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THE CHEMISTRY OF BIS-(TRIMETHYLSILYL)KETENE
AND A RATE DECOMPOSITION STUDY OF
BIS-SILYLATED ACETATES

By

Behrouz Cyrour

A DISSERTATION

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in partial fulfillment of the requirements
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DOCTOR OF PHILOSOPHY

Department of Chemistry

1980

ABSTRACT

THE CHEMISTRY OF BIS-(TRIMETHYLSILYL)KETENE AND A RATE OF DECOMPOSITION STUDY OF BIS-SILYLATED ACETATES

By

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Methyl, ethyl, and isopropyl bis-(trimethylsilyl)-acetate were prepared in 80-88% isolated yield by treating bis-(trimethylsilyl)ketene with the appropriate alcohol in the presence of methanesulfonic acid at room temperature.

The esters were converted quantitatively to the corresponding lithium enolates by reaction with one equivalent of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78°C . The THF solutions are stable for at least one hour at -78°C , but decomposes to bis-(trimethylsilyl)ketene at higher temperatures. The less substituted members of the series decompose faster than the more highly substituted enolates; $\text{R}=\text{Me} \rangle \text{Et} \rangle \text{i-C}_3\text{H}_7 \rangle \text{t-C}_4\text{H}_9$

Bis-(trimethylsilyl)ketene was reacted with methyl-lithium, n-butyllithium and tert-butyllithium at room temperature to give the corresponding α, α , -bis-(trimethylsilyl)ketone enolate.

α, α -bis-(trimethylsilyl) ketones were obtained in 75-85% yield by quenching the reaction mixtures with dilute acetic acid or H_2O .

The lithium enolate of α, α -bis-(trimethylsilyl)-acetone was reacted with trimethylchlorosilane to give

the corresponding silyl enol ether in quantitative yield. This enolate was also reacted with benzaldehyde to give the α -silylvinyl ketone.

The lithium enolate of α,α -bis-(trimethylsilyl)-acetone failed to react with aldehydes or ketones possessing one or more α -hydrogen, presumably due to the protonation of the enolate by carbonyl compounds with acidic α -hydrogens.

ACKNOWLEDGMENTS

The author wishes to extend his appreciation to Dr. Michael W. Rathke for his ideas, time and assistance throughout this project. Thanks are also given to Dr. Donald G. Farnum for serving as second reader and for his helpful comments.

Appreciation is also extended to past and present members of Dr. Rathke's research group who have always provided assistance and an enjoyable atmosphere in the Lab.

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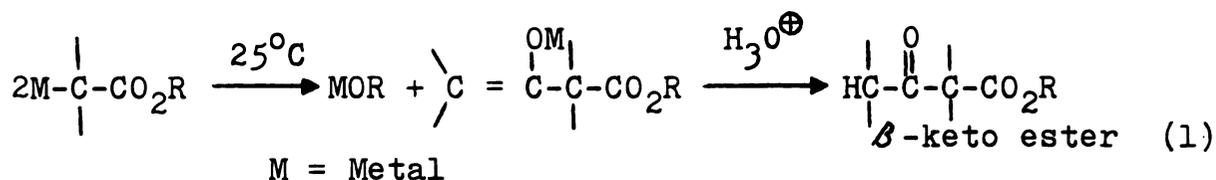
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CHAPTER I

PREPARATION OF α, α -BIS-(TRIMETHYLSILYL)ACETATES AND
EXAMINATION OF THEIR LITHIUM ENOLATE DECOMPOSITION

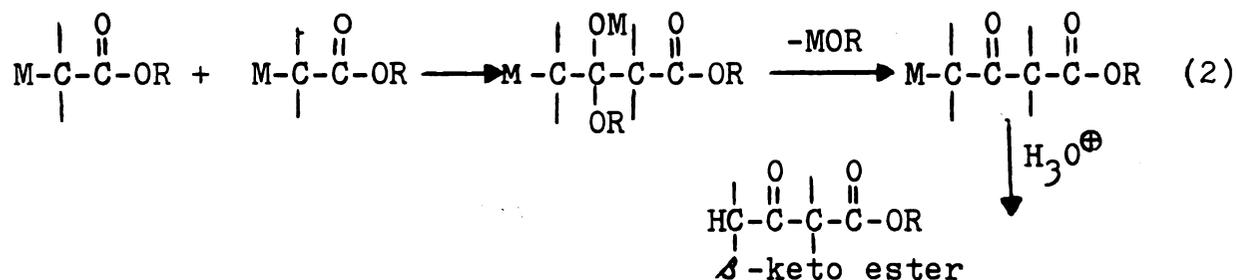
INTRODUCTION

Unlike ketone enolates,¹ the enolates of simple esters are not stable indefinitely at room temperature,² but decompose at varying rates to the corresponding β -keto esters (eq. 1).

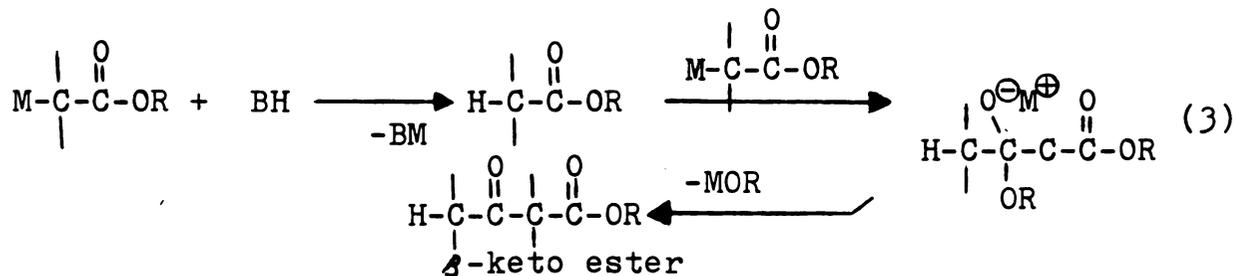


The decomposition to β -keto esters may occur by at least three pathways:

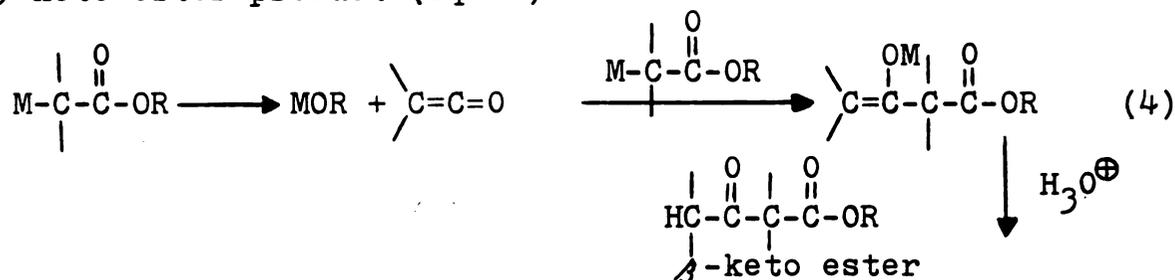
(a) Direct coupling of the ester enolate with a second molecule of enolate (eq. 2).



(b) An inverse Claisen condensation which entails removing a proton from the solvent or from amine and rapid condensation of the ester thus formed with another molecule of enolate³ (eq. 3).

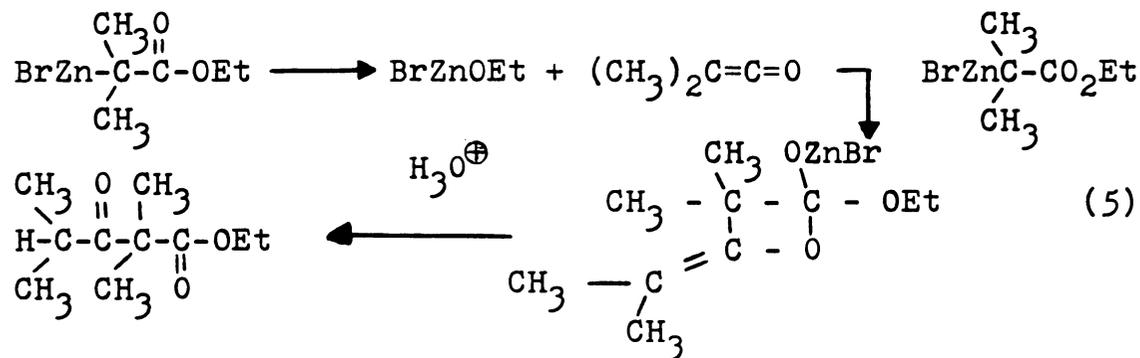


(c) Initial decomposition to a ketene which then condenses with a second molecule of enolate to give the observed β -keto ester product (eq. 4).



A study of the kinetic behavior of the decomposition of ester enolates, which showed first order kinetics,⁴ provided evidence against direct enolate coupling (pathway a).

The ketene intermediate (pathway c) to β -keto ester formation was suggested by Vaughan⁵ for the self condensation of the reagent prepared from ethyl α -bromo-~~isobutyrate~~ isobutyrate and zinc metal (eq. 5).

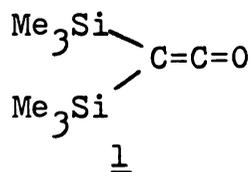
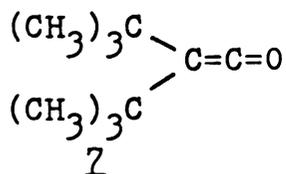


Ketene intermediates have also been proposed for the $E_{1\text{cb}}$ mechanism in the hydrolysis of malonic and β -keto esters.⁶⁻¹⁰

Recently, bis-(trimethylsilyl)ketene was isolated from the decomposition of lithium bis-(trimethylsilyl) acetate enolate.¹⁹

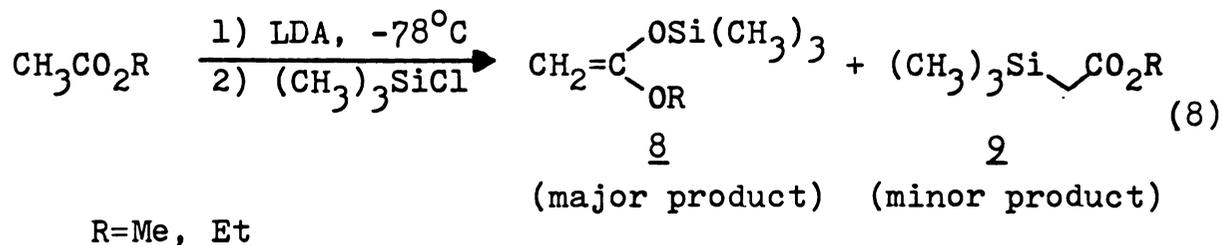
Since the direct δ -elimination of a metal alkoxide is a very rare occurrence, and the trapping of the ketene intermediate¹¹ was often not possible (for example, ketene trapping with dimethylamine or detection by an IR study of the solution was unsuccessful for lithio isobutyrate and lithio t-butyl acetate decomposition),¹² it was of interest to study this reaction in more detail. In particular, it was of interest to know what effect the R group in the alcohol portion of ester enolate has on the rate of elimination of metal alkoxide, M-OR.

Since the elimination of MOR to form ketene from most ester enolates is followed by a further rapid condensation of ketene, it was desirable to choose an ester which would produce a stable ketene, thereby simplifying the rate determination of the initial elimination. Both di-tert-butylketene,¹³ 2, and bis-(trimethylsilyl)ketene, 1, are reported to be very stable and unreactive to nucleophilic attack.

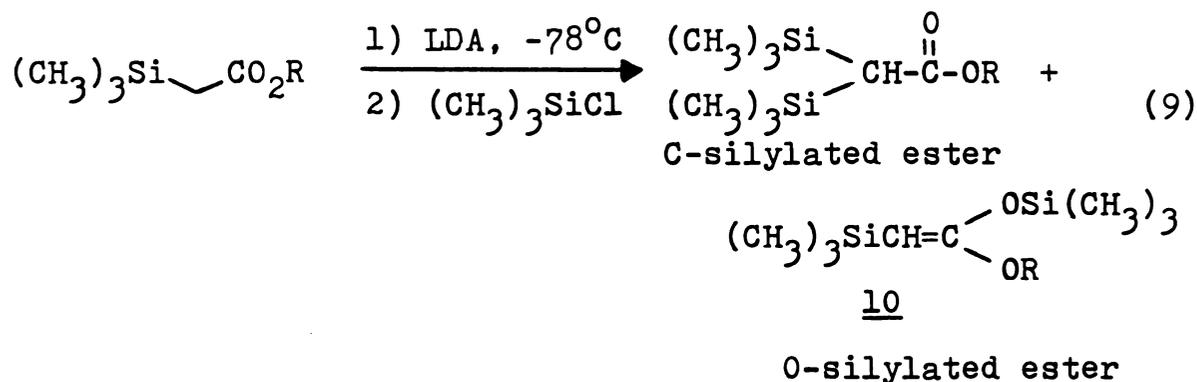


However, the esters leading to di-tert-butyl ketene are reported to be inert to amide bases such as LDA, presumably

gives 65% O-silylated and 35% C-silylated product.

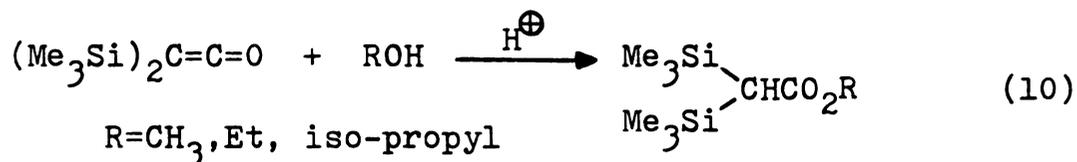


Also, in the second step of the silylation of 9, O-silylation would be a problem since α -substituted acetate enolates (except for tert butyl esters) give almost exclusively the O-silylated compound 10¹⁸ (eq. 9).



The O-silylated products obtained in the first and second step cannot be used for our study.

A reasonable preparation of methyl, ethyl and isopropyl bis-(trimethylsilyl)acetates would be the reaction of bis-(trimethylsilyl)ketene with the corresponding alcohol (eq. 10).

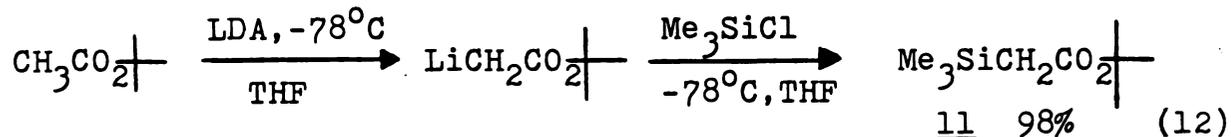


This stable ketene is readily available by the decomposition

RESULTS

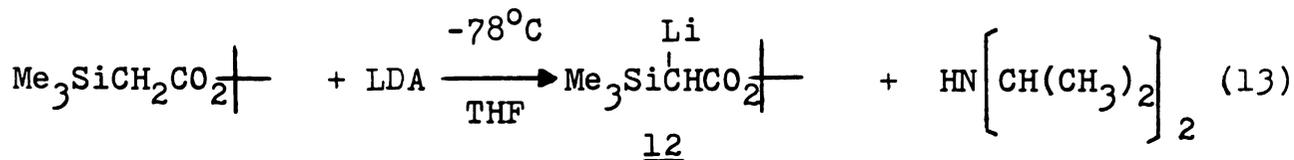
Preparation of Bis-(trimethylsilyl)ketene

Tert-butyl acetate was reacted with an equivalent of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78°C . The reaction mixture was stirred for 10 minutes at -78°C to complete enolate formation. One equivalent of trimethylchlorosilane was added and stirred for an additional 30 minutes to convert the enolate to tert-butyl (trimethylsilyl)acetate (eq. 12).

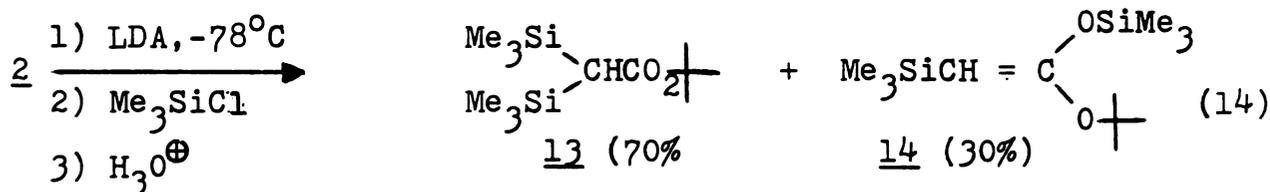


Quenching the solution with dilute hydrochloric acid is not desirable because, not only does remaining acid or water in the mono-silylated tert-butyl acetate, 11, destroy the newly formed enolate in the next step, but also the separation and distillation of 11 is time consuming. Therefore, the solution of 11 without quenching was transferred to an equivalent of LDA in THF at -78°C . The solution was stirred for 15 minutes to convert the mono-silylated tert-butyl acetate to the corresponding lithium enolate, 12,

(eq. 13).

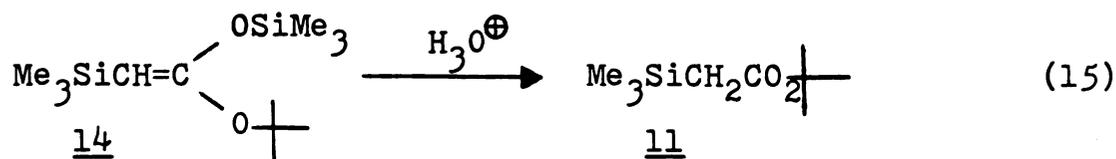


An equivalent of trimethylchlorosilane was added to the solution and the solution was stirred for 30 minutes at -78°C and for another 15 minutes at room temperature to convert 12 to tert-butyl bis-(trimethylsilyl)acetate 13 (70%) and 14 (30%) (eq. 14).

