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Norbornyne: A Cycloalkyne Reacting Like A Dicarbene

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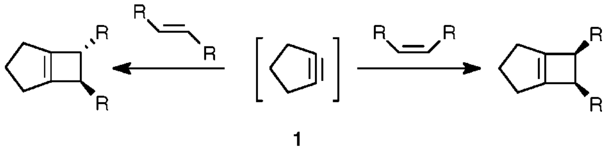
Cyclopentyne (**1**) is a fascinating highly strained cyclo-alkyne primarily because of its predilection for forming $[2+2]$ cycloadducts (Scheme 1).[1] As illustrated in the scheme, the complete retention of stereochemistry in this process bespeaks a concerted process, a most provocative result in light of the “rules” of Woodward and Hoffmann[2] that govern pericyclic reactions. Nonetheless, we found theoretical support for concert in this transformation through the use of semiempirical methodologies.[3] We now report experimental results that point toward a novel rationale for the stereospecific formation of $[2+2]$ cycloadducts that circumvents characterization of the process as a $[\pi 2s + \pi 2s]$ reaction. They also support the conjecture that distorted alkynes might exhibit reactivity consistent with their having the character of a dicarbene.[4]

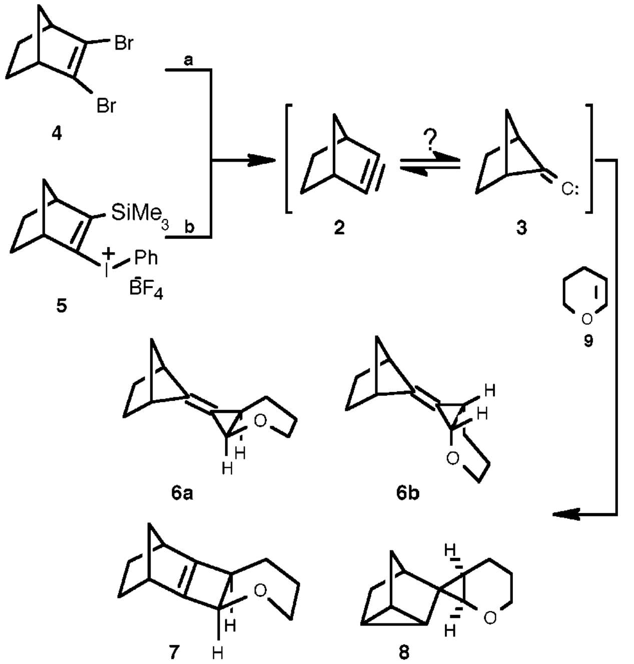
The synthesis of norbornyne (**2**, Scheme 2) has been claimed previously,[5] but its pericyclic chemistry with alkenes was not explored. Our studies of this chemistry, in which **2** was generated from the precursors **4** and **5**, revealed that cycloadducts **6ab**, **7**, and **8** were produced in overall yields of 40 and 10%, respectively (Scheme 2).[6] Variation in the ratios of cycloadducts from precursors **4** and **5** is thought to result from the potential role of lithium cation in the decomposition of **4**.[7] In this context, the ratio afforded by iodonium salt **5** is believed to represent the intrinsic reactivity of norbornyne (**2**).[8]

Methylenecyclopropanes **6ab** provide evidence for our long-sought goal of identifying a system wherein a simple cycloalkyne isomerizes to its isomeric alkylidenecarbene, in this case **3**.[9] Formation of cycloadduct **7** bespeaks the “usual” $[2 + 2]$ pericyclic mode of a strained cycloalkyne,[1] but that of the major product **8** is unprecedented in cycloalkyne chemistry. Consideration of a possible mechanism for its generation (Scheme 3) provides a framework for understanding the details of the “$[2 + 2]$” cycloadditions of cycloalkynes.

Scheme 1

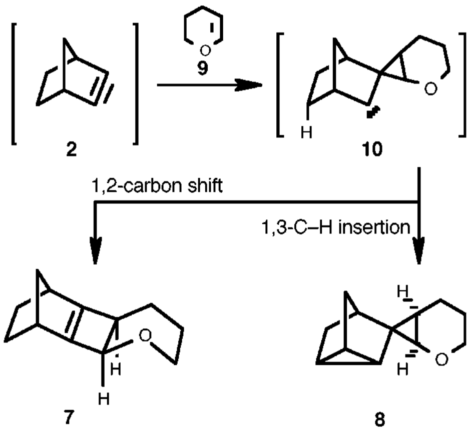


Scheme 2[a]



[a] (a) Li, THF, 60 °C, 1 h, 40%. Ratio of **6a:6b:7:8** = 1:1:9:18. (b) TBAF, CH_2Cl_2, −80 °C, 15 min, 10%. Ratio of **6a:6b:7:8** = 1:1:2.1:2.9.

