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Complex formation of *O*-carboxymethylcalix[4]resorcinolarene with alkaline metal and ammonium ions

S. N. Pod´yachev,[a]* ***A. R. Mustafina,***[a] ***and W. D. Habicher***[b]

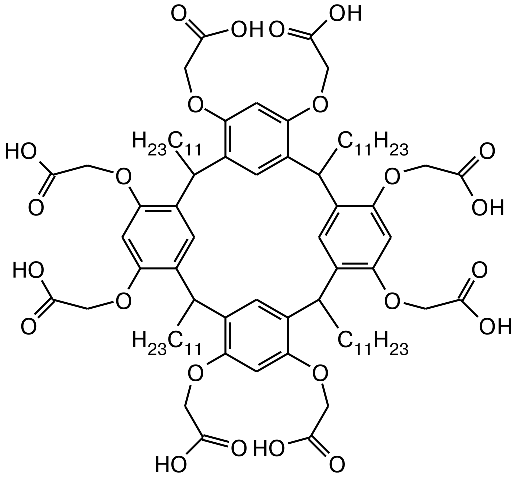
[a]*A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center of the Russian Academy of Sciences,*
8 ul. Akad. Arbuzova, 420088 Kazan, Russian Federation.
Fax: +7 (843 2) 75 2253. E-mail: spodyachev@iopc.kcn.ru
[b]*Drezden University of Technology, Institute of Organic Chemistry,*
13 Mommsenstrasse, D-01062 Drezden, Germany.
Fax: (035 1) 4633 4093

Complex formation of 3,5,10,12,17,19,24,26-octa(carboxymethoxy)-1,8,15,22-tetraundecylcalix[4]arene (H_8X) with Li^+, Na^+, K^+, and NH_4^+ ions was studied by ^1H NMR spectroscopy and pH-metry in water—DMSO solutions. Binding of one cation occurs during the stepped deprotonation of four carboxymethyl groups in H_8X. The K^+ ion was found to be bound more efficiently than Li^+ and Na^+. The further deprotonation to the penta- and hexaanion leads to the coordination with two cations. The most stable binuclear complex is formed with the Li^+ ion.

Key words: calix[4]resorcinolarene, complexes, alkaline metals, stability constants, pH-metry.

Introduction of functional groups into the calixresorcinolarene matrix allows its complex-forming ability toward metal ions to be widely varied.[1—4] One of commonly used methods for functionalization is the substitution of protons of hydroxyl groups by the corresponding functional group, for example, carboxymethyl. Although similar compounds have been synthesized long ago,[5] published data on their use as complexones for metal ions are scarce. However, the carboxy derivatives of calixarenes have already recommended themselves as efficient and selective complexones for rare-earth and transuranium metal ions.[3,4] Their complex formation with alkaline metal ions, whose presence remarkably affects the efficiency and selectivity of extraction of lanthanide ions, has also been found.[4]

In this work, the complex-forming properties of 3,5,10,12,17,19,24,26-octa(carboxymethoxy)-1,8,15,22-tetraundecylcalix[4]arene (H_8X) toward alkaline metal cations (Li^+, Na^+, K^+) and NH_4^+ (hereafter Cat^+) were studied by ^1H NMR spectroscopy and pH-metry.



H_8X

Experimental

Synthesis of H_8X was performed using a previously described procedure.[5] Commercial alkaline metal and ammonium chlorides (analytically pure grade) and alkali (Merck) were used. Water was twice distilled, and DMSO (reagent grade) was purified using a known procedure.[6]

^1H NMR spectra were recorded on a Unity-300 spectrometer (300 MHz) using Me_4Si as internal standard. Titration of H_8X with the initial concentration of $8.5 \cdot 10^{-3}$ mol L^{-1} was monitored by ^1H NMR in a D_2O—DMSO-d_6 (90 vol.%) solution. An alkali solution ($C = 8.5 \cdot 10^{-2}$ mol L^{-1}) with the similar composition of a water-organic solvent was used for titration. The alkali solution was prepared by dissolution of a saturated aqueous solution of the alkali with the known concentration.

pH-Metric titration was carried out at a variable volume on an I-130 instrument with an accuracy of ±0.05 pH units. The ionomer was calibrated by standard buffer solutions. To measure acidity in a water—DMSO (70 vol.%) solution, a described procedure[7,8] was used, according to which the ionomer was calibrated by standard buffer solutions in water. Then, to measure pH of a water-organic solution, the electrode was prelimi-

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narily soaked for 1 day in the corresponding water-organic solvent with a specified composition. The pH values of water-organic solutions were determined from the equation

$$\mathrm{pH} = \mathrm{pH}_{\mathrm{exp}} - \Delta\mathrm{pH},$$

where $\mathrm{pH}_{\mathrm{exp}}$ is the measured value in a mixed solvent, and $\Delta\mathrm{pH}$ reflects the difference in activities of protons in aqueous and water-organic solutions.

