

Conformational Characteristics of Free and Cesium Complexed *p*-H-Calix[6]arene Alkyl Ester Derivatives

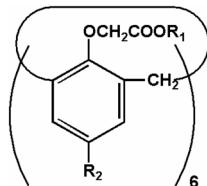
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Calixarenes have received much interest because of their versatile recognition properties toward a variety of ionic and organic guests including biomolecules, which result from the ease of functionalization at the lower rim or upper rim.¹⁻⁴ The conformational characteristics of calixarenes are also known to have strong effects on their complex formation behaviors.¹ Among the calixarene series, the appropriately functionalized calix[6]arenes are known to have a preference for cesium ion, which is one of the major components of nuclear wastes.^{1,5} Nevertheless, there are only a few reports on the complexation of cesium ion by calix[6]arenes and on the conformational behaviors of the complex and/or the free host itself.^{6,7} In this paper, we report the unusual conformational characteristics of *p*-H-calix[6]arene derivatives and their cesium ion complexes revealed by using ¹H, ¹³C and ¹³³Cs NMR spectroscopy at various temperatures.



- | | |
|--|----------------------|
| 1 : R ₁ = CH ₃ | R ₂ = tBu |
| 2 : R ₁ = CH ₂ CH ₃ | R ₂ = tBu |
| 3 : R ₁ = CH ₃ | R ₂ = H |
| 4 : R ₁ = CH ₂ CH ₃ | R ₂ = H |

bridged methylenes have been generally used to elucidate calixarene conformations in solution.⁸⁻¹⁰ According to their symmetries, both 1,2-alternate and 1,2,4-alternate conformers may have four different positions (ratio of 1:2:2:1) of the bridged methylene carbons. For the free host 4, as shown

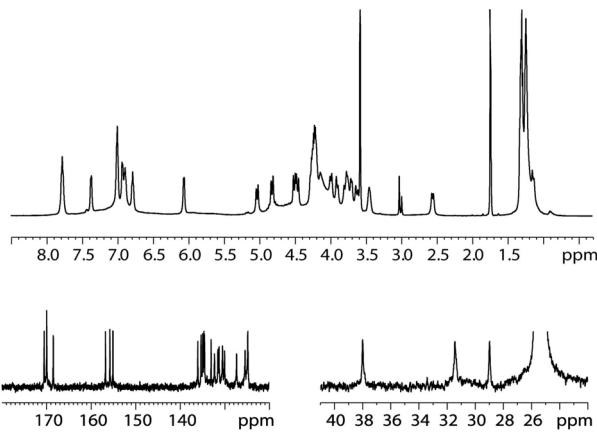


Figure 1. ¹H (top) and ¹³C NMR (bottom) spectra of free host 4 at 198 K in THF-d₈ and acetone-d₆ (5:1, v/v).

Because of the fast interconversion between conformations, at temperatures above 238 K, the ¹H NMR spectra of free *p*-H-calix[6]arene hosts, 3 and 4, maintained simple patterns. However, below 238 K, the peaks have started to split into multiple peaks, and finally the spectrum changed into a complicated one at 198 K, as shown in Figure 1. The sharp splitting occurred at 198 K means that the site exchange takes place more rapidly compared to *p*-*tert*-butylcalix[6]arene host 1, which showed a fully splitted ¹H spectrum at 238 K.⁷ The 1D and 2D-NMR spectra of the free host 4 at 198 K are well resolved and allow us to infer the conformational characteristics. The COSY spectrum shows that the phenyl proton resonances are constituted of nine different sites (six for *meta* and three for *para* protons), and the possible conformations which give rise to those splitting patterns are 1,2-alternate and/or 1,2,4-alternate forms. The ¹³C NMR spectrum also supports the above inference, because the carboxyl carbon and the aromatic carbons are divided into three parts with a 1:1:1 intensity ratio, as shown in Figure 1.

Besides the NMR splitting patterns reflecting the molecular symmetry, the absolute positions of ¹³C signals for the

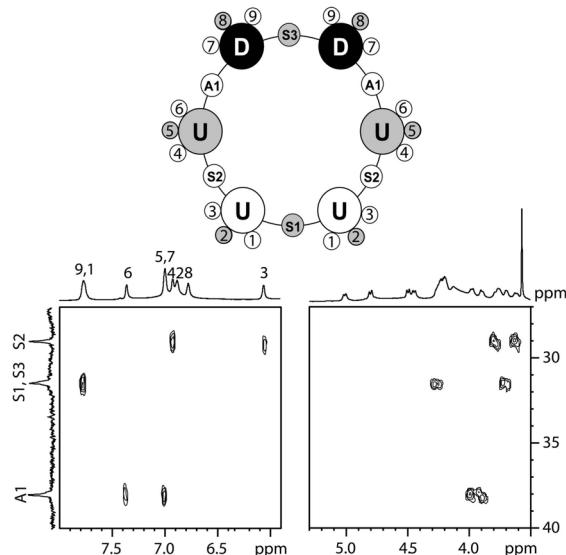


Figure 2. Partial HMBC (left) and HMQC (right) spectra of free host 4 at 198 K in THF-d₈ and acetone-d₆ (5:1, v/v), which show the multiple and single bond information between corresponding protons and carbons. Large, medium and small circles represent aryl moieties, bridged methylenes and phenyl protons, respectively.

