Theoretical Study of the Reaction Mechanisms Involved in the Thermal Intramolecular Reactions of 1,6-Fullerenynes

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Received: January 22, 2007; In Final Form: March 16, 2007

Substitution of a H atom by an alkyl group on the terminal carbon of the alkyne moiety of 1,6-fullerenynes has a strong impact on the products of the reaction undergone by this species after thermal treatment. While the reaction of 1,6-fullerenynes bearing an unsubstituted alkyne moiety results in the cycloaddition of the alkyne group to the fullerene double bond leading to cyclobutene-fused derivatives, the presence of an alkyl substituent leads to the formation of allenes. In the present work, we have performed an exhaustive theoretical analysis of all possible reaction mechanisms leading to cyclobutene-fused derivatives and allenes to offer an explanation of the reactivity differences observed. The results obtained show that formation of cyclobutene-fused derivatives occurs through a stepwise diradical reaction mechanism, while allene formation proceeds through a concerted way involving an uncommon intramolecular ene process. For the 1,6-fullerenynes bearing a substituted alkyne, the ene reaction path leading to allenes has an energy barrier somewhat lower than the stepwise diradical mechanism for the cyclobutene-fused derivative formation, thus explaining the outcome of the reaction.

Introduction

Enynes, and particularly 1,6-enynes, are important building blocks which have been successfully used, under transition-metal-catalyzed cyclization conditions, for the preparation of a wide variety of carbo- and heterocyclic systems.[1] On the other hand, the singular 3D geometry of fullerenes with carbon spheres containing 30 (C_{60}) or more (C_{70} and other giant fullerenes) highly reactive double bonds constitutes a unique scenario where a variety of different chemical reactions can be tested. Furthermore, the convex surface of fullerenes offers new possibilities for the study of new reactions and mechanisms under severe geometrical constraints on carbon atoms showing a rather unusual $sp^{2,3}$ hybridization.[2] With this in mind, during the past recent years, we have developed a new and highly versatile building block in which a double bond of the fullerene C_{60} core is used as the alkene component of the enyne moiety. These so-called 1,6-fullerenynes have proven to react very efficiently in a variety of important reactions involving alkenes and alkynes. Thus, in a first study, they were successfully used for the regioselective metal transition catalyzed [2 + 2 + 1] Pauson-Khand intramolecular cyclization to form, almost quantitatively, unprecedented modified fullerenes endowed with three or five fused pentagonal rings on the fullerene surface.[3]

In two recent works, the different intramolecular reactions undergone by 1,6-fullerenynes after noncatalyzed thermal treatment of alkyne-substituted fulleropyrrolidines have been described.[4,5] It has been shown that the presence of an alkyl group on the terminal carbon atom of the alkyne moiety in the 1,6-fullerenyne species has a strong impact on the reaction outcome. Thus, 1,6-fullerenynes with an unsubstituted alkyne moiety undergo a thermally induced [2 + 2] cyclization to form quantitatively new fullerene derivatives with a rather unusual cyclobutene-fused cyclopentane moiety.[4] On the other hand, 1,6-fullerenynes bearing an alkyne with an alkyl substituent yield efficiently allenes[6] instead of the expected cyclobutene derivatives.[5] Preliminary theoretical calculations have shown that the [2 + 2] cycloaddition in 1,6-fullerenynes leading to cyclobutene-fused fullerenes occurs in a concerted and highly asynchronous mechanism involving the alkyne triple bond and the closer fullerene double bond,[4] while formation of the allene structure takes place through an intramolecular ene reaction.[5]

To unravel the reasons why the presence of a methyl or alkyl group on the terminal carbon of the alkyne moiety leads to a different reaction product, in this work we analyze and compare all possible reaction mechanisms that lead to cyclobutene (see Scheme 1) and allene (see Scheme 2) formation from the simplest 1,6-fullerenynes with both unsubstituted (**1a**) and methyl-substituted (**1b**) alkynes with two main goals: (i) To compare the kinetics and thermodynamics of the diradical and the three possible carbene pathways for the formation of **3a** and **3b** from **1a** and **1b**, respectively, to find out the operative reaction mechanism and determine whether the presence of the methyl group is responsible for the inhibition of the cyclobutene formation in **1b**, and (ii) to study the mechanism for the formation of the allene **8** from the methyl-substituted derivative **1b** and to compare it to the mechanism leading to **3b** in order to discuss whether the allene reaction is kinetically or thermodynamically driven.

