

AN ABSTRACT OF THE THESIS OF

Michael James Smith for the degree of Doctor of Philosophy
in Chemistry presented on December 1, 1978

Title: THE HETEROATOM EFFECT IN INTRAMOLECULAR
CYCLIZATIONS OF ORGANOALUMINUM AND -LITHIUM
COMPOUNDS

Abstract approved: _____

Redacted for Privacy

Peter K. Freeman

Intramolecular cyclization of organometallic compounds represents a promising tool for synthesis in general. The use of strategically-placed heteroatoms in the cyclizing molecule can influence the stereochemistry and/or efficiency of an organometallic cyclization while providing for functionality in the cyclic product.

The work described herein first concerns cyclizations of organolithiums. Prepared from the appropriate halide, heteroatom-containing alkenyllithiums cyclized to produce five and six-membered rings in some cases when analogous systems without heteroatoms failed to cyclize. Allylic and homoallylic heteroatom systems cyclized with stereochemistry opposite to that obtained in the cyclization of alkyl-substituted counterparts. The inclusion of n-butyllithium in the reaction medium was found to accentuate the heteroatom's influence.

Organoaluminum cyclizations were also investigated. Prepared by the hydroalumination of a multiple bond, alkenylaluminum compounds with and without heteroatoms were cyclized. A homoallylic ether-containing alkenylaluminum cyclized with stereochemistry opposite to that of its methyl substituted replica. In cyclizations of 1,1-dialuminocompounds, prepared from enyne precursors, alkene cyclization products, due to dehydroalumination, were obtained when ether was excluded from the reaction mixture. In the presence of ether these systems did not dehydroaluminate and saturated cyclic products were obtained.

The Heteroatom Effect in Intramolecular Cyclizations
of Organoaluminum and -lithium Compounds

by

Michael James Smith

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

Completed December 1, 1978

Commencement June 1979

APPROVED:

Redacted for Privacy

Professor of Chemistry

in charge of major

Redacted for Privacy

Chairman of ~~Department~~ of Chemistry

Redacted for Privacy

Dean of Graduate School

Date thesis is presented December 1, 1978

Typed by Opal Grossnicklaus for Michael James Smith

ACKNOWLEDGEMENTS

Primary thanks go to Dr. Stan Wilson, my research advisor prior to his departure from the university in the summer of 1978. His guidance and friendship have always been and continue to be of great value to me.

Special thanks should also go to Professor Peter Freeman, who generously took time and effort to serve as my research advisor for the last portion of my graduate work.

To my colleagues, Dr. Bill Beavers, Dr. Steve Chum, Dr. (to be) Larry Bass, Dale Dei Rossi, Dean Regier, and all my other friends, both students and staff, go best wishes and thanks. May we meet again some day.

I'll just say, "Ciao," to that grand old man, Mario, a last true master craftsman in this day of mass production, and a dear friend.

Words could never sufficiently thank my parents for the part they played in this achievement. The respect for knowledge and accomplishment represented by this work is chiefly from them. The success is theirs, too, and I'm proud to share it with them.

Meredith, I'll never forget the role you played in helping me to this point. The success is yours, too.

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	HISTORICAL	3
	A. General	3
	B. Lithium	5
	1. With nitrogen	5
	2. With oxygen	8
	C. Aluminum	21
	1. With nitrogen	21
	2. With oxygen	22
III.	RESULTS AND DISCUSSION	31
	A. Lithium cyclizations	31
	B. Aluminum cyclizations	47
IV.	EXPERIMENTAL	66
	A. Lithium work	68
	B. Aluminum work	87
	REFERENCES AND NOTES	108

LIST OF TABLES

<u>Table</u>		<u>Page</u>
1.	Product Ratios for Methylation of Sulfoxides <u>15</u> and <u>19</u>	10

THE HETEROATOM EFFECT IN INTRAMOLECULAR CYCLIZATIONS OF ORGANOALUMINUM AND -LITHIUM COMPOUNDS

I. INTRODUCTION

There are two general approaches to exploring the realm of synthetic organic chemistry that remains uncharted. On the one hand there are those whose primary focus is the preparation of a specific desirable target molecule. There are those, certainly as valuable to continued progress, whose research purpose is developing general synthetic techniques of broad applicability that might be used in a large and varied number of individual quests for specific molecules. The research described in this paper is of the latter type. The technique being developed is efficient (poly)annelation, the process of forming (poly)cyclic products from acyclic precursors, and the method of annelation is organometallic cyclization.

The exploration of any new scientific frontier can validly be justified on the basis of pure science, a seeking of knowledge for knowledge's own sake. As anyone with some experience in the field of natural product structure can verify, efficient reactions forming cyclic compounds from acyclic precursors are valued tools in the synthetic chemist's repertoire. Thus, to the extent that it advances the sophistication of this technique, the research described herein possesses practical worth to complement its intrinsic value as

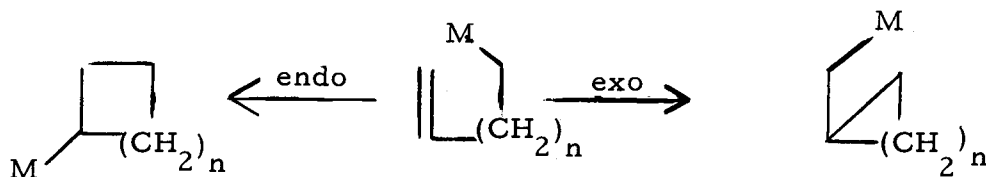
scientific inquiry.

The primary area of investigative interest in this research was the use of a heteroatom at various positions in the cyclizing organo-metallic compound, thereby influencing the stereochemistry, regio-chemistry, and efficiency of the cyclization, as well as providing for functionality in the cyclic product.

II. HISTORICAL

A. An excursion through the chemical literature provides testament to the importance and broad scope of intramolecular polyene cyclizations. These cyclizations may occur via carbonium ions (1), radicals (2), or organometallic moieties. Metals that have been employed to effect intramolecular cyclizations include: lithium (3), aluminum (4), magnesium (5), zirconium (6), titanium (7), gallium (8), indium (8), rhodium (9), nickel (10), iron (11), palladium (12), copper (13), thorium (14), and cobalt (15).

General examples and background discussion on the theory of cyclizations have recently been set forth (16) and need not be repeated here. One point that should be mentioned, however, is that intramolecular cyclizations can occur either by exocyclization, forming the smaller of two possible rings, or by endocyclization, which forms the larger of the two possible rings. In every example of intramolecular cyclization reported herein, except one (see p. 59), and in the



bulk of literature examples (5, 6, 7), the exocyclization product is

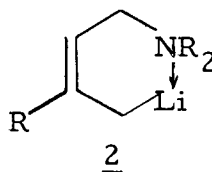
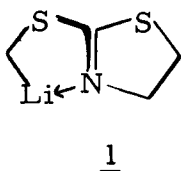
formed. A complete discussion of the theoretical basis for the exo-cyclization preference is provided elsewhere (16) and will not be reiterated here. A better use of this discussion space is the basis for the notion that a strategically placed heteroatom might influence the course of an organometallic cyclization.

To begin, a definition of the term "heteroatom" is in order. For most organic chemists the term is a label for elements like oxygen, nitrogen, sulfur, etc. For the purposes of this work, a heteroatom is an electronegative element bonded to carbon, and having unshared pairs of electrons and thus Lewis base potential; in its role as a heteroatom it forms a donor-acceptor interaction with a metal involving either intermolecular or intramolecular (as in the case with this research) electron pair transfer through space, forming a new donor-metal single bond in the limiting case. Thus, the heteroatom-metal interaction will be of a Lewis acid-Lewis base nature. An examination of the recent chemical literature, including a review paper on intramolecular coordination (17), provides numerous examples of heteroatom-metal complexation; while most reports deal with oxygen and nitrogen, sulfur (18, 19, 20, 21) and the halogens (22, 23, 24) also display coordination. In order to structure this discussion of the historical basis for the expectation of a heteroatom effect in organolithium and -aluminum cyclizations, it will be divided into these areas: nitrogen with lithium (and related metals); oxygen

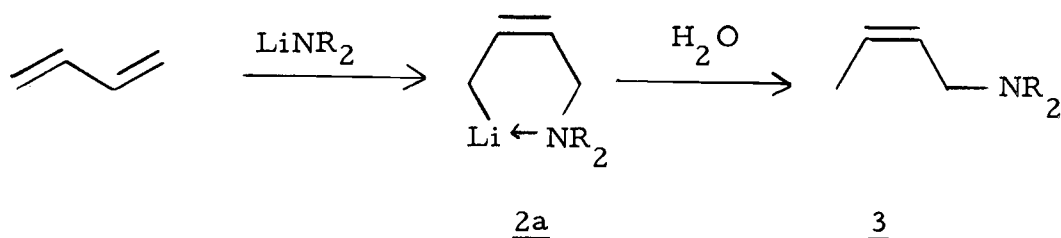
with lithium (and related metals); nitrogen with aluminum; and finally, oxygen with aluminum. Since this research employed only oxygen, the greatest portion of the attention will be affixed in that direction.

B. Alkylolithiums, in the absence of electron donors, normally exist as hexamers. In the presence of electron donors like diethyl ether or tetrahydrofuran (THF), the degree of association is lessened, usually to a tetramer with four lithiums at the four corners of a tetrahedron and alkyl groups centered on each of the faces. One electron pair donor would provide the lithium atom with a filled outer shell of electrons (25). This type of interaction would be observed to develop during a heteroatom-influenced organolithium reaction.

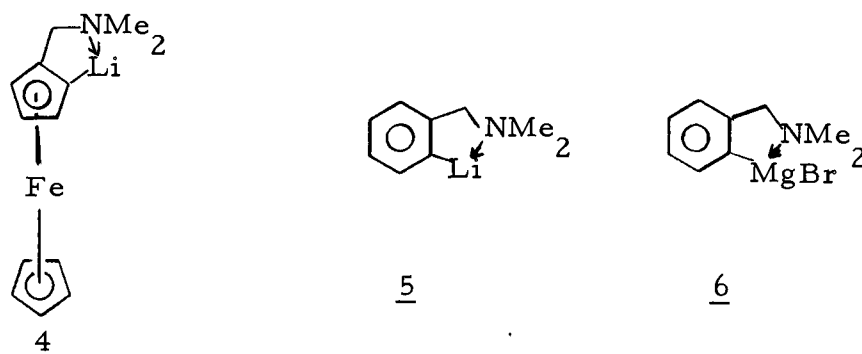
1. Nitrogen with lithium (and related metals). Intramolecular coordination of lithium by nitrogen, forming both five- (26) and six- (27) membered rings, as shown in structures 1 and 2, has been proposed to account for observed behavior. For example, 2a is prepared



and reacts as follows, giving product 3 with a cis to trans ratio of 24 to 1.



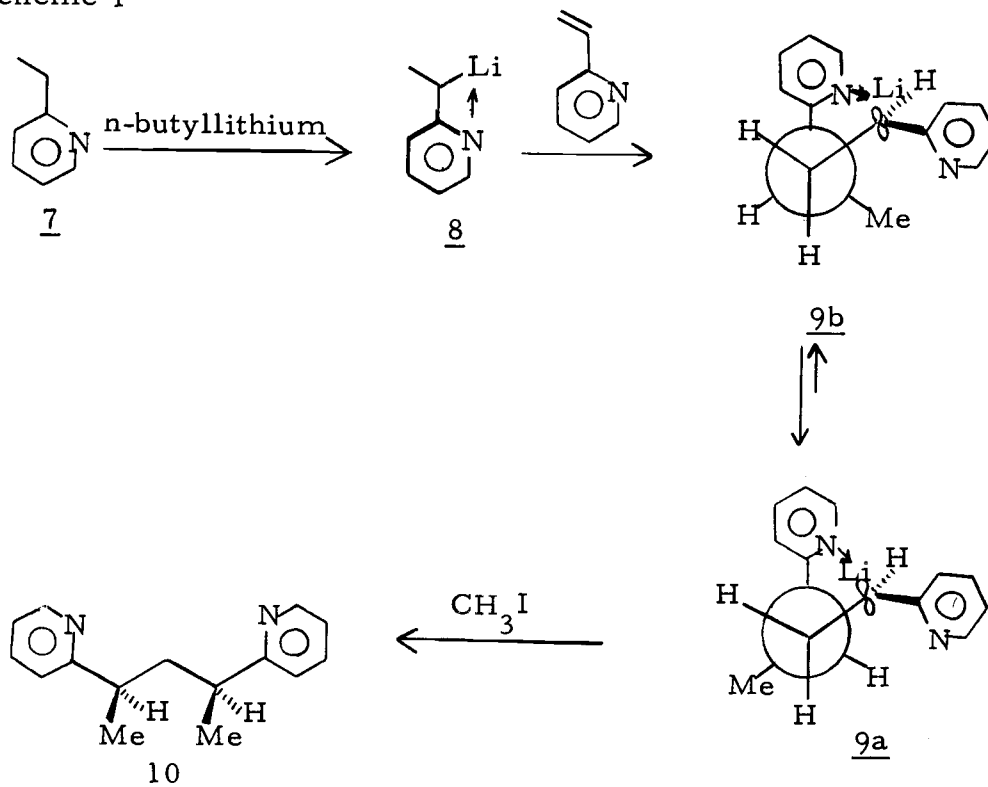
Exclusive ortho metallation of amino derivatives of ferrocene (28) and benzene (29), as well as facile formation of Grignard reagents



like 6 (30), can be ascribed to intramolecular complexation as depicted in 4, 5, and 6.

As summarized by Scheme 1, when compound 7 was treated with *n*-butyllithium, lithium reagent 8 resulted. Treatment of 8 with vinyl pyridine followed by methylation, provided product 10, with greater than 99% being the meso form (31). It is proposed that diastereomer 9a, which leads to the meso product, is more stable than its counterpart (9b), which would yield racemic products, due to nonbonded CH_3 -lone pair interaction and to the unfavorable gauche interaction

Scheme 1

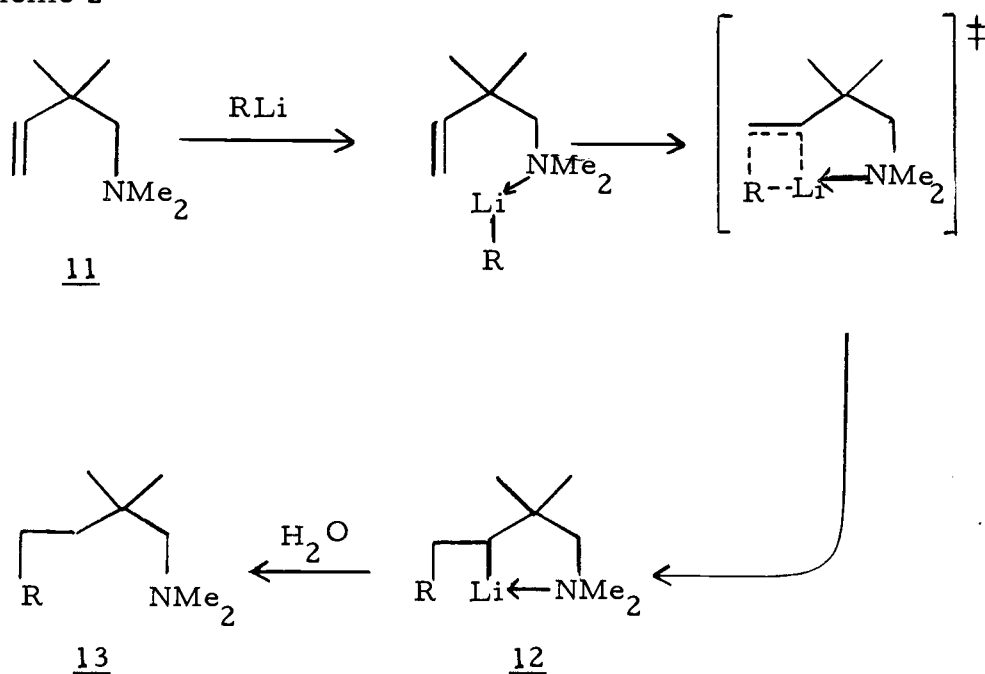


present in **9b**. The approach of methyl iodide from the least hindered side of **9a** results in the meso product formation.

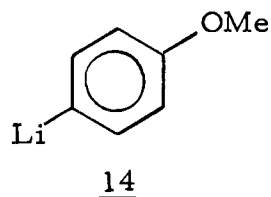
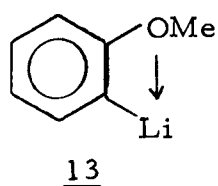
The addition of alkylolithium reagents to alkenyllithiums provides an important example in this area. Generally, lithium reagents do not add to nonconjugated olefins (32). Exceptions occur when strain is relieved, when the addition is intramolecular (*i.e.* cyclization), and when the addition results in a new lithium reagent of increased stability. The subject reactions fall into this last category in that the addition product is a lithium reagent stabilized by internal chelation. When treated with various alkylolithiums, alkenylamine **11** added to the lithium reagent regiospecifically, as shown in Scheme 2, to form

a complex-stabilized organolithium (12), which, upon hydrolysis, gave amine 13 in excellent yield (21).

Scheme 2



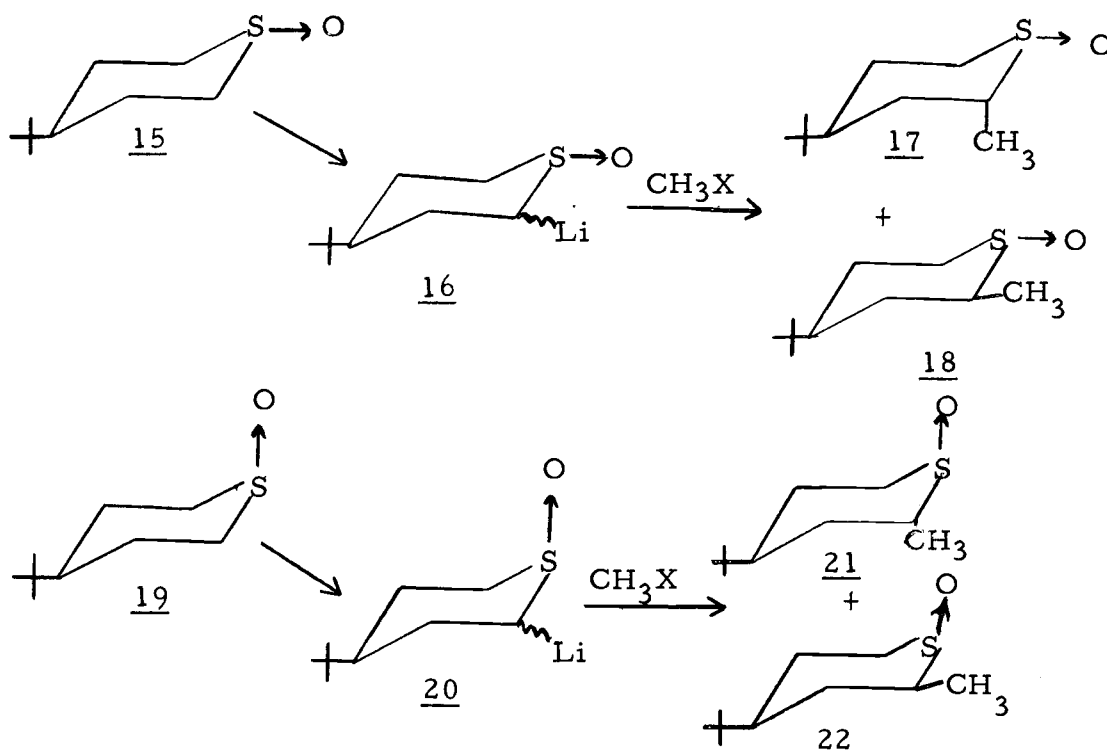
2. Oxygen with lithium (and related metals). Like the behavior cited above for aminoferrocenes and aminobenzenes, methoxyferrocenes (33) and methoxybenzenes (34) metallate only at the ortho position when treated with n-butyllithium. In related work, Beck and Siegel (35) proposed that enthalpy differences in the reaction of lithioanisoles 13 and 14 with ethanol (to form anisole) are primarily due to stabilization of 13 via intramolecular coordination. The ΔH of reaction for the ortho isomer (13) is lower than that of 14 by 8.3 kcal/mole



when the solvent is *n*-butyl ether. In *N,N,N',N'*-tetramethylethylenediamine (TMEDA), where better solvent coordinative stabilization is available to either isomer, the entropy difference is reduced to 2.8 kcal/mole.

The methylation of sulfoxides 15 and 19 via metallation followed by treatment with methylating agents afforded products 17 thru 22 in the yields indicated in Table I (36). Scheme 3 depicts the process.

Scheme 3

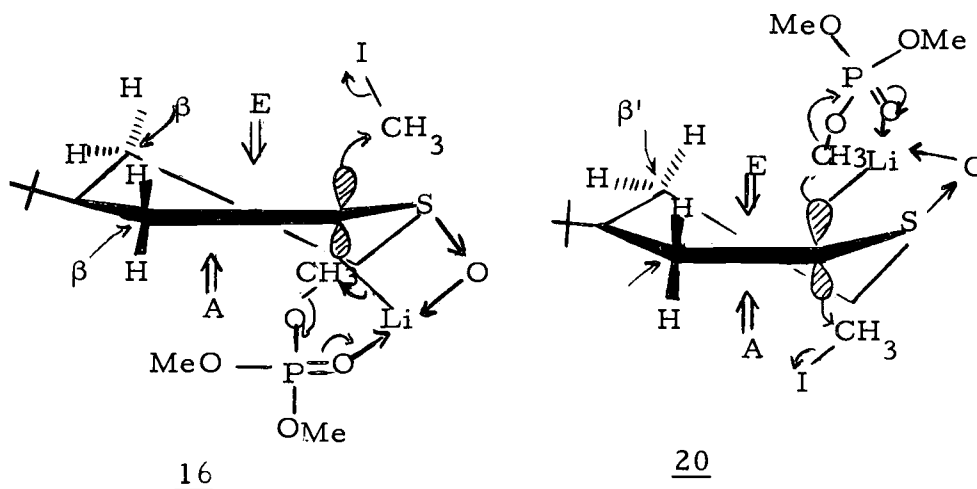


The authors explain this remarkable stereochemical result by an analysis of lithiated structures 16 and 20 and the role played by the cation in the methylation. C^{13} and H^1 NMR studies of the lithiated structures show them to be in the half chair conformation with planar metallated carbon, as depicted here (37). As indicated by Table I,

Table I. Product Ratios for Methylation of Sulfoxides 15 and 19

	X = -I	X = $-\overset{\text{O}}{\overset{\parallel}{\text{P}}}(\text{OMe})_2$	X = $-\overset{\text{O}}{\overset{\parallel}{\text{P}}}(\text{OMe})_2$ + added LiClO_4
Ratio of <u>17</u> / <u>18</u> (Reaction of <u>15</u>)	20/80	93/7	40/60
Ratio of <u>21</u> / <u>22</u> (Reaction of <u>19</u>)	100/0	30/70	92/8

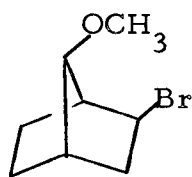
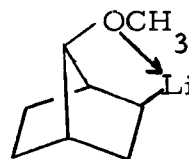
the approach of the methyl iodide, governed by steric considerations,



is trans to the chelated face, whereas trimethylphosphate, which

requires coordination to lithium, must attack cis. Note that equatorial attack (path E) is hindered, relative to axial attack, by the axial hydrogen on carbon β' and by the t-butyl group; this is borne out by the fact that for methyl iodide, stereospecificity is maximal when the steric factors work together (the reaction of 19) and least when they work against each other (the reaction of 15). Also, when lithium perchlorate was added to the reaction using trimethylphosphate, the requirement for coordinating with the internally complexed metal is greatly lessened and steric considerations weigh much more heavily in product ratio determination.

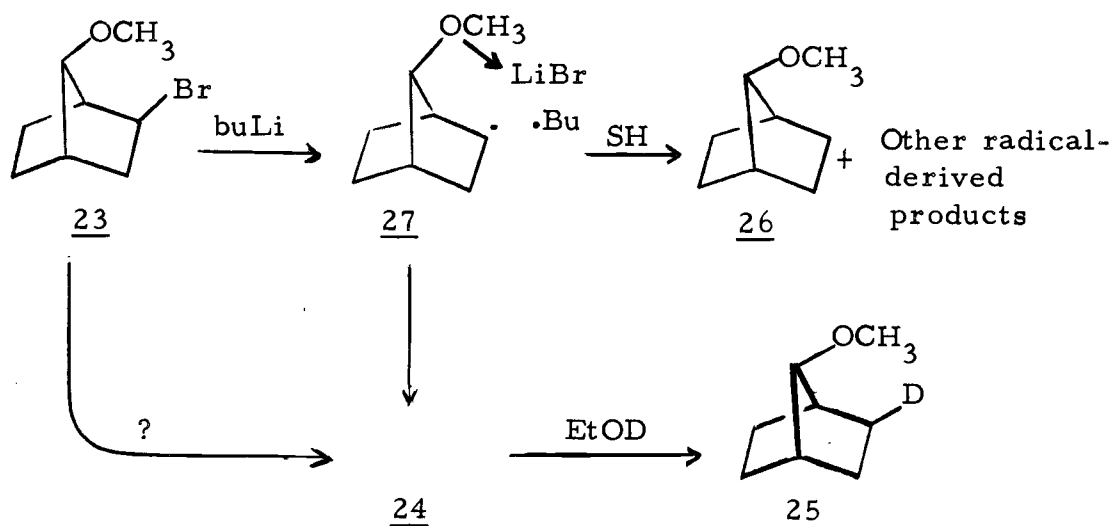
The treatment of compound 23 with n-butyllithium in hydrocarbon solvent at 0° was effected (38) in an effort to compare the

2324

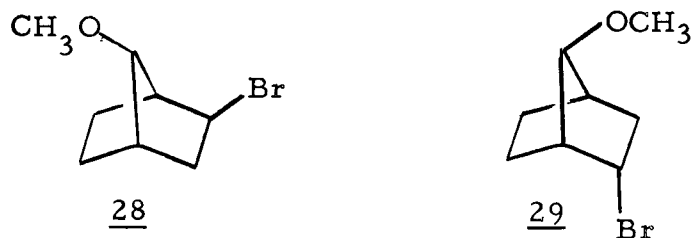
relative thermodynamic stabilities of an intramolecularly coordinated secondary lithium reagent (24) and a primary organolithium. As it turned out, little of 24 seems to have been formed in that upon quenching with $\text{C}_2\text{H}_5\text{OD}$, less than 10% of the products was deuterated ether (25). The other products, by far the major of them being ether 26, seem to be derived from radical sources, likely via a scheme such

as 4. The salient fact pointing up the importance of intramolecular coordination in the formation of 27 is that compounds 28 and 29, in

Scheme 4

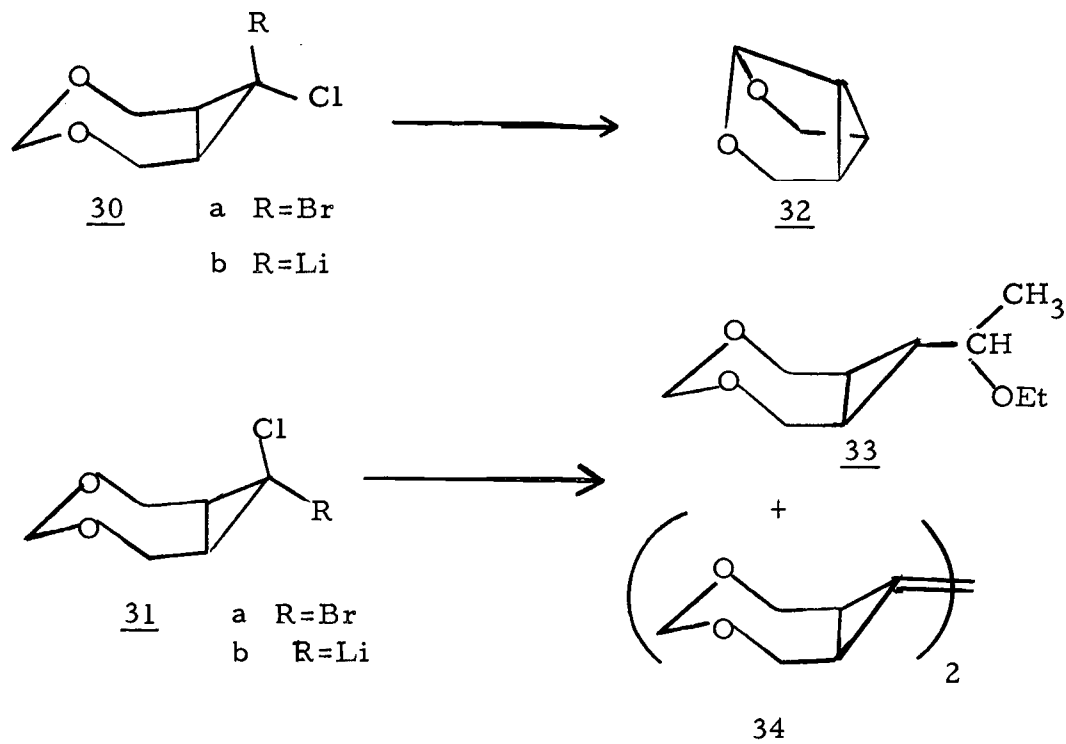


which complexing is unattainable, fail to react under the conditions of the reaction.



