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Approaches to Open Fullerenes: A 1,2,3,4,5,6-Hexaadduct of C_{60}

Shih-Ching Chuang, Fernando R. Clemente, Saeed I. Khan, K. N. Houk, and Yves Rubin*

*Department of Chemistry and Biochemistry, University of California,
Los Angeles, California 90095-1569*

rubin@chem.ucla.edu

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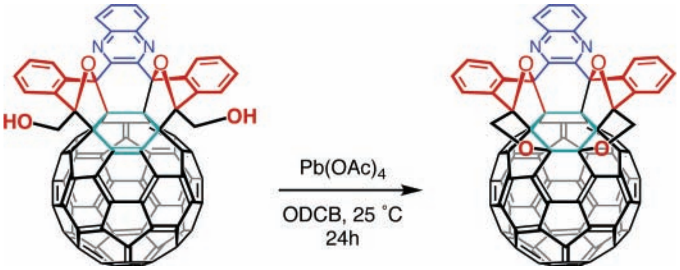
ABSTRACT



Complete saturation of a single six-membered ring on fullerene C_{60} has been achieved. The critical step in this first synthesis of a fully characterized 1,2,3,4,5,6-hexaadduct consisted of a remarkable double 5-exo-trig addition of alkoxyl radicals promoted by lead tetraacetate. Two possible opening pathways ([2 + 2 + 2] retrocycloadditions) for the newly synthesized compound were explored using quantum mechanical calculations. We found that the oxa bridges in the hexaadduct prevent ring opening through the retro[2 + 2 + 2] mechanism due to the high activation barrier and endothermicity of the reaction.

Endohedral fullerenes have properties that are often inherently distinct from those of empty fullerenes.[1] In fact, complexes of *transition metals* are the most conspicuously absent members of the series of isolated endohedral metallofullerenes, even if they are expected to have the most interesting properties. The demonstrated potential of synthetic organic approaches for these compounds ("molecular surgery") has recently highlighted the need for an expanded set of opening reactions.[2−4] These methods should eventually provide access to a wider array of elements trapped inside fullerene cages than those currently available.[5]

We obtained the first effectively open fullerene through an unexpected set of rearrangement and oxygenation reactions[2a] and showed that both H_2 and He can be inserted.[2b] Komatsu et al. further demonstrated that another H_2-complexed open fullerene can be reclosed.[3] Overall, a precise control of bond-breaking reactions within fullerene cages needs to be further scrutinized to generate wider openings. The limited set of reactions has for now kept the size of species inserted into C_{60} to the smallest atoms or molecules.

One of the potentially most effective scission mechanisms of the fullerene cage involves the complete saturation of a

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(1) (a) Saunders, M.; Jiménez-Vázquez, H. A.; Cross, R. J.; Mroczkowski, S.; Freedberg, D. I.; Anet, F. A. L. *Nature* **1994**, 367, 256−258. (b) Kobayashi, S.; Mori, S.; Iida, S.; Ando, H.; Takenobu, T.; Taguchi, Y.; Fujiwara, A.; Taninaka, A.; Shinohara, H.; Iwasa, Y. *J. Am. Chem. Soc.* **2003**, *125*, 8116−8117. (c) *Endofullerenes: A New Family of Carbon Clusters*; Akasaka, T., Nagase, S., Eds.; Kluwer Academic Publishers: Dodrecht, The Netherlands, 2002.

(2) (a) Schick, G.; Jarrosson, T.; Rubin, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 2360−2363. (b) Rubin, Y.; Jarrosson, T.; Wang, G.-W.; Bartberger, M. D.; Houk, K. N.; Schick, G.; Saunders: M.; Cross, R. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1543−1546.

(3) (a) Murata, Y.; Murata, M.; Komatsu, K. *Chem. Eur. J.* **2003**, *9*, 1600−1609. (b) Komatsu, K.; Murata, M.; Murata, Y. *Science* **2005**, *307*, 238−240. (c) Komatsu, K.; Murata, Y. *Chem. Lett.* **2005**, *34*, 886−891. (d) Murata, M.; Murata, Y.; Komatsu, K. *J. Am. Chem. Soc.* **2006**, *128*, 8024−8033.

