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The synthesis of new amphiphilic *p*-*tert*-butylthiacalix[4]arenes containing peptide fragments and their interaction with DNA†

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New water-soluble *p*-*tert*-butylthiacalix[4]arenes containing peptide and quaternary ammonium fragments in *cone* and 1,3-*alternate* conformations were synthesized and characterized. The interaction of the macrocycles with DNA was studied by UV-spectroscopy, DLS and TEM. It was shown that the interaction of the self-associates based on *p*-*tert*-butylthiacalix[4]arenes tetrasubstituted at the lower rim with glycine and quaternary ammonium fragments in *cone* and 1,3-*alternate* conformations with DNA led to the formation of particles of about 99–192 nm in size.

Introduction

Synthesis of the supramolecular systems for recognition of biomacromolecules is one of the promising fields of investigations in supramolecular chemistry and nanotechnology.[1–24] These systems can be applied for the formation of sensors, catalysts, biomimetic systems, selective extractants and drug delivery systems.[25–32] Synthetic receptors and aggregates based on them can be used as supramolecular systems.[6–24,33–37] The molecular platform for the synthesis of this type of receptors should meet certain requirements: first, it should be easily obtained and modified; second, it should recognize biomacromolecules. Calix[4]arene has been one of the most actively studied molecular platforms in the last decade.[38–51] The ability of synthetic receptors based on calixarene platform to recognize biopolymers is determined by the receptor conformation, type of functional groups and the ability of a macrocycle to self-assemble. According to the literature, calixarenes that are able to interact with biomacromolecules contain guanidinium, pyridinium, quaternary ammonium substituents,[52–56] amino groups,[57] amino acid[58] and phthalimide fragments.[59] It was also shown that the nanoscale particles based on amphiphilic calixarenes can form stable complexes with DNA.[60–62]

Previously, the formation of water-soluble supramolecular particles based on amphiphilic *p*-*tert*-butylthiacalix[4]arenes containing amide and quaternary ammonium fragments with alkyl, aryl, ester and phthalimide groups at the nitrogen atom in *cone* conformation was shown and applied for protein recognition.[63] According to the results[54–56,63] it can be expected that self-associates based on amphiphilic *p*-*tert*-butylthiacalix[4]-arenes containing the $-N^{+}R_3$ fragment in different conformations are able to interact with anionic macromolecules like DNA. To examine this hypothesis, the amphiphilic *p*-*tert*-butylthiacalix[4]arenes containing peptide and quaternary ammonium fragments in two conformations, *i.e. cone* and 1,3-*alternate*, were selected for the synthesis. The introduction of ammonium groups and peptide fragments in the structure of macrocycles is necessary for the creation of amphiphilic receptors based on *p*-*tert*-butylthiacalix[4]arene and also for the interaction of the macrocycles with DNA by the formation of hydrogen bonds and electrostatic forces. Amide fragments in the structure of macrocycles are necessary to create aggregates by self-association inspired by the formation of hydrogen bonds. The formation of nanoscale aggregates based on *p*-*tert*-butylthiacalix[4]arenes will increase the efficiency of the interaction of supramolecular systems with DNA by increasing the number of simultaneous multiple non-covalent interactions with biomacromolecules. Depending on the conformation of the calixarene (*cone* or 1,3-*alternate*), the formation of different types of self-associates can be observed. According to the literature,[64] macrocycles in the *cone* conformation (all four substituents located at one side of the macrocyclic platform) are able to form spherical particles – micelles, and in the case of macrocycles in 1,3-*alternate* conformation (two substituents located on each side of the macrocyclic ring) the formation of

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vesicles occurred. Thus, the influence of the structure and conformation of *p-tert*-butylthiacalix[4]arenes on their interaction with DNA will also be studied.

In this work, the synthesis of *p-tert*-butylthiacalix[4]arenes tetrasubstituted at the lower rim with peptide and quaternary ammonium groups in *cone* and 1,3-*alternate* conformations and the ability of the macrocycles to interact with DNA in aqueous solutions are described.

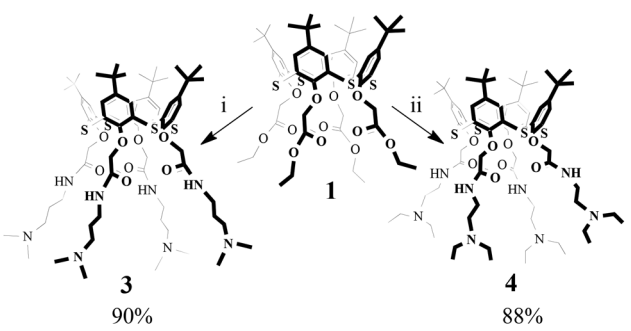
Results and discussion

Synthesis of quaternary ammonium salts based on *p-tert*-butylthiacalix[4]arene containing peptide fragments

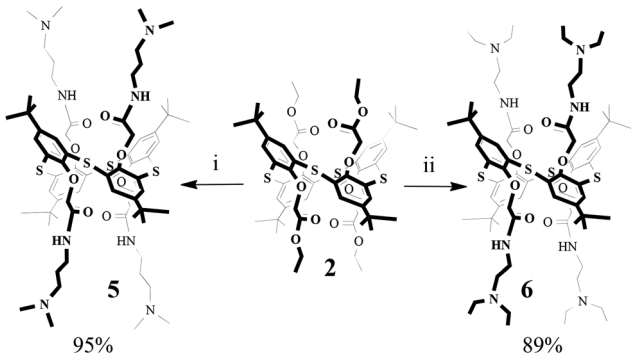
To synthesize target products, *i.e. p-tert*-butylthiacalix[4]arenes containing quaternary ammonium groups, the introduction of amide fragments in the structure of macrocycles followed by the interaction of amine groups with the halogenoalkanes was studied. According to the literature procedure,[65] compounds **3** and **4** were synthesized by the reactions of tetraester **1** in *cone* conformation with *N*,*N*-diethylethane-1,2-diamine and *N*,*N*-dimethylpropane-1,3-diamine (Scheme 1).

To synthesize *p-tert*-butylthiacalix[4]arenes containing tertiary amino groups in 1,3-*alternate* conformation, the reactions of tetraester **2** with *N*,*N*-diethylethane-1,2-diamine and *N*,*N*-dimethylpropane-1,3-diamine were studied (Scheme 2). The reactions were carried out in toluene-methanol (1 : 1) under 72 h reflux. Compounds **5** and **6** were obtained in excellent yields.

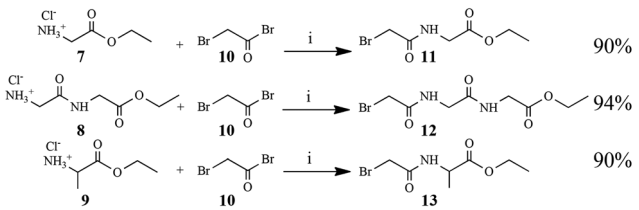
To synthesize alkylating reagents necessary to obtain quaternary ammonium salts based on *p-tert*-butylthiacalix[4]arene, according to the literature procedure,[66] the acylation of glycine ethyl ester hydrochloride **7**, glycylglycine ethyl ester hydrochloride **8** and L-alanine ethyl ester hydrochloride **9** with bromoacetyl bromide **10** was carried out in benzene at room temperature (Scheme 3). *N*-Bromoacetyl-glycine ethyl ester **11**, *N*-bromoacetyl-glycylglycine ethyl ester **12** and *N*-bromoacetyl-L-alanine ethyl ester **13** were obtained. The alkylating reagents **11–13** were chosen because of the presence of amino acid groups in their structure: glycine as a simple achiral amino acid and L-alanine as the closest chiral analogue of glycine.



