ORGANIC LETTERS

2005
Vol. 7, No. 3
507−510

Computational Investigation of the Reactivity of a Hexadienyne Derivative

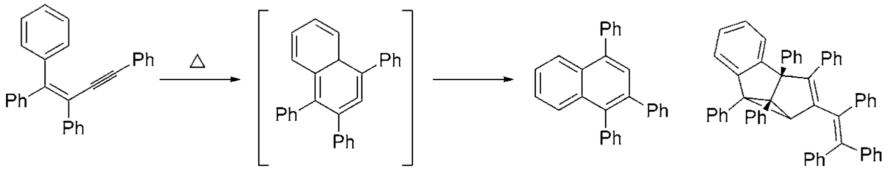
Aviva E. Litovitz,[†] Barry K. Carpenter,*[,†] and Henning Hopf*[,‡]

Department of Chemistry and Chemical Biology, Baker Laboratory,
Cornell University, Ithaca, New York 14853-1301, and Institut für Organische Chemie,
Technische Universität Braunschweig, Hagenring 30, 38106 Braunschweig, Germany

bkc1@cornell.edu; h.hopf@tu-bs.de

Received December 13, 2004

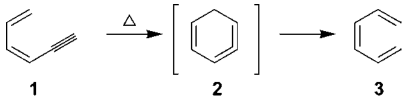
ABSTRACT



The mechanisms of perphenylbutenyne reactivity are examined through B3LYP and multireference ab initio calculations on model systems. Calculations for the formation of a naphthalene derivative suggest a process similar to that seen previously in the literature. A new mechanism for perphenylbutenyne dimerization to form a semibullvalene derivative is proposed and supported by calculations.

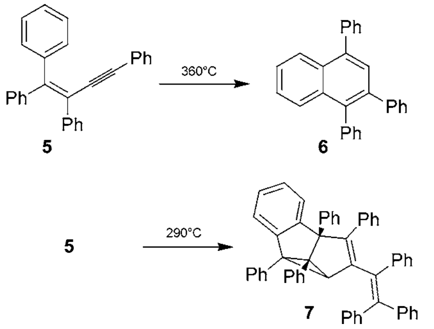
When heated, hexadienynes such as **1** are known to cyclize to aromatic products (Scheme 1).[1,2] More recently, it has been observed that some of these hexadienyne derivatives can also give new, more complex dimerization products.[3,4] Key to the diversity of products appears to be a high-energy cyclic allene or isobenzene structure (**2**) that is formed initially from the hexadienyne.[3,5] A better understanding of the reactivity of these strained allenes may lead to new synthetic routes to a variety of hydrocarbon skeletons.

Scheme 1. Cyclization of Hexadienynes



We chose to look more closely at one of these systems, the recently reported reactivity of perphenylbutenyne, **5** (Scheme 2).[4] Heating perphenylbutenyne in toluene for 7 h at 360 °C gave the anticipated aromatization product, 1,3,4-triphenylnaphthalene (**6**). However, heating for 5 h at 290 °C gave an unexpected product, the dimer **7**, a semibullvalene derivative.

Scheme 2. Reactivity of Perphenylbutenyne

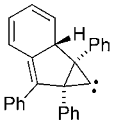


The original report of these experimental results was accompanied by a tentative mechanism that involved isomerization of the allene to a cyclopropylidene intermediate (**8**).[4]

[†] Cornell University.
[‡] Technische Universität Braunschweig.
(1) Hopf, H.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 680.
(2) Review: Zimmermann, G. *Eur. J. Org. Chem.* **2001**, 457.
(3) Hopf, H.; Berger, H.; Zimmermann, G.; Nuchter, U.; Jones, P. G.; Dix, I. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1187.
(4) Berger, H.; Hopf, H.; Dix, I.; Jones, P. G. *Eur. J. Org. Chem.* **2004**, 3401.
(5) Prall, M.; Kruger, A.; Schreiner, P. R.; Hopf, H. *Chem. Eur. J.* **2001**, *7*, 4386.