(4) (a) Iwamatsu, S.-I.; Uozaki, T.; Kobayashi, K.; Re, S.; Nagase, S.; Murata, S. *J. Am. Chem. Soc.* **2004**, *126*, 2668−2669. (b) Iwamatsu, S.; Murata, S.; Andoh, Y.; Minoura, M.; Kobayashi, K.; Mizorogi, N.; Nagase, S. *J. Org. Chem.* **2005**, *70*, 4820−4825. (c) Iwamatsu, S.; Murata, S. *Synlett* **2005**, *14*, 2117−2129.

(5) (a) Arce, M.-J.; Viado, A. L.; An, Y.-Z.; Khan, S. I.; Rubin, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3775−3776. (b) Rubin, Y. *Chem. Eur. J.* **1997**, *3*, 1009−1016. (c) Rubin, Y. *Chimia* **1998**, *52*, 118−126. (d) Rubin, Y. *Top. Curr. Chem.* **1999**, *199*, 67−91.

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single six-membered ring of C_{60} by a concerted σ-bond rearrangement (Figure 1).[2,5,6] The saturation of two out of three C═C bonds within a six-membered ring can be easily performed through a versatile double Diels−Alder reaction, which gives analogues of the *cis*-1 bis-isobenzofuran−C_{60} adduct **1** (Scheme 1).[7] However, because severe steric hindrance is imparted by these groups at the 1- and 4-positions of the cis-1 addition pattern, saturation of the third C═C bond (5,6-positions) has been exceedingly difficult to achieve.[8]

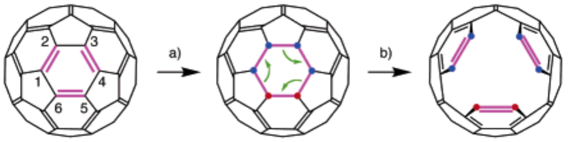
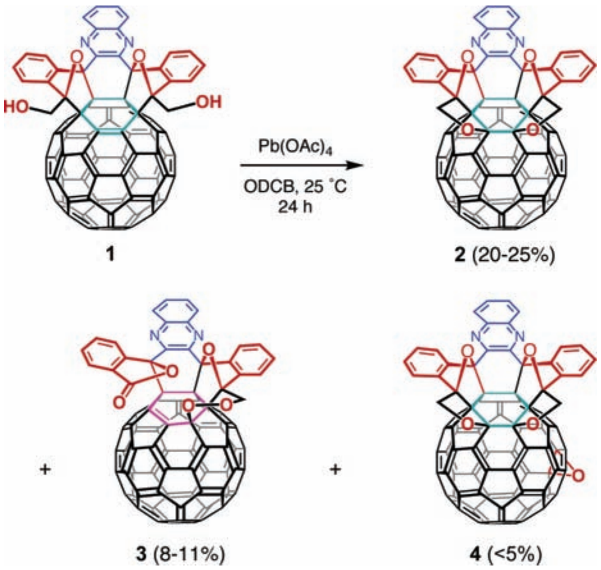


Figure 1. Formation of a wide opening on C_{60}: (a) addition of six saturating groups; (b) [2 + 2 + 2] ring opening of the 1,2,3,4,5,6-hexaadduct.

Scheme 1



Herein, we describe how functionalization of the desired third double bond can be achieved by two sequential 5-exo-trig additions of alkoxyl radicals generated from diol **1**.[9] Only one other example of such a reaction is known, that of phenoxyl radicals undergoing a similar 1,2-bisaddition to a C═C bond.[10] The 1,2,3,4,5,6-hexaadduct **2** was characterized by single-crystal X-ray diffraction.

