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1,4-Fullerenols C_{60}ArOH: Synthesis and Functionalization

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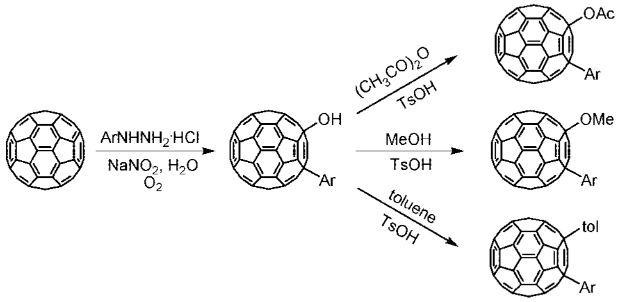
ABSTRACT



A mild and facile process for the preparation of 1,4-fullerenols C_{60}ArOH was achieved. The key intermediate 1,2-C_{60}Ar(NO_2) was identified to better understand the reaction mechanism. Further functionalizations including esterification, etherification, and arylation of the synthesized 1,4-C_{60}ArOH provided efficient access to versatile fullerene derivatives in the presence of *p*-toluenesulfonic acid.

Fullerenols consisting of 14−20 hydroxy moieties were first synthesized by Chiang et al. using nitronium chemistry[1] or aqueous acid reaction.[2] Other methods for the polyhydroxylation of fullerenes involved the hydrolysis of a fullerene intermediate formed through aqueous base reaction,[3] oleum,[4] nitrogen dioxide radicals,[5] or hydroboration.[6] These synthesized fullerenols were a mixture of fullerene compounds with different numbers of hydroxy groups and different chemical structures. In fact, the fullerenols prepared by the aqueous acid reaction of [60]fullerene (C_{60}) in the presence of sulfuric acid and potassium nitrate/nitric acid contained hemiketal moieties.[2b] In comparison, the fullerenols prepared by the $C_{60(\text{toluene})}$/$NaOH_{(\text{aq.})}$/TBAH method were structurally and electronically complex C_{60} radical anions with a molecular formula of $Na^{+}{}_{n}[C_{60}O_x(OH)_y]^{n-}$ (where $n = 2−3$, $x = 7−9$, and $y = 12−15$).[7] The synthesis of more structurally defined fullerenol with multiple addends was first achieved by Taylor and co-workers.[8] They treated $C_{70}Cl_{10}$ with benzene/$FeCl_3$ and obtained a minor product of fullerenol $C_{70}Ph_9OH$. Fullerenols $C_{60}Me_5OOH$, $C_{60}Me_5O_2OH$, and $C_{60}Me_4PhOOH$ were synthesized by the reaction of C_{60} with methyllithium[9] or the reaction of $C_{60}Cl_6$ with methyllithium followed by

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(1) Chiang, L. Y.; Upasani, R. B.; Swirczewski, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 10154.

(2) (a) Chiang, L. Y.; Swirczewski, J. W.; Hsu, C. S.; Chowdhury, S. K.; Cameron, S.; Creegan, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1791. (b) Chiang, L. Y.; Upasani, R. B.; Swirczewski, J. W.; Soled, S. *J. Am. Chem. Soc.* **1993**, *115*, 5453.

(3) Li, J.; Takeuchi, A.; Ozawa, M.; Li, X.; Saigo, K.; Kitazawa, K. *J. Chem. Soc., Chem. Commun.* **1993**, 1784.

(4) (a) Chiang, L. Y.; Wang, L.-Y.; Swirczewski, J. W.; Soled, S.; Cameron, S. *J. Org. Chem.* **1994**, *59*, 3960. (b) Chen, B.-H.; Huang, J.-P.; Wang, L. Y.; Shiea, J.; Chen, T.-L.; Chiang, L. Y. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1171. (c) Chen, B.-H.; Canteenwala, T.; Patil, S.; Chiang, L. Y. *Synth. Commun.* **2001**, *31*, 1659.

(5) Chiang, L. Y.; Bhonsle, J. B.; Wang, L.; Shu, S. F.; Chang, T. M.; Hwu, J. R. *Tetrahedron* **1996**, *52*, 4963.

