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CuI-Catalyzed Oxidative [3 + 2] Reaction of Fullerene with Amidines or Amides Using Air as the Oxidant: Preparation of Fulleroimidazole or Fullerooxazole Derivatives

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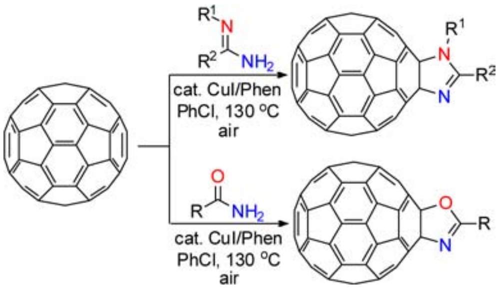
ABSTRACT



CuI-catalyzed oxidative reaction of amidines with C_{60} using air as the oxidant has been exploited for the easy preparation of fulleroimidazole derivatives. Furthermore, this kind of CuI-catalyzed [3 + 2] reaction has also been successfully applied in the synthesis of fullerooxazole derivatives starting from amides for the first time. The substrate scope is broad, and the process is particularly cheap and simple.

A great diversity of modifications of the fullerene spheroid has attracted the attention of many researchers, which allows the design of new promising fullerene-based materials with unique biological and technological properties. Numerous efforts for chemical modification of fullerenes have been made over the past two decades, involving various [2 + *n*] (*n* = 1−4) cycloadditions, radical additions, nuclophilic additions, and multiadditions.[1] The 1,3-dipolar cycloaddition reaction is one of the most used methodologies to construct five-membered ring-fused [60]fullerene derivatives containing one or two heteroatoms. Fulleroisoxazoles and fulleropyrazoles can be easily prepared from the reaction of C_{60} with the *in situ* generated nitrile oxide and nitrilimine, respectively.[2] Generally, most of the [60]fullerene derivatives possess poorer electron affinity than the pristine C_{60} due to the partial loss of conjugation, which raises the LUMO energy.[3] Fulleroimidazoles and fullerooxazoles, as isomers of fulleropyrazoles and fulleroisoxazoles, proved to have better electron acceptor character than C_{60} due to the presence of two electronegative atoms directly linked to the C_{60} core, which is beneficial for the preparation of a wide variety of organic photovoltaic devices. However, there were only a few reports on their preparation up to now. Photochemical reactions of C_{60} with acylazides[4] or rearrangement of the fulleroaziridines generated from the thermal reactions of

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(1) For books, see: (a) Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2005. (b) Langa, F.; Nierengarten, J.-F. *Fullerenes: Principles and Applications*; RSC Publishing: Cambridge, U.K., 2007.

(2) Perez, L.; El-Khouly, M. E.; de la Cruz, P.; Araki, Y.; Ito, O.; Langa, F. *Eur. J. Org. Chem.* **2007**, 2175–2185. (b) Yang, H.-T.; Ruan, X.-J.; Miao, C.-B.; Sun, X.-Q. *Tetrahedron Lett.* **2010**, *51*, 6056–6059. (c) Illescas, B. M.; Martín, N. *J. Org. Chem.* **2000**, *65*, 5986–5995.

(3) Echegoyen, L.; Echegoyen, L. E. *Acc. Chem. Res.* **1998**, *31*, 593–601.

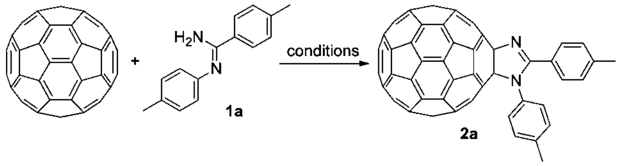
(4) Averdung, J.; Mattay, J.; Jacobi, D.; Abraham, W. *Tetrahedron* **1995**, *51*, 2543–2552.

