Synthesis of *C₅*-Symmetric Functionalized [60]Fullerenes by Copper-Mediated 5-Fold Addition of Reformatsky Reagents
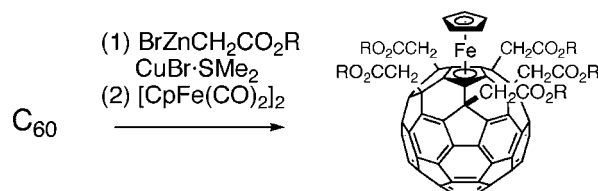
Takahiro Nakae, Yutaka Matsuo,* and Eiichi Nakamura*

Nakamura Functional Carbon Cluster Project, ERATO, Japan Science and Technology Agency, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

matsuo@chem.s.u-tokyo.ac.jp; nakamura@chem.s.u-tokyo.ac.jp

Received December 4, 2007

ABSTRACT

A variety of Reformatsky reagents were added five times to [60]fullerene in good yield in the presence of a stoichiometric amount of a copper(I) complex. The penta-addition products $C_{60}(CH_2CO_2R)_5H$ (R = Et, *t*-Bu, CH_2CF_3, $(CH_2CH_2O)_2Et$, and $CH_2CH_2CCSiMe_3$) can then be converted to the corresponding penta-hapto metal complexes. When the R group is a (–)-menthyl group, the corresponding metal complex comprises an organometallic complex with a coordination sphere consisting of a homochiral C_5-symmetric environment.

Polyfunctionalized fullerene materials have received much attention because of various applications in the life and materials sciences.[1] For the synthesis of such materials, control of regioselectivity when introducing multiple functional groups is a key issue[2–5] and may be achieved, for instance, by the addition of multifunctional tethered reactants[6] or by multiple additions of monofunctional reactants.[7] Penta-addition reactions of organocopper reagents that selectively

introduce five organic groups around one pentagon are interesting examples of the latter category.[8] The reaction is extremely selective and high yielding and can be carried out readily on a multigram scale. The functional group tolerance is also quite high as exemplified by the synthesis of $C_{60}(C_6H_4$-$CO_2Et)_5H$ from the corresponding ethyl 4-magneciobenzoate.[8c] One major limitation of this copper route, however, is that one can introduce aryl, alkenyl, methyl, and silylmethyl

(1) (a) Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley-VCH: Weinheim 2005. (b) Kadish, K. M.; Ruoff, R. S. *Fullerenes: Chemistry, Physics, and Technology*; John Wiley & Sons: New York, 2000. (c) Hirsch, A. *The Chemistry of Fullerenes*; Theme: Stuttgart, 1994. (d) *The Chemistry of Fullerenes*; Taylor, R., Ed.; World Scientific: River Edge, NJ, 1995.

(2) (a) Wang, G.-W.; Murata, Y.; Komatsu, K.; Wan, T. S. M. *Chem. Commun.* **1996**, 2059–2060. (b) Allard, E.; Delaunay, J.; Cousseau, J. *Org. Lett.* **2003**, *5*, 2239–2242. (c) Wang, Z.; Meier, M. S. *J. Org. Chem.* **2003**, *68*, 3043–3048.

(3) Wang, G.-W.; Zhang, T.-H.; Cheng, X.; Wang, F. *Org. Biomol. Chem.* **2004**, *2*, 1160–1163.

(4) Allard, E.; Rivière, L.; Delaunay, J.; Dubois, D.; Cousseau, J. *Tetrahedron Lett.* **1999**, *40*, 7223–7226.

(5) Zhang, T.-H.; Wang, G.-W.; Lu, P.; Li, Y.-J.; Peng, R.-F.; Liu, Y.-C.; Murata, Y.; Komatsu, K. *Org. Biomol. Chem.* **2004**, *2*, 1698–1702.

(6) (a) Isaacs, L.; Haldimann, R. F.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2339–2342. (b) Diederich, F.; Kessinger, R. *Acc. Chem. Res.* **1999**, *32*, 537–545. (c) Nakamura, E.; Isobe, H.; Tokuyama, H.; Sawamura, M. *Chem. Commun.* **1996**, 1747–1748. (d) Isobe, H.; Tokuyama, H.; Sawamura, M.; Nakamura, E. *J. Org. Chem.* **1997**, *62*, 5034–5041.

