Structure and Dynamics of *p*-Sulfonatocalix[4]arene and Its Hydration Shell. Nuclear Magnetic Relaxation Results

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The longitudinal ^{13}C spin−lattice relaxation times and {[1]H}−[13]C nuclear Overhauser factors of the aliphatic and aromatic carbon atoms of calix[4]arene-*p*-sulfonic acid (**1a**) and its pentasodium salt (**1b**) were measured for a solution in D_2O and a temperature range from 270 to 347 K; those of the calixarene (**1a**) were measured also for a solution in [²H₄]methanol and from 203 to 324 K. The results show that the extreme narrowing condition is not fulfilled for the ^{13}C relaxation data. For the aqueous solutions the longitudinal ^{2}H spin−lattice relaxation times of D_2O were determined as well. The observed relaxation times were fitted to the theoretical expressions for rotational motions of the molecules. The reorientational molecular dynamics showed Arrhenius behavior in all cases, and the corresponding activation parameters were evaluated. The rotational motion of the calixarene molecules is essentially isotropic in the investigated solutions. The order of the reorientation rates is methanolic solution of **1a** > aqueous solution of **1b** > aqueous solution of **1a**. The differences in the motional behavior are an indication of differing intermolecular interaction mechanisms between solvent and solutes and, in the case of the aqueous solutions, a different dynamical behavior of the water around the calixarene molecules. A scaling of the spectral densities with the generalized order parameter S^2 of the model-free approach by Lipari and Szabo has to be applied for quantitative interpretation of the relaxation data. This is caused by the existence of a very fast initial decay of the reorientational correlation function of the calixarene molecules, stemming from fast librational and/or internal motions in addition to the overall rotational diffusion process.

Introduction

Calix[*n*]arenes belong to a particularly interesting class of compounds regarding their host−guest interactions.[1] Calix[*n*]-arenes are cyclic compounds, easily obtained and modified according to the requirements for host molecules, which makes them superior to crown ethers and cyclodextrins. By sulfonation in the *para* position to the phenolic hydroxyl group water-soluble calixarenes are obtained,[2] being of great importance for potential applications. The proposed applications for water-soluble calixarenes span for example from recovery of uranium from aqueous solutions by complexation of the uranyl cation[1b] to encapsulation of fullerene C_{60},[3] utilization as catalysts and surfactants,[4] and nonenzymatic regioselective cleavage of ribonucleoside 2′,3′-cyclic phosphates.[5] Patents have been applied for the use of water-soluble calixarenes for therapy of thrombosis[6] and viral infections.[7] Furthermore, the application as a catalyst in the synthesis of acetonin, which is an important intermediate product in the production of pharmaceuticals and UV stabilizers, has been reported in a patent application.[8]

Calixarenes are flexible compounds that exist in different conformations. In solution, the conformers transform into each other. Calix[4]arenes exhibit mainly the cone conformation, stabilized by a ring of intramolecular hydrogen bonds between the phenolic hydroxyl groups.[1] This is also true for the water-soluble *p*-sulfonatocalix[4]arenes: In the solid state[9] as well as in aqueous solution[10] they exist predominantly in the cone conformation, although a permanent interconversion between

the two cone conformers occurs in the liquid.[10] During these cone−cone inversions the hydroxyl groups have to pass through the calixarene ring structure. For that the intramolecular hydrogen bonds have to be at least partially broken. Since this will proceed simultaneously with the forming of hydrogen bonds to surrounding water molecules, the hydration sphere becomes considerably important for this process.

