

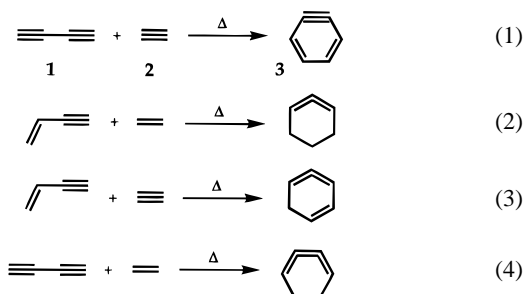
Thermolysis of 1,3,8-Nonatriyne: Evidence for Intramolecular [2 + 4] Cycloaromatization to a Benzyne Intermediate

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Cycloaromatizations have been of intense recent interest because of their potential involvement in the chemistry of antitumor agents.¹ In principle, aromatic rings might also be prepared directly by diyne + alkyne cycloaddition reactions, as exemplified by eq 1, which yields *o*-benzyne. This conceptually simple process is a logical extension of known enyne + alkene, enyne + alkyne, and diyne + alkene cycloadditions (eqs 2–4) which have been previously demonstrated in substances where the reacting components are held together by a three-carbon tether.^{2,3} In flash vacuum thermolysis experiments, the



intermediacy of strained cyclic cumulenes⁴ was supported by the observation of predictable secondary processes. We describe here experimental evidence for 1,3-diyne + alkyne [2 + 4] cycloaromatization (eq 1) as a new mode of Diels–Alder type cycloaddition. Although this process might seem geometrically improbable, ab initio computational studies support the feasibility of the parent diyne + alkyne cycloaddition step.⁵

1,3,8-Nonatriyne (**5**) was prepared in several steps as shown in Scheme 1. Alkylation of 1,4-bis(trimethylsilyl)butadiyne and subsequent TMS removal gave **5** in 50% overall yield. Flash vacuum thermolysis of pure **5** at 10^{-2} Torr in a quartz apparatus at 580 °C cleanly yielded two products, which were identified by comparison to authentic samples as indan (**7**, 86%) and indene (**8**, 14%). These accounted for >95% of the products, and no starting material remained. Some soot also formed in this pyrolysis but there was no evidence for the expected dimers of benzyne **6**. At 650 °C, the product ratio was 60:40, which suggests that indene is predominantly a secondary product of indan dehydrogenation. This has literature precedent⁶ and was confirmed by pyrolysis of indan under the same conditions.

The most straightforward route to the observed product is through intramolecular [2 + 4] cycloaddition to give benzyne derivative **6**. There is ample precedent for reduction of benzynes under similar pyrolytic reaction conditions.⁷ However, thermal

(1) For reviews, see: (a) Wisniewski-Grissom, J.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. (b) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207.

(2) Burrell, R. C.; Daoust, K. J.; Bradley, A. Z.; DiRico, K. J.; Johnson, R. P. *J. Am. Chem. Soc.* **1996**, *118*, 4218.

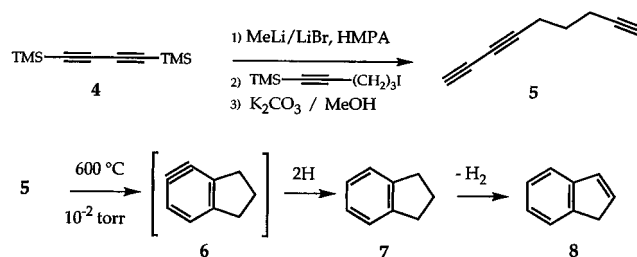
(3) Danheiser, R. L.; Gould, A. E.; Fernandez de la Predilla, R.; Helgason, A. L. *J. Org. Chem.* **1994**, *59*, 5514.

(4) Review: Johnson, R. P. *Chem. Rev.* **1989**, *89*, 1111.

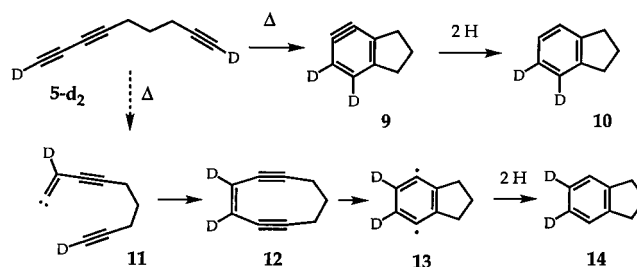
(5) For preliminary report, see: *Abstracts of Papers*, 213th National Meeting of the American Chemical Society, San Francisco, CA, April, 1997; American Chemical Society: Washington, DC, 1997; ORGN 0459.

(6) Penninger, J. M. L. *Int. J. Chem. Kinet.* **1982**, *14*, 761.

