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Synthesis and Self-Photooxygenation of Alkenyl-Linked [60]Fullerene Derivatives. A Regioselective Ene Reaction

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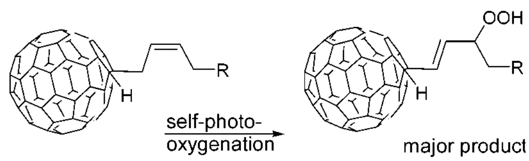
ABSTRACT



Alkenyl-linked C_{60} derivatives undergo self-photooxygenation regioselectively, by the preferential abstraction of allylic hydrogens on the fullerene side of the double bond.

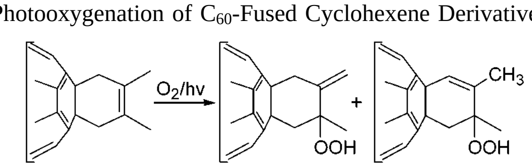
The photophysical and photochemical properties of the electron-deficient fullerene C_{60} has received intensive attention over the past 10 years.[1,2] The triplet excited state of C_{60} is formed with a quantum yield close to unity,[3] and by energy transfer to molecular oxygen, it produces large quantities of $^1O_2$ (eq 1). This useful photochemical property makes C_{60}

$$C_{60} \xrightarrow{h\nu} {}^1C_{60} \xrightarrow{\text{ISC}} {}^3C_{60} \xrightarrow{{}^3O_2} {}^1O_2 \qquad (1)$$

a potent sensitizer for the mild photooxygenation of simple alkenes and dienes.[4] It was also observed that fullerene C_{60} adducts that bear an oxidizable group are sensitive to oxygen and light.[5] Apparently, a self-sensitized photooxygenation of these derivatives leads to the formation of a variety of oxygenated adducts. This is a simple synthetic route for oxo functionalization of fullerene derivatives with increased solubility in solvents more polar than toluene or benzene.[6] This useful observation has been applied successfully in photosensitized studies of biological systems.[7] Only two reports so far deal with the self-sensitized ene photooxygenation of fullerene adducts. For example, Rubin and coworkers reported[8] previously an unexpected regioselectivity in the self-photooxygenation reaction of several adducts prepared by [4 + 2] cycloaddition to C_{60}. In particular, while photooxygenation of 1,2-dimethylcyclohexene affords preferentially the *exo* ene product in a 89/11 ratio, the self-photooxygenation of the corresponding C_{60}-fused cyclohexene derivative **1** showed reverse regioselectivity (Scheme 1). The rationalization of that result was based mainly on the favorable electrostatic or electronic interactions between the negative oxygen of the developing *endo*-perepoxide intermediate and the electron-deficient C_{60}.

Furthermore, in our previous study on the mechanism of [2 + 2] functionalization of C_{60} with butadienes, the

Scheme 1. Regioselectivity in the Self-Sensitized Photooxygenation of C_{60}-Fused Cyclohexene Derivative **1**



1   **1a** (15%)   **1b** (85%)

(1) Mattay, J.; Ulmer, L. Sotzmann, A. *Photophysics and Photochemistry of Fullerenes and Fullerene Derivatives*; Rumamurthy, V., Schanze, K. S., Eds. In *Molecular and Supramolecular Photochemistry*: Marcel Dekker: New York, 2001.
(2) Hirsh, A. *The Chemistry of the Fullerenes*; Thieme Verlag: Stuttgart, 1994.
(3) Arbogast, J. W.; Darmanyan, A. P.; Foote, C. S.; Rubin, Y.; Diederich, F. N.; Alvarez, M. M.; Anz, S. J.; Whetten, R. L. *J. Phys. Chem.* **1991**, *95*, 11.
(4) (a) Orfanopoulos, M.; Kambourakis, S. *Tetrahedron Lett.* **1994**, *35*, 1945. (b) Tokuyama, H.; Nakamura, E. *J. Org. Chem.* **1994**, *59*, 1135.
(5) Zhang, X.; Romero, A.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 11024.

