Short Communication

A Facile Method of Synthesis of a Calix[4]arene Amide and the Crystal Structure of a Self-assembled Calix[4]arene Amide *via* Van Der Waals Interaction

YONG WU, HUI-BIAO LIU, YONG-JIANG LIU, CHUN-YING DUAN, JUN HU and ZHENG XU⋆
Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing 210093, P. R. China

Abstract. A new facile method of synthesis of calix[4]arene amide *via* the aminolysis of the calix[4]arene esters was reported. One ethyl ester of the compound (**2**) was aminolysized by *n*-butylamine. The crystal structure of compound (**1**) shows that one ethyl ester of compound (**1**) enters into the cavity of another compound (**1**) forming a long chain host-guest supramolecule. From the 2D NMR data, the compound (**1**) does not assemble in THF or $CHCl_3$ solution. The CH-π interaction and crystallization energy might be the important driving forces for forming the self-assembled calix[4]arene.

1. Introduction

Self-organization is found as a general principle in nature, and the design and investigation of artificial molecules that are able to mimic this principle at least in part is a topic of current interest in supramolecular chemistry [1]. Assemblies of small molecules provide a means for exploring the intermolecular forces involved in molecular recognition and the chemical information that becomes expressed when the superstructure emerges. Calix[4]arenes have proved to be very useful building

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⋆ Author for correspondence.

blocks in the synthesis of receptors for cations, anions, and neutral molecules. The driving force of host-guest complexation involving electrostatic interactions, hydrogen bonding and the van der Waals interactions including CH-π interactions has received much attention [2]. Recently the behavior of hydrogen-bonded aggregates of calix[4]arene and the calix[4]arene assembly *via* van der Waals interaction were studied by many groups [3]. Here we report a new facile synthesis method and the crystal structure of calix[4]arene derivative (**1**), which shows a one-dimensional self-assembly chain *via* van der Waals interaction.

$$R_1 = CH_2COOCH_2CH_3, \quad R_2 = CH_2CONH(CH_2)_3CH_3$$
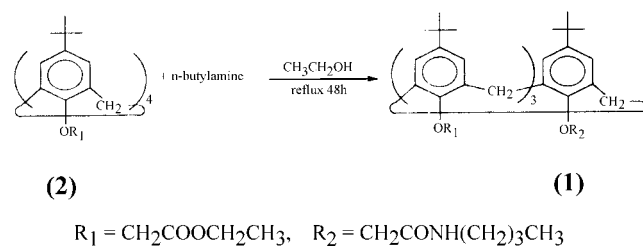
Scheme 1.

2. Synthesis

The starting reactant compound (**2**) is a sodium inclusion complex[4], which has been proved by ESI-MS and it is difficult to get compound (**2**) without sodium ion, but it does not matter to the aminolysis reactions. To a solution of 0.5 mmol of the calix[4]arene ester (**2**) in 20 ml of absolute ethanol was added 20 mmol of *n*-butylamine. The resulting mixture was heated under reflux for 48 h with stirring, and then the solvent was removed at room temperature under vacuo to get a white powder, which was washed with water and recrystallized from ethanol to get pure compound (**1**) [5]. Colorless transparent single crystals of compound (**1**) which were suitable for X-ray diffraction was obtained by evaporation of the ethanol solution for about 10 days at room temperature. The X-ray crystal structure and analysis of sodium in compound (**1**) by a Jarrell–Ash 1100 + 2000 inductively coupled plasma quantometer (ICP) shows that there is no sodium ion in compound (**1**), but ESI-MS data show that compound (**1**) contains a sodium ion. Maybe, the sodium ion entered into the calix[4]arene amide during the ESI-MS process, which came from the mobile phase water-ethanol. The reaction is a high selective aminolysis of only one of four ester groups and is the first example of the aminolysis reaction used in the synthesis of a calix[4]arene amide. Compound (**2**) can be aminolysized by a variety of amines, such as ethanolamine, *n*-propylamine, *n*-butylamine, *n*-heptylamine and diamine, to get the mono, bis, tetrakis and double bridged amides [6], which depends on the reaction conditions and the reactants. For example, on refluxing in absolute ethanol, all four ethyl esters of compound (**2**) are aminolysized by ethanolamine which is high selectivity, but one and two ethyl esters of compound (**2**) are aminolyzed by *n*-propylamine to get a mixture

