Saccharide Libraries as Potential Templates for Regio- and Chiroselective Introduction of Two Functional Groups into [60]Fullerene

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This paper reports regio- and chiroselective introduction of two boronic acid groups into [60]fullerene controlled by a saccharide used as a template molecule. The double [4+2] cycloadditions between [60]fullerene and 1:2 saccharide−boronic acid complexes **6**−**9** afforded [60]fullerene−bisadducts **12**. Their structures were identified on the basis of ^{1}H and ^{13}C NMR, UV−vis, and CD spectroscopy, mass spectrometry, and chiral HPLC analysis. When 3-*O*-methyl-D-glucose (**4**) was used as the template molecule, high regioselectivity was achieved which gave *trans*-4 isomer **12a** as a main isomer in 72.5% yield. The chiro- as well as regioselective preparation of *e* isomer **12c** was attained in 81.4% ee from the 55.7% yield racemic mixture by the reaction using the D-mannitol-3,4-carbonate template (**3**). When the enantiomers, D-threitol (D-**2**) and L-threitol (L-**2**) were used as the templates, *cis*-3 isomers **12b** and *ent*-**12b** with opposite chirality were yielded in 44.2 and 45.2% ee, respectively. On the other hand, 1-*O*-methyl-α-D-mannopyranoside template (**5**) featured nonselective cycloaddition.

Introduction

Recently, regioselective introduction of two functional groups into [60]fullerene has been of much concern.[1−8] The principle idea is to use a template molecule by which two functional molecules are arranged at the desired angle and distance. For example, when bifunctionalization (i.e., cyclopropanation,[2−4] [3+2] cycloaddition,[5,6] and [4+2] cycloaddition[7]) occurs on the [6,6] junction bonds between the two six-membered rings on [60]fullerene surface, the formation of eight different regioisomers (*cis*-1, *cis*-2, *cis*-3, *e*, *trans*-1, *trans*-2, *trans*-3, and *trans*-4)[9] is expected. It is not yet possible to selectively obtain one of these regioisomers, because of the lack of potential templates which can cover all of the possible spacer lengthes between the two [6,6] junction bonds on the [60]-fullerene surface. Furthermore, chiroselective bifunctionalization of [60]fullerene has scarcely been attained except for a few limited reports.[2,3,5] Is there any template family as a practical library that can overcome the problems described above? We recently noticed that the saccharide family could be a potential candidate, because naturally abundant saccharides can be used and their inherent chirality would be very useful for chiro- as well as regioselective bifunctionalization of [60]fullerene. This methodology will be achieved by utilizing the saccharide−boronic acid interaction,[10] in which boronic acids react with 1,2- or 1,3-diols in saccharide molecules to form cyclic boronate esters. Thus, we chose saccharides as templates and boronic acids as functional groups for regio- and chiroselective bifunctionalization of [60]-fullerene. Furthermore, when the saccharide−boronic acid interaction is used to make a memory for the original template saccharide on the [60]fullerene surface, one can expect that removal and rebinding of the saccharide templates can occur reversibly (Scheme 1). This reversible system between bifunctionalized [60]fullerene derivatives and template molecules has never been reported.

In a preliminary communication, we reported the regioselective double [4+2] cycloaddition between [60]-fullerene and saccharide−3,4-bis(bromomethyl)phenylboronic acid (1:2) complexes, which can generate *o*-quinodimethane species[11] to react with the two [6,6] junction bonds in [60]fullerene (Scheme 1).[12] The regiospectrum

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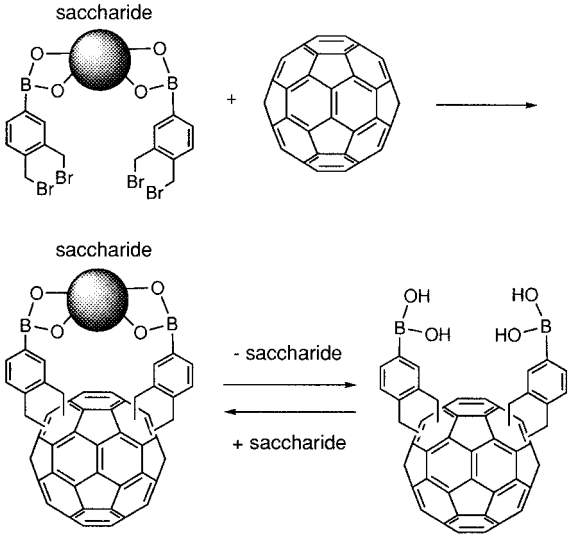
Scheme 1



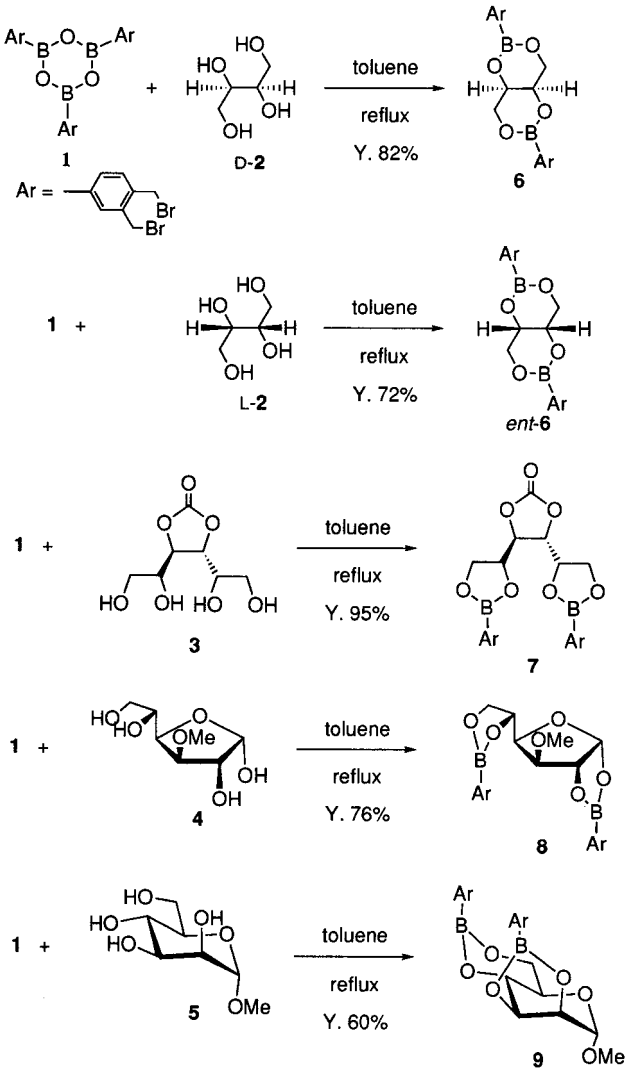
was closely related to a structure of the saccharide used as the template molecule. Here, we report a full account of this study including the new findings of the chiroselective introduction of two boronic acid groups into [60]fullerene, which is controlled by the inherent chirality of saccharide templates.

