

Lewis Acid-Assisted Nucleophilic Substitution of Fullerene Epoxide

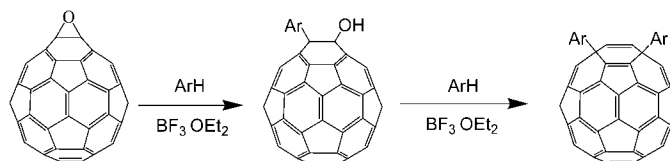
Yusuke Tajima,^{*,†} Takumi Hara,[‡] Takeshi Honma,[‡] Shiro Matsumoto,[‡] and Kazuo Takeuchi[†]

Nanomaterial Processing Laboratory, RIKEN, Hirosawa 2–1, Wako, Saitama 351-0198, Japan, and Graduate School of Science and Engineering, Saitama University, 255 Shimoohkubo, Saitama 338-8570, Japan

tajima@riken.jp

Received April 27, 2006

ABSTRACT



A 1,4-bis(phenyl)-1,4-dihydro[60]fullerene resulting from an efficient nucleophilic substitution has been obtained by reaction of a fullerene epoxide, C₆₀O, with nucleophilic aromatic compounds in the presence of boron trifluoride etherate as a Lewis acid.

Since fullerene epoxides were first detected, they have exhibited interesting properties applicable to new material development.^{1,2} They have also received attention for their possible application to the fields of electronic materials and biological sciences.^{3,4} The chemical transformation of fullerene epoxides, however, has scarcely been studied, despite the general recognition that they could serve as convenient starting materials for the synthesis of functionalized fullerene

derivatives.⁵ Recently, we succeeded in converting fullerene epoxides into 1,3-dioxolane derivatives arbitrarily.⁶ Reaction of a toluene solution of C₆₀O (**1**) with an excess amount of benzaldehyde in the presence of an *N*-(1-phenethyl)-2-cyanopyridinium salt as a Lewis acid led to the formation of a 1,3-dioxolane derivative of C₆₀ in a high yield. This implies the possibility of other nucleophilic substitutions of the epoxy rings on a fullerene cage. The chemical transformation of fullerene epoxide is expected to play an important role in the development of the functionalization of fullerenes because such transformations can readily afford a variety of mono- or polyfunctionalized fullerene derivatives with conservation of the epoxy ring arrangement on the fullerene surface, starting from regioisomeric fullerene polyepoxides. The recent development of the large-scale production of fullerene epoxide⁷ thus prompted us to develop a new methodology for the synthesis of polyfunctionalized fullerene derivatives by means of efficient chemical transformation of regioisomerically pure fullerene polyepoxides.⁸ Herein, we report on the efficient formation of 1,4-bisadducts from C₆₀O with aromatic nucleophilic compounds by Lewis acid-assisted nucleophilic substitution of the epoxy ring.

[†] Nanomaterial Processing Laboratory, RIKEN.

[‡] Saitama University.

(1) (a) Wood, J. M.; Kahr, B.; Hoke, S. H., II; Dejarme, L.; Cooks, R. G.; Ben-Amotz, D. *J. Am. Chem. Soc.* **1991**, *113*, 5907. (b) Creegan, K. M.; Robbins, J. L.; Robbins, W. K.; Millar, J. M.; Sherwood, R. D.; Tindall, P. J.; Cox, D. M. *J. Am. Chem. Soc.* **1992**, *114*, 1103.

(2) (a) Beck, R. D.; Brauchle, G.; Stroemer, C.; Kappes, M. M. *J. Chem. Phys.* **1995**, *102*, 540. (b) Winkler, K.; Costa, D. A.; Balch, A. L.; Fawcett, W. R. *J. Phys. Chem.* **1995**, *99*, 17431. (c) Lebedkin, S.; Ballenweg, S.; Gross, J.; Taylor, R.; Krätschmer, W. *Tetrahedron Lett.* **1995**, *36*, 4971. (d) Gromov, A.; Lebedkin, S.; Ballenweg, S.; Avent, A. G.; Taylor, R.; Krätschmer, W. *Chem. Commun.* **1997**, 209. (e) Gromov, A.; Ballenweg, S.; Giesa, S.; Lebedkin, S.; Hull, W. E.; Krätschmer, W. *Chem. Phys. Lett.* **1997**, *267*, 460. (f) Murray, R. W.; Iyyanar, K. *Tetrahedron Lett.* **1997**, *38*, 335. (g) Eisler, H.-J.; Hennrich, F. H.; Werner, E.; Hertwig, A.; Stoermer, C.; Kappes, M. M. *J. Phys. Chem. A* **1998**, *102*, 3889. (h) Kudo, T.; Akimoto, Y.; Shinoda, K.; Jeyadevan, B.; Tohji, K.; Nirasawa, T.; Waelchli, M.; Krätschmer, W. *J. Phys. Chem. B* **2002**, *106*, 4283.

