Complexation of cobalt(III)-containing complex monocations with calix[4]resorcinarenes in alkaline water–methanolic media

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It is shown by pH-metric titration that calix[4]resorcinarenes can bind cobalt(III)-containing complex monocations in alkaline water–organic media; the binding constants depend on the complex cation structure and are independent of the charge of the calix[4]resorcinarene anion.

Calix[4]resorcinarenes (H_8L) in alkaline media exist in the $[H_4L]^{4-}$ form, which can bind bulky ammonium cations according to the 'size-match rule'.[1] The dependence of binding constants on the structure of alkylammonium cations is the basis of using $[H_4L]^{4-}$ as an artificial receptor for molecular recognition of acetylcholine.[2] It has been shown previously[3] that in alkaline water–organic media, H_8L with four *cis*-arranged hydrophobic radicals ($R = C_6H_{13}$, C_7H_{15}) (structure **1**) can bind cobalt-containing complex cations according to equation (1) to give $[H_{8-k}L]^{k-}[Co(X)_n]^{m+}$ 'supercomplexes'.

$$H_8L + [Co(X)_n]^{m+} \longleftrightarrow [H_{8-k}L]^{k-}[Co(X)_n]^{m+} + kH^+ \qquad (1)$$

According to ^1H NMR spectroscopy data recorded in $[^2H_6]DMSO$, supercomplexes with $m = 2$, 3 are characterised by upfield-shifted signals of guest protons, whereas the upfield shifts for supercomplexes containing monocation are less than 0.1 ppm.[3] The solubility of supercomplexes decreases with an increase in m from 1 to 3. Monocation supercomplexes are most soluble in DMSO and precipitate only in water–MeOH solutions. So, the dependence of 'supercomplexation' constants on the structure of the metal-containing complex cations is of potential use in the molecular recognition of some metal-containing biologically important compounds by supercomplexation with calix[4]-resorcinarenes in water–organic media. The main goal of this work is a study of the association equilibria between octahedral cobalt(III)-containing complex monocations (Kt^+) with various ligands as the environment: isomers of $[Co(His)_2]^+$ with a *trans*-orientation of imidazoles (*trans*-i-) and *trans*-orientation of amino groups (*trans*-a-), where His^- is histidinate; $[Co(En)_2X]^+$, where En is ethylenediamine and $X = [C_2O_4]^{2-}$ or $[CO_3]^{2-}$ with H_8L ($R = C_6H_{13}$ or CH_3) in water–MeOH solutions (60% MeOH) at pH 8 to 11.

It is evident from elemental analysis data for substances precipitating from water–MeOH alkaline solutions of cobalt(III)-containing monocations and H_8L ($R = C_6H_{13}$)[†] that the composition of the precipitates differs considerably from that corresponding to a molar ratio of 1:1 for all monocations except *trans*-i-$[Co(His)_2]^+$ and depends on the solution pH. The molar ratio of H_8L and *trans*-a-$[Co(His)_2]^+$, $[Co(En)_2C_2O_4]^+$, $[Co(En)_2CO_3]^+$ monocations was determined by the 'host–guest' ratio of signal intensities in the ^1H NMR spectra recorded for solutions of the precipitates in $[^2H_6]DMSO$ and was found to vary from 3:1 to 1:1. So, it is most reasonable to assume that the variable composition of the precipitates is determined by the extent of supercomplex accumulation, which in turn depends on its stability and solution pH. The solubility of both H_8L and its supercomplexes in water–organic alkaline media depends on the length of the *cis*-arranged hydrophobic radicals (R). A decrease in R size to R = Me increases the solubility, which in turn makes it possible to investigate equilibria existing in water–MeOH alkaline solutions of cobalt(III)-containing monocations and H_8L ($R = CH_3$).[†]

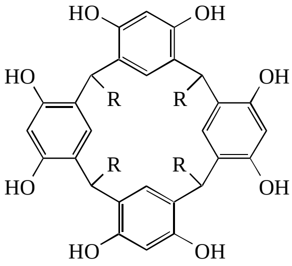
1 H_8L

Table 1 Stability constants of supercomplexes.

