



Aminoalkylated Calix[4]resorcinarenes as pH Sensitive “hosts” for Charged Metallocomplexes

YULIA E. MOROZOVA, LIUBOV S. KUZNETZOVA, ASIA R. MUSTAFINA, ELLA KH KAZAKOVA, VLADIMIR I. MOROZOV, ALBINA YU ZIGANSHINA* and ALEXSANDR I. KONOVALOV

A. E. Arbuзов Institute of Organic and Physical Chemistry, Kazan Scientific Center of the Russian Academy of Sciences, A. E. Arbuзов 8, 420083 Kazan, Russia

Abstract. On the basis of RCA, pH-potentiometry and EPR-spectroscopy data aminoalkylated derivatives were proved to bind metal ion complexes both in alkaline and in acidic media. Outer-sphere coordination is the only interaction mode in these host-guest complexes.

Key words: calix[4]resorcinarene, metallocomplex ions, supercomplexes, pH-metry, EPR-spectroscopy.

1. Introduction

From the wide spectrum of cyclic host molecules, crown-ethers are well known as platforms for cation binding receptors, cyclodextrins for neutral molecule-sensitive receptors and calixarenes and calixresorcinarenes for cation and anion binding. A variety of binding groups thus allows a selectivity of host-guest complexation under different working conditions. In this work the properties of substituted calix[4]resorcinarene and their ability to form metallocomplexes will be discussed.

2. Experimental

Compounds H_8L and H_8X were synthesized according to literature procedures [1, 2] (Figures 1 and 2). Complexes $[Co(en)_3]Cl_3$, $[Co(His)_2]ClO_4$, $[Cu(phen)_2(H_2O)](ClO_4)_2$, $[Cu(phen)(AA^-)(H_2O)]ClO_4$ were obtained as described previously [3–6], where **en** is ethylenediamine, **His** is histydidate, **phen** is 1,10-phenanthroline, **AA⁻** = **Tyr**, **Phal** are tyrosinat, phenylalaninat respectively.

pH-Titrations were carried out according to the procedure previously reported [7] in a thermostatted cell at $T = 25$ °C using I-130 ionomer with standardization of the glass electrode by aqueous buffer solutions followed by evaluation of the liquid/liquid potential according to a known procedure [8]. All titrations were made

* Author for correspondence.

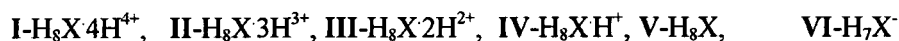
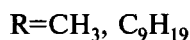
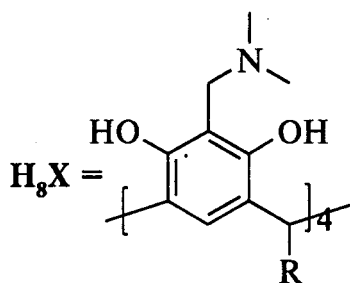
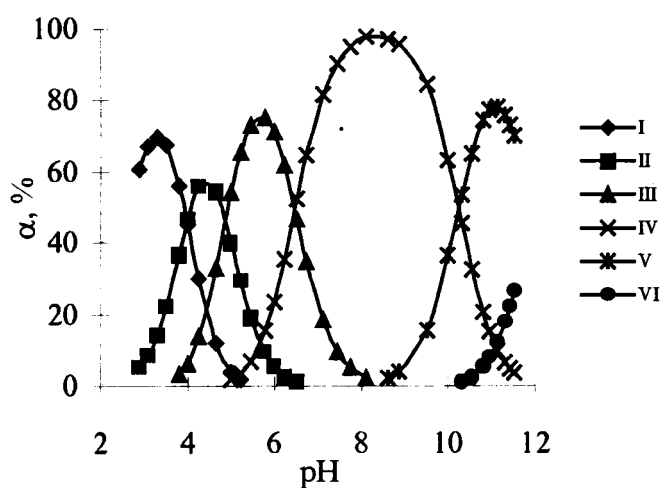


Figure 1. Distribution diagram for the system $\text{H}_8\text{X}\cdot 4\text{HCl}$.

for 0.002 M water-isopropanol solutions with 79 vol.% of isopropanol. The data points collected in the pH range 3–11 were used for calculations. The log β -values were calculated by use of a computer program “CPESP” [9].

