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Palladium-catalysed heteroannulation of [60]fullerene with *N*-benzyl sulfonamides and subsequent functionalisation†‡§

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The palladium-catalysed heteroannulation of [60]fullerene with various *N*-benzyl sulfonamides *via* C–H bond activation affords [60]fullerene-fused tetrahydroisoquinolines. In the presence of a Brønsted acid [60]fullerene-fused tetrahydroisoquinolines are transformed to [60]fullerene-fused indanes, in which the sulfonamide group can be removed or replaced with an aryl group.

A vast number of chemical reactions have been discovered to functionalise fullerenes since the 1990s.[1] Among them transition-metal-mediated or -catalysed reactions of fullerenes have attracted significant attention.[2] Palladium-catalysed reactions of [60]fullerene (C_{60}) have also been disclosed.[3,4] However, functionalisation of C_{60} *via* a C–H bond activation strategy is underdeveloped and limited to the Pd-catalysed reactions of C_{60} with anilides,[4a] benzamides[4b] and arlysulfonic acids.[4c] It was reported that the amide-directed *ortho* C–H bond activation occurred selectively at the benzamide phenyl ring rather than at the phenyl ring of the *N*-benzyl moiety for the Pd-catalysed reaction of C_{60} with *N*-benzyl benzamides.[4b] In continuation of our interest in Pd-catalysed C–H activation reactions[4,5] and in efforts to extend *N*-benzyl benzamides[4b] to other substrates, we have found that the usage of *N*-benzyl sulfonamides changes the site selectivity of the *ortho* C–H activation to the phenyl ring of the *N*-benzyl moiety (Fig. 1). Herein, we report this new finding and its application to the synthesis of C_{60}-fused tetrahydroisoquinolines from the Pd-catalysed heteroannulation of C_{60} with *N*-benzyl sulfonamides. Intriguingly, the obtained C_{60}-fused tetrahydroisoquinolines have been transformed to C_{60}-fused indanes through a Brønsted acid-promoted rearrangement. Furthermore, the sulfonamide group in C_{60}-fused indanes can be removed or replaced with an aryl group.

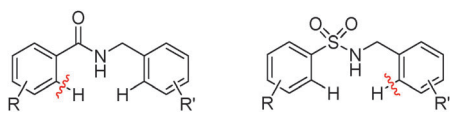
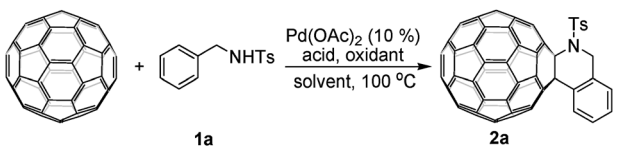


Fig. 1 Different site selectivity for the Pd-catalysed C–H bond activation of *N*-benzyl benzamides and *N*-benzyl sulfonamides.

Initially, we chose the Pd-catalysed reaction of C_{60} with *N*-benzyl-4-toluenesulfonamide (**1a**) as the model reaction for our optimization study. When a mixture of C_{60} (36.0 mg, 0.05 mmol), **1a** (5 equiv.) and $Pd(OAc)_2$ (10 mol%) in *O*-dichlorobenzene (4 mL) was heated at 100 °C for 2 h, only a trace amount of the product was identified (Table 1, entry 1). *p*-Toluenesulfonic acid (PTSA) was found to be beneficial to the C–H activation reaction of C_{60}.[4a] After addition of 2 equiv. of PTSA, C_{60}-fused tetrahydroisoquinoline **2a** was obtained in 13% yield (Table 1, entry 2). In contrast to the previously reported Pd-catalysed reaction of C_{60} with *N*-benzyl benzamides,[4b]

Table 1 Screening the Pd-catalysed reaction of C_{60} and *N*-benzyl-4-toluenesulfonamide[a]



1a **2a**

Entry	Acid	Oxidant	Solvent (mL)	Yield[b] (%)
1	None	$K_2S_2O_8$	ODCB (4)	Trace
2	PTSA	$K_2S_2O_8$	ODCB (4)	13 (81)
3	CSA	$K_2S_2O_8$	ODCB (4)	4 (44)
4	PWA	$K_2S_2O_8$	ODCB (4)	Trace
5	TFA	$K_2S_2O_8$	ODCB (4)	4 (49)
6[c]	TFA	$K_2S_2O_8$	ODCB (4)	29 (47)
7	**MesSA**	**$K_2S_2O_8$**	**ODCB (4)**	**28 (58)**
8	MesSA	Oxone	ODCB (4)	6 (40)
9	MesSA	$Cu(OAc)_2{\cdot}H_2O$	ODCB (4)	7 (78)
10	MesSA	AgOAc	ODCB (4)	3 (38)
11	MesSA	BQ	ODCB (4)	3 (38)
12[d]	MesSA	$K_2S_2O_8$	ODCB (4)	12 (63)
13	MesSA	$K_2S_2O_8$	ODCB(4)/DMSO (0.5)	NR
14	MesSA	$K_2S_2O_8$	ODCB(4)/CH_3CN (0.5)	NR
15	MesSA	$K_2S_2O_8$	ODCB(4)/dioxane (0.5)	NR