Results and Discussion

Preparation of 1:2 Saccharide−Boronic Acid Complexes. To access 1:2 saccharide−boronic acid complexes **6**−**9**, we selected five saccharides, D-threitol (D-**2**), L-threitol (L-**2**), D-mannitol-3,4-carbonate (**3**), 3-*O*-methyl-D-glucose (**4**), and 1-*O*-methyl-α-D-mannopyranoside (**5**), as templates. The complexes were prepared from 2,4,6-[3,4-bis(bromomethyl)phenyl]boroxin **1**[13] and the corresponding saccharides in refluxing toluene with azeotropic removal of water (Scheme 2). The products **6**−**9** were identified by means of spectral data and elemental analyses. For the complex obtained from **1** and threitol **2**, one can propose two different cyclic structures, a 1,2-adduct with two five-membered rings and a 1,3-adduct with two six-membered rings. Previously, we confirmed on the basis of the X-ray crystallographic study that in **6** the two boronic acids react with the 1,3-diols in threitol to form the two six-membered rings.[13] Extensive ^{1}H NMR and ^{1}H−^{1}H COSY studies of **8** showed that the saccharide moiety for **8** adopts the furanose form: the coupling constants of the saccharide moiety were very similar to those of 1,2:5,6-bisarylglucofuranose reported previously.[14]

Reaction between [60]Fullerene and 1:2 Saccharide−Boronic Acid Complexes. The intramolecular double additions between [60]fullerene and **6**−**9** were performed in refluxing toluene in the presence of 18-crown-6 and KI under a nitrogen atmosphere (Scheme 3). To avoid the intermolecular double addition giving bis-

Scheme 2



[60]fullerene connected with a saccharide−bisboronate moiety, we adopted the dilute-concentration conditions at 1×10^{-3} mol dm^{-3}. To simplify the product analysis, the saccharides in the product **10** were removed by treatment with aqueous 1.2 mol dm^{-3} HCl solution. Then, the boronic acid groups in **11** were protected with 2,2-dimethylpropane-1,3-diol. Finally, the desired bisadduct **12** was isolated by column chromatography (silica gel, toluene/chloroform) in 46−58% yields as a regioisomeric mixture.

Isomer Distribution of Bisadducts. To analyze the isomer distribution in **12**, the regioisomeric mixture of **12** was subjected to HPLC analysis using a COSMOSIL 5PBB column eluting with *n*-hexane/toluene (3:7 (v/v), 1.0 mL/min). The results are summarized in Table 1. In HPLC analysis, seven or eight peaks were always observable in the bisadduct region and the relative intensity changed depending on the saccharide template. Compounds **6**, *ent*-**6**, **7**, and **8** afforded a major peak for peak 7 (47.3%), peak 7 (47.8%), peak 8 (55.7%), and peak 6 (72.5%), respectively, indicating that a single regioisomer was selectively formed in each case. On the other hand, compound **9** featured a rather nonselective product

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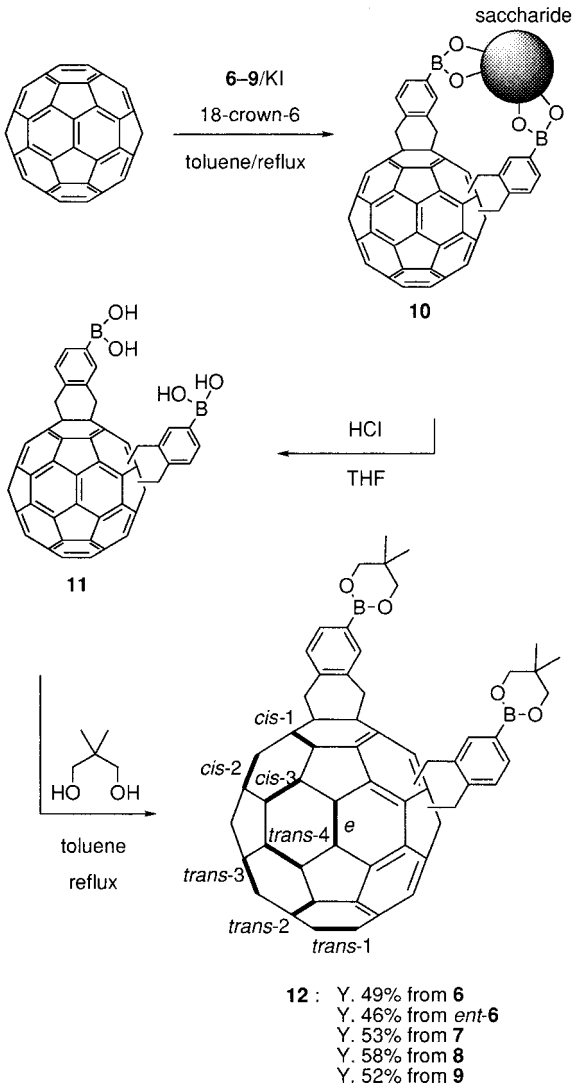
Scheme 3



12 : Y. 49% from **6**
Y. 46% from *ent*-**6**
Y. 53% from **7**
Y. 58% from **8**
Y. 52% from **9**

Table 1. Results of HPLC Analysis[a] for 12

peak no.	retention time/min	product percentage[b] in **12** obtained from				
		6	*ent*-**6**	**7**	**8**	**9**
1	39.6	1.5	2.9	4.2	0.2	5.6
2	41.5	2.3	5.3	4.3	1.5	7.5
3	43.0	5.4	8.5	3.4	3.0	11.4
4	46.5	7.8	5.8	10.5	3.7	15.2
5	49.7	12.3	8.1	7.7	3.6	23.7
6	51.2	11.3	10.7	14.2	72.5	15.6
7	52.9	47.3	47.8	0	0	0
8	54.1	12.1	10.9	55.7	15.5	21.0

[a] Conditions: stationary phase, COSMOSIL 5PBB (10 × 250 mm); eluent, *n*-hexane/toluene (3:7 (v/v)); flow rate, 1.0 mL/min. [b] Computed from the peak area obtained by the chromatogram followed at 350 nm.

distribution. The results imply that the saccharide changes the orientation between the two bis(bromomethyl)phenyl groups in **6**−**9** and the addition reaction occurs with the different [6,6] junction bonds on the [60]-fullerene surface.