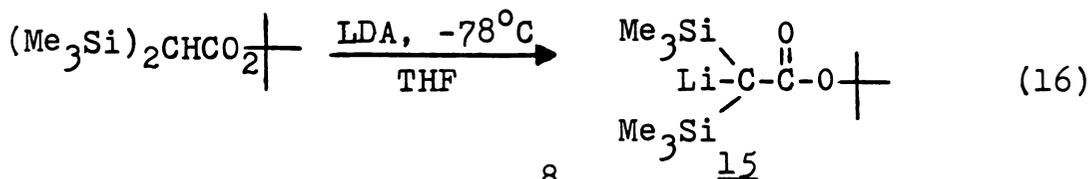


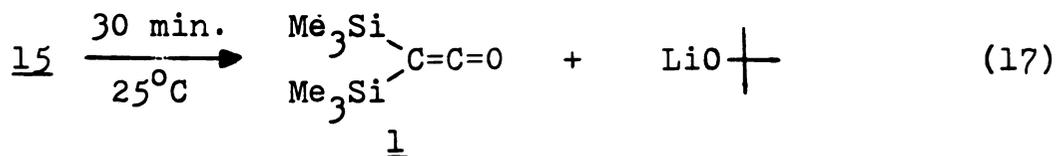
After quenching with 3M HCl and distillation, compound 13 was isolated in 60% yield.

Compound 14 was recovered and converted to the mono-silylated ester 11 (eq. 15) in the quenching step. 11 was then recycled for bis-silylation.



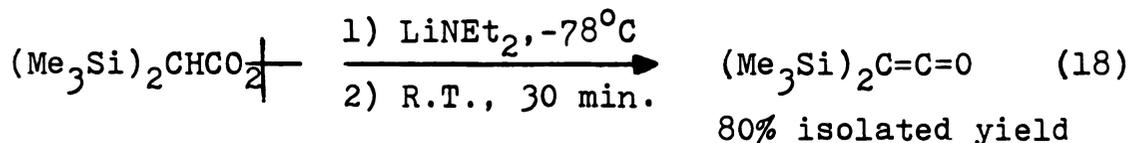
Pure 13 was treated with one equivalent of LDA in THF at -78°C for 15 minutes, then the solution was warmed to room temperature and stirred for 30 minutes to convert the enolate 15 to bis-(trimethylsilyl)ketene, 1, (eq. 16, 17).





Quenching with even dilute hydrochloric acid destroyed at least some of the ketene. Quenching with distilled water separated the ketene 1 from the aqueous layer without loss. Separation and careful distillation of the organic layer under reduced pressure gave a 60% yield of bis-(trimethylsilyl)ketene.

Some of the ketene was found in the evaporated solvent. From this, it was concluded that using a lower boiling solvent and dialkylamine in the reaction would simplify the separation. With this in mind, diisopropylamine (B.P. 85°C) was replaced with the relatively volatile diethylamine (B.P. 55°C); THF (B.P. 67°C) was replaced with diethylether (B.P. 34°C). Then diethylether and diethylamine were evaporated at 0°C under reduced pressure. The ketene was distilled under reduced pressure using an oil bath at approximately 30°C. With this improved procedure the yield of isolated ketene was increased from 60% to 80% (eq. 18).

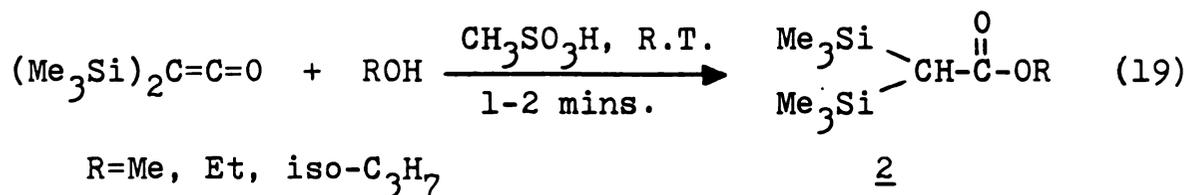


Preparation of Bis-(trimethylsilyl) acetates

Bis-(trimethylsilyl)ketene was added to an equivalent amount of the corresponding alcohol at room temperature without any solvent. No addition product was found after

reacting overnight. Only starting materials were found in the solution mixture.

The reaction was only slightly catalyzed by glacial acetic acid, but it was catalyzed by stronger acids such as concentrated sulfuric acid and methanesulfonic acid at room temperature. Bis-(trimethylsilyl)ketene was added dropwise to an equivalent amount of the corresponding alcohol containing 0.01% mole equivalent of methanesulfonic acid. The solution was stirred for 1-2 minutes. GLC analysis of the solution confirmed that the ketene was converted to the corresponding bis-(trimethylsilyl)acetate (eq. 19).

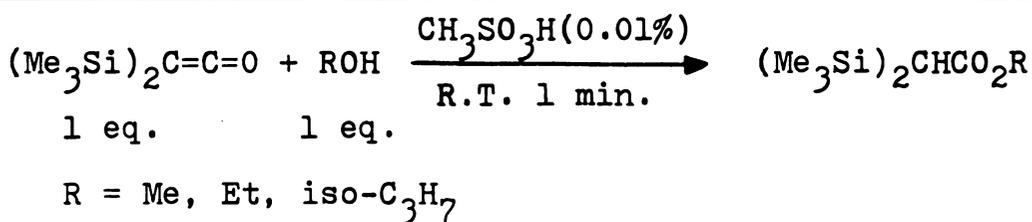


The colorless α,α bis-(trimethylsilyl) acetates, 2, are stable at room temperature indefinitely. The products 2 were distilled under reduced pressure, with isolated yields ranging from 80% to 88%.

The results obtained with methanesulfonic acid are summarized in Table 1.

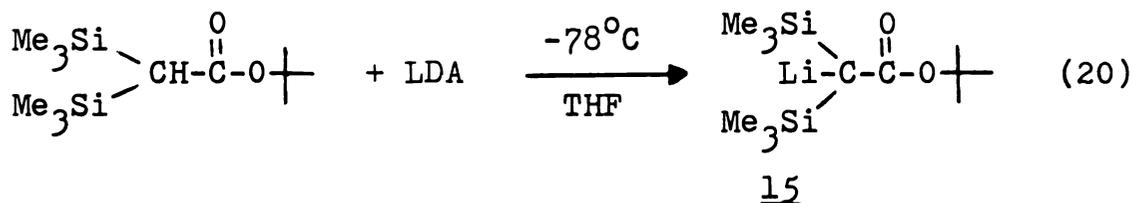
Table 1. Preparation of Bis-(trimethylsilyl) acetates

ROH	Reaction Condition	Product	Isolated % yield
MeOH	No solvent R.T. 1 min.	$(\text{Me}_3\text{Si})_2\text{CHCO}_2\text{CH}_3$	80
EtOH	No solvent R.T. 1 min.	$(\text{Me}_3\text{Si})_2\text{CHCO}_2\text{Et}$	81
Isopropyl -OH	No solvent R.T. 1 min.	$(\text{Me}_3\text{Si})_2\text{CHCO}_2^i\text{C}_3\text{H}_7$	88

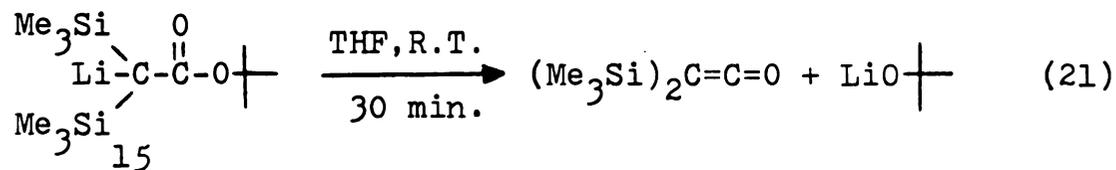


Decomposition study of Lithio tert-butyl Bis-(trimethylsilyl) acetate

Tert-butyl bis-(trimethylsilyl)acetate was added to an equivalent amount of LDA in THF at -78°C . The solution was stirred for 10 minutes to form the corresponding lithium enolate 15 (eq. 20).



15 is stable in solution at -78°C for at least 2 hours, but decomposes to bis-(trimethylsilyl)ketene and lithium tert-butoxide within 30 minutes at room temperature (eq. 21)



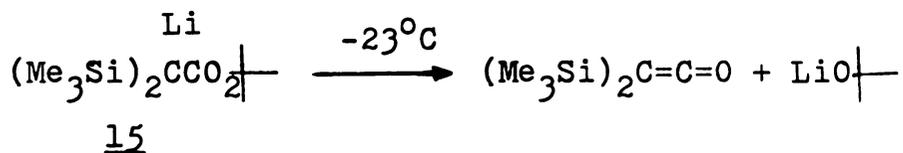
Although the decomposition of 15 is slow enough at room temperature to follow the rate of decomposition, because of the fast decomposition of the methyl analogues, even at 0°C, a temperature of -23°C was chosen for a comparison of rates.

Five μ l of a THF solution of the lithium enolate of tert-butyl bis-(trimethylsilyl)acetate at -78°C, was withdrawn and injected quickly onto the GLC. Only bis-(trimethylsilyl)ketene was observed, in quantitative yield by internal standard. Similar behavior was observed for the other lithium enolates of the bis-silylated acetates. From these observations, it was concluded that lithium enolates of bis-(trimethylsilyl)acetate decompose to bis-(trimethylsilyl)ketene on the GLC column (SE-30.5% on chromosorb W). Therefore, a THF solution of enolate 15 was warmed to -23°C in a CCl₄-Dry Ice bath. An internal standard was added and the rate of decomposition was followed by removing a small aliquot with a cooled syringe and adding the aliquot to sufficient water to quench the enolate to the ester.

After addition of pentane and drying over anhydrous magnesium sulfate, the amount of ketene formed was measured by GLC analysis. Results are shown in Table 2.

Table 2. The Rate of Decomposition of Lithio-tert-butyl bis (trimethylsilyl) acetate at -23°C .

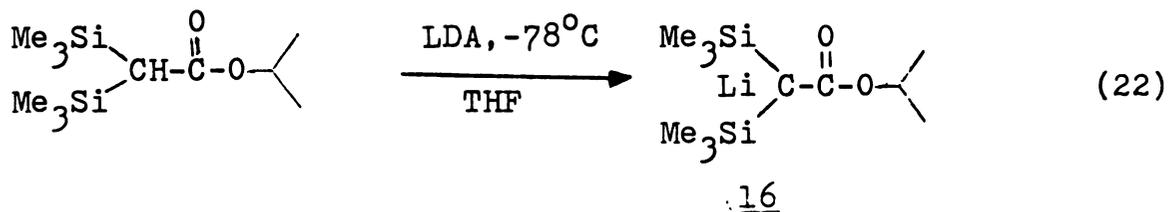
Time (min.) enolate stirred at -23°C	% ketene formed
7.5	13
30	28
60	33
100	37
200	50



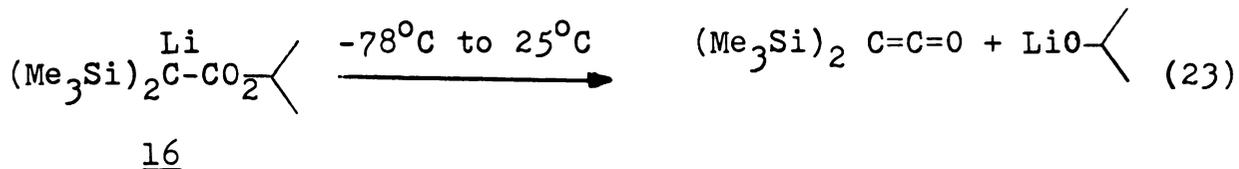
These data are presented graphically in Figure 1, by plotting the percent of produced ketene versus time. These data show that at -23°C , 3.3 hours are needed to convert half of the lithium enolate 15 to ketene.

Decomposition Study of Lithio-isopropyl Bis-(trimethylsilyl) acetate

Isopropyl bis-(trimethylsilyl)acetate was converted quantitatively to the corresponding lithium enolate 16, by treating with one equivalent of LDA in THF at -78°C for 10 minutes (eq. 22).



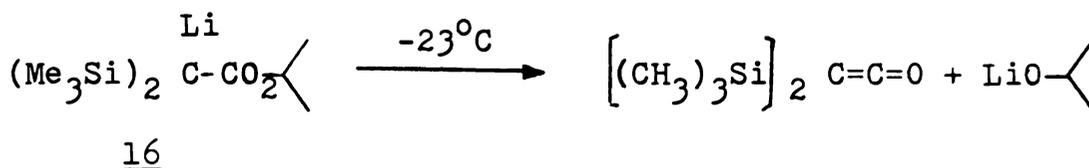
The enolate 16 is stable at -78°C for at least 1.5 hr. As the temperature is increased to 25°C , the enolate decomposes to bis-(trimethylsilyl)ketene and lithium isopropoxide (eq. 23).



The THF solution of this enolate 16 was warmed to -23°C in a CCl_4 -Dry Ice bath and an internal standard was added. At appropriate intervals, ketene formation was determined as before. The results are presented in Table 3.

Table 3. The Rate of Decomposition of Lithio-isopropyl Bis (trimethylsilyl) acetate at -23°C .

Time (min) enolate stirred at -23°C	% ketene formed
6	15
10	20
20	27
40	36
60	41
90	47
120	51



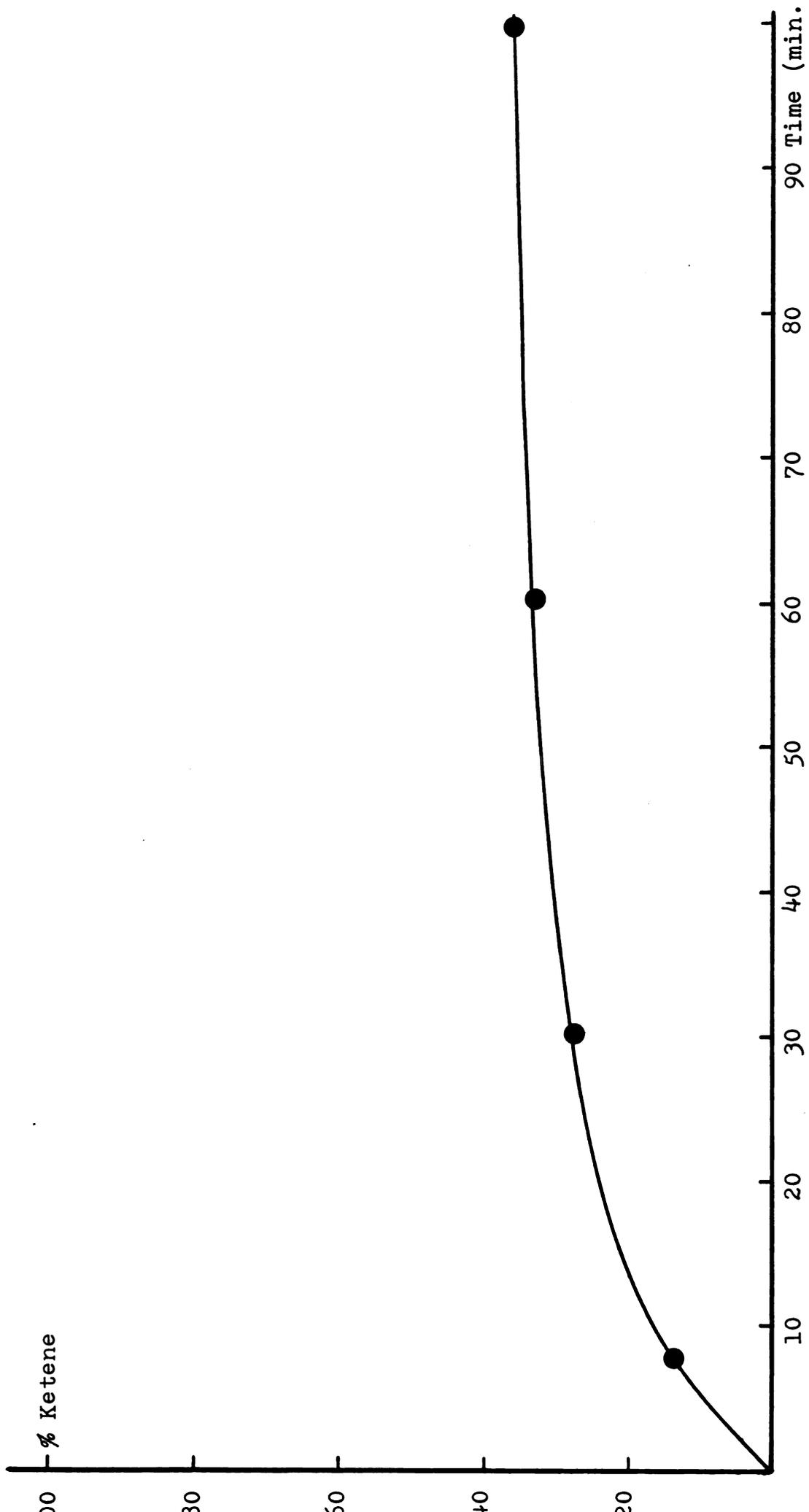


Figure 1. Rate of Decomposition of Lithio Tert-Butyl Bis-(trimethylsilyl)acetate at -23°C .

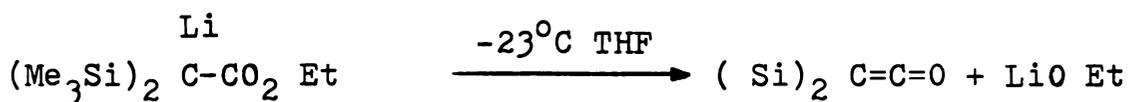
The data show that, after approximately 2 hours at -23°C , half of the Lithio-isopropyl bis-(trimethylsilyl) acetate has decomposed to ketene. The data are presented graphically in Figure 2 as before.

Rate of decomposition of Lithio-Ethyl and Methyl-Bis (trimethylsilyl) acetates

Ethyl and methyl bis-(trimethylsilyl)acetates were treated similarly. The results are presented in Tables 4 and 5.

