

AN ABSTRACT OF THE THESIS OF

RICHARD EDWARD BOLESTA for the degree of Master of Science
in Chemistry (Organic) presented on _____

Title: SILOXY-COPE REARRANGEMENTS OF THE TRANS-1-
VINYLCYCLOTRIDEC-3-EN-1-OL SYSTEM

Abstract approved: _____ **Redacted for privacy** _____
Dr. Richard W. Thies

The thermolysis of trans-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS) led to the formation of two major products: 4-vinylcyclotridecanone (VII) and cyclopentadec-5-en-1-one (VIII) after hydrolysis. Ketone VII is produced by a concerted [3, 3] sigmatropic shift, while ketone VIII is formed by a [1, 3] sigmatropic shift with a concerted or diradical mechanism.

The rates of reaction and activation parameters have been determined.

The large amount of [3, 3] shift product formed hinders the use of the siloxy-Cope rearrangement as a two-carbon ring expansion reaction for the thirteen member ring systems.

The synthetic scheme for the formation of 1-vinylcyclotridec-3-ene-1-ol produces only the trans-isomer.

Siloxy-Cope Rearrangements of the trans-1-
Vinylcyclotridec-3-en-1-ol System

by

Richard Edward Bolesta

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Master of Science

Completed September 1975

Commencement June 1976

APPROVED:

Redacted for privacy

Associate Professor of Chemistry
in charge of major

Redacted for privacy

Chairman of the Department of Chemistry

Redacted for privacy

Dean of Graduate School

Date thesis is presented

August 11, 1975

Typed by Opal Grossnicklaus for Richard E. Bolesta

ACKNOWLEDGEMENTS

"When I consider thy heavens, the work of thy fingers, the moon and the stars, which thou hast ordained; What is man that thou art mindful of him?" Psalms 8:3, 4.

I would like to thank all those who have contributed to the completion of my studies at Oregon State University. In particular I want to thank Dr. R. W. Thies for his guidance and understanding and the other members of our group, Phil Seitz and Janey Peng, for everything. Special thanks go to the Reichen family - mine away from home - and to my wife, Karen, for her love, patience, and help during this time.

TABLE OF CONTENTS

	<u>Page</u>
INTRODUCTION	1
RESULTS	10
DISCUSSION	19
EXPERIMENTAL	29
BIBLIOGRAPHY	41

LIST OF FIGURES

<u>Figure</u>		<u>Page</u>
1	Products from the pyrolysis of <u>trans</u> -1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS)	13
2	Relative chemical shifts of 4-vinylcyclotridecanone (VII) in $\text{Eu}(\text{fod})_3$ study	14
3	Relative chemical shifts of cyclopentadec-5-ene-1-one (VIII) in $\text{Eu}(\text{fod})_3$ study	15
4	Strain energy (S. E.) associated with some simple cyclic systems	25

LIST OF SCHEMES

<u>Scheme</u>		<u>Page</u>
1	Products from a chair-like transition state	4
2	Products from a boat-like transition state	5
3	Synthesis of <u>trans</u> -1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS)	11
4	Mechanism and products of cyclopropyl alcohol ring opening reaction	21
5	Concerted mechanism	23
6	Diradical mechanism	24

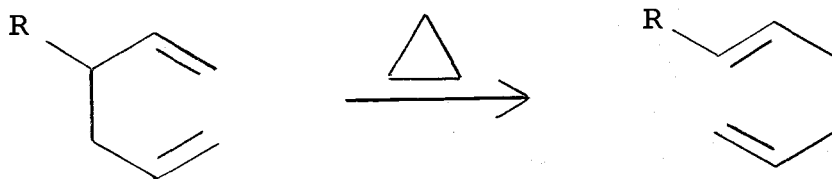
LIST OF TABLES

<u>Table</u>		<u>Page</u>
1	Relative percent of products formed from the thermolysis of VI-OTMS followed by hydrolysis	17
2	First order rate of disappearance of <u>trans</u> -1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS)	18
3	Activation energies for some siloxy-Cope rearrangements	22
4	Comparison of two siloxy-Cope rearrangements	26
5	Product comparison for some Siloxy-Cope rearrangements	27

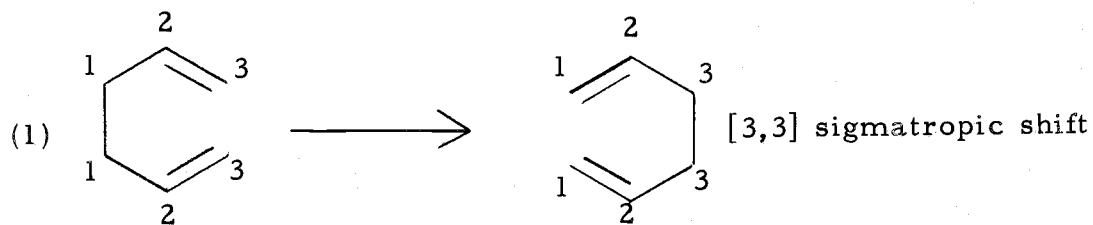
SILOXY-COPE REARRANGEMENTS OF THE TRANS- 1-VINYLCYCLOTRIDEC-3-EN-1-OL SYSTEM

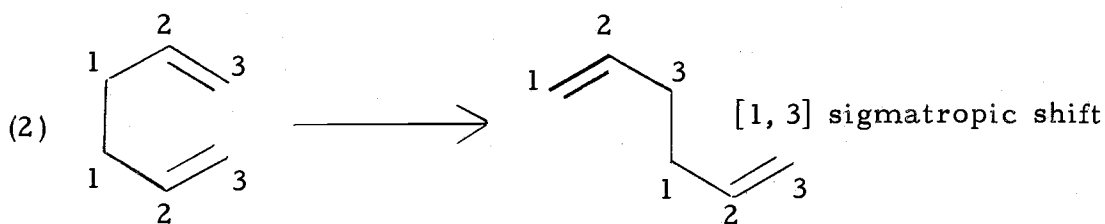
I. INTRODUCTION

Thermal rearrangements of 1,5-hexadiene systems are known as "Cope rearrangements"; a simple version is shown below.

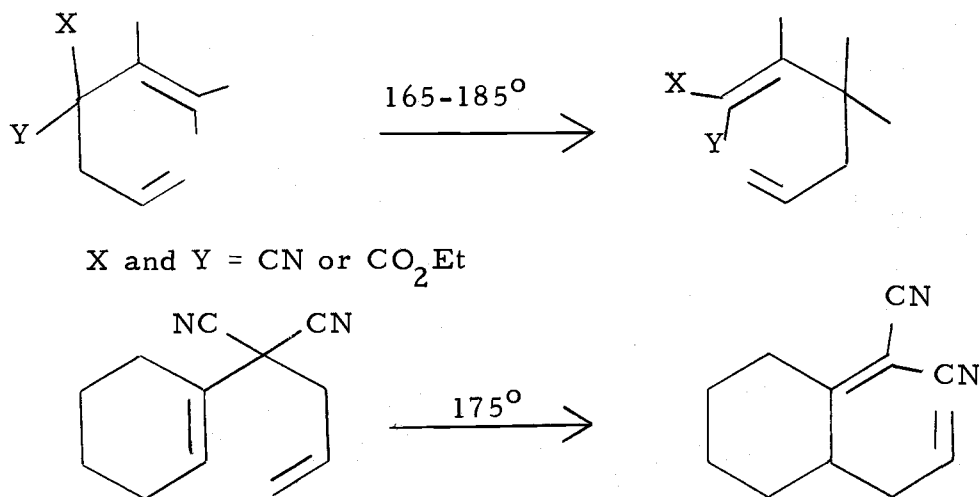


Cope rearrangements are members of a class of reactions called sigmatropic reactions. Sigmatropic reactions are defined as involving migration of a sigma bond that is flanked by one or more conjugated systems to a new position within the system (1). This bonding change can take place by either a concerted or nonconcerted mechanism. The systems are numbered by starting at the atoms to which the migrating sigma bond is attached. The reaction is called an [i, j] sigmatropic shift when the sigma bond migrates from position [1, 1] to position [i, j]. The following examples illustrate this terminology (eqs. 1 and 2).

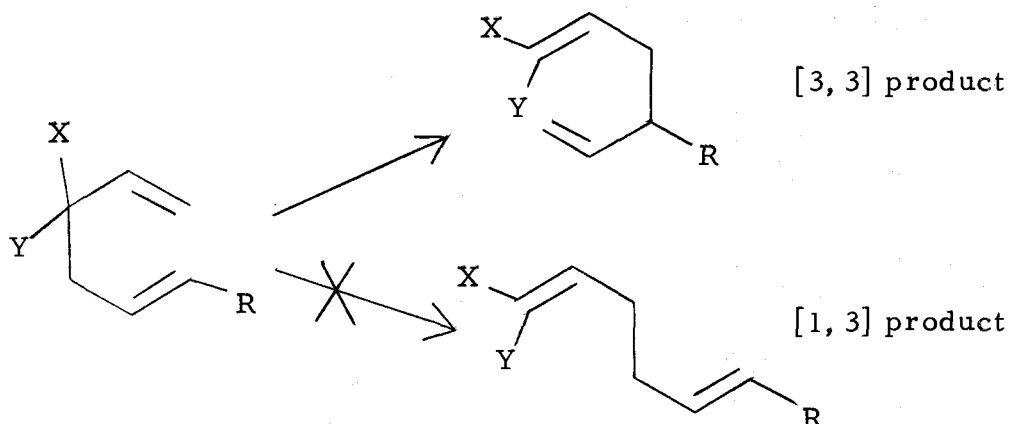




A. C. Cope and coworkers reported the thermal rearrangements of some diallyl compounds to isomeric diallyl compounds in 1940 (2, 3).

