

# Resorcarene-Based Receptor: Versatile Behavior in Its Interaction with Heavy and Soft Metal Cations

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Received: June 10, 2005; In Final Form: November 24, 2005

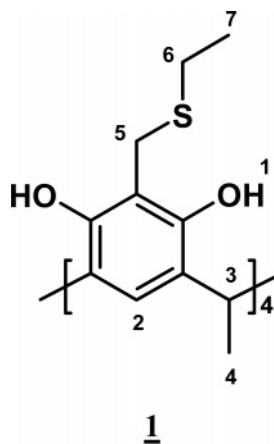
Standard solution Gibbs energies,  $\Delta_s G^\circ$ , of the resorcarene-based receptor 5,11,17,23-ethylthiomethylated calix[4]resorcarene, **1**, (characterized by  $^1\text{H}$  NMR and X-ray diffraction studies) in its monomeric state (established through partition experiments) in various solvents are for the first time reported in the area of resorcarene chemistry. Transfer Gibbs energies of **1** from hexane (reference solvent) to other medium are calculated. Agreement between  $\Delta_t G^\circ$  (referred to the pure solvents) and standard partition Gibbs energies,  $\Delta_p G^\circ$  (solvent mutually saturated) is found. Cation–ligand interactions were investigated through  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$  and  $\text{CD}_3\text{OD}$ ) and conductometric titrations in acetonitrile and methanol.  $^1\text{H}$  NMR data revealed the sites of interaction of **1** with the metal cation. The composition of the metal-ion complexes ( $\text{Ag}^+$  and  $\text{Pb}^{2+}$  in acetonitrile and  $\text{Ag}^+$  and  $\text{Cu}^{2+}$  in methanol) was established through conductometric titrations. Thus, complexes of 1:1 stoichiometry were formed between **1** and  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  in acetonitrile and  $\text{Cu}^{2+}$  in methanol. However, in moving from acetonitrile to methanol, the composition of the silver complex was altered. Thus, two metal cations are hosted by a unit of the ligand. As far as  $\text{Cu}^{2+}$  and **1** in acetonitrile is concerned, conductance data suggest that metalates are formed in which up to four units of  $\text{Cu}^{2+}$  are taken up per unit of resorcarene. The contrasting behavior of **1** with  $\text{Cu}^{2+}$  in acetonitrile relative to methanol is discussed. As far as mercury (II) is concerned, the unusual jump in conductance observed in the titration of  $\text{Hg}^{2+}$  with **1** in acetonitrile and methanol after the formation of a multicharged complex (undefined composition) is attributed to the presence of highly charged smaller units (higher mobility) resulting from the departure of pendant arms from the resorcarene backbone. Isolation of these species followed by X-ray diffraction studies corroborated this statement. The thermodynamic characterization of metal-ion complexes of  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  in acetonitrile and  $\text{Cu}^{2+}$  and  $\text{Ag}^+$  in methanol is reported. Final conclusions are given.

## Introduction

Calix[4]resorcarenes (resorcinarenes) are versatile compounds often obtained from the condensation reaction of resorcinol and aldehydes (aliphatic or aromatic) in acidic medium.<sup>1</sup> The general reaction was reported by Baeyer<sup>2,3</sup> in 1872. However, it was not until 1968 that the metacyclane structure of resorcarene derivatives was proved by X-ray crystallography.<sup>4,5</sup> Since then, many efforts have been devoted to the investigation of the chemical behavior of these macrocycles.<sup>6,7</sup> Resorcarenes have been used as platforms for the synthesis of functionalized receptors in the field of supramolecular chemistry.<sup>8,9</sup> However, the hosting ability of resorcarenes for positively charged species was first demonstrated by Schneider and co-workers in 1985.<sup>10,11</sup>

Resorcarene derivatives can be obtained through (i) functionalization of the two hydroxyl groups of the aromatic rings of the parent compound<sup>12,13</sup> or (ii) the introduction of suitable functionalities in the ortho position situated between the two OH groups of the aromatic rings.<sup>14–16</sup> On the basis of the latter approach, we have designed a resorcarene derivative with pendant arms containing sulfur donor atoms, namely, 5,11,17,-

23-ethylthiomethylated calix[4]resorcarene, **1**. The aim was to



find a receptor able to complex toxic metal cations while discriminating against those which are known to play a significant role in biological processes,<sup>17,18</sup> such as alkali, alkaline-earth, and some transition metal cations.<sup>19,20</sup> In this paper, we report the following: (i) the synthesis and characterization of **1** and its solubility in various solvents at 298.15 K. Given that the presence of two hydroxyl groups per monomer

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in the structure of **1** may lead to its dimerization or even polymerization of this ligand in aprotic media,<sup>21</sup> partition experiments were carried out. The aim was to establish the nature of the speciation in solution, prior to the use of solubility data for the calculation of the standard Gibbs energies of solution ( $\Delta_s G^\circ$ ) and transfer ( $\Delta_t G^\circ$ ) of **1** from a reference ( $s_1$ ) to another solvent ( $s_2$ ); (ii)  $^1\text{H}$  NMR, conductometric, and thermodynamic studies on the interaction of **1** with alkali, alkaline-earth, transition, and heavy metal cations in two solvents, acetonitrile, MeCN (dipolar aprotic solvent),<sup>22,23</sup> and methanol, MeOH<sup>22</sup> (protic solvent).

The outcome of these investigations is discussed and final conclusions are given.

## Experimental

**Chemicals.** Formaldehyde (37%, Across Organics), ethanethiol (97%, Aldrich Chem. Co), triethylamine (99.5%, Aldrich), methanol (HPLC grade, Fisher), hexane (HPLC grade, Aldrich), ethanol (HPLC grade, Hayman Ltd.), tetrahydrofuran (Aldrich), chloroform (Aldrich), propylene carbonate (Aldrich), dichloromethane (HPLC grade, Aldrich), dimethyl sulfoxide (Fisher), butan-1-ol (99%, Fisher), and propan-1-ol (99.7%, BDH) were used without further purification. The deuterated solvents (acetonitrile, methanol, and chloroform as well as tetramethylsilane) and all metal cation perchlorate salts (lithium, 99%; sodium monohydrate, 98%; potassium, 99%; rubidium, 99%; cesium, 98%; magnesium hexahydrate, 99%; calcium tetrahydrate, 99%; strontium hydrate; barium trihydrate, 99%; silver, 99.9%; lead trihydrate, 98%; cadmium hydrate; copper hexahydrate, 98%; zinc hexahydrate, 98%; nickel hexahydrate; and mercury hydrate, 98%) were purchased from Aldrich. The salts were dried over phosphorus pentoxide ( $\text{P}_4\text{O}_{10}$ ) under vacuum for several days before use. Potassium chloride (99%, Fisher) was recrystallized from deionized water and dried at 120 °C for 3 days before its use for conductometric measurements. Tetra-*n*-butylammonium perchlorate (Fluka) and tris-(hydroxymethyl)aminomethane (ultrapure 99%, Aldrich) were recrystallized from a water/methanol (50:50) mixture. The crystals were washed with methanol and dried at room temperature for 24 h. Then, these were stored for 3 days in a vacuum desiccator prior their use for the standard reaction in calorimetry. *N,N*-Dimethylformamide (HPLC grade, Fisher) and acetonitrile (HPLC, Hayman) were distilled as described elsewhere.<sup>24,25</sup>