(7) (a) Hirsch, A. *Top. Curr. Chem.* **1999**, *199*, 1–65. (b) Lamparth, I.; Maichle-Mössmer, C.; Hirsch, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1607–1609. (c) Hirsch, A.; Vostrowsky, O. *Eur. J. Org. Chem.* **2001**, 829–848. (d) Lamparth, I.; Herzog, A.; Hirsch, A. *Tetrahedron* **1996**, *52*, 5065–5075. (e) Camps, X.; Hirsch, A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1595–1596.

(8) (a) Sawamura, M.; Iikura, H.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 12850–12851. (b) Matsuo, Y.; Muramatsu, A.; Tahara, K.; Koide, M.; Nakamura, E. *Org. Synth.* **2006**, *83*, 80–87. (c) Zhong, Y.-W.; Matsuo, Y.; Nakamura, E. *Org. Lett.* **2006**, *8*, 1463–1466.

groups, but not alkyl groups, probably because the intermediary alkylcopper reagents decompose via β-elimination. Here, we report that Reformatsky reagents[9] undergo penta-addition to [60]fullerene in the presence of a stoichiometric amount of a copper(I) catalyst to produce $C_{60}(CH_2CO_2R)_5H$ (**1**) (eq 1). The product **1** is not exactly the desired penta-

(1)
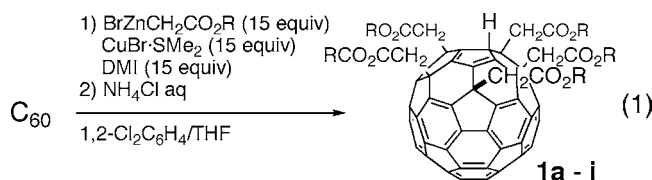
alkylated fullerene but can serve as its surrogate because one can install various alkyl groups and functional groups via the ester linkage without imposing steric effects on the central cyclopentadiene moiety. The utility of the products is illustrated by the smooth conversion of **1** to the C_5-symmetric iron and ruthenium complexes **4** and **5** (Scheme 1). The

Scheme 1. Derivatization of Pentafunctionalized Fullerene **1** into Methylated Compound **3** and Metal Complexes **4** and **5**
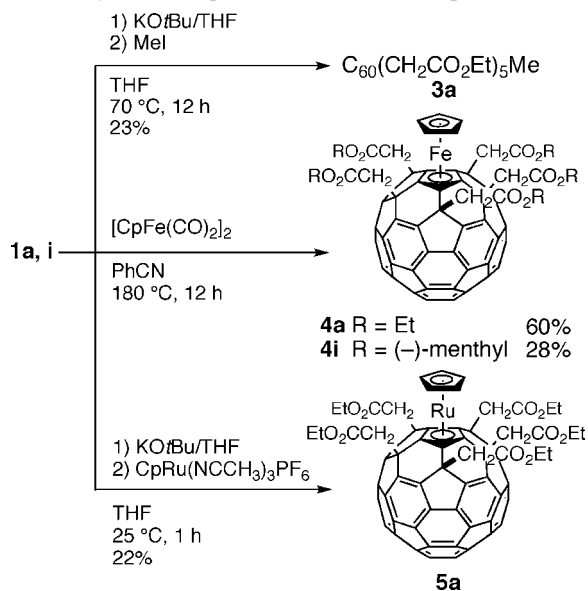
introduction of five equivalents of a chiral group as R groups (e.g., five (−)-menthyl groups) provides chiral C_5-symmetric molecules that belong to a rarely investigated class of chiral molecules.

