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Macrolactones and Crown Ethers Derived from Biphenyl. Electronic and Steric Influence of Substituents on its Complexation Ability

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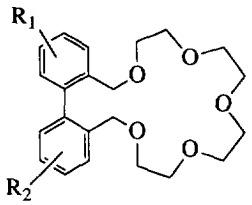
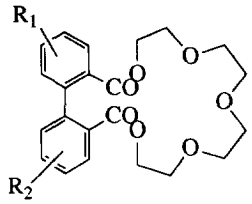
Abstract. Electronic effects as well as steric hindrance must be considered in order to compare the ability of macrolactones and crown ethers for complexing alkali cations and $Hg(SCN)_2$.

During the last few years our research group has been interested in studying crown ethers containing biphenyl units in their structures. Different reasons justify this interest: first, the rigidity of the biaryl framework would be used to design receptors presenting allosteric behaviour.[1,2] In addition, the chirality observed in some biphenyl derivatives could permit to prepare ligands for chiral recognition.[3]





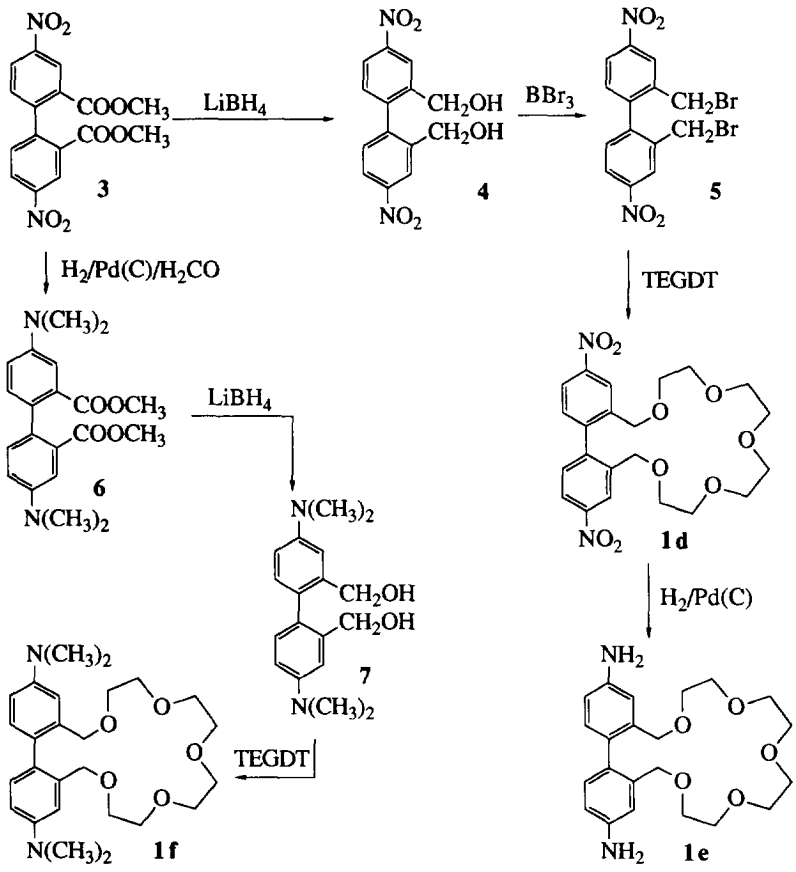
1a $R_1=R_2=$ 6-OCH_3
1b $R_1=R_2=$ 6-OH
1c $R_1=$ 6-OH; $R_2=$ 6'-OCH_3
1d $R_1=R_2=$ 4-NO_2
1e $R_1=R_2=$ 4-NH_2
1f $R_1=R_2=$ 4-$N(CH_3)_2$

2a $R_1=R_2=$ 6-OCH_3
2b $R_1=R_2=$ 4-NO_2
2c $R_1=R_2=$ 4-NH_2
2d $R_1=R_2=$ 4-$N(CH_3)_2$

Previous experiments[4] showed that the ability of biphenyl crown ethers and lactones to extract alkali picrates strongly depends on steric and electronic effects. In addition to compounds **1a-b** and **2a-b** previously studied, compounds **1c-f** and **2c-d** have been recently synthesized, in order to have more complete information about the influence of these factors. In this way, it was possible to study a series of compounds with sustituents of different electronic characteristics and placed in different positions.

