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A Density Functional Molecular Orbital Study of the C^2−C^7 and C^2−C^6 Cyclization Pathways of 1,2,4-Heptatrien-6-ynes. The Role of Benzannulation

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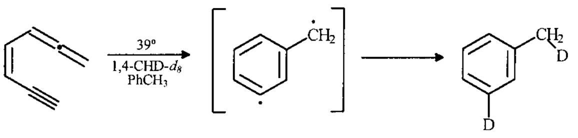
Abstract: The electronic factors influencing the competition between C^2−C^7 (Myers−Saito) and C^2−C^6 (Schmittel) cyclizations of 1,2,4-heptatrien-6-yne and 1-ethynyl-2-propadienylbenzene are investigated using Becke3LYP/6-31G* calculations. The relative energies of the biradical products formed upon cyclization are calculated using a simple bond additivity estimate and by direct calculation. Both approaches predict that benzannulation stabilizes the bis-dehydromethylfulvene biradical that forms upon C^2−C^6 cyclization with respect to the biradical that forms upon C^2−C^7 cyclization by ca. 10 kcal/mol. Transition state calculations predict that benzannulation decreases the barrier for C^2−C^6 cyclization, relative to that for C^2−C^7 cyclization, by 2.3 kcal/mol. The results suggest that benzannulation plays an important role in promoting C^2−C^6 cyclization.

Introduction

The antitumor antibiotic neocarzinostatin A (NCA) was discovered in a microbial fermentation broth in 1965.[1] Although it was known that NCA was composed of a highly unsaturated polyketide “chromophore” noncovalently associated with an apoprotein and that it was a potent DNA-cleaving agent,[2,3] the origin of its antitumor activity was unclear until 1987. In that year, Myers[4] proposed that the NCA chromophore (**1**) cyclized by a novel mechanism to form an indenyl diradical (**3**) capable of abstracting hydrogen atoms from the ribose rings of the DNA backbone (Scheme 1).

The first verification of the cyclization shown in Scheme 1, now termed the “Myers cyclization”, came from the studies of Myers et al.[5,6] and Saito and co-workers,[7] who independently reported the thermal cyclization of the (*Z*)-1,2,4-heptatrien-6-yne skeleton to α,3-tolyl diradicals (eq 1). Although novel, this cyclization had an obvious parallel in the cycloaromatization of (*Z*)-3-hexen-1,5-diyne to *p*-benzyne diradical first observed in the seminal studies of Bergman.[8−10] Unlike the cyclization of **2**, which is believed to be a rapid process,[11,12] the cyclization of (*Z*)-1,2,4-heptatrien-6-yne (**4**) was found to have a half-life of 20.5 h at 39 °C,[13] corresponding to an activation barrier of 22 kcal/mol. These initial reports stimulated a number of studies of the thermal cyclizations of related enyne−allene systems to aromatic diradicals.[14−22] It was found that the Myers cyclization was a general property of (*Z*)-enyne−allenes and could be triggered by a variety of reactions.



(1)

4 **5** **6**

Among those studies are the works of Schmittel[23−28] and others[29−31] in which an alternate cyclization of enyne−allenes

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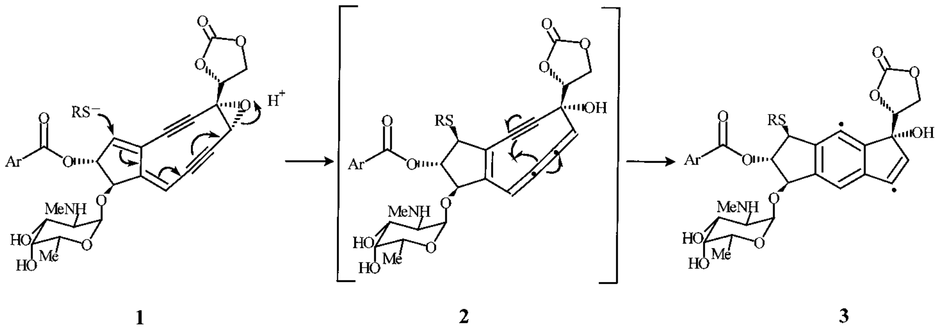
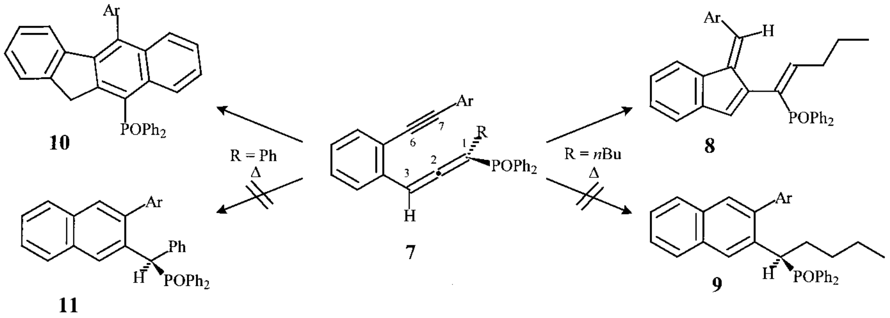
Scheme 1