**Synthesis of 1.** Ligand **1** was prepared by a Mannich type reaction.<sup>26</sup> To a solution of calix[4]resorcarene (2.5 g, 4.6 mmol) in an ethanol/chloroform (50:50) mixture, triethylamine (73.6 mmol, 10.25 mL), ethanethiol (73.6 mmol, 5.6 mL), and formaldehyde (110.4 mmol, 8.1 mL) were added. The reaction mixture was heated at 60 °C for several hours, and then, the solvent was removed by evaporation. Addition of methanol to the residue led to the formation of a precipitate which was filtered. The solid was recrystallized from a methanol/chloroform (70:30) mixture. The product **1** (80% yield) was characterized by  $^1\text{H}$  NMR (in  $\text{CD}_3\text{CN}$ ,  $\text{CD}_3\text{OD}$ , and  $\text{CDCl}_3$ ),  $^{13}\text{C}$  NMR in  $\text{CDCl}_3$ , and microanalysis. The results are as follows:

$^1\text{H}$  NMR (500 MHz, in  $\text{CD}_3\text{CN}$ );  $\delta$  (ppm),  $J$  (Hz):  $\delta$  = 7.54 (s, 2H, OH),  $\delta$  = 7.38 (s, 1H, H-2),  $\delta$  = 4.53 (q, 1H,  $J$  = 7.2, H-3),  $\delta$  = 3.80 (s, 2H, H-5),  $\delta$  = 2.37 (q, 2H,  $J$  = 7.3, H-6),  $\delta$  = 1.74 (d, 3H,  $J$  = 7.2, H-4),  $\delta$  = 1.15 (t, 3H,  $J$  = 7.1, H-7).

$^1\text{H}$  NMR (300 MHz, in  $\text{CD}_3\text{OD}$ );  $\delta$  (ppm),  $J$  (Hz):  $\delta$  = 7.23 (s, 1H, H-2),  $\delta$  = 4.57 (q, 1H,  $J$  = 7.2, H-3),  $\delta$  = 3.77 (s, 2H, H-5),  $\delta$  = 2.37 (q, 2H,  $J$  = 7.4, H-6),  $\delta$  = 1.69 (d, 3H,  $J$  = 7.2, H-4),  $\delta$  = 1.11 (t, 3H,  $J$  = 7.5, H-7).

$^1\text{H}$  NMR (500 MHz, in  $\text{CDCl}_3$ );  $\delta$  (ppm),  $J$  (Hz):  $\delta$  = 7.95 (s, 2H, OH),  $\delta$  = 7.30 (s, 1H, H-2),  $\delta$  = 4.59 (q, 1H,  $J$  = 7.2,

H-3),  $\delta$  = 3.87 (s, 2H, H-5),  $\delta$  = 2.39 (q, 2H,  $J$  = 7.3, H-6),  $\delta$  = 1.75 (d, 3H,  $J$  = 7.2, H-4),  $\delta$  = 1.22 (t, 3H,  $J$  = 7.3, H-7).

$^{13}\text{C}$  NMR (500 MHz,  $\text{CDCl}_3$ );  $\delta_c$  (ppm):  $\delta$  = 150.24 (C–OH),  $\delta$  = 125.90 (C–CH<sub>2</sub>–S),  $\delta$  = 122.50 (CH–aromatic),  $\delta$  = 110.05 (CH aromatic–C),  $\delta$  = 28.21 (CH bridge),  $\delta$  = 25.48 (C–CH<sub>2</sub>–S),  $\delta$  = 25.04 (S–CH<sub>2</sub>–CH<sub>3</sub>),  $\delta$  = 20.28 (CH<sub>3</sub> bridge),  $\delta$  = 14.48 (S–CH<sub>2</sub>–CH<sub>3</sub>).

Microanalysis carried out at the University of Surrey for  $\text{C}_{44}\text{H}_{56}\text{O}_8\text{S}_4$  gave calc: C, 62.83; H, 6.71. Found: C, 62.61; H, 6.73.

**Partition Experiments.** For the partition experiments carried out to investigate the speciation of the ligand in the solvents, we used the procedure reported in the literature.<sup>27</sup> Thus, the solvents methanol/hexane and acetonitrile/hexane were mutually saturated before use to avoid changes when mixed. For the partition experiments, solutions containing different concentrations of **1** ( $1.0 \times 10^{-5}$ – $1.5 \times 10^{-3}$  mol dm<sup>-3</sup>) were prepared in MeOH or MeCN saturated with hexane, Hex. Equal volumes of these solutions (10 cm<sup>3</sup>) and hexane (saturated with acetonitrile or methanol) were placed in separate tubes and shaken for 2 h. Then, these were left in a thermostat bath at 298.15 K for several hours to ensure that equilibrium was achieved. Samples of both phases were taken and the equilibrium concentrations of **1** in these solvents were determined by UV absorption spectrophotometry. Blank experiments in the absence of the receptor were carried out in all cases.

**Solubility Measurements.** Solubility data of **1** in different solvents at 298.15 K were obtained. Thus, saturated solutions were prepared by adding an excess amount of **1** to the appropriate solvent. The mixtures were left in a thermostated bath at the standard temperature for several days to ensure that the equilibrium between the solid and its saturated solution was achieved. Samples of the saturated solution were analyzed by the gravimetric method. Blank experiments were carried out. Solvate formation was checked by the De Ligny method.<sup>28</sup> Thus, an amount of the solid was placed in a desiccator under a saturated atmosphere of the appropriate solvent, as described elsewhere.<sup>29</sup>

**$^1\text{H}$  NMR Measurements.**  $^1\text{H}$  NMR measurements were recorded at 298 K using a Bruker AC-300 E pulsed Fourier transform NMR spectrometer. Typical operating conditions for routine proton measurements involved a “pulse” or flip angle of 30°, a spectral frequency (SF) of 300.135 MHz, a delay time of 1.60 s, an acquisition time (AQ) of 1.819 s, and line broadening of 0.55 Hz. A solution of **1** (0.5 mL) in the appropriate solvent ( $\text{CD}_3\text{CN}$ ,  $\text{CD}_3\text{OD}$ , and  $\text{CDCl}_3$ ) was placed in 5 mm NMR tubes using TMS as the internal reference.

**$^1\text{H}$  NMR Studies on the Interaction of 1 with Metal Cations.** The complexation behavior of **1** toward metal cations at 298 K was studied using a  $^1\text{H}$  NMR technique, by adding the metal-ion salt in excess ( $5 \times 10^{-3}$ – $6 \times 10^{-2}$  mol dm<sup>-3</sup>) into the NMR tube containing the ligand ( $1 \times 10^{-3}$ – $6 \times 10^{-3}$  mol dm<sup>-3</sup>) dissolved in the appropriate solvent. Changes in the chemical shifts upon the addition of the metal cation were measured and compared, using the spectra of the free ligand as a reference.

**Conductance Measurements.** For these measurements, a Wayne-Kerr model 7330 automatic LCR meter conductivity bridge at a frequency of 1 kHz was used. The conductance cell was a Russell-type glass-bodied electrode with a cell constant of  $0.99 \pm 0.01$  cm<sup>-1</sup>, determined using 0.1 mol dm<sup>-3</sup> aqueous KCl solution at 298.15 K.

