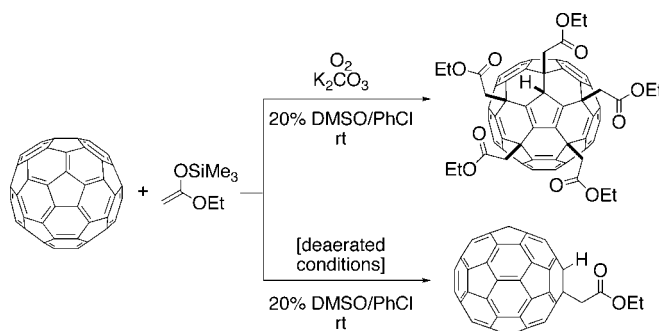# Mono- and Penta-Addition of Enol Silyl Ethers to [60]Fullerene

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ABSTRACT

The reaction of 1-alkoxy-1-siloxyethene with [60]fullerene in 20% DMSO/chlorobenzene at ambient temperature under an oxygen atmosphere gave a penta-addition product, while the reaction of 1-alkoxy-1-siloxyalkenes or 1,2-siloxyalkenes under argon gave monoaddition products. The new method has merits over the previously reported syntheses of these compounds in that the synthesis does not require the use of heavy metals or photolysis conditions, and it can be carried out under simple and mild conditions.

The scope of fullerene science has been significantly expanded by the development of the method for the synthesis to achieve selective additions of functional reactants to the fullerene molecules.[1] Chemical, physical, and biological activities of the resulting functionalized materials may exhibit properties that are similar to or entirely different from the properties of the pristine fullerene molecules.[2] Considerable developments in the science of functional fullerenes on a molecular level have been made. Nevertheless, practical aspects of the synthesis still need careful attention. Here we report that the monoaddition and penta-addition of enol silyl ethers derived from ketones and esters to [60]fullerene (C_{60}) can be achieved by a simple procedure and without the use of hazardous or heavy metal reagents. Thus, a mixture of C_{60} and an enol silyl ether **1** in DMSO/chlorobenzene at ambient temperature, either with or without molecular oxygen, results in the penta-addition or monoaddition of the corresponding ketone and ester groups to the fullerene molecule, respectively. The present synthesis requires simple synthetic operations and only light metals (silicon and

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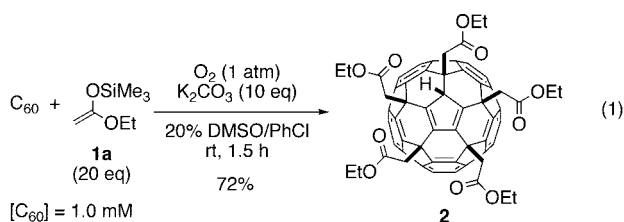
(1) (a) Lamparth, I.; Maichle-Mossmer, C.; Hirsch, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1607–1609. (b) Hirsch, A.; Vostrowsky, O. *Eur. J. Org. Chem.* **2001**, 829–848. (c) Lamparth, I.; Herzog, A.; Hirsch, A. *Tetrahedron* **1996**, *52*, 5065–5075. (d) Nierengarten, J. F.; Gramlich, V.; Cardullo, F.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2101–2103.

(2) (a) Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley-VCH: Weinheim, 2005. (b) Guldi, D. M.; Zerbetto, F.; Georgakilas, V.; Prato, M. *Acc. Chem. Res.* **2005**, *38*, 38–43. (c) Martín, N.; Sánchez, L.; Llescas, B.; Pérez, I. *Chem. Rev.* **1998**, *98*, 2527–2547. (d) Nakamura, E.; Isobe, H. *Acc. Chem. Res.* **2003**, *36*, 807–815. (e) Jensen, A. W.; Wilson, S. R.; Schuster, D. I. *Bioorg. Med. Chem.* **1996**, *4*, 767–779. (f) Da Ros, T.; Prato, M. *Chem. Commun.* **1999**, 663–669. (g) Nakamura, E.; Tokuyama, H.; Yamago, S.; Shiraki, T.; Sugiura, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2143–2151.
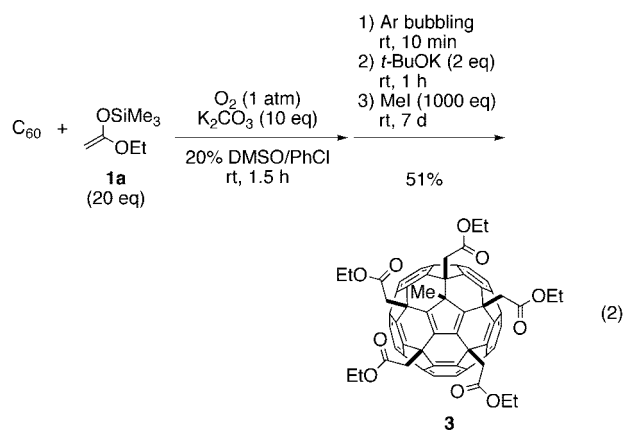
(3) (a) Nakae, T.; Matsuo, Y.; Nakamura, E. *Org. Lett.* **2008**, *10*, 621–623. (b) Matsuo, Y.; Muramatsu, A.; Tahara, K.; Koide, M.; Nakamura, E. *Org. Synth.* **2006**, *83*, 80–87. (c) Sawamura, M.; Iikura, H.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 12850–12851. (d) Matsuo, Y.; Nakamura, E. *Chem. Rev.* **2008**, *108*, 3016–3028.

