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Photocycloaddition of Biscyclopropyl Alkenes to C_{60}: An Unprecedented Approach toward *cis*-1 Tricyclic-Fused Fullerenes

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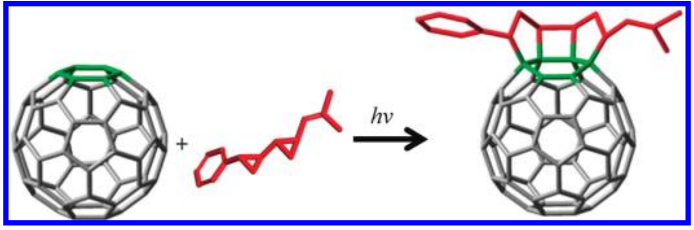
ABSTRACT



A novel, simple, and entirely regioselective tandem cycloaddition of biscyclopropyl-substituted alkenes to [60]fullerene has been revealed. This reaction affords *cis*-1 tricyclic-fused organofullerenes bearing the hitherto elusive 5−4−5 fused tricyclic ring system.

Cyclopropane-containing compounds are important and versatile building blocks in organic synthesis. They have been extensively used for the synthesis of carbocyclic ring systems including five- to nine-membered carbocycles.[1,2] In this context, we previously investigated the reactivity of vinyl monocyclopropane derivatives with different electrophiles, including C_{60}.[3] In sharp contrast, however, to their monocyclopropane analogues, the synthetic utility of biscyclopropane derivatives is still in its infancy. To date, there are only two examples of synthetic applications of such systems, which include the preparation of carbocyclic seven-membered rings[4a] and N-containing heterobicycles, respectively.[4b] Herein we report the unprecedented photochemical cycloaddition of biscyclopropyl-substituted alkenes with C_{60}. This simple one-step reaction proceeded in a totally regioselective manner affording in good yield the first example of *cis*-1 fullerene isomers featuring the hitherto elusive 5−4−5 tricyclic fused ring system. Semipreparative HPLC was employed to circumvent the inherently difficult challenge of separating and purifying all four stereoisomeric adducts, thus allowing for their unequivocal structural characterization by means of spectral studies (i.e., 1D/2D NMR, HRMS, UV−vis).

Our first goal was the preparation of 5- to 12-membered fused ring systems on C_{60}. To this purpose, we prepared vinyl biscyclopropane derivatives **9** and **10** (Scheme 1);[5] the key intermediate for this synthesis was the cyclopropanation of compound **4** with oxosulfonium salt **5**.[5,6a,7] The presence of a double bond next to the biscyclopropyl moiety was a prerequisite to observe the subsequent strain-driven cleavage

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(1) Selected reviews: (a) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051. (b) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117. (c) Thematic Issue on Cyclopropanes and Related Rings. *Chem. Rev.* **2003**, *103*, 931. (d) Wong, H. N. C.; Hon, M. Y.; Tse, C. W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165.

(2) For recent examples, see: (a) Saito, S.; Maeda, K.; Yamasaki, R.; Kitamura, T.; Nakagawa, M.; Kato, K.; Azumaya, I.; Masu, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 1830. (b) Bhargava, G.; Trillo, B.; Araya, M.; López, F.; Castedo, L.; Mascareñas, J. L. *Chem. Commun.* **2010**, *46*, 270. (c) Inagaki, F.; Sugikubo, K.; Miyashita, Y.; Mukai, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2206 and references therein.

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(5) For the synthetic details as well as the structural characterization, see the Supporting Information.