Scheme 1



Scheme 2



1,2-shifts are well-known for alkynes; one alternative mechanism (Scheme 2) would pass through vinylidene **11**. C–H bond insertion and Bergman cyclization^{1,8} might give *p*-benzyne **13** and, hence, indan.⁹ Eneidyne **12** is unknown, although larger ring homologues have been investigated.¹⁰ To distinguish these two paths, we prepared and pyrolyzed **5-d₂**. The ¹H NMR spectrum of the isolated indan cleanly showed an AB spin system for the aromatic hydrogens; these results are consistent with structure **10** and a [2 + 4] cycloaddition mechanism. Similar deuterium labeling was observed in the indene isolated from these reactions.

Ab initio calculations were carried out to estimate the geometric and energetic feasibility of a diyne plus alkyne cycloaddition. Stationary points were located at the MP2(FC)/6-31G* level, followed by analytic Hessian calculation and single-point MP4SDTQ/6-31G* energy evaluation.^{11,12} This level of theory correctly describes energetics of the parent Diels–Alder reaction to within a few kcal/mol.¹³ The transition state is predicted to have C_{2v} symmetry, with a nascent C–C bond distance of 2.196 Å; this is in good agreement with geometries of other pericyclic transition states.¹⁴ The predicted

(7) Benzyne reduction has been seen under a variety of conditions. (a) Berry, S. R.; Spokes, G. N.; Stiles, M. *J. Am. Chem. Soc.* **1962**, *84*, 3570. (b) Corbett, T. G.; Porter, Q. N. *Aust. J. Chem.* **1965**, *18*, 1781. (c) Bove, J. L.; Arrigo, J. R. *Chem. Ind.* **1984**, 803. (d) Brown, R. F. C.; Coulston, K. J.; Eastwood, F. W. *Tetrahedron Lett.* **1996**, *37*, 6819.

(8) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25. Lockhart, T. P.; Comita, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4082. Bharucha, K. N.; Marsh, R. M.; Minto, R. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 3120.

(9) As an alternative mechanism, a referee has suggested that 1,2-hydrogen shift at C-9 would give an intermediate carbene that could cyclize to cyclonon-3,5-diyne, which might further rearrange to indan. However, models show the divalent center in this intermediate to be >4 Å distant from the alkyne hydrogen, thus cyclization seems highly unlikely. By contrast, in carbene **11**, this distance is ca. 1.7 Å.

(10) Nicolau, K. C.; Zuccarello, G.; Ogawa, Y.; Schweiger, E. J.; Kumazawa, T. *J. Am. Chem. Soc.* **1988**, *110*, 4866.

(11) (a) Spartan, version 4.01; Wavefunction Inc.: Irvine, CA, 1993. (b) Gaussian 92, revision E.1; Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1992.

(12) For benzyne geometry, see: Hobza, P.; Zahradnik, R.; Hess, B. A.; Radziszewski, J. G. *Theor. Chim. Acta* **1994**, *88*, 233.

(13) (a) Bachrach, S.; Liu, M. J. *Org. Chem.* **1992**, *57*, 6736. (b) Rowley, D.; Steiner, H. *Discuss. Faraday Soc.* **1951**, *10*, 198.

(14) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682.

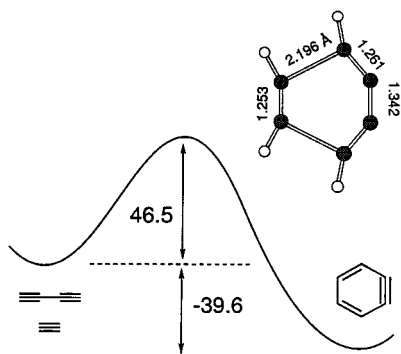


Figure 1. Free energy diagram (kcal/mol, 25 °C) and MP2/6-31G* transition state structure for the cycloaddition of acetylene with butadiyne.

free energy changes are summarized in Figure 1. Intramolecular reaction should decrease ΔG^\ddagger by ca. 5 kcal/mol because of the smaller $T\Delta S^\ddagger$ component. The large predicted reaction exothermicity is consistent with the formation of a new aromatic ring, while the high activation energy must derive from the dramatic molecular distortion necessary to reach the transition state geometry. Most notably, the predicted activation free energy is only 9.0 kcal/mol higher than that calculated for the cycloaddition of ethyne with butadiene.² The electronic features of this cycloaromatization transition state are unusual because two orthogonal orbital arrays must come together simultaneously. In this process, the out-of-plane π orbitals simply merge to form the aromatic ring π system, while the in-plane π bonds transform into σ bond orbitals and the in-plane benzyne π bond. Both transition state arrays are aromatic in this doubly symmetry allowed process. A stepwise cycloaddition is also possible; we have not yet explored the energetics of this process.

