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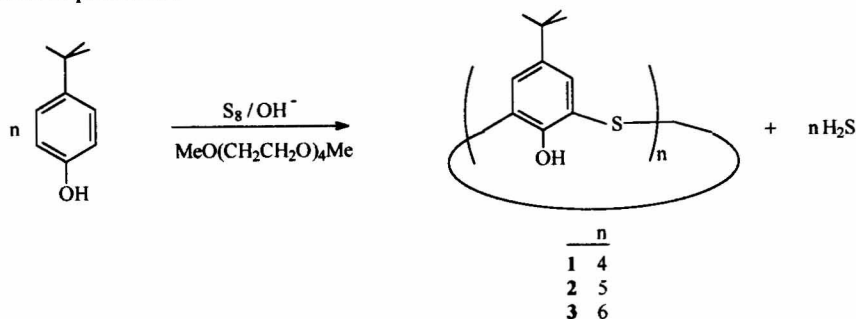
THIACALIXARENES

Abstract: In the present paper examples of thiacalixarenes, compounds belonging to heteracalixarenes, a new class of heterocycles, are described, showing their reactivity and application possibilities.

Thiacalixarenes, compounds now intensively studied ¹⁻⁷, are analogues of calixarenes ⁸⁻¹⁷ in which four methylene groups have been replaced by sulfur atoms. These species have interesting chemical and physicochemical properties, often different from those of parent calixarenes.

In the present work, a continuation of our papers concerning heteracalixarenes ^{18,19}, i.e. analogues of calixarenes containing heteroatoms in linkages of benzene units, examples of thiacalixarenes are described, pointing out their lower rim functionalization and oxidation of sulfur atoms.

The convenient synthesis of *p-t*-butylthiacalix[4]arene **1** involves the treatment of *p-t*-butylphenol with elemental sulfur and NaOH as a base catalyst ^{2,20}. In this reaction also thiacalixarenes **2** and **3** have been obtained as minor products.

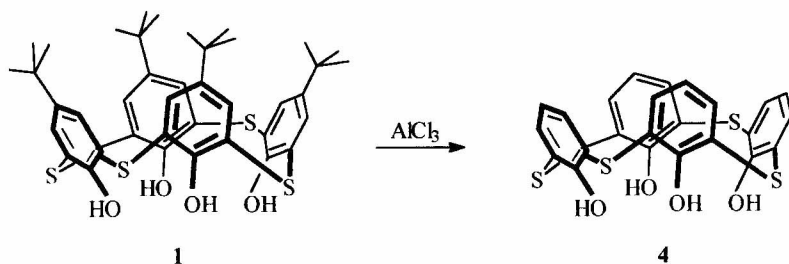


Inclusion properties of **1** with solvent molecules have been investigated using among others acetone, trichloromethane, tetrachloromethane and benzene as guests; the complexes formed have 1:1 stoichiometry. In the case of 1,2-dichloroethane, however, the 1:2 complex has been obtained in which one guest molecule is included in the cavity of **1**, while the second one is situated in the crystal lattice to form a clathrate type complex².

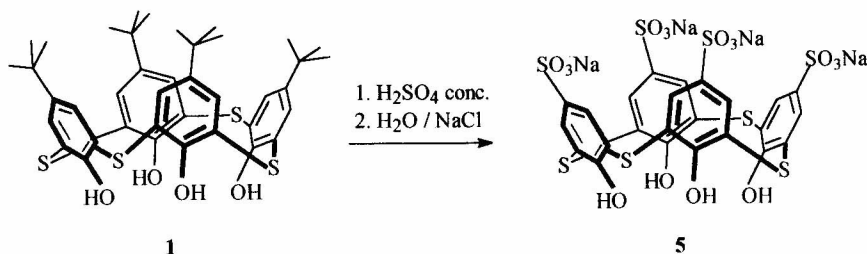
It was observed that the compound **1** in contrast to parent calixarene can quantitatively extract transition metal ions, e.g. Co^{2+} , Cu^{2+} and Zn^{2+} from an aqueous phase into chloroform^{21,22}.

The complex of **1** with Zn^{2+} ions $[\text{Zn}_4\text{L}(\text{H}_2\text{L})_2]$ ($\text{H}_4\text{L} = \mathbf{1}$) has been prepared *via* solvent extraction procedure and its structure determined by X-ray analysis. It was established that Zn^{2+} ions bind with **1** by bridging sulfur and oxygen atoms. The $\mathbf{1}\text{-Zn}^{2+}$ complex contains one L^{4-} and two H_2L^{2-} units in cone conformations fused at the lower rim by four Zn^{2+} ions²¹.

