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Optically pure fullerodendron formed by diastereoselective Diels–Alder reaction

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ABSTRACT

The Diels–Alder reaction between C_{60} and anthryl glycodendron, which has D- or L-gluconamides at the terminals, gave a new fullerene glycodendron conjugate. Interestingly, the diastereoselective cycloaddition reaction proceeded upon the treatment of C_{60} with the anthryl dendron **3**. Furthermore, optical pure fullerodendrons (−)-**4L** and (+)-**4D**, which were confirmed by ^{1}H and ^{13}C NMR spectroscopy, FT-IR, MALDI-TOF mass spectroscopic analysis, were isolated from the mixture of diastereomers. And their absolute configurations were predicted by the use of CD spectra.

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1. Introduction

Chiral fullerene derivatives are likely to play an important role in the area of materials science and medical chemistry.[1] In particular, fullerene glycoconjugates have attracted much attentions in the past two decades.[2–8] However, there are only a few examples of the synthesis and characterization of fullerene glycodendron conjugates.[9,10] Meanwhile, we have developed material chemistry based on poly(amidoamine) (PAMAM) fullerodendrons synthesized by the [4+2]cycloaddition reaction of C_{60} with anthryldendrons.[11–19] It is well-known that prebuilt PAMAM dendrimers offer several advantages as scaffolding for biologically relevant glycodendrimers, including sialic acid, sialyloligosaccharides, simple sugars, and cancer markers, such as T and Tn antigens.[20] Recently, we have reported the modification of dendrimer disulfides and anthryl dendrons to their glycoconjugates by the treatment of terminal amine groups of the PAMAM dendron unit with glucono-δ-lactone.[21,22] In this context, PAMAM dendritic wedge of our fullerodendron expected to be converted to glycoconjugate. These backgrounds prompted us to investigate the synthesis and characterization of fullerodendron having sugar moieties at the terminals by the use of the Diels–Alder reaction of C_{60} with anthryl glycodendron. Although a lot of reports described the Diels–Alder reaction of C_{60} with anthracene derivatives,[23–28] enantiomeric mono-adduct of anthracene and C_{60} is very limited. Schwenninger et al. observed barely separated signals of different enantiomers of C_2-symmetric adduct of [60]fullerene and 2,6-di-*tert*-butylanthracene using a chiral ^{1}H NMR shift reagent.[29] However, the separation of an optically pure [60]fullerene-anthracene mono-adduct has never been reported. Because of an increasing focus on developing syntheses[30,31,32] and applications[33,34]of enantiomerically pure fullerene derivatives, exploring a new type of chiral fullerene derivative is quite important. This paper describes that the separation of optically pure fullerodendron formed by the diastereoselective Diels–Alder reaction of C_{60} with the anthryl dendron having D- or L-gluconamides at the terminals. Diastereoselective and/or enantioselective addition reaction to spherical carbon cage is still quite rare. To our best knowledge, this is the first example of the diastereoselective [4+2]cycloaddition reaction of C_{60} with dendron and the diastereomeric separation of fullerene derivatives having dendritic architecture.

2. Results and discussion

2.1. Synthesis of fullerene glycodendron conjugates

Scheme 1 shows the synthesis of fullerene glycodendron conjugates **4** and **8**. First-generation PAMAM dendron **1** was employed for the preparation of fullerene glycodendron **4**. First, gluconamide arms of dendron **2** were introduced by the aminolysis of D- or L-glucono-1,5-lactone with the NH_2 groups of **1**. Subsequently, the acetylation of the hydroxyl groups of dendron **2** with acetic anhydride gave protected dendron **3**. Furthermore, Diels–Alder reaction between **3** and C_{60} afforded fullerene glycodendron **4**. The second generation fullerene glycodendron **8** was also synthesized using

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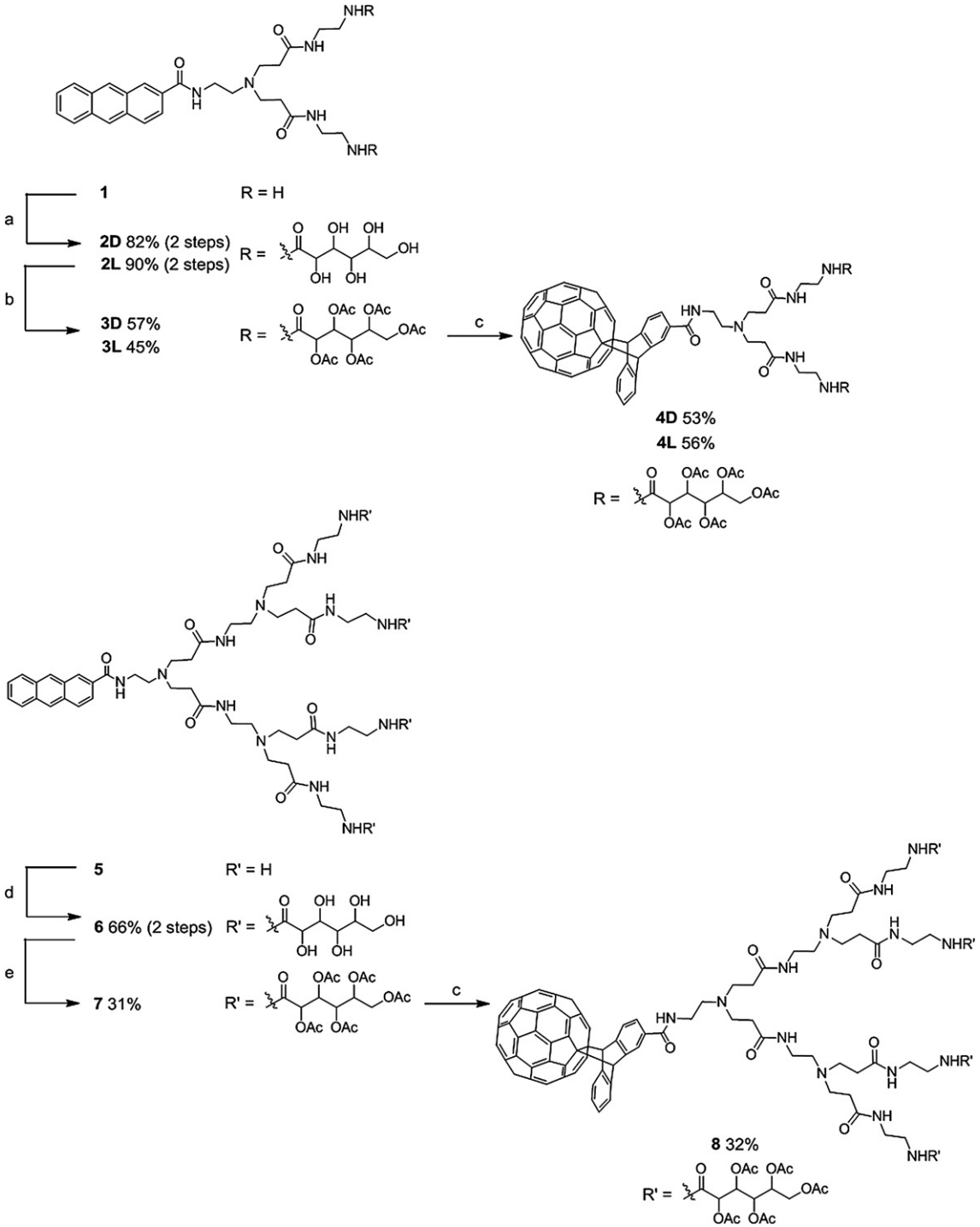


