Kinetics and Mechanism of the Sodium Cation Complexation by 5,11,17,23-Tetra-*p*-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene in Solution

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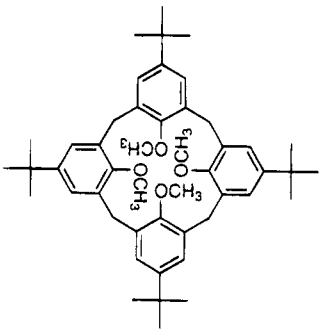
Abstract: The kinetics and the mechanism of complexation of the sodium cation by the title compound (**1**) were studied in a 1:1 (v/v) mixture of chloroform and acetonitrile using ^{23}Na and 2D-EXSY ^{1}H NMR. The results show the formation of a 1:1 complex where the calixarene is fixed in the cone conformation, $(Na,c)^+$, with an equilibrium constant of formation of $(9.3 \pm 0.7) \times 10^2$ at 320 K with $\Delta H = -22 \pm 2$ kJ mol^{-1} and $\Delta S = -7 \pm 5$ J mol^{-1} K^{-1}. The exchange of the sodium cation between the solvated and the complexed sites follows a dissociation/recombination mechanism, with a dissociation rate constant of 37.3 ± 0.4 s^{-1} at 300 K. The kinetic parameters for the dissociation are $\Delta H^{\ddagger} = 47 \pm 2$ kJ mol^{-1} and $\Delta S^{\ddagger} = -61 \pm 6$ J mol^{-1} K^{-1}. Calixarene **1** shows an intermediate behavior between crown ethers and cryptands for the complexation processes of the sodium cation in solution, dissociating with rates in the typical orders of magnitude found for crown ethers, but with rates of formation in the range of those typically found for cryptands.

Introduction

If, traditionally, the main object of chemistry has been the control and the rationalization of the association of atoms to form supraatomic structures, molecules, current problems include also the next level of association, supramolecular structures, controlled by non-covalent forces.[1−5] Synthetic chemists have designed and prepared a large number of specific compounds, receptacle molecules, that are well adapted for the recognition of other molecules or ions, forming with them host−guest complexes. A particular class of these compounds is currently receiving a lot of attention, calixarenes, cyclic oligomers of phenolic units linked through the ortho positions.[6−10] One of the main attractive properties of calixarenes is their versatility in hosting various types of guests: neutral, cationic, or anionic compounds.[11−16] However, while a large number of calixarene derivatives have been synthesized in the last decade, thermodynamic studies on their complexation properties are less frequent,[17−22] and the experimental kinetic and mechanistic studies are even rarer with, to the best of our knowledge, only studies dealing with very slow dissociation kinetics of calixspherands[23,24] and of a calix[4]arene ester.[25]

Depending upon the relative orientations of the para and phenolic sites, the calixarene tetramer can adopt four different conformations: cone (c), partial cone (pc), 1,2-alternate (alt,2), and 1,3-alternate (alt,3).[6] These different conformers all have distinct ^{1}H NMR spectra making their determination relatively simple.[6] In a previous paper,[26] the kinetics of interconversion of the four conformers of 5,11,17,23-tetra-*p*-*tert*-butyl-25,26,27,28−tetramethoxycalix[4]arene (**1**) were studied in two