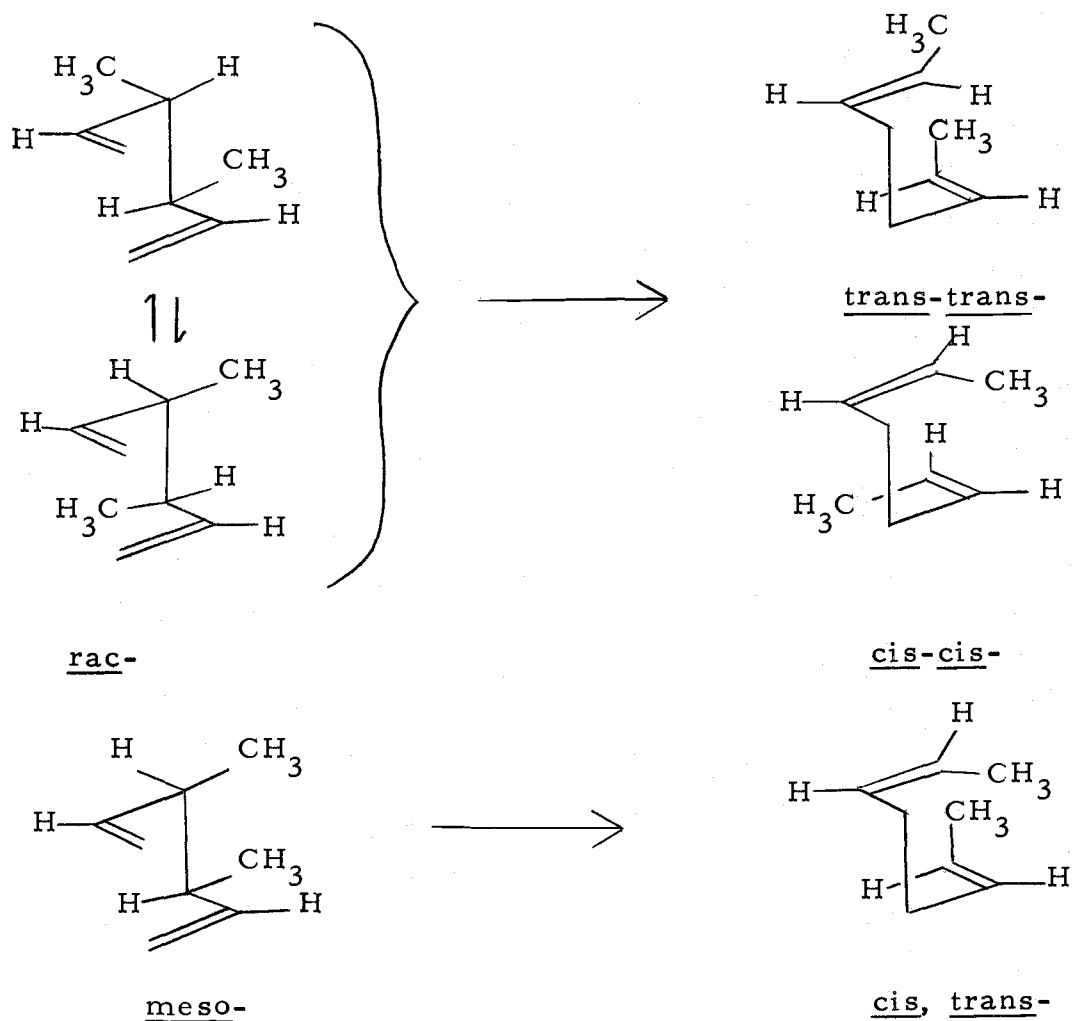


The tendency of the substituents to enter into conjugation with the double bond in the product is apparently the driving force for the rearrangement. A cyclic mechanism was proposed for this isomerization, by analogy with the Claisen rearrangement. In support of this mechanism, first-order kinetics and product composition resulting from intramolecular rearrangement were found. This was illustrated by the fact that, after rearrangement of a mixture of two diallyl compounds of comparable reaction rates, no exchange of allyl groups was observed. Cope and coworkers also observed only [3, 3] shift products for the rearrangement and no [1, 3] products.



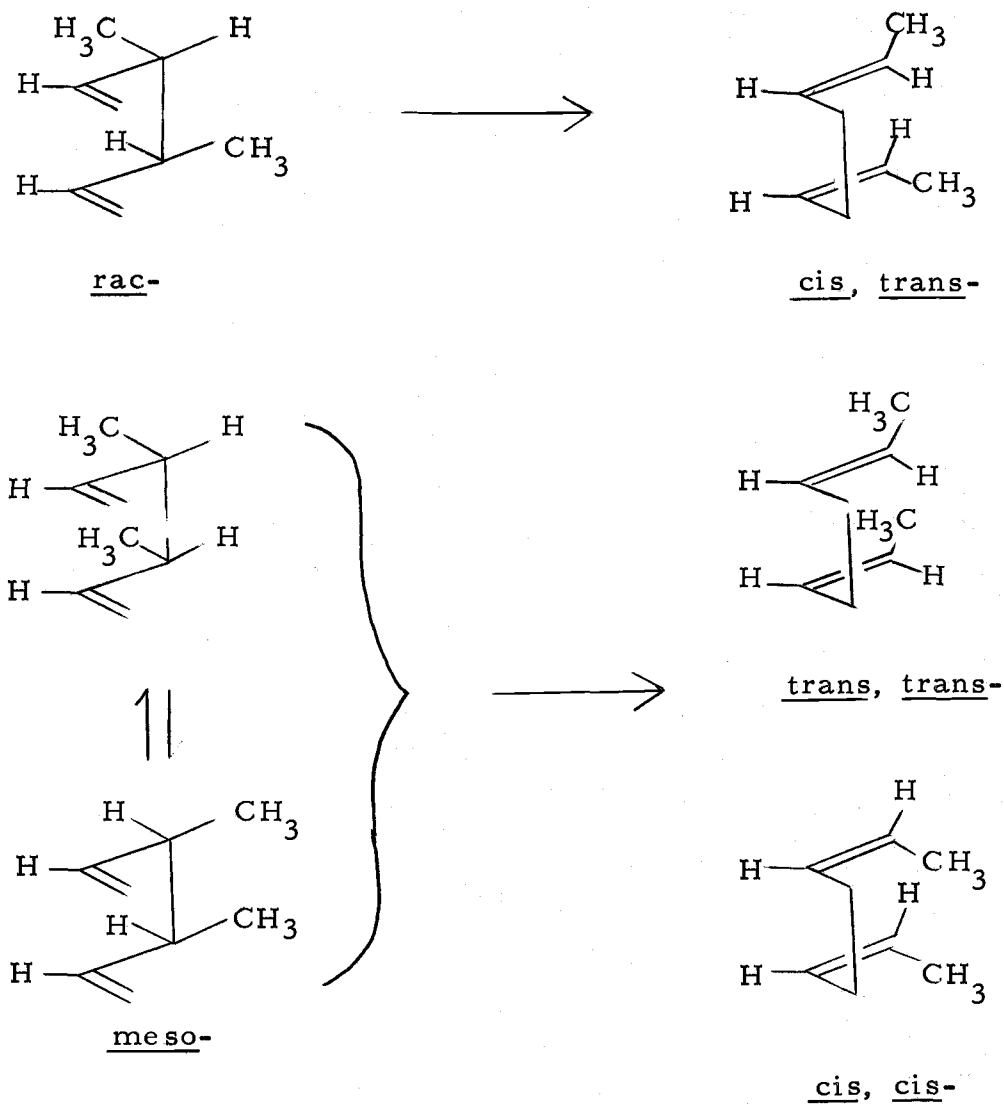
In 1947 Foster, Cope, and Daniels studied the kinetics of three biallyl systems at several temperatures and found the entropy of activation was about -12 e. u. (4). They pointed out that this considerable negative entropy of activation is in agreement with the cyclic mechanism since the cyclic transition state will have lost several degrees of freedom.

In 1961 Doering and Roth proved conclusively, in systems where constraints allow, the Cope rearrangement can proceed by a totally concerted mechanism and the transition state is chair-like rather than boat-like (5). They studied the rearrangement of meso- and rac-3,4-dimethyl-1,5-hexadiene to the isomeric 2,6-octadienes. In the case of the chair-like transition state (Scheme 1), rac-3,4-dimethyl-1,5-hexadiene can react in two ways to give cis, cis- or trans, trans-octadiene. meso-3,4-Dimethyl-1,5-hexadiene can form only cis, trans-octadiene.



Scheme 1. Products from a chair-like transition state.

Alternatively if a boat-like arrangement is favored in the transition state (Scheme 2), then rac-3,4-dimethyl-1,5-hexadiene would give the cis, trans-2,6-octadiene and the meso-isomer would produce a mixture of cis, cis- and trans, trans-2,6-octadiene.



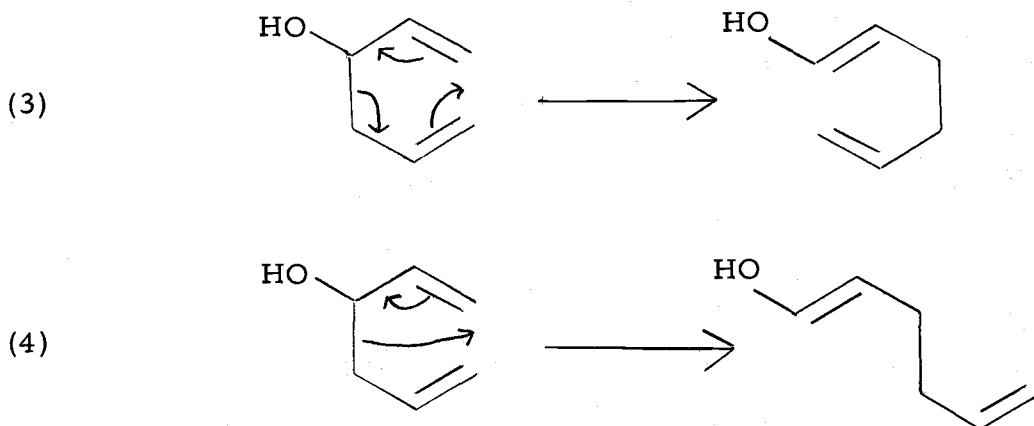
Scheme 2. Products from a boat-like transition state.

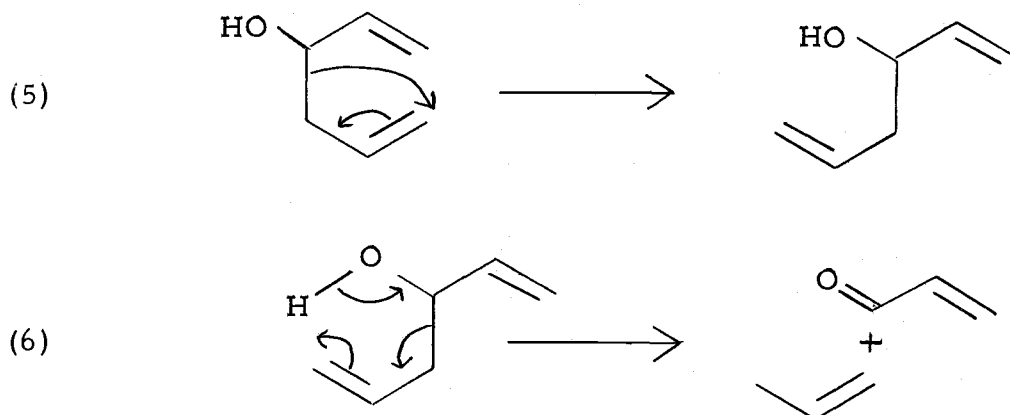
The result of the experiment was that meso-3,4-dimethyl-1,5-hexadiene rearranged at 225° almost exclusively (99.7%) to cis, trans-2,6-octadiene. Also, the rac- compound rearranged to a mixture of 10% cis, cis- and 90% trans, trans-octadiene. The retention of stereochemistry supports the concerted mechanism and the product

composition supports the chair-like transition state. Other workers have found the Cope rearrangement still occurs smoothly even when the transition state is constrained to the boat form rather than the preferred chair form, in such systems as cis-1,2-divinyl-cyclopropane and cyclobutane, and the 1-hydroxydicyclopentadienes (6, 7).

