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Outer-sphere interactions between octahedral chiral cobalt(III) complexes and water-soluble calixarenes*

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The structures and stability of outer-sphere associates of sulfonate derivatives of thiacalix[4]arene and calix[4]resorcinarene with coordinatively saturated cobalt(III) bis- and tris-chelates ($[Co(L\text{-}His)_2]^+$, $[Co(en)_2ox]^+$, $[Co(en)_3]^{3+}$, and $[Co(dipy)_3]^{3+}$) were compared based on the data from UV, CD, 1D ^1H NMR, and 2D (2D NOESY) ^1H NMR spectroscopy and conductometry. Outer-sphere association is accompanied by partial penetration of the chelate rings of the complexes into the hydrophobic cavity of calixarene, which induces changes in the spectroscopic and spectropolarimetric properties of the cobalt(III) complexes.

Key words: sulfonate derivatives of thiacalix[4]arene and calix[4]resorcinarene, octahedral cobalt(III) complexes, outer-sphere association, structure, stability.

Demands for compounds, which are able to recognize and selectively bind particular chemical species, generate a need for the construction of synthetic receptors imitating natural sensors. It is well known that efficiency of biological systems, in particular, high selectivity of molecular recognition, is associated with cooperative action of weak noncovalent forces.[1] Consequently, cooperative binding in guest—host complexes can be considered as a principle, which determines the molecular design of artificial receptors and sensors.[2] Evidently, for the cooperative effect to be manifested, guest—host binding should occur through numerous intermolecular interactions, whose efficiency depends on the structural compatibility between the guest and host. A bowl-like shape of calixarenes completely meets these requirements.[1,3,4] Calixarenes serve as convenient molecular platforms for the construction of three-dimensional structures, which contain cavities of various sizes and differ in the number and type of binding sites, the spatial arrangement of the binding groups, and the possibilities of forming asymmetric cavities and changing the balance between rigidity and flexibility of the receptor. Calixarene derivatives can be used for molecular[5,6] and enantiomeric[7,8] recognition of biologically important molecules. In addition, chiral cyclophanes can serve as building blocks for enantioselective self-organization,[9] which would be a prerequisite for the design of new materials. Further applications of enantioselective cyclophanes in chiral discrimination and enantioselective self-organization call for the development of new approaches to their recognition and separation.

It is known that outer-sphere association of cobalt tris-chelates with various counterions provides the basis for many efficient procedures for recognition and separation. In particular, enantioselectivity of outer-sphere association between cobalt tris-chelates and optically active anions as well as between oppositely charged cobalt complexes makes it possible to perform chromatographic separation of enantiomers of cobalt complexes with the use of eluents contaning chiral counterions as separating agents.[10—13] Two- or three-center Coulomb interactions and hydrogen bonding serve as a basis for chiral discrimination in the course of outer-sphere association of cobalt(III) tris-chelates.[14—16] Outer-sphere association

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with coordinatively saturated octahedral cobalt complexes plays an important role in solving such a complicated problem as structural and enantiomeric recognition of DNA molecules. Due to noticeable changes in the spectroscopic, spectropolarimetric, and electrochemical properties of cobalt complexes, which occur in the course of their outer-sphere complexation, octahedral cobalt complexes can be used as probes for the determination of the DNA structure.[17—19] Calixarenes containing ionized groups attached to a cyclophane matrix form stable outer-sphere associates with charged metal complexes.[20—22] Based on the published data, it can be concluded that charged coordinatively saturated cobalt(III) complexes are promising agents for recognition and separation of cyclophane molecules and ions. However, the data available in the literature are insufficient to reveal the main characteristic features of structural recognition of ionized calixarenes by charged coordinatively saturated complexes. Hence, the aim of the present study was to perform comparative analysis of the structural and thermodynamic parameters of the outer-sphere complexation of sulfonate derivatives of thiacalixarene (**1**) and calix[4]resorcinarene (**2**) with coordinatively saturated octahedral cobalt(III) complexes with different compositions.

Thiacalixarene **1** has a smaller cavity (Fig. 1) and contains charged sulfonate groups rigidly attached to the rim, unlike resorcinarene (**2**), in which the sulfonatomethyl substituents attached to the rim are more flexible. The coordinatively saturated octahedral cobalt(III) complexes $[Co(en)_3]^{3+}$ (**3**), $[Co(en)_2ox]^+$ (**4**) (en is ethylenediamine, ox = $C_2O_4^{2-}$), *trans*-im-$[Co(L\text{-}His)_2]^+$ (**5**) (*trans*-im signifies the *trans*-arranged imidazole fragments in the coordination sphere of the complex, L-His is L-histidine), and $[Co(dipy)_3]^{3+}$ (**6**) (dipy is 2,2´-dipyridine) were chosen as guests.

