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Synthesis and Functionalization of [60]Fullerene-Fused Imidazolines

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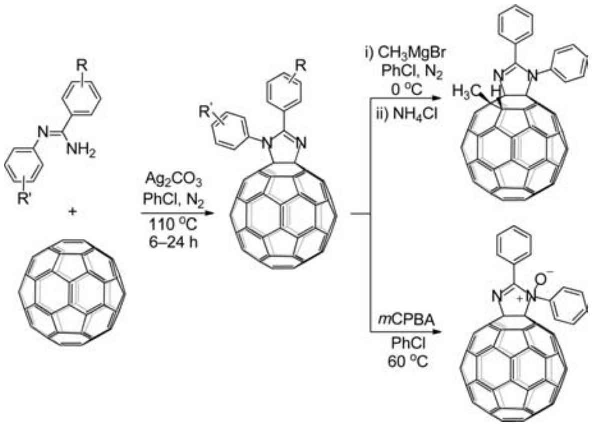
ABSTRACT



The silver carbonate promoted reaction of [60]fullerene with (*Z*)-*N*-arylbenzamidines afforded the unprecedented C_{60}-fused imidazoline derivatives in high yields. Substrates with both electron-donating and -withdrawing groups on aromatic rings could be employed. In addition, the electrochemistry and further selective functionalization of the obtained C_{60}-fused imidazolines were investigated.

Owing to potential applications in materials, medical chemistry, and nanotechnology,[1] various methodologies have been explored to functionalize fullerenes, and a large number of fullerene products have been prepared over the past two decades.[2] Transition-metal-mediated reactions of [60]fullerene (C_{60}) have attracted increasing attention. Although various reactions of C_{60} mediated by $Mn(OAc)_3$[3] and $Fe(ClO_4)_3$[4] have been reported, the utilization of other transition metal salts including silver salts in the radical reactions of fullerenes is underdeveloped.[5] In our previous work, we found that $Fe(ClO_4)_3$ could efficiently promote the radical reactions of C_{60} and afforded C_{60}-fused oxazolines,[6] dioxolanes,[7] and dioxaborolanes,[8] where an oxygen and a nitrogen atom or two oxygen atoms are connected to the C_{60} cage. Herein, we disclose that silver carbonate can promote the radical reaction of C_{60} with

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(1) For selected reviews, see: (a) Nakamura, E.; Isobe, H. *Acc. Chem. Res.* **2003**, *36*, 807. (b) Guldi, D. M.; Illescas, B. M.; Atienza, C. M.; Wielopolski, M.; Martín, N. *Chem. Soc. Rev.* **2009**, *38*, 1587. (c) Vougioukalakis, G. C.; Roubelakis, M. M.; Orfanopoulos, M. *Chem. Soc. Rev.* **2010**, *39*, 817.

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(3) For reviews, see: (a) Wang, G.-W.; Li, F.-B. *J. Nanosci. Nanotechnol.* **2007**, *7*, 1162. (b) Wang, G.-W.; Li, F.-B. *Curr. Org. Chem.* **2012**, *16*, 1109.

(4) For a review, see: Li, F.-B.; Wang, G.-W. *Sci. China Chem.* **2012**, *55*, 2009.

(5) AgOAc has been employed in the catalytic enantioselective 1,3-dipolar cycloadditions of fullerenes; see: (a) Filippone, S.; Maroto, E. E.; Martín-Domenech, Á.; Suarez, M.; Martín, N. *Nat. Chem.* **2009**, *1*, 578. (b) Maroto, E. E.; de Cózar, A.; Filippone, S.; Martín-Domenech, Á.; Suarez, M.; Cossío, F. P.; Martín, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 6060.

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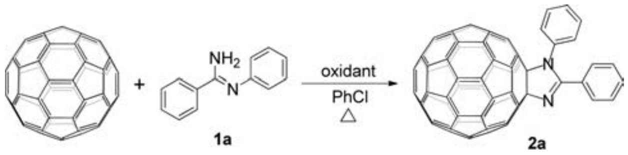
10.1021/ol400319w

(*Z*)-*N*-arylbenzamidines to provide C_{60}-fused imidazolines, in which two nitrogen atoms are attached to the fullerene moiety. In addition, further selective functionalization of the obtained C_{60}-fused imidazolines by a Grignard reagent and 3-chloroperbenzoic acid (*m*CPBA) is demonstrated.

