doi:10.1246/cl.2010.298

Reaction of Cage-opened Fullerene Derivative with Grignard Reagents and Subsequent Transannular Cyclization

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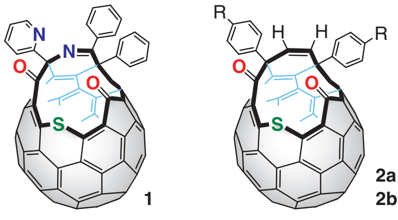
1,2-Addition of methyl and allyl Grignard reagents to a cage-opened fullerene derivative **2a** selectively proceeded at −20 °C in THF at one of the two carbonyl groups. Under acidic conditions, the resulting alcohol underwent a transannular cyclization. The elevated LUMO levels of these products were shown by electrochemical and theoretical investigations.

Since the first report[1] of a cage-opened fullerene derivative by Wudl et al., synthetic efforts have been made to create a large opening in the fullerene cage. Insertions of neutral entities such as He,[2,3] Ne,[4] Ar,[4] Kr,[4] H_2,[2,5,6] CO,[7] N_2,[4] H_2O,[8,9] NH_3,[10] and CH_4[11] into the cage through the opening have become reality.[12] Meanwhile, in our laboratory, C_{60} derivative **1** with a 13-membered-ring opening[13] has been synthesized (Chart 1) and after 100% insertion of H_2[14] it was transformed into the original form of C_{60} encapsulating H_2 ($H_2@C_{60}$)[15,16] via complete closure of the opening. This method has worked effectively for the representative higher fullerene, C_{70}, to give $H_2@C_{70}$ and $(H_2)_2@C_{70}$ encapsulating one and two molecules of H_2, respectively.[17,18] Since this is currently the only way to produce endohedral fullerenes by organic synthesis, better understanding of fundamental reactivity and properties of this unique compound **1** is essential for further improvement and extension of our method to realize as yet unknown endohedral fullerenes. However, studies on the reactions of **1** have been so far limited to only an oxidation of the sulfide to the sulfinyl moiety with *m*-chloroperoxybenzoic acid (MCPBA),[16] and a reduction of one of the carbonyl groups with $NaBH_4$.[19]

In this work, we have studied additions of organometallic nucleophiles such as methyl and allyl Grignard reagents to compound **2a** (Chart 1), which was newly prepared to overcome the low solubility of **1** in common organic solvents, such as THF, by installation of the long alkyl chains.[20] It should be mentioned that a reaction of methyl Grignard reagent with pristine C_{60} in 1,2-dichlorobenzene (ODCB) was reported to give a monoadduct Me–C_{60}–H in 46% yield by using DMF as an additive.[21] The DFT calculations[22] for model compound **2b** indicated that the LUMO is delocalized over the fullerene cage and not over the two carbonyl groups directly connected to the opening of fullerenyl π system (Figure 1). This result makes it difficult to predict the reaction course toward nucleophiles such as RMgX.



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2a, R = *n*-octyl
2b, R = Me

Chart 1.

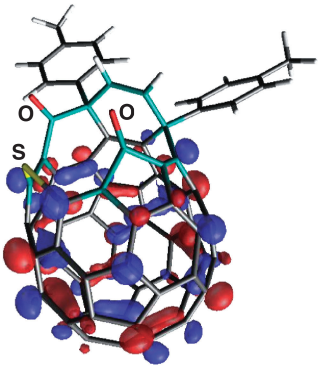
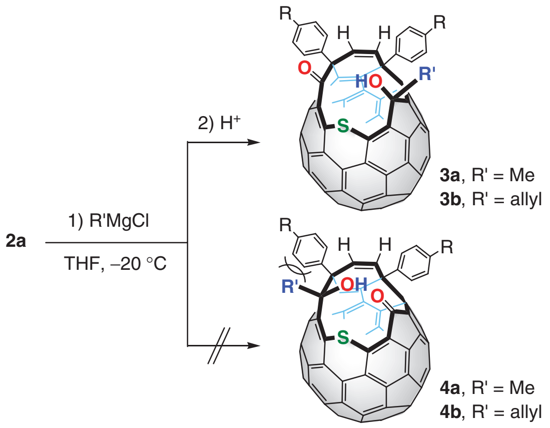


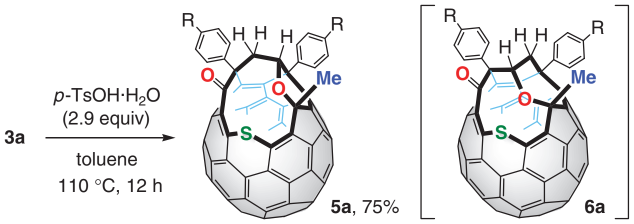
Figure 1. LUMO of **2b** calculated at the B3LYP/6-31G* level.

