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MACROMOLECULAR CHEMISTRY AND POLYMERIC MATERIALS

Nonionogenic Star-Shaped Calix[8]arenes: Synthesis and Ionophore Properties

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Abstract—New approach to the synthesis of star-shaped polymers based on calix[8]arene with amphiphilic arms of nonionogenic nature is described. The ionophore properties of the resulting polymer with respect to ions of alkali metals, europium, and uranium were studied by an example of a polymer containing residues of ω-cetyloligoethylene oxide as arms.

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Amphiphilic star-shaped systems based on calixarenes are presently an object of intensive research. On the one hand, this is due to the trend of systems of this kind toward formation of micelles with a narrow size distribution, which is of interest for development of systems for delivery of medicinal agents. On the other hand, this interest is caused by the presence of a calixarene ring, which tends to form complexes with low-molecular-weight compounds and metal ions [1]. Calix[n]arenes are cyclic oligomers produced in polycondensation of 4-*tert*-butylphenol with formaldehyde [2], with n determining the number of phenol residues in a macrocycle. The possibility of modifying calixarenes along both the upper and lower rims and varying the macrocycle size resulted in the synthesis of a wide variety of calixarene derivatives and in a study of their complex-forming properties [3]. In doing so, it was shown that introduction of amphiphilic structural groups and addition of surfactants to the system enhance the ionophore properties of the molecules.

Methods for synthesis of star-shaped, including amphiphilic, calixarene-containing polymers have been rather well developed [4–7]. In particular, methods of living polymerization have been used to obtain star-shaped polymers with arms having the form of block-copolymers of the acrylic acid–methyl acrylate [6] and polyethylene oxide–polystyrene [7] types. Despite the considerable advances in the application of the living radical polymerization, the synthesis of block-copolymers is limited by the small number of monomers that can be involved in processes of this kind. In addition, the ionophore properties of such macromolecules were almost not studied so far.

An original approach to the synthesis of calixarene-containing star-shaped polymers with nonionogenic arms of amphiphilic nature is based on the condensation method for synthesis of polymers [8]. In this case, the role of arms can be played by commercially available oligoethylene oxides with hydrophobic terminal groups.

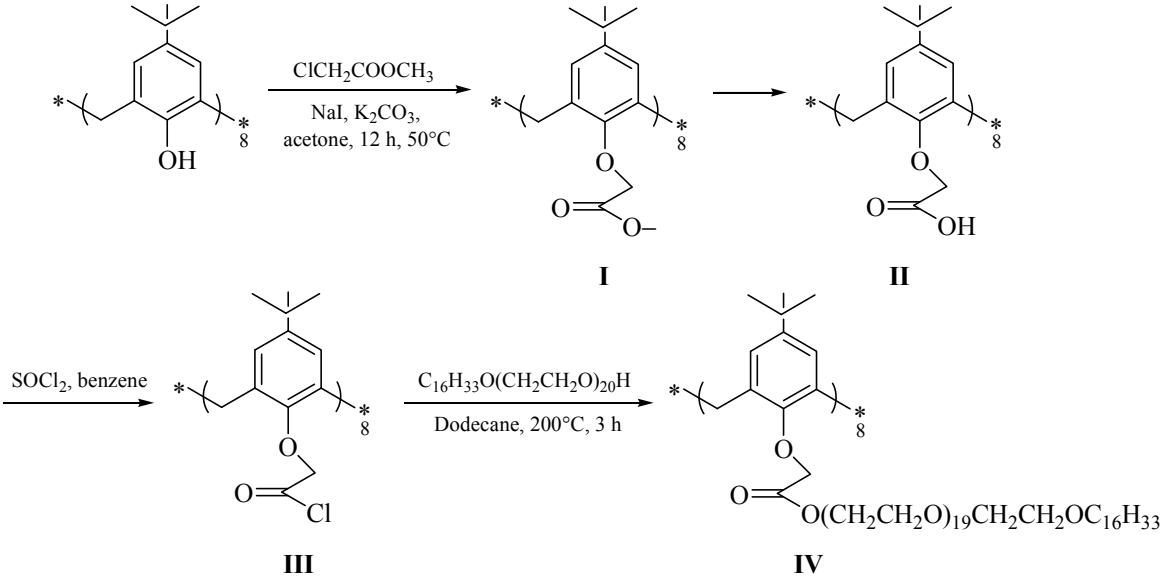
This communication describes the synthesis of an octafunctional monomer based on calix[8]arene and the corresponding star-shaped polymer with arms in the form of ω-cetyloligoethylene oxide (*MM* 1100) and presents the results of a study of its ionophore properties with respect to alkali metal ions.

EXPERIMENTAL

The scheme of the synthesis of the polymer under study is presented in Scheme 1.

