Aggregation of amphiphilic aminomethylated calix[4]resorcinarenes and the nonionic surfactant Triton-X-100 in organic solvents*

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Aggregation and intermolecular interactions of amphiphilic calix[4]resorcinarene (**1**), aminomethylated calix[4]resorcinarenes (AMC **2**—**7**) with different structures of the upper rim (including the oxazine structure in **6** and **7**) and hydrophobic substituents on the lower (**2**—**5**), upper (**6**), or both rims (**7**) in the absence and in the presence of the nonionic surfactant Triton-X-100 (**8**) and *p*-nitrophenol (**9**) in chloroform and 1,4-dioxane were studied by permittivity measurements and 2D ROESY ^{1}H NMR technique. The tendency of amphiphilic derivatives **1**—**7** toward self-aggregation and mixed aggregation with surfactant **8** primarily depends on the nature of both the solvent and the polar groups on the upper rim of calixarenes. In chloroform, AMC—**8** aggregates show interactions of the methyl and methylene groups of the hydrophobic substituents of AMC with the ethyleneoxy fragments of surfactant **8**, while in stable intermolecular complexes of **5** and **6** with compound **9**, the methylene groups of the long-chain radicals of the AMC strongly interact with the aromatic protons *ortho* to the hydroxy group of **9**. In 1,4-dioxane, calix[4]resorcinarenes **1** and **5** are bound in stable solvates, which prevents them from forming aggregates and mixed micelles.

Key words: aggregation, micellization, inter- and intramolecular interactions, critical micelle concentrations, amphiphilic compounds, aminomethylated calix[4]resorcinarene, nonionic surfactant Triton-X-100, mixed micelles, intermolecular associates, chloroform, 1,4-dioxane, 2D ROESY ^{1}H NMR technique, permittivity measurements.

Calix[4]resorcinarenes are macrocyclic compounds prepared from resorcinol and an aldehyde, which tend to form complexes with organic and inorganic cations, anions, and neutral molecules.[1,2] In recent years, these compounds have become an important class of "host" molecules because of the preparation of new structures on their basis, which are capable of trapping "guest" molecules such as cavitands, carcerands, and capsules formed in solutions *via* hydrogen bonding.[1,2]

Calix[4]resorcinarenes easily form multicomponent products, which makes them interesting objects in the study of processes of molecular recognition, transmembrane transport, and the formation of ionic channels.[3,4] In the crystalline state and in solution, calix[4]resorcinarenes can be solvated by organic solvents such as acetone, 1,4-dioxane, ethyl methyl ketone, ethyl acetate, DMF, *N*-methylpyrrolidone, methanol, 1,2-dimethoxybenzene, and acetonitrile.[5—10]

Because of their amphiphilic structure, calix[4]resorcinarenes were successfully used to obtain mono-[11—13] and multilayers[14,15] at interfaces and solid supports.[13—15,16] The solvent nature is known to strongly influence the intermolecular interactions (*e.g.*, aggregation of amphiphilic compounds) and the properties of the resulting aggregates since solvation, aggregation, and complexation compete in solution. For instance, it was found that lipophilic calix[4]resorcinarenes form multilayers, the number of which depend on the organic solvent (hexane, dichloromethane, and methanol) used for their preliminary dissolution.[14]

We found that amphiphilic calix[4]resorcinarenes **1**—**5** can form organized ensembles in water—DMF mixtures;[17—19] in the presence of surfactants in the same solutions[20] or in chloroform,[21] they give mixed aggregates that efficiently bind phosphorus acid esters and catalyze their hydrolysis and transesterification. The catalytic ef-

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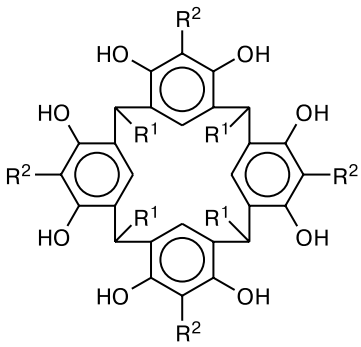
fects of individual aggregates of **1**—**5** and their mixed aggregates with surfactants are closely related to the structures of the resulting supermolecules in solution, which can be estimated by ^{1}H NMR spectroscopy using the nuclear Overhauser effect (2D NOESY, 2D ROESY); this technique is successfully employed to investigate 3D structures formed by large molecules and micellar aggregates and mixed micelles formed by various surfactant molecules.[22,23] The presence of the hydrophobic cavity in calix[4]resorcinarenes **1**—**7** [1,2] substantially complicates the pattern of the formation of mixed micelles (aggregates) and reactive intermolecular complexes compared to simple amphiphilic compounds such as typical surfactants. Apart from their aforementioned ability to form stable solvates, calix[4]resorcinarenes can trap surfactants or other substrates not only in their own cavity to give inclusion complexes (similar to "molecular necklaces" obtained from cyclodextrins and nonionic surfactants of the Triton-X-100 type[24]) but also in the cavity of capsules formed by calix[4]resorcinarenes.[25—27] This emerged from recent data[25] concerning a novel type of supramolecular structures constructed from analogs of **1** in chloroform in the presence of tetraalkylammonium (or phosphonium) salts or Bu_4SbBr. The resulting giant hexameric capsules can accommodate the mentioned guests and other organic molecules with suitable size. For this reason, aggregation of calix[4]resorcinarene derivatives in various solvents in the presence of guests tending to form intermolecular complexes or mixed aggregates and hence affect the calixarene reactivity is of topical interest.

