

Supramolecular Chemistry

A Copper-based Supramolecular Nanocapsule that Enables Straightforward Purification of Sc₃N-based Endohedral Metallofullerene SootsCarles Fuertes-Espinosa,^[a] Cristina García-Simón,^[a] Edison Castro,^[b] Miquel Costas,^{*[a]} Luis Echegoyen,^{*[b]} and Xavi Ribas^{*[a]}

Abstract: A self-assembled Cu^{II}-based nanocapsule enables efficient and straightforward isolation of Sc₃N@C₈₀ from arc-processed raw soot. The newly designed Cu^{II}-based supramolecular nanocapsule 5·(OTf)₈ was used to effectively entrap fullerenes and endohedral metallofullerenes (EMFs) with different affinities depending on their size and shape. Moreover, we took advantage of the sharply different entrapment abilities of the 5·(OTf)₈ cage in the solid state versus in solution to encapsulate all the species with the exception of Sc₃N@C₈₀ (both I_h and D_{5h} isomers), which remains pure in solution. HPLC quantification determined that up to 85% of the total Sc₃N@C₈₀ content in the initial mixture was recovered in very high purity (>99.5%). The complete release of the encapsulated species with an orthogonal solvent-washing strategy regenerates 5·(OTf)₈ ready to be re-used. This approach opens new opportunities for EMFs purification.

EMFs are intriguing fullerene-based nanomaterials due to their unique electronic properties.^[1,2] The small band gap of endohedral metallofullerenes (EMFs) (compared to those of empty fullerenes) places them as promising candidates for solar cells. Shielding of the entrapped metals or molecules by the fullerene cage confers high stability and low toxicity to EMFs, and are excellent materials for electronic and biomedical applications, such as in diagnostic radiology.^[3] However, applications of EMFs have not been fully exploited mainly because of the very high cost of these materials, due to extensive and time-

consuming HPLC procedures required for their purification.^[2,4] The large variety of species present in soot mixtures and their low solubility further complicates the purification of EMFs by standard HPLC.^[4] Several alternative non-chromatographic methods have been developed to purify EMF crude soots,^[4] most of them mainly based on the different chemical behavior of EMFs in comparison with empty fullerenes. Those include 2-aminoethanol extraction,^[5] the specific reactivity of EMFs with Lewis acids,^[6] functionalized silica^[7] or resins^[8] or the combination of both strategies by successive precipitation of EMFs with Lewis acids, followed by treatment with amino-functionalized silica gel (SAFA, stir and filter approach).^[9] In addition, the different redox properties between EMFs belonging to the same family and their selective exohedral functionalization can also be exploited to facilitate their separation.^[10]

Alternatively, the use of polyaromatic molecular receptors to incarcerate EMFs has also been investigated by different groups. In 2011, Ballester's and Echegoyen's groups reported the encapsulation of Sc₃N@C₈₀ in a receptor based on two cyclic β-pyrrole unsubstituted *meso*-tetraphenylbisorphyrins.^[11] Chiu's group synthesized a cyclotrimeratrylene-based hemicarceplexe capsule, able to host Sc₃N@C₈₀ within its inner cavity.^[12] Shinohara's group developed a size-selective host-guest complexation with cycloparaphenylene (CPP) to render mixtures enriched in Gd@C₈₂ from crude soot.^[13] However, to our knowledge, selective purification of EMFs from crude soots mediated by coordination nanocapsules have not been described yet.

In this context, in 2014 some of us reported the synthesis of a Pd^{II}-based tetragonal prismatic supramolecular nanocapsule (4·(BArF)₈, Figure 1a) capable of entrapping fullerenes (from C₆₀ to C₈₄) and to release them in a selective manner, offering a promising platform for their purification.^[14] Herein, we describe a novel Cu^{II}-based tetragonal prismatic nanocapsule 5·(OTf)₈ (Figure 1a) that enables isolation of highly pure (>99.5%) Sc₃N@C₈₀ from crude soot by selective host-guest complexation. The new nanocapsule shows enhanced encapsulation/release properties in comparison with 4·(BArF)₈, and its preparation is simpler. The inherently more labile nature of Cu^{II}-carboxylate coordination bonds in 5·(OTf)₈ compared to Pd^{II} in 4·(BArF)₈ are thought to be the reason for its enhanced performance, allowing easier access/release of the guests.

