ORGANIC LETTERS

2006
Vol. 8, No. 26
6075−6078

Switch of Electronic Reactivity in Fullerene C_{60}: Activation of Three *trans-4* Positions via Temporary Saturation of the *cis-1* Positions

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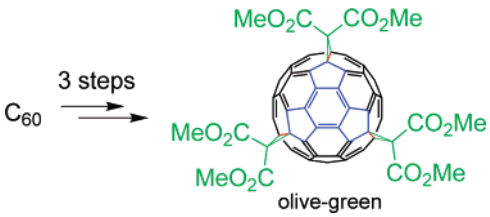
Received October 17, 2006

ABSTRACT



The regioselective functionalization of C_{60} with a *trans-4,trans-4,trans-4* trisaddition pattern is not feasible directly. We have found an indirect approach taking advantage of the modified electronic reactivity of *cis-1* bisadducts. The *cis-1* addition pattern electronically activates three *trans-4* C═C bonds on the opposite hemisphere of C_{60}, allowing further highly regioselective additions at these positions. Thermal removal of the *cis-1* blocking unit results in a *trans-4,trans-4,trans-4* trisadduct with C_{3v} symmetry.

Controlling the regioselectively of multiple additions to C_{60} has been a challenging aspect of fullerene chemistry because reactions usually give regioisomeric mixtures that can require tedious HPLC separation.[1] Tether-directed reactions have been used as ways to constrain reactive groups to add regioselectively and even enantioselectively to C_{60}.[2] Most of these approaches tend to limit the amount of regioisomers produced and usually favor additions to the inherently electronically activated *e*-positions, leading to multiadducts with high symmetry. T_h-symmetrical hexaadducts were discovered as early as 1991.[1c,3]

Among all of the possible regioisomeric trisadducts of C_{60} with a C_3-rotational axis of symmetry, the *all-cis-1* (**A**)[4] and *all-trans-4* (**C**) adducts[5] have been the most absent members of the series due to disfavored additions caused by high steric hindrance or electronically unfavorable reactivity, respectively (Figure 1). Bingel adducts with an *all-trans-4* pattern have not been isolated except in a macrocyclic addition approach in which only 2% of an olive-green adduct is produced.[6] Its formation remains ambiguous in the nontethered method.[7] In any method using a templated or tethered

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(7) Echegoyen, L. E.; Djojo, F.; Hirsch, A.; Echegoyen, L. *J. Org. Chem.* **2000**, *65*, 4994−5000.

10.1021/ol0625637 CCC: $33.50
Published on Web 12/01/2006

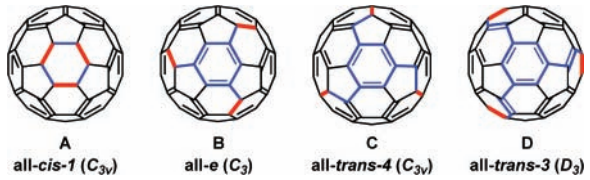


Figure 1. Trisadducts having a C_3 rotational axis.[6]

approach, the favored addition products are always dominated by the *e*,*e*,*e* or *trans*-3,*trans-3*,*trans-3* patterns.[8]

We have discovered that trisadducts of type **C** can be prepared via temporary electronic activation of the LUMO orbital coefficients at the *trans-4*,*trans-4*,*trans-4* positions in intermediately formed *cis-1* bisadducts. Figure 2 outlines

