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Comparison of Biradical Formation between Enediyne and Enyne–Allene. Ab Initio CASSCF and MRSDCI Study

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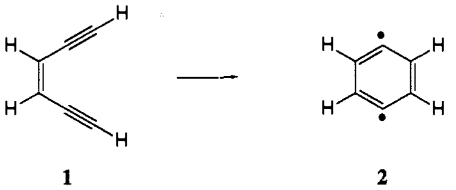
Abstract: We theoretically compared energetics of the Bergman-type biradical formation between enediyne and enyne–allene. The structures of transition states as well as reactants and products for the reaction of (*Z*)-hexa-1,5-diyn-3-ene (**1**) and (*Z*)-hepta-1,2,4-trien-6-yne (**3**) are determined at the CASSCF level. Energy calculations at the CASSCF and the MRSDCI level show that the reaction of enyne–allene **3** is more exothermic and its activation energy is lower than that of enediyne **1**, consistent with the experiments. The reaction of enyne–allene is more exothermic, since a π radical on the benzylic methylene group in the product of enyne–allene is more stable than the σ radical of the product of enediyne, partly because of the conjugation with the aromatic ring and partly because of the intrinsically stronger aryl–H bond than the alkyl–H bond. This conjugation, however, does not take place at the enyne–allene transition state where the methylene remains perpendicular. Thus, the lower activation energy for enyne–allene is not ascribed to the conjugation but to the smaller four-electron repulsion between the in-plane π bonds than that for enediyne.

Biradical formation from enediyne by the Bergman-type cyclization[1] is an essential step for realization of antitumor activities of such antibiotics as neocarzinostatin and esperamicin–calichemicin[2] and has drawn considerable attention.[3] The reaction of an enediyne system requires a substantial activation energy; for instance, the activation enthalpy for the reaction of (*Z*)-hexa-1,5-diyn-3-ene (**1**) (eq 1) has been evaluated to be 32 kcal/mol.[1c] Therefore, a strain imposed in a cyclic enediyne compound such as esperamicin shown below is considered to be indispensable to induce biradical formation at a low, such as body, temperature. However, very recently, Nagata et al. and Myers et al. have found that an enyne–allene system without a strain can produce a biradical at a lower temperature.[4,5] The Arrhenius activation barrier for the reaction of (*Z*)-hepta-1,2,4-trien-6-yne (**3**) (eq 2) has been measured to be 21–23 kcal/mol,[4b,5] substantially lower than that of the open-chain enediyne system having no strain mentioned above. With use of the group-equivalent assumption,[6] the heats of reaction of **1** and **3** have been estimated to be +14 and −15 kcal/mol, respectively.[1c,5] The exothermicity of **3** has been attributed to the conjugation between the methylene and the aromatic ring in the product α,3-didehydrotoluene (**4**). This conjugation has been considered to contribute also to the lower activation energy, and thus the transition-state structure has been proposed to have the terminal methylene twisted to facilitate the conjugation.[5]



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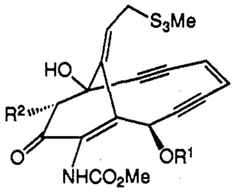
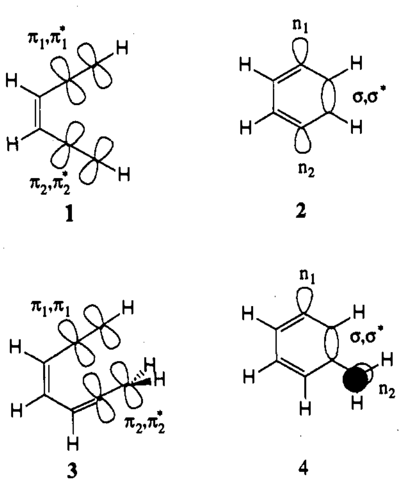
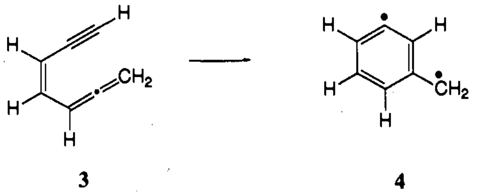


Chart I





(2)

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[1] (a) Lockhart, T. P.; Comita, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4082. (b) Lockhart, T. P.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4091. (c) Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660.