solvent systems. It was shown that the interconversion proceeds

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(1) Lehn, J. M. *Science* **1993**, *260*, 1762−1763.
(2) Lehn, J. M. *Science* **1985**, *227*, 849−856.
(3) Bein, T., Ed. *Supramolecular Architecture*; ACS Symp. Ser. No. 499; American Chemical Society: Washington, DC, 1992.
(4) Vögtle, F. *Supramolecular Chemistry. An Introduction*; Wiley: Chichester, 1991.
(5) Gorman, C. B.; Biebuyck, H. A.; Whitesides, G. M. *Chem. Mater.* **1995**, *7*, 252−254.
(6) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161−170.
(7) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989.
(8) van Loon, J.-D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proced. Int.* **1992**, *24*, 437−462.
(9) Shinkai, S. *Tetrahedron* **1993**, *49*, 8933−8968.
(10) Atwood, J. L.; Orr, G. W.; Juneja, R. K.; Bott, S. G.; Hamada, F. *Pure Appl. Chem.* **1993**, *65*, 1471−1476.
(11) Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1988**, *110*, 610−611.
(12) Andreetti, G. D.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1773−1779.
(13) Bauer, L. J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1985**, *107*, 6063−6069.
(14) Guilbaud, P.; Varnek, A.; Wipff, G. *J. Am. Chem. Soc.* **1993**, *115*, 8298−8312.
(15) Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 1709−1710.
(16) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Domiano, P. *J. Chem. Soc., Perkin Trans. 2* **1985**, 197−201.
(17) De Namor, A. F. D. *Pure Appl. Chem.* **1993**, *65*, 193−202.
(18) 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.
(19) Arnaud-Neu, F.; Barrett, G.; Harris, S. J.; Owens, M.; McKervey, M. A.; Schwing-Weill, M. J.; Schwinte, P. *Inorg. Chem.* **1993**, *32*, 2644−2650.
(20) Schwing, M-J.; Arnaud, F.; Marques, E. *Pure Appl. Chem.* **1989**, *61*, 1597−1603.
(21) Arnaud-Neu, F.; Schwing-Weill, M. J.; Ziat, K.; Cremin, S.; Harris, S. J.; McKervey, M. A. *New J. Chem.* **1991**, *15*, 33−37.

0002-7863/95/1517-8536$09.00/0

through one-step processes involving the partial cone conformation. All the values of the activation enthalpies are close ($\Delta H^{\ddagger} \approx 60$ kJ mol^{-1}), while the entropies of activation vary largely, indicating that the conformational exchange is under entropy control. In a recent paper, Fisher *et al.*[27] calculated the potential energies of the transition states for the three one-step processes to be in a narrow range of 2 kcal mol^{-1}, confirming our previous finding.

In this paper, the kinetics and mechanisms of complexation/decomplexation of the sodium cation complex with the calix[4]arene (**1**) are studied in a mixture of acetonitrile and chloroform, a system for which the kinetic parameters of the conformational interconversions were previously determined.[26]

Experimental Section

Chemicals and Solutions. 5,11,17,23-Tetra-*p-tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene (**1**) was synthesized from the tetrahydroxy derivative (Aldrich, 99%), as described earlier[26] following the procedure, slightly modified, of Gutsche *et al.*[28]

Sodium tetraphenylborate (Aldrich, 99.5%) was used as the sodium source. It was dried overnight at 60 °C under vacuum prior to use.

All measurements were made in binary mixtures of chloroform and acetonitrile (1:1 by volume). Acetonitrile-d_3 (99.5%) was purchased from Aldrich and chloroform-*d* (99.8%) from Cambridge Isotope Laboratories. Both solvents were dried over 4 Å molecular sieves. The solution used for the ^{1}H 2-D EXSY measurements was 37 mM in **1** and 17 mM in Na^+; the compositions of the solutions used for the 1D kinetics are given in the respective figure captions.

NMR Measurements. The ^{1}H NMR spectra were recorded on a Bruker AMX-500 NMR spectrometer at 500.14 MHz. All the samples were contained in 5 mm outer diameter tubes, and the spectra were recorded in deuterium locked mode and, in the case of the 2D measurements, without spinning to reduce T_1 noise. The temperature calibration was done with a thermocouple inserted in a non-spinning tube containing chloroform or water. The temperature was estimated to be reliable at ±0.5 K.

The longitudinal relaxation times of the methoxy protons of **1** were 0.7 and 0.3 s for the methylenic protons. A standard NOESY pulse sequence was used for the 2D exchange (2D-EXSY) experiments.[29-31] The ^{1}H NMR parameters were chosen to obtain quasiquantitative spectra: relaxation delay time 2 s ($\geq 3\ T_1$), 90° pulse 6.1 μs, sweep width 3.8 kHz, acquisition time 0.136 s, 16 scans of 1024 points by 256 slices with a total measuring time per spectrum of 2.5−3 h. Spectra were recorded at 260, 270, and 280 K. At each temperature, a series of six 2D-EXSY spectra were recorded, with mixing times (τ_m) ranging from 20 to 300 ms.

The ^{23}Na NMR parameters were chosen to obtain quantitative spectra: relaxation delay time 0.15−0.3 s ($>5\ T_1$), 80° pulses (9 μs), sweep width 6−60 kHz, acquisition time 0.13−0.3 s, 250−13000 scans of 512−2048 real points with a total measuring time per spectrum of typically 10−30 min. The spectra were referenced against 0.1 M NaCl in 10% D_2O and obtained at 123.30 MHz.

