Russian Chemical Reviews **79** (12) 1071 – 1097 (2010) © 2010 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2010v079n12ABEH004107

Molecular receptors and electrochemical sensors based on functionalized calixarenes

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Abstract. The approaches to the design of molecular receptors based on functionalized calixarenes aimed at recognition of ions and neutral organic compounds are considered; such receptors can serve as the basis for potentiometric and amperometric sensors. The application of the receptors is exemplified and analytical characteristics of the sensors are discussed. Particular attention is paid to the factors affecting the efficiency of recognition and selectivity and sensitivity of the developed sensors. The bibliography includes 173 references.

I. Introduction

Development of new highly efficient and selective sensors for the determination of biologically active compounds appears an urgent problem in progress of the modern electrochemical analysis. Successful solution of this problem depends to a great extent on characteristics of receptors providing molecular recognition of the analytes and, consequently, the analytical parameters for determinations thereof. In this connection, numerous investigations are now being carried out in both directed synthesis and studies of synthetic receptors and identification of the factors that determine interactions of the receptors with diverse analytes.

Originally, the interest in synthetic receptors was initiated by development of extraction methods for the separation and preconcentration. Later, this subject was evolved in potentiometric methods of analysis, particularly in creating new ion-selective electrodes (ISE) based on polymeric membranes.[1] The application of such currently known ionophores as valinomycin, crown ethers or dioctyl phenylphosphonate extended the range of compounds that can be determined by ISE and made it possible to produce competitive commercial devices that differ from glass electrodes in simple design and larger diversity of determined compounds. Further enlargement of the range of determined compounds and, in particular, development of ISE for the analysis of organic substrates, stimulated the search for new synthetic receptors and studies of factors responsible for their efficiency. It is noteworthy that synthesis of new receptors is also essential for the successful solution of relative problems implying molecular recognition of analytes. These include membrane technologies of separation, purification and concentration, solid-phase extraction, chromatographic separations *etc*.[2,3]

Macrocyclic compounds, specifically calixarenes and their analogues, belong to a group of promising receptors, the components of electrochemical sensors. Variation of structures of such receptors by changing the size and conformation of a macrocyclic platform and incorporating functional groups as substituents enable alteration of binding selectivity and efficiency of different substrates over broad range. These properties of calixarenes together with their accessibility, availability of the starting reagents and sufficiently elaborated theoretical concepts on the structure – property relationships allow one to consider calixarene-based receptors as very promising components of sensor devices and supramolecular structures, *viz*., ionic channels, nanoparticles and composite materials with functions of the molecular recognition.[3,4]

Rapid progress in the chemistry of calixarenes has been marked by publication of a series of monographs and reviews[4–7] in which problems of application of macrocyclic ligands in analytical chemistry were discussed together with other problems. In these monographs, primary attention was paid to the use of calixarenes in the separation and concentration of analytes, *e.g*., by chromatography and extraction. At the same time, the application of macrocyclic ligands as receptors in sensors received insufficient attention so far. The problems of embodiment of the ability of calixarenes to molecular recognition when incorporated in

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Received 18 September 2009
Uspekhi Khimii **79** (12) 1164 – 1192 (2010); translated by P M Chukurov

supramolecular structures and ISE membranes are far from being comprehensively clarified.

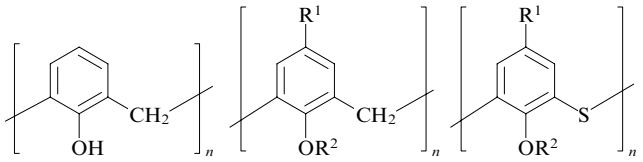
During the last decade, a considerable body of experimental data related to the use of calixarenes in different electrochemical sensors has been accumulated, but this was not generalized so far. In particular, newer methods for functionalization of calixarenes and their application in electrochemical sensors have been developed. These methods partially compensate drawbacks inherent in this group of receptors and make it possible to realize completely their advantages. In the present review, data are generalized on the use of functionalized calixarenes and their thia analogues in electrochemical sensors published over the last decade.

II. Features of molecular recognition by functionalized calixarenes

Application of calixarenes as molecular receptors is based, first of all, on their ability to bind selectively analytes. The structure–property relationships and mechanisms of binding different substrates by calixarenes were repeatedly discussed in the monographs and reviews[4–7] and are not considered in the present review. Nevertheless, it appears appropriate to consider the main structural peculiarities of calixarenes and their ability to recognize different molecules for subsequent discussion of properties of electrochemical sensors based on calixarenes.

Calixarenes are metacyclophanes with a basket-like geometry. According to the IUPAC Nomenclature, compound **1a** with $n = 4$ is named pentacyclo[19.3.1.1.1.1]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene.

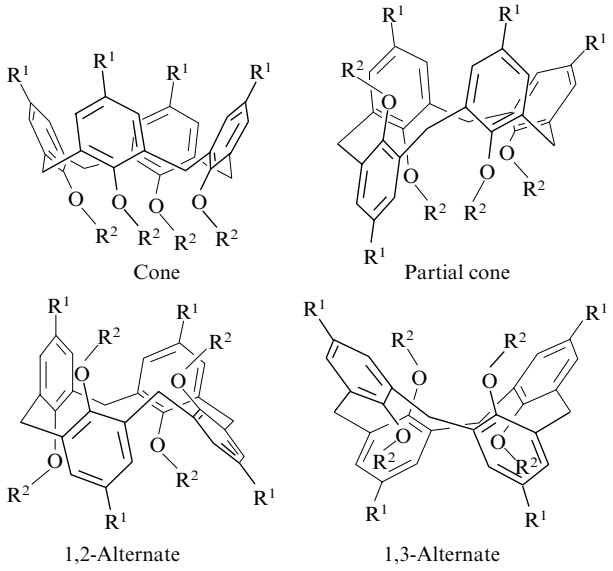
Cram proposed[8] an alternative nomenclature for such rings; in accordance with his nomenclature, compound **1a** is named [1.1.1.1]metacyclophane.[8] The term 'calixarene' (from the Latin *calix*, a bowl; 'arene' indicates the presence of aromatic rings in a molecule) was introduced for the first time by Gutsche[5,6] and now this term is generally accepted. The structure of calixarene **1b** enables functionalization of this compound in the upper and lower rims (hereinafter, R^1 and R^2 stand for substituents on the upper and lower rims, respectively). The combination of structural aryl fragments of the classic calix[4]arene **1a** produces an inner cavity with the average volume of 10 A^3.



1a **1b** **1c**

Compounds **1c** in which the bridging CH_2 groups are replaced by sulfur atoms, are named thiacalixarenes. Incorporation of bridging sulfur atoms increases to some extent the size of the cavity and its conformational flexibility. Heterocyclic analogues of calixarenes have been described, for example, calix[*n*]pyrroles.[9]

From synthetic considerations, tetra-, hexa- and octameric calix[*n*]arenes ($n = 4$, 6, 8) are the most accessible, although compounds with n up to 14 were also prepared.[2,3] Calixarenes exist in different conformations and stability of these conformations can be increased by incorporation of bulky substituents or bridging groups in the macrocyclic platform. For calix[4]arenes, such conformations are cone, partial cone and alternates.



Introduction of bulky alkyl substituents on the upper rim of calix[4]arenes additionally stabilizes the cone and partial cone conformations. Synthesis of lower rim esters and ethers, *e.g.*, *O*-acetyl and *O*-benzyl derivatives, pursued the same goal. Owing to specific features of the synthesis, tetrasubstituted and symmetrical 1,3-disubstituted calix[4]arenes are most available. In these cases, the upper rim usually contains bulky *tert*-butyl substituents stabilizing the cone conformation. A few receptors are known with functional groups in the upper-rim substituents and dimeric and trimeric calixarenes linked by relatively short bridges.

Calixarenes are characterized by high melting points, which virtually always are noticeably higher than those of acyclic analogues. Yet another characteristic feature of calixarenes is their low solubility in organic solvents, which often complicates purification and identification of these compounds and their incorporation into polymeric membranes of sensors. The nature of a substituent in the *para*-position of the phenol fragments substantially influences their solubility. Among calixarenes with non-polar substituents, allylcalixarenes have the highest solubility. Conversion of calixarenes into ethers and esters usually increases their soubility in non-polar media. Variation of substituents, particularly incorporation of sulfonate and carboxylate groups, favours attainment of relatively high solubility of these macrocycles in water (up to 0.3 mol · litre^{-1}).[10]

Calixarenes and their structural analogues (thiacalixarenes, calixpyrroles and so on) exhibit pronounced tendency to formation of supramolecular complexes, and this feature largely determines the prospects of application of these systems in analytical chemistry.[11,12] Supramolecular compounds of calixarenes with metal ions and small organic molecules are called 'host–guest' complexes, implying that an analyte ('guest') fits in a cavity formed by the phenol fragments or functional groups of substituents (predominantly on the lower rim). The 'host–guest' complexes can be regarded as a particular case of inclusion complexes. New functionalized calixarenes can form more complex interaction products with the analytes similar to outer-sphere complexes in coordination chemistry where the central metal ion is found outlying substantially away

from the calixarene platform. In some cases, calixarenes fix organic molecules by means of predominantly hydrophobic weak forces or the so-called π–π-stacking to produce structures similar to metallocenes or stacks of DNA base pairs. In these cases, the term 'host–guest', strictly speaking, cannot be applied, but it is sometimes used through habit. It is necessary to note that such supramolecular complexes with predominantly hydrophobic interactions did not find use so far in sensors designed for analysis of liquid media, but potentially can be used in the vapour-phase analysis of volatile organic compounds and certain gases.

The ability of calixarenes and their analogues to form supramolecular complexes is determined by multi-point interactions with involvement of the macrocyclic cavity and functional groups of the substituents. These include electrostatic, donor–acceptor, hydrophobic and π–π-stacking interactions of small molecules and ions with the aromatic system of the macrocyclic cavity. The formation of hydrogen bonds with non-substituted hydroxyl groups on the lower rim of calixarenes, carboxylate, hydroxyl and amino groups of substitiuents is also important. In many cases, such interactions are characterized by cooperative nature and proceed with several binding sites formed by functional groups at the upper or the lower rim. All of the above-mentioned interactions can be involved in the complexation process.

In all diversity of the synthesized functionalized calixarenes, only a limited number of factors that determine characteristics of binding is mentioned when discussing the efficiency and selectivity of molecular recognition. These factors are geometric conformity of sizes of a 'guest' and the binding site of a calixarene, the character and complementarity of arrangement of the corresponding functional groups that are involved in recognition as well as the cooperative nature of interactions, which is expressed as the ability of binding site in a 'host' molecule to fit the structure of a particular 'guest' and to bind molecules or ions in a concerted manner.[6,11] As has been noted earlier, studies of the complexation by novel calixarenes are mainly performed under experimental conditions that differ from the conditions of functioning of the same receptors in sensor devices. Therefore, the relationships established in coordination chemistry should be applied with caution when used for the interpretation of results obtained using the electrochemical sensors, particularly for selectivity and sensitivity of the analytical signals.

Several mechanisms of incorporation of molecules and ions ('guests') into complexes (Fig. 1) can be regarded, *viz*., partial submersion of a 'guest' into a macrocyclic cavity or interactions with functional groups of substituents on the upper or lower rims. In the latter case, cooperative interaction of the 'guest' molecules with the functional groups of several substituents that operate in a concerted manner can be distinguished from the non-cooperative interaction in which functional groups of only one substituent are involved in binding of one 'guest'. Binding with involvement of bridging sulfur atoms in thiacalixarenes can also take place with formation of oligomeric polynuclear supramolecular structures where the 'guest' molecule acts as a binding centre. The mode of interaction depends not only on the receptor structure but on the nature of the analyte. Thus bulky caesium ions interact with several substituents in the calixarene conformations cone, partial cone and 1,3-alternate. Smaller lithium ions can form separate bonds

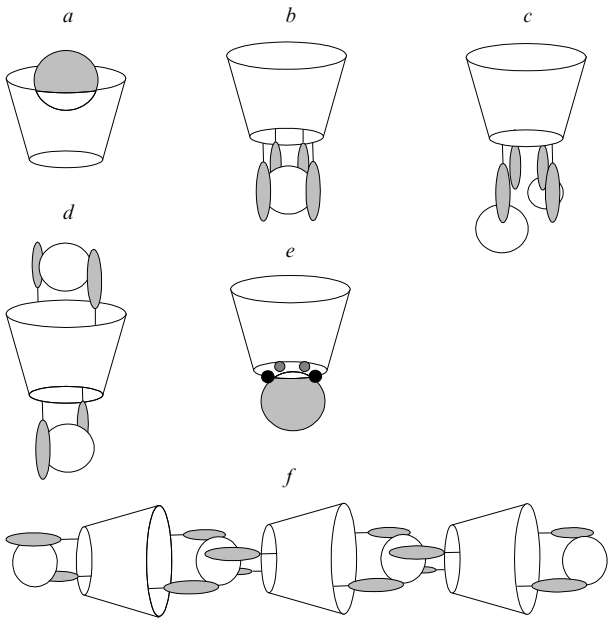


Figure 1. Schematic representation of possible structures of calixarene-based 'host–guest' complexes.
(*a*) a 'guest' incorporated in a macrocyclic cavity of a receptor, (*b*) cooperative interaction of a 'guest' with several substituents on the lower rim, (*c*) non-cooperative interaction of a 'guest' with one substituent, (*d*) formation of a complex with the composition 1 : 2 involving functional groups of substituents in the 1,3-alternate conformation or substituents at the upper and lower rims in the cone conformation, (*e*) interaction of a 'guest' with bridging sulfur atoms of thiacalixarene, (*f*) formation of supramolecular structures with bridging 'guest' ions.

with carboxylate and amide groups of substituents on the lower rim resulting in complexes with the composition 1 : 2, 1 : 3 or even 1 : 4. For the lower-rim tetrasubstituted receptors in the 1,3-alternate conformation, binding of one metal ion can decrease the binding efficiency of the second ion on the opposite side of the macrocyclic platform. This effect was named negative allosteric effect, it is expressed for bulky alkali metal cations. It explains the observed changes in stoichiometry of complexes from 1 : 2 to 1 : 1 in the series of ions with different radii.

The requirement of the geometric conformity between the 'guest' molecules and 'host' binding sites is also manifested in the dependence of the selectivity of ion binding on their radii. Thus *p-tert*-butylcalix[*n*]arenes can transfer metal ions from alkaline solutions through hydrophobic liquid membranes. The relative efficiency of transfer does not depend on the size of the macrocyclic cavity (value *n*). In all the series ($n = 4, 6, 8$), the same order of the increase in transfer efficiency was observed, which corresponded to the increase in the radii of the cations: $Li^+ \ll Na^+ K^+ < < Rb^+ < Cs^+$ (hereinafter, the formal charge of the central ion is given). The absolute rate of transfer increases with the increase in the size of the macrocycle and becomes maximum for the system Cs^+–calix[8]arene.[13,14] The geometric correspondence also determines the dependence of binding selectivity of organic and inorganic ions on the conformation of a calixarene. For example, tetraethers in the cone conformation selectively bind sodium ions, but in the other conformations they bind bulkier potassium ions.

In addition to the geometric correspondence, the efficiency of binding substantially depends on complementarity

between functional groups of a receptor and the corresponding groups of 'guest' molecules. In the case of metal ions, it is connected not only with the required size of a pseudo-cavity formed by substituents. The selectivity of ion binding by substituents is enabled also by a coordination saturation of central metal ions with involvement of functional groups of substituents that do not take part in formation of such a cavity. Such groups form also additional coordination bonds with oxygen atoms of the oxoions, for example, the uranyl ion.

The requirement of complementarity is even more important in the determination of organic compounds. The specificity and efficiency of this process largely depend on the ability of the groups mentioned to form donor–acceptor or hydrogen bonds. The achievement of such complementarity is one of principal goals in a molecular design of calixarene-based receptors. In general, the binding sites can be selected by comparison with the corresponding acyclic receptors, but their position in substituents and characteristics of interactions with complementary fragments of a 'guest' molecule depend on structures of substituents and configuration of a macrocyclic platform as a whole. The optimal choice of the receptor can be made on the basis of molecular modelling of structures for the receptor and the 'host–guest' complex with subsequent confirmation by X-ray and spectral methods of analysis.

Examples of successful design of calixarene-based molecular receptors will be given below. These receptors are employed in analytical studies but are not used in sensors so far. Of course, these examples do not exhaust all the multitude of calixarene-based receptors (there are more than 3000 publications devoted only to the recognition of metals), but they illustrate the main approaches to the synthesis of receptors over the last decade.

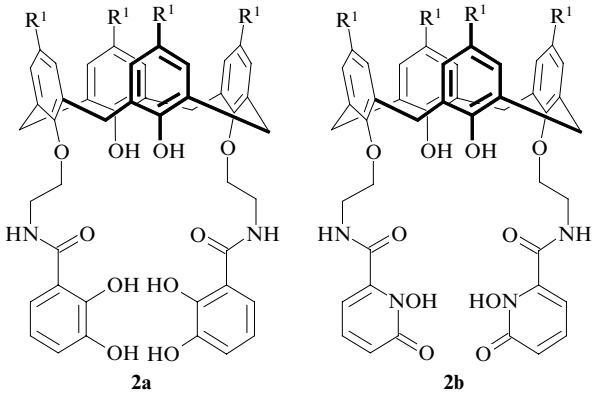
1. Receptors based on functionalized calix[4]arenes.

Functuionalization of calix[4]arenes extends the potential of the influence on the selectivity and efficiency of binding of the metal ions and organic compounds as compared with non-substituted calix[*n*]arenes. As a rule, substituents on the lower rim of a calixarene (more seldom, on the upper rim) are characterized by a conformational lability, which is sufficient for achievement of the required complementarity of the binding site.

The binding specificity of a metal ion is usually rationalized as the interaction of the ion with electron-donating groups and atoms in substituents within the framework of the theory of 'hard' and 'soft' acids and bases (HSAB).[15] Ions of alkali and alkaline-earth metals as 'hard' acids preferably interact with lone electron pairs of oxygen and nitrogen atoms.[14] Thus amide derivatives of 1,3-disubstituted calixarenes form stronger bonds with alkali metal ions than esters with analogous structures.[13] Additionally these derivatives exhibit selectivity to alkaline-earth metal ions (calcium, strontium, barium) as compared with alkali metals. On the contrary, 'softer' transition metal ions preferably interact with the sulfur atoms. In particular, silver, iron and mercury ions are selectively bound to thiacalixarenes, whereas alkali and alkaline-earth metal ions form stronger complexes with conventional calixarenes with the methylene bridges.[16,17] For the same reason, substituted thiacalixarenes are prone to formation of polynuclear supramolecular aggregates with ions and nanocrystals of elemental silver, in which heteroatoms of substituents and bridging sulfur atoms form coordination bonds with silver. Such supramolecular aggregates were found in organic solvents where the aggregates form regular nanoparticles and in thin films on a solid substrate. Structures of these aggregates were investigated by X-ray diffraction analysis, transmission electron and atomic-force microscopy.[16–19]

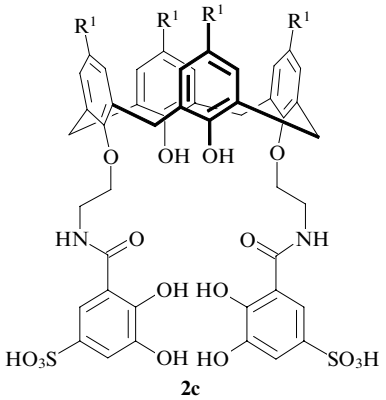
One of advantages of the use of the calixarene scaffold in molecular receptors is the possibilty of pre-organization (that is, achievement of the favourable arrangements of functional groups of the substituents that facilitate the formation of a complex with a substrate) due to the rigid macrocyclic cage. This reduces the energy expenditures for reorganization at the equilibrium receptor–complex and, as a consequence, increases stability of the complex. In the case of 1,3-disubstituted calix[4]arenes, non-substitiuted hydroxyl groups can act as an 'anchor' holding fixed the position of a 'guest' molecule relative to functional groups of the second pair of substituents, which participate properly in electrostatic or donor–acceptor interactions (see Fig. 1).

