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ANION EQUIVALENT.

THE OHIO STATE UNIVERSITY, PH.D., 1979
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TRIMETHYLSILYLALLYL ANION: A HOMOENOLATE ANION EQUIVALENT

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By

Edward E. Ehlinger, B.S.

The Ohio State University

1979

Reading Committee:
Professor G. Fraenkel
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Professor P. D. Magnus

Approved By

P. D. Magnus
Department of Chemistry
To Kim and Erin.
ACKNOWLEDGEMENTS

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PUBLICATIONS

New $\beta$-Acylcarbanion Equivalent Based on Allyltrimethylsilane
Chemistry, D. Ayalon-Chass, E. Ehlinger, and P. D. Magnus,

$\alpha$-Chloro-$\alpha$-trimethylsilyl Carbanion, a Reagent for Homologation
of Ketones and Aldehydes via $\alpha,\beta$-Epoxysilanes, C. Burford, F. Cooke,

Silicon in Synthesis. Unusual Transformations of 4-Hydroxybutenyl-

FIELDS OF STUDY

Organic Chemistry. Professor P. D. Magnus
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INTRODUCTION

Linderalactone (1) is a germacrolide sesquiterpene which contains a central six-membered ring with a quaternary carbon; the appended groups are methyl and vinyl. It exists as an equilibrium mixture of the two structures shown, which are interconvertible through the Cope rearrangement. It seemed apparent that an efficient synthesis of this system would deal with the construction of the central ring with its quaternary carbon early on. Hence, a useful intermediate and the initial goal of our synthetic effort was 3,5-dimethoxy-1,4-dihydro-1-methyl-1-vinyl benzene (2). This molecule contains the quaternary
center in the correct orientation to a masked 1,3-dicarbonyl system useful for the further elaboration of the structure. The element of symmetry present in 2 has potential use in simplifying regiochemistry in subsequent reactions. Further, it seemed that 2 could be derived from readily available simple aromatic substrates. The plan shown in Scheme I was developed for the production of 2.

**Scheme I**

\[
\begin{align*}
&\text{OH} \\
&\text{CH}_3\text{O} \\
&\text{OCH}_3 \\
\end{align*}
\]

\[
\begin{align*}
1. \text{Li/NH}_3 \\
2. \text{CH}_3\text{I} \\
\end{align*}
\]

\[
\begin{align*}
&\text{OH} \\
&\text{CH}_3\text{O} \\
&\text{OCH}_3 \\
\end{align*}
\]

\[
\begin{align*}
\text{LiAlH}_4 \\
\end{align*}
\]

\[
\begin{align*}
&\text{OH} \\
&\text{CH}_3\text{O} \\
&\text{OCH}_3 \\
\end{align*}
\]

\[
\begin{align*}
\text{CrO}_3 \\
\end{align*}
\]

\[
\begin{align*}
&\text{OH} \\
&\text{CH}_3\text{O} \\
&\text{OCH}_3 \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2=\text{P} \_3 \\
\end{align*}
\]

\[
\begin{align*}
&\text{OH} \\
&\text{CH}_3\text{O} \\
&\text{OCH}_3 \\
\end{align*}
\]
Thus, following the published procedure of van Bekkum, et al.,
3,5-dimethoxy-1,4-dihydro-1-methyl benzoic acid (3) was produced
nearly pure and in high yield (90%) by the treatment of 3,5-dimethoxy
benzoic acid with lithium and liquid ammonia, followed by quenching the
dianion with methyl iodide. Treatment of the acid with lithium
aluminum hydride converted it cleanly to 3,5-dimethoxy-4-hydro-1-
hydroxymethyl toluene (4) in high yield (80%). However, oxidation
of 4 to the corresponding aldehyde proved considerably more difficult
than had been anticipated. Pyridinium chlorochromate oxidation gave a preponderance of aromatic material, while Collins oxidation produced only 50-60% of the desired compound, contaminated by starting material and 3,5-dimethoxytoluene. The observation of 3,5-dimethoxy-toluene as the major contaminant led to a possible explanation for
the failure of the oxidation, which is outlined in Scheme II. The
first step in either oxidation method must be the formation of a species
with a leaving group attached to the alcoholic oxygen. Pathway a
then leads to the desired product by the usual mechanism for such
reactions, while pathway b is a fragmentation which leads to recovery
of aromaticity by the loss of formaldehyde, producing 3,5-dimethoxy-
toluene.

To circumvent this problem, we decided to make use of a variant
on the Peterson reaction. The original Peterson reaction, delineated
in Scheme III, is an alternative to the Wittig reaction for some systems,
and has the advantage of the absence of triphenylphosphine oxide in
the crude product mixture. Since the aldehyde required to use the
Peterson reaction could not be made cleanly in this case, we planned
Scheme II

\[ \text{CH}_3\text{O} - \text{OCH}_3 \xrightarrow{[O]} \text{CH}_3\text{O} - \text{OCH}_3 \xrightarrow{\text{a}} \] 

\[ \text{CH}_3\text{O} - \text{OCH}_3 \xrightarrow{\text{b}} \]

Scheme III

\[ R\text{C}=O + \text{CH}_2\text{Si(CH}_3)_3 \xrightarrow{} \text{[R\text{C}=O\text{Si(CH}_3)_3]} \xrightarrow{-\text{TMS}} R\text{=} \]
to treat the acid chloride from 3 with lithiomethyltrimethylsilane to arrive at the intermediate (6) shown in Scheme IV. Sodium borohydride or lithium aluminum hydride reduction of 6 would then produce 2 by in situ loss of trimethylsilyl oxide from the indicated intermediate.

**Scheme IV**

\[ \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{OH} \quad \text{SOCl}_2 \rightarrow \quad \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{Cl} \quad \text{CH}_2\text{Si(CH}_3\text{)}_3 \]

\[ \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{Si(CH}_3\text{)}_3 \quad \text{NaBH}_4 \text{ or LiAlH}_4 \rightarrow \quad \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{Si(CH}_3\text{)}_3 \]

\[ \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \quad \text{Si(CH}_3\text{)}_3 \quad \text{TMSO}^- \rightarrow \quad \text{CH}_3\text{O} \quad \text{OCH}_3 \quad \text{OCH}_3 \]
Preliminary experiments were done on a model system, 1-methyl-1-cyclohexanecarboxylic acid chloride. Lithiomethyltrimethysilane was made by reacting lithium metal with chloromethyltrimethylsilane in unsaturation-free dry pentane. The acid chloride was added to that solution. However, the best result obtained in this series of experiments was a 1:1 mixture of the desired α-trimethylsilyl ketone (6) and the ester (7) shown below.

![Chemical structures](image)

Presumably, water was contaminating the reaction, and the reaction to form lithiomethyltrimethylsilane was incomplete, since the formation of 7 would appear to require the presence of 1-methyl-1-cyclohexane carboxylic acid and chloromethyltrimethylsilane. This situation could doubtless have been improved, but the project was suspended indefinitely in favor of studying the reaction of chloromethyltrimethylsilanyl anion with carbonyl compounds.

Numerous examples exist in the literature of anions of the type Z-CH-Si(CH$_3$)$_3$ which react with carbonyl compounds to provide olefinic products, as shown in Scheme V. However, we discovered that chloromethyltrimethylsilane could be deprotonated with sBuLi in THF in the presence of TMEDA to give a species whose reactions indicated
it to be $\text{Cl}-\text{CH}-\text{Si}(\text{CH}_3)_3$. This anion reacts cleanly with carbonyl compounds to provide $\alpha,\beta$-epoxysilanes rather than vinyl chlorides. These compounds were previously available only through epoxidation of the corresponding vinyl silanes, which are not readily available.

Thus, treatment of benzophenone and fluorenone with the

Scheme VI

$$\text{ClCH}_2\text{Si}(\text{CH}_3)_3 \xrightarrow{s\text{BuLi}} \text{THF} \xrightarrow{\text{TMEDA}} \Theta \xrightarrow{\text{Si}(\text{CH}_3)_3} \text{Cl}$$

$9\text{a} (R = R^1 = \text{f})$

$9\text{b} (R, R^1 = \text{fluorenyl})$
chloromethyltrimethylsilyl carbanion gave >95% and 85% yields, respectively, of crude epoxy silanes containing traces of starting materials. The reaction did not proceed, however, when 6-methoxy-1-tetralone was used as the substrate presumably due to enolization.

α,β-epoxysilanes are known to hydrolyze under acidic conditions to aldehydes. Hence, the overall operation performed, shown in Scheme VII, can be termed reductive nucleophilic acylation. That is, not only does the reaction provide the homologous aldehyde from

Scheme VII

\[
\begin{align*}
\text{R} & \quad \rightarrow \\
\text{R} & \quad \rightarrow \\
\text{H} & \quad \rightarrow
\end{align*}
\]

a carbonyl compound, but it does so with reduction at the original electrophilic carbonyl carbon. This is one of the simplest procedures to effect this transformation, and the reagent is commercially available. Further work has been done on this process by other workers at The Ohio State University, under the direction of Professor P. D. Magnus.
General Experimental Information

All proton NMR spectra were obtained on either a Varian A-60 spectrometer or a Varian EM-360 spectrometer. Melting points were taken on a Thomas Hoover melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer 267 Grating Infrared Spectrophotometer. Elemental analyses were done by M-H-W Laboratories in Phoenix, Arizona. Mass spectral data were obtained on a Consolidated Electronic MS-9 Double Focusing mass spectrometer.
EXPERIMENTAL

3,5-Dimethoxy-1,4-dihydro-1-methyl Benzoic Acid. (3)². 3,5-Dimethoxybenzoic acid (.11 mole, 20g) was dissolved in liquid ammonia (1L) and the resulting solution was mechanically stirred. Lithium wire (.27mole, 1.9g) was added in portions, the last producing a lasting deep blue color in the solution. Methyl iodide (.44mole, 62g, 28ml) was added, discharging all color. The reaction mixture was stirred for 20 min., then the ammonia was allowed to evaporate over several hours, with stirring. All solutions used in the workup were kept ice cold. The residue was dissolved in water, layered with dichloromethane, and the resulting mixture was stirred vigorously on an ice bath. The pH was brought slowly to 7 with 8M hydrochloric acid, keeping the temperature below 2.5 °C. Saturated aqueous sodium dihydrogen phosphate was then added in portions, until white precipitate no longer formed in the aqueous phase and dissolved in the organic one with each portion. The mixture was transferred to a separatory funnel, and the phases separated. The aqueous phase was extracted, and the combined organics dried over MgSO₄. Removal of the solvent gave 19.6g (90%) of crude 3 which was nearly pure. IR (CHCl₃; cm⁻¹): 3400-2600m; 1700s; 1650m; 1405s; 1155s. NMR (CDCl₃/TMS; δ): 4.73 (s, 2H, vinyl protons); 3.56 (s, 6H, -OCH₃'s); 2.76 (s, 2H, allylic protons); 1.41 (s, 3H, -CH₃).
3,5-Dimethoxy-1,4-dihydro-1-hydroxymethyltoluene, (4).b Lithium aluminum hydride (.21 mole, 8.0g) was suspended in dry ether (250ml) and the mixture was stirred at 0°C under argon. 3,5-Dimethoxy-1,4-dihydro-1-methyl benzoic acid (3) (97mmole, 19.2g) was added quickly, as a solution in ether (80ml). The reaction mixture was brought slowly to room temperature and allowed to stir for 24 hours. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), it was quenched in stirred, iced saturated aqueous sodium sulfate layered with ether and stirred vigorously. The resulting slurry was suction filtered, and the phases were separated. The aqueous phase was extracted and the combined organics dried over MgSO₄. Removal of solvent yielded 14.2g (80%) of crude 4 as an oil. IR (CHCl₃, cm⁻¹): 3530w; 2960s; 1660s; 1445s. NMR (CDCl₃/TMS): 4.42 (s, 2H, vinyl protons); 3.54 (s, 6H, -OCH₃'s); 3.28 (s, 2H, methylene protons next to hydroxyl); 2.75 (s, 2H, allylic protons); 1.08 (s, 3H, -CH₃).

3,5-Dimethoxy-1,4-dihydro-1-methylbenzaldehyde, (5). Dry pyridine (32.6mmole, 2.6g, 2.6ml) was added in a dropwise fashion to a stirred, cooled (0°C) solution of chromium trioxide (16.3mmole, 1.6g) in dichloromethane (40ml). The resulting heterogeneous mixture was stirred 25 min. at 0-5°C. 3,5-Dimethoxy-1,4-dihydro-1-hydroxymethyltoluene (4) (2.7mmole, .5g) was added slowly as a solution in dichloromethane (10ml). When the starting material was destroyed, as judged by TLC (70% high petroleum ether, 30% EtOAc), the reaction was worked up. The dichloromethane was decanted from the tarry residue in the flask. The residue was washed with several portions of dichloromethane which were combined with the decanted liquid. The combined organics
were washed with cold sodium hydroxide and ice water, then dried over MgSO₄. Removal of the solvent left a material whose spectral data were complex, but showed an aldehyde proton in the NMR. A semicarbazone was made from the crude product, obtaining as crystals which were recrystallized from dichloromethane/isopropyl ether (mp 184-185°C). Analysis showed that the derivative was of the desired aldehyde, 3,5-dimethoxy-4-hydro-1-methyl benzaldehyde. Analysis: C_{11}H_{12}O_{3}N_{3} requires: C 55.23, H 7.11, N 17.57; found: C 54.74, H 7.26, N 17.48.

3,5-Dimethoxy-1,4-dihydro-1-methyl-benzaldehyde, (5) (Not produced).

Pyridinium chlorochromate (9.7mmole, 2.2g) and pyridine (11mmole, .87g, .89ml) were added to dry dichloromethane (10ml) and the mixture stirred at room temperature. 3,5-Dimethoxy-4-hydro-1-hydroxymethyl toluene (4) (5.4mmole, 1.0g) was taken up in dry dichloromethane (10ml) and added to the reaction mixture in one portion. The reaction was allowed to run for 1 hour, and then the solution was diluted with dry ether (10ml). The supernatant liquid was decanted from the tarry residue, which was washed with several portions of ether. The combined organics were gravity filtered, then passed through a short column of silica gel. The solvent was removed, leaving a product whose spectral data showed it to be a complex mixture of compounds, especially aromatics.

1-Methyl-cyclohexane Carboxylic Acid Trimethylsilylmethyl Ester, (8). Dry, olefin-free pentane (15ml) was placed in a 50ml flask fitted with a Dewar condenser. Lithium (16mmole, .11g) and chloromethyltrimethylsilane (8.2mmole, 1.0g, 1.2ml) were added, and the
reaction mixture stirred at reflux for 13h, at the end of which time the solution was dark purple. Most of the pentane was boiled off, and the solution was cooled to -74° under argon. THF (10ml, dry) was added, and when the solution was brought to -40°, the purple color present initially slowly disappeared. Upon addition of copper (I) iodide (4.1 mmole, .78g), the solution became milky grey, darkening to charcoal after 10min. After the solution was stirred for an additional 20min., 1-methyl-1-carboxylic acid chloride (4.1mmole, .66g) was added. A very fast reaction ensued, as judged by TLC (90% high petroleum ether, 10% EtOAc), giving rise to a single fast running spot concomitant with complete destruction of starting material. The reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted with dichloromethane and the combined organics washed with water. Removal of the dried (MgSO₄) solvent left a crystalline product whose spectral data showed it to be 8 (67%). IR (neat, cm⁻¹): 2920s; 1720s; 1245s; 1200s; 1155s; 1130s; 850s. NMR (CDCl₃/external TMS; δ): 3.98 (s, 2H, protons α to -TMS); 2.5-1.5 (envelope, 10H, ring protons); 1.36 (s, 3H, -CH₃); 0.30 (s, 9H, -TMS). MS: M⁺ at 228.

1-Methylcyclohexyl-trimethylsilylmethyl Ketone, (8). Lithiomethyl-trimethylsilane (6.5mmole, 8.1ml of a .8M solution in pentane) was added to dry diethyl ether (8ml) stirred under argon at -78°C. Copper(I) iodide (3.4mmole, .65g) was added, resulting in a suspension. The reaction mixture was warmed to -40°C, whereupon the mixture went from beige to dark grey to olive green. 1-Methyl-1-cyclonexane carboxylic acid chloride (3.1mmole, .5g) was added in a dropwise
fashion, and the reaction finished quickly, as judged by TLC (80% high petroleum ether, 20% EtOAc). The solution was warmed to 0°, then quenched in saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave a 1:1 mixture of 6 and 7. Two carbonyls were visible by IR, as well as two methyls and two sets of methylene protons α to the -TMS groups by NMR.

**1,1-Diphenyl-2-trimethylsilyl Ethylene Oxide**, (9a). To a stirred solution of chloromethyltrimethylsilane (6mmole, .74g, .84ml) in dry THF under argon were added sBuLi (4ml of a 1.5M solution in cyclohexane) and TMEDA (5.6mmole, .66g, .86ml). The resulting solution was stirred for 30min. at -75°, warmed to -55°, and benzophenone (2.7mmole, .5g) was added in a dropwise fashion as a solution in THF. The reaction was finished after 10min., as determined by TLC (90% high petroleum ether, 10% EtOAc). The reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted with dichloromethane and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent under vacuum gave a quantitative yield of the desired product. IR (neat, cm⁻¹): 3060w; 2950m; 1600w; 1495m; 1450m; 1250s; 840s; 955s; 900s. NMR (CDCl₃/TMS; δ): 7.41 (mult, 10H, aromatics); 2.89 (s, 1H, oxirane proton); 0.27 (s, 9H, -TMS). This compound was converted by acid hydrolysis to the corresponding aldehyde. (MS: Calc: 196.089; obs: 196.089).
1,1-(1-Fluorenyl)-2-trimethylsilyl Ethylene Oxide. (9b). To a stirred solution of sBuLi (4ml of a 1.5M solution in cyclonexane) and TMEDA (5.9mmole, .69g, .86ml) at -75° in dry THF under argon was added chloromethyltrimethylsilane (6.2mmole, .77g, .88ml) in a dropwise manner. The resulting solution was stirred at -75° for 30min., then warmed to -55°. Fluorenone (2.8mmole, .5g) was added dropwise as a solution in THF, and the reaction was monitored by TLC (90% high petroleum ether, 10% EtOAc). The reaction mixture was allowed to come to room temperature, and after 24h the reaction was judged complete by TLC. The solution was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted with dichloromethane, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .63g of the desired product (85%), contaminated with a small amount of the corresponding aldehyde, as judged by IR. IR (neat, cm⁻¹): 3060w; 2950m; 1715m (aldeneye); 1630m; 1600m; 1450s; 1250s; 840s. NMR (CDCl₃/TMS; δ): 9.12 (aldeneye proton); 7.6-7.0 (mult, 8H, aromatics); 3.08 (s, 1H, oxirane proton); 0.13 (s, 9H, -TMS). MS: C₉H₁₈O. Calc: 266.113; obs: 266.113. This compound was converted by acid hydrolysis to the corresponding aldehyde. (MS: C₁₀H₁₀O. Calc: 194.073; obs: 194.074.

