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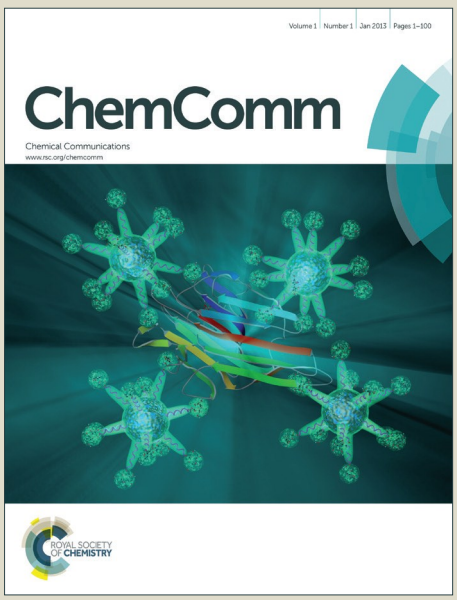

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Copper(I)-catalyzed heteroannulation of [60]fullerene with ketoxime acetates: preparation of novel 1-fulleropyrrolines

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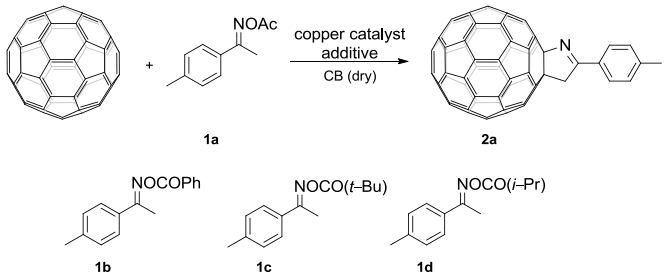
A cuprous bromide-catalyzed heteroannulation reaction of [60]fullerene with ketoxime acetates has been exploited to prepare the novel 1-fulleropyrrolines through the cleavage of N–O and C–H bonds and formation of C–C and C–N bonds under thermal conditions. A plausible mechanism for the formation of 1-fulleropyrrolines is proposed on the basis of the experimental results. The electrochemistry of the obtained products has also been investigated.

Over the past decades, tremendous reactions have been developed to obtain a diversity of fullerene derivatives, which have huge potential applications in materials, biology and nanoscience.[1] As one of the first investigated reactions of fullerenes, free radical reactions are still attractive protocols to synthesize fullerene derivatives.[2] Especially in recent years, increasing attentions have been paid to the transition-metal-catalyzed/promoted radical reactions for their excellent ability to create novel functional fullerenes and remarkable advantages such as high compatibility with a wide range of functional groups over the traditional peroxide- or light-initiated processes.[2b-f] The first-row transition metals such as Mn(III),[3] Fe(II)/Fe(III)[4] and Cu(I)/Cu(II)[3d,5] have been extensively exploited to functionalize fullerenes due to their availability, low toxicity, and ease of manipulation. However, the development of new methodologies for the transition-metal-catalyzed/promoted remains as a promising approach for the preparation of novel fullerene derivatives.[6]

The reaction of [60]fullerene (C_{60}) with nitrile ylides[7] has been employed to prepare C_{60}-fused pyrroline derivatives, of which the nitrogen atom does not link to the fullerene skeleton directly. Until now, there are only two reports on the synthesis of C_{60}-fused pyrroline derivatives with a nitrogen atom bonding to the fullerene cage directly.[3f,5c] Recently, the Wang[3f] and Yang[5c] groups realized the synthesis of 2-fulleropyrrolines, which have a nitrogen atom attached to the fullerene cage directly. To the best of our knowledge, the preparation of 1-fulleropyrrolines has never been achieved so far. Although they both possess a nitrogen atom bonding to the fullerene cage directly, 1-fulleropyrrolines have a C=N bond, whereas 2-fulleropyrrolines contain a C=C bond. On the other hand, oximes and their derivatives are valuable substances in transition-metal-catalyzed coupling reactions. Cleavage of the N–O bond in ketoxime carboxylates by a low valent transition metal such as Cu(I) shows a promising approach for the synthesis of nitrogen-containing compounds.[8] Herein, we develop a facile and efficient protocol to construct 1-fulleropyrrolines by Cu(I)-catalyzed heteroannulation of C_{60} with ketoxime acetates.

