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Straightforward supramolecular purification of C_{84} from fullerene extract

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Selective purification of fullerene mixtures via supramolecular encapsulation is an appealing strategy to circumvent the tedious HPLC chromatographic purification protocols. In this work, we utilize tetragonal prismatic nanocapsules of different cavity sizes and shapes to selectively encapsulate C_{84} from a mixture containing fullerenes ranging from C_{60} to C_{96} (fullerene extract), allowing to enrich C_{84} content from 0.7% to 86%. Moreover, terphenyl-based extra-large nanocapsules were prepared for the first time that can strongly bind the dumbbell-shaped azafullerene dimer $(C_{59}N)_2$ as a guest. Competition experiments between $(C_{59}N)_2$ and C_{84} allowed to deduce a $K_a > 1.0 \times 10^7$ M^{-1} for C_{84} in nanocapsule **6**·$(BArF)_8$. The preference of nanocapsule **7**·$(BArF)_8$ to bind C_{84}-D_2(22) among all IPR-isomers is also discussed.

Introduction

Higher fullerenes are stable compounds that are produced in very tiny quantities using the known arc-discharge methodology.[1] Besides the available C_{60} and C_{70}, the third more abundant fullerene found in soot is C_{84}, although its content is below 0.7%.[2] Moreover, the isolation of C_{84} is very challenging mainly due to the tedious HPLC purification required.[3, 4] In addition, it has 24 possible IPR-isomers, being C_{84}-D_2(22) and C_{84}-D_{2d}(23) isomers the most abundant (as empty fullerenes in a 2:1 ratio), which further handicaps the availability of pure samples.[5-8] Recently, even higher fullerenes such as C_{90}-D_{5h}(1) and C_{100}-D_{5d}(1), featuring a tubular shape and named as fullertubes, were isolated and crystallized from extract soot by Stevenson following a combined aminopropanol selective discrimination and intensive HPLC purification.[9]

As a consequence, finding a straightforward methodology for the purification of higher fullerenes is highly appealing, since it would bring the opportunity to extensively investigating the mostly unknown electronic properties and reactivity of higher fullerenes.[10] In this sense, supramolecular nanocages capable of encapsulating large guests such as fullerenes have been explored, mainly focusing on the most ready available fullerenes C_{60} and C_{70}.[11, 12] Modest attempts to encapsulate higher fullerenes were described by Nitschke in 2011 and Ribas in 2014.[13, 14] In the former, a self-assembled cubic cage bearing six Ni-porphyrin units trapped a mixture of higher fullerenes (C_{70}, C_{76}, C_{78}, C_{82} and C_{84}) from fullerene extract, in a non-selective manner.[13] On the other hand, our group designed and synthesized a tetragonal prismatic nanocapsule capable of encapsulating fullerenes ranging from C_{60} to C_{84} by squeezing the guests through the gates of the capsule (Figure 1a).[14, 15]

Supramolecular purification requires the facile release of guests and this has been achieved in a few selected cases, i.e. for C_{60},[14] C_{78}- and C_{80}-based uranium endohedral metallofullerenes (EMFs) (Figure 1b),[16, 17] and for C_{84} utilizing cyclotriveratrylene-based capsules.[18]

Despite the difficulty to dispose of milligram-scale amounts of C_{84}, an additional drawback is its occurrence as an IPR isomeric mixture (mainly D_2 and D_{2d}). The different reactivity of the double bonds depending on each isomer has been used as a successful strategy to crystallize the $(\eta^2\text{-}C_{84})Ir(CO)Cl(PPh_3)_2$ complex corresponding to the D_{2d} isomer.[19] Also, the kinetic resolution of the chiral D_2 isomer was reported via asymmetric osmylation triggering a Stone-Wales transformation.[20] Later in 1998, Shinohara reported the tedious multiple-step HPLC purification of D_2(22) and D_{2d}(23).[3] On the other hand, Echegoyen used a Bingel-retro-Bingel strategy to isolate the two enantiomers of C_{84}-D_2 and also C_{84}-D_{2d} as a pure isomer.[21]

