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COMMUNICATION

Highly regioselective 1,3-dipolar cycloaddition of diphenylnitrilimine to Sc₃N@I_h-C₈₀ affording a very stable, unprecedented pyrazole-ring fused derivative of endohedral metallofullerenes

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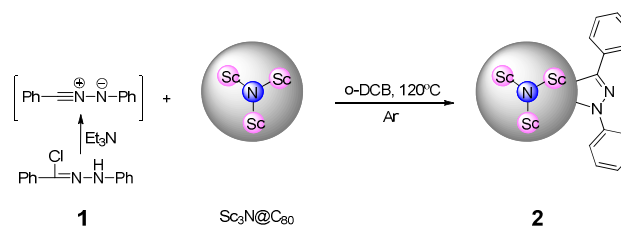
Formation of a very stable, unprecedented pyrazole-ring fused derivative of endohedral metallofullerenes was achieved from the first 1,3-dipolar cycloaddition reaction of Sc₃N@C₈₀ with diphenylnitrilimine in a highly regioselective manner.

Endohedral metallofullerenes (EMFs), a new family of carbon clusters formed by encapsulation of metallic species inside fullerene cages, have attracted considerable attention during recent years due to their unique structures, special electronic properties and potential applications in nanoscience, organic solar cell and biomedicine.¹⁻³ Chemical functionalization of EMFs has attracted increasing interest because it is not only helpful for understanding the intriguing properties of EMFs but also of practical significance for producing potentially applicable materials.⁴ To date, various approaches have been utilized to modify the outer cage of EMFs, such as disilylation, Diels–Alder reaction, 1,3-dipolar cycloaddition, Bingel–Hirsch reaction, [2+2] cycloaddition with benzyne, [2+1] cycloaddition with carbene, free-radical reaction and so on.⁴ Among these methods, the 1,3-dipolar cycloaddition is rather attractive and has been widely adopted to synthesize the nitrogen-heterocycle derivatives of EMFs because of its versatility. However, 1,3-dipolar cycloaddition of EMFs reported so far produced exclusively the corresponding derivatives with pyrrolidino-ring fused structures.⁵⁻⁸ Accordingly, it is eager to get novel derivatives of EMFs with different heterocycle structures, which may bear unexpected properties.

Nitrilimines, a special kind of reactive dipoles with a linear R-CN-NR structure, can readily undergo 1,3-dipolar cycloaddition with different double bonds of dipolarphiles.⁹⁻¹¹ This is also a powerful tool for the synthesis of various fullerene derivatives with pyrazole rings.^{12,13} Since pyrazoles are also a major class of five-membered nitrogen heterocycles in a wide variety of natural products and drug molecules, such structures have received great interest as a result of their broad range of biological activities.^{14,15} The reaction of nitrilimines and C₆₀ has been investigated previously,^{9,16,17} but nitrilimines have never been used to functionalize EMFs. In this context, for the first time we report the highly regioselective 1,3-dipolar cycloaddition reaction of Sc₃N@I_h-C₈₀ with diphenylnitrilimine (DPNI, **1**), which is generated in situ by dehydrohalogenation of N-phenylbenzenecarbohydrazonoyl chloride with triethylamine (Scheme 1).

Under argon atmosphere, Sc₃N@C₈₀ reacted with excess amount of N-phenylbenzenecarbohydrazonoyl chloride (ca. 5-fold) in the presence of triethylamine in *o*-dichlorobenzene (*o*-DCB) at elevated temperatures

(see Supporting Information for experimental details). The reaction progress was monitored by high performance liquid chromatography (HPLC) and the profiles are shown in Figure 1. Before reaction, a strong peak corresponding to Sc₃N@C₈₀ appeared at 40.6 min (Figure 1a). After 1 hour (Figure 1b), a new peak appeared at 19.0 min, which was later assigned as the target product (**2**). The intensity of the adduct peak continued to increase with prolonging reaction time and the content of Sc₃N@C₈₀ decreases simultaneously. The reaction was terminated after 5 hours (Figure 1c) when there was no significant increasing of the desired product **2** any longer. Interestingly, no bis-adducts or multi-adducts were detected in the reaction mixture, indicating a rather inert reactivity, and in other words, a high stability of the monoadduct **2**. After replacing *o*-DCB with toluene, the concentrated solution was subjected to HPLC separation which gave the adduct **2** in 38% isolated yield eventually.