(3) (a) Fedruco, M.; Costa, D. A.; Balch, A. L.; Fawcett, W. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 194. (b) Yang, S.-C.; Mieno, T. *Jpn. J. Appl. Phys., Part 1* **2001**, *40* (2B), 1067. (c) Zhai, R.-S.; Das, A.; Han, C.-C.; Canteenwala, T.; Chiang, L. Y.; Chuang, T. J. *J. Mater. Chem.* **2003**, *13*, 167.

(4) Li, J.; Takeuchi, A.; Yoshizawa, T.; Li, X.; Saigo, K.; Kitazawa, K. *Trans. Mater. Res. Soc. Jpn.* **1994**, 1185.

(5) Barrow, M. P.; Tower, N. J.; Taylor, R.; Drewello, T. *Chem. Phys. Lett.* **1998**, *293*, 302.

(6) Shigemitsu, Y.; Kaneko, M.; Tajima, Y.; Takeuchi, K. *Chem. Lett.* **2004**, *33* (12), 1604.

Reaction of a toluene solution of fullerene epoxide **1** in the presence of 5 equiv of boron trifluoride etherate ($\text{BF}_3 \cdot \text{OEt}_2$) at room temperature for 60 min led to the formation of 1,4-bis(*p*-tolyl)-1,4-dihydro[60]fullerene (**3a**) in 80.8% yield together with a very small amount of pristine fullerene C_{60} based on HPLC analysis. **3a** was purified by flash column chromatography on silica gel with *n*-hexane as an eluent.

A detailed spectral characterization of **3a** revealed that two *p*-tolyl moieties were introduced to the C_{60} core in a 1,4-addition pattern. The FT-IR spectrum is in good agreement with that in an earlier report.⁹ The characteristic vibrations for the 1,4-adduct were found at 1430, 1187, 573, and 527 cm^{-1} , and the C–H vibrations for toluene showed strong vibrations at 2963 and 810 cm^{-1} . The atmospheric pressure photochemical ionization (APPI) mass spectrum showed a molecular ion peak at m/z 902, which is 166 units more than **1**, corresponding to a 1:2 adduct of C_{60} and toluene–H. In the ^1H NMR spectrum, in addition to two doubles at 7.94 (2H), 7.93 (2H), 7.28 (2H), and 7.27 (2H) ppm for eight phenyl protons, one singlet methyl proton was observed at 2.46 (6H) ppm. The ^{13}C NMR showed the characteristic absorption of aromatic carbons in the *p*-tolyl group at 138.25 (2C), 136.91 (2C), 129.52 (4C), and 126.94 (4C) ppm, and two quaternary carbons of the C_{60} moiety were observed at 60.86 (2C) ppm. The UV–vis spectrum showed a characteristic absorption band around 450 nm. The 1,4-bisadduct structure for **3a** was evidently confirmed by comparing these spectra with FT-IR, ^1H NMR, and ^{13}C NMR spectra for the similar compounds.⁹

Reactions of **1** with other aromatic compounds under the same conditions as those described above were carried out, and the results are listed in Table 1. In anisole, *o*-xylene,

Table 1. Substitution of **1** with Aromatic Compounds

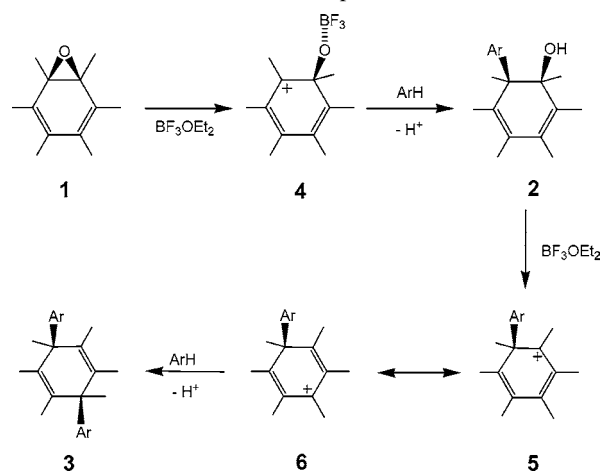
aromatic compound ^a	isolated yield of 2 (%) ^b	isolated yield of 3 (%) ^c
a toluene	0	80.8
b anisole	0	95.8
c <i>o</i> -xylene	0	76.5
d <i>m</i> -xylene	trace	45.3 ^d
e <i>p</i> -xylene	0	0
f 1,3,5-trimethylbenzene	35.3	trace
g chlorobenzene	0	0
h benzene	0	0

