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# Highly Regioselective Transformation of *out*/*out-equatorial* Bis(formylmethano)[60]fullerenes: Construction of Dissymmetric [60]Fullerene-Centered Triads

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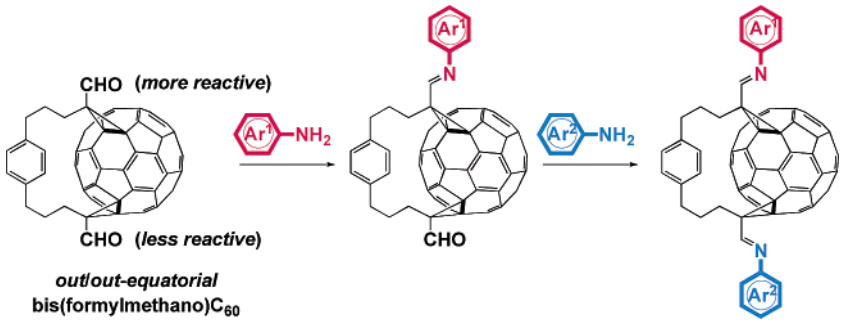


Three kinds of *out*/*out-equatorial* bis(formylmethano)[60]fullerenes (**1b**−**d**) were obtained by the tether-directed bifunctionalization of [60]fullerene with bis(α-formylsulfonium ylide)s. The condensation of aromatic amines with **1b**−**d** proceeded with an unexpectedly high regioselectivity to give one of two possible regioisomers of mono-imines as the main products (the ratio of the regioisomers, up to 97:3). By the transformation of the remaining formyl group in the mono-imines thus obtained, the corresponding dissymmetric bis-imines were efficiently synthesized.

## Introduction

For the construction of novel [60]fullerenes ($C_{60}$)-containing functional materials, bifunctionalized $C_{60}$s have been recognized as one of the most fundamental and useful components.[1] Since the development of an elegant and versatile method for the preparation of regio- and stereo-controlled bifunctionalized $C_{60}$s, the so-called tether-directed bifunctionalization, by Diederich et al., access to these attractive compounds have became easier; $C_{60}$ derivatives with a diversity of addition patterns and functional groups have been able to be efficiently synthesized.[2,3] Furthermore, several successful examples have been reported for the transformation of both addends to other functional groups, which are applicable to the construction of $C_{60}$-based functional molecules with a fascinating structure.[4] To date, however, there has been no report on the selective transformation of only one of two identical addends in bifunctionalized $C_{60}$s; this attempt has been regarded hardly possible, because the two addends are considered to be chemically equivalent and because their transformations might be anticipated to proceed essentially without influence with each other. Thus, the selective mono-transformation of two identical addends in bifunctionalized $C_{60}$s still remains as a challenging and unsettled target, even though the selective mono-transformation would give anisotropic $C_{60}$ derivatives with significant value from the viewpoints of synthetic chemistry and materials chemistry.

To achieve the first selective mono-transformation of two identical addends in bifunctionalized $C_{60}$, we focused on the regio- and stereochemistries of bifunctionalized $C_{60}$s. For a

(1) Kadish, K. M.; Ruo, R. S. *Fullerenes: Chemistry, Physics, and Technology*; Wiley-Interscience: New York, 2000.

(2) (a) Nierengarten, J.-F.; Gramlich, V.; Cardullo, D.-C. F.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2101−2103. (b) Nierengarten, J.-F.; Habicher, T.; Kessinger, R.; Cardullo, F.; Diederich, F.; Gramlich, V.; Gisselbrecht, J. P.; Boudon, C.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 2238−2276.

(3) Diederich, F.; Kessinger, R. *Acc. Chem. Res.* **1999**, *32*, 537−545.

(4) (a) Taki, M.; Takigami, S.; Watanabe, Y.; Nakamura, Y.; Nishimura, J. *Polym. J.* **1997**, *29*, 1020−1022. (b) Kessinger, R.; Thilgen, C.; Mordasini, T.; Diederich, F. *Helv. Chim. Acta* **2000**, *83*, 3069−3096. (c) Hino, T.; Hamada, M.; Kinbara, K.; Saigo, K. *Chem. Lett.* **2002**, 728−729. (d) Nierengarten, J.-F. *New J.* Chem. **2004**, *28*, 1177−1191.

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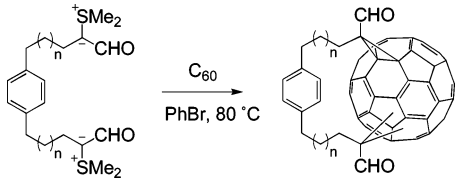
bifunctionalized $C_{60}$ with dissymmetric addends, 22 isomers are theoretically driven on the basis of eight possible addition patterns and three relative orientations of the functional groups (*in*/*in* and *in*/*out* diastereoisomers for the *trans*-1 bisadduct; *in*/*in*, *in*/*out*, and *out*/*out* diastereoisomers for the *trans*-2, *trans*-3, *trans*-4, *cis*-3, *cis*-2, and *cis*-1 bisadducts; *in*/*out* and *out*/*out* diastereoisomers for the *equatorial* bisadduct).[5−7] Only in the case of the *equatorial* addition pattern among the eight addition patterns, two [6,6]-bonds undergoing addition reactions are not equivalent to each other. Therefore, two functional groups in the *in*/*in*- and *in*/*out*-*equatorial* bisadducts should be theoretically unequivalent, and the two addends might show different reactivity toward properly selected reagents, reflecting the subtle but certain structural difference between them. On the other hand, unequivalent circumstance around two addends in a bifunctionalized $C_{60}$ is able to arise from another reason; in the cases of the *in*/*out* isomers of the *trans*-2, *trans*-3, *trans*-4, *cis*-3, *cis*-2, and *cis*-1 bisadducts, two addends are also unequivalent because of their relative orientation.[7] Although all of the eight isomers are candidates for substrates in the present study on the selective mono-transformation of bifunctionalized $C_{60}$s, the *in*/*out* isomers are generally obtained in very poor yields by a tandem bifunctionalization[7] and are hardly prepared by a tether-directed bifunctionalization.[6] Considering these aspects, an *out*/*out*-*equatorial* bisadduct is a sole bisadduct, which satisfies criteria; its synthetic accessibility and the unequivalence of two addends at the same time.

