

# Molecular recognition applied to sensors \*

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## Abstract

The role of molecular recognition by synthetic receptor molecules in the signal generation of CHEMFET sensors is discussed together with their self-organization on gold surfaces.

Keywords: Molecular recognition; Sensors

## 1. Introduction

Molecular recognition, combined with chemically modified field-effect transistors (CHEMFETs), is being used to develop selective sensors for cations [1]. For a further extension to the detection of anions and neutral molecules in solution, it will be necessary to design neutral receptor molecules that are able to recognize these species selectively. However, in contrast to the selective recognition of cations, the corresponding area of anion recognition is far less developed [2]. Although macrocycles and clefts with positively charged quaternary ammonium groups, guanidinium fragments or transition metal cations incorporated to aza-macrocycles are known to complex anions, selectivity is not easily introduced. Neutral macrocyclic and acyclic ligands that contain Lewis-acidic binding sites such as boron, silicon, tin, and mercury bind anions, but these structures lack the possibility of subtle structural variation that is the basis for the selectivity in cation and neutral guest complexation.

In nature, the selective complexation of anions takes place by hydrogen bonds; the selective recognition of phosphate and sulfate in biological systems by transport receptor proteins has recently been described [3].

## 2. Neutral anion receptors

We have very recently developed a novel class of neutral anion receptors **1** that contain a unique com-

bination of an immobilized Lewis-acidic binding site ( $\text{UO}_2^{2+}$ ) and additional amide  $\text{C}(\text{O})\text{-NH}$  groups, which can form favourable H-bonds with a coordinated anion guest (Fig. 1) [4,5]. The anion complexation has been systematically studied, both in the solid state by X-ray analysis, and in aprotic solutions by conductometry, cyclic voltammetry and NMR spectroscopy (see, for instance, Fig. 2). High selectivity for dihydrogen phosphate ( $\text{H}_2\text{PO}_4^-$ ) anions has been obtained. In the case of the preorganized ligands **1b** and **1d**, strong ( $K_{\text{ass}} > 10^5 \text{ M}^{-1}$  in MeCN-DMSO, 99:1) and selective complexation of  $\text{H}_2\text{PO}_4^-$  has been observed. Selectivities of  $>10^2$  and  $>10^3$  over  $\text{Cl}^-$  and  $\text{NO}_2^-$ , respectively, were obtained for receptor **1b**.

Currently we are applying the functionalized  $\text{UO}_2$ -salenes for the detection of  $\text{H}_2\text{PO}_4^-$  anion in CHEMFETs and as carriers in transport studies through supported liquid membranes (SLMs).