The detertiobutylation of **1** by aluminium chloride leads to **4**²³. The X-ray diffraction studies of **1** and **4** have been made. The X-ray analysis of **4** has shown that it undergoes a self-inclusion leading to trimeric units stabilized by edge-to-face interactions between aromatic moieties.



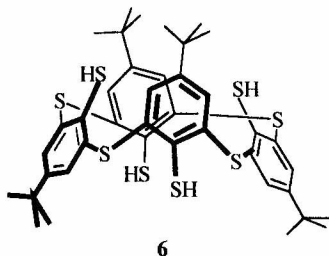
The thiacalix[4]arene tetrasulfonate **5**, a water soluble receptor has been obtained by sulfonation of **1**²⁴.



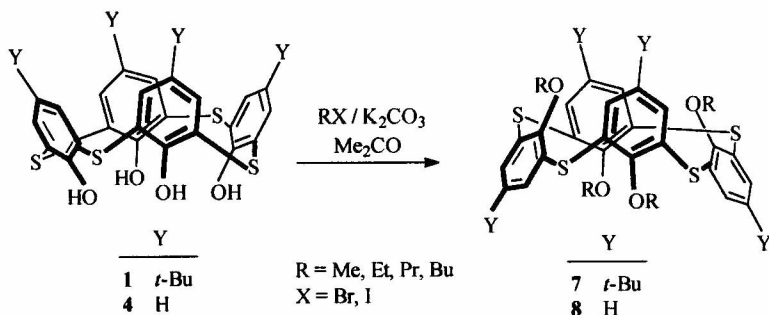
Thiacalixarene **5** binds small chlorinated organic compounds, such as CH_2Cl_2 , CHCl_3 and 1,2-dichloroethane in its hydrophobic cavity in aqueous solution forming 1:1 complexes. This property may be useful in the removal

of chlorinated organic compounds from water, an important activity in waste water and drinking water treatment. The addition of **5** to polluted water leads to the formation of host-guest complexes, in which **5** is a host. The subsequent trapping of complexes onto anion exchange resin results in almost complete removal of CH_2Cl_2 and CHCl_3 .²⁵

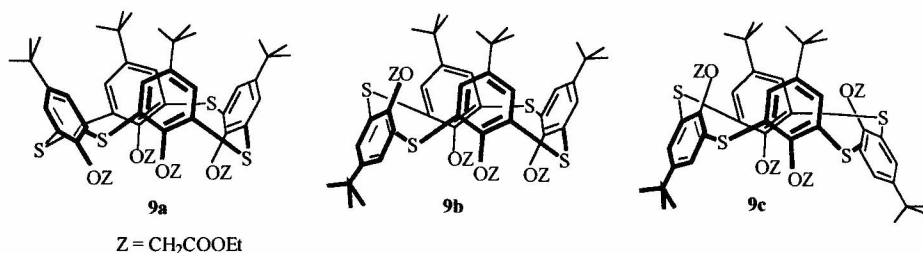
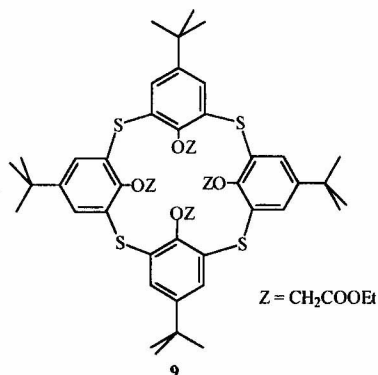
The synthesis of **6** bearing thiol groups at the lower rim has been reported and the 1,3-alternate conformation of this compound was determined in the solid state by X-ray analysis.²⁶



Thiacalixarenes **1** and **4** have been alkylated by alkyl bromides and iodides in the presence of K_2CO_3 or Cs_2CO_3 to give tetraalkylated species **7** and **8** existing in 1,3-alternate conformation in CDCl_3 solution at room temperature.^{27,28}



