Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2015, **25**, 177–179
Mendeleev Communications

‘Click chemistry’ in the synthesis of new amphiphilic *1,3-alternate* thiacalixarenes

Vladimir A. Burilov,*[a] Ramil I. Nugmanov,[a] Regina R. Ibragimova,[a] Svetlana E. Solovieva[a,b] and Igor S. Antipin[a,b]

[a] *A. M. Butlerov Chemical Institute, Kazan (Volga Region) Federal University, 420008 Kazan, Russian Federation*
[b] *A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of the Russian Academy of Sciences, 420088 Kazan, Russian Federation. Fax: +7 843 273 2253; e-mail: ultrav@bk.ru*

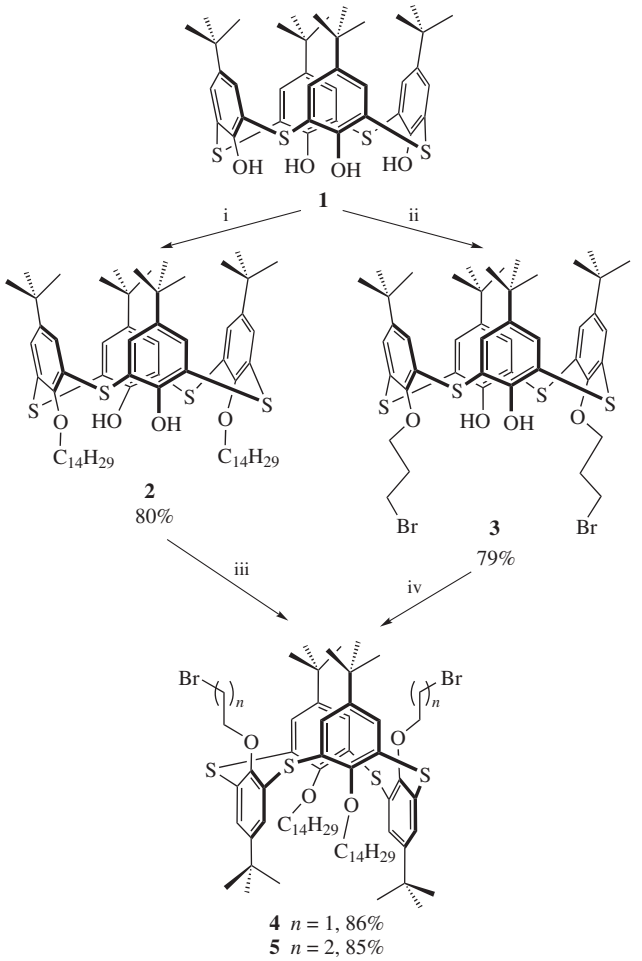
DOI: 10.1016/j.mencom.2015.05.005

Azidoalkyl-substituted *1,3-alternate p-tert*-butylthiacalix[4]arenes were subjected to click reactions with alkynes affording thus novel amphiphilic derivatives of this series.

Molecular recognition of membrane embedded receptors plays a key role in the biological processes associated with the cell signaling or transmitting of signals across cell membranes[1] as well as for the design of bio-inspired materials.[2] The applications of vesicular membranes with incorporated artificial receptors as carrier systems, reaction containers, switchable devices and sensor materials are in recent literature.[3] From this point of view, preparation of broad series of synthetic amphiphiles with receptor properties for recognition of different substrates is challenging.[4] Thiacalix[4]arenes have a great potential as amphiphilic receptors due to their unique properties: number of substituents, variety of stereoisomeric configurations, easy functionalization and preorganization effect.[3(a),5] Thus, the functionalization of a lower rim with amphiphilic and binding fragments can lead to novel type of biomimetic receptor molecules.

To achieve a wide variety of binding sites as well as amphiphilic properties thiacalix[4]arenes adopting *1,3-alternate* conformation are most promising since selective functionalization of upper and lower rims allows one to create two molecular domains with different characteristics. In this work we accomplished synthesis of the amphiphilic ‘clickable’ platform based on the azidoalkyl derivatives of *p-tert*-butylthiacalix[4]arene bearing in mind that the presence of azido group provides an easy way to a variety of amphiphilic receptor molecules by click reactions.

The first step was a preparation of precursors **4**, **5** containing ω-bromoalkyl and long chain alkyl groups starting from *p-tert*-butylthiacalix[4]arene **1**[6] (Scheme 1).† Selective functionalization of phenolic groups of thiacalixarene was carried out under Mitsunobu reaction conditions.[7] Two sequences of alkylation/bromoalkylation reactions were investigated (see Scheme 1), both of them having given practically the same yield of the expected precursors. Two singlets of thiacalixarene aromatic protons in ^{1}H NMR and cross-peaks between aromatic and methylene protons of alkyl and bromoalkyl fragments in NOESY spectra clearly show that compounds **4** and **5** adopt *1,3-alternate* configuration.



Scheme 1 *Reagents and conditions*: i, *n*-$C_{14}H_{29}OH$ (2.5 equiv.), PPh_3, DEAD, PhMe, 40 °C, 24 h; ii, $Br(CH_2)_3OH$ (2.5 equiv.), PPh_3, DEAD, PhMe, 40 °C, 24 h; iii, $Br(CH_2)_2OH$ (4 equiv.), PPh_3, DEAD, PhMe, 70 °C, 24 h; iv, *n*-$C_{14}H_{29}OH$ (4 equiv.), PPh_3, DEAD, PhMe, 70 °C, 24 h.

† *Compounds* **2** *and* **3**. An appropriate alcohol (6.9 mmol), *p-tert*-butylthiacalix[4]arene **1**[6] (2 g, 2.8 mmol), triphenylphosphine (2.22 g, 8.3 mmol) and diethyl azodicarboxylate (1.32 ml, 8.3 mmol) were dissolved in 20 ml of dry toluene under inert atmosphere. The reaction mixture was stirred at 40 °C for 24 h, and then the solvent was evaporated *in vacuo*. The crude material was washed twice with ethanol to give products **2** or **3**.

For **2**: yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ: 0.78 (s, 18 H, CMe_3), 0.88 (t, 6 H, Me, *J* 6.8 Hz), 1.31–1.19 (m, 36 H, CH_2), 1.33 (s, 18 H, CMe_3), 1.45–1.37 (m, 4 H, CH_2), 1.61–1.50 (m, 4 H, CH_2), 2.08–1.92 (m, 4 H, CH_2), 4.48 (t, 4 H, $ArOCH_2$, *J* 6.9 Hz), 6.94 (s, 4 H, H_{Ar}), 7.65 (s, 4 H, H_{Ar}), 7.95 (s, 2 H, OH).

For **3**: yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ: 0.83 (s, 18 H, CMe_3), 1.33 (s, 18 H, CMe_3), 2.58 (p, 4 H, CH_2, *J* 6.3 Hz), 3.83 (t, 4 H, CH_2Br, *J* 6.74 Hz), 4.59 (t, 4 H, OCH_2, *J* 5.86 Hz), 7.01 (s, 4 H, H_{Ar}), 7.66 (s, 4 H, H_{Ar}), 7.80 (s, 2 H, OH).