Nanocapsule 5·(OTf)₈ was synthesized by self-assembly of a tetracarboxylate Zn^{II}-porphyrin and a Cu^{II}-based molecular clip [Cu-1 b](OTf)₄ (Figure 1a). The [Cu-1 b](OTf)₄ molecular clip

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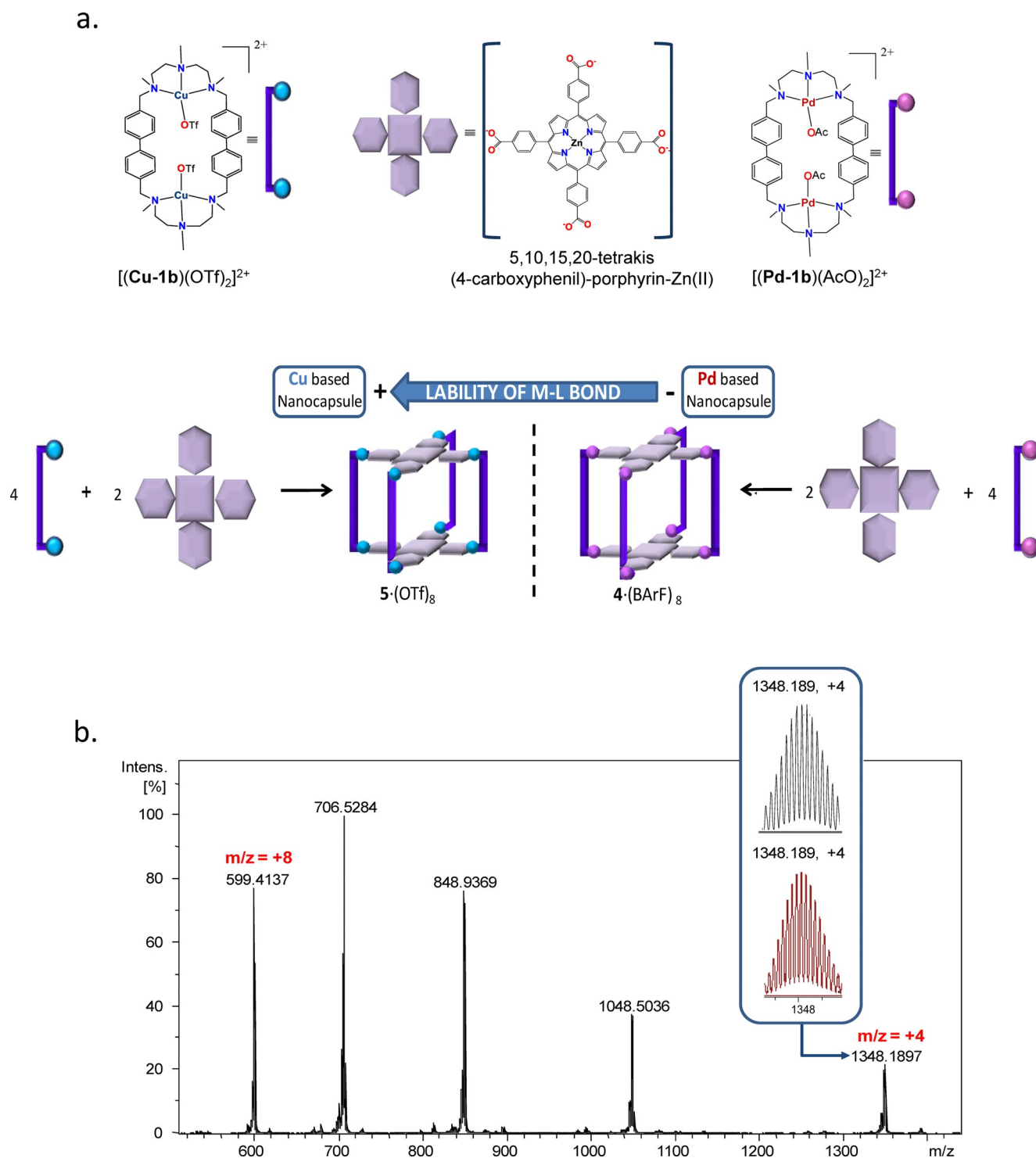


