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FULL PAPER

4,4′-Bis(dimethylamino)biphenyl containing binding sites. A new fluorescent subunit for cation sensing

Ana M. Costero,*[a] Rosario Andreu,[a] Elena Monrabal,[a] Ramón Martínez-Máñez,*[a] Félix Sancenón[a] and Juan Soto[b]

[a] *Departamento de Química Orgánica, Universidad de Valencia, Doctor Moliner, 50, Valencia, 46100-Burjassot, Spain*
[b] *Departamento de Química, Universidad Politécnica de Valencia, Camino de Vera s/n, 46071-Valencia, Spain*

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The emission behaviour of the 4,4′-bis(dimethylamino)biphenyl subunit covalently attached to aza-crown ethers is studied. Some new ligands have been synthesised in order to test the properties of this new fluorophore. The fluorescence of these new ligands and some other compounds previously described has been studied in acetonitrile in the presence of Ni^{2+}, Cu^{2+}, Zn^{2+}, Hg^{2+}, Pb^{2+}, Cd^{2+} and also in the presence of some alkali and alkaline-earth cations.

Introduction

There has been great interest in exploring fluorescence changes in luminescent molecular systems to signal the presence of a particular substance in solution.[1] In a chemical context, sensing of molecular substrates results from the combination of two different and well-defined functions: (1) recognition of the substrate; (2) signalling to the outside recognition of the event. Hence, the simplest and most logical approach to the design of a molecular sensor would involve the coupling of two distinct components, one devoted to perform function (1), and the other to function (2). To achieve this, different binding sites have been attached to suitable signalling subunits. The target goal is to develop systems where the coordination of a certain guest would produce a selective modification of an easily macroscopically measurable physical property of the signalling part. In this context the development of fluorescent systems is especially appealing due to the lower detection limit that can be achieved compared with absorbance measurements. In fact a large number of fluorescent signalling subunits have proved suitable for the development of new receptors for substrate sensing.[2]

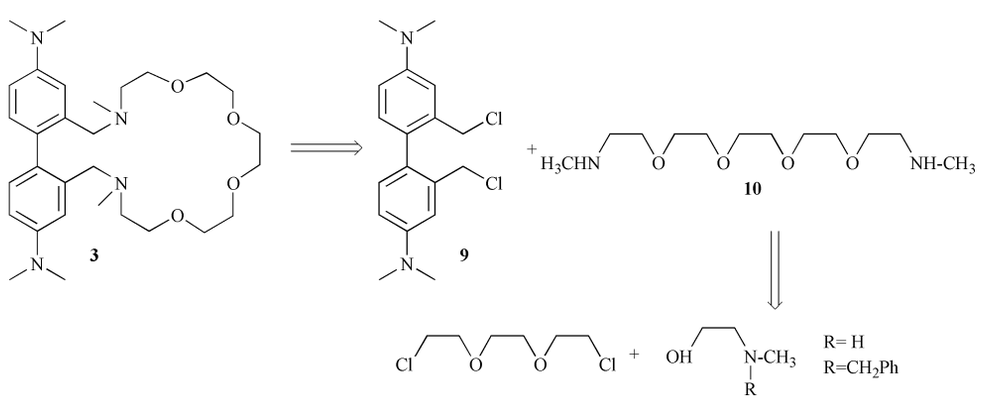
The recognition process should induce change in the intensity or the frequency of light emission. However, quenching does not appear to be the most desirable choice of fluorescent signalling of a recognition event in solution. The reason is that other species in solution, which may be present in a concentration much larger than that of the investigated analyte, can interfere, by quenching the fluorescence.

We have recently reported the use of 4,4′-bis(dimethylamino)biphenyl as a redox-active group in redox-responsive molecules.[3] This group was covalently attached to aza-crown ethers for electrochemical sensing of transition metal cations. On the other hand, the photophysical properties of the 4,4′-bis(dimethylamino)biphenyl subunit, to the best of our knowledge, have never been used for signalling the recognition of events. Therefore it was our aim to test the behaviour of this new fluorophore and so we have synthesised new aza-oxa macrocycles containing 4,4′-bis(dimethylamino)biphenyl and have studied their fluorescence behaviour in the presence of Ni^{2+}, Cu^{2+}, Zn^{2+}, Hg^{2+}, Pb^{2+}, Cd^{2+} and also in the presence of some alkali and alkaline-earth cations. A family of receptors have been synthesised varying in the size of the cavity, the number of N and O donor atoms and their relative position in the aza-crown ring.

Results and discussion

Synthesis

The studied compounds were those shown in Chart 1. Compounds **1**, **2** and **7** were prepared as described in the literature.[3] The first designed synthetic pathway for compound **3** involved the cyclization reaction between 2,2′-bis(chloromethyl)-4,4′-bis(dimethylamino)biphenyl[3b] (**9**) and 2,17-diaza-5,8,11,14-tetraoxaoctadecane (**10**) (Scheme 1). However all attempts to prepare this chain by reaction of 1,8-dichloride-3,6-dioxaoctane with *N*-methylethanolamine or *N*-benzyl-*N*-methyl-



