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Complex formation between water-soluble sulfonated calixarenes and C_{60} fullerene

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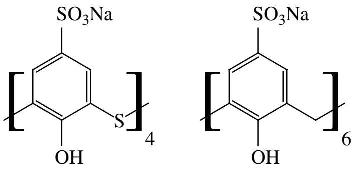
Abstract—The inclusion complexes of sulfonated thiacalix[4]arene **1** and calix[6]arene **2** sodium salts with C_{60} fullerene were investigated by photoluminescence (PL) and quantum-chemical methods. The stoichiometries of calixarene/C_{60} complexes were found to be 2:1 for **1** and 1:1 for **2**. Related quantum-chemical investigations show that C_{60} fullerene is included in a cavity composed of two half-bowl molecules of **1**. The C_{60} fullerene ball is located deep within the cavity of **2** and the negatively charged sulfonate arms probably inhibit the formation of the bowl-shaped capsule that was observed in the case of **1**.

The electron accepting ability of the fullerenes is known to inhibit the activity of redox enzymes[1–3] (e.g., nitric oxide synthase, thus providing a therapeutic approach for some neurodegenerative disorders[4]) and a large number of fullerene derivatives are competitive inhibitors of the human immunodeficiency virus (HIV) protease.[5] However, the very low solubility of fullerenes in aqueous solvents is a major difficulty hindering their application in clinical practice. Several strategies have been developed to increase the water solubility of fullerene derivatives.[6] One of them is the inclusion of C_{60} within water-soluble hosts such as cyclodextrins[7,8] and calixarenes.[9,10] Other approaches such as covalent functionalization of C_{60} with hydrophilic, ionic,[11,12] or nonionic[13,14] organic moieties or electrochemical/chemical reduction of C_{60} to a water-soluble anion[15] have also been utilized to overcome the natural water repulsion of C_{60} fullerene.

Williams et al. first used water-soluble calixarenes to include C_{60},[9] then two independent investigations showed that *p-tert*-butylcalix[8]arene selectively includes the C_{60} fullerene with 1:1 stoichiometry.[16,17] Subsequently efforts were made to study the supramolecular complexes of fullerenes with calixarenes.[6] It turned out that most calixarene–fullerene complexes exist only in the solid state, whereas in solvents they frequently dissociate or precipitate after formation. Therefore the existence of these complexes is difficult to prove by spectroscopic methods.[18]

In our recent papers,[19–21] the complexation behavior and the factors controlling the thermodynamic and kinetic stability or selectivity of some calixarene derivatives towards neutral π-electron deficient species were reported. A paper on the interaction of a water-soluble calixarene with iron ions has been published recently.[22]



1 **2**

Figure 1. Sulfonated thiacalix[4]arene **1** and calix[6]arene **2** investigated in this work.

Herein, we report our results on the inclusion complexes of two sulfonated calixarene derivatives (Fig. 1, the

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sodium salts of thiacalix[4]arene tetrasulfonate **1** and calix[6]arene hexasulfonate **2**) with C_{60} fullerene. In this investigation our earlier developed methodology, based on PL measurements and on Job's method, is used.

In order to investigate the interaction, 10^{-4} M aqueous solutions of **1** or **2** at pH = 7, buffered by TRIS and a 10^{-4} M toluene solution of fullerene were prepared. For the application of Job's method, these solutions were mixed at different molar ratios and the PL spectra of the aqueous phases were recorded. The peaks at 310 nm were used for data evaluation. Both calixarene derivatives showed higher PL intensity in the presence of C_{60} fullerene (Fig. 2). No considerable emission of C_{60} fullerene was observed in the absence of calixarenes. According to our earlier results[19–22] it was concluded that the spectral changes were induced by a weak interaction between the calixarene hosts and the C_{60} guest.

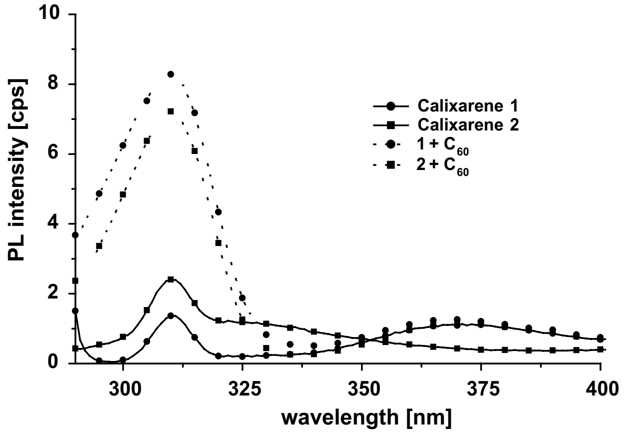

Figure 2. Spectral changes of calixarene derivatives **1** or **2** in the absence and in the presence of 10^{-4} M C_{60} fullerene.