EPR spectra were recorded on a Radiopan SE/X-2544 spectrometer for $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})](\text{ClO}_4)_2$ and $[\text{Cu}(\text{phen})(\text{AA}^-)(\text{H}_2\text{O})]\text{ClO}_4$ in water-isopropanol solutions ($c = 10^{-3}$ – 5×10^{-3} mol/L) both in the absence and in the presence of an equimolar quantity of H_8L and H_8X in the pH range 5–10, at $t = 25$ °C (CF-313,9; SW-100 mT; TC-0,3 s; ST-120 s; for complexes of $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$: AM-1 mT; At-5 db; $G-1 \times 10^5$; for complexes of $[\text{Cu}(\text{phen})(\text{AA}^-)(\text{H}_2\text{O})]^+$: AM-0.5 mT; At-7 db; $G-0,5 \times 10^5$).

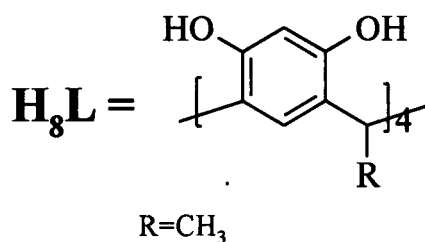
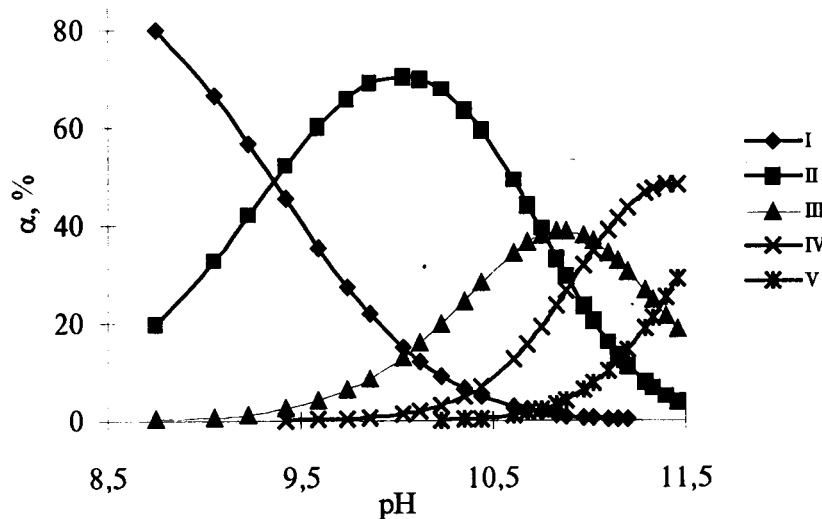


Figure 2. Distribution diagram for the system H₈L.

3. Results and Discussion

3.1. HOST PROPERTIES

Substituted calix[4]resorcinarenes were synthesized by the Mannich reaction [1]. They have eight hydroxy- and four alkylamino-groups. For this reason they can be protonated in acidic, deprotonated in alkaline or exist in zwitterionic form in neutral media. Dimethylaminoalkylated calix[4]resorcinarene's (H₈X) solubility depends both on the length of the cis-oriented hydrophobic radicals R and on the pH of solution. The compound H₈X with R = CH₃ was shown to be most soluble in water-containing solutions. Moreover it is reasonably soluble even in acidic (pH < 1) water solutions. Water-isopropanol mixture (79 vol.% of isopropanol) was used

Table I. pK_n-values of stepwise deprotonation of H₈X·4HCl and H₈L in water-isopropanol solution (*n* = 1–4 – are ascribed to deprotonation of protonated dimethylaminogroups, *n* = 5–8 – to deprotonation of hydroxy-groups).

	pK ₁	pK ₂	pK ₃	pK ₄	pK ₅	pK ₆	pK ₇	pK ₈
H ₈ X·4HCl	2.64	4.16	5.9	7.6	10.1	–	–	
H ₈ L	–	–	–	–	8.94	10.21	10.9	12.1

for pH-metric investigation of the acid-base and complexation properties of H₈X with both R=CH₃ and C₉H₁₉ over a wide pH range (2–11).

