¹H NMR Relaxation Time Studies of Molecular Motions in a 1,3-Alternate-Shaped Calix[4]arene Ensemble

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Abstract: The systematic studies through ¹H NMR longitudinal relaxation times (T_1) of an ionophoric 1,3-alternate-shaped calix[4]arene ester **1** were reported. The T_1 values were measured under proton-noise-decoupling conditions by the inversion-recovery technique. The terminal groups in an ethoxycarbonylmethoxybenzene unit in **1** move vigorously whereas the motion of the central ArCH₂Ar moiety is rather suppressed. K⁺ ion plays an important role as a template ion specifically to freeze the fluctuational motion of these terminal groups. The ethoxycarbonylmethoxybenzene unit features a 'seesaw motion' around the ArCH₂Ar moiety as central support. It is clear that the molecular motion of the calixarene skeleton is efficiently frozen through complexation with metal cations.

Key words: molecular machine, conformation, ¹H NMR, longitudinal relaxation times, T_1 , ionophore, calix[4]arene, supramolecule, metal cation, fluctuation

1 Introduction

Recently, although controlled molecular motions have been known (1-3), existing in a number of supramolecules ranging from purely organic structures to inorganic complexes, the field of "molecular machines and motors in supramolecular chemistry" is just emerging (4-6). Calixarene derivatives have been receiving increasing attention in the field of supramolecular chemistry (7). It has been shown that the 1,3-alternate-shaped calix[4]arene possessing two ester groups **1** exhibits high selectivity towards K⁺ (8). This is attributable to the internal size of the ionophoric cavity made up by the two OCH₂C=O groups, which is comparable with the ion size of K⁺ (9). In order to understand the selectivity for the metals, it is of great significance to access the conformational properties as for the controlled molecular motions characteristic of

1,3-alternate-shaped calix[4]arene. Among NMR spectroscopic methods, it is known that NMR relaxation-time studies could provide further insights into the conformational properties and binding dynamics (9-11). Herein, we describe systematic studies through ¹H NMR longitudinal relaxation times (T_1) of an ionophoric 1,3-alternate-shaped calix[4]arene ester **1**. The main purpose of this work is to clarify how the molecular segments composing the calixarene cavity change upon inclusion of K⁺.

2 Experimental

Materials: 2-(Ethoxycarbonylmethoxy)xylene **2** was used as a reference compound. The synthesis of 1,3-alternate-shaped 25,27-dipropoxy-26,28-bis(ethoxycarbonylmethoxy)-calix[4]arene **1** was described previously (12).

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Fig. 1 Substrates **1**, **1-K⁺ Ensemble**, and **2**.

T₁ Measurements. NMR samples consisted of 0.5 ml of solution in 5-mm o.d. tubes which were sealed under vacuum after degassing by 5 freeze-pump-thaw cycles. All glassware was washed with 0.01 M ethylenediaminetetraacetic acid (EDTA) solution to remove paramagnetic impurities. ¹H NMR spectra were recorded on a Varian Gemini-300 spectrometer operated at 300 MHz at room temperature (25°C) in the Fourier transform mode. Perdeuteriotetrahydrofuran (THF-d₈) was used as a solvent and tetramethylsilane (TMS) was used as an internal reference. Longitudinal relaxation times (T₁) values were measured under proton-noise-decoupling conditions by the inversion-recovery technique (13). A waiting time (T_w) of at least five times the longest relaxation time was used in each case. Three kinds of pulse sequence were used to determine T₁ for different carbon atoms. All spectra were recorded at 25°C, and each run took 8–14 h. T₁ values were determined by a linear least-squares, two-parameter fit of the experimental data directly performed by the spectrometer computer. At least ten points were included for each T₁ calculation (correlation coefficient $\gamma > 0.98$).

Fig. 2 Numbering Systems for Protons of the Substrates.

3 Results and Discussion

The chemical shifts and relaxation times (T₁) in species **1** and **2** are summarized in **Table 1** and **2**, respectively. The protons are numbered as shown in **Fig. 2**. As shown in **Table 1**, the calixarene derivative **1** shows a doublet for the ArCH₂Ar protons and this split pattern was not affected by the measurement temperature. This means that **1** adopts a 1,3-alternate conformation (7) and the oxygen-through-the annulus rotation is inhibited by the CH₂CO₂Et groups (14).

The δ -values for protons a, b and c of **1** are comparable to those for **2**. In contrast, the δ -values for aromatic protons e and f of **1** shift to higher magnetic field compared with those for **2**. As mentioned above, **1** adopts a 1,3-alternate conformation and is conformationally immobile. Thus, the CH₂CO₂Et moiety in **1** can not be affected by the ring current of the benzene moiety whereas proton e and f is always affected by the ring current. This is why the δ -values for proton e and f

Table 1 Chemical Shifts (δ) of Protons in **1**, **1-K⁺ Ensemble**, and **2**.^{a)}

Substrate	Proton δ / ppm						
	a	b	c	d _(exo)	d _(endo)	e	f
1	1.29	4.15	4.30	3.80	3.90	6.75	6.40
1-K⁺	1.40	3.92	3.98	3.84	3.86	7.38	7.05
2	1.26	4.18	4.33	2.53 ^{b)}		7.00	6.72

a) 25°C, THF-d₈, internal standard TMS, [**1**] = 0.10 mol dm⁻³, [Potassium Picrate] = 0.17 mol dm⁻³.

