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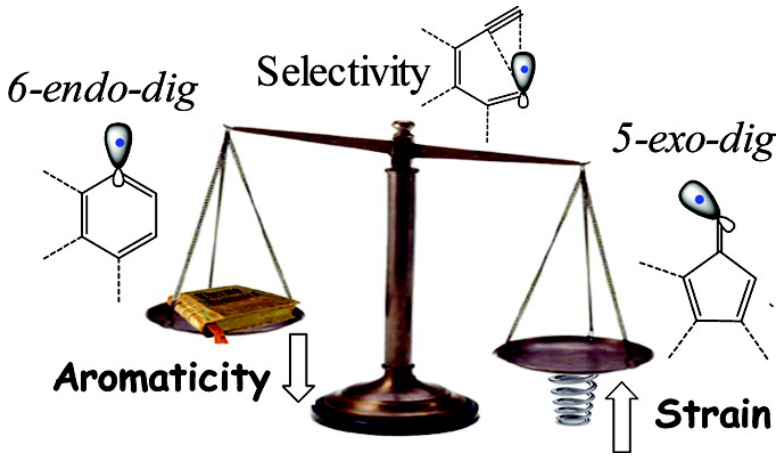

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Thermodynamic and Strain Effects in the Competition between 5-Exo-dig and 6-Endo-dig Cyclizations of Vinyl and Aryl Radicals

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Abstract: Electronic and structural factors controlling the competition between 5-exo-dig and 6-endo-dig cyclizations of sp^2-radicals were analyzed using a combination of available experimental data and computation. Although the stereoelectronically favored 5-exo pathways usually has the lower activation energy, formation of a new aromatic ring not only makes the 6-endo process favorable thermodynamically in conjugated systems but also lowers its activation barrier to the extent where the 5-exo/6-endo selectivity is controlled by subtle factors such as the different sensitivity of the two pathways to strain effects in polycyclic systems. In particular, the stronger sensitivity of the 5-exo pathway to strain leads to a crossover in selectivity. The 6-endo cyclization is kinetically favored in smaller (and strained) cycles, whereas the 5-exo cyclization has lower barriers in the larger rings.

1. Introduction

Conjugated molecules that incorporate acetylene moieties have valuable electronic properties[1] and serve as convenient building blocks in the synthesis of more advanced conjugated materials.[2] In particular, cascade radical cyclizations[3] provide an attractive approach to transforming polyacetylenes into new polycyclic frameworks and may be implicated in the formation of soot particles and carbon nanostructures. Many of such cyclizations involve intramolecular attack of an sp^2 hybridized radical[4] at a triple bond. The 6-endo and 5-exo modes of this process (commonly referred to as *dig*, or digonal cyclizations in the Baldwin classification[5]) are illustrated in Scheme 1. Note that these cyclizations do not need to follow the Bürgi−Dunitz trajectory and thus are stereoelectronically different from the analogous reactions of alkenes. On the other hand, stereoelectronic factors for the radical cyclizations of alkynes have interesting parallels in active field of cycloaromatization reactions (Scheme 1b).[6]

Several literature examples[7] indicate that the 5-exo pathway dominates when the acetylene and vinyl moieties are connected by a saturated bridge. However, the situation is more complicated when the bridge is unsaturated, and thus, the cyclization involves completely conjugated molecules. For example, the

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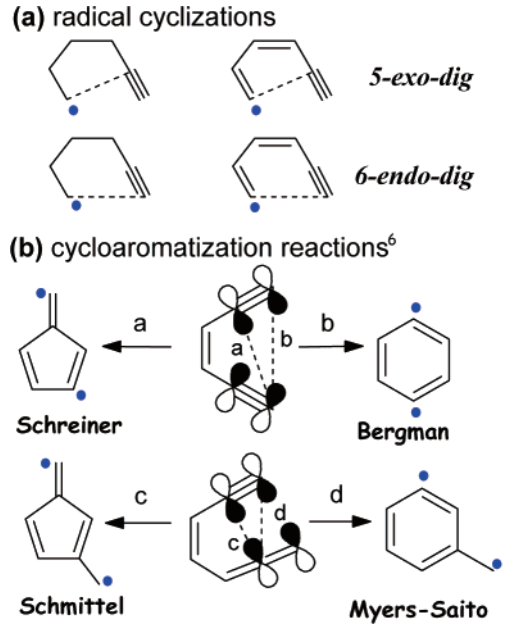
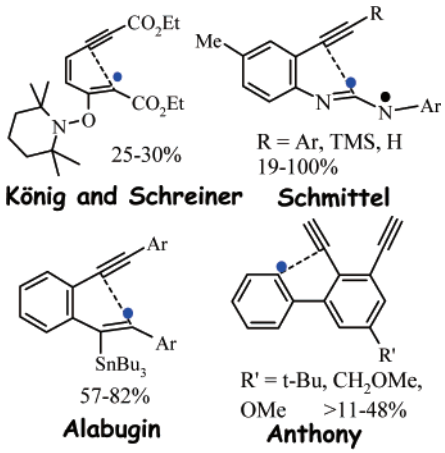
Scheme 1 [a]



[a] (a) 5-Exo-dig and 6-endo-dig cyclizations in parent and fully conjugated systems. (b) Selected cycloaromatization reactions.

6-endo cyclization of the parent conjugated 1,3-hexadiene-5-yn-1-yl radical has been considered as the key step in the formation of polycyclic aromatic hydrocarbons (PAH)[8] during combustion of hydrocarbons.[9] Most recently, Olivella and Solé[10] carefully studied the kinetic competition between 5-exo and 6-endo cyclizations in this system using both DFT and high level multiconfigurational (CASSCF and RCCSD(T)) calculations and found that the 5-exo activation barrier is only 1.4 kcal/mol lower than the 6-endo barrier (at the ZPVE-corrected RCCSD(T)6-311+G(3df,2p)//CASSCF/6-31G(d) level), a noticeable decrease in comparison to the difference between the respective trigonal cyclizations of the 5-hexene-1-yl radical.[11] The authors also suggested that the lowest energy pathway for the formation of phenyl radical involves the rearrangement of

Scheme 2. Selective 5-Exo-dig Cyclizations in Conjugated Systems[12−15,18]



the 5-exo product via bicyclo[3.1.0]hex-3,5-dien-2-yl radical intermediate instead of direct 6-endo cyclization.

Many of the literature cyclizations involving the addition of vinyl radicals to triple bonds in conjugated systems agree with the intrinsic preference for the 5-exo process. For example, König and Schreiner et al.[12] reported an example of the 5-exo-dig cyclization of an enediyne promoted by the 2,2,5,5-tetramethyl-4-piperidin-1-oxyl (TEMPO) radical (Scheme 2). Our group found recently that Bu_3Sn-initiated cyclizations of diaryl-substituted enediynes proceed through the same pathway but in considerably improved yields (vide infra),[13] thus providing a convenient synthetic approach to substituted fulvenes and indenes.[14] Through computational analysis of thermodynamics of competing 5-endo-, 5-exo-, and 6-endo-dig pathways, we also found that the 6-endo path is more exothermic and, thus, that 5-exo products should be formed under kinetic control.[13] Schmittel et al. found that triplet diradicals formed photochemically from enyne-carbodiimides (Scheme 2) and enyne-ketenimines undergo exclusively 5-exo-dig cyclization.[15]

However, several recent articles suggested that this "intrinsic preference" is not absolute and that 6-endo cyclization can compete with the 5-exo pathway in conjugated systems.[16] For example, Anthony and co-workers[17,18] reported several surprisingly efficient 6-endo cyclizations in constrained enediyne systems (Scheme 3). Matzger et al.[19] described thermal cycloaromatization of tri- and tetraynes where formation of the final product may proceed through a combination of 5-endo and 6-endo cyclizations.

