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A Novel Reaction of [60]Fullerene.
A Formal [2+2] Cycloaddition with Aryloxy- and Alkoxyketenes

Satoshi Matsui, Kazushi Kinbara, and Kazuhiko Saigo*

Department of Chemistry and Biotechnology, Graduate School of Engineering,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

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Abstract: [60]Fullerene reacted with aryloxy- and alkoxyketenes, generated *in situ* from the corresponding acid chlorides and triethylamine, to give the 1:2 adducts in good yields. The reaction proceeded via a formal [2+2] cycloaddition, followed by enolization and acylation. © 1999 Elsevier Science Ltd. All rights reserved.

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Many reactions for the functionalization of [60]fullerene have been developed on the basis of the electron-deficient characteristic of [60]fullerene.[1] Among the reactions, the Diels-Alder reaction,[2] 1,3-dipolar cycloaddition,[3] and [2+2] cycloaddition[4] are widely used for the functionalization, because the cycloadditions give the characterizable mono- and/or bisadducts in acceptable yields. Thus, [60]fullerene usually tends to exhibit electrophilicity, and nucleophilic reactions of [60]fullerene do not proceed readily, although a few exceptions have been reported.[5] On the other hand, ketenes, which are important components for the synthesis of cyclobutanones, β-lactams, etc., by [2+2] cycloadditions, show higher reactivity in the reaction with substrates having a more electron-rich double bond, indicating that they have an electrophilic character.[6] Consequently, the [2+2] cycloaddition of [60]fullerene with a ketene is expected to be difficult, although the reactions of [60]fullerene with the highly reactive *o*-quinodiketene and *o*-quinoketenemethane have been reported by [2+4] cycloaddition and [2+1] cycloaddition, respectively.[7]

In the course of our studies on the selective functionalizations of [60]fullerene, we carried out the reaction of [60]fullerene with ketenes, generated *in situ*, and found that the reactions with some ketenes gave the corresponding adducts. Herein we report a novel type of [2+2] cycloaddition of [60]fullerene.

We first attempted the reaction of [60]fullerene (1) with ketenes **2a** and **2b**, which were generated *in situ* from 2-phenylbutanoyl chloride and (4-methoxyphenyl)acetyl chloride, respectively, and triethylamine; however, no reaction was observed. In contrast, some reaction occurred in the case of phenoxyketene (**2c**).[8] When triethylamine (0.19 ml, 1.39 mmol, 10 eq.) was added to a solution of phenoxyacetyl chloride (0.19 ml, 1.39 mmol, 10 eq.) in chlorobenzene (30 ml) in the presence of **1** (100 mg, 0.139 mmol), followed by stirring of the reaction mixture for 50 min at ambient temperature, the spot of **1** completely disappeared and two new spots appeared on TLC. The immediate separation of the products by silica-gel column chromatography[9] (eluent: from toluene/hexane=1/3 to toluene) gave 84 mg of the main product (the less-polar component).[10]

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The FAB-MS spectrum of the isolated product showed peaks at m/z 988, 989, and 990,[11] which would be assigned to $(M)^+$, $(M+1)^+$, and $(M+2)^+$, respectively, for an adduct of **1** with **2c** in a molar ratio of 1:2. Consequently, the yield of the 1:2 adduct was calculated to be 61%.

The 1:2 adduct was characterized in detail by ^1H NMR, ^{13}C NMR, DEPT, and IR spectra.[12,13] Only one signal corresponding to a carbonyl carbon was detected at 165.18 ppm in the ^{13}C NMR spectrum, and a sharp absorption band was observed at 1800 cm^{-1} in the IR spectrum. These observations strongly suggest that the 1:2 adduct has only one carbonyl group. The existence of an alkenyl group is deduced from peaks at 152.95 and 152.83 ppm in the ^{13}C NMR spectrum and from an absorption at 1723 cm^{-1} in the IR spectrum. These data indicate that the 1:2 adduct contains an enol ester moiety. On the other hand, the sp^2 carbons, originated from **1**, appear as 25 peaks at 146.75-139.27 and 126.35 ppm, and signals at 76.24 and 76.21 ppm in the DEPT spectrum reveal the existence of two quaternary sp^3 carbons incorporated in the moiety of **1**, indicating that the product has C_S symmetry. On the basis of these observations and the interpretation thereof, the structure of the 1:2 adduct is assigned as **3c**.