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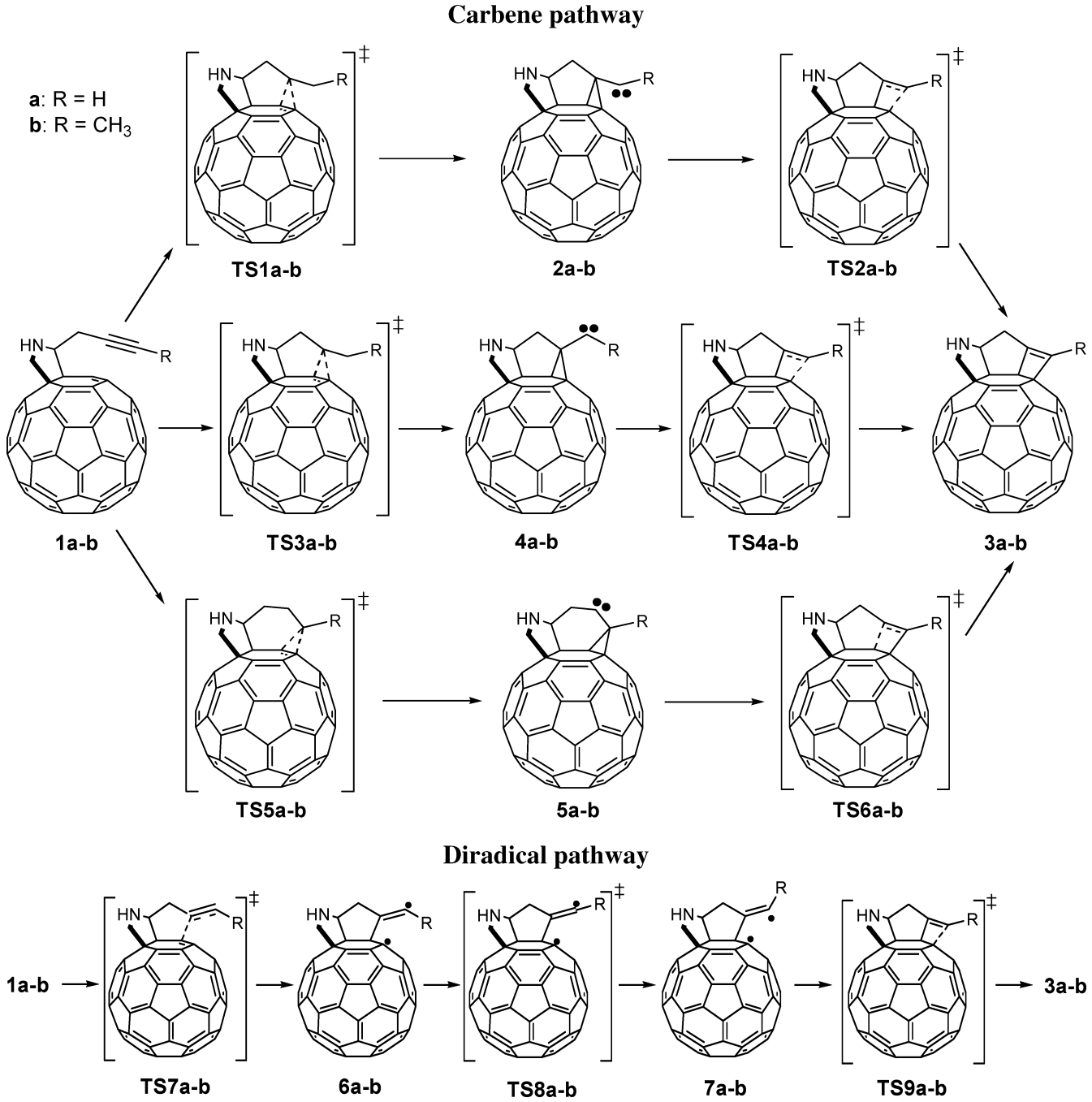
10.1021/jp0705368 CCC: $37.00
Published on Web 05/25/2007

