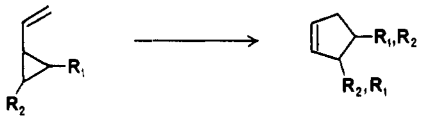
Communications

Synthesis of 3-Cyclopentenols by Alkoxy-Accelerated Vinylcyclopropane Rearrangement

Summary: Lithium salts of 2-vinyl-1-cyclopropanols undergo vinylcyclopropane rearrangement at room temperature, providing an efficient method for the conversion of 1,3-dienes to functionalized cyclopentenes.

Sir: Although the vinylcyclopropane rearrangement has been the subject of intensive mechanistic investigation,[1] to date this reaction has seen limited application in total synthesis.[2] Several features of this thermal rearrangement compromise its synthetic utility. High temperatures (frequently in the range 500–600 °C) are required to effect the reaction, particularly in sterically congested systems, and such conditions may not be compatible with highly functionalized synthetic intermediates. Rearrangements of 2,3-disubstituted 1-vinylcyclopropanes are regiochemically ambiguous and can result in mixtures of isomeric products.[3]

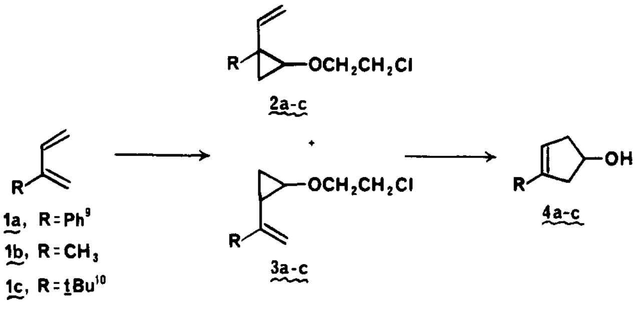


The intervention of side reactions further limits the scope of the thermal vinylcyclopropane rearrangement. Cyclopropanes bearing syn vinyl and CH groups are subject to homo-[1,5]-sigmatropic hydrogen migration and rarely undergo satisfactory vinylcyclopropane rearrangment.[3,4] Activation energies for homo [1,5] hydrogen shifts are typically 31–33 kcal/mol, significantly lower than the 48–52 kcal/mol required for normal thermal vinylcyclopropane rearrangements.

In this communication we describe an unusually facile vinylcyclopropane rearrangement which should not be subject to these limitations. We have found that the *lithium salts of 2-vinylcyclopropanols rearrange to cyclopentenols at 25 °C*.

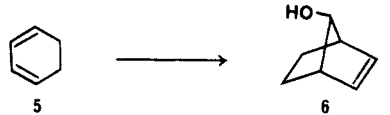
We report herein two alternate methods for the synthesis and rearrangement of 2-vinylcyclopropanols which provide efficient strategies for the two-step conversion of 1,3-dienes to functionalized cyclopentenes.

Scheme I



One convenient route to the requisite vinylcyclopropanols involves the reaction of the carbenoid :CHOCH$_2$CH$_2$Cl with conjugated dienes. Treatment of dienes **1a–c** (Scheme I) with 1.2 equiv of chloromethyl β-chloroethyl ether and 1.1 equiv of lithium 2,2,6,6-tetramethylpiperidide in diethyl ether according to the procedure of Olofson[5] generated mixtures of cyclopropyl ethers **2a–c** and **3a–c**[6] (**2a**,**3a**, 43%, 21:1; **2b** 42%; **2c**,**3c**, 54%, 2:3).[7] Ether cleavage and rearrangement of the resulting salts could then be effected in a single step. Exposure of the phenyl derivatives **2a**,**3a** to 5 equiv of *n*-butyllithium[8] in diethyl ether–hexane (0–25 °C, 1 h) directly afforded 3-phenyl-3-cyclopentenol (**4a**), mp 80–82 °C, in 90% yield following chromatographic purification.[11] Similar reaction of cyclopropyl ethers **2b** and **2c**,**3c** yielded cyclopropanol salts which were stable under these conditions. However, these alkoxides underwent smooth rearrangement at 25 °C in THF, in DME, or in diethyl ether containing at least 2 equiv of hexamethylphosphoric triamide (HMPT). Thus, reaction of **2b** and **2c**,**3c** with 5 equiv of *n*-butyllithium in 1:1 ether–HMPT (25 °C, 1 h) furnished **4b** and **4c** in 69 and 95% yield.[12]

When applied to cyclic dienes, this two-step sequence provides an attractive route to bicyclic [*n*.2.1]alkenols. 1,3-Cyclohexadiene was converted to *anti*-bicyclo[2.2.1]hept-2-en-7-ol (**6**) in 24% overall yield[13] in this fashion; the syn isomer of **6** was not detected in the crude rearrangement product.



