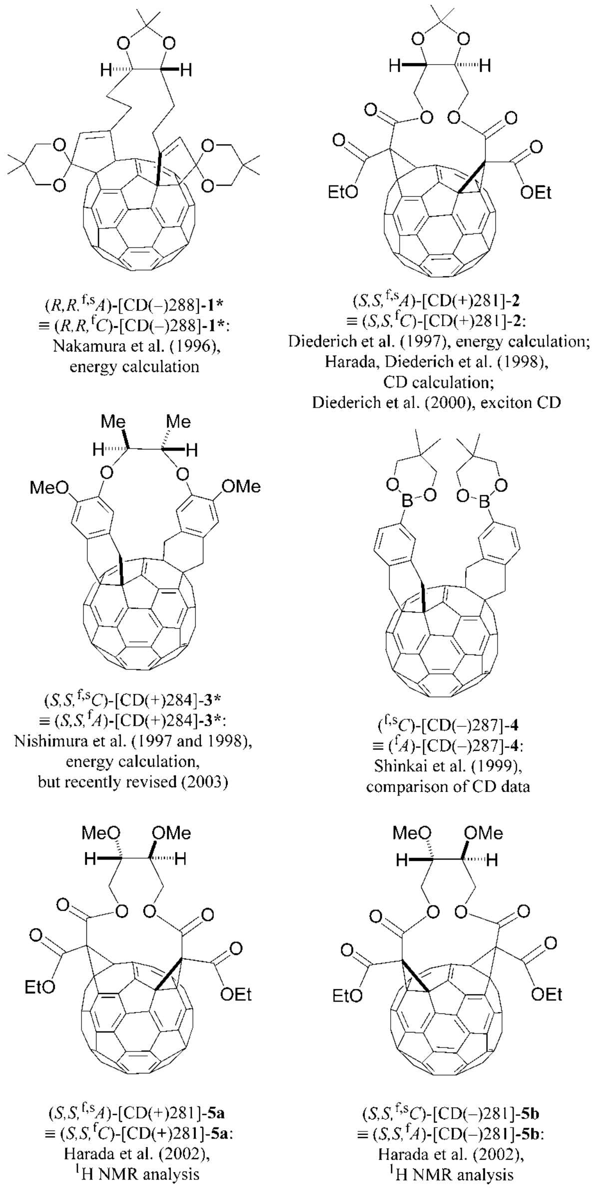
Chiral Fullerene Adducts

Conclusive Determination of the Absolute Configuration of Chiral C_{60}-Fullerene *cis*-3 Bisadducts by X-ray Crystallography and Circular Dichroism**

Shunsuke Kuwahara, Kazuhiro Obata,
Kazuhiro Yoshida, Takatoshi Matsumoto,
Nobuyuki Harada, Nobuhiro Yasuda, Yoshiki Ozawa,*
and Koshiro Toriumi



$(R,R,{}^{\mathrm{f,s}}A)$-[CD(−)288]-**1*** ≡ $(R,R,{}^{\mathrm{f}}C)$-[CD(−)288]-**1***: Nakamura et al. (1996), energy calculation

$(S,S,{}^{\mathrm{f,s}}A)$-[CD(+)281]-**2** ≡ $(S,S,{}^{\mathrm{f}}C)$-[CD(+)281]-**2**: Diederich et al. (1997), energy calculation; Harada, Diederich et al. (1998), CD calculation; Diederich et al. (2000), exciton CD

$(S,S,{}^{\mathrm{f,s}}C)$-[CD(+)284]-**3*** ≡ $(S,S,{}^{\mathrm{f}}A)$-[CD(+)284]-**3***: Nishimura et al. (1997 and 1998), energy calculation, but recently revised (2003)

$({}^{\mathrm{f,s}}C)$-[CD(−)287]-**4** ≡ $({}^{\mathrm{f}}A)$-[CD(−)287]-**4**: Shinkai et al. (1999), comparison of CD data

$(S,S,{}^{\mathrm{f,s}}A)$-[CD(+)281]-**5a** ≡ $(S,S,{}^{\mathrm{f}}C)$-[CD(+)281]-**5a**: Harada et al. (2002), ^{1}H NMR analysis

$(S,S,{}^{\mathrm{f,s}}C)$-[CD(−)281]-**5b** ≡ $(S,S,{}^{\mathrm{f}}A)$-[CD(−)281]-**5b**: Harada et al. (2002), ^{1}H NMR analysis

Scheme 1. Previously reported chiral C_{60}-fullerene *cis*-3 bisadducts together with their CD data and absolute configurations, which are designated by the new systematic nomenclature (${}^{\mathrm{f,s}}C$ and ${}^{\mathrm{f,s}}A$) as well as by the old nomenclature (${}^{\mathrm{f}}C$ and ${}^{\mathrm{f}}A$). The present study suggests that the absolute configuration should be revised in the case of compounds marked with the symbol *.