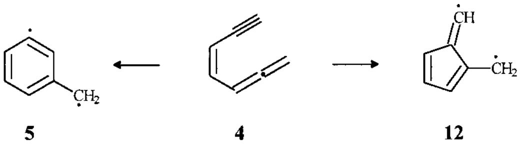


Scheme 2

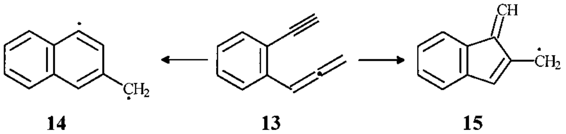


was observed (Scheme 2), leading not to the expected naphthyl diradical products (**9** and **11**) but rather to indenyl (**8**) and fluorenyl (**10**) products. These reactions were characterized by their apparent lack of dehydrotoluene-like diradical products and formation of a five-membered, rather than six-membered, ring. The products observed in these reactions result from C^2-C^6 cyclization, as opposed to the C^2-C^7 cyclization that occurs in the Myers−Saito reaction. Neither the precise mechanism of the C^2-C^6 cyclization nor the factors responsible for switching between the two cyclization pathways are well understood. Schmittel and co-workers have proposed that the C^2-C^6 cyclization, like the Myers cyclization, produces a diradical intermediate,[25,26] and recently reported the successful trapping of such an intermediate by 1,4-cyclohexadiene.[32,33] Recent theoretical work by Engels and Hanrath[34] and by Schreiner and Prall[35] on the cyclization of **4** supports a diradical C^2-C^6 cyclization pathway and estimates a 10 kcal/mol preference for the C^2-C^7 transition state ($\Delta G^{\ddagger} = 25$ vs 35 kcal/mol) in the parent hydrocarbon system. Schmittel has identified several factors that may switch a C^2-C^6 to a C^2-C^7 cyclization: bulky alkyne substituents that preferentially destabilize the C^2-C^7 transition state by steric congestion, aromatic substituents on the alkyne that stabilize an incipient radical at C7, and ring strain.[23−25,27]

One noteworthy feature in most of C^2-C^6 cyclizations is the benzannulation of the enyne−allene substrates. With the exception of two examples reported by Schmittel et al.,[28] all the enyne−allenes reported to undergo selective C^2-C^6 cyclization have been *o*-alkynylaryl allenes. However, whereas it has been shown that the size of the annulated ring is important,[28] the electronic perturbation introduced by the benzene ring has not been examined. Because the exothermicity of the Myers cyclization of **4** can be attributed in part to the stability of the aromatic product **5**,[36] one must question how the overall thermodynamics of cyclization are affected when one compares the competing cyclization pathways of (*Z*)-1,2,4-hexatriene-6-yne, **4**, and its benzannulated analogue **13** (eq 2).



(2a)



(2b)

In this work, we examine the thermodynamics of cyclization—by both C^2-C^6 and C^2-C^7 pathways—of **4** and **13** at the B3LYP/6-31G* level of theory to determine the effects of benzannulation. We show that benzannulation decreases the energy difference between the Myers and Schmittel biradicals by ca. 10 kcal/mol, and correspondingly decreases the energy difference between the C^2-C^7 and C^2-C^6 pathways by ca. 2 kcal/mol. These results show that the electronic modulation introduced by benzannulation plays an important role in promoting the C^2-C^7 cyclization reaction.

