Intramolecular Thermal Cyclization of Bicyclobutane and Allene

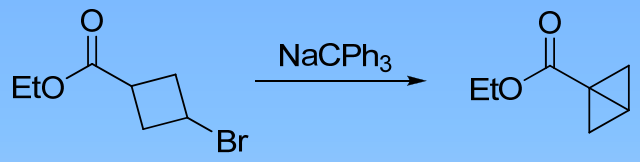
Research Topic Seminar

Mike Yang

March 13th, 2010

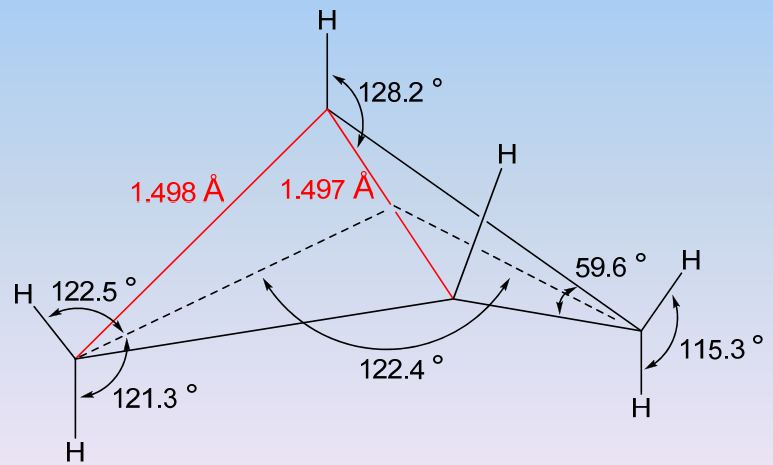
Bicyclobutane Background

- First prepared by Wiberg and Ciula in 1959



Wiberg, K. B.; Ciula, R. P. *J. Am. Chem. Soc.* **1959**, *81*, 5261

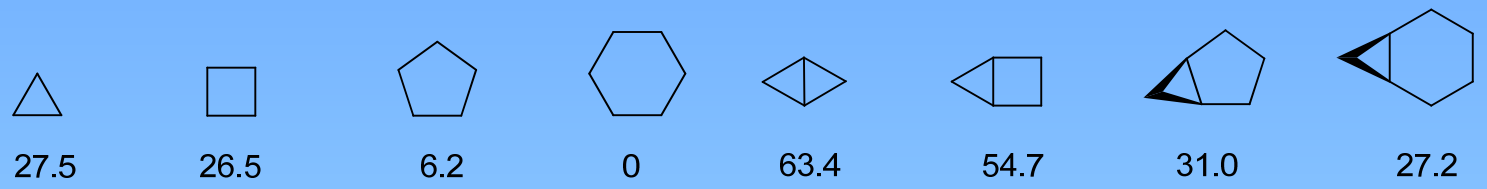
- Structural elucidation - vibrational spectra, NMR, electron diffraction, and microwave spectroscopy



Cox, K. W.; Harmony, M. D.; Nelson, G.; Wiberg, K. B. *J. Chem. Phys.* **1969**, *50*, 1976-1980.

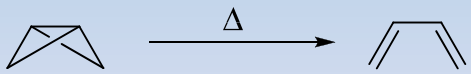
Strain in Bicyclobutane

- Bicyclobutane has high calculated strain energy (kcal/mol)



Wiberg, K. B. *Angew. Chem. Int. Ed.* **1986**, *25*, 312–322.

- Strain exceed sum of two cyclopropanes
  - 1,3 carbon-carbon interaction
    - Bauld, N. L.; Cessac, J.; Holloway, R. L. *J. Am. Chem. Soc.* **1977**, *99*, 8140–8144.
  - Baeyer strain
    - D. Baric, Z. B. Maksic, *Theor. Chem. Acc.* **2005**, *114*, 222–228.
- High kinetic barrier for thermal decompostion

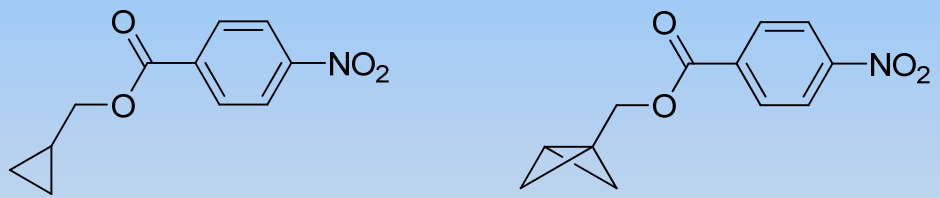


  - 40.6 kcal/mol
    - Frey, H. M.; Stevens, I. D. R. *Trans. Faraday Soc.* **1965**, *61*, 90–94.
  - 41.4 kcal/mol
    - Srinivasan, R.; Levi, A. A.; Haller, I. *J. Phys. Chem.* **1965**, *69*, 1775–1777.

p-Character of Bicyclobutane Central Bond

- High p-character of the bicyclobutane central bond
  - 96% *p*-character in the central C-C bond of bicyclobutane
    - Calculations: Newton, M. D.; Schulman, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 767–773.
  - 89% *p*-character in the central C-C bond of bicyclobutane
    - Coupling constants: Pomerantz, M.; Hillenbrand, D. *J. Am. Chem. Soc.* **1973**, *95*, 5809–5810.
  - 83% *p*-character in C-C bond of cyclopropane