1,1-[(1,2,3,4)-Tetrahydro-6-methoxynaphthyl]-2-trimethylsilyl

Ethylene Oxide. To a stirred solution of sBuLi (5.6mmole, 3.7ml of a 1.5M solution in cyclonexane) and TMEDA (5.6mmole, .65g, .84ml) in dry THF (5ml) under argon at -75° was added chloromethyltrimethylsilane (5.6mmole, .69g, .79ml). After stirring at -75° for 30min., the
solution was allowed to come to -55°, at which temperature 6-methoxy-1-tetralone (2.8mmole, .5g) was added dropwise as a solution in THF. The reaction mixture was allowed to come to room temperature, and after 24 hours complete loss of starting material was not achieved, as judged by TLC. None of the desired product was isolated after the usual workup.
CHAPTER TWO
REVIEW

PART ONE: HOMOENOLATE ANION EQUIVALENTS.

A great deal of work has been directed over the past ten years toward the development of efficient $\beta$-acyl anion equivalents. Such reagents would be capable of producing products formally derived from 1 or 2. Ideally, such reagents should be highly nucleophilic, and if

\[ R = H, \text{ alkyl} \]

the carbonyl is masked, it should be easily released. The synthetic uses of such reagents are clear; they would provide a three carbon extension, complete with a carbonyl at the end of the chain, which could be used for further elaboration. The approaches taken have been many and widely varied, but they can be roughly divided into two categories. The first group encompasses those systems which contain a protected carbonyl group with an activating group appended to the $\beta$ carbon. The second group consists of systems which try to take advantage of the ambident reactivity of heteroatomically substituted allylic anions.

Kondo and Tunemoto have described the use of $\beta$-sulfonyl acetals as homoenolate anion equivalents. These reagents are made by oxidation of the corresponding sulfides with meta-chloroperoxybenzoic acid.
acid. Deprotonation of 3 can be achieved with nBuLi in THF at -75°C,

\[
\begin{align*}
\phi S & \quad \text{MCPBA} \\
\rightarrow & \\
\phi S & \\
\end{align*}
\]

and the anion reacts with alkyl halides to give 80-90% yields of substituted sulfones. Hydrolysis is accomplished with aqueous acetic acid to provide \(\alpha,\beta\)-unsaturated carbonyl compounds in 70-80% yield, after basic \(\beta\)-elimination of the sulfonyle group. It is also possible to dialkylate the \(\beta\)-sulfonyl acetal anions; in those cases, mixtures of E and Z isomers are formed upon hydrolysis. The method will tolerate a methyl group \(\alpha\) to the acetal; in those cases, only E isomers result upon monoaalkylation. These reagents are operationally equivalent to 2.

Julia and Badet extended the versatility of \(\beta\)-sulfonyl acetals by performing a reduction prior to hydrolysis. Thus, if the alkylated \(\beta\)-sulfonyl acetal 4 is treated with sodium amalgam, followed by acid hydrolysis, the saturated ketone (or aldehyde) 5 is the product, in 70-80% from the the alkylated \(\beta\)-sulfonyl acetal. They also demonstrated the elimination sequence which produces \(\alpha,\beta\)-unsaturated carbonyl compounds. Thus, \(\beta\)-sulfonyl acetals were shown to be selectively
equivalent to 1 or 2, at least in their reactions with alkyl halides.

Along the same general lines, Ponaras developed the Grignard reagent 6 as a homoenolate anion equivalent. He showed that 6 would add to simple ketones to produce tertiary alcohols in high yield.

However, Eaton used the reagent 6 in a synthesis of the dilactone 7, and reported that 6 is of low reactivity and unstable. He observed decomposition of the anion 6 at room temperature and ready polymerization at 35°C. Further, he claimed that the addition reaction of 6 to the diketone frequently failed completely, for no apparent reason. Therefore, he developed a synthesis based upon the use of the known compound ethyl-3-lithiopropyl acetaldehyde acetal (9) as a 3-acyl anion unit. This sequence, shown in Scheme I, leads from 8 to 7 in
45% overall yield; the double addition of 9 can be done in one pot, since the anion of thiophenol is not sufficiently basic to initiate reverse aldol cleavage of 10 when the sequence is carried out quickly and the reaction mixture is kept cold. Ethyl-3-lithiopropyl acetaldehyde acetal is therefore operationally equivalent to the reduced form of 1.

Scheme I

\[ RLi = Li \]

\[ \text{RLi} \]

\[ \text{RLi} \]

\[ \text{RLi} \]

\[ 2 \text{SH} \]

\[ 1. \text{RLi} \]

\[ 2. \text{H}_2\text{O} \]

\[ 1. \text{H}_3\text{O}^+ \]

\[ 2. \text{H}_2\text{CrO}_4 \]
Recently Warren has developed the synthesis and use of \( \beta \)-diphenylphosphinoyl ketone acetals (I) as equivalents to \( \text{I} \)\(^{15} \). He has described routes to (I) which are amenable to introduction of the substituents \( R, R^1 \), and/or \( R^2 \). Deprotonation of (I) with BuLi in THF gives the corresponding anion which adds to carbonyl compounds with yields ranging from 80% to 70%. Treatment of these initial adducts with sodium hydride in THF gives Horner-Wittig products, of which (12) is an example, in >90% yield.

Seebach has shown that \( \beta \)-nitropropionyl chloride (13) can react with enolates to give cyclization products upon appropriate treatment.\(^{16} \)
When 13 is added to a pre-formed enolate, at \(-80^\circ C\) to \(-100^\circ C\), the 

\[
\begin{align*}
\text{Cl} & \quad \text{NO}_2 \\
\end{align*}
\]

reacts with the enolate to form 14 in a yield of 65-90%. At \(pH = 8.5\) in a buffer solution, 14 cyclizes to 15, which isomerizes to 16 upon use of prolonged reaction times. Thus, 13 is shown to be equivalent to the species 17.

\[
\begin{align*}
\text{17} \\
\end{align*}
\]

Bakuzis has investigated the reactions of a somewhat similar system, but his work has led to an equivalent of 1 which adds 1,4 to \(\alpha,\beta\)-unsaturated ketones. Under the influence of potassium t-butoxide in THF, the \(\beta\)-nitro ester 19 adds conjugatively to cyclopentenone and eliminates nitrous acid to form the adduct 19 in 52% yield. Likewise, addition of 18 to cyclohexane carboxaldehyde in the
presence of diisopropylamine and DMSO proceeded in 58\% yield.

Apparently, the condensation occurs faster than elimination of nitrous acid in those cases. That was not so for 20a, which had to be converted to 20b for use in the reactions shown.

Debal, Cuvigny, and Larcheveque used \( \alpha \)-carbon activation by the cyano group in their procedure.\(^{18}\) Thus, ketones 21, produced by 1,4 addition of cyanide to the corresponding enones, can be doubly deprotonated with two equivalents of LDA to give the dianion 22. Reaction of 22 with an alkyl halide leads to a mixture of the enolates.
23a and 23b. Elimination of cyanide from 23b occurs easily at room temperature, but if 23a is the predominant species formed, then enolate equilibration must be effected in a separate step. That process is not always efficient. In general, however,

yields of enones range from 50% to 80%, based on the starting cyano-ketone 21.

Caine has taken a very straightforward line in his attempt to develop a \( \beta \)-acyl anion system. The \( \beta \)-lithio carboxylate 24 is prepared from \( \beta \)-bromopropionic acid by successive treatment with nBuLi and lithium naphthalenide. This species adds to carbonyl compounds and, after
acid catalyzed cyclization, gives 30-70% of lactones \textsuperscript{25}. It is worthy of note that \textsuperscript{24} adds to the 2-methoxypropanyl derivative of androst-5-en-3\(\beta\)-ol-17-one to provide 28\% of \textsuperscript{26} after deprotection. Until the work described in the Discussion section of this chapter, this was the only \(\beta\)-acyl anion unit which had achieved addition to a 17-ketosteroid, presumably due to the steric hindrance and ease of enolization of the 17-carbonyl group.

Kuwajima introduced the use of 1-ethoxy-1-trimethylsiloxycyclopropane (\textsuperscript{27}) as a \(\beta\)-acyl anion equivalent which is used in conjunction with TiCl\(_4\).\textsuperscript{20} This reagent system affords lactones from aldehydes, and also reacts with acetals, as shown. Unfortunately, the reagent will not add to ketones.
Reich has developed an interesting equivalent based upon selenium chemistry. The dianion $28$ reacts with alkyl halides α to selenium and with alkyl halides or carbonyl compounds in the acetylenic position to give derivatives $29$. These compounds are oxidized, generally with peracid, to the selenoxides, which undergo rearrangement at $-30^\circ C$ to α-phenylselenoenones $30$. This rearrangement is postulated to proceed via the indicated intermediate. Overall yield of $30$ is in the range of 50-70%. Reich notes that the analogous reactions do not occur in the sulfur series to produce α-sulfenylation enones. Thus, he has established a reagent equivalent to the species $31$. 
Many attempts have been made to make use of the ambident reactivity of heteroatomically substituted allylic anions in the development of a homoenolate anion equivalent. A system such as 32, where Z has most often been a group containing O, S, P, or N, can usually be deprotonated to afford the allylic anion. Reaction with an electrophile at the γ end of the anionic system leads to intermediate 33 which contains a vinylheteroatom unit which is presumably convertible into a carbonyl group. On the other hand, reaction at the α carbon leads to 34 which in general has no such utility.

Thus, predominant, if not exclusive, γ attack of the allylic anion is the goal for one wishing to develop successful β-acyl anion chemistry based on allylic anions.

Evans has successfully metalated the allylic ethers 35 with sBuLi, and reacted the resulting anions with both alkyl halides and carbonyl compounds.
He found that alkyl halides produced mainly γ attack in isolated yields of 70-90%, while carbonyl compounds reacted preferentially at the α carbon, also in high yield. Mixtures of α and γ attack were obtained in nearly all cases, however. He also was able to show that if the counterion was zinc rather than lithium, the anions derived from 35 reacted with ketones and aldehydes exclusively at the α carbon of the allylic system.

Similarly, Still has shown that the silyl ethers 36 can be deprotonated, and the derived anions also react preferentially with alkyl halides at the γ position and with carbonyl compounds at the α position. As in Evans' work, all compounds 38 appeared with cis double bonds, leading Still to the notion that the reactive species in solution was 37. Compounds 38 were produced in 70-95% yield when $E^\ominus$ was an alkyl halide, and compounds 39 were produced in 70-90% when $E^\ominus$ was a carbonyl compound.
Still also offered a general rule of thumb for predicting the modes of reactivity for a given unsymmetrical allylic anion. According to this postulate, for unsymmetrical allylic anions where the lithium cation and the anion are closely associated, reaction with alkyl halides and protons occurs at the position of higher electron density, while reaction with carbonyl compounds occurs at the opposite site. Thus, for 40

\[
\begin{align*}
Y & \quad \text{Li} & \quad \text{Y} \\
40 & & 41 \\
\end{align*}
\]

where \(Y\) is an anion destabilizing group such as alkyl, -OR, or -NR\(_2\), the position of highest electron density, and hence the site of reaction with alkyl halides, is the \(\gamma\) position, as in 41. For \(Y = -SR\) or \(-BR\), however, the position of highest electron density is the \(\alpha\) carbon, as in 42, and the opposite regiochemistry obtains.

More recently, Evans has made use of the exclusive \(\alpha\)-attack of species 43 on ketones and aldehydes to develop an equivalent to 1 which, in effect, adds 1,4 to \(\alpha,\beta\)-unsaturated carbonyl compounds. 24

\[
\begin{align*}
\text{ZnCl} & \quad \Theta & \quad \Theta & \quad \Theta \\
X & \quad \text{R} & \quad \text{R} & \quad \text{R} \\
43 & & 44 & & \Delta [3,3] \\
\end{align*}
\]

\(X = \text{OR, SR}\)
Compound \(43\) adds to enones in high yield to give adducts \(44\), which rearrange on heating to the product ketones. The rearrangement to final product is a much milder process when \(X = SR\).

A scheme utilizing \([2,3]\) sigmatropic rearrangement of allylic sulfoxides has also been developed by Evans.\(^{25}\) For example, can be deprotonated with LDA and reacted with an alkyl halide to give \(46\). (The regiochemistry of addition is not as reliable with carbonyl compounds). The compounds \(46\) then rearrange very readily below room temperature to provide 50–80% overall yields of > 98% trans allylic alcohols, after cleavage of sulfur. This sequence, then, is equivalent to the use of the reduced form of \(2\).

Biellmann, some years earlier, had shown that allylic sulfides themselves could be deprotonated, and that the resulting allylic anions reacted with alkyl halides predominantly at the \(\alpha\) position.\(^{26}\) He also
participated in an investigation which found in part that the anion $47^-$ reacted with acetone primarily at the $\gamma$ carbon under a variety of conditions. These two studies established, though, that allylic sulfide anions could not be depended upon to provide exclusive regiochemistry of either type except in rare cases; mixtures normally obtained.

However, the idea of alkylation of an allylic sulfide anion was successfully used by Kondo and Masamune and also by Stotter in their independent but similar syntheses of Cecropia juvenile hormones. A key step in both sequences was the addition of $48^-$ to the indicated epoxide to achieve 70-90% yield of $49^-$ after dehydration. In that case, reaction of the anion $48^-$ with the epoxide occurred exclusively at the $\alpha$ carbon.

Seebach has investigated the alkylation reactions of the simplest sulfur substituted allylic anion, the dianion $50^-$. When reacted successively with two electrophiles, high yields (70-90%) of mixtures
of α and γ products are obtained. The γ adducts dominate, if only

\[ \text{HS} + \text{2 nBuLi} \xrightarrow{\text{TMEDA}} \text{2 Θ} \xrightarrow{\text{1. E}^1} \text{E}^1 \xrightarrow{\text{2. E}^2} \text{SE}^2 \text{E}^1 \text{(All cis)} \]

\[ \text{E}^1 = RX \text{ or } \text{R}^1 \xrightarrow{\text{R}} \text{O} \]

\[ \text{E}^2 = RX \]

slightly, in all cases. Further reactions of the γ product are illustrated for a specific case below. Those conversions established 50 as an

\[ \text{R} \xrightarrow{\text{CH}_3\text{SH}} \text{SCH}_3 \xrightarrow{\text{NBS CH}_3\text{CN/H}_2\text{O}} \text{Br} \xrightarrow{\text{R}} \text{75%} \text{CH}_3\text{CN/H}_2\text{O} \]

\[ \text{R} \xrightarrow{\text{AgNO}_3} \text{SCH}_3 \xrightarrow{\text{NBS CH}_3\text{CN/H}_2\text{O}} \text{R} \xrightarrow{\text{AgNO}_3} \text{60%} \text{CH}_3\text{CN/H}_2\text{O} \]

equivalent to 1, but one which requires separation of isomers to be effective.
Martin was able to achieve nearly exclusive (>95%) γ-alkylation of the anion \(5_1\), produced by sBuLi deprotonation of the corresponding allylic amine, with alkyl halides. However, treatment of \(5_1\) with a variety of carbonyl compounds led to nearly equal amounts of α and γ products. Additionally, if \(5_1\) was formed in the presence of zinc chloride, the resulting anion gave >95% α selectivity with carbonyl compounds, in line with Evans' work.

Ahlbrecht achieved more success with a more complicated allylic amine. The allylic anion \(5_2\), formed from the corresponding allylic amine with LDA in THF, undergoes the reactions shown; only γ reaction was observed. These reactions establish \(5_2\) as an equivalent of \(5\).
Seebach has very recently reported the metallated allylurea 53 which reacts almost exclusively at the \( \gamma \) position with carbonyl compounds in 80\% average yield.\(^{32}\)

Some disubstituted allylic systems have been examined. For example, Corey developed a new synthesis of \( \alpha,\beta \)-unsaturated aldehydes by using alkylation and subsequent hydrolysis of the allyl anion 55.\(^{33}\) Treatment of 54, produced in a short sequence from epichlorohydrin, with two equivalents of LDA produces the anion 55.

\[
\begin{align*}
\text{CH}_3\text{S} & \quad \text{SCH}_3 \\
\text{OCH}_3 & \\
\rightarrow & \\
2 \text{LDA} \\
\text{CH}_3\text{S} & \quad \text{SCH}_3 \\
\end{align*}
\]

As the anion is symmetrical, its reaction with alkylation agents can lead to only one product. Mercuric ion assisted hydrolysis then provides the desired unsaturated aldehyde. The reagent can also be

\[
\begin{align*}
\text{CH}_3\text{S} & \quad \text{SCH}_3 \\
\text{Br} & \\
\rightarrow & \\
\text{HgCl}_2 & \quad \text{H}_2\text{O} \\
\text{CH}_3\text{CN} & \\
\rightarrow & \\
\text{R} & \quad \text{O} \\
\text{H} & \\
90\%, R = \text{nC}_5\text{H}_{11} & \\
\end{align*}
\]
used to open epoxides as shown. That process has been used as a key step in a total synthesis of prostaglandin $\mathrm{F}_{2\alpha}$ (56). 34

$$\begin{align*}
\text{OCH}_3 + 55 & \rightarrow \text{OCH}_3 \\
\text{HO} & \rightarrow \text{HO} \\
\text{40\% other positional isomer}
\end{align*}$$
Taking a similar approach, Taguchi investigated the chemistry of the mixed disubstituted allylic anion \( \text{57} \). This anion, generated from the corresponding allyl compound with LDA, adds alkyl halides exclusively \( \alpha \) to sulfur, as may well have been predicted from a perusal of the literature on the anions generated from allylic ethers and sulfides. The compound \( \text{58} \) is obtained as a mixture of cis and trans isomers, which is converted to the corresponding \( \alpha,\beta \)-unsaturated aldehydes by mercuric ion catalyzed hydrolysis.

![Chemical structure](image)

\[ \phi S \rightarrow_{\text{LDA}} \phi S \rightarrow_{\text{RX}} + \]

\( \text{57} \)

\( \text{58} \)

60-80%

\[ \text{58} \rightarrow_{\text{Hg}^{+2}} \]

\[ \text{HCl/CH}_3\text{CN} \rightarrow \]

\[ \text{H} \rightarrow \]

70-95%

Martin has developed a Wittig reagent which adds a new twist to the theme of \( \beta \)-acylcarbanions. Triphenylphosphine hydrobromide reacts with methoxyallene to give the adduct \( \text{59} \). When \( \text{59} \) is
deprotonated with BuLi, the resulting ylid attacks carbonyl compounds to give dienes 60. Hydrolysis of 60 gives compounds 61 in 50-70% overall yield. Thus, 61 is the result of a reductive addition of 2; the original carbonyl oxygen has been removed.