We chose alkoxyl radicals as reactive intermediates because oxygen is the least sterically demanding of common radical intermediates. To avoid intermolecular side-reactions, we searched for a number of methods to simultaneously generate alkoxyl radicals that could undergo double cyclization, e.g., by forming an unstrained cyclic peroxide intermediate from **1** followed by thermolysis of the weak O−O bond. However, the latter peroxide could not be prepared. Ultimately, our quest was successful when we used $Pb(OAc)_4$ alone (Scheme 1). The concentration of diol **1** determined the outcome of the double radical addition.[11] At concentrations above 10^{-4} M, we isolated only oligomeric material, but we observed three new products (**2**−**4**) under more dilute conditions (Scheme 1). The yields of **2** and **3** increased steadily upon decreasing the concentration of **1**; its optimal concentration (1.0×10^{-5} M; 34 mg/3.0 L ODCB) was the lower limit for a practical scale. Doubling this concentration was also acceptable, but the yields of **2** were lowered to ca. 10%. The reactions typically proceeded for 24 h at 25 °C;[12] at 0 °C, 60 h was required to produce the compounds in similar yields.

We readily isolated compound **2** (25%), peroxide **3** (9%), and the epoxide byproduct **4** (5%) by column chromatography (SiO_2; toluene/EtOAc). The MALDI-TOF mass spectrum of **2** (m/z 1140) revealed two fewer hydrogen atoms than its precursor **1**. The ^1H NMR spectra of **2** and **3** both display sets of clean AB quartets; four methylene doublets appear for the asymmetric epoxide **4**. The ^1H NMR spectrum of **2** indicates that it possesses a plane of symmetry. The ^{13}C NMR spectrum of **2** has a signal for a new sp^3-hybridized carbon atom at 92.3 ppm, revealing that the two oxygen atoms have bonded symmetrically to two fullerene carbon atoms. We could not assign this signal with certainty, even with the assistance of 2D-HMBC data.

We confirmed the structure of **2** through a single-crystal X-ray analysis (Figure 2).[13] The C84−C85−C86 and C76−C77−C78 bond angles are 125.5(5) and 124.5(4)°, respectively; hence, there is enormous angle strain generated in the critical bond forming events affording the two new tetrahydrofuran rings. The eclipsing strain among the 1,2,3,4,5,6-addends is manifested by significant dihedral bond distortions, for example, 4.2° at one of two benzoxabicyclo[2.2.1]heptene units. The quinoxaline ring itself (C62−C69−C65−C66 dihedral angle = 172.4°) is axially distorted due to crystal packing forces.

The lack of symmetry in **3** makes its structural determination much more complex than that of **2**. Its very weak molecular ion at m/z 1142 (MALDI-TOF MS) and a base peak cluster at m/z 1126 imply that the original structure has lost a CH_2 group (m/z = 14) in addition to the two hydrogen atoms that were abstracted to form both alkoxyl

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(6) Vogel, E.; Altenbach, H.-J.; Sommerfeld, C.-D. *Angew. Chem., Int. Ed. Engl.* **1972**, *10*, 939−940.

(7) Chuang, S.-C.; Jarrosson, T.; Sander, M.; James, S.; Rozumov, E.; Khan, S. I.; Rubin, Y. Manuscript in preparation.

(8) A C_{3v}-tris-epoxide $C_{60}O_3$ has been postulated; see: Tajima, Y.; Takeuchi, K. *J. Org. Chem.* **2002**, *67*, 1696−1698.

(9) For reviews, see: (a) Feray, L.; Kuznetsov, N.; Renaud, P. *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol 2, pp 246−277. (b) Cekovic, Ž. *Tetrahedron* **2003**, *59*, 8073−8090.

(10) (a) Masutani, K.; Irie, R.; Katsuki, T. *Chem. Lett.* **2002**, *31*, 36−37. (b) Cardillo, B.; Cornia, M.; Merlini, L. *Gazz. Chim. Ital.* **1975**, *105*, 1151−1163.

(11) See the Supporting Information.

radicals (^{1}H NMR). We infer the presence of a lactone carbonyl group in **3** from its FT-IR (1780 cm^{-1}) and ^{13}C NMR (167.9 ppm) spectra. These data suggest that the initial β-cleavage of one alkoxyl radical fragmentation is followed by a rearrangement with concomitant oxygenation to produce the tentative structure **3**.[11] The ^{1}H, ^{13}C, HMBC, and HMQC NMR data are all consistent with the proposed structure.

