New Synthetic Reactions. Facile Synthesis of Oxaspiropentanes, Versatile Synthetic Intermediates[1]

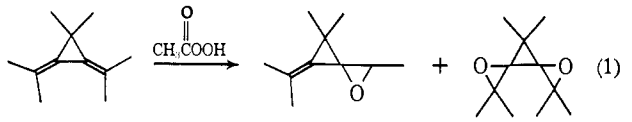
Barry M. Trost*[2] and Mitchell J. Bogdanowicz

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received February 23, 1973*

Abstract: The condensation of diphenylsulfonium cyclopropylide with aldehydes and ketones generates oxaspiropentanes in 59–100% yields. Whereas dialkyl and arylalkyl ketones allow easy isolation of these reactive compounds, the oxaspiropentanes from benzophenone and cyclopropyl methyl ketone are not isolable but rearrange to the cyclobutanones. 3-Methyloxaspiropentanes are equally accessible (83–100%) by use of diphenylsulfonium 2-methylcyclopropylide. With cyclohexanones equatorial attack occurs exclusively. Treatment of such intermediates with lithium diethylamide in hexane leads to 1-vinyl-1-cyclopropanols which may be directly derivatized with trimethylchlorosilane to give the silyl ethers. Base treatment of the vinylcyclopropanols generates 1-propionyl olefins, whereas acid treatment generates cyclobutanones. Thermal rearrangement produces the enolsilyl ethers of cyclopentanones which may be hydrolyzed with aqueous hydrochloric acid to the cyclopentanone or cleaved to the lithium enolate with methyllithium. The overall process is annelation of a cyclopentanone ring regiospecifically onto a carbonyl compound possessing an α-methyl or methylene group. This cyclopentane annelation method proceeds in overall yields of 73–85%.

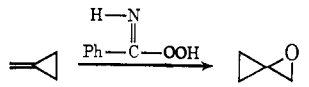
Oxaspiropentanes, monooxygen analogs of spiropentanes, are highly strained molecules which should exhibit remarkable chemical characteristics. Epoxides, oxygen relatives to cyclopropanes, have strain energies of approximately 28 kcal/mol compared with 27.5 kcal/mol for cyclopropane itself.[3] Therefore, the strain energy of oxaspiropentane may be equated to that of spiropentane which is 63 kcal/mol. This high strain energy should translate into unusual chemical reactivity accented by the normal reactivity of the epoxide toward ring opening.

Preparation of oxaspiropentanes has been limited to the epoxidations of an alkylidene cyclopropane. The first oxaspiropentane was reported by Crandall and Paulson[4] (eq 1), and the parent compound was pre-



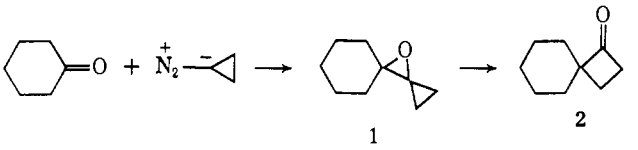
(1)

pared by Conia[5] (eq 2). Wiseman has proposed the



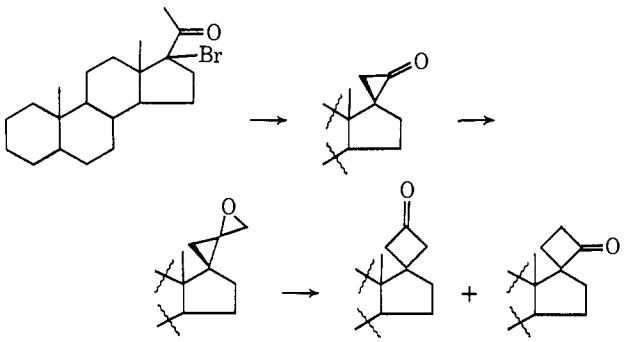
(2)

intermediacy of oxaspiropentane **1** in the formation of spiro[3.5]nonan-1-one (**2**) *via* the addition of diazocyclopropane to cyclohexanone.[6] Oxaspiropentane **1** was generated independently by epoxidation of cyclopropylidenecyclohexane.



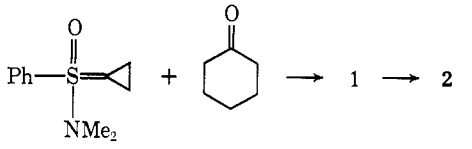
1 2

Other reactions may involve oxaspiropentanes as intermediates. Reaction of 17-halogen-16α-methyl-20-oxasteroids with excess dimethyloxosulfonium methylide leads to formation of cyclobutanones, possibly through the intermediate oxaspiropentane **3**.[7]



3

N,N-Dimethylaminophenyloxosulfonium cyclopropylide (**4**) reacts with cyclohexanone to obtain a cyclobutanone, **2**, in moderate yield *via* the oxaspiropentane **1**.[8] However, the preparation of oxaspiropentanes



4

from alkylidenecyclopropanes normally requires a tedious peracid epoxidation. Such acidic conditions are inherently incompatible with oxaspiropentanes and tend to cause ring opening. Thus, coupled with the

(1) For preliminary reports of portions of this work, see M. J. Bogdanowicz and B. M. Trost, *Tetrahedron Lett.*, 887 (1972); B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **95**, 289 (1973). This contribution represents part IX of this series on new synthetic reactions and methods.

(2) Camille and Henry Dreyfus Teacher-Scholar Grant Recipient.

(3) J. D. Cox, *Tetrahedron*, **19**, 1175 (1963).

(4) J. K. Crandall and D. R. Paulson, *J. Org. Chem.*, **33**, 991 (1968); J. K. Crandall and D. R. Paulson, *Tetrahedron Lett.*, 2751 (1969). A novel thiaspiropentane has been reported by J. G. Pacifici and C. Diebert, *J. Amer. Chem. Soc.*, **91**, 4595 (1969). An azaspiropentane has also recently been synthesized; see J. K. Crandall and W. W. Conover, *J. Chem. Soc., Chem. Commun.*, 33 (1973).

(5) J. R. Salaün and J. M. Conia, *Chem. Commun.*, 1579 (1971).

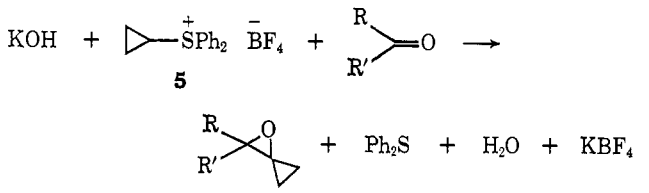
(6) J. R. Wiseman and H. F. Chan, *J. Amer. Chem. Soc.*, **92**, 4749 (1970).

(7) R. Wiechert, *Angew. Chem., Int. Ed. Engl.*, **9**, 237 (1970).

(8) C. R. Johnson, G. F. Katekar, R. F. Huxol, and E. R. Janiga, *J. Amer. Chem. Soc.*, **93**, 3771 (1971).

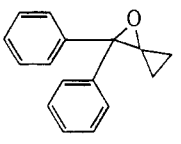
moderate yield preparation of alkylidenecyclopropanes[9] this method does not allow for an easy synthesis of oxaspiropentanes.

Sulfur ylides offer a facile approach to this problem since in contrast to phosphorus ylides they condense with carbonyl compounds to yield epoxides under strongly basic or neutral conditions. In this event the required ylide is a sulfonium cyclopropylide. Indeed, oxaspiropentanes are produced in high yields by treatment of an equimolar solution of cyclopropyldiphenylsulfonium fluoroborate (**5**) and a carbonyl partner with

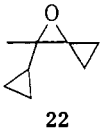


solid potassium hydroxide at 25° in dimethyl sulfoxide. Since dimethyl sulfoxide and hexane are immiscible, the *only* compounds extracted by hexane are the oxaspiropentane and diphenyl sulfide. Washing with a saturated aqueous sodium bicarbonate solution eliminates any traces of dimethyl sulfoxide from the hexane while leaving the oxaspiropentane intact. Although utilizing such basic solutions in treating the oxaspiropentane is recommended, remarkably, most oxaspiropentanes are stable for 5–10 min with 0.5 *N* protonic acids if partitioned between hexane and water. On the other hand, oxaspiropentanes cannot tolerate even mildly acidic media if more highly miscible systems, such as ether–water, are used. However, neutral or basic conditions may be employed for isolation. The byproduct of the ylide reaction, diphenyl sulfide, may be removed by distillation of the oxaspiropentane from the mixture at reduced pressure in base washed glassware.[9] It is essential that no acid be present or that the pot temperature not rise above 80° to avoid thermal rearrangement to cyclobutanones. Table I summarizes the synthetic scope of this reaction with various carbonyl compounds. Similarly, diphenyl-2-methylcyclopropylsulfonium fluoroborate (**17**) enables methyl-substituted oxaspiropentanes to be isolated under the same conditions as for **5** (Table II). It should be noted that the yields of these reactions were not optimized.

Attempts to extend the generality of this reaction to 6-methoxy-2-tetralone led only to enolization with resultant isolation of starting material. 3-Cyanocyclobutanone and spiro[3.5]nonan-1-one also failed to condense, possibly as a result of enolization. Isolation of oxaspiropentanes **21** and **22** was not possible under



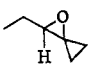
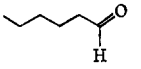
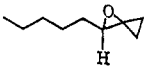
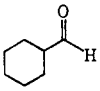
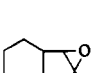
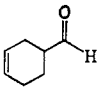
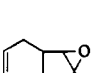
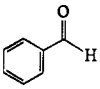
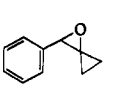
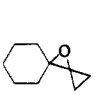
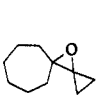
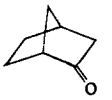
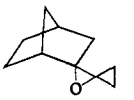
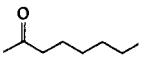
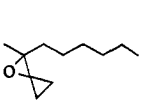
21



22

these conditions, only the corresponding cyclobutanones being isolated.[10] In these cases lability of the oxaspiropentanes toward ring expansion is a consequence of the highly stable cation formed by heterolysis of the carbon–oxygen bond.

