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Novel Methodology for the Preparation of Five-, Seven-, and Nine-Membered Fused Rings on C_{60}

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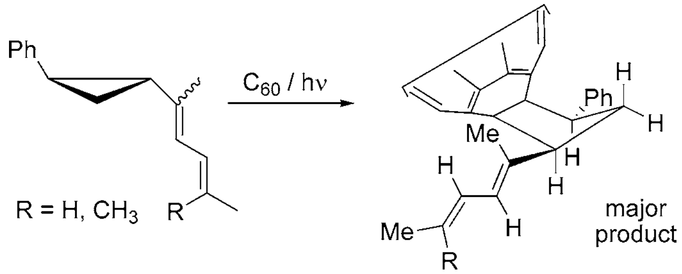
ABSTRACT



The photocycloaddition of dienyl cyclopropanes to C_{60} gives a new synthetic approach to yield stereospecifically five-, seven-, and nine-membered [60]fullerene adducts. Our results suggest the formation of a biradical intermediate between the dienyl substrate and C_{60}. An electron transfer between the triplet excited state of C_{60} and the dienyl substrate precedes the formation of the intermediate.

Many reactions for the functionalization of [60]fullerene have been developed on the basis of its electron-deficient behavior.[1] Photoinduced functionalization of [60]fullerene has attracted considerable interest because photoexcited C_{60} exhibits more electrophilicity than the ground state of C_{60}.[2] [60]Fullerene can easily be excited into its triplet state, $^3C_{60}$, in quantum yield near unity, elevating the reduction potential from −0.42 V vs SCE of the ground state to close to 1.14 V vs SCE of the triplet state.[3] Previously, we reported the [2 + 2] functionalization of C_{60} with moderately electron-rich *p*-methoxyarylalkenes[4] as well as with the less-electron-rich alkyl-substituted 1,3-butadienes.[4] Stereochemical and secondary kinetic isotope effects studies showed that the first (rate-determining) step of the reaction involves the formation of an open intermediate (dipolar or biradical) between the $^3C_{60}$ and the unsaturated substrate. Moreover, in the case of 2,4-hexadienes, it is noteworthy that the stereochemical studies favor the involvement of a biradical rather than a dipolar intermediate.

During the course of our studies on the mechanism of photocycloadditions of dienes and alkenes to C_{60}, we have developed a new synthetic approach to prepare functionalized

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[2] (a) Akasaka, T.; Ando, W. *J. Am. Chem. Soc.* **1993**, *115*, 10366. (b) Liou, K.-F.; Cheng, C.-H. *Chem. Commun.* **1996**, 1423. (c) Lawson, G. E.; Kitaygorodskiy, A.; Sun, Y.-P. *J. Org. Chem.* **1996**, *61*, 5913. (d) Akasaka, T.; Maeda, Y.; Wakahara, T.; Okamura, M.; Fujitsuka, M.; Ito, O.; Kobayashi, K.; Nagase, S.; Kako, M.; Nakadaira, Y.; Horn, E. *Org. Lett.* **1999**, *1*, 1509. (e) Mokami, K.; Matsumoto, S.; Okubo, Y.; Fujitsuka, M.; Ito, O.; Suenobu, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **2000**, *122*, 2236. (f) Akasaka, T.; Maeda, Y.; Wakahara, T.; Mizushima, T.; Ando, W.; Wälchli, M.; Suzuki, T.; Kobayashi, K.; Nagase, S.; Kako, M.; Nakadaira, Y.; Fujitsuka, M.; Ito, O.; Sasaki, Y.; Yamamoto, K.; Erata, T. *Org. Lett.* **2000**, *2*, 2671. (g) Imahori, H.; Tamaki, K.; Araki, Y.; Sekiguchi, Y.; Ito, O.; Sakata, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **2002**, *124*, 5165.

[3] (a) Arbogast, J. W.; Darmanyan, A. O.; Foote, C. S.; Rubin, Y.; Diederich, F. N.; Alvarez, M. M.; Anz, S. J.; Whetten, R. L. *J. Phys. Chem.* **1991**, *95*, 11. (b) Arbogast, J. W.; Foote, C. S.; Kao, M. *J. Am. Chem. Soc.* **1992**, *114*, 2277.

