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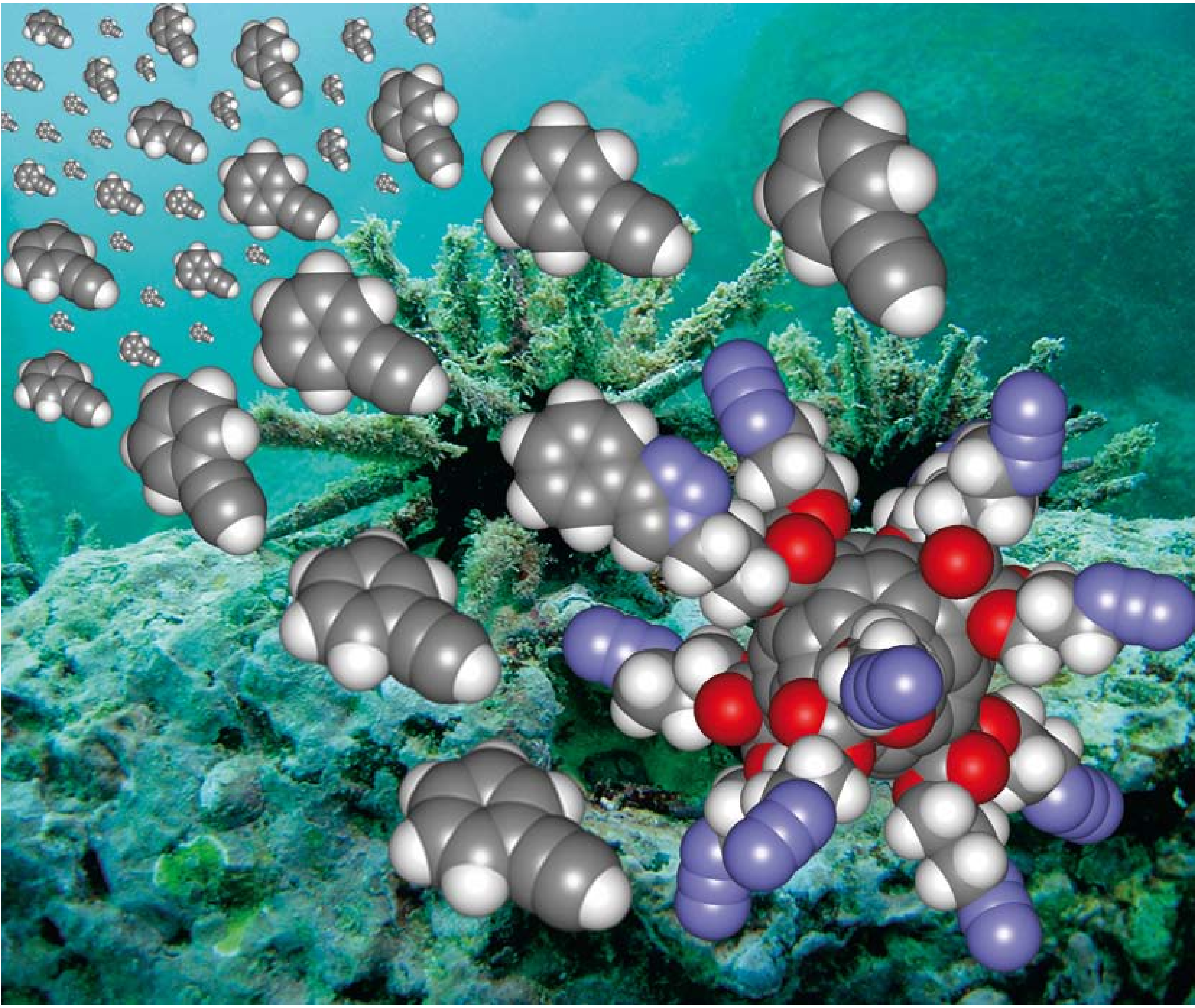

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Click chemistry for the efficient preparation of functionalized [60]fullerene hexakis-adducts†