Table I. Preparation of Oxaspiropentanes from **5**

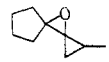
Aldehyde or ketone	Oxaspiropentane	% yield
	 **6**	100[a,c]
	 **7**	92[a]
	 **8**	89[a]
	 **9**	80[a]
	 **10**	87[a]
	 **11**	94[a]
	 **1**	97[a]
	 **12**	90[a]
	 **13**	92[b]
	 **14**	80[a,d]
	 **15**	92[a]
	 **16**	59[a]

[a] Isolated yields unless noted. [b] Oxaspiropentane was not separated from diphenyl sulfide; yield by nmr integration. [c] Oxaspiropentane flash distilled from initial reaction mixture at 25° (0.5 mm). [d] Crystalline solid, mp 26.5–27.0°.

(9) J. P. Chesick, *J. Amer. Chem. Soc.*, **85**, 2720 (1963); R. Noyori, H. Takaya, Y. Nakanisi, and H. Nozaki, *Can. J. Chem.*, 47, 1242 (1969); H. J. Bestman, *Angew. Chem.*, 77, 1011 (1965); E. E. Schweizer, *J. Org. Chem.*, 33, 337 (1968); K. Sisido, *Tetrahedron Lett.*, **28**, 3267 (1968).

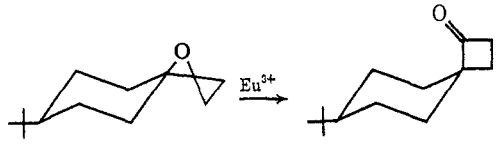
(10) (a) Attempted thin layer chromatography on alumina, Fluorisil, acetate-buffered Fluorisil, silica gel, or acetate buffered silica gel resulted in rearrangement of the oxaspiropentanes to cyclobutanones. (b) B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **95**, 5321 (1973).

Table II. Oxaspiropentanes from 17

Ketone	Oxaspiropentane	% yield
	 18	100[a,c]
	 19	83[a]
	 20	95[b]

[a] Isolated yields unless noted. [b] Oxaspiropentane was not separated from diphenyl sulfide; yield by nmr integration. [c] Oxaspiropentane flash distilled from initial reaction mixture at 25° (0.5 mm).

The reaction is highly stereoselective. Thus, reaction of 4-*tert*-butylcyclohexanone with **5** under the described conditions results in an oxaspiropentane with a sharp melting point, 26.5–27°, indicative of a single stereoisomer. The assignment as **14**, *i.e.*, that



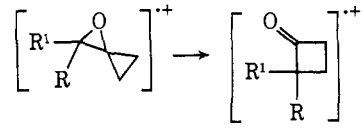
14 **23**

from equatorial attack, arises by consideration of its stereospecific rearrangement with europium(III) to a single cyclobutanone **23**[10] presumably with inversion at the migration terminus.

Although the yields were not optimized, the reaction time was dependent on the reactivity of the ketone or aldehyde. Most ketones react in excellent yield with **5** within 3 hr; however, longer reaction times may be used if a ketone is sterically hindered without fear of product decomposition. The yield of oxaspiropentane **1** is essentially the same regardless of the reaction time between 2 and 24 hr. Furthermore, diisopropyl ketone reacts with **5** to form only 23% of **16** after 2 hr, but 59% after 24 hr.

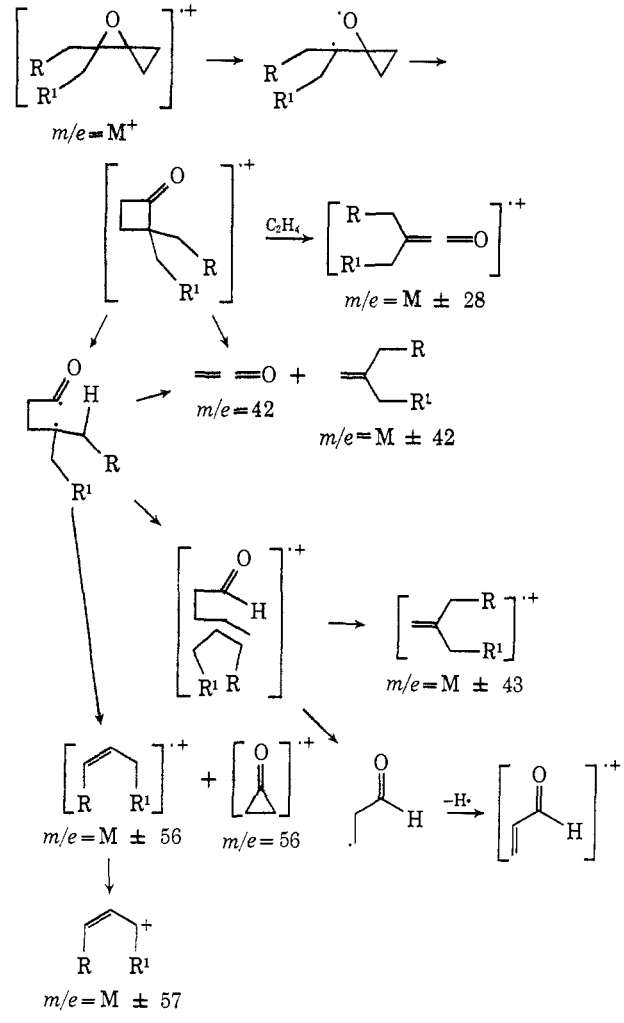
Oxaspiropentanes are distillable, isolable, and sometimes crystalline (*i.e.*, **14**) materials. Infrared analysis of these compounds allows an assignment of three absorptions due to the spiro-ring system, one near 3075 cm^{-1} assigned to the cyclopropyl proton stretch and two others at 1078 and 995–1020 cm^{-1}. It is interesting to note that spiropentanes exhibit two distinct bands at 1000–1010 and 1050 cm^{-1}.[11] The mass spectra also show fragmentation patterns characteristic of oxaspiropentanes. Most oxaspiropentanes exhibit mass spectral fragmentation patterns similar to those of the respective cyclobutanone derived from rearrangement of the oxaspiropentane. It is difficult, without labeling techniques, to ascertain whether the fragmentation pattern is truly the oxaspiropentane or that of the cyclobutanone resulting from rearrangement *prior* to ionization. The characteristic fragments lost are 28, 42, 56, and 57 mass units. The common fragment ions

(11) H. E. Simmons, E. P. Blanchard, and H. D. Hartzler, *J. Org. Chem.*, 31, 295 (1966).



are *m/e* 39, 41, 42, 55, 56, 57, and $M^+ - 56$, $M^+ - 42$, and $M^+ - 28$. Scheme I represents a rationalization of the observed major fragments.

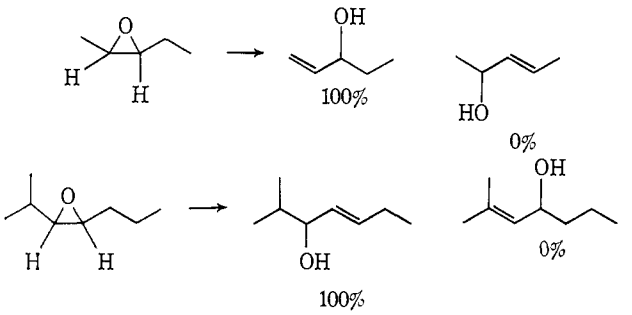
Scheme I. Fragmentation in Mass Spectrometer of Oxaspiropentanes



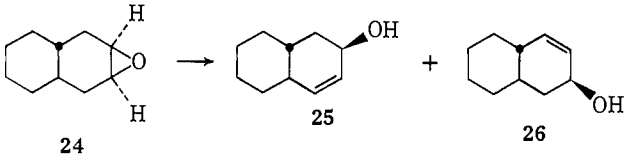
Nuclear magnetic resonance spectra of oxaspiropentanes show characteristic absorptions for the four cyclopropyl protons in the δ 0.7–1.1 range as an AA′-BB′ pattern. Oxaspiropentanes derived from an aldehyde exhibit an absorption for the epoxide proton in the δ 2.9–3.3 range. This region is quite typical for simple epoxide methines.

Oxaspiropentanes are anticipated to behave as highly reactive epoxides. Among the more interesting synthetically useful reactions of epoxides stands their ring opening to allyl alcohols.[12] This reaction employing a lithium dialkylamide, such as lithium diethylamide, exhibits unusually high orientational and stereochemical requirements for a base induced elimination reaction. The preference for elimination is primary ≫ secondary

(12) B. Rickborn and R. P. Thummel, *ibid.*, 34, 3583 (1969); R. P. Thummel and B. Rickborn, *J. Amer. Chem. Soc.*, 92, 2064 (1970); R. P. Thummel and B. Rickborn, *J. Org. Chem.*, 36, 1365 (1971); C. L. Kissel and B. Rickborn, *ibid.*, 37, 2060 (1972); R. P. Thummel and B. Rickborn, *ibid.*, 37, 3919, 4250 (1972).

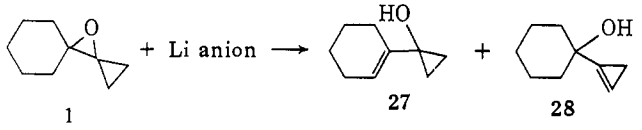


≫ tertiary as illustrated in the examples above. When only one type of hydrogen is available for reaction, the elimination occurs in an essentially statistically predicted manner. A very different result is observed with cyclic olefin epoxides where strong conformational preference exists. Thus, *trans*-2-octalin oxide (**24**)

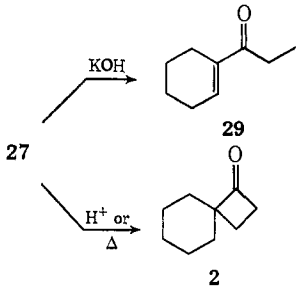


reacts readily with lithium diethylamide to give allyl alcohols **25** and **26** in a 98:2 ratio. The very high regioselectivity is in keeping with a cyclic syn-elimination mechanism where the ring opening has substantial stereoelectronic requirements. The favored direction of elimination is accounted for by the preferred abstraction of the axial hydrogen which enables a greater orbital overlap in the cyclic transition state.

Application of this rearrangement to an oxaspiropentane-type epoxide such as **1**, under various conditions with lithium dialkylamides and carbanions, affected rearrangement to allyl alcohols **27** and **28**.