Reformatsky reagent $BrZnCH_2CO_2Et$ was prepared in THF from metallic zinc powder (Kanto Chemical) and a bromoacetic acid ester and then allowed to react with 1 equiv of $CuBr \cdot SMe_2$ in a mixture of THF and N,N'-dimethyl-2-imidazolidinone. To obtain the cleanest possible product, it is essential to remove the unreacted zinc powder completely

(9) (a) Knochel, P.; Leuser, H.; Gong, L.-Z.; Perrone, S.; Kneisel, F. F. In *Handbook of Functionalized Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, 2005; Vol. 1, pp 251−346. (b) Knochel, P. In *Science of Synthesis*; O'Neil, I. A., Ed.; Georg Thime Verlag: Stuttgart, 2004; Vol. 3, pp 5−90. (c) Ocampo, R.; Dolbier, W. R., Jr. *Tetrahedron* **2004**, *60*, 9325−9374.

by filtration and to use excess Reformatsky reagent. [60]-Fullerene in 1,2-dichlorobenzene was added at once at 25 °C, and the mixture was stirred for 4 h at 25 °C. After acidic workup and filtration through a pad of silica gel, we obtained the pentafunctionalized [60]fullerene, for instance, $C_{60}(CH_2CO_2Et)_5H$ (**1a**) in 92% yield with 88% purity (HPLC) (Table 1, entry 1). For reasons yet unknown, the products prepared

Table 1. Copper-Mediated Penta-addition of Reformatsky Reagent to [60]Fullerene[a]

entry	$BrCH_2CO_2R$ (**2**)	product	yield[b] (%)	purity[c] (%)
1	$BrCH_2CO_2Et$ (**2a**)	**1a**	92 (40)[d]	88
2	$BrCH_2CO_2$(1-hexyl) (**2b**)	**1b**	91	86
3	$BrCH_2CO_2CH_2C_6H_5$ (**2c**)	**1c**	89	86
4	$BrCH_2CO_2$(*tert*-butyl) (**2d**)	**1d**	19[d]	
5	$BrCH_2CO_2$(1-adamantyl) (**2e**)	**1e**	30[d]	
6	$BrCH_2CO_2CH_2CF_3$ (**2f**)	**1f**	91	80
7	$BrCH_2CO(OCH_2CH_2)_3H$ (**2g**)	**1g**	29[d]	
8	$BrCH_2CO_2CH_2CH_2CCSiMe_3$ (**2h**)	**1h**	31[d]	
9	$BrCH_2CO_2$[(−)-menthyl] (**2i**)	**1i**	92	84

[a] The syntheses were carried out according the typical procedure described in footnote 10. Details are reported in the Supporting Information. [b] Unless otherwise noted, the yields are determined for the crude product on which the purity was assessed by HPLC. [c] Purity was determined by HPLC area ratio measured at 350 nm. [d] Yield of isolated product after purification by silica gel chromatography and preparative HPLC.

by this method were much more susceptible to air oxidation than any other similar compounds we have previously synthesized.[8] Thus, we could isolate pure samples of **1** in 40−50% isolated yield after careful chromatographic purification out of the crude product of 88% purity.

Other examples of the synthesis of the penta-adducts **1b−h** from the corresponding α-bromo acetates **2b−h** are shown in Table 1 (entries 2−8). The reactions of the Reformatsky reagents bearing 1-alkyl, benzyl, and *tert*-alkyl groups (entries 1−5) also proceeded smoothly (the lower yields in entries 4 and 5 are because of the oxidative loss of the product during purification). We examined the esters bearing fluorinated and polyoxo groups (entries 6 and 7), and these products showed higher solubility than the compounds in entries 1−5. The trifluoroethyl ester **2f** was soluble in methanol and acetone, which are generally not good solvents for organofullerenes. The polyether derivative **2g** was an oily material at room temperature and is highly soluble in various

common organic solvents, such as acetone and THF. A silylalkynyl group was found to survive the reaction conditions (entry 8). A rather bulky (−)-menthyl ester moiety could also be introduced smoothly (Table 1, entry 9).

