Макрогетероциклы
http://macroheterocycles.isuct.ru

DOI: 10.6060/mhc161293s

Iminodiacetic Derivatives of *p*−*tert*−Butylthiacalix[4]arene: Synthesis and Influence of Conformation on the Aggregation with Bismarck Brown Y

Olga A. Mostovaya,[a] Pavel L. Padnya,[a] Dmitry N. Shurpik,[a,b] Alena A. Vavilova,[a] Vladimir G. Evtugyn,[c] Yu. N. Osin,[c] and Ivan I. Stoikov[a@]

[a]*Kazan Federal University, A.M. Butlerov Chemical Institute, 420008 Kazan, Russian Federation*
[b]*RUDN University, Faculty of Science, Organic Chemistry Department, 117198 Moscow, Russian Federation*
[c]*Kazan Federal University, Interdisciplinary Centre for Analytical Microscopy, 420008 Kazan, Russian Federation*
[@]*Corresponding author E-mail: ivan.stoikov@mail.ru*

Three conformers (cone, partial cone and 1,3-alternate) of tetrasubstituted at the lower rim p-tert-butylthiacalix[4] arene derivatives with iminodiacetic fragments were synthesized and characterized. It was shown by spectral methods (UV-Vis, ^{1}H NMR and DOSY spectroscopy, DLS) and TEM that the monodisperse nano-sized particles are formed by self-assembly of synthetic octaacids in water with azo dye Bismarck brown Y in the case of the partial cone and 1,3-alternate conformations. It was found that the dye associates with the acid binding sites of the macrocycle.

Keywords: Thiacalix[4]arene, self-assembly, Bismarck brown Y, macrocyclic receptors.

Иминодиуксусные производные *п*—*трет*−бутилтиакаликс[4]−арена: синтез и влияние конформации на агрегацию с Бисмарком коричневым Y

О. А. Мостовая,[a] П. Л. Падня,[a] Д. Н. Шурпик,[a,b] А. А. Вавилова,[a] В. Г. Евтюгин,[c] Ю. Н. Осин,[c] И. И. Стойков[a@]

[a]*Казанский федеральный университет, Химический институт им. А.М. Бутлерова, 420008 Казань, Россия*
[b]*Российский университет дружбы народов, факультет физико-математических и естественных наук, 117198 Москва, Россия*
[c]*Казанский федеральный университет, Междисциплинарный центр "Аналитическая микроскопия", 420008 Казань, Россия*
[@]*E-mail: ivan.stoikov@mail.ru*

Три стереоизомера (конус, частичный конус и 1,3-альтернат) тетразамещённых по нижнему ободу иминодиуксусными фрагментами производных п-трет-бутилтиакаликс[4]арена были синтезированы и охарактеризованы. Спектральными методами (УФ, ЯМР ^{1}H и DOSY спектроскопией, ДСР) и методом ПЭМ показано, что образующиеся в результате самосборки синтезированных октакислот в воде ассоциаты при взаимодействии с азокрасителем Бисмарком коричневым Y в случае конформаций частичный конус и 1,3-альтернат формируют монодисперсные наноразмерные частицы. Установлено, что краситель связывается кислотными участками макроцикла.

Ключевые слова: Тиакаликс[4]арен, самосборка, Бисмарк коричневый Y, макроциклические рецепторы.

Introduction

The study of dyes is currently a very promising area of chemistry due to their widely application in medicine, microbiology, and forensic science. Bismarck brown Y (BBY) is frequently applied in histological microscopy,[1,2] for marking small fish.[3-5] Moreover, there is information about its use in the treatment of cancer.[6] For textile industry, the study of BBY binding can be used for extraction from the wastewaters.[7,8] Mutagenic influence of BBY to some aquatic organisms was reported despite relative harmlessness of azo dyes in low concentrations.[9] The covalent binding of some macrocyclic compounds with dyes offers opportunities to create sensory materials,[10] non-covalent interactions can be used for targeted delivery of drugs and diagnostic agents inside the cells.[11,12] It has been previously shown that non-covalent interaction of pillar[5]arene derivative with BBY leads to forming of nanometer-size aggregates.[13] In this regard, the study of the BBY binding with thiacalix[4] arene derivatives, which are analogs of pillar[5]arenes but significantly differ from them in the spatial structure and properties was interesting.[14-19] The macrocyclic platform of thiacalixarene has pronounced hydrophobic properties and readily undergoes functionalization by various fragments. The using of template method allows creating structures with binding groups located in a predetermined manner in the space,[16] and these species can applied in the development of a variety of sensors toward biologically important substrates.[20,21] Previously, a large number of selective extractants of metals,[21-23] biologically significant acids,[24-26] the anions,[23,27,28] biomacromolecules,[29,30] *etc*. has been obtained on the basis of thiacalixarene platform. In addition, the formation of different conformers of thiacalix[4]arene derivatives opens up additional possibilities for controlling the shape and size of the amphiphilic aggregates,[29] which distinguishes thiacalix[4]arene from pillararene. Thus, the study of the thiacalixarene derivatives binding with BBY can be of great practical importance.

This article describes the synthesis of three conformers (*cone*, *partial cone* and *1,3-alternate*) of the tetrasubstituted derivatives of *p-tert*-butylthiacalix[4]arene with iminodiacetic fragments and their interaction with BBY.

Experimental

All experiments (NMR, UV-Vis spectroscopy and DLS) were performed at 298 K. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (400.17 MHz for H-atoms) for 3–5 % solutions in DMSO-d_6 and methanol-d_4. The residual solvent peaks were used as an internal standard. The IR spectra were recorded on Spectrum 400 (Perkin Elmer) IR spectrometer. Elemental analysis was performed on Perkin–Elmer 2400 Series II instruments. Mass spectra (ESI) were recorded on an AmaZonX mass spectrometer (Bruker Daltonik GmbH, Germany). The drying gas was nitrogen at 300 °C. The capillary voltage was 4.5 kV. The samples were dissolved in acetonitrile (concentration ~10^{-6} g/ml). Melting points were determined using Boetius Block apparatus. The purity of the compounds was monitored by melting points, ^{1}H NMR and TLC on 200 μm UV 254 silica gel plate. The electronic absorption spectra were recorded on a spectrometer "Shimadzu UV-3600" in water in quartz cuvettes with thickness of the transmissive layer 1 cm. The matrix solutions of thiacalixarenes were prepared in methanol with a concentration of 5 mM. Then, the resulting solutions were diluted with deionized water to a concentration of 40 μM. In the course of the experiments the concentration of BBY was constant and was 10 μM. Thiacalixarenes concentrations ranged from 4 to 38.6 μM. The mixtures were incubated for 5 minutes.

Determination of Stoichiometry and Association Constants

Determination of stoichiometry of the complexes and association constants K_a by spectrophotometric titration. Series of the solutions of thiacalix[4]arene derivatives and BBY were prepared in water. The volume of the host and guest solutions varied from 2.75:0.25 to 0.25:2.75, respectively, with the total concentration of the host (H) and guest (G) being constant and equal to $2\cdot10^{-5}$ M. The solutions were shaken for 5 minutes. The absorbance A_i of the complexation systems was measured at the maximum absorbance wavelength for the complex.

The lgK_a values were determined from the plot of lg[G_nH]-lg[H] *versus* lg[G], which presents a straight line, slope of which equals to n. Association constants K_a were calculated using the intercept values.[31] Three independent experiments were carried out for each system.