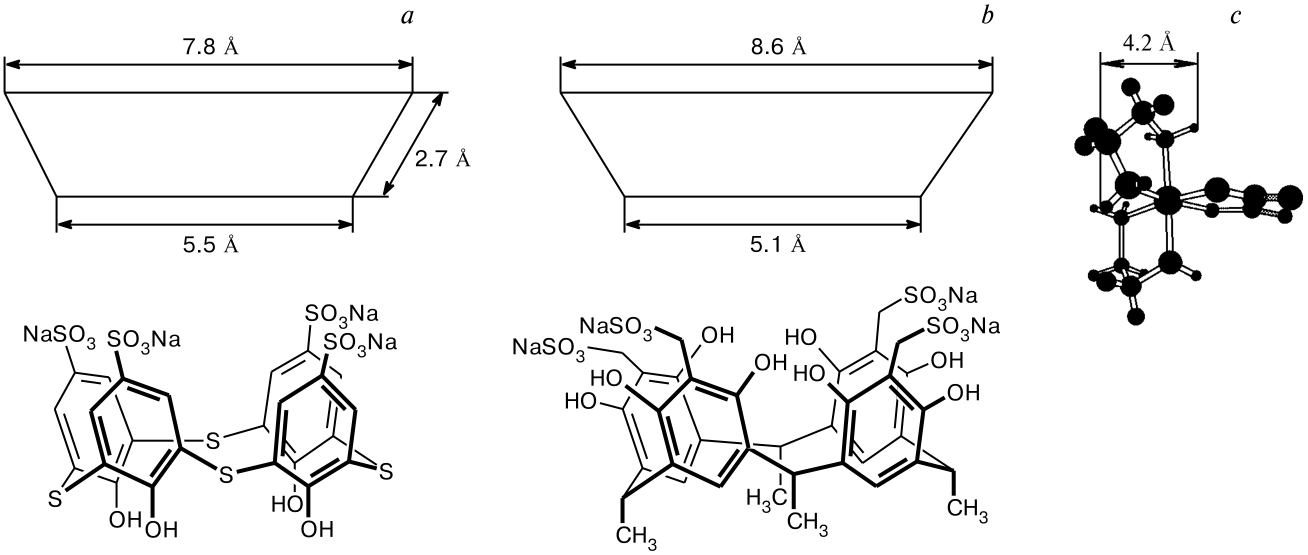
Complexes **3—6** were chosen because of the possibility of varying the charge, size, and geometry of the ligand environment about the central cobalt(III) ion with the aim of revealing the influence of the above-mentioned factors on the structural and thermodynamic parameters of their outer-sphere association with ionized calixarenes. Complexes **3—6** are diamagnetic and stable over a wide pH range, which enables one to study their reactions with calixarenes by different physicochemical methods, including NMR spectroscopy. In addition, it is of interest to compare the characteristic features of the outer-sphere association of cobalt(III) complexes with calixarenes and DNA, because cobalt tris-chelates have been well studied as probes in investigations of the structural and conformational features of DNA.[17—19]

Experimental

Compounds **1** and **2** were synthesized according to procedures described earlier.[23,24] The cobalt complexes were prepared according to known procedures: $[Co(en)_3]Cl_3$, Δ-, Λ-$[Co(en)_3]I_3$,[25] $[Co(en)_2ox]Cl$, Λ-$[Co(en)_2ox]Br$,[26] $[Co(dipy)_3](ClO_4)_3$,[27] and *trans*-im-$[Co(L\text{-}His)_2]ClO_4$.[28]

^{1}H NMR spectra were recorded on Bruker DRX-300 and Bruker DRX-500 instruments operating at 300 and 500.13 MHz. The chemical shifts were determined relative to the signals for the residual protons of the deuterated solvent D_2O (δ 4.86 at 20 °C). The concentrations of the guest and host were $1 \cdot 10^{-3}$ and $5 \cdot 10^{-4}$—$5 \cdot 10^{-3}$ mol L^{-1}, respectively.

The constants of outer-sphere association of the cobalt complexes with calixarenes and the upfield shifts of the signals for the protons of complexes **3—6** under conditions of 100% accu-



1 **2**

Fig. 1. Structures, sizes, and shapes of the cavities in compounds **1** (*a*) and **2** (*b*) and the size of the ethylenediaminate chelate ring in the $[Co(en)_2ox]^+$ complex (*c*).

mulation of the outer-sphere associates were calculated from the ^{1}H NMR spectroscopic data using the Benesi—Hildebrandt plot.[29]

Conductometry was used for the determination of the constants of outer-sphere association of resorcinarene **2** with tris-chelates $[Co(en)_3]^{3+}$ and $[Co(dipy)_3]^{3+}$. For this purpose, the ionic equivalent conductivities of the tetraanion of resorcinarene **2** and the $[Co(en)_3]^{3+}$ and $[Co(dipy)_3]^{3+}$ ions were determined by Eq. (1)

$$\lambda = \lambda^{eq} - \lambda^{eq}_{cion}, \quad (1)$$

where λ^{eq} is the equivalent conductivity of resorcinarene **2** or the $[Co(en)_3]Cl_3$ and $[Co(dipy)_3](ClO_4)_3$ complexes and λ^{eq}_{cion} is the ionic equivalent conductivity of the counterions. The conductivities λ^{eq}_{cion} for the sodium, chloride, and perchlorate ions were taken from the handbook.[30]

The conductivities of solutions containing different volume fractions of resorcinarene **2** and the cobalt complexes (ionic strength $I = 2.8 \cdot 10^{-3}$ mol L^{-1}) were measured at 20±0.1 °C on an inoLab Cond Level 1 conductometer. The equilibrium concentration of the associate ($Cat^{3+}A^{4-}$) was calculated from these data by Eq. (2). The stability constants of the outer-sphere associates of the cobalt complexes with calixarenes were calculated by the law of mass action from the calculated equilibrium concentrations of the associates according to a procedure,[13] which is widely used for evaluation of the stability constants of outer-sphere associates,

$$(\Delta\kappa \cdot 10^3)/\alpha = [Cat^{3+}A^{4-}], \quad (2)$$

where $\Delta\kappa$ is the deviation of the measured conductivities of solutions containing different volume fractions of resorcinarene **2** and the cobalt complexes from the conductivities calculated according to an additive scheme on the assumption that interactions are absent

$$\Delta\kappa \cdot 10^3 = \kappa_c \cdot \chi - \lambda_1^{eq}[Na_4A] - \lambda_2^{eq}[CatX_3], \quad (3)$$

where κ_c is the cell constant, χ is the measured conductivity, and λ_1^{eq} and λ_2^{eq} are the molar conductivities of resorcinarene **2** (Na_4A) and the complex ($CatX_3$), respectively.