Mathematical treatment of the pH-metric titration data of the hydrochloric tetra-salt H₈X·4HCl resulted in pK-values of the stepwise dissociation of the (NMe₂H)⁺ and OH groups (Table I). The pK-values of deprotonation of three (NMe₂H)⁺ groups are less than that of the Mannich base (pK = 7.3). The fourth (NMe₂H)⁺ group deprotonates (pK₄ = 7.6) very similar to pK of Mannich base. The pK-values for deprotonation of the OH groups of H₈X are greater than for unsubstituted H₈L (Table I). This is explained by the existence of intermolecular hydrogen bonding, resulting in H₈L deprotonation up to [H₄L]⁴⁻. The lower acidity of H₈X can be explained by disturbance of the intermolecular hydrogen bonding between OH-groups due to their hydrogen bonding with NMe₂-groups. For this reason H₈X and H₈L deprotonate up to the mono- and tetraanions respectively with increasing pH from 7 to 12 (Figures 1 and 2). Thus aminoalkylated H₈X can be used as pH-dependent hosts for both anion and cation guests. According to the “size match rule”, the most efficient guests for cyclophane-type structure of H₈L and H₈X are bulky organic ions [10] or metal-containing complex ions [11].

3.2. COMPLEXATION WITH METALLOCOMPLEXES IN BASIC MEDIA

pH-Titrimetric data shows that in neutral media H₈X exists in the molecular or zwitterionic form (Figure 1). Four NMe₂ groups provide binding sites for transition metal ions [12], but in view of the size of the “rim”, metal ion coordination with four dimethylamino-groups is improbable. The host-guest interaction was shown to occur with deprotonation of hydroxy groups resulting in the appearance of a negative charge on the “rim” of the host (Equation (1)) as well as in the formation of the host-guest complex [(H_{8-m}L)^{m-}]_p[Ktⁿ⁺]_q [7].



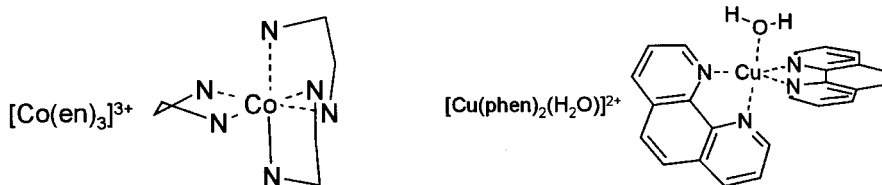
According to the literature [13, 14] dealing with complexation of crown-ethers and cyclodextrins with metal complexes, such host-guest complexation over the outer-sphere coordination is called supercomplexation. The supercomplex stability

constant (β) is calculated using Equation (2), where p , q are the moles of host and guest, respectively, and k is the degree of deprotonation.

$$\beta = [(\text{H}_{8-k/p}\text{L})_p(\text{Kt})_q]/([\text{H}_{8-k/p}\text{L}]^p[\text{Kt}]^q), \quad (2)$$