For the experimental determination of thermodynamic properties, Job's method was applied at four different temperatures in the range of 20–35 °C with a step size of 5 °C. The Jobs's curves obtained (Fig. 3) suggest that **1** and **2** form complexes with C_{60} fullerene with 2:1 and 1:1 stoichiometry, respectively. For quantitative evaluation of the Job's curves (where C refers to the calixarene host **1** or **2**; G is the C_{60} fullerene guest; CG and C_2G are the individual types of complexes formed in the studied systems; K_1 and K_2 denote the formation constants of the individual complexes, respectively) the following considerations apply. Assuming that the observed PL signal varies linearly with the concentrations, ΔF in such a system is described by Eq. 1

$$\Delta F = f_{CG}[CG] + f_{C_2G}[C_2G], \tag{1}$$

wherein $\Delta F = F - F_0$ is the difference between the PL intensity obtained with the calixarene–C_{60} system and the PL intensity of the calixarene with the same concentration. The measures of the PL signals, f_{CG} and f_{C_2G} could be observed for the individual C_iG ($i = 1, 2$) species relative to the PL signal of pure calixarene at the same concentrations. By definition,

$$f_{C_iG} = \left. \frac{F([C]) - F([C_iG])}{F([C])} \right|_{[C_iG]=[C]} \quad (i = 1, 2). \tag{2}$$

Using the expressions for the total concentration of the calixarene (Eqs. 3 and 4), the theoretical change of the PL signal in the system studied can be obtained by Eq. 5,

$$C_0 = [C] + K_1[C][G] + 2K_1K_2[C]^2[G], \tag{3}$$

$$G_0 = [G] + K_1[C][G] + K_1K_2[C]^2[G], \tag{4}$$

$$F - F_0 = \frac{G_0\{f_{CG}K_1[C] + f_{C_2G}K_1K_2[C]^2\}}{1 + K_1[C] + K_1K_2[C]^2}, \tag{5}$$

wherein C_0 is the analytical concentration of calixarene, [C] is the equilibrium concentration of calixarene, G_0 and [G] are the analytical and equilibrium concentrations of the C_{60} fullerene, respectively, K_i ($i = 1,2$) is the complex formation constant. Using Eq. 5 the values of K_1 and K_2 as well as f_{CG} and f_{C_2G} could be optimized iteratively: First, Eqs. 3 and 4 are solved numerically for given values of the formation constants and the f_{CG}, f_{C_2G} coefficients. Then, using the equilibrium concentration of the C_{60} fullerene for the given parameters, the theoretical change in the PL signal can be calculated.

We note here, that the K_i values are extraction constants rather than association constants (K_{ass}), which are related by the equation

$$K_{ass} = K_i \cdot K_d, \tag{6}$$

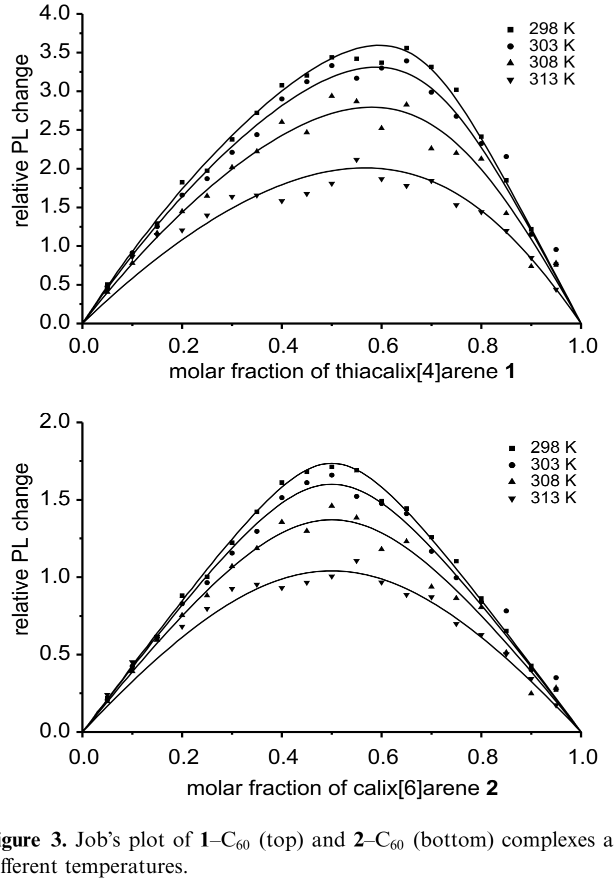

Figure 3. Job's plot of **1**–C_{60} (top) and **2**–C_{60} (bottom) complexes at different temperatures.

where K_d is the distribution coefficient of C_{60} from toluene to water.

However, it is known that the equilibrium in similar systems strongly depends on the temperature.[14] The thermodynamic parameters for the individual complexes formed in the calixarene–C_{60} system can be determined from the van't Hoff equation:

$$\ln K_i = -\frac{\Delta G_i}{RT} = -\frac{\Delta H_i}{RT} + \frac{\Delta S_i}{R} \quad (i = 1, 2), \tag{7}$$

where ΔG_i is the Gibbs free energy change, ΔS_i the entropy change and ΔH_i the enthalpy change associated with complex formation.

