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Hydrophilic [60]fullerene carboxylic acid derivatives retaining the original 60π electronic system

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Abstract—Water-soluble carboxylic acid derivatives of [60]fullerene retaining the original 60π electronic configuration are prepared from a tetra-*tert*-butyl ester of bis(fulleroid).

Improvement of solubility in polar and aqueous solvents has been considered as one of most important targets in fullerene-based organic chemistry, because the development of such hydrophilic fullerene derivatives not only enlarges the potentials of material sciences but also finds utility in the biochemical and pharmaceutical fields.[1–3] Polar substituents commonly increase the solubility in aqueous media, and, accordingly, synthetic procedures to introduce hydrophilic groups on the fullerene surface have been investigated for a long time.[4–7] The most successful and well-investigated examples are methano[60]fullerenes modified by polar groups, such as carboxylate, polyol, polyether.[4] However, the loss of the originally existing characteristic 60π conjugation during the transformations has constituted a significant problem. Because there is no way other than employing addition reactions to bind organic groups onto C_{60}, it is inevitable that the chemical modification of fullerenes consumes at least one π-electron pair in each reaction. Thence, increasing the solubility decreases the conjugate system of the products. Such π-electron-reducing derivatization might substantially deviate the electronic properties of the products from those of the parent compounds,[8] and, in this context, multi-functionalized compounds sustaining the parent fullerene core are highly desirable. Among numerous types of organic derivatives based on C_{60}, only fulleroid and bis(fulleroid) can retain the 60π conjugated structures. Although fulleroid isomerizes easily to methano[60]fullerene,[9] bis(fulleroid) is stable enough to create the isoelectronic fullerene derivatives.[10] Described herein are the preparation and characterization of hydrophilic bis(fulleroid) derivatives.

In our previous research regarding the thermal isomerization of the C_{60} cyclohexadiene derivative (**1**) to bis(fulleroid) (**2**),[10b] it was found that the *tert*-butyl ester of **1a** cleaved quantitatively at 150 °C in *o*-dichlorobenzene to give a carboxylic anhydride (**1b**). However, further chemical transformations of **1b**, such as hydrolysis and alcoholysis, were unsuccessful because of its insolubility in common organic solvents. On the other hand, the *tert*-butyl ester cleavage of **1a** and **2a** proceeded under mild acidic conditions to afford carboxylic acid derivatives.[11] For example, a reaction of **1a** with an excess amount of *p*-toluenesulfonic acid monohydrate (TsOH) in toluene at 90 °C gave the dicarboxylic acid derivative (**1c**) in a 85% yield. When trifluoroacetic acid (TFA) was employed in the reaction of **1a** under the same conditions, anhydride **1b** was obtained in a 83% yield. Similar hydrolysis of bis(fulleroid) **2a** mediated by TsOH gave the tetracarboxylic acid **2b** (86%), whereas the treatment with TFA afforded a mixture of **2b** and the dicarboxylic acid **2c** (Scheme 1).

The structures of the products were mainly confirmed by using ^{1}H and ^{13}C NMR, IR, UV/vis, and MS spectroscopy. In the ^{13}C NMR spectra of **1b** and **1c**, C_{2v} symmetrical 21 sp^2 carbons were observed together with 1 sp^3 carbon (64.4 ppm) of the fullerene core in each case. For **2b** and **2c**, on the other hand, C_s symmetrical

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Keywords: Fullerene; Carboxylic acid; Ester hydrolysis.

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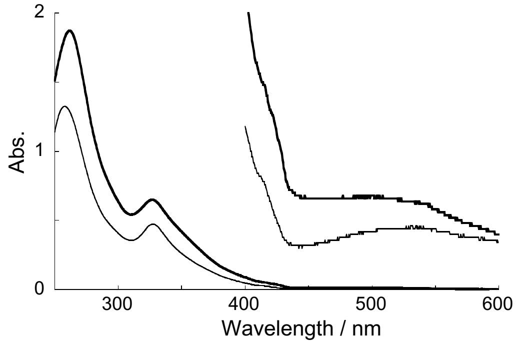


Figure 1. UV/vis spectrum of **2b** in 1,4-dioxane (plane line, 8.4×10^{-6}M) and in 0.01M K_2CO_3 aqueous solution (bold line, 1.4×10^{-5}M). Inset shows magnified spectrum (×20).

35 and 34 sp^2 carbons were observed together with 1 sp^3 carbon (57.8ppm for **2b** and 54.7ppm for **2c**), respectively, and the spectra were characteristic of the bis(fulleroid) derivatives. These results agree with the fact that all the products retain the original framework of the starting materials. The 58π and 60π electronic structures, respectively, for **1** and **2**, are also evident in typical UV/vis absorptions at λ_{max} 431 and 532nm, respectively (Fig. 1).[10c] According to the observed difference in the UV/vis spectra, compounds **1** and **2** showed different colors in solutions (**1**: brown, **2**: reddish purple). Carbonyl absorptions in the IR spectra give unequivocal evidence for the existence of COOH and anhydride groups. Carboxyl groups in **1c**, **2b**, and **2c** showed absorptions at $\nu < 1730\,cm^{-1}$ together with broad OH bands, and the C=O absorptions of the anhydride appeared at $\nu > 1760\,cm^{-1}$ (Table 1).