Calix[4]arenes **2** with catecholcarboxamide-, sulfocatecholcarboxamide- and *N*-hydroxypyridinecarboxamide-containing lower-rim substituents can serve as examples of the implementation of this approach. In spite of substantial remoteness of the core from the central ion, these calixarenes provide optimal coordination of the hydroxyl and amide groups around the central ion, which determines the required efficiency of binding. It turned out that calixarenes **2a** and **2b** (R^1 = H or Bu^t) predominantly bind the uranyl ion in acidic and neutral media and sulfocatecholcarboxamide derivative **2c** appeared more efficient in extraction from basic media.[20]



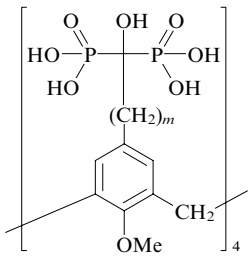
2a

2b



2c

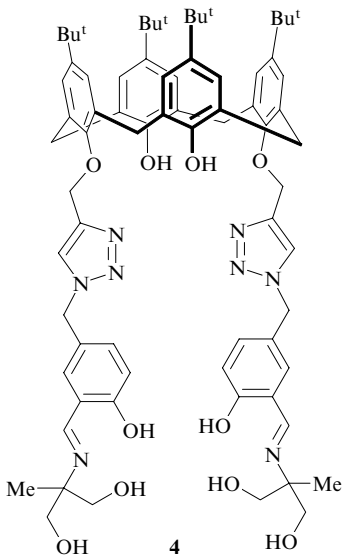
Upper-rim polyphosphorylated calix[4]arenes **3** containing methyl substituents on the lower rim are also uranyl receptors.[21]



3

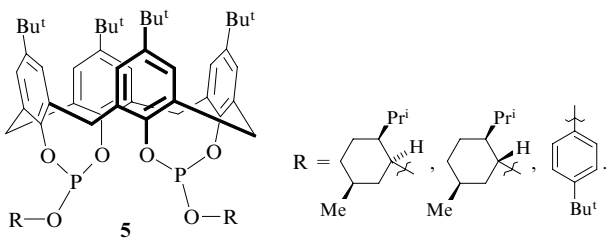
These receptors included four fragments of 1-hydroxymethylene-1,1-bis(phosphonic) acid [$R^1 = (CH_2)_mC(PO_3H_2)_2OH$] and differ from one another only in the length of spacers between these fragments and the calix[4]arene platform ($m = 0$, 1, 2). Calixarene with $m = 2$ manifested the highest affinity to the uranyl ion.

Among other 1,3-disubstituted calix[4]arenes, compound **4** containing Schiff base units derived from 2-amino-2-methylpropane-1,3-diol can be noted.[22] Interaction of this compound with the zinc ions was established by fluorescence and absorption spectroscopy.



4

Covalent cross-linking of calixarene substituents with formation of a cavitand-like ring offers additional options. This second ring not only holds fixed the required configuration of other functional groups but can itself act as a binding site. On the ground of synthesis, the majority of studies in this field were devoted to 1,3-disubstituted and tetrasubstituted calixarenes in the 1,3-alternate conformation. Bisphosphite derivatives of *p-tert*-butylcalix[4]arene **5** with chiral and achiral substituents can be noted as an exception, they form 1 : 1 complexes with the cations Pd^{2+} and Pt^{2+}.[23]

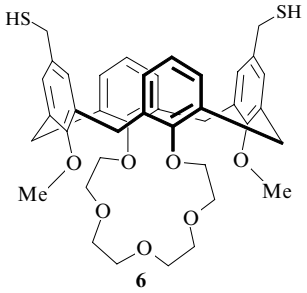


5

Calixcrown ethers have acquired wide distribution.[24–27] Incorporation of a calixarene moiety increases the efficiency of metal ion extraction as compared to ordinary crown ethers and to calixarenes with acyclic substituents containing the same functional groups.[25] Such calixcrown ethers in the cone conformation produce 1 : 1 complexes with ions that have sizes corresponding to the size of the polyoxyethylene cavity. In the case of tetrasubstituted calixarenes in the 1,3-alternate conformation, two oxyethylene rings can form at the opposite sides of the calixarene platform. Complexes of such calixarenes with metal ions can have stoichometry 1 : 1 or 1 : 2. In the former case, the interaction of the receptor with a cation decreases affinity of the second crown-ether fragment due to the negative allosteric effect. In the latter case, the interactions at the opposite sides of the calixarene platform are independent.

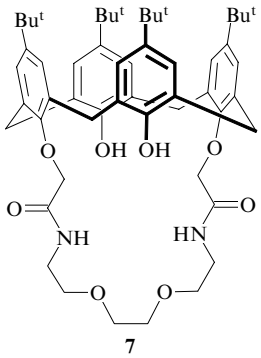
1,3-Calixcrown ethers differ favourably from classic crown ethers also owing to the possibility of variation of the hydrophilic–hydrophobic balance and, consequently, their solubility in water and organic solvents by changing lengths of hydrocarbon 'tails' in acyclic substituents. In particular, incorporation of sulfonate or fluorosulfonate groups makes it possible to obtain water-soluble receptors.

The other promising area[26–29] is the development of calixcrown-ethers with thiol groups that form self-assembling layers on gold. Such coatings are used in the immobilization of proteins and small charged molecules (tags) employed for the registration of molecular recognition. For example, a sensor for the detection of glucose was prepared by immobilization of the enzyme glucose oxidase and the redox tag (ferrocenecarboxylic acid) on the self-assembled layer of calix[4]crown-5 **6** on gold.[29]



6

Oxyethylene bridges can include additionally ester and amide groups as in calixarene **7**, which binds selectively the dichromate anion.[30]

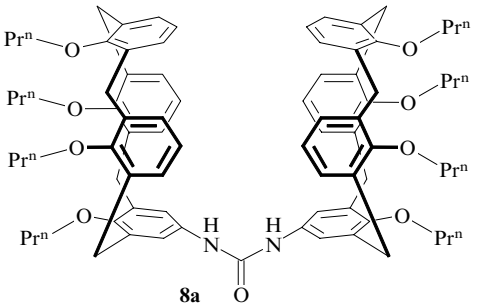


7

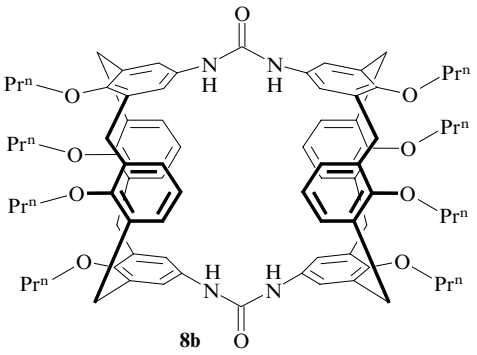
The next step in the strategy of covalent fixation of the favourable configuration of a receptor is the transition to oligomers, which contain several macrocyclic fragments arranged in chains through different bridges. This results

in the increase in both efficiency of binding (it can be used for increasing the extraction efficiency) and affinity to bulkier molecules or ions. Thus dimers of calix[4]arenes with oxyethylene bridges bind bulky *N*-methylpyridinium and *N*-methylpicolinium cations.[31] Similar oligomers are effective extractants of the alkali metal ions.[32] The possibility of selective transport of K^+ across bulk liquid membranes was established in which calixcrown oligomers with 2–5 macrocyclic fragments and ether, amide and ester groups in the lower-rim substituents served as carriers. The selectivity of transport in the K^+/Na^+ pair depended on the structures of substituents not linked to the crown-ether unit.

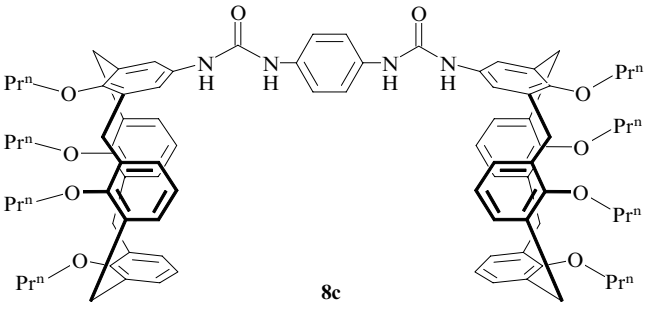
Calixarene oligomers may contain urea units as bridges. Thus bismacrocyclic receptors **8a–c** selectively bind the benzoate anion.[33]



8a



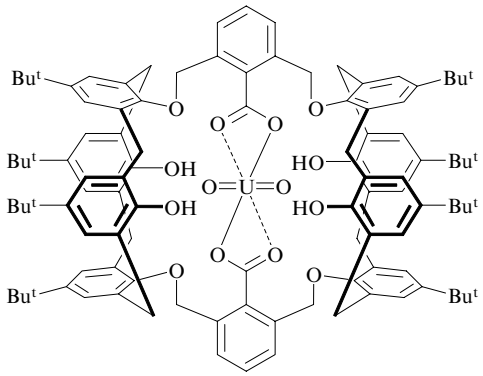
8b



8c

Analogous dimers with two and four bridges were described but these compounds have not been used so far for solution of analytical problems. Among other bridged structures, calix[4]arene **9** can be mentioned (shown is the structure of its complex), which is used for selective extraction of the uranyl cation in organic phase.[34]

By condensation of 1,3-disubstituted calix[4]arene hydrazide derivatives with calix[4]arene mono- and bis-benzaldehyde groups in substituents at the lower rim, bis- and tris(calixarenes) were prepared. These compounds are able to extract many metal cations and α-amino acids.[35] Asymmetric bis(calix[4]arenes) containing calixarene and thiacalixarene fragments can also bind metal cations and amino acids. The Hg^{2+} cations are predominantly bound as



9

compared with Ag^+ and the Cs^+ and K^+ cations in comparison with Na^+. Tris(calix[4]arenes) possess good extraction capacity with respect to heavy metal cations.[36]

2. Functionalized calix[6]arenes

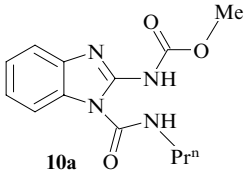
The increasing in the number of phenolic groups in a macrocycle results in an increase in possible conformations, and simultaneously makes the problems of their stabilization and selective synthesis more difficult. In particular, steric stabilization of the cone conformation for calix[6]-arenes can be achieved by incorporation of such bulky and branched substituents as 1,1,3,3-tetramethylbutyl groups in the upper rim.[37] Calix[6]arene-biscrown selectively binds caesium ions.[38] Publications in the 1990s were devoted to receptors based on calix[6]arenes with ester and amide substituents for recognition of the potassium ions,[39] primary amines,[40] carboxylic acids[41] (following conversion of acids into amines by treatment with sodium azide).

p-Sulfonatocalix[6]arene immobilized on the surface of gold nanoparticles was proposed as colorimetric probes to detect diaminobenzenes with the detection limits of 1 and 4 mol litre^{-1} for *m*- and *p*-diaminobenzene, respectively. For other aromatic amines (*o*-diaminobenzene, *o*-, *m*- and *p*-nitroanilines, *o*- and *p*-chloroanilines, *o*-, *m*- and *p*-toluidines, aniline) no analytical signals were observed.[42]

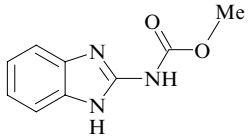
Carboxyl derivatives of *p*-*tert*-butylcalix[*n*]arenes ($n = 6$, 8) and their methyl esters were employed for extraction of benzidine, *p*-chloroaniline and α-naphthylamine with subsequent HPLC analysis.[43] Octacarboxylic acid on the basis of *tert*-butyl-calix[8]arene revealed the most pronounced affinity to all mentioned compounds .

Hexasubstituted at the upper rim, *p*-(*p*-sulfonatobenzylaza)calix[6]arene forms 1 : 1 complex with vitamin K_3 with equilibrium constant 4.95×10^3 litre mol^{-1}. This reaction has been used for spectrophotometric determination of vitamin K_3 in the concentration range $5.0 \times 10^{-7} - 3.0 \times 10^{-5}$ mol litre^{-1} [detection limit (c_{lim}) was found[44] to be 2.0×10^{-1} mol litre^{-1}].

The addition of *p*-sulfonatocalix[6]arene was shown[45] to enhance the fluorescence of benzoimidazole fungicides Benomyl (**10a**) and Carbendazim (**10b**).



10a



10b

3. Functionalized thiacalixarenes

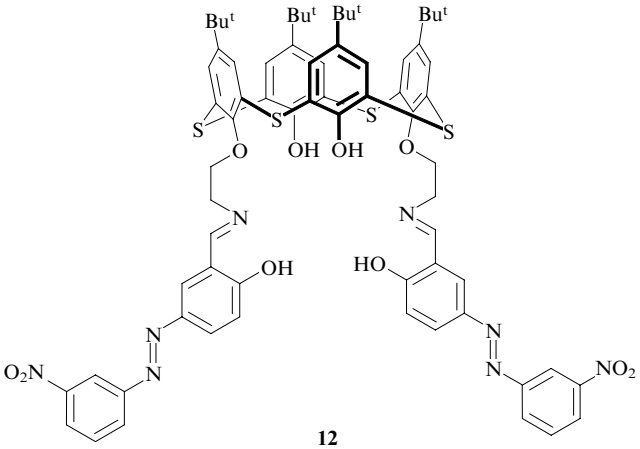
Thiaanalogues of calixarenes have been known for less than twenty years and lately they have attracted close attention of researchers as molecular platforms for development of sensors. Thiacalix[4]arenes can also exist in several conformations, *viz*., cone, partial cone and 1,3-alternate.[46] If substituents at the lower rim contain heteroatoms, tetrasubstituted thiacalix[4]arenes can form an additional pseudocavity and bind a substrate through eight heteroatoms (four bridging sulfur atoms among them). Variation of charges on the heteroatoms, their hybridization and length of a spacer that separates the macrocyclic platform and the heterocyclic fragment in a substituent makes it possible to create receptors for different cations. As regards the use of thiacalixarenes in sensors, it is very important that the bridging sulfur atoms allow fixation of thiacalixarenes on gold electrodes without additional supports. Thiacalixarenes form complexes with stoichiometry differing from 1 : 1 more often as compared with ordinary calixarenes. In the case of thiacalixarenes, an additional possibility arises to create structures with different substituents at the lower rim and sometimes at the upper rim (heterotopic receptors).

Direct incorporation of metal cations into a hydrophobic cavity of thiacalixarenes is effective only for large cations, for example Ag^+. For metal cations with low ionic radii, binding is possible provided the cation is included in a complex with an organic ligand that forms an outer-sphere inclusion complex with thiacalixarene.

The efficiency of binding of metal cations to *p-tert*-butylthiacalix[4]arenes tetrasubstituted on the lower rim and stoichiometry of the resulting complexes depend substantially on the thiacalixarene conformation. Thus the results of extraction of metal picrates (picrate extraction) show that macrocycles **11a**–**d** [R^1 = Bu^t: R^2 = $CH_2C(O)Ph$ (**a**), $CH_2C(O)NEt_2$ (**b**), $CH_2C(O)(NC_4H_8O$-cyclo) (**c**) and $CH_2C(O)(NC_4H_8$-cyclo) (**d**)] in the cone, partial cone and 1,3-alternate conformations form complexes with alkali metal ions in an organic phase with the stoichiometry 1 : 1, 1 : 2 and 1 : 4. In addition, macrocycle **11a** in the cone conformation preferably extracts the Na^+ cations, and macrocycle **11b** in the partial cone and 1,3-alternate conformations preferably extracts the K^+ cations. Substitution of the diethylamino group for the phenyl group results in the increase in the extent of the metal ion extraction. The same thiacalixarenes with substituents containing heterocycles (**11c**,**d**) extract more effectively the silver cation, which interacts with bridging sulfur atoms of the macrocyclic platform.[13]

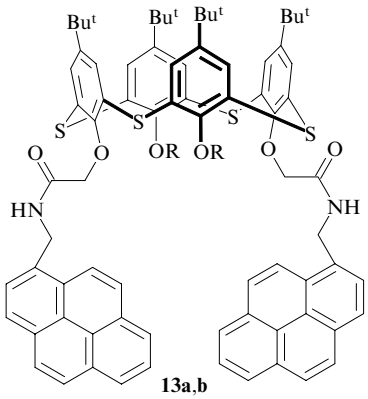
The selectivity of interactions of mono-, di-, tri- and tetra-substituted *p-tert*-butylthiacalix[4]arenes in different conformations, containing amide substituents, with ions of alkali, alkaline earth and transition metals was studied. Thus tetrakisbutylamide derivative [R^2 = $CH_2C(O)NHBu^n$] in the cone, partial cone and 1,3-alternate conformations exhibited affinity to Na^+ and K^+ cations, and 1,3-alternate bound also the Co^{2+} cations. It is established that dichromate anion is bound more strongly as compared with the picrate anion. In the case of the hexyl alkyl 'tail' in a substituent [R^2 = CH_2 $C(O)NHC_6H_{13}$-n], the efficiency of dichromate anion binding decreased.[47]

p-tert-Butylthiacalix[4]arene disubstituted at the lower rim (**12**) in the cone conformation was used as a chromogenic sensor to cation Cu^{2+} in mixtures THF–water (9 : 1).[48] This receptor selectively binds the Cu^{2+} cations in the presence of ions Li^+, Na^+, K^+, Cd^{2+}, Ni^{2+}, Zn^{2+}, Ag^+, Pb^{2+} and Hg^{2+}.



12

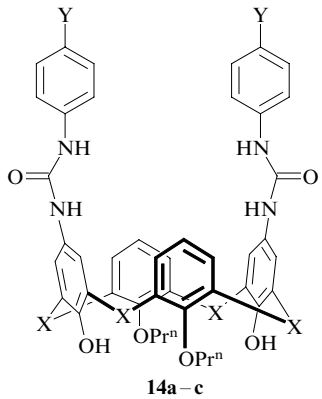
Disubstituted thiacalix[4]arenes with pyrene substituents (**13a,b**) in the cone conformation were used for fluorometric determination of ions Cu^{2+} and CN^-. Cations Li^+, Na^+, K^+, Ni^{2+}, Cd^{2+}, Zn^{2+}, Pb^{2+}, Ag^+, as well as anions F^-, Cl^-, Br^-, I^-, AcO^-, HSO_4^- , NO_3^- do not interfere. Depending on the nature of 'host' and 'guest', complexes with the stoichiometry 1 : 1 or 1 : 2 are formed in a mixture CH_2Cl_2–MeCN (1 : 1).[49]



13a,**b**

R = H (**a**), Pr^n (**b**).

Compounds **14a**–**c** containing two arylurea functions in the substituents on the upper rim were investigated as receptors for bromide, acetate and benzoate anions in polar organic solvents. The acetate and benzoate anions are bound more strongly and the stability constants of complexes increase in the series of calixarenes



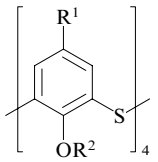
14a–**c**

X = CH_2: Y = Me (**a**), NO_2 (**b**); X = S, Y = Me (**c**).

14a < **14c** < **14b**.[50] At the same time, no complexes with the chloride anions were found.

1,3-Disubstituted thiacalix[4]arenes are receptors for the determination of α-hydroxy, α-amino acids and dicarboxylic acids; in this case, substrates with small substituents are bound according to a 'docking' mechanism (*i.e.*, enter the cavity formed by the macrocycle and substituents), but for bulky substrates thiacalixarenes operate as 'tweezers' ligands. For instance, oxalic acid is selectively bound to thiacalix[4]arene [$R^2 = CH_2$(Py-4)] (Py is pyridyl), and glutamic acid binds to a thiacalixarene containing two substituents $R^2 = CH_2CH_2NHBz$ at the lower rim and two nitro groups at the upper rim.[51]

Tetrasubstituted thiacalix[4]arenes exhibit more efficient complexation and transmembrane transport of inorganic cations as compared with conventional calix[4]arenes. For example, thiacalix[4]arenes **11b**, **15a**–**c** bind to cations Pd^{2+}, Ag^+, Cd^{2+}, Sm^{3+} and Ce^{3+}; for the amide substituents (compound **11b**), the efficiency of extraction decreases in the series $Au^{3+} > Pd^{2+} > Pt^{4+} > Ag^+$. Thiacalixarene **15a** with ether substituents efficiently extracts cations Sm^{3+}, compound **15b** extracts cations Sm^{3+} and Ce^{3+}, while Ag^+ is selectively extracted by compounds **15b**,**c**.[52]



11b, **15a**–**c**

$R^1 = Bu^t$: $R^2 = CH_2C(O)NEt_2$ (**11b**), CH_2CO_2Et (**15a**), H (**15b**); $R^1 = R^2 = H$ (**15c**).