Circular dichroism spectra were recorded on a JASCO 500A spectropolarimeter using a 10-mm cell at room temperature (~20 °C). The concentrations of the Δ- and Λ-$[Co(en)_3]I_3$ complexes were $6 \cdot 10^{-4}$ mol L^{-1}. The concentration of the (Λ-$[Co(en)_2ox]Br$) complex was $8 \cdot 10^{-4}$ mol L^{-1}. The concentrations of thiacalixarene **1** and sulfonatomethylated calix[4]resorcinarene **2** were varied from $6 \cdot 10^{-4}$ to $2.4 \cdot 10^{-3}$ mol L^{-1}.

The complexation constants were determined by processing the spectropolarimetric data using the CPESSP program.[31]

Electronic absorption spectra were recorded on a Specord UV VIS spectrometer using a 10-mm cell. The concentration of the $[Co(dipy)_3](ClO_4)_3$ complex was $5 \cdot 10^{-3}$ mol L^{-1}. The concentration of thiacalixarene **1** was varied from $1.25 \cdot 10^{-3}$ to $2.5 \cdot 10^{-3}$ mol L^{-1}.

Results and Discussion

Studies by ^{1}H NMR spectroscopy are widely used for estimating the structures and stabilities of guest—host complexes, when the constants of their formation are in a range of 10^2—10^4.[29] Very important characteristics of calixarene-based guest—host complexes are the upfield shift of the signals for the protons of the guest and the downfield shift of the signals for the protons of the host caused by shielding of the protons of the guest by the aromatic fragments involved in the cyclophane structure of the host.[29] The dependence of the upfield shifts of the signals for the methylene protons of complexes **3** and **4**, the protons of bis-histidinate complex **5**, and the aromatic protons of complex **6** on the concentration of thiacalixarene **1** is indicative of efficient binding, whose constant is higher than four orders of magnitude and cannot be correctly estimated by ^{1}H NMR spectroscopy. The dependences of the upfield shifts of the signals for the methylene protons of complex **4** on the concentration of thiacalixarene **1** are shown in Fig. 2. Unlike the constants of outer-sphere association of complexes **4** and **5** with thiacalixarene **1**, the corresponding constants for resorcinarene **2**, which have been determined earlier by ^{1}H NMR spectroscopy, are in a range of 100—250.[32] Since the associates formed by tris-chelates **3** and **6** with resorcinarene **2** precipitated, the binding constants of complexes of **3** and **6** with receptor **2** also cannot be determined under the concentration conditions used in ^{1}H NMR spectroscopy. To determine the constants of outer-sphere association of complexes **3—6** with calixarenes **1** and **2**, it is necessary to employ electron spectroscopy or conductometry, which enable one to decrease the concentrations of the interacting components by at least an order of magnitude. The results of conductometry (Fig. 3) demonstrate that $\Delta\kappa$ of solutions containing resorcinarene **2** and complexes **3** or **6** in different ratios depend on the mole fraction of the latter (see Eq. (3)).

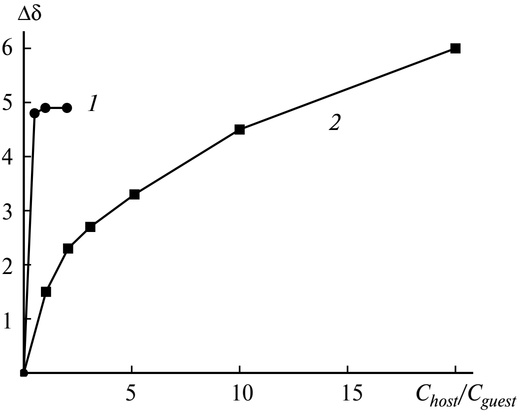


Fig. 2. Dependence of the change in the chemical shift of the signal for the protons of the CH_2 group ($\Delta\delta$) of the $[Co(en)_2ox]^+$ complex (**4**) ($C_4 = 3.5 \cdot 10^{-3}$ mol L^{-1}) in the ^{1}H NMR spectra of solutions of calixarenes **1** or **2** (*host*) and complex **4** (*guest*) in D_2O at 20 °C on the concentrations of compounds **1** ($C_1 = 1.5 \cdot 10^{-3}$—$7 \cdot 10^{-3}$ mol L^{-1}) (*1*) and **2** ($C_2 = 3.5 \cdot 10^{-3}$—$2 \cdot 10^{-2}$ mol L^{-1}): *1*, a mixture of **1** and **4**; *2*, a mixture of **2** and **4**.

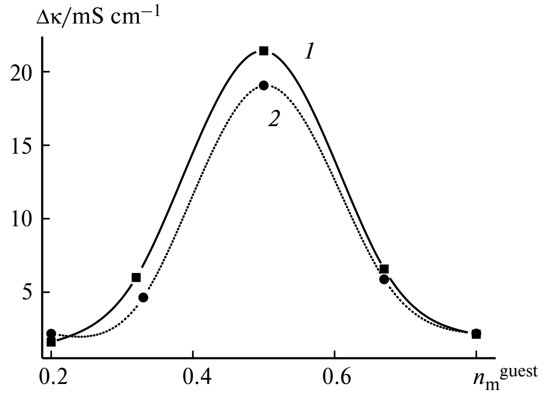


Fig. 3. Plot of Δκ for solutions containing resorcinarene **2** and complexes **3** and **6** *vs.* the mole fraction (n_m) of complexes **3** and **6**; $I = 2.8 \cdot 10^{-3}$ mol L^{-1}: *1*, $Co(en)_3Cl_3$; *2*, $Co(dipy)_3(ClO_4)_3$.