Scheme 1. Reaction between Sc₃N@C₈₀ and N-phenylbenzenecarbohydrazonoyl chloride in the presence of triethylamine.

The matrix-assisted laser desorption/ionization time-of-flight mass spectrum (MALDI-TOF MS) of **2** in a positive-ion linear mode showed a molecular ion peak at *m/z* 1303 with 1,1,4,4-tetraphenyl-1,3-butadiene as a matrix (Figure 2, inset), verifying the covalent attachment of the diphenylnitrilimine onto the fullerene cage. The peak at *m/z* 1109 is attributed to Sc₃N@C₈₀ due to the loss of the pyrazole entity from the product under laser desorption. This is consistent with our ¹H NMR result of **2** (Fig. S1, Supporting Information) which shows only one set of proton signals, confirming the presence of a single regioisomer.

The electronic configuration of **2** was investigated with UV-vis-NIR spectrometry. As illustrated in figure 2, the absorption spectrum of **2** resembles that of pristine Sc₃N@C₈₀, demonstrating that the electronic structure remains in the derivative. UV-vis-NIR spectrometry can also be a practical tool to determine the addition patterns of Sc₃N@C₈₀ cycloadducts which can adopt either a [5,6]- or a [6,6]-structure. According to the results from Dorn and coworkers, the [6,6]-pyrrolidino

adduct of $\text{Sc}_3\text{N}@C_{80}$ shows a new absorption band at 800–820 nm but the spectrum of the [5,6]-adduct resembles that of pristine $\text{Sc}_3\text{N}@C_{80}$.¹⁸ As a consequence of the featureless absorption spectrum, it is tentatively proposed that **2** is a [5,6]-adduct.

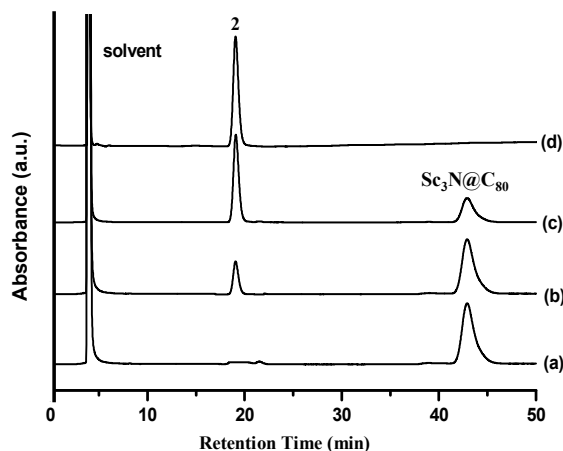


Fig. 1. HPLC profiles of the reaction mixture probed at different reaction times. (a) 0 h; (b) 1 h; (c) 5 h. (d) pure product **2** after HPLC separation. Conditions: Buckyprep column (Φ 10 mm \times 250 mm), 4 mL/min toluene flow, 330 nm detection wavelength.

The molecular structure of **2** was unambiguously determined by single-crystal X-ray diffraction (XRD) crystallography. Black crystals suitable for XRD measurements were obtained by slow diffusion of a carbon disulfide solution of **2** into hexane over a period of two weeks under 263K.

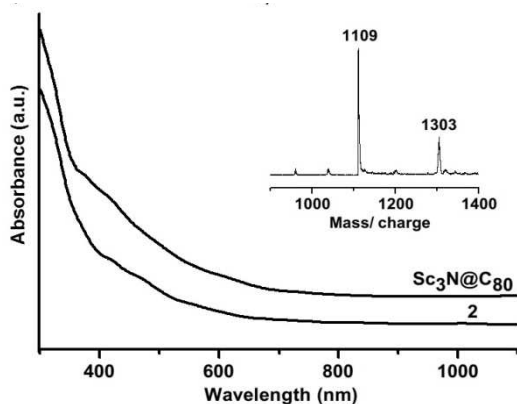


Fig. 2. UV-vis-NIR spectra of $\text{Sc}_3\text{N}@C_{80}$ and **2** in toluene. The inset shows the MALDI TOF spectrum of **2**.