Moreover, the ratio of 5-exo- and 6-endo-dig products can be very sensitive to the substitution pattern (e.g., in the

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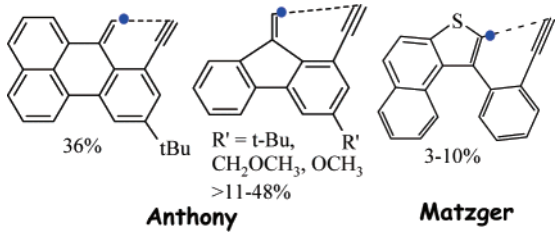
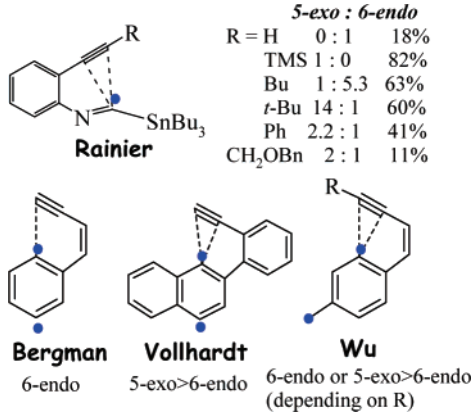
Scheme 3. Selective 6-Endo-dig Cyclizations[17−19]



Scheme 4. Examples of Competing 5-Exo-dig/6-endo-dig Cyclizations of Conjugated Radicals[20−23]



cyclizations of α-Bu_3Sn-imidoyl radicals reported by Rainier and Kennedy; Scheme 4).[20] Another intriguing example is provided by the topologically related diradicals produced in the course of Bergman and Myers−Saito cyclizations (Scheme 4). Although Bergman and co-workers reported only the formation of naphthalene product (>10%) in the "double cycloaromatization" of (*Z*,*Z*)-deca-3,7-diene-1,5,9-triyne,[21] Vollhardt and Matzger found both the 5-exo (19%) and the 6-endo (2.5%) products in a similar system.[22] Moreover, Wu and co-workers reported that, depending on the substitution, didehydrotoluene diradicals formed by the Myers−Saito cyclization yield either exclusively the 6-endo product (18%) or a mixture of 5-exo and 6-endo products in a ca. 4:1 ratio and a 63% combined yield.[23]

Thus, the growing body of available experimental evidence calls for a detailed theoretical study to provide a unified description of the disconnected experimental data, to identify possible inconsistencies, and to guide future development. We will outline the factors that control the selectivity of such digonal radical cyclizations and determine whether the basic stereoelectronic requirements for these reactions (exemplified by the Baldwin rules) are absolute or can be attenuated or even reversed by thermodynamic contributions to the reaction barriers.

To achieve this goal, we will organize our discussion according to the following plan. First, we will determine activation energies for the competing cyclization pathways in the parent systems. After the electronic effects for the archetypal cases are understood, we will investigate how the situation is changed by strain and thermodynamic effects. Because differences in thermodynamic contributions to alternative cyclizations modes may mask intrinsic stereoelectronic factors, we will separate thermodynamic contributions to the reaction barrier using Marcus theory.[24]

2. Computational Details and Method

All reactant, product, and transition state geometries involved in radical cyclizations were optimized at the UB3LYP/6-31G** level[25] using Gaussian 98 and 03 programs.[26] B3LYP was shown to provide results that are in good agreement with the higher level RCCSD(T)6-311+G(3df,2p)//CASSCF/6-31G(d) computations.[10] The broken-spin symmetry UB3LYP computations with both 6-31G** and cc-PVDZ basis sets were performed for the biradical systems to investigate the basis set effects on 6-endo cyclization. Accuracy of DFT description of biradical reactions was also evaluated with the single-point BD(T)/cc-pVDZ calculations (BD(T) = Brueckner Doubles calculation with a triples contribution).[6c,27,28] The zero-point energy correction on the barriers and other activation parameters ($\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$, and $\Delta S^{\ddagger}$) were obtained for selected radical cyclizations from frequency calculations. The nature of transition structures was confirmed by the presence of a single negative eigenvalue in the force constant matrix. The electronic properties of radical systems were analyzed by Natural Bond Orbital (NBO) computations using the NBO 4.0 program[29] implemented in Gaussian software.

3. Results and Discussion

Intrinsic Stereoelectronic Bias and Separation of Thermodynamic Contribution to the Reaction Barrier. In this article, we will separate intrinsic and thermodynamic contributions to the reaction barrier using Marcus theory,[24] which although originally developed for electron-transfer reactions has been successfully applied to a wide variety of organic reactions.[30−33] We will analyze the intrinsic stereoelec-

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Table 1. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distances (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of Radicals (**1**−**3**) at the UB3LYP/6-31G** Level

	5-exo					6-endo				
	r'(R)	r'(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_o	r''(R)	r''(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_o
1[a]	3.212	2.325	4.4	−38.2	18.3	3.874	2.409	8.9	−40.9	25.2
2	3.211	2.329	4.5	−32.3	16.8	3.743	2.412	7.2	−41.6	23.4
3	3.297	2.325	4.1	−38.0	18.1	3.726	2.422	11.5	−40.8	28.2

[a] The activation barriers at the BD(T)/cc-pVDZ//B3LYP/6-31G** level for 5-exo and 6-endo cyclizations are 5.7 and 9.2 kcal/mol, respectively.

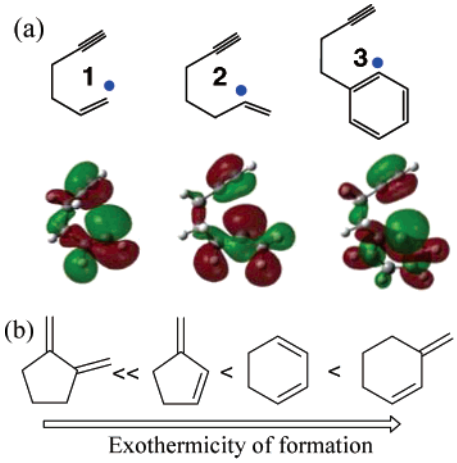


Figure 1. (a) SOMOs of model vinyl radicals (**1**−**3**) with a saturated bridge between the vinyl and acetylene moieties (UB3LYP/6-31G**). (b) Relative exothermicities for the formation of 5-exo- and 6-endo products from radicals **1** and **2**.

tronic requirements of related reactions by comparing the intrinsic barriers obtained from eq (1).[34]

$$\Delta E_o^{\ddagger} = \frac{\Delta E^{\ddagger} - (^1/_2)\Delta E_R + \sqrt{\Delta E^{\ddagger 2} - \Delta E^{\ddagger}\,\Delta E_R}}{2} \qquad (1)$$

Electronic and Structural Effects in the 5-Exo- and 6-Endo-Dig Cyclizations. A. Thermodynamic Contribution. In the next three sections, we will concentrate on the role of the thermodynamic component in the competition between the 5-exo and 6-endo cyclizations of hydrocarbon systems. We will start with the systems where exothermicities of the two reactions are comparable and proceed further by introducing significant thermodynamic bias to the 6-endo cyclization.

(a) Saturated Bridge. Computational results for the cyclizations of hexynyl-1-ene-5-yne-1-yl and hept-1-ene-6-yne-2-yl radicals **1** and **2** as well as their benzannelated "hybrid" **3** (Figure 1) are given in Table 1.[35] Higher level BD(T) computations suggest that DFT results are acceptable. To provide a better reference point for the discussion of completely conjugated systems in the following section, the barriers are given relative to the "near-attack" conformations.

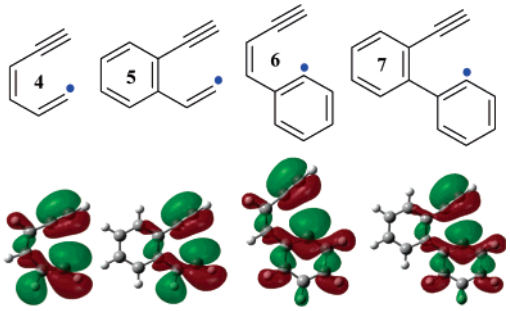


Figure 2. SOMOs of conjugated vinyl and aryl radicals (**4**−**7**) (UB3LYP/6-31G**).

All cyclizations are highly exothermic and have low activation barriers. Reaction energies for the six reactions in Table 1 are similar because in all of them a stronger σ-bond is formed at the expense of a weaker π-bond. The slight differences are due to the greater stability of endocyclic alkenes and *trans*-dienes relative to exocyclic alkenes and *cis*-dienes[36] (Figure 1). The trends in the activation barriers indicate a strong stereoelectronic preference for the 5-exo-dig cyclizations that have significantly lower barriers despite being slightly less exothermic than their 6-endo counterparts.[37] This preference is fully consistent with the shorter incipient $C_1\cdots C_5$ distances in the starting materials and with the lesser deformation needed to form the new bonds at the TS.