Scheme 1. Synthesis of fullerene glycodendron **4** and **8**. Reagents and conditions: (a) D- or L-gluconolactone, methanol, 50 °C, 18 h. (b) acetic anhydride, DMAP, triethylamine, DMF, 0 °C, 1 day. (c) C_{60}, *o*-dichlorobenzene, 40 °C, 7 days. (d) D-Gluconolactone, methanol, 50 °C, 4 days. (e) Acetic anhydride, pyridine, 0 °C to rt, 5 days.

the same procedure from the anthryl dendron **5** as shown in Scheme 1.

2.2. Diastereomeric separation of fullerene glycodendron conjugates

It is notable that the mono-adduct between 2-substituted anthracene and C_{60} possibly has enantiomers because there are prochiral carbon atoms in the 2-substituted anthracene (Fig. 1).

For instance, fullerene glycodendron **4L** should have two diasteromers, (+)-**4L** and (−)-**4L**, as shown in Figure 2. Surprisingly, diastereoselective Diels–Alder reaction of C_{60} with the dendrons **3D** or **3L** was proceeded to afford the two diastereomers, of which ratio was estimated to be 3:2 by ^{1}H NMR. For example, after the reaction of C_{60} with **3L**, ^{1}H NMR spectrum of the reaction mixture exhibited diastereomeric signal splitting, the bridge-head proton signals of anthracene moiety (Fig. 3a) and acetyl protons of sugar moieties (Fig. 3b). Fortunately, the diastereomeric separation of fullerene glycodendrons **4D** or **4L** was succeeded by silica-gel column chromatography (eluent, chloroform/methanol=30:1) and GPC, respectively, to give the optically pure **4D** (2.5 mg, 1.6%) or **4L** (59 mg, 5.6%), of which structures were confirmed by ^{1}H

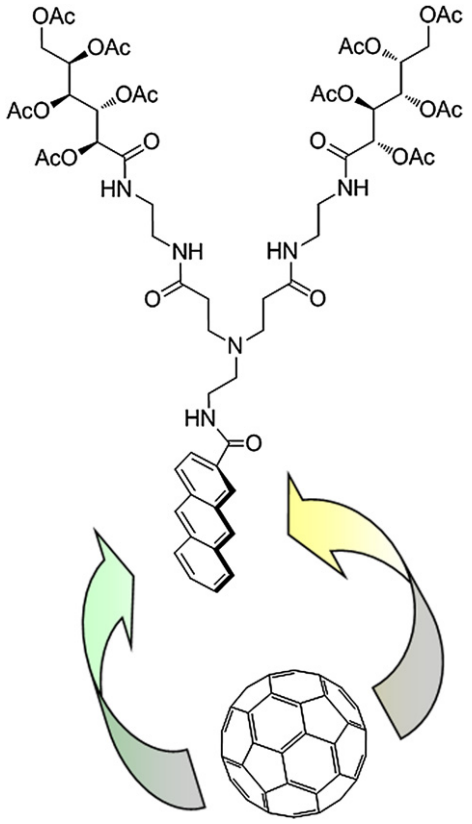


Figure 1. Schematic representation of diastereoselective Diels–Alder reaction.

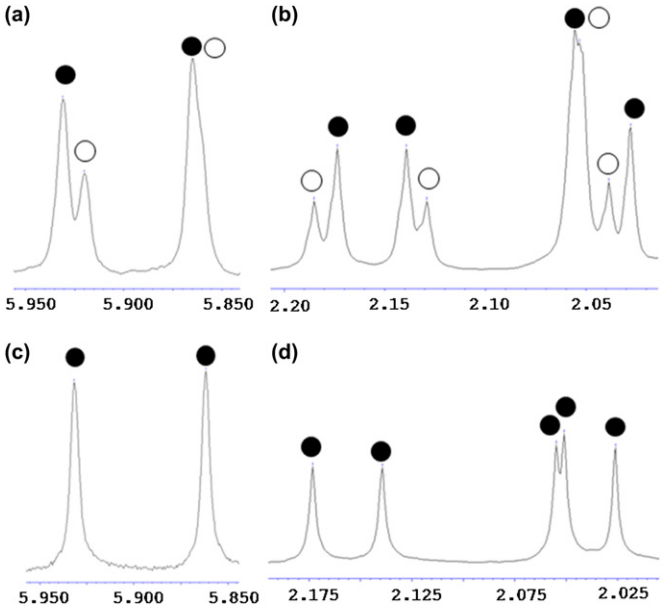


Figure 3. ^{1}H NMR spectra of the dendron **4L** before and after the diastereomeric separation. (a) Bridge-head protons before the separation. (b) Methyl protons of acetyl groups before the separation. (c) Bridge-head protons after the separation. (d) Methyl protons of acetyl groups after the separation.

