Solubilization and acidic and receptor properties of calix[4]resorcinarenes in aqueous solutions of oxyethylated dodecanol Brij-35

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Solubilization of calix[4]resorcinarenes (Cn) with a varied length of hydrophobic substituents (R = Me, Pr, C_5H_{11}, C_7H_{15}, C_9H_{19}, and $C_{11}H_{23}$) in aqueous solutions of oxyethylated dodecanol Brij-35 was studied by the solubility method and 1D and 2D ^{1}H NMR spectroscopy. The solubilization of Cn in micellar solutions of Brij-35 is caused by the formation of mixed Cn—Brij-35 aggregates and is weakened substantially with the elongation of R. It was shown by pH-metry and 1D ^{1}H NMR spectroscopy that the receptor properties of the Cn anions toward the tetramethylammonium cations in the mixed aggregates differ substantially from those for the monomeric molecules in aqueous-organic and aqueous solutions. In particular, the binding of the tetramethylammonium cations does not result in screening of their N—Me fragments with the cyclophane cavity of the receptor.

Key words: calix[4]resorcinarene, Brij-35, solubilization, complexation.

Researchers are interested in water-soluble calixarenes, first of all, due to their receptor properties toward various biologically significant substrates, because the majority of processes occur in an aqueous medium.[1] One of the methods to create water-soluble calixarenes is the introduction of ionized groups into their matrix.[2] Meanwhile, to transform calixarenes into the water-soluble state, one can use such a method as solubilization of surfactants (Surf) in aqueous solutions. From this point of view, micellar solutions of nonionogenic surfactants (NSurf) are of special significance,[3] because they provide the solubilization of receptors and their complexes with organic substrates and metal ions by micelles and, in addition, the separation of the micellar and aqueous phases using the so-called procedure of "cloud point extraction."[4—7] Both metal ions[4,5] and organic substrates[6,7] can thus be isolated from the aqueous phase. We have previously shown that calix[4]resorcinarenes with a varied chain length of hydrophobic substituents (from R = Me to R = $C_{11}H_{23}$) are efficiently solubilized in aqueous micellar solutions of oxyethylated isooctylphenols Triton X-100 (TX100) and Triton X-405 (TX405).[8,9] The NSurf studied differ only by the length of polar groups, while the structure of their hydrophobic fragment is the same. As follows from the data obtained, the number of oxyethyl units of NSurf has a decisive effect on the solubilization capacity of micelles formed by these surfactants. It was found[8,9] that the solubilization efficiency and the dissociation and stability constants of calix[4]resorcinarene complexes in micellar solutions of TX100 and TX405 depend on the length of hydrophobic substituents of cyclophanes. This indicates that the polarities of the environment and solvate state of calix[4]resorcinarenes depend on their hydrophobicity, which is caused, probably, by different efficiencies of all noncovalent intermolecular (including hydrophobic) interactions occurring in a mixed aggregate. In particular, it can be assumed that the elongation of the hydrophobic substituents is accompanied by resorcinarene molecule pulling deep into the mixed aggregate due to effective hydrophobic intermolecular interactions. Therefore, it seems of interest to estimate the localization of calix[4]resorcinarene inside the mixed aggregate and compare the acid-base and receptor properties of calix[4]resorcinarenes in aqueous solutions of oxyethylated dodecanol Brij-35

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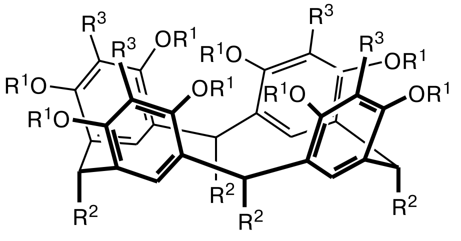
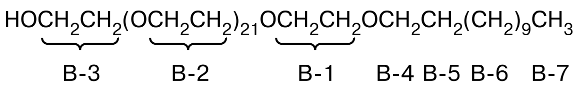
(23 oxyethylated units) with similar properties of monomeric calix[4]resorcinarenes. ^{1}H NMR spectroscopy is known to be efficient for studying the receptor properties of both cyclophane molecules[10] and mixed aggregates of ionic and nonionic surfactants.[11,12] However, in micellar solutions of TX100 and TX405, signals of aromatic protons of calix[4]resorcinarenes, which are most sensitive to the conformational state and complexation with organic molecules and ions, overlap with signals of aromatic protons of TX100 and TX405. The hydrophobic fragments of Brij-35 contain no aromatic protons, and signals of the methylenic protons of its oxyethyl chains do not overlap with signals of the protons of calix[4]resorcinarene. This makes it possible to analyze a change in chemical shifts of signals of protons of both Brij-35 and calix[4]resorcinarene for the formation of mixed calix[4]resorcinarene—Brij-35 aggregates.