The combination of Cu(I) and $NaHSO_3$/Na_2SO_3 has proven to be effective for coupling reactions of ketoxime carboxylates.[8] Therefore, we initially studied the reaction of C_{60} (36 mg, 0.05mmol) with 4-methylacetophenone oxime acetate (**1a**; 1.5 equiv) by using CuCl (0.2 equiv) and $NaHSO_3$ (10 equiv) in chlorobenzene (CB) at 150 ^{o}C under open air atmosphere (Table 1). To our delight, the desired product **2a** was obtained in 9% yield (entry 1). Encouraged by this result, different copper catalysts were next evaluated to improve the product yield. When CuI was used, a slight increase of yield to 14% was obtained (entry 2). However, no reaction occurred in the case of Cu_2O (entry 3). Notably, Cu(II) catalysts such as $CuCl_2$ and $CuBr_2$ could not improve the reaction efficiency (entries 4 and 5). To our satisfaction, when CuBr was used, the yield was significantly improved to 30% (entry 6). Screening of the additives demonstrated that $NaHSO_3$ was the best choice, while Na_2SO_3 and $Na_2S_2O_4$ gave **2a** in 11% and 17% yields, respectively (entries 7 and 8). When the amount of substrate **1a** was reduced to 1.0 equiv, an obvious decrease in yield was observed (entry 9). However, further increasing the amount of substrate **1a** to 2.0 equiv caused a slight decrease in yield, yet more C_{60} was consumed (entry 10). The increase or decrease of the amount of additive $NaHSO_3$ was also not beneficial to the reaction

Table 1. Optimization of reaction conditions for the reaction of C_{60} with 4-methylacetophenone oxime acetate **1a** catalyzed by copper salt[a]



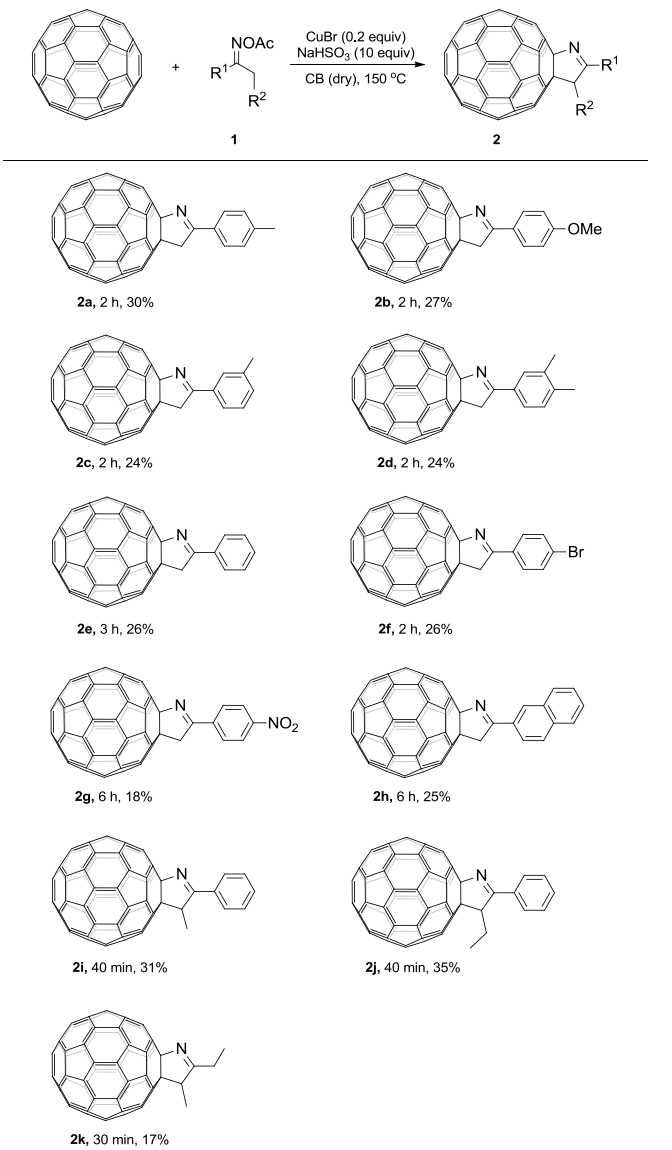
entry	catalyst	additive	molar ratio[b]	yield of **2a** (%)[c]
1	CuCl	$NaHSO_3$	1:1.5:0.2:10	9 (35)
2	CuI	$NaHSO_3$	1:1.5:0.2:10	14 (56)
3	Cu_2O	$NaHSO_3$	1:1.5:0.2:10	0
4	$CuCl_2$	$NaHSO_3$	1:1.5:0.2:10	8 (22)
5	$CuBr_2$	$NaHSO_3$	1:1.5:0.2:10	10 (25)
6	**CuBr**	**$NaHSO_3$**	**1:1.5:0.2:10**	**30 (51)**
7	CuBr	Na_2SO_3	1:1.5:0.2:10	11 (33)
8	CuBr	$Na_2S_2O_4$	1:1.5:0.2:10	17 (33)
9	CuBr	$NaHSO_3$	1:1.0:0.2:10	14 (40)
10	CuBr	$NaHSO_3$	1:2.0:0.2:10	26 (38)
11	CuBr	$NaHSO_3$	1:1.5:0.2:5	16 (27)
12	CuBr	$NaHSO_3$	1:1.5:0.2:15	27 (46)
13[d]	CuBr	$NaHSO_3$	1:1.5:0.2:10	22 (46)
14[e]	CuBr	$NaHSO_3$	1:1.5:0.2:10	25 (38)
15[f]	CuBr	$NaHSO_3$	1:1.5:0.2:10	16 (40)
16[g]	CuBr	$NaHSO_3$	1:1.5:0.2:10	19 (37)
17	–	$NaHSO_3$	1:1.5:0:10	0
18	CuBr	–	1:1.5:0.2:0	7 (18)
19[h]	CuBr	$NaHSO_3$	1:1.5:0.2:10	19 (40)
20[i]	CuBr	$NaHSO_3$	1:1.5:0.2:10	9 (57)
21[j]	CuBr	$NaHSO_3$	1:1.5:0.2:10	19 (23)