5 6

The oxygenation of lithiocyclopropanes[14] forms the basis of an alternate route to 2-vinylcyclopropanols which uti-

---

[1] Mil'vitskaya, E. M.; Tarakanova, A. V.; Plate, A. F. *Russ. Chem. Rev. (Engl. Transl.)* **1976**, *45*, 469. Gutsche, C. D.; Redmore, D. "Carbocyclic Ring Expansion Reactions"; Academic Press: New York, 1968; pp 163-70. Baldwin, J. E.; Andrews, G. D. *J. Am. Chem. Soc.* **1976**, *98*, 6705 and references cited therein.

[2] Trost, B. M.; Nishimura, Y.; Yamamoto, K.; McElvain, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 1328.

[3] For example, see: Paquette, L. A.; Henzel, R. P.; Eizember, R. F. *J. Org. Chem.* **1973**, *38*, 3257.

[4] Bahurel, Y.; Cottier, L.; Descotes, G. *Synthesis* **1974**, 118. Monti, S. A.; Cowherd, F. G.; McAninch, T. W. *J. Org. Chem.* **1975**, *40*, 2265. Mazzocchi, P. H.; Tamburin, H. J. *J. Am. Chem. Soc.* **1975**, *97*, 555.

[5] Barber, G. N.; Olofson, R. A. *Tetrahedron Lett.* **1976**, 3783.

[6] These ethers were produced as mixtures of syn and anti isomers.

[7] Isolated yields of compounds purified by chromatography. Infrared, ^{1}H NMR, and mass spectral data were fully consistent with the assigned structures.

[8] Schöllkopf, U.; Paust, J.; Al-Azrak, A.; Schumacher, H. *Chem. Ber.* **1966**, *99*, 3391. Schöllkopf, U.; Paust, J.; Patsch, M. R. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 859.

[9] Marvel, C. S.; Woolford, R. G. *J. Org. Chem.* **1958**, *23*, 1658.

[10] Korotkov, A. A.; Roguleva, L. F. *Zh. Org. Khim.* **1965**, *1*, 1180.

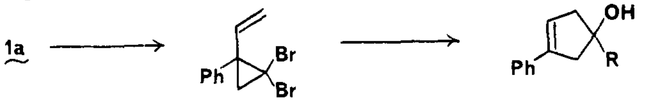
[11] Spectral data for this compound were in accord with that previously reported: Padwa, P. A.; Alexander, E. *J. Am. Chem. Soc.* **1970**, *92*, 5674.

[12] The infrared, ^{1}H and ^{13}C NMR, and high-resolution mass spectral data for these substances were fully consistent with the assigned structures.

[13] Spectral data for this compound were in accord with those previously reported: Tori, K.; Aono, K.; Hata, Y.; Mureyuki, R.; Tsuji, T.; Tanida, H. *Tetrahedron Lett.* **1966**, 9.

[14] Longone, D. T.; Wright, W. D. *Tetrahedron Lett.* **1969**, 2859.

lizes readily available dibromocyclopropanes. Reaction of diene **1a** with 1 equiv of $CHBr_3$ and 1.2 equiv of KO-*t*-Bu in pentane (0–25 °C, 15 h) produced **7** in 73% yield.[7] This



7

4a, R=H

9, R=CH_3

dibromocyclopropane was converted to **4a** in one pot in 45% yield by sequential treatment in THF with (a) 1 equiv of *n*-butyllithium (−100 °C, 0.5 h), (b) 1 equiv of methanol (−100 to −78 °C, 2 h), (c) 2 equiv of *tert*-butyllithium (−78 °C, 2 h), and (d) anhydrous CO_2-free oxygen (−78 °C, slowly bubbled through reaction mixture for 2 h), followed by stirring at 25 °C for 2 h. The tertiary cyclopentenol **9** was produced (40% yield)[12] by substituting 1 equiv of methyl iodide[15] for methanol in the above procedure.