The 5-exo barriers are relatively insensitive to structural changes in **1**−**3**, while the 6-endo barriers change significantly. As a result, the kinetic preference for the formation of 5-exo products significantly increases in **3**. It is interesting that the intrinsic barriers for both the 5-exo-"endo" and 6-endo-"endo" cyclizations of radical **1** are ca. 2 kcal/mol higher than that for the respective "exo" cyclizations of radical **2** (where "exo" and "endo" refer to the orientation of the double bond of the vinyl radical moiety relative to the formed cycle). Due to the unfavorable orientation of the radical orbital in the reactant, locking the reacting vinyl group in a benzene ring (**3**) leads to a further increase in the 6-endo barrier.

(b) Unsaturated Bridge. Introduction of a π-system between the triple bond and the vinyl radical (Figure 2) has two effects. First, it preorganizes the reacting functional groups for the bond-forming step. Such preorganization provides an entropic advantage over systems in which the vinyl radical and the triple bond are connected with a flexible saturated bridge.[38] In addi-

(33) Pericyclic reactions: (a) Yoo, H. Y.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 2877. (b) Aviyente, V.; Yoo, H. Y.; Houk, K. N. *J. Org. Chem.* **1997**, *62*, 6121. (c) Aviyente, V.; Houk, K. N. *J. Phys. Chem. A* **2001**, *105*, 383. (d) Alabugin, I. V.; Manoharan, B. B.; Lewis, F. *J. Am. Chem. Soc.* **2003**, *125*, 9329. Pericyclic reactions in transition metal complexes: (e) Kristjansdottir, S. S.; Norton, J. R. *J. Am. Chem. Soc.* **1991**, *113*, 4366. (f) Gisdakis, P.; Rösch, N. *J. Am. Chem. Soc.* **2001**, *123*, 697.

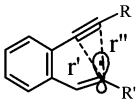
(34) (a) The $\Delta E^{\ddagger}$ term corresponds to E_a in the IUPAC nomenclature. For a more advanced but also more complicated parabolic model of radical addition reactions, see: (b) Denisov, E. T. *Russ. Chem. Rev.* **2000**, *69*, 153. (c) Denisov, E. T.; Denisova, T. G. *Russ. Chem. Rev.* **2000**, *71*, 417.

(35) The "near-attack" conformation was taken as the reactant to facilitate the comparison with conjugated radicals discussed in the rest of the article. As a result, the experimentally observed barriers for these flexible systems will be different from the computed values.

(36) Schleyer, P. v. R.; Puhlhofer, F. *Org. Lett.* **2002**, *4*, 2873.

(37) Experimental precedents for analogues of **1** will be discussed in detail in the following sections. Cyclizations of analogues of radical **2** show strong 5-exo-selectivity: (a) Journet, M.; Malacria, M. *J. Org. Chem.* **1994**, *59*, 6885. (b) Sha, C.-K.; Zhan, Z.-P.; Wang, F.-S. *Org. Lett.* **2000**, *2*, 2011.

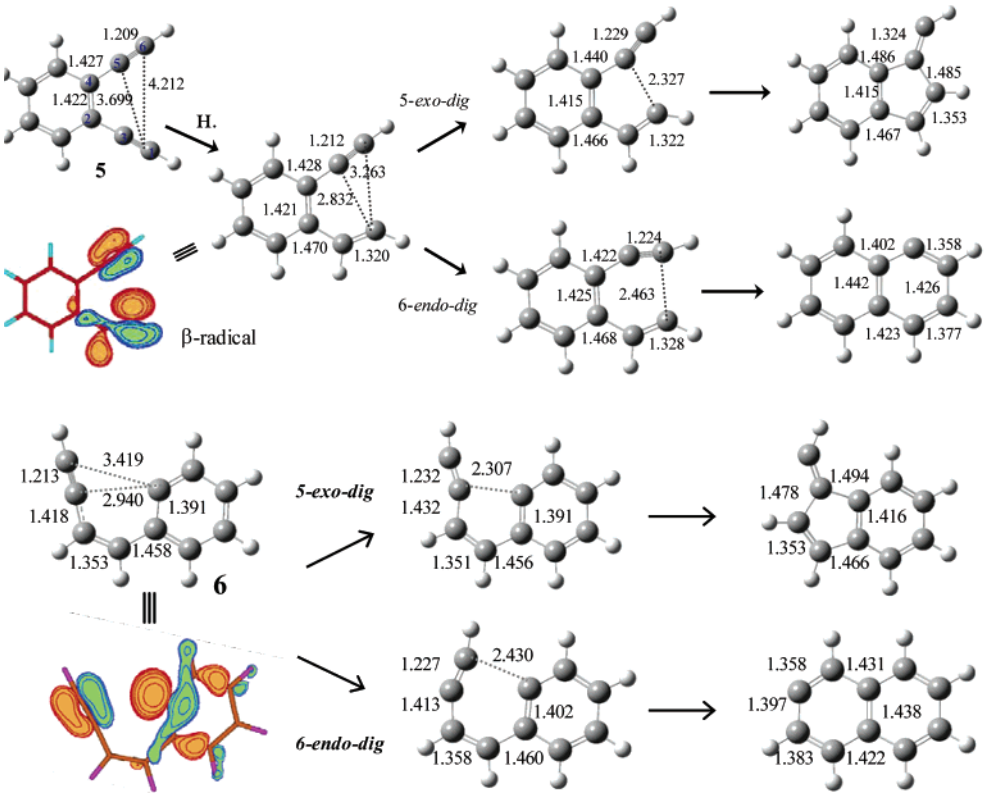
Table 2. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of the Radicals (**4**−**7**) at the UB3LYP/6-31G** Level



	5-exo					6-endo				
	r′(R)	*r*′(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0	*r*″(R)	*r*″(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0
4[a]	2.961	2.298	4.1	−35.0	17.1	3.433	2.481	4.7	−70.8	29.5
5[a,b]	2.832	2.327	2.4	−37.9	15.6	3.263	2.463	4.2	−62.2	26.0
6	2.940	2.307	3.6	−35.4	16.6	3.419	2.430	5.7	−59.8	27.5
7	2.649	2.376	0.5	−40.5	12.6	3.147	2.427	5.3	−56.3	25.8

[a] The activation barriers at the BD(T)/cc-pVDZ//B3LYP/6-31G** level for 5-exo and 6-endo cyclizations are, respectively, 5.3 and 6.1 kcal/mol for **4**, and 3.5 and 5.1 kcal/mol for **5**. [b] Computational results for the substituted radical **5** are given in the SI section (Tables S1 and S2).

Scheme 5. Structural Parameters (UB3LYP/6-31G**) of 5-Exo- and 6-Endo Cyclizations in Selected Conjugated Systems (**5** and **6**)[39] [a]



[a] See Table S2 in the SI for further details.

tion, the absence of conformational equilibrium between reactive and unreactive conformers simplifies computational analysis.

Second, the presence of an unsaturated bridge renders the 6-endo cyclization much more exothermic by providing aromatic stabilization to the products (Table 2). For example, the 36 kcal/mol difference in the stabilities of benzene and fulvene is directly translated into the 36 kcal/mol difference between the reaction energies of 5-exo and 6-endo cyclizations in the parent radical **4** (Figure 2). *From the practical perspective, substantial aromatic stabilization lowers the barrier for the 6-endo process, thus bringing it sufficiently close to the 5-exo cyclization barrier to allow selectivity to be controlled by subtle factors.* At the UB3LYP/6-31G** level, the difference in the activation energies of the two cyclizations of radical **4** is only 0.6 kcal/mol (within 1 kcal/mol from the higher level ZPVE-corrected RCCSD(T)6-311+G(3df,2p)//CASSCF/6-31G(d) results of Olivella and Solé).[10]

Finally, the incipient C···C bonds in the conjugated radicals **4**−**7** are 0.3−0.6 Å shorter than those in radicals **1**−**3** with a saturated bridge. This trend, along with the high exothermicities, accounts for very early transition states.