Tetrasubstituted *p-tert*-butylcalix[4]arenes and thiacalix[4]arenes containing *N*,*N*-dimethylaminocarbonylmethoxy and *N*,*N*-dimethylaminothiacarbonylmethoxy substituents at the lower rim were used for the extraction of the silver cations from nitrate solutions. The formation of 1 : 1 and 1 : 2 complexes calixarene–Ag^+ ion for derivatives of calixarene and thiacalixarene, respectively, was established in this case. The degree of this ion recovery was more than 90% with calixarene and more 99% with thiacalixarene.[52] *p-tert*-Butylthiacalix[4]arenes tetrasubsituted at the lower rim [$R^2 = CH_2Bz$ (**11a**), CH_2CO_2Et] in the cone conformation were used for the extraction of technetium(IV).[13]

p-tert-Butylthia[4]calixarenes functionalized with secondary amide groups at the lower rim strongly bind anions owing to hydrogen bonding with the amide functions. For example, thiacalixarene with substituents $R^2 = CH_2C(O)NH$(Naph) (Naph is 1-naphthyl) at the lower rim in the 1,3-alternate conformation can recognize the fluoride anion, in the cone conformation it recognizes fluoride and chloride anions and in the partial cone conformation this receptor allows one to establish the presence of either the fluoride and chloride anions (detected together) or the bromide anions.[13]

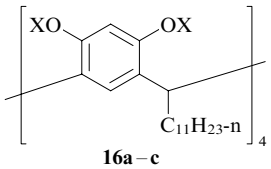
4. Calixarene-based receptors binding proteins and nucleic acids

One of the modern trends in the design of new synthetic receptors is the development of approaches to specific recognition of biopolymers. In addition to their application in analytical chemistry, such receptors can be useful in medicine as the basis for the design of new drugs and systems of their targeted delivery and for investigations into structures and functions of proteins and DNA, transfection of genes *etc*.[53] The design of receptors for biopolymer molecules is a very complex problem due to a large number of functional groups that can, in principle, bind to a receptor and due to the fact that all macromolecules are similar in structures to each other consisting of basically the same building blocks, *viz*., amino acid residues of proteins or nucleotides of nucleic acids. At present, the problem of recognition of individual proteins or oligonucleotides is not solved yet (with a few exceptions), but there are promising approaches that allow one to rely on positive solution of this problem in future.

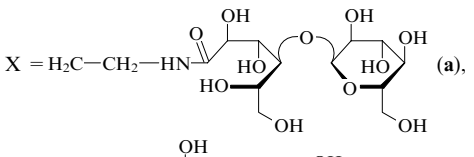
To date, several strategies of DNA recognition have been developed:[54–56] binding of DNA phosphate groups, individual oligonucleotides or a biopolymer as a whole.

Thus calix[4]arene with four propoxy groups attached to the lower rim and four semicarbazone units attached to the upper rim selectively binds the dihydrogenphosphate anions in the presence of the Cl^-, Br^-, I^-, HSO_4^-, ClO_4^- anions and the acetate anion.[57] Structurally similar calix[*n*]arenes with guanidine units [$NHC(NH_2)_2^+Cl^-$] in substituents at the upper rim ($n = 4$: $R^1 = Pr^n$, n-C_8H_{17}; $n = 6$, $R^1 = Me$; $n = 8$, $R^1 = Me$), bind both plasmid and linear DNA.[58]

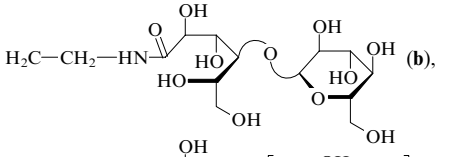
Glucocalixarenes **16a**–**c**, which form the so-called glucoclusters owing to self-assembly, represent a new class of receptors that bind DNA through the phosphate groups. These glucoclusters interact with phosphates,[59] nucleotides[60] and nucleic acids[61–63] to form either complexes with composition 1 : 1 or supramolecular aggregates[50] with the 'guest' : 'host' ratio > 10.



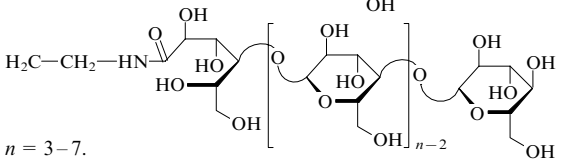
16a–**c**



(**a**),



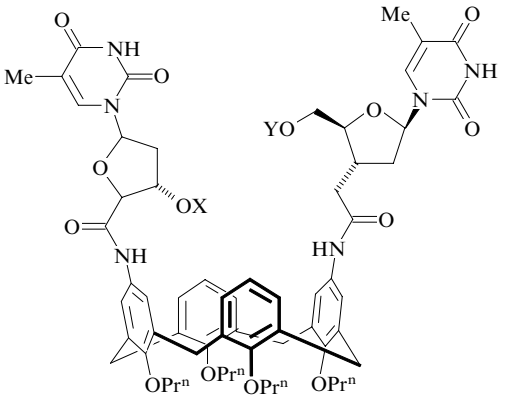
(**b**),



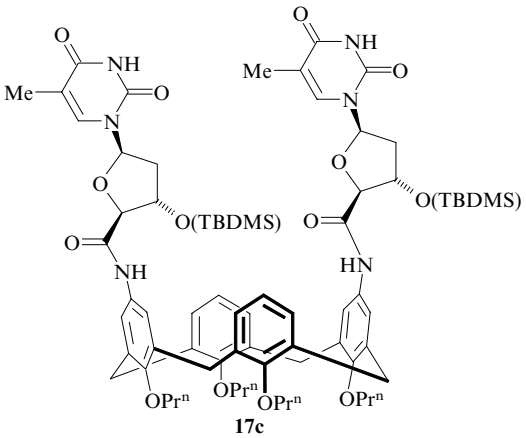
(**c**);

$n = 3–7$.

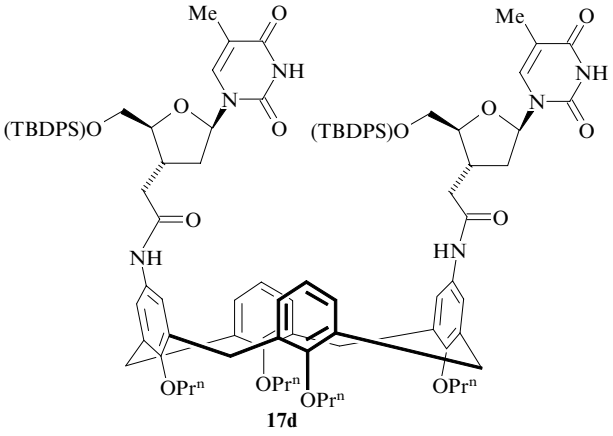
Calix[4]arenes containing DNA nucleosides as the functional groups of substituents (calixnucleosides **17a**–**d**) are capable to form complementary base pairs, hence they can selectively bind single-stranded DNA or RNA.[63]



17a,b



17c

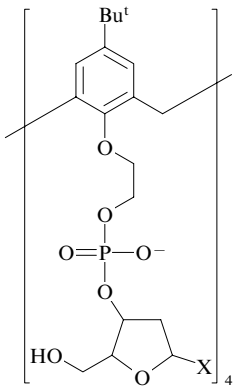


17d

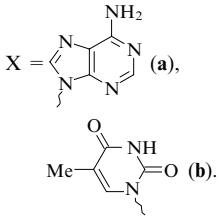
X = Y = H (**a**); X = TBDMS, Y = TBDPS (**b**); TBDMS is *tert*-butyldimethylsilyl, TBDPS is *tert*-butyldiphenylsilyl.

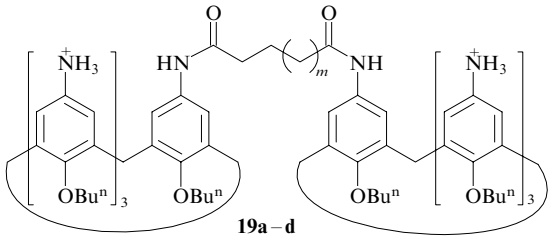
Apparently, the same mechanism (interaction of complementary nucleotides) underlies the inhibition of DNA amplification by calix[4]arenes **18a,b** bearing thymine or adenine fragments.[64]

For recognition of DNA molecule as a whole based on electrostatic multi-point interactions (with formation of polyionic complex), dimeric calix[4]arenes **19a–f** with amino groups in *para*-position on the upper rim and amide groups in bridging fragments were prepared.[54] The formation of complexes was established by changes in DNA melting temperatures and also by fluorescence experiments on displacement of intercalated ethidium bromide and quenching of fluorescein-labelled oligonucleotides. The association constants of complexes were in the range of 10^5-10^6 mol litre^{-1}.



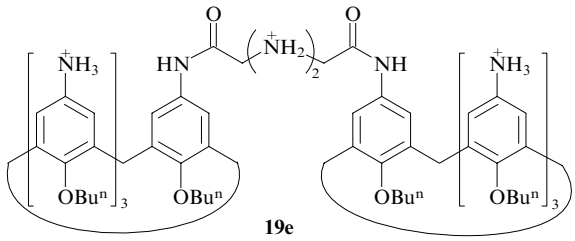
18a,b



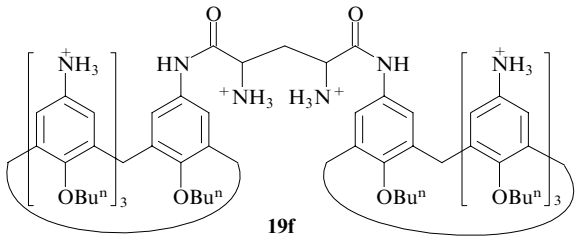


19a–d

m = 2 (**a**), 4 (**b**), 6 (**c**), 8 (**d**).



19e



19f

Binding of proteins to calixarene-based receptors is determined primarily by inherent charges of a protein globule and a receptor and by acid–base interactions of ionized amino acid residues on the protein surface. The above-mentioned calixcrown **6** was used for electrostatic immobilization of the enzyme glucose oxidase.[29] The same calixarene available commercially as ProLinker™ is a constituent of a biochip Proteochip™. It permits one to perform electrostatic immobilization of antibodies onto proteins-markers of oncological diseases.[26,28]

Calix[4]arenes with four benzylammonium or ethylphosphonate groups at the upper rim and long-chain alkyl substituents at the lower rim were used for colorimetric detection of proteins.[65] Calixarene-based receptors were embedded into vesicles formed by dimyristoylphosphatidylcholine — polydiacetylene as a chromatic polymer by means of hydrophobic interactions. The charged substituents at the upper rim interact with globular proteins, which results in their adsorption on the surface of vesicles and partial compensation of charges. These interactions in the lipid layer shift an equilibrium between the acetylene and diene forms of the polymer and the colour of vesicles changes

from blue (in the absence of a protein) to red. The proposed method gives the possibility to detect microgram quantities of extracellular soluble proteins and could be used in future for selective determination of individual proteins provided the corresponding selective receptors are developed.

Methods for the determination of compounds that form complexes with calixarenes were developed based on specific interaction of receptors with enzymes. For example, 1,3-disubstituted calix[4]arenes with substituents at the lower rim containing aromatic fragments form complexes with aromatic acids and their esters. This type of complex with a chromogenic substrate of the enzyme cholinesterase, indophenyl acetate, was shown to possess strong inhibitory properties.[66,67] It was suggested that the interaction of the complex with the active site of the enzyme results in formation of an enzyme–substrate inhibitory complex. Following its decomposition, calixarene is held close to the active site of the enzyme by hydrophobic interactions between phenolic groups of the calixarene macrocavity and tryptophan residues of the protein. As a result, calixarene spatially blocks the interaction of the active site of the enzyme with the substrate but does not interact directly with the active site. Good fit of geometric sizes of the complex calixarene–indophenyl acetate and the active site of cholinesterase is in favour of this mechanism. Some organic acids, such as benzoic or oxalic, compete with indophenyl acetate in the binding to calixarene, decrease concentration of the complex and suppress its inhibitory action onto the enzyme. This method allows one to detect spectrophotometrically micromolar concentrations of organic acids from kinetic curves of enzymatic hydrolysis of indophenyl acetate.

Other examples of calixarene-based inhibitors of enzymes can be mentioned. Thus 1,3-disubstituted calix[4]arenes with bisphosphonate substituents effectively inhibit alkaline phosphatase.[68] Amhiphilic calix[4]arene with four substituents at the upper rim containing cyclic tetrapeptides and four long-chain alkyl substituents at the lower rim forms a complex with cytochrome *c* preventing its redox transformations in the presence of reductants.[69] Some calix[4]arenes were also reported to inhibit Na^+, K^+-ATPase.[70] Other examples of the application of calix[*n*]arenes as receptors for protein sensing, as well as synthetic antibodies for the determination of proteins, biomarkers of neurodegenerative diseases, are given in a review article.[71]

Considering synthetic aspects of the design of calixarenes-based receptors as a whole, it is necessary to note that in the last years the research interests shifted to successive complication of receptor structures both regarding the number of functional groups in substituents and macrocyclic fragments and spatial pre-organization (formation of supramolecular aggregates, synthesis of polydentate calixarene ligands[55]). This is dictated mainly by the necessity to develop receptors for the recognition of biological macromolecules (proteins and nucleic acids) or for incorporation into supramolecular structures (lipid bilayers, vesicles, cell membranes, synthetic and natural ion channels). Calixarene oligomers[54] and polynuclear complexes increase the efficiency of extraction and transmembrane transport of small ions and organic molecules of biological importance, *e.g.* drugs, pesticides, *etc*. In particular, nanocrystals and films were described that are formed by regular layers of functionalized calixarenes and some other complex-forming agents, such as porphyrins, the formation and optical properties of which are determined by incorporation of metal ions into the lattice.[72] In future, such supramolecular structures can be used as the main element of chromophoric devices for the determination of both metal ions and compounds affecting self-organization processes in such systems. Ionic channels formed by non-covalent self-assembly of calixarenes and possessing definite selectivity with respect to transport of metal ions depending on their sizes are also promising issues.[73] Methods of preparation and properties of synthetic ion channels, in particular with macrocyclic ligands, are reviewed elsewhere.[74,75]

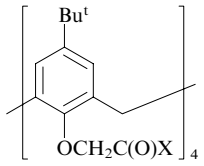
In all the described examples of molecular receptors, the proposed methods of functionalizing seldom took into account requirements related to the registration of complex formation. Stoichiometry of complexes and their structures are usually investigated by means of versatile methods, such as X-ray diffraction analysis and ^{1}H NMR titration. In the case of metal binding, picrate extraction received wide application where transfer of a metal–calixarene complex into an organic phase is accompanied by equivalent transfer of the picrate anion, which can be registered by spectrophotometry. However, these methods hardly meet demands to the registration of interaction, if the receptors are incorporated in sensors. Inclusion of additional functional groups, such as thiol or disulfide, can promote immobilization of the corresponding receptors on gold electrodes or on the surface of gold nanoparticles as, for example, in the case of calixarene **6**.[26,28,29] Functionalization of calixarenes with special substituents (so-called tags), which are used to record complexation, has been mentioned earlier in connection with fluorescence-aided detection of substrate binding to compound **13** (Ref. 49). Some additional examples of calixarene functionalization with electrochemically active groups will be given below in the consideration of amperometric sensors. Nevertheless, this field of investigations is being developed slowly so far.

Combination of calixarene-based receptors with nanotechnology is very promising, in particular, their incorporation in surface layers of nanoparticles or vesicles. Amphiphilic receptors, which combine hydrophobic linear functional groups in lower-rim substituents and upper-rim functional groups for binding 'guest' molecule, are in demand to this end. Although derivatization of calixarenes on the upper rim is still rarely used, such receptors have already been described.[65,76] Changes in lipid layer characteristics associated with incorporation of a 'guest' and not directly affecting the receptor molecule can be employed as an analytical signal. This provides a possibility of creating versatile receptor structures with common method of analytical signal measuring (changes in colour, surface tension, circular dichroism, resistance of charge transfer) and variable selectivity in relation to individual analytes. Such systems are required in proteomics and they can compete with the existing methods of multi-parameter evaluation of different control subjects on the basis of individual sensors.

III. Potentiometric sensors

Functionalized calixarenes-based receptors have been used as neutral ionophores in membrane-type ISE since a long time. As compared with their analogues, *i.e.*, crown ethers and dialkyl phosphonates, they advantageously differ by lower solubility in water, high stability against oxidation and hydrolysis and by weaker interactions with other membrane components, *e.g.*, plasticiziers, lipophilic salts

and organic solvents. Commercial products comprise, first of all, calix[4]arene acid derivatives **20** containing four oxyacetate substituents with aliphatic and cyclic alkyl groups.[77–80] Tetraethyl ester of this acid is produced commercially, it is a standard sodium ionophore of poly(-vinyl chloride) membrane ISE.[80]



X = OEt, $OC_{10}H_{21}$-n, NBu^n_2, O(C_6H_{11}-cyclo).

20

The main part of studies related to membrane ISE with calixarene-based receptors was published in the 1990s. Analytical characteristics of ISE and factors determining their sensitivity and selectivity were discussed in a number of reviews.[4, 53, 81, 82] Analogous data for ISE developed over the last decade are given in Table 1. The best values are presented for those receptors or polymeric membranes where different characteristics are reported. Sensitivity was defined as the slope of the concentration plot of the analytical signal in Nernstian coordinates $E - \log c$, where E is the ISE potential (in mV), c is the molar concentration of the potential-determining ion (this relationship is called electrode function). The selectivity of the ISE signal is quantitavely expressed conventionally as a selectivity constant (K) or its logarithm ($\log K$), which are measured with the separate solutions method. In some studies, instead of quantitative characteristics, ion series are presented in which the ISE signal changes regularly. If selectivity coefficients are given in a graphical form (as a diagram), then the order of changes in the corresponding coefficients is tabulated together with the interval in which selectivity coefficients change.

The classic most popular ISE contains an intewrnal reference electrode. A composition for manufacture of ion-selective membrane comprises PVC, plasticizer and a lipophilic salt that enables transfer of counter-ions across the membrane. In addition to factors mentioned in Section II, binding and membrane transfer of the potential-determining ion are affected also by solvation of the reactants in the membrane and acid–base interactions. As a result, changes in plasticizer composition, in particular, its polarity and ability to form donor–acceptor and hydrogen bonds, substantially influence sensitivity and selectivity of determination of potential-determining ions. As noted earlier, calixarenes are poorly soluble in water, which determines substantially long (up to six months) lifetimes of ISE. At the same time, thiacalixarene-based receptors with polar ester and amide groups are poorly soluble in tetrahydrofuran, the solvent, which is often used in membrane manufacture. Possibly, for this reason thiacalixarene-based receptors are rarely applied in membrane ISE.

Published data (Table 1) are limited to investigations of ISE characteristics on the basis of a small number of structurally similar receptors. This prevents establishing structure–property relationships from the measured selectivity coefficients. As an exception, studies should be mentioned in which analytical characteristics of tetrasubstituted thiacalix[4]arene-based sensors with nitrogen-containing substituents at the lower rim were described for thiacalixarenes in cone, partial cone and 1,3-alternate conformations.[100, 101] All the ISE studied demonstrated high selectivity to silver ions as compared with alkali and alkaline-earth metal ions. Among transition metals, the Hg^{2+} and Fe^{3+} cations gave close analytical signals. Although no pronounced dependence of selectivity and sensibility on the type of receptor conformation was established, 1,3-alternates still revealed somewhat better analytical characteristics in detection of the silver cations in comparison with other isomers. Better spatial accessibility of binding sites in 1,3-alternate as compared with other isomers is one of possible explanations of these facts. Preferable binding of iron and silver ions in comparison with alkali and alkaline-earth metal ions was supported also in the experiments with picrate extraction of these ions with the same receptors. But direct correlation of the data from potentiometry and extraction is not completely correct because iron(III) forms complexes with composition 1 : 2 in an organic phase (dichloromethane), which was not supported by potentiometric measurements. Qualitative agreement between relative extraction of metal ions and selectivity of their potentiometric determination with use of ISE containing calixarene-based Cs^+ receptor was established.[87]

Effects of acidity on potentiometric selectivity of calixarene-based ISE are associated with protonation–deprotonation of functional groups in substituents and hydrolytic stability of potential-determining and interfering ions at different pH. For example, in the determination of silver ions the increase in pH usually favours more selective determination of Ag^+, since interfering transition metal ions, as a rule, have tendency to undergo hydrolysis. In acidic solutions (pH 1.7–3.5), the selectivity coefficients usually do not depend or negligibly depend on pH, because in this range of acidity the fraction of transition-metal aquaions is virtually constant. In general, weakly acidic media (pH 3–5) are recommended for the determination of metal ions, since strong mineral acids can remove receptors containing basic groups.