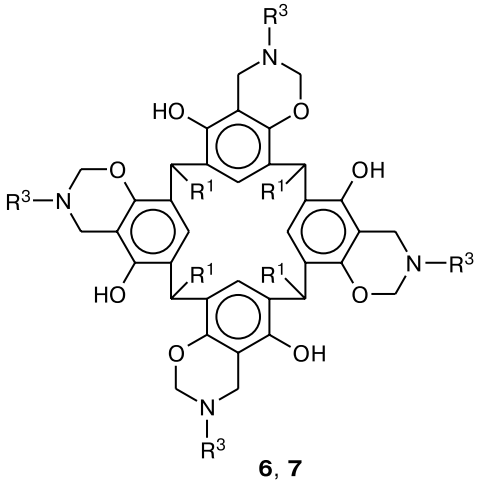
In the present work, we investigated aggregation and intermolecular interactions of calix[4]resorcinarenes in low-polarity solvents (chloroform and 1,4-dioxane) by permittivity measurements and the 2D ROESY ^{1}H NMR technique. The compounds studied were amphiphilic calix[4]resorcinarene (**1**), calix[4]resorcinarenes aminomethylated in the upper rim (AMC **2**—**7**) and containing a complex polar head group (**6**, **7**) and hydrophobic substituents on the lower (**2**—**5**), upper (**6**), or both rims (**7**), the nonionic surfactant Triton-X-100 (TX-100, **8**), and *p*-nitrophenol (**9**), which is usually used as a good leaving group in the study of the nucleophilic substitution kinetics of *p*-nitrophenyl esters; the way of aggregation of these compounds in nonaqueous solvents was also estimated.

Experimental

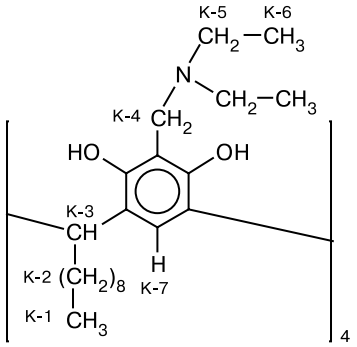
Calix[4]resorcinarenes **1**—**7** were prepared as described in Refs. 28—30. 1,4-Dioxane and chloroform were purified according to conventional procedures.[31] Reagent-grade Triton-X-100 (**8**) (Sigma) was used. Compounds **1**—**7** in the absence and in the presence of surfactant **8** in 1,4-dioxane or chloroform were

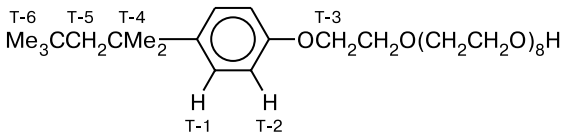


1—**5**



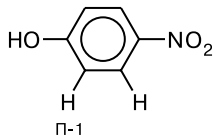
6, **7**





TX-100

8



PNP

9

	1	**2**	**3**	**4**	**5**	**6**	**7**
R^1	C_9H_{19}	C_6H_{13}	C_9H_{19}	$C_{11}H_{23}$	C_9H_{19}	Me	$C_{11}H_{23}$
R^2	H	CH_2NMe_2	CH_2NMe_2	CH_2NMe_2	CH_2NEt_2	—	—
R^3	—	—	—	—	—	$C_{10}H_{21}$	C_4H_9

studied by permittivity measurements. Essentially, we plotted the permittivity (ε) *vs.* the concentration for solutions of compounds **1**—**7** and **8** and their mixed systems and analyzed the resulting dependences (see Ref. 32). The permittivity measurements for series of solutions were performed on a setup consisting of a beat-frequency E12-I instrument and a temperature-controlled capacitor as a measuring cell.

