Tetrahedron 65 (2009) 7109–7114

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Supramolecular self-assemblies of stereoisomers of *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide groups at the lower rim with some metal cations

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ARTICLE INFO

Article history:
Received 9 January 2009
Received in revised form 21 May 2009
Accepted 11 June 2009
Available online 18 June 2009

Keywords:
Self-assembly
p-tert-Butyl thiacalix[4]arenes
Molecular recognition
Picrate extraction
Dynamic light scattering (DLS)

ABSTRACT

Novel *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide groups at the lower rim in *cone*, *partial cone* and *1,3-alternate* conformations were synthesized and their receptor properties toward metal ions of p- (Al^{3+}, Pb^{2+}) and d- (Fe^{3+}, Co^{3+}, Ni^{2+}, Cu^{2+}, Ag^{+}, Cd^{2+}) elements were investigated by picrate extraction and dynamic light scattering (DLS). It was shown that the *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide groups are effective extractants of soft metal cations. The complex stoichiometry depended on the receptor configuration. All the *p-tert*-butyl thiacalix[4]arene derivatives with hydrazide fragments were able to form nanoscale aggregates but did not show self-association abilities.

1. Introduction

Chemical and physical properties of nanomaterials differ dramatically from those molecules and depend on the their size, i.e., the quantity of atoms or molecules forming nanoscale structures.[1,2] The establishment of 'structure–property' relationships that control the size, shape and chemical properties of nanoscale aggregates on the spatial level is considered an important problems. Presently, the development of approaches to the synthesis and modification of the particles from 1 nm to 1 μm, and appropriate nanomaterials is one of the priority directions in the nanotechnology area.[1] As a rule, nanoparticles of a definite size can be formed by self-association processes. This can be most effectively achieved by non-covalent self-assembly affected by specially designed ligands spontaneously connecting via metal ions. One of the appropriate classes of host molecule used for this purpose, are macrocyclic polyphenols.[3,4] They have been successfully used for the design of a variety of receptor molecules showing complexation properties. Calix[4]arene-based receptors possessing unusual cavity dimensions have been synthesized via upper and lower rim functionalization. Their complexation properties highly depend on the nature and number of donor atoms of the substituents as well as conformation of the calix[4]arene moiety.[3–8]

In this work, novel *p-tert*-butyl thiacalix[4]arenes containing hydrazide units attached to the lower rim in *cone*, *partial cone* and *1,3-alternate* conformations have been synthesized and their receptor properties toward metal ions of p- (Al^{3+}, Pb^{2+}) and d- (Fe^{3+}, Co^{3+}, Ni^{2+}, Cu^{2+}, Ag^{+}, Cd^{2+}) elements were investigated by picrate extraction and dynamic light scattering (DLS).[9,10]

1.1. Synthesis of stereoisomers of tetrasubstituted at the lower rim *p-tert*-butyl thiacalix[4]arenes containing hydrazide fragments

The hydrazide fragments of the macrocycles are amenable to further modification by various reagents (Fig. 1). The introduction of the hydrazide groups at the lower rim of the *p-tert*-butyl thiacalix[4]arenes **1** were found to be very promising for the development of thiacalix[4]arene derivatives.

The interaction of tetraesters **2** with hydrazine hydrate in various solvents has been investigated (Table 1). The reaction was controlled by TLC. Typically, the stereoisomers of tetraesters **2** interact with the excess of hydrazine hydrate in ethanol.[11,12]

However, the reaction of tetraester **2** with a 10-fold excess of hydrazine hydrate in boiling ethanol led to formation of the target product **1** with high yields of 95% only in the case of the *partial cone*. No reaction was observed for *1,3-alternate*-**2** and the initial tetraester was quantitatively isolated from the reaction mixture. The replacement of the solvent by a mixture of ethanol/THF increased the solubility of initial tetraether-**2** in the *1,3-alternate* conformation

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doi:10.1016/j.tet.2009.06.045

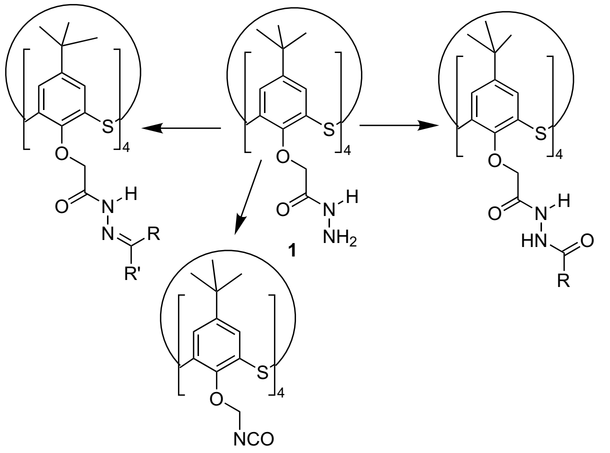

Figure 1. Scheme of possible synthetic modification of stereoisomers of tetrahydrazides on the basis of *p-tert*-butyl thiacalix[4]arene **1**.

