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THE CHEMISTRY OF α-SILYL CARBONYL COMPOUNDS

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1. INTRODUCTION

The chemistry of α-silyl carbonyl compounds began in the early 1950s. It has been reviewed four times.[1–4] As will hopefully become apparent in the subsequent pages, the chemistry of this interesting structural entity is varied, wide, and useful. The author has taken the liberty of using abbreviations. Although these are in common usage and for the most part well known, a list of the abbreviations used are as follows:

9-BBN	9-Borabicyclononane
BOMO	Benzyloxymethoxy
DCM	Dichloromethane
EE	Diethyl Ether
HMPA	Hexamethylphosphoric Triamide
LDA	Lithium Diisopropyl Amide
LiDMAN	Lithium Dimethylaminonaphthalene
PCC	Pyridinium Chlorochromate
TES	Triethylsilyl
THF	Tetrahydrofuran

2. SPECTROSCOPY

It was pointed out early on that the stretching frequency of trimethylsilyl acetone occurred at shorter wavelengths than that for the *tert*-butyl analog.[5] This was argued to be the result of an intramolecular interaction between the oxygen of the carbonyl and the electropositive silicon atom. This effect could, however, be explained by the electron-donating (+I) effect of the trimethylsilylmethyl group on the carbonyl. The carbonyl stretching frequency of α-silyl esters is some 20–25 cm^{-1} lower than that of normal esters, again a result of the inductive effect of the silylmethyl group.[6]

The stretching frequency of the carbonyl in methyl triethylsilylacetate in various solvents was studied.[7] In nonpolar solvents the stretching frequency is near 1735 cm^{-1} whereas in polar solvents it falls between 1715 and 1724 cm^{-1}. Some values along with the solvent are: cyclohexane (1738), decalin (1735), benzene (1724), carbon tetrachloride (1734), dichloromethane (1718), chloroform (1716), nitromethane (1724), acetonitrile (1723), and pyridine (1711).

Several aryldimethylsilyl acetones were prepared from the corresponding aryldimethylsilylmethylmagnesium chloride and acetic anhydride and the spectral properties reported.[8] It was found that the carbonyl stretching frequency of the α-aryldimethylsilyl ketones appeared at 1695 cm^{-1} and the C=C stretch in the silyl enol ethers at 1640 cm^{-1}.

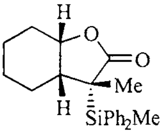
Musker and Ashby[9] showed that the ultraviolet spectrum of trimethylsilyl acetone gave a higher extinction coefficient for $n \rightarrow \pi^*$ transition than that for the *tert*-butyl analog. They argued that this was evidence for a possible orbital interaction between the *d*-orbitals of the silicon and carbonyl group resulting in a mixing of the *s*- and *np*-orbital character of the carbonyl group.

Mass spectra were recorded for a number of 1-(aryldimethylsilyl)-2-propanones and their corresponding enol silyl ethers.[10] The fragmentation patterns of the α-silyl ketone and the corresponding enol silyl ether were in all cases very similar. The use of normal mass spectrometry to distinguish the keto from the enol structure would not be reliable.

The natural abundance ^{29}Si NMR spectra of a wide variety of organosilanes were first published by Scholl, Maciel, and Musker.[11] Some of the data pertinent to this article are shown below.

> $(Me_3SiCH_2)_2(Me)\underline{Si}CH_2CO_2Et$ (−81.39 ppm); $(Me_3SiCH_2)(Me)_2\underline{Si}CH_2CO_2Et$ (−81.42 ppm); $Me_3\underline{Si}CH_2CH_2CO_2Et$ (−81.37 ppm); $EtMe_2\underline{Si}CH_2CO_2Et$ (−83.67 ppm); $Et_2Me\underline{Si}CH_2CO_2Et$ (−85.60 ppm); $Me_3SiOMe_2\underline{Si}CH_2CO_2Et$ (−87.39 ppm).

The X-ray crystal structures have been reported for the α-silyl carbonyl compounds **1**[12], **2**[13], **3**[14], and **4**[15].



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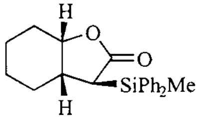

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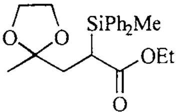

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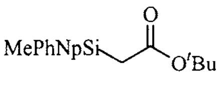

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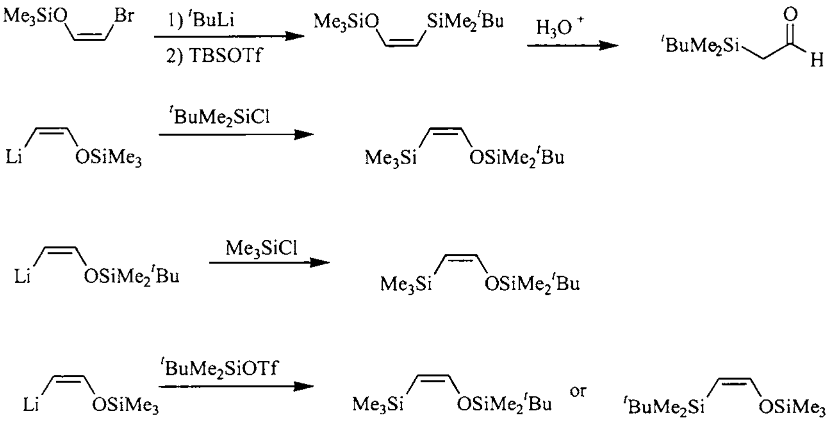
3. SYNTHESIS OF α-SILYL ALDEHYDES

The direct synthesis of α-silyl aldehydes has been slower than some of the other α-silyl carbonyl systems due to their increased instability and reactivity, making their isolation and purification more difficult. Sterically demanding groups either in the silyl moiety or in the rest of the molecule near the carbonyl can impart added stability to these systems.

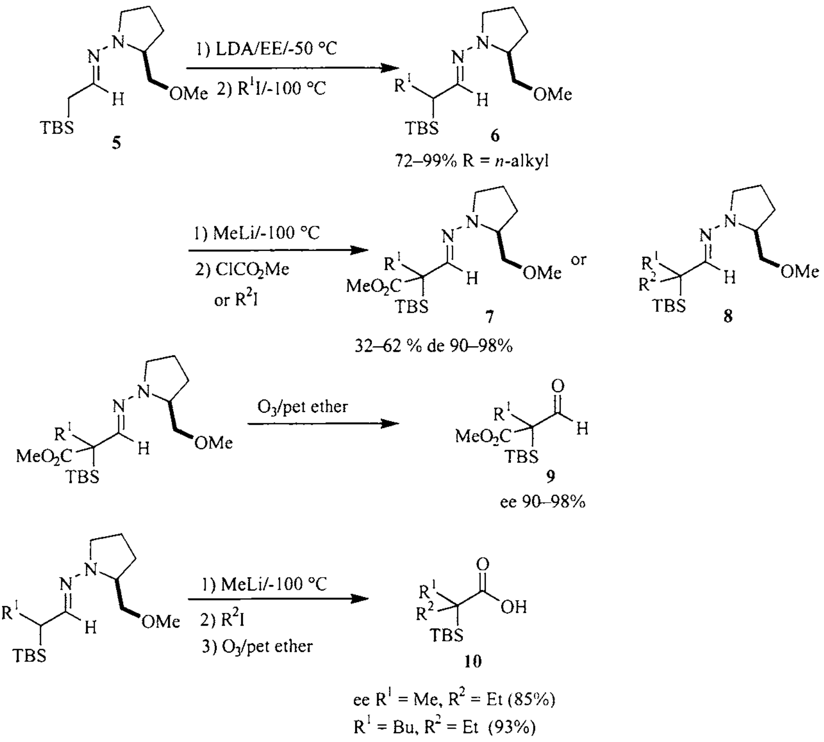
3.1. α-Silyl Aldehydes from Organometallic Reagents

An excellent entry into *tert*-butyldimethylsilylacetaldehyde has been reported starting from the trimethylsilyl enol ether of bromoacetaldehyde which was lithiated and the lithium reagent silylated with *tert*-butyldimethylchlorosilane in good yield.[16] Careful acid hydrolysis of the resulting trimethylsilyl enol ether provides *tert*-butyldimethylsilylacetaldehyde. This reaction was shown to occur with rearrangement of the silyl group when the silyl group is trimethylsilyl or triethylsilyl, as can be seen from the examples below.[17] The reaction of the β-trimethylsiloxyvinyllithium reagent with *tert*-butyldimethylchlorosilane provides the *tert*-butyldimethylsilyl enol ether of trimethysilylacetaldehyde. The reaction of the *tert*-butyldimethylsiloxyvinyllithium reagent with trimethylchlorosilane, however, gives the same product with migration of the *tert*-butyldimethylsilyl group, presumably due to its greater steric bulk. Treatment of the trimethylsiloxyvinyllithium reagent with *tert*-butyldimethylsilyl triflate gives either the rearranged or unrearranged product depending on the purity of the triflate with freshly distilled triflate providing unrearranged product and commercial triflate rearranged product.

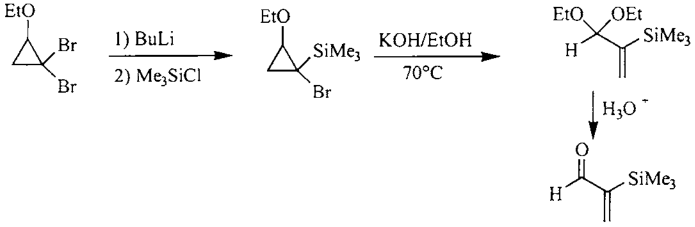


The α-*tert*-butyldimethylsilyl hydrazone **5** was deprotonated and alkylated to give **6**, which can then be deprotonated and carboethoxylated or alkylated to give **7** or **8**, respectively. Ozonolysis of the hydrazone gives the aldehyde **9** or the acid **10**.[18]

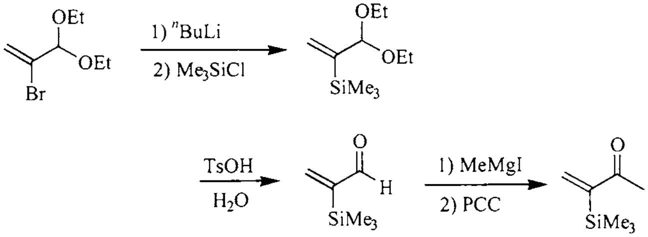
Lithiation-trimethylsilylation of 1,1-dibromoethoxycyclopropanes gives 1-trimethylsilyl-1-bromo-2-ethoxycyclopropanes which upon



treatment with potassium carbonate in an alcohol provide the acetal or ketal of an α-silyl-α,β-unsaturated aldehyde or ketone. Hydrolysis of the acetal or ketal gives rise to the α-silyl-α,β-unsaturated carbonyl derivative.[19]

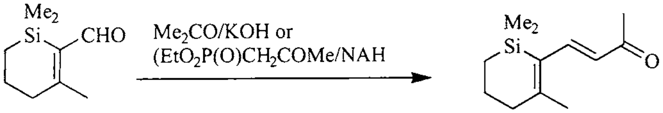


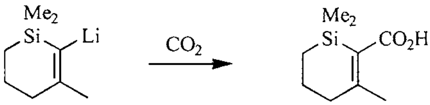
2-Trimethylsilylacrolein was synthesized and converted to 2-trimethylsilylbut-1-ene-3-one by treatment with methylmagnesium iodide and pyridinium chlorochromate.[20] This implies that the silylated acrolein could be an excellent precursor to a number of different α-silyl-α,β-unsaturated enones. (See Section 5 for a discussion of α-silyl enones.)



The α-bromovinylsilane **11** was converted via its Grignard reagent to α-silyl aldehyde **12**, which in turn was used to synthesize sila-β-ionone as a potential sila perfume.[21] The lithium reagent was also converted to the α-silyl acid **13**. Similar chemistry was used to prepare 2-trimethylsilyl-3-methylbut-2-enal.[22]

11 **12**





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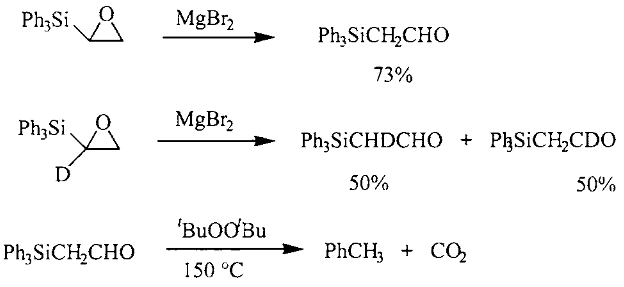
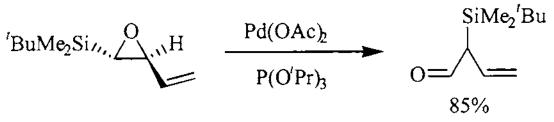
3.2. α-Silyl Aldehydes from Rearrangements

Eisch and Trainor[23] were the first to show that the isomerization of an α,β-epoxysilane could rearrange to the α-silyl aldehyde. Thus, they synthesized triphenylsilylacetaldehyde in good yield from the corresponding epoxide. This rearrangement was later shown to occur via opening of either the C_1–O or the C_2–O bonds, whereas the reaction with HCl leads to triphenylchlorosilane and acetaldehyde.[24] Wilt and

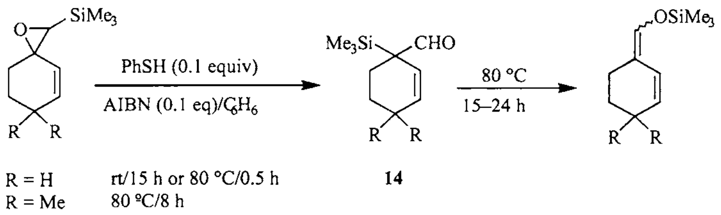
Kolewe[25] demonstrated that triphenylsilylacetaldehyde does not react with radicals in the same manner as its carbon analog, choosing to eliminate carbon dioxide instead.

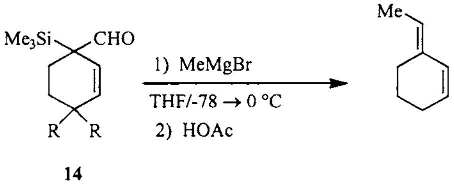


The rearrangement of an epoxysilane was used to prepare 2-trimethylsilylbut-3-enal.[26] Thus palladium(0) was found to rearrange vinyl α,β-epoxy *tert*-butyldimethylsilanes to β,γ-unsaturated α-silyl aldehydes. The carbonyl could be reacted, although in only poor yields, with nucleophiles.

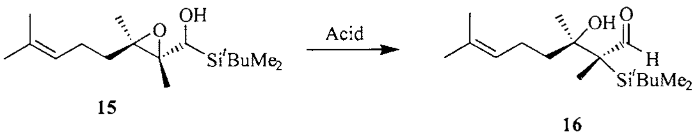


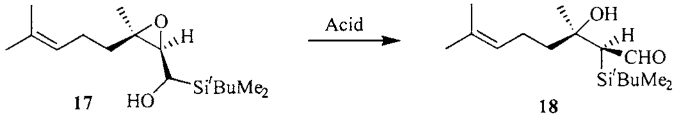
The thiyl radical-induced fragmentation of unsaturated epoxysilanes can be used to afford α-trimethylsilyl aldehydes.[27] The aldehyde **14** was shown to react stereospecifically with methylmagnesium bromide.



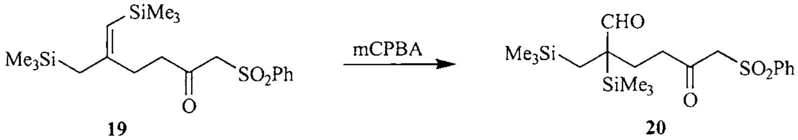


The α-hydroxy-β,γ-epoxysilanes **15** and **17** were shown to undergo acid-catalyzed rearrangement to the unstable α-silyl aldehydes **16** and **18**, respectively.[28]

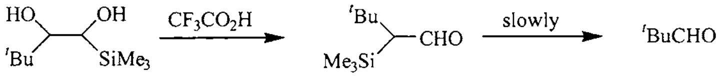


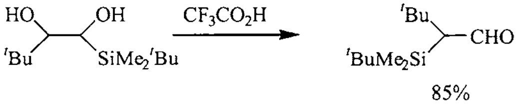


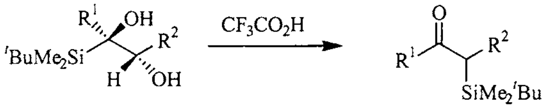
The epoxidation–rearrangement of vinylsilane **19** gives the α,β-bis(trimethylsilyl)aldehyde **20** in quantitative yield.[29]



A silapinacol rearrangement was employed for the synthesis of the elusive α-silyl aldehydes.[30] In the trimethylsilyl example the stability was aided by the bulky *tert*-butyl group in the α-position. The approach also works for the synthesis of β-ketosilanes. When the silyl group is *tert*-butyldimethylsilyl the stability is greater and the products are easier to isolate.





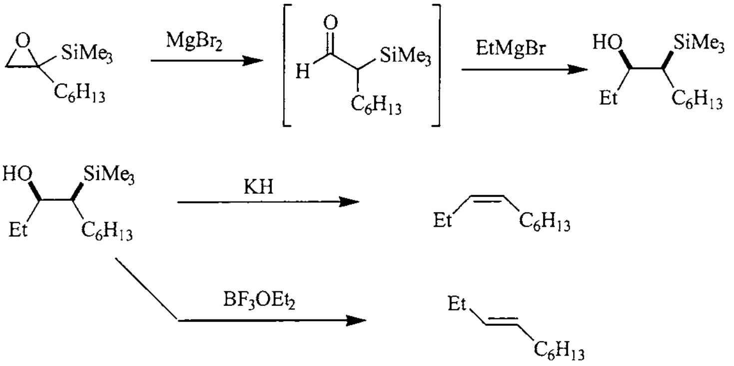


$R^1 = H, R^2 = {}^nC_6H_{13}$

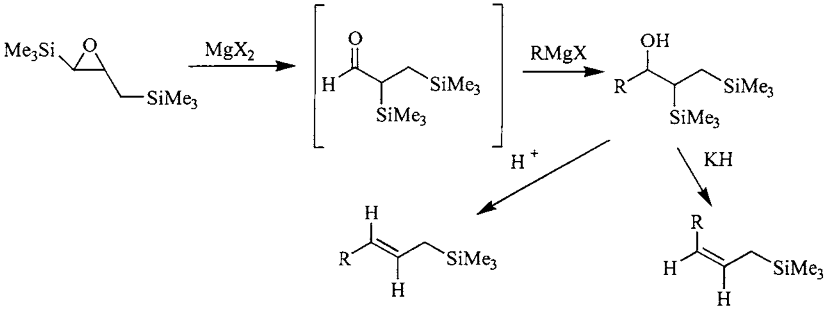
$R^1 = Ph, R^2 = H$

3.3. 'In Situ' Generation of α-Silyl Aldehydes

Hudrlik and co-workers[31] showed, in an example of the generation of an α-silyl carbonyl for the purpose of further reaction, that α,β-epoxysilanes when reacted with magnesium bromide generate α-silyl ketones or aldehydes. These were then trapped with nucleophilic reagents leading, in the case of their reaction with Grignard reagents, to olefins of defined stereochemistry.



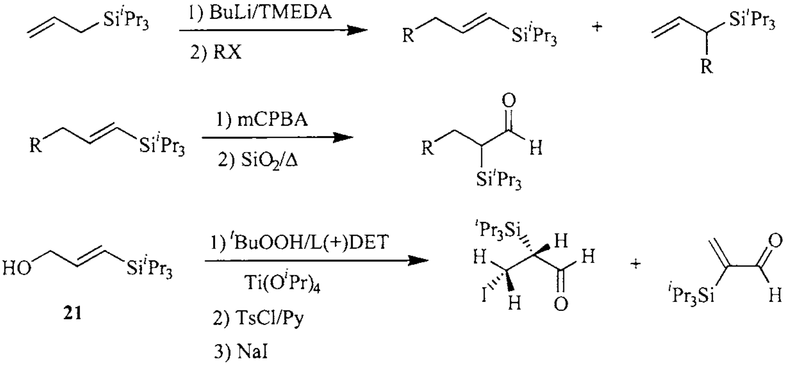
1,3-Bis(trimethylsilyl)propylene oxide reacts with magnesium halides present in a Grignard reagent to give 2,3-bis(trimethylsilyl)propanal, which reacts with the Grignard reagent to give a β-hydroxysilane, which can be eliminated in a Peterson fashion to either the (*E*)- or the (*Z*-allylsilane depending on whether the elimination is carried out with base or with acid.[32] The stereoselectivity is reasonably high.



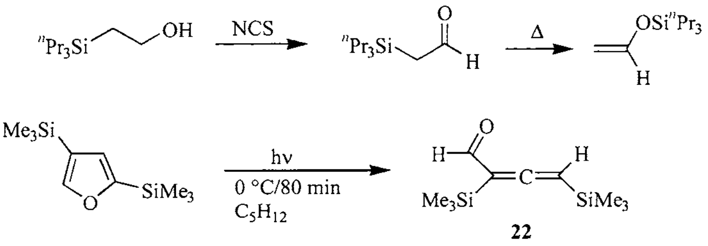
stereoselectivity >89:11

3.4. Miscellaneous Syntheses of α-Silyl Aldehydes

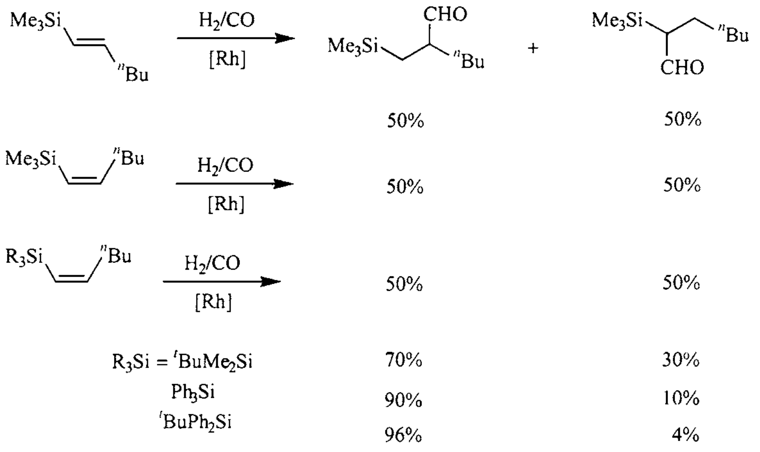
The alkylation of the lithium anion of allyltriisopropylsilane was shown to occur predominantly at the γ-position.[33] The resulting vinylsilanes could be treated with *m*-chloroperbenzoic acid and the epoxide rearranged to the α-triisopropylsilyl aldehyde in nearly quantitative yields. Interestingly, the vinylsilane **21** was subjected to the Sharpless epoxidation and this epoxide converted as shown to the optically active α-silyl aldehyde.



The *N*-chlorosuccinimide oxidation of 2-tri-*n*-propylsilylethanol gives tri-*n*-propylsilylacetaldehyde, which upon heating rearranges to the silyl enol ether of acetaldehyde.[34] The photolysis of 2,4-bis(trimethylsilyl)furan gives the α-trimethylsilylallenyl aldehyde **22**.[35]

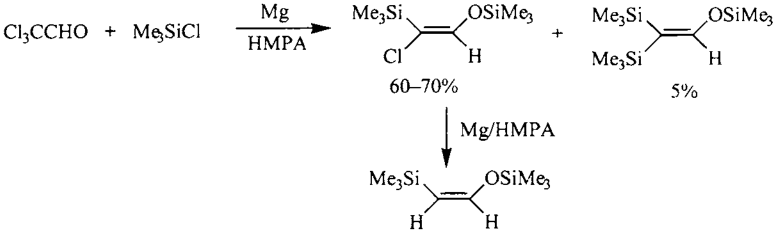


The hydroformylation of vinylsilanes was reported and it was found that with the trimethylsilyl derivatives the α:β ratio was nearly 1:1 for either the *cis*- or the *trans*-isomers, but that the larger silyl groups gave more of the β-product.[36] The hydroformylation of vinyltrimethylsilane and vinyltrimethoxysilane with a variety of catalysts was studied and shown to give a mixture of the α- and β-carbaldehyde products.[37]

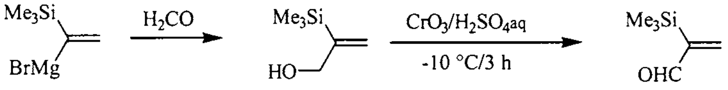


3.5. Species Related to α-Silyl Aldehydes

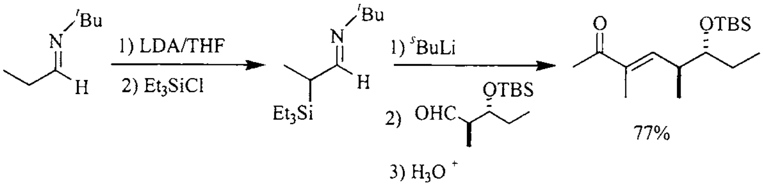
Several protected versions of α-silyl aldehydes have been reported. Chloral was reacted with trimethylchlorosilane/magnesium in HMPA solvent to give the silyl enol ether of (trimethylsilyl)chloroacetaldehyde and of bis(trimethylsilyl)acetaldehyde.[38] Treatment of the chloro derivative with magnesium in HMPA gave the reduced material, 1-trimethylsiloxy-2-trimethylsilylethylene, the trimethylsilyl enol ether of trimethylsilylacetaldehyde.



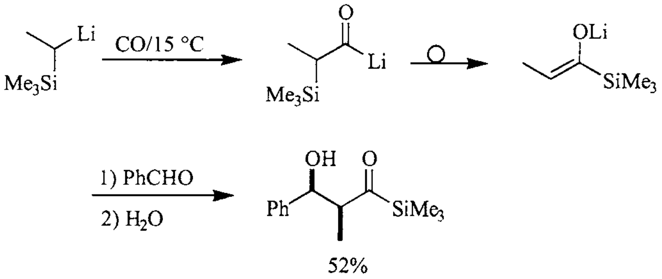
The Grignard reagent of 1-bromovinyltrimethylsilane was reacted with formaldehyde and the resulting allyl alcohol oxidized to the aldehyde.[39]



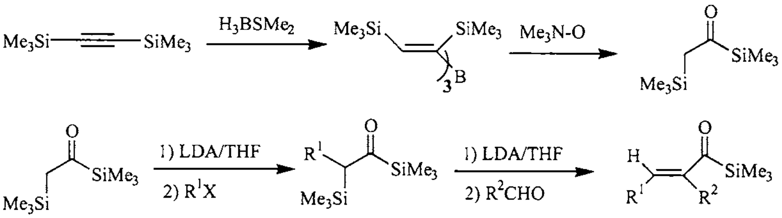
The *tert*-butyl imines of aldehydes are readily deprotonated–silylated to provide the α-silyl derivative. These derivatives show excellent promise for the vinylogation of aldehydes as illustrated.[40]



Other related species to the α-silyl aldehydes have appeared. Carbonylation of 1-trimethylsilylmethyllithium reagents gives rise to α-trimethylsilyl acyllithium intermediates which undergo a rearrangement to the lithium enolate of an acylsilane, which could be trapped with aldehydes.[41]

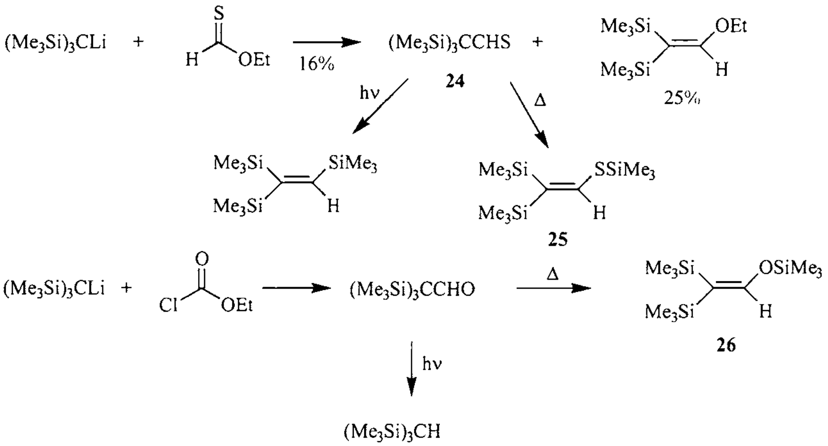


Miller and Zweifel[42] showed that the hydroboration–oxidation of bis(trimethylsilyl)acetylene provides trimethylsilylacetyl trimethylsilane in good yield. In a related paper, bis(trimethylsilyl)acetylene was hydroborated with borane methylsulfide complex to give the trisubstituted borane, oxidation of which with trimethylamine oxide gave (trimethylsilylacyl)trimethylsilane. Deprotonation–alkylation of this material gave the substituted systems **23**, which could be deprotonated and condensed with aldehydes to give α,β-unsaturated acylsilanes.



23

Tris(trimethylsilyl)methyllithium was reacted with ethyl thioformate to give tris(trimethylsilyl)thioaldehyde and the ethyl enol ether of α,α-bis(trimethylsilyl)acetaldehyde. Photolysis of **24** gives tris(trimethyl-

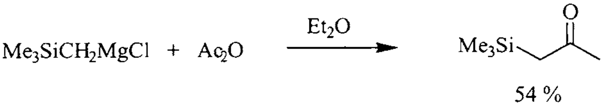


silyl)ethylene, whereas thermolysis gives the thioenol ether **25**. In contrast, reaction of ethyl formate with tris(trimethylsilyl)methyllithium gives the tris(trimethylsilyl)acetaldehyde which, upon photolysis, gives loss of carbon monoxide. Thermolysis gives the expected enol silyl ether **26**.[43]

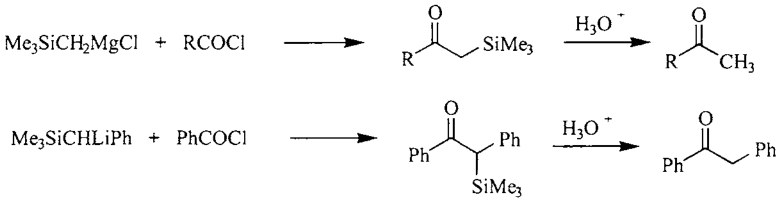
4. SYNTHESIS OF α-SILYL KETONES

4.1. Synthesis of α-Silyl Ketones from α-Silyl Organometallic Reagents

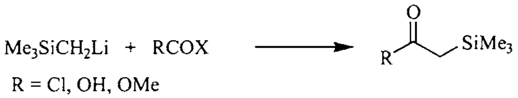
The reaction of α-silyl organometallic reagents with carboxylic acid derivatives has been used to provide α-silyl ketones. Hauser and Hance[44] were the first to show that the reaction of trimethylsilylmethylmagnesium chloride with acetic anhydride gives trimethylsilyl acetone.



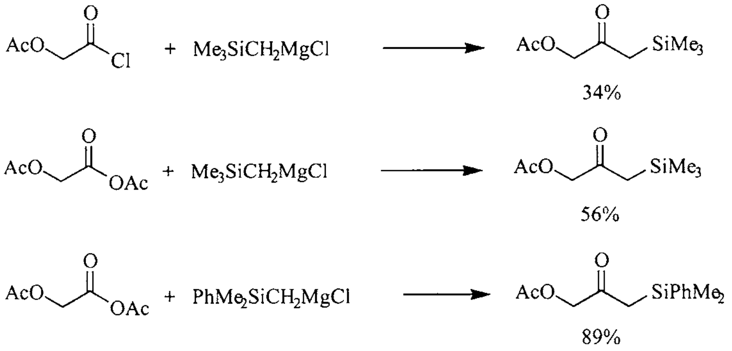
Chan and co-workers[45] showed that the reaction of acid chlorides with trimethylsilylmethylmagnesium chloride could be used to give methyl ketones via trimethylsilylmethyl ketones. Thus, the trimethylsilylmethyl unit is used as a hindered methyl group stopping the addition to the carbonyl at one. Protiodesilylation of the initially formed α-silyl ketone occurs readily upon acid workup of the reaction mixture. The reaction was extended to α-lithiobenzyltrimethylsilane as well.



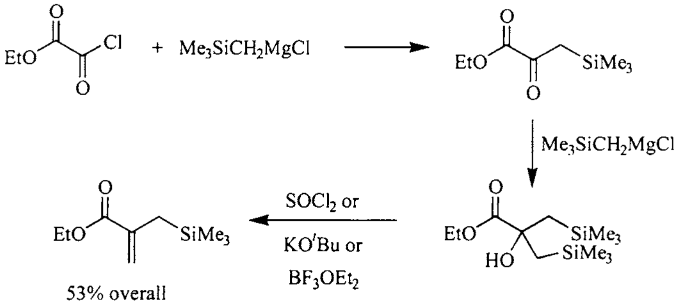
A series of β-ketosilanes was prepared by the reaction of trimethylsilylmethyllithium, available from transmetalation of trimethylsilyl(tributylstannyl)methane, with acid chlorides, acids, or esters.[46]



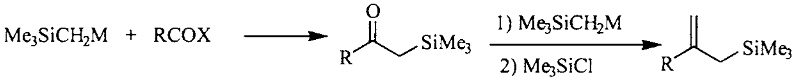
Trost and Schneider[47] synthesized 1-trimethylsilyl-3-acetoxy-2-propanone by the reaction of trimethylsilylmethylmagnesium chloride with acetoxyacyl chloride, and in better although still moderate yield with acetoxyacetic anhydride. The reaction of the more hindered dimethylphenylsilylmethylmagnesium chloride with the anhydride gives 1-(dimethylphenylsilyl)-3-acetoxy-2-propanone in excellent yield.



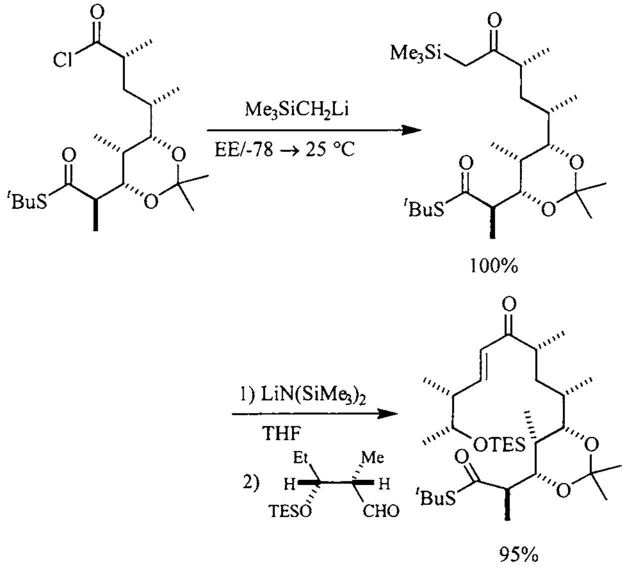
Haider[48] reacted trimethylsilylmethylmagnesium chloride with chloroethyl oxalate to give initially the α-silyl ketone which, being a relatively nonhindered ketone, adds a second equivalent of the Grignard reagent. A Peterson-type elimination of this adduct provides (2-ethoxycarbonylallyl)trimethylsilane, a potential synthon for the preparation of 2-methylene-4-alkanolides. This sequence indicates that trimethylsilylmethyl ketones will react faster with trimethylsilylmethylmagnesium chloride than will the ester group.



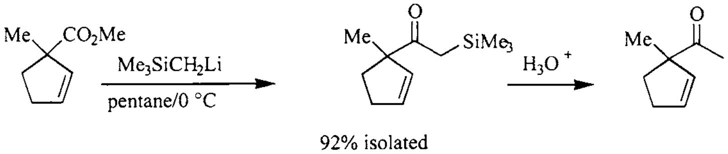
A similar approach to allylsilanes was used by Anderson and Fuchs[49] who converted acid chlorides and esters to allylsilanes from trimethylsilylmethyl organometallic reagents by the double addition–elimination sequence shown.

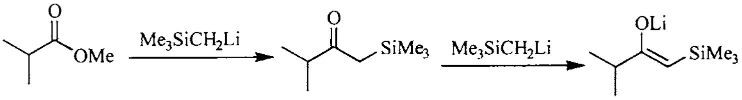


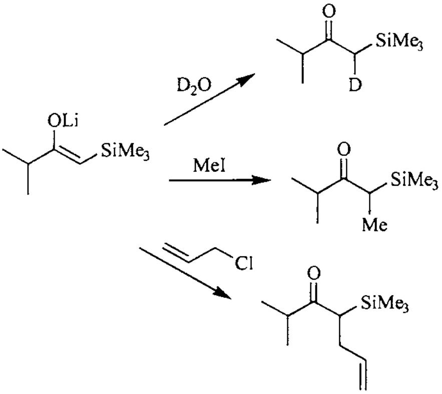
A trimethylsilylmethyl ketone was used by Masamune and co-workers[50] in the construction of precursors for the formation of macrocycles.



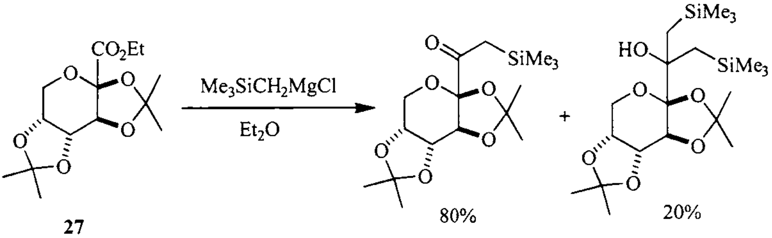
The reaction of secondary or tertiary methyl or ethyl esters with trimethylsilylmethyllithium was used to prepare α-trimethylsilyl ketones.[51] It was shown that the sterically hindered α-trimethylsilyl ketone reacts with the lithium reagent to give the enolate rather than to give addition to the carbonyl. The thusly generated enolate could be trapped with alkylating agents providing the more highly substituted α-trimethylsilyl ketone. Alternatively, the α-silyl ketones could be protiodesilylated to provide methyl ketones.





