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Mechanisms of Formation and Dissociation of a Cesium−Calix[4]arene Acetamide Complex in Solution: A Cs-133 Dynamic NMR Study

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The kinetics and mechanism of the cesium cation complexation by 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(*N*,*N*-diaethylaminocarbonyl)methoxy calix[4]arene (**1**) were studied in a binary mixture (1:1 by volume) of deuterated acetonitrile and deuterated chloroform using ^{1}H and ^{133}Cs NMR spectroscopy. The formation of cone complexes with 1:1 and 2:1 Cs^+/**1** stoichiometries is reported. The complex formation of the 1:1 complex is quantitative ($K_f > 10^4$ M^{-1}), and the equilibrium constant for the 2:1 complex is 3 ± 2 M^{-1} at 238 K. The first complexed Cs^+ is embedded in the cavity made of the four phenolic and four carbonyl oxygens, whereas it is suggested that the second Cs^+ is loosely bound by the amido groups. The second Cs^+ and the solvated Cs^+ are in fast exchange. The embedded Cs^+ is in slow exchange with solvated Cs^+. The decomplexation process of the 1:1 complex follows a unimolecular dissociation mechanism. It is characterized by $\Delta H^* = 67 \pm 2$ kJ/mol and $\Delta S^* = 40 \pm 3$ J/(mol K). An intramolecular exchange between the two bound cesium cations is not observed.

Introduction

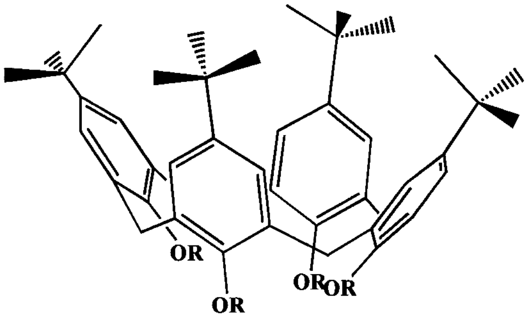
Calix[*n*]arenes are macrocyclic phenol−formaldehyde condensation oligomers which have received widespread attention due to their versatile recognition properties toward neutral, cationic, and anionic guests.[1−4] The selectivity of the complexation process can be controlled by substitutions, particularly at the phenolic oxygens, constituting what is currently referred to as the lower rim.[5−9] Of the many calix[4]arenes which have been chemically modified at the lower rim, ester, ketone, and amide derivatives have received particular attention because they display strong extracting and complexing properties toward alkali metal cations.[10] Thermodynamic and kinetic studies of the complex formation and dissociation processes are required to understand the factors and mechanisms responsible for the observed selectivity of the host−guest complexation in solution.[11] The kinetics and mechanisms of the alkali metal cation complexation by calix[4]arenes and their conformational interconversion in solution have been scarcely studied.[12−19]

In this paper, the complexation of the cesium cation by a calix[4]arene acetamide, 5,11,17,23-tetra-*tert*-butyl-25,26,27,-28-tetrakis(*N*,*N*-diaethylaminocarbonyl)methoxycalix[4]arene, **1** (Scheme 1), is studied by ^{1}H and ^{133}Cs NMR spectroscopies in a binary mixture of deuterated acetonitrile and chloroform. It is shown that the decomplexation of the 1:1 cesium−calix[4]arene acetamide complex (Cs^+, **1**) follows an unimolecular dissociation mechanism. The presence of small amounts of a 2:1 Cs^+/**1** complex does not lead to a competitive associative exchange mechanism.

Experimental Section

Chemicals and Solutions. The 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(*N*,*N*-diaethylaminocarbonyl)methoxycalix[4]arene was synthesized from the *p*-*tert*-butylcalix[4]arene derivative (Aldrich 99%) as described by Arduini et al.[5] Cesium triiodide (Johnson Matthey 99%) was used as the cesium cation source. CsI_3 was dried under vacuum overnight prior to use.

SCHEME 1



R=$CH_2CON(CH_2CH_3)_2$

All measurements were made in a binary mixture of deuterated chloroform and deuterated acetonitrile. Deuterated chloroform (99.8%) was purchased from Cambridge Isotope Laboratories, and deuterated acetonitrile (99.8%) was purchased either from Cambridge Isotope Laboratories or CDN Isotopes Pointe-Claire, Quebec, Canada. The solvents were dried over 4 Å molecular sieves before use.