In this work, we studied regularities of the solubilization of calix[4]resorcinarenes (Cn) with a varied length of hydrophobic radicals in micellar solutions of Brij-35 and the acidic and receptor properties of calix[4]resorcinarenes in micellar solutions of Brij-35 by the solubility method, pH-metry, and ^{1}H NMR spectroscopy.



Cn, P1, P9, P11



$$\mathrm{HO}\underbrace{\mathrm{CH_2CH_2}}_{\text{B-3}}(\mathrm{O}\underbrace{\mathrm{CH_2CH_2}}_{\text{B-2}})_{21}\mathrm{O}\underbrace{\mathrm{CH_2CH_2}}_{\text{B-1}}\mathrm{O}\underset{\text{B-4}}{\mathrm{CH_2}}\underset{\text{B-5}}{\mathrm{CH_2}}\underset{\text{B-6}}{\mathrm{(CH_2)_9}}\underset{\text{B-7}}{\mathrm{CH_3}}$$

Brij-35

	Cn	P1	P9	P11
R^1	H	H	CH_2CO_2Me	CH_2CO_2H
R^2	C_nH_{2n+1}	Me	C_9H_{19}	$C_{11}H_{23}$
R^3	H	CH_2SO_3Na	H	H

n = 1, 3, 5, 7, 9, 11

Experimental

Compounds Cn [13] and P1 [14] were synthesized according to known procedures. Compounds P9 and P11 were synthesized at the Department of Chemistry of the Dresden University of Technology using a procedure described in Ref. 15.

Commercial Brij-35 (ICN Biomedicals) and poly(ethylene glycol) PEG-4000 (Merck) were used. An industrial sample of tetramethylammonium bromide (TMA) was purified by recrystallization from methanol.

The amount of NSurf necessary to obtain a $2.0 \cdot 10^{-3}$ M solution of Cn, P1, P9, and P11 was determined by the successive introduction of small amounts of an aqueous solution of the surfactant with a concentration of $4 \cdot 10^{-2}$ mol L^{-1} into a water—Cn heterogeneous system at 25 °C until calix[4]resorcinarene dissolved completely. The solubilization capacity of micellar solutions is usually calculated by the expression[16]

$$S = (C_2 - C_{21})/(C_1 - C_{11}), \qquad (1)$$

where C_2 and C_1 are the concentrations of the solubilizate and NSurf, respectively; C_{11} is the concentration of the NSurf monomers, and C_{21} is the solubility of the solubilizate in water. Taking into account that the commonly used concentrations of Brij-35 are much higher than the critical micellization ($6.0 \cdot 10^{-5}$ mol L^{-1})[17] and the solubility of Cn in water is very low, the S value was calculated as

$$S = C_2/C_1. \qquad (2)$$

pH-Metric titration was carried out at a variable volume on an I-130 instrument with an accuracy of 0.05 pH units. A ionometer was calibrated by standard buffer solutions. The titrant was a $1.53 \cdot 10^{-3}$ M aqueous solution of KOH free of carbonate admixtures and with the same NSurf content as that in the titrated solution. The Cn concentration in titrated solutions was $2.0 \cdot 10^{-3}$ mol L^{-1}. The TMA : H_8L concentration ratio was maintained equal to 1 : 1, and titration was carried out in a range of pH 6—11. The titration curves of $1.0 \cdot 10^{-2}$ M solutions of hydrochloric acid with potassium hydroxide in water and in $8.5 \cdot 10^{-3}$ and $1.7 \cdot 10^{-2}$ M solutions of Brij-35 are identical, indicating that Brij-35 does not affect the parameters of the electrode system.

Experimental data were mathematically processed by a described procedure[8] using the CPESSP program.[18]

1D ^{1}H NMR spectra of solutions in D_2O were recorded on an MSL-400 instrument with a working frequency of 400.13 MHz, and chemical shifts were determined relatively to signals of residual protons in deuterated water. 2D ^{1}H NOESY spectra were also recorded in D_2O on a Bruker DRX-500 instrument with a working frequency of 500.13 MHz and a mixing time of 100 μs. The following concentrations of reagents were used: $C_{\mathrm{Cn}} = C_{\mathrm{TMA}} = 3.3 \cdot 10^{-3}$ mol L^{-1} and $C_{\text{Brij-35}} = 3.3 \cdot 10^{-3}$—$3.3 \cdot 10^{-2}$ mol L^{-1}.