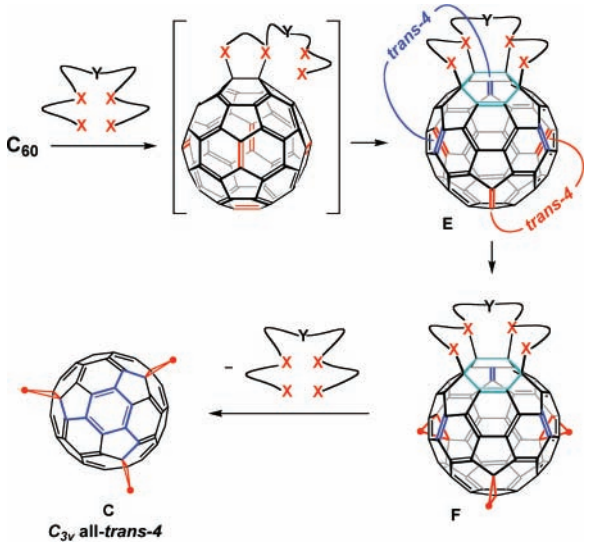
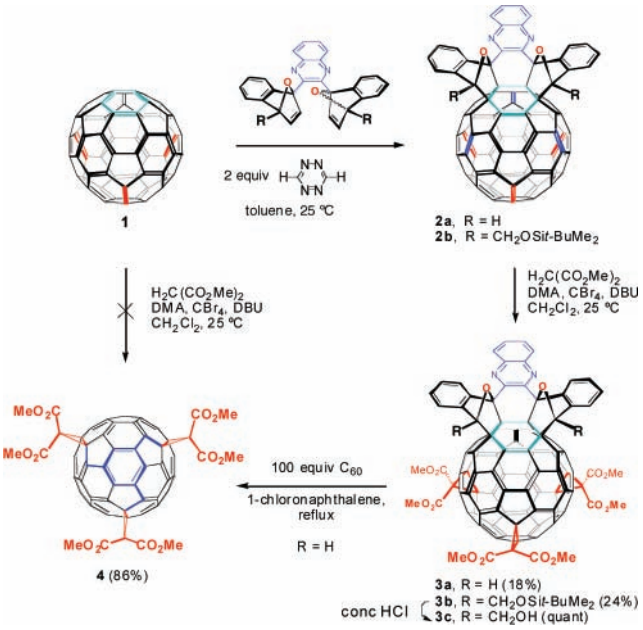


Figure 2. Electronic activation effect upon *cis-1* bisadduct formation (**E**), leading to the formation of *all-trans-4* trisadducts **C** via intermediate formation of **F**.

this basic principle: (a) A tethered *cis-1* bisadduct is easily formed from a linked reactive bis-1,3-diene X−X that is at the same time thermally removable through a retroaddition reaction. The LUMO configuration changes from mainly *e-edge*, *e-face*, and *trans-3* for a simple C_{60} monoadduct to the two sets of *all-trans-4*-related positions on each hemisphere shown in blue and red colors for the *cis-1* bisadduct. (b) Chemical functionalization at the least hindered lower hemisphere, followed by thermal removal of the *cis-1* addends, leaves the *all-trans-4* adduct **C**.

Our approach to form an orifice in C_{60} cages by saturating three double bonds within a six-membered ring[4,9] led us to prepare *cis-1* bis(isobenzofuran) adducts **2a**,**b** (Scheme 1).[10]

Scheme 1



We observed that the AM1-calculated LUMO orbital configuration for the *cis-1* adducts is dramatically different from that of regular monofunctionalized adducts of C_{60} (Figure 2).[11−14] Two sets of three *trans-4* related double bonds located on two separate hemispheres of structure **E** have very high LUMO coefficients at the double bonds shown in blue and red. Double bonds having the highest LUMO coefficients are most reactive toward nucleophilic reagents used in fullerene functionalization. Steric hindrance in adducts **2a** and **2b** caused by the large *cis-1* addends impinges on additions at the higher blue double bonds. As will be seen, only the lower red double bonds are functionalized with these particular systems.

The tris *trans-4* adduct **4** was obtained either by a stepwise addition−isolation approach, or by one-pot synthesis starting from the *cis-1* bis(isobenzofuran) adducts **2a**,**b**. Because stepwise synthesis requires purification of each sequential Bingel functionalization step, one-pot synthesis of **3a**,**b** from **2a**,**b** was first attempted. As we expected, several products including bis, tris, tetrakis, and higher adducts were obtained

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(11) See the Supporting Information for a graphic presentation of the LUMO configurations and density of compound **2a**.

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that were not readily separated from other isomers by column chromatography. This issue was resolved by using dimethyl anthracene (DMA) as the temporary templating agent.[1c] The amount of isomers readily decreased, and the tris-Bingel adducts **3a**,**b** were isolated in 18% and 26% yield, respectively, as bright orange solids (24 and 27% based on recovered starting materials, Scheme 1).[15] The addition pattern was unambiguously confirmed by an X-ray single-crystal structure of product **3c** formed by aqueous HCl treatment of silyl ether **3b** (Figure 3).[16] The bottom view of

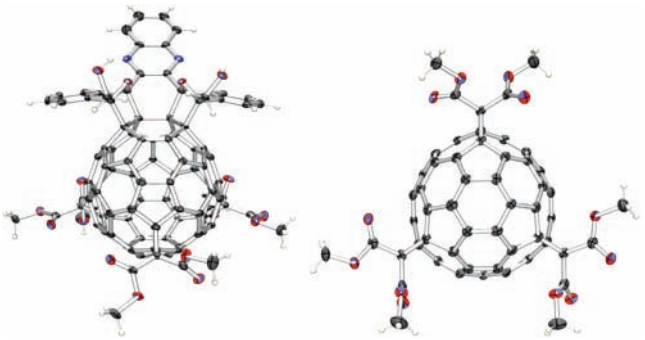

Figure 3. X-ray crystal structure of compound **3c**. Left: front view. Right: bottom view with bis(isobenzofuran) moiety omitted for clarity.