(6) Schneider, N. S.; Darwish, A. D.; Kroto, H. W.; Taylor, R.; Walton, D. R. M. *J. Chem. Soc., Chem. Commun.* **1994**, 463.

(7) Husebo, L. O.; Sitharaman, B.; Furukawa, K.; Kato, T.; Wilson, L. J. *J. Am. Chem. Soc.* **2004**, *126*, 12055.

(8) Birkett, P. R.; Avent, A. G.; Darwish, A. D.; Kroto, H. W.; Taylor, R.; Walton, D. R. M. *J. Chem. Soc., Chem. Commun.* **1996**, *10*, 1231.

(9) Al-Matar, H.; Hitchcock, P. B.; Avent, A. G.; Taylor, R. *Chem. Commun.* **2000**, *35*, 1071.

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hydrolysis.[10] Starting from fullerene peroxides with multiple OO^{t}Bu groups, Gan and co-workers have prepared a variety of closed-cage and open-cage fullerenols with at least one hydroxy group and/or hemiketal moiety.[11] The simplest fullerene diols $C_{60}(OH)_2$ and $C_{70}(OH)_2$ were prepared by the reaction of C_{60} and C_{70} with RuO_4 followed by acid hydrolysis.[12]

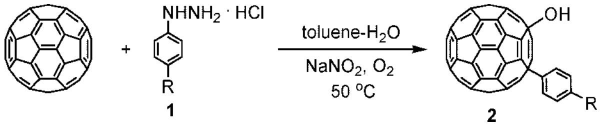
Monohydroxylated fullerenols with the general form of $C_{60}ROH$ are much less investigated, and only a few such compounds have been isolated and characterized until now.[13−17] Iyoda and co-workers synthesized $C_{60}R_FOH$ by the reaction of C_{60} with $(R_FCO)_2O$.[13] Irngartinger et al. prepared 1,2-$C_{60}(CN)OH$ via N−O bond cleavage of [60]fullereno[1,2*d*]isoxazole,[14] which was generated by the addition of fulminic acid to C_{60}.[18] Kitagawa et al. described the formation of fullerenols 1,4-$C_{60}ROH$ (R = $CHCl_2$, CCl_2CH_2Cl) from the hydrolysis of chlorofullerenes.[15] Tajima and co-workers recently reported the synthesis of 1-hydroxyl-2-(1,3,5-trimethylphenyl)-1,2-dihydro[60]fullerene (1,2-$C_{60}ArOH$) by the nucleophilic substitution of $C_{60}O$ in the presence of $BF_3{\cdot}Et_2O$.[16] More recently, Tuktarov et al. described the preparation of 1,2-$C_{60}HOH$ by the reaction of C_{60} with water catalyzed with Cp_2MCl_2.[17] Evidently, much more monohydroxylated fullerenols $C_{60}ROH$ with different functional groups and addition patterns are demanded due to their scarcity and the utility of the hydroxy group.[14−17]

In our earlier work, we reported that the reaction of C_{60} with 4-substituted phenylhydrazine hydrochlorides in refluxing chlorobenzene afforded 1-(4-substituted phenyl)-1,2-dihydro[60]fullerenes (1,2-$C_{60}ArH$).[19] Interestingly, we recently found that upon the addition of sodium nitrite ($NaNO_2$) the above reaction under moisture and aerobic conditions unexpectedly afforded 1-hydroxyl-4-(4-substituted phenyl)-1,4-dihydro[60]fullerenes (1,4-$C_{60}ArOH$). In this letter, we report this novel result and further transformation of the 1,4-$C_{60}ArOH$ into other versatile fullerene derivatives by esterification, etherification, and arylation.

Our recent work on the solvent-free reaction of C_{60} with an arylhydrazine hydrochloride and $NaNO_2$ under mechanical milling conditions, which led to the formation of a fullerotriazoline compound ($C_{60}ArN_3$),[20] promoted us to investigate the corresponding liquid-phase reaction. Surprisingly, the reaction of C_{60} (36.0 mg, 0.05 mmol) with 4-substituted phenylhydrazine hydrochlorides **1a−d** (0.1 mmol) and $NaNO_2$ (6.9 mg, 0.1 mmol) in a mixture of toluene (25 mL) and H_2O (1 mL) at 50 °C under air atmosphere afforded fullerenols 1,4-$C_{60}ArOH$, instead of $C_{60}ArN_3$ or 1,2-$C_{60}ArH$.

