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Separation and Characterization of [60]Fullerene Bisadducts Modified by 4,5-Dimethoxy-*o*-quinodimethane

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Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

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Abstract—The reaction of [60]fullerene with the *o*-quinodimethane species generated from 1,2-bis(bromomethyl)-4,5-dimethoxybenzene (**1**) was examined. Among possible regioisomers of bisadducts **2**, seven isomers (*trans*-1, *trans*-2, *trans*-3, *trans*-4, *e*, *cis*-3, and *cis*-2) were isolated by HPLC and characterized on the basis of NMR, FAB-MS, and/or UV–Vis spectroscopies.

Multiple addition to [60]fullerene becomes of increasing interest from the viewpoint of electronic,[1] electrochemical,[2] photophysical,[3] and chiroptical properties.[4] For example, the *cis*-3 *o*-quinodimethane bisadducts were found to exhibit red-shifted absorption and fluorescence spectra relative to [60]fullerene itself and the monoadduct.[3,5] The addition modes such as, *trans*-2, *trans*-3, and *cis*-3 lead to a chirality on the [60]fullerene core,[4] and the relationship between absolute configuration and CD spectra has been investigated.[4b] However, the drastic increase in the number of possible regioisomers with the number of additions is problematic from the synthetic aspects. Even in the bis-addition reactions occurring exclusively at [6,6] junctions, eight regioisomers are possible in principle. In addition, bisadditions usually take place without sufficient regioselectivity and the separation of resulting bisadducts requires highly sophisticated chromatographic techniques. Nevertheless, several research groups have succeeded in the isolation and characterization of a series of bisadduct regioisomers obtained by some typical reactions with [60]fullerene. Hirsch et al. successfully obtained and characterized the bisadducts from a Bingel–Hirsch reaction except for the *cis*-1 isomer that was absent for steric reasons.[6] Schuster et al. separated and characterized the six bisadducts accessible by Prato reaction and compared their UV spectra with those of Bingel–Hirsch bisadducts.[1] Concerning the bisadducts by Diels–Alder reaction, which is one of the most familiar and fundamental reactions of fullerene, there has been no systematic study on the isolation and characterization of regioisomers and the relationship between addition sites and spectroscopic properties. Although some regioisomers have been prepared by several research groups independently, all the possible bisadducts have not been isolated and characterized. The D_{2h}-symmetrical *trans*-1 bisadduct with anthracene was first isolated as Diels–Alder bisadduct by the reactions in solution[8] and crystals.[9] We have regioselectively synthesized the *e*, *cis*-3, and *cis*-2 bisadducts that are modified within only one hemisphere of [60]fullerene by using compounds in which two *o*-quinodimethane precursors are connected with an oligomethylene linkage.[5] Recently, the regioselective synthesis of a *trans*-4 bisadduct was also reported by using a dibenzo-18-crown-6 moiety as a bridging unit.[7] To the best of our knowledge, however, other Diels–Alder bisadducts, *trans*-2 and *trans*-3, have not been isolated yet. Thus, we have investigated the simple reaction of [60]fullerene with the *o*-quinodimethane species generated from 1,2-bis(bromomethyl)-4,5-dimethoxybenzene (**1**). As a result, both *trans*-2 and *trans*-3 Diels–Alder bisadducts were isolated from regioisomeric mixture of bisadducts **2** and characterized for the first time. In this paper, the isolation and characterization of the seven bisadducts obtained are described, and their spectroscopic properties are compared among regioisomers and also with those of other bisaddition products.

Results and Discussions

A mixture of [60]fullerene and **1** (2.5 equiv.)[10] was refluxed in *o*-dichlorobenzene in the presence of KI and 18-crown-6 for 4 days (Scheme 1). The purification by column chromatography on silica gel (eluent: toluene) afforded a regioisomeric mixture of bisadducts **2** in 38%, after the elution of unchanged [60]fullerene and the monoadduct. These bisadducts **2** were further subjected to preparative HPLC

