

Studies on the Intramolecular Inclusion Complexes of Functionalized Calix[4]arenes with CH_3X ($\text{X} = \text{CN}, \text{NO}_2$)[†]

ZHOU, Zhi-Xian(周稚仙) SHI, Ya-Lin(石雅琳) DU, Chen-Xia(杜晨霞)
XING, Yan-Jun(邢彦军) WU, Yang-Jie*(吴养洁)

Department of Chemistry, Zhengzhou University, Zhengzhou, Henan 450052, China

Two functionalized calix[4]arenes in cone conformation $\text{L}_{2,3}$ have been synthesized and their intramolecular inclusion complexes (1:1) with organic neutral molecules CH_3CN and CH_3NO_2 have been prepared and characterized, respectively. The X-ray crystallographic analysis shows that L_2 in $\text{L}_2 \cdot \text{CH}_3\text{CN} \cdot \text{C}_2\text{H}_5\text{OH}$ has C_4 symmetry and L_3 in $\text{L}_3 \cdot \text{CH}_3\text{NO}_2$ exhibits C_2 symmetry. The CH- π aromatic interactions between the CH group of the guest and the phenyl rings of the calix backbone have been proved to be able to stabilize the intramolecular inclusion complexes formed. The interaction is directional, but it is independent of the acidity of the guest. To gain information on CH- π interactions, suitable geometrical parameters have been calculated from the crystal data of intramolecular inclusion complexes. The results show that $\text{L}_3 \cdot \text{CH}_3\text{NO}_2$ with L_3 in C_2 symmetry can also be bound stably in the intramolecular inclusion complex, being consistent with the thermal analysis. The geometrical parameters and the results of the thermal analysis of $\text{L}_1 \cdot \text{CH}_3\text{CN}$ and $\text{L}_1 \cdot \text{CH}_3\text{NO}_2$ were also given and discussed.

Keywords calix[4]arene, intramolecular inclusion complex, CH- π interaction, molecular recognition, host-guest chemistry

Introduction

One of the most attractive features of calix[4]arenes is their cuplike structure, which was observed both in solid state and in solution. The cavity defined by the cone conformer of this macrocycle was extensively employed as a binding site for the recognition of neutral guests having

complementary size. It is well known that many of the calix[4]arenes show a spontaneous ability to retain the solvent from which they are crystallized. On the basis of the structural data available, the inclusion complexes of calix[4]arenes with such neutral organic molecules may be divided into two main categories: intramolecular and intermolecular complexes. In the first, one guest molecule is held inside the cavity of one host molecule with 1:1 stoichiometry. In the second, one guest molecule is demonstrated to be of clathrate character, in which the guest species is accommodated in continuous channels or layers within the crystal lattices.¹⁻³ Andreetti *et al.*⁴ and Mckerverey *et al.*⁵ were the first to report the crystallographic structure of intramolecular inclusion (1:1) complex of *p-t*-butyl-calix[4]arene with toluene and that of calix[4]arene derivative, tetraethyl *p-t*-butyl-calix[4]arene tetracarboxylate with non-aromatic molecule (CH_3CN), respectively. The introduction of substituents on the phenolic OH groups of *p-t*-butyl-calix[4]arene produces various derivatives. Hence the examples of such complexes (either intra- or inter-molecular) are particularly numerous in the case of calix[4]arene derivatives. However, to the best of our knowledge, only few studies on the crystal structures of intramolecular inclusion complexes of functionalized calix[4]arenes including calix[4]arene biscrowns with non-aromatic neutral organic molecule have been reported.⁵⁻⁹

