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Aziridinofullerene: A Versatile Platform for Functionalized Fullerenes

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Supporting Information

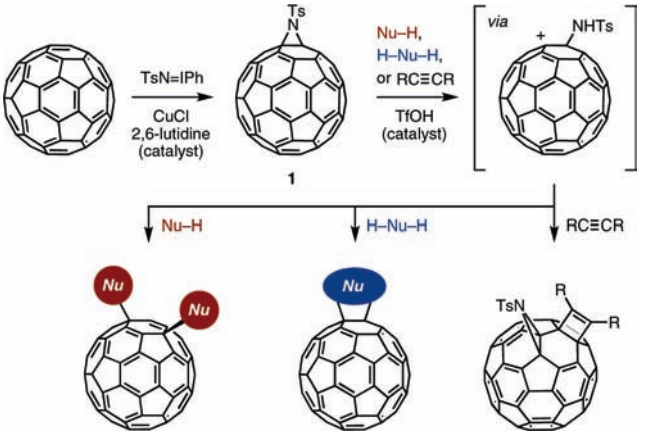
ABSTRACT: An aziridine moiety on the fullerene core can serve as an acid-triggered reacting template for the controlled synthesis of a range of functionalized fullerenes that are otherwise difficult to synthesize in an efficient and selective manner. A copper-catalyzed aziridination of C_{60} for the practical synthesis of aziridinofullerene **1** and acid-catalyzed reactions of **1** with mono- and bifunctional nucleophiles as well as alkynes are described. The rapid generation of structural diversity in a single chemical operation using the common platform **1** is notable.

Multiple addition reactions of fullerenes offer a significant opportunity for the creation of new nanocarbons with potential applications in biological and materials science.[1−3] As the degree and pattern of addition determine the electronic and chemical properties of the functionalized fullerenes, regiocontrol in multiple additions is critically important. During the last 15 years, chemists have uncovered several inherent regioselectivity principles in multiadditions and have also developed new concepts such as tethering and templating strategies for controlled multiple additions.[1−3] We now report that an aziridine moiety on the fullerene core can serve as an acid-triggered reacting template for the controlled synthesis of a range of functionalized fullerenes that are otherwise difficult to synthesize in an efficient and selective fashion (Scheme 1). In addition, a new copper-catalyzed aziridination of C_{60} for the practical synthesis of aziridinofullerene **1** has been developed, and a formal [2 + 2] cycloaddition of **1** with alkynes has been discovered (Scheme 1).[4]

Because of the inherent ring strain, we envisioned that the ring opening of the aziridine moiety in aziridinofullerene **1** should occur through the agency of Lewis or Brønsted acids,[5] allowing the facile introduction of a nucleophile onto the fullerene core. Unlike the case of typical aziridines, the resulting amino moiety could be further substituted by a nucleophile in the presence of acids through a carbocationic intermediate stabilized by the fullerene cage. We expected that this "aziridine" approach to fullerene functionalization would not only significantly increase the efficiency of nucleophile installation but also allow full control over the regiochemistry in multiple additions.[6] Clearly, the utility of this strategy depends heavily on the efficiency in accessing the aziridinofullerene platform and the efficiency, regioselectivity, generality, and diversity of the transformations of the aziridinofullerene. As we have demonstrated in a number of fullerene functionalizations, we expected that introducing the essence of molecular catalysis should offer enormous opportunities in this chemistry.[4]

In designing a new blueprint for controlled multiadditions to fullerenes, we became aware that there remains considerable room for investigation of the synthesis of aziridinofullerenes in terms of efficiency, selectivity, and practicality.[7] Thus, we first focused on the development of a selective and efficient aziridination reaction of C_{60}. Inspired by recent progress in metal-catalyzed aziridination of olefins,[5] we investigated the aziridination of C_{60} with iminophenyliodinane (TsN═IPh) using various metal complexes (Table 1).[8]