Isolation of Bisadducts. It seems difficult to isolate eight different isomers of bisadduct **12** and to identify the structure of each isomer. We thus decided to challenge the isolation of main regioisomers of peak 7 for **6**, peak 7 for *ent*-**6**, peak 8 for **7**, and peak 6 for **8**. We found that peak 6 (**12a**) can be easily isolated by recrystallization from dichloromethane/*n*-hexane. In contrast, the isolation of peak 7 (**12b** from **6**, *ent*-**12b** from *ent*-**6**) and peak 8 (**12c**) was achieved only by a HPLC separation method using a COSMOSIL 5PBB column eluting with *n*-hexane/toluene (3:7 (v/v), 0.5 mL/min). Finally, **12a**, **12b**, *ent*-**12b**, and **12c** can be obtained in 16%, 10%, 10%, and 11% isolated yield from **8**, **6**, *ent*-**6**, and **7**, respectively. The regioisomers isolated, **12a**, **12b**, *ent*-**12b**, and **12c**, showed a single peak, which is consistent with peak 6, peak 7, peak 7, and peak 8, in their HPLC chromatograms, respectively.

Identification of Bisadducts. The structures of **12a**, **12b**, *ent*-**12b**, and **12c** were identified to be *trans*-4, *cis*-3, *cis*-3, and *e*, respectively, on the basis of the molecular symmetry deduced from ^{1}H and ^{13}C NMR spectra.[15] The comparison of their UV−vis spectra with those reported in the preceding reports[9,16] also supported these assignments. The derivation of **12** to Nishimura's phenol derivative **13**[7] by treatment with H_2O_2[17] also afforded very helpful information for the structure identification of **12a**, **12b**, *ent*-**12b**, and **12c** (Scheme 4). The details of the assignment processes are described below.

In the ^{1}H NMR spectrum (toluene-d_8, 90 °C) of **12a**, one could observe one CH_3 proton peak (0.71 ppm, 12H) and one CH_2 proton peak (3.50 ppm, 8H) for the protective groups and four CH_2 proton peaks (4.04, 4.04, 4.12, and 4.19 ppm, 2H each) and three ArH proton peaks (7.42, 8.13, and 8.17 ppm, 2H each) for the *o*-xylenyl groups. This splitting pattern is commensurate with either C_2 symmetry (*cis*-3, *trans*-2, or *trans*-3) or C_s symmetry (*cis*-1, *cis*-2, *trans*-1, or *trans*-4).[9,16] Among them, the size of the saccharide template is actually too small or too large to give *cis*-1, *trans*-1, *trans*-2, and *trans*-3; therefore, these isomers can be excluded. The residual possible isomers are *cis*-2, *cis*-3, and *trans*-4. The solubility of **12a** into deuterated NMR solvents was not so high as to obtain a satisfactory ^{13}C NMR spectrum, so that we converted **12a** to more soluble **13a** by treatment with H_2O_2.[17] Compound **13a** did not coincide either with *cis*-2 or with *cis*-3, reported by Nishimura et al.[7] Furthermore, the ^{13}C NMR spectrum of **13a** (DMSO-d_6, 120 °C) gave 30 sp^2 carbon peaks and 2 sp^3 carbon peaks for the [60]-fullerene moiety. This splitting pattern is commensurate with C_s symmetrical *cis*-2 and *trans*-4.[9,16] As the summary of the results mentioned above, **12a** can be identified to be *trans*-4, which satisfies all of the above-mentioned information.

Bisadducts **12b** and *ent*-**12b** showed the same ^{1}H NMR spectrum ($C_2D_2Cl_4$, 90 °C), and the splitting pattern was commensurate with either C_2 symmetry or C_s symmetry.[9,16] In the ^{13}C NMR spectra ($C_2D_2Cl_4$, 90 °C) of **12b** and *ent*-**12b**, the splitting pattern with 28 sp^2 carbon peaks and 2 sp^3 carbon peaks for the [60]fullerene moiety indicates the C_2 symmetrical *cis*-3, *trans*-2, or *trans*-3.[18] Judging from the size of the template saccharides, only

(15) To obtain the clear spectra, the ^{1}H and ^{13}C NMR spectra of **12** and **13** were measured at high temperature (90−120 °C), since the spectra were broadened at room temperature because of the slow flipping motions around the two cyclohexene rings in **12** and **13**. For the flipping motion in methano[1,2]benzenomethano[60]fullerenes, see: Nakamura, Y.; Minowa, T.; Tobita, S.; Shizuka, H.; Nishimura, J. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2351−2357.

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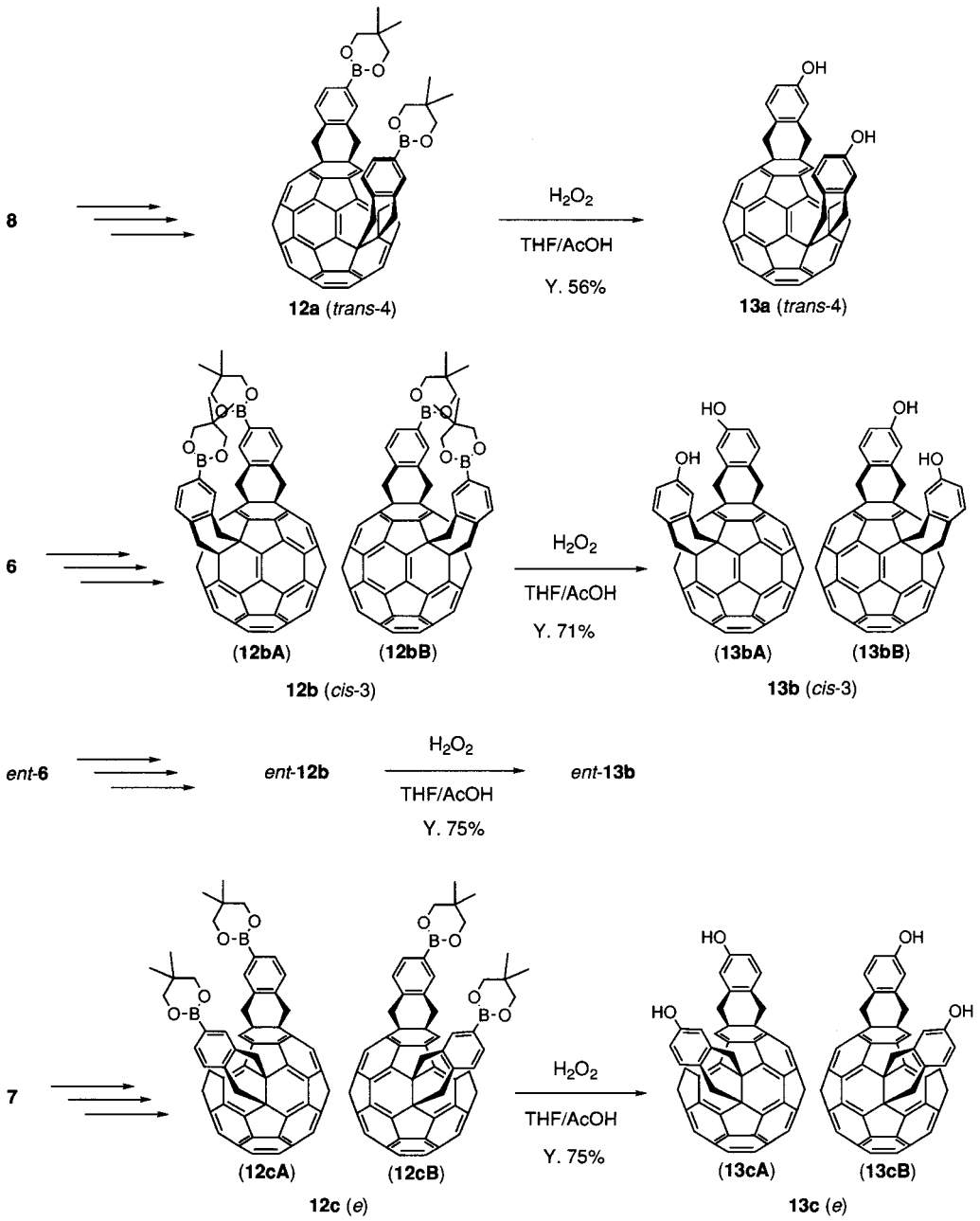
Scheme 4