[a]Unless otherwise noted, the reactions were performed in anhydrous CB at 150 ℃ under an open air atmosphere for 2 h. [b]Molar ratio refers to C_{60}:**1a**:catalyst:additive. [c]Yields in parentheses were based on consumed C_{60}. [d]The reaction time was 1 h. [e]The reaction time was 3 h. [f]The reaction was performed at 140 ℃. [g]The reaction was performed at 160 ℃. [h]The substrate was **1b**. [i]The substrate was **1c**. [j]The substrate was **1d**.

efficiency (entries 11 and 12). The reaction time and temperature were also varied. It was found that 2 h and 150 °C were the best reaction time and temperature (entries 13–16). Furthermore, control experiments confirmed that the reaction was totally shut down in the absence of CuBr, and the product yield was only 7% without $NaHSO_3$ (entries 17 and 18). These observations suggested that copper species was necessary and $NaHSO_3$ played an important role in this reaction. Finally, other different acetophenone oxime esters were tested under our catalytic system, and no further improvement in product yield was observed (entries 19–21). Thus, the optimal reaction conditions were a molar ratio of 1:1.5:0.2:10 for the reagents of C_{60}, **1a**, CuBr and $NaHSO_3$, and a temperature at 150 °C.

With the optimized reaction conditions established, the substrate scope of this transformation was investigated, and the results are presented in Table 2. Generally, the reaction of C_{60} with ketoxime acetates bearing electron-donating and -withdrawing groups on aromatic rings proceeded smoothly and gave the desired products **2a**–**2g** in 18–30% yields. Substrates bearing methyl, methoxy, bromo or nitro groups on the phenyl ring could be used and gave similar product yields (24–30%) except **1g**, which contained a strong electron-withdrawing NO_2 group. Aryl bromide was inert under our conditions, suggesting that the Cu(I) catalyst preferentially reacted with the N–O bond of the ketoxime acetate over the C–Br bond. Thus, the bromide-containing product could be further functionalized by undergoing subsequent cross-coupling reactions. In addition, 2-acetylnaphthalene oxime acetate **1h** could also employed and provided **2h** in 25% yield. It should be noted that prolonging the reaction time from 2 h to 6 h was essential for both **1g** and **1h** to obtain the synthetically valuable product yields. Intriguingly, ketoxime acetates derived from other aryl ketones such as propiophenone and n-butyrophenone showed better reactivity and afforded the desired products **2i** and **2j** in 31% and 35% yields, respectively. In addition, an alkyl ketoxime acetate was

Table 2. Results for the reaction of C_{60} with ketoxime acetates **1a–k** catalyzed by CuBr[a]