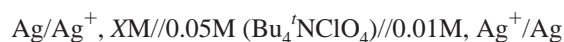
Conductometric titrations were carried out. Thus, a solution of the metal cation salt (concentration range depending of the

salt used, from  $8 \times 10^{-5}$  to  $1 \times 10^{-4}$  mol dm $^{-3}$ ) was placed in the conductometric cell in the appropriate solvent (25 cm $^3$ ) and titrated with a solution of the ligand (concentration range from  $1 \times 10^{-3}$  to  $2 \times 10^{-3}$  mol dm $^{-3}$ ) in the same solvent, and the conductance was measured after each addition. The temperature of the vessel was kept at 298.15 K using a thermostat.

**Titration Calorimetry.** Stability constants ( $\log K_s$ ) and enthalpies,  $\Delta_c H$ , of complexation of **1** with the appropriate metal cation at 298.15 K were determined by direct calorimetric titration using a Tronac 450 as an isoperibol titration calorimeter.<sup>30</sup> The reproducibility of the apparatus was checked by carrying out the standard reaction of protonation of an aqueous solution of tris-(hydroxymethyl)aminomethane (THAM) with an aqueous solution of hydrochloric acid (HCl, 0.1 mol cm $^{-3}$ ), suggested as a standard thermochemical reaction,<sup>31</sup> at 298.15 K. The value obtained ( $-47.57 \pm 0.08$  kJ mol $^{-1}$ ) was in good agreement with that reported by Wilson and Smith<sup>32</sup> ( $-47.49 \pm 0.25$  kJ mol $^{-1}$ ) at 298.15 K. As far as complexation studies are concerned, for stability constants lower than  $10^6$  ( $\log K_s = 6$ ), a solution of **1** ( $8 \times 10^{-4}$ – $3 \times 10^{-3}$  mol dm $^{-3}$  concentration range) was placed in the vessel (50 cm $^3$ ) in the appropriate solvent and the metal cation salt ( $3.0$ – $6.0 \times 10^{-2}$  mol dm $^{-3}$  concentration range) was placed in the same solvent in the syringe. The latter was added from a 2 cm $^3$  buret connected by a silicone tube to the reaction vessel after reaching thermal equilibrium. These experiments were repeated four times for each metal cation. Blank experiments were carried out in all cases to account for dilution effects resulting from the addition of the metal cation salt to the solvent placed in the calorimetric vessel.

For  $\log K_s$  values higher than 6, potentiometric titrations were carried out.

**Potentiometric Titrations. Determination of the Stability Constant.** Potentiometric titrations using silver electrodes<sup>33</sup> were carried out to determine the stability constant of **1** with the silver cation in MeOH. A schematic representation of the electrochemical cell is shown



The indicator and the reference silver electrode rods were immersed each in separate jacket-thermostated glass vessels. The reference electrode was immersed in a solution of silver perchlorate in MeOH ( $1 \times 10^{-3}$  mol dm $^{-3}$ ), and the indicator electrode was immersed in a solution of tetra-*n*-butylammonium perchlorate (TBAP), where the titration was performed and the activity of the free silver ion was measured. Tetra-*n*-butylammonium perchlorate (TBAP) was used to maintain the ionic strength (0.05 mol dm $^{-3}$ ) in all solutions, including the filling solution of the salt bridge between the two glass vessels. The titration vessel was equipped with a magnetic stirrer to ensure proper mixing after each addition.

A digital microprocessor pH/mV-meter, CAMLAB model HI 8417, was used to measure the potential changes during the course of the titration. The volume of the titrant was added stepwise using a micropipet.

For the calibration of the electrode, the silver perchlorate solution was titrated into the sample cell containing a TBAP (25 cm $^3$ , 0.05 mol dm $^{-3}$ ) solution in methanol. These data were used to calculate the standard electrode potential of the reference cell. Nernstian behavior was observed.

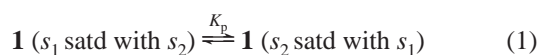
The second titration involved the formation of the silver–**1** complex. The ligand solution was added to the silver solution, the change in the potential was recorded, and a Hyperquad program<sup>34</sup> was used to calculate the stability constant values

derived from these measurements. Titrations were carried out in triplicate, and an average was calculated.

## Results and Discussion

**Effect of the Solvent.** The  $^1\text{H}$  NMR spectrum of **1** exhibited one signal for the OH protons in all the solvents investigated except in CD $_3$ OD where the OH signal is hardly detected probably due to a fast exchange with the bulk MeOH. Inspection of the NMR spectra reveals sharp signals for all the protons. No significant chemical shift changes are observed in moving from one solvent to another except for the OH signal which is deshielded in CDCl $_3$  relative to CD $_3$ CN. The presence of one signal for each proton in the ligand spectra in these solvents reveals the symmetrical structure of the ligand. It should be mentioned that the X-ray diffraction study of **1** (crystallized from a chloroform solution) shows a squashed “cone” conformation and four upper rim O–H $\cdots$ O bonds between the adjacent phenyl rings defining the cavity and arranged in the lattice as supramolecular centrosymmetric dimers (Figure 1a). The monomers in a dimer (Figure 1b) are linked to each other through hydrophobic interactions between one upper rim pendant group of a molecule and the cavity of the neighboring one. The dimer is further stabilized by a pair of intermolecular O–H $\cdots$ O bonds.

**Partition of 1.** In an attempt to confirm that **1** is predominately in its monomeric form in solution, two solvent systems were used. These are MeOH/Hex and MeCN/Hex. Therefore, partition data are referred to the process described in eq 1, taking hexane as the reference solvent ( $s_1$ ). In eq 1,  $s_2$  denotes MeOH or MeCN. In all cases, these solvents were mutually saturated ( $s_1$  satd with  $s_2$  and  $s_2$  satd with  $s_1$ ).

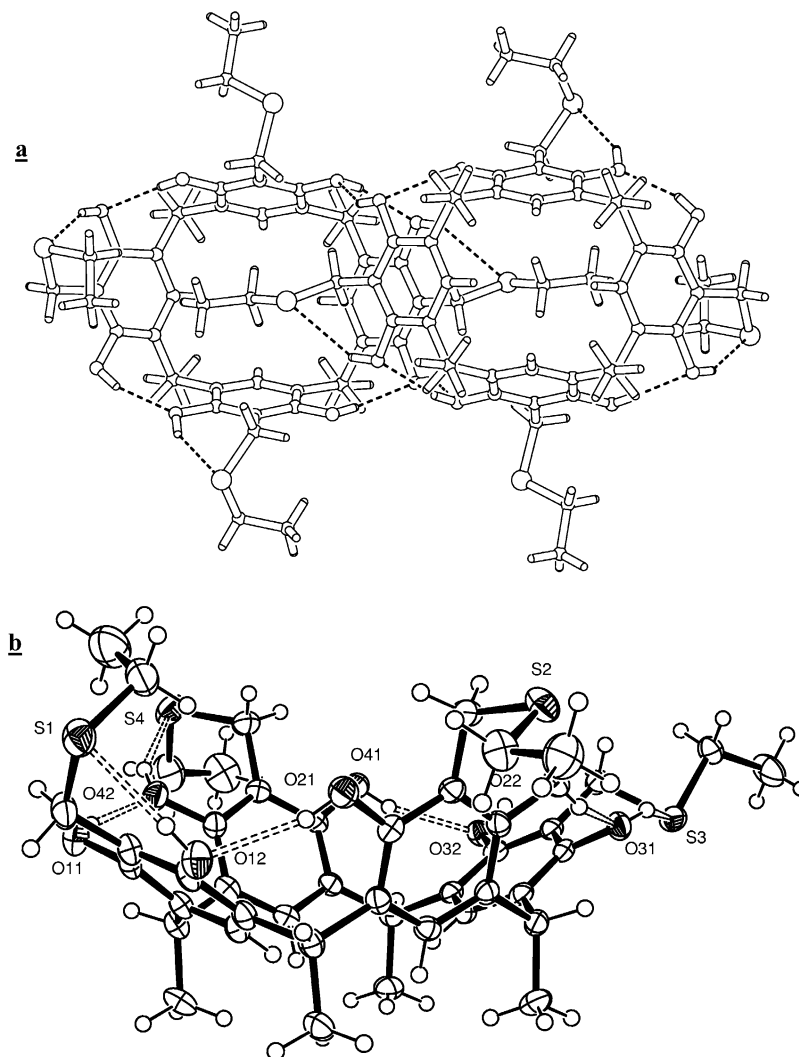


The thermodynamic equilibrium (partition) constant,  $K_p$ , is defined by eq 2

$$K_p = \frac{[\mathbf{1}]_{s_2} \gamma_{1(s_2)}}{[\mathbf{1}]_{s_1} \gamma_{1(s_1)}} \quad (2)$$