In this study, we first succeeded in the mono-transformation of two identical addends in a bifunctionalized $C_{60}$ with an excellent regioselectivity by using an *out*/*out*-*equatorial* bis(formylmethano)$C_{60}$, which was obtained by a tether-directed method. In addition, by transforming the two functional groups stepwise, a set of $C_{60}$-centered triads with a dissymmetric structure were efficiently synthesized.

## Results and Discussion

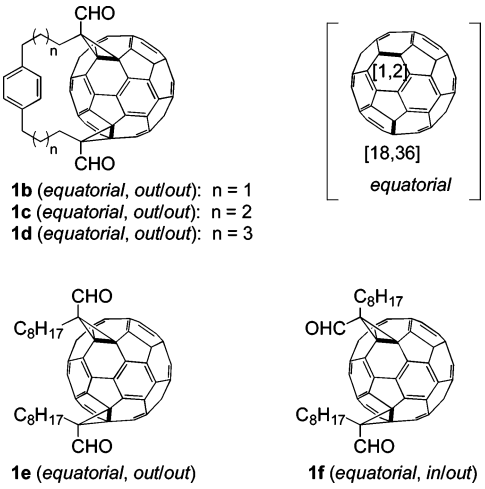
**Design and Synthesis of the *out*/*out*-*equatorial* Bis(formylmethano)$C_{60}$s 1b−d.** Among *out*/*out*-*equatorial* bisadducts possessing transformable functional groups, we selected *out*/*out*-*equatorial* bis(formylmethano)$C_{60}$s (**1**) as the substrates in this study on the basis of the following findings: (i) The formyl groups could be introduced to a $C_{60}$ core without any protecting groups and yet possessed sufficient reactivity to be transformed into various functional groups, such as acetals, imines, alkenes, alcohols, etc. For example, we have reported that the condensation of a formyl group on the methano-bridge carbon of methano$C_{60}$s with aromatic amines proceeded efficiently under mild conditions to give the corresponding imines.[7,8] (ii) A synthetic method for the preparation of bis(formylmethano)$C_{60}$s by using tethered bis(α-formylsulfonium ylide)s has already been established by our group, in which the proper choice of the tether moiety connecting the two sulfonium ylide moieties led to the efficient formation of the *out*/*out*-*equatorial* bisadducts.[9]

**TABLE 1. Synthesis of Bis(formylmethano)[60]fullerenes**




| entry | ylide | n | *cis*-2 | *cis*-3 | *equatorial* | *trans*-4 |
|---|---|---|---|---|---|---|
| 1 | **2a** | 0 | trace | 17% | n.d.[a] | n.d.[a] |
| 2 | **2b** | 1 | n.d.[a] | 9% | 30% | trace |
| 3 | **2c** | 2 | n.d.[a] | 9% | 23% | trace |
| 4 | **2d** | 3 | n.d.[a] | 6% | 22% | 3% |

[a] Not detected.




According to the method we have developed,[9] a series of bis(α-formylsulfonium ylide)s (**2a**−**d**) were prepared, of which the linkers connecting the aromatic core and the sulfonium ylide moieties were ethane-1,2-diyl, propane-1,3-diyl, butane-1,4-diyl, and pentane-1,5-diyl groups, respectively.[10] By using **2a**−**d** for the biscyclopropanation reaction of $C_{60}$, the corresponding bis(formylmethano)$C_{60}$s were obtained as mixtures of two or three regioisomers. All of the isomers were successfully isolated by preparative TLC, and their structural assignment was carried out on the basis of $^1$H and $^{13}$C NMR and UV−vis spectroscopy (Table 1). Although the reaction of **2a** did not give the *out*/*out*-*equatorial* bisadduct **1a** at all (entry 1), the other *out*/*out*-*equatorial* bisadducts **1b**−**d** were obtained as the main products, respectively (entries 2−4).[10] This observation indicates that the tether moiety in **1b** was minimum in length as the tether to connect the two methano-bridge carbons of an *equatorial* bisadduct. This assumption is further supported by the notable signal broadening of the $^1$H NMR spectrum of **1b**: in the

(5) (a) Hirsh, A.; Lamparth, I.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 437−438. (b) Schick, G.; Hirsh, A.; Mauser, H.; Clark, T. *Chem. Eur. J.* **1996**, *2*, 935−943. (c) Lu, Q.; Schuster, D. I.; Wilson, S. R. *J. Org. Chem.* **1996**, *61*, 4764−4768. (d) Nakamura, Y.; O-kawa, K.; Matsumoto, M.; Nishimura, J. *Tetrahedron* **2000**, *56*, 5429−5434. (e) Nakamura, Y.; Takano, N.; Nishimura, T.; Yashima, E.; Sato, M.; Kudo, T.; Nishimura, J. *Org. Lett.* **2001**, *3*, 1193−1196.

(6) For selected examples of the formation of *in*/*out* $C_{60}$ bisadducts by the tether-directed method, see: (a) Taki, M.; Sugita, S.; Nakamura, Y.; Kasashima, E.; Yashima, E.; Okamoto, Y.; Nishimura, J. *J. Am. Chem. Soc.* **1997**, *119*, 926−932. (b) Reference 2a. (c) Nakamura, Y.; O-kawa, K.; Nishimura, J. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 865. (d) Nakamura Y.; Suzuki, M.; Imai, Y.; Nishimura, J. *Org. Lett.* **2004**, *6*, 2797−2799. (e) Sergeyev, S.; Schar, M.; Seiler, P.; Lukoyanova, O.; Echegoyen, L.; Diederich, F. *Chem. Eur. J.* **2005**, *11*, 2284−2294.

(7) Ito, H.; Ishida, Y.; Saigo, K. *Tetrahedron Lett.* **2005**, *46*, 8757−8760.

(8) Hamada, M.; Hino, T.; Kinbara, K.; Saigo, K. *Tetrahedron Lett.* **2001**, *42*, 5069−5071.

(9) Ito, H.; Ishida, Y.; Saigo, K. *Tetrahedron Lett.* **2006**, *47*, 3095−3098.

(10) See Supporting Information.

spectrum of **1d** with relatively long linkers, only a set of sharp peaks were observed for all of the protons, whereas signals in the spectrum of **1c** were observed as partially broadened peaks. On the other hand, **1b** with the shortest linkers gave a spectrum with significantly broadened peaks, most likely due to the constrained structure of the tether part, of which the mobility was considered to be comparable to the $^1$H NMR time scale.

