

# Metal Ion Recognition Properties of Self-Assembled Monolayers

## ABSTRACT

The advent of self-assembled monolayers (SAMs) formed by organosulfur compounds on gold opened the possibility of designing molecular architectures at the electrode-solution interface and to control the reactivity of the electrode so that it becomes selectively responsive to a given species. In this article, a summary of SAMs designed for molecular recognition events will be presented, with special emphasis in metal ion recognition from our recent work with cyclic and acyclic polyether SAMs on gold. A series of dithia-crown-tetrathiafulvalene (TTF) derivatives with one or two disulfide groups has been prepared, and their SAMs on gold have been characterized by electrochemistry and by reflection-absorption infrared spectroscopy (RAIRS). These SAMs are extremely stable upon repeated electrochemical potential scans and can selectively recognize alkali metal ions. Acyclic polyether derivatives can also self-assemble on gold to yield selective metal ion recognition domains. Some of the SAMs prepared with new polyether derivatives are able to detect potassium cations selectively when templated in their presence. These structures are believed to result as a consequence of ion "imprinting" during the process of SAM formation. Finally, the first report of the self-assembly of different conformers of *p*-tert-butylcalix[4]crown-6 derivatives on gold electrodes and their conformationally-controlled Cs<sup>+</sup> recognition is discussed.

## 1. INTRODUCTION

Organic monolayer films, which contain well-defined surface environments, offer the level of structural control required for detailed studies of organic surfaces.<sup>1</sup> Interfacial interactions play an essential role in electrochemistry,<sup>2</sup> chromatography,<sup>3</sup> formation of detection devices, switches and sensors<sup>4</sup> and biological membranes, including cellular interactions and cell-surface biochemistry.<sup>5</sup> The complexity of these systems and their frequent lack of defined structure has made the preparation of well-ordered and easily characterized model systems (for example: organic monolayer films)



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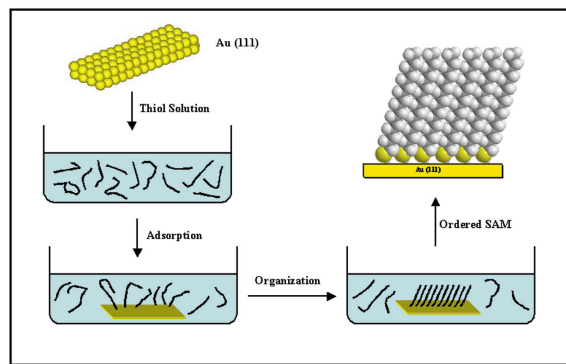
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essential to gain insight into fundamental interactions involved in such systems. Of all the types of monolayer films studied, monolayers prepared by adsorption of alkanethiols on gold, silver, and platinum are particularly useful.<sup>1</sup>

Self-assembled monolayers (SAMs) rely on strong specific interactions between an adsorbate and a substrate to drive the spontaneous formation of a monolayer film (see **Figure 1**). To prepare a SAM the substrate is simply immersed in a dilute (ca. 1mM) solution of the adsorbate at room temperature for

an interval varying from a few minutes to several days, depending on the system. Gold substrates are commonly employed, and typically, organosulfur compounds (including dialkyl sulfides, dialkyl disulfides and thiols) are used as adsorbates. The densely packed, oriented films that result are thermodynamically stable and mechanically robust. SAMs of organosulfur derivatives on gold can be removed from the solutions from which they form and immersed in other solvents without apparent desorption. In addition, their ease of preparation and characterization, their flexibility in functionalization of terminal group at the monolayer surface, and the inertness of gold towards most organic functional groups has resulted in considerable activity in this field since the first publication by Nuzzo and Allara.<sup>6</sup>

SAMs have been characterized and studied by a range of techniques including ellipsometry, transmission elec-



**Figure 1.** Formation process of self-assembled monolayers (SAMs)

tron microscopy (TEM), contact angle determination, reflection adsorption infrared spectroscopy (RAIRS), X-ray photoelectron spectroscopy (XPS) and electrochemistry.<sup>1</sup> Of all these techniques, electrochemistry is particularly convenient to characterize SAM structures and that is the main reason why most of the experimental and theoretical analyses mentioned in this article include electrochemical studies.

In this article we will concentrate on monolayers of alkyl-sulfur compounds on gold, with special emphasis on our own research in metal ion recognition and molecular templating in self-assembled monolayers of cyclic and acyclic polyethers. First, we will discuss the phenomena of molecular recognition in SAMs. We will then summarize the principal examples of SAM structures prepared for the recognition and sensing of metal ions. The main portion of the article is devoted to the presentation of our work with cyclic and acyclic polyether SAMs on gold. Because of the strong S-Au interactions, thiol, disulfide and sulfide adsorbates were used as anchoring points for the formation of the SAMs.

## 2. MOLECULAR RECOGNITION ON FUNCTIONALIZED SAMs

Molecular recognition phenomena have been extensively studied in the last two decades, probably because of the realization of the widespread importance of non-covalent interactions in biochemistry.<sup>7</sup> In living systems, 3-D molecular structures control substrate recognition properties. Molecular organization and molecular recognition are intimately related and respond to the same kind of intermolecular forces, such as ion-dipole, hydrogen bonding, van der Waals, aromatic  $\pi$ - $\pi$  stacking, and other similarly weak interactions. Therefore, detailed studies of the interplay between self-assembly forces and binding phenomena are relevant and important.