Sturtz has explored some interesting chemistry of allylic anions having phosphonamide substituents. His investigations have led to a reagent system which functions as an equivalent of a β-carboxyl anion. The general scheme is presented below; substituents can be borne at the β and γ carbons, but are left out of the example for clarity. When the allylic system 62 is deprotonated with nBuLi, the resulting allylic anion rearranges to the alkoxide 63. This species may in turn be deprotonated with nBuLi to derive the dianion 64. This dianion reacts exclusively at the γ position with both epoxides and carbonyl compounds to provide lactones after hydrolysis, with yields ranging from 30-50%.
Finally, in a very recent publication containing many useful references to the homo enolate anion field in general, Evans has also made use of phosphonamide stabilized allylic anions. He has shown that the phosphorodiamidite will add to \( \alpha,\beta \)-unsaturated aldehydes to give species of the general form. These compounds can be deprotonated with nBuLi to provide the allylic anions, which undergo reactions with both carbonyl compounds and alkylating agents to give nearly exclusively the products of \( \gamma \) attack; significant mixtures of \( \alpha \) and \( \gamma \) were obtained only when methyl iodide was used. The adducts and can be transformed into lactones and esters in good yield as shown in the second following figure.
\[ \text{Et}_3\text{Si-O-P[N(CH}_3\text{)\textsubscript{2}]_2} + R\text{-C}==\text{CH} \rightarrow R\text{-C}==\text{CH}_2\text{Y} \]

\[ \text{nBuLi} \rightarrow R\text{-C}==\text{CH}_{\text{OSiEt}_3}\text{Y} \]

\[ R = H, \phi, \text{CH}_3 \]

\[ Y = \text{P[N(CH}_3\text{)\textsubscript{2}]_2} \]

\[ \text{F}^- / \text{THF} \rightarrow R^2\text{-CO}_2R^1 \rightarrow 60-70\% \text{ overall} \]

\[ \text{CH}_3\text{O}^- \rightarrow \text{CH}_3\text{OH} \rightarrow R^1\text{-CO}_2\text{CH}_3 \rightarrow 60-70\% \text{ overall} \]
PART TWO: CARBANIONS α TO SILICON

Silicon is less electronegative than carbon, as indicated by its position directly below carbon in the periodic table. It is energetically favorable to replace carbon-silicon bonds with oxygen-silicon or halogen (usually fluorine)-silicon bonds, since the latter are stronger. Organosilicon compounds undergo nucleophilic substitution at silicon much more easily than corresponding carbon analogs, an effect which is due not only to the reduced electronegativity of silicon compared with carbon, but also the the presence of empty d-orbitals on silicon. These are available for coordination with a nucleophile before departure of the leaving group. Silicon is able to stabilize an α-carbanion, but not so well as sulfur or phosphorous.

In general, organosilanes can be metalated by alkylolithiums; usually nBuLi or sBuLi has been used. Thus tetramethylsilane can be deprotonated with nBuLi in the presence of TMEDA, but the anion mixture gives only 36% yield of product when reacted with chlorotrtrimethylsilane. α-Halosilanes react with magnesium or lithium

\[
\text{(CH}_3\text{)}_4\text{Si} \xrightarrow{n\text{BuLi}} \text{(CH}_3\text{)}_3\text{SiCH}_2\text{Li} \xrightarrow{\text{TMSCl}} \text{(CH}_3\text{)}_3\text{Si} \xrightarrow{\text{Si(CH}_3\text{)}_3}
\]

to produce the corresponding metalated species. In fact, this process (the full scheme is shown below, second figure) is the only method for making α-lithiovinylsilanes, since reaction of alkyl-lithiums with vinylsilanes results only in addition of the alkyl-lithium
to the vinylsilane double bond, producing a saturated α-lithiosilane.\(^{43}\) (That this undesired process is also synthetically useful will be illustrated later.)

\(\alpha\)-Silyl carbanions can also be prepared by cleavage of carbon-silicon bonds, usually with oxygen nucleophiles; the reaction is
favored by the difference in bond energies mentioned earlier. Methyl lithium will not perform an analogous displacement.

\[
\text{[(CH}_3\text{)}_3\text{Si}])_4\text{C} \xrightarrow{\text{NaOCH}_3 / \text{HMPA}} \text{[(CH}_3\text{)}_3\text{Si}])_3\text{CNa} + \text{(CH}_3\text{)}_3\text{SiOCH}_3
\]

Phosphorous and sulfur ylides containing silicon have been prepared by silylation of the unsubstituted ylid and subsequent deprotonation.

\[
\phi_3\text{P=CH}_2 + \text{(CH}_3\text{)}_3\text{SiCl} \xrightarrow{\text{1. RX}} \phi_3\text{P=CHSi(CH}_3\text{)}_3
\]

\[
\text{R}_2\text{N-S=CHR'} + \text{(CH}_3\text{)}_3\text{SiCl} \xrightarrow{\text{1. RX}} \text{R}_2\text{N-S=CRR'Si(CH}_3\text{)}_3
\]

Possibly the most important uses of α-silyl carbanions are the Peterson reaction and its variants. The reaction was first described by D. Peterson in 1968. Treatment of a carbonyl compound with the Grignard reagent provides adduct. Mild acid hydrolysis

\[
\text{(CH}_3\text{)}_3\text{SiCH}_2\text{MgCl} \xrightarrow{\text{RX}} \text{(CH}_3\text{)}_3\text{SiOH}
\]

\[
\text{(CH}_3\text{)}_3\text{SiOH} \xrightarrow{\text{H}_2\text{O}^\oplus} \text{(CH}_3\text{)}_3\text{SiR'} + \text{H}_2\text{O}
\]
gives a $\beta$-hydroxysilane, which eliminates triethylsiloxide upon
treatment with potassium hydride or sodium hydride in THF to yield
an olefin. The reaction is thus an alternative to the Wittig reaction,
and has been touted as cleaner and operationally simpler.

The reaction has been used to convert the ketone 71 into $\beta$-gorgonene,
and $\beta$-ionone into the methylene derivative 72. In the latter example,
elimination to the olefin was achieved in situ by treatment of the
$\beta$-alkoxysilane intermediate with acetyl chloride, after which product
was presumably formed via the mechanism shown below.
Chan demonstrated an elegant application of the reactivity of alkyl-lithiums with vinylsilanes in his synthesis of the Gypsy moth sex pheromone, disparlure (76). The alkyl-lithium 73 added to triphenylvinylsilane to generate the new lithio species 74. This compound underwent the

\[
Li^+ \cdot Si^3 + CH_3CH_2CHO \rightarrow 75
\]

Peterson reaction with undecanal to give a 1:1 mixture of the geometric isomers of 75, which was converted into the final product. The corresponding Wittig reagent required several steps to prepare.

Hudrlik has shown that olefins can also be generated from \( \varepsilon \)-hydroxy-silanes by acidic treatment, and further that such olefins are formed with the opposite stereochemistry from those obtained in the basic treatment, for a given stereoisomer of the \( \varepsilon \)-hydroxysilane. This is illustrated below. Compounds 77 and 78, prepared independently, lead to the two geometrical isomers of 4-octene under the conditions
shown. Hudrlik also demonstrated that α-ketosilanes could be converted stereoselectively into olefins. Thus, 79 was reduced stereoselectively by diisobutylaluminum hydride to a single diastereomer, 80. This α-hydroxysilane then provided cis or trans olefinic products under the conditions shown.
Acid chlorides can be converted into $\beta$-ketosilanes using $\alpha$-silyl carbanions; these species can suffer nucleophilic attack at silicon to yield ketones.\footnote{53}

\[
\text{\((CH_3)_3SiCH_2MgCl + RCOCl \rightarrow R CO\text{Si(CH}_3)_3\)}
\]

\[
\text{Nuc}
\]
The bis-trimethylsilyl carbanion [81] has been prepared, and its reactions with carbonyl compounds lead nonstereoselectively to moderate yields of vinylsilanes. Vinyl silanes can be epoxidized with peracids, and the resulting \( \alpha, \beta \)-epoxysilanes yield aldehydes upon acid hydrolysis.

The cuprate [82] has been prepared and added to cyclohexenone to provide, after a further series of steps, the product of acyl anion addition in a conjugate sense.
It is possible to deprotonate $\alpha,\beta$-epoxysilanes to silicon, and the anions made in this way react with a variety of electrophiles.\(^5^7\)

$\alpha,\beta$-Epoxysilanes also rearrange at high temperatures (600°C) to silylenol ethers.\(^5^8\)

\[
\begin{align*}
\phi_3\text{Si} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \q
Vinyl sulfoxides and vinyl phosphonates can be prepared by the reaction of the anions \( \text{84} \) with carbonyl compounds. These are special cases of the Peterson reaction, and proceed nonstereospecifically.\(^{60}\)

\[
\begin{align*}
(\text{CH}_3)_3\text{Si} & \text{X} & \text{Li} & \xrightarrow{\text{R1 CO}} & \text{R} & \text{CO} & \text{R1} & \text{X} \\
\text{84} & & & \text{X} = -\text{P(\text{OEt})}_2, -\text{S}\phi \\
\end{align*}
\]

Reductive nucleophilic addition of a carboxyl group to aldehydes and ketones can be effected with dithiane \( \text{85} \) via a ketene thiaoacetal,\(^{61}\) while compound \( \text{86} \) functions as a formyl anion equivalent in reactions with alkylating agents.\(^{62}\)

\[
\begin{align*}
\text{85} & \xrightarrow{\text{R CO}} \text{R} & \text{CO}_2 & \text{H} \\
\end{align*}
\]

Silicon substituted allylic anions have been reported.\(^{63}\) The lithio derivative of triphenylallylsilane \( \text{87} \) reacts with electrophiles...
to give mixtures of \( \alpha \) and \( \gamma \) attack, with \( \gamma \) attack being the major process. The corresponding Grignard reagent displays the opposite trend. The disilylated anion \( \overset{88}{\phi_3Si} \) is also known, but few of its

\[
\begin{align*}
\phi_3Si & \xrightarrow{nBuLi, TMEDA} \phi_3Si^+ \\
& \xrightarrow{E^+} \phi_3Si= \ E + \phi_3Si
\end{align*}
\]

\[ E = CO_2, \ \phi \phi \phi, \ \overset{87}{\circ} \]

\[
\begin{align*}
M & = Li \quad \text{major} \quad \text{minor} \\
\text{TMSCl, CH}_3I & \quad M = MgBr \quad \text{minor} \quad \text{major}
\end{align*}
\]

reactions have been reported. Chan has been able to produce

\[
\begin{align*}
\overset{88}{\phi_3Si} \overset{88}{\phi_3Si} \overset{88}{\phi_3Si}
\end{align*}
\]

moderate yields of 1,3 dienes by reaction of the trimethylsilylallyl anion with carbonyl compounds under the influence of magnesium bromide.\(^{64}\)

\[
\begin{align*}
(CH_3)_3Si & \xrightarrow{sBuLi, HMmPA} (CH_3)_3Si \overset{88}{\phi_3Si} \\
& \xrightarrow{1. MgBr_2} (CH_3)_3Si \overset{88}{\phi_3Si} \\
& \xrightarrow{2. R \ \text{R}} \ (CH_3)_3Si \overset{88}{\phi_3Si}
\end{align*}
\]

\[
\begin{align*}
\overset{88}{\phi_3Si} \overset{88}{\phi_3Si} \overset{88}{\phi_3Si}
\end{align*}
\]

major

\[
\begin{align*}
\overset{88}{\phi_3Si} \overset{88}{\phi_3Si} \overset{88}{\phi_3Si}
\end{align*}
\]

minor
Seyferth has reported the production and reactions of the gem-chloro-(trimethylsilyl)allyl anion (89). That species produces mixtures of α and γ attack in all cases examined, including methyl iodide, aldehydes, and ketones, except when it reacts with trimethylsilyl chloride and triethyltin chloride. Those cases produce γ adducts exclusively.
DISCUSSION

Allyltrimethylsilane is a commercially available compound,\textsuperscript{66} that can be deprotonated with sBuLi in THF in the presence of an equivalent of TMEDA to give the trimethylsilylallyl anion (I). The reaction

\begin{equation}
(CH_3)_3Si \overset{\text{sBuLi/THF/Ar}}{\overset{\text{TMEDA/\(-78^\circ\text{C}\)}}{\longrightarrow}} (CH_3)_3Si^\ominus
\end{equation}

mixture requires warming from \(-78^\circ\text{C}\) to \(-40^\circ\text{C}\) for complete formation of the anion I. The solution may then be recooled to \(-78^\circ\text{C}\) for addition of the substrate, or it may be warmed further to at least \(0^\circ\text{C}\) and used. The anion I, having ambident reactivity, could have produced dienes from carbonyl compounds by attack from the \(\alpha\) carbon of the allylic system followed by the loss of trimethylsiloxide from the initial adduct (see Scheme I). Reaction at the \(\gamma\) carbon was the desired process, as \(\delta\)-hydroxy vinylsilanes would be the products. The \(\gamma\) adducts are, in principle, convertible into carbonyl compounds. In fact, when the anion I was treated with a variety of carbonyl compounds, \(\delta\)-hydroxy vinylsilanes were the sole products (see Table I). The adducts were obtained nearly pure from the crude reaction mixtures; they did not require purification for use in subsequent reactions. The vinylsilane double bond was exclusively trans in all cases, from proton and \(^{13}\)NMR spectra (\(J_{AB} = 19\text{Hz}\)).
$\gamma + RCO \rightarrow RCOOR \rightarrow \text{Si(CH}_3\text{)}_3 \rightarrow \text{Si(CH}_3\text{)}_3$

**Table I**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Vinyl silane</th>
<th>(yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{HO-CH}_3\text{Si(CH}_3\text{)}_3$</td>
<td>2</td>
<td>$(88%, 65%$ distilled)</td>
</tr>
<tr>
<td>$\text{HO-CH}_3\text{Si(CH}_3\text{)}_3$</td>
<td>3</td>
<td>$(84%, 53%$ distilled)</td>
</tr>
<tr>
<td>$\text{HO-CH}_3\text{Si(CH}_3\text{)}_3$</td>
<td>4</td>
<td>$(&gt;95%)$</td>
</tr>
<tr>
<td>$\text{HO-CH}_3\text{Si(CH}_3\text{)}_3$</td>
<td>5</td>
<td>$(89%)$</td>
</tr>
<tr>
<td>$\text{HO-CH}_3\text{Si(CH}_3\text{)}_3$</td>
<td>6</td>
<td>$(&gt;98%)$</td>
</tr>
</tbody>
</table>
Several different methods were found to unmask the carbonyl functionality inherent in the vinylsilane, but all except one proceeded through the corresponding 6-hydroxy-α,β-epoxysilanes. The epoxysilanes were produced cleanly and in high yield (80-95%) from the vinylsilanes by treatment with meta-chloroperoxybenzoic acid in dichloromethane. These were rapid reactions, usually requiring 10-30 min, during which time the temperature was raised from 0°C to room temperature. Often, this oxidation step improved the purity of the material, by TLC analysis.

Treatment of the 6-hydroxy-α,β-epoxysilane derived from cyclopentanone with peracetic acid led to moderate yields of the corresponding spirolactone, but the crude product required separation. Jones oxidation of the 6-hydroxy-α,β-epoxysilane derived from cyclohexanone produced approximately the same result. However, when 6-hydroxy-α,β-epoxysilanes were treated with BF₃·Et₂O in neat methanol, the corresponding spirocyclic methyl lactols were produced in good yield (50-95%) nearly pure. These compounds could be converted quickly, cleanly and efficiently (60-80%) to spirolactones by use of the Jones oxidation. These processes are outlined in Scheme II. (See pg 68 for two steroid examples.) Thus, the highest yields of purest products were formed via the methyl lactols, even though that procedure was a step longer.
Table II

<table>
<thead>
<tr>
<th>Substrate</th>
<th>5-Hydroxy-(\alpha,\beta)-epoxysilane (yield)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="#">Image of compound with OH and Si(CH(_3)(_3))</a></td>
<td><a href="#">Image of compound with OH and O-Si(CH(_3)(_3))</a> (78%)</td>
</tr>
<tr>
<td><a href="#">Image of compound with HO and Si(CH(_3)(_3))</a></td>
<td><a href="#">Image of compound with HO and O-Si(CH(_3)(_3))</a> (95%)</td>
</tr>
<tr>
<td><a href="#">Image of compound with HO and Si(CH(_3)(_3))</a></td>
<td><a href="#">Image of compound with HO and O-Si(CH(_3)(_3))</a> (94%)</td>
</tr>
<tr>
<td><a href="#">Image of compound with HO and Si(CH(_3)(_3))</a></td>
<td><a href="#">Image of compound with HO and O-Si(CH(_3)(_3))</a> (89%)</td>
</tr>
</tbody>
</table>

*Yield of material pure enough to use directly in subsequent reactions.
Table III

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product (Yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Substrate 8" /></td>
<td><img src="image2" alt="Product 11" /> (97%)*</td>
</tr>
<tr>
<td><img src="image3" alt="Substrate 9" /></td>
<td><img src="image4" alt="Product 12" /> (78%)*</td>
</tr>
<tr>
<td><img src="image5" alt="Substrate 10" /></td>
<td><img src="image6" alt="Product 13" /> (51%)*</td>
</tr>
<tr>
<td><img src="image7" alt="Substrate 11" /></td>
<td><img src="image8" alt="Product 14" /> (74%)**</td>
</tr>
<tr>
<td><img src="image9" alt="Substrate 12" /></td>
<td><img src="image10" alt="Product 15" /> (66%)37**</td>
</tr>
<tr>
<td><img src="image11" alt="Substrate 13" /></td>
<td><img src="image12" alt="Product 16" /> (62%)37**</td>
</tr>
</tbody>
</table>

*Yields of material pure enough to use directly in subsequent reactions.
**Isolated yield.
Additionally, treatment of the 6-hydroxy vinylsilanes themselves with peracetic acid led to moderate (50-60%) yields of spirolactones. Although the crude products from these reactions also required separation to obtain pure material, this reaction has the advantage of being the second step of a two step sequence leading from a carbonyl compound to the corresponding spirolactone.

These reactions, summarized below, establish the trimethylsilyl-allyl anion as a useful homoenolate anion equivalent. It is not only nucleophilic enough to provide high yields of initial adducts, but an efficient, high yielding process is available to release the masked carbonyl group.