Under these conditions, 1,3-alternate-shaped calix[4]arene **1** totally exists as its K⁺ ensemble (**8**).

b) 2,6-Dimethyl groups of a reference compound **2**.

shift to higher magnetic field.

It is reported that **1** can bind K^+ through interactions with two oxygens in the OCH_2CO moiety and the association constant (K) in THF is $\log K = 4.4$ (8). Hence, we consider that **1** exists totally as a K^+ ensemble under the measurement conditions. The large association constant observed for **1** is rationalized as for the fitness between the ionophoric cavity formed by two ester groups and the ionic size of K^+ . In addition, the structure pre-organized to the 1,3-alternate conformation is also important. As for **1**, the δ -values in the presence of K^+ generally shift to lower magnetic field, which effect is attributed to the electron-withdrawing nature of K^+ . There are one exception, that is, the OCH_2CO protons shift to higher magnetic field by 0.32 ppm. As illustrated in **Fig. 3**, the OCH_2CO protons are forced to be located on the benzene ring when the two oxygens coordinate to K^+ . Thus, these protons undergo a ring current effect which causes the upfield shift. Interestingly, the difference in δ -values between H_{exo} and H_{endo} in **1** becomes smaller (0.10 ppm in the absence of K^+ ; 0.02 ppm in the presence of K^+). This means briefly that H_{exo} is less shielded whereas H_{endo} is more shielded. In calix[4]arenes with C_{2v} symmetry two confronting phenol units are more or less coplanar while the other two confronting phenol units are parallel to each other. This 'flattening' effect in the absence of K^+ causes the fluctuational motion of the $ArCH_2Ar$ linkage so that H_{endo} is placed in the plane of the aromatic rings while H_{exo} is placed above the aromatic rings. It is known that $\Delta\delta$ between H_{exo} and H_{endo} in calix[4]arene serves as a measure of the 'flattening': $\Delta\delta$ is generally ~ 0.2 ppm for a system in the 1,3-alternate conformation and in the 'flattening' conformation, $\Delta\delta$ is significantly decreased (9). The decrease of $\Delta\delta$ -values upon inclusion of K^+ implies the occurrence of 'flattening' of one face-to-face phenol unit which interacts with K^+ . On the other hand, the 1H NMR spectrum for **2** was scarcely changed by the addition of excess K^+ .

The T_1 -values for hydrogen nuclei were summarized in **Table 2**, in which T_1 -values decrease in the order **2** > **1** > **1-K⁺ Ensemble**. This implies that the T_1 -value for 1H relaxation is primarily controlled by the molecular weight. The T_1 -values for most protons decrease when **1** formed the ensemble with K^+ , indicating that K^+ acts as a template ion to suppress ring fluctuational motion. Among six different protons in **1-K⁺ Ensemble**, the T_1 decrease was observed for methyl

Fig. 3 Co-ordination of K^+ with Ester Moiety.

protons (proton a, $\Delta T_1 = 2.05$ s for H^a). This change means that the molecular motion of the ester groups, which is possible in the absence of K^+ , is considerably frozen by complexation with K^+ . The T_1 decrease for the aromatic protons (proton e and f) is also noteworthy (proton e: $\Delta T_1 = 0.38$ s for H^e ; proton f: $\Delta T_1 = 0.40$ s for H^f). This suggests that the freezing effect occurring at the ester moieties through interaction with K^+ is transmitted to the aromatic rings. On the other hand, the T_1 -values for the $ArCH_2Ar$ protons (proton d), which serve as connectors of the aromatic rings, change to a smaller extent.

The foregoing results demonstrate that, in 1,3-alternate-shaped calix[4]arene **1**, terminal groups in an ethoxycarbonylmethoxybenzene unit move vigorously whereas the motion of the central $ArCH_2Ar$ moiety is rather suppressed. This indicates that the molecular motion of the $EtOCOCH_2O$ - moiety is also suppressed through interactions with K^+ . K^+ ion plays an important role as a template ion specifically to freeze the fluctuational motion of these terminal groups. Eventually, the ethoxycarbonylmethoxybenzene unit features a 'seesaw motion' around the $ArCH_2Ar$ moiety as central support.

In conclusion, the present paper shows the systematic

Table 2 Relaxation Times (T_1) of Protons in **1**, **1-K⁺ Ensemble**, and **2**.^{a)}

Substrate	Proton T_1 / s					
	H^a	H^b	H^c	H^d	H^e	H^f
1	2.53	1.03	0.40	0.15 ^{b)}	0.70	0.80
1-K⁺	0.48	— ^{c)}	0.20	0.11 ^{b)}	0.32	0.40
2	5.64	5.23	4.13	3.72	5.00	5.07

a) Measurement conditions are shown in footnote a in **Table 1**.

b) The T_1 for $H_{(endo)}$; the peaks for $H_{(exo)}$ overlapped with those for H^b .

c) The T_1 value could not be obtained as for the overlap of signals from H^b and $H_{(exo)}$.^{d)}

study on ^1H NMR relaxation times of a 1,3-alternate-shaped calix[4]arene. It is clear that the molecular motion of the calixarene skeleton is efficiently frozen through complexation with metal cations. Further examination on the conformational motions in 1,3-alternate-shaped calix[4]arene possessing two ester groups as molecular machine is now under investigation.

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