The reaction conditions and yields for the reaction of C_{60} with 4-substituted phenylhydrazine hydrochlorides **1a−d** and $NaNO_2$ leading to 1,4-$C_{60}ArOH$ **2a−d** are listed in Table 1.

Table 1. Reaction Conditions and Yields for the Reaction of C_{60} with **1a−d** and $NaNO_2$[a]



product	R	reaction time (h)	yield[b]	recovered C_{60}
2a	CH_3	6	18%	59%
2b	CH_3O	6	19%	69%
2c	H	6	14%	50%
2d	Cl	12	20%	64%

[a] All reactions were performed in toluene−H_2O solution (v/v, 25:1) in air at 50 °C; molar ratio of C_{60}:**1**:$NaNO_2$ = 1:2:2. [b] Isolated yield.

As can be seen from Table 1, 4-substituted phenylhydrazine hydrochlorides with both electron-donating and electron-withdrawing groups on the phenyl ring could be employed in this reaction. Higher reaction temperature resulted in decreased product yields.

1,4-Fullerenols **2a−d** were fully characterized by HRMS, ^{1}H NMR, ^{13}C NMR, FT-IR, and UV−vis spectra. The 1,4-addition pattern was established by the typical broad peak at around 440 nm in their UV−vis spectra. Further evidence for the assignment of **2a−d** as 1,4-adducts came from the ^{13}C NMR spectra, which had at least 46 peaks for the sp^2-carbons of the C_{60} skeleton, consistent with their C_1 symmetry.

1,2-Fullerenols $C_{60}ArOH$ carrying only bulky aryl groups could be isolated from the nucleophilic substitution of $C_{60}O$ with a bulky arene such as 1,3,5-trimethylbenzene in the presence of $BF_3{\cdot}Et_2O$.[16] In contrast, our synthesized fullerenols are another type of products, i.e., 1,4-adducts, and a bulky aryl group was not required.

It should be noted that all of the sodium nitrite, water, and oxygen in the system played crucial roles for the successful synthesis of 1,4-fullerenols **2a−d**. In an attempt to neutralize the HCl in phenylhydrazine hydrochlorides, other bases such as NEt_3, pyridine, 4-dimethylaminopyridine, aq NaOH, and aq K_2CO_3 were used to replace $NaNO_2$ in the above reaction. However, none or only trace amounts of 1,4-$C_{60}ArOH$ along with some unidentified products could be obtained in any of these cases. The reaction in anhydrous toluene at 50 °C under air atmosphere afforded only 1,2-$C_{60}ArH$, with the products just the same as those at higher temperature[19] yet in much lower yields. Nevertheless, the

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(10) Al-Matar, H.; Abdul-Sada, A. K.; Avent, A. G.; Fowler, P. W.; Hitchcock, P. B.; Rogers, K. M.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2.* **2002**, 53.

(11) For selected examples, see: (a) Huang, S.; Xiao, Z.; Wang, F.; Gan, L.; Zhang, X.; Hu, X.; Zhang, S.; Lu, M.; Pan, Q.; Xu, L. *J. Org. Chem.* **2004**, *69*, 2442. (b) Xiao, Z.; Yao, J.; Yang, D.; Wang, F.; Huang, S.; Gan, L.; Jia, Z.; Jiang, Z.; Yang, X.; Zheng, B.; Yuan, G.; Zhang, S.; Wang, Z. *J. Am. Chem. Soc.* **2007**, *129*, 16149. (c) Yao, J.; Xiao, Z.; Gan, L.; Yang, D.; Wang, Z. *Org. Lett.* **2008**, *10*, 2003.

(12) Meier, M. S.; Kiegiel, J. *Org. Lett.* **2001**, *3*, 1717.

(13) Yoshida, M.; Morinaga, Y.; Iyoda, M.; Kikuchi, K.; Ikemoto, I.; Achiba, Y. *Tetrahedron Lett.* **1993**, *34*, 7629.

(14) Irngartinger, H.; Weber, A. *Tetrahedron Lett.* **1997**, *38*, 2075.