of two products. Also, there are no reactions with benzylamine and aniline. It is clear that as the activity of the amine decreases the aminolysis reactions become gradually more difficult. The steric effect of the amines is an important factor. The aminolysis reactions do not take place with high steric hindrance amines, such as cyclohexylamine, t-butyl amine and diethylamine. A strong base such as NaH promotes the aminolysis reaction. For example, in DMF solution containing NaH, all four ethyl esters are aminolysized by n-butylamine at room temperature reacting for 24 h. These results can be understood by the mechanism of the aminolysis reaction [7]. As a comparison with the usual method [8], the new method reported here is facile, economic and high yield.

3. Crystal Structure

Colorless transparent single crystal of compound (**1**) contains solvated ethanol and is stable for about two hours when exposed to the air. The crystal structure has been determined on a Siemens P4 diffractometer using $\omega/2\theta$ scan. The crystal of compound (**1**) belongs to the monoclinic space group $P2_1/n$, with $a = 13.411(6)$, $b = 25.346(7)$, $c = 19.482(4)$ Å; $\alpha = 90$, $\beta = 106.13(3)$, $\gamma = 90°$, $V = 6362(4)$ Å^3, $D_c = 1.092$ mg cm^{-3}, $Z = 4$. Accurate cell parameters were derived from least-squares fitting of the setting angles of 25 independent reflections in the range of 4.99–15.67°. Of the 10,350 measured independent reflections, 5251 were observed with $T \geq 2\sigma$, and were used for the structure refinements. At final convergence, $R_1 = 0.0796$, $wR_2 = 0.1574$ and GOF = 1.046. The molecular structure and the molecular packing view are shown in Figure 1. It shows that one ethyl ester of compound (**1**), which is more extended and closer to the plane composed of four oxygen atoms of phenols, enters into the cavity of another compound (**1**) to form a long chain host-guest supramolecule. Each molecule of compound (**1**) acts as both host and guest for another molecule. The normal distances of C(45) of the guest compound (**1**) to the four phenyl ring planes and the distances of C(45) to the centers of the four phenyl rings (A, B, C and D) in the host compound (**1**) are 3.597, 3.691, 3.492, 3.453, 3.610, 3.714, 3.492 and 3.467 Å respectively. They are almost the same. It means that the alkyl chain almost locates at the center of the calix[4]arene cavity. Checking the distances between the alkyl chain and the phenol rings, we might deduce that the CH-π interaction plays an important role in the formation of the host-guest complex.