Host-guest complexation accompanied by protonation or deprotonation has been investigated by a pH-titrimetric method. It was carried out for both H_8X and H_8L in the presence of octahedral tris- and bis-chelates of Co(III) ($[\text{Co}(\text{en})_3]^{3+}$, $[\text{Co}(\text{His})_2]^+$) and some bis-chelates of Cu(II) ($[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$, $[\text{Cu}(\text{phen})(\text{AA}^-)(\text{H}_2\text{O})]^+$), where **en** is ethylenediamine, **phen** is 1,10-phenanthroline, **AA**⁻ = **His**⁻, **Tyr**⁻, **Phal**⁻ are: histidinate, tyrosinate, phenylalaninate, respectively. Due to the $\log \beta$ -values presented in Table II, $[\text{Co}(\text{en})_3]^{3+}$, $[\text{Co}(\text{His})_2]^+$ and $[\text{Cu}(\text{phen})(\text{AA}^-)(\text{H}_2\text{O})]^+$ bind with the monoanion of H_8X ($[\text{H}_7\text{X}]^-$) forming supercomplex 111 with $\log \beta$ -values close to those for the unsubstituted calix[4]resorcinarene ($[\text{H}_7\text{L}]^-$). Further deprotonation of 111 to 112 or 113 occurs with pK-values, which are very similar for both H_8X and H_8L (Table II).

For $[\text{Co}(\text{en})_3]^{3+}$ and $[\text{Co}(\text{His})_2]^+$ outer-sphere coordination was proved to be the only interaction mode due to the stability of the inner-sphere of ligands in both $[\text{Co}(\text{His})_2][\text{H}_7\text{L}]$ and $[\text{Co}(\text{en})_3][\text{H}_5\text{L}]$ supercomplexes, which was derived from ¹H NMR and elemental analysis data [11]. While $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ and $[\text{Cu}(\text{phen})(\text{AA}^-)(\text{H}_2\text{O})]^+$ cations have a water molecule in the axial position, which may be substituted by donor atoms of H_8L or H_8X . Unfortunately, substitution of a water molecule cannot be detected by ¹H NMR or elemental analysis data.



On the other hand $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ is coordinated with $[\text{H}_7\text{X}]^-$ forming a 111 supercomplex with a $\log \beta$ -value, which is greater than for the unsubstituted calix[4]resorcinarene. Further deprotonation of this supercomplex from 111 to 112 occurs with a pK-value that is also close to those for the unsubstituted form. For this reason only for $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ do the presence of NMe_2 groups affects the $\log \beta$ -value of supercomplexation. The effect of the NMe_2 -groups may be explained as inner-sphere coordination of Cu(II) by the NMe_2 groups of H_8X or by more effective outer-sphere coordination due to intermolecular proton transfer from the OH to the NMe_2 group and the appearance of additional negative charge on the “rim”. EPR-spectra are sensitive to the nature and geometry of the inner-sphere environment of Cu(II), and they were obtained for both free

Table II. log β -Values of stability of supercomplexes 111 and pK-values of their deprotonation up to 112 and 113 (**en** is ethylenediamine, **His** is histyinate, **phen** is 1,10-phenantroline, **Tyr** is tyrosinate, **Phal** is phenylalaninate).

H ₈ T	Kt ⁿ⁺	log β_{111} [H ₇ T] ⁻ + Kt ⁿ⁺ = [H ₇ T] ⁻ [Kt] ⁿ⁺	pK 111 = 113 + 2H ⁺	pK 111 = 112 + H ⁺
H ₈ L	[Co(His) ₂] ⁺	2.8	19.6	–
	[Co(en) ₃] ³⁺	3.0	17.3	–
	[Cu(phen) ₂ (H ₂ O)] ²⁺	3.6	–	9.4
	[Cu(phen)(Phal)(H ₂ O)] ⁺	3.5	–	9.0
	[Cu(phen)(Tyr)(H ₂ O)] ⁺	3.2	–	9.3
H ₈ X	[Co(His) ₂] ⁺	3.0	20.8	–
	[Co(en) ₃] ³⁺	3.4	18.3	–
	[Cu(phen) ₂ (H ₂ O)] ²⁺	4.7	–	10.7
	[Cu(phen)(Phal)(H ₂ O)] ⁺	3.3	–	9.6
	[Cu(phen)(Tyr)(H ₂ O)] ⁺	3.1	–	9.6