In practice, $\Delta\mathrm{pH}$ was determined by measurement of the pH of solutions of hydrochloric acid with different concentrations in a mixed solvent ($\mathrm{pH}_{\mathrm{w+s}}$) and in water ($\mathrm{pH}_{\mathrm{w}}$) using the equation

$$\Delta\mathrm{pH} = \mathrm{pH}_{\mathrm{w+s}} - \mathrm{pH}_{\mathrm{w}}.$$

Solutions were titrated in the pH 6—12 range with the H_8X concentration equal to $2.2 \cdot 10^{-3}$ mol L^{-1} at a guest : host ratio of 1 : 1. The choice of the mixed solvent, concentrations used, and the guest : host ratio is caused by the necessity of providing a satisfactory solubility for the initial components and reaction products. A solution of $\mathrm{Bu^n{}_4N^+OH^-}$ in a water—DMSO mixture ($C = 2.4 \cdot 10^{-2}$ mol L^{-1}) free of carbonate admixtures was used as titrant. Experimental data were processed by the CPESSP program.[9]

For the chosen basis species (macrocycle H_8X and metal cation Cat^+), the reaction equations of the type

$$\mathrm{H_8X} \rightleftharpoons \mathrm{H}_{8-k}\mathrm{X}^{k-} + k\,\mathrm{H}^+, \qquad (1)$$

$$m\,\mathrm{H_8X} + n\,\mathrm{Cat}^+ \rightleftharpoons \{([\mathrm{H}_{8-k}\mathrm{X}]^{k-})_m(\mathrm{Cat}^+)_n\}^{n-km} + k\,\mathrm{H}^+, \qquad (2)$$

characterized by intrinsic equilibrium constants were written.

According to Eq. (2), the stoichiometry of any complex formed can be characterized by the set of *m*, *n*, and *k*, where *m* is the number of the $[\mathrm{H}_{8-k}\mathrm{X}]^{k-}$ calix[4]resorcinolarene anions involved in the reaction, *n* is the number of cations, and *k* is the charge of the $[\mathrm{H}_{8-k}\mathrm{X}]^{k-}$ anion-host.

The mathematical model was a set of *q* equations (1) and (2). The dissociation and complex formation constants ($\beta_{i...q}$) corresponding to the minimum of the Fischer functional (*F*) were determined by the iteration procedure performed according to the CPESSP program

$$F = \sum_m (\bar{n} - \bar{n}_q)^2 \cdot \frac{1}{\sigma^2(\bar{n})^2},$$

$$\bar{n}_q = \sum_k n_i\alpha_i,$$

where σ^2 is dispersion, $\bar{n}$ and $\bar{n}_q$ are the experimental and calculated Bjerrum functions in the *m*th point, respectively, n_i is the number of protons involved in equilibria (1) and (2) for the *i*th species, and α_i is the formation extent of the *i*th species calculated taking into account the approximated β_i constant.

Results and Discussion

The pH-metric titration was carried out using $\mathrm{Bu^n{}_4N^+OH^-}$ as titrant. Its cation is not almost coordinated with unsubstituted calix[4]resorcinolarene (stability constant $K = 0.01$)[10] due to the large size and cannot efficiently be coordinated by carboxymethyl groups. As should be expected, an increase in the charge of the calix[4]resorcinolarene anion decreases the acidity of its protons, which is confirmed by an increase in $\mathrm{p}K_i$ for different steps of H_8X deprotonization obtained by mathematical processing of the pH-metric titration data using the CPESSP program.[9]

$$\mathrm{H_8X} \rightleftharpoons \mathrm{H_7X^-} + \mathrm{H^+} \qquad (\mathrm{p}K_1 = 5.78 \pm 0.01)$$

$$\mathrm{H_7X^-} \rightleftharpoons \mathrm{H_6X^{2-}} + \mathrm{H^+} \qquad (\mathrm{p}K_2 = 6.89 \pm 0.02)$$