(c) Role of Benzannelation in Conjugated Systems. The 6-endo cyclizations of benzannelated radicals **5**−**7** are less exothermic because the gain in aromatic stabilization in the benzene → naphthalene transformation is less than that for the formation of benzene. Again, the difference in the stabilities of benzfulvene and naphthalene accounts almost exactly for the 24.5 kcal/mol difference in the exothermicities of the 5-exo and 6-endo cyclizations of radicals **5** and **6** (Table 2 and Scheme 5). Since radical **5** is 2.5 kcal/mol less stable than its isomer **6**, both cyclizations of **5** are more exothermic and proceed through lower barriers. Finally, formation of phenanthrene in the 6-endo cyclization of radical **7** provides even less aromatic stabilization than in above, further decreasing the thermodynamic bias for the 6-endo cyclization.

Interestingly, changes in the 6-endo intrinsic barriers are almost completely compensated by variations in the thermody-

(38) For examples of using unsaturation in the bridge to alleviate unfavorable enthropy contributions to cyclization reactions, see: Byrne, L. A.; Gilheany, D. G. *Synlett* **2004**, *6*, 933.

namic contribution, and thus, the activation barriers change only slightly. In contrast, the 5-exo barriers vary to a larger extent because the relatively constant thermodynamic components do not mask the stereoelectronic contributions. As a result, the 5-exo preference increases to 1.8−2.1 kcal/mol for benzannelated systems **5** and **6** (Table 2). Nevertheless, this is still considerably smaller than in the nonconjugated systems given above (Table 1), and only in the case of radical **7** where the thermodynamic bias for the 6-endo process is the smallest, there is a substantial (∼5 kcal/mol) preference for the 5-exo cyclization.

Structural features of stationary points along the 5-exo and 6-endo reaction paths of radicals **5** and **6** are compared in Scheme 5. Both cyclizations proceed through relatively early reactant-like transition states where both the triple bond lengths and hybridization at the reacting carbons change only slightly from those in the reactant. Although the incipient C···C distances are much shorter in radical **6**, the transition states for the more exothermic cyclizations of radical **5** occur somewhat earlier than in the respective cyclizations of radical **6** in accord with the Hammond−Leffler postulate.[40] Geometries of the products reflect hyperconjugative delocalizing interactions that involve the radical centers and vicinal σ(C−C) bonds.[41]

(d) Aryl Substitution−Thermodynamic and Steric Contributions. Because the thermodynamic contribution significantly decreases the difference in the activation barriers for the two cyclizations, one may expect the above kinetic preferences to be sensitive to further structural modifications.[42] A practical way to modify the electronic properties of the reacting moieties and to further differentiate between the two cyclizations is to introduce aryl substituents at the terminal carbons. The presence of such substituents imposes a dramatic effect on the cyclization. First, it disfavors the 6-endo process, especially in the case of α,ω-disubstituted reactants (Figure 3), where repulsion of two Ph-substituents in the naphthalene product provides ca. 4−6 kcal/mol of steric destabilization (Scheme 6).[6c] Second, if the reactant radical is stabilized by benzylic conjugation, the conjugation is invariably lost in the 6-endo process. In contrast, the products of 5-exo cyclization do not suffer from the steric repulsion between the terminal substituents and when the 5-exo cyclization proceeds onto an aryl-substituted triple bond in **8** which is stabilized by benzylic conjugation. Thus, both steric and thermodynamics contribute to the further decrease in the 5-exo barrier.

The intrinsic barriers for 5-exo cyclizations of radicals **9** and **10** are almost identical, whereas the 6-endo intrinsic barrier slightly increases, which suggests that steric interaction between the terminal substituents is already present at the TS stage. Interestingly, the intrinsic barriers for radicals **5** and **9** are also similar, suggesting that the deactivating effect of benzylic conjugation is compensated by the difference in hybridization and geometry. Aryl-substituted radicals have little s-character and almost linear geometry at the radical center, whereas simple vinyl radicals have a significant amount of s-character and are noticeably bent. In addition to the usual consequences for chemical reactivity and orbital energies, hybridization also controls molecular geometry and determines the direction in which the radical orbitals are projected in space (the valence angles) as well as the relative size of the two orbital lobes.[43] Such differences in the projection trajectory should have stereoelectronic consequences for the attack at the acetylene π-system.

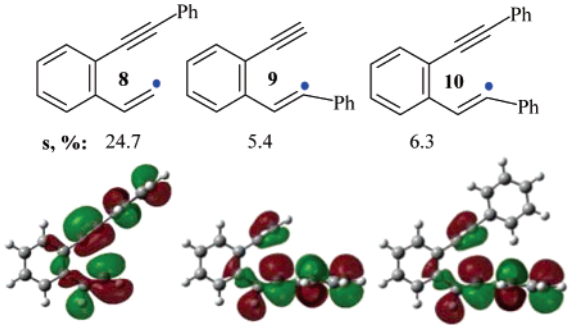
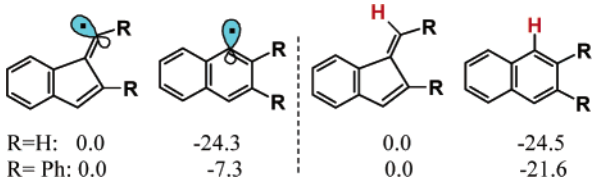


Figure 3. SOMOs and s-character in singly occupied NBOs of aryl-substituted vinyl radicals (**8**−**10**) (UB3LYP/6-31G**).

Scheme 6. Relative Energies of Fulvenes, Naphthalenes, and Respective Radicals at the UB3LYP/6-31G** Level



B. Contrasting Effects of Strain on the Two Cyclizations. The final experimentally relevant factor that may influence the 5-exo/6-endo selectivity is strain. This factor should be especially important in cascade radical cyclizations in Scheme 3 where rigid polycyclic frameworks are created as the result of sequential cyclizations. We estimated these effects by annealing a cyclopentene ring at all possible positions of radical **5**. Remarkably, independent of the exact pattern (**14**−**16**) in Figure 4, such a structural change leads to an inversion of selectivity

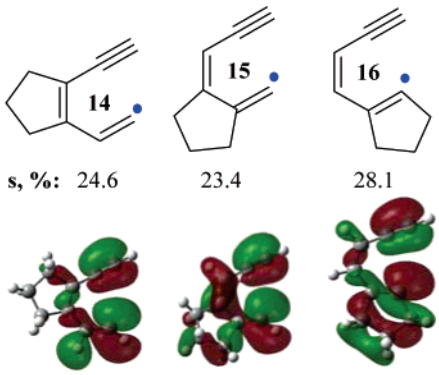


Figure 4. SOMO and s-character in singly occupied NBOs in vinyl radicals (**14**−**16**) containing the saturated rings (UB3LYP/6-31G**).

(39) The *Z*-fulvene radical obtained from **5** is 0.1 kcal/mol more stable than the *E*-isomer formed from **6**.
(40) (a) Leffler, J. E. *Science* **1953**, *117*, 340. (b) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.
(41) These interactions lead to increased bond order between the radical carbon and adjacent atoms and decreased bonding in the vicinal bonds. Interestingly, the elongation of vicinal C−C bond is more pronounced in the fulvene radical where the only C−C bond is available to delocalize the spin density in contrast to the naphthyl radical where two C−C bonds are involved.
(42) Moreover, Olivella and Solé had shown that 5-exo product can rearrange in the 6-endo product under conditions when the former radical is not trapped by H-abstraction. Even though the TS for the rearrangement is rather high in energy relative to the 5-exo product, it is still lower in energy than the barrier for direct 6-endo cyclization.
(43) For a seminal contribution, see: (a) Bent, H. A. *Chem. Rev.* **1961**, *61*, 275. For a detailed discussion of the role of hybridization in chemical properties of nonbonding orbitals see: (b) Alabugin, I. V.; Manoharan, M.; Zeidan, T. A. *J. Am. Chem. Soc.* **2003**, *125*, 14014. For the effect of hybridization in X−H bonds, see: (c) Alabugin, I. V.; Manoharan, M.; Peabody, S.; Weinhold, F. *J. Am. Chem. Soc.* **2003**, *125*, 5973. (d) Alabugin, I. V.; Manoharan, M.; Weinhold, F. *J. Phys. Chem. A* **2004**, *108*, 4720.