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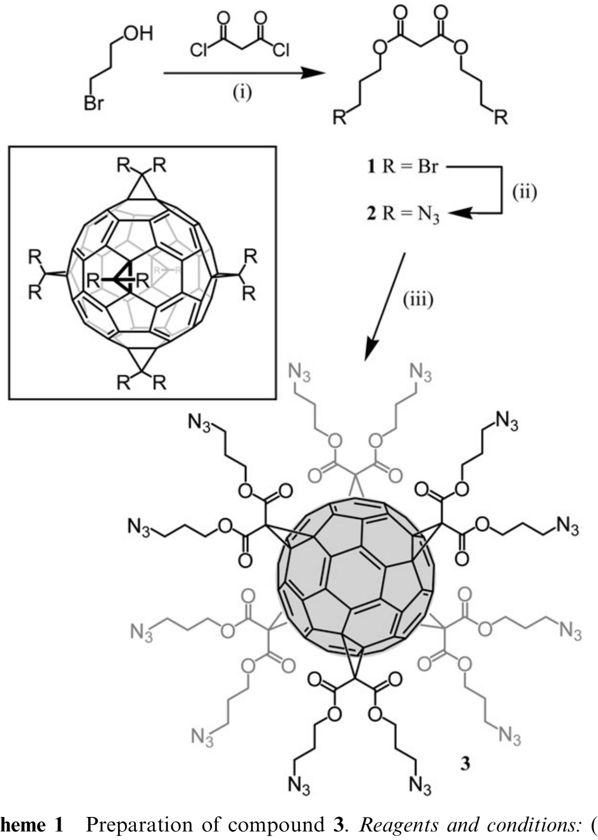
A T_h-symmetrical C_{60} hexakis-adduct bearing 12 peripheral azide groups has been prepared and used to produce functionalized derivatives by the copper mediated Huisgen 1,3-dipolar cycloaddition of azides and alkynes.

Fullerene hexakis-adducts with a T_h-symmetrical octahedral addition pattern have received increasing attention in the past few years.[1] Apart from their aesthetically appealing chemical structure resulting from their high symmetry, fullerene hexa-adducts are also unique three-dimensional molecules for the preparation of new materials such as liquid crystals.[2] On the other hand, hexakis-adducts with interesting photophysical properties have also been reported.[3] As far as the synthesis of fullerene hexakis-adducts is concerned, most of them have been prepared by the one-pot reaction of C_{60} with malonates under the conditions initially developed by Hirsch[4] and further improved by Sun.[5] Whereas these reaction conditions are efficient for the synthesis of fullerene hexakis-adducts when starting from relatively simple malonates, structurally more complicated systems are generally obtained in rather low yields and/or HPLC is often required for their purification. In order to overcome this problem, we have decided to produce a simple C_{60} hexakis-adduct derivative bearing 12 terminal groups allowing its further functionalization. The grafting of 12 building blocks onto this core requires, however, an extremely efficient reaction to obtain functionalized derivatives with good yields. Indeed, click chemistry[6] appears to be perfectly suited for our purpose. In this paper, we show that the copper mediated Huisgen 1,3-dipolar cycloaddition of azides and alkynes resulting in 1,2,3-triazoles, one of the most powerful click reactions to date,[6] is an ideal tool to efficiently produce functionalized hexa-substituted fullerenes. To this end, we have prepared a C_{60} hexakis-adduct bearing 12 azide groups (**3**) allowing the attachment of 12 alkyne units *via* click reaction.

The preparation of compound **3** is depicted in Scheme 1. Reaction of malonyl dichloride with 3-bromopropan-1-ol in the presence of pyridine afforded malonate **1** in 83% yield. Subsequent treatment with sodium azide in DMF at room temperature gave **2** in 95% yield. Hexakis-adduct **3** was then readily synthesized by the reaction of C_{60} (1 equiv.) with **2** (10 equiv.), CBr_4 (100 equiv.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 20 equiv.) in *o*-dichlorobenzene (ODCB) at room temperature. The mixture was stirred for 72 h and evaporated. The resulting sample was separated on a silica-gel column in a relatively straightforward fashion to obtain **3** in 62% yield.