Cyclopropene **28** was identified by the presence of a sharp doublet, J = 1.5 Hz, about δ 1.00 in the nmr spectra which was coupled to a sharp triplet at δ 6.53, J = 1.5 Hz. Also, infrared analysis showed an absorption at 1640 cm^{-1} characteristic of a monoalkylcyclopropene.[13] However, attempted isolation of **28** resulted only in polymeric decomposition. The desired product **27** was identified on the basis of its spectro-



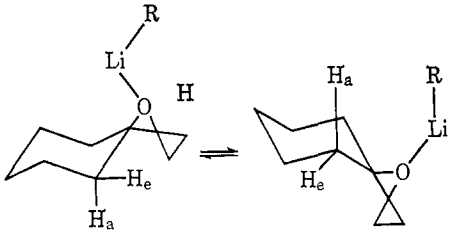
scopic properties and chemical behavior. Aqueous potassium hydroxide affected ring cleavage to 1-propionylcyclohexene (**29**), whereas acid treatment or thermolysis in ethanol afforded cyclobutanone **2**. A summary of the effect of base and solvent on this elimination appears in Table III.

Table III. Reaction of **1** with Various Lithium Reagents[a]

Base	Solvent	27:28
	Ether	No reaction
	Ether	1.00:1.23
	Ether	1.00:6.25
	Ether	1.50:1.00
	Pentane	9.00:1.00
	Ether	1.00:7.60
	Ether	1.00:1.27
	Pentane	3.50:1.00

[a] Ratio was determined by nmr integration of the vinyl proton of **27** to the vinyl proton of **28**.

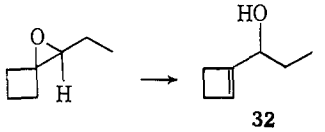
These results may be rationalized by consideration of the stereochemical features of the reaction. Two conformers are possible for the lithium dialkylamide–oxaspiropentane complex, that in which the "O" is axial or the conformer where "O" is equatorial. It is



"O" axial "O" equatorial

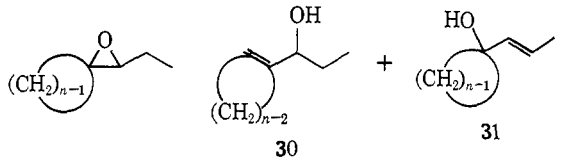
evident that the only conformer which will allow the preferred removal of the axial hydrogen in the cis elimination is the "O" equatorial conformer. If the oxygen is axial the stereoelectronic requirements make the removal of the cis-equatorial hydrogen highly unlikely. However, for this conformer removal of a cyclopropyl hydrogen allows efficient overlap of the developing p orbitals of the incipient double bond, a factor more important than the developing strain energy of a cyclopropene.

This same type of argument applies to the product distribution obtained in the base induced ring opening of propylidenecycloalkane oxides in which a reversal of the normal orientational preferences is only seen for the six-membered ring case (see Table IV). It is interesting to note that propylidene cyclobutanone oxide results in 77% cyclobutene **32** upon reaction with



(13) K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.*, 83, 1226 (1961).

Table IV. Reaction of Propylidenecycloalkane Oxide with Lithium Diethylamide[a]



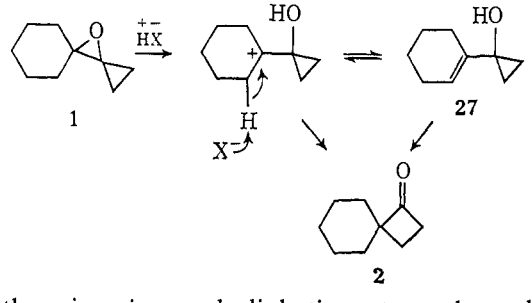
30 31

n	Time, hr[b]	Product distribution 30	31
4	6	77	15
5	1	100	0
6	49	5	95
7	5	98	2
8	2	100	0
12	22	84	12

[a] Reference 12. [b] The reactions were followed by vpc; this is the time required to effect complete loss of starting epoxide.

lithium diethylamide in ether. Nevertheless, whereas the formation of **31** rather than 1-propenylcyclobutanol does not introduce a significant additional strain to the system, formation of cyclopropene **28** increases the strain by approximately 27 kcal/mol.[14] This can be viewed as a measure of the energy difference between removal of an equatorial hydrogen with poor p-orbital overlap and removal of a cyclopropyl hydrogen leading to cyclopropene.

The drastic change in the selectivity of proton removal with different solvents is amply rationalized by the shifting of equilibrium between the two possible conformers "O" axial and "O" equatorial. Ether can effectively compete with the oxaspiropentane in complexation with the lithium dialkylamide. Thus, the oxaspiropentane exists minly uncomplexed as the "O"-axial conformer, leading to **28**. Alternatively, pentane does not solvate the lithium species resulting in a tighter lithium dialkylamide–oxaspiropentane complex. Lithium is tied up only with the epoxide oxygen resulting in the "bulkier" group driving the equilibrium toward the "O"-equatorial conformer leading to **27**.

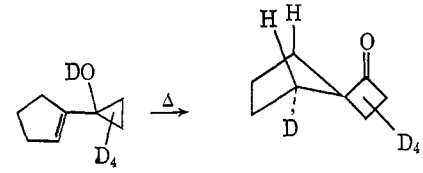


1 2 27

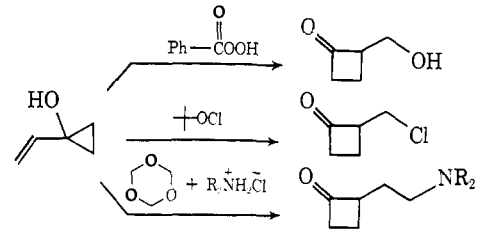
In other ring sizes and aliphatic systems there should be a strong preference against cyclopropene formation due to either a proper juxtaposition of the ring proton or ring conformational mobility.[12] It is curious to note that vinylcyclopropanol has also been detected upon attempted rearrangement of oxaspiropentanes to cyclobutanones with protonic acids possessing possible basic anions. Thus, hydrochloric, hydrobromic, and hydroiodic acids serve both as an acid (ring opening) and a base (proton removal) in opening oxaspiropentanes to these intermediates.

(14) K. B. Wiberg, W. J. Bartley, and F. P. Lossing, *J. Amer. Chem. Soc.*, 84, 3980 (1962); P. v. R. Schleyer, J. E. Williams, and K. E. Blanchard, *ibid.*, 92, 2377 (1970); for a review, see G. L. Closs, *Advan. Alicyclic Chem.*, 1, 50 (1966).

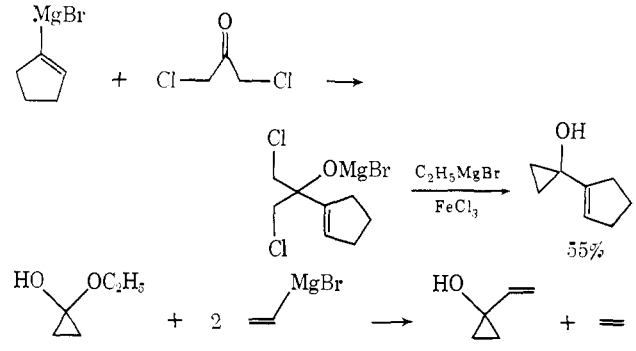
Vinylcyclopropanols have already proved to be useful intermediates for a variety of transformations. Thus, they suffer thermal ring enlargement which involves an intramolecular cis addition of the proton on the double bond with inversion at the migration terminus. They undergo ready ring expansion with a



variety of electrophilic reagents to form substituted cyclobutanones as reported by Wasserman.[15,16] For



these reactions Conia[17] and Wasserman[15,16] developed



preparations of vinylcyclopropanols necessitating the preparation of a vinyl halide with subsequent addition of a cyclopropane moiety. The difficulty in preparing the vinyl halide in good yields renders this approach less attractive. However, the facile preparation of vinylcyclopropanols from readily available ketones opens a wide field of synthetic transformations heretofore extremely difficult.

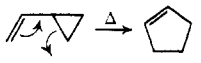
In addition, vinylcyclopropanols have an important substructure, the vinylcyclopropane moiety, a unit characterized by thermal rearrangement to cyclopentenes.[18] The discovery of many important natural

(15) H. H. Wasserman, R. E. Cochoy, and M. S. Baird, *J. Amer. Chem. Soc.*, 91, 2375 (1969).

(16) H. H. Wasserman, H. W. Adickes, and O. Espejo de Ochoa, *ibid.*, 93, 5586 (1971).

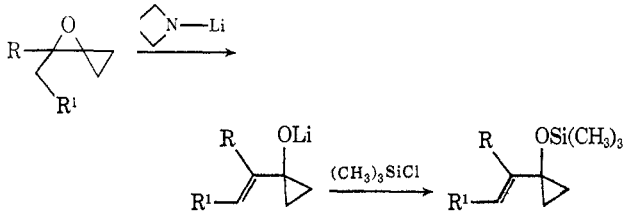
(17) J. R. Salaün and J. M. Conia, *Tetrahedron Lett.*, 2849 (1972).

(18) W. von E. Doering and W. R. Roth, *Angew. Chem., Int. Ed. Engl.*, 2, 115 (1963); H. M. Frey, *Advan. Phys. Org. Chem.*, 4, 147 (1966); J. Wiemann and S. L. Thithan, *Bull. Soc. Chim. Fr.*, 199 (1958); S. F. Birch, R. A. Dean, and N. J. Hunter, *J. Org. Chem.*, 23, 1390 (1958); N. P. Neureiter, *ibid.*, 24, 2044 (1959); C. G. Overberger and A. E. Borchert, *J. Amer. Chem. Soc.*, 82, 4896 (1960); E. Vogel, K. H. Ott, and K. Gajek, *Justus Liebigs Ann. Chem.*, 644, 172 (1961); M. C. Flowers and H. M. Frey, *J. Chem. Soc.*, 3547 (1961); E. Vogel, *Angew. Chem., Int. Ed. Engl.*, 1, 53 (1962); A. D. Kettey and J. L. McClanahan, *J. Org. Chem.*, 30, 940, 942 (1965); P. D. Bartlett and G. D. Sargent, *J. Amer. Chem. Soc.*, 87, 1297 (1965); M. J. Jorgenson and C. H. Heathcock, *ibid.*, 87, 5264 (1965); M. R. Willcott and V. H. Cargle, *ibid.*, 89, 723 (1967); L. Skattebol, *Tetrahedron*, 23, 1107 (1967); W. R. Roth and A. Friedrich, *Tetrahedron Lett.*, 2607 (1969); M. R. Willcot and V. H. Cargle, *J. Amer. Chem. Soc.*, 91, 4310 (1969); S. Masamune, S. Takada, N. Nakatsuka, R. Vukov, and E. N. Cain, *ibid.*, 91, 4322 (1969); R. A. Clark, *Tetrahedron Lett.*, 2279 (1971).



products containing five-membered rings such as the prostaglandins,[19] several sesquiterpene antibiotics,[20] and various flavor and fragrance principles[21] requires new methods for cyclopentane synthesis.[22]

Whereas vinylcyclopropanols rearrange thermally to cyclobutanones rather than cyclopentanones, an alternative method for utilization of this important substructure in ring expansion reactions was investigated through the protection of the hydroxyl group with a trimethylsilyl ether linkage.[23] Treatment of an oxaspiropentane with lithium diethylamide in hexane at 25° effected ring opening with formation of a lithium vinylcyclopropanoxide. Work-up of the reaction with trimethylchlorosilane results in a siloxyvinylcyclopropane. The silyl ethers of vinylcyclopropanols can be



purified by distillation *in vacuo* or by chromatography on silica gel (see Table V).