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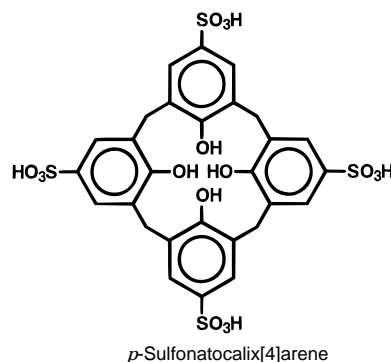
Until now, the dynamic properties of calixarenes, *i.e.*, the conformational flexibility, have been investigated mainly by dynamic ^{1}H NMR spectroscopy,[1] by which kinetics on a time scale of about $10-10^5$ s^{-1} are accessible. Dynamics on faster time scales, such as reorientations of the whole molecule or of molecular segments, are studied very efficiently by measurement of relaxation data. The overall and segmental mobility of calix[*n*]arenes and one of their methyl ethers were studied by measurement of their ^{13}C spin−lattice relaxation times;[11] the motional behavior of free *p-tert*-butylcalixarene ester derivatives

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and the influence of host−guest interactions were assessed by [1]H[12−14] and [13]C[13] spin−lattice relaxation times. The data in these investigations were interpreted in a qualitative manner, and no quantitative values for the motional dynamics were given. Recently, the determination of diffusion coefficients for *p-tert*-butylcalix[*n*]arenes by dynamic light scattering[15] and pulsed field gradient NMR methods[16] were reported. In the latter work also the effect of possible host−guest interactions between small organic molecules and calixarenes was studied. All data mentioned above were obtained for solutions in organic solvents.

The dynamic and conformational properties of the calixarenes are of great importance for their host characteristics when interacting with guests. In order to gain a deeper understanding of the host properties of calixarenes, the rotational dynamics of water-soluble *p*-sulfonatocalix[4]arene (**1**) are investigated by NMR methods in the present work. To our knowledge, this is the first experimental study of the motional behavior of water-soluble calixarenes. The rotational dynamics of **1** and water are obtained for solutions of the acid form (**1a**) and the pentasodium salt (**1b**). Furthermore, a solution of **1a** in methanol is also studied.

Theoretical Background

Relaxation of [13]C Nuclei. The relaxation of ^{13}C nuclei in medium-sized molecules and for moderate magnetic fields is generally determined by dipolar interactions with directly bonded protons. When the relaxation times are measured under ^{1}H decoupling conditions, the cross-relaxation term vanishes,[17] and the intramolecular dipolar longitudinal relaxation rate ($1/T_1^{DD})_i$ for relaxation of ^{13}C nucleus i by n_H protons j is connected to the molecular reorientations by[17]

$$\left(\frac{1}{T_1^{DD}}\right)_i = \frac{1}{20} n_H (2\pi D_{ij})^2 [J(\omega_C - \omega_H) + 3J(\omega_C) + 6J(\omega_C + \omega_H)] \quad (1)$$

with the dipolar coupling constant

$$D_{ij} = (\mu_0/4\pi)\gamma_C\gamma_H(\hbar/2\pi)r_{ij}^{-3} \quad (2)$$

where μ_0 is the permeability of vacuum, γ_C and γ_H are the magnetogyric ratios of the ^{13}C and ^{1}H nuclei, respectively, $\hbar = h/2\pi$ with the Planck constant h, and r_{ij} is the length of the internuclear vector between i and j. The $J(\omega)$ are the spectral densities with the resonance frequencies of the ^{13}C and ^{1}H nuclei, ω_C and ω_H, respectively.

The nuclear Overhauser (NOE) factor η_i of carbon atom i for relaxation by n_H protons j is given by[17,18]

$$\eta_i = \frac{\gamma_H}{\gamma_C} \frac{\sum_{j=1}^{n_H} \sigma_{ij}}{\sum_{j=1}^{n_H} \rho_{ij} + \rho_i^*} \quad (3)$$

where σ_{ij} is the cross-relaxation rate, ρ_{ij} the dipolar relaxation rate, and ρ_i^* the so-called leakage term, which represents the contribution of all other relaxation mechanisms to relaxation of ^{13}C nucleus i and which reduces the NOE factor. Usually, intermolecular dipolar contributions can be neglected for ^{13}C nuclei with directly bonded protons. Under ^{1}H decoupling conditions the sum of ρ_{ij} over all n_H interacting protons gives the dipolar spin−lattice relaxation rate $(1/T_1^{DD})_i$. For relaxation of ^{13}C exclusively *via* the intramolecular dipolar interaction,