Scheme 1 (i) $NH_2(CH_2)_3NMe_2$, $CH_3OH/C_6H_5CH_3$, reflux[65]; (ii) $NH_2(CH_2)_2NEt_2$, $CH_3OH/C_6H_5CH_3$, reflux.[65]



Scheme 2 (i) $NH_2(CH_2)_3NMe_2$, $CH_3OH/C_6H_5CH_3$, reflux; (ii) $NH_2(CH_2)_2NEt_2$, $CH_3OH/C_6H_5CH_3$, reflux.

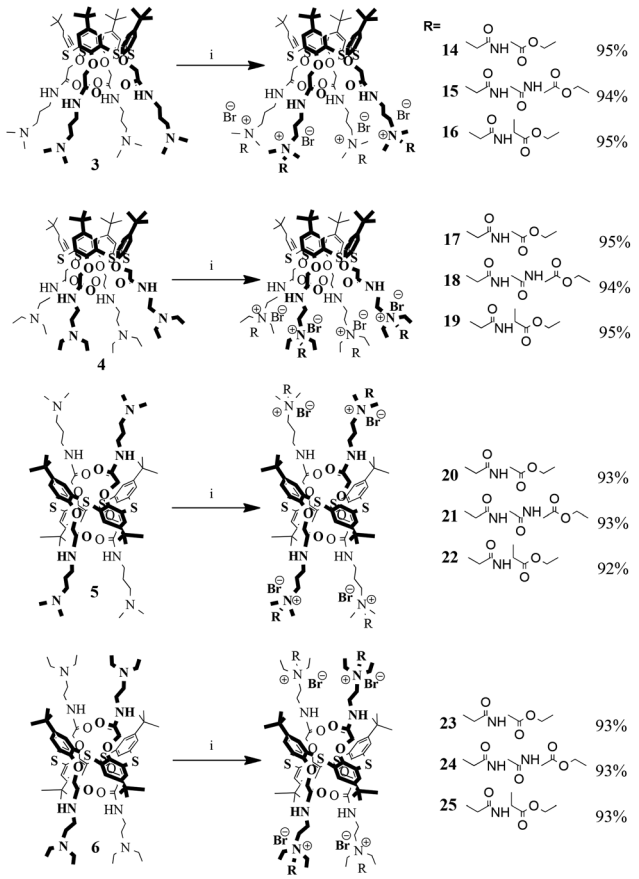


Scheme 3 (i) $NaHCO_3$, C_6H_6/H_2O.[66]

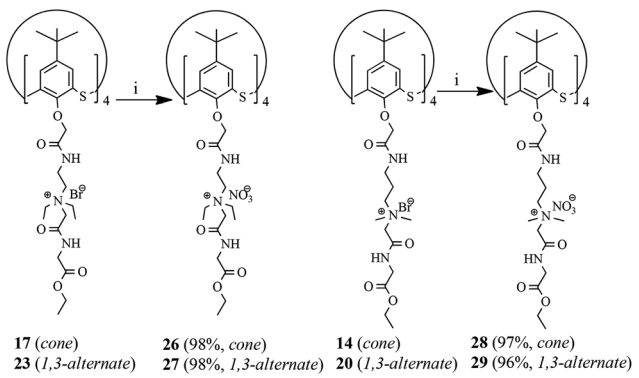
The quaternary ammonium salts **14–25** containing amino acid and peptide fragments were obtained in excellent yields by the interaction of the *p-tert*-butylthiacalix[4]arenes **3–6** containing tertiary amino groups with methyl and ethyl fragments at the nitrogen atom in *cone* and 1,3-*alternate* conformations with alkylating agents **11–13** (Scheme 4). The reactions were carried out in acetonitrile under 8 h reflux.

To study the complexing properties of *p-tert*-butylthiacalix[4]arenes containing amide, quaternary ammonium and amino acid fragments, the model salts **26–29** were obtained. The replacement of bromide anions in quaternary ammonium salts **14**, **17**, **20**, **23** by nitrate anions is necessary to avoid the formation of hydrogen bonds between bromide anions and biomacromolecules. It would significantly complicate the determination of the interaction between *p-tert*-butylthiacalix[4]arenes and DNA.[67,68] The interaction of quaternary ammonium salts **14**, **17**, **20**, **23** with silver nitrate in acetonitrile at room temperature produced the compounds **26–29** with quantitative yields (Scheme 5). The absence of bromide anions in the structure of obtained macrocycles was confirmed by ion chromatography.

Thus, water-soluble *p-tert*-butylthiacalix[4]arenes containing peptide and quaternary ammonium fragments were synthesized as potential receptors for biomacromolecules. The structure and composition of the synthesized compounds **5**, **6**, **14–29** were determined by ^1H and ^{13}C NMR, IR spectroscopy, mass spectrometry and elemental analysis.



Scheme 4 (i) RBr, CH_3CN, reflux.



Scheme 5 (i) $AgNO_3$, CH_3CN.

The study of complexing properties of *p-tert*-butylthiacalix[4]-arenes tetrasubstituted at the lower rim with peptide fragments toward DNA

The interaction of synthesized thiacalix[4]arenes **26–29** with the DNA from salmon sperm in 5 mM Tris-HCl buffer was studied by UV spectroscopy. The DNA from this source was chosen as a model substrate because of its relatively low molecular weight and small size. To determine optimal experimental conditions, electronic spectra of the compounds were studied. It was found that maximum absorption of DNA and calix[4]arenes **26–29** coincide at 260 nm. In order to specify optimal experimental conditions for studying the interaction of the macrocycles with DNA, the effect of concentration on the absorption spectra of the substances was studied. Based on these results, 0.019 mg ml^{-1} concentration of DNA was used in the following experiments. The intensity of absorption of DNA taken at this concentration was about 0.5 and allowed varying the concentration of the compounds in a wide range.

It was shown by UV spectroscopy that the interaction between thiacalix[4]arenes **26–29** and DNA led to a hypochromic effect at 260 nm, however, the shift of maximum of absorption was not observed. According to the literature,[69] the decrease of the absorption intensity (hypochromic effect) during the interaction of receptors with DNA can be explained by changing of the structure of the polynucleotide. It is interesting to note that the rise of baseline in UV spectra was observed during the interaction of thiacalix[4]arenes **26–29** with DNA. Probably, it can be due to the aggregation of the DNA with thiacalix[4]arenes. Furthermore, the solutions of biomacromolecules were not able to absorb and scatter light (Rayleigh scattering); hence, they could exert artificially increased absorption. Fig. 1 shows the absorption spectrum of DNA, thiacalix[4]arene **29** and their mixture as an example.

The data obtained demonstrate the aggregation of synthetic macrocycles **26–29** with DNA. According to the results, we would like to confirm an interaction of a biopolymer with receptors that leads to the formation of aggregates and to estimate their size by dynamic light scattering (DLS).

DLS is widely used to study colloidal particles, macromolecules and molecular assemblies.[70] To confirm the aggregation of macrocycles with DNA, the size of particles based on thiacalix[4]arene/DNA was determined, and self-association of DNA and compounds **26–29** was studied.

It was shown by DLS that in the absence of macrocycles the particles with a hydrodynamic diameter of about 5 nm were observed in DNA solution (0.048 mg ml^{-1}). However, the value of polydispersity was high (PDI ~ 0.5).