**Assignment of $^{13}$C NMR Signals of Formyl Groups in *out*/*out-equatorial* Bis(formylmethano)C$_{60}$s 1b−d.** As a probe to detect the transformation of the formyl groups in the *out*/*out-equatorial* bis(formylmethano)C$_{60}$s **1b**−**d**, we focused on the $^{13}$C NMR signals of the methano-bridge carbons. In the $^{13}$C NMR spectra, *equatorial* biscyclopropanated C$_{60}$s usually give two signals around 50 ppm assignable to two methano-bridge carbons embedded in the [6,6]-junctions at the [1,2] and [18,36] positions,[11] which are suitable for monitoring the conversion of the formyl groups. Unfortunately, however, analytical methods for the assignment of these two signals have been despairingly limited to date. As far as we know, only $^{13}$C NMR 2D INADEQUATE is a practical method, which still has some problems in convenience and generality.[12]

On the other hand, we have reported the synthesis and characterization of the *out*/*out* and *in*/*out* isomers of an *equatorial* bis(formylmethano)C$_{60}$ having no tether moiety (**1e** and **1f**, respectively), which were prepared by a tandem C$_{60}$ bifunctionalization, followed by chromatographic separation.[7] The diastereoisomers **1e** and **1f** might be useful as references for the NMR signal assignment of the addends at the [1,2] and [18,36] positions.

In the case of the *in*/*out-equatorial* isomer **1f**, the formyl group on the [18,36] methano-bridge carbon taking an *out*-orientation ([18,36]-CHO) should be more reactive than that of the other formyl group on the [1,2] methano-bridge carbon taking an *in*-orientation ([1,2]-CHO), upon comparing the steric congestion around these two formyl groups. When the condensation of the formyl groups in **1f** with an equimolar amount of aniline was conducted, the carbon signal of the methano-bridge carbon at a higher magnetic field decreased preferentially. It means that the more reactive formyl group locates on the [18,36] methano-bridge carbon in the case of **1f** and that the methano-bridge carbon appears at a higher magnetic field. Moreover, our preliminary study revealed that the chemical shifts of the $^{13}$C signals of the addends in bifunctionalized C$_{60}$s are little affected by their orientation (*in* or *out*) but are determined by their positions. With these facts in mind, we attempted the assignment of the $^{13}$C NMR signals of the methano-bridge carbons in **1b**−**d**. All of the *equatorial* bisadducts **1b**−**f** showed two signals at around 52 and 50 ppm. On the basis of the universal relationship between the position of an addend and its chemical shift mentioned above, the signals observed at around 52 and 50 ppm were assigned to the [1,2] and [18,36] methano-bridge carbons, respectively (Table 2).

**TABLE 2. Assignment of $^{13}$C NMR Signals Attributable to the Methano-bridge Carbons in the *equatorial* Bis(formylmethano)[60]fullerenes 1b−f**

| | $\delta$/ppm (orientation) | |
|---|---|---|
| | [1,2] | [18,36] |
| **1b** (*equatorial*, *out*/*out*) | 52.66 (*out*) | 50.38 (*out*) |
| **1c** (*equatorial*, *out*/*out*) | 52.10 (*out*) | 49.78 (*out*) |
| **1d** (*equatorial*, *out*/*out*) | 52.30 (*out*) | 50.13 (*out*) |
| **1e** (*equatorial*, *out*/*out*) | 52.29 (*out*) | 49.78 (*out*) |
| **1f** (*equatorial*, *in*/*out*) | 52.95 (*in*) | 49.97 (*out*) |

**Regioselective Condensation of the *out*/*out-equatorial* Bis(formylmethano)C$_{60}$s *equatorial*-1b−d with Aniline.** Three kinds of *out*/*out-equatorial* bis(formylmethano)C$_{60}$s (**1b**−**d**) with a well-defined structure were successfully prepared. Then, we attempted the selective transformation of one of the two formyl groups. Among various reactions in which formyl groups can participate, we selected the imine formation with an aromatic amine promoted by a TiCl$_4$/1,4-diazabicyclo[2,2,2]octane (DABCO) system, owing to its mild reaction conditions, high efficiency, and irreversibility.[13]

Quite interestingly, the mono-imination of **1b** proceeded efficiently with an unexpectedly high regioselectivity. For example, when the condensation of **1b** with aniline (1.0 equiv) was conducted in $CH_2Cl_2$ in the presence of TiCl$_4$ (25 equiv)/DABCO (234 equiv) and the resultant mixture was subjected to GPC separation, a mixture of the mono-imines **3b**($R^1$ = Phe) and **3b′**($R^2$ = Phe), the bis-imine **4b**($R^1$, $R^2$ = Phe), and unreacted **1b** were obtained in 73%, 15%, and 12% yields, respectively. The $^1$H and $^{13}$C NMR analyses of the mixture of mono-imines **3b**($R^1$ = Phe) and **3b′**($R^2$ = Phe) revealed that one of the two regioisomers was predominantly generated with a surprisingly high selectivity (major:minor = 95:5). Moreover, the peak integral of the $^{13}$C NMR signal at around 52 ppm was obviously small compared with the signal at around 50 ppm. On the basis of these observations, we could unequivocally conclude that the [1,2]-CHO group was selectively converted to an imino group (Table 3, entry 1). From the ratio of the products, the rate constant ratio was calculated to be $k_{[1,2]}$:$k_{[18,36]}$ = 9:1. Worth noting is the fact that the isolated yield of the mono-iminated species (73%) was much higher than the theoretical yield of 50%, calculated on the assumption that the two formyl groups have an identical reactivity. The high yield of the mono-imines thus observed is in good agreement with the finding that the reaction of the [1,2]-CHO was nine times faster than that of the [18,36]-CHO, and clearly shows the advantage of this reaction for a practical application. The highly regioselective reaction thus we found was most likely kinetically controlled, because under the conditions we adopted, the condensation of a primary amine with an aldehyde generally proceeds in an irreversible manner.[13b,14]