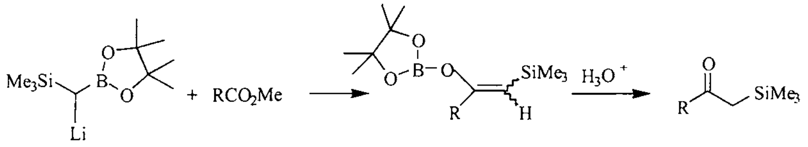


The reaction of trimethylsilylmethylmagnesium chloride with an ester was used to convert the ester **27** to a methyl ketone.[52] The large steric effect of this Grignard reagent allows the reaction to stop at the monoaddition stage with only a moderate amount of the bis-addition product. Subsequent removal of the trimethylsilyl group gives the methyl ketone.



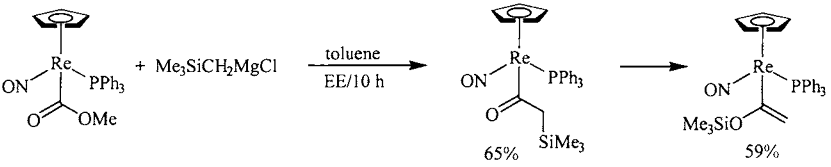
27

The α-trimethylsilyl-α-boryllithium reagent **28** was reacted with methyl esters to give α-silyl ketones via the boron enolate.[53] The products proved difficult to purify when prepared by this procedure, however.

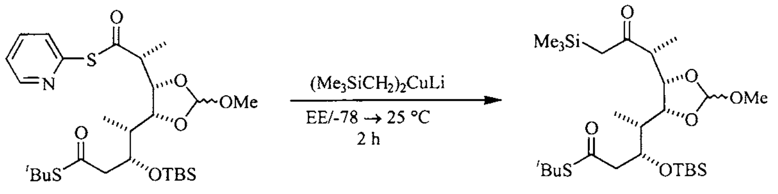


28

The reaction of trimethylsilylmethylmagnesium chloride with an ester to form a trimethylsilylmethyl ketone was employed in the synthesis of a trimethylsilylacyl rhenium complex.[54] Thermal isomerization provides the enol silyl ether.

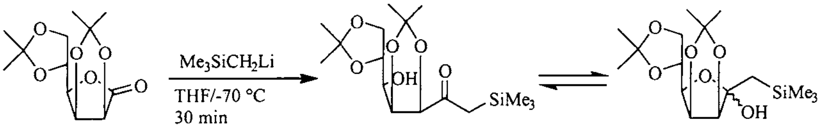


Masamune and coworkers[55] reacted lithium bis(trimethylsilylmethyl)cuprate with 2-pyridylthio ester **29** to give the trimethylsilylmethyl ketone **30**, which was used in a synthesis of the aglycone of tylosin. Trimethylsilylmethyllithium was reacted with the aldolactone **31** to give the trimethylsilylmethyl ketone in equilibrium with the hemiacetal.[56]



29

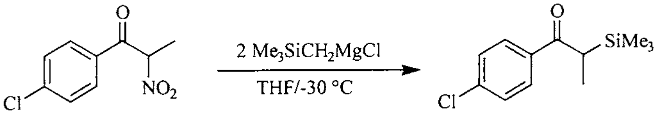
30

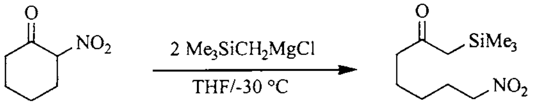


31

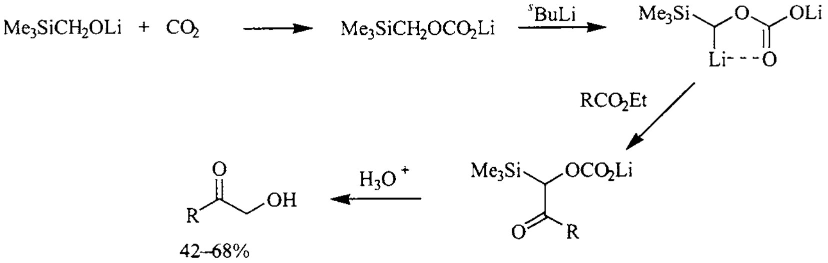
A very convenient entry into α-(methyldiphenylsilyl) ketones was shown to be the reaction of the readily prepared α-(methyldiphenylsilyl) ester with an excess of a Grignard reagent. This reaction only proceeds with primary Grignard reagents and results in the formation of the magnesium enolate of the α-silyl ketone regioselectively on the side opposite to that bearing the bulky methyldiphenylsilyl group.[6,57] Interestingly the addition of vinylmagnesium bromide results in the addition of two equivalents of the Grignard reagent, the second being the Michael addition to the enone produced in the first addition. (See Sections 11.2 and 12.2 for the reactions of α-silyl ketones and α-silyl esters with nucleophiles.)

The reaction of α-nitro ketones with two equivalents of trimethylsilylmethylmagnesium chloride results in trimethylsilylmethyl ketones.[58] When the α-nitro ketone is a cyclic ketone the product is a nitroalkyltrimethylsilyl ketone.





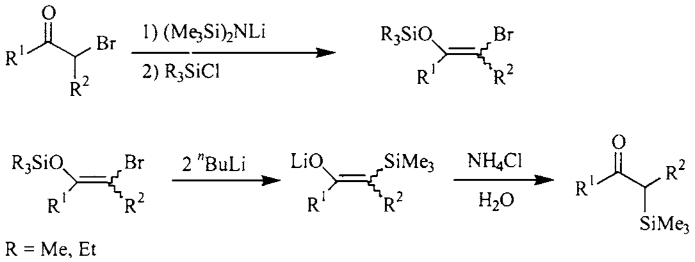
Trimethylsilylmethoxylithium can be reacted with carbon dioxide to give the lithium salt of the corresponding carbonate, deprotonation of which gives the α-silyllithium reagent.[59] This in turn can be reacted with esters, amides, acid chlorides, or nitriles to give α-silyl ketones as intermediates on the way to α-hydroxy ketones, which were isolated in good overall yields. The trimethylsilylmethoxylithium thus represents a methanol dianion equivalent.



Trimethylsilylmethylmagnesium chloride was reacted with the carbonyl ligand of complex **32** to give the trimethylsilylacetyl complex **33**.[60] The X-ray crystal structure showed it to be a heptavalent oxirane complex of molybdenum.

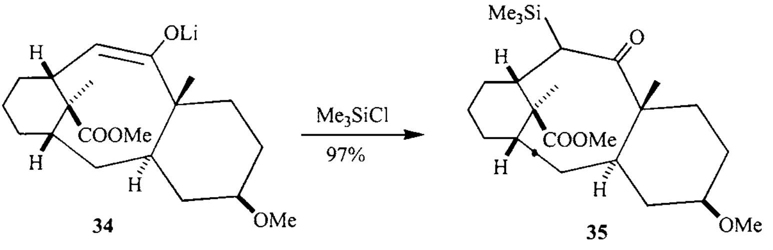
$$\underset{\mathbf{32}}{MoCl_2(CO)_2(PMe_3)_3} + Me_3SiCH_2MgCl \xrightarrow{EE} \underset{\substack{\mathbf{33}\\ 60\text{–}70\%}}{MoCl(\eta^2COCH_2SiMe_3)(CO)(PMe_3)_3}$$

Wiemer and co-workers[61] showed that the enolates of α-bromoketones could be O-trimethylsilylated and the resulting bromosilyl enol ethers reacted with butyllithium giving rise to a rearrangement and α-silyl ketones upon hydrolysis.



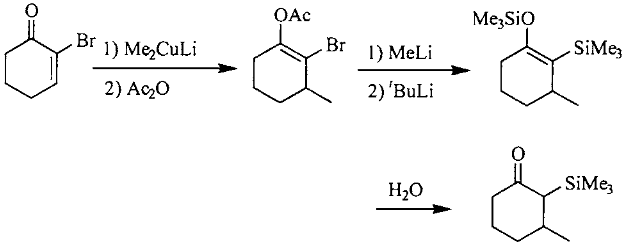
4.2. Synthesis of α-Silyl Ketones by Direct Silylation

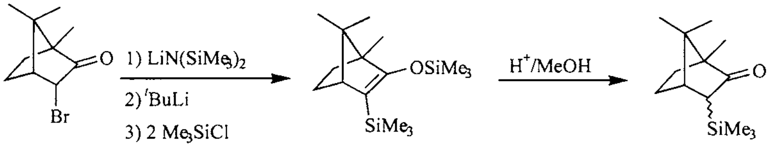
Only one report of the direct C-silylation of the lithium enolate of a ketone has been reported and it is to be found in highly sterically demanding taxol systems. Thus, treatment of the lithium enolate **34** with trimethylchlorosilane results in the formation of the α-silyl ketone **35**.[62] This highly unusual reaction is likely due to the steric hindrance found in the O-silylated product.



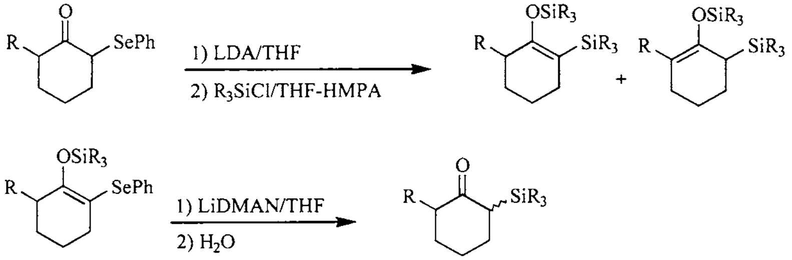
2-Bromocyclohexenone was reacted with lithium dimethylcuprate and then acetic anhydride to give the enol acetate, which upon treatment with a combination of methyllithium and *tert*-butyllithium gave the

2-lithio lithium enolate in a regiospecific manner.[63] Trimethylsilylation-hydrolysis of this dianion lead to the α-trimethylsilyl cyclohexanone.

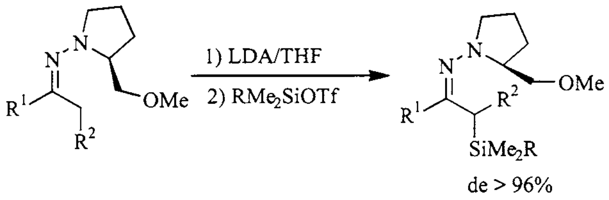


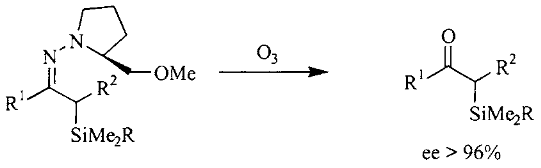


The trimethylsilyl enol ether of α-phenylseleno ketones can be converted to the vinyllithium reagent by way of metal–metal exchange. The resulting lithium reagent can then be trimethylsilylated and hydrolyzed to produce α-trimethylsilyl ketones in good yields.[64]



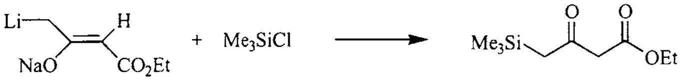
Lithiation of optically active hydrazones followed by silylation with either *tert*-butyldimethylchlorosilane or thexyldimethylchlorosilane gives the α-silylated hydrazone with high diastereomeric excess.[65] Treatment of the α-silylated hydrazone with ozone yields the α-silyl ketone with high enantiomeric excess.

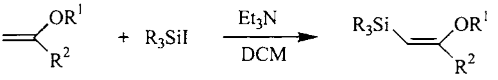




R = ^{t}Bu; Thexyl

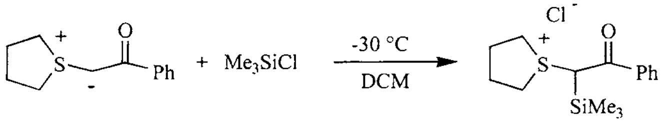
Reaction of the dianion of ethyl acetylacetonate with trimethylchlorosilane gives ethyl trimethylsilylacetylacetonate.[66] The reaction of trimethyl- or triethyliodosilane with enol ethers in the presence of an amine is reported to give β-silyl enol ethers, the enol ether of an α-silyl ketone.[67]





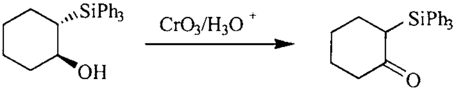
R^1 = H, alkyl; R^2 = alkyl; R_3Si = Me_3Si, Et_3Si

Benzoyl sulfonium ylide was reacted with trimethylchlorosilane to give an α-silyl-α-sulfonium ketone, which underwent reaction with the chloride ion present to give ultimately hexamethyldisiloxane and the trimethylsilyl-free sulfonium salt.[68]

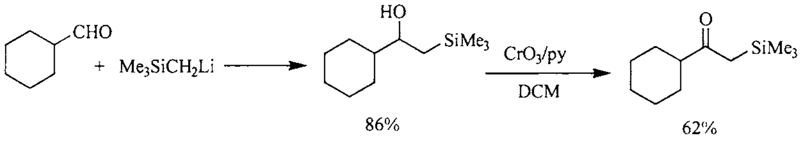


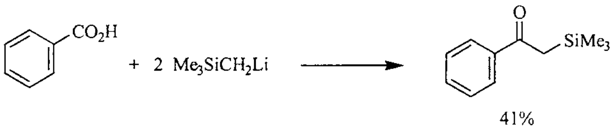
4.3. Synthesis of α-Silyl Ketones by Oxidation Reactions

Peddle[69] showed that 2-triphenylsilylcyclohexanone could be synthesized by the oxidation of the corresponding *trans*-2-triphenylsilylcyclohexanol, prepared by the reaction of triphenylsilyllithium on cyclohexene oxide.

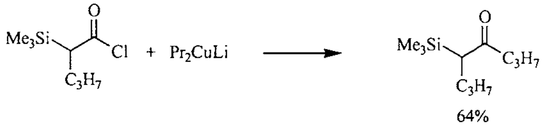


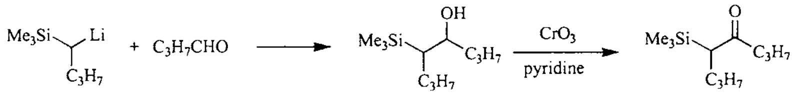
Ruden and Gaffney[70] showed that trimethylsilylmethyllithium in ether would react with aldehydes to give β-hydroxysilanes, which could be oxidized with Collin's reagent to give the α-silyl ketone in good yields. They also showed that the reaction of a carboxylic acid with two equivalents of the lithium reagent provides the trimethysilylmethyl ketone.



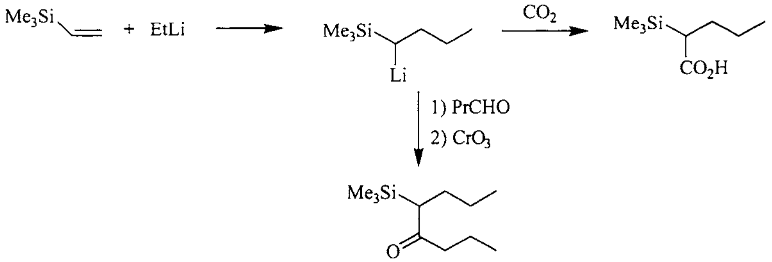


Hudrlik and Peterson[71] showed that the reaction of α-trimethylsilyl acid chloride with dialkylcuprates gives α-silyl ketones. They were also the first to show the successful oxidation of β-hydroxy silanes with Collin's reagent, a reaction that has subsequently been utilized in the preparation of many other α-silyl ketones.

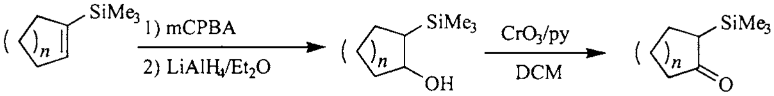




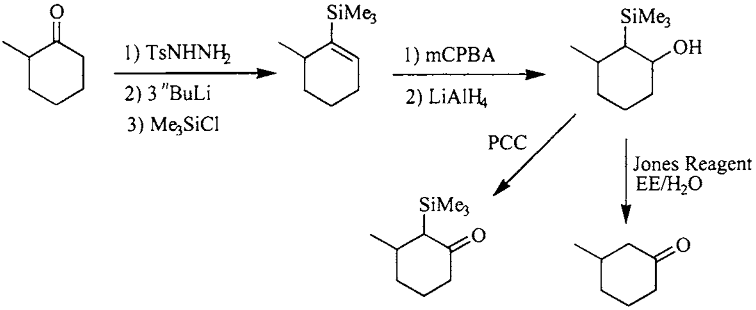
The addition of ethyllithium to vinyltrimethylsilane gives an α-silyllithium reagent, which was reacted with carbon dioxide to give the α-silyl acid or with butanal and then oxidation to give the α-silyl ketone.[72]



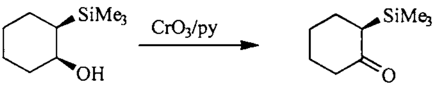
The synthesis of cyclic α-trimethylsilyl ketones was accomplished by the epoxidation of cycloalkenyltrimethylsilanes, opening of the epoxide with lithium aluminum hydride and Collin's oxidation of the resulting β-hydroxysilane.[73]

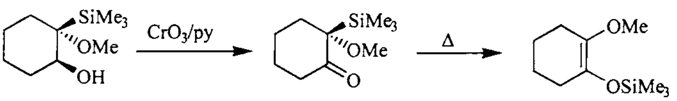


Paquette and co-workers[74] showed how the 1,2-transposition of a carbonyl group can be accomplished through a β-ketosilane as an intermediate. Thus, the ketone is subjected to a Shapiro reaction and the lithium reagent trimethylsilylated to give the least substituted vinylsilane, which is epoxidized and reacted with lithium aluminum hydride to provide the β-hydroxysilane. This is oxidized with concomitant desilylation to give the transposed ketone. Careful oxidation with pyridinium chlorochromate gives the α-silyl ketone.



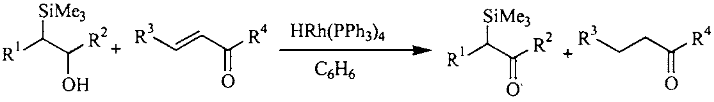
Davis and co-workers[75] showed that *cis*-2-trimethylsilylcyclohexanol could be readily oxidized to 2-trimethylsilylcyclohexanone with Collin's reagent. The material could be successfully distilled below 98 °C. The α-methoxy derivative of the above was also oxidized to the α-silyl





ketone, which was isomerized to the methoxy trimethylsiloxycyclohexene upon distillation.

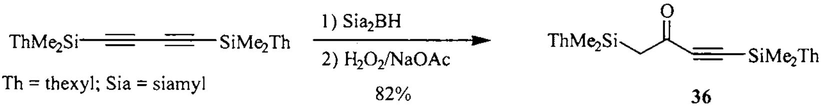
A clever oxidation of β-hydroxysilanes utilizing an enone as the oxidant and hydridotetrakis(triphenylphosphine) as a catalyst gives α-trimethylsilyl ketones in good yields.[76]



Enones used were 3-buten-2-one and cyclohexenone

5 examples 23 - 97%

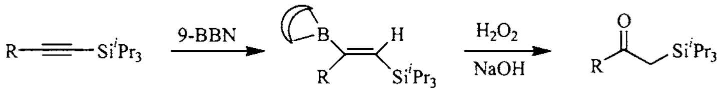
The monohydroboration of bis(trimethylsilyl)butadiyne followed by oxidation produces the α-trimethylsilyl ketone **36**.[77]



Th = thexyl; Sia = siamyl

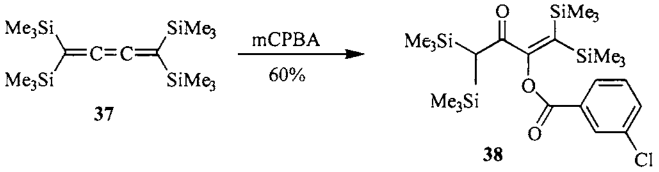
36

Soderquist and co-workers[78] have shown that 1-silyl acetylenes, where the silyl group is sufficiently sterically hindered, in particular the triisopropylsilyl group, are hydroborated with 9-BBN to place the boron on the β-carbon. Alkaline hydrogen peroxide oxidation provides the α-silyl ketone in excellent yields.



R = Me 90%, Pr 83%

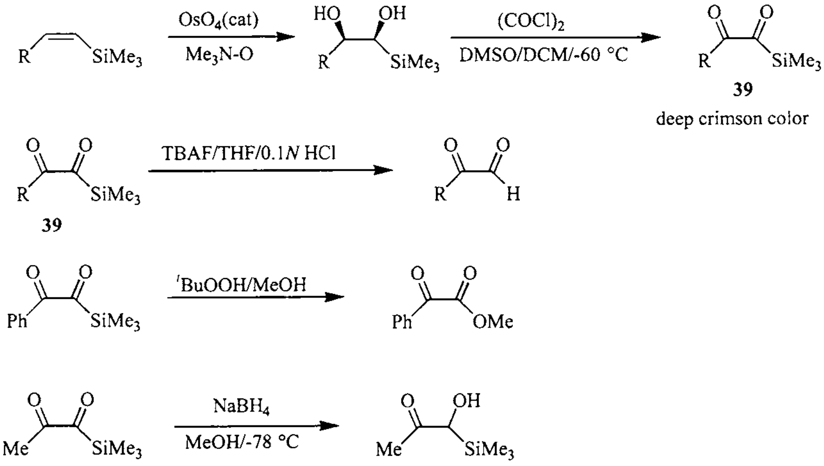
The reaction of 1,1,4,4-tetrakis(trimethylsilyl)butatriene, **37**, with *m*-chloroperbenzoic acid gives the epoxide on one of the terminal double bonds. This material reacts with the *m*-chlorobenzoic acid present in the reaction mixture to give the α,α-bis(trimethylsilyl) ketone **38**.[79]



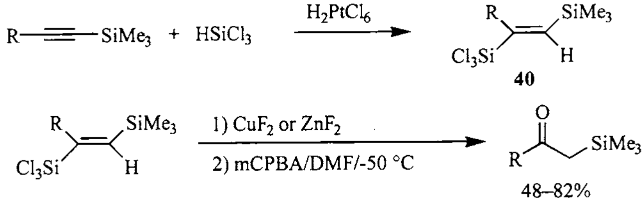
37

38

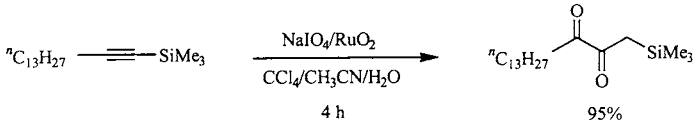
The osmium tetroxide-catalyzed dihydroxylation of *cis*-vinylsilanes followed by Swern oxidation leads to α-ketoacylsilanes, **39**, an unusual α-silyl ketone system. Oxidation with chromium trioxide and pyridine gives only the aldehyde with desilylation.[80] Sodium borohydride reduction occurs selectively at the acylsilane carbonyl.



Ethynylsilanes can be hydrosilated with trichlorosilane to give the β-trichlorosilylvinylsilane, **40**, which can be fluorinated and oxidized to provide trimethylsilylmethyl ketones in good yields.[81]



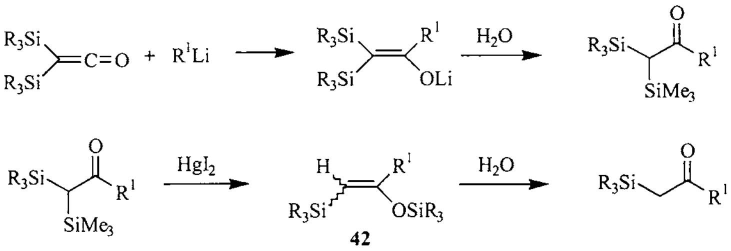
A mild oxidation of acetylenes to 1,2-diketones was reported. This was used to prepare the α-silyl ketone **41**.[82]



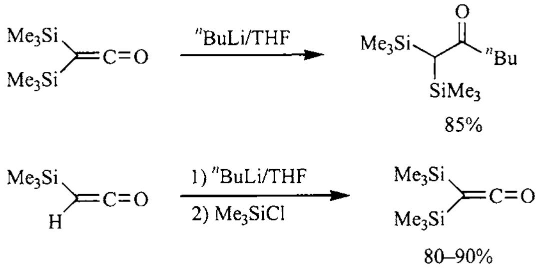
41

4.4. Synthesis of α-Silyl Ketones from Silyl Ketenes

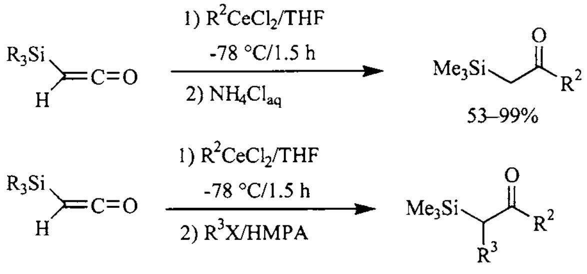
Bis(trimethylsilyl)ketene reacts with *n*-butyllithium or methyllithium to give bis(trimethylsilylmethyl)ketones in moderate yields. These were rearranged to the silyl enol ethers, **42**, under the influence of mercuric iodide.[83]

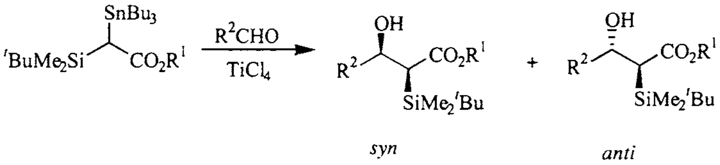


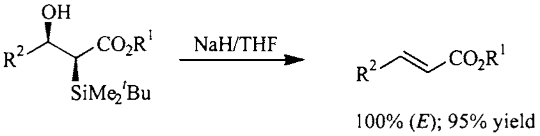
Bis(trimethylsilyl)ketene was shown to react with butyllithium in the normal fashion, whereas trimethylsilylketene is deprotonated.[84]

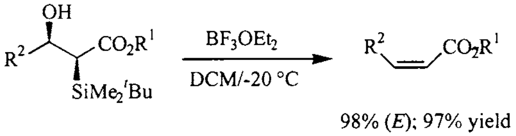


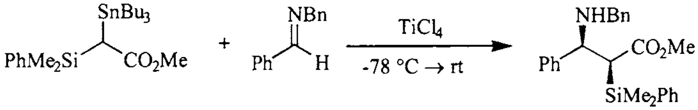
Silyl ketenes were shown to react with alkyldichlorocerium reagents to give α-silyl ketones in good yields.[85] If the intermediate is reacted with an alkyl halide in the presence of HMPA rather than simply protonated, the substituted α-silyl ketone is isolated. This work was expanded to include the electrophilic reaction of the α-stannyl-α-silyl esters with aldehydes and aldimines leading to (*E*)- or (*Z*)-α,β-unsaturated esters and α-silyl-β-amino ketones.[86] This latter conversion was used in the preparation of cyclic carbamates.

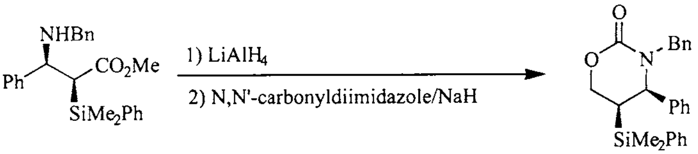




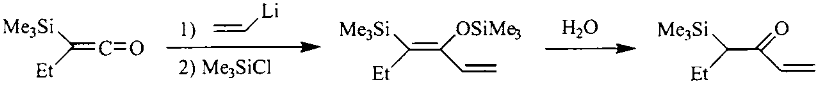




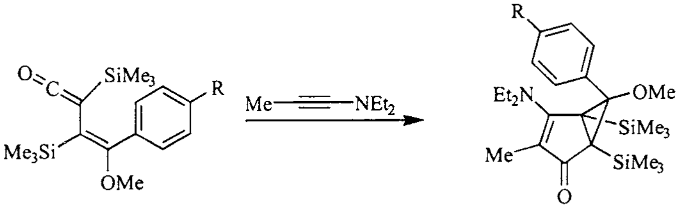




The enol silyl ethers of α-trimethylsilyl ketones were prepared directly from the reaction of lithium reagents with trimethylsilyl ketenes. The enol silyl ethers are hydrolyzable to the α-trimethylsilyl ketones.[87]



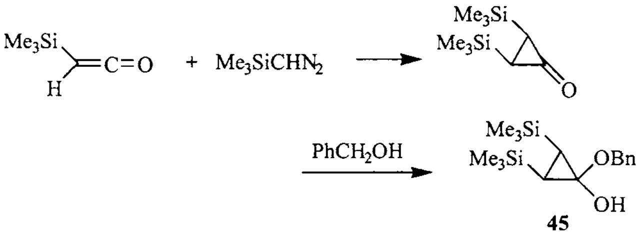
The silylated ketene **43** was reacted with 1-diethylaminopropyne to give α-silyl ketone **44** in addition to two other adducts.[88]



43

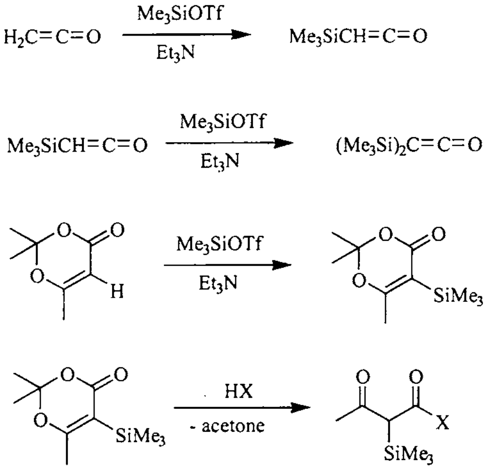
44

The reaction of trimethylsilyl ketene with trimethylsilyldiazomethane gives *cis*-2,3-bis(trimethylsilyl)cyclopropanone. Treatment of this with benzyl alcohol gives the benzyl hemiacetal **45**.[89]



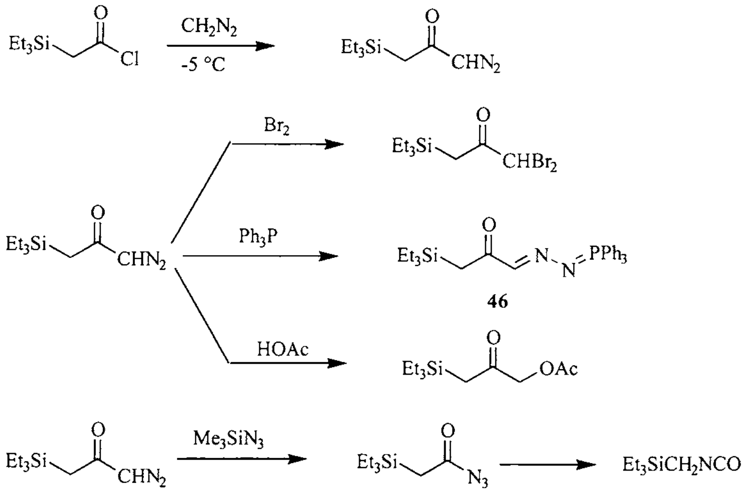
45

The reaction of ketene, trimethylsilylketene, and the acetone adduct of diketene with trimethylsilyl triflate in the presence of triethylamine provide the corresponding α-trimethylsilyl carbonyls.[90]



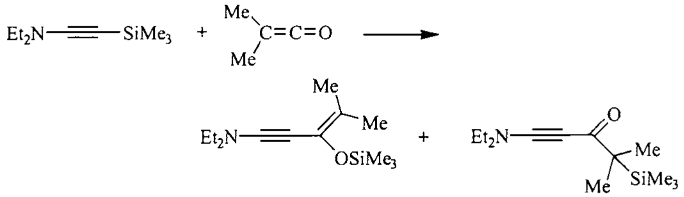
X = OMe, NMe$_2$, SPh

Triethylsilylacetyl chloride was reacted with diazomethane to give the diazomethyl ester, which was reacted with bromine to give dibromomethyltriethylsilylmethyl ketone, with triphenylphosphine to give adduct **46**, and with acetic acid to give the α-acetoxyketone. The reaction with trimethylsilyl azide gives the acyl azide, which rearranges to the acyl isocyanate. This was reacted with methanol to give the corresponding carbamate.[91]

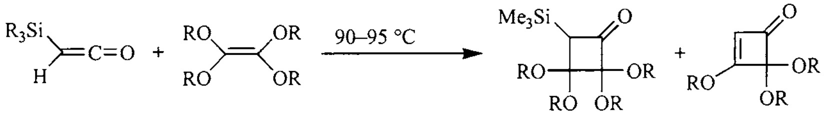


46

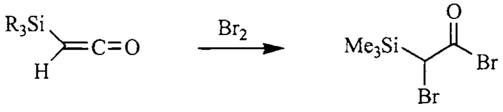
The reaction of trimethylsilyl ynamines with ketenes can provide both the silyl enol ether and the α-silyl ketone.[92]



Trimethylsilyl ketene reacts with tetraalkoxyethylenes to give 2-trimethylsilylcyclobutanones in addition to the product of elimination of trimethylalkoxysilane, namely the cyclobut-2-en-1-one.[93]



Trimethylsilylketene was reacted with bromine to give the α-trimethylsilyl-α-bromoacyl bromide, **47**, which upon treatment with triethylamine gives the trimethylsilylbromoketene.[94] The α-silyl acid bromide **47** was reacted with an imine to give the silylated β-lactam.



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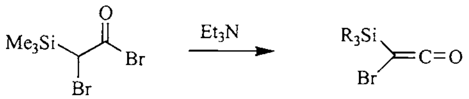

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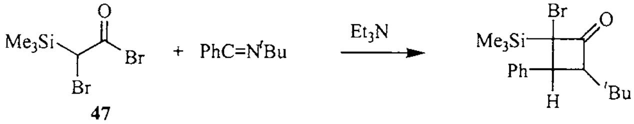
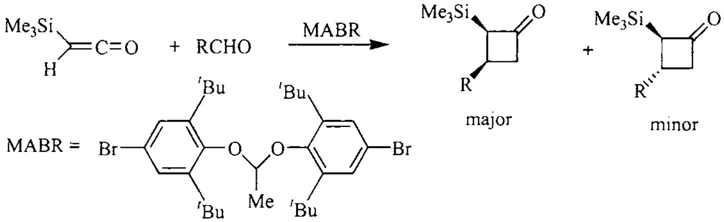
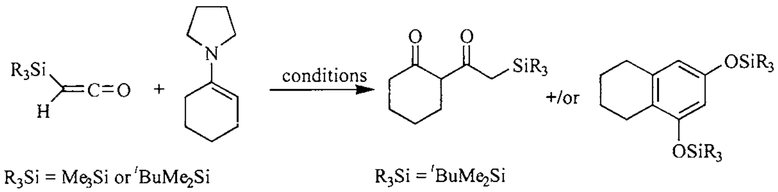


47

The reaction of trimethylsilylketene with aldehydes catalyzed by MABR leads to α-trimethylsilyl-β-lactones with the *cis*-diastereomer predominating, except in the case of pivaldehyde.[95]

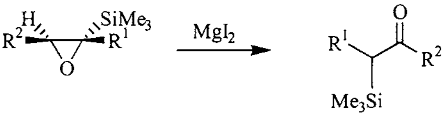


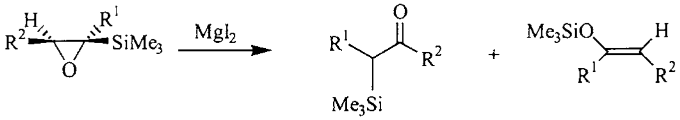
The reaction of trimethylsilyl (or *tert*-butyldimethylsilyl) ketene with imines provides α-trimethylsilyl (or *tert*-butyldimethylsilyl) ketones in addition to aromatics.[96]



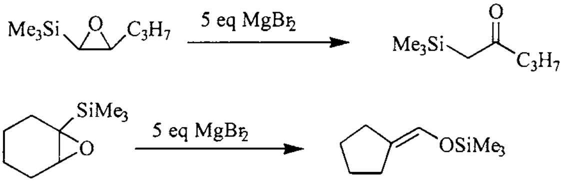
4.5. Synthesis of α-Silyl Ketones from Epoxysilanes

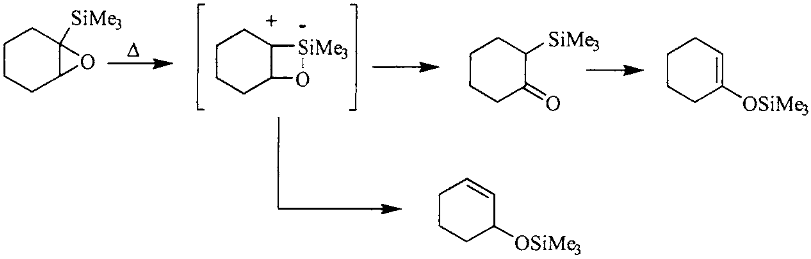
The magnesium iodide ring opening of trimethylsilyl oxiranes can lead to α-trimethylsilyl ketones when the stereochemistry of the oxirane is *E*.[97] The *Z*-isomers lead to the trimethylsilyl enol ethers. Both reaction pathways involve migration of a hydrogen.



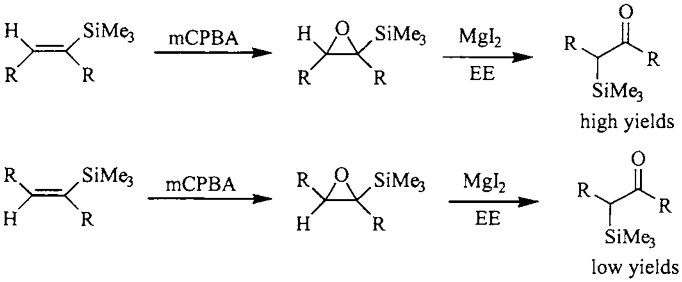


α,β-Epoxysilanes were shown by Hudrlik and co-workers to react with magnesium bromide to give β-ketosilanes and silyl enol ethers depending on the structure of the starting epoxide.[98] They argued for an α-silyl ketone in the thermolysis of epoxysilanes to enol silyl ethers and O-silylated allyl alcohols as well.[99]

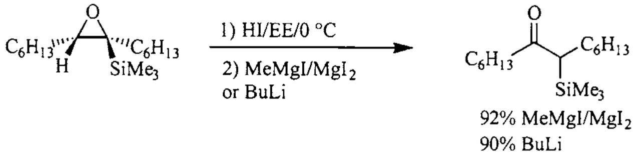


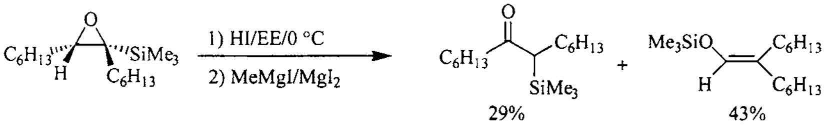


Utimoto and co-workers[100] reported the magnesium iodide promoted rearrangement of epoxysilanes obtained from (*E*)-vinylsilanes to give good yields of β-ketosilanes. The rearrangement of the epoxysilane obtained from (*Z*)-vinylsilanes, however, gave low yields of the ketosilane. (For a similar example see Section 3.3 and ref. 31.)



