A Novel [60]Fullerene-Calixarene Conjugate Which Facilitates Self-Inclusion of the [60]Fullerene Moiety into the Homooxacalix[3]arene Cavity

Atsushi Ikeda,[a] Shigeki Nobukuni,[a] Hiromi Udzu,[a] Zhenlin Zhong,[a] and Seiji Shinkai*[a]

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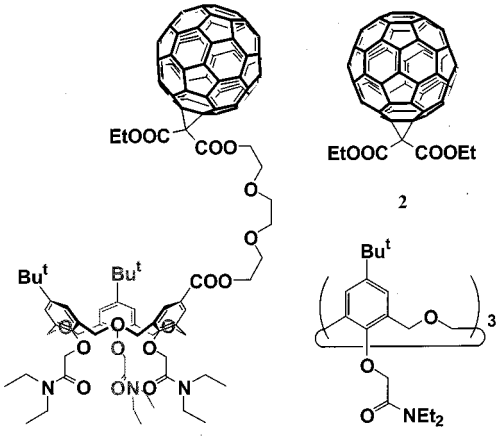
A novel calixfullerene **1**, in which a homooxacalix[3]arene moiety conjugates with a [60]fullerene moiety through a triethylene glycol chain, exhibits interesting self-complexation–decomplexation properties in response to the solvent polarity. In $CDCl_3$, **1** exists predominantly as conformer I with a free [60]fullerene moiety and the open calixarene cavity. In $CHCl_3/CH_3CN$ (1:1, v/v), however, **1** exists predominantly as the self-inclusion conformer II with the [60]fullerene moiety capped by the intramolecular calixarene moiety. This is a unimolecular event but not an aggregate formation event because the concentration effect on the stoichiometry in the ^1H NMR spectroscopy and molecular weight determination in vapor pressure osmometry are all commensurate with a unimolecular process. The complexation–decomplexation exchange rate is slower than the NMR time scale, which has enabled us to estimate the equilibrium constant [conformer II/conformer I = 0.72 in $CHCl_3/CH_3CN$ (24:1, v/v) at 27 °C].

Introduction

In the field of host-guest chemistry, much attention has been devoted toward the use of half-bowl-shaped host molecules such as calixarenes,[1–5] cyclodextrins,[6] cyclotriveratrylene,[7] resorcinarenes[8] and other macrocyclic molecules[9] to design receptor molecules which can form stable host-guest-type complexes with large guest molecules. Particular interest is now focused on the inclusion of globular-shaped fullerenes.[10] The host-guest-type interactions in these inclusion complexes have successfully been applied to the purification of fullerenes,[2] water-solubilization of fullerenes,[5,6] photocleavage of DNA,[5] design of photovoltaic cells,[11] etc. In spite of a large number of studies on the inclusion complexes of fullerenes in organic solvents, only few attempts have so far been extended to the fullerene-related interdisciplinary research areas. It is undoubted that one major reason for this is related to the low association constants between the receptor molecules and [60]fullerene in organic solvents. Although calixarene dimers[3] and a capsular molecule[4] have relatively high association constants by including [60]fullerene in the three-dimensional cavities, the association constants are not yet sufficiently high for applying these systems to photochemical and electrochemical fields where [60]fullerene should play an important role as an electron pool. One possible approach to solve this low association-constant problem is to connect a receptor moiety intramolecularly to [60]fullerene by a flexible linker. A few [60]fullerene derivatives connected to calix[*n*]arenes have already been reported.[12] In 1994, we reported a calixfullerene[12a] in which the [60]fullerene moiety is connected to a lower rim OH group in calix[8]arene. Although this conjugate could form an intramolecular inclusion complex in the solid state, no clear evidence for inclusion of the [60]fullerene moiety in the calixarene cavity was obtained in the solution state. Reexamining the structure of the calixfullerene in light of the results described below about calixarene–fullerene interactions, we found that the possible reasons are that the calix[8]arene moiety in which one of the OH groups was alkylated has only very weak binding ability and that the [60]fullerene moiety is connected onto a lower rim which is on the opposite side to the cavity. We thus designed and synthesized a novel calixfullerene **(1)** in which the [60]fullerene moiety is connected to an upper rim OH group of a cone-conformation homooxacalix[3]arene moiety (which is known to interact with [60]fullerene[2a]) through a triethylene glycol chain. Since [60]fullerene and its derivatives are poorly soluble in polar solvents,[13] one may expect that the [60]fullerene moiety is desolvated in these polar solvents and should be able to be captured by the π-aromatic homooxacalix[3]arene cavity. This means, if it really occurs, that in **1** the complexation–decomplexation processes can be readily controlled by the solvent effect.



[a] Department of Chemistry and Biochemistry, Graduate School of Engineering, Kyushu University,
Fukuoka 812–8581, Japan
Fax: (internat.) +81-92/642-3611
E-mail: seijitcm@mbox.nc.kyushu-u.ac.jp

