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Synthesis and conformational analysis of a calix[4]arene–fullerene conjugate[†]

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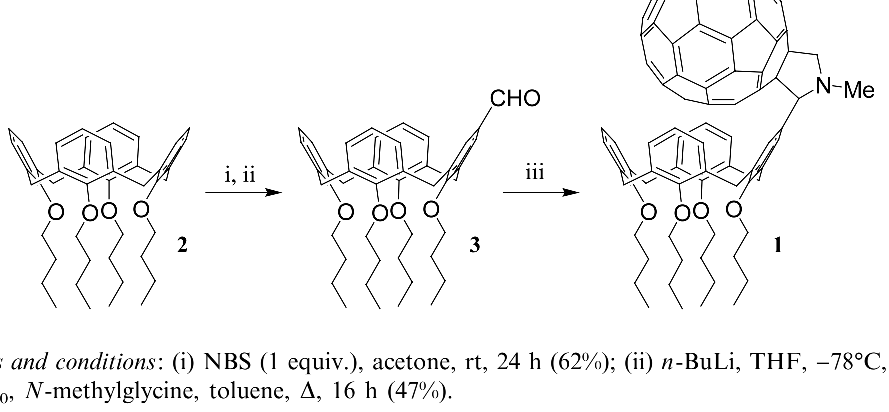
Abstract—A cone-calix[4]arene derivative bearing a fulleropyrrolidine group on the upper-rim has been prepared and interesting self-complexation–decomplexation properties in response to the temperature evidenced. © 2001 Elsevier Science Ltd. All rights reserved.

The conformational isomerism of calix[*n*]arenes has been extensively investigated and a number of strategies developed to immobilize the various conformers, thus affording a great number of cavities different in size and shape.[1] Therefore, the calix[*n*]arene skeletons have become important tools in host–guest chemistry.[1] In 1994, two independent studies[2] have shown that *p*-*tert*-butylcalix[8]arene selectively includes C_{60} in carbon soot and forms a precipitate with 1:1 stoichiometry. This discovery was the starting point to the study of supramolecular complexes of fullerenes with a variety of host systems.[3] In recent years, covalent assemblies of such macrocyclic receptors with C_{60} have been prepared with the aim to study the intramolecular association of the two components.[4] In particular, Shinkai and co-workers have shown that a homooxacalix[3]arene moiety connected to a C_{60} unit through a flexible spacer exhibits interesting self-complexation–decomplexation properties in response to the solvent polarity.[4a] The synthesis of calix[*n*]arene ($n=4$ or 5) derivatives bearing a fulleropyrrolidine group on the upper-rim has been reported by Wang and Gutsche.[4b] However, self-complexation could not be evidenced due to the conformational mobility of the macrocyclic rings making NMR studies difficult. As part of this research, we now report the synthesis of a related calix[4]arene–fullerene conjugate. Thanks to the conformationally immobile tetra-*O*-alkylated cone-calix[4]-arene skeleton used for the functionalization of the fullerene sphere, conformational analysis could be achieved. Interestingly, whereas the fulleropyrrolidine group is rotating freely at high temperature, only the self-complexed conformer is seen at low temperature.



Scheme 1. *Reagents and conditions*: (i) NBS (1 equiv.), acetone, rt, 24 h (62%); (ii) *n*-BuLi, THF, −78°C, 1 h, then DMF, −78°C to rt (46%); (iii) C_{60}, *N*-methylglycine, toluene, Δ, 16 h (47%).

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[†] Dedicated to Professor Vincenzo Balzani on the occasion of his 65th birthday.