Table 4. The Rate of Decomposition of Lithio-Ethyl-Bis (trimethylsilyl) acetate at -23°C .

Time (min) enolate stirred at -23°C	% ketene formed
5	29
10	43
20	52
40	54
60	69



These data show that less than 20 min. is needed for the decomposition of half of the lithio ethyl bis-(trimethylsilyl)acetate and less than 5 minutes for the methyl ester at -23°C . These data are presented graphically in Figures 3 and 4.

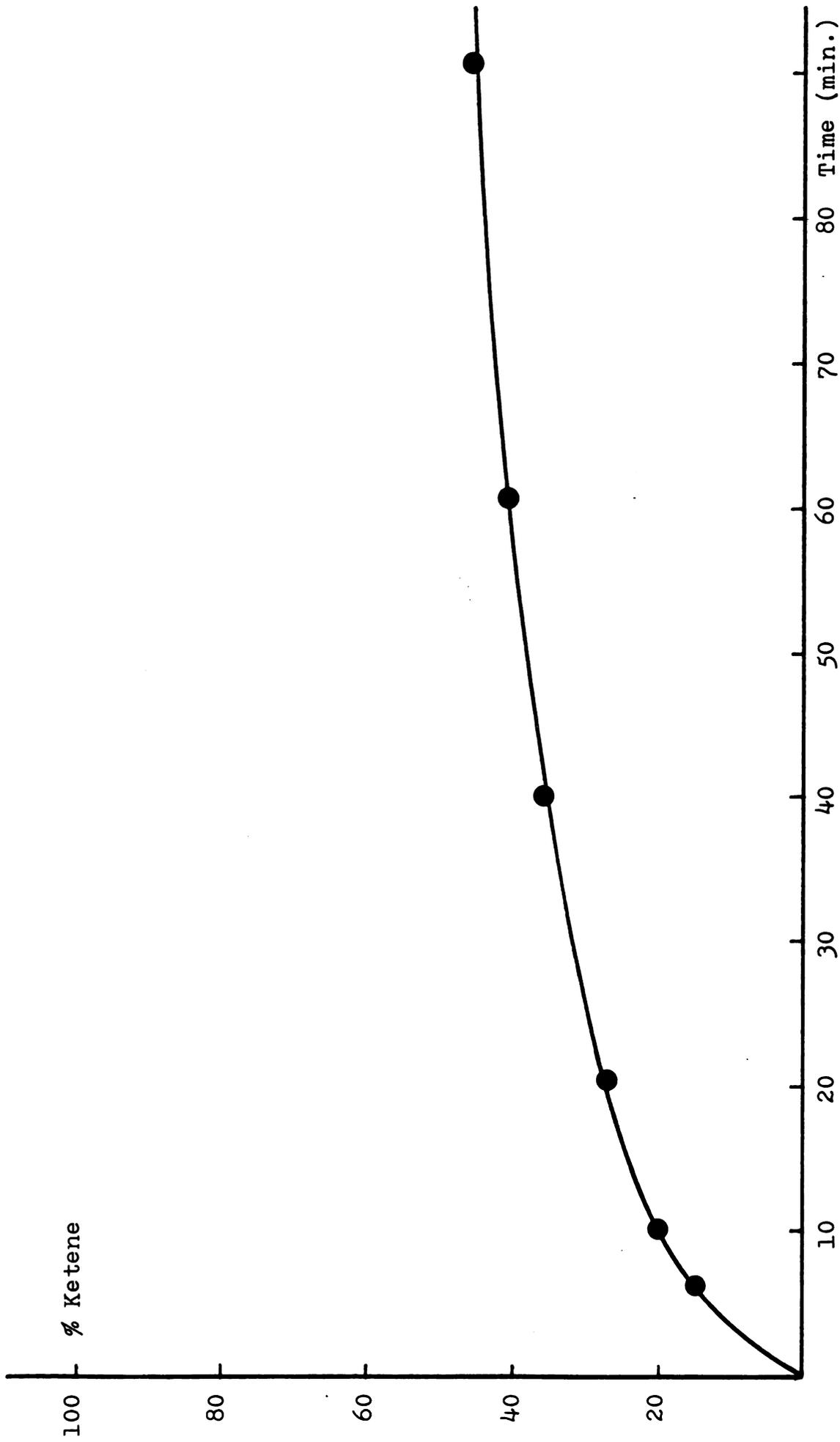
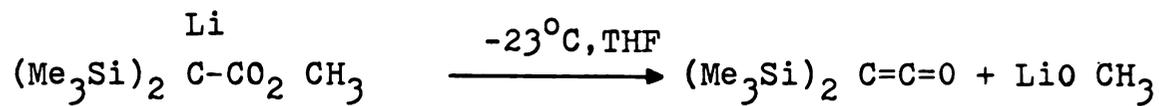


Figure 2. Rate of Decomposition of Lithio Isopropyl Bis-(trimethylsilyl)acetate at -23°C .

Table 5. The Rate of Decomposition of Lithio Methyl Bis-(trimethylsilyl)acetate at -23°C .

Time (min.) enolate stirred at -23°C	% ketene formed
2	25
4	41
5	50
10	65
15	70
20	75
40	81



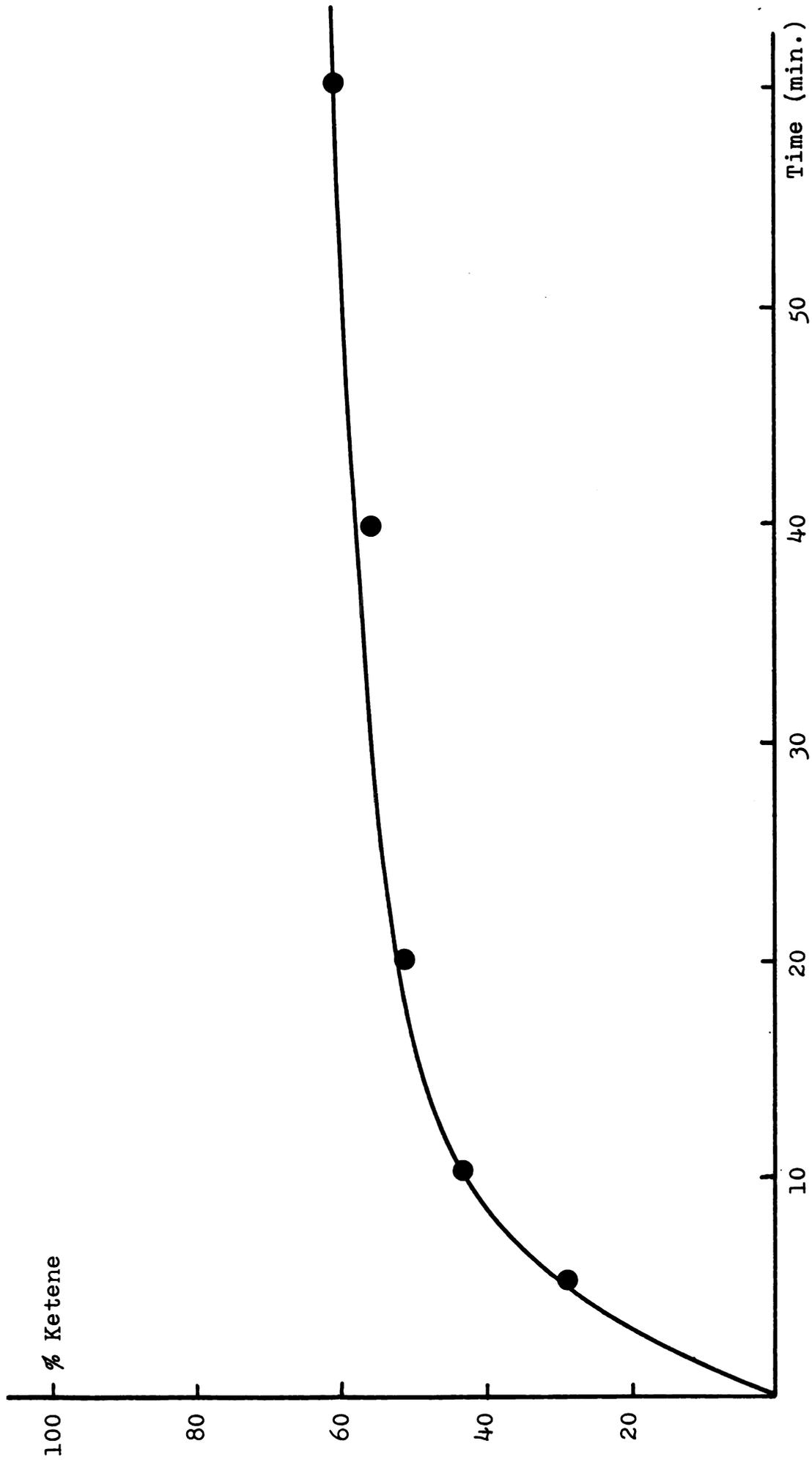


Figure 3. Rate of Decomposition of Lithio Ethyl Bis-(trimethylsilyl)acetate at -23°C .

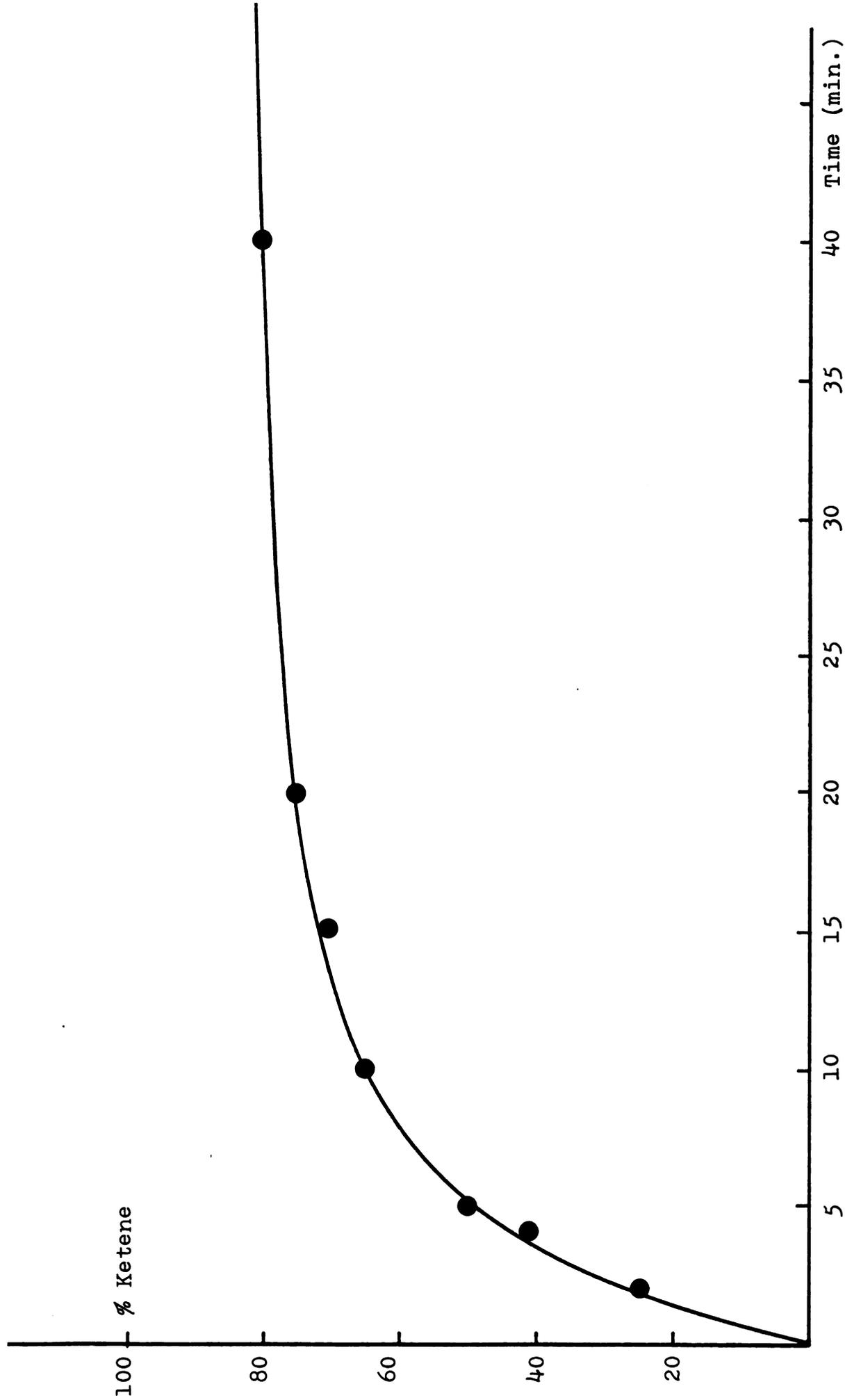
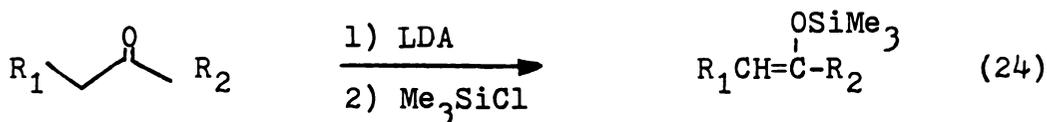


Figure 4. Rate of Decomposition of Lithio Methyl Bis-(trimethylsilyl)acetate at -23°C .

DISCUSSION

Preparation of α, α -Bis-(trimethylsilyl)acetates

Trialkylchlorosilanes react with ketone enolates to produce O-silylated products exclusively²⁰⁻²⁴ (eq. 24). Ketones substituted on the α position with trialkylsilyl groups are unstable relative to their O-silylated isomers²⁵ and rearrange to the O-silylated isomer under the influence of heat or catalyst²⁶ (eq. 25).



Silylation of ester enolates with trialkylhalosilanes can occur on either the carbon or oxygen atom (Fig. 5).

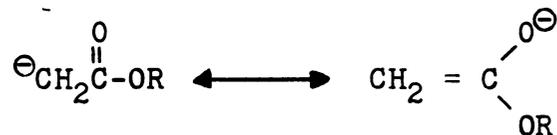
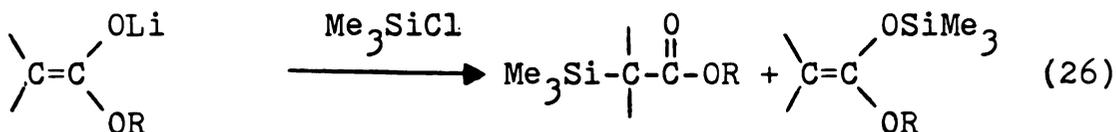
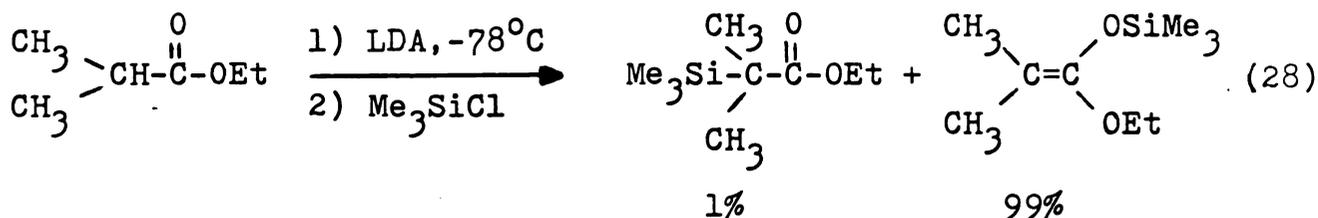
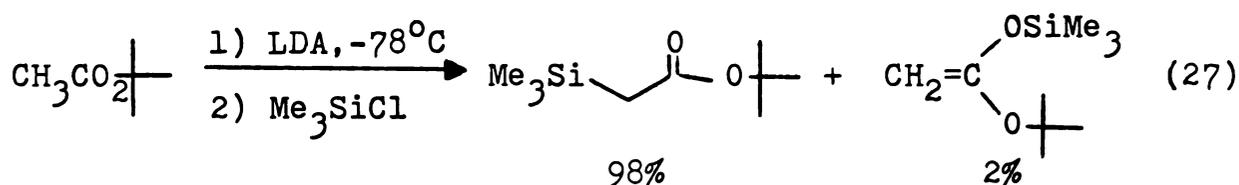


Figure 5. Ester enolates resonance structures.

The ratio of C to O-silylated product depends heavily on the structure of the ester enolate used (eq. 26).



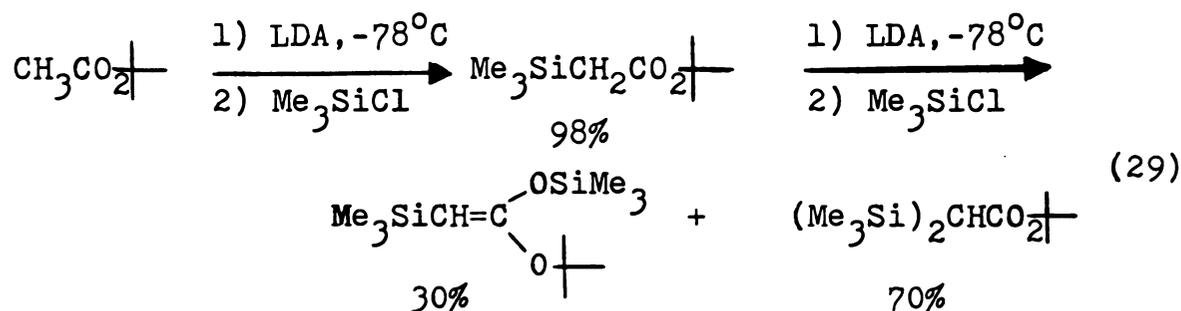
It has been reported¹⁷ that the reaction path is determined by steric factors: substitution on the alcohol portion of the ester favors C-silylation while substitution on the alpha carbon of the ester favors O-silylation (eq. 27, 28).



