Cyclodextrin-[60]fullerene conjugates: synthesis, characterization, and electrochemical behavior

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Abstract—Three different functionalized β-cyclodextrins (β-CDs) bearing the C_{60} moiety linked covalently have been prepared in good yields by reaction between the parent β-CD and [60]fullerene via 1,3-dipolar cycloaddition. These compounds have been fully spectroscopically characterized and their electrochemical behavior has been investigated. Surprisingly, the electrochemical properties of the C_{60} cage remain unaltered even after chemical functionalization, making these systems very appealing as supramolecular hosts for electron-transfer processes.
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1. Introduction

Since its discovery, [60]fullerene has been considered as a powerful building block in material sciences and medicinal chemistry due to its unique properties. In particular, C_{60} shows a noticeable electron acceptor capability as well as singular photophysical[1] and electrochemical behavior.[2] All these properties have been exploited in the fabrication of pioneering organic photovoltaic devices[3] as well as in the construction of supramolecular architectures.[4] In addition, fullerene and its derivatives exhibit satisfactory enzyme-inhibiting,[5] radical quenching,[6] and DNA-cleavage abilities.[7]

On the other hand, cyclodextrins (CDs) represent one of the most studied molecular receptors in the field of supramolecular chemistry due to their capability to include various guest molecules in the hydrophobic cavity.[8] While the supramolecular complexation of C_{60} by CDs is a well explored topic,[9] only few works are reported on the CD-C_{60} conjugates. In fact, to the best of our knowledge, the first CD derivatized with fullerene showing water solubility has been described by Samal and Geckeler.[10] Photodriven DNA-cleaving properties

have been successfully tested by Liu et al. in a β-CD-C_{60} and in a bis-β-CD-C_{60} conjugate.[11] Rassat and co-workers have devoted a lot of effort in the search for internal complexation in water of fullerene in the CD cavity in bis-CD-C_{60} systems although they mainly detected the presence of aggregates.[12]
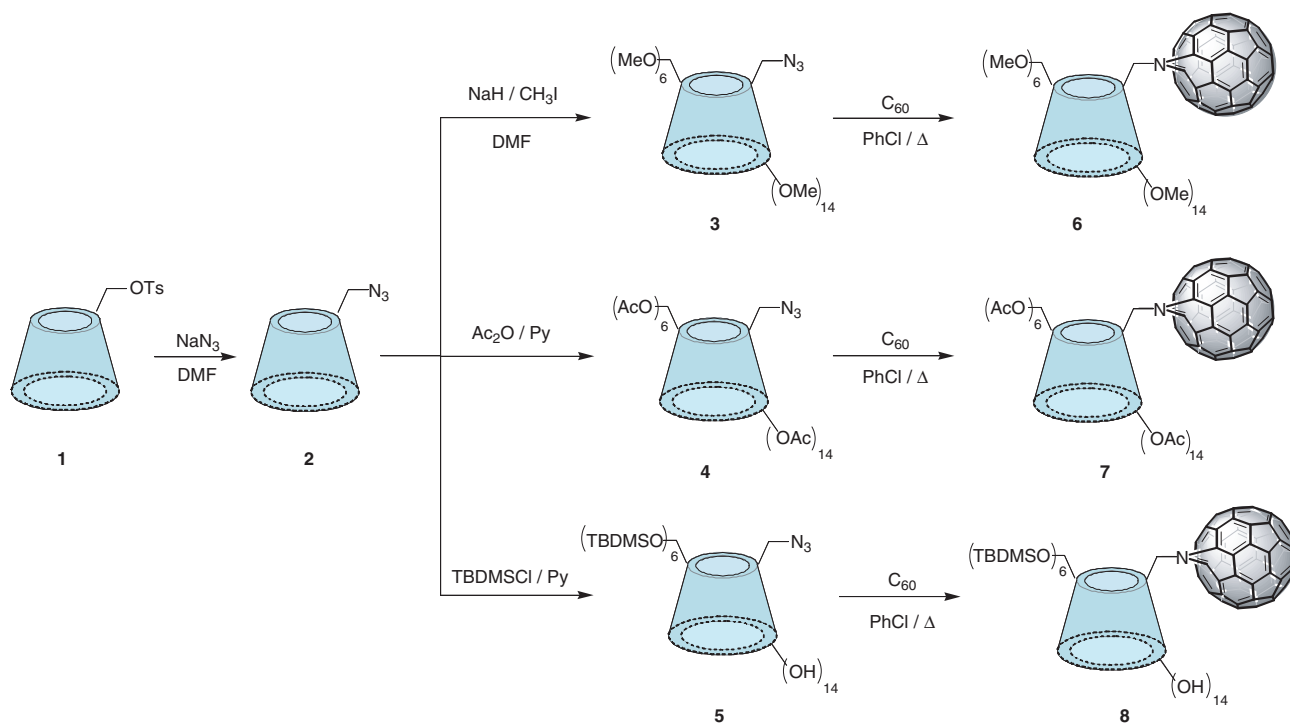
In this letter, we present the synthesis, the spectroscopical characterization and the electrochemical investigation of three novel CD-C_{60} conjugates (**6**–**8**) with the aim to furnish new systems that combine the binding ability of cyclodextrins with the well known electrochemical properties of [60]fullerene. Furthermore, changes in chemical structures should be reflected into different CD-cavity receptivity with the subsequent effect toward complexation.

