

# Calix[4]resorcinarene: molecular recognition in Langmuir films

Piotr Prus<sup>a</sup>, Marek Pietraszkiewicz<sup>a</sup>, Renata Bilewicz<sup>b,\*</sup>

<sup>a</sup> Institute of Physical Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Kasprzaka 44 / 52, Poland

<sup>b</sup> Department of Chemistry, Warsaw University, Pasteura 1, 02-042 Warsaw, Poland

## Abstract

The interaction between calix[4]resorcinarene derivatives and amino acids is presented in this paper. Langmuir film technique was used to control this interaction. © 2001 Elsevier Science B.V. All rights reserved.

**Keywords:** Langmuir films; Calix[4]resorcinarene; Amino acids; Surface potential

## 1. Introduction

Molecular recognition of ions and neutral molecules is one of the mainstream topics in supramolecular chemistry. Calixarenes can deliver an outstanding variety of the receptor structures that can, in principle, recognize cationic and anionic species as well as neutral molecules, depending on the substituents attached to the pre-formed calixarene skeleton. The availability of modified calixarenes is much higher than in the case of other synthetic receptors. Development of chiral receptors based on calixarenes may provide not only new analytical tools for controlling the enantiomeric purity, but also a means for the separation of enantiomers. It should be noted that the attractiveness of calixarenes relies on their possibilities to form the molecular cavities of various size and depth. This feature is particularly important for rational design and synthesis of specific receptors for particular molecules or ions that differ in size, functionalities, and shape [5–7].

## 2. Experimental

The calix[4]resorcinarenes 1–3 (Fig. 1) were prepared as described earlier [1–4]. All reagents were purchased from Aldrich, and used without purification.

The Langmuir apparatus KSV-5000 with Wilhelmy plate-type microbalance was used for all experiments.

Surface potential and surface pressure measurements were performed simultaneously as a function of molecular area. Software version KSV 5000 was used. The apparatus was isolated from the environment in a laminar flow hood at  $20 \pm 1$  °C. The accuracy of measurements was  $\pm 0.1$  mN m<sup>-1</sup> for surface pressure,  $\pm 0.01$  Å<sup>2</sup> molecule<sup>-1</sup> for molecular area and  $\pm 5$  mV for surface potential. Water was purified by Milli-Q water purification system (18.2 MΩ). Concentration of calixarene solutions was 1 mg/ml in chloroform distilled over calcium hydride. Phosphate buffers were used to adjust the required pH, and the concentrations of amino acids were 10<sup>-2</sup> M. All experiments were repeated at least three times. The Langmuir isotherms recorded upon compression and decompression were found to overlap, indicating that no aggregation occurred in the systems studied.

## 3. Results and discussion

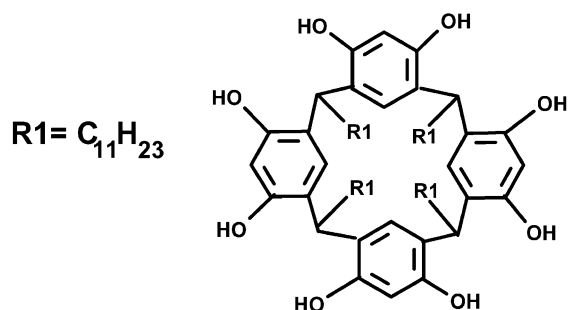
The properties of monolayers of the calixarenes have been studied using subphases of pH in the range 2.7–6.6. In case of unsubstituted calix[4]resorcinarene 1, no significant changes in the  $A_0$  or SP values were observed in the pH range 2.70–6.60. On the contrary, for the calix[4]resorcinarene with nitrogen containing substituents 2 and 3,  $A_0$  increased with the decreasing pH value.