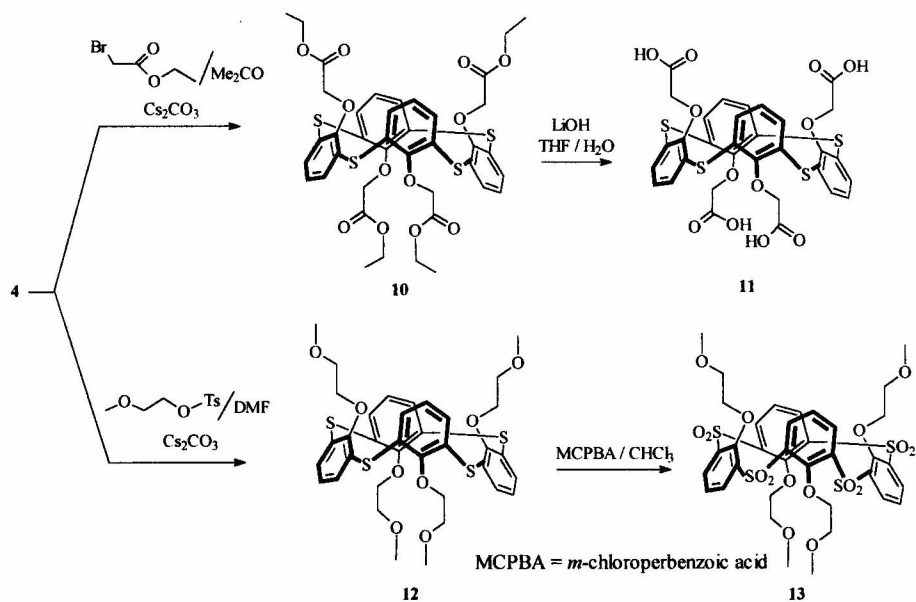
The reaction of **1** with ethyl bromoacetate in the presence of M_2CO_3 ($\text{M}=\text{Na}, \text{K}, \text{Rb}$) has been investigated in the aspect of determination of the conformer distribution. This *O*-functionalization leads to thiacalixarenes **9** adopting cone, partial cone and 1,3-alternate conformations^{29,30}, **9a-c**, respectively^{29,30}.



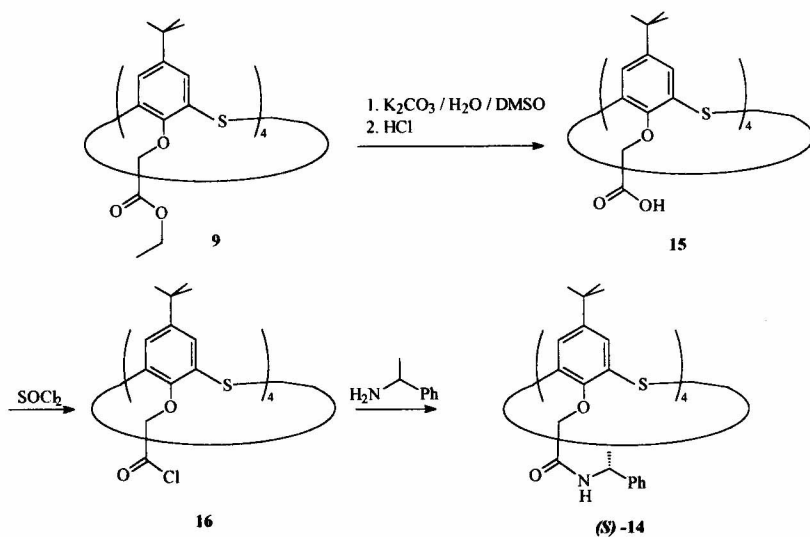
It was found that the isomer distribution depended on the base used; cone and partial cone conformations of **9** prefer Na^+ and K^+ , respectively, while 1,3-alternate conformation prefers Rb^+ , due to the fact that the cavity size of **9** increases in the order cone < partial cone < 1,3-alternate conformation^{30,31}. It should be pointed out that the ion selectivity of cone **9** is higher than that of the analogous parent calixarene containing methylene groups instead of sulfur atoms. Thiocalixarene **9** is promising for use in sensory systems such as ion-selective electrodes and in chemically modified field effect transistors³⁰.

Compounds **1** and **4** adopt cone conformation in the solid state, however in solution above the room temperature the rapid interconversion between different conformers takes place. For the design of new building blocks the species of a 1,3-alternate conformation are necessary; they are achieved by the introduction of bulky substituents at the lower rim, which makes impossible the interconversion between conformers³².