$\rho_i^* = 0$, the NOE factor reaches its maximum value and depends only on the reorientational molecular dynamics[17,18]

$$\eta_{i,max} = \frac{\gamma_H}{\gamma_C} \frac{6J(\omega_H + \omega_C) - J(\omega_H - \omega_C)}{J(\omega_H - \omega_C) + 3J(\omega_C) + 6J(\omega_H + \omega_C)} \quad (4)$$

Aromatic ^{13}C nuclei relax even in moderate magnetic fields partially *via* the chemical shift anisotropy (CSA) mechanism. The corresponding longitudinal relaxation rate of ^{13}C nucleus i is given by

$$\left(\frac{1}{T_1^{CSA}}\right)_i = \frac{1}{15} \gamma_C^2 H_0^2 (\Delta\sigma_i)^2 J(\omega_C) \quad (5)$$

with the magnetic field strength H_0 and the chemical shift anisotropy $\Delta\sigma = \sigma_\| - \sigma_\perp$ for an axially symmetric chemical shift tensor with $\sigma_\|$ and $\sigma_\perp$ as the components parallel and perpendicular to the main principal axis of the chemical shift tensor.

When discussing the various mechanisms[17] contributing to the ^{13}C relaxation of the calixarenes, it is reasonable to assume that the aliphatic methylene ^{13}C nuclei relax exclusively *via* the dipolar relaxation mechanism, and the experimental relaxation times can be equated to the dipolar ones, whereas for the relaxation of the aromatic methine ^{13}C nuclei the CSA mechanism also makes a contribution. Thus, for the aromatic ^{13}C nuclei the total longitudinal relaxation rate is determined by the relation

$$\left(\frac{1}{T_1}\right)_i = \left(\frac{1}{T_1^{DD}}\right)_i + \left(\frac{1}{T_1^{CSA}}\right)_i \quad (6)$$

Relaxation of [2]H Nuclei. Nuclei with nuclear spin quantum numbers greater than $^1/_2$ possess electric quadrupole moments eQ. The longitudinal relaxation rates caused by quadrupolar interaction are for nuclei with a nuclear spin quantum number of $I = 1$ like the ^{2}H nuclei:[19]

$$\frac{1}{T_1^{EQ}} = \frac{3}{40} (2\pi\chi)^2 [J(\omega) + 4J(2\omega)] \quad (7)$$

with the nuclear quadrupole coupling constant $\chi = eQq/h$; q is the electric field gradient which is closely related to the local symmetry of the electric field at the nucleus. Furthermore, it is assumed in eq 7 that the asymmetry parameter can be neglected, which is normally justified for ^{2}H nuclei.

Spectral Densities. Usually, the spectral densities are connected to the effective correlation times τ_c for reorientation of the corresponding internuclear [13]C−[1]H vectors by[19]
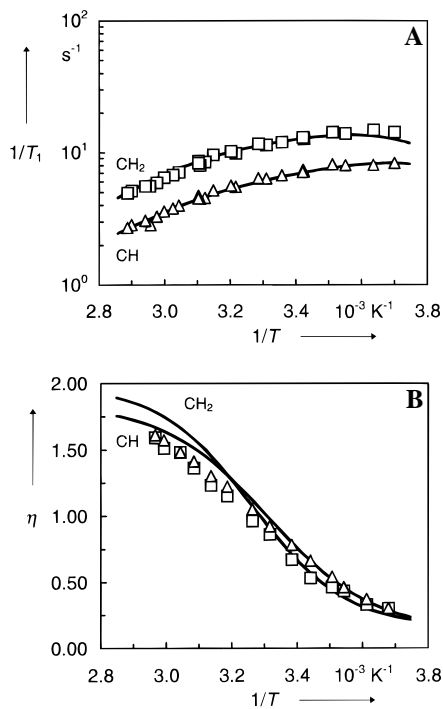
$$J(\omega) = \frac{2\tau_c}{1 + (\omega\tau_c)^2} \quad (8)$$