Computational Methods

All calculations were carried out by using the Becke3LYP/6-31G* level of theory[37−39] with the Gaussian 98 program.[40] Energies and frequencies of closed-shell molecules and monoradicals were calculated

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by using restricted and unrestricted procedures, respectively. The calculations for the biradicals were carried out by using an unrestricted wave function, and the open-shell singlet state was specified by using the command GUESS=ALTER in the input and switching the HOMO and LUMO for the β electron.[41] The wave function that results from this procedure is formally a 50:50 mixture of singlet and triplet states,[42] as shown in eq 3, where ψ_a and ψ_b are the singly occupied orbitals, and 1 and 2 indicate the electrons in those orbitals.

$$^{50:50}\psi = [\psi_a(1)\alpha(1)\psi_b(2)\beta(2) - \psi_a(2)\alpha(2)\psi_b(1)\beta(1)] \qquad (3)$$

The energy obtained from this wave function is a combination of the energies of the open-shell singlet and the triplet states:

$$E_{50:50} = {}^1/_2(E_{\mathrm{sing}} + E_{\mathrm{trip}}) \qquad (4)$$

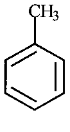
Therefore, the energy of the open-shell singlet can be calculated by using $E_{\mathrm{sing}} = 2E_{50:50} - E_{\mathrm{trip}}$. This "sum method" for calculating the energies of singlet biradicals is not applicable to all biradicals,[43] but should give accurate results for the dehydrotoluenes and dehydrofulvene biradicals because the wave functions are required by symmetry to be purely open-shell.[36] For the dehydrotoluenes, the energies of the open-shell singlets and the triplets are nearly the same, such that the difference between $E_{50:50}$ and E_{sing} is small. Energies and frequencies were calculated at the optimized geometry for the 50:50 wave function. It is expected that the geometries of the singlet and triplet states are similar and the structural differences between the 50:50 biradical and the singlet should be small.

All the energy differences reported in this work contain zero-point energy and thermal corrections, and correspond to 298 K enthalpies. The zero-point energies and thermal corrections were obtained from the calculated harmonic frequencies, which have not been scaled to account for anharmonicity.

Results and Discussion

In this section, we report calculations of the energies of the benzannulated and nonbenzannulated Myers–Saito and Schmittel biradicals. We start by describing calculations of methyl-substituted fulvene and benzfulvene to provide a basis for bond additivity calculations of the biradical enthalpies. In the second section, we provide simple bond additivity estimates of the enthalpies of formation of **5**, **12**, **14**, and **15**. In the same section, more refined estimates are obtained using calculated bond dissociation energies. In the third section, we compare the bond additivity estimates with the directly calculated energy differences between the biradicals and address the differences that are observed. In the final section, we provide results for the calculations of the transition states for the reactions and discuss why the C^2-C^6 cyclization pathway is favored in certain systems.

Methylfulvene and Methylbenzfulvene Enthalpies of Formation. As an alternative to calculating the energies of the biradicals, we first sought to estimate them using bond additivity. However, to do so requires knowledge of the energies of the hydrocarbons from which the biradicals are derived. The experimental enthalpies of formation of toluene and 2-methylnaphthalene, **16** and **17**, are 12.0 and 27.8 kcal/mol, respectively,[44] but the enthalpies of formation of methylfulvene (**18**) and the methyl-substituted benzofulvene (**19**) are not known.



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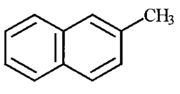

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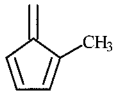

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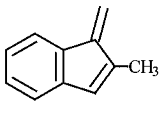
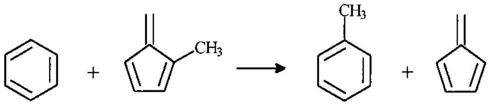