Nonconcerted versions of the Cope reaction have been postulated (6, 8, 9).

Numerous examples of the rearrangement of 3-hydroxy-1,5-hexadiene systems have been reported. In general these systems can rearrange thermally in four different ways: a [3, 3] sigmatropic shift leading to an enol (eq. 3), a [1, 3] sigmatropic shift leading to an enol (eq. 4), a [1, 3] sigmatropic shift not leading to an enol (eq. 5), and β -hydroxyolefin cleavage (eq. 6). All four can be symmetry allowed, concerted rearrangements (e.g., $[\pi^2_s + \sigma^2_s + \pi^2_s]$, $[\pi^2_s + \sigma^2_a]$, $[\pi^2_s + \sigma^2_a]$, and $[\sigma^2_s + \sigma^2_s + \pi^2_s]$ respectively) (10). Nonconcerted versions of all are known (11).

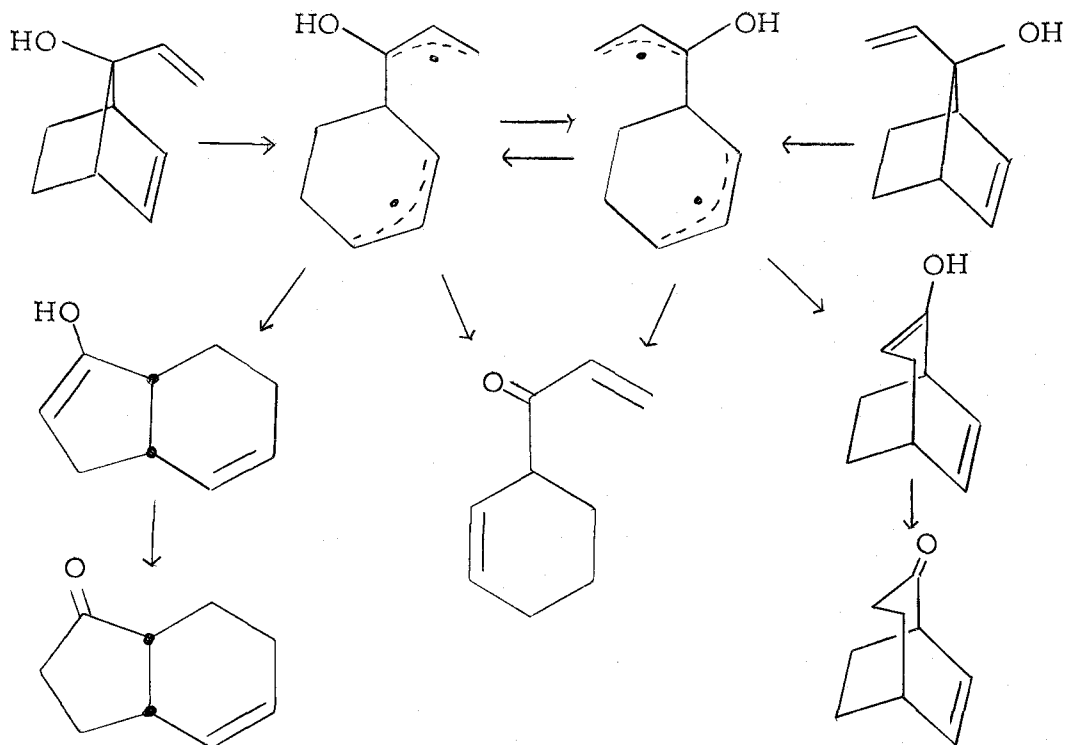




The above transformations which lead to enol forms have been termed oxy-Cope rearrangements (12).

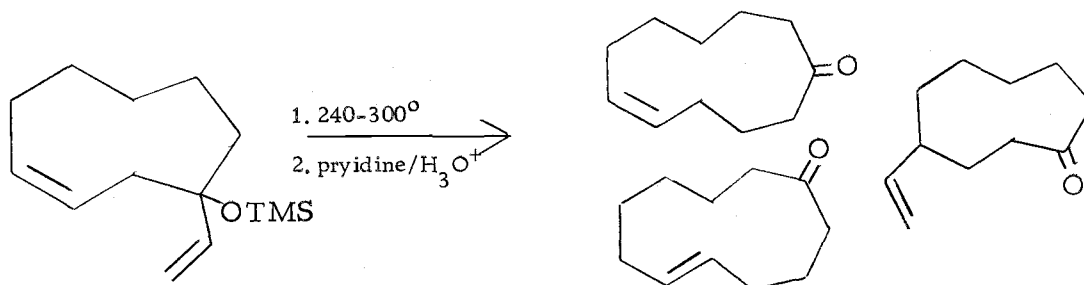
A. Viola and coworkers studied reactions of methyl-substituted open-chain 1,5-hexadien-3-ol systems (13). Pyrolyzing samples at temperatures ranging from 340° to 390°, they found production of cleavage products predominated at the higher temperatures, whereas the [3,3] sigmatropic shift was favored at lower temperatures. They found no intermolecular coupling products and none of either [1,3] shift product. The authors concluded the reactions were concerted proceeding through a cyclic six-member transition state.

Studies on certain bicyclic and medium-size ring systems show both [1,3] and [3,3] oxy-Cope rearrangements, and β -hydroxyolefin cleavage, all via diradical intermediates. Berson and Jones studied the thermal rearrangements of epimeric 7-vinylbicyclo [2.2.1] hept-2-en-7-ols (11).



Since both epimers react at almost the same rate, the authors postulated a diradical mechanism for the rearrangement of both epimers.

R. W. Thies has shown that β -hydroxycyclofin cleavage (eq. 6) may be eliminated using trimethylsilyl ethers of the alcohol, a procedure which results in higher yields (14, 15). The pyrolysis of 1-trimethylsiloxy-1-vinylcyclohex-3-ene was studied. Both [1, 3] and [3, 3] shift products were found as shown below.

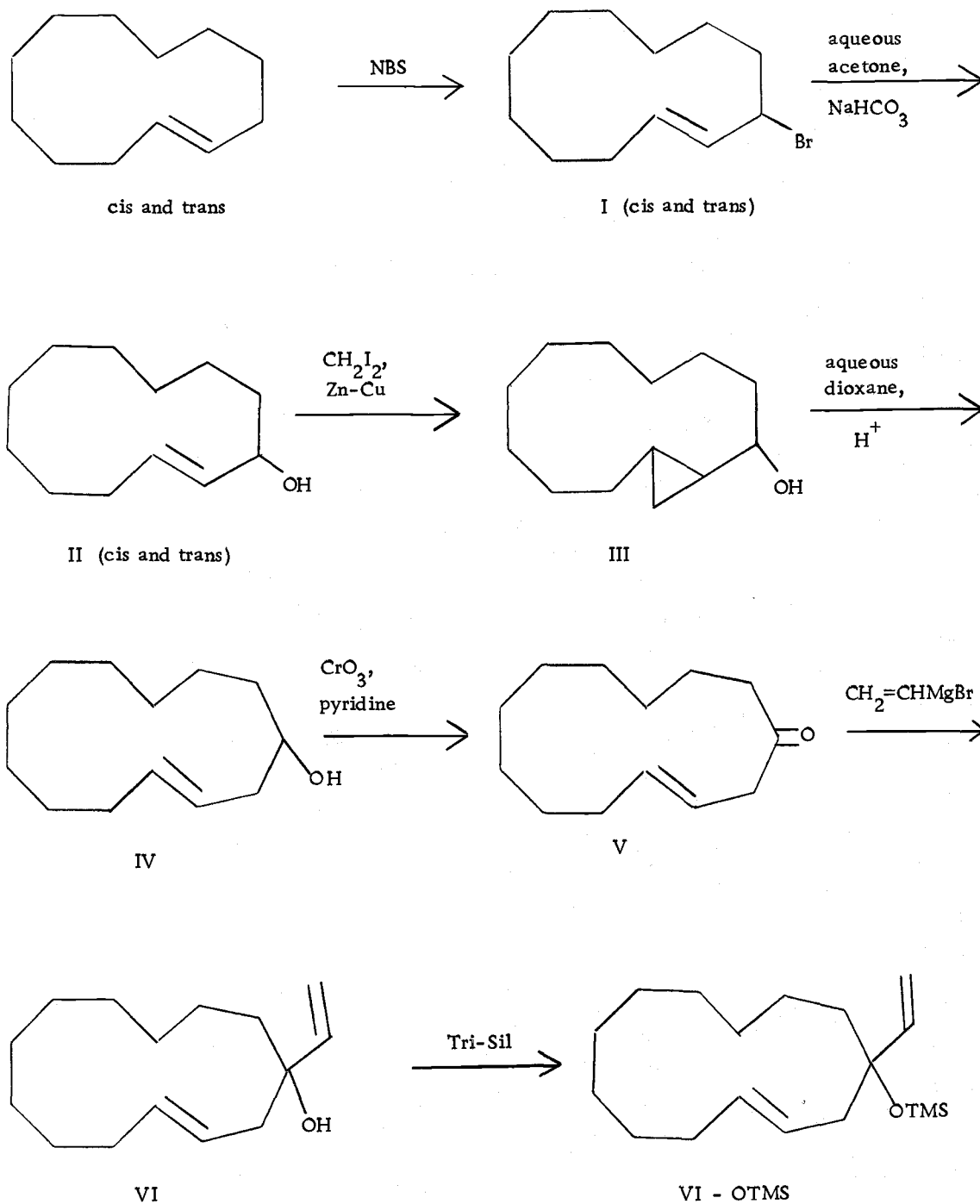


This rearrangement was thought to proceed via a diradical intermediate (16). The eight and ten-member ring homologs have also been studied (17, 18).

Recently Berson has questioned the idea that a diradical intermediate is involved in [1, 3] shift rearrangements (19). He argued there are three possible pathways to rearrangement: allowed concerted (e. g. $\pi^2_s + \sigma^2_a$), forbidden concerted (e. g. $\pi^2_s + \sigma^2_s$), and diradical. Using simple molecular theory, he predicted the transition state energy of the forbidden process to be intermediate between that of the allowed process and the diradical, thus making diradical formation the least favored pathway. The author's stereochemical labeling studies of small-ring and bicyclic systems indicate a lack of diradical intermediacy. Even though the stereochemistry does not support a diradical mechanism, the activation parameters are consistent with, and were previously taken as evidence for, the formation of a diradical.