In eq 2,  $\gamma_{1(s_2)}$  and  $\gamma_{1(s_1)}$  denote the activity coefficients of **1** in the two solvents. Since **1** is a nonelectrolyte and provided that low concentrations are used,  $\gamma$  values are considered to be  $\cong 1$ . Thus, Table 1 reports the  $K_p$  values obtained at different concentrations of the ligand,  $c_l$ , in the Hex–MeOH and Hex–MeCN solvent systems. These data are used to derive the standard partition Gibbs energy,  $\Delta_p G^\circ$  of **1** in these solvent systems. The fact that no changes are observed in the  $\Delta_p G^\circ$  values by altering the ligand concentration provides a clear indication that the monomeric species predominates in solution. Given that the behavior of nonelectrolytes in propylene carbonate is often similar to that in acetonitrile led us to assume that monomeric species are also predominant in propylene carbonate. Having determined the nature of species in these solvents, we proceeded with the determination of the solubility of this ligand in different media at 298.15 K, as discussed below.

**Solubility and Derived Standard Gibbs Energies of Solution and Transfer.** Although a considerable amount of work has been carried out with resorcarenes and their derivatives, quantitative information on their solubility in different media is almost nonexistent. Indeed, this is limited to a few systems.<sup>35</sup> These data are particularly relevant for (i) the selection of the solvent to be used in solution studies<sup>36</sup> and (ii) the calculation of the standard solution Gibbs energies,  $\Delta_s G^\circ$ , of these



**Figure 1.** X-ray structure of **1**. (a) View of the coupled pair of **1** as seen down the calix axis. The molecules in the dimer are symmetry related to each other by a crystallographic inversion center. Sulfur and oxygen atoms are indicated by large and medium size open disks, respectively. (b) Side view of **1** (monomer in a dimer).

**TABLE 1: Partition Constants and Derived Partition Gibbs Energies of **1** in the Hexane–Methanol and Hexane–Acetonitrile Solvent Systems at 298.15 K**

Hexane–Methanol		
$c^a$ (mol dm <sup>-3</sup> )	$K_p$	$\Delta_p G^\circ$
$3.16 \times 10^{-5}$	12.73	-6.31
$7.36 \times 10^{-5}$	12.72	-6.30
$9.47 \times 10^{-4}$	12.73	-6.31
$1.05 \times 10^{-4}$	12.72	-6.30
average	$12.73 \pm 0.01$	$-6.31 \pm 0.01$
Hexane–Acetonitrile		
$c^a$ (mol dm <sup>-3</sup> )	$K_p$	$\Delta_p G^\circ$
$1.09 \times 10^{-5}$	80.87	-10.89
$4.35 \times 10^{-5}$	80.85	-10.89
$1.09 \times 10^{-4}$	80.86	-10.89
$1.41 \times 10^{-4}$	80.84	-10.89
average	$80.85 \pm 0.01$	$-10.89 \pm 0.01$

<sup>a</sup> The term  $c$  = initial concentration of **1** in methanol or acetonitrile.

compounds in various solvents from which corresponding data for the transfer process,  $\Delta_t G^\circ$ , from a reference solvent to another can be obtained. The latter parameter provides information regarding the differences in solvation of these macrocycles in different media. Solubility data of **1** in aprotic and protic solvents are reported in Table 2. These are the results of three

**TABLE 2: Solubility, Derived Standard Gibbs Energies of Solution, and Standard Transfer Gibbs Energies from Hexane of **1** in Various Solvents on the Molar Scale at 298.15 K**

solvent <sup>a</sup>	solubility (mol dm <sup>-3</sup> )	$\Delta_s G^\circ$ (kJ mol <sup>-1</sup> )	$\Delta_t G^\circ_{(\text{Hex} \rightarrow \text{s})}$ (kJ mol <sup>-1</sup> )
Hex	$(9.51 \pm 0.01) \times 10^{-5}$	$22.95 \pm 0.01$	0
MeCN	$(8.56 \pm 0.09) \times 10^{-3}$	$11.80 \pm 0.02$	-11.15
MeOH	$(3.20 \pm 0.19) \times 10^{-3}$	$14.2 \pm 0.1$	-8.72
EtOH	$(1.81 \pm 0.01) \times 10^{-2}$	$9.94 \pm 0.01$	-13.81
1-BuOH	$(1.40 \pm 0.01) \times 10^{-2}$	$10.58 \pm 0.01$	-12.37
1-PrOH	$(6.79 \pm 0.06) \times 10^{-3}$	$12.37 \pm 0.02$	-10.58
PC	$(3.50 \pm 0.02) \times 10^{-2}$	$8.31 \pm 0.02$	-14.64
butanone	too soluble		
THF	too soluble		
CH <sub>2</sub> Cl <sub>2</sub>	too soluble		
DMF	too soluble		
DMSO	too soluble		

<sup>a</sup> Abbreviations used: acetonitrile (MeCN), methanol (MeOH), ethanol (EtOH), butanol (1-BuOH), propan-1-ol (1-PrOH), hexane (Hex), propylene carbonate (PC), tetrahydrofuran (THF), dichloromethane (DCM), *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO).

analytical measurements carried out on the same saturated solution. The standard deviation of the data is also included in this table. It should be noted that solvate formation was observed when **1** was exposed to saturated atmospheres of *N,N*-dimeth-