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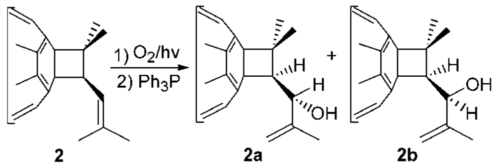
Scheme 2. Self-Sensitized Photooxygenation of Cycloadduct **2**



unsaturated cycloadduct **2** was produced[9] (Scheme 2). Because this adduct bears an oxidizable alkene moiety, it undergoes facile self-sensitized ene photooxygenation and produces, after reduction, a mixture of the *threo/erythro* allylic alcohols **2a** and **2b** as the only products.

We report here the preparation and self-photooxygenation of a series of alkenyl-linked[C_{60}] derivatives that produce a variety of oxo-functionalized ene products. The reactions are regioselective and show preferential abstraction of the allylic hydrogens on the fullerene side of the double bond.

The preparation of the desired C_{60}-substituted alkenes was achieved by the reaction of the C_{60}^{2-} anion with allylic bromides. It is well-known that the C_{60}^{2-} anion, generated electrochemically[10] or chemically,[11] can be alkylated by alkyl halides to give adducts $C_{60}R_2$ in good yields (40−60%). Kadish and co-workers[11b] have investigated the mechanism of this two-step reaction by measuring the rate constants of each step and comparing them with those for genuine electron transfer and S_N2 reactions. According to the proposed mechanism, electron transfer from the C_{60}^{2-} to the RX gives the radical pair ($C_{60}{}^{\bullet-}R^{\bullet}X^-$), where the R−X bond is cleaved upon dissociative electron transfer. Facile radical coupling in the radical pair gives the intermediate anion RC_{60}^-. The addition of a second alkyl halide R′X to RC_{60}^- occurs by a S_N2 pathway to yield the final product $R(R')C_{60}$.

In the present study the C_{60}^{2-} dianion was prepared selectively by the reaction of C_{60} with sodium methylthiolate[12] ($CH_3S^-Na^+$) in acetonitrile at room temperature under an argon atmosphere. In a typical procedure, C_{60} (40 mg, 0.055 mmol) and a 10-fold molar excess of sodium methylthiolate salt were mixed in dry acetonitrile (30 mL) under an argon atmosphere, and the mixture was stirred for 1 h at room temperature. After the generation of the C_{60}^{2-} (dark red color) the allylic bromide was added with a syringe until the color of the solution turned to dark green, which is characteristic of the RC_{60}^- anion. The RC_{60}^- was protonated with acetic acid while the color of the reaction mixture became brown. The solid residue was washed with acetonitrile, and the fullerene products were purified by flash column chromatography (SiO_2, hexane).

The trisubstituted alkene **3**, bearing a C_{60} substituent as the sensitizer, was prepared from the coupling of 4-bromo-2-methyl-2-butene with the dianion of C_{60}. The allylic bromide was used in a 6-fold molar excess, relative to C_{60}, and after protonation of the intermediate RC_{60}^- anion and flash column chromatographic purification, ^{1}H NMR spectroscopy revealed the formation of the adducts **3a** and **3b** in a 85/15 ratio (Figure 1). These adducts were poorly separated

