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$FeCl_3$-Mediated Cyclization of [60]Fullerene with *N*-Benzhydryl Sulfonamides under High-Speed Vibration Milling Conditions

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ABSTRACT

The $FeCl_3$-mediated reaction of [60]fullerene with *N*-benzhydryl sulfonamides afforded C_{60}-fused indane derivatives using the high-speed vibration milling technique. A possible reaction mechanism involving the unprecedented $FeCl_3$-mediated homolytic C−N bond cleavage of *N*-benzhydryl sulfonamides is proposed. The electrochemistry of the obtained C_{60}-fused indanes was also investigated.

Due to the poor solubility of fullerenes in common organic solvents, the solvent-free mechanochemical reaction has particular significance in the chemical functionalization of fullerenes.[1] In 1996, the first mechanochemical reaction of [60]fullerene (C_{60}) conducted under solvent-free and high-speed vibration milling (HSVM) conditions was reported.[2] Following that, many types of reactions such as Diels−Alder reactions, 1,3-dipolar cycloadditions, nucleophilic additions, and radical reactions have been explored.[1] In most cases, these reactions performed under the HSVM conditions led to higher yields compared to the liquid-phase counterparts. More importantly, some HSVM-promoted reactions provide unexpected products that cannot be generated by liquid-phase reactions. For example, the HSVM technique has been applied to the reaction of C_{60} with various potassium salts, alkaline metals, or amines to give fullerene dimers and trimers,[3] which are still elusive by the common liquid-phase protocols.

On the other hand, Lewis acids have been utilized in fullerene functionalization. For instance, $AlCl_3$- or $FeCl_3$-mediated Friedel−Crafts-type hydroarylation reactions of C_{60},[4a−f] $AlCl_3$-mediated tandem acetylation of 1,2-HC_{60}Ar with acetyl chloride,[4d] and $FeCl_3$-mediated synthesis of fullerenyl esters[5] have been reported. Recently we disclosed

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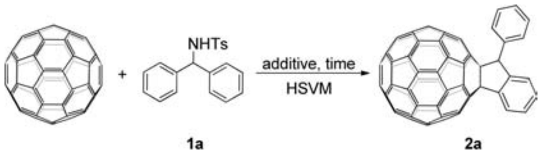
that the addition of $AlCl_3$ to the $Mn(OAc)_3$-mediated reaction of C_{60} with active methylene compounds substituted with an aryl or a benzyl group could switch the reaction pathway and afford aryl-annulated products.[6] However, the Lewis acid mediated reaction of fullerenes under solvent-free mechanochemical conditions has not been described. Herein, we report the solvent-free $FeCl_3$-mediated reaction of C_{60} with *N*-benzhydryl sulfonamides under the HSVM conditions.

Initially, the reaction of C_{60} with *N*-benzhydryl 4-toluenesulfonamide (**1a**) was chosen as the model reaction to screen the reaction conditions. Much to our delight, when a mixture of C_{60} (0.02 mmol), **1a** (2 equiv), and $FeCl_3$ (2 equiv) was milled under the HSVM conditions for 1 h, C_{60}-fused indane **2a** was obtained in 23% yield (Table 1, entry 1). Increasing the amount of $FeCl_3$ further to 3 equiv improved the product yield to 27% (Table 1, entry 2). However, prolonging the reaction time to 1.5 h was not beneficial (Table 1, entry 3 vs 2). Efforts to enhance the product yield proved fruitless by replacing $FeCl_3$ with $FeCl_3 \cdot 6H_2O$, $Fe(NO_3)_3$, $ZnBr_2$, $AlCl_3$, *p*-toluenesulfonic acid (PTSA), $Ce(NH_4)_2(NO_3)_6$ (CAN), or $Mn(OAc)_3 \cdot 2H_2O$ (Table 1, entries 4–10). In addition, when the reaction was performed in *o*-dichlorobenzene or 1,1,2,2-tetrachloroethane at 120 °C for 12 h, no desired product was found (Table 1, entries 11 and 12), demonstrating the advantages of the solvent-free mechanochemical reaction over the liquid-phase reaction. Therefore, the molar ratio of 1:2:3 for the regents C_{60}, **1a**, and $FeCl_3$ and milling time of 1 h were chosen as the optimized reaction conditions.