The possibility of using electron spectroscopy for analysis of the efficiency of outer-sphere association is determined by sensitivity of the intensity of d-d transitions to the outer-sphere binding with counterions. For chiral isomers of cobalt(III) tris-chelates, the absorption bands corresponding to d-d transitions possess optical activity. The absorption bands in CD spectra of tris-chelates are more sensitive to outer-sphere association with counterions than absorption bands in electronic absorption spectra. The constants of outer-sphere association were determined by ^{1}H NMR and CD spectroscopy and conductometry (Table 1). The results of these studies demonstrate that calixarene **1** forms more stable outer-sphere associates than calixarene **2**. For both receptors, the association constants decrease in the series $[Co(en)_3]^{3+} > [Co(dipy)_3]^{3+} > Co(L\text{-}His)_2]^{+} > [Co(en)_2ox]^{+}$.

Analysis of the upfield shifts and cross-peaks in 2D ^{1}H NMR spectra (NOESY) allows one to estimate the mutual arrangement of a metal complex and calixarene.[29] The results of our study showed (Fig. 4) that the interactions of all the complexes under consideration with receptors **1** and **2** lead to upfield shifts of the signals for the protons of the corresponding chelate rings of complexes **3—6**. The upfield shifts of the signals for the protons of the complexes enable one to estimate not only the mutual arrangement of the chelate rings with respect to the charged rim of the receptors but also the dynamics of outer-sphere associates.[33] The size of the ethylenediaminate fragment (see Fig. 1) is such that only one of them can be shielded by the hydrophobic cavities of both receptors (Fig. 5). However, the same upfield shifts are observed for all three ethylenediaminate fragments. This is indicative of free rotation resulting in averaging of the upfield shifts of the signals for the methylene protons of cobalt(III) tris-ethylenediaminate. Outer-sphere association of complex **4** with receptor **2** is accompanied by a larger upfield shift of the methylene protons compared to that observed in the case of outer-sphere association with receptor **1** (Fig. 4, *a*). This fact correlates with the size of the hydrophobic cavity of the receptor (see Fig. 1) and indicates that the ethylenediaminate fragment can penetrate deeper into the more capacious cavity of receptor **2**.

Table 1. Logarithms of the stability constants (β/L mol^{-1}) of the guest—host outer-sphere associates of compounds **1** and **2** with the cobalt complexes determined by different physicochemical methods (in parentheses)

Compound	logβ (method)	
	1	**2**
$[Co(en)_3]^{3+}$	>7 (CD)	4.1±0.07 (cond.*)
$[Co(dipy)_3]^{3+}$	—	3.7±0.06 (cond.*)
$[Co(en)_2ox]^{+}$	4.0±0.1 (CD)	2.0±0.04 (^{1}H NMR)
$[Co(His)_2]^{+}$	—	2.4±0.05 (^{1}H NMR)

* Conductometry.

In the CD spectra of complex **3** in aqueous solutions, the intensities of absorption bands (Δε) caused by d-d transitions reflect the conformational state of the chelate rings. Hence, it is of interest to estimate the change in Δε for complex **3** induced by outer-sphere association with receptors **1** and **2**. The conformational state of complex **3** in aqueous solutions is a superposition of the two limiting *lel* and *ob* conformations of the ethylenediaminate chelate ring. In the *lel* conformation, the C—C bond is almost parallel to the threefold axis of the tris-chelate (Fig. 6, *a*), whereas this bond in the *ob* conformation is perpendicular to this axis[9] (Fig. 6, *b*). As for the changes in the spectropolarimetric properties of complex **3**, the structural and thermodynamic parameters of the outer-sphere coordination of **3** by cyclic and acyclic polyanions and the changes in the spectropolarimetric properties induced by this coordination are of most interest. Coulomb attractions and two- or three-center intermolecular hydrogen bonds are the driving forces for the outer-sphere coordination by such anions.[14—16] These interactions lead to the conformational shift of the ethylenediaminate chelate ring toward the *lel* conformation, in which the protons of the NH groups are most accessible for intermolecular hydrogen bonding.[14—16] This, in turn, leads to a decrease in Δε of the major component (E, 490 nm) and an increase in Δε of the additional component (A_2, 435 nm) of the $^1A_{1g}$-$^1T_{1g}$ d-d transitions.[16] It is known[19] that the outer-sphere association of complex **3** with DNA gives rise to a wider spectrum of intermolecular interactions, in particular, to the hydrophobic effect. However, in spite of a more complex character of interactions, the changes in the CD spectrum of complex **3** induced by outer-sphere association with DNA are analogous to those observed in the case of association with simple polyanions, such as tartrates.[34] Therefore, the outer-sphere coordination of complex **3** by various polianions and DNA leads to an increase in the percentage of the *lel* conformation. Con-