At the outset of our studies, the Ag_2CO_3-promoted reaction of C_{60} with (*Z*)-*N*-phenylbenzamidines (**1a**) was chosen to screen the reaction conditions. The reaction of C_{60} with **1a** and Ag_2CO_3 in a molar ratio of 1:1:1 at 110 °C for 10 h gave **2a** in 10% yield (Table 1, entry 1). Increasing the amount of Ag_2CO_3 to 2 equiv provided **2a** in 24% yield (Table 1, entry 2). An additional increase of **1a** to 2 equiv resulted in a 42% yield (Table 1, entry 3). When the molar ratio was enhanced to 1:3:2, the product yield could be further improved to 56% (Table 1, entry 4). It was found that an inert atmosphere was important, as the reaction in open air or an oxygen atmosphere significantly decreased the product yield (Table 1, entries 5 and 6).

Table 1. Optimization of the Reaction Conditions of C_{60} with **1a**[a]



entry	oxidant	molar ratio[b]	temp (°C)	time (h)	yield (%)[c]
1	Ag_2CO_3	1:1:1	110	10	10 (100)
2	Ag_2CO_3	1:1:2	110	10	24 (92)
3	Ag_2CO_3	1:2:2	110	10	42 (75)
4	**Ag_2CO_3**	**1:3:2**	**110**	**10**	**56 (95)**
5[d]	Ag_2CO_3	1:3:2	110	10	18 (50)
6[e]	Ag_2CO_3	1:3:2	110	10	17 (37)
7	Ag_2CO_3	1:3:3	110	10	55 (72)
8	Ag_2CO_3	1:4:2	110	10	54 (66)
9	Ag_2CO_3	1:3:2	90	10	18 (100)
10	Ag_2CO_3	1:3:2	130	10	54 (63)
11	Ag_2CO_3	1:3:2	110	8	46 (87)
12	Ag_2CO_3	1:3:2	110	12	51 (67)
13	AgOAc	1:3:2	110	10	8 (38)
14	Ag_2O	1:3:2	110	10	40 (75)
15	$Mn(OAc)_3 \cdot 2H_2O$	1:3:2	110	10	12 (71)
16	$Cu(OAc)_2 \cdot H_2O$	1:3:2	110	10	14 (50)
17	$FeCl_3 \cdot 6H_2O$	1:3:2	110	10	4 (80)

[a] All reactions were carried out under a nitrogen atmosphere unless otherwise indicated. [b] Molar ratio refers to C_{60}/**1a**/oxidant. [c] Isolated yield; the values in parentheses were based on consumed C_{60}. [d] The reaction was carried out in open air, and **1a** was recovered in 96% yield when C_{60} was omitted from the system under the same conditions. [e] The reaction was carried out under an oxygen atmosphere, and **1a** was recovered in 98% yield when C_{60} was omitted from the system under the same conditions.

Increasing the amount of either **1a** or Ag_2CO_3 further was not beneficial to achieve a higher yield, yet more C_{60} was consumed (Table 1, entries 7 and 8). When the temperature was lowered to 90 °C, **2a** was obtained in only 18% yield (Table 1, entry 9). When the temperature was increased to 130 °C, the yield dropped slightly to 54% accompanied by more byproducts (Table 1, entry 10). Shortening or prolonging the reaction time led to a lower yield (Table 1, entries 11 and 12). The efficiency of other silver salts was also examined. Ag_2O and AgOAc could promote the reaction, but both of them gave an inferior yield compared to Ag_2CO_3 (Table 1, entries 13 and 14). Disappointingly, when $Mn(OAc)_3 \cdot 2H_2O$, $Cu(OAc)_2 \cdot H_2O$, or $FeCl_3 \cdot 6H_2O$ was employed as the oxidant, **2a** was isolated in much lower yields (Table 1, entries 15–17). Therefore, the molar ratio of 1:3:2 for the regents C_{60}, **1a**, and Ag_2CO_3 and the temperature of 110 °C in chlorobenzene under a nitrogen atmosphere were chosen as the optimized reaction conditions (Table 1, entry 4).

