9.80 mmol) was added and the reaction was heated under reflux for an additional hour. Then, the starting amine was distilled and dichloromethane was added to the residue. The obtained suspension was filtered and the solvent was evaporated in vacuo. Distillation in vacuo of the crude oil gave the title compound **2** (1.79 g, 91%) as a clear oil, bp 250°C at 0.5 mm Hg; ν_{max} (liquid film) 3340, 2840, 1450, 1360, 1100, 1030 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.58-3.52 (14 H, m, C$\underline{H}_2$O, O$\underline{H}$), 2.60 (4 H, t, *J* 5.3 Hz, C$\underline{H}_2$N), 2.54 (4 H, t, *J* 5.3 Hz, C$\underline{H}_2$N), 2.28 (6 H, s, NC$\underline{H}_3$); δ_C (62.5 MHz, $CDCl_3$) 70.2, 69.1, 59.1, 58.7, 56.5, 42.6; HRMS (EI): MH$^+$ found 265.2127. $C_{12}H_{28}N_2O_4$ requires 265.2127.

Synthesis of N,N'-dimethyl-6,9-diaza-3,12-dioxatetradecane-1,14-diol (3). N,N'-dimethyl-1,2-ethanediamine (1.0 g, 11.34 mmol) was added to a suspension of 5-chloro-3-oxapetanol (11.86 ml, 113.40 mmol) and sodium carbonate (10.0 g, 72.35 mmol) in toluene (110 ml). The mixture was heated under reflux for two days in a Dean-Stark system. After cooling, the mixture was filtered and the solvent and the unreacted starting materials were evaoparted under vacuum. The residue was distilled to give the title compound 3 (2.74 g, 92%) as a clear oil, bp 240°C at 0.5 mm Hg; ν_{max} (liquid film) 3383, 2871,1470, 1354, 1120, 1061 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 4.50 (2 H, broad s, O$\underline{H}$), 3.70-3.40 (12 H, m, C$\underline{H}_2$O), 2.70-2.50 (8 H, m, C$\underline{H}_2$N), 2.19 (6 H, s, NC$\underline{H}_3$); δ_C (62.5 MHz, $CDCl_3$) 72.4, 67.8, 61.1, 56.8, 54.4, 42.2; HRMS (EI$^+$): MH$^+$ found 265.2126. $C_{12}H_{29}N_2O_4$ 265.2127.

Synthesis of 2,2'-tetramethylbenzidine-N,N'-dimethyl-6,15-diaza-22-crown-6 (4).General Procedure. Dry sodium hydride (0.170 g, 7.10 mmol) was added under an inert atmosphere to a solution of N,N'-dimethyl-3,12-diaza-6,9-dioxatetradecane-1,14-diol (0.188 g, 0.71 mmol) in dry THF (40 ml). The mixture was heated under reflux for 2 hours and then, sodium iodide (0.013 g, 0.09 mmol) was added. Subsequently, a solution of 2,2-bis(chloromethyl)4,4'-bis(dimethylamino) biphenyl (2)[3a] (0.240 g, 0.71 mmol) in dry THF (50 ml) was added dropwise over 3 hours. The reaction was additionally heated for 17 hours. the reaction was quenched with water and then, the solvent was evaporated in vacuo. The residue was dissolved in ethyl acetate (75 ml) and the organic phase was washed with water (3x25 ml) and dried with sodium sulphate. The solvent was romeved in vacuo and the crude material was purified by column chromatography (neutral alumina) to give the title compound **4** (0.252 g, 67%) as a dark yellow oil , ν_{max} (liquid film) 2920, 1607, 1550, 1492, 1350, 1203, 1121, 1030 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 6.93 (2 H, d, *J* 8.4 Hz, Ar-H), 6.89 (2 H, d, *J* 2.7 Hz, Ar-H), 6.64 (2 H, dd, *J* 8.4, 2.7 Hz, Ar-$\underline{H}$), 4.31 (2 H, *J* 12.2 Hz, Ar-C$\underline{H}_a$H$_b$), 4.24 (2 H, *J* 12.2 Hz, Ar-CH$_a\underline{H}_b$), 3.62-3.45 (12 H, m, C$\underline{H}_2$O), 2.97 (12 H, s, Ar-NC$\underline{H}_3$), 2.82-2.67 (8 H, m, C$\underline{H}_2$N), 2.38 (6 H, s, NC$\underline{H}_3$); δ_C (62.5 MHz, $CDCl_3$) 149.7, 137.2, 130.9, 127.8, 111.8, 111.2, 71.3, 70.3, 68.2, 67.9, 56.6, 56.3, 42.9, 40.6; HRMS (EI$^+$): M$^+$ found 528.3693. $C_{30}H_{48}N_4O_4$ requires 528.3676.