Our previous study has showed that the *O*-[*o*-

* E-mail: wyj@zzu.edu.cn

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(alkoxycarbonyl) benzyl] (alkoxy = methoxy or ethoxy)-substituted calix[4]arenes in cone conformation exhibit high extractibility for K^+ ,¹⁰ and *O*-[*m*-(methoxycarbonyl)benzyl] tetra-substituted calix[4]arene (**L**₁) seems to recognize tetrabutyl ammonium cation. In order to obtain the crystal of **L**₁, the mixed solvent of CH_3CN , CH_3OH and $CHCl_3$ was used. Surprisingly, a single-crystal of **L**₁· CH_3CN was formed. In a similar way, a single-crystal of **L**₁· CH_3NO_2 was also obtained.¹¹ Since single-crystal X-ray diffraction remains the most important technique for determining the structure of inclusion compounds, from the data reported in the literature and the crystal data of **L**₁· CH_3CN and **L**₁· CH_3NO_2 ,¹¹ it can be deduced that stable intramolecular complexes can be formed only when the calix[4]arene host is blocked in rigid cone conformation, and the guest possesses acidic CH groups.

Recently, specific CH- π interactions between the CH groups of the guest and the electron-rich aromatic nuclei of the host have been hypothesized to stabilize such intramolecular inclusion complexes formed.¹² In order to give an insight into these supramolecular interactions, suitable geometrical descriptors, which define the host geometry and the orientation of the guests in the complexes, have been selected. The symmetry of the host was defined through the angle θ between each phenyl ring of the calix backbone and the *R* plane by the bridging methylene carbon atoms of the calix[4]arenes.⁶ To take account of the co-operative effect by the four aromatic nuclei present in the receptor site, the global interaction of the methyl group with the aromatic cavity was evaluated by the sum of $\Sigma d_{1,4}$, rather than only by *d* which is the distance between the methyl carbon atom and the centroids of the aromatic rings of the calix[4]arenes. The position of the

CH_3CN or CH_3NO_2 in the cavity could also be expressed by the height *h*, that is, the distance of the methyl carbon atom from the reference plane *R*.⁶

As indicated in this paper, two novel hosts in the cone conformation, *O*-{*m*-[ethoxycarbonyl] and *m*-[methoxycarbonyl]benzyl} tetra- and di-substituted calix[4]arenes (**L**_{2,3}) were synthesized and their intramolecular inclusion complexes with CH_3CN and CH_3NO_2 have been prepared and characterized, respectively.

As reported, thermal gravimetry (TG) and differential scanning calorimetry (DSC) are also useful tools for the study of thermal stability of inclusion compounds.¹³ The thermal analysis studies of the intramolecular inclusion complexes have also been performed.

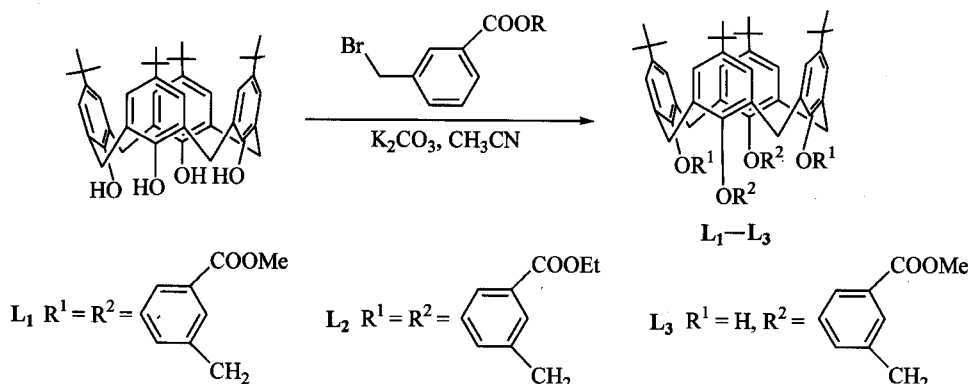
Results and discussion

The functionalized calix[4]arenes **L**_{2,3} were prepared as shown in Scheme 1.

Intramolecular inclusion (1:1) complexes of **L**₂ with CH_3CN and **L**₃ with CH_3NO_2 have been characterized by X-ray diffraction. The crystal data are listed in Table 1. The molecular structures of **L**₂· CH_3CN and **L**₃· CH_3NO_2 are given in Figs. 1 and 2, respectively. The geometrical parameters, θ , $\Sigma\theta_{1,4}$, *d*, $\Sigma d_{1,4}$, *h*, *etc.* of the intramolecular complexes have been calculated from the crystal data which are summarized in Table 2. In addition, there exist structural ethanol molecules in the crystal packing which play a crucial role in stabilizing the lattice, so the chemical formula of crystal complex between **L**₂ and CH_3CN should be **L**₂· CH_3CN · C_2H_5OH .