(19) For some recent synthetic efforts, see T. K. Schaaf and E. J. Corey, *J. Org. Chem.*, 37, 2921 (1972), and references therein; M. P. L. Caton, E. C. J. Coffee, and G. L. Watkins, *Tetrahedron Lett.*, 773 (1972); E. J. Corey and T. Ravindranathan, *ibid.*, 4753 (1971); C. J. Sih, R. G. Salomon, P. Price, R. Sood, and G. Peruzzotti, *ibid.*, 2435 (1972), and references therein; H. L. Slates, Z. S. Zelawski, D. Taub, and N. L. Wendler, *J. Chem. Soc., Chem. Commun.*, 304 (1972); J. Fried, C. H. Lin, J. C. Sih, P. Dalven, and G. F. Cooper, *J. Amer. Chem. Soc.*, 94, 4342 (1972); J. Fried, J. C. Sih, C. H. Lin, and P. Dalven, *ibid.*, 94, 4343 (1972), and references therein; P. Crabbe, A. Cervantes, and A. Guzman, *Tetrahedron Lett.*, 1123 (1972).

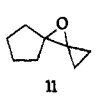
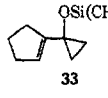
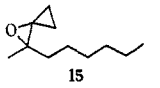
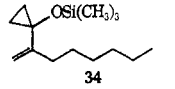
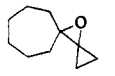
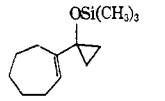
(20) For example, hirsutic acid [F. W. Comer, F. McCapra, I. H. Oureshi, and A. I. Scott, *Tetrahedron*, 23, 4761 (1967); F. W. Comer and J. Trotter, *J. Chem. Soc. B*, 11 (1966)] and pentalenolactone [D. G. Martin, G. Slomp, S. Mizsak, D. J. Duchamp, and C. G. Chidester, *Tetrahedron Lett.*, 4901 (1970); S. Takeuchi, Y. Ogawa, and H. Yonehara, *ibid.*, 2737 (1969)]. For recent efforts toward hirsutic acid, see P. T. Lansbury, N. Y. Wang, and J. E. Rhodes, *Tetrahedron Lett.*, 2053 (1972); F. Sakan, H. Hashimoto, and A. Ichihara, *ibid.*, 3703 (1971).

(21) For some recent synthetic efforts, see J. A. Marshall, W. F. Huffman, and J. A. Ruth, *J. Amer. Chem. Soc.*, 94, 4691 (1972); J. A. Marshall and A. E. Greene, *J. Org. Chem.*, 37, 982 (1972); J. E. McMurry and T. E. Glass, *Tetrahedron Lett.*, 2575 (1971); G. Büchi and B. Egger, *J. Org. Chem.*, 36, 2021 (1971); J. E. McMurry and J. Melton, *J. Amer. Chem. Soc.*, 93, 5309 (1971).

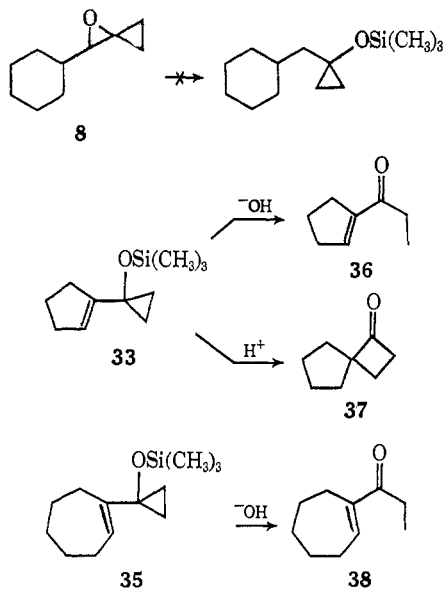
(22) For recent developments in the synthesis of cyclopentane ring systems, see R. A. Ellison and W. D. Woessner, *J. Chem. Soc., Chem. Commun.*, 529 (1972); J. E. McMurry and J. Melton, *J. Amer. Chem. Soc.*, 93, 5309 (1971); J. E. McMurry and T. E. Glass, *Tetrahedron Lett.*, 2575 (1971); E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sathe, D. J. Scharf, and G. Tori, *J. Amer. Chem. Soc.*, 92, 7428 (1970); S. M. Wanieb and R. J. Cvetorich, *Tetrahedron Lett.*, 1233 (1972); W. Hartmann, H. M. Fischler, and H. G. Heine, *ibid.*, 853, 857 (1972); A. I. Meyers and N. Nazarenko, *J. Org. Chem.*, 38, 175 (1973); P. T. Lansbury, *Accounts Chem. Res.*, 5, 311 (1972); W. S. Johnson, M. B. Gravestock, R. J. Parry, R. F. Myers, T. A. Bryson, and D. H. Miles, *J. Amer. Chem. Soc.*, 93, 4330 (1971); J. M. Conia and M. L. Lerwirend, *Tetrahedron Lett.*, 2101 (1968); P. E. Eaton and R. H. Mueller, *J. Amer. Chem. Soc.*, 94, 1014 (1972); J. M. Conia, *Bull. Soc. Chim. Fr.*, 3057 (1968); P. Beslin and J. M. Conia, *ibid.*, 959 (1970); T. A. Spencer, A. L. Hall, and C. F. v. Reyn, *J. Org. Chem.*, 33, 3369 (1968); G. Büchi and B. Egger, *ibid.*, 36, 2021 (1971); W. F. Berkowitz and A. A. Ozoris, *ibid.*, 36, 3787 (1971); E. J. Corey and S. W. Walinsky, *J. Amer. Chem. Soc.*, 94, 8932 (1972); G. Stork and G. L. Nelson, *ibid.*, 93, 3091 (1971); R. Noyori, K. Yokoyama, S. Makino, and Y. Hayakawa, *ibid.*, 94, 1772 (1972); J. Ficini, J. d'Angelo, J. P. Genet, and J. Noire, *Tetrahedron Lett.*, 1569 (1971).

(23) Higher yields and cleaner products were obtained in the oxy-Cope rearrangement using trimethylsiloxy derivatives: R. W. Thies, *Chem. Commun.*, 237 (1971); R. W. Thies, *J. Amer. Chem. Soc.*, 94, 7074 (1972).

Table V. Preparation of Siloxyvinylcyclopropanes

Oxaspiropentane	Siloxyvinylcyclopropane	% isolated yields
 11	 33	94
 15	 34	96
 12	 35	91

Attempts to extend the reaction to include oxaspiropentane ring opening to a tertiary center, *i.e.*, **8**, failed. The chemical reactivity characteristic of silyl ethers **33** and **35** is similar to that of vinylcyclopropanols.[15,16] Thus, **33** or **35** may be transformed in aqueous base to **36** or **38** and **33** in aqueous acid to **37**.



Thermolysis of siloxyvinylcyclopropanes **33–35** by passing a hexane solution through a conditioned[24] hot tube packed with glass helices at 330° with a contact time of 4 sec led to smooth quantitative rearrangement to the enol silyl ethers listed in Table VI.

Vinylcyclopropanes without siloxy substitution have been investigated, and the activation energy for vinylcyclopropane rearrangements ranges from 48 to 53 kcal/mol for compounds containing only carbon and hydrogen.[25] A typical vinylcyclopropane has a half-life of 1 sec at 460°.[26] For example, the activation energy and half-life of vinylcyclopropane **39** rearranging to **40** are 51.3 kcal/mol and 3.05 hr at 340°.[27] It should be noted that the isomerization to cyclopentene proceeds with a considerably lower energy of activation than other cyclopropane isomerizations.[18] Further

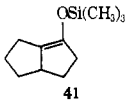
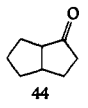
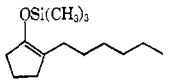
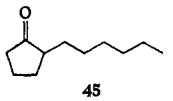
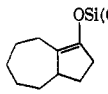
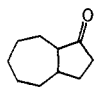
(24) The column was silylated prior to thermal rearrangement of the silyl ethers. This silylation prevented decomposition of the silyl ethers which occurred on an unconditioned column.

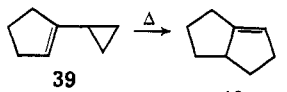
(25) M. R. Willcott, R. L. Cargill, and A. B. Sears, *Progr. Phys. Org. Chem.*, 9, 25 (1972).

(26) J. A. Berson and M. R. Willcott, *J. Org. Chem.*, 30, 3569 (1965).

(27) G. R. Branton and H. M. Frey, *J. Chem. Soc. A*, 1342 (1966).

Table VI. Rearrangement of Siloxyvinylcyclopropanes

Siloxyvinylcyclopropane	Enolsilane	% yield	Ketone	% yield
33	 41	89	 44	96
34	 42	97	 45	98
35	 42	99	 46	90

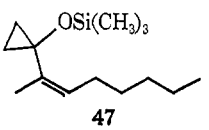


39 40

lowering of the activation energy should be anticipated by substitution on the cyclopropane ring.[28] Berson estimated the stabilizing effect of an oxygen α to a radical from the oxy-Cope rearrangement[29] to be approximately 2.4 kcal/mol. Furthermore, a comparison between the oxy-Cope and siloxy-Cope failed to reveal a significant difference in the rate of rearrangement.[23]

Assuming an upper limit of 1 sec for the half-life of **37** at 330°, and using the parameters for compound **39**, the activation energy of the siloxyvinylcyclopropane rearrangement is estimated to be 42 kcal/mol. Thus, the siloxy group on a cyclopropyl ring lowers the activation energy by approximately 9 kcal/mol. However, this may be a lower limit to the decrease in energy since the half-life of the reaction at 330° may be much less than 1 sec. At present, no satisfactory explanation exists for the discrepancy with Berson's interpretations.