Here, τ_c corresponds to τ_2, the time constant for the exponential decay of the second-rank Legendre polynomial P_2. In the extreme narrowing case, when the product of the molecular reorientational correlation time and resonance frequency is much less than unity ($\omega\tau_c \ll 1$), eq 8 reduces to

$$J(\omega) = 2\tau_c \quad (9)$$

The temperature dependence of the correlation times is often described by an Arrhenius equation:

$$\tau_c = \tau_0 \exp(E_a/RT) \quad (10)$$

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Figure 1. Experimental and calculated (—) ^{13}C relaxation rates $1/T_1$ and $\{^1H\}-^{13}$C NOE factors η of the aliphatic (CH$_2$, $\square$) and aromatic (CH, $\triangle$) carbon atoms of calix[4]arene-*p*-sulfonic acid (**1a**) as a function of reciprocal temperature $1/T$ for a solution in D$_2$O with mole fraction $x = 0.0040$ (solution **A**).

Figure 2. Experimental and calculated (—) ^{13}C relaxation rates $1/T_1$ and $\{^1H\}-^{13}$C NOE factors η of the aliphatic (CH$_2$, $\square$) and aromatic (CH, $\triangle$) carbon atoms of pentasodium calix[4]arene-*p*-sulfonate (**1b**) as a function of reciprocal temperature $1/T$ for a solution in D$_2$O with mole fraction $x = 0.0040$ (solution **B**).
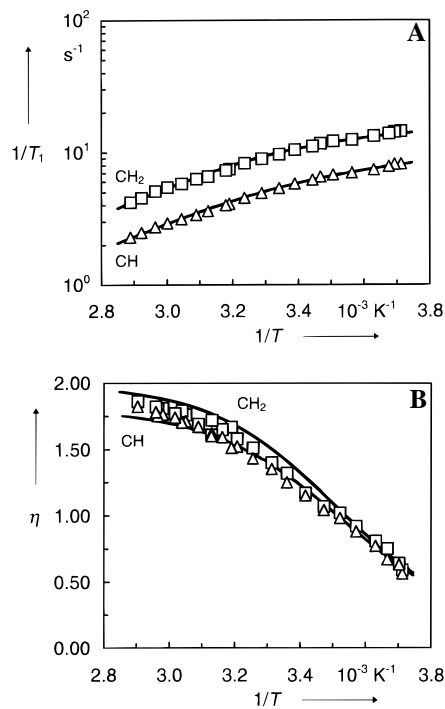
with the activation energy E_a, the temperature T, and the gas constant R. In order to take into account very fast internal motions, the "model-free" approach by Lipari and Szabo[20] has often been used. It reduces the spectral density by a factor S^2, the generalized order parameter:

$$J(\omega) = S^2 \frac{2\tau_c}{1 + (\omega\tau_c)^2} \quad \text{and} \quad 0 \leq S^2 \leq 1 \qquad (11)$$
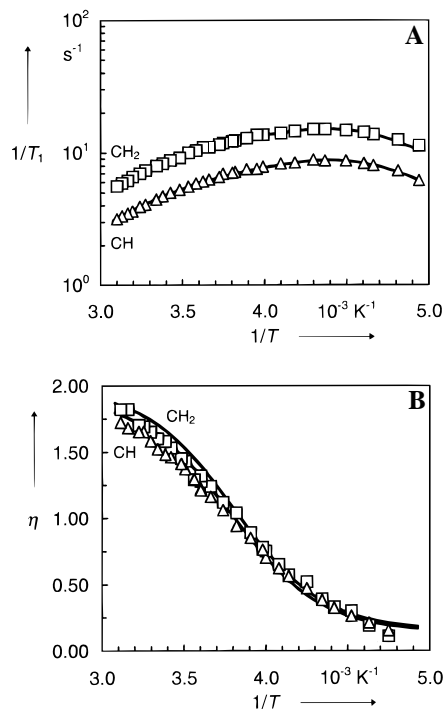
Results