Synthesis of 2,2'-tetramethylbenzidine-N,N'-dimethyl-9,12-diaza-22-crown-6 (5). The product was prepared following the general procedure from 2,2'-bis(chloromethyl)-4,4'-bis(dimethylamino)biphenyl (0.668 g, 1.98 mmol) and N,N'-dimethyl-6,9-diaza-3,12-dioxatetradecano-1,14-diol (0.524 g, 1.98 mmol). The crude product was purified by chromatography (neutral alumina) to give the title compound 5 (0.356 g, 34%) as a yellow solid, mp 75°C; ν_{max} (KBr) 2870, 1451, 1307, 1226, 1204, 1011 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 6.97 (2 H, d, *J* 7.9 Hz, Ar-$\underline{H}$), 6.95 (2 H, d, *J* 2.8 Hz, Ar-$\underline{H}$), 6.67 (2 H, dd, *J* 7.9, 2.8 Hz, Ar-$\underline{H}$), 4.45-4.20 (4 H, m, Ar-C$\underline{H}_2$), 3.65-3.40 (12 H, m, C$\underline{H}_2$O), 3.00 (12 H, s, Ar-NC$\underline{H}_3$), 2.70-2.50 (8 H, m, C$\underline{H}_2$N), 2.28 (6 H, s, NC$\underline{H}_3$); δ_C (62.5 MHz, $CDCl_3$) 149.2, 136.9, 130.3, 127.6, 111.4, 110.7, 70.8, 69.9, 69.0, 68.1, 55.9, 53.7, 42.6, 40.2; HRMS (EI$^+$) M$^+$ found 528.3670. $C_{30}H_{48}N_4O_4$ 528.3676.

Synthesis of the complex. General procedure. One equivalent of the salt in acetone was added to one equivalent of the ligand in acetone. In each case the minimun amounts of acetone to dissolve the ligand and the salt were employed. The mixture was stirred in a stoppered tube for 4 hours and then the solvent was slowly evaporated to give the different complexes.

$4\cdot Hg(CN)_2$. Yellow solid, mp 90-91°C; [Found: C, 46.8; H, 5.9; N, 10.2. $C_{32}H_{52}O_6HgN_6$: requires C, 46.9; H, 6.4; N, 10.2]; δ_H (250 MHz, CD_3OD) 6.82 (2 H, d, *J* 2.4 Hz, Ar-$\underline{H}$), 6.81 (2 H, d, *J* 8.5 Hz, Ar-$\underline{H}$), 6.62 (2 H, dd, *J* 8.5, 2.4 Hz, Ar-$\underline{H}$), 4.25 (4 H, s, Ar-$C\underline{H}_2$), 3.53-2.36 (12 H, m, $C\underline{H}_2O$), 2.85 (12 H, s, Ar-$NC\underline{H}_3$), 2.79-2.46 (8 H, m, $C\underline{H}_2N$), 2.18 (6 H, s, $NC\underline{H}_3$); δ_C (62.5 MHz, CD_3OD) 151.5, 144.4, 138.0, 132.1, 129.6, 113.9, 113.1, 73.0, 71.1, 68.8, 68.1, 58.7, 58.6, 41.2, 41.0.

$4\cdot Cd(NO_3)_2$. Yellow wax, [Found: C, 45.1; H, 6.5; N, 10.4. $C_{30}H_{52}O_{12}CdN_6$ requires C, 44.8; H, 6.5; N, 10.4]; δ_H (250 MHz, CD_3OD) 6.84 (2 H, d, *J* 8.5 Hz, Ar-$\underline{H}$), 6.81 (2 H, d, *J* 2.8 Hz, Ar-$\underline{H}$), 6.63 (2 H, dd, *J* 8.5, 2.8 Hz, Ar-$\underline{H}$), 4.28 (2 H, *J* 11.6 Hz, Ar-$C\underline{H}_aH_b$), 4.21 (2 H, *J* 11.6 Hz, Ar-$CH_a\underline{H}_b$), 3.65-3.43 (12 H, m, $C\underline{H}_2O$), 3.35-3.10 (8 H, m, $C\underline{H}_2N$), 2.85 (12 H, s, Ar-$NC\underline{H}_3$), 2.72 (6 H, s, $NC\underline{H}_3$); δ_C (62.5 MHz, CD_3OD) 151.5, 137.4, 132.2, 131.3, 114.2, 113.3, 73.0, 71.3, 65.6, 65.5, 57.0, 56.8, 41.9, 41.1.