Compound **4** possesses an epoxide moiety, as indicated by an additional oxygen atom in its mass spectrum (*m*/*z* 1156) and two oxygenated carbon atoms at 76.6 and 80.6 ppm in its ^{13}C NMR spectrum. Presumably, **4** arises from the epoxidation of **2**, most likely mediated by lead peroxides generated from adventitious O_2. The ^{1}H, ^{13}C, HMBC, and HMQC NMR data are all consistent with the proposed structure. The placement of the epoxide bond corresponds to the most reactive site of this framework.[14] It is noteworthy that we did not observe any products arising from α-hydrogen atom abstraction during the formation of **2**.[9]

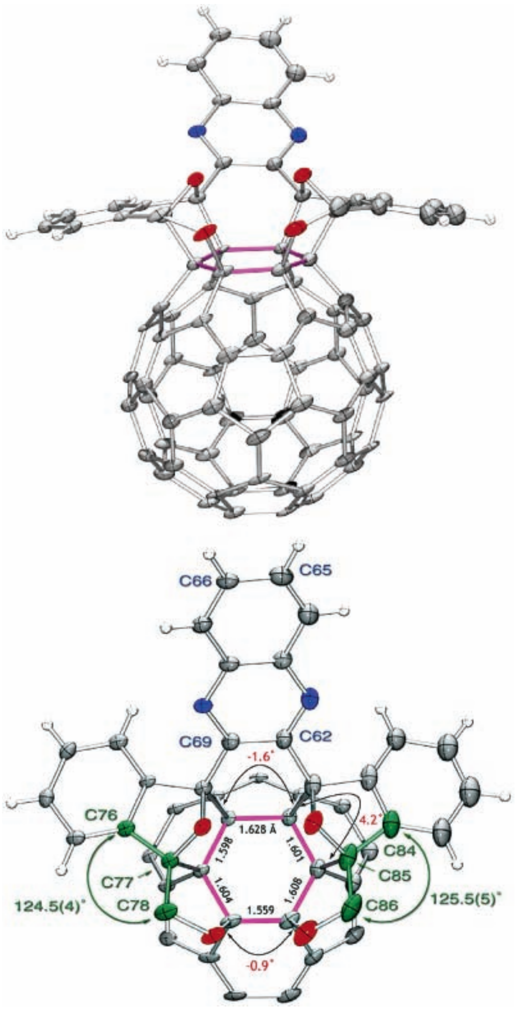

Figure 2. Two views of the structure of **2** in the crystal.

The successful synthesis of this first closed 1,2,3,4,5,6-hexaadduct of C_{60} (**2**) gave us the opportunity to reexamine the energetics of the sigmatropic [2 + 2 + 2] ring-opening reaction in fullerenes.[15] We investigated the origin of the stability of **2** toward ring opening at the B3LYP/6-31G*//PM3 level of theory by computing the energetics of two independent pathways.[16] The product **5o-2**, obtained by breaking the C−C bonds shared by the hexasubstituted six-membered ring and three adjacent five-membered rings, is 44.8 kcal/mol higher in energy than the closed form, **2** (Figure 3). This concerted retro-[2 + 2 + 2] cycloaddition is highly unfavorable: its energy barrier is 61.0 kcal/mol. The alternative open form, **6o-2**, is 61.3 kcal/mol higher in energy than **2** and possesses an even higher activation energy.