It is known that one of the main difficulties in synthesis of star-shaped polymers is the full functionalization of all groups of a calixarene in the "from the ring" approach. In this context, of particular importance in using condensation methods is the

Scheme 1.



choice of the type of interacting groups of monomers and the method by which the reaction is performed. The procedure for synthesis of star-shaped calixarenes with arms of the oligoethylene type [9], based on the Williamson reaction, is rather labor-consuming and, as reported by the authors, cannot yield products with the molecular mass of the arms exceeding 800, which is due to the occurrence of side processes in the synthesis of the target product. At the same time, it is well known that the reaction of activated acid derivatives with alcohols is one of the most efficient ways to synthesize polyesters because the esterification reaction proceeds quantitatively. In this context, with the synthetic approach to the star-shaped calixarenes with arms of nonionogenic amphiphilic nature chosen, it is the most appropriate to preliminarily synthesize calixarene derivatives containing carboxy terminal groups, and upon activation of these groups, to perform esterification with the corresponding alcohols. As amphiphilic oligomers with terminal hydroxy groups were chosen commercial ω-alkyloligoethylene oxides. The advantage of this scheme is that a single macrocyclic monomer can be used to obtain a wide variety of star-shaped polymers with different lengths of the hydrophilic and hydrophobic moieties of the arm.

A known method for synthesis of octakis-(carbethoxymethoxy)calix[8]arene [10] is based on the Claisen reaction between calixarene and haloacetic acid esters in a system constituted by potassium carbonate, potassium iodide, and acetone or potassium hydride and DMFA. Despite the comparative simplicity of the method, preparatively acceptable yields of the target product can only be obtained upon a prolonged (>100 h) heating. It was found that, by using iodo derivatives, which can be in situ produced by the reaction with sodium iodide, instead of chloro(bromo) acetates, the reaction duration can be reduced to 5 h without any noticeable decrease in the yield of octaacid. Octakis(carbethoxymethoxy)calix[8]arene used as the monomer was synthesized by the standard method, by reacting the corresponding acid, readily produced by alkaline hydrolysis of the octaester, with thionyl chloride.

One of the most difficult tasks to be solved in synthesis of star-shaped systems with a large number of arms is the full functionalization of active centers of the monomer. As a rule, this is done by using an excess amount of one of the components. Esterification under the conditions of the Einhorn reaction (THF–pyridine, 0–2°C) yields a mixture, isolation of the target compound from which is rather difficult because of the high solubility of all the components in most of organic solvents and water and the close polarities of the target and by-products. Application of the high-temperature acceptorless polycondensation technique, which makes it possible to use reagents in equimolar ratios and is known [11] to provide a quantitative yield of the product in reaction between the hydroxy group

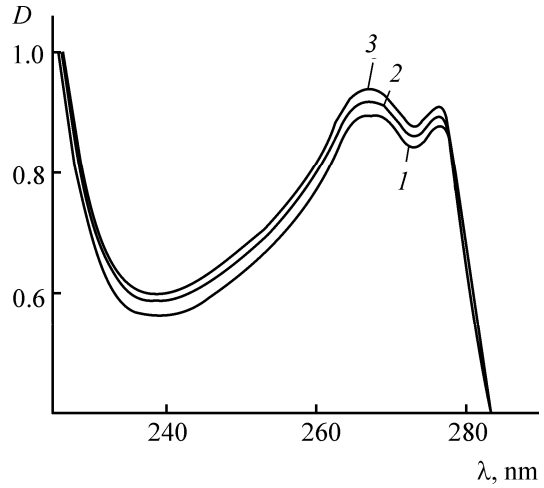


Fig. 1. UV absorption spectra of star solution at different potassium chloride concentrations. Star concentration 1×10^{-4} M. (*D*) Optical density and (λ) wavelength. KCl concentration (M): (*1*) 0, (*2*) 2×10^{-4}, and (*3*) 5×10^{-4}.

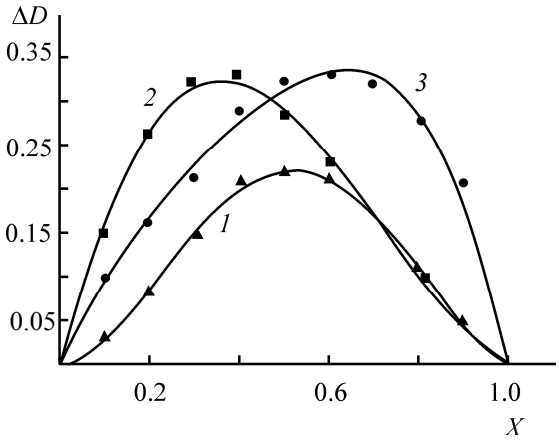


Fig. 2. Diagrams of isomolar series (Job diagrams) for (*1*) CsCl–**IV**, (*2*) $UOP_2(NO_3)_2$–**IV**, and (*3*) KCl–**IV** mixtures in methanol. Total component concentration 5×10^{-5} M. (Δ*D*) Difference in optical densities and (*X*) molar fraction of a salt.

and acyl chloride, leads to the target product with high yield and >98% degree of substitution.