**TABLE 3:  $^1\text{H}$  NMR Chemical Shifts ( $\Delta$ ) and Chemical Shifts Changes ( $\Delta\delta$ ) of the Ligand Protons **1** by the Addition of Heavy and Transition Metal Cations in  $\text{CD}_3\text{CN}$  at 298 K**

protons	$\text{CD}_3\text{CN } \delta$ (Free <b>1</b> ) (ppm)	$\Delta\delta$ (ppm)				
		$\text{Zn}^{2+}$	$\text{Cd}^{2+}$	$\text{Pb}^{2+}$	$\text{Ag}^+$	$\text{Hg}^{2+}$
H-1	7.54	0.03	0.02	0.20	0.03	
H-2	7.38	−0.01	0.00	0.13	0.02	0.08
H-3	4.53	−0.01	−0.02	0.05	0.00	−0.01
H-4	1.74	−0.01	0.01	0.04	0.03	0.03
H-5	3.80	−0.04	−0.02	0.16	0.15	0.46
H-6	2.37	−0.01	0.01	0.05	0.13	
H-7	1.15	−0.01	0.00	0.07	−0.13	0.12

ylformamide, dimethyl sulfoxide, tetrahydrofuran, butanone, and dichloromethane. In the absence of solvate formation, the standard Gibbs energies of solution,  $\Delta_s G^\circ$ , were calculated from solubility data. For this purpose, the following expression was used:

$$\Delta_s G^\circ = -RT \ln S \quad (3)$$

In eq 3,  $R$ ,  $T$ , and  $S$  denote the gas constant, the absolute temperature (K), and the solubility (molar scale), respectively. Combination of  $\Delta_s G^\circ$  values in two solvents leads to the calculation of the transfer Gibbs energies,  $\Delta_t G^\circ$ , from a reference solvent  $s_1$  to the other solvent  $s_2$ . Given that hexane was chosen as the reference solvent in the calculation of  $\Delta_p G^\circ$  values, for comparative purposes, the same solvent is selected for the evaluation of  $\Delta_t G^\circ$  values. These are also reported in Table 2 and are referred to the process,



which differs from that shown in eq 1 in that in this process the pure rather than the mutually saturated solvents are involved. Excellent agreement is found between the  $\Delta_t G^\circ$  (Table 2) and  $\Delta_p G^\circ$  (Table 1) values in the Hex-MeCN and the Hex-MeOH solvent systems. These findings are indicative of the fact that the mutual solubility of the solvents involved is very low; this statement is based on previous work which demonstrated that for systems involving solvents of low mutual solubility  $\Delta_p G^\circ \cong \Delta_t G^\circ$ .<sup>37,38</sup>

**$^1\text{H}$  NMR Studies.** Having determined the solubility of **1** in various solvents,  $^1\text{H}$  NMR measurements were carried out to assess the interaction of this ligand with metal cations in  $\text{CD}_3\text{CN}$  and  $\text{CD}_3\text{OH}$ . No chemical shift changes were observed by the addition of alkali ( $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ , and  $\text{Cs}^+$ ) and alkaline-earth metal cations ( $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Sr}^{2+}$ , and  $\text{Ba}^{2+}$ ) salts to **1** in these solvents. As far as transition and heavy metal cations in  $\text{CD}_3\text{CN}$  are concerned, the most significant changes are observed for the ligand protons upon the addition of  $\text{Hg}^{2+}$ ,  $\text{Ag}^+$ , and  $\text{Pb}^{2+}$  cation salts (see Table 3). Thus, the addition of the  $\text{Pb}^{2+}$  salt to **1** in  $\text{CD}_3\text{CN}$  leads to downfield changes in H-2 and H-6 and, particularly, in H-1. These findings may suggest that both the oxygen and to a lesser extent the sulfur donor atoms provide the sites of interaction of this ligand with this cation. A different behavior is observed for the soft metal cations ( $\text{Ag}^+$  and  $\text{Hg}^{2+}$ ) in this solvent. Thus, for the  $\text{Ag}^+$  cation, downfield shifts are found for H-5 and H-6, whereas an upfield shift is observed for H-5. These observations suggest that the interaction of this cation with **1** occurs through the sulfur (soft) donor atom. Distortion in the spectra of **1** was observed upon the addition of  $\text{Hg}^{2+}$  which did not allow the detection of all the proton signals. However, the significant downfield shift observed for H-5 and to a lesser extent H-7 appears to indicate that the cation–macrocycle interaction occurs through the sulfur donor atom.

**TABLE 4:  $^1\text{H}$  NMR Chemical Shifts ( $\Delta$ ) and Chemical Shifts Changes ( $\Delta\delta$ ) of the Ligand Protons **1** by the Addition of Heavy and Transition Metal Cations in  $\text{CD}_3\text{OD}$  at 298 K**

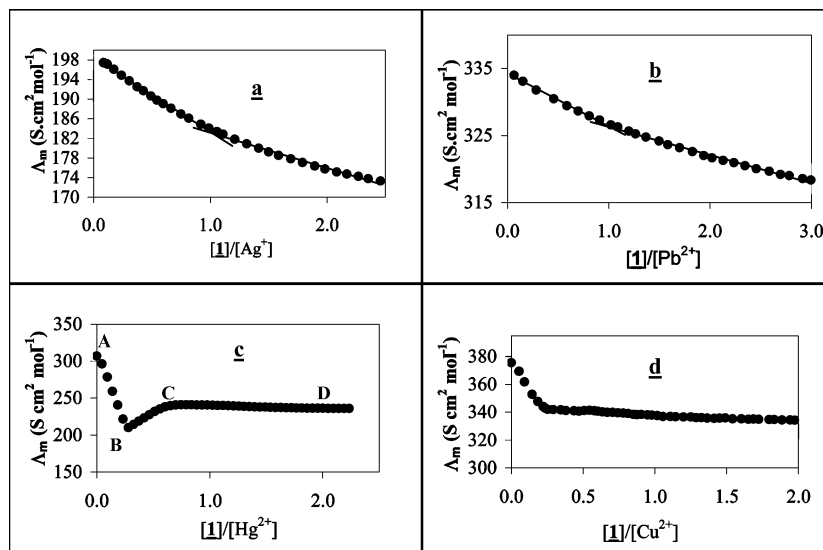
protons	$\text{CD}_3\text{OD } \delta$ (Free <b>1</b> ) (ppm)	$\Delta\delta$ (ppm)				
		$\text{Zn}^{2+}$	$\text{Cd}^{2+}$	$\text{Pb}^{2+}$	$\text{Ag}^+$	$\text{Hg}^{2+}$
H-2	7.38	0.01	0.01	0.07	0.22	0.08
H-3	4.53	0.00	−0.01	−0.01	0.07	−0.04
H-4	1.74	0.00	−0.01	0.01	0.13	−0.01
H-5	3.80	0.00	−0.01	0.01	0.39	0.18
H-6	2.37	−0.01	−0.01	0.01	0.29	0.23
H-7	1.15	0.00	0.01	0.03	−0.07	0.11

In moving from  $\text{CD}_3\text{CN}$  to  $\text{CD}_3\text{OD}$  (Table 4), significant chemical shift changes were observed for  $\text{Ag}^+$  and  $\text{Hg}^{2+}$ . Thus, for the former cation, the downfield shifts observed in H-5 and H-6 are quite significant and strongly suggest that the sulfur donor atoms are the sites of interaction of **1** with this cation. In fact, the shifts observed for these protons are far more pronounced than those found for this system in  $\text{CD}_3\text{CN}$ . It should be noted that this cation is known to be highly solvated in  $\text{CD}_3\text{CN}$  relative to  $\text{CD}_3\text{OD}$  and, therefore, a weaker interaction of  $\text{Ag}^+$  and **1** is expected in the former relative to the latter solvent. On the basis of the chemical shift change observed in H-2 and H-4, the participation of the oxygen donor atoms cannot be excluded although this is likely to be weak relative to that involving the sulfur donor atoms. As far as  $\text{Hg}^{2+}$  and **1** in  $\text{CD}_3\text{OD}$  are concerned, the downfield shifts observed in H-5, H-6, and H-7 are indicative of the fact that the interaction of this ligand and  $\text{Hg}^{2+}$  in this solvent takes place through the sulfur donor atoms.