NMR Measurements. The ^{1}H and ^{133}Cs NMR spectra were recorded on a Bruker AMX-500 NMR spectrometer at 500.14 and 65.59 MHz, respectively. The ^{1}H NMR spectra were referenced to chloroform (7.24 ppm) and the ^{133}Cs spectra to 0.01 M CsCl in 20% D_2O (0 ppm at 300 K).

^{133}Cs NMR Spectra. The parameters were chosen to obtain quantitative spectra. At relaxation delay of 0.5−4 s ($>5T_1$), a 90° pulse of 14 μs, an acquisition time of 0.01−2 s, and a sweep width of 20 kHz were used and 32−10000 scans were accumulated per spectrum.

The longitudinal relaxation times, T_1, were measured by the inversion−recovery technique. A 90° pulse of 14 μs and 10 delay times (1 ms to 2.56 s) and relaxation delays of at least 0.75 s were used. The data were fitted to the equation $I(\tau) = M_0(1 - ke^{\tau/T_1})$, and M_0, k, and T_1 were determined by a nonlinear

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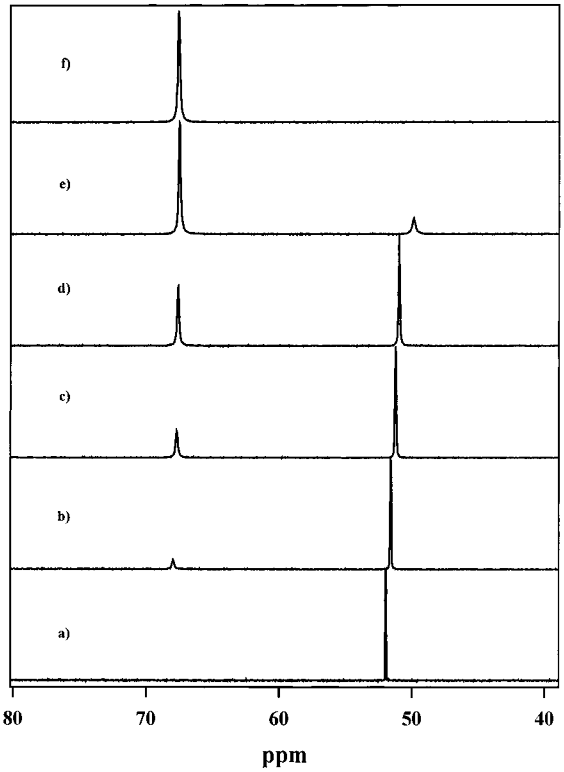


Figure 1. ^{133}Cs NMR spectra of 30 mM CsI_3 in the absence (a) and the presence (b−f) of various amounts of **1** at 238 K: (a) 0; (b) 4.5; (c) 9.9; (d) 15.2; (e) 25.4; (f) 36.7 mM.

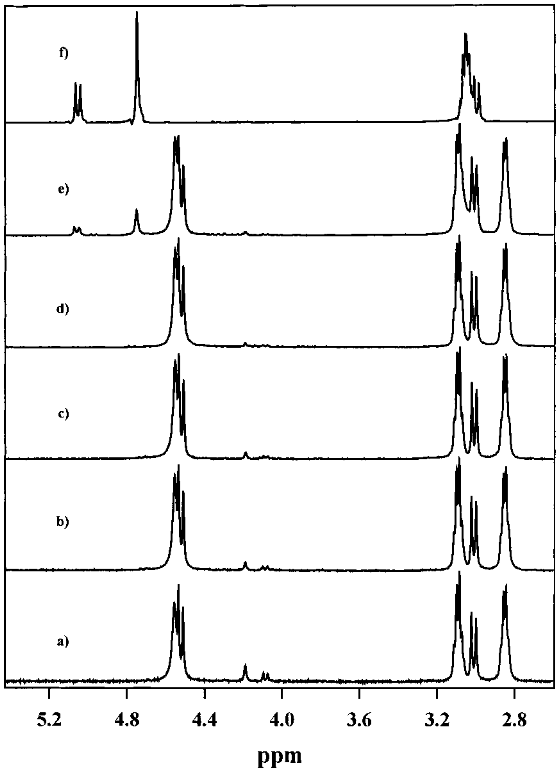


Figure 2. ^{1}H NMR spectra of various amounts of **1** in the presence (a−e) and absence (f) of 30 mM CsI_3 at 238 K: (a) 4.5; (b) 9.9; (c) 15.2; (d) 25.4; (e) 36.7; (f) 32.6 mM.

regression analysis. The T_1 values were determined at 255, 265, 274, 283, and 292 K. They were found to be respectively 120, 132, 174, 202, and 220 ms for the complexed Cs^+ and 150, 173, 179, 201, and 245 ms for the solvated Cs^+.