With the optimized conditions in hand, we started to investigate the scope of the reaction. We were pleased to find that (*Z*)-*N*-arylbenzamidines (**1a**–**g**) with both electron-donating and -withdrawing groups could be employed and furnished the desired [60]fullereoimidazolines **2a**–**g** in 42–59% isolated yields, higher than those of most monoadducts. (*Z*)-*N*-Arylbenzamidines bearing a methyl, chlorine, or methoxy group in both aryl rings could undergo the Ag_2CO_3-promoted cycloaddition reaction to C_{60}. Intriguingly, ortho-substituted substrates proceeded well and even provided higher product yields (Table 2, entries 3 and 5). In addition, the chlorine group in products **2c**, **2d**, and **2g** (Table 2, entries 3, 4, and 7) may be used as a handle for coupling reactions.

The structures of C_{60}-fused imidazolines **2a**–**g** were fully established by their MALDI-TOF MS, ^1H NMR, ^{13}C NMR, IR, and UV–vis spectra. All products **2a**–**g** exhibited correct molecular weights in their mass spectra. The ^{13}C NMR spectra of **2a**–**g** except **2c** clearly exhibited no more than 30 peaks in the range of 134–149 ppm for the sp^2-carbons of the fullerene cage and two peaks at 85–87 and 93–94 ppm for the two sp^3-carbons of the fullerene skeleton, consistent with the C_s symmetry of their molecular structures. However, because of the steric hindrance of Cl at the ortho position, the ^{13}C NMR spectrum of **2c** exhibited 45 peaks for the sp^2-carbons of the fullerene skeleton, along with two peaks for the two sp^3-carbons of C_{60} cage, agreeing with its C_1 symmetry. The chemical shifts for the two C_{60} sp^3-carbons of **2a**–**g** are close to those of fullerene derivatives with the nitrogen atom attached to the C_{60} skeleton.[6,9] The typical chemical shifts at 163–164 ppm in the ^{13}C NMR spectra indicated the presence of the amidine moiety. The UV–vis spectrum of all products showed a peak at 427–428 nm, which is the characteristic peak for 1,2-adducts of C_{60}.

Although the exact pathway leading to **2a**–**g** remains to be clarified, a plausible mechanism is outlined in Scheme 1. First, the reaction of *N*-arylbenzimidamide **1** with Ag_2CO_3 generates **3**, which undergoes homolytic cleavage of the nitrogen–silver bond to provide radical species **4**. A similar Cu-catalyzed process was recently reported.[10]

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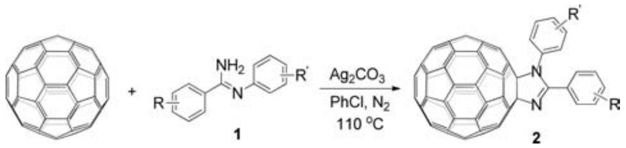
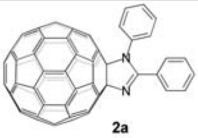
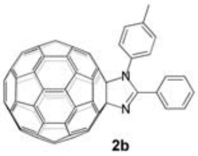
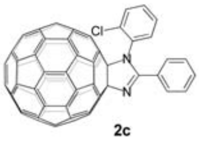
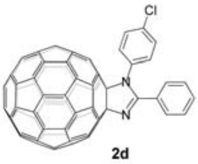
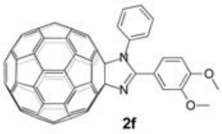
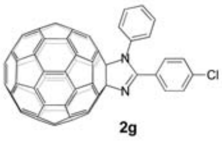
(10) Wang, Y.-F.; Zhu, X.; Chiba, S. *J. Am. Chem. Soc.* **2012**, *134*, 3679.

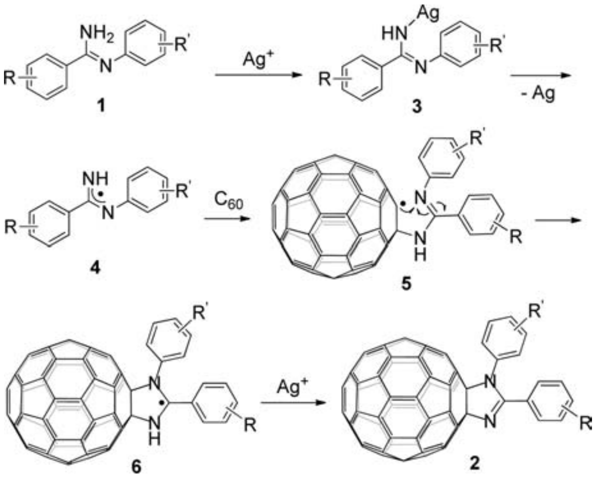
Table 2. Reaction Conditions and Yields for the Reaction of C_{60} with **1a**−**g** in the Presence of Ag_2CO_3[a]