Several mechanisms may be postulated for the alkoxy-accelerated vinylcyclopropane rearrangement: (a) homolytic cyclopropane cleavage to a stabilized diradical intermediate (**10**), followed by internal coupling; (b) initial

10

11

heterolytic cleavage to an aldehyde (**11**), followed by aldol cyclization; (c) a concerted [1,3] sigmatropic rearrangement. Dramatic acceleration of [3,3][16] and [1,3][17] sigmatropic shifts by alkoxide substituents in other systems have been observed recently, although these rearrangements commonly involve the reaction of *potassium* alkoxides in highly dissociating media. Richey[18] has previously noted the accelerating effect of methoxyl and dimethylamino substituents on the thermal vinylcyclopropane rearrangement. Perhaps significant is the exclusive formation of the anti isomer **6**, as expected for a concerted reaction controlled by orbital symmetry[19] and subjacent orbital[20] effects.

Further studies are underway to clarify the mechanism of this rearrangement, to define the scope and limitations of the process, and to develop improved methodology for the synthesis of 2-vinylcyclopropanols.

Acknowledgment. This investigation was supported in part by a Pennwalt Corp. grant from the Research Corp.

Registry No. 1a, 2288-18-8; **1b**, 78-79-5; **1c**, 2495-32-1; **2a**, 72926-75-1; **2b**, 72926-76-2; **2c**, 72926-77-3; **3a**, 72938-30-8; **3c**, 72926-78-4; **4a**, 27856-20-8; **4b**, 72926-79-5; **4c**, 72926-80-8; **5**, 592-57-4; **6**, 694-70-2; **7**, 58189-55-2; **9**, 72926-81-9.

---

[15] The alkylation of *gem*-lithiobromocyclopropanes has been described: Hiyama, T.; Kitiani, K.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 949.

[16] Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.

[17] Thies, R. W.; Seitz, E. P. *J. Chem. Soc., Chem. Commun.* **1976**, 846. Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050. Wilson, S. R.; Mao, T. M.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559. Franzus, B.; Scheinbaum, M. L.; Waters, D. L.; Bowlin, H. B. *J. Am. Chem. Soc.* **1976**, *98*, 1241.

[18] Simpson, J. M.; Richey, H. G. *Tetrahedron Lett.* **1973**, 2545. Richey, H. G.; Shull, D. W. *Ibid.* **1976**, 575.

[19] Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chimie: Weinheim/Bergstr., Germany, 1970; pp 121–2.

[20] Berson, J. A.; Salem, L. *J. Am. Chem. Soc.* **1972**, *94*, 8917.

[21] CONACyT (Mexico) predoctoral fellow.

Rick L. Danheiser,* Carlos Martinez-Davila[21]
John M. Morin, Jr.

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received January 10, 1980

Perturbed Pericyclic Reactions: Stereochemical Consequences of Heterosubstitution. A Qualitative Mechanistic Model Based on the Nonpreservation of Orbital Topology[1]

Summary: The CNDO/B potential energy surfaces for ring closure of 1- and 2-hetereosubstituted butadienes leads to results unexpected from a naive application of the Woodward–Hoffmann rules; however, the deviations are rationalizable in terms of nodal shifts within the highest occupied π molecular orbital of the dienoids as ring closure sets in.

Sir: The idea implied by orbital symmetry conservation for analyzing the course of reactions, first proposed by Woodward and Hoffmann[2] and others,[3,4] has been expressed in a variety of ways.[5-18] The isomorphism has been demonstrated rigorously for a few of the cases[19] as well as extended to a hierarchy of symmetry rules.[20] The conceptual simplicity of the various methods coupled to their efficacious application to molecular systems containing no symmetry has had a profound effect on recent theoretical and experimental developments. Two of the currently more popular expressions of the orbital symmetry principle due to Dewar[5] and Zimmerman[6] postulate that molecules without symmetry survive the analysis because orbital topology is conserved across the potential energy surface for reaction.[21] Indeed, a wide variety of presumably concerted heterocyclic transformations have been rationalized as being consistent with this postulate. In the present contribution semiempirical MO calculations are presented to show that this is not necessarily the case for certain heteroelectrocyclic reactions which are isoelectronic with the butadiene/cyclobutene interconversion. One prediction of particular importance concerns the

---

[1] Perturbed Pericyclic Reactions. 3. For part 2 see L. Carlsen and J. P. Snyder, *Tetrahedron Lett.*, 2045 (1977). For part 1 see B. Schilling and J. P. Snyder, *J. Am. Chem. Soc.*, **97**, 4422 (1975).