[2] (a) Edo, K.; Mizugaki, M.; Koide, Y.; Seto, H.; Furihara, K.; Otake, N.; Ishida, N. *Tetrahedron Lett.* **1985**, *26*, 331. (b) Golik, J.; Clardy, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Monishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.; Doyle, T. W. *J. Am. Chem. Soc.* **1987**, *109*, 3461. (c) Golik, J.; Clardy, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Monishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.; Doyle, T. W. *J. Am. Chem. Soc.* **1987**, *109*, 3462. (d) Lee, M. D.; Dunne, T. S.; Siegel, M. M.; Chang, C. C.; Morton, G. O.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3464. (e) Lee, M. D.; Dunne, T. S.; Siegel, M. M.; Chang, C. C.; Morton, G. O.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3466. (f) Myers, A. G. *Tetrahedron Lett.* **1987**, *28*, 4493. (g) Myers, A. G.; Proteau, P. J.; Handel, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 7212. (h) Myers, A. G.; Proteau, P. J. *J. Am. Chem. Soc.* **1989**, *111*, 1146. (i) Saito, I.; Kawabata, T.; Fujiwara, T.; Sugiyama, H.; Matsurra, T. *J. Am. Chem. Soc.* **1989**, *111*, 8302.

[3] (a) Magnus, P.; Lewis, R. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 6921. (b) Nicolaou, K. C.; Ogawa, Y.; Zuccarello, G.; Kataoka, H. *J. Am. Chem. Soc.* **1988**, *110*, 7247. (c) Wender, P. A.; Harmata, M.; Jeffrey, D.; Mukai, C.; Suffert, J. *Tetrahedron Lett.* **1988**, *29*, 909. (d) Schreiber, S.; Kiessling, L. *Tetrahedron Lett.* **1989**, *30*, 433. (e) Kende, A. S.; Smith, C. A. *Tetrahedron Lett.* **1989**, *29*, 4217. (f) Tomioka, K.; Fujita, H.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 851. (g) Mantlo, N. B.; Danishefsky, S. J. *J. Org. Chem.* **1989**, *54*, 2781. (h) Hirama, M.; Fujiwara, K.; Shigematsu, K.; Fukazawa, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4120. (i) Snyder, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 7630. (j) Haseltine, J. N.; Danishefsky, S. J.; Schulte, G. *J. Am. Chem. Soc.* **1989**, *111*, 7638.

[4] (a) Nagata, R.; Yamanaka, H.; Okazaki, E.; Saito, I. *Tetrahedron Lett.* **1989**, *30*, 4995. (b) Nagata, R.; Yamanaka, H.; Murahashi, E.; Saito, I. Private communication.

[5] Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057.

[6] Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

0002-7863/91/1513-1907$02.50/0

In this paper, we will report some theoretical evidence for the difference of the reaction between the enediyne and the enyne–allene system. For this purpose, we determined the structures of the transition states (TSs) as well as the reactants and the products for the reactions of **1** and **3** (eqs 1 and 2) using the complete active space self-consistent field (CASSCF) method. For energy calculation, in addition to the CASSCF method, we carried out the multireference single and double configuration interaction (MRSDCI) calculations. At all the levels, reaction 2 was calculated to be more exothermic and have a lower activation energy than reaction 1. The difference in the energy of reaction will be analyzed by comparing the energies of reaction 2 and those of the methyl-substituted version of reaction 1 (eq 3). The activation energy difference will be discussed on the basis of the overlap between the in-plane π bonds.

Method of Calculations

The structures of the reactants, the transition states, and the products for reactions 1 and 2 were determined by the four-electron four-orbital CASSCF (CASSCF4) method[7] with the MIDI1 basis set.[8] To designate the computational level, we used the standard notation. For instance, CASSCF4/MIDI1 indicates the calculation level by the CASSCF4 method with the MIDI1 basis set. During the reactions, four in-plane π electrons of **1** and **3** are transformed into two electrons of the newly formed CC σ bond and two unpaired electrons of the respective products. Therefore, these four electrons are allowed to spin-couple completely; i.e., they are taken active in the CASSCF4 wave functions. The four orbitals chosen are schematically shown in Chart I. On the other hand, out-of-plane π MOs of the reactants remain doubly occupied and smoothly become the aromatic π MOs of the products.

The structures of stationary points for reaction 1 were determined under the C_{2v} symmetry constraint. On the other hand, the C_s symmetry restriction was imposed on the structures of **3** and **4**; the CH bonds of the allenic methylene of **3** are assumed to be out of the symmetry plane, while those of **4** lie in the symmetry plane. For the TSs connecting **3** and **4**, we searched structures under no symmetry constraint as well as those under the C_s constraint with the out-of-plane CH bonds similar to those in **3**.