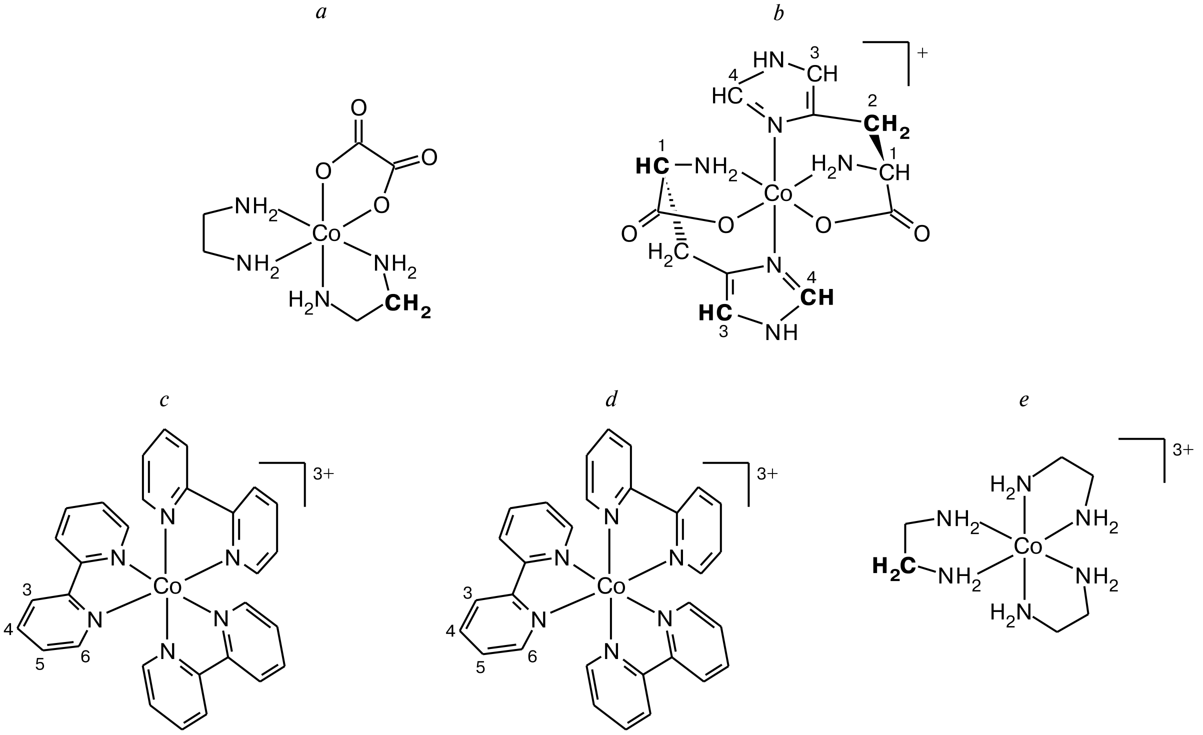


Figure	Δδ		Assignment
	CIS(**1**)	CIS(**2**)	
a	−0.48	−0.6	CH_2
b	−0.13	−0.13	$C(2)H_2$
	−0.23	−0.07	C(1)
	−0.33	−0.35	C(3)H
	−0.06	−0.09	C(4)H

Figure	Δδ		Assignment
	CIS(**1**)	CIS(**2**)	
c	−0.44	—	C(3)H
	−0.59	—	C(4)H
	−0.3	—	C(5)H
	−0.51	—	C(6)H

Figure	Δδ		Assignment
	CIS(**1**)	CIS(**2**)	
d	−0.22	−0.19	C(3)H
	−0.47	−0.47	C(4)H
	−0.31	−0.31	C(5)H
	−0.38	−0.39	C(6)H
e	−0.58	—	CH_2

Fig. 4. Upfield shifts of the signals for the protons of complexes **3—6** in the ^1H NMR spectra under the conditions of 100% accumulation of the complexes with compounds **1** (**CIS 1**) and **2** (**CIS 2**): *a*, $[Co(en)_2ox]^+$, *b*, $[Co(His)_2]^+$; *c*, $[Co(dipy)_3]^{3+}$ in H_2O; *d*, $[Co(dipy)_3]^{3+}$ in a H_2O—20 vol.% DMSO mixture; *e*, $[Co(en)_3]^{3+}$.

sequently, the opposite effect (Fig. 7, *a*), *e.g.*, an increase in the rotational power of the major component and a decrease in the rotational power of an additional component, is indicative of the *lel—ob* inversion of the chelate ring. Receptors **1** and **2** differ from cyclic and acyclic polyanions primarily in that they have a hydrophobic cavity. It is known[33] that an CH-π interaction is the main driving force for interactions between the hydrocarbon fragments and the hydrophobic cavity of cyclophanes. Hence, it is reasonable to suppose that CH-π interactions of the hydrocarbon fragments with the cavity of receptors **1** and **2** are responsible for the *lel—ob* inversion of the ethylenediaminate chelate ring. According to the published data, the *lel* conformation of the ethylenediaminate chelate ring of **3** is most stable and, hence, occurs as the major one at room temperature.[35] Broadening of the signal for the methylene protons in the ^1H NMR spectrum observed with increasing temperature is a consequence of

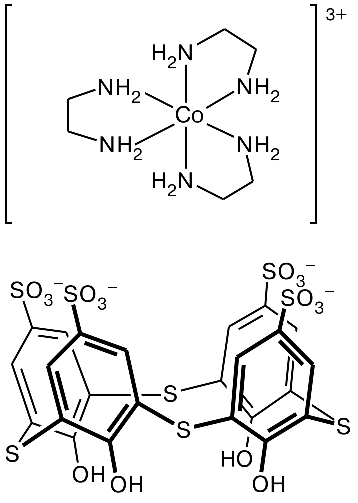


Fig. 5. Scheme of the mutual arrangement of $[Co(en)_3]^{3+}$ and the cavity of compound **1**.

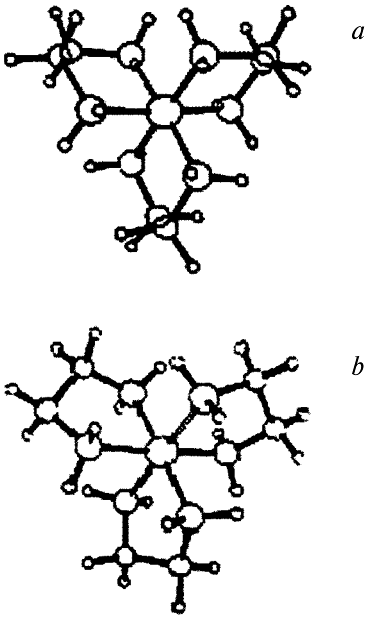


Fig. 6. Conformations of the chelate rings in $[Co(en)_3]^{3+}$: *a*, the *lel* conformation, in which the —C—C— bond is parallel to the threefold axis of the tris-chelate; *b*, the *ob* conformation, in which the —C—C— bond is perpendicular to the threefold axis of the tris-chelate.