[a] Unless indicated otherwise, all reactions were performed in the indicated solvent at 100 °C for 2 h, molar ratio of C_{60}/**1a**/$Pd(OAc)_2$/oxidant/acid = 1/5/0.1/5/2. [b] Isolated yield. Values in parentheses are based on consumed C_{60}. [c] 0.5 mL of TFA was used. [d] Molar ratio of C_{60}/**1a**/$Pd(OAc)_2$/oxidant/acid = 1/3/0.1/3/2. Ts = 4-toluenesulfonyl, ODCB = *O*-dichlorobenzene, DMSO = dimethyl sulfoxide.

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† Dedicated to Professor Koichi Komatsu on the occasion of his 70th birthday.

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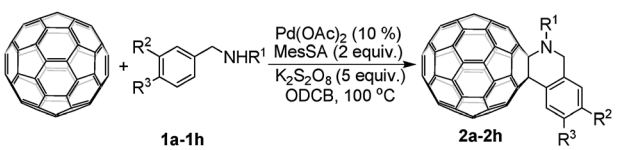
§ Electronic supplementary information (ESI) available: Experimental procedures for the synthesis, spectral data and NMR spectra of compounds **2a–2h**, **3a–3h** and **4a–4c**. See DOI: 10.1039/c2cc33923d

replacing the amide group with the sulfonamide group switches the C–H bond activation selectivity to the benzylamine moiety. The use of camphorsulfonic acid (CSA), 12-phosphotungstic acid (PWA) or trifluoroacetic acid (TFA) in place of PTSA led to obvious decrease in the product yield of **2a** (Table 1, entries 3–5). To our delight, if TFA was employed as the cosolvent, a yield of 29% (47% based on the consumed C_{60}) was obtained (Table 1, entry 6). In addition, mesitylenesulfonic acid dihydrate (MesSA) was superior to TFA in terms of both the amount of the used acid and product yield based on consumed C_{60} (58% *vs.* 47%) (Table 1, entry 7 *vs.* entry 6). After the acid was selected, several other oxidants including oxone, $Cu(OAc)_2{\cdot}H_2O$, AgOAc and *p*-benzoquinone (BQ) were explored, and $K_2S_2O_8$ was found to be the best oxidant for the reaction (Table 1, entries 8–11 *vs.* entry 7). Decreasing the amount of **1a** and $K_2S_2O_8$ reduced the product yield to 12% (Table 1, entry 12 *vs.* entry 7). Disappointingly, no reaction occurred when CH_3CN, DMSO and 1,4-dioxane were employed as cosolvents (Table 1, entries 13–15).

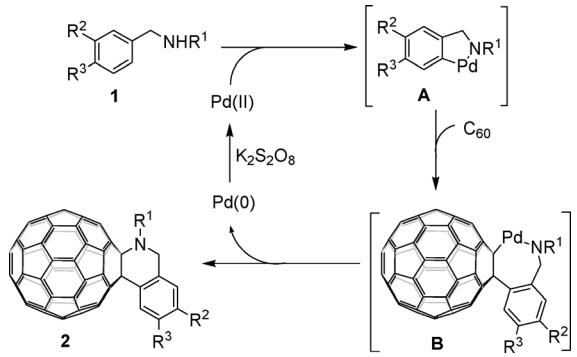
With the optimal conditions (Table 1, entry 7) in hand, the substrate scope and limitation were investigated by employing a wide array of *N*-benzyl sulfonamides. The reaction conditions, product yields along with recovered C_{60} are shown in Table 2. Substrates bearing electron-withdrawing group (4-Cl) and electron-donating groups (4-Me, 4-MeO, 3,4-$(Me)_2$) on the benzylamine moiety were all tolerated. Substrates **1b** and **1c** gave products **2b** and **2c** in 22% and 30% yields, respectively (Table 2, entries 2 and 3). Under the employed standard conditions, substrate **1d** tended to generate more byproducts, thus the reaction temperature and the amount of MesSA were lowered, and the desired product could be obtained in 17% yield (Table 2, entry 4). The corresponding product of *N*-(3,4-dimethylbenzyl)-4-toluenesulfonamide **1e** was regioselectively formed in 33% yield due to steric hindrance (Table 2, entry 5). On the other hand, different functional groups