^{13}C Relaxation Data. The longitudinal ^{13}C spin−lattice relaxation times T_1 of the aliphatic (CH$_2$) and aromatic (CH) carbon atoms of calix[4]arene-*p*-sulfonic acid (**1a**) and its pentasodium salt (**1b**) were measured for a solution in D$_2$O (solution **A** and **B**, respectively) and a temperature range from 270 to 347 K; those of the calixarene **1a** also for a solution in [^{2}H$_4$]methanol (solution **C**) and a range from 203 to 324 K. The observed relaxation rates ($1/T_1$) are presented in Figures 1A−3A as functions of the reciprocal temperature $1/T$. While the relaxation rates of the ^{13}C nuclei in solution **B** are monotonically increasing, the data points for solution **A** show a maximum at lowest temperatures, which is even more pronounced for solution **C** because for the methanolic solution smaller reorientation rates could be reached at lower temperatures. The corresponding measured $\{^1H\}-^{13}$C NOE factors η are plotted as a function of reciprocal temperature $1/T$ in Figures 1B−3B. As is seen from the figures, the NOE factors are decreasing with increasing reciprocal temperature.

^{2}H Relaxation Data. The longitudinal quadrupolar ^{2}H spin−lattice relaxation times T_1^{EQ} of the D$_2$O in both aqueous solutions **A** and **B** were determined for a temperature range from 273 to 340 K. The logarithmic plot of the observed relaxation rates $1/T_1^{EQ}$ as a function of the reciprocal temperature $1/T$ is given in Figure 4.

Figure 3. Experimental and calculated (—) ^{13}C relaxation rates $1/T_1$ and $\{^1H\}-^{13}$C NOE factors η of the aliphatic (CH$_2$, $\square$) and aromatic (CH, $\triangle$) carbon atoms of calix[4]arene-*p*-sulfonic acid (**1a**) as a function of reciprocal temperature $1/T$ for a solution in CD$_3$OD with mole fraction $x = 0.0040$ (solution **C**).

Rotational Molecular Dynamics in the Calixarene Solutions. In order to evaluate the reorientational dynamics of the calixarene molecules in the solutions, the experimental longitudinal relaxation rates and the NOE factors of the aliphatic methylene ^{13}C nuclei were fitted simultaneously with eqs 1, 4, 10, and 11. For fitting the relaxation data of the aromatic ^{13}C nuclei, additionally eqs 5 and 6 have to be applied. The

TABLE 1: Best Fit Parameters for the ^{13}C Relaxation Data of the Calix[4]arene-*p*-sulfonic Acid (1a) and Its Pentasodium Salt (1b)[a]

compd/solution (solvent)	carbon atom	no. of data points	τ_0/fs	E_A/kJ mol^{-1}	S^2	$|\Delta\sigma|$/ppm	χ^2
1a/A		39					
(D$_2$O)	CH$_2$		8 ± 1	29.0 ± 0.4	0.743 ± 0.007		91
	CH		25 ± 6	25.6 ± 0.6	0.68 ± 0.02	280 ± 30	28
1b/B		45					
(D$_2$O)	CH$_2$		74 ± 10	21.7 ± 0.3	0.81 ± 0.01		29
	CH		110 ± 20	20.5 ± 0.5	0.73 ± 0.01	320 ± 30	12
1a/C		57					
(CD$_3$OD)	CH$_2$		670 ± 60	15.2 ± 0.2	0.827 ± 0.007		98
	CH		740 ± 60	15.0 ± 0.2	0.79 ± 0.01	190 ± 20	27