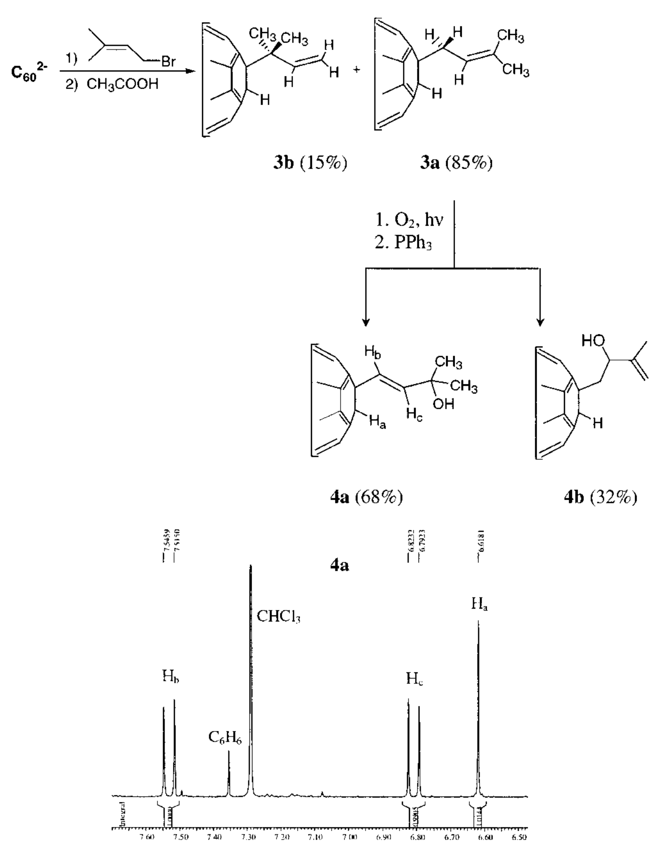


Figure 1. Preparation and sensitized self-oxygenation of adduct **3a**.

on a Cosmosil 5C18-MS reverse phase column but could not be separated by flash column chromatography.

The formation and characterization of the adduct **3b** confirms the electron-transfer mechanism from the C_{60}^{2-} to the alkyl halide, which was proposed by Kadish and co-workers. The allylic radical formed when the R−Br bond is cleaved upon dissociative electron transfer from C_{60}^{2-} is a hybrid of the resonance structures **I** and **II** (Scheme 3).

Coupling of the $C_{60}{}^{\bullet-}$ with the C1 or the C3 radical center leads to the formation of **3a** and **3b**, respectively. The primary carbon of the delocalized radical (Scheme 3) adds preferentially to $C_{60}{}^{\bullet-}$, most probably for steric reasons. In the ^{1}H NMR spectrum of **3** the hydrogen atom connected

(6) Ruoff, R. S.; Tse, D. S.; Malhotra, R.; Lorents, D. C. *J. Phys. Chem.* **1993**, 97, 3379.

(7) (a) An, Y.-Z.; C.-h. B.; Aderson, J. L.; Sigman, D. S.; Foote, C. S.; Rubin, Y. *Tetrahedron* **1996**, *89*, 5179. (b) Boutorine, A. S.; Tokuyama, H.; Takasugi, M.; Isobe, H.; Nakamura, E.; Helene, C. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2462.

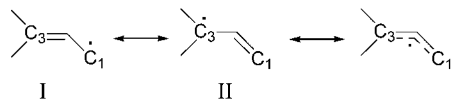
(8) An, Y.-Z.; Viado, A. L.; Arce, M.-J.; Rubin, Y. *J. Org. Chem.* **1995**, *60*, 8330.

(9) Vassilikogiannakis, G.; Chronakis, N.; Orfanopoulos, M. *J. Am. Chem. Soc.* **1998**, *120*, 9911.

(10) Caron, C.; Subramanian, R.; D′Souza, F.; Kim, J.; Kutner, W.; Jones, M. T.; Kadish, K. M. *J. Am. Chem. Soc.* **1993**, *115*, 8505.

(11) (a) Subramanian, R.; Kadish, K. M.; Vijayashree, M. N.; Gao, X.; Jones, M. T.; Miller, M. D.; Krause, K. L.; Suenobu, T.; Fukuzumi, S. *J. Phys. Chem.* **1996**, *100*, 16327. (b) Fukuzumi, S.; Suenobu, T.; Hirasaka, T.; Arakawa, R.; Kadish, K. M. *J. Am. Chem. Soc.* **1998**, *120*, 9220.