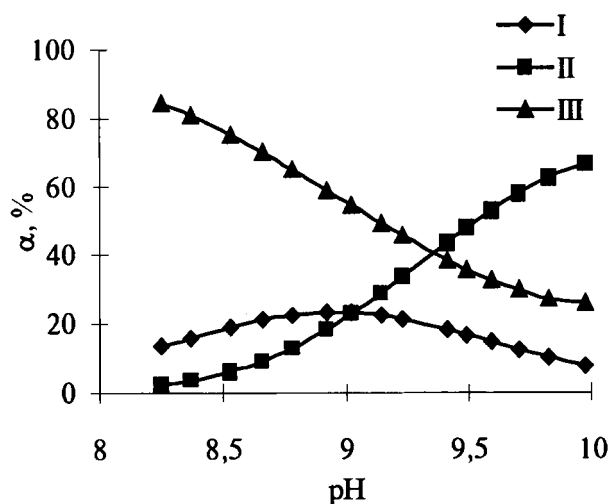


Figure 3. Distribution diagram for the system $H_8L + [Cu(phen)(Tyr)(H_2O)]^+$. I. α_{111} . II. α_{112} . III. $\alpha_{[Cu(phen)(Tyr)(H_2O)]^+}$.

guests $[Cu(phen)_2(H_2O)]^{2+}$, $[Cu(phen)(AA)(H_2O)]^+$ and bound ones in water-isopropanol solutions. Changes in the EPR-spectra were observed over the pH range 5–10 and occurred in the inner-sphere of Cu(II) cation both with H_8L and H_8X .

As was shown in [6, 15] Cu(II) in these complexes has a tetrahedrally distorted square-pyramidal geometry with the four nitrogen atoms of two **phen** or two nitrogen atoms of **phen** and an α -amino nitrogen and carboxylate oxygen atoms at the equatorial position and a water molecule at an axial position. From RCA-data [6] complex $[Cu(phen)(Phal)(H_2O)]ClO_4$ exists in both stacked and unstacked forms, while the form with intermolecular stacking between coordinated **phen** and **Tyr** dominates for $[Cu(phen)(Tyr)(H_2O)]ClO_4$ complexes.

The addition of both H_8L and H_8X does not lead to any changes in the EPR-spectra of $[Cu(phen)(Tyr)(H_2O)]^+$, but in the pH range 8–10 the signals were broader. According to the distribution of supercomplexes with pH (Figure 3) supercomplexation occurs in the pH range 8–10. Supercomplexation resulted in no variation in the magnetic parameters of Cu(II) indicating no changes in the inner-sphere environment. pH-Dependent broadening of EPR-components may be ascribed to residual anisotropy as a result of the restriction of diffusion movement due to outer-sphere coordination of $[Cu(phen)(Tyr)(H_2O)]^+$ by anions of H_8L and H_8X .

The pH-dependence of the $[Cu(phen)_2(H_2O)]^{2+}$ signals in the EPR-spectra were due to the equilibrium of two conformations. The presence of H_8L and H_8X gave similar shifts to those observed from a change in pH due to outer-sphere coordination of $[Cu(phen)_2(H_2O)]^{2+}$ by the negatively charged “rim” of H_8L and H_8X .