the formation of *cis*-3 is possible as the structures of **12b** and *ent*-**12b**.

The ^{1}H and ^{13}C NMR spectra ($C_2D_2Cl_4$, 90 °C) of **12c** gave the two sets of proton and carbon peaks for the two boronic acid groups, respectively, suggesting that the two boronic acid groups in **12c** are chemically unequivalent.[19] Since the spectral behavior is observable only for C_1 symmetrical *e*, **12c** was identified to be *e*.[9,16]

The UV−vis spectra of **12a**, **12b**, *ent*-**12b**, and **12c** are also supportive of their proposed structure. It is already known that the UV−vis spectra of [60]fullerene−bisadducts depend on the addition pattern rather than on the nature of the substituent.[9,16] In the UV−vis spectra of **12a**, **12b**, *ent*-**12b**, and **12c** in dichloromethane, the characteristic absorption maxima were observed at 643 and 708 nm for **12a**, at 661 and 731 nm for **12b**, at 661 and 731 nm for *ent*-**12b**, and at 423 nm for **12c**, respectively (Figure 1). These maxima are consistent with those in the previous reports.[9,16]

The spectral data of phenol derivatives **13b** (*ent*-**13b**) and **13c** coincide with those of *cis*-3 and *e* reported by Nishimura et al., respectively.[7] In contrast, **13a** shows different spectral behavior compared to *cis*-2, *cis*-3, and *e* reported by Nishimura et al.[7] As a summary of the foregoing findings deduced from the spectral data and the derivation, **12a**, **12b** (*ent*-**12b**), and **12c** are unequivocally identified to be *trans*-4, *cis*-3, and *e*, respectively.[20]

Optically Active Bisadducts. Since C_2 symmetrical

(18) Although the theoretical number of sp^2 carbon peaks for the [60]fullerene moiety as well as the benzene moieties in **12b** and *ent*-**12b** should be 34, the peak number observed was 33. Probably, a peak of the adjacent carbon to the boron atom would be missing.

(19) Theoretically, the total number of sp^2 carbon peaks for the [60]-fullerene moiety as well as the benzene moieties in **12c** should be 68. However, it was very difficult to count all of the sp^2 carbon peaks due of the overlapping of some peaks.

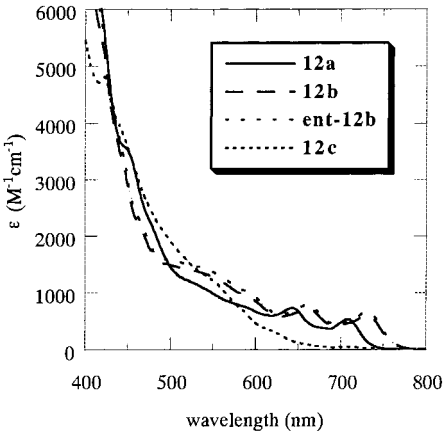


Figure 1. Absorption spectra of **12a**, **12b**, *ent*-**12b**, and **12c** in dichloromethane.

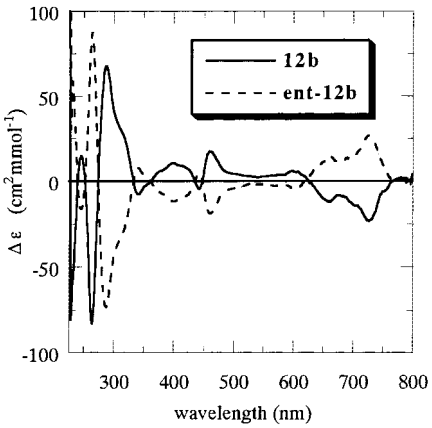


Figure 2. CD spectra of **12b** and *ent*-**12b** in dichloromethane (2×10^{-5} mol dm^{-3}, 1 cm cell).

cis-3 and C_1 symmetrical *e* addition patterns are chiral, one can expect that **12b**, *ent*-**12b**, and **12c** are chiroselectively yielded from **6**, *ent*-**6**, and **7** because of the inherent chirality of saccharide templates, D-**2**, L-**2**, and **3**, respectively. Thus, two pairs of enantiomers **12bA**/**12bB** and **12cA**/**12cB** are available, and one of the two possible enantiomers should be preferentially formed in each reaction of **6**, *ent*-**6**, and **7** (Scheme 4). This chiroselectivity was investigated on the basis of the CD (circular dichroism) spectra and HPLC analysis with a chiral packed column.

As expected, **12b** and *ent*-**12b** were CD-active in dichloromethane, and the spectral shape was symmetrical to each other (Figure 2). The molar circular-dichroic absorptions ($\Delta\epsilon$) of **12b** and *ent*-**12b** are as large as those of chiral *cis*-3 isomers reported previously.[2,3,5] The strong Cotton effects observed in these spectra are mainly due to strong chiroptical contributions from the chiral fullerene chromophore in **12b** and *ent*-**12b** with C_2 symmetry.[21] The optical purities of these compounds were estimated by a HPLC method (CHIRALCEL OD-H) developed by

(20) Three isomers (in-in, out-in, and out-out) in **12a**, **12b**, and *ent*-**12b** are available, in principle, owing to the direction of the $B(OCH_2C(CH_3)_2CH_2O)$ group in the benzene ring. Judging from the size of the template saccharides and the splitting patterns of the ^{1}H and ^{13}C NMR spectra, the out-in and out-out isomers can be excluded. Thus, **12a**, **12b**, and *ent*-**12b** isolated here are the in-in isomer. Also, two isomers (in and out) are available in **12c**. Similarly, **12c** is identified as in isomer. For an explanation of the concept of the in-in, out-in, and out-out isomers and the in and out isomers, see refs 2−7.