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



entry	additive	molar ratio[b]	time (h)	yield (%)[c]
1	$FeCl_3$	1:2:2	1	23 (56)
2	**$FeCl_3$**	**1:2:3**	**1**	**27 (66)**
3	$FeCl_3$	1:2:3	1.5	25 (60)
4	$FeCl_3 \cdot 6H_2O$	1:2:2	1	trace
5	$Fe(NO_3)_3$	1:2:2	1	0
6	$ZnBr_2$	1:2:2	1	0
7	$AlCl_3$	1:2:2	1	0
8	PTSA	1:2:2	1	0
9	CAN	1:2:2	1	0
10	$Mn(OAc)_3 \cdot 2H_2O$	1:2:2	1	0
11[d]	$FeCl_3$	1:2:2	12	0
12[e]	$FeCl_3$	1:2:2	12	0

[a] All reactions were performed under the HSVM conditions for 1 h and repeated twice. [b] Molar ratio refers to C_{60}/**1a**/additive. [c] Isolated yield; that in parentheses was based on consumed C_{60}. [d] The reaction was performed in *o*-dichlorobenzene (2 mL) at 120 °C. [e] The reaction was performed in 1,1,2,2-tetrachloroethane (4 mL) at 120 °C.

With the optimized conditions in hand, a series of *N*-benzhydryl sulfonamides were examined to investigate the scope and limitation of the reaction. Substrates bearing weak electron-donating (4-Me and 3,4-$(Me)_2$) or electron-withdrawing (4-Cl and 4-Br) groups on the phenyl ring of benzhydryl moieties could be employed and afforded the corresponding products. It should be noted that the regioselectivity was highly dependent on the electronic property of the two aryl moieties, and the cyclization occurred exclusively on the more electron-rich phenyl ring probably due to the electron-deficient nature of the fullerene moiety. All substrates gave only one product except for **1b**. In addition, the reaction selectively occurred at the less hindered position of the phenyl ring (Table 2, entry 3). Compared with **1d**, substrate **1e** containing a chloro group at the ortho position also proceeded well and provided a comparable product yield (Table 2, entry 5 vs 4). Substrate **1f** bearing the electron-deficient chloro group on both phenyl rings obviously retarded the reaction, giving product **2f** in only 16% yield (Table 2, entry 6). Replacement of the Ts group by the less electron-withdrawing methylsulfonyl (Ms) group reduced the reactivity and resulted in a lower yield (Table 2, entry 8 vs 7). A larger-scale reaction could be performed by using 50.0 mg of C_{60} with the same reagent ratio, albeit at lower efficiency. For example, the product yield of **2g** was decreased from 41% (64% based on consumed C_{60}) with 14.4 mg of C_{60} for 1 h to 28% (51% based on consumed C_{60}) with 50.0 mg of C_{60} for 2 h. The chloro and bromo groups in products **2d**–**g** (Table 2, entries 4–8) may be used as a handle for further coupling reactions. The methods for the synthesis of fulleroindanes are still limited.[4d,6,7] The synthesis of fulleroindane **2a** was previously reported by us and required three steps starting from C_{60}.[7] Obviously, the present mechanochemical protocol in only one step is much more concise and efficient.

It is intriguing that the reaction of C_{60} with substrate **1i** did not afford the desired product **2i**. Instead, an unexpected Diels–Alder type product **3** was obtained in 15% yield (Scheme 1). This method provides a new route to the construction of C_{60}-fused polycycles.[8]

Product **2a** is a known compound, and its identity was confirmed by comparison of its spectral data with those reported in the literature.[7] New compounds **2b**–**g** and **3** were unambiguously characterized by HRMS, ^1H NMR, ^{13}C NMR, FT-IR, and UV–vis spectral data. All MALDI mass spectra of these products gave the correct molecular ion peaks. The ^{13}C NMR spectra of **2c**–**g** and **3** clearly exhibited at least 45 peaks in the range of 133–159 ppm for the sp^2-carbons of the fullerene cage and two peaks in the 68–76 ppm range for the two sp^3-carbons of the fullerene skeleton, consistent with the C_1 symmetry of their