Scheme 3



Norbornyne (**2**), a highly bent cycloalkyne, is expected to have a low-lying LUMO for the in-plane π-like bond.[10] Approach of dihydropyran at one end of the triple bond of **2** would foster a HOMO−LUMO interaction with this low-lying orbital. This interaction, coupled with mixing of the LUMO of dihydropyran with the HOMO of the “normal” out-of-plane π-bond of **2** could lead in one step to cyclopropylcarbene **10**, which could then function as a common intermediate leading to **7** and **8** (Scheme

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[1] (a) Fitjer, L.; Modaressi, S. *Tetrahedron Lett.* **1983**, *24*, 5495−5498. (b) Gilbert, J. C.; Baze, M. E. *J. Am. Chem. Soc.* **1984**, *106*, 1885−1886.

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

[3] (a) Gilbert, J. C.; Kirschner, S. *Tetrahedron Lett.* **1993**, *34*, 599−602. (b) Gilbert, J. C.; Kirschner, S. *Tetrahedron Lett.* **1993**, *34*, 603−606. (c) Gilbert, J. C.; Kirschner, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1105−1106. (d) Gilbert, J. C.; Kirschner, S. *Tetrahedron* **1996**, *52*, 2279−2290.

[4] Lu. P. J.; Pan, W.; Jones, M., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 8315−8318; Suhadra, C. P.; Pan, W.; Jones, M., Jr. *Tetrahedron* **1999**, *55*, 14547−14554.

[5] Gassman, P. G.; Gennick, I. *J. Org. Chem.* **1980**, *45*, 5211−5213.

[6] (a) Structures of adducts **6ab**, **7**, **8**, and **11** were proven by HRMS and multidimensional NMR spectroscopy. In addition, the NMR data for adduct **8** was analyzed by the SESAMI[6b] structure elucidation program and provided one and only one structure solution which corresponds to adduct **8**. (b) Madison, M. S.; Schultz, K.; Andrey, A.; Munk, M. E. *Internet J. Chem.* **1998**, *1*, 34. (c) We thank Prof. Morton Munk (Arizona State University) for performing this calculation and for permission to cite.

[7] Gilbert, J. C.; McKinley, E. G.; Hou, D. R. *Tetrahedron* **1997**, *29*, 9891−9902; Gilbert, J. C.; Hou, D. R.; Grimme, J. W. *J. Org. Chem.* **1999**, *64*, 1529−1534.

[8] The ratios of cycloadducts afforded from the decomposition of **5** showed a modest temperature dependence over the range −80−25 °C and did not approach that for precursor **4**.

[9] Isomerization of an alkyne to its isomeric alkylidenecarbene in a polycyclic framework has been reported. Marchand, A. P.; Namboothiri, I. N. N.; Ganguily, B.; Bott, S. G. *J. Am. Chem. Soc.* **1998**, *120*, 6871−6876.

[10] Strozier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340−1343.

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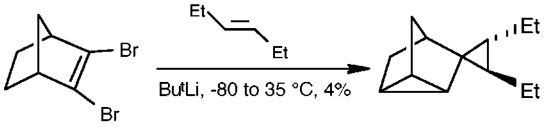
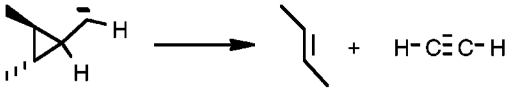
3). There is literature precedent for both the 1,2-carbon shift, which is known to occur with retention of configuration at the migrating carbon atom,[11a] and the 1,3-C−H insertion.[11b] There has been speculation that strained cycloalkynes might behave as though they were vicinal dicarbenes, but experimental evidence for this for a thermally generated species has not been obtained.[4,12] The formation of **8** provides the most compelling evidence to date in support of the dicarbene hypothesis.

Reaction of norbornyne (**2**), generated from dibromide **4**, with *trans*-3-hexene was found to afford **11**,[6a] the only adduct produced in the reaction (eq 1). The retention of the stereochemistry present in the alkene is consistent with the cyclopropanation step being the result of a concerted singlet process. The cleavage of a cyclopropylcarbene to an alkyne and an alkene, the reverse of this process, is known to occur with retention of configuration (eq 2);[13] applying the Principle of Microscopic Reversibility[14] lends support to the proposition that norbornyne is functioning as though it were a singlet dicarbene in its cycloaddition to alkenes.