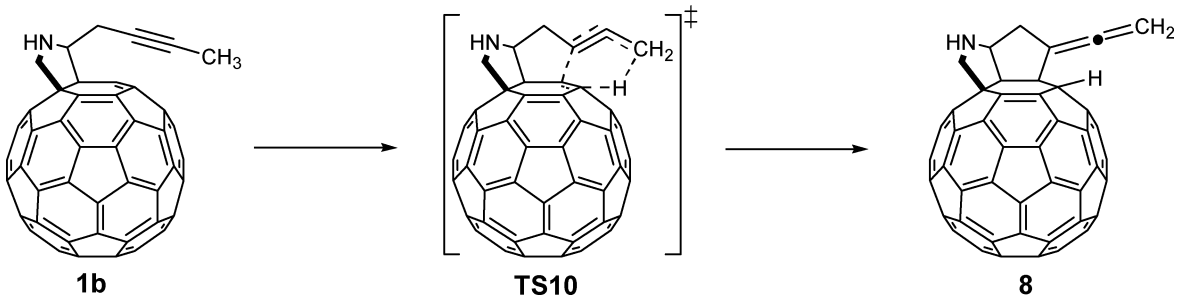
SCHEME 1: Schematic Representation of the Carbene and Diradical Possible Pathways for the Intramolecular Cycloaddition



Computational Details

Full geometry optimizations have been carried out with the two-layered ONIOM approach[7] using the Gaussian 03 program.[8] The density functional theory (DFT) B3LYP method[9] together with the STO-3G basis set[10] was used for the low-level calculations, while the same hybrid density functional B3LYP method with the 6-31G* basis set[11] was employed for the high-level system. For all stationary points, single-point B3LYP energy calculations have been performed at the ONIOM2-(B3LYP/6-31G*:B3LYP/STO-3G) optimized geometries employing the 6-31G** basis set (B3LYP/6-31G**//ONIOM2-(B3LYP/6-31G*:B3LYP/STO-3G)). For all systems, only the lowest-lying singlet state has been considered in the calculations. For open-shell singlet species, the geometry optimizations and single-point energy calculations were performed within the unrestricted methodology, while for the closed-shell singlet molecules the restricted formalism was used. Theoretical treatment of singlet diradical species requires multiconfigurational or multireference methods due to strong static electron configuration, but, unfortunately, these methods can only be applied to relatively small systems because they are extremely computationally demanding. In our study, the size of the systems analyzed prevents the use of such sophisticated ab initio methods. As an alternative, we have used the unrestricted UB3LYP method (with guess=mix) in broken symmetry. This method improves the modeling of singlet diradical states at the expense of introducing some spin contamination from unwanted states of higher spin.[12] Although this is not the most appropriate method to treat singlet diradical species, it has been shown that it can be used provided that the overlap between the open-shell

SCHEME 2: Schematic Representation of the Ene Pathway



orbitals is small (the unpaired electrons are located in separated atomic centers), as happens in the diradical systems studied in the present work.[12h] In addition, the experience shows that this method provides a good combination of accuracy and efficiency. In particular, it has been successfully employed to compare reaction paths involving diradicals with those for concerted, closed-shell pathways.[13,14] All transition structures (TSs) found have been characterized by computing the vibrational harmonic frequencies; TSs have a single imaginary frequency with the expected eigenvector (transition vector) related to the approach of the two reaction centers.

Results and Discussion

A theoretical analysis of the four different possible reaction paths depicted in Scheme 1 has been carried out to determine the nature of the reaction mechanism for both R = H and CH_3. We have located all intermediates and TSs involved in the so-called carbene and diradical pathways. The carbene reaction mechanism proposed first by Gilbert and co-workers involves a [2 + 1] cycloaddition to give a cyclopropylcarbene intermediate that in a subsequent step evolves through 1,2-C shift to the final product.[13c,g,15,16] As can be seen in Scheme 1, there are three different possibilities for the carbene pathway. The diradical mechanism, first suggested by Olivella and co-workers,[17] involves a diradical intermediate that already comprises one of the two C−C bonds to be formed. This diradical mechanism has been also considered by several authors for the reaction between cyclopentyne and ethene.[13c,g,15,16]