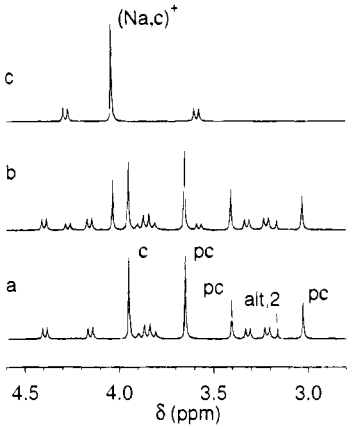
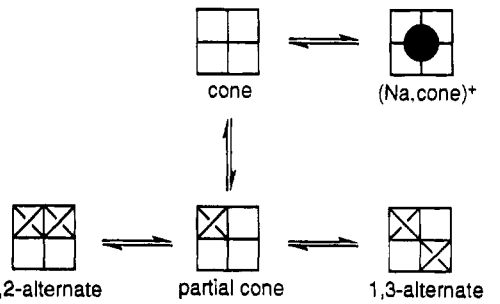


Figure 1. ^{1}H NMR (methoxy/methylenic region) of 30 mM **1** in the presence of $NaBPh_4$ at 260 K, showing the formation of a Na^+−**1** complex with the calixarene fixed in the cone conformation. [$NaBPh_4$] = 0 (a), 4.4 (b), and 40 mM (c).

Scheme 1



Data Treatment. The analysis of the 2-D EXSY data was performed as described earlier,[26] except that the methylene cross peaks were used for the (Na,c)$^+$−c exchange to avoid overlapping peaks (see Figure 2). The complete bandshape analysis (CBA) was carried out using the DNMR5 program.[32]

Results and Discussion

Figure 1a shows the ^{1}H NMR spectrum of a solution of **1** in a 1:1 mixture of acetonitrile-d_3 and chloroform-*d*. The methoxy peaks corresponding to three of the four conformers in slow exchange on the ^{1}H NMR time scale are indicated (cone (c); partial cone (pc); 1,2-alternate (alt,2)); the singlet corresponding to the methoxy peak of the 1,3-alternate (alt,3) has a low intensity and is obscured by the methylenic resonances of the pc conformer but its cross peaks can be clearly seen in the 2D measurements (vide infra) giving a chemical shift of 3.14 ppm. Upon addition of sodium tetraphenylborate, one singlet and a pair of doublets, respectively at 4.04, 3.58, and 4.28 ppm, superimpose on the spectrum of **1**, whose resonances do not shift (Figure 1b).[33] When a slight excess of $NaBPh_4$ is added to **1**, only these new signals can be observed (Figure 1c), which have to be attributed to the sodium complex of the cone conformer (Na,c)$^+$. A similar behavior could be observed for the aromatic and for the *tert*-butyl parts of the spectra. This titration demonstrates the strong affinity of the sodium cation for the cone conformer of **1**. No other sodium−conformer complex could be detected in the sensitivity limits of the ^{1}H NMR experiment. The set of the equilibria of conformer interconversion and of complexation can be described by Scheme 1. The (Na,c)$^+$ peaks remain narrow even at 320 K while all the other peaks are exchange broadened at room temperature (the alt,3 peak broadened already at 260 K) indicating rather slow cation exchange.

(22) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767−2777.
(23) Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.-E.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567−7575.
(24) Bakker, W. I. I.; Haas, M.; Khoobeattie, C.; Ostaszewski, R.; Franken, S. M.; Den Hertog, H. J.; Verboom, W.; Dezeeuw, D.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 123−133.
(25) Jin, T.; Ichikawa, K. *J. Phys. Chem.* **1991**, *95*, 2601−2606.
(26) Blixt, J.; Detellier, C. *J. Am. Chem. Soc.* **1994**, *116*, 11957−11960.
(27) Fisher, S.; Grootenhuis, P. D. J; Groenen, L. C.; van Hoorn, W. P.; van Veggel, F. C. J. M.; Reinhoudt, D. N.; Karplus, M. *J. Am. Chem. Soc.* **1995**, *117*, 1611−1620.
(28) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409−426.
(29) Perrin, C. L.; Dwyer, T. J. *Chem. Rev.* **1990**, *90*, 935−967.
(30) Jeener, J.; Meier, B. H.; Bachmann, P.; Ernst, R. R. *J. Chem. Phys.* **1979**, *71*, 4546−4553.
(31) Ernst R. R.; Bodenhausen G.; Wokaun A. *Principles of Nuclear Magnetic Resonance in One and Two Dimensions*; Clarendon Press: Oxford, 1987.
(32) Stephenson D. S.; Binsh G. *QCPE* **1978**, *11*, 365.
(33) Iwamoto, K.; Ikeda, A.; Araki, K.; Harada, T.; Shinkai, S. *Tetrahedron* **1993**, *49*, 9937−9946.