We next carried out the reactions of **1** with other ketenes **2d-i**, generated *in situ*. The results are summarized in Table 1. The corresponding 1:2 adducts[14] were obtained in moderate yields when aryloxy- and alkoxyketenes **2d-g** were used.[8] In contrast, no reaction proceeded when chloroketene (**2h**) and phthalimidoylketene (**2i**) were employed, even though they similarly have an electronegative element at the α-position.

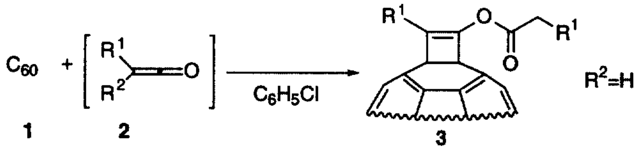


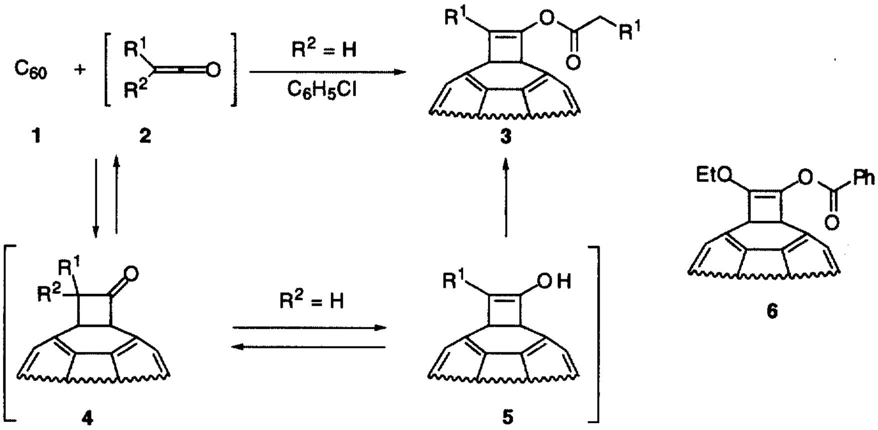
Table 1. [2+2] Cycloaddition of [60]fullerene with acid chlorides and triethylamine.

Entry	2	R^1	R^2	Reaction time	Yield [%]
1	**2a**	C_6H_5	C_2H_5	24 h	no reaction
2	**2b**	*p*-$CH_3OC_6H_4$	H	12 h	no reaction
3	**2c**	C_6H_5O	H	50 min	61
4	**2d**	*p*-ClC_6H_4O	H	11 h	39
5	**2e**	$C_6H_5CH_2O$	H	7.5 h	58
6	**2f**	C_2H_5O	H	7.5 h	58
7	**2g**	CH_3O	H	9 h	37
8	**2h**	Cl	H	24 h	no reaction
9	**2i**	Phthalimido	H	24 h	no reaction

The reaction mechanism of this cycloaddition, especially insofar as to reasonably explain the difference in reactivity between **2c-g** and **2h-i**, is not clear at present. However, it is considered that for the formation of **3** the alkoxy substituent at the α-position of the ketenes has some effect on the stabilization of the intermediate or transition-state.

Scheme 1 shows a plausible reaction route from the starting materials to the 1:2 adduct: The 1:1 adduct **4** is formed by the [2+2] cycloaddition of **1** with **2**. When the R^2 of **4** is a hydrogen, the cycloadduct **4** would be able to transform into the enol **5**, which is easily acylated with **2** or its precursor (acid chloride) to give the 1:2 adduct **3**.[15] The enolization and the following acylation steps are strongly supported by the fact that enol ester **6** was obtained in 34 % yield in addition to the corresponding 1:2 adduct **3f** (29% yield) when **1** was allowed to react with 7 equivalents of **2f** in the presence of 30 equivalents of benzoyl chloride in chlorobenzene for 4 h.