The fullerene C_{60} is a symmetrical and achiral molecule. However, an addition reaction at two chiral positions of the C_{60} skeleton, for example, a *cis*-3 addition,[1] makes the π-electron system of fullerene chiral in the resulting bisadduct. Synthetic and configurational studies of such chiral fullerene bisadducts have been carried out by many research groups (Scheme 1). For example, Nakamura et al. first synthesized the chiral bisadduct **1** by using a chiral tether and tentatively assigned its absolute configuration as $R,R,{}^{\mathrm{f,s}}A$[1] (≡ $R,R,{}^{\mathrm{f}}C$[1]) on the basis of MM2/Monte Carlo calculations.[2] Diederich and co-workers synthesized the chiral bisadduct **2** as the sole product of a double Bingel reaction. The absolute stereochemistry of [CD(+)281]-**2** was determined to be $S,S,{}^{\mathrm{f,s}}A$ (≡$S,S,{}^{\mathrm{f}}C$), because the results of molecular-mechanics calculations indicated that of the two possible diastereomeric bisadducts, diastereomer $(S,S,{}^{\mathrm{f,s}}A)$-**2** is much more stable than the other diastereomer $(S,S,{}^{\mathrm{f,s}}C)$-**2**.[3] The same absolute configuration was assigned by the theoretical calculation of circular-dichroism (CD) spectra of chiral bisadducts and related compounds based on the π-electron SCF-CI-DV MO method, as reported by the Harada and Diederich groups.[4] Later, Diederich and co-workers applied the CD exciton chirality method to related compounds and confirmed their previous assignment.[5] Nishimura and co-workers synthesized the chiral bisadduct **3** by using a chiral tether prepared from 2,3-butanediol,[6] and tentatively assigned its absolute configuration as shown in Scheme 1 on the basis of the results of molecular-mechanics calculations. Shinkai and co-workers reported the synthesis of the boron-containing chiral bisadduct **4**, the absolute configuration of which was assigned by the comparison of its CD spectrum with that of **2**.[7] As shown in Scheme 1, however, those assignments of absolute configuration disagreed with one another: Compound $({}^{\mathrm{f,s}}A)$-**1** (≡$({}^{\mathrm{f}}C)$-**1**) showed a negative CD Cotton effect at 288 nm, whereas $({}^{\mathrm{f,s}}A)$-**2** (≡ $({}^{\mathrm{f}}C)$-**2**) exhibited a positive Cotton effect at 281 nm. The CD spectra of $({}^{\mathrm{f,s}}A)$-**1** and $({}^{\mathrm{f,s}}A)$-**2** were thus opposite in sign despite their identical chiral π-electron systems in the C_{60} skeleton. The bisadduct $({}^{\mathrm{f,s}}C)$-**3** (≡ $({}^{\mathrm{f}}A)$-**3**) showed a positive Cotton effect at 284 nm, in disagreement with the assignment of $({}^{\mathrm{f,s}}A)$-**2**, which exhibits a positive

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[*] S. Kuwahara, K. Obata, Dr. K. Yoshida, Dr. T. Matsumoto,
Prof. Dr. N. Harada
Institute of Multidisciplinary Research for Advanced Materials
Tohoku University
2-1-1 Katahira, Aoba, Sendai 980-8577 (Japan)
Fax: (+81) 22-217-5667
E-mail: n-harada@tagen.tohoku.ac.jp

Dr. N. Yasuda
SPring-8/Japan Synchrotron Radiation Research Institute (JASRI)
1-1-1 Kouto, Mikazuki-cho, Hyogo 679-5198 (Japan)

Dr. Y. Ozawa, Prof. Dr. K. Toriumi
Graduate School of Material Science
University of Hyogo
3-2-1 Kouto, Kamigori-cho, Hyogo 678-1297 (Japan)