lithium, and/or sodium, for preparation of the enol silyl ethers), whereas the previously described synthesis[3] of the penta-addition product **2** requires careful control of reaction conditions and the use of heavy metals (zinc and copper).

We first describe the penta-addition of a ketene silyl acetal to C_{60}. By allowing C_{60} to react with 20 equiv of a ketene silyl acetal **1a** and 10 equiv of K_2CO_3 in 20% DMSO in chlorobenzene under an atmospheric pressure of oxygen at ambient temperature, we obtained a penta[[(ethoxycarbonyl)-methyl] adduct $C_{60}(CH_2CO_2Et)_5H$ **2**[3a] in 72% yield (by HPLC analysis) (eq 1). The ketene silyl acetal **1a** was synthesized by deprotonation of ethyl acetate with lithium diisopropylamide in the presence of chlorotrimethylsilane.[4] While the selective penta-addition of organocopper reagents to C_{60} has been well studied,[3] the penta-addition of the ketene silyl acetal was also found to proceed regioselectively. This finding implies that the selectivity was induced by the intrinsic property of C_{60} rather than organocopper reagents.

$$C_{60} + \text{(1a, OSiMe}_3\text{, OEt)} \xrightarrow[\substack{\text{20% DMSO/PhCl} \\ \text{rt, 1.5 h} \\ 72\%}]{\substack{O_2 \text{ (1 atm)} \\ K_2CO_3 \text{ (10 eq)}}} \textbf{2} \quad (1)$$

1a (20 eq)

$[C_{60}] = 1.0$ mM

The product **2** decomposed easily during workup[3a,5] and was isolated in 21% yield after purification by GPC, using toluene as eluent. To obtain an air-stable derivative of **2** that can be easily purified, we methylated the product in situ (eq 2).[6] The penta-adduct was first prepared under oxygen, which was later replaced with argon on completion of the reaction and then was deprotonated with potassium *tert*-butoxide followed by treatment with excess iodomethane to yield the air-stable and thermally stable methylated penta-adduct **3**. This stable product was easily isolated by silica gel column chromatography in 51% yield.[7]

$$C_{60} + \text{(1a, OSiMe}_3\text{, OEt)} \xrightarrow[\substack{\text{20% DMSO/PhCl} \\ \text{rt, 1.5 h}}]{\substack{O_2 \text{ (1 atm)} \\ K_2CO_3 \text{ (10 eq)}}} \xrightarrow[\substack{51\%}]{\substack{\text{1) Ar bubbling} \\ \text{rt, 10 min} \\ \text{2) } t\text{-BuOK (2 eq)} \\ \text{rt, 1 h} \\ \text{3) MeI (1000 eq)} \\ \text{rt, 7 d}}} \textbf{3} \quad (2)$$

1a (20 eq)

