

Synthesis of [60]Fullerene-Fused Sultones via Sulfonic Acid Group-Directed C—H Bond Activation

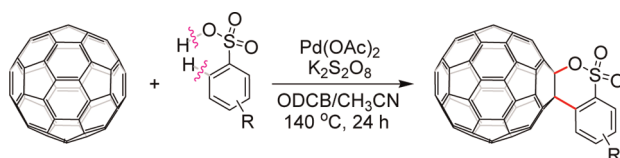
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Received March 22, 2012

ABSTRACT



Functionalization with the sulfonic acid group as the directing group in a C—H activation reaction has been revealed for the first time. [60]Fullerene has been employed in the unprecedented palladium-catalyzed C—H activation reaction of arylsulfonic acids to afford [60]fullerene-fused sultones.

Transition-metal-mediated or -catalyzed reactions of fullerenes have provided useful methods for the preparation of a wide range of functionalized fullerene derivatives.¹ Our previous work in this direction has been focused on the free-radical reactions of [60]fullerene (C₆₀), which was mainly promoted by Mn(OAc)₃² and Fe(ClO₄)₃.³ Recently, we have developed the Pd-catalyzed reactions of C₆₀ and obtained novel C₆₀-fused indoline and isoquinolinone derivatives in a highly regioselective manner.⁴

On the other hand, C—H bond activation has emerged as one of the most important methodologies to construct C—C and C—X (X = heteroatom) bonds in organic synthesis.⁵ A directing group is usually required to achieve high regioselectivity. A diverse range of directing groups, such as amides, anilides, pyridines, oxime ethers, quinolines, oxazolines, and amines, have been reported for C—H activation reactions.⁵ However, only one type of acids, that is, carboxylic acid, has been exploited to direct C—H bond activations, and C—H halogenation, arylation, alkylation, olefination, hydroxylation, and carboxylation reactions

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have been successfully realized.⁶ Our interest in C–H activation reactions^{4b,c,7} prompted us to explore another type of organic acids for directing C–H functionalization. *p*-Toluenesulfonic acid (TsOH) has been added frequently to promote Pd-catalyzed C–H activation reactions by increasing the electrophilicity of the Pd(II) center.^{4b,8} Pd(OTs)₂ has also been employed as the palladium source in a few C–H activation reactions.^{8b,9} Just like carboxylic acids, it is possible that arylsulfonic acids can be functionalized via sulfonic acid group-directed C–H activation. However, such TsOH derivatives have not been reported in all the aforementioned cases.^{4b,8,9} The electron-deficient aryl ring of arylsulfonic acids is less prone to the C–H activation step compared to that of aryl carboxylic acids. We have addressed this challenge, and herein report the synthesis of sultones by Pd-catalyzed reaction of arylsulfonic acids with C₆₀ via unprecedented sulfonic acid group-directed C–H bond activation.

The readily available TsOH (**1a**) was chosen as a model substrate. Our initial attempts to olefinate TsOH failed with both acrylate esters and styrene under conditions previously employed for aromatic carboxylic acids¹⁰ or other combinations of Pd(OAc)₂, oxidants, and solvents. Gratifyingly, when C₆₀ was utilized, TsOH could be functionalized to give C₆₀-fused sultone derivative **2a**. This sultone construction via Pd-catalyzed sp² C–H activation of arylsulfonic acids has no precedent in the literature.

This reaction of C₆₀ (36.0 mg, 0.05 mmol) with TsOH (3 equiv) was screened in the presence of different palladium catalysts (10 mol %), oxidants (3 equiv), and solvents. The results are summarized in Table 1. Because of the poor solubility of TsOH in ODCB, a mixture of ODCB (4 mL) and CH₃CN (0.5 mL) was first used as the solvent to afford product **2a** in 30% yield (73% based on consumed C₆₀) when the reaction was catalyzed with Pd(OAc)₂ (Table 1, entry 1). However, the absence of CH₃CN as the cosolvent lowered the yield to 11% (Table 1, entry 2). Replacing CH₃CN with DMSO and DMF generated only a trace amount of the desired product (Table 1, entries 3 and 4). Further examination of other oxidants, including Cu(OAc)₂, Cu(OTf)₂, AgOAc, Ag₂O, Ag₂CO₃, oxone, BQ, and PhI(OAc)₂, proved that K₂S₂O₈ was the best for this reaction with Pd(OAc)₂ as the catalyst and provided the highest product yield (Table 1, entry 1 vs entries 5–12). Similar superior performance of CH₃CN and K₂S₂O₈ was also observed previously for the Pd-catalyzed reaction of C₆₀ with anilides via C–H bond activation.^{4b} The exact reason is unknown now, although the inefficiency of DMSO and DMF compared to CH₃CN might be due to their stronger coordination to the palladium species and