Acidity produces the most pronounced effect on the ISE signal in determination of organic amines.[110] Changes in pH determine not only relative strength of amine binding in comparison with large metal cations (Tl^+, Cs^+, Rb^+), but also relative strength of binding of quaternary alkylammonium cations, protonated tertiary amines and amino acids.

Influence of pH on characteristics of a calibration curve may also serve as an additional argument supporting the suggested mechanism of interaction between a receptor and an analyte. For example, the slope of a calibration curve (sensitivity of determination) allows one to evaluate the charge of the potential-determining ion. The maximum value of ISE signal (with the use of ionophore **41**) in determination of benzoic acid is achieved at pH 3.0, which can be considered as evidence of involvement of non-dissociated benzoic acid molecules in complex formation. This conclusion was supported by data from ^{1}H NMR titration.[112]

For anions, pH values influence, first of all, selectivity of determination of anions of weak acids. For example, determination of phosphate anions is carried out at pH 7.0–7.2 corresponding to the largest accumulation of monohydrogenphosphate.[107, 108] Under these conditions, the major part of organic acids exists in non-dissociated form, which knowingly increases selectivity of the hydrogen phosphate analytical signal. Probably, in more basic media ISE selectivity to hydrogen phosphate anions is reduced.

Table 1. Analytical characteristics of ISE with calixarene-based receptors.

Calixarene [a]	Method of incorporation in the sensor	Determined ion (compound)	Main electrode parameters [b]	Selectivity of determination [c]	Ref.
21	PVC membrane	Na^+	$\Delta c = 5\times10^{-4}-1\times10^{-1}$, $S = 52.9-58.3$, $c_{lim} = 10^{-4}$	$Na^+ > K^+ > Cs^+, Li^+$; $K = (1.55-13.8)\times10^{-3}$	83
1b (R^1 = Bu^t, R^2 = Et, n = 4)	PVC membrane on polypyrrole doped with the $[3,3'\text{-}Co(1,2\text{-}C_2B_9H_{11})_2]^-$ ions	Na^+	$\Delta c = 3.0\times10^{-6}-1\times10^{-1}$, $S = 58\pm2$, $c_{lim} = 1.45\times10^{-6}$	log$K$ = −2.20 (K^+), −2.97 (Li^+), −3.04 (Cs^+), −4.60 (Mg^{2+}), −4.60 (Ca^{2+})	84
22a,**b**	PVC membrane	K^+	$\Delta c = 1\times10^{5}-1\times10^{-1}$, $S = 48.8-55.3$, $c_{lim} = 2\times10^{-6}$	interference of Rb^+; $NH_4^+ > Ag^+ > Pb^{2+} > Cd^{2+} > Sr^{2+} > Cs^+ > Cu^{2+} > Na^+ > Ba^{2+} > Ni^{2+} > Co^{2+} > Li^+ > Ca^{2+}, Mg^{2+} > Zn^{2+}$; log$K$ from −1 to −5	85
23	PVC membrane	Cs^+	$\Delta c = 10^{-6}-10^{-1}$, $S = 55$	$Cs^+ > Rb^+ > K^+$, $NH_4^+ > Na^+ > Li^+$; log$K$ from −0.5 to −4.1	86, 87
24 (R = H, Bu^t; n = 4–6)	the same	Tl^+	$\Delta c = 10^{-6}-10^{-2}$, $S = 55-56$, $c_{lim} = 6\times10^{-7}$ (n = 5, R = H), 3×10^{-7} (n = 5, R = Bu^t)	n = 5, R = H: log$K$ = −0.5 (Cs^+), −1.6 (Rb^+), −2.7 (K^+), −4.0 (Na^+), −3.5 (Ag^+)	88
25	"	Co^{2+}	$\Delta c = 9.2\times10^{-6}-1\times10^{-1}$, $S = 29.0\pm1.0$, $c_{lim} = 4.0\times10^{-6}$	$K = 9\times10^{-2}$ (Li^+), 3×10^{-2} (NH_4^+), 8.1×10^{-1} (Na^+), 2.8×10^{-2} (K^+), 1.1×10^{-2} (Ag^+), 1×10^{-2} (Hg_2^{2+}), 3.6×10^{-2} (Cu^{2+}), 3.7×10^{-2} (Ni^{2+}), 2.3×10^{-2} (Ca^{2+}), 3.4×10^{-2} (Cd^{2+}), 2.2×10^{-2} (Mg^{2+}), 1.4×10^{-2} (Ba^{2+}), 1.7×10^{-2} (Pb^{2+}), 8.8×10^{-1} (Zn^{2+}), 1.6×10^{-2} (Sr^{2+}), 1.4×10^{-2} (Cr^{3+}), 1.4×10^{-2} (Al^{3+}), 2.7×10^{-2} (Fe^{3+})	89
1c (R^1 = Bu^t R^2 = H)	"	Co^{2+}	$\Delta c = 1\times10^{-6}-1.0\times10^{-1}$, $S = 30\pm0.1$	$K = 4.8\times10^{-3}$ (Ag^+), 1.6×10^{-3} (Na^+), 1.3×10^{-3} (K^+), 9.5×10^{-4} (Ca^{2+}), 2.0×10^{-3} (Cs^+), 1.0×10^{-3} (Li^+), 8.2×10^{-4} (Mg^{2+}), 4.4×10^{-3} (Cu^{2+}), 6.8×10^{-3} (Hg^{2+}), 6.5×10^{-3} (Pb^{2+}), 9.0×10^{-4} (Ba^{2+}), 7.2×10^{-3} (Zn^{2+}), 9.3×10^{-4} (Sr^{2+}), 4.0×10^{-3} (Ni^{2+}), 3.3×10^{-3} (Cr^{3+})	90
26	"	Pb^{2+}	$\Delta c = 10^{-6}-10^{-1}$, $S = 24.2-30.1$, $c_{lim} = 0.63-1.6$	$K^+ > Ca^{2+} > Cu^{2+} > NH_4^+ > Cd^{2+} > Ni^{2+} > Co^{2+} > Zn^{2+}$; log$K$ from −0.2 to −4.7	91
27	"	Pb^{2+}	$\Delta c = 10^{-6}-10^{-2}$, $S = 29.4$, $c_{lim} = 10^{-6.1}$	interference of Ag^+, Hg^{2+}, Hg_2^{2+} (log$K$ > 1); $Pb^{2+} > Cs^+ > K^+ > NH_4^+ > Fe^{2+} > Mn^{2+}, Al^{3+} > Cu^{2+}, Mg^{2+} > Sr^{2+} > Ba^{2+} > Cd^{2+} > Ca^{2+} > Co^{2+}$	92
1b (R^1 = Bu^t, R^2 = H, n = 6, 8)	PVC membrane on a platinum wire	Pb^{2+}	$\Delta c = 10^{-6}-10^{-1}$, $S = 30\pm1$, $c_{lim} = 6\times10^{-7}$	$K = 3\times10^{-3}$ (Na^+), 5.5×10^{-3} (K^+), 9.3×10^{-3} (Ag^+), 4.8×10^{-4} (Mg^{2+}), 8.0×10^{-4} (Ca^{2+}), 1.3×10^{-4} (Ba^{2+}), 2.0×10^{-4} (Sr^{2+}), 7.9×10^{-4} (Mn^{2+}), 1.6×10^{-3} (Co^{2+}), 6.3×10^{-3} (Ni^{2+}), 4.8×10^{-3} (Cu^{2+}), 1.3×10^{-3} (Zn^{2+}), 7.6×10^{-3} (Cd^{2+}), 2.9×10^{-2} (Hg^{2+}), 5.1×10^{-3} (Cr^{3+}), 3.5×10^{-3} (Fe^{3+}), 2.4×10^{-3} (Al^{3+})	93

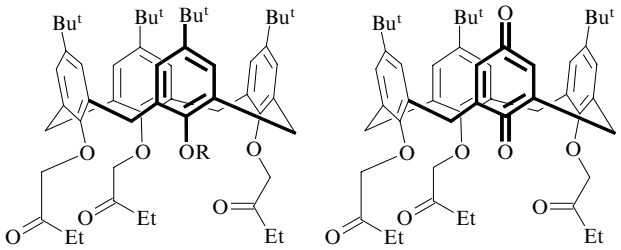
Table 1 (continued).

Calixarene [a]	Method of incorporation in the sensor	Determined ion (compound)	Main electrode parameters [b]	Selectivity of determination [c]	Ref.
28	inclusion in an isodecyl acrylate — methyl metacrylate copolymer	Cu^{2+}	$\Delta c = 10^{-5}-10^{-2}$, $S = 55.4$	$\log K = -2.0$ (K^+), -3.7 (Ca^{2+}), -3.9 (Mg^{2+})	94
29	PVC membrane	Hg^{2+}	$\Delta c = 7.5\times10^{-6}-1\times10^{-2}$, $S = 61.1\pm0.8$, $c_{lim} = 4.5\times10^{-7}$	$Ag^+ > Pb^{2+} > K^+$, $Li^+ > Fe^{2+}$, Cu^{2+}, $Ca^{2+} > Co^{2+}$, Ba^{2+}, $Sr^{2+} > Zn^{2+}$, Cd^{2+}	95
23, **30**	the same	Ag^+	$\Delta c = 10^{-5}-10^{-1}$, $S = 58.9$, $c_{lim} = 6.31\times10^{-6}$	$\log K = -2.35$ (Na^+), -2.65 (K^+), -4.57 (Mg^{2+}), -4.10 (Ba^{2+}), -3.42 (Cd^{2+}), -3.45 (Pb^{2+}), -2.0 (Hg^{2+})	96, 97
31	"	Ag^+	$\Delta c = 5\times10^{-6}-10^{-2}$, $S = 57$, $c_{lim} = 10^{-5.3}$	interference of Hg^{2+} ($\log K > 1$); $Pb^{2+} > Ni^{2+} > NH_4^+ > K^+ > Na^+ >$ $> Cu^{2+} > Zn^{2+} > Mg^{2+} > Ca^{2+}$ ($\log K$ from -2 to -5)	98
32	"	Ag^+	$\Delta c = 5\times10^{-6}-1\times10^{-1}$, $S = 39-53$	$\log K$ from -4.5 to -4.3 (alkali, alkaline-earth and transition metals), from -3.4 to -3.5 (Pb^{2+}), from -1.8 to -1.6 (Hg^{2+})	99
33	adsorption on polyaniline	Ag^+	$\Delta c = 2\times10^{-7}-1\times10^{-2}$, $S = 55-70$, $c_{lim} = 1\times10^{-7}-2.5\times10^{-8}$	$\log K$ from -3.96 to -6.53 (K^+), from -2.80 to -6.28 (Na^+), from -3.30 to -6.31 (Cu^{2+}), from -4.44 to -6.90 (Cd^{2+}), 0.05–1.78 (Hg^{2+}), from 1.20 to -1.20 (Fe^{3+})	100, 101
Sulfonato-calix[*n*]-arenes ($n = 6, 8$)	adsorption on polypyrrole and poly(3,4-ethylene-dioxythiophene)	Ag^+	$\Delta c = 10^{-5}-10^{-1}$, $S = 55-62$, $c_{lim} = 1\times10^{-5}$	$\log K = -3$ (H^+, polythiophene); $Li^+ > Na^+$, $K^+ > Mg^{2+} > Ca^{2+}$, NH_4^+, $Mn^{2+} > Zn^{2+} > Co^{2+}$ ($\log K$ from -2 to -4.5)	102
34	PVC membrane	Ag^+	$\Delta c = 5\times10^{-6}-1\times10^{-1}$, $S = 58$, $c_{lim} = 10^{-5.5}-10^{-5.8}$	$Hg^{2+} > NH_4^+$, $K^+ > Na^+$, $Fe^{3+} > Zn^{2+}$, Cu^{2+}, $Ni^{2+} > Co^{2+}$, $Cd^{2+} > Ca^{2+}$, Mg^{2+}; $\log K$ from -2.5 to -5.5	103
35	the same	Ag^+	$\Delta c = 10^{-6}-10^{-2}$, $S = 60$, $c_{lim} = 4\times10^{-7}$	$\log K$ from -2.5 to -2.8 (Hg^{2+}), < -4.0 (Cu^{2+}, K^+, Pb^{2+}, Na^+, Ni^{2+}, Ca^{2+}, Zn^{2+})	104
36	"	Ag^+	$\Delta c = 5\times10^{-8}-1\times10^{1}$, $S = 61.4$, $c_{lim} = 1\times10^{-8}$	$Hg^{2+} > Pb^{2+} > Fe^{2+} > Fe^{3+} > Na^+$, $Li^+ > Ca^{2+} > Cs^+ > Na^+$, $Tl^+ > Cu^{2+}$, $Ba^{2+} > Ni^{2+} > Cd^{2+} > Zn^{2+} > Al^{3+}$; $\log K$ from -2 to -6	105
1b ($R^1 = Bu^t$, $R^2 = H$, $n = 6$)	PVC membrane or a wire coated with Nafion and triphenylphosphine oxide	UO_2^{2+}	$\Delta c = 10^{-5}-10^{-1}$, $S = 27$	$K = 6.1\times10^{-3}$ (Na^+), 8.1×10^{-3} (K^+), 7.8×10^{-3} (Mg^{2+}), 6.6×10^{-3} (Ca^{2+})	106
37	PVC membrane	HPO_4^{2-}	$\Delta c = 1.8\times10^{-5}-1\times10^{-1}$, $S = 33-44$	$1/K = 9.0$ (chloride), 8.8 (nitrite), 9.0 (nitrate), 9.6 (thiocyanate), 0.05 (sulfate), 3.0 (hydrogencarbonate), 50 (perchlorate)	107
38	the same	HPO_4^{2-}	$\Delta c = 5.5\times10^{-5}-1\times10^{-1}$, $S = 33-28$, $c_{lim} = 5\times10^{-5}$	$1/K$ from 7.5 to 100 (nitrate, sulfate, chloride, perchlorate, acetate, thiocyanate)	108
39	"	CO_3^{2-}	$\Delta c = 5\times10^{-4}-1\times10^{-1}$, $S = 29$, $c_{lim} = 1.2\times10^{-4}$	$K = 1.9\times10^{-2}$ (salycilate), 2.1×10^{-2} (iodide)	109

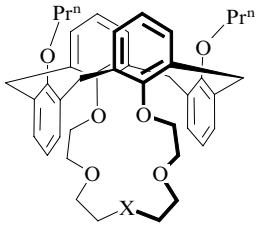
Table 1 (continued).

Calixarene [a]	Method of incorporation in the sensor	Determined ion (compound)	Main electrode parameters [b]	Selectivity of determination [c]	Ref.
40	PVC membrane	Cl^-	$\Delta c = 1\times10^{-1}-5\times10^{-5}$, $S = 55.69$, $c_{lim} = 2.51\times10^{-5}$	$\log K = -3.00$ (nitrite), -3.75 (tartrate), -4.31 (citrate), -3.65 (carbonate), -3.00 (acetate), -2.60 (nitrate), -1.40 (thiocyanate), -4.00 (sulfate), -2.10 (hydroxide), -2.65 (fluoride), -2.50 (azide), -2.70 (perchlorate), -1.30 (bromide), -1.80 (iodide)	110
24 (R = H, Bu^t; n = 6, 8)	the same	organic amines	$\Delta c = 10^{-5}-10^{-2}$ (norepinephrine), $S = 50-57$	n = 6: $Tl^+ > Cs^+ > Rb^+ >$ phenylalanine > alkylamines > Alk_4N^+; n = 8: phenylalanine > Tl^+, K^+, Rb^+, $Cs^+ > Na^+ > NH_4^+ > Li^+$	111
1b ($R^1 = Bu^t$, R^2 = H, n = 4, 6, 8)	"	pyridoxine	$n = 8: \Delta c = 6.2\times10^{-6}-1\times10^{-1}$, $S = 60.4$, $c_{lim} = 1.6\times10^{-6}$; $n = 4, 6: \Delta c = 1\times10^{-5}-1\times10^{-1}$, $S = 51.6$ (n = 6), 40.1 (n = 4)	Ca^{2+}, Cu^{2+} and Zn^{2+} do not interfere; cyanocobalamine, thiamine hydrochloride, nicotinamide and *p*-aminobenzoic acid	112
41	"	benzoic acid	$\Delta c = 5\times10^{-2}-5\times10^{-4}$, $S = 30$, $c_{lim} = 2\times10^{-4}$	$\log K = -0.42$ (chloride), -1.22 (phosphate); the ascorbate, citrate and acetate anions and glucose do not interfere	113

[a] Structures of compounds **21**–**41** are given below; [b] Δc is the interval of determined concentrations (mol litre^{-1}); S is the slope of the electrode function [mV (pC)$^{-1}$]; c_{lim} is the detection limit (mol litre^{-1}); [c] K is the selectivity constant.

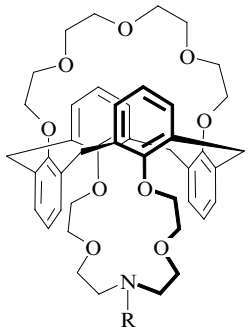


21 (R = H, Me, Bn)



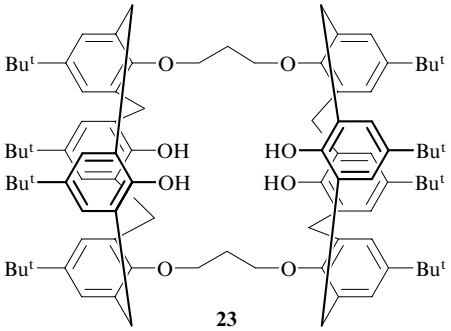
22a

X = O, NR (R = H, Ph).

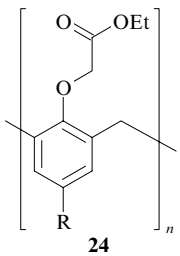


22b

R = H, Ph.

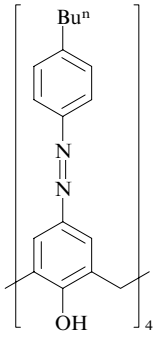


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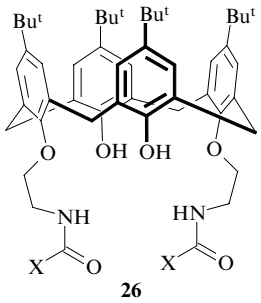


24

R = H, Bu^t; n = 4–6.

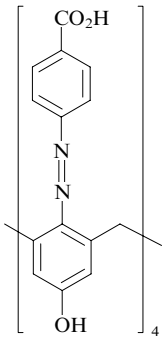


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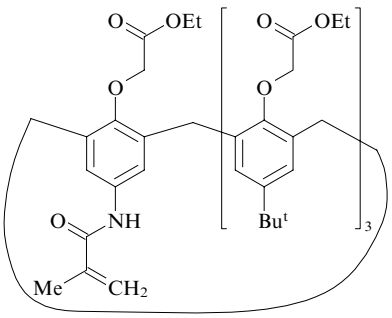


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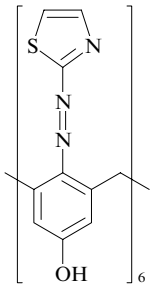
X = Me, Et, 4-$O_2NC_6H_4$, 4-Py.