Figure 1. a) Schematic representation of the building blocks (top) used for the self-assembly of molecular clips $[(\text{Cu-1b})\cdot(\text{OTf})_2]_4$ or $[(\text{Pd-1b})\cdot(\text{AcO})_2]_4$ and tetracarboxylated Zn^{II} -porphyrin to form the supramolecular nanocapsules $5\cdot(\text{OTf})_8$ (bottom left) or $4\cdot(\text{BARF})_8$ (bottom right). b) HRMS spectrum of $5\cdot(\text{OTf})_8$ (simulated spectrum of selected peaks is shown in red).

was synthesized analogously to the previously reported Pd clip,^[14] and characterized by high resolution mass spectrometry (HRMS), ultraviolet-visible spectroscopy (UV/Vis), infrared spectroscopy (FT-IR) (Supporting Information Figures S1–S3) and combustion analysis. Nanocapsule $5\cdot(\text{OTf})_8$ shows better solubility in acetonitrile than its Pd analogue $4\cdot(\text{OTf})_8$; therefore,

counteranion exchange with BARF is not required to enhance its solubility in acetonitrile (Figure 1 a).^[14] The HRMS (Figure 1 b) and the UV/Vis spectrum (Supporting Information Figure S4) strongly suggest that nanocapsule $5\cdot(\text{OTf})_8$ retains its integrity in solution. $5\cdot(\text{OTf})_8$ was also characterized by FT-IR (Supporting Information Figure S5).

We first explored the ability of $5\cdot(\text{OTf})_8$ to act as a host for the encapsulation/release of fullerenes. Immediate inclusion of C_{60} occurred after mixing an acetonitrile solution of $5\cdot(\text{OTf})_8$ with a toluene solution of C_{60} , in a 1:1 molar ratio. UV/Vis titration experiments indicated the formation of a 1:1 adduct $\text{C}_{60}\subset 5\cdot(\text{OTf})_8$ ($K_a = 3.53(\pm 0.4) \times 10^6 \text{ M}^{-1}$, Supporting Information Figure S6). In addition, HRMS analysis showed exclusively the peaks corresponding to the $\text{C}_{60}\subset 5\cdot(\text{OTf})_8$ complex (Figure 2a).

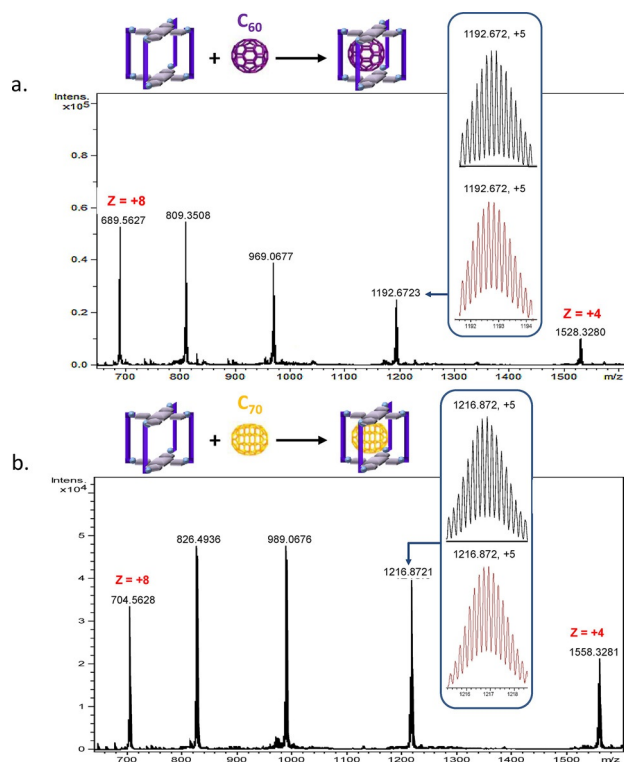


Figure 2. a) HRMS spectrum of $\text{C}_{60}\subset 5\cdot(\text{OTf})_8$ host-guest adduct generated in solution (9:1, toluene/acetonitrile). Simulated spectrum of selected peaks is shown in red. b) HRMS spectrum of $\text{C}_{70}\subset 5\cdot(\text{OTf})_8$ host-guest adduct generated in solution (9:1, toluene/acetonitrile). Simulated spectrum of selected peaks is shown in red.