Scheme 1 Preparation of compound **3**. *Reagents and conditions:* (i) CH_2Cl_2, pyridine, 0 °C to rt, 18 h (83%); (ii) NaN_3, DMF, rt, 16 h (95%); (iii) C_{60}, ODCB, DBU, CBr_4, rt, 72 h (62%). Inset: detailed view of the octahedral addition pattern of a T_h symmetrical fullerene hexa-adduct.

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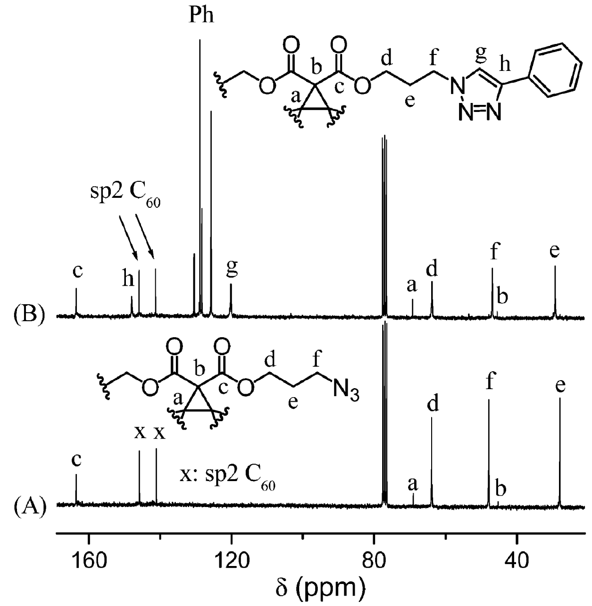
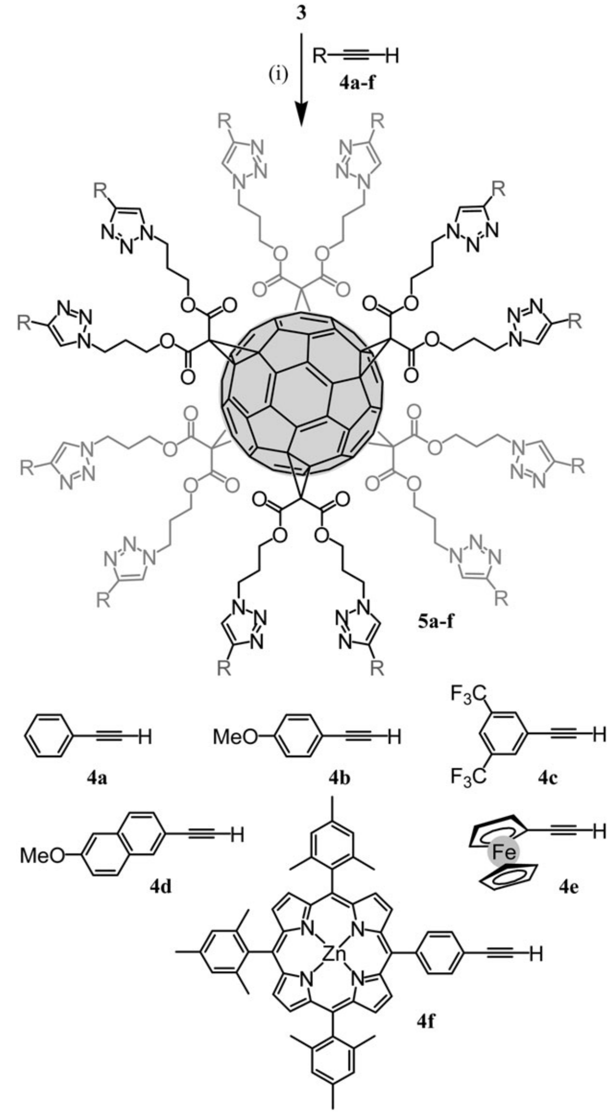


Fig. 1 ^{13}C NMR spectra ($CDCl_3$, 75 MHz) of **3** (A) and **5a** (B).