10.1021/ol401909z

C_{60} with azidoformates or hydroxamic acid derivatives[5] is the earlier method to synthesize fullerooxazoles. Recently, the Gao group reported an electrochemical method for the preparation of fullerooxazoles through aerobic oxidations of dianionic C_{60} in PhCN solution.[6] The Wang and Minakata groups developed a one-step approach starting from nitriles or amides mediated by $Fe(ClO_4)_3 \cdot 6H_2O$[7] or *t*-BuOI,[8] respectively. We also developed a $PhI(OAc)_2/I_2$-mediated [3 + 2] reaction of C_{60} with amides for the preparation of fullerooxazoles.[9] As for the fulleroimidazoles, only the Wang group reported their preparation through the silver carbonate promoted reaction of [60]fullerene with *N*-arylbenzamidines.[10] Nevertheless, these reactions have some limitations. The reaction of C_{60} with acylazides always produces the azafulleroid as a byproduct. Furthermore, the azides are classified as highly explosive and toxic. The electrochemical method always results in some serious side reactions, which dramatically decreases its practicability. Wang's method needs an excessive amount of nitriles up to 100 equiv. Silver carbonate is an expensive reagent, and a stoichiometric amount is needed. In continuation of our interest in fullerene chemistry,[11] herein, we reported the CuI-catalyzed oxidative reaction of C_{60} with amidines or amides using air as the oxidant for the easy preparation of fulleroimidazole or fullerooxazole derivatives.

Copper-mediated inter- or intramolecular reactions of β-enamino carbonyl compounds could afford various azaheterocycles.[12] Stimulated by the structural analogy of amidines with enamine carboxylates, the Chiba group developed a copper-catalyzed intramolecular aerobic [3 + 2]-annulation reaction of *N*-alkenyl amidines for the preparation of bi- and tricyclic amidines.[13] Most recently, the Neuville and Chen groups reported the copper-catalyzed reaction of the amidines with terminal alkynes or nitroalkenes for the preparation of polysubstituted imidazoles, respectively.[14] Inspired by their results, we envisioned that similar oxidative processes could occur through Cu(*n*)-mediated aerobic reactions of C_{60} with amidines, which would lead to the formation of fulleroimidazole derivatives.

Table 1. Screening of the Reaction Conditions[a]



entry	Cu	ligand	[C_{60}/**1a**/Cu/L]	time (h)	yield (%)[b]
1	CuI	none	1:3:3:0	10	6 (85)
2	CuBr	none	1:3:3:0	10	trace
3	CuCl	none	1:3:3:0	10	0
4	$CuCl_2$	none	1:3:3:0	10	trace
5	$CuBr_2$	none	1:3:3:0	10	trace
6	$Cu(OAc)_2 \cdot H_2O$	none	1:3:3:0	10	trace
7	$Cu(OTf)_2$	none	1:3:3:0	10	0
8	CuI	pyridine	1:3:3:3	10	8 (81)
9	CuI	Bpy	1:3:3:3	10	13 (77)
10	CuI	TMDEA	1:3:3:3	10	14 (80)
11	CuI	PMDETA	1:3:3:3	10	trace
12	CuI	Phen	1:3:3:3	10	37 (75)
13	CuI	Phen	1:3:0.3:0.3	10	35 (84)
14[c]	CuI	Phen	1:3:0.3:0.3	24	9 (90)
15	CuI	Phen	1:2:0.2:0.2	10	27 (79)
16	CuI	Phen	1:2:0.4:0.4	10	34 (86)
17[d]	CuI	Phen	1:2:0.4:0.4	10	0

[a] All the reactions were carried out with 0.05 mmol of C_{60}, 0.1 mmol of **1a**, and proper additives in 10 mL of chlorobenzene at 130 °C under air unless specified otherwise. [b] Isolated yield; the values in parentheses are based on consumed C_{60}. [c] The reaction was operated at 70 °C. [d] The reaction was carried out under a nitrogen atmosphere.

We began our investigation with the reaction between C_{60} and *N*-(*p*-tolyl)-4-methylbenzamidine (**1a**) in the presence of different copper reagents (Table 1). The reaction of C_{60} with **1a** and CuI in a molar ratio of 1:3:3 at 130 °C for 10 h gave the desired product **2a** in 6% yield. Other copper salts such as CuCl, CuBr, $CuCl_2$, $CuBr_2$, $Cu(OAc)_2$, and $Cu(OTf)_2$ were not effective in this reaction (entries 2−7). Next, the reaction of C_{60} with **1a** and CuI was carried out in the presence of different ligands such as pyridine, TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine), Bpy (2,2′-bipyridine), PMDETA (pentamethyldiethylenetriamine), and Phen (1,10-phenanthroline) to improve the yield (Table 1, entries 8−12). The results showed that 1,10-phenanthroline (Phen) was the best ligand and afforded **2a** in 37% yield. Reducing the CuI and Phen to catalytic amounts also gave a good yield of **2a** (Table 1, entry 13). When the temperature was lowered to 70 °C, **2a** was obtained in only 9% yield after 24 h (Table 1, entry 14). Further reducing the amount of **1a**,