19

Therefore, they have been determined computationally. The enthalpy of formation of 2-methylfulvene can be calculated by using the enthalpy change for the isodesmic reaction shown in eq 5. The energy for this reaction, calculated to be 0.3 kcal/mol, reflects the difference between substituting hydrogen with methyl in benzene and fulvene. Using the enthalpies of formation of benzene and fulvene, 19.8 and 53.6 kcal/mol, respectively,[44] along with the energy of toluene listed above gives $\Delta H_{\mathrm{f},298}(\mathbf{18}) = 45.4$ kcal/mol. This values agrees with that obtained by Schreiner and Prall[35] at the coupled-cluster level of theory using an alternate isodesmic approach. The enthalpy of formation of the methyl-substituted benzofulvene (**8**) can be obtained by using the reaction shown in eq 6. The calculated enthalpy change for this reaction is 11.9 kcal/mol, which means that the methyl-substituted benzofulvene is 11.9 kcal/mol more stable with respect to 2-methylnaphthalene than 2-methylfulvene is with respect to toluene. This result mainly reflects the differences in the π stabilization energies of the molecules involved; at the Hückel level of theory the energy change for eq 6 is predicted to be 0.185β. From the calculated result for eq 6, the enthalpy of formation of methylbenzfulvene, **19**, is found to be 48.5 kcal/mol.



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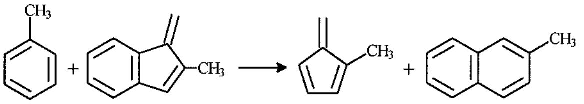

(6)

16 **19** **18** **17**

Bond Additivity Calculations. To a first approximation, the enthalpies of formation of biradicals **5**, **12**, **14**, and **15** can be calculated by using a bond additivity assumption. For example, the enthalpy of formation of **5** can be estimated by using the sequential C–H bond cleavages as shown in eq 7, assuming bond dissociation enthalpies equal to those in toluene (89.8 ±

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[40] Gaussian 98, Revision A.6; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1998.

[41] Schreiner and Prall (ref 35) have suggested that the B3LYP approach suffers from artifactual symmetry breaking, based on their observation that they obtain a significantly lower energy for an essentially planar, C_1, structure than for the C_s biradical. Using the GUESS=ALTER command, we found a C_s state with a geometry and energy identical to those of the C_1 biradical reported by Schreiner and Prall indicating that symmetry breaking does not occur in this case. We did obtain their results by using the GUESS=MIX command.

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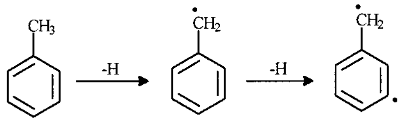
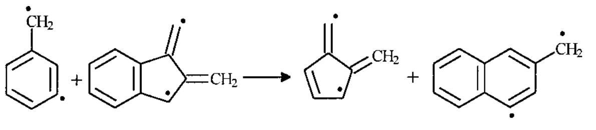


(7)

0.5 kcal/mol)[45] and benzene (113.5 ± 0.6 kcal/mol).[46] The value obtained using this approach is 111.1 kcal/mol. Because **5** has a small singlet−triplet splitting,[35,36] the bond additivity estimate is expected to be close to the enthalpy of formation of the singlet biradical.[47]

The bond additivity estimate for the enthalpy of formation of **5** is significantly higher than the reported experimental value of 103 ± 3 kcal/mol.[36] However, all of the reliable molecular orbital calculations that have been carried out[35,36] (vide infra) give values of $\Delta H_{f,298}$(**5**) close to that obtained from bond additivity, suggesting that the reported enthalpy of formation may need to be reevaluated. Moreover, even if the experimental enthalpy of formation is correct and the calculations are giving energies that are too high, the error should be systematic for all the biradicals because they are electronically similar. Therefore, whereas the absolute energies may not be correct, the relative energies should be more accurate.

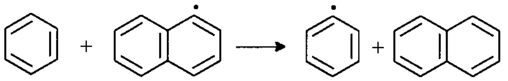
The bond dissociation enthalpies in toluene and benzene can also be applied to calculate the enthalpy of formation of biradical **14**, giving $\Delta H_{f,298}$(**14**) = 126.1 kcal/mol. The energies of the Schmittel biradicals are calculated by using the C−H bond dissociation energy in ethylene (111.2 ± 0.8 kcal/mol)[48] and that for the allylic C−H bond in propylene (88.8 ± 0.4 kcal/mol).[45] These bond dissociation energies lead to $\Delta H_{f,298}$(**12**) = 141.2 kcal/mol and $\Delta H_{f,298}$(**15**) = 144.2 kcal/mol. Therefore, the energy difference between the Myers−Saito and Schmittel biradicals is 30.1 for the parent, nonbenzannulated case, but is only 18.1 kcal/mol in the benzannulated system. The relative energy difference for these biradicals, 12.0 kcal/mol, is most easily understood as the enthalpy change for the reaction shown in eq 8. The difference between the relative stabilities of the two systems as calculated above is due to the difference in the relative energies of the benzannulated and nonbenzannulated hydrocarbons.