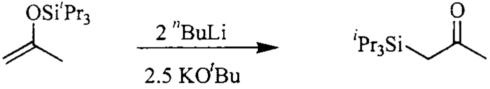
The magnesium bromide-catalyzed rearrangement of α-trimethylsilyl epoxides has been shown to give α-trimethylsilyl ketones. It was further shown that the iodohydrin resulting from the reaction of α-trimethylsilyl epoxides with hydroiodic acid reacts with a mixture of methylmagnesium iodide and magnesium iodide or with butyllithium to give α-trimethylsilyl ketones.[101,102] The original configuration of the epoxysilane and therefore the iodohydrin has an influence on the reaction.

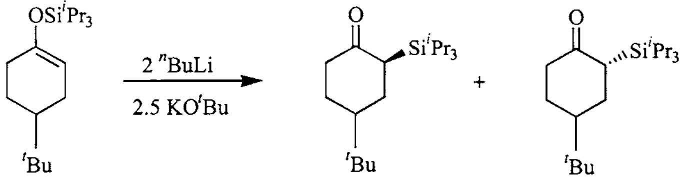


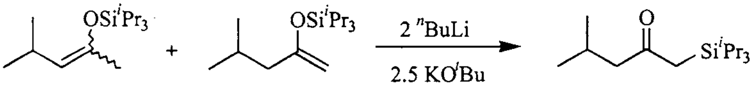


4.6. Synthesis of α-Silyl Ketones by Rearrangement Reactions

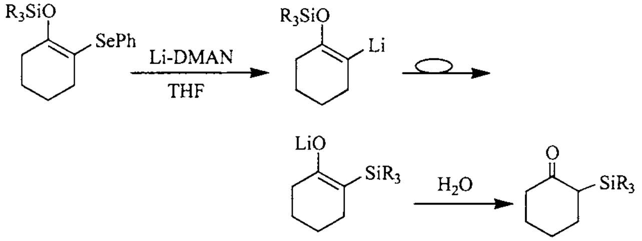
Corey and Ruecker[103] have shown that triisopropylsilyl enol ethers are rearranged to α-triisopropylsilyl ketones with a combination of butyllithium/potassium *tert*-butoxide. The least substituted α-silyl ketone is preferred. The diisopropylmethylsilyl group also rearranged in this manner, but the less hindered trimethylsilyl group did not.



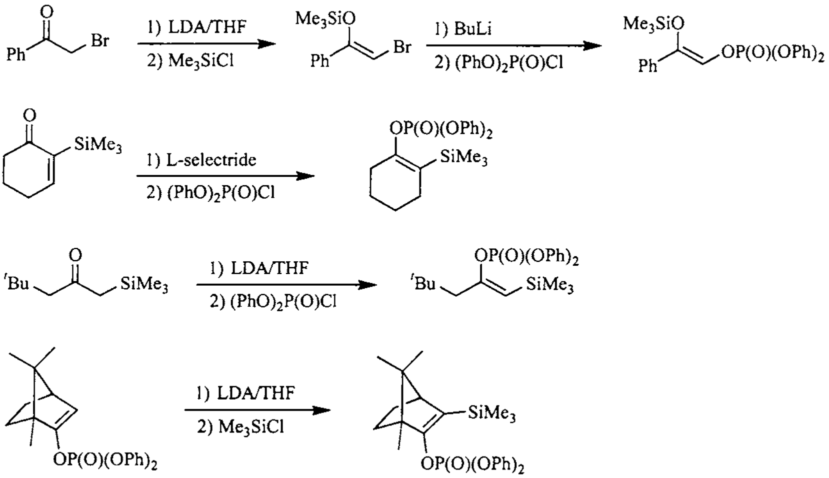




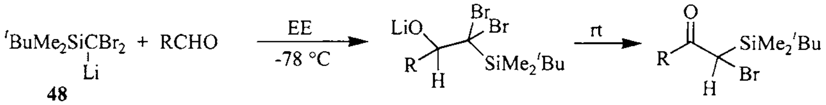
The trialkylsilyl enol ethers of α-phenylseleno ketones can be converted to their lithium reagents via metal–metal exchange.[104] The resulting β-siloxyvinyllithium reagent then undergoes a rearrangement to the lithium enolate of the α-silyl ketone. Wiemer and co-workers[61] employed a variation on the Brook rearrangement to prepare α-trimethylsilyl ketones.



Four approaches to vinyl silane phosphonates, the thermodynamic phosphonate ester of α-trimethylsilyl ketones, were worked out and reported by Wiemer and co-workers.[105] The first of these, building on the chemistry first developed by Kowalski,[63] involves the use of α-bromoketones. The second utilizes an α-trimethylsilyl-α,β-unsaturated ketone and conjugate hydride addition to generate the enolate of an α-trimethylsilyl ketone. The third approach simply deprotonates an α-trimethylsilyl ketone. This approach is limited by the relative steric situation on either side of the carbonyl group. The fourth approach starts with an enol phosphonate which is deprotonated and trimethylsilylated.



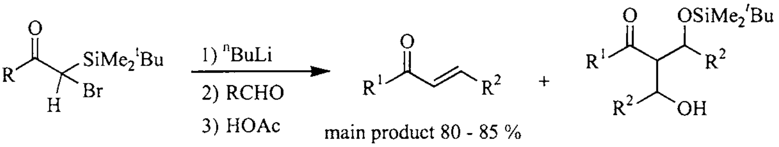
tert-Butyldimethylsilyldibromomethyllithium, (**48**) was reacted with aldehydes to generate initially the β-alkoxysilane, which undergoes rearrangement to the α-*tert*-butyldimethylsilyl-α-bromoketone, **49**, in moderate yields.[106] These interesting α-silyl ketones were converted to the regiospecifically generated lithium enolates and condensed with aldehydes to ultimately give enones in good yields. The reaction of the enolate with aldehydes also leads to bis-addition of the aldehyde, one equivalent to the lithium enolate and the second to the α-silyl ketone, which can react like a silyl enol ether. The yield of the bis-adduct increased with an increase in the amount of aldehyde added.



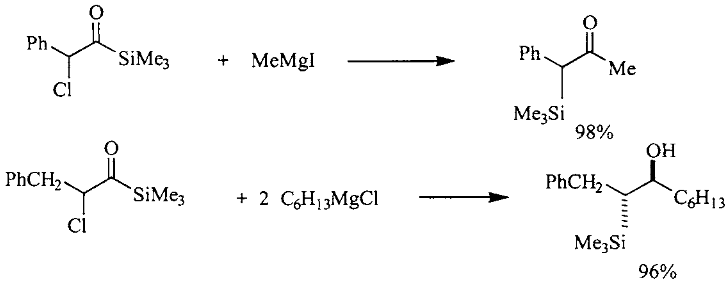
48

(R = Ph, PhCH=CH, $^nC_6H_{13}$, c-C_6H_{11}, $^tC_4H_9$; yields 42 - 76 %)

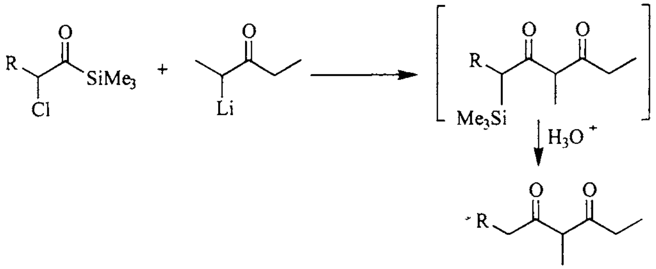
49



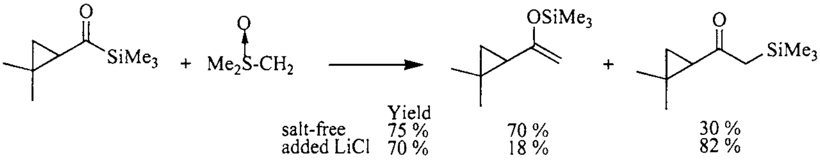
Treatment of α-chloroacyl trimethylsilanes with Grignard reagents gives α-trimethylsilyl ketones in good yields as a result of migration of the trimethylsilyl group.[107] Grignard reagents that contain β-hydrogens first give reduction with trimethylsilyl group migration and an intermediate α-silyl aldehyde, which then undergoes attack of a second Grignard reagent leading to a β-hydroxysilane. This sequence is marked by the Cram addition of the second equivalent of Grignard reagent to the α-silyl aldehyde as evidenced by the elimination of the β-hydroxysilane which with base leads to the *Z*-olefin via a *syn*-elimination and with acid leads via *anti*-elimination to the *E*-olefin.



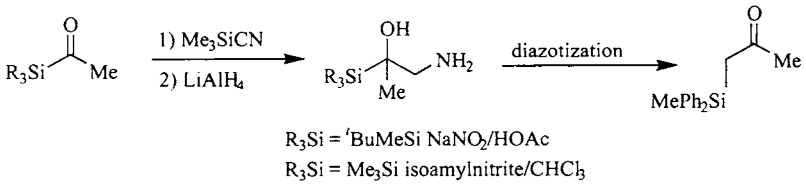
α-Chloroacylsilanes were shown to react with lithium ketone enolates to give, after protiodesilylation, substituted 1,3-diketones.[108]



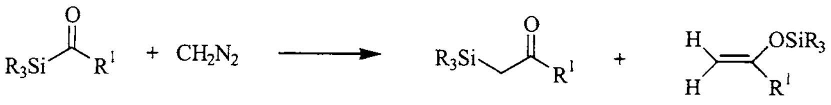
The reaction of acylsilanes with sulfur ylides in THF produces the enol silyl ethers and the β-ketosilanes.[109] The silyl enol ethers are favored under salt-free conditions and the β-ketosilanes in the presence of inorganic salts.



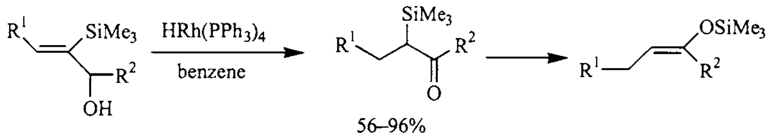
Cunico and Kuan[110] used a Tiffeneau–Demjanov reaction to prepare α-trimethylsilyl ketones from acyltrimethylsilanes. Thus, they reacted the acyltrimethylsilane with trimethylsilyl nitrile to provide the trimethylsilylated cyanohydrin, which was reduced to the β-aminoalcohol. The β-aminoalcohol was then subjected to diazotization to give the α-silyl ketone.

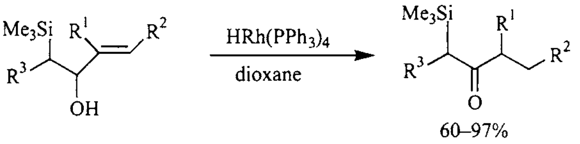


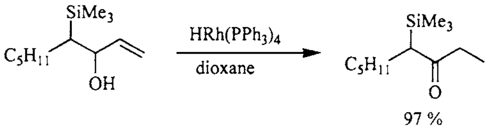
Brook and co-workers[111] showed that acylsilanes would react with diazomethane to insert a methylene group between the silicon and the acyl groups. A mixture of the α-silyl ketone and the silyl enol ether was obtained.



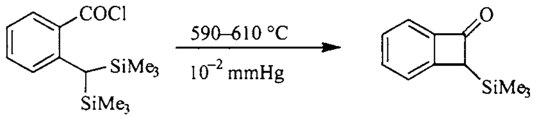
Sato and co-workers[112,113] have shown that the rhodium(I)-catalyzed isomerization of 2-trimethylsilyl-1-ene-3-ols leads to α-silyl ketones, which can then be thermally isomerized to silyl enol ethers. This reaction was extended to 4-trimethylsilyl-1-en-3-ols as well.[114] A full report of these rearrangement approaches to α-silyl ketones has been published.[115]



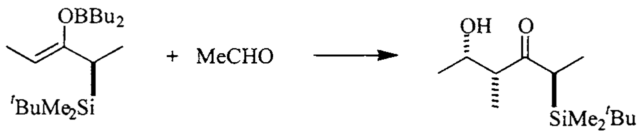




o-Trimethylsilylmethylbenzoyl chlorides were shown to give benzocyclobutanones upon thermolysis at low pressure.[116] When the benzyl position was substituted with two trimethylsilyl groups an α-trimethylsilylbenzocyclobutanone was obtained.

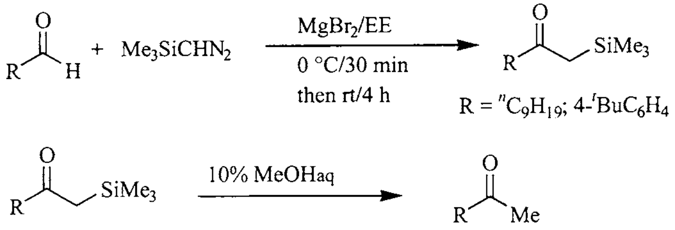


Condensation of the boron enolate **50** with acetaldehyde leads to the α-silyl-β-hydroxy ketone with excellent stereospecificity.[117]



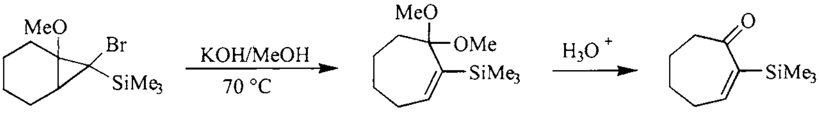
50

The reaction of trimethylsilyldiazomethane with aldehydes in the presence of magnesium bromide gives trimethylsilylmethyl ketones in good yields when worked up with water.[118] If the workup is carried out under acidic conditions protiodesilylation occurs to give the methyl ketone.



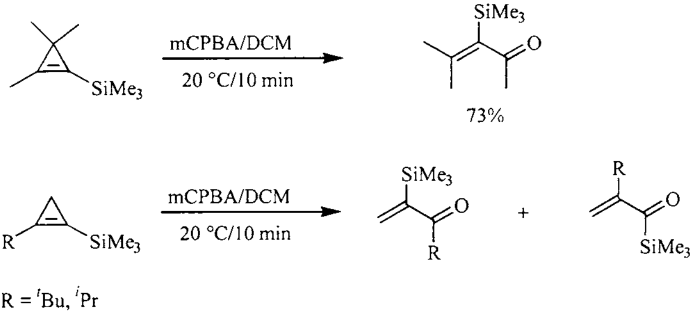
5. SYNTHESIS OF α-SILYL ENONES

Lithiation-trimethylsilylation of the 1,1-dibromocyclopropane provides the α-bromosilane **51**, which upon treatment with potassium carbonate in an alcohol and then acid, gives the α-silyl enone **52**.[19]

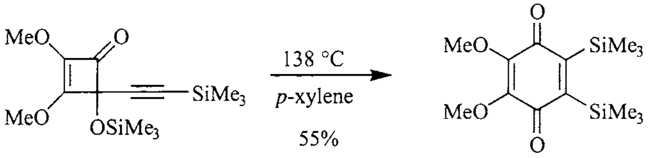


51 **52**

The *m*-chloroperbenzoic acid oxidation of 1-trimethylsilylcyclopropenes produces 2-trimethylsilylbuten-3-ones in good yields.[119]

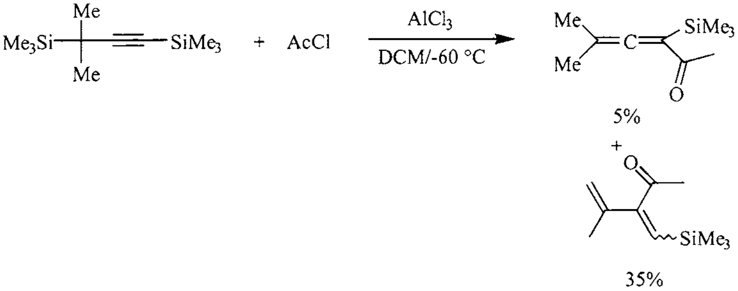


Thermolysis of the cyclobutenone **53** produces the trimethylsilyl-substituted quinone **54**.[120]

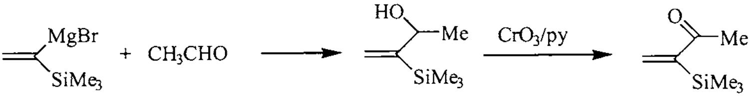


53 **54**

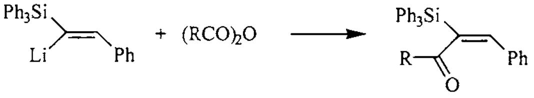
1,3-Bis(trimethylsilyl)propynes, when treated with acetyl chloride in the presence of aluminum chloride, yield α-trimethylsilylallenyl ketones.[121]



The synthesis of 3-(trimethylsilyl)-but-3-en-2-one, which has been shown to be an excellent Michael acceptor has been reported in *Organic Synthesis*.[122]

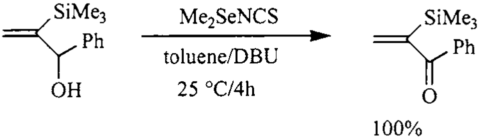


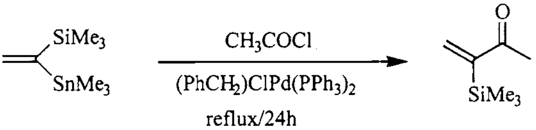
α-Silyl-α,β-unsaturated ketones can also be synthesized by the reaction of 1-silyl-1-lithio (or halomagnesio) ethylenes with acid anhydrides.[123] This reaction was first reported by Hauser and Hance.[44] 2-Trimethylsilylacrolein was synthesized and converted to 2-trimethylsilylbut-1-ene-3-one by treatment with methylmagnesium iodide and pyridinium chlorochromate.[20] This implies that the silylated acrolein could be an excellent precursor to a number of different α-silyl-α,β-unsaturated enones.



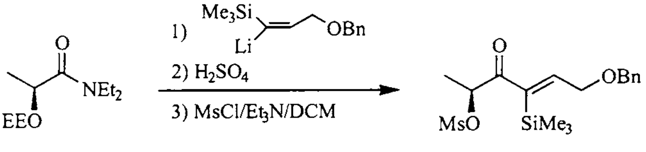
R = Me, Ph

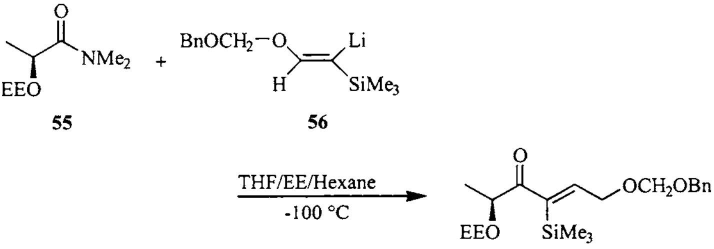
2-Trimethylsilyl allyl alcohols have been shown to be readily oxidized to the important 2-trimethylsilylbut-2-enones in very high yields.[124] 1-Trimethylsilylvinyltrimethyltin was cross-coupled with acetyl chloride to give 2-trimethylsilylbuten-3-one.[125]





α-Lithiovinylsilanes have been reacted with amides to give α-silyl-α,β-unsaturated ketones.[126] The vinylsilyl group can be useful in directing the stereochemistry of the reduction of the keto functionality. Reaction of *Z*-isomeric α-lithiovinylsilane **55** with amide **56** gave the α-trimethylsilyl enone **57**.[127] The reaction of α-trimethylsilylvinyl-

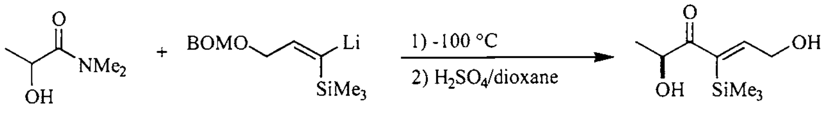




55 **56**

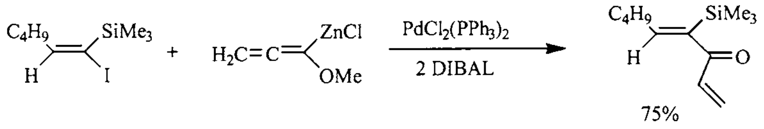
57

lithium reagent **58** with the hydroxyamide **59** was shown to give the α-trimethylsilylenone **60**.[128]

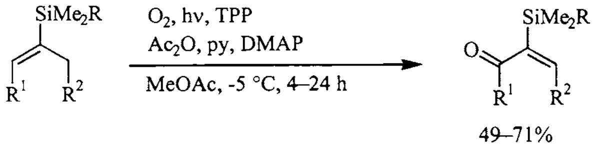


58 **59** **60**

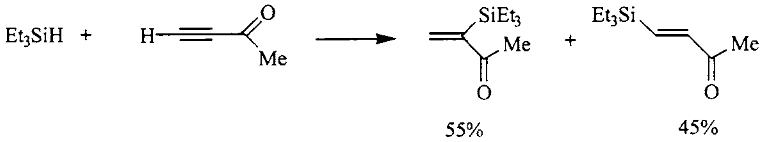
The palladium-catalyzed cross-coupling of α-alkoxyorganozinc reagents with α-trimethylsilylvinyl iodides provides α-trimethylsilyl-α,β-unsaturated ketones in good yields.[129]



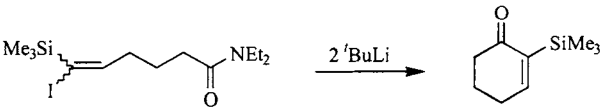
A one-pot synthesis of α-silyl enones via the photooxygenation of vinylsilanes was reported. The yields are moderate to good.[130]



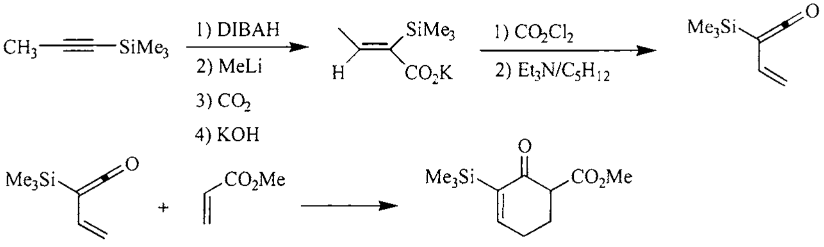
The hydrosilation of methylethynyl ketone with triethylsilane and chloroplatinic acid gives a 55:45 mixture of the α-triethylsilyl- to β-triethylsilyl-α,β-unsaturated ketone.[131]



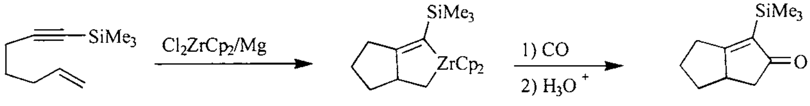
Negishi and co-workers[132] have demonstrated that α-iodovinylsilanes of a suitable structure for cyclizations can lead to α-silyl-α,β-unsaturated ketones upon metal–halogen exchange cyclization.



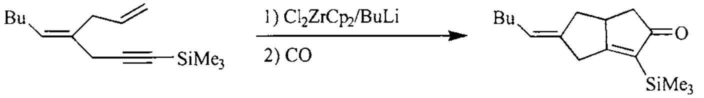
α-Trimethylsilyl vinyl ketene was prepared starting from 1-trimethylsilylpropyne as outlined below. This ketene was cycloadded to electron deficient olefins to give α-trimethylsilylcyclohexenones.[133]



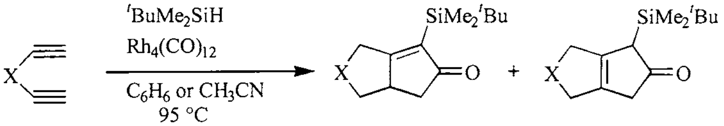
The cyclization of 6-enylethynylsilanes with a zirconium catalyst followed by carbonylation results in α-silyl-α,β-unsaturated cyclopentenones.[134,135]



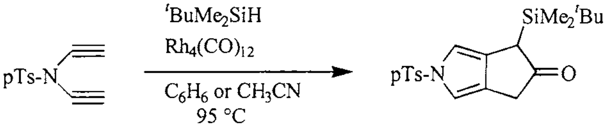
14 examples 55–65%



The reaction of 1,6-diynes with *tert*-butyldimethylsilane in the presence of a rhodium catalyst provides cyclic α-silyl cyclopentenones and cyclopentanones.[136]

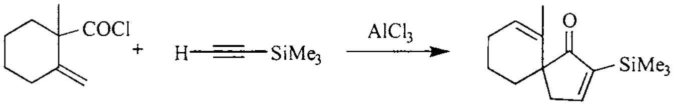


X		
CH$_2$	60	0
C(CO$_2$Me)$_2$	14	0
NBn	8	31
O	35	0
CH$_2$CH$_2$	0	0

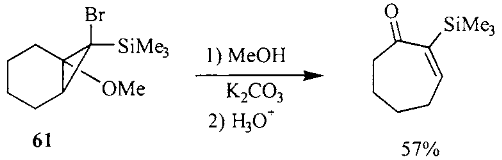


72%

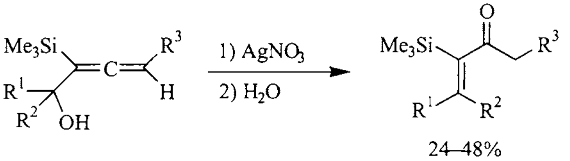
β,γ-Unsaturated acyl chlorides were reacted with trimethylsilylacetylene to give α-trimethylsilyl-α,β-unsaturated ketones as the predominant products.[137]



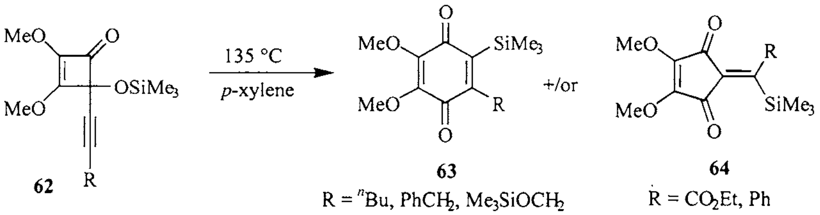
The 1-trimethylsilyl-1-bromo-2-methoxycyclopropane **61** when treated with alkaline methanol and then acidified gives the 2-trimethylsilylcycloheptenone in good yield.[138]



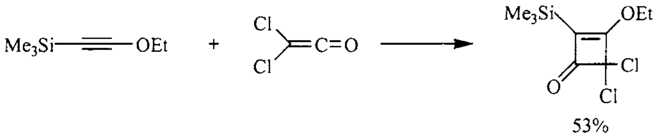
α-Trimethylsilyl-α-allenic alcohols can be isomerized to α-trimethylsilyl-α,β-unsaturated ketones with silver nitrate in moderate yields.[139]



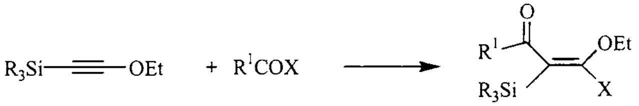
The acetylenic trimethylsiloxycyclobutenones **62** can be thermolyzed to the trimethylsilylated quinone **63**.[140] When the R group of the ethynyl substituent is electron withdrawing such as a carboethoxy group or a phenyl group the alkylidene cyclopentanedione **64** is formed.



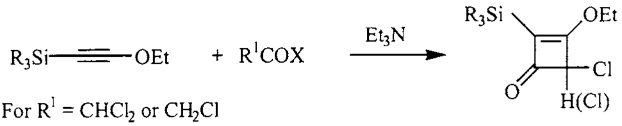
Trimethylsilylethoxyacetylene was reacted with dichloroketene to give the cycloadduct, which is the ethyl enol of the α-silylcyclobutanedione.[141]



Trialkylsilylethoxyacetylenes were reacted with acyl chlorides or trifluoroacetic anhydride to give α-silyl-α,β-unsaturated ketones.[142]

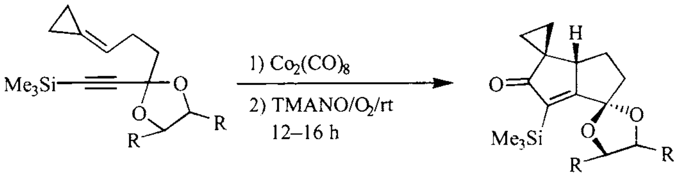


R = Me, Et; $R^1 = CCl_3, CHCl_2, CH_2Cl, CF_3$; X = Cl, O_2CCF_3



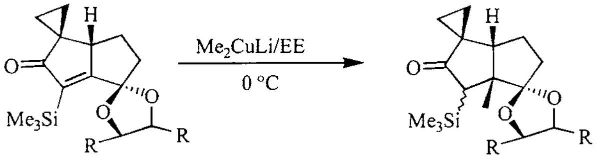
For $R^1 = CHCl_2$ or CH_2Cl

The dicobalt octacarbonyl-catalyzed carbonylation of **65** provided the α-trimethylsilyl enones **66**.[143] These α-silyl enones were reacted with lithium dimethylcuprate and then protiodesilylated with double bond migration.



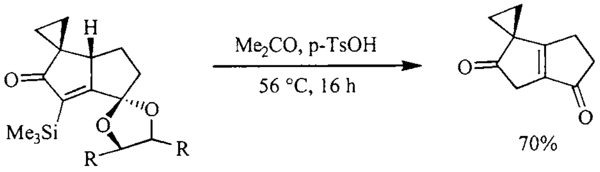
65

66



66

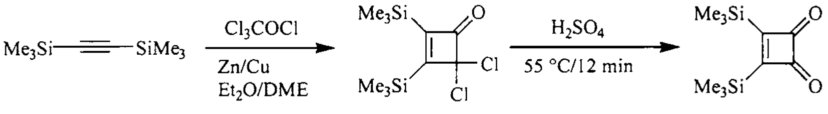
86%

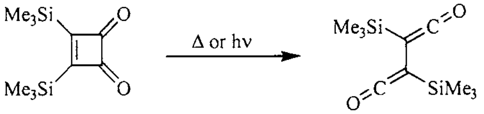


66

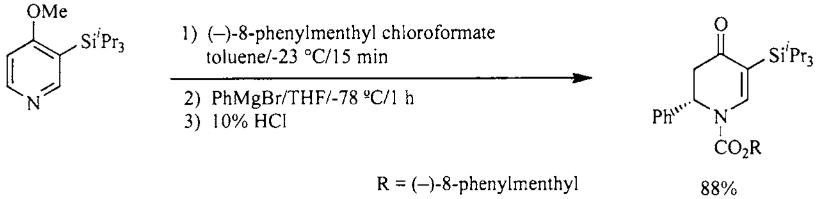
70%

Zhao and Tidwell[144] were able to prepare a stable bis-ketene via a route that proceeds through the intermediacy of a bis trimethylsilyl cyclobuten-1,2-dione.

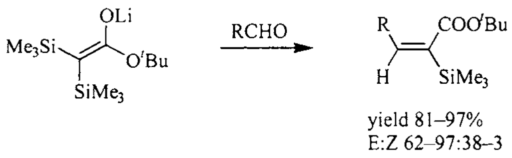


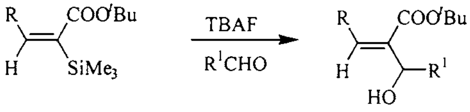


An asymmetric synthesis of dihydropyridones, which are also α-silyl-α,β-unsaturated ketones, was reported.[145]



Deprotonation of *tert*-butyl α,α-bis(trimethylsilyl)acetate followed by condensation with and aldehyde results in the formation of the α-trimethylsilyl-α,β-unsaturated ester in high yield and with high *E* stereoselectivity. These α-trimethylsilyl-α,β-unsaturated esters can be condensed directly with aldehydes under the influence of fluoride ion.





6. SYNTHESIS OF α-SILYL CARBOXYLIC ACIDS

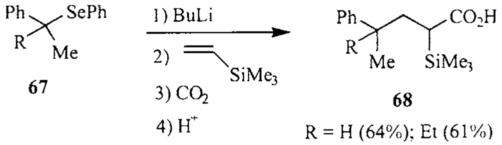
6.1. α-Silyl Carboxylic Acids from α-Silyl Organometallic Reagents

Sommer and co-workers[147] were the first to report the synthesis of trimethylsilylacetic acid, which they prepared by the simple reaction of trimethylsilylmethylmagnesium chloride with carbon dioxide. Other silylacetic acids were prepared in the same general fashion. All were found to be less acidic than pivalic acid as a result of the greater +I effect of the silylmethyl group.

$$\mathrm{RMe_2SiCH_2MgCl} + \mathrm{CO_2} \longrightarrow \mathrm{RMe_2SiCH_2CO_2H}$$

$(\mathrm{R} = \mathrm{Me}, \mathrm{Me_3SiO}, \mathrm{Ph})$

The selenide **67** was converted to the lithium reagent, which was in turn added to vinyltrimethylsilane, resulting in an α-trimethylsilyllithium reagent which was carboxylated to give the α-trimethylsilyl acid **68**.[148]

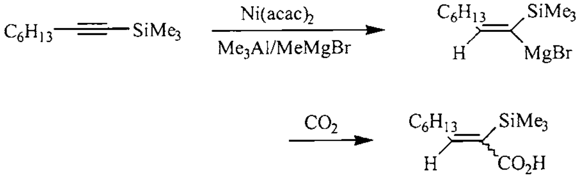


67

68

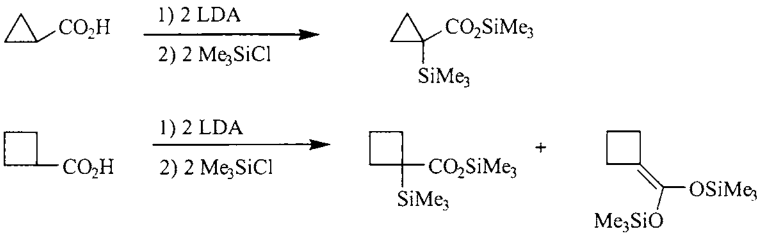
R = H (64%); Et (61%)

The nickel-catalyzed addition of Grignard reagents to ethynylsilanes gives the α-bromomagnesiovinylsilane, which can be reacted with carbon dioxide to give an α-silyl-α,β-unsaturated acid.[149]

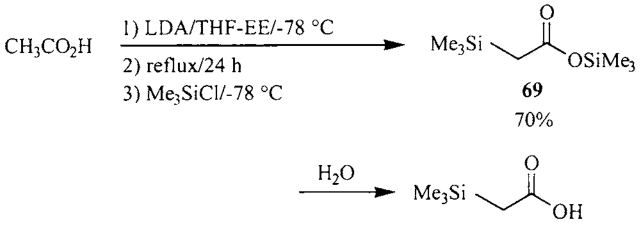


6.2. α-Silyl Carboxylic Acids from Lithiated Carboxylic Acids

Cyclopropane carboxylic acid reacts with two equivalents of lithium diisopropyl amide and the dianion trimethylsilylates to give the α-trimethylsilyl acid as its trimethylsilyl ester in high yield.[150,151] The cyclobutyl homolog, however, gives a mixture of the C-silylated and O-silylated products.



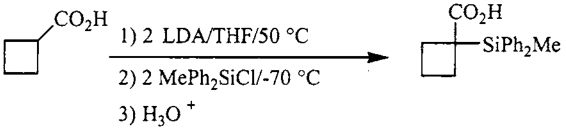
It was found that reaction of the dianion of acetic acid with trimethylchlorosilane gives a mixture of trimethylsilyl trimethylsilylacetate, the α-trimethylsilyl ester of the trimethylsilyl ester of acetic acid, and bis(trimethylsilyl)ketene acetal. However, if the enolate is formed in a mixture of ether and THF and refluxed for 24 h prior to quenching with trimethylchlorosilane a 70% yield of the α-silyl ester is achieved.[152] Hydrolysis of the silyl ester **69** provides trimethylsilylacetic acid. Bellassoued and Gaudemar[153] have shown, however, that the deprotonation–trimethylsilylation of trimethylsilylacetate gives exclusively the C-trimethylsilylated product when the lithium enolate is allowed to stand at –70 °C overnight prior to the trimethylchlorosilane quench. Alternatively, if the enolate is immediately quenched at –20 °C the O-trimethylsilylated ketene acetal is obtained in moderate yield. Employment of the sodium enolate gives the O-silylated derivative exclusively.

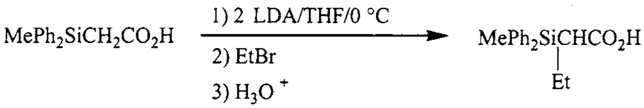


69
70%

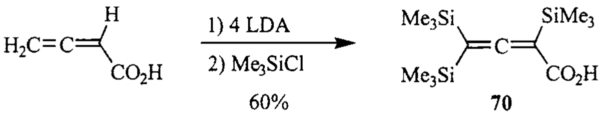
The dianions of several carboxylic acids were treated with methyldiphenylchlorosilane to give the α-silyl carboxylic acid after hydrolysis.[154] The α-silyl acids could be alkylated via their dianions as well.

$$CH_3CO_2H \xrightarrow[\substack{\text{2) 2 } MePh_2SiCl\text{/-70 °C} \\ \text{3) } H_3O^+}]{\text{1) 2 LDA/THF/50 °C}} MePh_2SiCH_2CO_2H$$

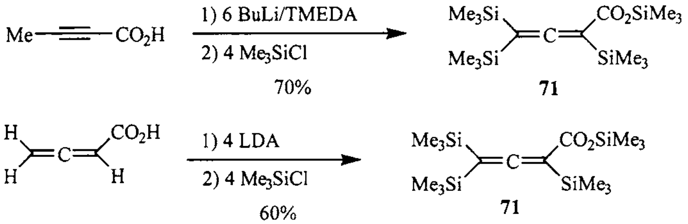




The reaction of either allenic or propargylic acid with four equivalents of LDA followed with trimethylsilylation provides the trimethylsilylated allenic acid **70** in moderate yield.[155]

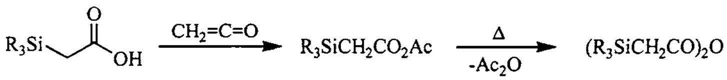


The polylithiation of 2-butynoic acid followed by trimethylsilylation leads to **71** in good yield. This same product can be obtained by a similar sequence on 2,3-butadienoic acid.[156]



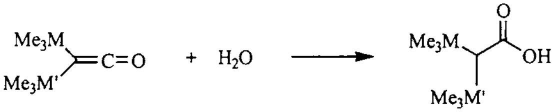
6.3. Miscellaneous Syntheses of α-Silyl Carboxylic Acids

Trialkylsilylacetic acids were reacted with ketene to give the mixed anhydride, which upon thermolysis gives trialkylsilylacetic anhydride.[157] This reacts with thionyl chloride to give the acid chloride and with trimethylsilylmethylmagnesium chloride to give trimethylsilylacetic acid anhydride.