Taylor, Chaney and Deck reported an instance of intramolecular complexation in a carbenoid (39), as depicted in Scheme 5. Dihalides 30a and 31a were treated with methyllithium to give carbenoids 30b

Scheme 5

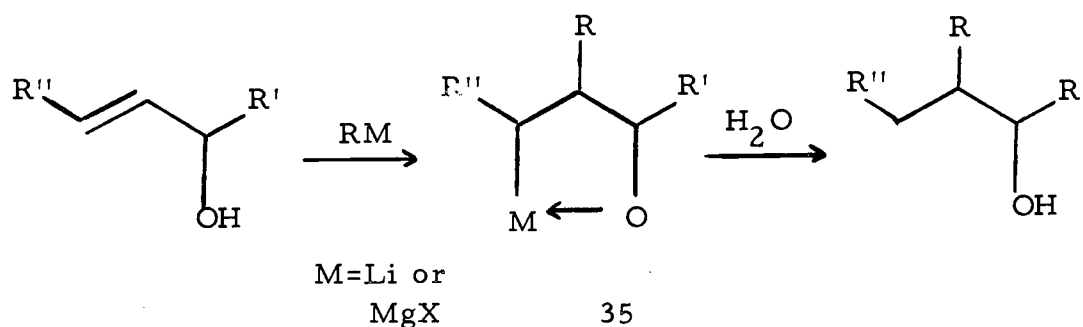


and 31b. Thermolysis of 30b gave almost exclusively the intramolecular insertion product (32), while thermolysis of 31b gave primarily insertion into the C-H bond of the ether solvent (33) and dimerization (34), both intermolecular processes. The products can be explained most easily by invoking an internally-complexed structure for 30b; the carbenoid center is thereby held in close proximity to the C-H bond into which it eventually inserts. In 31b there is no such complexation possible, and no intramolecular reaction is observed.

Oxygen functions can facilitate addition of organometallic reagents to carbon-carbon double bonds as did nitrogen and sulfur (as discussed above). In that this approximates a heteroatom-influenced

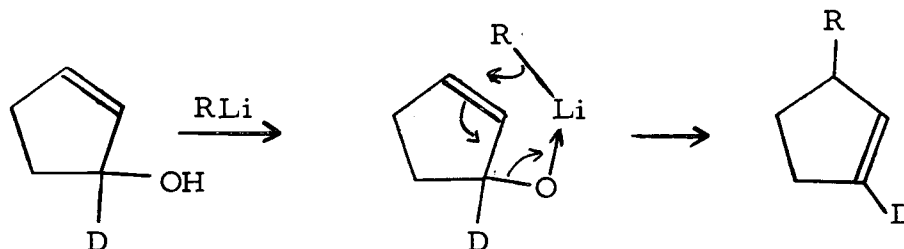
lithium cyclization, it merits special consideration. Recent examples of such behavior include the following: Both Grignard and organolithium reagents add to the double bonds of allylic alcohols. Felkin, Swierczewski, and Tambute' reported (40) that reactive (allyl or benzyl) organomagnesium and ordinary alkyllithiums in the presence of TMEDA react with allylic alcohols as in Scheme 6. The regiochemistry is such that a five-membered complex-containing ring (35) is formed by the addition. Crandall and Clark (41) reported similar

Scheme 6



findings, noting additionally that the conversion to Scheme 6a occurs.

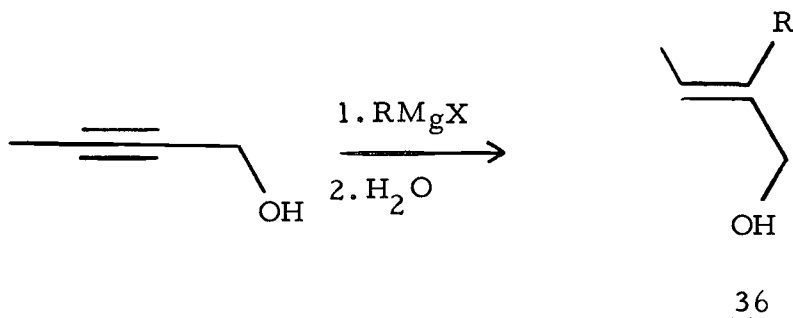
Scheme 6a



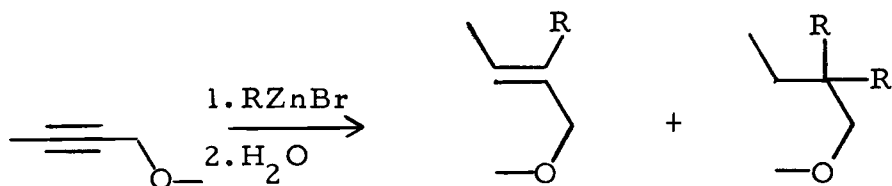
Quelet, Broquet and d'Angelo reported like behavior in the reaction of Grignard and lithium reagents with allylic acetals (42).

Propargylic alcohols and ethers are active to organometallic addition; isolated, unactivated triple bonds are unresponsive to the addition of organometallics except under heroic conditions (43).

Richey and Von Rein made the preliminary report (44) of the addition of Grignard reagents to propargylic alcohols (Scheme 7). As noted for allylic systems, the regiochemistry is such that a five-membered ring complex is formed. This is reflected in the product's geometry (36). A recent study done by Frangin and Grandemar (45) focuses on Scheme 7

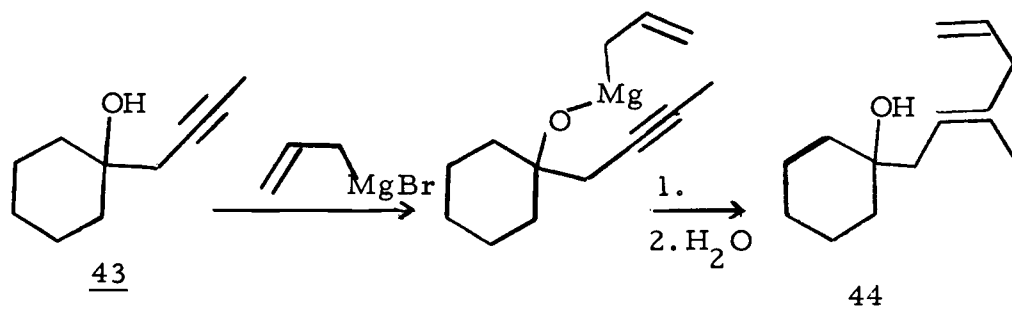


the action of organozinc reagents on propargylic ethers and alcohols. Depending on the substrate and reaction conditions, either one or two organozinc add across the triple bond, always with the regiochemistry that allows a five-membered ring complex, as shown in the following reaction.

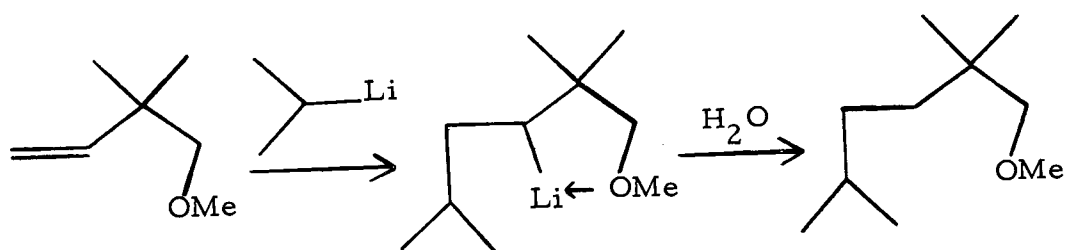
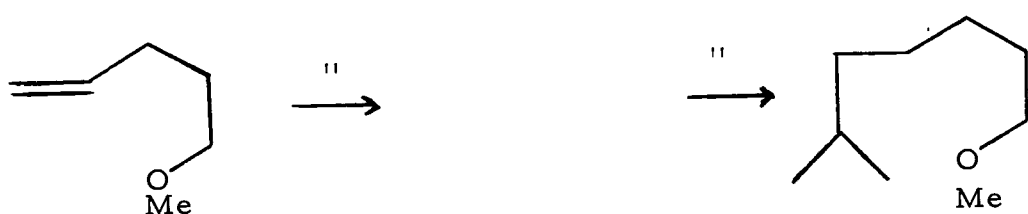
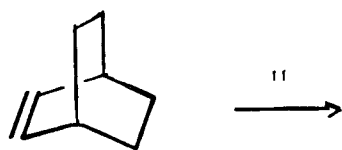


Studies dealing with the oxygen function removed farther than the allylic position point up further examples of a heteroatom effect. Veefkind, Bukelhaupt, and Klumpp reported the addition of isopropyl-lithium to various nonallylic ethers (46); examples are given in Scheme 8. As expected, in adduct 37, the five-membered chelate is formed in preference to the six-membered isomer. In 38 the six-membered ring prevails over the seven-membered possibility. The reactivity of 39 compared to the lack thereof displayed by 41 and 42 shows once again the importance of intramolecular coordination. The stereochemistry and regiochemistry of 40 had not been determined by the authors.

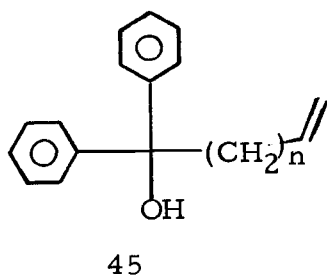
Eisch and Merkley made an early report (47) dealing with the addition of Grignard reagents to ynol 43. When allyl magnesium bromide reacts as depicted in Scheme 9, product 44 is formed having



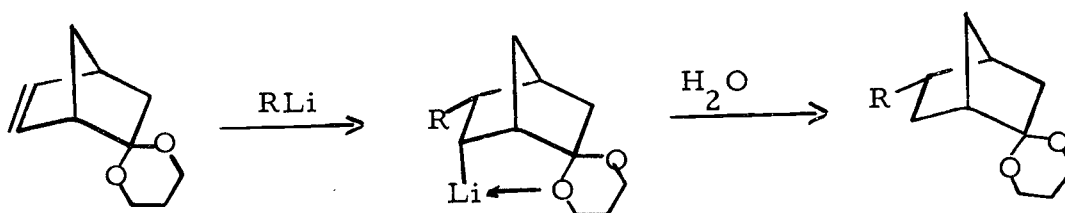
Scheme 8

3738394041No addition
takes place42

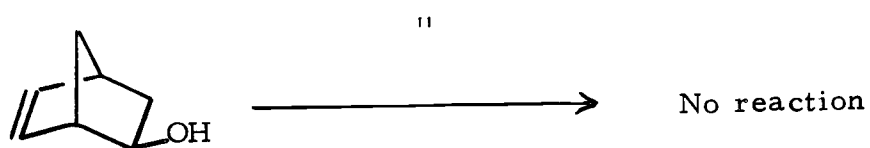
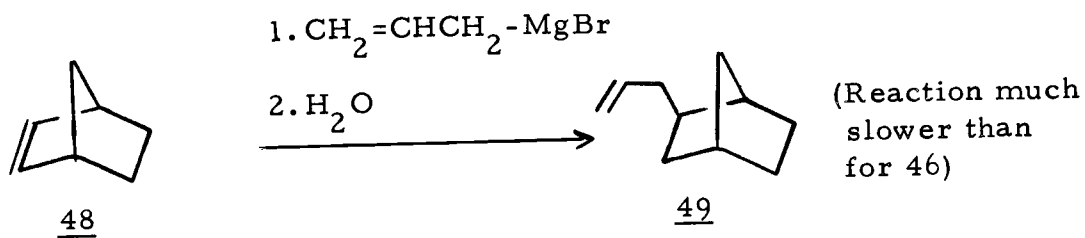
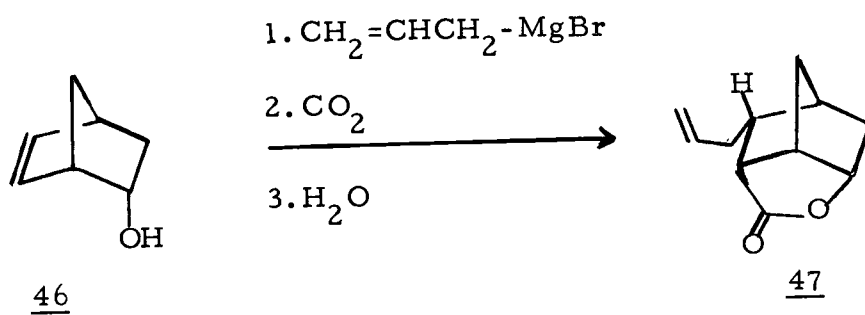
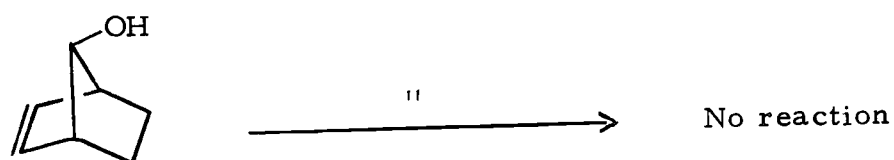
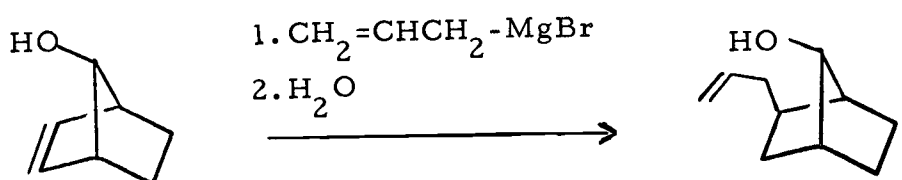
the regiochemistry (attachment of the magnesium to the carbon nearer to the oxygen, thus forming a five-membered ring) and stereochemistry (cis addition of the organomagnesium reagent) as depicted. The importance of oxygen participation is emphasized by the fact that for 45, the reaction with allyl Grignard reagents is fastest for $n=1$ and



slows as n increases until at $n=4$ there is no addition to the double bond. Richey et al. reported (48) similar Grignard additions to bicyclic alkenols as depicted in Scheme 10. The studies show that the addition of allyl magnesium bromide is cis and that heteroatom participation can overcome the inclination for exo attack (compare 46 to 47 with 48 to 49). Similar work by Kool and Klumpp (49), given in the following reaction, demonstrates that the same principles hold for alkyllithiums acting on alkenylketal systems.



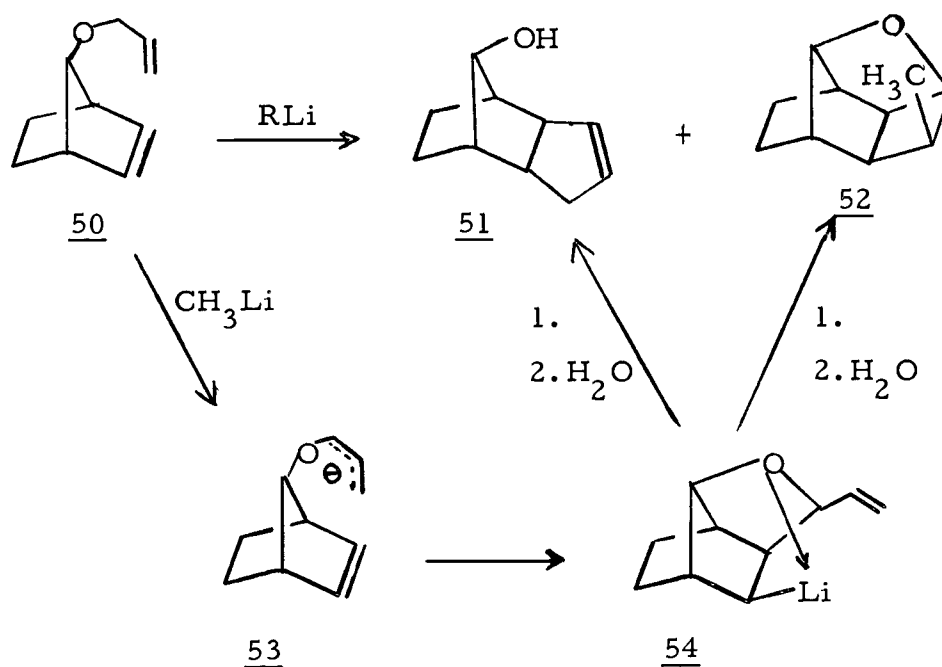
Scheme 10



A last study in this area was done by Klumpp and Schmitz (50).

When treated with methyllithium, dienyli ether 50 forms a lithium reagent that cyclizes to give 51 and 52. Scheme 11 portrays the reaction and sets forth the mechanism proposed by the authors. The

Scheme 11

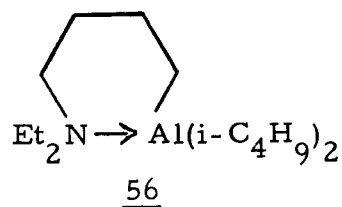
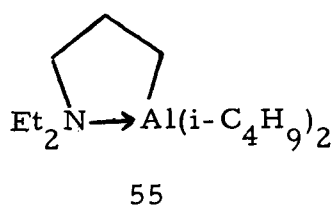


conversion of 50 to 53 has much precedent (51). The reaction from 53 to 54 is an intramolecular addition of a coordinated lithium reagent to a homoallylic ether's double bond. The conversion of 54 to 51 is, formally at least, an endocyclization followed by elimination of a lithium alkoxide, while the conversion producing 52 is an exocyclization of a secondary lithium reagent to an allylic ether's double bond. Both processes have precedent in material that has been previously

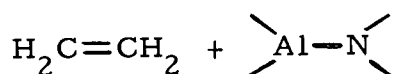
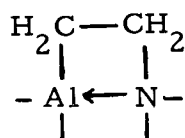
discussed.

C. Aluminum, when bonded to three groups, possesses six outer electrons. For this reason, trivalent aluminum acts as a Lewis acid in that it can acquire a filled outer shell by accepting an electron pair from a Lewis base. Electron pair acceptance by aluminum is one of the most important aspects of its chemistry (52).

1. Nitrogen with aluminum. Zakharkin and Savina (53b) propose intramolecular donor-acceptor complexes in compounds like 55 and 56. These compounds have significant thermal stability; compound 55 begins to decompose only at 250°. They can be vacuum



distilled. Unlike aluminum compounds without internal complexing, organoaluminums like 55 and 56 give molecular weight values corresponding to their empirical formulae, i.e. are monomeric. β -amino aluminum compounds decompose producing ethylene (54), likely due to the ring strain introduced by the complex. Trimethylamine forms

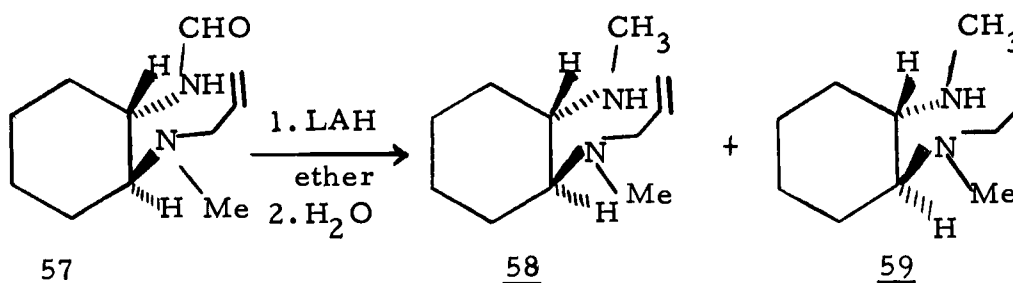


a complex with trimethylaluminum whose structure has been

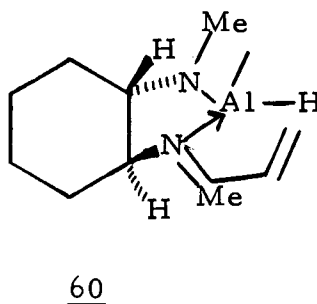
elucidated by electron diffraction (55), and shown to be roughly tetrahedral about the aluminum atom.

Szmuskovicz, Musser, and Laurian reported (56) an unusual double bond reduction by lithium aluminum hydride (LAH), shown in Scheme 12, in which the nitrogen atoms participate to effect the

Scheme 12

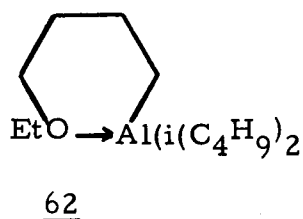
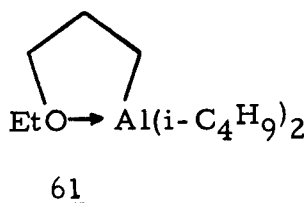


reduction to 59, possibly as is indicated in structure 60.



2. Oxygen with aluminum. Bahr and Muller (53a) and later Zakharkin and Savina (53b) have studied internally-complexed organoaluminum compounds in which an ether function serves as the electron pair donor. Like their nitrogen-containing counterparts, these compounds have cyclic structures, e.g. 61 and 62, and display

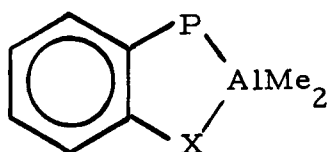
physical properties substantiating their lack of intermolecular association. When ethyl allyl ether is hydroaluminated with diisobutylaluminum hydride (DIBAL), compound 61 is obtained; heating of



61 to 160°-180° results in dissociation to liberate cyclopropane.

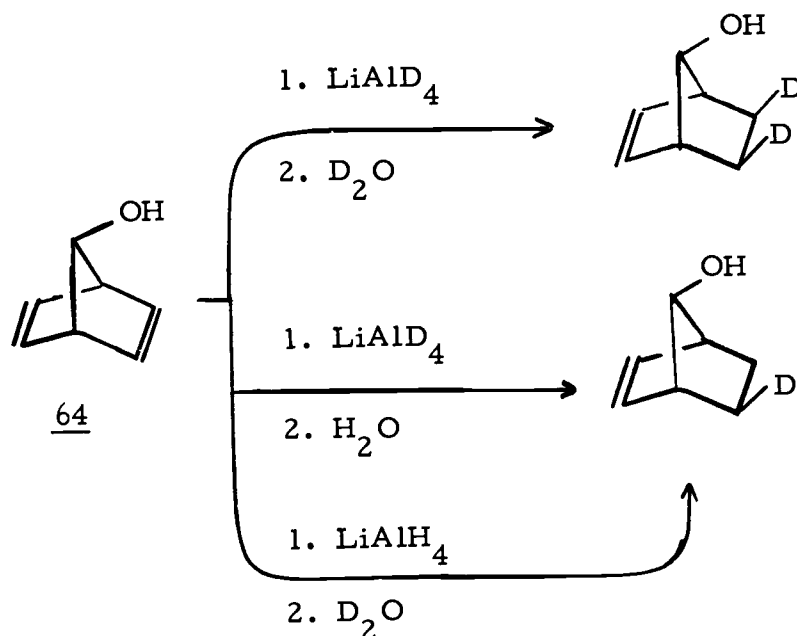
The α -phenoxy substituted aluminum reagent decomposes at 90° to 100° (22). The explanation of the relative stabilities is that phenoxide is a more stable anion than is ethoxide. This result is in line with the previously mentioned thermal stability (to 250°) of the amino-substituted analogue.

Pasynkiewicz et al. studied coordinative interaction in ortho-substituted dimethylaluminum phenoxides (57). The subject compounds (72) were studied via proton magnetic resonance, infrared (ir) spectroscopy, and cryoscopy. The study concluded that 63a has little intramolecular coordination and that the carbonyl oxygen in 63c proved to be an excellent donor ligand. The methoxy substituent, as present in 63b, is intermediate in donating ability. This result is reasonable, given the highly polarized nature of the carbonyl function, the somewhat polarized nature of the methoxy group, and the essentially nonpolar nature of the methyl substituent.

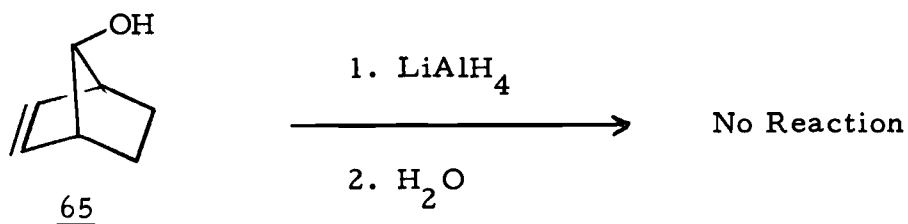
63

- a. $X=CH_3$
- b. $X=OCH_3$
- c. $X=CO_2CH_3$

An area of this topic that will be allotted a significant amount of discussion is that of lithium aluminum hydride reduction of carbon-carbon double bonds which are in the close proximity of an oxygen function. Normally, isolated double bonds are not reduced by LAH. A conveniently available oxygen atom can change that situation as the reactions in Scheme 13 indicate (58). The most significant point is Scheme 13



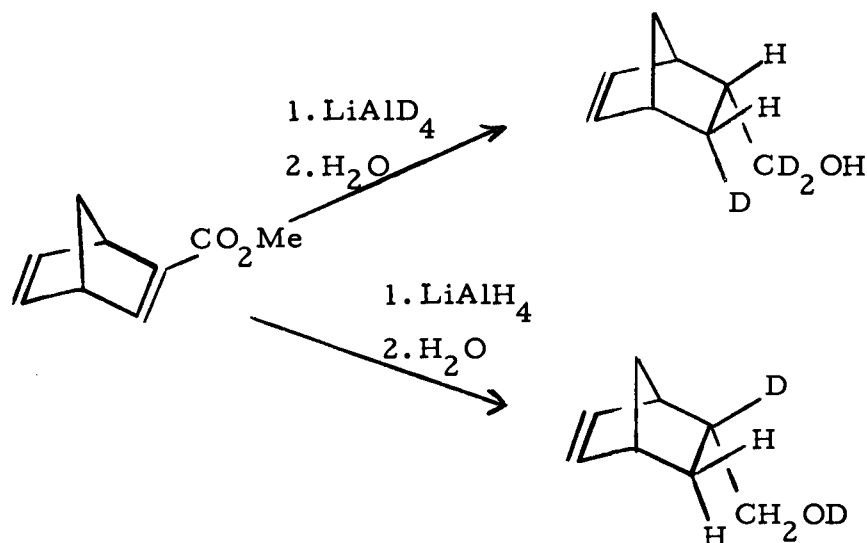
Scheme 13 (continued)



made by the contrast in the reactivities of 64 and 65: The oxygen is requisite for the reduction of the carbon-carbon double bond, likely serving to complex with the aluminum, thereby "locking in" the reducing agent over the point of attack.