The new crown derivatives have been prepared through different pathways. Thus, compound **1c** was obtained from **1a** by a demethylation reaction using nucleophilic conditions ($NaSCH_2CH_3$/DMF).[5] The synthesis of **1d** was achieved from 4,4´-dinitro-2,2'-diphenic acid dimethyl ester, **3**, that was reduced with $LiBH_4$ to give alcohol **4**;[6] from it, **5** was prepared by reaction with boron tribromide.[7] Cyclization of **5** with tetraethylene glycol ditosylate (TEGDT) yields **1d** in 6.2%. Catalytic hydrogenation of **1d** allowed us to

isolate **1e**. On the other hand, compound **2c** was prepared by reduction of **2b** under catalytic conditions. This compound proves to be very unstable even at low temperature and under inert or reducing atmosphere. Compound **1f** was prepared using **3** as starting material. Thus, **3** was converted into **6** by reaction with formaldehyde under reducing conditions (H_2 and Pd(C)).[8] Reduction of compound **6** gave the alcohol **7** and from it **1f** could be synthesized under the appropriate conditions.



Macrolactones **2c-d** were prepared from **2b**. Thus, **2c** was obtained through catalytic hydrogenation and as it was suspected, this compound proves to be even more unstable than compound **1e**. On the other hand, the reaction of **2b** with formaldehyde and hydrogen under catalytic conditions afforded **2d**.

COMPLEXATION STUDIES

Mercury Derivatives

All the studied crown ethers were able to form solid complexes with $Hg(SCN)_2$. The ^1H NMR spectra of these compounds in d_6-acetone allowed us to determine the corresponding complexation constants. These

calculations could be done because, in all cases, sufficient separation between one signal of the free ligand and the same one of the complexed form was observed. The results obtained are shown in Table 1.

Compounds **1a-c** have electron donating groups in the biphenyl system and in all the cases substituents are in the 6,6' positions. Consequently, no great differences in complexation constants should be expected for all these ligands. However, compound **1b** showed a value lower than those observed in compounds **1a** and **1c**. This fact could only be explained if some structural characteristic hindered the crown from adopting a conformation suitable for complexing the guest. Molecular mechanics calculations using MACROMODEL[9] showed that ligand **1b** presented one hydrogen bond between the -OH group on one phenyl ring and the oxygen of the benzyl ether corresponding to the other aromatic ring. Even though theoretical calculations described ligand conformations in gas phase, the presence of this hydrogen bond agreed with the lower value of the association constant observed for **1b**.

Table 1. Complexation Constants (K_a (M^{-1}), d_6-acetone, 25°C)

Ligand	$Hg(SCN)_2$	Na^+
1a	$2.7\ 10^3$	96.9
1b	$6.1\ 10^2$	83.3
1c	$5.3\ 10^3$	358.6
1d	$2.3\ 10^2$	42.3
1f	$1.0\ 10^3$	106.7
2a	------	19.4
2b	------	------
2d	------	28.0

In adition, molecular mechanic calculations showed a clear difference between **1b** and **1c** (Figure 1). Compound **1c** also possessed one hydrogen bond in its structure, but in this case it is formed between the -OH hydrogen and the oxygen of the methoxy group. This fact permits the oxygens to direct their lone pair toward the metal atom in a more effective way.