The error on the temperature measurements was estimated to be 0.5 K.

Data Treatment. The line widths, intensities, and chemical shifts were determined by fitting each peak with a Lorentzian line shape. The integrals were calculated analytically using these line widths and intensities.

Results and Discussion

Figure 1 shows the ^{133}Cs NMR spectra of variable amounts of **1** in the presence of 30 mM of cesium triiodide, CsI_3, in a binary mixture of deuterated acetonitrile and deuterated chloroform at 238 K. In the absence of **1,** the $^{133}Cs^+$ resonance is observed at 52 ppm, which, in the conditions of this study, corresponds to the solvated cation, since, as it has been shown before,[12] the contact ion pair eventually formed between Cs^+ and I_3^- is dissociated, at least to a very large extent. Upon addition of **1**, a new signal appears at 68 ppm, whose chemical shift does not depend on the concentration of **1**. The resonance of the solvated Cs^+ is slightly shifted toward lower frequencies, indicating a fast exchange with at least one other species formed upon addition of **1**.

Figure 2 shows the ^{1}H NMR spectra, in the region 2.7−5.3 ppm, of various amounts of **1** in the presence (Figure 2a−e) and in the absence (Figure 2f) of 30 mM CsI_3. The spectrum of the uncomplexed calixarene is characteristic of the cone conformation. No other conformations can be detected. In the presence of CsI_3, one of the AB doublets of the methylenic bridges is displaced to lower frequencies (5.05 to 4.52 ppm). The singlet is attributed to the O−CH_2−CO moiety (4.75 to 4.55 ppm). The two amido methylene groups in slow exchange are better resolved, at 3.08 and 2.85 ppm. These shifts are in agreement with the formation of a 1:1 complex in the cone conformation. Interestingly, in the cases of a large excess of the Cs^+ salt, additional peaks are observed at 4.19 ppm (singlet) and 4.08 ppm (doublet). They can be attributed to another complex, also in the cone conformation, with a 2:1 Cs^+/calixarene stoichiometry. This assignment is further supported by the fact that the intensities of this complex decrease compared to those of the major complex upon addition of **1**. The same behavior is observed in the aromatic part of the spectrum, with the integrals of the various peaks in excellent agreement with the attribution done above. In the *tert*-butyl part of the spectrum, the shifts are too small to be observed. The chemical shifts of the two complexes and of free **1** are given in Table 1. On the basis of ^{1}H NMR integrals, the equilibrium constant for the complex formation of the 2:1 complex is calculated to be 3 ± 2 M^{-1} at 238 K.

The temperature dependence of the ^{133}Cs NMR spectra of 30 mM CsI_3 and 15.2 mM **1** are shown in Figure 3. For $T >$ 255 K, the line width of the two signals increases with increasing temperatures, indicating a chemical exchange between solvated and complexed Cs^+. Above 300 K the two signals coalesce. For temperatures greater than 265 K, it was possible to determine the exchange rate between the two sites by a complete band shape analysis using the DNMR5 software.[20] The fits at 265, 283, and 300 K, using the DNMR5 software, are shown in Figure 4. At all temperatures, the agreement between the experimental and calculated spectra is excellent.

As mentioned above, the two signals coalesce above 300 K (Figure 3i). Figure 5 gives the ^{133}Cs NMR line widths (top) and chemical shifts (bottom) of 30 mM CsI_3 and variable amounts of **1** at 328 K. The chemical shift and line widths variations are characteristic of a system under moderately fast exchange. The contributions of the exchange to the observed line width ($\Delta\nu_{ex}$) is related to the pseudo-first-order rate