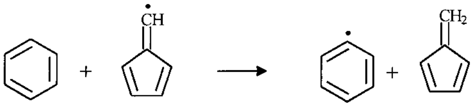
(8)

5 **15** **12** **14**

More refined estimates of the energies of the biradicals can be obtained by using bond dissociation energies that more closely mirror those in **16**−**19**. The bond dissociation energies for the α-position in naphthalene and the vinyl positions in fulvene and benzofulvene were calculated by using isodesmic reactions involving benzene and phenyl radical, as shown in eqs 9a−c. For example, it can be readily shown that the enthalpy change for the hydrogen atom transfer reaction shown in eq 9a is the difference between the bond dissociation energy in benzene and that in the α-position of naphthalene. Similarly, the enthalpies for the reactions shown in eqs 9b and 9c are the difference between the bond energy in benzene and that for the vinylic C−H bond in fulvene and benzfulvene, respectively. The bond dissociation energies for the methyl positions in **17**−**19** were obtained in analogous fashion by comparison with toluene and benzyl radical (eqs 10a−c). The calculated bond dissociation enthalpies are indicated in Figure 1. The naphthyl and vinylic C−H bond dissociation energies are found to be within 0.3 kcal/mol of that in benzene,[46] consistent with previous computational[49,50] and experimental[50] results. Moreover, the methyl C−H bond dissociation energy in 2-methylnaphthalene is similar to that in toluene. On the other hand, the methyl C−H bond dissociation energies in fulvene and benzofulvene are significantly different from each other and from the bond dissociation energy in toluene. The difference in the bond dissociation energies in **18** and **19** is due to the geometry difference between the two radicals. The important features of the structures of the corresponding radicals are shown in Figure 2. The 2-methylfulven-7-yl radical (**18a**) has a C_{2v} structure and the radical is delocalized over carbons 3, 4, and 5 (see numbering in Figure 2). The 1-methylene-2-methylinden-9-yl radical (**19a**) has the electrons unevenly distributed over carbons 3 and 7a (the spin densities are 0.58 and 0.16, respectively) as expected for a benzylic-like structure. The difference in the bond energies in **18** and **19** indicates that the allylic stabilization of the radical in **18a** is more favorable than the benzylic stabilization of the radical in **19a**.

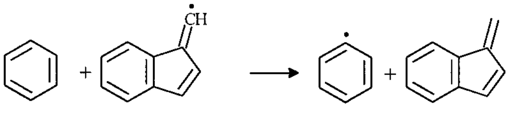


(9a)



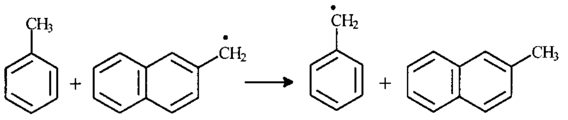
(9b)

20a **20**



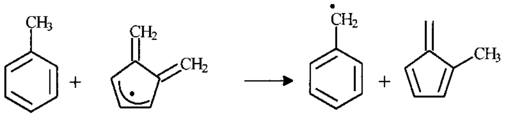
(9c)

21a **21**



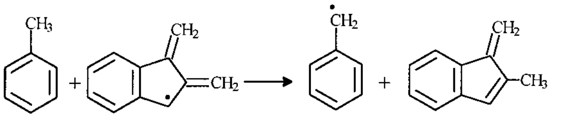
(10a)

16 **17a** **16a** **17**



(10b)

16 **18a** **16a** **18**



(10c)