thus inhibiting the catalytic reaction.^{4b} With K₂S₂O₈ as the oxidant, various Pd catalysts were screened (Table 1, entries 13–16). It was found that Pd(TFA)₂ gave comparable yield to that of Pd(OAc)₂ (Table 1, entry 13 vs entry 1), while PdCl₂, Pd(PPh₃)₂Cl₂, and Pd(PPh₃)₄ exhibited slightly lower yields (Table 1, entries 14–16 vs entry 1). A control experiment showed that the absence of a palladium catalyst under otherwise identical conditions did not produce any **2a** (Table 1, entry 17). With economic considerations, the optimized reaction conditions were thus chosen as follows: Pd(OAc)₂ and K₂S₂O₈ as the catalyst and oxidant, respectively, in ODCB/CH₃CN = 8:1 at 140 °C for 24 h.

Table 1. Screening the Reaction Conditions for the Pd-Catalyzed Reaction of C₆₀ with **1a**^a

entry	catalyst	oxidant	solvent (mL)	yield of 2a (%) ^b
1	Pd(OAc) ₂	K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	30 (73)
2	Pd(OAc) ₂	K ₂ S ₂ O ₈	ODCB (4)	11 (61)
3	Pd(OAc) ₂	K ₂ S ₂ O ₈	ODCB/DMF (4:0.5)	trace
4	Pd(OAc) ₂	K ₂ S ₂ O ₈	ODCB/DMSO (4:0.5)	trace
5	Pd(OAc) ₂	Cu(OAc) ₂	ODCB/CH ₃ CN (4:0.5)	6 (33)
6	Pd(OAc) ₂	Cu(OTf) ₂	ODCB/CH ₃ CN (4:0.5)	5 (25)
7	Pd(OAc) ₂	AgOAc	ODCB/CH ₃ CN (4:0.5)	11 (31)
8	Pd(OAc) ₂	Ag ₂ O	ODCB/CH ₃ CN (4:0.5)	trace
9	Pd(OAc) ₂	Ag ₂ CO ₃	ODCB/CH ₃ CN (4:0.5)	trace
10	Pd(OAc) ₂	oxone	ODCB/CH ₃ CN (4:0.5)	10 (27)
11	Pd(OAc) ₂	BQ	ODCB/CH ₃ CN (4:0.5)	trace
12	Pd(OAc) ₂	PhI(OAc) ₂	ODCB/CH ₃ CN (4:0.5)	18 (41)
13	Pd(TFA) ₂	K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	31 (72)
14	PdCl ₂	K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	24 (80)
15	PdCl ₂ (PPh ₃) ₂	K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	27 (77)
16	Pd(PPh ₃) ₄	K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	26 (79)
17		K ₂ S ₂ O ₈	ODCB/CH ₃ CN (4:0.5)	0 (0)

^a All reactions were carried out with C₆₀ (36.0 mg, 0.05 mmol), catalyst (0.005 mmol), TsOH (28.5 mg, 0.15 mmol), and oxidant (0.15 mmol) in the indicated solvent at 140 °C for 24 h in air. ^b Isolated yield. Values in parentheses were based on consumed C₆₀.

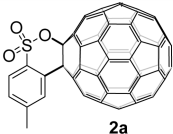
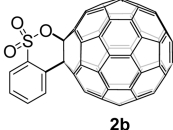
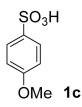
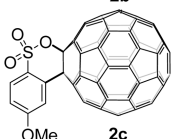
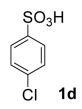
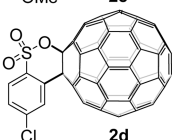
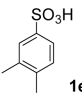
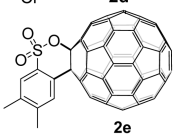
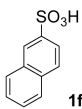
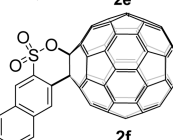
The scope of this annulation reaction was investigated next by exploring different arylsulfonic acids. As shown in Table 2, a variety of arylsulfonic acids reacted efficiently to afford the desired C₆₀-fused sultones in synthetically valuable yields. Arylsulfonic acids with both electron-donating (Table 2, entries 1, 3, and 5) and electron-withdrawing (Table 2, entry 4) substituents on the phenyl ring could be smoothly transformed into the desired products in 18–30% yields (60–81% based on consumed C₆₀). β-Naphthylsulfonic acid (**1f**) could also be employed and furnished sultone **2f** in 22% yield (69% based on consumed C₆₀). In principle, two isomers could