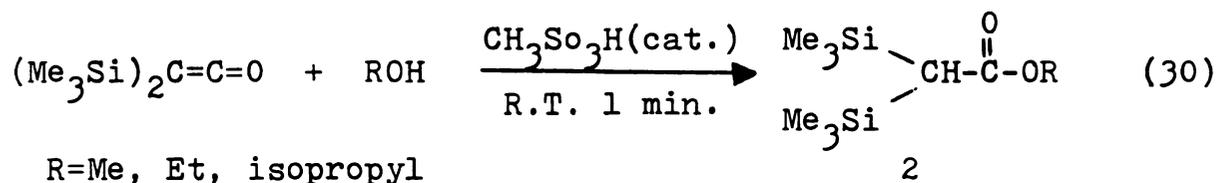
Tert-butyl acetate enolate gives almost exclusively C-silylated ester while ethyl isobutrate gives exclusively O-silylated product. Methyl, ethyl and isopropyl acetates give mostly (more than 60%) O-silylated products. We thought that the preparation of methyl, ethyl, and isopropyl bis-(trimethylsilyl) acetate for our decomposition rate studies of the corresponding lithio enolates would be difficult, because silylation of the lithium enolate of these acetates would give mostly O-silylated products.

Furthermore, silylation of the mono-silylated acetates to produce the desired bis-silylated acetates would be much

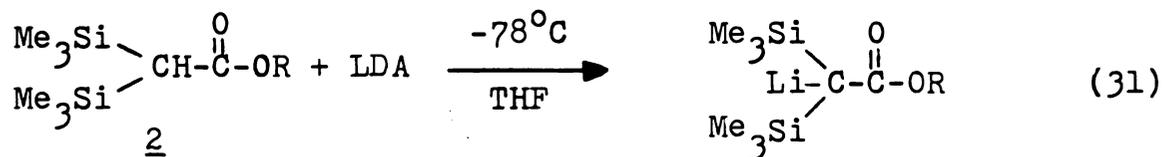
more difficult, because as mentioned above, α -substituted acetate enolates usually give almost exclusively O-silylated product. Therefore, methyl, ethyl, and isopropyl bis-(trimethylsilyl)acetates 2 are unlikely to be produced in a sufficient yield by successive silylation of corresponding acetates in the manner of the tert-butyl analogues (eq. 29).

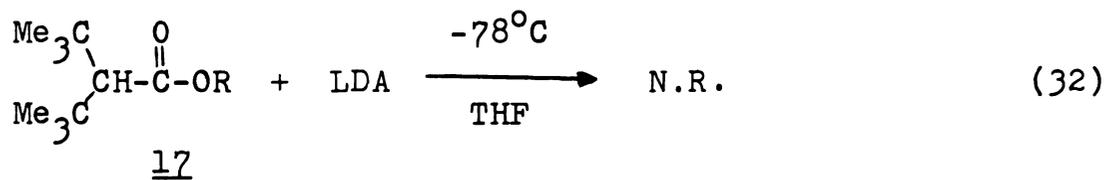


Methyl, ethyl and isopropyl bis-(trimethylsilyl)-acetates were prepared by addition of bis-(trimethylsilyl)-ketene to methanesulfonic acid in a solution of the appropriate alcohol (eq. 30).



To observe the effect of the R group on the rate of decomposition of the enolates of these esters, 2 was converted to the corresponding lithium enolate by treatment with LDA in THF at -78°C . It has been reported¹⁴ that the carbon analogues 17 are inert toward LDA (eqs. 31, 32).





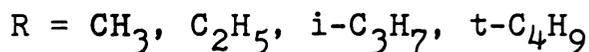
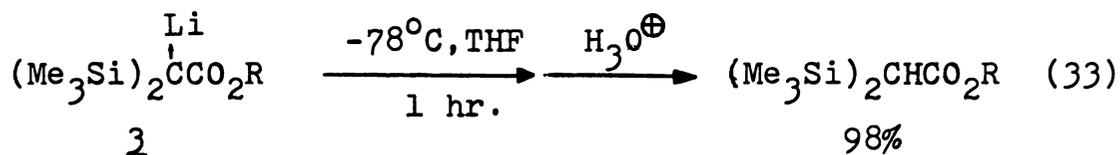
This is probably due to two factors:

(1) The Si-C (1.87Å) bond is longer than C-C (1.54Å)²⁷ bond which decreases steric hindrance in the case of the silicon analogues.

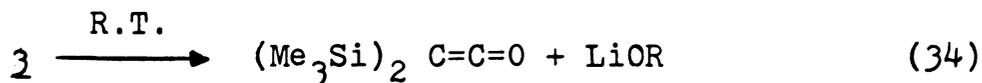
(2) The enhanced acidity of a Si-C-H group, compared with C-C-H, may also be an important factor in the greater reactivity of silicon analogues towards base. Such acidity is due to the vacant 3d-orbitals on the silicon atom which are of suitable energy for back bonding with a filled 2p-orbital on the adjacent carbon atom, thus stabilizing the adjacent carbanion.²⁸

Decomposition Study of Lithio Bis-(trimethylsilyl)acetates

All of the lithium enolates of bis (trimethylsilyl) acetate **2** which we studied were stable at -78°C in THF solution for at least 1 hour (eq. 33), but as the temperature



was increased, the enolates decomposed to the stable bis (trimethylsilyl)ketene and lithium alkoxide (eq. 34).



Three mechanisms have been suggested for converting simple ester enolates to β -keto esters (Figure 6).

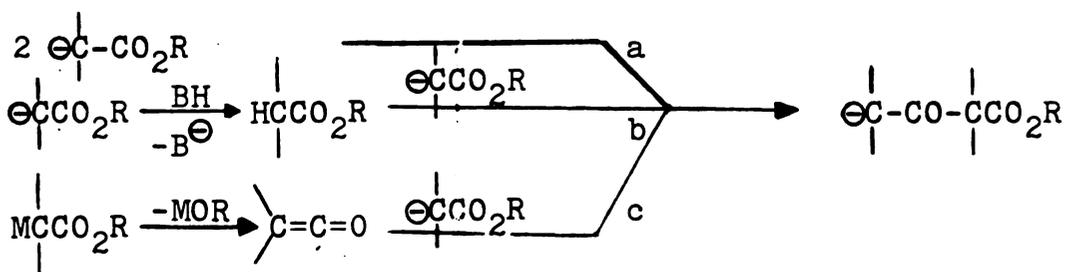
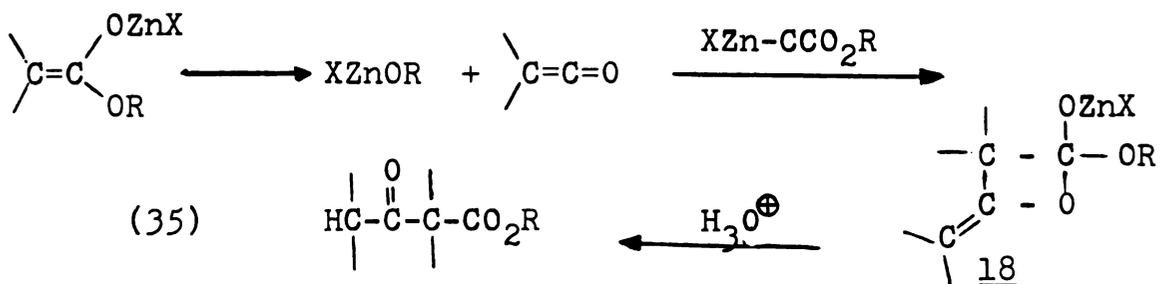


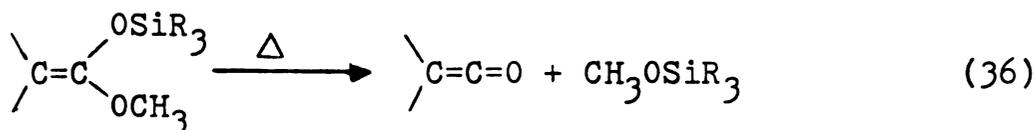
Figure 6. Three Proposed Pathways of Ester Enolates Decomposition.

A study of the kinetic behavior in the decomposition of ester enolates⁴ provided evidence against direct enolate coupling (path a). Path a requires that the decomposition be second order in enolate concentration, while the kinetic study showed the decomposition to be first order. A ketene intermediate has been proposed for the decomposition of zinc enolates. The reaction of this intermediate with the ester enolate is believed to produce a dimer, 18, which upon hydrolysis, yields β -keto esters⁵ (eq. 35).

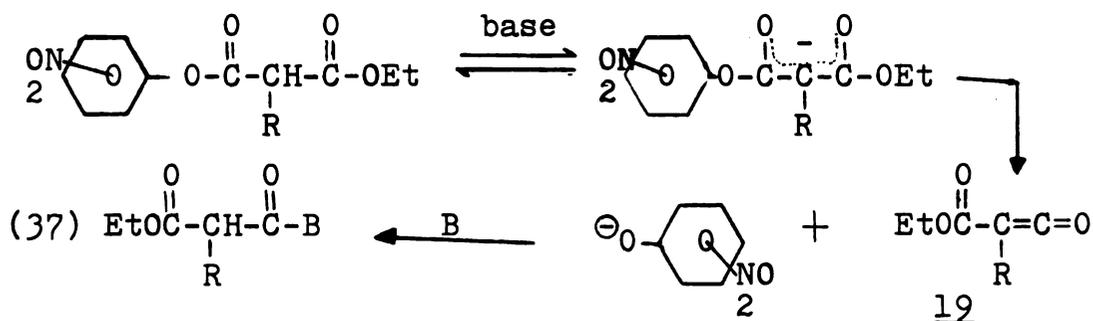


Ketene is produced in the thermal decomposition of

silicon ester enolates²⁹ (eq. 36).



Bruice and Pratt⁸ have proposed an E_{1cb} mechanism involving a ketene intermediate in the hydrolysis of ortho and para-nitrophenyl acetate esters (eq. 37).



They reported that this ketene intermediate, 19, was trapped using aniline buffers.

Rebek and co-workers⁹ have reported a technique for the detection of reaction intermediates from an insoluble polymeric precursor. The intermediates are detected by trapping them on a second solid phase suspended in the same solvent. An acyl transfer to 21 has been observed when the precursor 20 was treated with triethylamine in dioxane (Figure 7). Unlike a classical trapping experiment, a direct reaction of precursor and trapping agent is physically prohibited in this three-phase system. This method is especially suited for the detection of nucleophilic catalysis.

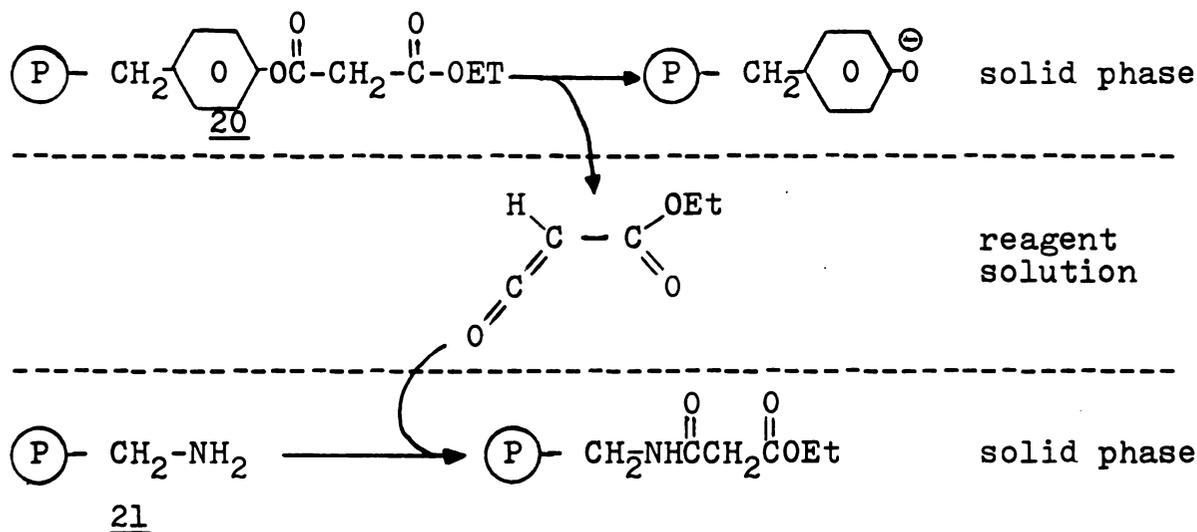
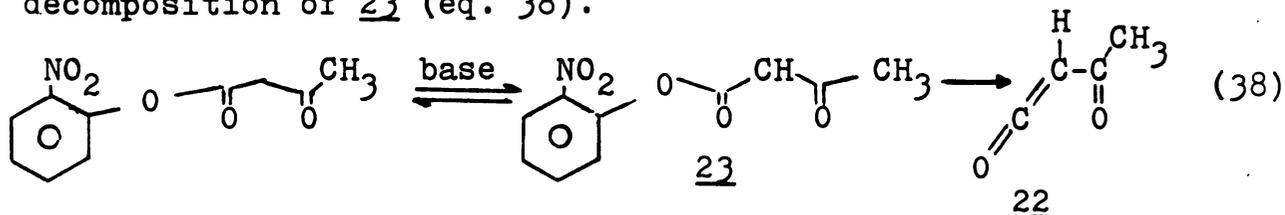
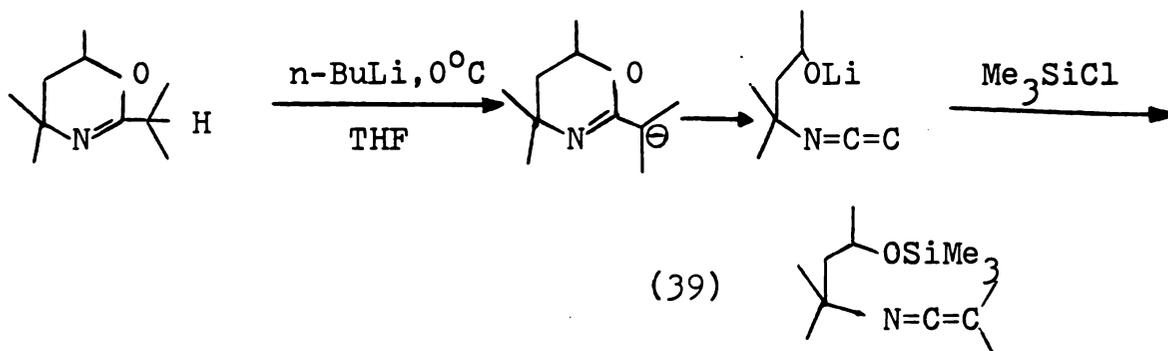


Figure 7. Three Phase System for the Trapping of Reaction Intermediates.

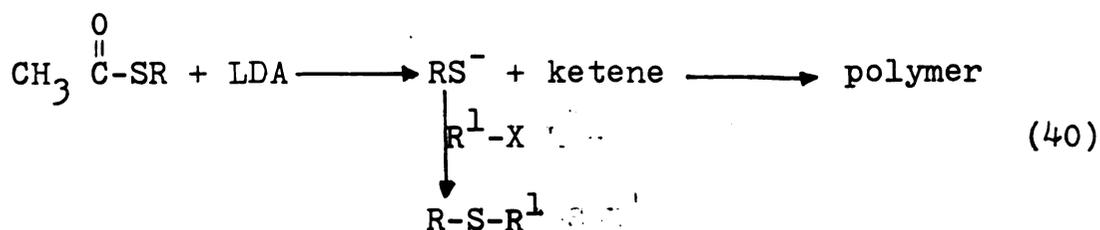
Ketene 22 has been trapped by this procedure in the decomposition of 23 (eq. 38).



In the reaction between isoalkyloxazolines and n-butyllithium, Meyers and co-workers¹⁰ have suggested a ketene-imine intermediate (eq. 39) which can be trapped with trimethylchlorosilane.



Decomposition of thiol ester enolates to ketene or ketene polymers also has been reported.³⁰ Preliminary evidence indicates that the sequence of events in the formation of mercaptide ion involves initial removal of an α -proton from thiol ester followed by the decomposition of this intermediate into a mercaptide ion and a ketene (eq. 40).



Under the basic conditions involved, ketene polymerization occurs readily.^{31,32} Thus, when a thiol ester of diphenylacetic acid was used, a gum having characteristics of a diphenylacetic acid was obtained.³⁰ However, there is no report in the literature on what effect R groups have on the rate of decomposition of thiol ester enolates. Also, isolation of stable ketene from decomposition of hindered thiol ester enolates has not been reported.

Decomposition studies of a wide variety of acetate enolates have also shown some evidence to support ketene intermediates.¹² Moreover, bis-(trimethylsilyl)ketene has been successfully isolated from the decomposition of lithio bis-(trimethylsilyl)acetate. Since there was some ambiguity in the decomposition studies of ester enolates and because the direct β -elimination of a metal alkoxide is a very rare occurrence, it was of interest to study this

reaction in more detail.

The objective of this study was to determine the rate of decomposition of different bis-silylated acetate enolates and to observe what effect the R group on the alcohol portion of these enolates had on the rate of decomposition. Data from Tables 2, 3, 4 and 5 indicates that the rate of decomposition of the enolates at -23° depends on the size of the R group.

Comparison of the relative rates of decomposition between methyl, ethyl, isopropyl and tert-butyl bis-(trimethylsilyl)acetate enolates, clearly indicates that the methyl ester enolate decomposition is the fastest while tert-butyl ester enolate decomposition is the slowest of the series (Figure 8).