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The synthesis of the calix[4]arene–fullerene conjugate **1** is depicted in Scheme 1. Monobromination of the tetra-*O*-alkylated cone-calix[4]arene **2**[5] by treatment with 1 equiv. of NBS followed by lithiation and subsequent quenching with DMF afforded aldehyde **3**. For both **2** and **3**, the cone conformation was deduced from the ^{1}H and ^{13}C NMR spectra. In particular, the ^{13}C NMR chemical shifts (around δ 31 ppm) of the methylene groups connecting the aromatic rings were in good agreement with a cone conformation as previously shown in the literature.[6] The functionalization of C_{60} with calix[4]arene **3** is based on the 1,3-dipolar cycloaddition of the azomethine ylide generated in situ from **3** and *N*-methylglycine.[7] In a typical procedure, a solution of **3** (200 mg), C_{60} (235 mg) and *N*-methylglycine (158 mg) in toluene (300 ml) was refluxed under argon for 16 h. After cooling, the resulting solution was evaporated to dryness and column chromatography (SiO_2, toluene/hexane 4:1) yielded **1** (200 mg, 47%).

All of the spectroscopic and elemental analysis results were consistent with the proposed molecular structure.[8] In particular, the FAB mass spectrum of **1** shows the expected molecular ion peak at 1424.3 (MH^+, calculated for $C_{107}H_{62}NO_4$: 1424.47). The characteristic bands of a fulleropyrrolidine derivative[7] at 430 and 702 nm are seen in the UV–vis spectrum of **1** recorded in CH_2Cl_2. As shown by Gutsche and Wang for related derivatives,[4b] the comparison of the absorption spectra of **1** and analogous fullerene derivatives lacking the calixarene moiety does not reveal any significant perturbation that might reflect an intramolecular association in **1** between the C_{60} moiety and the cavity of the calixarene. The ^{1}H NMR spectrum of **1** shows all the anticipated signals but some of them are broad at room temperature (Fig. 1). A variable-temperature NMR study revealed a reversible narrowing of all these peaks showing that a dynamic effect occurs. This indicates restricted rotation of the calixarene substituent on the pyrrolidine ring.[9] In the ^{1}H NMR spectrum of **1** recorded in $CDCl_2CDCl_2$ at 120°C, four distinct AB quartets are seen for the four methylene groups connecting the aromatic rings and four sets of signals are observed for the OCH_2 groups in full agreement with the C_1 symmetry of **1** resulting from the presence of the asymmetric C atom in the pyrrolidine ring. This lack of symmetry is also evidenced by the signal dispersion in the aromatic region and by the pair of doublets centered at δ 4.4 and 5.1 ppm corresponding to the resonances of the two protons of the methylene group of the pyrrolidine rings. It should be noted that the structure of **1** was also confirmed by the 2D-COSY and NOESY spectra recorded at room temperature in CD_2Cl_2 and an unambiguous attribution could be achieved.

The ^{1}H NMR spectra of **1** in $CDCl_3$ revealed the presence of only one conformer by decreasing the temperature (Fig. 1). Typically, aromatic protons of calix[4]arenes are observed around δ 6.6–7.5 ppm.[6] In the ^{1}H NMR spectra of **1** recorded at low temperatures, some of the aromatic protons resonate around 5.5–6.1 ppm. This dramatic up-field shift must be the result of the close proximity of the fullerene sphere suggesting that compound **1** adopts a conformation in which the C_{60} unit is located atop the calix[4]arene macrocycle. Computational studies[10] have been performed to evaluate the relationship between the potential energy and the relative position of the calix[4]arene macrocycle and the fulleropyrrolidine moiety (Fig. 2). The molecule has been optimized with fixed values of the torsion angle for rotation about the bond between the pyrrolidine ring and the benzene group attached to it. This angle has been increased stepwise from 0 to 360°, leading to the potential energy diagram shown in Fig. 2. Two minima of different energy have been found, the lowest-