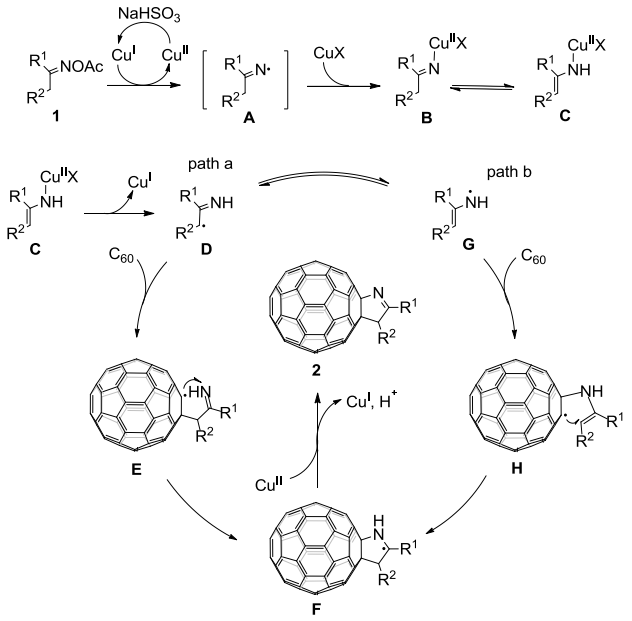
[a]Unless otherwise noted, the reactions were performed with C_{60} (0.05 mmol), **1** (0.075 mmol), CuBr (20 mol %), and $NaHSO_3$ (0.50 mmol) in anhydrous CB at 150 ℃.

also a suitable substrate, and **2k** could be obtained in 17% yield under our conditions.

The structures of products **2a**–**k** were unambiguously characterized by MALDI-TOF MS or ESI FT-ICR MS, ^{1}H NMR, ^{13}C NMR, FT-IR and UV-vis spectra. All of the mass spectra of these products gave the correct molecular ion peaks. Their ^{1}H NMR spectra displayed the expected chemical shifts as well as the splitting patterns for all protons. The ^{13}C NMR spectra of **2a**–**h** exhibited no more than 30 peaks in the range of 135–156 ppm for the sp^2-carbons of the fullerene cage and two peaks at 65–66 ppm and 99–101 ppm for the two sp^3-carbons of the fullerene skeleton, consistent with the C_s symmetry of their molecular structures. In the ^{13}C NMR spectra of **2i**–**k**, there were more than 49 peaks in the range of 134–157 ppm with some overlapping ones for the 58 sp^2-carbons of the fullerene cage and two peaks at 70–71 ppm and 99-100 ppm for the two-sp^3 carbons of the fullerene skeleton, consistent with the C_1 symmetry of their molecular structures. The chemical shifts at 65–71 ppm and 99-101 ppm for the two sp^3-carbons of the fullerene skeleton are close to the reported data of other fullerene derivatives with a nitrogen atom and a carbon atom attached to the fullerene skeleton. The peak at 171–183 ppm in the ^{13}C NMR spectra and the absorption at 1780–1806 cm^{-1} in the IR spectra belonged to the C=N bond of the 1-pyrroline moiety. Their UV–vis spectra exhibited a peak at 428–429 nm, which is the characteristic absorption for 1,2-adducts of C_{60}.

To gain more insight into the reaction mechanism, some control experiments were conducted. Addition of a free radical scavenger such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) or 2,2-azobisisobutyronitrile (AIBN) to the reaction mixture severely prohibited the current cyclization reaction, indicating that a radical pathway might be involved. Furthermore, we have detected the coupling product **3a** formed between the 1-(p-tolyl)ethanimino moiety from **1a** and the isobutyronitrile radical from AIBN (see Electronic Supplementary Information).