Determination of Particle Size

The determination of the hydrodynamic particle size by DLS method. The particle size was determined by size analyzer of nanoparticles Zetasizer Nano ZS (Malvern). The tool is equipped with a 4 mW He-Ne laser, laser operating at a wavelength of 633 nm and incorporates noninvasive backscatter optics (NIBS). The measurements were performed at a detection angle of 173°, and the measurement position within the one-use polystyrene cuvette was automatically determined by the software. The results were processed with the DTS (Dispersion Technology Software 4.20) software package. Deionized water with resistivity > 18.0 MΩ·cm was used for the preparation of solutions. Deionized water was obtained using a Millipore-Q purification system. The experiments were carried out in water. The solutions of thiacalix[4]arenes ($5\cdot10^{-3}$ M) in methanol and BBY ($3\cdot10^{-4}$ M) in water were filtered through the nylon filters with a pore size of 450 nm. Then an aliquot of thiacalix[4]arene solution (120 μl) was adjusted with deionized water to 10 ml ($6\cdot10^{-5}$ M). Tested mixtures of thiacalix[4]arenes and BBY in a molar ratio of 1:1 were prepared in polystyrene cuvettes without additional filtering. During the experiments the concentration of mixtures varied from $5\cdot10^{-6}$ to $5\cdot10^{-5}$ M. The determination of the particle sizes was carried out in 1 hour after sample preparation. To assess the kinetic stability of the systems, the measurements were also carried out under similar conditions after 1 and 7 days.

The determination of particle size by transmission electronic microscopy method. Analysis of samples was carried out in a transmission electron microscope Hitachi HT7700 Exalens. Sample preparation: samples of compounds **7-9** (10^{-5} M) and their equimolar mixtures with BBY have been prepared similarly to studies by DLS method. Suspension (10 μl) was placed on a carbon coated 3 mm copper grid, drying was performed at room temperature. After drying, a grid was placed in a transmission electron microscope. Analysis was held at an accelerating voltage of 100 kV in TEM mode.

The determination of particle size by optical microscopy method. Analysis of samples was carried out in a universal optical microscope AxioImager M2 in transmitted light mode. Sample preparation: samples of compound **7** (10^{-5} M) and its equimolar mixtures with BBY have been prepared similarly to studies by DLS method. 100 μl suspension was placed on a glass slide and covered with a cover glass. Imaging and analysis were performed in AxioVision Rel.48 program.

^{1}H Diffusion Ordered Spectroscopy (DOSY)

The spectra were recorded on a Bruker Avance 400 spectrometer in methanol-d_4. DOSY experiments were performed using the STE bipolar gradient pulse pair (stebpgp1s) pulse sequence. 16 Scans of 16 data points were collected. The maximum gradient strength produced in the z direction was 5.35 G·mm^{-1}. The duration of the magnetic field pulse gradients (δ) was optimized for each diffusion time (Δ) in order to obtain a 2 % residual signal with the maximum gradient strength. The values of δ and Δ were 1.800 μs and 100 ms, respectively. The pulse gradients were incremented from 2 to 95 % of the maximum gradient strength in a linear ramp.[32-34]

Synthesis

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(hydroxycarbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arenes (cone ***1****, partial cone* ***2****, 1,3-alternate* ***3****)* were synthesized according to the literature procedure.[35]

The hydrochloride of ethyl ester of iminodiacetic acid.[36] To a suspension of iminodiacetic acid (20.00 g, 0.15 mol) in ethanol (190 ml, 3.1 mol) the thionyl chloride (33 ml, 0.45 mol) was slowly added dropwise. The reaction mixture was refluxed for 1 hour. After cooling the precipitated crystals were filtered, washed with diethyl ether and dried under reduced pressure over phosphorus pentoxide for two days. The yield of product is 30.60 g (90 %). T_{melt}=54 °C (Lit. 74 °C, recrystallized from acetone).[36]

General procedure for the synthesis of compounds ***4-6.*** The mixture of the corresponding stereoisomer of compounds **1-3** (1.00 g, 1.05 mmol) and thionyl chloride (10.0 ml, 84.0 mmol) was refluxed for 1.5 hours. Then, the excess of thionyl chloride was removed under reduced pressure and the residue was dried under reduced pressure for two hours. Then, the hydrochloride of ethyl ester of iminodiacetic acid (1.90 g, 8.4 mmol) and triethylamine (2.33 ml, 16.8 mmol) in 50.0 ml of methylene chloride were added to the resulting acid chloride of tetraacid. The reaction mixture was stirred at room temperature for 12 hours. Then 10 ml of 2M HCl was added, stirred at room temperature for 30 min. The organic phase was separated, the aqueous phase was washed with methylene chloride (3×10 ml), and the combined organic phases were dried over molecular sieves (3 Å). The molecular sieves were filtered off. The filtrate was concentrated on a rotary evaporator and dried in vacuum over phosphorus oxide.

*5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di(ethoxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (cone-****4****).* Yield: 1.30 g (88 %). White powder. T_{melt}=96 °C. El. Anal. Calcd for $C_{80}H_{108}N_4O_{24}S_4$ (%): C, 58.66; H, 6.65; N, 3.42; S, 7.83. Found (%): C, 58.62; H, 6.44; N, 3.19; S, 7.55. MS (ESI) *m/z*: calcd for $[M+Na]^+$: 1659.6; found 1659.8. IR ν_{max} cm^{-1}: 1186 (COC), 1669 (C(O)-NR), 1734 (C(O)-OR). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.05 (s, 36H, $(CH_3)_3C$), 1.17 (t, 12H, $^3J_{HH}$=7.1 Hz, OCH_2CH_3), 1.21 (t, 12H, $^3J_{HH}$= 7.1 Hz, -OCH_2CH_3), 4.06 (q, 8H, $^3J_{HH}$=7.1 Hz, OCH_2CH_3), 4.08 (s, 8H, -NCH_2CO-), 4.15 (q, 8H, $^3J_{HH}$=7.1 Hz, OCH_2CH_3), 4.38 (s, 8H, -NCH_2CO), 5.34 (s, 8H, OCH_2CO), 7.28 (s, 8H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 169.57, 169.44, 169.30, 157.48, 145.70, 134.62, 128.93, 70.66, 61.35, 60.85, 49.67, 48.38, 34.16, 31.26, 14.45.

*5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di(ethoxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (partial cone-****5****).* Yield: 1.28 g (86 %). White powder. T_{melt}=86 °C. El. Anal. Calcd for $C_{80}H_{108}N_4O_{24}S_4$: C, 58.66; H, 6.65; N, 3.42; S, 7.83. Found: C, 58.72; H, 6.55; N, 3.38; S, 7.43. MS (ESI) *m/z*: calcd for $[M+Na]^+$: 1659.6; found 1659.8. IR ν_{max} cm^{-1}: 1183 (COC), 1675 (C(O)-NR), 1740 (C(O)-OR). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.00 (s, 18H, $(CH_3)_3C$), 1.18–1.33 (m, 24H, OCH_2CH_3), 1.28 (s, 9H, $(CH_3)_3C$), 1.30 (s, 9H, $(CH_3)_3C$), 4.07–4.32 (m, 48H, -OCH_2CH_3, NCH_2CO), 4.52 (AB-q, 2H, $^2J_{HH}$ = 13.2 Hz, OCH_2), 4.73 (s, 2H, OCH_2), 5.03 (AB-q, 2H, $^2J_{HH}$ = 13.2 Hz, OCH_2), 5.40 (s, 2H, OCH_2), 7.07 (d, 2H, $^4J_{HH}$ = 2.5 Hz, ArH), 7.42 (d, 2H, $^4J_{HH}$ =2.5 Hz, ArH), 7.63 (s, 2H, ArH), 7.64 (s, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 170.02, 169.54, 169.37, 169.26, 168.36, 167.60, 158.81, 158.36, 157.01, 146.47, 146.16, 144.93, 135.91, 135.36, 135.13, 134.32, 129.05, 127.87, 127.70, 126.79, 71.51, 68.59, 68.06, 61.44, 61.30, 61.21, 61.02, 60.85, 60.70, 49.68, 49.39, 48.48, 47.72, 34.34, 34.26, 34.12, 31.54, 31.22, 31.12, 14.57, 14.48, 14.37.