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Table 2. Results for the Pd-Catalyzed Reaction of C₆₀ with Arylsulfonic Acids **1a–f**^a

entry	arylsulfonic acid 1	product 2	yield of 2 (%) ^b
1			30 (73)
2			24 (77)
3 ^c			18 (60)
4			26 (74)
5			22 (81)
6			22 (69)

^a Unless otherwise specified, all reactions were performed with C₆₀ (36.0 mg, 0.05 mmol), **1** (0.15 mmol), K₂S₂O₈ (40.5 mg, 0.15 mmol), and Pd(OAc)₂ (1.1 mg, 0.005 mmol) in ODCB (4 mL)/CH₃CN (0.5 mL) at 140 °C for 24 h. ^b Isolated yield by column chromatography. Values in parentheses were based on consumed C₆₀. ^c Substrate **1c** (30.9 mg, 0.15 mmol) was first dissolved in acetonitrile (0.5 mL) and then added to the ODCB (4 mL) solution of C₆₀ (36.0 mg, 0.05 mmol), Pd(OAc)₂ (2.2 mg, 0.01 mmol), and K₂S₂O₈ (40.5 mg, 0.15 mmol).

be produced for the reaction with both **1e** and **1f**. The regioselective formation of **2e** and **2f** may be governed by steric factors.^{4,7} It should be pointed out that the 18–30% yields (60–81% based on consumed C₆₀) of **2a–f** are comparable with the reported yields for most other monoadducts^{2–4,11} in fullerene chemistry, as C₆₀ has 30 reactive C=C bonds and tended to give a mixture of

regioisomers from bisadducts and multiadducts when overreacted.

The structures of C₆₀-fused sultones **2a–f** were fully characterized by HRMS, ¹H NMR, ¹³C NMR, FT-IR, and UV–vis spectroscopy. The high-resolution mass spectra of **2a–f** displayed the correct molecular ion peaks. The ¹H NMR spectra of **2a–f** showed all expected signals, with one less aromatic proton than the starting material **1a–f** due to the removal of one proton during the C–H activation process. In the ¹³C NMR spectra of **2a–f**, there were 29–30 peaks including two half-intensity ones in the 134.60–153.19 ppm region for the 58 sp²-carbons of the C₆₀ moiety, consistent with their C_s symmetry. The two sp³-carbons of the C₆₀ skeleton were located at 97.56–98.25 ppm and 59.91–60.38 ppm, close to those of the previously reported C₆₀-fused lactone derivatives.¹¹ It should be pointed out that the very low solubility of **2c** prevented us from obtaining its ¹³C NMR spectrum with good signal/noise ratio. The IR spectra of **2a–f** showed two strong absorptions at 1370–1377 and 1190–1200 cm^{–1} due to the sultone group. Their UV–vis spectra exhibited a peak at 421–422 nm, which is a characteristic absorption for the 1,2-adducts of C₆₀.^{2–4,11}

Sultones exhibit biological activities¹² and are synthetically valuable heterocycles that can react with a variety of compounds to afford other useful products.¹³ It is expected that our C₆₀-fused sultones can be further elaborated to produce functionalized fullerenes. Indeed, we successfully achieved the ring-opening of C₆₀-fused sultone **2a** by treating with excess BF₃·OEt₂ in ODCB at 150 °C and obtained arylsulfonic ester-substituted hydrofullerene **3** in 86% yield (Scheme 1). To the best of our knowledge, the unusual ring-opening of a sultone by BF₃·OEt₂ is also unprecedented. Hydrofullerene **3** was likely formed via the BF₃-mediated cleavage of diethyl ether followed by hydride transfer (see the Supporting Information).¹⁴ The acidic hydrogen attached to the fullerene skeleton in hydrofullerene **3** could be easily deprotonated with KO^tBu in THF at room temperature.¹⁵ The color of the solution changed immediately from brown to dark green, indicating the formation of a monoanion C₆₀R[–]. Further nucleophilic substitution reaction of the in situ generated C₆₀R[–] with CH₃I gave 1,4-bisadduct **4** in 82% yield (Scheme 1).¹⁶ When the monoanion C₆₀R[–] was treated with I₂, the singly bonded dimer **5** existed as a mixture of *racemic* and *meso* isomers and was formed in 91% yield by coupling of the monomer radicals C₆₀R[•],¹⁷ which were produced by one-electron oxidation of C₆₀R[–] with I₂ (Scheme 1).¹⁶