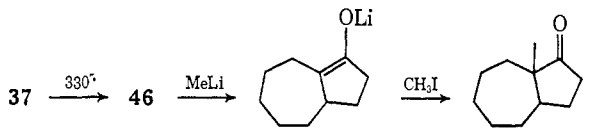
Hydrolysis of the enol silyl ethers unmasked the carbonyl groups to give the respective cyclopentanones. The results are listed in Table VI. To examine the orientational selectivity with an unsymmetrical oxaspiropentane, the case of 2-*n*-hexyl-2-methyloxaspiropentane (**15**) was explored. Utilizing the lithium diethylamide cleavage reaction with subsequent silylation produces regioselectively a single siloxyvinylcyclopropane **34**. Absence of the isomeric silyl ether **47** was inferred from the nmr data, where the vinyl



47

region appears as two finely split singlets integrating for two protons. Silyl ether **47** would only have a one proton signal appearing as a broad triplet. Furthermore, **47** should show a finely split three proton singlet for the vinyl methyl group which is completely absent in the nmr obtained in the preparation of **34**. Transformation of **34** *via* a hot tube pyrolysis to **42** with subsequent hydrolysis generated a homogeneous ketone **45**.

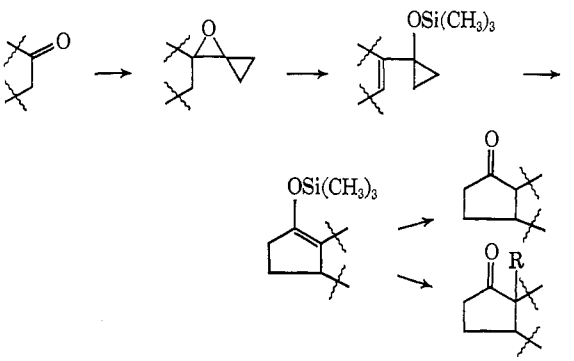
Utilization of this cyclopentane annelation results in an enol silane which may be transformed into an enolate by the method of Stork[30] and House.[31] Such an enolate may be alkylated to introduce further alkyl groups. Thus, treatment of the pyrolysate from **35** with methyllithium in dimethoxyethane followed by methyl iodide produced the perhydroazulenone derivative **48** with the



37 46 48

methyl group only at the bridgehead carbon as a mixture of trans and cis isomers. The assignment of configuration was based on the downfield shift of the methyl group observed for the cis isomer (δ 1.17) compared to that of the trans isomer (δ 1.13).[32,33]

We have demonstrated the ability to produce oxaspiropentanes of various substitution patterns from readily available carbonyl compounds. The utility of oxaspiropentanes in a facile ring opening to vinylcyclopropanols becomes synthetically important in view of the ring expansion to cyclobutanones promoted by electrophiles.[15,16] Further, these intermediates have now been demonstrated to be readily converted into enol derivatives of cyclopentanones. This process (eq 3), combined with its regioselectivity and the ability



(3)

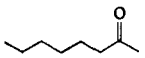
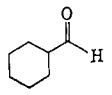
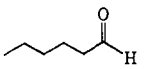
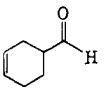
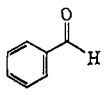
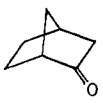
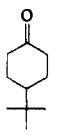
to introduce further alkyl groups regiospecifically, is one of the most versatile cyclopentanone syntheses available. Although this sequence is a four-step sequence in which some steps may be combined, the overall yield from starting carbonyl compound to annelated cyclopentanone is excellent, 73–85%.

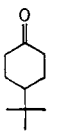
Experimental Section

General. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Unless otherwise stated, infrared spectra were determined in carbon tetrachloride solution on a Beckman IR-8 spectrophotometer; ultraviolet spectra were determined in 95% ethanol on a Cary Model 15 spectrometer. Nmr spectra were determined in carbon tetrachloride solution on Varian A60 or A60A spectrometers; chemical shifts are given in δ with TMS as the internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; bs, broad

(28) K. W. Egger, D. M. Golden, and S. W. Benson, *J. Amer. Chem. Soc.*, **86**, 5420 (1964).
(29) J. A. Berson and E. J. Walsh, *J. Amer. Chem. Soc.*, **90**, 4730 (1968).
(30) G. Stork and P. F. Hudrlik, *ibid.*, **90**, 4462, 4464 (1968).
(31) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969); H. O. House, M. Gall, and H. D. Olmstead, *ibid.*, **36**, 2361 (1971).
(32) H. O. House and B. M. Trost, *ibid.*, **30**, 2502 (1965).
(33) P. T. Lansbury, P. C. Briggs, T. R. Demmin, and G. E. DuBois, *J. Amer. Chem. Soc.*, **93**, 1311 (1971).

Table VII. Preparation of Oxyspiropentanes

Ketone	Wt, g (mmol)	5, g (mmol)	KOH, g (mmol)	Time, hr	Oxaspiropentane: Bp, °C (mm)	Oxaspiropentane: Wt, g (mmol)	% yield
	3.84 (30.0)	10.99 (35)	2.80 (50)	18	54 (1.0)	4.64 (27.6)	92[b]
	2.10 (25.0)	7.85 (25.0)	2.80 (50)	3	25 (1.0)[a]	2.91 (23.5)	94[b]
	2.24 (20.0)	6.24 (20.0)	2.24 (40)	3	60 (0.5)[a]	2.74 (18.0)	90[b]
	2.24 (20.0)	6.60 (21.0)	2.24 (40)	3	58 (0.3)	2.70 (17.8)	89[b]
	2.00 (20.0)	6.28 (20.0)	2.25 (40)	1.5	50 (20)[a]	2.57 (18.4)	92[b]
	0.58 (10.0)	3.45 (11.0)	1.12 (20)	2	25 (0.3)[c]	0.98 (10.0)	100[b]
	1.14 (10.0)	3.14 (10.0)	1.12 (20)	24	25 (0.1)[a]	0.91 (5.9)	59[b]
	0.98 (10.0)	3.92 (12.5)	1.12 (20)	4	26 (1.0)	1.33 (9.7)	97[b,f]
	1.15 (10.4)	3.70 (11.8)	1.15 (20.5)	2.25	60 (0.5)[a]	126 (8.3)	80[b]
	1.06 (10.0)	3.14 (10.0)	1.12 (20.0)	0.5			87[d]
	1.10 (10.0)	3.14 (10.0)	2.80 (50)	10			92[d]
	2.31 (15)	5.64 (18.0)	1.97 (35)	10	80 (1.0)[e]	2.33 (12.0)	80[b]

Ketone	Wt, g (mmol)	5, g (mmol)	KOH, g (mmol)	Time, hr	Bp, °C (mm)	Wt, g (mmol)	% yield
	0.84 (10.0)	3.28 (10.0)	1.12 (20)	1	50 (0.5)[a]	1.15 (8.3)	83[b]
	1.54 (10.0)	3.28 (10.0)	1.12 (20)	4			95[d]
	0.29 (5.0)	1.69 (5.15)	0.5 (10)	1	25 (0.5)[c]	0.60 (5.0)	100[b]

[a] Flash distilled, temperature indicates pot temperature. [b] Isolated yield. [c] Flash distilled from the reaction mixture directly into a −78° trap. [d] Nmr based yield. [e] Crystalline solid, mp 26.5–27.0°. [f] Retention time of 12 min on a 5 ft × 0.25 in. 10% KOH and 10% Carbowax 20M on Chromosorb W at 125°.

singlet; mult, multiplet. Coupling constants are given in hertz. Mass spectra were taken on the AE1 MS 902 high resolution mass spectrometer or a Consolidated Electronic Corporation 103C mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 98 mA. All exact mass determinations were obtained on the MS-902 instrument. Vpc analyses were performed on an Aerograph Model 90P instrument with a helium flow rate of 60 ml/min.

All experiments were carried out under an atmosphere of dry nitrogen unless noted otherwise. In experiments requiring dry solvents, ether, tetrahydrofuran, and dimethoxyethane were distilled from sodium–benzophenone. Methylene chloride and dimethyl sulfoxide were distilled from calcium hydride. Apparatus for experiments requiring dry conditions were dried either by flaming under reduced pressure or in a nitrogen stream, or drying in an oven at 120° for 12 hr.

During work-up of the reactions, general drying of the solvent was performed over anhydrous magnesium sulfate unless otherwise stated.

Thin layer or preparative thick layer plates were made of E. Merck AG Darmstadt silica gel PF-254 activated by drying for 2 hr at 140°. The general eluent was 10% ether in hexane unless described in the text. Removal of material from the silica gel was accomplished by successive washings with ether.

Preparation of Oxaspiropentanes. Method A. Generation of Diphenylsulfonium Cyclopropylide in Dimethyl Sulfoxide with Potassium Hydroxide. Under nitrogen, a solution of cyclopropyldiphenylsulfonium fluoroborate or diphenyl-2-methylcyclopropylsulfonium fluoroborate and the ketone in dimethyl sulfoxide was prepared at room temperature in a 50-ml flask. In one portion powdered potassium hydroxide was added and the solution stirred for the desired time. The reaction mixture was then directly extracted with 3 × 150-ml portions of hexane. The hexane was washed with a saturated aqueous sodium bicarbonate solution to remove any traces of dimethyl sulfoxide and then dried over anhydrous sodium sulfate (magnesium sulfate may cause rearrangement). Removal of the solvent *in vacuo* yields an oil which is a mixture of the oxaspiropentane and diphenyl sulfide. The oxaspiropentane is purified by distillation *in vacuo* from the diphenyl sulfide. Table VII lists the results for each carbonyl compound.

Spectral Properties of Oxaspiropentanes. 2-*n*-Hexyl-2-methyloxaspiropentane (15): ir (CCl_4) 3086, 2967, 2937, 2870, 1408, 1377, 1209, 1163, 1143, and 1000 cm^{-1}; nmr (CCl_4) δ 0.75–1.0 (mult, AA'BB' over a triplet, J = 7 Hz, 7 H), 1.32 (s, 3 H), 1.1–1.7 (mult, 10 H); ms *m/e* (%) 168 (5), 153 (1), 150 (10), 112 (14), 111 (10), 98 (12), 70 (38), 69 (33), 56 (100). *Anal.* Calcd for $C_{11}H_{20}O$: 168.15141. Found: 168.15243.