[2] R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

[3] K. Fukui, *Tetrahedron Lett.*, 2009, 2427 (1965); *Acc. Chem. Res.*, **4**, 57 (1971).

[4] H. C. Longuet-Higgens and E. W. Abrahamson, *J. Am. Chem. Soc.*, **87**, 2045 (1965).

[5] M. J. S. Dewar, *Tetrahedron, Suppl.*, **8**, (1966); *Chem. Soc., Spec. Publ.*, **No. 21**, 177 (1967); *Angew. Chem.*, **83**, 859 (1971); *Angew. Chem., Int. Ed. Engl.*, **10**, 761 (1971). For information on orbital isomerism, see M. J. S. Dewar, S. Kirschner, and H. W. Kollmar, *J. Am. Chem. Soc.*, **96**, 5240 (1974); M. J. S. Dewar, S. Kirschner, H. W. Kollmar, and L. E. Wade, *ibid.*, **96**, 5242 (1974).

[6] H. E. Zimmerman, *J. Am. Chem. Soc.*, **88**, 1564, 1566 (1966); *Science*, **153**, 837 (1966); *Acc. Chem. Res.*, **4**, 272 (1971).

[7] P. Millie, *Bull. Soc. Chim. Fr.*, 4031 (1966).

[8] L. Salem, *J. Am. Chem. Soc.*, **90**, 543, 553 (1968).

[9] W. T. A. M. van der Lugt and L. J. Oosterhoff, *Chem. Commun.*, 1235 (1968); *J. Am. Chem. Soc.*, **91**, 6042 (1969); *Mol. Phys.*, **18**, 177 (1970); J. J. C. Mulder and L. J. Oosterhoff, *Chem. Commun.*, 305, 307 (1970); W. J. van der Hart, J. J. C. Mulder, and L. J. Oosterhoff, *J. Am. Chem. Soc.*, **94**, 5724 (1972).

[10] C. Trindle, *J. Am. Chem. Soc.*, **92**, 3251, 3255 (1970).

[11] W. A. Goddard, III, *J. Am. Chem. Soc.*, **92**, 7520 (1970); **94**, 793 (1972).

[12] R. G. Pearson, *Theor. Chim. Acta*, **16**, 107 (1970); *Acc. Chem. Res.*, **4**, 152 (1971); *Pure Appl. Chem.*, **27**, 145 (1971); *J. Am. Chem. Soc.*, **94**, 8287 (1972); *Top. Curr. Chem.*, **41**, 75 (1973).

[13] E. B. Wilson and P. S. C. Wang, *Chem. Phys. Lett.*, **15**, 400 (1972).

[14] R. H. Hudson, *Angew. Chem.*, **85**, 63 (1971); *Angew. Chem., Int. Ed. Engl.*, **12**, 36 (1973).

[15] N. D. Epiotis, *Angew. Chem.*, **86**, 825 (1974); *Angew. Chem., Int. Ed. Engl.*, **13**, 751 (1974).

[16] D. M. Silver and M. Karplus, *J. Am. Chem. Soc.*, **97**, 2645 (1975).

[17] A. Rassat, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **274**, 730 (1972).

[18] E. A. Halevi, *Angew. Chem.*, **88**, 664 (1976); *Angew. Chem., Int. Ed. Engl.*, **15**, 593 (1976).

[19] A. C. Day, *J. Am. Chem. Soc.*, **97**, 2431 (1975).

[20] D. M. Silver, *J. Am. Chem. Soc.*, **96**, 5969 (1974).

[21] Trindle's more rigorous analysis[10] rests on the assumption that an "allowed" reaction pathway does not involve a change in nodal structure.

0022-3263/80/1945-1341$01.00/0