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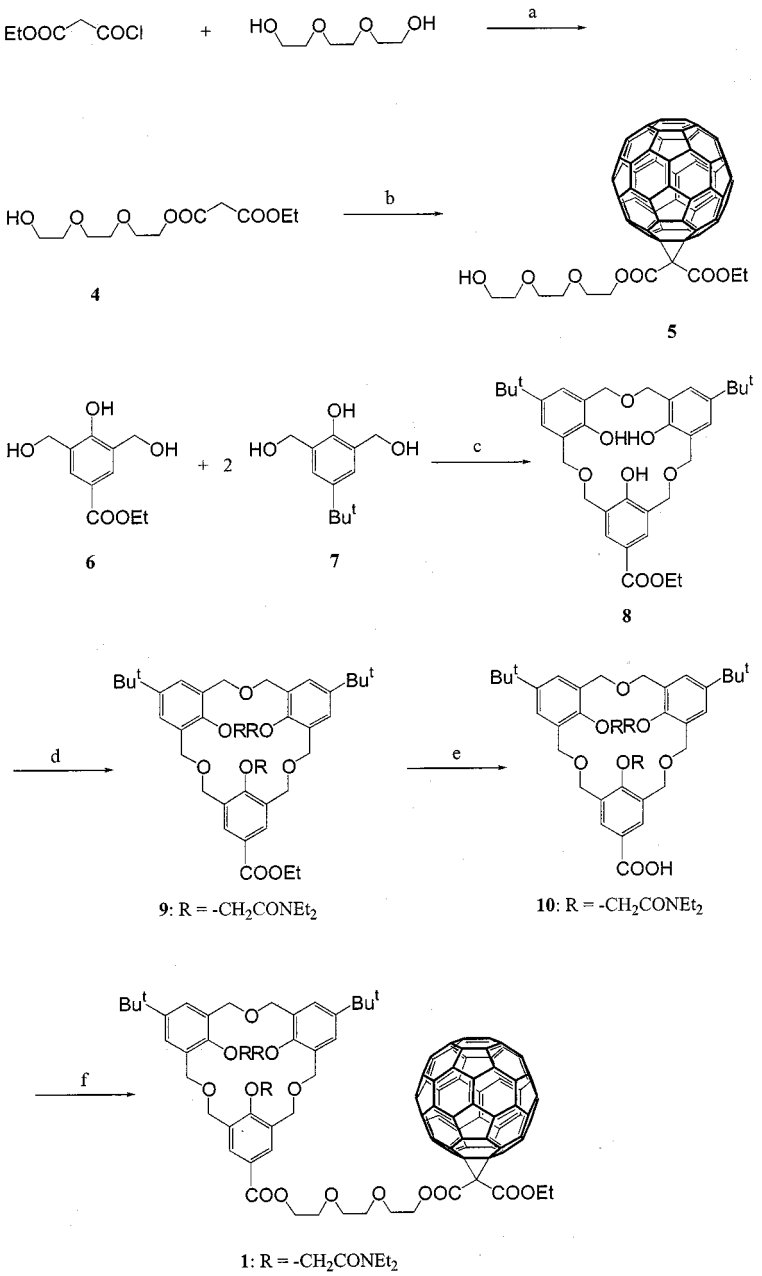
Results and Discussion

Synthesis of Compound 1

The synthetic route for compound **1** is depicted in Scheme 1. Fuji et al. previously reported the stepwise synthesis of homooxacalix[3]arenes bearing different substituents on the upper rim.[14] We designed a more convenient one-step procedure to reach compound **8** with two *tert*-butyl and one ethyl ester groups on the upper rim. The isolated yield is 26% which is comparable to that of Fuji's method (ca. 15−30%). Treatment of **8** with *N*,*N*-diethylchloroacetamide yielded cone-**9**, in which interconversion between cone- and partial-cone-conformations is suppressed by the bulky diethylacetamide substituents on the phenolic oxygens.[15] In the last step, a calixarene moiety and a [60]fullerene moiety were coupled with the flexible triethylene glycol chain so that the homooxacalix[3]arene moiety can include the [60]fullerene moiety in its own cavity.

UV/Vis Absorption Spectroscopy

We measured the UV/Vis absorption spectra of **1** (0.10 mM) as a function of the solvent composition. As shown in Figure 1a, the absorption band near 425 nm shows a hypochromic shift with increase in the CH_3CN



Scheme 1. Synthesis of compound **1**; reagents and reaction conditions: (a) ethyl malonyl chloride (1.0 equiv.), pyridine, dry CH_2Cl_2, room temperature, 36 h, 72%; (b) CBr_4 (1.0 equiv.), DBU (2.0 equiv.), toluene, room temperature, 12 h, 28%; (c) **6** (0.33 equiv.), *p*-xylene, reflux, 22 h, 26%; (d) 2-chloro-*N*,*N*-diethylacetamide (5 equiv.), NaH (5 equiv.), NaI (0.25 equiv.), reflux, 6 h, 22%; (e) NaOH (3.0 equiv.), EtOH/H_2O, room temperature, 3 days, 88%; (f) **8** (1.0 equiv.), EDC (1.0 equiv.), DMAP (1.0 equiv.), CH_2Cl_2, room temperature, 18 h, 21%

concentration. However, a similar spectral change was observed for the UV/Vis absorption spectra of **2** (0.10 mM) without the intramolecular calixarene cavity (Figure 1b). These results imply that these spectral changes are caused by a change in the solvent polarity. Clear evidence for the intramolecular interaction of **1** was not obtained in polar solvents by UV/Vis absorption spectroscopy. Presumably, the spectral change induced by the fullerene−calixarene interaction is smaller in asymmetrically substituted [60]fullerenes than in symmetrically unmodified [60]fullerene.[8c]

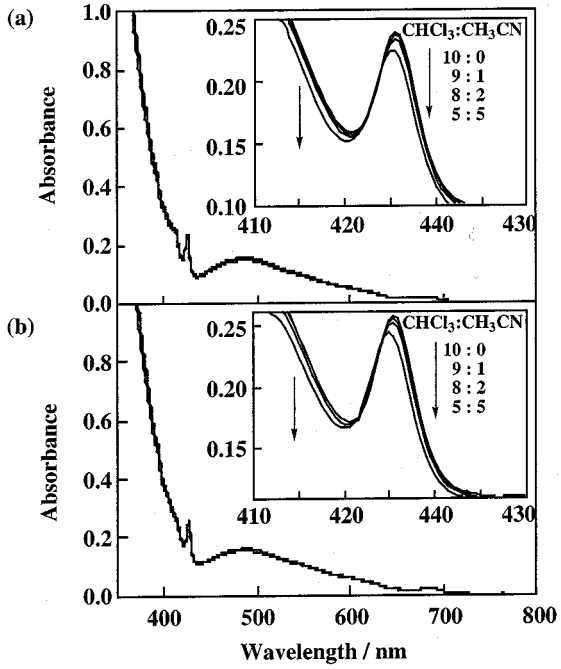


Figure 1. UV/Vis spectra of (a) **1** (0.1 mM) and (b) **2** (0.1 mM) in $CDCl_3/CD_3CN$ = 1:0, 9:1, 4:1 and 1:1 (v/v) at 25 °C