We wanted to investigate the reaction of an electrophilic species with 6-hydroxy vinylsilanes, and we hoped thereby to expand the versatility of the 6-hydroxy vinylsilane-to-spirolactone sequence. That is, if 6-hydroxy vinylsilanes suffered electrophilic attack with ring closure to the tetrahydrofuran derivative shown in Scheme III, then it should be possible to produce spirolactones by nucleophilic attack on silicon followed by hydrolysis and oxidation of the intermediate dinydrofuran. Of course, E would have to be an atom or group of atoms able to support either a positive or negative charge.
This sequence completely eliminates the need to produce a 6-hydroxy-
α,β-epoxysilane; it would thus be useful in systems which would not
tolerate peracid. A model study was undertaken, using as substrate
the 6-hydroxy vinylsilane derived from adamantanone. This compound
is crystalline and is available in high yield from the process described
earlier.
Thus, 2-(3-trimethylsilylprop-2-enyl)-adamantan-2-ol (6) was treated, under a variety of conditions, with both molecular chlorine and bromine. These reactions all provided very messy mixtures of compounds. Treatment with phenylselenyl bromide generated in situ by cleavage of diphenyldiselenide with bromine provided no identifiable products. However, when the model 6-hydroxy vinylsilane was reacted with N-bromosuccinimide in THF at room temperature, two major products appeared, concomitant with complete destruction of starting material. It was then found that one product or the other could be produced alone at will by varying the temperature at which the reaction was run. When the model system 6 was treated with N-bromosuccinimide in THF at 0°C, cyclization did indeed occur, but the product was the oxetane \( \text{17}(92\%) \) rather than the desired tetrahydrofuran derivative. \(^{69}\) Alternatively, if 6 was treated with N-bromosuccinimide in THF at reflux, the crystalline silylbromodiene \( \text{18} \) was obtained as the sole product (>95%). Compound 18 apparently arose from in situ acid
Scheme IV

17

NBS/THF
0°C

cat. THF/
HCl reflux

19

DMSO
40-45°C
KF.2 H_2O

NBS/THF
reflux

6

18
catalyzed ring opening of the oxetane 17, followed by loss of water, since when 17 was refluxed in THF in the presence of a catalytic amount of hydrochloric acid, 18 was obtained. The structure of compound 18 was firmly established by subsequent reactions.

When 18 was reacted with potassium fluoride dihydrate in DMSO at -40°C, the sole product, produced in quantitative yield, was the bromodiene 19. The configuration of the vinyl bromide double bond in this molecule was confirmed as the one shown in two ways. First, computer modeling of the proton NMR for pure 19 showed coupling constants for the three olefinic protons which indicated that the terminal double bond was cis. The calculated coupling constants are shown in Scheme V. The second confirmation of structure made use of the sequence shown in Scheme VI. When the oxetane 17 was treated

Scheme V

![Scheme V](image)

\[ J_{1,2} = 10.8 \text{Hz} \]
\[ J_{2,3} = 6.96 \text{Hz} \]
\[ J_{1,3} = -1.21 \text{Hz} \]
with potassium fluoride dihydrate in DMSO at 40-45°C, the bromoalcohol \( \text{20} \) was produced (76%). When \( \text{20} \) was dehydrated using thionyl chloride and pyridine, compound \( \text{19} \) was once more obtained; spectral data for the compound \( \text{19} \) produced via the two different routes were identical. Further, the \( \text{cis} \) double bond of \( \text{20} \) is predicted by stereochemical considerations. That is, when \( \text{6} \) is treated with NBS in THF at 0°C, the oxetane \( \text{17} \) is produced with the relative stereochemistry shown (see Scheme VII). If a \text{trans} coplanar arrangement is assumed for the
involved C-O and C-Si bonds during ring opening, then the product should have a \textit{cis} double bond, as shown.
Therefore, the compound $19$ does, in fact, possess the configuration shown about the terminal double bond, which means that $18$ must have the configuration shown. That requires explanation, as does the fact that a proton, not the trimethylsilyl group, was lost from compound $17$ during the formation of $18$. Conventional thought in organosilicon chemistry until now would dictate that any time a positive charge is produced from a trimethylsilyl group, and is in the same plane as the C-Si bond, that group should be lost to provide an unsaturated, desilylated product. An explanation for both proton loss and double bond stereochemistry is shown in Scheme VIII.

When $17$ reacts with acid (HBr in the NBS reaction mixture) at THF reflux, loss of water occurs to provide the allylic cation shown. This cation can exist as the 5-membered bromonium ion $21$. Models show that in $21$, the trimethylsilyl group prefers a quasi-equatorial conformation, while the proton on the same carbon is quasi-axial. The adamantyl group may enhance these preferences, by pushing the trimethylsilyl group out of the way. In its quasi-axial orientation, the proton's C-H bond is perfectly aligned with the $\pi$ orbitals of the adjacent double bond, while the trimethylsilyl group is necessarily out of that plane. Due to this favorable overlap, the proton is lost to quench the positive charge on the ring, rather than the trimethylsilyl group, thus leading to the observed product. The 5-membered ion $21$ also accounts for the cis stereochemistry of the vinyl bromide formed upon proton loss.
Thus, we have shown that bromine addition to a δ-hydroxy vinylsilane can lead cleanly and efficiently to interesting functional arrays, but not yet to a non-epoxidative procedure for the production of spiro-lactones.

There are a number of steroidal compounds containing spirolactones appended at the 17 position which are diuretics by virtue of the fact that they are aldosterone blockers. Some of these are shown in Scheme IX. Many others have been synthesized, but most are analogs.
of 22, such as 24. Since 24 is much more active than 22, and 22 is easily convertible to 24, an efficient synthesis of 22 is highly desirable. The most often used synthesis of 22 to date is shown in Scheme X. 73

We undertook a synthesis of 22 based upon the methodology developed earlier for the introduction of spirolactone units at carbonyl sites.

Unfortunately, we found that the trimethylsilylallyl anion made in the usual way would only add to the 17 carbonyl of 3-methoxyandrost-3,5-dien-17-one (23) in 30-40% isolated yield after hydrolysis of the dienol ether; the balance of the material was recovered starting material, presumably arising from enolization. This reaction required 10 equivalents of reagent, and the addition was done at 0°C. However, an observation was made in the Kalamazoo laboratories of The UpJohn
Company\textsuperscript{74} which surmounted this problem. They omitted TMEDA from the reaction mixture, and substituted an equivalent amount of anhydrous zinc chloride. This enhanced the effective nucleophilicity of the anion to the point that after acid hydrolysis, 85-95\% of the desired product was obtained, nearly pure without chromatography, using only 4.5 equivalents of the reagent. This was a surprising discovery, in light of the fact that other similar allyl anion systems undergo exclusive $\alpha$ attack when treated in the same way.\textsuperscript{75}

\begin{equation}
\begin{array}{c}
\text{CH}_3 O \\
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
\text{CH}_3 O \\
\end{array}
\end{equation}

If done carefully, meta-chloroperbenzoic acid oxidation of best poor yields of the corresponding epoxide, always accompanied by extensive decomposition of the ring A enone. However, the Sharpless oxidation\textsuperscript{76} provided high yields (90-95\%) of very clean product, the $\delta$-hydroxy-$\alpha,\beta$-epoxysilane $\text{25}$. Direct production of the spirolactone from $\text{24}$ and $\text{25}$ were attempted, but yields were not good for those processes, and difficult chromatographic separations were required. The best route to $\text{22}$ was found to be through oxidation of the methyl
lactol 26, which was formed upon treatment of the epoxide 25 with 
$\text{BF}_3 \cdot \text{Et}_2 \text{O}$ in methanol (90–95%). (See Scheme XI). Jones oxidation

25 \[ \text{BF}_3 \cdot \text{Et}_2 \text{O} \quad \text{CH}_3 \text{OH} \] 26

22

$\text{H}_2 \text{CrO}_4$ 
$\text{H}^\circ$
of 26 provided 22 in 50% yield after isolation by chromatography over silica gel. None of the intermediates along this sequence from 23 to 22 require purification, and the overall yield on a 5g run is 35-40% pure compound after chromatography following the Jones procedure.

This process was applied to estrone methyl ether (27)\(^{77b}\), providing 25% overall yield of pure spirolactone 31. This compound can be seen as a possible precursor to 23. Part of the reason for the lower overall yield in this case is that chromatography was required after the initial step. From that operation, we obtained a 70% yield of 28 and a 20% yield of 32.\(^{77b}\) The origin of 32 from the reaction of estrone methyl ether and the trimethylsilylallyl anion is not yet known. The by-product 32 interfered with the subsequent Sharpless oxidation\(^{76,77a}\), and had to be removed from the product mixture prior to that operation.
These reactions establish that the trimethylsilylallyl anion is a useful homoenolate anion equivalent which is nucleophilic enough under defined conditions to add in high yield to a carbonyl group even as highly hindered and easily enolizable as those in the 17 position of a steroid. In fact, only one other homoenolate anion equivalent has ever added to 17-ketosteroids in useful yields, even though numerous such equivalent species are known.
General Experimental Information

All proton NMR spectra were obtained on either a Varian A-60 spectrometer or a Varian EM-360 spectrometer. Melting points were taken on a Thomas Hoover melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer 267 Grating Infrared Spectrophotometer. Elemental analyses were done by M-H-W Laboratories in Phoenix, Arizona. Mass spectral data were obtained on a Consolidated Electronic MS-9 Double Focusing mass spectrometer.
EXPERIMENTAL

4-Cyclohexyl-4-hydroxy-1-trimethylsilylbut-1-ene. (4). To a solution of sBuLi (36mmole, 36ml of a 1.0M solution in cyclohexane) and TMEDA (36mmole, 4.2g, 5.5ml) in dry THF (10ml) under argon at -78°C was added allyltrimethylsilane (36mmole, 4.1g, 5.7ml) in a dropwise fashion. The resulting solution was warmed to -40°C for 10-15min recooled to -78°C, and cyclohexane carboxaldehyde (18mmole, 2.0g, 2.2ml) was added dropwise. The reaction was followed by TLC (80% high petroleum ether, 20% EtOAc), and destruction of starting material gave rise to a set of twin spots. The reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO₄) solvent yielded 4.07g (100%) of crude product, pure enough for use in Subsequent reactions.

IR (neat, cm⁻¹): 3410m; 2920s; 1615m; 1450s; 1250s; 840s. NMR (δ, δ):
5.91 (mult, 2H, vinyl protons, J_AB = 18.5Hz); 2.43 (s, 1H, -OH);
2.23 (mult, 3H, protons γ and δ to -TMS); 2.0-1.0 (envelope, 11H, cyclohexyl ring); 0.16 (s, 9H, -SiMe). MS: C₁₃H₂₆OSi; calc: 226.175; obs: 226.176, 226 (85%), 211 (100%), 185 (59%).

2-(3-Trimethylsilylprop-2-enyl) adamantane-2-ol, (6). To a stirred solution of sBuLi (34mmole, 34ml of a 1.0M solution in cyclohexane) and TMEDA (34mmole, 3.9g, 5.1ml) in dry THF (10ml) under argon at -78°C was added allyltrimethylsilane (34mmole, 3.9g, 5.4ml). The solution was allowed to come to -40°C for 10-15min., then warmed further to 0°C for 20min. Adamantanone (6.7mmole, 1.0g) was added.
as a solution in THF (5ml) in a dropwise fashion. The solution was warmed to just below room temperature and stirred for 30min. The reaction was complete very quickly, as judged by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried solvent gave 1.77g (100%) of crude product (sublimes; mp 70-75°C), pure enough for use in subsequent reactions. IR (neat, cm⁻¹): 3400s; 2900s; 1615m; 1250s; 840s. NMR (CDCl₃/\(\phi;\delta\)): 5.87 (mult, 2H, vinyl protons); \(\int_{AB} = 18\)Hz); 2.48 (d, 2H, protons γ to -TMS, \(\int_{AX} = 6\)Hz); 1.77 (center of broad envelope, 14H, adamantyl system); 0.05 (s, 9H, -TMS). MS: \(\text{C}_{16}\text{H}_{26}\text{Si}\) (M⁺ - H₂O; loss of water from tertiary alcohol). calc: 246.180; obs: 246.181. 246 (28%), 231 (28%), 223 (100%). Analysis \(\text{C}_{16}\text{H}_{26}\text{Si}\) required: C 72.73, H 10.60; found: C 73.00, H 10.79.

1-(3-Trimethylsilylprop-2-enyl)cyclohexanol, (2). Allyltrimethylsilane (.13mole, 14.8g, 20.6ml) was added in a dropwise fashion to a stirred solution of sBuLi (.13mole, 92.8ml of a 1.4M solution in cyclonexane) and TMEDA (.13mole, 15.1g, 19.6ml) in dry THF (40ml) under argon at -78°C. The resulting solution was warmed to -30°C and stirred at that temperature for 30 min. The cyclohexanone (51mmole, 5.0g, 5.3ml) was added dropwise, and the reaction was followed by TLC (80% high petroleum ether, 20% EtOAc). When the reaction was judged to be finished by TLC, it was worked up by quenching it in saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with
water. Removal of the dried (MgSO\textsubscript{4}) solvent left 9.49g (88%) of the desired product, as an oil, contaminated with a trace of cyclohexanone. Vacuum distillation (bp 66-70°C at 0.025mmHg) provided 7.00g (65%) of pure product. IR (neat, cm\textsuperscript{-1}): 3410m; 2930s; 1615w; 1250m; 840m.

NMR (\(\delta\), \(\beta\)): 6.03 (mult, 2H, vinyl protons; \(J_{AB} = 18.5\)Hz); 2.37 (d, 2H, protons \(\gamma\) to -TMS; \(J_{AX} = 6\)Hz); 1.58 (s, 10H, ring protons); 0.21 (s, 9H, -TMS). MS: (M\textsuperscript{+} - H\textsubscript{2}O; loss of water from tertiary alcohols) C\textsubscript{12}H\textsubscript{22}Si: calc: 194.149; obs: 194.150, 197 (48%), 194 (100%), 179 (100%). Analysis: required C 67.92, H 11.32; found C 68.14, H 11.50. (CDCl\textsubscript{3}/TMS; H\textsubscript{2}): 141.762, 135.451 (vinyllic carbons); 71.075 (hydroxyl-bearing carbon); 49.908, 25.828 (allylic carbon and carbon \(\gamma\) from -OH bearing carbon); 37.576, 22.235 (four carbons \(\alpha\) and \(\beta\) from -OH bearing carbon); 1.165 (-CH\textsubscript{3}'s on -TMS).

1-(3-Trimethylsilylprop-2-enyl)cyclopentanol, (3). Allyltrimethylsilane (.16mole, 18.2g, 25.3ml) was added in a dropwise fashion to a stirred solution of sBuLi (.15mole, 107ml of a 1.4M solution in cyclohexane) and TMEDA (.15mole, 17.4g, 22.6ml) in dry THF (50ml) under argon at -75°C. The solution was allowed to come slowly to -30°C, and was stirred at that temperature for 30 min. Cyclopentanone (60mmole, 5.0g, 5.3ml) was added dropwise. The reaction was finished immediately, as judged by TLC (80% high petroleum ether, 20% EtOAc). It was quenched by pouring it into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO\textsubscript{4}) solvent gave 9.98g (84%) of the desired adduct. The product was purified by vacuum distillation, giving 6.25g (53%) of pure product (bp 66-70°C at 0.025mmHg). IR (neat, cm\textsuperscript{-1}): 3400s; 2950s; 1615m;
1247s; 864s; 840s. NMR (δ, δ): 6.13 (comp mult, 2H, vinyl protons, \( J_{\text{AB}} = 19\text{Hz} \)); 2.50 (d, 2H, protons γ to -TMS, \( J_{\text{AX}} = 6\text{Hz} \)); 2.24 (s, 1H, -OH); 1.73 (s, 8H, ring protons); 0.20 (s, 9H, -TMS). MS: \( \text{C}_{11}\text{H}_{20}\text{Si}(M^+ - \text{H}_2\text{O}; \text{loss of water from tertiary alcohol}) \): 183 (100%), 180 (79%), 169 (69%).

1-(3-Trime thylsilylprop-2-enyl)cyclohex-2-en-1-ol (5). Allyltrimethylsilane (15mmole, 1.7g, 2.4ml) was added dropwise to a stirred solution of sBuLi (15mmole, 15ml of a 1.0M solution in cyclohexane) and TMEDA (15mmole, 1.7g, 2.2ml) in dry THF under argon at -75°C. The solution was allowed to warm to -40°C for 10-15min., then recooled to -75°C. Cyclohexenone (10mmole, 1.0g, 1.0ml) was added dropwise. The reaction was finished instantly, as judged by TLC (80% high petroleum ether, 20% EtOAc), and gave one major and one minor product. The reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 1.86g (89%) of what appeared via spectral data to be the 1,2 adduct contaminated by some of the 1,4 adduct. The product was purified by vacuum distillation (bp 68-70°C at .2mmHg). IR (neat, cm⁻¹): 3420s, 2960s, 1620m, 1250s, 850s. NMR (δ, δ): 6.05 (comp. mult, 4H, overlapping vinyl systems); 2.45 (d, 2H, protons γ to -TMS, \( J_{\text{AX}} = 6\text{Hz} \)); 1.75 envelope, 6H, ring protons); 0.17 (s, 9H, -TMS). MS: \( \text{C}_{12}\text{H}_{22}\text{OSi} \): calc: 210.144; obs: 210.144.

4-Cyclohexyl-1,2-epoxy-4-hydroxy-1-trimethylsilylbutane (7). 4-Cyclohexyl-4-hydroxy-1-trimethylsilylbut-1-ene (4) (1.9mmole, .5g) was dissolved in dichloromethane and the resulting solution stirred
at 0°C. Meta-chloroperoxybenzoic acid (2.9 mmole, 0.48 g) was added and the solution allowed to come to room temperature. The reaction was worked up when a faint starting material spot was still visible by TLC (80% high petroleum ether, 20% EtOAc), to prevent over-oxidation. The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 0.36 g (78%) of a product whose spectral data indicated it to be the desired compound, contaminated with a trace of starting material (visible by IR and NMR). IR (neat, cm⁻¹): 3420m; 2930s; 1250m; 845s. NMR (δ, δ): 3.07 (envelope, 1H, proton p to -TMS); 2.0–1.0 (envelope, 15H, ring protons and others); 0.18 (d, 9H, isomeric -TMS groups).

2-(2,3-Epoxy-3-trimethylsilylpropyl)adamantan-2-ol (8) (not produced).

Triton B (0.114 mmole, 19.1 mg, 0.05 ml of a 40% solution in methanol) was added to a solution of 2 (1.14 mmole, 0.3 g) and t-butyldihydroperoxide (1.25 mmole, 0.11 g, 0.12 mm) in benzene (5 ml) at room temperature. The reaction was monitored by TLC (80% high petroleum ether, 20% EtOAc), and did not proceed, even upon addition of a further equivalent each of t-butyldihydroperoxide and Triton B.