^a All reactions were performed according to the procedure described in the text. ^{b,c} All of the reactions were accomplished until the complete disappearance of the starting material **1**. ^d The overall yield of the structural isomeric mixture of the 1,4-adduct.

and *m*-xylene, the reaction produced the corresponding 1,4-bisadducts (**3b**, **3c**, and **3d**) in 45–95% yields, whereas

neither the 1,2- (**2e**) nor 1,4-bisadduct (**3e**) was produced in *p*-xylene. Purification of 1,4-bisadducts **3a**, **3b**, and **3c** was easily carried out with HPLC apparatus, but **3d** was not well-separated because of the formation of structural isomers. In the case of 1,3,5-trimethylbenzene, the corresponding 1-(substituted-phenyl)-2-hydroxyl-1,2-dihydro[60]fullerene (**2f**) was dominantly formed instead of a 1,4-bisadduct, as identified by UV–vis, APPI mass, ^1H , and ^{13}C NMR spectra. Usually, the sp^3 carbons of the C_{60} cage were observed to be shifted downfield ca. 10 ppm for the 1,2-adducts relative to those for the 1,4-adducts.⁹ The two peaks at 86.9 and 72.0 ppm for the two sp^3 carbons of the fullerene core in **2f** indicate a typical structure of a 1,2-adduct.⁹ This suggests that the 1,4-bisadduct formation from **1** proceeds stepwise via 1,2-adduct **2** as an intermediate. Actually, the formation of **2d** can be observed as a transient intermediate in the course of the reaction in *m*-xylene. With respect to the UV–vis spectrum beyond wavelengths of 300 nm, **2d** is identical with **2f**. The reaction in benzene and chlorobenzene scarcely proceeded even above 75 °C, and no product was observed. Thus, it appears that the progress of the reaction depends considerably on the nucleophilicity of the aromatic compound. In the absence of $\text{BF}_3 \cdot \text{OEt}_2$, no reaction was observed in any solvent. From this general behavior, it may be concluded that the first substitution of **1** to obtain **2** occurs via a carbocationic intermediate **4** generated with the assistance of the Lewis acid, followed by a nucleophilic attack of an aromatic compound on the cation. In the transformation of **2** into **3**, it is reasonable to assume that the substitution of the hydroxyl group proceeded by an $\text{S}_{\text{N}}1$ -type mechanism with allylic rearrangement as shown in Scheme 1.

Scheme 1. Proposed Mechanism for the Substitution of **1** with Aromatic Compounds^a



^a Part of the fullerene surface is shown.

Generally, the Lewis acid-assisted substitution of the epoxy group is considered to follow a concerted $\text{S}_{\text{N}}2$ -like mecha-

(7) The large-scale supply of fullerene epoxides is planned by Frontier Carbon Corporation in Japan.

(8) Tajima, Y.; Takeuchi, K. *J. Org. Chem.* **2002**, *67*, 1696.

nism involving a backside attack of a nucleophilic reagent on an epoxide carbon atom.¹⁰ However, such a backside attack on the fullerene epoxide is rather unrealistic because the fullerene cage occupies the entire side opposite the epoxy ring. The first substitution of the epoxy ring on a fullerene, therefore, would take place with an energetically unfavorable S_N1-like attack of a nucleophilic reagent on the carbocation generated by the C–O bond cleavage of the epoxy ring. On the other hand, the second substitution for **2** might take place by an S_N2'-type mechanism, in which the nucleophilic attack on the residual hydroxyl group can occur first, followed by the elimination of –OH on the side that has an allylic rearrangement.¹¹ The fact that no reaction proceeded in the absence of the Lewis acid catalyst suggests that the second substitution occurs by an S_N1-type mechanism with allylic rearrangement, where **3** is formed via carbocationic intermediates **5** and **6** with an allylic resonance,¹² generated with the assistance of BF₃·OEt₂. No formation of a 1,2-bis-(substituted-phenyl)adduct was observed in any of the cases, presumably because of the steric hindrance between two substituents.