Table 1
The reaction of hydrazine hydrates with stereoisomers of tetraesters **2**

Initial compound	Solvent	Excess of $NH_2NH_2 \cdot H_2O$, equiv	Time of reaction, h	Yield, %
1,3-Alternate-**2**	Ethanol	10	48	No reaction
1,3-Alternate-**2**	Ethanol/THF (1:1)	10	48	92
Partial cone-**2**	Ethanol	10	40	95
Cone-**2**	Ethanol	10	14	Inseparable mixture of products
Cone-**2**	Ethanol	2	10	Inseparable mixture of products
Cone-**2**	Ethanol/diethyl ether (1:4)	1.25	30	74
Cone-**2**	Ethanol/diethyl ether (1:4)	1.5	30	87
Cone-**2**	Ethanol/diethyl ether (1:4)	5	20	67
Cone-**2**	Diethyl ether	1.5	30	No reaction

and provided the formation of the target product, i.e., *1,3-alternate*-**1** with high yields up to 92%.

The hydrazinolysis of *cone*-**2** stereoisomer in boiling ethanol resulted in formation of inseparable mixture of the products. It was supposed that the collateral reaction of hydrolysis can take place simultaneously with hydrazinolysis. Decreasing the excess of hydrazine hydrate to 2 equiv did not suppress the side reactions so that inseparable products were isolated from reaction media. The hydrazinolysis of *cone*-**2** tetraester was also investigated in softer conditions, i.e., in the presence of 1.5-fold excess of hydrazine hydrate in boiling diethyl ether. The initial tetraester **2** was quantitatively isolated from the reaction mixture. Probably, a proton donating solvent should be preferably used for this reaction. Indeed, the hydrazinolysis reaction in a mixture of ethanol/diethyl ether (1:4) in the presence of 1.5 equiv of $NH_2NH_2 \cdot H_2O$ resulted in formation of the target product, tetrahydrazide *cone*-**1**, with a yield of 87%. The decrease of hydrazine hydrate excess diminished the amount of initial compound involved in the reaction (yield 74%, 1.25 equiv of $NH_2NH_2 \cdot H_2O$). The increase of hydrazine hydrate/tetraester-**2** ratio leads to the increase of the contribution of other unexpected by-reactions so that the yield of the target product decreased.

The significant difference in reactivity of stereoisomers can be explained by different solubility of initial tetraesters **2**. Poorly soluble *1,3-alternate*-**2** reacts for 48 h whereas more soluble *partial cone*-**2** for 40 h at the temperature of boiling ethanol. *Cone*-**2** is well soluble in most polar solvents and was completely converted within 30 h at the temperature of boiling diethyl ether (Fig. 2). Obviously, the collateral reactions following the hydrazinolysis of *cone*-**2** in strict conditions (ethanol, reflux) can be caused by mutual interactions of hydrogen bonds of hydrazide fragments of the product *cone*-**1**.

The structure and composition of the tetrahydrazides of thiacalix[4]arene obtained in this work were determined by elemental analysis and a number of spectroscopic methods. In the mass-spectra of compounds **1** the peak of a molecular ion was tracked.

The hydrazinolysis of tetraesters *partial cone*-**2** has not been described in the literature. As the reaction was conducted in rather soft conditions, it is necessary to confirm the conformation of the macrocyclic rings of compounds **1**.

Partial cone structures of **1** are notable due to less symmetry of the structures, i.e., amide protons of this macrocycle give three signals in the ^{1}H NMR spectrum (Fig. 3). Signals of three associated amide fragments located on one side of the macrocyclic platform give two singlets (8.96 and 8.50 ppm) with intensity ratio 1:2, respectively. The amide and amine protons of the isolated hydrazide group on the other side of macrocyclic platform give a triplet (4.45 ppm) and a doublet (2.26 ppm), respectively. The chemical shifts in the strong field of the hydrazide protons prove this fragment is included in the macrocyclic cavity formed by the aromatic fragments. Recorded IR-spectra of the *partial cone*-**1** recorded contained absorption bands of associated (3330 cm^{-1}) and non-associated (3425 cm^{-1}) amide groups both in the solid state and solution.

The configuration of the macrocycles obtained by the hydrazinolysis of tetraester *cone*-**2** and *1,3-alternate*-**2** can be determined by correlation of chemical shifts of *tert*-butyl group protons, aromatic ring and oxymethylene protons in the ^{1}H NMR spectra (Fig. 3). In the *1,3-alternate*-**1** conformer, the protons of the –OCH_2 group are located in the shielded zone of neighboring aromatic rings of the macrocycle, and their signals in the ^{1}H NMR spectrum were recorded in higher fields than those of the *cone*-**1** conformer (4.57 and 4.86 ppm, respectively) (Fig. 3).[13] The chemical shifts of aromatic protons were less dependent on the conformation of the macrocyclic ring, they drift to weaker field in the range from *cone*-**1** to *1,3-alternate*-**1** stereoisomer. This is evidence for the shielding effect of neighboring aryl fragments in the cone stereoisomer on the aryl protons of macrocycle ring.[13] The signals of protons of the *tert*-butyl groups of *cone*-**1** stereoisomer were found at higher field in comparison with those of *1,3-alternate*-**1** stereoisomer.[13] Probably, this effect is due to the spatial location of the *tert*-butyl groups of *cone*-**1** stereoisomer, entering the shielding zone of the neighboring fragments of the marocycle.[13] Thus, the structures of those compounds obtained by the hydrazinolysis of tetraester *cone*-**2** and *1,3-alternate*-**2** correspond to *cone*-**2** and *1,3-alternate*-**2** stereoisomers.