Critical micelle concentrations were estimated to within 2% (error was determined by the accuracy of preparing solutions of required concentrations by successive dilution and the accuracy of measuring the solution permittivity).

1D and 2D ROESY ^{1}H NMR spectra were recorded on a Bruker MSL-400 spectrometer (400.132 MHz). Deuterated 99.5% $CDCl_3$ and dioxane-d_8 were purchased from RNTs Applied Chemistry. Proton numbering used in Results and Discussion for compounds **4**, **8**, and **9** is indicated in the scheme.

2D ROESY pulse sequence was D_0—90°—t_1—spin lock—t_2; D_0 = 3 s, $t_{spin\ lock}$ = 0.8 s, $t_{90°\ pulse}$ = 28 μs, NS = 16, DS = 2, T = 298 K, matrix 512×512, TPPI mode. The average time of the experiment was 4 h; the concentrations of compounds **1**—**9** were $5 \cdot 10^{-2}$ mol L^{-1}. In mixed systems, the ratio of the reagents was 1 : 1.

Results and Discussion

The critical micelle concentration (CMC) whenever revealed by any physical method is known to be a key factor for description and detection of aggregation processes in solution.[33] At present, the term "micelle" is used to denote any soluble one-, two-, or three-dimensional nanosized aggregate spontaneously and reversibly formed from amphiphilic molecules or ions in aqueous (normal micelles) or nonaqueous media (inverted micelles).[34] Aggregation of amphiphilic molecules in nonpolar media has been successfully investigated by methods measuring solvent polarization, in particular, permittivity measurements.[35—37] This is because amphiphilic molecules in nonpolar media interact *via* their polar head groups; these are mostly dipolar interactions. The formation of associates make molecules more or less polar, thus affecting the dielectric parameters of solutions. The permittivity (ε) characterizes the polarization of a medium (total dipole orientation of its species) in the applied electric field. Insofar as ε is structurally dependent and sensitive to any bond rearrangement, its concentration function $\varepsilon = f(C)$ (where C is the concentration of medium species) is informative as regards structuration or aggregation processes. Several cases are possible when determining CMC from $\varepsilon = f(C)$ to identify processes occurring in these systems.[36—38]

If the components of a mixture do not affect each other, then $\varepsilon = f(C)$ is a linear function. The slope of this straight line characterizes the polarizability of the medium. The nonlinearity is a measure of intermolecular interactions between the components of a mixture. During aggregation (micellization) processes, the slope of the function $\varepsilon = f(C)$ changes at the CMC point, usually in two ways: ε either jumps[36] or gives a plateau.[37] The former is characteristic of linearly ordered premicellar subunits forming "chain associates" with unidirectional dipole moments of species, which increases ε values with an increase in the associate concentration.[33] Further association at higher concentrations can give rise to multipolar aggregates ("quadrupoles") in which the dipoles of associated species exhibit an antiparallel orientation to give nonpolar head-to-head aggregates. Note that such aggregates need no chain associates as precursors and can form even at the first step of aggregation. In this case, ε changes only slightly at higher-than-CMC concentrations to give a plateau in ε *vs.* C coordinates. Supposedly, the point at which the curved line $\varepsilon = f(C)$ changes to a linear one corresponds to the initiation of aggregation (micellization), *i.e.*, CMC.[36—39]

Such a shape of the functions $\varepsilon = f(C)$ was obtained for compounds **1**—**8** in chloroform; therefore, they behave, in this solvent, like surfactants forming nonpolar aggregates. This is illustrated with the ε *vs.* C plots for compounds **8** and **3** (Fig. 1, curves *1*, *2*) and for compound **8** in the presence of different concentrations of **3** or **7** in chloroform (Fig. 2). The figures show distinct break points corresponding to CMC. The CMC of compounds **1**—**8** and those of mixed micelles based on compounds **1**, **3**, **5**—**7**, and **8** in chloroform are given in Table 1.

Some assumptions of the type of the resulting aggregates can be made when analyzing the CMC values and the shapes of the plots obtained. Note that the CMC of compound **1** ($5 \cdot 10^{-4}$ mol L^{-1}) is virtually one order of magnitude higher than the CMC of a typical nonionic surfactant **8** ($6 \cdot 10^{-5}$ mol L^{-1}). Aminomethylation of compound **1** decreases CMC to $7 \cdot 10^{-5}$ to $9 \cdot 10^{-5}$ mol L^{-1} for calix[4]resorcinarenes **3**—**5**. Most likely, this is due to the zwitterionic form of aminomethylated calix[4]resorcinarenes (AMC),[40] in contrast to nonionic compound **1**.