$$\mathrm{H_6X^{2-}} \rightleftharpoons \mathrm{H_5X^{3-}} + \mathrm{H^+} \qquad (\mathrm{p}K_3 = 7.67 \pm 0.08)$$

$$\mathrm{H_5X^{3-}} \rightleftharpoons \mathrm{H_4X^{4-}} + \mathrm{H^+} \qquad (\mathrm{p}K_4 = 7.91 \pm 0.15)$$

$$\mathrm{H_4X^{4-}} \rightleftharpoons \mathrm{H_3X^{5-}} + \mathrm{H^+} \qquad (\mathrm{p}K_5 = 7.57 \pm 0.05)$$

$$\mathrm{H_3X^{5-}} \rightleftharpoons \mathrm{H_2X^{6-}} + \mathrm{H^+} \qquad (\mathrm{p}K_6 = 9.29 \pm 0.1)$$

No deprotonation of the seventh and eighth protons is observed up to pH 12. Figure 1, *a* presents the plot of the distribution of the deprotonated H_8X forms *vs.* experimental Bjerrum function ($\bar{n}$), reflecting the number of equivalents of the added alkali

$$\bar{n} = [C_{\mathrm{alk}}V - (V + V_0)10^{-\mathrm{pOH}}]/C_{\mathrm{H_8X}}V_0,$$

where V_0 and V are the volumes of the titrated solution and added alkali; C_{alk} and $C_{\mathrm{H_8X}}$ are the concentrations of the alkali and titrated solution.

Therefore, the upfield shift of the signal from the methylene protons of the $\mathrm{CH_2COOH}$ groups with an increase in the alkali concentration (Fig. 2), which is observed during titration of H_8X with $\mathrm{Bu^n{}_4N^+OH^-}$, is a result of the successive dissociation of the carboxyl fragments. In the case of titration by alkaline metal hydroxides, the upfield shift of the signals is insignificant (see Fig. 2). This can indicate the addition of the metal ions to the $\mathrm{CH_2COO^-}$ groups, which should exert an effect analogous to protonation.

The addition of equimolar amounts of alkaline metal chlorides to a solution of H_8X in a water—DMSO mixture increases the acidity of the carboxylic groups. This allows the quantitative estimation of the stoichiometry and stability constants of the formed complexes using the pH-metric titration data.

The mathematical model of complex formation processes, which includes the amount, stoichiometry, and constants of formation of complexes necessary for adequate description of experimental data, was chosen using the CPESSP program. The search for the adequate model for the complex formation of the $\mathrm{Li^+}$, $\mathrm{Na^+}$, $\mathrm{K^+}$, and $\mathrm{NH_4{}^+}$ ions with H_8X was based on the assumption that any $[\mathrm{H}_{8-k}\mathrm{X}]^{k-}$ deprotonated form can bind the metal and ammonium ions according to Eq. (2).

The pH-metric titration data were obtained at the 1 : 1 concentration ratio of H_8X to the corresponding chlo-