Table 2. Results of Chiral HPLC Analysis[a] and Enantiomeric Excess (% ee) of 13a, 13b, *ent*-13b, and 13c

	retention time/min (peak intensity/%)	% ee
13a	29.1 (100)[b]	
13b	39.3 (72.1)	44.2
	51.6 (27.9)	
ent-**13b**	39.3 (27.4)	45.2
	51.6 (72.6)	
13c	29.4 (9.3)[b]	81.4
	72.8 (90.7)[b]	

[a] Conditions: stationary phase, CHIRALCEL OD-H (4.6 × 250 mm); eluent, *n*-hexane/2-propanol (9:1 (v/v)); flow rate, 1.0 mL/min. [b] *n*-Hexane/2-propanol (7:3 (v/v)).

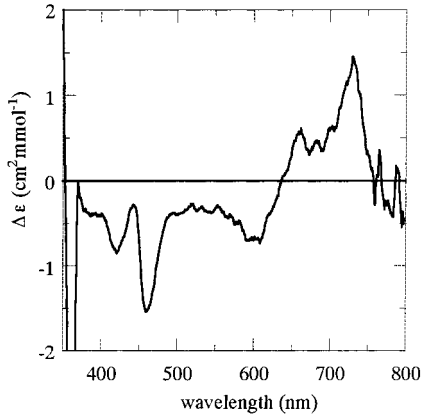


Figure 3. CD spectrum of **12c** in dichloromethane (2×10^{-4} mol dm^{-3}, 1 cm cell).

Nishimura and Okamoto's groups.[7,22] The chromatograms of **13b** and *ent*-**13b** showed the two peaks with different intensity, and the intensity ratio of the two peaks was exchanged in each case of **13b** and *ent*-**13b** (Table 2). On the basis of the results of the chiral HPLC analysis, the enantiomeric excesses of **12b** and *ent*-**12b** were estimated to be 44.2% ee and 45.2% ee, respectively (Table 2).[23] Although **12c** with C_1 symmetry was also CD-active in dichloromethane, the $\Delta\epsilon$ values of **12c** were smaller by 1 or 2 orders of magnitude compared to those of **12b** and *ent*-**12b** with C_2 symmetry (Figure 3). The similar weak Cotton effects in *e* isomer were also reported by Diederich et al.[3] We assign the weak Cotton effects to induced circular dichroism[24] originating from the perturbation of the achiral fullerene chromophore in **12c** by the local asymmetry based on the direction of the $B(OCH_2C(CH_3)_2CH_2O)$ group in the benzene ring. Bisadduct **12c** showed the high enantiomeric excess of 81.4% ee, which was deduced from chiral HPLC analysis of **13c** (Table 2).[23] On the other hand, **12a** with achiral C_s symmetry was CD-silent in dichloromethane, and as expected, **13a** gave a single peak in HPLC analysis with a chiral packed column (Table 2).

(21) (a) Hawkins, J. M.; Meyer, A.; Nambu, M. *J. Am. Chem. Soc.* **1993**, *115*, 9844−9845. (b) Herrmann, A.; Rüttimann, M.; Thilgen, C.; Diederich, F. *Helv. Chim. Acta* **1995**, *78*, 1673−1704.

(22) Okamoto, Y.; Yashima, E. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1020−1043.

(23) Although we attempted the optical resolution of **12b**, *ent*-**12b**, and **12c**, it was not achieved by using any chiral stationary phases.

(24) The Cotton effects due to induced circular dichroism were found in some [60]fullerene derivatives having a chiral substituent. For example: (a) Bianco, A.; Maggini, M.; Scorrano, G.; Toniolo, C.; Marconi, G.; Villani, C.; Prato, M. *J. Am. Chem. Soc.* **1996**, *118*, 4072−4080. (b) Wilson, S. R.; Lu, Q.; Cao, J.; Wu, Y.; Welch, C. J.; Schuster, D. I. *Tetrahedron* **1996**, *52*, 5131−5142.

As a summary of the foregoing findings with the CD spectra and chiral HPLC analyses, it is clear that the double additions between [60]fullerene and **6**, *ent*-**6**, and **7** chiroselectively afforded the optically active **12b**, *ent*-**12b**, and **12c**, respectively. The stereospectrum depends on the inherent chirality of saccharides used as the template molecules. In particular, **6** and *ent*-**6** afforded the opposite enantiomers (**12bA**/**12bB**) preferentially, as deduced from the sign of the Cotton effects in CD spectra (Figure 2) and the peak intensity in chiral HPLC analysis (Table 2).

Concluding Remarks

In this study, we have demonstrated that saccharides are very useful as a versatile template for regio- and chiroselective introduction of two functional groups into [60]fullerene. The addition patterns in the double additions between [60]fullerene and 1:2 saccharide−boronic acid complexes highly reflect the structure of saccharides used as the template molecules. In particular, the inherent chirality of saccharide templates plays a decisive role in the chiroselective double additions leading to chiral [60]fullerene−bisadducts. It is now possible to chiroselectively prepare each enantiomer of chiral [60]fullerene−bisadducts by utilizing either a D-saccharide or a L-saccharide as a template molecule.

In the [60]fullerene−bisadducts obtained here, the arrangement of the two boronic acid groups would be complementary to the angle and the distance of the original saccharide used as the template molecule. When saccharide−boronic acid interaction is utilized, rebinding of the bifunctionalized [60]fullerene with the original saccharide template should occur selectively. This idea would serve to create the concept of "memory storage for the template molecule" as found in the molecular imprinting technique.[25] This implies that the molecular imprinting can be realized even in homogeneous solution using reactive C=C double bonds in the solubilized [60]fullerene surface. We believe that this study is applicable not only to the regio- and chiroselective preparation of various bifunctional [60]fullerene derivatives but also to a new technique for molecular imprinting.

Experimental Section

General Considerations. All melting points are uncorrected. IR spectra were measured as KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$, toluene-d_8, $C_2D_2Cl_4$, or DMSO-d_6 with tetramethylsilane as the internal standard. Mass spectra (negative SIMS) were measured in 2-nitrobenzyl alcohol. UV−vis and CD spectra were measured in dichloromethane. The isomer distribution was determined by HPLC using a COSMOSIL 5PBB column (10 × 250 mm) eluting with *n*-hexane/toluene (3:7 (v/v), 1.0 mL/min). The enantiomeric excess was determined by HPLC using a CHIRALCEL OD-H column (4.6 × 250 mm) eluting with *n*-hexane/2-propanol (7:3−9:1 (v/v), 1.0 mL/min). Column chromatography was carried out on silica gel (Wako C-300). Compound **3** was prepared according to a method described previously.[26] The preparations of **1** and **6** were already reported.[13] D-Threitol (D-**2**), L-threitol (L-**2**), and methyl-α-D-mannopyranoside (**5**) were purchased from SIGMA Co. Ltd. 3-*O*-Methyl-D-glucose (**4**) was purchased from Wako Pure Chemical Industries, Ltd.