Scheme 1

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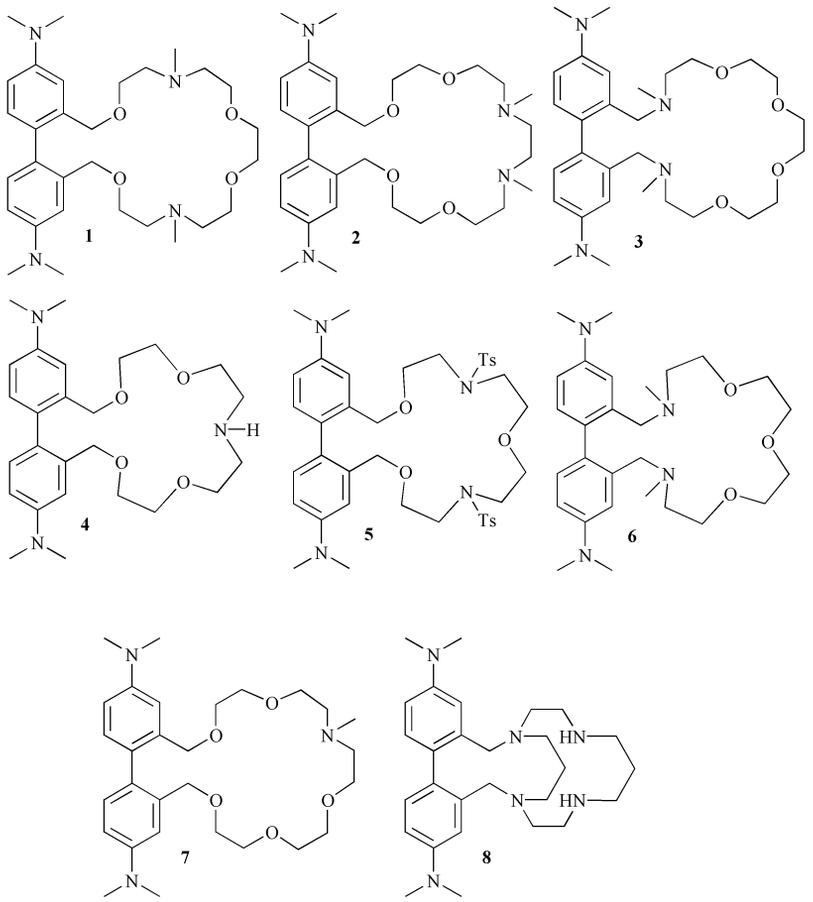
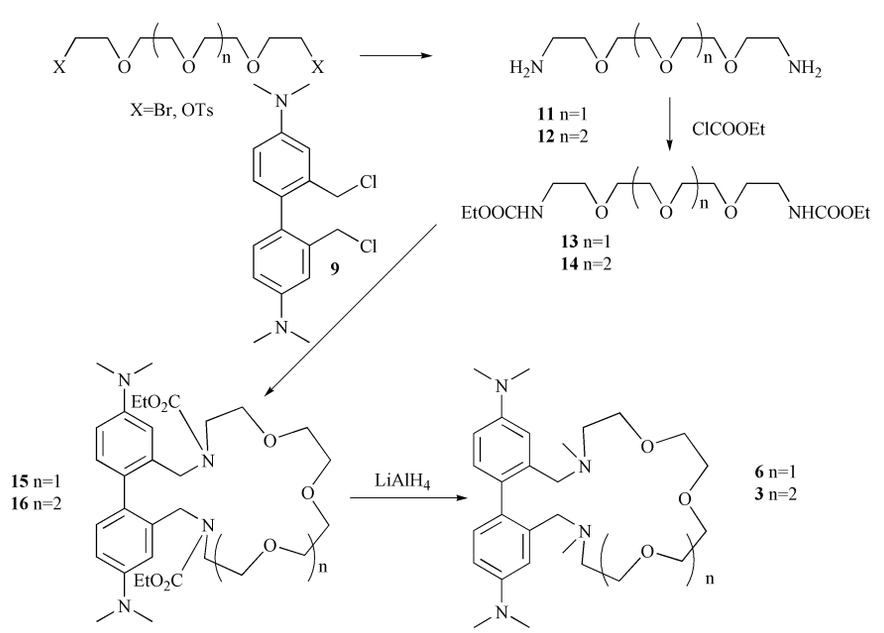


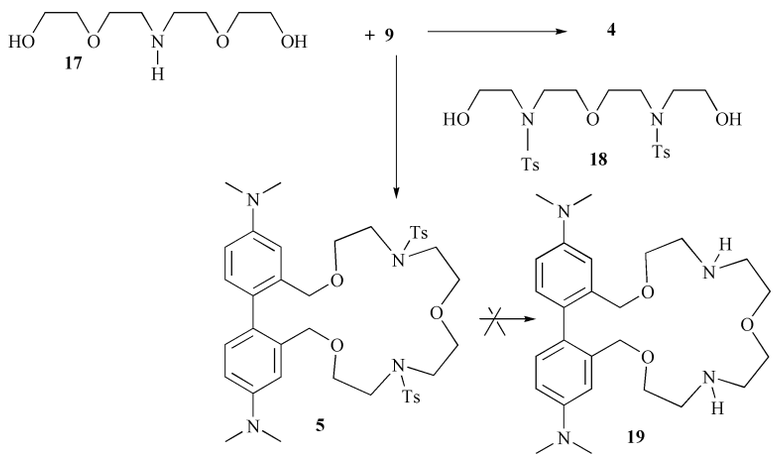
Chart 1



Scheme 2

ethanolamine in strong basic medium failed and only elimination products were isolated. Finally, aza-crown ethers **3** and **6** were obtained through the method outlined in Scheme 2. *N*,*N*′-Bis-(ethoxycarbonyl)-1,11-diamino-3,6,9-trioxaundecane (**13**), and *N*,*N*′-bis(ethoxycarbonyl)-1,14-diamino-3,6,9,12-tetraoxatetradecane (**14**), were prepared by an alternative procedure to that described by Hodgkison and Sutherland.[4] The free amines, 3,6,9-trioxaundecane-1,2-diamine (**11**), and 3,6,9,11-tetraoxatetradecane-1,14-diamine (**12**),[5] were prepared by treating tetra(ethyleneglycol)di-*para*-tosylate and penta(ethyleneglycol)-di-*para*-tosylate respectively with ammonium hydroxide under pressure. The bis-carbamate compounds, **13** and **14**, were prepared from the free amines by reaction with ethylchloroformate. The overall yields for the desired compounds were higher when this procedure was used probably because of the fewer number of steps. Cyclic compounds **15** and **16** were obtained by cyclization of the appropriate bis-carbamates with compound **9**. Treatment of **15** and **16** with lithium aluminium hydride produced ligands **6** and **3**, respectively.[6]