^{1}H NMR Spectroscopy

Compound **1** gives a very complicated ^{1}H NMR spectrum in $CDCl_3$ (Figure 2a). As shown in Figure 2, however, the spectrum changes significantly upon addition of CD_3CN: the peaks marked with open circles decrease with the increase in the ratio of CD_3CN, whereas the peaks marked with filled circles increase. All the peaks observed in $CDCl_3$ or $CDCl_3/CD_3CN$ = 1:1 (v/v) can be assigned with the aid of ^{1}H-^{1}H COSY spectroscopy to two conformers: conformer I (open circle) and conformer II (filled circle). The equilibrium constant (= conformer I/conformer II) decreases with the addition of CD_3CN, namely, 3.40, 1.39. 0.20, 0.29 and 0.00 in $CDCl_3/CD_3CN$ = 1:0, 24:1, 9:1, 4:1 and 1:1 (v/v), respectively. To confirm that none of these two conformers is the degradation product, we carried out the following three experiments with a solution used for Figure 2d, in which **1** predominantly exists as conformer II. Firstly, a thin-layer chromatogram showed that conformer II in this solution gives the same R_f value as highly purified **1**. Secondly, the MALDI-TOF MS measurement established that conformer II has the same molecular weight as **1**. Finally, the solution was once evaporated to dryness and the residue was dissolved again in $CDCl_3$. The ^{1}H NMR spectrum of the solution thus obtained was identical to that in Figure 2a. These results unambiguously support the view that conformer II is not the degradation product of **1** but one solvent−dependent conformer of **1**. In a **2** + **3** mixed system (2.0 mM each), on the other hand, no new ^{1}H NMR peak appears upon addition of CH_3CN.

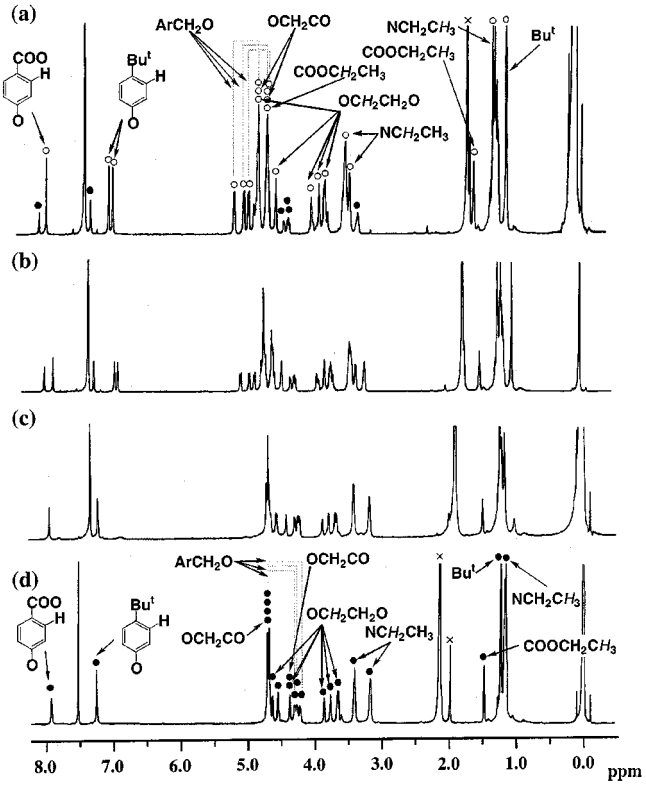


Figure 2. ^{1}H NMR spectra (600 MHz, 27 °C) of **1** (2.0 mM) in $CDCl_3/CD_3CN$ = (a) 1:0, (b) 24:1, (c) 9:1 and (d) 1:1 (v/v)

In $CDCl_3$, conformers I and II have three pairs of doublets for the $ArCH_2OCH_2Ar$ methylene protons (conformer I: δ = 4.53 and 4.90, 4.55 and 4.82 and 4.70 and 5.04; conformer II: δ = 4.21 and 4.67, 4.23 and 4.65 and 4.28 and 4.63) and three different kinds of ArH protons [conformer I: δ = 6.89, 6.91 and 7.83; conformer II: δ = 7.13 (the b_1 and b_2 protons in Figure 3 overlap with each other) and 7.93] (Table 1). This splitting pattern is commensurate with a structure of C_s symmetry (Figure 3). It is known that in cone-homooxacalix[3]arene the chemical shift difference ($\Delta\delta_H = \delta_{Heq} - \delta_{Hax}$) between axial ($H_{ax}$) and equatorial ($H_{eq}$) protons in the $ArCH_2OCH_2Ar$ methylene groups is useful as a measure for the phenyl units′ inclination:[2b,16] in conventional calix[*n*]arenes the phenyl rings are more flattened with the increase in the $\Delta\delta_H$, whereas the reverse correlation is seen for homooxacalix[3]arenes.[2b] The $\Delta\delta_H$ values for conformer I are 0.28, 0.36 and 0.38 ppm. In contrast, the $\Delta\delta_H$ values for conformer II are increased to 0.36, 0.43 and 0.49 ppm. These results indicate that the phenyl groups in conformer II are less flattened than those in conformer I; undoubtedly, this conformational change is induced by inclusion of the [60]fullerene moiety into the cavity.[2b,17] Furthermore, the peaks of the $ArCH_2OCH_2Ar$ methylene protons in conformer II appear very close to

Table 1. Chemical shifts and Δδ of $ArCH_2OCH_2Ar$ methylene protons

Conformer I			Conformer II		
δ_{Heq} (ppm)	δ_{Hax} (ppm)	Δδ (ppm)	δ_{Heq} (ppm)	δ_{Hax} (ppm)	Δδ (ppm)
4.90	4.53	0.37	4.67	4.21	0.36
4.82	4.55	0.27	4.65	4.23	0.42
5.04	4.70	0.26	4.63	4.28	0.35

$\Delta\delta = \delta_{Heq} - \delta_{Hax}$.