10.1021/ol047447n CCC: $30.25

A potential problem with this mechanism was that the



8

cyclopropylidene might be inaccessibly high in energy with respect to the cyclic allene, as it is known to be in similar cases.[6] The present calculations were undertaken to see whether that was the case for the reaction under study, and, if so, whether an alternative could be proposed.

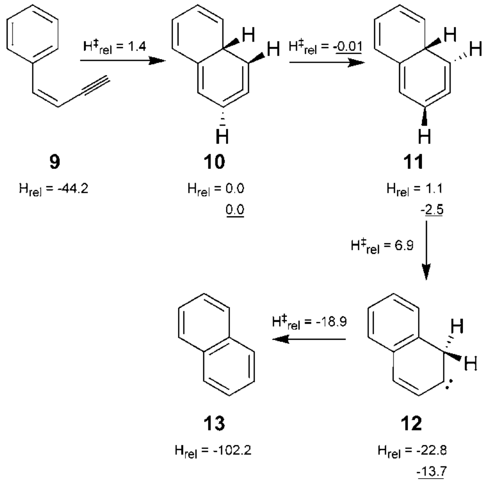
The calculations were carried out at the B3LYP/6-31+G-(d,p)[7−9] level unless otherwise noted. Although multiconfigurational methods better describe singlet biradical intermediates, the size of the present system would make such calculations very time-consuming.

Unrestricted density functional theory (DFT) has been shown to describe singlet biradicals reasonably well in many cases,[5,10] and so that method was employed here. The calculations were also simplified by removing pendant phenyl groups (as shown in Schemes 3−5). The second molecule of perphenylbutenyne in the bimolecular mechanism (Scheme 5) was represented by acetylene.

Of the two products, the formation of the naphthalene was the simpler to explain (Scheme 3). According to our calculations, the cyclization to the cyclic allene **10** occurs over an enthalpy barrier of 45.6 kcal/mol to give the allene at 44.2 kcal/mol relative to the starting material, **9**. These values are somewhat larger than those reported for similar cyclic allenes[5] as here aromaticity is lost in the cyclization.

Naphthalene formation is then predicted to occur through two [1,2] hydrogen shifts, again comparable to similar systems.[5] Before the first hydrogen migration can take place, **10** must isomerize so that the two adjacent hydrogens are on opposite faces (as in **11)**. The transition state for this isomerization could not be found at the B3LYP level so the multireference method CASPT2-g3(10,10)/cc-pVDZ//CASSCF(10,10)/6-31G(d)[11,12] was used to calculate the two cyclic allene isomers, the transition state between them and the cyclic carbene (Scheme 3). The transition state between the two allene isomers is slightly lower in enthalpy than **10**, when zero-point energies are included, implying that the isomerization is essentially barrierless.

Scheme 3. Enthalpies for the Formation of Naphthalene Relative to Cyclic Allene **10** (kcal/mol)[a]



[a] B3LYP/6-31+G(d,p) enthalpies are in plain text and CASPT2-g3(10,10)/cc-pVDZ//CASSCF(10,10)/6-31G(d) enthalpies are underlined.

After the isomerization to form **11** a [1,2] hydrogen shift gives the carbene **12**. Multireference calculations located both singlet states of **12**. DFT calculations gave only one singlet carbene with both carbene electrons paired in the sp^2 in-plane orbital ($^1A'$). Using multireference methods, we were able to find enthalpies for this closed-shell carbene as well as for the open-shell singlet carbene with one carbene electron in the sp^2 in-plane orbital and the other in a π-orbital ($^1A''$). The closed-shell carbene is more stable by 1.8 kcal/mol according to the CASPT2 results.