*5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di(ethoxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (1,3-alternate-****6****).* Yield: 1.38 g (93 %). White powder. T_{melt}=67 °C. El. Anal. Calcd for $C_{80}H_{108}N_4O_{24}S_4$: C, 58.66; H, 6.65; N, 3.42; S, 7.83. Found: C, 58.43; H, 6.74; N, 3.51; S, 7.71. MS (ESI) *m/z*: calcd for $[M+K]^+$ 1675.6; found 1675.8. IR ν_{max} cm^{-1}: 1184 (COC), 1665 (C(O)-NR), 1740 (C(O)-OR). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.20 (s, 36H, $(CH_3)_3C$), 1.23 (t, 24H, $^3J_{HH}$ = 7.1 Hz, OCH_2CH_3), 4.12 (q, 8H, $^3J_{HH}$ = 7.1 Hz, OCH_2CH_3), 4.15 (s, 8H, -NCH_2CO-), 4.17 (q, 8H, $^3J_{HH}$ = 7.1 Hz, OCH_2CH_3), 4.28 (s, 8H, -NCH_2CO-), 4.67 (s, 8H, OCH_2CO), 7.48 (s, 8H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 169.88, 169.53, 167.66, 157.96, 145.90, 134.59, 127.31, 68.28, 61.40, 60.84, 49.45, 48.52, 34.29, 31.24, 14.56.

General procedure for the synthesis of compounds ***7-9.*** The mixture of the compounds **4-6** (0.30 g, 0.183 mmol) in tetrahydrofuran (1.7 ml) and a solution of lithium hydroxide monohydrate (0.307 g, 7.32 mmol) in water (3.3 ml) were stirred at room temperature for 10 minutes. Then 10 ml of 2 M HCl was added, and THF was evaporated from the reaction mixture. The precipitate was filtered, washed with water and dried under reduced pressure over phosphorus pentoxide for two days.

*5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di-(hydroxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (cone-****7****).* Yield: 0.23 g (89 %). White powder. T_{melt}=192 °C. El. Anal. Calcd for $C_{64}H_{76}N_4O_{24}S_4$: C, 54.38; H, 5.42; N, 3.96; S, 9.07. Found: C, 54.47; H, 5.45; N, 4.00; S, 9.10. MS (ESI) *m/z*: calcd for $[M–H^+]^-$ 1411.4; found 1411.5. IR ν_{max} cm^{-1}: 1193 (COC), 1644 (C(O)-NR), 1727 (C(O)-OH). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.04 (s, 36H, $(CH_3)_3C$), 3.96 (s, 8H, -NCH_2CO-), 4.26 (s, 8H, -NCH_2CO), 5.32 (s, 8H, OCH_2CO), 7.23 (s, 8H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 171.45, 171.05, 169.47, 157.74, 145.32, 134.33, 128.95, 70.48, 49.71, 48.69, 34.11, 31.30.

*5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di-(hydroxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (partial cone-****8****).* Yield: 0.25 g (93 %). White powder. T_{melt}=237 °C. El. Anal. Calcd for $C_{64}H_{76}N_4O_{24}S_4$: C, 54.38; H, 5.42; N, 3.96; S, 9.07. Found: C, 54.37; H, 5.76; N, 4.12; S, 9.05. MS (ESI) *m/z*: calcd for $[M–H^+]^-$ 1411.4, found 1411.5. IR ν_{max} cm^{-1}: 1194 (COC), 1669 (C(O)-NR), 1727 (C(O)-OH). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.00 (s, 18H, $(CH_3)_3C$), 1.30 (s, 9H, $(CH_3)_3C$), 1.31 (s, 9H, $(CH_3)_3C$), 3.81–4.24 (m, 16H, NCH_2), 4.52 (AB-q, 2H, $^2J_{HH}$=13.0 Hz, OCH_2), 4.72 (s, 2H, OCH_2), 5.01 (AB-q, 2H, $^2J_{HH}$=13.0 Hz, OCH_2), 5.39 (s, 2H, OCH_2), 7.04 (d, 2H, $^4J_{HH}$=2.4 Hz, ArH), 7.49 (d, 2H, $^4J_{HH}$=2.4 Hz, ArH), 7.60 (s, 2H, ArH), 7.69 (s, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 171.64, 171.27, 171.12, 169.99, 168.29, 167.48, 158.90, 158.54, 157.20, 146.38, 146.18, 144.63, 135.71, 135.50, 134.88, 134.35, 129.13, 127.89, 127.63, 126.70, 71.32, 70.80, 49.67, 49.19, 48.53, 47.61, 34.58, 34.42, 34.13, 31.57, 31.46, 31.20.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-[{di-(hydroxycarbonylmethyl)iminocarbonyl}-methoxy]-2,8,14,20-tetrathiacalix[4]arene (*1,3-alternate-****9*****)). Yield: 0.24 g (92 %). White powder. T_{melt}=173 °C. El. Anal. Calcd for $C_{64}H_{76}N_4O_{24}S_4$: C, 54.38; H, 5.42; N, 3.96; S, 9.07. Found: C, 54.12; H, 5.33; N, 3.92; S, 9.15. MS (ESI) *m/z*: calcd for $[M–H^+]^-$ 1411.4, found 1411.5. IR ν_{max} cm^{-1}: 1186 (COC), 1655 (C(O)-NR), 1727 (C(O)-OH). ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ_H ppm: 1.20 (s, 36H, $(CH_3)_3C$),

4.09 (s, 8H, -NCH_2CO-), 4.16 (s, 8H, -NCH_2CO-), 4.65 (s, 8H, OCH_2CO), 7.53 (s, 8H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C ppm: 171.41, 171.17, 167.53, 158.09, 145.93, 134.70, 127.26, 68.28, 49.29, 48.07, 34.33, 31.33.

Results and Discussion

Synthesis

Acid groups were chosen to provide binding the dye, which is an inherent base. Due to the fact that BBY contains four amino groups, for enhancement of the binding it was decided to use diacetic fragments as the binding sites. For preparation of macrocyclic structures containing eight carboxylic fragments for complexation the tetraacids in *cone*-**1**, *partial cone*-**2** and *1,3-alternate*-**3** conformations were chosen as precursors.

The appropriate acid chlorides were obtained by the interaction of tetraacids in *cone*-**1**, *partial cone*-**2** and *1,3-alternate*-**3** conformations with thionyl chloride and then were treated with the hydrochloride of ethyl ester of iminodiacetic acid[37] in dichloromethane in the presence of triethylamine (Scheme 1).

The esters of α-amino acids are readily hydrolysable. These esters can be frequently cleaved by boiling with water or using an aqueous solution of hydroxides of alkali and alkaline earth metals.[38] The hydrolysis of amides generally requires more hard conditions than the hydrolysis of the corresponding esters, for example, boiling for several hours with concentrated aqueous acid solutions or concentrated solutions of caustic alkali.[38]

Due to the fact that the compounds **4**-**6** contain both amide and ester fragments, the conditions of ester group hydrolysis should be rather mild to avoid the destruction of amide bond. For this reason, aqueous solution of the lithium hydroxide in tetrahydrofuran (THF) was used.

