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X-Ray Crystallographic Studies of a 1,3-Alternate-calix[4]arene•Na⁺ Complex. Is the Cation-π Interaction Operative between the Benzene Rings and Na⁺?

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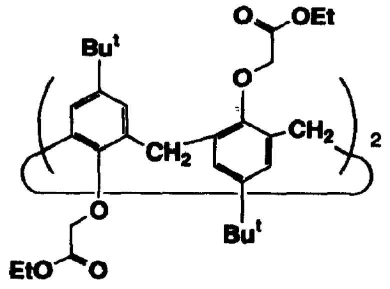
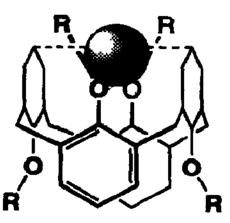
Abstract: The structure of a 1,3-alternate-calix[4]arene•Na^+ complex was determined by X-ray crystallography for the first time. It showed that two well-preorganized oxygen bases ($OCH_2C{=}O$ groups) contribute to the Na^+-binding whereas two π-basic benzene rings, unlike those for the K^+ complex, are not involved. The complex adopts a highly symmetrical structure, which is the origin of the facile "Na^+-tunneling" across the 1,3-alternate-calix[4]arene cavity.

Tetrakis((ethoxycarbonyl)methoxy)calix[4]arene with a 1,3-alternate conformation (1,3-alternate-**1**) is an interesting molecule because of its unique structural charactreristics: for example, (i) a metal-binding site is composed of two "hard" oxygenic ligands and two "soft" π-basic benzene rings, (ii) there are such two binding-sites at the two sides of the calix[4]arene cavity, and (iii) the two binding-sites are linked with each other by a π-basic tunnel. The structural characteristics are reflected by the unique metal-binding properties: for example, (i) 1,3-alternate-**1** forms a 1:1 **1**/Na^+ complex as well as a 1:2 **1**/Na^+ complex[1] and (ii) in the 1:1 complex Na^+ vibrates between two metal-binding sites through the π-basic tunnel.[2,3] In spite of these intriguing metal-binding properties, the metal-binding mechanism is not understood in detail. For example, $K_{1:1}$ for the formation of the 1:1 **1**/Na^+ complex ($10^{4.38}$ M^{-1} in $CDCl_3$:CD_3OD = 1:1 v/v at -50 °C) is much greater than the $K_{1:2}$ for the formation of the 1:2 **1**/Na^+ complex ($10^{0.60}$ M^{-1}).[1] This may be due to the electrostatic repulsion between two Na^+ ions or may be due to the first Na^+-induced conformational change which is unfavorable to the second Na^+-binding (*i.e.*, the allosteric effect observed for certain bis(crown ether)s[4,5]). It is known that in the binding of K^+ and Ag^+ to 1,3-alternate-calix[4]arenes not only $M^+\cdots O$ electrostatic interaction but also the $M^+\cdots$benzene cation-π interaction participates in the binding event,[2,3] but it is still ambiguous if the similar cation-π interaction is operative in the binding of Na^+. The fact that the $K_{1:1}$ for 1,3-alternate-**1** ($10^{4.10}$ M^{-1} in THF at 30 °C) is greater than that for cone-**1** ($10^{3.95}$ M^{-1})[1] may be related to the π-base participation in the 1,3-alternate-**1**•Na^+ complex. We considered that these difficult problems can be solved only by the X-ray crystallographic study. Here, we address the first example for the X-ray structure of the 1,3-alternate-calix[4]arene•Na^+ complex.[6]



1,3-Alternate-1



π-Base participation in 1,3-alternate-calix[4]arene•metal complexes

Recrystallization of 1,3-alternate-**1** and $NaClO_4$ (1:1 molar ratio) from chloroform-methanol gave colorless crystals. The elemental analysis[7] established that the stoichiometry of the crystals is 1:1. The method for the X-ray crystallographic analysis is similar to those described previously.[3,6] The crystal data are summarized in Table 1 and the X-ray structure is illustrated in Fig. 1.[8]

One can raise a number of interesting points about the X-ray structure. Firstly, Na^+ interacts only with two $OCH_2C{=}O$ groups but not with the benzene rings: that is, in the present system the π-bases do not participate in the Na^+-binding. Then, why is the $K_{1:1}$ for 1,3-alternate-**1**•Na^+ based on the interaction between Na^+ and two $OCH_2C{=}O$ groups greater than that for cone-**1**•Na^+ based on the interaction between Na^+ and four $OCH_2C{=}O$ groups? In Table 2 we compare the dihedral angles (θ) between the mean plane of the four $ArCH_2Ar$ methylene carbons and each benzene ring. The θ values for 1,3-alternate-**3** (the structure is illustrated in Table 2) predicted by the MM3 computation[9] are very close to 90°. In 1,3-alternate-**2**, on the other hand, the θ values are significantly smaller than 90°, indicating that the benzene rings are flattened to relax the steric crowding among *O*- and para-substituents. It is acceptable to consider that the θ values in metal-uncomplexed 1,3-alternate-**1** should be similar to those in 1,3-alternate-**2** because their structures are similar to each other. It is seen from Table 1 that although Ph_1 is a little more flattened than that in 1,3-alternate-**2**, the residual three θ values are very similar to those in 1,3-alternate-**2**. This implies that in 1,3-alternate-**1** the distance between two $OCH_2C{=}O$ groups is suitably "preorganized" to the Na^+-binding. In cone-**1**, in constant, four $OCH_2C{=}O$ groups must be significantly flattened upon Na^+-binding.[10] Hence, one can consider that the difference in the preorganization explains why 1,3-alternate-**1** using only two $OCH_2C{=}O$ groups possesses the $K_{1:1}$ greater than cone-**1** using four $OCH_2C{=}O$ groups. Since the first Na^+-binding does not induce a serious conformational change, the relation of $K_{1:1} > K_{1:2}$ is attributable to the electrostatic repulsion but not to the allosteric effect.