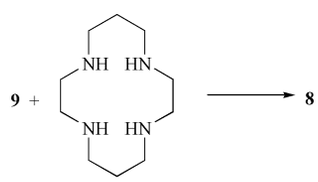
Compounds **4** and **5** were prepared by reaction of **9** with 6-aza-3,9-dioxaundecane-1,11-diol[7] (**17**), and *N*,*N*′-di-(*para*-toluensulfonyl)-3,9-diaza-5-oxaundecane-1,11-diol[8] (**18**),



Scheme 3

respectively (Scheme 3). The cyclization reactions were carried out under conditions similar to those described for compound **1**. All attempts to obtain the unsubstituted ligand **19** from **5** through a detosylation reaction failed even though different conditions were used. Thus, when reduction conditions were used ($LiAlH_4$ or Red-Al)[9] the starting material was recovered and when HBr/AcOH/PhOH[10] or H_2SO_4 was used[11] a complex mixture of products was obtained. This latter behaviour could be due to the presence of the 4,4′-bis(dimethylamino)biphenyl subunit which experiences an easy oxidation process to give the corresponding radical cation.

Finally, compound **8** was prepared from **9** and cyclam as shown in Scheme 4. The reaction was carried out in DMF and



Scheme 4

in the presence of K_2CO_3.[8] A main product could be isolated from this reaction in 54% yield. The structure of compound **8** was established by spectroscopic experiments. Thus its ^1H NMR spectrum showed two different chemical shifts for H_a and $H_{a'}$. One of these hydrogen atoms appears at a higher chemical shift as a consequence of the presence of the aromatic rings that affect each hydrogen in a different way (Chart 2).

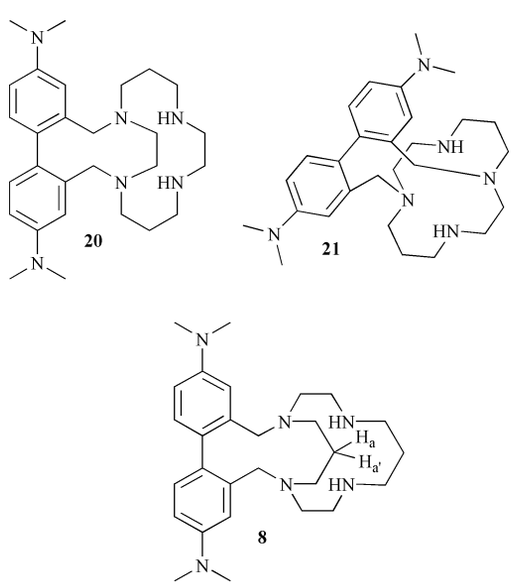


Chart 2

On the other hand, complexes of ligand **3** and **6** with $Hg(CN)_2$, $Pb(NO_3)_2$ and $Cd(NO_3)_2$ were prepared and identified by using NMR techniques. Comparative studies of the ^1H NMR data for the complexes and ligands **1** and **3** demonstrated that coordination of the cation with the nitrogen atoms is different in both types of complex. Thus, Table 1 shows the shift observed in the most significant signals for both ligands and complexes. It is clear that coordination of the cation depends on the position of the nitrogen atoms. The observed values ($\Delta\delta$ 0.50 and 0.48 ppm respectively for $Pb(NO_3)_2$ and $Cd(NO_3)_2$ with ligand **1** and 0.16 and 0.17 ppm respectively for the same salts with ligand **3**) can be related to the proximity of the metal cation to the nitrogen atoms. The position of these atoms in compound **1** allows them to be more flexible and to generate stronger interactions with the cations than those observed in ligand **3** (where the nitrogen atoms are in more fixed positions). The different behaviour of the mercury salt could be explained by taking into account its covalent character.

Fluorescence studies

Studies have been carried out with the aim of characterizing the fluorescence behaviour of the 4,4′-bis(dimethylamino)biphenyl subunit and the effect that the presence of different guests has on its emission behaviour. Receptors **1**–**8** have been designed in order to cover a wide range of structural characteristics; the ring size, the number of N donor atoms, their relative position on the ring and the nature of the N-substituted groups. Several experiments were carried out in order to establish the influence of each factor on the fluorescence behaviour under complexing conditions.

Firstly, the emission behaviour of compounds **1**, **2** and **3** was studied. These compounds show an UV-Vis sprectrum with bands in the UV region centred at 270 nm. Excitation at λ = 270 nm gave an emission band at 370 nm. Addition of alkali, alkaline-earth cations and anions (Cl^-, Br^- and HSO_4^-) to acetonitrile solutions of **1**, **2** or **3** did not produce any important change in the emission spectrum. More interesting results were observed in the presence of transition metal cations (see Fig. 1). For **1** and **2**, the Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+} metal ions produce a partial quenching of the emission band centred at 370 nm. In contrast, in the presence of Pb^{2+}, both ligands experience a selective red shift of *ca.* 50 nm of the emission band (see Fig. 1). Compound **3** also shows selective behaviour. The presence of Cu^{2+} produces a new band at *ca.* 570 nm, 200 nm shifted from the emission band of the free receptor. This new band is only obtained in the presence of Cu^{2+} and other metal ions such as Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} just produce a quenching of the 367 nm emission band. Studies carried out with ligands **1** and **3** showed that there was a linear correlation between optical change and metal ion concentration. On the other hand, the detection limits were 0.7 ppm for Pb^{2+} with

Table 1 Shifts observed in the most significant signals for ligands **1** and **3** and their complexes with $Pb(NO_3)_2$, $Cd(NO_3)_2$ and $Hg(CN)_2$