It is well known that the two guests, nitromethane and acetonitrile, exhibit very different acidity, and fur-

Scheme 1



thermore, the acidity of the latter is weaker than that of the former (CH_3CN $pK_{\text{aDMSO}} = 31.3$, CH_3NO_2 $pK_{\text{aDMSO}} = 17.2$).¹⁴ However, based on the geometrical data Σd_{1-4} and h , $\text{L}_1 \cdot \text{CH}_3\text{CN}$ is slightly stabler in comparison with $\text{L}_1 \cdot \text{CH}_3\text{NO}_2$.

The results of the thermal analysis show that the DSC curve of L_1 displays only an endothermic peak near 171 °C which corresponds to melting, that the onset of the initial endothermic peak of $\text{L}_1 \cdot \text{CH}_3\text{CN}$ is near 136 °C with a maximum at 139 °C, and the end is at 142 °C which corresponds to the release of the guest CH_3CN , that the onset of the initial endothermic peak of the $\text{L}_1 \cdot \text{CH}_3\text{NO}_2$ is near 64 °C with a maximum at 77 °C and the end is at 84 °C. From the comparison with the data of the guests included in the L_1 , it can be concluded that the first release of $\text{L}_1 \cdot \text{CH}_3\text{NO}_2$ is thermally easier than that of $\text{L}_1 \cdot \text{CH}_3\text{CN}$. The results obtained are in agreement with those obtained by the geometric parameters Σd_{1-4} and h as mentioned above.

Based on the above discussion, it can be concluded that CH_3X guests are bound preferentially by hosts having a C_4 or near C_4 symmetry, and that the $\text{CH}-\pi$ interaction is directional, but it is independent of the acidity of the guests, which indicates that the classical hydrogen bond does not play a major role.⁶

To gain information of $\text{CH}-\pi$ interactions of intramolecular complex, in which host is in C_4 symmetry and guest bearing CH_3 group, L_2 was chosen to be a new host. Elemental analysis and ^1H NMR study have confirmed that L_2 is quite similar to L_1 with the same cone conformation and near C_4 symmetry, because the difference between them is only that the methoxy in the methoxycarbonyl group in L_1 is displaced by ethoxy in L_2 .

In the course of the crystallization for preparing the intramolecular complexes between L_2 and CH_3CN or CH_3NO_2 , the former does form stable crystal suitable for X-ray structural analysis as expected. The crystal data are shown in Table 1, and the geometrical parameters are