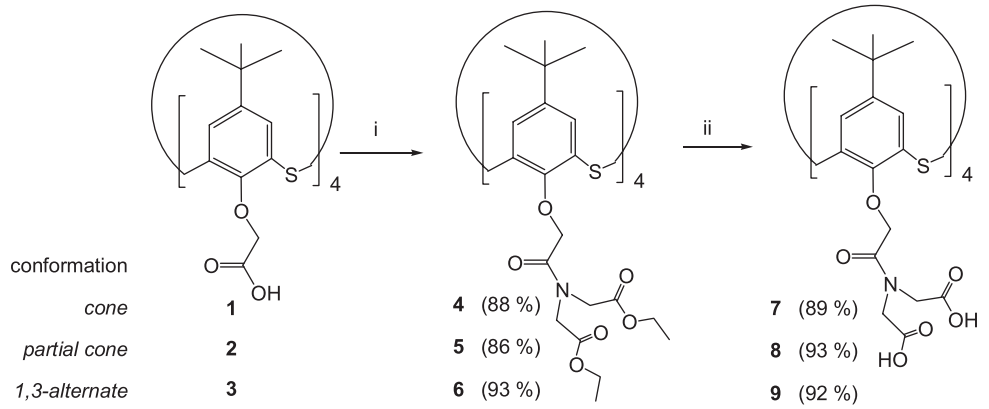
The hydrolysis of octaesters **4**-**6** (Scheme 1) with lithium hydroxide in the mixture of THF and H_2O was studied. The reaction proceeds for 10 minutes at room temperature. With increasing time or increasing temperature of the reaction mixture, the impurities, probably, the products of amide bond hydrolysis, are always present in addition to the major product. The amount of such impurities increased with the synthesis duration according to TLC data and ^{1}H NMR spectra. Fast reaction can be explained by a low steric congestion of ethoxycarbonyl groups as well as the autocatalytic effect resulted from the hydrolysis of the carboxyl groups in closely spaced adjacent space not yet hydrolyzed. As a result, each subsequent ester group is hydrolyzed faster than the previous one.

The structure and composition of the thiacalix[4] arene derivatives **4**-**9** obtained in three conformations (*cone*, *partial cone*, *1,3-alternate*) were characterized by ^{1}H, ^{13}C NMR, IR spectroscopy, ESI mass spectrometry and the elemental analysis.

Table 1 summarizes the values of chemical shifts and the constants of spin-spin interaction (Hz) of characteristic protons in the compounds **4**-**9**. In the ^{1}H NMR spectra, the *cone* and *1,3-alternate* stereoisomers significantly differ in chemical shifts of protons of *tert*-butyl, oxymethylene and aromatic fragments. However, the spectral picture becomes more complicated for *partial cone* stereoisomers due to the reduction of the structure symmetry. The signals of protons of *tert*-butyl groups appear as three singlets with an intensity ratio of 2:1:1, those of aromatic and oxymethylene protons as two singlets and AB-quadruplet.

The conformation of *p-tert*-butylthiacalix[4]arene derivatives is usually determined by using the two-dimensional NMR spectroscopy techniques.[39-43] However, in one-dimensional ^{1}H NMR spectra, the compounds **4**-**9** obtained can be distinguished by characteristic signals of the protons, which can clearly establish the conformation of the macrocycle. The conformational correlation of *cone* **4** and **7** stereoisomers, and *1,3-alternates* **6** and **9** tetrasubstituted at the lower rim of *p-tert*-butylthiacalix[4] arene can be realized by comparison of the chemical shifts of protons of $OCH_2C(O)$ groups in the ^{1}H NMR spectra. The signals of oxymethylene protons in *cone* stereoisomer exerted downfield shift if compared to similar signals of the protons in *1,3-alternate* stereoisomer for all the synthesized compounds.[44]

It should be noted that ethoxyl and imidomethylene protons give a pair of similar signals (the triplet and quartet for CH_3CH_2O group and singlet for NCH_2CO group) of equal intensity. This fact indicates that the diastereotopic ethylacetimide fragments are located at the amide nitrogen atom (Table 1).



Scheme 1. Reagents and conditions: i – 1) $SOCl_2$, reflux, 2) $Cl^-NH_2^+(CH_2COOEt)_2$, CH_2Cl_2, NEt_3; ii – 1) LiOH, THF/H_2O, 10 min, 2) 2 M HCl.

Table 1. The chemical shifts of protons in the ^{1}H NMR spectra of compounds **4-9** in DMSO-d_6 (400 MHz, 298 K).

Compound	*cone*		*partial cone*		*1,3-alternate*	
	4	**7**	**5**	**8**	**6**	**9**
t-Bu	1.05	1.04	1.00, 1.28, 1.30	1.00, 1.30, 1.31	1.20	1.20
NCH_2CO	4.08, 4.38	3.96, 4.26	4.07–4.32 (m)	3.81–4.24 (m)	4.15, 4.28	4.09, 4.16
OCH_2CO	5.34	5.32	4.52 ($^2J_{HH}$=13.2 Hz), 4.73, 5.03 ($^2J_{HH}$=13.2 Hz), 5.40	4.52 ($^2J_{HH}$=13.0 Hz), 4.72, 5.01 ($^2J_{HH}$=13.0 Hz), 5.39	4.67	4.65
ArH	7.28	7.23	7.07 ($^4J_{HH}$=2.5 Hz), 7.42 ($^4J_{HH}$=2.5 Hz), 7.63, 7.64	7.04 ($^4J_{HH}$=2.4 Hz), 7.49 ($^4J_{HH}$=2.4 Hz), 7.60, 7.69	7.48	7.53

Spectral Study of BBY Binding by the Macrocycles ***7-9***

Initially the interaction of the synthesized compounds **7-9** with BBY was studied by UV-Vis spectroscopy in water. Currently, an interest in the study of reactions in aqueous media regularly grows,[45] as the widespread use of water as an environmentally friendly solvent in many reactions within the concept of "green chemistry". Furthermore, water allows to form a lot of hydrogen bonds with polar molecules, thus affecting the substrate binding. Finally, all the important interactions in the living beings are carried out in an aqueous medium. It turned out that in the spectra of BBY and the macrōcycles, the absorption maximum peaks corresponding to π-π* transitions of the aromatic fragments overlap in the area of 280 nm (Figure 1).[46] A little "blue" shift of the absorption maximum from 463 to 455 nm accompanied by a hyperchromic effect was observed due to the interaction of the azo dye with all the acids conformers (Figures 1, 2). The dye concentration of 10 μM was chosen because of limited solubility of the macrocycles in water (no more than 60 μM), whereas possible variation of a calixarene concentration was much wider. Initially, the stoichiometry of 1:1 was determined for all the complexes by a method of constructing curves of isomolar series (Figure 2). The determination of the association constants of the complexes showed that all three conformers form complexes with similar association constants. The dye is most effectively bonded by the macrocycle in a *cone*-**7** conformation (lgK_a 4.0±0.3). The other conformers bind BBY slightly weaker: lgK_a for *partial cone*-**8** is equal to 3.2±0.1 and lgK_a for *1,3-alternate*-**9** is 3.8±0.1.

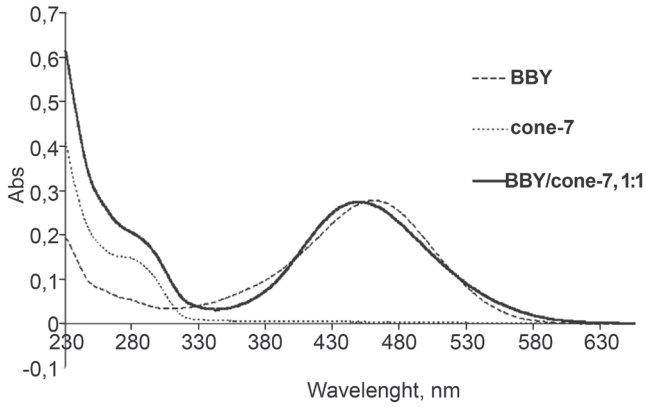


Figure 1. The UV-Vis spectra of the *cone*-**7** (10 μM), BBY (10 μM) and their mixture (1:1) in water, 298 K.

