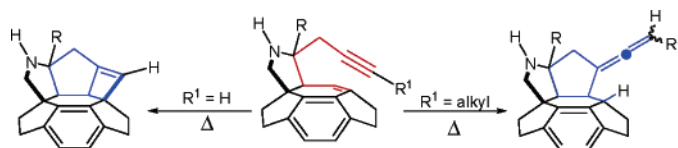# Intramolecular Ene Reaction of 1,6-Fullerenynes: A New Synthesis of Allenes

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ABSTRACT

Thermal treatment of 1,6-fullerenynes bearing an alkyl group on the terminal carbon of the alkyne moiety leads quantitatively to new allenes through a reaction mechanism involving an intramolecular ene process. This reaction outcome is in contrast to that recently found for free terminal alkynes which form cyclobutene derivatives through a [2+2] cyclization mechanism.

1,6-Enynes in which fullerene C_{60} is used as the alkene component (1,6-fullerenynes) are singular and versatile building blocks which have been successfully used for the regioselective transition-metal-catalyzed [2+2+1] Pauson–Khand cyclization to form unprecedented modified fullerenes endowed with three or five fused pentagonal rings on the fullerene surface.[1] Furthermore, 1,6-fullerenynes undergo a noncatalyzed thermally induced [2+2] cyclization to form new fullerene derivatives bearing a cyclobutene-fused cyclopentane moiety, whose existence as a useful and elusive intermediate has received much attention due to its academic and practical interest.[2] ONIOM(UB3LYP/6-31G*:AM1) theoretical calculations predicted that this general reaction

occurs in a concerted and highly asynchronous mechanism between the alkyne group and the closer fullerene double bond.[3]

In this communication, we describe the strong impact that the presence of a methyl or alkyl group on the alkyne moiety in the 1,6-fullerenyne has on the reaction outcome. The thermal treatment of the novel alkyne-substituted fulleropyrrolidines (**2a–c, 3**) does not form the expected alkyl-substituted cyclobutene derivatives through a [2+2] cyclization, and instead, new allene derivatives (**4a–c, 5**) are obtained in a highly efficient way through a different mechanism involving an *intra*molecular *ene* reaction.[4]

The chemistry of allenes is currently a field of interest because of the role that these—almost neglected—compounds play in the mechanisms of enzyme inhibitors, cytotoxic agents, or antiviral agents. They have also been isolated and

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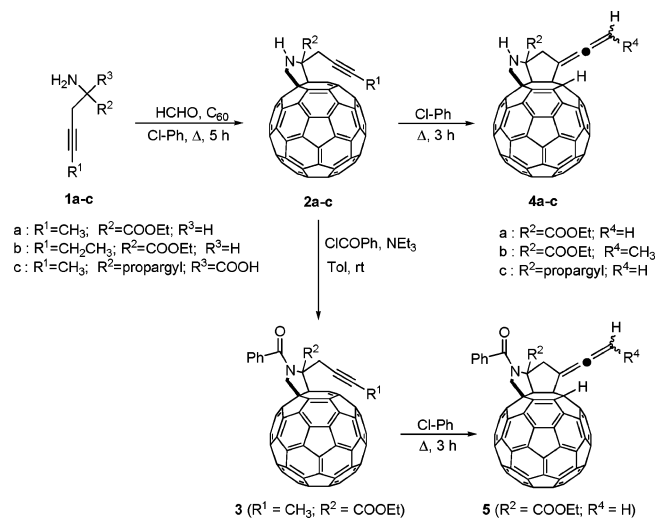
(4) Some examples of intermolecular ene reactions involving fullerenes have previously been reported. See, for example: (a) Cronakis, N.; Orfanopoulos, M. *Org. Lett.* **1999**, *1*, 1909. (b) Miles, W. H.; Smiley, P. M. *J. Org. Chem.* **1996**, *61*, 2559. (c) Komatsu, K.; Murata, Y.; Sugita, N.; Wan, T. S. M. *Chem. Lett.* **1994**, 635. (d) Wu, S.; Shu, L.; Fan, K. *Tetrahedron Lett.* **1994**, *35*, 919.

characterized from many natural products, and up to now, over 150 compounds comprising this functionality in their structure are known.[5] Moreover, allenes are emerging as valuable building blocks for a wide variety of synthetic applications, thus discarding the old belief of being highly unstable compounds.[6] Only very few examples are known in the literature on the preparation of allenes from enynes, and they involve the use of a Lewis catalyst[7] or allenyl radicals.[8] To the best of our knowledge, only two allene compounds have previously been reported by thermal intramolecular ene reaction of enynes, and they involve the use of high temperature (210 °C) with a moderate yield in one case[9] and the formation of a nonisolated allene intermediate in the other.[10] Very recently, the first intermolecular ene reaction of arynes with alkynes to form a wide variety of symmetric and asymmetric allenes has been thoroughly reported.[11] Therefore, in the present communication, we report the first detailed account of the synthesis of allenes by simple and efficient thermal noncatalyzed intramolecular ene cyclization from readily available fuller-1,6-enynes.