(15) Kitagawa, T.; Sakamoto, H.; Takeuchi, K. *J. Am. Chem. Soc.* **1999**, *121*, 4298.

(16) Tajima, Y.; Hara, T.; Honma, T.; Matsumoto, S.; Takeuchi, K. *Org. Lett.* **2006**, *8*, 3203.

(17) Tuktarov, A. R.; Akhmetov, A. R.; Pudas, M.; Ibragimov, A. G.; Dzhemilev, U. M. *Tetrahedron Lett.* **2008**, *49*, 808.

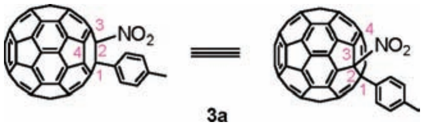
(18) Imgartinger, H.; Weber, A.; Esther, T. *Liebigs Ann.* **1996**, 1845.

(19) Chen, Z.-X.; Wang, G.-W. *J. Org. Chem.* **2005**, *70*, 2380.

(20) Chen, Z.-X.; Zhu, B.; Wang, G.-W. *Lett. Org. Chem.* **2008**, *5*, 65.

presence of water would lead to 1,4-C_{60}ArOH at the expense of 1,2-C_{60}ArH. When more than 0.5 mL of water was added, the formation of 1,2-C_{60}ArH was completely suppressed. When the reaction was conducted under a nitrogen atmosphere and otherwise the same conditions, no 1,4-C_{60}ArOH was produced, indicating that oxygen was indispensable.

The thin-layer chromatography (TLC) monitoring of the reaction showed that a less polar product was formed at the early stage of the reaction but disappeared at the end of the reaction. We surmised that this product was probably the precursor of 1,4-C_{60}ArOH. Fortunately, we managed to isolate the product (14%) along with 1,4-fullerenol **2a** (9%) from the reaction of C_{60} with **1a** in a shorter reaction time (2 h). The product proved to be 1-(4-methylphenyl)-2-nitro-1,2-dihydro[60]fullerene (**3a**) (Figure 1) by detailed spectral characterization.



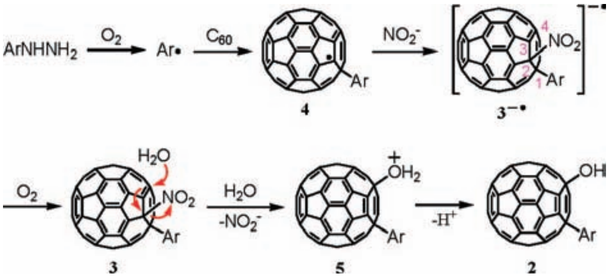
3a

Figure 1. Structure of **3a**.

The HRMS (+ESI) of **3a** gave a peak at 880.0387 for $C_{67}H_7NNaO_2^+$, corresponding to the $[M + Na]^+$ peak. In the IR spectrum of **3a**, the strong absorptions at 1556, 1341, and 805 cm^{-1}, which were close to 1572, 1328, and 815 cm^{-1} for the nitro group in polynitrofullerenes,[5] exhibited the existence of the nitro group rather than the nitrite group. In the ^{13}C NMR spectrum of **3a**, there were 25 peaks with some overlapping ones in the range of 153−134 ppm for the sp^2 carbons of the fullerene skeleton, accompanied with the peaks at 106 and 69 ppm for the two sp^3 carbons of the fullerene cage. These ^{13}C NMR data are fully consistent with its molecular structure with a C_s symmetry. The 1,2-addition pattern of product **3a** was obvious in its UV−vis spectrum, which showed a characteristic sharp peak at 420 nm. Nitrofullerene **3a** represents the first example of the fully characterized and structurally defined fullerene compounds with the nitro group directly attached to the fullerene cage, even though polynitrofullerenes $C_{60}(NO_2)_n$ as a mixture[5] and a multiadduct of C_{60} bearing a ONO_2 group[11a] have been reported.