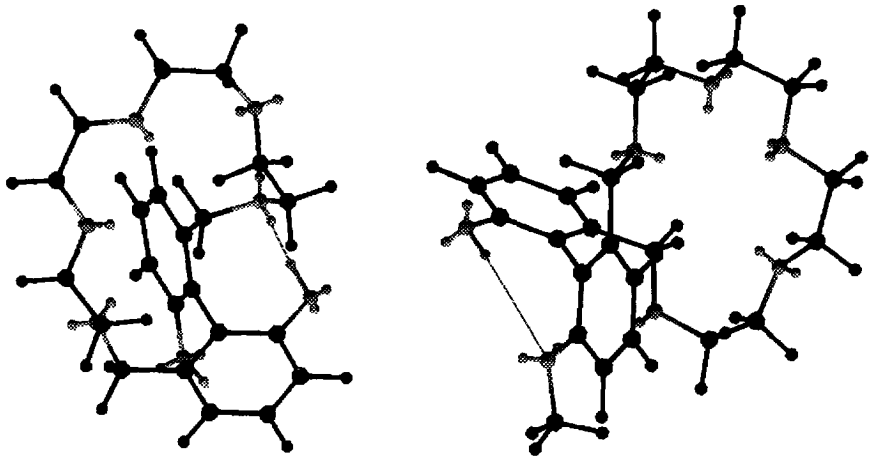


Fig. 1. Molecular modeling structures of **1b** and **1c**

Compound **1d** has the substituents, two nitro groups, in the 4,4' positions; so no steric hindrance should be expected. However, a decrease in $Hg(SCN)_2$ complexation was observed with this ligand. This fact could be explained using electronic considerations; but inductive electron withdrawal to the benzylic oxygen, produced by the presence of both nitro groups, must be so weak that this effect is negligible. However, small conformational changes could explain the observed behaviour. In fact, macromodel experiments showed a conformation for **1d** that is different to that obtained for **1a-c**. In this conformation, the crown moiety is laying close to one of the aromatic rings (Figure 2). Even though, a similar situation seems to be present in compound **1f**, more careful observations demonstrated that in **1d** the distances between oxygens (1), (2), and (3) and one of the carbons in the ortho positions of the nitro group were markedly shorter than that observed in **1f**. This fact could fix the ligand in a conformation less suitable for complexing the metal which could explain the smaller value of the association constant.

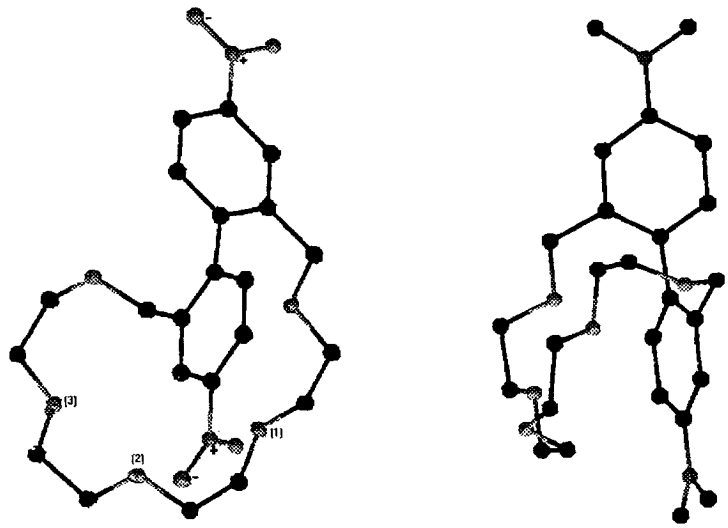


Fig. 2. Molecular modeling structures of **1d** and **1f**.

On the other hand, clear differences were observed between **1d** and **1f** and 4,4'-dinitrobiphenyl and 4,4'-dimethylaminobiphenyl, respectively. Thus, the dihedral angle in compounds **1d** and **1f** are around 90° while the values for the corresponding 4,4'-disubstituted biphenyls are close to 36°. Thus, the dihedral angles observed in **1d** and **1f** are similar to that calculated for **1a-c**.

In lactones **2a-c** no complexation with $Hg(SCN)_2$ was observed. Macromodel studies of these compounds (Figure 3) showed that whereas one carbonyl group is coplanar to its aromatic ring, the other is almost perpendicular.[10] This position of the carbonyl group not only produces a strong steric hindrance but also prevents one oxygen directing its lone pairs toward the cavity. These two effects make the conformation unsuitable for complexing the mercury atom since one of the SCN groups should pass through the cavity which is hindered by the presence of the carbonyl group.