L-Threitol-1,3:2,4-bis[-3,4-bis(bromomethyl)phenylboronate] (*ent*-6) (General Procedure). A suspension of **1** (869 mg, 1.0 mmol) and L-**2** (183 mg, 1.5 mmol) in dry toluene (150 mL) was heated at the reflux temperature with azeotropic removal of water (Dean−Stark) for 2 h under a nitrogen atmosphere. After the reaction mixture was cooled to room temperature, it was evaporated in vacuo to dryness. The solid residue was purified by recrystallization from dichloromethane/*n*-hexane to give *ent*-**6** in 72% yield (720 mg, 1.08 mmol) as colorless prisms. The spectral data of *ent*-**6** coincided with those of **6**:[13] mp 176−177 °C (**6**; 176−177 °C).[13]

D-Mannitol-1,2:5,6-bis[3,4-bis(bromomethyl)phenylboronate]-3,4-carbonate (7). According to the same procedure used for the synthesis of *ent*-**6**, **7** was obtained by complexation of **1** (869 mg, 1.0 mmol) with **3**[26] (312 mg, 1.5 mmol) in dry toluene (230 mL) for 3 h in 95% yield (1.07 g, 1.42 mmol): colorless prisms (dichloromethane/*n*-hexane); mp 90−91 °C; IR (KBr) ν_{max} 2973, 2909, 1828, 1798, 1610, 1412 (ν_{BC}), 1356 (ν_{BO}), 1217, 1098, 785, 681 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.32 (dd, J = 6.0, 9.9 Hz, 2H, CH_2), 4.50 (d, J = 10.6 Hz, 2H, CH), 4.62 (ddd, J = 9.9, 10.6, 13.6 Hz, 2H, CH), 4.65, 4.66 (s, each 4H, CH_2Br), 4.77 (dd, J = 6.0, 13.6 Hz, 2H, CH_2), 7.31, 7.60 (d, J = 7.6 Hz, each 2H, ArH), 7.71 (s, 2H, ArH). Anal. Calcd for $C_{23}H_{22}B_2Br_4O_7$: C, 36.75; H, 2.95. Found: C, 37.12; H, 3.14.

3-*O*-Methyl-D-glucofuranose-1,2:5,6-bis[3,4-bis(bromomethyl)phenylboronate] (8). According to the same procedure used for the synthesis of *ent*-**6**, **8** was obtained by complexation of **1** (87 mg, 0.1 mmol) with **4** (29 mg, 0.15 mmol) in dry toluene (30 mL) for 13 h in 76% yield (84 mg, 0.114 mmol): white powder (dichloromethane/*n*-hexane); mp 154−155 °C; IR (KBr) ν_{max} 2980, 2951, 1647, 1437 (ν_{BC}), 1368 (ν_{BO}), 1220, 1080, 679, 608 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.57 (s, 3H, OMe), 3.98 (d, J = 3.2 Hz, 1H, H-3), 4.18 (dd, J = 3.2, 6.1 Hz, 1H, H-4), 4.42 (d, J = 7.2 Hz, 2H, H-6), 4.65 (s, 8H, CH_2Br), 4.87 (dt, J = 6.1, 7.2 Hz, 1H, H-5), 4.93 (d, J = 4.5 Hz, 1H, H-2), 6.25 (d, J = 4.5 Hz, 1H, H-1), 7.36 (d, J = 7.8 Hz, 1H, ArH), 7.39 (d, J = 7.8 Hz, 1H, ArH), 7.71 (dd, J = 1.2, 7.8 Hz, 1H, ArH), 7.74 (dd, J = 1.2, 7.8 Hz, 1H, ArH), 7.77 (d, J = 1.2 Hz, 1H, ArH), 7.81 (d, J = 1.2 Hz, 1H, ArH). Anal. Calcd for $C_{23}H_{24}B_2Br_4O_6$: C, 37.45; H, 3.28. Found: C, 37.81; H, 3.45.

Methyl-α-D-mannopyranoside-2,3:4,6-bis[3,4-bis(bromomethyl)phenylboronate] (9). According to the same procedure used for the synthesis of *ent*-**6**, **9** was obtained by complexation of **1** (869 mg, 1.0 mmol) with **5** (305 mg, 1.5 mmol) in dry toluene (300 mL) for 14 h in 60% yield (660 mg, 0.895 mmol): white powder (dichloromethane/*n*-hexane); mp 190−192 °C; IR (KBr) ν_{max} 2957, 2911, 1611, 1439 (ν_{BC}), 1374 (ν_{BO}), 1331 (ν_{BO}), 1210, 1082, 683, 613 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.57 (s, 3H, OMe), 3.87−3.99 (m, 3H), 4.26−4.34 (m, 1H), 4.58 (d, J = 7.2 Hz, 1H), 4.65−4.75 (m, 1H), 4.67, 4.68, 4.69, 4.71 (s, each 2H, CH_2Br), 5.13 (s, 1H, H-1), 7.37 (d, J = 7.5 Hz, 1H, ArH), 7.42 (d, J = 7.5 Hz, 1H, ArH), 7.78 (dd, J = 1.1, 7.5 Hz, 1H, ArH), 7.80 (dd, J = 1.1, 7.5 Hz, 1H, ArH), 7.84 (d, J = 1.1 Hz, 1H, ArH), 7.89 (d, J = 1.1 Hz, 1H, ArH). Anal. Calcd for $C_{23}H_{24}B_2Br_4O_6$: C, 37.45; H, 3.28. Found: C, 38.09; H, 3.34.

General Procedure for the Reaction between [60]-Fullerene and Saccharide−Bisboronates 6−9. To a solution of [60]fullerene (72 mg, 0.1 mmol), 18-crown-6 (1.06 g, 4.0 mmol), and pottasium iodide (166 mg, 1.0 mmol) in dry toluene (100 mL) was added **6**−**9** (0.1 mmol) under a nitrogen atmosphere, and the mixture was heated at the reflux temperature for 40 h. After the reaction mixture was cooled to room temperature, it was evaporated in vacuo to dryness. The residue was washed with water and dissolved in THF (20 mL). Hydrochloric acid (1.2 mol dm^{-3}, 10 mL) was added to the THF solution at room temperature under an argon atmosphere, and the mixture was stirred for 12 h. The reaction mixture was washed with 1% sodium bisulfite brine solution, washed with brine, dried over anhydrous magnesium sulfate, and evaporated in vacuo to dryness. The residue was washed with methanol to give crude **11** as a brown solid. The crude **11** and 2,2-dimethylpropane-1,3-diol (21 mg, 2.0 mmol) in dry toluene

(25) For comprehensive reviews for the molecular imprinting technique, see: (a) Wulff, G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1812−1832. (b) Kriz, D.; Ramström, O.; Mosbach, K. *Anal. Chem.* **1997**, *69*, 345A-349A.