The ten-electron ten-orbital CASSCF (CASSCF10) calculations[9] with the MIDI4 basis set[8] were also carried out at the CASSCF4/MIDI1-optimized structures. In these CASSCF10 calculations, the six out-of-plane π electrons were included in the active space as well to allow more flexible spin-coupling of the out-of-plane π orbitals. (We will refer to the CASSCF4/MIDI1 and the CASSCF10/MIDI4 levels of calculation as levels A and B, respectively.) In addition, in order to take into account the electron correlation related to the σ electrons, we carried out MRSDCI calculations using the CASSCF10/MIDI4 natural orbitals.[10] In the MRSDCI calculations for **1**, **2**, **3**, and the transition states, the four configurations that give the total weight of more than 99% in the CASSCF4 wave functions are chosen as the reference configurations. They are $(\pi_1 + \pi_2)^2(\pi_1 - \pi_2)^2$, $(\pi_1 + \pi_2)^2(\pi^*_1 + \pi^*_2)^2$, $(\pi_1 - \pi_2)^2(\pi^*_1 - \pi^*_2)^2$, and $(\pi_1 + \pi_2)^1(\pi_1 - \pi_2)^1\,(\pi^*_1 + \pi^*_2)^1\,(\pi^*_1 - \pi^*_2)^1$ for the reactants and the transition states and $(\sigma)^2(n_1 - n_2)^2$, $(\sigma)^2(n_1 + n_2)^2$, $(n_1 - n_2)^2(\sigma^*)^2$, and $(\sigma)^1(n_1 - n_2)^1(n_1 + n_2)^1(\sigma^*)^1$ for **2**. For **4**, which has a π unpaired electron, three congfigurations, which gave the total weight of 99.9% in the CASSCF4 wave function, $((\sigma)^2(n_1)^1(n_2)^1$, $(n_1)^1(n_2)^1(\sigma^*)^2$, and $(\sigma)^1(n_1)^1(n_2)^1(\sigma^*)^1)$ are used as the reference configurations. Excitations from 1s orbitals of the carbons were not taken into account. The MRSDCI calculations with the threshold of 10 μhartree for perturbation selection of configurations showed that the reference configurations had a weight of 85–86% in all in the MRSDCI wave functions. The MRSDCI energies calculated with the threshold of 10 μhartree were extrapolated to estimate the full CI energies with the Feller and Davidson formula,[11a] which incorporated the correction of the unlinked terms[11b] as well as the extrapolation to the value without the perturbation selection.[11c]

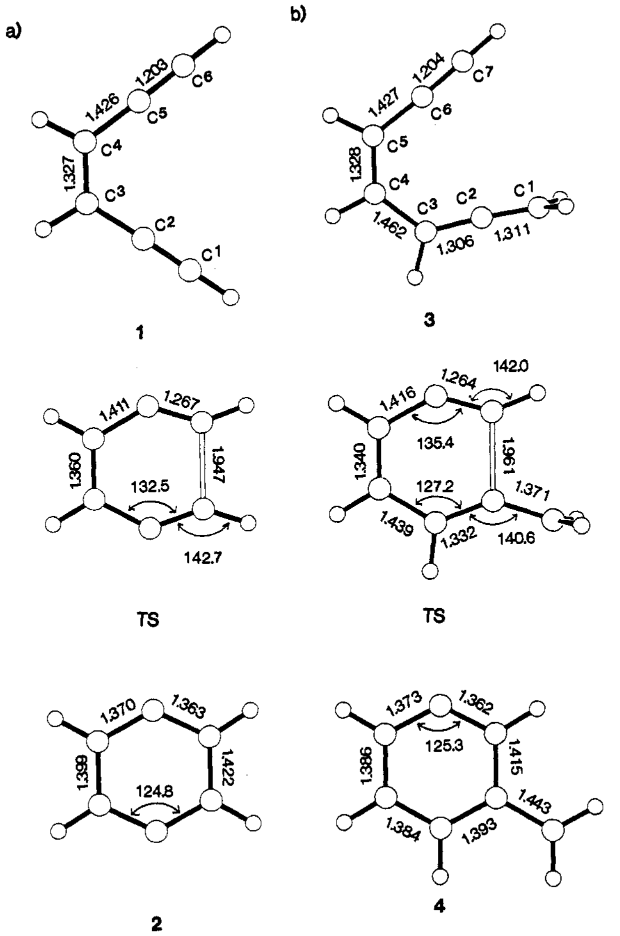

Figure 1. CASSCF4/MIDI1-optimized structures (Å and deg) of (a) **1**, **2**, and the transition state for reaction 1 and (b) **3**, **4**, and the transition state for reaction 2.

In comparing reactions 1 and 2, we need to calculate the energies of the following fragments: ketene, propyne, and benzyl and *o*-tolyl radicals. The structures of ketene and propyne were determined at the restricted Hartree–Fock (RHF) level with the MIDI1 basis set.[12] The energies were also calculated by several more sophisticated methods: the two-electron two-orbital CASSCF (CASSCF2) method with the MIDI1 basis set, the CASSCF4 method with the MIDI4 basis set, and the MRSDCI method with the MIDI4 basis set.[9] In the CASSCF2 calculation, two π electrons in only one π orbital are in the active space, though there are two occupied π orbitals. This CASSCF2/MIDI1 calculation is equivalent to level A above, since only the in-plane π electrons but not the out-of-plane π electrons are correlated. On the other hand, the CASSCF4/MIDI4 calculation for ketene and allene where all the π electrons are correlated is equivalent to level B. In the MRSDCI calculations, the CASSCF4/MIDI4 natural orbitals are used and all the configurations in the CASSCF2 wave functions are included as the reference configurations. 1s orbitals of the carbons were frozen in the MRSDCI calculations.