Molecular recognition on a functionalized monolayer surface, in which the model surface is constructed from a mixed monolayer of alkanethiolates and receptor-terminated alkanethiolates on gold films, is shown schematically in **Figure 2**. This system permits the examination of the individual parameters that impact recognition, such as solvent/ligand and solvent/receptor interactions, and the impact that the surface environment has on the ability of the receptor on the surface to recognize ligands from solutions.<sup>8</sup>

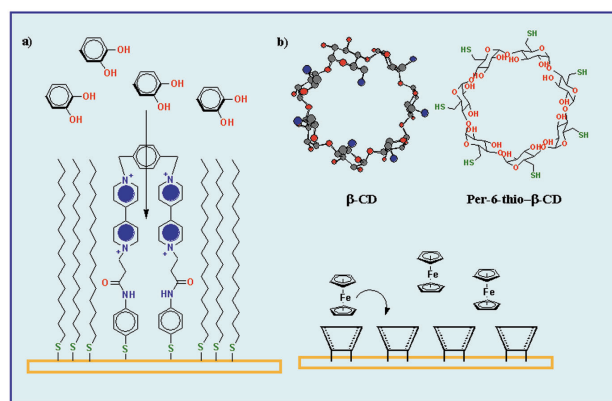
Several articles have described molecular recognition phenomena involving SAMs.<sup>9</sup> For instance, Kaifer and Rojas designed and synthesized a redox-active receptor, based on the well-known host cyclobis(paraquat-*p*-phenylene) (see **Figure 3a**), that chemisorbs on gold electrode surfaces, where it binds electron-rich aromatic guests, such as the biologically relevant compounds catechol and indole, allowing their voltammetric detection at micromolar concentration levels.<sup>10</sup> Another approach of the same authors relies on the synthetic modification of well-known receptors in order to drive

their interfacial self-assembly.<sup>11</sup> For this purpose, per-6-thio- $\beta$ -cyclodextrin (**Figure 3b**) was prepared in two steps from  $\beta$ -cyclodextrin. This derivative chemisorbs on gold and generates stable, but imperfect monolayers. The authors developed a simple procedure to "patch" the defects of these monolayers with a solution of ferrocene and pentanethiol, while the cyclodextrin cavities were protected. However, this procedure may also inactivate a fraction of the surface-attached cavities. The resulting monolayers exhibit excellent binding ability towards appropriate species in the contacting solution.



**Figure 2.** Molecular recognition on a functionalized monolayer surface

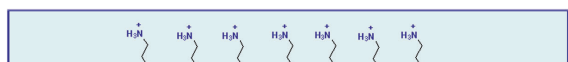
The voltammetric data showed that ferrocene and *m*-toluic acid molecules are included in the cavities of the interfacial receptors and the relative binding strengths correlate well with those observed in the solution phase.



**Figure 3.** Molecular recognition at the electrode-solution interface. (a) Idealized representation of the interfacial binding event between a cyclobis(paraquat-*p*-phenylene) derivative and catechol, (b) interfacial binding properties of a thiolated  $\beta$ -cyclodextrin derivative

SAM structures have also been prepared for the recognition and sensing of metal ions, some of which are electrochemically active.<sup>12</sup> One of us reported the first example of the use of the well-known ammonium-crown ether interaction as the driving force for the formation of SAMs via specific interactions at the electrode-solution interface.<sup>13</sup> The principle, as illustrated in **Figure 4**, involves initially the formation of a thiolated SAM terminated in ammonium groups, followed by a secondary self-assembly of the crown-fullerene monolayer driven by the interaction between the crown ethers and the ammonium groups.<sup>13</sup>

Since the fullerene group is electroactive, it is very easy to detect the current for the first reduction of the fullerene moiety to its monoanionic state. The current detected for the same solution of the methanofullerene in the absence of a cystamine monolayer can be easily subtracted from that observed in the presence of the monolayer to obtain the surface concentration effect. After simulation and appropriate calibration of the electrode surface area, a surface coverage of  $1.4 \times 10^{-10}$  mol/cm<sup>2</sup> was determined. Assuming an area per molecule of  $100 \text{ \AA}^2$  for the C<sub>60</sub> group, a close-packed coverage of  $1.9 \times 10^{-10}$  mol/cm<sup>2</sup> is calculated. This means that about 75% of the surface is covered by this double self-assembly driven process.



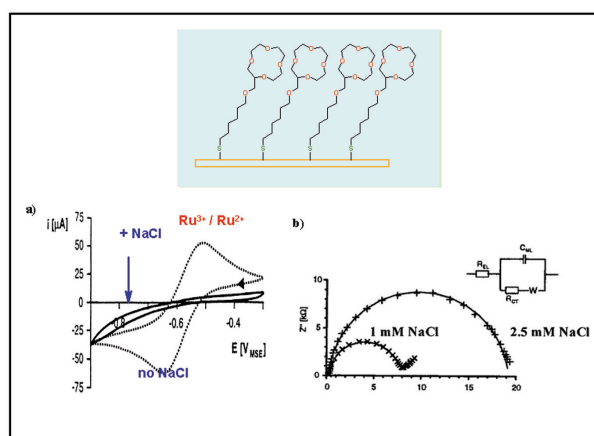
**Figure 4.** Formation of a cystamine monolayer on gold followed by its interaction with a benzo[18]crown-6 methanofullerene. A secondary monolayer of fullerenes is formed by self-assembly due to molecular recognition between the ammonium groups and the crown ether