In the marked contrast with compound **3**, the diastereoselectivity was not observed in the Diels–Alder reaction of the second generation anthryl glycodendron **7** with C_{60}, i.e., ^{1}H NMR spectrum of the fullerene glycodendron **8** in the reaction mixture exhibited diastereomeric signal splitting with a ratio of 1:1. Unfortunately, diastereomeric separation of the fullerene glycodendron **8** was not succeeded.

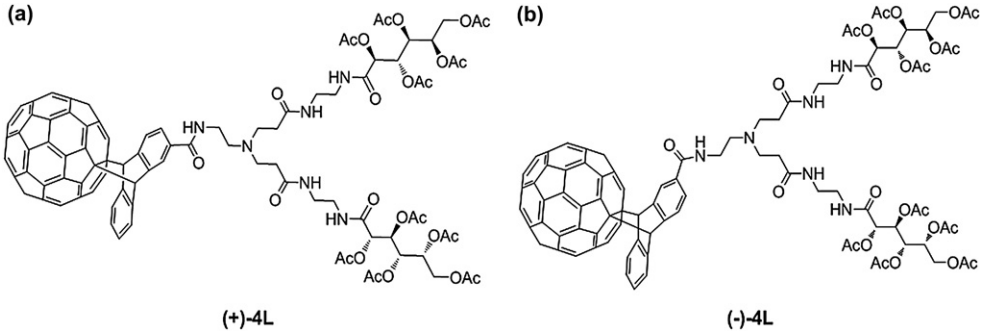


Figure 2. The structures of two diastereomers of fullerene glycodendron **4L**.

and ^{13}C NMR spectroscopy, FT-IR, and MALDI-TOF mass spectroscopic analysis. For example, in the ^{1}H NMR spectrum of **4L** ($CDCl_3$), singlet signals of the bridge-head and acetyl groups were observed at δ 2.02 (s, 6H), 2.05 (s, 6H), 2.06 (s, 6H), 2.14 (s, 6H), 2.17 (s, 6H), 5.86 (s, 1H), and 5.94 (s, 1H) as shown in Figure 3c and d.

Furthermore, the MALDI-TOF mass spectrum of fullerene glycodendron **4L** clearly showed the parent peak at *m/z* 1989.189, which is good agreement with the calculated molecular weight of **4L** ($[M]^-$, calcd 1989.486) (Fig. 4.). The UV–vis spectrum of fullerene glycodendron **4L** in $CHCl_3$ exhibited two absorption maxima at 433 and 704 nm, in which the former band is known to be a characteristic absorption band in the 1:1 adduct on the 6,6-ring junction of C_{60} (Fig. 5). It is notable that the fullerene glycodendron **4L** is stable in $CDCl_3$ solution (at room temperature for at least 1 month in a sealed tube), and neither retro Diels–Alder reaction nor racemization was observed.

The reason for the face selectivity in the Diels–Alder reaction of the anthryl glycodendron **3** is still unclear. However, it is likely that the selectivity may be influenced by the steric hindrance between C_{60} and dendritic wedge, which provide asymmetric space via chiral recognition of gluconamide terminals. Although we carried out the reaction of C_{60} with dendron **3** in various temperatures, from 0 °C to 40 °C, temperature dependence of the diastereoselectivity was not observed. To our knowledge, this is the first example of the diastereoselective [4+2] addition reaction of C_{60} with dendron, and the diastereomeric separation of fullerene derivatives having dendritic architecture.

Although it is valuable to reduce the long reaction time (7 days) of the Diels–Alder reaction (step c, Scheme 1), very mild reaction conditions are quite important to obtain the fullerodendrons in good yields. For instance, to check the possibility to accelerate the

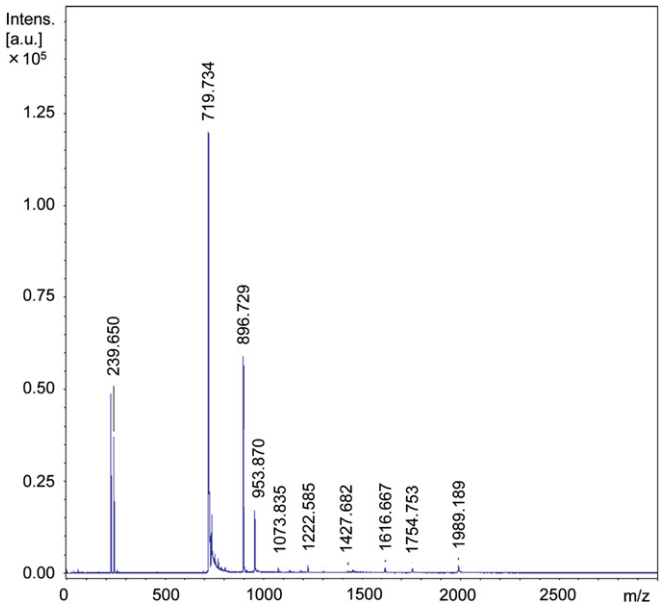


Figure 4. MALDI-TOF MS spectrum of fullerene glycodendron **4L**.

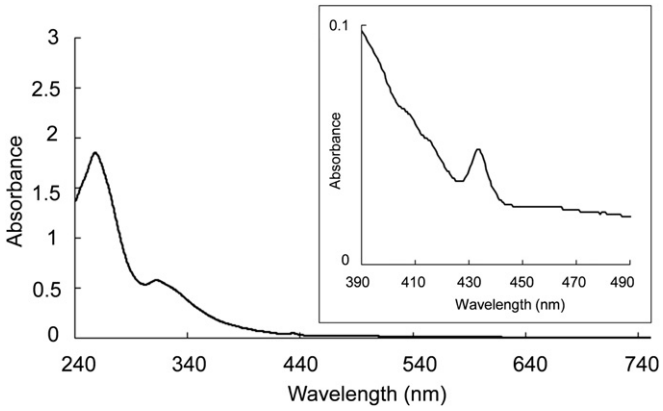


Figure 5. UV–vis spectrum of fullerene glycodendron **4L** in $CHCl_3$ solution (15 μM). Inset: Enlarged absorption spectrum in the visible region from 390 to 490 nm.