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[60]fullerenes with various fused rings. To our knowledge, there is no other available method.

Herein, we present a new methodology for the preparation of five-, seven-, and nine-membered fused rings by the photochemical addition of 2-(*trans*-2'-phenylcyclopropyl)-5-methyl-2,4-hexadiene (**1**)[5] to C_{60}. Vinylcyclopropane derivatives are effectively used as mechanistic probes in the investigation of radical[6] or dipolar[7] cycloadditions to a carbon−carbon double bond. Apart from the synthetic ability, the formation of ring-opened, rearranged products can provide useful information on the intermediate or on the radical cation if an electron-transfer process[8] is the case.

A solution of C_{60} and a 30-fold excess of **1** as an 80:20 *E*/*Z* mixture in deoxygenated toluene, in the absence of light, did not react after 24 h at solvent reflux. However, upon irradiation with a xenon lamp (Variac Eimac Cermax 300 W), a rapid reaction was detected by HPLC on a Cosmosil 5C18-MS reverse-phase column. Two major peaks appeared in the HPLC chromatogram in a 60:40 ratio, within just a few minutes of irradiation, indicating the formation of a mixture of C_{60} cycloadducts. The mixture of products was formed in 60% yield, based on the recovered C_{60}. Purification through flash column chromatography (SiO_2, hexane/CH_2Cl_2 = 4:1) led to the isolation of the fullerene products (Scheme 1) in two fractions, the first one containing the seven- and nine-membered cycloproducts (the less polar compounds) and the second one containing the major cycloproduct with a five-membered ring (the more polar compound). The ^{1}H NMR spectrum (Figure 1) of the major cycloproduct displays four multiplet signals which correspond to the cyclopentane ring protons of the rearranged derivative ***E-syn*-2**. ^{1}H homonuclear decoupling experiments reveal the following coupling pattern for the protons on the cyclopentane ring: $-CH-CH_2-CH-$ (Table 1). The two methine protons resonate at lower fields as a doublet of a doublet each, and the diastereotopic methylene protons resonate at higher fields as multiplets. Consequently, a regiospecific cleavage of the more substituted cyclopropane bond occurs.

Scheme 1. Photochemical Ring-Opening Cycloaddition of a Mixture of ***E*-**, ***Z*-1** to C_{60}

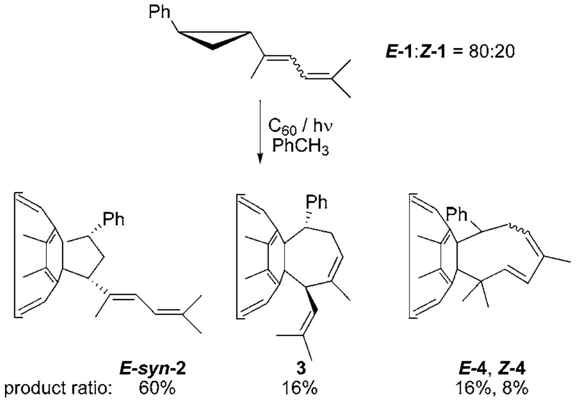

Figure 1. Stereochemistry and ^{1}H NMR of ***E-syn*-2**.