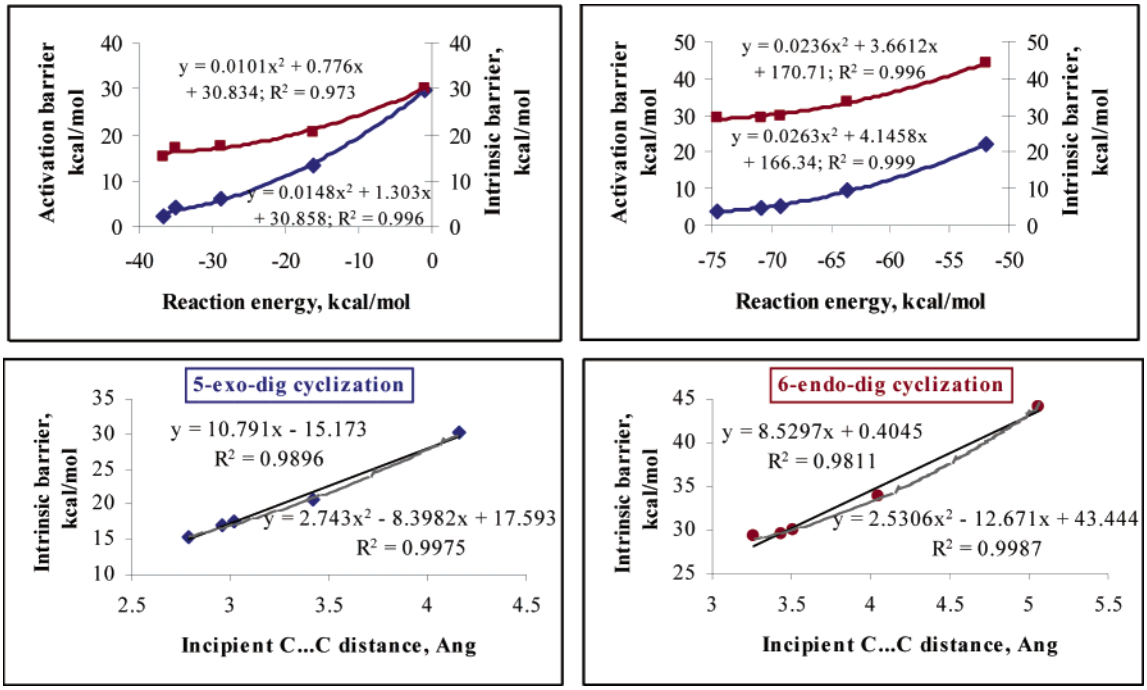
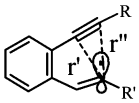


Figure 5. Correlation of reaction energy and incipient C···C distance in reactant with activation and intrinsic barriers for 5-exo and 6-endo cyclizations of cyclic hexa-1,3-diene-5-yne-1-yl derivatives (**14**, **17**−**19**).

Table 3. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of the Phenyl-Substituted Vinyl Radicals (**8**−**10**) in Figure 3 at the UB3LYP/6-31G** Level



	5-exo					6-endo				
	r'(R)	r'(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0	r''(R)	R''(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0
R═Ph, R′═H (**8**)	2.772	2.449	0.6	−43.7	13.8	3.238	2.404	4.6	−56.4	24.8
R═H, R′═Ph (**9**)	2.894	2.259	5.0	−27.9	15.9	3.340	2.628	6.3	−51.1	25.4
R═R′═Ph (**10**)	2.906	2.347	3.6	−32.9	15.8	3.396	2.340	9.9	−40.2	26.1

Table 4. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of the Radicals (**14**−**16**) in Figure 4 at the UB3LYP/6-31G** Level

	5-exo					6-endo				
	r'(R)	r'(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0	r''(R)	r''(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0
14	3.022	2.266	6.1	−28.8	17.5	3.511	2.483	5.4	−69.2	30.0
15	2.983	2.279	5.4	−30.9	17.4	3.452	2.483	4.8	−69.1	29.1
16	3.018	2.247	6.5	−30.9	18.8	3.469	2.481	4.3	−70.9	28.9

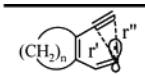
and renders the 6-endo cyclization a kinetically preferred pathway (Table 4).

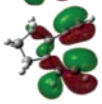
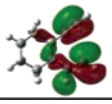
We have investigated the origin of this phenomenon more thoroughly by varying the ring size in radical **14**. The resulting changes in the reaction and activation energies of the two cyclizations are summarized in Table 5. As ring size decreases, the C1−C5 (or C1−C6) distance in the reactant and the activation energy of both 5-exo and 6-endo cyclizations of radicals derived from ring-fused enediynes increase. However, the sensitivities of the two cyclizations to the ring size effect are drastically different,[44] with the 5-exo cyclization being much more affected by ring strain effects than its 6-endo counterpart.[45] This observation suggests that five-membered rings are more strained than six-membered rings and is consistent with the much stronger variations in the incipient C···C distance in the TS in the case of 5-exo cyclizations (Table 5). For example, the change from $n = 0$ (**4**) to $n = 1$ (**17**) introduces ∼34 kcal/mol of strain in the 5-exo cyclization product, whereas the relative destabilization is only 19 kcal/mol for 6-endo cyclization. Differences between the acyclic and cyclobutene ($n = 2$, **18**) systems are still significant: 19 (5-exo) versus 7 kcal/mol (6-endo). *As a result of these differences, an increase in the product strain should result in a 5-exo → 6-endo crossover in*

(44) Interestingly, 5-endo-dig cyclization of an isomeric hex-1,3-diene-5-yne-2-yl radical is also highly sensitive to strain effects. Alabugin, I. V.; Manoharan, M. *J. Am. Chem. Soc.* **2005**, *127*, 9534.

(45) For a rare example of 6-endo-dig selectivity in reactions of alkyl radicals in polycyclic systems, see: (a) Breithor, M.; Herden, U.; Hoffmann, H. M. R. *Tetrahedron* **1997**, *53*, 8401. (b) Hoffmann, H. M. R.; Herden, U.; Breithor, M.; Rhode, O. *Tetrahedron* **1997**, *53*, 8383. The 6-endo-dig cyclizations of vinyl radicals have also been enforced in some cascade reactions where polycyclic strain slowed the alternative 5-exo-dig mode. (c) Albrecht, U.; Wartchow, R.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 910.

Table 5. Incipient C···C Distances (Å) along with the Activation Energies, Reaction Energies, and Intrinsic Barriers ΔE_o (all in Kcal/Mol) for 5-Exo and 6-Endo Cyclizations of Ring-Fused Strained Systems Calculated at the UB3LYP/6-31G** Level along with s-Character of Radical Carbon (%)[a]



		5-exo					6-endo				
	SOMO	s-char	r'(R)	r'(TS)	$\Delta E^{\neq}$	ΔE_r	ΔE_o	r"(R)	r"(TS)	$\Delta E^{\neq}$	ΔE_r	ΔE_o
n = 1 (**17**)		24.32	4.155	2.197	29.6	-1.0	30.1	5.068	2.482	22.1	-51.9	44.2
n = 2 (**18**)		24.14	3.422	2.227	13.4	-16.3	20.7	4.049	2.489	9.5	-63.6	33.8
n = 3 (**14**)		24.56	3.022	2.266	6.1	-28.8	17.5	3.511	2.483	5.4	-69.2	30.0
N = 4 (**19**)		24.81	2.793	2.323	2.4	-36.6	15.2	3.257	2.470	3.9	-74.5	29.3

[a] Values for $n = 0$ are given in Table 2.

selectivity, thus leading to the situation where the 6-endo pathway becomes kinetically favored in the more strained systems. As we will show later in this article, this observation is of practical value in the design of selective radical processes and in understanding available experimental results.[46]

The correlations between the barrier heights and reaction energies are shown in Figure 5. Although the correlations seem to be almost linear, the slopes (0.72 for 5-exo and 0.84 for 6-endo) are greater than those in the commonly used Evans−Polanyi−Semenov relation (0.25) between activation energy and reaction enthalpy in radical additions to alkenes.[47] Although the quality of correlations is noticeably improved by the parabolic fit, the coefficients in these equations are different from those given in the Marcus Eq 1. This is not surprising: not only the shapes of the reactant and product potential energy surfaces differ from parabolas[48] but the intrinsic activation barrier itself should also change due to the strain effects.