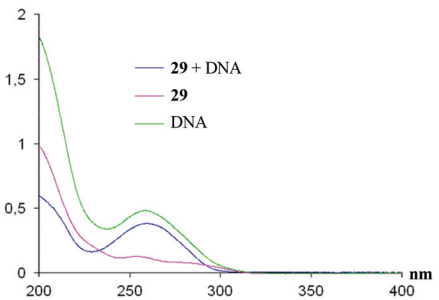


Fig. 1 UV spectra of thiacalix[4]arene **29** (1×10^{-4} M), DNA (0.019 mg ml^{-1}) and mixture – DNA (0.019 mg ml^{-1}) and thiacalix[4]arene **29** (1×10^{-4} M).

Table 1 Size of particles and polydispersity index obtained with macrocycles **26–29** at different concentrations in Tris-HCl buffer (pH 7.5)

The concentration of thiacalix[4]arene	Particle size (d, nm); PDI			
	26	**27**	**28**	**29**
1×10^{-3} M	141.6 (0.13)	99.7 (0.21)	75.4 (0.21)	92.8 (0.19)
8×10^{-4} M	161.6 (0.18)	104.3 (0.22)	145.5 (0.22)	139.9 (0.20)
1×10^{-4} M	208.9 (0.26)	207.4 (0.28)	201.2 (0.23)	425.7 (0.23)
1×10^{-5} M	389.5 (0.37)	239.5 (0.40)	244.7 (0.25)	824.5 (0.40)
1×10^{-6} M	488.7 (0.40)	896.0 (0.41)	453.7 (0.40)	1004.0 (0.41)

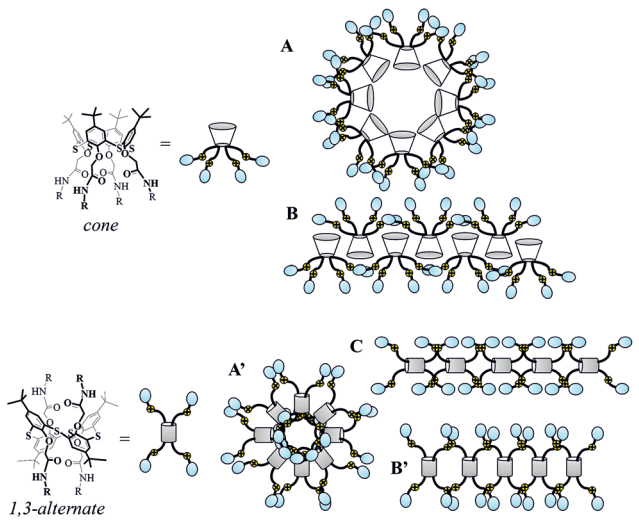


Fig. 2 Possible paths for the formation of supramolecular associates.

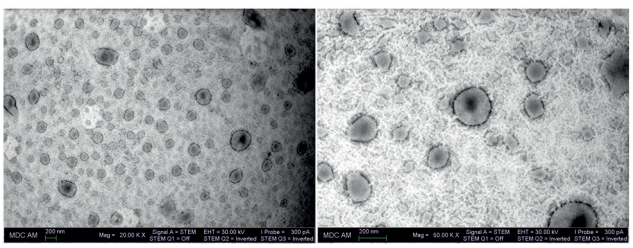


Fig. 3 TEM images of self-associates based on thiacalix[4]arene **28** at 10^{-5} M concentration.

The solutions of thiacalix[4]arenes **26**, **28** (*cone*) and **27**, **29** (1,3-*alternate*) at different concentrations (10^{-3}–10^{-6} M) were studied. The consistent increase in the size of aggregates corresponded to the decrease in the concentration observed for macrocycles **26–29** with no respect for the macrocycle conformation. The value of polydispersity was increased simultaneously (Table 1). It can be assumed that the increasing size of aggregates with decreasing thiacalix[4]arene concentration can be explained by changing the shape of self-associates (Fig. 2). As a rule, spherical aggregates (Fig. 2(A and A′)) should be smaller than the elongated self-associates (Fig. 2(B, B′ and C)).[35]

The nanoscale aggregates formed by the *p-tert*-butylthiacalix[4]arene **28** containing amide, quaternary ammonium and amino acid fragments in *cone* conformation were also investigated by transmission electron microscopy (TEM). The existence of spherical nanoparticles with the sizes very close to those determined by DLS (Table 1) was confirmed (Fig. 3).

The interaction of macrocycles **26**, **28** and **27**, **29** in *cone* and 1,3-*alternate* conformations with DNA was studied. In the case of aggregates based on DNA and macrocycles **26**, **28** in *cone* conformation, the increase of the size of associates was observed for decreasing thiacalix[4]arene concentration. Then, the formation of aggregates with a minimum size of about 191.6 nm and 166.6 nm, respectively, occurred at 10^{-5} M concentration. The polydispersity index of these systems changed in the same direction. In the case of associates based on DNA and the thiacalix[4]arenes **27**, **29** in 1,3-*alternate* conformation, the size of aggregates and polydispersity index decreased with the concentration of thiacalix[4]arenes. The minimum size of aggregates was also observed at 10^{-5} M concentration (98.7 nm and 131.0 nm, respectively) (Table 2).

It was shown that DNA can interact with macrocycles[54–56] and self-associates based on them.[60–62] It can be assumed that in the case of formation of aggregates based on a macrocycle and DNA with sizes larger than the size of self-associates

Table 2 Size of particles and polydispersity index obtained with macrocycles **26–29** and DNA (0.048 mg ml^{-1}) in Tris-HCl buffer (pH 7.5)

The concentration of thiacalix[4]arene	Particle size (d, nm); PDI			
	DNA and **26**	DNA and **27**	DNA and **28**	DNA and **29**
8×10^{-4} M	528.2 (0.30)	700.5 (0.25)	295.5 (0.50)	695.3 (0.33)
1×10^{-4} M	926.7 (0.74)	630.5 (0.21)	757.7 (0.70)	559.3 (0.27)
1×10^{-5} M	191.6 (0.21)	98.7 (0.11)	166.6 (0.09)	131.0 (0.16)

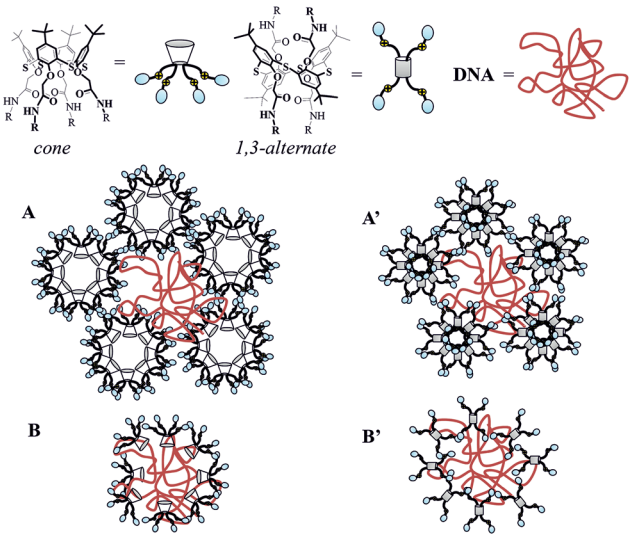


Fig. 4 Possible paths for the formation of aggregates based on amphiphilic calixarenes **26**, **28** and **27**, **29** and DNA.