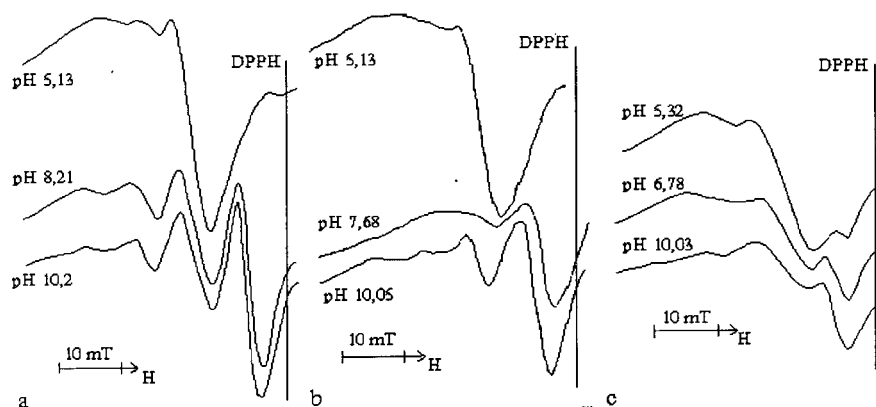


Figure 4. pH dependence of the parallel portion of the EPR-spectra for the solution of the systems. (a) $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$. (b) $\text{H}_8\text{L}\cdot[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$. (c) $\text{H}_8\text{X}\cdot[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$.

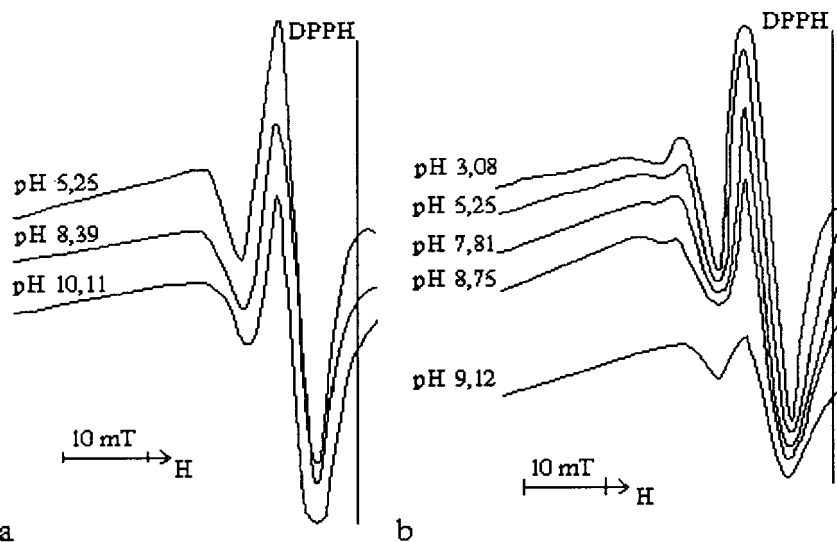


Figure 5. pH dependence of the parallel portion of the EPR-spectra for the solution of the systems: (a) $[\text{Cu}(\text{phen})(\text{Tyr})(\text{H}_2\text{O})]^{+}$. (b) $\text{H}_8\text{X}\cdot[\text{Cu}(\text{phen})(\text{Tyr})(\text{H}_2\text{O})]^{+}$.

anions. When coordinated by H_8L and H_8X anions $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ displayed a decrease of intensity which can be probably ascribed to dimerisation, which cannot be detected from pH-metric data, but is detectable from EPR-spectroscopy due to its high sensitivity.

The EPR-data showed that even for Cu(II)-containing complexes with a soft central ion and a water molecule as an easily substituted group, outer-sphere coordination is the only interaction mode in supercomplexation with H_8L and H_8X . Thus, the main reason for NMe_2 -groups affecting $\log \beta$ -values is the appearance