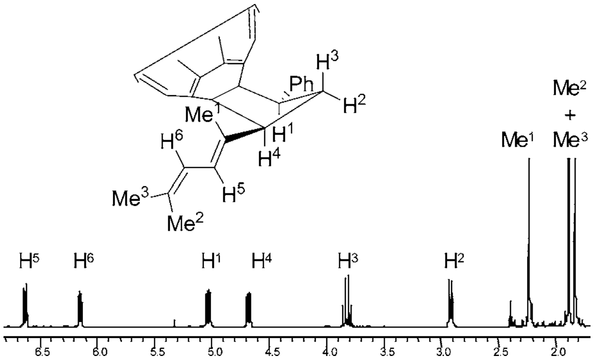

Table 1. Some Spectroscopic Data of ***E-syn*-2**

	CH^1	CH^2	CH^3	CH^4	CH^5	CH^6	Me^1
^{1}H	5.05	2.94	3.83	4.70	6.65	6.15	2.25
^{13}C	59.9	34.6	34.6	64.0	127.5	127.1	16.8

The configurational assignment of the protons on the cyclopentane ring was determined by difference nuclear Overhauser effect (DNOE) experiments. The methine signal at 5.05 ppm (H^1) was identified as benzylic on the basis of the positive enhancement between H^1 and *o*-phenyl protons. The methine signal at 4.70 ppm (H^4) was identified as allylic on the basis of the positive enhancement between H^4 and vinylic protons at 6.65 ppm. Substantial positive enhancement was displayed between the methylene proton which resonates at 2.94 ppm (H^2) and the methine protons, H^1 and H^4, revealing their syn configuration as well as the axial-like positions of the methine protons on the cyclopentane ring. Consequently, the thermodynamically more stable five-membered ring was formed where the 1,3-substituents, phenyl and dienyl groups, possess the equatorial-like positions on the ring. Moreover, the values of anti and syn coupling constants (J_{anti} = 13.0 Hz and J_{syn} = 4.38 Hz) are consistent with dihedral angles close to 180° for the anti hydrogens and 47° for the syn hydrogens.[9]

The resolved ^{13}C NMR spectrum displays for the fullerene skeleton two signals at 75.7 and 76.0 ppm due to the two

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(5) For preparation of **1** and **7**, see Supporting Information.

(6) (a) Shimizu, N.; Nishida, S. *J. Chem. Soc., Chem. Commun.* **1972**, 389. (b) Rudolph, A.; Weedon, A. *Can. J. Chem.* **1990**, *68*, 1590. (c) Becker, D.; Galili, N.; Haddad, N. *Tetrahedron Lett.* **1996**, *37*, 8941. (d) Adam, W.; Curci, R.; D'Accolti, L.; Dinoi, A.; Fusco, C.; Gasparrini, F.; Kluge, R.; Paredes, R.; Schulz, M.; Smerz, A. K.; Veloza, L. A.; Weinkötz, S.; Winde, R. *Chem.−Eur. J.* **1997**, *3*, 105.

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(8) (a) Kataoka, F.; Nishida, S. *Chem. Lett.* **1980**, 1115−18. (β) Tsuji, T.; Nishida, S. *Acc. Chem. Res.* **1984**, *17*, 56. (b) Nishida, S.; Murakami, M.; Mizuno, T.; Tsuji, T.; Oda, H.; Shimizu, N. *J. Org. Chem.* **1984**, *49*, 3928.

(9) Constantino, M. G.; da Silva, G. V. *Tetrahedron* **1998**, *54*, 11363.

sp^3-hybridized junction carbons, and the rest of the sp^2-hybridized signals are in the spectral range between 125 and 160 ppm. The protonated carbons were assigned using DEPT and H−C correlation experiments. Analysis of the H−C coupling in the gHMQC NMR spectrum confirms the proposed structure. Both methylene protons H^2 and H^3 exhibit a cross-peak with the methylene carbon of the cyclopentane ring at 34.6 ppm. The benzylic and allylic methine carbon signals of the cyclopentane ring resonate at 59.9 and 64.0 ppm, respectively. The olefinic carbon signals of the dienyl group resonate at 121.1 and 127.5 ppm, whereas the methyl carbons resonate at 16.8, 18.3, and 26.4 ppm.

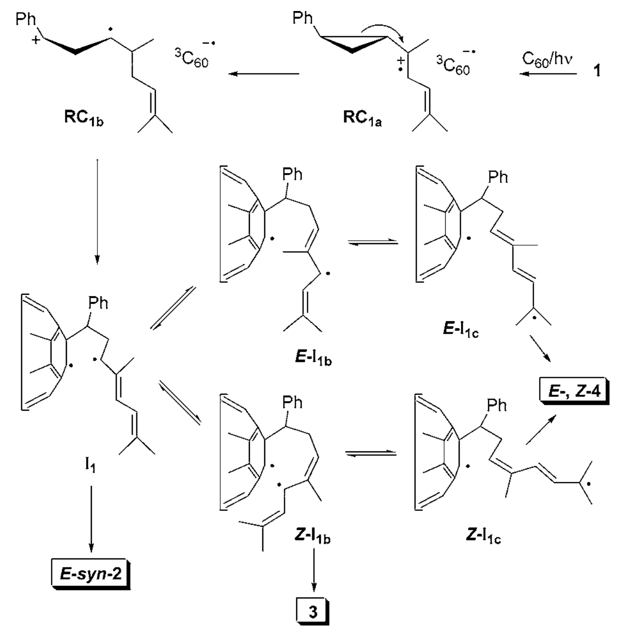
Analysis of the H−C three-bond coupling in the gHMBC NMR spectrum combined with DNOE experiments on the allylic methine hydrogen H^4 revealed the stereochemistry of the dienyl group. Specifically, in the gHMBC NMR spectrum, the olefinic hydrogen which resonates at 6.15 ppm (H^6) couples with the two methyl carbons at 18.3 (Me^2) and 26.4 ppm (Me^3), and the other olefinic hydrogen at 6.65 ppm (H^5) couples with the methyl carbon at 16.8 ppm (Me^1) and the allylic cyclopentane carbon at 64.0 ppm ($C-H^4$). Moreover, spacial proximity of olefinic hydrogen which resonates at 6.65 ppm (H^5) with H^4 and methyl hydrogens at 18.3 ppm (Me^2) was determined. The above spectroscopic data reveal *E*-stereochemistry on the dienyl group (Figure 1).