In this work, we envisioned that modular tetragonal prismatic nanocapsules with larger cavities could be designed to selectively host C_{84} and higher fullerenes. Based on a) the poor affinity of C_{84} previously observed for the biphenyl-macrocycle-based nanocapsule, and b) the affinity of the large guest $C_{60}\subset10$[CPP] for a 1,2-diphenylethyne-macrocycle-based nanocapsule (Figure 1c),[22] we reasoned that the latter could serve as an ideal host for C_{84}. Moreover, a larger terphenyl-macrocycle-based nanocapsule is reported for the first time and the host-guest chemistry with fullerenes of variable size and shape is explored.

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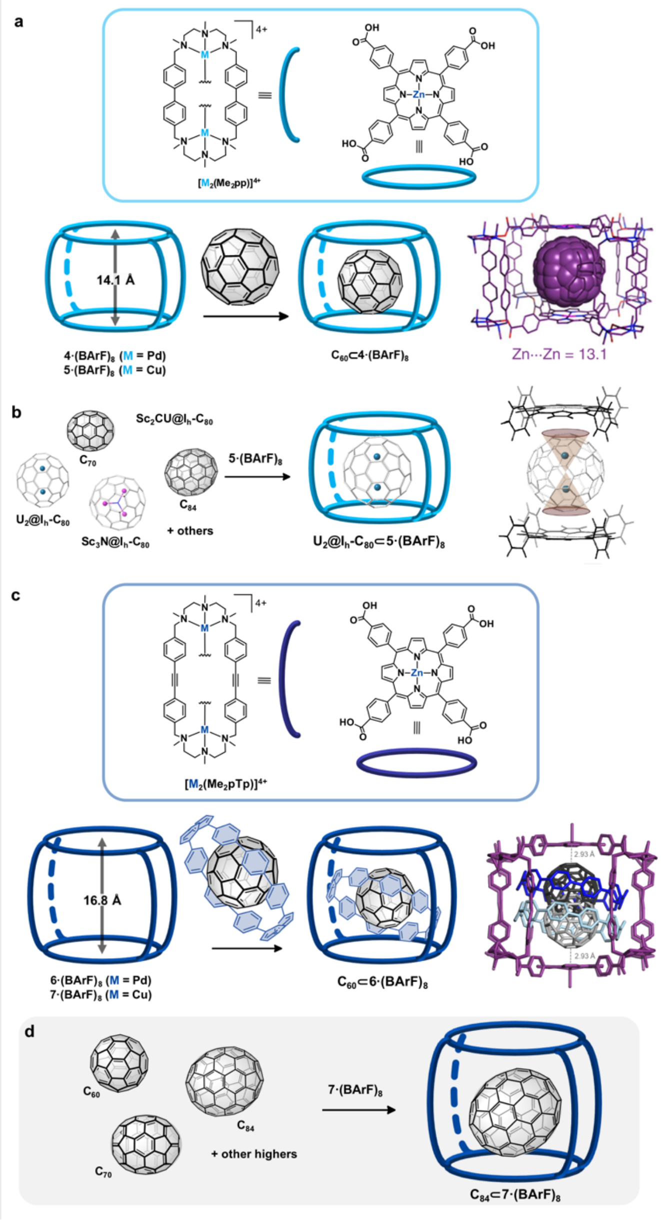

Figure 1. Supramolecular encapsulation of fullerenes and EMFs for **a)** the purification of C_{60},[14] and **b)** the purification of U-based C_{80}-EMFs.[16] **c)** Three-shell matryoshka-like assembly featuring encapsulated $C_{60}\subset$[10]CPP.[22] **d)** Selective encapsulation of C_{84} in nanocapsule **7**·$(BArF)_8$ (this work).