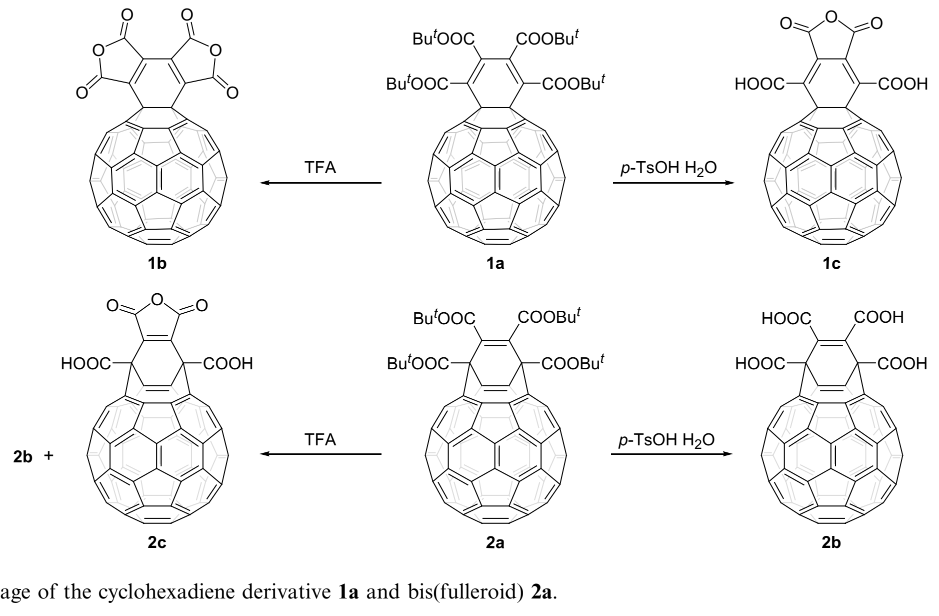
In contrast to the starting esters (**1a** and **2a**), the products were poorly soluble in commonly used solvents for fullerene derivatives such as toluene and *o*-dichlorobenzene. On the other side, the solubility of the carboxylic acid derivatives (**1c**, **2b**, and **2c**) increased in polar solvents such as THF, 1,4-dioxane, and a mixture of toluene and methanol. The highly insoluble carboxylic anhydride derivative (**1b**) was found to be slightly soluble in a mixed solvent of 1,4-dioxane and carbon disulfide (3:2 v/v), and its ^{13}C NMR spectrum was observed in the solvent (Table 1).

Table 1. Selected data of the products

Product	^{13}C NMR spectra		
	Number of sp^2 C (symmetry)	Chemical shifts of CO (δ/ppm)	IR spectra (ν_{CO}/cm^{-1})
1b	21 (C_{2v})	161.49, 156.92[a]	1837, 1765
1c	21 (C_{2v})	162.03, 157.55[b]	1772, 1716
2b	35 (C_s)	171.39, 165.91[b]	1725
2c	34 (C_s)	169.22, 161.13[b]	1836, 1772, 1718

[a] Observed in a 3:2 mixture of 1,4-dioxane-d_8 and CS_2.
[b] Observed in 1,4-dioxane-d_8.

Bis(fulleroid) tetracarboxylic acid **2b**, which is insoluble in neutral water is soluble in basic aqueous media such as 0.01M K_2CO_3. It is known that in the case of water-soluble C_{60} derivatives a considerable broadening of the UV/vis bands, especially 425nm absorption, is recommended.[6a,12] For **2b**, the UV/vis spectrum in 1,4-dioxane was virtually identical to that of **2a** in CH_2Cl_2. On the other hand, in 0.01N K_2CO_3 aqueous solution, detectable broadening was observed in the range of 450–500nm (Fig. 1). The approximate concentration of the corresponding saturated solution was estimated as the order of 10^{-4}M.[12] Although we could not find comparable numerical data of previously reported carboxylic acid derivatives, the solubility of **2b** seemed to be similar or rather lower than those of the known hydrophilic compounds. The characteristic figure of **2b** is that all hydrophilic carboxyl groups assemble in one part of the fullerene surface, whereas the carboxyl groups of other examples, which are multi-adducts of malonic acid, spread to some extent on the surface. It



Scheme 1. Ester cleavage of the cyclohexadiene derivative **1a** and bis(fulleroid) **2a**.

has been known that aggregation affected by the geometric factors of the hydrophobic and hydrophilic groups plays an important role in the solubility of the fullerene derivatives.[2] Further studies on the influence of aggregation on solubility of the products are now underway.

We have recently succeeded to synthesize novel endohedral complexes incorporating small molecules from the bis(fulleroid) derivatives.[13] In the field of medicinal science, applications of the water-soluble endohedral metallofullerenes have been investigated as contrast agents for MRI (magnetic resonance imaging).[4d,7a] Therefore, this methodology has a large potentiality in the synthesis of various fullerene-based materials modified inside as well as outside of their surface.

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Supplementary data

Experimental procedures as well as spectroscopic data of the products (**1b**, **1c**, **2b**, and **2c**) are available. This material is available online (at doi:10.1016/j.tetlet.2004.09.072) with the paper in Science-Direct.

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