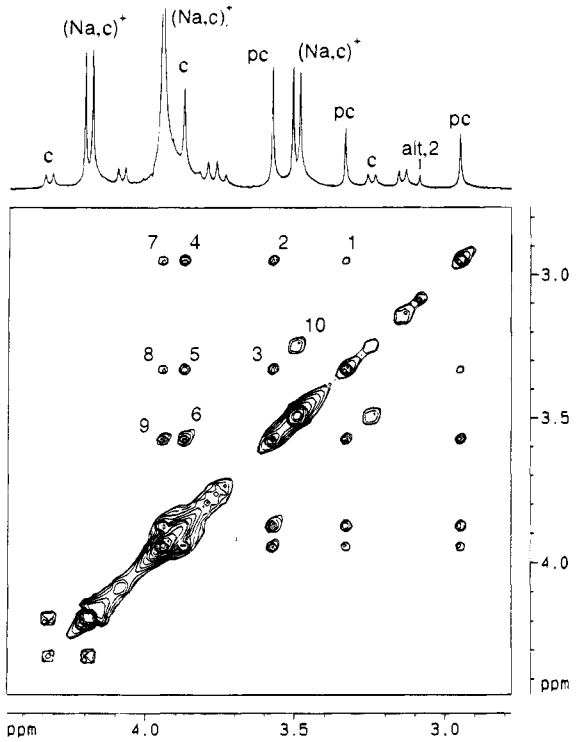


Figure 2. ^{1}H 2-D EXSY NMR spectrum of a solution 17 mM in $NaBPh_4$ and 37 mM in **1** at 260 K in a 1:1 mixture of acetonitrile-d_3 with chloroform-*d*. The mixing time was 300 ms. The cross peaks used in the analysis are numbered: partial cone−partial cone (1, 2, 3), partial cone−cone (4, 5, 6), partial cone−$(Na^+,cone)^+$ (7, 8, 9), and cone−$(Na^+,cone)^+$ (10). Peaks 1−9 are methoxy cross peaks while peak 10 is a methylene cross peak.

Table 1. A Comparison between the Apparent Rate Constants (in s^{-1}) of the Conformational Interconversion of **1** with and without $NaBPh_4$

	1			**1** + $NaBPh_4$		
exchange	260 K	270 K	280 K	260 K	270 K	280 K
pc-alt,2			0.20(2)			0.25(4)
c-alt,3	0.073(6)			0.045(3)		
pc-pc	0.33(2)	1.5(2)	4.1(8)	0.31(1)	1.9(1)	4.5(5)
pc-c	1.3(2)	3.7(4)	8.7(9)	1.2(2)	3.7(5)	10(2)
pc-alt,3	1.6(4)			1.4(4)		
c-alt,2			0.19(3)			0.20(3)
$(Na,c)^+$-pc				0.09(2)	0.37(1)	0.76(3)
$(Na,c)^+$-c				0.60(2)	1.43(3)	2.5(2)
$(Na,c)^+$-alt,2						0.03(1)

An example of a 2D EXSY ^{1}H NMR spectrum at 260 K of a mixture of complexed and uncomplexed **1** is shown on Figure 2. Given the number of peaks and of cross peaks, and, consequently, the overlaps between them, given also the low intensity of the peaks of the minor species (alt,2 and alt,3), the useful temperature range for studying the kinetics of a given exchange is limited. However, from the cross peak intensities at various mixing times, the rate constants for the following equilibria could be determined at three temperatures: pc ⇌ pc; pc ⇌ c; $(Na,c)^+$ ⇌ c and $(Na,c)^+$ ⇌ pc. Moreover, the rate constants could be determined at one temperature for the following equilibria: c ⇌ alt,3; pc ⇌ alt,3; c ⇌ alt,2; pc ⇌ alt,2; and $(Na,c)^+$ ⇌ alt,2. The rate constants involving the sodium cation in the above equilibria are apparent rate constants, since they can be the result of associative mechanisms and/or multi-step processes. This point is analyzed and discussed below. The results are summarized in Table 1, together with the results of our previous study on the free ligand. In the limits of the experimental errors, the interconversion rate constants for uncomplexed **1** are identical with our previous results. The