2. Synthesis

The synthesis of CD-C_{60} conjugates **6**–**8** takes place in a parallel way, as depicted in Scheme 1. The mono-6-azido-β-CD (**2**),[13] obtained from the readily available mono-6-tosyl-β-CD **1**,[14] is reacted with methyl iodide, acetic anhydride, and *tert*-butyldimethylsilyl chloride to afford the parent cyclodextrin **3**–**5**, respectively, in high yields. Spectroscopical data matched those reported in the literature. Hence, such azido-CDs are in turn reacted with fullerene, in refluxing chlorobenzene for 24 h, following a well established protocol,[15] via

Scheme 1.

1,3-dipolar cycloaddition to give rise the corresponding azafulleroid **6**–**8** in 40–49% yields.

The CD-C_{60} derivatives so obtained have been readily purified by flash chromatography (silica gel, DCM/MeOH from 99:1 to 95:5, for **8** also 1% water is needed). These CD-C_{60} conjugates are soluble in all the common organic solvents as well as in THF/H_2O mixtures with up to 90% of water.[16]

All CD-C_{60} conjugated (**6**–**8**) have been satisfactorily characterized by means of FT-IR, UV–vis, ^{1}H and ^{13}C NMR, and MS techniques.[17] FT-IR spectra clearly showed the disappearance of N_3 stretching band at $\sim$2100 cm^{-1} and the subsequent appearance of a new set of bands in the 750–500 cm^{-1} region, characteristic of C_{60}. The UV–vis spectra in dichloromethane and in THF/H_2O 1:9 (v/v) mixtures for target compounds **6**–**8** are reported in Figure 1. Similar spectra were recorded for the three cyclodextrin–fullerene systems despite differences in the solubilizing group nature, namely methyl, acetyl, and TBDMS. All spectra show the typical absorption features of azafulleroid mono-adduct: a strong band at $\sim$257 nm and a shoulder at $\sim$325 nm very similar to that of fullerene itself. It