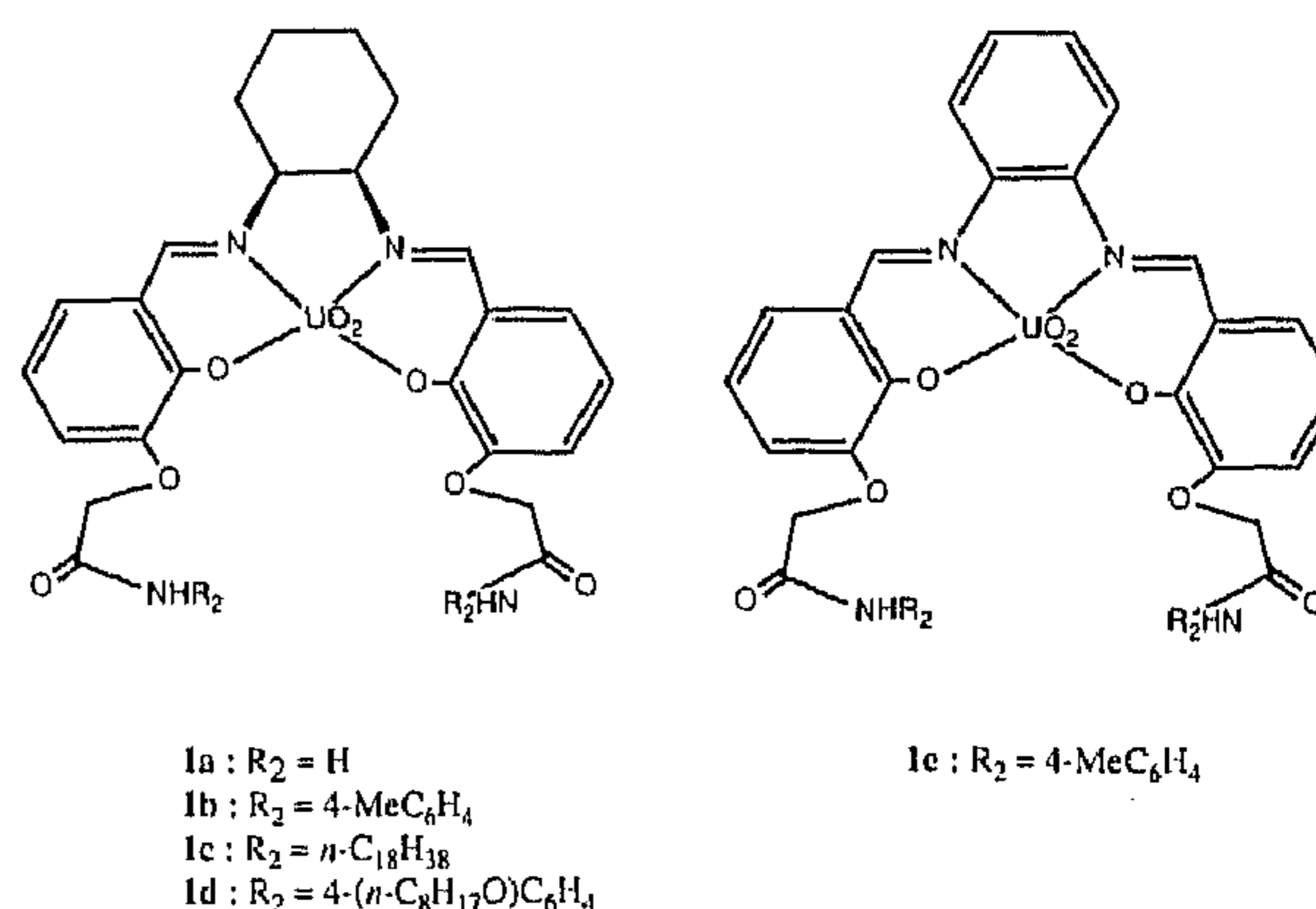


Fig. 1. Structure of anion receptors (1a-e).

\* Plenary lecture.

