

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

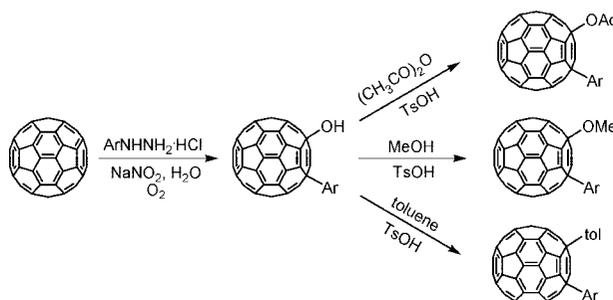
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ABSTRACT



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 chemistry¹ 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 $C_{60}(\text{toluene})/NaOH_{(aq.)}/TBAH$ 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 fullereneol 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 fullereneol $C_{70}Ph_9OH$. Fullerenols $C_{60}Me_5OOH$, $C_{60}Me_5O_2OH$, and $C_{60}Me_4PhOOH$ were synthesized by the reaction of C_{60} with methyllithium⁹ or the reaction of $C_{60}Cl_6$ with methyllithium followed by

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hydrolysis.¹⁰ Starting from fullerene peroxides with multiple OO^tBu groups, Gan and co-workers have prepared a variety of closed-cage and open-cage fullereneols with at least one hydroxy group and/or hemiketal moiety.¹¹ The simplest fullerene diols C₆₀(OH)₂ and C₇₀(OH)₂ were prepared by the reaction of C₆₀ and C₇₀ with RuO₄ followed by acid hydrolysis.¹²

Monohydroxylated fullereneols with the general form of C₆₀ROH are much less investigated, and only a few such compounds have been isolated and characterized until now.^{13–17} Iyoda and co-workers synthesized C₆₀R_FOH by the reaction of C₆₀ with (R_FCO)₂O.¹³ Irgartinger et al. prepared 1,2-C₆₀(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 C₆₀.¹⁸ Kitagawa et al. described the formation of fullereneols 1,4-C₆₀ROH (R = CHCl₂, CCl₂CH₂Cl) 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-C₆₀ArOH) by the nucleophilic substitution of C₆₀O in the presence of BF₃·Et₂O.¹⁶ More recently, Tuktarov et al. described the preparation of 1,2-C₆₀HOH by the reaction of C₆₀ with water catalyzed with Cp₂MCl₂.¹⁷ Evidently, much more monohydroxylated fullereneols C₆₀ROH with different functional groups and addition patterns are demanded due to their scarcity and the utility of the hydroxy group.^{14–17}

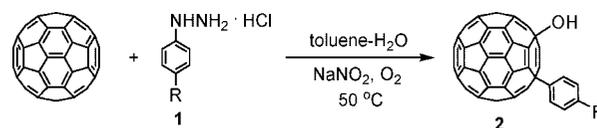
In our earlier work, we reported that the reaction of C₆₀ with 4-substituted phenylhydrazine hydrochlorides in refluxing chlorobenzene afforded 1-(4-substituted phenyl)-1,2-dihydro[60]fullerenes (1,2-C₆₀ArH).¹⁹ Interestingly, we recently found that upon the addition of sodium nitrite (NaNO₂) the above reaction under moisture and aerobic conditions unexpectedly afforded 1-hydroxyl-4-(4-substituted phenyl)-1,4-dihydro[60]fullerenes (1,4-C₆₀ArOH). In this letter, we report this novel result and further transformation of the 1,4-C₆₀ArOH into other versatile fullerene derivatives by esterification, etherification, and arylation.

Our recent work on the solvent-free reaction of C₆₀ with an arylhydrazine hydrochloride and NaNO₂ under mechanical milling conditions, which led to the formation of a fullerotriazolone compound (C₆₀ArN₃),²⁰ promoted us to investigate the corresponding liquid-phase reaction. Surprisingly, the

reaction of C₆₀ (36.0 mg, 0.05 mmol) with 4-substituted phenylhydrazine hydrochlorides **1a–d** (0.1 mmol) and NaNO₂ (6.9 mg, 0.1 mmol) in a mixture of toluene (25 mL) and H₂O (1 mL) at 50 °C under air atmosphere afforded fullereneols 1,4-C₆₀ArOH, instead of C₆₀ArN₃ or 1,2-C₆₀ArH.

The reaction conditions and yields for the reaction of C₆₀ with 4-substituted phenylhydrazine hydrochlorides **1a–d** and NaNO₂ leading to 1,4-C₆₀ArOH **2a–d** are listed in Table 1.

Table 1. Reaction Conditions and Yields for the Reaction of C₆₀ with **1a–d** and NaNO₂^a



product	R	reaction time (h)	yield ^b	recovered C ₆₀
2a	CH ₃	6	18%	59%
2b	CH ₃ O	6	19%	69%
2c	H	6	14%	50%
2d	Cl	12	20%	64%

^a All reactions were performed in toluene–H₂O solution (v/v, 25:1) in air at 50 °C; molar ratio of C₆₀:**1**:NaNO₂ = 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, ¹H NMR, ¹³C 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 ¹³C NMR spectra, which had at least 46 peaks for the sp²-carbons of the C₆₀ skeleton, consistent with their C₁ symmetry.