The signal of the amide protons of *cone*-**1** is recorded in unusually weaker field (at 9.90 ppm) (Fig. 3), probably, due to strong hydrogen bonding between all the four hydrazide groups located on one side of the macrocyclic platform.[13] This fact was proved by the IR-spectrum of *cone*-**1** which did not contain the absorption bands of non-associated amide groups.[13]

In the *1,3-alternate*-**1** conformer, the signals of the protons of the amide group in the ^{1}H NMR spectrum are recorded as narrow singlets at 7.37 and 3.58 ppm, respectively, probably due to fast conformational exchange between the associated and non-associated forms. In the IR-spectra of *1,3-alternate*-**1** in the solid state and solution (chloroform, 0.05 M) the signals of associated and non-associated amide groups were observed.[13]

Thus, three stereoisomers of *p-tert*-butyl thiacalix[4]arene **1** containing hydrazide fragments were synthesized by the interaction of tetraester-**2** stereoisomers of *p-tert*-butyl thiacalix[4]arene with

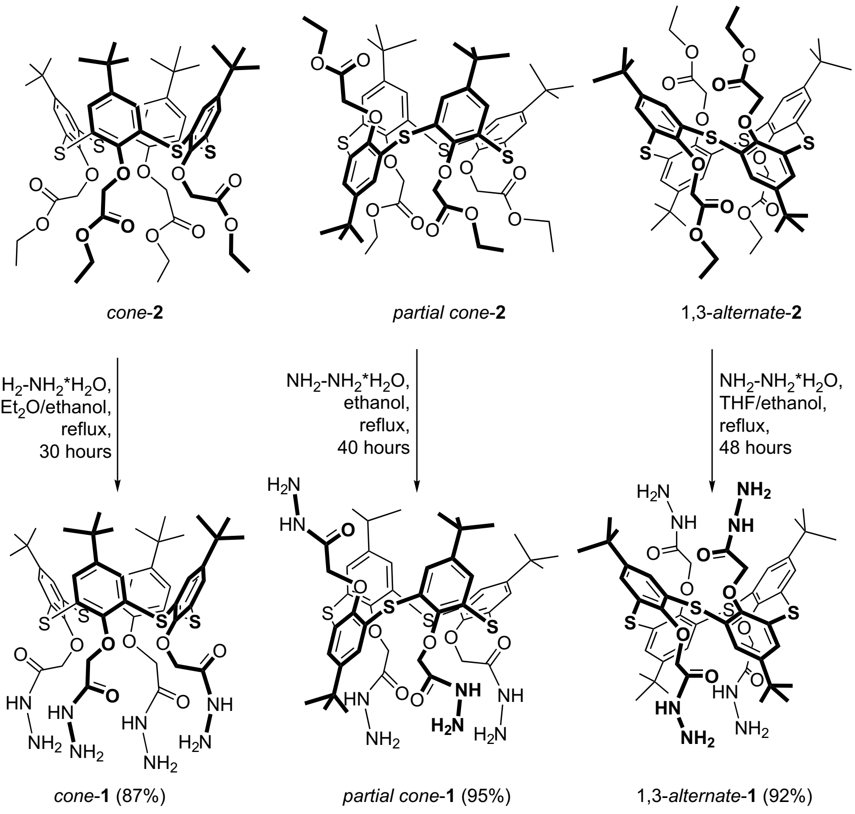

Figure 2. Synthetic approaches to the synthesis of hydrazides of *p-tert*-butyl thiacalix[4]arene by hydrazinolysis of tetraester-**2** stereoisomers with hydrazine hydrate.