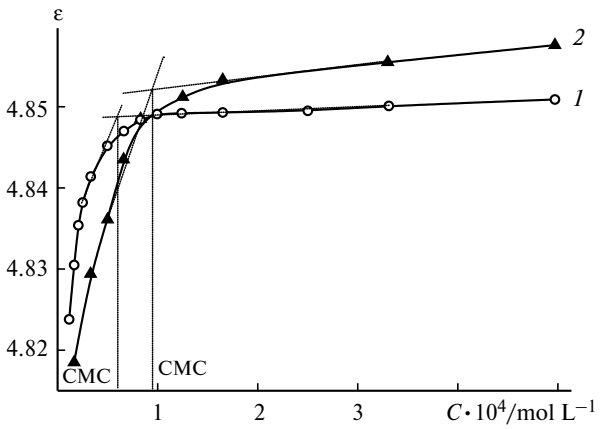


Fig. 1. Plots of the permittivity ε *vs.* the concentration for solutions of (*1*) TX-100 and (*2*) compound **3** in chloroform.

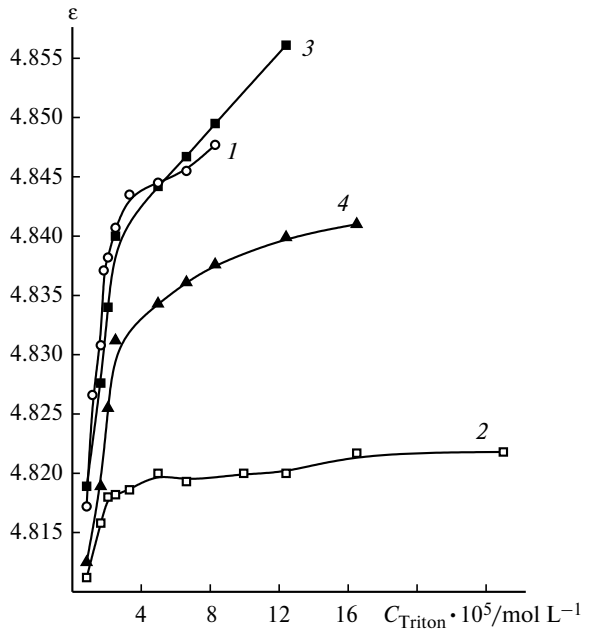


Fig. 2. Plots of the permittivity ε *vs.* the concentration of TX-100 (**8**) for its solutions in chloroform in the presence of compounds (*1*, *2*) **3** and (*3*, *4*) **7** for C_3 = (*1*) $2 \cdot 10^{-5}$ and (*2*) $2 \cdot 10^{-4}$ mol L^{-1} and C_7 = (*3*) $3 \cdot 10^{-5}$ and (*4*) $8 \cdot 10^{-5}$ mol L^{-1}.

Table 1. CMC for calix[4]resorcinarenes **1**—**7**, the nonionic surfactant Triton-X-100 (**8**), and their mixed aggregates in chloroform

Compound	CMC /mol L^{-1}	System	CMC /mol L^{-1}
1	$5 \cdot 10^{-4}$	**8**	$6 \cdot 10^{-5}$
2	$1 \cdot 10^{-4}$	**8·2**	—
3	$9 \cdot 10^{-5}$	**8·3**	$2 \cdot 10^{-5}$
4	$8.5 \cdot 10^{-5}$	**8·4**	—
5	$7 \cdot 10^{-5}$	**8·5**	$2 \cdot 10^{-5}$
6	$1 \cdot 10^{-4}$	**8·6**	$2.5 \cdot 10^{-5}$
7	$7 \cdot 10^{-5}$	**8·7**	$2.5 \cdot 10^{-5}$

Because of this, they are more able to form head-to-head aggregates (similarly to "inverted micelle precursors of ionic surfactants"[33]) than uncharged compound **1**. The somewhat higher CMC ($1 \cdot 10^{-4}$ mol L^{-1}) of compounds **6** and **2** are accounted for by the insufficient lipophilicity of the radicals on the lower rim of both AMC and, for AMC **6**, by the complicated structure of head groups, which prevents the formation of head-to-head aggregates because of steric hindrances at the N atoms. For AMC **7**, which contains shorter hydrocarbon radicals bound to the N atoms and lipophilic radicals on the lower rim, the CMC is lower than that of its analog **6** (see Table 1).