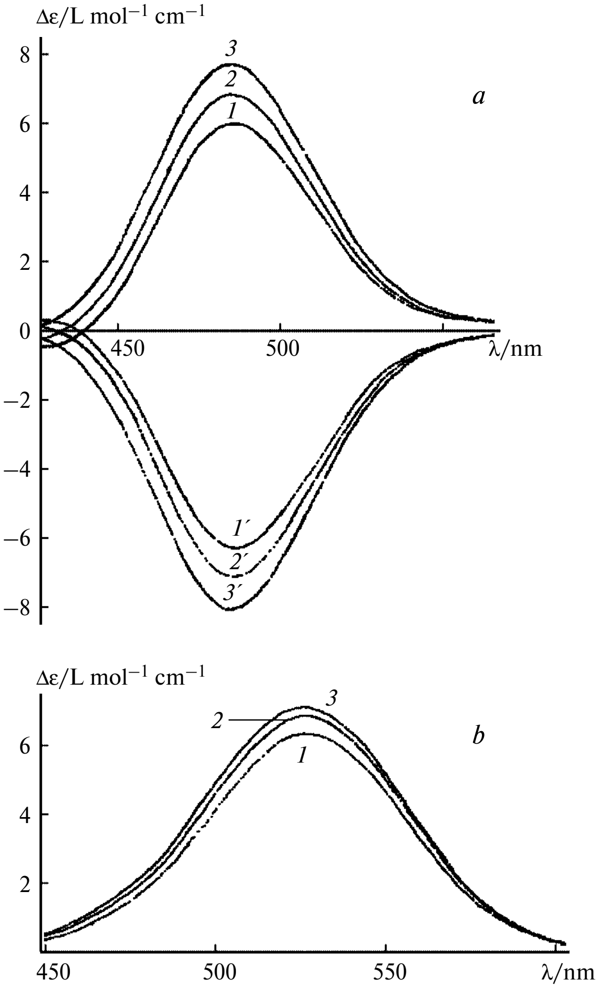


Fig. 7. CD spectra of the (*a*) Λ-$[Co(en)_3]^{3+}$ (*1*) and Δ-$[Co(en)_3]^{3+}$ (*1′*) complexes ($C = 6 \cdot 10^{-4}$ mol L^{-1}) and their mixtures with compound **1** in ratios of 1 : 1 ($C = 6 \cdot 10^{-4}$ mol L^{-1}) (*2*, *2′*) and 1 : 2 ($C = 1.2 \cdot 10^{-3}$ mol L^{-1}) (*3*, *3′*); (*b*) the Λ-$[Co(en)_2ox]^+$ complex (*1*) ($C = 8 \cdot 10^{-4}$ mol L^{-1}) and its mixtures with compound **1** in ratios of 1 : 1 ($C = 8 \cdot 10^{-4}$ mol L^{-1}) (*2*) and 1 : 2 ($C = 1.6 \cdot 10^{-3}$ mol L^{-1}) (*3*).

an increase in the percentage of the *(ob)$_3$* conformer. Hence, a decrease in the width of the signal for the methylene protons in going from free complex **3** to its outer-sphere associate with **1** and the fact that an analogous increase in the temperature of a solution of this outer-sphere associate is not accompanied by broadening of this signal (Fig. 8) confirm the fact of stabilization of the *ob* conformation of the chelate rings induced by outer-sphere association.

As expected, the replacement of one ethylenediaminate chelate ring with the oxalate anion leads to a decrease in the binding constant of complex **4** compared to that of complex **3** (see Table 1). The complexation-induced shift (CIS) for complex **4** is somewhat smaller than that for **3** (see Fig. 4, *a*). Since the upfield shifts for $[Co(en)_2ox]^+$ and $[Co(en)_3]^{3+}$ are averaged over eight and twelve protons, respectively, the ethylenediaminate (en) ring in complex **4** is shielded by the cavity of the receptor to a smaller extent compared to the en ring in complex **3**. However, the outer-sphere coordination of complex **4** by receptor **1**, unlike that of **3**, is characterized by the presence of cross-peaks in the 2D ^{1}H NMR spectrum (2D NOESY) of the corresponding outer-sphere associate (Fig. 9, *b*), which is indicative of a short contact between the methylene protons of the ethylenediaminate ring of complex **4** and the aromatic protons of receptor **1**. A substantial increase in the intensities of the cross-peaks in the 2D ^{1}H NMR spectrum (2D NOESY)[36] of the outer-sphere associate of receptor **1** with complex **4** compared to the intensities of the cross-peaks for **3** is most probably attributable to the presence of the oxalate anion in the coordination sphere of cobalt(III), which hinders free rotation of the tris-chelate with respect to the negatively charged rim and increases the correlation time of the interacting protons of the ethylenediaminate chelate ring and the aromatic protons of receptor **1**. A change in the spectropolarimetric properties of tris-chelate **4** upon the outer-sphere association with receptors **1** and **2** is analogous to the corresponding change observed for **3** (see Fig. 7, *b*). Interestingly, the interaction of the ethylenediaminate chelate ring of **4** with the more capacious cavity of receptor **2** leads to a smaller change in Δε for the $^1A_{1g}$-$^1T_{1g}$ d-d transitions (from 84703 to 92234.5 L mol^{-1} cm^{-1}) and, hence, to a smaller conformational shift of the chelate ring com-