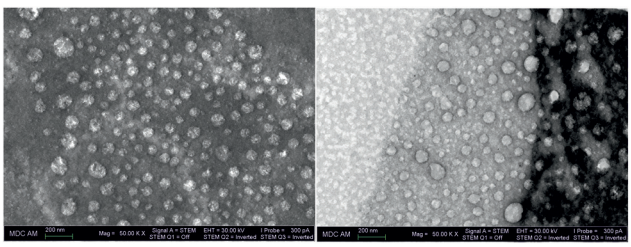


Fig. 5 TEM images of aggregates based on macrocycle **28** (10^{-5} M) and DNA (0.048 mg ml^{-1}).

based on macrocycles **26**, **28** and **27**, **29**, the interaction of self-associates with DNA took place (Fig. 4(A and A′)). However, the size of aggregates based on a macrocycle and DNA becomes smaller than the size of self-associates based on thiacalix[4]-arenes **26**, **28** and **27**, **29** at 10^{-5} M concentration of the receptors. In this case, it can be assumed that DNA interacts with single molecules of thiacalix[4]arenes instead of their self-associates (Fig. 4(B and B ′)).

The shape and the size of self-associates based on the macrocycle **28** and DNA with a hydrodynamic diameter of about 166.6 nm determined by DLS were also investigated by TEM. Fig. 5 shows TEM images of the spherical nanoparticles formed by the thiacalix[4]arene **28** with DNA. According to the TEM, the size of the aggregates is comparable with the hydrodynamic diameter measured by DLS (Table 2).

Thus, it was determined by UV spectroscopy that thiacalix-[4]arenes tetrasubstituted at the lower rim with peptide fragments are able to effectively interact with DNA. It was shown by DLS that most monodisperse systems based on thiacalix[4]-arenes and DNA with a small diameter of the aggregates (less than 200 nm) are able to form at a 10^{-5} M concentration of thiacalix[4]arenes **26–29**. The existence of spherical self-associates based on macrocycle **28** and spherical aggregates formed by thiacalix[4]arene **28** with DNA was confirmed by TEM.

Conclusions

Thus, water-soluble *p-tert*-butylthiacalix[4]arenes tetrasubstituted at the lower rim with amide and quaternary ammonium groups with peptide fragments in *cone* and 1,3-*alternate* conformation were synthesized. Thiacalix[4]arenes as complexing agents toward salmon sperm DNA were studied by UV spectroscopy, dynamic light scattering and transmission electron microscopy. It was determined that water-soluble *p-tert*-butylthiacalix[4]arenes tetrasubstituted at the lower rim in the *cone* and 1,3-*alternate* conformations are able to form associates with hydrodynamic diameters of about 75–142 nm at 10^{-3} M concentrations in aqueous solution. It was shown that the interaction of water-soluble thiacalix[4]arenes (10^{-5} M) with salmon sperm DNA (0.048 mg ml^{-1}) leads to the formation of monodisperse nanoparticles with polydispersity index equal to 0.09–0.21 and hydrodynamic diameter of about 99–192 nm. These results open new opportunities to obtain innovative sensors and drug delivery systems.

Experimental

General

The ^{1}H and ^{13}C NMR spectra of compounds (3–5% solution in $CDCl_3$, $(CD_3)_2SO$) were recorded on 400 MHz and 100 MHz Bruker Avance 400 spectrometer using $CDCl_3$ and $(CD_3)_2SO$ as the internal standard.

The IR spectra were recorded on Spectrum 400 (Perkin Elmer) IR spectrometer. The IR spectra from 4000 to 400 cm^{-1} were considered in this analysis. The spectra were measured with 4 cm^{-1} resolution and 14 scans co-addition.

Elemental analysis was performed on Perkin–Elmer 2400 Series II instruments.

Mass spectra (MALDI-TOF) were recorded on an Ultraflex III mass spectrometer in the 4-nitroaniline matrix.

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^{-1}).

Melting points were determined using Boetius Block apparatus. The purity of the compounds was monitored by melting and boiling points, and ^{1}H NMR and thin layer chromatography (TLC) on 200 μm UV 254 silica gel plate using UV-light (254 nm).

To determine the presence of anions in the aqueous solutions of thiacalixarene, ion chromatography ICS-5000 DIONEX was performed.

In this work, the following reagents and solvents were used: acetonitrile (chemical pure), benzene (chemical pure), bromo-

acetyl bromide (chemical pure), distilled water, sodium hydrogen carbonate (chemical pure), *N*,*N*-dimethylpropane-1,3-diamine (chemical pure), *N*,*N*-diethylethane-1,2-diamine (chemical pure), methanol (chemical pure), silver nitrate (chemical pure), toluene (chemical pure), glycine ethyl ester hydrochloride (chemical pure), glycylglycine ethyl ester hydrochloride (chemical pure), L-alanine ethyl ester hydrochloride (chemical pure), salmon sperm DNA (Fluka Biochemika; protein content <5%, molecular weight 384 000), Tris-HCl (Sigma).

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arenes (*cone*-1 and 1,3-*alternate*-2) were synthesized according to the literature procedure.[71]

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl)aminopropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene (*cone*-3) was synthesized according to the literature procedure.[65]

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl)aminoethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]-arene (*cone*-4) was synthesized according to the literature procedure.[65]

General procedure for the synthesis of the compounds 5 and 6

In a round bottom flask equipped with a magnetic stirrer and a reflux condenser, the compound **2**[71] (0.50 g, 0.46×10^{-3} mol) in 30 ml of a mixture of toluene and methanol (1 : 1) was dissolved. *N*,*N*-dimethylpropane-1,3-diamine or *N*,*N*-diethylethane-1,2-diamine (1.00 ml) was added. The reaction mixture was refluxed for 72 h. The solvent was removed under reduced pressure. The precipitate was washed with water and dried under reduced pressure over phosphorus pentoxide.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl)aminopropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene (1,3-*alternate*-5). White powder, yield: 0.57 g (95%). Mp: 81 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.24 (s, 36H, $(CH_3)_3C$), 1.76 (m, 8H, –$NCH_2CH_2CH_2NH$), 2.23 (s, 24H, $(CH_3)_2N$), 2.37 (m, 8H, –$NCH_2CH_2CH_2NH$), 3.37 (m, 8H, $NCH_2CH_2CH_2NH$), 4.05 (s, 8H, OCH_2CO), 7.57 (s, 8H, ArH), 8.29 (br.s, 4H, CONH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.23, 157.07, 147.18, 133.59, 127.26, 71.42, 57.64, 45.37, 38.13, 34.25, 31.12, 27.18; $IR_{\nu max}$ 1649 (C=O), 2952, 3312 (NH); MALDI-TOF: calcd for $[M + H]^+$ m/z = 1290.9, $[M + Na]^+$ m/z = 1312.9, $[M + K]^+$ m/z = 1328.9, found m/z = 1290.2, 1312.2, 1328.2; El. Anal. Calcd for $C_{68}H_{104}N_8O_8S_4$: C, 63.32; H, 8.13; N, 8.69; S, 9.94. Found: C, 63.02; H, 8.72; N, 8.73; S, 9.51.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl)aminoethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]-arene (1,3-*alternate*-6). White powder, yield: 0.54 g (89%). Mp: 181 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.03 (t, $^3J_{HH}$ = 7.1 Hz, 24H, (CH_3CH_2–), 1.24 (s, 36H, $(CH_3)_3C$), 2.57 (q, $^3J_{HH}$ = 7.1 Hz, 16H, –CH_2CH_3), 2.65 (t, $^3J_{HH}$ = 6.8 Hz, 8H, –NCH_2CH_2NH), 3.39 (m, 8H, NCH_2CH_2NH), 4.06 (s, 8H, OCH_2CO), 7.57 (s, 8H, ArH), 8.06 (t, $^3J_{HH}$ = 5.3 Hz, 4H, CONH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.34, 156.96, 147.10, 133.61, 127.36, 71.19, 51.56, 47.17, 37.27, 34.23, 31.15, 11.91; $IR_{\nu max}$ 1661 (C=O), 2964, 3322 (NH); MALDI-TOF: calcd for $[M + H]^+$ m/z = 1344.9, found m/z = 1344.0; El. Anal. Calcd for $C_{72}H_{112}N_8O_8S_4$: C, 64.25; H, 8.39; N, 8.33; S, 9.53. Found: C, 64.65; H, 8.12; N, 7.88; S 9.05.