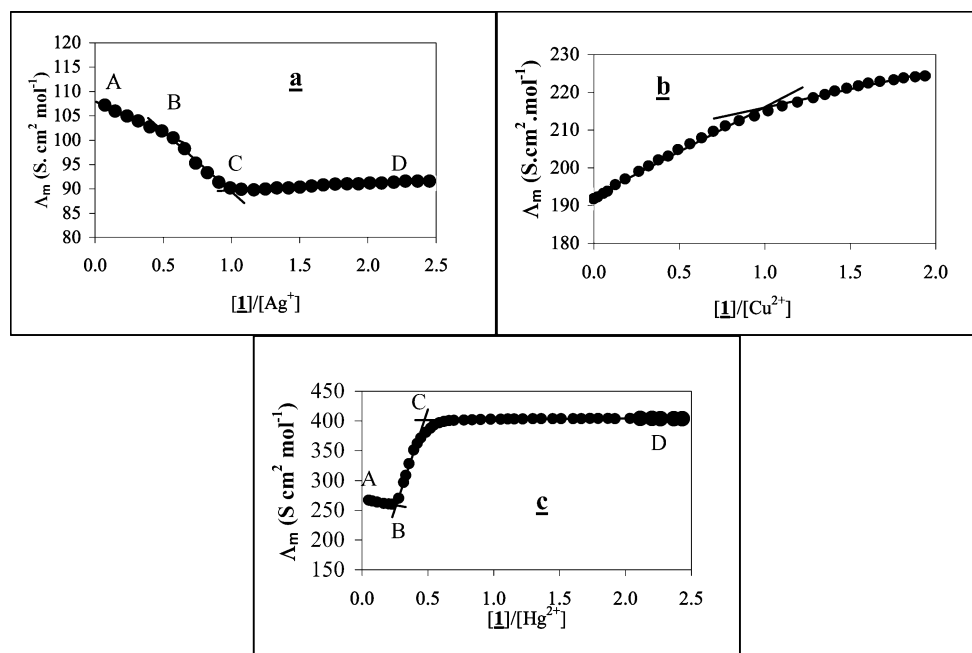
Conductance measurements were carried out in an attempt to determine the composition of the cation complexes. These are discussed in the following section.

**Conductometric Studies. (A) In Acetonitrile.** Plots of molar conductance,  $\Lambda_m$ , as a function of the ligand to metal cation ( $\mathbf{1}:\text{M}^{n+}$ ) ratio for the titration of  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  with **1** in acetonitrile are shown in Figure 2a and b, respectively. Extrapolation to the intersection of the linear portions of the titration curve yields the composition of these complexes (1:1 stoichiometry). The decrease in conductance observed upon the addition of **1** to the metal-ion-salt solution may be attributed to a size increase in moving from the free (higher mobility) to the complex (lower mobility) cation in this solvent. However, the shape of the titration curves is typical of the behavior of weak complexes.

As far as mercury(II) is concerned, the conductometric titration curve of this cation and **1** in MeCN at 298.15 K is shown in Figure 2c. A decrease in conductance due to complex formation is observed from A to B. However, a sharp break is found at a rather unusual ligand/metal cation stoichiometry ( $\sim 0.3$ ), as if several cations were interacting per unit of ligand. However, the increase in conductance observed from B to C suggests the formation of smaller units with high mobility as a result of the decomposition of the complex. Again, from the break in conductance observed at C, it is not possible to establish the composition of the complex. No further changes are observed from C to D. A similar situation is found for  $\text{Cu}^{2+}$  and **1** in MeCN, where a sharp break is observed at a ligand/metal cation ratio of 0.2 (Figure 2d) suggesting the formation of metalated complexes. No changes in conductance were observed by the addition of the ligand to solutions containing alkali, alkaline-earth, and some transition metal cations ( $\text{Ni}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Zn}^{2+}$ ) in this solvent. These findings were indicative of the fact that either very weak complexes are formed or no complexation takes place between this ligand and these cations



**Figure 2.** Conductometric titration curve for the addition of **1** to (a)  $\text{Ag}^+$ , (b)  $\text{Pb}^{2+}$ , (c)  $\text{Hg}^{2+}$ , and (d)  $\text{Cu}^{2+}$  (perchlorate as counterion) in MeCN at 298.15 K.



**Figure 3.** Conductometric titration curve for the addition of **1** to (a)  $\text{Ag}^+$ , (b)  $\text{Cu}^{2+}$ , and (c)  $\text{Hg}^{2+}$  (perchlorate as counterion) in MeOH at 298.15 K.

in this solvent. In an attempt to gain further insight on these interactions, we proceeded with conductometric measurements in methanol and these are now discussed.

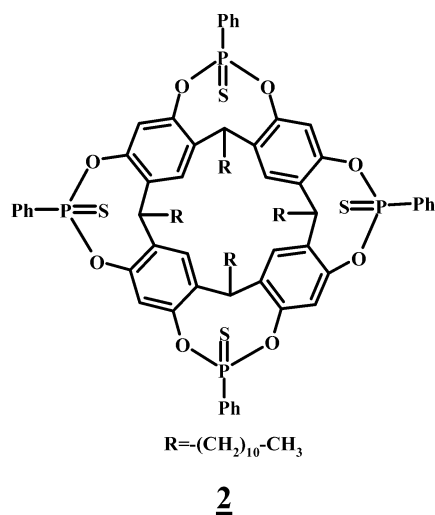
**(B) In Methanol.** The results in MeOH differ from those in MeCN in that no changes were observed by the addition of  $\text{Pb}^{2+}$  to **1** in this solvent. This finding indicates that either very weak or no complexation takes place in this solvent. This is also corroborated by the  $^1\text{H}$  NMR data which indicate that no chemical shift changes are observed by the addition of the metal cation salt to **1** in  $\text{CD}_3\text{OD}$ . On the other hand, the conductometric curve for the titration of  $\text{Ag}^+$  with **1** in this solvent (Figure 3a) shows the first change in curvature at a ligand-to-cation ratio of 0.5 which corresponds to a complex of 1:2 composition. Further addition of the ligand led to the formation of a 1:1 complex with the expected decrease in conductance. No further changes are observed in the  $\Lambda_m$  values from C to D. The change in complex composition in moving from acetonitrile (1:1 ligand/metal cation complex) to methanol (1:2 complex)

could be attributed to the higher solvation of the silver cation in the former relative to the latter solvent.<sup>39</sup> Unlike in acetonitrile, the interaction of **1** and  $\text{Cu}^{2+}$  in methanol leads to the formation of a 1:1 complex and this is shown in Figure 3b.

Figure 3c shows the conductometric titration curve of  $\text{Hg}^{2+}$  and **1** in methanol. For this particular system in this solvent, a small decrease in conductance is observed from A to B. However, this is followed by a dramatic increase in the  $\Lambda_m$  values from B to C. In fact, this jump in conductance in methanol is much higher than the one observed in acetonitrile. Distinctive breaks are shown at the ligand/metal cation ratios of 0.25 and close to 0.5.

In an attempt to explain these findings, previous work reported in the literature is considered. Highly metalated complexes involving resorcarene derivatives have been reported.<sup>40,41</sup> Illustrative examples are those resulting from the interaction of these macrocycles and cobalt metal-ion salts. Thus, complexes containing 8 and 16 cobalt cations have been shown.