Scheme 3. Resonance Structures of the Allylic Radical Formed via Dissociative Electron Transfer from C_{60}^{2-} to 4-Bromo-2-methyl-2-butene

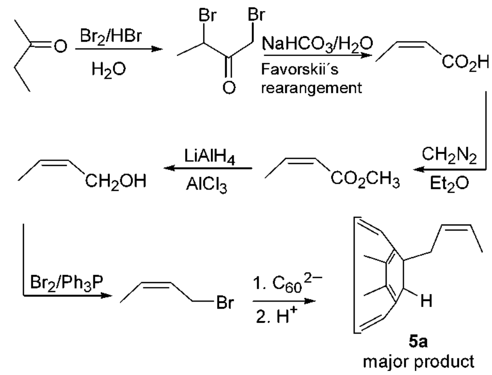


on the fullerene core had a characteristic[2] absorption at 6.47 ppm due to the deshielding effect of C_{60}. The UV−vis absorption spectrum showed a strong absorption at 437 nm that is characteristic[13] of 1,2-adducts of C_{60}. The MALDI-TOF MS spectrum of **3** showed the molecular ion of C_{60} at 720, thus indicating the decomposition of **3** under the spectrometric conditions.

A solution of **3a/3b** in toluene was irradiated in the presence of oxygen with a Variac Eimac 300-W Xenon lamp as the light source. The self-oxidation reaction was monitored by HPLC. The complete disappearance of **3a** was observed within 15 min, in contrast with adduct **3b**, which was unreactive even after prolonged irradiation. This result was not surprising, since it is well-known that terminal alkenes that lack allylic hydrogens are unreactive to singlet oxygen.[14] After reduction with PPh_3, the reaction mixture was chromatographed on silica gel using a mixture of hexane and ethyl acetate (4/1) as eluent. The structure of the oxo functionalized **4a** and **4b** fullerene adducts were determined by ^{1}H NMR spectroscopy. Adduct **4a** was formed in 68% relative yield in favor to **4b** by the preferential abstraction of the allylic hydrogen next to C_{60}. Accounting for the statistical factor, a single methylene hydrogen of **3a** is seven times more reactive than methyl hydrogens, leading to the observed regioselectivity. It is worth noting here that although the hydrogen connected to the fullerene core in substrate **3a** is slightly acidic,[15] under the photooxygenation conditions the material is stable and apart from the ene products **4a** and **4b**, no other products were detected.

To study further this regioselectivity and obtain more information about its origin, a series of disubstituted alkenes, bearing the C_{60} substituent at one terminal of the double bond and alkyl substituents of variable sizes at the other, were prepared. Allylic bromides[16] *cis*-1-bromo-2-butene, *cis*-1-bromo-2-pentene, *cis*-1-bromo-4-phenyl-2-butene, *cis*-1-bromo-5-methyl-2-hexene, and *cis*-1-bromo-5,5-dimethyl-2-hexene were chosen as the appropriate substrates for the alkylation of C_{60}^{2-}. As an example, the synthesis of the fullerene adduct **5a**, derived from the coupling of the *cis*-1-bromo-2-butene[17] with C_{60}^{2-}, is shown in Scheme 4.

Scheme 4. Synthesis of Adduct **5a** from the Coupling of the *cis*-1-Bromo-2-butene with C_{60}^{2-}



The isomeric products derived from the coupling of the various allylic bromides and the fullerene dianion are shown in Scheme 5. According to the resonance structures of the allylic radical formed upon dissociative electron transfer from C_{60}^{2-} to the allylic bromide, and taking into account the geometrical isomerization of the allylic radicals,[18] the formation of adducts **Xa**, **Xb**, and **Xc** can be easily explained. The structures of **Xa**, **Xb**, and **Xc** were determined by ^{1}H NMR spectroscopy by using homonuclear decoupling experiments. Compounds **Xa**, **Xb**, and **Xc** had similar retention times on a Cosmosil 5C18-MS reverse phase column and were isolated as the isomeric mixture by flash column chromatography (SiO_2, hexane).

The self-sensitized photooxygenation of the isomeric mixture **Xa**/**Xb**/**Xc** was performed in toluene by irradiating the reaction mixture in the presence of oxygen. Alkenes **Xa** were self-oxidized, and after 5−7 h of irradiation a 60−70% conversion was measured by HPLC. *trans*-Alkene **Xb** showed negligible reactivity[19] relative to the *cis* analogue, whereas **Xc** was not photooxidized at all.[20] After reduction with triphenylphosphine, the reaction mixture was chromatographed on silica gel by using chloroform as eluent. The structures of the isolated oxygenated fullerene adducts **Ya** and **Yb** were determined by ^{1}H NMR spectroscopy. The results are summarized in Scheme 6.