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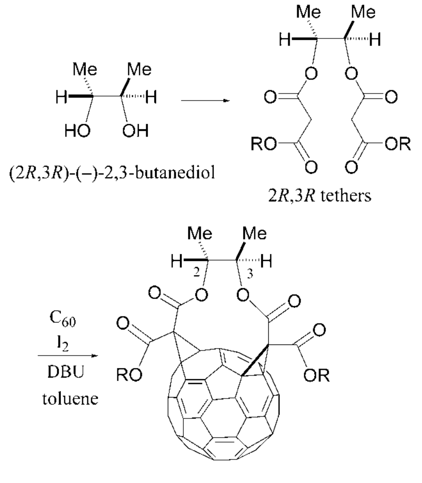
Cotton effect at 281 nm. These results clearly indicated that some configurational assignments were erroneous.

What is the main reason for such disagreement? In most cases of the preparation of *cis*-3 bisadducts by using a chiral tether, only one of two possible diastereomers had been isolated, and its configuration had been assigned based on the assumption that the isolated diastereomer should be more stable than the other diastereomer. To judge which of the diastereomers was more stable, their relative steric energies were calculated by empirical MM (molecular mechanics) methods. Thus, there were two problems of ambiguity in these studies. The first is that the major product isolated is not necessarily the most stable compound if the reaction is kinetically controlled. The second is that the MM method used for the calculation of steric energy is empirical, and therefore the results might not always be correct.

To overcome the drawbacks of previous studies for the assignment of absolute configuration, we employed a different strategy: If a loose and more flexible chiral tether with known absolute configuration was used, two possible diastereomers would be obtained, and therefore it should be relatively straightforward to determine their absolute stereostructures by comparing ^{1}H NMR spectroscopic data for two diastereomers. Thus, the double Bingel reaction of C_{60} with (2*S*,3*S*)-(−)-2,3-dimethoxybutane-1,4-diyl bis(ethyl malonate) yielded the chiral bisadducts [CD(+)281]-**5a** and [CD(−)281]-**5b** as expected; their CD spectra were almost mirror images of one another, thus reflecting the opposite chirality of the π-electron systems in the two C_{60} skeletons (Scheme 1).[8] The analyses of ^{1}H NMR spectroscopic chemical-shift and coupling-constant data led to the absolute-configuration assignments (*S*,*S*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**5a** (≡(*S*,*S*,$^{\mathrm{f}}$*C*)-[CD(+)281]-**5a**) and (*S*,*S*,$^{\mathrm{f,s}}$*C*)-[CD(−)281]-**5b** (≡(*S*,*S*,$^{\mathrm{f}}$*A*)-[CD(−)281]-**5b**), respectively; the results were consistent with those reported by Diederich, and co-workers[3,5] as well as by Harada, Diederich, and co-workers.[4] Although these assignments by ^{1}H NMR spectroscopic analysis were more reliable than the previous assignments, we wanted to confirm our results by X-ray crystallography, the most unambiguous and conclusive method for the determination of absolute configuration. Recently, we succeeded in obtaining single crystals of a chiral C_{60}-fullerene bisadduct of the *cis*-3 type, and we report herein the first X-ray crystallographic determination of its absolute configuration.

It was known that chiral fullerene derivatives hardly ever crystallized as single crystals suitable for X-ray diffraction experiments. To our knowledge, no one had succeeded in determining the absolute configuration of chiral C_{60}-fullerene bisadducts of the *cis*-3 type by X-ray crystallography, and this situation prompted us to take up the challenge of crystallizing derivatives. To obtain single crystals, we prepared the chiral C_{60}-fullerene bisadducts **6**–**12** of the *cis*-3 type from (2*R*,3*R*)-(−)-2,3-butanediol, the absolute configuration of which would be useful as an internal reference for determining the absolute stereostructures of the adducts (Scheme 2). The ethyl ester [CD(+)280]-**6** had been prepared previously by Diederich and co-workers (see Supporting Information).[5,9] Besides the bisadducts **7** and **12** with aliphatic side chains, derivatives **8**–**11** with aromatic side chains were synthesized in the expectation that π–π stacking between neighboring molecules would promote the molecular packing in the crystal lattice.