[a] The C−H bond lengths r_{C-H} were taken to be 109 ppm for the aromatic methine and 111 pm for the aliphatic methylene group. The error of the experimental data in the fitting procedure was assumed to be 3% for the relaxation rates and 7.5% for the NOE factors.
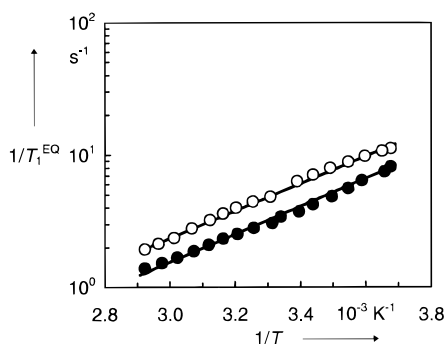
Figure 4. Experimental and calculated (−) quadrupolar ^{2}H relaxation rates $1/T_1^{EQ}$ of D$_2$O in the aqueous solution of calix[4]arene-*p*-sulfonic acid (1a) (○, mole fraction $x = 0.0040$, solution **A**) and of pentasodium calix[4]arene-*p*-sulfonate (1b) (●, mole fraction $x = 0.0040$, solution **B**) as a function of reciprocal temperature $1/T$.
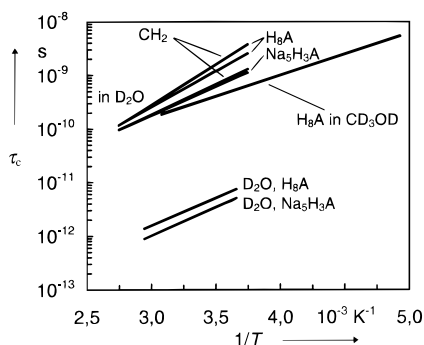
Figure 5. Correlation times τ_c of the calix[4]arene-*p*-sulfonic acid (1a) and its pentasodium salt (1b) in solutions **A** to **C** and correlation times of the D$_2$O molecules in solutions **A** and **B** as a function reciprocal temperature $1/T$.

corresponding parameters of the best fit, *i.e.*, the parameters of rotational molecular motion, are listed in Table 1. The longitudinal relaxation rates and NOE factors calculated from the best fit parameters are also presented in Figures 1−3. The correlation times obtained from these parameters are shown in Figure 5.

The rotational dynamics of the water molecules in the aqueous solutions were evaluated from the ^{2}H relaxation rates by fitting the data with eqs 7, 8, and 10, for which the best fit parameters are contained in Table 2. The calculated quadrupolar relaxation rates are compared to the experimental values in Figure 4. For calculating the reorientational motion, we assumed a nuclear quadrupole coupling constant for the D$_2$O molecules of 255 kHz, which is the value for pure D$_2$O.[22]

Discussion

^{13}C Relaxation Data. The curvature in the plots of the relaxation rates as well as the occurrence of the maxima (Figures

TABLE 2: Best Fit Parameters for the ^{2}H Relaxation Data of D$_2$O for the Calix[4]arene-*p*-sulfonic Acid (1a) and Its Pentasodium Salt (1b) in Aqueous Solutions A and B[a]

solution (dissolved compd)	no. of data points	τ_0/fs	E_A/kJ mol^{-1}	χ^2
A (1a)	16	2.0 ± 0.2	19.7 ± 0.3	19
B (1b)	17	1.1 ± 0.1	20.2 ± 0.3	19

[a] The nuclear quadrupole coupling constant of the ^{2}H nuclei was assumed to be 255 kHz.[22] The error of the experimental relaxation rates in the fitting procedure was assumed to be 3%.