### 3. SELF-ASSEMBLED MONOLAYERS OF CYCLIC AND ACYCLIC POLYETHERS

The field of supramolecular chemistry started with the selective binding of alkali metal cations by natural, as well as by synthetic macrocyclic ligands, the crown ethers and the cryptands.<sup>14</sup> This led to the emergence of molecular recognition as a new emphasis area of chemical research that has continued to expand across disciplines. However, it was relatively recently that Reinhoudt *et al.*<sup>15</sup> and Bryce *et al.*<sup>16</sup> reported, almost simultaneously, the incorporation of crown-ether groups into SAMs and their use as potential metal ion sensors. Reinhoudt *et al.* described the reversible and selective complexation of electrochemically inactive metal ions from aqueous solutions to self-assembled monolayers of 12-crown-4 and 15-crown-5 adsorbates as monitored both by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). Characterization of the crown ether monolayer by cyclic voltammetry in the presence of Ru(NH<sub>3</sub>)<sub>6</sub>Cl<sub>3</sub> showed that the heterogeneous electron transfer from the gold electrode to the redox couple in aqueous solution was hardly influenced by the presence of the SAM. The large current density

of the redox waves around  $-0.56 \text{ V}_{\text{MSE}}$  indicated that the redox couple can easily access the electrode surface. Addition of NaCl to the electrolyte led to a drastic decrease of the faradaic current for the 12-crown-4 derivative modified electrode as shown in **Figure 5a**. Hence, complexation of metal cations by the SAM generates surface-confined positive charge that repels the positively charged redox couple thus attenuating its redox current.<sup>15a</sup> This means that cyclic voltammetry allows the detection of metal cation complexation by the monolayer.

More interestingly, the Reinhoudt group used electrochemical impedance spectroscopy (EIS) to quantitatively determine the interactions between the SAMs and the metal ions. This technique enables the detection of interfacial ion recognition phenomena when both guest ion and host monolayer are electrochemically inactive, by detecting changes of the charge-transfer resistance induced by metal ion binding (see **Figure 5b**). Gold electrodes modified with a SAM of 12-crown-4 detect Na<sup>+</sup> even in the presence of a 100-fold excess of K<sup>+</sup> and, as a result of the high surface density of crown ethers, sandwich complexes are formed.<sup>15</sup>



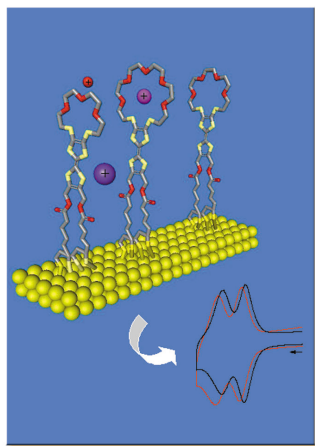
**Figure 5.** (a) Cyclic voltammograms of the 12-crown-4 derivative modified gold electrode in aqueous solutions. The dotted CV is recorded in 100 mM Et<sub>4</sub>NCl + 1 mM Ru(NH<sub>3</sub>)<sub>6</sub>Cl<sub>3</sub>; the solid CV is recorded in 14 mM NaCl + 86 mM Et<sub>4</sub>NCl + 1 mM Ru(NH<sub>3</sub>)<sub>6</sub>Cl<sub>3</sub>, (b) Impedance spectra of the 12-crown-6 derivative modified gold electrode in solutions containing 1 mM NaCl (X) and 2.5 mM NaCl (+). Fits to the spectra are indicated by the solid lines. Inset shows the Randles equivalent circuit, used to fit the spectra, consisting of an electrolyte resistance ( $R_{EL}$ ), a monolayer capacitance ( $C_{ML}$ ), a charge-transfer resistance ( $R_{CT}$ ), and a diffusion element ( $W$ )

#### 3.1. Crown-Ether Annelated Tetrathiafulvalene Derivatives

In the case of metal cation recognition, the efficiency of the electroactive tetrathiafulvalene (TTF) framework has been recently demonstrated with crown TTF derivatives (**Figure 6**).<sup>16-18</sup> The redox-active TTF can exist in three stable redox states (TTF<sup>0</sup>, TTF<sup>+</sup>, and TTF<sup>2+</sup>), and for this reason TTF derivatives have been extensively used in materials chemistry.<sup>19</sup> Yip *et al.*<sup>17</sup> first reported SAMs

on gold electrodes of *n*-mercaptoalkyl tetrathiafulvalenecarboxylate terminated in a thiol group, even though the SAMs were relatively unstable. Subsequently, a TTF incorporating four thiol groups, which forms very robust SAMs on gold, was described<sup>18</sup> and more recently, Amabilino and coworkers have prepared monolayers of TTF derivatives linked to a gold surface through 1,2-ethylene dithiolate groups.<sup>20</sup> As mentioned before, Bryce *et al.*<sup>16</sup> were the first ones to incorporate crown-ether groups into TTF-SAMs, and their use as potential metal ion sensors was clearly demonstrated. Positive potential shifts of the first oxidation wave of the TTF unit were observed upon metal binding, similar to those observed in solution, e.g.,  $\Delta E^{1/2}$  for  $\text{Na}^+$  and  $\text{Ba}^{2+} = 45$  mV. In these monolayers, if the potential scanned was limited to the first wave, the CV response was recorded for at least 1000 cycles. However, the electroactivity gradually decreased when the potential was scanned beyond the first oxidation.<sup>16</sup>