Compound	δ ^{1}HNMR					
	$N–CH_3$	$\Delta\delta$ (ppm)	$CH_2–N$	$\Delta\delta$ (ppm)	$CH_2–O$	$\Delta\delta$ (ppm)
1	2.38		2.83–2.67		3.62–3.45	
1·$Pb(NO_3)_2$	2.75	0.37	3.40–3–10	0.50	3.65–3.47	0
1·$Cd(NO_3)_2$	2.72	0.34	3.35–3.10	0.48	3.65–3.43	0
1·$Hg(CN)_2$	2.18	−0.20	2.79–2.46	−0.12	3.53–3.36	0
3	2.19		2.72–2.32		3.68–3.43	
3·$Pb(NO_3)_2$	2.29	0.10	2.87–2.50	0.16	3.70–3.10	−0.15
3·$Cd(NO_3)_2$	2.25	0.06	2.84–2.50	0.17	3.55–3.22	0.17
3·$Hg(CN)_2$	2.00	−0.19	2.70–2.45	0.05	3.56–3.20	0.17

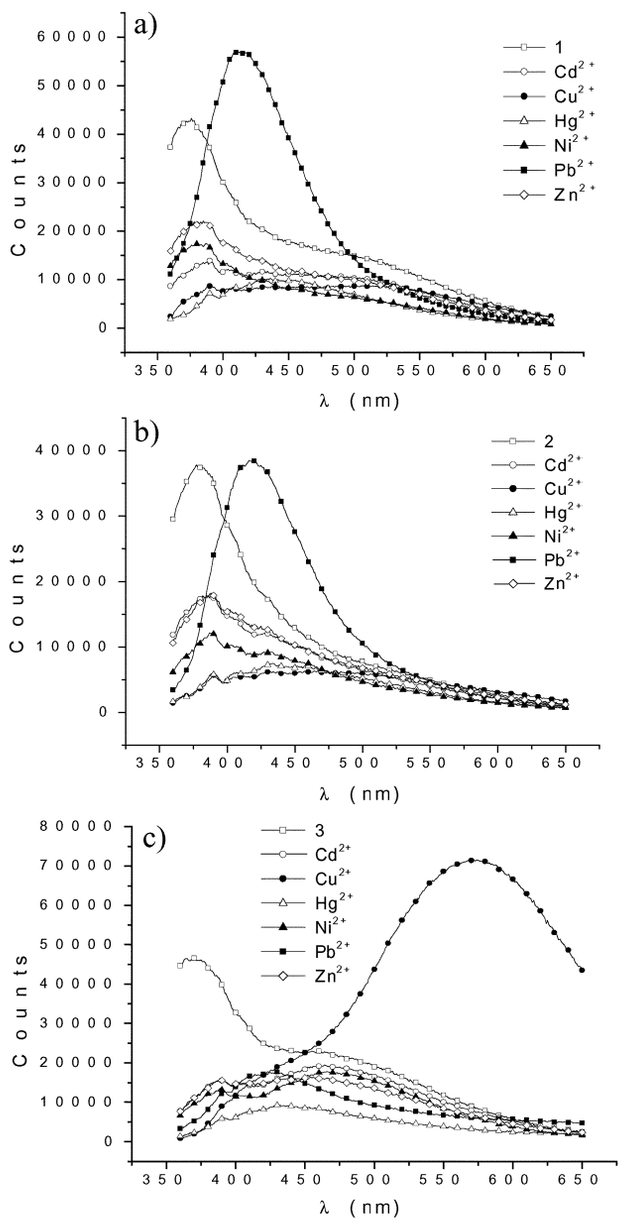


Fig. 1 Emission spectrum of a) **1**, b) **2** and c) **3** in acetonitrile in the presence of Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pd^{2+}.

ligand **1** and 0.2 ppm for Cu^{2+} with ligand **3**. The observed behaviour points out that there is a remarkable dependence on the relative position of the nitrogen atoms in the aza-crown and selectivity toward a particular cation. Transition metal ions are known to quench fluorescence very effectively, however it has also been shown that Cu^{2+}, Ni^{2+} and Pb^{2+} can cause fluorescence enhancement in a cryptand-based fluorophore due to the strong cryptate effect.[12] Similarly to the results observed by Bharadwaj *et al.*,[13] we have not observed any significant reduction wave in the cyclic voltammogram of Cu^{2+}·**3** in the range −1.0 to 1.0 (*vs.* SCE). The absence of the redox process $Cu^{2+} \longrightarrow Cu^{+}$ in the complex could explain the enhancement of the fluorescence observed in Cu^{2+}·**3**.

By contrast, the red-shift of the fluorescence emission observed remains unexplained because it is too important ($\Delta\lambda$ = 200 nm) to be only due to a metal ion induced change in polarity around the fluorophore. This emission could well be a result of an interaction involving the chromophore in its excited state.[14] This possibility is supported by the high stability of the complex. In fact, the complexation costant (in CD_3CN) was determined by a non-linear least-squares analysis of the fluorescence intensity at 370 nm *versus* the Cu^{2+} concentration using the equation derived for 1 : 1 complexes.[15] The obtained value was log $K = 6.30 \pm 0.2$ which agrees with the idea of a stable complex. Similar reasons could explain the shift observed for Pb^{2+}·**1**. Additionally, the complexation constant for Cu^{2+}·**3** could be determined and its value was log $K = 6.30 \pm 0.2$

In order to have a wider knowledge about this different response, the influence of the cavity size was also studied. For this reason, studies on compound **6** were also carried out. Thus, compound **6** has only five coordinating atoms in the cavity with the two nitrogen atoms in the same relative positions as in compound **3**. The absorption and emission spectra of the free receptor **6** in acetonitrile is, as expected, similar to that of **3** with UV bands at 269 nm that produced upon excitation a fluorescence band centred at 372 nm. In the presence of the metal cations Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} there is a quenching of the fluorescent band at 372 nm, but for Cu^{2+} a new band centred at *ca.* 525 is observed. This band is similar to that found for the Cu^{2+}·**3** system, although it is less intense for **6** than for compound **3**. In this sense, compound **8** also showed an analogous behaviour with a unique band at 425 nm for Cu^{2+} although its intensity is very poor compared with that of Cu^{2+}·**3**.