A common method for determining the number of arms of a star-shaped polymer is selective decomposition of the product. In this case, however, the number of arms can be found from NMR and UV spectroscopic data by taking into account the known molecular mass and the polydispersity of commercial ω-cetyloligo-ethylene oxide (Brij58@; MM 1100, M_w/M_n = 1.1). NMR data fail to provide a sufficient analytical accuracy because of the significant differences in the content of aliphatic and aromatic protons, whereas UV spectroscopic data make it possible to determine the relative content of aromatic moieties with a sufficient accuracy. Comparison of data obtained by measuring the absorption of ethanolic solutions of the polymer and model octaethyl ester at 270 nm shows that, under the synthesis conditions used, the degree of substitution of acyl chloride groups with residues of ω-cetyloligoethylene oxide was 7.8–7.9.

The ionophore properties of the star-shaped polymer obtained were studied by an example of chlorides of alkali metals (Li, Na, K, Rb, Cs) and europium chloride and uranyl nitrate. These cations were chosen because they tend to form complexes with "oxygen" ligands of the carbonyl and ester type.

The formation of a complex between a molecule of the star-shaped polymer and a metal cation is accompanied by an increase in the absorption in the range 270–280 nm (Fig. 1), characteristic of the π–π* transition in substituted benzene rings.

Such a change in the absorption spectra can be attributed to the formation of a complex between the metal cation and polymer, in which the binding of the cation to the microcycle occurs in the close vicinity of aromatic units, as observed in the case of compound **II** [10].

The molecular composition of the complexes was determined by the isomolar series method (Job's method) (Fig. 2) [12]. This was done using the systematic increase in the absorption of a methanol solution of the polymer upon addition of a metal chloride solution in the same solvent. It was found that lithium, sodium, and europium chlorides form no complexes of a certain composition with the polymer under study: K^+ and Rb^+ form complexes of composition 4 $(M^+)_2$; Cs, complexes of 1 : 1 composition; and UO_2^{2+}, complexes of 1 : 2 composition. This behavior well correlates with variation of the ionic radius of the cation and agrees with the known data [9] on the complementarity of the calix[8]arene molecule and the cesium ion.

The apparent instability constants of the complexes were estimated photometrically by the "saturation curve" method [12] (Table 1). It can be seen from these data that the stability of the complexes increases in the order potassium–rubidium–cesium, which is

Table 1. Composition and apparent instability constants of **IV**–metal salt complexes

Cation	Composition of a complex (polymer–metal)	log β	Ionic radius of cations, Å [10]
K^+	1:2	5.13	2.02
Rb^+	1:2	5.07	1.86
Cs^+	1:1	4.53	1.65
UO_2^{2+}	2:1	4.61	3.10

Table 2. Fraction of metal picrate extracted into a solution of **IV** in methylene chloride. Polymer and salt concentration 1.35×10^{-4} M, 20°C

Extractive agent	Extracted		
	KCl	RbCl	CsCl
IV	0.263	0.373	0.506
I	0.255	0.298	0.201
Brij58@	0.012	0.015	0.015

probably due to an increase in the ionic radius and in the most probable coordination number of a cation in this series.

It should be noted that the binding constants of complexes of the polymer under study with salts of alkali metals are comparable with the binding constants of these cations with dibenzo-18-crown-6 [13] [log β 5.0 (K^+), 4.2 (Rb^+), 3.5 (Cs^+)], a typical representative of the class of crown esters, with an antibate dependence of the stability of the complex on the ionic radius of a cation observed in the case of compound **IV**. This is, apparently, a consequence of the large size of the calix[8]arene ring, compared with that of cyclohexaethylene oxide.

The ionophore properties of the polymer were also studied by the method of extraction of picrates of alkali metals into a solution of the polymer in methylene chloride, previously used for semiquantitative analysis of the ionophore properties of low-molecular-weight calixarenes [10]. The equilibrium concentrations of picrate ions were found spectrophotometrically from the absorption at a wavelength of 335 nm. It was found in a blank run that picrates are not extracted from the aqueous phase into methylene chloride in the absence of surfactants.

It can be seen in Table 2 that the star-shaped polymer is the best extracting agent, compared with the low-molecular-weight analog, and the extraction efficiency increases with the ionic radius of a cation, which correlates with the increase in the binding constants in this series. It might be assumed that the extractive capacity of the polymer under study increases, compared with the low-molecular-weight analog, because the structure contains residues of polyethylene oxide, which is known to be a podand for alkali metal cations. However, the extractive capacity of ω-cetyloligoethylene oxide solutions (Brij58@) for alkali metal cations is incomparably small relative to the extractive capacity of the polymer (Table 2). This gives reason to believe that the complexation in the system under study is governed by the interaction of a metal ion with oxyacetate groups directly bonded to the macrocycle, which is primarily determined by the molecular architecture of the polymer.