The asymmetric unit contains a whole molecule of **2** and two CS_2 molecules intercalating in between the fullerene cages.¹⁹ Both the cage and the internal cluster suffer from disorder although the pyrazole moiety is fully ordered. The cage has two disordered positions with relative abundance of 0.67:0.33. Inside the cage, the N atom and a scandium atom, which is close to one of the sites of addition, are fixed but each of the other two scandium atoms displays two respective disordered positions with a relative ratio of 0.60:0.40. By considering the geometrical relationships and the occupancy values, we allow the minor cage to encapsulate the minor metal sites while the major ones are grouped together (Figure S2, Supporting information).

Figure 3 shows the X-ray structure of **2** consisting of only the major components from two orthogonal viewing directions. The cycloaddition occurs at a [5,6]-bond junction. The C1–C2 bond length (1.61 Å) at the sites of addition falls in the range of a C–C single bond, confirming a close-cage structure. This value is very close to that of the corresponding [5,6]-pyrrolidino $\text{Sc}_3\text{N}@C_{80}$ (1.619 Å).²⁰ In the pyrazole ring, the C81–N2 bond length (1.291 Å) is shorter than the N2–N3 distance (1.399 Å), which is the evidence to confirm the relative positions of C81 and N2.

The lone pair of electrons on N2 in the pyrazole ring is located over a hexagonal ring rather than over the opposite pentagonal ring of the C_{80} cage (Figure 3a). This may be a result of steric hindrance.

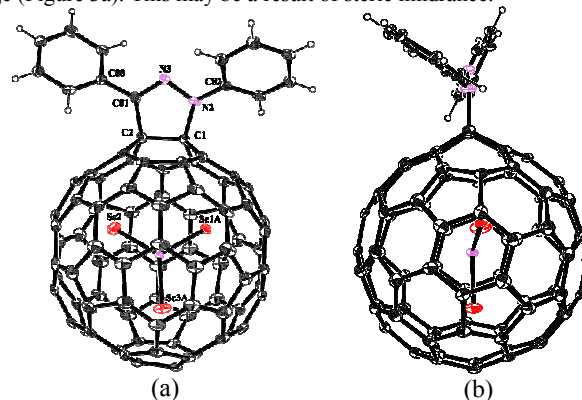


Fig. 3. Ortep drawing of **2** showing thermal ellipsoids at the 30% probability level from two orthogonal viewing directions. Only the major cage orientation (0.67 occupancy) and the major metal sites (0.60 occupancy for Sc1A and Sc3A) are shown. Solvent molecules, the minor cage orientation and minor metal sites are omitted for clarity.

In pristine $\text{Sc}_3\text{N}@C_{80}$, it is believed that the Sc_3N cluster tends to adopt a dynamic motion rather than being fixed because of the high cage symmetry and the relatively small cluster size. However, X-ray structure of **2** demonstrated here that the motion of the cluster has been largely hindered upon exohedral functionalization. Even considering the minor sites of the two disordered Sc atoms, the Sc_3N cluster is located in such a way that two Sc atoms point to the respective *para*-positions of the cage carbons at the sites of addition, while the remaining one directs to a [5,6]-bond junction opposite the addend. This is similar to the previous X-ray results of the corresponding [5,6]-pyrrolidino derivatives of $\text{Sc}_3\text{N}@C_{80}$. Moreover, the sum of the three Sc–N–Sc angles (356.0°) suggests that the trimetallic nitride cluster slightly derives from a coplanar structure. This is most probably due to the distortion of the C_{80} cage by exohedral modification. The Sc–N distances of the Sc_3N cluster (1.9859 Å – 2.050 Å) are shorter than the shortest distances (2.217 Å – 2.240 Å) between each scandium atom and the nearby cage carbon atoms. Another interesting finding is that the pyrazole ring is nearly coplanar with the major Sc_3N set (Figure 3b) in spite that two of the scandium atoms slightly leave the plane.