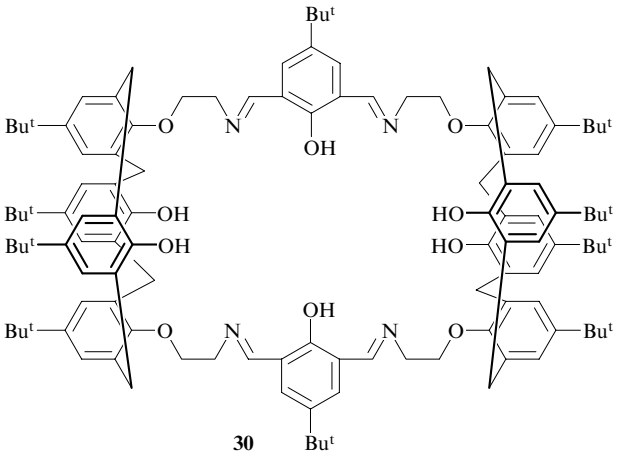
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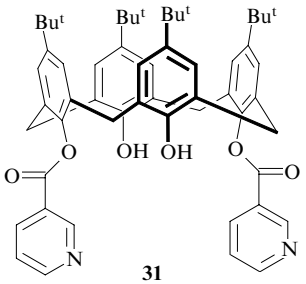
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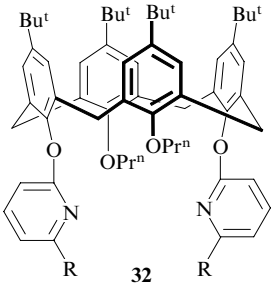
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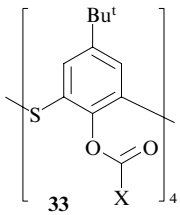


31

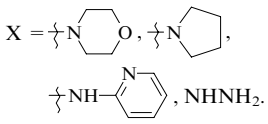


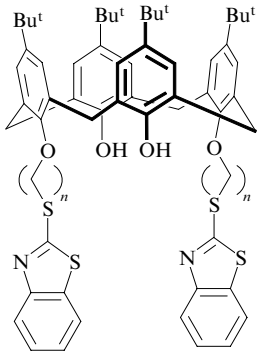
32

R = CH_2PPh_2, CH_2OH.

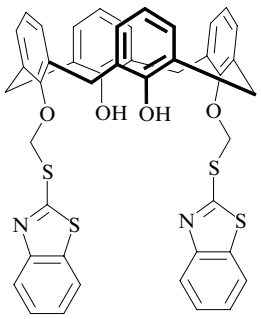


33

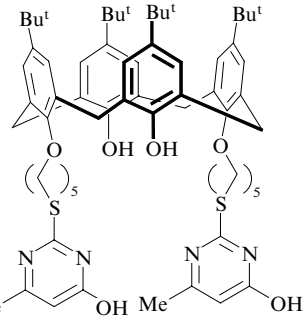
X = 



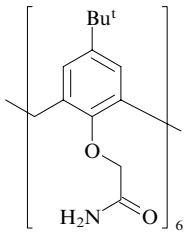
34 (*n* = 2, 3)



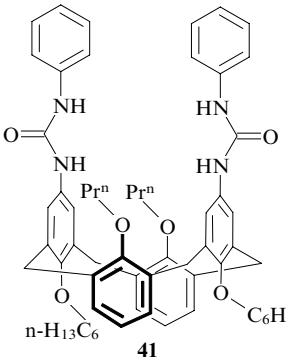
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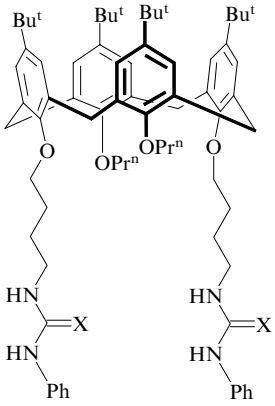
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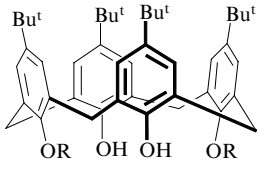
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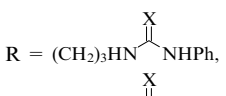
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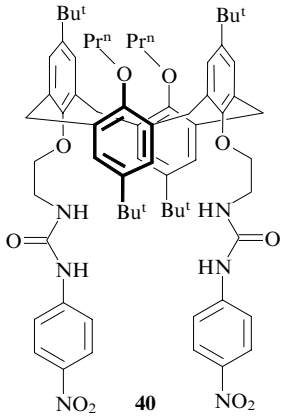
38 (X = O, S)



39

R = 

(X = O, S).



40

It is noteworthy that in some cases the same calixarene-based receptors demonstrate different selectivity in different ISE. For example, *p-tert*-butylcalix[6]arene was used in the assembly of sensors toward the Pb^{2+} (Ref. 93) and uranyl ions;[106] in the latter case, sufficiently high potentiometric selectivity was found in the pair UO_2^{2+}/Pb^{2+}. Moreover, the same calixarene was used [114] in a chemoresistor to the nickel ions. Thus, the same receptor in different devices produced selective response to three different ions. *p-tert*-Butylcalixarene thermally evaporated to the field-effect-transistor gate [115, 116] or gold [117] produced potentiometric and impedimetric response to the Cu^{2+} ions. The same receptor incorporated in the Langmuir–Blodgett films on glassy carbon selectively accumulated the silver ions, which were further determined by means of stripping voltammetry.[118] At the same time, *p-tert*-butylcalix[4]arene in PVC membrane produces selective response to the Co^{2+} ions with selectivity coefficients of 4.4×10^{-3} relative to the Cu^{2+} ions and 4.8×10^{-3} relative to Ag^+.[90] Cadmium-selective ISE with internal reference filling were fabricated; polymeric membranes of these ISE contained thiacalix[4]arene or *p-tert*-butylthiacalix[4]arene [selectivity coefficients $K = 1 \times 10^{-3}$ (Ag^+) and 9×10^{-3} (Cu^{2+})].[119]

That great discrepancy of the results of different studies can be related to the features of measurements of the membrane ISE signal. Its potential depends, first of all, on the ratio of potential-determining ion concentrations in the solution to be analyzed and in the internal reference solution. The electrode must be pre-conditioned to achieve equilibrium distribution of the determined ion in the membrane. Thus the binding sites of calixarenes are saturated with the potential-determining ion from the reference solution. This suppresses the effect of ions with similar binding characteristics but present in solutions at substantially lower concentrations. As far as in these cases calixarenes and their thia-analogues do not contain substituents with functional groups that selectively bind the determined ion, the selectivity of response is governed basically by properties of the ion from the reference solution. In solid-state sensors, including field-effect transistors and 'coated wire' electrodes (where the polymeric membrane is deposited directly onto the surface of the metal wire), the internal reference solution is absent, but the sensor is soaked in the solution of the potential determined ion. This results in the same consequences, *i.e.* saturation of the binding sites with the analyte. Hence, the selectivity changes similar to that of a conventional membrane ISE with the same receptor described above.

The selectivity coefficients in Table 1 were obtained by the separate solution method.[1] Not in all cases this method takes into consideration concurrent interactions of determined and interfering ions if both are present in the solution. In addition, the method describes the signal selectivity insufficiently adequately for different charges of determined and interfering ions. The use of corrections, for example in calculations of the so-called unbiased selectivity coefficients,[1, 120] can change the absolute values of the selectivity coefficients by two or more orders of magnitude. This has special importance for ions that are easily hydrolyzed since in the processes of selectivity measurements the acidity control or correction of pH values in solution of a metal salt are not usually specified. The formation of the hydroxo ions with lower inherent charge as compared with the nominal value can drastically affect the estimation of selectivity.

Nevertheless, the selectivity coefficient can be considered as one of few quantitative characteristics of the ISE receptors. It is not even their absolute values that are discussed most often, but rather changes in these values or the metal series constructed according to the selectivity coefficients. The latter are used for correct choice of working conditions in signal measurements under variations of membrane and receptor composition or conditions of measurements. In general, the published selectivity series agree with the factors considered in Section II in relation to the efficiency of metal ion recognition. Both the increase in the size of the calixarene cavity and incorporation of functional groups that can form chelate complexes with metal ions at both the upper and the lower rims, favour the formation of complexes with larger ions. The trend of preferable binding of 'soft' transition metal ions with thiacalixarenes and sulfur-containing calixarenes as compared with the alkali and alkaline-earth metal ions was also confirmed. But even for structurally similar receptors, the order of change in selectivity does not coincide and can substantially differ owing to changes in plasticizer polarity and pH. That is why, the problem of quantitative characterization of ISE selectivity should be solved separately for each receptor and sensor.

In addition to membrane ISE, other electrode devices exist that differ in the mode of incorporation of a calixarene-based receptor into the membrane. Development of such sensors aims at solution of two problems, *viz.*, miniaturization of a sensor and increase in operational stability of a signal. Incorporation of receptors in polymeric layers deposited directly on the surface of a sensor and application of calixarene without carrier directly on a transducer can be placed in the category of relatively new technologies.

Preparation of polymeric membrane *in situ* suggests deposition of a polymer layer on the surface of a transducer by a physical process or a chemical reaction from receptor-containing solution. It is possible to incorporate the receptor into a pre-formed polymeric film using electrostatic or physical (non-specific) adsorption.

As an example of the former approach, silicone-based membrane ISE prepared by sol–gel technology [78] can be mentioned. To this end, halogenosilane was made to react with a receptor containing a trialkoxysilyl substituent. As a result, the produced siloxane contained calixarene-based receptor fixed in the film by covalent bonds Si–O–Si. This sensor is characterized by lesser response time and lower detection limit of sodium ion (10 μmol litre^{-1}) in comparison with polymeric membranes prepared by conventional methods.

In a similar way, receptor **28**, an analogue of commercial ionophore to sodium ions,[80] was incorporated into a membrane.[94] Polymerization was carried out in mixtures of isodecyl and methyl metacrylates, and the ionophore also contained an acrylate fragment which was incorporated in the polymer chain in the course of polymerization. This ISE produced more stable signal and had longer life-time as compared with an analogue in which the receptor was added into a PVC matrix. At the same time, this ISE with the receptor incorporated into the co-polymer was inferior to conventional analogue regarding its selectivity and sensitivity.

In the calixarene-based solid-state sensors, electroconducting polymers, *e.g.*, polypyrrole,[84, 102] polyaniline [100, 101] and polythiophene,[102] are used as the polymer base of ion-selective membranes. These polymers undergo reversible

redox reactions, and equilibrium of these reactions and consequently the potential of a polymer will depend on the charge of the film and will change upon formation of a calixarene complex with a metal ion. Application of electroconducting polymers permits one to exclude internal reference solution from ISE and also removes limitations regarding the size and geometry of the transducer. The receptors are fixed on the sensor surface by electrostatic interactions (sulfonatocalixarenes[102]) or non-specific adsorption. Additional coating of polypyrrole with a PVC film containing a receptor[84] was described. The drawbacks of these sensors include the effect of a doping ion flow on the signal value, since this flow arises upon change in the oxidation state of the polymer. The potential of polyaniline depends on pH, because doping is accompanied by protonation of the nitrogen atoms in the polymer. These drawbacks are partly compensated by application of outer membranes with additional doping components. For polyaniline, the pH-dependence of the response is suppressed by interaction of protonated fragments of the polymer with heteroatoms of functional groups in substituents. In particular, the use of tetrasubstituted calixarenes with morpholide, hydrazide, pyrrolidide and amidopyridine substituents on the lower rim results in a more than twofold decrease in the slope of the pH-dependence of ISE potential.[101] Suppression of the pH-dependence of the polyaniline potential was also manifested in attainment of sufficiently high selectivity coefficient in the pair potential-determining ion (Ag^+) – proton ($\log K \approx 3$). Some other examples of polymeric membrane manufacture with incorporation of calixarenes are discussed in Section IV.2.

Attempts were undertaken to deposit calixarenes directly onto surface of a transducer without a polymeric support. Thus calix[*n*]arenes ($n = 4-8$) were deposited on a field-effect transistor gate by thermal evaporation in vacuum at 800 – 1000 °C. The thus produced sensors showed responses to the Na^+ ions ($n = 4$) and Ni^{2+} ($n = 6$) with slopes of calibration curve of 56 and 24 mV $(pC)^{-1}$, respectively.[115, 116, 118] Thiacalix[4]arene and *p*-*tert*-butylthiacalix[4]arene deposited on gold film electrode by vacuum spray-coating produced potentiometric response to the Cu^{2+} ions.[117]

The developed calixarene-based receptors are characterized by effective performances for real objects. For example, ISE were successfully used for titrimetric determination of silver ion-containing antibiotic Argosulfan,[100] chloride anions in natural water samples.[96, 97] An electrode with calix[6]arene **24** was used as the indicating electrode in precipitation titration of the Tl^+ ions (KI as a titrant),[88] that with calixarene **25** was used in complexometric titration of the Co^{2+} ions.[89] The possibility of the determination of the cobalt ions in wastes and beer was also established.[90]

Considering application of calixarene-based receptors in ISE as a whole, it is necessary to emphasize that the majority of studies was devoted to traditional objects of the potentiometric analysis, *viz*., sodium, potassium and cesium ions in the case of calixarene-based receptors and silver ions in the case of thiacalixarene-based receptors. The list of objects is expected to be expanded, first of all, owing to inclusion of anions and neutral organic compounds, in particular biopolymers. These are especially demanded due to the priority development of synthesis of receptors to proteins and nucleic acids. However, the mechanism of signal generation in this kind of ISE is not as obvious as in the determination of metal ions. The interaction with a neutral substrate does not change the charge of the surface layer or charge distribution in the membrane of traditional ISE. Therefore, new approaches are required. Thus, a concept of displacement, which is used, for example, in ligand displacement immunoassay,[121] will probably be successful. The essence of this concept is the reaction of an analyte biomolecule with an immunocomplex resulting in displacement of a labelled ligand from this complex. In the case of ISE, an analyte protein would react with a complex calixarene – metal ion resulting in displacement of this ion from the complex; the metal ion can be determined potentiometrically. Implementation of this approach seems very promising, but will require assessment of non-specific interactions of proteins with the metal ions. This method of signal registration is of universal character and may be used to develop ISE with similar constructions, but varied receptors, for the determination of different biomolecules.

The second promising approach to the determination of biomolecules is based on the use of specific binding, which limits mobility and ability to complexation of a potential-determining ion, for generation of an analytical signal. This can include formation of polyionic complexes or specific affinity interactions of the type antigen – antibody or DNA – intercalator. Competitive interactions with binding sites of the analyte ion and the biopolymer will change the ISE signal. The main advantage of such an approach as compared with direct potentiometric determination of polyelectrolytes including proteins and DNA is higher sensitivity of determination. According to the Nernst equation, the slope of a calibration curve ($0.059/n$, where n is the charge of a potential-determining ion) in the case of polyelectrolytes sharply decreases in comparison with singly and doubly charged metal ions. Potentiometric determination of surfactants by means of barium-selective ISE[122] and determination of protamine and heparin[123, 124] can be mentioned as examples of such an approach. Calixarene-based receptors in these ISE can provide selective concentration of biopolymers thus increasing the efficiency of competition for the potential-determining ion and, consequently, sensitivity of the method. Earlier, an example of such receptors and practice of their application in biochips for protein immobilization has been discussed.[26, 28]

Other potential field of the application of calixarene-based receptors in ISE is miniaturization of sensors. Owing to the inherent sizes and amphiphilic character of many calixarene receptors, they can be used in membranes without additional plasticizers[94] and sometimes without lipophilic salts.[100, 101] Such approaches are implemented in solid-state ISE on the base of electropolymerized materials and in sensors based on co-polymers with covalently linked supports. Single examples are known where analytical characteristics of traditional ISE were compared with those of microsensors with the same receptors.[84] As a rule, this comparison is still not in favour of miniature devices: the latter have narrower range of determined concentrations and higher detection limits with the same calibration curve slope and sensors' lifetimes. The application of other technologies for the preparation of surface layers with regular ultrathin coatings on current collector will eliminate, as we can believe, these drawbacks.

IV. Voltammetric sensors

Voltammetric detection of complex formation involving functionalized calixarenes imposes high requirements to

the composition and structure of sensor surface layer. Since the macrocyclic cavity under ordinary conditions is electrochemically inactive, oxidation or reduction of functional groups of substituents can proceed only at definite orientation of receptor on the electrode surface. It should also be noted that the formation of continuous layer of calixarene on the electrode surface results in substantial diffusion resistance of charge transfer across the interface electrode–solution due to very low electroconductivity and ion-exchange activity of the calixarene platform. These factors determine fairly low surface concentrations of calixarene-based receptors and, as a consequence, their weak influence on sorption accumulation of depolarizer molecules or ions. For these reasons, calixarenes often lose competition with traditional modifiers of amperometric sensors, which are used for sorption preconcentration of analytes on the surface of sensor.

Nevertheless, advantages of calixarene-based receptors promote studies on their electrochemical properties with subsequent application for amperometric determination of 'guest' molecules both in solutions and on the electrode surface.[125]

At present, all investigations in this field are carried out in the following directions:

— investigations of oxidation of the calixarene macrocyclic cavity and the effect on the oxidation of complex-forming low-molecular compounds;

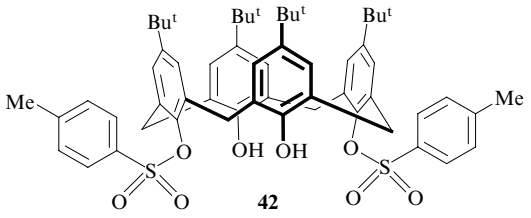
— synthesis of electrochemically active groups, such as ferrocene or cobaltocene covalently bound to the calixarene platform and their use for registration of amperometric signal;

— incorporation of calixarene-based receptors in electrochemically active coatings characteristics of which are affected by transfer of protons or charged 'guest' particles;

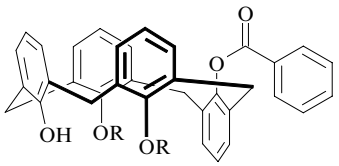
— the use of substituted calixarenes for sorption accumulation of analytes with subsequent determination of these compounds by means of direct or inversion voltammetry.

1. Electrochemical properties of calixarenes

Traditional non-substituted calixarenes and calixarenes with alkyl or alkoxy substituents on the upper and lower rims do not exhibit electrochemical activity in aqueous solutions. In organic solvents (acetonitrile, dichloromethane), irreversible oxidation of calix[n]arenes and *p-tert*-butylcalix[*n*]arenes ($n = 4, 6$) to the corresponding quinones was established. Usually, in cyclic voltammogram a peak of irreversible oxidation is detected at 1.55–1.9 V *vs.* $Ag/AgNO_3$ electrode (0.01 mole litre^{-1}).[126] The oxidation of calixarenes non-substituted at the upper rim results in passivation of a glassy carbon electrode in the second and subsequent cycles of potential scan and this phenomenon is accompanied by a sharp decrease in recored currents. In the absence of passivation at platinum electrodes, repeated cycles of potential scan reveal pairs of quasi-reversible peaks in the range of medium potentials (1.2–1.5 V) corresponding to the primary oxidation products of the calixarene macrocycle. Preparative electrolysis confirmed the formation of diquinones with adjacent (1,2) and opposite (1,3) positions of quinonoid rings. Analogous oxidation products were found for substituted calixarenes **42** (Ref. 127) and **43**, **44** (Ref. 128). In the latter case, the cyclic voltammogram also contained peaks assigned to the phenoxyl radical and a monoquinone derivative of the initial calixarene.



42

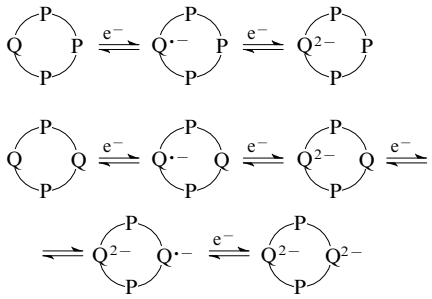


43, **44**

R = Pr^n (**43**), Bn (**44**).

The general pattern of electrochemical transformations of calixarene mono- and diquinones is shown in Scheme 1.[125]

Scheme 1



Q is a quinonoid fragment; P is a phenolic fragment.

It should be noted that estimation of a number of transferred electrons (like selection of intermediate steps of protonation) have only hypothetic character. Whereas the products of preparative electrolysis of calixarenes were isolated and identified, their cathodic reduction was studied exclusively by electrochemical methods.