Analogously, the $\text{C}_{70}\subset 5\cdot(\text{OTf})_8$ complex was instantaneously formed upon mixing $5\cdot(\text{OTf})_8$ with C_{70} ($K_a = 1.76(\pm 0.7) \times 10^7 \text{ M}^{-1}$, see Figures S7 (Supporting Information) and Figure 2b). The inclusion of higher fullerenes was also observed by HRMS by using fullerene extract (C_{60} 70%, C_{70} 28%, higher fullerenes 2%) (Supporting Information Figure S8a).

Subsequently, the release of the entrapped fullerenes was attempted. As previously reported, by applying a solvent washing protocol, which exploits the orthogonal solubility of the nanocapsule and fullerenes, the latter can be easily recovered.^[14] Gratifyingly, the complete release of C_{60} and C_{70} from $5\cdot(\text{OTf})_8$ was successfully achieved using this methodology, fully recovering $5\cdot(\text{OTf})_8$ after the process (confirmed by HRMS) (Figure 3 and Supporting Information Figure S9). The latter is remarkable because C_{70} could not be released from $4\cdot(\text{BARF})_8$.^[14] Presumably, the lability of metal-coordination bonds (Cu-carboxylate) endows $5\cdot(\text{OTf})_8$ with some degree of structural flexibility in regard to the intramolecular porphyrin-

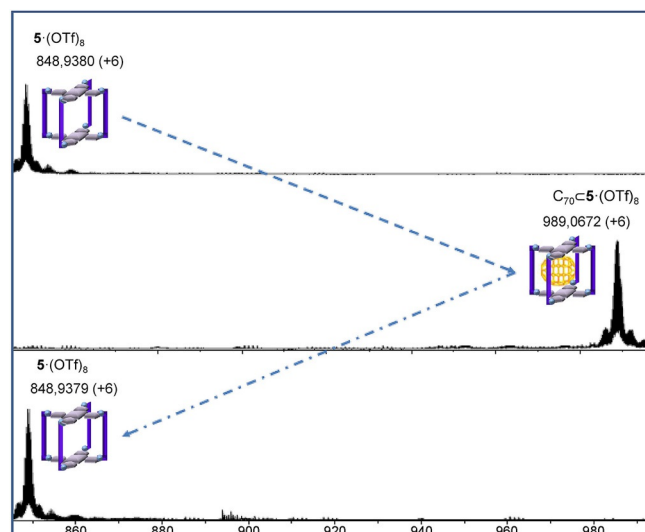


Figure 3. Solid-state extraction of fullerene C_{70} from $5\cdot(\text{OTf})_8$. HRMS monitoring of the C_{70} extraction-washing protocol using pure C_{70} in $5\cdot(\text{OTf})_8$ in solid phase.

porphyrin distance ("breathing ability") that enables the remarkable fast binding and release of the fullerenes.

The ability of $5\cdot(\text{OTf})_8$ to bind EMFs from EMF-based soots was explored. The species present in a Sc_3N -based soot were first determined by HPLC (Supporting Information Figure S10). A toluene solution of the soot was then mixed with a solution of $5\cdot(\text{OTf})_8$ in acetonitrile (1:1 molar ratio, assuming that all the species are $\text{Sc}_3\text{N}@C_{80}$, final mixture 9:1 toluene/acetonitrile). The HRMS of the inclusion compounds exhibited the ion peaks corresponding to $\text{C}_{60}\subset 5\cdot(\text{OTf})_8$, $\text{C}_{70}\subset 5\cdot(\text{OTf})_8$, $\text{Sc}_3\text{N}@C_{68}\subset 5\cdot(\text{OTf})_8$, $\text{Sc}_3\text{N}@C_{78}\subset 5\cdot(\text{OTf})_8$ and $\text{Sc}_3\text{N}@C_{80}\subset 5\cdot(\text{OTf})_8$ (major peak) (Supporting Information Figure S11). In parallel, UV/Vis titration experiments of $5\cdot(\text{OTf})_8$ with $\text{Sc}_3\text{N}@(\text{I}_h)\text{-C}_{80}$ in toluene/acetonitrile (9:1) demonstrated the formation of a 1:1 host-guest adduct, $\text{Sc}_3\text{N}@C_{80}\subset 5\cdot(\text{OTf})_8$, with a high association constant of $K_a = 2.02(\pm 0.6) \times 10^7 \text{ M}^{-1}$ (Supporting Information Figure S12). Remarkably, all the entrapped species can be completely released by applying our previously reported solvent washing protocol (Supporting Information Figure S13).