Results and discussion

Pd-based nanocapsule **6**·$(BArF)_8$ and Cu-based nanocapsule **7**·$(BArF)_8$ were prepared following literature procedures (Figure 1c).[22] These nanocapsules, featuring a cavity height of 16.8 Å, were dissolved in toluene:CH_3CN (9:1) and exposed to 100 eq. of fullerene extract (70% C_{60}, 28% C_{70} and 2% higher fullerenes – from C_{76} to C_{96}, of which C_{84} was the most abundant and accounts for a 0.7%), at room temperature (Figure 2a). It was rapidly observed by HRMS monitoring that the nanocapsules remained empty after short periods of time and therefore, longer periods of time were tested. Despite the low content of higher fullerenes in the extract, after 7 days, selective encapsulation of C_{84} occurred and $C_{84}\subset$**7**·$(BArF)_8$ is detected as major thermodynamic product by HRMS (Figure 2b and 3), indicating very good size and shape complementarity between the capsule and C_{84}.

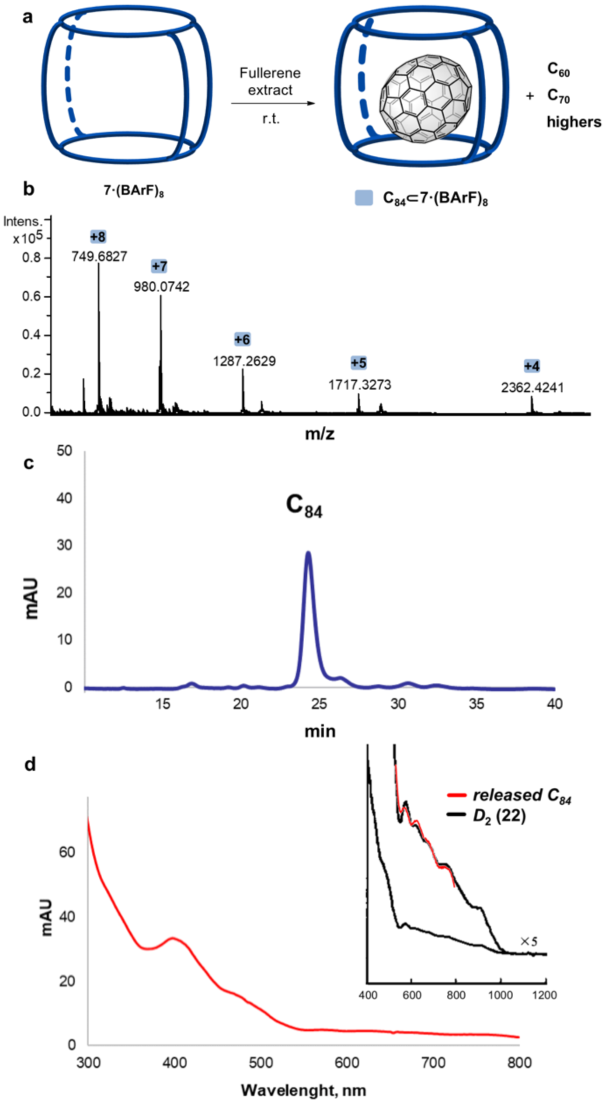

Figure 2. a) Schematic representation of the selective encapsulation of C_{84} in nanocapsule **7**·$(BArF)_8$ from a fullerene extract. **b)** HRMS (ESI^+) monitoring for **7**·$(BArF)_8$ upon addition of 100 eq. of fullerene extract and stirring at room temperature for 7 days in toluene. **c)** HPLC-DAD chromatogram recorded after the disassembly of the nanocapsule **d)** UV-vis spectra of the peak at 24.3 min corresponding to C_{84} fullerene [inset showing an amplification of the 500-800 nm range and matching with the reported spectrum for isomer D_2 (22)].

Indeed, upon removal of the solvent, redissolution in CH_3CN and treatment with acid (HOTf) to disassemble the nanocapsule, the guests were released and the predominant fullerene C_{84} was predominantly detected by HPLC (Buckyprep M column, toluene eluent, Figure 2c) and characterized by UV-vis spectroscopy (Figure 2d) and by MALDI mass spectrometry (*m/z* = 1008.24, Figure S16). However, with a careful examination of the HRMS spectra (Figure 3a), weak *m/z* ions corresponding to $C_{70}\subset$**7**·$(BArF)_8$ complex were also observed, indicating that the nanocapsule encapsulated small quantities of the abundant C_{70} (28%). Moreover, other weak *m/z* ions were present, attributed to other encapsulated higher fullerenes (C_{76}, C_{78}, C_{82}, C_{86}, C_{88}, C_{90}, C_{92}, C_{94} and C_{96}), despite their very low content.