Calixarenes can form insoluble oxidative polycondensation products on electrode surfaces. This property was used for the preparation of a film containing fullerene as a mediator of electron transfer. Fullerene C_{60} and *p-tert*-butylcalix[8]arene were deposited on glassy carbon and then IR-irradiated. With the use of the thus modified electrodes, voltammograms were obtained and reversible redox peaks were found and assigned to fullerene molecules strongly bound to the surface layer.[129]

Positions and heights of redox peaks for calixarene macrocycles depend on the presence of 'guest' ions in solution. This can be used for the determination of these ions. Thus it was established[130] that the positions of oxidation peaks of the lower-rim tetrasubstituted *p-tert*-butylcalix[4]arene ($R^2 = CH_2CO_2Et$) measured by square-wave voltammetry at a platinum electrode in acetonitrile depend on the nature and concentrations of metal ions in solution. The Li^+, Na^+ and K^+ ions suppress oxidation processes, decrease the current of a peak at 1.2 V and shift the peak (registered at 1.45 V in the absence of these ions) to higher anodic potentials. The effect of ions decreases in the series $Na^+ > Li^+ > K^+$, which coincides with the corresponding series of stability constants of complexes with calixarene.

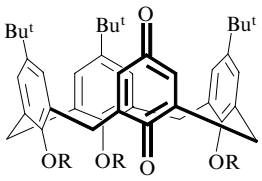
A method of recognition of the alkali metal cations was proposed, which is based on the effect of these metals on the oxidation of *p-tert*-butylcalix[4]arene 1,3-disubstituted with

fragments $CH_2C(O)NEt_2$ at a platinum electrode in dichloromethane. In the absence of these ions, irreversible anodic peaks at 1.51 and 1.78 V and one cathodic peak at 0.05 V were found in cyclic voltammograms. In the presence of lithium, sodium, potassium or caesium chlorates (1–2 mol. equiv.), additional anodic peaks in the interval from 70.2 to 0.06 V appeared in cyclic voltammograms, and the cathodic peak shifted into the interval from −0.23 to −0.44 V. These changes in cyclic voltammograms depend on the nature of a cation.[131]

Similar results were obtained for calixarenes with diphenylphosphinoylmethoxyl substituents at proximal positions of the lower rim. The corresponding 1,2-diquinone-calixarene was first obtained under conditions of preparative electrolysis, which further was studied by CV with rotating platinum electrode in dichloromethane. The positions and the number of oxidation peaks depended on the concentration of the silver ions added to the solution.[132]

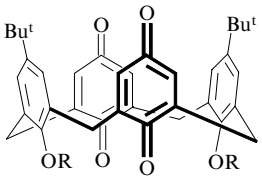
In the cases of thiacalix[4]arene and *p-tert*-butylthiacalix[4]arene, only one oxidation peak was found in cyclic voltammograms at 1.53 and 1.55 V, respectively. The potential of this peak shifts approximately to an equal extent in the presence of equimolar amounts of the K^+, Na^+, Cs^+, Li^+, Rb^+, Co^{2+}, Ni^{2+} and Cu^{2+} ions. In the system H_2O–MeCN, an additional oxidation peak appears at 0.55 V. The Cd^{2+} and Co^{2+} ions shift this peak to more positive potentials and simultaneously increase the current value whereas the Ni^{2+} ions suppresses it completely. The potential of the main oxidation peak of thiacalix[4]arene shifts to 1.7 V in the presence of the Cd^{2+} ions and the current increases with an increase in concentration of the Cd^{2+} ions up to the equimolar ratio with the receptor. This is considered as evidence of thiacalixarene–Co^{2+} complex formation with the stoichiometry 1 : 1.[133]

Quinone-calixarenes synthesized chemically or by preparative electrolysis of conventional calixarenes reveal high activity in electrochemical reactions. The addition of the NH_4 , Li^+, Na^+, K^+ and La^{3+} ions shifts potentials of redox peaks of mono- (**45a**) and 1,3-diquinone derivatives (**45b**) of *p-tert*-butylcalix[4]arene (200–1000 mV) without substantial change in current.[125]



45a

R = CH_2CO_2Et.



45b

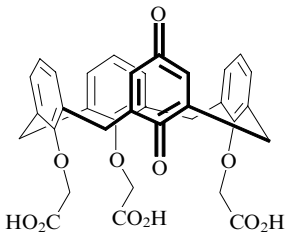
R = $CH_2C(O)NHBu^n$, CH_2CO_2Et, CH_2CO_2Me.

Changes in positions of cathodic peaks are most informative, since electrochemically reduced quinone is stabilized by 'guest' cations. In particular, quantitative determination of the Na^+, Ca^{2+} and La^{3+} ions in acetonitrile in the presence of the quinone-calixarenes is based on these electrochemical properties.

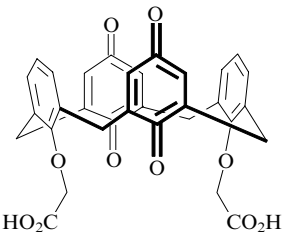
Receptor **45b** (R = $CH_2C(O)NHBu^n$, CH_2CO_2Et) forms complexes with the NH_4^+, Na^+ and K^+ ions, which results in appearance of an additional irreversible peak assigned to reduction of the complex.[134] Depending on the concentration of the 'guest', the height of this peak corresponds to transfer of one or two electrons, which is connected presumably with stabilization of the intermediate radical anion and dianion (see Scheme 1). The ammonium cations, which form hydrogen bonds with the oxygen atoms of the quinone fragments, stabilize the radical anion to a greater extent than the metal cations. This results in appearance of an additional one-electron peak at more positive potentials as compared with reduction of the free ligand. In the case of the Na^+ and K^+ ions, all peaks of the free ligand disappear after addition of one equivalent of these cations and their subsequent addition does not produce changes in cyclic voltammograms.

Proton-donor compounds (independently on the sizes of their molecules) also influence electrochemical behaviour of quinone-calixarenes. Thus dopamine, histamine, pyruvate, glycine, maleic acid and the ammonium ion shift cathodic peaks of reduction of diquinone-calixarenes and these shifts are proportional to the concentrations of these substances.[125]

Electrochemical properties of mono- (**46a**) and diquinone-calix[4]arenes (**46b**) with carboxyl groups at the lower rim were studied by constant-current and square-wave voltammetry with the use of glassy carbon and silver electrodes.[135]



46a

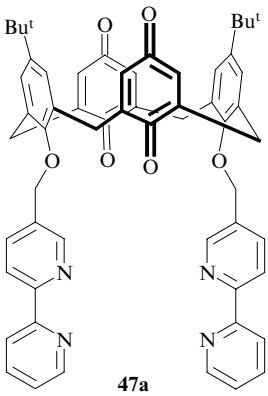


46b

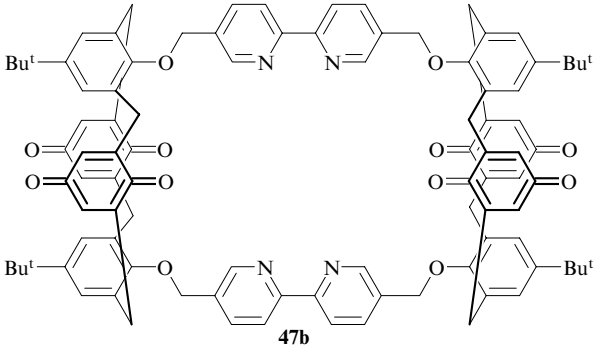
These receptors in neutral and basic aqueous solutions are characterized in cyclic voltammograms by only one conjugated reversible redox pair of peaks at 0.12 V *vs.* Ag/AgCl electrode. In the case of monoquinone **46a**, the addition of the Ca^{2+} ions results in appearance of a new peak at −0.12 V, the height of this peak increasing with the increase in the concentration of the Ca^{2+} ions. 500- and 1000-fold excesses of the Na^+ and K^+ ions, respectively, and 50-fold excess of the Mg^{2+} ions do not interfere with this determination. The same monoquinone-calixarene exhibits one quasi-reversible peak of two-electron reduction at a glassy carbon electrode in aqueous solution.[136] The most pronounced influence of the Ca^{2+} ions is manifested at pH 8 where reversibility of the signal increases and the value of the peak current increases by 50%–70%. Two one-electron redox peaks are observed in the presence of equimolar amount of the Ca^{2+} ions at pH 10. For the first peak, the current increases linearly with concentration of the Ca^{2+} ions up to the molar ratio 1 : 1, which corresponds to stoichiometry of the formed complex.

Recognition of the ammonium, potassium and barium cations with 2,2′-bipyridyl-containing quinone-calix[4]-arenes **47** in acetonitrile was studied by CV method at a disk glassy carbon electrode. Two quasi-reversible peaks are observed in cyclic voltammograms of compound **47a** at −1.07 and −1.15 V relative to Ag/AgNO3 corresponding to one-electron reduction of each quinone. In the case of biscalixarene **47b**, a single intense peak of reduction at −1.11 V was found. In addition, cyclic voltammograms of compounds **47a** and **47b** contained the second irreversible

peak at −1.82 and −1.91 V, respectively, which was assigned to formation of dianion forms of quinones.



47a



47b

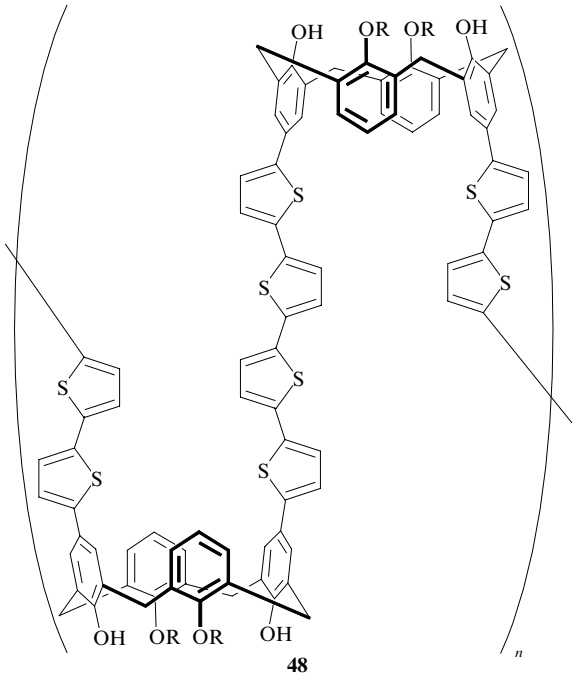
The addition of the ammonium ion (1 or 2 equiv.) to calixarene **47a** resulted in a shift of the first reduction peak, which became completely irreversible, to less negative potentials (−0.89 V). Reverse scan of the potential gave two new intense oxidation peaks in cyclic voltammograms (E_a = 0.2 and 0.71 V), and the second irreversible reduction peak shifted to a more negative region (E_k = −2.18 V). Similar results were obtained in the case of biscalixarene **47b**.

Similar changes in voltammograms associated with formation of complexes and changes in stability constants in the redox processes were also observed for the K^+ and Ba^{2+} ions. In all cases, complexes with stoichiometry 1 : 1 formed. The stability of the K^+ complex appeared higher by one order of magnitude than that of ammonium complex, and the Ba^{2+} cation forms more stable complex with mono-derivative **47a** than with biscalixarene **47b**.[137]

2. Electrochemical reactions of functional groups in substituted calixarenes

Some studies were devoted to preparation of polymers with covalently linked calixarenes. Electrochemical polymerization of calix[4]arenes modified with N-substituted pyrrole residues at the upper rim [R^2 = Me, R^1 = NHC(O)$(CH_2)m$(cyclo-NC_4H_4), where m = 2 or 4] in a potentiodynamic regime with multiple scan of a potential at a platinum electrode in acetonitrile produced a film of a polymer on the electrode surface, the stability of which increased with lengthening of the methylene spacer in the pyrrole-containing substituent.[138]

Similar films of thiophene oligomers with calixarenes (**48**) were obtained at platinum microelectrodes using electrolysis in a potentiodynamic regime in dichloromethane.[139]

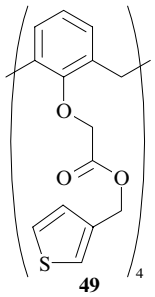


48

Cyclic voltammograms of polymeric products contained two redox peaks at 0.22 and 0.45 V; oxidation at higher potentials resulted in polymer destruction.

The main purpose of preparation of polymers with incorporated calixarenes is to enhance stability of the surface film. In addition, some polymerization products (polypyrrole and polythiophene) are electrochemically active and can influence electrochemical properties of a 'guest', as was noted for potentiometric sensors.[100–102] As an example, sensor on the base of an electrode coated with polypyrrole film can be mentioned. This polymer was doped with sulfonate derivative of calix[6]arene held in the layer by electrostatic forces.[140] This sensor made it possible to determine the uranyl ion, which formed complex with calixarene. The formation of the complex changes the reversibility of the uranyl peaks in cyclic voltammograms; in this case the 'guest' ion can be not only accumulated, but desorbed by changing the electrode potential and pH of the solution. This allows one to regenerate the sensor after measurements. Polypyrrole exhibits stabilizing properties and suppresses the tendency of the uranyl ion to disproportionation and pH-dependence of uranyl redox reactions.

Tetraesters of calix[4]arene with thiophene fragments (**49**) exhibited affinity to the K^+, Na^+ and NH_4^+ cations.



49

The formation of complexes in acetonitrile was detected by characteristic changes in an irreversible oxidation

peak in the range of 1.2 – 1.6 V, which was attributed to oxidation of phenol rings of the macrocycle. This compound undergoes electropolymerization with formation of an electroconducting film on the electrode surface in multiple cyclic scans of the potential. The increase in heights of redox peaks in the range of 0.8 – 1.2 V, which are attributed to thiophene fragments, can be considered as a evidence of polymerization. Polymerization was also observed in mixtures of calixarene **49** and methylthiopnene.[141]

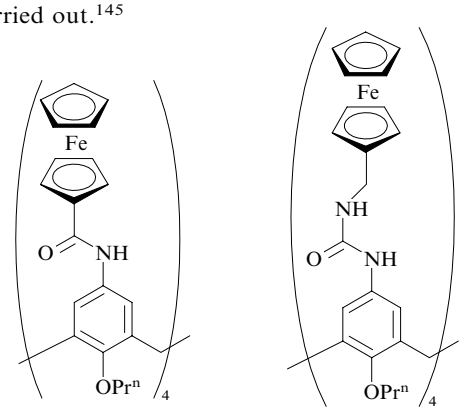
Metallocenes are very effective markers of the complexation involving calixarenes. Ferrocene substituents in side chains retain the ability to undergo reversible one-electron redox reactions and characteristics of these reactions are determined by the nearest neighbours of these substituents, size of the macrocycle and by number of ferrocene residues in the ligand. Thus polyferrocene derivatives of *p-tert*-butylcalix[*n*]arenes ($n = 4$, 6, 8) containing different amounts of ferrocene substituents at the upper and lower rims (at the bridging carbon atoms and in the aromatic ring) are characterized by different positions of redox peaks in cyclic voltammograms in acetonitrile. The smallest potentials of anodic and cathodic peaks (0.55 and 0.29 V, respectively) were observed for calix[4]arene with four ferrocene substituents at the bridging carbon atoms. Anodic and cathodic peaks in the range of potentials 0.59 – 0.66 and 0.35 – 0.38 V, respectively, were observed for calixarenes with eight substituents at the upper rim and four substituents at the lower rim. Potentials of anodic and cathodic redox peaks of the ferrocene substituents increased in the series $n = 6 < n = 4 < n = 8$, and occurred in the intervals of 0.70 – 0.78 and 0.48 – 0.56 V, respectively.[142]

One of the reasons for substantial changes in potentials of redox peaks of the ferrocene substituents depending on microenvironment, in particular on the presence of 'guest' molecules, is self-association processes with incorporation of an oxidized form of the receptor into the macrocyclic cavity or coordination of this form with lower non-substituted phenolic groups of calixarene. Such processes were investigated using ^{1}H NMR spectroscopy and homogeneous electron exchange rate constants between ferrocene fragments were calculated.[143] The appearance of only one peak in cyclic voltammograms irrespective the number of such substituents in the molecule can be considered as evidence of electron exchange between the ferrocene substituents.

Steric hindrance in the electron transfer and the effect of coordination result in substantial shifts (up to 200 mV and more) of the corresponding redox-peaks in the anodic region as compared with cyclic voltammograms of non-substituted ferrocene. Obviously, any processes affecting the intra- and intermolecular electron exchange will determine electrochemical characteristics of the complex and the receptor.

Oxidation of ferrocene produces cationic sites and due to this process substituted calixarenes can be used as receptors to anions. The application of calix[n]arene **50a** substituted with ferrocenecarboxamide fragments at the upper rim for the determination of phosphate anions was described. Dependences of cyclic voltammograms of tetraferrocenylamidocalix[4]arene, pentaferrocenylamidocalix[5]arene and bis(ferrocenylamido)calix[4]arene in mixtures acetonitrile – dichloromethane on concentrations of inorganic anions were studied. All these ligands produced one quasi-reversible oxidation peak in the interval of potentials 0.12 – 0.2 V (relative to Ag/Ag^+ electrode). In the presence of phosphate, sulfate and chloride anions, cathodic shifts of peak potentials were observed, which had maximum value for equivalent amount of the HPO_4^{2-} anions.[144]

Comparative investigation of complex formation of ferrocenyl-containing calix[4]arenes **50a** and **50b** with the chloride, benzoate and dihydrogenphosphate anions was carried out.[145]

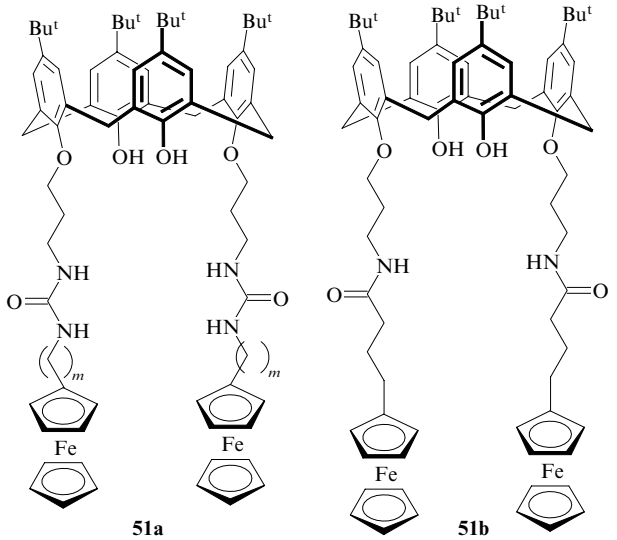


50a **50b**

According to X-ray diffraction and ^{1}H NMR titration data, the complex has 'guest' : 'host' stoichiometry 2 : 1.

The reversibility of electron transfer with participation of ferrocenyl substituents was established by CV for both free and bound receptors. Incorporation of a 'guest' results in increase in potential difference in direct and reverse processes up to 85 – 100 mV. By means of square-wave voltammetry in mixtures dichloromethane – acetonitrile, the possibility of separation of signals for free and bound receptors was established. The maximum separation (220 mV) was observed for the dihydrogenphosphate anion at the equivalent ratio anion : receptor. The changes in the signal of ferrocenyl substituents can be used for both the investigation of complex formation and quantitative determination of anions, for example, in their chromatographic separation.

Similar receptors **51** with longer spacers that separate ferrocene and the macrocycle gave selective response to dihydrogenphosphate anion.[146] The stability of the complexes with **51** was lower than that with **50a** and **50b** since the peaks for both the complex and the free receptor were



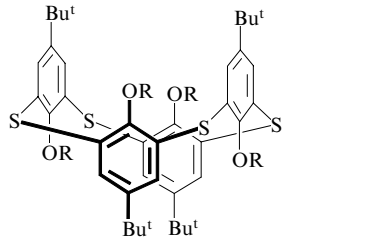
51a **51b**

$m = 1, 3$.

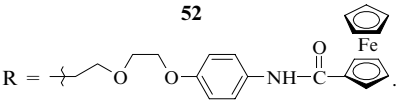
found in voltammograms even in the presence of an excess of a 'guest'.

It was established that in acetonitrile, dimethylformamide and dichloromethane the anodic peak of irreversible oxidation of the amide fragments at 0.55 V can be found in cyclic voltammograms only in the presence of bases, whereas the signal of the ferrocenyl substituents is not affected by addition of a base. Recognition of the dihydrogenphosphate anion by urea fragments of ligand **51a**, in contrast to receptor **50b**, occurs at a fairly long distance from ferrocenyl substituents. This excludes their direct interaction with the 'guest'. Thus, it can be proposed that the electrochemical response observed in this case is connected with incorporation of a counter-ion in the complex.