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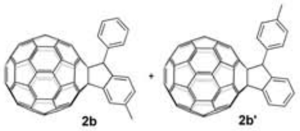
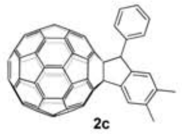
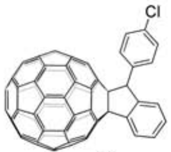
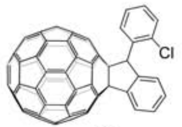
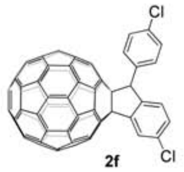
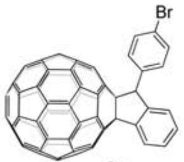
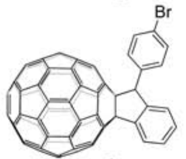
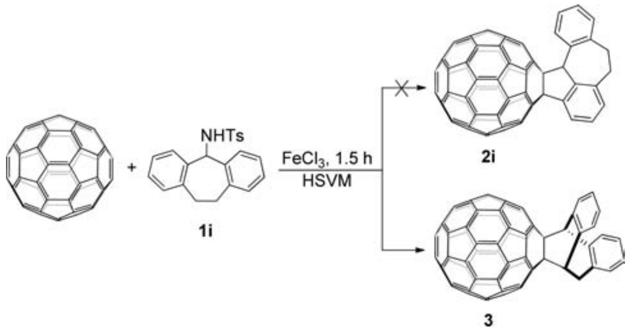
Table 2. Results for the Reaction of C_{60} with *N*-Benzhydryl Sulfonamides **1a**−**h** in the Presence of $FeCl_3$ under the HSVM Conditions[a]

entry	substrate **1**	product **2**	yield of **2** (%)[b]
1	$R^1 = H$ $R^2 = H$ $R^3 = Ts$	 **2a**	27 (66)
2[c]	$R^1 = 4\text{-}Me$ $R^2 = H$ $R^3 = Ts$	 **2b** + **2b′** **2b**:**2b′** = 2:1	15 (38)
3	$R^1 = 3,4\text{-}(Me)_2$ $R^2 = H$ $R^3 = Ts$	 **2c**	30 (59)
4	$R^1 = H$ $R^2 = 4\text{-}Cl$ $R^3 = Ts$	 **2d**	38 (61)
5	$R^1 = H$ $R^2 = 2\text{-}Cl$ $R^3 = Ts$	 **2e**	35 (60)
6	$R^1 = 4\text{-}Cl$ $R^2 = 4\text{-}Cl$ $R^3 = Ts$	 **2f**	16 (32)
7	$R^1 = H$ $R^2 = 4\text{-}Br$ $R^3 = Ts$	 **2g**	41 (64)
8	$R^1 = H$ $R^2 = 4\text{-}Br$ $R^3 = Ms$	 **2g**	23 (43)

[a] All reactions were performed with 0.02 mmol of C_{60}, 0.04 mmol of **1**, and 0.06 mmol of $FeCl_3$ under the HSVM conditions for 1 h, repeated twice. [b] Isolated yield; that in the parentheses was based on consumed C_{60}. [c] Products **2b** and **2b′** could not be separated from each other by preparative HPLC.

Scheme 1. $FeCl_3$-Promoted Reaction of C_{60} with *N*-Benzhydryl Sulfonamide **1i** under HSVM Conditions



molecular structures. It is noteworthy that line broadenings for four aryl protons and four aryl carbons were observed in the NMR spectra of fulleroindanes **2** except for **2e** due to the restricted rotation of the R^2-containing phenyl ring. The broadened peaks became narrower and well-resolved ones, when **2d**, for example, was heated to 70 °C in $CHCl_2CHCl_2$/DMSO-d_6. A similar phenomenon for the restricted rotation of the phenyl substituent in fulleropyrrolidines has been documented.[9] In contrast, the rotation of the aryl ring in **2e** is prevented by its ortho-chloro substituent and, thus, gave well-resolved NMR peaks at room temperature. The peak numbers and splitting patterns of the ^1H NMR peaks of **2e** remained unchanged, and no coalescence was observed from 12 to 70 °C in $CHCl_2CHCl_2$/DMSO-d_6, indicating the existence of only one diastereoisomeric conformer and thus the high diastereoselectivity of the reaction.[9] Their UV−vis spectra displayed characteristic peaks at around 430 nm, which is a diagnostic absorption for 1,2-adducts of C_{60}.[2,3a,3b,6,7]

To gain more insight into the reaction mechanism, we carried out the MALDI-TOF MS analysis of the reaction mixture of C_{60}, **1g**, and $FeCl_3$ under our HSVM conditions and observed the formation of the benzhydryl dimer **4** (Figure 1). In the absence of C_{60}, dimer **4** was also formed by treating **1g** with $FeCl_3$. Furthermore, when an equimolar amount of 2,2,6,6-tetramethylpiperidine-*N*-oxide (TEMPO) was added to the reaction system, compound **2g** could not be obtained. These results suggested that *N*-benzhydryl radicals were most likely generated from *N*-benzhydryl sulfonamides via the $FeCl_3$-meditated C−N bond cleavage under the HSVM conditions. To the best of our knowledge, the Lewis acid promoted homolytic C−N bond cleavage of *N*-benzhydryl sulfonamides is unprecedented, although the corresonding $FeCl_3$-meditated heterolytic C−N bond cleavage has been reported.[10]

On the basis of the above experimental results, a plausible mechanism for the formation of fulleroindanes **2a**−**g**

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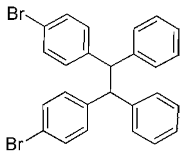

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Figure 1. Benzhydryl dimer **4**.