C_s-symmetric trisadduct **3c** clearly shows that the three Bingel addends are located at the saturated *exo* CC bonds of three peripheral five-membered rings pointing away from a central 6-membered ring. The formation of this repetitive addition pattern is consistent with the predictions from AM1 semiempirical calculations that high LUMO coefficients are turned on at these locations in *cis-1* bisadduct **2a** and in the ensuing Bingel addition intermediates (two isomers are formed in the first Bingel addition and two isomers in the second Bingel additions).[11]

Removal of the bis(isobenzofuran) moiety from **3a** is the key to obtain the final *trans-4*,*trans-4*,*trans-4* Bingel trisadduct **4**. According to thermogravimetric analysis (TGA), the bis(isobenzofuran) moiety of compound **2a**[10] undergoes retroaddition around 300 °C in the crystalline state. Initial attempts to effect retroaddition in the presence of maleic anhydride (MA) or *N*-methylmaleimide (NMM) in solution failed to remove the bis(isobenzofuran) moiety because the MA or NMM adducts are much less stable than the starting material **2a**.[17] However, refluxing compound **3a** in the presence of an excess of C_{60} in boiling 1-chloronaphthalene (bp 265 °C) successfully transferred the bis(isobenzofuran) moiety to pristine C_{60} by formation of the equally thermally stable *cis-1* adduct **2a** (Scheme 1).[18] A similar example in using C_{60} as an effective trapping reagent has been recently reported.[19]

The Bingel addends are thermally stable under these conditions and do not come off or walk over the fullerene moiety. The walk of malonate addends has been observed under reductive conditions, but not thermally.[7,20] This notion is further supported by the MALDI-ICR mass spectra of compound **3b** (Figure 4). Only the parent ion bears a bis-

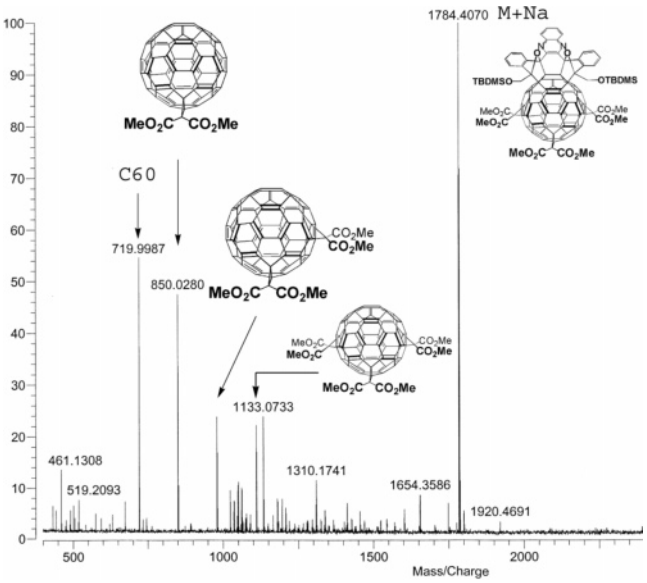

Figure 4. MALDI-TOF mass spectrum of compound **3b**.

(isobenzofuran) moiety; all of the main fragment ions bear only malonate units.

The olive-green *trans-4*,*trans-4*,*trans-4* Bingel trisadduct **4** is very stable. Its structure is confirmed by a unique singlet at 3.98 ppm for the methyl ester protons in the ^{1}H NMR spectrum. The ^{13}C spectrum only shows 10 peaks for sp^2 carbons of the C_{60} moiety, with eight peaks having twice the intensity of the two other peaks. The features in the UV−vis absorption spectrum of trisadduct **4** are identical to those of the *trans-4*,*trans-4*,*trans-4* trisadduct prepared by Hirsch et al. using the macrocyclic trismalonate addition approach.[6] Four typical and strong absorptions appear at 466,