Polyynes are known to be explosive,¹⁵ and Vollhardt has recently shown that such explosions might generate ordered carbon arrays.¹⁶ One sample of triyne **5** underwent a mild explosion during reduced pressure distillation, with instantaneous formation of heavy soot. Similarly, purification by preparative gas chromatography at 130 °C resulted in an injector port filled with fine black powder; this material is currently being analyzed.

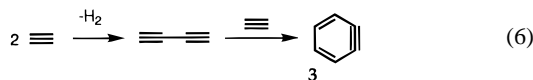
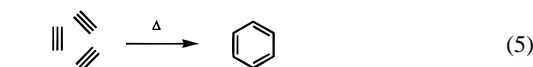
Both our experiments and model ab initio calculations are thus consistent with intramolecular [2 + 4] cycloaromatization of triyne **5** to benzyne **6**. Further reaction gives indan and indene. This cycloaddition has little precedent, but might potentially be involved in diverse high-temperature processes such as the Berthelot benzene synthesis. In 1866, Berthelot

(15) (a) Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes and Cumulenes*; Elsevier Publishing Company: Amstrdam, 1981; references therein. (b) For a review of polyyne structures, see: Bunz, U. H. F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1073.

(16) Boese, R.; Matzger, A. J.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1997**, *119*, 2052.

(17) Berthelot, M. *Liebigs Ann. Chem.* **1867**, *141*, 173.

reported the thermal trimerization of acetylene to benzene.¹⁷ Concerted cyclotrimerization (eq 5) is very unlikely because this will have large enthalpic and entropic barriers.¹⁸ Among many possible stepwise mechanisms, Fields and Meyerson proposed dimerization of acetylene to butadiyne followed by [2 + 4] cycloaddition (eq 6) to give benzene.¹⁹ In support of



this mechanism, they observed that co-pyrolysis of acetylene and phthalic anhydride yielded naphthalene and other aromatics. Both the thermal dimerization of acetylene²⁰ and the reduction of benzyne to benzene⁷ are preceded, but experimental evidence for the key cycloaddition step has been scant. The present data are consistent with the mechanism depicted in eq 6. Beyond this, one of the enduring questions in combustion chemistry is the mechanism for formation of aromatic rings.²¹ Some types of flames are rich in alkynes, and we speculate that cycloadditions such as those shown in eqs 1–4 may play an important role in six-membered ring formation in combustion.

Our results thus support the existence of a sixth mode of Diels–Alder cycloaddition, thus completing this series of pericyclic reactions. This new mode of cycloaromatization complements the many electrocyclizations that have been reported.^{1,22}

Acknowledgment. We are grateful to the National Science Foundation for support of this research and to the Pittsburgh Supercomputer Center for a generous allocation of supercomputer time. We thank Professors Curt Wentrue and Charles Zercher for helpful discussions.

Supporting Information Available: Selected characterization data and spectra (5 pages). See any current masthead page for ordering and Internet access information.

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(18) For theoretical studies, see: (a) Houk, K. N.; Gandour, R. W.; Strozier, R. W.; Rondan, N. G.; Paquette, L. A. *J. Am. Chem. Soc.* **1979**, *101*, 6797. (b) Bach, R. D.; Wolber, G. J.; Schlegel, H. B. *J. Am. Chem. Soc.* **1985**, *107*, 2837. (c) Wagenseller, P. E.; Birney, D. M.; Roy, D. *J. Org. Chem.* **1995**, *60*, 2853.

(19) (a) Fields, E. K.; Meyerson, S. *Tetrahedron Lett.* **1967**, 571. (b) Fields, E. K.; Meyerson, S. In *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic: New York, 1968; Vol. 6, p 1. (c) Brown, R. F. C. *Pyrolytic Methods in Organic Synthesis*; Academic: New York, 1980; p 65.

(20) Kiefer, J. H.; Von Drasek, W. A. *Int. J. Chem. Kinet.* **1990**, *22*, 747.

(21) For example, see: (a) Miller, J. A.; Melius, C. F. *Combust. Flame* **1992**, *91*, 21. (b) Miller, J. A.; Volponi, J. V.; Pauwels, J.-F. *Combust. Flame* **1996**, *105*, 451. (c) Melius, C. F.; Miller, J. A.; Evleth, E. M. *Symp. (Int.) Combust.* **1992**, *24*, 621–8.

(22) As this paper was completed, a related cycloaromatization was reported: Miyawaki, K.; Suzuki, R.; Kawano, T.; Ueda, I. *Tetrahedron Lett.* **1997**, *38*, 3943.