For *o*-tolyl and benzyl radicals, we carried out the restricted open-shell Hartree–Fock ROHF/MIDI1 geometry optimization[12] under the C_s and the C_{2v} symmetry restriction and calculated the energies at the optimized structures by the seven-electron seven-orbital CASSCF (CASSCF7) method[9] with the MIDI4 basis set, in which six out-of-plane π electrons and one unpaired electron are active. When two σ electrons of the newly formed CC σ bond and one unpaired electron are neglected, the ROHF and the CASSCF7 calculations here are equivalent to levels A and B, respectively.

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(7) We used the HONDO7 program for the CASSCF4 calculations: Dupuis, M.; Watts, J. D.; Viller, H. O.; Hurst, G. J. B. HONDO7; Quantum Chemistry Program Exchange, No. 544.

(8) Tatewaki, H.; Huzinaga, S. *J. Comput. Chem.* **1980**, *1*, 205.

(9) We used the MOLPRO88 program: Knowles, P.; Werner, H.-J.; Elbert, S. T. MOLPRO88; 1988.

(10) Davidson, E. R.; McMurchie, L. E.; Elbert, S. T.; Langhoff, S. R.; Rawlings, D.; Feller, D. MELD; IMS Computer Center Library Program, No. 030.

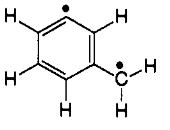
(11) (a) Feller, D.; Davidson, E. R. *J. Chem. Phys.* **1983**, *80*, 1006. (b) Davidson, E. R.; Silver, D. W. *Chem. Phys. Lett.* **1977**, *52*, 403. (c) Langhoff, S. R.; Davidson, E. R. *J. Chem. Phys.* **1976**, *64*, 4699.

(12) We used the IMS version of GAUSSIAN86,[12a] in which Obara integral and derivative codes[12b] are implemented. (a) Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; DeFrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fluder, E. M.; Topiol, S.; Pople, J. A. GAUSSIAN86; Carnegie-Mellon Quantum Chemistry Publishing Unit, Carnegie-Mellon University: Pittsburgh, PA 15213, 1986. (b) Obara, S.; Honda, M.; Nakano, H.; Sakano, F.; Takada, S.; Miyake, Y. KOTO; IMS Computer Center Library Program, No. 070.

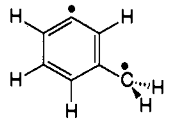
Results and Discussion

Optimized Structures and Energetics for Reactions of Enediyne 1 and Enyne–Allene 3. The CASSCF4/MIDI1-optimized structures of the reactants, the products, and the transition states for reactions 1 and 2 are shown in Figure 1. The CC bond lengths at the transition state of reaction 1 are closer to those of **1** than to those of **2**, indicating that the transition state is located early on the reaction path; the C^1C^2 (C^5C^6) and the C^3C^4 bonds become longer by 40 and 46% of the change between **1** and **2**, respectively, while the C^2C^3 (C^4C^5) bond becomes shorter by 27% of the change. Though **2** should have a D_{2h} structure, its optimized structure has a lower symmetry of C_{2v} due to the artifact of the CASSCF4, in which C^1C^6 σ electrons are correlated but C^3C^4 σ electrons are not; the correlated C^1C^6 bond is slightly longer than the uncorrelated C^3C^4 bond.

The product of reaction 2 (**4**) has the methylene CH bonds in-plane because of the conjugation between the aromatic π and the methylene π orbitals.[13] For **4**, we preliminarily determined two structures with the CH bonds being in-plane (**4a**) and out-of-plane (**4b**) by the unrestricted Hartree–Fock (UHF) method[12]



4a



4b

with the MIDI1 basis set and calculated the energies at the CASSCF10/MIDI4 level. The in-plane structure is more stable by 18.1 and 12.1 kcal/mol at the UHF/MIDI1 and the CASSCF10/MIDI4 levels, respectively. This energy difference is ascribable to the conjugation.