- Solvolysis of bicyclobutane is 1000x faster than the cyclopropyl derivative



k_{rel} 1 >1000

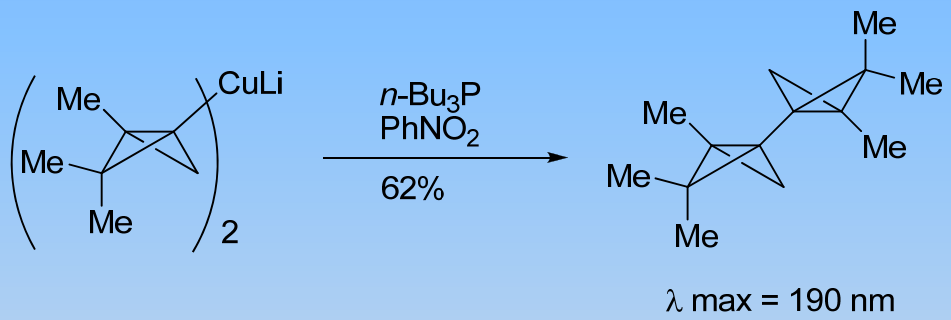
Wiberg, K. B.; Lampman, G. M.; Ciula, R. P.; Connor, D. S.; Schertler, P.; Lavanish, J. *Tetrahedron* **1965**, *21*, 2749.

- Bridgehead proton is acidic due to its high *s* character

Closs, G. L.; Larrabee, R. B. *Tetrahedron Lett*. **1965**, *21*, 287.

Conjugation of Bicyclobutane Central Bonds

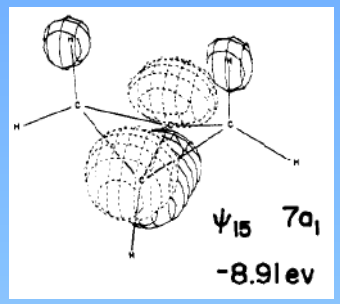
- Red shift in conjugated bicyclobutanes



Moore, W. R.; Costin, C. R. *J. Am. Chem. Soc.* **1971**, *93* , 4910–4912.

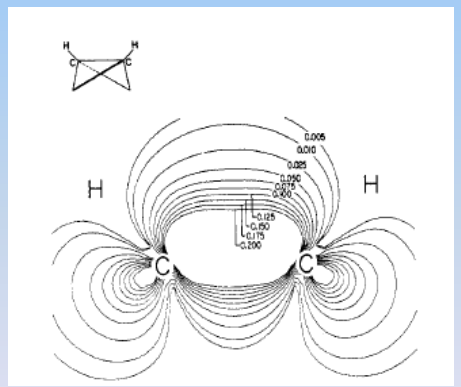
HOMO of Bicyclobutanes

- HOMO of a bicyclobutane is associated with the central bond



Wiberg, K. B.; Ellison, G. B.; Peters, K. S. *J. Am. Chem. Soc.* **1977**, *99*, 3941–3946.

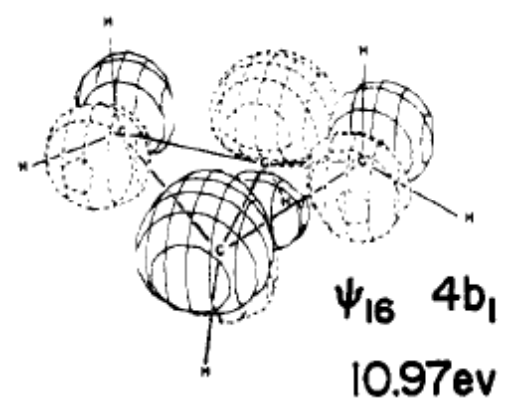
- Electrophilic attach approaches from an equatorial trajectory



Newton, M. D.; Schulman, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 767–773.

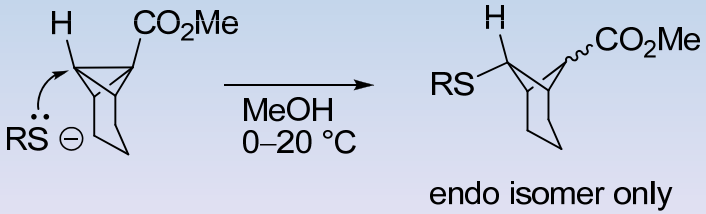
LUMO of Bicyclobutanes

- LUMO also associated with the central bond



Wiberg, K. B.; Ellison, G. B.; Peters, K. S. *J. Am. Chem. Soc.* **1977**, *99*, 3941–3946.

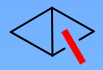
- Equatorial attack of nucleophile

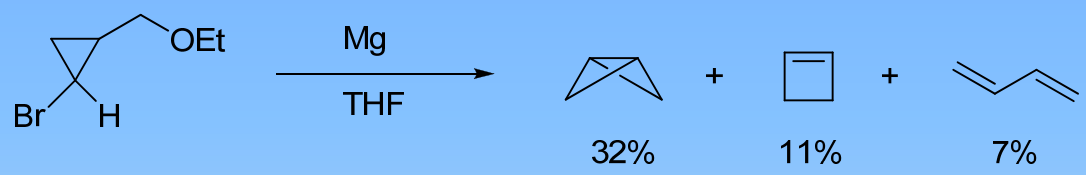


endo isomer only

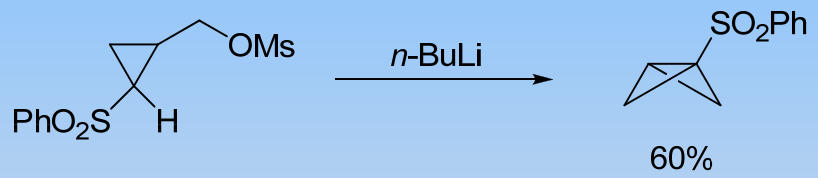
Lehn, J. M.;Wipff, J. *J. Chem. Soc. Chem. Comm.* **1973**, 747–748.