The ^1H NMR spectrum of the less polar fraction displays the presence of three opened-ring cycloproducts **3**, ***E*-4**, and ***Z*-4** (Scheme 1), the first one bearing a seven-membered ring and the other two bearing a nine-membered ring with *E*- and *Z*-stereochemistry on the trisubstituted double bond. These products could not be separated by flash column chromatography. The proposed structures and their stereochemistries were determined by a combination of 1D and 2D NMR experiments. The hybridization of the protonated carbons as well as the assignment of the diastereotopic methylene hydrogens of these cycloadducts were confirmed by gHMQC NMR experiments. The coupling pattern $-CH-CH_2-CH-$ was deduced by ^1H homonuclear decoupling experiments. DNOE experiments revealed all spacial approximations, confirming the formation of these cyclic adducts and determining the trans stereochemistry of the 1,5-substituents, phenyl and alkenyl groups, of the product **3**.

Consumption of **1** was dramatically suppressed by addition of 10 equiv of rubrene, a well-known triplet quencher.[3b] Moreover, neither irradiation nor heating led to cycloreversion or decomposition of these cycloadducts. These results suggest the nonreversible formation of the adducts through the triplet excited state of C_{60}. The proposed mechanism that could account for the formation of the ring-fused C_{60} derivatives can be best rationalized via the geminate radical ion pair produced by the photoinduced electron transfer from the dienyl group of **1** to $^3C_{60}$ shown in Scheme 2. The incipient radical cation RC_{1a} undergoes ring opening to RC_{1b} before combining with its geminal radical anion of $^3C_{60}$.

Coupling of the rearranged radical ion pair forms the biradical intermediate $\mathbf{I}_1$, where the allylic radical delocalizes in the dienyl group and ultimately cyclizes to the three isolated cycloadducts. In Scheme 2, ring opening of RC_{1a} is shown to be attributed to cyclopropylcarbinyl cation rearrangement according to a previous report.[10]

Scheme 2. Proposed Mechanism in the Cycloadditon Reaction of **1** to C_{60}



The possibility that the disubstituted bond of cyclopropane of **1** acts as an electron donor to the $^3C_{60}$, in a $[2\sigma + 2\pi]$ photocycloaddition, was also examined. For this purpose, the chemical reactivities of 1,2-diphenylcyclopropane[11] **5** and 1-methyl-2-phenylcyclopropane[11] **6** were examined with C_{60}, under photochemical conditions identical to those described previously (Figure 2). No cycloaddition took place after prolonged irradiation in toluene solution. This is in agreement with the proposed electron-transfer mechanism outlined in Scheme 2, excluding the possibility of a $[2\sigma + 2\pi]$ cycloaddition.

Figure 2. Substrates utilized to examine their chemical reactivity with C_{60} under photochemical conditions.