We have been able to locate the three possible cyclopropylcarbene intermediates and the TSs that connect these intermediates with reactants and products. The B3LYP/6-31G**//ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) relative energies referred to reactants of intermediates, TSs, and products for these carbene routes are listed in Table 1. Figures 1 and 2 show drawings of the structures of reactants **1a** and **1b** and products **3a** and **3b**, respectively. The colored atoms in Figure 1 constitute the small system treated at the high level of theory within the ONIOM approach for all species analyzed in this work (optimized *xyz* coordinates of all species are given as Supporting Information). As can be seen in Table 1, the energy barriers involved in the pathways from reactants to products through these cyclopropylcarbene intermediates have been found always to be larger than 57.8 kcal·mol^{-1}, and, for this reason, this mechanism has been rejected. It is worth noting that, for the particular case of the cyclopentyne and ethene cycloaddition, the carbene and diradical mechanisms compete and the most favored pathway obtained depends on the level of calculation employed.[13c,g] However, in our systems **1a** and **1b** that have nonstrained triple bonds (in contrast to cyclopentyne or benzyne[13c]), the carbene pathway can be totally ruled out.

TABLE 1: Relative Energies (kcal·mol^{-1}) Referred to Reactant 1 for All Intermediates, Transition Structures, and Products of the Carbene Pathway (Scheme 1)

	ΔE			ΔE	
species	R = H	R = CH_3	species	R = H	R = CH_3
1	0.00	0.00	**TS4**	62.51	64.80
TS1	57.84	64.80	**TS5**	52.90	63.44
2	56.63	53.66	**5**	51.95	55.12
TS2	57.63	56.09	**TS6**	68.07	67.31
TS3	57.31	58.83	**3**	−12.39	−12.16
4	56.30	57.84			

The second reaction mechanism that we have analyzed is the diradical pathway shown in Scheme 1. We have been able to locate the two intermediates and the three TSs involved in the transformation of **1a** → **3a** and also the corresponding systems for the path from **1b** → **3b**. The relative energies of all species implicated in these diradical pathways are given in Table 2. In addition, Figure 3 depicts the energetically highest TSs (**TS9a** and **TS9b**) involved in these processes, while Figure 4 shows the optimized molecular structure of intermediate **6b**. The **1** → **3** reactions are found to be exothermic by 12.4 and 12.2 kcal·mol^{-1} for R = H and CH_3, respectively. The highest energy barrier of 36.6 and 34.5 kcal·mol^{-1} for R = H and CH_3, respectively, are found for the last step of the diradical reaction mechanism. Our previous study[4] at the UB3LYP/6-31G*//ONIOM2(UB3LYP/6-31G*:AM1) level of theory yield an energy barrier of 27.5 kcal·mol^{-1} for the **1a** → **3a** process. In that study, we were unable to find diradical intermediates, so we concluded that the reaction was concerted but with a very asynchronous TS. As can be seen in Table 2, intermediate species **6** and **7** are not very stable, and, in this situation,

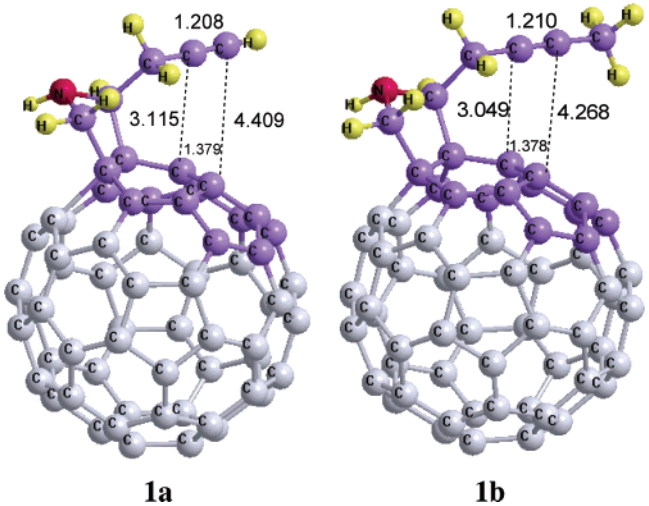


Figure 1. Optimized structures for reactants **1** (ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G)) with the most relevant bond distances. Colored atoms constitute the small system treated at high level in the ONIOM approach (distances in angstroms).