These factors notwithstanding, we found that the differences in intrinsic energies correlate very well with the incipient distances between the reacting carbons. Moreover, Figure 5 suggests that the effect of strain is significant in the TS for $n = 1, 2$ but not for the larger cycles ($n = 3, 4$) where the intrinsic activation energies ΔE_o are not significantly different from the acyclic case. Intriguingly, *this region of increased strain corresponds to the crossover point between the 5-exo and 6-endo pathways*, suggesting that the Marcus Eq 1, although not perfect, should be suitable for the semiquantitative separation of the intrinsic activation energies.

The difference in the above correlations provides further insight into the contrasting sensitivities of the 5-exo and 6-endo cyclizations to strain. Both thermodynamic and intrinsic terms are important for the 5-exo path as illustrated by a much steeper dependence of the activation energy from reaction exothermicity compared to analogous correlation with the intrinsic barrier (Figure 5). In contrast, in the case of 6-endo cyclization the observed increase in the activation barrier rather closely parallels the trend in the intrinsic barrier.

Comparison of Theory and Experiment. Comparison of theory and experiment serves a dual purpose: (a) testing and refining theory and (b) providing both an insight into and a quality check of the experimental data. With this notion in mind, let us proceed to the critical evaluation and comparison of the available experimental data. We will start with three cases where theory and experiment are in a perfect agreement and continue to the discussion of two more complicated systems where such agreement is yet to be found.

(a) Nonconjugated Systems. Here the experimental data are unambiguous and clearly indicate that 5-exo cyclization is a preferred pathway (Scheme 7). This notion is in a perfect agreement with the computational data in Table 6, which provides 4−7 kcal/mol lower barriers for the 5-exo path.[49] Introduction of a nitrogen atom (**20**−**22**) slightly lowers barriers for both cyclizations, but the exact position of the nitrogen hardly matters: it can be attached to the benzene ring or to the triple bond without significant changes in the reaction PES.

On the other hand, introduction of an amide moiety significantly lowers the cyclization barriers and renders them more

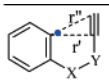
(46) This observation is not limited to dig cyclizations. For selected examples of similar strain effects on the competition between radical 6-endo-trig and 5-exo-trig cyclizations, see: (a) Kametani, T.; Honda, T. *Heterocycles* **1982**, *19*, 1861. (b) Kano, S.; Yuasa, Y.; Asami, K.; Shibuya, S. *Heterocycles* **1988**, *27*, 1437. For the effect on Bergman cyclization, see: (c) Jones, G. B.; Wright, J. M.; Plourde, G., II; Purohit, A. D.; Wyatt, J. K.; Hynd, G.; Fouad, F. *J. Am. Chem. Soc.* **2000**, *122*, 9872.

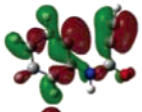
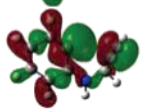
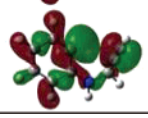
(47) (a) Evans, M. G. *Discuss. Faraday Soc*. **1947**, *2*, 271. (b) Evans, M. G.; Gergely, J.; Seaman, E. C. *J. Polym. Sci*. **1948**, *3*, 866. (c) Semenov, N. N. *Some Problems in Chemical Kinetics and Reactivity* (Engl. Transl.); Princeton Press: Princeton, NJ, 1958; p 29. (d) Fischer, H.; Radom, L. *Angew. Chem., Int. Ed*. **2001**, *40*, 1340 and references therein. (e) Shaik, S. S.; Canadell, E. *J. Am. Chem. Soc.* **1990**, *112*, 1446. (f) Coote, M. L.; Wood, G. P. F.; Radom, L. *J. Phys. Chem. A* **2002**, *106*, 12124. (g) Gómez-Balderas, R.; Coote, M. L.; Henry, D. J.; Radom, L. *J. Phys. Chem. A* **2004**, *108*, 2874. (h) Henry, D. J.; Coote, M. L.; Gómez-Balderas, R.; Radom, L. *J. Am. Chem. Soc*. **2004**, *126*, 1732. (i) Henry, D. J.; Parkinson, C. J.; Mayer, P. M.; Radom, L. *J. Phys. Chem. A* **2001**, *105*, 6750. (j) Gómez-Balderas, R.; Coote, M. L.; Henry, D. J.; Fischer, H.; Radom, L. *J. Phys. Chem. A* **2003**, *107*, 6082. (k) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1993**, *115*, 11050. (l) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 6284. (m) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc*. **1994**, *116*, 11938. (n) Batchelor, B. N.; Fischer, H. *J. Phys. Chem.* **1996**, *100*, 9794.

(48) Note, however, that the systematic error caused by the first factor can be decreased by limiting the discussion to the *relative* trends in *similar* reactions as it is done in this article.

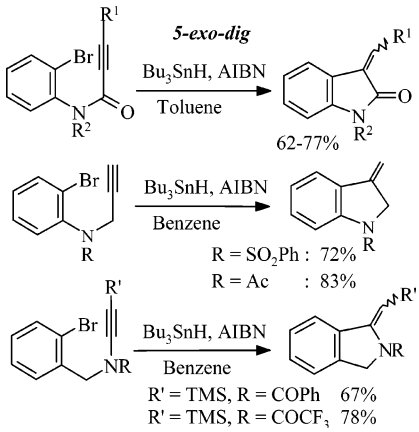
(49) Note that these barriers are likely to be different from those determined experimentally due to the presence of other conformers of the conformationally flexible reactants. However, the *relative* barriers for the 5-exo and 6-endo processes can be directly compared with experimental differences because both cyclizations proceed from the same "near-attack" conformer.

Table 6. SOMOs, s-Character (%) of the Radical Centers, Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of Radicals (**20**−**22**) with the Amide and Amine Bridges at the UB3LYP/6-31G** Level

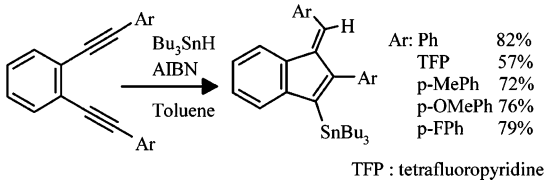


Reactant		5-exo					6-endo				
SOMO	s,%	r'(R)	r'(TS)	$\Delta E^{\neq}$	ΔE_r	ΔE_o	r"(R)	r"(TS)	$\Delta E^{\neq}$	ΔE_r	ΔE_o
X=NH, Y=CO **20**		23.89	2.788	2.379	1.2	-45.2	15.6	3.276	2.448	5.2	-55.0	25.2
X=NH, Y=CH_2 **21**		23.00	3.155	2.342	3.5	-40.3	18.0	3.823	2.440	10.1	-43.9	27.7
X=NMe_2, Y=CH_2 **22**		23.47	3.502	2.378	3.8	-40.8	18.6	4.358	2.425	10.5	-43.8	28.1

Scheme 7. 5-Exo-dig Cyclizations of Aryl Radicals with Saturated Bridge between the Acetylene and Aryl Moieties



Scheme 8. Bu_3SnH-Promoted 5-Exo-dig Radical Cyclization of 1,2-Bis(arylethynyl) Benzenes

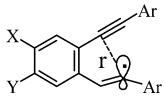


exothermic. The observed increase in exothermicity is more pronounced in the case of 6-endo cyclization where the classic amide (**21**) resonance (n(N) → π^*(C═O) interaction) increases the C═N double bond character in the ring and the aromatic character in the newly formed six-membered ring. However, this contribution is still not sufficient to lower the barrier for the 6-endo cyclization below that for the 5-exo cyclization.

(b) Cyclizations of Substituted Enediynes. The first example of such cyclizations was reported by König and Schreiner et al.[12] in reactions of carboxyl-substituted enediynes with the stable TEMPO radical where the mixture of stereisomeric fulvenes was formed in 25−30% yield. Our group[13,14] found recently that Bu_3Sn-initiated cyclizations of diaryl-substituted enediynes also proceed through the 5-exo pathway and provide 57−82% yields of tin-substituted fulvenes (Scheme 8).