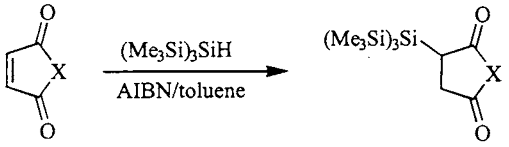
$R_3Si = MeEt_2Si, MePr_2Si$

Bis(trimethylsilyl)ketene and trimethylsilyltrimethylgermylketene react with water to give the corresponding α,α-dimetalated acetic acid.[158]



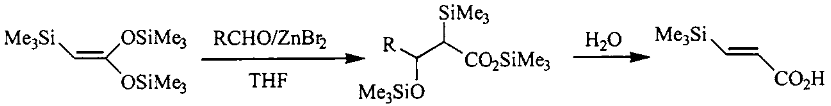
M = M' = Si or Ge; M = Si, M' = Ge

It was shown that although the hydrosilylation of methyl acrylate or methyl crotonate with tris(trimethylsilyl)silane occurs to give primarily the β-silyl product, tris(trimethylsilyl)silane was shown to hydrosilylate maleic anhydride and *N*-methylmaleimide under free radical conditions to give the α-silyl carbonyl system in good yields.[159]



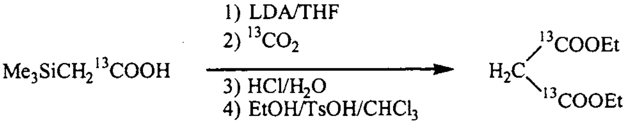
X = O, 89%; NMe, 83%

The bis(trimethylsilyl)ketene acetal of trimethylsilylacetic acid, prepared in 91% yield by deprotonation–trimethylsilylation of trimethylsilyl trimethylsilylacetate, reacts with aldehydes to give β-trimethylsiloxy-α-trimethylsilyl carboxylates, which are hydrolyzed to α,β-unsaturated acids.[160]

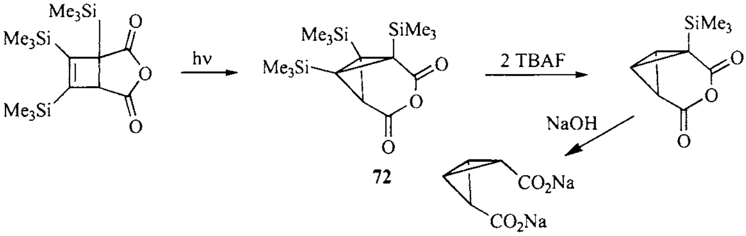


52–97%

The deprotonation–carboxylation of [1-^{13}C]trimethylsilylacetic acid was used to prepare [1,3-$^{13}C_2$]malonic acid diethyl ester.[161]



Photolysis of the trisilylated cyclobutenedicarboxylic acid anhydride gives the silylated bicyclobutane derivative **72**.[162] Interestingly, treatment of this material with tetrabutylammonium fluoride serves to remove the two trimethylsilyl groups that are β to the carbonyl groups. Basic hydrolysis both opens the anhydride and removes the α-trimethylsilyl group.



72

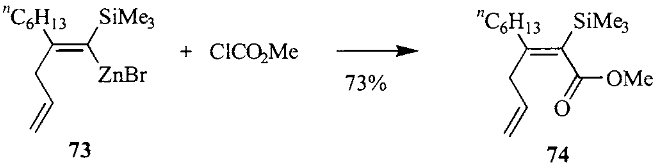
7. SYNTHESIS OF α-SILYL ESTERS

7.1. Synthesis of α-Silyl Esters from α-Silyl Organometallic Reagents

Reaction of trimethylsilylmethylmagnesium chloride with ethyl chloroformate gives ethyl trimethylsilylacetate.[163] They also reported on the acid and base sensitivity of this ester as well as its reaction with bromine to give trimethylbromosilane and ethyl bromoacetate.

$$Me_3SiCH_2MgCl + ClCO_2Et \longrightarrow Me_3SiCH_2CO_2Et$$

Reaction of the α-trimethylsilylzinc reagent **73** with methyl chloroacetate gives the α-silyl ester **74** in good yield and with moderate stereoselectivity.[164]

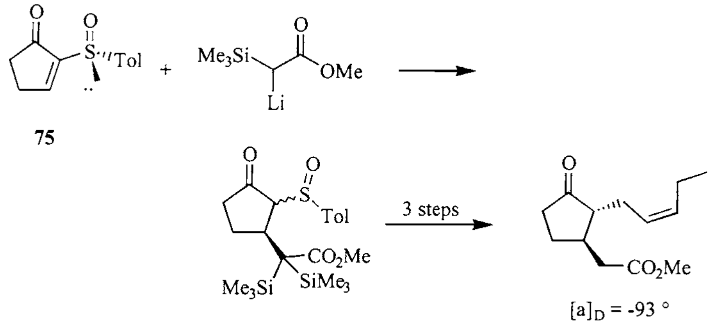


73

74

7.2. Synthesis of α-Silyl Esters from Ester Enolates

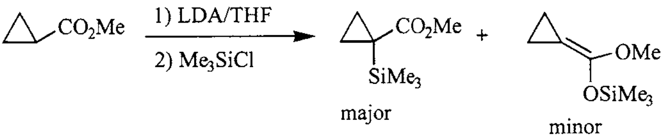
Employing the optically active sulfoxide **75** and methyl lithio(trimethylsilyl)acetate, Posner and Asirvatham[165] prepared (–)-methyl jasmonate with the highest optical rotation yet reported.



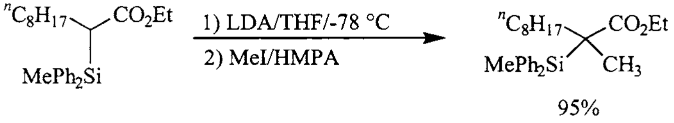
As part of a study showing the benefits of activating zinc with trimethylchlorosilane in the Reformatsky reaction it was found that ethyl bromoacetate reacts with trimethylchlorosilane-activated zinc and then with trimethylchlorosilane to give ethyl trimethylsilylacetate in good yield.[166] Hance and Hauser[167] reported the preparation of the sodium enolate of ethyl isobutyrate and its reaction with trimethylchlorosilane to give ethyl trimethylsilylisobutyrate, but it is likely that the O-silylated material was isolated instead.

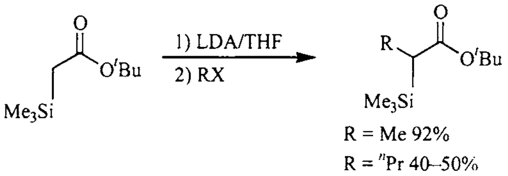
$$BrCH_2CO_2Et \xrightarrow[\text{2) } Me_3SiCl]{\text{1) } Zn/Me_3SiCl(act)} Me_3SiCH_2CO_2Et$$

Ainsworth and co-workers[168] found that the lithium enolate of methyl cyclopropane carboxylate was both C- and O-trimethylsilylated with the C-silylated product predominating.

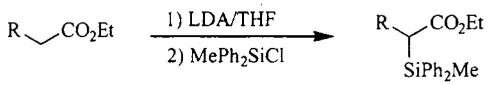


The alkylation of α-(methyldiphenylsilyl)esters with methyl iodide and allyl bromide was shown.[6] Helmchen and Schmierer[169] used the alkylation of *tert*-butyl trimethylsilylacetate in the chain extension of esters. Hudrlik and co-workers[170] showed that the alkylation of *tert*-butyl trimethylsilylacetate leads to substituted α-silyl esters.

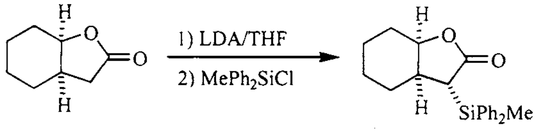




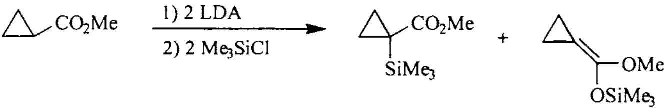
Larson and Fuentes[171] reported that the direct C-silylation of the lithium enolates of esters with methyldiphenylchlorosilane is possible. For example, trimethylsilylation of the lithium enolate of ethyl acetate gives predominantly the O-silylated ketene acetal, quenching of the enolate with dimethylphenylchlorosilane gives a 50:50 mixture of the C- and the O-silylated products and quenching with methyldiphenylchlorosilane gives exclusively the C-silylated product. This C-diphenylmethylsilylation is also possible with α-substituted acetates, but not with α,α-disubstituted acetates. The reaction was shown to occur with inversion of configuration at silicon and to also occur with lactones.[6]



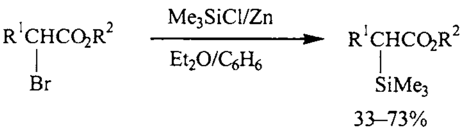
$$(R)\text{-1-NpPhMeSi*Cl} + \text{LiCH}_2\text{CO}_2\text{Et} \xrightarrow[\text{inversion}]{\text{THF}} (S)\text{-1-NpPhMeSi*CH}_2\text{CO}_2\text{Et}$$



The lithium enolate of methyl cyclopropylcarboxylate is trimethylsilylated primarily at carbon.[172]



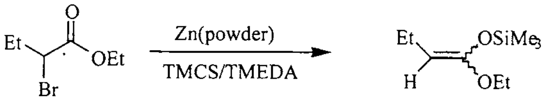
Fessenden and Fessenden[173] showed that under Reformatsky-type conditions α-bromo esters could be C-silylated.



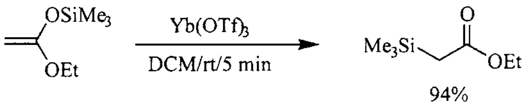
$$\underset{\text{Br}}{\text{R}^1\text{CHCO}_2\text{R}^2} \xrightarrow[\text{Et}_2\text{O/C}_6\text{H}_6]{\text{Me}_3\text{SiCl/Zn}} \underset{\text{SiMe}_3}{\text{R}^1\text{CHCO}_2\text{R}^2}$$

33–73%

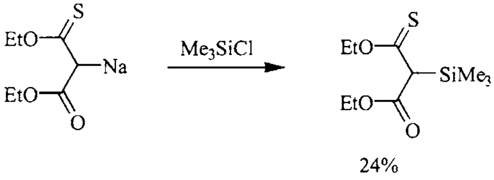
The reaction of several α-bromo esters with a zinc–copper couple and trimethylchlorosilane in the presence of TMEDA was studied and the results were the formation of the silyl ketene acetals, except in the case of ethyl bromoacetate which gave a small amount of the α-silyl ester.[174] This is in contrast to the reaction in the absence of TMEDA in which the α-silyl esters are observed.



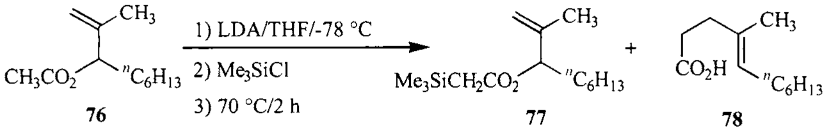
The O- to C-migration of the trimethylsilyl group of trimethylsilyl ketene acetals can be brought about with a catalytic amount of lanthanoid trifluorosulfonates.[175]



The sodium enolate of the monothiomalonic ester was reacted with trimethylchlorosilane to give the light sensitive C-trimethylsilylated ester.[176]

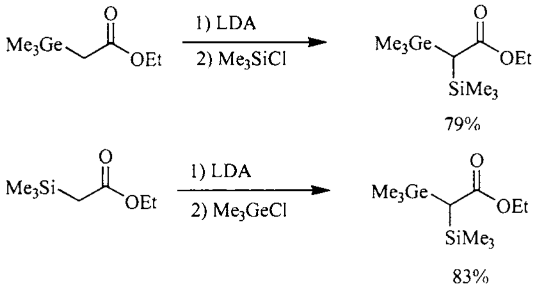


Katzenellenbogen and Christy[177] reported the C-trimethylsilylation of the lithium enolate of **76** to give **77** along with the Claisen rearrangement product **78**. When the sequence shown below was carried out the Claisen product was obtained in 80% yield.

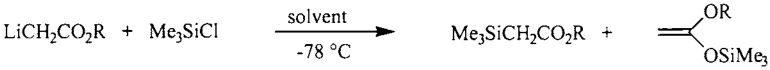


76 **77** **78**

Deprotonation-trimethylsilylation of *tert*-butyl trimethylgermylacetate gives the α-germyl-α-silyl ester as does the reverse sequence of germylation of *tert*-butyl trimethylsilylacetate.[178]

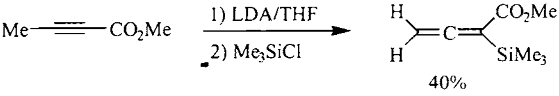


Rathke and Sullivan[179] reported the lithium enolates of various acetates to give the C-silylated acetate. The bulkier the alcohol group of the ester the greater the amount of C-silylation, presumably due to steric reasons. Also the use of HMPA as a cosolvent with THF leads to more C-silylation.

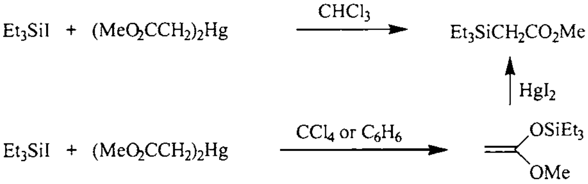


R	Solvent	Yield (%)	
Me	THF	35	65
Me	THF/HMPA	40	60
Et	THF	40	60
Et	THF/HMPA	90	10
^{t}Bu	THF	98	2
^{t}Bu	THF/HMPA	99	<1

The deprotonation–trimethylsilylation of methyl prop-1-ynoate produces methyl 2-trimethylsilylallenoate in moderate yield.[180]

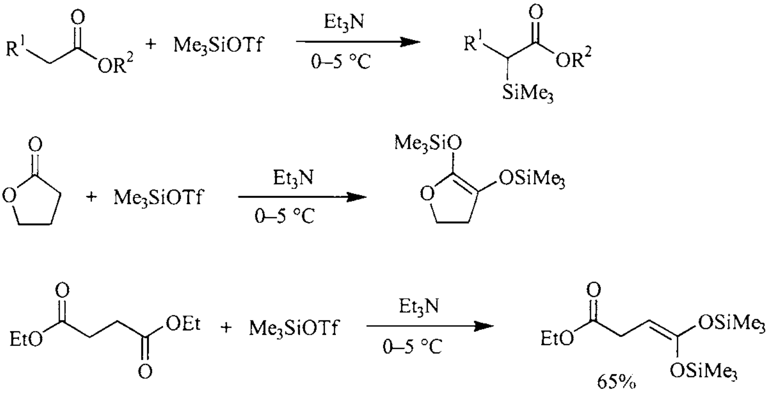


Triethylsilyl iodide was shown to react with bis(carbomethoxymethyl)mercury to give methyl triethylsilylacetate.[181] This reaction was shown to be solvent-dependent giving the C-silylated material in chloroform and the O-silylated product in benzene or carbon tetrachloride. The O-silylated ketene acetal can be isomerized to the silylacetate with mercuric iodide.

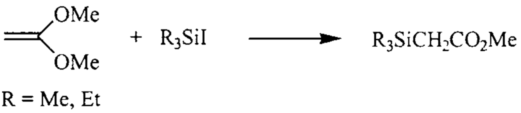


7.3. Synthesis of α-Silyl Esters via Direct Silylation

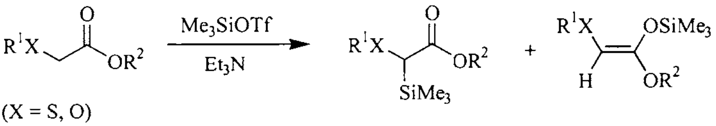
Simchen and Emde[182] showed that the reaction of esters and certain lactones with trimethylsilyl triflate and triethylamine gives the α-trimethylsilyl ester or lactone. O-silylation is sometimes seen, however.



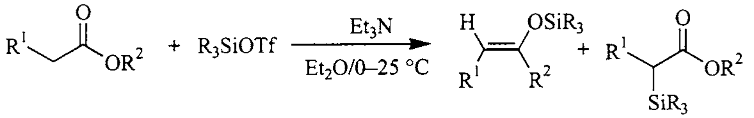
The reaction of dialkyl ketene acetals with trialkylsilyl iodides gives α-silyl acetates in nearly quantitative yields.[183]



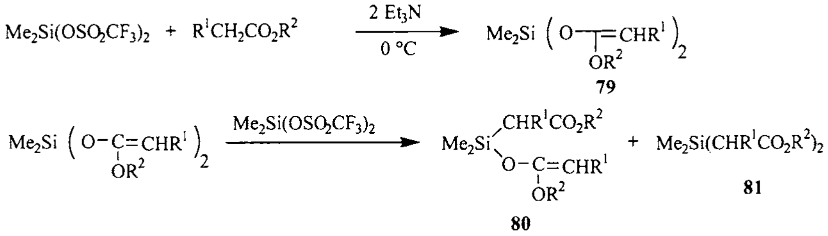
The reaction of trimethylsilyl triflate with esters and thioesters in the presence of triethylamine was shown to give a mixture of C- and O-silylated products depending on the structure of the ester.[184]



The reaction of trimethylsilyl triflate with esters was shown to lead to either the silyl ketene acetal or the α-silyl ester depending on the conditions of the reaction and the structure of the ester.[185] The equilibration of the silyl ketene acetal/α-silyl ester mixture with trimethylsilyl triflate was demonstrated. The more rapid hydrolysis of the silyl ketene acetal allows for the isolation of the pure α-silyl esters.

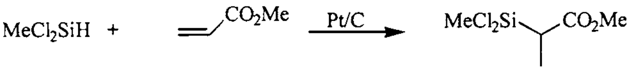


The reaction of dimethylsilylditriflate with esters in the presence of triethylamine provides the ketene acetal **79**, which in the presence of excess silyl triflate isomerizes to the mixture of **80** and **81**.[186]

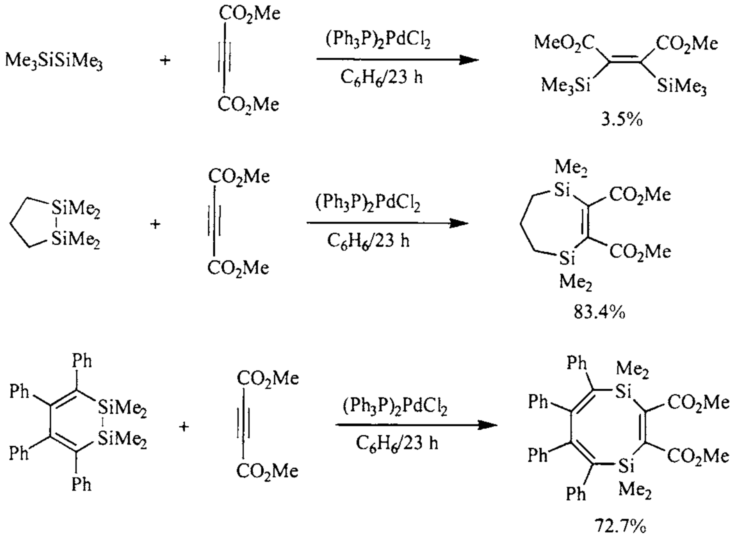


7.4. Synthesis of α-Silyl Esters via Hydrosilation

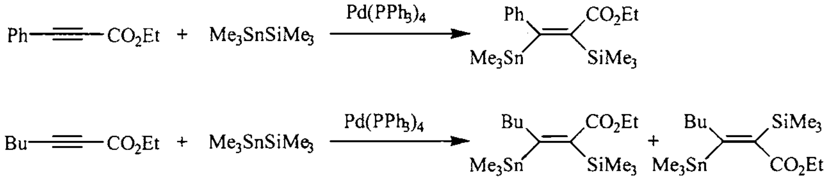
The hydrosilation of α,β-unsaturated esters with different silanes and various catalysts was shown to give mixtures of the α- and the β-silyl esters.[187] The hydrosilation of methyl acrylate with methyldichlorosilane catalyzed by platinum on charcoal gives the α-silyl ester.[188] This same reaction was also reported to give a mixture of the α- and the β-silyl derivatives.[189] Sommer and co-workers[190] also reported this reaction to occur to place the silyl group at the α-position. A similar study was carried out by Ojima and Kumagi[191] who also looked into the hydrosilation of α,β-unsaturated nitriles.



Disilanes, especially those of strained cyclic structure, were shown to add to dimethylacetylene dicarboxylate under the influence of palladium(II) catalysts.[192] Hexamethyldisilane reacts only poorly.



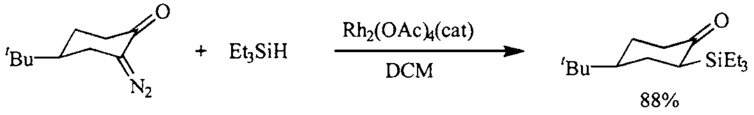
(Trimethylstannyl)trimethylsilane was shown to add to ynoates to place the trimethylsilyl group on the α-carbon to the ester group.[193] The addition is not stereospecific.



Doyle and co-workers[194] prepared α-silyl ketones and esters by the rhodium-catalyzed reaction of α-diazo ketones and esters with silanes. The carbene insertion mechanism accounts for the retention of configuration at silicon in the reaction. Rijkens and co-workers[196] first showed the reaction of ethyl diazoacetate with triethylsilane to give ethyl triethylsilylacetate in 40% yield.

$$Et_3SiH + N_2CHCOR \xrightarrow[DCM]{Rh_2(OAc)_4} Et_3SiCH_2COR$$

$R = OEt, Ph, PhCH_2, C_7H_{15}, {}^tBu$



$$\text{(S)-(+)-1-NpPhMeSiH} + N_2CHCO_2Et \xrightarrow[\text{DCM}]{Rh_2(OAc)_4\text{(cat)}} \text{(R)-(–)-NpPhMeSiCH}_2CO_2Et$$

Seyferth and co-workers[196] showed that chloro(carbomethoxy)carbene and bromo(carbomethoxy)carbene could be inserted into the Si–H bond to give the corresponding α-silyl ester in moderate yield.

$$PhHgCCl_2CO_2Me + Et_3SiH \longrightarrow \underset{47\%}{Et_3SiCHClCO_2Me}$$

$$PhHgCBr_2CO_2Me + Et_3SiH \longrightarrow \underset{35\%}{Et_3SiCHBrCO_2Me}$$

The reaction of 1,1,1-trifluoropropylsilanes with ethyl diazoacetate give the corresponding α-silyl ester.[197] The reaction of an Si–H bond with ethyl diazoacetate was studied as a function of the groups attached to silicon.[198] It was found that the presence of a phenyl group enhanced the reaction of the carbene with the Si–H bond. Even dialkylamino substituted silyl hydrides react with ethyl diazoacetate at the Si–H bond.[199]

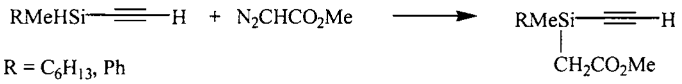
$$(CF_3CH_2CH_2)_nMe_{3-n}SiH + N_2CHCO_2Et \xrightarrow[80\ °C]{Cu} (CF_3CH_2CH_2)_nMe_{3-n}SiCH_2CO_2Et$$

$n = 1,2$

$$R^1R^2MeSiH + N_2CHCO_2Et \xrightarrow[90\ °C]{Cu} R^1R^2MeSiCH_2COEt$$

$R^1 = Et_2N$; $R^2 = Me$
$R^1 = R^2 = Et_2N$

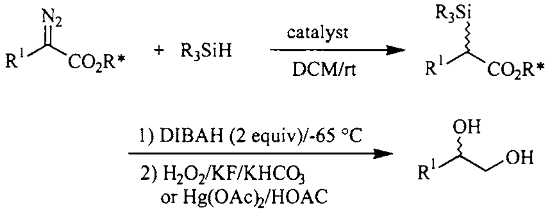
Although the reactions of n-hexyldimethylsilylacetylene and phenyldimethylsilylacetylene with methyl diazoacetate were shown to give the methyl 4-silylbut-3-ynoate, the reaction of methyl diazoacetate with *n*-hexyl- or phenylmethylsilylacetylene gives the α-silyl acetate instead.[200] It has also been shown that the Si–H bond is more reactive towards the ethoxycarbony carbene than are double bonds.[201] A related paper studied the effect of the ethynyl groups on the reaction.[202]



$$RMeHSi{-}C{\equiv}C{-}H + N_2CHCO_2Me \longrightarrow \underset{\displaystyle CH_2CO_2Me}{RMeSi}{-}C{\equiv}C{-}H$$

$R = C_6H_{13}$, Ph

The asymmetric insertion of a metal carbene into the Si–H bond was demonstrated by the use of metal carbene complexes derived from optically active α-diazo esters.[203] The diastereomeric α-silyl esters were converted to diols of moderate enantiomeric excess.



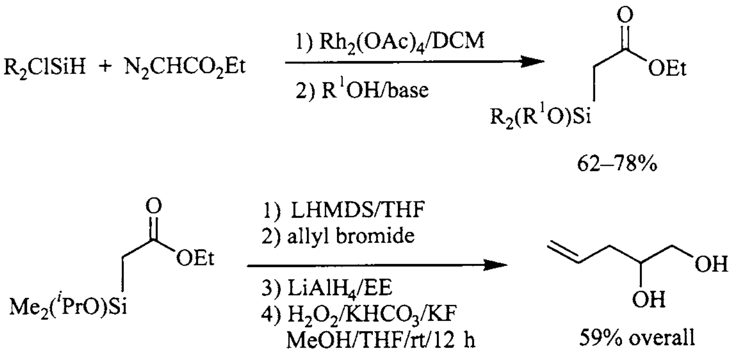
R_1 = Me, ^{i}Bu, Bn, $CH_2CO_2{}^tBu$; R* = (−)-menthyl, (+)-menthyl, 2-phenylcyclohexyl; catalyst = $Rh_2(OAc)_4$, $Cu(acac)_2$, $Cu(OTf)_2$, $Cu(OTf)_2$/sparteine.

The insertion of carboethoxycarbene, generated from ethyl diazoacetate, into the Si–H bond was shown to occur with retention of configuration at silicon and was used to prepare (+)-ethyl (1-naphthyl)phenylmethylsilylacetate by the reaction of (+)-(1-naphthyl)phenylmethylsilane with ethyl diazoacetate in 21% yield.[204]

$$(S)\text{-}(+)\text{-1-NpPhMeSiH} + N_2CHCO_2Et \xrightarrow{\text{CuCl}} (R)\text{-}(+)\text{-1-NpPhMeSiCH}_2CO_2Et$$

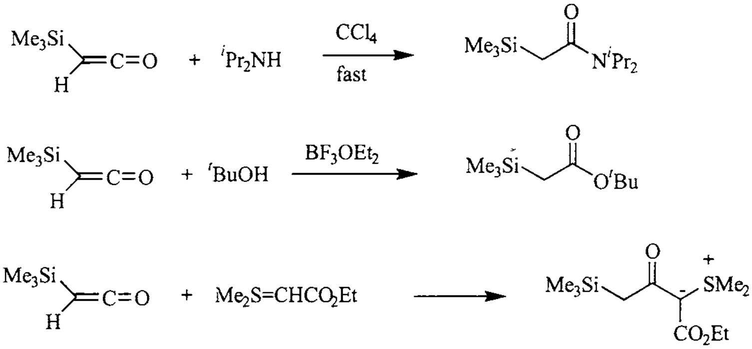
21%

The synthesis of α-(alkoxydialkylsilyl)acetates was accomplished by the reaction of ethyl diazoacetate with dialkylchlorosilanes followed by alkoxylation.[205] These α-silyl esters were alkylated, reduced, and oxidized to give terminal diols.

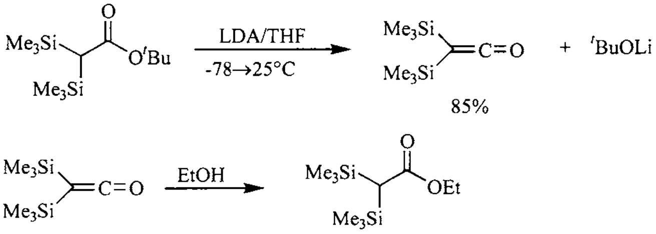


7.5. Synthesis of α-Silyl Esters from Silyl Ketenes

Ruden[206] reported the reactions of trimethylsilylketene with diisopropylamine, *tert*-butanol and carboxyethyldimethylsulfonium ylide. The reaction with *tert*-butanol is very slow in the absence of a catalyst, but very fast in the presence of boron fluoride etherate.



tert-Butyl bis(trimethylsilyl)acetate, when deprotonated and allowed to react in the absence of other reagents, loses lithium *tert*-butoxide and forms bis(trimethylsilyl)ketene in excellent yield.[207] This ketene reacts with ethanol to give ethyl bis(trimethylsilyl)acetate as expected.

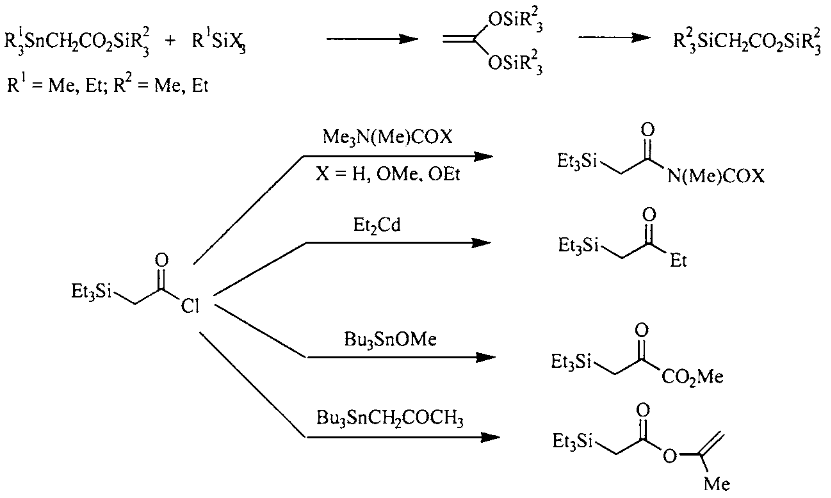


The reaction of trialkylsilyl ketenes with trialkylmethoxytin gives the α-silyl α-stannyl ester.[208]

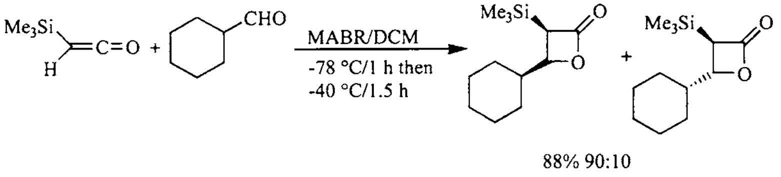
$$R^1_3SiC{=}C{=}O + R^2_3SnOMe \longrightarrow R^1_3Si\underset{\displaystyle R^2_3Sn}{C}HCO_2Me$$

$R^1 = Me, Et; R^2 = Et, {}^nBu$

α-Trialkylstannyl esters react with chlorosilanes to give both the O- and the C-silylated products.[209] In the reaction with trimethylchlorosilane the C-isomer was obtained, but with trimethyl- or triethylsilyl iodide the O-isomer was found, possibly due to isomerization of the C-isomer.[210] Triethylsilylacetyl chloride was used as the starting material for a variety of α-triethylsilyl carbonyl systems.[211]

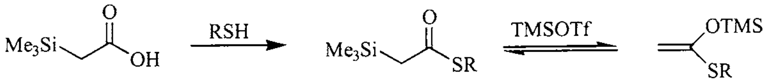


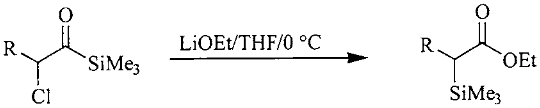
α-Trimethylsilyl-β-butyrolactones were prepared from trimethylsilyl ketene and aldehydes.[212]



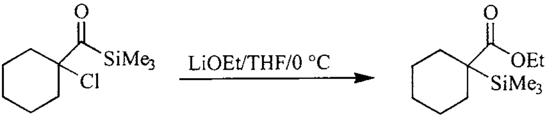
7.6. Synthesis of α-Silyl Esters from Rearrangements

Tajima and co-workers[213] have shown that trimethylsilyl acetic acid reacts readily with mercaptans to give the corresponding thioester, which in turn can be reacted with trimethylsilyl triflate to give the thermodynamically more stable thio trimethylsilyl ketene acetal in equilibrium with the α-silyl mercaptoester. α-Chloroacyltrimethylsilanes were reacted with lithium ethoxide to give α-trimethylsilyl esters in good yields.[214]

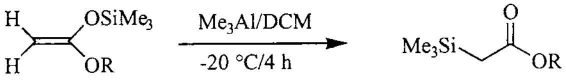




4 examples 83–87%

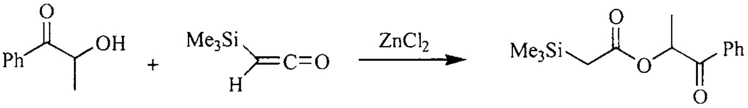


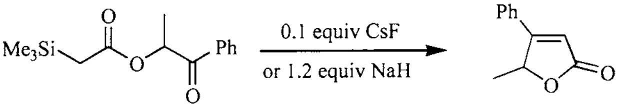
The O- to C-migration of the trimethylsilyl group to produce α-trimethylsilyl esters directly from trimethylsilyl ketene acetals is catalyzed by trialkylaluminum reagents.[215]

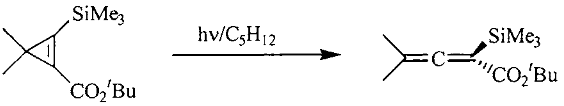


R = C_6H_{13} (90%), C_4H_9 (73%), C_2H_5 (84%)

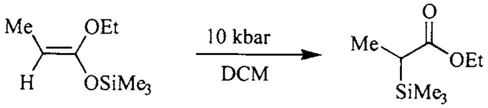
The zinc chloride-catalyzed reaction of alcohols with silyl ketenes was used to prepare α-silyl esters containing functional groups.[216] These functionalized α-silyl esters can then be employed in cyclization reactions. The photolysis of 2-trimethylsilylcyclopropene carboxylic esters gives α-trimethylsilyl allenates.[217]





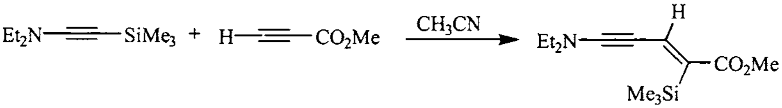


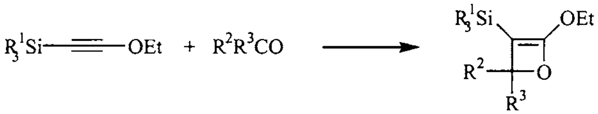
Yamamoto and co-workers reported the rearrangement of trimethylsilyl ketene acetals to α-trimethylsilyl esters under high pressure.[218]



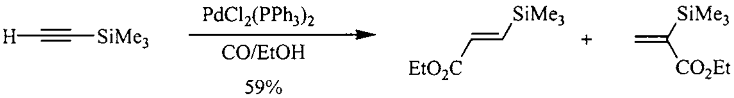
7.7. Synthesis of α-Silyl Esters from Unsaturated Silanes

The reaction of silylynamines with ynoates gives α-silyl-α,β-unsaturated esters.[219] Trialkylsilyl ethoxyacetylenes react with aldehydes and ketones to provide the α-silyl ketene acetals of butyrolactones.[220]

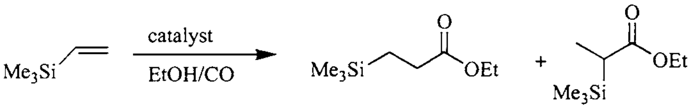




The hydroethoxycarbonylation of ethynylsilanes under catalysis by palladium(II) gives predominantly the (*E*)-β-ethoxycarbonylvinylsilane[221] ester, with only small amounts of the α-trimethylsilyl ester when palladium(II) catalysts are employed, but greater amounts of the α-trimethylsilyl ester when dicobalt octacarbonyl is used as the catalyst.[222,223] These reactions apply also to the synthesis of β- and α-trimethylsilylacetic acids and to α-substituted β- or α-trimethylsilyl esters.



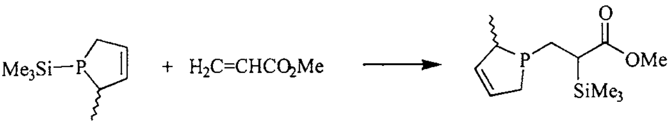
The carbonylation of vinyltrimethylsilane was shown to give primarily the β-trimethylsilyl ester.