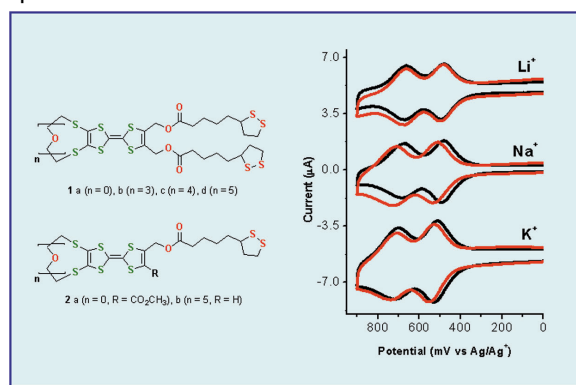
The use of multiple anchoring sites provides very strong adherence of organic compounds to metal surfaces, especially when sulfur atoms are contained within the same ring structure, in which case they exhibit a chelate effect.<sup>21</sup> For this reason, the use of thiocetic acid derivatives as anchoring groups for SAMs has recently received considerable attention.<sup>22</sup> In addition, the commercial availability of thiocetic acid (1,2-dithiolane-3-valeric acid) stimulated us to prepare compound **1a-d** and **2a,b** shown in **Figure 7**.<sup>23</sup> The compounds were directly synthesized in high yield by reacting the corresponding alcohols with thiocetic acid in the presence of 1,3-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP), using  $\text{CH}_2\text{Cl}_2$  as solvent.<sup>10-12</sup>



**Figure 6.** SAMs of different crown-ether annelated tetrathiafulvalenes for metal cation recognition

RAIRS is a useful technique that provides information about monolayer formation and also about the degree of organization. Comparison of the conventional transmission spectrum with those of the monolayers of **1a-d** reveal in the higher frequency region, a disorder or liquid-like packing around the environment of the methylene chains in the monolayer (almost the same wavelength  $\approx 2925$   $\text{cm}^{-1}$ ). Increasing the size of the appended crown apparently results in disordered monolayers.

On the other hand, in the lower frequency range for the monolayer of **1b**, the  $-\text{C}=\text{O}$ ,  $-\text{C}=\text{C}-$  and  $-\text{C}-\text{O}-\text{C}-$  stretchings are very weak, but the  $-\text{C}-\text{S}$  stretching at  $666$   $\text{cm}^{-1}$  is very intense. These observations indicate that the two  $-\text{C}=\text{O}$  groups and the  $-\text{C}=\text{C}-$  are oriented almost parallel to the metal surface, whereas the  $-\text{C}-\text{S}$  part, from the crown, is more perpendicular. In contrast, the RAIRS spectra of the monolayers of **1c** and **1d** show intense peaks for the  $-\text{C}=\text{O}$  and  $-\text{C}-\text{O}-\text{C}-$  stretching, but none is observed for the  $-\text{C}-\text{S}$  stretching, indicating that the orientation for the  $-\text{C}=\text{O}$  group in these structures is more perpendicular to the surface than in the case of **1b**.



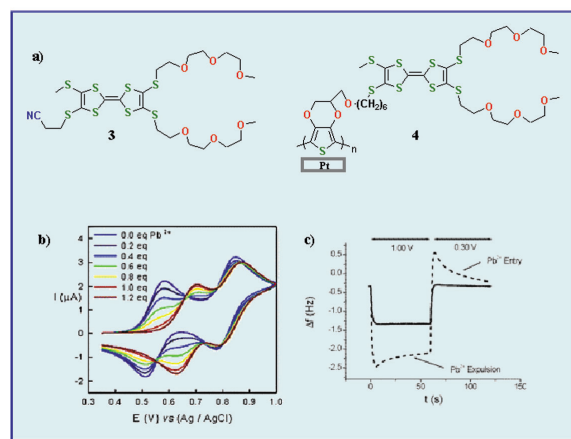
**Figure 7.** Crown-ether annelated tetrathiafulvalene derivatives **1a-d** and **2a,b** and CV analysis of the SAMs of **1d** in THF solutions containing different alkali metal ions ( $\text{Li}^+$ ,  $\text{Na}^+$  and  $\text{K}^+$ )

The CVs of the SAMs obtained with derivatives **1a-d** and **2a,b** showed the expected two one-electron oxidation processes corresponding to the radical cation and dication of TTF respectively (**Figures 6 and 7**). The electrochemical response of these SAMs is consistent with a redox system confined to the electrode surface: the anodic and cathodic peak-to-peak separations are less than 20 mV in all cases, and the full width at half-maximum is 95-110 mV. Also, both oxidative peak currents are proportional to the scan rate (not shown).<sup>23</sup> These SAMs are extremely stable and their electrochemical response remains essentially unchanged, especially for **1a-d**. The latter exhibit almost the same current response even after more than 1000 potential scan cycles.

The effect of adding alkali metal ions to these SAMs varied for the different compound- $\text{M}^+$  combinations. A significant anodic shift was observed for both the first and second redox processes of the SAMs of **1b**, **1c**, **1d**, and **2b** in THF solution when  $\text{Na}^+$  was added. The largest anodic shift observed was for **1d-Na**<sup>+</sup> (60 mV) (see **Figure 7**). However, there is no potential shift observed for the SAMs of **1a** or **2a**, where no crown ether groups are present. These results indicate that the interaction of the metal ion with the dithia-crown ether must be responsible for the potential shifts. The affinity sequence for the SAMs of **1b** and **1d** was  $\text{Na}^+ > \text{K}^+ > \text{Li}^+$ . However for **1c**, the order is  $\text{Na}^+ \approx \text{K}^+ > \text{Li}^+$ , similar to the solution behavior of the corresponding crown ethers.<sup>23</sup>