$4\cdot Pb(NO_3)_2$. Yellow wax, [Found: C, 39.9; H, 5.7; N, 9.27. $C_{30}H_{52}O_{12}PbN_6$ requires C, 40.1; H, 5.8; N, 9.4]; δ_H (250 MHz, CD_3OD) 6.84 (2 H, d, *J* 8.6 Hz, Ar-$\underline{H}$), 6.81 (2 H, d, *J* 2.4 Hz, Ar-$\underline{H}$), 6.63 (2 H, dd, *J* 8.6, 2.4 Hz, Ar-$\underline{H}$), 4.28 (2 H, *J* 11.6 Hz, Ar-$C\underline{H}_aH_b$), 4.22 (2 H, *J* 11.6 Hz, Ar-$CH_a\underline{H}_b$), 3.65-3.47 (12 H, m, $C\underline{H}_2O$), 3.40-3.10 (8 H, m, $C\underline{H}_2N$), 2.85 (12 H, s, Ar-$NC\underline{H}_3$), 2.75 (6 H, s, $NC\underline{H}_3$); δ_C (62.5 MHz, CD_3OD) 151.5, 137.4, 132.2, 129.8, 114.2, 113.3, 73.0, 71.3, 65.4, 56.9, 56.7, 41.8, 41.1.

$5\cdot Hg(CN)_2$. Yellow solid, mp 95-96°C; [Found: C, 46.8; H, 6.3; N, 10.2. $C_{32}H_{52}O_6HgN_6$ requires C, 46.9; H, 6.4; N, 10.2]; δ_H (250 MHz, CD_3OD) 6.87 (2 H, d, *J* 2.6 Hz, Ar-$\underline{H}$), 6.75 (2 H, d, *J* 8.4 Hz, Ar-$\underline{H}$), 6.57 (2 H, dd, *J* 8.4, 2.6 Hz, Ar-$\underline{H}$), 4.19 (2 H, *J* 12.8 Hz Ar-$C\underline{H}_aH_bO$), 4.12 (2 H, *J* 12.8 Hz Ar-$CH_a\underline{H}_bO$), 3.51-3.20 (12 H, m, $C\underline{H}_2O$), 2.81 (12 H, s, Ar-$NC\underline{H}_3$), 2.80-2.40 (8 H, m, $C\underline{H}_2N$), 2.14 (6 H, s, $NC\underline{H}_3$); δ_C (62.5 MHz, CD_3OD) 151.6, 138.2, 132.0, 129.6, 126.3, 113.6, 113.0, 73.5, 72.4, 71.2, 67.5, 59.3, 57.0, 41.3, 39.6.

$5\cdot Cd(NO_3)_2$._ (Diastereoisomeric mixture) Yellow wax, [Found: C, 45.1; H, 6.2; N, 10.7. $C_{30}H_{52}O_{12}HgN_6$ requires C, 44.9; H, 6.5; N, 10.5]; δ_H (250 MHz, $CDCl_3$) 6.99 (2 H, d, *J* 8.3 Hz, Ar-$\underline{H}$), 6.91 (2 H, d, *J* 8.3 Hz, Ar-$\underline{H}$), 6.88 (2 H, d, *J* 2.4 Hz, Ar-$\underline{H}$), 6.66 (4 H, dd, *J* 8.3, 2.4 Hz, Ar-$\underline{H}$), 4.61-4.16 (8 H, m, Ar-$C\underline{H}_2O$), 3.90-3.20 (24 H, m, $C\underline{H}_2O$), 2.99 (12 H, s, Ar-$NC\underline{H}_3$), 2.98 (12 H, s, Ar-$NC\underline{H}_3$), 2.90-2.60 (16 H, m, $C\underline{H}_2N$), 2.46 (6 H, s, $NC\underline{H}_3$); δ_C (62.5 MHz, $CDCl_3$) 149.8, 149.4, 137.7, 136.1, 131.5, 130.5, 127.9, 112.8, 111.7, 111.3, 111.2, 72.1, 71.7, 71.1, 71.0, 69.2, 67.8, 66.0, 65.5, 578.1, 57.3, 55.6, 54.8, 43.8, 42.8, 40.8, 40.6.

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