TABLE 1: ^{1}H NMR Chemical Shifts of Free and Complexed 1 at 238 K

region	1:1 complex	2:1 complex	free
aromatic	6.95	6.98	6.82
Ar−C**H**$_2$−Ar	4.52 (d), 3.01 (d), $J = 12$ Hz	4.08 (d), $J = 11$ Hz	5.05 (d), 2.99 (d) $J = 13$ Hz
O−C**H**$_2$−C=O	4.55	4.19	4.75
N−C**H**$_2$−CH$_3$	3.08 (q), 2.85(q), $J = 7$ Hz		3.05 (2q)
tert-butyl	0.9		0.87
N−CH$_2$−C**H**$_3$	0.88 (t), 0.82 (t), $J = 7$ Hz		0.85 (t), 0.78 (t), $J = 7$ Hz

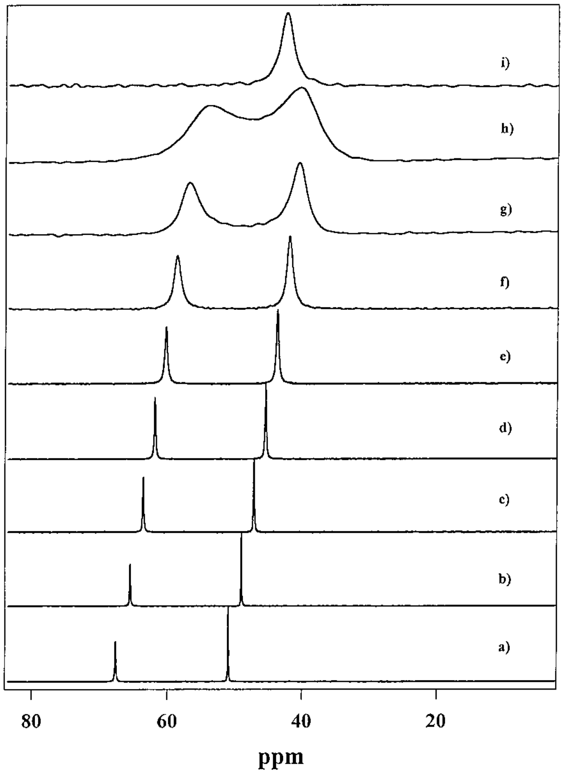


Figure 3. ^{133}Cs NMR spectra of 30 mM CsI$_3$ and 15.2 mM **1** at various temperatures: (a) 238; (b) 246; (c) 255; (d) 265; (e) 274; (f) 283; (g) 292; (h) 300; (i) 328 K.

constants k_A and k_B (Scheme 2a) through eq 1[11,21] and the observed chemical shifts are the weighted average of all contributions.[22,23]

$$\Delta\nu_{ex} = 4p_A p_B \pi(\nu_A - \nu_B)^2(k_A + k_B)^{-1} \qquad (1)$$

This exchange regime permits an easy test of the exchange mechanism since the rate constants are directly obtained from the measured line width. The plot of the line width as a function of the [**1**]/[Cs$^+$] ratio goes through a maximum for [**1**]/[Cs$^+$] $\approx$ 0.4, and the curve is not symmetrical with respect to the maximum (Figure 5, top). The chemical shifts are directly proportional to [**1**]/[Cs$^+$] for [**1**]/[Cs$^+$] $<$ 1 and constant for [**1**]/[Cs$^+$] $>$ 1, confirming that the complex formation is quantitative, i.e., $K > 10^4$ M^{-1} at 328 K (Figure 5, bottom). This is in good agreement with $K = 10^{3.6}$ M^{-1} in acetonitrile at 298 K, a result published by Arnaud-Neu et al.[8] It is reasonable to assume a larger equilibrium constant for the complex formation in the binary mixture of chloroform and acetonitrile than in acetonitrile due to the lower donicity of chloroform. These results allow discrimination between the two possible mechanisms for the decomplexation of the Cs$^+$−calixarene complex. Under conditions of a quantitative complex formation, if the associative interchange mechanism (Scheme 2c) was operative, the line width variations have to be symmetrical with respect to [**1**]/[Cs$^+$] = 0.5.[21,24] Obviously, this is not the case (Figure 5, top).