Synthesis of Bicyclobutanes
Disconnection: Lateral Bond Part I

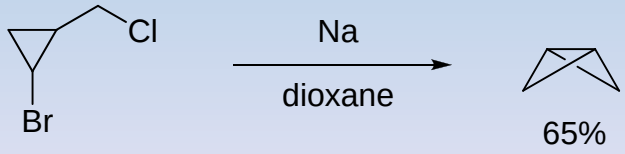
- Ring-closure of lateral bond 
  - Ionic reactions
    - Grignard



    - Deprotonation

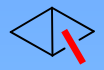


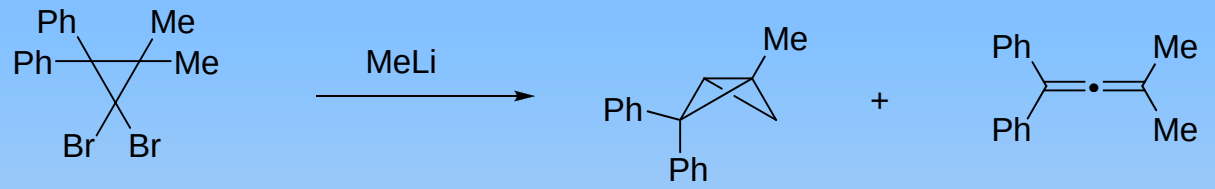
    - Metal reduction of C-X bond



S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

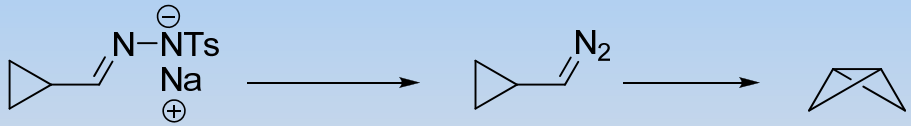
Synthesis of Bicyclobutanes
Disconnection: Lateral Bond Part II

- Ring-closure of lateral bond 
  - Carbenes
    - From Dibromocyclopropanes



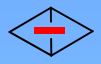
73% 27%

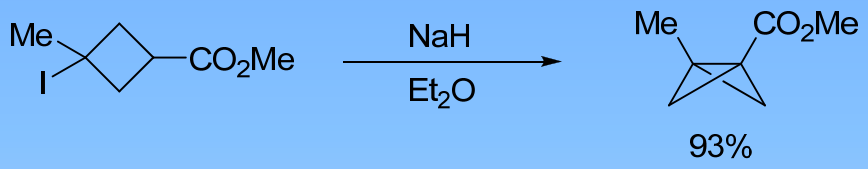
    - From decomposition of diazocompounds



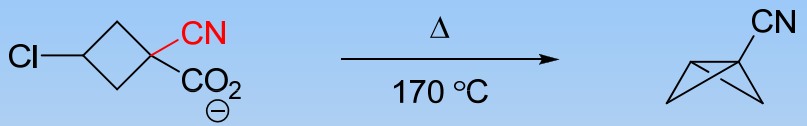
S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

Synthesis of Bicyclobutanes Disconnection: Central Bond

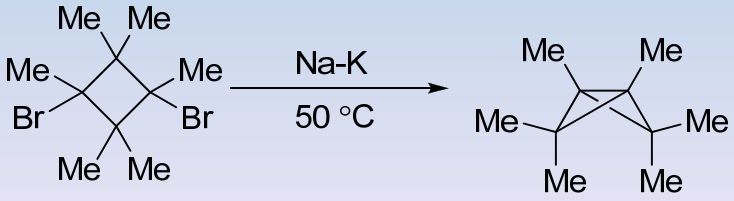
- Ring-closure of the central bond 
  - Deprotonation



  - Decarboxylation

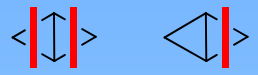


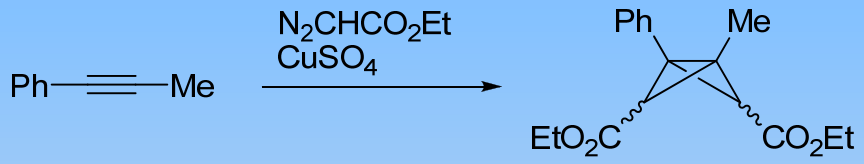
  - Wurtz coupling



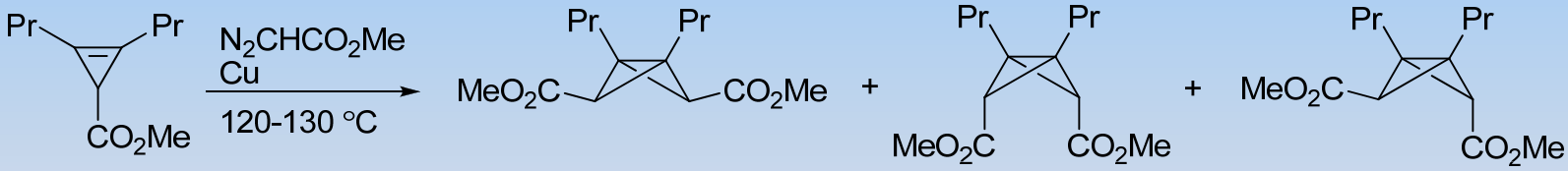
S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