The chemical structure of compound **3** was easily confirmed by ^1H and ^{13}C NMR analysis. As shown in Fig. 1, the ^{13}C NMR spectrum of fullerene hexakis-adduct **3** is in full agreement with its T_h-symmetrical structure and shows the three expected fullerene resonances (δ = 69.0 for the sp^3 C atom; 141.1 and 145.8 ppm for the two different sp^2 C atoms), a signal for the bridgehead C atom (δ = 45.2 ppm), a signal for the carbonyl group (δ = 163.5 ppm), and three signals for the $(CH_2)_3$ linker (δ = 28.0, 47.9 and 63.8 ppm). It is worth noting that compound **3** is quite unstable in the solid state but reasonably stable in solution. Upon purification, it is best to use polyazide **3** for the click reactions within the next 12 hours to obtain good yields.

The reaction conditions for the 1,3-dipolar cycloaddition of compound **3** with terminal alkynes were first adjusted with phenylacetylene (**4a**) (Scheme 2). Under optimized conditions, a mixture of **3** (1 equiv.), **4a** (13 equiv.), $CuSO_4 \cdot 5H_2O$ (0.1 equiv.) and sodium ascorbate (0.3 equiv.) in CH_2Cl_2–H_2O was vigorously stirred at room temperature for 12 h. After work-up and purification, compound **5a** was thus obtained in 78% yield.

The reaction conditions used for the preparation of **5a** from phenylacetylene were then applied to the terminal alkynes **4b–f**.[7] The clicked derivatives **5b–f** were thus obtained in 56 to 81% yields. The structure of compounds **5a–f** was confirmed by their ^1H and ^{13}C NMR spectra as well as by mass spectrometry. Inspection of the ^1H NMR spectra clearly indicates the disappearance of the CH_2-azide signal at δ 3.33 ppm. IR data also confirmed that no azide (2092 cm^{-1}) residues remain in the final products. Importantly, the ^1H NMR spectra of **5a–f** show the singlet typical of the 1,2,3-triazole unit at *ca.* δ 7.5–7.8 ppm as well as the signal corresponding to the CH_2-triazole protons at *ca.* δ 4.3–4.4 ppm. Finally, the two expected resonances of the C atoms of the 1,2,3-triazole unit are clearly observed in the ^{13}C NMR spectra of **5a–f**. As a typical example, the ^{13}C NMR spectrum of **5a** is depicted in Fig. 1.



Scheme 2 Preparation of compounds **5a–f**. *Reagents and conditions:* (i) $CuSO_4 \cdot 5H_2O$, sodium ascorbate, CH_2Cl_2, H_2O, rt, 12 h (**5a**: 78%, **5b**: 61%, **5c**: 56%, **5d**: 63%, **5e**: 81%, **5f**: 74%).

