

Chemo- and stereocontrolled alkylation of 1,2-disubstituted at the lower rim 1,2-*alternate* *p*-*tert*-butylthiacalix[4]arene

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1,2-*Alternate* *p*-*tert*-butylthiacalix[4]arene bearing at the lower rim 1,2-positioned acetamide fragments reacts with ethyl bromoacetate to give mono-O-alkylation product when Na₂CO₃ is used as a base and O,O',N,N'-tetraalkylation one in the case of K₂CO₃.

The common approach to design of synthetic receptors is modification of macrocyclic molecular platform by variation of substituents which provides optimal spatial orientation of binding sites.¹ To choose such substituents, one should consider a number of requirements: availability of starting macrocycle, sufficient conformation rigidity of the molecular platform providing optimal spatial orientation of binding sites, existence of highly effective common procedures for functionalization of the molecular platform.^{2,3} Products of cyclocondensation of phenols and sulfur, namely thiacalix[4]arenes, are in a good agreement with these requirements.^{4,5}

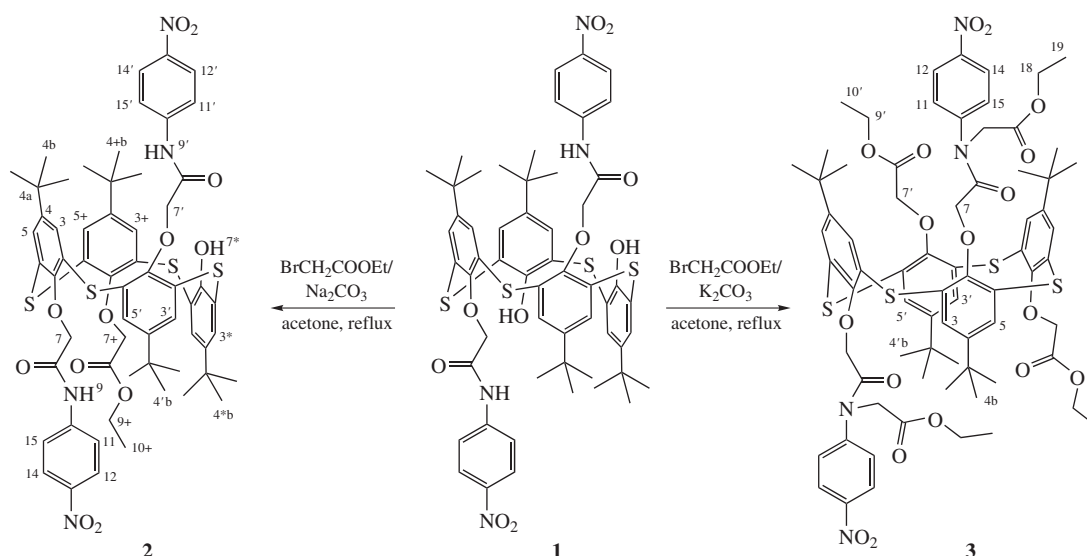
Carboxamide fragment, which contains two different binding sites – proton-donor NH group and lone electron pair of carbonyl group is very promising for this purpose. Depending on the substitution pattern of amide group, such thiacalixarenes either can serve as hosts for anion binding (in the case of secondary amide group),⁶ or as extragents of metal cations (in the case of tertiary amide group).^{7–9} Thus, interest to N-alkylation of secondary amide fragments attached to thiacalix[4]arene platform is obvious.

In the literature, there are only several examples of partially substituted at the lower rim thiacalix[4]arenes in 1,2-*alternate* conformation.⁴ Therefore, studying of reactivity of 1,2-disubstituted 1,2-*alternate* *p*-*tert*-butylthiacalix[4]arene **1** bearing *N*-(4-nitrophenyl)acetamide fragments¹⁰ seemed topical. Macro-

cycles modified by ester fragments are known to recognize alkali metal cations due to their coordination with carbonyl and alkoxy oxygen atoms.¹¹ Ethyl bromoacetate is a favourable reactant for the introduction of ester group into the macrocyclic platform.^{12–14}

In this work, macrocycle **1** was modified by its treatment with ethyl bromoacetate in acetone using sodium and potassium carbonates as the bases, in analogy with the published data.¹⁵ In the case of sodium carbonate, monosubstitution product **2** is formed in 87% yield, with the 1,2-*alternate* conformation of the macrocycle being retained, whereas the use of potassium carbonate leads to formation of O,O',N,N'-tetrasubstitution product **3** accompanied by a conformation change of thiacalix[4]arene platform into 1,3-*alternate* stereoisomer (Scheme 1).

The structures of new thiacalix[4]arene derivatives **2** and **3** were established based on ¹H, ¹³C NMR and IR spectroscopy, mass spectrometry (EI, ESI) and elemental analysis. The 2D NOESY ¹H–¹H NMR spectrum of compound **2** displays cross-peaks between spatially close protons, namely, between *tert*-butyl and aryl protons (H^{4a}_b/H¹¹, H¹⁵/H^{4a}_b, H¹¹/H^{4b}, H¹⁵/H^{4b}, H¹¹/H^{4b}, H¹⁵/H^{4b}), between oxymethylene protons and aromatic protons of the macrocycle (H^{7a}/H^{5'}, H^{7a}/H³, H^{7a}/H^{5*}), and between hydroxyl proton and nitrophenylamide protons (H^{7*}/H^{9'}, H^{7*}/H^{11'}, H^{7*}/H^{15'}), which clearly testifies that macrocycle **2** has 1,2-*alternate* conformation.



Scheme 1