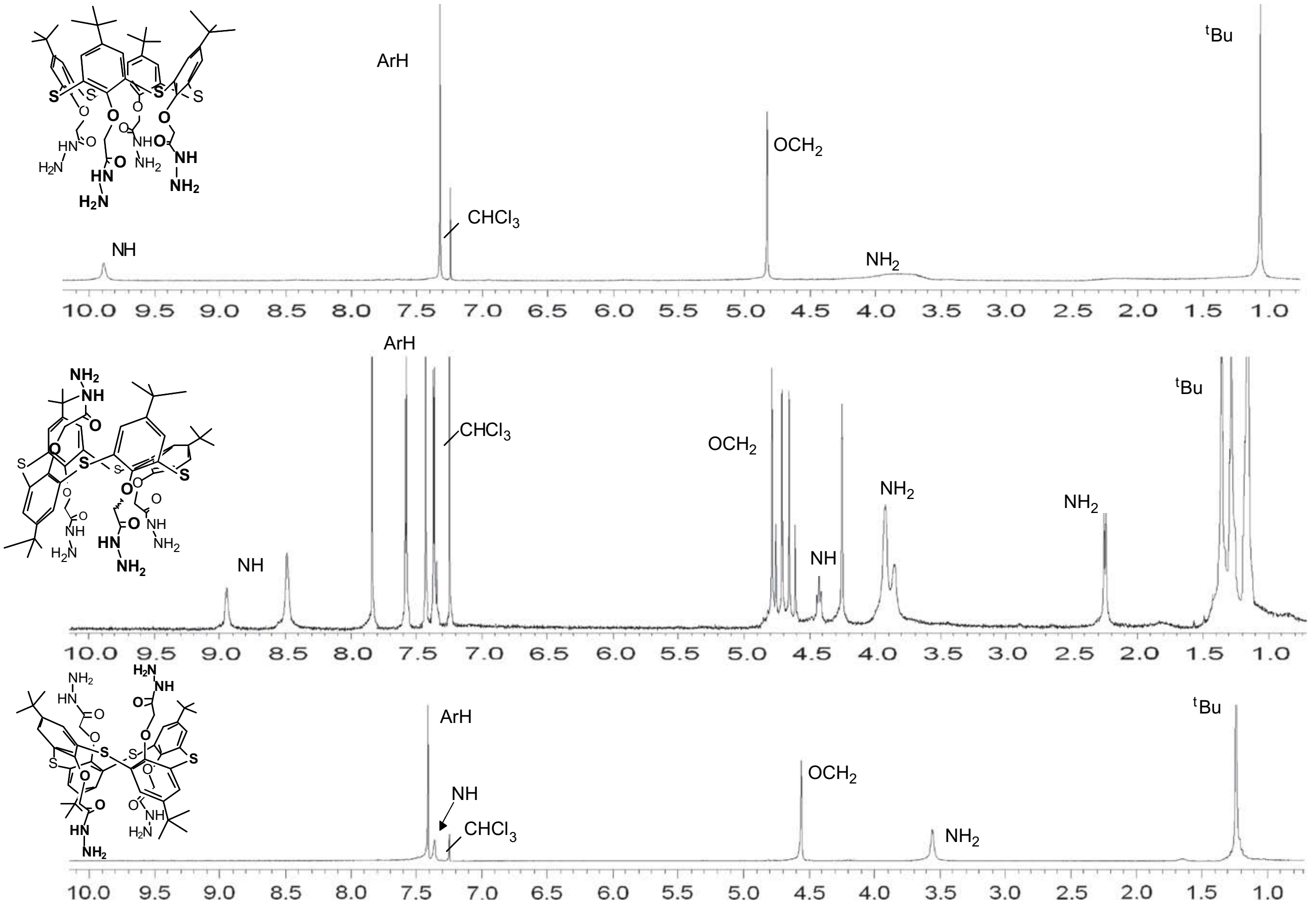

Figure 3. ^{1}H NMR spectra ($CDCl_3$, 300 MHz, δ, ppm) of stereoisomers of *p-tert*-butyl thiacalix[4]arenes **1** functionalized with hydrazide groups.

hydrazine hydrate. The structures of the tetrahydrazides were determined by elemental analysis and spectroscopic methods. The analysis of ^{1}H NMR and IR spectra of the above compounds showed that the hydrazinolysis of tetraesters **2** did not change the conformation of the macrocycles. The chemical environment of the coordination centers responsible for cation (the cavity formed by oxygen atoms of phenyl and carbonyl groups and amine groups of hydrazide fragments) and anion binding (amide protons) differ for all the three stereoisomers of tetrahydrazide **1**.

1.2. Picrate extraction method, the extraction constants log K_{ex} and the complex stoichiometry

The abilities of *p-tert*-butyl thiacalix[4]arene tetrasubstituted with the hydrazide fragments in three conformations for the molecular recognition of alkaline, alkaline-earth metals and p- and d-element ions were estimated using the picrate extraction method.[13] It was shown that the *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide groups are effective extractants of the soft metal cations[13] and the complex stoichiometry depended on the receptor configuration. Each stereoisomer of *p-tert*-butyl thiacalix[4]arenes-**1**, i.e., *cone*, *partial cone* and *1,3-alternate*, forms complexes with different stoichiometry (Table 2). As was established the complex stoichiometry of some cations with macrocycle in *cone* configuration differed from 1:1. Only nickel ions gave a 1:1 complex with the *cone* stereoisomer. Other metals gave complexes with *p-tert*-butyl thiacalix[4]arene of different ratios (2:1—Fe^{3+}, 2:3—Al^{3+}, Pb^{2+}, 1:2—Cu^{2+}, Ag^+, Cd^{2+}, Co^{3+}) (Table 2).

Table 2
Extraction constants (log K_{ex}) and stoichiometry (n) of the complexes of **1** with cations of p- and d-elements in organic phase[a]

	Cations	n	log K_{ex}
Cone (**1**)	Fe^{3+}	0.48±0.02	4.99±0.06
	Ni^{2+}	1.12±0.08	8.05±0.31
	Al^{3+}	1.61±0.10	7.17±0.21
	Pb^{2+}	1.56±0.12	8.44±0.04
	Cd^{2+}	1.88±0.08	10.90±0.33
	Co^{3+}	1.88±0.10	10.73±0.36
	Cu^{2+}	2.30±0.28	13.36±1.17
	Ag^+	1.99±0.15	10.01±0.60
Partial cone (**1**)	Al^{3+}	0.93±0.05	4.91±0.11
	Fe^{3+}	0.81±0.05	5.13±0.11
	Ag^+	1.11±0.04	6.06±0.15
	Ni^{2+}	1.15±0.08	7.09±0.23
	Cu^{2+}	1.23±0.11	7.48±0.37
	Pb^{2+}	1.17±0.07	5.94±0.17
1,3-Alternate (**1**)	Cu^{2+}	0.42±0.03	3.68±0.08
	Ag^+	1.22±0.06	5.78±0.21
	Fe^{3+}	0.43±0.14	3.82±0.29

'±' Standard deviation.