Synthesis of Bicyclobutanes – Disconnection: Multiple Lateral bonds I

- Cyclopropanation of alkynes or cyclopropenes 
  - Double carbene insertion



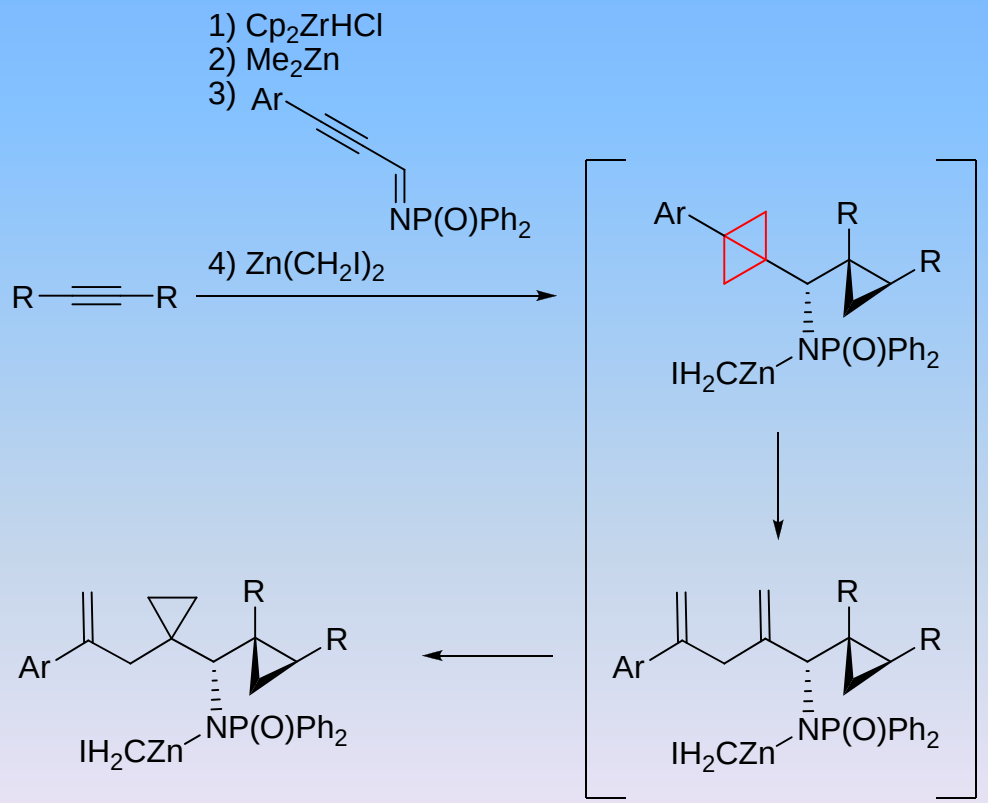
  - Insertion not diastereoselective



S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

Synthesis of Bicyclobutanes – Disconnection: Multiple Lateral bonds II

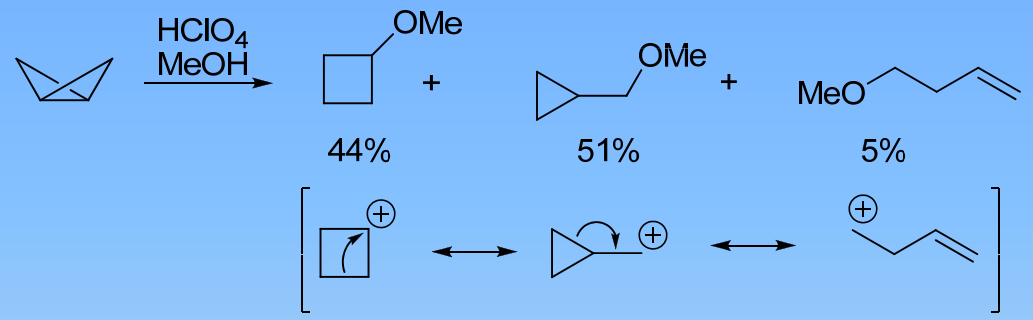
- Cyclopropanation of alkynes with zinc carbenoids

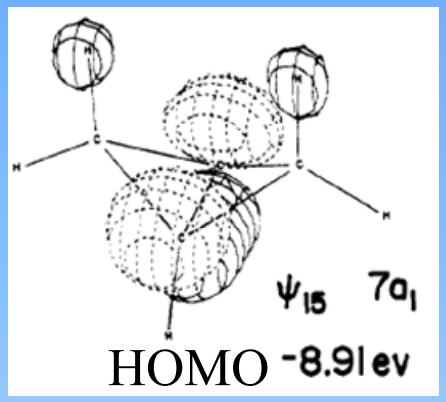


Wipf, P.; Stephenson, C. R. J.; Okumura, K. *J. Am. Chem. Soc.* **2003**, *125*, 14694–14695.