2-(2,3-Epoxy-3-trimethylsilylpropyl)adamantan-2-ol (8). In dry CH₂Cl₂ (15 ml) δ (3.8 mmole, 1.0 g) was dissolved and stirred at 0°C. Meta-chloroperoxybenzoic acid was added in portions over several hours until the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc). The solution was poured into aqueous sodium sulfite layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with aqueous sodium bicarbonate
and water. Removal of the dried (MgSO₄) solvent gave 1.01g (95%) of crude product as white crystals of sufficient purity to use in subsequent reactions. IR (Nujol mull, cm⁻¹): 3400s; 2900s; 1250m, 850m. NMR (CDCl₃/δ; δ): 2.99 (mult, 1H, proton β to -TMS); 2.3-1.9 (envelope, 5H, protons α and γ to -TMS, and protons α to -OH); 1.77 (s, 12H, adamantyl system); 0.04 (s, 9H, -TMS). MS: C₁₆H₂₆OSi (M⁺ - H₂O; loss of water from tertiary alcohol): calc: 262.176; obs: 262.176. 263 (29%), 262 (100%), 248 (53%).

1-(2,3-Epoxy-3-trimethylsilylpropyl)cyclohexanol (9). Meta-chloroperoxycarboxylic acid (1.2mmole, 0.21g) was added to a stirred solution of 1-(3-trimethylsilylprop-2-enyl)cyclohexanol (2) (0.8mmole, 0.17g) in dichloromethane at 0°C. A rapid reaction occurred, giving a single product, as judged by TLC (80% high petroleum ether, 20% EtOAc). The reaction was quenched in saturated aqueous sodium bisulfite layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with saturated aqueous sodium bicarbonate and water. Removal of the dried (MgSO₄) solvent gave 0.17g (94%) of the desired product of sufficient purity to use in subsequent reactions. IR (neat, cm⁻¹): 3430m; 2920s; 1245s; 840s. NMR (δ, δ): 3.28 (mult, 1H, proton β to -TMS); 2.08 (d, 2H, protons γ to -TMS); 1.9-1.5 (envelope, 10H, ring protons); 0.19 (s, 9H, -TMS). MS: M⁺ - H₂O: C₁₆H₂₆OSi; calc: 210.144; obs: 210.144. 210 (100%), 207 (36%), 195 (83%).

1-(2,3-Epoxy-3-trimethylsilylpropyl)cyclopentanol (10). 1-(3-Trimethylsilylprop-2-enyl)cyclopentanol (3) (2.0g, 10nmole) was taken up in dichloromethane (10ml) and the resulting solution was stirred at 0°C. Meta-chloroperoxycarboxylic acid (1nmole, 1.9g, 2.4g of material 80-90% in meta-chloroperoxycarboxylic acid) was added, and the reaction
mixture was allowed to come to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the reaction mixture was poured into saturated aqueous sodium bisulfite layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with aqueous sodium bicarbonate and water. Removal of the dried (MgSO₄) solvent gave 1.90g (89%) of crude product of sufficient purity for use in subsequent reactions. IR (neat, cm⁻¹): 3450m; 2960s; 1252s; 845s. NMR 1.9-1.5 (mult, 10H, ring protons and protons γ to -TMS); 0.07 (s, 9H, -TMS). MS: C₁₁H₂₀O₆ (M⁺ - H₂O; loss of water from tertiary alcohol): calc: 196.128; obs: 196.129. 196 (89%), 185 (74%), 181 (100%).

2-Methoxyadamantanespiro-2'-tetrahydrofuran (II). 2-(2,3-Epoxy-3-trimethylsilylpropyl)-adamantan-2-ol (8) (2.7mmole, .75g) was dissolved in methanol (5ml) and the resulting solution was stirred at 0°C. Then BF₃·Et₂O (6.8mmole, .96g, .83ml) was added dropwise, after which the reaction was allowed to come slowly to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .58g (97%) of crude product, pure enough for use in subsequent reactions. IR (neat, cm⁻¹): 2910s; 1455m; 1205m; 1105s; 1050s. NMR (CCl₄/δ, δ): 4.85 (mult, 1H, proton between oxygens); 3.26 (s, 3H, -OCH₃); 2.5-2.0 (mult, 6H, protons α to spiro-carbon and protons in the lactol ring); 1.81 (mult, 12H, adamantyl protons).
1-Oxa spiro[4.5]decane, (12). 1-(2,3-Epoxy-3-trimethylsilylpropyl)-cyclohexanol (9) (6.6mmole, 1.5g) was taken up in neat methanol and the solution was stirred at 0°C. BF₃·Et₂O (13mmole, 1.8g, 1.6ml) was added, and the solution was allowed to warm slowly to room temperature. When the reaction was complete, as judged by TLC (80% high petroleum ether, 20% EtOAc), it was quenched in saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 0.80g (78%) of the crude desired product pure enough for use in subsequent reactions. IR (neat, cm⁻¹): 2930s; 1450s; 1045s. NMR (CDCl₃/TMS; δ): 4.83 (mult, 1H, proton between oxygens); 3.81 (s, 3H, -OCH₃); 1.79 (mult, 4H, lactol protons); 1.47 (s, 10H, ring protons). Analysis: C₁₀H₁₈O₂ required: C 70.59, H 10.59; found: C 70.55, H 10.35. MS: C₁₀H₁₈O₂: calc: 170.131; obs: 170.132. 170 (56%), 139 (100%), 138 (62%).

1-Oxaspiro[4.4]nonane (13). 1-(2,3-Epoxy-3-trimethylsilylpropyl)-cyclopentanol (10) (7.0mmole, 1.5g) was dissolved in methanol (5ml) and the resulting solution was stirred at 0°C. BF₃·Et₂O (14mmole, 2.0g, 1.7ml) was added dropwise, and the solution was allowed to come slowly to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 0.56g (51%) of crude product pure enough for use in subsequent reactions. IR (neat, cm⁻¹): 3450 (impurity); 2960s; 1100s; 1045s. NMR (CDCl₃/TMS; δ): 4.82 (mult, 1H, proton between oxygens); 3.21 (s, 3H,
-OCH₃); 2.0–1.7 (mult, 4H, lactol protons); 1.63 (s, 8H, ring protons).
MS: C₉H₁₆O₂: calc: 156.115; obs: 156.115. 156 (22%), 127 (100%), 125 (50%).

1-Oxaspiro-2-hydroxy[4.4]nonane. 1-(2,3-Epoxy-3-trimethylsilyl-
propyl)cyclopentanol (10) (2.0mmole, 0.42g) was taken up in 20% aqueous
THF (5ml) and the resulting solution was stirred at room temperature after
the addition of 7 drops of concentrated sulfuric acid. When the reaction
was judged complete by TLC (80% high petroleum ether, 20% EtOAc),
the reaction mixture was poured into saturated aqueous sodium
bicarbonate, layered with dichloromethane. The aqueous phase was
extracted, and the combined organics dried over MgSO₄. Removal of
solvent left 0.13g (56%) of the desired product, contaminated with
trace amounts of silicon- and carbonyl-containing compounds. The
spectral data were not very helpful in confirming structure, but confir-
mation was achieved through subsequent transformation to 1-oxaspiro-
2-oxo[4.4]nonane (see page 84), in 38% crude yield.

2-Oxoadamantanespiro-2'-tetrahydrofuran, (14). In acetic acid (8ml)
6 (3.8mmole, 1.0g) was dissolved at room temperature, and the resulting
solution was stirred magnetically. Peracetic acid (19mmole, 2.5ml of
a 40% solution) was added, as well as concentrated sulfuric acid (3
drops). Within one hour, destruction of starting material was complete,
by TLC, (80% high petroleum ether, 20% EtOAc) and one major and one
minor product were evident only when the plate was visualized with
iodine. The reaction mixture was poured into saturated aqueous sodium
bisulfite layered with dichloromethane. The aqueous phase was
extracted, and the combined organics were washed with aqueous sodium
bicarbonate and water. Removal of the dried (MgSO₄) solvent gave a
quantitative yield of a mixture which contained the desired product and a second carbonyl containing compound. Separation by preparative layer chromatography (80% low petroleum ether, 20% EtOAc) provided .24g (31%) of pure product. Spectral data were identical to those obtained by Jones Oxidation of the corresponding methyl lactol.

2-Oxoadamantanespiro-2'-tetrahydrofuran (14). 2-Methoxyadamantanespiro-2'-tetrahydrofuran (11) (2.2mmole, .50g) was taken up in acetone and the resulting solution was stirred at 0°C. The Jones reagent (11mmole, 1.4ml of a solution 8M in chromic acid) was added dropwise. The reaction was complete in 10min., as judged by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was treated with isopropanol, and then poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .36g (80%) of nearly pure product, as large crystals. Sublimation of a small sample showed the crude to be 92% pure. IR (CHCl₃; cm⁻¹): 2920s; 1758s; 1455m; 1220m; 1000m. NMR (CCl₄/TMS; δ): 2.5-2.0 (mult, 6H, lactone protons and protons α to the spiro-carbon on the adamantyl system); 1.80 (s, 12H, adamantyl protons). MS: C₅₉H₈₁O₂: calc: 206.131; obs: 206.131. 206 (60%), 160 (67%), 149 (100%). Mp: 124-128°C.

1-Oxa[spiro-2-oxo[4.4]nonane (15). 1-Oxa[spiro-2-methoxy[4.4]nonane (13) (2.6mmole, .40g) was dissolved in acetone and the resulting solution was stirred at 0°C. The Jones reagent (13mmole, 1.6ml of a solution 8M in chromic acid) was added dropwise, and the solution was allowed to come to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was treated with isopropanol
and poured into saturated aqueous sodium bicarbonate layered with dichloromethane. Removal of the dried (MgSO₄) solvent gave \(0.27\) g (75\%) of crude product. Preparative layer chromatography (80\% low petroleum ether, 20\% EtOAc) showed the crude to be 88\% pure. IR (neat, cm\(^{-1}\)): 2960\text{m}; 1770\text{s}; 1165\text{s}; 930\text{m}. NMR (CDCl\(_3\)/TMS; \(\delta\)): 2.33 (mult, 4H, lactone protons; AA'BB' system); 1.76 (s, 8H, ring protons). MS: \(C_9H_{14}O_2\); calc: 154.099, obs: 154.100. 154 (28\%), 111 (100\%).

1-Oxaospiro-2-oxo[4.4]nonane (15). 1-Oxaospiro-2-hydroxy[4.4]nonane (0.92 mmole, 0.13 g) was taken up in acetone, and the Jones reagent (0.61 mmole CrO₃)\(^{67}\) was added at room temperature. Immediate formation of a green precipitate occurred, and the reaction was judged to be complete by TLC (80\% high petroleum ether, 20\% EtOAc). A few drops of isopropanol were added, then the solution was poured into a saturated aqueous solution of potassium carbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics dried over MgSO₄. Removal of the solvent gave \(0.05\) g (38\%) of crude product. IR (neat, cm\(^{-1}\)): 2950\text{s}; 1770\text{s}; 1160\text{s}. NMR (CDCl\(_3\)/TMS; \(\delta\)): 2.33 (mult, 4H, lactone protons, AA'BB' system); 1.76 (s, 8H, ring protons).

1-Oxaospiro-2-oxo[4.4]nonane (15). 1-(2,3-Epoxy-3-trimethylsilylpropyl)-cyclopentanol (10) (0.44 mmole, 0.10 g) was dissolved in acetone (3 ml) and the resulting solution was stirred at \(0^\circ\)C. The Jones reagent\(^{67}\) (1.3 mmole CrO₃, 0.16 ml of a solution 8M in CrO₃) was added dropwise. The reaction was allowed to come to room temperature, and two further equivalents of the reagent were added over two days. Many intermediates were visible by TLC (80\% high petroleum ether, 20\% EtOAc) over that time, but when no further change occurred and the starting material had been destroyed, the reaction mixture was poured into
of the dried ($\text{MgSO}_4$) solvent yielded 0.05g (70%) of a mixture of the desired product and a second carbonyl-containing compound. IR (neat, $\text{cm}^{-1}$): 3420m; 2930s; 1775s; 1715m.

1-Oxaspiro-2-oxo[4.4]nonane (15). 1-(2,3-Epoxy-3-trimethylsilyl-propyl)cyclopentanol (10) (2.3mmole, 0.5g) was stirred at room temperature in acetic acid (5ml). Three drops of concentrated sulfuric acid were added, followed by 10ml of 30% hydrogen peroxide. The reaction was allowed to proceed 12 hours, and was judged complete at the end of that time. The reaction was worked up in saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics dried over MgSO$_4$. Removal of the solvent gave 0.14g (44%) of a mixture of the desired lactone and the corresponding hydroxy-acid ($\nu_{\text{max}}$ 1770cm$^{-1}$ and 1760cm$^{-1}$).

1-Oxaspiro-2-oxo[4.4]nonane (15). To a stirred solution of 1-(3-trimethylsilylprop-2-enyl)cyclopentanol (3) (7.6mmole, 1.5g) in acetic acid (5ml) at 0°C was added peracetic acid (4.9ml of a 40% solution). The reaction was allowed to come slowly to room temperature, and was judged complete after several hours, by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics dried over MgSO$_4$. Removal of the solvent gave 0.55g (52%) of the desired crude product. IR (neat, $\text{cm}^{-1}$): 2950s; 1770s; 1160s.
5-Cyclonexyl-2-oxotetrahydrofuran. 4-Cyclonexyl-4-hydroxy-1-trimethylsilylbut-1-ene (6.7mmole, 1.5g) was taken up in acetic acid (3ml) and the resulting solution was stirred at 0°C. Six ml of peracetic acid (40% solution) were added, and the reaction mixture was allowed to come to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO\textsubscript{4}) solvent gave what appeared by spectral data to be a mixture of the desired lactone ($\nu_{\text{max}}$ 1775cm\textsuperscript{-1}) and the corresponding hydroxy acid. Attempts to lactonize the hydroxy acid by treatment of the crude product with polyphosphoric acid failed.

1-Oxaspiro-2-oxo[4,5]decane (16). 1-(3-Trimethylsilylprop-2-enyl)-cyclohexanol (2) (12mmole, 2.5g) was taken up in acetic acid (5ml) and stirred at 0°C. Ten ml of peracetic acid (40% solution) were added, and the reaction was allowed to come to room temperature. Three drops of concentrated sulfuric acid were added. After several hours, the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), and was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO\textsubscript{4}) solvent gave 0.86g (47%) of crude product. IR (neat, cm\textsuperscript{-1}): 2920s; 1765s. NMR ($\phi$, $\delta$): 2.24 (mult, 2H, protons $\alpha$ to carbonyl); 1.9-1.0 (envelope, 12H, remaining protons). MS: C\textsubscript{9}H\textsubscript{14}O\textsubscript{2}; calc: 154.099; obs: 154.100, 154 (39%), 141 (100%), 135 (84%).
1-Oxaspiro-2-oxo[4.5]decane (12) (3.8mmole, .65g) was taken up in acetone and the resulting solution was stirred at 0°C. The Jones reagent (18mmole, 2.4ml of a solution 8M in chromic acid) was added dropwise, and the solution was allowed to come to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was treated with isopropanol and poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .44g (76%) of crude product. Preparative layer chromatography showed that the crude was 82% pure. IR (neat, cm⁻¹): 2940s; 1770s; 1195w; 960w. NMR (CDCl₃/TMS, δ): 2.21 (mult, 4H, lactone protons; AA'BB' system); 1.62 (s, 10H, ring protons). MS: C₂₂H₄₂O₂: calc: 340.084, obs: 140.084. 140 (31%), 111 (100%), 98 (85%).

3-Chloro-2-trimethylsilyladamantanespiro-2'-tetrahydrofuran. (Not produced). In 2ml of carbon tetrachloride, 2 (.76mmole, .2g) was dissolved and the resulting solution was stirred at room temperature. Chlorine (10ml of a .78M solution in carbon tetrachloride) was added in portions over two days, eventually leading to destruction of starting material and production of two products by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave a colorless oil whose spectral data showed a complex mixture of products.
3-Bromo-2-trimethylsilyladamantanespiro-2'-tetrahydrofuran. (Not produced). Compound 2 (0.76mmole, 0.2g) was taken up in carbon tetrachloride (3ml) and the resulting solution was stirred at 0°C. Neat bromine was added dropwise until the solution, initially light yellow, became orange. TLC (80% high petroleum ether, 20% EtOAc) showed complete destruction of starting material, so the reaction mixture was poured into 3N sodium hydroxide layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 0.32g of a product mixture whose spectral data showed no identifiable product.

3-Bromo-2-trimethylsilyladamantanespiro-2'-tetrahydrofuran. (Not produced). Compound 2 (0.76mmole, 0.2g) was dissolved in dichloromethane (2ml) and the resulting solution was stirred at 0-10°C. Bromine was added as a solution in dichloromethane until complete destruction of starting material was achieved, by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was poured into water layered with dichloromethane. The aqueous phase was extracted, and the combined organics were dried over MgSO₄. Removal of the solvent gave us no identifiable product.
3-Phenylselenyl-2-trimethylsilyladamantanespiro-2'-tetrahydrofuran.

(Not produced). Compound 6 (.76mmole, .2g) was taken up in dichloromethane (2ml) and the resulting solution was stirred at room temperature in the presence of potassium carbonate (.76mmole, .10g). To this solution was added a CH\textsubscript{2}Cl\textsubscript{2} solution of phenylselenyl bromide prepared in situ by addition of bromine (.53mmole, .53ml of a 1M solution in CH\textsubscript{2}Cl\textsubscript{2}) to diphenyl diselenide (.57mmole, .18g) at room temperature. Destruction of starting material was complete by TLC (80% high petroleum ether, 20% EtOAc), so the reaction mixture was poured into water layered with dichloromethane. The aqueous phase was extracted, and the combined organics were dried over MgSO\textsubscript{4}. Removal of the solvent gave no identifiable product.

2-Bromo trimethylsilylmethyladamantanespiro-2'-oxetane (17) Compound 6 (3.8mmole, 1.0g) was dissolved in dry THF (20ml) and the resulting solution was stirred at 0°C. N-bromosuccinimide (5.7mmole, 1.0g) was added as a solid all in one portion. When the reaction was judged complete by TLC (95% high petroleum ether, 5% EtOAc), the reaction mixture was quenched in saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (MgSO\textsubscript{4}) solvent gave 1.2g (92%) of crude product, pure enough to use in subsequent reactions. IR (heat, cm\textsuperscript{-1}): 2900s; 1450m; 1250s; 970s; 850s. NMR (CDCl\textsubscript{3}/δ, δ): 4.57 (q, OH, proton α to -TMS); 3.33 (d, 1H, proton α to -TMS); 2.4-1.75 (envelope, 4H, protons γ to -TMS and adamantyl protons α to the spiro-spiro-carbon); 1.66 (s, 12H, adamantyl system); .15 (s, 9H,-TMS). C\textsuperscript{13} (CDCl\textsubscript{3}, ppm): 85.446 (spiro-carbon); 74.182
There were 14 carbon signals in all, consistent with the proposed structure. Decoupling experiments confirmed the proton assignments.