The permittivity *vs.* concentration plots for both amphiphilic compounds **8** and **3** (see Fig. 1) show two segments: that of increasing ε with an increase in their concentration and a plateau. Since surfactant **8** shows a tendency toward intermolecular hydrogen bonding (IHB), the former segment (see Fig. 1, curve *1*) may be indicative of further polarization of the solution *via* the formation of an "oligomeric net" of hydrogen-bonded molecules of **8**; *i.e.*, linear associates ("chains") composed of polar dimers accumulate in this segment. With an increase in the concentration of compound **8**, these associates unite into premicelles (quadrupoles) to give closed inverted micelles. Calixarenes **1**—**7** primarily tend to form intramolecular hydrogen bonds competing with IHB. Most likely, compounds **1**—**7** undergo self-aggregation without forming chain associates. The aggregation of calix[4]resorcinarenes near CMC involves head-to-head structures analogous to inverted micelle nuclei or premicellar surfactant aggregates.

The CMC for a mixture of compounds **8** and **3** at the concentration of **3** $C_3 = 2 \cdot 10^{-5}$ mol L^{-1}, at which AMC **3** exists in the molecular form, is $2 \cdot 10^{-5}$ mol L^{-1} (see Fig. 2, curve *1*). This value is substantially lower than the CMC of these individual compounds, which suggests their mixed aggregation in chloroform. At the CMC point, the ratio $n = C_8/C_3 = 1$; *i.e.*, at the low concentrations of AMC, the resulting associate **8·3** contains one AMC molecule per molecule of TX-100 (**8**).

With an increase in C_3 to $1 \cdot 10^{-4}$ mol L^{-1} (see Fig. 2, curve *2*), at which AMC **3** is associated in chloroform (see Table 1), the CMC of its mixture with surfactant **8** is $2 \cdot 10^{-5}$ mol L^{-1} and $n = 0.2$. Therefore, even at the first step of micellization, the mixed micelle **8·3** consists of one TX-100 and five AMC molecules, which agrees with the formation of hexameric capsules of compound **1** in chloroform.[26,27]

Analogous results were obtained for mixtures of compound **8** with AMC **6** or **7** containing the oxazine rings in their head groups (see Fig. 2, curves *3*, *4*). In these systems, irrespective of the concentration of AMC, the CMC is $2.5 \cdot 10^{-5}$ mol L^{-1}, which is lower than the CMC of its components (see Table 1). The mixed TX-100—AMC **7** associate is considered to be 1 : 1 at $C_7 = 3 \cdot 10^{-5}$ mol L^{-1} and 1 : 3 at $C_7 = 8 \cdot 10^{-5}$ mol L^{-1}. Because a nonpolar head-to-head aggregate must include an even number of molecules, the above ratios of AMC to TX-100 in mixed micelles are fairly acceptable. The difference between the compositions of the mixed aggregates **8·3** and **8·7** (1 : 5 and 1 : 3, respectively) is due to the structural dissimilarity between the head groups of these compounds. Compound **7** containing the oxazine fragments capable, according to X-ray diffraction data,[30] of sterically hindering access for molecules to the upper rim of calix[4]resorcinarenes forms mixed micelles with a lower ratio (compared to **3**), which are less stable and more polar.

This is evident from the plots in Fig. 2. For instance, curves *1* and *3* for solutions of **8·3** and **8·7** show virtually

equal ε values at the CMC point, which characterize the polarity of mixed 1 : 1 aggregates, and their permittivities are close to those for individual micelles **8** and **3** (see Fig. 1). If the micelle polarity is conventionally estimated in terms of ε at the CMC point, then mixed 1 : 1 micelles **8**·**3** and **8**·**7** are significantly more polar than 1 : 5 and 1 : 3 aggregates (Fig. 2, curves *2*, *4*). The least polar 1 : 5 aggregate **8**·**3** seems to be of highest symmetry and stability. Because mixed micellization proceeds competitively, a flexible, mobile guest molecule of TX-100 can be assumed to seek to penetrate, through its ethyleneoxy fragment, into the polar core formed by the head groups of cumbersome AMC molecules. Analysis of the ε values at the CMC point (see Figs. 1, 2) showed that mixed micelles **8**·**3** or **8**·**7** with a low content of amphiphilic TX-100 molecules are more stable than the micelles of the starting compounds and mixed 1 : 1 aggregates **8**·**3** and **8**·**7**.

Analysis of the ε vs. C plots for compounds **1**, **5**, **6**, and **8** in 1,4-dioxane revealed that calixarenes **1**, **5**, and **6** differ from typical surfactant **8** in aggregation behavior in this solvent.