The versatility of the cage was further exploited by soaking a solid sample of $5\cdot(\text{OTf})_8$ in a toluene solution of fullerene extract (10:1 fullerene extract/ $5\cdot(\text{OTf})_8$ molar ratio, assuming that all the fullerenes are C_{60}). The HRMS of the solid (isolated and dissolved in acetonitrile) showed $\text{C}_{60}\subset 5\cdot(\text{OTf})_8$ and $\text{C}_{70}\subset 5\cdot(\text{OTf})_8$ as the unique signals (with preference for C_{60} in a 4:1 ratio, Supporting Information Figure S8b). On the other hand, in the encapsulation performed in solution the ion peak corresponding to $\text{C}_{70}\subset 5\cdot(\text{OTf})_8$ was detected as the main species by HRMS (Supporting Information Figure S8a). These results showed that $5\cdot(\text{OTf})_8$ preferentially encapsulated the smaller fullerenes in the solid state, in contrast to the results obtained in solution (K_a for $\text{C}_{70} > K_a$ for C_{60} , see above). This different selectivity behavior exhibited by the nanocapsule in solution or in solid phase might be rationalized by a higher structural rigidity of the capsule in the solid state, making its internal cavity more

restricted and selective for smaller fullerenes. In contrast, when the nanocapsule is used in solution, the flexibility of its structure increases, making its internal cavity more accessible for larger fullerenes.

Based on these observations and aiming at circumventing a tedious work-up that must result from the similar K_a of the different species in solution, we hypothesized that the Sc_3N -based EMF soot could be purified by encapsulating smaller species using $5\cdot(\text{OTf})_8$ in the solid state. To evaluate this hypothesis, two parallel experiments were performed. First, stoichiometric amounts of solid $5\cdot(\text{OTf})_8$ were mixed with a toluene solution of Sc_3N -based soot (Figure 4). As expected, pref-

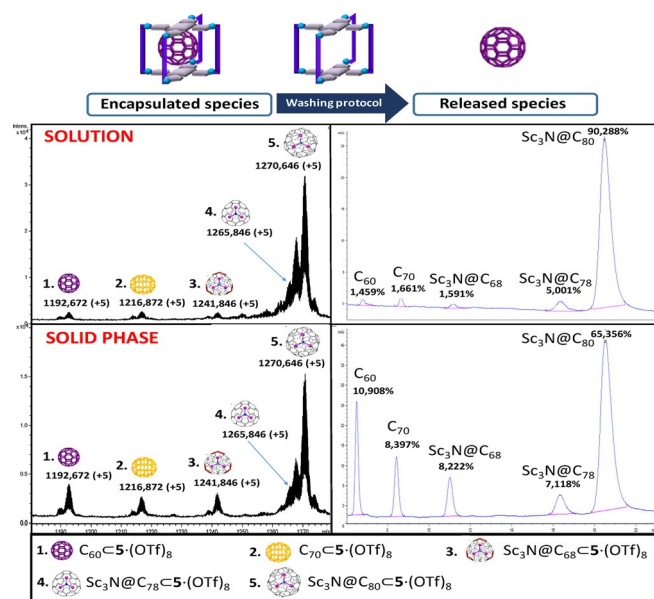


Figure 4. HRMS spectrum of Sc -based crude soot $\cdot 5\cdot(\text{OTf})_8$ host-guest complex generated (top left) in solution (9:1, toluene/acetonitrile) and (bottom left) in solid phase of $5\cdot(\text{OTf})_8$. HPLC chromatogram of the species released through our solvent-washing protocol from the Sc -based crude soot $\cdot 5\cdot(\text{OTf})_8$ host-guest complex generated in solution (top right) and in the solid phase (bottom right). The molar ratio soot: $5\cdot(\text{OTf})_8$ was 4:1, assuming that all the species are $\text{Sc}_3\text{N}@C_{80}$. The drawing of EMFs are reprinted with permission from reference [4]; Copyright (2013) American Chemical Society.