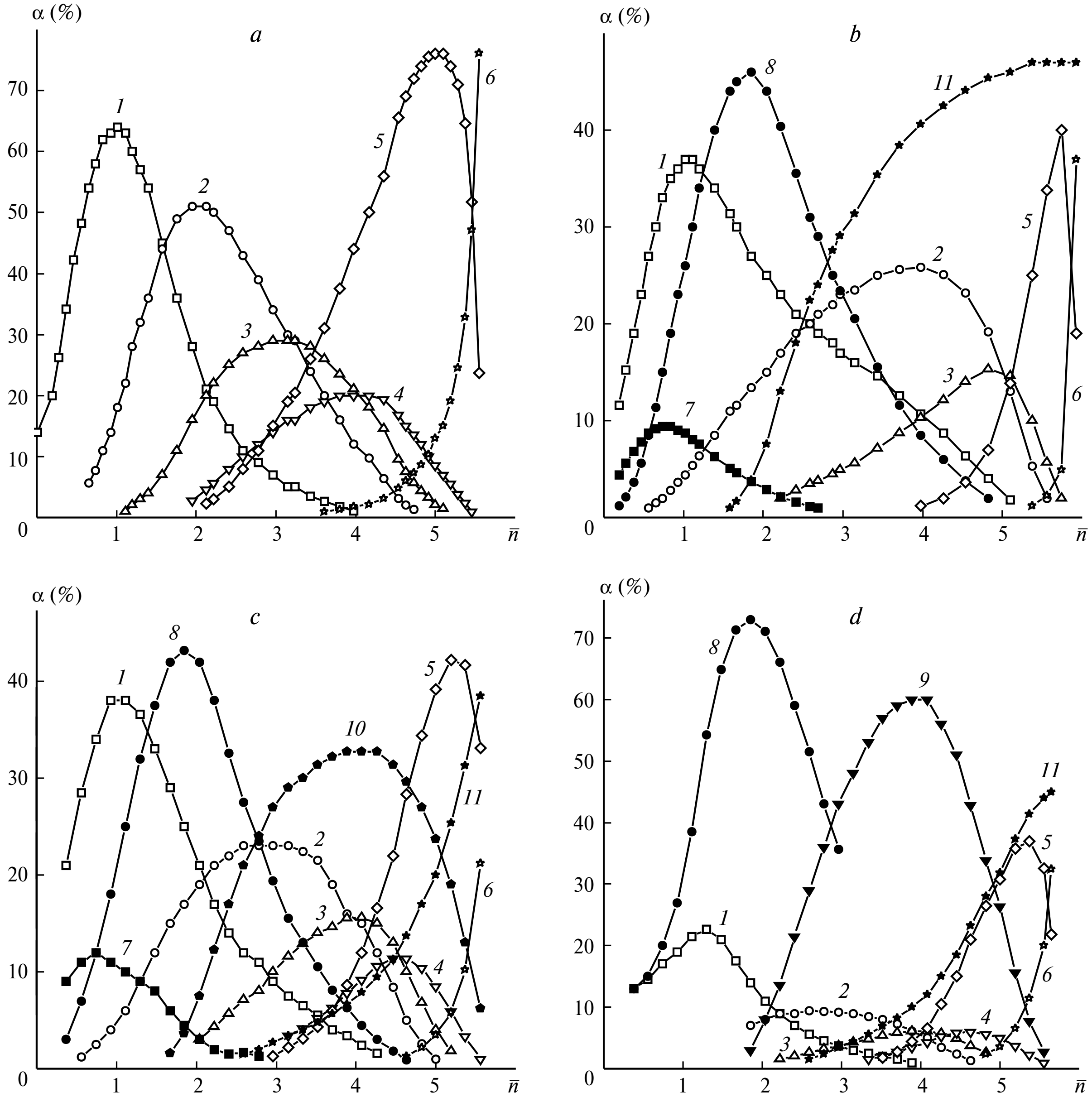

Fig. 1. The plot of the formation extent (α) of the ionized forms in solution *vs.* Bjerrum function ($\bar{n}$) for the H_8X compound (*a*) and H_8X—Cat^+ system ($Cat^+ = Li^+$ (*b*), Na^+ (*c*), and K^+ (*d*)). Ionized forms: H_7X^- (*1*), H_6X^{2-} (*2*), H_5X^{3-} (*3*), H_4X^{4-} (*4*), H_3X^{5-} (*5*), H_2X^{6-} (*6*), $[Cat^+H_7X^-]$ (*7*), $[Cat^+H_6X^{2-}]^-$ (*8*), $[Cat^+H_4X^{4-}]^{3-}$ (*9*), $[Cat^+{}_2H_3X^{5-}]^{3-}$ (*10*), and $[Cat^+{}_2H_2X^{6-}]^{4-}$ (*11*).

ride. Taking into account this fact and the tendency of complexones with the cyclophanic structure to form 1 : 1 complexes, we can assume the predominant formation of complexes with a similar composition. For example, it was found for the H_8X—Na^+ system by the iteration procedures that the experimental data are described by complexes with the composition $m = 1$, $n = 1$, $k = 1$; $m = 1$, $n = 1$, $k = 2$; $m = 1$, $n = 1$, $k = 3$; and $m = 1$, $n = 1$, $k = 5$ with $F = 0.26$. However, the introduction of the complexes with the composition 1, 2, k into the stoichiometry matrix showed that the complexes with $m = 1$, $n = 2$, $k = 5$ and $m = 1$, $n = 2$, $k = 6$ noticeably improved adequacy of the experimental data description ($F = 0.14$). The formation extent of the complex with $m = 1$, $n = 1$, $k = 1$ is at most 12% (see Fig. 1, *c*). However, its exclusion from the stoichiometry matrix increases the Fischer functional ($F = 0.66$). The stoichiometry and equilibrium constants of complex formation calculated for Eq. (3)

$$m\,[H_{8-k}X]^{k-} + n\,Cat^+ \rightleftharpoons \{([H_{8-k}X]^{k-})_m(Cat^+)_n\}^{n-km}, \qquad (3)$$

for the H_8X—Cat^+ systems ($Cat^+ = Li^+$, Na^+, K^+, NH_4^+) characterized by the lowest F value are presented in Table 1.