(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)280]-**6**, R = Et
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**7**, R = Pr
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**8**, R = CH_2Ph
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**9**, R = $CH_2C_6H_4$-4-Br
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**10**, R = $CH_2C_6H_4$-3-Br
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)282]-**11**, R = $CH_2PhC_6H_4$-2-Br
(*R*,*R*,$^{\mathrm{f,s}}$*A*)-[CD(+)281]-**12**, R = $CH_2(CH_2)_4CH_3$

Scheme 2. Synthesis of chiral fullerene *cis*-3 bisadducts by the Bingel reaction.

We attempted the crystallization of these compounds **6**–**12** many times from various solvents and solvent mixtures. However, in all cases but one, amorphous solids were obtained. When the ethyl ester [CD(+)280]-**6** was recrystallized from chloroform/hexane (1:1), extremely thin, red plate crystals were obtained (see Supporting Information). The crystals formed had a thickness of just 1–2 μm, which is too thin for conventional X-ray diffractometers. Therefore, the extremely strong synchrotron X-ray radiation at the SPring-8 in Hyogo (Japan) was required for the X-ray diffraction experiment: X-ray 22.00 keV, $\lambda = 0.5633$ Å, data collected at 100 K, red thin plate, $0.100 \times 0.075 \times 0.002$ mm, monoclinic, space group $P2_1$ (#4), $Z = 2$, $a = 9.9890(11)$, $b = 9.984(2)$, $c = 21.047(5)$ Å, $\beta = 102.193(12)°$, $V = 2051.7(7)$ Å^3, 4375 unique reflections.[11] The structure was solved by direct methods and refined by full-matrix least-squares analysis, whereby all non-hydrogen atoms were refined isotropically, whereas all hydrogen atoms were placed at their idealized positions: $R = 0.180$ for 3110 reflections with $I > 2\sigma(I)$ and 329 parameters (Figure 1). Although the final *R* value remained large, the absolute configuration of the bisadduct [CD(+)280]-**6** was clearly determined as $^{\mathrm{f,s}}$*A* (≡ $^{\mathrm{f}}$*C*) by using the 2*R*,3*R* absolute configuration of the tether moiety as an internal reference.

The molecular packing in the unit lattice is shown in Figure 1. The tether moieties of two molecules are in contact with one another, thus leading to the non-C_2-symmetrical conformation of the two ethyl ester groups on each fullerene. In contrast, the compound has a C_2-symmetric structure in the solution state, as proved by ^{1}H and ^{13}C NMR spectroscopy (see Supporting Information). The X-ray crystallographic

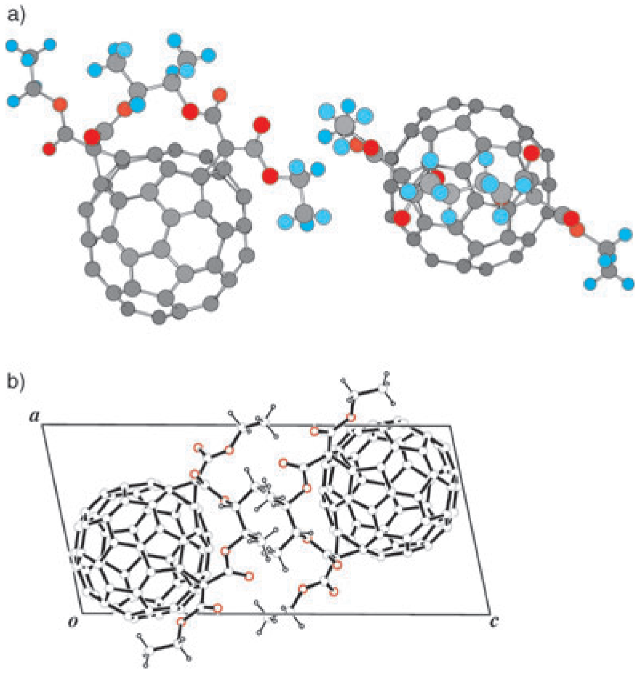


Figure 1. a) Absolute stereostructure of the C_{60}-fullerene bisadduct ($R,R,^{\mathrm{f,s}}A$)-[CD(+)280]-**6**, as determined by X-ray crystallography. b) Projection of the X-ray crystal structure of ($R,R,^{\mathrm{f,s}}A$)-[CD(+)280]-**6** along the *b* axis.