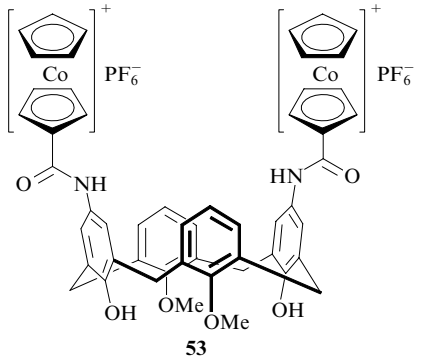
Application of calixarenes with ferrocenyl substituents for the determination of metal cations is limited to only a few examples. Thus calixarene **52** in the 1,3-alternate conformation recognizes the Eu^{3+} ions and the dihydrogenphospate anions.[147]



52

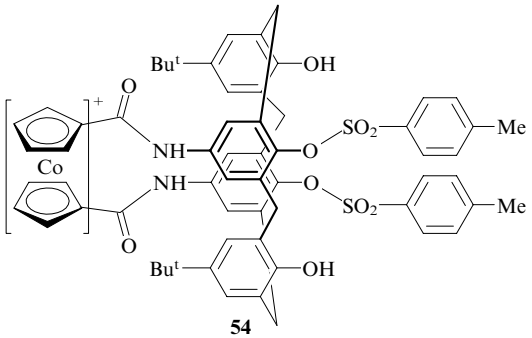


A reversible redox peak in the interval 0.5–0.6 V *vs*, the saturated calomel electrode (SCE) is observed in cyclic voltammograms of calixarene. The formation of complexes leads to changes in the potential of the calixarene peak up to 0.45–0.35 V in the presence of the Eu^{3+} cations and to 0.4–0.1 V in the presence of the dihydrogenphosphate anions. The acetate and bromide anions and the Na^+, K^+, Mg^{2+} and Cu^{2+} cations do not interfere. Determination of the La^{3+} cations using biscalix[4]arene with ester functional groups and ferrocenyl substituent in the bridge connecting the monomers was described.[148] In addition to ferrocene, cobaltocene [125, 149–151] and Ru^{2+} bipyridyl complex [129] were used as electrochemically active components of substituents in calixarene-based receptors to anions. Calix[4]arene **53** containing two cobaltocenyl substituents on the upper rim exhibited receptor properties towards anions of organic acids, particularly the adipinate dianion.[149]



53

Calixarene **54** with one cobaltocenyl substituent possessed similar properties.



54

Calixarenes with ruthenium bipyridyl complex as a substituent manifested affinity to the dihydrogenphosphate anion. The shift of potentials for the redox peak in cyclic voltammograms serves as an analytical signal as in the case of ferrocenyl substituents. Other examples of calixarenes modified with electrochemically active substituents, *e.g.*, transition metal complexes, can be found in a review.[152]

3. Voltammetric detection of complex formation on the base of a 'guest' signal

Calixarene-based receptors were used in several studies for selective preconcentration of 'guest' molecules on the surface of a transducer with its subsequent determination using its redox response. This approach does not differ in principle from traditional adsorption voltammetry, direct or stripping one.

p-tert-Butylcalix[4]arene tetrasubstituted with 2-sulfanylethoxy groups on the lower rim was deposited on the surface of a screen-printed carbon electrode. The thus produced sensor was suitable for determination of traces of lead by voltammetry following its cathodic accumulation from alkali solutions at −1.4 V (*vs.* SCE).[153] The peak of the lead ion oxidation at −0.42 V, registered by stripping voltammetry, served as an analytical signal. The range of determined concentrations constituted 5–100 ng ml^{-1} with the limit of detection of 5 ng ml^{-1}. The presence of the Cr^{3+}, Hg_2^{2+} and Zn^{2+} ions with concentrations 1.3, 0.72, 0.72 μg ml^{-1}, respectively, in the analyzed solution did not interfere. the Cd^{2+} ions at a concentration of 400 ng ml^{-1} produced anodic peak at −0.83 V in cyclic voltammograms. This sensor was used for lead determinations on spiked river water samples.

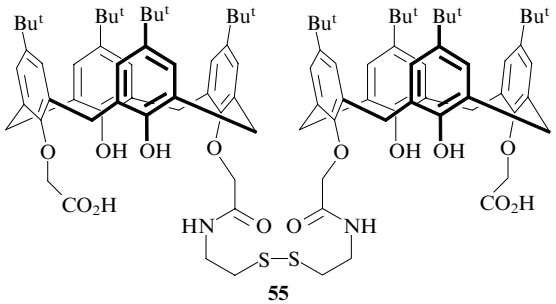
The same receptor in the screen-printed graphite electrode was applied for cadmium determination.[154] It was proposed to separate steps of metal accumulation and subsequent signal measurement, which was carried out in another electrolyte. Commercially available non-substituted calix[4]arene suppressing the influence of redox-active impurities was additionally incorporated in the modifying layer of the sensor. The limit of detection of the Cd^{2+} ions was 2.8 ng ml^{-1}, the upper boundary of detectable concentrations was 350 ng ml^{-1}.

Lead determination using *p-tert*-butylcalix[6]arene containing phosphinoxide substituents on the lower rim [$R^2 = CH_2CH_2P(O)Ph_2$] was reported.[155] Earlier, adsorption voltammetry was applied for determination of the silver ions with calix[4]arenes with nitrogen- and sulfur-containing substituents [156, 157] and for determination of the Hg_2^{2+} , Pb^{2+} and Cu^{2+} ions with calix[4]arene containing thioamide substituents.[158, 159]

The Langmuir–Blodgett films are very suitable supports of amphiphilic calixarenes. Self-assembly process and the presence of substituents differing in lipophilic properties on the upper and lower rims provide the required orientation of calixarenes in the surface layer. Small thickness of the layer ensures minimum diffusion resistance to transfer of the analyte ion and, consequently, quick and reproducible response. Glassy carbon electrodes coated with the Langmuir–Blodgett films containing *p*-allylcalix[4]arene, were used for the determination of trace amounts of the Tl^+ and Cd^{2+} ions in natural water samples by anodic inverse voltammetry. In a phosphate buffer, the linear dependence of a signal was obtained for the concentration intervals of 5–250 μg litre^{-1} for the Tl^+ ions and 10–300 μg litre^{-1} for the Cd^{2+} ions. The detection limit was 1 and 2.2 μg litre^{-1} (5×10^{-9} and 2×10^{-8} mol litre^{-1}), respectively.[160]

p-tert-Butylthiacalix[4]arene was used for Hg^{2+} determination by stripping and differential pulse voltammetry.[161] This receptor was incorporated in the Langmuir–Blodgett film produced by applying a solution of thiacalixarene in chloroform on water with subsequent evaporation of the solvent, compression of the film and its transfer on the surface of glassy carbon. The formation of a 'host–guest' complex with the mercury ions was investigated on the water–air interface by UV-spectroscopy and on the surface of glassy carbon by electrochemical impedance spectroscopy and atomic force microscopy. This sensor gave possibility to determine the Hg^{2+} ions in the concentration range of 5×10^{-10}–1.5×10^{-7} mol litre^{-1} with the detection limit of 2×10^{-10} mol litre^{-1}. Interfering influence of other metal ions was investigated in binary solutions containing 150-fold excess of interfering ions. Changes in the signal values did not exceed 2.5 rel.% as compared with those obtained in the absence of the interfering ions. The sensor was applied for the determination of mercury in natural and drinking water samples. The results of this study contradict to some extent to earlier investigation[118] by the same authors where the same *p-tert*-butylthiacalix[4]-arene-based sensor was used for the determination of the silver ions. The range of determined concentrations constituted 5×10^{-9}–2×10^{-6} mol litre^{-1}, the detection limit was 3×10^{-9} mol litre^{-1}. It is of note that the authors reported approximately the same parameters of the signal selectivity, 1 rel.%–3 rel.%. Possibly, such a substantial difference in the behaviour of the sensors is connected with the fact that the determination of mercury was performed at high concentrations of chlorides, which bind silver in insoluble chloride, whereas determination of the Ag^+ ions was carried out in nitric acid as a supporting electrolyte.

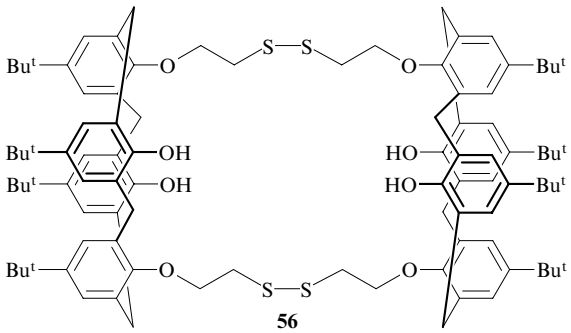
Self-assembly of bis(*p-tert*-butylcalix[4]arene) **55** with a disulfide bridge was applied to modify the surface of a gold electrode.[162]



55

An anodic peak at 0.25 V (*vs.* SCE) was found in cyclic voltammograms of the modified electrode in the presence of uranyl sulfate and a cathodic peak at 0.05 V, the peaks are assigned to redox-pairs UO_2^{2+}/UO_2^+ or UO_2^{2+}/U^{IV}. Determination was carried out in the concentration range of 10–300 μg litre^{-1}. Similar signals were registered in cyclic voltammograms with electrodes modified with polypyrrole and hexasulfonatocalix[6]arene.[140] The potentials and reversibility of peaks depend on pH. Presumably, the cathodic peak corresponds to reduction of the UO_2^{2+} ion, and the anodic peak corresponds to oxidation of the UO_2^+ ion. The appearance of new peaks at pH < 3 is explained by UO_2^+ disproportionation with formation of the UO_2^{2+} ions and U^{IV} compounds. The same method was applied for immobilization of hexasulfonatocalix[6]arene on the surface of a gold electrode pre-coated with a monolayer of cysteamine;[163] the limit of detection of the uranyl ion was 1 mg litre^{-1}.

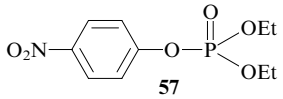
Determination of the silver ions with use of transfer currents in a four-electrode system may be considered as a new approach.[164] Dichloroethane served as an organic phase and bis(*p-tert*-butylcalix[4]arene) **56** as a ionophore. Measurements were performed in the cyclic voltammetry mode with variations of ratio Ag^+ : ionophore. The formation of complexes with stoichiometry 1 : 1 and 1 : 2 and log *K* (complex association constants) 12.4 and 14.5, respectively, was established. By differential pulse voltammetry, linear concentration dependence was obtained for the Ag^+ ions in the interval of $(2-10)\times10^{-5}$ mol litre^{-1} with the detection limit of 3.5×10^{-6} mol litre^{-1}. Such ions as Li^+, Na^+, K^+, Rb^+, Cs^+, Zn^{2+}, Cd^{2+}, Cu^{2+}, Ni^{2+} and Fe^{2+} do not interfere.



56

There are a limited number of publications devoted to voltammetric determination of organic molecules as 'guests'. In addition to limitations connected with a fewer number of receptors to organic compounds, this is explained by electrochemical inertness of potential 'guests' involved in complex formation, and, consequently, by the absence of signals in cyclic voltammograms. In the cases where these signals can be obtained, the mechanisms of electrode reactions remain unstudied.

For example, an amperometric sensor for the determination of pesticide parathion (**57**) was developed. Deposition of 1,4-crown-4-*p-tert*-butylcalix[6]arene on the surface of a glassy carbon electrode was performed with the use of the sol–gel technology.[165]



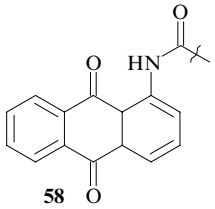
57

A cathodic peak at -1.18 V and an anodic peak at -0.29 V (*vs.* SCE) were registered in cyclic voltammograms following incubation of the sensor in a phosphate buffer solution (pH 6.5) containing the pesticide. The interval of determined parathion concentrations constituted $5.0 \times 10^{-9} - 1.0 \times 10^{-4}$ mol litre^{-1}, the detection limit was 1.0×10^{-9} mol litre^{-1}.

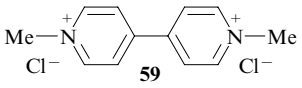
An indirect method of ascorbic acid determination was proposed based on its oxidation in the presence of the Co^{2+}, Ni^{2+}, Mn^{2+}, Cu^{2+} and Pb^{2+} cations, which were fixed on an electrode as complexes with *p-tert*-butylcalix[4]-arene and *p-tert*-butylcalix[6]arene. The interval of determined concentrations of ascorbic acid constituted 0.07 – 400 mg litre^{-1}, the detection limit was 30 μg litre^{-1} (Ref. 166).

Similar method was used for the registration of a signal of a cholinesterase sensor in which the electrode was modified with 1,3-disubstituted *p-tert*-butylcalix[4]-arenes.[167] Butyrylthiocholine served as a substrate for this enzyme. The current connected with the oxidation of an enzymatic hydrolysis product, *viz.*, thiocholine, increased in the presence of the copper ions fixed in the complex. The established electrocatalytic effect can be applied also for the determination of activity of the native enzyme or of the copper ions in micromolar concentrations.

Electrochemical reactions were used for a study of complex formation of *p-tert*-butylcalix[6]arene monosubstituted on the lower rim with amide groups and anthraquinone fragments (R^2 = **58**) with methylviologen **59**.[168]



58



59

In addition to changes in signals for the anthraquinone moiety and methylviologen, the catalytic activity of the complex in the cathodic reduction of oxygen was established. The current of the oxygen reduction peak in cyclic voltammograms increased 1.5 times as compared with non-modified electrode and the potential of this peak shifted to the region of less negative potentials to -0.63 V (with a bare glassy carbon electrode and an electrode modified only with calixarene, the redox peaks were observed at potentials of -0.75 and -0.7 V, respectively).

V. Conclusion

Modern approaches to the synthesis of functionalized calixarenes allow one to obtain diverse receptors capable of molecular recognition of different ions and neutral molecules. Since the 1980s, commercial application of calixarene-based receptors has begun and somewhat later, this was followed by commercial production of ISE with calixarene-based receptors to the sodium and lead ions. Molecular design of calixarene-based receptors firstly developed extensively: the amount and composition of functional groups of substituents on the upper and lower rims gradually increased. This gave the possibility to achieve substantial progress over a comparatively short period, first of all, in sensing the alkali, alkaline-earth and transition metal ions. The obtained analytical characteristics of ISE are not inferior in selectivity and sensitivity to electrodes with traditional ionophores. Now, probably, we can speak about successful accomplishment of this step and transition to supramolecular level of receptor organization. It is characterized by structural complication of recognition sites and application of oligomeric associates rather than separate molecules in sensors. Regularity and concerted involvement in reactions with an analytes and a support (transducer) is a characteristic feature of these associates. Such receptors can be synthesized from monomeric fragments covalently bound by bridging structures (di- and trimeric calixarenes). In the first stage, these oligomers were employed to solve the problem of an increase in the efficiency of receptors as extractants. Currently, the functional groups of the bridging fragments take part in the recognition together with substituents on the upper and lower rims of a macrocycle. Such polytopic receptors are most suitable for the recognition of organic compounds with different functional groups spatially separated from one another (amino acids, proteins, oligonucleotides). Supramolecular structures can also be obtained by self-assembly and self-association through non-covalent (electrostatic and donor – acceptor) interactions between separate 'building blocks' on a common support. Varying the polarity and charge of this support allows fabrication of polyelectrolyte complexes and synthetic analogues of lipid. In this case, the possibility arises not only to register the process of complexation itself, but also the influence of the complexation on the supramolecular object as a whole (changes in regularity of structure, optical characteristics, viscosity and so on). Examples of such cooperative process, in electrochemical sensors among other, were described. For example, binding of amino acids to amphiphilic calixarenes results in the corresponding changes in resistance to charge transfer of the surface layer and this can be discovered in CV of electron transfer mediators and in changes in electrochemical impedance parameters.[166] Similar approaches can be realized in two-phase systems where the registered currents relate to charge transfer across the interface. Electrochemically inactive compounds can be determined by this method. In addition to silver determination,[164] such methods were used for the determination of organic compounds, for example, biogenic amines and amino acids.[75,166] These examples are not connected as yet with solution of analytical problems, but the perspectives of a given approach are evident.

It is noteworthy that in spite of advantages in the field of directed immobilization of calixarene-based receptors (among them, self-assembly on gold electrodes and preparation of the Langmuir – Blodgett films) the problems of diffusional and spatial limitations of an access of analytes to the receptor binding sites remain topical, especially in amperometric sensors. Possibly, the methods applied in enzyme and immuno-sensors would be helpful, since the problem of establishment of the access and required spatial coordination of the receptor and the 'guest' is also topical. Additional mediators providing electronic transfer in a dielectric layer of receptor by means of a relay (jump) mechanism can be used for the solution of this problem. Long-chain linkers that separate the binding site and surface of a transducer to decrease spatial resistance to interactions of bulky biomolecules are popular.

Receptors combining the calixarene platform with carbon nanotubes or fullerenes (covalently bound to receptors) would appear in the near future. Now chemoresistors on the basis of single-walled carbon nanotubes and polythiophenes

with grafted amphiphilic calixarenes are known. The resistance of these structures in air changes owing to complexation of calixarenes with volatile aromatic substrates.[169]

Sulfonate derivatives of calixarenes are used for solubilization and separation of single-walled carbon nanotubes due to their effective adsorption on the walls with subsequent electrostatic repulsion of separate tubes.[170] Such supramolecular receptor structures would appear in future in electrochemical sensors for measurements in liquid media.

Chemistry of calixarene-based dendrimers begins to emerge.[171–173] Calix-dendrimers increase the stability of biopolymers in their immobilization in a surface layer of a sensor and also provide sufficiently high diffusional permeability of the surface layer with respect to transfer of ionophore guest molecules and mediators of electron transfer in amperometric registration of a signal. Such investigations of supramolecular structures are also needed in other fields of chemistry, particularly in creation of systems for drug delivery in gene therapy and in developing of molecular devices as components of biocomputers.