In the mono-imination of bis(formylmethano)C$_{60}$s with longer tether moiety, **1c** and **1d**, regioselective reactions again occurred. The $^{13}$C NMR monitorings revealed the preferential consumption of the [1,2]-CHO to the [18,36]-CHO in both cases. Compared with the reaction of **1b**, these two reactions resulted in a lower selectivity (Table 3, entries 2 and 3, **3c**($R^1$ = Phe):**3c′**($R^2$ = Phe) = 60:40, **3d**($R^1$ = Phe):**3d′**($R^2$ = Phe) = 62:38). In addition, the isolated yields of the mono-iminated compounds were notably lower than that of the reaction of **1b** (34% and 39% yields, respectively). Such decrease in chemical

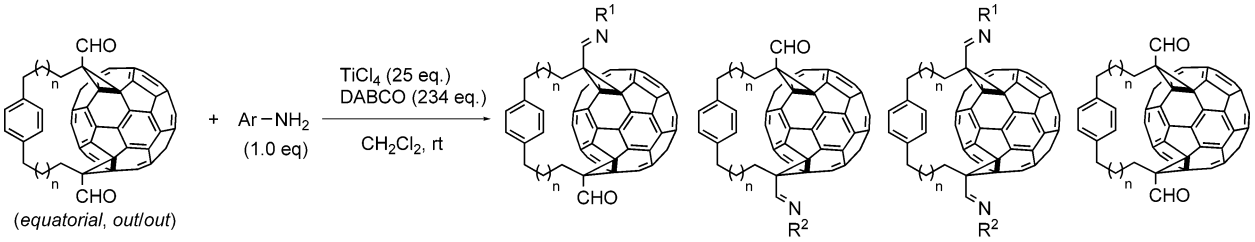
(11) For the numbering system of the carbon atoms in C$_{60}$, see: Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1993**, 813−824.

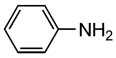
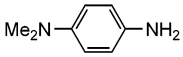
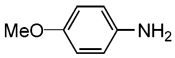
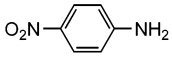
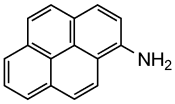
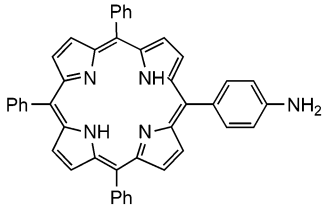
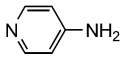
(12) Ball, G. E.; Burley, G. A.; Chaker, L.; Hawkins, B. C.; Williams, J. R.; Keller, P. A.; Pyne, S. G. *J. Org.* Chem. **2005**, *70*, 8572−8574.

(13) Higuchi, M.; Kimoto, A.; Shiki, S.; Yamamoto, K. *J. Org. Chem.* **2000**, *65*, 5680−5684. (b) Higuchi, M.; Shiki, S.; Yamamoto, K. *Org. Lett.* **2000**, *2*, 3079−3082.

(14) Inconsistent with general cases using TiCl$_4$/DABCO, an irreversible nature of the imination reaction was proved in our system, by using other substrates; in the transformation of the remaining formyl group of **3b** with an aromatic amine other than that used for the first imination, the products due to the scrambling of the amino groups were not observed.

**TABLE 3. Regioselective Mono-imination of the *out*/*out-equatorial* Bis(formylmethano)[60]fullerenes 1b−d with Aromatic Amines**




| entry | aromatic amine | (Ar–$NH_2$) | bis(formylmethano)$C_{60}$ | isolated yield /% | | | |
|---|---|---|---|---|---|---|---|
| | | | | **3** + **3'** | (**3**:**3'**)[a] | **4** | **1**$_{recoverd}$ |
| 1 |  | (Phe–$NH_2$) | **1b** | 73 | (95:5) | 15 | 12 |
| 2 | | | **1c** | 34 | (60:40) | 14 | 18 |
| 3 | | | **1d** | 39 | (62:38) | 20 | 23 |
| 4 |  | (*p*-DAPhe–$NH_2$) | **1b** | 59 | (93:7) | 16 | 29 |
| 5 |  | (*p*-MPhe–$NH_2$) | **1b** | 55 | (95:5) | 24 | 0 |
| 6 |  | (*p*-NPhe–$NH_2$) | **1b** | 55 | (96:4) | 23 | 15 |
| 7 |  | (1-Pyr–$NH_2$) | **1b** | 59 | (95:5) | 16 | 20 |
| 8 |  | (TPP–$NH_2$) | **1b** | 73 | (97:3) | 14 | 12 |
| 9 |  | (Pyd–$NH_2$) | **1b** | 44 | (89:11) | 4 | 31 |

[a] Total yield of a mixture of the regioisomers **3** and **3′**. Ratio of the regioisomers was determined by $^1$H NMR.

yield is reasonably elucidated by the difference in regioselectivity rather than by the difference in efficiency between the reactions; in the case of a reaction with a low selectivity, the formation of the undesired bis-imine **4b**−**d**($R^1$, $R^2$ = Phe) is inevitable, which significantly reduces the yields of mono-imines. In fact, the conversion of aniline was not so different between the three reactions, which could be roughly estimated by the equation $\text{conversion}_{\text{aniline}} = \text{yield}_{\text{mono-imine}} + 2(\text{yield}_{\text{bis-imine}})$.

Thus, the highly regioselective mono-transformation of a bifunctionalized $C_{60}$ was accomplished by using **1b**. As far as we know, the reaction demonstrated here is the first example of a synthetic method to easily access regio- and diastereoregulated bifunctionalized $C_{60}$s having different functional groups.

As the origin of the difference in reactivity between two formyl groups, which are apparently equivalent to each other, the following two factors might be possible: the difference in electronic state and that in steric hindrance. To clarify the reason, a control experiment was conducted by using an analogous *out*/*out-equatorial* bisadduct (**1e**) lacking a tether moiety. In the mono-imination of **1e**, almost the same amounts of the mono-imines **3e**($R^1$ = Phe) and **3e′**($R^2$ = Phe) were generated. Therefore, the main reason of the moderate to excellent regioselectivity, observed in the reactions of **1b**−**d**, is concluded to be the difference in steric congestion arising from the relative orientation of the tether moiety and the two formyl groups, rather than the difference in inherent reactivity.