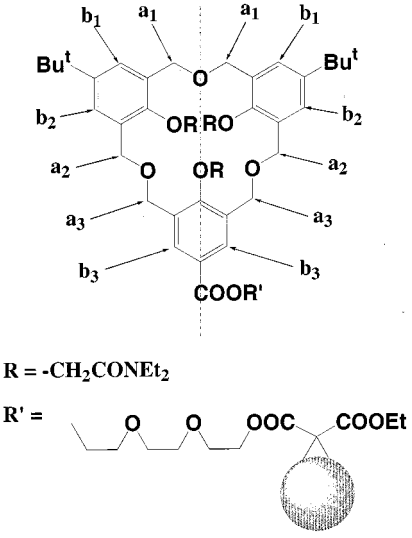


Figure 3. Symmetry of compound **1**

Table 2. NOE peak intensities (%) of the ArH protons with respect to the methyl protons in the malonate group of **1** [$CDCl_3$/CD_3CN = 24:1 (v/v), 27 °C]

	b_1	b_2	b_3
Conformer I	0.05[a]	0.04[a]	0.07
Conformer II	0.11[b]		0.09

[a] The b_1 and b_2 protons could not be assigned. The protons at δ_H = 6.89 and 6.91 were tentatively assigned to b_1 and b_2, respectively. – [b] The b_1 and b_2 protons overlapped with each other.

each other [$\Delta\delta_{Hax}$ = 0.07 ppm (4.21–4.28 ppm) and $\Delta\delta_{Heq}$ = 0.04 ppm (4.63–4.67 ppm) compared to those for conformer I, $\Delta\delta_{Hax}$ = 0.29 ppm (4.53–4.82 ppm) and $\Delta\delta_{Heq}$ = 0.22 ppm (4.82–5.04 ppm)]. These results consistently suggest that the calixarene ring of conformer II has a C_{3v} symmetrical structure. One may consider, therefore, that conformer II includes the [60]fullerene moiety in the cavity. To further confirm the [60]fullerene inclusion, we conducted a nuclear Overhauser effect (NOE) experiment on **1** in $CDCl_3/CD_3CN$ (24:1, v/v), where conformers I and II exist in a nearly 1:1 ratio (400 MHz, 25 °C). Table 2 shows the NOE peak intensities of the ArH protons with respect to the methyl group of the malonate. These results establish that the distance between the homooxacalix[3]arene moiety and the [60]fullerene moiety in conformer II is shorter than that in conformer I. This trend is clearly commensurate with a conformation featuring inclusion of the [60]fullerene moiety.

Evidence for the Self-Inclusion

The foregoing spectral findings can be explained in three different ways: (i) self–inclusion of the [60]fullerene moiety (Figure 4a), (ii) intermolecular inclusion to form the dimer (Figure 4b), and (iii) higher-order oligomerization (Figure 4c). To evaluate which phenomenon is really taking place in solution, we examined the concentration effect on the spectroscopic properties. In the ^1H NMR spectrum, the ratio of I vs. II is scarcely affected by a change in the concentration of **1** ([**1**] = 0.5–5.0 mM, $CDCl_3$, room temperature). These result shows that the equilibrium between the two conformers I and II is a concentration-independent, intramolecular event (i). Furthermore, the average molecular weight determined by vapor pressure osmometry (VPO) in $CHCl_3/CH_3CN$ (1:1, v/v) is 1361 ± 600. This value is in agreement with that calculated for monomeric **1** (theoretical MW = 1867).

As a summary of the foregoing findings, one can now propose that conformer II includes the [60]fullerene moiety into its own cavity (as shown in Figure 4a). The equilibrium constant can be readily estimated from the ^1H NMR spec-

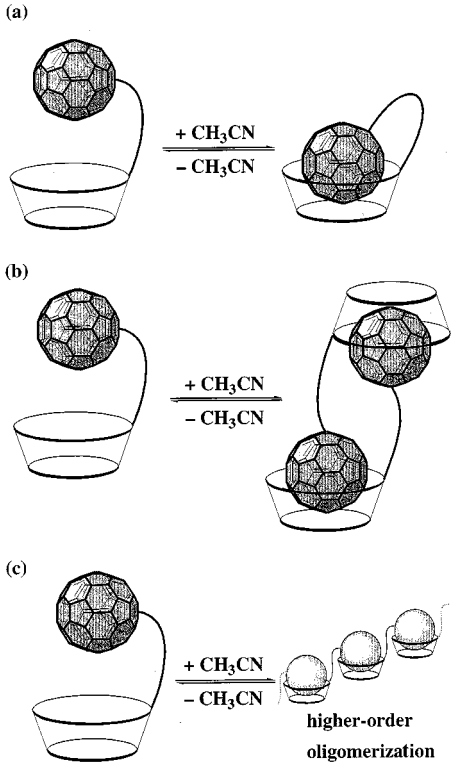


Figure 4. Possible interactions between calixarene-[60]fullerene or [60]fullerene-[60]fullerene; (a) an intramolecular event in which the [60]fullerene moiety is intramolecularly included in the calixarene cavity, (b) an intermolecular event in which the [60]fullerene moiety is intermolecularly included in the other calixarene cavity and (c) an intermolecular event in which the [60]fullerene moieties aggregate by themselves