1,2-Fullerenols C₆₀ArOH carrying only bulky aryl groups could be isolated from the nucleophilic substitution of C₆₀O with a bulky arene such as 1,3,5-trimethylbenzene in the presence of BF₃·Et₂O.¹⁶ In contrast, our synthesized fullereneols 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 NEt₃, pyridine, 4-dimethylaminopyridine, aq NaOH, and aq K₂CO₃ were used to replace NaNO₂ in the above reaction. However, none or only trace amounts of 1,4-C₆₀ArOH 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-C₆₀ArH, with the products just the same as those at higher temperature¹⁹ yet in much lower yields. Nevertheless, the

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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.

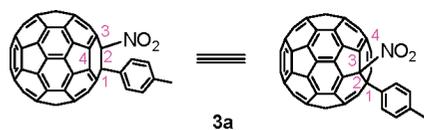
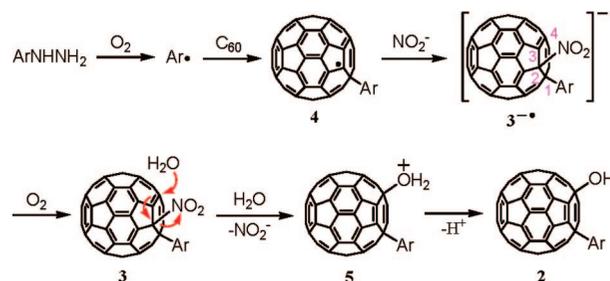


Figure 1. Structure of **3a**.

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 mixture⁵ 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 fullerenylic radicals **4** are the same as the previously proposed ones.¹⁹ The addition of the nitrite anion to radicals **4** results in radical anions **3^{-•}**, 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

Scheme 1. Proposed Reaction Mechanism



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 $NO_2^•$ radical could be formed in the reaction mixture and adds to the radical intermediates **4**.

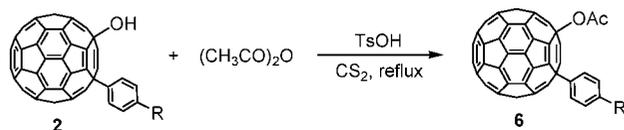
Fullerenols have great synthetic potential due to the hydroxyl group. Esterification was first attempted by the reaction of 1,4-fullerenol **2a** with acetic acid employing DCC/DMAP (1:2:2:0.2) under a nitrogen atmosphere.¹⁴ The reaction in toluene/acetonitrile (v/v, 9:1) for 72 h at room temperature 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 h¹⁷ 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 acetoxyated 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 methoxyated 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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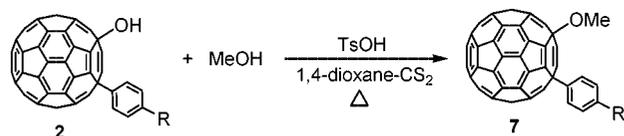
Table 2. Reaction Conditions and Yields for the Acetylation of Fullerenols **2a–d** in the Presence of TsOH^a

product	R	reaction time (h)	yield ^b	recovered fullereneol
6a	CH ₃	6	74%	11%
6b	CH ₃ O	6	70%	23%
6c	H	6	82%	7%
6d	Cl	6	64%	23%

^a All reactions were performed in CS₂ at an oil bath temperature of 80 °C; molar ratio of **2**:Ac₂O:TsOH = 1:2:2. ^b Isolated yield.

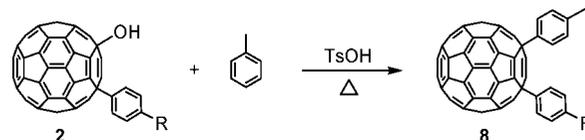
must be the same in the 1,4-C₆₀(Ar)₂ products prepared by the Lewis acid-assisted nucleophilic substitution of C₆₀O.¹⁶ However, the 1,4-C₆₀(Ar)Ar' products with two different aryl groups could be achieved by our protocol.

The structures of products **7a–d** and **8a–d** were fully established by their MS, ¹H NMR, ¹³C 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 C₁ molecular symmetry deduced from their ¹³C NMR spectra except for **8a**. Due to the same two addends, 1,4-adduct **8a** showed much fewer peaks (31 peaks) for the sp² carbons along with one peak at 60 ppm for the two sp³ carbons of the C₆₀ cage in its ¹³C NMR spectrum, agreeing with its C₂ symmetry. It is noteworthy that the δ_c value for the sp³ carbon of C₆₀ attached to the oxygen atom was close to each other in **2a–d** (ca. 74 ppm), **6a–d** (76–78 ppm¹⁹), and **7a–d** (79–80

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 fullereneol
7a	CH ₃	60	26%	47%
7b	CH ₃ O	60	46%	39%
7c	H	60	37%	50%
7d	Cl	50	44%	46%

^a All reactions were performed in 1,4-dioxane-CS₂-MeOH solution (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 fullereneol
8a	CH ₃	10	71%	7%
8b	CH ₃ O	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.

ppm), but the corresponding sp³ carbon was upfield shifted by more than 14 ppm in **8a–d** (ca. 60 ppm) because of the addend change to an aryl group.

Fullerenyl cation intermediates have been produced by dissolving 1,4-C₆₀ROH (R = CHCl₂, CCl₂CH₂Cl) in CF₃SO₃H¹⁵ or by treating 1,2-C₆₀ArOH with BF₃·Et₂O.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 Ac₂O, 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 C₆₀ArOH 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 C₆₀Ar(NO₂) was isolated and characterized. A possible mechanism for the formation of 1,4-fullerenols involving C₆₀Ar(NO₂) 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 ¹H NMR and ¹³C 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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