Diels–Alder reaction using microwave irradiation[35–38], we examined the model reaction employing anthryl dendron **9**, which have methyl ester groups at the terminals, and C_{60} (Scheme 2). Upon microwave irradiation at 45 °C for 14 h, a maximum yield of the [4+2] cycloadduct **10** was obtained in 48% yield. On the other hand, the reaction at 45 °C for 4 days without microwave irradiation afforded **10** in 83% yield. Hence, microwave irradiation technique is not so efficient in our case. It is notable that PAMAM dendritic wedge has the advantage of biocompatibility, but this property causes the degradation under vigorous reaction conditions.

The CD spectra of optically pure fullerene glycodendrons (+)-**4D** and (−)-**4L**, obtained by the diastereomeric separation of **4D** or **4L**, in $CHCl_3$ solutions are shown in Figure 6. Each compound shows an identical Cotton effects near 265 and 290 nm. It is concluded that (+)-**4D** and (−)-**4L** are enantiomers, because their CD spectra display the expected mirror image shapes. Furthermore, the compounds show identical Cotton effects near 430 nm (Fig. 6, inset). Wilson et al. proposed the sector rule to determine the absolute configuration of optically pure fullerene derivatives as shown in Figure 7.[39] The vertical axis is drawn through the 6-6 $C(sp^3)$–$C(sp^3)$ bond. Location of atoms in + or − sectors defines the sign of the Cotton effect at 430 nm, which is used to determine the absolute configuration of attached groups. Since isolated optically pure **4L** has positive Cotton effect at 430 nm, the absolute configuration can be ascribed to (−)-**4L** as shown in Figure 1b. On the other hand, since isolated **4D** has negative Cotton effect at 430 nm, the absolute configuration can be ascribed to (+)-**4D**.

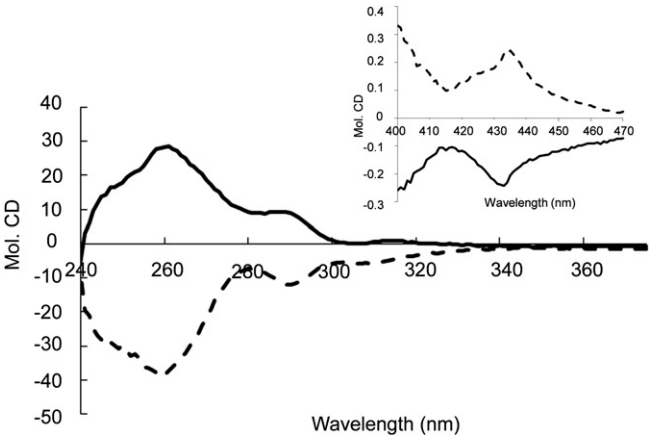


Figure 6. CD spectra of (+)-**4D** (solid line) and (−)-**4L** (dash line) in $CHCl_3$ solution (15 μM). Inset: CD spectra of (+)-**4D** (solid line) and (−)-**4L** (dash line) in the visible region from 400 to 470 nm in $CHCl_3$ solution (600 μM).

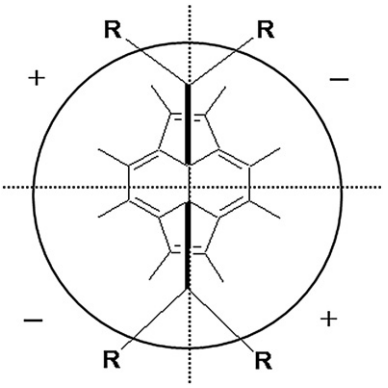
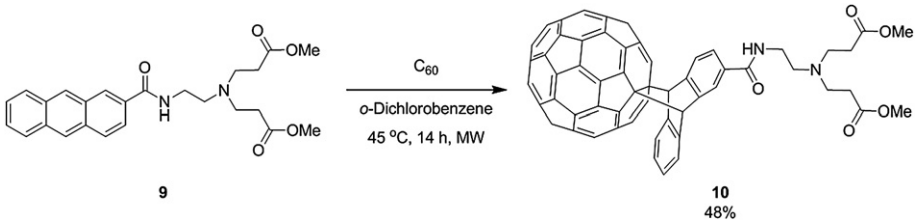


Figure 7. Sector rule for C_{60} derivatives.



Scheme 2. Synthesis of fullerodendron **10** under microwave irradiation.

3. Conclusions

In conclusion, the synthesis of the fullerene glycodendrons **4** and **8** was succeeded. Diastereoselective Diels–Alder reaction of dendron **3** with C_{60} was evidenced by the ^{1}H NMR spectra after the reaction, in which fullerene glycodendron **4** exhibited diastereomeric signal splitting with a ratio of 3:2. On the other hand, the fullerene glycodendron **8** exhibited diastereomeric signal splitting with a ratio of 1:1 after the corresponding Diels–Alder reaction. The diastereomeric separation of fullerene glycodendrons **4** was succeeded by silica-gel column chromatography to give the optically pure (+)-**4D** and (−)-**4L**, of which CD spectra display the expected mirror image shapes. The absolute configuration of optically pure fullerene glycodendrons (+)-**4D** and (−)-**4L** was predicted by the use of sector rule. We are currently exploring the applications for the synthesis of several fullerene derivatives because it is expected that fullerene glycodendron conjugates formed by Diels–Alder reaction are considerably useful for the application of fullerene to pharmaceutical science.