General procedure for the synthesis of the compounds 14–25

In a round bottom flask equipped with a magnetic stirrer and a reflux condenser, the compounds **3–6** (0.20 g, 0.15×10^{-3} mol) were dissolved in 10 ml acetonitrile. *N*-Bromoacetyl-glycine ethyl ester **11**[66], *N*-bromoacetyl-glycylglycine ethyl ester **12**[66] and *N*-bromoacetyl-L-alanine ethyl ester **13**[66] (0.62×10^{-3} mol) were added. The reaction mixture was refluxed for 8 h. The solvent was removed under reduced pressure. The precipitate was washed with water and dried under reduced pressure over phosphorus pentoxide.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammonium-propyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetra-bromide (*cone*-14). White powder, yield: 0.34 g (95%). Mp: 114 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.12 (s, 36H, $(CH_3)_3C$), 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 2.32 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.51 (s, 24H, $(CH_3)_2N^+$), 3.55 (m, 8H, $NHCH_2CH_2CH_2N^+$), 4.01 (m, 8H, $NHCH_2CH_2CH_2N^+$), 4.02 (d, $^3J_{HH}$ = 5.8 Hz, 8H, $NHCH_2CO$), 4.16 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.70 (s, 8H, N^+CH_2CO), 5.03 (s, 8H, OCH_2CO), 7.36 (s, 8H, ArH), 8.68 (br.s, 4H, $NHCH_2CH_2CH_2N^+$), 9.28 (t, 4H, $^3J_{HH}$ = 5.8 Hz, $NHCH_2CO$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.11, 168.94, 163.71, 157.80, 147.70, 134.91, 128.13, 74.43, 65.32, 63.20, 61.47, 51.85, 41.23, 36.19, 34.31, 31.08, 23.17, 14.16; $IR_{\nu max}$ 1199 (COC), 1675 (C=O), 2960, 3331 (N–H); ESI: calcd for $[M - 2\ Br^-]^{2+}$ m/z = 1012.9, $[M - 3\ Br^-]^{3+}$ m/z = 648.7, $[M - 4\ Br^-]^{4+}$ m/z = 466.6, found m/z = 1012.9, 649.0, 466.5; El. Anal. Calcd for $C_{92}H_{144}Br_4N_{12}O_{20}S_4$: C, 50.55; H, 6.64; N, 7.69; S, 5.87. Found: C, 50.11; H, 6.90; N, 7.38; S, 6.00.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{([ethoxycarbonylmethyl]amidocarbonylmethyl)amidocarbonylmethyl})ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (*cone*-15). White powder, yield: 0.34 g (94%). Mp: 113 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.08 (s, 36H, $(CH_3)_3C$), 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.97 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.21 (s, 24H, $(CH_3)_2N^+$), 3.25 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.55 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.85 (d, $^3J_{HH}$ = 5.5 Hz, 8H, $NHCH_2CO$), 3.87 (d, $^3J_{HH}$ = 5.3 Hz, 8H, $NHCH_2CO$), 4.09 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.15 (s, 8H, N^+CH_2CO), 4.84 (s, 8H, OCH_2CO), 7.40 (s, 8H, ArH), 8.50 (t, $^3J_{HH}$ = 5.5 Hz, 4H, CONH), 8.54 (t, $^3J_{HH}$ = 5.9 Hz, 4H, $NHCH_2CH_2CH_2N^+$), 8.89 (t, $^3J_{HH}$ = 5.3 Hz, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.63, 168.38, 168.24, 163.14, 158.03, 146.58, 134.27, 128.00, 74.37, 62.93, 62.11, 60.47, 51.16, 41.59, 40.59, 35.40, 33.90, 30.69, 22.76, 14.03; $IR_{\nu max}$ 1197 (COC), 1667 (C=O), 2964, 3056 (N–H); ESI: calcd for $[M - 4\ Br^-]^{4+}$ m/z = 523.7, found m/z = 523.8; El. Anal. Calcd for $C_{100}H_{156}Br_4N_{16}O_{24}S_4$: C, 49.75; H, 6.51; Br, 13.24; N, 9.28; S, 5.31. Found: C, 48.62; H, 6.04; Br, 12.05; N, 7.19; S, 3.55.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonyl[*S*-methyl]methyl)amidocarbonylmethyl})-ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix-[4]arene tetrabromide (*cone*-16). White powder, yield: 0.32 g (95%). Mp: 116 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.07 (s, 36H, $(CH_3)_3C$), 1.18 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.31 (d, $^3J_{HH}$ = 7.3 Hz, 12H, CH_3CH), 1.97 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.19 (s, 24H, $(CH_3)_2N^+$), 3.25 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.56 (m, 8H, $NHCH_2CH_2CH_2N^+$), 4.09 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.16 (s, 8H, N^+CH_2CO), 4.27 (m, 4H, CH_3CH), 4.82 (s, 8H, OCH_2CO), 7.39 (s, 8H, ArH), 8.53 (t, $^3J_{HH}$ = 5.4 Hz, 4H, $NHCH_2CH_2CH_2N^+$), 9.03 (d, $^3J_{HH}$ = 6.6 Hz, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.72, 168.27, 168.13, 162.96, 157.91, 146.66, 134.39, 128.11, 128.04, 74.21, 62.80, 61.71, 60.80, 51.18, 47.97, 35.36, 33.90, 30.69, 22.64, 16.53, 14.00; $IR_{\nu max}$ 1157 (COC), 1676 (C═O), 2961, 3330 (N–H); ESI: calcd for $[M - 4\ Br^-]^{4+}$ m/z = 480.6, found m/z = 480.5; El. Anal. Calcd for $C_{96}H_{152}Br_4N_{12}O_{20}S_4$: C, 51.42; H, 6.83; Br, 14.25; N, 7.50; S, 5.72. Found: C, 51.62; H, 6.74; Br, 14.82; N, 7.33; S, 5.96.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniu-methyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (*cone*-17). White powder, yield: 0.34 g (95%). Mp: 111 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.12 (s, 36H, $(CH_3)_3C$), 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.53 (t, $^3J_{HH}$ = 7.0 Hz, 24H, $CH_3CH_2N^+$), 3.74 (m, 8H, $NHCH_2CH_2N^+$), 3.88 (m, 8H, $NHCH_2CH_2N^+$), 3.96 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 4.03 (q, $^3J_{HH}$ = 7.0 Hz, 16H, $CH_3CH_2N^+$), 4.16 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.66 (s, 8H, N^+CH_2CO), 4.98 (s, 8H, OCH_2CO), 7.35 (s, 8H, ArH), 8.94 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CH_2N^+$), 9.51 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.87, 168.78, 163.60, 157.30, 147.73, 134.98, 128.24, 74.14, 61.39, 57.50, 57.03, 56.44, 41.12, 34.26, 33.69, 31.09, 14.17, 8.48; $IR_{\nu max}$ 1198 (COC), 1676 (C═O), 2962, 3314 (N–H); ESI: calcd for $[M - 2\ Br^-]^{2+}$ m/z = 1041.2, $[M - 3\ Br^-]^{3+}$ m/z = 667.5, $[M - 4\ Br^-]^{4+}$ m/z = 480.6, found m/z = 1041.5, 667.6, 480.6; El. Anal. Calcd for $C_{96}H_{152}Br_4N_{12}O_{20}S_4$: C, 51.42; H, 6.83; Br, 14.25; N, 7.50; S, 5.72. Found: C, 51.17; H, 6.70; Br, 13.90; N, 7.68; S, 5.86.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl)amidocarb-onylmethyl})ammoniumethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (*cone*-18). White powder, yield: 0.35 g (94%). Mp: 120 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.08 (s, 36H, $(CH_3)_3C$), 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.28 (t, $^3J_{HH}$ = 6.9 Hz, 24H, $CH_3CH_2N^+$), 3.50–3.58 (m, 24H, $CH_3CH_2N^+$, $NHCH_2CH_2N^+$), 3.66 (m, 8H, $NHCH_2CH_2N^+$), 3.84 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 3.87 (d, $^3J_{HH}$ = 5.9 Hz, 8H, $NHCH_2CO$), 4.09 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.14 (s, 8H, N^+CH_2CO), 4.86 (s, 8H, OCH_2CO), 7.40 (s, 8H, ArH), 8.50 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CH_2N^+$), 8.50 (br.s, 4H, $NHCH_2CO$), 8.94 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.44, 168.25, 168.12, 163.01, 157.64, 146.56, 134.51, 128.03, 71.07, 60.52, 56.60, 55.98, 55.14, 41.50, 40.56, 33.77, 31.98, 30.55, 14.04, 7.47; $IR_{\nu max}$ 1196 (COC), 1668 (C═O), 2960, 3212 (N–H); ESI: calcd for $[M - 3\ Br^-]^{3+}$ m/z = 743.6, $[M - 4\ Br^-]^{4+}$ m/z = 537.7, found m/z = 743.7, 537.7; El. Anal. Calcd for $C_{104}H_{164}Br_4N_{16}O_{24}S_4$: C, 50.56; H, 6.69; Br, 12.94; N, 9.07; S, 5.19. Found: C, 50.52; H, 6.51; Br, 12.92; N, 8.79; S, 4.78.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonyl[*S*-methyl]methyl)amidocarbonylmethyl})-ammoniumethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]-arene tetrabromide (*cone*-19). White powder, yield: 0.32 g (95%). Mp: 116 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.08 (s, 36H, $(CH_3)_3C$), 1.18 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.30 (d, $^3J_{HH}$ = 7.3 Hz, 12H, CH_3CH), 1.31 (t, $^3J_{HH}$ = 7.2 Hz, 24H, $CH_3CH_2N^+$), 3.48–3.61 (m, 24H, $NHCH_2CH_2N^+$, $N^+CH_2CH_3$), 3.67 (m, 8H, $NHCH_2CH_2N^+$), 4.09 (s, 8H, N^+CH_2CO), 4.11 (m, 8H, CH_3CH_2O–), 4.26 (m, 4H, CH_3CH), 4.87 (s, 8H, OCH_2CO), 7.40 (s, 8H, ArH), 8.81 (br.s, 4H, $NHCH_2CH_2N^+$), 9.23 (br.s, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.71, 169.17, 162.88, 157.56, 146.56, 134.64, 127.81, 73.96, 60.62, 56.43, 56.23, 55.32, 47.98, 33.81, 32.34, 30.66, 16.47, 13.98, 7.39; $IR_{\nu max}$ 1157 (COC), 1676 (C═O), 2964, 3316 (N–H); ESI: calcd for $[M - 2\ Br^-]^{2+}$ m/z = 1069.5, $[M - 3\ Br^-]^{3+}$ m/z = 686.3, $[M - 4\ Br^-]^{4+}$ m/z = 494.6, found m/z = 1069.1, 685.9, 494.7; El. Anal. Calcd for $C_{100}H_{160}Br_4N_{12}O_{20}S_4$: C, 52.26; H, 7.02; N, 7.31; S, 5.58. Found: C, 52.52; H, 6.96; N, 7.22; S, 5.43.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammonium-propyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (1,3-*alternate*-20). White powder, yield: 0.34 g (93%). Mp: 112 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 1.18 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.20 (s, 36H, $(CH_3)_3C$), 1.93 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.18 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.21 (s, 24H, $(CH_3)_2N^+$), 3.52 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.94 (d, $^3J_{HH}$ = 5.8 Hz, 8H, $NHCH_2CO$), 3.99 (s, 8H, OCH_2CO), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.16 (s, 8H, N^+CH_2CO), 7.60 (s, 8H, ArH), 8.04 (br.s, 4H, $NHCH_2CH_2CH_2N^+$), 9.08 (t, $^3J_{HH}$ = 5.8 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.96, 163.15, 155.94, 147.57, 130.02, 128.24, 69.59, 64.45, 63.42, 61.54, 52.62, 41.10, 36.94, 34.42, 31.52, 29.70, 23.32, 14.16; $IR_{\nu max}$ 1677 (C═O), 2959, 3202 (N–H); ESI: calcd for $[M - 2\ Br^-]^{2+}$ m/z = 1012.9, $[M - 3\ Br^-]^{3+}$ m/z = 648.7, $[M - 4\ Br^-]^{4+}$ m/z = 466.6, found m/z = 1013.0, 649.0, 466.6; El. Anal. Calcd for $C_{92}H_{144}Br_4N_{12}O_{20}S_4$: C, 50.55; H, 6.64; Br, 14.62; N, 7.69; S, 5.87. Found: C, 50.90; H, 6.27; Br, 14.57; N, 7.12; S, 5.94.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{([ethoxycarbonylmethyl]amidocarbonylmethyl)amidocarbo-nylmethyl})ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (1,3-*alternate*-21). White powder, yield: 0.35 g (93%). Mp: 120 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.18 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.19 (s, 36H, $(CH_3)_3C$), 1.97 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.13 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.20 (s, 24H, $(CH_3)_2N^+$), 3.52 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.84 (br.s, 8H, $NHCH_2CO$), 3.86 (br.s, 8H, $NHCH_2CO$), 3.96 (s, 8H, OCH_2CO), 4.08 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.12 (s, 8H, N^+CH_2CO), 7.59 (s, 8H, ArH), 8.04 (br.s, 4H, $NHCH_2CH_2CH_2N^+$), 8.52 (t, $^3J_{HH}$ = 5.8 Hz, 4H, CONH), 8.90 (br.s, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6)