[a] Extraction conditions: $[L]_{org.,init}=10^{-4}$ to 2.5×10^{-3} M, $[MPic_n]_{aq,init}=2.32\times10^{-4}$ M.[14]

The stoichiometry of *partial cone* and *1,3-alternate* complexes is either 2:1 or 1:1. It means that in this case both pairs of functional groups interact with a guest ion independently of each other and structural changes caused by the ion complexation on one side of *1,3-alternate* and *partial cone* do not cause significant hindrance for binding on the other side. For *p-tert*-butyl thiacalix[4]arenes-**1** in *partial cone* and *1,3-alternate* conformations, only 2:1 complexes of *1,3-alternate* with Cu^{2+} and Fe^{3+} cations were found and log K_{ex} did not exceed 3.8. The formation of 1:1 complexes is typical for all the three stereoisomers with silver (*partial cone*, *1,3-alternate*) and nickel (*cone*, *partial cone*), thus the values of extraction constants logarithms did not depend on the conformation of the receptors and varied from 5.8 to 8.1. The amount of the extracted cations essentially decreased in the range *cone*, *partial cone*, *1,3-alternate*.

1.3. Self-assembly of aggregates consist of *p-tert*-butyl thiacalix[4]arenes derivatives and metal cations in organic phase

The ability of the systems consisting of *p-tert*-butyl thiacalix[4]arenes **1** and nitrates of p- and d-elements to self-assemble has been investigated by dynamic light scattering (DLS) in the same conditions as picrate extraction. The hydrodynamic diameters of the nanoaggregates and polydispersity index of the systems were determined 3 h after the solution preparation at 20 °C. The kinetic stability of the systems was proved in repeated measurements performed under similar conditions after 28 h. Figure 4 shows the intensity size distributions for the complex of thiacalix[4]arene functionalized with hydrazide units in *1,3-alternate* configuration with iron cations.

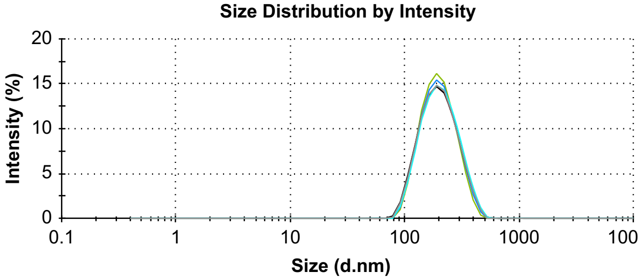

Figure 4. Intensity size distributions for the system consisting of molecular *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide units in *1,3-alternate* configuration and iron cations in CH_2Cl_2 (HPLC).

All the *p-tert*-butyl thiacalix[4]arene derivatives with hydrazide fragments are able to form nanoscale aggregate with some metal cations but they did not show self-association features (Table 3–5).

The decrease in the complexation ability determined by the picrate extraction was observed for the stereoisomers in the range

Table 3
Size of aggregates (hydrodynamic diameter of peak 1, 2, 3 mean intensity—d_1, d_2, d_3, nm) and peak 1, 2, 3 area intensity (S_1, S_2, S_3, %) for the system consisting of *p-tert*-butyl thiacalix[4]arene derivative **1** in *cone* conformation and cations of p- and d-elements in CH_2Cl_2 (HPLC), polydispersity index (PDI)

Cations	d_1, nm/S_1, %		d_2, nm/S_2, %		d_3, nm/S_3, %		PDI	
	3 h	28 h	3 h	28 h	3 h	28 h	3 h	28 h
Al^{3+}	—	—	—	—	—	—	—	—
Co^{3+}	2.1±2.0/38.8±39.9	8.0±0.6/56.2±3.9	526.5±917.4/61.2±39.9	629.7±129.8/43.8±3.9	—	—	0.50±0.45	0.50±0.05
Fe^{3+}	—	—	137.7±2.6/100	110.5±7.5/99.6±0.6	—	5385.0±2223.6/0.4±0.5	0.05±0.02	0.13±0.02
Ni^{2+}	2.1±5.7/8.3±13.6	5.0±1.3/16.7±14.1	224.3±23.1/91.7±13.6	457.3±39.3/79.4±12.6	—	3850.0±796.9/3.9±4.2	0.30±0.20	0.71±0.22
Cu^{2+}	5.3±1.7/30.6±2.5	5.7±1.6/37.4±21.1	187.5±15.7/50.8±1.6	102.8±26.8/47.8±20.6	4215.0±437.2/18.6±4.0	4960.0±783.4/14.2±11.9	0.18±0.06	0.32±0.08
Cd^{2+}	—	8.5±4.9/11.4±6.9	—	142.3±69.6/82.2±13.7	—	4784.5±1177.3/6.4±9.0	—	0.19±0.04
Ag^+	3.9±4.0/21.6±9.2	8.5±2.6/11.2±2.8	244.2±206.0/20.6±22.6	56.3±8.4/87.7±3.0	2572.0±1086.5/57.8±24.4	5308.7±684.5/1.1±1.4	1.00±0.00	0.28±0.06
Pb^{2+}	—	—	—	—	—	—	—	—

'±' Standard deviation.
'—' No aggregates observed.