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

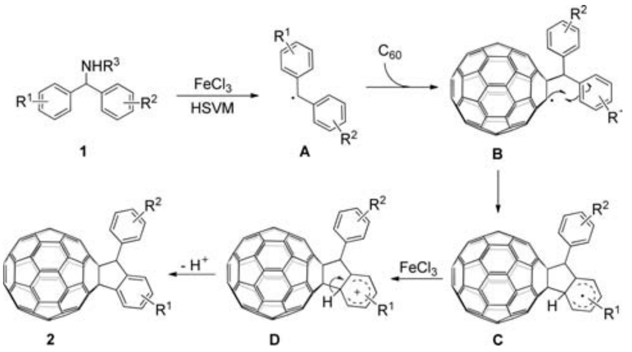

Table 3. Half-Wave Reduction Potentials (V) of C_{60}, PCBM, **2a**, **2c**−**g**, and **3**[a]

compd	E_1	E_2	E_3
C_{60}	−1.076	−1.460	−1.925
PCBM	−1.160	−1.538	−2.050
2a	−1.165	−1.540	−2.069
2c	−1.182	−1.566	−2.113
2d	−1.153	−1.530	−2.059
2e	−1.159	−1.534	−2.068
2f	−1.142	−1.526	−2.058
2g	−1.156	−1.540	−2.078
3	−1.174	−1.550	−2.090

[a] Versus ferrocene/ferrocenium. Experimental conditions: 1 mM of compound 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: 20 mV s^{-1}.

is outlined in Scheme 2. Initially benzhydryl radicals **A** are generated from N-benzhydryl sulfonamides **1** through the $FeCl_3$-mediated homolytic C−N bond cleavage. Addition of radicals **A** to C_{60} provides fullerenyl radicals **B**, which can undergo intramolecular cyclization to give radicals **C**. Due to the electron deficiency of fullerenyl radicals **B**, the cyclization selectively occurred on the more electron-rich phenyl ring. Oxidation of radicals **C** by the Fe^{3+} species results in aryl cations **D**.[11] Loss of H^+ from cations **D** leads to the formation of C_{60}-fused indanes **2**. Although the reaction most likely proceeds in a radical process via the homolytic C−N bond cleavage, the alternative pathway via a sequence of heterolytic C−N bond cleavage followed by addition of the formed carbocation to C_{60} and final intramolecular Friedel−Crafts arylation cannot be completely excluded and may operate simultaneously.

Table 3 summarizes the half-wave reduction potentials of C_{60}, PCBM, **2a**, **2c**−**g**, and **3**. It can be seen that the first reduction potentials (E_1) of fulleroindanes **2** and polycycle **3** are 66−106 mV more negative than that of C_{60}. Notably, most of them were comparable to that of PCBM. Furthermore, the onset reduction potential of **2c** (−1.182 V) and **3** (−1.174 V) are even more cathodically shifted relative to PCBM (−1.160 V). Since the LUMO levels of fullerene compounds are estimated by their onset reduction potentials (LUMO $= -(E_1 + 4.8)$ eV).[12] The high LUMO levels of fulleroindanes **2** and **3** imply a potential application as acceptors in organic photovoltaic devices.[13]

In summary, we have disclosed that the solvent-free $FeCl_3$-mediated reaction of C_{60} with N-benzhydryl sulfonamides under high-speed vibration milling conditions affords the scarce C_{60}-fused indanes, which cannot be obtained in the liquid-phase counterparts. The intriguing formation of fulleroindane derivatives is believed to proceed via a sequence that includes the unprecedented $FeCl_3$-mediated homolytic C−N bond cleavage of N-benzhydryl sulfonamides, radical addition to C_{60}, intramolecular radical annulation, and oxidation. The fulleroindane derivatives may be utilized in solar cells.

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Supporting Information Available. Experimental procedures, spectral data, NMR spectra, MS of reaction mixtures, and voltammograms. 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.