In the case of the compound **7** in the *cone* conformation (concentration of receptor more than 20 μM), a significant rise of the base line was observed in the UV-Vis spectrum due to light scattering caused by aggregates formed.[47] Indeed, it is logical to expect for this conformation the formation of micelles, because the molecules of such a compound are amphiphilic. There are pronounced hydrophobic (macrocycle)

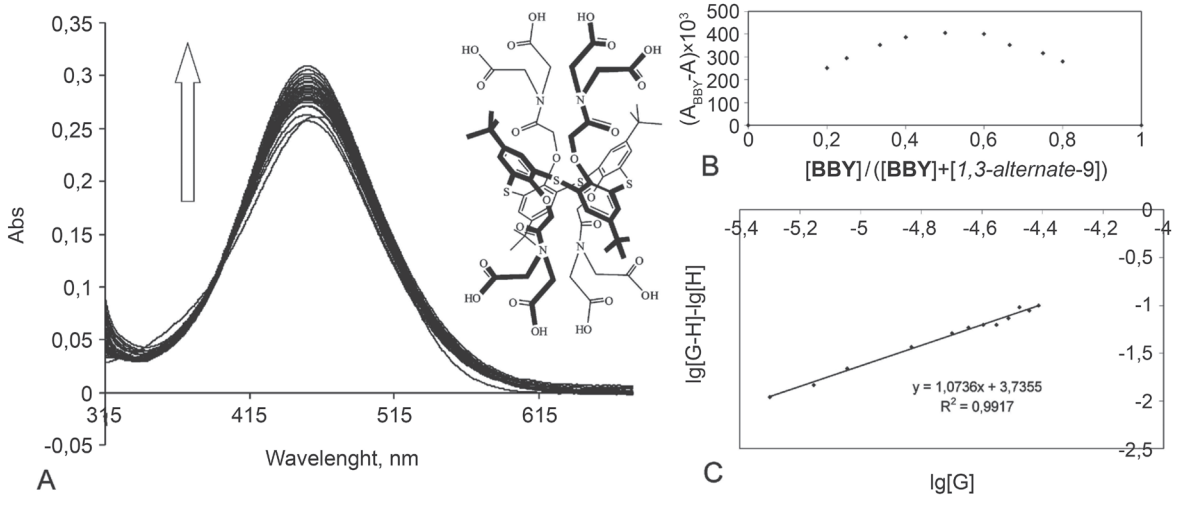


Figure 2. Spectrophotometric titration of complexation system between BBY (10 μM) and *1,3-alternate*-**9** in water (A); the Job's plot (B) and the calculation of the association constant of the complex between BBY and *1,3-alternate*-**9** (C).

and hydrophilic (substituents) parts that offer the surfactants properties (Figure 3A). The experiment made by DLS widely used for the study of colloidal systems, macromolecules and molecular associates, has fully confirmed this prediction. It was found that the compound in the *cone* conformation formed polydisperse system in aqueous solutions consisting of large associates with a particle size of about 700–800 nm (Table 2). In addition, it was confirmed by TEM.

It can be clearly seen in the Figure 4A, that micron sized particles are formed due to self-assembly of the *cone*-**7** that is well correlated with large PDI values determined for this conformer by DLS. There is a small number of particles of about 2–3 μm (up to 6 μm) but the majority of the particles has the size of about 0.5–1 μm in a good agreement with the DLS data. Application of TEM made it possible to establish the existence of very large aggregates of about 6 μm in size (Figure 4B). Even bigger increase of the PDI (to 1.000) followed by a significant reduction in particle size was observed after the dye addition. Indeed, Figure 4C shows a large number of spherical associates of about 40–60 nm in size, which agree with the DLS results. The compounds **8** and **9** existing in *partial cone* and *1,3-alternate* conformation form self-associates which are much smaller in size (Table 2). Possibly, such a significant difference in the size against the *cone* conformer can be explained by principal difference in the molecule structure from the other conformers. As a consequence, the particles of another type are formed. Thus, for the *cone* conformation one can expect the formation of spherical particles – micelles resulting in orientation of hydrophobic moieties of molecule inside creating a micelle core. The polar acid fragments are directed outside (Figure 3A).

In the case of the *1,3-alternate* and *partial cone*, the molecules have an essentially different structure. The hydrophobic macrocyclic part is enclosed between the polar hydrophilic groups, so that the formation of vesicles can be expected. Their polar groups are directed into the water, between them, a hydrophobic hydrocarbon layer is located (Figure 3B and C). It is interesting, that minimal PDI values were observed for a *partial cone* conformation indicating preferential formation of one type of particles. The study of the BBY solutions by DLS showed that the dye forms aggregates in the water. The particle size increases with dilution (Table 2) in contrast to macrocyclic compounds where strong correlation was not found between a compound concentration and the size of aggregates. It is supposed that changes in the size of associates depending on the concentration of the molecules forming them and it can be attributed to various forms of the particles in solution. Thus, spherical aggregates are usually lesser than extended ones of

Table 2. The size distribution of the number and polydispersity index of thiacalixarenes **7**-**9** and their complexes with BBY (1:1) at various concentrations in water.

	The particle size (d), nm / PDI						
Concentration, M	BBY	*cone*-**7**	*cone*-**7** with BBY	*partial cone*-**8**	*partial cone*-**8** with BBY	*1,3-alternate*-**9**	*1,3-alternate*-**9** with BBY
$5 \cdot 10^{-5}$	85.02 / 0.242	885.7 / 0.751	41.40 / 1.000	33.40 / 0.212	44.94 / 0.218	45.83 / 0.300	41.64 / 0.246
$1 \cdot 10^{-5}$	170.3 / 0.187	698.2 / 0.892	76.04 / 1.000	44.97 / 0.329	30.93 / 0.212	44.37 / 0.341	44.65 / 0.245
$5 \cdot 10^{-6}$	191.1 / 0.167	741.0 / 0.884	53.51 / 1.000	51.23 / 0.289	28.91 / 0.387	43.17 / 0.373	39.17 / 0.273

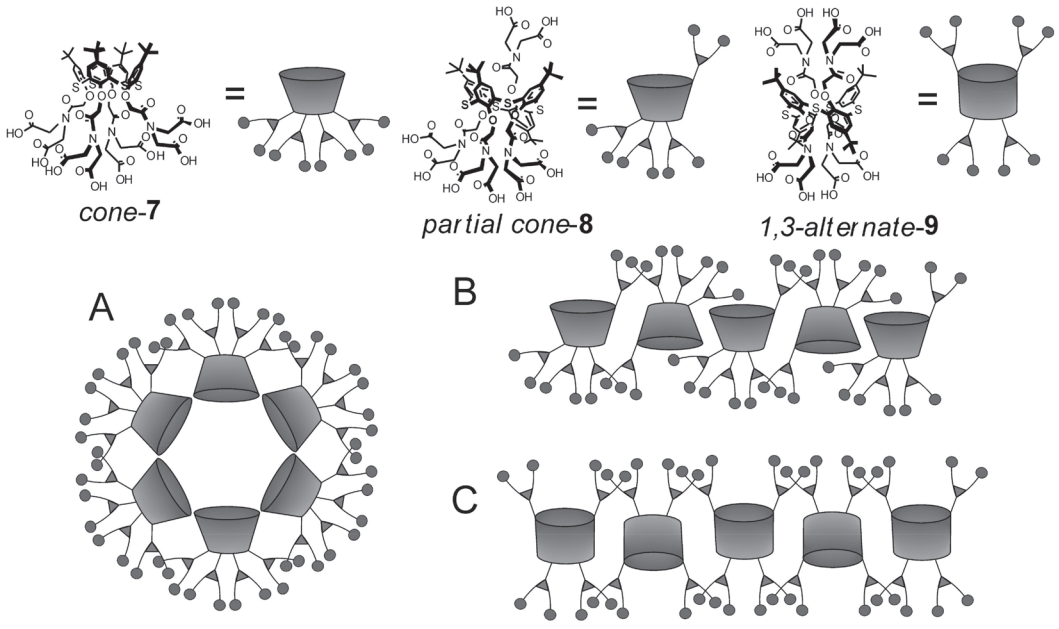


Figure 3. Possible paths for the formation of supramolecular associates.