Table 4
Size of aggregates (hydrodynamic diameter of peak 1, 2, 3 mean intensity—d_1, d_2, d_3, nm) and peak 1, 2, 3 area intensity (S_1, S_2, S_3, %) for the system consisting of *p-tert*-butyl thiacalix[4]arene derivative **1** in *partial cone* conformation and cations of p- and d-elements in CH_2Cl_2 (HPLC), polydispersity index (PDI)

Cations	d_1, nm/S_1, %		d_2, nm/S_2, %		d_3, nm/S_3, %		PDI	
	3 h	28 h	3 h	28 h	3 h	28 h	3 h	28 h
Al^{3+}	—	—	—	345.1±50.2/98.4±2.4	—	4493.3±1686.3/1.6±2.4	—	0.24±0.08
Co^{3+}	—	—	—	—	—	—	—	—
Fe^{3+}	—	—	153.7±25.1/81.8±33.2	224.1±11.6/96.8±3.2	4393.3±2593.7/18.2±33.2	5431.3±146.9/3.2±3.2	0.36±0.31	0.37±0.07
Ni^{2+}	—	1.0±0.1/15.9±10.6	272.5±65.3/100	389.7±98.3/84.1±10.6	—	—	0.26±0.14	0.30±0.15
Cu^{2+}	—	1.1±1.0/21.7±14.0	403.8±102.9/87.8±8.8	335.6±237.3/63.8±19.0	3434.0±369.7/11.2±7.2	4249.7±534.7/14.5±21.3	0.43±0.15	0.33±0.14
Cd^{2+}	—	—	—	—	—	—	—	—
Ag^{+}	—	—	—	63.7±6.1/99.3±0.7	—	4642.5±625.4/0.7±0.7	—	0.22±0.02
Pb^{2+}	—	1.2±4.7/8.7±10.2	—	493.9±935.8/91.3±10.2	—	—	—	0.34±0.01

'±' Standard deviation.
'—' No aggregates observed.

Table 5
Size of aggregates (hydrodynamic diameter of peak 1, 2, 3 mean intensity—d_1, d_2, d_3, nm) and peak 1, 2, 3 area intensity (S_1, S_2, S_3, %) for the system consisting of *p-tert*-butyl thiacalix[4]arene derivative **1** in *1,3-alternate* conformation and cations of p- and d-elements in CH_2Cl_2 (HPLC), polydispersity index (PDI)

Cations	d_1, nm/S_1, %		d_2, nm/S_2, %		d_3, nm/S_3, %		PDI	
	3 h	28 h	3 h	28 h	3 h	28 h	3 h	28 h
Al^{3+}	—	—	—	—	—	—	—	—
Co^{3+}	—	—	—	—	—	—	—	—
Fe^{3+}	—	—	183.8±64.5/100	233.0±24.3/100	—	—	0.15±0.17	0.06±0.03
Ni^{2+}	—	—	—	—	—	—	—	—
Cu^{2+}	—	—	788.3±205.7/100	210.1±103.7/94.0±9.3	—	3520.0±762.4/6.0±9.3	0.55±0.87	0.29±0.16
Cd^{2+}	—	—	—	—	—	—	—	—
Ag^{+}	1.4±0.7/13.3±10.8	—	348.8±91.5/86.7±10.8	131.4±19.9/99.8±0.3	—	5120.0±113.8/0.2±0.3	0.57±0.16	0.15±0.01
Pb^{2+}	—	—	—	—	—	—	—	—

'±' Standard deviation.
'—' no aggregates observed.

cone, *partial cone*, *1,3-alternate* together with the number of cations able to form aggregates with the macrocycles. One can see (Table 3–5) all investigated compounds **1** form kinetically stable nanoscale particles with silver(I), copper(II) and iron(III) cations.

Thus, the hydrodynamic diameter of particles formed with silver cations varies from 8.5 to 131.0 nm, that with copper from 1.1 to 211.0 nm, and with iron from 111.0 to 233.0 nm. Also when aggregation was measured at various time intervals, the polydispersity index was decreasing due to kinetic stabilization of system. The opposite tendency was observed for the systems consisting of *p-tert*-butyl thiacalix[4]arene derivatives and nickel cations. The polydispersity index in these systems increased. Nanoscale aggregates consisting of *p-tert*-butyl thiacalix[4]arenes **1** and silver, cobalt, nickel and copper cations have diameters of about 1.0–5.3 nm, the equilibrium of their formation is shifted toward lower accumulation, the dispersion intensity of these particles increases. It was shown that the decrease of log K_{ex} for the *partial cone* with aluminum(III) and lead(II) cations lead to the decrease of aggregating rate but not for iron(III) cations. Only *p-tert*-butyl thiacalix[4]arenes in the *cone* configuration are able to form nanoscale particles with cadmium(II), cobalt(II), copper(II) and silver(I) cations. For them, high values of the extraction constant (log $K_{ex}=10$) and stoichiometry ratio (cation/*p-tert*-butyl thiacalix[4]arene—1:2) were determined by the picrate extraction method. These systems are able to form several particles with various hydrodynamic diameters. *p-tert*-Butyl thiacalix[4]arene **1** in the *cone* configuration does not form aggregates with aluminum(III) and lead(II) cations. As was shown, this system had another values of stoichiometry ratio (cation/*p-tert*-butyl thiacalix[4]arene—2:3) determined by the picrate extraction method. However, *partial cone* stereoisomer **1** with a different orientation of the binding site is able to form nanoscale particles with these cations, even with low extraction constants. Irrespective of the configuration, all the stereoisomers of *p-tert*-butyl thiacalix[4]arenes form nanoscale particles with cations of p- and d-elements for which identical values of the stoichiometry were determined by picrate extraction. It should be mentioned as a general tendency, that a decrease in the size of the substrates results in an increase of the hydrodynamic size aggregates.