At the TS for reaction 2, this conjugation may take place, and in such a case the methylene is expected to take a conformation between those of **3** and **4**. First, we started the TS search under the C_s symmetry constraint with the out-of-plane CH bonds of the allenic methylene. The resultant structure is shown in Figure 1. The methylene rotation around the C^1C^2 bond by 10, 20, 45, and 90° (in-plane methylene) from this TS leads to higher energies by 0.4 (0.3), 1.5, 9.7, and 18.1 kcal/mol at the CASSCF4 (CASSCF10) level, respectively. Further, we started the TS search without any symmetry restriction from the structure with the methylene rotated by 45° around the C^1C^2 bond from the C_s transition state. This trial in fact gave the same C_s TS structure. These results indicate that reaction 2 passes through the C_s transition state with the out-of-plane CH bonds of allenic methylene and that the methylene rotation therefore must take place *after* this TS is passed. The conjugation that favors the in-plane methylene of **4** is at the TS not large enough to compensate the loss of the $C{=}CH_2$ in-plane π bond. The short $C{=}CH_2$ distance of 1.37 Å at the TS indicates that the π bond has not yet been broken. We note here that the UHF/MIDI1 calculation gave a TS structure having a nearly in-plane methylene, though at the CASSCF10/MIDI4 level this UHF structure is 9.0 kcal/mol higher in energy than the CASSCF4 structure in Figure 1. High-spin contaminations in the UHF wave function seem to make the π bond unrealistically weak and the results unreliable.

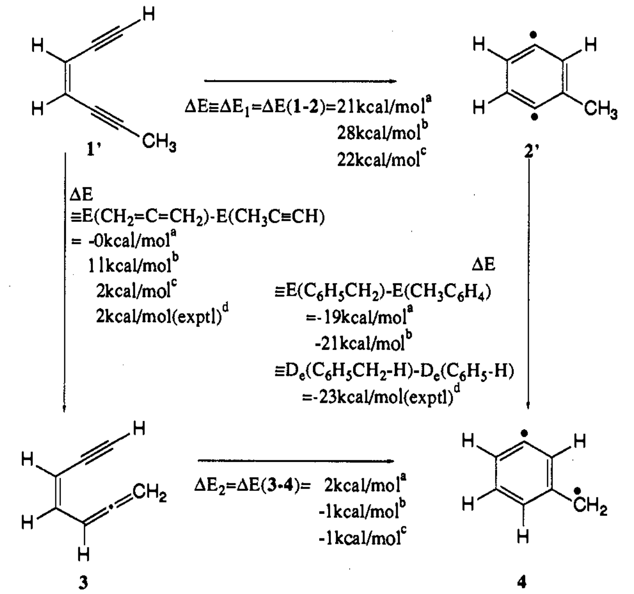
The TS structure for reaction 2 in Figure 1 is very similar to that for reaction 1; the partially formed CC bond distances are 1.95 and 1.96 Å for reactions 1 and 2, respectively, and the bending angles around the reaction centers are 141–143°.

Table I. Energies for Biradical Formation Relative to the Reactants (kcal/mol) Calculated at the CASSCF4/MIDI1-Optimized Structures

method	reactant[a]	TS	product
	Reaction 1		
CASSCF4/MIDI1	−228.0737	45.3	20.7
CASSCF10/MIDI4	−229.2166	44.7	28.3
MRSDCI/MIDI4	−229.5986	37.6	22.0
estimated[b]			14[c]
	Reaction 2		
CASSCF4/MIDI1	−266.8776	35.5	2.1
CASSCF10/MIDI4	−268.1762	33.3	−1.2
MRSDCI/MIDI4	−268.6852	19.1	−0.7
estimated[b]			−15[d]

[a] Total energy in hartrees. [b] Estimated from the heat of formation of the reactant, which is calculated based on the group additivity assumption,[6] and that of the biradical product, which is estimated according to the equations $\Delta H_f(C_6H_6) + 2D_e(C_6H_5{-}H) - D_e(H{-}H)$ for reaction 1 and $\Delta H_f(C_6H_5CH_3) + D_e(C_6H_5{-}H) + D_e(C_6H_5CH_2{-}H) - D_e(H{-}H)$ for reaction 2. [c] Reference 1c. [d] Reference 5.

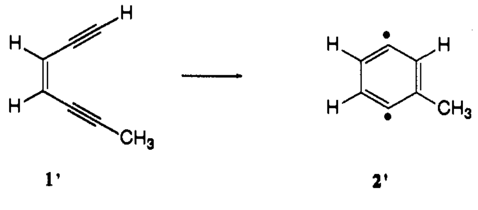
Scheme I



[a] Level A: CASSCF4/MIDI1, **1**, **2**, **3**, and **4**; CASSCF2/MIDI1, allene and propyne; ROHF/MIDI1, $CH_3C_6H_4$ and $C_6H_5CH_2$. [b] Level B: CASSCF10/MIDI4, **1**, **2**, **3**, and **4**; CASSCF4/MIDI4, allene and propyne; CASSCF7/MIDI4 for $CH_3C_6H_4$ and $C_6H_5CH_2$. [c] MRSDCI/MIDI4. [d] Reference 14.

