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The solid-state structure of calix[4]arene dihydroxyphosphonic acid–L-lysine complex

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Abstract

The solid-state structure of calix[4]arene dihydroxyphosphonic acid with L-lysine shows a high degree of complexity. The system presents three independent molecules of amino acid, all in different conformational structures, associated with four molecules of calixarene, in the presence of a relatively high number of solvent molecules. The general topology of the complex is guided by the layer of two dimeric units of calixarene molecules and by the large network of hydrogen bonds generated by the molecules of lysine. The arrangement of lysine molecules in the crystal generates a 1-D ladder network.

Keywords: Calixarene; Dimers; Lysine; Conformation; Hydrogen bonds

1. Introduction

All biological systems have predefined three-dimensional shape [1] given by their component molecules, changes in structural geometry along with bonding and isomerism having radical influence on their activity [2]. The study of molecular recognition involves the overview of all intra- and intermolecular interactions, in order to establish the selective binding of a certain molecule with respect to another [3]. By virtue of their relatively flexible side chains, the amino acids are mainly responsible for protein bindings in living systems [4].

The availability of molecules that can bind selectively to a target molecule has been extensively studied in the recent years [5,6].

The complexation abilities of calix[4]arene dihydroxyphosphonic acid, **1**, a water soluble calixarene derivative presenting two polar functionalisations on the lower rim, represent a growing interest in supramolecular chemistry [7]. Due to the anionic character of these functional substitutions, this calixarene generates astonishing architectures in solid-state complexes with aliphatic as well as with heterocyclic amines. The ubiquitous dimeric motif described by the interdigitation of aromatic rings of facing calixarenes is present in all the reported structures. Thus the topologies present in these complexes are all related to this dimeric association of calixarene molecules and generated the following: hexagonal arrangement of the dimeric units forming aquachannels in the complex with propanediamine [8] or individual dimeric units separated by an envelope of aliphatic amines in the complex with hexanediamine [9]. Molecular cages of amines were observed in the structures with heterocyclic amines, like phenanthroline [10], whereas the complex with bipyridyl ligands generates a 1-D ladder structure [11].

The solid-state structure of calix[4]arene dihydroxyphosphonic acid complex with L-lysine, in aqueous media, is reported here. The preferred conformations adopted by the amino acid molecules and the hydrogen bonds they develop with the molecular environment represent the main subject of the description.

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2. Experimental section

2.1. Synthesis and crystal growth

The synthesis of calix[4]arene dihydroxyphosphonic acid (**1**) was carried out according to the literature method. The measured physical data were in full accord with published data [12].

The crystallization of the complex was realised by employing the solvent diffusion technique. Solution of 0.01 M of **1** was prepared in ethanol. The solution of amino acid was prepared in MilliQ water at the same concentration. The two solutions were deposited in layers into test tubes, in the following order: amino acids solution/water/ethanol/calixarene solution, in such a way that there was the formation of an interface between the two solvents with different densities. Crystals were obtained after several weeks.

2.2. X-ray crystallographic study

The crystal data were collected at 100(2) K on a Nonius KappaCCD diffractometer using MoKα radiation. Data were corrected for Lorentz and polarisation effects but not for absorption. The two structures were solved using direct methods and Fourier techniques (SHELXS 97) and were refined by full matrix least squares on F^2 (I > 2σ (I)) using the program SHELXL 97.

All H-atoms were included in geometric positions and refined as 'riding' atoms with isotropic thermal parameters based upon the corresponding bonding carbon atom [$U_{iso} = 1.2U_{eq}$, $U_{iso} = 1.5U_{eq}$ for CH_3 and OH hydrogens].

Crystal data and refinement details are summarized in Table 1.

Table 1
X-ray crystallographic and experimental data for the complex of calix[4]arene dihydroxyphosphonic acid with L-lysine

Complex of **1** with	L-Lysine
Chemical formula	$4C_{28}H_{22}O_{10}P_2 \cdot 3C_6H_{15}N_2O_2 \cdot 2C_2H_5OH \cdot 7H_2O$
Formula mass (g mol^{-1})	2981.43
Space group	$P2_1$
a (Å)	10.7934(2)
b (Å)	29.3481(5)
c (Å)	21.8847(4)
β (°)	91.974 (1)
Z	2
V (Å^3)	6928.2(2)
ρ_{calc} (g cm^{-3})	1.429
Data collection	
Diffractometer detector	KappaCCD
Radiation *λ* (Å)	MoKα
T (K)	100(2)
θ range (°)	2.61–26.38°
Crystal colour	Colourless
Crystal size (mm)	0.22 × 0.10 × 0.10
μ (mm^{-1})	0.197
No. of reflections measured	45,902
R_{int}	0.128
No. of independent reflections	14,392
No. of reflections with $F_o > 4\ \sigma(F_0)$	8413
No. of parameters/restraints	1879/1
$R(F^2)$	0.146
$R(F^2)$ [I > 2σ(I)]	0.078
Goodness of fit on F^2	1.02

3. Results and discussion

The asymmetric unit of the complex of **1** with L-lysine is generated by the complicity of four molecules of calix[4]arene dihydroxyphosphonic acid with three molecules of lysine, in the presence of two molecules of ethanol and seven water molecules.

Notable structural and geometrical differences are observed for the components of the two molecular species, starting with the four individual molecules of **1** (denoted **1A**, **1B**, **1C** and **1D**). The structural characteristics of these molecules may be described by intramolecular interactions. The phenolic oxygen atoms are involved in intramolecular hydrogen bonds except for molecule **1A** where one of the unsubstituted phenolic oxygen atoms is involved in hydrogen bonding to a water molecule. In molecule **1D** one of the phenolic oxygens forms a bifurcated hydrogen bond (see Table 3).

As expected, all four independent molecules of **1** are present in the cone conformation. The cone angles formed by the substituted phenolic rings and by the unsubstituted ones, respectively, are described as follows: 26.3(3)°, 106.2(3)°; 28.3(3)°, 106.8(3)°; 29.8(3)°, 103.2(3)°; and 27.2(3)°, 111.0(3)°, for the four molecules **1A**, **1B**, **1C** and **1D**, respectively. From the above values the conformation of the four crystallographically independent calixarene molecules can be described as 'flattened cone'. This is a consequence of the fact that the geometry of the calixarene molecules presents certain flexibility at the level of aromatic core, which adapts itself in order to allow the most favorable interactions with the local environment (Fig. 1).

The presence of four independent molecules of **1** as building elements of the complex induces formation of two structural dimeric units characterized by interdigitation of the aromatic crowns of two opposite calixarene molecules. Thus, the two angles formed by the *para*-carbon atoms describing the interdigitation are of 165.1(3) and 163.5(3)° (Fig. 2) and represent a deeper interdigitation than in the previously described structures based on calix[4]arene dihydroxyphosphonic acid [7,10,11], for which average values of 158° are generally observed. Nevertheless, recently, a similar value of interdigitation was observed for the complex of **1** with melamine mono-cations [13].

A remarkably large network of short aromatic contacts occur between neighbouring dimers, as: 3.85(1), 3.94(1), 3.74(1), 3.84(1), 3.98(2), 3.990(1), 4.00(2), 3.77(2), 3.99(2) and 3.74(1) Å. Besides these short aromatic contacts, there are dipolar interactions between the carbon atoms of the ethanol molecules with the aromatic cycles of 3.98(2),