These results suggest a large preference for the 5-exo cyclization that agrees very well with the significantly lower calculated barrier for this pathway in the diphenyl-substituted

Table 7. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of Diaryl-Substituted Systems (**23**−**27**) at the UB3LYP/6-31G** Level[a]



	r(R)	r(TS)	$\Delta E^{\neq}$	ΔE_r	ΔE_o
Ar═*p*-F−Ph, X═Y═H (**23**)	2.898	2.341	3.5	−32.8	15.6
Ar═*p*-OMe-Ph, X═Y═H (**24**)	2.895	2.355	3.6	−32.7	15.7
Ar═TFP, X═Y═H (**25**)	2.915	2.303	3.1	−32.8	15.0
Ar═Ph, X═F, Y═H (**26**)	2.908	2.346	3.6	−33.1	15.8
Ar═Ph, X═H, Y═F (**27**)	2.898	2.350	3.5	−33.1	15.7

[a] Data for Ar═Ph, X═Y═H are available in Table 3.

enediyne **10** (Table 3). Both benzannelation and the presence of terminal aromatic substituents promote the 5-endo pathway, accounting for high selectivity and good reaction yields (see Table 7 for the effect of the nature of aryl substitutent).[50] Although the situation is less favorable in the case of the diesters reported by König and Schreiner et al. (radical pattern **5**), the combination of steric and conjugative effects of the terminal substituents still should be sufficient to provide the rather high 5-exo/6-endo selectivity.

(c) Cyclization of Polycyclic Radicals. Theory and experiment are once again in a perfect agreement in describing two interesting radical-induced cyclization cascades discovered by Anthony et al.[17,18] A particularly intriguing case is illustrated in Scheme 3 where formation of an aryl radical is followed by a sequence of 5-exo and 6-endo cyclizations.[17] Taking into account the previously discussed 5-exo preference for radical **5**, it may seem surprising why the last step in this cascade as well as a similar step in an earlier report[18] (Scheme 3) and the final step in a topologically related reaction described by Matzger and co-workers[19] proceed via the 6-endo path.

However, the computed activation energies (Scheme 9) suggest that the combination of 5-exo and 6-endo pathways suggested by Anthony for acetylenes without terminal substitution indeed follows the lowest activation energy path. The first (5-exo) step (**28** → **30**) in the cascade proceeds through a very low barrier: not only is the TS relatively unstrained but the

(50) The lower yield in the case of the bis-TFP (tetrafluoropyridinyl) enediyne is due to the formation of acyclic products rather than the competition with 6-endo cyclization.

Scheme 9. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distances (Å) for the Cyclizations of 2,3-Diethynylbiphenyl Radical at the UBLYP/6-31G** Level

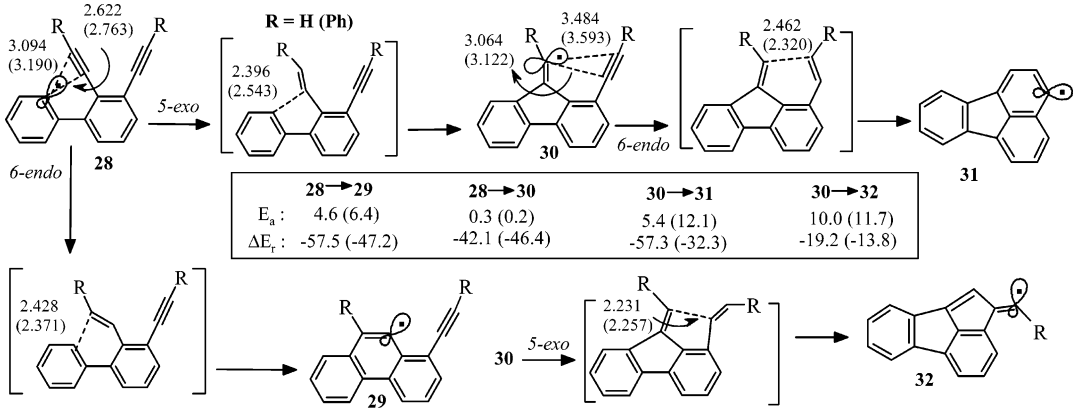
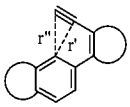


Table 8. Activation Barriers, Reaction Energies, and Intrinsic Barriers (all in kcal/mol) along with the Incipient C···C Distance (Å) for 5-Exo-dig and 6-Endo-dig Cyclizations of Radicals (**33**−**36**) at the UB3LYP Level with cc-PVDZ and 6-31G** Basis Sets



		5-exo					6-endo				
	method	r′(R)	r′(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0	r″(R)	r″(TS)	$\Delta E^{\ddagger}$	ΔE_r	ΔE_0
33[a]	I[b]	2.901	2.291	4.2	−34.2	17.0	3.444	2.437	5.7	−58.1	26.9
	II[c]	2.948	2.291	4.1	−34.4	16.9	3.426	2.421	21.8[e]	−58.7	46.5
34	I	2.932	2.295	1.2	−41.9	14.7	3.524	2.441	3.7	−58.1	23.5
	II[d]	2.904	2.292	NA	NA	NA	3.491	2.445	NA	NA	NA
35	I	2.822	2.335	1.4	−36.8	13.6	3.281	2.424	5.7	−54.2	25.6
	II	2.796	2.361	1.0	−39.8	13.6	3.259	2.427	5.9	−55.6	26.4
36	I	2.809	2.337	1.4	−38.0	13.9	3.273	2.418	5.6	−55.3	25.9
	II	2.811	2.342	1.3	−38.7	13.9	3.269	2.397	19.8[e]	−54.5	42.7

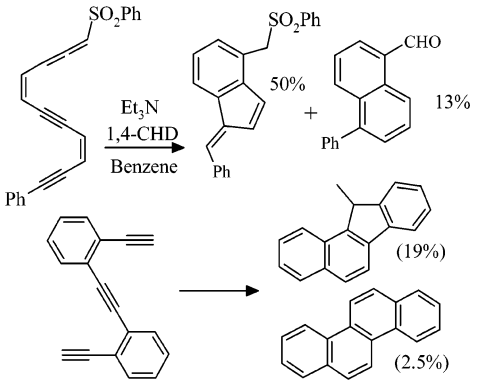
[a] The activation barriers at the BD(T)/cc-pVDZ//B3LYP/6-31G** level for 5-exo and 6-endo cyclizations are 5.8 and 10.2, respectively. [b] Calculated at the UB3LYP/cc-PVDZ level. [c] Calculated at the UB3LYP/6-31G** level. [d] The 6-31G** geometries of *reactant and products* of both cyclizations show unusual cumulenic Lewis structures, *but the* 5-exo and 6-endo TSs exhibit proper saddle point geometries in which the 5-exo TS is 1.8 kcal/mol more stable. [e] The barriers for 6-endo cyclizations of both **33** and **36** are strongly overestimated. Nevertheless, the TS geometries seem to be acceptable because the single-point calculations at UB3LYP/cc-PVDZ and BD(T) levels provide results comparable to those for the monoradical species (see the Supporting Information and Tables S6 and S7 for more detail).

cyclization may also be assisted even further by the buttressing effect of the second ethynyl moiety. On the other hand, after a five-membered ring is formed in the first step, the second 5-exo cyclization (**30** → **32**) should proceed via a TS annealed to a polycyclic skeleton. As discussed in detail in the earlier section on strain effects, the presence of such a structural feature significantly increases strain in the 5-exo TS, explaining the ca. 10 kcal/mol increase in the reaction barrier. In contrast, the 6-endo step (**30** → **31**) of the intermediate radical does not suffer as much from the strain (the barrier increases by less than 1 kcal/mol). Interestingly, these effects may be partially compensated by Ph-substitution at the acetylene moiety that renders the final step in the analogous cascade significantly less selective, thus allowing for the formation of the 5-exo/5-exo product as well.[51]

Thus, it is the first step in the cyclization cascade that sets up the selective 6-endo process in the second step by restraining the TS geometry. The observed increase in the 5-exo barriers in the polycyclic cases is analogous to the trends discussed above in the section dealing with the effects of strain at the selectivity in the case of radicals **14**−**19**.