1A−3A) results from the fact that the extreme narrowing condition is not fulfilled for the measured relaxation rates. Otherwise, the relaxation function $\ln(1/T_1) = f(1/T)$ would give straight lines when eqs 9 and 10 were valid. The relaxation rates of the methylene ^{13}C nuclei is approximately double of that for the aromatic nuclei because of the interaction with two directly bonded protons in the former case instead of only one proton in the latter. In the range of extreme narrowing the NOE factors would be constant and expected to be either equal to the maximum value $\eta_{i,\text{max}}$ in eq 4 for the methylene or smaller than $\eta_{i,\text{max}}$ for the aromatic ^{13}C nuclei. The differing behavior of the experimental values (Figures 1B−3B) also points to the fact that the condition of extreme narrowing is no longer fulfilled. The values even reach for the methanolic solution **C** the value of 0.154 for $\eta_{i,\text{max}}$ at $\omega\tau_c \gg 1$ (Figure 3B). It is also seen from the figures that deviations from the extreme narrowing case are much earlier visible for NOE factors than for longitudinal relaxation rates.

^{2}H Relaxation Data. The logarithmic plot of the observed relaxation rates $1/T_1^{EQ}$ as a function of the reciprocal temperature $1/T$ shows the typical behavior for relaxation in the extreme narrowing regime, *i.e.*, a straight line (*cf.* Figure 4).

Rotational Molecular Dynamics in the Calixarene Solutions. From Table 1 and Figure 5 it is deduced that the reorientation of the calixarene molecules in the methanolic solution **C** is fastest, followed by the aqueous solution **B** of the salt. At higher temperatures, however, the reorientation rates become similar. The faster reorientation in solution **C** can be attributed to the lower viscosity of the solvent.

When both aqueous solutions are compared with each other, the rotational dynamics is faster in solution **B** (pentasodium salt 1b) than in solution **A** (sulfonic acid 1a). Since the hydrated calixarene anions should be equally charged in both solutions, the different dynamical behavior cannot be easily explained by differences in the interaction of the calixarene anions with their hydration shell. On the other hand, a different dynamical behavior of the surrounding solvent, caused by differing properties of the counterions of the calixarene anions, could be taken into consideration. In fact, the reorientation of the bulk water molecules is slower in solution **A** of the sulfonic acid

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(**1a**) (Figure 5) as also indicated by the greater relaxation rates $1/T_1^{eq}$ (Figure 4) and the greater value of τ_0 (Table 2). However, this finding is in contrast to the "structure-forming" strength of both counterions in simple aqueous solutions:[21] the $B^{\pm}$ or $B'^{\pm}$ coefficients of H_3O^+ and Na^+ (being a measure for the reorientation rates of the hydration shell water molecules) are almost equal or contrary to the effect observed in this study.

The activation energies for reorientation of the water molecules also show discrepancies to this latter concept. The activation energy for reorientation of the water molecules is identical for both solutions (*cf.* Table 2). While these values are comparable to that of pure water,[22] the values for τ_0 are higher. In the aqueous salt solution **B** the activation energy for reorientation of the calixarene molecules is of the same magnitude as that for the bulk water reorientation, as one would expect for a Debye-like reorienting particle in a viscous medium. In contrast to that, in solution **A** the activation energies for reorientation of the water and calixarene molecules are significantly different. In conclusion, we consider these discrepancies as indicative for differing host—guest interactions between the calixarene and its counterions. However, further elucidation of these findings is beyond the scope of this study.

Furthermore, it becomes evident from the data that the correlation times for reorientation of both observed kinds of ^{13}C nuclei in the calixarene molecules are very similar over the considered temperature range or that they are even identical within the error limits in case of solutions **B** and **C**. Because of this and also because of the shape of the calixarene molecules, it is reasonable to assume a more or less isotropic rotational motion of the calixarene molecules, especially in the methanolic solution **C**.

The generalized order parameter S^2, which describes the spatial restriction of fast internal motions, deviates significantly from unity and is always larger for the methylene ^{13}C nuclei. Unfortunately, no further information about the possible physical process causing this phenomenon is obtained from that value, except that a very fast motion is existing besides the rotational diffusion contributing to ^{13}C relaxation of the calixarene molecules.