The synthesis of the novel starting 1,6-fullerenynes (**2a–c**) was carried out by 1,3-dipolar cycloaddition reaction of the respective azomethine ylides, which were in turn generated in situ from methyl- or ethyl-propargyl containing glycine derivatives **1a–c**[12] and formaldehyde to C_{60} in refluxing chlorobenzene for 5 h following Prato's procedure.[13] These new 1,6-fullerenynes were obtained as stable brown solids in moderate (16–32%) yields (55–64% based on recovered fullerene). 1,6-Fullerenyne **3** was readily prepared in 90% yield by benzoylation reaction of compound **2a**. Further thermal treatment of the so-formed 1,6-fullerenynes (**2a–c**, **3**) by heating in refluxing chlorobenzene for 3 h afforded new fulleroallenes (**4a–c**, **5**) in quantitative yields (Scheme 1).[14]

It is interesting to note that this highly efficient intramolecular cyclization reaction leads to compounds **4a–c** and **5** bearing different substituents on the C-2 of the pyrrolidine ring (ester or propargyl) and on the N atom (hydrogen or acyl). Furthermore, the reaction proceeds with a methyl or ethyl group on the terminal alkynyl carbon atom, thus showing the versatility of this reaction. Because fulleropyrrolidines **2a–c** and **3** can be considered to be isolable intermediates in the obtention of allene derivatives **4a–c** and

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(14) Allenes **4a–c** were obtained as byproducts in the formation of 1,6-fullerenynes **2a–c** in 6–10% yield of the isolated compound.

Scheme 1. Thermal Ene Reaction of 1,6-Fullerenynes **2a–c** and **3**

a : R^1=CH$_3$; R^2=COOEt; R^3=H
b : R^1=CH$_2$CH$_3$; R^2=COOEt; R^3=H
c : R^1=CH$_3$; R^2=propargyl; R^3=COOH

a : R^2=COOEt; R^4=H
b : R^2=COOEt; R^4=CH$_3$
c : R^2=propargyl; R^4=H

3 (R^1 = CH$_3$; R^2 = COOEt)

5 (R^2 = COOEt; R^4 = H)

5 from the starting substituted glycines, formaldehyde and [60]fullerene, we carried out the preparation of the allenes from compounds **1a–c** in a one-pot synthesis. Thus, reaction of **1c** with formaldehyde and C_{60} in refluxing chlorobenzene for 8 h led to the formation of the expected allene **4c** in 30% yield, together with unreacted pristine C_{60} and a mixture of regioisomeric bisadducts.[15]

The structures of the novel compounds **2a–c** and **3** and **4a–c** and **5** were unambiguously determined by UV/vis, FTIR, and ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. The structure of the 1,6-fullerenynes is perfectly established, showing in the ^{1}H NMR spectra the methyl group connected to the alkyne moiety as a singlet at around 1.95 ppm in **2a,c** and **3** and the ethyl group as a triplet at 1.22 ppm and a multiplet (quartet of triplets, $J^3 = 7.5$ Hz, $J^5 = 2.3$ Hz) at 2.32 ppm in **2b**. On the other hand, allenes **4a–c** showed, in addition to the expected pyrrolidine protons at around 4.7 and 5.1 ppm, the presence of the hydrogen atom on the fullerene sphere as a singlet at around 6.5 ppm as a diagnostic signature in the ^{1}H NMR spectra. In allene **5**, the presence of the acyl group on the nitrogen atom has a strong impact on the δ values of the pyrrolidine hydrogen atoms, which are significantly shifted to a lower field (5.4 and 5.6 ppm) in comparison with allenes **4a–c**. The two hydrogen terminal atoms of the allene unit appear as two ddd's at around 5.4 and 5.6 ppm in **4a,c** and **5**. Furthermore, the characteristic allene central carbon atom appears at 204.0 ppm in **4a,c** and **5** bearing two hydrogen terminal atoms on the allene moiety, whereas this signal is upfield shifted (200.6 ppm) when a methyl group is present (**4b**).

As expected, compound **4b** bearing a hydrogen atom and a methyl group on the terminal carbon of the allene unit was

(15) This one-step process is not, however, as clean as that involving the isolation of the intermediate 1,6-fullerenyne as revealed by the HPLC analysis of the monitored reaction. Retention times corresponding to a mixture of bisadducts as well as other nonidentified byproducts were observed in the HPLC chromatogram.

obtained as a mixture of diastereomers in a 3.5:1 ratio (determined by ^{1}H NMR) due to the atropisomerism of the allene group, showing the hydrogen atom and the methyl group at 6.04 and 1.93 ppm (major isomer) and 5.80 and 2.13 ppm (minor isomer), respectively.