The relative enthalpies for the closed-shell carbene, **12**, and the cyclic allene, **10**, differ markedly at the two computational levels. At the CASPT2 level, **12** is located at −13.7 kcal/mol with respect to **10**, whereas B3LYP gives a value of −22.8 kcal/mol. The CASPT2 result is probably more trustworthy, because the cyclic allene has significant multireference character. Given this discrepancy, multireference calculations ideally would be performed on the transition states leading to **12** and to naphthalene but such transition-state searches would be very computationally

---

(6) Bettinger, H. F.; Schleyer, P. v. R.; Schreiner, P. R.; Schaefer, H. F. *J. Org. Chem.* **1997**, *62*, 9267.

(7) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T., Jr.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revision B.05; Gaussian, Inc.: Pittsburgh, PA, 2003.

(8) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

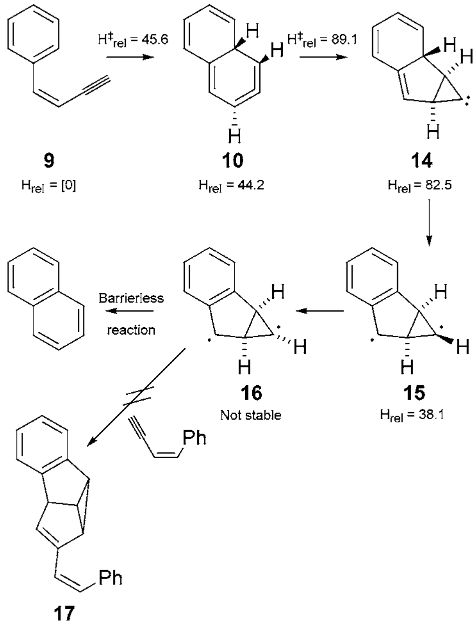
(9) Unrestricted calculations were performed on open-shell species. Restricted calculations were stability checked if questionable.

(10) Cramer, C. *Essentials of Computational Chemistry*; John Wiley & Sons Ltd.: West Sussex, England, 2002.

(11) Andersson, K.; Barysz, M.; Bernhardsson, A.; Blomberg, M. R. A.; Cooper, D. L.; Fleig, T.; Fulscher, M. P.; de Graaf, C.; Hess, B. A.; Karlstrom, G.; Lindh, R.; Malmqvist, P.-Å.; Neogrady, P.; Olsen, J.; Roos, B. O.; Sadlej, A. J.; Schutz, M.; Schimmelpfennig, B.; Seijo, L.; Serrano-Andres, L.; Siegbahn, P. E. M.; Stalring, J.; Thorsteinsson, T.; Veryazov; V.; Widmark, P.-O. *MOLCAS*, Version 5.4; Lund University: Sweden, 2002.

(12) Zero point energy (ZPE) corrections were calculated at the CASSCF level. They were scaled by 0.942 so that the ZPE of the closed-shell carbene at the CASSCF level matched the ZPE of the B3LYP calculations. The active space for these calculations included all π and π^* orbitals as well as the carbene sp^2 and p orbitals.

Scheme 4. DFT Enthalpies for the Previously Proposed Pathway Relative to the Phenylbutenyne (kcal/mol)