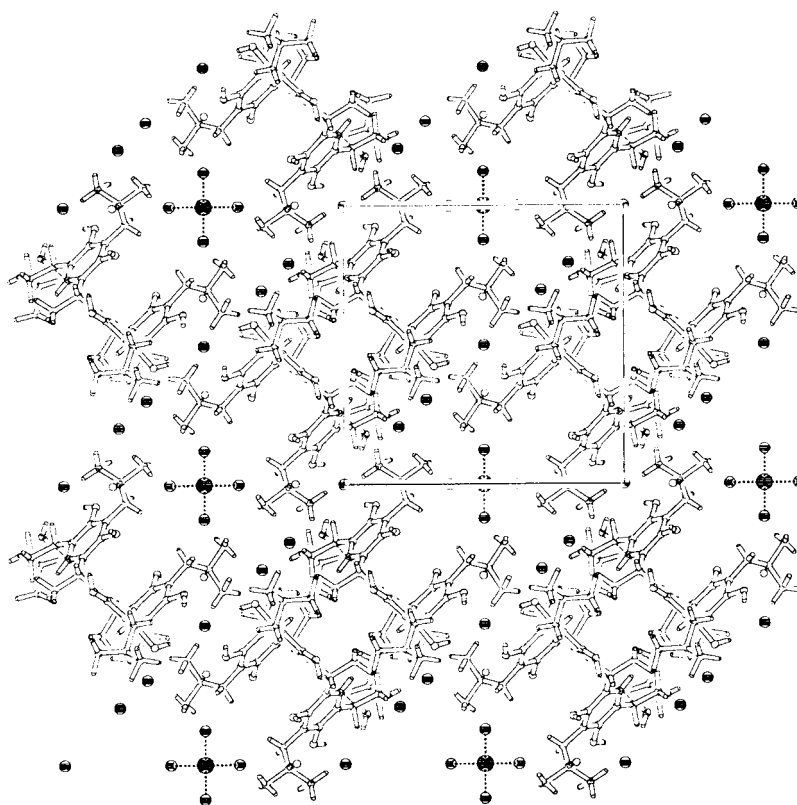


Figure 6. The monolayer arrangement in the crystal. View along the *c* axis.

of additional deprotonated centers on the “host’s rim” due to the existence of zwitterionic forms.

It was also found that $[\text{H}_7\text{L}]^-$ binds all $\text{Cu}(\text{II})$ -containing complexes with $\log \beta$ -values which are independent of the charge and the structure of the complexed cation, while $[\text{H}_7\text{X}]^-$ prefers $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ as the guest (Table II). According to [7] $\log \beta$ -values for $\text{Co}(\text{III})$ -containing monocations do not increase with further deprotonation of $[\text{H}_7\text{L}]^-$ up to $[\text{H}_4\text{L}]^{4-}$. Taking everything into account it was proposed that both $[\text{Co}(\text{His})_2]^+$ and $[\text{Cu}(\text{phen})(\text{AA})(\text{H}_2\text{O})]^+$ should not be affected by NMe_2 -groups. In contrast, $\log \beta$ -values for cations $[\text{Cu}(\text{phen})_2(\text{H}_2\text{O})]^{2+}$ and $[\text{Co}(\text{en})_3]^{3+}$ increase with deprotonation of $[\text{H}_7\text{L}]^-$.

3.3. COMPLEXATION WITH METALLOCOMPLEX ANIONS IN ACIDIC MEDIA

Dimethylaminoalkylated calix[4]resorcinarene H_8X ($\text{R} = \text{CH}_3$) protonated in acidic media $[\text{H}_8\text{X} \cdot 4\text{H}]^{4+}$ should be able to form supercomplexes with complex anions. The ionic compound $2(\text{C}_{44}\text{H}_{64}\text{O}_8\text{N}_4)^{4+} \cdot (\text{ZnCl}_4)^{2-} \cdot 6\text{Cl}^- \cdot 4\text{H}_2\text{O}$ was obtained from the aminomethylated calix[4]resorcinarene H_8X and zinc chloride in HCl wa-

