Coupling of Alkylarene and Pentamethyl[60]fullerene by Iridium-catalyzed Benzylic C–H Bond Activation

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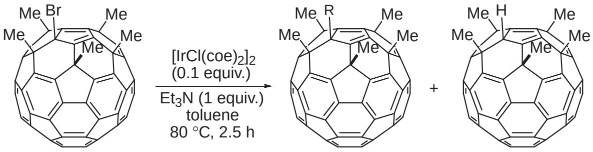
Heating of $C_{60}Me_5Br$ in toluene in the presence of an iridium catalyst and triethylamine results in benzylation of the fullerene core to yield $C_{60}Me_5CH_2C_6H_5$. The reaction is general for various alkylarenes, and probably takes place via iridium-catalyzed activation of a benzylic C–H bond.

Among popular topics of metal-catalyzed C–H bond activation,[1] selective activation of one type of C–H bond over the others is a relatively unexplored field of research. For instance, conversion of an aromatic C–H bond into a C–C bond[2] is a ubiquitous reaction, but selective activation of a benzylic C–H bond in an alkylarene compound in preference to other aromatic C–H bonds in the same molecule is not an easy task.[3] It is partly due to a thermodynamic reason: The C–H bond activation of the methyl group of toluene is a process usually thermodynamically less favored than the aryl C–H bond activation at the meta- and para-position.[4] To achieve the selectivity, ideas of utilizing steric effects to direct the catalyst toward activation of the methyl group of toluene have been examined successfully,[5] but the extension of such approaches beyond toluene remains yet to be investigated. Herein, we report alkylation of the cyclopentadiene moiety of pentamethyl[60]fullerene, $C_{60}Me_5H$,[6] with an alkylarene in the presence of an iridium catalyst. This transformation allows introduction of a variety of (alkyl)(aryl)methyl groups to the carbon atom surrounded by the five methyl groups. The method is complementary to previously reported methods of alkylation of $C_{60}Me_5H$ in that it allows introduction of a secondary benzylic group to the hindered position of the molecule.[7]

The new reaction was discovered in the course of attempted synthesis of iridium–fullerene complexes. The first synthetic approach to $Ir(\eta^5\text{-}C_{60}Me_5)(CO)_2$ relying on the reaction of an anion, $K(C_{60}Me_5)$, with $[IrCl(CO)_2]_2$ took place smoothly to give the iridium–fullerene complex.[8] A polarity-reversed approach relying on the reaction of bromo(pentamethyl)[60]fullerene, $C_{60}Me_5Br$ (**1**)[9] with one equivalence of $[IrCl(coe)_2]_2$ (coe = cyclooctene) in toluene at 25 °C for 120 h unexpectedly gave benzyl(pentamethyl)[60]fullerene, $C_{60}Me_5(CH_2Ph)$ (**2**) in 33% yield (100% conversion of **1**). Clearly, a C–H bond activation of the solvent molecule took place.[10] The reaction afforded $C_{60}Me_5H$ (**3**, 50%) and several oxidized products such as $C_{60}Me_5O_3H$[11] as by-products. We found that the reaction of **1** with 10 mol % of $[IrCl(coe)_2]_2$ in the presence of triethylamine (1 equiv.) in toluene at 80 °C for 2.5 h afforded **2** and **3** in 41 and 43% yield, respectively (Scheme 1 and Table 1, Entry 1). Other bases were examined without success: e.g., pyridine and 1,8-diazabicyclo[5.4.0]undec-7-ene. No such benzylation reaction was found in the same reaction of the more sterically hindered molecule, $C_{60}Ph_5H$.



1 **2**: R = Bn, 41% **3**, 43%

Scheme 1.

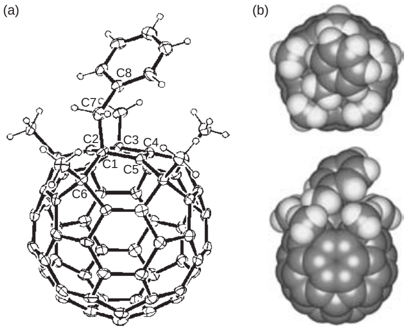


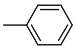
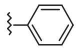
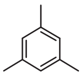
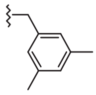
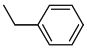
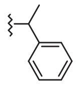
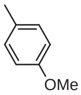
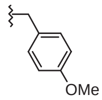
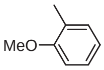
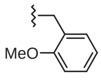
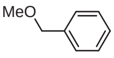
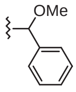
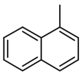
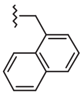
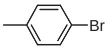
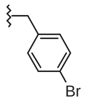
Figure 1. Crystal structure of **2**. (a) ORTEP drawing with 30% probability level ellipsoids. (b) Space-filling models from top and side view. Selected bond length (Å) and angles (°): C1–C2 = 1.522(11), C2–C3 = 1.357(11), C3–C4 = 1.494(10), C4–C5 = 1.366(12), C5–C1 = 1.529(12), C1–C7 = 1.592(12), C7–C8 = 1.511(13); C6–C1–C7 = 107.2(7), C1–C7–C8 = 117.0(7).