Using **4** as a backbone, its derivatives **10** - **13** bearing ester, acid and ether groups blocked in 1,3-alternate conformation have been synthesized in the following procedures.

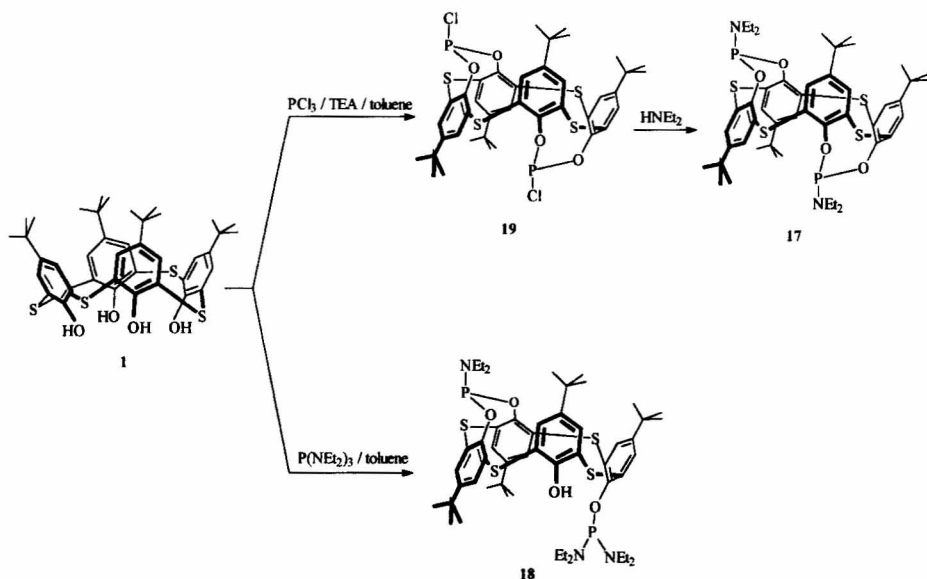


In the study of chiral stationary phases for direct separation of enantiomers by gas chromatography, the synthesis of tetramide (*S*)-**14** useful as a chiral selector for gas separation of enantiomers has been performed. In the first step of this procedure thiacalixarene **1** reacts with ethyl bromoacetate and Na_2CO_3 in acetone to give tetraester **9** existing in the cone conformation. The hydrolysis of **9** leads to the tetracarboxylic acid **15** which was converted into acid chloride **16**; its reaction with (*S*)-1-phenylethylamine afforded the tetramide (*S*)-**14**.³³

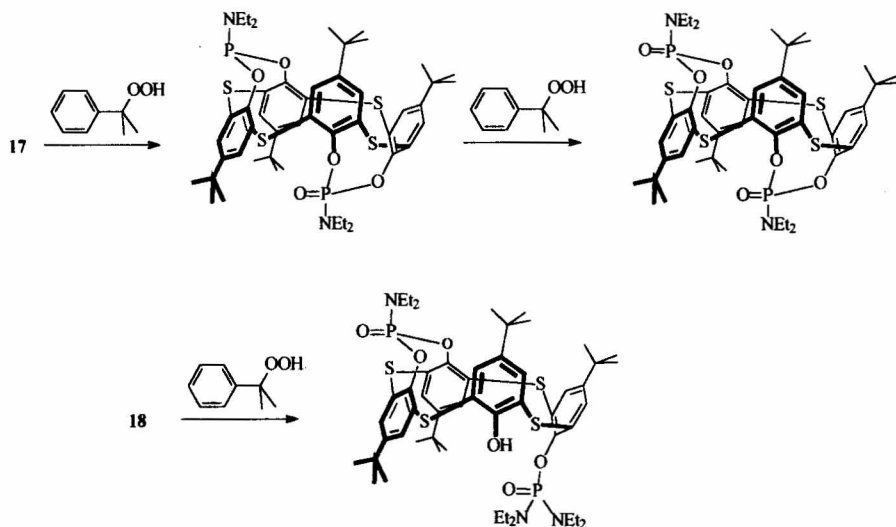


The (*S*)-**14**-coated column showed good separations of enantiomeric aminoacid, amine and alcohol derivatives. It should be pointed out that the analogous parent calixarene with methylene groups instead of sulfur atoms does not exhibit any enantioselectivity³³.