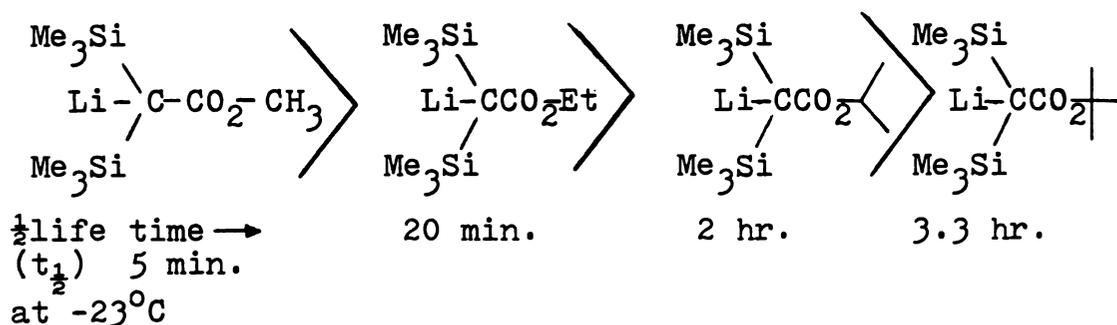


Figure 8. Comparison of Half Life Stability ($T_{\frac{1}{2}}$) of Bis-(trimethylsilyl) acetate Enolates.

As Figure 8 shows, the rate of decomposition for bis-silylated acetate enolates decreases as the alkyl substitution of R increases. The relative rate of decomposition is presented graphically on the following page (Figure 9).

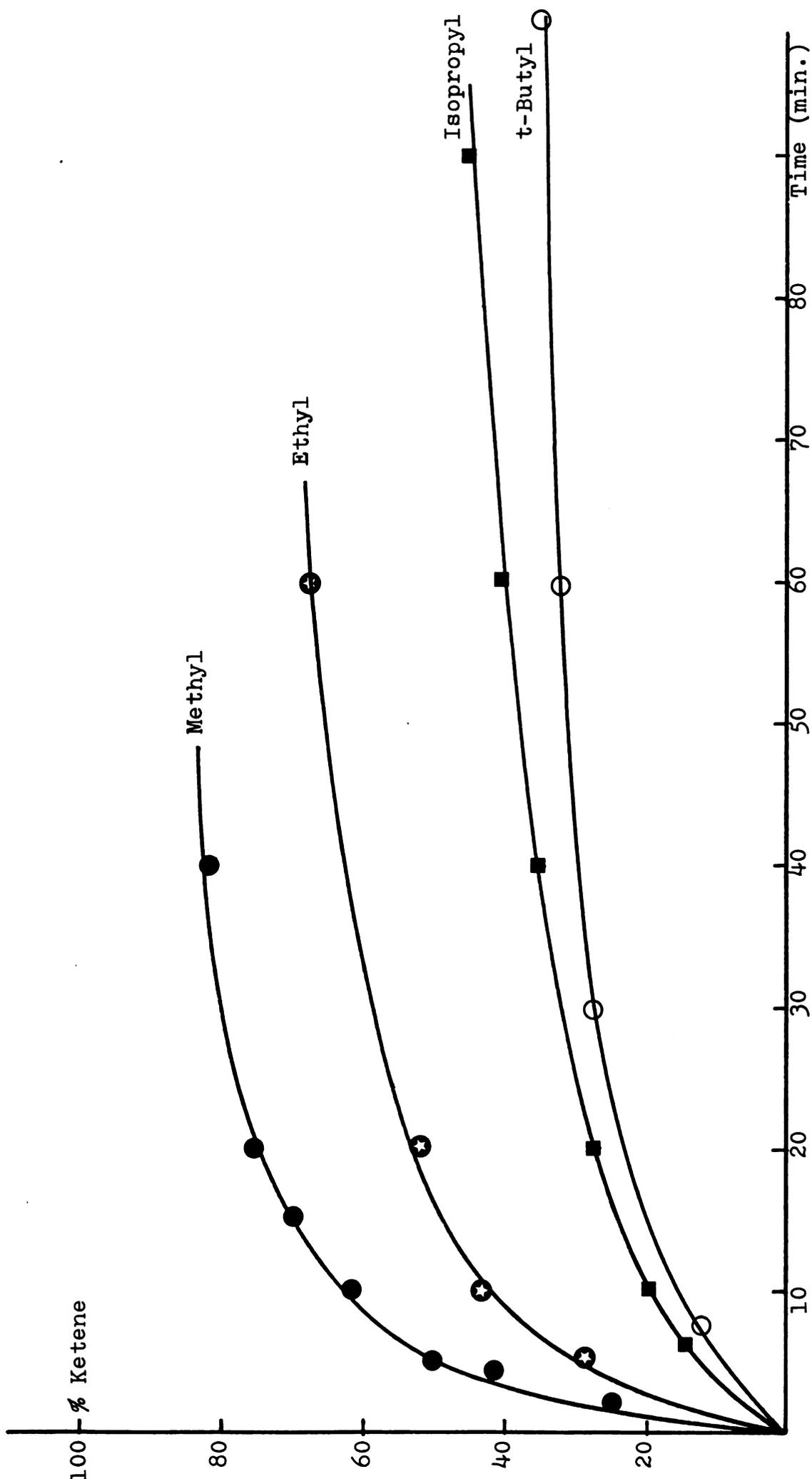
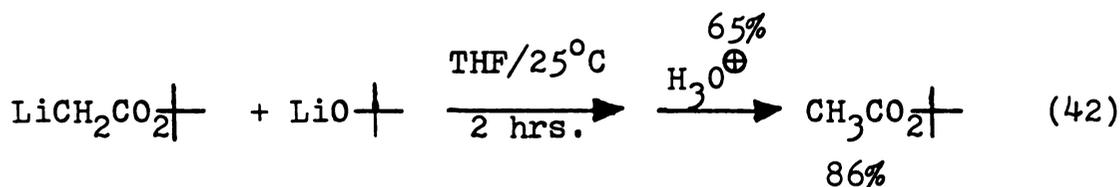
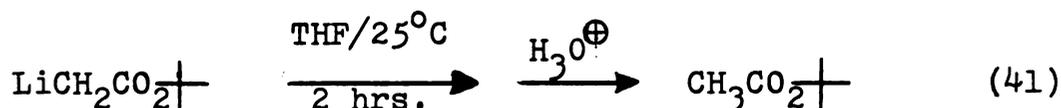
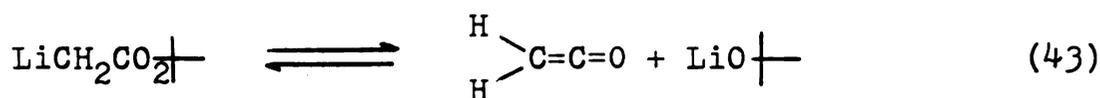


Figure 9. Rate of Decomposition of Methyl, Ethyl, Isopropyl and t-Butyl Bis-Silylated Lithium Enolates

If steric relief is assumed to be the driving force in the formation of ketene, then the tert-butyl bis-silylated ester enolate should be the least stable of the series, because the tert-butyl bis-silylated enolate is more hindered than the others. Therefore, other factors must be involved in the decomposition reaction. In studying lithio-tert butyl acetate, Woodbury¹² observed that the rate of decomposition decreased in the presence of lithium-t-butoxide (eqs. 41, 42).

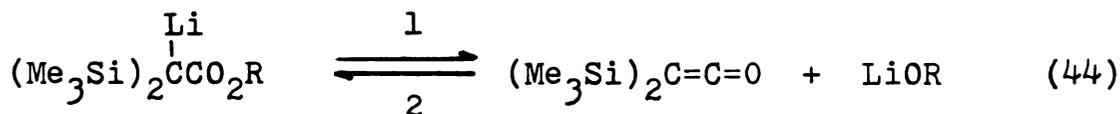


He concluded that the ketene formation was reversible (eq. 43).



As expected, an increase in the lithium t-butoxide concentration would force the equilibrium towards the enolate and slow the decomposition rate. This does not occur with ethyl acetate enolate, probably because ethoxide anion is a weaker base than tert-butoxide anion. If this occurs in the decomposition of lithio bis-(trimethylsilyl) acetates (eq. 44), then one would expect that with increasing PK_b of RO^- , the equilibrium would be driven

to the left in eq. 44.



Since bis-(trimethylsilyl)ketene was isolated quantitatively from the decomposition of corresponding enolates, it can be assumed that the reaction proceeds to completion. This is probably due to the steric effect of bis-(trimethylsilyl)ketene which prevents the nucleophilic attack of alkoxides on the ketene.

As the basicity of RO^- increases, the corresponding enolate should become more stable, the relative PK_b 's of the leaving groups are:



If enolate decomposition is related to the basicity of the leaving group, then enolate decomposition should be in accordance with Figure 8.

An ambiguity arose when we plotted the logarithm of the decomposition rate of enolates versus time. Contrary to our expectations, data from Tables 2, 3, 4 and 5 did not fit a straight line which would confirm the first order decomposition of enolates studied.

In conclusion, it seems that the stability of bis-silylated acetate enolates increases with increasing basicity of the leaving group (RO^-).

EXPERIMENTAL

1. Materials

Ester

Tert-butyl acetate was commercially available from Aldrich Chemical Company, and used without further purification.

Ethers

Anhydrous diethylether, was commercially available and used without further purification.

Tetrahydrofuran (THF), was commercially available from Aldrich Chemical Company. THF was distilled from the sodium ketyl of benzophenone and stored under argon.

Amines

Diisopropylamine was obtained from Aldrich Chemical Company. It was used after distillation from calcium hydride (bp 84°C, 760 mmHg) and stored under argon.

Diethylamine was obtained from Matheson Coleman & Bell Company. It was distilled from calcium hydride (bp 55, 760 mmHg), stored under argon and molecular sieve.

n-butyllithium

n-butyllithium was obtained as a 1.5M hexane solution

from Aldrich Chemical Company and titrated prior to use by the Watson-Eastham method.³³

Trimethylsilylchlorosilane

Trimethylchlorosilane was obtained from Aldrich Chemical Company. It was distilled (bp 57°C, 760mmHg) and stored under argon.

Alcohols

Absolute methanol, ethanol and isopropanol were obtained from Aldrich Chemical Company and used without further purification.

2. Preparation of tert-butyl bis-(trimethylsilyl)acetate

A dry 500 ml side arm round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and mercury bubbler. The flask was flushed with argon and charged with 100 ml of distilled THF and 13.4 ml (100 mmole) of distilled diisopropylamine was injected by syringe. The flask was cooled to 0°C in an ice bath and 66.7 ml of 1.5 M solution of n-butyllithium was added dropwise over 10 minutes. The ice bath was removed and flask was immersed in a Dry Ice-acetone bath. 13.4 ml (100 mmole) of tert-butyl acetate was added dropwise over a period of 10 minutes. The solution was stirred an additional 10 minutes. Then 12.8 ml (100 mmoles) of distilled trimethylchlorosilane was injected dropwise over 10 minutes. The solution was stirred for another 15 minutes. The Dry Ice-acetone bath was removed and the solution in the flask was transferred by

Teflon tubing to a 1000 ml round-bottomed containing 100 m moles lithium diisopropylamide under argon in 100 ml THF at -78°C . The solution was stirred for 15 minutes and another 12.8 ml (100 m mole) of distilled trimethylchlorosilane was added dropwise over a 10 minute period. The mixture was stirred for 30 minutes at -78°C . Then the dry ice-acetone bath was removed and the solution was stirred for 15 minutes at room temperature.

100 ml of 3 M aqueous HCl was injected. The aqueous layer was separated in a 1000 ml separatory funnel and discarded. THF and diisopropylamine were evaporated from the organic layer under reduced pressure. The mono silylated tert-butyl acetate was distilled under reduced pressure (bp 67°C , 13 mmHg) and was used for further silylation. The tert-butyl bis-(trimethylsilyl) acetate was then distilled under reduced pressure (bp 61°C , 0.4 mmHg). The yield was 14.4 g (60%) of pure tert-butyl bis-(trimethylsilyl)acetate.

3. Preparation of bis-(trimethylsilyl)ketene

A dry 500 ml side-armed round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and a mercury bubbler. The flask was flushed with argon and 125 ml of anhydrous diethyl ether was injected into the flask. 15.6 ml (150 m mole) of diethylamine was added. The flask was immersed in an ice bath. Then 100 ml of n-butyllithium (1.5M, 150 m mole) was added

by syringe over 15 minutes to the stirring solution. After stirring for an additional 10 minutes, the flask was put in a dry ice-acetone bath and 39 g (150 m mole) of pure tert-butyl bis-(trimethylsilyl) acetate was added over a 10 minute period. The reaction mixture was stirred for an additional 20 minutes at -78°C , warmed to room temperature and stirred 30 minutes longer. 100 ml distilled water was injected into the flask. The two layers were separated in a separatory funnel. The organic layer was poured into a 500 ml side armed round-bottomed flask equipped with a magnetic stirring bar, septum inlet, a short vertical condenser and a gas inlet valve on top of the condenser. The flask was immersed in an ice bath and stirred. The solvents (hexane, diethylamine and diethylether) were removed under reduced pressure. The ice bath was removed for 30 minutes and the solvent evaporation was completed. The remaining ketene residue was distilled under reduced pressure (bp. 20°C , 2 mm Hg) and afforded 20.2 g (80%) of pure bis (trimethylsilyl) ketene. $^1\text{H NMR}(\text{CCl}_4) \delta$ 0.25(S) IR (neat) 2085cm^{-1} and 1295cm^{-1} (Lit 2085, 1295cm^{-1}).

4. Preparation of Methyl bis-(trimethylsilyl)acetate

A dry 25 ml side armed round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and a mercury bubbler. The flask was flushed with argon and was charged with 0.8 ml (20 m mole) of methanol and 5 micro liters (0.01 mole) of methanesulfonic acid as a

catalyst. Then 4.0 ml (20 m mole) of pure bis-(trimethylsilyl)ketene was added dropwise to the solution at room temperature. GLC analysis of the solution on 6 foot 5% SE-30 column confirmed that all of the ketene was converted to methyl bis-(trimethylsilyl)acetate within one minute. Bulb-to-bulb distillation of this solution under reduced pressure (.95 mm, 49-51°C) gave 3.5 g (80%) of methyl bis-(trimethylsilyl)acetate.

Product Analysis:

bp 49-51°C/0.95 mm, Density 0.911

IR (neat), 1700 cm^{-1} strong C=O absorption

^1H NMR (CCl_4): δ 0.14 (s, 18H), δ 1.53 (s, 1H), δ 3.46 (s, 3H)

5. Preparation of Ethyl bis-(trimethylsilyl)acetate

A 25 ml side-armed round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and a mercury bubbler. The flask was flushed with argon and charged by 1.1 M ml (20 m mole) of absolute ethanol and 5 micro liters (0.01 m mole) of methanesulfonic acid as a catalyst. Then 4.00 ml (20 m mole) of pure bis-(trimethylsilyl)ketene was added dropwise to the solution at room temperature. After stirring 1 minute, GLC analysis of the solution of 6¹, 5% SE-30 column confirmed that the ketene was converted to ethyl bis-(trimethylsilyl)acetate. Bulb-to-bulb distillation of this solution under reduced pressure gave 3.9 g (81%) of pure ethyl bis-(trimethylsilyl)acetate.

Product Analysis:

B.P. 57-59°C/ 1.1 mm, Density = 0.8519

IR(neat) 1720 cm^{-1} strong C=O absorption

^1H NMR(CCl_4): δ 0.23 (s, 18H), δ 2.3 (t, 3H), δ 1.6 (s, 1H)
 δ 4.1 (q, 2H)

6. Preparation of Isopropyl bis-(trimethylsilyl)acetate

The same procedure was applied as with the methyl and ethyl analogues. Bulb-to-bulb distillation of the solution in final step gave 4.32 g (87.8%) of isopropyl bis-(trimethylsilyl)acetate.

Product Analysis:

B.P. 63-65°C/ 1.1 mm, Density = 0.8621

IR(neat) 1720 cm^{-1} strong absorption for C=O

^1H NMR (CCl_4): δ 4.85 (s, 1H), δ 1.5 (s, 1H), δ 1.2 (d, 6H)
 δ 0.15 (s, 18H).

7. Rate of Decomposition of Bis-(trimethylsilyl)acetate Lithium Enolate

The following procedure is representative for all rate decomposition studies of the lithio bis-silylated acetates.

A dried 10 ml side armed round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and a mercury bubbler. The flask was flushed with argon and charged with 1 ml g dry THF. 0.155 (1.0 m mole) freshly distilled diisopropylamine was added. The flask was immersed in an ice bath. Then 0.73 ml of a 1.5 M

solution (1.1 m mole) of n-butyl lithium was added dropwise. After a few minutes the flask was placed in a dry ice-acetone bath. Then 1 m mole of desired bis-silylated acetate was added dropwise and stirred an additional 10 minutes at -78°C . The flask was then placed in a carbon tetrachloride-dry ice bath (-23°C) and 0.21 ml (1.00 m mole) of undecane was injected into the solution as the internal standard. At appropriate intervals, approximately 0.1 ml aliquots of the solution were removed using a cooled syringe and quenched by injecting it into approximately 50 ml H_2O in a small vial. Approximately 0.15 ml of pentane was added into the vial. The solution was dried over anhydrous magnesium sulfate and analyzed for ketene. The results are presented in Tables 2, 3, 4 and 5.

