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The first synthesis of a water-soluble α-cyclodextrin/C_{60} supramolecular complex using anionic C_{60} as a building block

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This letter is dedicated to the memory of Professor Junyuan Gao

Abstract—A novel supramolecular inclusion complex of α-CD/C_{60} was synthesized using anionic C_{60}. The reaction progress was monitored in situ by visible and near-IR spectroscopy. The obtained complex was characterized by UV–vis, ^{13}C NMR, MALDI-TOF, and cyclic voltammetry. The induction and dispersion forces are considered to be the major driving forces for the formation of a resulting α-CD/$C_{60}{}^{\cdot -}$ inclusion complex.

The formation of non-covalent bonding supramolecular inclusion complexes with cyclodextrins (CDs) has been shown to be an effective method to solubilize fullerenes in aqueous solution.[1–12] The resulting γ-cyclodextrin-bicapped C_{60} complex has displayed interesting properties such as DNA cleaving ability,[13] dinitrogen fixation,[14] and reduction of C=C, C=O and N–N$^+$ bonds[15] under mild conditions. Several methods have been developed for the preparation of water-soluble CD/fullerene complexes, including refluxing,[1–3] kneading,[4] stirring,[5,6] ultrasonic evaporating,[7] and solid state ball/high-speed vibration milling.[11,12] However, due to the size compatibility between the CD cavity and the C_{60} diameter, the studies are mostly limited to γ-CD/C_{60} rather than the α- and β-CD analogs. The cavity size of γ-CD is 8.4 Å[16] which is the closest match to the van der Waal's diameter of C_{60} (1 nm)[17] among the three CDs. For the cyclodextrins with a smaller cavity diameter, there are few papers reported on β-CD[6,18] (6.6 Å[16]), and no reports on the preparation of an inclusion complex between α-CD (5.2 Å[16]) and C_{60}. It is of significance to investigate the formation of inclusion complexes of C_{60} and CDs with a small cavity size, since it reveals cavity size effects on encapsulation of large hydrophobic molecules like C_{60}, and provides more insights into the formation of supramolecular complexes between cyclodextrins and fullerenes. The α-CD is an ideal model for such purposes, and the preparation of an α-CD/C_{60} inclusion complex is of interest because it makes it possible to study the cyclodextrins/C_{60} inclusion complexes systematically.

C_{60} possesses strong electron-accepting abilities, and its anionic species are easily generated due to the large spacing of the formal potential of each individual redox process.[19] Anionic C_{60} has been used as the starting materials in many reactions;[20,21] however, it has not been used in the preparation of CD/C_{60} supramolecular complexes. Here we report the preparation of supramolecular complex of α-CD and C_{60} using monoanionic C_{60}, which was generated by a chemical reduction. Preliminary results indicate that anionic C_{60} can form an inclusion supramolecular complex with α-cyclodextrin, while the neutral C_{60} cannot under the same conditions.

C_{60} was reduced by a 10-fold molar equivalent of a sodium salt of 1-methylnaphthalene radical anion under

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Keywords: Fullerene; Cyclodextrin; Anions; Supramolecular chemistry.

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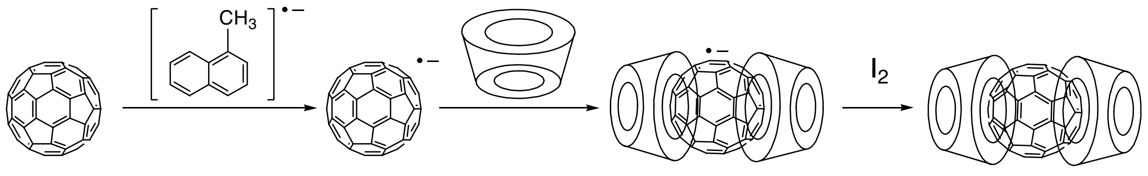

Scheme 1. Illustration of the preparation of α-CD/C_{60} using $C_{60}{}^{\bullet -}$.

argon in freshly distilled DMF. The 1-methylnaphthalene radical anion was prepared using deaerated DMF solution according to a previously reported method.[22] Typically 0.28 mmol methylnaphthalene radical anion was added to 20 mg of C_{60} (0.028 mmol) and vigorously stirred for 3 h under argon at ambient temperature. α-CD (0.14 mmol) was then added to this solution and stirred for 3 h. After that, iodine (0.14 mmol) was added to oxidize the α-CD/$C_{60}{}^{\bullet -}$ to neutral α-CD/C_{60}. The solvent was then removed under vacuum and a yellow-brown crude product was obtained. The product was washed with methanol, and dried in vacuo, yielding a brown solid α-CD/C_{60} complex. The process of synthesis is elucidated in Scheme 1.