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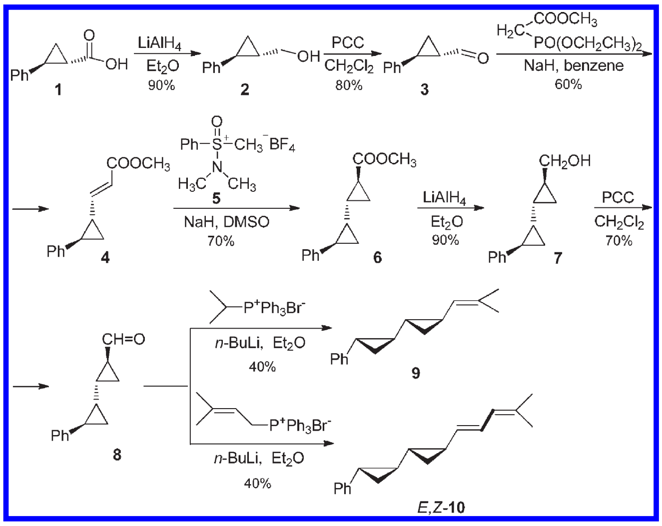
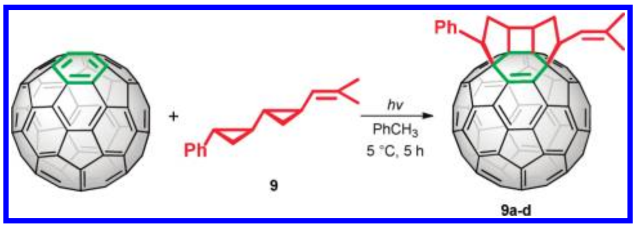
of both cyclopropane rings,[6] upon an electron transfer reaction with C_{60} (vide infra), as previously observed in related monocyclopropane analogues.[3] Accordingly, it should be expected that rearranged biscyclopropane derivatives **9** and **10** could spontaneously cyclize with C_{60} to form n-membered fused ring systems (for alkene **9**, $n = 5, 7, 8, 10$; for alkene **10**, $n = 5, 7–10, 12$).

Scheme 1. Preparation of Compounds **9** and *E*,*Z*-**10**



Initially, the reaction of C_{60} with a 30-fold excess of **9** in deoxygenated toluene was investigated. No products were observed at solvent reflux in the absence of light for 12 h, whereas this reaction took place readily upon irradiation using a xenon lamp (Variac Eimac Cermax 300 W, $\lambda > 280$ nm) at 5–10 °C. Reversed-phase HPLC analysis of the reaction mixture showed two major, partially overlapping peaks after 5 h of irradiation. These peaks corresponded to a complex mixture of C_{60} cycloadducts. Contrary to our initial expectations, the only compounds obtained from this mixture in 60% yield (80% based on recovered C_{60}) were assigned as the unanticipated *cis*-1 tricyclic-fused fullerene derivatives **9a**–**d** (Scheme 2). To the best of our knowledge, this is the first example of a fused 5–4–5 tricyclic ring system on the same fullerene hexagonal ring. The end result of this reaction may be regarded as a tandem (3 + 2) cycloaddition of two cyclopropyl rings into adjacent double bonds of C_{60}.

Scheme 2. Reaction of **9** with C_{60} in Toluene



It should be noted that the isolation of isomers **9a**–**d** was not a trivial endeavor. It was only achieved after laborious chromatographic separation, including a two-step semipreparative HPLC process (for details see the Supporting Information (SI)). To demonstrate the difficulty of HPLC separations for **9a** and **9b** stereoisomers (1:1, major products), Figure S15 indicates elution differences of only 129 and 124 min, respectively, and a clear lack of baseline resolution. These stereoisomers were effectively separated and purified after successive recycling of overlapping subfractions. The mixture of **9c** and **9d** isomers was found to be inseparable under several conditions which, however, did not prevent their structural characterization.

The structure of all new fullerene adducts has been unambiguously established by the combined use of 1D and 2D NMR techniques (^{1}H, ^{13}C, ^{1}H–^{1}H COSY, ^{1}H–^{13}C HMQC, ^{1}H–^{13}C HMBC, ^{1}H homonuclear decoupling and ^{1}H–^{1}H NOE difference), UV/vis spectroscopy, and high resolution mass spectrometry (see the SI). In particular, the NMR spectra of the isolated products all exhibit similar ^{1}H/^{13}C NMR patterns, showing them to be diastereomers of *cis*-1 tricyclic 5–4–5-fused fullerenes **9a**–**d**, thus demonstrating the totally regioselective nature of the 2-fold cycloaddition of **9** across the same hexagonal ring of C_{60} (Scheme 2). The ^{13}C NMR spectra of C_1 symmetric compounds **9a**–**d** each display 60 resonances for the fullerene carbon atoms: 56 sp^2 resonances in the region of 133.1–156.1 ppm and four single intensity characteristic resonances in the region 67.4–71.5 ppm which, based on HMQC experiments, are assigned to sp^3-hybridized fullerene carbons. The absence of the characteristic cyclopropyl proton absorption in the upfield ^{1}H NMR region (~0.5–2.3 ppm) indicates cyclopropane ring-opened structures for compounds **9a**–**d**. Moreover, the ^{1}H NMR spectrum of these adducts shows, apart from the existence of two methyl group resonances at 1.82–2.00 ppm, the presence of the characteristic vinyl proton of **9a**–**d**, which appears as a doublet centered at 5.64–5.90 ppm with a coupling constant of $^3J_{HH} = 9.5–10$ Hz. The H–H coupling pattern in isolated products was deduced by ^{1}H homonuclear decoupling, ^{1}H–^{13}C HMBC, and ^{1}H–^{1}H COSY experiments (see the SI) giving results consistent with the assignment of structures **9a**–**d**. Difference nuclear Overhauser effect (DNOE) experiments provided all spatial proximity information, including the *cis*/*trans* stereochemistry of the 1,3-cyclopentane substituents, and confirmed the formation of these cyclic adducts as shown in Figure 1 (also see Figure S40, SI). The energy-minimized molecular structures of **9a**–**d** obtained from molecular mechanics calculations (Figure 1) correlate perfectly with the information obtained from the spectroscopic analysis. More importantly, the coupling constant values between the neighboring cyclopentane protons support their *anti* or *syn* relative configuration ($^3J_{HH(syn)} = 6–9.5$ Hz and $^3J_{HH(anti)} = 9.5–13.5$ Hz) as depicted in Figure 1.