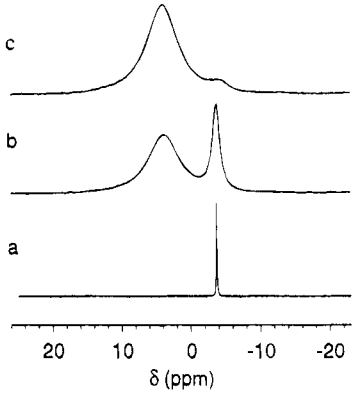


Figure 3. ^{23}Na NMR spectra of 30 mM $NaBPh_4$ in the presence of various amounts of **1** at 320 K: 0 (a), 27 (b), and 76 mM (c).

apparent exchange rates for $(Na,c)^+$ ⇌ pc and for $(Na,c)^+$ ⇌ alt,2 are both slower than the apparent exchange rate for $(Na,c)^+$ ⇌ c. These observations corroborate the validity of Scheme 1. For the reasons mentioned above, these data could be obtained only at three temperatures, in a 20 K temperature range. The activation parameters which, in those conditions, could be calculated only approximately, with large limits of errors, are in reasonable agreement with those previously determined on the uncomplexed ligand.[26]

Figure 3 shows examples of ^{23}Na NMR spectra of $NaBPh_4$ titrated with **1**, at 320 K. Upon addition of the calixarene, the peak at −3.7 ppm, corresponding to the uncomplexed sodium cation, broadens, most plausibly because of chemical exchange. Concurrently, a broad signal attributed to the complexed sodium cation appears at 3.9 ppm. On the basis of the ^{1}H NMR results (Figure 1), one expects the titration to be apparently quantitative, and, consequently, to observe only the signal of the complexed species for ratios ϱ $(=[\mathbf{1}]_{tot}/[NaBPh_4]_{tot})$ larger than 1. However, a residual signal remains near −4 ppm for ϱ values larger than 1. These ^{23}Na NMR spectra can provide direct information on the kinetics of the sodium complexation, but before one can analyse the line shapes one has to resolve the apparent contradiction with the ^{1}H NMR data. In order to test for the possibility of formation of complexes of stoichiometries other than 1:1, a total concentration study was done, for a ratio value ϱ = 0.63, and for $[NaBPh_4]_{tot}$ ranging from 1.9 to 31 mM (supporting information). The percentage of the complexed species is given in Figure 4, as a function of $[NaBPh_4]_{tot}$. It is expressed as $\varrho' = [(Na,c)^+]/[Na^+]_{tot}$, for which $\varrho' = \varrho$ if the complexation is quantitative. These results could be interpreted on the basis of the formation of a 1:1 complex, following eq 1

$$Na^+ + \mathbf{1} \rightleftarrows (Na, c)^+ \qquad (1)$$

Equation 2 was derived on the basis of the above equilibrium,

$$K = \frac{\varrho'}{(1-\varrho')(\varrho-\varrho')[NaBPh_4]_{tot}} \qquad (2)$$

and an equilibrium constant of formation of the complex, K, could be calculated to be $(9.3 \pm 0.7) \times 10^2$ at 320 K, as shown in Figure 4. The same approach could be applied at several temperatures, showing an increase of K in decreasing the temperature. For temperatures below 280 K, the formation of the complex could be considered quantitative ($K \geq 10^4$).[34] This explains the apparent discrepancy with the ^{1}H NMR results which had to be taken at and below 280 K. The thermodynamic parameters of the complexation are $\Delta H = -22(2)$ kJ mol^{-1} and $\Delta S = -7(5)$ J mol^{-1} K^{-1} (supporting information).

(34) Stöver, H. D. H.; Delville, A.; Detellier, C. *J. Am. Chem. Soc.* **1985**, *107*, 4167−4171.