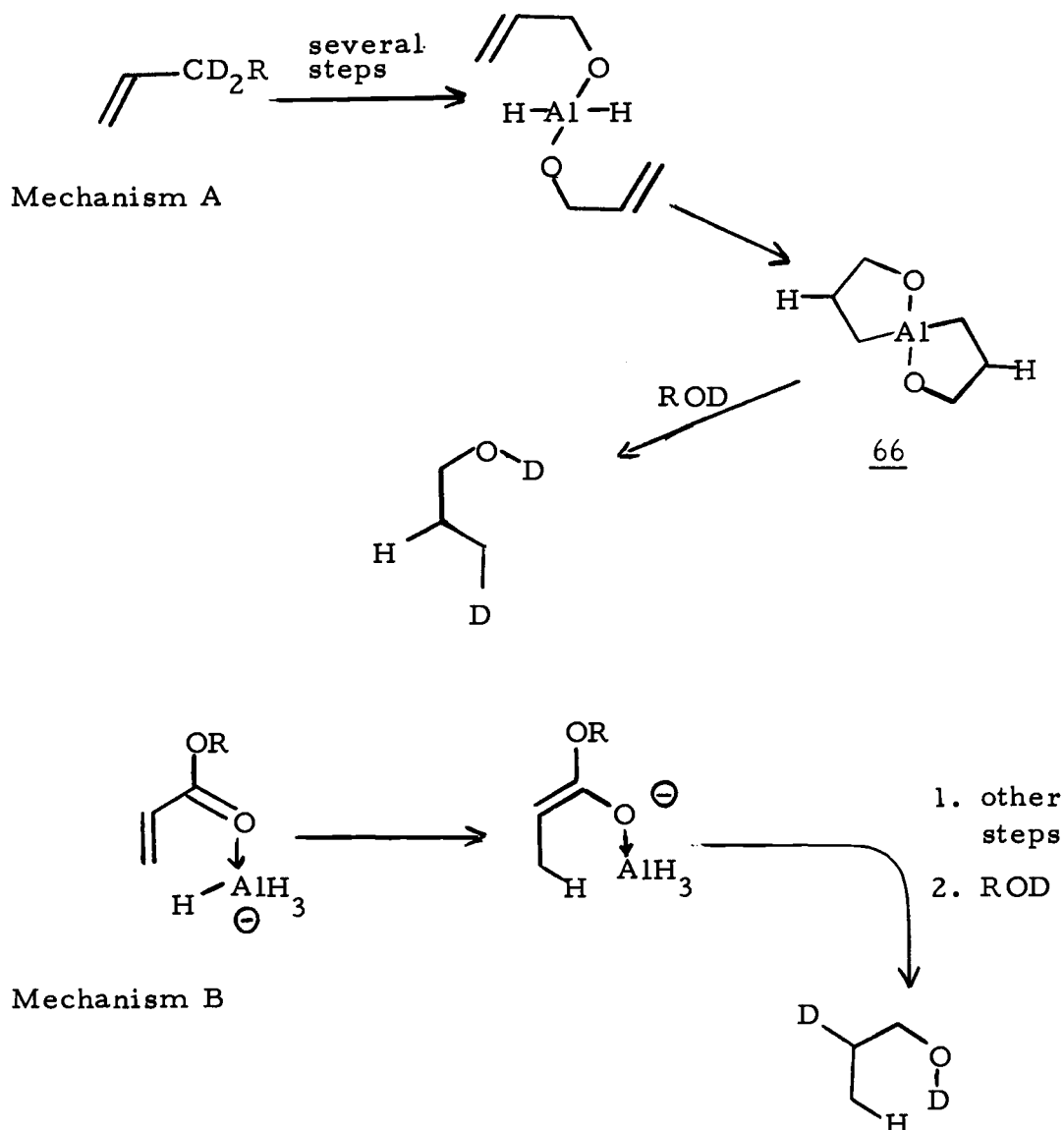
Insight into the mechanism of such reductions was obtained by the recent study of Jackson, Norman, and Rae (59) which is outlined by the reactions in Scheme 14. The literature contains two mechanistic notions on reactions like the one above; these are set forth

Scheme 14



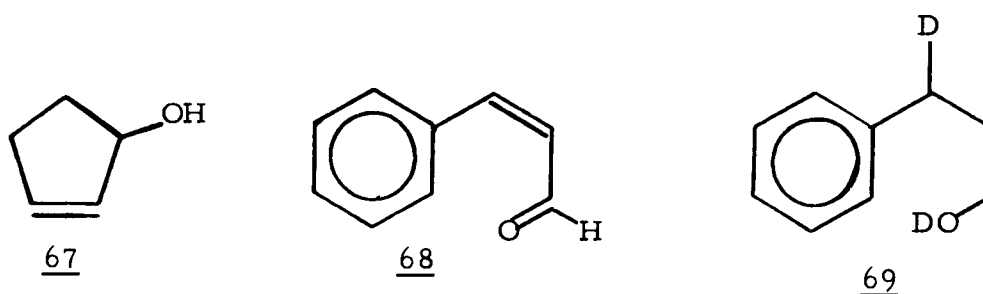
in Scheme 15. In mechanism A, the reducing agent transfers its

Scheme 15

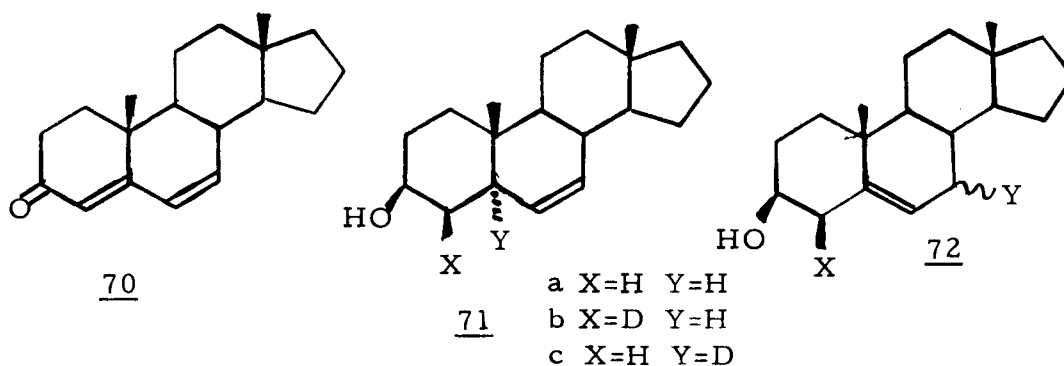


hydride to the (former) α carbon and in mechanism B the hydride is delivered in a Michael fashion to the β carbon. The reaction displayed in Scheme 14 seems to follow the conjugate addition pathway, that is, mechanism B. Another piece of evidence for the latter mechanism is that alcohol 67 is not reduced by LAH (60). However,

all the evidence does not support mechanism B. When compound 68 was treated with LAH, followed by work-up with deuterium source, 69

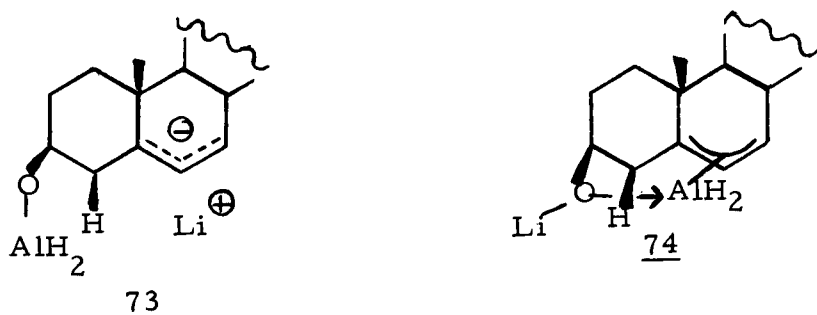


was the product. Note that 69 contains the deuterium label at the β carbon (from ROD) and a hydrogen (from LAH) at carbon α (61). This product must be derived from an intermediate like 66. Another piece of evidence for mechanism A, and a rather interesting bit of chemistry at the same time, is the LAH reduction of 70 (62). When



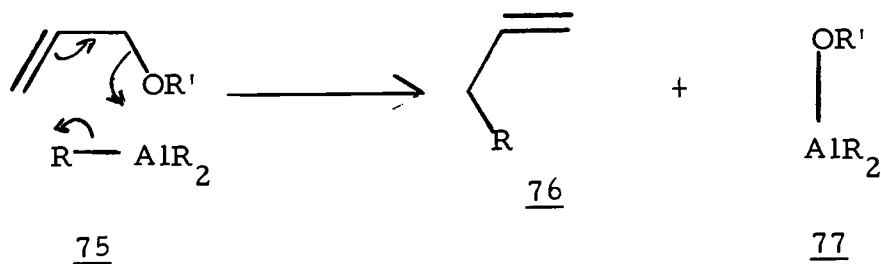
the reduction is carried out in THF, compounds 71a and 72a result. Reduction with lithium aluminum deuteride gives 71b and 72b, both with deuterium in the 4β position. Reduction by LAH followed by D_2O quench gives 71c and 72c. These results are consistent with a

mechanism involving passage of a hydride from the complexed reducing agent to the α carbon, forming an allylic anion in the process with either the lithium cation serving as counter ion (73), or with an aluminum-allyl species (74) similar to 66 mentioned in mechanism A above. The allyl-aluminum species could be either of the π -allyl type or an interconverting pair of sigma-bonded allyl-aluminum



compounds (63). Since the π -allyl ligand is a four electron donor, if 74 is the reaction intermediate, and if it involves π -type bonding, complexation with oxygen would no longer be required after the hydride is passed stereospecifically to the 4 β position.

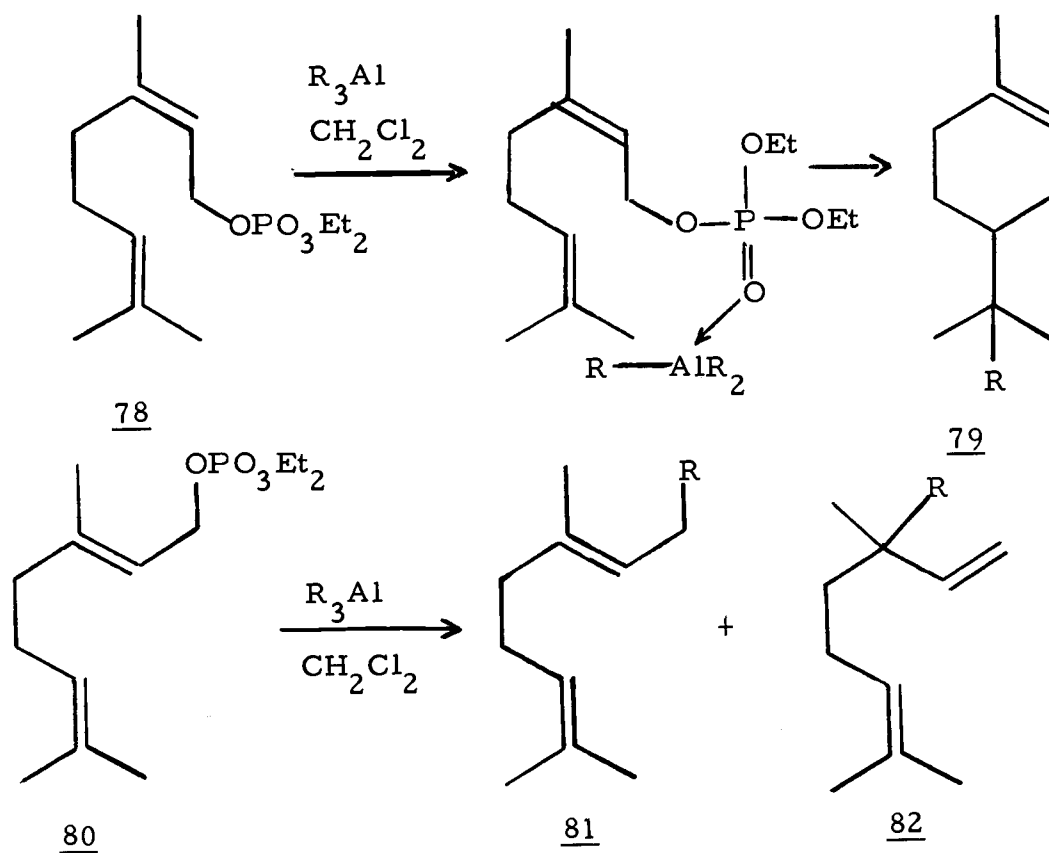
A final point of attention, addition of organoaluminum compounds to alkenes that have a proximal oxygen function, will now be discussed; note that this is equivalent to a heteroatom-influenced organoaluminum cyclization. Zakharkin and Savina addressed the subject of reaction of trialkylaluminum compounds with allylic ethers (18). Derived from a transition state like 75, the products were 76 and 77, and are analogous to the process of an endocyclization followed by an elimination. A recent example of this type of behavior was



reported by Kitagawa *et al.* (64) and that work is as follows in

Scheme 16. The contrast in reactivity between 78 and 80 is

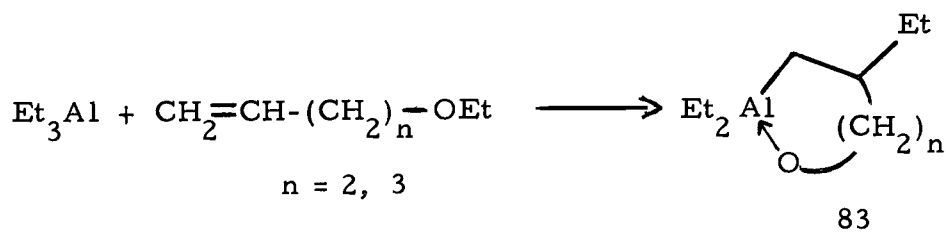
Scheme 16



interesting in that it points up the importance of complexation between aluminum and oxygen. Note that the formation of 79 and 82 effectively

proceeds through a transition state like 75. Other leaving groups on the geranyl substrate (80) have been employed yielding various ratios of 81 and 82 (65).

Nonallylic ethers (and amines) also react with trialkylaluminums (53b) to yield complexed products like 83. It is significant that the regiochemistry of the formation of 83 is completely analogous to an



exocyclization. Also significant is the observation that the $n=2$ product contains a six-membered ring chelate and the $n=3$ product contains a seven-membered chelate.

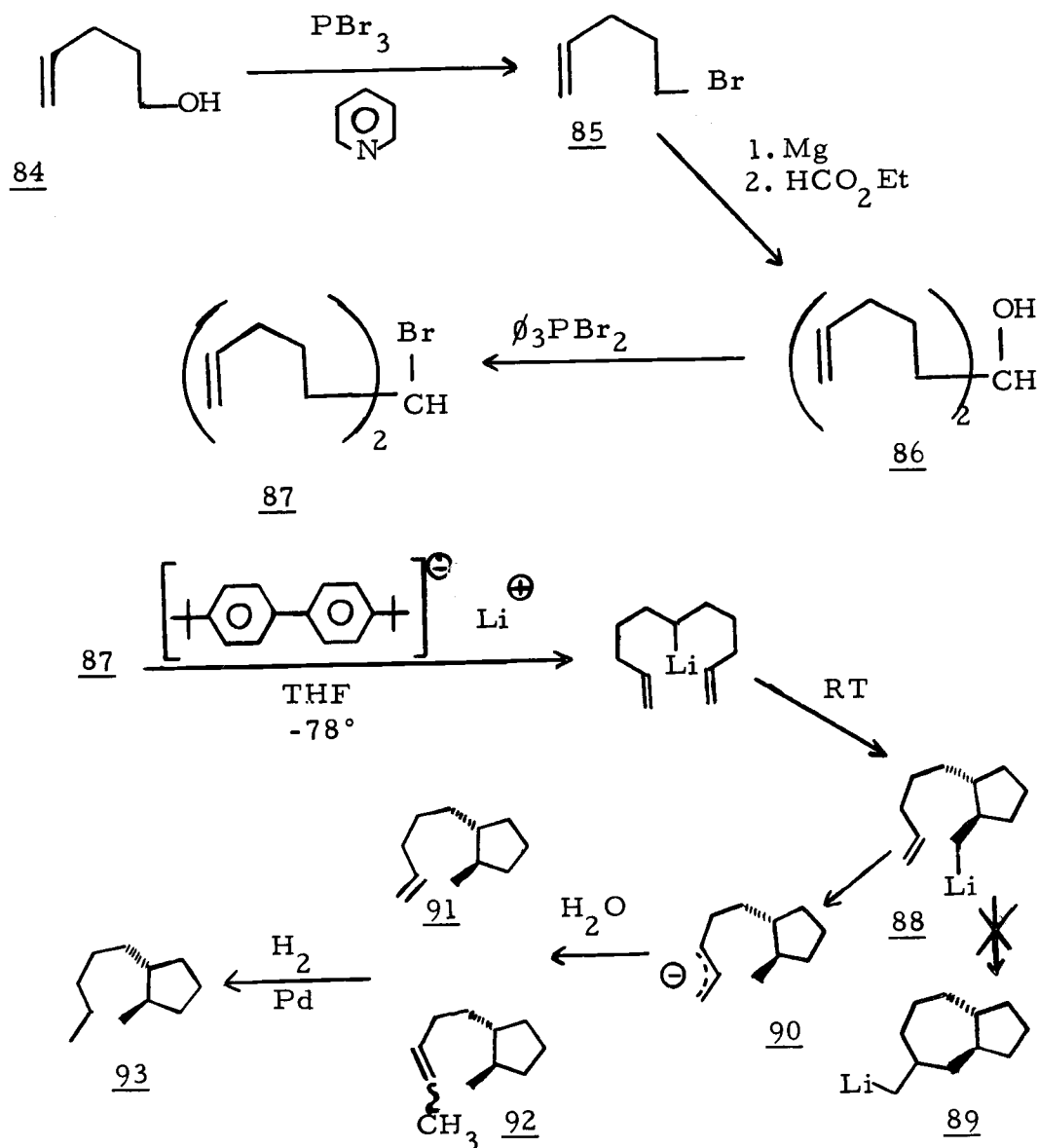
To summarize, a large body of evidence for interaction between heteroatom and metal has been presented. In terms of the research to be described in the following pages, the most significant portion, due to its close analogy, was the influencing of intermolecular addition of alkyllithiums and alkylaluminums to heteroatom-containing alkenes.

III. RESULTS AND DISCUSSION

A. Lithium Cyclizations. Any organometallic cyclization involves two basic processes. These are the formation of the alkenyl-metallic compound from a suitable precursor, and the subsequent intramolecular addition (i.e., cyclization) of this organometallic reagent to its own double bond. A host of procedures for the preparation of alkenyllithiums is available to the organic chemist (66); these include reaction of an organic halide with lithium metal, metallation, metal-halogen exchange, and organic halide with lithium radical anion. A recent example of this last technique that is particularly impressive in its virtually quantitative yield is the reaction of lithium p, p'-di-t-butylbiphenyl with alkyl halides to form organolithiums (67). Since the studies reported herein focus on the action of the alkenyllithium compound after its formation, preparation was generally accomplished by the simple reaction of the appropriate alkenyl halide with lithium dispersion (having 2% sodium, in mineral oil) in diethyl ether solvent, rather than a more involved method that might provide a better yield.

The first cyclization (along with preparation of the linear precursor) reported here is given in Scheme 17. Likely the bicyclic lithium reagent (89) was not formed, because after the initial cyclization to form 88, an allylic proton was abstracted by the primary alkyllithium moiety before the second cyclization could occur. This

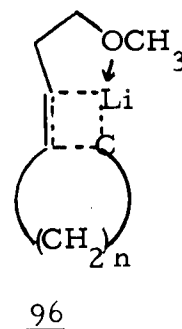
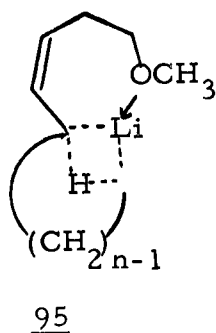
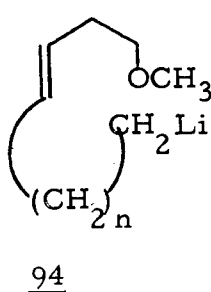
Scheme 17



abstraction leads to stabilized lithium reagent 90. The quench of 90 gives 91 and cis and trans 92, the mixture thereof giving, upon catalytic hydrogenation, a single compound whose structure is consistent for that depicted above for 93. It was the troublesome allylic proton abstraction experienced here and in other systems (68) that

prompted investigation into the use of heteroatoms to disfavor abstraction, enhance cyclization, and control stereoselectivity.

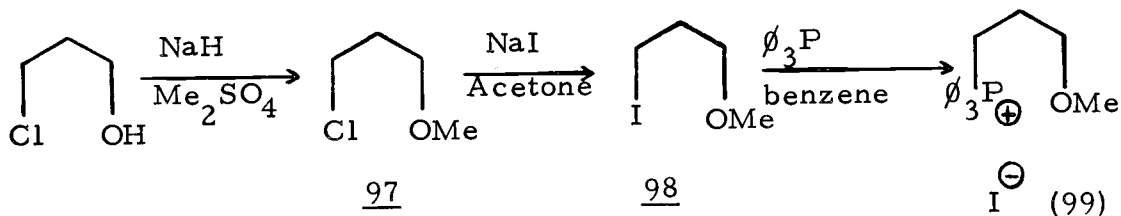
Starting with a lithium reagent like 94, 95 and 96 compare transition states leading to abstraction and cyclization, respectively. As has been indicated above, a five-membered complexation (96) is greatly preferred to a seven-membered ring of complexation (95). In fact, heteroatom involvement in 95 would be nearly impossible in the case of a trans double bond; this is not true for the cyclization



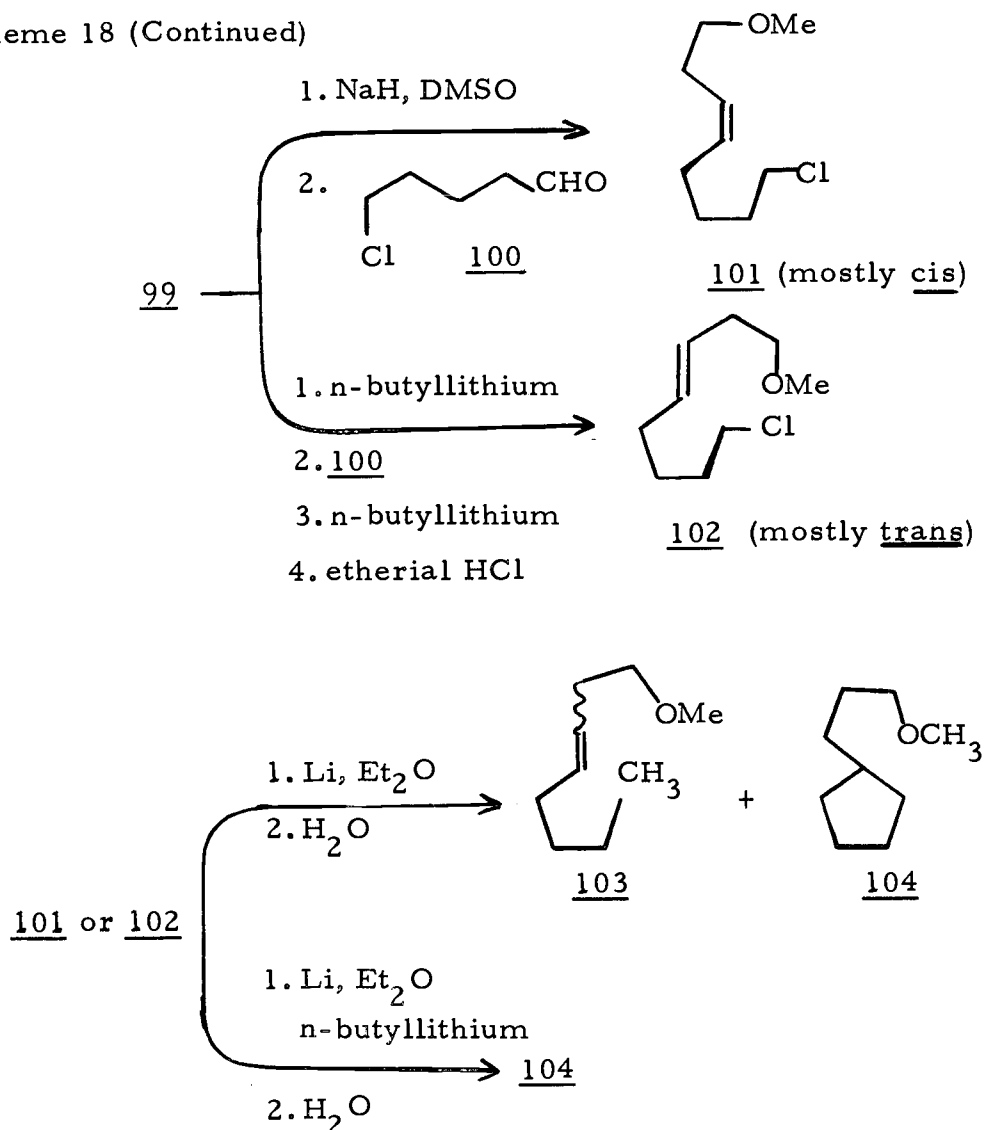
transition state (96).

The lithium reagent of 101 or 102, prepared as in Scheme 18, did cyclize to give product 104 as is indicated.

Scheme 18

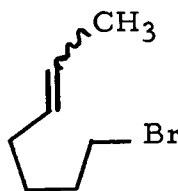


Scheme 18 (Continued)



A number of interesting features should be noted. The first is the interesting stereochemical outcomes of the two Wittig reactions. The normal Wittig produced 101 of mostly (90%) cis geometry. The product (102) of the Schlosser modification (69) was 60% trans and 40% cis. Either mixture of isomers reacted with lithium dispersion to give mostly (about 75%) cyclic product (104). When n-butyllithium was added to the reaction mixture, only cyclic product 104 was obtained, in 41% yield. The cyclization of 101 or 102 contrasts with the

behavior of 105 which gave no cyclic product under either set of reaction conditions (70). These results offer palpable proof that some



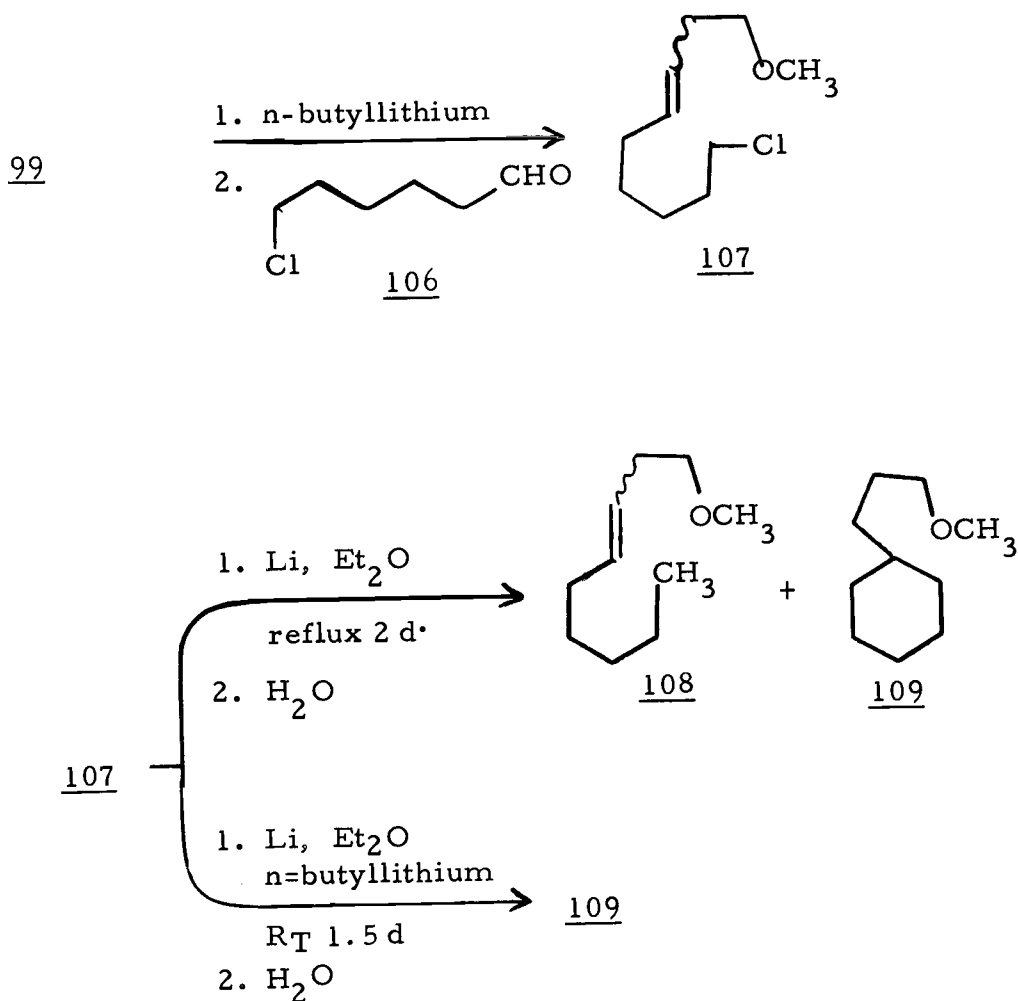
105

metal-heteroatom interaction of the type depicted in structure 96 must exist and state conclusively that heteroatoms can influence the efficiency of an organometallic cyclization.

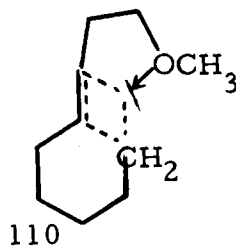
Since Grignard reagents can be formed in excellent yields (71a), it was hoped that treatment of 101 with magnesium might effect the cyclization in increased yield. However, treatment with magnesium in ether produced only the linear reduced product (103), and treatment in THF with magnesium turnings or with "supermagnesium" (71b) left only unreacted starting material.

The cyclization to form a six-membered ring is generally much less favorable, and thus slower, than is formation of five-membered rings, according to kinetics studies. Compound 107, a homologue of 101, was synthesized by an analogous reaction scheme in order to determine if the heteroatom interaction was sufficiently influential to bring about cyclization to the six-membered ring. Without added n-butyllithium, there was only about 15% cyclized product (109) after two days of refluxing. A catalytic amount (0.1 equivalent) of

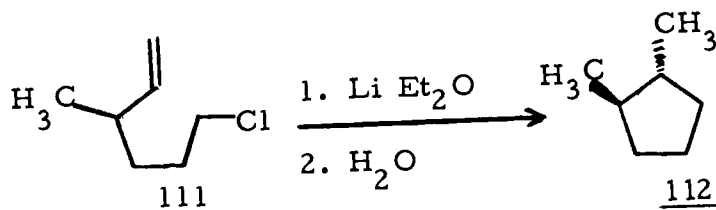
1-bromo-butane added prior to addition of the halide (107) resulted in 85% cyclization after 1.5 days at RT, and addition of a full equivalent of n-butyllithium resulted in complete cyclization. The



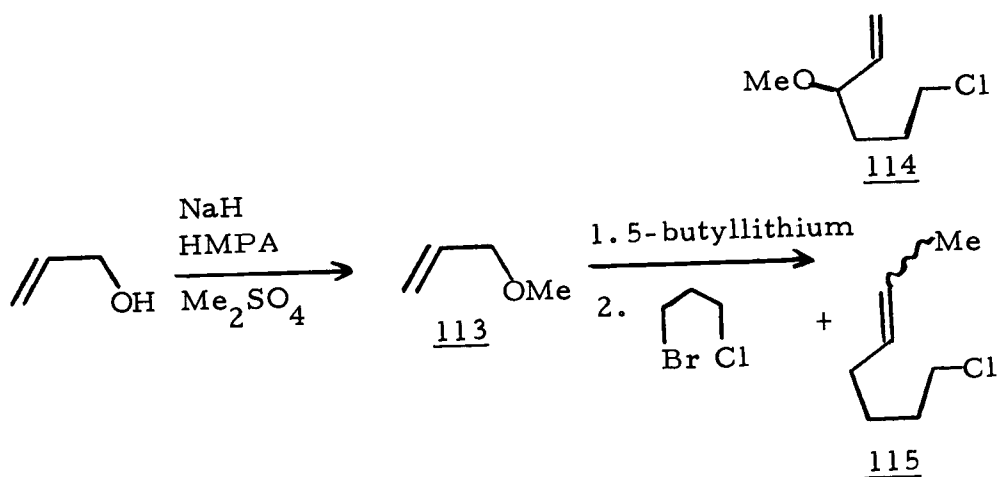
impressive fact that the lithium reagent of 107 cyclizes when no cyclization occurs without the heteroatom, requires some intramolecular coordination in the cyclization transition state, as portrayed in 110.