In order to have a better understanding of the reaction, the progress of the preparation of α-CD/C_{60} with anionic C_{60} as the guest was monitored by near-IR spectroscopy in an air-tight quartz cuvette under argon at room temperature. Figure 1b–d shows the generation of $C_{60}{}^{\bullet -}$ after 10-fold 1-methylnaphthalene radical anion was added at different time intervals. The characteristic absorption bands of the C_{60} monoanion appeared at 1074, 1035, 993, 935 nm,[23] with the maximum reached in cal 3 h and without the generation of $C_{60}{}^{2-}$. The DMF solution of α-CD was then added to the solution and stirred for 3 h. No distinct spectral change was observed except for a slight decrease of absorbance probably due to the dilution effect, indicating that the monoanion of the α-CD/C_{60} inclusion complex has similar absorption bands as those of C_{60}. The same absorptions were also observed for the γ-CD/$C_{60}{}^{\bullet -}$.[24] Iodine was added to the solution at the end of the reaction, and the characteristic absorption bands of $C_{60}{}^{\bullet -}$ disappeared at once. It thus confirms that the complexation reaction occurred between α-CD and $C_{60}{}^{\bullet -}$, and that the resulting complex was oxidized back to the neutral form after the addition of iodine.

The color of a concentrated aqueous solution of the α-CD/C_{60} complex is yellow-brown, changing to yellow when diluted. The aqueous solution of α-CD/C_{60} is stable for at least several months, while the solid can stand much longer without decomposition. Figure 2 shows the UV–vis spectra of the aqueous solution of α-CD/C_{60} and C_{60} in *n*-hexane. The α-CD/C_{60} displays three bands at 226, 267 and 337 nm, which are red shifted with respect to the reported bands of the γ-CD/C_{60} complex (214–215, 260, and 333 nm)[7,12] in aqueous solution and C_{60} in *n*-hexane (211, 256, and 328 nm)[25], respectively. The characteristic spike of C_{60} at 409 nm and the broad band at 540 nm are missing for the α-CD/C_{60} complex, indicating that aggregation occurs in aqueous solution.[26] Similar aggregations were also observed for the water-soluble conjugate of β-CD and C_{60}[27] and other water-soluble C_{60} derivatives.[28–30] Since the cavity of α-cyclodextrin is smaller than that of γ-cyclodextrin, the greater part of hydrophobic C_{60} surface will be exposed to the aqueous phase, which may result in more aggregation than the counterpart of γ-CD/C_{60}.[30] The solubility of the complex in water is estimated to be 8.5×10^{-5} M by using the absorption coefficient $\varepsilon = 5.19 \times 10^4$ at $\lambda_{\max}$ 330 nm for C_{60} in cyclohexane.[12] The actual solubility for the complex may be higher

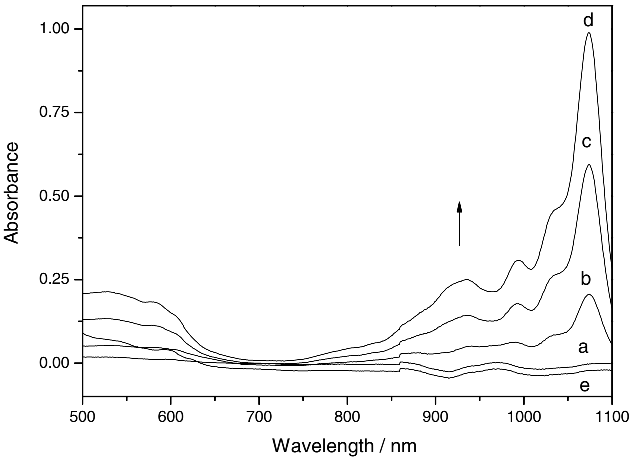

Figure 1. In situ monitoring of the complexation progress between the C_{60} monoanion and α-CD. C_{60} was reduced by 10-fold excess 1-methylnaphthalene anions in deaerated DMF at 298 K in 3 h. (a) C_{60}, (b)–(d) generation of $C_{60}{}^{\bullet -}$ at different time intervals during the reduction, (e) after adding iodine.