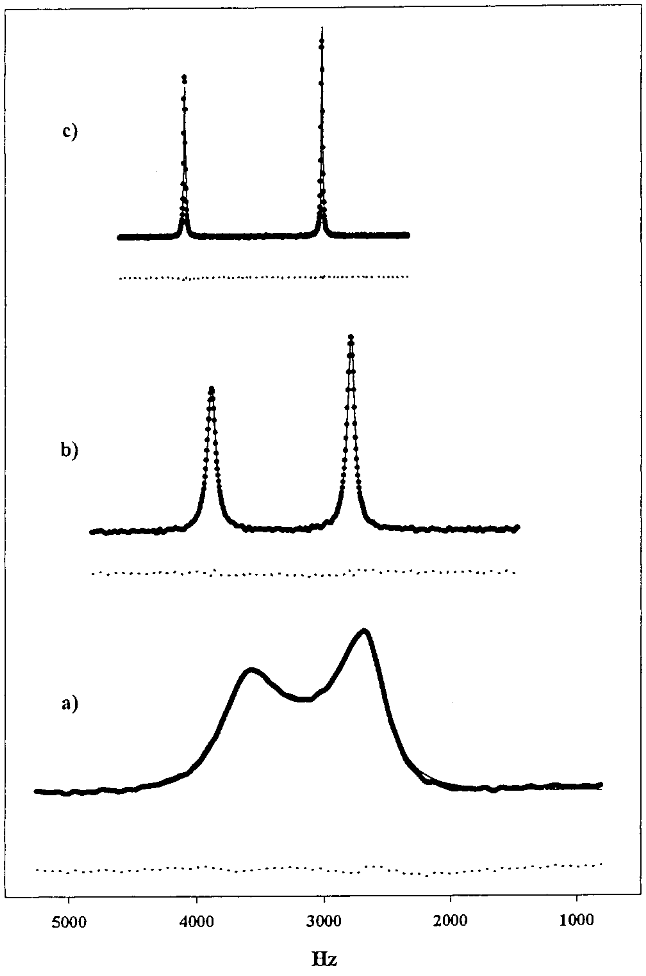


Figure 4. ^{133}Cs NMR spectra of 30 mM CsI$_3$ and 15.2 mM **1** at (a) 300 K ($k = 1708 \pm 6$s^{-1}), (b) 283 K ($k = 249 \pm 1$ s^{-1}), and (c) 265 K ($k = 43 \pm 1$ s^{-1}): (●) measured spectrum; (−) fit with DNMR5; (···) difference.

In the hypothesis of a dissociative mechanism, shown in Scheme 2b, the relationship between $k_A + k_B$ and k_{-1} is given by eq 2.[21,24,25] This equation can be applied since the complex formation is quantitative, as shown by the chemical shift variations (see above). The relationship between $k_A + k_B$ and (1 − [**1**]/[Cs$^+$]$_{tot}$ is shown in Figure 6. Indeed, the relationship is linear and extrapolates to the origin within the error limit. The slope gives k_{-1}, the rate constant characterizing the unimolecular dissociation process shown in Scheme 2b. At 328 K $k_{-1} = 1.8 \pm 0.2 \times 10^4$ s^{-1}.

$$k_A + k_B = k_{-1}\left(1 - \frac{[\mathbf{1}]}{[\mathrm{Cs}^+]_{tot}}\right)^{-1} \qquad (2)$$