The interaction between Cn with $n = 5$ (hereinafter C5) and TMA in neutral micellar solutions of Brij-35 was estimated by conductometry. For this purpose, we measured the electroconductivity of an aqueous solution of TMA with a concentration of $2.0 \cdot 10^{-3}$ mol L^{-1}, solutions of TMA ($2.0 \cdot 10^{-3}$ mol L^{-1}) in the presence of Brij-35 ($8.0 \cdot 10^{-3}$—$2.0 \cdot 10^{-2}$ mol L^{-1}), and solutions of TMA ($2.0 \cdot 10^{-3}$ mol L^{-1}) containing Brij-35 ($8.0 \cdot 10^{-3}$—$2.0 \cdot 10^{-2}$ mol L^{-1}) and C5 ($2.0 \cdot 10^{-3}$ mol L^{-1}). Measurements were carried out at 20.0±0.1 °C using an inoLab Cond Level 1 conductometer.

Results and Discussion

The data presented in Fig. 1 make it possible to compare the solubilization capacities of Brij-35 micelles toward calix[4]resorcinarenes with different hydrophobici-

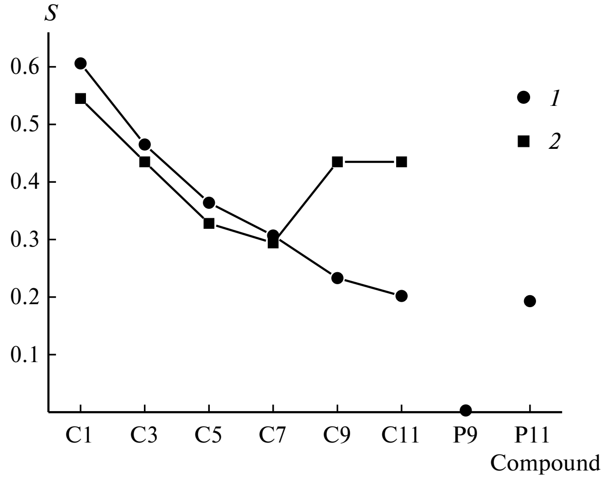


Fig. 1. Solubilization capacities (*S*) of micellar solutions of Brij-35 (*1*) and TX405[8,9] (*2*) for calix[4]resorcinarenes with varied hydrophobicity.

ties. As follows from the data obtained, the *S* value of micellar solutions of Brij-35 decreases with the elongation of the hydrophobic radical of calix[4]resorcinarenes. For calix[4]resorcinarenes C1, C3, C5, and C7 (Cn with $n = 1, 3, 5$, and 7, respectively), the solubilization capacity of micellar Brij-35 solutions almost coincides with that for TX405, although the oxyethyl chain of Brij-35 (23 OCH_2CH_2 units) is much shorter than that of TX405 (40 OCH_2CH_2 units). Calix[4]resorcinarenes with the hydrophobic substituents (C9, C11) are remarkably more efficiently solubilized in micellar solutions of TX405 than in Brij-35 solutions.

It is known that the distribution coefficient of organic compounds between the aqueous phase and NSurf micelles is satisfactorily described in the framework of the Abraham model.[19] The model is linear and includes the following terms:

$$\log SP = c + rR_2 + s\pi^{H}{}_2 + a\Sigma\alpha^{H}{}_2 + b\Sigma\beta^{H}{}_2 + v(V_x/100),$$

where SP is a physicochemical property of a solution, for instance, the distribution coefficient of a substance between the aqueous and micellar phases; c, r, s, a, b, and v are the regression coefficients; R_2 is the excessive molar refraction; and $\pi^{H}{}_2$, $\Sigma\alpha^{H}{}_2$, $\Sigma\beta^{H}{}_2$, and V_x are the parameters describing the dipolarity/polarizability, effective proton-donor ability, proton-acceptor ability, and molar volume of the solubilized substance, respectively. Since the main moving forces of solubilization in micellar solutions of NSurf are the formation of hydrogen bonds with oxyethyl chains composing the polar layer and hydrophobic interactions with alkyl chains of surfactants forming a lipophilic core of a micelles, then, according to the Abraham model, the higher the proton-donor ability and the large the molar volume of the solute, the higher is the solubilization efficiency.[6,20] Therefore, the sharp decrease in the efficiency of solubilization on going from compound C9 to compound P9 with the methoxycarbonyl groups is quite regular, while the solubilization efficiency of calixarene P11 is compared to that of C11 with the carboxyl groups (see Fig. 1). At the same time, according to this model, one should expect an increase in the efficiency of solubilization with the elongation of the hydrophobic radicals on going from C1 to C11, because this elongation results in an increase in the molar volume and molar refraction of the molecule.[21] However, the experimentally observed decrease in the solubilization capacity of micellar solutions of Brij-35 with the elongation of the hydrophobic radicals in compounds from C1 to C11 contradicts the Abraham model. Thus, the regularities of formation of Cn—TX405 and Cn—Brij-35 mixed aggregates differ from those for phenols and their derivatives, whose solubilization agrees with the Abraham model.[6]