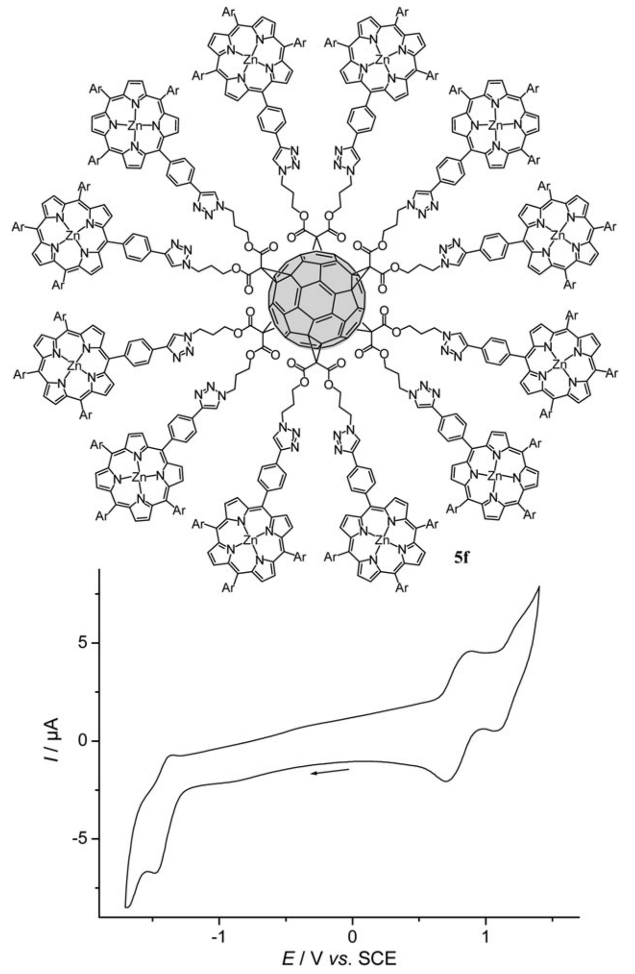
The electrochemical properties of compounds **5b**, **5e** and **5f** were determined by cyclic voltammetry (CV) and Osteryoung square wave voltammetry (OSWV). All the experiments were performed at room temperature in CH_2Cl_2 solutions containing tetra-*n*-butylammonium tetrafluoroborate (0.1 M) as supporting electrolyte, with a Pt wire as the working electrode and a saturated calomel electrode (SCE) as a reference. Potential data are collected in Table 1. As a typical example, the cyclic voltammogram obtained from **5f** is shown in Fig. 2.

Compound **5b** exhibits an irreversible cathodic process at −1.59 V *vs.* SCE. As already observed for related hexa-substituted C_{60} derivatives,[8] the high degree of addition on the fullerene cage disrupts the π conjugation, making the reduction more difficult when compared to mono-functionalized fullerenes.[9] In the anodic region, compound **5b** presents an irreversible peak at +1.51 V *vs.* SCE which can likely be attributed to the oxidation of the benzenoid rings in the 'cubic'

Table 1 Electrochemical data of **5b**, **5e** and **5f** determined by OSWV on a Pt working electrode in CH_2Cl_2 + 0.1 M $^{n}Bu_4NBF_4$ at room temperature[a]

	Reduction			Oxidation	
	E_3	E_2	E_1	E_1	E_2
5b			−1.59	+1.51	
5e			−1.55	+0.55	
5f	−1.82	−1.58	−1.38	+0.88	+1.23

[a] OSWVs were obtained using a sweep width of 20 mV, a frequency of 10 Hz, and a step potential of 5 mV; Fc^+/Fc is observed at +0.57 ± 0.01 V *vs.* SCE under these conditions.



5f

Fig. 2 Cyclic voltammogram of **5f** on a Pt electrode at v = 0.1 V s^{-1} in CH_2Cl_2 + 0.1 M $^{n}Bu_4NBF_4$ (Ar = mesityl).

cyclophane substructure of the fullerene hexa-adduct core.[10] In the cathodic region, compound **5e** revealed the typical electrochemical response of dendrimers with peripheral ferrocene subunits.[11] Indeed, the 12 ferrocene moieties in **5e** behave as independent redox centers and their oxidation is observed at +0.55 V *vs.* SCE. Whereas the oxidation centered on the fullerene core could not be clearly seen for compound **5e** in the available potential window, an irreversible peak at *ca.* −1.6 V *vs.* SCE corresponding to the reduction of the C_{60} hexa-adduct core is clearly observed in the anodic region.

As shown in Fig. 2, the cyclic voltammogram recorded for compound **5f** shows the two characteristic Zn(II)-porphyrin-centered oxidations.[12]

In the cathodic part, the reduction of the hexa-substituted fullerene core is masked by the first reduction of the 12 Zn(II)-porphyrin subunits. The latter is, however, easily observed by OSVW (see ESI†).

In conclusion, a new approach based on click chemistry has been developed for the efficient functionalization of fullerene hexakis-adducts. As click reactions are modular, tolerant to a wide range of functional groups, and high yielding, a large number of functionalized fullerene hexakis-adducts should become easily accessible by using this synthetic approach. Further efforts are currently under way in our group to prepare related derivatives with new properties for various applications.

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