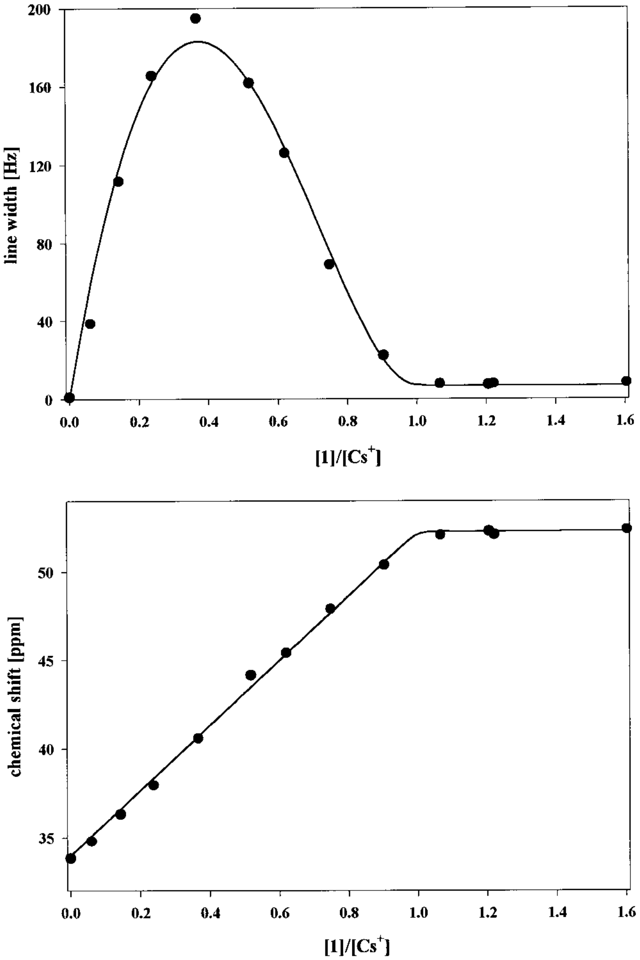


Figure 5. ^{133}Cs NMR line width (top) and ^{133}Cs NMR chemical shift (bottom) of 30 mM CsI_3 and various amounts of **1** at 328 K: (●) experimental line width or chemical shift. The solid line is the best fit calculated on the basis of eqs 1 and 2.

SCHEME 2

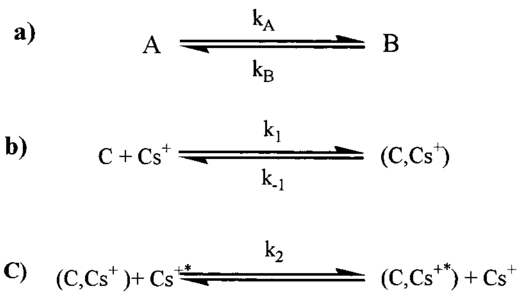


Figure 7 shows the rate constants for the dissociation of the (**1**, Cs$^+$) complex as a function of the temperature. The data points in the slow exchange regime from 265 to 300 K were obtained by a full band shape analysis and in the regime of a moderate fast exchange at 328 K from the line width as a function of the $[\mathbf{1}]_{tot}/[Cs^+]_{tot}$ ratio using eq 2. The agreement between the data obtained by the two methods in different kinetic regimes is excellent. An Eyring plot of this exchange process is characterized by $\Delta H^*= 67 \pm 2$ kJ/mol and $\Delta S^*= 40 \pm 3$ J/(mol K) (Figure 7).

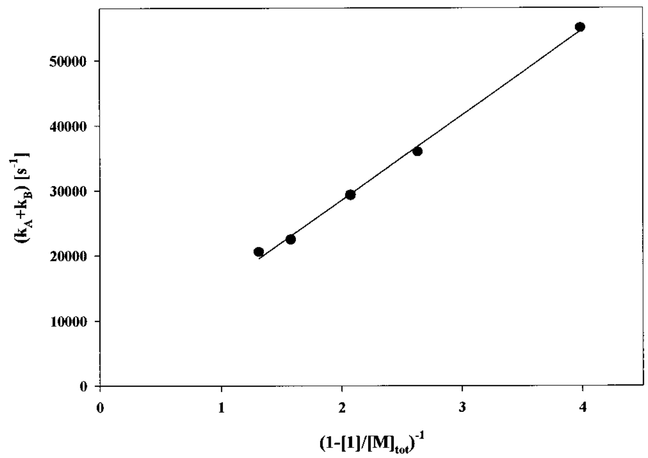


Figure 6. $(k_A + k_B)$ as a function of $1 - [\mathbf{1}]/[Cs^+]_{tot}$ at 328 K for 30 mM CsI_3 and various amounts of **1**. $k_{-1} = 1.8 \pm 0.2 \times 10^4$ s^{-1}.

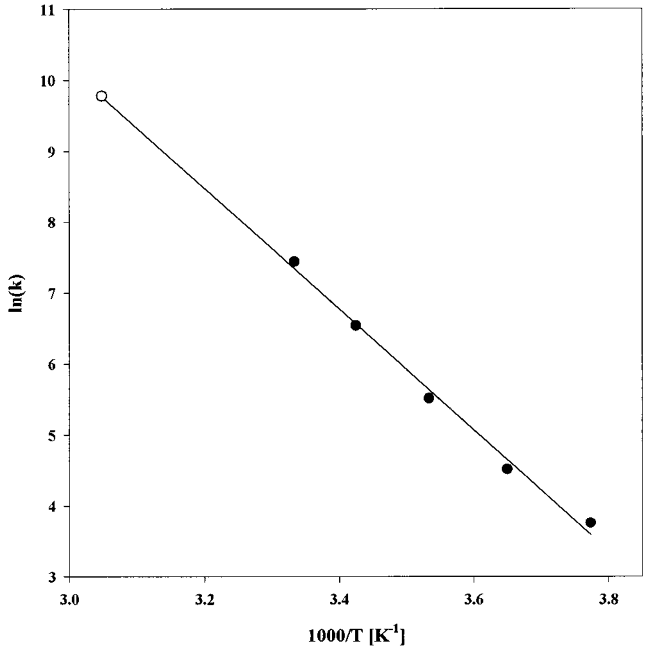
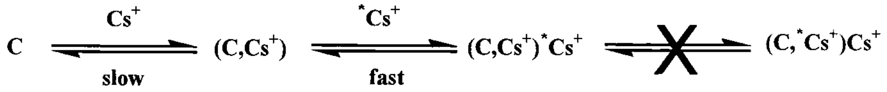