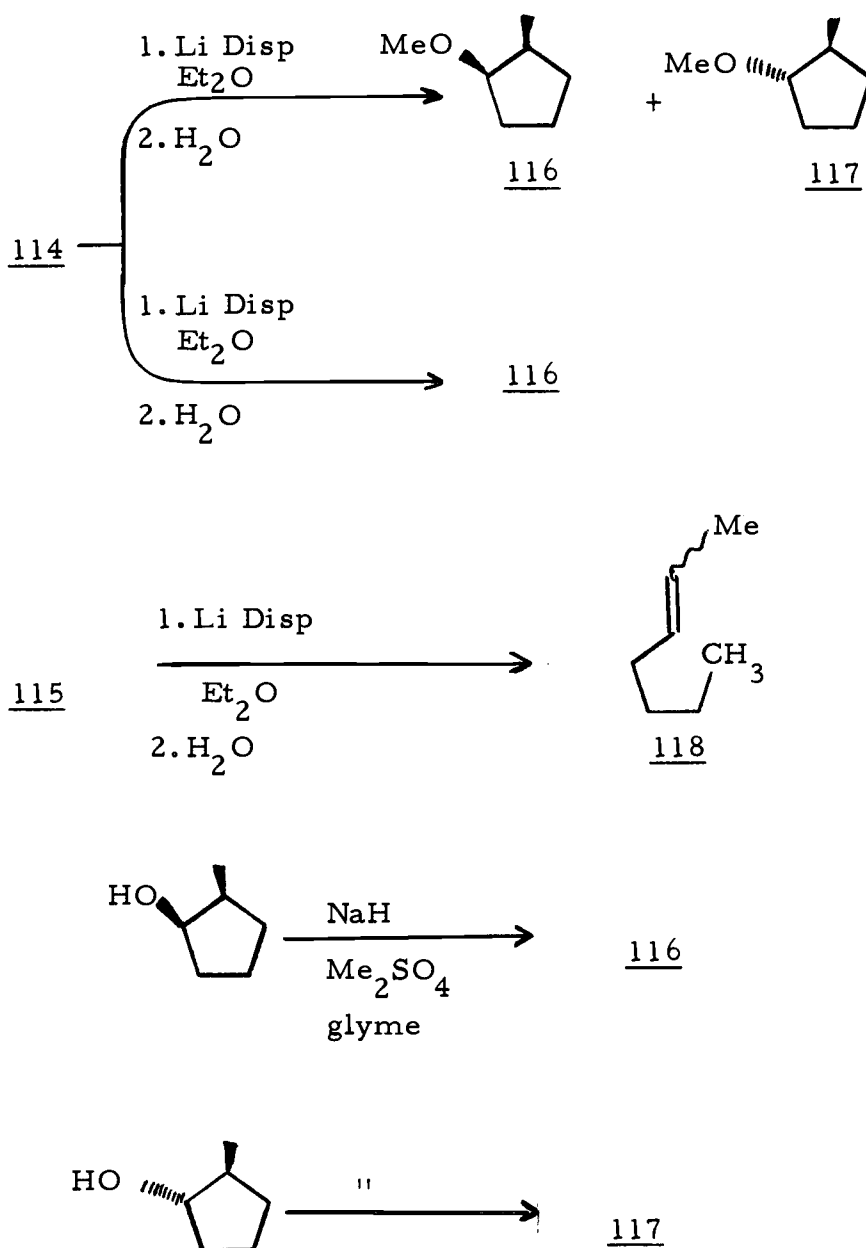
The lithium reagent of 111 was prepared and cyclized to give virtually exclusive (97%) trans cyclic isomer 112 (72), likely due to steric influence in the transition state (73). In order to determine



a possible heteroatom influence on the stereochemistry of cyclization, halide 114 was prepared along with isomer 115, as in Scheme 19, Scheme 19



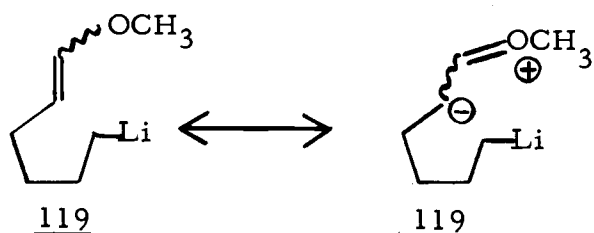
Scheme 19 (Continued)



according to the procedure of Evans (51). When treated with lithium dispersion in ether, 114 gave only cyclic products, a 50/50 ratio (by NMR integration; products were not separated) of cis/trans

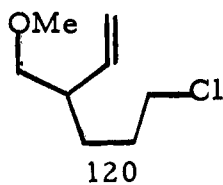
isomeric products (116 and 117). These two isomers were prepared independently from the appropriate cis and trans alcohols, as is indicated in the preceding reactions. A mixture of these authentic isomers of known stereochemistry gave an NMR spectrum identical to that obtained from the cyclization product mixture (116 and 117). While this result is not stereospecific, the indication is that a heteroatom effect is competing with the steric effect predominating in the cyclization of 114. When the effect of the presence of n-butyllithium on heteroatom-influenced cyclizations was recognized, 114 was treated with lithium in the presence of n-butyllithium. As is indicated above, the cyclization under these conditions gave a single product having an NMR spectrum identical to that of the independently prepared cis ether (116). This remarkable result will be discussed at the end of this section.

As is indicated above, compound 115 failed to cyclize. This may be due to the heteroatom's electron donor capability, as indicated in 119b a resonance form of 119, which is the lithium reagent derived from halide 115. In an exocyclization, the lithium bearing carbon attacks the carbon bearing a negative charge in 119b: this process is



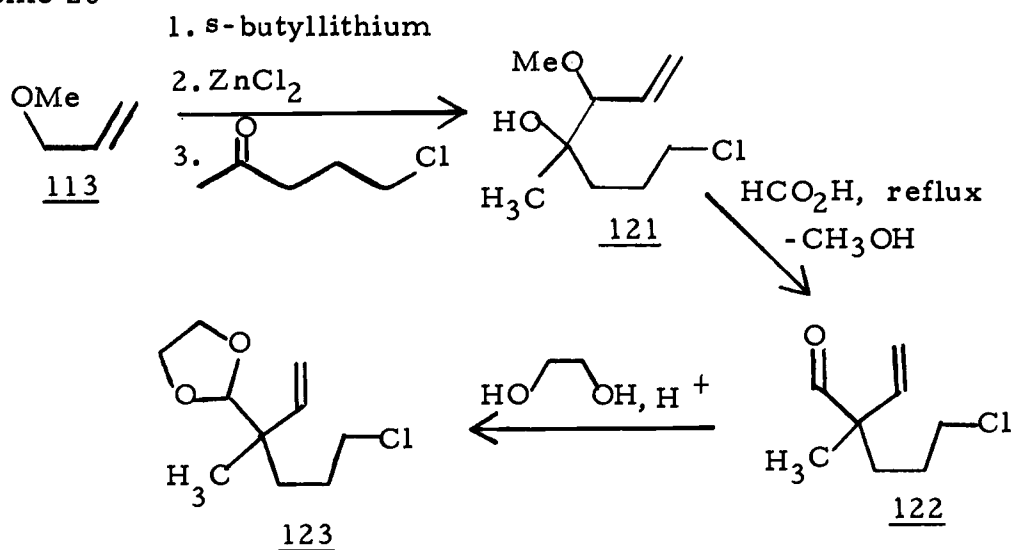
unfavorable in that it involves bringing together of like charges, ergo no cyclization. A much more likely reaction would involve proton abstraction from the allylic position (having precedent in the reaction that forms 114 and 115) or metallation of the oxygen-bearing vinyl position, for which there is excellent precedent (74).

The synthesis of 120, possessing a homoallylic ether, was pursued in the hope of determining the capability it might show in directing a cyclizing organolithium moiety in a particular face of the



double bond. Several attempts to prepare 120 were fruitless. The timely publication of an interesting rearrangement (75) allowed the synthesis of a suitable alternative to 120. This alternative (123), an acetal rather than an ether, was prepared as in Scheme 20. The only

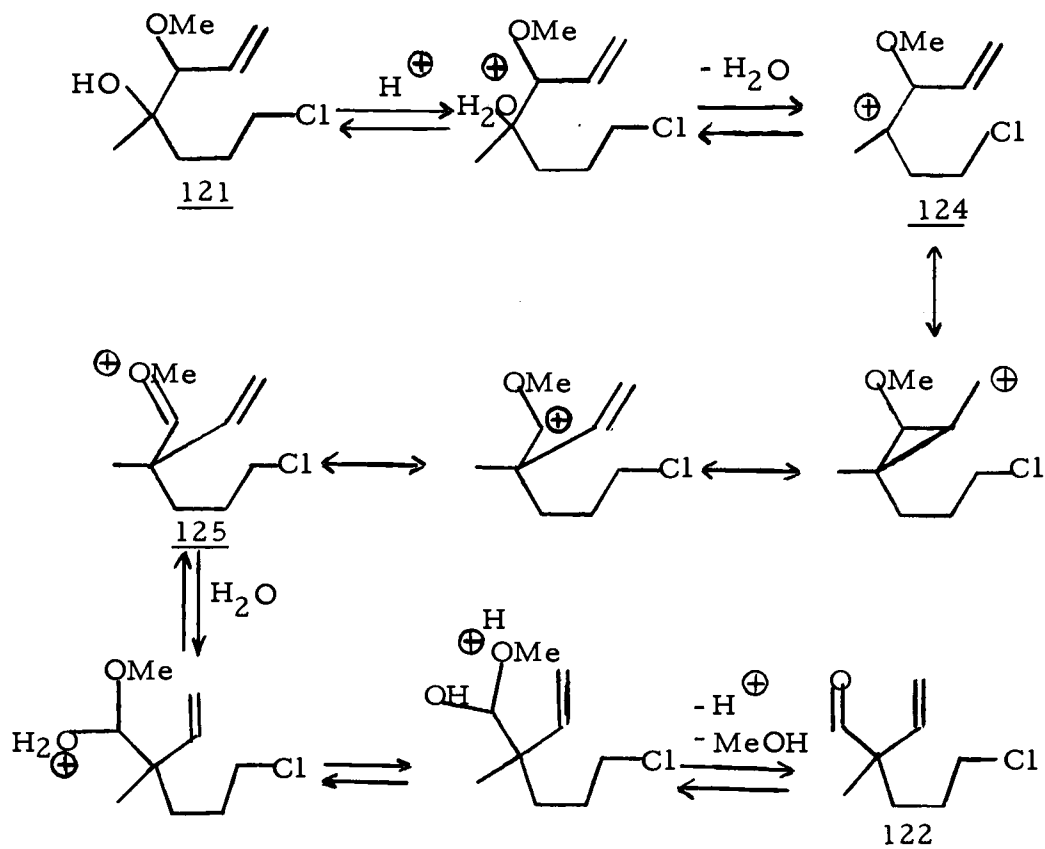
Scheme 20



product of the initial reaction is 121; this is in contrast to the analogous preparation of 114. The agency of this stereoselectivity is the use of zinc chloride in the reaction medium. This is hypothesized to convert the allylic lithium reagent first formed into an allylic zinc compound. The former tends to alkylate at either allylic position, giving mostly reaction at the γ -position; the zinc counterpart, however, gives only α -alkylation as is evidenced by this example.

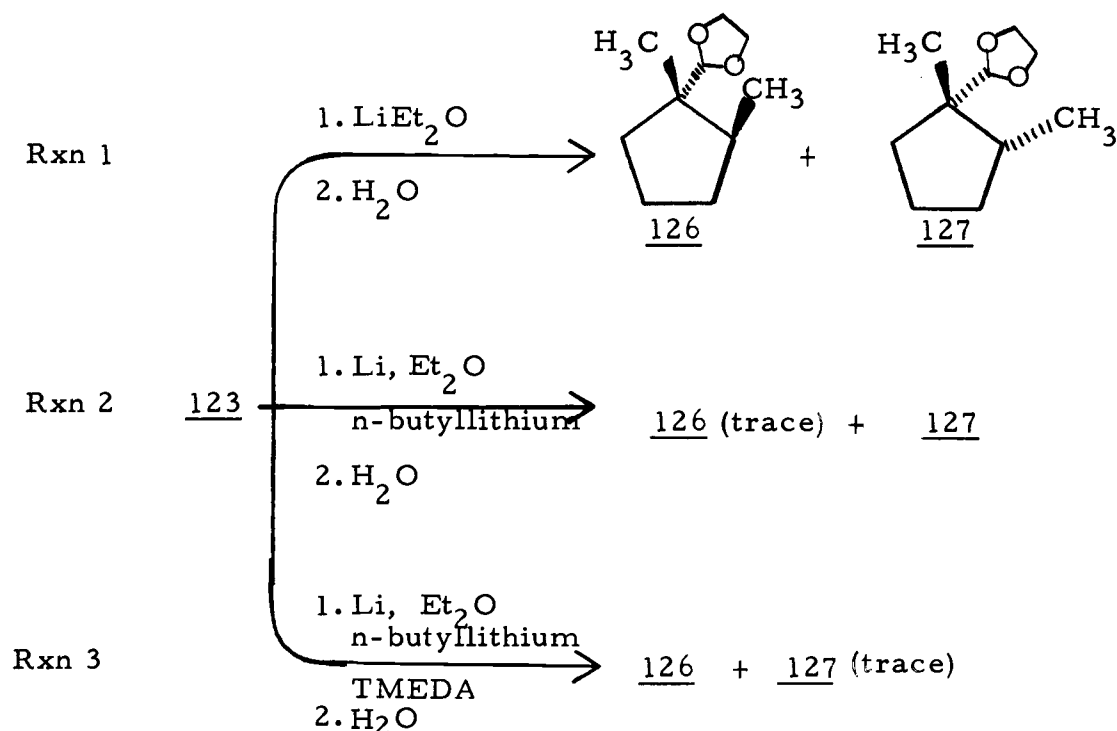
Also noteworthy is the semipinacolic rearrangement (121 to 122) which likely proceeds by a mechanism similar to that provided in Scheme 21. Intermediate carbonium ion 124 is stabilized in that it

Scheme 21



is cyclopropylcarbinyl and has a form (125) in which charge is resonated to an oxygen atom.

The cyclization of the lithium reagent of 123 was effected as indicated below. Preparation of the lithium reagent of 123 in ether



gives only cyclic products, but of both possible stereochemistries.

The products, not separable of GLC, are in the proportion of 40% 126 and 60% 127, by NMR integration of the mixture. When n-butyllithium was present, the reaction was fairly stereospecific, giving predominantly (over 90%) one stereoisomer in 33% yield, and assigned the trans-dimethyl stereochemistry (126). When the reaction was effected using lithium dispersion, n-butyllithium (1.6 equivalents),

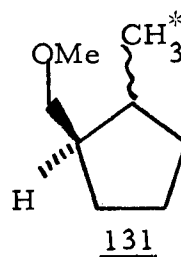
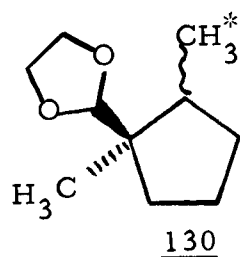
and TMEDA (2.7 equivalents), the other cyclic product (127) was produced as the major (over 90%) stereoisomeric product in 44% yield based on starting halide.

Synthetically, the results of reactions 2 and 3 are intriguing. To be able to effect stereospecific cyclizations producing either isomer depending on the use or non-use of TMEDA is a synthetically attractive attribute of heteroatom-controlled organometallic cyclizations.

Compounds 126 and 127 were not independently synthesized. Rather, the stereochemistries were assigned on the basis of comparison of NMR spectra to those of similar compounds of known stereochemistry, and by chemical precedent. From the work discussed below on aluminum, compounds 128 and 129 were cyclization products that were also independently synthesized. As will be discussed later, the stereochemistries were thus established and are as



indicated in the structures above. A comparison of the chemical shifts of the methyl doublets due to H* in structures 130 (representing 126 and 127) and 131 (representing 128 and 129) shows that H* is relatively upfield for 126 and the trans isomer (128) and relatively downfield for 127 and the cis isomer (129). This analogy offers



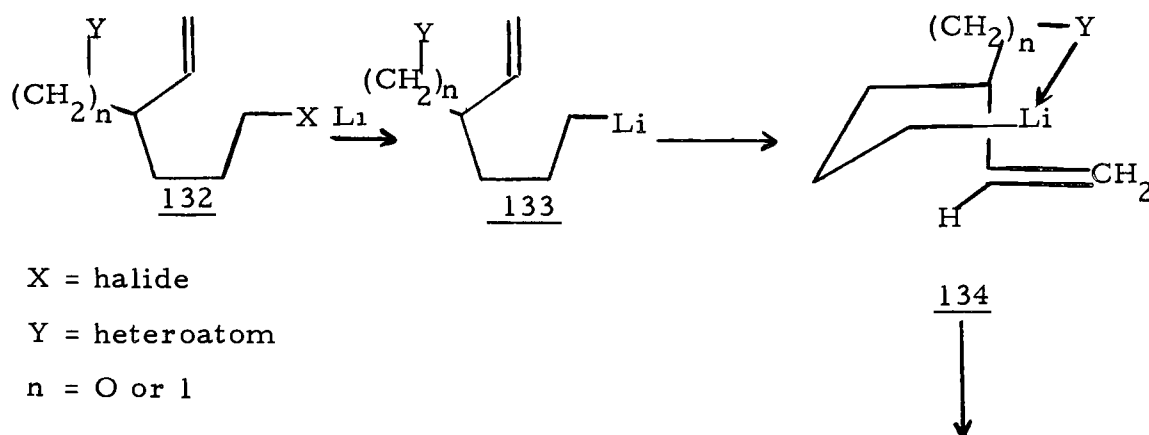
	H* doublet: δ values
<u>127</u>	0.95-1.00 (downfield)
<u>126</u>	0.87-0.93 (upfield)
<u>129</u>	0.97-1.03 (downfield)
<u>128</u>	0.80-0.86 (upfield)

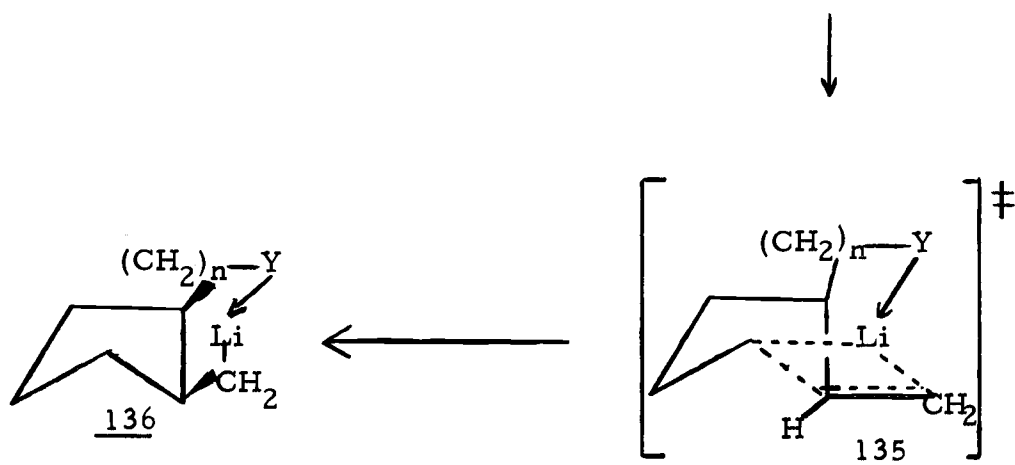
a basis for the stereochemical assignments made for 127 (trans-dimethyl) and 126 (cis-dimethyl).

Probably the most convincing reason for the structural assignments made above is chemical precedent. In all cases reported above in which the cyclization of a heteroatom compound was carried out both with and without the presence of *n*-butyllithium, the reaction with

same showed an enhancement of the heteroatom's influence. In the reaction at hand, enhancement would mean increased percentages of the trans-dimethyl product (127), again supporting the proposed structural formulae.

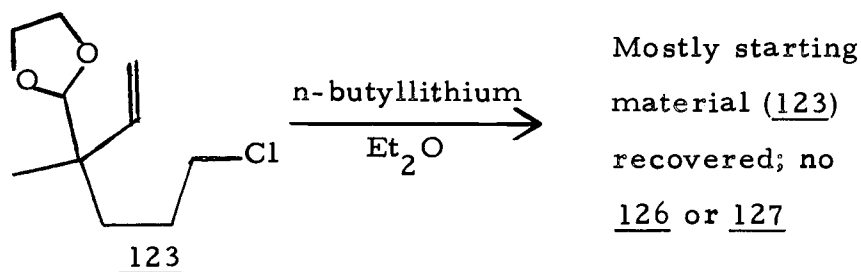
System 123 is the final example an organolithium cyclization to be reported here. At this point a discussion of the stereochemical outcome of the allylic heteroatom-influenced cyclization is appropriate. The results obtained for the cyclizations of 101, 102, and 107 indicate (since they do cyclize) that an interaction between the metal and the heteroatom begins to form in the approach to the transition state (76). Based on this, for allylic or homoallylic system 132, the initial action after formation of the lithium reagent (133) would be the evolution of the intramolecularly-complexed species (134). With the lithium atom locked on the heteroatom's side of the incipient ring as in transition state 135, the result is the cis relationship between the





heteroatom and the lithium-bearing carbon. A transition state like 135 could be invoked in the cyclization reactions of 114 and 123.

One topic that remains untouched is the enhancement of the heteroatom effect by the presence of n-butyllithium. A control experiment shown below ruled out the possibility of a metal-halogen exchange somehow being responsible for the stereoselectivity attained.



It is likely that the increased heteroatom influence in the presence of n-butyllithium involves changes in the aggregates in which lithium reagents generally exist. In the presence of donor solvents like ether, alkyllithiums are usually tetramers (77). In the presence of n-butyllithium, mixed tetramers are likely. TMEDA is reported (78) to break down the aggregates of alkyllithiums due to its strong bidentate chelated complex with lithium. The TMEDA would be expected to

complex with lithium more strongly than could the heteroatom; with the heteroatom impotent, steric considerations become dominant. To make worthwhile hypotheses, an in-depth knowledge of the nature of aggregation in cyclizing alkenyllithium systems in various environments would be required. That knowledge is not available in the current state-of-the-art, and thus a definitive statement is presently not possible. Also, it is well to remember that the primary goal of this research was the evolution of efficient synthetic tools rather than investigation into mechanistic pathways.

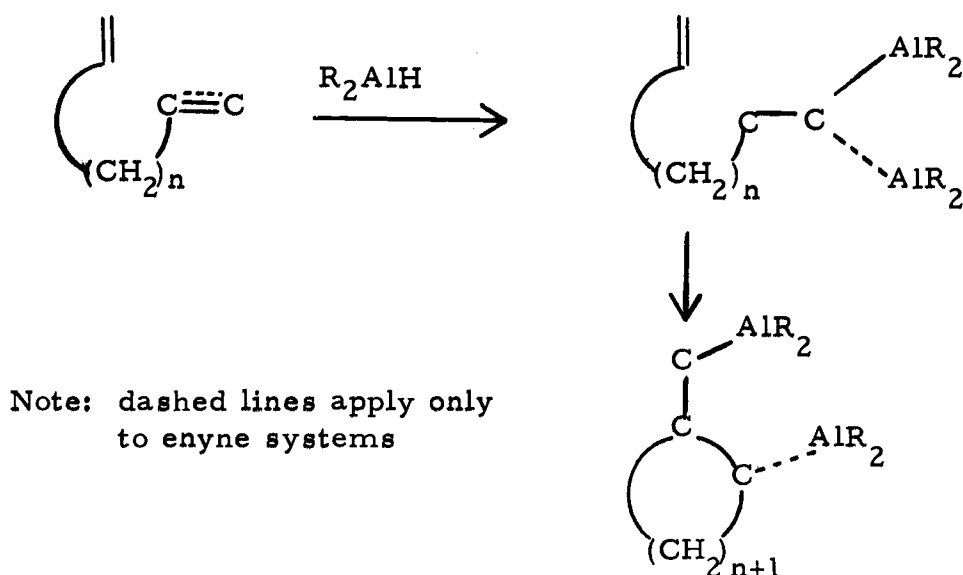
By way of summary, heteroatoms have been shown to have potential in influencing the efficiency and/or the stereochemistry of organolithium cyclizations. Systems like 101 and 107, whose counterparts gave only noncyclic products, cyclized completely. Other systems (114 and 123) were cyclized stereospecifically, with stereochemistry opposite to that obtained with non-heteroatom analogues.

b) Aluminum cyclizations. Intramolecular cyclizations of alkenyl-aluminum compounds have been shown to be promising synthetic tools (16). The use of heteroatom complexation to influence stereochemistry while providing for functionality in the cyclic product would enhance the synthetic utility of organoaluminum cyclizations. The following portion of the thesis describes work done in that direction.

An organoaluminum cyclization involves hydroalumination of a

multiple bond by a dialkylaluminum hydride species to form the alkenyl-aluminum compound which can then undergo carbocyclization to form the desired ring compound. This flow of events is depicted in Scheme 22. If a terminal triple bond is available, a double

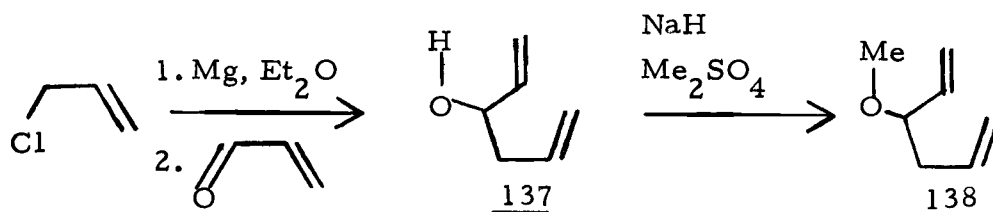
Scheme 22

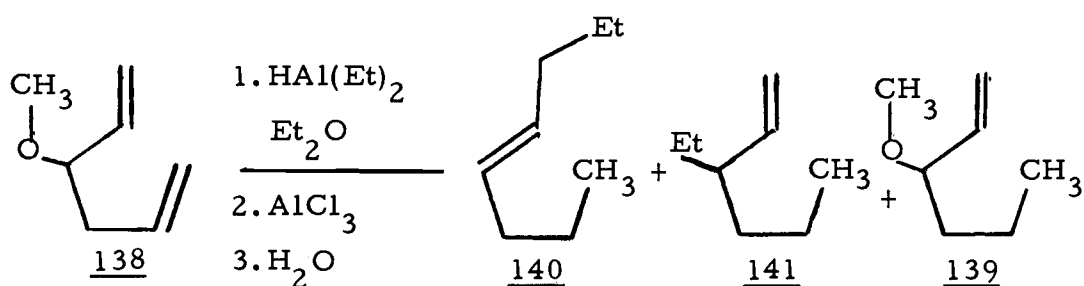
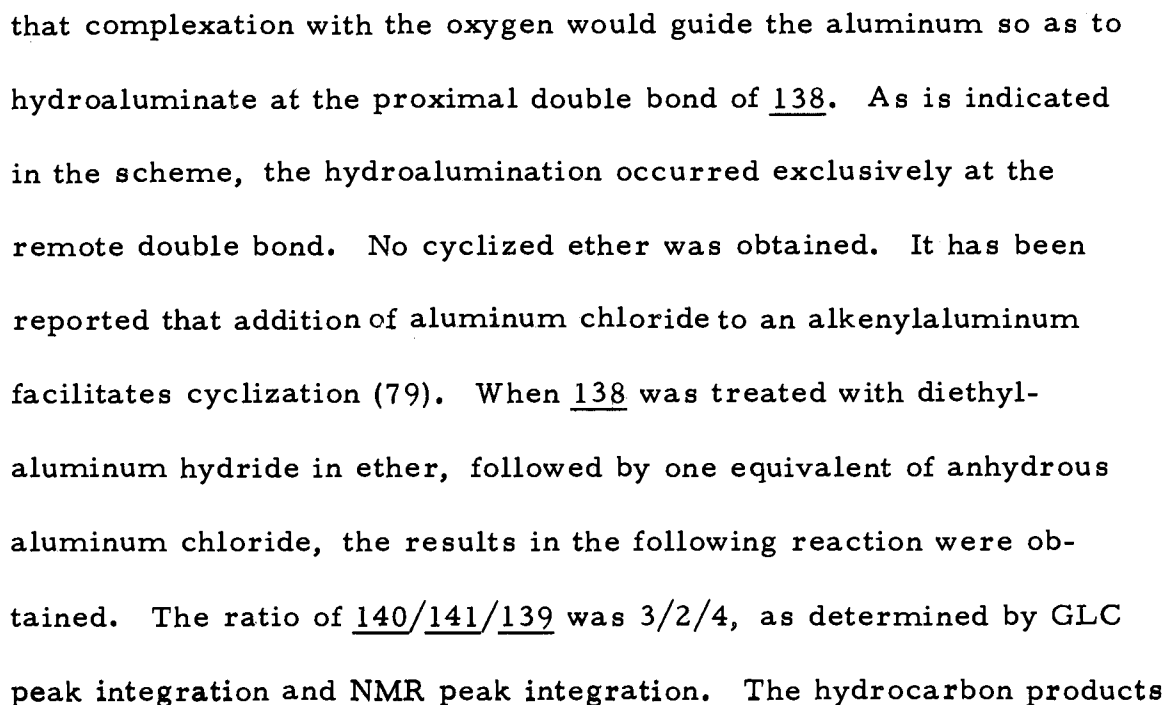


hydroalumination, with anti-Markovnikov regiochemistry, occurs in preference to single hydroalumination at the double bond.