Again, tetraphosphinitoresorcarene ligands are known to form cluster structures with silver(I) and copper(II) halides.<sup>42</sup> More recently, cation interaction between silver(I) and mercury(II) and tetrathiophosphonate calix[4]resorcarene **2** (a ligand with a common feature to **1** in that it contains sulfur donor atoms in its pendant arms), have been reported.<sup>43</sup>



As far as **2** and silver are concerned, a complex of 1:2 (ligand/metal cation) stoichiometry was found. Isolation of this complex from acetone led to the formation of a self-assembled complex containing two units of ligand and four silver(I) picrate moieties,  $2_2(AgPi)_4$ . Acetone and chloroform are aprotic solvents, and as such, these offer a suitable media for the formation of self-assembled complexes. This statement is further corroborated by the conductometric studies of  $Cu^{2+}$  and **1** in acetonitrile relative to methanol. Indeed, while in the dipolar aprotic medium, a metalated complex was formed, a 1:1 complex was found in methanol. For **1** and  $Ag^+$ , there is no evidence on the formation of self-assembled complexes. The fact that interaction of **1** with  $Ag^+$  in acetonitrile led to the formation of a 1:1 complex in this dipolar aprotic solvent excludes the possibility of self-assembled complex formation in a protic solvent such as methanol. The essence of these findings is that as far as resorcarenes and calixarenes are concerned the formation of different complex species in solution is strongly dependent on the solvent.

The unusual behavior observed in the conductometric titration curves of **1** and  $Hg^{2+}$  in acetonitrile and methanol led us to attempt to isolate the complex. A single-crystal X-ray diffraction study performed on the solid obtained from a MeCN solution revealed the mercury salt  $(SC_2H_5)_9Hg_6 \cdot 3ClO_4 \cdot H_2O$ . A molecular diagram of the complex is shown in Figure 4a, while Figure 4b is a view of the crystal packing, reflecting the polymeric structure of the salt. It should be noted, in Figure 4a, that three  $Hg^{2+}$  ions are linearly coordinated to two sulfur atoms while the remaining cations (the other three  $Hg^{2+}$  ions) are in a tetrahedral environment of sulfur atoms. Therefore, we concluded that the mercury(II) complex most likely decomposes into a quinone resorcarene.

Having identified the composition of the complexes formed between **1** and metal cations in acetonitrile ( $Ag^+$  and  $Pb^{2+}$ ) and in methanol ( $Ag^+$  and  $Cu^{2+}$ ), we proceeded with the thermodynamics of these systems in these solvents and the results are now discussed.

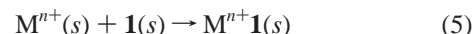
**Thermodynamics of Complexation.** Stability constants and derived standard Gibbs energies,  $\Delta_c G^\circ$ ; enthalpies,  $\Delta_c H^\circ$ ; and entropies,  $\Delta_c S^\circ$ , for  $Ag^+$  and  $Pb^{2+}$  in acetonitrile and for  $Ag^+$

**TABLE 5: Thermodynamics of the Complexation of **1** with Metal Cations in Acetonitrile and Methanol at 298.15K**

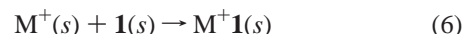
<b>1</b> (L:M)	$\log K_s$	$\Delta_c G^\circ$ (kJ mol <sup>-1</sup> )	$\Delta_c H^\circ$ (kJ mol <sup>-1</sup> )	$\Delta_c S^\circ$ (J mol <sup>-1</sup> K <sup>-1</sup> )
Acetonitrile				
$Pb^{2+}$	$2.83 \pm 0.01^a$	$-16.14 \pm 0.01$	$-35.7 \pm 0.1^a$	-66
$Ag^+$	$3.20 \pm 0.01^a$	$-18.25 \pm 0.01$	$-28.3 \pm 0.5^a$	-34
Methanol				
$Cu^{2+}$	$3.4 \pm 0.1^a$	$-19.5 \pm 0.6$	$-2.9 \pm 0.5^a$	56
$Ag^+$				
(1:1)	$9.53 \pm 0.04^b$	$-54.4 \pm 0.2$	$-32.4 \pm 0.04^a$	74
(1:2)	$7.21 \pm 0.04^b$	$-41.1 \pm 0.2$	$-24.50 \pm 0.04^a$	57
overall	$16.74 \pm 0.08$	$-95.5 \pm 0.4$	$-56.90 \pm 0.08$	130

<sup>a</sup> Calorimetric data. <sup>b</sup> Potentiometric data.

and  $Cu^{2+}$  in methanol at 298.15 K are listed in Table 5. For  $Ag^+$  and  $Pb^{2+}$  in MeCN and  $Cu^{2+}$  in MeOH, these data are referred to the process



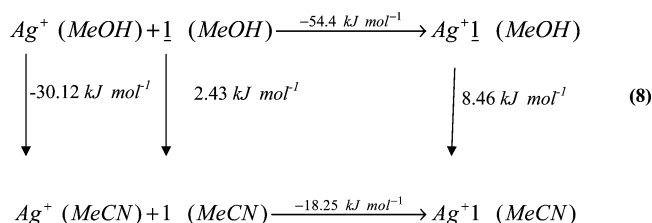
In eq 5,  $M^{n+}$  and  $M^{n+}\mathbf{1}$  denote the free and complex cation, respectively. For  $Ag^+$  and **1** in methanol, the processes taking place are those shown in eqs 6 and 7.



In all cases, these equations are representative of the processes taking place in solution. This statement is based on the fact that the working range of concentration is that at which the electrolytes are predominately in their ionic forms in solution.<sup>44–46</sup>

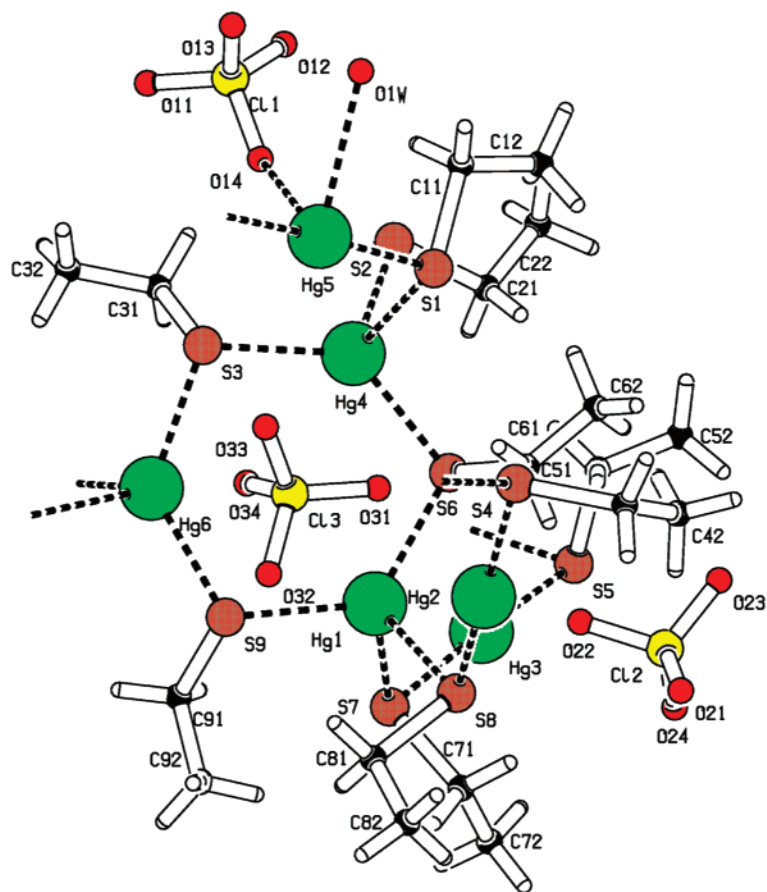
The results in Table 5 clearly show that, in acetonitrile, the lead and silver complexes are relatively weak. In both cases, the process is enthalpically controlled and entropically destabilized. The higher stability of silver and **1** relative to  $Pb^{2+}$  and this ligand in this solvent is due to the lower decrease in entropy of the former relative to the latter system. This is mainly attributed to the higher desolvation of  $Ag^+$  (highly solvated in acetonitrile) relative to  $Pb^{2+}$  in this solvent. Indeed, the desolvation of the cation will lead to a decrease in enthalpic stability with an entropy increase as reflected in these data. This statement is further corroborated in the results obtained for  $Ag^+$  and **1** in methanol, the latter solvent being a poorer solvator for this cation than acetonitrile. This is reflected in the  $\Delta_c G^\circ$  ( $Ag^+$ )<sub>(MeOH→MeCN)</sub> =  $-30.12$  kJ mol<sup>-1</sup> (ref 39, data based on the  $Ph_4AsPh_4B$  convention).<sup>47</sup>