Using Eq. 7, inserting this expression for the formation constants into the Eqs. 3–5, the fluorescence change in Eq. 5 can be expressed as a function of the ΔH_i, ΔS_i values and the f_{CG}, f_{C_2G} coefficients.

The thermodynamic parameters associated with the K_i values were determined from the Job's curves by an iterative solution of Eqs. 1–5 using the expression of K_i values from the van't Hoff equation (Eq. 7). In the case of host **1** (Fig. 3 top, Table 1), the enthalpy, entropy, and also the Gibbs free energy changes for both complexation steps are nearly the same. The complexation of **2** with the fullerene guest shows higher energy changes (Fig. 3 bottom, Table 2), however, with 1:1 calixarene–fullerene stoichiometry.

Table 1. Thermodynamic parameters of complexation of calixarene **1** with C_{60} fullerene

Coord. step	Log K_i	Log β_i	ΔG^0 (kJ mol^{-1})	ΔH^0 (kJ mol^{-1})	ΔS^0 (J K^{-1} mol^{-1})
1	5.08 (5)	5.08	−28.97 (8)	−37.11 (5)	−27.32 (3)
2	4.98 (5)	10.06	−28.43 (8)	−38.41 (5)	−33.46 (3)

Table 2. Thermodynamic parameters of complexation of calixarene **2** with C_{60} fullerene

Coord. step	Log K_i	Log β_i	ΔG^0 (kJ mol^{-1})	ΔH^0 (kJ mol^{-1})	ΔS^0 (J K^{-1} mol^{-1})
1	5.48 (4)	5.48	−31.29 (8)	−42.37 (5)	−37.17 (3)

Our related quantum-chemical calculations show that C_{60} fullerene is included in a cavity composed of two half-bowl molecules of **1** (Fig. 4). Interestingly, the C_{60} fullerene ball lies much more deeply in the cavity of **2**. The close proximity of the negatively charged sulfonate arms probably inhibits the formation of the bowl-shaped capsule found in the case of **1**.

In summary, we can conclude that water-soluble tetrasulfonated thiacalix[4]arene and hexasulfonated calix[6]arene form complexes with C_{60} fullerene exhibiting 2:1 and 1:1 stoichiometry, respectively. This observation makes these compounds promising candidates to overcome the natural water-repulsive character of C_{60} fullerene.

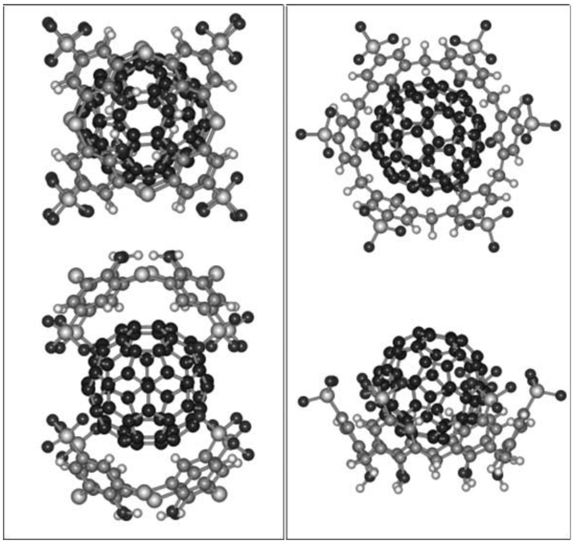

Figure 4. Top and side views of the equilibrium conformations of **1**–C_{60} (left) and **2**–C_{60} (right) complexes calculated by quantum-chemical methods.

Experimental

Both hosts were synthesized as described in the literature. Thus, thiacalix[4]arene-tetrasulfonate salt **1** was obtained by the *ipso* sulfonation of *p-tert*-butylthiacalix[4]arene,[23] while calix[6]arene-hexasulfonate salt **2** was prepared by direct sulfonation of the parent calix[6]-arene with concentrated sulfuric acid.[24] A highly sensitive Fluorolog τ3 spectrofluorometric system (Jobin-Yvon/SPEX) was used to investigate the photoluminescence (PL) spectra of the different solutions. For data collection a photon counting method with 0.4 s integration time was used. Excitation and emission bandwidths were set to 1 nm. A 1 mm layer thickness of the fluorescent probes with front face detection was used to eliminate the inner filter effect. The fluorometric experiments were carried out at pH = 7.0 using TRIS, Tris(hydroxymethyl)aminomethane (Merck) buffer. The exact pH value was reached by the addition of 0.1 M HCl. The equilibrium conformations of calixarene derivatives and their complexes with C_{60} fullerene were studied with semi-empirical AM1 (Austin Model) method, followed by ab initio HF/6-31G* calculations. The Fletcher–Reeves geometry optimization method was used for the investigation of the conformers. All calculations were carried out with the HyperChem Professional 7 program package.[25]

Acknowledgements

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