Bond lengths and angles within compound (**1**) are unexceptional. The carbon atoms of four phenyl rings are coplanar with deviations of 0.007, 0.017, 0.019 and 0.020 Å respectively. The dihedral angles between the phenyl ring plane and the plane composed of four oxygen atoms from phenols are 63.5°, 61.8°, 63.1° and 63.5°. This indicates that compound (**1**) adopts an almost rigid cone geometry in the solid state. The inclusion complex forming has played an important effect on the conformation.
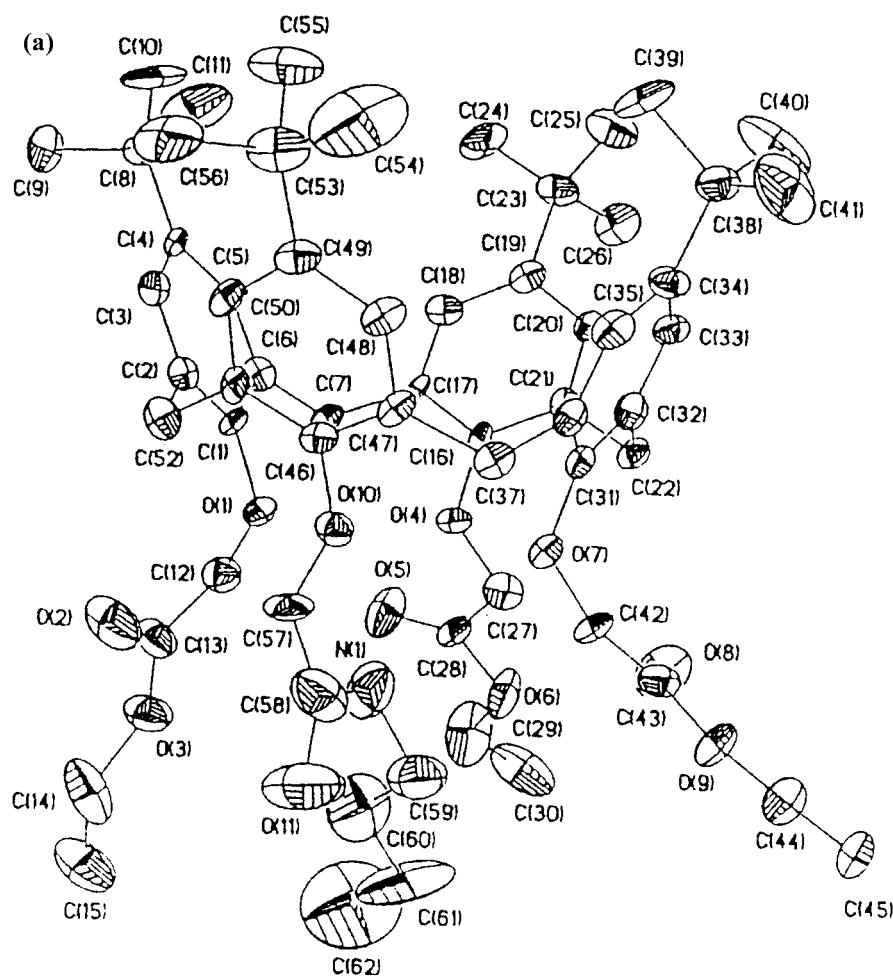
Figure 1. (a) The single crystal structure of compound (**1**); (b) one chain is chosen from the crystal cell. The *p-t*-butyl groups are omitted for clarity.

The crystallography data show that there is a hydrogen bond between the nitrogen atom of the $CH_2C(O)NH(CH_2)_3CH_3$ moiety and the oxygen atom of the phenol unit. The length and angle of N(1)—H—O(10) are 2.634 Å and 100.6°, respectively. It would be the hydrogen bond that restricts the rotation of the *n*-butyl group and induces the bending of the amine chain. It is the reason that the ethyl and not the *n*-butyl group which enters into the cavity of the host compound (**1**).