(26) Hough, L.; Priddle, J. E.; Theobald, R. S. *J. Chem. Soc.* **1962**, 1934−1938.

(20 mL) was heated at the reflux temperature with azeotropic removal of water (Dean−Stark) for 2 h under a nitrogen atmosphere. After the reaction mixture was cooled to room temperature, it was evaporated in vacuo to dryness. The residue was purified by silica gel column chromatography eluting with toluene to give a trace amount of [60]fullerene and monoadduct and eluting with toluene/chloroform (1:1 (v/v)) to give **12** as a regioisomeric mixture.

65,72-Bis(4,4-dimethyl-2,6-dioxa-1-boracyclohexanyl)-1,2:34,35-bis(methano[1,2]benzenomethano)[60]fullerene (12a). In the reaction of **8**, the isolation of main isomer **12a** from the regioisomeric mixture was performed by recrystallization from dichloromethane/*n*-hexane: dark brown solid; mp >450 °C; IR (KBr) ν_{max} 2955, 2930, 2880, 1476, 1422 (ν_{BC}), 1341, 1320 (ν_{BO}), 1293, 1246, 1181, 1123, 668, 527 cm^{-1}; ^{1}H NMR (toluene-d_8, 90 °C) δ 0.71 (s, 12H, Me), 3.50 (s, 8H, CH_2), 4.04 (s, 4H, CH_2), 4.12, 4.19 (d, J = 14.4 Hz, each 2H, CH_2), 7.42, 8.17 (d, J = 7.4 Hz, each 2H, ArH), 8.13 (s, 2H, ArH); MS (negative SIMS, NBA) m/z 1152 (M^-), 1151 [$(M-H)^-$]; UV−vis (dichloromethane) λ_{max} (ϵ) 708 (530), 643 (730), 450 (sh, 3522), 307 (47 739), 264 (92 000), 233 (127 910) nm. Anal. Calcd for $C_{86}H_{34}B_2O_4$: C, 89.60; H, 2.97. Found: C, 89.18; H, 3.08.

65,73-Bis(4,4-dimethyl-2,6-dioxa-1-boracyclohexanyl)-1,2:16,17-bis(methano[1,2]benzenomethano)[60]fullerene (12b). In the reaction of **6**, the isolation of main isomer **12b** from the regioisomeric mixture was performed by HPLC (COSMOSIL 5PBB column) eluting with *n*-hexane/toluene (3:7 (v/v), 0.5 mL/min). An analytical sample of **12b** was obtained as a dark brown solid by recrystallization from dichloromethane/*n*-hexane: mp >450 °C; IR (KBr) ν_{max} 2955, 2926, 2880, 1476, 1422 (ν_{BC}), 1341, 1320 (ν_{BO}), 1293, 1246, 1183, 1123, 664, 525 cm^{-1}; ^{1}H NMR ($C_2D_2Cl_4$, 90 °C) δ 1.04 (s, 12H, Me), 3.79 (s, 8H, CH_2), 3.95, 4.02 (d, J = 13.3 Hz, each 2H, CH_2), 4.23, 4.30 (d, J = 13.8 Hz, each 2H, CH_2), 7.45, 7.87 (d, J = 7.3 Hz, each 2H, ArH), 7.88 (s, 2H, ArH); ^{13}C NMR ($C_2D_2Cl_4$, 90 °C) δ 23.12 (CH_3), 32.90 (C), 43.99, 45.75 (CH_2), 61.93, 65.67 (fullerene-sp^3 C), 73.58 (OCH_2), 128.04 (sp^2 CH), 130.36 (sp^2 C), 134.53, 134.55 (sp^2 CH), 134.69, 136.09, 137.22, 137.41, 139.48, 140.91, 141.92, 142.04, 142.84, 142.92, 143.23, 143.40, 145.94, 145.97, 146.23, 146.30, 146.68, 147.04. 147.20, 147.22, 147.54, 148.57, 148.90, 149.85, 150.18, 150.59, 150.82, 152.47, 154.98 (sp^2 C); MS (negative SIMS, NBA) m/z 1152 (M^-); UV−vis (dichloromethane) λ_{max} (ϵ) 731 (595), 661 (725), 395 (sh, 6500), 261 (98 750), 232 (118 000) nm; CD (dichloromethane) λ_{max} ($\Delta\epsilon$) 726 (−23.48), 658 (−11.25), 608 (5.51), 461 (17.48), 442 (−4.40), 399 (10.67), 341 (−7.70), 287 (67.57), 264 (−83.00), 246 (14.61) nm. Anal. Calcd for $C_{86}H_{34}B_2O_4 \cdot 0.75(C_6H_{14})$: C, 89.28; H, 3.68. Found: C, 88.91; H, 3.49.

65,73-Bis(4,4-dimethyl-2,6-dioxa-1-boracyclohexanyl)-1,2:16,17-bis(methano[1,2]benzenomethano)[60]fullerene (*ent*-12b). According to the same procedure used for the synthesis of **12b**, *ent*-**12b** was isolated and purified. The spectral data of *ent*-**12b** coincided with those of **12b** except those for CD spectra: CD (dichloromethane) λ_{max} ($\Delta\epsilon$) 726 (26.70), 658 (14.45), 608 (−3.76), 461 (−18.90), 442 (4.51), 399 (−11.83), 341 (7.50), 287 (−73.23), 264 (87.07), 246 (−16.35) nm.