16 **19a** **16a** **19**

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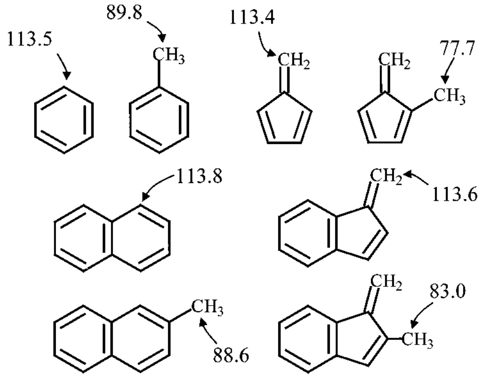
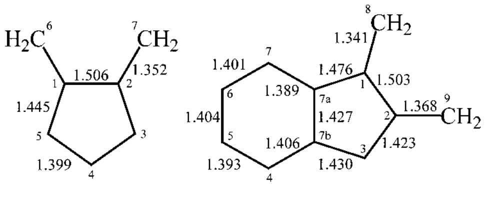


Figure 1. Carbon-hydrogen bond dissociation energies determined at the B3LYP/6-31G* level of theory using the isodesmic reactions shown in Scheme 1. The values for benzene and toluene are taken from refs 46 and 45, respectively.

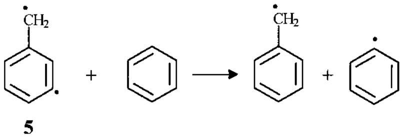


18a **19a**

Figure 2. Bond lengths (in Å) for the 2-methylfulven-7-yl (**18a**) and 1-methylene-2-methylinden-9-yl (**19a**) radicals calculated at the B3LYP/6-31G* level of theory.

The difference in the methyl C−H bond dissociation energies in **18** and **19** affects the estimated relative energies of the biradicals. Using the bond dissociation energies shown in Figure 1, the enthalpies of formation of **5**, **12**, **14**, and **15** are calculated to be 111.1, 132.4, 126.5, and 142.4 kcal/mol, respectively, and the energy for eq 8 is calculated to be 5.5 kcal/mol. Therefore, using the methyl C−H bond dissociation energies in the methyl-substituted fulvenes, the energy difference between the Myers−Saito and Schmittel biradicals is only 5.5 kcal/mol less in the benzannulated system.

Biradical Calculations and Comparison with Additivity. Last, the differences in the relative stabilities of the biradicals were determined by calculating directly the enthalpy change for the reaction shown in eq 8. The energies of the singlet biradicals were obtained from the energies for the 50:50 states and the triplets as described above. At the Becke3LYP/6-31G* level of theory, the enthalpy of eq 8 is calculated to be 10.5 kcal/mol. The absolute enthalpies of formation of the biradicals can be calculated by using the Biradical Stabilization Energies (BSEs),[51] which are the enthalpy changes for the reactions shown in eqs 11a−d and are a measure of the extent to which enthalpies of formation deviate from bond additivity. The BSEs for biradicals **5**, **12**, **14**, and **15**, are 1.8, −4.8, 1.8, and −0.2 kcal/mol, respectively, which lead to enthalpies of formation of 109.3, 137.2, 124.7, and 142.6 kcal/mol, respectively. For comparison, Schreiner and Prall[35] calculated a value of +0.6 kcal/mol for the BSE of **5** and an energy difference of 23.7 kcal/mol between **5** and **12** at the BLYP/cc-pVTZ//BLYP/cc-pVDZ level of theory, ca. 4 kcal/mol lower than what is found here.



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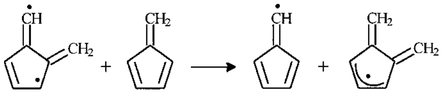
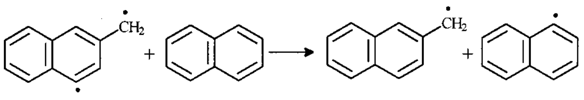
(11a)



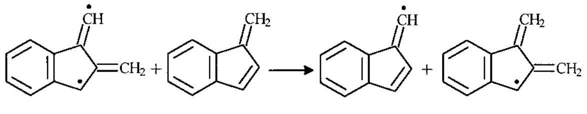
12

(11b)



14

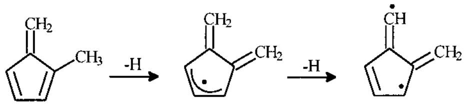
(11c)