We made several interesting observations pertinent to the reaction mechanism and useful for the improvement of synthetic efficiency. First, LC-MS analyses of the penta-addition reaction mixture (Figure S1 in Supporting Information) suggested the presence of the compounds **4a**, **5a**, **6**, **7**, and **8**, illustrated in Figure 1. The indicated structures were
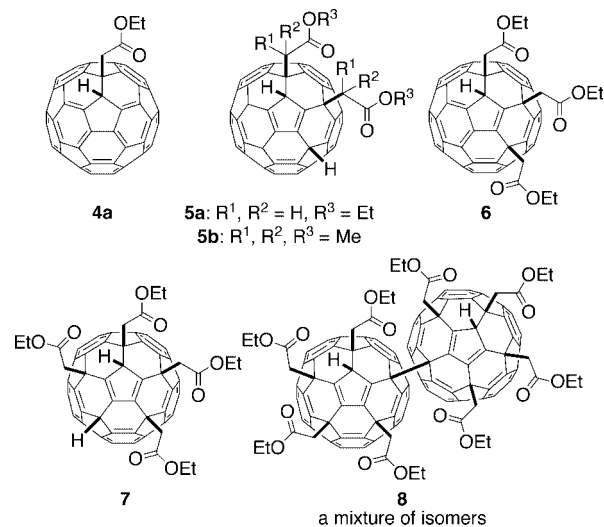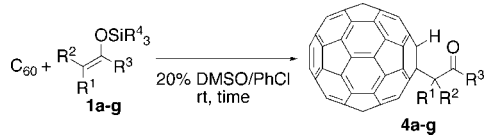


Figure 1. Penta-addition reaction intermediates.

4a

5a: R^1, R^2 = H, R^3 = Et
**5b**: R^1, R^2, R^3 = Me

6

**7**

8
a mixture of isomers

assigned on the basis of their eventual conversion to the penta-adduct **2**. When we carried out the reaction of the ketene silyl acetal of methyl isobutyrate **1b** under an argon atmosphere (although the possibility of the presence of adventitious oxygen cannot be excluded), we isolated a small quantity of the diadduct intermediate **5b** (10% yield, Figure 1) together with a monoadduct **4b** (vide infra). This bulky ketene acetal and the related enol silyl ethers **1c**−**g** (Table 1) did, however, not afford the penta-addition product under the oxygen atmosphere.

Second, the use of DMSO was crucial for the reaction to proceed with a good yield (and with a smell of dimethyl-sulfide). The highest yield of 72% was obtained in a 20% DMSO/chlorobenzene solvent system (Table S1 in Supporting Information). No reaction took place without DMSO, while 10% DMSO/chlorobenzene and 30% DMSO/chlorobenzene mixtures gave yields of 46% and 66%, respectively. No further improvements were obtained. Note that fullerene is insoluble in DMSO. DMSO was found to be unique among polar solvents: HMPA, N,N'-dimethylpropyleneurea (DMPU), and 1,3-dimethyl-2-imidazolidinone (DMI) did not promote the reaction (<5% to 15% yields were obtained under comparable reaction conditions). It should be noted that in the previously reported tetra-amination reaction, all of these solvents showed rate acceleration effects under similar conditions.[8] It is possible that DMSO not only provides a polar environment but also actively participates in the oxidation step.[9,10]

(4) Oisaki, K.; Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5644–5645.

(5) While we consider that the decomposition is due to oxidation of **2**, the reason why **2** survives the oxidative reaction conditions is unclear.

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

(7) The low methylation yield is due to the electron-withdrawing ester functionality, which lowers the nucleophilicity of the penta-adduct anion.

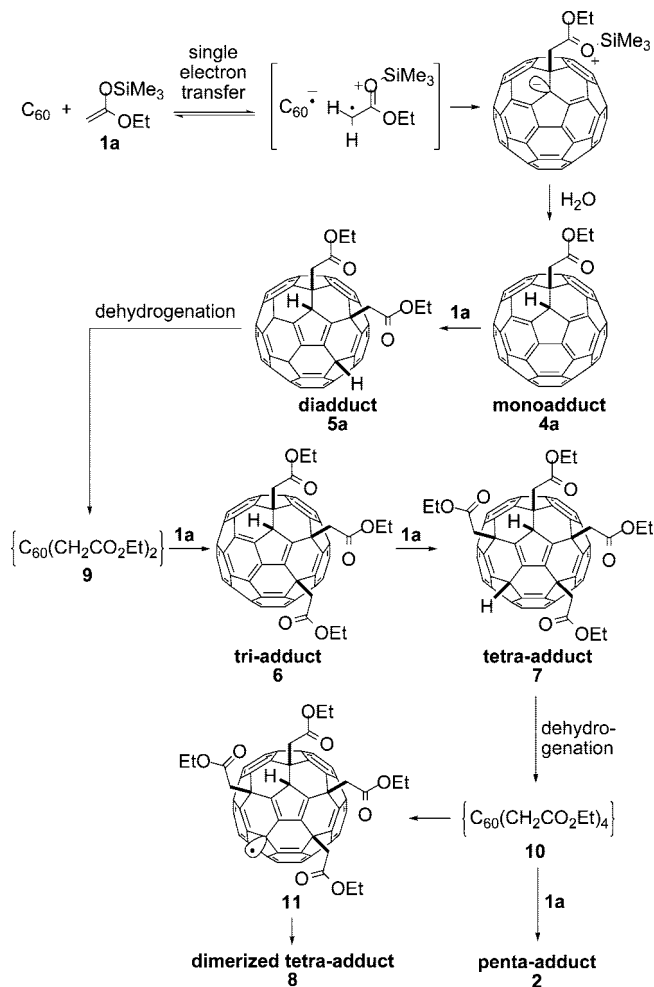**Table 1.** Monoaddition of Ketene Silyl Acetals to C_{60}