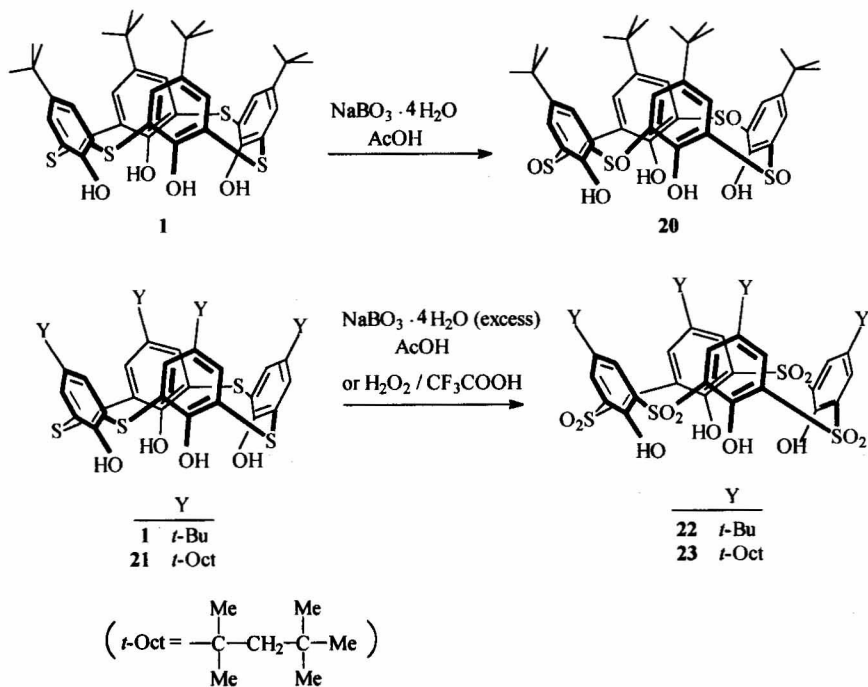
In the investigation of phosphorus containing thiacalixarenes³⁴, diamide **17** and triamide **18** have been obtained using **1** as starting material. The reaction of **1** with PCl_3 gave chloride **19** converted by treatment with diethylamine into diamide **17**, and the phosphorylation with $\text{P}(\text{NEt}_2)_3$ afforded triamide **18**¹. Thiacalixarene **1** adopts in solution the cone conformation, while compounds **17** and **18** exist as 1,2-alternate conformers.



The oxidation of **17** and **18** has been investigated using cumene hydroperoxide, as shown below¹.

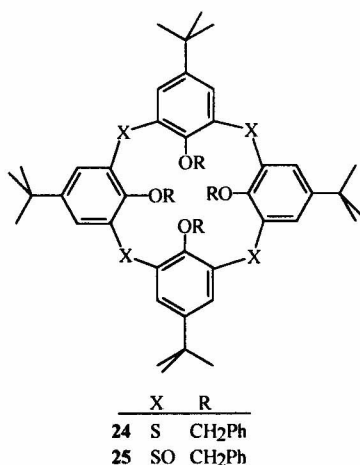


Compound 1 has been oxidized by NaBO_3 to give sulfinylcalixarene **20**^{35,36}. The oxidation of 1 and 21 with an excess of NaBO_3 or with hydrogen peroxide afforded sulfonylcalixarenes **22** and **23**, respectively^{35,37}.

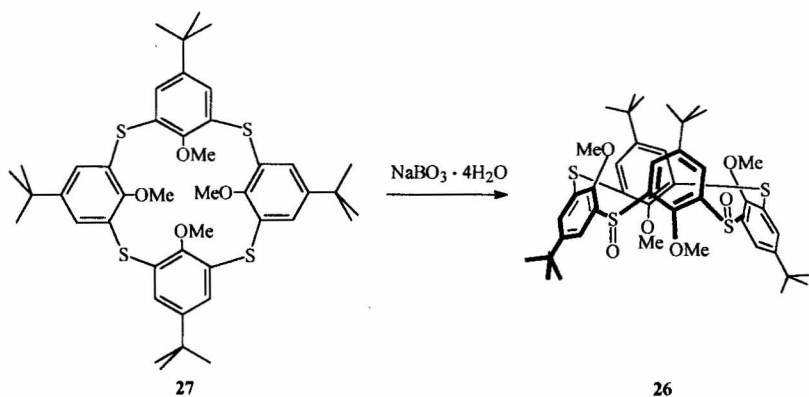


Compounds **20**, **22** and **23** exist in cone conformations. The binding abilities of **1** and **20** - **23** depend on the presence of S, SO or SO₂ groups. Thiocalixarenes extract well transition metal ions, while their affinity to alkaline metal ions is low. However, in the contrast, the sulfonylcalixarene **23** prefers alkaline metal ions over transition metal ions, and the sulfinylcalixarene **20** can form complexes so with transition metal ions (except for Cu²⁺ ion) as well as with alkaline metal ions³⁵.