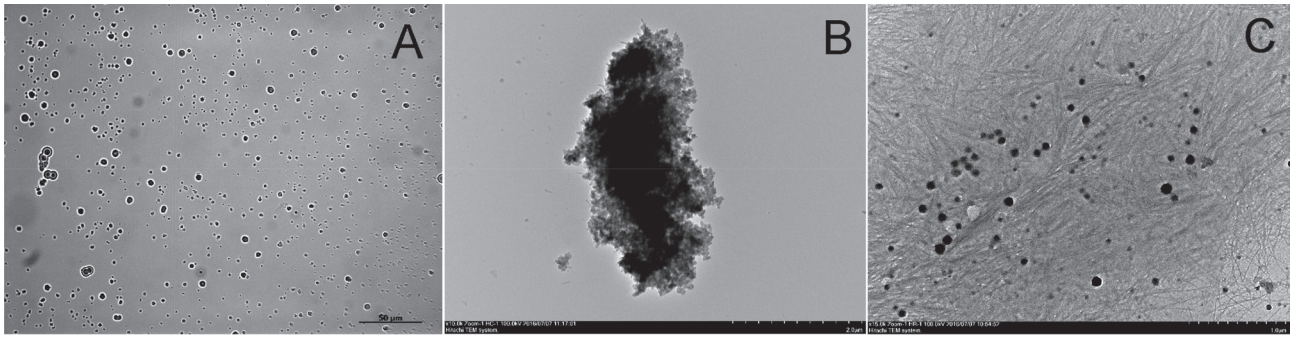


Figure 4. The optical microscope image of *cone*-**7** ($1 \cdot 10^{-5}$ M) (A); TEM images of *cone*-**7** ($1 \cdot 10^{-5}$ M) (B) and an equimolar mixture of *cone*-**7** ($1 \cdot 10^{-5}$ M) with BBY (C).

the same mass.[29,48] Probably, aggregates form changes with dilution due to the thermodynamic reasons (mainly due to the entropy change of the system).[49] It is interesting that the size of the particles formed by self-association of the dye with *partial cone*-**8** and *1,3-alternate*-**9** do not differ in size from the particles formed by the macrocycles themselves. The complexation is confirmed by the absence of rather large associates related to self-association of BBY (Table 2). In order to establish the nature of the interaction of thiacalix[4] arenes **7**-**9** obtained with the dye, ^{1}H NMR spectroscopy was used. In our previous studies[39,40] on amphiphilic thiacalix[4] arenes, two possible ways of formation of aggregates were shown. The first one involves the coordination of BBY molecules with binding acidic groups of the macrocycle (Figure 5, A and B),[40] while the second way assumes incorporation of the azo dye between the calixarene molecules constituting the aggregate (Figure 5, A' and B').[39] Furthermore, the aromatic moiety of BBY is intercalated between the hydrophobic "bowls" of the macrocycles with simultaneous orientation of the amino groups of the dye to the carboxyl functions of the compounds **7**-**9**. All of the ways proposed correlate well with the stoichiometry of the complexes of 1:1, previously found for all the macrocycles by UV-Vis spectroscopy.

The initial record of the ^{1}H NMR spectra in methanol-d_4 has confirmed the complexation. The selection of other solvents instead of water was required because of poor solubility of the macrocycles investigated that prevented preparation of the solutions with a concentration sufficient for NMR spectroscopy. However, for the compound *cone*-**7** the formation of the colloidal systems was observed even in methanol both for individual compound and its mixture with the dye. This makes the NMR method less informative.

The biggest changes were observed in the spectrum of the BBY complex with *partial cone*-**8** (Figure 6). Probably, this was due to the asymmetrical structure of the macrocycle which resulted in binding dye with losses of symmetry. This lead to the appearance of additional doublet at 5.9 ppm with the constant of the spin-spin interaction of $^4J_{HH}$=2.4 Hz related to the protons H_e becoming non-equivalent. Meanwhile, overlapping unresolved multiplets at 6.5–6.6 ppm for the free dye underwent upon complexation with **8** the slight upfield shift in the area of 6.47–6.54 ppm. Fine structure indicated also losses in the equivalency of the H_d and H_f protons of BBY. As a result, a superposition of two AB-spin systems of these protons belonging to different aromatic rings of the dye took place in the ^{1}H NMR spectrum. The signals of the H_a, H_b and H_c

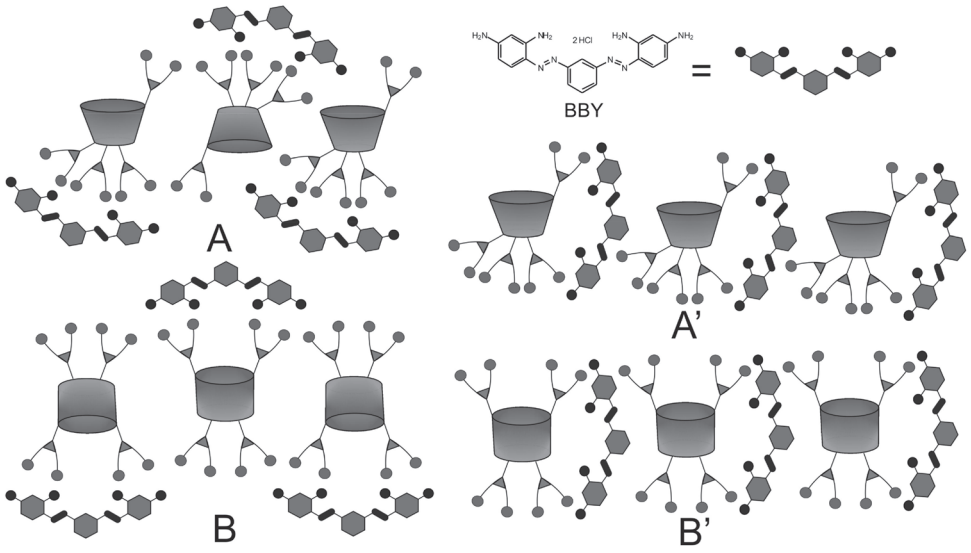


Figure 5. Possible paths for the formation of aggregates based on thiacalixarenes **8**, **9** and BBY.

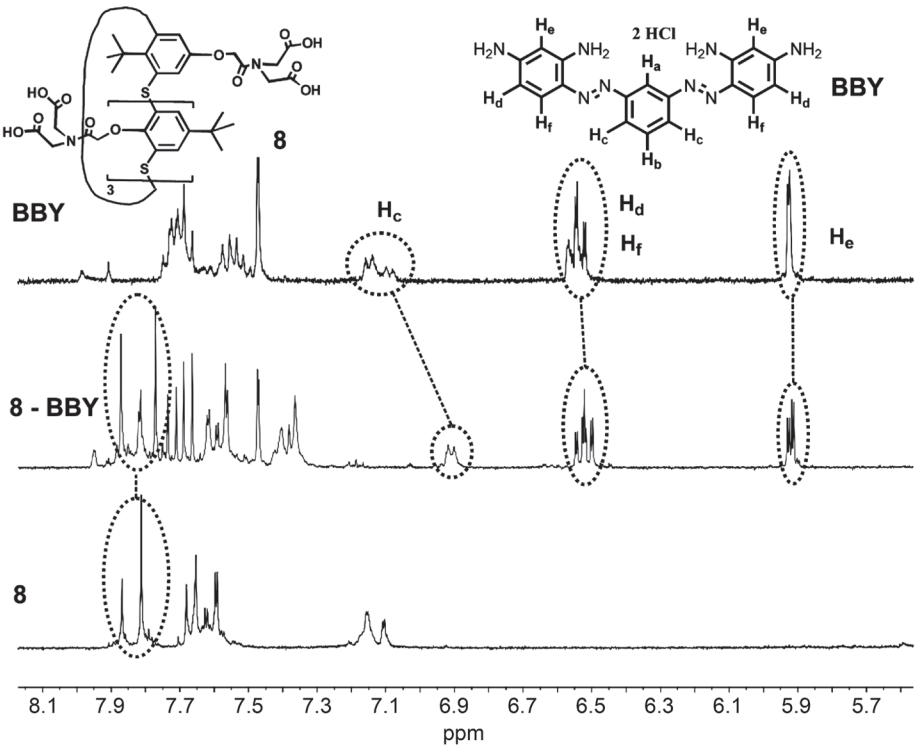


Figure 6. The fragments of ^{1}H NMR spectra (methanol-d_4, 298 K, 400 MHz) of BBY ($2.5\cdot10^{-3}$ M), *partial cone*-**8** ($2.5\cdot10^{-3}$ M) and their complex ($2.5\cdot10^{-3}$ M).

protons and those of the amino groups of free azo dye were in the field of 7.05–8.00 ppm.