(15) **Synthesis of Tris-Bingel Bis-isobenzofuran C_{60} Adduct 3a.** 9,10-Dimethylanthracene (102 mg, 0.497 mmol) was added to a solution of *cis-1* adduct **2a** (108 mg, 0.100 mmol) in toluene (250 mL) at ambient temperature under argon, and then the mixture was stirred for 2 h. Tetrabromomethane (593 mg, 1.79 mmol) and DBU (276.5 mg, 1.82 mmol) were then added. Dimethyl malonate (39 mg, 0.298 mmol) in toluene (10 mL) was injected slowly into the solution over 2 h using a mechanical syringe pump, and the mixture was stirred for 24 h at ambient temperature. The solvent was evaporated under reduced pressure, and the residue was dissolved in CS_2. Flash chromatography on silica gel was performed using toluene as eluent to recover the starting material (27 mg). Slowly increasing the polarity of the eluent (toluene/EtOAc, from 90:1 to 30:1) eluted the tris-Bingel adduct **3a** as a bright-orange solid: yield 18% (24% based on recovered starting material); $R_f = 0.13$ (toluene/EtOAc 30:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 3.78 (s, 6H), 3.84 (s, 6H), 3.94 (s, 6H), 6.40 (s, 2H), 7.39−7.43 (m, 4H), 7.51−7.54 (m, 2H), 7.90 (dd, $J = 6.4$, 3.4 2H), 8.01 (d, $J = 7.5$ Hz, 2H), 8.30 (dd, $J = 6.4$, 3.4 Hz, 2H); ^{13}C NMR (125.8 Hz, $CDCl_3$) δ (ppm) 45.59, 46.69, 53.61, 53.67, 53.80, 68.68, 69.26, 70.18, 70.45, 73.70, 77.92, 88.32, 94.84, 120.35, 126.84, 127.61, 129.21, 129.88, 131.44, 133.61, 138.14, 138.57, 139.28, 139.41, 139.89, 140.14, 142.10, 142.43, 142.62, 142.64, 142.92, 143.40, 143.76, 143.84, 143.90, 144.10, 144.68, 145.44, 145.93, 146.47, 146.87, 148.53, 148.80, 149.20, 149.66, 151.44, 151.49, 152.98, 153.29, 164.09, 164.12, 164.16; FTIR (KBr) ν (cm^{-1}) 753, 836, 919, 962, 1013, 1058, 1122, 1250, 1742, 2853, 2923, 2958, 3022; MALDI-LRMS calcd for $C_{99}H_{32}N_2O_{14}$ 1472.2, found 1472.9. See the Supporting Information for spectral data of compound **3b**.

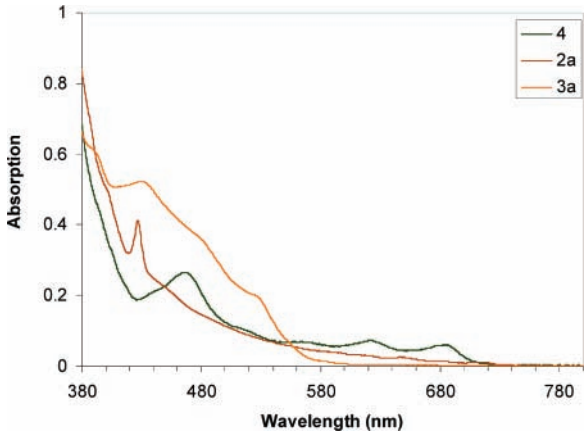

Figure 5. UV−vis spectra of compounds **2a** (9.7×10^{-5} M), **3a** (5.0×10^{-5} M), and **4** (1.0×10^{-4} M) in $CHCl_3$.

565, 622, and 684 nm (Figure 5). The olive-green color is unique and different from that of the D_3 *all-trans-3* (cherry-red),[21] C_3 *all-e* (orange-red),[22] and C_{3v} *all-cis-1* (brown)[4] adducts.

The isolation of the C_{3v}-symmetric *all-trans-4* Bingel trisadduct **4** eliminates a question about its stability;[7] the unknown compound of Echegoyen's study[7] does not seem to be an *all-trans-4* adduct because the UV−vis absorption spectra do not match.

In summary, we have introduced a new concept for the synthesis of multiple adducts of fullerenes, in which a temporary blockage of double bonds on C_{60} alters the electronic structure of the whole molecule. The advantages of this approach lie in the use of the easily formed bis(isobenzofuran) moiety leading to a stable *cis-1* bisadduct which activates three C═C bonds in *trans-4* positional relationships. The activated C═C bonds can be functionalized to give a C_s-symmetrical pentakisadduct. Removal of the bis-(isobenzofuran) moiety through Diels−Alder transfer to C_{60} as the trapping agent affords an *all-trans-4* trisadduct not easily attainable in other ways.