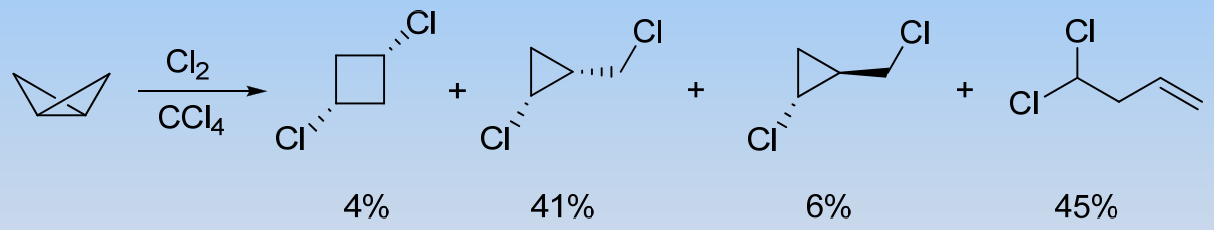
Electrophilic Addition to Bicyclobutanes

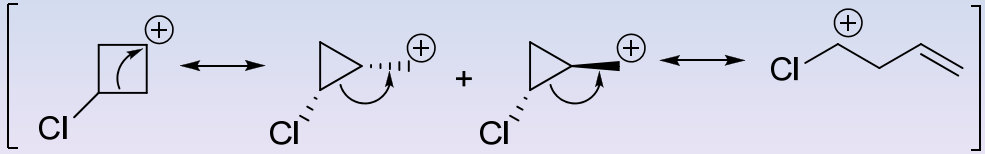
- Acid-catalyzed addition to bicyclobutanes