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(12) **Synthesis of Hexaadduct 2, Peroxide 3, and Epoxide 4.** $Pb(OAc)_4$ (264 mg, 0.600 mmol) was added to a solution of diol **1** (34 mg, 0.030 mmol, 10^{-5} M) in dry ODCB (3 L). The resulting mixture was stirred at room temperature for 24 h. The progress of the reaction was monitored by TLC. The reaction mixture was passed through a short plug of silica gel using CH_2Cl_2 as the eluent to remove most of the ODCB solvent. A dark brown solution was collected when CH_2Cl_2/EtOAc (1:1) was used as the eluent. The solvents were evaporated under reduced pressure. Flash chromatography was conducted using a gradient of EtOAc/toluene (from 0 to 20%) to obtain compounds **2**, **3**, and **4** in 25, 9, and 5% yields, respectively. Compound **2**: $R_f = 0.4$ (CH_2Cl_2/EtOAc, 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.22 (d, $J = 11.6$ Hz, 2H), 5.60 (d, $J = 11.6$ Hz, 2H), 7.21 (d, $J = 7.5$ Hz, 2H), 7.30 (t, $J = 7.5$ Hz, 2H), 7.45 (t, $J = 7.5$ Hz, 2H), 7.92−7.96 (m, 4H), 8.36 (dd, $J = 6.5, 3.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 65.32, 74.55, 83.73, 92.29, 96.53, 102.52, 119.95, 127.15, 127.74, 129.56, 130.00, 131.85, 134.46, 137.02, 137.19, 137.65, 138.46, 140.18, 140.96, 141.76, 141.79, 141.94, 142.88, 143.07, 143.26, 143.28, 143.30, 143.55, 143.61, 143.88, 144.15, 144.25, 144.41, 144.50, 144.88, 146.10, 146.60, 146.65, 146.68, 148.26, 148.59, 148.89, 149.24; FTIR (KBr) ν (cm^{-1}) 524, 754, 1049, 1459, 1514, 2851, 2916, 3045; HRMS (MALDI) calcd for $C_{86}H_{16}N_2O_4$ 1140.1110, found 1140.0373. Compound **3**: $R_f = 0.54$ (CH_2Cl_2/EtOAc, 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.33 (d, $J = 11.3$ Hz, 1H), 5.43 (d, $J = 11.3$ Hz, 1H), 7.26 (d, $J = 7.3$ Hz, 1H), 7.33 (td, $J = 7.4, 0.8$ Hz, 1H), 7.39 (td, $J = 7.5, 1.1$ Hz, 1H), 7.70 (td, $J = 7.4, 0.9$ Hz, 1H), 7.75 (td, $J = 7.6, 1.3$ Hz, 1H), 7.84 (td, $J = 8.4, 1.5$ Hz, 1H), 7.89 (td, $J = 8.4, 1.6$ Hz, 1H), 8.01 (d, $J = 8.1$ Hz, 2H), 8.03 (dd, $J = 7.6, 0.9$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.29 (dd, $J = 8.4, 1.2$ Hz, 1H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm) 66.47, 66.78, 75.85, 84.37, 84.62, 89.58, 94.65, 102.60, 119.64, 125.75, 127.32, 128.22, 130.01, 130.08, 130.29, 130.37, 130.75, 130.85, 131.90, 132.02, 132.05, 135.42, 135.50, 135.92, 138.09, 138.53, 139.05, 139.65, 140.32, 140.80, 141.26, 141.41, 141.57, 141.79, 142.29, 142.42, 142.46, 142.70, 142.76, 142.91, 143.14, 143.26, 143.43, 143.46, 143.51, 143.59, 143.68, 144.00, 144.13, 144.16, 144.40, 144.54, 144.60, 144.66, 144.83, 144.84, 145.08, 145.12, 145.58, 145.64, 145.85, 145.95, 146.78, 147.01, 147.47, 147.54, 147.76, 147.79, 147.81, 147.86, 148.37, 148.59, 149.19, 149.33, 149.53, 149.91, 167.87; FTIR (KBr) ν (cm^{-1}) 527, 748, 1030, 1067, 1260, 1461, 1506, 1780, 2852, 2917, 2950; HRMS (MALDI) calcd for $C_{85}H_{14}N_2O_4$ 1126.0954, found 1126.0460. Compound **4**: $R_f = 0.02$ (CH_2Cl_2/EtOAc, 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.06 (d, $J = 11.5$ Hz, 1H), 5.28 (d, $J = 11.5$ Hz, 1H), 5.35 (d, $J = 11.5$ Hz, 1H), 5.43 (d, $J = 11.5$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 2H), 7.22−7.23 (m, 1H), 7.28−7.35 (m, 3H), 7.72 (d, $J = 7.5$ Hz, 1H), 7.74 (d, $J = 7.5$ Hz, 1H), 7.90 (dd, $J = 6.4, 3.5$ Hz, 2H), 8.24 (dd, $J = 6.4, 3.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 64.68, 65.30, 72.05, 73.95, 76.56, 80.55, 81.96, 83.62, 89.47, 90.03, 95.66, 95.78, 102.07, 102.98, 119.48, 120.07, 126.81, 126.83, 127.17, 127.34, 129.01, 129.12, 129.77, 129.79, 131.46, 131.48, 133.52, 134.63, 135.99, 136.35, 137.23, 137.39, 137.54, 139.55, 140.67, 140.86, 141.04, 141.22, 141.56, 141.62, 141.81, 142.01, 142.22, 142.29, 142.46, 142.47, 142.79, 142.84, 142.86, 142.91, 143.85, 143.88, 143.95, 143.97, 144.30, 144.46, 144.57, 144.77, 144.83, 144.86, 144.89, 144.96, 145.01, 145.04, 145.05, 145.18, 145.90, 146.18, 146.21, 146.37, 146.64, 146.74, 147.46, 147.59, 147.75, 147.93, 148.16, 148.87, 148.97, 149.11, 149.21. HRMS (MALDI) calcd for $[M + Na]^+$ $C_{86}H_{16}N_2O_5Na$ 1179.0957, found 1179.0947.