Finally, experiments in acetonitrile carried out with ligands **4**, **5** and **7** in the presence of the metal cations Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} allowed us to obtain information about the influence of the nitrogen substituents in the fluorescence response. UV-Vis spectra of **4**, **5** and **7** gave absorption bands at 271, 260 and 260 nm. Upon excitation to these λ values emission bands at 370, 450 and 420, respectively were observed for **4**, **5** and **7**. In the presence of metal ions, the most relevant feature for these receptors is that only a partial quenching was noticed but no shift or appearance of new waves was observed. Thus, for instance, compound **7** (which can be related to ligand **2**) did not present a red shift of the emission band upon Pb^{2+} complexation as receptor **2** did. All these data confirm that the fluorescence response depends on the flexibility as well as on the cavity size of the macrocyclic receptor.

Additional emission studies in an aqueous environment (1,4-dioxane : water 70 : 30 v/v) have also been carried out for receptors **1**, **2** and **3** as a function of pH. Receptors **1**, **2** and **3**

have two very different types of nitrogen atoms; those in the macrocycle and those on the biphenyl group. In a previous paper[3] we determined that the nitrogens in the macrocycle are more basic that those on the biphenyl. For instance, protonation constants for receptor **1** were determined and the logarithms of the stability constants for processes $\mathbf{1} + H^+ \rightleftharpoons H\cdot\mathbf{1}^+$, $H\cdot\mathbf{1}^+ + H^+ \rightleftharpoons H_2\cdot\mathbf{1}^{2+}$ and $H_2\cdot\mathbf{1}^{2+} + H^+ \rightleftharpoons H_3\cdot\mathbf{1}^{3+}$ were log $K = 8.31$, log $K = 7.16$ and log $K = 3.79$, respectively. The first two protonations are of the nitrogens in the aza-oxa macrocycle whereas the third corresponds to the protonation of the *N*-dimethylamino group. The second protonation of the bis-(dimethylamino)biphenyl group was too acidic to be determined. These stability constants indicate that at neutral or basic pH the predominant species are those with the aza-oxa macrocycle protonated, whereas only at acidic pH (*ca.* < 4) the species containing protonated dimethylamino groups predominate. Compounds **1**, **2** and **3** show an absorption and emission spectra in 1,4-dioxane : water (70 : 30 v/v) similar to those described above in acetonitrile. Addition of protons to basic solutions of these ligands results in a quenching of the emission band. Fig. 2 plots the relative emission intensity of compounds

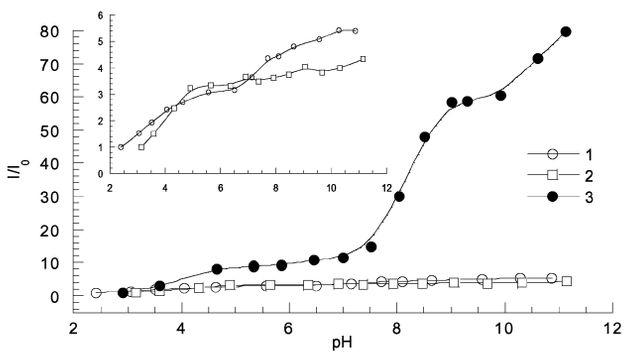


Fig. 2 Plot of the relative intensity of the emission fluorescence band at 370 nm of **1**, **2** and **3** as a function of the pH in dioxane : water 70 : 30 v/v.

1, **2** and **3** as a function of pH. The quenching of fluorescence by protonation of amines is unusual even though quenching of fluorescence by protonation of pyridines is known.[16] Normally, amines transfer an electron to the photoproduced vacancy in the HOMO of the fluorophore which quenches fluorescence. However, in the studied compounds, the diaminobiphenyl fluorophore has a rather high energy HOMO (due to its easy oxidizability), so PET from the amine is not probable.

For compounds **1** and **2**, the smaller pH dependence at pH 5–11 is because the ring N's are too far away to influence the fluorophore. Below pH 5 the fluorescence intensity falls because the anilinic nitrogen protonates and the absorption loses intensity. For compound **3**, the larger fluorescence–pH dependence above pH 7 is due to the ring N's being closer to the fluorophore; these results agree with the pK_a values previoulsy calculated. However, different reasons must explain the obtained results at pH 7–11. The explanation can be due to the fact that biphenyls try to flatten in the excited state.[17] At pH > 9 the two ring N's are free, and the biphenyl flattens normally when excited and the fluorescence is high. At lower pH values, one ring N protonates and forms a hydrogen bond with the other ring N. At still lower pH values, both ring N's protonate and the two repel each other. In either case, the two phenyl rings in biphenyl are now unable to flatten either because of an attraction or a repulsion and thus, fluorescence decreases.

Conclusions

Some new receptors containing aza-crown coronands and a photoactive group derived from biphenyl have been synthesised and characterised. To the best of our knowledge this is the first time that 4,4′-bis(dimethylamino)biphenyl groups have been used as fluorescent subunits in the design of new ligands based on the binding site and fluorescent signalling subunit concept. Ligands **1** and **2** showed a remarkable fluorescence response for Pb^{2+} and **3** shows a fluorescence response for Cu^{2+}. These receptors are new chemosensors for Pb^{2+} and Cu^{2+} sensing in acetonitrile. Additional studies pointed out that the position of the nitrogen donors within the cavity has a strong influence on the response against these metal ions. Additional modifications (size of the cavity, different susbtituents on the nitrogen atoms, *etc*.) have also been studied but they do not seem to improve selectivity. Studies in 1,4-dioxane : water 70 : 30 v/v for **1**, **2** and **3** as a function of the pH showed a noticeable behaviour with a reduction in the intensity of the fluorescent emission band when the proton concentration increases.