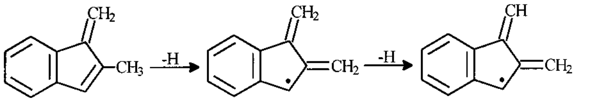
15

(11d)

The directly calculated energy difference in the relative energies of the benzannulated and nonbenzannulated biradicals is ca. 5 kcal/mol higher than that obtained from the bond additivity estimate that utilized the calculated bond dissociation enthalpies. The origin of the difference between these two results lies with the bond dissociation energies used for the bond additivity estimate. As noted above, the radical **18a** is stabilized by allylic resonance and adopts a C_{2v} geometry, such that the electron density is equally distributed between carbons 3 and 5. However, as noted by Schreiner and Prall,[35] the Schmittel biradical, formed by removing a hydrogen atom from C6, is not a completely delocalized π radical, but has slightly alternating single and double bonds. Moreover, whereas the electron spin densities on carbons 3 and 5 are 0.51 in the radical, they are 0.55 and 0.43, respectively, in the biradical such that the spin is more localized on C3. This change occurs because it reduces the electron repulsion between the two unpaired electrons by putting them in different regions of the molecule.[52] A similar effect has been noted for the open-shell singlet in phenyl nitrene.[53] However, the introduction of bond alternation in the biradical is accompanied by a loss in the allylic stabilization that was gained upon formation of the radical (eq 12), which leads to a second bond dissociation energy that is higher than that in the methylene position in 2-methylfulvene, accounting for the observed BSE. In contrast, although the benzannulated biradical also has a bond-alternated structure, it is not significantly different from the structure of **19a**, and the benzylic stabilization is not disrupted when the biradical is formed (eq 13). This is because the spin densities at the 7a and 8 positions in the radical are already very small, with values of 0.16 and 0.01, respectively (compared to values of 0.51 and 0.31 in analogous positions in **18a**), and the electron distribution does not have to change significantly to reduce the repulsion



(12)



(13)

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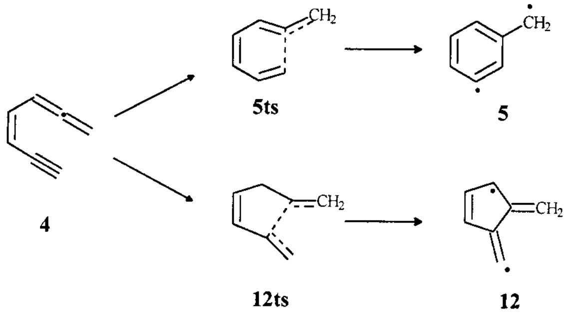
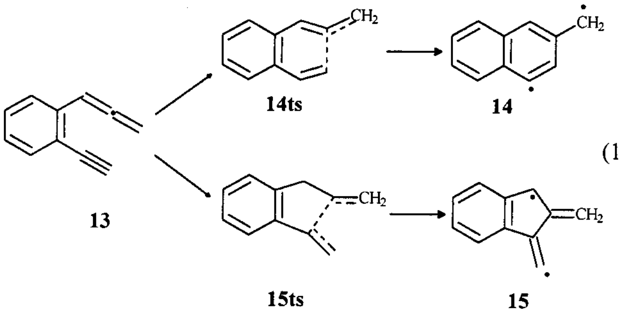
between the electrons. Therefore, the second C−H bond dissociation energy is similar to that in benzofulvene.

Transition State Calculations. The calculations described above indicate that benzannulation decreases the energy difference between the Myers−Saito and Schmittel biradical products by ca. 10 kcal/mol as compared to the nonbenzannulated system. To examine the effect that the change in thermochemistry has on product formation, we calculated the geometries and energies of the reaction transition states (eqs 14−15). For the nonbenzannulated system (eq 14), at the restricted B3LYP/6-31G* level of theory the 298 K enthalpy difference between the transition states for the Myers−Saito and Schmittel cyclization pathways, **5ts** and **12ts**, respectively, is calculated to be 7.2 kcal/mol. However, because the products of the cyclizations are open-shell biradicals, the calculations were also carried out at the UB3LYP/6-31G* level of theory. The geometry and energy obtained for the Myers−Saito transition state, **5ts**, at this level of theory are identical to those obtained from the restricted calculation, and the expectation value for s^2 is found to be 0.00, indicating a closed-shell singlet. On the other hand, although the geometry of the Schmittel transition state, **12ts**, does not change significantly, the energy of this species is ca. 0.1 mhartree lower than that obtained from the restricted calculation. Moreover, the expectation value for s^2 found in this calculation is 0.148, indicating partial open-shell character. Given the small value for s^2, the energy of the singlet should be similar to that of the mixed state. Therefore, with unrestricted wave functions, the energy difference between the transition states of the two reactions is 7.1 kcal/mol, 0.1 kcal/mol lower than was found with the restricted calculation.[54−56]