Equilibrium	Kt^+	lg β
$[H_7L]^- + Kt^+ = [H_7LKt]$	*trans*-i-$[Co(His)_2]^+$	17.96
	trans-a-$[Co(His)_2]^+$	15.0
	$[Co(En)_2C_2O_4]^+$	13.2
	$[Co(En)_2CO_3]^+$	14.1
$[H_6L]^{2-} + Kt^+ = [H_6LKt]^-$	*trans*-i-$[Co(His)_2]^+$	19.2
	trans-a-$[Co(His)_2]^+$	16.3
	$[Co(En)_2C_2O_4]^+$	14.7
	$[Co(En)_2CO_3]^+$	14.5
$[H_5L]^{3-} + Kt^+ = [H_5LKt]^{2-}$	*trans*-i-$[Co(His)_2]^+$	20.1
	trans-a-$[Co(His)_2]^+$	17.3
	$[Co(En)_2C_2O_4]^+$	15.7
	$[Co(En)_2CO_3]^+$	15.0
$[H_4L]^{4-} + Kt^+ = [H_4LKt]^{3-}$	*trans*-i-$[Co(His)_2]^+$	20.2
	trans-a-$[Co(His)_2]^+$	17.7
	$[Co(En)_2C_2O_4]^+$	16.2
	$[Co(En)_2CO_3]^+$	15.5

Since supercomplexation is accompanied by deprotonation in accordance with equilibrium (1), the pH-metric titration method is applicable for the evaluation of supercomplexation constants.[†]

The deprotonation of H_8L occurs in four steps. The first proton is the most acidic ($pK_1 = 7.9$), the second one is less acidic than the first one ($pK_2 = 9.4$) but more acidic than the third and fourth ones ($pK_3 = 10.2$, $pK_4 = 11.2$). pH-Metric titration curves for H_8L with $[Co(X)_n]^{m+}$ in a concentration ratio of 1:1 differ from the similar curve for H_8L.

It was shown by a mathematical treatment of the pH-metric data that this difference is caused by equilibrium (1), where $k = 1$–4. pH-Metric data recorded for various H_8L : monocation concentration ratios (1:1, 1:2, 2:1) prove the stoichiometry of the supercomplexes to be 1:1 in this concentration range. Table 1 lists the stability constants (β) of the supercomplexes.

[†] H_8L ($R = Me$, C_6H_{13}) were synthesised according to a reported procedure.[4] *trans*-i- and *trans*-a-$[Co(His)_2]ClO_4$, $[Co(En)_2C_2O_4]Cl$ and $[Co(En)_2CO_3]Cl$ were synthesised according to procedures reported in refs. 5–7. pH-Metric titrations were carried out in a thermostatted cell at $T = 25$ °C using I-130 ionomer. The measurement of the pH of water–MeOH solutions was carried out by standardisation of a glass electrode by aqueous buffer solutions followed by evaluation of the liquid/liquid potential according to a known procedure.[8] Mathematical treatment of pH-metric titration data was carried out by the CPESSP program.[9] A pH-metric titration was carried out for both H_8L and cobalt(III)-containing monocations in order to detect all equilibria possible in their mixtures simultaneously with supercomplexation.

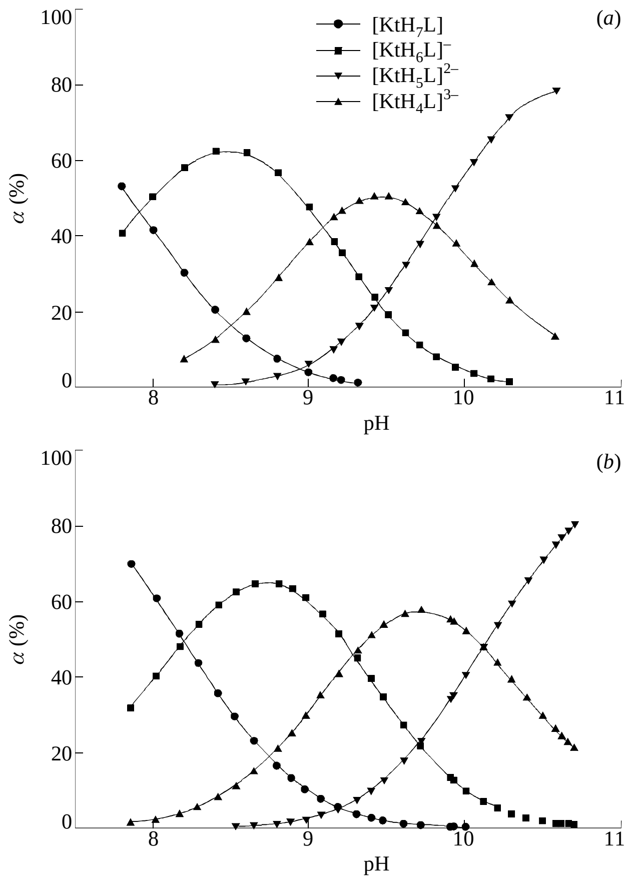

Figure 1 Distribution of supercomplexes as a function of pH for monocations (Kt^+): (*a*) $Kt^+ = [Co(En)_2C_2O_4]^+$ and (*b*) $Kt^+ =$ *trans*-i-$[Co(His)_2]^+$.