To obtain more detailed information about the contribution of the tether part to the regioselective transformation, the molecular modeling of **1b** was carried out. A PM3 calculation showed that the [1,2]-CHO in **1b** is oriented to the direction opposite to the tether part (Figure 1a, top view), whereas the [18,36]-CHO is located in a sterically hindered environment surrounded by the propane-1,3-diyl chain and the phenylene core, which would disturb the nucleophilic attack of an amine (Figure 1a, side view). Such a characteristic structure around the [18,36]-CHO was most likely due to the highly constrained conformation of the tether part of **1b**. On the other hand, the molecular modelings of **1c** and **1d** revealed that such sterically congested conformations around the [18,36]-CHO were again unavoidable (Figure 1b and c, side view). However, owing to

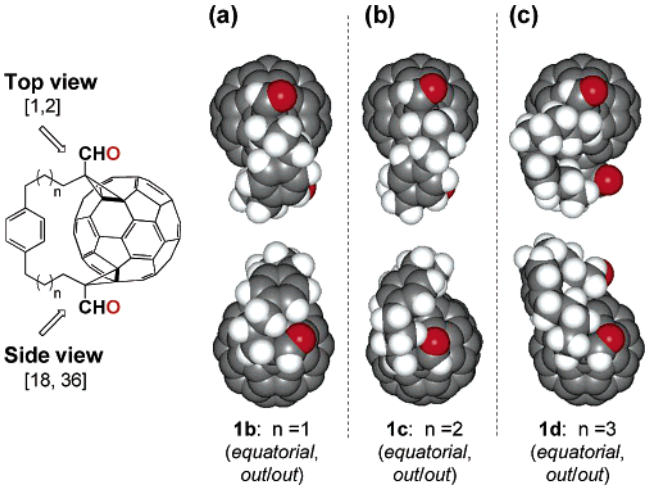



**FIGURE 1.** PM3-optimized structures of the *out*/*out-equatorial* bis-(formylmethano)$C_{60}$s: (a) **1b**, (b) **1c**, and (c) **1d**.

the relatively long oligomethylene chains, the degree of "shielding" for the [18,36]-CHO would be reduced, compared with that of **1b**.

**Regioselective Condensation of *out*/*out-equatorial* Bis-(formylmethano)$C_{60}$ 1b with Various Aromatic Amines.** To clarify the scope of the present regioselective mono-imination, various aromatic amines were employed for the condensation with **1b**. The reactions of **1b** with the aniline derivatives (Table 3, entries 4−6), possessing an electron-donating (*p*-DAPhe-$NH_2$ and *p*-MPhe-$NH_2$) or -withdrawing (*p*-NPhe-$NH_2$) substituent at the 4-position, proceeded very smoothly to give the corresponding mono-imines in good yields (55−59%) with an excellent regioselectivity (**3b**:**3b′** = 93:7−96:4). The results suggested that the introduction of an electron-withdrawing group brought a favorable effect on the regioselectivity, whereas an electron-donating group had an opposite effect; this tendency is in good agreement with the relative nucleophilicity of these aniline derivatives. In addition, 1-pyrenamine (1-Pyn-$NH_2$), which possesses a highly expanded $\pi$-conjugation system, was found to be applicable to this reaction to give a mixture of the corresponding mono-imines in satisfactory yield with a sufficient regioselectivity (entry 7). Interestingly, the condensation of **1b** with 4-(10,15,20-triphenylporphyrin-5-yl)phenylamine (TPP-$NH_2$) gave the corresponding mono-imine in the highest yield with the best regioselectivity among the reactions examined (entry 8). Considering the peculiar properties of the porphyrin and $C_{60}$ units, the cooperation of these units,[15] and the potential of further derivertization of the remaining formyl group, the resultant mono-imine is expected to be an attractive component for the construction of $C_{60}$-containing dye arrays.[16] Moreover, the condensation with the heteroaromatic amine, 4-pyridinamine (4-Pyd-$NH_2$), could also be conducted, although the yield and regioselectivity were lowered to some extent compared with those of the other amines (entry 9). Thus, the regioselective imination was found to be generally applicable to various aromatic amines to afford dissymmetrically bifunctionalized $C_{60}$ derivatives efficiently. In all cases of the iminations, in which various aromatic amines were employed, two regioisomers of the mono-imines **3b** and **3b′** had quite similar polarity, so that we could not separate them by chromatography. However, the major isomers **3b** were adequately enriched in all cases (**3b**:**3b′** = 89:11−97:3), which enabled us to assign the NMR signals of the major isomers (see Experimental Section).