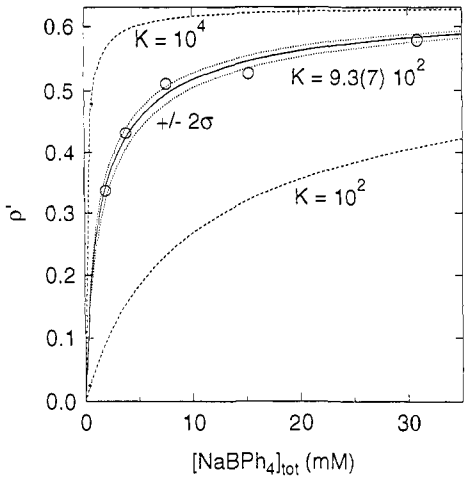


Figure 4. Nonlinear regression analysis of $\varrho' = [(Na,c)^+]/[NaBPh_4]_{tot}$ as a function of $[NaBPh_4]_{tot}$ for the calculation of the equilibrium constant of formation of the complex. The circles are experimental points, the solid line represents the best fit to the model, and the dashed lines are calculated for various values of K (10^4, 10^2, and the calculated $K \pm 2\sigma$).

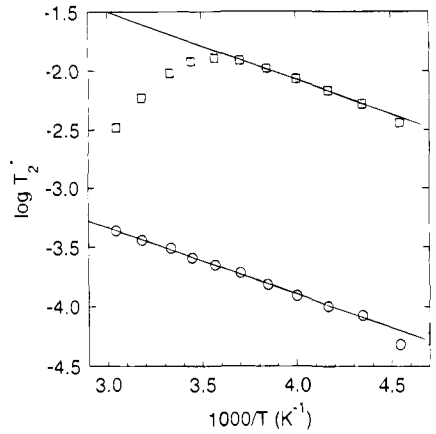


Figure 5. Log T_2^* (^{23}Na) of a 50 mM $NaBPh_4$ and 30 mM **1** solution as a function of T^{-1}: (□) uncomplexed $^{23}Na^+$; (○) $(^{23}Na,c)^+$.

Figure 5 shows the apparent transverse relaxation time, $T_2^* = 1/(\pi\Delta\nu_{1/2})$, where $\Delta\nu_{1/2}$ is the line width at half-height of the ^{23}Na signal, for the free and complexed sodium cations of a 50 mM sodium and 30 mM calixarene solution as a function of temperature. At lower temperatures, where the exchange broadening is negligible, the measured line width originates only from quadrupolar and inhomogeneity contributions to the relaxation.[35-38] In the case of the uncomplexed sodium, the contribution to the exchange can be obtained from an extrapolation to the higher temperatures where there is a measurable exchange broadening (Figure 5). In the case of the broad line width of the complexed sodium cation, the exchange contribution remains in the error limits of the measurement at all temperatures. Since, from the approach described above and shown in Figure 5 the line width in the absence of exchange can be obtained, a full line shape analysis could be performed on all the ^{23}Na spectra, using the DNMR5 software.[32] An observed rate constant for the complexation, k_A, is obtained from the full line shape analysis, with two examples shown in Figure 6. The exchange studied by ^{23}Na NMR is given in eq 3, where k_A and k_B are pseudo-first-order rate constants for the forward and reverse reactions, respectively. M^+ represents the solvated sodium, and $(M,C)^+$ the complexed sodium. The pseudo-first-order rate constant k_A can only be interpreted in a meaningful way if the corresponding mechanism of exchange is known. Two limiting mechanistic hypotheses, of a dissociative exchange (association/recombination mechanism) shown in eq 4 and of

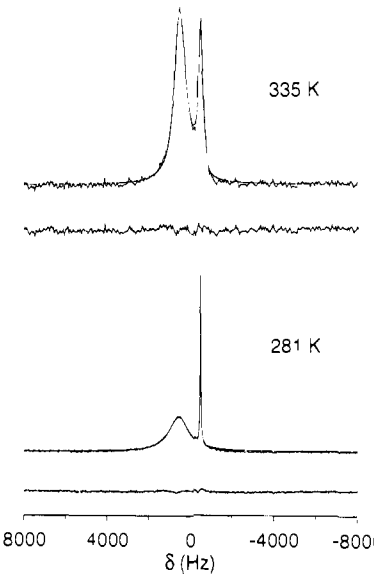


Figure 6. ^{23}Na NMR spectra of $[\mathbf{1}]_{tot} = 28.3$ mM and $[NaBPh_4]_{tot} = 32.3$ mM at 281 and 335 K showing the measured spectrum, the fit from DNMR5, and the difference.