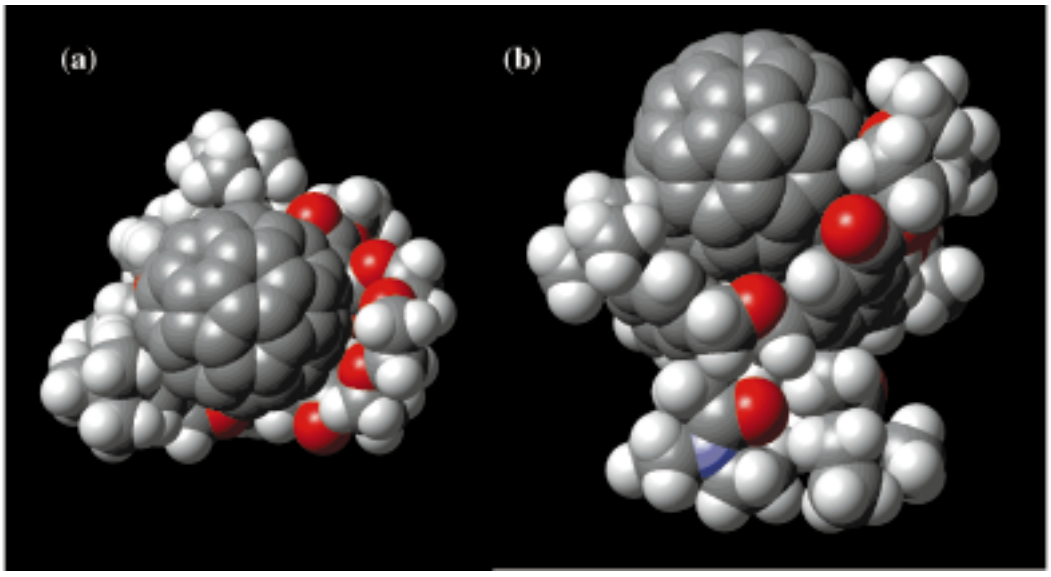


Figure 5. Energy-minimized structure of conformer II: (a) top view and (b) side view

tra to be conformer I/conformer II = 0.72 in $CDCl_3$/CD_3CN (24:1, v/v) at 27 °C. The energy-minimized structure of conformer II was generated by computational molecular modeling (Figure 5). Very interestingly, the calixarene moiety has C_{3v} symmetry which agrees well with the results obtained from NMR spectroscopy.

Conclusion

In conclusion, the present paper presents the first unequivocal evidence for intramolecular inclusion of [60]fullerene in its own cavity. The complexation−decomplexation exchange rate is slower than the NMR time scale, which has enabled us to estimate the equilibrium constant for self-inclusion. In addition, the ratio between complexed conformer II and decomplexed conformer I is independent of the concentration but can be controlled by the solvent effect. Particularly, **1** exists as conformer II in 100% purity in $CDCl_3/CD_3CN$ (1:1, v/v). Based on the foregoing findings, one can foresee several intriguing extensions: for example (i) one may estimate "unimolecular" chemical and physical properties of [60]fullerene derivatives in polar solvents, (ii) one may suppress undesired photodimerization of [60]fullerene, and (iii) one may dissolve [60]fullerene derivatives in high concentration even in polar solvents. We believe that these extensions would result in fruitful findings in fullerene functionalization.

Experimental Section

Melting points were determined on a Micro Melting Point Apparatus (Yanaco MP-500D) and uncorrected. The routine ^1H and ^{13}C NMR measurements and the specific measurements such as 2D COSY and VT NMR were carried out with a Bruker AC-250P (250 MHz) or DRX 600 (600 MHz) spectrometer. On the other hand, the NOE measurements were carried out with a JEOL GX-400 (400 MHz) spectrometer. UV/Vis spectra were measured on a Shimadzu UV-2500PC spectrometer. Mass spectra were performed with a PerSeptive Voyager RP spectrometer. Vapor pressure osmometry measurements were carried out with a Knauer Vapor Pressure Osmometry. Model buildings and molecular dynamics calculations were performed with an Insight II/Discover 98 software packaged in the context of the Molecular Simulations Inc. (MSI). All calculations were performed with the Extensive Systematic Force Field (ESFF). The initial calculation was carried out in vacuo by molecular dynamics (MD) minimization around 500 K, followed by molecular mechanics (MM). The syntheses of compounds **2**,[18] **3**,[19] **6**[20] and **7**[21] were described previously. In the elemental analyses, even though the samples were dried at room temperature under vacuum for a few days, the solvent molecules could not be removed (as frequently seen for solid calixarenes).

Ethyl 2-[2-(2-Hydroxyethoxy)ethoxy]ethyl Malonate (4): Triethylene glycol (2.00 g, 13.3 mmol) and pyridine (0.35 g, 4.4 mmol) were mixed in 30 mL of dry CH_2Cl_2. To this solution was added an ethyl malonyl chloride solution (0.33 g, 2.2 mmol) in 10 mL of dry CH_2Cl_2 from a dropping funnel for 1 h. The mixture was stirred at room temperature for 36 h. The reaction was stopped with aqueous 1 N HCl solution and the organic layer was separated, washed twice with water and dried over $MgSO_4$. After evaporation to dryness, the residue was purified twice by column chromatography (silica gel, $CHCl_3$). Yield 0.42 g (72%). − ^1H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.34−4.31 (m, 2 H, OCH_2), 4.22 (q, J = 7.1 Hz, 2 H, $COOCH_2CH_3$), 3.75−3.50 (m, 10 H, OCH_2), 3.42 (s, 2 H, $COCH_2CO$), 2.79 (s, 1 H, OH), 1.28 (t, J = 7.1 Hz, 3 H, $COCH_2CH_3$). − $C_{11}H_{20}O_7{\cdot}H_2O$ (282.29): calcd. C 49.99, H 7.63; found C 49.77, H 7.52.