Scheme 1. Aziridinofullerene 1 as a Platform for Functionalized Fullerenes



In early experiments, we identified that the aziridination of C_{60} with TsN═IPh did not occur under the influence of standard catalysts such as $Rh_2(OAc)_4$, $Cu(OTf)_2$, and CuCl (entries 1−3). While searching for a ligand-accelerating effect in the reaction, we found that *N*-tosyl[1,2]aziridino[60]fullerene (**1**) could be obtained in 25% yield when C_{60} (1.0 equiv) was treated with TsN═IPh (1.0 equiv) in the presence of CuCl (20 mol %) and pyridine (40 mol %) in 1,2-$Cl_2C_6H_4$ at room temperature (entry 6).[9] Among the various copper salts (entries 6−9) and pyridine-based ligands (entries 10−16) examined, we identified as the best system the combination of CuCl and 2,6-lutidine, which furnished **1** in 41% yield (entry 14). With this system, it was possible to reduce the catalyst loading to 2 mol % without loss of reactivity (43%; entry 15).

Having established a new protocol for the fullerene aziridination, we subsequently embarked on the acid-catalyzed double nucleophilic substitution of **1** with aromatic compounds. Among various Lewis/Brønsted acids investigated, we found that trifluoromethanesulfonic acid (TfOH) is an effective catalyst for such reactions (see the Supporting Information for details).[10]

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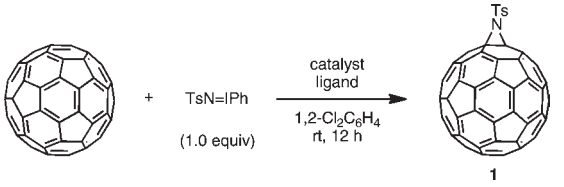
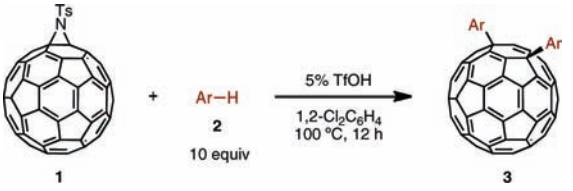
Table 1. Effect of the Ligand in Cu-Catalyzed Aziridination of C_{60}[a]

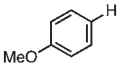
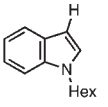
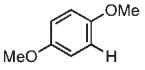
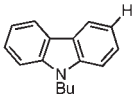
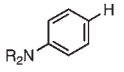
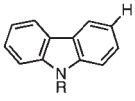
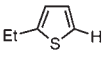
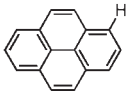


entry	catalyst	ligand	yield (%)[b]	entry	catalyst	ligand	yield (%)[b]
1	$Rh_2(OAc)_4$	—	<1	9	CuI	pyridine	<1
2	$Cu(OTf)_2$	—	<1	10	CuCl	4-MeOpy	24
3	CuCl	—	<1	11	CuCl	4-CNpy	10
4[c]	CuCl	2,2′-bpy	<1	12	CuCl	2-picoline	39
5	CuCl	PPh_3	10	13	CuCl	quinoline	37
6	CuCl	pyridine	25	14	CuCl	2,6-lutidine	41
7	$CuCl_2$	pyridine	23	15[d]	CuCl	2,6-lutidine	43
8	CuBr	pyridine	<5	16	CuCl	2,6-di*t*Bupy	<1

[a] Reaction conditions: C_{60} (30 μmol), TsN=IPh (30 μmol), catalyst (20 mol %), ligand (40 mol %), 1,2-$Cl_2C_6H_4$, rt, 12 h. Abbreviations: bpy, bipyridyl; py, pyridine. [b] Isolated yield. [c] 20 mol % ligand was employed. [d] Reaction conditions: C_{60} (600 μmol), TsN=IPh (600 μmol), CuCl (2 mol %), ligand (4 mol %), 1,2-$Cl_2C_6H_4$, rt, 12 h.