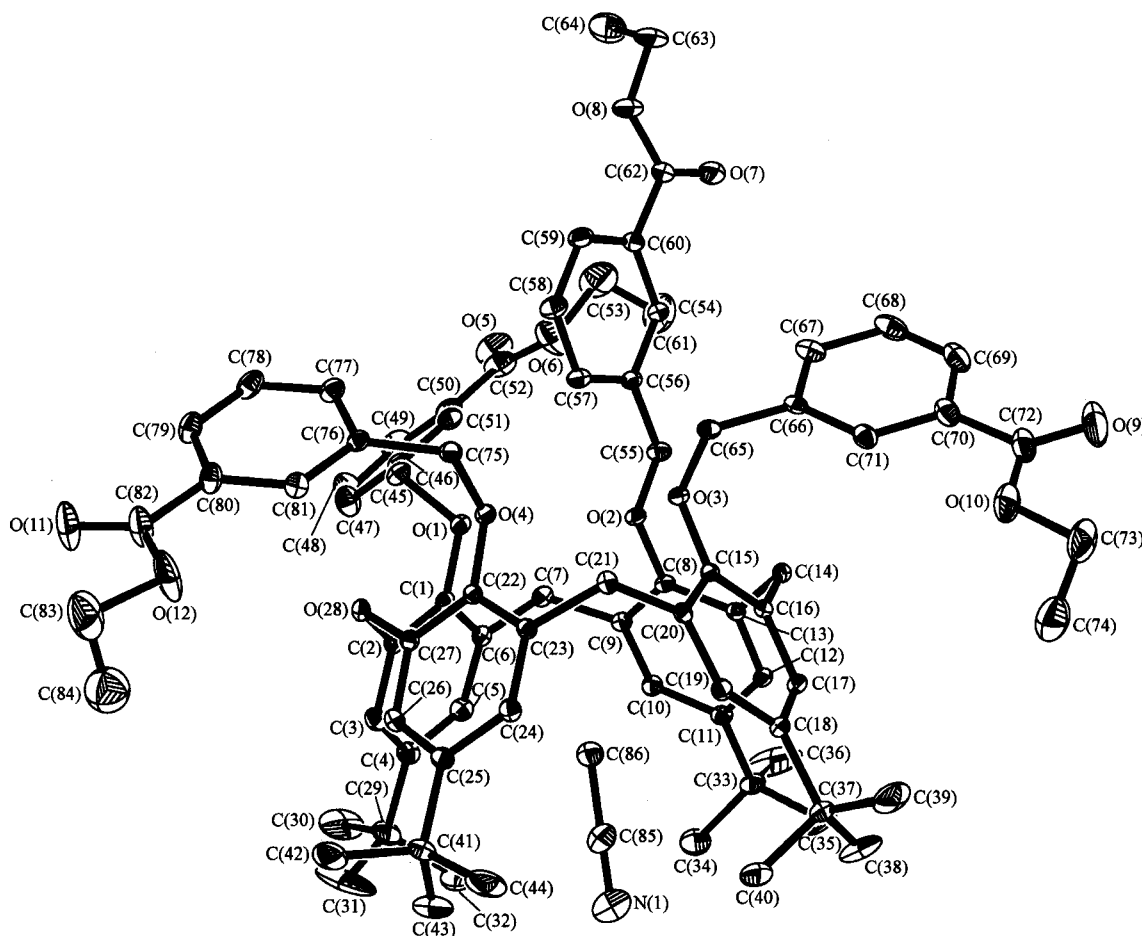


Fig. 1 Molecular structure of $\text{L}_2 \cdot \text{CH}_3\text{CN}$.

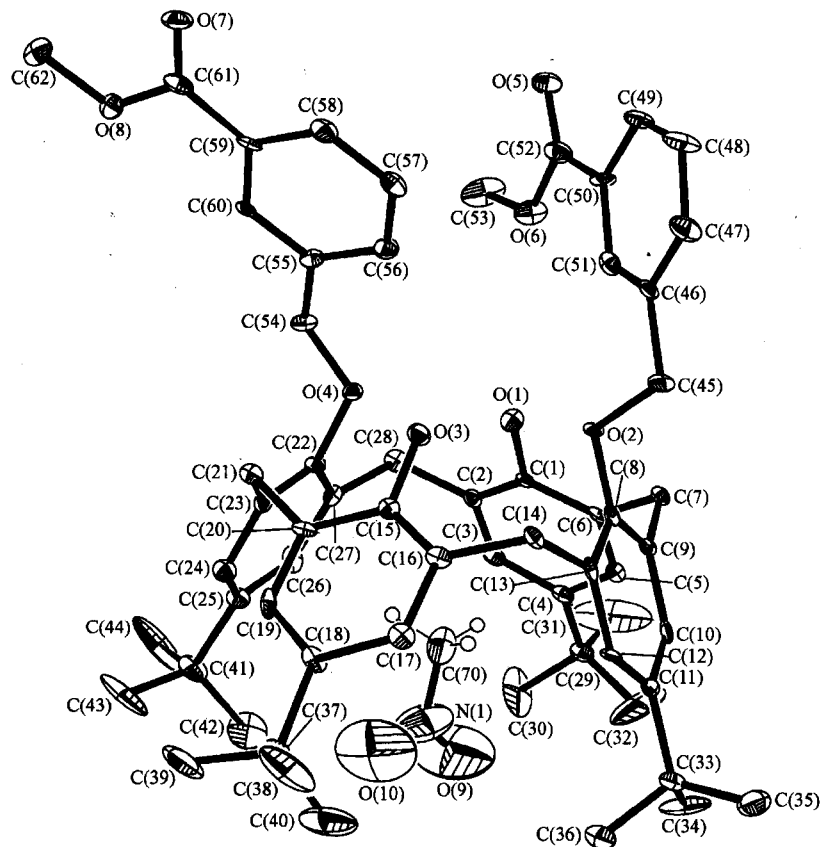


Fig. 2 Molecular structure of $L_3 \cdot CH_3NO_2$.