Secondly, we have to discuss why K^+ can enjoy the π-base participation[3] while Na^+ cannot. In the present system, the distances from Na^+ to the para-carbons are 3.32 and 3.88. Å. Since the sum of the half thickness of the benzene π-electron cloud (1.70 Å) and the Na^+ radius (1.16 Å) is 2.86 Å, Na^+ cannot interact with the π-bases. On the other hand, the sum of the half thickness of the benzene π-electron cloud and the K^+ radius (1.65 Å) is 3.35 Å. This value is large enough to interact with the π-bases around the para-carbons. Although the "softer" K^+ may interact with the π-base more favorably than the "harder" Na^+,[11] the Na^+ / K^+ difference in 1,3-alternate-**1** is ascribed to the steric problem.

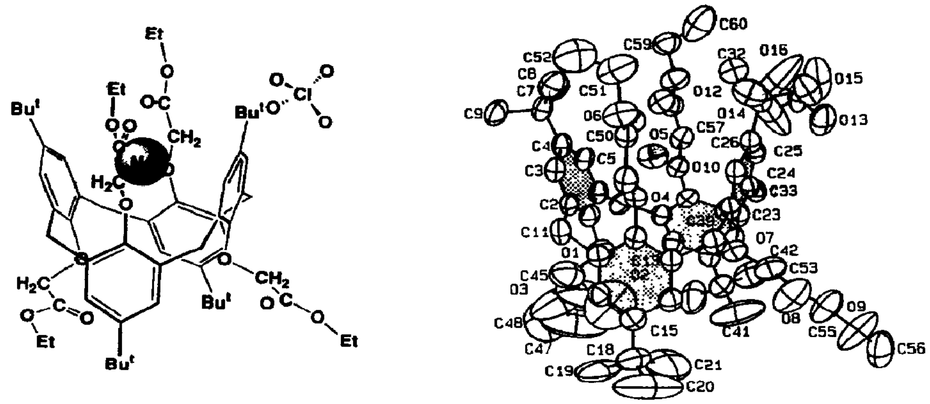


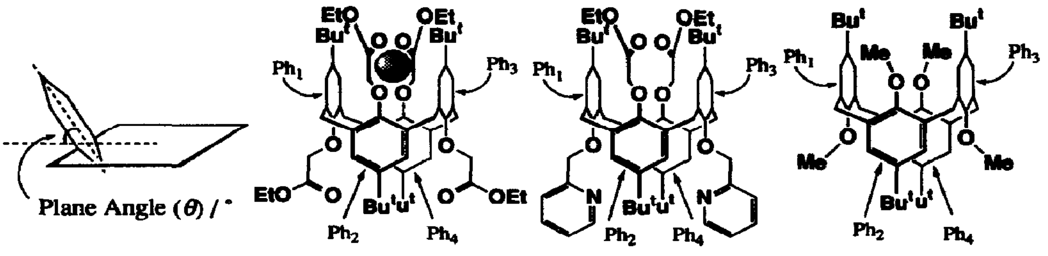
Fig. 1 X-Ray strucuture of the 1,3-alternate-1•NaClO4 complex.

Table 1 Crystal data

Empirical formation	$C_{60}H_{80}ClNaO_{16}$	V / Å^3	6144.7(9)
Space group	$P2_1/n$	Z	4
a / Å	21.546(2)	D_{calc} / g cm^{-3}	1.206
b / Å	20.057(2)	observed reflections	10979
c / Å	14.2618(6)	R	0.088
β / °	94.460(6)	R_w	0.115

Table 2 Comparison of the dihedral angles (θ)

	1,3-Alternate-1•Na$^+$	1,3-Alternate-2	1,3-Alternate-3
	X-ray	X-ray	MM3
Ph$_1$	-74.9	-86.5	-88.0
Ph$_2$	78.2	79.6	87.8
Ph$_3$	-75.5	-78.6	-87.9
Ph$_4$	70.9	73.9	88.0



1,3-Alternate-1•Na$^+$ complex

1,3-Alternate-2

1,3-Alternate-3

Thirdly, the ^{1}H NMR studies established that Na$^+$ bound to 1,3-alternate-**1** can enjoy the "metal-tunneling" across the π-basic cavity.[3] However, they did not tell us if the hopping of Na$^+$ from one binding-site to another binding-site accompanies the conformational change.[1] The X-ray structure in Fig. 1 and the dihedral angles in Table 2 show that 1,3-alternate-**1** adopts a nearly symmetrical structure although Na$^+$ is bound only to one binding-site. This means that the "metal-tunneling" can take place without accompanying the conformational change. We believe that the absence of the conformational change may facilitate the Na$^+$-tunneling in 1,3-alternate-**1**•Na$^+$.

In conclusion, the present study is the first example for the X-ray structure determination of the conformationally-immobile 1,3-alternate-calix[4]arene•Na$^+$ complex. The study has provide several clues to explain how Na$^+$ is bound to the binding-site in 1,3-alternate-calix[4]arene and why Na$^+$ can enjoy the "metal-tunneling". We believe that these lines of basic knowledge are useful to understand the relative contribution of the oxygen base and the π-base to the metal-binding and provide guiding principles for the design of π-basic ion channels,[11] calix[4]arene-based nano-tubes,[12] *etc.*

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7. Anal. Calcd for $C_{60}H_{80}O_{12}$•$NaClO_4$: C, 64.59; H, 7.23%. Found: C, 63.71; H, 7.24%.

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