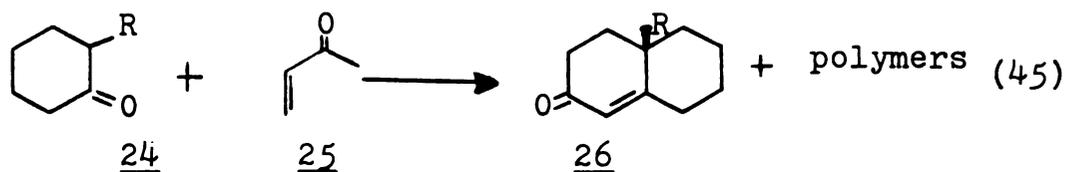
CHAPTER II

REACTIONS OF BIS-(TRIMETHYLSILYL)KETENE

INTRODUCTION

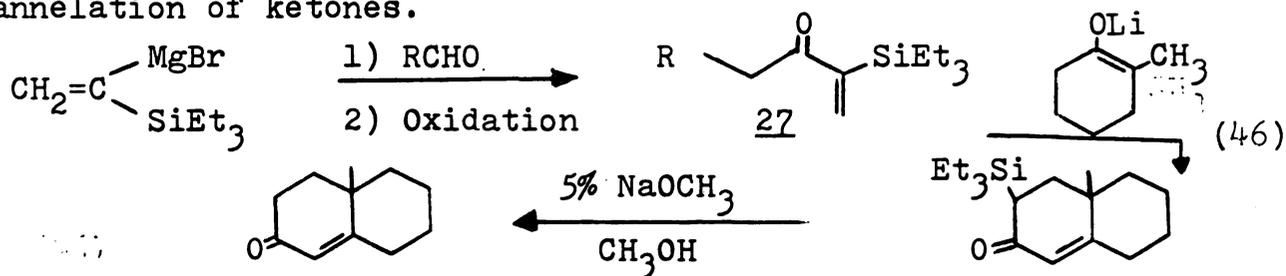
The annelation of 2-alkylcyclohexanones 24 with methyl vinyl ketones 25 is an important route to the fused poly-cyclic system 26,³⁴ (eq. 45). While condensation at the less substituted α carbon of the 2-alkylcyclohexanone can be carried out efficiently using the corresponding enamines,³⁵ the conditions required for reaction at the more substituted site result in low yields due to polymerization of the vinyl ketone³⁶ (eq. 45).

This difficulty is avoided by the use of alkyl halides instead of vinyl ketones,^{37,38} but a number of steps are then required to transform the added alkyl group into the 3-keto alkyl function.



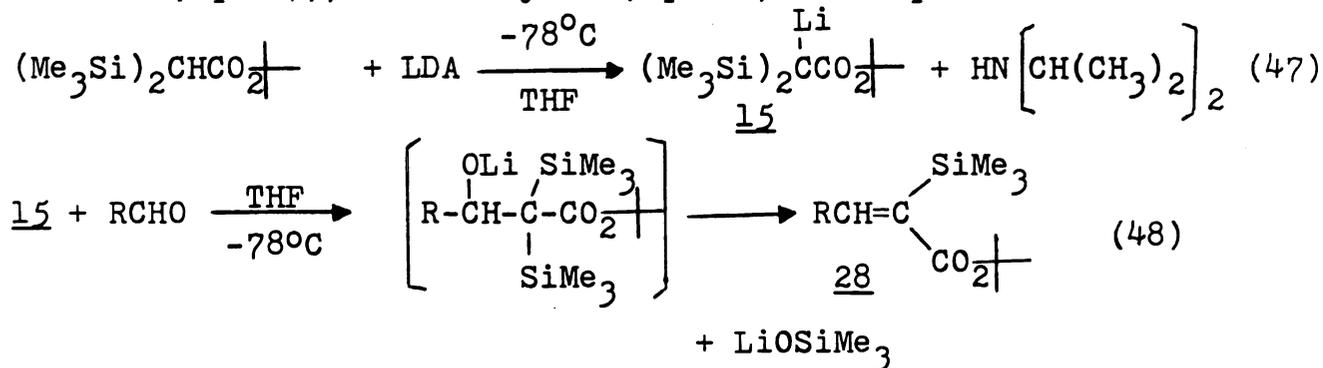
The problem with simple vinyl ketones, such as methyl vinyl ketone, stems from the similar base strengths and reactivities of the enolate ions derived from the starting material and the Michael adduct (1, 4 adduct).

There is good evidence that silicon with its vacant 3d orbitals can stabilize an adjacent negative charge^{39,40,41} and can be easily removed after cyclization. Taking advantage of this principle, Stork⁴² has reported the synthesis and use of α -silylated vinyl ketones 27 (eq. 46) for the annelation of ketones.



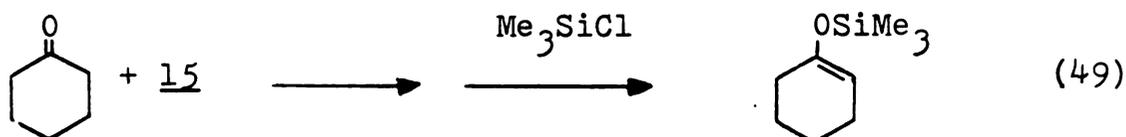
However, this preparation of α -silyl vinyl ketones requires several steps from commercially available vinyl silanes.⁴³

The synthesis of α -silyl vinyl esters 28 by reacting lithio-tert-butyl bis-(trimethylsilyl) acetate 15 (obtained by reaction of the corresponding ester, 13, with LDA (eq. 47)) and aldehydes (eq. 48) was reported¹⁸.

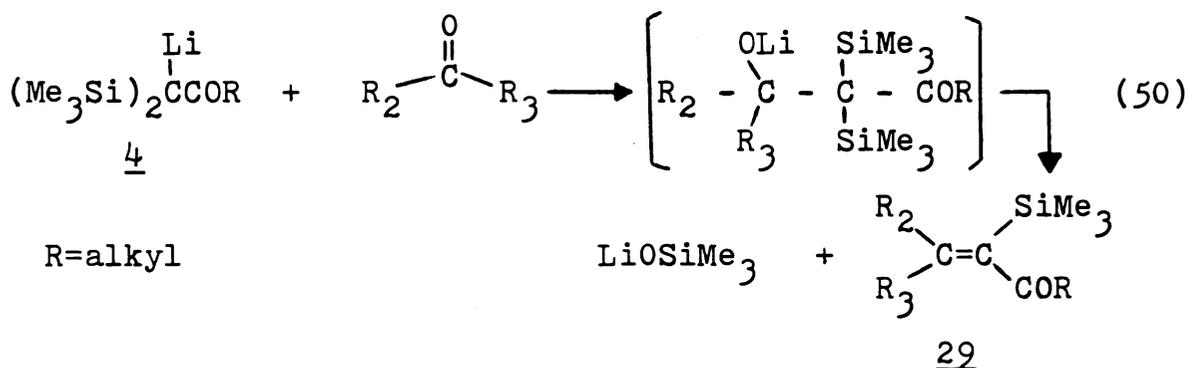


The reagent, 15, failed to react with ketones. Thus, addition of cyclohexanone to a solution of 15 gave only recovered tert-butyl bis (trimethylsilyl) acetate and the lithium enolate of cyclohexanone (eq. 49) which was trapped

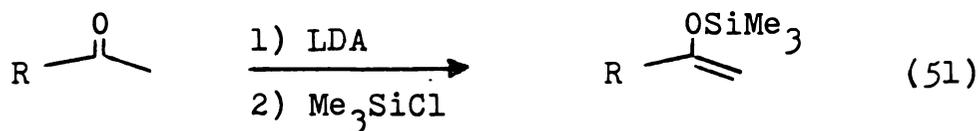
by trimethylchlorosilane.



We thought that the ketone analogue of 15 (i.e. 4) would be more efficient and probably would be able to convert both aldehydes and ketones to their corresponding α -silyl-vinyl ketones 29 (eq. 50).

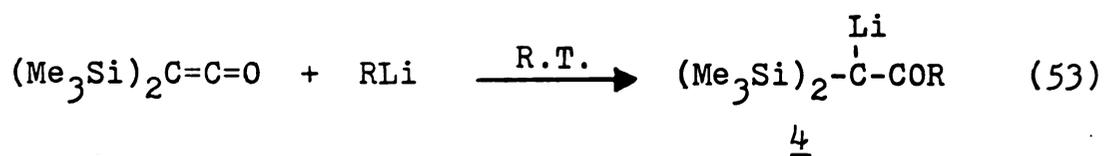


This procedure would be a convenient synthesis of the α -silyl vinyl ketones which are very useful Michael acceptors.⁴⁴ However, the bis-silylated ketones required to prepare 4 are not available by successive silylation of the ketones. Treatment of trimethylchlorosilane with a ketone enolate usually leads to a silyl enol ether (O-silylated product) rather than the C-Silylated Ketone⁴⁵⁻⁴⁷ (eq. 51).



Since α, α bis-silylated ketones could not be prepared by this procedure, we decided to prepare reagent 4 by treating alkyl lithium and Grignard reagents with bis

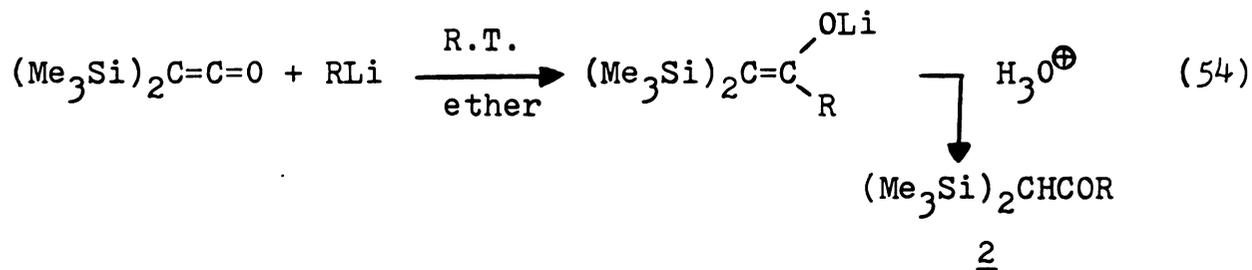
(trimethylsilyl)ketene, available from lithio-tert-butyl bis-(trimethylsilyl)acetate 15 (eq. 52, 53).



RESULTS

1. Preparation of α,α -Bis-silylated ketones

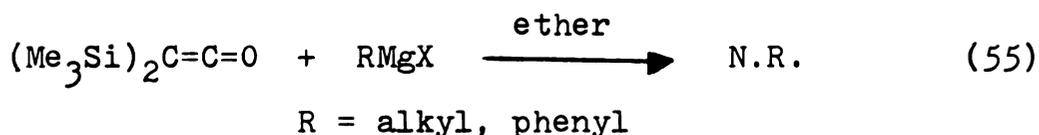
Alkyl lithium reagents were added to an ethereal solution containing an equivalent amount of bis-(trimethylsilyl)ketene at room temperature. Individual solutions were stirred at room temperature for periods of time ranging from one hour to 8 hours, depending on the R group of the alkyl lithium reagent. After complete reaction, the resulting enolates were converted to the colorless, stable, α,α bis-(trimethylsilyl) ketones 2 by quenching with acetic acid (eq. 54).



The α,α -bis-(trimethylsilyl) ketones were decomposed on a 30.5% SE GlC column. Consequently, the yields were determined by $^1\text{H-NMR}$. The yields ranged from 75% to 85% by NMR analysis.

Grignard reagents such as methyl magnesium iodide in ether were added dropwise to ethereal solutions containing an equivalent amount of bis-(trimethylsilyl)-

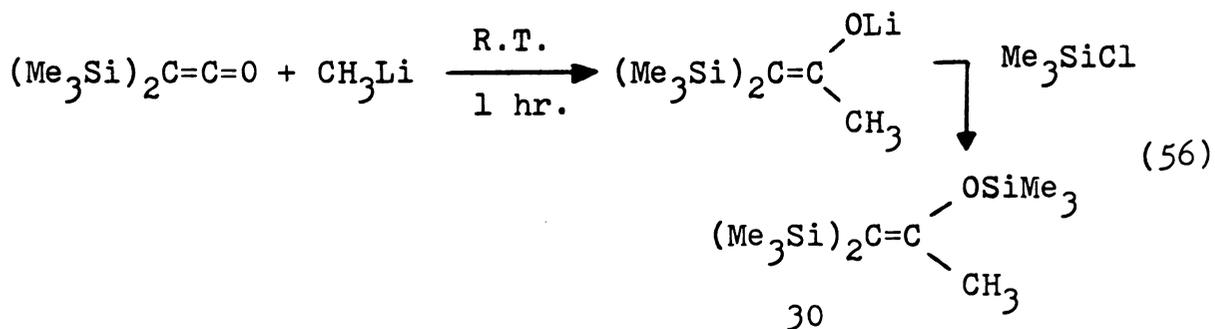
ketene at room temperature. The solutions were stirred for 1 hour, but no products were detected by GLC. No product was found in the mixture even after stirring overnight. Ketene was recovered quantitatively by GLC using an internal standard. The same observation was made with ethyl magnesium iodide and phenyl magnesium bromide even at reflux for one hour (eq. 55).



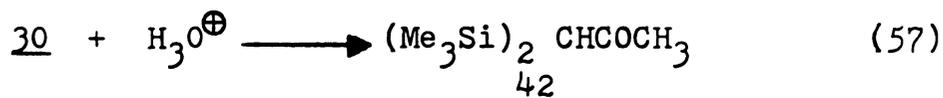
2. Reaction of the Enolate Formed by Adding Methyl lithium to Bis-(trimethylsilyl)ketene

A. With Trimethylchlorosilane.

Methyl lithium was added to an ethereal solution containing an equivalent of bis-(trimethylsilyl)ketene at room temperature. The solution was stirred for one hour to complete the reaction. Then one equivalent of distilled trimethylsilylchlorosilane was added. The GLC analysis of the solution without quenching gave the desired addition product 30 as the only product, identified by its $^1\text{H NMR}$ spectrum (eq. (56)).



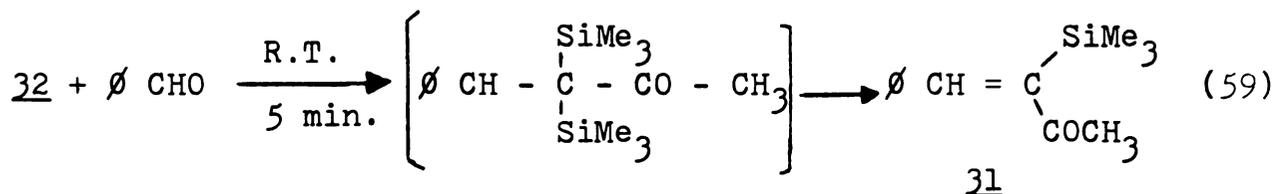
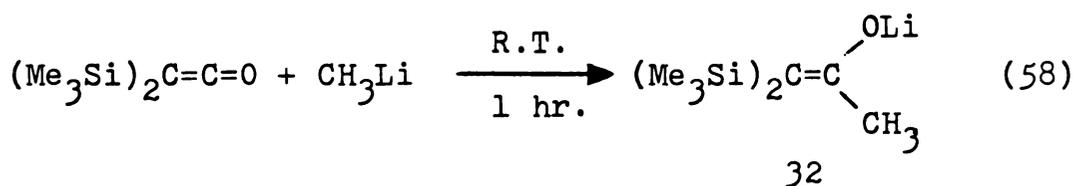
Quenching the solution with 3 M HCl converted the product 30 to α,α -bis-(trimethylsilyl)acetone (eq. 57).



Attempted purification of the product 30 by distillation under reduced pressure was unsuccessful. Only a black tar was formed.

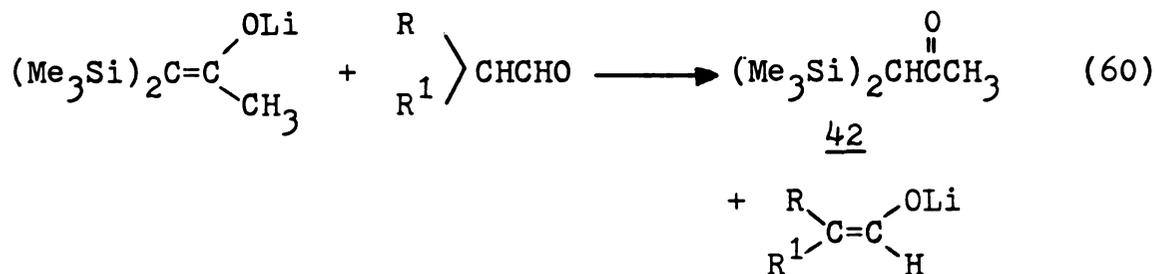
B. With Aldehydes.

One equivalent of methyl lithium was added dropwise to an equivalent of bis-(trimethylsilyl)ketene in ether at room temperature. The solution was stirred for one hour to convert the ketene to the enolate. Then freshly distilled benzaldehyde was added dropwise by syringe. After 5 minutes, the enolate was converted to the corresponding vinyl ketone, 31, (eq. 58, 59). The product 31 was identified by its ^1H NMR spectrum.



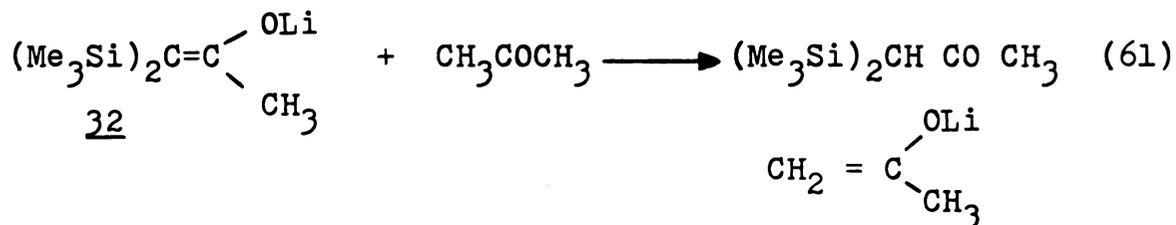
The same procedure was followed with acetaldehyde and propionaldehyde. The products were identical to the

quenching product,⁴² both by GLC retention time and ^1H NMR (eq. 60).