The solubility of calix[4]resorcinarenes in micellar solutions of Brij-35 decreases noticeably on going from H_2O to D_2O, which prevents the dispersion of compounds C9 and C11 under the concentration conditions we are interested in, namely, achievement of a concentration of $3.33 \cdot 10^{-3}$ mol L^{-1}, which is optimum for an NMR experiment at a 6—10-fold concentration excess of Brij-35. Therefore, ^1H NMR spectroscopic data were obtained only for compounds C1, C3, C5, and C7. It should be noted that the chemical shifts of NSurf change remarkably (Table 1) even in a sixfold concentration excess of Brij-35 over the latter compounds. In particular, the upfield shifts of signals of the B-4 protons are observed (from δ 3.46 to 3.40—3.43) and, to a less extent, of the B-1 protons (see Table 1), whereas the formation of Brij-35—sodium dodecyl sulfate and Brij-35—cetyltrimethylammonium bromide mixed aggregates leads to the downfield shift of almost the same value.[12] The chemical shifts of signals of the B-2 protons remain virtually

Table 1. Chemical shifts (δ±0.01) of signals of the B-1, B-2, and B-4 protons in a micellar solution of Brij-35 ($C = 0.0198$ mol L^{-1}) in the absence and presence of Cn ($C = 0.0033$ mol L^{-1}) and signals of the aromatic protons of Cn

Compound	Protons				
	B-1	B-2	B-4	H_a	H_b
Brij-35	3.59	3.69	3.46	—	—
C1	3.60	3.69	3.40	7.16	6.28
C3	3.56	3.68	3.41	7.08, 7.10	6.30
C5	—	3.68	3.41	7.08	6.29
C7	—	3.70	3.42, 3.43	7.08, 7.09, 7.10	6.30

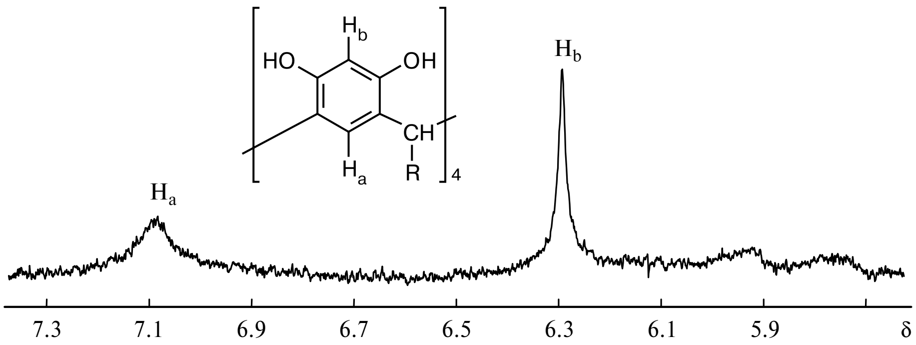


Fig. 2. Signals of aromatic protons of compound C5 ($C = 3.3 \cdot 10^{-3}$ mol L^{-1}) in a micellar solution of Brij-35 ($C = 1.3 \cdot 10^{-2}$ mol L^{-1}).