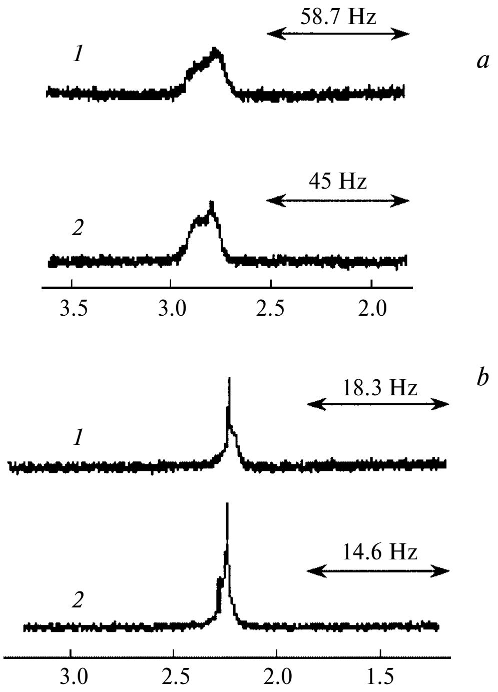


Fig. 8. Signals for the methylene protons of the [Co(en)$_3$]Cl$_3$ complex in the ^{1}H NMR spectra in D$_2$O: *a*, [Co(en)$_3$]Cl$_3$ ($C = 1 \cdot 10^{-3}$ mol L^{-1}) at 80 °C (*1*) and 20 °C (*2*); *b*, a mixture of [Co(en)$_3$]Cl$_3$ and compound **1** in a ratio of 1 : 1 ($C = 1 \cdot 10^{-3}$ mol L^{-1}) at 80 °C (*1*) and 20 °C (*2*).

pared to that induced by interaction with receptor **1** (from 84703 to 99438 L mol^{-1} cm^{-1}). Therefore, more efficient shielding of **4**, which takes place in the case of interaction with receptor **2** (see Fig. 4, *a*), correlates with neither the change in $\Delta\varepsilon$ of the $^1A_{1g}$-$^1T_{1g}$ d-d transitions (see Fig. 7, *b*) nor with the binding constant (see Table 1).

An increase in the size of the chelate ring from en to dipy in going from complex **4** to complex **6** results in a decrease in stability of the corresponding outer-sphere associates with receptor **2** (see Table 1). In contrast to the signals for the protons of the ethylenediaminate fragments, which undergo an upfield shift averaged due to free rotation, the signals for the protons of dipy undergo different upfield shifts in the case of outer-sphere association with receptor **1** in an aqueous solution (see Fig. 4, *c*). In an aqueous dimethyl sulfoxide (20 vol.%) solution (DMSO is required to increase solubility of the outer-sphere associate with resorcinarene **2**), the upfield shifts of the signals for the protons of dipy have similar values for the associates with receptors **1** and **2** (see Fig. 4, *d*). The two-dimensional NMR spectra of the corresponding outer-sphere associates show intense cross-peaks, which are indicative of interactions between the aromatic protons H(6) of the dipy residue and receptor **1**, all aromatic protons of the dipy residue and the methylene protons of the sulfonatomethylated groups of **2** (see Fig. 9, *c*). The presence of cross-peaks, which are assigned to close contacts between the protons of dipy and the CH$_2$SO$_3^-$ groups of the receptor, is evidence that the dipyridyl fragment is much more rigidly fixed inside the charged rim of receptor **2** compared to the ethylenediaminate chelate ring. This fact is consistent with the sizes of dipy and en. In the