erential encapsulation of the smaller species was observed compared to the experiment with the nanocapsule in solution. With these results in hand, an excess of solid $5\cdot(\text{OTf})_8$ was added to a toluene solution of Sc_3N -based soot (6:1 $5\cdot(\text{OTf})_8$ /soot molar ratio, assuming that all the species are $\text{Sc}_3\text{N}@C_{80}$). The supernatant was increasingly enriched in $\text{Sc}_3\text{N}@C_{80}$ over time, being the unique species in solution at the end of the experiment. The encapsulation process was monitored by HPLC analysis of the supernatant (Figure 5). At the end of the experiment (after 5 h stirring), we observed that the species remaining in the supernatant corresponded uniquely to $\text{Sc}_3\text{N}@C_{80}$ (also analyzed by MALDI, Supporting Information Figure S14).

Strikingly, fractions of $\text{Sc}_3\text{N}@C_{80}$ with up to 99.5% purity were obtained in a single and operationally simple step. On

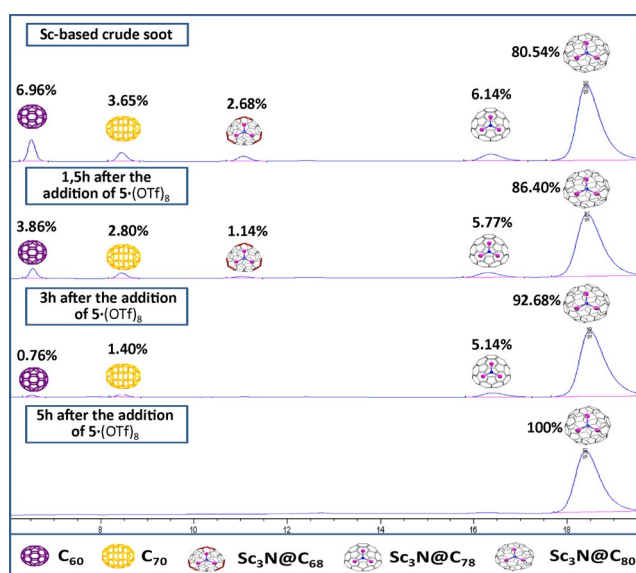


Figure 5. Sc_3N -based soot purification protocol using $5\cdot(\text{OTf})_8$ in the solid phase, by HPLC monitoring of the remaining supernatant.

the other hand, HPLC analysis of the purified fraction determined that the ratio between the two isomers of $\text{Sc}_3\text{N}@C_{80}$ (I_h and D_{5h}) remains essentially unaltered, indicating that the nanocapsule $5\cdot(\text{OTf})_8$ does not discriminate between the isomeric $\text{Sc}_3\text{N}@C_{80}$ cages (Figure 6). The quantification by HPLC of

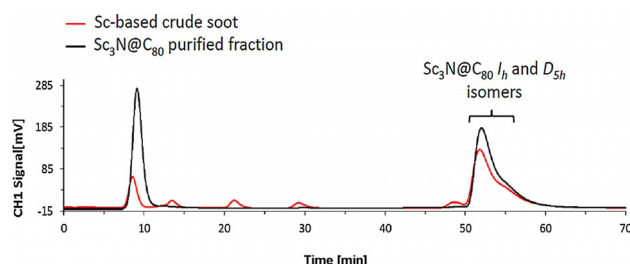


Figure 6. HPLC chromatograms of Sc -based crude soot and $\text{Sc}_3\text{N}@C_{80}$ purified fraction, from which I_h and D_{5h} isomers cannot be separated. Experimental conditions: 1.8×10^{-4} M in toluene, approximate concentration assuming that all the species are $\text{Sc}_3\text{N}@C_{80}$; HPLC separation using a 5-PBB column ($\phi = 4.6$ ID \times 250 mm); flow: 1.2 mL min^{-1} .

the purified fraction determined that approximately 60% of $\text{Sc}_3\text{N}@C_{80}$ contained in the initial soot was recovered. The species encapsulated in $5\cdot(\text{OTf})_8$ were completely released by a solvent-washing procedure and empty $5\cdot(\text{OTf})_8$ was ready to be re-used (see Supporting Information Figure S15).