The benzylated product **2** was characterized by NMR and HR-MS as well as X-ray crystallographic analysis.[12] The ^1H and ^{13}C NMR spectra exhibited signals characteristic of the C_s symmetric structure. The ORTEP drawing and CPK models are shown in Figure 1. Bond lengths of the top pentagon (C1 to C5) are in good agreement with an ordinary cyclopentadiene structure. The bond distance between C1 and C7 (1.592(12) Å) is considerably longer than an ordinary $C(sp^3)$–$C(sp^3)$ bond (1.54 Å), likely due to steric hindrance.

As summarized in Table 1, a variety of arenes bearing alkyl or substituted alkyl side chains (used as a solvent) have been found to take part in the reaction albeit in poor to moderate yield. The major product besides the desired one was the reduction product **3**. When mesitylene was used as a solvent, 3,5-dimethylbenzyl adduct of fullerene was obtained (Entry 2). The use of ethylbenzene as a solvent resulted in introduction of a 1-phenylethyl group ($C_{60}Me_5(CHMePh)$) (Entry 3). The C–H bond activation approach is a synthetically useful reaction, since the synthesis of this compound by the conventional method by using $C_{60}Me_5K$ and an adequate halide is not a synthetically viable reaction.

4-Methoxytoluene and benzyl methyl ether are more reactive than toluene and smoothly afforded the benzyl activation

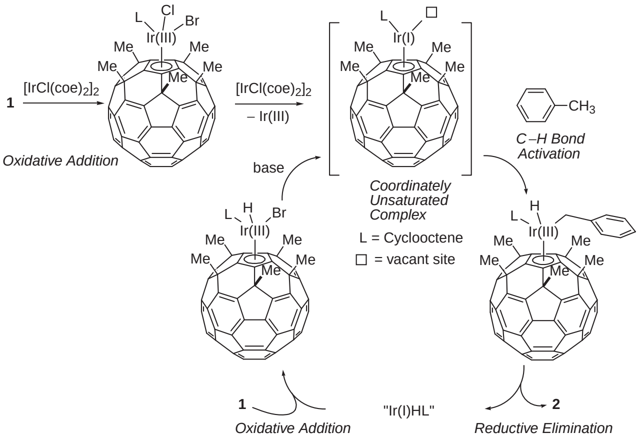
Table 1. Iridium-catalyzed alkylation of $C_{60}Me_5H$ with alkylarenes[a]

Entry	Solvent	R	Time/h	Yield/%[b]
1			2.5	41
2			1.5	37
3			2	32[c]
4			1.5	40[c]
5			3.5	13
6			1	36
7			6	19
8			2.5	25

[a] A solution of **1**, $[IrCl(coe)_2]_2$ (0.1 mol %), and Et_3N (1.0 equiv.) in an alkylarene (3.8 mM solution) was heated under argon at 80 °C. [b] Determined by ^1H NMR. [c] Isolated yield.

products (Entries 4 and 6). 2-Methoxytoluene was much less reactive probably due to the steric effect of the flanking methoxy group (Entry 5). In all three cases, we did not observe products due to methoxy-group activation. Similarly, sterically hindered 1-methylnaphthalene reacted rather slowly (Entry 7). 4-Bromotoluene gave $C_{60}Me_5(CH_2C_6H_4Br)$ in 25% yield (Entry 8). The bromo group did not affect the reaction rate and the yield (cf. Entry 1). We did not detect any products due to the reaction of the bromine atom. The bromo product offers possibilities of further elaboration of the product.

A possible catalytic pathway is discussed below (Scheme 2). The iridium(I) cyclooctene complex undergoes oxidative addition to the fullerene–bromine bond to form an Ir(III)–fullerene intermediate. A second molecule of the iridium(I) complex reduces the intermediate to generate a coordinatively unsaturated Ir(I)-intermediate. It reacts with the C–H bond of toluene to give an Ir(III)$C_{60}Me_5$–benzyl complex. Reductive elimination produces the alkylated product **2** and an Ir(I) complex, which then reacts with **1** to generate a bromo–hydro Ir(III)-complex. Reduction of this complex by triethylamine regenerates the coordinatively unsaturated complex. A possibility of intervention of radical intermediates cannot be discounted.



Scheme 2.

In summary, we found an interesting instance of the chemoselective control of C–H bond activation, where the alkyl side chain of alkylarene compounds is selectively alkylated by the cyclopentadienyl moiety of $C_{60}Me_5$. This reaction is a rare example of transition metal-mediated catalytic chemical modification of fullerenes,[13] and will serve to expand the molecular library of functionalized fullerenes.

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References and Notes

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9 Procedure for synthesis of **1** will be described elsewhere.

10 We confirmed that **2** was obtained by the reaction of $KC_{60}Me_5$ with benzyl bromide.

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