in Figure 1, only three bridged methylene carbon peaks are observed; one at 38 ppm and two near 31 ppm (29 and 32 ppm) which represent *anti* and *syn* orientations of connected phenyl groups, respectively.^{8–10} The C–H correlation NMR experiments (HMBC and HMQC) have revealed that the two *syn* bridged methylene carbon signals (S1 and S3, see Figure 2) have been overlaid at 32 ppm. These data indicate that *p*-H-calix[6]arene ethyl ester derivative **4** preferentially adopts an unusual 1,2-alternate conformation at low temperature. In contrast, if it were a 1,2,4-alternate conformation, there would be more carbon peaks around 37 ppm than around 31 ppm. To our knowledge, there is no report that shows a 1,2-alternate conformation for calix[6]arene derivatives. Also, this behavior is different from host **1** having *tert*-butyl groups on the upper rim, as we have reported earlier,⁷ which has a 1,2,3-alternate conformation at low temperature. Most of simple calix[6]arenes reported have cone or 1,2,3-alternate conformers.^{6–8} The methyl ester analogue **3** has shown similar splitting patterns at low temperature, but it was found to have no such preferential conformation at 198 K.

Upon complexation with cesium ion, the methylene resonances (ArCH_2Ar) of hosts **3** and **4** split into a pair of doublets around 3.5–4.5 ppm, indicating that the complexes formed have a cone conformation. There are also two broad signals (with a 2:1 intensity ratio) for the aromatic protons in the ^1H NMR spectrum. However, as the temperature lowered, the aromatic peaks of **3** and **4** separated into four peaks corresponding to two sets of 2:1 ratios with the same integral values (see Figure 3). Additionally, the methylene peaks in

$\text{COOCH}_2\text{CH}_3$ of **4** separated into two peaks (at 4.2 and 4.1 ppm) of equal intensity at low temperature. All these observations imply that there are site exchanges between two equivalent conformations that have C_{3v} symmetry. The existence of this kind of site exchange could be confirmed by the cross peaks between two sets of phenyl proton peaks and between two methylene peaks in $\text{COOCH}_2\text{CH}_3$ of **4** in the EXSY NMR spectrum at 238 K, as shown in Figure 3. These kinds of conformational⁶ and site exchange¹¹ were also observed in the complex **2**+ Cs^+ .

The exchange rate constant k for the conformational exchange can be obtained by line-shape fitting, and the results for the **3**+ Cs^+ complex are shown in Figure 4. The calculations reproduced temperature-dependent NMR spectra successfully for both of the cesium complexes of **3** and **4**. These results support that the site exchange between two equivalent C_{3v} conformers occurs over the observed range of temperatures.

Although the compound **1** does not complex well with the Cs^+ ion, weak signals due to the cone-type complex were observed in the ^1H NMR spectrum for the mixture of **1** and Cs^+ . As seen in the other complexes, the signals from the complex have changed at low temperature. For example, the aromatic and *tert*-butyl proton signals were broadened and finally separated into two peaks, while a pair of doublets from ArCH_2Ar remained the same throughout the observed temperature range. This is again interpreted as the site exchange between two equivalent conformations having C_{3v} symmetry, which can be seen in other cesium complexes of **2**, **3** and **4**.

The ^{133}Cs spectra show that all the hosts form *endo*-type complexes with cesium ions because the cesium resonance peaks undergo upfield shifts referenced to free cesium ion differing from the complexes of calix[4]arene derivatives.¹² As shown in Figure 5, however, the upfield shifts of the Cs^+ complexes of **3** and **4** are much smaller (*ca.* –8 ppm) than