To this end, we reasoned that encapsulation might be even more selective by performing a solid/liquid experiment with the nanocapsule suspended as a solid in a toluene solution of the fullerene extract. This strategy was previously successfully applied in the purification of U-based EMFs owing to the restricted flexibility of the nanocapsule.[15-17] Upon suspending **7**·$(BArF)_8$ in a toluene solution of 100 eq. of fullerene extract, at room temperature for 12 hours, no improvement of the selectivity was observed (Figure 3b). However, elongating the time to 7 days, the C_{70} and C_{76} *m/z* ions disappeared, all *m/z* ions of higher fullerenes were diminished while, the one corresponding to C_{84} was enhance (Figure 3c). The comparison was performed considering the relative intensity of the *m/z* peaks with respect to the C_{84} *m/z* ion peak in the HRMS spectra. The peak intensity corresponding to C_{78} was decreased from 6.4% to 1.7%, the one for C_{82} decreased from 10.7% to 3.4%, C_{86} from 14.3% to 13.3%, C_{88} from 4.8% to 3.3%, C_{90} from 10.7% to 5.0%, C_{92} from 6.2% to 3.3% and finally, the *m/z* peak intensities for C_{94} and C_{96} were both decreased from 3.5 to 3.3%. The latter revealed that C_{84} was the most thermodynamically favored guest among all fullerenes present in the extract. The quantification of the C_{84} enrichment was performed by first disassembling the capsule upon acid treatment, followed by HPLC analysis. Integration of the peaks in the and HPLC chromatogram indicated a ~125-fold enrichment of C_{84} (from 0.7% in the initial soot to 86% in the encapsulated mixture). By selective collection of the peak corresponding to C_{84}, 2.2 mg of pure C_{84} were isolated and ^{13}C NMR spectroscopic characterization was attempted to decipher whether the nanocapsule was able to select among different C_{84} isomers. Despite recording the spectrum on a 500 MHz NMR (equipped with a cryoprobe) for 3 days (1.6×10^5 scans, CS_2:acetone-d^6, 40 mM $Cr(acac)_3$ as relaxing agent and d1 = 2s),[4] weak peaks were detected probably due to the low concentration of C_{84} (Figures S17-S18). However, careful inspection of the UV-vis spectrum of C_{84} liberated from the nanocapsule (HPLC-DAD) pointed towards the accumulation of C_{84}-D_2(22) (Figure 2d) which is one of the main isomers of C_{84} present in the fullerene extract. The latter might indicate a slight preference of nanocapsule **7**·$(BArF)_8$ to bind C_{84}-D_2(22) among all IPR-isomers contained in the starting fullerene extract (see Figure 2d and S15).