Very recently, Sallé *et al.* have reported the preparation of a modified surface with the TTF-derivative **3**, which

exhibits unprecedented electrochemical recognition properties among TTF-based ligands.<sup>24</sup> The CV of **3** exhibits a shift of  $E^1_{ox}$  in the presence of  $Pb^{2+}$  with good selectivity. The binding of the metal is accompanied by the concomitant appearance of a new redox system at +120 mV (**Figure 8b**), which corresponds to the reversible oxidation of the  $3 \cdot Pb^{2+}$  complex. These recognition properties were conserved at a solid-liquid interface with poly(**4**). The demonstration of the modulation of the binding affinity of the modified surface, as a function of the potential applied, is given by electrochemical quartz crystal microbalance (EQCM) analysis and by direct measurement of residual  $Pb^{2+}$  in solution by atomic absorption (AA). EQCM is a very informative technique for probing mass-transport processes within thin films. A first set of experiments was carried out without lead and showed a drastic decrease of the frequency on applying a +1.0 V, corresponding to a mass increase due to the entry of  $ClO_4^-$  (see **Figure 8c**). Upon reduction at +0.3 V, the frequency then increases sharply (mass decrease) to a plateau corresponding to the initial values ( $ClO_4^-$  exit). When  $Pb^{2+}$  is present, once the very rapid  $ClO_4^-$  migration is finished at +1.0 V (or +0.3 V),  $Pb^{2+}$  migration can be detected during the oxidation process (slow increase of  $\Delta f$ ,  $Pb^{2+}$  expulsion), as well as during the reduction process (slow decrease of  $\Delta f$ ,  $Pb^{2+}$  binding). From these data, a clear picture of the complexation-expulsion sequence occurring along one scan is obtained.<sup>24</sup>

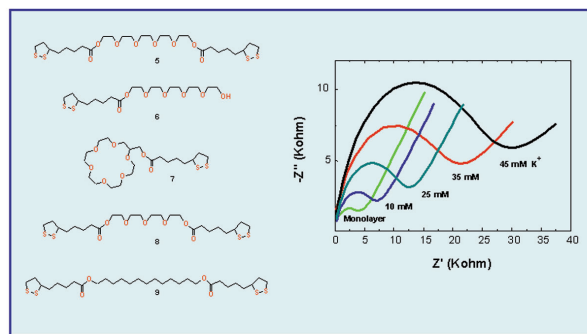


**Figure 8.** (a) TTF based redox-switchable ligands **3** and **4** for binding of  $Pb^{2+}$ , (b) CV response of a  $10^{-3}$  mol solution of **3**, Acetonitrile/ $CH_2Cl_2$  1/1, with  $Pb^{2+}$  ( $Pb(ClO_4)_2$ ),  $Bu_4NClO_4$  (0.1 mol/L), Ag/AgCl, Pt (1mm diameter),  $100\text{ mVs}^{-1}$ , (c) EQCM response of poly(**4**)film, acetonitrile,  $Bu_4NClO_4$  (0.05 mol/L), solid line without  $Pb^{2+}$ , dashed line with  $Pb^{2+}$

### 3.2. Acyclic Oligo(ethyleneglycols) (OEGs) SAMs

In addition to using electrochemical techniques to detect ion binding by crown bearing SAMs, we decided to probe the effect of the degree of preorganization of the host on ion binding and selectivity. The compounds chosen, see **Figure 9**, were very floppy podands (exhibiting essentially no preorganization) to see if they were able to form ion binding domains on the surface (similar to

crown ethers) via the process of self-assembly.<sup>25</sup> Compounds **5-9** (**Figure 9**) were easily synthesized starting from the corresponding glycols and by reaction of these with thioctic acid in  $CH_2Cl_2$  in the presence of DCC and DMPA.<sup>25</sup> Compounds **5** and **6** were obtained from the same reaction as two separate products.



**Figure 9.** Bis-thioctic ester derivatives of oligoethyleneglycols (**5-9**) for SAMs formation and impedance response of monolayer **5** in the absence and in the presence of varying amounts of  $[K^+]$

The monolayers prepared were characterized using reflection absorption infrared spectroscopy, cyclic voltammetry or impedance spectroscopy and reductive desorption.

The RAIRS showed that the essential features are similar for all compounds studied, since they are structurally similar. In the higher frequency region there are two absorption bands due to methylene stretching vibrations from both alkyl and oligoethylene glycol (OEG) fragments. The peak positions of the respective methylene vibration bands in the monolayer are almost the same when compared to the transmission spectra of the compounds, indicating that the alkyl chains in all of the monolayers are in a liquid-like disordered state.<sup>26</sup> Analysis of the spectra in the lower frequency region shows a strong absorption band in the region of  $1740\text{--}1721\text{ cm}^{-1}$  for the  $-C=O$  stretching of the carbonyl group. Furthermore, absorption bands between  $1126\text{--}1129\text{ cm}^{-1}$  are attributed to the parallel polarized  $-C-O-C-$  stretching mode of the OEG part of the monolayer. Shoulders are also observed in the lower frequency region of the  $-C-O-C-$  stretching band at  $1118\text{ cm}^{-1}$  for **5** and  $1121\text{ cm}^{-1}$  for **8**, corresponding to the  $-C-O-C-$  stretching mode perpendicular to the OEG helical axis. Finally, a sharp peak was observed at  $1138\text{ cm}^{-1}$  for **7**, characteristic of the  $C-O$  stretching mode of the ether group.