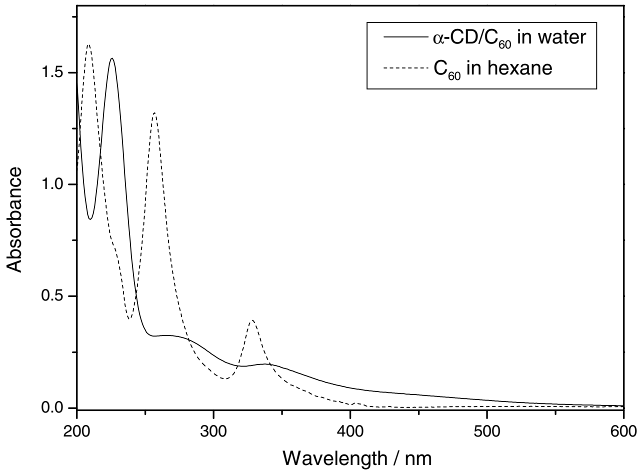

Figure 2. UV–vis spectrum of α-CD/C_{60} in water and the C_{60} in *n*-hexane.

due to the broadening of the peak used for calculation. It is found that the solution of the complex is stable in the presence of an excess of α-CD and thus difficult to purify. When the complex is purified by removing the excess of α-CD, it is difficult to dissolve the complex in water again. Similar behavior has been observed for the γ-CD/C_{60} complex.[9]

The formation of the α-CD/C_{60} complex was further confirmed by MALDI-TOF and ^{13}C NMR. Mass spectrometry provides direct evidence of the formation of CD/C_{60} inclusion complexes, and is considered along with NMR as one of the important characterizations for the CD/fullerene complexes.[10] The MALDI-TOF mass spectrometry of the α-CD/C_{60} complex (see Fig. 3) shows peaks at $m/z = 1715$, 1731, and 2703, which are assigned to [α-CD/C_{60}(1:1)+Na]$^+$, [α-CD/C_{60}(1:1)+K]$^+$, and [α-CD/C_{60}(2:1)+K]$^+$, respectively. Previous studies have shown that a supramolecular complex with a 2:1 (CD:C_{60}) stoichiometry is formed exclusively for γ- and β-cyclodextrin.[2,6,9,10,12,14] In addition the fullerene complexes and even fullerene compounds tend to decompose in a gas phase during mass spectrometry characterization; thus it is possible that the peaks corresponding to a 1:1 α-CD/C_{60} moiety are due to the fragmentation of the 2:1 α-CD/C_{60} in the gas phase. Figure 4 shows the ^{13}C NMR spectrum of a water solution of the α-CD/C_{60} complex. A single resonance at 142.1 ppm from the carbon atoms of the C_{60} moiety and the resonances due to α-CD at 59.5 (C6), 70.9 (C2 and C5), 72.4 (C3), 80.2 (C4), and 100.4 (C1) ppm were observed. The results clearly indicate the formation of a water-soluble supramolecular complex between α-CD and C_{60}. The presence of one resonance for C_{60} indicates that the obtained complex has one composition. The chemical shift for C_{60} of α-CD/C_{60} is the same as that of γ-CD/C_{60} obtained using the current protocol, suggesting that the complex of α-CD/C_{60} has the same stoichiometry of CD and C_{60} as that of γ-CD/C_{60} analog. Since the water-soluble supramolecular complex with a 2:1 (CD:C_{60}) stoichiometry is formed strictly for γ-CD/C_{60},[10] it is reasonable to conclude that the obtained α-CD/C_{60} has a 2:1 (CD:C_{60}) stoichiometry.

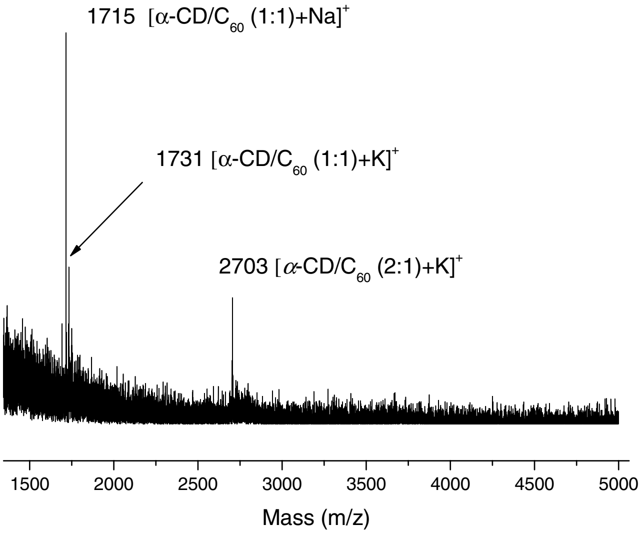

Figure 3. MALDI-TOF of the α-CD/C_{60} complex.