Keywords: fullerenes bisadduct; Diels–Alder reaction; *o*-quinodimethane.
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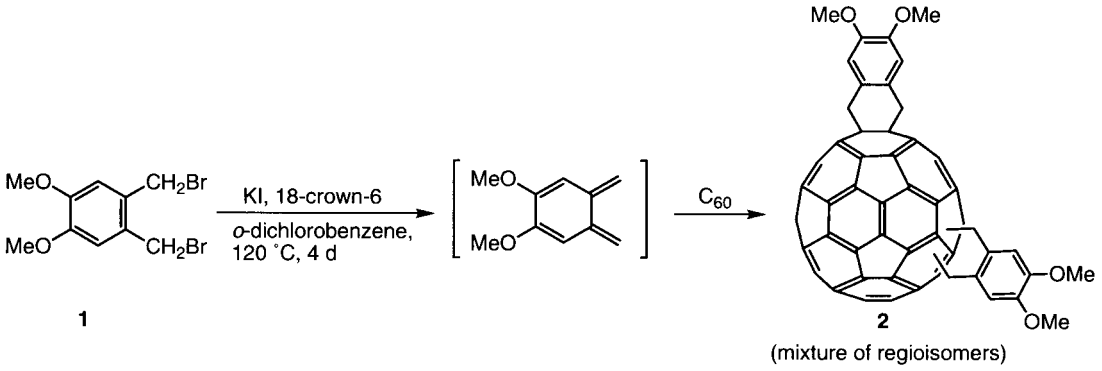

Scheme 1.

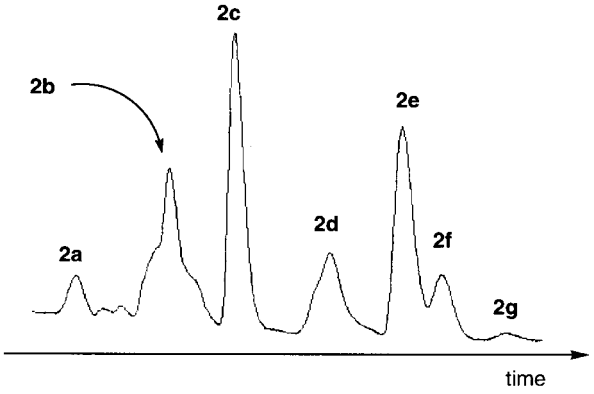

Figure 1. HPLC chromatogram of regioisomeric mixture of bisadducts **2**. Conditions: stationary phase, RPFULLERENE column (20×250 mm); eluent, toluene/acetonitrile (1:3 (v/v)); flow rate, 10 mL/min; detection, UV 335 nm.

using an RPFULLERENE column (eluent: toluene/acetonitrile (1:3 (v/v)). As shown in Fig. 1, mainly seven peaks (**2a**–**g**) were observed in a ratio of 4:16:29:15:27:1:8 and each fraction was repeatedly collected.

The structures of **2a**–**g** were characterized by FAB-MS, ^{1}H and ^{13}C NMR, and/or UV–Vis spectroscopy. All products **2a**–**g** indicated the molecular ion peak (M^+=1048) corresponding to the desired bisadduct in FAB-MS spectra. The ^{1}H and ^{13}C NMR spectra were measured in 1,1,2,2-tetrachloroethane-d_2 at 120°C, since the spectra were extremely broadened at room temperature due to the slow flipping motion of the cyclohexene rings. Selected ^{1}H NMR spectral data of **2a**–**e** are summarized in Table 1. For **2f** and **2g**, well-defined NMR spectra were not obtained because of their low yields.

Bisadduct **2a** exhibits a quite high symmetry as demonstrated by the only three singlets corresponding to the equivalent four aromatic, eight methylene, and twelve methoxy protons. This observation apparently indicates the D_{2h}-symmetrical *trans*-1 bisadduct. In the ^{1}H NMR spectrum of **2e**, both aromatic and methoxy protons were observed as three singlet peaks with an integral ratio of 2:1:1. This spectral pattern can be accomplished only by the *e*-bisadduct with C_s symmetry. The ^{13}C NMR spectrum, in which about thirty [60]fullerene sp^2 carbon peaks are observed, is also compatible with this addition pattern. On the other hand, **2b**–**d** afforded two aromatic and two methoxy proton peaks, suggesting the C_s or C_2 symmetry. Their ^{13}C NMR spectra exhibiting 28–30 peaks due to the [60]fullerene sp^2 carbons also supported such symmetry.[11] It appears quite difficult, however, to identify **2b**–**d** only from the symmetry of the NMR spectra, since C_s symmetry can result from the *cis*-1, *cis*-2, and *trans*-4 and C_2 symmetry from *cis*-3, *trans*-3, and *trans*-2 bisadducts. Among them, the *cis*-1 isomer is most unlikely to be formed due to steric hindrance. The *cis*-2 isomer can also be excluded, because there are no low-field-shifted aromatic protons characteristic of *cis*-2 isomers[5] in the ^{1}H NMR spectra of **2b**–**d**. Therefore, *trans*-2, *trans*-3, *trans*-4, and *cis*-3 bisadducts are possible candidates for **2b**–**d**.