Experimental

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 with a Cambridge Instrument and a Reichter Termovar. NMR spectra were recorded with Bruker AC-250 and Varian Unity-300/400 spectrometers. Chemical shifts were reported in parts per million downfield from $SiMe_4$. Spectra taken in $CDCl_3$ were referenced to either $SiMe_4$ or residual $CHCl_3$. When the spectra were recorded in acetone-d_6, the residual solvent was taken as reference. Mass spectra were taken with a VG-AUTOSPEC mass. Fluorescence measurements were made with an Edinburgh Analytical Instrument using **1**–**8** with concentration *ca.* 1.0×10^{-5} mol dm^{-3} in acetonitrile and in the presence of different metal ions (Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+}; metal-to-ligand ratio 1 : 1). For some compounds fluorescence measurements were also made in 1,4-dioxane : water (70 : 30 v/v) as a function of the pH.

Preparations

Synthesis of compound 15. Dry sodium hydride (0.054 g, 2.23 mmol) was added under an inert atmosphere to a solution of *N*,*N*′-bis(ethoxycarbonyl)-3,6,9-trioxaundecane-1,11-diamine (0.30 g, 0.89 mmol) in dry DMSO (9 ml). The mixture was heated at room temperature for 2 h. Then, a solution of 2,2′-bis(chloromethyl)-4,4′-bis(dimethylamino)biphenyl (0.30 g, 0.89 mmol) in dry DMSO (6 ml) was added. The reaction was kept for two days at room temperature under an inert atmosphere. Then, the solvent was evaporated under vacuum and the crude product was purified by column chromatography (silical gel, hexane–ethyl acetate 1 : 9 to ethyl acetate–methanol 98 : 2) to give the product as a light yellow oil (0.176 g, 33%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.97 (2H, m, Ar–H), 6.65 (4H, m, Ar–H), 4.63 (1H, AB, $J = 16.9$, $ArCH_A$), 4.58 (1H, A′B′, $J = 16.9$, Ar–$CH_{A'}$), 4.20–4.08 (4H, m, CO_2CH_2), 4.01 (2H, AB,A′B′, $J = 16.9$ Ar–CH_B, Ar–$CH_{B'}$), 3.70–3.20 (16H, m, CH_2N, CH_2O), 2.96 (12H, s, Ar–N–CH_3), 1.26 (3H, t, $J = 7.2$, $CO_2CH_2CH_3$), 1.18 (3H, t, $J = 7.0$, $CO_2CH_2CH_3$) ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 156.6 (s), 149.6 (s), 137.1 (s), 130.9 (d), 127.2 (s), 110.5 (d), 110.1 (d), 70.4 (2 × t), 69.7 (t), 61.0 (t), 50.3 (t), 48.2 (t), 40.5 (q), 14.6 (q). HRMS (EI^+) calc. for $C_{32}H_{48}N_4O_7$ *m*/*z* 600.3523; found 600.3528. Anal. Calc. for $C_{32}H_{48}N_4O_7$: C, 64.00%, H, 8.00%; N, 9.33%. Found: C, 63.92%; H, 7.98%; N, 9.31%.

Synthesis of compound 16. Compound **16** was prepared from *N*,*N*′-bis(ethoxycarbonyl)-3,6,9,12-tetraoxatetradecane-1,14-diamine (0.339 g, 0.89 mmol) and 2,2′-bis(chloromethyl)-

4,4′-bis (dimethylamino)biphenyl (0.30 g, 0.89 mmol) following the procedure described in the synthesis of compound **15**. Compound **16** was isolated as a yellow oil (0.115 g, 20%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.97–6.90 (2H, m, Ar–H), 6.74–6.63 (4H, m, Ar–H), 4.66 (1H, AB, J = 15.7, $ArCH_A$), 4.64 (1H, A′B′, J = 15.7, Ar–$CH_{A'}$), 4.17–3.92 (6H, m, Ar–CH_B, $CH_{B'}$, $ArCO_2CH_2$), 3.72–3.18 (20H, m, CH_2N, CH_2O), 2.96 (12H, s, Ar–N–CH_3), 1.28–1.12 (6H, m, $CO_2CH_2CH_3$). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 156.5 (s), 149.7 (s), 136.5 (s), 131.2 (d), 128.3 (s), 112.0 (d), 110.9 (d), 70.9 (t), 70.7(2 × t), 70.5 (t), 61.1 (t), 49.9 (t), 45.8 (t), 40.6 (q), 14.5 (q). HRMS (FAB$^+$) $(M + 1)^+$ calc. for $C_{34}H_{53}N_4O_8$ *m*/*z* 645.3863; found 645.3840. Anal. Calc. for $C_{34}H_{52}N_4O_8$: C, 63.33%, H, 8.07%; N, 8.69%. Found: C, 63.34%; H, 8.11%; N, 8.65%.

Synthesis of compound 6. Lithium aluminium hydride (0.052 g, 1.36 mmol) was slowly added to a stirred solution of **15** (0.100 g, 0.17 mmol) in dry diethyl ether (6 ml) under an inert atmosphere. The mixture was stirred for 3 h at room temperature and then the reaction was quenched with some drops of water. The suspension was filtered and the solid was washed several times with diethyl ether. The organic phases were gathered and the solvent was eliminated to give **6** as a white oil that became solid after some time (0.058 g, 70%). mp 76–77 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.99 (2H, d, J = 2.7 Hz, Ar–H), 6.93 (2H, d, J = 8.3 Hz, Ar–H), 6.64 (2H, dd, ^1J = 8.3 Hz, ^2J = 2.7 Hz, Ar–H), 3.52 (2H, AB, J = 13.5 Hz, $ArCH_A$), 3.62–3.46 (12H, m, CH_2O), 3.10 (2H, AB, J = 13.5 Hz, Ar–CH_B), 2.98 (12H, s, Ar–N–CH_3), 2.55 (2H, dt, ^1J = 12.9 Hz, ^2J = 6.3 Hz NCH_CCH_2O), 2.43 (2H, dt, ^1J = 12.9 Hz, ^2J = 6.3 Hz, NCH_DCH_2O). 2.16 (6H, s, N–CH_3). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.6 (s), 138.6 (s), 131.0 (d), 129.9 (s), 113.1 (d), 110.5 (d), 71.0 (t), 70.5 (t), 69.5 (t), 59.4 (t), 57.0 (t), 43.3 (q), 40.8 (q). HRMS (EI$^+$) calc. for $C_{28}H_{44}N_4O_4$ *m*/*z* 484.3413; found 484.3410. Anal. Calc. for $C_{28}H_{44}N_4O_3$: C, 69.42%, H, 9.09%; N, 11.57%. Found: C, 69.38%; H, 9.07%; N, 11.53%.