As can be seen from Fig. 3b, the function $\varepsilon = f(C)$ is linear for solutions of calixarene **1** at $C_1 < 8 \cdot 10^{-5}$ mol L^{-1}, which indicates the presence of individual molecules of compound **1** and 1,4-dioxane in solution below this concentration. Then, the slope of the function $\varepsilon = f(C_1)$ slightly diminishes to give new rigorous linearity up to very high concentrations of calixarenes (see Fig. 3). Such a behavior of the system can be associated with the formation and accumulation of a stable solvate of compound **1** with 1,4-dioxane with an increase in C_1. A comparison of the slopes of these two linear segments of the function $\varepsilon = f(C)$ (Fig. 3) suggests that such a solvate is less polar than a calixarene molecule. An analogous behavior was observed for AMC **5**. Obviously, a solvate of compound **1** or **5** with 1,4-dioxane mainly involves hydrogen bonds

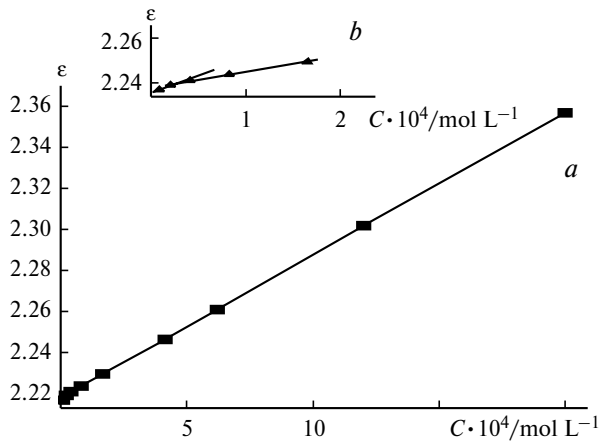


Fig. 3. Plot of the permittivity *vs.* the concentration of compound **1** for its solution in 1,4-dioxane.

between the O atoms of 1,4-dioxane and the hydroxy groups of calix[4]resorcinarenes, through which self-association occurs.

For a solution of compound **6** in 1,4-dioxane, two segments are also distinguishable: ε grows in the first segment below CMC = $2 \cdot 10^{-3}$ mol L^{-1} and then gradually comes to a plateau, which can be associated with the formation of head-to-head aggregates in equilibrium with less stable (than for compounds **1** and **5**) solvates of **6** in 1,4-dioxane. Note that the CMC of this compound in 1,4-dioxane is 20 times higher than in chloroform.

The behavior of compounds **1**, **5**, and **6** in 1,4-dioxane is determined by the structures of upper-rim polar head groups responsible for solvability. According to X-ray diffraction data,[6] a stable crystalline solvate of calix[4]resorcinarene ($R^1 = C_{11}H_{23}$) with 1,4-dioxane is built from asymmetric species containing the above compounds in the 1 : 4 ratio; one 1,4-dioxane molecule is over the hydrophilic rim, while the others are chaotically arranged in the hydrophobic "tails". Calix[4]resorcinarenes **3** and **5**, which also allow free access for solvent molecules to the hydroxy and amino groups of the upper rim, form either crystalline solvates or inclusion compounds, depending on the structure of the amino group.[40] In contrast, four oxazine fragments in AMC **6** can hinder the formation of solvates,[30] which is a probable reason for their self-aggregation at sufficiently high concentrations.

As in chloroform, the function $\varepsilon = f(C)$ for Triton-X-100 (**8**) in 1,4-dioxane shows a plateau and the CMC is $5 \cdot 10^{-5}$ mol L^{-1}, which approximately equals that in chloroform. Therefore, in contrast to calixarenes **1** and **5**, the self-association of TX-100 (**8**) in 1,4-dioxane is not impeded, which can be explained by the instability of its solvates with 1,4-dioxane or by the fact that the self-association of compound **8** in 1,4-dioxane (as in chloroform) follows a different mechanism from that for calix[4]resorcinarenes **1** and **5**.

In contrast to solutions in chloroform, addition of AMC **5** ($C_5 = 4 \cdot 10^{-4}$ mol L^{-1}) to surfactant **8** in 1,4-dioxane changes neither its CMC nor the slope of the function $\varepsilon = f(C_8)$. This suggests that a stable solvate of AMC **5** with 1,4-dioxane precludes its mixed aggregation with compound **8** in this solvent. Apparently, 1,4-dioxane effectively blockades the polar head groups of AMC **5**, thus preventing not only self-association of AMC but also the formation of its mixed aggregates with another amphiphilic compound **8**.

The 2D ROESY technique allows visualization of a pattern of dipolar interactions existing between spatially close protons in a system. We used this technique to study intermolecular interactions in systems containing calix[4]resorcinarenes **1**, **3**, **5**, and **6** in the absence and in the presence of TX-100 in chloroform and 1,4-dioxane.