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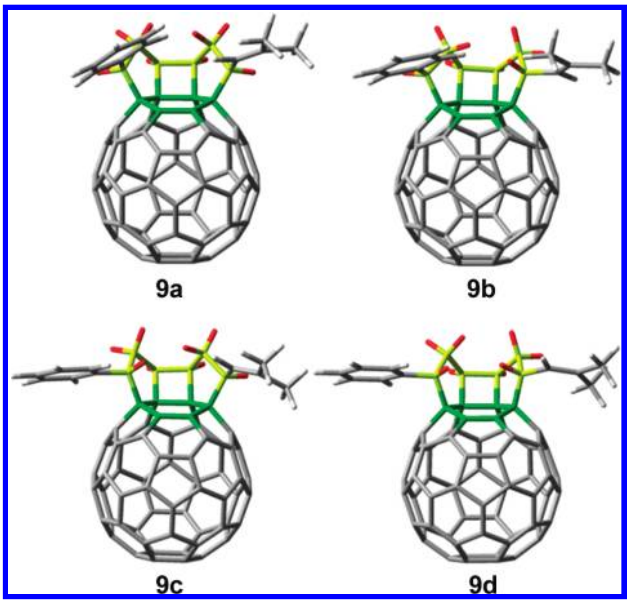

Figure 1. MM2-optimized structures of **9a**−**9d** (the cyclopentane hydrogens, red; the carbon framework of the addend, yellow; the corresponding hexagonal fullerene framework, green).

Further evidence is provided by UV−vis spectroscopy, which has proven to be a powerful tool in determining the addition pattern of C_{60} bisadducts; the electronic absorption spectra of [60]fullerene bisadducts are typically sensitive toward the addition pattern rather than the type of addends.[8−10] Herein, the UV/vis absorption spectra of compounds **9a**−**d** exhibit the typical features of the hitherto known *cis*-1 bisadducts, with a characteristic absorption at 433 nm, together with shoulders at 334 nm (Figure 2).[9−17] Finally, the high-resolution FAB mass spectra of **9a**−**d** exhibit pseudomolecular ion peaks at *m*/*z* 933.1630−933.1652 $[M + H]^+$, consistent with the molecular weight of **9a**−**d**. The above spectral studies all support the C_1 symmetric structures of **9a**−**d** with *cis*-1 regiochemistry, as depicted in Figure 1.

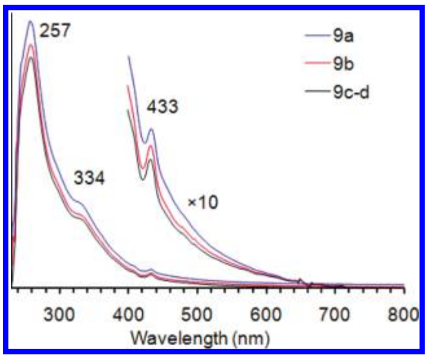

Figure 2. UV/vis spectra of compounds **9a**−**d**.