To obtain better energetics at the CASSCF4/MIDI1 structures thus obtained, we carried out the CASSCF10/MIDI4 and the MRSDCI/MIDI4 calculations, as shown in Table I. At all the levels of calculation, reaction 2 is more favorable than reaction 1, consistent with the experiments.[4,5] Reaction 2 is almost thermoneutral, while reaction 1 is endothermic by about 20 kcal/mol at the CASSCF4 and the MRSDCI levels and 28 kcal/mol at the CASSCF10 level. The difference of 8 kcal/mol between the two levels of calculation will be discussed later. The activation barrier for reaction 2 is 11 kcal/mol lower than that for reaction 1 at the CASSCF levels and 19 kcal/mol at the MRSDCI level. Both reactions 1 and 2 are calculated to be more endothermic than, but their differences to be nearly equal to, what is obtained from the estimated heat of formation of the reactants and the products (see footnote *b* of Table I);[1c,5] the difference between the two reactions was reproduced well.

Analysis of Energetics of Reactions between Enediyne 1 and Enyne–Allene 3. In order to analyze the difference in the energy of reaction between reactions 1 and 2 ($\Delta E_1 - \Delta E_2$), we considered Scheme I. The top row in Scheme I is reaction 3, the methyl-substituted version of reaction 1. The reactant **1'** and product



1' **2'** (3)

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(13) For benzyl, in which the conformation with in-plane methylene is the minimum, see: Dorigo, A. E.; Li, Y.; Houk, K. N. *J. Am. Chem. Soc.* **1989**, *111*, 6942.

Table II. Energy Difference between Ketene and Propyne (kcal/mol) Calculated at RHF/MIDI1-Optimized Structures[a]

method	*E*(ketene) – *E*(propyne)
RHF/MIDI1	2.0
CASSCF2/MIDI1	–0.1
CASSCF4/MIDI4	10.8
MRSDCI/MIDI4	1.5

[a] Total energies of propyne are *E*(RHF/MIDI1) = –115.1789 hartrees, *E*(CASSCF2)/MIDI1 = –115.2025 hartrees, *E*(CASSCF4/MIDI4) = –115.7635 hartrees, and *E*(MRSDCI/MIDI4) = –115.9909 hartrees.

2′ of reaction 3 are isomers of **3** and **4**, respectively; **1′** is transformed into **3** through propynyl–ketenyl isomerization and **2′** into **4** through H migration from the methyl group to the phenyl ring. Consequently, the difference in the energy of reaction between reactions 3 and 2 ($\Delta E_3 - \Delta E_2$) corresponds to the difference in the energy of reaction between the propynyl–ketenyl isomerization and the H migration ($\Delta E(\mathbf{1'} \rightarrow \mathbf{3}) - \Delta E(\mathbf{2'} \rightarrow \mathbf{4})$) as shown in Scheme I. The estimated heat of reaction shows that reaction 3 is more endothermic by only 2 kcal/mol than reaction 1. (Heats of formation calculated by the group-additivity assumption are 126.8 and 117.2 kcal/mol for **1** and **1′**, respectively.[6] Those of **2** and **2′** were calculated by the equations $\Delta H_f(C_6H_6)$ (19.8) + $2D_e(C_6H_5\text{–}H)$ (2(110.9)) – D_e(H–H) (104.2) = 137.4 kcal/mol and $\Delta H_f(C_6H_5CH_3)$ (11.95) + $2D_e(C_6H_5\text{–}H)$ (2(110.9)) – D_e(H–H) (104.2) = 129.6 kcal/mol.[14]) The effect of methyl substitution is not large. Thus, in Scheme I the ab initio energetics for reaction 1 are used as that for reaction 3.

For the process **1′** → **3** in Scheme I, we used the energy for propyne to allene isomerization. The group-additivity calcultion shows that **1′** → **3** is 1 kcal/mol endothermic, and the experimental heat of formation shows that the propyne to allene isomerization is 2 kcal/mol endothermic; the difference between the two processes is quite small.

The RHF/MIDI1-optimized structures of ketene and allene are shown in Figure 2, and the energy difference calculated at the several levels are shown in Table II. The CASSCF4/MIDI4 (level B) ΔE(propyne → ketene) is calculated to be 10.8 kcal/mol, which is larger than the experimental heat of reaction above as well as the theoretical ΔE(propyne → ketene) of –0.1 kcal/mol at the CASSCF2/MIDI1 level (level A) and 2.0 kcal/mol at the RHF/MIDI1 level. In order to investigate this discrepancy, we carried out the MRSDCI calculation to obtain ΔE(propyne → ketene) of 1.5 kcal/mol. At the MP4SDQ/6-31G* level, ΔE(propyne → ketene) has been calculated to be 1.4 kcal/mol.[15] These results show that the π–π electron correlation stabilizes propyne more than ketene, since in propyne four π electrons are closer to each other, and that σ–σ and σ–π electron correlations taken into account in the MRSDCI and MP4 calculations compensate the difference in the π–π electron correlation between propyne and ketene. The CASSCF2 wave function for propyne and ketene (level A) gives a more balanced description. Therefore, level A results are better to use in comparison between reactions 1 and 2 than level B results.