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(5) (a) Banks, M. R.; Cadogan, J. I. G.; Gosney, I.; Hodgson, P. K. G.; Langridge-Smith, P. R. R.; Rankin, D. W. H. *J. Chem. Soc., Chem. Commun.* **1994**, 1365–1366. (b) Banks, M. R.; Cadogan, J. I. G.; Gosney, I.; Hodgson, P. K. G.; Langridge-Smith, P. R. R.; Millar, J. R. A.; Taylor, A. T. *Tetrahedron Lett.* **1994**, *35*, 9067–9070.

(6) Hou, H.-L.; Gao, X. *J. Org. Chem.* **2012**, *77*, 2553–2558.

(7) Li, F.-B.; Liu, T.-X.; Wang, G.-W. *J. Org. Chem.* **2008**, *73*, 6417–6420.

(8) Takeda, Y.; Enokijima, S.; Nagamachi, T.; Nakayama, K.; Minakata, S. *Asian J. Org. Chem.* **2013**, *2*, 91–97.

(9) This work ($PhI(OAc)_2/I_2$-Mediated [3 + 2] Reaction of [60]Fullerene with Amides for the Preparation of Fullerooxazoles) has been submitted to *Tetrahedron Letters* (Revisions being processed).

(10) He, C.-L.; Liu, R.; Li, D.-D.; Zhu, S.-E.; Wang, G.-W. *Org. Lett.* **2013**, *15*, 1532–1535.

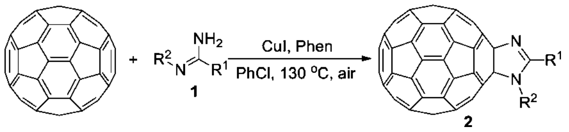
(11) (a) Yang, H.-T.; Ren, W.-L.; Miao, C.-B.; Dong, C.-P.; Yang, Y.; Xi, H.-T.; Meng, Q.; Jiang, Y.; Sun, X.-Q. *J. Org. Chem.* **2013**, *73*, 1163–1170. (b) Yang, H.-T.; Tian, Z.-Y.; Ruan, X.-J.; Zhang, M.; Miao, C.-B.; Sun, X.-Q. *Eur. J. Org. Chem.* **2012**, 4918–4922. (c) (b) Yang, H.-T.; Ruan, X.-J.; Miao, C.-B.; Sun, X.-Q. *Tetrahedron Lett.* **2010**, *51*, 6056–6059. (d) Yang, H.-T.; Ruan, X.-J.; Miao, C.-B.; Xi, H.-T.; Jiang, Y.; Meng, Q.; Sun, X.-Q. *Tetrahedron Lett.* **2009**, *50*, 7337–7339.

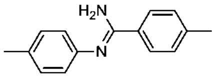
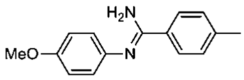
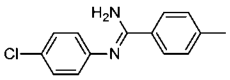
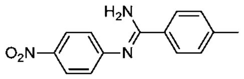
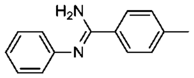
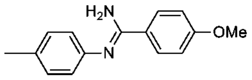
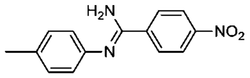
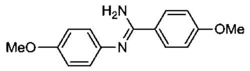
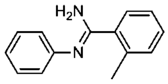
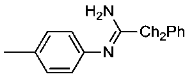
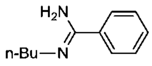
(12) (a) Toh, K. K.; Wang, Y.-F.; Ng, E. P. J.; Chiba, S. *J. Am. Chem. Soc.* **2011**, *133*, 13942–13945. (b) Würtz, S.; Rakshit, S.; Neumann, J. J.; Dröge, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 7230–7233. (c) Cheung, C. W.; Buchwald, S. L. *J. Org. Chem.* **2012**, *77*, 7526–7537. (d) Neumann, J.; Suri, M.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 7790–7794. (e) Yan, R.-L.; Luo, J.; Wang, C.-X.; Ma, C.-W.; Huang, G.-S.; Liang, Y.-M. *J. Org. Chem.* **2010**, *75*, 5395–5397. (f) Wang, L.; Ackermann, L. *Org. Lett.* **2013**, *15*, 176–179.