As a result of the association with the *partial cone*-**8**, slight upfield shift of the group of multiplets to 6.85–7.95 ppm has been observed. It can be assumed that the upfield shift of the dye signals can be attributed to the shielding the protons of dye aromatic fragments caused by the macrocycle.

In the ^{1}H NMR spectrum of the complex BBY with *1,3-alternate*-**9**, additional peaks in the area of the *tert*-butyl protons of the macrocycle appeared, *i.e.* the singlet at 1.23 ppm in addition to the peak at 1.25 ppm. Probably, weakly expressed upfield shift can be associated with an additional shielding of the protons of *tert*-butyl groups resulted from ionization of the carboxyl fragments in the interaction with the base. There are significant changes in the ^{1}H NMR spectrum for the protons of the methylene substituents. In the spectrum of free macrocycle, the singlets at 4.21 and 4.75 ppm in the ratio of 2:1 are related to the protons of NCH_2 and OCH_2 groups, respectively. In the spectrum of associated macrocycle, the number of signals increases due to the loss of the molecule symmetry in the complexation with one dye molecule. Thus, the signals of the methylene group protons bonded to the oxygen atoms are substantially shifted to low fields and appear as two singlets with the ratio of 1:1 at 4.90 and 5.06 ppm. The multiplet at 4.09–4.30 ppm formed from closely spaced and overlapping signals corresponded to 16 protons of the methylene groups at the nitrogen atoms. In addition to the aromatic protons of BBY, changes were also observed similarly to those corresponded to the complexation of the dye with the *partial cone*-**8**. The only difference was found for the protons H_e: owing to the symmetrical structure of the macrocycle **9**, such protons are also equivalent due to the formation of a symmetric complex. Together with established stoichiometry of complexation 1:1, this testifies binding of the dye molecule only from one side of the macrocycle. Probably, we observe negative allosteric effect resulted from the substrate binding on one side of the macrocycle. The geometry of the binding site on the other side changes making binding of the other dye molecule impossible.[24,50,51]

The DLS method was used in order to confirm aggregation in methanol. The concentration of solutions was chosen the same as that in the NMR study. It was found that in the case of *cone* conformation, large self-associates are formed in methanol (Table 3). For other conformations, small particles with dimensions in order of 1.1 nm can indicate the formation of dimers.[48] It is interesting, that only for the compound *cone*-**7** an increase of the aggregate size was observed as a result of interaction with BBY. For the other conformations, the same tendency of decrease

Table 3. The size distribution by number and polydispersity index of thiacalix[4]arenes **7-9** and their complexes with BBY (1:1, $2.5\cdot10^{-3}$ M) in methanol.

The particle size (d), nm / PDI						
BBY	*cone*-**7**	*cone*-**7** with BBY	*partial cone*-**8**	*partial cone*-**8** with BBY	*1,3-alternate*-**9**	*1,3-alternate*-**9** with BBY
0.668 / 0.767	306.1 / 1.000	675.9 / 0.454	1.109 / 0.914	0.899 / 1.000	1.114 / 0.576	0.771 / 1.000

of the aggregate size with the dye compared with the self-associates occurred in the aqueous solutions (Table 3). Such a small size of the associates of the macrocycles with the dye can be interpreted as the destruction of the dimers to form complexes consisting of a single molecule of the guest and the host.

Thus, data obtained using ^{1}H NMR spectroscopy and DLS made it possible to conclude that the dye binding is carried out with orientation of its amino groups toward acid fragments of the macrocycle without the intercalation between the "bowls" of the cyclophane (Figure 5, A and B).

The final confirmation of the association between the synthesized octaacids **8** and **9** and the BBY was obtained by the diffusion-ordered spectroscopy (DOSY). This approach provides information about the formation of host-guest associates.[32,33] This experiment allowed establishing formation of the complexes based on the values of the diffusion coefficients of BBY and macrocycles **8** and **9**, as well as their 1:1 mixtures (**8**-BBY and **9**-BBY). Initially, the diffusion coefficients of thiacalix[4]arenes and dye were identified ($2.5\cdot10^{-3}$ M) (Table 4). Compounds **8** and **9** in the presence of BBY showed a significant reduction in their diffusion rate (Table 4). This indicates the formation of host-guest associates in both cases. Besides, decrease in diffusion of the dye molecule during the formation of the complex was observed in both cases. This indicates reduction of the mobility of the guest molecule (BBY) due to complexation. The last but not least, that ensures in the formation of the host-guest associates between macrocycles and BBY is that the peaks of the complexes **8**-BBY and **9**-BBY are located on the horizontal line in the DOSY spectra.

Table 4. The diffusion coefficients of pure compounds **8**, **9**, BBY and their complexes in CD_3OD (400 MHz, 298 K).

Compounds	$D\cdot10^{-10}$, $m^2\cdot s^{-1}$
partial cone-**8**	4.10
1,3-alternate-**9**	3.86
BBY	2.18
partial cone-**8** with BBY	1.75
1,3-alternate-**9** with BBY	1.82

Conclusions

The interaction of tetrasubstituted at the lower rim *p-tert*-butylthiacalix[4]arene derivatives with iminodiacetic fragments (*cone*, *partial cone* and *1,3-alternate* conformers) with Bismarck brown Y was studied. Self-assembly of all the studied compounds with BBY was shown by UV-Vis and NMR spectroscopy, DLS and TEM. No significant difference in selectivity of the dye interaction was found by electronic absorption spectroscopy for all the macrocycle conformers. These results are in similar values of appropriate association constants of the complexes formed. The polydisperse systems with the size of the aggregates in order of 40–60 nm were formed in the interaction with the dye except that with *cone* conformation showed the formation of large micrometer sized self-assembly particles. The BBY addition leads to significant decrease of the particle size in the *cone* conformation (to 60 nm) maintaining a high polydispersity of the system. The research carried out offered the perspectives for use of the octaacids based on the macrocyclic platform to create sensory materials on azo dye BBY.

Acknowledgements. The work was supported by the Russian Science Foundation (№16-13-00005).