Synthesis of compound 3. Compound **3** was prepared from **16** (0.10 g, 0.02 mmol) and lithium aluminium hydride (0.049g, 1.28 mmol) following the procedure described in the synthesis of compound **6**. **3** was isolated as a white oil (0.069 g, 81%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.01 (2H, d, J = 2.7 Hz, Ar–H), 6.93 (2H, d, J = 8.4 Hz, Ar–H), 6.64 (2H, dd, ^1J = 8.4 Hz, ^2J = 2.7 Hz, Ar–H), 3.68–3.43 (16H, m, CH_2O), 3.57 (2H, AB, J = 13.9 Hz, $ArCH_A$), 3.20 (2H, AB, J = 13.9 Hz, Ar–CH_B), 3.00 (12H, s, Ar–N–CH_3), 2.72–2.32 (4H, m,CH_2N), 2.19 (6H, s, N–CH_3) ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.4 (s), 138.3 (s), 131.0 (d), 129.5 (s), 112.8 (d), 110.3 (d), 70.8 (t), 70.5 (t), 70.4 (t), 69.4 (t), 59.9 (t), 56.7 (t), 43.3 (q), 40.7 (q). HRMS (FAB$^+$) $(M + 1)^+$ calc. for $C_{30}H_{49}N_4O_4$ *m*/*z* 529.3754; found 529.3732. Anal. Calc. for $C_{30}H_{48}N_4O_4$: C, 68.18%, H, 9.09%; N, 10.60. Found: C, 68.20%; H, 9.07%; N, 10.62%.

Synthesis of compound 4. Dry sodium hydride (0.214 g, 8.90 mmol) was added, under an inert atmosphere, to a solution of 6-aza-3,9-dioxaundecane-1,11-diol (0.172 g, 0.89 mmol) in dry THF (40 ml). The mixture was heated at reflux for 2 h and then sodium iodide (0.012 g, 0.08 mmol) was added. Subsequently, a solution of 2,2-bis(chloromethyl)-4,4′-bis(dimethylamino)biphenyl (0.30 g, 0.89 mmol) in dry THF (50 ml) was added dropwise over 3 h. The reaction was additionally heated for 17 h. The reaction was quenched with water and then the solvent was evaporated under vacuum. The residue was dissolved in ethyl acetate (50 ml) and the organic phase was washed with water (2 × 25 ml) and dried with sodium sulfate. The solvent was eliminated under vacuum and the crude was purified by column chromatography (neutral alumina) to give **4** as a dark yellow oil (0.110 g, 27%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.95 (2H, d, J = 8.4 Hz, Ar–H), 6.84 (2H, d, J = 2.6 Hz, Ar–H), 6.65 (2H, dd, ^1J = 8.4 Hz, ^2J = 2.6 Hz, Ar–H), 4.48 (2H, AB, J = 11.7 Hz, Ar–CH_A), 4.20 (2H, AB, J = 11.7 Hz, Ar–CH_B), 3.78–3.30 (13H, m, CH_2O, NH), 3.11–3.06 (4H, m, CH_2N), 2.98 (12H, s, NCH_3). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.6 (s), 136.7 (s), 130.9 (d), 128.0 (s), 112.2 (d), 111.3 (d), 71.7 (t), 70.2 (t), 69.4 (t), 66.0 (t), 47.7 (t), 40.5 (q). HRMS (EI$^+$) calcd for $C_{26}H_{39}N_3O_4$ *m*/*z* 457.2941; found 457.2944. Anal. Calc. for $C_{26}H_{39}N_3O_4$: C, 68.27%; H, 8.53%; N, 9.19%. Found: C, 68.30%; H, 8.51%; N, 9.22%.

Synthesis of compound 5. The product was prepared following the general procedure from *N*,*N*′-di(*para*-toluensulfonyl)-3,9-diaza-6-oxaundecane-1,11-diol (0.711 g, 1.42 mmol) and 2,2′-bis(chloromethyl)-4,4′-bis(dimethylamino)biphenyl (0.480g, 1.42 mmol). **5** was purified by column chromatography (neutral alumina) as a white solid (0.456g, 42%). mp 61 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.67 (4H, d, J = 8,5 Hz, Ar–H), 7.28 (4H, d, J = 8.5 Hz, Ar–H), 6.92 (2H, d, J = 8.3 Hz, Ar–H), 6.81 (2H, d, J = 2.6 Hz, Ar–H), 6.63 (2H, dd, ^1J = 8.3 Hz, ^2J = 2.6 Hz, Ar–H), 4.18 (4H, s, Ar–CH_2O), 3.56–3.24 (16H, m, CH_2O, CH_2N), 2.96 (12H, s, N–CH_3), 2.41 (6H, s, CH_3–Ar). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.7 (s), 143.2 (s), 137.2 (s), 136.9 (s), 130.9 (d), 129.6 (d), 128.0 (s), 127.0 (d), 111.9 (d), 111.3 (d), 71.4 (t), 71.0 (t), 69.2 (t), 48.9 (t), 40.6 (q), 21.5 (q). HRMS (FAB$^+$) $(M + 1)^+$ calc. for $C_{40}H_{52}N_4S_2O_7$ *m*/*z* 764.3277; found 764.3308. Anal. Calc. for $C_{40}H_{52}N_4S_2O_7$: C, 62.82%, H, 6.80%; N, 7.32%; S, 8.37%. Found: C, 62.79%; H, 6.75%; N, 7.31%; S, 8.40%.