Acknowledgment. We thank the NSF for Grant Nos. CHE-0080942 (Y.R.), CHE-9871332 (X-ray), CHE-9974928 (NMR), DGE-0114443 (TGA), the Alfred P. Sloan Research Foundation, and ACS-PRF for support of this work.

Supporting Information Available: Spectral data and crystallographic information files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) See the Supporting Information for the synthesis of compound **3c**. Physical data of compound **3c**: quantitative, $R_f = 0.48$ (CH_2Cl_2/MeOH 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.74 (br), 3.77 (s, 6H), 3.83 (s, 6H), 3.93 (s, 6H), 4.88 (s, 4H), 7.20 (br, 2H), 7.40 (t, $J = 6.9$ Hz, 2H), 7.51 (t, $J = 7.4$, 2H), 7.90 (dd, $J = 6.1$, 3.1 Hz, 2H), 7.98 (d, $J = 7.4$ Hz, 2H), 8.29 (dd, $J = 5.4$, 3.1 Hz, 2H). ^{13}C NMR (125.8 Hz, $CDCl_3$) δ (ppm) 45.58, 46.72, 53.61, 53.68, 53.81, 60.22, 68.68, 69.24, 70.11, 70.50, 75.25, 78.77, 93.09, 95.59, 119.99, 126.94, 127.66, 129.30, 129.87, 131.60, 133.51, 138.24, 138.56, 139.21, 139.33, 139.95, 140.89, 141.46, 142.57, 142.62, 142.64, 142.72, 143.38, 143.41, 143.63, 143.69, 144.11, 144.48, 145.45, 146.05, 146.43, 146.62, 147.60, 148.84, 149.06, 149.19, 151.10, 151.49, 152.79, 164.04, 164.10, 164.14; FTIR (KBr) ν (cm^{-1}) 730, 751, 956, 1054, 1123, 1251, 1435, 1746, 2851, 2919, 2953, 3013, 3544; HRMS $[M + Na]^+$ calcd for $C_{101}H_{36}N_2NaO_{16}$ 1555.1963, found 1555.1667. X-ray diffraction data: orange prism, approximate dimensions 0.6 mm × 0.2 mm × 0.2 mm, triclinic, space group $P\bar{1}$, $Z = 2$, $a = 16.235(3)$ Å, $b = 18.066(3)$ Å, $c = 18.447(3)$ Å, $a = 104.899(3)°$, $b = 114.991(3)°$, $g = 93.152(3)°$, $V = 4655.4(13)$ Å^3, temperature = 100 (2) K, $R_1 = 0.066$, Rw = 0.1758, GoF = 0.812.

(17) Tobia, D.; Harrison, R.; Phillips, B.; White, T. L.; DiMare, M.; Rickborn, B. *J. Org. Chem.* **1993**, *58*, 6701−6706.

(18) **Synthesis of Tris-*trans-4*-Bingel Adduct 4.** A solution of tris-Bingel **3a** (4 mg, 2.72 mmol) and C_{60} (195 mg, 0.271 mmol) in 1-chloronaphthalene (40 mL) was flushed with argon for 15 min and then heated under reflux for 30 min. The reaction mixture was cooled, hexanes (20 mL) were added, and then the mixture was passed through a short plug of silica gel. Toluene was used initially to elute out C_{60}. Subsequently, a mixture of toluene and EtOAc (3:1) was used to obtain all of the polar materials. The solvent was evaporated under reduced pressure, and then the residue was submitted to chromatography (toluene then toluene/EtOAc, 60:1) to obtain the *cis-1* adduct **2a** (2.8 mg, $R_f = 0.46$ (toluene/EtOAc 20:1)). The olive-green tris-Bingel adduct **4** was obtained in 86% yield after eluting with toluene/EtOAc (30:1). Compound **4**: $R_f = 0.39$ (toluene/EtOAc 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 3.98 (s, 18H); ^{13}C NMR (125.8 Hz, $CDCl_3$) δ (ppm) 48.20, 53.95, 70.44, 71.31, 135.28, 140.82, 141.19, 141.87, 142.43, 142.86, 142.92, 144.79, 145.58, 147.70, 164.28; FTIR (KBr) ν (cm^{-1}) 1252, 1732, 2851, 2924; MALDI-LRMS $[M]^+$ calcd for $C_{75}H_{18}O_{12}$ 1110.08, found 1110.05.

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