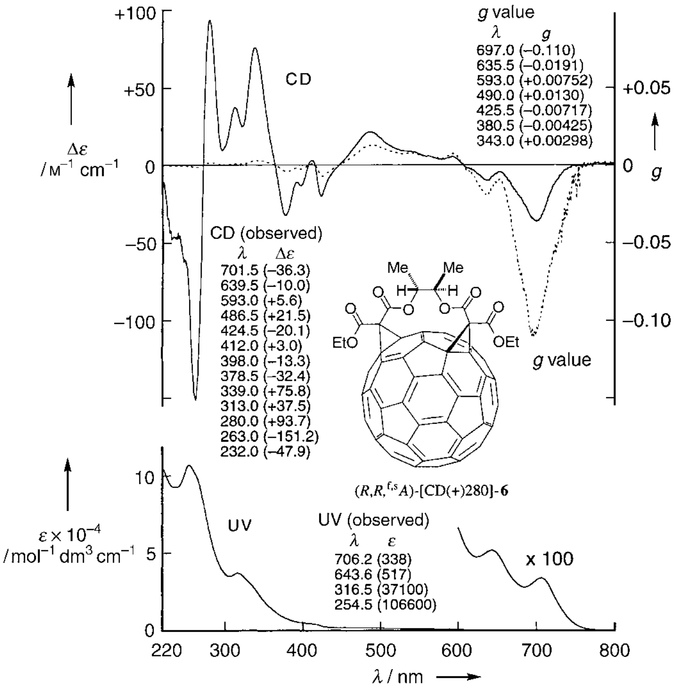


Figure 2. CD and UV spectra and *g*-value curve of the bisadduct ($R,R,^{\mathrm{f,s}}A$)-[CD(+)280]-**6** in $ClCH_2CH_2Cl$: CD and UV, solid lines; *g* value ($g=\Delta\varepsilon/\varepsilon$), dotted line.

analysis revealed that the *c* axis is perpendicular to the main plane of the extremely thin plate crystal. These data explain the reason why compound **6** crystallizes as extremely thin plate crystals: When the compound packs along the *c* axis, two bare spherical regions of the C_{60} skeleton have to come into contact with one another, and no effective interaction suitable for fixing two molecules is expected. Therefore, the crystal hardly grows along the *c* axis at all. On the other hand, when the crystal grows along the *a* and *b* axes, parts of the tether come into contact with one another to favor the molecular packing. This is the mechanism of formation of extremely thin plate crystals.

The bisadduct ($R,R,^{\mathrm{f,s}}A$)-**6** (≡ ($R,R,^{\mathrm{f}}C$)-**6**) exhibits the CD and UV spectra shown in Figure 2. The CD spectrum shows an intense positive Cotton effect ($\Delta\varepsilon=+93.7$) at 280 nm. Therefore, the absolute configuration of the bisadduct was designated as ($R,R,^{\mathrm{f,s}}A$)-[CD(+)280]-**6** (≡ ($R,R,^{\mathrm{f}}C$)-[CD(+)280]-**6**). As the CD spectra of chiral C_{60}-fullerene *cis*-3 bisadducts, including derivatives **1**–**6**, are similar to one another in shape (Table 1), the results obtained in this study clearly indicate that the compounds that exhibit a positive Cotton effect at around 280 nm should have the $^{\mathrm{f,s}}A$ (≡ $^{\mathrm{f}}C$) absolute configuration, whereas the opposite enantiomers with a negative Cotton effect at around 280 nm should have the $^{\mathrm{f,s}}C$ (≡ $^{\mathrm{f}}A$) absolute configuration. Therefore, our previous assignments of ($S,S,^{\mathrm{f,s}}A$)-[CD(+)281]-**5a** and ($S,S,^{\mathrm{f,s}}C$)-[CD(−)281]-**5b** by ^{1}H NMR spectroscopic analysis were corroborated by this study (Table 1). The assignment of ($S,S,^{\mathrm{f,s}}A$)-[CD(+)281]-**2** by Diederich and co-workers was also confirmed. On the other hand, the results of this study suggest that the absolute configuration of the bisadduct [CD(−)288]-**1** should be revised as $R,R,^{\mathrm{f,s}}C$ (Table 1). Similarly, we propose the absolute configuration $S,S,^{\mathrm{f,s}}A$ for [CD(+)284]-**3** (Table 1).