Compound 138 was prepared as per Scheme 23. It was expected

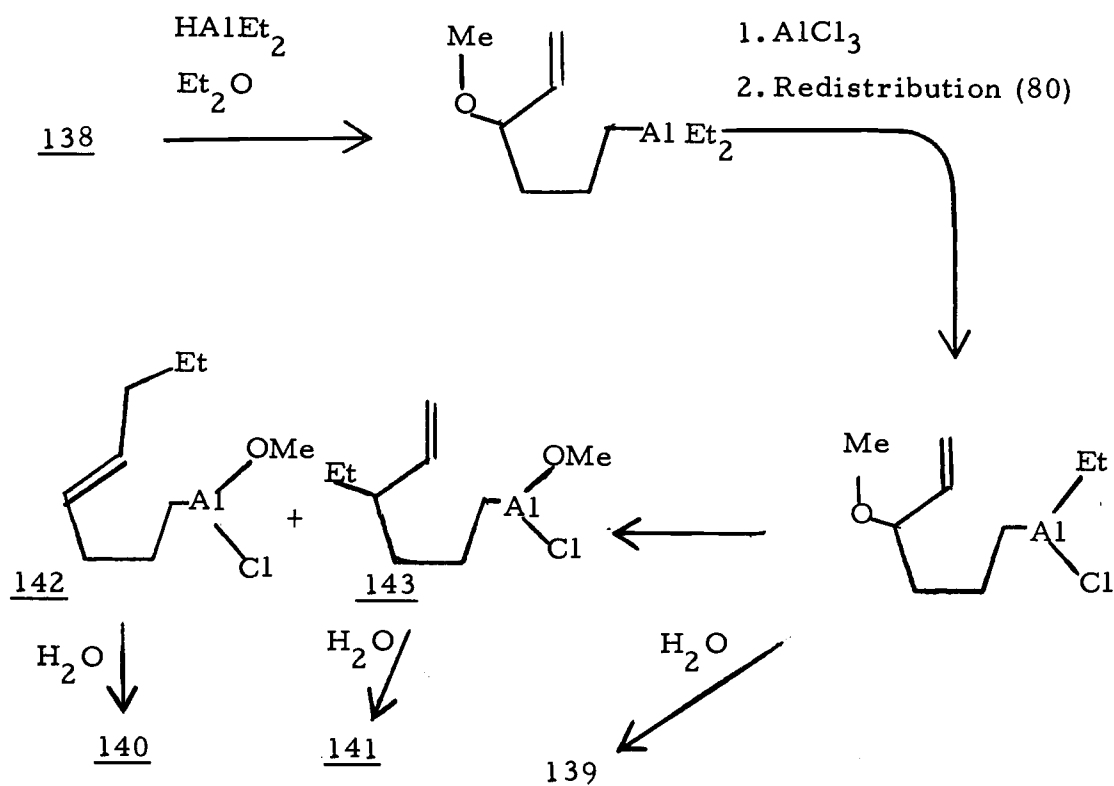
Scheme 23





seem to be derived (Scheme 24) from the transfer, likely intramolecular, of an ethyl group which brings about the exodus of the methoxy to form an aluminate species (142 or 143). This result has ample precedent, being entirely analogous to Kitagawa's work (64) discussed

Scheme 24

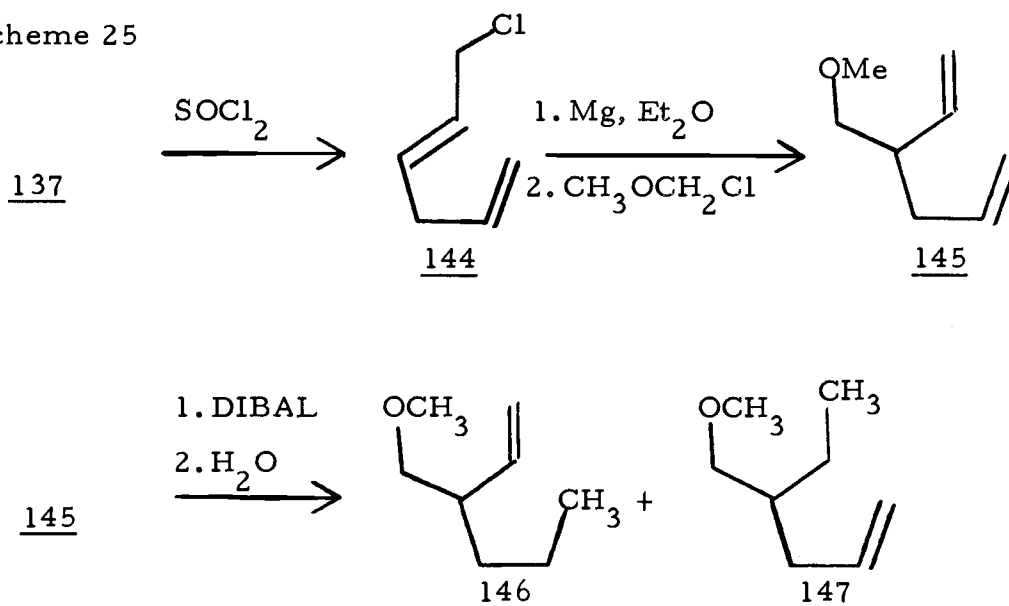


above (page 29). No cyclohexene could be identified in the reaction products. Its formation would have been by a reaction analogous to the formation of 142 with the metal end of the alkenyl ether being passed to the double bond (endocyclization) rather than the ethyl group's passage.

The hydroalumination of 138 seemed to indicate that if a chelate ring was being formed, the six-membered ring was preferred to the five-membered ring. The next logical step was the synthesis of a system pitting a six-membered chelate ring against a seven-membered chelate ring. This involved preparation and hydroalumination of homoallylic ether 145 as in Scheme 25. There was again no cyclic product

produced. The linear reduced products were unexpected in their ratio; the major portion of the hydroalumination occurred again at the distant double with the ratio of 146/147 being about 9/1, as determined by

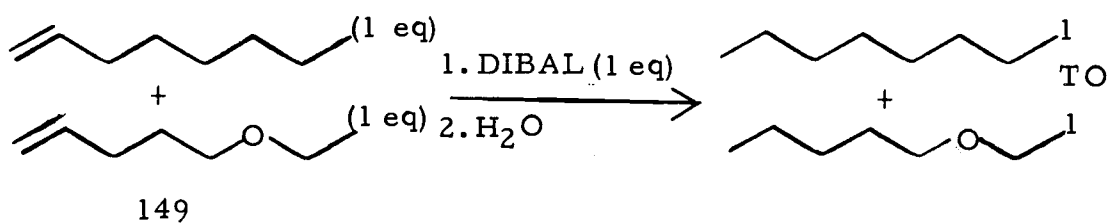
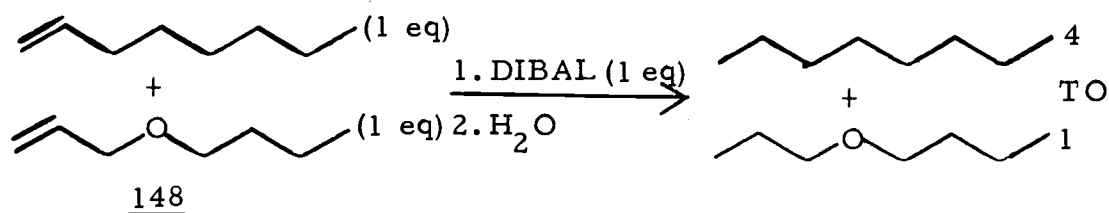
Scheme 25



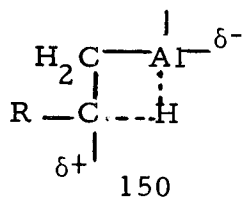
NMR peak integration. Addition of aluminum chloride resulted in the same products, with 146 again greatly predominating.

The results of hydroalumination of 138 and 145 seemed to indicate that, rather than guiding the aluminum to the near double bond as had been expected, there seemed to be a tendency to hydroaluminate as far from the oxygen as possible; this was termed the "oxyphobic effect" (81). In order to further study this phenomenon, the competition experiments outlined in Scheme 26 were performed. The results given in Schemes 23, 25, and 26 all support the notion of an oxyphobic tendency. The possibility exists that this is due to the fact that oxygen, being a better Lewis base than is a double bond, monopolizes the

Scheme 26



vacant site on a nearby aluminum in the hydroalumination transition state. The degree of availability of that site determines the rate at which the hydroalumination occurs. Double bonds more remote from the oxygen experience less interference in the hydroalumination transition state, and thus react faster. Another possible factor in the oxyphobic proclivity is the inductive effect of oxygen. In the transition state for addition of H-Al to a double bond, some positive charge build-up on carbon, as indicated in 150, has been postulated (82). The electron withdrawing effect of oxygen would disfavor such



a transition state. The inductive basis for the oxyphobic predilection is not in accord, however, with the fact that a competition experiment

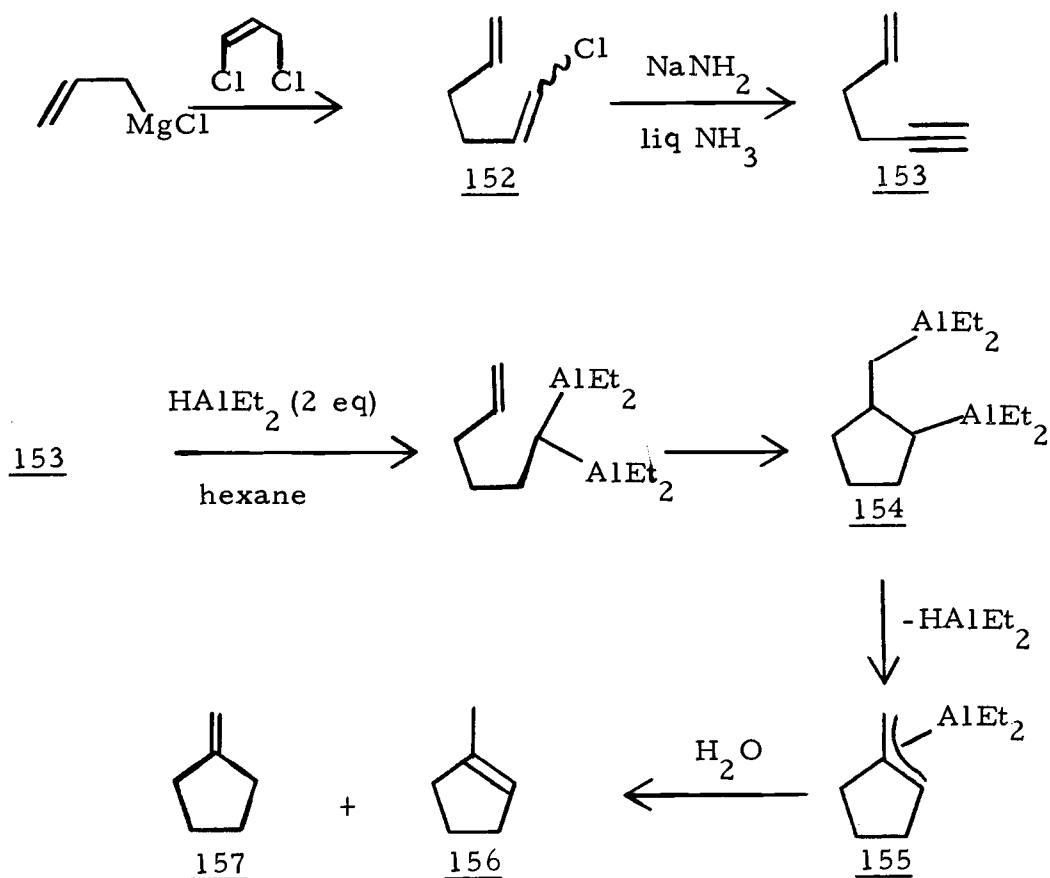
between 1-octene and allyltrimethylsilane (151) for a limited amount of alkylaluminum hydride showed the reaction rate of 1-octene to be faster. The inductive premise would predict that silicon's electron release (electronegativity: Silicon = 1.74, Carbon = 2.50; using Allred-Roschow (83) formula) should stabilize the transition state and accelerate the reaction. That this does not happen could have other causes (e.g., steric in the case of allyltrimethylsilane), but it does cast doubt on the inductive basis for the oxyphobic tendency.

As the heteroatom-diene systems, 138 and 145, had not shown promise as cyclization tools, attention was shifted to heteroatom-enyne systems. The notion, touched on above in the discussion of the basis for the oxyphobic effect, was that, with two aluminum atoms on the former terminal alkyne carbon, the heteroatom could not interact strongly with both in the transition state. Thus, it might influence the stereochemistry of attack of the organoaluminum moiety without curtailing its chemical reactivity. To acquire a background for the heteroatom work, hydrocarbon enyne systems were first investigated.

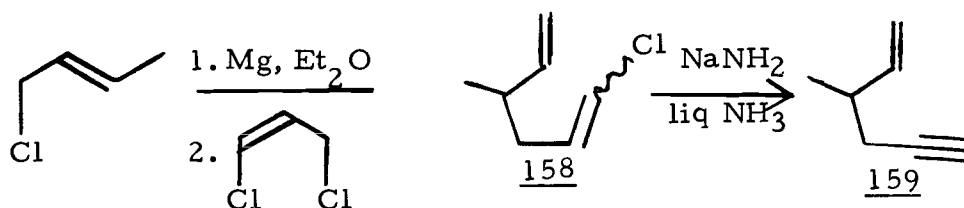
The addition of dialkylaluminum hydrides to 1-alkynes was reported to give mono- and dihydroalumination when carried out in hydrocarbon or ether solvents, respectively (84). Results presented in the following pages contradict that statement as dihydroalumination apparently occurred in either solvent. Prepared as indicated, compound 153 dihydroaluminated and cyclized giving alkenes 156 and 157

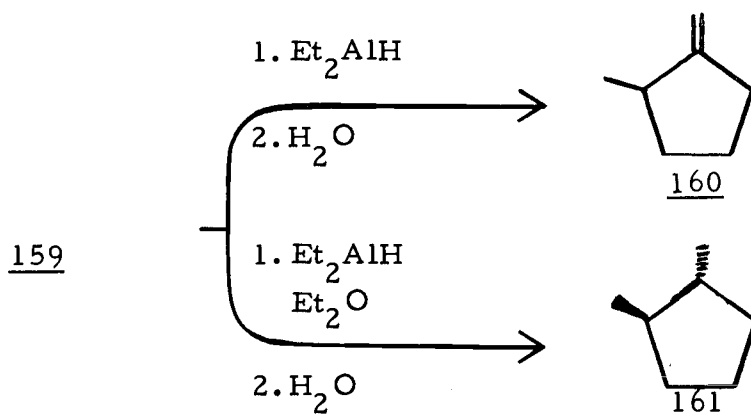
in a ratio of 1.0 to 1.33 respectively (Scheme 27). Products 156 and 157 appear to be derived from the dialuminocyclopentane (154), by way of allylaluminum compound 155, possessing either σ or π -type bonding (see discussion on p. 28 above).

Scheme 27

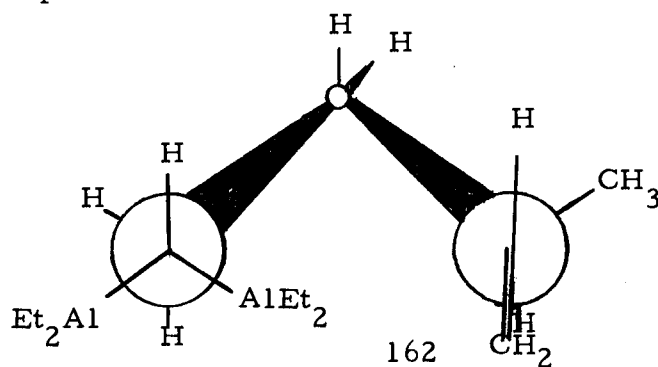


Compound 159 was prepared in a manner analogous to 157 and cyclized as is indicated in the following reactions. As before, in the

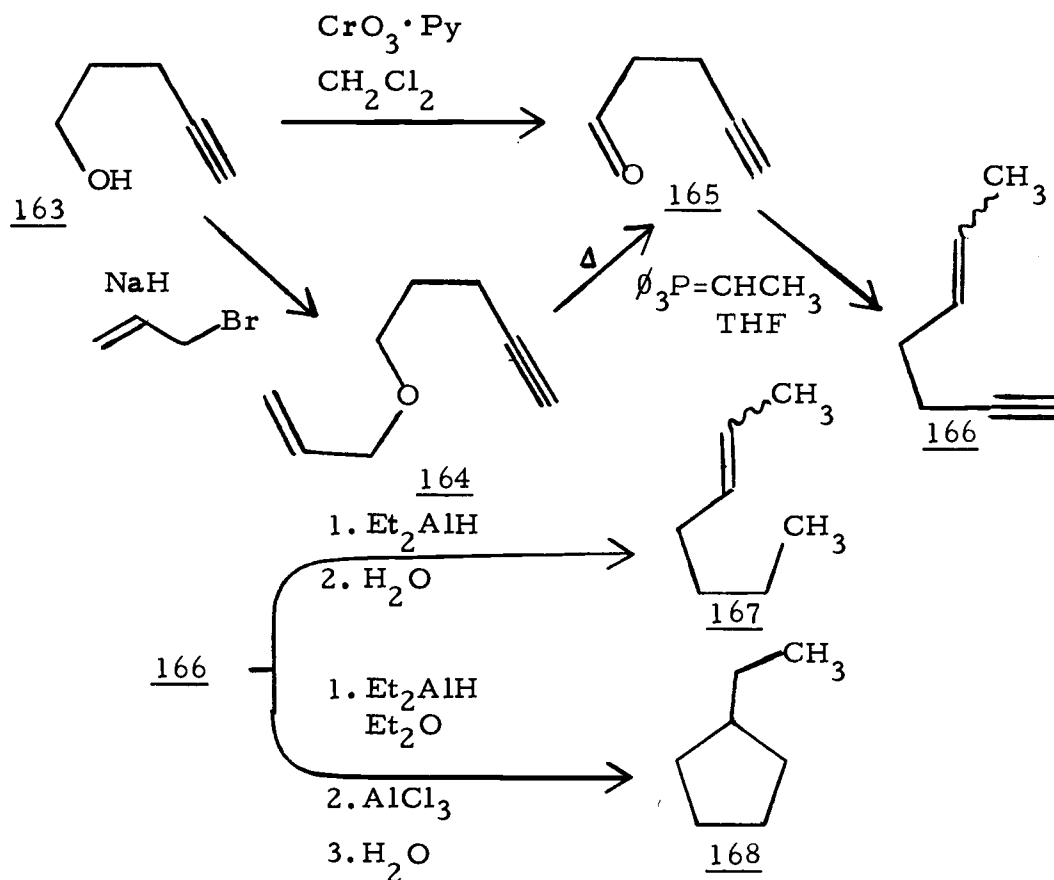




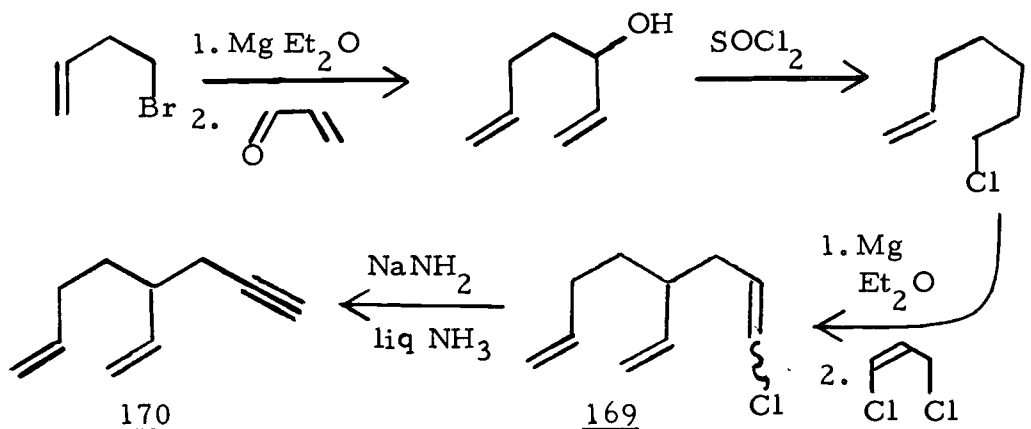
absence of ether, dehydroalumination occurred giving 2-methylmethylenecyclopentane (150). As is indicated in the above reactions the presence or absence of ether did not determine the extent of hydroalumination but rather whether dehydroalumination occurred or not. For example, in the presence of two equivalents of ether, no dehydroalumination was observed and the sole product was saturated hydrocarbon 161, afforded in 68.6% yield and of the trans stereochemistry. The stereospecific formation of 161 can be explained on a steric basis using Stefani's argument (73). Structure 162 shows a reasonable reaction coil for the aluminum reagent of 159. The methyl's occupation of the more stable quasiequatorial position leads to the trans stereochemistry in the product.



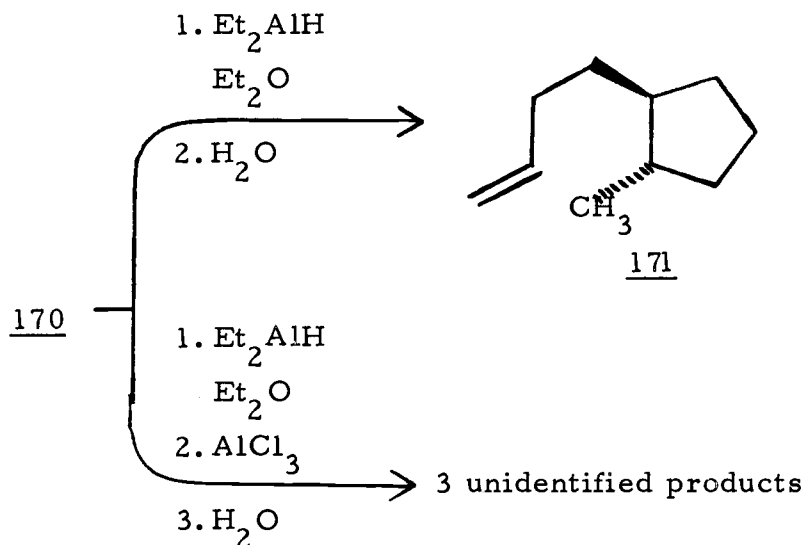
Enyne 165 was prepared as indicated. Alcohol 163, prepared by Organic Synthesis methods (85), was converted to aldehyde 165 both by Collins oxidation (86) and through ether 164 (87). The reaction of 166 and diethylaluminum hydride without the presence of aluminum chloride gave primarily linear reduced products (167). A small GLC peak (approximately 5% of the reaction products) had the same retention time as cyclic product 168. Reaction in the presence of ether and aluminum chloride produced one major product identified as the cyclic isomer (168) by comparison of its mass spectrum with that of an authentic sample of ethylcyclopentane.



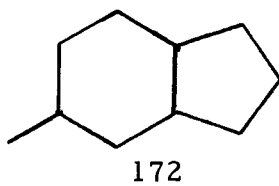
A final enyne hydrocarbon system was 170, prepared as shown from a sample of 169 obtained from P. W. Chum. Without added aluminum chloride, the reaction gave only a single cyclization (to 171).



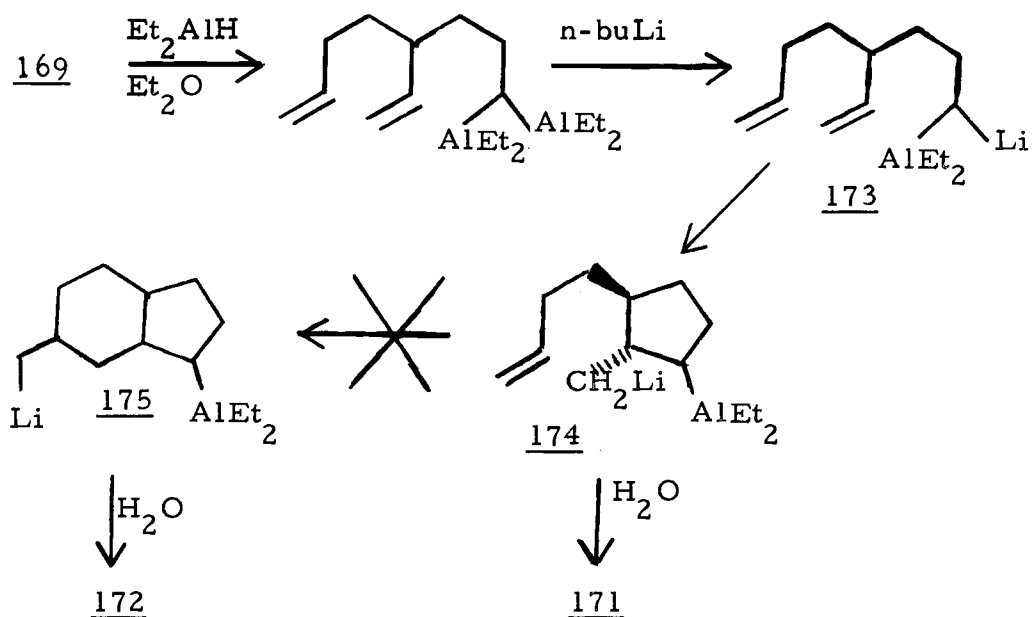
Alkene 171 possessed an NMR spectrum identical to that of 2-(3-butenyl) methylcyclopentane, produced by the lithium cyclization of 5-bromo-1,9-decadiene and of proven stereochemistry (88). When



anhydrous aluminum chloride was added, three unidentified compounds were obtained. None were 171 or the hoped-for product, 172 (whose NMR spectrum had previously been obtained (88)).

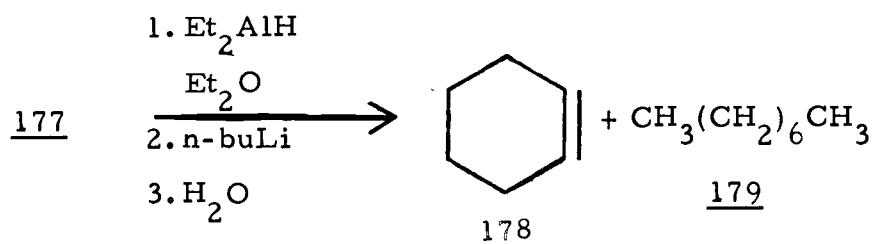
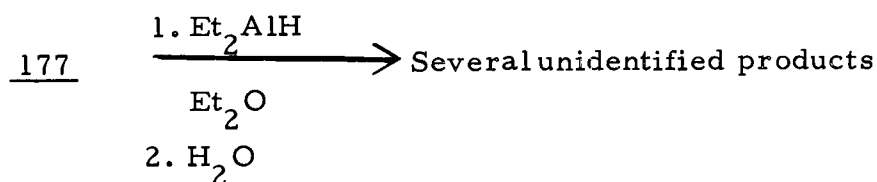
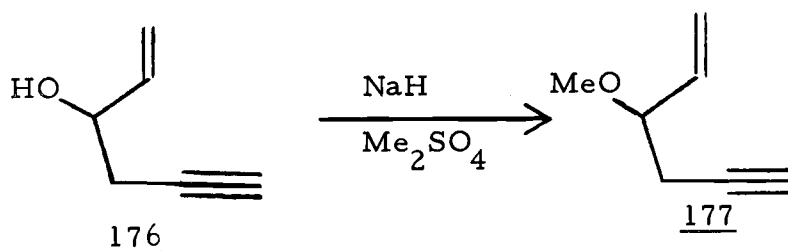


Another approach to the bicyclization of 170 was the report (89) that 1,1-dialumino compounds can be converted into 1-alumino-1-lithio compounds (173, for example) by treatment with n-butyllithium. Since conversion of 174 into 175 is known to proceed without the aluminum (90), it was hoped that the sequence indicated would carry through to bicyclic product 172. The approach was not successful and provided only monocyclic product 171 upon quench, however.



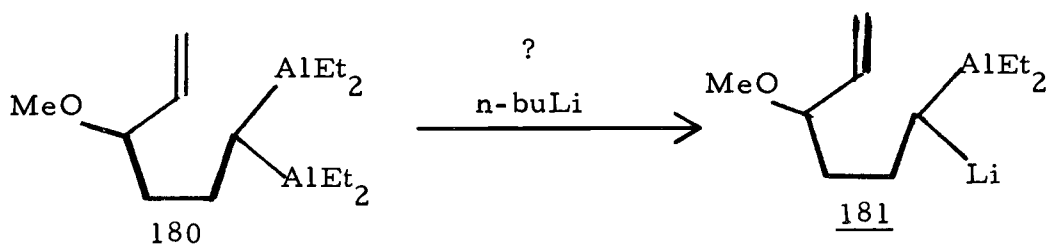
Having set the foundation for beginning to investigate hetero-atom-influenced enynaluminum cyclizations, the synthesis of 177 was

accomplished and the cyclization attempted. Alcohol 176 was obtained by the method of Viola and MacMillan (91).