II. RESULTS

In a continuation of previous studies involving the oxy-Cope rearrangement, in particular by incorporating the 1,5-hexadiene system into a large ring system rather than into a medium ring system, we proposed to synthesize and study the rearrangements of trans-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS). The compound of interest was synthesized according to the route shown in Scheme 3. Compound I was prepared by the action of N-bromosuccinimide on a mixture of cis- and trans-cyclododecene. Hydrolysis of the resulting allylic bromide led to the formation of cyclododec-2-en-1-ol (II). Reaction of the allylic alcohol (II) with methylene iodide and zinc-copper couple produced cyclopropyl alcohol (III), which was ring-opened under acid-catalyzed conditions to give trans-cyclotridec-3-en-1-ol (IV). Analysis of IV by glc showed one peak. After photolysis of IV in benzene, analysis showed the starting material and peak of slightly longer retention time. By analogy with other systems studied (20, 16), we presume that photolysis interconverts the cis- and trans- isomers and that the longer retention time peak is the cis- isomer. Since analysis of IV before photolysis showed only one peak, and the ir spectrum shows absorption characteristic of trans-olefin, we presume IV to be only the trans-isomer. Oxidation of the homoallylic alcohol (IV) with the Collins procedure (21) led



Scheme 3. Synthesis of *trans*-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS).

to trans-cyclotridec-3-ene-1-one (V) which, when reacted with vinyl magnesium bromide, resulted in formation of alcohol VI. The synthesis was completed by reaction of alcohol VI with Tri-Sil (Pierce Chemical Company) in dimethyl sulfoxide to yield trans-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS). The product was purified by preparative gas chromatography or bulb to bulb vacuum transfer. Compound VI-OTMS was photolyzed in benzene and analyzed by glc. Using the rationale mentioned previously, it was shown to be only the trans-isomer. The trimethylsilyl ether (VI-OTMS) was heated in sealed, evacuated ampoules then hydrolyzed to yield varying ratios of the products shown in Figure 1. After isolation by preparative gas chromatography, assignment of structure of 4-vinylcyclotridecanone (VII) and cyclopentadec-5-en-1-one (VIII) was based on high resolution mass spectroscopy, infra-red spectroscopy, and nmr studies. Mass spectroscopy gave verification of the empirical formula $C_{15}H_{26}O$ for the ketones. The infra-red spectra of ketones VII and VIII showed carbonyl bands at 1709 cm^{-1} . The vinyl ketone VII showed the characteristic pattern for the vinyl group in the nmr spectrum.

Europium shift studies, using $\text{Eu}(\text{fod})_3$ shift reagent, in combination with decoupling experiments were performed to determine the position of the vinyl group in ketone VII and the double bond in ketone VIII. As the shift reagent complexes with the oxygen atom, the protons near it shift downfield due to paramagnetic anisotropy effect.

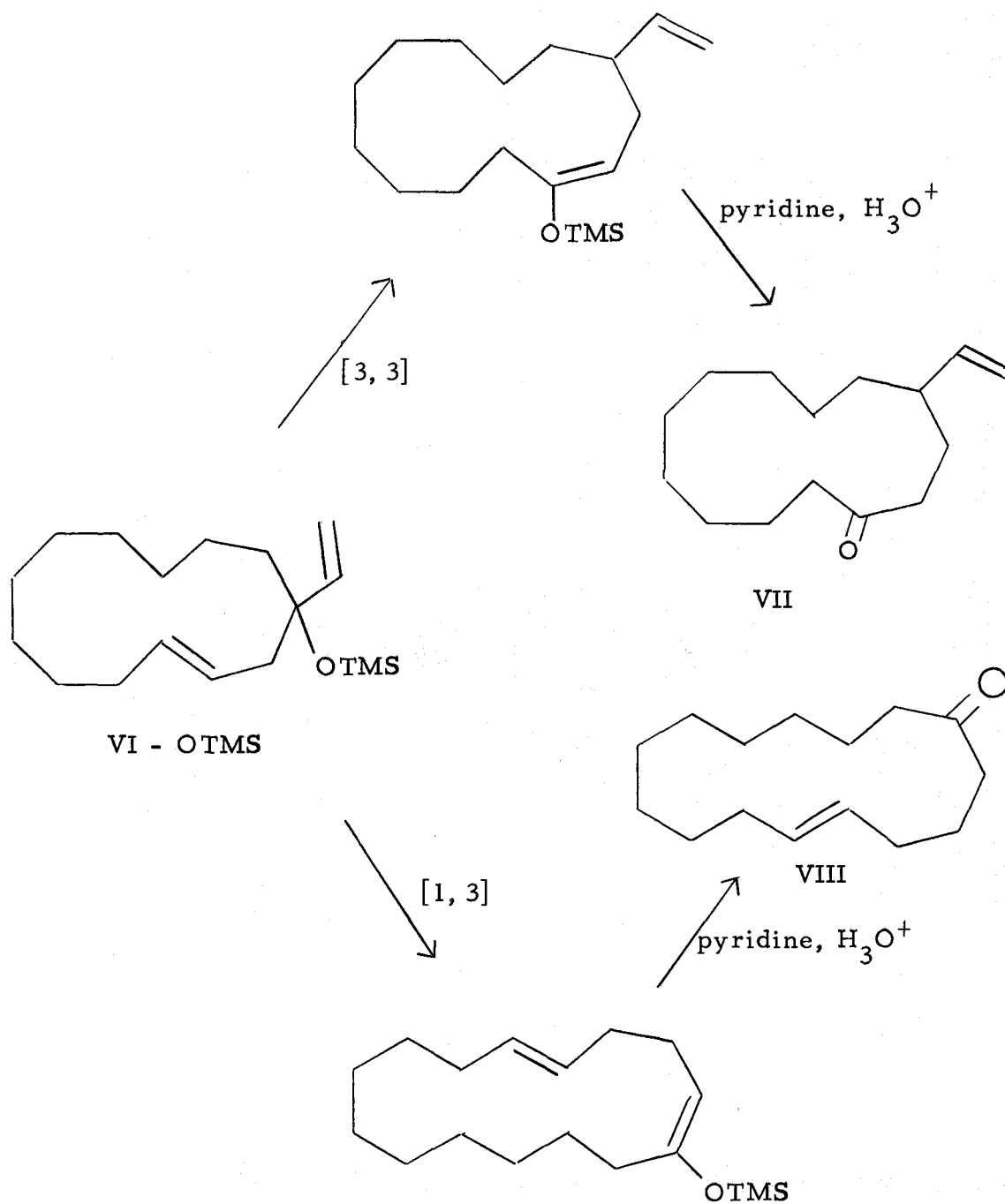
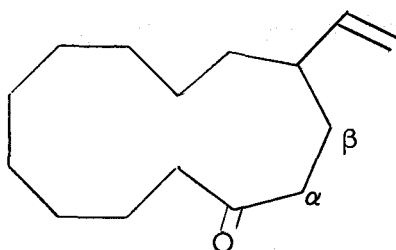


Figure 1. Products from the pyrolysis of *trans*-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS).

The protons closer to the complex move faster than those farther from it. When the protons move far enough apart, decoupling experiments are made possible. Before adding shift reagent to VII, the nmr spectrum showed a fourteen proton multiplet at 1.1-1.4 δ , a four proton multiplet at 1.4-1.8 δ , a one proton multiplet at 1.8-2.2 δ , a four proton multiplet at 2.3-2.5 δ , and a three proton multiplet at 4.9-5.8 δ . A reasonable assignment for the α protons is 2.3-2.5 δ , for the allylic proton is 1.8-2.2 δ , and for the β protons is 1.4-1.8 δ . After shift reagent was added and separation achieved (Figure 2), the β protons were irradiated and the α protons decoupled. Then the allyl proton was irradiated and the β protons decoupled. This study shows that the vinyl group is in the γ position.

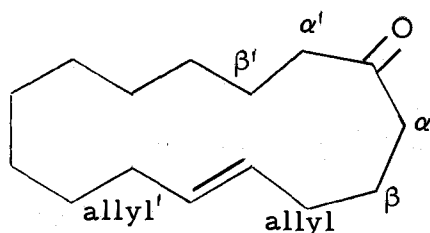


VII

	Chemical shifts (δ)		
	α	β	allyl
Before $\text{Eu}(\text{fod})_3$	2.3-2.5	1.4-1.8	1.8-2.2
1st addition of $\text{Eu}(\text{fod})_3$	4.9-5.2	3.2-3.6	3.6-3.9
2nd addition of $\text{Eu}(\text{fod})_3$	---	7.2-8.0	8.4-8.9

Figure 2. Relative chemical shifts of 4-vinylcyclotridecanone (VII) in $\text{Eu}(\text{fod})_3$ study.

Before adding shift reagent to VIII, the nmr spectrum showed a twelve proton multiplet at 1.1-1.5 δ , a four proton multiplet at 1.5-1.8 δ , a four proton multiplet at 1.8-2.2 δ , and a four proton multiplet at 2.2-2.5 δ . A reasonable assignment for the α protons is 2.2-2.5 δ , for the allylic protons is 1.8-2.2 δ , and for the β protons is 1.5-1.8 δ . These assignments were later confirmed by shift reagent, *i. e.*, the α protons which are closer to the carbonyl moved downfield faster than β protons which in turn moved downfield faster than allylic protons (Figure 3). After shift reagent had been added



VIII

	Chemical shifts (δ)					
	α	β	allyl	α'	β'	allyl'
Before Eu(fod) ₃	2.2-2.5	1.5-1.8	1.8-2.2	2.2-2.5	1.5-1.8	1.8-2.2
After Eu(fod) ₃	5.2-5.4	4.0-4.3	2.8-3.1	5.4-5.6	3.2-3.5	2.3-2.6

Figure 3. Relative chemical shifts of cyclopentadec-5-en-1-one (VIII) in Eu(fod)₃ study.

and the allyl protons were irradiated, the β and the olefinic patterns sharpened. When the β protons were irradiated the α protons decoupled. This study shows that the double bond is in the δ - ϵ position.

After ketone VIII was reduced to an alcohol, it was photolyzed in benzene and analyzed on glc. Using the rationale mentioned previously, ketone VIII was shown to be greater than 97% the trans-isomer.

Kinetic runs were conducted using sealed, evacuated ampoules containing ca. 10 mg of sample. The product ratio of the thermolysis was found to be temperature dependent. As the temperature of pyrolysis is increased, the relative amount of [1, 3] product to [3, 3] product increases as shown in Table 1. The rate of disappearance of VI-OTMS showed first order behavior. Table 2 presents the variation of rate with temperature and the resulting activation parameters. It was found that hydrolysis of the enol forms occurred spontaneously to some extent during some pyrolyses, but it was not determined what conditions caused this to happen. The extent was negligible for the kinetic runs. Samples were analyzed after complete hydrolysis in refluxing pyridine/ H_3O^+ solution.