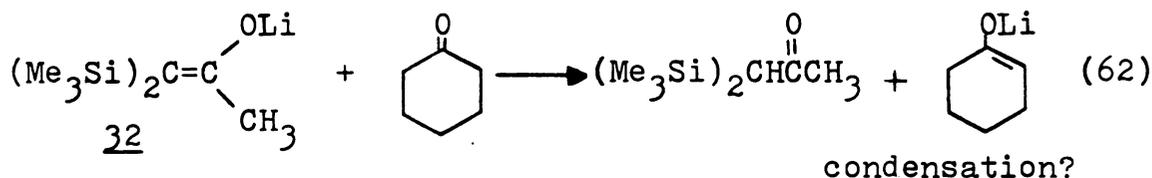


C. With Ketones.

One equivalent of methyl lithium was added to an ethereal solution containing one equivalent of bis-(trimethylsilyl)ketene at room temperature to complete the reaction. Then one equivalent of acetone was added and the reaction mixture stirred for one hour. Analysis of the reaction mixture by GLC gave the quenching product, α, α -bis-(trimethylsilyl)acetone (eq. 61).

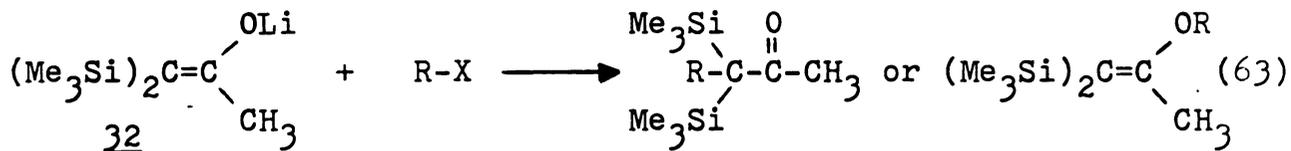


The same procedure was followed with cyclohexanone. In this case, a product other than α, α -bis-(trimethylsilyl)-acetone was found in the reaction mixture. The ^1H NMR of this product was similar to the self condensation product of the cyclohexanone enolate (eq. 62).



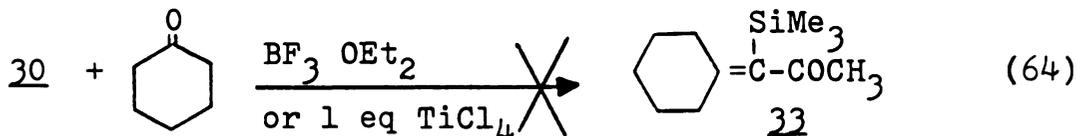
D. With Alkylhalides.

An equivalent amount of methyl or ethyl iodide was added to the enolate 32 formed as before. GLC analysis of the solution after stirring at room temperature gave several products with higher boiling points than the starting materials, but all attempts to isolate and identify these products were unsuccessful (eq. 63).



3. Reaction of $(\text{Me}_3\text{Si})_2\text{C}=\text{C}(\text{OSiMe}_3)\text{CH}_3$, 30, with Ketones.

An ethereal solution of 30 was prepared. One equivalent amount of cyclohexanone was added to the solution at -78°C . Then 3 drops of $\text{BF}_3 \cdot \text{OEt}_2$ was injected as a catalyst. The solution was stirred for 1.5 hours at -78°C and then 30 minutes at room temperature. Only trace amounts of an unidentified compound was formed. It definitely was not the expected product 33 (eq. 64).

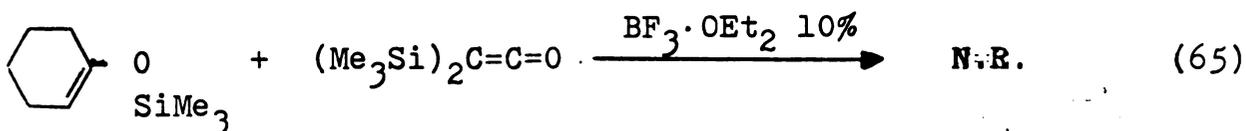


The same reaction was done with an equivalent of TiCl_4 with similar results. More than 80% of cyclohexanone was recovered from the solution after work up.

4. Reaction of the Bis (trimethylsilyl) Ketene with Silylenol ethers.

An equivalent amount of bis-(trimethylsilyl)ketene containing 10% mole equivalent of $\text{BF}_3 \cdot \text{OEt}_2$ as a catalyst was injected dropwise to a preformed solution of cyclohexanone silyl enol ether.

None of the expected addition product was detected by GLC after 30 minutes stirring at 0°C . A trace amount of an unknown compound was detected on the GLC after solution was stirred overnight at room temperature (eq. 65).

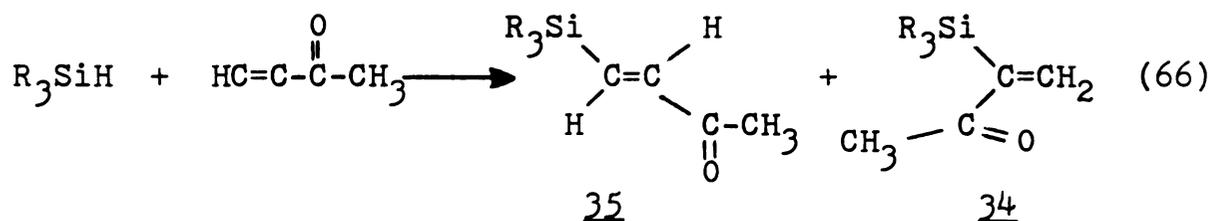


DISCUSSION

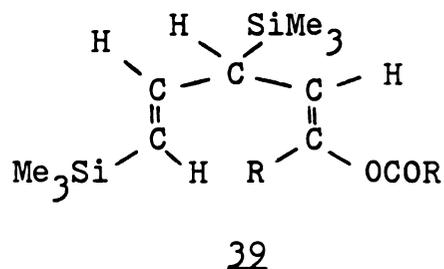
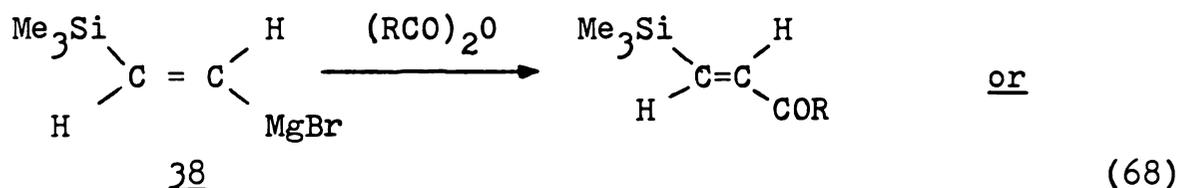
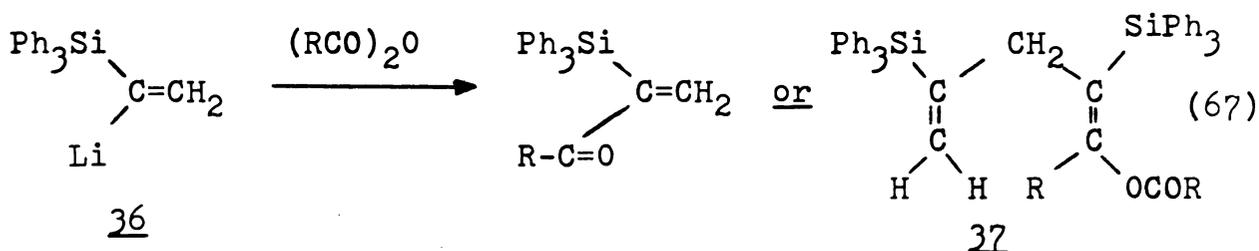
Synthesis of α -Silylated Vinyl Ketones.

Stork⁴² and Boeckman⁴⁴ have shown that α -silyl vinyl ketones undergo Michael addition reactions with a number of electrophiles. A valuable synthetic application of α -silyl vinyl ketones is in the annelation of ketones to fused polycyclic systems.⁴⁹ Several methods are reported for the preparation of α -silyl vinyl ketones in the literature.

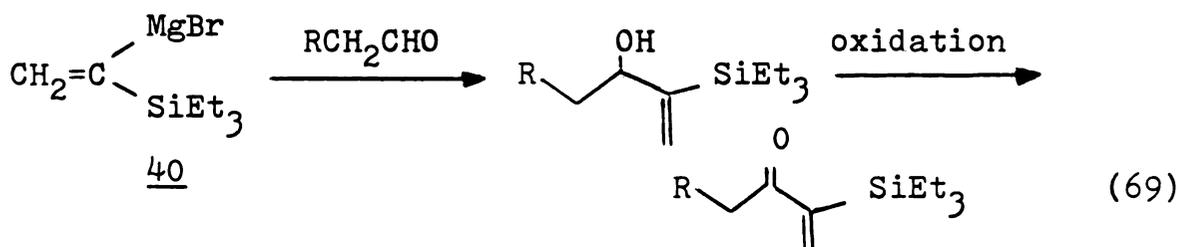
Hydro-silylation of acetylenic ketones^{50,51} yields a mixture of silyl vinyl ketones, 34, and 35, from which it is difficult to separate the desired α -silylated product (eq. 66).



Brook and Duff⁵² have described a general route to both α and β -silyl vinyl ketones by the coupling of silyl vinyl organometallic reagents 36 and 38 with acid anhydrides (eq. 67, 68).



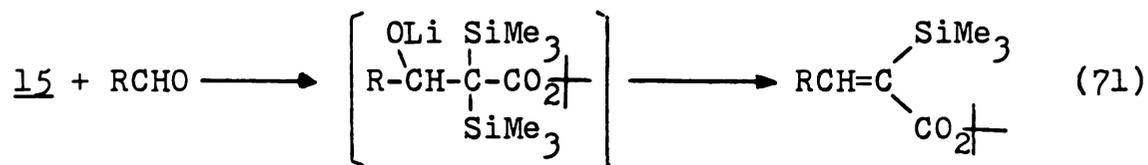
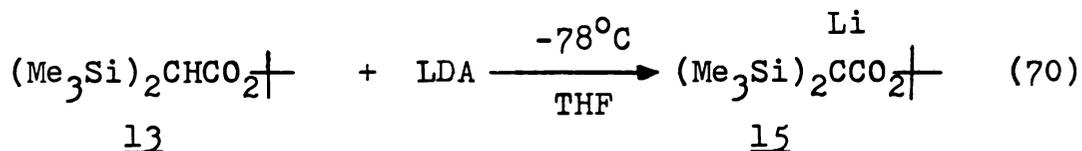
α and β -silyl vinyl ketones were found to be very sensitive towards 1, 4-addition reactions and therefore low temperatures were necessary to minimize production of 37 and 39. However, the yields varied from 30-80% under optimum conditions. The trimethylsilyl Grignard reagents, 38, gave none of the expected product with benzoic anhydride under any conditions. Stork⁴⁸ used a similar procedure for the preparation of α -silyl vinyl ketones (eq. 69).



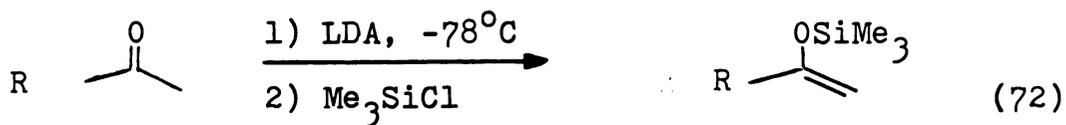
Several steps are required to prepare Grignard reagent

40 from commercially available vinyl silanes.⁴³

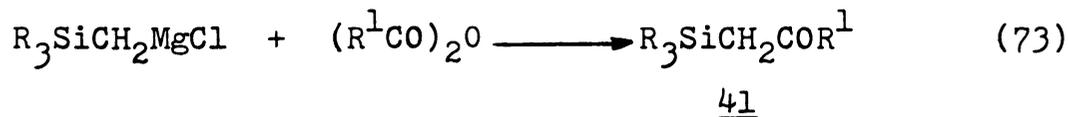
It has been reported¹⁸ that lithio tert-butyl bis-(trimethylsilyl)acetate 15, obtained by treatment of the corresponding ester 13 with LDA (eq. 70), reacts with aldehydes to give α -silyl vinyl esters (eq. 71).



Reagent 15 fails to react with ketones presumably due to steric effects.¹⁸ Bis silylation of ketones on carbon has not yet been reported because the silylation of ketone enolates with trimethylchlorosilane usually leads to silyl enol ethers (O-silylated product) rather than C-silylated ketones⁴⁵⁻⁴⁷ (eq. 72).

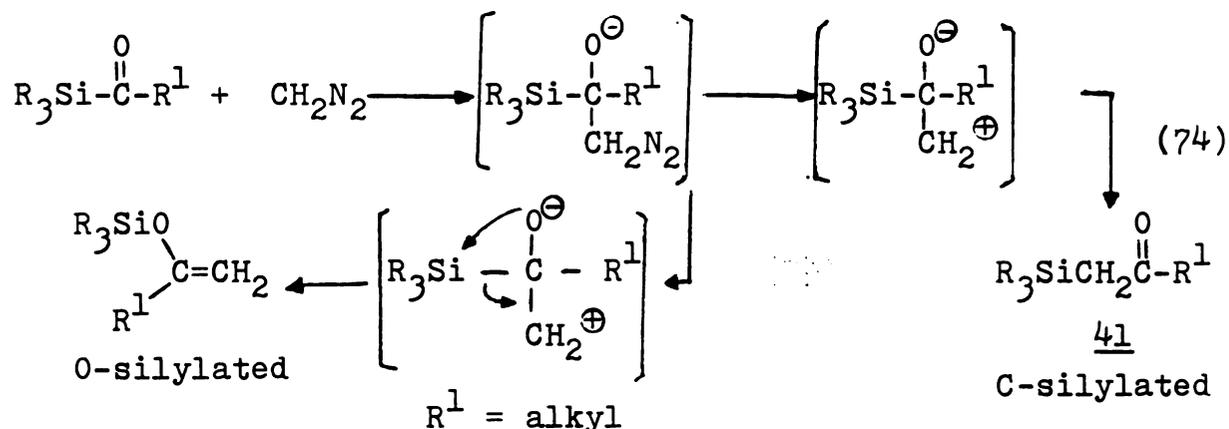


Mono C-silylated ketones can be synthesized by other methods. Hauser⁵³ prepared C-silylated ketones by the reaction of acid anhydrides with trialkylsilylmethyl magnesium halides (eq. 73).

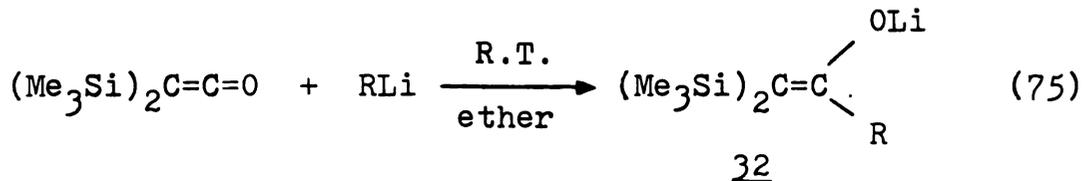


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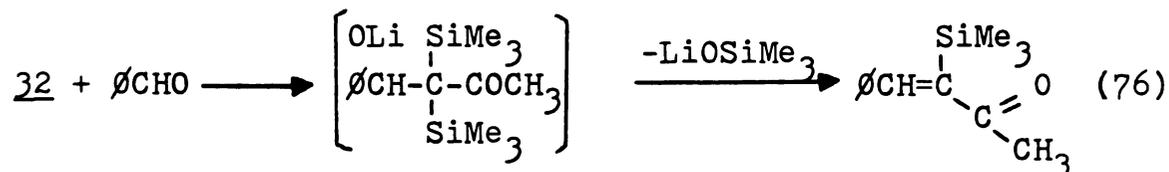
Brook⁵⁴ reported that acylsilanes react with diazomethane to form a mixture of O- and C-silylated products (eq. 74).



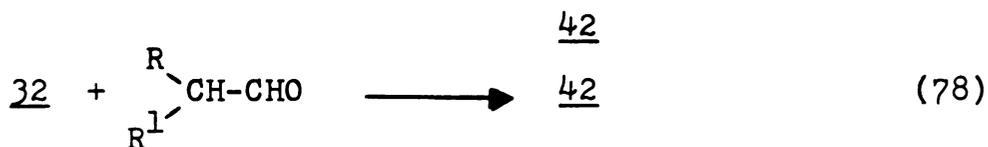
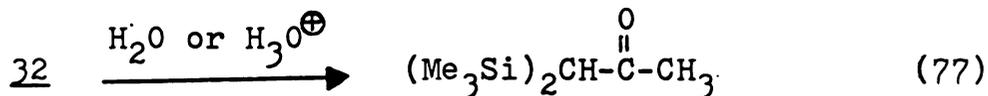
C-silylation of the β -keto silanes has not yet been reported. Although it has been reported that hindered ketenes such as di-*t*-butyl ketene¹³ and bis (trimethylsilyl) ketene are unreactive to nucleophilic attack, the ketone analogues of 15 were prepared by the addition of alkyl lithium reagents to an ethereal solution of bis (trimethylsilyl) ketene which is formed by decomposing 15 at room temperature (eq. 75).



Using methyl lithium, the enolate formed was reacted with aldehydes and ketones. Only benzaldehyde was converted to the expected α -silyl vinyl ketone (eq. 76).



All other aldehydes and ketones having at least one α -hydrogen gave the same product with enolate 32 as did H_2O or dilute acetic acid (eq. 77-79).

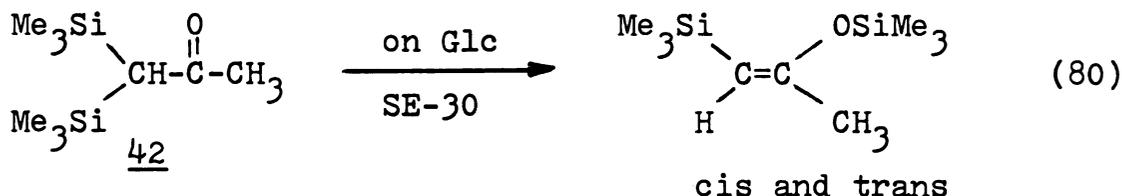


That means that the enolate 32 is protonated by aldehydes and ketones having α -hydrogen, again probably due to steric effects.