The $\log\beta$ values for various monocations presented in Table 1 depend on the nature of the cobalt(III)-containing monocation and increase in the series: $[Co(En)_2C_2O_4]^+ <$ $< [Co(En)_2CO_3]^+ <$ *trans*-a-$[Co(His)_2]^+ <$ *trans*-i-$[Co(His)_2]^+$. The deviation of the precipitate composition from the molar ratio of 1:1 for *trans*-a-$[Co(His)_2]^+$ and $[Co(En)_2X]^+$ ($X =$ $= [CO_3]^{2-}$, $[C_2O_4]^{2-}$) is caused by the lower stability of their supercomplexes in comparison with *trans*-i-$[Co(His)_2]^+$. Figure 1 shows the distribution of supercomplexes as a function of pH, illustrating that supercomplex $[Co(En)_2C_2O_4]H_7L$ (*a*) has lower stability than *trans*-i-$[Co(His)_2]H_7L$ (*b*).

It is known from Schneider's data that $[H_4L]^{4-}$ interacts with ammonium compounds (NR_4^+) forming a symmetrical structure with the cation located in the centre of the tetraanion 'rim', which possesses four $OH\cdot\cdot O^-$ donor centres. The energy of such an interaction consists of hydrophobic and electrostatic contributions, of which the latter is the major contribution. As stated previously,[3] metal-containing complexes must be positively charged to be coordinated by calix[4]resorcinarenes. According to ^1H NMR spectroscopic data, the higher the positive charge of the cobalt(III)-containing 'guest', the larger the upfield shift of the 'guest' proton signals.[3] Thus, the electrostatic contribution is not the only one, but it is essential in the Gibbs energy of supercomplexation. However, the small increase in stability of the supercomplexes with further deprotonation from $[H_7L]^-$ to $[H_4L]^{4-}$ (Table 1) disagrees with the major role of the electrostatic contribution. Further deprotonation of $[H_7L]^-$ results in the formation of other deprotonated centres, which in turn may lead to a multipoint interaction of the cation with the 'host's rim' and to an increase in supercomplex stability. Alkali metal ions are known to form complexes with calix[4]arene monoanions, forming an asymmetric structure in which the cation is located closer to one of the phenolic oxygen atoms.[10] So, it is reasonable to assume that the properties of a supercomplex based on $[H_7L]^-$ are governed by the asymmetric monocation location, which is closer to one of the deprotonated $OH\cdot\cdot O^-$ donor centres on the rim of $[H_7L]^-$. The experimentally observed small increase, or independence, of $\log\beta$ upon deprotonation of $[H_7L]^-$ to $[H_4L]^{4-}$ shows that only one deprotonated centre on the 'host's rim' is essential in monocation interaction with both $[H_7L]^-$ and $[H_4L]^{4-}$.

The dependence of $\log\beta$ values on the structure of the complex monocation is most evident for *trans*-i-$[Co(His)_2]^+$ and *trans*-a-$[Co(His)_2]^+$, which are isomers with a *trans* arrangement of imidazole and amine fragments, respectively.[5]

In spite of the structural differences, all of the monocations under consideration are characterised by a *cis*-arrangement of two negatively charged carboxyl groups; this arrangement should be preferable for supercomplexation to the *trans*-arrangement. The *trans*-arrangement of two negatively charged donor centres in the coordination sphere can be obtained for $[Co(En)_2Y_2]^+$, where Y^- is a monoanion. Unfortunately, such complexes are less stable in alkaline media than $[Co(En)_2X]^+$, where X^{2-} is a chelate, which makes impossible the accurate determination of their association constants.

So, according to the dependence of the stability of the supercomplexes on the structure of the complex cation, the latter can be recognised by calix[4]resorcinarenes in water–organic media. The small increase of supercomplex stability with an increase in the charge on the host's rim from $[H_7L]^-$ to $[H_4L]^{4-}$ is unusual. It is probably due to the extra stability of the monocation asymmetric location closer to one deprotonated donor centre in both $[H_7L]^-$- and $[H_4L]^{4-}$-containing supercomplexes, which in turn leads to independence of the Gibbs energy of supercomplexation on the charge of the 'host's rim'.

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