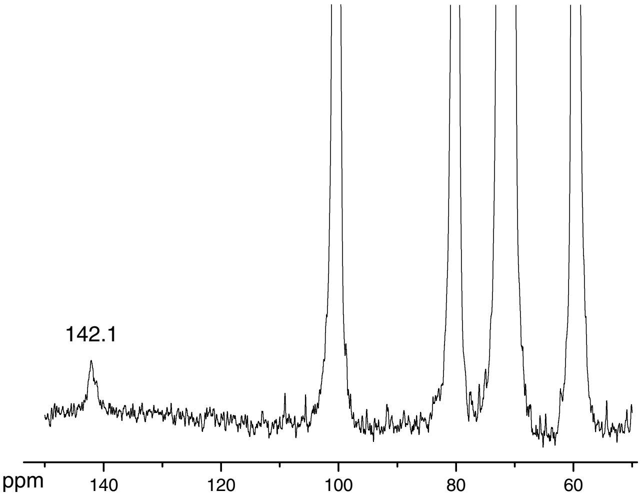

Figure 4. ^{13}C NMR spectrum of the α-CD/C_{60} complex in water.

Cyclic voltammetry (CV) of the obtained α-CD/C_{60} complex in DMF containing 0.05 M $LiClO_4$ was performed with a glassy carbon disk as the working electrode. The complex undergoes three reversible one-electron reductions, and the $E_{1/2}$ values are located at −0.30, −0.76, and −1.35 V, respectively, similar to those of the γ-CD/C_{60} complex.[7] No electrochemical reduction wave was detected for the complex in aqueous solution, probably due to the aggregation in water.[30]

Experiments have shown that the current method also works well when β- and γ-CD are used for the formation of the corresponding supramolecular complex with C_{60}.[31,32] In order to probe further into the effect of anionic C_{60} toward the reaction, control experiments were performed where neutral C_{60} was used as the guest molecule to react with α-cyclodextrin in a mixture of DMF and toluene with stirring under similar experimental conditions. No inclusion supramolecular complex of α-CD and C_{60} was detected. Thus the anionic C_{60} plays a crucial role in the complexation reaction.

Studies of cyclodextrin inclusion complexes have shown that the driving forces for the complex formation are categorized as hydrophobic interaction, dipole–dipole, dipole-induced dipole, and dispersion forces.[16] The observation that anionic C_{60} has a better complexing ability with cyclodextrin than neutral C_{60} indicates that the hydrophobic interaction between the fullerene and the cavity of CD is not the major contributor during the formation of the complex, because the neutral C_{60} should be more hydrophobic than the anionic one. Instead the induction and dispersion forces must be the major driving forces during the formation of α-CD/$C_{60}{}^{\cdot -}$ inclusion complex, since the anionic C_{60} carries more electron density and thus has a greater polarizability to enhance the induction and dispersion components, which in turn result in a stronger interaction with α-CD.[16] The situation is similar to the case of 4-nitrophenolate and 4-nitrophenol, where 4-nitrophenolate exhibits a better complexation ability with α-CD than 4-nitrophenol because of the enhanced induction and dispersion forces caused by the increasing electron density.[33] After the formation of the α-CD/$C_{60}^{\cdot-}$ supramolecular complex, the negative charge was removed by iodine. The complex is then probably stabilized by the n–π donor–acceptor interactions between the n-orbitals of the CD oxygen atoms and the π-system of C_{60} as proposed previously for the complex of γ-CD/C_{60}.[2]

Since the cavity of α-CD is much smaller than the diameter of C_{60}, it is not possible to form a penetrating complex, but to form a shallow inclusion complex at van der Waal's contact distance. A similar structure has been reported for the inclusion complex between cyclotriveratrylene (CTV) and C_{60}, where C_{60} adopts a position at van der Waal's contact distance above the concave surface of the CTV macrocycle as shown by the X-ray structure.[34]

In conclusion, we have synthesized and characterized a novel water-soluble supramolecular complex of α-CD and C_{60} by using the C_{60} monoanion. The current protocol extends the type of cyclodextrin for the formation of a supramolecular complex with C_{60} to those with a much smaller cavity size. It indicates that the induction and dispersion forces between cyclodextrin and anionic C_{60} play important roles during the formation process of the supramolecular complex. The method has the potential to prepare other kinds of supramolecular complexes between CD and fullerenes. The elucidation of complexation mechanism details and properties of the water-soluble α-CD/C_{60} supramolecular complex is currently in progress.

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31. *UV–vis for β-CD/C_{60} complex in H_2O*: $\lambda_{\max}$ (ε) = 222, 268, and 334 nm; ^{13}C NMR for β-CD/C_{60} complex (150 MHz, in H_2O) in ppm: δ 142.1 (C_{60}), 100.9 (C1), 70.9 (C2), 72.3 (C3), 80.2 (C4), 71.3 (C5), 60.4 (C6 of complexed CD), 59.4 (C6).
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