unchanged (see Table 1), which is quite natural if we take into account their number. The chemical shifts of the B-4 protons in the two-component calix[4]resorcinarene—Brij-35 system increase by 0.03 ppm with an increase in the hydrophobicity of calix[4]resorcinarene on going from C1 to C7 (see Table 1). Unlike the ^{1}H NMR spectra in organic and aqueous-organic solutions, the signals of aromatic protons of calix[4]resorcinarenes are strongly broadened (especially the signal of the H$_a$ proton) or look like a superposition of several signals, indicating their magnetic nonequivalence (Fig. 2; Table 1). The chemical shift of the signal of the aromatic H$_a$ protons in compound C1 (δ 7.16) somewhat differs from that for compounds C3, C5, and C7 (in an interval of 7.08—7.10 ppm) (see Table 1). This agrees with the lowest hydrophobicity and the highest solubility in water of calixarene C1 in the series of studied resorcinarenes Cn. The chemical shifts of signals of the H$_b$ protons are almost the same for compounds C1, C3, C5, and C7 and range within δ 6.28—6.30. When the Brij-35 concentration is varied, the position and width of the signals of the aromatic protons of C1 do not remarkably change; however, the chemical shifts of the signals of the NSurf protons depend on the C1 to Brij-35 ratio (Fig. 3). As follows from the presented dependence, the greatest upfield shift is observed when the C1 to Brij-35 concentration ratio is equal to ~0.35—0.4. It is of interest that the chemical shift of signals of the B-4 protons increases with either the decrease or increase in the $C_{\mathrm{Cn}}/C_{\mathrm{Brij\text{-}35}}$ ratio from 0.35—0.4. The increase in the chemical shift observed with a decrease in $C_{\mathrm{Cn}}/C_{\mathrm{Brij\text{-}35}}$ from 0.35—0.4 agrees with the accumulation of intrinsic aggregates of Brij-35. A similar increase in the chemical shift of signals of the B-4 protons with an increase in the $C_{\mathrm{Cn}}/C_{\mathrm{Brij\text{-}35}}$ ratio indicates a change in the composition and structure of the mixed aggregates. Thus, changes in the ^{1}H NMR spectra indicate the interaction of calix[4]resorcinarenes with oxyethyl chains of Brij-35, and an upfield shift of signals of the B-4 protons can indicate their partial screening by the aromatic fragments of calix[4]resorcinarenes characteristic of "host—guest" interactions.[10] This pattern was observed, in particular, for the CH—π interaction of oxyethyl fragments of crown ether with water-soluble calix[4]resorcinarene P1.[22] However, in addition to the upfield shift of signals of protons of the fragments that partially immersed into the cavity, the CH—π interactions of oxyethyl fragments of crown ether with the hydrophobic cavity of P1 are accompanied by the downfield shift of signals of the aromatic protons of the "host." [22] It is interesting that a similar CH—π interaction is observed for P1 binding with poly(ethylene glycol) (PEG-4000), which is indicated by the downfield shift of the H$_a$ signal of the aromatic protons of P1 from δ 6.65 to δ 6.80 when P1 was mixed with PEG-4000 in an equimolar concentration ratio ($C_{\mathrm{PEG}} = C_{\mathrm{P1}} = 3 \cdot 10^{-3}$ mol L^{-1}). However, as already mentioned, the variation of the C1 : Brij-35 concentration ratio has almost no effect on the chemical shift values of the H$_a$ and H$_b$ protons. The data of 2D NMR NOESY spectroscopy (Fig. 4), namely, a correlation between the chemical shifts of signals of the H$_b$ aromatic proton and B-4, B-1, and B-3 protons and of the H$_a$ proton and B-1 and B-3 protons of Brij-35 indicates a tight contact of the oxyethyl chains of the latter with the resorcinol fragments of C5, which confirms that they interact. Weaker cross-

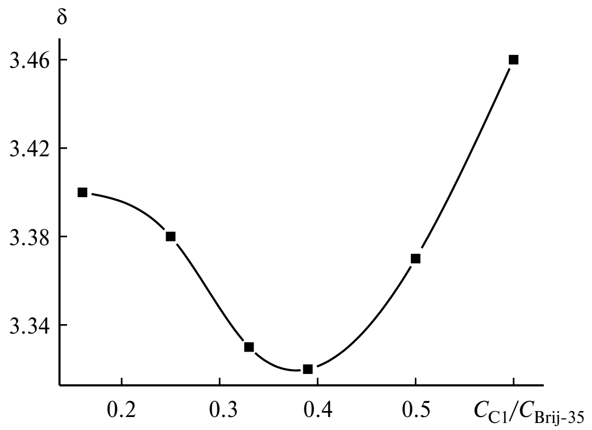


Fig. 3. Dependence of the chemical shifts of signals of the B-4 protons of Brij-35 in the C1—Brij-35 system on the ratio of the C1 and Brij-35 concentrations in D$_2$O.