Table 2 Pd-catalysed heteroannulation of C_{60} with *N*-benzyl sulfonamides[a]



Entry	Product	R^1, R^2, R^3	Time (h)	Yield[b] (%)	Recovered C_{60} (%)
1	**2a**	R^1 = Ts, R^2 = R^3 = H	2.0	28 (58)	52
2	**2b**	R^1 = Ts, R^2 = H, R^3 = Cl	3.5	22 (57)	61
3	**2c**	R^1 = Ts, R^2 = H, R^3 = Me	1.5	30 (63)	52
4[c]	**2d**	R^1 = Ts, R^2 = H, R^3 = MeO	6.0	17 (61)	72
5	**2e**	R^1 = Ts, R^2 = R^3 = Me	1.5	33 (63)	47
6	**2f**	R^1 = Bs, R^2 = R^3 = H	2.0	31 (56)	45
7	**2g**	R^1 = Cs, R^2 = R^3 = H	2.5	23 (54)	59
8	**2h**	R^1 = Ms, R^2 = R^3 = H	3.0	22 (47)	53

[a] Unless indicated otherwise, all reactions were performed in ODCB at 100 °C, molar ratio of C_{60}/**2**/$Pd(OAc)_2$/$K_2S_2O_8$/MesSA = 1/5/0.1/5/2. [b] Isolated yield. Values in parentheses are based on consumed C_{60}. [c] The reaction was performed in ODCB at 80 °C, molar ratio of C_{60}/**2d**/$Pd(OAc)_2$/$K_2S_2O_8$/MesSA = 1/5/0.2/5/1. Bs = benzenesulfonyl, Cs = 4-chlorobenzenesulfonyl, Ms = methanesulfonyl.



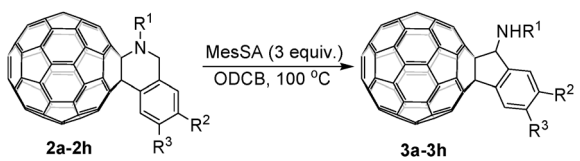
Scheme 1 Proposed mechanism for the formation of C_{60}-fused tetrahydroisoquinolines.

attached to the nitrogen atom such as benzenesulfonyl (Bs) (**1f**), 4-chlorobenzenesulfonyl (Cs) (**1g**), and methanesulfonyl (Ms) (**1h**) worked well and gave the corresponding products **2f**, **2g** and **2h** in 22–31% yields (Table 2, entries 6–8).

The exact pathway leading to **2** is unknown now. On the basis of the suggested mechanisms in the literature,[4,5] a proposed mechanism is shown in Scheme 1. Palladation of *N*-benzyl sulfonamides **1** with $Pd(OAc)_2$ produces intermediate **A**, followed by insertion of C_{60} to generate intermediate **B**. Similar processes have been suggested previously.[4a,b] Subsequent reductive elimination produces C_{60}-fused tetrahydroisoquinolines **2** and Pd(0). The latter is oxidized to Pd(II) by $K_2S_2O_8$ to complete the catalytic cycle.

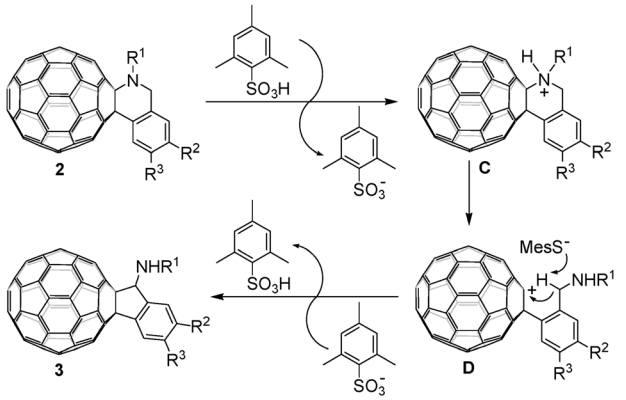
Intriguingly, we found that treatment of **2a** with 3 equiv. of MesSA afforded a rearrangement product, *i.e.*, C_{60}-fused indane **3a**, in 70% yield (Table 3, entry 1). Until now, the access to C_{60}-fused indane derivatives is limited.[6] We thus extended this conversion to other fullerotetrahydroisoquinolines **2b–2h**. Substrates bearing both electron-withdrawing group (**2b**) and electron-donating groups (**2c–2e**) on the benzylamine moiety could furnish the rearrangement products in acceptable yields (62% for **3b**, 65% for **3c**, 48% for **3d** and 67% for **3e**) (Table 3, entries 2–5). On the other hand, substrates containing different sulfonamide groups such as BsNH (**2f**),