- Addition of halogens

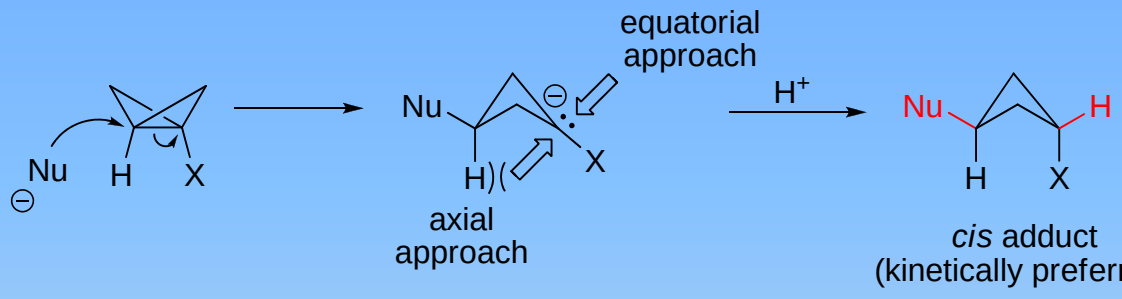


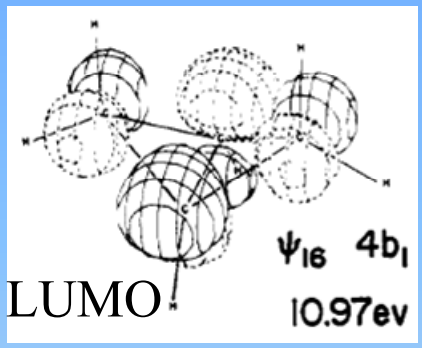


S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

Nucleophilic Addition to Bicyclobutanes

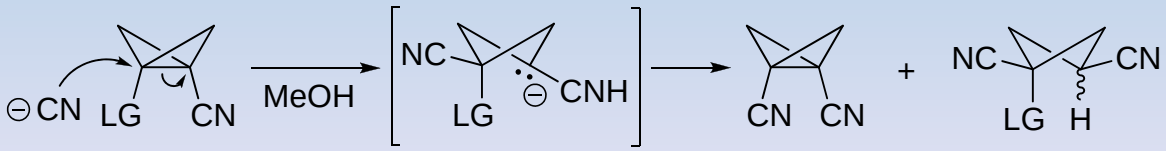
- Nucleophilic addition





  - Equatorial attack by the nucleophile
  - *cis* adduct = kinetic product

- Addition-elimination reactions

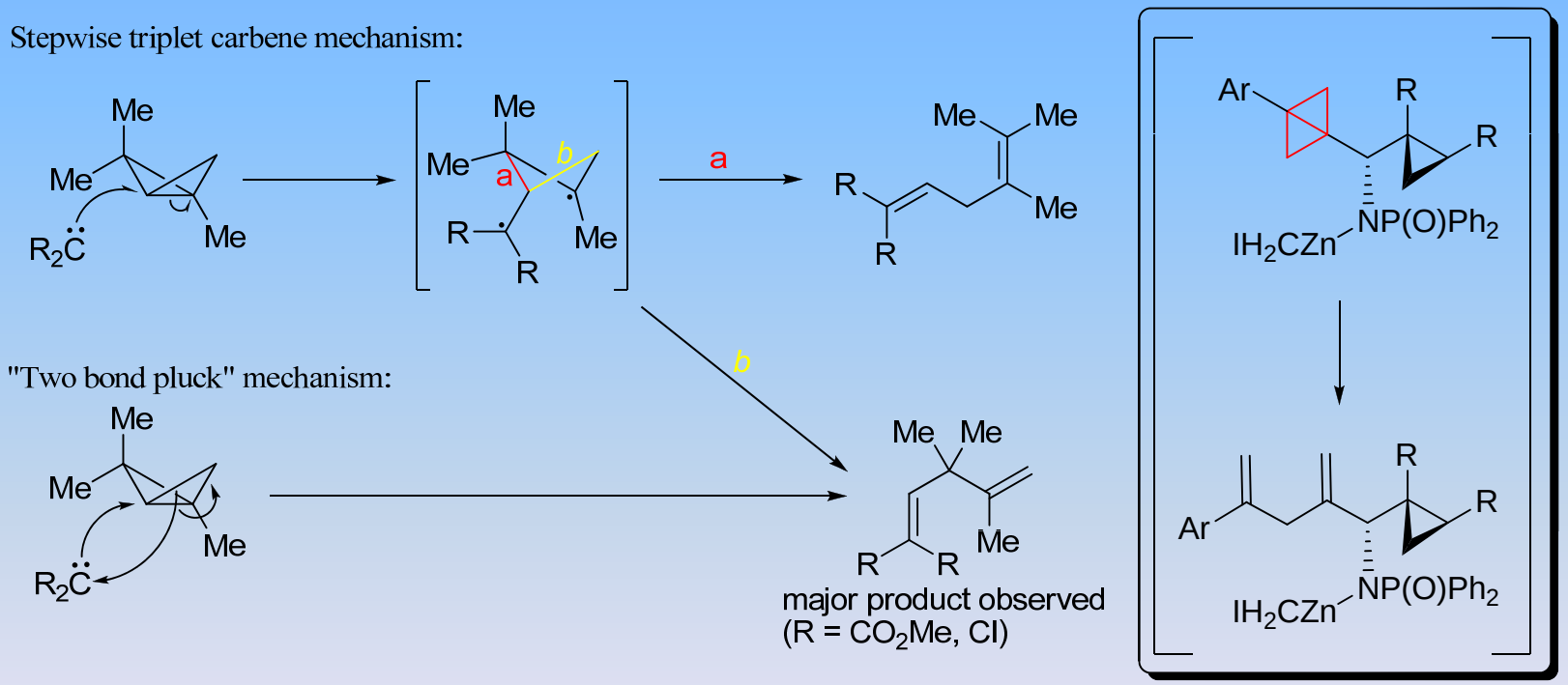


LG = Cl	17%	40%
LG = Br	60%	0%

S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.

Reactions of Bicyclobutanes with Carbenes

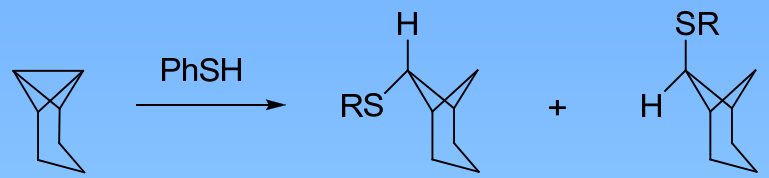
- In addition to C-H insertion, carbenes can react with bicyclobutanes to form skip dienes.



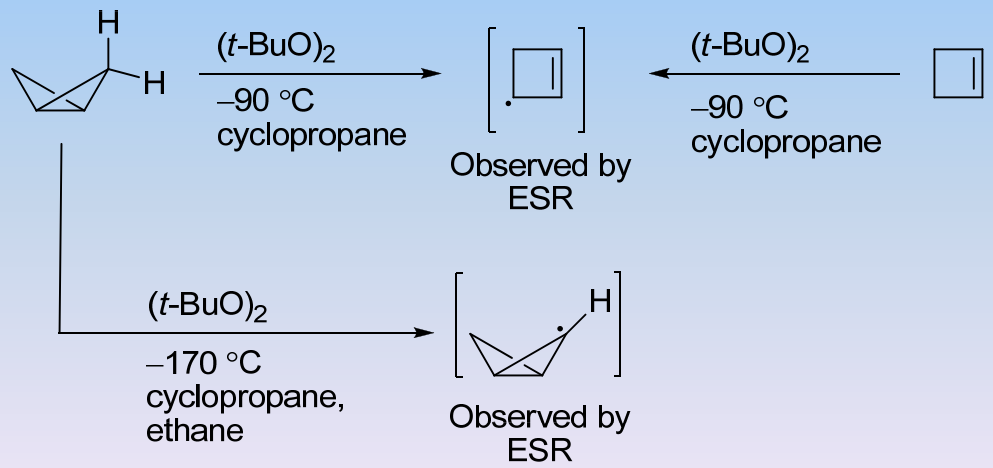
Jackson, J. E.; Mock, G. B.; Tetef, M. L.; Zheng, G.-X.; Jones, M., Jr. *Tetrahedron* **1985**, *41*, 1453–1464.