To corroborate this statement, complexation of **1** and  $Ag^+$  in the two solvents (Table 5) and transfer Gibbs energy data for the cation, the ligand (Table 2) and the complex cation (obtained via the cycle shown below) from MeOH to MeCN are inserted in the following thermodynamic cycle (expressed in terms of Gibbs energies)

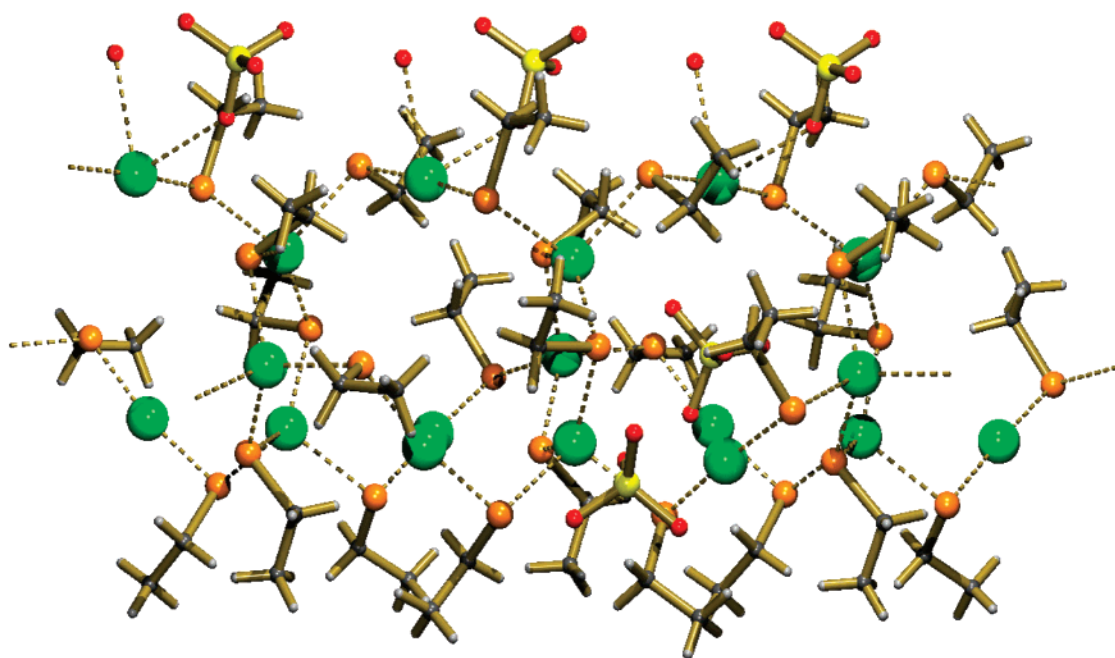


The data in the cycle clearly illustrates that it is the lower solvation of the free cation in MeOH relative to MeCN which contributes most significantly to the higher stability of the

(a)



(b)



**Figure 4.** X-ray structure of the reaction products derived from the interaction of  $\text{Hg}^{2+}$  and **1** in acetonitrile solution: (a) asymmetric unit content of the  $(\text{SC}_2\text{H}_5)_6\text{Hg}_6 \cdot 3\text{ClO}_4 \cdot \text{H}_2\text{O}$  salt, showing the linear and tetrahedral coordination around the  $\text{Hg}(\text{II})$  ions (in dashed lines); (b) crystal packing, showing the polymeric structure of  $(\text{SC}_2\text{H}_5)_6\text{Hg}_6 \cdot 3\text{ClO}_4 \cdot \text{H}_2\text{O}$ .

complex in the former relative to the latter solvent. To a much lesser extent, complex solvation (higher in MeOH than in MeCN) also contributes favorably to the higher stability in the alcohol relative to the aprotic solvent.

Unlike in MeCN, the complexation process in methanol is enthalpically and entropically favorable. However, while  $\text{Ag}^+$

is controlled by enthalpy, the opposite occurs for  $\text{Cu}^{2+}$  and this ligand in this solvent. This is now being investigated.

### Conclusions

From the above discussion, the following conclusions are drawn: (1) The analysis of solution equilibria involving



resorcaren derivatives containing hydroxy groups in aprotic media is by no means a trivial issue. In these media, assembled systems resulting from self-association of resorcarenes may be formed. Partition measurements involving two aprotic and one protic solvent revealed that as far as this receptor is concerned, **1** is predominantly in its monomeric state in these solvents. (2) A rather versatile behavior is shown by this ligand in its complexation with metal cations. Electrical conductance provided key information regarding the composition of metal-ion complexes as well as their decomposition. Thus, the sharp increase in conductance observed for mercury(II) in the presence of an excess of ligand in acetonitrile and methanol is likely to be due to the breakage of the complex (as reflected in the X-ray structure of the isolated material) with the formation of multicharged polymeric species with higher mobility. As far as  $\text{Cu}^{2+}$  is concerned, the poor solvation of  $\text{Cu}^{2+}$  in acetonitrile [ $\Delta_r G^\circ \text{Cu}^{2+}(\text{H}_2\text{O} \rightarrow \text{MeCN}) = 50.21 \text{ kJ mol}^{-1}$ , data based on the  $\text{Ph}_4\text{AsPh}_4\text{B}$  convention]<sup>47</sup> favors the formation of metalates in this solvent, whereas a complex of 1:1 (metal cation/ligand) stoichiometry is found in methanol. Indeed, the rather positive entropy and the lower enthalpic stability (Table 5) shown for this system in methanol strongly suggest that the metal cation may undergo strong desolvation upon complexation in this alcohol. These results contrast with those for  $\text{Ag}^+$ . As any cation having a  $d^{10}$  electronic configuration,  $\text{Ag}^+$  back-bonds its d electrons to acetonitrile<sup>48</sup> and, therefore, it is well solvated in this solvent. As a result, it is reluctant to interact with the ligand to the extent that the complex stability reflects the formation of a weak complex in this solvent. In fact, taking into account the  $\Delta_r G^\circ$  value of reactants and product from acetonitrile to methanol (as shown by the thermodynamic cycle, eq 8), it follows that it is the solvation changes that the cation undergoes in these two solvents that is the main contributor to the higher complex stability observed for this cation and **1** in methanol relative to acetonitrile. It is a general phenomenon that a good solvator for the reactants is a poor medium for complexation.<sup>36</sup>

**Acknowledgment.** The authors thank the European Commission for the financial support provided under Contract ICA-CT-2002-10055 and ICA-CT-2004-509159.

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