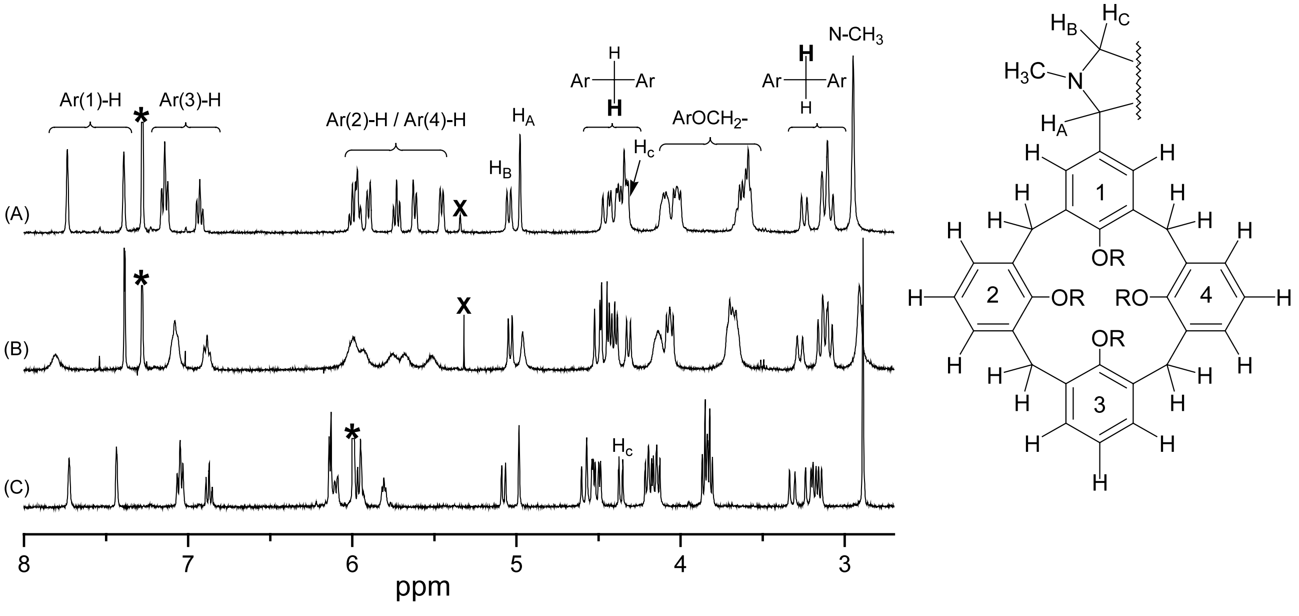

Figure 1. ^{1}H NMR spectra of **1** (400 MHz) at (A) −40°C ($CDCl_3$, ★: solvent peak, **X**: CH_2Cl_2 impurity); (B) 30°C ($CDCl_3$, ★: solvent peak, **X**: CH_2Cl_2 impurity); and (C) 120°C ($CDCl_2CDCl_2$, ★: solvent peak).