Thus, the ability of *p-tert*-butyl thiacalix[4]arenes to form nanoscale aggregates with cations of p- and d-elements depends on the macrocycle configuration, possible paths of the coordination of the metal cations with the ligands, the size of cations, and also on the stoichiometry and value of extraction constants of the systems.

2. Conclusion

Thus, new *p-tert*-butyl thiacalix[4]arenes functionalized with hydrazide groups at the lower rim in *cone*, *partial cone* and *1,3-alternate* conformations were synthesized and their receptor properties for metal ions of p- (Al^{3+}, Pb^{2+}) and d- (Fe^{3+}, Co^{3+}, Ni^{2+}, Cu^{2+}, Ag^{+}, Cd^{2+}) elements were studied using picrate extraction method and dynamic light scattering (DLS). As was established, the investigated thiacalix[4]arenes are effective extractants of soft metal cations. The complex stoichiometry depended on the receptor configuration. All the *p-tert*-butyl thiacalix[4]arene derivatives with hydrazide fragments are able to form nanoscale aggregate on the addition of metal cations but did not show self-association abilities. It was shown that the ability of *p-tert*-butyl thiacalix[4]arenes to form nanoscale aggregates with cations of p- and d-elements depends on the macrocycle configuration, possible paths of the coordination of the metal cations with the ligands and the size of cations.

3. Experimental

3.1. 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(hydrazidocarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene *cone* (1)

Cone (**2**) (1.06 g, 1.05 mmol) was put into round-bottom flask and diethyl ether (20 mL), ethanol (5 mL) and hydrazine hydrate

(0.3 mL, 6.3 mmol) were added and refluxed for 30 h. Then the reaction mixture was cooled to room temperature, the sediment (colorless crystals) was filtered, washed by diethyl ether (3×10 mL) and dried at lower pressure. The remainder was crystallized from isopropanol. Yield: 0.82 g (87%). Mp: 258 °C. ^{1}H NMR (300 MHz, 373 K, $CDCl_3$) δ 9.90 (s, 4H; CONH), 7.34 (s, 8H; Ar–H), 4.86 (s, 8H; OCH_2CO), 3.95 (s, 8H; NH_2), 1.10 (s, 36H; *t*-Bu–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 158.0, 147.9, 134.8, 128.2, 75.0, 34.1, 30.9. IR (KBr) ν_{max} 1266 (COC), 1675 (C=O), 3324 (NH). IR (0.05 M, $CHCl_3$) ν_{max} 1265 (COC), 1670 (C=O), 3330 (NH). MS MALDI-TOF, *m*/*z*: 1010 $[M+H]^+$, 1032 $[M+Na]^+$. MS (ESI): calcd for $[M+H]^+$ *m*/*z*=1009.4, calcd for $[M+Na]^+$ *m*/*z*=1031.4, calcd for $[M+K]^+$ *m*/*z*=1047.3, found $[M+H]^+$ *m*/*z*=1009.5, $[M+Na]^+$ *m*/*z*=1031.4, $[M+K]^+$ *m*/*z*=1047.3. El. Anal. Calcd for $C_{48}H_{64}N_8O_8S_4$: C, 57.12; H, 6.39; N, 11.10; S, 12.71. Found: C, 57.11; H, 6.66; N, 15.37; S, 9.88.

3.2. 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(hydrazidocarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene *partial cone* (1)

Partial cone (**2**) (1.06 g, 1.05 mmol) was put into a round-bottom flask and ethanol (15 mL) and hydrazine hydrate (2.0 mL, 41.0 mmol) were added and refluxed for 40 h. Then the solvent was evaporated at lower pressure, the dry sediment was dissolved in dichloromethane (20 mL), mixed with water (50 mL) for 30 min. The organic layer was separated, washed with water (3×15 mL) and dried (mol. sieves, 3 Å). The remainder was crystallized from ethanol/methylene chloride. Yield: 0.90 g (95%). Mp: 226 °C. ^{1}H NMR (300 MHz, 373 K, $CDCl_3$) δ 8.96 (s, 1H; CONH), 8.50 (s, 2H; CONH), 7.85 (s, 2H; Ar–H), 7.59 (d, $^{4}J_{HH}$=2.6 Hz, 2H; Ar–H), 7.44 (s, 2H; Ar–H), 7.38 (d, $^{4}J_{HH}$=2.6 Hz, 2H; Ar–H), 4.80 (s, 2H; OCH_2CO), 4.64, 4.75 (AB-qv, $^{2}J_{HH}$=14.2 Hz, 4H; OCH_2CO), 4.45 (t, $^{3}J_{HH}$=4.3 Hz, 1H; CONH), 4.27 (s, 2H; OCH_2CO), 3.94 (s, 4H; NH_2), 3.86 (s, 2H; NH_2), 2.26 (d, $^{3}J_{HH}$=4.3 Hz, 2H; NH_2), 1.37 (s, 9H; *t*-Bu–H), 1.30 (s, 9H; *t*-Bu–H), 1.17 (s, 18H; *t*-Bu–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 168.3, 165.5, 158.4, 156.5, 152.4, 149.6, 148.8, 137.1, 135.5, 131.1, 128.4, 128.3, 127.8, 126.9, 126.0, 74.1, 72.6, 64.6, 34.7, 31.0, 34.5, 34.3, 31.2. IR (KBr) ν_{max} 1260 (COC), 1680 (C=O), 2962 (Ar–H), 3217–3545 (N–H). IR (0.05 M, $CHCl_3$) ν_{max} 1265 (COC), 1670 (C=O), 3330, 3416 (NH). MS MALDI-TOF, *m*/*z*: 1010 $[M+H]^+$, 1032 $[M+Na]^+$. El. Anal. Calcd for $C_{48}H_{64}N_8O_8S_4$: C, 57.12; H, 6.39; N, 11.10; S, 12.71. Found: C, 56.94; H, 6.56; N, 11.10; S, 12.91.