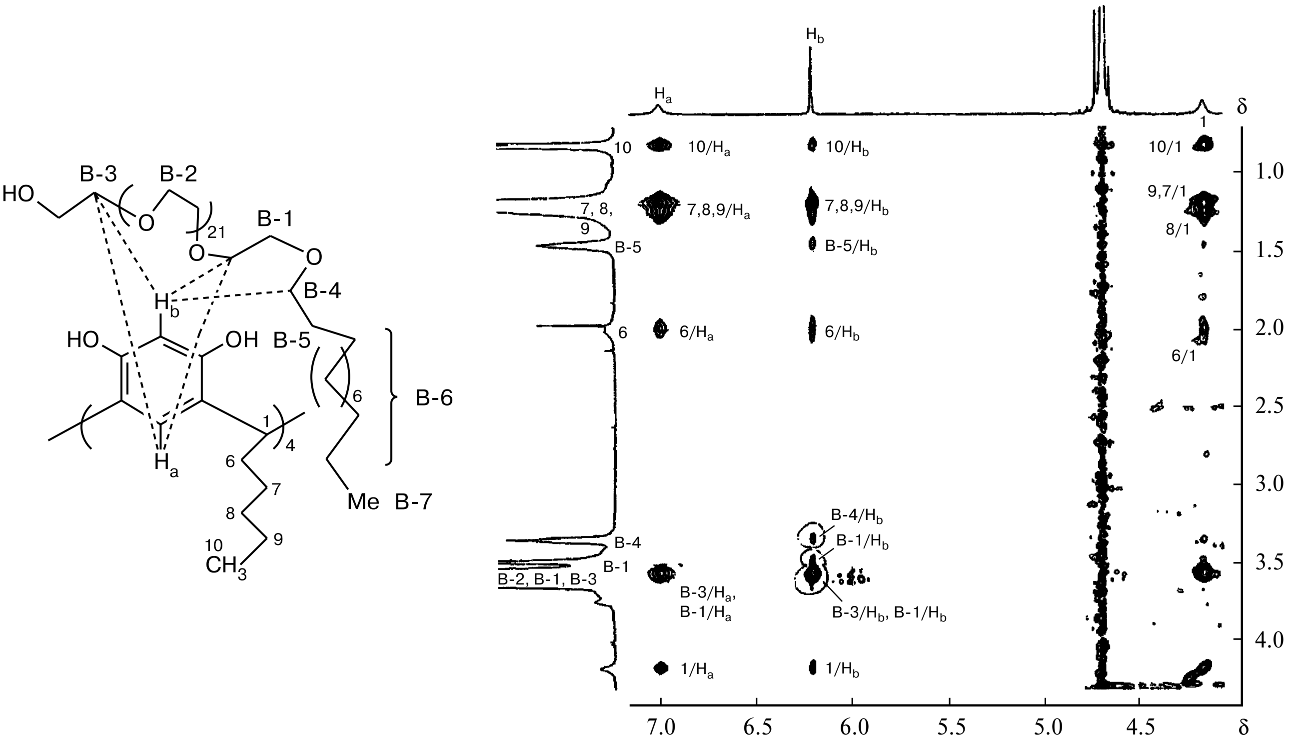


Fig. 4. 2D NOESY spectrum of compound C5 ($C = 3.3 \cdot 10^{-3}$ mol L^{-1}) in the presence of Brij-35 ($C = 1.3 \cdot 10^{-2}$ mol L^{-1}) in D_2O and the scheme of interaction of protons of compounds C5 and Brij-35 in D_2O (dotted line connects the protons that give cross-peaks; cross-peaks of aliphatic protons of C5 are not shown).

peaks, indicating a spatial closeness of the H_a and H_b aromatic protons and the B-5 protons of Brij-35, are also observed. Therefore, unlike the complexation of the monomeric P1 anion with PEG, the CH—π interaction does not contribute remarkably to the binding of Cn with the oxyethyl chains of Brij-35 in a mixed aggregate. It should be also emphasized that the stability of the Cn—Brij-35 mixed aggregates is determined not only by the efficiency of Cn interaction with the oxyethyl fragments of Brij-35, because Cn is not dissolved in aqueous solutions of PEG. However, the direct proof of their interaction cannot be obtained from the 2D spectra because of overlapping of the signals of the protons of the hydrophobic fragments of C5 and Brij-35. Thus, the interaction of the resorcinol fragments with the oxyethyl fragments of Brij-35 (first of all, the formation of intermolecular hydrogen bonds) and the interaction of the hydrophobic fragments of Cn and Brij-35 are the main driving forces for the formation of Cn—Brij-35 mixed aggregates.

According to the data of pH-metry, the addition of four equivalents of alkali results in calix[4]resorcinarene (H_8L) deprotonation to form the corresponding tetraanion $[H_4L]^{4-}$. In solutions of Brij-35, as in solutions of TX-405,[9] the dissociation constants of four protons of calix[4]resorcinarenes (p$K_{1,4}$) change nonmonotonically with the elongation of the hydrophobic radicals of the latter, and these constants depend on the calix[4]resorcinarene : NSurf concentration ratio (Table 2). The above-presented NMR spectroscopic data indicate that the phenolate groups of calix[4]resorcinarene are localized deep

Table 2. General dissociation constants p$K_{1,k}$±δ[a] of calix[4]resorcinarenes (H_8L) and the stability constants logβ$_k$±δ[a] of the 1 : 1 complexes of the $[H_{8-k}L]^{k-}$ anions (*k* is the degree of deprotonation) and TMA in aqueous solutions of Brij-35

$C_{\text{Brij-35}}$/mol L^{-1}	p$K_{1,k}$, logβ$_k$	Calix[4]resorcinarene					
		C1	C3	C5	C7	C9	C11
0.017	pK_1	8.98	8.87	9.02	9.07	9.41	9.36
0.017	p$K_{1,2}$	19.5	19.3	19.3	19.5	21.1	19.8
0.017	p$K_{1,3}$	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
0.017	p$K_{1,4}$	42.5	42.1	41.6	42.2	44.3	42.2
0.017	logβ$_1$	2.17	1.73	2.54	—[b]	—[b]	3.28
0.017	logβ$_2$	—[b]	—[b]	—[b]	—[b]	3.9	—[b]
0.017	logβ$_4$	5.9	4.0	5.2	3.2	4.8	5.7
0.0085	pK_1	7.62	9.57	8.48	9.45	9.45	9.69
0.0085	p$K_{1,2}$	—[b]	—[b]	18.7	20.8	—[b]	—[b]
0.0085	p$K_{1,3}$	27.2	32.4	29.4	—[b]	—[b]	32.19
0.0085	p$K_{1,4}$	38.2	43.7	39.9	42.4	42.4	42.9
0.0085	logβ$_1$	—[b]	3.26	—[b]	—[b]	2.66	3.16
0.0085	logβ$_2$	—[b]	—[b]	2.95	4.6	—[b]	—[b]
0.0085	logβ$_4$	4.4	7.2	3.7	4.8	6.1	6.1