ter solution. The X-ray data is given in [16]. The calixarene molecule exists in the protonated cationic form and exhibits a 1,3-diplanar shape with the two opposite phenolic rings bearing the dimethylamino-groups almost parallel to one another. The crystal superstructure is rather interesting. Two calixarene molecules are facing each other with their “planar” **A** resorcinolic rings forming bilayer lipophilic regions. On the other hand the **B** resorcinolic rings incorporate a “supercavity” large enough to encompass the anion $[\text{ZnCl}_4]^{2-}$. This motif is organized into infinite one-dimensional stacks, which are surrounded by a hydrophilic layer consisting of the NH^+Me_2 , OH-groups, Cl^- and H_2O , forming a solvating shell. The coplanar stacks are packed with a constant shift into monolayers. Every next monolayer is twisted by 90° with respect to the previous one, which explains why all guests have a lipophilic covering. The $[\text{ZnCl}_4]^{2-}$ anion is surrounded by ten calixarene molecules and one Cl^- is placed on the C_2 axis forming an anion «pseudo-channel». A hydrogen bonding system forms a three-dimensional network with a direction which does not coincide with the stacks and monolayers. The aminomethylated calixarene fragments are not involved in the first coordination sphere of the metal ion. Electrostatic forces and the size of complexation are important in this case.

Acknowledgments

Acknowledgment is made to the Stefan Batory Foundation for support of this work presented at the 1st International Conference of Supramolecular Science & Technology (Zakopane, Poland, 1998). We also gratefully acknowledge financial support by the Russian Foundation of Basic Research (Grant No. 98-03-33051).

References

1. J. Matsuskita and T. Matsui: *Tetrahedron Lett.* **46**, 7433 (1993).
2. L. M. Tunstad, J. A. Tucker, E. Dalcanale, J. Weiser, J. A. Bryant, J. C. Sherman, R. C. Helgerson, C. B. Knobler, and D. J. Cram: *J. Org. Chem.* **54**, 1305 (1989).
3. J. Corey and J. C. Bailar: *J. Am. Chem. Soc.* **81**, 2620 (1959).
4. S. Bagger and H. Jensen: *Acta Chem. Scand.* **A32**, 659 (1978).
5. W. R. McWhinnie: *J. Inorg. Nucl. Chem.* **26**, 15 (1964).
6. J. Sugimori, H. Masuda, N. Ohata, K. Koiwai, A. Odani, and O. Yamauchi: *Inorg. Chem.* **36**, 576 (1997).
7. A. R. Mustafina, V. V. Skripacheva, Yu. G. Yelistratova, E. Kh. Kazakova, S. N. Pod'yachev, V. Ye. Katayev, and A. I. Konovalov: *Mendeleev Commun.* **2**, 71–73 (1998).
8. F. Jordan: *J. Phys. Chem.* **77**, 2681 (1973).
9. Yu. I. Sal'nikov, F. V. Devyatov, N. E. Zhuravleva, and D. V. Golodnitskaya: *Zh. Neorg. Khim.* **29**, 2273 (1984) [*J. Inorg. Chem. USSR (Engl. Transl.)*]. **29**, 1299 (1984).
10. H.-J. Schneider, D. Guttes, and U. Schneider: *J. Am. Chem. Soc.* **110**, 6449 (1988).
11. A. R. Mustafina, V. V. Skripacheva, Yu. G. Yelistratova, E. Kh. Kazakova, A. R. Burilov, and A. I. Konovalov: *Koord. Khim.* **23**, 609 (1997) [*J. Coord. Chem. (Engl. Transl.)*]. **23**, 568 (1997).
12. C. D. Gutsche and K. Ch. Nam: *J. Am. Chem. Soc.* **110**, 6153 (1998).
13. D. D. MacNicol, J. J. McKendrick, and D. R. Wilson: *Chem. Soc. Rev.* **7**, 65 (1978).

14. F. Peter, M. Gross, M. W. Hosseini, J.-M. Lehn, and R. B. Sessions: *J. Chem. Soc., Chem. Commun.* 1067 (1981).
15. N. Hisayoshi and N. Yukinao: *Bull. Chem. Soc. Jap.* **51**, 1386 (1978).
16. A. T. Gubaidullin, Y. E. Morozova, A. R. Mustafina, E. Kh. Kazakova, I. A. Litvinov, and A. I. Konovalov: *Mendeleev. Commun.* **1**, 9 (1999).