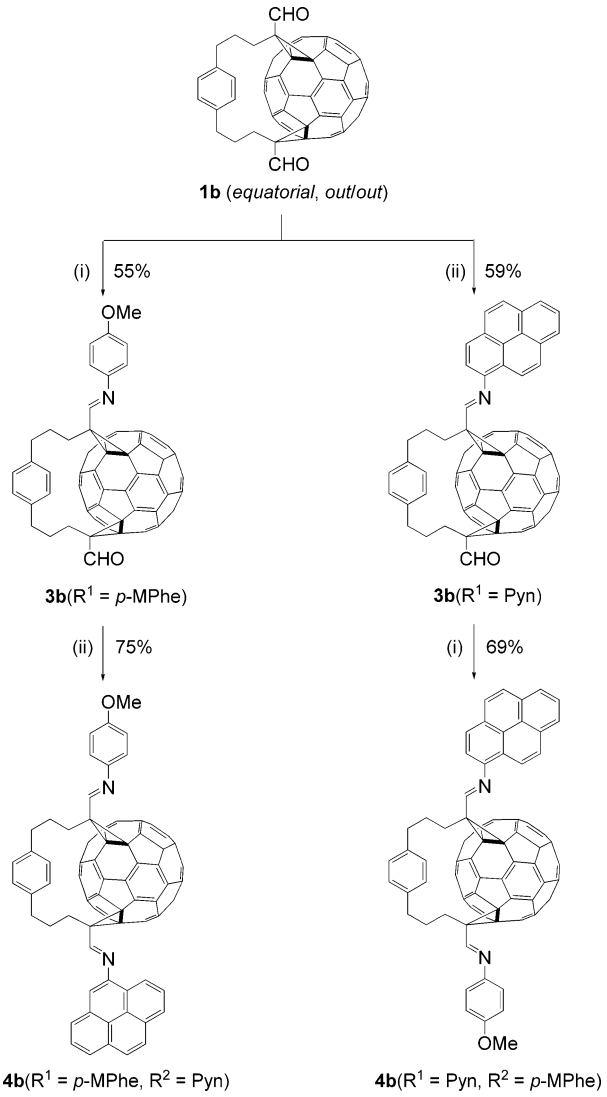
**Construction of $C_{60}$-Centered Dissymmetric Dye Triads.** The success in the mono-transformation of two addends in bis-(formylmethano)$C_{60}$s prompted us to apply the reaction to the construction of dissymmetric triads containing a $C_{60}$ core at the center by the transformation of the remaining formyl group in order to demonstrate an example for the full utility of the regiocontrolled mono-imination. Although formyl groups are potentially converted into various functional groups, we selected a dissymmetric bis-imination; two different amines were used for the first and second iminations. When 4-methoxyaniline and 1-pyrenamine are used as the amino parts for the bis-imination of **1b**, a pair of triads, **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe), are possible, taking into account the dissymmetric structure of **1b**. By repetitively conducting two mono-iminations in a proper order, either of the two triads should be prepared. For example, the condensation of the mono-imine **3b**($R^1$ = *p*-MPhe), prepared by the reaction of 4-methoxyaniline with **1b** as described above, with 1-pyrenamine under conditions similar to those of the mono-imination of **1b**, followed by GPC separation, gave a fraction containing compound(s) with a *m*/*z* value of 1267.27, which is consistent with the value expected for the dissymmetric bis-imines **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) (69%). The solid mass obtained upon concentrating the fraction exhibited a quite simple $^1$H NMR spectrum with one set of signals, indicating that the solid mass consisted of one species. Because the products due to the scrambling of the amino groups, such as **4b**($R^1$, $R^2$ = *p*-MPhe) and **4b**($R^1$, $R^2$ = 1-Pyn), were hardly detectable through the reaction, the main product was undoubtedly concluded to be the target bis-imine **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) (Scheme 1, left).[17] This observation strongly support the mechanism that this imination reaction is an irreversible process, which is one of the main reasons for the regioselectivity observed in the mono-imination of **1b**.[13b] By conducting two mono-iminations in a reverse order, the other triad **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) was successfully prepared; the condensation of **1b** with with 1-pyrenamine selectively afforded the mono-imine **3b**($R^1$ = 1-Pyn) (59% yield), which was easily converted to the dissymmetric bis-imine **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) (75%) by a similar procedure (Scheme 1, right).[17] Worth noting is the surprisingly high total yields for the synthesis of the two triads, despite their dissymmetric structure.

(15) For selected examples of $C_{60}$−porphyrin hybrids, see: (a) Imahori, H.; Hagiwara, K.; Aoki, M.; Akiyama, T.; Taniguchi, S.; Okada, T.; Shirakawa, M.; Sakata, Y. *J. Am. Chem. Soc.* **1996**, *118*, 11771−11782. (b) Dietel, E.; Hirsch, A.; Eichhorn, E.; Rieker, A.; Hackbarth, S.; Roder, B. *Chem. Commun.* **1998**, 1981−1982. (c) Tashiro, K.; Aida, T.; Zheng, J. Y.; Kinbara, K.; Saigo, K.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1999**, *121*, 9477−9478.

(16) Luo, C.; Guldi, D. M.; Imahori, H.; Tamaki, K.; Sakata, K. *J. Am. Chem. Soc.* **2000**, *122*, 6535−6551. Imahori, H.; Guldi, D. M.; Tamaki, K.; Yoshida, Y.; Luo, C. P.; Sakata, Y.; Fukuzumi, S. *J. Am. Chem.* Soc. **2001**, *123*, 6617−6628. Herranz, M. A.; Illescas, B.; Martin, N.; Luo, C. P.; Guldi, D. M. *J. Org.* Chem. **2000**, *65*, 5728−5738.

(17) For the synthesis of dissymmetric bis-imines **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe), mixtures of regioisomers **3b** and **3b′** (**3b**($R^1$ = *p*-MPhe):**3b′**($R^2$ = *p*-MPhe) = 95:5 for **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn), and **3b**($R^1$ = 1-Pyr):**3b′**($R^2$ = 1-Pyr) = 95:5 for **4b**($R^1$ = 1-Pyn. $R^2$ = *p*-MPhe)) as the starting materials. As a result, the resultant bis-imines were also the mixture of regioisomers. Fortunately, the two regioisomers **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) could by separated from each other by HPLC. See Experimental Section.

**SCHEME 1. Synthesis of [60]Fullerene-Centered Dissymmetric Triads 4b($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and 4b($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe)**[a]




[a] Reagents and conditions: (1) $TiCl_4$ (25 equiv), DABCO (234 equiv), 4-methoxyaniline (1.0 equiv), $CHCl_2$, rt. (ii) $TiCl_4$ (25 equiv), DABCO (234 equiv), 1-pyrenamine (1.0 equiv), $CH_2Cl_2$, rt.

Quite interestingly, in HPLC analyses, the elution times of two triads thus obtained were significantly different (column, Merck LiChroCART Si60; eluent, toluene; retention time for **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn), 9.7 min; retention time for **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe), 10.7 min). Furthermore, the two triads exhibited UV−vis spectra distinguishable from each other (Figure 2). These observations imply the difference in physical properties between **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe).

## Conclusion

We first demonstrated the selective transformation of one of two addends in bifunctionalized $C_{60}$s by using three kinds of *out*/*out*-*equatorial* bis(formylmethano)$C_{60}$s (**1b**−**d**). The condensation of the formyl groups in **1b** with aniline proceeded predominantly at the [1,2] position to give the corresponding mono-iminated product with an unexpectedly high regioselectivity. The regioselective imination was found to be generally

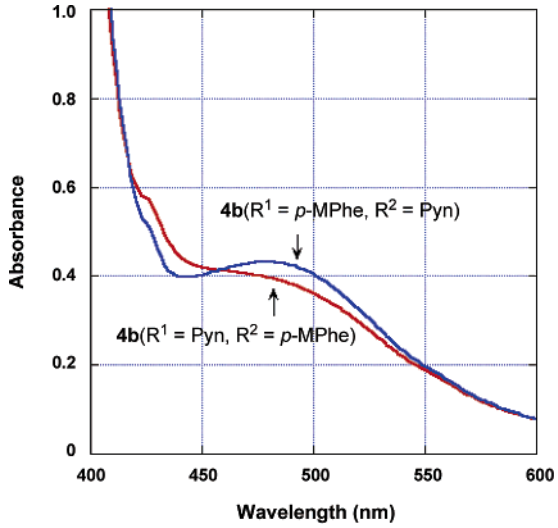



**FIGURE 2.** UV−vis Spectra of [60]Fullerene-Centered Dissymmetric Triads **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) in $CHCl_3$.

applicable to various aromatic amines. Furthermore, $C_{60}$-centered triads with a sequence-controlled structure were efficiently synthesized by applying this reaction. The synthetic method developed here would provide reliable routes to access dissymmetrically functionalized $C_{60}$ derivatives, which are expected to expand the scope of $C_{60}$-containing molecular devises.