Radical Reactions of Bicyclobutanes

- Addition to the central bond

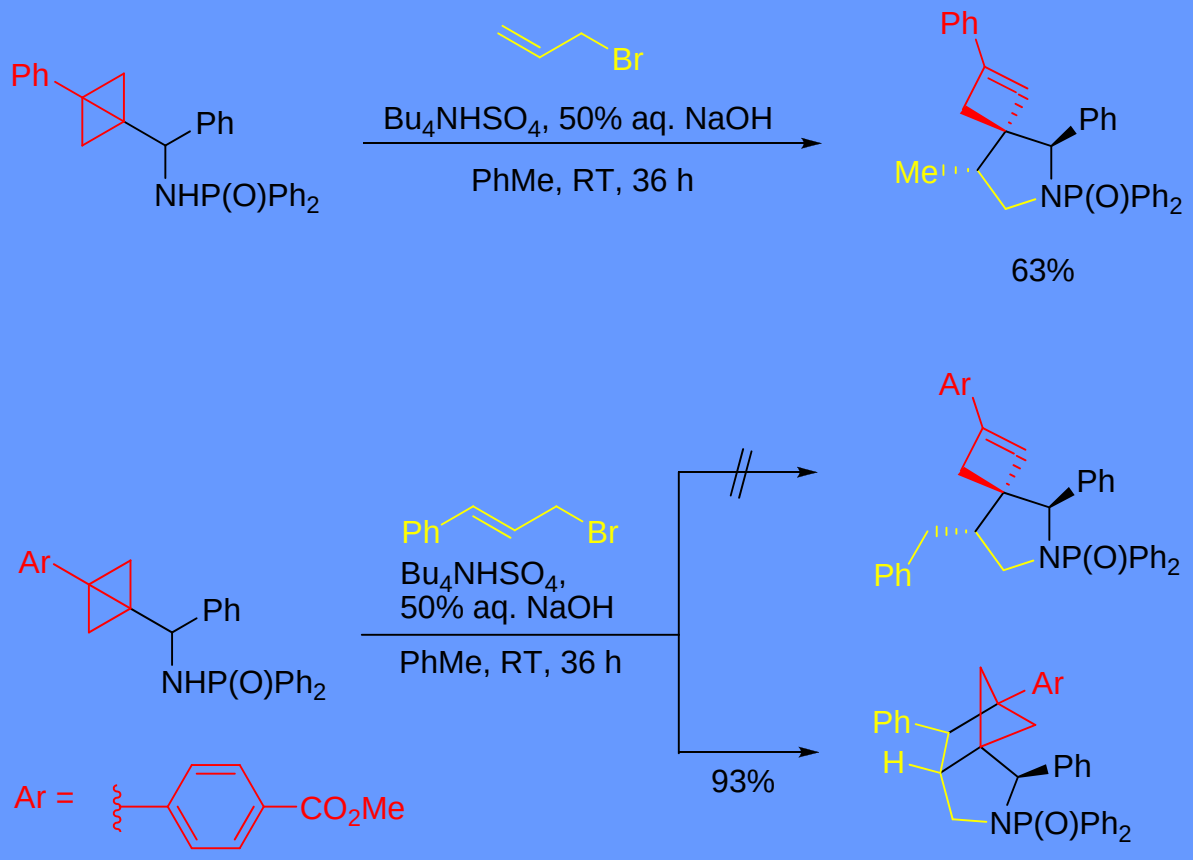


- Hydrogen abstraction



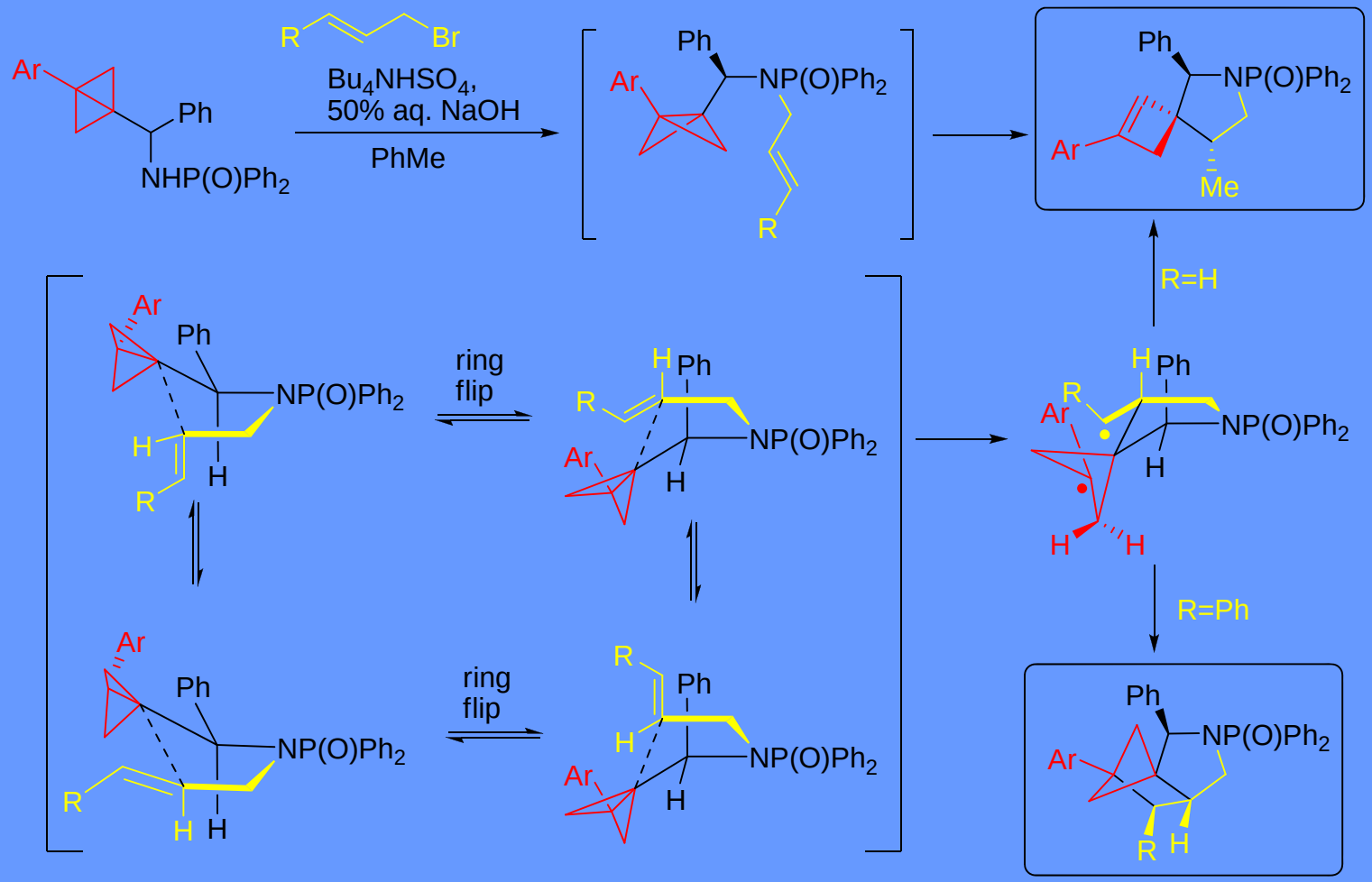
S. Hoz, in *The Chemistry of the Cyclopropyl Group*, ed. Z. Rappoport, J. Wiley & Sons, New York, **1987**, vol 1, ch. 19.
Krusic, P. J.; Jesson, J. P.; Kochi, J. K. *J. Am. Chem. Soc.* **1969**, *91*, 4566–4568.