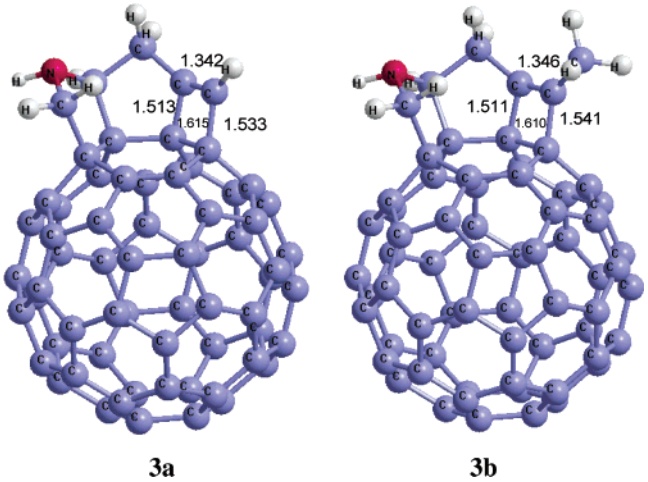


Figure 2. Optimized structures for the products **3** (ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G)) with the most relevant bond distances (in angstroms).

TABLE 2: B3LYP/6-31G//ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) Relative Energies (kcal·mol^{-1}) Referred to Reactant 1 for All Intermediates, Transition Structures, and Products Together with Their $\langle S^2 \rangle$ Values for the Diradical (Scheme 1) and the Ene Pathways (Scheme 2)**

	ΔE		$\langle S^2 \rangle$	
species	R = H	R = CH_3	R = H	R = CH_3
1	0.00	0.00	0.00	0.00
TS7	31.69	29.63	0.55	0.59
6	29.93	28.35	0.96	0.93
TS8	33.38	30.75	0.92	0.88
7	31.37	29.11	1.02	1.02
TS9	36.62	34.50	0.88	0.91
3	−12.39	−12.16	0.00	0.00
TS10		33.88		0.00
8		−9.46		0.00

intermediates **6** and **7** may be obtained as minima or not in the potential energy surface depending on the level of theory used. The current calculations are done using a higher level of theory than in our previous study and, therefore, are more reliable. In this sense, we have to correct our definition of the reaction mechanism and conclude that the transformation from **1a** → **3a** goes through a stepwise diradical reaction mechanism. The intermediates **6** and **7** and the TSs **TS7**, **TS8**, and **TS9** have some diradical character, with the carbon atom of the CH (or $C(CH_3)$) end of the 1,6-enyne structure having a localized α electron, while the unpaired β electron is delocalized mainly around the colored pyracylene unit of C_{60} in Figure 1.

The large spin contamination (see Table 2) of intermediates **6** and **7** and TSs **TS8** and **TS9** wave functions (approximated by the Slater determinant constructed by using the corresponding Kohn−Sham orbitals) is consistent with a roughly speaking 1:1 mixture of singlet and triplet states and indicates significant diradical character. Clearly, this spin-contaminated wave functions cannot be the correct solution for singlet diradical species. However, as said before, several studies have indicated that the broken-symmetry UB3LYP method provides a reasonable modeling of singlet diradicals and that for large systems this method provides the best ratio between the computational cost and the reliability of the results.[13,14,18]

It is well-known that, for radical species, substitution of a H atom attached to the C atom carrying the unpaired electron by a methyl group stabilizes the radical.[19] This observation is in agreement with the fact that, as compared to reactants **1a,b**, all

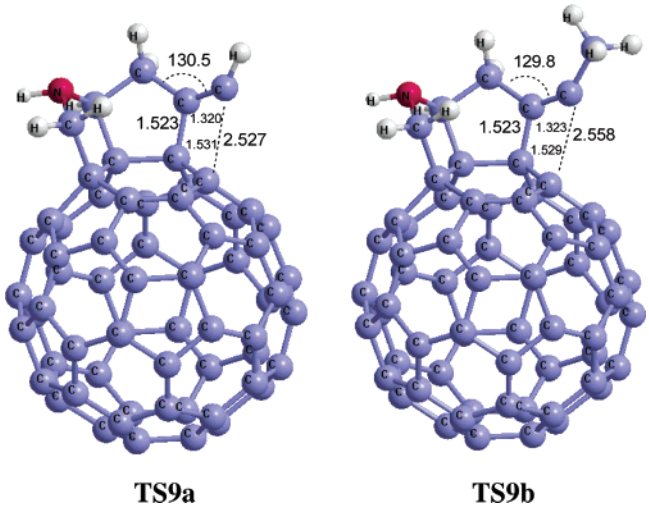


Figure 3. Optimized structures for the transition structures highest in energy of the diradical pathways (ONIOM2(UB3LYP/6-31G*:UB3LYP/STO-3G)) with the most relevant bond distances and angles (distances in angstroms and angles in degrees).