The 2D ROESY spectra of TX-100 (**8**) in chloroform and 1,4-dioxane show only cross-peaks responsible for

the intramolecular interactions T-1↔T-6, T-1↔T-7, T-1↔T-8, and T-2↔T-3, T-2↔T-4.

The 2D ROESY spectra of calixarenes **1**, **5**, and **6** in chloroform and 1,4-dioxane also exhibit trivial cross-peaks indicating the K-1↔K-7, K-2↔K-7, K-3↔K-7, K-1↔K-2, and K-2↔K-3 intramolecular interactions, which is unambiguous evidence for the cone conformation of these compounds in the solvents studied.

In addition, the 2D ROESY spectra of calixarenes **1**, **5**, and **6** in 1,4-dioxane show distinct cross-peaks for intermolecular interactions between the methylene protons of 1,4-dioxane and the K-1 and K-2 protons of **1**, **5**, and **6** and the K-5 and K-6 protons of AMC **5**, which was confirmed by the X-ray diffraction data[7] on the arrangement of 1,4-dioxane molecules in the upper and lower rims of calix[4]resorcinarenes.

A different pattern was obtained for calixarenes **1**, **5**, and **6** in chloroform. Their 2D ROESY spectra contain only trivial cross-peaks (K-2↔K-7, K-1↔K-2, and K-2↔K-3) and no cross-peaks for intermolecular interactions with the solvent.

A comparison of the 1D ^{1}H NMR spectra of AMC **5** in dioxane and chloroform confirms the formation of head-to-head aggregates of calixarenes in chloroform. The 1D ^{1}H NMR spectrum of AMC **5** in dioxane shows a singlet at δ 3.8 for the NCH_2 group (K-4). In chloroform, this singlet changes into the AB system with J_{AB} = 14 Hz, which indicates the fixed position of the N atom and the hindered rotation of the NCH_2 fragment. In addition, the signal for the OH group at δ 5.5 in 1,4-dioxane disappears when passing to chloroform. These facts are easily explained in terms of the aforesaid formation of AMC aggregates in chloroform *via* hydrogen bonds involving the head groups of AMC. A similar pattern was found for a mixture of AMC **5** and TX-100 (**8**), which confirms mixed aggregation of these compounds in chloroform.

Mixed aggregation of **1**, **5**, and **6** with **8** in $CDCl_3$ and the absence of this process in 1,4-dioxane also become evident from the 2D ROESY data obtained in these solvents. For instance, the spectrum of a mixture of calixarene **1** and surfactant **8** in 1,4-dioxane (Fig. 4) contains cross-peaks for the intermolecular interactions of the methylene protons of dioxane with K-1, K-2, and K-7 of calixarene **1** and with the T-2 and T-8 protons of compound **8**. However, this spectrum shows no cross-peaks responsible for proton interactions between compounds **8** and **1**, **5**, and **6**.

A similar pattern was observed for mixtures of compounds **5** and **6** with surfactant **8**; *i.e.*, the spectrum contains cross-peaks of the methylene protons of dioxane with the K-1, K-2, K-5, and K-6 protons of calixarenes **5** and **6** and with the protons of compound **8**, while proton interactions between compounds **8** and **5** (or **6**) were not detected.

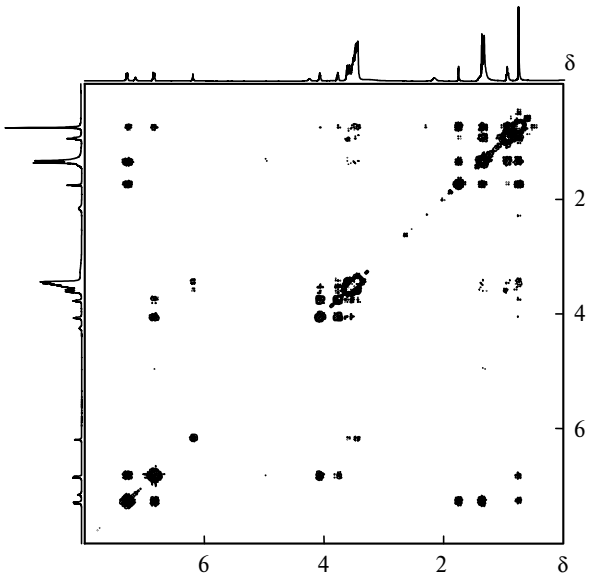


Fig. 4. 2D ROESY ^{1}H NMR spectrum of compounds **1** and **8** in 1,4-dioxane-d_8.