(d) Cascade Cyclizations of Triynes. In contrast to the above sections, not all of the experimental results discussed in this part agree with the computational findings. The results are summarized in Scheme 4 where the three topogically similar reactions of diradical species display contrasting 5-exo/6-endo selectivities. Since these cyclizations are structurally analogous to the respective reactions of radicals **6** and **7**, one should expect the preferential formation of the 5-exo product under kinetic control conditions. Such a preference would be slightly larger for the system described by Vollhardt and Matzger (similar to radical **7**, Figure 2) than for the systems described by the Bergman and Wu groups (Scheme 10). The latter systems are closer to radical **6** where the difference between the 5-exo and 6-endo barriers is almost 3 kcal/mol less than in the case of radical **7**.

Scheme 10. Selected Double Cyclizations of Triynes[22,23]



(51) Formation of products resulting from addition of the initiating Sn radicals to one of the triple bonds is also possible.

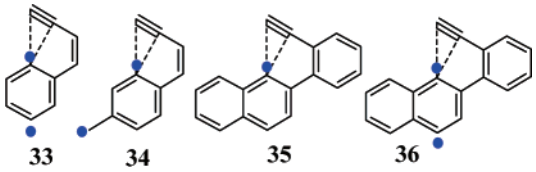


Figure 6. Structures of diradicals and radicals relevant to cascade 5-exo-dig and 6-endo-dig cyclizations of triynes.

From the earlier studies on reactivity of *p*-benzynes (H-atom abstraction),[52] one may expect that, due to the loss of the stabilizing "through-bond" interaction between the two radical centers,[53] the reactions of *p*-benzyne diradicals should be about 3−5 kcal/mol less exothermic than analogous reactions of monoradicals. This decrease in the thermodynamic component should be partially translated in the cyclization barrier as well.

As far as the computational aspects are concerned, there are several practical considerations that have to be discussed first. Most importantly, despite the topological similarity, reactions of diradicals are very different from analogous reactions of monoradicals from the theoretical perspective.[54] This difference stems from the multiconfigurational character of electronic *p*-benzyne wave function and renders theoretical studies of diradical reactivity particularly challenging. In fact, although the relative trends in energetics of *formation* of *p*-benzyne species are described reasonably well by BLYP and B3LYP fuctionals,[53] application of DFT methods to *reactions* of *p*-benzyne diradicals puts one in uncharted territory.[27]

To avoid the complications associated with the multiconfigurational character of diradical wave functions, we calculated PES for the radical additions using respective monoradicals (Figure 2). This modification allowed us to use B3LYP calculations with accuracy comparable to our results in other hydrocarbon radical systems discussed earlier in this article. Moreover, since the selectivity should be controlled by the *differences* in the activation barriers, the 5-exo/6-endo competition is unlikely to change significantly in analogous reactions of diradical species (Figure 6).

The computational results are in excellent agreement with the more recent report of Vollhardt and Matzger, who found that intramolecular trapping of a *p*-benzyne diradical formed by the Bergman cyclization yields a ca. 8/1 mixture of 5-exo and 6-endo products. This difference is in a qualitative agreement with the 4.9 kcal/mol preference for the 5-exo path (Table 8), especially if one considers the relatively low mass balance with the concomitant uncertainty about experimental accuracy. The low isolated yields of the products suggest partial decomposition along the reaction path which is likely to take a heavier toll on the less stable 5-exo products.

The most recent set of results of Wu and co-workers is also consistent with the slight preference for the 5-exo-dig cyclization. In this case, the presence of a terminal Ph group at the reacting acetylene moiety accounts for the higher yield of the 5-exo product as discussed in the previous sections. The increased overall yield can be a consequence of the milder conditions needed for thermal activation of Myers−Saito cyclization relative to the Bergman cyclization.

Interestingly, the 5-exo preference decreases from 4.3 to 1.5 kcal/mol when going from Vollhardt's radical **35-I** to Bergman's intermediate **33-I** (Table 8), providing a possible explanation for the increased yield of the 6-endo product reported by the groups of Bergman and Wu. Low thermal stability of the fulvene products provides a possible explanation for their absence. One can also speculate that the mechanism for the formation of 6-endo product may be more complex than a simple kinetic partitioning of the initially formed diradical along the two competing paths. Indeed, it was suggested earlier that, in the parent system, the initially formed fulvene radical may rearrange to the more thermodynamically stable phenyl radical (the 6-endo product),[10] providing a possible explanation for the observed 6-endo selectivity. However, this pathway can only increase the isolated amounts of the 6-endo-products when H-abstraction is remarkably slow.

It is interesting that BS-UB3LYP fails rather dramatically to provide an acceptable description in some cases (e.g., it strongly overestimates the 6-endo cyclization barrier for diradicals **33** and **36**; Figure 6). Such results are the artifacts of DFT as it is readily illustrated by comparing 6-endo barriers with the DFT results for related *mono*radicals **6** and **35** and with the TS energies obtained by the higher level coupled-cluster BD(T) computations. Even though 6-endo activation energies are improved by using a cc-PVDZ basis set and BS-UBLYP/6-31G** activation energies for the 5-exo processes seem reasonable, such aberrations suggest that one has to be extremely careful in applying DFT to multiconfigurational *p*-benzyne species (a more detailed discussion of these observations is given in the SI).

4. Conclusions

We analyzed the interplay of stereoelectronic and thermodynamic contributions to the activation barriers for 5-exo-dig and 6-endo-dig radical cyclizations of aryl and vinyl radicals. UB3LYP/6-31G** provides an acceptable description of selectivity in simple systems but should be applied with caution to the cyclizations of diradical species. The 5-exo-pathway has a 3−7 kcal/mol lower barrier when the vinyl moiety and the triple bond are connected through a saturated bridge. In completely conjugated systems, the kinetic preference for 5-exo-dig cyclization is noticeably decreased by the favorable thermodynamic contribution to the formation of aromatic 6-endo products. As a result, the difference between 5-exo and 6-endo barriers in polycyclic systems can be readily overturned by the high sensitivity of the 5-exo cyclization to the strain effects. The role of such effects in generation of pentagons in the process of carbon nanotubes formation is under current investigation.

Acknowledgment. We thank the Florida State University Supercomputing Center and the National Center for Supercomputing Application (NCSA, UIUC) for providing computational facilities. We are grateful to the National Science Foundation (CHE-0316598) and to the Material Research and Technology (MARTECH) Center at Florida State University for the support of this research (to I.A.), to Professor Robert Bergman (UC

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(53) (a) Squires, R. R.; Cramer, C. J. *J. Phys. Chem. A* **1998**, *102*, 9072. (b) Davico, G. E.; Bierbaum, V. M.; DePuy, C. H.; Ellison, G. B.; Squires, R. R. *J. Am. Chem. Soc*. **1995**, *117*, 2590. (c) Logan, C. F.; Chen, P. *J. Am. Chem. Soc.* **1996**, *118*, 2113. (d) Schottelius, M. J.; Chen, P. *J. Am. Chem. Soc.* **1996**, *118*, 4896. (e) Hoffner, J.; Schottelius, J.; Feichtinger, D.; Chen, P. *J. Am. Chem. Soc*. **1998**, *120*, 376. (f) Kraka, E.; Cremer, D. *J. Am. Chem. Soc*. **2000**, *122*, 8245. (g) Kraka, E.; Cremer, D. *J. Comput. Chem.* **2001**, *22*, 216. (h) Stahl, F.; Moran, D.; Schleyer, P. v. R.; Prall, M.; Schreiner, P. R. *J. Org. Chem.* **2002**, *67*, 1453. (i) Winkler, M. *J. Phys. Chem. A* **2005**, *109*, 1240. (j) Alabugin, I. V.; Manoharan, M. *J. Am. Chem. Soc.* **2003**, *125*, 4495.
(54) Zhang, D. Y.; Borden, W. T. *J. Org. Chem.* **2002**, *67*, 3989.

Berkeley) for a stimulating discussion, and to Mr. Aaron Pearson (Colorado State University) for his artistic contribution to the graphical abstract.

Supporting Information Available: Activation parameters (E_a, $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$, $\Delta S^{\ddagger}$) and reaction energies for the cyclizations of benzannelated enediyne initiated by H, SnH_3, and didehydronaphthalene radicals along with the bond lengths at different DFT and QCISD(T) levels. Activation and reaction energies for cyclizations of radicals **11**−**13**, **31**−**36** at different DFT levels. Complete citations for Gaussian 98 and Gaussian 03 (ref 26). Cartesian coordinates of all stationary point geometries. This material is available free of charge via the Internet at http://pubs.acs.org.

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