$PdCl_2(PPh_3)_2$	98%	2%
$PdCl_2(PhCN)_2$	95%	5%
$Co_2(CO)_8$	7%	93%

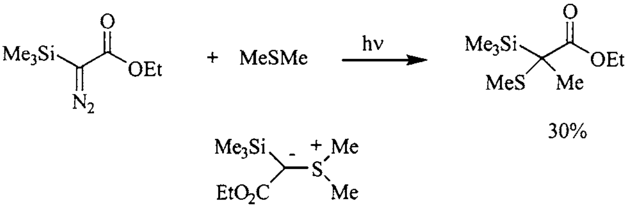
7.8. Miscellaneous Syntheses of α-Silyl Esters

The addition of the silylphosphine **82** to methyl acrylate provides the α-silyl ester **83**.[224]



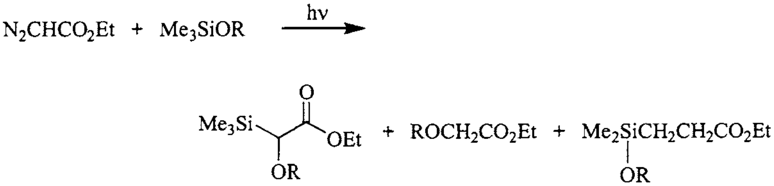
82 **83**

Ethyl trimethylsilyldiazoacetate was reacted with disulfides under the influence of light to give insertion into the C–S bond resulting in an α-trimethylsilyl α-thio ester.[225] The reaction proceeds *via* the sulfur ylide **84** as shown by low temperature NMR.



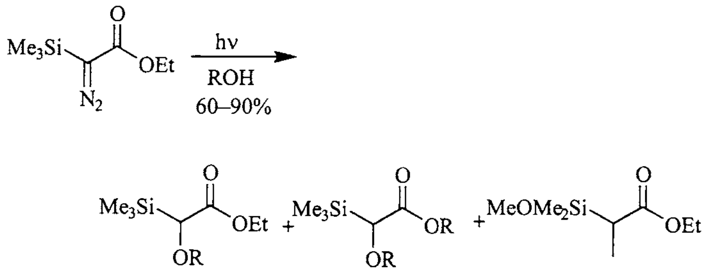
84

The ethyl diazoacetate generated carboethoxycarbene was shown to insert into the Si–O bond of alkoxytrimethylsilanes to give an α-alkoxy-α-trimethylsilyl ester.[226]

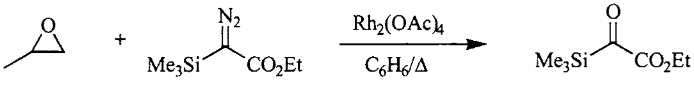


R = Me	28%	5%	10%
R = Et	31%	14%	14%

The photolysis of ethyl diazotrimethylsilylacetate in the presence of an alcohol leads to α-alkoxy-α-trimethylsilyl esters along with α-dimethylalkoxysilyl esters, which are thought to come from a silene intermediate.[227]

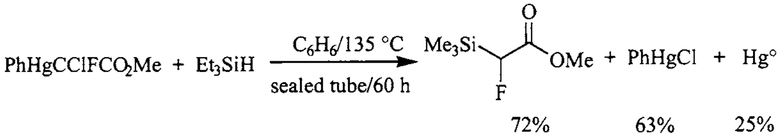


The dirhodium tetraacetate-catalyzed deoxygenation of epoxides with diazo esters was reported. When this was carried out with propylene oxide and **85** the silyl keto ester **86** was formed.[228]

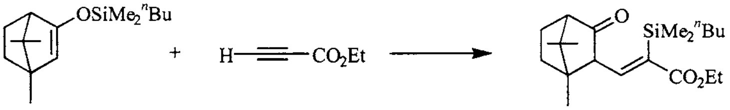


85 **86**

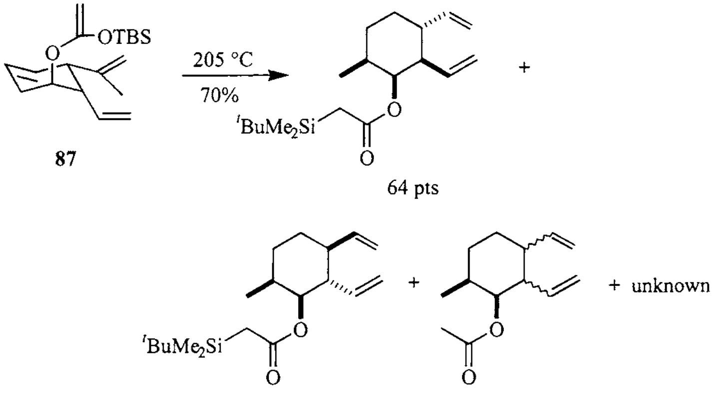
Seyferth and Woodruff[229] reported the insertion of carbomethoxymethylfluorocarbene, generated by the mercurial route, into the Si–H bond of triethylsilane to provide methyl fluoro(triethylsilyl)acetate.



Whereas enol silyl ethers were shown to react with ethyl propiolate to give [2+2] cycloaddition products, the reaction of the enol silyl ether of camphor gives α-silyl esters in a noncyclization process.[230]



In a study of the preparation of some (*E*,*E*)-cyclohexadienes, structures such as **87** were subjected to a tandem Cope–Claisen rearrangements.[231] There is a C- to O-migration of the *tert*-butyldimethylsilyl group involved after the Cope rearrangement, however, that therefore does not allow for the desired subsequent Claisen rearrangement. In the case of the ketene acetal of the isobutyrate unit there is some of the tandem Cope–Claisen product.



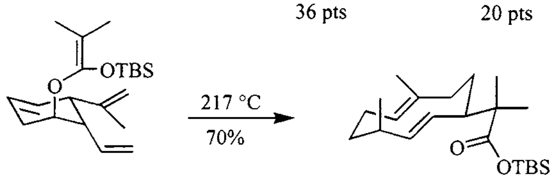
87

64 pts

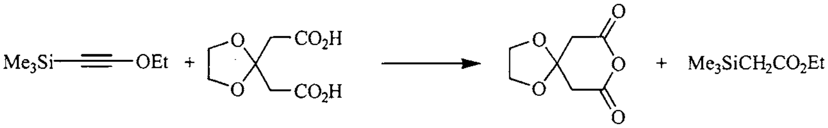
36 pts

20 pts

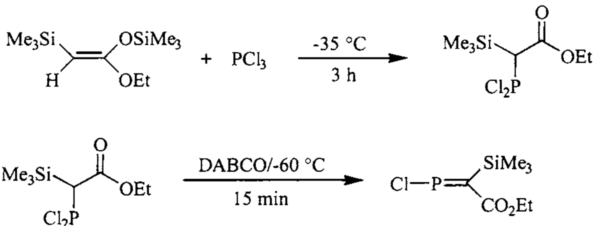
10 pts



Ethoxytrimethylsilylacetylene has been used as the anhydride of ethyl trimethylsilylacetate in a facile synthesis of acid anhydrides.[232]

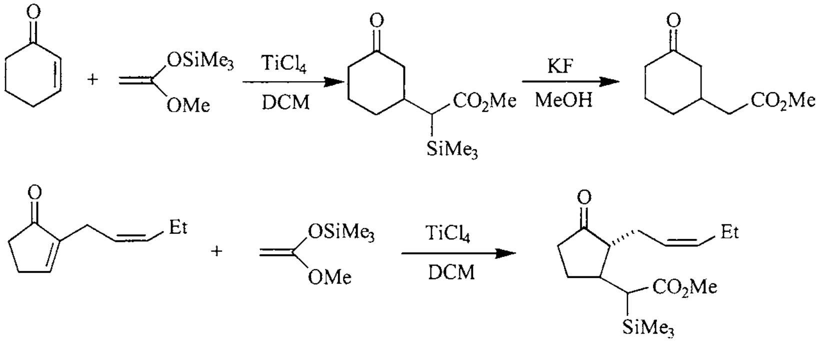


The trimethylsilyl ketene acetal of ethyl trimethylsilylacetate was reacted with phosphorous trichloride to give the α-trimethylsilyl-α-dichlorophosphinylacetate, which was eliminated with DABCO to the phosphaalkene **88**.[233]

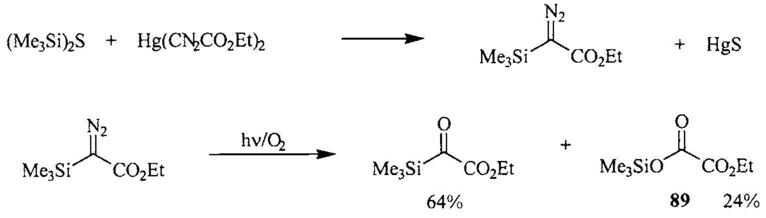


88

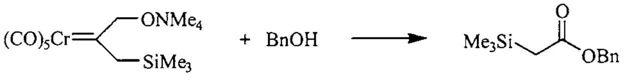
Trimethylsilylketene acetals were shown to react with cyclohexenones and cyclopentenones under the influence of titanium tetrachloride to give Michael addition to the enone and trapping of the trimethylsilyl group to the ester group rather than at the oxygen of the ketone enolate.[234] Potassium fluoride in methanol serves to remove the trimethylsilyl group.



Bis(ethyl)diazoacetoxymercury was shown to react with bis(trimethylsilyl)sulfide to give mercuric sulfide and ethyl diazotrimethylsilylacetate, which upon photooxidation yields the acylsilane **89**, which is also an α-silyl ester.[235]

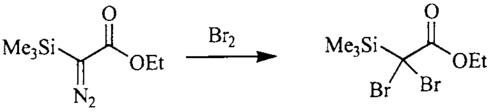


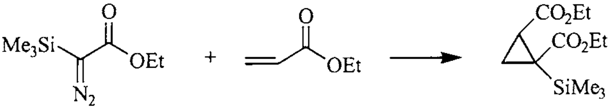
The reaction of chromium complex **90** with benzyl alcohol results in the formation of benzyl trimethylsilylacetate in poor yield.[236]



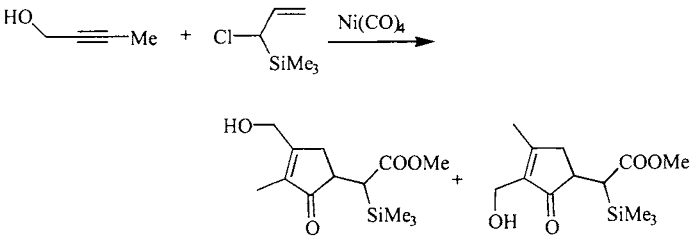
90

Some reactions of ethyl trimethylsilyl(diazo)acetate lead to α-trimethylsilyl esters.[237] For example, the reaction with bromine gives the α,α-dibromo acetate, and the reaction with ethyl acrylate gives the cyclopropane.



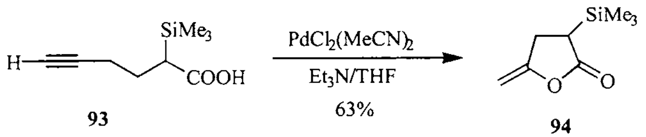


The reaction of propargyl alcohols with 3-chloro-3-trimethylsilyl-1-propene and nickel tetracarbonyl provides the lactones **91** and **92**.[238]

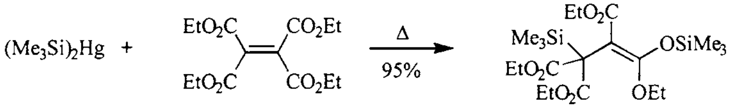


91 24% **92** 8%

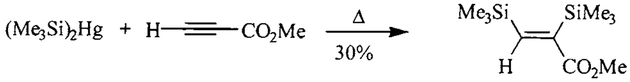
The intramolecular, palladium-catalyzed cyclization of 3-ethynyl carboxylic acids provides 4-pentene-4-olides in excellent yields.[239] When this reaction was carried out with the α-silyl acid **93**, the enolide **94** was obtained in 63% yield. The reaction of bis(trimethylsilyl)mercury with tetrakis(carboethoxy)ethylene gives the trimethylsilylated ester **95**.[240]



93 **94**



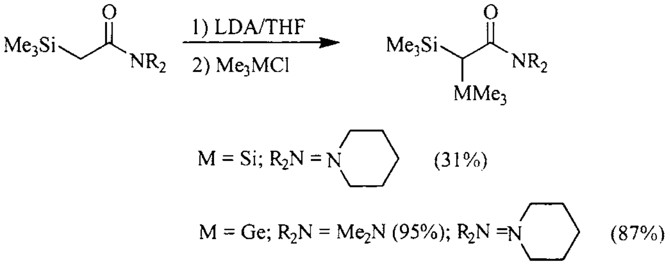
95

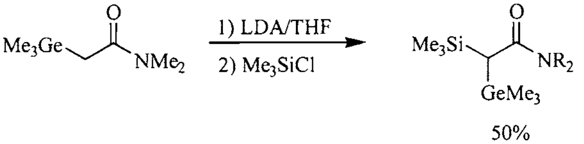


8. SYNTHESIS OF α-SILYL AMIDES

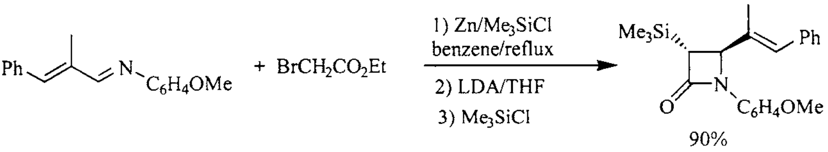
8.1. Synthesis of α-Silyl Amides from Enolates

Trimethylsilylacetamides were deprotonated and the anion quenched with trimethylchlorogermane or trimethylchlorosilane to give the α,α-bismetallo derivatives.[241]

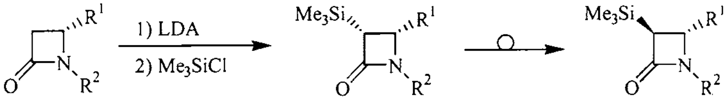




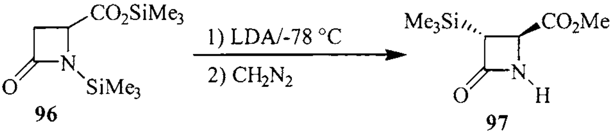
The condensation of ethyl bromoacetate with enimines promoted by zinc-trimethylchlorosilane gives β-lactams, with concomitant trimethylsilylation at carbon.[242]

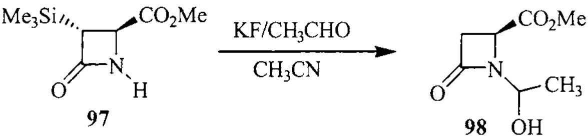


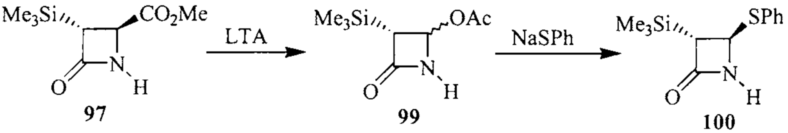
The deprotonation–trimethylsilylation of 1,4-disubstituted β-lactams occurs to place the trimethylsilyl group on carbon cis to the 4-substituent. The *cis*-isomer converts to the *trans*-isomer, however.[243] The C-trimethylsilylated β-lactam was reacted with acyl chlorides and aldehydes.



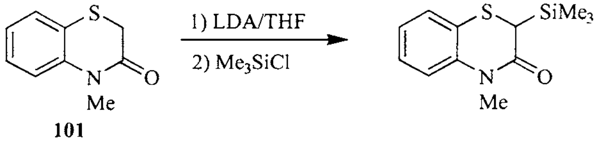
Treatment of the bis-trimethylsilylated acetidinone **96** with lithium diisopropylamide results in a 1,4-O → C migration resulting in the α-trimethylsilylacetidinone **97** after workup.[244] This material can be reacted with potassium fluoride in the presence of the electrophile acetaldehyde to give the nitrogen adduct with loss of silicon **98**. Lead tetraacetate treatment of **97** gives **99** which can be reacted with nucleophiles to give the substituted acetidinones **100**.



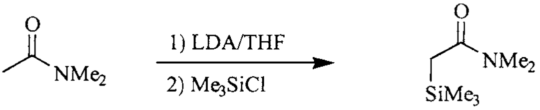


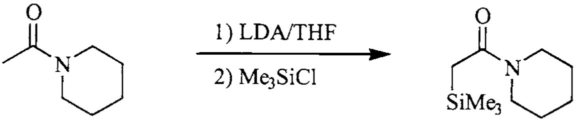


Amide **101** was C-trimethylsilylated via its lithium enolate in good yield.[245]



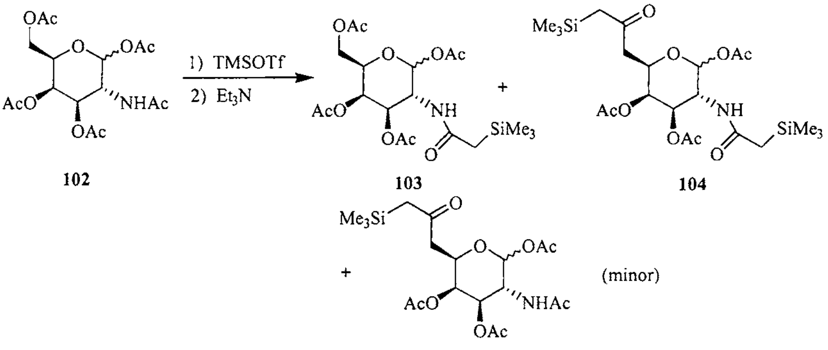
It has been shown that *N*,*N*-dimethylacetamide is directly C-trimethylsilylated as is the pyrrolidine amide.[246]



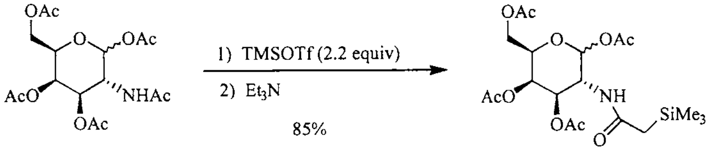


8.2. Synthesis of α-Silyl Amides via Direct Silylation

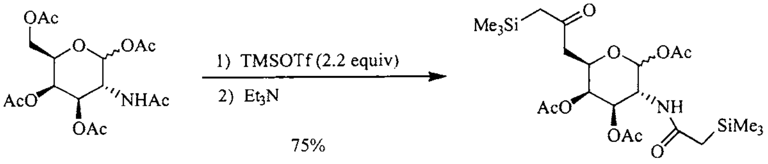
The reaction of the GlcNAc peracetate, **102**, with trimethylsilyl triflate and triethylamine results in a mixture of three products as shown. The predominant formation of the trimethylsilylated amide, **103**, or the bis-silylated, **104**, can be accomplished.[247]



102 **103** **104** **105**

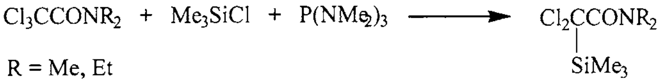


102 **103**



102 **104**

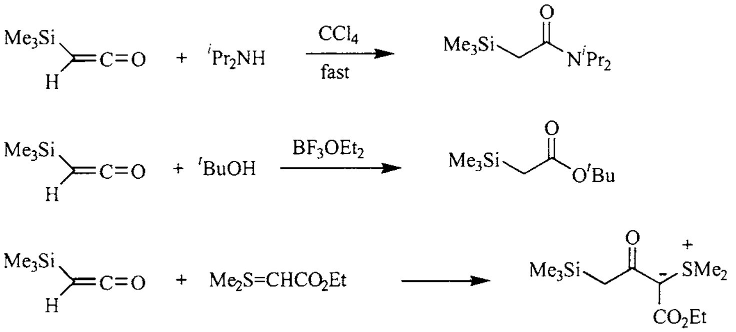
The reaction of dimethyl (or diethyl)trichloroacetamide with trimethylchlorosilane in the presence of tris(dimethylamino)phosphine gives the α-silyl-α,α-dichloroacetamide.[248]



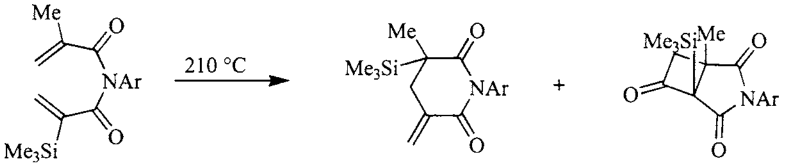
$$\begin{array}{l} Cl_3CCONR_2 + Me_3SiCl + P(NMe_2)_3 \longrightarrow Cl_2C(SiMe_3)CONR_2 \\ R = Me, Et \end{array}$$

8.3. Synthesis of α-Silyl Amides by Miscellaneous Methods

Ruden[249] reported the reactions of trimethylsilylketene with diisopropylamine, *tert*-butanol, and carboxyethyldimethylsulfonium ylide. The reaction with *tert*-butanol is very slow in the absence of a catalyst, but very fast in the presence of boron fluoride etherate.



Thermal rearrangement of **106** provides the cyclic and bicyclic α-trimethylsilyl lactams **107** and **108**.[250]



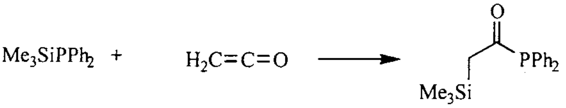
106 **107** 21% **108** 57%

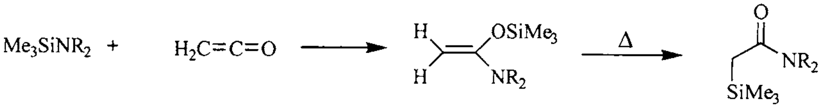
Trimethyltribromoacetoxysilane was reacted with triphenylphosphine and trimethyl(diethylamino)silane to give *N*,*N*-diethyl(trimethylsilyl)dibromoacetamide, along with trimethylbromosilane and triphenylphosphine oxide, in good yield.[251]

$$Me_3SiO_2CCBr_3 + Ph_3P + Me_3SiNEt_2 \longrightarrow$$

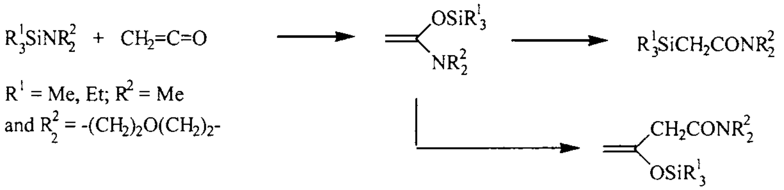
$$\begin{array}{ccccc} Et_2NCOCBr_2SiMe_3 & + & Me_3SiBr & + & Ph_3PO \\ 77\% & & 95\% & & 97\% \end{array}$$

Phosphino- and aminotrimethylsilanes were shown to react with ketene to give the α-silyl carbonyl system.[252] The reaction of the aminosilanes was shown to give initially the O-silylated product, which then isomerized to the C-silylated isomer.

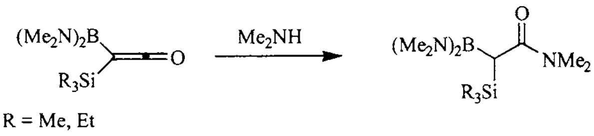




Dialkylaminosilanes react with ketene to give initially the O-silylated ketene aminal, which rearranges to the C-silylated isomer or reacts with a second equivalent of ketene.[253]

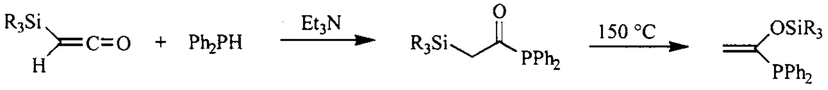

$R^1 = Me, Et; R^2 = Me$
and $R^2_2 = -(CH_2)_2O(CH_2)_2-$

Bis(dimethylamino)boryltrialkylsilyl ketenes react with dimethylamine to give the α-boryl-α-silylamide.[254] (For the synthesis of the boryl ketene see ref. 255.) The reaction of ethyl trialkylsilylacetates with dialkylamino halides gives the corresponding α-trialkylsilyl amide.[256] The reaction of silylketenes with diphenylphosphine gives diphenyltrimethylsilylacylphosphine.[257] The reaction with dialkylphosphites leads directly to the O-silylated derivatives instead.


R = Me, Et

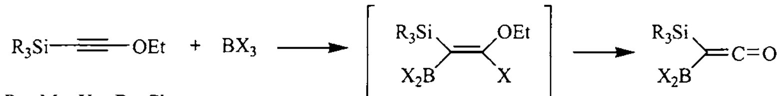
$$R^1_3SiCH_2CO_2Et + R^2NX_2 \longrightarrow R^1_3SiCH_2CONR^2_2$$

$R^1 = Et, Pr, {}^nBu; R^2 = Et, Pr$, and $R^2_2 = -(CH_2)_5-$



9. SYNTHESIS OF α-SILYL KETENES

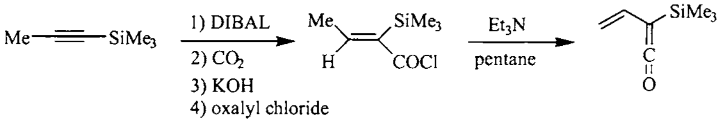
Trimethylsilylethoxyacetylene, a material much more thermally stable than ethoxyacetylene itself, was reacted with boron trihalides to give addition of B–X to the triple bond with the boron adding to the carbon containing the trimethylsilyl group.[258] Hydrolysis of the adduct leads to α-dihaloboryl silylketenes **109**. Reaction of this ketene with methanol leads to methyl trimethylsilylacetate.

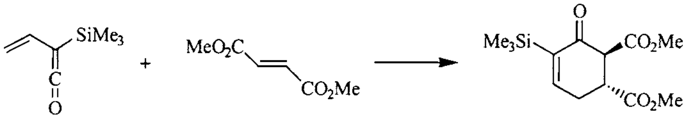


R = Me; X = Br, Cl
R = Et; X = Br

109

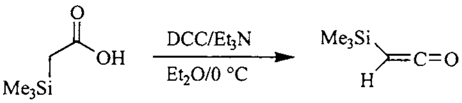
(Trimethylsilyl)vinylketene was prepared from 1-trimethylsilylpropyne and found to be a stable vinylketene and, at the same time, a reactive enophile in [4+2] cycloadditions with activated olefins.[259]



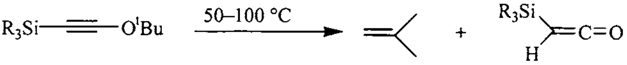


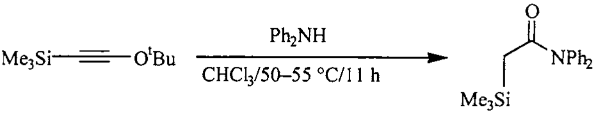
62%

Treatment of trimethylsilyl acetic acid with dicyclohexylcarbodiimide gives trimethylsilylketene in good yield.[260] It was shown that 1-*tert*-butoxy-2-silylethynes thermally eliminate isobutene to give silyl ketenes. This allows the "in situ" generation of silyl ketenes in the presence of nucleophiles.[261]



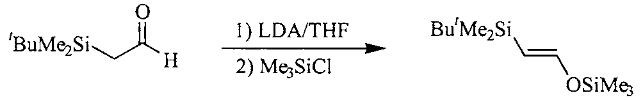
63%

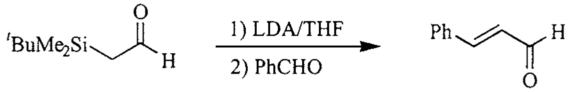




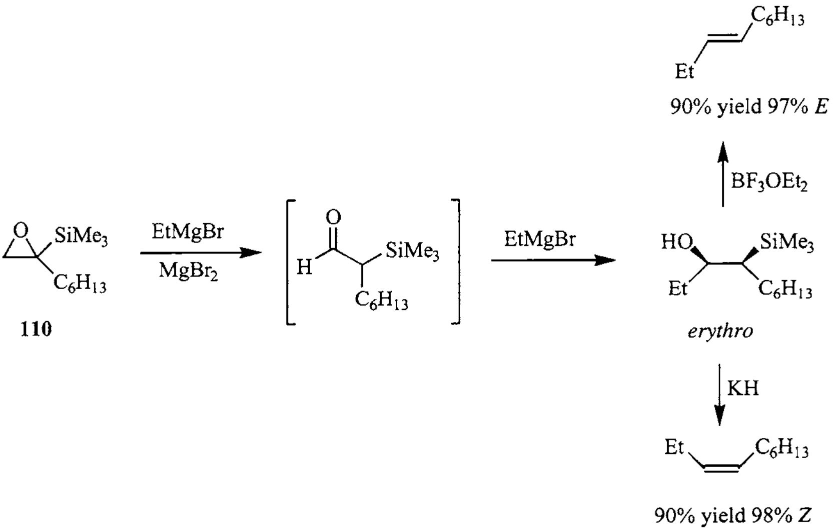
10. REACTIONS OF α-SILYL ALDEHYDES

tert-Butyldimethylsilylacetaldehyde was deprotonated and the lithium enolate reacted with trimethylchlorosilane or benzaldehyde.[262]

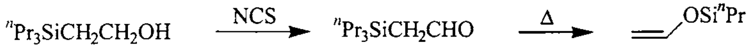




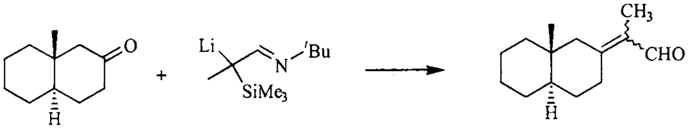
Hudrlik and co-workers[31] showed that α,β-epoxysilanes are precursors to α-trimethylsilyl ketones and aldehydes. These key materials can be generated in the presence of Grignard reagents, which then trap them. The presence of magnesium bromide brings about the rearrangement of the epoxysilane to the α-silyl carbonyl isomer. The reaction of epoxide **110** with ethylmagnesium bromide/magnesium bromide gives addition of the ethylmagnesium bromide to the aldehyde in a Cram manner leading to the erythro β-hydroxysilane. This undergoes elimination to either the *Z*- or *E*-olefin depending on the conditions.



N-Chlorosuccinimide oxidation of 2-tri-*n*-propylsilylethanol gave tri-*n*-propylsilylacetaldehyde, which thermally rearranged, as expected, to tri-*n*-propylsilyloxyethylene.[263]

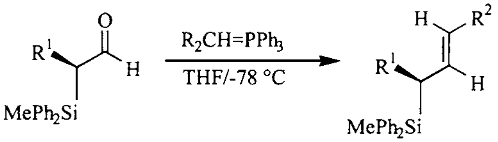


The *tert*-butylimine of 2-trimethylsilylpropionaldehyde was lithiated and reacted with decalone **111** to give the corresponding α,β-unsaturated aldehyde.[264]



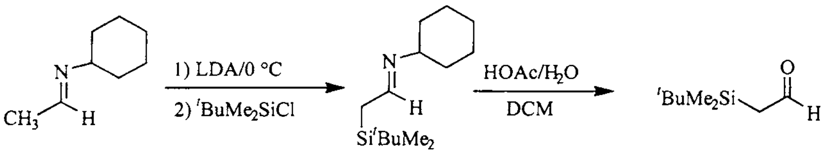
111

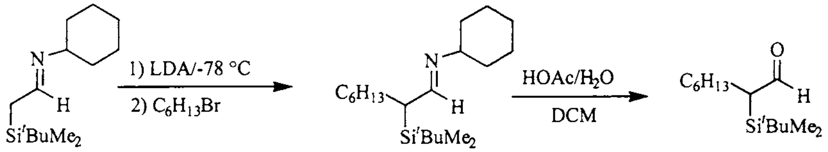
Optically active allylsilanes, **112**, can be prepared by the reaction of alkylidene triphenylphosphoranes with α-silyl aldehydes.[265] Conversion of the allylsilane back to the starting α-silyl aldehyde confirmed that the Wittig reaction occurs without racemization.



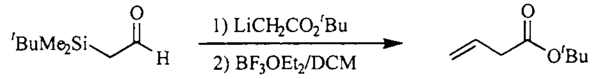
112

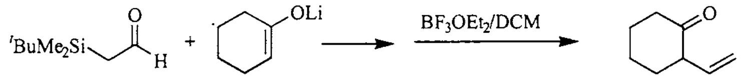
Hudrlik and Kulkarni[266] demonstrated that the cyclohexyl imine of acetaldehyde could be deprotonated and *tert*-butyldimethylsilylated and that the resulting α-silyl imine could be carefully hydrolyzed to give *tert*-butyldimethylsilylacetaldehyde. An alkylation–hydrolysis sequence led to substituted α-silyl aldehyde **113**. Reaction of the *tert*-butyldimethylsilylacetaldehyde with the lithium enolate of *tert*-butyl acetate or of cyclohexanone lead to the corresponding β,γ-unsaturated ester and vinylcyclohexanone, respectively.





113

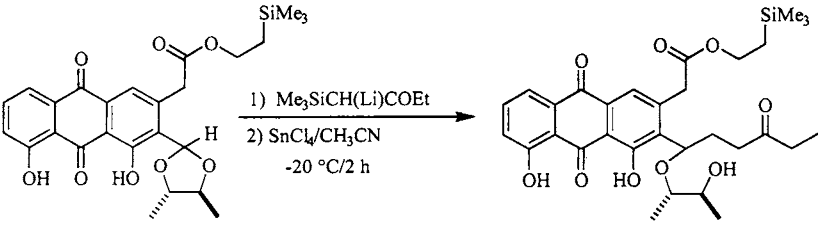




11. REACTIONS OF α-SILYL KETONES

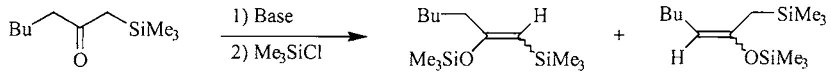
11.1. Reactions of the Enolates of α-Silyl Ketones

Kishi and co-workers[267] used a diastereoselective β-alkoxy ester synthesis in a practical preparation of 11-deoxydaunomycinone and related materials.

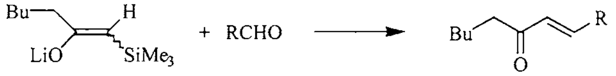


85–90% plus 5% epimer

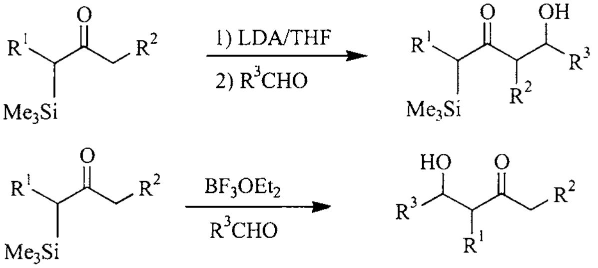
The regioselectivity of the deprotonation of trimethylsilylmethylsilyl ketones was studied. It was found that lithium dialkylamides, with the exception of lithium hexamethyldisilazide, give greater deprotonation on the side containing the trimethylsilyl group.[268] The difference found with the lithium hexamethyldisilazide could stem from the longer Si–C bond in the substrate and the longer Si–N bond in the base providing more steric hindrance on that side of the molecule in this case. Both 1-trimethylsilylhexyllithium and 1-trimethylsilylethyllithium give very high regioselectivity with deprotonation on the trimethylsilyl side of the molecule. The resulting α-trimethylsilyl enolate ions react with aldehydes to give α,β-unsaturated ketones in good yields.



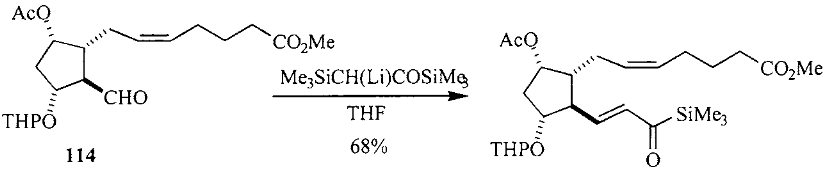
Base		
R_2NLi	80–89%	11–20%
$(Me_3Si)_2NLi$	24%	76%
$Me_3SiCHLiR$	96–98%	2–4%



It was shown by Kuwajima and co-workers[269] that α-trimethylsilyl ketones can be used to generate enolate chemistry from either side of the carbonyl group by taking advantage of the bulk of the trimethylsilyl group to permit selective deprotonation in the one case and utilizing the trimethylsilyl group to produce the enolate chemistry in the other.



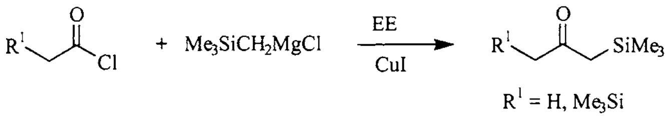
The enolate of trimethylsilylacetyltrimethylsilane was reacted with aldehyde **114** in the preparation of some prostaglandins such as **115**.[270]

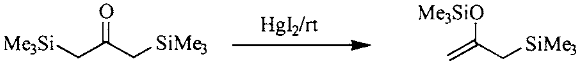


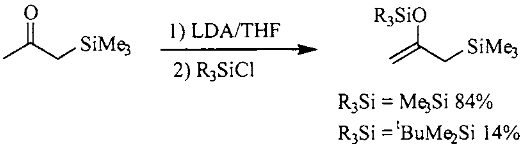
114

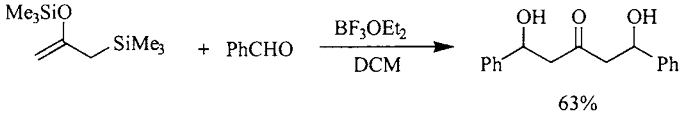
115

It was found that the formation of the kinetic silyl enol ether of trimethylsilylacetone gives a reagent that can be used as the synthetic equivalent of the α,α′-dianion of acetone.[271] The reagent can be prepared either by the isomerization of 1,3-bis(trimethylsilyl)-2-propanone, or the silylation of the kinetic enolate of trimethylsilylacetone. The preferred reagent, 2-trimethylsiloxytrimethylsilylpropene, was shown to react with electrophiles in the presence of a Lewis acid catalyst to give the bis-adduct. The example with benzaldehyde is shown. It was shown that the reaction is sequential with the reagent reacting as a silyl enol ether first and then as an α-trimethylsilyl ketone.