Reductive desorption of the monolayer of **5**, **7** and **8** in 0.5 M KOH was used to estimate the surface coverage.<sup>27</sup> In all three cases an irreversible cathodic wave was observed at ca.  $-0.9\text{ V vs Ag/AgCl}$ , which corresponds to the surface attached thiolate groups. Integrating the current under the cathodic wave, and normalizing the results on the basis of the number of sulfurs presumably bonded to the surface provides an estimated surface coverage of  $6.2 \times 10^{-11}$ ,  $4.6 \times 10^{-11}$ ,

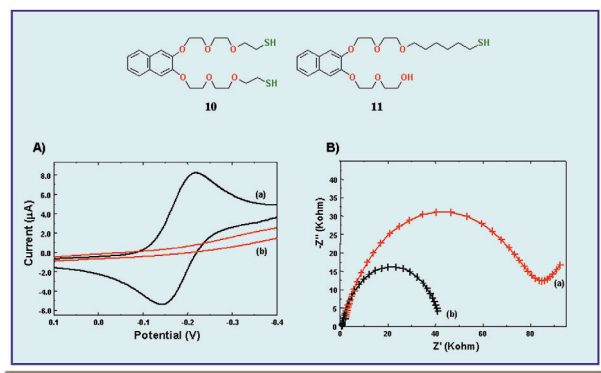
and  $3.3 \times 10^{-11}$  for **5**, **7**, and **8** respectively. These values are lower than that observed for a thiocetic acid (which is the anchoring segment for all the compounds) monolayer on gold.<sup>28</sup> The reduced surface coverage is partly due to the larger size and the presence of the two disulfide functionalities in **5** and **8** and due to the presence of the terminal crown ether group in **7**.

Ion recognition at the interface of these structures was probed by impedance spectroscopy, since none of the structural components of the SAMs are electroactive. Compound **9** forms a monolayer with an initial charge transfer resistance ( $R_{CT}$ ) of 25 K $\Omega$ , but it exhibits no  $R_{CT}$  changes upon exposure to either  $K^+$  or  $Na^+$ . The mono ester compound **6** has almost no charge transfer blocking ability and behaves essentially as a bare gold electrode.

The more interesting results are for the monolayers constituted by **5** and **8**, which exhibit selective ion responses. The  $K^+$  binding ability of monolayer **5** is summarized in **Figure 9**. Based on the results obtained,<sup>25</sup> it is fair to say that a monolayer of **5** can act as a reversible and highly selective sensor for  $K^+$  over  $Na^+$  and in the case of a monolayer of **8** this selectivity is reversed (not shown).<sup>25</sup> The selectivity for  $K^+$  over  $Na^+$  or viceversa suggests the formation of surface-confined pseudo-18-crown-6 or pseudo-15-crown-5 structures. Indeed, these selectivities are similar to those exhibited by 15-crown-5 or 18-crown-6 in aqueous solution<sup>29</sup>, making them potentially useful monolayer sensors.

### 3.3. Ion Imprinted SAMs for Ion Sensing

While molecular recognition sites can be introduced in a SAM as preformed entities (such as the cyclic and acyclic crown ethers described above), they can form



**Figure 10.** Polyether derivatives with the capability of imprinting binding sites for potassium cations. A) Cyclic voltammogram of 1mM  $Ru(NH_3)_3^{3+/2+}$  in 0.1 M tetraethylammonium chloride at (a) bare gold bead electrode and (b) Compound **10** modified gold bead electrode at a scan rate of 100 mV/s. B) Complex impedance plot at dc bias of -0.20 V versus Ag/AgCl in 1 mM  $Ru(NH_3)_3^{3+/2+}$  in a 0.1 M aqueous solution of tetraethyl ammonium chloride for (a) monolayer of **10** grown in the presence of  $K^+$  in solution and (b) monolayer grown without any  $K^+$  in solution. The frequency range used was 1 KHz to 0.1 Hz with a 5 mV rms signal at 10 steps per decade

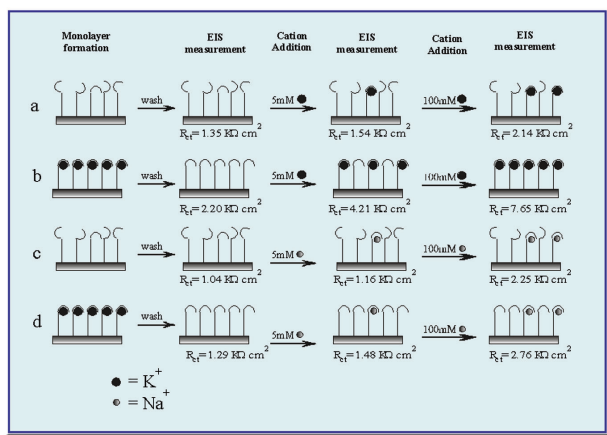
via self-assembly of non-organized groups under the action of molecular imprinting. The latter means that the growth of the SAM occurs in the presence of an appropriate analyte that templates the aggregation of groups that collectively form the recognition motif.<sup>30</sup> We have recently prepared new acyclic polyether thiol compounds that exhibit selective  $K^+$  recognition if imprinted during SAM formation (structures **10** and **11** in **Figure 10**).<sup>31</sup>