summarized in Table 2. Nevertheless, the solid complex between L_2 and CH_3NO_2 has not been obtained so far.

As shown in Table 2, the complex between L_2 and CH_3CN has fourfold symmetry with the phenyl ring of the L_2 inclined by θ from 112.4° to 120.3° , the $\sum \theta_{1-4}$ is 460.9° . Each benzoate site can be considered as a π -conjugated system. The interplanar angles between the carboxyl groups and the connected phenyl rings are 3.1° , 8.8° , 7.9° and 1.6° , respectively. All the carbonyl groups are directed towards outside of the cavity to reduce the steric crowding in the narrow calix range as that of the $L_1 \cdot CH_3CN$.¹¹ The interplanar angles between the benzoate site and the connected phenyl ring of the calix backbone are 50.7° , 82.4° , 125.4° and 67.4° , respectively.

The acetonitrile molecule lies on the crystallographic fourfold axis with the nitrogen atom directed *exo* and the methyl group pointing inside the intramolecular cavity facing the aromatic nuclei of the calix backbone. The d is from 0.3612 nm to 0.3685 nm which is shorter than the sum of van der Waals radius 0.38 nm. This clearly

elucidates that there are CH- π interactions. The θ , $\sum \theta_{1-4}$, d , $\sum d_{1-4}$ and h are shown in Table 2, indicating that the complex between L_2 and CH_3CN has similar stability with that of $L_1 \cdot CH_3CN$, and slightly stabler than $L_1 \cdot CH_3NO_2$. These results are consistent with those of thermal analysis (DSC), that is, the onset of the initial endothermic peak of $L_2 \cdot CH_3CN$ (for clarity, the composition of solid state used in thermal analysis being $L_2 \cdot CH_3CN$) is $84.3^\circ C$ and the end is at $138^\circ C$.

It is interesting to note that L_3 formed intramolecular complex with nitromethane, $L_3 \cdot CH_3NO_2$, as shown in Fig. 2, which has similar stability as the complexes $L_1 \cdot CH_3CN$ and $L_2 \cdot CH_3CN$. The crystal data and geometrical parameters are shown in Tables 1 and 2, respectively.

L_3 has C_2 symmetry in $L_3 \cdot CH_3NO_2$. The interplanar angles of different phenyl rings of the calix backbone with respect to the reference plane R are: 129.2° and 127.4° for the phenolic rings and 109.3° and 116.1° for the phenyl rings of the benzoate site. Each benzoate can also be considered as a π -conjugated system, the interplanar angles between the carboxyl group and the con-

Table 1 Crystallographic data of $L_2 \cdot CH_3CN \cdot C_2H_5OH$ and $L_3 \cdot CH_3NO_2$

	$L_2 \cdot CH_3CN \cdot C_2H_5OH$	$L_3 \cdot CH_3NO_2$
Formula	$C_{88}H_{105}NO_{13}$	$C_{63}H_{75}NO_{10}$
Formula weight	1384.73	1006.24
Wavelength	0.71073	0.71073
T (K)	291	291
Crystal size (mm)	0.40 × 0.40 × 0.30	0.30 × 0.30 × 0.20
Crystal system	Monoclinic	Triclinic
Space group	$P2(1)/c$	$P-1$
a (nm)	1.8566(4)	1.2594(4)
b (nm)	1.3216(3)	1.6835(6)
c (nm)	3.3287(7)	2.8424(9)
α (°)	90	106.656(7)
β (°)	95.15(3)	96.381(6)
γ (°)	90	97.465(6)
V (nm ³)	0.81348(28)	0.56544(33)
Z	4	4
D_c (g·cm ⁻³)	1.131	1.182
$F(000)$	2976	2160
θ range (°)	1.10 to 27.62	1.28 to 21.00
Independent reflections	14270 ($R_{int} = 0.0000$)	12120 ($R_{int} = 0.0564$)
Reflections collected	14270	15408
R	0.0865	0.1012
wR	0.2172	0.2000
Goodness-of-fit	1.077	1.118
Data/restraints/parameters	14266/4/900	12117/0/1189
Largest diff. peak and hole ($\times 10^3$ e/nm ³)	0.496/ - 0.345	0.337/ - 0.308