Thus, the characterization of these bisadducts was attempted on the basis of UV–Vis spectra, which are known to be generally dependent mainly on the addition patterns and almost independent of the kind of substituents on addends, at least for *o*-quinodimethane bisadducts.[3] Fig. 2 shows the UV–Vis spectra of **2a**–**g** in CCl_4 at room temperature. The spectrum of **2d** exhibits two broad bands with maxima at 643 and 708 nm, which are characteristic of *trans*-4 bisadducts as reported in the literature.[7,12] The spectra of

Table 1. ^{1}H NMR spectral data for bisadducts **2a**–**e** (measured in 1,1,2,2-tetrachloroethane-d_2 at 120°C)

Compound	δ(Ar)[a]	δ(OMe)[a]
2a	7.31 (4H)	4.05 (12H)
2b	7.29 (2H), 7.22 (2H)	4.04 (6H), 4.01 (6H)
2c	7.27 (2H), 7.03 (2H)	4.03 (6H), 3.93 (6H)
2d	7.14 (2H), 7.01 (2H)	3.98 (6H), 3.92 (6H)
2e	7.07 (1H), 7.06 (2H), 7.01 (1H)	3.97 (6H), 3.94 (3H), 3.91 (3H)

[a] All the signals were observed as singlets.

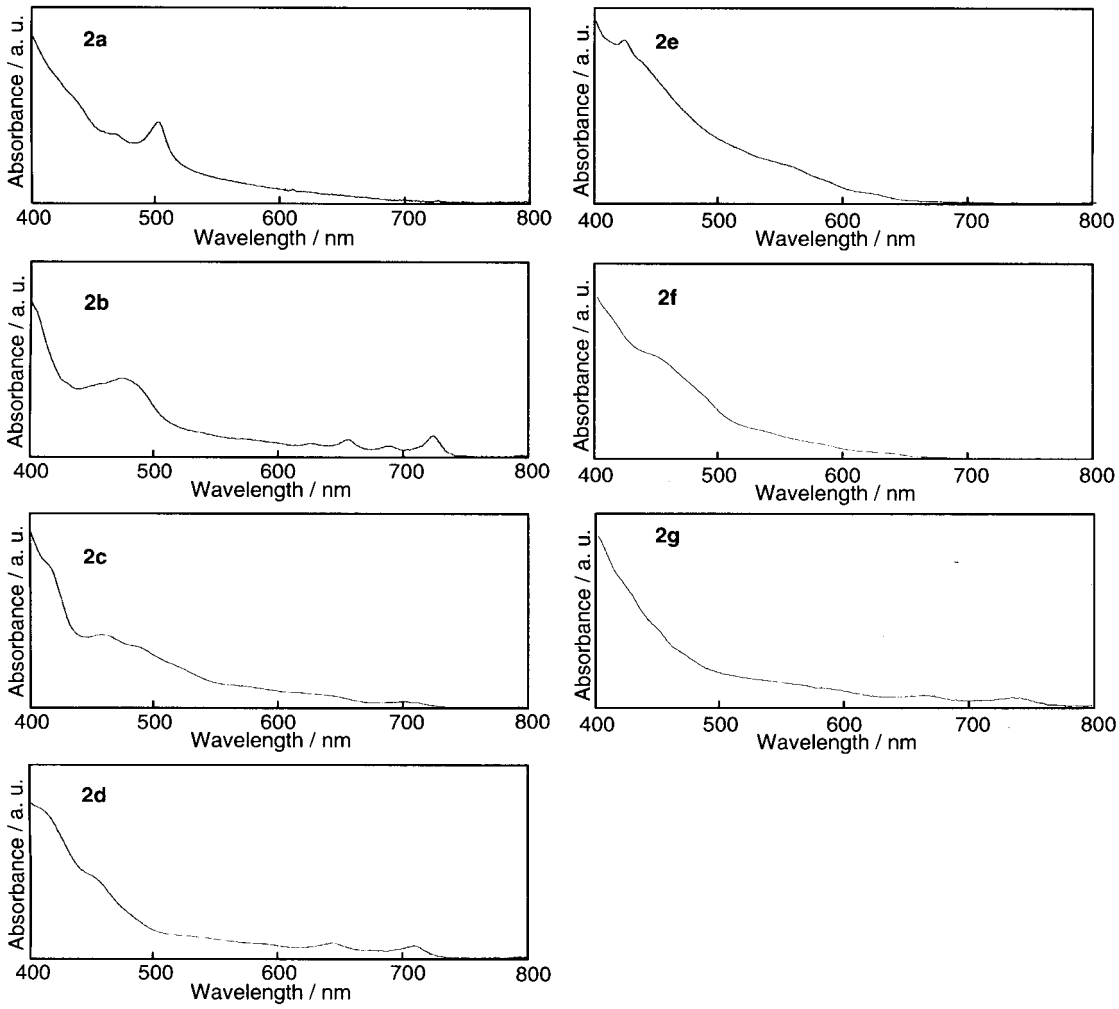

Figure 2. UV–Vis spectra of **2a–g** in CCl_4 at room temperature.

both **2b** and **2c** are apparently inconsistent with that of *cis*-3 isomers, whose longest absorption band would extend up to ca. 750 nm.[5] Since there have been no reports on the UV–Vis spectra of *trans*-2 and *trans*-3 *o*-quinodimethane bisadducts, the assignment of **2b** and **2c** was accomplished by the comparison with the spectra of the corresponding [60]fullerene-*N*-methylpyrrolidine bisadduct regioisomers (Prato bisadducts).