The quality of these SAMs was investigated by observing their effect on the voltammetric behavior of the  $Ru(NH_3)_6^{3+/2+}$  couple present in solution. An almost complete disappearance of the Faradaic current was evident for the monolayer modified electrode as shown in **Figure 10(A)**. The voltammetric features suggest that the SAM of compound **10** is capable of providing an effective barrier for electron transfer to the redox species in solution. **Figure 10(B)** shows the impedance response of a monolayer of **10** grown on a gold electrode in the absence of  $K^+$  (curve b) and that of a monolayer of  $K^+$  grown in the presence of  $K^+$  (curve a). The  $R_{CT}$  values obtained are 82.9 and 49.9 K $\Omega$  for parts a and b respectively, indicating a reasonably effective blocking monolayer in both cases.<sup>31</sup> The impedance response corresponding to the monolayer alone (b) contains no diffusion part. On the contrary, a small linear component is present in the lower frequency domain for the response of the monolayer grown in the presence of  $K^+$ , so the impedance data has been treated following two modified Randle's equivalent circuits.<sup>32</sup> Rate constants were calculated to be  $3.0 \times 10^{-4}$  and  $6.1 \times 10^{-4}$  cm/s for the reactions in parts a and b of **Figure 10(B)**, respectively. Although the decrease in the rate constants in both cases is four orders of magnitude relative to the rate constants of the redox couple at a bare gold electrode ( $> 1$  cm/s)<sup>33</sup> the decrease is larger for the monolayer grown in the presence of  $K^+$ .

The different impedance experiments performed suggest the presence of two different binding states for  $K^+$  in the surface-confined structure. The primary  $K^+$  can be removed irreversibly and slowly in contrast to the second one, which exchanges reversibly and quickly. No  $K^+$  incorporation occurs within preformed monolayers.

To probe the selectivity of this templating effect during SAM formation, monolayers were also grown in the presence of other metal ions.<sup>31a</sup> With  $Ba^{2+}$  and  $Ca^{2+}$  the impedance responses are mostly dominated by diffusional components.  $Cs^+$  shows some effects and is incorporated partially in the monolayer while the presence of  $Na^+$  has no effect and leads to an almost identical behavior to that of a simple monolayer. Definitely, the  $R_{CT}$  values in all of these cases are below that observed with  $K^+$ , indicating some selective templating during monolayer formation. RAIRES suggested a more organized and oriented ethylene glycol helix in the monolayer of **10** grown in the presence of  $K^+$ . Based on the results obtained with **10**, receptor **11** was designed

to be used in a cation templating process upon self-assembly on the gold surface.



**Figure 11.** Cartoon representation of the binding of metal cations by a SAM of **11** grown: a) in the absence of KCl (A), and immersed in different  $[K^+]$ , b) in the presence of 0.1M KCl (B), and immersed in different  $[K^+]$ , c) in the absence of KCl (A), and immersed in different  $[Na^+]$ , d) in the presence of 0.1M KCl (B), and immersed in  $[Na^+]$

Two kinds of SAMs were prepared using **11**, in the absence (A) or in the presence (B) of  $K^+$  and the charge transfer resistances ( $R_{CT}$ ) of both SAMs were measured in the presence of increasing concentrations of KCl. These results, as well as the ability of A and B to recognize sodium cations are summarized in Figure 11.<sup>31b</sup> These results show that it is possible to imprint  $K^+$  binding sites into SAMs when the monolayer is assembled on gold in the presence of this metal cation.

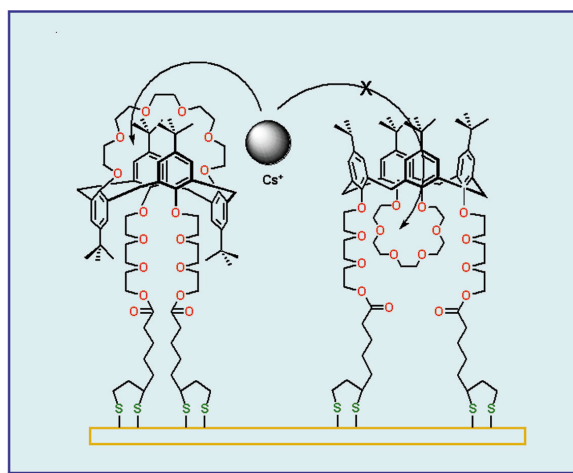
### 3.4. Self-Assembled Monolayers of Calix[4]arene Derivatives

Calix[4]arenes, when suitably modified, can serve as host for a wide range of metal ions, and are ideal platforms to develop receptors for molecular recognition by the incorporation of an appropriate sensory group.<sup>34</sup> Calix[4]crown-6 compounds, in which the pentaethylene glycol unit connects with the 1,3-dialkoxy calyx[4]arene frame, exhibit highly selective complexation towards alkali and alkaline-earth metal ions. They can present four different conformations, described as 1,3-alternate, 1,2-alternate, cone and partial cone, which play crucial roles in the selectivity for different metal cations. Calix[4]crown-6 in its 1,3-alternate conformation is particularly attractive because it exhibits remarkable efficiency to extract cesium ion from nuclear wastes.<sup>35</sup> For this purpose, a number of cesium-ion electrodes based on 1,3-alternate-calix[4]crown-6 derivatives have been prepared and their behavior in solution reported.<sup>36</sup>

The incorporation of calix[4]crown-6 derivatives into SAMs to study their ion recognition properties was only recently reported by Ji *et al.*<sup>37</sup> and we have carried out the preparation of two conformational isomers of bis-thioctic ester derivatives of *p-tert*-butylcalix[4]crown-6,