[a] $0.05 < \delta < 0.1$.

[b] The accumulation of this complex species is <15%.

in the polar layer of the mixed aggregate, because the aromatic H_b proton exists in the immediate vicinity to the B-4, B-1, and B-3 protons of Brij-35 (see Fig. 4). Thus, the change in $pK_{1,4}$ with the elongation of the hydrophobic radical of Cn reflects the change in the polarity of the micropolarity of the phenolate rim of calix[4]resorcinarene and, therefore, its localization inside the polar layer. The latter depends on the efficiency of interaction of solubilized species with the hydrophobic core of the mixed aggregate.

To compare the receptor properties of compounds C1, C3, C5, and C7 in micellar solutions of Brij-35 with the receptor properties of calix[4]resorcinarenes in aqueous and aqueous-organic solutions, we analyzed changes in the ^{1}H NMR spectra upon the addition of TMA to the calix[4]resorcinarene—Brij-35 system. It is known[23] that in aqueous-organic solutions the neutral form of calix[4]resorcinarene (H_8L) and TMA are bound inefficiently, and no changes in the ^{1}H NMR spectra of both the guest and host are observed at their equimolar concentration ratio. According to the data of conductometry, the electroconductivity of TMA (168 μS cm^{-1} at $C = 2.0 \cdot 10^{-3}$ mol L^{-1}) remains almost unchanged with an increase in the Brij-35 concentration in the range from $8.0 \cdot 10^{-3}$ to $2.0 \cdot 10^{-2}$ mol L^{-1}, indicating no noticeable binding of TMA and Brij-35 aggregates. The electroconductivity of TMA also remains unchanged when equimolar amounts of Cn are added to micellar TMA solutions. Thus, in the micellar media studied, no remarkable binding of H_8L and TMA is observed at their equimolar ratio under neutral conditions. The deprotonation of monomeric H_8L to tetraanions $[H_4L]^{4-}$ in aqueous-organic media results in a more efficient binding with TMA accompanied by spectral changes: the upfield shift of signals of the TMA protons and the downfield shift of signals of the aromatic protons of $[H_4L]^{4-}$. These effects are caused by the immersion of the N—Me fragments of TMA into the calix[4]resorcinarene cavity.[22—24]

The addition of TMA to the $[H_4L]^{4-}$—Brij-35 two-component system results in an insignificant upfield shift ($\Delta\delta$ 0.1—0.3) of signals of its protons. The shift value is virtually independent of the hydrophobicity of Cn but depends on the Brij-35 concentration (Fig. 5). Such a small change in the chemical shift of the TMA protons can be a consequence of either a small fraction of accumulation of the corresponding complex or the absence of the CH—π interaction between the Me fragments of TMA and the hydrophobic cavity of Cn. The stability of the TMA complexes with the $[H_4L]^{4-}$ tetraanions of varied hydrophobicity (C1—C11) was determined by pH-metric titration (Fig. 6). As follows from the data obtained (see Table 2), the binding under discussion is rather efficient to result in a significant (>70%) accumulation of the corresponding complex (Fig. 7). Thus, according to the

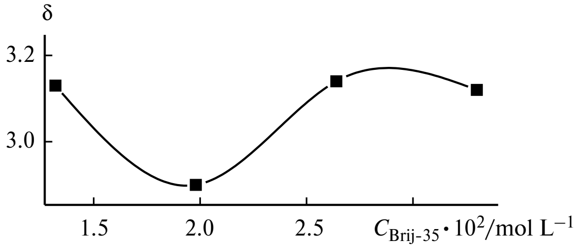


Fig. 5. Dependence of the chemical shifts of signals of the protons of TMA ($C = 3.3 \cdot 10^{-3}$ mol L^{-1}) in the presence of equimolar amounts of C5 at pH $\geq$ 11 in micellar solutions of Brij-35 in D_2O on the concentration of Brij-35.

