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Selective fluoride ion recognition by a thiacalix[4]arene receptor containing *N*-(4-nitrophenyl)acetamide and 1-amidoanthraquinone fragments

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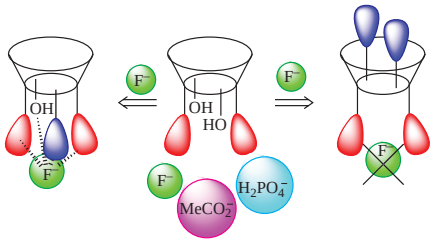
New derivatives of thiacalix[4]arene, tri- and tetrasubstituted at the lower rim by *N*-(4-nitrophenyl)acetamide and 1-amidoanthraquinone fragments were synthesized. Their ability for recognition and binding of some anions (F^-, Cl^-, Br^-, I^-, $MeCO_2^-$, $H_2PO_4^-$, NO_3^-) was examined by UV spectroscopy, and a selective receptor for fluoride ion giving a 1 : 1 complex was invented.



A variety of objects of supramolecular chemistry and their ability to exhibit properties characteristic of highly organized biomolecules, such as molecular recognition, catalysis, active and selective transport has led to the rapid development of the chemistry of synthetic receptors.[1–5]

The design and synthesis of systems capable of recognizing anions continues to be one of the actual problems of organic chemistry. In particular, the fluoride ion plays an important role in living organisms, being one of the constituents of the mineral metabolism. It determines the bone status, its strength and toughness, correct formation of the skeleton, conditions and growth of hair, nails and teeth.[1] Usually, synthetic receptors for halide anions contain proton-donor groups, *e.g.*, amide, hydroxyl, urea.[6–10]

Calixarenes and thiacalixarenes are widely used as building blocks in the design of host molecules due to their unique three-dimensional structure as well as simplicity of functionalization of the macrocyclic platform[11–16] and possibility of existence of different conformational isomers (*cone*, *partial cone*, *1,2-alternate*, and *1,3-alternate*).

The synthesis of differently substituted at the lower rim *p-tert*-butylthiacalix[4]arene is more difficult than that of macrocycles substituted with the same fragments. Regioselective functionalization of the lower rim of thia-analogue of calix[4]arene is greatly complicated, because it requires comprehensive selection of the reaction conditions (ratio of reactants, temperature, and synthesis duration).

Development of selective 1,3-dialkylation of the lower rim of *p-tert*-butylthiacalix[4]arene with 2-bromo-*N*-(4-nitrophenyl)-acetamide[17] provided differently substituted synthetic receptors, allowing one to study the influence of the conditions on the functionalization of partially substituted derivatives with amide fragments. With the aim of the introduction of additional binding sites in thiacalixarene, special attention was paid to the functionalization of the macrocycle **1** with *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)acetamide fragment containing polar NH group and chromophoric moiety required for spectrophotometrical detection of the complex formation. The 1-amidoanthraquinone fragment is also known as OFF–ON photo-switchable receptor realizing the ESIPT (excited-state intramolecular proton transfer) mechanism[18] including fluorescent sensors on its basis.[19] In this regard, we supposed to modify the thiacalixarene **1** structure with substituents containing 1-amidoanthraquinone fragment by alkylation of free phenolic hydroxyls and to study the complexation properties of the obtained compounds towards a variety of single-charged anions.

The interaction of the 1,3-disubstituted thiacalix[4]arene **1** with 2-bromo-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)acetamide according to the reported procedure[20] in the presence of alkali carbonates in acetone was studied. As a result, tri- and tetrasubstituted derivatives **2** and **3** were isolated from the reaction mixtures on using Na_2CO_3 and K_2CO_3, respectively (Scheme 1). The yields of products **2** and **3** (24 and 14%, respectively) were not as high, probably due to the steric hindrance of the reaction centre. In accordance with two-dimensional NMR data, macrocycle **2** possesses the *cone* conformation and macrocycle **3**, the *1,3-alternate* one. When cesium carbonate was used, only the starting compounds were quantitatively isolated instead of the expected tetrasubstituted product. Structures of products **2** and **3** were characterized by ^1H, ^{13}C, 2D NOESY NMR, IR spectroscopy, mass spectrometry, and their composition was confirmed by elemental analysis.[†]

The IR spectrum of trisubstituted thiacalix[4]arene **2** contained an absorption band of stretching vibrations of hydroxyl group

[†] *General procedure for the synthesis of compounds* **2** *and* **3**. The mixture of 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-26,28-bis[*N*-(4-nitrophenyl)aminocarbonylmethoxy]-2,8,14,20-tetrathiacalix[4]arene **1** (1.00 g, 0.93 mmol), an anhydrous alkali carbonate (0.39 g, 3.72 mmol Na_2CO_3 or 0.51 g, 3.72 mmol K_2CO_3) and 2-bromo-*N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)acetamide (1.28 g, 3.72 mmol) in 60 ml of dry acetone was refluxed for 60 h. After cooling, the solid residue from the reaction mixture was removed by filtration (in the case of Na_2CO_3, after evaporation under reduced pressure). The residue was dissolved in chloroform and washed with 2 M HCl. The organic layer was dried over molecular sieves, filtered and evaporated under reduced pressure. Crystallization of the resulting solid from tetrahydrofuran–methanol mixture gave pure samples of **2** and **3**.