entry	product	time (h)	yield of **2** (%)[b]	recovered C_{60}
1	 **2a**	10	56 (95)	41
2	 **2b**	12	49 (80)	39
3	 **2c**	10	59 (76)	22
4	 **2d**	24	44 (71)	38
5	 **2e**	6	56 (74)	24
6	 **2f**	18	47 (85)	45
7	 **2g**	24	42 (75)	44

[a] All reactions were carried out at 110 °C under a nitrogen atmosphere with a molar ratio of C_{60}/**1**/Ag_2CO_3 = 1:3:2. [b] Isolated yield; the values in parentheses were based on consumed C_{60}.

Scheme 1. Proposed Reaction Mechanism for the Formation of **2a**−**g**



The radical addition of **4** to C_{60} will give fullerenyl radical **5**. Alternatively, the intermediate **5** may also be formed by the homolytic addition of **3** to C_{60}.[6] Intramolecular cyclization of **5** produces radical **6**.

Although the addition of a carbon-centered radical to the N-terminus of the C=N bond is rare, the formed radical in **6** is stabilized by two nitrogen substituents and a phenyl group.[11] Oxidation of radical **6** by another Ag^+ species with the loss of H^+ affords **2**. Therefore, 2 molar equiv of Ag(I) were required, and the molar ratio of C_{60}/**1a**/Ag_2CO_3 = 1:3:2 was used to achieve higher conversions and product yields. However, the concerted [3 + 2] annulation process of amidines to C_{60} via a nitrene intermediate cannot be excluded.[10]

Table 3 shows the half-wave reduction potentials of products **2a**−**g** together with C_{60}. The first reduction potentials are generally shifted anodically by ca. 100 mV for most monoadducts of C_{60}. However, the E^1 of **2a**−**g** showed a smaller negative shift (30−50 mV) relative to that of C_{60}, due to the two attached heteroatoms.[9d,12] Therefore, fullereoimidazolines **2a**−**g** may be utilized as low-lying LUMO acceptors in organic photovoltaic devices by choosing appropriate donor material.[12]

Table 3. Half-Wave Reduction Potentials of **2a**−**g** Along with C_{60}[a]

compd	E^1	E^2	E^3
C_{60}	−1.077	−1.456	−1.911
2a	−1.117	−1.493	−2.013
2b	−1.119	−1.493	−2.013
2c	−1.114	−1.493	−2.016
2d	−1.111	−1.485	−1.997
2e	−1.114	−1.490	−2.010
2f	−1.124	−1.504	−2.026
2g	−1.116	−1.498	−2.018

[a] Potential in V versus a ferrocene/ferrocenium couple. Experiment conditions: 0.20 mM of **2a**−**g**/C_{60} and 0.1 M of *n*-Bu_4NClO_4 in anhydrous *o*-dichlorobenzene; reference electrode: SCE; working electrode: Pt; auxiliary electrode: Pt wire; scanning rate: 50 mV s^{-1}.

Further functionalization of the synthesized fullereoimidazolines was also attempted by using **2a** as a representative compound. After **2a** was treated with CH_3MgBr in chlorobenzene at 0 °C for 5 min and subsequently quenched by NH_4Cl, the regioselective product **7a** with a

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(11) Friestad, G. K. *Tetrahedron* **2001**, *57*, 5461.