Ethyl 2-[2-(2-Hydroxyethoxy)ethoxy]ethyl 1,2-Methano[60]fullerene-61,61-dicarboxylate (5): [60]Fullerene (0.58 g, 0.80 mmol) and **4** (0.21 g, 0.80 mmol) were mixed in 250 mL of toluene. After cooling to 0 °C, carbon tetrabromide (0.27 g, 0.80 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.02 g, 1.60 mmol) were added to this solution. The mixture was stirred at room temperature for 12 h. The reaction was quenched with water and the organic solution was separated, washed twice with water and dried over $MgSO_4$. After evaporation to dryness, the residue was purified twice by column chromatography (silica gel, toluene and then $CHCl_3$). Yield

0.22 g (28%); M.p. >350 °C (decomp.). − ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 4.67 (t, *J* = 4.5 Hz, 2 H, OCH_2), 4.57 (q, *J* = 7.0 Hz, 2 H, $COOCH_2CH_3$), 3.89 (t, *J* = 4.5 Hz, 2 H, OCH_2), 3.75−3.68 (m, 6 H, OCH_2), 3.62 (t, *J* = 4.5 Hz, 2 H, OCH_2), 1.50 (t, *J* = 7.2 Hz, 3 H, $COOCH_2CH_3$). − $C_{71}H_{18}O_7$·0.41$CHCl_3$ (1031.79): calcd. C 83.12, H 1.80; found C 82.88, H 2.05. − MS [MALDI-TOF, 2-(4-hydroxyphenylazo)benzoic acid matrix]: *m*/*z*: calcd. 1005.3 $[M + Na]^+$; found 1005.7.

7-Ethoxycarbonyl-15,23-di-*tert*-butyl-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene-25,26,27-triol (8): 2,6-Bis(hydroxymethyl)-4-*tert*-butylphenol **(6)** (0.28 g, 1.35 mmol) and 4-hydroxy-3,5-bis(hydroxymethyl)benzoic acid ethyl ester **(7)** (0.10 g, 0.45 mmol) were mixed in 30 mL of *p*-xylene in a 100 mL flask equipped with a Dean−Stark collector. The mixture was stirred at reflux temperature for 22 h. After evaporation to dryness, the residue was purified by column chromatography [silica gel, ethyl acetate/hexane = 1:10 (v/v)]. Yield 0.07 g (26%); M.p. 131.2−133.2 °C. − ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 9.38 (s, 1 H, OH), 8.47 (s, 2 H, OH), 7.84 (s, 2 H, ArH), 7.14 (s, 4 H, ArH), 4.73 (s, 12 H, $ArCH_2O$), 4.32 (q, *J* = 7.1 Hz, 2 H, $COOCH_2CH_3$), 1.36 (t, *J* = 6.9 Hz, 3 H, $COOCH_2CH_3$), 1.25 [s, 18 H, $C(CH_3)_3$]. − $C_{35}H_{44}O_8$·0.7$CH_3COOC_2H_5$ (654.40): calcd. C 69.38, H 7.64; found C 69.17, H 7.42.

7-Ethoxycarbonyl-15,23-di-*tert*-butyl-25,26,27-tris(*N*,*N*-diethylaminocarbonylmethoxy)-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene (9): Compound **8** (0.80 g, 1.35 mmol) was treated with sodium hydride (60% oil susp., 0.26 g, 6.50 mmol) and sodium iodide (0.05 g, 0.33 mmol) in 55 mL of dry THF at 60 °C under a nitrogen stream. After 1 h, 2-chloro-*N*,*N*-diethylacetamide (0.88 g, 6.50 mmol) was added and the mixture was stirred at reflux temperature for 6 h. After cooling, the mixture was diluted with aqueous 1.0 M acetic acid and extracted with $CHCl_3$. The organic solution was washed twice with water and dried over $MgSO_4$. After evaporation to dryness, the residue was purified by column chromatography [silica gel, $CHCl_3$/acetone = 1:1 (v/v)]. Yield 0.27 g (22%); M.p. 127.0−129.3 °C. − ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.81 (s, 2 H, ArH), 6.92 (s, 2 H, ArH), 6.87 (s, 2 H, ArH), 5.03 (d, *J* = 13.2 Hz, 2 H, $ArCH_2O$), 4.90 (d, *J* = 12.6 Hz, 2 H, $ArCH_2O$), 4.83 (d, *J* = 13.2 Hz, 2 H, $ArCH_2O$), 4.78−4.61 (m, 4 H, $ArCH_2O$, $ArOCH_2$), 4.59−4.50 (m, 8 H, $ArCH_2O$ and $ArOCH_2$), 4.31 (q, *J* = 7.1 Hz, 2 H, $COOCH_2CH_3$), 3.42−3.34 (m, 12 H, NCH_2CH_3), 1.35 (t, *J* = 7.1 Hz, 3 H, $COOCH_2CH_3$), 1.30−1.13 (m, 18 H, NCH_2CH_3), 1.02 [s, 18 H, $C(CH_3)_3$]. − $C_{53}H_{77}N_3O_{11}$·0.2$CHCl_3$ (956.05): calcd. C 66.83, H 8.14, N 4.39; found C 66.77, H 8.31, N 4.46. − MS [MALDI-TOF, 2-(4-hydroxyphenylazo)benzoic acid matrix]: *m*/*z*: calcd. 955.2 $[M + Na]^+$; found 955.0.

7-Carboxy-15,23-di-*tert*-butyl-25,26,27-tris(*N*,*N*-diethylaminocarbonylmethoxy)-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene (10): Compound **9** (80 mg, 0.086 mmol) was treated with aqueous 1.27 M NaOH solution (0.9 mL, 0.25 mmol) and 3 mL of EtOH. The mixture was stirred at room temperature for 3 days. The mixture was diluted with aqueous 1.0 M HCl solution and the resultant solution was extracted with $CHCl_3$. The organic solution was washed twice with water and dried over $MgSO_4$. After evaporation to dryness, the residue was used for the next step. Yield 70 mg (88%). − ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.55 (s, 2 H, ArH), 7.01 (s, 4 H, ArH), 4.97−4.87 (m, 6 H, $ArCH_2O$), 4.77 (s, 2 H, $ArOCH_2$), 4.65−4.49 (m, 10 H, $ArCH_2O$ and $ArOCH_2$), 3.47−3.28 (m, 12 H, NCH_2CH_3), 1.25−1.13 (m, 18 H, NCH_2CH_3), 1.10 [s, 18 H, $C(CH_3)_3$]. − $C_{51}H_{73}N_3O_{11}$·0.5$CHCl_3$ (963.81): calcd. C 64.18, H 7.69, N 4.36; found C 64.28, H 7.95, N 4.66. − MS [MALDI-TOF, 2-(4-hydroxyphenylazo)benzoic acid matrix]: *m*/*z*: calcd. 926.5 $[M + Na]^+$; found 929.0.