Synthesis of compound 8. 2,2′-Bis(chloromethyl)-4,4′-bis-(dimethylamino)biphenyl (0.30 g, 0.89 mmol), cyclam (0.17 g, 0.95 mmol) and potassium carbonate (0.61 g, 4.45 mmol) were heated at 70 °C in 10 ml of DMF for 24 h. After this time the solvent was removed by distillation and the residue was dissolved in water (60 ml). The aqueous phase was extracted with ethyl acetate (3 × 50 ml) and the organic phase after having been dried with sodium sulfate was evaporated. Compound **8** was purified by column chromatography (neutral alumina, AcOEt : MeOH 98 : 2) to give a white solid (54%). mp 152–153 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.28 (2H, d, J = 8.0Hz, Ar–H), 6.70 (2H, d, J = 8.0 Hz, Ar–H), 6.62 (2H, s, Ar–H), 4.31 (4H, dd, ^1J = 15.1 Hz, ^2J = 7.2 Hz), 3.58–3.19 (12H, m, N–CH_2), 2.92 (12H, s, N–CH_3), 2.68 (2H, s, NH), 2.57 (4H, t, J = 4.7 Hz, N–CH_2), 1.89–1.76 (3H, m), 1.69–1.60 (1H, m). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.7 (s), 134.9 (s), 129.7 (s), 127.6 (d), 113.6 (d), 111.8 (d), 61.5 (t), 56.3 (t), 52,6 (t), 48.3 (t), 44.5 (t), 40.5 (q), 27.6 (t), 25.9 (t). HRMS (FAB$^+$) $(M)^+$ calc. for $C_{28}H_{44}N_6$ *m*/*z* 464.6958; found 464.6949. Anal. Calc. for $C_{28}H_{44}N_6$: C, 72.41%, H, 9.48%; N, 18.10%. Found: C, 62.43%; H, 9.45%; N, 18.10%.

Synthesis of complexes. General procedure

One equivalent of the salt in acetone was added to one equivalent of the ligand in acetone. In every case the minimun amount of acetone to dissolve the ligand and the salt were employed. The mixture was stirred in a stoppered tube for 4 h and then the solvent was slowly evaporated to give the different complexes.

3·Hg(CN)$_2$. Yellow wax. Yield 82%. ^{1}H NMR (250 MHz, CD_3OD) δ 6.86 (2H, d, J = 2.7 Hz, Ar–H), 6.80 (2H, d, J = 8.4 Hz, Ar–H), 6.61 (2H, dd, ^1J = 8.4 Hz, ^2J = 2.7 Hz, Ar–H), 3.56–3.20 (20H, m, Ar–CH_2,CH_2O), 2.84 (12H, s, Ar–NCH_3), 2.70–2.45 (4H, m, CH_2N), 2.00 (6H, s, NCH_3). ^{13}C NMR (62.5 MHz, CD_3OD) δ 151.5 (s), 143.7 (s, CN), 137.3 (s), 132.8 (d), 131.7 (s), 114.8 (d),113.1 (d), 71.7 (t), 71.5 (t), 71.4 (t), 69.8 (t), 60.9 (t), 57.8 (t), 42.8 (q), 41.2 (q). MS (FAB$^+$) $(M)^+$ 780. Anal. Calc. for $C_{32}H_{48}N_6O_4Hg$: C, 49.19%, H, 6.19%; N, 10.76%. Found: C, 49.26%; H, 5.99%; N,10.68%.

3·Cd(NO$_3$)$_2$. Yellow wax. Yield 73%. ^{1}H NMR (250 MHz, CD_3OD) δ 6.88 (2H, d, J = 8.4 Hz, Ar–H), 6.77 (2H, d, J = 2.7 Hz, Ar–H), 6.69 (2H, dd, ^1J = 8.4 Hz, ^2J = 2.7 Hz, Ar–H),

3.89–3.77 (4H, m, Ar–CH_2), 3.55–3.22 (16H, m, CH_2O), 2.86 (12H, s, Ar–NCH_3), 2.84–2.50 (4H, m, CH_2N), 2.25 (6H, s, NCH_3). ^{13}C NMR (62.5 MHz, CD_3OD) δ 151.5 (s), 135.3 (s), 132.8 (d), 130.7 (s), 116.0 (d),113.8 (d), 71.7 (t), 71.1 (t, t), 67.6 (t), 61.2 (t), 57.7 (t), 42.6 (q), 40.8 (q). MS (FAB$^+$) $(M + 1)^+$ 765. Anal. Calc. for $C_{30}H_{48}N_6O_{10}Cd$: C, 47.09%, H, 6.32%; N, 10.98%. Found: C, 47.98%; H, 6.30%; N, 11.01%.

3·Pb(NO$_3$)$_2$. Yellow wax. Yield 77%. ^{1}H NMR (250 MHz, CD_3OD) δ 6.90 (2H,d, J = 8.4 Hz, Ar–H), 6.76 (2H, d, J = 2.6 Hz, Ar–H), 6.71 (2H, dd, ^1J = 8.4 Hz, ^2J = 2.6 Hz, Ar–H), 3.95 (2H, AB, J = 13.5 Hz, Ar–CH_A), 3.70–3.10 (18H, m, Ar–CH_B, CH_2O), 2.88 (12H, s, Ar–NCH_3), 2.87–2.50 (4H, m, CH_2N), 2.29 (6H, s, NCH_3). ^{13}C NMR (62.5 MHz, CD_3OD) δ 151.6 (s), 134.4 (s), 132.9 (d), 130.4 (s), 116.0 (d), 114.1 (d), 71.7 (2 × t), 71.1 (t), 67.2 (t), 60.9 (t), 42.3 (q), 40.8 (q). MS (FAB$^+$) $(M + 1)^+$ 860. Anal. Calc. for $C_{32}H_{48}N_6O_{10}Pb$: C, 41.90%, H, 5.63%; N, 9.77%. Found: C, 41.85%; H, 5.60%; N, 9.79%.

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