Figure 7. Eyring plot for 30 mM CsI_3 and 15.2 mM **1**: (●) determined by a complete band shape analysis; (○) determined at 328 K using eq 2. $\Delta H^* = 67 \pm 2$ kJ/mol and $\Delta S^* = 40 \pm 3$ J/(mol K).

The ^{133}Cs chemical shifts of the (**1**, Cs$^+$) complex is on the order of 50 ppm at 300 K. This is compatible with a capped structure of the calixarene lower rim substituents around the Cs$^+$. This shift is comparable to the shifts observed in the case of the sandwich complexes between 18-crown-6 (18C6) and Cs$^+$, $[Cs(18C6)_2]^+$ as reported by Popov et al.[26] In both cases it is expected that all solvent molecules are expelled from the Cs$^+$ cation coordination sphere. The ^{133}Cs shift of the (**1**,Cs$^+$) complex is in the same order of magnitude as the one observed for the 2:1 Cs$^+$/calix[6]arenehexaamide complex (63 ppm). In this case the Cs$^+$ coordination sphere is made of four phenolic and four carbonyl oxygens as shown by the X-ray structure.[27] It is reasonable to assume the same coordination sphere for the (**1**,Cs$^+$) complex of this study.

This study shows the formation of a 2:1 Cs$^+$/**1** complex in detectable amounts with the calixarene in a cone conformation, as it is the case for the 1:1 complex. One can propose the hypothesis that the second Cs$^+$ cation is linked through the amido groups, while the first Cs$^+$ cation is embedded into the cavity formed by the phenolic and carbonyl oxygens, with a structure similar to the K$^+$ complex, as shown by an X-ray study.[5] The coordination of the Cs$^+$ cation by the amido groups

SCHEME 3



leaves access to solvent molecules and rapid dissociation of the complex. On the contrary, the Cs$^+$ cation embedded in the inner oxygen cavity is not accessible to solvent molecules. It requires a much larger energy barrier to overcome to allow for the dissociation of the complex. This model is compatible with the experimental observation that a complexed Cs$^+$, presumably in the 2:1 complex is in fast exchange with solvated Cs$^+$, while the solvated and the 1:1 complexed Cs$^+$ are in slow exchange. Interestingly, this does not allow for an internal exchange of the two Cs$^+$ cations inside the 2:1 complex. This prohibits an associative exchange mechanism, where the 2:1 complex would be an intermediate in the exchange of the solvated and the 1:1 complexed cations, as it was shown to be the case for crown ethers in low donicity solvents.[11] This discussion is depicted in Schemes 2 and 3.

The 2:1 complex is in slow exchange with the 1:1 complex on the ^{1}H NMR time scale (Figure 2). However, a complexed cation in the 2:1 complex is in fast exchange with solvated Cs$^+$ on the ^{133}Cs NMR time scale (Figure 1). Since the equilibrium constant for the formation of the 2:1 complex is known from the ^{1}H NMR spectra, the lower and upper limit for the Cs$^+$ exchange between the solvated Cs$^+$ and the 2:1 complex can be estimated at 238 K. For the formation of the 2:1 complex, i.e., (Cs$^+$, **1**) + Cs$^+$ → ((Cs$^+$)$_2$, **1**), lower and upper limits of respectively 90 and 400 s^{-1} and 1000 and 10000 s^{-1} for the 2:1 complex formation and dissociation processes are estimated. This corresponds to free activation energies (ΔG^*) for the 2:1 complex formation of 47−49 kJ/mol. For the dissociation, ΔG^* is in the range of 40−45 kJ/mol. This can be compared to $\Delta G^*=$ 57kJ/mol for the dissociation of the 1:1 complex. These values are in good agreement with the proposed model for the structures of the 2:1 complex and with Scheme 3.