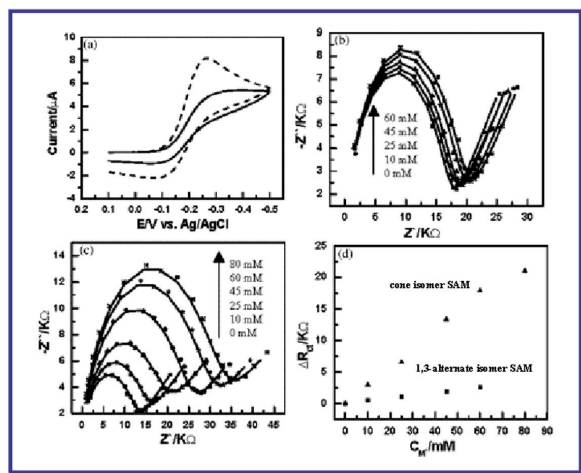
which form stable SAMs on gold and show reversible and selective complexation of metal ions. SAMs derived from the 1,3-alternate derivative bind  $Cs^+$  while those from the cone isomer do not (see **Figure 12**).<sup>38</sup>

**Figure 13a** shows the CV response for the  $Ru(NH_3)_6^{3+/2+}$  redox couple at a SAM modified gold electrode with the 1,3-alternate isomer (dotted line) and the CV response for the  $Ru(NH_3)_6^{3+/2+}$  redox couple with the same SAM modified gold electrode after addition of 45 mM CsCl (solid line). Addition of CsCl results in a drastic reduction of the cathodic current and in the almost complete disappearance of the corresponding anodic current, most probably due to the inhibition of electron transfer at the interface caused by strong repulsion between the 1,3-alternate calix[4]-crown-6 bound cations and the positively charged  $Ru(NH_3)_6^{3+/2+}$  redox couple.<sup>38</sup> In contrast, the CV response at a cone-calix[4]crown-6 gold electrode shows almost no change when CsCl is added to the electrolyte. This means that the cone-calix-[4]crown-6 isomer can not bind  $Cs^+$ , but the 1,3-alternate isomer can recognize  $Cs^+$  very efficiently. Impedance spectroscopy was employed to investigate further the interfacial ion recognition process. The totally different impedance responses for  $Cs^+$  of SAMs of 1,3-alternate and cone-calix-[4]crown-6 isomers ( see **Figures 13b** and **13c**) confirm the selective binding of  $Cs^+$  to the 1,3-alternate isomer. The fitting of all the impedance data were done by the program Equivalent Circuit. **Figure 13d** shows a plot of  $\Delta R_{ct}$  versus  $[Cs^+]$  for SAMs of both isomers. The SAMs of the 1,3-alternate isomer show a linear increase in  $R_{ct}$  with increasing concentration of  $Cs^+$ . This is in contrast to the lack of a response to  $Cs^+$  for the SAM of the cone isomer.<sup>38</sup>



**Figure 12.**  $Cs^+$  recognition in SAMs of *p-tert*-butylcalix[4]crown-6 isomers

The recognition ability of SAMs of these isomers and their 1,2-alternate and partial-cone equivalents for different metal cations was also systematically investigated. Although SAMs of the 1,3-alternate isomer can bind with  $Cs^+$  to some extent, all other SAMs show no recognition ability for alkali metal cations. However, all SAMs serve as good sensors for alkaline metal cations such as  $Ca^{2+}$  and  $Ba^{2+}$ .<sup>39</sup>



**Figure 13.** (a) Cyclic voltammogram of  $\text{Ru}(\text{NH}_3)_6^{3+/2+}$  in 0.1 M  $\text{Et}_4\text{NCl}$  at a SAM of the 1,3-alternate isomer calix-[4]crown-6 modified gold electrode before (dashed line) and after (solid line) addition of  $\text{Cs}^+$  to the electrolyte at a scan rate of 100 mV/s. (b) Impedance response of the electrode modified by a SAM of the cone isomer calix-[4]crown-6 in the absence and in the presence of increasing  $[\text{Cs}^+]$ . The solid lines represent the fits of the experimental points. (c) Impedance response of SAMs of the 1,3-alternate isomer calix-[4]crown-6 modified gold electrode in the absence and presence of increasing  $[\text{Cs}^+]$ . (d) Comparative plot of  $\Delta R_{\text{ct}}$  versus concentration of  $[\text{Cs}^+]$  for SAMs of both isomers

## 4. SUMMARY AND CONCLUSIONS

In this article we have briefly reviewed the principal requirements for the formation of SAMs for molecular recognition, and we have showed the cation binding behavior of different surface-active compounds based on crown-ethers, oligoethylene glycols or polyether derivatives. When incorporated as SAMs on gold these compounds are able to detect ion binding events on the surface.

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The dithia-crown annelated TTF compounds show well-defined surface confined redox waves, and their corresponding SAMs are extremely stable under a wide variety of conditions. The latter are able to recognize metal ions, and the process can be easily monitored following the potential shift of the TTF group, which can serve as a voltammetric sensor for electrochemically inactive ions.

SAMs prepared with the bis-thioctic ester podand derivatives show higher ion binding selectivities than those of analogous crown ethers. These glycols form ion recognition domains on gold, which are surprisingly selective for ion sensing. We have also considered semirigid structures with ethylene glycol arms that selectively detect potassium cations when their SAMs are imprinted in their presence. The concept of ion imprinted SAMs for sensing application shows considerable promise. Judicious choice of structures with various degrees of rigidity and preorganization could result in selective and sensitive systems for ion sensing.

Finally, we have demonstrated how two isomers of *p-tert*-butylcalix[4]crown-6 derivatives form stable SAMs by taking advantage of the adsorption of bis-thioctic ester on gold electrodes, and their  $\text{Cs}^+$  recognition is completely dependent on the conformational orientation of the compounds. These isomers are able to differentiate alkaline earth metal cations from alkali metal cation and consequently, they could be used as sensors.

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