64,72-Bis(4,4-dimethyl-2,6-dioxa-1-boracyclohexanyl)-1,2:18,36-bis(methano[1,2]benzenomethano)[60]fullerene (12c). According to the same procedure used for the synthesis of **12b**, **12c** was isolated and purified: reddish brown solid; mp >450 °C; IR (KBr) ν_{max} 2957, 2928, 2880, 1476, 1422 (ν_{BC}), 1341, 1320 (ν_{BO}), 1293, 1246, 1181, 1121, 666, 527 cm^{-1}; ^{1}H NMR ($C_2D_2Cl_4$, 90 °C) δ 1.02, 1.06 (s, each 6H, Me), 3.76, 3.81 (s, each 4H, OCH_2), 3.80−4.31 (m, 8H, CH_2), 7.47 (d, J = 7.4 Hz, 1H, ArH), 7.48 (d, J = 7.4 Hz, 1H, ArH), 7.82, 7.85 (s, each 1H, ArH), 7.89 (d, J = 7.4 Hz, 2H, ArH); ^{13}C NMR ($C_2D_2Cl_4$, 90 °C) δ 22.00, 22.02 (CH_3), 31.78, 31.81 (C), 44.95, 45.04, 45.23, 45.26 (CH_2), 64.43, 64.52, 64.81, 64.92 (fullerene-sp^3 C), 72.46, 72.51 (OCH_2), 126.90, 126.96, 132.98, 133.03, 133.52, 133.58 (sp^2 CH), 134.84, 135.75, 136.37, 136.41, 136.74, 136.77, 137.12, 137.16, 137.50, 137.54, 140.29, 140.54, 140.75, 141.09, 141.64, 141.86, 141.90, 142.46, 142.99, 143.84, 144.53, 144.69, 144.77, 145.01, 145.17, 145.91, 145.93, 146.18, 146.21, 146.26, 146.54, 146.57, 147.10, 147.36, 148.10, 148.14, 148.16, 148.19, 149.15, 150.45, 150.91, 154.66, 154.68, 154.75, 154.78, 155.06, 155.50, 155.62, 155.71, 161.74, 161.75, 163.76 (sp^2 C); MS (negative SIMS, NBA) m/z 1152 (M^-); UV−vis (dichloromethane) λ_{max} (ϵ) 423 (4812), 400 (sh, 5459), 315 (40 351), 232 (119 550) nm; CD (dichloromethane) λ_{max} ($\Delta\epsilon$) 730 (1.45), 667 (0.49), 609 (−0.74), 460 (−1.55), 421 (−0.86) nm. Anal. Calcd for $C_{86}H_{34}B_2O_4 \cdot 0.2(CH_2Cl_2)$: C, 88.50; H, 2.96. Found: C, 88.58; H, 3.11.

65,72-Dihydroxy-1,2:34,35-bis(methano[1,2]benzenomethano)[60]fullerene (13a) (General Procedure). To a solution of **12a** (57 mg, 0.05 mmol) in acetic acid (0.5 mL) and THF (5 mL) was added 30% H_2O_2 (0.5 mL) at 0 °C, and the mixture was stirred for 50 h at room temperature under an argon atmosphere. The reaction mixture was extracted with toluene and washed with 1% ammonium sulfate aqueous solution and water. The organic phase was dried over anhydrous magnesium sulfate and evaporated in vacuo to dryness. The solid residue was purified by silica gel column chromatography eluting with toluene/ethyl acetate (19:1 (v/v)) to give **13a** in 56% yield (27 mg, 0.028 mmol). An analytical sample was obtained as a dark brown solid by recrystallization from dichloromethane/*n*-hexane: mp >450 °C; IR (KBr) ν_{max} 3442 (ν_{OH}), 2923, 1615, 1501, 1456, 1354, 1269, 1217, 1150, 770, 695, 527 cm^{-1}; ^{1}H NMR (DMSO-d_6, 120 °C) δ 4.21 (br s, 4H, CH_2), 4.35, 4.44 (d, J = 13.8 Hz, each 2H, CH_2), 6.86 (dd, J = 2.4, 8.0 Hz, 2H, ArH), 6.94 (d, J = 2.4 Hz, 2H, ArH), 7.42 (d, J = 8.0 Hz, 2H, ArH), 8.96 (s, D_2O-exchange, 2H, OH); ^{13}C NMR (DMSO-d_6, 120 °C) δ 42.65, 42.69 (CH_2), 63.73, 64.39 (fullerene-sp^3 C), 113.83, 114.43 (sp^2 CH), 127.79 (sp^2 C), 127.89 (sp^2 CH), 129.23, 133.67, 134.75, 137.29, 137.55, 138.41, 140.05, 140.09, 140.23, 140.67, 141.14, 141.41, 142.32, 143.49, 143.75, 143.80, 144.50, 145.13, 145.24, 145.30, 146.56, 146.96, 147.19, 147.21, 148.44, 148.55, 150.29, 152.21, 152.33, 154.16, 156.30, 156.50 (sp^2 C); MS (negative SIMS, NBA) m/z 960 (M^-); UV−vis (cyclohexane/2-propanol = 1:1 (v/v)) λ_{max} (ϵ) 709 (756), 643 (921), 450 (sh, 3994), 309 (52 903), 266 (100 000), 227 (139 240) nm. Anal. Calcd for $C_{76}H_{16}O_2 \cdot 1.1(C_6H_{14})$: C, 93.97; H, 3.00. Found: C, 93.58; H, 2.58.

65,73-Dihydroxy-1,2:16,17-bis(methano[1,2]benzenomethano)[60]fullerene (13b). According to the same procedure used for the synthesis of **13a**, **13b**[7] was prepared from **12b**. An analytical sample was obtained as a dark brown solid by silica gel column chromatography eluting with toluene: mp >450 °C; ^{1}H NMR (DMSO-d_6, 120 °C) δ 3.79, 4.00 (d, J = 13.7 Hz, 2H, CH_2), 4.18, 4.28 (d, J = 13.7 Hz, 2H, CH_2), 6.85 (dd, J = 2.3, 8.0 Hz, 2H, ArH), 6.90 (d, J = 2.3 Hz, 2H, ArH), 7.30 (d, J = 8.0 Hz, 2H, ArH), 8.61−9.27 (br s, 2H, OH).

65,73-Dihydroxy-1,2:16,17-bis(methano[1,2]benzenomethano)[60]fullerene (*ent*-13b). According to the same procedure used for the synthesis of **13a**, *ent*-**13b**[7] was prepared from *ent*-**12b**. An analytical sample was obtained as a dark brown solid by silica gel column chromatography eluting with toluene: mp >450 °C.

64,72-Dihydroxy-1,2:18,36-bis(methano[1,2]benzenomethano)[60]fullerene (13c). According to the same procedure used for the synthesis of **13a**, **13c**[7] was prepared from **12c**. An analytical sample was obtained as a reddish brown solid by silica gel column chromatography eluting with toluene/ethyl acetate (19:1 (v/v)): mp >450 °C; ^{1}H NMR (DMSO-d_6, 120 °C) δ 3.81−3.99 (br m, 2H, CH_2), 4.10−4.29 (br m, 6H, CH_2), 6.82, 6.85 (dd, J = 2.4, 8.4 Hz, each 1H, ArH), 6.91, 7.00 (d, J = 2.4 Hz, each 1H, ArH), 7.34, 7.36 (d, J = 8.4 Hz, each 1H, ArH), 8.93, 9.00 (s, each 1H, OH).

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