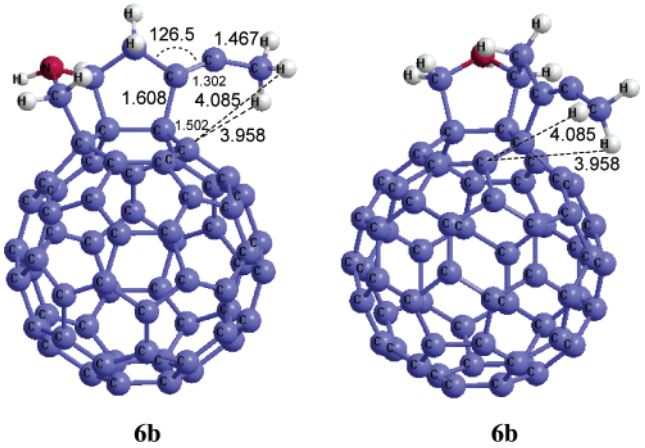


Figure 4. Two different views of the optimized structure for the intermediate **6b** in the diradical pathway (ONIOM2(UB3LYP/6-31G*:UB3LYP/STO-3G)) with the most relevant bond distances and angles (distances in angstroms and angles in degrees).

species having radical character in the diradical pathway are about 1.5−2.5 kcal·mol^{-1} more stabilized for R = CH_3 than for R = H (see Table 2). Thus, formation of cyclobutene derivatives is kinetically favored by methyl substitution by about 2 kcal·mol^{-1}. Finally, we briefly mention that our preliminary calculations[4] indicated that the cycloaddition of ethyne to ethene has an energy barrier of about 7 kcal·mol^{-1} higher than that corresponding to cycloaddition that transforms **1a** into **3a**.

Finally, as said before, reactant **1b** experimentally evolves to product **8** and not product **3b**. For this reason, we have analyzed for this system the ene reaction path that leads from **1b** to **8** (see Scheme 2). The ene reactions are defined as a six-electron pericyclic process between an alkene (or alkyne) bearing an allylic hydrogen (an "ene") and an electron-deficient multiple bond (an enophile) to form two σ-bonds with the migration of the π-bond. The ene reaction is mechanistically related to the Diels−Alder reaction, but, in the former, the two electrons of the allylic C−H σ-bond replace two π-electrons of the diene in the latter. For this reason, the activation energy is greater, and higher temperatures are generally required than in the Diels−Alder reactions.[20] However, intramolecular ene reactions are normally much more facile than their intermolecular counterparts,[21] and even simple olefins and acetylenes

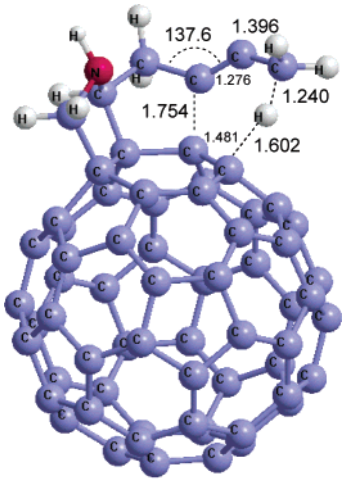


Figure 5. Optimized structure for the transition structure highest in energy of the ene pathway (ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) with the most relevant bond distances and angles (distances in angstroms and angles in degrees).

can be used as enophiles in intermolecular thermal ene cyclizations. Moreover, in our reactant **1b**, the low-lying LUMO of the C_{60} cage should facilitate this kind of cycloaddition. Some ene reactions containing a triple bond in the ene group have been reported.[22,23]