A different pattern arises for mixtures of compounds **1**, **5**, and **6** with surfactant **8** in chloroform (Fig. 5). In this solvent, the spectrum shows distinct cross-peaks for intermolecular interactions of the methyl and methylene groups of the hydrophobic substituents in calixarenes **1**, **5**, and **6** (no matter whether they are above (as in **6**) or below (**1**, **5**) the rim) with the ethyleneoxy fragments of surfactant **8** (T-3). These groups are spatially very close (< 4 Å). With consideration of the foregoing data, the formation of mixed head-to-head aggregates **6**·**8** and **5**·**8** can be represented as follows. *N*-Alkyl substituents

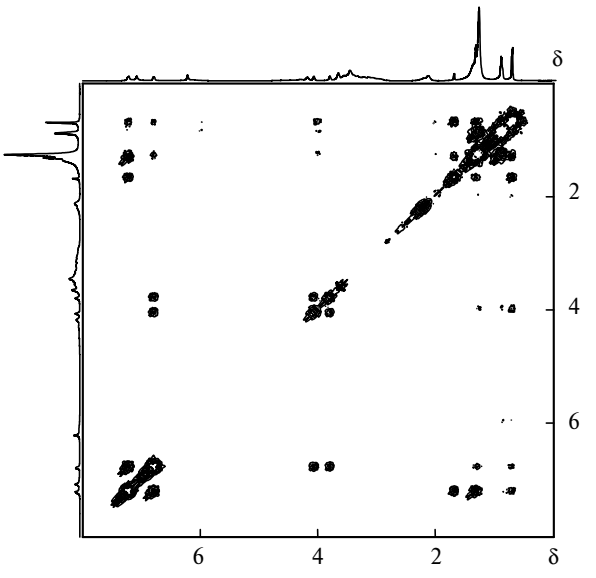


Fig. 5. 2D ROESY ^{1}H NMR spectrum of compounds **1** and **8** in $CDCl_3$.

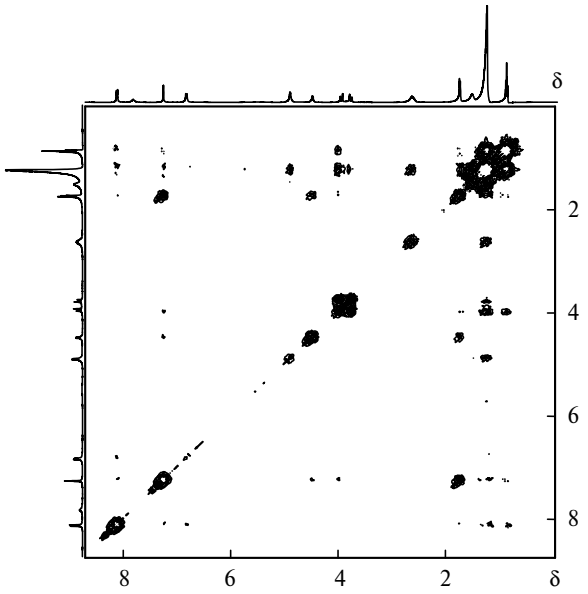


Fig. 6. 2D ROESY ^{1}H NMR spectrum of compounds **5** and **9** in $CDCl_3$.

in AMC **6** are in the close vicinity of its head polar groups (interactions of the *N*-alkyl groups with the polar ethyleneoxy fragment of compound **8** were detected by the ROESY NMR technique). In the mixed aggregate **5·8**, the ethyleneoxy fragments tending to shrink or extend, depending on the environment (see Ref. 22), are close to the polar core of the inverted micelle (between K-3 and K-2).

A very interesting pattern was obtained in the reactions of calix[4]resorcinarenes **5** and **6** with compound **9** (Fig. 6). As with mixed aggregates **5·8** and **6·8**, the spectra always contain pronounced K-2↔P-1 cross-peaks indicating the formation of stable intermolecular head-to-head complexes (in *p*-nitrophenol **9**, the hydroxy group serves as a head similarly to the ethyleneoxy fragments of compound **8**).

Thus, the aggregation and intermolecular interactions of various amphiphilic calix[4]resorcinarenes with the nonionic surfactant Triton-X-100 in chloroform and 1,4-dioxane was studied by permittivity measurements and 2D ROESY ^{1}H NMR technique. In chloroform, all the compounds involved were found to form aggregates and mixed aggregates in the form of inverted micelle. Strong intermolecular interactions between the hydrocarbon substituents of aminomethylated calix[4]resorcinarenes and the aromatic protons *ortho* to the hydroxy group of *p*-nitrophenol in chloroform unambiguously indicate the solubilization of *p*-nitrophenol by AMC aggregates, with location of their sites involved in this process. In 1,4-dioxane, the aggregation of calix[4]resorcinarenes, in contrast to Triton-X-100, is prevented by the formation of their stable solvates.

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