In principle, cycloaddition to $\text{Sc}_3\text{N}@I_h-C_{80}$ produces two different mono-adduct isomers, namely, [5,6]- and [6,6]-adducts. Both experimental and computational results proposed that the [5,6]-adduct is more thermodynamically stable and the [6,6]-adduct is more favored kinetically.²¹ This is particularly true for the pyrrolidino-derivatives of $\text{Sc}_3\text{N}@I_h-C_{80}$. Several groups have demonstrated that the 1,3-dipolar reactions of various azomethine ylide reagents to $\text{Sc}_3\text{N}@I_h-C_{80}$ generate both [5,6]- and [6,6]-cycloadducts.²⁰ Upon heating, the [6,6]-adduct changes to the corresponding [5,6]-adduct, indicating a reaction mechanism involving both kinetic and thermodynamic pathways.²⁰ In contrast, our study found here that the addition of **1** to $\text{Sc}_3\text{N}@I_h-C_{80}$ exclusively gave rise to the [5,6]-adduct **2**, suggesting a pure thermodynamic process. This result was closed to the previous reported that the pyrazolo-fullerenes have better thermal stability than other cycloadducts.¹² This methodology would be useful for the functionalization of other EMFs because of the high regio-selectivity and the high yield. For example, addition of N-triphenyl azomethine ylide to $\text{La}_2@C_{80}$ afforded two isomers which are not separable from each other even using exhaustive HPLC.²² By using **1**, however, it can be anticipated that only the [5,6]-adduct will be obtained. Moreover, previous reports also revealed that the relative stability of the [5,6]-adduct versus [6,6]-adduct is highly dependent on the cluster size inside the fullerene cage.²³ It will be interesting to perform the reaction of **1** with other $\text{M}_3\text{N}@I_h-C_{80}$ compounds containing different clusters to see whether the [6,6]-adduct will appear or not, which may add new insights into the art of reactivity control of EMFs via the cluster effect.

In addition, Martin and coworkers reported that the N-ethyl pyrrolidino- $\text{Sc}_3\text{N}@I_h\text{-C}_{80}$ underwent retro-1,3-dipolar reaction under heating.²⁴ Similarly, the corresponding pyrazolo-fullerenes also underwent retro-cycloaddition reaction under negative ESI mass spectrometric conditions.²⁵ However, the current pyrazole-ring fused derivative **2** proves quite stable. After the chlorobenzene solution of **2** was refluxed for 8 hours, its HPLC chart remains unchanged at all. Such a high thermal stability promises its future use in the construction of donor-acceptor conjugates and related devices. Furthermore, our results found that no bis- or multi-adducts were formed in the reaction, showing the inert reactivity of **2**. This can be an advantage in future works for the selective synthesis of mono-adducts of EMFs.

In conclusion, we have introduced a facile process for the synthesis of novel EMF-derivatives bearing a pyrazole ring. The regioselective 1,3-dipolar cycloaddition between $\text{Sc}_3\text{N}@C_{80}$ and nitrilimine, which was generated in situ from N-phenylbenzenecarbohydrazonoyl chloride in the presence of triethylamine, produced a single adduct in reasonable yield. The product has been characterized with a collection of experimental tools such as MALDI-TOF mass spectroscopy, NMR, UV-vis-NIR spectrometry and X-ray crystallography which firmly established the [5,6]-cycloaddition pattern. Formation of only one isomer suggests that the reaction involves merely a thermodynamic process. Further studies demonstrated that the derivative is very stable even under heating conditions, suggesting its practical applications in related fields. This simple method which shows high regioselectivity and produces derivatives of high stability, can be easily extended to the functionalization of other EMFs. Following works are ongoing in our laboratory.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures, ¹H NMR spectrum and X-ray structures of **2**. See DOI: 10.1039/c000000x/

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