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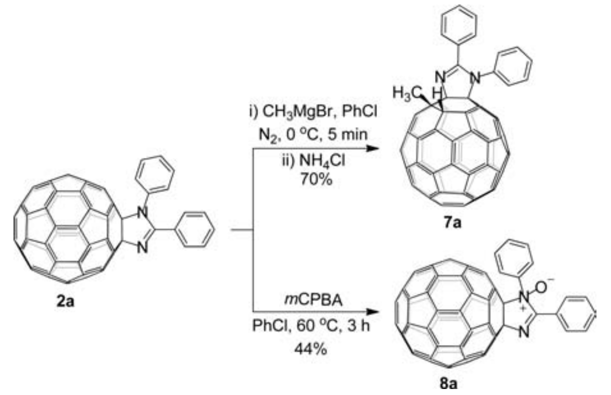
Scheme 2. Further Functionalization of **2a**



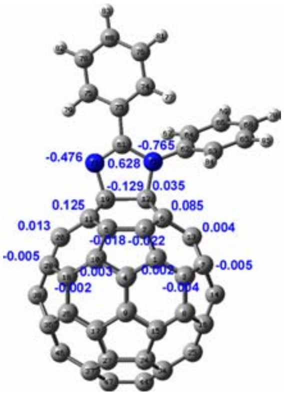
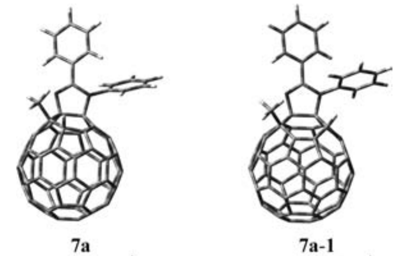


Figure 1. Partial NBO charge distribution of **2a**.

1,2,3,4-configuration was isolated in 70% yield (Scheme 2). In the ^1H NMR spectrum of **7a**, two singlets for the methyl group and fullerenyl proton were located at 2.71 and 5.94 ppm besides those for the two phenyl groups. The ^{13}C NMR of **7a** exhibited 53 peaks in the 152−129 ppm range for the sp^2-carbons of the fullerene skeleton and four peaks at 87.46, 82.98, 59.58, and 57.39 ppm for the four sp^3-carbons of the C_{60} cage. The amidino carbon showed little chemical shift compared to that of **2a**, suggesting that it remained unchanged. The UV−vis spectrum of **7a** exhibited the typical feature of fullerene products with a 1,2,3,4-configuration (see Figure S1 in the Supporting Information).[13] To better understand the regioselectivity for the Grignard addition reaction, the NBO charge distribution of **2a** was calculated at the B3LYP/3-21G* level. As shown in Figure 1, the fullerenyl carbon with a positive charge of +0.125 should be the site of attack by CH_3MgBr.



7a
0.0 kJ·mol^{-1}

7a-1
28.6 kJ·mol^{-1}

Figure 2. Optimized structures and relative energies of **7a** and its regioisomer **7a-1**.

The protonation of the formed fullenenyl anion could afford **7a** or its regioisomer **7a-1**. The introduction of an unfavorable [5,6] double bond in isomeric **7a-1** would increase its formation energy.

Indeed, theoretical calculations at the B3LYP/3-21G* level showed that **7a** was more stable than **7a-1** by 28.6 kJ·mol^{-1} (Figure 2). It should be pointed out that although the amidino carbon atom had the largest positive charge of +0.628, the Grignard reagent did not attack the C=N bond. The addition mode of CH_3MgBr to C_{60}-fused imidazolines here is different from that to C_{60}-fused lactones, which underwent either a reductive ring opening[14] or addition to the C=O bond of the lactone moiety.[15]

Furthermore, the nitroxide **8a** could be prepared in 44% yield after treatment of **2a** with *m*CPBA at 60 °C for 3 h. Product **8a** was also fully characterized. The addition of the oxygen atom to **2a** lowered the symmetry from C_s to C_1, and thus the ^{13}C NMR of **8a** exhibited 52 peaks for the sp^2-carbons of the fullerene cage in the range of 149−135 ppm. The δ_C of the amidino carbon that was located at 162.96 ppm indicated that the oxygenation did not occur at the C=N bond. This result was supported by the calculated larger negative density at the nitrogen atom bearing the phenyl group (−0.765) compared to the imino nitrogen atom (−0.476) (Figure 1).

In summary, Ag_2CO_3 has been successfully applied to the radical reaction of C_{60} with (*Z*)-*N*-arylbenzamidines affording unprecedented C_{60}-fused imidazolines. [60]-Fulleroimidazolines can be further functionalized to give regioisomeric products with a 1,2,3,4-configuration or nitroxide products, which would be difficult to synthesize by existing methods.

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Supporting Information Available. Experimental procedures, spectral data, spectra, and computation details. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.