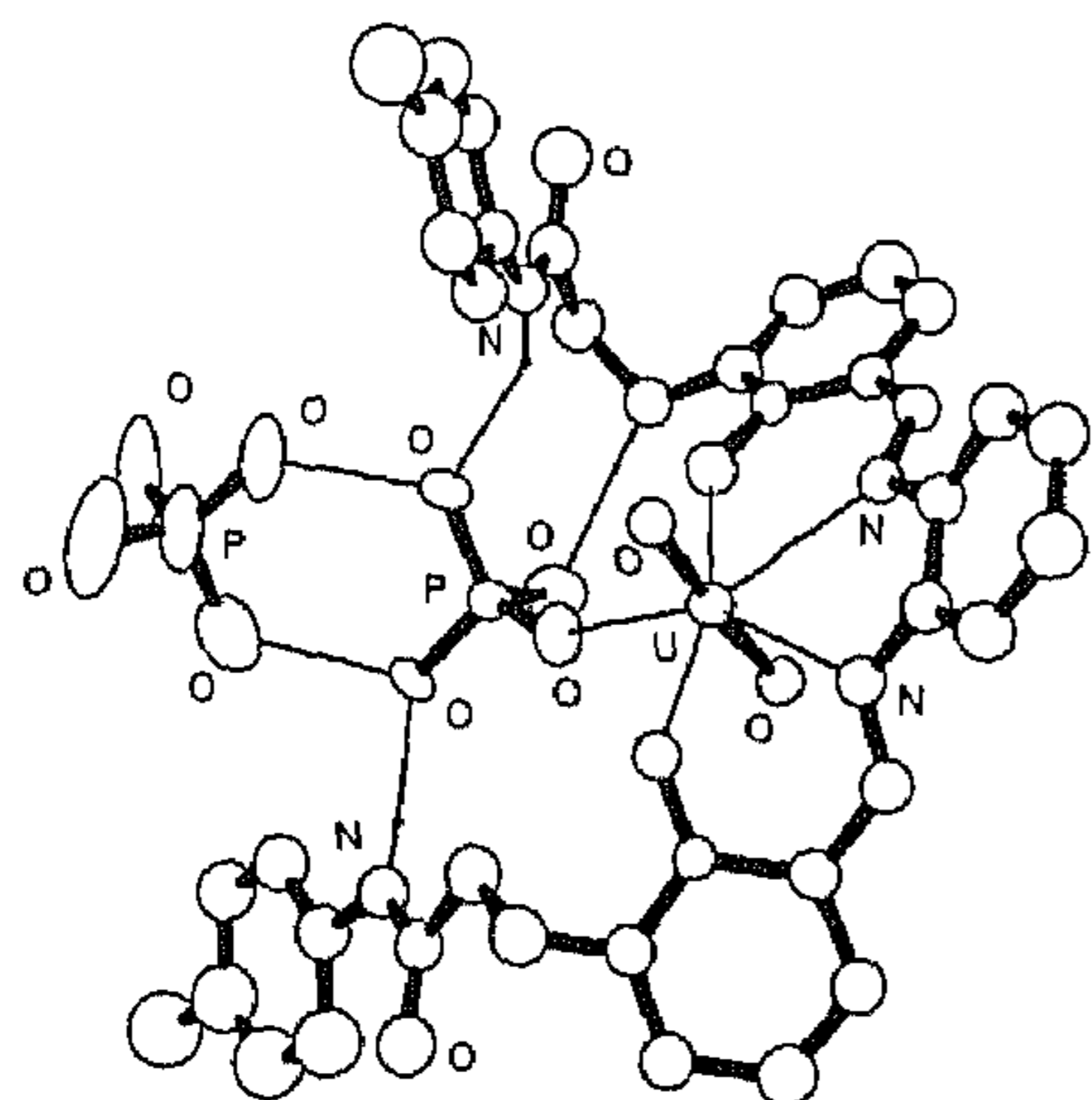
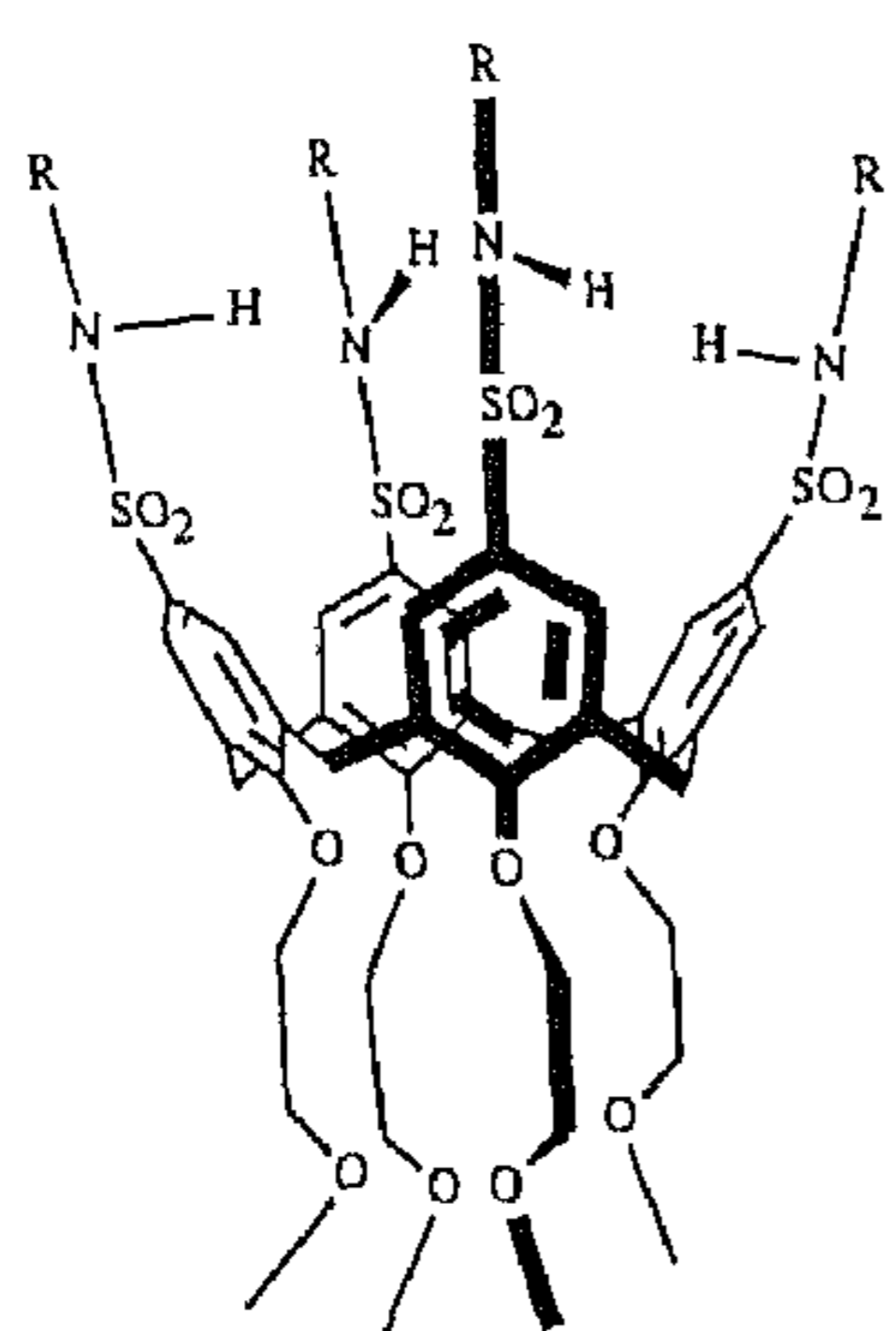