4. NMR Spectra

From the two dimensional H-H COSY spectrum, the chemical shifts (ppm) of the ethyl groups are 1.36–1.41 (multiplet) and 4.28–4.34 (multiplet) in THF-d_8 solution. There are no great differences among the three ethyl groups, which means
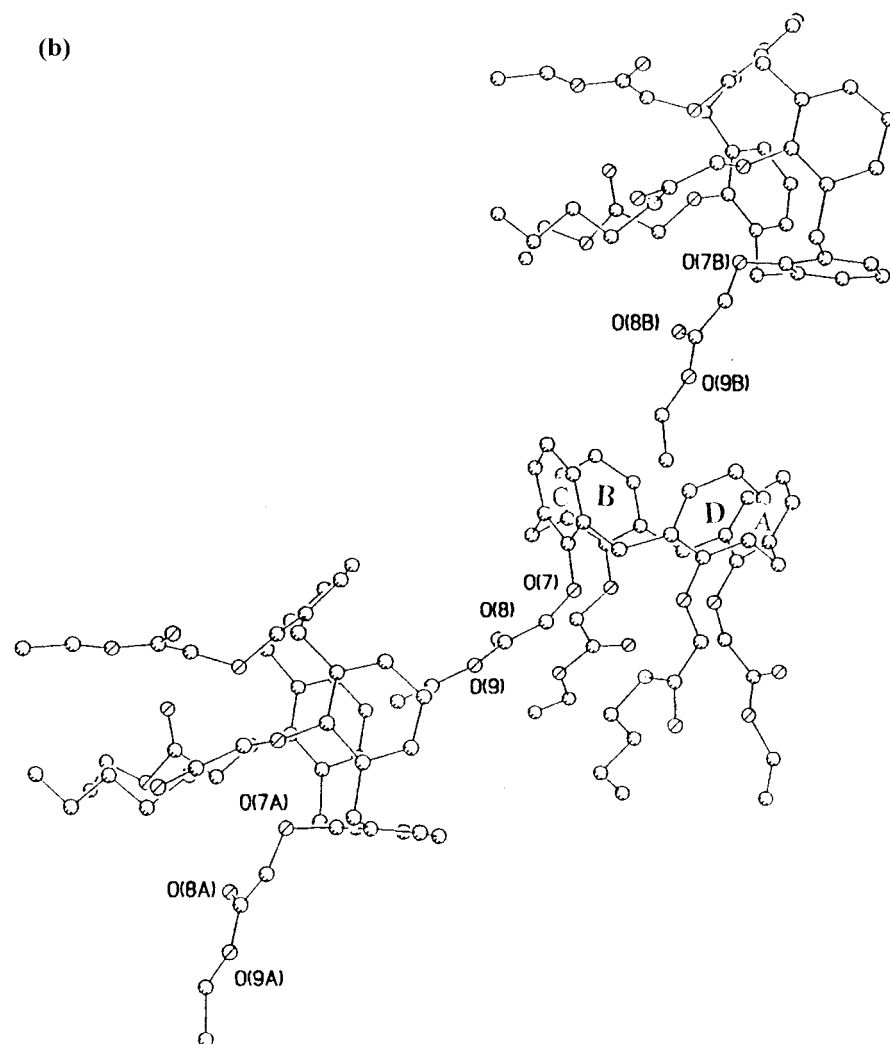
(b)

Figure 1. (Continued)

that their chemical circumstances are almost the same. The same result is found in CDCl$_3$ solution, except that the chemical shifts do differ slightly. So, there is no self-assembly of compound (**1**) whether in THF or CHCl$_3$ solution. From the two-dimensional H-H Noesy spectrum in THF-d$_8$ solution, we can see there are no proton-couplings between the ethyl groups and the *p-t*-butyl phenol units [9], which means that the ethyl group does not enter into the cavity of host compound (**1**). This result provides a further evidence: compound (**1**) doesn't assemble in THF solution. Comparing with the crystal structure of compound (**1**), it could be deduced that compound (**1**) forms a self-assembly host-guest aggregate in the solid state to produce more compact packing and to decrease the energy. Probably,

the crystallization energy acts as another important driving force for host-guest complexation.

In conclusion, we have reported a new facile method – the aminolysis of calix[4]arene ester for synthesizing the calix[4]arene amide, and the crystal structure of a self-assembled calix[4]arene amide via van der Waals interaction. The CH-π interaction and crystallization energy might be the important driving forces for forming the self assembled calix[4]arene amide.

Acknowledgment

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5. Yield (90%); mp 100–103 °C; ESI-MS: m/z 1043 [M + Na$^+$]; IR (KBr): 1754 cm^{-1} $\nu_{C=O(ester)}$, 1679 cm^{-1} $\nu_{C=O(amide)}$; ^{1}H NMR (THF-d$_8$, 500 MHz) δ 1.07–1.10 (t, 3H), 1.21 (s, 27H), 1.26 (s, 9H), 1.37–1.41 (m, 9H), 1.49–1.53 (m, 2H), 1.72–1.77 (m, 2H), 3.32–3.38 (m, 4H), 3.45–3.49 (m, 2H), 4.28–4.34 (m, 6H), 4.56 (s, 2H), 4.76–4.79 (d, 2H), 4.85–4.91 (m, 4H), 4.98–5.00 (d, 2H), 5.01–5.04 (d, 2H), 6.94–7.02 (m, 8H); Anal. Calcd. For C$_{62}$H$_{85}$O$_{11}$N: C, 73.01; H, 8.34; N, 1.37. Found: C, 72.71; H, 8.54; N, 1.30.

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9. H-H Noesy spectrum of compound (**1**): after picking out the cross peaks in the same positions of the H-H COSY spectrum, the proton-couplings are only found between the *p-t*-butyl group and the phenyl group.