The value of 190 ± 20 ppm for the chemical shift anisotropy of the calixarene molecule in solution **C** (see Table 1) is in accord with the absolute value of 182.9 ppm for benzene observed in liquid crystalline solvents.[23] The values for the calixarene anions in the aqueous solutions **A** and **B** are equal within the error limits but differ significantly from the former. This can be explained by the different electron densities of the neutral and negatively charged calixarene molecules in methanolic and aqueous solutions, respectively.

Conclusions

In the present study the rotational dynamics of water-soluble *p*-sulfonatocalix[4]arene (**1**) and of water as solvent has been investigated for the first time quantitatively and over a large temperature region by measuring ^2H and ^{13}C relaxation data. Significant differences for the dynamical behavior in the different solutions have been observed. The measured relaxation data of the calixarene molecules show even for the highest temperature deviations from the extreme narrowing condition; *i.e.*, the molecular reorientational motion is already at ambient temperatures relatively slow. It is concluded from the data that the rotational motion is essentially isotropic. Besides rotational dynamics, also information about the electronic structure of the differently charged calixarene molecules was obtained from fitting the relaxation data (chemical shift anisotropy). The evaluation of reorientational dynamics of the calixarene mol-

ecules and their hydration shell by measuring relaxation data is thus an appropriate tool to investigate the properties of these host molecules and the influence of different solvents.

Methods

Synthesis and Sample Preparation. For synthesis of the calix[4]arene-*p*-sulfonic acid (**1a**) either the calix[4]arene was sulfonated by a procedure of Scharff *et al.*[24] after dealkylation[25] of the commercial *p-tert*-butylcalix[4]arene (Fluka) or compound **1a** was synthesized in one step from the *p-tert*-butylcalix[4]-arene according to Gömer *et al.*[8] The pentasodium salt **1b** was obtained from **1a** by neutralization with sodium hydrogen-carbonate and recrystallized by dissolving in water and precipitating with methanol.

Compounds **1a** and **1b** were dissolved in ^2H_2O (solutions **A** and **B**, respectively) and additionally **1a** in $[^2H_4]$methanol (solution **C**) to give solutions with a mole fraction of $x = 0.0040$, which corresponds to one calixarene molecule per 250 water molecules. The samples were degassed by five freeze—pump—thaw cycles.

NMR Measurements. ^2H and ^{13}C NMR measurements were performed on a Bruker AM 250 spectrometer ($B_0 = 5.875$ T, $\nu_0(^1H) = 250.13$ MHz, $\nu_0(^2H) = 38.25$ MHz, $\nu_0(^{13}C) = 62.90$ MHz, internal lock for the ^{13}C measurements ^2H_2O or $[^2H_4]$methanol). Measurements of the spin—lattice relaxation times were carried out with the inversion-recovery pulse sequence under ^1H broad-band decoupling and repeated five times; those for the NOE factors were repeated 3—10 times. The spin—lattice relaxation times and NOE factors were extracted from signal heights, the relaxation times were calculated by a three-parameter exponential fit implemented in the spectrometer software. Temperatures were determined before and after measurement of the relaxation data by temperature-dependent ^1H chemical shift measurements[26] of neat 1,2-ethanediol or methanol. The error in the temperature was estimated to be ± 1 K. The mean standard deviations of the mean experimental data were below 2% for the relaxation times and less than 7% for the NOE factors. However, the "real" error for the relaxation times is believed to be about 3% and for the NOE factors between 5 and 10%. Further details concerning experimental techniques and sample preparation are given in ref 27.

Data Evaluation. The model parameters were obtained with the aid of a FORTRAN 77 program which performed a χ^2 fit by the Levenberg—Marquardt method[28] to all experimental relaxation data simultaneously. In order to obtain reasonable results for the χ^2 test and for the standard deviations of the fitted parameters, a mean standard deviation of 3% for the spin—lattice relaxation times and of 7.5% for the NOE factors was assumed.

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