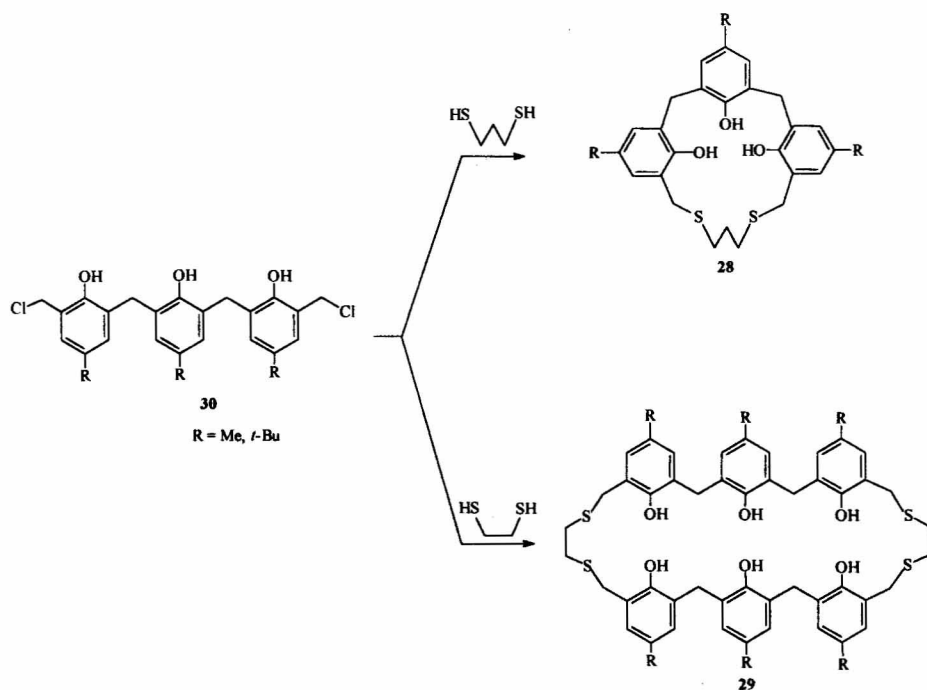
The oxidation of **1** by NaBO₃ gives sulfinylcalixarene as only one isomer *trans-trans-trans-20*, i.e. a species in which four sulfinyl groups are situated in an up-down-up-down manner^{35,36}. In order to obtain *cis-cis-cis-20*, i.e. the isomer in which four sulfinyl groups are arranged on the same side of the macrocycle plane, the following procedure has been used. At first **1** was tetra-*O*-benzylated to give **24**; in this way the structure has been blocked in the cone conformation. The next step was the oxidation with NaBO₃ of the sulfur linkages into sulfinyl groups, affording tetraether **25** in which all four S=O groups are situated in a *cis-cis-cis* manner, almost in an equatorial orientation, due to the presence of bulky benzyl units. The subsequent cleavage of the ether bonds results in the *cis-cis-cis-20*³⁸.



Chiral disulfinyldithiocalix[4]arene **26** existing in the 1,3-alternate conformation containing two *trans*-sulfinyl groups has been obtained by NaBO₃ oxidation of the two proximal epithio linkages in thiocalixarene **27**³.



Compounds **28** and **29** belong to homothiocalix[4]arenes. They have been synthesized by treatment of triphenol **30** with 1,3-propanedithiol or 1,2-ethanedithiol, respectively³⁹.



One should mention here also troponoid tetrathiacyclophanes **31** and **32** related to thiacalixarenes, obtained by condensation of 2,7-dibromotropone with 1,3-bis(mercaptomethyl)benzene⁴⁰.

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Tiakaliksareny

Streszczenie: W artykule przedstawiono przykłady tiakaliksarenów, związków należących do heterakaliksarenów, stanowiących nową klasę układów heterocyklicznych, z omówieniem ich reaktywności i możliwości zastosowań.