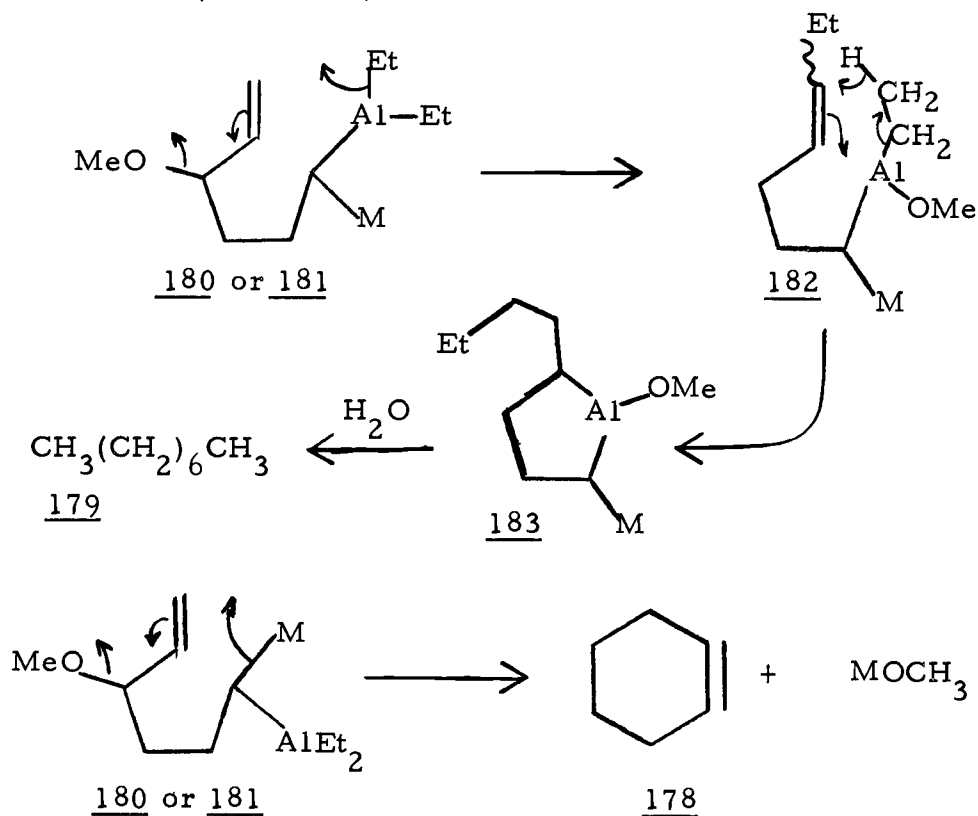


Noteworthy is the reaction of 177 with diethylaluminum hydride followed by n-butyllithium. The products, as indicated above, might be explained by the reactions in Scheme 28. It is unknown whether

Scheme 28



Scheme 28 (Continued)

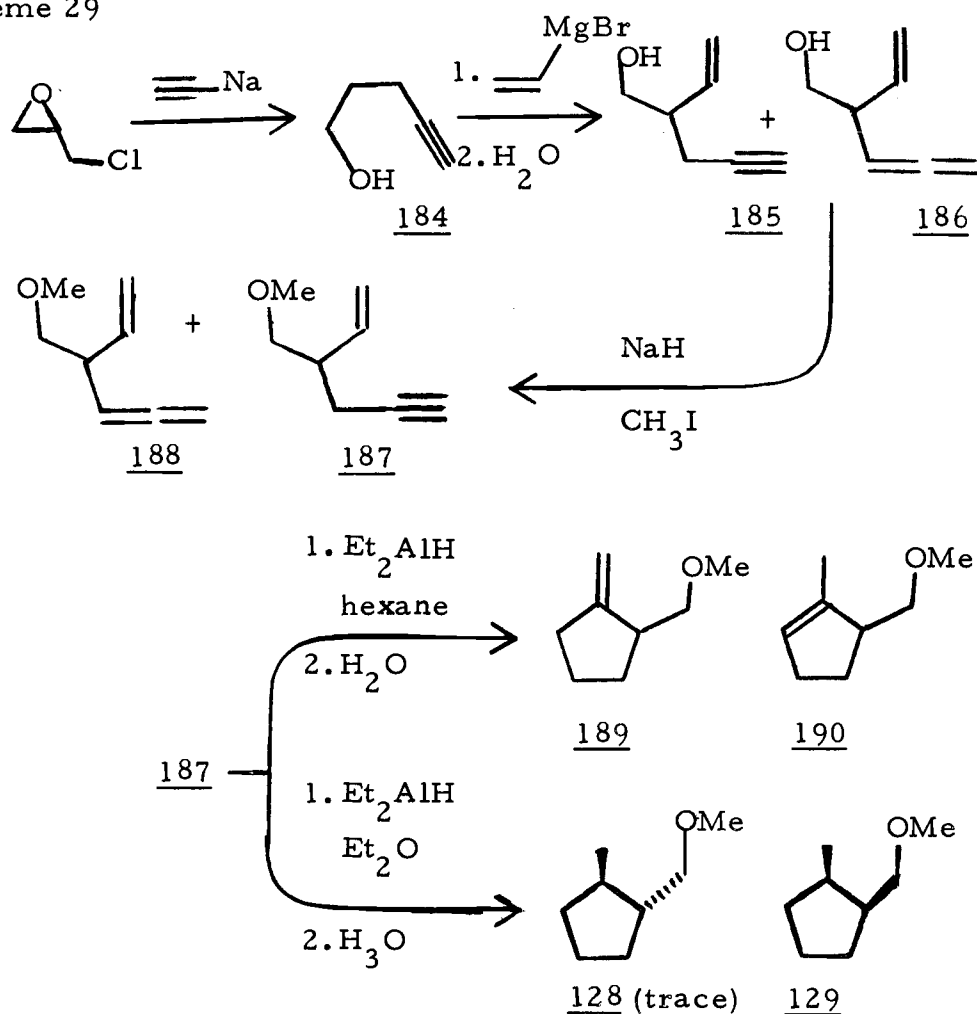


181 is actually formed; this could be determined by treatment of the reaction mixture with methyl iodide after the addition of butyllithium. It is known that 1,1-dialumino compounds fail to react with methylating agents, while the lithium containing counterpart (181) certainly would (89). In any case, the reactions proposed for the dimetallic reagent (180 or 181) have well established precedent in both aluminum (page 28 above) and lithium (page 14 above) chemistry. The process of conversion of 182 into 183 might be thought of as involving intermediate production of an alkylalkoxyaluminum hydride which then accomplishes an intramolecular hydroalumination to give 183 (92).

Compound 177 had not provided the hoped-for model system for

heteroatom-influenced organoaluminum cyclizations. The observed susceptibility of the allylic heteroatom prompted a turn of attention to the synthesis of 187, a homoallylic system. That synthesis as well as the successful cyclization of 187 are outlined in Scheme 29.

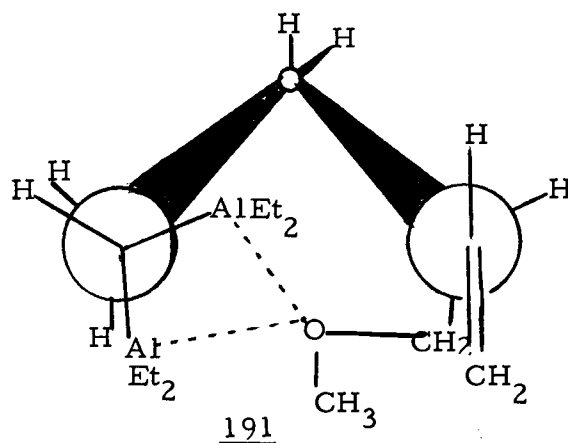
Scheme 29



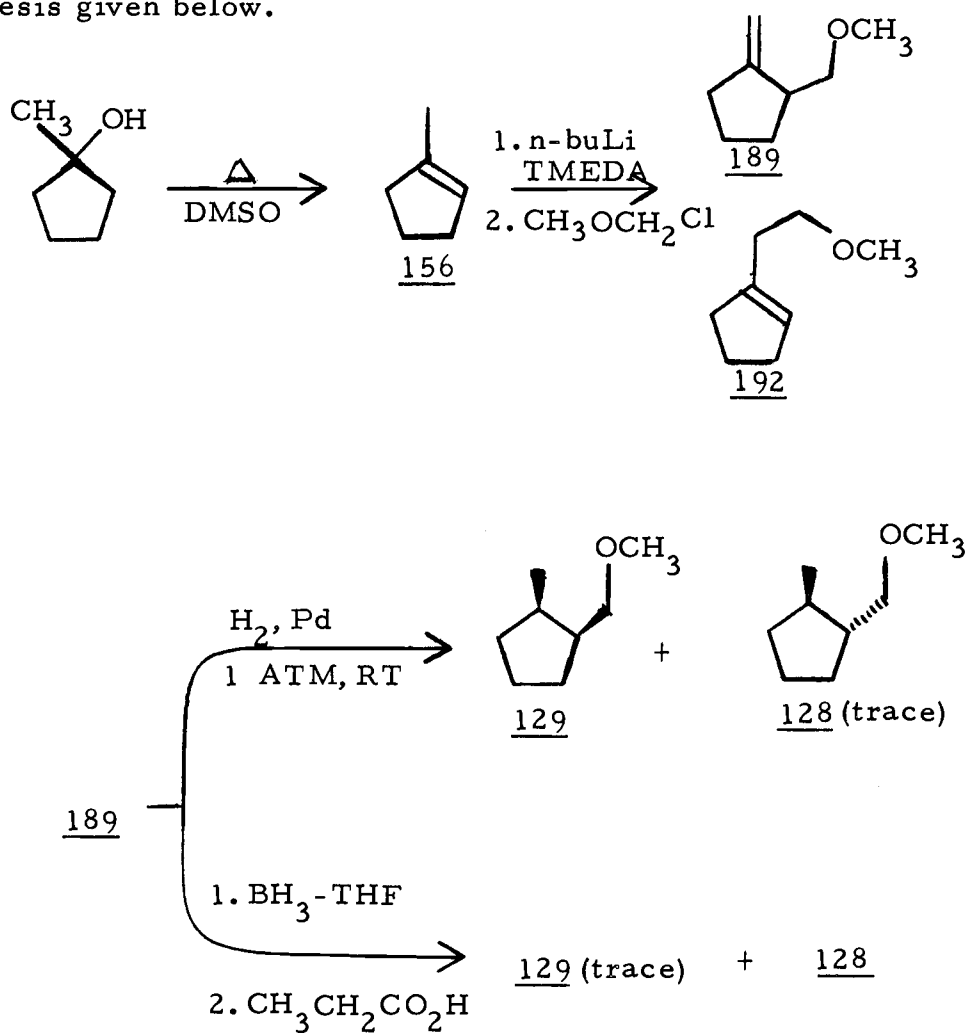
The preparation of 187 contains a reaction that is especially interesting in light of the subject of this thesis. Vinyl magnesium bromide adds across the double bond of alcohol 184, which was prepared by the method of Sondheimer *et al.* (93), to provide isomeric

alcohols 185 and 186 (94). The addition of the Grignard is similar to several examples mentioned in the historical section above, in which an organometallic adds across the double bond of an allylic alcohol. The regiochemistry is in keeping with the examples discussed above.

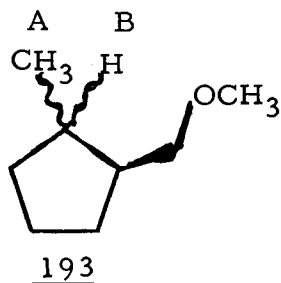
As observed before, the cyclization of 187 produces alkenes when the reaction is run in hydrocarbon solvent. The internal oxygen apparently cannot stop the dehydroalumination, likely because it cannot tie-up both aluminum atoms. However, addition of ether to the reaction mixture results in the formation of the saturated product (129) of essentially one stereochemistry, even if the ether is in ten times excess. The stereochemistry was determined to be cis, fortuitously in direct contrast to the cyclization of the allylic methyl substituted enyne (158); this demonstrates the dominance of the heteroatom effect over steric effects. The following representation (191) of a possible reaction coil would explain the cis product geometry. The requirement is for some interaction between the oxygen and each aluminum atom. Bridging is a well established phenomenon in aluminum chemistry, especially for heteroatom ligands (52b). In this case the interaction may well be best described by a three center bond. This bonding concept is commonly invoked in the chemistry of boron, and also in its isoelectronic partner, aluminum, e.g. hydrides (95).



The stereochemistry of 129 was ascertained by the independent synthesis given below.



The reductions of 189 offer an interesting contrast. The catalytic hydrogenation gives mainly a product identical to the major cyclization product (129). Based on steric predictions this should be the cis isomer. The hydroboration-protonolysis of 189 gives a major product identical to the minor product of the cyclization of 128, assigned the trans stereochemistry. The production of the trans isomer rather than the cis which might be expected as it results from the approach of the borane from the least hindered side of the double bond can be explained in either of two ways. The initially formed cis isomer could isomerize to the more stable trans isomer (96) prior to protonolysis, which has been reported but only at much higher reaction temperatures. A more engaging explanation, at least in terms of its correspondence to the subject of this thesis, involves the heteroatom guiding the borane by a Lewis interaction into the face of the double bond on its own side of the ring; this results in the trans product. The stereochemistries assigned to isomers 128 and 129 are supported by the NMR chemical shift data depicted for structure 193.



δ Values (average)

	<u>129</u>	<u>128</u>
H ^A	1.00	0.82
H ^B	1.80	2.08

By way of summary, it would seem that allylic ethers are too susceptible to undesired side reactions to be useful for organo-aluminum cyclizations. The triple bond work in general proved potentially useful in that it offers cyclization capability along with selectivity in the point of initial hydroalumination; this would be critical in the polycyclization of multi-ene systems. The triple bond systems also lend themselves to heteroatom influence in that, having two aluminum atoms, they have one to complex with the heteroatom and one to complex with (and subsequently cyclize into) an appropriate double bond. The homoallylic heteroatom enyne system (187) combines all of these features and its cyclization performance testifies to the potential of the systems for which it serves as a model.

IV. EXPERIMENTAL

General Laboratory Procedures and Conditions

All temperatures are uncorrected. Nuclear magnetic resonance (NMR) spectra were obtained on Varian EM-360 (60 MHz) and Varian HA-100 (100 MHz) spectrometers. Unless otherwise specified, tetramethylsilane was used as an internal reference, and the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, J = coupling constant in Hertz. Infrared (IR) spectra were obtained on Perkin-Elmer 137 sodium chloride spectrophotometer. Low resolution mass spectra were obtained from an Atlas CH7 instrument using a 70 eV excitation potential. High resolution mass spectra were obtained from a CEC 110B instrument.

Gas-liquid chromatography (GLC) analyses were carried out on a Varian 920 (thermal conductivity detector, using 1/4 in. columns) and a Hewlett-Packard 5720A (thermal conductivity detector, using 1/8 in. columns). The chromatograms were recorded by either a Hewlett-Packard 7123A recorder, a Linear Instruments 445 recorder, or a Sargent-Welch XKR recorder.

For yield determinations by GLC analysis, a hydrocarbon internal standard was added to reaction product solutions. Equal molar responses were assumed using the thermal conductivity detector. All peak areas needed to calculate yields were determined by use of a

Hewlett Packard integrator model 3373B, or by cutting out and weighing.

Safety and efficiency dictate that persons following experimental procedures described herein involving organometallics (for example, all cyclizations) should be familiar with and follow appropriate precautions and prescribed procedures for handling air-sensitive reagents (97).

Analytical and preparative GLC work was conducted using the following columns:

Column A: OV-17 (5%) on Chromosorb G, 1/4 in. X 10 ft.

Column B: SE-30 (20%) on Chromosorb P, 1/4 in. X 15 ft.

Column C: SE-30 (20%) on Chromosorb P, 1/4 in X 6 ft.

Column D: SE-30 (25%) on Chromosorb P, 1/4 in. X 4 ft.

Column E: Carbowax (20%) on Chromosorb P, 1/4 in. X 20 ft.

Column F: OV-17 (5%) on Chromosorb G, 1/4 in. X 18 ft.

Column G: Carbowax (25%) on Chromosorb P, 1/4 in. X 45 ft.

(glass)

Column H: OV-17 (5%) on Chromosorb P, 1/4 in X 6 ft.

All elemental analyses of analytical samples were performed by Gailbraith Laboratories, Inc. (Galbraith Laboratories, Inc., P. O. Box 4187, Knoxville, Tennessee).

5-Bromo-1-pentene (85)

To a solution of 43.35 g (0.5 mole) of 4-penten-1-ol (84), which was prepared by the method of Kharasch and Fuchs (98), 150 mL of anhydrous ethyl ether, and 5 mL of pyridine, maintained at 0°, was added 19.0 mL of phosphorus tribromide (freshly distilled) dropwise over a 1.5 hour period. The reaction was refluxed five hours, then poured onto ice/5% ammonium chloride. The layers were separated and the organic washed thrice with 5% aqueous sodium bicarbonate. The ether layer was dried (saturated brine, then magnesium sulfate) and the solvent removed by rotary evaporation. Simple distillation afforded 30.23 g (40.3% yield) of the desired halide, bp 55° (55 mm). NMR (CCl₄) δ 5.43-6.10 (m, 1H), 4.85-5.20 (m, 2H), 3.27-3.46 (t, J=6.9Hz, 2H), 1.63-2.41 (m, 4H).

1,10-Undecadien-6-ol (86)

To a mixture of 12.5 g (0.51 mole) of magnesium turnings and 250 mL of anhydrous ether, which was maintained at 0°, was dropwise added a solution of 37.59 g (0.25 mole) of 5-bromo-1-pentene (85) in 35 mL of dry ether over a four hour period. After three hours of maintenance at 0°, the reaction flask was cooled to -22° and 9.34 g (0.126 mole) of ethyl formate (dried over calcium chloride) in 15 mL of dry ether was added over a 15 minute period. After coming to RT

over a one hour period, the reaction was poured over ice/5% ammonium chloride. The aqueous layer was washed twice with ether, and the combined organic layers were washed with 5% sodium bicarbonate and dried (saturated brine, then anhydrous potassium carbonate). Solvent was removed by rotary evaporation and the resulting oil simply distilled to give 16.46 g (78% yield) of 86, bp 60-61° (0.1 mm). NMR (CCl₄) δ 5.58-6.00 (m, 2H), 4.86-5.13 (m, 4H), 3.43-3.64 (t, J=5.0 Hz, 1H), 1.94-2.24 (m, 4H), 1.85 (s, 1H), 1.31-1.70 (m, 8H).

6-Bromo-1, 10-undecadiene (87)

To a solution of 28 g (0.107 mole) of dried (in a high vacuum desiccator for three hours) triphenylphosphine and 75 mL of dried (over silica gel) acetonitrile, which was maintained at 0°, was added 5.12 mL (0.10 mole) of bromine over a 45 minute period. After an additional 45 minutes of stirring, a solution of 14.77 g (0.088 mole) of 1, 10-undecandien-6-ol in 15 mL of acetonitrile was added dropwise over a period of forty minutes. After stirring 16 hours, 3 g of sodium carbonate was added. The reaction was stirred three additional hours and the supernatant yellow solution was decanted; the precipitate was washed once with acetonitrile and the combined acetonitrile layers rotovaped to remove solvent. The resulting material was dissolved in pentane, washed (water), dried (saturated brine, then magnesium

sulfate), and simply distilled to give 12.25 g (60.3% yield) of the subject compound, bp 51° (0.1 mm). NMR (CCl_4) δ 5.55-6.00 (m, 2H), 4.86-5.18 (m, 4H), 3.82-4.08 (quintet, $J=6\text{Hz}$, 1H), 1.96-2.25 (m, 4H), 1.32-1.92 (m, 8H).

3-Chloro-1-methoxypropane (97)

Employing a procedure similar to the convenient general methylation procedure of Diner et al. (99), a solution of 30.95 g (0.328 mole) of commercial (Columbia Organic Chemicals) 3-chloro-1-propanol, 48.3 g (0.34 mole) of methyl iodide, 175 mL of THF, and 5 mL of HMPA was maintained at 0° . To this was added 15.74 g (0.328 mole) of sodium hydride (50% in mineral oil) in ten equal portions over a 1/2 hour period. The reaction was stirred 24 hours at RT, and then components boiling under 70° were removed by simple distillation (1 atm) until the volume had been reduced by 2/3. The reaction flask was cooled to 0° , and 25 mL of saturated aqueous ammonium chloride was added slowly. After addition of 75 mL of pentane, the solution was washed (water, 1% sulfuric acid, 5% sodium bicarbonate) and dried (saturated brine, then anhydrous magnesium sulfate). Simple distillation afforded 21.02 g (59% yield) of 97, bp 109° (1 atm). NMR (CCl_4) δ 3.56-3.68 (t, $J=6.0\text{ Hz}$, 2H), 3.44-3.55 (t, $J=6.0\text{ Hz}$, 2H), 3.34 (s, 3H), 1.86-2.12 (quintet, $J=6.0\text{ Hz}$, 2H); ir (neat) 2960, 1450, 1120, 1016 (cm^{-1}).

3-Iodo-1-methoxypropane (98)

A solution of 16.57 g (.153 mole) of 3-chloro-1-methoxypropane (97), 68.5 g (.456 mole) of sodium iodide, and 325 mL of reagent grade acetone was refluxed for 18 hours, then evaporated. The residue was dissolved in water and extracted with ether. The extract was washed with 0.1 N sodium thiosulfate, dried (saturated brine, then anhydrous magnesium sulfate), and simply distilled to give 24.6 g (80.2% yield) of iodoether 98, bp 51° (10 mm). NMR (CCl₄) δ 3.22-3.48 (m, 7H), 1.91-2.19 (quintet, J=6.0Hz, 2H).

3-Methoxyprop-1-yltriphenylphosphonium iodide (99)

A solution of 16.7 g (0.0835 mole) of 3-iodo-1-methoxypropane (98), 125 mL of dried (stored over molecular sieves, then remaining water azeotroped off) benzene, and 27.29 g (0.1 mole) of triphenylphosphine was refluxed 3.6 days, giving a voluminous white precipitate, which was filtered from the cold reaction solution, washed with 100 mL of benzene, and dried under 60 μ vacuum and gentle warming for three hours. The dried precipitate amounted to 37.45 g (97% yield) of 99. NMR (CDCl₃) δ 7.68-8.01 (m, 15H), 3.63-4.04 (m, 4H), 3.33 (s, 3H), 1.73-2.16 (m, 2H).

8-Chloro-1-methoxy-3-octene (primarily cis) (101)

The general procedure for the Wittig reaction was that of Findlay et al. (100). A solution of 12 mL of freshly distilled (from LAH) dimethylsulfoxide (DMSO) and 0.77 g (0.81 mole) of sodium hydride (57% in mineral oil) was stirred at 80° for 45 minutes. To the cooled (0°) solution was added 7.73 g (0.0167 mole) of 3-methoxyprop-1-yltriphenylphosphonium iodide (99) dissolved in 30 mL of DMSO. After 1/2 hour at RT, 2.0 g (0.067 mole) of 5-chloropentanal (100), which had been prepared by the procedure of Cuvigny et al. (101), was added to the deep red solution, which decolorized immediately upon the addition. The solution was heated to 80° for 18 hours, then one mL of water was added. The product was extracted with pentane, and the pentane layer dried over anhydrous magnesium sulfate. Solvent was distilled off and the resultant was vacuum transferred. The product was purified by preparative scale GLC (column B, 150°) to give 1.60 g (47.7% yield) of 101. Injection on column G (151°) shows two peaks: A, 9.7% by integration and retention time of 12 hours, is the trans isomer. B, 90.3% by integration and retention time of 12.5 hours, is the cis isomer. NMR (CCl₄) δ 5.32-5.50 (m, 2H), 3.43-3.56 (t, J=6 Hz, 2H), 3.14-3.37 (m, 5H), 1.92-2.39 (m, 4H), 1.48-1.89 (m, 4H); ir (neat) 3025, 2800, 1120 (cm⁻¹). Anal. Calcd for C₉H₁₇OCl: C, 61.17; H, 9.69. Found: C, 60.91; H, 9.51.

8-Chloro-1-methoxy-3-octene (primarily trans) (102)

The procedure employed was that of Schlosser (69). To a solution of 15 mL of dry THF, 10 mL of dry ether, and 4.47 g (0.011 mole) of 99, maintained at -78° , was added 4.36 mL (0.01 mole) of n-butyllithium (2.29 M). The solution was stirred at RT for 15 minutes and then recooled to -78° , and 1.16 g (0.098 mole) of 100 dissolved in 7 mL of ether was added dropwise. The temperature was kept below -60° for twenty minutes after which time 4.36 mL of n-butyllithium was added, restoring a deep orange color. After stirring two hours at RT, 13.02 mL (0.01 mole) of etherial hydrogen chloride (0.7683 M) was added. After twenty hours at RT, water was added and the organic layer extracted with pentane. The pentane layer was dried (saturated brine, then anhydrous magnesium sulfate), the solvent evaporated, and the remainder vacuum transferred to give 1.23 g (71.7% yield) of the subject compound which was further purified by preparative scale GLC as before (see preparation of 101, above). The product ratios were: trans, 58% and cis, 42%. The NMR was virtually identical to that of 101, as was the ir, except that this product possessed a large ir peak at 970 cm^{-1} also. Anal. Calcd for $\text{C}_9\text{H}_{17}\text{OCl}$: C, 61.17; H, 9.69. Found: C, 61.02; H, 9.59.

9-Chloro-1-methoxy-3-nonene (107)

A solution of 12.79 g (0.03 mole) of 3-methoxyprop-1-yltriphenylphosphonium iodide (99), 36 mL of ether, and 50 mL of THF was cooled to -78° , and to this was added 14 mL (0.0294 mole) of n-butyllithium (2.1 M). The reaction contents were raised to RT and stirred for one hour. The flask was cooled to 0° , and 3.8 g (0.028 mole) of 6-chlorohexanal (106), prepared by the procedure of Cuvigny *et al.* (101), was added in one portion. After two hours at RT, ten mL of saturated aqueous ammonium chloride was added. The organic products were extracted using pentane, dried (saturated brine, then anhydrous magnesium sulfate) and solvent removed. Simple distillation gave 3.28 g (61.9% yield) of the desired product (107), bp 72° (0.3 mm). NMR (CCl_4) δ 5.20-5.56 (m, 2H), 3.43-3.56 (t, $J=6.1$ Hz, 2H), 3.23-3.40 (m, 5H), 1.98-2.30 (m, 4H), 1.33-1.97 (m, 6H); mass spectrum m/e 190.113 (Calcd for $\text{C}_{10}\text{H}_{19}\text{OCl}$: 190.112). Anal. Calcd for $\text{C}_{10}\text{H}_{19}\text{OCl}$: C, 62.97; H, 10.04. Found: C, 62.71; H, 9.90.

Allyl-methyl ether (113)

A solution of 10 mL of HMPA, 3.7 mL (0.054 mole) of allyl alcohol, and 5.7 mL (0.06 mole) of dimethyl sulfate was cooled to 0° , and to it was added 3.5 g (0.081 mole) of sodium hydride (57% in

mineral oil) in ten equal portions. Gas was evolved and the reaction was brought to 90° over a two hour period. A distilling head, condenser, and ice-cooled receiver were put in place and over a two hour period, 2.06 g (53% yield) of the clear liquid (113) was collected, bp 46° (1 atm). NMR (CCl₄) δ 5.64-6.04 (m, 1H), 5.02-5.33 (m, 2H), 3.80-3.91 (d of t, J=5.2, 1.1 Hz, 2H), 3.26 (s, 3H).

6-Chloro-3-methoxy-1-hexane (114) and

6-Chloro-1-methoxy-1-hexene (115)

To a solution of 150 mL of dry THF and 5.34 g (0.074 mole) of allyl-methyl ether (113), which was maintained at -78°, was added 51.4 mL (0.075 mole) of s-butyllithium (1.46 M). After stirring for one hour, 12.6 g (0.08 mole) of 1-bromo-3-chloropropane was added over a two minute period. The reaction flask was allowed to come to RT over 1 1/2 hours, and was stirred at RT for two additional hours. The reaction was cooled to 0° and two mL of saturated aqueous ammonium chloride was added. The organic layer was washed with 5% sodium bicarbonate, dried (saturated brine, then anhydrous magnesium sulfate) and solvent removed by simple distillation. Vacuum transfer of the residue afforded 6.18 g (63% yield) of a mixture of 114 and 115 in a ratio of 16 to 84, respectively (by GLC integration). The isomers were separated by preparative scale GLC using column A at 155°. Compound 114: Retention time 3.8 minutes;

NMR (CCl_4) δ 5.49-5.86 (m, 1H), 5.08-5.30 (m, 2H), 3.42-3.62 (m, 3H), 3.22 (s, 3H), 1.50-2.04 (m, 4H); mass spectrum m/e 148.065 (Calcd for $\text{C}_7\text{H}_{13}\text{OCl}$: 148.065). Compound 115: Retention time 5.8 minutes; NMR (CCl_4) δ 5.78-6.34 (m, 1H), 4.14-4.76 (m, 1H), 3.55 (s, 1H), 3.42-3.49 (t, $J=3.3$ Hz, 2H), 1.37-2.21 (m, 6H).

cis-2-Methoxymethylcyclopentane (116)

The standard procedure for conversion of alcohols into ethers (see 3-chloro-1-methoxypropane (97)) was used to prepare the subject compound from 20 mL of dried (distilled from LAH) glyme, 3.0 mL (0.033 mole) of dimethyl sulfate, 1.75 g (0.0175 mole) of commercial (Chemical Samples Company) cis-2-methylcyclopentanol, and 0.80 g (0.019 mole) of sodium hydride (57% in mineral oil). The product was obtained by preparative scale GLC (column F, 178°). NMR (CCl_4) δ 3.39-3.56 (m, 1H), 3.22 (s, 3H), 1.21-1.99 (m, 7H), 0.91-0.98 (d, $J=6.3$, 3H).

trans-2-Methoxymethylcyclopentane (117)

Using the standard procedure for conversion of alcohols into ethers (see 3-chloro-1-methoxypropane (97)), the subject ether was prepared from 2.0 g (0.02 mole) of trans-2-methylcyclopentanol (Aldrich Chemical Company), 3.6 mL (0.04 mole) of dimethyl sulfate,

30 mL of dry glyme, and 0.90 g (0.021 mole) of sodium hydride.

The product was isolated by preparative scale GLC (column F, 180°).

NMR (CCl_4) δ 3.12-3.38 (m, 4H), 1.41-2.00 (m, 7H), 0.93-1.00 (d, $J=6.3$ Hz, 3H).