Intramolecular Cyclization of Bicyclobutane-alkene



Wipf, P.; Walczak, M. A. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 4172–4175.

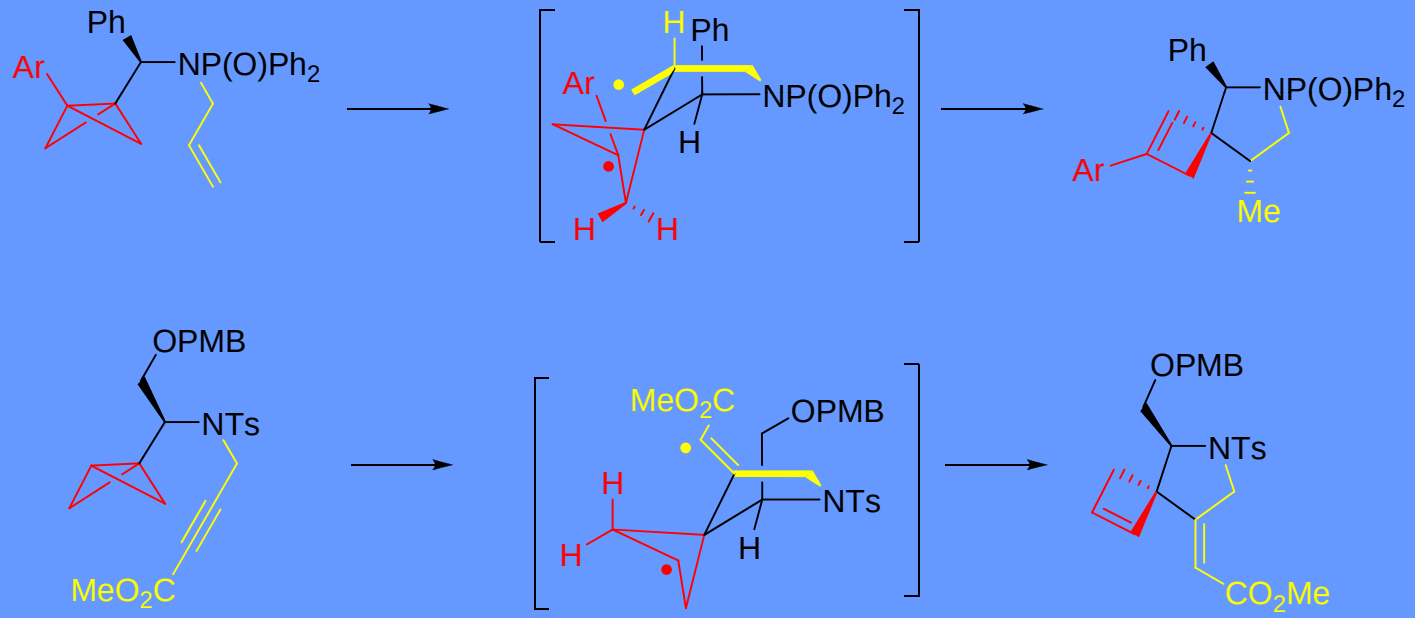
Mechanism of the Thermal Bicyclobutanes-alkene Intramolecular Cyclization



Wipf, P.; Walczak, M. A. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 4172–4175.
Walczak, M. A. A.; Shin, B.-k.; Wipf, P.; Saxena, S. *Org. Biomol. Chem*. **2009**, *7*, 2363–2366.

Cyclization with Alkynoates

- Difference in hybridization between vinyl and alkyl radical influences selectivity in hydrogen abstraction.



Acknowledgement

- Professor Wipf
- Wipf Group
- University of Pittsburgh Chemistry Department
- NIH P50 program