Table 2 Geometrical parameters of compounds L_{1-3} with CH_3CN or CH_3NO_2

	$L_1 \cdot CH_3CN$	$L_1 \cdot CH_3NO_2$	$L_2 \cdot CH_3CN \cdot C_2H_5OH$	$L_3 \cdot CH_3NO_2$
d_1^a (nm)	0.3683	0.3689	0.3612	0.3687
d_2 (nm)	0.3662	0.3665	0.3685	0.3564
d_3 (nm)	0.3664	0.3706	0.3624	0.3824
d_4 (nm)	0.3662	0.3675	0.3679	0.3515
Σd_{1-4} (nm)	1.4671	1.4735	1.460	1.459
θ_1^b (°)	113.5	116.6	113.7	129.2
θ_2 (°)	112.8	114.3	120.3	109.3
θ_3 (°)	115.2	114.8	112.4	127.4
θ_4 (°)	119.4	118.7	114.5	116.1
θ_{1-4} (°)	460.9	464.4	460.9	481.9
h^c (nm)	0.2796	0.2826	0.2765	0.2634

^a d is the distance between the methyl carbon (CH_3X) and the centroids of each phenyl ring of the calix backbone; ^b θ is the angle between phenyl ring of the calix backbone and the R plane defined by the bridging methylene carbons of calixarenes; ^c h is the distance of the methyl carbon atom from the R plane.

nected benzene ring are 7.0° and 8.4°, respectively.

The nitromethane lies on the crystallographic axis

with the nitro group directed *exo* and the methyl group pointing inside the intramolecular cavity facing the aro-

400 MHz) δ : 8.11 (s, 2H, ArOH), 8.04 [t, $J = 9.2$ Hz, 4H, ArH (ester)], 7.35 [t, $J = 7.8$ Hz, 2H, ArH (ester)], 7.17 [s, 2H, ArH (ester)], 7.05 [s, 4H, ArH (calix)], 6.79 [s, 4H, ArH (calix)], 5.09 (s, 4H, OCH₂Ar), 4.24 (d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 3.87 (s, 6H, OCH₃), 3.27 (d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 1.28 [s, 18H, C(CH₃)₃], 0.945 [s, 18H, C(CH₃)₃]; IR (KBr) ν : 3434, 2962, 866, 1725, 1599, 1481, 1364, 1297, 1115, 1200, 1028, 978, 880, 749 cm⁻¹; Anal. calcd for C₆₂H₇₂O₈: C 78.78, H 7.68; found C 78.68, H 7.66.

Preparation of the single crystals of the intramolecular inclusion complexes

Crystals of complexes L₁·CH₃CN and L₁·CH₃NO₂ were prepared according to the reported procedure.¹¹

Crystal of complex L₂·CH₃CN suitable for X-ray crystallography was obtained by slowly evaporating the solution of L₂ in CHCl₃-C₂H₅OH containing a small amount of acetonitrile. Crystal L₃·CH₃NO₂ was obtained in a similar manner for L₂·CH₃CN when CH₃NO₂ was used instead of CH₃CN.

X-Ray crystal determination

A colorless prismatic crystal was mounted on a glass fiber. All measurements were made on a Rigaku-1V imaging plate area detector with graphite monochromated MoK α radiation. The data were collected for Lorentz and polarization effects. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were defined anisotropically. Hydrogen atoms were included but not refined. All calculations

were performed using the teXsan crystallographic software package.

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