On the basis of the above experimental results, a plausible reaction mechanism for the formation of 1,4-C_{60}ArOH is shown in Scheme 1. The first two steps leading to fullerenyl radicals **4** are the same as the previously proposed ones.[19] The addition of the nitrite anion to radicals **4** results in radical anions $\mathbf{3}^{-\bullet}$, which are oxidized, presumably by oxygen, to the neutral products **3**. The attack of H_2O at the C4 position of **3** with the leaving of the nitrite anion via a S_N2' mechanism gives intermediates **5**, and subsequent loss of proton generates 1,4-fullerenols **2**. Similar S_N2' processes on the fullerene cage have been reported.[4a,21] The proposed mechanism shown in Scheme 1 perfectly explains why fullerenols **2** were formed as 1,4-adducts from 1,2-adducts **3**. The proposed conversion of **3** to **2** was substantiated by the fact that **2a** was obtained in 43% yield by treating **3a** in toluene/water at 50 °C for 36 h. However, other alternative pathways cannot be ruled out. For example, the first step might also be oxidized by $NaNO_2$; the $NO_2^{\bullet}$radical could be formed in the reaction mixture and adds to the radical intermediates **4**.

Scheme 1. Proposed Reaction Mechanism



Fullerenols have great synthetic potential due to the hydroxyl group. Esterification was first attempted by the reaction of 1,4-fullerenol **2a** with acetic acid employing DCC/DMAP (1:2:2:0.2) under a nitrogen atmosphere.[14] The reaction in toluene/acetonitrile (v/v, 9:1) for 72 h at room temperature afforded only 25% of the desired **6a**. The DMAP-catalyzed reaction of **2a** with acetic anhydride (Ac_2O, 100 equiv) in pyridine at 110 °C for 8 h[17] gave only a trace of **6a** along with a mixture of polar unidentified products. The above two conditions[14,17] were reported to be effective for the esterification of 1,2-fullerenols. These results may indicate that a 1,4-fullerenol is less reactive than a 1,2-fullerenol.

Fortunately, we found that the acetylation of 1,4-fullerenol **2a** as well as its analogues **2b**−**d** worked very well with Ac_2O in the presence of *p*-toluenesulfonic acid (TsOH). The reaction conditions and product yields for acetoxylated fullerenes **6a**−**d** along with recovered fullerenols **2a**−**d** are listed in Table 2. The esterification reaction was efficient and gave products **6a**−**d** in 64−82% yields after 6 h. The identities for products **6a**−**d** were evidently confirmed by comparing their spectral data with the reported ones.[19]

The etherification of fullerenols **2a**−**d** with methanol could be realized by TsOH in a mixture of solvents. The reaction conditions and product yields for methoxylated fullerenes **7a**−**d** along with recovered fullerenols **2a**−**d** are listed in Table 3. It is noteworthy that **7a** could also be obtained in 71% yield by treating **3a** with methanol at 50 °C for 36 h, further supporting the last two steps in Scheme 1.

The arylation of fullerenols **2a**−**d** with toluene could also be successfully achieved in the presence of TsOH. The reaction conditions and product yields of the arylated fullerenes **8a**−**d** along with recovered **2a**−**d** are listed in Table 4. It should be pointed out that the two aryl groups

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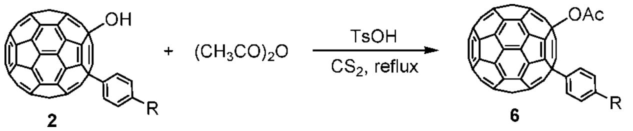
(21) Avent, A. G.; Abdul-Sada, A. K.; Clare, B. W.; Kepert, D. L.; Street, J. M.; Taylor, R. *Org. Biomol. Chem.* **2003**, *1*, 1026.

Table 2. Reaction Conditions and Yields for the Acetylation of Fullerenols **2a−d** in the Presence of TsOH[a]



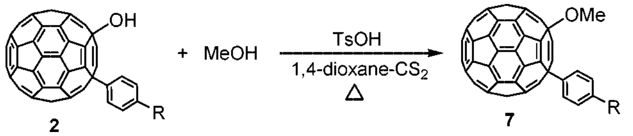
product	R	reaction time (h)	yield[b]	recovered fullerenol
6a	CH_3	6	74%	11%
6b	CH_3O	6	70%	23%
6c	H	6	82%	7%
6d	Cl	6	64%	23%

[a] All reactions were performed in CS_2 at an oil bath temperature of 80 °C; molar ratio of **2**:Ac_2O:TsOH = 1:2:2. [b] Isolated yield.

must be the same in the 1,4-$C_{60}(Ar)_2$ products prepared by the Lewis acid-assisted nucleophilic substitution of $C_{60}O$.[16] However, the 1,4-C_{60}(Ar)Ar′ products with two different aryl groups could be achieved by our protocol.