4. Experimental

4.1. General

The NMR spectra were measured using a JEOL AL300 spectrometer using $CDCl_3$ and DMSO-d_6 as solvents tetramethylsilane as an internal standard. Matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF MS) was performed on an Autoflex mass spectrometer, Bruker Daltonics Inc. Sinapinic acid or Dithranol was used as the matrix. Fourier-transform infrared spectra (FT-IR) were recorded on a Shimadzu IRAffinity-1 spectrometer. The GPC experiments were performed using a LC-918 V (Japan Analytical Industry Co.) with JAIGEL 1H, 2H (eluent: chloroform) and JAIGEL GS-320 (eluent: methanol). UV–vis spectra were measured using a Shimadzu UV-3150 spectrometer. CD spectra were recorded (240–370 nm and 400–470 nm) using a JASCO J-720 spectrometer. Each spectrum was the result of averaging two scans, which were subtracted by the solvent baseline. All spectra were recorded at room temperature with quartz cell of 1 cm path length. Microwave irradiation experiment was carried out using a Biotage Initiator™. The reaction was performed with temperature and power-controlled program in a glass vial (0.5–2 mL) sealed with a Teflon septum. Temperature was measured externally by an IR sensor. The reaction time was counted when the reaction mixture was reached the stated temperature. Pressure was measured by a non-invasive sensor integrated into the cavity lid.

Unless otherwise noted, the reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Chemical Industries Co. Ltd., Kanto Kagaku Co. Ltd., Nacalai Tesque, Acros Organics and Aldrich Chemical Co. Methanol, triethylamine, DMF, pyridine and acetic anhydride used as reaction solvents were distilled by general method. Other reagents were used without further purification. The first-generation poly(amidoamine) dendron **1**, compounds **2D** and **9** were synthesized according to the previous reported procedures.[12,22]

4.2. Reaction procedures and spectral data

4.2.1. Synthesis of anthryl glycodendron ***2L***. A solution of **1** (0.896 g, 1.82 mmol) in dry methanol (10 mL) was slowly added to a solution of L-glucono-1,5-lactone (3.24 g, 18.2 mmol) in dry methanol (175 mL) at 50 °C, and the solution was stirred for 18 h under a nitrogen atmosphere. The solution was left overnight at 4 °C, then precipitate was filtered, washed with methanol and acetone to afford **2L** (1.39 g, 1.64 mmol, 90%). Compound **2L**: yellow solid; mp 168–171 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.26 (t, J=6.9 Hz, 4H), 2.64 (t, J=6.6 Hz, 2H), 2.75 (t, J=6.9 Hz, 4H), 3.14 (br s, 10H), 3.39–3.44 (m, 4H), 3.49–3.50 (m, 4H), 3.56–3.61 (m, 2H), 3.92–3.94 (m, 2H), 4.00 (t, J=4.5 Hz, 2H), 4.35 (t, J=5.7 Hz, 2H), 4.45 (d, J=7.2 Hz, 2H), 4.54 (dd, J=5.7, 6.0 Hz, 4H), 5.38 (d, J=5.1 Hz, 2H), 7.55–7.58 (m, 2H), 7.78 (br s, 2H), 7.90–7.93 (m, 3H), 8.11–8.17 (m, 3H), 8.55 (t, J=5.7 Hz, 1H), 8.63 (br s, 2H), 8.71 (s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 33.2, 38.18, 38.22, 49.4, 53.5, 63.3, 70.1, 71.5, 72.2, 73.5, 123.5, 125.88, 125.94, 126.3, 127.7, 127.98, 128.04, 128.17, 128.23, 130.1, 131.3, 131.5, 131.6, 132.1, 166.1, 171.7, 172.8; MALDI-TOF (m/z): calcd for $C_{39}H_{57}N_6O_{15}$, 849.380 $[M+H]^+$; found, 849.614 $[M+H]^+$, 871.627 $[M+Na]^+$; IR (KBr, cm^{-1}) ν 3311, 2944, 1644, 1544.

4.2.2. Synthesis of anthryl glycodendron ***3D***. A mixture of **2D** (0.300 g, 0.354 mmol), triethylamine (2.94 mL, 21.2 mmol), and 4-dimethylaminopyridine (0.397 g, 3.54 mmol) in dry DMF (20 mL) was added to acetic anhydride (1.66 mL, 17.7 mmol) at 0 °C, and the solution was stirred for 24 h under a nitrogen atmosphere. After evaporation under reduced pressure below 50 °C, the residue was added to water and extracted with chloroform. The organic layer was washed with saturated sodium hydrogen carbonate solution and brine. The chloroform solution was dried over $MgSO_4$. After the removal of the solvent, the residue was purified by column chromatography on silica gel (chloroform/methanol, 30:1) and GPC to afford **3D** (0.258 g, 0.303 mmol, 57%). Compound **3D**: yellow solid; mp 94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.019 (s, 6H), 2.020 (s, 6H), 2.04 (s, 6H), 2.12 (s, 6H), 2.15 (s, 6H), 2.29–2.35 (m, 2H), 2.46–2.48 (m, 6H), 2.77–2.80 (m, 2H), 2.92–3.15 (m, 8H), 3.58 (br s, 1H), 3.84 (br s, 1H), 4.11 (dd, J=6.0, 6.3 Hz, 2H), 4.31 (dd, J=3.0, 9.3 Hz, 2H), 5.06–5.07 (m, 2H), 5.21 (d, J=4.8 Hz, 2H), 5.44 (t, J=6.0 Hz, 2H), 5.67 (t, J=4.8 Hz, 2H), 7.31 (br s, 2H), 7.49–7.52 (m, 2H), 7.78 (br s, 2H), 8.01–8.02 (m, 4H), 8.29 (br s, 1H), 8.44 (s, 1H), 8.56 (s, 1H), 8,76 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.41, 20.42, 20.6, 20.7, 20.8, 33.4, 37.7, 37.9, 49.4, 51.7, 61.6, 68.7, 69.1, 69.4, 71.9, 122.9, 125.9, 126.25, 126.34, 128.0, 128.2, 128.3, 128.6, 129.0, 130.2, 130.4, 132.0, 132.1, 132.8, 166.7, 167.7, 169.87, 169.88, 170.1, 170.3, 170.6, 173.4; MALDI-TOF (m/z): calcd for $C_{59}H_{77}N_6O_{25}$, 1269.486 $[M+H]^+$; found, 1269.392 $[M+H]^+$, 1307.371 $[M+K]^+$; IR (KBr, cm^{-1}) ν 3394, 3311, 3081, 2959, 1750, 1649, 1543, 1219.