[1] The spectra of **2b** and **2c** are quite similar to those of *trans*-2 and *trans*-3 Prato bisadducts, respectively; especially, a broad band around 480 nm is characteristic of *trans*-2 bisadducts. Thus, it is reasonable to assign **2b** and **2c** as *trans*-2 and *trans*-3, respectively. This assignment seems to be reasonable also from the consideration of the order of chromatographic elution, since **2a** and **2d** are *trans*-1 and *trans*-4, respectively. The spectra of **2a** and **2d**, which have been already identified by NMR, support their addition patterns. The rather sharp band around 500 nm in **2a** is similar to that in the *trans*-1 Prato bisadduct. The weak, sharp band at 430 nm observed in **2e** is also typical of *e*-bisadducts including the Prato bisadduct.[1,5] The UV–Vis spectra of **2f** and **2g** provide decisive evidences for their assignments, though their NMR spectra were not accessible; **2f** and **2g** exhibit quite similar spectra to those of the *cis*-2 and *cis*-3 *o*-quinodimethane bisadducts reported previously, respectively.[5] Thus, **2a**, **2b**, **2c**, **2d**, **2e** **2f**, and **2g** were assigned as *trans*-1, *trans*-2, *trans*-3, *trans*-4, *e*, *cis*-2, and *cis*-3, respectively. The order of elution apparently corresponds to the positional relationship between the two addition sites, except for **2f** and **2g**; the regioisomers attacked at more remote positions are eluted in earlier retention times. The UV–Vis spectrum of each regioisomer of *o*-quinodimethane bisadducts possessing six-membered rings was found to resemble that of the corresponding Prato bisadducts with five-membered rings rather than that of Bingel–Hirsch bisadducts with three-membered rings; the electronic-properties of *o*-quinodimethane bisadducts are relatively similar to those of Prato bisadducts. With respect to these two types of bisadducts, their UV–Vis spectra depend on addition sites rather than what is attached to the fullerene surface.