The structures of products **7a−d** and **8a−d** were fully established by their MS, ^{1}H NMR, ^{13}C NMR, FT-IR, and UV−vis spectra. All etherified and arylated fullerenes **7a−d** and **8a−d** are 1,4-adducts, which are supported by the peak at ca. 440 nm in their UV−vis spectra and the C_1 molecular symmetry deduced from their ^{13}C NMR spectra except for **8a**. Due to the same two addends, 1,4-adduct **8a** showed much fewer peaks (31 peaks) for the sp^2 carbons along with one peak at 60 ppm for the two sp^3 carbons of the C_{60} cage in its ^{13}C NMR spectrum, agreeing with its C_2 symmetry. It is noteworthy that the δ_c value for the sp^3 carbon of C_{60} attached to the oxygen atom was close to each other in **2a−d** (ca. 74 ppm), **6a−d** (76−78 ppm[19]), and **7a−d** (79−80 ppm), but the corresponding sp^3 carbon was upfield shifted by more than 14 ppm in **8a−d** (ca. 60 ppm) because of the addend change to an aryl group.

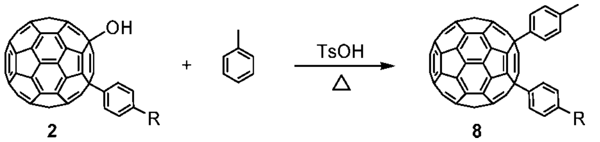
Table 3. Reaction Conditions and Yields for the Methoxylation of Fullerenols **2a−d** in the Presence of TsOH[a]



product	R	reaction time (h)	yield[b]	recovered fullerenol
7a	CH_3	60	26%	47%
7b	CH_3O	60	46%	39%
7c	H	60	37%	50%
7d	Cl	50	44%	46%

[a] All reactions were performed in 1,4-dioxane-CS_2-MeOH solution (v/v/v, 2:1:1) at an oil bath temperature of 100 °C; molar ratio of **2**:TsOH = 1:5. [b] Isolated yield.

Table 4. Reaction Conditions and Yields for the Arylation of Fullerenols **2a−d** in the Presence of TsOH[a]



product	R	reaction time (h)	yield[b]	recovered fullerenol
8a	CH_3	10	71%	7%
8b	CH_3O	12	53%	16%
8c	H	2	62%	11%
8d	Cl	2	66%	13%

[a] All reactions were performed in toluene at an oil bath temperature of 80 °C; molar ratio of **2**:TsOH = 1:5. [b] Isolated yield.

Fullerenyl cation intermediates have been produced by dissolving 1,4-C_{60}ROH (R = $CHCl_2$, CCl_2CH_2Cl) in CF_3SO_3H[15] or by treating 1,2-C_{60}ArOH with BF_3•Et_2O.[16] We believe that the esterification, etherification, and arylation of fullerenols **2a−d** in the presence of TsOH should also proceed through the formation of the corresponding fullerenyl carbocations, followed by the reaction with Ac_2O, MeOH, and toluene. TsOH was preferred in our protocol because it was cheap and environmentally friendly and showed high efficiency for all three transformations.

In summary, 1,4-fullerenols C_{60}ArOH were synthesized via the reaction of [60]fullerene with 4-substituted phenylhydrazine hydrochlorides and sodium nitrite under moisture and aerobic conditions at 50 °C. The key and unprecedented intermediate $C_{60}Ar(NO_2)$ was isolated and characterized. A possible mechanism for the formation of 1,4-fullerenols involving $C_{60}Ar(NO_2)$ via a S_N2' pathway was proposed. Further transformations of the 1,4-fullerenols through esterification, etherification, and arylation were also carried out in the presence of *p*-toluenesulfonic acid.

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Supporting Information Available: Detailed experimental procedures and characterization data, as well as the ^{1}H NMR and ^{13}C NMR spectra of **2a−d**, **3**, **7a−d**, and **8a−d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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