4.2.3. Synthesis of anthryl glycodendron ***3L***. A mixture of **2L** (0.270 g, 0.318 mmol), triethylamine (2.65 mL, 19.1 mmol), and 4-dimethylaminopyridine (0.357 g, 3.18 mmol) in dry DMF (20 mL) was added to acetic anhydride (1.50 mL, 15.9 mmol) at 0 °C, and the solution was stirred for 24 h under a nitrogen atmosphere. The same workup procedures mentioned above afforded **3L** (0.220 g, 0.173 mmol, 45%). Compound **3L**: yellow solid; mp 94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 6H), 2.03 (s, 6H), 2.04 (s, 6H), 2.13 (s, 6H), 2.15 (s, 6H), 2.28–2.52 (m, 6H), 2.60–2.75 (m, 2H), 2.83–3.33 (m, 12H), 4.12 (dd, J=6.0, 6.0 Hz, 2H), 4.31 (dd, J=2.7, 9.6 Hz, 2H), 5.04–5.10 (m, 2H), 5.21 (d, J=4.8 Hz, 2H), 5.45 (t, J=6.3 Hz, 2H), 5.71 (t, J=4.8 Hz, 2H), 7.16 (br s, 1H), 7.51 (t, J=3.9 Hz, 2H), 7.80 (br s, 2H), 8.01–8.02 (m, 4H), 8.29 (br s, 1H), 8.44 (s, 1H), 8.57 (s, 1H), 8.81 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 20.6, 20.67, 20.74, 20.8, 33.5, 37.7, 37.8, 39.9, 49.5, 51.7, 61.6, 68.7, 69.2, 69.4, 72.0, 122.9, 125.9, 126.3, 126.4, 128.1, 128.2, 128.3, 128.6, 129.1, 130.2, 130.5, 132.0, 132.1, 132.8, 166.7, 167.6, 169.88, 169.91, 170.1, 170.3, 170.6, 173.4; MALDI-TOF (m/z): calcd for $C_{59}H_{77}N_6O_{25}$, 1269.486 $[M+H]^+$; found, 1269.549 $[M+H]^+$; IR (KBr, cm^{-1}) ν 3399, 3312, 3083, 2961, 1758, 1649, 1546, 1219.

4.2.4. Synthesis of fullerene glycodendron ***4D***. A mixture of C_{60} (114 mg, 0.158 mmol) and **3D** (100 mg, 0.0787 mmol) in *o*-dichlorobenzene (9 mL) was stirred at 40 °C for 7 days under a nitrogen atmosphere. The solution was separated by column

chromatography on silica gel (chloroform/methanol, 30:1) to afford **4D** (85 mg, 42.7 μmol, 53%) as diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03–2.04 (m, 6H), 2.05–2.06 (m, 12H), 2.13–2.14 (m, 6H), 2.17–2.19 (m, 6H), 2.26–2.41 (m, 8H), 2.64 (br s, 2H), 3.16–3.27 (m, 8H), 3.51 (br s, 2H), 4.10–4.18 (m, 2H), 4.31–4.40 (m, 2H), 5.06–5.11 (m, 2H), 5.21 (t, *J*=4.8 Hz, 2H), 5.46 (t, *J*=6.3 Hz, 2H), 5.66–5.72 (m, 2H), 5.87 (s, 1H), 5.93 (d, *J*=3.3 Hz, 1H), 7.47–7.51 (m, 2H), 7.60 (br s, 1H), 7.73–7.85 (m, 4H), 8.14 (d, *J*=3.6 Hz, 2H), 8.30 (br s, 1H), 8.49 (s, 1H); MALDI-TOF (*m/z*): calcd for $C_{119}H_{77}N_6O_{25}$, 1989.486 $[M+H]^+$; found, 1989.810 $[M+H]^+$.

*4.2.5. Synthesis of fullerene glycodendron **4L**.* A mixture of C_{60} (0.578 g, 0.801 mmol) and **3L** (0.678 g, 0.534 mmol) in *o*-dichlorobenzene (51 mL) was stirred at 40 °C for 7 days under a nitrogen atmosphere. The same workup procedures mentioned above afforded **4L** (0.595 g, 0.299 mmol, 56%) as diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96–1.97 (m, 6H), 1.98–2.00 (m, 12H), 2.06–2.07 (m, 6H), 2.10–2.12 (m, 6H), 2.24–2.47 (m, 8H), 2.55 (br s, 2H), 3.10–3.25 (m, 8H), 3.45 (br s, 2H), 4.05–4.11 (m, 2H), 4.24–4.28 (m, 2H), 5.02 (br s, 2H), 5.14 (t, *J*=5.4 Hz, 2H), 5.39 (t, *J*=5.1 Hz, 2H), 5.61–5.66 (m, 2H), 5.80 (s, 1H), 5.86 (d, *J*=3.3 Hz, 1H), 7.40–7.43 (m, 2H), 7.55 (br s, 1H), 7.67–7.77 (m, 4H), 8.08 (d, *J*=3.6 Hz, 1H), 8.27 (br s, 1H), 8.43 (s, 1H); MALDI-TOF (*m/z*): calcd for $C_{119}H_{77}N_6O_{25}$, 1989.486 $[M+H]^+$; found, 1990.138 $[M+H]^+$.