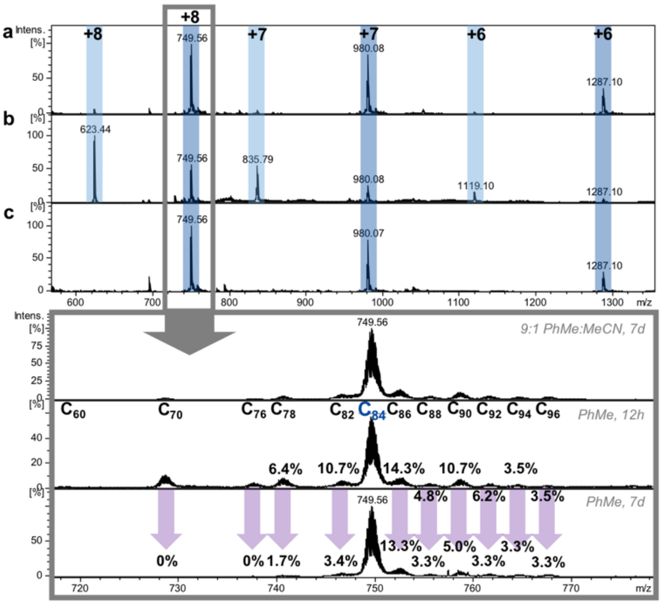

Figure 3. Study of the binding affinity in time and solution/solid phase. HRMS (ESI+) monitoring for encapsulation of C_{84} fullerene. **a)** **7**·$(BArF)_8$ in solution (toluene:CH_3CN = 9:1), 100 eq. of fullerene extract, r.t., 7 days (liquid/liquid). **b)** **7**·$(BArF)_8$ in the solid state (suspension in toluene), 100 eq. of fullerene extract, r.t., 12 hours. **c)** **7**·$(BArF)_8$ in the solid state (suspension in toluene), 100 eq. of fullerene extract, r.t., 7 days.

In an effort to improve the selective binding of higher fullerenes, we designed a nanocapsule with larger cavity, by introducing a terphenyl-macrocycle-based clip with a calculated cavity height of 18.4 Å (Figure 4a). The Pd-based **8**·$(BArF)_8$ and Cu-based **9**·$(BArF)_8$ nanocapsules were synthesized following an analogous procedure. The encapsulation of fullerenes present in the extract was not successful and HRMS spectrometric investigation of the reaction mixture revealed the major *m/z* ions corresponding to empty nanocapsules. This clearly indicated that the cavities of **8** and **9** were too large to stabilize any of the higher fullerenes being present in the extract.

With this in mind, we reasoned that the dumbbell-shaped azafullerene dimer $(C_{59}N)_2$ might show an enhanced affinity for nanocapsules **8** and **9** due to its large size. The association constant of $(C_{59}N)_2$ guest in **8**·$(BArF)_8$ host was calculated by UV-vis titration, finding a $K_a = 4.3\ (\pm 1.0) \times 10^7\ M^{-1}$. This value is comparable to the association constant measured for the encapsulation of C_{60} in the Pd-based biphenyl nanocapsule, reported in 2014.[14] A similar value was calculated for the Cu-analogue **9**·$(BArF)_8$ ($K_a = 1.3\ (\pm 0.6) \times 10^7\ M^{-1}$). As expected, the association constant decreased upon shrinking the cavity size, leading to a $K_a = 1.0\ (\pm 1.1)\ 10^7\ M^{-1}$ for **6**·$(BArF)_8$, $1.6\ (\pm 0.1) \times 10^6\ M^{-1}$ for **7**·$(BArF)_8$ and $9.4\ (\pm 0.5) \times 10^5\ M^{-1}$ for the smaller biphenyl-based nanocapsule **4**·(BArF)$_8$,[15] featuring a cavity height of 14.1 Å (see Figures 4b).

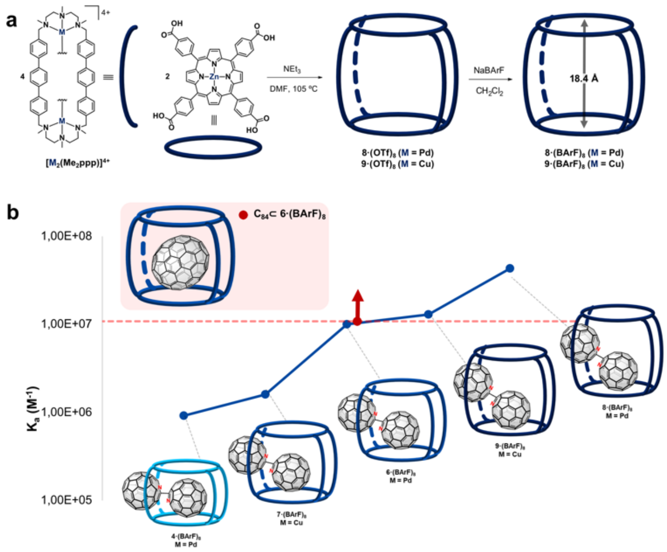

Figure 4. a) Synthesis of terphenyl-based tetragonal prismatic nanocapsules **8**·(BArF)$_8$ (Pd-based) and **9**·(BArF)$_8$ (Cu-based). b) Comparative association constants (K$_a$) of (C$_{59}$N)$_2$ with different sized nanocapsules and estimation of the K$_a$ for C$_{84}$⊂**6**·(BArF)$_8$ (see Figure 5).