Table 2. TfOH-Catalyzed Reactions of 1 with Aromatic Compounds 2

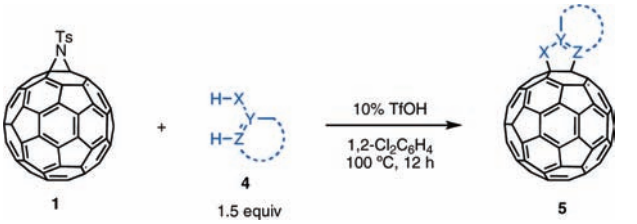


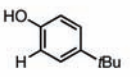
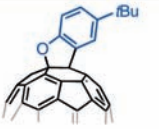
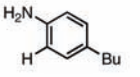
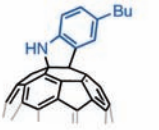
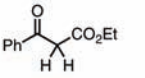
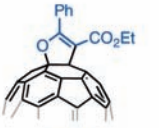
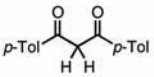
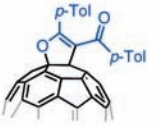
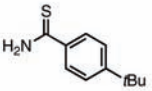
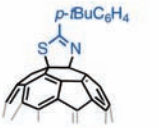
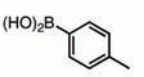
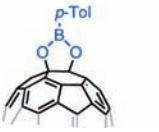
entry	Ar–H		3 (yield[a])	entry	Ar–H		3 (yield[a])
1[b]		(2a)	3a (81%)	5		(2e)	3e (88%)
2[c]		(2b)	3b (90%)	6		(2f)	3f (86%)
3[d]		(2c)	3c (95%)	7[d]		(2g)	3g (85%)
4		(2d)	3d (94%)	8		(2h)	3h (94%)

[a] Isolated yield. [b] The catalyst loading was 10 mol %. [c] The catalyst loading was 30 mol %. [d] R = *p*-1-nonylphenyl.

Representative results are shown in Table 2. For example, electron-rich benzene derivatives such as anisole (**2a**), 1,4-dimethoxybenzene (**2b**), and aniline derivative **2c** reacted with **1** at the para (for **2a** and **2c**) or ortho (for **2b**) position. The 1,4-diarylation reaction also occurred with electron-rich heteroarenes such as thiophenes, indoles, and carbazoles (entries 4−7). Notably, the reaction displayed excellent regioselectivity with regard to both the heteroarene ring (at most nucleophilic carbons) and the fullerene core (in 1,4-addition mode). Pyrene (**2h**) also reacted smoothly with **1** to give planar-sphere hybrid hydrocarbon **3h** in 94% yield (entry 8).

Table 3. TfOH-Catalyzed Reactions of 1 with Bifunctional Nucleophiles 4



entry	substrate 4		5 (yield[a])	
1		4a		5a (96%)
2[b]		4b		5b (62%)
3		4c		5c (86%)
4		4d		5d (87%)
5[b]		4e		5e (67%)
6[c]		4f		5f (57%)

[a] Isolated yield. [b] The reaction time was 48 h. [c] 3 equiv of **4f** was employed.

We next envisioned that organic compounds having two potential nucleophilic sites could be employed in the TfOH-catalyzed reaction of **1** to afford cyclized products (Table 3). Indeed, under the catalytic influence of TfOH, 4-*tert*-butylphenol (**4a**) reacted with **1** to furnish the dihydrobenzofuran derivative **5a** in 96% yield (entry 1). The cyclization occurred in a 1,2-addition mode on the fullerene core and at the OH group and aromatic ortho C−H bond of **4a**. Although a longer reaction time was required, aniline derivative **4b** also reacted in a similar fashion to afford dihydroindole **5b** (entry 2). It was also found that 1,3-dicarbonyl compounds possessing two acidic C−H bonds, such as **4c** and **4d**, reacted with **1** to furnish dihydrofuran derivatives **5c** and **5d**, respectively (entries 3 and 4).[11] When thiobenzamide **4e** was used as the substrate, dihydrothiazole **5e** was formed in 67% yield (entry 5). Interestingly, the reaction