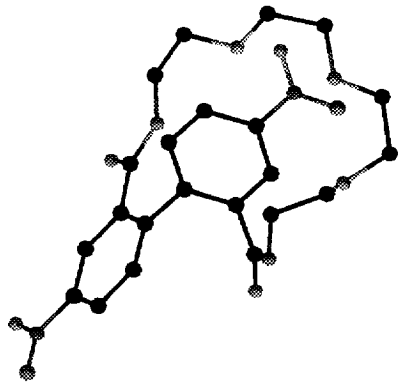


Fig. 3. Molecular modeling structure of **2b**

Alkali Metals

With alkali metals, exchange is usually rapid and the weight average of free and bound species is observed in NMR experiments. However, titration of the studied crown compounds with sodium picrate in acetone-d_6 resulted in a gradual shift in the NMR peaks. In this way, plots of $\Delta\nu$ *vs.* amounts of Na^+ added gave association constant values in each case. Nonlinear least-squares regression analysis of data was required. The obtained result are reflecting in Table 1.

The studied crown ethers showed smaller association constant values in Na^+ than in $Hg(SCN)_2$ complexation. In principle, this fact could be surprising because it is established that crown ether complex alkali better than transition cations. However, there are not any contradiction because it is also known that $Hg(SCN)_2$ is not an ionic compound. Thus, solvent polarity had stronger influence in ionic species what presented smaller association constant. From the point of view of ligands the ability to complex sodium picrate kept the same order previously observed.

In lactones **2a** and **2d**, complexation was observed but with very low association constant values. These results could be explained due to the smaller size and spherical shape of Na^+ what produce lower sterical repulsions and can be complexing by four oxygens. Compound **2b** is unable to complex the cation what can be explained by the presence of a fixed conformation similar to that discribed for **1d**.

EXPERIMENTAL SECTION

Synthesis General.

All comercially available reagents were used without further purification. Air-water sensitive reactions were performed in flame-dried glassware under argon. Tetrehydrofurane and ethyl ether were distilled from Na-K amalgam.

Melting points were taken on a Cambridge Instrument and a Reichert Termovar. TLC analysis were carried out on 0.2 mm Merck PC 60F 245 silica gel plates and column chromatographies on Merck 60 A-CC silica gel.

NMR spectra were recorded on a Bruker AC-250, Varian Unity-300 and 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 Spectrometer.

*Synthesis of **1a-b** and **2a-b**.* All them were obtained as has been previosly described[1,4].

*Synthesis of 6-hydroxy-6'-methoxy-2,2'-biphenyl-19-C-5 (**1c**).*

A 0.5 M. solution of NaEtS in dry DMF was prepared in a flask under argon atmosphere. Then, 7.4 ml. (3.7 mmol) of this solution were added to **1a** (0.4 g, 0.928 mmol) and the resulting solution was heated at 115-120ºC under argon for 24 h. The cooled mixture was then acidified with 10% aqueous HCl and extracted with EtOAc (3x10 ml). The combined organic extracts were washed with 10% aqueous NaOH (3x5ml). The chilled basic solution was acidified with 10% aqueous HCl and extracted with EtOAc (3x10ml). The combined organic extracts were washed with water and dried on $MgSO_4$. Removal of solvent by rotatoty evaporation afforded **1c** as a yellow oil (45% yield). ^{1}HNMR (250 MHz, $CDCl_3$) δ 7.57 (1H, s, -OH), 7.29 (1H, t, J=7.9Hz), 7.14 (1H, t, J=7.4Hz), 7.12 (1H, d, J=7.9Hz), 7.00 (1H, dd, J_1=7.4Hz, J_2=0.75Hz), 6.93 (1H, d, J=7.4Hz), 6.82 (1H, dd, J_1=7.9Hz, J_2=1,18Hz), 4.20 (2H, dd, J_1=13.77Hz, J_2=3.36Hz), 4.07 (2H, d, J=1.53Hz), 3.62 (3H, s), 3.52-2.83 (16H, m). ^{13}CNMR (62.5MHz, $(CD_3)_2CO$) 157.42(s), 154.58(s), 140.15(s), 139.59(s), 128.79(d), 128.34(d), 123.80(s), 122.74(s), 120.54(d), 119.57(d), 114.77(d), 110.13(d), 71.31(t), 71.19(t), 70.99(t), 70.80(t), 70.66(t), 70.55(t), 70.41(t), 70.36(t), 55.36(q). HRMS (FAB) calcd. for $C_{23}H_{30}O_7$, 418.1991; found 418.1992.