3-Oxadispiro[2.1.4.0]nonane (11): ir (CCl_4) 3086, 1183, 1134, 1085, 1022, 1000, 988, 949 cm^{-1}; nmr (CCl_4) δ 0.90 (mult, AA'BB', 4 H), 1.81 (bs, 8 H); ms *m/e* (%) 124 (16), 96 (16), 82 (19), 67 (100). *Anal.* Calcd for $C_8H_{12}O$: 124.08810. Found: 124.08924.

3-Oxadispiro[2.1.6.0]undecane (12): ir (CCl_4) 3070, 1000, 925 cm^{-1}; nmr (CCl_4) δ 0.85 (mult, AA'BB', 4 H), 1.7 (mult, 12 H); ms *m/e* (%) 152 (9), 124 (15), 95 (80), 81 (100), 66 (81), 54 (72). *Anal.* Calcd for $C_{10}H_{16}O$: 152.12011. Found: 152.12047.

2-Cyclohexyloxaspiropentane (8): ir (CCl_4) 3096, 1342, 1001, 970, 850, and 839 cm^{-1}; nmr (CCl_4) δ 0.93 (mult, AA'BB', 4 H), 1.0–2.2 (mult, 11 H), 3.04 (bd, J = 7 Hz, 1 H); ms *m/e* (%) 152 (3), 134 (13), 124 (25), 96 (11), 95 (25), 81 (100), 67 (65). *Anal.* Calcd for $C_{10}H_{16}O$: 152.12011. Found: 152.12021.

2-*n*-Pentyloxaspiropentane (7): ir (CCl_4) 3077, 1002, 877 cm^{-1}; nmr (CCl_4) δ 0.89 (mult, AA'BB', 4 H), 0.90 (t, J = 7 Hz, 3 H), 1.0–1.8 (mult, 8 H), 3.23 (t, J = 7.5 Hz, 1 H); ms *m/e* (%) 140 (3), 112 (25), 85 (42), 68 (68), 56 (100), 55 (94). *Anal.* Calcd for $C_9H_{16}O$: 140.12011. Found: 140.12003.

2-Ethyloxaspiropentane (6): ir (CCl_4) 3088, 1180, 1134, 1085, 1000 cm^{-1}; nmr (CCl_4) δ 0.85 (mult, AA'BB', 4 H), 0.96 (t, J = 7 Hz, 3 H), 1.6 (qd, J = 7 Hz, J = 6 Hz, 2 H), 3.20 (t, J = 6 Hz, 1 H); ms *m/e* (%) 98 (10), 70 (53), 69 (13), 55 (100). *Anal.* Calcd for $C_7H_{10}O$: 98.07316. Found: 98.07326.

2,2-Diisopropyloxaspiropentane (16): ir (CCl_4) 3077, 1078, 1065, 1020, 979, 920, 876, 838 cm^{-1}; nmr (CCl_4) δ 0.70–1.10 (mult, 4 H), 0.94 (d, J = 7 Hz, 6 H), 0.96 (d, J = 7 Hz, 6 H), 2.07 (sept, J = 7 Hz, 2 H); ms *m/e* (%) 154 (14), 139 (5), 126 (10), 111 (40), 97 (36), 83 (62), 69 (98), 55 (80), 43 (97), 41 (100). *Anal.* Calcd for $C_{10}H_{18}O$: 154.13576. Found: 154.13567.

3-Oxadispiro[2.1.5.0]decane (1): ir (CCl_4) 3067, 1078, 1047, 1001, 906, 864 cm^{-1}; nmr (CCl_4) δ 0.58–1.02 (mult, AA'BB', 4 H), 1.60 (bs, 10 H); ms *m/e* (%) 138 (32), 120 (5), 110 (30), 96 (50), 81 (100), 67 (87). *Anal.* Calcd for $C_9H_{14}O$: 138.10446. Found: 138.10519.

2-(Cyclohex-3-ene)oxaspiropentane (9): ir (CCl_4) 3096, 3035, 1647, 1000, 842, 655 cm^{-1}; nmr (CCl_4) δ 0.88 (mult, AA'BB', 4 H), 1.2–2.2 (mult, 7 H), 3.18 (bd, J = 6.5 Hz, 1 H), 5.57 (bs, 2 H); ms *m/e* (%) 150 (6), 122 (21), 93 (24), 80 (50), 79 (87), 68 (100), 54 (50). *Anal.* Calcd for $C_{10}H_{14}O$: 150.10446. Found: 150.10437.

2-Phenyloxaspiropentane (10): ir (CCl_4) 3086, 1078, 1066, 1020, 1002, 973, 910, 889, 862, 690 cm^{-1}; nmr (CCl_4) δ 0.8–1.2 (mult, 4 H), 4.14 (s, 1 H), 7.20 (bs, 5 H); ms *m/e* (%) 146 (4), 119 (7), 118 (7), 117 (12), 115 (6), 105 (13), 104 (100), 103 (13), 91 (8), 90 (8), 89 (7), (12), 77 (8), 63 (7), 51 (9), 50 (4), 39 (9). *Anal.* Calcd for $C_{10}H_{10}O$: 146.07316. Found: 146.07347.

6-*tert*-Butyl-3-oxadispiro[2.1.5.0]decane (14): ir (CCl_4) 3091, 1078, 995, 945, 907, 844 cm^{-1}; nmr (CCl_4) δ 0.7–0.9 (mult, 4 H), 0.92 (s, 9 H), 1.1–1.9 (mult, 9 H); ms *m/e* (%) 194 (12), 166 (10), 137 (11), 123 (10), 109 (17), 96 (40), 81 (33), 57 (100). *Anal.* Calcd for $C_{13}H_{22}O$: 194.16706. Found: 194.17025.

6-*tert*-Butyl-1-methyl-3-oxadispiro[2.1.5.0]decane (20). Diphenyl sulfide was not separated from this sample: ir (CCl_4) 3077, 1366, 1079, 1050, 1021, 1000, 969 cm^{-1}; nmr (CCl_4) δ 0.47 (mult, 1 H), 0.92 (s, 9 H), 1.0–2.0 (14 H).

2,2,3-Trimethyloxaspiropentane (18): ir (CCl_4) 3079, 1408, 1374, 1202, 1126, 1105, 1007, 969, 910, 870, 848 cm^{-1}; nmr (CCl_4) δ 0.48 (mult, 1 H), 0.7–1.2 (mult, 2 H), 1.12 (bs, 3 H), 1.32 (s, 3 H), 1.33 (s, 3 H); ms *m/e* (%) 112 (9), 97 (3), 70 (100), 55 (69), 42 (63), 41 (52). *Anal.* Calcd for $C_7H_{12}O$: 112.08881. Found: 112.08930.

1-Methyl-3-oxadispiro[2.1.4.0]nonane (19): ir (CCl_4) 3070, 1085, 1045, 997, 969, 916, 870, 845 cm^{-1}; nmr (CCl_4) δ 0.5 (mult, 1 H), 0.7–1.2 (mult, 2 H), 1.11 (bs, 3 H), 1.76 (bs, 8 H); ms *m/e* (%) 138 (11), 96 (55), 67 (100). *Anal.* Calcd for $C_9H_{14}O$: 138.10446. Found: 138.10458.

4,7-Methano-3-oxadispiro[2.1.5.0]decane (13). Diphenyl sulfide was not separated from this sample: ir (CCl_4) 3077, 1302, 1096, 1080, 1022, 995, 942 cm^{-1}; nmr (CCl_4) δ 0.7–1.0 (mult, 4 H), 1.1–1.9 (mult, 8 H), 2.0 (bs, 1 H), 2.3 (bs, 1 H).

Generation of Diphenylsulfonium Cyclopropylide with Potassium *tert*-Butoxide in Dimethyl Sulfoxide at 25°. Method B. To Obtain Oxaspiropentanes. A solution of cyclohexanone (0.98 g, 10 mmol), cyclopropyldiphenylsulfonium fluoroborate (3.14 g, 10 mmol), and dimethyl sulfoxide was stirred at room temperature. A 1.24 *M* solution of potassium *tert*-butoxide in dimethyl sulfoxide (8.0 ml) was added over a 3-min period. As the base was added, an intense yellow-orange color appeared which disappeared rapidly and then reappeared upon addition of more base. Near 1 equiv of base, the color did not appear as intense and diminished more slowly. The mixture was stirred for 5 min and then extracted with 2 × 50 ml of pentane. The pentane was washed with 3 × 25 ml of a saturated aqueous sodium bicarbonate solution, then dried over anhydrous sodium sulfate. The pentane was evaporated to an oil which was flash distilled at 26° (1 mm) to yield an oil, 1.30 g, 94%. This oil was spectroscopically identical with cyclopropylidenecyclohexane oxide **1** obtained *via* the previous procedure A.

Generation of Lithium Dialkylamides. The dialkylamine (1.50 mmol) was dissolved in 1.0 ml of dry (distilled from sodium–benzophenone ketyl) tetrahydrofuran. This solution was cooled to −78° and *n*-butyllithium in hexane (1.00 ml, 1.5 mmol of a 1.50 *M* solution) added. This solution (approximately 0.4 *M*) was used after mixing 15 min.

Reaction of Lithium Bases with 3-Oxadispiro[2.1.5.0]decane in Ether. Cyclopropylidenecyclohexane oxide (500 mg, 3.62 mmol) in 15 ml of ether was cooled to −78°. A solution (1 equiv) of the previously prepared lithium base (see Table III) was added and the solution stirred at −78° for 10 min. The mixture was warmed to room temperature and stirred for 2 hr. Ether (20 ml) was then added along with 20 ml of water. The ether was separated and the aqueous layer extracted with 25 ml of ether. The ether layers were combined, dried, and evaporated to yield a product for nmr analysis. The results are listed in Table III.