is noteworthy that, in THF/H_2O 1:9 mixtures, the electronic band at lower wavelength is slightly bathochromi-cally shifted and, at the same time decreases in intensity in comparison with the absorption at $\sim$325 nm (Abs_{260}/Abs_{330} ratio: $\sim$3.6 in DCM, $\sim$2.4 in THF/H_2O 1:9, see inset in Fig. 1). In addition in DCM the band offset is 100 nm blue-shifted. Such electronic behavior for C_{60} derivatives has been previously observed and ascribed to the formation of the colloidal cluster generated from the self association of fullerene moieties.[18]
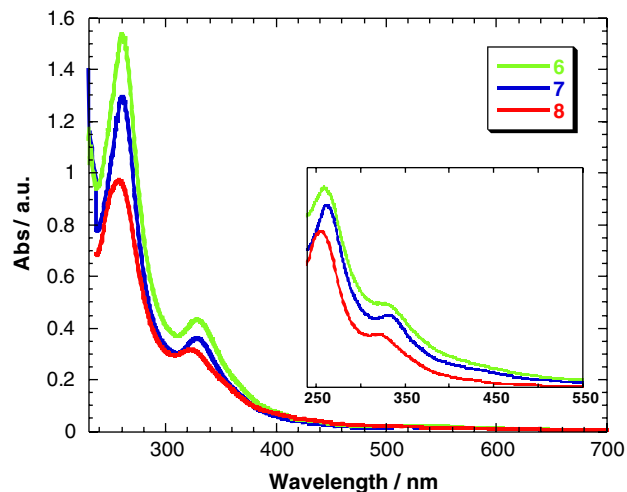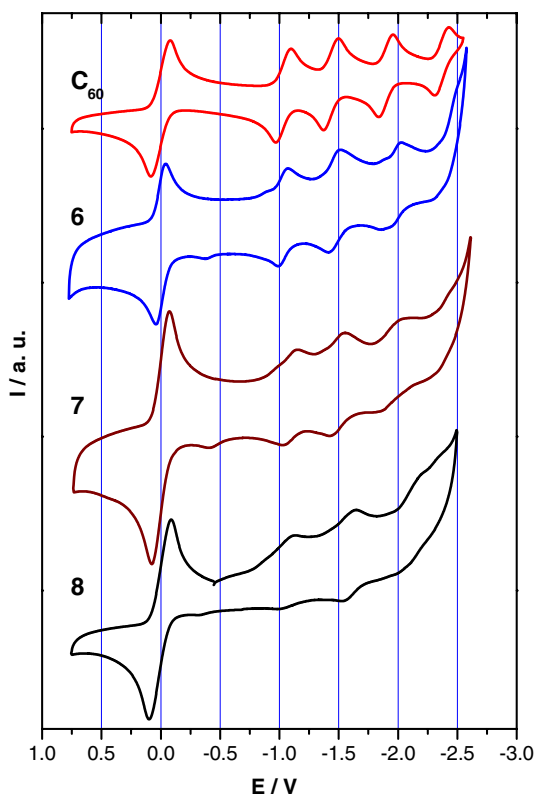

Figure 1. UV–vis spectra of derivatives **6**–**8** in dichloromethane. Inset shows spectra recorded in THF/H_2O 1:9 (v/v) mixtures.

^{1}H NMR spectra of title compounds **6**–**8** were very similar to those of the corresponding precursors. The presence of more than 17 signals (about 32) between 135 and 150 ppm in the ^{13}C NMR spectra is symptom-atic for the open form of the [5,6] adducts due to its lower symmetry, C_s, with respect to the C_{2v} of [6,6] closed adducts. This finding is in agreement with that previously observed for other CD-C_{60} systems in which fullerene is covalently connected to the CD through an azo-bridge.[19] Finally MALDI-TOF experiments showed the presence of the molecular ion peak for all the structures suggested.

3. Electrochemistry

The redox properties of the electroactive CD-C$_{60}$ systems were determined by cyclic voltammetry (CV) measurements at room temperature in *ortho*-dichlorobenzene/acetonitrile (*o*DCB/MeCN, 4/1 v/v) mixtures as solvent, adding ferrocene as an internal reference. The electrochemical data, shown in Figure 2 and collected in Table 1, display the presence of four reduction processes for **6**–**8**.