Table 1. Relative percent of products formed from the thermolysis of VI-OTMS followed by hydrolysis.^a

T °C	Time, min.	Relative Product Percentages		
		VI	[3, 3]	[1, 3]
245.9	930	59.9	29.3	10.8
245.9	1240	56.4	31.5	12.1
245.9	1340	54.1	33.5	12.4
245.9	1480	48.2	36.6	15.2
245.9	1690	44.5	39.9	15.6
245.9	1810	38.7	43.8	17.5
245.9	2625	31.1	49.2	19.7
254.1	210	85.0	9.9	5.1
254.1	660	58.9	30.4	10.7
254.1	720	48.9	35.7	15.4
254.1	870	49.3	35.8	14.9
254.1	870	49.3	34.9	15.8
254.1	1050	40.6	39.9	19.5
254.1	1140	39.6	41.7	18.8
254.1	1290	35.7	44.1	20.2
284.4	20	89.3	7.0	3.8
284.4	55	72.8	16.0	11.2
284.4	60	63.7	21.4	14.8
284.4	75	60.1	24.1	15.8
284.4	75	58.6	24.7	16.7
284.4	80	54.2	27.3	18.5
284.4	105	42.8	33.0	24.1
284.4	150	33.8	38.4	27.8
284.4	150	31.0	40.2	28.8
298.6	20	62.6	20.0	17.4
298.6	25	54.7	24.8	20.5
298.6	30	49.5	27.6	22.9
298.6	35	43.7	30.1	26.2
298.6	45	34.6	35.3	30.1
298.6	50	30.9	37.1	32.0
298.6	60	25.6	40.2	34.2
298.6	65	20.8	42.3	36.9

^aAll samples were pyrolyzed in a NaNO₂-KNO₃ fused salt bath.

Table 2. First order rate of disappearance of trans-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS).^a

$T^{\circ}\text{C}^{\text{b}}$	$k \times 10^5 \text{ (sec}^{-1}\text{)}^{\text{c}}$	Correlation Coefficient
245.9	$0.69 \pm .05$	0.997
254.1	$1.34 \pm .08$	0.984
284.4	$13.3 \pm .60$	0.992
298.6	39.0 ± 0.5	0.998
	<u>E_a</u>	<u>log A</u>
[3, 3] process	41.8	12.3
[1, 3] process	50.3	15.5

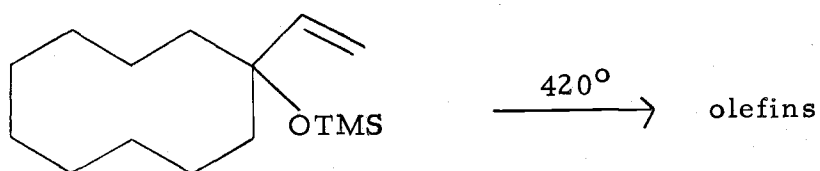
^aRates were measured by R. W. Thies.

^bDetermined by a platinum resistance thermometer in a $\text{NaNO}_2\text{-KNO}_3$ fused salt bath.

^cThe rate constant is obtained by a least-squares plot of 7-9 data points at each temperature.

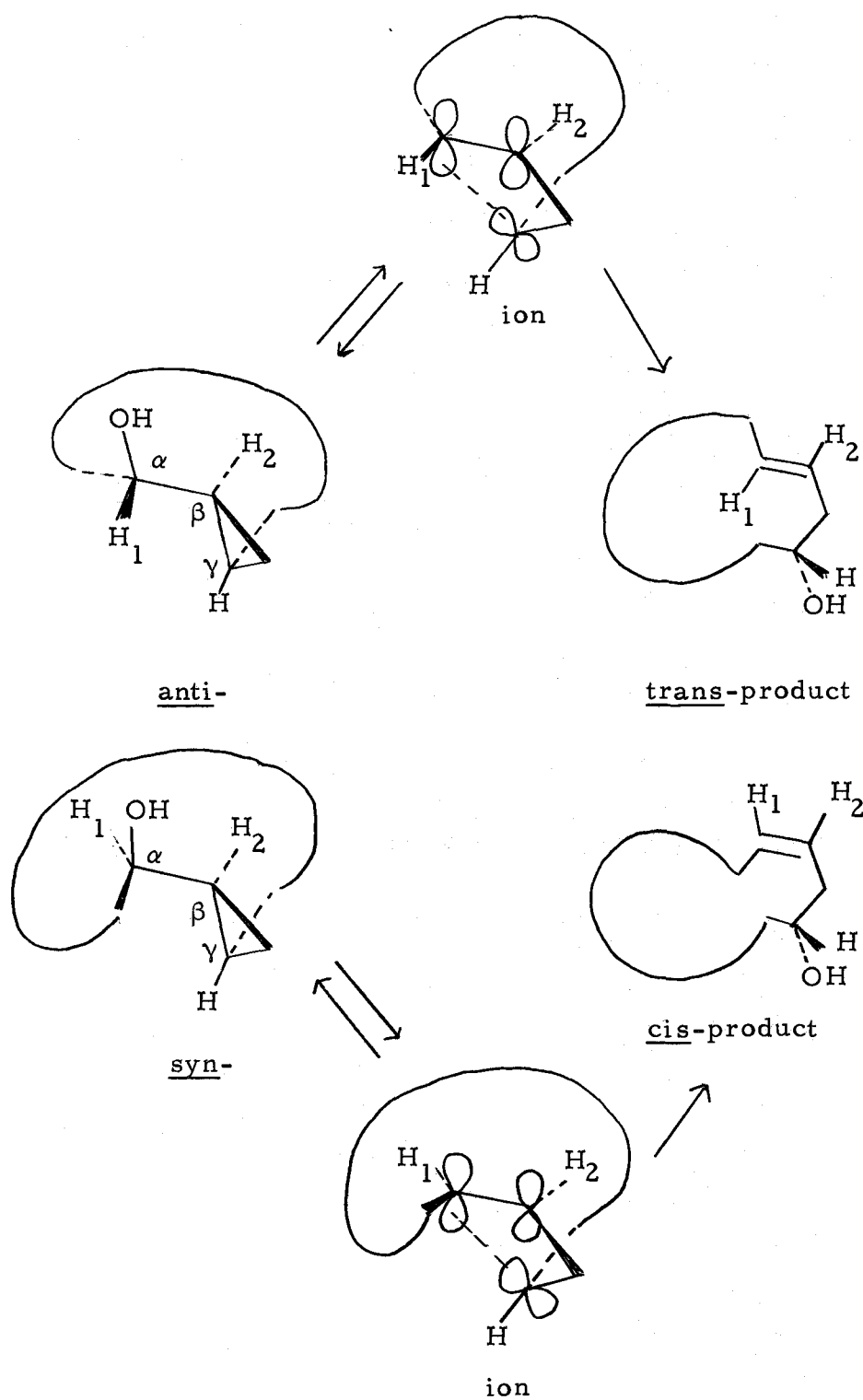
III. DISCUSSION

Thies and coworkers have investigated the oxy-Cope and siloxy-Cope rearrangements of medium-size ring compounds (16, 17, 18) in an attempt to uncover the mechanism of reaction, *i. e.*, either concerted or diradical. The synthetic utility as a two-carbon ring expansion reaction was also discussed. In this respect, the influence of ring strain was thought to be an important factor since it affects the rate of reaction. This in turn governs the temperatures which must be used for the thermolysis. It was shown by the thermolysis of 1-trimethylsiloxy-1-vinylcyclodecane that if an excessive temperature is necessary other reactions can compete with the siloxy-Cope rearrangement (18).



The present study was undertaken on a system where ring strain is small relative to the other systems studied to determine if the siloxy-Cope could have any synthetic utility in large ring compounds. Would ring expansion occur readily, or would the temperature necessary for reaction be too high and cause side reactions? Could any conclusions about the mechanism of reaction be drawn?

It is interesting to note that in the synthetic scheme for the formation of 1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS) only the trans-isomer is formed. This stereospecificity can be traced back to the formation of trans-cyclotridec-3-en-1-ol (IV) from bicyclo[10.1.0]dodecan-2-ol (III). It has been shown that stereochemical selectivity is expected from reactions proceeding by way of homoallylic ions formed by anchimeric assistance of the $C_{\beta}-C_{\gamma}$ bond in the cyclopropyl precursor (22). The cyclopropane can be either syn or anti to the alcohol function (Scheme 4). For the $C_{\beta}-C_{\gamma}$ bond of the cyclopropane ring of the anti-epimer to participate in the isomerization, rotation about the $C_{\alpha}-C_{\beta}$ bond must occur so as to take place H_1 and H_2 in a trans relationship in the ion and thus in the product. Conversely, a cis relationship of H_1 and H_2 is expected in the ionization of the syn-epimer. Since homoallylic alcohol IV has been shown to be only the trans-isomer, it may be concluded that cyclopropyl alcohol III formed in the Simmons-Smith reaction (23) is only the anti-epimer. This result is in agreement with the work of Poulter, Friedrich, and Winstein (24) and Thies and Billigmeier (18). This result is novel in that other workers prepared cyclopropyl alcohols from allylic alcohols with only cis double bonds in the ring, while this study involves an allylic alcohol with a trans double bond.



Scheme 4. Mechanism and products of cyclopropyl alcohol ring opening reaction.

Table 3 shows the E_a values for some analogous siloxy-Cope reactions which rearrange primarily by the [1, 3] process (18).

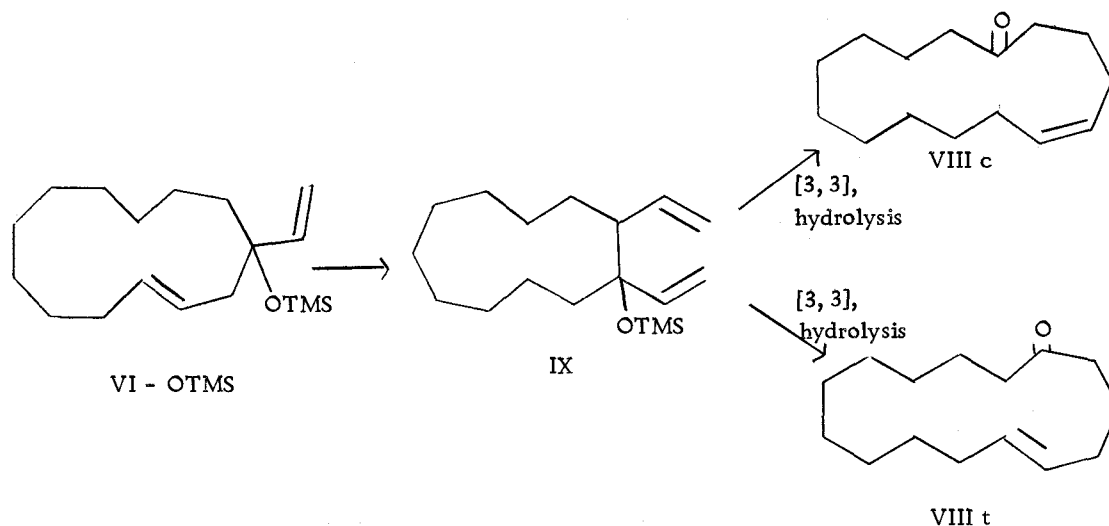
Table 3. Activation energies for some siloxy-Cope rearrangements.