*Synthesis of 4,4'-dinitro-2,2'-diphenic acid dimethyl ester (**3**).*

4,4'-dinitro-2,2'-diphenic acid (1.5 g, 4.51 mmol) was disolved in methanol (25 ml) and concentrated sulfuric acid (1.5 g) was added. The solution was refluxed for 12 h. The solid obtained was separated by filtration and the reaction kept under the same conditions for another 12 h. and additional precipitated was separated. The mixture of solid was washed with cold $NaHCO_3$ (10%) and then with water. After dried **3** was obtained as a white solid (95%). m.p. 174ºC. ^{1}HNMR (250 MHz, $CDCl_3$) δ 8.9 (1H, d, J=2.5Hz), 8.4 (1H, dd, J_1=8.4Hz, J_2=2.5Hz), 4.7 (1H, d, J=8.4Hz), 3.7 (3H, s).

*Shynthesis of 2,2'-bis(hydroxymethyl)-4,4'-dintrobiphenyl (**4**).*

A solution of 4,4'-dinitro-2,2'-diphenic acid dimethyl ester (1g, 2.77 mmol) in ethyl ether (125 ml) was added to a suspension of $LiBH_4$ (0.484g, 22.16mmol) in ethyl ether (50ml). The mixture was stirred at room temperature for 16 hours in a stoppered flask with a $CaCl_2$ tube. Then it was quenched with H_2O (30ml) and the aqueous layer was washed with ethyl acetate (2x15ml). All the organics were joined and dried over Na_2SO_4 and the solvent was removed under vacuum to give a crude product that was purified by flash chromatography through a silica gel column (hexane/ethyl acetate 1/1). 0.59 g of dialcohol **4** were obtained (70% yield). mp 156ºC. ^{1}HNMR (250 MHz $(CD_3)_2CO$) δ 8.67 (1H, d, J= 1.76Hz), 8.37(1H, dd, J_1=8.3, J_2=2.14Hz), 7.48(1H, d, J=8.33Hz), 4.63(1H, d, J=14.23Hz), 4.52(1H, d, J=14.23Hz). ^{13}CNMR (62.5MHz, $(CD_3)_2CO$) 153.43(s), 148.39(s), 147.41(s), 135.36(d), 127.19(d), 126.83(d), 65.94(t).

Synthesis of 2,2'-bis(bromomethyl)4,4'-dinitrobiphenyl (5).

A solution of **4** (0.5g, 1.64 mmol) in CH_2Cl_2 (50 ml) was cooled at -20°C. Then BBr_3 was carefully added with a dry syringe (0.49ml, 4.92mmol) and the mixture was allowed to reach room temperature and stirred for 2 additional days with moisture exclusion. The reaction was quenched with H_2O (20ml) and the organic layer was washed with H_2O (2x20ml), dried over Na_2SO_4 and the solvent was removed under vacuum to give 0.64g of **5** (91% yield). mp 120°C. ^{1}HNMR (250 MHz, $CDCl_3$) δ 8.45(1H, d, J=2.16Hz), 8.29(1H, dd, J_1=8.39, J_2=2.2Hz), 7.49(1H, d, J=8.40Hz), 4.34(1H, d, J=10.63Hz), 4.16(1H, d, J=10.63Hz). ^{13}CNMR (62.5MHz, $CDCl_3$) 148.48(s), 143.48(s), 137.83(s), 130.90(d), 125.87(d), 123.37(d), 29.15(t).