*4.2.6. Diastereomeric separation of fullerene glycodendron **4D**.* Compound **4D** (85 mg, 42.7 μmol) was separated by column chromatography on silica gel (chloroform/methanol, 30:1) and GPC to afford optically pure (+)-**4D** (2.5 mg, 1.26 μmol, 1.6%). The other diastereomer was not obtained in good purity. Compound (+)-**4D**: brown solid; mp 165 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03 (s, 6H), 2.05 (s, 6H), 2.06 (s, 6H), 2.14 (s, 6H), 2.17 (s, 6H), 2.26–2.53 (m, 6H), 2.60–2.70 (m, 2H), 2.80–2.95 (m, 2H), 3.04–3.29 (m, 6H), 3.51 (br s, 1H), 3.88 (br s, 1H), 4.15 (dd, *J*=6.0, 6.0 Hz, 2H), 4.33 (dd, *J*=2.7, 9.6 Hz, 2H), 5.06–5.11 (m, 2H), 5.22 (d, *J*=4.8 Hz, 2H), 5.46 (t, *J*=5.7 Hz, 2H), 5.72 (t, *J*=4.8 Hz, 2H), 7.72–7.85 (m, 5H), 8.14–8.17 (m, 1H), 8.29 (br s, 1H), 8.50 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 20.61, 20.66, 20.73, 20.8, 22.7, 23.4, 33.4, 34.1, 36.3, 37.8, 37.9, 39.9, 49.6, 50.1, 51.7, 53.7, 56.8, 57.7, 60.4, 61.6, 61.7, 68.8, 69.2, 69.4, 71.9, 72.0, 72.2, 125.1, 125.8, 125.9, 126.1, 126.6, 127.1, 127.6, 132.5, 136.7, 136.8, 136.9, 139.83, 139.86, 139.91, 141.0, 141.19, 141.24, 141.51, 141.53, 141.6, 141.8, 141.9, 142.07, 142.12, 142.2, 142.3, 142.46, 142.49, 142.86, 142.92, 144.53, 144.58, 145.18, 145.21, 145.25, 145.29, 145.34, 145.35, 145.39, 145.46, 145.58, 145.6, 146.11, 146.13, 146.4, 147.49, 147.52, 155.15, 155.21, 155.3, 166.6, 167.5, 169.8, 169.9, 170.1, 170.2, 170.5, 173.4; MALDI-TOF (*m/z*): calcd for $C_{119}H_{76}N_6O_{25}$, 1988.486 $[M]^-$; found, 1987.952 $[M]^-$; IR (KBr, cm^{-1}) ν 3292, 2943, 1750, 1649, 1535, 1217, 526.

*4.2.7. Diastereomeric separation of fullerene glycodendron **4L**.* Compound **4L** (0.595 g, 0.299 mmol) was separated by column chromatography on silica gel (chloroform/methanol, 30:1) and GPC to afford optically pure (−)-**4L** (59 mg, 29.6 μmol, 5.6%). The other diastereomer was not obtained in good purity. Compound (−)-**4L**: brown solid; mp 165 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.02 (s, 6H), 2.05 (s, 6H), 2.06 (s, 6H), 2.14 (s, 6H), 2.17 (s, 6H), 2.25–2.54 (m, 6H), 2.63–2.65 (m, 2H), 2.88 (m, 2H), 3.01–3.30 (m, 6H), 3.49 (br s, 1H), 3.88 (br s, 1H), 4.15 (dd, *J*=6.0, 6.3 Hz, 2H), 4.33 (dd, *J*=3.0, 9.6 Hz, 2H), 5.06–5.11 (m, 2H), 5.22 (d, *J*=5.1 Hz, 2H), 5.46 (t, *J*=4.8 Hz, 2H), 5.72 (t, *J*=4.8 Hz, 2H), 5.86 (s, 1H), 5.94 (s, 1H), 7.23 (br s, 2H), 7.49–7.51 (m, 2H), 7.75–7.85 (m, 5H), 8.15–8.18 (m, 1H), 8.32 (br s, 1H), 8.51 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 20.62, 20.67, 20.7, 20.8, 33.42, 33.45, 37.8, 37.9, 39.9, 40.0, 49.65, 49.67, 58.1, 61.7, 68.8, 69.22, 69.24, 69.4, 69.5, 72.01, 72.04, 72.27, 72.29, 125.2, 125.8, 125.96, 125.98, 126.1, 126.58, 126.6, 127.6, 132.5, 136.7, 137.0, 139.88, 139.92, 140.0, 141.0, 141.58, 141.63, 141.96, 142.0, 142.12, 142.16, 142.2, 142.3, 142.48, 142.52, 142.54, 144.57, 144.59, 144.61, 144.63, 145.21, 145.23, 145.34, 145.40, 145.45, 145.53, 146.2, 146.4, 147.5, 155.2, 155.25, 155.3, 166.7, 169.89, 169.98, 170.1, 170.2, 170.3, 170.6, 173.4; MALDI-TOF (*m/z*): calcd for $C_{119}H_{76}N_6O_{25}$, 1988.486 $[M]^-$; found, 1989.189 $[M]^-$; IR (KBr, cm^{-1}) ν 3404, 3311, 3074, 2939, 1750, 1643, 1537, 1218, 527.

*4.2.8. Synthesis of anthryl glycodendron **6**.* A solution of **5** (0.632 g, 0.666 mmol) in dry methanol (10 mL) was slowly added to a solution of D-glucono-1,5-lactone (2.37 g, 13.3 mmol) in dry methanol (125 mL) at 50 °C, and the solution was stirred for 4 days under a nitrogen atmosphere. The precipitate was filtered and washed with methanol and acetone to afford **6** (0.727 g, 0.438 mmol, 66%).Compound **6**: yellow solid; mp 110–112 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.16 (t, *J*=6.9 Hz, 8H), 2.25 (t, *J*=7.8 Hz, 4H), 2.40 (t, *J*=6.9 Hz, 4H), 2.62 (t, *J*=6.6 Hz, 8H), 2.74 (t, *J*=6.6 Hz, 4H), 3.12 (br s, 20H), 3.49 (br s, 8H), 3.56–3.61 (m, 4H), 3.91 (d, *J*=6.0 Hz, 4H), 3.99 (t, *J*=4.8 Hz, 4H), 4.08 (q, *J*=5.1 Hz, 2H), 4.33 (t, *J*=5.4 Hz, 4H), 4.42 (d, *J*=6.9 Hz, 4H), 4.51 (dd, *J*=4.2, 11.4 Hz, 8H), 5.36 (d, *J*=4.8 Hz, 4H), 7.55–7.58 (m, 2H), 7.79–7.92 (m, 10H), 8.11–8.17 (m, 3H), 8.56 (br s, 1H), 8.63 (s, 2H), 8.71 (s, 1H); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 33.3, 38.2, 38.3, 49.4, 63.3, 70.1, 71.5, 72.2, 73.5, 125.9, 128.0, 128.17, 128.21, 130.1, 131.3, 131.5, 166.2, 171.4, 171.6, 172.8; MALDI-TOF (*m/z*): calcd for $C_{71}H_{117}N_{14}O_{31}$, 1661.793 $[M+H]^+$; found, 1661.908 $[M+H]^+$; IR (KBr, cm^{-1}) ν 3300, 2943, 1646, 1236.