This trend was clearly seen by the dependence of surface potential on the pH (Scheme 1), where for the substituted calixresorcinarenes, the values become higher with decreasing pH, as expected for protonation of the molecules. This might be, therefore, attributed to the sequential protonation of nitrogen atoms in the ephedrine

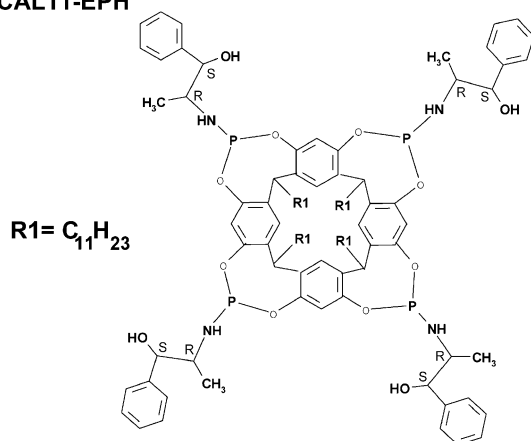
\* Corresponding author. Tel.: +48-22-822-0211; fax: +48-22-822-5996.

E-mail addresses: viayner@ichf.edu.pl (P. Prus), pietrasz@ichf.edu.pl (M. Pietraszkiewicz), bilewicz@chem.uw.edu.pl (R. Bilewicz).

## 1. CAL11



## 2. CAL11-EPH



## 3. CAV11P-PhEt

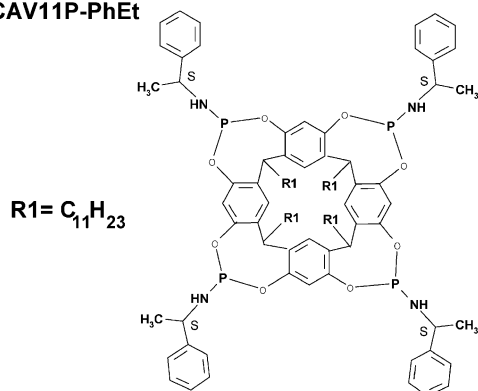
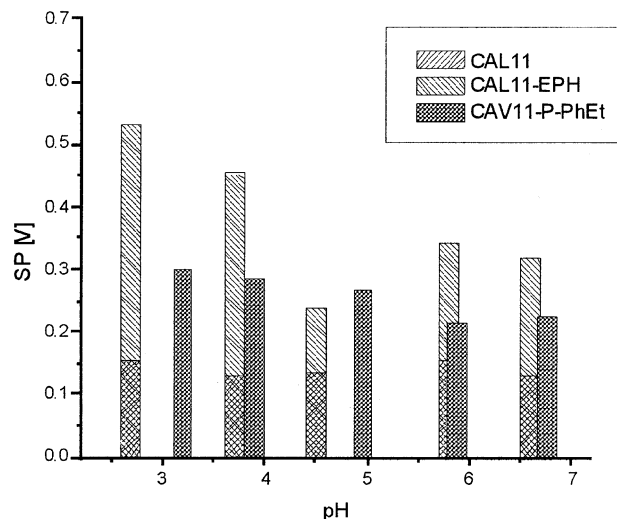


Fig. 1. Formulas of the calix[4]resorcinarenes studied.

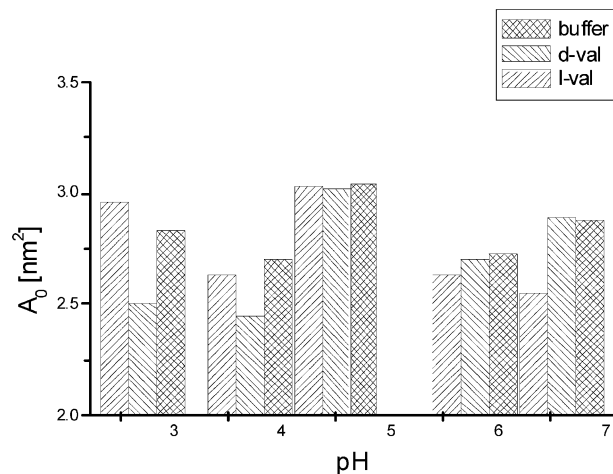
units leading to the increase of electric dipole moments of the molecules and reflected in the value of the surface potential. As can be seen from Scheme 1, the surface potential of the nonderivatized calixarene, where no nitrogen centers are present, is distinctly lower, its value remaining approximately constant and with only ca. 0.1 V throughout the whole pH range studied.