To further explore this different selectivity, an excess of solid nanocapsule was added to an equimolar mixture of C_{60} , C_{70} and $\text{Sc}_3\text{N}@C_{80}$ (I_h - D_{5h} mixture) in toluene (6:1:1 $5\cdot(\text{OTf})_8$ / C_{60} / C_{70} / $\text{Sc}_3\text{N}@C_{80}$ molar ratio). The encapsulation process was monitored by HPLC analysis, clearly showing selective uptake of C_{60} and C_{70} , leaving the $\text{Sc}_3\text{N}@C_{80}$ (I_h - D_{5h} mixture) in solution after 11 hours in a single step (Figure 7). The mass recovery of $\text{Sc}_3\text{N}@C_{80}$ was 85% as determined by HPLC quantification.

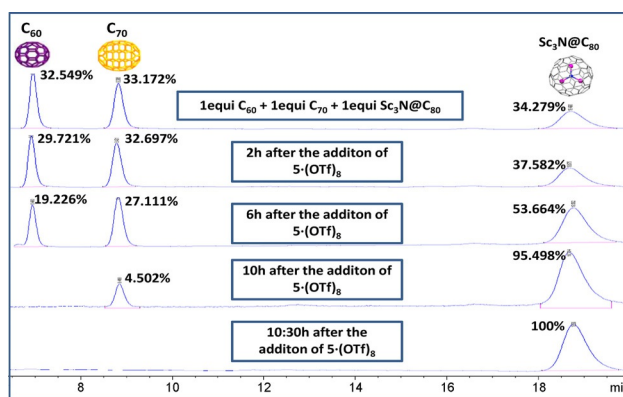


Figure 7. Purification process of an equimolar mixture of C_{60} , C_{70} and $Sc_3N@C_{80}$ (I_h - D_{5h} mixture) using $5\cdot(OTf)_8$ in the solid phase (1:6 C_{60} : $5\cdot(OTf)_8$ molar ratio) by HPLC monitoring of the remaining supernatant.

In summary, a Cu^{II} -based supramolecular nanocapsule $5\cdot(OTf)_8$ has been prepared and enables efficient and simple purification of $Sc_3N@C_{80}$ contained in a Sc_3N -based fullerene soot. Simply by soaking a solid sample of the Cu^{II} -based supramolecular nanocapsule $5\cdot(OTf)_8$ in a toluene solution of Sc_3N -based EMF soot, only $Sc_3N@C_{80}$ (I_h - D_{5h} mixture, >99.5%) is obtained in a single step. Furthermore, up to 85% recovery of the total amount of $Sc_3N@C_{80}$ from the initial mixture was attained. The species encapsulated during the process can be released and the nanocapsule can be easily recovered and directly re-used. To the best of our knowledge, this is the first EMF soot purification protocol mediated by a coordination nanocapsule. Further development of supramolecular versatile platforms for EMFs soot purification is currently being pursued in our laboratories,^[15] and the exploitation of the distinctive encapsulation of the nanocapsules in the solid state is thought to offer new opportunities in fullerene and EMF purification.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: copper · fullerenes · scandium nitride · soot purification · supramolecular nanocapsules

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- [15] Longer reaction experiments (from 5 h to 4 days) using substoichiometric amounts of solid $5\cdot(OTf)_8$ (4:1 Sc_3N -based soot/ $5\cdot(OTf)_8$ molar ratio, assuming that all the species are $Sc_3N@C_{80}$) showed a preferential encapsulation of $Sc_3N@C_{68}$ and $Sc_3N@C_{78}$ (Supporting Information Figure S16). Additional experiments will be performed in order to further explore and understand the selectivity of the $5\cdot(OTf)_8$ nanocapsule toward these EMFs.

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