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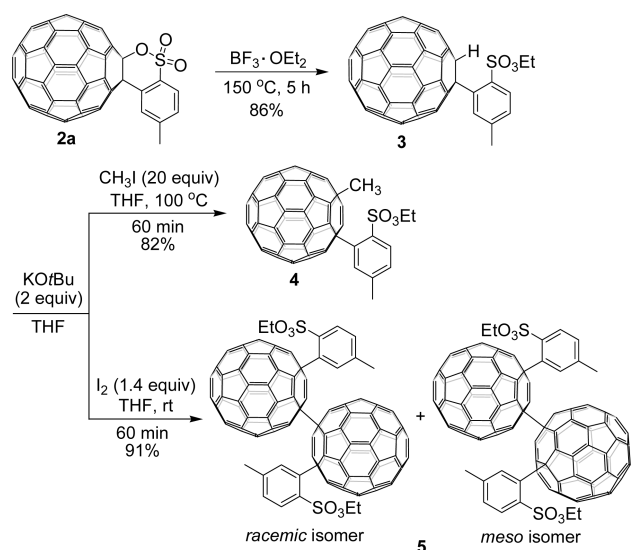
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Scheme 1. Ring-Opening and Further Functionalization of Sultone **2a**

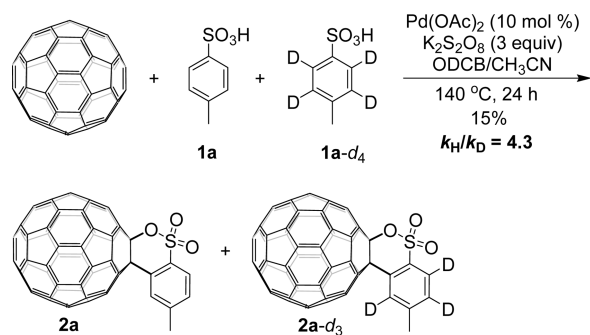


To gain insight into the reaction mechanism for the formation of sultones **2**, we performed a kinetic isotope effect (KIE) study. Experiments revealed that the Pd-catalyzed reaction of C_{60} with 1.5 equiv of **1a** and 1.5 equiv of **1a-d₄** exhibited a primary kinetic isotope effect $k_H/k_D = 4.3$ (Scheme 2).

During our work, Bedford et al. reported the Pd-catalyzed *ortho*-selective halogenation of anilides in the presence of TsOH, and identified that the orthopalladated species of TsOH was actually the catalyst.¹⁸ Nevertheless, the palladacyclic complex was fragile and underwent rapid loss of TsOH.¹⁸ Therefore, the C–H functionalization of arylsulfonic acids is viewed to be extremely difficult. Although the exact reaction mechanism for the formation of **2** is currently unknown, the reaction is believed to proceed through the sulfonic acid group-directed *ortho* sp^2 C–H bond activation to afford the same palladacycles,¹⁸ which undergo subsequent cyclization with C_{60} to eventually afford sultones **2**.

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Scheme 2. Kinetic Isotope Effect Study for the Formation of Sultone **2a**



In summary, we have addressed the challenge of using the sulfonic acid group for directing C–H activation reactions for the first time. C_{60} could be successfully utilized in the Pd-catalyzed C–H activation of arylsulfonic acids leading to C_{60} -fused sultones, albeit the attempts to olefinate TsOH with acrylates and styrenes failed. The present reaction involves the cleavage of C–H and O–H bonds as well as the formation of C–C and C–O bonds. The unprecedented ring-opening of C_{60} -fused sultones was achieved by heating with $BF_3 \cdot OEt_2$, and could be further functionalized to 1,4-adduct and singly bonded fullerene dimer.

Acknowledgment. The authors are grateful for financial support from the National Natural Science Foundation of China (21132007, 20972145) and National Basic Research Program of China (2011CB921402).

Supporting Information Available. Experimental procedures, characterization data, and the 1H NMR and ^{13}C NMR spectra of products **2a–f**, **3–5**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.