δ 169.56, 168.33, 168.19, 163.31, 156.77, 146.77, 133.06, 127.50, 70.81, 62.61, 62.05, 60.47, 51.21, 41.56, 40.49, 35.80, 33.81, 30.75, 22.60, 14.04; $IR_{\nu max}$ 1197 (COC), 1667 (C═O), 2962, 3214 (N–H); ESI: calcd for $[M - 3\ Br^-]^{3+}$ m/z = 724.8, $[M - 4\ Br^-]^{4+}$ m/z = 523.7, found m/z = 724.7, 523.7; El. Anal. Calcd for $C_{100}H_{156}Br_4N_{16}O_{24}S_4$: C, 49.75; H, 6.51; Br, 13.24; N, 9.28; S, 5.31. Found: C, 49.94; H, 6.21; Br, 13.16; N, 9.14; S, 5.63.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonyl[*S*-methyl]methyl)amidocarbonylmethyl})-ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]-arene tetrabromide (1,3-*alternate*-22). White powder, yield: 0.31 g (92%). Mp: 118 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.18 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.20 (s, 36H, $(CH_3)_3C$), 1.32 (d, $^3J_{HH}$ = 7.3 Hz, 12H, CH_3CH), 1.95 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.17 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.22 (s, 24H, $(CH_3)_2N^+$), 3.55 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.99 (s, 8H, OCH_2CO), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.16 (s, 8H, N^+CH_2CO), 4.29 (m, 4H, CH_3CH), 7.59 (s, 8H, ArH), 8.53 (br.s, 4H, $NHCH_2CH_2CH_2N^+$), 9.03 (br.s, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.95, 167.16, 163.12, 157.21, 146.19, 133.00, 127.66, 70.94, 62.56, 61.67, 60.77, 51.21, 48.13, 35.77, 33.79, 30.76, 22.59, 16.52, 13.99; $IR_{\nu max}$ 1157 (COC), 1676 (C═O), 2958, 3193 (N–H); ESI: calcd for $[M - 4\ Br^-]^{4+}$ m/z = 480.6, found m/z = 480.5; El. Anal. Calcd for $C_{96}H_{152}Br_4N_{12}O_{20}S_4$: C, 51.42; H, 6.83; Br, 14.25; N, 7.50; S, 5.72. Found: C, 51.53; H, 6.59; Br, 14.53; N, 7.10; S, 5.31.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniu-methyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (1,3-*alternate*-23). White powder, yield: 0.34 g (93%). Mp: 114 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.29 (s, 36H, $(CH_3)_3C$), 1.48 (t, $^3J_{HH}$ = 7.0 Hz, 24H, $CH_3CH_2N^+$), 3.61–3.67 (m, 24H, $CH_3CH_2N^+$, $NHCH_2CH_2N^+$), 3.91 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 3.95 (m, 8H, $NHCH_2CH_2N^+$), 4.08 (s, 8H, OCH_2CO), 4.14 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.68 (s, 8H, N^+CH_2CO), 7.48 (s, 8H, ArH), 7.53 (br. s, 4H, $NHCH_2CH_2N^+$), 9.60 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.88, 168.66, 163.50, 156.34, 147.50, 131.35, 126.92, 70.51, 61.49, 57.30, 56.45, 55.94, 41.05, 34.44, 33.54, 31.41, 14.18, 8.16; $IR_{\nu max}$ 1199 (COC), 1678 (C═O), 2962, 3190 (N–H); ESI: calcd for $[M - 4\ Br^-]^{4+}$ m/z = 480.6, found m/z = 480.5; El. Anal. Calcd for $C_{96}H_{152}Br_4N_{12}O_{20}S_4$: C, 51.42; H, 6.83; Br, 14.25; N, 7.50; S, 5.72. Found: C, 51.11; H, 6.78; Br, 14.51; N, 7.16; S, 5.83.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl)amidocarb-onylmethyl})ammoniumethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetrabromide (1,3-*alternate*-24). White powder, yield: 0.35 g (93%). Mp: 124 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.19 (t, $^3J_{HH}$ = 7.2 Hz, 12H, CH_3CH_2O–), 1.21 (s, 36H, $(CH_3)_3C$), 1.31 (t, $^3J_{HH}$ = 7.1 Hz, 24H, $CH_3CH_2N^+$), 3.45 (m, 8H, $NHCH_2CH_2N^+$), 3.51–3.58 (m, 24H, $CH_3CH_2N^+$, $NHCH_2CH_2N^+$), 3.86 (br.s, 8H, $NHCH_2CO$), 3.88 (br.s, 8H, $NHCH_2CO$), 4.05 (s, 8H, OCH_2CO), 4.09 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.13 (s, 8H, N^+CH_2CO), 7.60 (s, 8H, ArH), 8.23 (br. s, 4H, $NHCH_2CH_2$), 8.51 (t, $^3J_{HH}$ = 6.0 Hz, 4H, CONH), 8.93 (br. s, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.70, 168.48, 168.36, 163.28, 157.84, 147.44, 131.21, 127.54, 72.31, 61.69, 59.65, 55.87, 55.05, 41.49, 40.56, 33.89, 32.44, 30.85, 14.00, 7.40; $IR_{\nu max}$ 1197 (COC), 1666 (C═O), 2964, 3216 (N–H); ESI: calcd for $[M - 3\ Br^-]^{3+}$ m/z = 743.6, $[M - 4\ Br^-]^{4+}$ m/z = 537.7, found m/z = 743.6, 537.5; El. Anal. Calcd for $C_{104}H_{164}Br_4N_{16}O_{24}S_4$: C, 50.56; H, 6.69; Br, 12.94; N, 9.07; S, 5.19. Found: C, 50.35; H, 6.35; Br, 12.50; N, 7.10; S, 4.81.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonyl[*S*-methyl]methyl)amidocarbonylmethyl})-ammoniumethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]-arene tetrabromide (1,3-*alternate*-25). White powder, yield: 0.31 g (93%). Mp: 118 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.22 (s, 36H, $(CH_3)_3C$), 1.32 (d, $^3J_{HH}$ = 7.3 Hz, 12H, CH_3CH), 1.34 (t, $^3J_{HH}$ = 7.2 Hz, 24H, $CH_3CH_2N^+$), 3.47 (m, 8H, $NHCH_2CH_2N^+$), 3.51–3.59 (m, 24H, $N^+CH_2CH_3$, $NHCH_2CH_2N^+$), 4.09 (s, 8H, N^+CH_2CO), 4.09–4.11 (m, 16H, OCH_2CO, CH_3CH_2O–), 4.29 (m, 4H, CH_3CH), 7.60 (s, 8H, ArH), 8.27 (br.s, 4H, $NHCH_2CH_2N^+$), 9.18 (br.s, 4H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.07, 168.53, 163.05, 157.69, 146.60, 133.71, 127.89, 71.05, 61.32, 56.87, 56.29, 55.71, 48.45, 34.51, 32.49, 31.36, 17.09, 14.49, 7.92; $IR_{\nu max}$ 1157 (COC), 1676 (C═O), 2964, 3185 (N–H); ESI: calcd for $[M - 4\ Br^-]^{4+}$ m/z = 494.7, found m/z = 494.5; El. Anal. Calcd for $C_{100}H_{160}Br_4N_{12}O_{20}S_4$: C, 52.26; H, 7.02; Br, 13.91; N, 7.31; S, 5.58. Found: C, 52.12; H, 6.92; Br, 13.40; N, 7.56; S, 5.38.