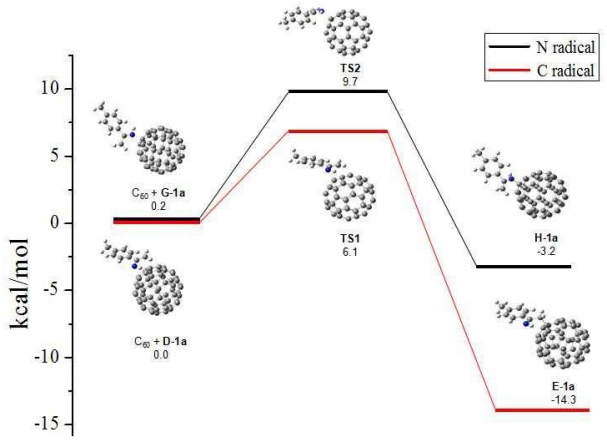
Based on the above results and previous literature on copper-catalyzed radical reactions, a plausible mechanism for the formation of novel 1-fulleropyrrolines **2a**–**k** is proposed and depicted in Scheme 1. This transformation is initiated via one-electron oxidation of **1** by Cu^{I}, which results in formation of imino radical **A**. The radical intermediate **A** reacts rapidly with another Cu^{I} to give N–Cu^{II} species **B**. Tautomerization of the imino–Cu^{II} complex **B** gives the enamino–Cu^{II} intermediate **C**.[8] Cleavage of the N–Cu bond of **C** forms a radical intermediate **D**, which can be captured by C_{60} to produce the fullerenyl radical **E**. **E** then undergoes cyclization to generate radical **F**, which is converted to **2** by oxidation with a Cu^{II} species accompanied by proton elimination. Tautomerization of **D** can also give **G**, which attacks C_{60} to afford fullerenyl radical **H**. The cyclization of **H** generates the same **F**. The formed Cu^{II} species can be reduced by sodium bisulfite to regenerate the active Cu^{I}, which enters into the next catalytic cycle. To further probe the preferred reaction pathways between the additions of **D** and **G** to C_{60}, computational study at the B3LYP/6-31G (d) level with the Gaussian 09 program for the reaction of C_{60} with **1a** was performed, and the energy profiles are depicted in scheme 2. The energy of radical intermediate **D**-



Scheme 1 Proposed reaction mechanisms for the formation of **2**

1a is close to that of **G**-**1a**. However, the formation of the fullerenyl radical **H**-**1a** requires an activation energy of 9.5 kcal/mol, 3.4 kcal/mol higher than the formation of **E**-**1a**. Furthermore, the fullerenyl rdical **E**-**1a** is more stable than **H**-**1a** by 11.1 kcal/mol. Therefore, the product formation via **E** should be more favourable.

The half-wave reduction potentials of products **2a**–**k** along with those of C_{60} have been investigated, and the results are summarized in Table 3. The obtained products had essentially the same CV behaviours and showed three reversible redox processes under our conditions. Due to the attached heteroatom, the first reduction potentials of 1- fulleropyrrolines **2a**–**k** were generally shifted negatively by 70–90 mV relative to that of C_{60}. Similar trends were observed in the values of their second (Δ = 60–80 mV) and third (Δ = 120–150 mV) reduction potentials.[9,10] Therefore, the synthesized 1-fulleropyrroline may have the potential application in organic photovoltaic devices by utilizing



Scheme 2 Computational calculation result

Table 3. Half-wave reduction potentials of **2a**–**k** and C_{60}[a]

compound	E_1	E_2	E_3
C_{60}	–1.080	–1.473	–1.934
2a	–1.166	–1.555	–2.083
2b	–1.165	–1.550	–2.076
2c	–1.153	–1.535	–2.056
2d	–1.164	–1.548	–2.076
2e	–1.152	–1.531	–2.046
2f	–1.152	–1.535	–2.057
2g	–1.137	–1.550	–2.097
2h	–1.158	–1.541	–2.060
2i	–1.155	–1.539	–2.073
2j	–1.152	–1.537	–2.068
2k	–1.170	–1.560	–2.104

[a]Potential V versus a ferrocene/ferrocenium couple. Experiment conditions: 0.1 mM of **2a-k**/C_{60} and 0.1 M of *n*-Bu_4NClO_4 in anhydrous ODCB; reference electrode: SCE; working electrode: Pt; auxiliary electrode: Pt wire; scanning rate: 20 mV s^{-1}.

appropriate donor acceptor.[10]

In conclusion, we have successfully developed a facile and efficient method for the synthesis of novel 1-fulleropyrrolines through the cuprous bromide-catalyzed heteroannulation of C_{60} with ketoxime acetates. This process involves the Cu(I)-catalyzed N–O bond cleavage, activation of sp^3 C–H bond and C–C/C–N bond formation.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures, spectral data and NMR spectra of **2**, mechanism study, half-wave reduction potentials, CVs and DPVs of **2**. See DOI: 10.1039/c000000x/

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