entry	substrate		eq	time (h)	product	yield[a] (%)	recovery of C_{60} (%)
1	(OSiMe$_3$, OEt)	**1a**	20	3	**4a**	62(59)[b]	15
2	(OSiMe$_3$, OMe)	**1b**	5.0	0.5	**4b**	68(80)[b]	11
3	(OSiMe$_3$[c], OMe)	**1c**	5.0	1	**4c**	62	14
4	Ph (OSiMe$_3$[d], OMe)	**1d**	5.0	6	**4d**	52	23
5	Me$_3$SiO (OSiMe$_3$)	**1e**	10	3	**4e**	55	16
6	Me$_3$SiO (OSiMe$_3$)	**1f**	10	4	**4f**	42	20
7	Me$_3$SiO (OSiMe$_3$)	**1g**	10	5	**4g**	42	18

[a] Isolated yield. [b] Yield of photoreaction under optimized conditions (see ref 12a). [c] E/Z = 34/66. [d] E/Z = 56/44.

Third, we found that the presence of either K_2CO_3 or Li_2CO_3 accelerates the reaction (Table S2 in Supporting Information). The penta-addition reaction without such an additive afforded the product **2** in 64% yield in 3 h, whereas the reaction with K_2CO_3 was much faster and gave a higher yield of 72% in 1.5 h. This observation suggests that the presence of a base is beneficial in certain steps of the overall reaction.

Interestingly, we noted the formation of a high molecular weight product ([M]$^-$: m/z = 2138.34), which can be assigned to a dimerized tetra-adduct **8**. When the concentration of the reaction mixture was increased five times from 1.0 mM C_{60} to 5.0 mM, the yield of **2** decreased from 72% to 26%, and there was an increase in **8**, as confirmed by HPLC.[11]

We suggest a possible reaction pathway of the penta-addition (Scheme 1) on the basis of the above observations as well as the pathway of the penta-addition of organocopper reagents.[3] The first step, the monoaddition reaction of ketene

(8) (a) Isobe, H.; Tanaka, T.; Nakanishi, W.; Lemiègre, L.; Nakamura, E. *J. Org. Chem.* **2005**, *70*, 4826–4832. (b) Isobe, H.; Chen, A.-J.; Solin, N.; Nakamura, E. *Org. Lett.* **2005**, *7*, 5633–5635.

(9) Dehydrogenation of $C_{60}H_2$ is accelerated in the presence of oxidants such as O_2 and 2,3-dichloro-5,6-dicyanobenzoquinone. (a) Becker, L.; Evans, T. P.; Bada, J. L. *J. Org. Chem.* **1993**, *58*, 7630–7631. (b) Meier, M. S.; Corbin, P. S.; Vance, V. K.; Clayton, M.; Mollman, M. *Tetrahedron Lett.* **1994**, *35*, 5789–5792.

(10) In the 20% DMSO/chlorobenzene solvent system, formation of a small amount of penta-adduct **2** was observed even under deoxygenated conditions.

(11) Isolation of dimerized tetra-adduct **8** was difficult since the product was unstable to air-oxidation and also the dimer comprises a complex mixture of isomers.

Scheme 1. Plausible Reaction Pathway

silyl acetal **1a** to fullerene, has long been known as a photochemical reaction that involves an single electron transfer or SET mechanism.[12] We recently found a related SET reaction in the tetra-addition of secondary amines to fullerene that occurs in the dark, in the presence of a polar solvent such as DMSO or DMF, which stabilizes the intermediate radical ion pair.[8] The monoadduct **4a** and diadduct **5a** may be isolated in low yield under certain conditions. For the diprotio diadduct **5a** to accept further ketene silyl acetal molecules, it must lose two hydrogen atoms at this stage, to generate the diadduct **9**. We consider that molecular oxygen and DMSO participate in this dehydrogenation step as oxidants, and the base additive (K_2CO_3 or Li_2CO_3) assists such oxidative removal of the hydrogen atoms.[13] We expect that **9** reacts with two moles of the ketene silyl acetal in a way similar to reaction in the path from C_{60} to **5a** to afford the tetra-adduct **7**. The formation of a dimer

(12) (a) Tokuyama, H.; Isobe, H.; Nakamura, E. *J. Chem. Soc., Chem. Commun.* **1994**, 2753–2754. (b) Mikami, K.; Matsumoto, S.; Ishida, A.; Takamuku, S.; Suenobu, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 11134–11141.