Synthesis of 4,4'-dinitro-2,2'-biphenyl-19-C-5 (1d).

A mixture of **5** (0.3g, 0.7mmol) and tetraethylene glycol (0.136g, 0.7mmol) in dry THF (40ml) was slowly added with a syringe pump to a suspension of NaH (0.058g, 2.4mmol) in THF (25ml) at room temperature and under inert atmosphere. The reaction was stirred in these conditions overnight. CH_2Cl_2 was added (500ml) and the whole was washed with distilled water (3x150ml).(WARNING: A violent reaction might occur between NaH and CH_2Cl_2). The organic layer was dried over Na_2SO_4 and the solvent removed under vacuum. The crude product was flash chromatographed through a silica gel column (hexane/ethyl acetate 2/1) to afford 0.020 g of **1d** as a red oil (6.2% yield) ^{1}HNMR (250 MHz, $CDCl_3$) δ 8.47(1H, d, J=2.35Hz), 8.21(1H, dd, J_1=8.32, J_2=2.40Hz), 7.29(1H, d, J=8.33Hz), 4.44(1H, d, J=12.00Hz), 4.23(1H, d, J=12.00Hz), 3.67-3.32(8H, m). ^{13}CNMR(62.5MHz, $CDCl_3$) 125.60(s), 123.14(s), 119.27(d), 112.76(d), 108.88(d), 107.64(s), 71.46(t), 71.41(t), 71.18(t), 71.06(t). HRMS (FAB) calcd for $C_{22}H_{26}N_2O_9$, 462.1638; found 462.1638.

Synthesis of 4,4'-diamino-2,2'-biphenyl-19-C-5 (1e).

1d (0.130 g, 0.28 mmmol) was disolved in EtOH (10 ml) and Pd/C 10% (20 mg) was added. The mixture was stirred under hydrogen atlmosphere at room temperature until the starting material was consumed. The suspension was quickly filtered up and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (ethyl acetate) to afford **1e** in 20% yield. Very unstable compound. ^{1}HNMR (250 MHz, CD_3OD) δ 6.78 (1H, d, J=2.46Hz), 6.70 (1H, d, J=7.35Hz), 6.51(1H, dd, J_1=7.35Hz, J_2=2.46Hz), 4.53 (2H, s broad), 4.20 (1H, d, J= 11.30 Hz), 4.06(1H, d, J=11.30Hz), 3.55-3.28(8H, m).

Synthesis of 4-4'-dimethylamino-2,2'-diphenic acid dimethyl ester (6).

A heterogeneous solution of 4,4'-dinitro-2,2'-diphenic acid dimethyl ester (0.5g, 1.66 mmol), formaldehyde (0.75 ml, 30% solution in H_2O) and 10% Pd-C (40 mg) in ethanol (50 ml) was stirred under H_2 atmosphere at room temperature for 24 hours. The reaction mixture was filtered up and the solvent was removed under vacuum. The crude material was taken up in $CHCl_3$ and then washed with 1 N HCl (2x30ml). The aqueous layer was carefully basified with Na_2CO_3 until a solid appeared. This solution was extracted with $CHCl_3$ (3x30ml) and the organic layer was dried over Na_2SO_4. The solvent was distilled to give 0.265 g of **6.** mp 140°C ^{1}HNMR (250 MHz, $CDCl_3$) δ 7.27(1H, d, J=4.16Hz), 7.07(1H,d,J=8.49Hz), 6.80(1H, dd, J_1=8.30, J_2= 2.60Hz), 3.62(3H, s), 3.00(6H, s). ^{13}CNMR(62.5MHz, $CDCl_3$) 169.27(s), 149.52(s), 132.23(d), 131.10(s), 115.97(d), 113.99(d), 52.42(q), 41.25(q).

Synthesis of 2,2'-bis(hydroxymethyl)-4,4'-dimethylaminobiphenyl (7).