Ring size	E_a , kcal/mole
8 (cis)	53.9
10 (cis)	50.4
9 (cis)	47.7
10 (trans)	45.1

As shown in the results section, the E_a for the pyrolysis of VI-OTMS is 50.3 for the [1, 3] process. This relatively high E_a coupled with the fact that the [3, 3] process is preferred over the [1, 3] process, at temperatures comparable to those used in other systems studied, suggests that a two-carbon ring expansion in large-member rings is not as synthetically useful as in medium-size rings.

The two ketones (VII and VIII) formed in the pyrolysis of VI-OTMS after hydrolysis result formally from a [3, 3] and a [1, 3] sigmatropic shift respectively. Any loss of trans stereochemistry from the starting material, in the formation of ring-expanded products, requires the process to occur by more than one concerted step or by a diradical.

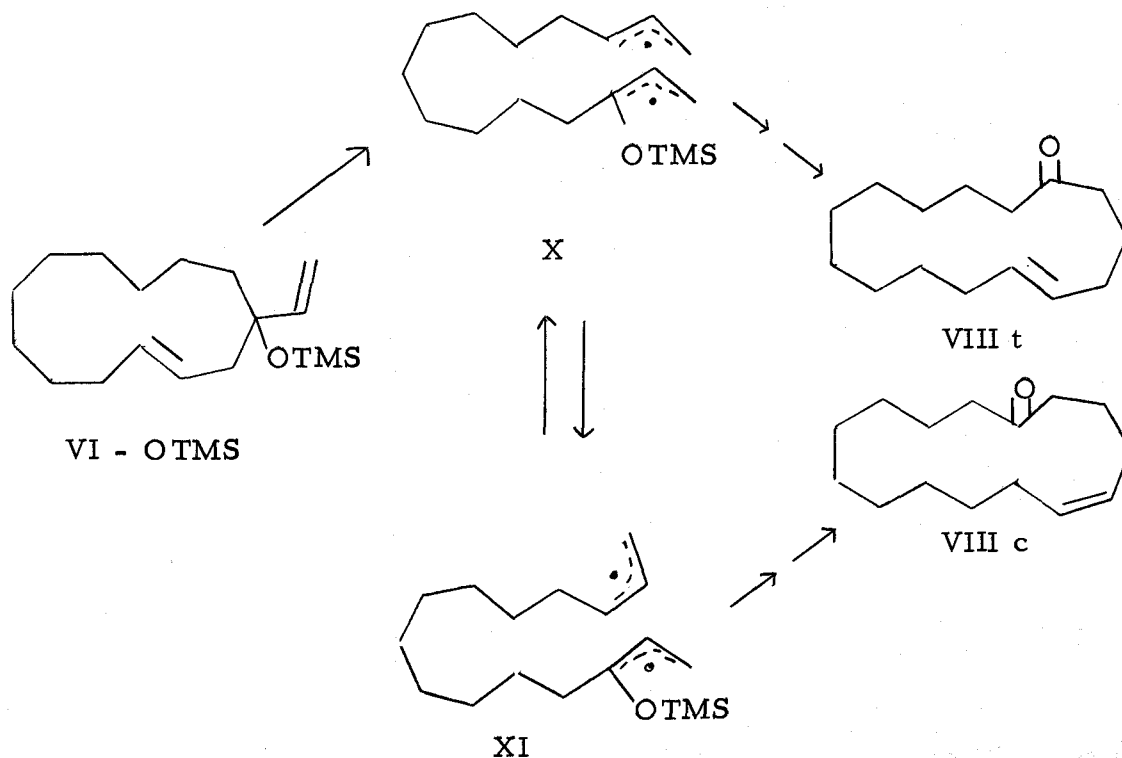
One possible concerted pathway which leads to stereochemical crossover is shown in Scheme 5.



Scheme 5. Concerted mechanism.

The divinyl intermediate (IX) could be formed with syn or anti stereochemistry, either of which could rearrange to give the cis-isomer (VIIIc) or the trans-isomer (VIIIt) after hydrolysis. The divinyl intermediate was not observed as a product of the pyrolysis, but this is expected because it is of higher energy than starting material or products and likely to rearrange immediately upon formation. Since the hydrolysis product of the divinyl compound IX was not found, the rearrangement of IX must be as fast or faster than its formation. This is reasonable because [3, 3] shifts are often faster than [1, 3] shifts. The divinyl compound was isolated in the eight-membered ring analog of this work (17). Other possible concerted mechanisms have been postulated (16).

A second pathway of rearrangement consistent with loss of stereochemistry involves intermediacy of a diradical (Scheme 6).



Scheme 6. Diradical mechanism.

Once formed, X could undergo ring closure to form VIII t after hydrolysis, or the allyl group could rotate to form XI. Ring closure could then occur to form VIII c after hydrolysis. Rotation of the allyl group must be slow with respect to ring closure, to form the trans-isomer, so that only a small amount of cis-isomer is formed.

The results of the thermolysis are consistent with either a concerted or a diradical mechanism for the [1,3] process. Figure 4 shows ring strain energies (S. E.) associated with simple cycloalkenes

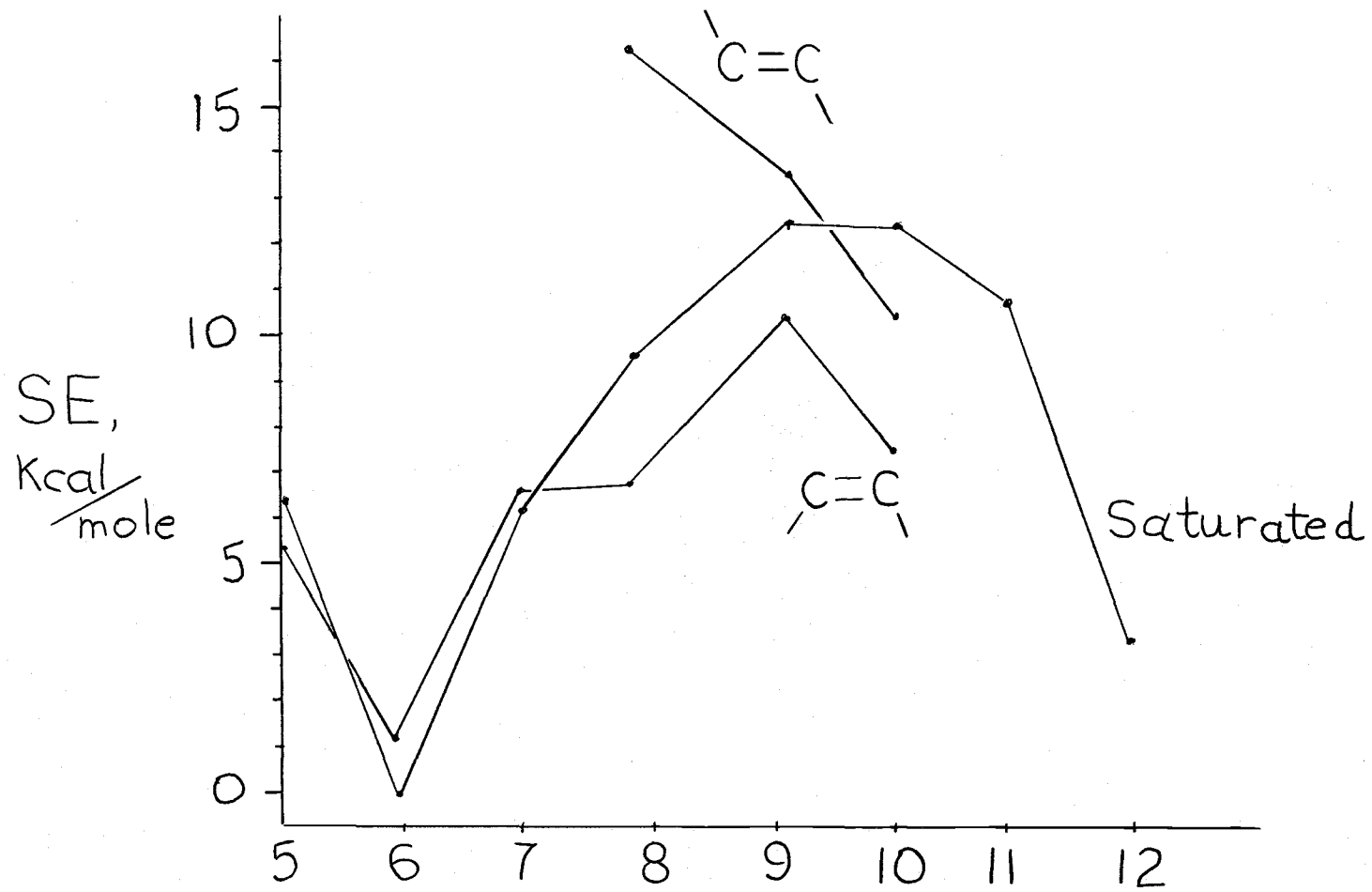


Figure 4. Strain energy (S. E.) associated with some simple cyclic systems.

and cycloalkanes (25, 26). The value for the strain energy of trans-cyclotridecene has not been determined, but if we look at the trend in Figure 4, we can see that S.E. drops in all systems as ring size increases above nine carbons. From this trend we can expect the S.E. of trans-cyclotridecene to be much less than it is in the medium-size rings. Now, for a diradical mechanism we would expect the E_a to be inversely proportional to the S.E., i. e., a smaller S.E. produces a higher E_a and thus a slower rate. Table 4 compares the S.E., E_a , and rates of VI-OTMS and the much more strained trans-1-trimethylsiloxy-1-vinylcyclodecene (XI). As is noticed from the

Table 4. Comparison of two siloxy-Cope rearrangements.