an associative exchange shown in eq 5, will be considered.[35-38]

$$M^+ \underset{k_B}{\overset{k_A}{\rightleftharpoons}} (M,C)^+ \qquad \begin{matrix} A & & B \end{matrix} \tag{3}$$

$$M^+ + C \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (M,C)^+ \tag{4}$$

$$(M + C)^+ + M^{*+} \underset{k_2}{\overset{k_2}{\rightleftharpoons}} (M^*,C)^+ + M^+ \tag{5}$$

k_A is related to k_{-1} and to k_2 by eq 6.[36,39]

$$k_A = k_{-1}\,[(M,C)^+]/[M^+] + k_2\,[(M,C)^+] \tag{6}$$

Since the equilibrium constant of complexation is not very large, the usual formalism, consisting of linearizing eq 6,[36,39] cannot be applied here. The combined analysis of the data obtained at 320 K, from a variation of the concentration of calixarene with a constant sodium concentration (such as in Figure 3) and from a variation of the total concentrations for a constant ratio (supporting information), is shown on Figure 7. $k_A/[(Na,c)^+]$ is given as a function of $[Na^+]^{-1}$. The result is a straight line, extrapolating to zero, in full agreement with eq 6, showing the absence of a significant associative mechanism component to the exchange. This conclusion was valid at all temperatures used in this study. The rates k_{-1} were then calculated from eq 6, with k_2 equal to zero, for various concentrations and temperatures. The result is given as Figure 8 in the form of an Eyring plot, from which the activation parameters for the dissociation of the complex $(Na,c)^+$ are obtained: $\Delta H^\ddagger = 47(2)$ kJ mol^{-1} and $\Delta S^\ddagger = -61(6)$ J mol^{-1} K^{-1}. The rate constants for the exchange could also be calculated from 2D EXSY on the ^1H NMR spectra at three temperatures. The results agree with the ^{23}Na NMR results, in the limits of the experimental errors. For example, at 270 K,

(35) Delville, A.; Stöver, H. D. H.; Detellier, C. *J. Am. Chem. Soc.* **1987**, *109*, 7293-7301.
(36) Brière, K. M.; Detellier, C. *New J. Chem.* **1989**, *13*, 145-150.
(37) Graves, H. P.; Detellier, C. *J. Am. Chem. Soc.* **1988**, *110*, 6019-6024.
(38) Brière, K. M.; Detellier, C. *J. Phys. Chem.* **1992**, *96*, 2185-2189.
(39) Detellier, C. In *Practical Spectroscopy*; Popov A. I., Hallenga K., Eds.; Marcel Dekker: New York, 1990; Ser. Vol. 11, pp 521-566.

Table 2. Comparison of the Na^+−Ligand Dissociation Kinetics of Various Na^+−Ligand Systems As Determined by ^{23}Na NMR[a]

ligand	solvent	$\Delta H^{\ddagger}$, kJ mol^{-1}	$\Delta S^{\ddagger}$, J mol^{-1} K^{-1}	$\Delta G^{\ddagger}_{300K}$ kJ mol^{-1}	ref
18C6	AN[b]	32(2)	−65(8)	52	37
DB18C6	AN	40(2)	−44(8)	53	35
C211	DMSO	69.5(0.4)	17.4(1.2)	64	43
monensin	MeOH	43.0	−66	63	44
BCAD[c]	$CDCl_3$/MeOH (2:1 v:v)	56(7)	−39(21)	68	25
1	AN/$CDCl_3$ (1:1 v:v)	47(2)	-61(6)	68	this work

[a] All systems follow the association/dissociation mechanism (Equation 4). [b] Acetonitrile. [c] As **1**, but $OCH_2CO_2C_2H_5$ is the substituent at the phenolic positions instead of OCH_3.

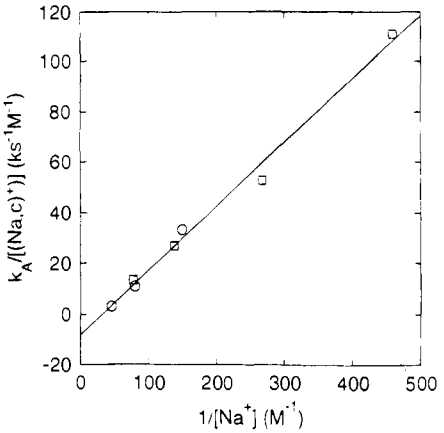


Figure 7. $k_A/[(Na,c)^+]$ as a function of $[Na^+]^{-1}$ (see eq 7), at 328 K. The squares were measured at a constant $R = 0.63$ with $[NaBPh_4]_{tot}$ between 1.92 and 15.3 mM while the circles were measured at $[NaBPh_4]_{tot} = 30.9$ mM with R ranging from 0.3 to 0.96.