Although much faster (10 °C, 30 min), the reaction of C_{60} with **10** afforded again in high yield (80%) an even more complex mixture of several stereoisomers apparently due to the presence of an extra double bond that increased the number of possible stereoisomers. This complex mixture was difficult to separate and could not be fully characterized. Importantly, however, the spectral analysis of this crude mixture indicated again the formation of *cis*-1 stereoisomers, thus validating the versatility of the present method.

The precise mechanism involved in this reaction is still unclear, but the unique structure of the observed products **9a**−**d** provides strong evidence for its rationalization. A plausible mechanism for the addition of **9** to C_{60} is depicted in Scheme 3. Specifically, the mechanism should be initiated by photoinduced electron transfer (PET) from the double bond of **9** to $^3C_{60}*$, thus forming the corresponding geminate radical ion pair. The incipient radical cation **9I** undergoes a facile ring opening of the two cyclopropane rings to form **9III** before combining with its geminal radical anion $^3C_{60}{}^{\bullet -}$. In each case, a regiospecific cleavage of the more substituted cyclopropane bond occurs, by virtue of the stability of a secondary over a primary carbon radical. At this point forward, two reaction pathways may be considered for the coupling of the radical ion pair. On one hand (pathway A), the coupling of distonic radical cation **9III** with $C_{60}{}^{\bullet -}$ produces 1,4-cycloadduct **9V** which, in turn, spontaneously undergoes an intramolecular [2 + 2] photocycloaddition reaction to produce the final adducts **9a**−**d**. The facility of this latter process may be ascribed, at least in part, to the release of the strain induced by the energetically unfavorable $C^2{=}C^3$ double bond at a [5,6] ring junction of C_{60}. On the other hand (pathway B), radical coupling of **9III** with $C_{60}{}^{\bullet -}$ followed by an intramolecular nucleophilic addition to the proximal double bond generates in situ the 1,3-dipolar intermediate **9VII** which, ultimately, cyclizes to adducts **9a**−**d** via an intramolecular 1,3-dipolar addition to the adjacent [6,6]-double bond of C_{60}.

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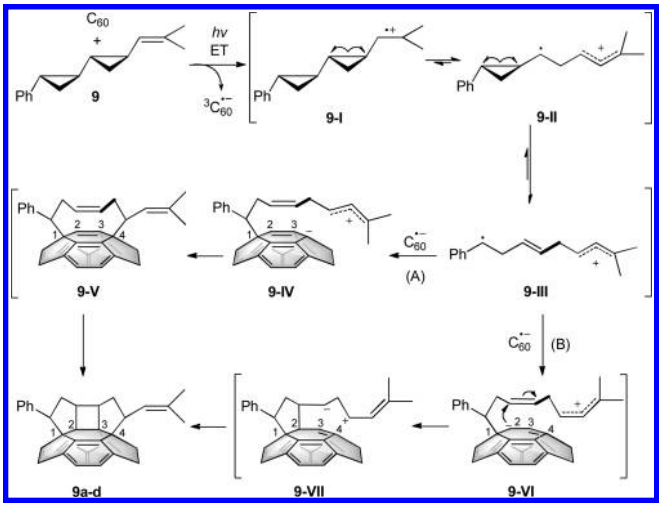
Scheme 3. Proposed Mechanism for the Cycloaddition of **9** and C_{60}, under PET Conditions



At this point it is worth noting that 1,2,3,4-tetrahydro[60]fullerenes display interesting photophysical properties.[18] They have also attracted considerable research interest due to their utility as ideal precursors of open-cage fullerenes through a stepwise approach of saturating all three double bonds of a six-membered ring on C_{60}.[11,19] More importantly, this is the first example of such an elegant cycloaddition reaction that provides a highly efficient route for the direct and completely regioselective *cis*-1 functionalization of C_{60}.[20]

In summary, we have disclosed a tandem (3 + 2) cycloaddition of vinyl biscyclopropane derivatives with C_{60}. This novel reaction affords, in a single synthetic step, smoothly, and in good yield, a novel class of fullerene *cis*-1 bisadducts containing the hitherto elusive 5−4−5 tricyclic fused ring system. The reaction is totally regioselective thus demonstrating its potential for sterically demanding fullerene functionalizations such as the construction of highly congested 1,2,3,4-tetrahydro[60]fullerene derivatives. Further exploration of the characteristics and scope of this novel reaction is currently in progress.

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Supporting Information Available. Detailed experimental procedures, spectral data, and copies of 1D/2D NMR, HRMS, and UV−vis spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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