## Experimental Section

**Mono-imination of 1b with Aromatic Amines. Typical Procedure.** To a $CH_2Cl_2$ solution (15 mL) of **1b** (15.0 mg, 15.6 $\mu$mol) and 1,8-diazabicyclo[2,2,2]octane (DABCO) (409 mg, 3.65 mmol) were successively added a $CH_2Cl_2$ solution of aniline (0.21 M, 73 $\mu$L, 15.6 $\mu$mol) and $TiCl_4$ (74 mg, 390 $\mu$mol). After being stirred overnight at room temperature, the mixture was subjected to a short alumina column chromatography eluted by $CH_2Cl_2$. The resultant solution was concentrated under reduced pressure, and the resultant residue was subjected to preparative GPC to give a mixture of mono-imines **3b**($R^1$ = Phe) and **3b′**($R^2$ = Phe) (11.8 mg, 11.4 $\mu$mol, 73%), bis-imine **4b**($R^1$, $R^2$ = Phe) (2.6 mg, 2.3 $\mu$mol, 15%), and unreacted **1b** (1.8 mg, 1.9 $\mu$mol, 12%).

**3b**($R^1$ = Phe): a mixture with **3b′**($R^2$ = Phe) (**3b**($R^1$ = Phe):**3b′**($R^2$ = Phe) = 95:5). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 6.7−6.9 (m, 2H), 7.1−7.2 (m, 1H), 7.2−7.3 (m, 4H), 7.46 (t, $J$ = 7.8 Hz, 2H), 8.69 (s, 1H), 10.51 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 24.34, 25.45, 26.14, 29.69, 34.83, 36.11, 50.04, 50.20, 74.69, 75.84, 120.85, 126.40, 129.32, 129.77, 130.68, 137.63, 138.24, 138.63, 139.05, 139.84, 140.13, 140.47, 141.21, 141.71, 141.97, 142.05, 143.01, 143.09, 143.30, 143.63, 143.73, 143.73, 143.82, 143.91, 143.98, 144.05, 144.25, 144.29, 144.51, 144.54, 144.60, 144.64, 144.82, 144.85, 144.97, 145.29, 145.33, 145.67, 145.74, 145.83, 146.04, 146.18, 146.28, 146.36, 146.40, 146.52, 146.78, 147.18, 147.27, 148.08, 148.68, 151.39, 159.30, 195.44; MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{82}H_{24}NO$ calcd 1038.19, found 1038.18.

**3b**($R^1$ = *p*-DAPhe): a mixture with **3b′**($R^2$ = *p*-DAPhe) (**3b**($R^1$ = *p*-DAPhe):**3b′**($R^2$ = *p*-DAPhe) = 93:7). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 3.01 (s, 6H), 6.8−7.3 (m, 4H), 6.80 (d, $J$ = 8.1 Hz, 2H), 7.28 (d, $J$ = 8.1 Hz, 2H), 8.73 (s, 1H), 10.51 (s, 1H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{84}H_{29}N_2O$ calcd 1081.23, found 1080.15.

**3b**($R^1$ = *p*-MPhe): a mixture with **3b′**($R^2$ = *p*-MPhe) (**3b**($R^1$ = *p*-MPhe):**3b′**($R^2$ = *p*-MPhe) = 95:5). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 3.86 (s, 3H), 6.7−6.9 (m, 2H), 6.98 (d, $J$ = 9.0 Hz, 2H), 7.1−7.2 (m, 1H), 7.2−7.3 (m, 1H), 7.26 (d, $J$ = 9.0 Hz, 2H),

8.71 (s, 1H), 10.51 (s, 1H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{83}H_{26}NO$ calcd 1068.20, found 1068.14.

**3b**($R^1$ = *p*-NPhe): a mixture with **3b′**($R^2$ = *p*-NPhe) (**3b**($R^1$ = *p*-NPhe):**3b′**($R^2$ = *p*-NPhe) = 96:4). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.2 (m, 11H), 3.2−3.5 (m, 1H), 6.7−6.9 (m, 2H), 7.1−7.2 (m, 1H), 7.2−7.3 (m, 1H), 7.31 (d, $J$ = 8.7 Hz, 2H), 8.34 (d, $J$ = 8.7 Hz, 2H), 8.68 (s, 1H), 10.51 (s, 1H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{82}H_{23}N_2O_3$ calcd 1083.17, found 1083.16.

**3b**($R^1$ = 1-Pyn): a mixture with **3b′**($R^2$ = 1-Pyn) (**3b**($R^1$ = 1-Pyn):**3b′**($R^2$ = 1-Pyn) = 95:5). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 6.7−7.0 (m, 2H), 7.1−7.2 (m, 1H), 7.4 (m, 1H), 7.73 (d, $J$ = 8.1 Hz, 1H), 8.0−8.1 (m, 3H), 8.2−8.3 (m, 4H), 8.71 (d, $J$ = 9.3 Hz, 1H), 8.96 (s, 1H), 10.51 (s, 1H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{92}H_{28}NO$ calcd 1062.22, found 1062.20

**3b**($R^1$ = TPP): a mixture with **3b′**($R^2$ = TPP) (**3b**($R^1$ = TPP):**3b′**($R^2$ = TPP) = 97:3). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 6.8−7.2 (m, 4H), 7.63 (d, $J$ = 8.1 Hz, 2H), 7.7−7.9 (m, 9H), 8.1−8.3 (m, 6H), 8.33 (d, $J$ = 8.1 Hz, 2H), 8.8−8.9 (m, 7H), 8.94 (d, $J$ = 4.8 Hz, 2H), 10.4 (s, 1H), 12.21 (s, 2H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{120}H_{47}N_5O$ calcd 1574.39, found 1574.33.

