

Dedicated to the 110th anniversary of M.I. Kabachnik's birth

## Synthesis of Macrocyclic Stereoisomers Substituted with Oligolactide Fragments

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**Abstract**—Acylation of *cone* and *1,3-alternate* stereoisomers of hydrazides of *p*-*tert*-butylthiacalix[4]arene tetrasubstituted at the lower rim with *S,S*-lactide in dimethylsulfoxide has afforded the macrocyclic oligolactide derivatives containing 16 (*cone*) to 24 (*1,3-alternate*) lactide fragments. It has been shown that nanosized aggregates (80 nm) are formed with silver nitrate in the case of the *cone* stereoisomer containing the oligolactide fragments at one side of the macrocyclic rim, whereas submicron particles (400 nm) are formed in the case of the *1,3-alternate* conformation when the substituents are at different sides of the macrocycle.

**Keywords:** L-lactide, *p*-*tert*-butylthiacalix[4]arene, oligolactide, antibacterial properties

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Biodegradable oligomers [1] and polymers [2] are attractive as they are ecologically compatible [3] and bioresorbable [4]. These materials open novel possibilities for medicinal applications [5, 6] and are green alternatives to plastics obtained from oil refining products. Modification of the structure and properties of biodegradable polymers is among the most important fields of their research [7]. The introduction of spatially pre-arranged blocks to impart the self-assembly features [8, 9] is at the edge of polymer science and supramolecular chemistry. It has been shown that the spatially organized materials prepared via modification of cyclophanes are promising in the development of electrochemical sensors [10, 11].

Self-assembly of derivatives of *p*-*tert*-butylthiacalix[4]arene with *d*-metal ions [12] extends the possibility of creating biocompatible materials. The possibility of forming crystalline metal-organic framework structures [13] and supramolecular associates [14] is a promising approach to the development of nanostructured materials with structure and morphology defined by the nature of the transition metal as well as the chemistry of the functional groups and spatial structure of the cyclophane [9, 10].

Oligolactide derivatives of *p*-*tert*-butylthiacalix[4]arene were prepared starting from tetrahydrazide-substituted *p*-*tert*-butylthiacalix[4]arenes **1** and **2** [15]

which exhibit high efficiency of binding with transition metal cations and are prone to supramolecular self-assembly of nanostructured associates and aggregates via the formation of hydrogen bonds and due to the involvement of the *d*-metal cations in the coordination bonds with sulfur atoms [16].

We have earlier demonstrated that amino derivatives of *p*-*tert*-butylthiacalix[4]arene exhibit sufficient nucleophilicity for the interaction with L-lactide to occur [17]. In view of the sufficiently high nucleophilicity of the hydrazide groups [15], derivatives **1** and **2** were interesting objects for the acylation with L-lactide as well. By analogy with the reference data [18, 19], the interaction of macrocycles **1** and **2** with excess of L-lactide was performed in anhydrous DMSO. The target products **3** and **4** were isolated with yield 45 and 55%, respectively (Scheme 1).

IR spectra of oligo(L-lactide) derivatives of *p*-*tert*-butylthiacalix[4]arene **3** and **4** contained the absorption bands corresponding to the oligolactide fragments: hydroxyl (3492 and 3386 cm<sup>-1</sup>) and carbonyl (1684 and 1646 cm<sup>-1</sup>) groups stretching. <sup>1</sup>H NMR spectra of compounds **3** and **4** showed the characteristic signals of the protons of oligolactide moieties. Analysis of the integral intensities ratio of the methyne and methyl groups of the hydroxyl-containing fragments of lactate and ester-linked lactate fragments revealed the