Compound 1: Compound **5** (70 mg, 0.077 mmol), 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide (EDC) (15 mg, 0.077 mmol) and 4-(dimethylamino)pyridine (DMAP) (9.0 mg, 0.077 mmol) were mixed in 5 mL of dry CH_2Cl_2. The mixture was stirred at room temperature for 18 h. The organic solution was washed twice with saturated aqueous ammonium solution and once with brine and then dried over $MgSO_4$. After evaporation to dryness, the residue was purified by column chromatography [silica gel, $CHCl_3$:MeOH = 20:1 (v/v)]. Yield 30 mg (21%); M.p. 132.0−134.0 °C.

Conformer I: ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.83 (s, 2 H, ArH), 6.91 (s, 2 H, ArH), 6.86 (s, 2 H, ArH), 5.04 (d, *J* = 13.8 Hz, 2 H, $ArCH_2O$), 4.90 (d, *J* = 13.2 Hz, 2 H, $ArCH_2O$), 4.82 (d, *J* = 13.2 Hz, 2 H, $ArCH_2O$), 4.76−4.62 (m, 6 H, $ArCH_2O$, $ArOCH_2$ and OCH_2), 4.62−4.48 (m, 10 H, $ArCH_2O$, $ArOCH_2$ and $COOCH_2CH_3$), 4.46−4.39 (m, 2 H, OCH_2), 3.94−3.85 (m, 2 H, OCH_2), 3.83−3.75 (m, 2 H, OCH_2), 3.75−3.64 (m, 4 H, OCH_2), 3.49−3.27 (m, 12 H, NCH_2CH_3), 1.49 (t, *J* = 7.1 Hz, 3 H, $COOCH_2CH_3$), 1.25−1.05 (m, 18 H, NCH_2CH_3), 1.01 [s, 18 H, $C(CH_3)_3$].

Conformer II: ^{1}H NMR [600 MHz, $CDCl_3$/CD_3CN = 1:1 (v/v), 25 °C]: δ = 7.90 (s, 2 H, ArH), 7.23 (s, 4 H, ArH), 4.77−4.65 (m, 10 H, $ArCH_2O$ and $ArOCH_2$), 4.65−4.58 (m, 2 H, OCH_2),), 4.54 (q, *J* = 7.2 Hz, 2 H, $COOCH_2CH_3$), 4.38−4.32 (m, 4 H, $ArOCH_2$ and OCH_2), 4.31−4.17 (m, 6 H, $ArCH_2O$), 3.87−3.78 (m, 2 H, OCH_2), 3.77−3.70 (m, 2 H, OCH_2), 3.70−3.53 (m, 4 H, OCH_2), 3.40−3.33 (m, 6 H, NCH_2CH_3), 3.20−3.10 (m, 6 H, NCH_2CH_3), 1.46 (t, *J* = 7.2 Hz, 3 H, $COOCH_2CH_3$), 1.22 [s, 18 H, $C(CH_3)_3$], 1.19−1.10 (m, 18 H, NCH_2CH_3). − $C_{122}H_{89}N_3O_{17}$·1.88CH_2Cl_2 (2028.69): calcd. C 73.34, H 4.61, N 2.07; found C 73.04, H 4.85, N 2.15. − MS [MALDI-TOF, 2-(4-hydroxyphenylazo)benzoic acid matrix]: *m*/*z*: calcd. 1892.1 $[M + Na]^+$; found 1890.6.

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[1] [1a] T. Suzuki, K. Nakashima, S. Shinkai, *Chem. Lett.* **1994**, 699−702. − [1b] J. L. Atwood, G. A. Koutsantonis, C. L. Raston, *Nature* **1994**, *368*, 229−231.

[2] [2a] A. Ikeda, M. Yoshimura, S. Shinkai, *Tetrahedron Lett.* **1997**, *38*, 2107−2110. − [2b] A. Ikeda, Y. Suzuki, M. Yoshimura, S. Shinkai, *Tetrahedron* **1998**, *54*, 2497−2508. − [2c] K. Araki, K. Akao, A. Ikeda, T. Suzuki, S. Shinkai, *Tetrahedron Lett.* **1996**, *37*, 73−76. − [2d] K. Tsubaki, K. Tanaka, T. Kinoshita, K. Fuji, *Chem. Commun*. **1998**, 895−896. − [2e] T. Haino, M. Yanase, Y. Fukazawa, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 259−260. − [2f] T. Haino, M. Yanase, Y. Fukazawa, *Tetrahedron Lett*. **1997**, *38*, 3739−3742. − [2g] N. S. Isaacs, P. J. Nichols, C. L. Raston, C. A. Sandova, D. J. Young, Chem. Commun. 1997, 1839−1840. − [2h] P. E. Georghiou, S. Mizyed, S. Chowdhury, *Tetrahedron Lett*. **1999**, *40*, 611−614.

[3] [3a] M. Yanase, T. Haino, Y. Fukazawa, *Tetrahedron Lett.* **1999**, *40*, 2781−2784. − [3b] T. Haino, M. Yanase, Y. Fukazawa, *Angew. Chem. Int. Ed.* **1998**, *37*, 997−998. − [3c] J. Wang, C. D. Gutsche, *J. Am. Chem. Soc.* **1998**, *120*, 12226−12231.