(13) Li, Y. -J.; Wang, G. -W.; Li, J. -X.; Liu, Y. -C. *New J. Chem.* **2004**, *28*, 1043–1047.

of tetra-adduct **8** under high-concentration conditions is a good indication of the intermediacy of a neutral radical intermediate **11**, which may have generated from the tetra-adduct radical anion during the SET reaction in which the desired penta-adduct **2** was formed.[14]

The molecular oxygen acts as an acceptor of electrons in the penta-addition reaction, which in turn suggests that monoaddition would predominate in the absence of molecular oxygen. Indeed, when conducting the reaction under an argon atmosphere in the presence of DMSO, for instance, the monoadduct **4a** from **1a** was obtained in 62% yield.[15] This yield was comparable to the one obtained under the previous photoreaction (Table 1, yield in parenthesis).

The monoaddition reaction proceeded both with substituted and unsubstituted ketene silyl acetals **1a–d** to afford moderate yields, varying from 52 to 68% (Table 1, entries 1–4). Substituted ketene silyl acetals gave better reaction yields in shorter reaction time (entries 2 and 3), suggesting that electron donation from the ketene acetal is an important feature of the reaction.[16] In agreement with this hypothesis, 1,2-siloxyalkenes **1e–g** (i.e., enol silyl ethers of 2-hydroxyketones) provided the monoadducts (Figure 2) in moderate
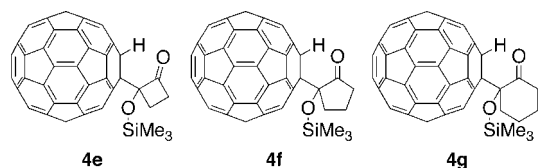

Figure 2. Structure of ketone-functionalized monoadducts.

yields (Table 1, entries 5–7). It is interesting to note that the reaction of C_{60} with **1e** has been reported to give a [4 + 2] cycloaddition product when the reaction is carried out in a nonpolar solvent.[17] These enol silyl ethers were synthesized by reductive cyclization of 1,2-dicarboxylic acid diester in the presence of sodium and chlorotrimethylsilane.[18] However, these substrates did not take part in the penta-addition reaction even under an oxygen atmosphere, probably due to the bulkiness of the carbonyl groups.

In conclusion, we have found that the addition of enol silyl ethers to C_{60} can now be achieved without recourse to the use of heavy metals and photoirradiation, under simple and mild reaction conditions. The use of DMSO was found to be crucial. The reaction performed under an oxygen atmosphere afforded a penta-addition product, but the reaction under argon afforded a monoaddition product. Through the monoaddition, we have introduced ketone, a versatile functional group, to C_{60} under mild conditions, and the monoadducts with a cyclic siloxyketone moiety would be a precursor for further derivatization through Lewis acid-promoted rearrangement reactions.[18] The penta-adduct reported here has already been used in a study of photocurrent generation,[19] and monoadducts may also prove to be useful for other applications.

Supporting Information Available: Supplemental data, experimental procedures, and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(14) Dimerization of the tetra-adduct **8** most likely follows the mechanism of C_{60} dimerization to form $C_{120}H_2$. Tanaka, T.; Komatsu, K. *J. Chem. Soc., Perkin Trans.* **1999**, *1*, 1671–1675.

(15) Some overreacted byproducts were observed in the syntheses of monoadducts due to the presence of DMSO, which presumably acts as an oxidant.

(16) Fukuzumi, S; Fujita, M.; Otera, J.; Fujita, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10271–10272.

(17) Garcia, T. T.; Luftmann, H.; Wolff, C.; Mattay, J. *J. Org. Chem.* **1997**, *62*, 2752–2756.

(18) (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 961–963. (b) Shimada, J.; Hashimoto, K.; Kim, B.-J.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1759–1773. (c) Nakamura, E.; Kuwajima, I. *Org. Synth.* **1987**, *65*, 17–25.

(19) Matsuo, Y.; Kanaizuka, K.; Matsuo, K.; Zhong, Y.-W.; Nakae, T.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 5016–5017.