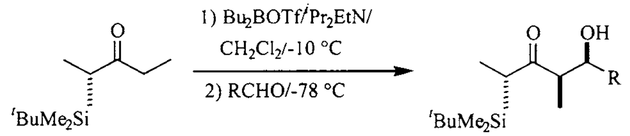


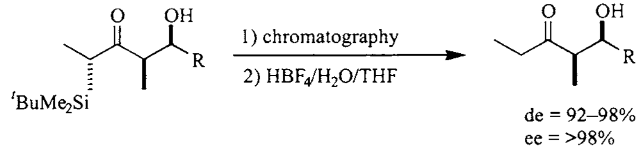




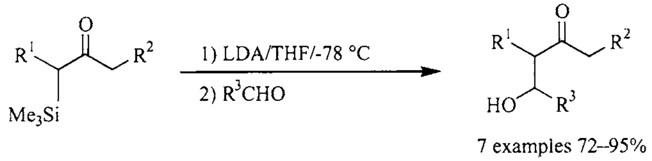


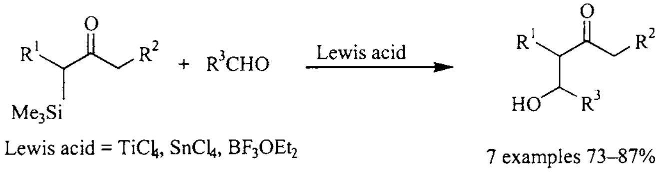
(*R*)-(–)-2-(*tert*-Butyldimethylsilyl)-3-pentanone was converted to its boron enolate in a regiospecific manner on the side opposite to that bearing the bulky silyl group and this boron enolate condensed with aldehydes and then desilylated to yield optically active β-hydroxy ketones in high optical purity.[272] Here the silyl group is an excellent tool for the asymmetric induction and for the regiospecific enol formation. This approach was used to synthesize sifophilure.

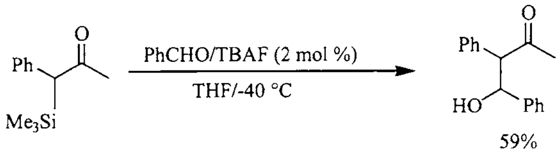


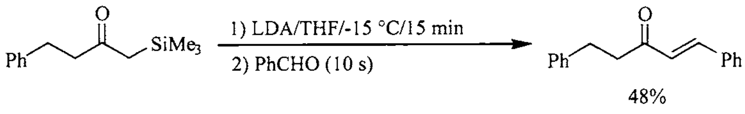


α-Trimethylsilyl ketones were shown to be very useful in directing the site of aldol condensations of the ketone.[273] Deprotonation of the α-silyl ketone with LDA occurs on the side opposite to the bulky trimethylsilyl group and hence condensation of the anion with aldehydes occurs away from the trimethylsilyl group. On the other hand, Lewis acid-catalyzed condensation of the α-silyl ketone with aldehydes occurs at the α-position containing the trimethylsilyl group. The steric effect of the trimethylsilyl group in the absence of another substituent is not enough to direct the deprotonation to the opposite side of the molecule as is seen below.

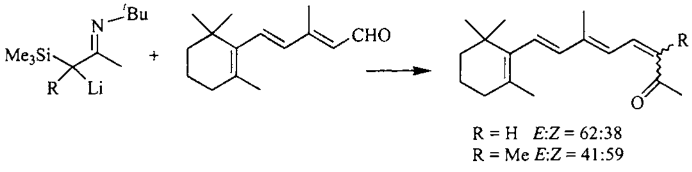




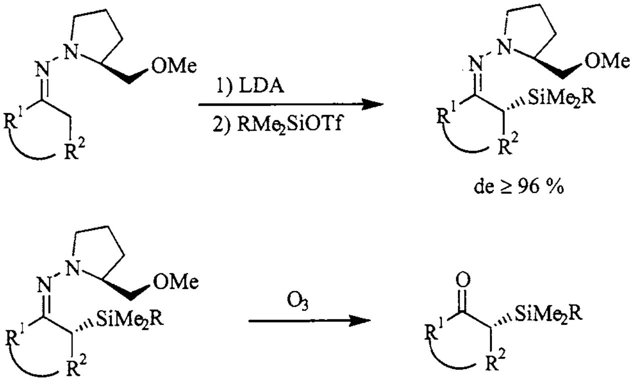




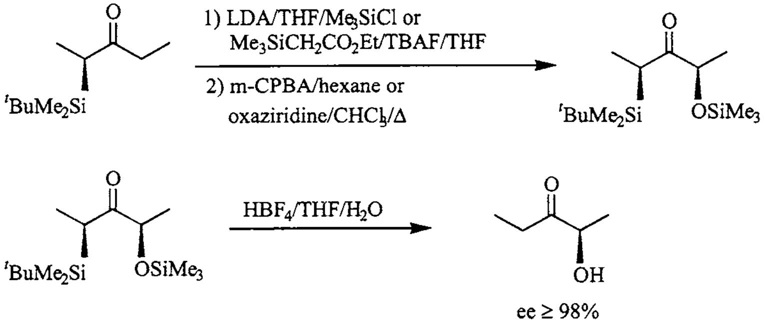
α-Trimethylsilyl tert-butylimines were deprotonated and the enolates reacted with ketones and aldehydes to give unsaturated ketones after hydrolysis of the imine to the ketone.[274] An interesting feature is that substantial *Z*-product is obtained.



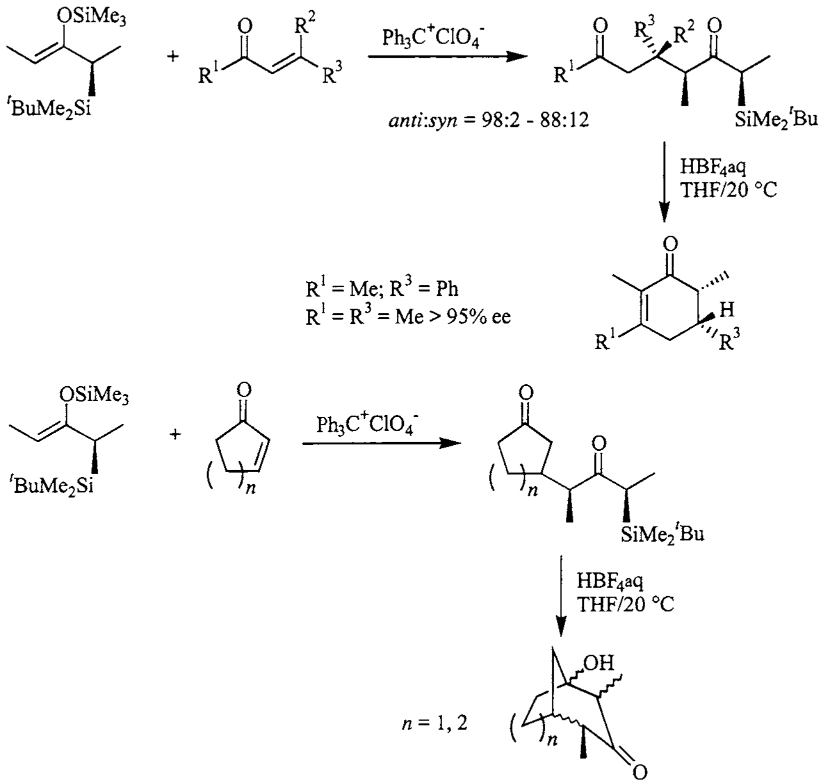
Enders and Lohray[275] showed that the enantioselective synthesis of α-silyl ketones and aldehydes was possible via the metalated SAMP (–)-(*S*)-1-amino-2-(methoxymethyl)pyrrolidine or RAMP (+)-(*R*)-1-amino-2-(methoxymethyl)pyrrolidine hydrazones. The diastereoselectivity of the formation of the α-silyl hydrazones is high as is the enantioselectivity of the corresponding α-silyl ketones or aldehydes. It was further shown that the formation of the trimethylsilyl enol ether of the α-silyl ketone could be converted to the α-silyl-α′-trimethylsiloxy ketone, which could, in turn be desilylated to the optically active α-hydroxyketone.



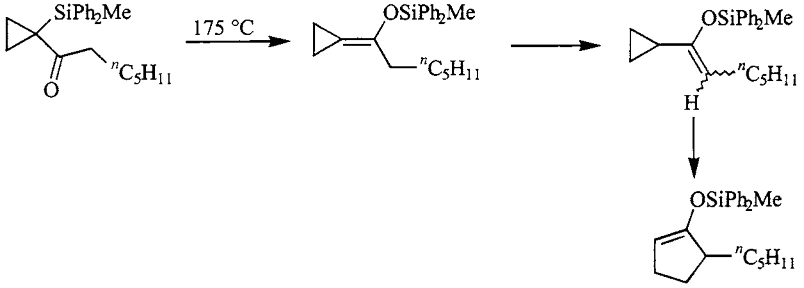
R = ^{t}Bu, Thexyl; R^1 = Et, Ph, 2-Np, 2,4-diMeOC_6H_3, H; R^2 = Me, Ph, Bn, $^n C_6H_{13}$.



A silicon-directed diastereo- and enantioselective Mukaiyama–Michael addition/aldol condensation sequence was employed using a single enantiomer of an α-silyl ketone as shown below.[276]



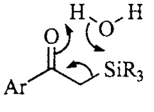
The thermal rearrangement of 1-(methyldiphenylsilyl)cyclopropyl ketones was shown to lead to an unstable cylopropylidene enol silyl ether, which further rearranges to a vinyl cyclopropane and ultimately give the enol silyl ether of a cyclopentanone.[277]



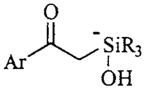
The enol silyl ethers of trimethylsilylmethylphenyl ketone and trimethylsilylacetone were prepared by a variety of methods.[278] A mixture of regio- and stereoisomers was obtained where possible.

11.2. Reactions of α-Silyl Ketones with Nucleophiles

The mechanism of the hydrolysis of various aryl silylmethyl ketones was studied under neutral- and base-catalyzed conditions.[279] It was determined that under neutral conditions a transition state involving a water molecule acting as both acid and base (electrophile and nucleophile!) was involved as illustrated in **116**. Under basic conditions attack of hydroxide on silicon is postulated as shown in **117**.

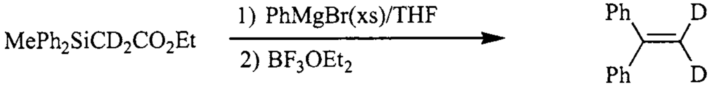


116

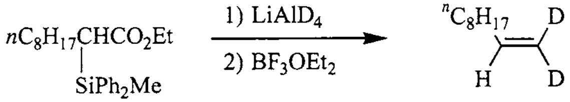


117

Larson and Cruz de Maldonado[280] showed that the introduction of the diphenylmethylsilyl group to esters allowed for the simple preparation of various deuterated olefins as shown below.

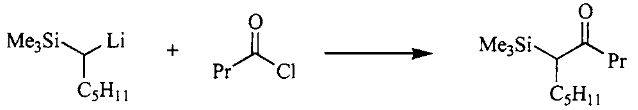


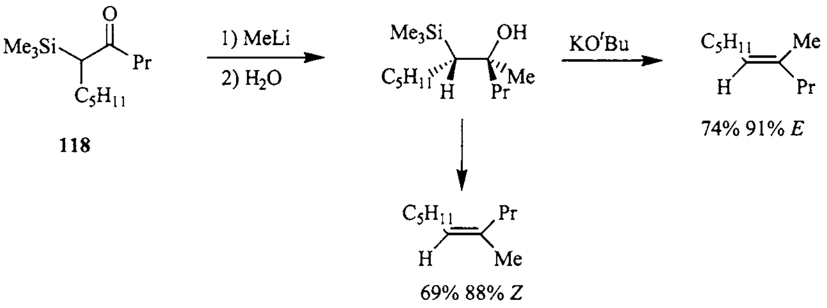
67%



57%

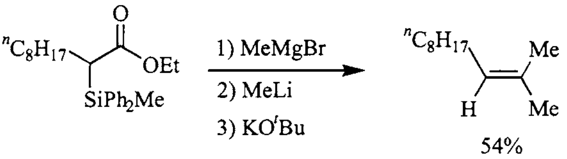
Utimoto and co-workers[281] showed that 5-trimethylsilyldecan-4-one, **118**, prepared by the reaction of 1-trimethylsilylhexyllithium and butyryl chloride, could be reacted stereoselectively with methylmagnesium bromide or better with methyllithium to give β-hydroxysilanes, which could be eliminated *syn* or *anti* to provide *E*- or *Z*-olefins. Larson and Hernández[282] showed that the diphenylmethylsilyl group gives greatly improved stereoselectivity in this reaction sequence.

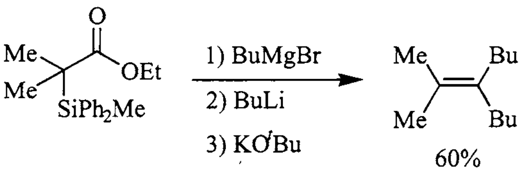


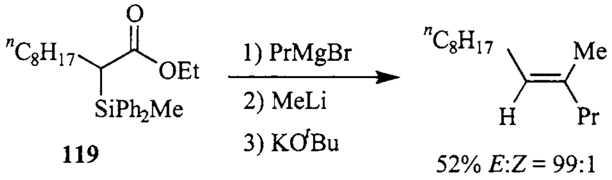


118

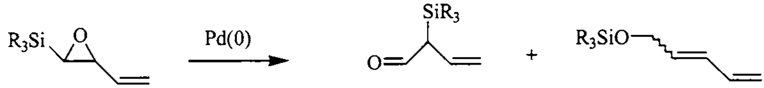
Hernández and Larson[282] further showed that the reaction of α-substituted and α,α-disubstituted ethyl(diphenylmethylsilyl)acetates react sequentially with a Grignard reagent, a lithium reagent, and then potassium *tert*-butoxide to give tri- and tetrasubstituted olefins, respectively. In one case ester **119** was reacted with *n*-propylmagnesium bromide, methyllithium, and then eliminated in base to give essentially pure (*E*)-4-methyl-4-dodecene. Acid catalyzed elimination gave a 70:30 *E:Z* ratio of olefins probably due to a *syn* elimination of the β-silyl lithium alkoxide intermediate prior to the acid addition. These results are to be compared with those of Utimoto and co-workers shown above and of Hudrlik and co-workers.[31]



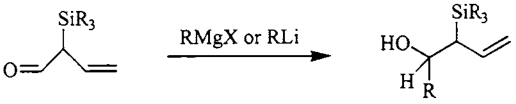




α-Trialkylsilyl-β,γ-unsaturated aldehydes were shown to be formed by the Pd(O)-catalyzed rearrangement of α-silyl-β-vinyloxiranes. The α-silyl aldehydes are only isolable when there are sterically demanding *tert*-butyl or isopropyl groups on the silicon; otherwise the corresponding enol silyl ether is formed. The α-silyl aldehyde was reacted with Grignard and organolithium reagents to give β-hydroxysilanes in high diastereomeric excess. The reaction can also be carried out with the "in situ" generation of the α-silyl aldehyde.[283]

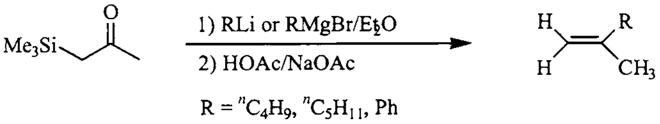


R_3Si = $^tBuMe_2Si$; $^iPr_3Si$; Me_3Si; Et_3Si; $PhMe_2Si$



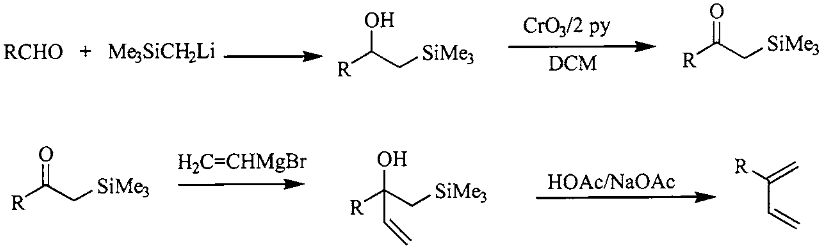
R_3Si = $^tBuMe_2Si$; $^iPr_3Si$; yields = 63–94%; de = 54–98%

Trimethylsilyl acetone was shown to react with lithium or Grignard reagents to give the corresponding olefin after elimination.[284]

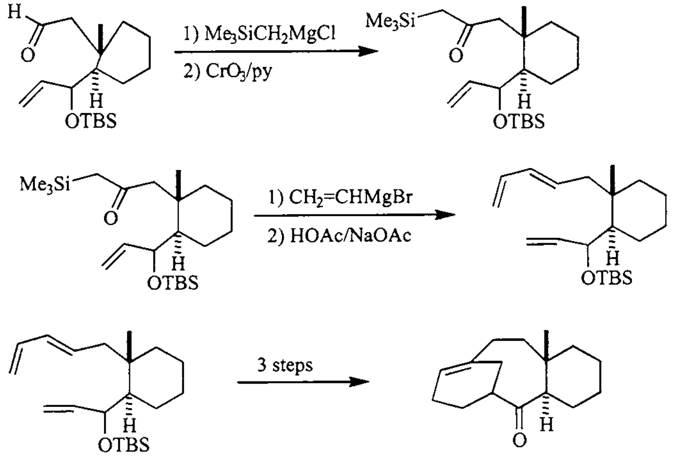


Jenkins and co-workers[285] used the reaction of trimethylsilylmethyllithium with aldehydes followed by oxidation to prepare α-silyl ketones.

These were in turn reacted with vinylmagnesium halides or vinyllithium reagents and the β-hydroxysilane so produced eliminated to provide dienes.

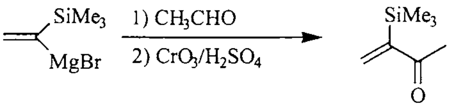


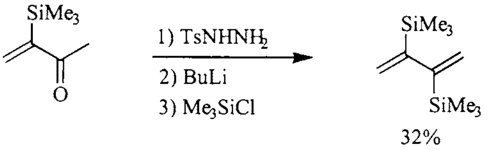
An α-silyl ketone was used to generate a 1,3-butadiene for a key intramolecular Diels–Alder step in an approach to the ring system of taxane, **120**.[286]



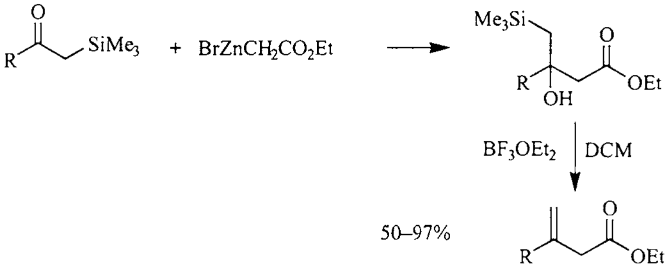
120

1-Trimethylsilylvinylmagnesium bromide was reacted with acetaldehyde and this product then oxidized to give 2-trimethylsilylbut-1-en-3-one.[287] This was subjected to the Shapiro reaction and the lithium reagent trimethylsilylated to give 2,3-bis(trimethylsilyl)-1,3-butadiene, which can be used as a substituted diene in Diels–Alder reactions.

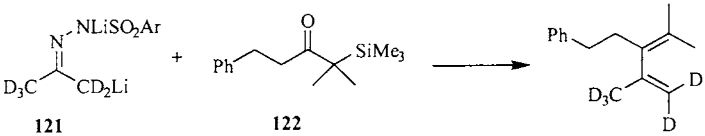




Trimethylsilylmethyl ketones, prepared by the reaction of trimethylsilylmethylmagnesium chloride with acid chlorides, were reacted with ethyl bromozinc acetate and the resulting β-hydroxy silane eliminated to give β-methylene esters in good yields.[288]

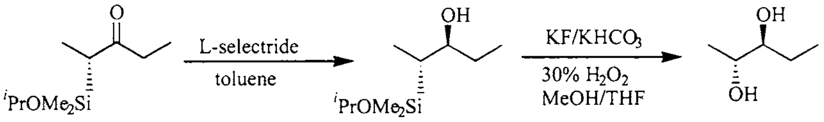


Treatment of the α-silyl ketone **121** with the anion of **122** was used to prepare the labeled diene **123**.[289]

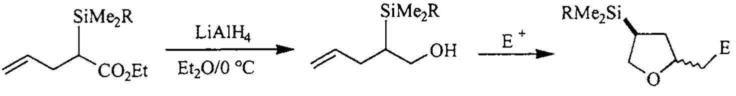


121 **122** **123**

By using the SAMP/RAMP technique, Enders and Nakai[290] were able to silylate with the isopropoxydimethylsilyl group, which could later be oxidized to the hydroxyl function. In this way they were able to convert chiral α-silyl ketones to diastereomeric diols in good yields and high diastereoselectivity.

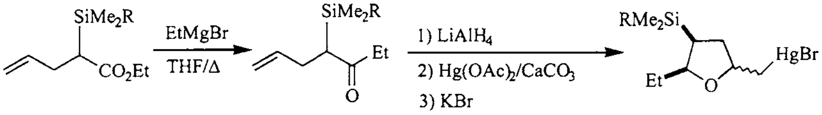


The lithium–aluminum hydride reduction of α-allyl-α-silyl esters provides the β-hydroxysilane, which upon treatment with electrophiles produces the 4-silyl tetrahydrofurans **124**.[291] It also proved possible to react the α-silyl ester with a Grignard reagent followed by the reduction/cyclization sequence to give the tetrahydrofurans.

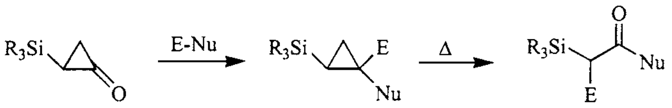


124

R = Me, Ph, OiPr, 4-methylthiophenyl; E^+ = PhSeCl, NIS, $Hg(OAc)_2$, $Hg(TFA)_2$, $Hg(NO_3)_2$

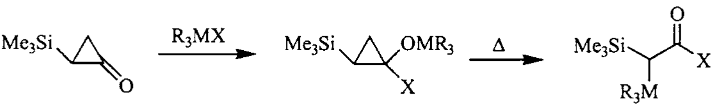


Trialkylsilylcyclopropanones were reacted with a variety of reagents, which give addition to the carbonyl group. The resulting carbonyl adducts underwent ring opening upon heating.[292]



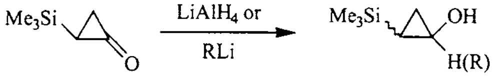
R_3Si = Me_3Si, Et_3Si; E-Nu = MeOH, Me_2NH, (–)-menthol, H_2O, Et_3SiOH, Et_3SnOMe, Bu_3SnOMe, Me_3SiNMe_2; Et_3SnNMe_2, $Me_3SiP(O)(OEt)_2$

Trimethylsilylcyclopropanones were shown to react with methoxy- or aminosubstituted silanes, germanes or stannanes to give addition to the carbonyl group.[293]

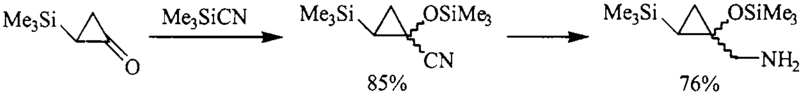


R = Me, Et, Bu; M = Si, Ge, SnX = MeO, Me_2N, Et_2N

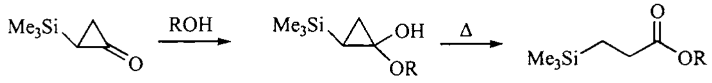
Trimethylsilylcyclopropanone was shown to react normally with lithium aluminum hydride or organolithium reagents to give the β-hydroxysilane, which, of course, does not undergo a facile elimination as do other β-hydroxysilanes.[294]



Trimethylsilylcyclopropanone reacts normally with trimethylsilyl nitrile to give the silylated cyanohydrin in good yield. Reduction provides the ethanol amine.[295]



Trimethylsilylcyclopropanone was reacted with water, alcohols, secondary amines and triethylsilanol to give the adduct of the carbonyl group.[296] These derivatives upon further heating gave ring opening and 3-trimethylsilylpropionic acid derivatives. In addition the reaction of 2-trimethylsilylcyclopropanones with a variety of nucleophiles was reported.[297]

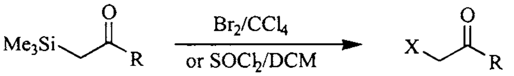


R = OH, MeO, Me_2N, Et_3SiO

11.3. Electrophilic Reactions of α-Silyl Ketones

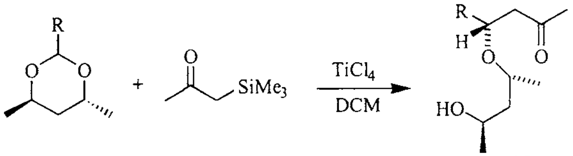
The electrophilic bromination of α-silyl ketones was used in the preparation of 1,3-diene epoxides.[298]

The reaction of α-silyl ketones with bromine or with thionyl chloride provides good yields of the α-halo ketone.[299]



X = Br 55–90%
X = Cl 64–89%

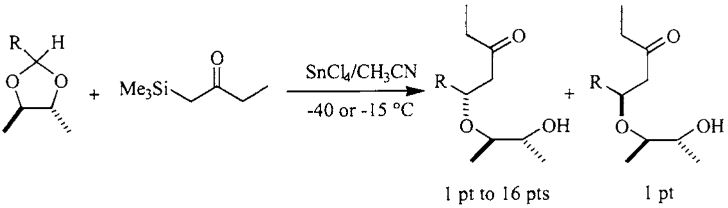
Johnson and co-workers[300] found that trimethylsilyl acetone reacts equally as the silyl enol ether with acetals derived from (*R*,*R*)-2,4-pentanediol. These reactions give diastereomer **125** predominantly.



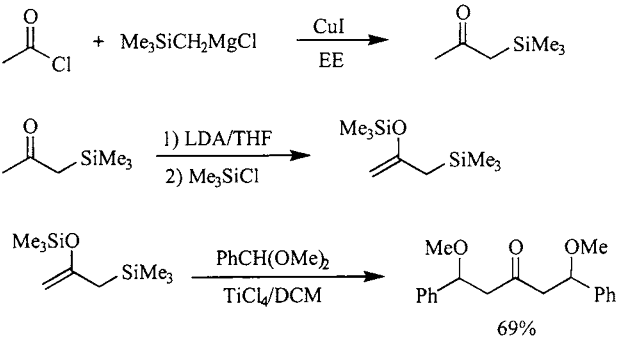
125

R = ${}^{n}C_8H_{17}$, c-C_6H_{11}, $H_2C{=}CHCH_2CH_2$; 92–93% yields; diastereoselectivity >97:3.

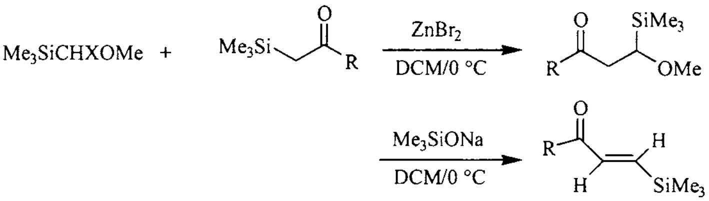
The reaction of 1-trimethylsilyl 2-butanone directly with chiral acetals derived from (*R*,*R*)-2,3-butane diol in the presence of tin tetrachloride to give the corresponding β-alkoxy ketone with moderate diastereoselectivity.[301]



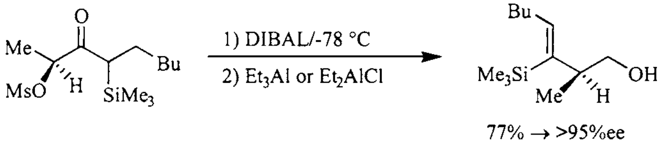
Formation of the silyl enol ether of the kinetic enolate of trimethylsilylacetone leads to a reagent, which can react with electrophiles in both the α- and α′-positions.[302]



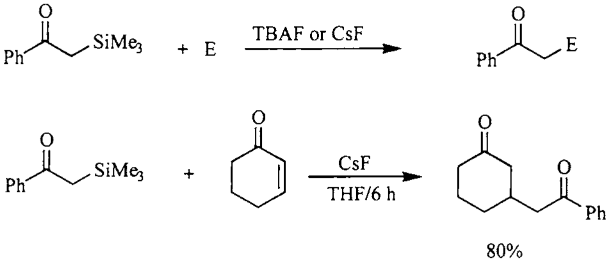
Trimethylsilylmethyl ketones were electrophilically reacted with methoxyhalomethyltrimethylsilane under the influence of zinc bromide to give β-methoxy-β-trimethylsilyl ketones, which upon elimination give β-trimethylsilyl α,β-unsaturated ketones.[303]



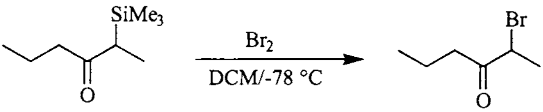
α-Silyl-α,β-unsaturated ketones containing an α′-mesyl group were shown to undergo a reductive rearrangement with migration of the vinylsilyl group and inversion at the α′-position.[304]



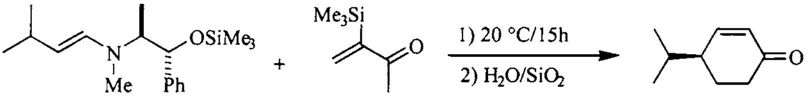
It has been shown that α-silyl ketones react with carbon electrophiles under the influence of fluoride ion catalysis.[305] The electrophiles reacted were benzaldehyde, cyclohexenone, benzyl bromide, allyl bromide, phenacyl bromide, benzoyltrimethylsilane, and 2-furoyltrimethylsilane.



The bromination of 2-trimethylsilylhex-3-one provided the 2-bromoketone directly.[306]

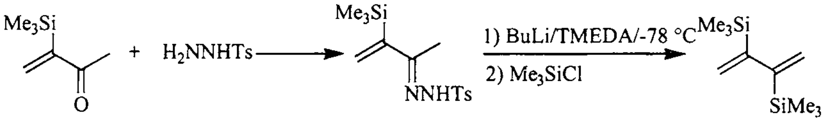


Ito and co-workers[307] have found that the reaction of optically active enamines with 3-trimethylsilylbuten-2-one gives cyclohexenones in relatively good enantiomeric excess.

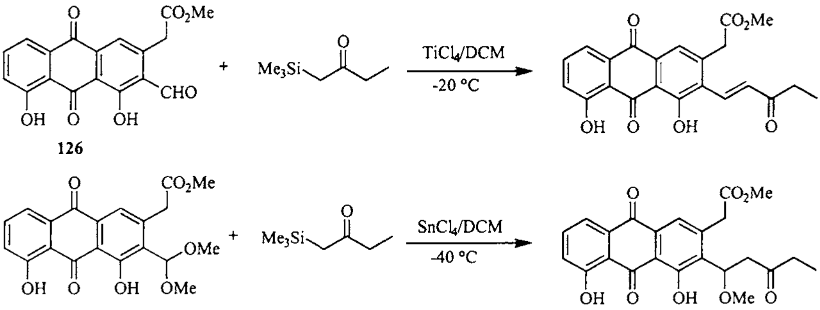


50% yield 53% ee (S)

The tosylhydrazone of 2-trimethylsilylbut-3-one was used in a Shapiro reaction to prepare 2,3-bis(trimethylsilyl)buta-1,3-diene, which was, in turn, used as a Diels–Alder diene in its reaction with various dienophiles.[308]



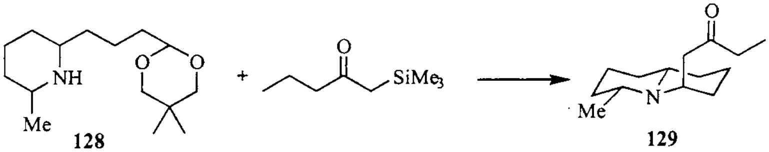
Kishi and co-workers[301,309] utilized the Lewis acid condensation of 1-trimethylsilyl 2-butanone with aldehyde **126** or better with the acetal **127** in a practical total synthesis of (±)-aklavinone and aklavin.



126

127

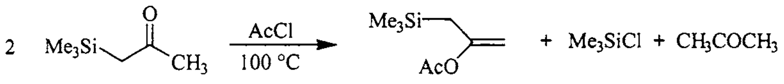
In a procedure, which employs an α-trimethylsilyl ketone as a substitute for a regiospecifically generated enol silyl ether, Ryckman and Stevens were able to prepare piperidine **129** from **128**.[310]



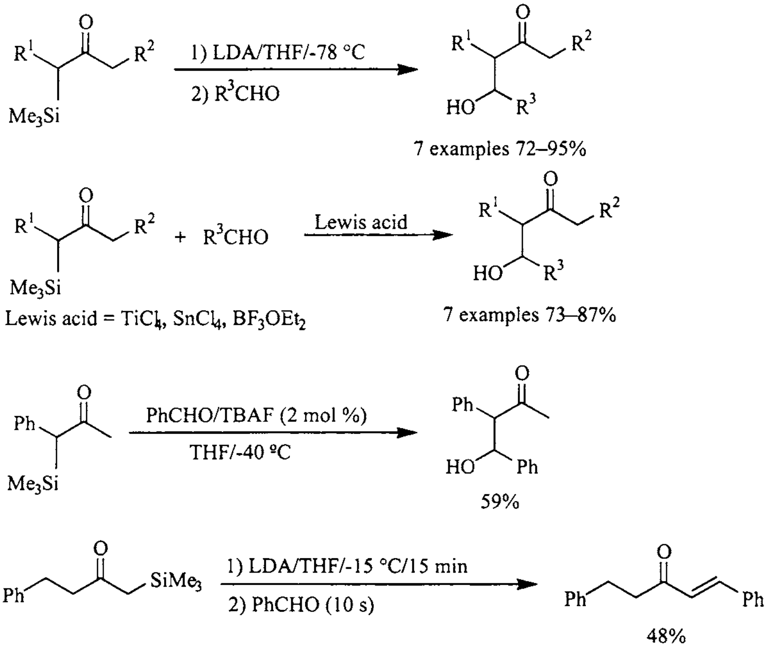
128

129

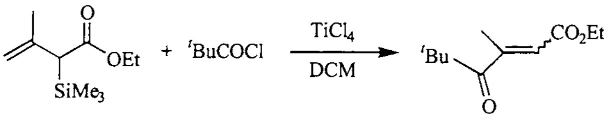
Two equivalents of trimethylsilyl acetone react with acetyl chloride at 100 °C to give acetone, trimethylchlorosilane and 2-acetoxy-3-trimethylsilylpropene.[311]

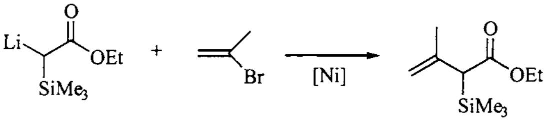


α-Trimethylsilyl ketones were shown to be very useful in directing the site of aldol condensations of the ketone.[273] Deprotonation of the α-silyl ketone with LDA occurs on the side opposite to the bulky trimethylsilyl group and hence condensation of the anion with aldehydes occurs away from the trimethylsilyl group. On the other hand, Lewis acid-catalyzed condensation of the α-silyl ketone with aldehydes occurs at the α-position containing the trimethylsilyl group. The steric effect of the trimethylsilyl group in the absence of another substituent is not enough to direct the deprotonation to the opposite side of the molecule as is seen below.

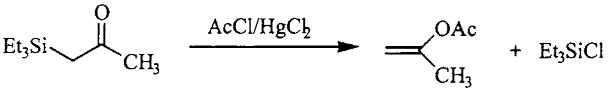


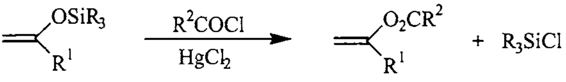
In order to circumvent the problems of α- versus γ-attack of the enolate ions prepared from α,β-unsaturated esters, Katzenellenbogen and Albaugh-Robertson[312] turned to the use of α-trimethylsilyl-β,γ-unsaturated esters, prepared by the nickel-catalyzed vinylation of ethyl trimethylsilylacetate. These esters react as allylsilanes with double bond transposition to give the γ-substituted product with excellent regioselectivity.



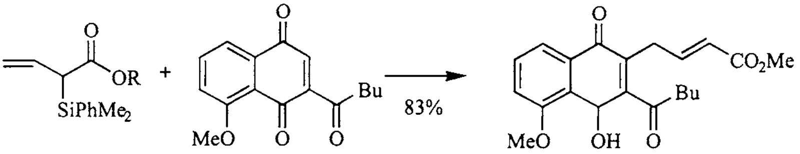


Triethylsilylacetone was shown to react with acetyl chloride in the presence of mercuric chloride to give the enol acetate of acetone.[313] Enol silyl ethers also give enol acetates under the same conditions, thus it is not clear whether the silyl ketone is reacting or if it is first isomerized to the enol silyl ether prior to reacting.





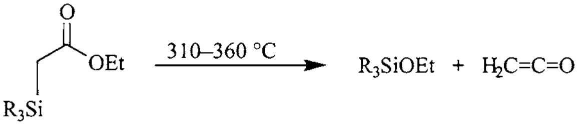
A derivative of the Katzenellenbogen ester, methyl 2-phenyldimethylsilylbut-3-enoate, was deprotonated and then reacted with quinone **130** to give the product of allylation **131**.[313]



130 **131**

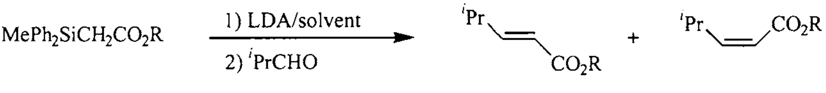
12. REACTIONS OF α-SILYL ESTERS

The first order, thermal elimination of ethyl α-silylacetates was studied kinetically.[314] It was found that the substitution of a phenyl group for a methyl group of the trimethylsilyl group resulted in a slightly faster rate due to the favorable electronic effect, but that the substitution of two or three of the methyls by phenyl groups hindered the rate due to steric factors.

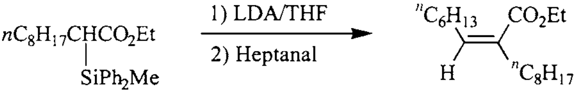


12.1. Enolate Reactions of α-Silyl Esters

Larson and co-workers[315] studied the stereochemical manifestations of changes in the steric requirements of the ester group of the reaction of lithium enolates of α-(methyldiphenylsilyl) esters with isobutyraldehyde. It was found that more of the *E*-isomer is formed at −78 °C than at 0 °C at which temperature the *Z*-isomer predominates. More *Z*-isomer is also obtained when the reaction is carried out in the presence of 12-crown-4, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine or HMPA. It is argued that the lack of stereoselectivity is a result not of the mode of addition of the enolate to the aldehyde, but rather of the mode of elimination in which a carbonyl stabilized intermediate which can rotate is involved.