6 was reduced with $LiBH_4$ in the same conditions than were used to get **4**. **7** was obtained in a 65% yield. mp 178°C. ^{1}HNMR (250 MHz, $CDCl_3$) δ 7.10(1H, d, J=2.51Hz), 7.04(1H, d, J=8.30Hz), 6.80(1H, dd, J_1=8.31, J_2=2.60Hz), 4.38(2H, m), 4.21(1H, m), 3.00(6H, s). ^{13}CNMR (62.5MHz, $CDCl_3$) 150.77(s), 141.48(s), 131.25(d), 128.56(s), 112.82(d), 111.67(d), 63.04(t), 40.58(q).

Synthesis of 4,4'-dimethylamino-2,2'-biphenyl-19-C-5 (1f).

A mixture of NaH (0.390 g, 1.63 mmol) and **7** (0.820 g, 2.7 mmol) in dry THF (150 ml) was refluxed under argon for 20 hours. Then a solution of tetraethylene glycol ditosylate (1.57 g, 3.13 mmol) in THF (75 ml) was added dropwise for a period of 8 hours with a syringe pump. The whole was stirred under argon overnight. The reaction was cooled at room temperature and stopped with H_2O (5 ml). The suspension was filtered up and the solvent distilled. The crude was taken up in ethyl acetate (50 ml) and washed with distilled H_2O (3x20ml). The organics were joined and dried over Na_2SO_4 and the solvent was removed under vacuum. The crude was flash-chromatographed through a silica gel column (hexane/ethyl acetate 1/1) to afford 0.210g of **1f** (17% yield) mp 90°C. ^{1}HNMR (250 MHz, acetone-d_6) δ 7.08(1H, d, J=2.55Hz), 7.00 (1H, d, J=8.34Hz), 6.81(1H, dd, J_1=5.63, J_2=2.67Hz), 4.46(1H, d, J=11.80), 4.33(1H, d, J=11.80), 3.71-3.50(8H, m), 3.10(6H, s). ^{13}CNMR (62.5MHz, acetone-d_6) 150.29(s), 138.36(s), 130.91(d), 128.64(s), 112.62(d), 111.46(d), 71.63(t), 71.08(t), 70.88(t), 70.81(t), 70.31(t), 40.34(q). HRMS (FAB) calcd for $C_{26}H_{38}N_2O_5$, 458.2781; found 458.2781.

Synthesis of 4,4'-diaminomacrolactone (2c)

2b was reduced in the same conditions descrived to get **1e**. **2c** was separated in 95% yield. **2c** is a very unstable compound. ^{1}HNMR (250 MHz, $CDCl_3$) δ 7.30(1H, d, J=2.45Hz), 6.93(1H, d, J=8.15Hz), 6.77(1H, dd, J_1=8.15Hz, J_2=2.45Hz), 4.20-4.09(2H, m), 3.71-3.36(6H,m). ^{13}CNMR (62.5MHz, $CDCl_3$) 168,15(s), 145.64(d), 134.01(s), 132.22(d), 130.96(s), 118.49(d), 116.91(d), 71.37(t), 71.09(t), 69.30(t), 64.06(t). HRMS (FAB) calcd for $C_{22}H_{22}N_2O_{11}$, 490.1223; found 490.1225

Synthesis of 4,4'-dimethylaminomacrolactone (2d)

Compound **2d** was prepared, from a solution of **7** (0.65g, 1.32 mmol), formaldehyde (1.17ml, 30% solution in H_2O) and 10% Pd-C (125mg) in ethanol, in a similar way to **6**. The residue was chromatographed through a silica gel column (hexane/ethyl acetate 1/3) to afford 0.4 g of **9** (62% yield). mp 134°C. ^{1}HNMR (250 MHz, CDCl3) δ 7.33(1H, d, J=2.67Hz), 7.09(1H, d, J=8.49Hz), 6.83(1H, dd, J_1=8.50, J_2=2.73Hz), 4.18(2H, t, 4.87Hz), 3.71-3.36(6H, m), 2.99(6H, s). ^{13}CNMR (62.5MHz, $CDCl_3$) 168.20(s), 148.99(s), 131.54(d), 131.36(s), 130.31(s), 115.16(d), 113.58(d), 71.10(t), 70.55(t), 68.78(t), 63.64(t), 40.58(q). HRMS (FAB) calcd for $C_{26}H_{34}N_2O_7$, 486.2366 found 486.2366.