In conclusion, we have shown that the decomplexation of the 1:1 cesium−calix[4]arene acetamide complex (Cs$^+$, **1**) follows an unimolecular dissociation mechanism. The presence of small amounts of a 2:1 Cs$^+$/**1** complex does not lead to a competitive associative exchange mechanism.

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References and Notes

(1) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161−170.
(2) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989.
(3) Bohmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713−745.
(4) Takeshita, M.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1088−1097.
(5) Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D.; Calestani, G.; Ugozzoli, F. *J. Inclusion Phenom.* **1988**, *6*, 119−134.
(6) Arnaud-Neu, F.; Barrett, G.; Corry, D.; Cremin, S.; Ferguson, G.; Gallagher, J. F.; Harris, S. J.; McKervey, M. A.; Schwing-Weill, M. *J. Chem. Soc., Perkin Trans. 2* **1997**, 575−579.
(7) Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M. J.; Seward, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 8681−8691.
(8) Arnaud-Neu, F.; Schwing-Weill, M. J.; Ziat, K.; Cremin, S.; Harris, S. J.; McKervey, M. A. *New J. Chem.* **1991**, *15*, 33−37.
(9) Arnaud-Neu, F.; Barrett, G.; Cremin, S.; Deasy, M.; Ferguson, G.; Harris, S. J.; Lough, A. J.; Guerra, L.; McKervey, M. A.; Schwing-Weill, M. J.; Schwinte, P. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1119−1125.
(10) McKervey, M. A.; Schwing-Weill, M.; Arnaud-Neu, F. Cation Binding by Calixarenes. In *Comprehensive Supramolecular Chemistry*; Gokel, G., Ed.; Elsevier Science: Oxford, U.K., 1996; Vol. 1, Chapter 15, pp 537−603 and references therein.
(11) Detellier, C. Complexation Mechanisms. In *Comprehensive Supramolecular Chemistry;* Gokel, G., Ed.; Elsevier Science. Oxford, U.K., 1996; Vol. 1, Chapter 9, pp 357−375.
(12) Meier, U. C.; Detellier, C. *J. Phys. Chem. A* **1998**, *102*, 1888−1893.
(13) Israeli, Y.; Detellier, C. *J. Phys. Chem. B* **1997**, *101*, 1897−1901.
(14) Blixt, J.; Detellier, C. *J. Am. Chem. Soc.* **1994**, *116*, 11957−11960.
(15) Blixt, J.; Detellier, C. *J. Am. Chem. Soc.* **1995**, *117*, 8536−8540.
(16) Soi, A.; Bauer, W.; Mauser, H.; Moll, C.; Hampel, F.; Hirsch, A. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1471−1478.
(17) Groenen, L. C.; van Loon, J.-D.; Verboom, W.; Harkema, S.; Casnati, A.; Ungaro, R.; Pochini, A.; Ugozzoli, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 2385−2392.
(18) Bakker, W. I. I.; Haas, M.; Khoobeattie, C.; Ostaszewski, R.; Franken, S. M.; Denhertog, H. J.; Verboom, W.; Dezeeuw, D.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 123−133.
(19) Groenen, L. C.; Ruel, B. H. M.; Casnati, A.; Timmerman, P.; Verboom, W.; Harkema, S.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Tetrahedron Lett.* **1991**, *32*, 2675−2678.
(20) Stephenson, D. S.; Binsh, G. *QCPE 11, 365*; 1978.
(21) Delville, A.; Stöver, H. D. H.; Detellier, C. *J. Am. Chem. Soc.* **1987**, *109*, 7293−7301.
(22) Woessner, D. E. *J. Chem. Phys.* **1961**, *35*, 41−48.
(23) Meiboom, S.; Gill, D. J. *J. Chem. Phys.* **1957**, *27*, 1411−1412.
(24) Brière, K. M.; Detellier, C. *J. Phys. Chem.* **1987**, *91*, 6097−6099.
(25) Delville, A.; Stöver, H. D. H.; Detellier, C. *J. Am. Chem. Soc.* **1985**, *107*, 4172−4175.
(26) Mei, E.; Popov, A. I.; Dye, J. L. *J. Phys. Chem.* **1977**, *81*, 1677−1681.
(27) Meier, U. C.; Detellier, C. To be published.