4,4-(2-Adamantyl)-cis-1-bromo-1-trimethylsilylbutadiene (18).

Compound 6 (3.8mmole, 1.0g) was dissolved in dry THF (20ml). The resulting solution was stirred and gradually warmed to reflux, whereupon N-bromosuccinimide (5.7mmole, 1.0g) was added in one portion. When the reaction was judged complete by TLC (95% high petroleum ether, 5% EtOAc), the solution was cooled and poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO$_4$) solvent gave 1.24g (100%) of crystalline product. The product was purified by preparative layer TLC (95% high petroleum ether, 5% EtOAc), giving .45g (38%) pure product (mp 92-97°C). IR (Nujol mull; cm$^{-1}$): 6.55 (q, 2H, vinyl protons; $J_{AB} = 11$Hz); 2.96 (s, 1H, allylic proton syn to vinyl silane); 2.46 (s, 1H, allylic proton anti to vinyl silane); 1.85 (s, 12H, adamantyl protons); 0.17 (s, 9H, -TMS). MS: C$_{16}$H$_{25}$SiBr$_7^+$; calc: 324.091; obs. 324.092. C$^{13}$ (CDCl$_3$; ppm): 157.832 (carbon $\delta$ to -TMS); 133.558 (carbon $\gamma$ to -TMS); 130.305 (carbon bearing -TMS); 115.643 (carbon $\gamma$ to -TMS); 1.747 (-TMS methyls); 41.218-28.546 (adamantane carbons). The spectrum showed 11 carbon signals. Analysis: C$_{16}$H$_{25}$SiBr$_7^+$; required: C 59.26, H 7.72; found: C 59.25, H 7.96.

2-(cis-3-Bromoprop-2-enyl)adamantan-2-ol (20). Compound 17 (1.7mmole, .59g) was dissolved in dry DMSO (5ml), and the resulting solution was stirred and heated at 40-45°C after the addition of
potassium fluoride dihydrate (5.1mmole, 0.48g). When the reaction was judged complete by TLC (95% high petroleum ether, 5% EtOAc), the solution was poured into water layered with ether. The aqueous phase was extracted, and the combined organics were dried over MgSO₄. Removal of the solvent gave 0.35g (76%) of crude crystalline product. A small amount was purified by preparative layer TLC (90% high petroleum ether, 10% EtOAc). IR (Nujol mull, cm⁻¹): 3320s; 2920s; 1625m; 1050m; 745m. NMR (CDCl₃/ø, ø): 6.23 (t, 2H, vinyl protons); 2.56 (d, 2H, allylic methylene group); 2.2-1.3 (envelope, 14H, adamantyl system). MS: (M⁺ -H₂O; loss of water from tertiary alcohol). C₁₃H₁₇Br₇₉: calc: 252.051; obs: 252.052, 254 (70%), 252 (65%), 219 (100%). C₁³ (CDCl₃; ppm): 130.669 (carbon bearing Br); 109.696 (carbon 8 to Br); 75.347 (carbon bearing -OH); 38.984-27.284 (carbon 7 to Br and the ring system). Mp 117-119°C. Analysis: C₁₃H₁₉OBr₇₉: required: C 57.78, H 7.05; found: C 57.35, H 7.10.

4,4-(2-Adamantyl)-cis-1-bromo-1-trimethylsilylbutadiene, (18).

Compound 17 (0.29mmole, 0.10g) was taken up in dry THF (2ml) and the resulting solution was brought to reflux and treated with 1 drop of 1M hydrochloric acid. After several hours, total destruction of the starting material and production of the desired product was evident by TLC (90% high petroleum ether, 10% EtOAc). The solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave an oil whose spectral data showed that it was crude 18.

4,4-(2-Adamantyl)-cis-1-bromobutadiene, (19). Compound 18 (1.0 mmole, 0.34g) was dissolved in dry DMSO (5ml). The resulting solution
solution was stirred and heated at 40-45°C after the addition of potassium fluoroide dihydrate (3.0mmole, .28g). When the reaction was judged complete by TLC (high petroleum ether), the solution was poured into water layered with ether. The aqueous phase was extracted and the combined organics were dried over MgSO₄. Removal of the solvent gave .25g (100%) of crude 19 as an oil. The product was purified by preparative layer TLC (high petroleum ether). IR (neat, cm⁻¹): 2900s; 1640w; 1450m; 1295m; 720m. NMR (CDCl₃/ δ, δ): 6.82 (mult, 1H, proton on carbon bearing Br); 6.01 (mult, 2H, other vinyl protons); 2.88 (s, 1H, allylic proton syn to the vinyl bromide); 2.45 (s, 1H, allylic proton anti to the vinyl bromide); 1.85 (s, 12H, adamantyl system). MS: C₁₃H₁₇Br₇⁻: calc: 252.051; obs: 252.052.254 (100%), 252 (96%). C₁₃ (CDCl₃: ppm): 157.007 (carbon δ to Br); 127.780 (carbon γ to Br); 113.313 (carbon bearing Br); 106.030 (carbon α to Br); 41.120-28.546 (adamantyl carbons). There were 10 carbon signals in evidence.

4,4-((2-Adamantyl)-cis-1-bromobutadiene, (19). Compound 18 (.37 mmole, .10g) was dissolved in dry pyridine (2ml), and the resulting solution was stirred at 0°C. Thionyl chloride (8 drops) was added dropwise. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into water layered with ether. The aqueous phase was extracted, and the combined organics were dried over MgSO₄. Removal of the solvent gave a dark oil whose spectral data confirmed it as crude 19. MS:


4,4-((2-Adamantyl)-1,2-epoxy-1-trimethylsilylbut-3-ene. Compound 2 (.71mmole, .2g) was dissolved in benzene (3ml), and the resulting
solution was stirred at 10°C for 2 days in the presence of a catalytic amount of para-toluenesulfonic acid. At the end of that time, the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent left an oily product which produced white crystals when treated with dry ether. Spectral data showed this material to be 4,4-(2-adamantyl)-1,2-epoxy-1-trimethylsilylbut-3-ene. IR (Nujol mull, cm⁻¹): 2920s; 1455m; 1250m; 1020m; 1000m; 845m. NMR (CDCl₃/TMS; δ): 5.04 (d, 1H, vinyl protons); 3.32 (mult, 1H, proton β to -TMS); 2.2-1.4 (envelope, 15H, adamantyl system and proton α to -TMS); 0.05 (s, 9H, -TMS). MS: C₁₆H₂₆O Si: calc: 262.175; obs: 262,176. 262 (54%), 237 (42%), 236 (100%).

Estrone methyl ether, (27). Estrone (19mmole, 5.0g), potassium carbonate (96mmole, 13.2g), and methyl iodide (.48mmole, 68g, 30ml) were combined in acetone (125ml), and the resulting reaction mixture was refluxed for 30 hours. The reaction was quenched in saturated aqueous ammonium chloride layered with chloroform. The aqueous phase was extracted, and the combined organics were washed with aqueous ammonium chloride and water. Removal of the dried (MgSO₄) solvent gave 5.04g (97%) of pure estrone methyl ether. IR (Nujol mull; cm⁻¹): 2920s; 1740s; 1610m; 1510s. NMR (CDCl₃/TMS; δ): 6.90 (mult, 3H, aromatics); 3.75 (s, 3H, -OCH₃); 3.2-1.3 (envelope, 15H, aliphatics); 0.88 (s, 3H, -CH₃). MS: M⁺ at 284. 285 (24%), 284 (100%). Mp (low pet. ether/CHCl₃): 169-171°C.

17α-Hydroxy-17α-(3-trimethylsilyl)prop-2-enyl)-4-androsten-3-one (24). To a stirred solution of sBuLi (0.1mole, 100ml of a 1.0M solution in
cyclohexane) and TMEDA (0.1mole, 11.6g, 15.0ml) in dry THF (20ml) under argon at -78^oC was added allytrimethylsilane (0.1mole, 11.4g, 16.0ml) in a dropwise fashion. The resulting solution was allowed to come to -40^oC for 10-15 min., then allowed to warm further to 0^oC. After 30 min. stirring, the solution was treated with a THF (15ml) slurry of 3-methoxy-androst-3,5-dien-17-one (6.7mmole, 2.0g). When no further reaction occurred after several hours by TLC (50% high petroleum ether, 50% EtOAc), the workup was done, even though starting material was still present. The solution was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Most of the solvent (dried over MgSO_4) was removed and a mass spectrum was taken. Crude IR and NMR were indicative of a mixture of product and starting material. MS: C_{26}H_{42}O_{2}Si: calc: 414.295; obs: 414.296. The crude product was taken up in ether (30ml) and stirred at room temperature with 20ml of 6M hydrochloric acid. In a short time, TLC (50% high petroleum ether, 50% EtOAc) showed no further enol ether present. Comparison with an authentic sample of androst-4-ene-3,17-dione showed that to be the minor component of a 2 component product mixture. The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (MgSO_4) solvent left a material which was chromatographed over silica to give 0.71g (26%) pure product. IR (neat, cm\(^{-1}\)): 3440m; 2940s; 1670s; 1615m; 1250s; 850s. NMR (\(\phi, \delta\)): 6.4-5.7 (mult, 2H, vinyl silane, \(J_{AX} = 18.5\) Hz);
5.85 (s, 1H, proton α to carbonyl); 2.8-1.1 (envelope, 20H, aliphatics);
1.06 (s, 3H, -CH₃ in A ring); 0.91 (s, 3H, -CH₃ next to -OH); 0.24 (s

17α-Hydroxy-17β-(3-trimethylsilylprop-2-enyl)-4-androsten-3-one (24).
To a stirred solution of sBuLi (68mmole, 56.7ml of a 1.2M solution in

cyclohexane) in dry THF (45ml) at -78°C under argon was added allyl-
trimethylsilane (76mmole, 8.7g, 12.1ml). Then anhydrous zinc
chloride (68mmole, 9.2g) was added. The solution was allowed to come
to -35°C, resulting in dissolution of most of the zinc chloride. After
30 min., 3-methoxyandrost-3,5-dien-17-one (17mmole, 5.0g) was added
dropwise as a solution in THF (40ml). When the reaction was judged
complete by TLC (80% high petroleum ether, 20% EtOAc), 40ml of satu-
rated aqueous ammonium chloride was added after the cooling bath was
removed. The dense precipitate so formed was filtered off, and the cake
was washed with water and THF. The aqueous phase was extracted with
THF, and the combined organics were washed with aqueous ammonium
chloride and dried over MgSO₄. Removal of solvent left a solid residue
which was taken up in dichloromethane (20ml) and treated with 7.5ml of
concentrated sulfuric acid in 20ml of water at 35°C for 30min. The solu-
tion was quenched in saturated aqueous sodium bicarbonate layered
with dichloromethane. The aqueous phase was extracted, and the
combined organics washed with water. Removal of the dried solvent
gave 5.64g (82%) of crude 24 pure enough to use in subsequent reactions.

IR (neat, cm⁻¹): 3440m; 2940s; 1670s; 1615m; 1250s; 850s. NMR (CDCl₃/

φ, δ): 5.83 (mxt, 2H, vinyl protons; Jₐ₈ = 19Hz); 5.67 (s, 1H, olefinic
proton); 2.4-1.3 (envelope, 22H, aliphatics); 1.15 (s, 3H, -CH₃ in A
ring); 0.87 (s, 3H, -CH₃ in D ring); 0.02 (s, 9H, -TMS). MS:
3-Methoxy-17α-(3-trimethylsilyl)prop-2-enyl)-1,3,3(10)-estratrien-17β-ol, (28). To a stirred solution of sBuLi (99mmole, 70.7ml of a 1.4M solution in cyclohexane) in dry THF (60ml) under argon at -78°C was added allyltrimethylsilane (11mole, 12.5g, 17.4ml). To the resulting solution was added anhydrous zinc chloride (99mmole, 13.5g). The heterogeneous reaction mixture was warmed to -20°C whereupon most of the zinc chloride dissolved. After 45 min., estrone methyl ether (27) (18mmole, 5.0g) was added as a slurry in THF. When the reaction was judged complete by TLC (70% high petroleum ether, 30% EtOAc), the cooling bath was removed and 60ml of saturated aqueous ammonium chloride were added, producing a dense white precipitate, which was filtered off. The filter cake was washed with THF and water. The aqueous phase was extracted, and the combined organics were washed with aqueous ammonium chloride and dried over MgSO₄. Removal of solvent gave a crude product which was chromatographed over silica gel to give 4.71g (66%) of pure 28, as well as .97g (19%) of the product of simple reduction at the 17 position, as identified by IR, NMR, and an accurate mass measurement. IR (CHCl₃; cm⁻¹): 3540w; 2950s; 1610m; 1500s; 1250s; 870s, 840s. NMR (CDCl₃/TMS; δ): 7.3-6.5 (mult, 3H, aromatics); 5.90 (mult, 2H, vinyl protons; J_AB = 19Hz); 3.72 (s, 3H, -OCH₃); 2.70 (mult, 3H, benzylic protons); 2.33 (d, 2H, allylic protons; J_AX = 5Hz); 1.9-1.1 (envelope, 14H, aliphatics); 0.90 (s, 3H, -CH₃); 0.05 (s, 9H, -TMS). MS: .
Compound \( ^{17a}(2,3\text{-Epoxy}-3\text{-trimethylsilylpropyl})-17a\text{-hydroxy}-4\text{-androstene-3-one} \), (25). (Not produced). Compound 24 (0.62mmole, 0.25g) was taken up in dichloromethane and the resulting solution stirred at room temperature. Metachloroperoxybenzoic acid was added in increments as the destruction of starting material was followed by TLC (60% high petroleum ether, 40% EtOAc). Starting material was absent only after 2.3mmole (0.40g) had been added. The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO\(_4\)) solvent left a product whose spectral data showed extensive loss of the enone portion of the molecule.

\( ^{17a}(2,3\text{-Epoxy}-3\text{-trimethylsilylpropyl})-17a\text{-hydroxy}-4\text{-androstene-3-one} \), (25). Compound 24 (7.5mmole, 3.0g) was dissolved in benzene (20ml), and the resulting solution was treated with VO(acac)\(_2\) (0.075mmole, 0.02g), stirred, and brought to reflux. Tert-butylhydroperoxide (8.2mmole, 0.74g) was added in a dropwise fashion, and the reaction mixture was refluxed for several hours. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was cooled and poured into aqueous sodium bisulfite. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO\(_4\)) solvent gave 3.03g (97%) of crude product. The product can be purified by preparative layer chromatography (70% high petroleum ether, 30% EtOAc). IR (CHCl\(_3\), cm\(^{-1}\)): 3480w; 2955s; 1665s; 1615w; 1250s; 845s. NMR (CDCl\(_3\)/\( \delta \)): 5.64 (s, 1H, olefinic proton);
3.00 (mult, 1H, proton β to -TMS); 2.5-1.3 (envelope, 23H, aliphatic system); 1.15 (s, 3H, -CH₃ in A ring); 0.86 (s, 3H, -CH₃ in D ring); -0.02 (s, 9H, -TMS). MS: C₂₅H₄₀O₃Si: calc: 416.275; obs: 416.275. 416 (100%), 399 (100%), 384 (39%). Mp (EtOAc/low pet. ether): 147-150°C.

17α-(2,3-Epoxyl-3-trimethylsilylpropyl)-3-methoxy-1,3,5(10)-estratrien-17β-ol. (29). Compound 28 (10mmole, 4.1g) was dissolved in benzene (20ml). The resulting solution was treated with VO(acoc)₂ (.10mmole, .026g) and brought to reflux. Tert-butyl hydroperoxide (1mmole, .99g) was added dropwise, and the reflux continued for 6 hours. The solution was then cooled and poured into aqueous sodium bisulfite/sodium chloride layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave 3.76g (91%) of crude epoxide pure enough to use in subsequent reactions. IR (CHCl₃, cm⁻¹): 2920s; 1610m; 1500s; 1255s; 845s. NMR (CDCl₃/TMS, δ): 7.3-6.5 (mult, 3H, aromatics); 3.76 (s, 3H, -OCH₃) 3.17 (mult, 1H, proton β to -TMS); 2.82 (mult, 3H, benzylic protons); 3.0-1.1 (envelope, 16H, aliphatics)) .92 (s, 3H, -CH₃; 0.09 (s, 9H, -TMS). Mp (EtOAc): 125-130°C.

α-(3-Oxo-17α-hydroxy-4-androstene-17α-yl)propionaldehyde Cyclosemiacetal Methyl Glycoside (26). Compound 25 (1.2mmole, 0.50g) was dissolved in methanol (2ml), and the resulting solution was stirred at 0°C. Then BF₃·Et₂O (2.4mmole, .34g, .30ml) was added, and the solution was allowed to come to room temperature. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc) after several hours, the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase
was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .40g (93%) of crude product pure enough to use in subsequent reactions. IR (CCl₄, cm⁻¹): 2950s; 1680s; 1620w; 1050s. NMR (CDCl₃/TMS, δ): 5.69 (s, 1H, olefinic proton); 4.89 (mult, 1H, proton between oxygens); 3.30 (s, 3H, -OCH₃); 2.6-1.4 (envelope, 23H, aliphatics); 1.17 (s, 3H, -CH₃ in A ring); 0.92 (d, 3H, -CH₃ in D ring). MS: C₉H₁₄O₂: calc: 358.251; obs: 358.251. 358 (12%), 327 (39%), 326 (100%).