(12) (a) Subramanian, R.; Boulas, P.; Vijayashree, M. N.; D'Souza, F.; Jones, M. T.; Kadish, K, M. *J. Chem. Soc., Chem. Commun.* **1994**, 1847. (b) Allard, E.; Riviére, L.; Delaunay, J.; Dubois, D.; Cousseau, J. *Tetrahedron Lett.* **1999**, *40*, 7223.

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(14) For recent reviews on singlet oxygen, see: (a) Stratakis, M.; Orfanopoulos, M. *Tetrahedron* **2000** *56*, 1595. (b) Clennan, E. L. *Tetrahedron* **2000**, *56*, 6945.

(15) Fagan, P. J.; Krusic, P. J.; Evans, D. H.; Lerke, S. A.; Johnston, E. *J. Am. Chem. Soc.* **1992**, *114*, 9697.

(16) Bromo-2-methyl-2-butene and *cis*-1-bromo-2-pentene, **6a**, were prepared from the corresponding allylic alcohols by using $Ph_3P{\cdot}Br_2$ as the brominating reagent. *cis*-1-Bromo-5,5-dimethyl-2-hexene and *cis*-1-bromo-5-methyl-2-hexene were synthesized according to the literature: Ando, K. *Tetrahedron Lett.* **1995**, *36*, 4105. *cis*-1-Bromo-4-phenyl-2-butene was prepared as follows: Wittig reaction between phenylacetaldehyde and the stabilized ylide from triphenyl phosphine and bromo-ethylacetate, gave the corresponding α,β-unsaturated esters as a mixture of two stereoisomers (*cis*/*trans* = 25/75). The *cis* ester was separated by flash column chromatography on silica gel by using hexane as eluent. Reduction with $LiAlH_4/AlCl_3$ followed by bromination with $Ph_3P{\cdot}Br_2$ afforded the desired allylic bromide in good yield.

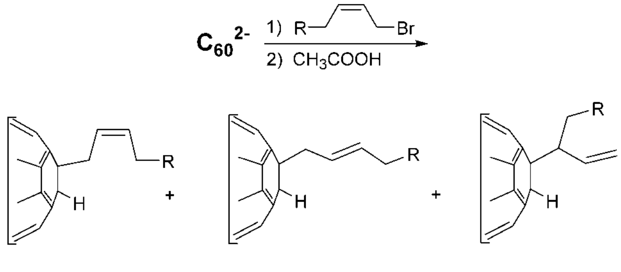
(17) *cis*-1-Bromo-2-butene was obtained from the key intermediate *cis*-methyl-2-butenoate: Orfanopoulos, M.; Smonou, I.; Foote, C. S. *J. Am. Chem. Soc.* **1990**, *112*, 3607.

(18) Crawford, R. J.; Hamelin, J.; Strehlke, B. *J. Am. Chem. Soc.* **1971**, *93*, 3810.

(19) Singlet oxygen ene reaction with *cis*-butene proceeds 20 times faster than that of the *trans* isomer: see ref 17.

(20) (a) Foote, C. S. *Acc. Chem. Res.* **1968**, *1*, 104. (b) Hurst, J. R.; Wilson, S. L.; Schuster, G. B. *J. Am. Chem. Soc.* **1982**, *104*, 2065.

Scheme 5. Synthesis of Disubstituted Alkenes Bearing C_{60} as the Large Substituent

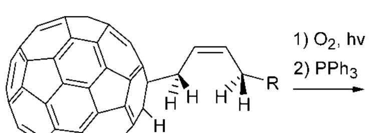


Xa **Xb** **Xc**

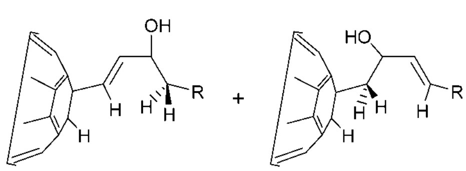
Allylic bromide	Fullerene adducts		
(R-)	**Xa** (%)	**Xb** (%)	**Xc** (%)
H-	**5a** (60)	-	**5c** (40)
CH_3-	**6a** (77)	**6b** (8)	**6c** (15)
Ph-	**7a** (67)	**7b** (20)	**7c** (13)
$(CH_3)_2CH$-	**8c** (74)	**8b** (15)	**8c** (11)
$(CH_3)_3C$-	**9a** (80)	**9b** (11)	**9c** (9)