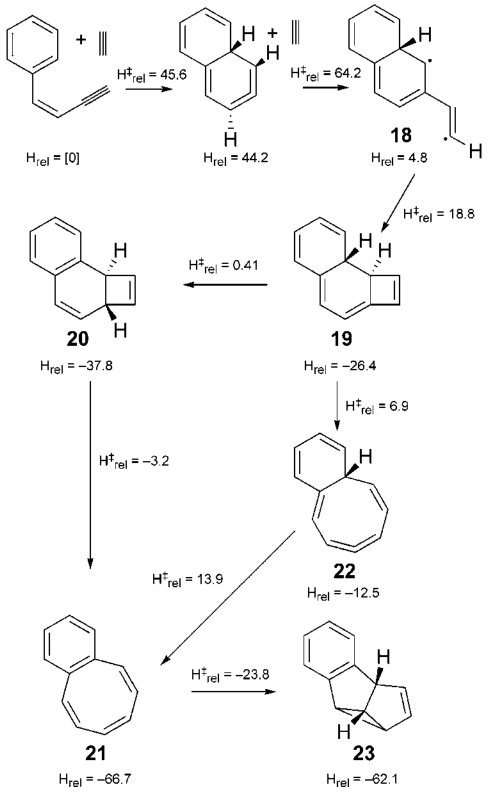


demanding. DFT calculations have the transition state to naphthalene at a relatively low enthalpy of −18.9 kcal/mol so its exact magnitude is unimportant. The transition state between **11** and **12**, however, is likely to be the rate-determining step for the formation of naphthalene. It should thus be noted that this activation enthalpy is unlikely to be quantitatively correct.

Besides the naphthalene product, a semibullvalene derivative (**7**) was experimentally observed, product of the dimerization of the starting material. It is here that our understanding of the mechanism differs from that previously suggested.[4] The original proposal is illustrated in Scheme 4 along with our calculated enthalpies relative to the starting phenylbutenyne (**9**). After formation of the cyclic allene as discussed above, it was suggested that the reaction could proceed through the cyclopropylidene **14**. The calculations show that **14** should be inaccessible, with an enthalpy for the intermediate of 82.5 kcal/mol and an activation enthalpy for its formation of 89.1 kcal/mol relative to **9**. Even at the elevated temperature of 290 °C, this is too high a barrier to be crossed at a reasonable rate.

It was then suggested in the original paper that, after a [1,3] hydrogen shift to form the resonance-stabilized biradical, **15**, the intermediate could react with another equivalent of the starting material to form the final isolated product. For this to occur, the cyclopropyl radical must first epimerize so that the vicinal hydrogens are all on the same face. This second cyclopropyl biradical, **16**, was not a stationary point under the computational method used; it led without barrier to naphthalene. Naphthalene is an observed product of the reaction, but its formation through this route does not explain the generation of the dimer. The calculations thus illuminated two significant problems with the previously suggested mechanism: the high energy of the cyclopropylidene intermediate and the favored formation of naphthalene through this pathway instead of the observed intermolecular reaction.

Scheme 5. DFT Enthalpies for the Newly Proposed Mechanism Relative to the Phenylbutenyne and Acetylene (kcal/mol)



Because of these issues with the above mechanism, alternative ways to generate the dimer were explored (Scheme 5). Allenes are known to participate in [2 + 2] cycloadditions[2] and this seemed a likely route as an alternative to the cyclopropylidene intermediate. We propose reaction of the cyclic allene with the triple bond of another molecule of the perphenylbutenyne. To lessen the size of the calculation, the phenyl substituents that are in the experimental materials were removed and the second molecule of perphenylbutenyne was replaced with acetylene. With these changes, the product biradical (**18**) has an enthalpy of 4.8 kcal/mol with an activation enthalpy of 64.2 kcal/mol with respect to the starting phenylbutenyne and acetylene. This is a rather large enthalpy barrier, albeit lower than the barrier to cyclopropylidene formation discussed above (89.1 kcal/mol). Because of our simplifications to the system, biradical intermediate **18** and the transition state leading to it lack the resonance stabilization that would be provided in the original material by the α-phenyl ring. The effect of this stabilization on the activation enthalpy barrier can be estimated by comparing the enthalpies for addition of a methyl radical to acetylene and to the β carbon of phenylacetylene.[13] These model reactions are much more exothermic than the formation of **18**. Thus we estimate an upper limit on the magnitude of phenyl stabilization in **18** by the difference in reaction enthalpies for the methyl additions to acetylene and phenylacetylene and a lower limit by the activation enthalpy difference between these additions. Based on these calculations, we would expect the enthalpy barrier to be 1.9−5.4 kcal/mol lower than the calculated 64.2 kcal/mol for the system in Scheme 5. However, the resulting barrier height is still too high for large amounts of the semibullvalene product to form at 290 °C, as is found experimentally. The discrepancy is likely because of difficulties in modeling this reaction at the B3LYP level of theory.