The reaction of alkyllithium with bis-(trimethylsilyl)-ketene can be used as a general route in preparing α,α -bis-(trimethylsilyl)ketones. Because the Grignard reagents could easily be prepared from a wide variety of alkyl halides, an attempt was made to use Grignard reagents instead of alkyl lithium. But bis-(trimethylsilyl)ketene was totally unreactive towards Grignard reagents.

During the GLC analysis of α,α -bis-silylated ketones, it was observed that α,α bis-silylated acetone 42 partially

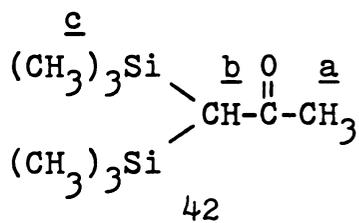
decomposed on the Glc column (30.5%-SE on chromosorb W). The ^1H NMR investigation of the decomposed mixture showed that the decomposition occurred by the migration of a silyl group (eq. 80).



The migration was confirmed by the following observations:

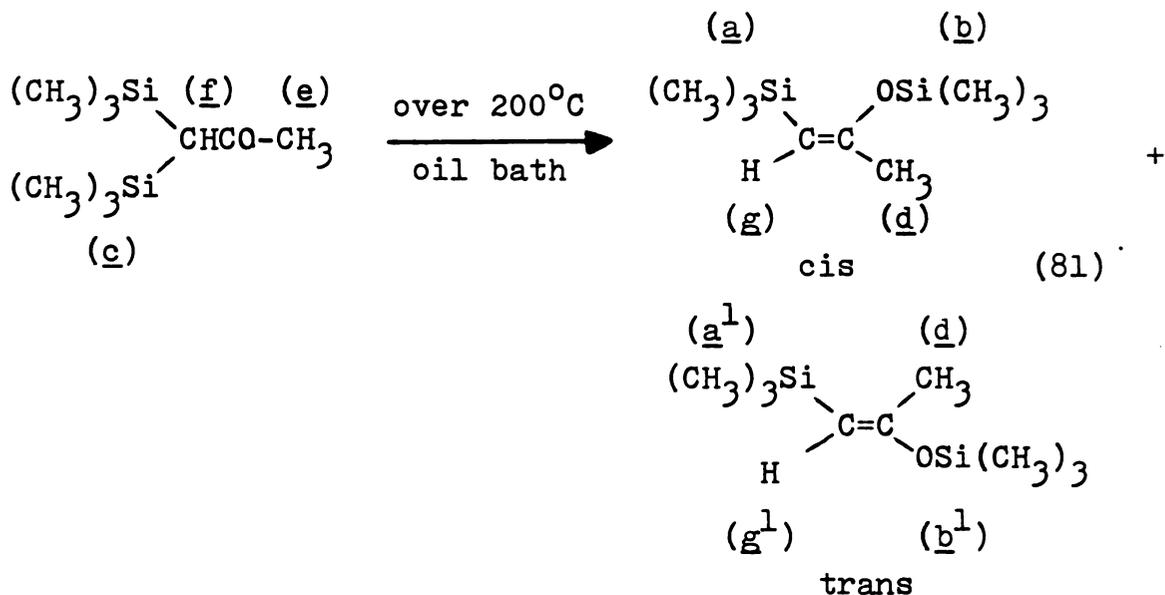
1) Pure α,α bis-(trimethylsilyl)acetone, prepared by treating methyl lithium with bis-(trimethylsilyl)ketene and quenching with 3M HCl, was heated in a sealed tube in oil bath. No change was observed until 200°C. When the temperature rose above 200°C a yellow color formed.

2) The ^1H NMR of bis (trimethylsilyl)acetone 42 in CCl_4 possesses



a singlet at δ 0.27 ppm (18H) for the methyl groups on silicon (protons c), a singlet at δ 2.01 ppm (3H) for the methyl ketone group (protons a), and a singlet at δ 2.31 ppm (1H) for the α -proton (proton b). But the ^1H NMR of the heated yellow solution (decomposed solution) possesses five

singlets at 0.1-0.27 ppm for the trimethyl silyl groups; one for the remaining bis-silylated acetone (e) and four (a, a¹, b, b¹) for the cis and trans migrated products (eq. 81).



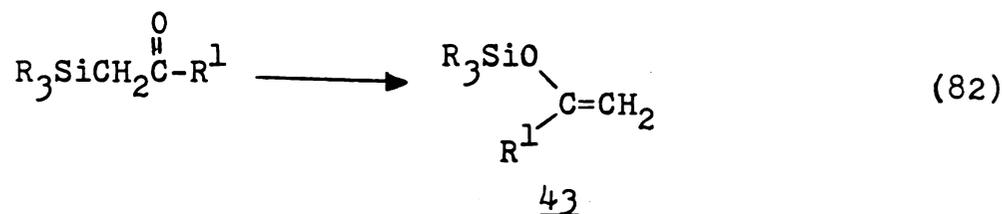
Two singlets at 1.8-2.00 ppm, for the cis and trans methyl groups (d, d¹ protons), one singlet at 2.01 ppm for the methyl of the remaining bis-silylated acetone (e proton), one singlet at 2.31 ppm for the α -proton of the remaining silylated acetone (f) and one singlet at 4.4 ppm for cis (g) and trans (g¹) vinyl protons were observed.

3) The IR spectrum of α, α -bis-silylated acetone possesses a strong carbonyl absorption at 1680 cm^{-1} . This strong absorption decreased after heating to over 200°C

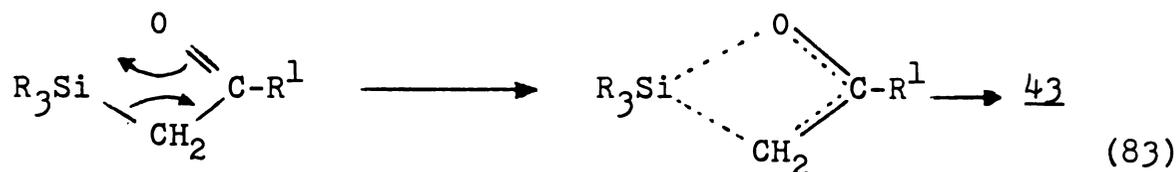
and instead, an absorption appeared at 1620 cm^{-1} for a carbon-carbon double bond.

4) The ^1H NMR and IR spectra of α,α bis (trimethylsilyl) acetone, collected from the GLC column outlet (30.5% SE) were the same as that for the heated solution discussed previously. From these data it was concluded that the α,α bis (trimethylsilyl) acetone decomposes by migration of a trimethylsilyl group (eq. 81) if heated over 200°C .

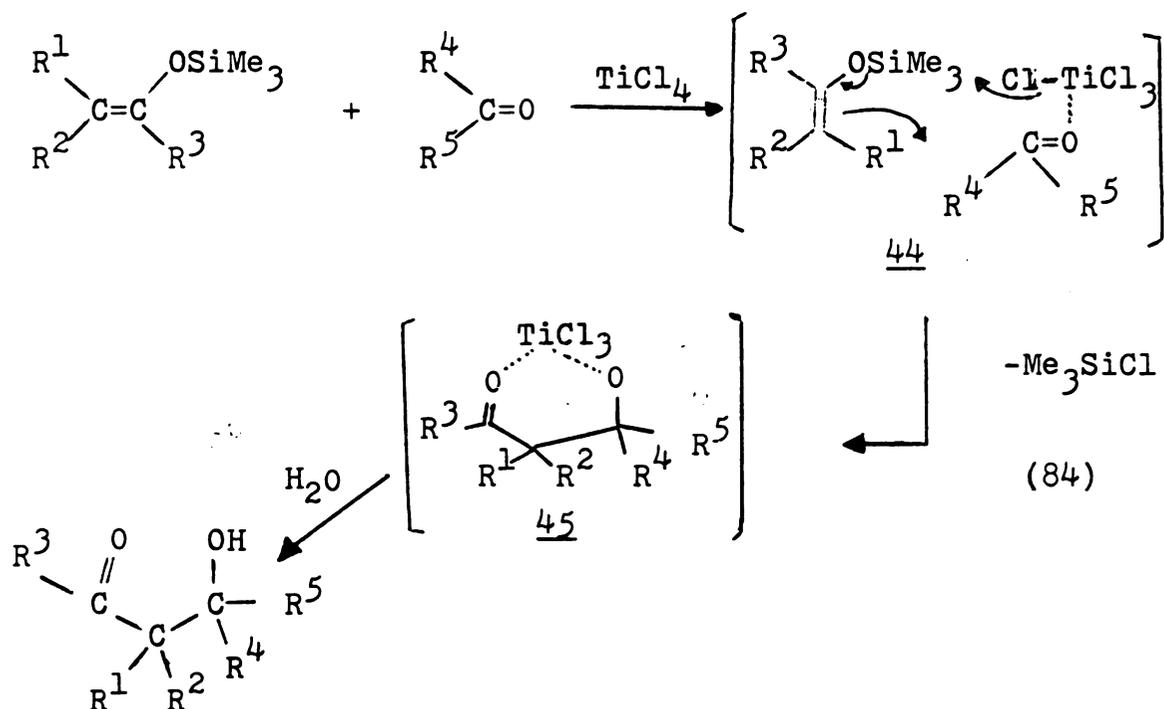
A similar type of decomposition has been reported by Brook^{25,26} for β -keto silanes (α -silylated ketones) on prolonged heating at temperatures from 80 - 175°C (eq. 82).



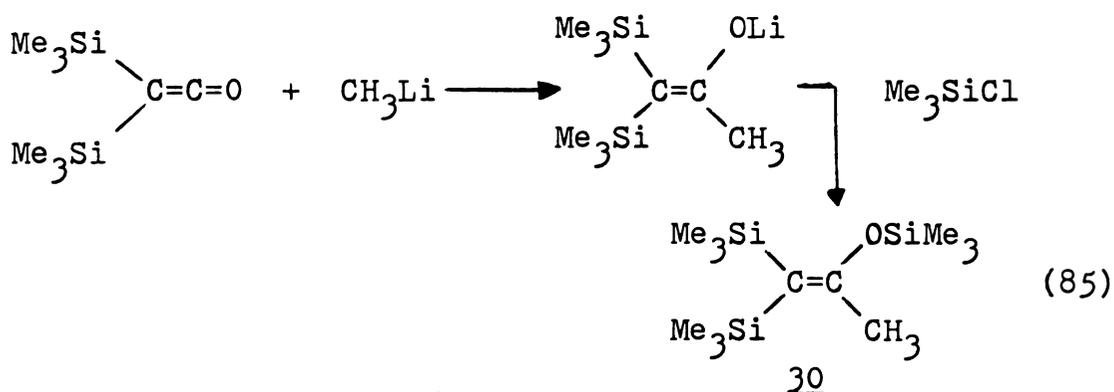
Related arrangements of trialkylsilyl acetones catalyzed by mercuric iodide or trialkyl silyl iodide have also been described.⁵⁴ It has been suggested that this reaction proceeds via a four-centered activated complex (eq. 83).



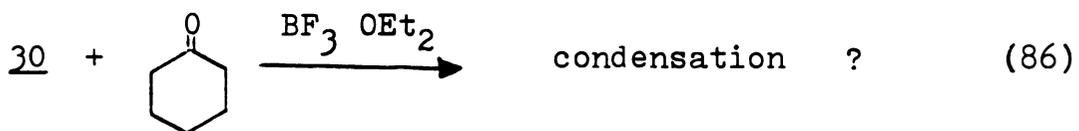
A crossed aldol reaction has been reported between silyl enol ethers and carbonyl compounds activated by titanium tetrachloride⁵⁵ (eq. 84).



Therefore, the enolate formed by addition of methyl-lithium to bis-(trimethylsilyl)ketene was reacted with trimethylchlorosilane (eq. 85) to yield the corresponding silylenolether (30).



Silylenolether 30 was treated with cyclohexanone in the presence of $BF_3 \cdot OEt_2$ with no detectable amounts of the corresponding α -silylvinyl ketone formed (eq. 86).



The same reaction was performed in the presence of TiCl_4 ; none of the expected α -silylvinyl ketone was observed by GLC. It appears that the reaction is prevented by the steric effect of bulky trimethylsilyl groups which disfavor the formation of transition states 44 or 45 (see eq. 84).

EXPERIMENTAL

1. Materials

Ketene

Bis-(trimethylsilyl)ketene was prepared from t-butyl acetate by the procedure described in Chapter I and stored under argon at 0°C.

Alkylolithium Reagents

Methylolithium, n-butyllithium and tert-butyllithium were available from the Aldrich Chemical Company as standard solutions which were titrated prior to use.⁵⁶

Trimethylchlorosilane

Trimethylchlorosilane was commercially available from the Aldrich Chemical Company and used after distillation (bp 57°C, 760 mm Hg).

Aldehydes

Acetaldehyde was available from Aldrich Chemical Company. It was distilled (bp 21°C 760 mm) prior to use. Benzaldehyde was also available from Aldrich Chemical Company and distilled prior to use (bp 178°C).

Ketones

Acetone was commercially available from Aldrich Chemical

Company and distilled prior to use (b.p. 56°C). Cyclohexanone was also available from Aldrich Chemical Company distilled prior to use (b.p. 155°C).

2. Preparation of α,α -Bis-(trimethylsilyl) Ketones.

The following procedure is typical for preparing bis-(trimethylsilyl) ketones. Argon was flushed through a 25 ml side-armed round-bottomed flask, which was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and mercury bubbler. The flask was charged with 5 ml anhydrous ether and 0.9 ml (5 mmoles) of methyl lithium in ether was added dropwise over 2 minutes. The solution was stirred for 1 hour at room temperature. Then 2.5 ml of 2 M solution of HCl was added to quench the solution. The aqueous layer was separated and organic solvent was removed under reduced pressure. The product was identified by its $^1\text{H NMR}$ and IR spectrum. The yield was determined to be 75%. $^1\text{H NMR}$ of α,α -bis-(trimethylsilyl) acetone in CCl_4 : 0.27 ppm (s, 18H), 2.01 (s, 3H), 2.31 (s, 1H), relative to TMS. IR, strong absorption at 1680 cm^{-1} for the carbonyl group.

3. Reactions of α,α -Bis-(trimethylsilyl)acetone Enolate.

A. With Trimethylchlorosilane.

Argon was flushed through a 25 ml side-armed round-bottomed flask, equipped with magnetic stirring bar, septum inlet, gas inlet valve and mercury bubbler. The flask was

charged with 5 ml anhydrous ether. Then 0.9 ml (5 m moles) of bis-(trimethylsilyl)ketene was injected and 3.4 ml of a 1.6 M (5.44 m moles) solution of methyllithium in ether was added dropwise over a 2 minute period. The solution was stirred for 1 hour at room temperature to convert the ketene to the corresponding enolate. Then 0.64 ml (5 m moles) of distilled trimethylchlorosilane was added dropwise. Stirring was continued for 1 hour.

The product, 30, was identified by its ^1H NMR spectrum in CCl_4 : Three singlets for three different kinds of trimethylsilyl groups at 0.27-0.4 ppm and one singlet for the methyl group at 2.00 ppm, relative to the TMS.

B. With Benzaldehyde.

A 10 ml side-armed round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, gas inlet valve and mercury bubbler. The flask was flushed with argon, 2 ml anhydrous ether and 0.18 ml (1 m mole) of pure bis-(trimethylsilyl)ketene were injected into flask. Then 0.7 ml of a 1.6 M (1.1 m mole) solution of the methyllithium in ether was added dropwise. The mixture was stirred for 1 hour, then 0.056 ml (1 m mole) of distilled benzaldehyde was injected dropwise. The solution was stirred for 5 minutes. GLC analysis showed that all of the enolate was converted to the desired product in quantitative yield. The ^1H NMR of product, 31, in CCl_4 was: 0.33 (S, 9H) for the trimethylsilyl group, 2.02 (S, 3H) for the methyl group,

δ 6.76 (S, 1H) for the vinyl proton (due to the phenyl ring) and δ 7.58 (S, 5H) for the phenyl.

C. With other Aldehydes.

The same procedure was followed with acetaldehyde and is a butyraldehyde. The results were the same as in quenching the enolate. No α -silylated vinyl product was detectable; instead, α, α bis-(trimethylsilyl)acetone was found in the solution.

D. With Ketones.

The same procedure as before was followed to make 1 mmole of the ketone enolate. 0.104 ml (1 mmole) distilled cyclohexanone was added dropwise. The reaction was stirred for 0.5 to 1.5 hours. After quenching with sufficient water, none of the desired α -silyl vinyl ketone was found in the solution. The same result was observed for acetone.

E. Reaction of the Enolate with Alkylhalides.

1 mmole of ketene enolate was made by the above procedure. Then 62 ml (1 mmole) of distilled methyl iodide was injected dropwise at room temperature. New products were observed by Glc but all attempts to isolate and identify these products were unsuccessful. The same result was observed with ethyl iodide.

4. Attempt to React $(\text{Me}_3\text{Si})_2\text{C}=\text{C}\begin{matrix} \text{OSiMe}_3 \\ \text{CH}_3 \end{matrix}$, 30, with Ketones.

A 1 mmole ethereal solution of 30 was formed as described previously in this chapter. The flask was immersed in a dry ice-acetone bath and 0.104 ml (1 m mole) of cyclohexanone was added over 1 minute. 3 drops of $\text{BF}_3 \cdot \text{OEt}_2$ was added as a catalyst to the flask. The solution was stirred for 1.5 hours at -78°C . Then the solution was warmed to room temperature and stirred 30 minutes longer. None of the expected product was detected by Glc analysis.

The same experiment was done using an equivalent of TiCl_4 instead of $\text{BF}_3 \cdot \text{OEt}_2$. The solution was quenched with sufficient water at -78°C . No product was formed and more than 80% of the starting cyclohexanone was recovered, using Glc analysis.

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