These reduction waves correspond unambiguously with the first four quasireversible reductions of the fullerene sphere.[2] On the other hand, CV of compound **7** shows a broadened third wave that, at first glance, seems to proceed from the combined reduction of C$_{60}$ and C=O groups, as previously observed.[20] However, additional squared wave voltammetry (SWV) experiments, in this case, evidenced no electrochemical contribution from carbonyl groups. It is interesting to note that, for CD-C$_{60}$ systems **6** and **8**, the first reduction potential is 60 mV less negative than that of **7** and the same with that of pristine C$_{60}$. To better understand if this behavior stems from some kind of supramolecular organization or it is simply characteristic for these systems, further CV experiments have been carried out. Mixtures of C$_{60}$ and precursors **3**–**5** in 1:1 and 1:2 stoichiometric ratios have been prepared and the voltammograms recorded showed no changes in the potentials. In addition, no shift in the reduction potential after dilution of **6**–**8** solutions was observed. All these data demonstrate that the good electrochemical response is intramolecular and is own for these systems. In this case, in agreement with the data reported in the literature for azafulleroids,[21] the cathodic shift in potentials produced upon saturation of one fullerene double bond, is corrected by the better electron accepting ability of azafulleroid due to the presence of the electronegative nitrogen atom. In addition, further stabilization for the C$_{60}^{\cdot-}$ specie may be derived from when the fullerene cage is in correspondence of the small rim of CD, as evidenced by preliminary molecular mechanics simulations.

In summary, we have prepared and characterized three new CD-C$_{60}$ conjugates. The spectroscopical data collected clearly indicate that fullerene cage is connected to the CD moiety as the open form of the [5,6] adducts. The electrochemical study, carried out for the first time on such CD-C$_{60}$ systems, revealed that, even after chemical functionalization the electrochemical properties of the fullerene moiety remain totally unaltered. This behavior suggests that these electroactive species are appealing electron acceptor–host systems for further photophysical studies in the search for energy and electron-transfer processes toward small electron donor guests such as ferrocene and tetrathiafulvalene. Further investigations in this sense are currently underway.

Figure 2. Voltammogram of compounds **6**–**8** and C$_{60}$ as reference (see Table 1 for experimental conditions).

Table 1. Redox potentials of C$_{60}$ and **6**–**8** (V vs Fc/Fc$^+$)[a]

Compound	$E_{1/2}^1$	$E_{1/2}^2$	$E_{1/2}^3$	$E_{1/2}^4$
C$_{60}$	−1.03	−1.43	−1.89	−2.35
6	−1.03	−1.46	−1.94	−2.46
7	−1.09	−1.48	−1.94	−2.40
8	−1.03	−1.58	−2.11	−2.32

[a] Working electrode: GCE; quasireference electrode: Ag/Ag$^+$; counter electrode: Pt; 0.1 M Bu$_4$NClO$_4$; scan rate: 200 mV s^{-1}; concentration: 0.3–0.6 × 10^{-3} M; solvent: *o*DCB/MeCN (4:1 v/v); ferrocene was added as an internal reference. Values were determined within the experimental error of ±5 mV.

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16. For the latter case, qualitative solubility tests were performed by diluting 1 ml of 1.2×10^{-4} M in THF stock solutions of CD-C_{60} with water to the final volume of 10 ml and UV spectra were recorded (final concentration 1.2×10^{-5} M).