References

1. E Bakker, E Pretsch *Angew. Chem., Int. Ed.* **46** 5660 (2007)
2. F Arnaud-Neu, M-J Schwing-Weill *Synth. Met.* **90** 157 (1997)
3. K Gloe *Macrocyclic Chemistry: Current Trends and Future Perspectives* (Dordrecht: Springer, 2005)
4. A Ikeda, S Shinkai *Chem. Rev.* **97** 1713 (1997)
5. C D Gutsche *Calixarenes Revisited (Monograph in Supramolecular Chemistry)* (Cambridge: Royal Society of Chemistry, 1998)
6. *Calixarenes in the Nanoworld* (Eds J Vicens, J Harrowfield, L Baklouti) (Dordrecht: Springer, 2007)
7. P Lhotvk *Top. Curr. Chem.* **255** 65 (2005)
8. D J Cram *Science* **219** 1177 (1983)
9. J L Sessler, P Anzenbacher, K Jursikova, H Miyaji, J W Genge, N A Tvermoes, W E Allen, J A Shiver *Pure Appl. Chem.* **70** 2401 (1998)
10. V Böhmer *Angew. Chem., Int. Ed. Engl.* **34** 713 (1995)
11. W Sliwa, M Deska *ARKIVOC* (i) 87 (2008)
12. D Diamond, K Nolan *Anal. Chem.* **73** 22A (2001)
13. A I Konovalov, I S Antipin *Mendeleev Commun.* **18** 229 (2008)
14. I I Stoikov, O A Omran, S E Solovieva, S K Latypov, K M Enikeev, A T Gubaidullin, I S Antipin, A I Konovalov *Tetrahedron* **59** 1469 (2003)
15. A D Garnovskii, A P Sadimenko, O A Osipov, G V Tsintsadze *Zhestko-Myagkie Vzaimodeistviya v Koordinatsionnoi Khimii* (Hard-Soft Interaction in Coordination Chemistry) (Rostov-on-Don: Rostov-on-Don State University, 1986)
16. E A Yushkova, I I Stoikov *Langmuir* **25** 4919 (2009)
17. Y K Agrawal, J P Pancholi *Indian J. Chem., Sect. A* **46** 1373 (2007)
18. J Sýkora, M Himl, I Stibor, I Císařová, P Lhoták *Tetrahedron* **63** 2244 (2007)
19. M N Kozlova, S Ferlay, N Kyritsakas, M W Hosseini, S E Solovieva, I S Antipin, A I Konovalov *Chem. Commun.* 2514 (2009)
20. A Leydier, D Lecerclé, S Pellet-Rostaing, A Favre-Reguillon, F Taran, M Lemaire *Tetrahedron* **64** 11319 (2008)
21. E Migianu-Griffoni, C Mbemba, R Burgada, D Lecerclé, F Taran, M Lecouvey *Tetrahedron* **65** 1517 (2009)
22. R K Pathak, K M Ibrahim, C P Rao *Tetrahedron Lett.* **50** 2730 (2009)
23. P Maji, S S Krishnamurthy, M Nethaji *Polyhedron* **27** 3519 (2008)
24. M S Wong, P F Xia, P K Lo, X H Sun, W Y Wong, S M Shuang *J. Org. Chem.* **71** 940 (2006)
25. Y Okada, Z Miao, M Mizutani, J Nishimura *Chem. Lett.* **35** 392 (2006)
26. Y S Lee, E K Lee, Y W Cho, T Matsui, I C Kang, T S Kim, M H Han *Proteomics* **3** 2289 (2003)
27. S Choi, E Y Choi, D J Kim, J H Kim, T S Kim, S W Oh *Clin. Chim. Acta* **339** 147 (2004)
28. S W Oh, J D Moon, H J Lim, D Y Park, T S Kim, J B Park, M H Han, M Snyder, E Y Choi *FASEB J.* **19** 1335 (2005)
29. H-S Jung, K-S Song, T Kim *Bull. Korean Chem. Soc.* **28** 1792 (2007)
30. A Yilmaz, A Kaya, H K Alpoguz, M Ersoz, M Yilmaz *Sep. Purif. Technol.* **59** 1 (2008)
31. A Arduini, A Pochini, A Secchi *Eur. J. Org. Chem.* 2325 (2000)
32. S-L Gong, Z-L Zhong, Y-Y Chen *React. Funct. Polym.* **51** 111 (2002)
33. V Stastny, P Lhotak, V Michlova, I Stibor, J Sykora *Tetrahedron* **58** 7207 (2002)
34. P Schmitt, P D Beer, M G B Drew, P D Sheen *Tetrahedron Lett.* **39** 6383 (1998)
35. F Yang, Y Ji, L Zheng, H Guo, J Lin *Supramol. Chem.* **18** 177 (2006)
36. B S Creaven, D F Donlon, J McGinley *Coord. Chem. Rev.* **253** 893 (2009)
37. F Vocanson, M Perrin, R Lamartine *J. Inclusion Phenom. Macrocycl. Chem.* **39** 127 (2001)
38. S W Ko, Y S Yang, J H Mun, K-M Park, S S Lee, K C Nam *Bull. Korean Chem. Soc.* **23** 1379 (2002)
39. W H Chan, A W M Lee, D W J Kwong, W L Tam, K Wang *Analyst* **121** 531 (1996)
40. W H Chan, A W M Lee *Analyst* **119** 2809 (1994)
41. A W M Lee, W H Chan, Y S Lam *Analyst* **120** 2841 (1995)
42. C Han, L Zeng, H Li, G Xie *Sens. Actuators, B* **137** 704 (2009)
43. S Erdemir, M Bahadir, M Yilmaz *J. Hazard. Mater.* **168** 1170 (2009)
44. Y Zhou, H Xu, L Wu, C Liu, Q Lu, L Wang *Spectrochim. Acta, Part A* **71** 597 (2008)
45. N L Pacioni, V N S Occello, M Lazzarotto, A V Veglia *Anal. Chim. Acta* **624** 133 (2008)
46. E A Shokova, V V Kovalev *Zh. Org. Khim.* **39** 13 (2003) [a]
47. S P Singh, A Chakrabarti, H M Chawla, N Pant *Tetrahedron* **64** 1983 (2008)
48. M Kumar, J N Babu, V Bhalla, A Dhir *Inorg. Chem. Commun.* **12** 332 (2009)
49. R Kumar, V Bhalla, M Kumar *Tetrahedron* **64** 8095 (2008)
50. J Kroupa, I Stibor, M Pojarova, M Tkadlecová, P Lhoták *Tetrahedron* **64** 10075 (2008)
51. I I Stoikov, L I Garifullina, D Sh Ibragimova, I S Antipin, A I Konovalov *Izv. Akad. Nauk, Ser. Khim.* 1125 (2004) [b]
52. A Zaghbani, C Fontàs, M Hidalgo, R Tayeb, M Dhahbi, F Vocanson, R Lamartine P Seta *Mater. Sci. Eng., C* **28** 985 (2008)
53. R Ludwig *Microchim. Acta* **152** 1 (2005)
54. C J Breitkreuz, R Zadmard, T Schrader *Supramol. Chem.* **20** 109 (2008)
55. L Baldini, A Casnati, F Sansone, R Ungaro *Chem. Soc. Rev.* **36** 254 (2007)
56. R V Rodik, V Boyko, V I Kalchenko *Curr. Med. Chem.* **16** 1630 (2009)
57. H M Chawla, S P Singh *Tetrahedron* **64** 741 (2008)
58. M Dudic, A Colombo, F Sansone, A Casnati, G Donofrio, R Ungaro *Tetrahedron* **60** 11613 (2004)
59. O Hayashida, K Mizuki, K Akagi, A Matsuo, T Kanamori, T Nakai, S Sando, Y Aoyama *J. Am. Chem.* Soc. **125** 594 (2003)
60. Y Aoyama, T Kanamori, T Nakai, T Sasaki, S Horiuchi, S Sando, T Niidome *J. Am. Chem. Soc.* **125** 3455 (2003)
61. J Budka, M Tkadlecová, P Lhoták, I Stibor *Tetrahedron* **56** 1883 (2000)
62. A Casnati, F Sansone, R Ungaro *Acc. Chem. Res.* **36** 246 (2003)
63. S J Kim, B H Kim *Tetrahedron Lett.* **43** 6367 (2002)
64. G M L Consoli, G Granata, E Galante, I Di Silvestro, L Salafia, C Geraci *Tetrahedron* **63** 10758 (2007)
65. S Kolusheva, R Zadmard, T Schrader, R Jelinek *J. Am. Chem. Soc.* **128** 13592 (2006)
66. I I Stoikov, A A Khrustalev, D Sh Ibragimova, E E Stoikova, G A Evtugyn, I S Antipin, A I Konovalov *Zh. Obshch. Khim.* **75** 305 (2005) [c]

67. E E Stoikova, G A Evtugyn, S V Beljakova, A A Khrustalev, I I Stoikov, I S Antipin, H C Budnikov, A I Konovalov *J. Inclusion Phenom.* **39** 339 (2001)
68. A Vovk, V Kalchenko, O Muzychka, V Tanchuk, I Muravyova, A Shivanyuk, S Cherenok, V Kukhar *Phosphorus, Sulfur, Silicon Relat. Elem.* **183** 625 (2008)
69. H Hamuro, M C Calama, H S Park, A D Hamilton *Angew. Chem., Int. Ed. Engl.* **36** 2689 (1997)
70. T Veklich, O Shkrabak, S Kosterin *Ann. UMCS Pharm.* **21** 253 (2008)
71. A W Coleman F Perret, A Moussa, M Dupin, Y Guo, H Perron *Top. Curr. Chem.* **277** 31 (2007)
72. R De Zorzi, N Guidolin, L Randaccio, R Purrello, S Geremia *J. Am. Chem. Soc.* **131** 2487 (2009)
73. O Lawal, K S J Iqbal, A M Amohamadi, P Razavi, H T Dodd, M C Allen, S Siddiqui, F Fucassi, P J Cragg *Supramol. Chem.* **21** 55 (2009)
74. I I Stoikov, I S Antipin, A I Konovalov *Usp. Khim.* **72** 1190 (2003) [*Russ. Chem. Rev.* **72** 1055 (2003)]
75. K S J Iqbal, P J Cragg *Dalton Trans.* 26 (2007)
76. S Friedman, S Kolusheva, R Volinsky, L Zeiri, T Schrader, R Jelinek *Anal. Chem.* **80** 7804 (2008)
77. K Kimura, T Miura, M Matsuo, T Shono *Anal. Chem.* **62** 1510 (1990)
78. Y Tsujimura,T Sunagawa, M Yokoyama, K Kimura *Analyst* **121** 1705 (1996)
79. T Grady, A Cadogan, T McKittrick, S J Harris, D Diamond, M A McKervey *Anal. Chim. Acta* **336** 1 (1996)
80. *Sodium Ionophore X*. Fluka Product Number: 71747 CAS: 97600-39-0 MDL Number: MFCD00145373
81. R Ludwig, N T K Dzung *Sensors* **2** 397 (2002)
82. A Cadogan, D Diamond, M R Smyth, M Deasy, M A McKervey, S J Harris *Analyst* **114** 1551 (1989)
83. Y D Kim, H Jeong, S O Kang, K C Nam, S Jeon *Bull. Korean Chem. Soc.* **22** 405 (2001)
84. I A M de Oliveira, D Risco, F Vocanson, E Crespo, F Teixidor, N Zine, J Bausells, J Samitier, A Errachid *Sens. Actuators, B* **130** 295 (2008)
85. S Kim, H Kim, K H Noh, S H Lee, S K Kim, J S Kim *Talanta* **61** 709 (2003)
86. L Chen, H Ju, X Zeng, X He, Z Zhang *Anal. Chim. Acta* **447** 41 (2001)
87. E M Choi, H Oh, S W Ko, Y-K Choi, K C Nam, S Jeon *Bull. Korean Chem. Soc.* **22** 1345 (2001)
88. T Katsu, K Ido, K Takaishi, H Yokosu *Sens. Actuators, B* **87** 331 (2002)
89. P Kumar, Y-B Shima *Talanta* **77** 1057 (2009)
90. V K Gupta, A K Jain, M A Khayat, S K Bhargava, J R Raisoni *Electrochim. Acta* **53** 5409 (2008)
91. L Chen, J Zhang, W Zhao, X He, Y Liu *J. Electroanal. Chem.* **589** 106 (2006)
92. J Lu, R Chen, X He *J. Electroanal. Chem.* **528** 33 (2002)
93. V S Bhat, V S Ijeri, A K Srivastava *Sens. Actuators, B* **99** 98 (2004)
94. E Malinowska, L Gawart, P Parzuchowski, G Rokicki, Z Brzózka *Anal. Chim. Acta* **421** 93 (2000)
95. J Lu, X Tong, X He *J. Electroanal. Chem.* **540** 111 (2003)
96. R K Mahajan, I Kaur, V Sharma, M Kumar *Sensors* **2** 417 (2002)
97. V Bhalla, M Kumar, H Katagiri, T Hattori, S Miyano *Tetrahedron Lett.* **46** 121 (2005)
98. L Chen, X He, B Zhao, Y Liu *Anal. Chim. Acta* **417** 51 (2000)
99. L Chen, X Zeng, H Ju, X He, Z Zhang *Microchem. J.* **65** 129 (2000)
100. G A Evtugyn, I I Stoikov, S V Beljyakova, R V Shamagsumova, E E Stoikova, A Yu Zhukov, I S Antipin, H C Budnikov *Talanta* **71** 1720 (2007)
101. G A Evtugyn, I I Stoikov, S V Belyakova, E E Stoikova, R V Shamagsumova, A Yu Zhukov, I S Antipin, H C Budnikov *Talanta* **76** 441 (2008)
102. Z Mousavi, J Bobacka, A Ivaska *Electroanalysis* **17** 1609 (2005)
103. X Zeng, L Weng, L Chen, X Leng, Z Zhang, X He *Tetrahedron Lett.* **41** 4917 (2000)
104. W Ngeontae,W Janrungroatsakul, N Morakot, W Aeungmaitrepirom, T Tuntulani *Sens. Actuators, B* **134** 377 (2008)
105. J Lu, D Pang, X Zeng, X He *J. Electroanal. Chem.* **568** 37 (2004)
106. J Ramkumar, B Maiti *Sens. Actuators, B* **96** 527 (2003)
107. V K Gupta, R Ludwig, S Agarwal *Anal. Chim. Acta* **538** 213 (2005)
108. F Kivlehan, W J Mace, H A Moynihan, D W M Arrigan *Anal. Chim. Acta* **585** 154 (2007)
109. H K Lee, H Oh, K C Nam, S Jeon *Sens. Actuators, B* **106** 207 (2005)
110. J N Babu, V Bhalla, M Kumar, R K Mahajan, R K Puri *Tetrahedron Lett.* **49** 2772 (2008)
111. T Katsu, N Okaki, K Watanabe, K Takaishi, H Yokosu *Anal. Sci.* **19** 771 (2003)
112. V D Vaze, A K Srivastava *J. Pharm. Biomed. Anal.* **47** 177 (2008)
113. A Krajewska, P Lhoták, H Radecka *Sensors* **7** 1655 (2007)
114. H Barhoumi, A Maaref, R Mlika, C Martelet, N Jaffrezic-Renault, L Ponsonnet *Mater. Sci. Eng., C* **25** 61 (2005)
115. M B Ali, C Bureau, C Martelet, N Jaffrezic-Renault, R Lamartine, H Ben Ouada *Mater. Sci. Eng., C* **7** 83 (2000)
116. M B Ali, N Jaffrezic-Renault, C Martelet, H Ben Ouada, J Davenas, M Charbonnier *Mater. Sci. Eng., C* **14** 17 (2001)
117. M V Ali, R B Chabanne, F Vocanson, C Dridi, N Jaffrezic, R Lamartine *Thin Solid Films* **495** 368 (2006)
118. F Wang, Q Liu, Y Wu, B Ye *J. Electroanal. Chem.* **630** 49 (2009)
119. V K Gupta, A K Jain, R Ludwig, G Maheshwari *Electrochim. Acta* **53** 2362 (2008)
120. E Bakker *Anal. Chem.* **69** 1061 (1997)
121. T T Ngo *Anal. Lett.* **38** 1057 (2005)
122. K N Mikhel'son *Ros. Khim. Zh.*. **52** (2) 30 (2008) [d]
123. A Shvarev, E Bakker *Anal. Chem.* **77** 5221 (2005)
124. J Langmaier, E Samcová, Z Samec *Anal. Chem.* **79** 2892 (2007)
125. T D Chung *J. Inclusion Phenom. Mol. Recogn. Chem.* **32** 179 (1998)
126. A Pailleret, G Herzog, D W M Arrigan *Electrochem. Commun.* **5** 68 (2003)
127. R Vataj, A Louati, C Jeunesse, D Matt *J. Electroanal. Chem.* **565** 295 (2004)
128. A Louati, J Spraula, V Gabelica, P Kuhn, D Matt *Electrochem. Commun.* **8** 761 (2006)
129. N-Q Li, B Zhou, H-X Luo, W-J He, Z-J Shi, Z-N Gu, X-H Zhou *J. Solid State Electrochem.* **2** 253 (1998)
130. A Pailleret, D W M Arrigan *Electrochem. Commun.* **3** 24 (2001)
131. R Vataj, A Louati, C Jeunesse, D Matt *Electrochem. Commun.* **2** 769 (2000)
132. R Vataj, H Ridaoui, A Louati, V Gabelica, S Steyer, D Matt *J. Electroanal. Chem.* **519** 123 (2002)
133. T H Kim, J K Lee, J H Bok, J S Kim, H Kim *Electrochim. Acta* **49** 3759 (2004)
134. D Choi, T D Chung, S K Kang, S K Lee, T Kim, S Chang, H Kim *J. Electroanal. Chem.* **387** 133 (1995)
135. J Park, S K Kang, T D Chung, S K Chang, H Kim *Microchem. J.* **68** 109 (2001)
136. S K Kang, T D Chung, H Kim *Electrochim. Acta* **45** 2939 (2000)
137. H C Y Bettega, J C Moutet, G Ulrich, R Ziessel *J. Electroanal. Chem.* **406** 247 (1996)
138. A Buffenoir, G Bidan, L Chalumeau, I Soury-Lavergne *J. Electroanal. Chem.* **451** 261 (1998)
139. H.Yu B.Xu T.M.Swager. *J. Am. Chem. Soc.* **125** 1142 (2003)
140. K Kaneto, G Bidan *Thin Solid Films* **331** 272 (1998)
141. A Pailleret, D W M Arrigan, J K Browne, M A McKervey *J. Mater. Chem.* **12** 2665 (2002)
142. J Han, Y H Cai, L Liu, C G Yan, Q Li *Tetrahedron* **63** 2275 (2007)
143. R M Nielson, J T Hupp *Inorg. Chem.* **35** 1402 (1996)
144. P A Gale, Z Chen, M G B Drew, J A Heath, P D Beer *Polyhedron* **17** 405 (1998)

145. A J Evans, S E Matthews, A R Cowley, P D Beer *Dalton Trans.* 4644 (2003)
146. E Métay, M C Duclos, S Pellet-Rostaing, M Lemaire, J Schulz, R Kannappan, C Bucher, E Saint-Aman, C Chaix *Eur. J. Org. Chem.* 4304 (2008)
147. D Guo, Z Liu, J Ma, R Huang *Tetrahedron Lett.* **48** 1221 (2007)
148. G D Brindley, O D Fox, P D Beer *J. Chem. Soc. Dalton Trans.* 4354 (2000)
149. P D Beer *Chem. Commun.* 689 (1996)
150. P D Beer, M G B Drew, D Heseka, K C Nam *Chem. Commun.* 107 (1997)
151. A Kaifer, M Gymez-Kaifer, in *Supramolecular Electrochemistry* (Weinheim: Wiley-VCH, 1999) p. 114
152. P D Beer, E J Hayes *Coord. Chem. Rev.* **240** 167 (2003)
153. K C Honeychurch, J P Hart, D C Cowell, D W M Arrigan *Sens. Actuators, B* **77** 642 (2001)
154. K C Honeychurch, J P Hart, D C Cowell, D W M Arrigan *Electroanalysis* **14** 177 (2002)
155. G McMahon, S O'Malley, K Nolan, D Diamond *ARKIVOC* (vii) 23 (2003)
156. K M O'Connor, G Svehla, S J Harris, M A McKervey *Talanta* **39** 1549 (1992)
157. K M O'Connor, G Svehla, S J Harris, M A McKervey *Anal. Proc.* **30** 137 (1993)
158. D W M Arrigan, G Svehla, S J Harris, M A McKervey *Electroanalysis* **6** 97 (1994)
159. D W M Arrigan, G Svehla, S J Harris, M A McKervey *Anal. Proc.* **29** 27 (1992)
160. H Dong, H Zheng, L Lin, B Ye *Sens. Actuators, B* **115** 303 (2006)
161. F Wang, X Wei, C Wang, S Zhang, B Ye *Talanta* **80** 1198 (2010)
162. C J Evans, G P Nicholson *Sens. Actuators, B* **105** 204 (2005)
163. A Becker, H Tobias, Z Porat, D Mandler *J. Electroanal. Chem.* **621** 214 (2008)
164. P O'Dwyer, V J Cunnane *J. Electroanal. Chem.* **581** 16 (2005)
165. C Li, C Wang, B Guan, Y Zhang, S Hu *Sens. Actuators, B* **107** 411 (2005)
166. W M Hassen, C Martelet, F Davis, S P J Higson, A Abdelghani, S Helali, N Jaffrezic-Renault *Sens. Actuators, B* **124** 38 (2007)
167. G A Evtugyn, I I Stoikov, G K Budnikov, E E Stoikova *Zh. Anal. Khim.* **58** 1284 (2003) [e]
168. S Hu, C Xu, Y He, L Meng, D Cui *Microchem. J.* **65** 311 (2000)
169. F Wang, Y Yang, T M Swager *Angew. Chem., Int. Ed.* **47** 8394 (2008)
170. L J Hubble, T E Clark, M Makha, C L Raston *J. Mater. Chem.* **18** 5961 (2008)
171. A-M Caminade, Y Wei, J-P Majoral *C.R. Acad. Sci., Ser. IIc: Chim.* **12** 105 (2009)
172. N Cheriaa, R Abidi, J Vicens *Tetrahedron Lett.* **46** 1533 (2005)
173. L Baklouti, N Cheriaa, M Mahouachi, R Abidi, J S Kim, Y Kim, J Vicens *J. Inclusion Phenom. Macrocycl. Chem.* **54** 1 (2006)

[a] — *Russ. J. Org. Chem. (Engl. Transl.)*
[b] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[c] — *Russ. J. Gen. Chem. (Engl. Transl.)*
[d] — *Mendeleev Chem. J. (Engl. Transl.)*
[e] — *J. Anal. Chem. (Engl. Transl.)*