[4] [4a] A. Ikeda, M. Yoshimura, H. Udzu, C. Fukuhara, S. Shinkai, *J. Am. Chem. Soc*. **1999**, *121*, 4296−4297. − [4b] A. Ikeda, M. Yoshimura, H. Udzu, C. Fukuhara, S. Shinkai, *Tetrahedron* **2000**, *56*, 1825−1832.

[5] [5a] R. M. Williams, J. W. Verhoeven, *Recl. Trav. Chim. Pays-Bas*, **1992**, *111*, 531−532. − [5b] A. Ikeda, T. Hatano, M. Kawaguchi, H. Suenaga, S. Shinkai, *Chem. Commun.* **1999**, 1403−1404.

[6] Y. Kuroda, H. Nozawa, H. Ogoshi, *Chem. Lett*. **1995**, 47−48 and reference therein.

[7] [7a] J. W. Steed, P. C. Junk, J. L. Atwood, M. J. Barnes, C. L. Raston, R. S. Burkhalter, *J. Am. Chem. Soc*. **1994**, *116*, 10346−10347. − [7b] J. L. Atwood, M. J. Barnes, M. G. Gardine, C. L. Raston, *Chem. Commun*. **1999**, 193−194. − [7c] J.-F. Nierengarten, L. Oswald, J.-F. Eckert, J.-F. Nicoud, N. Armaroli, *Tetrahedron Lett*. **1999**, *40*, 5681.

[8] [8a] F. C. Tucci, D. M. Rudkevich, J. Rebek Jr., *J. Org. Chem.* **1999**, *64*, 4555−4559. − [8b] P. Timmerman, W. Verboom, F. C. J. M. van Veggel, J. P. M. van Duynhoven, D. N. Reinhoudt, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2345−2348. − [8c] P. Timmerman, K. G. A. Nierop, E. A. Brinks, W. Verboom, F. C. J. M. van Veggel, W. P. van Hoorn, D. N. Reinhoudt, *Chem. Eur. J.* **1995**, *1*, 132−143.

[9] M. M. Garcia, M. I. C. Uribe, E. B. Palacios, F. L. Ochoa, A. Toscano, J. A. Cogordan, S. Rios, R. Cruz-Almanza, *Tetrahedron* **1999**, *55*, 6019−6026.

[10] [10a] S. Shinkai, A. Ikeda, *Pure Appl. Chem*. **1999**, *71*, 275−280. − [10b] A, Ikeda, S. Shinkai, *Chem. Rev.* **1997**, *97*, 1713−1734. − [10c] A. L. Balch, M. M. Olmstead, *Coord. Chem. Rev.* **1999**, *185−186*, 601−617. − [10d] M. J. Hardie, C. L. Raston, *Chem. Commun*. **1999**, 1153−1163.

[11] T. Hatano, A. Ikeda, T. Akiyama, S. Yamada, M. Sano, Y. Kanekiyo, S. Shinkai, *J. Chem. Soc., Perkin Trans. 2* **2000**, 909−912.

[12] [12a] M. Takeshita, T. Suzuki, S. Shinkai, *J. Chem. Soc., Chem. Commun*. **1994**, 2587−2588. − [12b] A. Ikeda, S. Shinkai, *Chem. Lett*. **1996**, 803−804. − [12c] M. Kawaguchi, A. Ikeda, S. Shinkai, *J. Chem. Soc., Perkin. Trans. 1* **1998**, 179−184. − [12d] M. Kawaguchi, A. Ikeda, I. Hamachi, S. Shinkai, *Tetrahedron Lett.* **1999**, 8245−8249. − [12e] A. Soi, A. Hirsch, *New J. Chem.*, **1999**, 1337−1339.

[13] R. S. Ruoff, D. S. Tse, R. Malhotra, D. C. Lorents, *J. Phys. Chem.* **1993**, *97*, 3379−3383.

[14] K. Tsubaki, T. Otsubo, K. Tanaka, K. Fuji, T. Kinoshita, *J. Org. Chem.* **1998**, *63*, 3260−3265.

[15] The reversing of the benzene ring in homooxacalix[3]arene is prohibited when the R group on the phenolic oxygen is *n*-butyl or larger groups: [15a] K. Araki, K. Inada, H. Otsuka, S. Shinkai, *Tetrahedron* **1993**, *49*, 9465−9478. − [15b] K. Araki, N. Hashimoto, H. Otsuka, S. Shinkai, *J. Org. Chem.* **1993**, *58*, 5958−5963.

[16] C. D. Gutsche, *Calixarenes*; Royal Society of Chemistry: Cambridge, **1989**.

[17] These $\Delta\delta_H$ values are smaller than those for homooxacalix[3]arene−[60]fullerene complexes in nonpolar organic solvents (0.68 and 0.72 ppm; ref. 5) but are comparable to those for a water-soluble homooxacalix[3]arene−[60]fullerene complex in water (0.32 ppm; ref. 22). The results suggest that the complexation mechanism in polar solvent is different from that in nonpolar organic solvents. Judging from the smaller UV Vis spectral changes, one may regard that in polar solvents, the CH(*tert*-butyl)-π interaction operates more effectively than the π-π interaction.

[18] X. Camps, A. Hirsch, *J. Chem. Soc., Perkin Trans 1* **1997**, 1595−1596.

[19] [19a] B. Dhawan, C. D. Gutsche, *J. Org. Chem.* **1983**, *48*, 1536−1539. − [19b] P. Zerr, M. Mussrabi, J. Vicens, *Tetrahedron Lett.* **1991**, *32*, 1879−1880.

[20] F. Hanus, E. Fuchs, *J. Prakt. Chem.* **1939**, *153*, 327−336.

[21] A. Zinke, R. Ott, E. Legewie, A. Hassaneim, G. Zankle, *Monatsh. Chem*. **1956**, *87*, 552−559.

[22] T. Hatano, A. Ikeda, S. Shinkai, unpublished data.

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