7- Chloro-3-methoxy-4-methyl-1-hepten-4-ol (121)

Following the procedure of Evans et al. (75), a solution of 150 mL of dry THF and 50 mL (50 mmole) of *s*-butyllithium (1.0 M) was maintained at -78° and to this was added 3.6 g (50 mmole) of allylmethyl ether. The reaction mixture was brought to -45° and stirred at that temperature for 45 minutes. To this was dropwise added a solution of 6.8 g (50 mmole) of anhydrous zinc chloride and 29 mL of dry THF. To the reaction was added a solution of 6.2 g (51.4 mmole) 5-chloro-2-pentanone (Aldrich Chemical Company) and 10 mL of THF over one minute's duration. The temperature was raised to -15° and after ten minutes, quenched with three mL of saturated aqueous ammonium chloride. Solids were removed by filtration, the solvent evaporated, and the residue dissolved in ether. The etherial solution was washed with water, dried (saturated brine, then anhydrous sodium sulfate), and the solvent evaporated. The subject compound was simply distilled, affording 6.06 g (63% yield) of 121, bp 74° (0.3 mm). NMR (CCl_4) δ 5.51-5.91 (m, 1H), 5.15-5.45 (m, 2H), 3.47-3.64 (t, $J=6.0$ Hz, 2H), 3.27-3.40 (m, 4H),

2.26 (s, 1H, position temperature variant), 1.41-2.04 (m, 4H), 1.06-1.09 (d, $J=2.6$ Hz, 3H); ir (neat) 3575, 3000, 1640, 1087, 935 (cm^{-1}). Anal. Calcd for $\text{C}_9\text{H}_{17}\text{O}_2\text{Cl}$: C, 56.10; H, 8.89. Found: C, 56.25; H, 8.78.

2-(3-Chloro-1-propyl)-2-methyl-3-butenal (122)

A solution of 2.5 g (0.054 mole) of freshly distilled formic acid (97%-99%) and 1.91 g (0.01 mole) of 7-chloro-3-methoxy-4-methyl-1-hepten-4-ol (121) was refluxed one hour according to the procedure of Evans et al. (75). The resulting brown mixture was extracted with ether, washed with saturated potassium carbonate and dried (saturated brine, then sodium sulfate). Solvent was removed and the resultant vacuum transferred to give 0.77 g (48% yield) of the desired aldehyde. NMR (CCl_4) δ 9.31 (s, 1H), 5.67-5.94 (d of d, $J=10.5$, 17 Hz, 1H), 5.24-5.36 (d of d, $J=1.0$, 10.5 Hz, 1H), 5.05-5.24 (d of d, $J=1.0$, 17 Hz, 1H), 3.45-3.60 (m, 2H), 1.71-1.80 (m, 4H), 1.19 (s, 3H); ir (neat) 2760, 1735, 1640 (cm^{-1}). Anal. Calcd for $\text{C}_8\text{H}_{13}\text{ClO}$: C, 59.81; H, 8.16. Found: C, 59.80; H, 8.08.

2-(3-Chloro-1-propyl)-2-methyl-3-butenal ethylene acetal (123)

A solution of 1.3 g (8.1 mmole) of aldehyde 122, 2.51 g (40 mmole) of ethylene glycol, 40 mL of benzene and 0.04 g of p-tolyl-sulfonic acid was refluxed using a Dean-Stark trap for one day,

according to the procedure of Davol (102). The cooled solution was washed (5% aqueous sodium bicarbonate, then water), and dried (saturated brine, then anhydrous sodium sulfate). Solvents were evaporated and the remaining oil subjected to simple distillation, giving 1.26 g (76% yield) of the title acetal (123), bp 61° (0.5 mm). NMR (CCl_4) δ 5.67-5.95 (d of d, $J=10.5$, 17 Hz, 1H), 5.06-5.19 (d of d, $J=1.8$, 10.5 Hz, 1H), 4.97-5.14 (d of d, $J=1.8$, 17 Hz, 1H), 4.54 (s, 1H), 3.76-3.95 (m, 4H), 3.43-3.55 (t, $J=6.0$ Hz, 2H), 1.43-2.00 (m, 4H), 1.03 (s, 3H). Anal. Calcd for $\text{C}_{10}\text{H}_{17}\text{O}_2\text{Cl}$: C, 58.67; H, 8.37. Found: C, 58.67; H, 8.27.

General Method for Cyclization of Alkenyl Halides with Lithium Dispersion (containing 2% sodium in mineral oil)

All cyclizations were done under a nitrogen atmosphere. An excess of lithium dispersion was washed with anhydrous ether. Anhydrous ether solvent was added, followed by the addition of ten drops of 1, 3-dibromo-propane to activate the metal. The reaction was stirred one hour and was then cooled to 0°. When n-butyllithium was to be added it was added at this point. The alkenyl halide was then added in one portion and the reaction was allowed to come to RT and stir for the indicated time. For quenching, the contents of the flask were cooled to -22° (using a Dry Ice/tetrachloroethylene bath) and the liquid contents were removed by pipet and squirted onto ice/ammonium

chloride. The ether layer was vacuum transferred and, where appropriate, a hydrocarbon internal standard was added. GLC analysis was as indicated for each cyclization.

Cyclization of 6-Bromo-1,10-undecadiene (87) (formation of lithium reagent by dianion method (67))

To a stirred solution of 200 mL of dry THF and 10.60 g (40 mmole) of freshly sublimed p, p'-di-t-butylbiphenyl was added 0.21 g (30 mmole) of lithium metal cut into small pieces. After five hours at RT, the reaction mixture was cooled to -78°, and 1.03 g (4.46 mmole) of 87 dissolved in 5 mL of THF was added over a five minute period. The reaction mixture was allowed to stand overnight. The reaction was quenched by cautious addition of water; 0.634 g (4.46 mmole) of n-decane was added as internal standard. The bulk of the product (46% yield based on n-decane) was composed of three components which were isolated together by preparative scale GLC (column F, 151°), and showed an NMR vinyl region typical of a mixture of terminal and 1,2-disubstituted double bonds. This mixture was hydrogenated catalytically (Palladium on charcoal) to give a single product, isolated by preparative scale GLC (column F, 162°), and consistent with the trans-2-methyl-1-pentylcyclopentane structure (93). NMR (CCl₄) δ 1.07-2.00 (m, 16H), 0.78-1.05 (m, 6H).

Cyclization of 8-Chloro-1-methoxy-3-octene (101)

The general cyclization procedure was employed using 0.54 g of lithium dispersion, 30 mL of ether solvent, and 0.36 g (2.0 mmole) of the title compound (101). The reaction time was 18 hours. As internal standard, 0.262 g (2.0 mmole) of n-decane was added to the solution after vacuum transfer. Two product peaks were isolated by preparative scale GLC (column H, 104°). The linear reduced product (103), 18.6% yield, based on n-nonane, had a retention time of 6.5 minutes. NMR (CCl_4) δ 5.15-5.57 (m, 2H), 3.19-3.40 (m, 5H), 1.89-2.40 (m, 4H), 1.20-1.47 (m, 4H), 0.87-1.00 (5, J=6.5 Hz, 3H). The second product was identified as the cyclic isomer, 104, produced in 37.9% yield, based on n-nonane, and possessing a retention time of 8.0 minutes. NMR (CCl_4) δ 3.18-3.37 (m, 5H), 0.96-1.94 (m, 13H). Anal. Calcd for $\text{C}_9\text{H}_{18}\text{O}$: C, 75.99; H, 12.76. Found: C, 75.87; H, 12.78.

The reaction was repeated just as above except for addition of one equivalent of n-butyllithium (2.29 M in hexane) just prior to addition of 101 (see general cyclization procedure). Only one product was obtained in 41% yield based on n-nonane, and was isolated by preparative scale GLC (column A, 141°, retention time was 4.0 minutes). The product possessed an NMR spectrum identical to that of 104.

Attempted Cyclization of 8-Chloro-1-methoxy-3-octene
(101) (using magnesium)

To a mixture of 2.0 g (0.082 g atom) of magnesium turnings and 25 mL of anhydrous ether was added 0.1 g of 1,3-dibromopropane. The reaction was stirred one hour and 0.4 g (2.3 mmole) of 101 was added in one portion. The reaction was stirred eight days at RT and quenched by dropwise addition of saturated aqueous ammonium chloride. After drying (saturated brine, then anhydrous magnesium sulfate), the ether layer was vacuum transferred and solvent evaporated. A single product isolated by preparative scale GLC (column D, 120°, retention time was 2.0 minutes), and it possessed an NMR spectrum identical to that of linear reduced 103.

The reaction was repeated using the Reike method (71b) of Grignard formation. To a solution of 50 mL of THF and 0.216 g (2.27 mmole) of anhydrous magnesium chloride was added 0.0615 g (1.57 mg atom) of metallic potassium cut into small pieces. The reaction mixture was refluxed one day resulting in a black suspension of "supermagnesium." The reaction mixture was cooled to 0° and 0.25 g (1.4 mmole) of 101 was added in one portion. After refluxing two days GLC analysis (column D, 113°) showed starting material 101 remained and that there was no product formation. The reaction was terminated.

Cyclization of 9-Chloro-1-methoxy-3-nonene (107)

The general cyclization procedure was employed using 0.57 g of lithium dispersion, 20 mL of ether solvent, and 0.44 g (2.3 mmole) of the title compound (107). The reaction was refluxed for two days. Two product peaks were isolated by preparative scale GLC (column D, 126°). The linear reduced product (108) had a retention time of 2.4 minutes, and accounted for 80% of the reaction products (by GLC peak integration). NMR (CCl_4) δ 5.35-5.52 (m, 2H), 3.24-3.43 (m, 5H), 1.96-2.35 (m, 4H), 1.23-1.50 (m, 6H), 0.88-1.01 (t, $J=6.1$ Hz, 3H). Anal. Calcd for $\text{C}_{10}\text{H}_{20}\text{O}$: C, 76.86; H, 12.90. Found: C, 77.06; H, 12.93. The cyclic product (109) amounted to 20% of the reaction products and had a retention time of 2.8 minutes. NMR (CCl_4) δ 3.20-3.41 (m, 5H), 1.09-1.88 (m, 15H); mass spectrum m/e 156.151 (Calcd for $\text{C}_{10}\text{H}_{20}$: 156.151). Anal. calcd for $\text{C}_{10}\text{H}_{20}\text{O}$: C, 76.86; H, 12.90. Found: C, 75.50; H, 12.51.

The reaction was repeated as above except that one equivalent of n-butyllithium was added just prior to the addition of the halide 107, and one equivalent of undecane was added as internal standard. GLC analysis showed one product (109), the cyclic isomer, afforded in 16% yield based on undecane. The product was isolated by preparative scale GLC (Column D, 125°, retention time 2.4 minutes), and possessed an NMR spectrum identical to that of the second product of the previous cyclization (109).

Cyclization of 6-Chloro-3-methoxy-1-hexene (114)

The general cyclization procedure described on page 79 above was followed using 0.55 g of lithium dispersion, 25 mL of ether solvent, and 0.26 g (1.7 mmole) of the title compound (114). The reaction time was 3.5 hours and 0.194 g (1.7 mmole) of n-octane was added as internal standard. Analysis by GLC (Column F, 160°, retention time was 11.4 minutes) showed one product peak, of 34% yield by peak integration, relative to n-octane. Isolation of the product by preparative scale GLC afforded material having an NMR spectrum identical to that of a 50/50 mixture of 116 and 117 independently synthesized above.

The reaction was repeated as above but one equivalent of n-butyllithium was added prior to the addition of the title compound (114). GLC analysis and preparative scale isolation (Column F, 141°, 14.6 minutes) established that the single product formed (116), obtained in 40% yield relative to n-octane, was identical in retention time (coinjection gave one peak) and NMR spectrum to the cis ether (116), independently prepared above.

Attempted Cyclization of 6-Chloro-1-methoxy-1-hexene (115)

Following the general procedure for lithium cyclization, 0.13 g (0.88 mmole) of the subject compound was subjected to cyclization

conditions using 0.50 g of lithium dispersion, 20 mL of dry ether, and 0.125 g (0.88 mmole) of n-decane as internal standard. The reaction time was three hours. GLC analysis showed one major product (column A, 180°, retention time 3.2 minutes), of 53.5% yield, based on n-decane. The product (118) is a mixture of cis and trans linear enol ethers (118). NMR (CCl₄) δ 6.14-6.33 and 5.73-5.89 (two m, 1H), 4.14-4.76 (m, 1H), 3.48 and 3.56 (two s, 3H), 1.81-2.46 (m, 2H), 1.21-1.52 (m, 2H), 0.86-0.99 (two t, J=6.1 Hz, 3H).

Cyclization of 2-(3-Chloro-1-propyl)-2-methyl-3-butenal ethylene acetal (123)

Employing the general cyclization procedure, 0.32 g (1.56 mmole) of the title compound was cyclized using 0.53 g of lithium dispersion, and 25 mL of ether as solvent. One product peak was observed by GLC analysis (column D, 140°, retention time: 4.1 minutes), and isolated by preparative scale GLC. The single peak contained two cyclic products, 126 and 127, in a ratio of 40% 126 to 60% 127 (as determined by NMR peak integrations). The NMR spectra of 126 and 127 are included in the following experimental entries.

The above procedure was repeated, also using 1.6 equivalents of n-butyllithium and one equivalent of undecane as internal standard; reaction time was 1.5 hour. Analysis and product isolation by GLC (column C, 126°, retention time: 15.0 minutes) showed one isomer,

afforded in 33% yield, and assigned structure 127, of the trans-dimethyl stereochemistry. NMR (CCl_4) δ 4.58 (s, 1H), 3.66-3.99 (m, 4H), 1.14-1.95 (m, 7H), 0.86-1.00 (m, 6H). Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_2$: C, 70.54; H, 10.66. Found: C, 70.38; H, 10.50.

The above procedure was repeated, again using one equivalent of undecane as internal standard and 1.6 equivalents of n-butyllithium. The reaction time was 2 hours. Immediately following the addition of the title compound (123), 2.7 equivalents of TMEDA were added to the reaction mixture. An additional wash with buffered solution (pH 4.0) was employed in the work-up to remove TMEDA. GLC analysis (column C, 120° , 15.0 minutes retention time) showed a single product, afforded in 44% yield, based on undecane. Isolated by preparative scale GLC, the product was assigned the cis-dimethyl stereochemistry (126). NMR (CCl_4) δ 4.50 (s, 1H), 3.66-3.99 (m, 4H), 1.09-2.00 (m, 7H), 0.87-0.93 (d, $J=6.0$ Hz, 3H), 0.78 (s, 3H).

The general procedure was repeated as a control experiment, without lithium metal present; 2.5 equivalents of n-butyllithium were employed, and the retention time was two hours. GLC analysis and preparative scale isolation (column C, 120°) showed that 126 and 127 were not present and that the only observed material possessed a retention time and NMR spectrum identical to that of the starting material (123).

3-Methoxy-1, 5-hexadiene (138)

The standard procedure for conversion of an alcohol into an ether (see 3-chloro-1-methoxypropane (97)) was employed to prepare 9.82 g (57% yield) of 3-methoxy-1, 5-hexadiene (138) from 15.05 g (0.153 mole) of 1, 5-hexadien-3-ol (available from Aldrich Chemical Company), 150 mL of THF, 10.0 mL of HMPA, 17.5 mL (0.184 mole) of dimethyl sulfate, and 8.56 g (0.178 mole) of sodium hydride (50% in mineral oil). The product was obtained by simple distillation, bp 106° (1 atm). NMR (CCl_4) δ 5.46-6.00 (m, 2H), 4.91-5.30 (m, 4H), 3.45-3.62 (m, 1H), 3.21 (s, 3H), 2.00-2.41 (m, 2H).

6-Chloro-1, 4-hexadiene (144)

To a solution of 12.2 mL (0.17 mole) of thionyl chloride and 125 mL of dry ether was added a solution of 15.96 g (0.16 mole) of 1, 5-hexadien-3-ol (137) and 90 mL of ether over a 1.5 hour period. The reaction was stirred 18 hours and then subjected to rotary evaporation to remove solvent and hydrogen chloride. The solution, still strongly acidic, was washed with 1% aqueous sodium carbonate until the washes were blue to litmus. The organic layer was dried (saturated brine, then anhydrous sodium sulfate), and simply distilled, affording 17.06 g (91% yield) of the title compound, bp 74° (100 mm). NMR (CCl_4) δ 5.45-6.01 (m, 3H), 4.92-5.22 (m, 2H), 3.97-4.03

(d, $J=5.9$ Hz, 2H), 2.72-2.93 (m, 2H).

3-Methoxymethyl-1, 5-hexadiene (145)

A mixture of 3.0 g (0.125 g atom) of magnesium turnings, 16 mL of dry ether, and 0.1 g of 1,3-dibromopropane were stirred 30 minutes at RT. The mixture was cooled to 0°, and a solution of 5.0 g (0.043 mole) of 6-chloro-1,4-hexadiene (144) and 16 mL of dry ether was dropwise added over a two hour period. After completion of addition, the Grignard solution was stirred at 0° for two hours and then allowed to come to RT and stir overnight. To the Grignard reagent, recooled to 0°, was added dropwise a solution of 3.3 mL (0.0435 mole) of chloromethylmethyl ether and five mL of ether. After completion of addition, the reaction was stirred three hours, and then quenched by pouring onto ice-ammonium chloride. After separation of layers, the aqueous layer was washed with ether, and the combined ether layers were washed with 5% aqueous sodium bicarbonate and dried (saturated brine, then magnesium sulfate). Solvent was removed by rotary evaporation and the resultant simply distilled, providing 1.95 g (36% yield) of compound 145, bp 80° (98 mm). NMR (CCl_4) δ 5.50-5.95 (m, 2H), 4.88-5.25 (m, 4H), 3.22-3.41 (m, 5H), 2.03-2.49 (m, 3H).

Competitive Reduction of 1-Octene vs. n-Butyl allyl ether (148) with DIBAL

A mixture of 0.60 g (5.25 mmole) of ether 148, prepared by the method of Wantanabe, Conlon, and Hwa (103), and 0.59 g (5.25 mmole) of 1-octene in three mL of hexane was reduced by 1.86 g (2.63 mmole) of DIBAL (20% by weight in hexane). The reaction was refluxed for 17 hours, and then cooled to -22°. The reaction was quenched by cautious addition of water to the reduction solution. The copious aluminum salts were removed from the hexane layer by centrifuging, and the organic layer was vacuum transferred. The resulting mixture was subjected to GLC analysis (column E, 80°). From relative peak areas, the ratio of octane to reduced ether was found to be 3.7 to 1.0.

Competitive Reduction of 1-Octene vs. 5-Ethoxy-1-pentene (149) with DIBAL

A mixture of 0.58 g (5.08 mmole), prepared by the method of Zakharkin and Savina (53b), of ether 149 and 0.57 g (5.08 mmole) of 1-octene in three mL of hexane was reduced by 1.80 g (2.53 mmole) of DIBAL (20% by weight in hexane). The reaction conditions, work-up, and analysis were as in the previous experimental entry. From the relative peak areas, it was found that the ratio of octane to reduced ether was 1.0 to 1.0.

Competitive Reduction of 1-Octene vs. Allyltrimethylsilane (151) with Diethylaluminum Hydride

A mixture of 0.731 g (6.4 mmole) of allyltrimethylsilane (151), obtained from Aldrich Chemical Company, and 0.718 g (6.4 mmole) of 1-octene in two mL of hexane was subjected to reduction by 5.0 mL (6.4 mmole) of diethylaluminum hydride for 15 hours at 45°. The quench, work-up, and analysis were as in the previous experimental entry. The relative peak areas indicated that the ratio of reduced silane to octane was 0.71 to 1.0.

1-Chloro-1,5-hexadiene (152)

Allyl magnesium chloride was prepared by the method of Kharasch and Fuchs (98) from 38.3 g (0.5 mole) of allyl chloride, 240 mL of anhydrous ether, and 13.3 g (0.547 g atom) of magnesium turnings. The Grignard reagent solution was cooled to 0°, and a solution of 66.6 g (0.6 mole) of 1,3-dichloropropene and 50 mL of dry ether was added dropwise over two hours. The reaction was allowed to come to RT gradually over one hour and was stirred for two days. The reaction mixture was quenched by pouring onto ice/ammonium chloride. Layers were separated, with the aqueous layer extracted with pentane. The combined organic layers were dried (saturated brine, then anhydrous magnesium sulfate) and

solvent removed. Distillation through a six inch Vigreux column provided the vinyl chloride product (152), bp 117-119° (1 atm). NMR (CCl_4) δ 5.65-6.56 (m, 3H), 5.00-5.32 (m, 2H), 2.20-2.66 (m, 4H).

1-Hexen-5-yne (153)

In a method similar to that of Sondheimer et al. (104), a solution of 12.5 g (0.1 mole) of 1-chloro-1,5-hexadiene (152) and 40 mL of ether was added over a two hour period to sodamide in refluxing ammonia (prepared from 14.1 g (0.61 g atom) of metallic sodium in 0.3 L of ammonia (105)). After completion of addition, the reaction vessel was allowed to boil off ammonia over a 1.5 day period. The reaction mixture was cooled to 0° and 100 mL of pentane was added followed by the dropwise addition of 90 mL of saturated aqueous ammonium chloride. The layers were separated, and the aqueous washed twice with pentane. The combined organic layers were washed (2% sulfuric acid, then 5% aqueous sodium bicarbonate) and dried (saturated brine, then anhydrous magnesium sulfate). Solvent was removed by distillation through an 18 inch glass helix-filled column, and the resulting material was purified by preparative scale GLC (column C, 71°). NMR (CCl_4) δ 5.64-6.05 (m, 1H), 4.93-5.20 (m, 2H), 2.20-2.43 (m, 4H), 1.76-1.84 (5, J=2 Hz, 1H).

1-Chloro-4-methyl-1,5-hexadiene (158)

Using the procedure set forth for 1-chloro-1,5-hexadiene (152), the title compound was prepared using 90.55 g (1.0 mole) of commercial crotyl chloride in 160 mL of ether, 43.2 g (1.8 g atom) of magnesium turnings in 350 mL of ether, and 82.0 mL (0.9 mole) of 1,3-dichloropropene in 100 mL of ether. The title compound was afforded by distillation, 79.9 g (68% yield) of 158, bp 83-90° (110 mm), being obtained. NMR (CCl₄) δ 5.52-6.12 (m, 3H), 4.86-5.11 (m, 2H), 1.97-2.39 (m, 3H), 0.98-1.80 (m, 3H).

3-Methyl-1-hexen-5-yne (159)

The standard method for conversion of a vinyl chloride into an alkyne (see 1-hexen-5-yne (153)) was employed to prepare 18.3 g (63.5% yield) of the subject compound, using 40.0 g (0.306 mole) of 1-chloro-4-methyl-1,5-hexadiene (158). 100 mL of dry ether, 31.0 g (1.35 g atom) of sodium metal, and about one L of liquid ammonia. After removal of the bulk of solvent by simple distillation, the product was distilled using a spinning band column, providing 159, bp 87° (1 atm). NMR (CCl₄) δ 5.56-6.02 (m, 1H), 4.90-5.21 (m, 2H), 2.10-2.56 (m, 3H), 1.82-1.87 (t, J=2.3 Hz, 1H), 1.08-1.14 (d, J=6 Hz, 3H); mass spectrum m/e 94.075 (Calcd for C₇H₁₀: 94.078).

Allyl 4-pentynyl ether (164)

Following the standard procedure for conversion of an alcohol into an ether (see 3-chloro-1-methoxypropane (97)) 13.22 g (0.157 mole) of 4-pentyn-1-ol (163), prepared by the method of Jones *et al.* (85), was converted into 12.65 g (64.9% yield) of the title ether by use of 7.95 g (0.17 mole) of sodium hydride (50% in mineral oil), 110 mL of THF, and 24.2 g (0.2 mole) of allyl bromide. The prescribed work-up afforded the product (164), bp 58° (20 mm). NMR (CCl₄) δ 5.66-6.08 (m, 1H), 5.03-5.38 (m, 2H), 3.89-3.97 (d of t, J=1.3), 5.7 Hz, 2H), 3.42-3.64 (t, J=6.0 Hz, 2H), 2.19-2.36 (t of d, J=2.8, 7.0 Hz, 2H), 1.61-1.94 (m, 3H).

4-Pentynal (165) from Pyrolysis of 164

Under the slow flow of nitrogen, 7.3 g (0.059 mole) of neat ether 164 was passed through a vertical preheating column (200°) into an 18 inch vertical, glass bead-filled column (460°). After collection in a Dry Ice/acetone-cooled trap, the crude product was simply distilled using a Hickman (short path) apparatus, and affording 2.86 g (59% yield) of 4-pentynal (165), bp 67° (45 mm) (literature value: 70° @ 50 mm (106)). NMR (CCl₄) δ 9.75 (s, 1H), 2.36-2.81 (m, 4H), 1.88-1.94 (t, J=2.3 Hz, 1H); ir (neat) 2787, 2135, 1730 (cm⁻¹).

4-Pentynal (165) from Oxidation of 163

Employing the improved general procedure of Ratcliffe and Rodehorst (86) for the Collins Oxidation (107) of alcohols to aldehydes, 0.79 g (32% yield) of the title compound was prepared from the addition of 2.5 g (0.03 mole) of 4-pentyn-1-ol (163) to a solution of 28.9 mL (0.36 mole) of pyridine, 400 mL of dry methylene chloride, and 18 g (0.18 mole) of chromium trioxide. The reaction was stirred for 15 minutes after addition of the alcohol, and the supernatant solution was decanted from the tarry, black deposit that formed during the reaction. The solution was filtered through celite, and washed thrice with 5% aqueous sodium hydroxide, once with 5% hydrochloric acid, and once with 5% sodium bicarbonate. After drying (saturated brine, then anhydrous magnesium sulfate), the methylene chloride was removed by distillation through an 18-inch glass helix-filled column. The resulting oil was simply distilled to give 165, bp 65° (42 mm). The NMR spectrum was identical to that of the compound prepared in the previous experimental section.

5-Hepten-1-yne (166)

Using the standard Wittig procedure (see 9-chloro-1-methoxy-3-nonene (107)), the title compound was prepared (108) from 7.5 g (20 mole) of a commercial sample (Aldrich Chemical Company) of

ethyltriphenylphosphonium bromide in 22 mL of ether, and 50 mL of THF, to which was added 9.1 mL (20 mmole) of n-butyllithium followed by 1.19 g (14 mmole) of 4-pentynal (165). The reaction time was 1.5 hours at RT. After work-up and drying as before, the product was isolated by preparative scale GLC (Column C, 70°). NMR (CCl₄) δ 5.56-5.69 (m, 2H), 2.14-2.43 (m, 4H), 1.74-1.85 (t, J=2.0 Hz, 1H), 1.60-1.71 (d, J=5.0 Hz, 3H).

4-Vinyl-7-octen-1-yne (170)

Using the standard procedure for elimination of hydrogen chloride from vinyl chlorides (see 1-hexen-5-yne (153)), 170 was prepared from 3.44 g (0.02 mole) of 1-chloro-4-vinyl-1,7-octadiene (169), prepared by P. W. Chum (109), 2.56 g (0.11 g atom) of sodium, and 150 mL of liquid ammonia. After work-up, 1.68 g (62.6% yield) of the desired product was further purified by preparative scale GLC using column D at 130°. NMR (CCl₄) δ 5.50-5.99 (m, 2H), 4.81-5.15 (m, 4H), 1.92-3.37 (m, 5H), 1.80-1.86 (t, J=2.1 Hz, 1H), 1.21-1.71 (m, 2H); mass spectrum m/e 134.109 (Calcd for C₁₀H₁₄: 134.110); m/e 133.101 (Calcd for C₁₀H₁₃: 133.102).

3-Methoxy-1-hexen-5-yne (177)

The standard method for conversion of an alcohol into an ether

(see 3-chloro-1-methoxypropane (97)) was employed to convert 3.0 g (0.025 mole) of 1-hexen-5-yne-3-ol (176), prepared by the method of Viola and MacMillan (91), into the title compound. The reaction employed 40 mL of dry glyme, 1.87 mL (0.02 mole) of dimethyl sulfate, and 1.18 g (0.025 mole) of sodium hydride. The reaction time was 20 hours at 50°. Evaporation of solvent afforded 2.9 g of crude 177 which was simply distilled to give 2.45 g (69% yield) of the desired ether (177), bp 110-112° (1 atm). NMR (CCl₄) δ 5.67-5.93 (m, 1H), 5.15-5.38 (m, 2H), 3.52-3.76 (m, 1H), 3.28 (s, 3H), 2.10-2.61 (m, 2H), 1.79-1.85 (t, J=3 Hz, 1H); ir (neat) 3405, 3200, 2160, 1430, 1100, 995, 928 (cm⁻¹).

3-Methoxymethyl-1-hexen-5-yne (187) and
4-Methoxymethyl-1,2,5 hexatriene (188)

The standard procedure for conversion of an alcohol to an ether (see 3-chloro-1-methoxypropane (97)) was employed to convert a mixture of alcohols 185 and 186, prepared by the method of Cortois et al. (94) from alcohol 184 (93), into 6.9 g (86% yield) of a mixture of 187 and 188. In the reaction, 60 mL of THF, 14.19 g (0.1 mole) of methyl iodide, 3.8 g (0.079 mole), and 8.4 g (0.076 mole) of 185 and 186 were used. The reaction time was 24 hours at RT. The products were isolated by preparative scale GLC (column B, 130°). NMR (CCl₄) δ 187: 5.60-5.98 (m, 1H), 4.98-5.23 (m, 2H), 3.34-3.40

(d, $J=5.0$ Hz, 2H), 3.31 (s, 3H), 2.24-2.57 (m, 3H), 1.79-1.85 (t, $J=2.5$ Hz, 1H); mass spectrum m/e 124.086 (Calcd for $C_8H_{12}O$: 124.089); m/e 123.081 (Calcd for $C_8H_{11}O$: 123.081). 188: 5.60-5.96 (m, 1H), 4.97-5.22 (m, 3H), 4.61-4.76 (m, 2H), 2.26-2.40 (m, 5H), 2.83-3.08 (m, 1H).