$\Delta E(\mathbf{2'} \rightarrow \mathbf{4})$ corresponds to the bond energy difference between the C_6H_4–H and $C_6H_4CH_2$–H bonds. In the calculation, this difference is approximated by the bond energy difference between the $CH_3C_6H_4$–H and $C_6H_5CH_2$–H bonds, which in turn corresponds to the energy difference between the tolyl and benzyl radicals. The calculations of radicals would be easier than those of biradicals. The ROHF/MIDI1 (level A) optimized structures for *o*-tolyl and benzyl radicals are shown in Figure 2.[12] At these optimized structures, the energies were calculated by the CASSCF7/MIDI4 method (level B). The calculations at levels A and B gave energy differences of 18.7 and 20.6 kcal/mol (Table III), respectively, which are similar to the experimental bond energy difference between the C_6H_5–H and the $C_6H_5CH_2$–H bonds; experimentally, the C_6H_5–H bond (110.9 kcal/mol) is 23 kcal/mol stronger than the $C_6H_5CH_2$–H bond (88.0 kcal/mol).[14] The difference in bond energy is partly due to the fact that the π radical on methylene is stabilized by the conjugation with the aromatic ring, leading to the $C_6H_5CH_2$–H bond, which is weaker than the C_6H_5–H bond. As mentioned above, this stabilization was calculated to be 12.1 kcal/mol at the CASSCF10/MIDI4 level. The remaining differences of 10 kcal/mol is ascribable to the intrinsic stronger aryl–H bond than the alkyl–H bond; the bond dissociation energy is, for instance, 100.3 kcal/mol for the CH_3CH_2–H bond vs 110.9 kcal/mol for C_6H_5–H bond.[14]

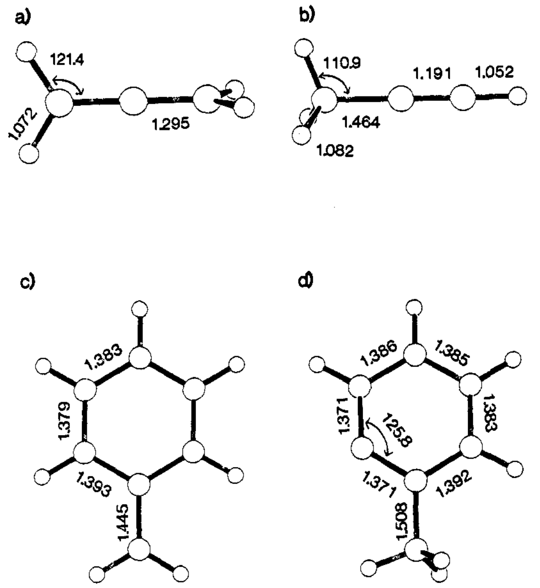

Figure 2. RHF/MIDI1-optimized structures (Å and deg) for (a) ketene and (b) propyne and ROHF/MIDI1-optimized structures (Å and deg) for the (c) benzyl and (d) *o*-tolyl radicals.

Table III. Energy Difference between *o*-Tolyl and Benzyl Radicals (kcal/mol) Calculated at ROHF/MIDI1-Optimized Structures[a]

method	*E*(benzyl) – *E*(*o*-tolyl)
ROHF/MIDI1	–18.7
CASSCF7/MIDI4	–20.6

[a] Total energies of the *o*-tolyl radical are *E*(ROHF/MIDI1) = –267.4841 hartrees and *E*(CASSCF7/MIDI4) = –268.7650 hartrees.

The energetics for some steps in the cycle shown in Scheme I are taken from a similar reaction of smaller molecules, and thus the energetics of the cycle are only approximately closed. However, it is safe to say that $\Delta E_3 - \Delta E_2$, and thus $\Delta E_1 - \Delta E_2$ is dominated by the energetics of the H migration. This implies that the reaction producing a radical on the methylene attached to the aromatic ring would be more exothermic and thus thermodynamically more favorable. Further attention should be paid to the difference between ΔE_1 and ΔE_2. The $\Delta E_1 - \Delta E_2$ at level B is different from that at level A and the MRSDCI level. The unbalanced treatment of the electron correlation effect at level B mentioned above stabilizes **1** artificially, compared to the others, to make reaction 1 more endothermic.