Compound	S.E.	E_a	$10^5 k(\text{sec}^{-1})$
XI	10.7	45.1	32.1 at 280°
VI-OTMS	$\ll 10.7$	50.3	13.3 at 284°

table, VI-OTMS has much less S.E. than XI and, as was predicted for a diradical, a larger E_a and slower rate of rearrangement. This result can also be explained by a concerted mechanism. Since XI has more S.E. it would be higher on the energy scale than VI-OTMS, while the products would be approximately equal in energy because the S.E. of the products are about equal. Since the transition state for a concerted reaction resembles products to some degree and the product of rearrangement of XI has lost more S.E. than that of the VI-OTMS case, we would expect the transition state of XI to lose S.E. relative to that of VI-OTMS in going to products of equal energy. Therefore

we would predict XI to have a smaller E_a and faster rate.

Another important point to consider is that in the large ring system studied, the ratio of [3, 3] to [1, 3] shift products is much greater than it is in analogous medium ring systems, as shown in Table 5 (16, 18).

Table 5. Product comparison for some siloxy-Cope rearrangements.

Ring size	Temp.	% Conversion	Relative product % after hydrolysis	
			[3, 3]	[1, 3]
9 (cis)	299.0	49.0	12	88
10 (cis)	295.2	49.4	9	91
10 (trans)	280.0	51.0	11	89
VI-OTMS	298.6	50.5	55	46

This result can be explained in terms of a concerted mechanism for the [3, 3] shift. In the medium-size ring compounds shown, it is relatively difficult for the molecule to achieve the chair-like or boat-like transition state necessary for the concerted [3, 3] shift. But as ring size is increased to thirteen carbons, more flexibility is gained. Thus it is easier to obtain the proper geometry and relatively more [3, 3] product is produced. Some rigidity must still be present in the thirteen member ring since the E_a of 41.8 kcal/mole for rearrangement is higher than expected for a concerted process with no constraints. Typical values of E_a for such a

concerted process are ca. 23-35 kcal/mole (8, 27).

Finally, the relative increase in [1, 3] shift product with increasing temperature is due to entropy effects. Since the [3, 3] shift process has the more ordered transition state, its ΔS^\ddagger term will be more negative than the ΔS^\ddagger term for the [1, 3] process. According to the equation $\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$, as temperature is increased and the ΔS^\ddagger term is negative, the $|-T\Delta S^\ddagger|$ term becomes more positive and the free energy term less favorable for the [3, 3] process. Thus at high temperature the [1, 3] process is favored relative to the [3, 3] process.

IV. EXPERIMENTAL

General Information

The infrared spectra were measured on a Beckman IR-8 or a Perkin-Elmer Model 621. NMR spectra were measured on Varian Associates HA-100 or EM360 instruments. Mass spectra were obtained on an Atlas CH7 or CEC 110B instrument. High resolution mass spectra were obtained with the CEC 110B instrument at the University of Oregon. All gas chromatography analyses were done with a Varian Aerograph Series 1200 gas chromatograph, fitted with flame ionization detector. The following columns were used:

Column A: 25' x 0.01" UCON LB 550X capillary;

Column B: 1/8" x 10' column packed with 10% DEGS on
ChW 60/80;

Column C: 50' x 0.01" DEGS PLOT capillary.

Helium flow through the 1/8" column was ca. 25 ml/min. The helium flow through the 0.01" capillary column was ca. 4 ml/min. A Hewlett-Packard 3373B integrator was used to determine peak areas. Preparative gas chromatography was done on a Gow-Mac instrument with a 1/4" x 4', 10% DEGS on CHW column.

Preparative Detail

3-Bromocyclododecene (I). A 200 g sample of distilled

technical grade cyclododecene, 220 g of freshly opened N-bromo-succinimide, and 1.25 l of carbon tetrachloride were added to a three-neck round bottom flask fitted with nitrogen inlet, mechanical stirrer, and dry ice condenser. The reaction mixture was stirred and heated to reflux before adding one spatula tip of benzoyl peroxide initiator. Reflux was continued for one hour, during which time a vigorous reaction occurred. The reaction mixture was filtered, the filter cake washed with additional carbon tetrachloride and discarded. The filtrate was washed with saturated sodium bicarbonate solution, then twice with water. The organic layer was evaporated, and the crude product was taken directly on to the next reaction without further purification. A small sample of the product was purified by vacuum distillation to yield a light yellow oil: bp 90-100° (0.6 mm); ir (neat) 3020 (vinyl), 1650 (olefin), 1460, 1445, 970, 950, 758 cm^{-1} ; nmr (CCl_4 , δ) 1.0-1.8 (m, 14H), 1.8-2.4 (m, 4H), 5.1-6.7 (m, 3H).

Cyclododec-2-en-1-ol (II). The previously prepared 3-bromocyclododecene (I) and 1.5 l of 60% aqueous acetone were added to a one-neck round bottom flask fitted with dry ice condenser. The reaction mixture was heated to reflux for 1.5 hours. As this two phase reaction progressed, the two layers reversed positions. The lower water layer was discarded, and the organic layer was washed with water, saturated brine solution, and dried over anhydrous

magnesium sulfate. Vacuum distillation was used to purify the product (68 g, 31% for two reactions): bp 103-105^o (0.15 mm); glc on Column B shows one peak; ir (neat) 3375 (OH), 1650 (olefin), 1460, 1445, 1015, 975 cm⁻¹; nmr (CCl₄, δ) 1.1-1.8 (m, 16H), 1.8-2.2 (m, 2H), 2.3 (s, 1H), 3.8-4.2 (M, 1H), 5.0-5.7 (m, 2H). The infrared spectrum matches that of the same compound synthesized by a different route (28).

Bicyclo[10.1.0] dodecan-2-ol (III). An 18 g sample of zinc-copper couple [prepared by the LeGoff method (29)], 23 g of methylene iodide dissolved in 60 ml of anhydrous ether, and a crystal of iodine were added to a three-neck round bottom flask fitted with nitrogen inlet, mechanical stirrer, condenser, and pressure-equalizing dropping funnel. The mixture was stirred with the oil bath at 50^o. Once the violet color of the zinc-copper couple had formed, 20.7 g of the alcohol (II) in 65 ml of anhydrous ether was added in two minutes without the reaction becoming vigorous. A second portion of methylene iodide (45 g) in 20 ml of anhydrous ether was added in 15 minutes. Analysis of the reaction mixture on column A at a temperature of 100^o indicated complete reaction eight hours after final addition of methylene iodide. The flask was allowed to cool and the reaction mixture was quenched with saturated ammonium chloride solution until two phases appeared. The reaction mixture was vacuum filtered through celite. The pad was washed with a small

amount of anhydrous ether and discarded. The ether and aqueous phases were separated, the aqueous phase discarded, and the solvent rotary evaporated from the product. The Simmons-Smith product (23) was purified by liquid chromatography to yield a low melting white solid (11.5 g, 52%); glc on Column B shows one peak; ir (CCl_4) 3670 (OH), 3525 (OH), 3070 (cyclopropane), 3050 (cyclopropane), 1460, 1455, 1075, 1025, 985 cm^{-1} ; nmr (CCl_4 , δ) 0.1-1.0 (m, 4H), 1.0-2.3 (m, 19H), 2.5-2.9 (m, 1H); mass spectrum: a good analysis was not attainable because no parent peak could be found, but a P-18 was found at the proper mass.

trans-Cyclotridec-3-en-1-ol (IV). A 20.5 g sample of cyclopropyl alcohol (III), 150 ml of 0.12 M perchloric acid, and 585 ml of dioxane were added to a two-liter round bottom flask, equipped with condenser and magnetic stirrer. The solution was heated, with stirring to 85°. Analysis of the solution on column A at a temperature of 85° indicated the reaction was complete after 3 hours. The reaction solution was divided into two portions, and the first portion poured into a solution of 1500 ml of 50:50 ether-pentane and 75 ml of water. The resulting two layers were separated, and the organic layer washed once with a saturated sodium bicarbonate solution and then once with a saturated brine solution. The above procedure was reported for the second portion of the reaction solution. The two portions were combined and dried over anhydrous

magnesium sulfate. The solvent was evaporated, and the residue, upon cooling, was a low melting white wax (15 g, 75%); glc on Column B shows one peak; ir (CCl_4) 3400 (OH), 1700, 1460, 1445, 973 cm^{-1} ; nmr (CCl_4 , δ) 1.1-1.5 (m, 16H), 1.6 (s, 1H), 1.8-2.4 (m, 4H), 3.4-3.8 (m, 1H), 5.2-5.5 (m, 2H); mass spectrum m/e 196.181 (calcd. for $\text{C}_{13}\text{H}_{24}\text{O}$ m/e 196.183).

trans-Cyclotridec-3-en-1-one (V). A 9.49 g sample (120 mmol) of dry pyridine and 150 ml of methylene chloride were added to a one-neck round bottom flask equipped with a magnetic stirrer. To this solution was added 6.00 g (60 mmol) of chromium trioxide with stirring. The flask was stoppered with a drying tube, and the mixture was allowed to stir for 15 minutes at room temperature. At the end of this time, 1.96 g (10 mmol) of the homoallylic alcohol (IV) was added in a small amount of methylene chloride. A tarry, black deposit separated immediately. The reaction mixture was allowed to stir an additional 15 minutes before 50 ml of anhydrous ether was added to coagulate the chromium salts. The mixture was gravity filtered, and the residue washed with 200 ml of anhydrous ether. The two organic phases were combined and washed three times with 100 ml portions of 5% aqueous sodium hydroxide, once with a 100 ml portion of 5% aqueous hydrochloric acid, once with a 10 ml portion of aqueous sodium bicarbonate, once with a 100 ml portion of saturated copper sulfate, and once with a 100 ml portion of saturated brine

solution. The product was dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated. This oil was taken on to the next reaction without further purification (crude yield 100%); glc on Column B shows one peak; ir (neat) 1710 (carbonyl), 1460, 1455, 1360, 972 cm^{-1} ; nmr (CCl_4 , δ) 1.0-1.9 (m, 14H), 1.9-2.2 (m, 2H), 2.2-2.5 (t, 2H), 2.8-3.1 (d, 2H), 5.3-5.6 (m, 2H); mass spectrum m/e 194.167 (calcd. for $\text{C}_{13}\text{H}_{22}\text{O}$ m/e 194.168).

trans-1-Vinylcyclotridec-3-en-1-ol (VI). A 1.82 g sample (75 mmol) of magnesium, and 5 ml of a solution composed of 8.03 g of freshly distilled vinyl bromide (75 mmol) in 30 ml of dry tetrahydrofuran were added to a three-neck round bottom flask fitted with magnetic stirrer, pressure equalizing dripping funnel, dry ice condenser, and nitrogen inlet. The reaction was stirred and warmed with a heat gun until evidence of a reaction was apparent. The reaction mixture was diluted with an additional 30 ml of tetrahydrofuran; then the remaining portion of vinyl bromide solution was added dropwise to maintain reflux. The addition required ca. 30 minutes, after which the reaction mixture was allowed to stir an additional 30 minutes. The flask was cooled to 0° and 5.7 g (29 mmol) of the ketone (V) in 40 ml of dry tetrahydrofuran was added slowly (ca. 10 minutes). Analysis of an aliquot of the reaction mixture on column B at 120° showed the reaction to be complete 20 minutes after addition of the ketone. The reaction was quenched by

the slow addition of 50 ml of a saturated ammonium chloride solution. The reaction mixture was poured into 350 ml of 50:50 ether-pentane solution, the layers separated, and the organic layer washed three times with 200 ml portions of water and once with a 200 ml portion of saturated brine solution. The organic layer was dried over anhydrous magnesium sulfate and filtered. Solvent was evaporated to leave a viscous yellow oil (5.9 g, 91%); glc on Column B shows one peak; ir (neat) 3450 (OH), 3125 (vinyl), 1640 (vinyl), 1460, 1445, 1420, 1125, 1070, 980, 920 cm^{-1} ; nmr (CCl_4 , δ) 1.0-1.7 (m, 16H), 1.7-2.1 (m, 2H), 2.1-2.2 (d, 2H), 2.4-2.6 (s, 1H), 4.8-6.3 (m, 5H); mass spectrum m/e 222.198 (calcd. for $\text{C}_{15}\text{H}_{26}\text{O}$ m/e 222.198).

trans-1-Trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS).