Table 3 Conversion of fullerotetrahydroisoquinolines **2a–2h** to fulleroindanes **3a–3h** promoted by MesSA[a]

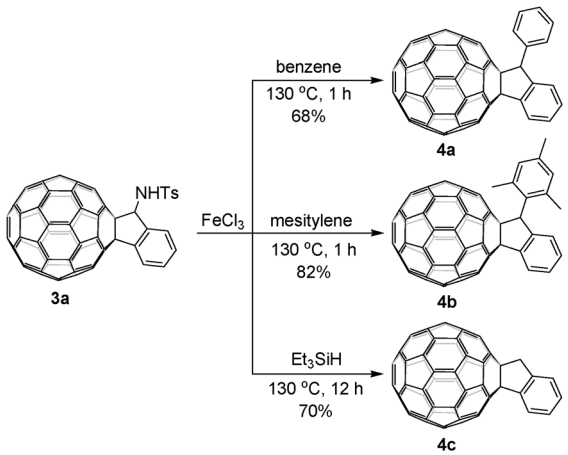


Entry	3	R^1, R^2, R^3	Time (h)	Yield[b] (%)	Recovered **2** (%)
1	**3a**	R^1 = Ts, R^2 = R^3 = H	9	70 (77)	9
2	**3b**	R^1 = Ts, R^2 = H, R^3 = Cl	14	62 (70)	11
3	**3c**	R^1 = Ts, R^2 = H, R^3 = Me	4	65 (81)	20
4	**3d**	R^1 = Ts, R^2 = H, R^3 = MeO	10	48 (72)	33
5	**3e**	R^1 = Ts, R^2 = R^3 = Me	2.5	67 (88)	22
6	**3f**	R^1 = Bs, R^2 = R^3 = H	8	72 (77)	7
7	**3g**	R^1 = Cs, R^2 = R^3 = H	9	74 (84)	14
8	**3h**	R^1 = Ms, R^2 = R^3 = H	6	58 (69)	16

[a] All the reactions were performed in ODCB at 100 °C, molar ratio of **3**/MesSA = 1/3. [b] Isolated yield. Values in parentheses are based on consumed material.



Scheme 2 Proposed mechanism for conversion of C_{60}-fused tetrahydroisoquinolines **2** to C_{60}-fused indanes **3**.



Scheme 3 Transformation of fulleroindane **3a**.

CsNH (**2g**), and MsNH (**2h**) worked well and gave products **3f–3h** in 58–74% yields (Table 3, entries 6–8). This appealing reaction might proceed *via* protonation to generate ammonium intermediate **C**, subsequent ring opening to afford fullerenyl cation **D**,[2f] and final ring closure with the assistance of mesitylenesulfonate ions ($MesS^-$) to produce **3** (Scheme 2).

These fulleroindanes could be synthetic precursors for further transformation *via* C–N bond cleavage, as shown in Scheme 3 with **3a** as an example. The Friedel–Crafts type reactions of **3a** with benzene and mesitylene were successfully achieved when a mixture of ODCB and ArH (v/v = 3/1) was used in the presence of $FeCl_3$ at 130 °C for 1 h. The rare C_{60}-fused indane derivatives **4a** and **4b** were obtained in 68% and 82% yields, respectively. Treatment of compound **3a** with $FeCl_3$ and Et_3SiH at 130 °C for 12 h produced the simplest C_{60}-fused indane **4c** in 70% yield.

In summary, we have discovered an effective way for the synthesis of C_{60}-fused tetrahydroisoquinolines *via* Pd-catalysed heteroannulation of C_{60} with *N*-benzyl sulfonamides *via* C–H bond activation. Intriguingly, change of the directing group from the amide group to the sulfonamide group switches the C–H activation selectivity to the benzylamine moiety. A novel rearrangement of C_{60}-fused tetrahydroisoquinolines in the presence of mesitylenesulfonic acid dihydrate has been found to give C_{60}-fused indanes, in which the sulfonamide group can be replaced with an aryl group in the presence of $FeCl_3$/arene or removed by $FeCl_3/Et_3SiH$.

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Notes and reference

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