Fig. 2. X-ray structure of  $1e \cdot 2H_2PO_4^-$  complex [5].



- 2a: R = H  
 2b: R = *n*-Pr  
 2c: R = *tert*-Bu  
 2d: R =  $CH_2CH_2NHC(O)Me$

Fig. 3. Structure of receptors (2a–d).

In addition, we have investigated another synthetic receptor mimicking the phosphate and sulfate binding proteins. We recently prepared such molecules, **2** (Fig. 3), in which four or eight amido C(O)NH moieties are preorganized on a rigid calix[4]arene platform. These are capable of selective binding of hydrogen sulfate ( $HSO_4^-$ ) anions [6]. For instance, receptor **2d** exhibits a selectivity for  $HSO_4^-$  of about  $10^2$  over  $Cl^-$  and  $NO_3^-$ . Obviously, the three-dimensional cavity of **2d** complexes the tetrahedral  $HSO_4^-$  better than the spherical  $Cl^-$  and the planar  $NO_3^-$ . To the best of our knowledge, **2a–d** represent the first anion receptors selectivity for  $HSO_4^-$ .

### 3. Bifunctional receptors

The next phase of our research is the design of bifunctional neutral receptors that contain both anionic and cationic binding sites, and are therefore capable of the simultaneous complexation of anionic and cationic species in apolar solvents.

We have synthesized receptors **3** and **4**, which consist of both a uranyl-containing salene part (for the complexation of the anion) and a crown ether or a calix[4]arene tetraester based ionophore, for the complexation of the cation (Fig. 4) [7,8]. The simultaneous complexation of alkali metal cations ( $Na^+$  and  $K^+$ ) and  $H_2PO_4^-$  anions has been proved by  $^1H$  NMR spectroscopy, cyclic voltammetry, FAB spectrometry, and liquid–liquid extraction experiments.

Previously in our laboratory, cation carrier-assisted transport of lipophilic alkali metal salts has been studied. A preliminary investigation showed a significant transport through an SLM of alkali metals chloride and dihydrogen phosphate, both hydrophilic salts, assisted by novel neutral bifunctional receptors. To the best of our knowledge, this is the first example of carrier-assisted co-transport, in which the anion and cation of a hydrophilic salt are bound and transported simultaneously through the SLM.

### 4. Towards the sensing of neutral molecules

Sensors for neutral molecules cannot be based on CHEMFETs because these devices require the variation of a membrane potential. Therefore, we are developing receptor molecules that have a recognition site, and in addition secondary binding sites, for self assembly in a monolayer (2–3 nm thick) on a gold surface.