Synthesis of the complexes of 1a, 1b, 1c, 1d, 1f with $Hg(SCN)_2$. General procedure.

To one equivalent of the crown ether in acetone was added one equivalent of $Hg(SCN)_2$ in acetone. In every case the minimum amount of acetone to dissolve the crown ether 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. **1a•Hg(SCN)$_2$** (mp 208°C) ^{1}HNMR (250 MHz, $(CD_3)_2CO$) δ 7.31 (1H, t, J=7.5Hz), 7.13 (1H,

d, J=7.5Hz), 6.93 (1H, d, J= 7.5Hz), 4.18 (2H, s), 3.67-3.43 (11H, m).**1b•Hg(SCN)$_2$** (mp 173°C) ^{1}HNMR (250 MHz, $(CD_3)_2CO$) δ 7.94 (1H, s, -OH), 7.15 (1H,t,J= 7.54Hz), /.08 (1H, d, J= 7.54Hz), 6.83 (1H, d, 7.55Hz), 4.36 (1H, d, 10.95Hz), 4.22 (1H, d, 10.95Hz), 3.77-3.24 (8H, m). **1c•Hg(SCN)$_2$** (mp 194°C) ^{1}HNMR (250 MHz, $(CD_3)_2CO$) δ 8.01 (1H, s, -OH), 7.27 (1H, t, J=7.97Hz), 7.12 (2H, m), 7.00 (1H, dd, J_1=7.75Hz, J_2=0.99Hz), 6.89 (1H, d, J=7.75), 6.80 (1H, dd, J_1=7.98Hz, J_2=1,15Hz), 4.32 (2H, d, J=10.95Hz), 4.19 (2H, d, J=10.95Hz), 3.73-3.40 (16H, m). **1d•Hg(SCN)$_2$** (mp 170°C) ^{1}HNMR (250 MHz, $(CD_3)_2CO$) δ 8.54 (1H, d, 2.41Hz), 8.25 (1H, dd, 2.41Hz), 7.52 (1H, d, 8.45), 4.58 (2H, dd, J_1=15.53Hz, J_2=11.10Hz), 3.89-3.43 (8H, m). **1f•Hg(SCN)$_2$** (mp 125°C) ^{1}HNMR (250 MHz, $(CD_3)_2CO$) δ 6.90 (1H, d, J=2.45Hz), 6.77 (1H, d, 8.40Hz), 6.67 (1H, dd, J_1=8.40Hz, J_2= 2.45Hz), 4.62 (1H. d. 10.34Hz), 4.14 (1H, d, J=10.30Hz), 3.72-3.36 (8H, m), 2.91 (3H, s).

Association Constants of the Complexes with Hg(SCN)$_2$ Determination. General Procedure.

0.0015 mmol of the complex were dissolved in 0.9ml of acetone-d_6 and placed in an NMR tube. The tube was capped with a Teflon tape and the NMR spectra were recorded at 298K. From the part of the spectra where different signals were observed for both species in solution (ligand and complex), a ratio R between free form and complex could be determined and from it Ka values could be obtained.

Association Constants of the Complexes with Sodium Picrate Determination. General Procedure.

All titrations were done at constant host concentration To a solution of the host (20mmol) in acetone-d_6 (0.5ml) aliquots of 50 µl of a 50mM guest solution in acetone were added. The solvent level was kept constant in every moment by evaporation and the different spectra recorded at 298K The chemical shift data obtained for the benzylic or -CH_2- linked to the phenolic oxygen signals with the variable guest concentration were plot in a curve that was fitted By using a nonlinear least-squares regresion analysis.

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10. IR of **2b** shows two different carbonyl frequencies at 1708 cm^{-1} (no-conjugated) and 1723 cm^{-1} (conjugated)

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