As Table 1 demonstrates, the chemical shifts in these bisadducts are closely related to the relative position of addition sites or the order of elution; both aromatic and methoxy protons are deshielded in the order of **2a**, **b**, **c**, **d**, and **e**. This tendency, ascribable to the curvature of the fullerene surface, is also observed in the Bingel–Hirsch and Prato bisadducts.[1]

The optical resolution of chiral bisadducts **2b** and **2c** with C_2

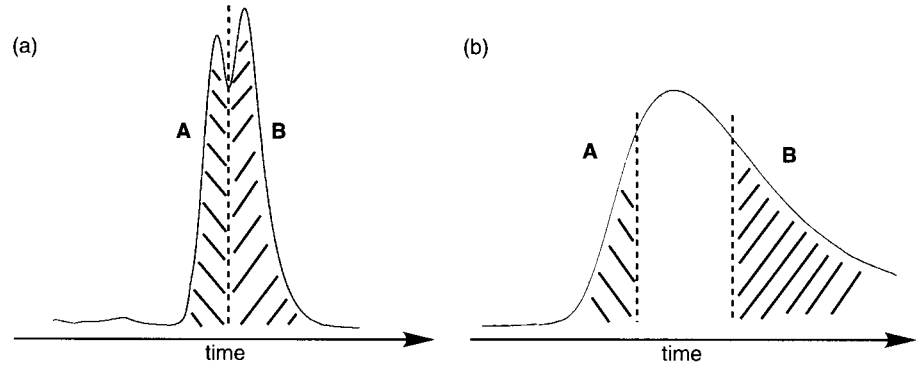

Figure 3. HPLC chromatograms of: (a) **2b**; and (b) **2c** by a CHIRALCEL OD HPLC column (10×250 mm) (eluent: hexane/2-propanol (5:2 (v/v)).

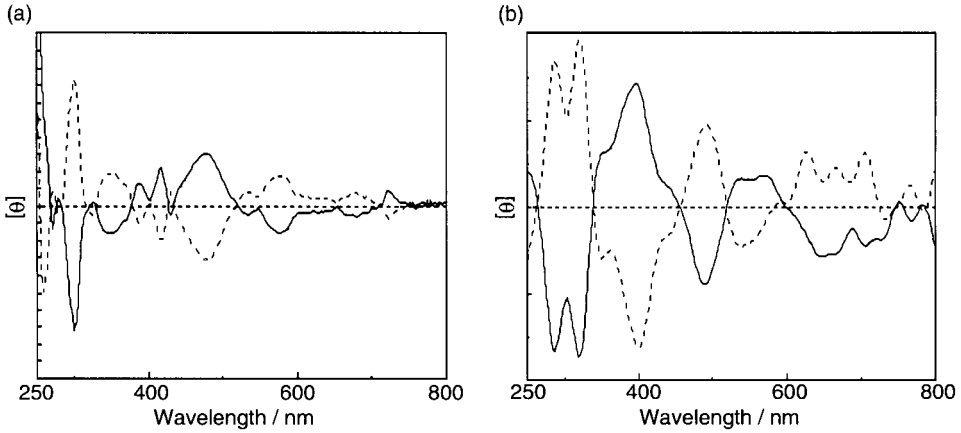

Figure 4. CD spectra of (a) **2b** and (b) **2c** in cyclohexane at room temperature. Solid and dotted lines correspond to part **A** and **B**, respectively, of HPLC chromatograms.

symmetry was attempted on a CHIRALCEL OD HPLC column (eluent: hexane/2-propanol (5:2 (v/v)). As Fig. 3 illustrates, **2b** affords two peaks that are not completely separated. On the contrary, **2c** affords a single broad peak, though various elution conditions such as eluent composition or flow rate were examined. Thus, the CD spectra of the front part **A** and tail part **B** of each bisadduct were examined. All the fractions were CD-active, as shown in