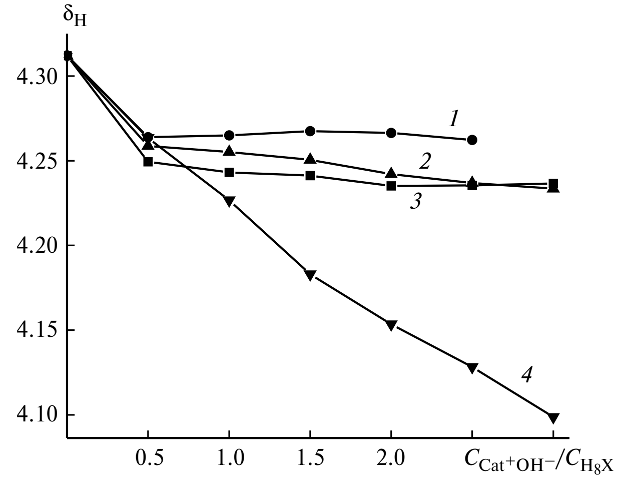

Fig. 2. Change in the chemical shifts (δ_H) of the averaged signal from the methylene protons of the CH_2COOH groups in H_8X in the ^1H NMR spectrum in a D_2O—DMSO-d_6 (90 vol.%) solution with addition of KOH (*1*), LiOH (*2*), NaOH (*3*), and $Bu^n{}_4N^+OH^-$ (*4*).

The $[H_7X]^-$ form containing one deprotonated carboxyl group at the 1 : 1 molar ratio binds the Li^+ and Na^+ cations but does not bind the K^+ cations (see Table 1). This can be caused by a higher charge density of the first two cations and, hence, by a higher efficiency of electrostatic interactions with the carboxylate anion. The enhanced stability of the complex with $m = 1$, $n = 1$, $k = 1$ for the $NH_4{}^+$ ion is a result, most likely, of its additional stabilization due to the hydrogen bond. The increase in the stability of the complex on going from $m = 1$, $n = 1$, $k = 1$ to $m = 1$, $n = 1$, $k = 2$ indicates the involvement of two carboxylate anions in coordination. The stability constant of the complex with $m = 1$, $n = 1$, $k = 2$ increases in the series $Li^+ < Na^+ < NH_4{}^+ < K^+$. This tendency indicates that the efficiency of bidentate coordination is caused by the sizes of the bound cation. The K^+ ion is characterized by the significant formation extent of the form with $m = 1$, $n = 1$, $k = 4$. Further deprotonation results in the formation of complexes of the calix[4]resorcinolarene penta- and hexaanions with two cations (see Fig. 1, *d*). Coordination of two Li^+ ions by the hexaanion affords the most stable complex, whose formation extent is substantial already at $\bar{n} = 2$ (see Fig. 1, *b*), unlike complexes of other cations. The stability of the binuclear complexes decreases on going to Na^+ and K^+. Thus, when mononuclear complexes are formed, the largest K^+ ion is most efficiently bound, while it is the Li^+ ion for the formation of a binuclear complex.

Table 1. Stability constants (logβ) of the complexes formed in the H_8X—Cat^+ system at a ratio of 1 : 1 ($C = 2 \cdot 10^{-3}$ mol L^{-1})

Cat^+	$\{([H_{8-k}X]^{k-})_m(Cat^+)_n\}^{n-km}$			logβ /L mol^{-1}
	m	*n*	*k*	
Li^+	1	1	1	2.3±0.5
	1	1	2	3.7±0.1
	1	2	6	11.9±0.2
Na^+	1	1	1	2.4±0.1
	1	1	2	3.6±0.05
	1	2	5	3.9±0.1
	1	2	6	9.6±0.3
K^+	1	1	2	4.6±0.08
	1	1	4	5.7±0.3
	1	2	6	10.9±0.2
$NH_4{}^+$	1	1	1	2.83±0.06
	1	1	2	4.27±0.04
	1	2	7	>16.5