2-Methoxymethylmethylenecyclopentane (189)

To 10 mL (24 mmole) of *n*-butyllithium (2.4 M) was added 3.6 mL (24 mmole) of TMEDA. A solid precipitate formed, and was dissolved by gentle warming and agitation. To this solution was added 1.93 g (23.5 mmole) of 1-methylcyclopentene (155), prepared by the method of Traynelis et al. (110) from 1-methylcyclopentanol. The solution was allowed to sit at RT for 36 hours, and then was added dropwise via syringe to a solution (maintained at -78°) of 1.82 mL (24 mmole) of chloromethylmethyl ether and 45 mL of THF. The reaction contents were warmed to RT over a one hour period, and most of the hexane/THF solvent was then taken off by simple distillation. The salts were dissolved in water, and the residue was extracted with pentane. The pentane extract was washed thrice with 2% sulfuric acid and once with 5% aqueous sodium bicarbonate. After drying (saturated brine, then anhydrous magnesium sulfate), the pentane layer was evaporated and the residue simply distilled to give 1.16 g (39% yield) of a mixture of 189 and 192, bp $133-135^\circ$ (1 atm).

GLC analysis and preparative scale isolation (column E, 158°) show two products. The first product was 189, 68.3% of the reaction products, as determined by GLC peak areas, and had a retention time of 13.8 minutes. NMR (CCl_4) δ 4.74-4.94 (m, 2H), 3.06-3.46 (m, 5H), 2.49-2.74 (m, 1H), 2.12-2.40 (m, 2H), 1.44-1.99 (m, 4H). The other product, 192, which amounted to 31.7% of the reaction products, as determined by GLC peak integration, had a retention time of 18.6 minutes. NMR (CCl_4) δ 5.27-5.40 (m, 1H), 3.33-3.47 (t, $J=6.8$ Hz, 2H), 3.26 (s, 3H), 2.12-2.45 (m, 6H), 1.80-2.01 (m, 2H).

cis-2-Methoxymethyl-1-methylcyclopentane (129) (111)

To a suspension of 0.042 g of palladium on charcoal in 5 mL of absolute ethanol, under a hydrogen atmosphere at atmospheric pressure, was added 0.22 g (1.75 mmole) of 2-methoxymethylmethylenecyclopentane (189). After 14 hours of stirring at RT, the catalyst was removed by filtration and 0.25 g (1.75 mmole) of n-decane was added. The resulting solution was subjected to GLC analysis and preparative scale isolation (column C, 97°), and two products were observed. The first product, 129, 49% yield based on the internal standard, had a retention time of 11.8 minutes. NMR (CCl_4) δ 3.06-3.66 (m, 5H), 1.30-1.97 (m, 8H), 0.96-1.02 (d, $J=5.9$ Hz, 3H). The second product, 7% yield based on n-decane, was not isolated, but

had a retention time (12.5 minutes) identical with that of 128, prepared below.

trans-2-Methoxymethyl-1-methylcyclopentane (128)

To a solution, maintained at 0°, of 0.31 g (2.46 mmole) of 2-methoxymethylmethylenecyclopentane (189) and 1.25 mL of THF was added 0.9 mL (0.9 mmole) of borane-THF complex (1.0 M in THF). The solution was stirred at RT for 20 minutes and then was heated to reflux for ten hours. After recooling to 0°, 0.28 g (3.7 mmole) of propanoic acid was added to the reaction and the flask contents were refluxed overnight. After again cooling to 0°, 2.25 mL (6.75 mmole) of 3M aqueous sodium hydroxide was added. Organic material was extracted with three mL of pentane, and the pentane layer was dried with saturated brine washing followed by anhydrous sodium sulfate. To the dried solution was added 0.35 g (2.46 mmole) of n-decane as internal standard. GLC analysis indicated the presence of two products. The first product, having a retention time identical to that of 129, prepared and identified above, was not isolated and amounted to less than 3% yield based on n-decane. The second product, which had a retention time of 11.4 minutes (column C), amounted to 59% yield based on n-decane, and was assigned structure 128. NMR (CCl₄) δ 3.03-3.41 (m, 5H), 1.92-2.30 (m, 1H), 1.10-1.82 (m, 7H), 0.80-0.86 (d, J=5.8 Hz, 3H).

General Method for Cyclization of Alkadienes and Alkynes with Dialkylaluminum Hydrides

All cyclizations were done under a nitrogen atmosphere. To a solution, maintained at 0°, of the cyclization substrate and solvents, as prescribed, was added the dialkylaluminum hydride. The solution was stirred at 0° for thirty minutes after which time it was allowed to stir as prescribed in each case. When *n*-butyllithium was to be included, it was added to the reaction mixture, recooled to 0°, two hours after the addition of the dialkylaluminum hydride. When aluminum chloride was to be included, it was first subjected for four hours to 0.1 mm vacuum dessication, and then added to the reaction mixture, recooled to 0°, in one portion twelve hours after addition of the aluminum hydride reagent. Reactions were quenched by the cautious addition of saturated aqueous ammonium chloride to the reaction solution, maintained at -22° by use of a Dry Ice/tetrachloroethylene bath. Voluminous aluminum salts were removed by centrifuging and the organic layer was vacuum transferred. Where appropriate, a hydrocarbon internal standard was added. GLC analysis was as indicated in each case.

Attempted Cyclization of 3-Methoxy-1, 5-hexadiene (138)

The general cyclization procedure was employed using 0.59 g (5.26 mmole) of 3-methoxy-1, 5-hexadiene (138), three mL of hexane,

and 3.75 g (5.27 mmole) of DIBAL. The reaction was refluxed 19 hours. The single product (139) peak was collected by preparative scale GLC (column E, 150°, retention time of 9.1 minutes). NMR (CCl_4) δ 5.45-5.83 (m, 1H), 5.01-5.25 (m, 2H), 3.25-3.73 (m, 1H), 3.21 (s, 3H), 1.24-1.65 (m, 4H), 0.82-1.06 (m, 3H).

The reaction, executed as above, but with deuterium oxide quench, gave a single product (139-d), 100% monodeuterated according to low voltage mass spectroscopy. The product possessed an NMR spectrum identical with the above except that the upfield multiplet was at δ = 0.78-1.02 and integrated to two protons.

The reaction was repeated as above, with the addition of one equivalent of anhydrous aluminum chloride twelve hours after addition of the hydride. Three products (139, 140, and 141) were isolated by GLC (column C, 62°). Compound 139 was identical to the product of the first reaction above in GLC retention time and NMR spectrum, and amounted to 43.9% of the reaction products, by peak integration. Compound 140, identified by mass spectrum and NMR spectrum as 4-octene, and amounting to 34% of the product material. Compound 141 was identified as 3-ethyl-1-hexene by its mass and NMR spectra, and was produced as 22.3% of the reaction products (112).

Attempted Cyclization of 3-Methoxymethyl-1,5-hexadiene (145)

Using the general cyclization procedure, 0.40 g (3.2 mmole)

of the title compound in 3.0 mL of hexane was treated with 2.38 g (3.4 mmole) of DIBAL. The reaction time was 21.5 hours at reflux. One GLC peak, representing 146 and 147, was the predominant product, and was isolated by preparative scale GLC (column G, 140°, retention time of 7.8 minutes). NMR (CCl_4) δ 5.43-5.97 (m, 1H), 4.86-5.10 (m, 2H), 3.15-3.38 (m, 5H), 1.95-2.34 (m, 1.3H), 1.12-1.63 (m, 6.9H), 0.78-1.01 (m, 3H).

Cyclization of 1-Hexen-5-yne (153)

The general procedure for cyclization was employed using 0.27 g (3.37 mmole) of the title compound (153), 1.2 mL of hexane and 5.15 mL (6.66 mmole) of diethylaluminum hydride (1.3 M in hexane). At the prescribed time, 0.385 g (3.37 mmole) of octane was added as internal standard. A mixture of isomeric products (156 and 157) was isolated by GLC (column B, 70°, retention time of 12 minutes), which showed the yield of the mixture of 156 and 157 to be 47.1% based on octane. The isomeric mixture was not separable by GLC. The NMR spectrum was identical to that of a mixture of commercial (Aldrich Chemical Company) 1-methylcyclopentene (156) and methylene-cyclopentane (157). Integration of the vinyl proton regions shows the ratio of 156 to 157 to be 1.0 to 1.33.

Cyclization of 3-Methyl-1-hexen-5-yne (159)

The general cyclization procedure was employed using 0.3 g (3.18 mmole) of 159, 1.5 mL of hexane, and 5.0 mL (6.46 mmole) of diethylaluminum hydride. The reaction was analyzed by GLC (column E, 91°) and the single product peak was isolated by preparative scale GLC. The product was identified as 2-methylmethylenecyclopentane (160) and possessed a GLC retention time of 7.3 minutes. NMR (CCl_4) δ 5.67-5.86 (m, 2H), 2.16-2.56 (m, 3H), 1.17-2.06 (m, 4H), 1.05-1.12 (d, J=6.3 Hz, 3H).

The reaction was repeated using 3.8 mL of diethyl ether as solvent instead of hexane. One equivalent of nonane was added as internal standard. GLC analysis (column E, 98°) shows a single product of 7.1 minutes retention time, which was afforded in 68.6% yield relative to the internal standard. This product showed an NMR spectrum identical to that of trans-1,2-dimethylcyclopentane (161) (113).

Cyclization of 5-Hepten-1-yne (166)

The general procedure for cyclization was executed, utilizing 80 mg (0.85 mmole) of the title compound, 1.0 mL of hexane, and 1.38 mL (1.78 mmole) of diethylaluminum hydride. The reflux time was two hours. GLC analysis (column E, 91°) showed two product

peaks. The first peak was isolated by preparative scale GLC (retention time 8.7 minutes) and accounted for 90% of the products. This product, designated 167, was identified as 2-heptene. NMR (CCl_4) δ 5.29-5.52 (m, 2H), 1.87-2.28 (m, 2H), 1.58-1.63 (d, $J=4.8$ Hz, 3H), 1.21-1.51 (m, 4H), 0.80-1.05 (m, 3H). The second product was not isolated, but possessed a retention time identical to that of an authentic sample of ethylcyclopentane (168).

The reaction was repeated as before, but with inclusion of 2.0 equivalents of diethyl ether in the solvent, and with addition of one equivalent of aluminum chloride. Reflux time was 40 hours (in a 48° oil bath). GLC analysis (column E, 91°, retention time: 9.4 minutes) showed one major product whose retention time was identical to that of an authentic sample of ethylcyclopentane (168) (114) and which was identified as that compound by comparison of mass spectra.

Cyclization of 4-Vinyl-7-octen-1-yne (170)

The general procedure for cyclization was employed, using 0.19 g (1.41 mmole) of the title compound (170), 0.31 mL (3.0 mmole) of diethyl ether, and 2.16 mL of diethylaluminum hydride. GLC analysis and preparative scale isolation (column D, 140°, retention time of 6.0 minutes) of the single product peak establishes it to be trans 2-(3-butenyl)methylcyclopentane (171) by a comparison of NMR spectra of the reaction product and a sample of proven structure (88).

The reaction described above was repeated using the reagents specified and also 2.2 equivalents of aluminum chloride. Reaction time was 40 hours at 42°. One equivalent of nonane was added as internal standard. GLC analysis and preparative scale isolation (column E, 160°) showed the following three products: Product A, retention time of 9.5 minutes, 16.7% based on nonane, had a mass spectral molecular ion peak at 140. The NMR spectrum is consistent with 2-butylmethylcyclopentane. Product B, retention time of 11.6 minutes, had a molecular ion peak at 140 and a yield of 5.6% based on nonane. Product C, amounting to 12.8% based on nonane, had a retention time of 12.7 minutes and a molecular ion at 138. NMR (CCl₄) δ 1.91-2.40 (m, 5H), 1.54-1.85 (m, 5H), 1.18-1.50 (m, 5H), 0.79-1.02 (m, 3H).

The procedure was repeated, with the inclusion of addition of one equivalent of n-butyllithium. The reaction temperature was 50° and the time was two days. One product peak was isolated by preparative scale GLC (column C, 140°, retention time of 3.2 minutes), and it was identical to the previously obtained trans-2(3-butenyl)-methylcyclopentane (171).

Attempted Cyclization of 3-Methoxy-1-hexen-5-yne (177)

The general procedure for cyclization was utilized, using 0.34 g (3.09 mmole) of 177, 3.0 mL hexane, and 2.96 mL (6.17 mmole) of

diethylaluminum hydride. The reaction was refluxed for 15 hours.

Analysis by GLC (column D, 89°) showed a multitude of products, each in small quantity. None were isolated or identified.

The previous reaction procedure was repeated, with the inclusion of two equivalents of diethyl ether in the reaction solvent, and with the addition of 2.1 equivalents of n-butyllithium. Analysis and product isolation by GLC (column C, 88°) showed two products, the first being identical (NMR and Mass Spectrum) with cyclohexene, and the second being identical (NMR and Mass Spectrum) with octane (115).

Cyclization of 3-Methoxymethyl-1-hexen-5-yne (187)

The general procedure for the cyclization was employed, using 0.17 g (1.37 mmole) of the title compound (187), 1.5 mL of hexane, and 2.2 mL (2.74 mmole) of diethylaluminum hydride. The reaction was run for 16 hours at 70°. GLC analysis (column D, 116°, 5.7 minutes) showed a single product peak which appears to be mostly 189 with a trace of isomer 190. NMR (CCl_4) δ 5.35-5.36 (m, due to 190); the rest of the NMR spectrum was identical to the independently-synthesized 189 prepared above.

The procedure was repeated using 3.1 mL of diethyl ether and one equivalent of decane as internal standard. The reaction was stirred two days at 42°. GLC analysis and preparative scale isolation (column B, 150°) showed two products: The first and major

product had a retention time of 5.1 minutes, and amounted to 75.6% relative to decane. It possessed an NMR spectrum identical to independently synthesized cis-2-methoxymethylmethylcyclopentane (129). The minor product had a retention time of 6.0 minutes. It was 5.4% relative to the internal standard. It possessed an NMR spectrum identical to that of independently synthesized trans-2-methoxymethylcyclopentane (128).

REFERENCES AND NOTES

1. (a) W. S. Johnson, Accounts of Chem. Res., 1, 1 (1968).
(b) K. E. Harding, J. L. Cooper, and P. M. Puckett, J. Amer. Chem. Soc., 100, 993 (1978).
(c) R. A. Volkmann, G. C. Andrews, and W. S. Johnson, ibid., 97, 4777 (1975).
(d) R. A. Markezich, W. E. Willy, B. E. McCarry, and W. S. Johnson, ibid., 95, 4414 (1973).
(e) W. S. Johnson, K. Wiedhaupt, S. F. Brady, and G. L. Olson, ibid., 96, 3979 (1974).
(f) P. A. Bartlett and W. S. Johnson ibid., 95 7501 (1973).
(g) P. A. Bartlett, J. T. Brauman, W. S. Johnson, and R. A. Volkmann, ibid., 95, 7503 (1973).
(h) W. S. Johnson, N. P. Jensen, J. Hooz, and E. J. Leopold. ibid., 90, 5872 (1968).
2. (a) R. C. Lamb, P. W. Ayers, and M. K. Toney, ibid., 85, 3483 (1963).
(b) M. Julia, Accounts of Chem. Res., 4, 386 (1971).
(c) M. Julia, Rec. Chem. Prog., 25, 3 (1964).
3. B. J. Wakefield, "The Chemistry of Organolithium Compounds," Pergamon Press, New York, N.Y. 1974.
4. (a) K. Ziegler, "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Corp., New York, 1960. p. 234.
(b) T. W. Dolzin and J. P. Oliver, J. Organomet. Chem., 78, 165 (1974).
(c) A. A. Antonov, C. F. Brodovskaya, N. S. Nanetkin, and V. I. Smetanyuk, Neftekhimiya, 15, 264 (1975).
5. E. A. Hill, J. Organomet. Chem., 91, 123 (1975).

6. C. A. Bertelo and J. Schwartz, J. Amer. Chem. Soc., 98, 262 (1976).
7. L. G. Channell, ibid., 94, 6867 (1972).
8. J. St. Denis, T. Dolzen, and J. P. Oliver, ibid., 94, 8260 (1972).
9. (a) K. Sakai and O. Oda, Tetrahedron Lett., 4375 (1972).
(b) H. Arai and J. Halpern, Chem. Commun., 1571 (1971).
(c) J. A. Evans, D. R. Russel, A. Gright, and B. L. Shaw, ibid., 841 (1971).
10. P. W. Jolly and G. Wilke, "The Organic Chemistry of Nickel, Volume II," Academic Press, New York, 1975.
11. (a) J. Y. Mirour, J. L. Roustan, C. Charrier, J. Collin, and J. Benaini, J. Organomet. Chem., 51, C24 (1973).
(b) N. Genco, D. Marten, S. Raghu, and M. Rosenblum, J. Amer. Chem. Soc., 98, 848 (1976).
12. (a) D. R. Coulson, ibid., 91, 200 (1969).
(b) B. M. Trost and T. R. Verhoeven, ibid., 99, 3867 (1977).
(c) E. Forsellini, G. Bonbieri, B. Crociani, and T. Boschi, Chem. Commun., 1203 (1970).
13. J. K. Crandall, P. Battioni, J. T. Wehlacz, and R. Bindra, J. Amer. Chem. Soc., 97, 7171 (1975).
14. T. J. Marks and W. A. Wachter, ibid., 98, 703 (1976).
15. K. P. C. Vollhardt and R. L. Funk, ibid., 99, 5483 (1977).
16. P. W. Chum, "The Intramolecular Cyclization of Organo-aluminum Compounds," Doctoral Thesis, Oregon State University, 1978.
17. A. K. Prokof'ev, Russian Chem. Rev., 45, 519 (1976).

18. L. I. Zakharkin and L. A. Savina, Bull. Acad. Sci. USSR, Engl. Transl., 420 (1959).
19. G. E. Coates and R. N. Mukherjae, J. Chem. Soc., 1295 (1964).
20. K. H. Thiele, M. Heinrich, W. Brüser, and S. Shröder, Z. Anorg. Allg. Chem., 432, 221 (1977).
21. A. H. Veeffkind, J. Schaaf, F. Bickelhaupt, and G. Klumpp, Chem. Commun., 722 (1971).
22. L. I. Zakharkin and L. A. Savina, J. Gen. Chem. USSR, Engl. Transl., 35 1144 (1965).
23. (a) F. P. Boer, J. J. Flynn, H. F. Freedman, and S. V. McKinley, J. Amer. Chem. Soc., 89, 5068 (1967).
(b) F. P. Boer, G. A. Boarakian, H. H. Freedman, and S. V. McKinley, ibid., 92, 1225 (1970).
24. (a) G. Wittig and J. Heyn, Ann. Chem., 726, 57 (1969).
(b) G. Wittig and J. Meske-Schuller, ibid., 711, 65 (1969).
(c) G. Wittig and V. Meyer, Chem. Ber., 96, 329 (1963).
25. See ref. 3, chapter 1.
26. K. Hirai, H. Matsuda, and Y. Kishida, Tetrahedron Lett., 4359 (1971).
27. K. Takabe, T. Kaligiri, and J. Takana, ibid., 4009 (1972).
28. D. Slocum, B. Rockett, and C. Hauser, J. Amer. Chem. Soc., 87, 1241 (1965).
29. F. Johes, M. Zinn, and C. Hauser, J. Org. Chem., 28, 663 (1963).
30. F. Jones and C. Hauser, ibid., 27, 701 (1962).
31. C. Tien and T. Hogen-Esch, J. Amer. Chem. Soc., 98, 7109 (1976).

31. C. Tien and T. Hogen-Esch, J. Amer. Chem. Soc., 98, 7109 (1976).
32. J. Mulvaney and Z. Gardlund, J. Org. Chem., 30, 917 (1965).
33. D. Slocum, B. Koonsvitsky, and C. Ernst, J. Organomet. Chem., 38, 125 (1972).
34. (a) D. Shirley, J. Johnson, and J. Hendrix, ibid., 11, 209 (1968).

(b) D. Slocum and D. Sugarman "Directed Metallation" Adv. Chem. Ser., 130, Ed. by A. Langer, American Chemical Society, Washington, 1974, p. 227.

(c) D. Slocum and B. Koonsvitsky, J. Org. Chem., 38, 1675 (1973).

(d) R. Ellison and F. Kotsonis, ibid., 38, 4192 (1973).
35. P. Beak and B. Siegel, J. Amer. Chem. Soc., 96, 6803 (1974).
36. G. Chassaing, R. Lett, and A. Marquet, Tetrahedron Lett., 471 (1978).
37. R. Lett and A. Marquet. ibid., 1579 (1975).
38. E. Boerhorst, R. Schmitz, and C. Klumpp, ibid., 3347 (1975).
39. (a) K. Taylor and J. Chaney, J. Amer. Chem. Soc., 98, 4158 (1976).

(b) K. Taylor, J. Chaney, and J. Deck, ibid., 98, 4163 (1976).
40. H. Felkin, G. Swierczewski, and A. Tambute', Tetrahedron Lett., 707 (1969).
41. (a) J. K. Crandall and A. Clark, ibid., 325 (1969).

(b) J. K. Crandall and A. Clark, J. Org. Chem., 37, 4236 (1972).
42. R. Quelet, C. Broquet, J. d'Angelo, and H. Normant, C. R. Acad. Sc. Paris, C, 1316 (1967).

43. See ref. 3, chapter 7.
44. H. Richey and F. Von Rein, J. Organomet. Chem., 20, P32 (1969).
45. Y. Frangin and M. Grandemar, ibid., 142, 9 (1977).
46. A. Veefkind, F. Bickelhaupt, and G. Klumpp, Recl. Trav. Chim. P. B., 88, 1058 (1969).
47. J. Eisch and J. Merkley, J. Organomet. Chem., 20, P27 (1969).
48. H. Richey, C. Wilkins, B. Brown, and R. Moore, Tetrahedron Lett., 723 (1976).
49. M. Kool and G. Klumpp, ibid., 1873 (1978).
50. G. Klumpp and R. Schmitz, ibid., 2911 (1974).
51. (a) D. A. Evans, G. Andrews, and B. Buckwater, J. Amer. Chem. Soc., 96, 5560 (1974).
- (b) W. C. Still and T. L. Macdonald, ibid., 96, 5561 (1974).
- (c) J. Hartmann, M. Stahle, and M. Schlosser, Synthesis, 888 (1974).
52. (a) S. Pasynkiewicz, Pure and Applied Chemistry, 30, 509 (1972).
- (b) T. Mole and E. Jeffery, "Organoaluminum Compounds," Elsevier Publishing Company, Amsterdam, 1972.
- (c) K. Henold and J. Oliver, Organometallic Reactions, 5, 387 (1975).
- (d) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, New York, 1972.
- (e) G. Bruno, "The Use of Aluminum Alkyls in Organic Synthesis," The Ethyl Corporation, Baton Rouge, La., 1970, with Supplement, 1972.
53. (a) G. Bähr and G. Müller, Chem. Ber., 88, 1765 (1955).

- (b) L. Zakharkin and L. Savina, Bull. Acad. Sci. USSR, Engl. Transl., 970 (1960).
54. L. Zakharkin and L. Savina, ibid., 1600 (1964).
55. G. Anderson, F. Forgaard, and A. Haaland, Chem. Commun., 480 (1971).
56. J. Szmuszkowicz, J. Musser, and L. Laurian, Tetrahedron Lett., 1412 (1978).
57. S. Pasynkiewicz, K. Starowieyski, A. Peregudov, and D. Kravtsov, J. Organomet. Chem., 132, 191 (1977).
58. B. Franzus and E. Snyder, J. Amer. Chem. Soc., 87, 3423 (1965).
59. W. R. Jackson, J. Norman, and I. Rae, Tetrahedron Lett., 2061 (1978).
60. H. Brown and H. Hess, J. Org. Chem., 34, 2206 (1969).
61. F. Hochstein and W. Brown, J. Amer. Chem. Soc., 70, 3484 (1948).
62. M. Fetizon, H. Huy, and P. Mourgues, Tetrahedron, 34, 209 (1978).
63. (a) J. Eisch and G. R. Husk, J. Organomet. Chem., 4, 415 (1965).
- (b) H. Lehmkuhl and D. Reinehr, ibid., 23, C25 (1970).
- (c) H. Hoberg, Angew. Chem. Int. Ed. Engl., 5, 513 (1966).
64. Y. Kitagawa, S. Hashimoto, S. Iemura, H. Yamamoto, and H. Nozaki, J. Amer. Chem. Soc., 98, 5030 (1976).
65. S. Hashimoto, Y. Kitagawa, S. Iemura, H. Yamamoto, and H. Nozaki, Tetrahedron Lett., 2615 (1976).
66. See ref. 3, pp. 19-71.
67. P. Freeman and L. Hutchinson, Tetrahedron Lett., 1849 (1976).

68. S. Wilson, unpublished results.
69. (a) M. Schlosser and K. Christmann, Angew. Chem. Int. Ed. Engl., 5, 126 (1966).
- (b) M. Schlosser and K. Christmann, Justus Liebigs Ann. Chem., 708, 1 (1967).
- (c) M. Schlosser, K. Christmann, and A. Piscala, Chem. Ber., 103, 2814 (1970).
- (d) E. Corey and H. Yamamoto, J. Amer. Chem. Soc., 92, 226 (1970).
70. S. Wilson, unpublished results.
71. (a) R. Reike, Acc. Chem. Res., 10, 301 (1977).
- (b) R. Reike and S. Bales, J. Amer. Chem. Soc., 96, 1775 (1974).
72. S. Wilson, unpublished results.
73. A. Stefani, Helv. Chim. Acta, 57, 1346 (1974).
74. C. Chavdarian and C. Heathcock, J. Amer. Chem. Soc., 97, 3822 (1975).
75. D. Evans, C. Simms, and G. Andrews, ibid., 99, 5453 (1977).
76. See ref. 3, p. 91.
77. See ref. 3, chapter 1.
78. See ref. 52 (d), p. 203.
79. See ref. 16, pp. 45-46.
80. T. Mole, "Organometallic Reactions, Volume 1," E. Becker and M. Tsutsui, Ed., Wiley-Interscience, New York, 1970, p. 1.
81. Name attributed to D. DeiRossi.
82. K. Egger, Internat. J. Chem. Kinetics, 1, 459 (1969).

83. A. Allred, J. Inorg. Nuclear Chem., 17, 215 (1961).
84. G. Zweifel, G. Clark, and R. Lynd, Chem. Commun., 1593 (1971), and refs. cited therein.
85. (a) L. Brooks and H. Snyder, "Organic Syntheses, Coll. Vol. 3," E. Horning, Ed., J. Wiley, New York, 1955, p. 698.
- (b) E. Jones, G. Eglinton, M. Whiting, "Organic Syntheses, Coll. Vol. 4," N. Rabjohn, Ed., J. Wiley, New York, 1963, p. 755.
86. R. Ratcliffe and R. Rodehorst, J. Org. Chem., 35, 4000 (1970).
87. E. Marvel and D. Titterington, private communication of unpublished results.
88. S. Wilson, unpublished results.
89. G. Zweifel and R. Steele, Tetrahedron Lett., 6021 (1966).
90. S. Wilson, unpublished results.
91. A. Viola and J. MacMillan, J. Amer. Chem. Soc., 90, 6141 (1968).
92. See ref. 52 (a), and ref. 52 (b), p. 121.
93. L. Haynes, I. Heilbron, E. Jones, and F. Sondheimer, J. Chem. Soc., 1584 (1947).
94. G. Courtois, B. Mauze, and L. Miginiac, J. Organomet. Chem., 72, 309 (1974).
95. (a) See ref. 52 (d), pp. 109-111.
- (b) See ref. 52 (b), pp. 56-58.
96. G. Zweifel and H. Brown, J. Amer. Chem. Soc., 86, 393 (1964).
97. D. F. Schriver, "The Manipulation of Air-Sensitive Compounds," McGraw-Hill Book Company, New York, 1969.

98. M. Kharasch and C. Fuchs, J. Org. Chem., 9, 359 (1944).
99. U. Diner, F. Sweet, and R. Brown, Can. J. Chem., 44, 1591 (1966).
100. J. Findlay, W. MacKay, and W. Bowers, J. Chem. Soc., (C), 2631 (1970).
101. T. Cuvigny, J. Le Borgne, M. Larcheveque, and H. Normant, J. Organomet. Chem., 70, C5 (1974).
102. J. Davoll, J. Chem. Soc., 131 (1960).
103. W. Wantanabe, L. Conlon, and J. Hwa, J. Org. Chem., 23, 1666 (1958).
104. F. Sondheimer, D. Ben-Efraim, and R. Wolovsky, J. Amer. Chem. Soc., 83, 1675 (1961).
105. T. Vaughn, R. Vogt, J. Nieuwland, ibid., 56, 2120 (1934).
106. F. Bohlmann and R. Miethe, Chem. Ber., 100, 3861 (1967).
107. J. Collins, W. Hess, and F. Frank, Tetrahedron Lett., 3363 (1968).
108. For the use of 4-pentynal (165) in a similar Wittig reaction see U. Meissner, A. Gensler, and H. Staab, Angew. Chem. Int. Ed. Engl., 15, 365 (1967).
109. 169: NMR (CCl_4) 5.32-6.12 (m, 4H), 4.83-5.15 (m, 4H), 1.90-2.41 (m, ⁴5H), 1.20-1.67 (m, 2H).
110. V. Traynelis, W. Hergenrother, H. Hanson, and J. Valicenti, J. Org. Chem., 29, 123 (1964).
111. 2-Methoxymethyl-1-methylcyclopentane has been prepared by M. Gadzhiev et al. (M. Gadzhiev, A. Shikhmamedbekova, L. Vorob'ev, and I. Mamedov, Zh. Org. Kh. Engl. Transl., 10 1381 (1974)), but apparently not stereospecifically.
112. Information on 140 and 141 kindly provided by W. A. Beavers, private communication. Based on R. Bates, W. Beavers, M. Greene, and J. Klein, J. Amer. Chem. Soc., 96, 5640 (1974).

113. S. Wilson, unpublished results.
114. Kindly provided by P. W. Chum.
115. Cyclohexene and octane are available from Aldrich Chemical Co.