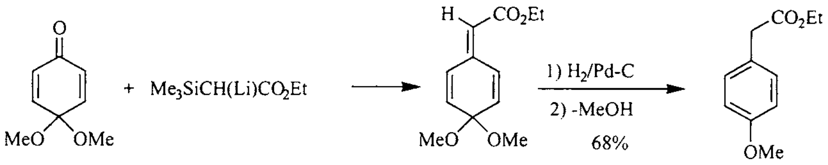


Larson and co-workers[316] were able to prepare α-substituted-α,β-unsaturated esters via the reaction of the lithium enolates of α-(methyldiphenylsilyl) esters with aldehydes. The reaction showed only moderate stereselectivity in favor of the *Z*-isomer.

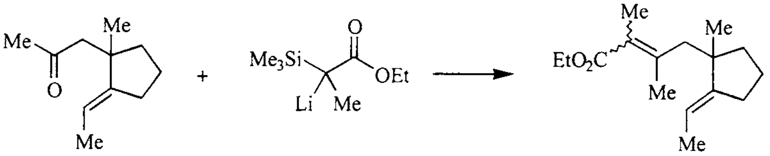


62% yield *Z*:*E* = 71:29

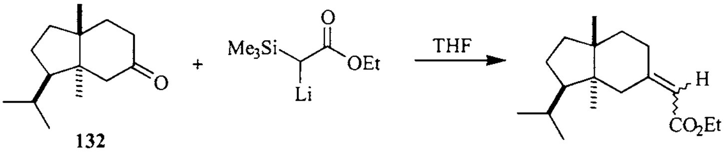
The reaction of the lithium enolate of ethyl trimethylsilylacetate with monoprotected *p*-quinones was used for the arylation of anions as shown below.[317]



Snider and Beal[318] utilized the lithium reagent of ethyl trimethylsilylpropionate as a part of their intramolecular ketene cycloaddition approach to seychellene. The Horner–Emmons approach to the necessary α,β-unsaturated esters was not successful.

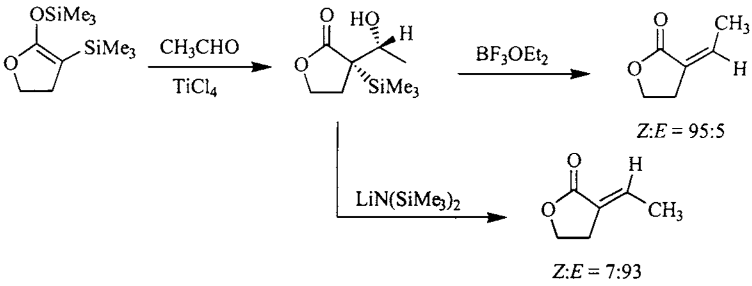


The reaction of ethyl trimethylsilyl(lithio)acetate with ketone **132** was used in a synthesis of (–)-retigeranic acid. Unfortunately, the ratio of *Z*- and *E*-isomers was not given.[319]

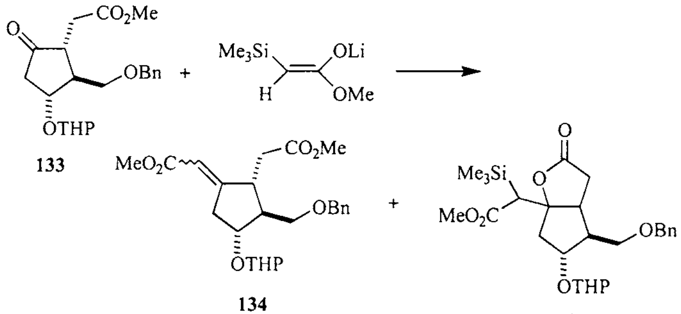


132

The condensation of the trimethylsilylketene acetal of 2-trimethylsilyl γ-butyrolactone with acetaldehyde leads to stereospecific formation of the β-hydroxysilane, which can be eliminated to give predominantly the (*Z*)- or the (*E*)-α-ethylidene-γ-butyrolactone.[320]

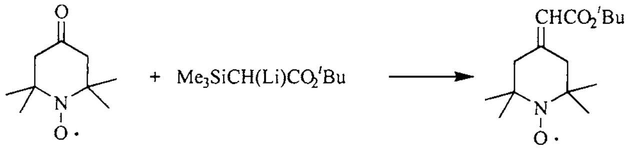


Methyl trimethylsilylacetate was used to provide **134** from ketone **133**. The reaction proceeds in good yield. A small amount of lactone **135** is also obtained.[321]



133 **134** **135**

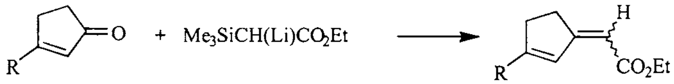
tert-Butyl trimethylsilyl(lithio)acetate was shown to react with the 4-oxo-piperinoxyl **136** to give the olefination product in excellent yield.[322]



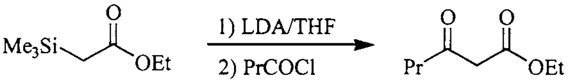
136

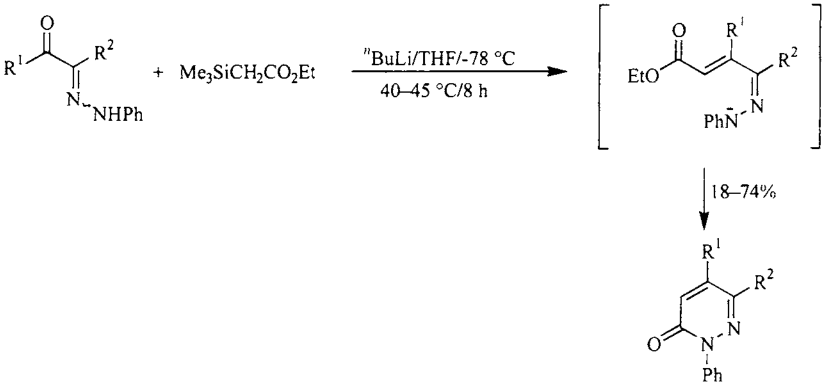
90.5%

The reaction of 3-substituted cyclopentenones with ethyl trimethylsilyl(lithio)acetate was shown to give the dienoic ester as an *E*/*Z* mixture.[323]

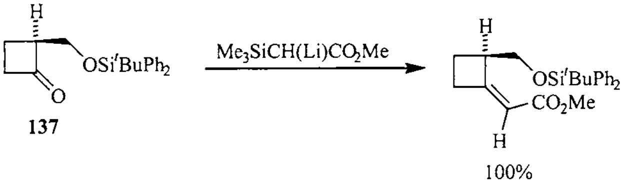


Ethyl trimethylsilyllithioacetate was reacted with butyroyl chloride to give the α-keto ester.[324] The reaction of the lithium enolate of ethyl trimethylsilylacetate with α-ketophenylhydrazones leads to 3-(2H)-pyridazinones.[325]

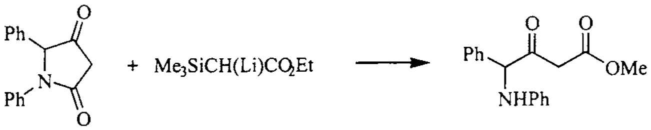




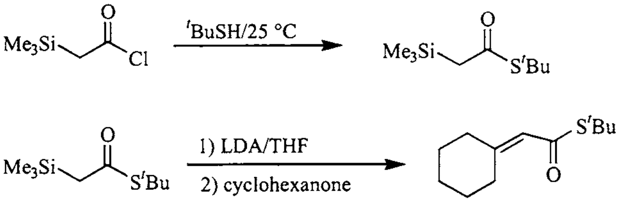
The reaction methyl trimethylsilyl(lithio)acetate with cyclobutanone **137** gave only the *Z*-diastereoisomer in a synthesis of (+)-grandisol.[326]


137

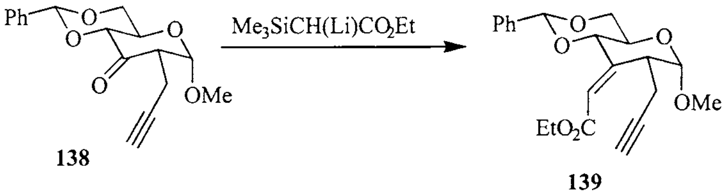
Azasuccinic acid anhydrides were reacted with methyl trimethylsilyl(lithio)acetate to give γ-amino-β-keto esters.[327]



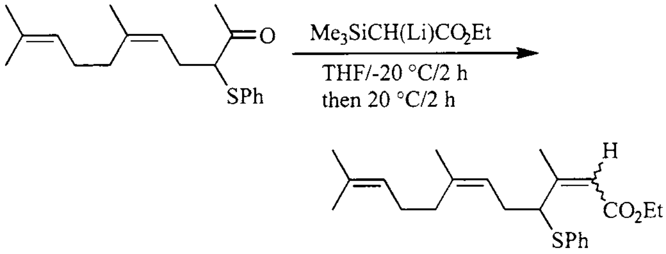
Trimethylsilylacetyl chloride was reacted with *tert*-butylthiol to give the thioester. This was deprotonated and the resulting enolate reacted with cyclohexanone to give the α,β-unsaturated ester.[328]



The reaction of ethyl trimethylsilyl(lithio)acetate with **138** provides **139** as the only isomer.[329] The corresponding Horner–Emmons reagent gives the *Z*-isomer and the axial propargyl derivative in a 6.1:3.3 ratio.

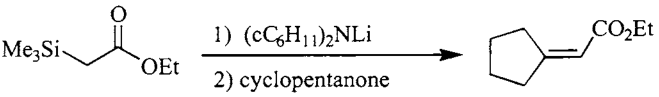


It was shown that the reaction of methyl α-(thiophenoxy)ketones with the lithium enolate of ethyl trimethylsilylacetate gives a mixture of the isomeric α,β-unsaturated esters with the *Z*-isomer predominating.[330]



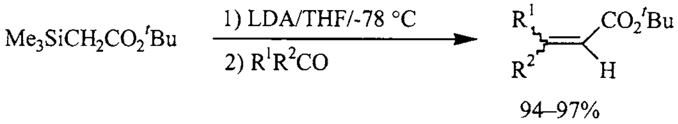
70% *Z*:*E* = 88:12

Shimoji and co-workers[331] were the first to show that the enolate of ethyl trimethylsilylacetate would react in a Peterson fashion to give α,β-unsaturated esters. The stereospecificity of this reaction is not good, however. The reaction provides an improvement over the Horner–Emmons procedure for the readily enolizable ketones such as cyclopentanone.

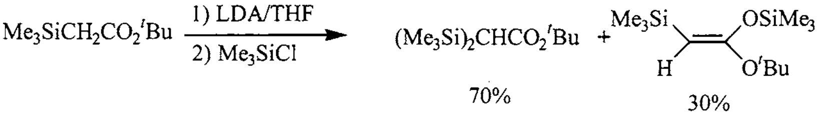


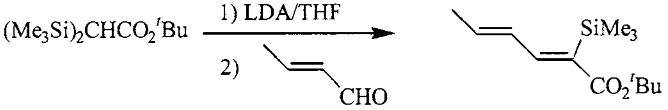
81%

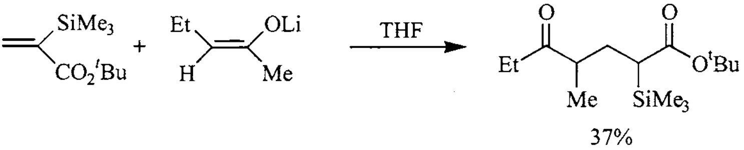
tert-Butyl trimethylsilylacetate was deprotonated and reacted with aldehydes and ketones to give the α,β-unsaturated *tert*-butyl esters in excellent yields.[332]



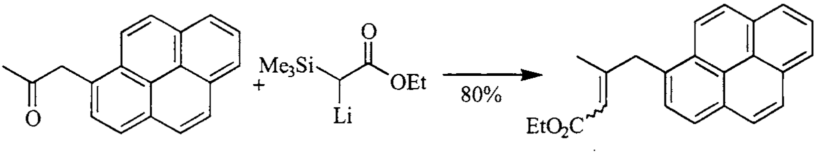
tert-Butyl bis(trimethylsilyl)acetate was prepared by trimethylsilylation of the lithium enolate of *tert*-butyl trimethylsilylacetate.[333] This product was accompanied by about 30% of the silyl ketene acetal. Deprotonation of the bis(trimethylsilyl)acetate is accomplished in the normal fashion and condensation of this enolate with aldehydes, but not ketones, which are deprotonated, gives α-trimethylsilyl-α,β-unsaturated esters. In one example *tert*-butyl-2-trimethylsilylacrylate was shown to be a Michael acceptor, although the yield of the adduct was a modest 37%.





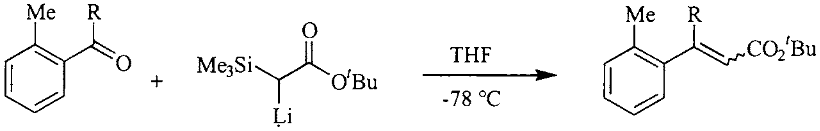


Ethyl trimethylsilyl(lithio)acetate was used successfully to convert the pyrenyl ketone **140** to the α,β-unsaturated ester **141**.[334] Unfortunately, the *E*:*Z* ratio was not reported. Both the Wittig and Horner–Emmons approaches performed poorly in this transformation.



140 **141**

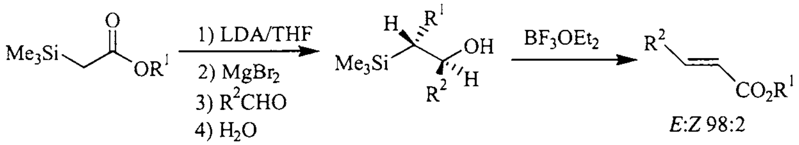
The substituted acetophenones **142** were converted to their α,β-unsaturated esters.[335] The best reagent proved to be *tert*-butyl trimethylsilyl(lithio)acetate. The Horner–Emmons approach worked well for R = Me and Et and the Reformatsky approach worked well only for R = Me.



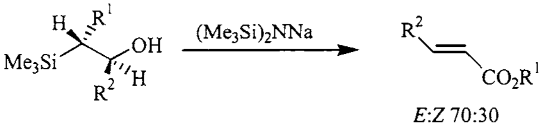
142

R = Me (58%), Et (60%), ^{i}Pr (52%)

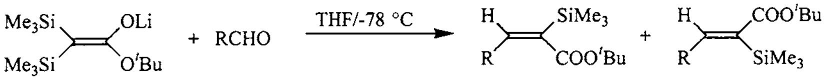
Larcheveque and Deval[336] deprotonated some trimethylsilylacetates with lithium diisopropylamide and then converted the lithium enolate to the bromomagnesium enolate. The condensation of the bromomagnesium enolate with aldehydes gave only a single diastereomeric β-hydroxysilane. Dehydroxysilylation of the diastereomerically homogeneous β-hydroxysilane with boron trifluoride etherate gave the (*E*)-α,β-unsaturated esters in good yield and high selectivity. On the other hand, the elimination under basic conditions with sodium bis(trimethylsilyl)amide gave an *E*:*Z*-isomer ratio of only 70:30. Straight thermolysis of the intermediate β-bromomagnesiumalkoxy silane in HMPA gives an *E*:*Z*-ratio of 15–29:85–71. This implies the intermediacy of an enolate anion which could rotate as an intermediate in the base-promoted elimination.



R^1 = Me, Et, ^{i}Pr; R^2 = Bu, Ph, ^{i}Pr)

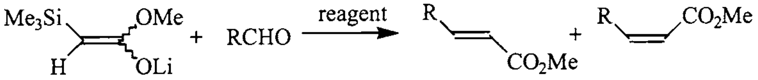


The geometric control of the reaction of the enolates of *tert*-butyl bis(trimethylsilyl)acetate with aldehydes to give 2-trimethylsilyl-3-substituted acrylates was investigated as a function of the counterion of the enolate and the aldehyde.[337] It was found that lithium and potassium enolates give a high degree of the *E*-isomer, but magnesium and aluminum enolates tend to give more of the *Z*-isomer. The arguments in this work do not consider, however, the possibility of enolate formation during the elimination step.



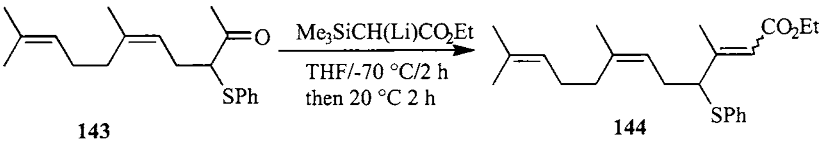
R = ^{t}Bu; $M^+ = Li^+$ Or K^+	> 99	< 1
R = ^{t}Bu; $M^+ = BrMg^+$	30	1
R = ^{t}Bu; $M^+ = Et_2Al^+$	1	9

The reaction of trimethylsilyl ketene acetal of methyl trimethylsilylacetate was used in a study of the stereoselectivity of the conversion of aldehydes to α,β-unsaturated esters.[338] Best results for the generation of the *E*-geometry were obtained with aluminum chloride in carbon tetrachloride and zinc chloride in benzene. The best reagent for the generation of the *Z*-diastereomer was titanium tetrachloride in dichloromethane.



$AlCl_3/CCl_4$	96	4
$ZnCl_2/C_6H_6$	96	4
$TiCl_4$/DCM	5	95

The reaction of ketone **143** with ethyl trimethylsilyl(lithio)acetate provides an 88:12 *Z*/*E* ratio of unsaturated esters **144**.[339]

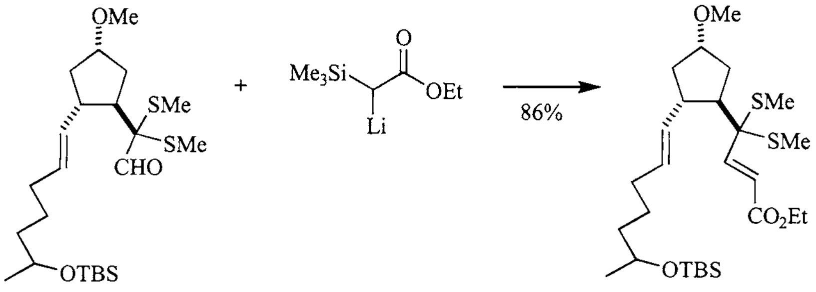


143

144

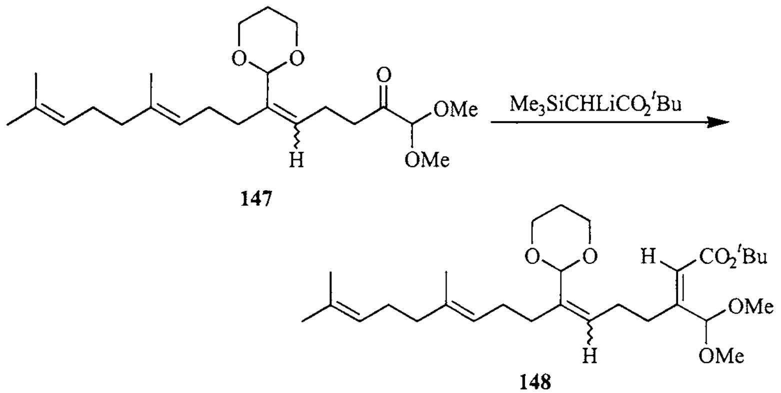
70% yield *Z*/*E* = 88:12

In an approach to brefeldin-A, ethyl trimethylsilyl(lithio)acetate was reacted with α,α-bis(methylthio)aldehyde **145** to give **146**.[340]



145 **146**

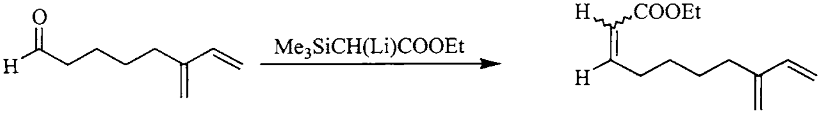
The α,α-bis(methoxy)ketone **147** was reacted with *tert*-butyl trimethylsilyl(lithio)acetate to give **148**, predominantly as the *Z*-diastereomer.[341] The condensation of ethyl trimethylsilyl(lithio)acetate was used in a synthesis of retinal and rhodopsin analogs.[342]



147

148

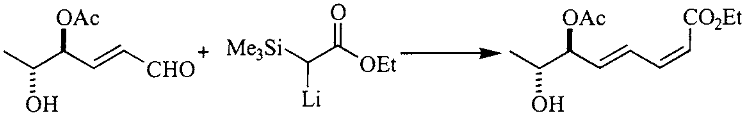
Whereas the sodium Horner–Emmons reagent gives essentially only the *E*-isomer in its reaction with **149**, the ethyl trimethylsilyl(lithio)acetate gives a 57:43 mixture of (*E*)- to (*Z*)-α, β-unsaturated esters.[343]



149

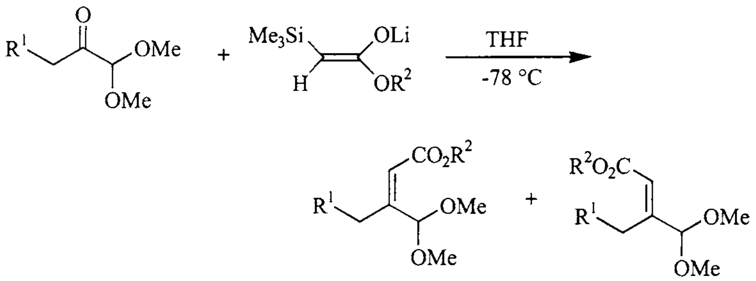
E:*Z* = 57:43

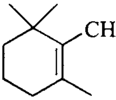
Ethyl trimethylsilyl(lithio)acetate was reacted with acrolein derivatives in order to produce ethyl dienoates. The stereoselectivity was not high, however.[344]



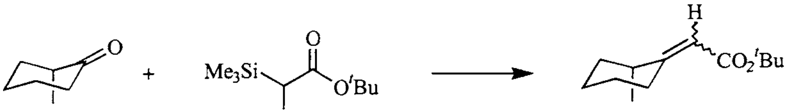
Z:E = 2:1

The stereoselectivity of the addition of the Peterson type olefination versus the Horner–Emmons methodology for the formation of α,β-unsaturated esters was tested in their reactions with the dimethylacetals of α-ketoaldehydes.[345] The Horner–Emmons reagent gave only very poor yields, whereas the lithium enolate of α-trimethylsilylesters gave good yields and very good stereoselectivity for the Z-isomers.



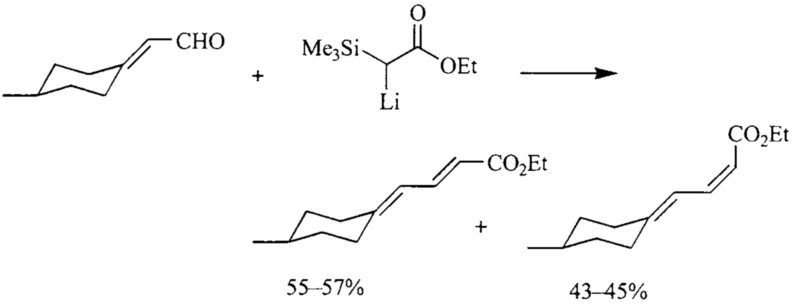
R^1	R^2			Yield
H	Me	56	44	55
H	^{t}Bu	89	11	63
Bu	^{t}Bu	84	16	79
	^{t}Bu	90	10	71

tert-Butyltrimethylsilyl(lithio)acetate was reacted with cyclohexanones as part of a synthesis of chiral cyclohexylidenepropenes by Duraisamy and Walborsky.[346] Both the α-silyl ester and the Horner–Emmons approaches gave the E-diastereomer selectively, with the α-silyl ester providing a slightly higher percentage of the E.

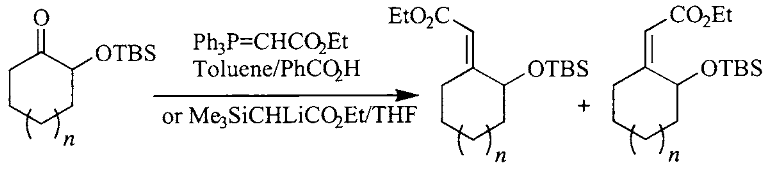


E:Z = 4:1

The olefination of 4-methylcyclohexylidene carbaldehyde with ethyl trimethylsilyl(lithio)acetate gives a mixture of *E*- and *Z*-diastereomers with the *E*-isomer predominating slightly.[347]

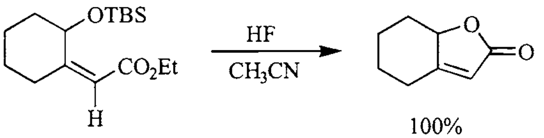


In a further study on the stereochemistry of the Peterson approach to α,β-unsaturated esters, α-*tert*-butyldimethylsilyloxycycloalkanones were reacted with both ethoxycarbonylmethylenetriphenylphosphorane and ethyl trimethylsilyl(lithio)acetate with the phosphorus system giving high yields of the *E*-diastereomer and the trimethylsilyl reagent the *Z*-diastereomer as the major product.[348] It is argued that the Wittig approach is under thermodynamic control, whereas the trimethylsilyl ester reaction is under kinetic control. This finding was put to use in the synthesis of fused butenolides.[349]



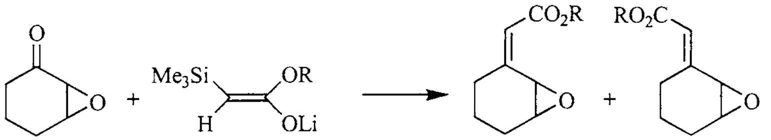
A = $Ph_3P{=}CHCO_2Et$
B = $Me_3SiCHLiCO_2Et$

n	method			Yield
0	A	97	3	52
0	B	33	67	64
1	A	96	4	80
1	B	14	86	68
2	A	94	6	27
2	B	8	92	50



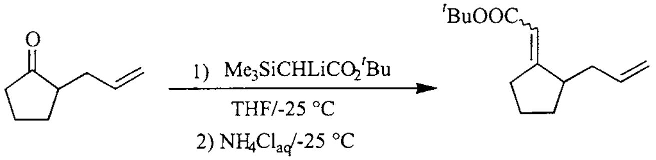
100%

The stereoselective alkoxycarbonylmethylenation of substituted cyclohexanones was realized by their reaction with the lithium or potassium enolate of α-trimethylsilyl esters. Here again the Horner–Emmons approach gave poor results.[350] Examples of the results from the reaction with 2,3-epoxycyclohexanone are given.

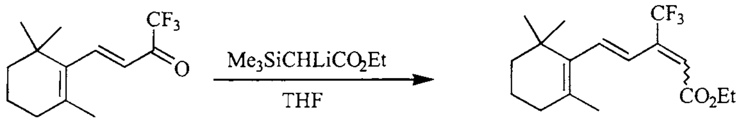


M	R			Yield
Li	^{t}Bu	78	22	60
K	Et	92	8	60
$(EtO)_2P(O)CHNaCO_2Et$		50	50	70

The reaction of the lithium enolate of *tert*-butyl trimethylsilylacetate with 2-allylcyclopentanone gives a mixture of the (*Z*)- and (*E*)-α,β-unsaturated esters, which upon saponification with trifluoroacetic acid gave the unsaturated acid in a *Z*:*E* ratio of 2:1.[351]

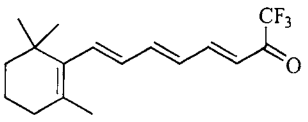


The reaction of ketone **150** with ethyl trimethylsilyl(lithio)acetate provides the corresponding α,β-unsaturated ester in good yield.[352] Similar results were obtained in the reaction of the extended ketone **151**.[353]



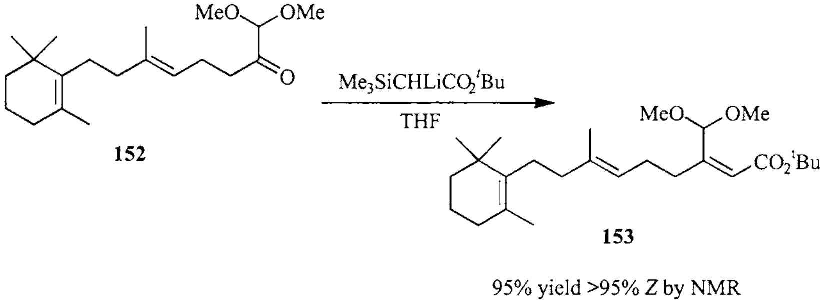
150

98% 1:1 *E*:*Z*

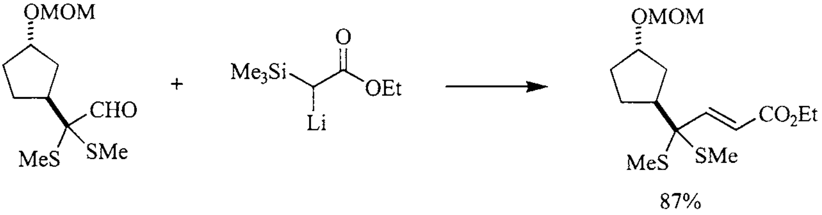


151

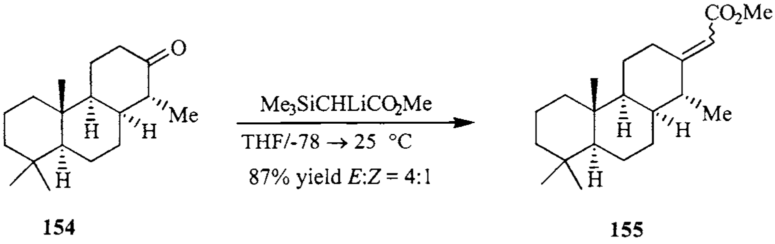
The reaction of *tert*-butyl trimethylsilyl(lithio)acetate with ketone **152** gives a 95% yield of the α,β-unsaturated ester **153**, which was shown by NMR to be greater than 95% *Z*-isomer.[354]



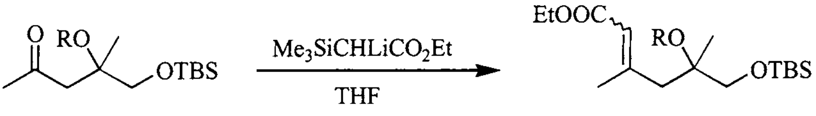
Ethyl trimethylsilyl(lithio)acetate was reacted with α,α-dimethylthioaldehydes to give very high (*E*)-α,β-unsaturated esters.[355]



The lithium enolate of methyl trimethylsilylacetate was reacted with steroidal ketone **154** to give a 4:1 E:Z mixture of α,β-unsaturated esters **155** in excellent yield.[356] The reaction of **154** with the Wadsworth–Emmons reagent gave only a 30% conversion to **155**, probably due to enolization of the ketone.



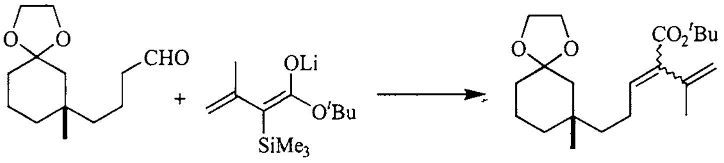
The reaction of the lithium enolate of ethyl trimethylsilylacetate with the substituted ketone **156** gives a 1:2.3 *Z*:*E* mixture of α,β-unsaturated esters.[357]



156

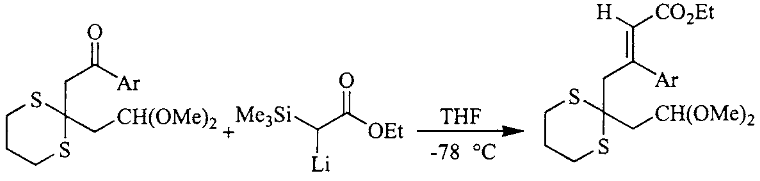
R = CH_3SCH_2 *Z*:*E* = 1:2.3

The lithium enolate of *tert*-butyl 2-trimethylsilyl-3-methylbut-3-enoate was used to prepare dienoate **157** as a 2:1 mixture of *E*- and *Z*-diastereomers.[358]



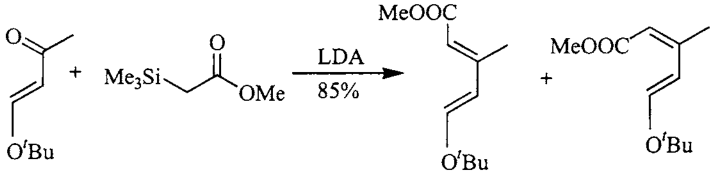
157

The reaction of aldehyde **158** with the Horner–Emmons–Wittig reagent gave only poor yields of the desired α,β-unsaturated ester, but the Peterson olefination approach with ethyl trimethylsilyl(lithio)acetate provided a good yield of an approximate 50:50 mixture of the diastereomeric unsaturated esters, **159**.[359]



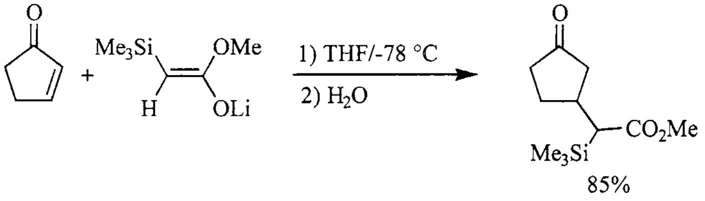
158 **159**

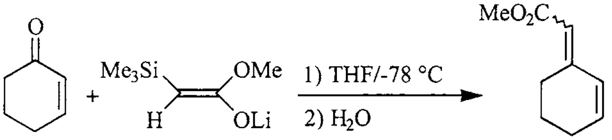
The lithium enolate of methyl trimethylsilylacetate was used to prepare the dienes **160** and **161**, which were used as dienes in the construction of aklavinones. This procedure, however, was discarded in favor of a Wittig procedure due to the difficulty in obtaining the enol ethers.[360]

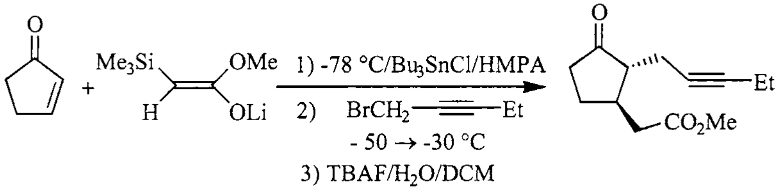


160 67% **161** 33%

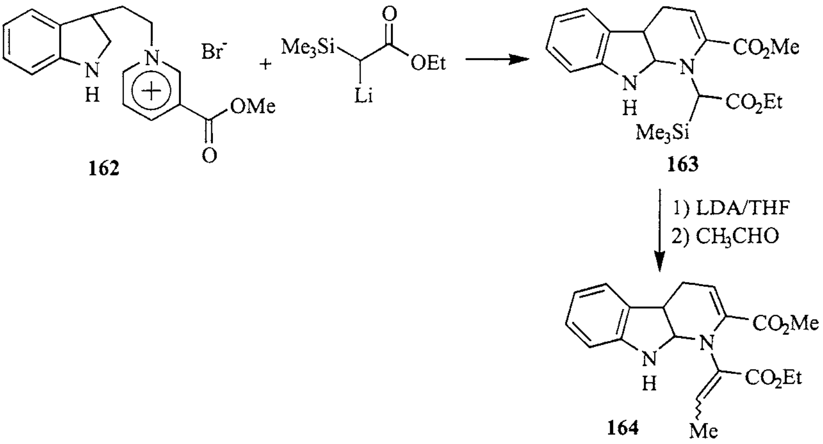
The lithium enolate of methyl trimethylsilylacetate was shown to react in a Michael fashion with cyclopentenones, but not with cyclohexenone with which it reacted in a 1,2-manner.[361] This finding was utilized in an addition to the many syntheses of methyl jasmonate.







The pyridinium bromide **162** was reacted with ethyl trimethylsilyl(lithio)acetate to give **163**, which was in turn deprotonated and reacted with acetaldehyde to give the α,β-unsaturated ester **164**.[362]

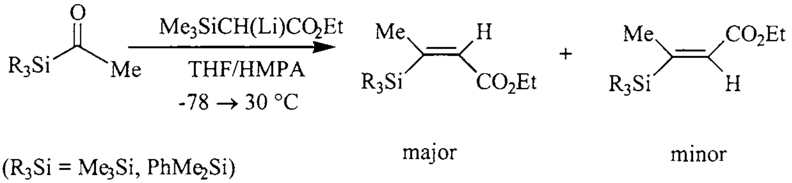


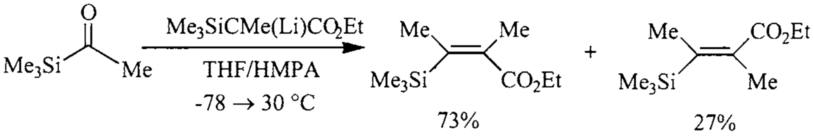
162

163

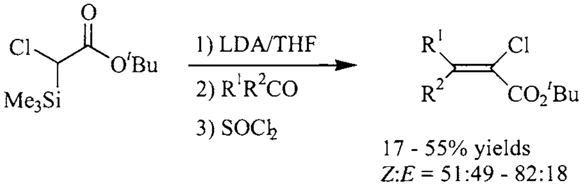
164

Acylsilanes were reacted with the lithium enolates of α-trimethylsilyl esters to give the β-silyl-α,β-unsaturated esters in moderate yields.[363]

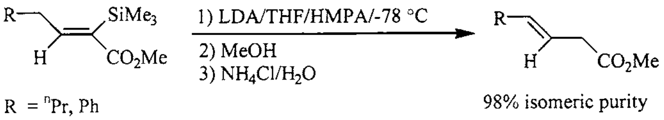


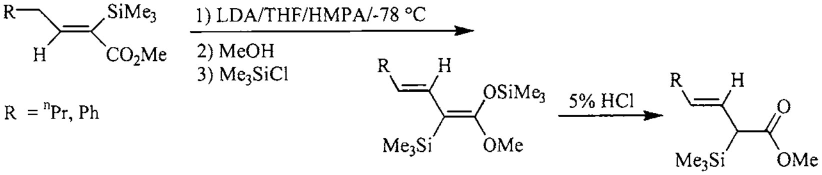


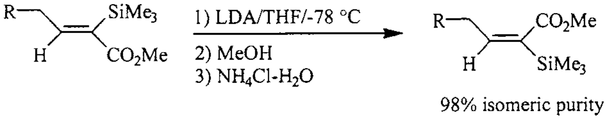
Deprotonation–trimethylsilylation of *tert*-butylchloroacetate gives *tert*-butyl chloro(trimethylsilyl)acetate, which can in turn be deprotonated and reacted with aldehydes and ketones.[364] This was done by Chan and co-workers, who were thusly able to prepare α-chloro-α,β-unsaturated esters. The elimination of the β-alkoxysilane is not as facile as in other systems and is best carried out by the addition of thionyl chloride. The stereoeselectivity favors the *Z*-isomer.