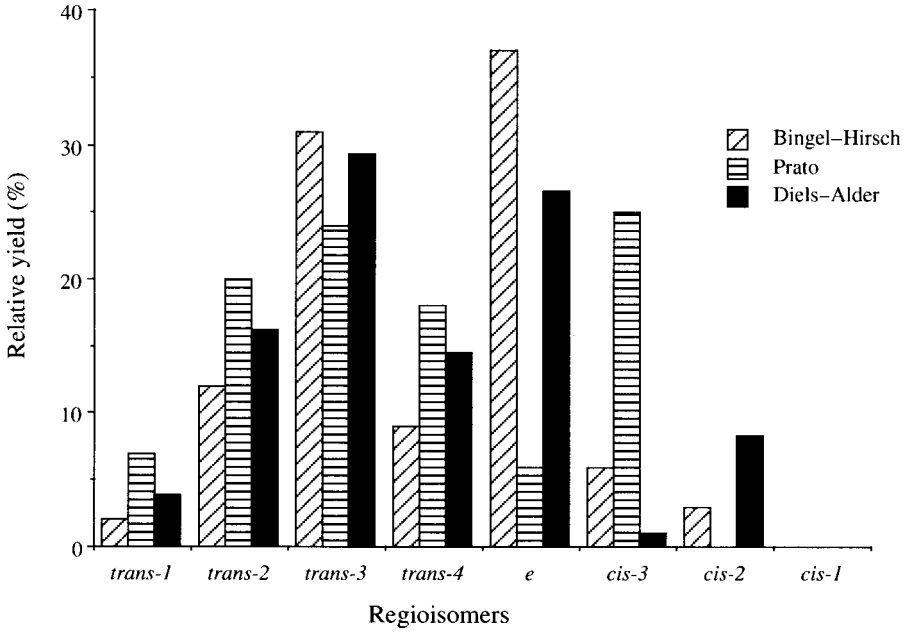

Figure 5. Comparison of regioselectivity in the *o*-quinodimethane bisaddition using **1** with those of the Bingel–Hirsch and Prato bisadditions.

Fig. 4. Furthermore, parts **A** and **B** of respective bisadducts display mirror images to each other, indicating the enantiomeric relationship. This observation shows that **2b** and **2c** are chiral bisadducts (*trans*-2, *trans*-3, or *cis*-3). The spectral shapes of **2b** and **2c** are entirely different from those of the *cis*-3 *o*-quinodimethane bisadducts reported previously,[4a] as in the case of UV–Vis spectra. The strong Cotton effects in these spectra mainly originate from the chiral fullerene core modified by two *o*-quinodimethanes asymmetrically. The CD spectra of some *trans*-2 and *trans*-3 bisadducts, such as osmylated ones[13] and cyclopropanated ones,[14] have so far been reported, but there are no spectral features characterizing each regioisomer including **2b** and **2c**. At this moment, unfortunately, it seems that CD spectra are not available for the distinction between *trans*-2 and *trans*-3 bisadducts.

Fig. 5 illustrates the comparison of regioselectivity in the *o*-quinodimethane bisaddition using **1** with those of the Bingel–Hirsch and Prato bisaddition. The regioselectivity of the bisaddition produced by **1** is relatively similar to that of the Bingel–Hirsch bisaddition rather than that of the Prato bisaddition; *trans*-3 and *e* isomers were obtained as major isomers.

Experimental

General

NMR spectra were recorded on a JEOL α-500 FT NMR spectrometer with tetramethylsilane as an internal standard. Preparative HPLC for the separation of bisadduct regioisomers was performed with a Shimadzu LC-6AD pump, an SPD-6A UV spectrophotometric detector, an FCV-100B fraction collector, and a C-R4A chromatopac. FAB Mass spectra were taken by a JEOL JMS-HX110A mass spectrometer. Absorption spectra were recorded on a Hitachi U3210 spectrophotometer. CD spectra were taken by a JASCO J-720W spectropolarimeter. Precursor **1** was prepared by the method in Ref. 10.

Preparation of [60]fullerene bisadducts 2

To a mixture of [60]fullerene (720 mg, 1.0 mmol), KI (1.66 g, 10 mmol), and 18-crown-6 (2.64 g, 10 mmol) dissolved in *o*-dichlorobenzene (400 mL) was added **1** (810 mg, 2.5 mmol). The mixture was refluxed in the dark for 4 days. After cooled to room temperature, the mixture was washed with aq. 5% KCl, aq. 5% $Na_2S_2O_3$, and water and dried over magnesium sulfate. After the solvent was evaporated under reduced pressure, the residue was chromatographed on silica gel (eluent; toluene), to give unchanged [60]fullerene, monoadduct, and regioisomeric mixture of bisadducts **2a**–**g** as brown-colored powder. These bisadducts were separated and isolated by HPLC using an RPFULLERENE column (20×250 mm) with an eluent of toluene/acetonitrile (1:3 (v/v)). Both **2b** and **2c** were separated into the respective enantiomers by chiral HPLC using a CHIRALCEL OD column (10×250 mm) with an eluent of hexane/2-propanol (5:2 (v/v)) (flow rate; 7 mL/min).