α-(17β-Hydroxy-3-methoxy-1,3,5(10)-estratrienyl)propionaldehyde Cyclosemiacetal Methyl Glycoside, (30). 17α-(2,3-Epoxy-3-trimethylsilylpropyl)-3-methoxy-1,3,5(10)-estratrien-17β-ol (29) (.84mmole, .35g) was taken up in methanol, creating a slurry. This mixture was stirred at 0°C, and BF₃·Et₂O (2.1mmole, .30g, .26ml) was added, causing dissolution of the starting material. The reaction mixture was allowed to warm to room temperature, and was stirred for three days. The solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .24g (80%) of crude product pure enough to use in subsequent reactions. IR (CHCl₃: cm⁻¹): 2940s; 1610m; 1500s; 1040s. NMR (CDCl₃/TMS, δ): 7.3-6.4 (mult, 3H, aromatics); 4.86 (mult, 1H, proton between oxygens); 3.70 (s, 3H, -OCH₃ in A ring); 3.26 (s, 3H, -OCH₃ of protected lactol); 2.73 (mult, 3H, benzylic protons); 2.3-1.1 (envelope, 16H, aliphatics); 0.86 (d, 3H, -CH₃). MS: C₂₃H₂₂O₃: calc: 356.235; obs: 356.236. 356 (48%), 325 (34%), 324 (100%).
3-(3-Oxo-17α-hydroxy-4-androsten-17α-yl)propanoic Acid Lactone

(22) (not produced). Compound 24 (.375mmole, .15g) was dissolved in glacial acetic acid (2ml), and peracetic acid (1ml of a 40% solution) was added, followed by 5 drops of concentrated sulfuric acid. When the reaction was judged over by TLC (60% high petroleum ether, 40% EtOAc), the reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO₄) solvent left a product whose IR showed complete absence of the enone portion of the molecule.

3-(3-Oxo-17α-hydroxy-4-androsten-17α-yl)propanoic Acid Lactone, (22). Compound 25 (.60mmole, .25g) was dissolved in acetone (1ml) and the resulting solution was stirred at 0°C. To the solution were added .5ml of water, the Jones reagent (3.0mmole, .38ml of a solution 8M in chromium trioxide), and 3 drops of concentrated sulfuric acid. When the reaction was judged complete by TLC (70% high petroleum ether, 30% EtOAc; double development), several drops of isopropyl alcohol were added. The solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave .14g (70%) of crude product, contaminated with some second carbonyl-containing compound, as seen by IR. IR (CCl₄, cm⁻¹): 2960s; 1790s; 1755s; 1695s; 1630w. NMR (CDCl₃/δ, δ): shows single olefinic signal at 5.70, but also shows two different D ring methyl groups. MS: C₂₂H₃₀O₃: calc: 342.219; obs: 342.221. The material was separated by preparative layer chromatography. The
second carbonyl containing compound was found to have an accurate mass identical to that of the desired product.

3-(3-Oxo-17α-hydroxy-4-androstene-17α-yl)propionic Acid Lactone, \( (22) \). Compound \( 26 \) (5.6mmole, 2.0g) was dissolved in acetone (10ml), and the resulting solution was stirred at 0°C. An excess of the Jones reagent\(^\text{67} \) (28mmole, 3.5ml of a solution 8M in chromium trioxide) was added in a dropwise fashion, causing precipitation of green solids. Several drops of isopropyl alcohol were added, and the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO\(_4\)) solvent gave 1.31g (68%) of crude \( \delta \). The crude product was chromatographed over silica gel, yielding .92g (48%) of pure product. IR (CHCl\(_3\), \( \text{cm}^{-1} \)): 2950s; 1765s; 1665s; 1620w. NMR (CDCl\(_3\)/TMS, \( \delta \)): 5.70 (s, 1H, olefinic proton); 2.6-1.3 (envelope, 23H, aliphatics); 1.20 (s, 3H, -CH\(_3\) in ring A); 0.97 (s, 3H, -CH\(_3\) in ring D). MS: \( C_{22}H_{30}O_3 \); calc: 342.219; obs: 342.220. 342 (99%), 300 (29%), 286 (100%). Mp (EtOAc) 148-151°C.

3-[3-Methoxy-17β-hydroxy-1,3,5(10)-estratrien-17α-yl]propanoic Acid Lactone, \( (31) \). \( \beta \)-(17β-Hydroxy-3-methoxy-1,3,5(10)-estratrienyl)propionaldehyde cyclosemiacetal methyl glycoside \( (30) \) (5.0mmole, 1.8g) was dissolved in acetone (10ml), and the resulting solution was stirred at 0°C. The Jones reagent\(^\text{67} \) (25mmole, 3.1ml of a solution 8M in CrO\(_3\)) was added dropwise, causing precipitation of green solids. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc; double development), a small quantity of isopropyl alcohol
was added. The solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave 1.12g (66%) of crude product which was purified by chromatography over silica gel, giving .52g (30%) of pure product. IR (CHCl₃, cm⁻¹): 2940s; 1765s; 1610m; 1500s; 1170s. NMR (CDCl₃/TMS, δ): 7.3-6.5 (mult, 3H, aromatics); 3.76 (s, 3H, -OCH₃); 2.84 (mult, 3H, benzylic protons); 2.6-1.1 (envelope, 16H, aliphatics); 0.95 (s, 3H, -CH₃). MS: C₂₂H₂₈O₃: calc: 340.204; obs: 340.204. 341 (22%), 340 (100%). Mp. (EtOAc): 150-152°C.
Many substituted allenic anions are known, and some have been put to use in synthetic sequences as acyl anion equivalents.\(^79\) Leroux has used the allenic system in a synthesis of \(\alpha,\beta\)-unsaturated carbonyl compounds.\(^80\) Similarly, \(2\) can lead to \(\delta\)-ketoesters or

\[
\begin{align*}
\text{R} = & -\text{TMS}, \text{-CH}_3 \\
\beta\text{-thiomethylbutenolides in high yield.} & \text{The potential for selective hydrolysis inherent in the adducts of } 3 \text{ has been exploited by Carlson.} \text{ Additionally, deprotonation of } 4 \text{ and reaction of the resulting anion with carbonyl compounds can lead to furanones, as shown in the third following figure.}
\end{align*}
\]
The work which sparked interest in the allenic anion field was that done by Hoff, Brandsma, Arens, et al. (see ref. 79) on α-lithio methoxyallene. They showed that the methyl ether of propargyl alcohol could be rearranged to methoxyallene in high yield simply by refluxing it in the presence of potassium t-butoxide. Methoxyallene can be deprotonated with nBuLi in ethereal solutions, and the resulting anion reacts well with carbonyl compounds and alkylating agents. Hydrolysis of such adducts provides products derived from the formal addition of the acyl anion $\Sigma$. Hoff, Brandsma, and Arens reported the
failure of α-lithiomethoxyallene to give the dianion when treated with an additional equivalent of alkyl lithium. However, Leroux and Mantione reported generation of the analogous species at -75°C.  

Can be alkylated twice, with the first group entering exclusively next to the phenyl substituent.

We hoped to make use of α-lithiomethoxyallene as an acyl anion equivalent which would add conjugatively to α,β-unsaturated carbonyl systems. Heathcock has reported the cuprate from α-methoxyvinyl-lithium, and has shown that it undergoes 1,4 addition to conjugated enones. We planned to generate the analogous cuprate, hoping to achieve eventual annulation, following conjugate addition, as in Scheme I. Such a sequence would provide a useful method of synthesizing n.n.3.0 1,4-dicarbonyl systems.
Simple addition of reprecipitated copper (I) iodide to a THF solution of α-lithiomethoxyallene does not produce the cuprate 9; only 1,2-adduct is formed when such a solution is treated with 2-cyclohexen-1-one. Heathcock has observed identical behavior in the case of α-methoxyvinylolithium (see ref. 85). However, the cuprate 8, from α-methoxyvinylolithium can be formed if dimethylsulfide is added to the reaction mixture. Unfortunately, this was not the case for the system under investigation here, and after numerous attempts, we were forced to abandon our pursuit of 9. No more than a few percent of 1,4-adduct were ever observed in any experiment, even though the temperature, solvent, and order of addition of the reactants were all varied.

Still, methoxyallene offered another synthetic use, if it could be deprototenated and made to react γ, rather than α, to the methoxyl group. That is, if the dianion 6 could be formed, it should react with carbonyl compounds and alkylating agents at the γ position, providing
butenolides and $\alpha,\beta$-unsaturated aldehydes, respectively, after appropriate treatment of the initial adducts. Thus, it would be a very simple $\beta$-acyl vinyl anion equivalent.

As mentioned earlier, it was reported elsewhere that $\tilde{6}$ could not be formed, and that turned out to be substantially true. Spectral evidence for the formation of $\tilde{6}$ and its subsequent reaction with adamantanone in the desired sense was obtained, however, when methoxyallene was treated sequentially with two equivalents of nBuLi in ether. Two different
methoxyl groups were evident in the NMR, as well as the allenic AB system of 11 overlapping with the singlet due to the allene terminus of 10. The ratio of 10 to 11 by NMR was 1:1. As this was unsatisfactory for synthetic purposes, we blocked the α position of methoxyallene by deprotonation and reaction with chlorotrimethylsilane. That alkylation provided a quantitative yield of the disubstituted allene 12. This allene could be deprotonated with nBuLi or tBuLi (which gave less clean product mixtures), and the resulting anion reacted well with carbonyl compounds, usually in ~90% yield, to provide adducts of the type 13. The idea of having compounds 13 is illustrated in Scheme III, for the cyclopentanone...
Scheme II

\[ \text{OCH}_3 \quad \text{Si(CH}_3)_3 \quad \text{OCH}_3 \quad \text{Si(CH}_3)_3 \]

\[ \text{R} \quad \text{R'} \quad \text{OH} \quad \text{R'} \quad \text{CH}_3 \text{O} \quad \text{Si(CH}_3)_3 \]

\[ 13 \]

13a: R, R' = cyclopentyl
13b: R, R' = cyclohexyl
13c: R = H, R' = C_9H_{19}
13d: R, R' = adamantyl
13e: R = H, R' = C_3H_7
13f: R = H, R' = 5-methyl furfuryl

case. Treatment of 13a with aqueous acid should lead to ring closure, to give reactive intermediate 14 which contains an allyl silane unit. If 14 underwent the desilylation reaction seen before for allyl silanes, then the enol ether 15 would be the result. 15 would then be easily hydrolyzable to the corresponding spirolactone. This sequence would
provide a non-epoxidative route to spirolactones, the goal which was sought in Chapter Two, using bromine addition to $\eta$-hydroxyvinylsilanes.

When $13a$ was subjected to either perchloric acid or hydrochloric acid treatment in aqueous THF, the butenolide $17$ rather than the saturated spirolactone predicted, was the product. Scheme IV shows the postulated course of the reaction. The intermediate $14$ is apparently produced, but rather than undergoing protodesilylation, it simply expels, at least formally, the trimethylsilyl anion, which captures a proton and is lost as trimethylsilane in the workup. The loss of trimethylsilyl anion is completely unprecedented in the literature, but simply seems the only way to rationalize the product observed. The yield of butenolide in the cyclopentanone case is often nearly quantitative, but for the
other substrates indicated in Scheme II, the hydrolysis using identical conditions is not as good, with one exception (see below). Small amounts of 18 and 19 can be obtained, but decomposition reactions dominate the hydrolyses of the other adducts, presumably via elimination pathways.
We had hoped to prove the loss of silane from intermediate $14$ by making adduct $20$ and subjecting it to the hydrolysis conditions. 1-Dimethylphenylsilylmethoxyallene can be formed in quantitative yield analogously to 1-trimethylsilylmethoxyallene, and its anion (formed via nBuLi) undergoes identical reactions with carbonyl compounds. Thus, $20$ was easily produced. If it lost dimethylphenylsilane during the hydrolysis, it would easily be detected, since dimethylphenylsilane has a boiling point of 155°C. Unfortunately, hydrolysis of $20$ under conditions used before to produce $17$ led to none of the desired product, and in fact to no major isolable product. However, two pieces of circumstantial evidence exist for the reaction sequence depicted in Scheme IV.

One other adduct for which the hydrolysis goes well is the one from decanal, $13c$. The product, however, is not the corresponding butenolide, but rather the furan $21$. This product can be seen to arise from an intermediate analogous to $14$. However, the presence of a proton in place of one of the alkyl groups of $14$ allows the 1,4 loss of methanol to provide the observed aromatic product.
Also, if allowed to stand neat in the cold or stirred at room temperature in dichloromethane, adduct 13a isomerizes to a single compound tentatively identified as 14. The reaction is very clean when done using the former method; the NMR signal for the allene proton disappears completely, and an AB quartet takes its place. The IR shows complete loss of the hydroxyl group of 13a.
Unfortunately, the production of butenolides by the reaction of 3-lithio-1-trimethylsilylmethoxyallene with ketones followed by hydrolysis is a very limited reaction sequence. It only works well to produce the butenolide 17. More work in this area is merited, since discovery of efficient hydrolysis conditions would provide a simple, high yielding method of butenolide formation. 88
General Experimental Information

All proton NMR spectra were obtained on either a Varian A-60 spectrometer or a Varian EM-360 spectrometer. Melting points were taken on a Thomas Hoover melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer 267 Grating Infrared Spectrophotometer. Elemental analyses were done by M-H-W Laboratories in Phoenix, Arizona. Mass spectral data were obtained on a Consolidated Electronic MS-9 Double Focusing mass spectrometer.
EXPERIMENTAL

83 Propargyl Alcohol Methyl Ether. A 1 l Morton flask equipped with a mechanical stirrer was charged with 50% sodium hydroxide (110 ml) and 44 ml of distilled water. Propargyl alcohol (1.0 mole, 56.0 g, 58.2 ml) was added slowly, causing formation of a dense white precipitate. Dimethylsulfate (.6 mole, 75.7 g, 56.9 ml) was added carefully, keeping the temperature below 60°C. When the addition was complete, the reaction mixture was heated at 50-60°C for 2 hours. The crude product was distilled from the reaction flask at 62-63°C. Accumulated water in the distillate was pipetted out, and the product was fractionated from calcium chloride (bp 59-60°C), giving 44.81 g (64%) of pure product. NMR (CDCl₃/TMS, δ): 4.10 (d, 2H, protons α to -OCH₃, J₆=2 Hz); 3.34 (s, 3H, -OCH₃); 2.50 (mult, 1H, acetylenic proton). MS:
C₉H₁₆O: calc: 70.042; obs: 70.042.

83 Methoxyallene. Dry propargyl alcohol methyl ether (.64 mole, 44.81 g) was refluxed over potassium t-butoxide (.11 mole, 12.3 g) for 3 hours. Then the reaction flask was cooled and evacuated to a pressure of about 20 mmHg. Methoxyallene was trapped in a receiver cooled to -78°C (39.41 g, 88%). NMR (CDCl₃/δ, δ): 6.69 (t, 1H, proton α to -OCH₃, J₆=5.5 Hz); 5.41 (d, 2H, allene terminus); 3.39 (s, 3H, -OCH₃).

1-(l-Methoxypropadienyl)cyclohex-2-enol. To a solution of nBuLi (11 mmole, 18.3 ml of a .6 M solution in pentane) in dry THF (11 ml) stirred under argon at -78°C was added methoxyallene (11 mmole, .77 g).
The solution was warmed to -20°C for 10-15 min., then copper(I)-iodide (5.7 mmole, 1.1 g) was added, causing a dark brown color to appear in the solution. After 10 min., 2-cyclohexen-1-one (5.2 mmole, 0.5 g, 0.5 ml) was added dropwise over 30 min., while the temperature was kept between -10°C and -15°C. After 1 hour, the reaction was judged complete by TLC (30% high petroleum ether, 20% EtOAc), and the mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed repeatedly with dilute ammonium hydroxide followed by water, to remove acculated solids. Removal of the dried (Na₂SO₄) solvent left a dark brown mobile oil whose IR showed it to be the 1,2 addition product. IR (neat, cm⁻¹): 3440s; 2930s; 1950w; 1650vw; 1460m; 1200m; 1050m. MS: C₁₀H₁₄O₂; calc: 166.099; obs: 166.099. 166 (82%), 151 (54%), 148 (100%).

1-(1-Methoxypropadienyl)cyclohex-2-enol. To a solution of dimethyl sulfide (84 mmole, 5.2 g, 6.1 ml) stirred in dry THF (20 ml) at -25°C under argon was added precipitated copper (I) iodide (23 mmole, 4.4 g). Most of the solid dissolved, giving the resulting solution a lime green color. To this solution was added a solution of 1-lithio-1-methoxy allene prepared by dropwise addition of methoxy allene (44 mmole, 3.1 g) to a stirred solution of nBuLi (44 mmole, 27.5 ml of a 1.6 M solution in hexane) in dry THF (10 ml) under argon at -25°C. The resulting solution was dark brown. After 30 min. further stirring, 2-cyclohexen-1-one (21 mmole, 2.0 g, 2.0 ml) was added dropwise. The reaction was judged to give one major product, by TLC (60% high petroleum ether, 40% EtOAc). The reaction mixture was poured into
dilute aqueous ammonium chloride layered with ether. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (Na$_2$SO$_4$) solvent gave what appeared to be a mixture of 1,2 and 1,4 addition products. (IR: $\nu_{\text{max}}$ 3450 cm$^{-1}$ and 1710 cm$^{-1}$). NMR was indicative of almost exclusive 1,2 product.

3-((1-Methoxypropadienyl)cyclohexanone (Not produced.) To a solution of dimethyl sulfide (21mmole, 1.3g, 1.5ml) in dry THF (10ml) stirred under argon at -40°C was added reprecipitated copper (I) iodide (5.7mmole, 1.1g). To this solution was added a solution of 1-lithio-1-methoxy allene made by adding methoxy allene (5.7mmole, .40g) to a stirred solution of nBuLi (5.7mmole, 3.6ml of a 1.6M solution in hexane) in dry THF (10ml) under argon at -78°C. After 30 min., 2-cyclohexen-1-one (5.2mmole, .5g, .5ml) was added in a dropwise fashion. No reaction of any kind was observed.

1-((1-Methoxypropadienyl)cyclohex-2-enol. To a solution of nBuLi (5.7mmole, 3.5ml of a 1.6M solution in hexane) in dry THF (5ml) stirred under argon at -25°C was added methoxy allene (5.7mmole, .40g). After 20-30 min., 2-cyclohexen-1-one (5.2mmole, .5g, .5ml) was added in a dropwise fashion. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the reaction mixture was poured into saturated aqueous ammonium chloride layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried (MgSO$_4$) solvent yielded .71g (82%) of crude product, containing just a trace of the corresponding 1,4 addition product, by IR. IR (neat, cm$^{-1}$): 3440s; 2930s; 1955m; 1460s; 1200s; 1055s. NMR (CDCl$_3$/TMS, $\delta$): 5.75 (mult,
2H, vinyl protons); 5.50 (s, 2H, allene terminus); 3.43 (s, 3H, -OCH₃); 2.55 (s, 1H, -OH as determined by D₂O wash); 1.79 (envelope, 6H, ring protons). MS: C₁₀H₁₄O₂: calc: 166.099; obs: 166.100. 166 (70%), 151 (44%), 148 (100%).