The cyclopentadienyl moiety in compound **1a** can be methylated[11] or converted to the corresponding buckyferrocene **4a**[12] and buckyruthenocene **5a**.[13] (Scheme 1). The structures were analyzed by ^{1}H, ^{13}C NMR, IR, and HRMS and, for **4a**, also by X-ray crystallographic analysis (Figure 1).
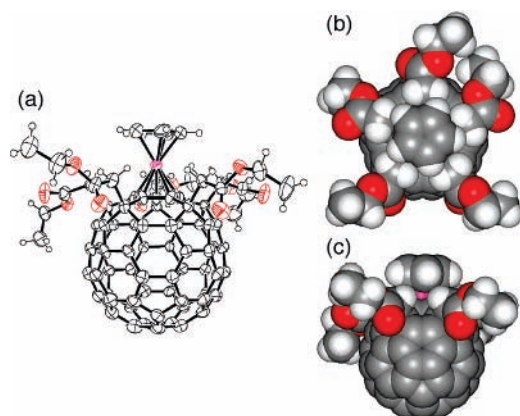
Figure 1. Molecular structure of **4a** (a) ORTEP drawing. (b) Top view of a CPK model. (c) Side view of a CPK model.

Complex **4a** underwent reversible one-electron oxidation and one-electron reduction ($E_{1/2}^{ox} = 0.38$ and $E_{1/2}^{red} = -1.48$ V vs Fc/Fc$^+$) (Figure S1, Supporting Information). The oxidation potential was higher than that of pentamethyl-buckyferrocene Fe(C$_{60}$Me$_5$)Cp ($E_{1/2}^{ox} = 0.22$ V vs Fc/Fc$^+$),[12] and it is consistent with the electron-withdrawing effects of the five esters through the fullerene cage (note that the ester group and the fullerene conjugation system are not directly conjugated).

The chirality of the (−)-menthol moieties in **1i** provides an interesting opportunity to create a chiral C_5-symmetric environment around a metal atom. Thus, the penta-adduct **1i** was converted into the ferrocene compound (**4i**) in 28% yield. The ^{1}H and ^{13}C NMR data for **4i** indicated a C_5-symmetric structure, indicating either free rotation of the menthyl group on the NMR time scale or that all menthyl groups are oriented in the same conformation making a C_5-symmetric chiral structure. The CD spectrum of **4i** exhibited a strong negative Cotton effect at 273 nm (Figure S2, Supporting Information). Chiral C_5 symmetric compounds have found use in biological applications,[14] and the preparation of **4i** suggests the utility of C_5 chirality in catalysis[15] and materials chemistry.

In conclusion, we have shown that a variety of alkyl groups and functional groups can be introduced to a fullerene core with the aid of the Reformatsky reagent in the presence of a copper complex. It is possible that zinc to copper transmetalation is involved as the first step of the reaction[16] and, if so, that the subsequent reactions follow a pathway similar to those in the penta-addition of the organocopper reagent based on Grignard reagents.[8] Ester linkage has served as a useful tool for construction of fullerene molecular array such as donor−acceptor hybrid molecules.[17] We expect that the flexibility of the present Reformatsky approach will allow us to synthesize a wide variety of functional fullerene derivatives thus far unavailable by other methods. The utility of the chiral C_5-symmetric organometallic compounds is of considerable interest and will be investigated in the near future.

Supporting Information Available: Experimental procedures, spectroscopic data for all new compounds, and CIF file for **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL702874W

(11) Hamasaki, R.; Matsuo, Y.; Nakamura, E. *Chem. Lett.* **2004**, *33*, 328−329.

(12) Sawamura, M.; Kuninobu, Y.; Toganoh, M.; Matsuo, Y.; Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2002**, *124*, 9354−9355.

(13) Matsuo, Y.; Kuninobu, Y.; Ito, S.; Nakamura, E. *Chem. Lett.* **2004**, *33*, 68−69.

(14) Isobe, H.; Cho, K.; Solin, N.; Werz, D. B.; Seeberger, P. H.; Nakamura, E. *Org. Lett.* **2007**, *9*, 4611−4614.

(15) Kagan, H. B. *Ann. N. Y. Acad. Sci.* **1980**, *333*, 1−15.

(16) Kuwajima, I.; Doi, Y. *Tetrahedron Lett.* **1972**, *13*, 1163−1166.

(17) Guldi, D. M.; Aminur Rahman, G. M.; Sgobba, V.; Ehli, C. *Chem. Soc. Rev.* **2006**, *35*, 471−487.