Table 1: CD spectral data and correct absolute configurations of chiral C_{60}-fullerene bisadducts of the *cis*-3 type.

	This study	Ref. [8]	Ref. [2]	Ref. [3]	Ref. [6]	Ref. [7]
compound	**6**	**5a**	**1**	**2**	**3**	**4**
absolute configuration	$R,R,^{\mathrm{f,s}}A$	$S,S,^{\mathrm{f,s}}A$	$R,R,^{\mathrm{f,s}}C$[a]	$S,S,^{\mathrm{f,s}}A$	$S,S,^{\mathrm{f,s}}A$[a]	$^{\mathrm{f,s}}C$
CD $\Delta\varepsilon$	−36.3	−38.9	+4.69[b]	−37.0	−36.3	+26.7
λ_{ext} [nm]	701.5	696.5	720.0	706.0	737.0	726.0
CD $\Delta\varepsilon$	+93.7	+99.3	−75.0[b]	+89.0	+60.6	−73.2
λ_{ext} [nm]	280.0	280.5	288.0	281.0	284.0	287.0

[a] Revised absolute configuration as suggested by this study. [b] Values are 1/1000 of the $\Delta\varepsilon$ values reported in reference [2], which are too large.

We observed unique phenomena in the CD and UV spectra of C_{60}-fullerene bisadducts of the *cis*-3 type. For example, ($R,R,^{\mathrm{f,s}}A$)-[CD(+)280]-**6** exhibits a very weak UV band at 706.2 nm ($\varepsilon=338$), as shown in Figure 2; this band is due to the forbidden π–π* transition as a result of the small ε value. In the corresponding region, the CD spectrum shows an intense negative Cotton effect at 701.5 nm ($\Delta\varepsilon=-36.3$). The curve of the dissymmetry ratio, *g* ($g=\Delta\varepsilon/\varepsilon$), was calculated as illustrated in Figure 2: the maximum value found is $g=-0.110$ at 697.0 nm. This *g* value is much larger than that of the n–π* forbidden transition of chiral ketones and that of the π–π* allowed transition of other compounds with strong CD absorption: n–π*, (*R*)-(+)-3-methylcyclohexanone, $g = +0.03$ at 298 nm;[12] π–π*, (+)-hexahelicene, $g = +0.007$ at 325 nm; π–π*, exciton-coupling CD of (2*S*,3*S*)-butanediyl bis(4-bromobenzoate), $g = +0.00035$ at 252 nm. A similar large *g* value was also observed for the bisadduct (*S*,*S*,$^{f,s}A$)-[CD(+)281]-**5a**: $g = -0.126$ at 696 nm. To our knowledge, these *g* values for chiral C_{60}-fullerene *cis*-3 bisadducts are the largest found for chiral organic compounds. Why does this transition in chiral fullerenes give rise to such a large *g* value? The phenomenon can be interpreted as follows: This π–π* transition is electronically forbidden as described above, but is magnetically allowed, because the molecular orbitals occupied by the π electrons are spherical, as they reflect the shape of the fullerene. Therefore, the transition contains a lot of angular momentum, thus yielding a large magnetic moment and generating an intense CD Cotton effect, with the result that this transition has a very large *g* value.

In conclusion, we have determined the absolute configuration of a chiral C_{60}-fullerene bisadduct of the *cis*-3 type by X-ray crystallography. We could establish the general rule that chiral C_{60}-fullerene bisadducts with a *cis*-3 relationship that show a positive Cotton effect in their CD spectrum at around 280 nm have the $^{f,s}A$ configuration, whereas those that show a negative Cotton effect have the $^{f,s}C$ configuration.

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[9] (*R*,*R*,$^{f,s}A$)-[CD(+)280]-**6**: red thin plates recrystallized from hexane/$CHCl_3$ (1:1); m.p. > 360 °C; $[\alpha]_D^{28} + 3950$ ($c = 0.0214$, $CHCl_3$). The physical data obtained (see Supporting Information) almost agree with those reported by Diederich and coworkers.[5] However, in the case of the ^1H NMR coupling constant between the two equivalent hydrogen atoms at the 2- and 3-positions, our value of $J_{2,3} = 9.1$ Hz, which was obtained by the ^{13}C satellite band method,[8,10] is consistent with the antiperiplanar conformation of 2-H and 3-H observed in the crystalline state (Scheme 2).

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