*4.2.9. Synthesis of anthryl glycodendron **7**.* A suspension of **6** (100 mg, 60.2 μmol) in dry pyridine (0.576 mL) was added to dry acetic anhydride (0.576 mL, 6.02 mmol) at 0 °C, and the solution was stirred for 5 days under a nitrogen atmosphere. After evaporation under reduced pressure below 50 °C, the residue was purified by column chromatography on silica gel (chloroform/methanol, 20:1) to afford **7** (47 mg, 18.7 μmol, 31%). Compound **7**: mp 66–68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 12H), 2.05 (s, 12H), 2.06 (s, 12H), 2.10 (s, 12H), 2.18 (s, 12H), 2.29–2.40 (m, 12H), 2.66 (br s, 12H), 3.17 (br s, 12H), 3.38 (br s, 8H), 4.12 (dd, *J*=6.0, 6.0 Hz, 4H), 4.30 (dd, *J*=3.3, 9.0 Hz, 4H), 5.06–5.07 (m, 4H), 5.25 (d, *J*=4.2 Hz, 4H), 5.46 (t, *J*=6.0 Hz, 4H), 5.68 (t, *J*=4.8 Hz, 4H), 7.47–7.54 (m, 6H), 7.82 (br s, 6H), 7.99–8.03 (m, 4H), 8.29 (br s, 1H), 8.46 (s, 1H), 8.57 (s, 1H), 8.73 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 20.58, 20.61, 20.7, 33.6, 33.7, 37.4, 38.4, 39.9, 40.0, 49.7, 49.8, 52.0, 61.5, 68.7, 69.1, 69.5, 69.7, 72.0, 123.3, 126.1, 126.3, 128.0, 128.1, 128.4, 130.5, 132.0, 132.1, 132.6, 166.8, 169.6, 169.7, 169.9, 170.2, 170.3, 170.5, 173.5; MALDI-TOF (*m/z*): calcd for $C_{111}H_{157}N_{14}O_{51}$, 2502.004 $[M+H]^+$; found, 2502.429 $[M+H]^+$; IR (KBr, cm^{-1}) ν 3378, 2958, 1754, 1651, 1219.

*4.2.10. Synthesis of fullerene glycodendron **8**.* A mixture of C_{60} (34 mg, 47.2 μmol) and **6** (79 mg, 31.5 μmol) in *o*-dichlorobenzene (2.7 mL) was stirred at 40 °C for 7 days under a nitrogen atmosphere. The solution was separated by column chromatography on silica gel (chloroform/methanol, 10:1) and GPC to afford **8** (32 mg, 9.93 μmol, 32%). **8**: mp 112–114 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04–2.20 (m, 60H), 2.33 (br s, 16H), 2.67 (br s, 8H), 3.17 (br s, 12H), 3.40 (br s, 8H), 4.13 (dd, *J*=6.0, 6.3 Hz, 4H), 4.31 (dd, *J*=3.0, 9.0 Hz, 4H), 5.05–5.10 (m, 4H), 5.25 (d, *J*=4.2 Hz, 4H), 5.46 (t, *J*=4.8 Hz, 4H), 5.68 (t, *J*=4.8 Hz, 4H), 5.87 (s, 1H), 5.92 (d, *J*=3.9 Hz, 1H), 7.48–7.51 (m, 6H), 7.77–7.84 (m, 9H), 8.12 (t, *J*=6.0 Hz, 1H), 8.46 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.46, 20.48, 20.49, 20.8, 29.7, 33.63, 33.66, 33.7, 38.46, 38.50, 40.09, 40.13, 49.83, 49.84, 49.87, 49.90, 58.16, 58.17, 61.6, 68.8, 69.1, 69.6, 72.05, 72.07, 72.3, 126.1, 127.6, 136.9, 139.90, 139.92, 139.94, 141.2, 141.6, 141.99, 142.01, 142.23, 142.25, 142.57, 142.59, 143.0, 144.59, 144.61, 145.18, 145.29, 145.34, 145.37, 145.40, 145.43, 145.44, 146.2, 146.5, 166.9, 169.86, 169.90, 169.93, 170.28, 170.30, 170.32, 170.6, 173.55, 173.57;

MALDI-TOF (*m/z*): calcd for $C_{171}H_{157}N_{14}O_{51}$, 3222.004 $[M+H]^+$; found, 3221.816 $[M+H]^+$; IR (KBr, cm^{-1}) ν 3396, 2923, 1750, 1653, 1433, 1221, 562.

*4.2.11. Synthesis of fullerodendron **10** under microwave irradiation.* A mixture of C_{60} (25 mg, 34.7 μmol) and **9** (30.3 mg, 69.4 μmol) in *o*-dichlorobenzene (2.0 mL) was stirred at 45 °C for 14 h under a nitrogen atmosphere under microwave irradiation. The solution was separated by column chromatography on silica gel (chloroform) to afford **10** (19.3 mg, 16.7 μmol, 48%). The spectral data of fullerodendron **10** was the same as our previous report.[12]

5. Supplementary data

Characterization data for compounds **2L**, **3D**, **3L**, **4D** (before and after the diastereomeric separation), **4L** (before and after the diastereomeric separation), and **6**–**8**, and copies of ^1H NMR, ^{13}C NMR, MALDI-TOF MS and FT-IR spectra of these compounds.

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Supplementary data

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