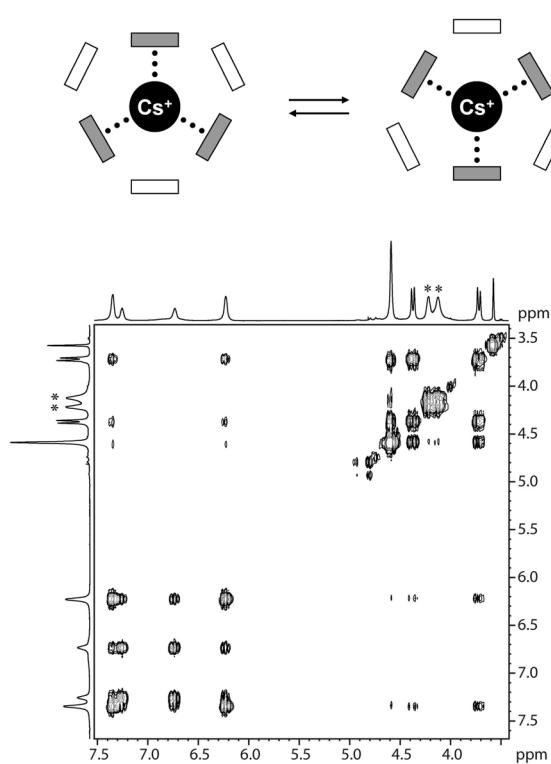


Figure 3. Site exchange scheme (top) and the EXSY spectrum of **4**+ Cs^+ at 238 K (bottom) in THF-d_8 and acetone-d_6 (5:1, v/v). The two methylene peaks in $\text{COOCH}_2\text{CH}_3$ are marked by asterisks.

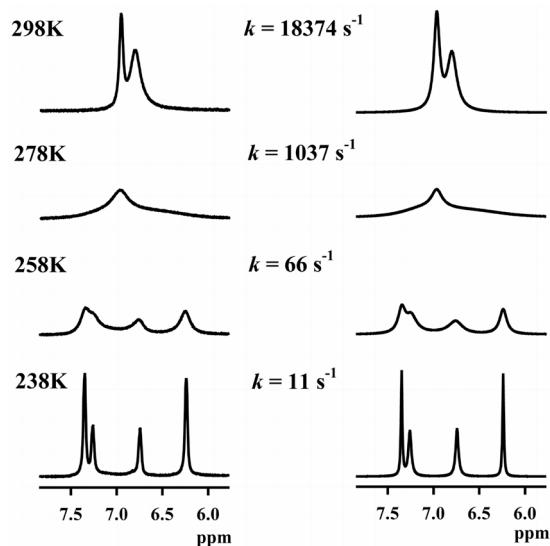


Figure 4. Temperature-dependent ^1H NMR line-shapes of phenyl protons in **3**+ Cs^+ in THF-d_8 and acetone-d_6 (5:1, v/v). Observed (left) and fitted (right) spectra with indicated exchange rate k .

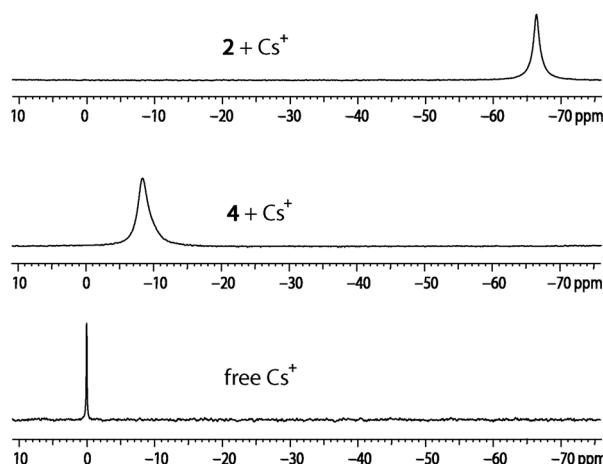


Figure 5. ^{133}Cs spectra of free Cs^+ , $\mathbf{4}+\text{Cs}^+$, and $\mathbf{2}+\text{Cs}^+$ at 298 K in THF-d₈ and acetone-d₆ (5:1, v/v). Note that the chemical shifts are referenced to free cesium ions.

those of **1** and **2** (*ca.* -70 ppm). This might be caused by the absence of *tert*-butyl groups on the upper rim of calix[6]-arene. The presence of *tert*-butyl groups makes it easier to lock the cesium ion deeply into the aromatic cavity, where it experiences stronger ring currents.

In summary, we have found that *p*-H-calix[6]arene ethyl ester derivative **4** preferentially adopts an unusual 1,2-alternate conformation at low temperatures. The *endo*-type complex formation of **3** and **4** with cesium ions was confirmed by Cs^+ NMR, and the complexes were found to undergo mutual interconversions between two equivalent conformations having C_{3v} symmetry over the observed temperatures.

Experimental Section

The calix[6]arene derivatives **1-4** were prepared following the reported standard procedures.¹³ Cesium picrate was prepared by the treatment of cesium hydroxide with picric acid and purified by crystallization from ethanol. Due to the limited solubility of calixarenes and cesium picrate (as a

guest), a binary mixture of THF-d₈ and acetone-d₆ (5:1, v/v) was used for the NMR experiments. All the deuterated solvents were purchased from Aldrich and Sigma Chemical Co. and used without further purification. 1D and 2D-NMR experiments were performed on Bruker Avance 600 and 800 spectrometers. The ^1H and ^{13}C NMR spectra were referenced to THF and the ^{133}Cs NMR spectra were referenced to free cesium ions. The concentration of all solutions was fixed at 0.05 M.

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