Reaction of Lithium Diethylamide with Cyclopropylidenecyclohexane Oxide in Pentane. Cyclopropylidenecyclohexane oxide (0.500 g, 3.62 mmol) in 25 ml of pentane was cooled to −78°. A solution of previously prepared lithium diethylamide (4.0 mmol) was added and the mixture stirred for 15 min. The mixture was warmed to room temperature and stirred for 2 hr. Water (20 ml) was added to stop the reaction. The resulting mixture was extracted with 2 × 20 ml of ether. The ether extracts were combined, dried, and evaporated *in vacuo* to yield a product for nmr analysis.[34] The results are listed in Table III. 1-(Cyclohex-1′-ene)-cyclopropan-1-ol (**27**): nmr (CCl_4) δ 0.68 (mult, AA'BB', 4 H), 1.33–1.83 (bs, 4 H), 1.83–2.33 (bs, 4 H), 2.00 (bs, 1 H), 5.65 (bs, 1 H). A sample was collected from a vpc column, 5 ft × 0.25 in. 5% SE-30 on Chromosorb W at 110° retention time 9 min, for ir and mass spectral data: ir (CCl_4) 3623, 3472, 3106, 3020, 2941, 2865, 2853, 1668, 1447, 1435, 1212, 1135, 1076, 1035, 1005, 917 cm^{-1}; ms *m/e* (%) 138 (6), 120 (11), 110 (20), 96 (24), 81 (100), 67 (81). *Anal.* Calcd for $C_9H_{14}O$: 138.10446. Found: 138.10491. Nmr evidence for 1-(cycloprop-1′-ene)cyclohexanol (**29**): nmr (CCl_4) δ 1.00 (d, J = 1.5 Hz, 2 H), 1.58 (bs, 10 H), 6.53 (t, J = 1.5 Hz, 1 H); ir (CCl_4) 1640 cm^{-1}.[35]

Rearrangement of 1-(Cyclohex-1′-ene)cyclopropan-1-ol (27) to 1-Propanoylcyclohexene (29). Cyclopropanol **32** (92 mg, 0.667 mmol) was dissolved in 10 ml of 2% potassium hydroxide in 50% aqueous ethanol. This solution was mixed for 24 hr, after which it was extracted with 2 × 20 ml of ether. The ether was dried and

(34) Ratio was determined by nmr integration of the vinyl proton of **27** to the vinyl proton of **28**.

(35) F. L. Carter and V. F. Frampton, *Chem. Rev.*, 64, 497 (1964).

evaporated *in vacuo* to yield 89 mg (96%) of an oil. The oil was analyzed by vpc,[36] which indicated that only one compound was present, **29**, which had a retention time of 9.4 min at 100°. 1-Propanoylcyclohexene (**32**): uv (EtOH) 232 (7620); ir (CCl_4) 3040, 2976, 2933, 2865, 2833, 1667, 1639, 1453, 1447, 1431, 1425, 1377, 1340, 1755, 1198, 1134, 1075, 1005, 973, 918, 893, 839 cm^{-1}; nmr (CCl_4) δ 1.05 (t, J = 7 Hz, 3 H), 1.63 (bs, 4 H), 2.25 (bs, 4 H), 2.57 (quart, J = 7 Hz, 2 H), 6.80 (bs, 1 H); ms *m/e* (%) 138 (19), 120 (5), 109 (51), 96 (23), 81 (100), 67 (52). *Anal.* Calcd for $C_9H_{14}O$: 138.10446. Found: 138.10320.

Preparation of Siloxyvinylcyclopropanes. A hexane (10 ml) solution of the oxaspiropentane and 2 equiv of diethylamine was cooled to −78°. A 1.5 *M* *n*-butyllithium solution in hexane was added slowly over a 2-min period. The solution was stirred for 5 min at −78°, then warmed to 25° with continued stirring. After the allotted time, trimethylchlorosilane was added (addition time was less than 1 min) followed by 2 ml of dimethoxyethane. After an additional 10 min of stirring, 75 ml of hexane was added to ensure complete precipitation of any salts. The salts were removed by filtration through a sintered glass funnel. The solid was washed with 25 ml of hexane and the combined hexane portions were concentrated *in vacuo*. The resultant oil was subjected to 0.2 mm of pressure at 25° to remove any traces of solvent. Distillation of silyl ethers *in vacuo* resulted in pure compounds (see Table VIII).

Table VIII. Preparation of Siloxyvinylcyclopropanes

Oxaspiro-pentane	Wt, g (mmol)	Diethylamine, g (mmol)	*n*-Butyllithium, ml (mmol)
15	1.00 (5.95)	0.87 (11.9)	7.9 (11.9)
11	1.24 (10.0)	1.46 (20.0)	13.4 (20)
13	1.54 (10.1)	1.46 (20.0)	13.3 (20)
Product	**Wt, g (mmol)**	**% yield**	**Bp, °C (mm)**
34	1.36 (5.66)	96	75 (0.2)
33	1.84 (9.4)	94	52 (0.3)
35	2.04 (9.1)	91	62 (0.1)

2-(1-Trimethylsiloxycyclopropyl)oct-1-ene (34): ir (CCl_4) 3096, 1639, 1250, 1027, 1005, 840 cm^{-1}; nmr (CCl_4) δ 0.08 (s, 9 H), 0.6–0.8 (mult, 4 H), 0.9 (t, J = 7 Hz, 3 H), 1.35 (bs, 9 H), 2.15 (bt, J = 7 Hz, 2 H), 4.75 (mult, 1 H), 4.91 (mult, 1 H); ms *m/e* (%) 240 (5), 225 (2), 169 (83), 73 (100). *Anal.* Calcd for $C_{14}H_{28}OSi$: 240.19093. Found: 240.19048.

1-(1′-Trimethylsiloxycyclopropyl)cyclopentene (33): ir (CCl_4) 3086, 3077, 1636, 1350, 1250, 1229, 1073, 1029, 1000 cm^{-1}; nmr (CCl_4) δ 0.02 (s, 9 H), 0.6–0.9 (mult, 4 H), 1.6–2.4 (mult, 6 H), 5.38 (mult, 1 H); ms *m/e* (%) 196 (12), 168 (32), 147 (38), 130 (73), 95 (31), 73 (100), 58 (50). *Anal.* Calcd for $C_{11}H_{20}OSi$: 196.12833. Found: 196.12830.

1-(1′-Trimethylsiloxycyclopropyl)cycloheptene (35): ir (CCl_4) 3089, 1250, 1024, 894 cm^{-1}; nmr (CCl_4) δ 0.03 (s, 9 H), 0.6–0.8 (mult, 4 H), 1.2–1.8 (mult, 6 H), 1.8–2.4 (mult, 4 H), 5.61 (t, J = 7 Hz, 1 H); ms *m/e* (%) 224 (15), 181 (52), 73 (100). *Anal.* Calcd for $C_{13}H_{24}OSi$: 224.15963. Found: 224.15940.

Acid Hydrolysis of 1-(1′-Trimethylsiloxycyclopropyl)cyclopentene (33). A few drops of the silane was dissolved in 1 ml of tetrahydrofuran and a drop of 6 *N* hydrochloric acid added. After 10 min, hexane and water were added. The hexane was separated and evaporated. The infrared spectra of the product were identical with spiro[3.4]octan-1-one.[37]

Basic Hydrolysis of 1-(1′-Trimethylsiloxycyclopropyl)cyclopentene (33). A few drops of the silane was dissolved in 1 ml of methanol and a drop of 9 *N* aqueous sodium hydroxide was added. After 10 min, hexane and water were added. The hexane was separated and evaporated *in vacuo*. The product had spectral properties characteristic of 1-propionylcyclopentene (**36**).[38] Purification was effected by vpc collection from a 5 ft × 0.25 in. 5% SE-30 on Chromosorb W column at 100°, retention time 4.4 min: uv λ_{max} (ϵ) 237 nm (10,800); ir (CCl_4) 3084, 1669, 1616, 1377, 1175, 1078, 1037, 957, 925, 901 cm^{-1}; nmr (CCl_4) δ 1.04 (t, J = 7 Hz, 3 H), 1.5–2.8 (mult, 6 H), 2.60 (q, J = 7 Hz, 2 H), 6.52 (bs, 1 H); ms *m/e* (%) 124 (25), 109 (2), 95 (100), 67 (27). *Anal.* Calcd for $C_8H_{12}O$: 124.08881. Found: 124.08894.

Basic Hydrolysis of 1-(1′-Trimethylsiloxycyclopropyl)cycloheptene (35). A few drops of the silane was dissolved in 1 ml of methanol and a drop of 9 *N* aqueous sodium hydroxide added. After 10 min, hexane and water were added. The hexane was separated and evaporated *in vacuo*. The spectral properties of the resultant oil were in accord with 1-propionylcycloheptene:[39] uv λ_{max} (ϵ) 235 nm (8110); ir (CCl_4) 3058, 1667, 1634, 1372, 1330, 1229, 1182, 1134, 961 cm^{-1}; nmr (CCl_4) δ 1.02 (t, J = 7 Hz, 3 H), 1.2–2.0 (mult, 6 H), 2.1–2.5 (mult, 4 H), 2.51 (q, J = 7 Hz, 2 H), 6.88 (t, J = 8 Hz, 1 H); ms *m/e* (%) 152 (23), 123 (100), 95 (64), 67 (27). *Anal.* Calcd for $C_{10}H_{16}O$: 152.12011. Found: 152.11995.

Thermal Rearrangements of Siloxyvinylcyclopropanes. A Pyrex tube, 2.5 × 40 cm, filled with glass helices (4 mm) has a gas volume of 125 ml. This column was conditioned at 25° to remove active sites by washing with a saturated aqueous sodium bicarbonate solution followed by water, acetone, hexane, *O,N*-bistrimethylsilylacetamide (or trimethylchlorosilane followed by diethylamine), and finally hexane. Passing a stream of nitrogen through the tube heated to 330° at a rate such that the contact time of the compound on the column is 4 sec results in complete rearrangement of the siloxyvinylcyclopropanes.

A solution of the silane was dissolved in hexane. This solution was passed through the column dropwise over a 15-min period. Collection of the effluent in a −78° 8-in. trap filled with Pyrex helices (4 mm) resulted in an enol silane after *in vacuo* removal of the hexane.

Starting with 2-(1′-trimethylsiloxycyclopropyl)oct-1-ene (**34**) (0.200 g, 0.83 mmol) in 5 ml of hexane, there was recovered 0.194 g (97%) of 1-trimethylsiloxy-2-*n*-hexylcyclopentene (**42**): ir (CCl_4) 1681, 1252, 1208, 883, 841 cm^{-1}; nmr (CCl_4) δ 0.19 (s, 9 H), 0.92 (t, J = 6 Hz, 3 H), 1.32 (bs, 8 H), 1.7–2.4 (mult, 8 H); ms *m/e* (%) 240 (10), 225 (3), 169 (50), 147 (100), 73 (74). *Anal.* Calcd for $C_{14}H_{28}OSi$: 240.19093. Found: 240.19079.

Starting with 1-(1′-trimethylsiloxycyclopropyl)cyclopentene (**33**) (0.300 g, 1.53 mmol) in 6 ml of hexane, there was recovered 0.267 g (89%) of 2-trimethylsiloxybicyclo[3.3.0]oct-1(2)-ene.