Below, procedures for synthesis of the star-shaped polymer and intermediates are described and detailed experimental information is presented.

Octa-*tert*-butylcalix[8]arene was synthesized by the known technique [15]. Methyl chloroacetate (Aldrich) and ω-cetyloligoethylene oxide (M_w = 1000 g mol^{-1}, Brijc58@, Aldrich) were used without additional purification, whereas the rest of the solvents and thionyl chloride were purified by distillation just prior to use.

NMR spectra were obtained on Bruker AC400 instruments (400 MHz) for solutions in DMSO and chloroform, and UV spectra, with Varian Cary and SF-26 spectrophotometers.

Octamethyl ester of 5,11,127,23,29,35,41,47-octa-*tert*-butyl-9,50,51,52,53,54,55,56-octakis(carbomethoxy)calix[8]arene (I). A mixture of dry sodium (3 g, 20 mmol) and methyl chloroacetate (2 g, 18 mmol) in 50 ml of dry acetone was agitated at room temperature for 20 min, then the precipitated NaCl was filtered off. To the resulting solution of methyl iodine acetate were added 5 g (36 mmol) of potassium carbonate and 1.3 g (1 mmol) of octa-*tert*-butylcalix[8]arene in the form of a suspension in 100 ml of acetone. The reaction mixture was boiled for 5 h. After the solvent was removed, the product was twice recrystallized from ethanol to give 1.4 g (77%), mp 239–240°C. ^{1}H NMR spectrum ($CDCl_3$) (ppm): 1.10 s (72H), 3.52 s (24H), 4.05 s (16H), 4.07 s (16H), 6.97 s (16H).

5,11,17,23,29,35,41,47-Octa-*tert*-butyl-9,50,51,52,-53,-54,55,56-octakis(carbethoxymethoxy)calix[8]-

arene (II). A suspension of 1.87 g (1 mmol) of octaester in 50 ml of 50% ethanol containing 3.20 g (80 mmol) of sodium hydroxide was boiled for 2.5 h. After the mixture was cooled and neutralized, the precipitate formed was filtered off, dried, and recrystallized from methanol to give 1.60 g of the product (90%), mp 239–240°C, ^{1}H NMR spectrum ($CDCl_3$) (ppm): 1.10 s (72H), 3.5 s (24H), 4.07 s (16H), 6.92 s (16H).

5,11,17,23,29,35,41,47-Octa-*tert*-butyl-9,50,51,52,-53,54,55,56-octakis(chlorocarbonyloxymethoxy)-calix[8]arene (III). To a suspension of 1.60 g (0.9 mmol) of **II** in 6 ml of benzene was added a solution of 2 ml (27 mmol) of thionyl chloride in 6 ml of benzene. The mixture was boiled for 40 h. The solvent and the excess amount of thionyl chloride were removed in a water-jet-pump vacuum and the product was washed with petroleum ether and dried. Yield 0.59 g (34.6%), mp 150–152°C. ^{1}H NMR spectrum ($CDCl_3$) (ppm): 1.17 s (72H), 3.5 s (24H), 4.72 s (16H), 6.92 s (16H).

Octa(*n*-hexadecyloxydecaethylene glycol) ester of 5,11,17,23,29,35,41,47-octa-*tert*-butyl-9,50,51,52,-53,54,55,56-octakis(carboxymethoxy)calix[8]arene (IV). A solution of 0.27 g (0.14 mmol) of **III** and 1.27 g (1.13) of ω-hexadecyl ester of decaethylene glycol (Brijc58@) in 2 ml of dodecane was heated in the atmosphere of argon at 180°C for 2 h. On cooling the mixture, the solvent was removed in a vacuum, and the polymer was reprecipitated from chloroform into hexane and dried in a vacuum (20°C, residual pressure 0.1 Torr) to constant weight to give 1.1 g of the product (84%). ^{1}H NMR spectrum ($CDCl_3$) (ppm): 0.88 s (CH_3), 1.23–1.36 m (CH_2), 3.36–3.51 m (OCH_2CH_2O), 4.29 t (OCH_2), 6.92 s (Ar–H).

CONCLUSIONS

(1) A synthesis was developed of a star-shaped polymer based on calixarene with arms of the amphiphilic nature using polycondensation methods.

(2) The capacity of the resulting polymer for complexation with metal ions was studied.

(3) It was found that introduction of diphilic substituents into the molecule of a macrocycle substantially enhances its ionophore properties.

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