Since the insolubility of pure C$_{84}$ precluded the calculation of the association constant with **6**·(BArF)$_8$, we circumvented this problem by performing a competition experiment exposing (C$_{59}$N)$_2$⊂**6**·(BArF)$_8$ to fullerene extract, in toluene solvent. After 4 days, a full exchange of the encapsulated azafullerene dimer by fullerene C$_{84}$ was observed by HRMS (Figure 5), thus indicating a K$_a$ value higher than 1.0 x 10^7 M^{-1} for C$_{84}$⊂**6**·(BArF)$_8$ (Figure 4b).

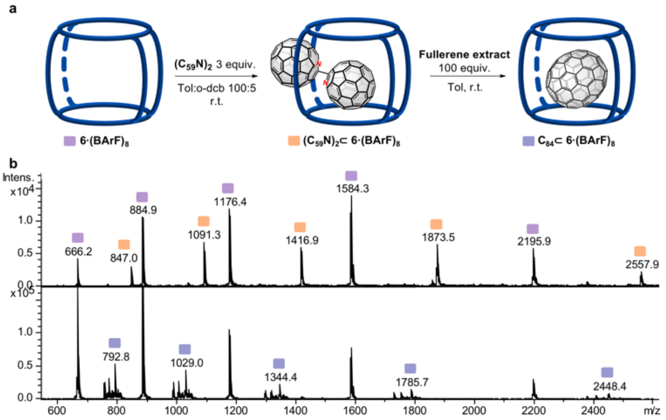

Figure 5. Competitive host-guest binding studies of azafullerene dimer (C$_{59}$N)$_2$ and fullerene extract with nanocapsule **6**·(BArF)$_8$ **a)** HRMS of (C$_{59}$N)$_2$⊂**6**·(BArF)$_8$ and **b)** HRMS upon exposure to fullerene extract showing complete replacement of (C$_{59}$N)$_2$ to form C$_{84}$⊂**6**·(BArF)$_8$.

Conclusions

In summary, we have successfully developed an efficient, one-step protocol for the enrichment of C$_{84}$ (up to 86%) directly from fullerene extract, utilizing nanocapsule **7**·(BArF)$_8$ which features a large cavity (16.8 Å height). Enlargement of the cavity height to 18.4 Å was accomplished by employing a terphenyl-based molecular clip towards the construction of nanocapsules **8**·(BArF)$_8$ and **9**·(BArF)$_8$. However, in this case, the cavity was proven too large to host even the higher fullerenes (> C$_{90}$). On the contrary, the the extra-large terphenyl-based nanocapsules were perfectly sized to host the dumbbell-shaped azafullerene dimer (C$_{59}$N)$_2$.[15] Comparison of the association constants of (C$_{59}$N)$_2$ with nanocapsules **4**, **6**, **7**, **8** and **9**, differing in their size, together with the results derived from a competition experiment between (C$_{59}$N)$_2$ and fullerene extract, allowed us to conclude that the association constant of C$_{84}$ with nanocapsule **6** must be greater than 1.0 x 10^7 M^{-1}. Moreover, nanocapsule **7**·(BArF)$_8$ shows a slight preference to bind C$_{84}$-*D*$_2$(22), among all IPR-isomers contained in the starting fullerene extract. This study shows that supramolecular design is a key tool for the selective encapsulation of fullerenes featuring different size and that fine-tuning of these tetragonal prismatic nanocapsules is a successful strategy to improve the selectivity for a targeted fullerene. In future work, further efforts will be guided towards further fine tune the capsules architecture in order to be able to more precisely separate the different isomers of C$_{84}$ following our well stablished purification strategy.

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