Thiacalix[4]arenes with terminal thiol groups at the lower rim: synthesis and structure*

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Methods were developed for the synthesis of ω-mercaptoalkoxy derivatives of thiacalix[4]arenes in the 1,3-alternate conformation containing different numbers (2—5) of methylene spacers at the lower rim. The hydrazinolysis of the corresponding thioacetates is the most efficient method for the synthesis of these compounds.

Key words: thiacalix[4]arenes, thiols, lower rim, 1,3-alternate stereoisomer, mercapto derivatives, bromo derivatives.

Natural and synthetic macrocyclic compounds show promise for studies in the field of supramolecular chemistry, because the structural features of these compounds are favorable for a sharp enhancement of the complexity of intermolecular interactions due to the formation of multistate coordination centers. Calixarenes have additional advantages associated primarily with the unique possibilities of their functionalization and the fine tuning between the three-dimensional structures of the host and the desired guest. The use of thiacalix[4]arenes 2 (see Refs 1—5) as a molecular platform for the design of intellectual receptor and self-organized supramolecular systems is very attractive, because the replacement of the methylene bridges in the classical calixarene by sulfur atoms gives rise to new properties.3,4,6—11 In this connection, it is important to develop approaches to the directed functionalization of this macrocycle, in particular, by introducing organosulfur fragments. The presence of functional sulfur-containing groups at the lower or upper rim of the macrocycle, in addition to four bridging sulfur atoms of the thiacalixarene platform, offers great possibilities for the design of highly selective host molecules based on thiophilic metal ions,12 the construction of highly organized nanolayers on the metal surface,13—17 and the design of sensors based on ion-selective electrodes.18—20

In addition, these sulfur-containing groups have a great synthetic potential for further modifications of the macrocyclic structure.

* Dedicated to Academician A. I. Konovalov on his 75th birthday.

Results and Discussion

In the present study, we synthesized new O-substituted thiacalix[4]arenes in the 1,3-alternate conformation containing ω-bromo- (3), ω-acetoxy- (4), or ω-mercaptoalkyl groups (5) linked by methylene spacers of different length (from two to five units). The structures of the new compounds were determined by different physical methods, such as 1D and 2D NMR spectroscopy, IR spectroscopy, and MALDI-TOF mass spectrometry. The purity of the compounds was checked by TLC and elemental analysis.

<table>
<thead>
<tr>
<th>Compound</th>
<th>X</th>
<th>R</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂</td>
<td>H</td>
</tr>
<tr>
<td>2</td>
<td>S</td>
<td>H</td>
</tr>
<tr>
<td>3a—e</td>
<td>S</td>
<td>(CH₂)₂ Br, n = 2 (a), 3 (b), 4 (c), 5 (d), 6 (e)</td>
</tr>
<tr>
<td>4a—d</td>
<td>S</td>
<td>(CH₂)SC(O)CH₃, n = 2 (a), 3 (b), 4 (c), 5 (d)</td>
</tr>
<tr>
<td>5a—d</td>
<td>S</td>
<td>(CH₂)₂S₇H, n = 2 (a), 3 (b), 4 (c), 5 (d)</td>
</tr>
</tbody>
</table>
We chose ω-bromoalkyl derivatives 3 as the starting compounds for the synthesis of thiol-containing thiacalix[4]arenes.

ω-Bromoalkyl derivatives 3b—e were synthesized (in 36—75% yields) in acetone in the presence of potassium carbonate and a catalytic amount of potassium iodide with the use of an twenty-fold excess of the alkylating reagent (Scheme 1). The reaction with 1,3-dibromo-propane afforded the target product in 75% yield; the reactions with other compounds under consideration, in 36—52% yields. Therefore, the yield of the target products substantially decreases as the number of methylene units in dibromoalkanes increases.

Scheme 1

Reagents and conditions: acetone, Br(CH₂)nBr, K₂CO₃; 

An increase in the number of methylene fragments in α,ω-dibromoalkanes leads to an increase in their conformational flexibility and enhances the possibility of being involved in the simultaneous interactions with two phenolic hydroxy groups of calixarene, which can give rise to either products containing bridging substituents or cross-linked bis-calixarenes and oligomeric products. The use of an excess amount of dibromoalkanes reduces the formation of bis-calixarenes. Thus, in addition to compound 3e (M⁺ = 1373 m/z), compound 6 was detected in the reaction mixture. The latter compound is a cross-linking product of two phenol groups at the lower rim through 1,6-dibromohexane, whereas two other aromatic rings in 6 are replaced by bromohexyloxy fragments.

The MALDI TOF mass spectra obtained in different conditions ((E)-2-cyano-3-(4-hydroxyphenyl)acrylic acid or p-nitroaniline as the matrix) show the molecular ion peak of compound 6 (Fig. 1), M⁺ = 1126, [M + Na]⁺ = 1148, [M + K]⁺ = 1164. The NMR data for the reaction mixture suggest that compound 6 is the cross-linking product of two opposite rather than adjacent phenol groups, because only two singlets for the protons of the aromatic moieties at δ 7.30 and 7.31 and two singlets for the protons the tert-butyl groups at δ 1.28 and 1.29 are observed in the chemical shift region of aromatic rings. The numbers and multiplicities of the signals for the product resulting from the cross-linking of the adjacent aromatic rings should be different.

Compound 3a (n = 2) cannot be prepared by direct alkylation with dibromoethane. Heating of thiacalixarene 1 with 1,2-dibromoethane in DMF in the presence of K₂CO₃ at 80 °C affords compound 7 in the cone conformation as a result of cross-linking of the adjacent hydroxy groups by a spacer consisting of two methylene units. For classical calixarenes, the cross-linking was not observed.

![MALDI TOF mass spectrum of compound 6](image-url)