17. A typical procedure for the preparation of CD-C_{60} from CD-N_3: a solution of the corresponding CD-N_3 (1 mmol) and C_{60} (1 mmol) in refluxing chlorobenzene (15 ml) was stirred under argon during 24–48 h. The solvent was evaporated in vacuo and the residue was purified by chromatography on silica gel (CS_2 first, then CH_2Cl_2/MeOH from 99:1 to 95:5) to afford the respective product as a black powder.
Selected spectroscopical data for **6**: ^{1}H NMR (500 MHz, CDCl$_3$/CS$_2$, TMS) δ: 5.36 (m, 1H), 5.07–4.97 (m, 6H), 4.23–3.15 (m, 102H, at 3.62, 3.48, and 3.36 are present the –OCH$_3$ signals); ^{13}C NMR (125 MHz, CDCl$_3$/CS$_2$) δ: 144.97, 144.77, 144.68, 144.64, 144.57, 144.39, 144.28, 144.23, 144.11, 144.05, 143.99, 143.91, 143.82, 143.70, 143.62, 143.38, 143.28, 143.25, 143.07, 143.05, 142.89, 142.74, 142.55, 142.53, 142.50, 142.43, 140.59, 139.12, 139.02, 135.96, 133.64, 99.97, 81.93, 80.07, 73.15, 71.29, 70.88, 61.46, 60.10, 58.70; FT-IR(KBr): 2927, 2839, 1458, 1365, 1215, 1161, 1087, 1045, 667 cm^{-1}; MALDI-TOF MS calcd for $[C_{122}H_{109}NO_{34}]^+$: m/z 2131.683; found: 2131.645.
Selected spectroscopical data for **7**: ^{1}H NMR (500 MHz, CDCl$_3$/CS$_2$, TMS) δ: 5.45–5.25 (m, 7H), 5.12–5.00 (m, 7H), 4.86–4.64 (m, 7H), 4.54–4.09 (m, 21H), 3.73–3.45 (m, 7H), 2.07 (m, 60H); ^{13}C NMR (125 MHz, CDCl$_3$/CS$_2$) δ: 170.05–168.85 (C=O), 146.19, 146.04, 145.93, 145.78, 145.21, 144.99, 144.92, 144.71, 144.51, 144.40, 144.33, 144.13, 144.00, 143.94, 143.70, 143.64, 143.19, 143.02, 142.90, 142.87, 142.59, 142.07, 141.95, 140.72, 140.68, 139.40, 138.40, 138.15, 137.62, 136.59, 135.73, 134.06, 96.39, 83.22, 70.58, 70.12, 69.98, 69.30, 62.25, 20.38; FT-IR(KBr): 3020, 2958, 1747, 1431, 1369, 1234, 1041, 667, 601 cm^{-1}; MALDI-TOF MS calcd for $[C_{142}H_{109}NO_{54}]^+$: m/z 2691.581; found: 2691.597.
Selected spectroscopical data for **8**: ^{1}H NMR (500 MHz, CDCl$_3$/CS$_2$, TMS) δ: 6.72 (m, 7H, OH$_2$), 5.18 (m, 7H, OH$_3$), 4.86 (m, 7H, H$_1$), 4.05–3.55 (m, 42H, H$_2$–H$_3$–H$_4$–H$_5$–H$_{6a,b}$), 0.94–0.75 (54H, ^{t}Bu–Si), 0.16–0.16 (m, 36H, Me$_2$Si); ^{13}C NMR (125 MHz, CDCl$_3$/CS$_2$) δ: 147.43, 146.49, 146.22, 145.99, 145.11, 144.94, 144.90, 144.65, 144.52, 144.43, 144.36, 144.32, 144.22, 144.02, 143.90, 143.59, 143.31, 143.25, 143.16, 142.87, 142.75, 142.66, 142.27, 141.30, 140.94, 140.37, 138.24, 138.19, 137.20, 135.30, 134.29, 101.88, 81.54, 73.47, 73.16, 72.39, 72.10, 61.42, 25.73, 18.05, -5.16, -5.29; FT-IR(KBr): 3421, 3294, 2950, 2931, 2896, 1462, 1400, 1250, 1083, 1045, 837, 687, 594 cm^{-1}; MALDI-TOF MS calcd for $[C_{138}H_{153}NNaO_{34}]^+$: m/z 2558.879; found: 2558.896.

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