(13) **X-ray data for 2:** red plates ($0.6 \times 0.1 \times 0.05$ mm^3) were grown from CS_2/benzene; space group $C2/c$; $a = 53.619(8)$ Å; $b = 12.361(2)$ Å; $c = 18.615(3)$ Å; $\beta = 108.317(2)°$; $V = 11713(3)$ Å^3; $Z = 8$; $T = 120$ K; N_{ref} (unique) = 14532; $R_1 = 0.123$; $R_w = 0.335$.

(14) Chuang, S.-C.; Rubin, Y. A full account of the reactivity of compound **1** toward cyclopropanation (Bingel reaction) will be reported elsewhere.

(15) Irle, S.; Rubin, Y.; Morokuma, K. *J. Phys. Chem. A* **2002**, *106*, 680−688.

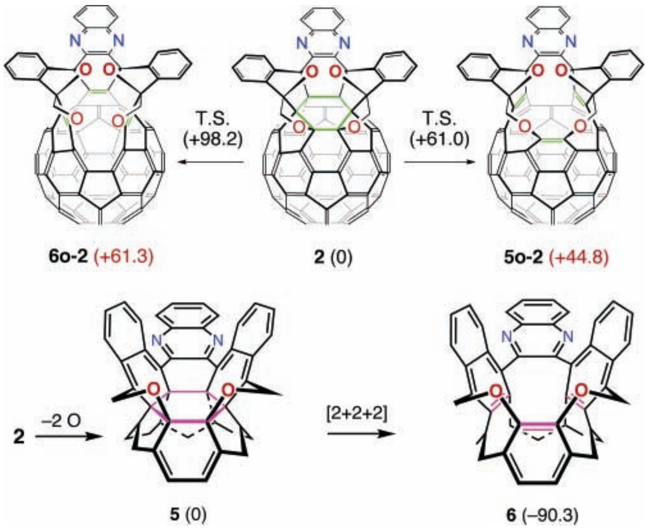

Figure 3. Calculated energies (kcal·mol^{-1}) of [5,6] vs [6,6] ring openings.

These results are consistent with our experimental observations. Interestingly, a significant factor affecting the ring opening process is that the pathway leading to **5o-2** generates two strained oxabenzonorbornadiene C═C bonds; i.e., the strained bicyclic nature of these two addends prevents the ring opening reaction. Deoxygenation, for example, into the *o*-quinodimethane intermediate **5**, should lead to [2 + 2 + 2] retrocycloaddition with high exothermicity (by 90.3 kcal/mol) to give the [5,6] open fullerene **6**, aromatization being the driving force.

In conclusion, we have achieved the first synthesis of a highly strained 1,2,3,4,5,6-hexaadduct of C_{60} and have computationally rationalized that its [2 + 2 + 2] ring opening is disfavored by high internal bond strain. We are currently investigating several routes for the deoxygenation of compound **2**.[17]

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Supporting Information Available: Spectral data for **2**−**4**; crystallographic information files (CIF) for **2**; Cartesian coordinates of all optimized structures and computed total energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Calculations were performed using Gaussian 98, revision A.9: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

(17) Preliminary results indicate that reductive opening of both epoxy bridges occurs under McMurry conditions: Chuang, S.-C.; Rubin, Y. Unpublished results.