Even with this large enthalpic barrier, the dimer was not formed when the experiment was run at higher temperatures (360 °C).[4] The entropic demands of dimerization in the rate-determining step probably preclude the formation of the semibullvalene derivative at higher temperatures.

After the formation of the biradical, all barrier heights in Scheme 5 are substantially lower, giving a more facile route to the dimer than the mechanism of Scheme 4. The biradical **18** can cyclize with two different stereochemistries; the more stable product isomer is shown (**19**). Two mechanistic alternatives were considered at this point. A [1,5] hydrogen shift to **20** can occur, followed by electrocyclic ring opening giving **21**. Alternatively, the order can be reversed with the cyclobutene ring opening to give allene **22** followed by the [1,5] hydrogen shift to generate **21**. Both routes regenerate aromaticity and relieve the strain of the cyclobutene ring. The first pathway has lower enthalpy barriers and so is preferred.

In this first pathway, one can look at the reactivity of **20** as involving the electrocyclic ring opening of either the cyclohexadiene or cyclobutene rings; both of these openings would result in the same bridging bond breaking but in differing double-bond placement. The allowed processes have the six-membered ring opening in a disrotatory fashion or the four-membered ring opening in a conrotatory fashion.[14] It is the conrotatory opening that would result in the less-strained cyclooctatetraene. As well, the movement of double bonds in a cyclohexadiene-ring opening would break the aromaticity of the adjacent aromatic ring. In this case, then, both the preferred stereochemistry of the ring opening and the stability of the aromatic ring work together to predict that the ring opening will be of the cyclobutene moiety to give the cyclooctatetraene derivative **21**.

As cyclooctatetraene species are known to interconvert with semibullvalene structures[15] and the mechanistic target was the semibullvalene **23** (observed as **7**), the pathway of Scheme 5 continued to look plausible. A transition state was found that led directly from **21** to **23**. Normally, semibullvalene derivatives can undergo Cope rearrangements.[16] In this case, however, the loss of aromaticity necessitated by the rearrangement raises the energy of the other possible product, making it no longer a stationary point. Thus only one semibullvalene product is observed.

An analysis of these mechanisms allows us to make some predictions for experiment. The two mechanisms for the dimerization differ in that the addition of the second molecule of perphenylbutenyne occurs in the original proposal as a last, low-energy step (Scheme 4), whereas in the proposal given here, this addition occurs earlier in the rate-determining step (Scheme 5). Thus an experimental first-order dependence on the concentration of reagent in formation of the dimer would support the original proposal and a second-order dependence would support the second mechanism. As well, the two pathways result in different bond connectivities in the final products. Therefore, an isotopic-labeling experiment would also help discriminate between the two routes to the dimerization. Both of these experiments would help us further determine which mechanism is more plausible or perhaps suggest that it is an entirely different process that is involved in this new pathway.

Acknowledgment. Support of this work by the National Science Foundation (grant CHE-0212149 to B.K.C.) and the Department of Energy (grant DE-FG02-98ER14857 to B.K.C.) is gratefully acknowledged. A.E.L. thanks the National Science and Engineering Research Council of Canada for a Postgraduate Scholarship.

Supporting Information Available: Cartesian coordinates, absolute energies, and frequencies for all stationary points. This material is available free of charge via the Internet at http://pubs.acs.org.

OL047447N

---

[13] In all of the reactions with acetylene, it is the cis form of the vinyl radical that forms first. The cis form rearranges over a relatively low barrier to the more stable trans form of the radical. In contrast, the phenyl-stabilized radicals are linear.

[14] Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, 1970.

[15] Martin, H.-D.; Urbanek, T.; Walsh, R. *J. Am. Chem. Soc.* **1985**, *107*, 5532.

[16] March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley & Sons: New York, 1992.