Since the conjugation between the methylene and aromatic ring does not take place at the TS of reaction 2, the difference in the activation energy is not ascribable to the conjugation. The higher activation barrier for reaction 1 may be ascribed to the larger four-electron repulsion due to the larger overlap between two in-plane π bonds. In Figure 3, the CASSCF10 natural orbitals for the transition states, which are in the symmetry plane, are shown. The occupation numbers of ϕ_1 and ϕ_2 are close to 2.0, suggesting that the repulsion between in-plane π orbitals is large. The repulsion is expected to be larger in reaction 1, since the two in-plane π bonds in **1** are located to be syn with respect to the partially formed CC bond. This discussion also suggests than an electron-withdrawing substituent would decrease the electron

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(14) *CRC Handbook of Chemistry and Physics*, 68th ed.; Weast, R. C., Ed.; CRC Press: Boca Raton, FL, 1988.

(15) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

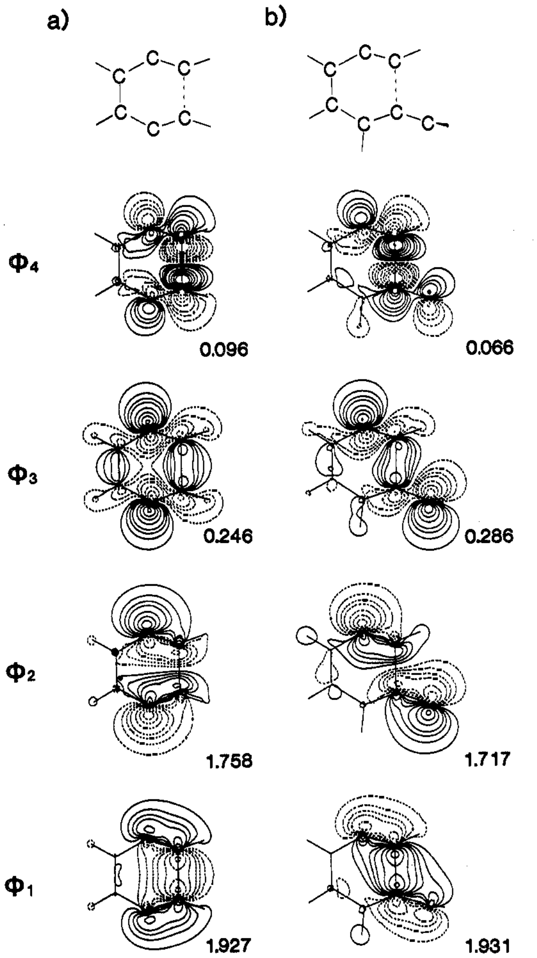
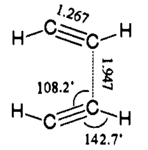


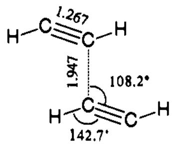
Figure 3. Selected CASSCF10 natural orbitals calculated at the transition states for reactions (a) 1 and (b) 2 with the occupation numbers.

density of π orbitals to reduce the repulsion and thus lower the activation barrier.

In order to obtain further support of this idea, we carried out the CASSCF4 calculations for acetylene dimers shown below, the conformations of which are cis (**5a**) and trans (**5b**) to mimic the transition states of reactions 1 and 2, respectively. The structures are taken from the transition state for reaction 1. In these calculations, only in-plane π electrons are correlated. The calcualtions show that the cis structure is 12 kcal/mol higher in energy than the trans structure. This difference is close to that in the activation energy between reactions 1 and 2, supporting the above idea. Bernardi et al. have determined the transition-state structure for cycloaddition of two ethylenes by the CASSCF method with the STO-3G and the 4-31G basis sets,[16] to show that the trans transition state is 6 kcal/mol more stable than the cis transition state.



5a



5b

Concluding Remarks

In this paper, we compared the energetics of the biradical formation between (*Z*)-hepta-1,2,4-trien-6-yne and (*Z*)-hexa-1,5-diyn-3-ene, the models of the enyne–allene and the enediyne systems, respectively, with the CASSCF and the MRSDCI methods. The present computational results show that the reaction of (*Z*)-hepta-1,2,4-trien-6-yne is more exothermic and requires a lower activation energy than (*Z*)-hexa-1,5-diyn-3-ene, qualitatively agreeing with the experiments. In the reaction of the eneyne–allene system, a π radical on the benzylic methylene is formed, which is more stable than the σ radical of the product of the enediyne system. This results in the more exothermic enyne–allene reaction. Also, the in-plane π bonds of the enyne–allene system are located anti with respect to the partially formed CC σ bond, which leads to the smaller four-electron repulsion at the transition state and thus the lower activation energy. Those of the enediyne system are located syn, and thus the four-electron repulsion is larger.

Acknowledgment. We are grateful to Dr. R. Nagata and Prof. I. Saito for suggestions and valuable discussions. The calculations were carried out at the IMS computer center.

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(16) Bernardi, F.; Bottoni, A.; Robb, M. A.; Schlegel, H. B.; Tonachini, G. *J. Am. Chem. Soc.* **1985**, *107*, 2260.