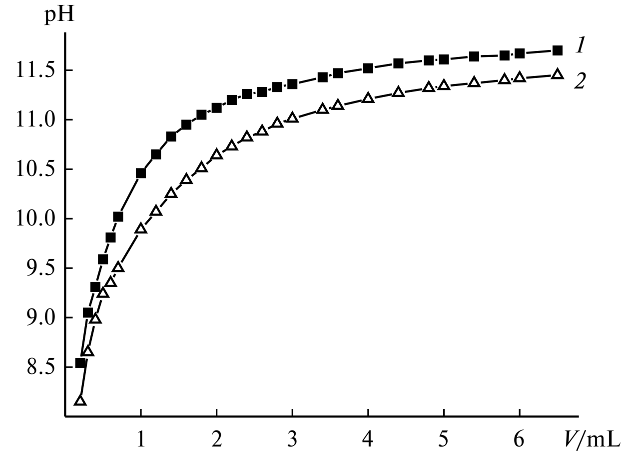


Fig. 6. Curves of pH-metric titration of compound C3 (*1*) and the C3—TMA system (*2*) ($C_{C3} = C_{TMA} = 2.0 \cdot 10^{-3}$ mol L^{-1}) in micellar solutions of Brij-35 ($C = 8.5 \cdot 10^{-3}$ mol L^{-1}).

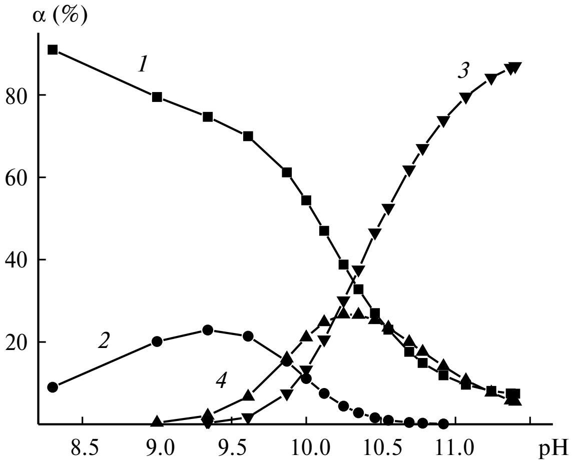


Fig. 7. Distribution of the 1 : 1 complexes formed between the $[H_{8-k}L]^{k-}$ anions with different degrees of dissociation (k) and TMA cation in a micellar solution of Brij-35 ($C = 0.017$ mol L^{-1}): α_{TMA} (*1*), α_1 (*2*), α_2 (*3*), and α_4 (*4*) (α_k is the degree of accumulation of the TMA complex with the $[H_{8-k}L]^{k-}$ anion).

pH-metric titration data, the $[H_4L]^{4-}$ anion in micellar solutions of Brij-35 binds TMA with at least the same efficiency as in $H_2O—Pr^iOH$ mixtures ($\log\beta = 6.6$).[8] Therefore, such a small change in the chemical shift of signals of the TMA protons (see Fig. 5) is caused by the absence of screening of its Me fragments by the hydrophobic cavity of $[H_4L]^{4-}$.

It should be mentioned that only for compound C1 the addition of equimolar amounts of TMA to the system results in the splitting of the signal of the aromatic H_b proton into two signals, one of which exhibits the downfield shift from δ 6.28 to δ 6.30, whereas the second signal (being considerably less intense) undergoes the downfield shift (to δ 5.90). The interaction with TMA does not induce downfield shifts of signals of the aromatic protons of $[H_4L]^{4-}$ with the elongation of the hydrophobic substituents in Cn ($n \geq 3$). Since compound C1 is the most hydrophilic in the chosen series of calixresorcinarenes, the splitting of the signals of the H_b proton can be assumed to be caused by the existence of both the micelle-bound and free forms of the $[H_4L]^{4-}$ tetraanion. The latter species interacts with the TMA cation *via* the mechanism known for aqueous-organic media.[23]

As can be seen from the data in Fig. 7, the presence of equimolar amounts of TMA shifts the equilibrium of dissociation of the hydroxy protons of Cn to the formation of deprotonated forms $[H_{8-k}L]^{k-}$ (k is the degree of deprotonation). The data obtained indicate that TMA is bound by the solubilized Cn anions. However, this binding, as mentioned above, is not accompanied by screening of the N—Me groups of TMA characteristics of "host—guest" complexes involving monomeric calix[4]resorcinarenes. Thus, the receptor properties of the $[H_4L]^{4-}$—Brij-35 system differ from those for the monomeric $[H_4L]^{4-}$ anions.

In our opinion, the efficient interaction of calix[4]resorcinarenes with oxyethyl and alkyl chains of Brij-35 decreases the polarity of their microenvironment. Therefore, the binding of TMA occurs mainly due to electrostatic interactions with phenolate fragments of solubilized anions. In this case, the N—Me fragments do not virtually immerse into the cyclophane cavity of $[H_4L]^{4-}$.

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