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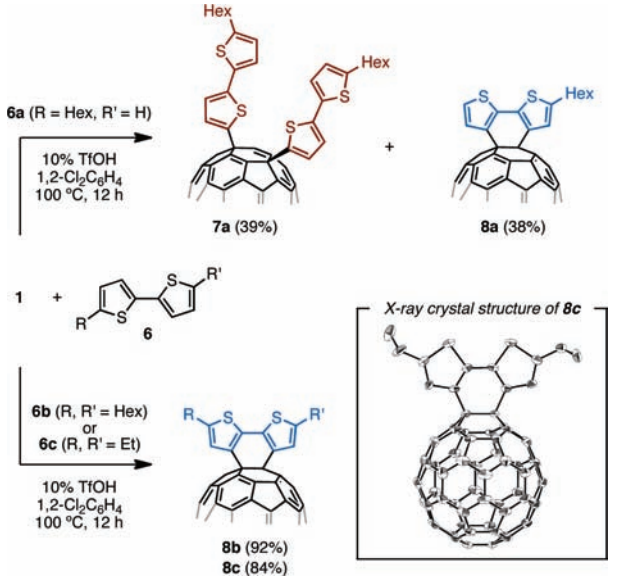
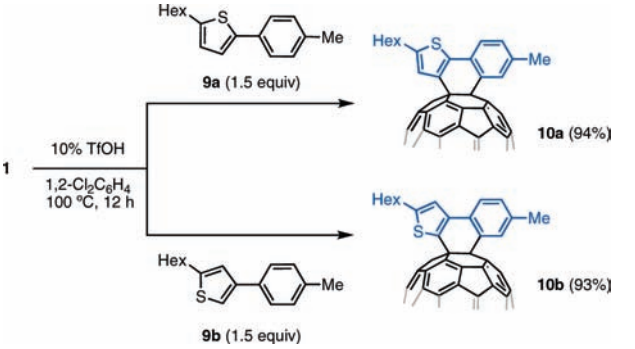
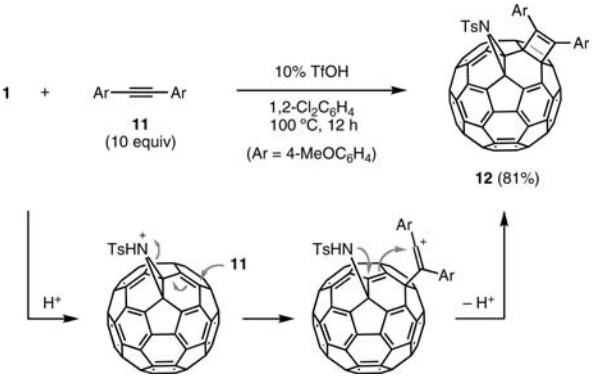
Scheme 2. TfOH-Catalyzed Reactions of 1 with 2,2′-Bithiophenes 6



Scheme 3. TfOH-Catalyzed Reactions of 1 with Arylthiophenes 9



Scheme 4. TfOH-Catalyzed Reaction of 1 with Alkyne 11



using *p*-tolylboronic acid (**4f**) gave the corresponding boronate ester **5f** (entry 6). This reaction represents a new synthetic method for generating protected fullerene diols, which are known to be difficult to synthesize and are unstable in a free-hydroxy form.[12]

During the investigation, we found the unique cyclization reaction using 2,2′-bithiophene derivatives **6** (Scheme 2). Treatment of **1** and 5-(1-hexyl)-2,2′-bithiophene (**6a**) in the presence of a catalytic amount of TfOH afforded two products. In addition to the expected 1,4-bisadduct **7a** (39% yield), the formation of fused fullerene derivative **8a** (38% yield) was indicated from the NMR and mass spectrometry analyses. As the 3- and 3′-positions in the 2,2′-bithiophene structure are generally less reactive than the 5- and 5′-positions for both steric and electronic reasons, the formation of **8a** was intriguing. We further found that fused fullerene derivatives **8b** and **8c** were exclusively formed when 5,5′-dialkyl-2,2′-bithiophenes **6b** and **6c**, respectively, were subjected to the reaction with **1**. The ^{13}C NMR spectra of **8b** and **8c** indicated that they have C_{2v} symmetry, which is in accordance with the fused structures. Gratifyingly, the structure of **8c** was unambiguously determined by single-crystal X-ray diffraction analysis (Scheme 2). These results clearly show that 2,2′-bithiophenes can act as both a monofunctional nucleophile (as shown in Table 2) and a bifunctional nucleophile (as shown in Table 3) in the TfOH-catalyzed reaction with **1**.