Resorcin[4]arenes **5** are well suited for this purpose. In addition to the 'cone'-like cavity formed by the four aromatic units, four points of attachment are available for alkyl chains at the methine linkage. These parallel chains are oriented perpendicular with respect to the annulus of the macrocycle. By connecting four 11-thiatheneicosyl chains to the methine linkages, adsorbates have been obtained that are able to form well-packed monolayers (Fig. 5); the sulfur atoms bind to the gold [9]. The monolayers have been characterized with various surface-analytical techniques (XPS, SPR and PIERS).

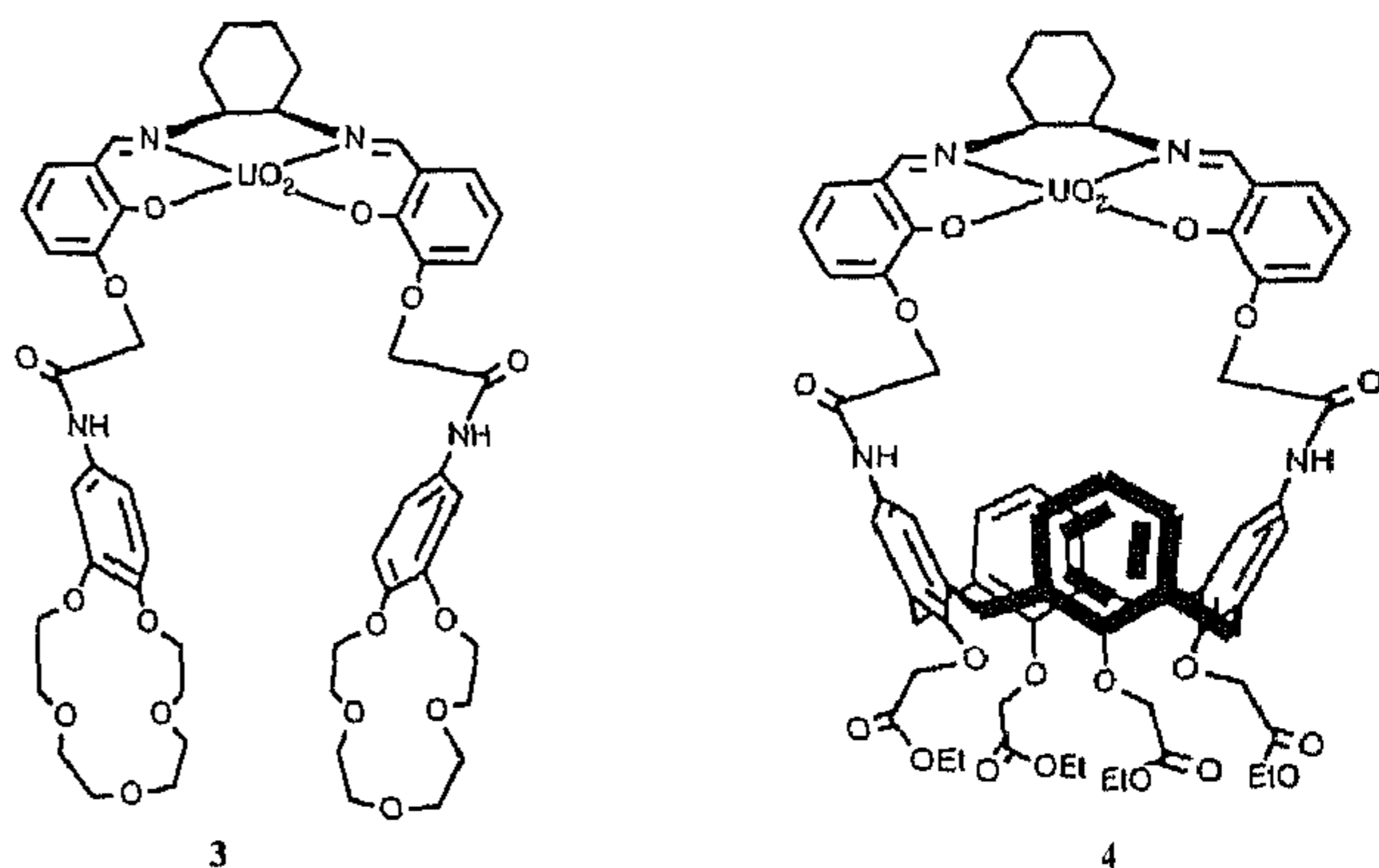


Fig. 4. Structures of bifunctional receptors (3,4).