3.3. 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(hydrazidocarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene *1,3-alternate* (1)

1,3-Alternate (**2**) (1.06 g, 1.05 mmol) was put into a round-bottom flask and ethanol (15 mL), THF (15 mL) and hydrazine hydrate (2.0 mL, 41.0 mmol) were added and refluxed for 48 h, concentrated at lowered pressure to 10 mL. After that, diethyl ether (10 mL) was added. The sediment (white crystals) was filtered, washed by diethyl ether (3×5 mL), dried at lower pressure. Further, the sediment was dissolved in 10 mL of methylene chloride and mixed with 20 mL of water. The organic layer was separated, washed by water (3×10 mL), dried (mol. sieves, 3 Å) and evaporated in vacuum. The remainder was crystallized from the ethyl alcohol/methylene chloride. Yield: 0.87 g (92%). Mp: 274 °C. ^{1}H NMR (300 MHz, 373 K, $CDCl_3$) δ 7.41 (s, 8H; Ar–H), 7.37 (s, 4H; CONH), 4.57 (s, 8H; OCH_2CO), 3.58 (s, 8H; NH_2), 1.26 (s, 36H; *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 154.7, 148.8, 128.5, 127.2, 68.3, 34.5, 31.3. IR (KBr) ν_{max} 1270 (COC), 1676 (C=O), 3416, 3320 (NH). IR (0.05 M, $CHCl_3$) ν_{max} 1263 (COC), 1676 (C=O), 3415, 3321 (NH). MS MALDI-TOF, *m*/*z*: 1011 $[M+H]^+$, 1033 $[M+Na]^+$. El. Anal. Calcd for $C_{48}H_{64}N_8O_8S_4$: C, 57.12; H, 6.39; N, 11.10; S, 12.71. Found: C, 56.91; H, 6.55; N, 10.86; S, 12.59.

3.4. Determination of extraction parameters

3.4.1. *Extraction constants log K_{ex} and stoichiometry of the complexes*

Extraction experiments were performed at various ligand concentrations (1×10^{-4} to 2.5×10^{-4} M). Silver picrate was prepared by stepwise addition of a 1.6×10^{-2} M of $AgNO_3$ to 2.32×10^{-4} M aqueous picric acid solution. In this case, the solutions were weakly acidic (pH 4). Other picrates were prepared by stepwise addition of a 3.02×10^{-4} M of $Al(NO_3)_3$, $Pb(NO_3)_2$, $Fe(NO_3)_3$, $Co(NO_3)_3$, $Ni(NO_3)_2$, $Cu(NO_3)_2$, $Cd(NO_3)_2$ to 2.32×10^{-4} M aqueous picric acid solution; in this case, the solutions were weakly acidic (pH 4). The log K_{ex} and n values were determined from the plot of $\log(a/1-a)$ versus $\log[L]_{org.}$ as described elsewhere.[15] Three independent experiments were carried out for each system.

3.5. Dynamic light scattering (DLS)

The particle sizes were determined by Zetasizer Nano ZS instrument at 20 °C. The instrument contains a 4 mW He–Ne laser operating at a wavelength of 633 nm and incorporates non-invasive backscatter optics (NIBS). The measurements were performed at the detection angle of 173° and the measurement position within the quartz cuvette was automatically determined by the software. The solutions of the investigated systems were prepared by addition of silver nitrate to 10 mL of 10^{-4} M solution of thiacalixarene derivatives in CH_2Cl_2 (HPLC). The mixture was mechanically shaken for 2 h and then magnetically stirred in thermostated water bath at 20 °C for 1 h. The final concentration of silver nitrate in 10 ml CH_2Cl_2 (HPLC) was 2.32×10^{-4} M. Three independent experiments were carried out for each combination of a ligand and metal nitrate.

Acknowledgements

The financial support from RFBR (08-03-91106-CRDF), CRDF (RUC1-2910-KA-07), joint program of CRDF and Ministry of Science and Education of Russian Federation 'Fundamental Researches and Higher Education' (REC-007) is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.045.

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