General procedure for the synthesis of the compounds 26–29

In a round bottom flask equipped with a magnetic stirrer, compounds **17**, **23** and **14**, **20** (0.46×10^{-3} mol) were dissolved in 10 ml of acetonitrile. Silver nitrate (1.84×10^{-3} mol) was added. The reaction mixture was refluxed for 10 h. Silver bromide was filtered. The solvent was removed under reduced pressure. The precipitate was dried under reduced pressure over phosphorus pentoxide.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniu-methyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetranitrate (*cone*-26). White powder, yield: 0.09 g (98%). Mp: 112 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.07 (s, 36H, $(CH_3)_3C$), 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.28 (t, $^3J_{HH}$ = 7.0 Hz, 24H, $CH_3CH_2N^+$), 3.54 (m, 8H, $NHCH_2CH_2N^+$), 3.55 (q, $^3J_{HH}$ = 7.0 Hz, 16H, $CH_3CH_2N^+$), 3.63 (m, 8H, $NHCH_2CH_2N^+$), 3.94 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.11 (s, 8H, N^+CH_2CO), 4.84 (s, 8H, OCH_2CO), 7.40 (s, 8H, ArH), 8.80 (t, $^3J_{HH}$ = 4.8 Hz, 4H, $NHCH_2CH_2N^+$), 9.10 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.96, 165.21, 163.60, 157.56, 146.94, 134.56, 127.94, 74.05, 60.79, 56.36, 56.08, 54.95, 40.70, 33.91, 32.23, 30.73, 14.01, 7.37; $IR_{\nu max}$ 1197 (COC), 1679 (C═O), 2957, 3279 (N–H); ESI: calcd for $[M - 2\ NO_3^-]^{2+}$ m/z = 1023.3, $[M - 3\ NO_3^-]^{3+}$ m/z = 661.5, $[M - 4\ NO_3^-]^{4+}$ m/z = 480.6, found m/z = 1023.1, 661.3, 480.6; El. Anal. Calcd for