Scheme 1



More detailed experimental and theoretical studies are in progress in order to clarify the mechanism.

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(8) The ketenes would be generated *in situ* from acid chloride **2c-2g** and triethylamine. Although the presumed ketenes have never been directly detected under the dehydrochlorination conditions used, their presence has been inferred from the products. For example, see: Arrieta, A.; Lecea, B.; Cossío, F. P. *J. Org. Chem.* **1998**, *63*, 5869.

(9) Merck Kieselgel 60 was used for the column chromatography.

(10) The more-polar component (ca. 17 mg) was partially decomposed during the silica-gel column chromatography. The ^{1}H NMR and FAB-MS spectra of the more-polar component indicated that it was a mixture of multi-adducts.

(11) The FAB mass spectrum was recorded on a JEOL JMS AX-505H. The 1:2 adduct: m/e 990 ($(M+2)^+$), 989 ($(M+1)^+$), 988 (M^+), 722 (([60]fullerene+2)$^+$), 721 (([60]fullerene+1)$^+$), 720 (([60]fullerene)$^+$).

(12) The ^{1}H NMR ($CDCl_3$), ^{13}C NMR and DEPT (CD_2Cl_2/CS_2 (1/1) with $Cr(acac)_3$) spectra were recorded on a Varian Mercury 300, and the infrared spectrum was recorded on a Jasco IR 810. The 1:2 adduct: ^{1}H NMR (300 MHz, $CDCl_3$) δ=7.65-6.90 (m, 10H, arom), 4.86 (s, 2H, CH_2); ^{13}C NMR (75 MHz, CD_2Cl_2/CS_2 (1/1) with $Cr(acac)_3$) δ=165.18 (1C, CO), 157.52 (C_6H_5O), 154.99 (C_6H_5O), 152.95 (alkene), 152.83 (alkene), 146.75 (6C), 146.43 (2C), 146.20 (2C), 146.16 (2C), 146.03 (4C), 145.48 (2C), 147.45 (2C), 145.37 (2C), 145.33 (2C), 145.09 (2C), 144.54 (2C), 144.46 (2C), 142.98 (4C), 142.89 (2C), 142.58 (4C), 142.36 (2C), 142.31 (2C), 142.11 (2C), 141.94 (2C), 140.94 (C), 140.27 (2C), 140.17 (2C), 139.62 (2C), 139.27 (2C), 130.07 (C_6H_5O), 129.84 (C_6H_5O), 126.35 (C), 125.70 (C_6H_5O), 122.34 (C_6H_5O), 119.74 (C_6H_5O), 114.78 (C_6H_5O), 76.24 (sp^{3}fullerene), 76.21 (sp^{3}fullerene), 64.76 (CH_2); DEPT spectrum δ=130.07 (CH), 129.84 (CH), 125.70 (CH), 122.34 (CH), 119.74 (CH), 114.78 (CH), 64.76 (CH_2); IR (KBr) cm^{-1} 1800, 1723, 1595, 1495, 1190, 1125, 755, 530.

(13) In a ^{13}C NMR measurement, the relaxation time of the quaternary sp^3 carbons in [60]fullerene backbones is known to be long. Subsequently, we used a relaxation agent, $Cr(acac)_3$, for the measurement of the ^{13}C NMR spectra of **3**.

(14) All of the products were characterized by ^{1}H NMR, ^{13}C NMR, DEPT, and IR spectra, and FAB-MS; their fundamental skeletons were the same as that of **3c**.

(15) There has been a report on the [2+2] cycloaddition of alkoxyketenes with electron-rich olefins, accompanied by enolization-acylation. See: Bellus, D. *J. Org. Chem.*, **1979**, *44*, 1208.