The energies of all species implicated in our investigated ene pathway are given in Table 2. In addition, Figure 5 depicts the TS (**TS10**) involved in this process. This **TS10** is identical for restricted and unrestricted calculations, and its wave function is spin-unrestricted stable. As can be seen in Figure 5, this TS has reactant-like structure as expected for an exothermic reaction in the light of the Hammond postulate.[24] This **TS10** bears some resemblance with the TS recently found by Jayanth et al.[23] for the ene reaction between benzyne and propyne. In this latter case, however, the TS was much earlier and the energy barrier was much lower (2.4 kcal·mol^{-1}) than in our **TS10** as expected from the fact that benzyne is more reactive than C_{60} in cycloaddition reactions. We have found that **TS10** is about 0.6 kcal·mol^{-1} more stable than **TS9b**. This difference increases by an additional 1.6 kcal·mol^{-1} if we take into account Gibbs energies at 500 K (the temperature of the reaction) computed with the ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) method. Since the reaction is exothermic by only 9.5 kcal·mol^{-1} (2.7 kcal·mol^{-1} less exothermic than reaction **1b** → **3b**), we can conclude that formation of **8** from **1b** is kinetically driven. However, one could in principle change from kinetic to thermodynamic control by increasing the temperature or the time of the reaction. Finally, prompted by a recent paper that analyzes a radical ene reaction mechanism between propene and cyclopropene,[25] we have analyzed the possibility of a radical pathway that goes directly from **6b** to **8**. All attempts to locate a TS directly connecting **6b** and **8** have been unsuccessful, and all optimization processes starting from appropriate initial structures have led to **TS10**. As can be seen in Figure 4, the distance between the H atom to be transferred and the C atom in the fullerene cage is about 4 Å. For the reaction between propene and cyclopropene the equivalent distance is about 1 Å shorter.[25] Therefore, either the big C_{C60}−H distance in **6b** makes the H transfer unfeasible and justifies the lack of TS connecting **6b** and **8** or the radical **6b** to **8** and concerted **1b** to **8** pathways merge in a single transition structure **TS10**.[26] To differentiate between these two possibilities, it would be necessary to compute a PES involving the C_{enyne}−C_{C60}, C_{enyne}−H, and C_{C60}−H bond lengths. Unfortunately, computational limitations prevent the study of such PES. However, this unsolved question does not alter the main conclusion of our study; i.e., a simple replacement of a H atom by a methyl group in the enyne fragment leads to a remarkable change of reaction mechanism from a [2 + 2] stepwise diradical mechanism for **1a** (R = H) to an ene reaction mechanism for **1b** (R = CH_3, Scheme 1).

Conclusions

We have analyzed by means of theoretical calculations two different intramolecular reactions undergone by 1,6-fullerenynes. Our results confirm that, for these species, simple replacement of a H atom by a methyl group on the terminal carbon atom of the alkyne moiety drastically changes the reaction outcome from cyclobutene-containing fullerenes in the unsubstituted systems to allene-containing fullerenes for the methyl-substituted species. Our results show that cyclobutene formation in the unsubstituted species occurs through a diradical pathway with two intermediates and three transition structures, the highest in energy having an energy barrier of about 36.6 kcal·mol^{-1}. The change of a H atom by a methyl group reduces the energy barrier of the diradical pathway by about 2 kcal·mol^{-1}, thus favoring the reaction. Therefore, compared to the unsubstituted species, the methyl group does not inhibit the cyclobutene formation. Indeed, it favors it as expected from the fact that the methyl group stabilizes radical species. Nevertheless, **1b** prefers to react through an unusual concerted ene reaction mechanism involving the triple and C−H bonds of the alkyne moiety and the closer double bond of the fullerene cage. The Gibbs energy barrier for the allene formation from **1b** is lower than that corresponding to the cyclobutene formation by about 2.2 kcal·mol^{-1}, despite the latter product being thermodynamically preferred by about 2.7 kcal·mol^{-1}.

Acknowledgment. Financial help has been furnished by the Spanish MEC Projects Nos. CTQ2005-08797-C02-01/BQU and CTQ2005-02609/BQU, CAM Project S-0505/PPQ/0225, and the DURSI Project No. 2005SGR-00238. M.G. and M.A. thank the MEC for research grants, and S.F. thanks CAM for a postdoctoral contract. We also acknowledge the Centre de Supercomputació de Catalunya (CESCA) for partial funding of computer time. We thank the reviewers for helpful comments.

Supporting Information Available: ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) optimized *xyz* coordinates and B3LYP/6-31G**//ONIOM2(B3LYP/6-31G*:B3LYP/STO-3G) energies of all reactants, transition structures, and products of the reaction mechanisms studied (see Schemes 1 and 2). This material is available free of charge via the Internet at http://pubs.acs.org.

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