$C_{96}H_{152}N_{16}O_{32}S_4$: C, 53.12; H, 7.06; N, 10.32; S, 5.91. Found: C, 53.43; H, 6.79; N, 9.92; S, 5.70.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(2′,2′-diethyl-2′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniumethyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetranitrate (1,3-*alternate*-27). White powder, yield: 0.09 g (98%). Mp: 112 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.20 (s, 36H, $(CH_3)_3C$), 1.31 (t, $^3J_{HH}$ = 7.0 Hz, 24H, $CH_3CH_2N^+$), 3.47 (m, 8H, $NHCH_2CH_2N^+$), 3.52–3.57 (m, 24H, $CH_3CH_2N^+$, $NHCH_2CH_2N^+$), 3.96 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 4.07 (s, 8H, OCH_2CO), 4.11 (q, $^3J_{HH}$ = 7.0 Hz, 8H, CH_3CH_2O–), 4.12 (s, 8H, N^+CH_2CO), 7.59 (s, 8H, ArH), 7.60 (t, $^3J_{HH}$ = 4.8 Hz, 4H, $NHCH_2CH_2N^+$), 9.10 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.11, 163.57, 156.90, 153.40, 146.11, 133.04, 127.44, 74.38, 60.72, 56.45, 55.09, 45.76, 40.80, 33.77, 31.83, 30.84, 14.06, 7.23; $IR_{\nu max}$ 1199 (COC), 1681 (C═O), 2960, 3266 (N–H); ESI: calcd for $[M - 2\ NO_3^-]^{2+}$ m/z = 1023.3, $[M - 3\ NO_3^-]^{3+}$ m/z = 661.5, $[M - 4\ NO_3^-]^{4+}$ m/z = 480.6, found m/z = 1023.0, 661.4, 480.7; El. Anal. Calcd for $C_{96}H_{152}N_{16}O_{32}S_4$: C, 53.12; H, 7.06; N, 10.32; S, 5.91. Found: C, 53.49; H, 6.86; N, 10.47; S, 5.59.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetranitrate (*cone*-28). White powder, yield: 0.09 g (97%). Mp: 113 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.08 (s, 36H, $(CH_3)_3C$), 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.94 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.18 (s, 24H, $(CH_3)_2N^+$), 3.24 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.50 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.92 (d, $^3J_{HH}$ = 5.7 Hz, 8H, $NHCH_2CO$), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.12 (s, 8H, N^+CH_2CO), 4.80 (s, 8H, OCH_2CO), 7.40 (s, 8H, ArH), 8.51 (t, $^3J_{HH}$ = 5.2 Hz, 4H, $NHCH_2CH_2CH_2N^+$), 9.04 (t, $^3J_{HH}$ = 5.7 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.26, 173.56, 168.87, 163.20, 151.96, 139.67, 133.52, 79.31, 67.87, 67.09, 66.00, 56.47, 45.97, 40.59, 39.15, 35.94, 27.72, 19.27; $IR_{\nu max}$ 1199 (COC), 1672 (C═O), 2963, 3310 (N–H); ESI: calcd for $[M - 2\ NO_3^-]^{2+}$ m/z = 995.2, $[M - 3\ NO_3^-]^{3+}$ m/z = 642.8, $[M - 4\ NO_3^-]^{4+}$ m/z = 466.6, found m/z = 995.0, 642.7, 466.5; El. Anal. Calcd for $C_{92}H_{144}N_{16}O_{32}S_4$: C, 52.26; H, 6.86; N, 10.60; S, 6.07. Found: C, 52.23; H, 6.83; N, 10.09; S, 5.93.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*-(3′,3′-dimethyl-3′-{(ethoxycarbonylmethyl)amidocarbonylmethyl})ammoniumpropyl)carbamoylmethoxy]-2,8,14,20-tetrathiacalix[4]arene tetranitrate (1,3-*alternate*-29). White powder, yield: 0.09 g (96%). Mp: 113 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 12H, CH_3CH_2O–), 1.20 (s, 36H, $(CH_3)_3C$), 1.94 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.17 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.20 (s, 24H, $(CH_3)_2N^+$), 3.51 (m, 8H, $NHCH_2CH_2CH_2N^+$), 3.95 (d, $^3J_{HH}$ = 5.8 Hz, 8H, $NHCH_2CO$), 4.00 (s, 8H, OCH_2CO), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 8H, CH_3CH_2O–), 4.13 (s, 8H, N^+CH_2CO), 7.60 (s, 8H, ArH), 8.03 (t, $^3J_{HH}$ = 5.6 Hz, 4H, $NHCH_2CH_2CH_2N^+$), 9.04 (t, $^3J_{HH}$ = 5.8 Hz, 4H, $NHCH_2CO$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.77, 167.24, 163.84, 156.92, 145.96, 132.96, 127.46, 70.96, 62.44, 61.67, 60.73, 51.31, 40.65, 35.96, 33.88, 30.73, 22.51, 13.88; $IR_{\nu max}$ 1197 (COC), 1679 (C═O), 2962, 3280 (N–H); ESI: calcd for $[M - 2\ NO_3^-]^{2+}$ m/z = 995.2, $[M - 3\ NO_3^-]^{3+}$ m/z = 642.8, $[M - 4\ NO_3^-]^{4+}$ m/z = 466.6, found m/z = 995.0, 642.7, 466.6; El. Anal. Calcd for $C_{92}H_{144}N_{16}O_{32}S_4$: C, 52.26; H, 6.86; N, 10.60; S, 6.07. Found: C, 52.59; H, 6.97; N, 10.74; S, 6.27.

The study of the interaction of the synthesized thiacalix[4]-arenes 26–29 with DNA by UV spectroscopy

UV-vis spectra were recorded by using a "Shimadzu UV-3600" spectrometer; the cell thickness was 1 cm, slit width was 1 nm. The experiments were performed in 5 mM Tris-HCl buffer (pH 7.5). The DNA concentration was 0.019 mg ml^{-1}, the concentration of receptors was 10^{-4} M. The recording of the absorption spectra of the mixtures of DNA with thiacalixarenes was carried out in 1 hour after mixing the solutions at 20 °C.

Determination of the hydrodynamic size of the particles by DLS

The particle size was determined by a 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 noninvasive backscatter optics (NIBS). The measurements were performed at a detection angle of 173°, and the measurement position within the quartz 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 5 mM Tris-HCl buffer (pH 7.5). The buffer and solutions of thiacalixarenes (10^{-3} M) were filtered through the nylon filters with a pore size of 450 nm. During the experiments, DNA concentration (0.048 mg ml^{-1}) remained constant, concentration of receptors varied from 10^{-3} to 10^{-6} 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 3 and 5 hours.

Determination of the shape and the size of the particles by TEM

Imaging was carried out with a Carl Zeiss Merlin scanning electron microscope. Images were processed with a STEM detector on a 300 mesh copper grid coated with Formvar. Probe preparation was carried out using a negative staining protocol with 2% uranyl acetate solution. The DNA concentration was 0.048 mg ml^{-1}, the concentration of thiacalix[4]-arene **28** was 10^{-5} M. The recording of the images of the mixtures of DNA with thiacalixarenes was carried out in 1 hour after mixing the solutions at 20 °C.

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