The ene reaction of the fullerene C_{60} substituted alkene of the general type **Xa** shows a consistent regioselectivity for double bond formation closer to the fullerene substituent. For example, when the R group is hydrogen or methyl, compounds **5a** and **6a**, the preferential abstraction of hydrogen adjacent to the fullerene group is greater than 67%. A similar regioselectivity trend is observed when R is a phenyl group, substrate **7a**. Again the major isomer is the product with the double bond on the side of the fullerene group. This result indicates that nonbonding sreric interactions play a more important role than conjugation with the π system of the phenyl ring in the transition state of this reaction. As the size of the R group becomes larger, the regioselectivity toward the fullerene group decreases. This is demonstrated with substrate **8a**, where the preferential hydrogen abstraction is slightly higher on the fullerene side. When R is *tert*-butyl, **9a**, competition for the two allylic sides leads to nearly equal hydrogen abstraction from the two methylene sides. It is useful to note here that photosensitized ene oxidation of 5,5-dimethyl-2-*cis*-hexene[14a] showed regioselectivity similar with that of substrate **5a**. This comparison might indicate that unlike the rationalization[8] for the regioselectivity of the self-photooxygenation of C_{60}-fused cyclohexene derivative **1**, the nonbonding steric interactions dictate the regioselectivity. Electrostatic factors from fullerene group most probably play a negligible role in the transition state of this reaction.

Scheme 6. Regioselective Ene Photooxygenations of Fullerene Derivatives **Xa**



Xa

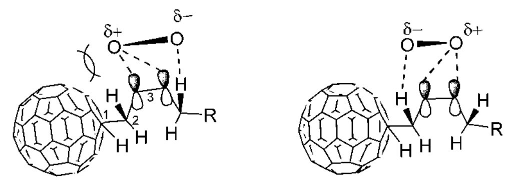


Ya **Yb**

Xa	R-	**Ya** (%)	**Yb** (%)
5a	H	**10a** (67)	**10b** (33)
6a	CH_3-	**11a** (70)	**11b** (30)
7a	Ph-	**12a** (66)	**12b** (34)
8a	$(CH_3)_2CH$-	**13a** (59)	**13b** (41)
9a	$(CH_3)_3C$-	**14a** (52)	**14b** (48)

Examination of the possible transition states TS_I and TS_{II} leading to the minor and major products provides an insight into this regioselectivity (Scheme 7). In transition state TS_{II},

Scheme 7



TS_I less favorable TS_{II} more favorable

leading to the major product, the nonbonding interactions involving the large fullerene moiety are smaller than those at the transition state TS_I leading to the minor product. As the size of the substituent on both sides of the double bond become similar, as in compound **9a**, the nonbonding interactions in TS_I and TS_{II} become isoenergetic, leading to equal amounts of the two isomeric ene products. This explanation in terms of nonbonding steric interactions is similar to that of the ene reaction of singlet oxygen with simple alkenes and has been discussed extensively.[14a] It is interesting to note that the regioselectivity is independent of solvent polarity. Self-photooxygenation of compound **9a** in toluene, 1,2-dichlorobenzene, and benzonitrile gave similar ratios of the two ene products (within experimental error).

In conclusion, the self-photooxygenation of C_{60}-allyl substituted *cis* alkenes ocurrs by the preferential abstraction of an allylic hydrogen next to the fullerene group. The hydrogen atom linked to the fullerene frame is unreactive under the photoogygenation conditions.

Acknowledgment. We thank Greek Secretariat of Research and Technology (PENED 1999) for financial support and for research fellowship to N.C.

Supporting Information Available: ^1H NMR, spectral data for **3a,b, 4a,b, 5a,c, 6a−c, 7a−c, 8a−c, 9a−c,** and **10a,-10b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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