A 1.0 ml sample of alcohol (VI) was mixed with 3.0 ml of dry dimethylsulfoxide and 2.0 ml of Tri-Sil in a screw-capped vial. The mixture was shaken for 15 minutes, then allowed to stand for 30 minutes. Pentane was added until the volume of the mixture was doubled. The mixture was shaken again; the top layer was pipetted off, washed with water, and dried over anhydrous magnesium sulfate. The product was purified further by use of an Aldrich Kugelrohr (a bulb to bulb vacuum transfer apparatus). The product was transferred at 0.25 mm with the air bath at 100°; glc on Column A shows one peak; ir (CCl_4) 3110, 1455, 1445, 1415, 1225, 1055, 975, 920,

835 cm^{-1} ; nmr (CCl_4 , δ) 0.9-1.7 (m, 16H), 1.7-2.1 (m, 2H), 2.1-2.3 (d, 2H), 2.4 (s, 1H), 4.8-6.3 (m, 5H); mass spectrum m/e 294.230 (calcd. for $\text{C}_{15}\text{H}_{34}\text{OSi}$ m/e 294.237).

Ampoule Pyrolysis of trans-1-Trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS)

Pyrex ampoules (10 ml) were washed with acetone, water, and concentrated ammonium hydroxide then dried overnight at 120° in an oven. In a typical analytical run, 10 μl of sample was added to an ampoule, which was then evacuated at 0.1 mm for 30 minutes and sealed. The ampoule was placed in an aluminum block oven maintained by a Proportionul temperature controller or in a fused salt bath maintained by a Bailey temperature controller.

The above procedure was also used with larger ampoules (65 ml and 250 ml) using proportionately larger sample sizes.

Hydrolysis of Pyrolysis Products

The crude mixture from the pyrolysis was hydrolyzed by refluxing 10 μl of sample in 0.5 ml of a solution consisting of 10 ml pyridine, 1 ml of water, and two drops of concentrated hydrochloric acid. The sample was extracted into 5 ml of ether and washed twice with 2 ml portions of 10% sulfuric acid, once with a 2 ml portion of saturated carbonate, and dried over anhydrous magnesium sulfate.

The reaction mixture was then analyzed on Column B or Column C.

It was found that under some conditions partial hydrolysis occurred spontaneously during pyrolysis.

Identification of Pyrolysis Products (After Hydrolysis)

Structural assignment for 4-vinylcyclotridecanone (VII). The structure was assigned by spectral properties: ir (CCl_4) 3110, 1790, 1709, 1645, 1460, 1440, 1405, 1350, 1250, 1220, 905 cm^{-1} ; nmr (CCl_4 , δ) 1.1-1.4 (m, 14H), 1.4-1.8 (m, 4H), 1.8-2.2 (m, 1H), 2.3-2.5 (m, 4H), 4.9-5.8 (m, 3H); mass spectrum m/e 222.196 (calcd. for $\text{C}_{15}\text{H}_{26}\text{O}$ m/e 222.198). Europium shift studies combined with decoupling experiments support the assignment of the vinyl group to the 4-position.

Structural assignment for cyclopentadec-5-en-1-one (VIII). The structure was assigned by spectral properties: ir (CCl_4) 1790, 1709, 1455, 1445, 1365, 1215, 970 cm^{-1} ; nmr (CCl_4 , δ) 1.1-1.5 (m, 12H), 1.5-1.8 (m, 4H), 1.8-2.2 (m, 4H), 2.2-2.5 (m, 4H), 5.2-5.4 (m, 2H); mass spectrum m/e 222.196 (calcd. for $\text{C}_{15}\text{H}_{26}\text{O}$ m/e 222.198). Europium shift studies combined with decoupling experiments support the assignment of the double bond to the 5-position.

Photolysis Experiments

Photolysis of *trans*-1-trimethylsiloxycyclotridec-3-ene (IV-OTMS). A solution of 100 mg of IV-OTMS in 10 ml of benzene was irradiated for 1 hour in a quartz tube in a Rayonet photochemical reactor. After hydrolysis as above, the sample was analyzed on Column A at 110°. This produced ca. a 70:30 mixture of IV and a slightly longer retention time component we presume to be the cis-isomer.

Photolysis of *trans*-1-trimethylsiloxy-1-vinylcyclotridec-3-ene (VI-OTMS). A solution of 10 μ l of VI-OTMS in a 2 ml of benzene was irradiated for 1 hour as above. The sample was analyzed on Column C at 135°. This produced ca. an 87:13 mixture of VI-OTMS and a slightly longer retention time component we presume to be the cis-isomer.

Photolysis of cyclopentadec-5-en-1-ol. Cyclopentadec-5-en-1-one (VIII) was reduced with lithium aluminum hydride to cyclopentadec-5-en-1-ol. A 20 mg sample was photolyzed in benzene for 50 minutes. The sample was analyzed on Column C at 135°. This produced ca. an 87:13 mixture of the starting alcohol and a slightly longer retention time component we presume to be the cis-isomer.

Kinetic Experiments

A series of 10-ml ampoules was introduced into a $\text{NaNO}_2/\text{KNO}_3$ fused salt bath which was maintained by a Bailey Model 124 proportional controller. Ampoules were removed at appropriate intervals and quenched in the draft of a fume hood. Each ampoule was hydrolyzed and analyzed as above. The log of the ratio of the alcohol VI over the sum of VI, VII, and VIII was plotted vs. time. Least-squares plots utilized the equation $\ln(A_t - A_\infty) = kt + c$, where A_t and A_∞ are percents of VI at time t and time infinity (10 half-lives).

Table 6. Retention times of compound on various glc columns.

Column	Compound	Temperature	Retention Time, min.
A	IV (trans)	110	12.6
A	IV (cis)	110	14.0
A	VI	100	9.2
A	VI-OTMS	100	3.3
A	VII	100	5.2
A	VIII	100	8.0
B	II	120	8.6
B	III	120	13.8
B	IV	120	15.4
B	V	120	8.4
B	VI	122	17.0
C	VI	135	11.8
C	VI-OTMS	135	3.0
C	VII	135	8.0, 30.2 ^a
C	VIII _t	135	10.8, 40.5 ^a
C	VIII _c	135	41.5 ^a

^aLow flow; 6.4 minutes for solvent to elute.

BIBLIOGRAPHY

1. R. E. Lehr and A. P. Marchand, Orbital Symmetry, Academic Press, Inc., New York, 1972, p. 7.
2. A. C. Cope, C. M. Hoffmann and E. M. Hardy, J. Am. Chem. Soc., 62, 1843, (1940).
3. A. C. Cope, K. E. Hoyle and D. Heyl, ibid., 63, 1852 (1941).
4. E. G. Foster, A. C. Cope and F. Daniels, ibid., 1893, (1947).
5. W. von E. Doering and W. R. Roth, Tetrahedron, 18, 67 (1962).
6. E. Vogel, Angew. Chem., Int. Ed. Engl., 2, 1 (1963).
7. R. B. Woodward and T. V. Katz, Tetrahedron, 5, 70 (1959).
8. G. S. Hammond and C. D. DeBoer, J. Am. Chem. Soc., 86, 899 (1964).
9. J. A. Berson and E. J. Walsh, Jr., J. Am. Chem. Soc., 90, 4730 (1968).
10. R. B. Woodward and R. Hoffmann, Angew. Chem., 81, 797 (1969); Angew. Chem. Int. Ed. Engl., 8, 781 (1969).
11. J. A. Berson and M. Jones, Jr., J. Am. Chem. Soc., 86, 5017, 5019 (1964).
12. J. A. Berson and M. Jones, Jr., ibid., 86, 5019 (1964).
13. A. Viola, E. J. Torio, K. K. Chen, G. M. Glover, U. Nayak and P. J. Kocienski, ibid., 89, 3462 (1967).
14. R. W. Thies and M. T. Wills, Tetrahedron Letters, 513, (1970).
15. R. W. Thies, Chem. Commun., 237 (1971).
16. R. W. Thies, J. Am. Chem. Soc., 94, 7074 (1972).
17. R. W. Thies, M. T. Wills, A. W. Chin, L. E. Schick and E. S. Walton, ibid., 95, 5281 (1973).

18. R. W. Thies and J. E. Billigmeier, *ibid.*, 96, 200, (1974).
19. J. A. Berson, *Accounts Chem. Res.*, 5, 406 (1972).
20. M. A. Golub and C. L. Stephens, *J. Phys. Chem.*, 70, 3576 (1966).
21. R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, 35, 4000 (1970).
22. M. Găsić, D. Whalen, B. Johnson, S. Winstein, *J. Am. Chem. Soc.*, 89, 6382 (1967).
23. H. E. Simmons and R. D. Smith, *ibid.*, 80, 5323, (1958).
24. C. D. Poulter, E. C. Friedrich, and S. Winstein, *ibid.*, 91, 6892 (1969).
25. J. Sicher, *Progr. Stereochem.*, 3, 202 (1962).
26. R. B. Turner and W. R. Meador, *J. Am. Chem. Soc.*, 79, 4133 (1957).
27. M. J. Goldstein, M. S. Benzon, *ibid.*, 94, 5119 (1972).
28. W. Kirchhof, *Chem. Ber.*, 93, 2712 (1960).
29. E. LeGoff, *J. Org. Chem.*, 29, 2048 (1964).