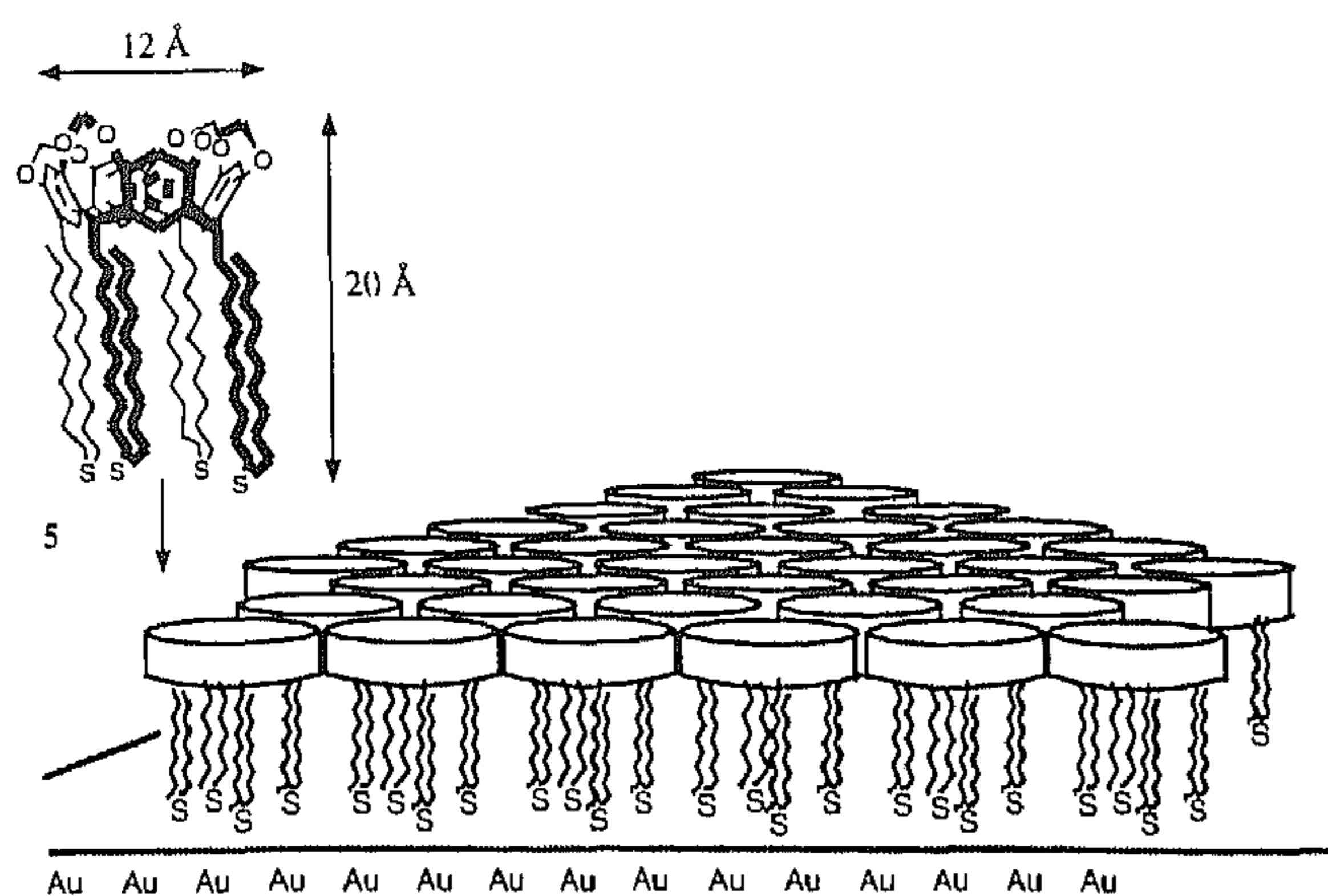


Fig. 5. Schematic representation of monolayers of 5.

The interaction with different neutral molecules is currently under investigation. The first results show a selectivity for tetrachloroethylene over other chlorinated hydrocarbons.

## 5. Conclusions

The complexation of both cationic and anionic species can be achieved by synthetic receptors. These can be applied in thin membranes deposited on top of an ISFET gate surface. For neutral molecules other types of sensors are needed and self-assembled monolayers of receptors on gold are promising in this respect.

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