1-(1-Methoxypropadienyl)cyclopentanol. To a stirred solution of methoxyallene (9.0mmole, 3.7ml of a 2.45M solution in hexane). After being stirred for 30min., the resulting solution was treated successively with TMEDA (9.0mmole, 1.0g, 1.3ml) and tBuLi (9.0mmole, 4.7ml of a 1.9M solution in pentane). After a further 30min. stirring, the solution was treated with cyclopentanone (610mmole, .5g, .52ml). After an hour, the reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 1-(1-methoxypropadienyl)cyclopentanol as the major product, rather than 1-(3-methoxypropadienyl)cyclopentanol.

2-(1-Methoxypropadienyl)adamantan-2-ol (10). To a stirred solution of nBuLi (5.0mmole, 2.2ml of a 2.3M solution in n-hexane) in dry ether (5ml) under argon at -78°C was added methoxyallene (5.0mmole, .35g). After 30min., tBuLi (5.0mmole, 2.6ml of a 1.9M solution in n-pentane) was added. After a further 30min., the solution was warmed to -45°C and adamantanone (3.3mmole, .5g) was added dropwise as a solution in ether. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave .73g (100%) of 2-(1-Methoxypropadienyl)adamantan-2-ol, rather than
2-(3-methoxypropadienyl)adamantan-2-ol. IR (neat, cm⁻¹): 3450m; 2900s; 1949w; 1450m; 1190m; 937m. NMR (CDCl₃/TMS, δ): 5.50 (s, 1H, allenyl protons); 3.39 (s, 3H, -OCH₃); 1.73 (br, s, 14H, adamantyl system). MS: C₁₄H₂₀O₂: calc: 220.146; obs: 220.147.

1-Trimethylsilylmethoxyallene, (I). To a stirred solution of nBuLi (14mole, 61ml of a 2.3M solution in hexane) in dry ether (20ml) under argon at -78°C was added methoxyallene (.14mole, 10.0g). After 30min. stirring, the solution was treated with trimethylsilyl chloride (.15mole, 16.4g, 19.2ml). The reaction mixture was brought to -40°C, and stirred for 1 hour, during which time LiCl precipitated from solution. The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with ether. The aqueous phase was extracted and the combined organics were washed with water and dried over MgSO₄. The resulting solution was pumped down to 20mmHg, producing 16.12g (81%) of essentially pure product. IR (neat, cm⁻¹): 2940s; 1920m; 1250s; 1125s; 845s. NMR (CCl₄/δ): 5.16 (s, 2H, allenyl protons); 3.43 (s, 3H, -OCH₃); 0.18 (s, 9H, -TMS).

1-Dimethylphenylsilylmethoxyallene. To a stirred solution of nBuLi (32mmole, 20ml of a 1.6M solution in hexane) in dry ether (20ml) under argon at -78°C was added methoxyallene (32mmole, 2.2g). After 30 min., dimethylphenylsilyl chloride (29mmole, 5.0g, 4.8ml) was added in a dropwise fashion. The temperature was then allowed to come slowly to 10°C, causing precipitation of lithium chloride between -20°C and 10°C. The solution was poured into saturated aqueous sodium bicarbonate layered with ether. The aqueous phase was extracted, and the combined organics were washed with water. The resulting solution
was pumped down to 20mmHg, providing 5.9g (100%) of essentially pure product. IR (neat, cm⁻¹): 3075w; 3055w; 2965m; 1915w; 1430m; 1255m; 1130s; 980m; 825s. NMR (CDCl₃/TMS, δ) 7.24 (mult, 5H, aromatics); 5.10 (s, 2H, allenyl protons); 3.36 (s, 3H, -OCH₂); 0.34 (s, 6H, -CH₃'s on Si).

1-Triphenylsilylmethoxyallene. (Not produced). To a stirred solution of nBuLi (1.0mmole, 1.2ml of a 1.6M solution in n-hexane) in dry ether (5ml) under argon at -78°C was added methoxyallene (1.9 mmole, 13g). After 30min., triphenylsilyl chloride (1.7mmole, 0.50g) was added as a slurry in ether. The temperature of the reaction mixture was allowed to come successively to -35°C and room temperature. After some time, the solution was poured into saturated aqueous sodium bicarbonate layered with ether. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent left a product whose spectral data showed that it contained none of the desired product.

1-(3-Methoxy-3-trimethylsilylpropadienyl)cyclohexanol, (13b) To a solution of nBuLi (15 mmole, 9.4 ml of a 1.6M solution in n-hexane) in dry THF (5ml) stirred under argon at -75°C was added 1-trimethylsilylmethoxyallene (15mmole, 2.1g). The resulting solution was stirred at -78°C for 30min., at the end of which time cyclohexanone (10mmole, 1.0g, 1.0ml) was added in a dropwise fashion. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the
reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried \((\text{MgSO}_4)\) solvent gave 2.20 (92%) of crude product, pure enough for use in subsequent reactions. IR (neat, \(\text{cm}^{-1}\)): 3440\(\text{m}\); 2930\(\text{s}\); 1885\(\text{w}\); 1450\(\text{m}\); 1250\(\text{s}\); 845\(\text{s}\). NMR (CDCl\(_3\)/\(\phi\), 6): 5.54 (\(s\), \(1\text{H}\), allenyl proton); 3.36 (\(s\), 3\(\text{H}\), \(-\text{OCH}_3\)); 2.5-1.3 (envelope, 10\(\text{H}\), cyclohexyl protons); 0.1 (\(s\), 9\(\text{H}\), -TMS).

1-(3-Methoxy-3-trimethylsilylpropadienyl)decanol, (13c). To a stirred solution of tBuLi (4.8mmole, 2.5ml of a 1.9M solution in pentane) and TMEDA (4.8mmole, .56g, .73ml) in dry THF (5ml) under argon at -78°C was added 1-methoxy-1-trimethylsilylallene (4.8mmole, .68g). The resulting solution was stirred for 30min., and decanal (3.2mmole, .50g, .60ml) was added in a dropwise fashion. When the reaction was complete, as judged by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics washed with water. Removal of the dried \((\text{MgSO}_4)\) solvent gave .92g (97%) of crude product, pure enough to use in subsequent reactions. IR (neat, \(\text{cm}^{-1}\)): 3380\(\text{m}\); 2920\(\text{s}\); 1250\(\text{m}\); 845\(\text{s}\). NMR (CDCl\(_3\)/\(\phi\), 6): 5.70 (d, \(1\text{H}\), allenyl proton); 3.36 (s, 3\(\text{H}\), \(-\text{OCH}_3\)); 2.35 (s, \(1\text{H}\), -OH); 1.22 (s, 17\(\text{H}\), alkyl chain protons); 0.93 (mult, 3\(\text{H}\), \(-\text{CH}_3\) at end of alkyl chain); 0.10 (s, 9\(\text{H}\), -TMS).

1-(3-Methoxy-3-trimethylsilylpropadienyl)cyclopentanol, (13a). To a stirred solution of nBuLi (18mmole, 11.2ml of a 1.6M solution in n-hexane) in dry THF (8ml) under argon at -78°C was added 1-methoxy-1-trimethylsilylallene (18mmole, 2.6g). After 20min., cyclopentanone
(12mmole, 1.0g, 1.0ml) was added in a dropwise fashion. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 2.55g (94%) of crude product... Vacuum distillation (65-70°C at 0.15mmHg) gave 1.38g (51%) of pure compound. IR (neat, cm⁻¹): 3440m; 2960s; 1250s; 1120s; 845s. NMR (CCl₄, δ): 5.80 (s, 1H, allenyl proton); 3.39 (s, 3H, ring protons); 0.12 (s, 9H, -TMS). MS: C₁₂H₂₂O₂Si; calc: 226.139; obs: 226.140. 226 (59%), 208 (42%), 195 (100%).

1-(3-Methoxy-3-trimethylsilylpropadienyl)cyclopentanol, (I3a).

To a stirred solution of tBuLi (9.0mmole, 4.7ml of a 1.9M solution in n-pentane) and TMEDA (9.0mmole, 1.0g, 1.3ml) in dry THF (6ml) under argon at -78°C was added 1-methoxy-1-trimethylsilylallene (9.0 mmole, 1.3g) in a dropwise fashion. The resulting solution was stirred for 30min., then cyclopentanone (6.0mmole, .5g, .52ml) was added to it. The reaction was finished immediately by TLC (80% high petroleum ether, 20% EtOAc), and the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave .73g (56%) of crude product, which was purified by sublimation to give .57g (41%) of the pure compound as a waxy solid. IR (Nujol mull; cm⁻¹): 3270m; 2930s; 1920w; 1460m; 1250m; 1120m; 970m; 850m. NMR (CDCl₃, δ):
5.80 (s, 1H, allenyl proton); 3.35 (s, 3H, -OCH₃); 1.70 (s, 8H, ring protons); 0.10 (s, 9H, -TMS). MS: C₁₂H₂₂O₂Si: calc: 226.139; obs: 226.139, 226 (59%), 208 (42%), 195 (100%).

2-(3-Methoxy-3-trimethylsilylpropadienyl)adamantan-2-ol, (13d) To a solution of tBuLi (5.0 mmole, 2.6 ml of a 1.9 M solution in n-pentane) and TMEDA (5.0 mmole, 0.58 g, 0.75 ml) stirred in dry THF (5 ml) under argon was added at -78°C 1-methoxy-1-trimethylsilylallene (5.0 mmole, 0.71 g). The resulting solution was stirred for 30 min., and then adamantalone (3.3 mmole, 0.5 g) was added dropwise as a solution in dry THF. The reaction was judged complete immediately by TLC (80% high petroleum ether, 20% EtOAc), and the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent left 0.96 g (100%) of crude product, pure enough to use in subsequent reactions. IR (neat, cm⁻¹): 3450m; 2900s; 1910w; 1455m; 1250s; 1120s; 970s; 850s. NMR (CDCl₃, δ): 6.11 (s, 1H, allenyl proton); 3.39 (s, 3H, -OCH₃); 2.37 (s, 1H, -OH); 1.77 (envelope, 14H, adamantyl system); 0.14 (s, 9H, -TMS).

1-(3-Methoxy-3-trimethylsilylpropadienyl)butanol, (13e). To a stirred solution of tBuLi (11 mmole, 610 ml of a 1.9 M solution in pentane) in dry THF (6 ml) under argon at -78°C was added 1-methoxy-1-trimethylsilylallene (11 mmole, 1.6 g). After 30 min., butyaldehyde (7.3 mmole, 0.52 g, 0.64 ml) was added in dropwise fashion. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the
combined organics were washed with water. Removal of the dried (MgSO$_4$) solvent gave 0.84 g (54%) of crude product. IR (neat, cm$^{-1}$): 3410m; 2960m; 1886w; 1255m; 855s. NMR (CCl$_4$/TMS, 6): 5.71 (d, 1H, allenyl proton; J = 5Hz); 3.42 (s, 3H, -OCH$_3$); 1.8-0.8 (envelope, 8H, aliphatics); 0.20 (s, 9H, -TMS).

1-(5-Methylfurfuryl)-4-methoxy-4-trimethylsilylbuta-2,3-dienol (13f). To a stirred solution of tBuLi (9.0 mmole, 4.7 ml of a 1.9 M solution in pentane) in dry THF (5 ml) under argon at -78°C was added 1-methoxy-1-trimethylsilylallene (9.0 mmole, 1.3 g). After a short period of stirring, the solution was brought to -40°C, and 5-methylfurfural (4.5 mmole, .5 g, .45 ml) was added dropwise. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc; not very clean), the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO$_4$) solvent gave 1.08 g (96%) of crude product. IR (neat, cm$^{-1}$): 3400m; 2950m; 1885w; 1250s; 845s. NMR (CCl$_4$/TMS, 6): 5.5-5.5 (mult, 4H, furan, alleny1, and allylic protons); 3.37 (s, 3H, -OCH$_3$); 2.24 (s, 3H, -CH$_3$); 0.12 (s, 9H, -TMS). (Also minor signals indicating impurities).

1-(3-Dimethylphenylsilyl-3-methoxypropadienyl)cyclopentanol (20). To a stirred solution of nBuLi (9.0 mmole, 5.6 ml of a 1.6 M solution in hexane) in dry THF (6 ml) was added 1-dimethylphenylsilyl-1-methoxyallene (9.0 mmole, 1.8 g). After 45 min. cyclopentanone (6.0 mmole, .50 g, .52 ml) was added in a dropwise fashion. When the reaction was judged complete by TLC (80% high petroleum ether, 20% EtOAc),
the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent gave 1.67g (96%) of crude product, pure enough to use in subsequent reactions. IR (neat, cm⁻¹): 3430m; 2970s; 1920w; 840s, 820s. NMR (CCl₄/δ, δ): 7.25 (mult, 5H, aromatics); 5.67 (s, 1H, allenyl proton); 3.37 (s, 3H, -OCH₃); 1.60 (s, 8H, ring protons); 0.38 (s, 6H, -CH₃'s on Si). MS: C₁₁H₂₂O₂Si: calc: 288.155; obs: 288, 155. 288 (60%), 274 (100%), 272 (100%).

2-Methoxy-2-trimethylsilyl-1-oxaspiro[4.4]non-3-ene, (14). 1-(3-Methoxy-3-trimethylsilylpropadienyl)cyclopentanol (1.3mmole, .30g) was allowed to stand in a refrigerator for 30 days. At the end of that time, the desired cyclization product was the sole isolated product. IR (neat, cm⁻¹): 2950s; 1585w; 1250s; 1100s; 840s. NMR (CCl₄/TMS, δ): 4.67 (q, 2H, vinyl protons; JAB = 2Hz); 3.16 (s, 3H, -OCH₃); 1.65 (envelope, 8H, ring protons); 0.14 (s, 9H, -TMS).

1-Oxaspiro-2-oxo[4.4]non-3-ene, (17). 1-(3-Methoxy-3-trimethylsilylpropadienyl)cyclopentanol (2.2mmole, .5g) was taken up in 20% aqueous THF (10ml) and the resulting solution was stirred at 0°C. Perchloric acid (15 drops of a 70% solution) was added in a dropwise fashion, resulting in immediate destruction of starting material and production of one major product by TLC (80% high petroleum ether, 20% EtOAc). The solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted and the combined organics washed with water. Removal of the dried (MgSO₄) solvent gave .30g (100%) of crude product. Purification
by preparative layer TLC (80% high petroleum ether, 20% EtOAc) gave 0.09g (30%) of pure product. IR (neat, cm⁻¹): 2960s; 1750s; 1600w; 1155s; 1070m; 990m; 940m; 820m. NMR (CDCl₃/TMS, δ): 6.65 (q, 2H, olefinic protons; Jₐb = 5.5Hz); 1.90 (s, 8H, ring protons). MS: C₈H₁₀O₂: calc: 138.068; obs: 138.068. 138 (100%), 126 (41%), 111 (32%).

2-Oxoadamantanespiro-2'-dihydrofuran, (I). 2-(3-Methoxy-3-trimethylsilylpropadienyl)adamantan-2-ol (1.7mmole, 0.5g) was taken up in 20% aqueous THF (5ml) and the resulting solution was stirred at 0°C. Perchloric acid (20 drops of a 70% solution) was added. When destruction of starting material was evident by TLC (80% high petroleum ether, 20% EtOAc), the reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal of the dried (MgSO₄) solvent left a dark oil from which the product was crystallized with high petroleum ether in low yield. IR (Nujol mull, cm⁻¹): 2920s; 1740m; 1595w; 1455s. NMR (CDCl₃/TMS, δ): 6.90 (q, 2H, vinyl protons; Jₐb = 6Hz); 2.5-1.5 (envelope, 14H, adamantyl system). MS: C₁₃H₁₆O₂: calc: 204.115; obs: 204.116.

1-Trimethylsilyl-5-nonanylfuran, (1I). 1-(3-Methoxy-3-trimethylsilylpropadienyl)decanol (1.7mmole, 0.5g) was dissolved in 20% aqueous THF (5ml), and the resulting solution was stirred at 0°C. Perchloric acid (20 drops of a 70% solution) was added dropwise, and the reaction was over in 20 min. as judged by TLC (80% high petroleum ether, 20% EtOAc). The reaction mixture was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted, and the combined organics were washed with water. Removal
of the dried (MgSO₄) solvent gave 0.40 g (89%) of crude product. IR (neat, cm⁻¹): 2920 s; 2855 m; 1250 m; 845 m. NMR (CCl₄/TMS, δ): 6.07 (q, 2H, furan protons, Jₐb = 3 Hz); 2.55 (mult, 2H, allylic protons); 1.27 (s, 14H, alkyl chain); 0.90 (mult, 3H, -CH₃ at end of chain); 0.23 (s, 9H, -TMS). MS: C₁₀H₃₀OSi: M⁺ at 266.
REFERENCES


\[
\begin{align*}
\text{OCH}_3 & + \phi_3 \text{P} + \text{OEt} \rightarrow \phi_3 \text{P} \text{Et} \\
& \rightarrow \phi_3 \text{P} \text{Et} \\
\end{align*}
\]

A


35. See references 12-18.


50. Ibid.


66. Petrarch System, Inc.


68. Yields as low as the mid-50's were only obtained for lower molecular weight substrates; volatility may have been the major contributing factor to loss of product in those cases.

69. This result is in accordance with Baldwin's Rules (J. E. Baldwin, J.C.S. Chem. Comm., 734 (1976)). That is, the oxetane 3 is the product of 4-exo-tet closure, which is favored over 5-endo-tet closure.

   It is interesting that when the epoxide from 2 was treated with p-toluene sulfonic acid in benzene, dehydration was the only reaction; no ring closure products at all were observed. One might have expected 5-endo-tet closure in that case, considering the transformation already established from 5-hydroxy-α,β-epoxy-silanes to 5-membered methyl lactols. Thus, the latter reaction must be proceeding by a pathway such as the one shown in Scheme I', rather than by ring closure concomitant with epoxide opening, as might otherwise have been imagined.
Scheme I'

2. \( p-TsOH \) →

\[
\begin{align*}
\text{HO} & \quad \text{Si}(\text{CH}_3)_3 \\
\text{O} & \quad \text{BF}_3 \cdot \text{Et}_2 \text{O} \\
\text{CH}_3 \text{OH} & \quad \text{HO} \\
& \quad \text{Si}(\text{CH}_3)_3 \\
& \quad \text{BF}_3 (\text{H}) \\
& \quad \text{HOCH}_3
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \text{Si}(\text{CH}_3)_3 \\
\text{O} & \quad \text{BF}_3 (\text{H}) \\
\text{Si}(\text{CH}_3)_3 & \quad \text{BF}_3 (\text{H}) \\
\text{HOCH}_3 & \quad \text{OCH}_3
\end{align*}
\]
70. (a) Dr. Charles Cottrell is thanked for his tenacious work on these NMR experiments.


74. Dr. J. Parikh is thanked for this initial observation.


   (e) L. Brandsma, H. E. Wijers, and J. F. Arens, Recueil, 82, 1040