To obtain further information on the stereochemistry of the photocycloaddition reaction of dienyl cyclopropanes to C_{60}, 2-(*trans*-2'-phenylcyclopropyl)-2,4-hexadiene (**7**)[5] was prepared as a mixture of ***E*-*cis*-7**, ***Z*-*cis*-7**, ***E*-*trans*-7**, and ***Z*-*trans*-7**. The ratio of trans/cis was measured by ^1H NMR to be 78:22. The stereochemistry of the terminal disubstituted

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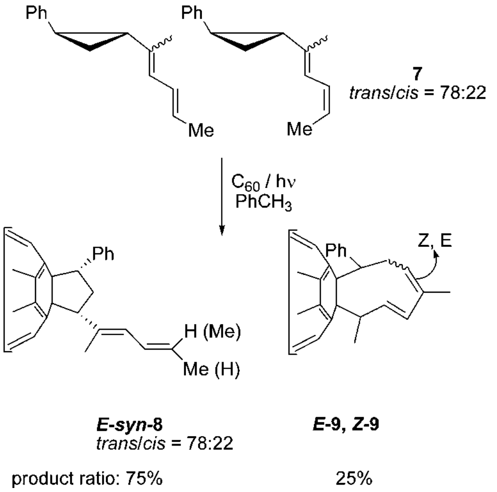
[10] Hatzimarinaki, M.; Roubelakis, M. M.; Orfanopoulos, M. *J. Am. Chem. Soc.* **2005**, *127*, 14183.

[11] Cyclopropanes **5** and **6** were prepared according to the literature: Petersen, R. J.; Skell, P. S. *Org. Synth. Coll.* **1973**, *5*, 929.

double bond was determined by a ^{1}H homonuclear decoupling experiment. Cycloaddition of the isomeric mixture of **7** to C_{60} under photochemical conditions identical to those described previously produced two cycloproducts, cyclopentane ***E*-*syn*-8** and a mixture of cyclononanes ***Z*-**, ***E*-9** (Scheme 3).

Scheme 3. Photochemical Ring-Opening Cycloaddition of a Mixture of **7** to C_{60}



The most important finding is the stereochemistry of the terminal double bond in the cyclopentane ***E*-*syn*-8** cycloadduct, determined by a ^{1}H homonuclear decoupling experiment (Figure 3). Upon irradiation of the terminal vinylic methyl groups, Me^2 and $Me^{2'}$ at 1.81 and 1.79 ppm, the multiplets of H^7 and $H^{7'}$ at 5.80 and 5.61 ppm collapsed to doublets with coupling constants $J = 13.9$ and 10.7 Hz, respectively. These values are typical for *trans*- and *cis*-alkyl-substituted double bonds.[12] The ratio of trans/cis of ***E*-*syn*-8** was measured by ^{1}H NMR to be 78:22. Consequently, the stereochemistry of the disubstituted double bond remained intact in the cyclopentane adduct. This finding is in agreement with the known propensity of allylic radicals to resist rotation around the partial double bonds.[13] In other words, this result supports the formation of biradical intermediate $\mathbf{I}_7$, which permits rotation around the C^3-C^4 bond but resists rotation around the C^5-C^6 and C^7-C^8 partial double bonds (Figure 4).

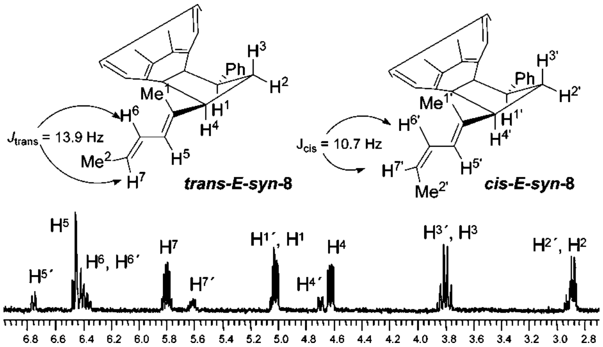


Figure 3. Stereochemistry and ^{1}H NMR of ***E*-*syn*-8**.

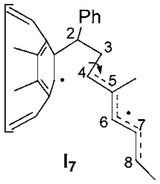


Figure 4. Biradical intermediate $\mathbf{I}_7$.

In conclusion, a novel photochemical functionalization of [60]fullerene with cyclopropyl-dienes is reported. Ring-opening products are smoothly formed bearing five-, seven-, and nine-membered rings. All findings support the formation of a biradical intermediate which is preceded by an electron-transfer step between the diene and $^3C_{60}$.

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Supporting Information Available: Detailed experimental procedures and 1D and 2D NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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