A further structural confirmation was based on 2D NMR experiments. Thus, Figure 1a shows the HMQC NMR
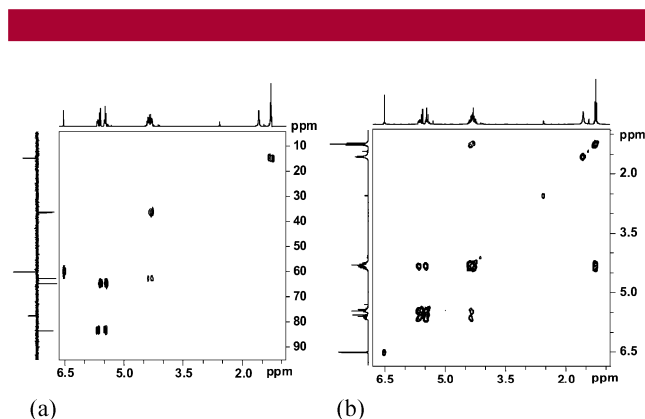
Figure 1. (a) HMQC NMR spectrum of compound **4a** combined with a DEPT experiment. (b) COSY experiment of compound **4a**.

spectrum combined with a DEPT experiment of compound **4a**, as a representative example. The three methylene groups and two allenic protons (coupled with the signal at 83.7 ppm) are clearly observed; the spectrum also shows the characteristic proton (6.5 ppm) attached to a C_{sp^3} of the fullerene core (60.2 ppm). Furthermore, the COSY experiment (Figure 1b) of **4a** shows the coupling of the allenic protons with the methylene group of the cyclopentane ring.

The structure of the novel compounds has also been supported by cyclic voltammetry (CV) in o-dichlorobenzene/acetonitrile (4:1) as solvent at room temperature, tetrabutylammonium perchlorate as the supporting electrolyte, and using Ag/Ag$^+$ as a reference electrode (see Supporting Information). Because of the characteristic shapes of the redox waves and their unequivocal position on the potential scale, CV has been labeled as "electrochemical spectroscopy".[16] In our case, the presence of one and two saturated double bonds in the precursor 1,6-fullerenynes (**2a−c**, **3**) and the final allene products (**4a−c**, **5**), respectively, should have a strong impact on the reduction potential values of the fullerene unit (see Supporting Information, Table SI1).

Intermediate fulleropyrrolidines **2a−c** and **3** show four reversible reduction waves, whereas three reversible waves were observed for the C$_{60}$ unit in **4a−c** and **5**. A sizable negative shift of the reduction potentials (50−80 mV) relative to pristine C$_{60}$ ($E^{1/2}_{red}$ = −0.800, −1.209, −1.673, −2.127 V) was observed for **2a−c**, due to the saturation of one double bond in the fullerene unit, which raises the LUMO energy. cis-1-Biscycloadducts **4a−c** showed, however, a larger negative shift (120−130 mV) relative to the parent C$_{60}$ (see Supporting Information, Table SI1) which corre-

sponds to the saturation of two double bonds of the fullerene moiety, in agreement with previous mono- and biscycloadducts on the fullerene surface.[17] Compounds **3** ($E^{1/2}_{red}$ = −0.827, −1.229, −1.752, −2.196 V) and **5** ($E^{1/2}_{red}$ = −0.876, −1.275, −1.932 V) showed lower negative shifts in comparison with their related compounds **2a−c** and **4a−c**, respectively, due to the presence of the electron-withdrawing benzoyl group on the pyrrolidine nitrogen atom.

Unlike compounds **2a−c** and **3**, allene derivatives **4a−c** and **5** showed the presence of two weak waves at around −0.40 and −1.70 V, the first one being irreversible and only observed in the reoxidation process (Figure 2). The intramo-
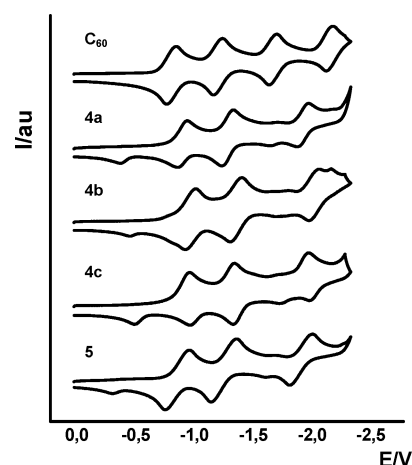
Figure 2. Cyclic voltammograms of compounds **4a−c** and **5** and C$_{60}$ measured in o-DCB/MeCN (4:1) at 100 mV s^{-1}.

lecular thermal cyclization of 1,6-fullerenynes affords regioselectively cis-1 isomers bearing two fused pentagonal rings on the same fullerene hexagonal ring. These new allene derivatives are suitably functionalized for further chemical transformations in the search for more complex modified fullerenes.