(14)

The difference between the transition state energies for the rearrangements of the benzannulated systems, eq 15, calculated at the RB3LYP/6-31G* level of theory is 5.9 kcal/mol, slightly lower than that obtained for the nonbenzannulated case. However, with the UB3LYP calculation, the difference between the transition states for the two reactions, **14ts** and **15ts**, is lowered to 4.8 kcal/mol, 2.3 kcal/mol lower than that for the nonbenzannulated system. As described above, the difference between the restricted and unrestricted results is due to a lower energy for the Schmittel transition state, **15ts**, at the UB3LYP level ($\langle s^2 \rangle = 0.283$), whereas the results for the Myers−Saito transition state, **14ts**, are the same with both procedures.[54] The resulting conclusion is that benzannulation is calculated to lower the energy difference between the barriers for the Myers−Saito and Schmittel cyclization, as predicted on the basis of the reaction thermochemistry.



(15)

C^2-C^7 vs C^2-C^6 Cyclization. The results described above, along with those reported previously, suggest that the switching of cyclization pathways observed by Schmittel and co-workers is due to a combination of effects. Whereas benzannulation is calculated to lower the barrier by 2.3 kcal/mol, the experimental results[27,57] have shown that it alone is not sufficient to make the C^2-C^6 cyclization the favored process. Similarly, at the AM1 level of theory,[27] a phenyl substituent at C7 stabilizes the Schmittel biradical by ca. 6 kcal/mol, which is likely not sufficient to switch the pathways. However, the combination of benzannulation and phenyl substitution is known to result in both C^2-C^6 and C^2-C^7 cyclization.[23−28] Therefore, experimental results are in agreement with the predictions from this work that the electronic benefits of benzannulation promote the C^2-C^6 cyclization pathway.

Schreiner and Prall[35] have shown that the C^2-C^6 cyclization pathway can also be promoted by incorporating the enyne−allene in a cyclic system, and that the barrier for Schmittel cyclization is lower for eight- and nine-member rings. The results obtained in this work indicate that the Schmittel pathways will be even more favored if these systems are benzannulated.

Conclusions

Calculations of the energies of Myers−Saito and Schmittel biradicals indicate that benzannulation plays a significant role in promoting C^2-C^6 cyclization of 1,2,4-heptatrien-6-yne. The energy difference between the Schmittel and Myers−Saito biradicals is 10.5 kcal/mol less for the benzannulated system than for the parent case, which is attributed to the difference in π stabilization energies in benzene, fulvene, naphthalene, and benzofulvene. This stability is reflected in the transition states, as the energy difference between the C^2-C^6 and C^2-C^7 cyclization pathways is 2.3 kcal/mol lower for the benzannulated case than for the nonbenzannulated system. The results indicate that the electronic perturbation provided by benzannulation favors the C^2-C^6 pathway.

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Supporting Information Available: Calculated geometries, energies, and frequencies for all the species discussed (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(54) Because the energy of the triplet is very high, the energy of the singlet is likely slightly lower than that of the mixed state. Yamaguchi and co-workers (refs 55 and 56) have estimated the singlet energy by using the equation $E_{\mathrm{mix}} = (1 - x)E_{\mathrm{sing}} + xE_{\mathrm{trip}}$, where $x = \langle s^2 \rangle/2$, to account for the contribution of the triplet state to the energy. If we apply this approximation to the systems described here, then the energy difference between **5ts** and **12ts** is 5.7 kcal/mol and the difference between **14ts** and **15ts** is 2.0 kcal/mol, such that benzannulation stabilizes the transition state by 3.7 kcal/mol.

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