References

1. Graham E.T. *Biotech. Histochem.* **1997**, *72*, 119–122.
2. Graham E.T., Trentham W.R. *Biotech. Histochem.* **1998**, *73*, 178–185.
3. Lawler G.H., Fitz-Earle M., Fish J. *Res. Board Can*. **1968**, *25*, 255–266.
4. Baker J.A., Modde T. *Trans. Am. Fish. Soc.* **1977**, *106*, 334–338.
5. Ewing R.D., McPherson B.P., Satterthwaite D. *The Progressive Fish-Culturist* **1990**, *52*, 231–236.
6. Kutushov M.V. US Patent WO 2009084982 A1, filed 2008, issued 2009.
7. Chao A.Ch., Shyu Sh.Sh., Lin Yu.Ch., Mi F.L. *Bioresour. Technol.* **2004**, *91*, 157–162.
8. Kumar B.G.P., Miranda L.R., Velan M. *J. Hazard. Mater*. **2005**, *126*, 63–70.
9. Soriano J.J., Mathieu-Denoncourt J., Norman G., Solla de S.R., Langlois V.S. *Environ. Sci. Pollut. Res*. **2014**, *21*, 3582–3591.
10. Ko Y.G., Sung B.H., Choi U.S. *Colloids Surf., A* **2007**, *305*, 120–125.
11. Seo J.W., Ang J., Mahakian L.M., Tam S., Fite B., Ingham E.S., Beyer J., Forsayeth J., Bankiewicz K.S., Xu T., Ferrara K.W. *J. Controlled Release* **2015**, *220*, 51–60.
12. Lu Y., Hu Q., Lin Y., Pacardo D.B., Wang C., Sun W., Ligler F.S., Dickey M.D., Gu Zh. *Nat. Commun.* **2015**, *6*, 10066.
13. Shurpik D.N., Padnya P.L., Basimova L.T., Evtugin V.G., Plemenkov V.V., Stoikov I.I. *Mendeleev Commun.* **2015**, *25*, 432–434.
14. Fernández-Rosas J., Gómez-González B., Pessêgo M., Rodríguez-Dafonte P., Parajó M., Garcia-Rio L. *Supramol. Chem.* **2016**, *28*, 464–474.
15. Cao D., Meier H. *Asian J. Org. Chem*. **2014**, *3*, 244–262.
16. Morohashi N., Narumi F., Iki N., Hattori T., Miyano S. *Chem. Rev*. **2006**, *106*, 5291–5316.
17. Tan L.L., Yang Y.W. *J. Inclusion Phenom. Macrocycl. Chem*. **2015**, *81*, 13–33.
18. Song N., Yang Y.W. *Sci. China Chem*. **2014**, *57*, 1185–1198.
19. Zhou Y., Li H., Yang Y.W. *Chin. Chem. Lett*. **2015**, *26*, 825–828.
20. Evtugyn G.A., Shamagsumova R.V., Padnya P.V., Stoikov I.I., Antipin I.S. *Talanta* **2014**, *127*, 9–17.
21. Wang L., Wang X., Shi G., Peng C., Ding Y. *Anal. Chem*. **2012**, *84*, 10560–10567.
22. Zhao H., Zhan J., Zou Z., Miao F., Chen H., Zhang L., Cao X., Tian D., Li H. *RSC Adv*. **2013**, *3*, 1029–1032.
23. Kumar R., Lee Y.O., Bhalla V., Kumar M., Kim J.S. *Chem. Soc. Rev*. **2014**, *43*, 4824–4870.
24. Mostovaya O.A., Agafonova M.N., Galukhin A.V., Khayrutdinov B.I., Islamov D., Kataeva O.N., Antipin I.S., Konovalov A.I., Stoikov I.I. *J. Phys. Org. Chem*. **2014**, *27*, 57–65.
25. Stoikov I.I., Zhukov A.Yu., Agafonova M.N., Sitdikov R.R., Antipin I.S., Konovalov A.I. *Tetrahedron* **2010**, *66*, 359–367.
26. Kalchenko O., Drapailo A., Shishkina S., Shishkin O., Kharchenko S., Gorbatchuk V., Kalchenko V. *Supramol. Chem*. **2013**, *25*, 263–268.
27. Zlatušková P., Stibor I., Tkadlecová M., Lhoták P. *Tetrahedron* **2004**, *60*, 11383–11390.

28. Pérez-Casas C., Höpfl H., Yatsimirsky A.K. *J. Inclusion Phenom. Macrocyclic Chem*. **2010**, *68*, 387–398.
29. Padnya P.L., Andreyko E.A., Mostovaya O.A., Rizvanov I.Kh., Stoikov I.I. *Org. Biomol. Chem*. **2015**, *13*, 5894–5904.
30. Khairutdinov B., Ermakova E., Sitnitsky A., Stoikov I., Zuev Y. *J. Mol. Struct*. **2014**, *1074*, 126–133.
31. Yushkova E.A., Stoikov I.I., Zhukov A.Yu., Puplampu J.B., Rizvanov I.Kh., Antipin I.S., Konovalov A. *RSC Adv*. **2012**, *2*, 3906–3919.
32. Sundaresan A.K., Gibb C.L., Gibb B.C., Ramamurthy V. *Tetrahedron* **2009**, *65*, 7277–7288.
33. Yakimova L.S., Shurpik D.N., Gilmanova L.H., Makhmutova A.R., Rakhimbekova A., Stoikov I.I. *Org. Biomol. Chem.* **2016**, *14*, 4233–4238.
34. Dais P., Misiak M., Hatzakis E. *Anal. Methods* **2015**, *7*, 5226–5238.
35. Stoikov I.I., Smolentsev V.A., Antipin I.S., Habicher W.D., Gruner M., Konovalov A.I. *Mendeleev Commun*. **2006**, *16*, 294–297.
36. Tietze L.F., Eicher T., Diederichsen U., Speicher A. *Reactions and Synthesis in the Organic Chemistry Laboratory*. Wiley-VCH: Weinheim, **2007**. 668 p.
37. Stoikov I.I., Sitdikov R.R., Padnya P.L., Antipin I.S. *Uchenye Zapiski Kazanskogo Universiteta. Seriya Estestvennye Nauki* **2011**, *153*, 190–205 (in Russ.).
38. Fieser L.F., Fieser M. *Reagents for Organic Synthesis*. John Wiley: NY, **1967**. 1457 p.
39. Andreyko E.A., Padnya P.L., Stoikov I.I. *J. Phys. Org. Chem*. **2015**, *28*, 527–535.
40. Andreyko E.A., Padnya P.L., Stoikov I.I. *Colloids Surf., A* **2014**, *454*, 74–83.
41. Vavilova A.A., Nosov R.V., Yagarmina A.N., Mostovaya O.A., Antipin I.S., Konovalov A.I., Stoikov I.I. *Macroheterocycles* **2012**, *5*, 396–403.
42. Andreyko E.A., Padnya P.L., Daminova R.R., Stoikov I.I. *RSC Adv*. **2014**, *4*, 3556–3565.
43. Vavilova A.A., Nosov R.V., Mostovaya O.A., Stoikov I.I. *Macroheterocycles* **2016**, *9*, 294–300.
44. Klochkov V.V., Khairutdinov B.I., Klochkov A.V., Tagirov M.S., Thiele C.M., Berger S., Vershinina I.S., Stoikov I.I., Antipin I.S., Konovalov A.I. *Russ. Chem. Bull*. **2004**, *53*, 1466–1470.
45. Oshovsky G.V., Reinhoudt D.N., Verboom W. *Angew. Chem. Int. Ed*. **2007**, *46*, 2366–2393.
46. Brown D.W., Floyd A.J., Sainsbury M. *Organic Spectroscopy*. John Wiley: NY, **1988**. 258 p.
47. Freifelder D. *Physical Biochemistry, Applications to Biochemistry and Molecular Biology*. W.H. Freeman and Company: San Francisco, 2nd edn, **1982**.
48. Yushkova E.A., Stoikov I.I. *Langmuir* **2009**, *25*, 4919–4928.
49. Manoharan V.N. *Science* **2015**, *349*, 1253751.
50. Tomiyasu H., Zhao J.L., Ni X.L., Zeng X., Elsegood M.R.J., Jones B., Redshaw C., Teat S.J., Yamato T. *RSC Adv*. **2015**, *5*, 14747–14755.
51. Tomiyasu H., Jin C.C., Ni X.L., Zeng X., Redshaw C., Yamato T. *Org. Biomol. Chem.* **2014**, *12*, 4917–4923.

Received 29.12.2016
Revised 25.03.2017
Accepted 28.03.2017