2a (*trans*-1). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 393 K) δ 7.31 (4H, s), 4.80 (8H, s), 4.05 (12H, s); FAB MS *m*/*z* 1048 (M^+).

2b (*trans*-2). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 393 K) δ 7.29 (2H, s), 7.22 (2H, s), 4.73 (2H, d, *J*=13.7 Hz), 4.55 (2H, d, *J*=13.7 Hz), 4.55 (2H, d, *J*=14.0 Hz), 4.45 (2H, d, *J*=14.0 Hz), 4.04 (6H, s), 4.01 (6H, s); ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K) δ 161.60, 155.26, 155.16, 154.75, 149.67, 149.64, 148.21, 147.28, 146.95, 164.88, 146.66, 146.63, 145.72, 145.34, 145.32, 144.42, 144.22, 143.98, 142.96, 142.89, 142.69, 142.31, 141.80, 141.76, 139.92, 139.59, 131.00, 130.82, 113.58, 113.51 (CH), 64.97, 64.87 (C_{60} sp^3-C), 57.02 (MeO), 45.31, 44.86 (CH_2); FAB MS *m*/*z* 1048 (M^+).

2c (*trans*-3). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 393 K) δ 7.27 (2H, s), 7.03 (2H, s), 4.59 (2H, d, *J*=13.9 Hz), 4.50 (2H, d, *J*=13.9 Hz), 4.27 (2H, d, *J*=13.7 Hz), 4.17 (2H, d, *J*=13.7 Hz), 4.03 (6H, s), 3.93 (6H, s); ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K) δ 160.78, 157.95, 157.80, 156.84, 149.57, 149.47, 149.45, 148.85, 148.85, 148.80, 148.62, 148.43, 146.02, 145.86, 145.77, 145.59, 145.55, 145.43, 145.21, 144.56, 143.99, 143.89, 142.92, 141.85, 141.73, 141.44, 139.95, 136.38, 134.98, 130.77, 129.18, 128.36, 113.32 (CH), 65.60, 65.38 (C_{60} sp^3-C), 56.97 (MeO), 45.45, 44.08 (CH_2); FAB MS *m*/*z* 1048 (M^+).

2d (*trans*-4). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 393 K) δ 7.14 (2H, s), 7.01 (2H, s), 4.40 (2H, d, *J*=13.7 Hz), 4.33 (2H, d, *J*=13.8 Hz), 4.17 (4H, s), 3.98 (6H, s), 3.92 (6H, s); ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K) δ 156.76, 154.60, 153.17, 152.90, 152.50, 149.72, 149.50, 149.44, 148.53, 147.44, 146.64, 146.48, 146.44, 145.79, 144.99, 144.55, 144.44, 143.37, 142.79, 142.45, 141.98, 141.56, 141.38, 138.93, 136.03, 134.99, 130.69, 130.46, 129.17, 128.36, 113.29 (CH), 65.09, 64.83 (C_{60} sp^3-C), 56.93 (MeO), 44.90, 43.93 (CH_2); FAB MS *m*/*z* 1048 (M^+).

2e (*e*). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 393 K) δ 7.07 (1H, s), 7.06 (2H, s), 7.01 (1H, s), 4.16 (6H, m), 3.97 (6H, s), 3.94 (3H, s), 3.91 (3H, s) (The peaks of two methylene protons were not clearly assigned due to the overlap with methoxy proton peaks and broadening.); ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K) δ 161.97, 155.73, 154.80, 150.62, 149.40, 149.31, 148.32, 147.52, 146.73, 146.40, 146.33, 146.12, 145.35, 145.19, 144.98, 144.88, 144.72, 143.98, 143.14, 142.67, 142.11, 141.80, 141.25, 140.95, 137.73, 136.54, 135.03, 130.83, 130.45, 113.20 (CH), 65.30, 65.00, 64.80 (C_{60} sp^3-C), 56.94 (MeO), 45.05, 44.75 (CH_2); FAB MS *m*/*z* 1048 (M^+).

2f (*cis*-2). FAB MS *m*/*z* 1048 (M^+).

2g (*cis*-3). FAB MS *m*/*z* 1048 (M^+).

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11. Although the total number of the [60]fullerene sp^2 carbon peaks is theoretically different in case of C_2 (28 signals) and C_s (30 signals) symmetry, it was difficult to distinguish between C_2 and C_s due to the overlapping of some peaks.
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