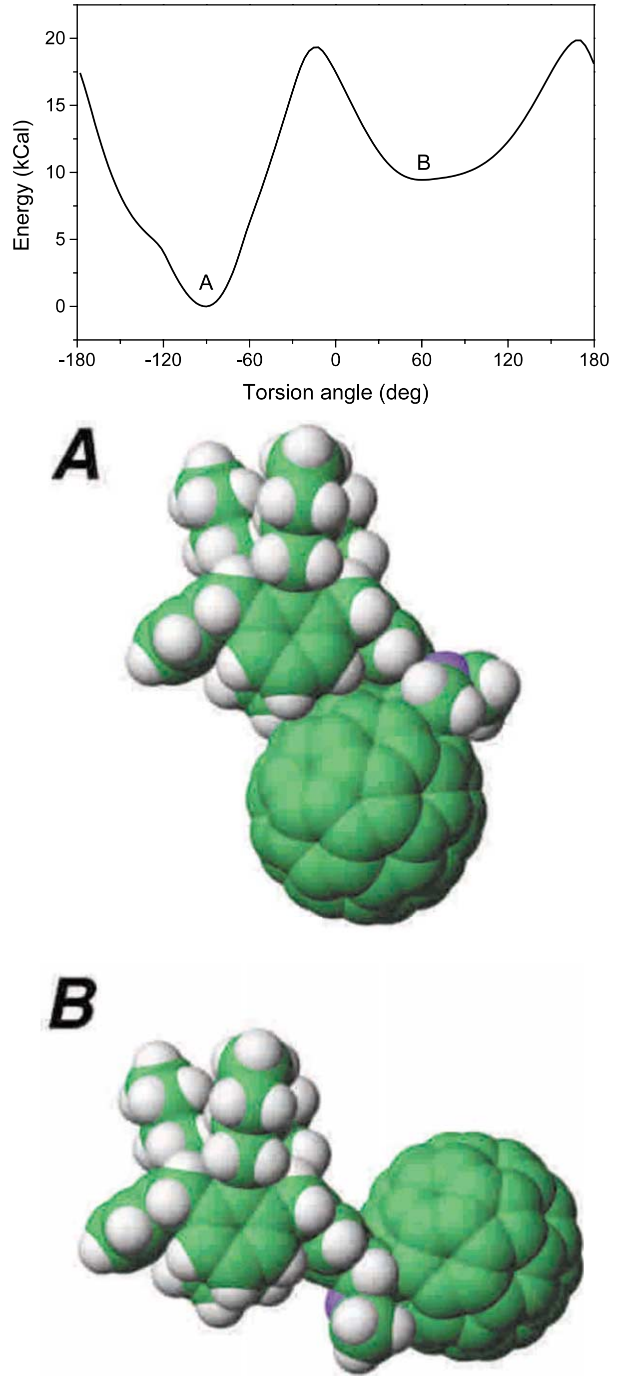

Figure 2. Top: calculated potential energy diagram of compound **1** for rotation about the bond between the pyrrolidine ring and the benzene group attached to it. Bottom: theoretical structures of the two conformers corresponding to the two minima.

energy conformation being the one with the fulleropyrrolidine moiety located atop the cavity of the calix[4]arene macrocycle, i.e. the self-complexed conformer (Fig. 2, conformer **A**). The second stable conformer in which the two moieties are far apart (Fig. 2, conformer **B**) is located ca. 10 kcal/mol higher in energy. The calculations are therefore in good agreements with the ^{1}H NMR studies suggesting that compound **1** adopts a self-complexed conformation at low temperature. It is worth noting that for the calculated conformer **A**, the calix[4]arene adopts a pinched-cone conformation. It should however be mentioned that a structure with a regular-cone-shaped calix[4]arene could be observed with the pcff forcefield, but the energy decay from the corresponding pinched-cone conformation was not significant enough to conclude with accuracy between these two theoretical structures. However, the ^{1}H NMR spectra recorded at low temperature showing only a dramatic up-field shift for the signals corresponding to the protons of the aromatic rings Ar(2) and Ar(4) (Fig. 1) but not for those of Ar(3) suggests that the calix[4]arene core adopts the pinched-cone conformation in which the benzene rings Ar(2) and Ar(4) are in close proximity of the fullerene core but not Ar(3). In addition, it must also be noted that the rotational energy barrier between the conformers **A** and **B** is about 15–20 kcal/mol, in good agreement with some experimental values found for the rotation of phenyl substituent on the pyrrolidine ring of phenyl–fulleropyrrolidine derivatives.[9] Thus, the dynamic exchange can occur at high temperature as suggested by the ^{1}H NMR studies.

In conclusion, the fulleropyrrolidine group in **1** is rotating freely at high temperature but only the self-complexed conformer is observed at low temperature. Compound **1** can be seen as a covalent assembly of two components able to perform mechanical-like movements of relatively large amplitudes (rotation of the fulleropyrrolidine group) as a consequence of an external stimulus (temperature). Therefore, calix[4]arene–fullerene conjugate **1** presents characteristic features that makes it an interesting building block for the preparation of new molecular machines.[11]

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