As follows from the titration data monitored by the ^1H NMR spectra (see Fig. 2), already at the 1 : 1 concentration ratio of the added alkali (LiOH, NaOH, KOH) to H_8X the upfield shift of the methylene protons of the CH_2COOH groups decreases compared to the similar value for $Bu^n{}_4N^+OH^-$. Further increase in the concentration of NaOH and LiOH to two equivalents also results in an insignificant (unlike $Bu^n{}_4N^+OH^-$) decrease in the chemical shift, whereas it remains virtually unchanged with an increase in the KOH concentration. In the H_8X—alkaline metal chloride system at $\bar{n} = 2.5$—3 for the Na^+ and Li^+ ions, dimeric complexes with the penta- and heptaanions are accumulated, whereas the monomeric complex with the tetraanion ($m = 1$, $n = 1$, $k = 4$) is predominant in the presence of KCl (see Fig. 1), which results, probably, in different chemical shifts.

It is known that intramolecular hydrogen bonds between the resorcinol fragments are the main factor stabilizing the "cone" conformation in unsubstituted calix[4]resorcinolarene.[10] The substitution of the resorcin protons by the carboxymethyl groups affords a conformationally mobile complexone with predomination of the 1,3-diplanar conformation with the C_{2v} symmetry in solution.[5] As shown[11] by NMR spectroscopy, the silver cation is coordinated by octafunctionalized calix[4]resorcinolarene containing amide groups through the O atoms of four amide groups when the conformation of the host molecule is 1,3-diplanar. It is reasonable to assume that the 1,3-diplanar conformation is also predominant in binding of both one and two alkaline metal ions by the H_8X anions (Fig. 3).

Thus, the successive deprotonation of four carboxymethyl groups of H_8X results in bonding of one metal ion, and the K^+ cation is bound with the highest stability constant in the series Li^+, Na^+, and K^+. The further deprotonation of H_8X to the penta- and hexaanions leads to coordination with two cations, and the most stable binuclear complex is formed with the Li^+ ion. The selective change in stability with an increase in the ion radius indicates, most likely, the involvement of several carboxymethyl groups in coordination with the metal ion.

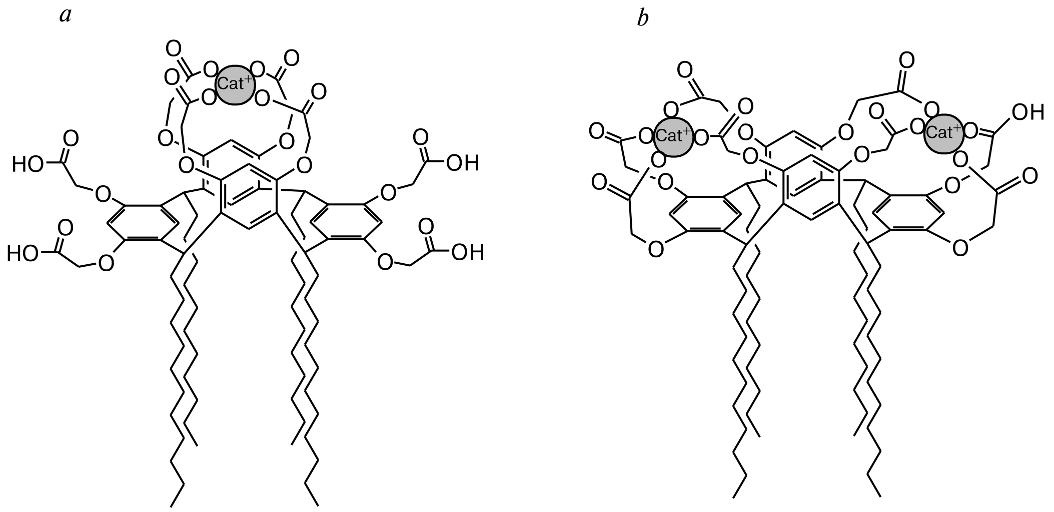

Fig. 3. Model assumed for the complex formation of the H_8X anion in the 1,3-diplanar conformation with one (*a*) and two (*b*) cations.

The formation of one or two active donor sites in H_8X can be favored by the 1,3-diplanar conformation of calix[4]resorcinolarene in solution stabilized by coordination with one or two metal ions.

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