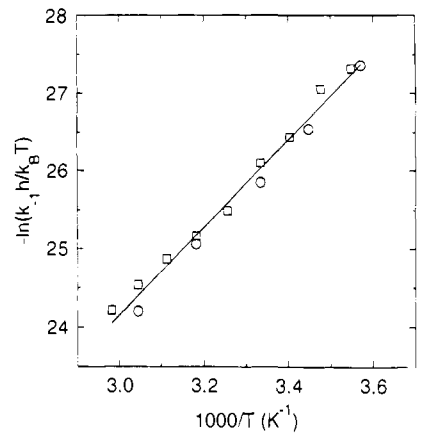


Figure 8. Eyring plot for two different series of measurements: (○) $[\mathbf{1}]_{tot} = 28.3$ mM and $[NaBPh_4]_{tot} = 32.3$ mM and (□) $[\mathbf{1}]_{tot} = 30$ mM and $[NaBPh_4]_{tot} = 50$ mM.

$\Delta G^{\ddagger}$ determined from ^1H 2D EXSY is 65 kJ mol^{-1}, to be compared with a $\Delta G^{\ddagger}$ of 63.5 kJ mol^{-1} from the ^{23}Na NMR study. Given the possibility of systematic errors, both on the ^{23}Na results, since the ^{23}Na lines for the complex are very broad, and on the EXSY results, since there are overlaps between the cross peaks, the agreement between the two independent measurements is quite gratifying.

Table 2 gives for comparison the activation parameters for the dissociation of a few Na^+−ligand systems, crown ethers, cryptand, antibiotic ionophore, and the calixarene of this study. In all cases, the exchange mechanism was shown to be dissociation/recombination (eq 4). The rate constant for the dissociation is in the order of magnitude of the cryptand or monensin cases, slower than crown ethers. However, the dissociation is characterized by activation parameters similar to the "open" systems, like crown ethers and monensin, with an enthalpy of activation primarily due to the rupture of the Na^+−O bonds, with a concurrent resolvation of the cation.[35] This is in contrast to the "closed" system, such as the C2111 cryptand, characterized by a much larger enthalpy of dissociation, and a positive entropy of activation. The rate constant for the formation of the complex $(Na,c)^+$ (k_1) can be calculated to be 5×10^5 mol^{-1} s^{-1} at 300 K. In strong contrast to the case of crown ethers, for which the formation of the complex is generally close to the diffusion-controlled limit,[40] in the case of calixarene **1**, the rate of formation is much slower, comparable to rate constants characteristic of cryptands[41] or of spherands.[23] Similarly to cryptands, the complexation of the sodium cation, the entrance of the cation in the ligation cage, necessitates conformational reorganization of the chelating ring of the calixarene while in the case of crown ethers, and particularly of 18C6, the conformation of the solvated crown is the most suitable one for the capture of the cation, showing a preorganization for complexation.[42] This is also in agreement with recent calculations showing the lack of preorganization for the complexation of cations in water in the case of *p-tert*-butylcalix-[4]arenetetraamide.[14]

In summary, calixarene **1** has the interesting characteristic of showing an intermediate behavior between crown ethers and cryptands for the complexation processes of the sodium cation in solution, dissociating like a crown ether, but forming the complex like a cryptand. This results in a thermodynamic equilibrium constant of formation of $(Na,c)^+$ which is several orders of magnitude smaller than in the cases of both cryptands and crown ethers.

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Supporting Information Available: Two figures showing ^{23}Na NMR spectra for various total concentrations of $NaBPh_4$ and ln$K$ as a function of T^{-1}, for the equilibrium given in eq 1 (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(40) Lockhart, J. C. *J. Chem. Soc., Faraday Trans. 1* **1986**, *82*, 1161−1167.
(41) Cox, B. G.; Garcia-Rosas, J.; Schneider, H. *J. Am. Chem. Soc.* **1982**, *104*, 2434−2437.
(42) Troxler, L.; Wipff, G. *J. Am. Chem. Soc.* **1994**, *116*, 1468−1480.
(43) Lincoln, S. F.; Brereton, I. M.; Spotswood, T. M. *J. Chem. Soc., Faraday Trans. 1* **1985**, *81*, 1623−1630.
(44) Degani, H. *Biophys. Chem.* **1977**, *6*, 345−349.