In the presence of D- and L-isomer of amino acids in the subphase, no enantiomeric differentiation was observed for achiral compounds and with no significant amino acid



Scheme 1. Dependence of surface potential in monolayers of calix[4]resorcinarenes 1–3 on buffer solutions.

influence on the surface area  $A_0$ . The chiral calix[4]resorcinarene displayed a different behaviour in the Langmuir monolayer on a subphase containing D- and L-valine, namely, clear differences were observed for subphases of different pH. At pH 3.66 or lower, the D-valine form was the one recognized. The surface pressure and surface potential isotherms were shifted significantly towards smaller molecular areas compared to the isotherm obtained on pure buffer subphase, and the surface pressure corresponding to the collapse of the monolayer was distinctly lower, indicating remarkable interaction of the D-valine with the chiral calixarene. While passing to pH 4.50, no enantiomeric recognition was observed: all three isotherms are overlapping. At pH 5.80, the L-valine enantiomer was recognized. At still higher pH, the collapse pressure differences were



Scheme 2. Dependence of molecular area of calix[4]resorcinarene 3 on buffer solution with amino acids.

even more pronounced which may be interpreted as due to lower flexibility of the host molecules involved in the interactions with the valine enantiomer in solution upon the compression of the monolayer. As shown on the Scheme 2, the recognized isomer formed films with always-lower values of  $A_0$ . For lower pH, isomer D is the one recognized while for high pH, the isomer L. In this case, we can control the recognition process by modifying the pH of the subphase. Mannich-type calix[4]resorcinarenes show high dependence of the surface area for pH subphase because they display high flexibility, and changing of their conformation can reduce the effect induced by recognition of amino acids. Phosphorus cavitands are less flexible now, therefore less dependent on pH, while enantioselection exhibits strong pH dependence. The changes in pH of the subphase containing guest enantiomeric molecules had a profound effect on the type and magnitude of enantioselection. Therefore, preparation of new calix[4]resorcinarene receptors rigidly and totally insensitive to pH changes remains to be a challenged in the synthesis of these macrocycles. Introduction of carboxamide, or sulphonamide enantioselecting groups may be a solution, and work in this direction is in progress in our laboratory.

## Acknowledgements

This work was supported by the Polish State Committee for Scientific Research, Grant No. 3T09A 025 011, and a BST grant from the Department of Chemistry, Warsaw University.

## References

- [1] M. Pietraszkiewicz, P. Prus, R. Bilewicz, *Pol. J. Chem.* 73 (1999) 2035.
- [2] M. Pietraszkiewicz, P. Prus, R. Bilewicz, *Pol. J. Chem.* 73 (1999) 1845.
- [3] P. Prus, M. Pietraszkiewicz, R. Bilewicz, *Supramol. Chem.* 10 (1998) 17.
- [4] M. Pietraszkiewicz, P. Prus, W. Fabianowski, *Pol. J. Chem.* 72 (1998) 1068.
- [5] C.D. Gutsche, J. Calixarenes, F. Stoddart (Eds.), *Monogr. Supramol. Chem., R. Soc. Chem.* (1989) 27–66.
- [6] V. Böhmer, Calixarenes: a versatile class of macrocyclic compounds, in: J.E.D. Davies (Ed.), *Topics in Inclusion Science*, Kluwer Academic Publishing, Dordrecht, The Netherlands, 1991, pp. 3–26.
- [7] R. Yanagihara, M. Tominaga, Y. Aoyama, *J. Org. Chem.* 59 (1994) 6865.