**3b**($R^1$ = 4-Pyd): a mixture with **3b′**($R^2$ = 4-Pyd) (**3b**($R^1$ = 4-Pyd):**3b′**($R^2$ = 4-Pyd) = 89:11). $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.5 (m, 12H), 3.86 (s, 3H), 6.7−6.9 (m, 2H), 6.98 (d, $J$ = 9.0 Hz, 2H), 7.1−7.2 (m, 1H), 7.2−7.3 (m, 1H), 7.26 (d, $J$ = 9.0 Hz, 2H), 8.71 (s, 1H), 10.51 (s, 1H); MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{81}H_{23}N_2O$ calcd 1039.18, found 1038.25.

**Mono-imination of 1c−e with Aniline.** The mono-imination was conducted in a similar procedure to that for the mono-imination of **1b** with aromatic amines as described above.

**Synthesis of Dissymmetric Bis-imine 4b($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn).** To a $CH_2Cl_2$ solution (12 mL) of **3b**($R^1$ = *p*-MPhe) (containing 5% **3b′**($R^2$ = *p*-MPhe), 12 mg, 12 $\mu$mol) and DABCO (300 mg, 2.7 mmol) were successively added a $CH_2Cl_2$ solution of 1-pyrenamine (2.5 mg, 12 $\mu$mol) and $TiCl_4$ (55 mg, 288 $\mu$mol). After being stirred overnight at room temperature, the mixture was subjected to a short alumina column chromatography eluted by $CH_2Cl_2$. The resultant solution was concentrated under reduced pressure, and the resultant residue was subjected to preparative GPC to give the dissymmetric bis-imine **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) containing 6% of **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) (11 mg, 8.7 $\mu$mol, 75%). The analytical sample of **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) (containing **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) <1%) was obtained by recycling preparative HPLC.

**4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn): IR (KBr) 2925, 2852, 1636, 1504, 1458, 1246, 1181, 1036, 842, 525; $^1$H NMR ($CDCl_3$) $\delta$ 2.0−3.0 (m, 10H), 3.2−3.3 (m, 1H), 3.6−3.8 (m, 1H), 3.86 (s, 3H), 6.8−6.9 (m, 2H), 6.98 (d, $J$ = 9 Hz, 2H), 7.1−7.2 (m, 1H), 7.26 (d, $J$ = 9 Hz, 2H), 7.5 (m, 1H), 7.73 (d, $J$ = 8.1 Hz, 1H), 8.0−8.1 (m, 3H), 8.2−8.3 (m, 4H), 8.70 (s, 1H), 8.78 (d, $J$ = 9.3 Hz, 1H), 9.04 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 24.09, 25.34, 28.91, 29.79, 34.86, 36.70, 47.84, 49.98, 55.55, 78.73, 114.46, 115.98, 122.24, 123.13, 124.81, 125.19, 125.24, 125.69, 126.28, 127.04, 127.28, 127.68, 130.04, 130.15, 130.78, 131.38, 131.50, 137.25, 137.52, 138.41, 138.66, 139.10, 139.95, 139.83, 140.14, 140.96, 141.02, 141.55, 141.81, 141.90, 142.6, 142.84, 143.05, 143.21, 143.54, 143.63, 143.78, 143.96, 144.00, 144.04, 144.22, 144.32, 144.44, 144.47, 144.69, 144.75, 144.85, 145.19, 145.14, 145.35, 145.45, 145.61, 145.64, 145.76, 145.95, 146.09, 146.30, 146.35, 146.48, 146.77, 147.08, 147.16, 149.47, 149.90, 157.45, 158.53, 160.45; MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{99}H_{35}N_2O$ calcd 1267.27, found 1267.27.

**Synthesis of Dissymmetric Bis-imine 4b($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe).** The condensation was conducted by a procedure similar to that for the synthesis of **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) by using **3b**($R^1$ = 1-Pyn) containing 5% of **3b′**($R^2$ = 1-Pyn) to give the dissymmetric bis-imine **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) containing 5% of **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) (75%). The analytical sample of **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe) (containing **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn) <1%) was obtained by recycling preparative HPLC.

**4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe): IR (KBr) 2923, 2851, 1636, 1503, 1458, 1246, 1180, 1035, 843, 524; $^1$H NMR ($CDCl_3$) $\delta$ 1.9−2.1 (m, 1H), 2.4−2.8 (m, 7H), 3.0−3.3 (m, 3H), 3.4−3.6 (m, 1H), 3.86 (s, 3H), 6.8−6.9 (m, 2H), 6.99 (d, $J$ = 9 Hz, 2H), 7.2 (m, 1H), 7.31 (d, $J$ = 9 Hz, 2H), 7.4 (m, 1H), 7.73 (d, $J$ = 8.1 Hz, 1H), 8.0−8.1 (m, 3H), 8.2−8.3 (m, 4H), 8.71 (d, $J$ = 9.3 Hz, 1H), 8.79 (s, 1H), 8.96 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.74, 25.72, 28.73, 30.07, 35.04, 36.26, 47.43, 50.42, 55.58, 78.89, 114.55, 115.99, 122.23, 123.12, 124.86, 125.04, 125.14, 125.18, 125.28, 125.67, 126.24, 126.96, 127.31, 127.54, 130.02, 130.76, 131.44, 131.56, 137.47, 137.62, 138.42, 138.69, 138.98, 139.68, 140.14, 140.90, 141.58, 141.82, 141.85, 141.93, 142.71, 142.87, 143.06, 143.19, 143.49, 143.66, 143.77, 143.81, 143.99, 144.07, 144.24, 144.35, 144.38, 144.42, 144.46, 144.64, 144.68, 144.98, 145.22, 145.22, 145.35, 145.50, 145.62, 145.64, 145.76, 145.95, 146.36, 146.47, 146.51, 146.54, 146.80, 147.11, 147.16, 149.54, 150.15, 157.59, 158.71, 160.35; MALDI-TOF-MS (dithranol) for $[M + H]^+$ $C_{99}H_{35}N_2O$ calcd 1267.27, found 1267.27.

**Supporting Information Available:** Synthetic procedures and characterization data of **2a**−**d**; structural assignment of bis(formylmethano)$C_{60}$s; $^1$H and $^{13}$C NMR spectra of **3b**, **4b**($R^1$ = *p*-MPhe, $R^2$ = 1-Pyn), and **4b**($R^1$ = 1-Pyn, $R^2$ = *p*-MPhe). This material is available free of charge via the Internet at http://pubs.acs.org.

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