Upon treatment of **2a** with MeMgCl (5.0 equiv) in THF at −20 °C, the color of the solution immediately changed from dark red to dark brown. After 70 min the mixture was quenched with trifluoroacetic acid and subjected to a chromatographic purification over SiO_2 to give product **3a** as a dark brown solid in 46% yield. The ^1H NMR of **3a** exhibited a singlet for the hydroxy group (δ 5.20) and the ^{13}C NMR showed one carbonyl carbon signal (δ 199.4) together with a deshielded sp^3 carbon signal (δ 92.53) in line with the 1,2-addition of MeMgCl to the carbonyl group of **2a** (Scheme 1). The addition of MeMgCl to **2a** in the presence of $CeCl_3$ gave the same product **3a**, albeit in a lower yield (39%). Allyl magnesium chloride also reacted with **2a** in a manner similar to MeMgCl to afford alcohol **3b** in 9% yield, while no carbonyl addition was observed when EtMgCl or Me_3SiCH_2MgCl was employed. The additions of methyl and allyl Grignard reagents to the other carbonyl group in **2a** to give **4a** and **4b** did not occur presumably due to the effect of steric hindrance by the adjacent phenyl group as judged by the result of DFT calculations; the all electron energy, ΔE, for **4a** was calculated to be higher than **3a** by 9.5 kcal mol^{-1}.

Alcohol **3a** is stable under ambient conditions. However, a transannular cyclization took place upon heating a solution of **3a** in refluxing toluene in the presence of *p*-TsOH (2.9 equiv) for 12 h (Scheme 2). Chromatographic purification over SiO_2 afforded **5a** in 75% yield as a brown solid. The DFT calculations (B3LYP/6-31G*) showed that both transformations of **3a** to **5a** and to **6a** are highly exothermic ($\Delta E = -29.3$ and -22.7 kcal mol^{-1}, respectively). Although the spectroscopic information[20] did not allow their clear distinction, we considered the product to be **5a** because of its lower energy than **6a** ($\Delta\Delta E = -6.6$ kcal mol^{-1}). This reaction is useful to confine small entities,



Scheme 1. Additions of the Grignard reagents to **2a**.



Scheme 2. Transannular cyclization of **3a**.

Table 1. Electrochemical reduction potentials[a] of C_{60}, **2a**, **3a**, and **5a** and calculated LUMO levels[b]

Compound	E_{red}^1/eV	E_{red}^2/eV	E_{red}^3/eV	LUMO/eV
C_{60}	−1.09	−1.49	−1.95	−3.23
2a	−1.12	−1.52	−2.01	−3.18
3a	−1.22	−1.59	−2.10	−3.04
5a	−1.24	−1.62	−2.14	−3.00

[a] V vs. ferrocene/ferrocenium couple: all reduction potentials were recorded in ODCB at room temperature with 0.1 M Bu_4NBF_4 as supporting electrolyte. Scan rate was 20 mV s^{-1}.
[b] Calculated at the B3LYP/6-31G* level.

such as molecular H_2, to the fullerene cage.[19] Actually, the encapsulated hydrogen of H_2@**5a** did not escape at all upon heating the solution at 180 °C for 24 h, as judged from the unchanged ^{1}H NMR signal of H_2@**5a** (δ −7.82 in ODCB-d_4), while that of H_2@**2a** (δ −7.46 in ODCB-d_4) completely escaped under the same conditions.

We then measured the electrochemical properties of the newly obtained derivatives **2a**, **3a**, and **5a**, in order to disclose the redox behavior of the fullerenyl π systems, which were severely ruptured by a large opening and should be affected by the inductive effects from the functional groups at the rim of the opening. Table 1 summarizes the first to third one-electron reduction potentials (E_{red}^1, E_{red}^2, and E_{red}^3) of the products and C_{60}, recorded by differential pulse voltammetry, together with the calculated LUMO levels for the corresponding model compounds **2b**, **3c**, and **5c** (R = Me). The E_{red}^1 value of **2a** is comparable to that of C_{60} in accordance with our previous report for **1**,[13] the cathodic shift being only 30 mV. The E_{red}^1 values of **3a** and **5a** were cathodically shifted to a similar extent (by 130 and 150 mV, respectively) with reference to that of C_{60}. This is apparently caused by the transformation of one of the carbonyl groups by the addition of MeMgCl. Note that the partial cleavage of the π conjugation of **2a** by the methyl group should be minimally effective since the carbonyl group is not involved in the LUMO (vide supra). The observed E_{red}^1 values are in good agreement with the higher levels of the LUMOs than that of C_{60} predicted by calculations (Table 1).

In summary, we have shown that the 1,2-addition of methyl and allyl Grignard reagents to cage-opened C_{60} derivative **2a** selectively takes place at the less hindered carbonyl group. The obtained alcohol **3a** undergoes transannular cyclization under acidic conditions. The decreased electron affinity of **3a** and **5a** was also demonstrated by the experimental and computational data.

This research was supported in part by the Global COE Program "Integrated Materials Science" (#B-09) and a Grant-in-Aid for Scientific Research on Innovative Areas (No. 20108003, "pi-Space") from MEXT, Japan. We thank Prof. Masaharu Nakamura for helpful comments.

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