Encouraged by the discovery of the fused reaction mode of 2,2′-bithiophenes, we next examined the reaction using arylthiophenes (Scheme 3). Thus, 5-tolylthiophene (**9a**) and 4-tolylthiophene (**9b**) were reacted with **1** under the catalytic influence of TfOH to give the corresponding fused fullerenes **10a** and **10b** in excellent yields.[13] The reaction of **9a** occurred at the 3-position of thiophene ring. In the case of **9b**, where there are two possible sites on the thiophene ring leading toward fused products, the cyclization took place exclusively at the 5-position. These fullerene-fused π-electron systems (**8** and **9**), which have significant potential as interesting optoelectronic materials, would be notoriously difficult to synthesize by other existing methods.

In all of the above-mentioned TfOH-catalyzed reactions, the aziridine moiety of **1** served as a traceless template. During an investigation trying to insert an alkyne into the C−N bond of **1**, we accidentally discovered a formal [2 + 2] cycloaddition of **1** and alkyne. Thus, treatment of **1** with tolan derivative **11** in the presence of TfOH catalyst furnished the formal [2 + 2] cycloaddition adduct **12** in 81% yield (Scheme 4). The molecular structure of **12** was unambiguously determined by X-ray crystal structure analysis (see the Supporting Information for details). The reaction might proceed through acid-catalyzed nucleophilic attack on **1** by the alkyne followed by aziridine-regenerating double ring closure, as shown in Scheme 4. In view of the general difficulty in achieving [2 + 2] cycloadditions of fullerenes and alkynes,[14] the importance of having the aziridine moiety fused on the fullerene core is obvious. As depicted in Scheme 4, the aziridine moiety might act as an electron reservoir, making a stepwise [2 + 2] cycloaddition feasible. Although the reaction mechanism is debatable, this result signifies the immense opportunity for further utilization of aziridinofullerenes.

In summary, we have demonstrated that aziridinofullerene **1** is a versatile platform for the synthesis of a variety of functionalized fullerenes via acid-catalyzed ring-opening reactions. The rapid generation of structural diversity in a single chemical operation using the common platform **1** is notable. The fact that most of the architecturally and electronically interesting fullerenes obtained in this study are new compounds speaks well for the potential of the present strategy in the generation of as-yet-unexplored nanocarbons for various applications.

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■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, characterization data for all of the fullerene derivatives, and crystallographic data for **8c** and **12** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) There is one report on the catalyzed aziridination of C_{60} (albeit low-yielding) in a patent (see: Duczek, W.; Niclas, H.-J.; Radeck, W. German Patent DE 19645374, 1998.) However, it was not possible to produce the corresponding aziridinofullerene in our laboratory.

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(10) Minakata recently reported that **1** reacts with toluene (employed as a solvent) in the presence of $BF_3 \cdot Et_2O$ (10 equiv) to give the corresponding 1,4-ditolylated C_{60}.[7b]

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(13) We recently developed two Pd-catalyzed C−H bond arylation reactions of thiophenes whose regiochemical outcomes are complementary to each other (α- and β-selective) [see: (a) Yanagisawa, S.; Ueda, K.; Sekizawa, H.; Itami, K. *J. Am. Chem. Soc.* **2009**, *131*, 14622. (b) Ueda, K.; Yanagisawa, S.; Yamaguchi, J.; Itami, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 8946.]. Coupling these reactions with the present cyclization reaction using arylthiophenes **9** will significantly enhance its utility.

(14) (a) For intramolecular [2 + 2] cycloadditions of fuller-1,6-enynes, see ref 2h. For the reactions using aminoalkynes, see:(b) Zhang, X.; Romero, A.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 11024. (c) Bernstein, R.; Foote, C. S. *Tetrahedron Lett.* **1998**, *39*, 7051.