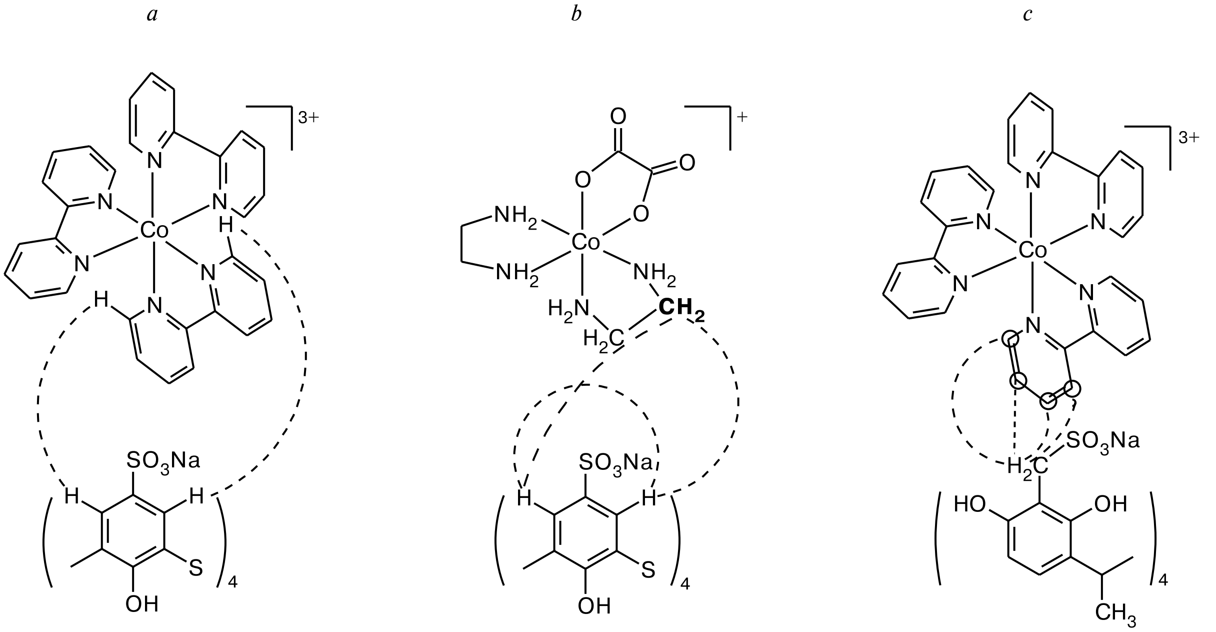


Fig. 9. Scheme of interactions of compound **1** with [Co(dipy)$_3$]$^{3+}$ (*a*) and [Co(en)$_2$ox]$^+$ (*b*) and interactions of compound **2** with [Co(dipy)$_3$]$^{3+}$ (*c*) according to the data from two-dimensional ^{1}H NMR spectroscopy (2D NOESY) (protons, which give cross-peaks, are linked by a dashed line).

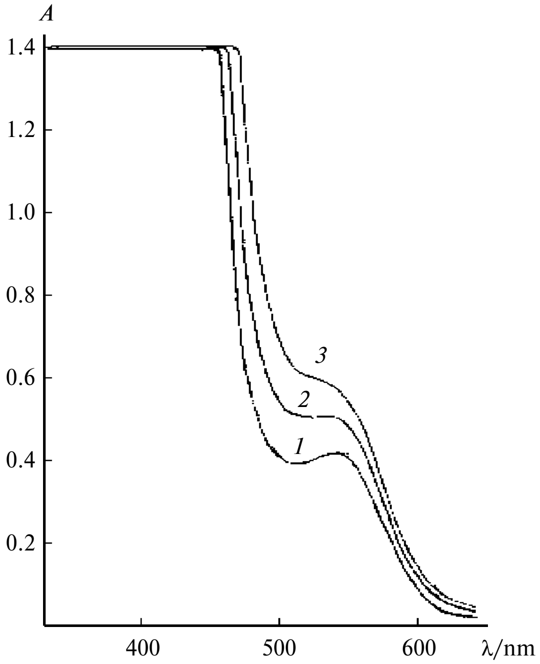


Fig. 10. Electronic absorption spectra of the $[Co(dipy)_3](ClO_4)_3$ complex ($C = 5 \cdot 10^{-3}$ mol L^{-1}) (*1*) and its mixtures with compound **1**; the $[Co(dipy)_3](ClO_4)_3$: **1** ratios are 1 : 0.25 (*2*) and 1 : 0.5 (*3*); the cell length is 10 mm.

electronic absorption spectrum of **6**, the bands assigned to d-d transitions are masked by an intense charge-transfer band. However, it is known that the characteristics of this band (ε and λ) are also sensitive to the outer-sphere coordination to DNA.[19] In particular, a small bathochromic shift and the hypsochromic effect in the case of interaction with DNA result from stacking interactions with the aromatic fragments of the purine and pyrimidine bases of DNA.[19] If the bathochromic shift and a decrease in ε of the charge-transfer band caused by stacking interactions with DNA were attributable to flattening of the chelate ring, a very small (by several nanometers) hypsochromic shift induced by outer-sphere coordination to receptor **1** and a small increase in the intensity of the charge-transfer band would be indicative of the opposite effect (Fig. 10). Therefore, the CH-π interaction of the dipyridyl fragment with the cavity of receptor **1** is not accompanied by flattening of **1** characteristic of stacking interactions with DNA.

The sizes of the histidinate fragments of $[Co(L\text{-}His)_2]^+$ also hinder free rotation of the histidinate fragment with respect to the rims of both receptors. As a result, the upfield shifts of different protons are not averaged, as evidenced by the ^1H NMR spectroscopic data presented in Fig. 4, *b*. However, the upfield shifts of the protons of the histidinate fragments are substantially smaller than the analogous values for **4** (see Fig. 4 *a*, *b*), although the outer-sphere associate of **5** with receptor **2** is more stable than the corresponding associate of **4** (see Table 1). In addition, unlike other complex cations, for which equal or even larger upfield shifts are observed in going from the smaller (**1**) to larger (**2**) receptor (see Figs. 1 and 4), association of **5** with **1** leads to a more substantial shielding of the H(1) proton compared to that observed for associates of **5** with **2**. Presumably, the outer-sphere association of complex **5**, unlike association of tris-chelates **3**, **4**, and **6**, is determined predominantly by interactions with the charged sulfonate groups at the rim of the receptor without a substantial contribution from CH-π interactions. This assumption is consistent with the absence of cross-peaks in the corresponding 2D ^1H NMR spectra (2D NOESY) of the outer-sphere associates with both receptors. The CD spectra of complex **5** are insensitive to outer-sphere association with both receptors due to the presence of the more rigid chelate ring, which is formed through tridentate coordination of the L-His$^-$ anion to the cobalt cation and whose conformation remains unchanged in the course of outer-sphere association. The constant of outer-sphere association of complex **5** with receptor **2** is higher than the corresponding value for **4**. Therefore, analogously to the tetraalkylammonium cations,[4] the binding constants of the complexes under study with ionized receptors **1** and **2** are determined predominantly by the contribution of Coulomb interactions.

To summarize, it should be noted that outer-sphere association of tris-chelates with calixarenes occurs through multicenter noncovalent interactions, among which Coulomb and dispersion (CH-π) interactions are of most importance. By contrast, two- or three-center hydrogen bonding is the main driving force for the outer-sphere association with polyanions and DNA. It is known that multicenter interactions are necessary for both the structural and enantiomeric selectivity of the guest—host complex formation (the larger the interface between the substrate and the receptor, the higher the efficiency of these interactions). Consequently, the above-described tris-chelates are promising agents for recognition and separation of ionized calixarenes.

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