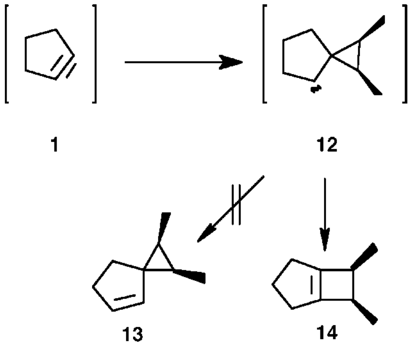


4 **11** (1)



(2)

Scheme 4



We believe that the hypothesis outlined in Scheme 3 is applicable to cyclopentyne (**1**) itself (Scheme 4). In this case, initial [2 + 1] cycloaddition as outlined for **2** and dihydropyran affords the intermediate cyclopropylcarbene **12**. There are two viable intramolecular reaction channels for this intermediate, namely, 1,2-C−H insertion and 1,2-carbon shift. Previous studies of this type of carbene show the 1,2-carbon shift to be its preferred fate, often to the complete exclusion of 1,2-C−H insertion.[15] Thus, it is not surprising that the novel mechanism currently being proposed was not unveiled previously since [2 + 2] cycloadducts such as **14** would be the only expected products.

The propositions illustrated in Schemes 3 and 4 are well-precedented experimentally and nicely rationalize the [2 + 2] cycloadditions of **1** and **2** in a manner consistent with the rules of Woodward and Hoffmann. Moreover, high-level DFT calculations by Professor S. Bachrach are consistent with the hypotheses of these schemes.[16] For example, cyclopentyne and norbornyne are both calculated to undergo concerted [2 + 1] cycloadditions with alkenes to afford cyclopropylcarbenes. However, repeated attempts to find the transition state for a concerted [2 + 2] cycloaddition of **1** and **2** to alkenes using DFT methodologies have failed, despite the fact that such a pathway was found previously using semiempirical approaches.[3ab,17ab]

The hypothesis of Scheme 4 is testable, and experiments designed to accomplish this are in progress. Whether the hypothesis that bent cycloalkynes react as though they were dicarbenes applies to benzyne is an intriguing issue and merits exploration as well.

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Supporting Information Available: Synthetic and experimental procedures for **4** and **5** as well as multidimensional NMR spectra used to establish structures for adducts **7** and **8** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) (a) Freeman, P. K.; Kuper, D. G. *J. Org. Chem.* **1965**, *30*, 1047−1049; Wilt, J. W.; Kosturik, J. M.; Orlowski, R. C. *J. Org. Chem.* **1965**, *30*, 1052. (b) Krieger, H.; Masar, S. E.; Routsalainen, H. *Suom. Kemistil.* **1966**, *39B*, 237; Shapiro, R. H. *Tetrahedron Lett.* **1966**, 3401−3407; Powell, J. W.; Whiting, M. C. *Tetrahedron* **1959**, *7*, 305−310; Reusch, W. W.; DiCarlo, M. W.; Traynor, L. *J. Org. Chem.* **1961,** *26*, 1711−1713.

(12) Photochemically promoted “dicarbene” chemistry has been reported: Shim, S. C.; Lee, T. S *J. Org. Chem.* **1988**, *53*, 2410−2413; Lee, T. S.; Lee, S. J.; Shim, S. C. *J. Org. Chem.* **1990**, *55*, 4544−4549; Lee, S. J.; Shim, S. C. *Tetrahedron Lett.* **1990**, *31*, 6196−6200; Shim, S. C. *J. Am. Chem. Soc., Chem. Commun.* **1996**, 2609−2614.

(13) Berson, J. A.; Bauer, W.; Campbell, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 7515−7516.

(14) Cope, A. C.; Haven, A. C., Jr.; Ramo, F. L. Trumbull, E. R. *J. Am. Chem. Soc.* **1952**, *74*, 4867−4871.

(15) (a) Kirmse W.; Pook, K. H. *Angew. Chem., Int. Ed. Engl.* **1966**, *6*, 594; Wiberg K. B., Burgmaier, G. J.; Warner, P. *J. Am. Chem. Soc.* **1971**, *93*, 246−247. (b) Sullivan, M. B.; Cramer, C. J. *J. Am. Chem. Soc.* **2000**, *122*, 5588−5596.

(16) Bachrach, S.; Gilbert, J. C.; Laird, D. W. J. Am. Chem. Soc. **2001**, *123*, 6706−6707.

(17) (a) Kirschner, S. Unpublished results cited in Gilbert, J. C.; Kirschner, S. *Adv. Theor. Interesting Mol.* **1998**, *4*, 203−244. (b) Laird, D. Unpublished results.