Electrochemical data for the first three reductions of C₆₀, **1**, **3a**, and **3b** are given in Table 2, and Figure 1 shows

Table 2. Half-Wave Potentials^a of C₆₀, C₆₀O, and 1,4-Adducts by Cyclic Voltammetry

compound	first	second	third
C ₆₀	–0.85	–1.23	–1.68
1	–0.81	–1.34	–1.69
3a	–0.91	–1.30	–1.77
3b	–0.90	–1.30	–1.76

^a V vs Ag/AgCl. (n-Bu)₄NPF₆ (0.1 M) in 1,2-dichlorobenzene. Scan rate = 100 mV/s. Solutions were deaerated by an N₂ purge prior to the experiments.

multicyclic voltammograms of **3a** and **3b** in 1,2-dichlorobenzene containing 0.1 M (n-Bu)₄NPF₆. Both 1,4-adducts exhibit three well-defined, reversible electroreductions between 0.0 and –2.0 V by multi-CV, as opposed to the irreversible reduction of fullerene epoxide **1**.^{2b} The first reduction potentials of the 1,4-adducts are shifted to a

(9) (a) Chen, Z.-X.; Wang, G.-W. *J. Org. Chem.* **2005**, *70*, 2380. (b) Kadish, K. M.; Gao, X.; Caemelbecke, E. V.; Suenobu, T.; Fukuzumi, S. *J. Phys. Chem. A* **2000**, *104*, 3878.

(10) Blackett, B. N.; Coxon, J. M.; Hartshorn, M. P.; Lewis, A. J.; Little, G. R.; Wright, G. J. *Tetrahedron* **1970**, *26*, 1311.

(11) Bordwell, F. G. *Acc. Chem. Res.* **1970**, *3*, 281.

(12) (a) Reed, C. A.; Kim, K.-C.; Bolskar, R. D.; Mueller, L. *J. Science* **2000**, *289*, 101. (b) Mueller, L. J.; Elliott, D. W.; Kim, K.-C.; Reed, C. A.; Boyd, P. D. W. *J. Am. Chem. Soc.* **2002**, *124*, 9360. (c) Kitagawa, T.; Sakamoto, H.; Takeuchi, K. *J. Am. Chem. Soc.* **1999**, *121*, 4298. (d) Murata, Y.; Cheng, F.; Kitagawa, T.; Komatsu, K. *J. Am. Chem. Soc.* **2004**, *126*, 8874. (e) Kitagawa, T.; Yangsoo, Lee.; Hanamura, M.; Sakamoto, H.; Konno, H.; Takeuchi, K.; Komatsu, K. *Chem. Commun.* **2002**, 3062.

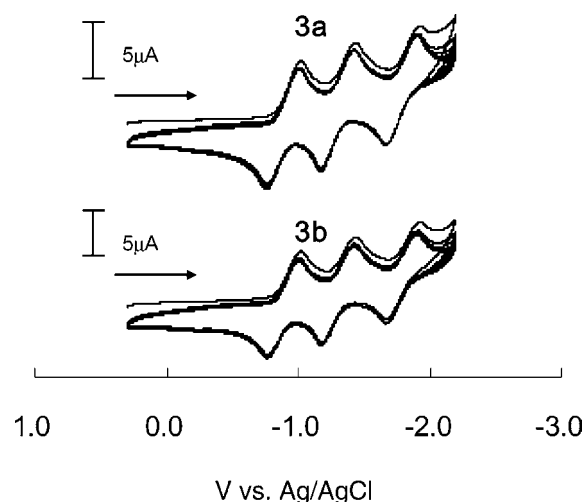


Figure 1. Multicyclic voltammogram of **3a** and **3b** at 500 mV/s in 1,2-dichlorobenzene containing 0.1 M (n-Bu)₄NPF₆.

negative potential by ca. 100 mV relative to that of **1** as a starting material and are more negative than C₆₀. The electrochemical behaviors of **3a** and **3b** are analogous to those of some comparable 1,4-adducts previously reported.^{9b,13} The shifts relative to C₆₀ in the second and third reduction peaks of **3a** and **3b** are more negative than those of the first reduction peaks. The difference between nucleophilic substituents has little influence on the electrochemistry of the 1,4-bisadduct.

In conclusion, the present study has shown that the reaction of C₆₀O with the nucleophilic aromatic compound in the presence of BF₃·OEt₂ gave the 1,4-bisadduct of C₆₀ in excellent yields. The results indicate that the reaction proceeds via 1,2-adduct formation by a Lewis acid-assisted S_N1-type mechanism with allylic rearrangement. The direct substitution of an epoxide oxygen atom on a fullerene epoxide, a versatile and advantageous synthetic methodology reported here, provides highly regioselective access to a variety of fullerene adducts.

Acknowledgment. Thanks are due to Frontier Carbon Co. for assisting in the preparation of fullerene epoxides. Very helpful discussions with Dr. Yasujiro Murata (Kyoto University), Dr. Mikio Hoshino (RIKEN), and Mr. Hiroki Osedo (Toray) are also gratefully acknowledged.

Supporting Information Available: Experimental procedures and NMR, UV–vis, and MS spectra for new compounds **2f**, **3a**, **3b**, and **3c**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL0610183

(13) Ford, W. T.; Nishioka, T.; Qiu, F.; D'Souza, F.; Choi, J. *J. Org. Chem.* **2000**, *65*, 1071.