To determine the reaction mechanism for the formation of the allene derivatives (**4a−c**, **5**) from 1,6-fullerenynes and to unravel the reason they do not undergo the alternative [2+2] cyclization to the cyclobutene derivative, we have performed density functional theory (DFT) calculations[18] with a two-layered ONIOM approach[19] using the Gaussian 03 program.[20]

As a model of **2a−c**, we have considered R$_1$ = CH$_3$ and R$_2$ = H in **2** and we have analyzed for this system the ene reaction path that leads to the allene. The energies of all species implicated in our investigated ene pathway are given in Supporting Information, Table SI2. In addition, Figure 3 depicts the TS (**TS1**) involved in this process. As it is shown, this TS has a reactant-like structure as expected for an

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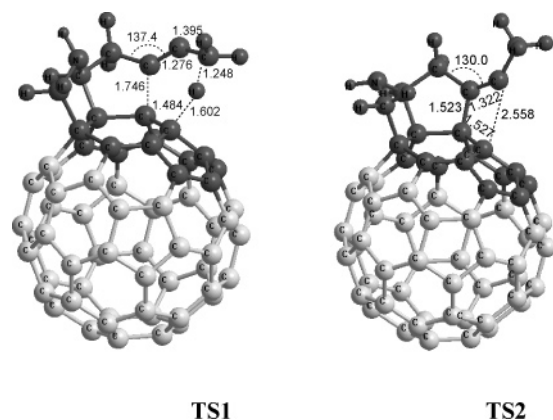
Figure 3. ONIOM2(UB3LYP/6-31G*:BVWN/STO-3G) optimized structures for the most important transition states of the ene reaction (**TS1**) and the diradical (**TS2**) pathways with the most relevant bond distances and angles (distances in angstroms and angles in degrees). Darkened atoms constitute the small system treated at a high level in the ONIOM approach.

exothermic reaction in light of the Hammond postulate.[21] **TS1** bears some resemblance to the TS recently found by Jayanth[10] for the ene reaction between benzyne and propyne.

TS1 is about 0.7 kcal mol^{-1} more stable than the TS found in the pathway to form the [2+2] cycloadduct (**TS2**) (Figure 3). This difference increases by an additional 1.8 kcal mol^{-1} if we take into account the zero-point energy plus the thermal corrections at 298 K computed with the ONIOM2(B3LYP/6-31G*:BVWN/STO-3G) method. Because the reaction is exothermic by only 9.5 kcal mol^{-1} (5 kcal mol^{-1} less exothermic than the reaction forming the [2+2] cycloadduct),

we can conclude that formation of allenes from fullerenynes is kinetically driven. However, one could in principle change from kinetic to thermodynamic control by increasing the temperature of the reaction.

In summary, we have found a new reactivity of 1,6-fullerenynes (**2a–c, 3**), thus emerging them as an important class of building blocks in fullerene chemistry. In this study, we have shown that a simple replacement of a H atom by a methyl or alkyl group in the alkyne fragment of the 1,6-fullerenyne results in a completely different reaction outcome, leading to unprecedented allene-containing fullerenes. Theoretical calculations predict that allene formation proceeds through an unusual concerted ene reaction mechanism involving an alkyne and a fullerene double bond. These results show that easily isolable and stable allenes can be obtained from suitably functionalized readily available 1,6-fullerenynes. Work is currently in progress to show the general scope of this new synthesis of the less-known allenes to other non-fullerene-containing 1,6-enynes from the appropriate substituted glycines.

Supporting Information Available: Spectroscopic data. Tables with energies and *xyz* optimized coordinates for the reactant, transition state, and product of the ene reaction. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) The BVWN method together with the STO-3G basis set was used for the low-level calculations, and the hybrid density functional B3LYP method with the 6-31G* basis set was employed for the high-level system in the ONIOM approach used. The darkened atoms in Figure 3 constitute the small system treated at the high level of theory within the ONIOM approach for all species analyzed in the present work. For all stationary points, single-point B3LYP energy calculations have been performed at the ONIOM2(B3LYP/6-31G*:BVWN/STO-3G) optimized geometries employing the 6-31G** basis set (B3LYP/6-31.G**//ONIOM2(B3LYP/6−31.G*:BVWN/STO-3G)). For open-shell species, the geometry optimizations and single-point energy calculations were performed within the unrestricted methodology, and in the closed-shell species singlet molecules, the restricted formalism was used. All stationary points found have been characterized as either minima or transition states (TSs) by computing the vibrational harmonic frequencies.

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