(13) Wang, Y.-F.; Zhu, X.; Chiba, S. *J. Am. Chem. Soc.* **2012**, *134*, 3679–3682.

(14) (a) Neuville, L.; Li, J. *Org. Lett.* **2013**, *15*, 1752–1755. (b) Tang, D.; Wu, P.; Liu, X.; Chen, Y.-X.; Guo, S.-B.; Chen, W.-X.; Li, J.-G.; Chen, B.-H. *J. Org. Chem.* **2013**, *78*, 2746–2750.

Table 2. Substrate Scope of Cu-Catalyzed Synthesis of Fulleroimidazole from C_{60} and Amidines[a]



entry	substrate	product	yield (%)[b]
1		**2a**	34 (86)
2		**2b**	30 (90)
3		**2c**	29 (79)
4		**2d**	24 (87)
5		**2e**	33 (88)
6		**2f**	48 (76)
7		**2g**	26 (73)
8		**2h**	31 (77)
9		**2i**	35 (88)
10		**2j**	0
11		**2k**	0

[a] All the reactions were performed with a molar ratio of C_{60}/amidines/CuI/phen = 1:2:0.4:0.4 in 10 mL of chlorobenzene at 130 °C for 8–12 h under air. [b] Isolated yield; the values in parentheses are based on consumed C_{60}.

Scheme 1. CuI-Catalyzed Oxidative Reaction of C_{60} with Benzamide

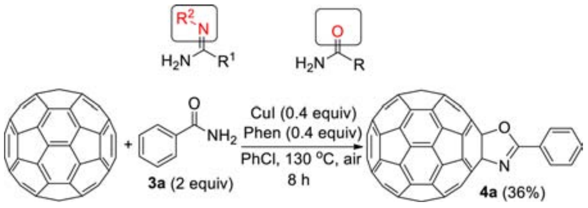
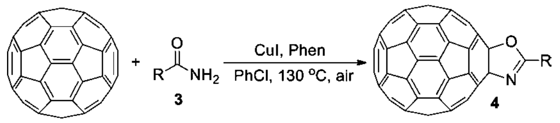
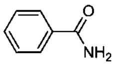
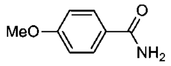
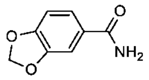
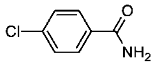
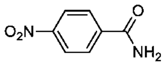
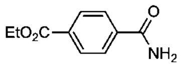
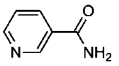
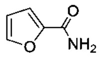
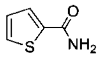
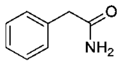
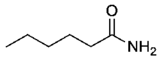
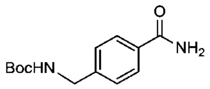


Table 3. Cu-Catalyzed Synthesis of Fullerooxazole from C_{60} and Amide[a]



entry	substrate	product	yield (%)
1		**4a**	36 (82)
2		**4b**	20 (87)
3		**4c**	22 (69)
4		**4d**	26 (79)
5		**4e**	23 (74)
6		**4f**	18 (85)
7		**4g**	31 (70)
8		**4h**	22 (76)
9		**4i**	20 (72)
10		**4j**	27 (82)
11		**4k**	31 (87)
12		**4l**	24 (79)

[a] All the reactions were performed with a molar ratio of C_{60}/amidine/CuI/phen = 1:2:0.4:0.4 in 10 mL of chlorobenzene at 130 °C for 6–10 h under air.

CuI, and Phen to 2, 0.2, and 0.2 equiv led to an obvious decrease in the yield of **2a** (35% to 27%, Table 1, entry 15 vs 13). Using 2 equiv of **2a** and increasing the amount of CuI and Phen from 0.2 to 0.4 equiv improved the yield to 34% (Table 1, entry 16). O_2 was crucial to the reaction, and no reaction occurred under a nitrogen atmosphere (Table 1, entry 17). From the viewpoint of atom economy, the molar ratio of C_{60}, **1a**, CuI, and Phen as 1:2:0.4:0.4 and the temperature of 130 °C in chlorobenzene under air were chosen as the optimal reaction conditions (Table 1, entry 16).

With the optimum reaction conditions in hand, we next investigated the substrate scope of the CuI-catalyzed oxidative synthesis of fulleroimidazoles (Table 2). When R^1 and R^2 are both aryl groups, all of the substrates gave good yields of **2**. The electronic effect of the substituent group on the phenyl ring has no significant influence on the reaction. An electron-donating group gave a slightly higher yield. However, when either R^1 or R^2 was replaced by an alkyl group, the reaction failed.