Starting with 1-(1′-trimethylsiloxycyclopropyl)cycloheptene (**35**) (0.500 g, 2.23 mmol) in 10 ml of hexane, there was recovered 0.493 g (99%) of 10-trimethylsiloxybicyclo[5.3.0]dec-1(10)-ene.

Acid Hydrolysis of the Enol Silanes. The enol silanes from thermal rearrangement of siloxyvinylcyclopropanes were dissolved in 10 ml of tetrahydrofuran and 5 drops of 6 *N* hydrochloric acid was added. After 10 min, water (100 ml) and hexane (100 ml) were added to the reaction mixture. The hexane was removed and the aqueous layer was extracted twice with 100-ml portions of hexane. Combination of the hexane extracts, drying over anhydrous magnesium sulfate, and evaporation *in vacuo* resulted in the corresponding ketones (see Table IX).

Table IX

Enol silane	Wt, g (mmol)	Ketone	Wt, g (mmol)	% yield
42	0.194 (0.81)	**45**	0.133 (0.79)	98
41	0.267 (1.36)	**44**	0.161 (1.29)	96
43	0.493 (2.20)	**46**	0.299 (1.97)	90

2-*n*-Hexylcyclopentanone (45) was purified by tlc: R_f 0.5; ir (CCl_4) 1745, 1408, 1263, 1151, 1094, 1015 cm^{-1}; nmr (CCl_4) δ 0.91 (t, J = 6 Hz, 3 H), 1.3 (b mult, 10 H), 1.5–2.4 (mult, 7 H); ms *m/e* (%) 168 (8), 84 (100). *Anal.* Calcd for $C_{11}H_{20}O$: 168.15141. Found: 168.15179.

Bicyclo[3.3.0]octan-2-one (44) was collected from vpc at 100°[40] (retention time 5.5 min): ir (CCl_4) 1739, 1410 cm^{-1}; nmr (CCl_4) δ 1.0–2.9 (mult, 12 H); ms *m/e* (%) 124 (34), 106 (6), 95 (57), 80 (56), 67 (100). *Anal.* Calcd for $C_8H_{12}O$: 124.08881. Found: 124.08860.

Bicyclo[5.3.0]decan-2-one (46):[41] ir (CCl_4) 1737, 1406, 1379,

(36) Column: 5 ft × 0.25 in. 5% SE-30 on Chromosorb W.
(37) I. V. Zaitseva, E. M. Auvinen, and I. A. Favorskaya, *Zh. Obshch. Khim.*, 33, 3501 (1963).
(38) N. Jones, H. T. Taylor, and E. Rudd, *J. Chem. Soc.*, 1342 (1961).
(39) A. Maccioni and E. Marongiv, *Ann. Chim. (Rome)*, 46, 252 (1956).
(40) A. C. Cope and W. R. Schmitz, *J. Amer. Chem. Soc.*, 72, 3056 (1950).
(41) C. D. Gutsche and I. Y. C. Tao, *J. Org. Chem.*, 28, 883 (1963).

1348, 1152, 1117 cm^{-1}; nmr (CCl_4) δ 1.1–2.3 (mult, 16 H); ms *m/e* (%) 152 (43), 123 (28), 109 (100), 96 (47), 95 (38), 83 (94), 81 (52), 67 (63), 55 (59), 41 (60). *Anal.* Calcd for $C_{10}H_{16}O$: 152.12011. Found: 152.11997.

Methylation of 2-Trimethylsiloxybicyclo[5.3.0]dec-1-ene (43). A solution of 2-trimethylsiloxybicyclo[5.3.0]dec-1-ene (56 mg, 0.25 mmol) in 3 ml of 1,2-dimethoxyethane with a few milligrams of triphenylmethane as an indicator was treated with methyllithium at 25° until a color persisted. Then methyl iodide (0.3 ml) was added and the mixture stirred for 2 min. Water was added and the product extracted with 2 × 50 ml portions of hexane. An oil, 29 mg (71%), was obtained upon evaporation of 1-methylbicyclo-[5.3.0]decan-2-one (**48**). The oil was a single spot by tlc on silica gel: ir (CCl_4) 1736, 1412, 1374 cm^{-1}; nmr (CCl_4) δ 1.13 (s) and 1.17 (s) total 3 H, cis and trans isomers; 1.2–2.3 (mult, 15 H); ms *m/e* (%) 166 (0.4), 151 (16), 110 (100), 95 (75), 81 (77), 68 (42), 67 (56), 55 (43), 41 (67). *Anal.* Calcd for $C_{11}H_{18}O$: 166.13576. Found: 166.13321.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs. We also thank the National Science Foundation and the Wisconsin Alumni Research Foundation for support in the purchase of nmr and mass spectrometric facilities.

New Synthetic Reactions. A Versatile Cyclobutanone (Spiroannelation) and γ-Butyrolactone (Lactone Annelation) Synthesis[1]

Barry M. Trost*[2] and Mitchell J. Bogdanowicz

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received February 23, 1973*

Abstract: The condensation of aldehydes and ketones with diphenylsulfonium cyclopropylide followed by acid treatment upon work-up leads directly to cyclobutanones in 44–97% yields *via* intermediate oxaspiropentanes. With cyclic ketones (a spiroannelation process), the reaction is highly stereoselective. With diphenylsulfonium 2-methylcyclopropylide, spiroannelation generates 3-methylcyclobutanones predominantly indicating preferential migration of the secondary carbon atom in the intermediate oxaspiropentane. Treatment of the cyclobutanones with basic hydrogen peroxide, sodium hypobromite, or hypochlorous acid effects smooth (82–100%) conversion to the corresponding γ-butyrolactones in which the more substituted carbon atom migrates exclusively and with retention of configuration. The high yields associated with these reactions and the ubiquitous nature of the carbonyl group make these methods valuable entries into cyclobutanones and γ-butyrolactones.

Examination of past and present literature shows the lack of a general method for the preparation of substituted cyclobutanones from aldehydes and ketones as starting materials. Nevertheless, many cyclobutanones have been prepared and described in the literature.[3,4] Basically, only a few of these methods are generally useful, some of which are summarized in Table I. The evolving utility of cyclobutanones as intermediates in synthesis led us to explore a method based on the ubiquitous carbonyl function. Our earlier finding of the formation of spiro[5.3]nonan-2-one in the quenching of the reaction of cyclopropyllithium and triphenylsulfonium fluoroborate with cyclohexanone suggested the use of cyclopropyl sulfur ylides.[5] This new cyclobutanone synthesis transforms a carbonyl carbon into the 2 carbon of a cyclobutanone ring through the intermediacy of an α-oxycyclopropylcarbinyl cation. An electrofugal center attached to the cyclopropane ring drastically modifies the chemical behavior of the latter. While the ready interconversion of cyclopropylcarbinyl, cyclobutyl, and homoallyl systems[6] causes product control of reactions proceeding by a cyclopropylcarbonium ion path to be frequently difficult, reactions involving oxycyclopropylcarbonium ion intermediates can be expected to be unidirectional. On the assumption that an oxycyclopropylcarbonium ion is the final stage of the acid catalyzed ring opening of an oxaspiropentane, the product of rearrangement of α-oxycyclopropylcarbinyl systems should be cyclobutanones. Some α-oxycyclopropylcarbinyl systems have been studied in recent years;[7–10] however, the applicability was limited due to the difficulties associated

(1) For preliminary reports of portions of this work, see (a) B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, **93**, 3773 (1971); (b) M. J. Bogdanowicz and B. M. Trost, *Tetrahedron Lett.*, 923 (1973). This manuscript represents part X of this series.

(2) Camille and Henry Dreyfus Teacher–Scholar Grant Recipient.

(3) For a series of articles dealing with cyclobutanones, see (a) J. M. Conia and J. Gore, *Bull. Chim. Soc. Fr.*, 726, 735, 744, 752, 755, 763, 768, 773 (1963); (b) J. M. Conia and J. Salaun, *ibid.*, 1957 (1964); (c) J. M. Conia and C. Faget, *ibid.*, 1963 (1964); (d) J. M. Conia and J. Bore, *ibid.*, 1968 (1964); (e) J. M. Conia, H. Gore, J. Salaun, and L. Ripoll, *ibid.*, 1976, 1981 (1964); (f) J. M. Conia and J. Salaun, *ibid.*, 2747, 2751, 2755 (1965); (g) H. Audier, J. M. Conia, M. Fetizon, and J. Gore, *ibid.*, 787 (1967); (h) J. Gore, C. Djerassi, and J. M. Conia, *ibid.*, 950 (1967); (i) J. Gore, J. M. Denis, P. Leriverend, and J. M. Conia, *ibid.*, 2432 (1968); (j) J. Salaun and J. M. Conia, *ibid.*, 3730, 3735 (1968); (k) J. Salaun and J. M. Conia, *Chem. Commun.*, 1358 (1970); (l) J. M. Conia and J. R. Salaun, *Accounts Chem. Res.*, **5**, 33 (1972).

(4) For a comprehensive review of cyclobutane chemistry, see D. Seebach, S. Beckman, and H. Geiger in "Methoden der Organischen Chemie," Band IB, Teil 4, E. Mueller, Ed., Georg Thieme Verlag, Stuttgart, 1971.

(5) B. M. Trost, R. W. LaRochelle, and M. J. Bogdanowicz, *ibid.*, 3449 (1970).

(6) M. Hanack and H. J. Schneider, *Fortschr. Chem. Forsch.*, **8**, 554 (1967).

(7) H. H. Wasserman, R. E. Cochoy, and M. S. Baird, *J. Amer. Chem. Soc.*, **91**, 2376 (1969); H. H. Wasserman, H. W. Adickes, and O. E. de Ochoa, *ibid.*, **93**, 5586 (1971).

(8) J. R. Salaun and J. M. Conia, *Tetrahedron Lett.*, 2849 (1972).

(9) L. Crombie, M. L. Games, and D. J. Pointer, *J. Chem. Soc. C*, 1347 (1968); H. W. Thielmann and H. Hecker, *Justus Liebigs Ann. Chem.*, **728**, 158 (1969); N. J. Turro and R. B. Gagosian, *J. Amer. Chem. Soc.*, **92**, 2036 (1970); E. E. Wenkert, R. A. Mueller, E. J. Reardon, S. S. Sathe, D. J. Scharf, and G. Tosi, *ibid.*, **92**, 7428 (1970).

(10) H. H. Wasserman and D. C. Clagett, *ibid.*, **88**, 5368 (1966).