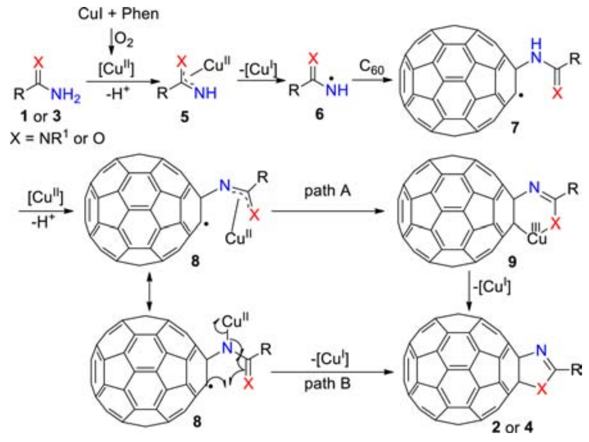
Amides have structure similarity with amidines only with the change of C=N double bonds to C=O double bonds (Scheme 1). We were inquisitive about whether the amides could also react with C_{60} under similar conditions to produce the fullerooxazoles. Up to now, there were only a few reports on the synthesis of oxazoles directly from the reaction of amides with alkenes such as treating 2-chloro-2-cyclopropylideneacetates with carboxamides under basic conditions through a domino transformation involving a Michael addition followed by an intramolecular nucleophilic substitution,[15] the NIS-mediated reaction of glucal with amide.[16] The Minakata group developed a *t*-BuOI mediated reaction of amides with olefins for the preparation of a variety of oxazoles, and they also applied this method in the preparation of fullerooxazoles.[8,17]

Benzamide **3a** was chosen to test this possibility. To our delight, when C_{60} was treated with benzamide **3a** (2 equiv) in the presence of CuI (0.4 equiv) and Phen (0.4 equiv) in chlorobenzene at 130 °C for 8 h, the oxidative cycloaddition product, fullerooxazole **4a**, was produced in 36% yield (Scheme 1). It is the first time to realize such a CuI-catalyzed [3 + 2] reaction of amides. Inspired by this result, we next investigated the scope of this Cu-catalyzed oxidative synthesis of fullerooxazoles (Table 3). It could be seen that the reaction was tolerant to various functional groups. Aryl amides with either an electron-donating or -withdrawing group on the phenyl ring gave a good yield of **4**. Heterocyclic amides **3g**–**i** also reacted with C_{60} to give corresponding fullerooxazoles **4g**–**i**. Alkyl amides were also applicable, and ester or carbamate groups were also tolerated in this reaction.

All of the known products were confirmed throuth comparison of their spectral data with those reported in the literature.[7–10] The identification of new compounds **2a**–**h**, **4c**, **4h**, and **4i** was fully confirmed by their MS, ^{1}H NMR, ^{13}C NMR, FTIR, and UV–vis spectra (see Supporting Information).

In view of the reported Cu-catalyzed oxidative reaction of enamines and amidines,[12–14] a proposed mechanism is described in Scheme 2. One-electron oxidation of amidine **1** or amide **3** by Cu^{II} species (described as $[Cu^{II}]$) generated from Cu^{I} with molecular oxygen[18] would provide nitrogen radical **6**, which was captured by C_{60} to afford fullerene radical **7**. Further reaction of **7** with Cu^{II} generated **8**. In path A, **8** could transform to a six-membered ring Cu(III) intermediate **9**, which underwent elimilation of Cu(I) to generate **2** or **4**. In path B, homolytic cleavage of the N–Cu bond and subsequent intramolecular cyclization would generate **2** or **4**.

Scheme 2. Proposed Reaction Mechanism



In summary, CuI-catalyzed oxidative intermolecular reaction of amidines or amides with C_{60} using air as an oxidant has been exploited for the easy preparation of fulleroimidazole or fullerooxazole derivatives. The process, which used copper as the catalyst and air as the co-oxidant, is particularly cheap, simple, and atom efficient. Further investigations on the Cu-catalyzed oxidative reaction of amides with alkynes, other olefins, and nitriles are currently underway.

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Supporting Information Available. Experimental procedures, spectral data of new compounds, and NMR spectra of the products. 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.