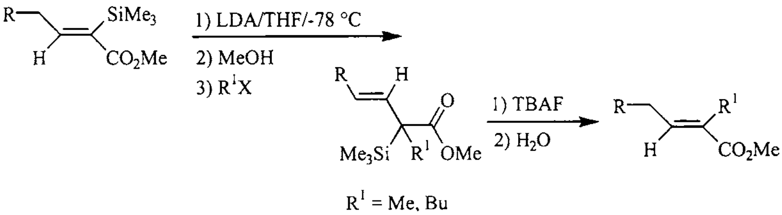


Zweifel and co-workers[365] were able to deprotonate (*E*)-α-trimethylsilyl-α,β-unsaturated esters and convert them to β,γ-unsaturated esters and α-trimethylsilyl-β,γ-unsaturated esters. The *E*-isomers required LDA in the presence of HMPA for deprotonation, whereas the *Z*-isomers could be deprotonated with LDA in THF alone. Deuteration experiments showed that the initial protonation occurs on the α-carbon followed by protiodesilylation. Alkylation of the anion of the α-trimethylsilyl-α,β-unsaturated esters gives the α-alkylation product, which when treated with tetrabutylammonium fluoride provide the (*E*)-α,β-unsaturated ester.

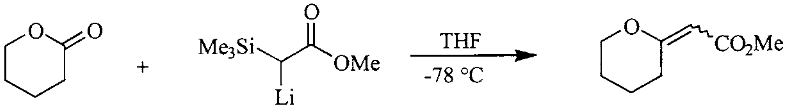




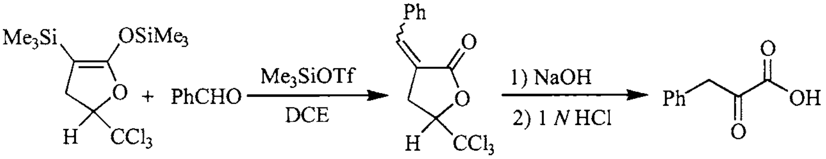




Methyl trimethylsilyl(lithio)acetate was reacted with δ-valerolactone to give the cyclic enol ether.[366]

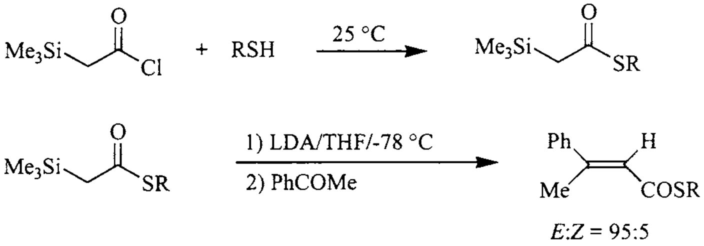


The cyclic trimethylsilyl ketene acetal **165** was reacted with aldehydes in the presence of trimethylsilyl triflate to yield α-oxo carboxylic acids.[367]

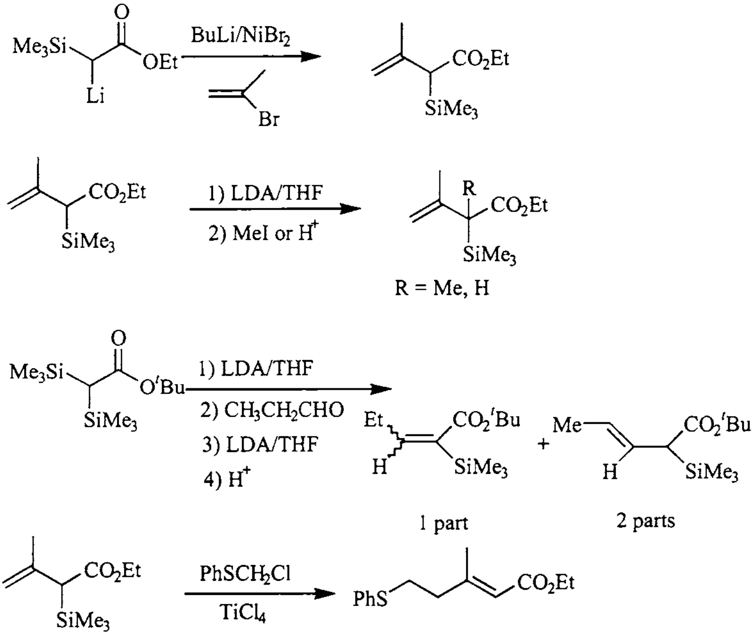


165

Trimethylsilylacetyl chloride was reacted with thiols to give the thiol esters. This was in turn converted to α,β-unsaturated thiol esters in good yields by simple deprotonation followed by condensation with an aldehyde or ketone.[368] The stereoselectivity of the reaction was very high in favor of the *E*-isomers.

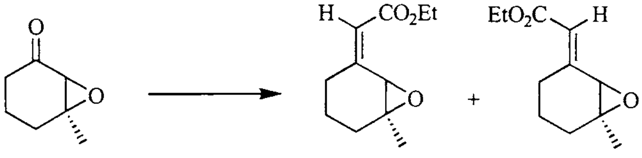


In order to bring about clean γ-substitution of an α,β-unsaturated ester Katzenellenbogen and Albaugh-Robertson resorted to the use of ethyl 2-trimethylsilylbut-3-enoates, which react with electrophiles as allyltrimethylsilanes with double bond transformation resulting in introduction of the electrophile in the γ-position.[369] The 2-trimethylsilylbut-3-enoates were synthesized by vinylation of ethyl trimethylsilyl(lithio)acetate, a Peterson olefination with *tert*-butyl bis(trimethylsilyl)acetate, followed by deprotonation–protonation of the 2-trimethylsilyl 2-butenoates.



Aldehydes and acid chlorides were also reacted

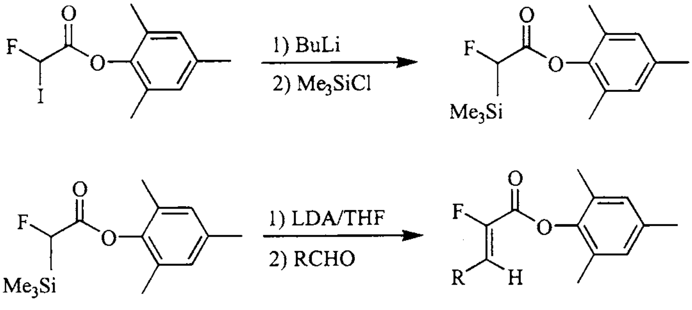
The reaction of ethyl trimethylsilyl(lithio)acetate with epoxyketone **166** was reported.[370] This gives a *Z*:*E* ratio of α,β-unsaturated esters of 78:22. When this conversion was carried out with triethyl sodium phosphonoacetate the *Z*:*E* ratio was 55:45. Related chemistry was reported for the α-trimethylgermyl acetates.[371]



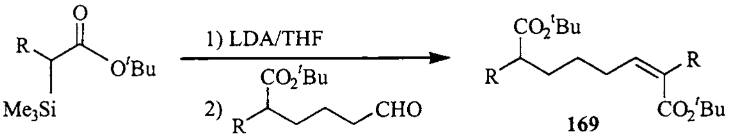
166

$Me_3SiCH(Li)CO_2Et$	78%	22%
$(EtO)_2P(O)CH(Na)CO_2Et$	55%	45%

Welch and Herbert[372] reported the reaction of the lithium enolate of 2,4,6-trimethylphenyl trimethylsilyl(fluoro)acetate, prepared by direct trimethylsilylation of the lithium enolate of the ester, in good yields with aldehydes and in poorer yields with ketones to give α,β-unsaturated ester with *Z*:*E* diastereomeric ratios of as high as 50:1.



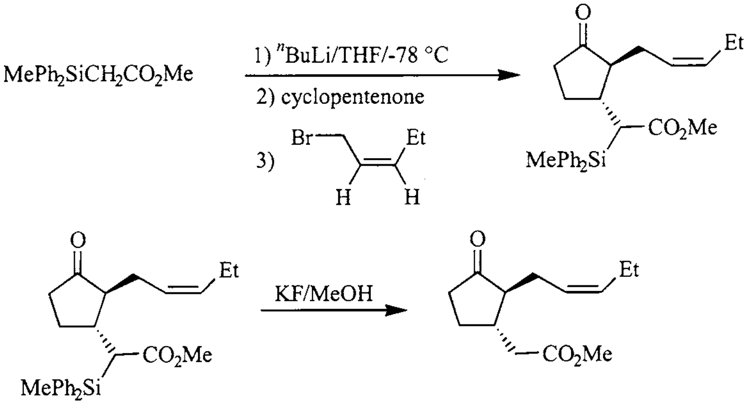
The lithium enolate **167** was reacted with aldehyde **168** to give the (*Z*)-α,β-unsaturated ester **169** along with 30% of the *E*-isomer.[373]



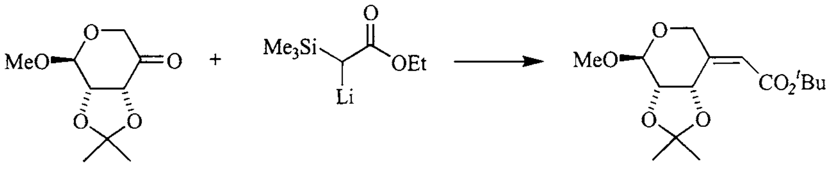
167 **168** **169**

73% yield; 70% (*Z*)

The conversion of cyclopentenone to (±)-methyl jasmonate was accomplished by the Michael addition of the lithium enolate of methyl α-(methyldiphenylsilyl)acetate to cyclopentenone and trapping of the enolate ion with *cis*-1-bromopent-2-ene and finally protiodesilylation with potassium fluoride in methanol.[374] The ethyl ester also works well in this sequence and both of these α-(methyldiphenylsilyl)acetates are better than the trimethylsilyl derivatives.



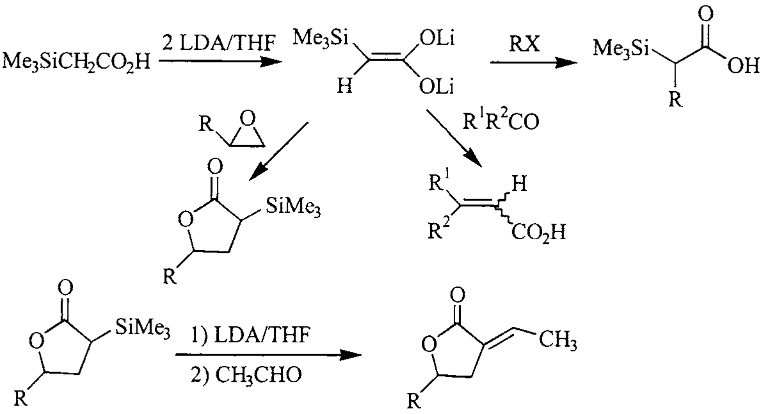
The reaction of *tert*-butyl trimethyl(lithio)acetate on ketone **170** was used in the synthesis of neopatulin.[375] The reaction gave a high degree of *Z* selectivity, whereas the Wittig approach gave greater than 80% of the *E*-isomer. This is somewhat consistent with the results of Larson and co-workers.[348,349]



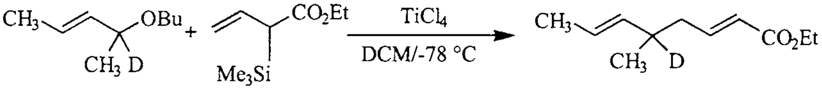
170

88% yield Z:E = 88:12

The dianion of trimethylsilylacetic acid was reacted with alkyl halides to give α-substituted trimethylsilyl acids with aldehydes and ketones to give α,β-unsaturated carboxylic acids and with epoxides to give, after treatment with acid, 3-trimethylsilyl 5-substituted-γ-butyrolactones.[376] These lactones could be deprotonated and condensed with aldehydes to give α-alkylidene-γ-butyrolactones.

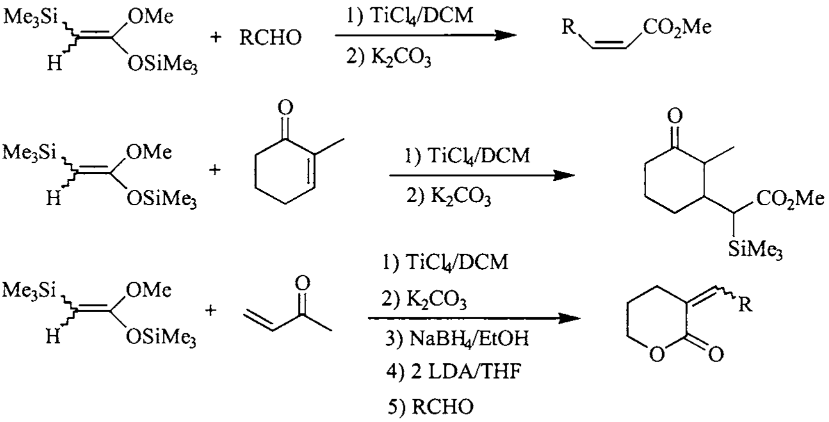


Ethyl 2-trimethylsilyl 3-butenoate was condensed with allyl butyl ether **171** to give the equivalent of γ-alkylation of the ester enolate as a result of double bond transposition of the allylsilane.[377]

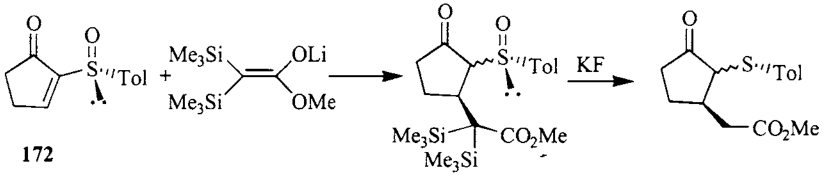


171

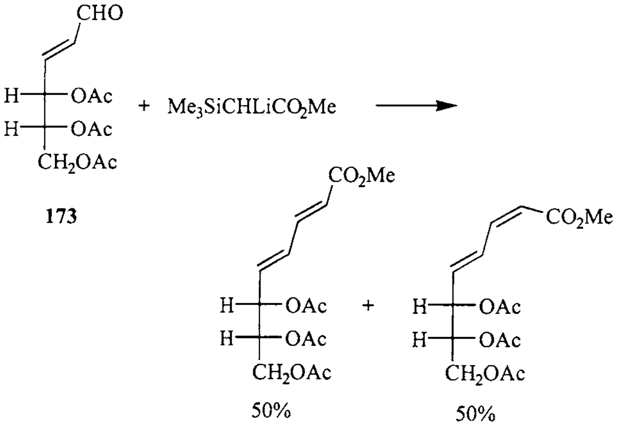
In a variation on the reaction of the lithium enolate of α-silyl esters with aldehydes, the trimethylsilyl ketene acetal of methyl trimethylsilylacetate was reacted with aldehydes leading to α,β-unsaturated esters as well.[378] This reagent reacts with enones to give addition of the trimethylsilylacetate group to the β-position. This adduct with acyclic enones can lead to α-alkylidene lactones.



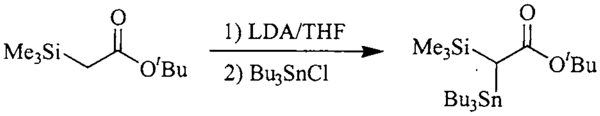
A highly enantioselective synthesis of (–)-methyl jasmonate was accomplished by employing the stereospecific conjugate addition of methyl bis(trimethylsilyl)lithioacetate to the chiral sulfoxide **172** as the key step.[379] The silyl groups were conveniently removed with fluoride ion.

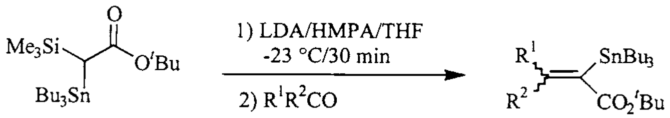

172

In an attempt to prepare *E:Z* dienoates methyl trimethylsilyl(lithio)acetate was reacted with α,β-unsaturated aldehyde **173**. This reagent gave the best stereoselectivity for the *E:Z* diastereomer.[380]


173

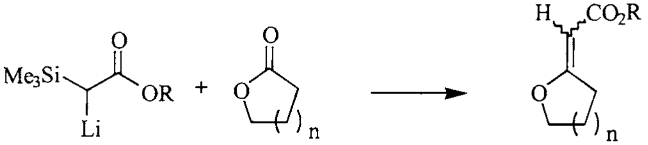
tert-Butyl trimethylsilylacetate can be deprotonated and stannylated to give the α-silyl α-stannyl derivative. Deprotonation of this interesting organometallic species followed by reaction of the enolate with an aldehyde or ketone gives the α-stannyl-α,β-unsaturated ester via beta elimination of trimethylsilanol rather than of tributylstannol.[382]





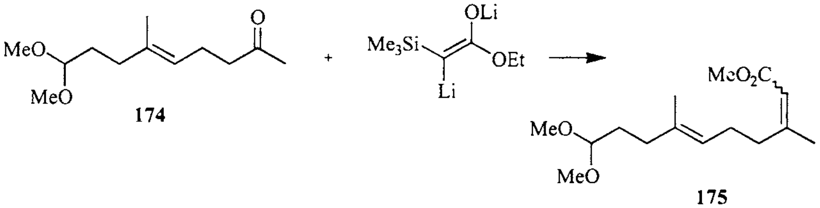
20–70% Z:E 63:37 - 31:69

The lithium enolate of methyl or *tert*-butyl trimethylsilylacetate was reacted with lactones to give tetrahydro-2-pyranylidene and tetrahydro-2-furylidene acetates in moderate yield.[384]

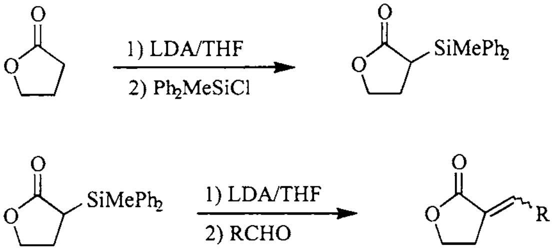


26–70%; E:Z 44:56 - 23:77

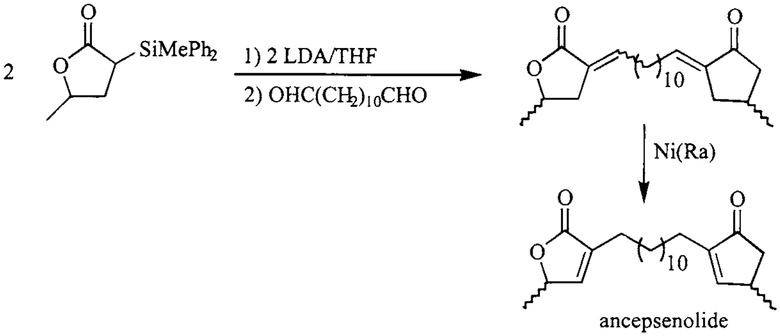
The lithium enolate of ethyl trimethylsilylacetate was reacted with protected keto aldehyde **174** to give a Z:E mixture of α,β-unsaturated esters **175**.[383]



Larson and Betancourt de Perez[384] took advantage of the direct C-diphenylmethylsilylation of the lithium enolates of γ-butyrolactones to prepare the α-silylated lactones. Deprotonation of these followed by reaction with aldehydes provides the α-ylidene lactones. This methodology was used in efficient synthesis of ancepsenolide.

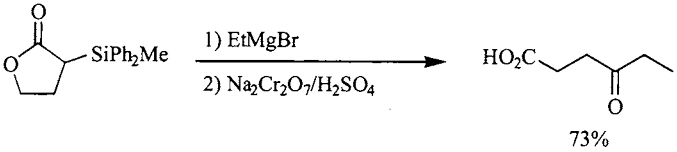


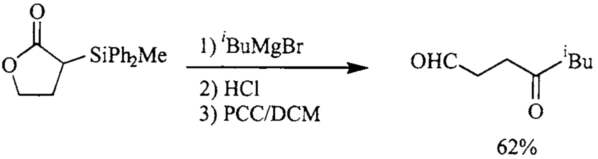
0–89% yields $Z > E$ except with CH_3CHO

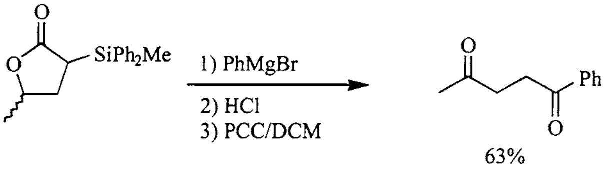


12.2. Reactions of α-Silyl Esters with Nucleophiles

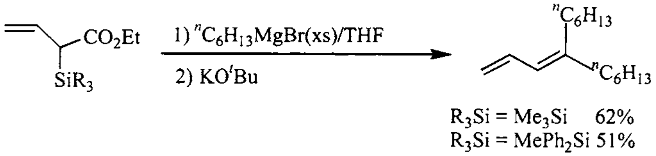
The reaction of α-(methyldiphenylsilyl)lactones with organomagnesium reagents results in 4-oxo carboxylic acids, 4-oxo ketones, or 4-oxo aldehydes, depending on the substitution of the lactone.[12,385]



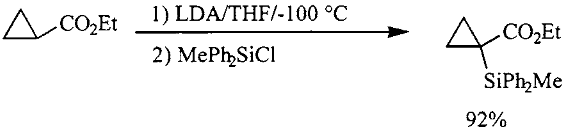


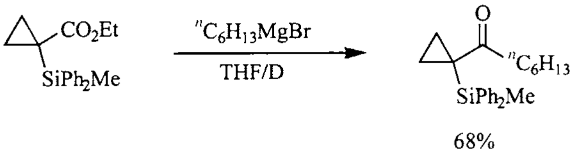


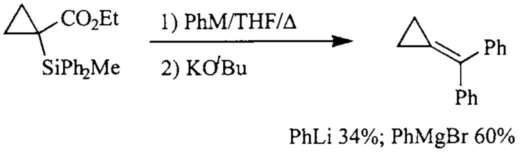
Larson and co-workers[386] demonstrated that 1,3-dienes could be readily prepared by the reaction of organomagnesium, but not organolithium reagents, with α-silyl-β,γ-unsaturated esters followed by elimination.



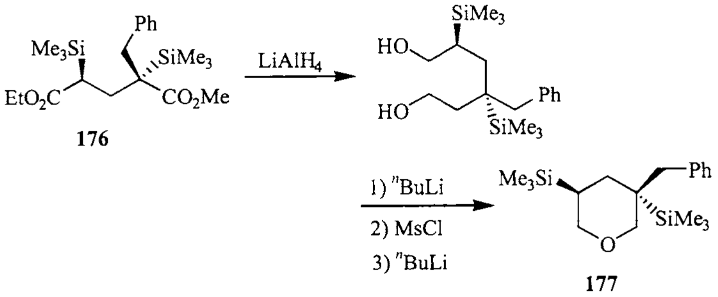
The reaction of ethyl 1-(diphenylmethylsilyl)cyclopropane carboxylate with organolithium and organomagnesium reagents results in the synthesis of the corresponding α-silyl ketone and, in the case of a bis-addition of the organometallic reagent, a Peterson-type olefination to cyclopropylidene derivatives.[387]



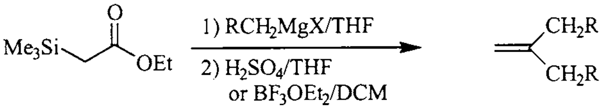




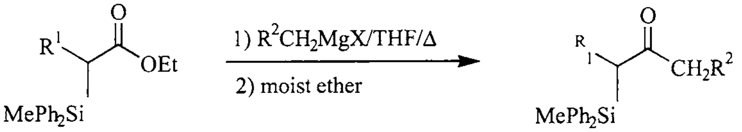
The reduction–cyclization of **176** gives the pyran **177** with a high degree of stereospecificity.[388]



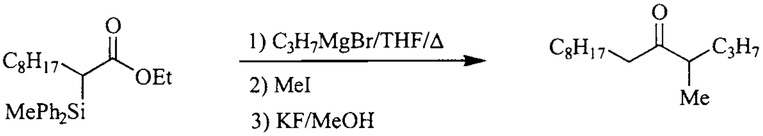
Larson and Hernández[389] showed that the reaction of ethyl diphenylmethylsilylacetate with Grignard reagents in refluxing THF followed by elimination leads to 1,1-disubstituted olefins in good yields. This reaction requires high purity magnesium to avoid numerous side reactions.

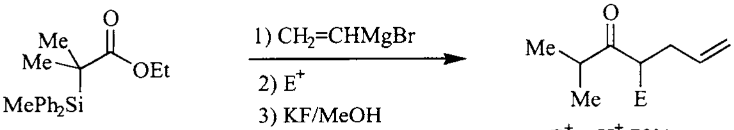


A number of α-silyl esters were reacted with primary Grignard reagents to give, after careful workup with moist ether, the α-silyl ketones in good to excellent yields.[390,391] The α-silyl ketones can be readily desilylated with potassium fluoride in methanol. The intermediate α-silyl ketones are deprotonated by excess Grignard reagent as evidenced by methylation of the magnesium enolate. Vinylmagnesium bromide was found to add to give the intermediate α,β-unsaturated ketone, which undergoes a Michael addition of the second equivalent of vinylmagnesium bromide. The methodology of converting an ester to its α-diphenylmethylsilyl ester and that to a ketone was used in a very short synthesis of a component of the sex pheromone of the Douglas Fir Tussock Moth. This reaction was extended to the synthesis of monoprotected 1,4-[57b] and 1,5-diketones.[57c]



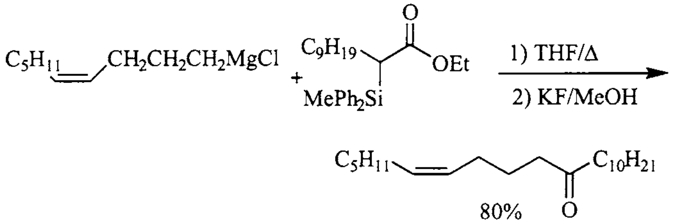
30 examples 22–94%



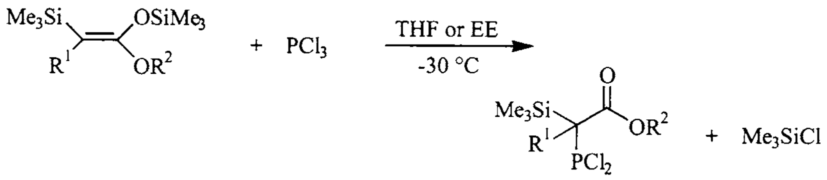


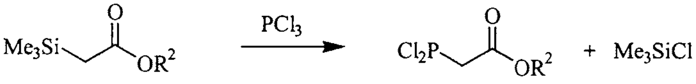
$E^+ = H^+$ 78%

$E^+ = MeI$ 75%



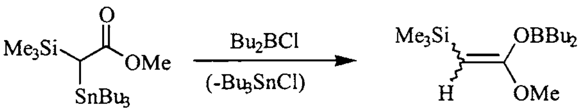
The trimethylsilyl ketene acetals of α-trimethylsilyl esters was reacted with phosphorous trichloride to give the α-dichlorophosphinyl derivative.[392] The α-trimethylsilyl *N,N*-dimethylacetamide reacts to give replacement of the trimethylsilyl group by the dichlorophosphinyl group.



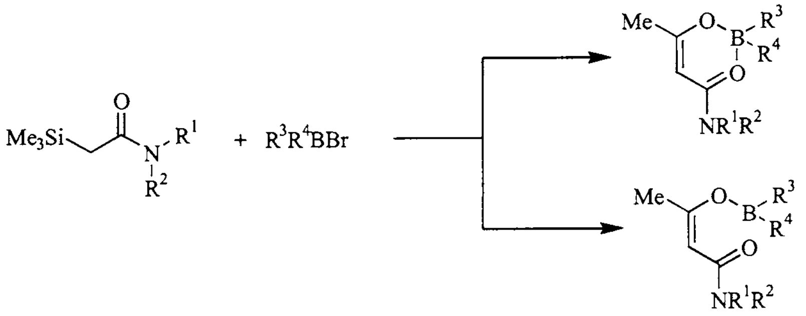


12.3. Reactions of α-Silyl Esters with Electrophiles

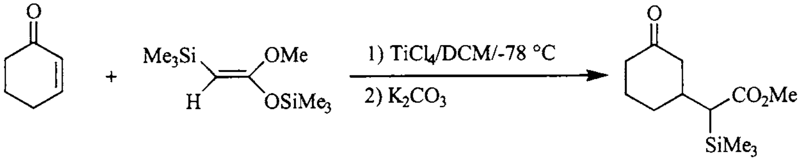
Treatment of α-trimethylsilyl-α-tributylstannyl esters with boron halides gives the α-trimethylsilyl boron ketene acetal via elimination of tributyltin halide.[393]

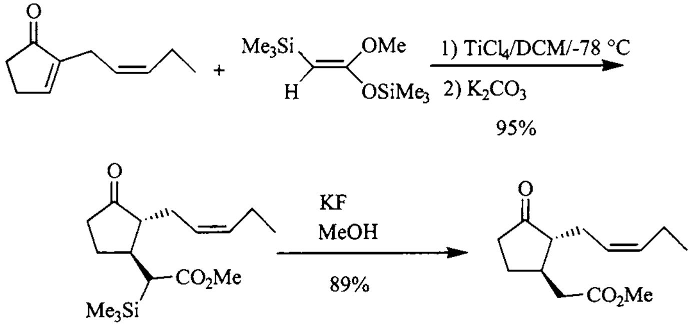


α-Trimethylsilyl *N,N*-dialkylacetamides were reacted with dialkylbromoboranes to give 4-oxo-1,2-oxaborato-5-cyclohexenes or the corresponding open-chain compound depending on the substitution of the amide.[394] Evans and Gauchet-Prunet used the Katzenellenbogen approach to 5-hydroxy esters, which were subsequently used to diastereoselectively prepare 1,3-diols.[395]

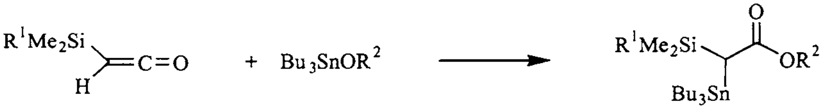


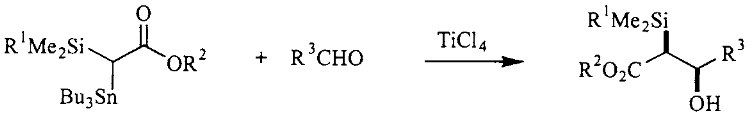
The trimethylsilyl ketene acetal of methyl trimethylsilylacetate has been Michael added in high yields to cyclic enones. This was used in a high-yield synthesis of methyl jasmonate.[396]



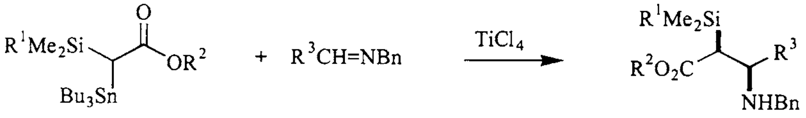


tert-Butyldimethyl(or diphenyl)silylketene was shown to react with tributylalkoxytins providing α-silyl α-stannyl esters.[86,397] These interesting species react with aldehydes or imines under the influence of titanium tetrachloride catalysis to give α-silyl-β-hydroxy(or amino)esters in good to excellent yields.





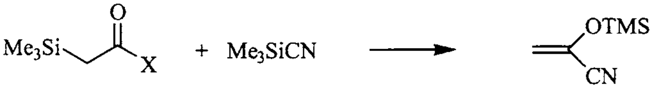
41–89% yield: *syn* = 52-96 de

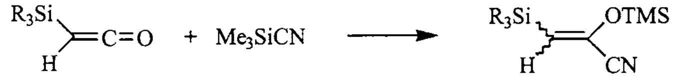


64–94% yield: *syn* ≥96 de

13. REACTIONS OF α-SILYL CARBOXYLIC ACIDS

Trimethysilyl acetyl chloride reacts with trimethylsilyl cyanide to give the α-cyanotrimethylsilyl vinyl ether.[398] Similar compounds are obtained by the addition of trimethylsilyl nitrile to silyl ketenes.





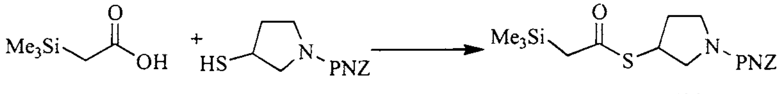
$R_3Si = Me_3Si, Et_3Si$

The reaction of trimethylsilylmethylmagnesium chloride with ^{13}C-labeled carbon dioxide gave the labeled trimethylsilylacetic acid. This was used to prepare diethyl malonate labelled at each carboxyl carbon.[399]

$$Me_3SiCH_2MgCl + {}^{13}CO_2 \longrightarrow Me_3SiCH_2{}^{13}CO_2H$$

$$\xrightarrow[\substack{\text{2) } {}^{13}CO_2 \\ \text{3) HCl} \\ \text{4) EtOH/TsOH}}]{\text{1) LDA/THF}} H_2C({}^{13}CO_2Et)_2$$

The reaction of trimethylsilylacetic acid with optically active thiols **178** produces the α-trimethylsilyl thioesters **179**, which were reacted with acetidinones to give **180**.[400] These are useful intermediates in the synthesis of carbapenums.



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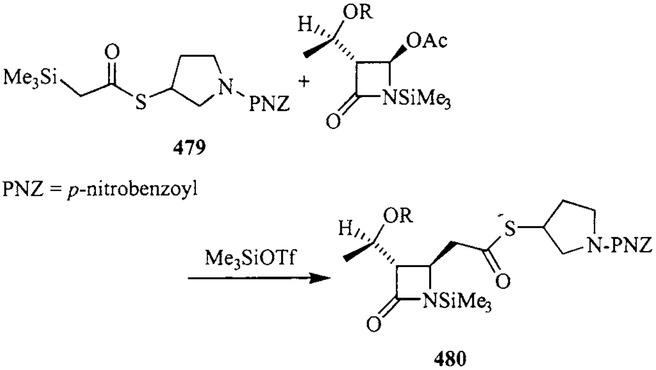
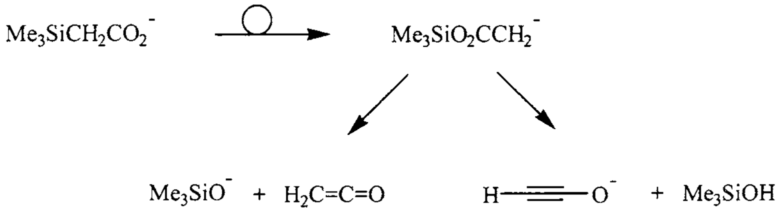


479

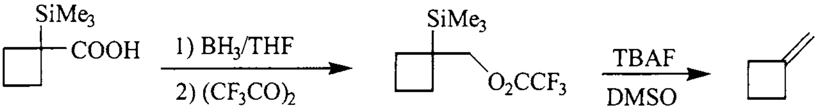
PNZ = *p*-nitrobenzoyl

480

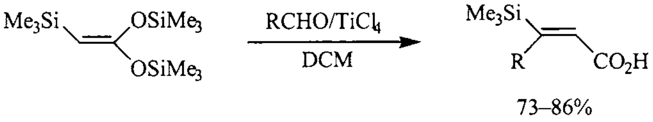
It was shown that the anion of trimethylsilylacetic acid rearranges to the enolate ion of acetoxytrimethylsilane in the gas phase and that this enolate decomposes by two pathways, one generating ketene and trimethylsiloxide ion and the other providing trimethylsilanol and the deprotonated ketene.[401]



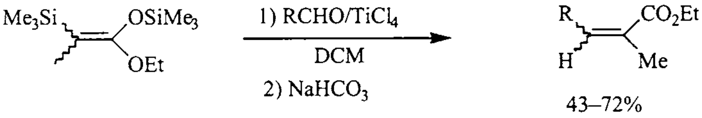
Paquette and co-workers[402] found that it was possible to produce the β-trifluoroacetate of 1-trimethylsilylcyclobutane carboxylic acid and bring about the β-elimination to the methylenecyclobutane. Such a sequence proved not possible with the corresponding cyclopropyl systems.



The reaction of the bis(trimethylsilyl)ketene acetal of trimethylsilyl acetic acid was also shown to react with aldehydes to give α,β-unsaturated acids directly when titanium tetrachloride was used as the catalyst.[403]

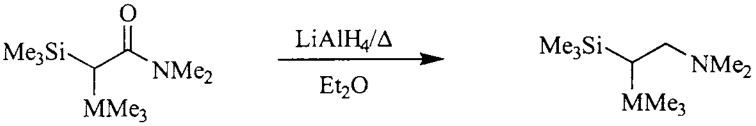


The trimethylsilyl ketene acetal of ethyl trimethylsilylpropionate was shown to give α,β-unsaturated esters upon reaction with aldehydes in the presence of titanium tetrachloride.[404]



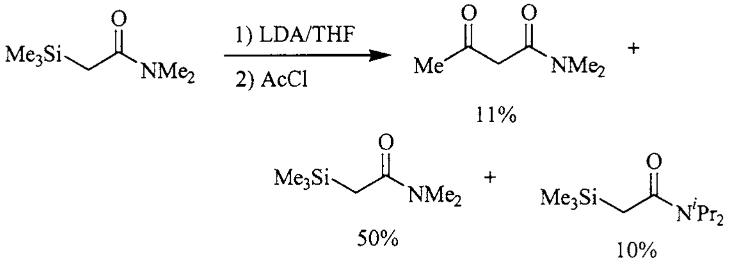
14. REACTIONS OF α-SILYL AMIDES

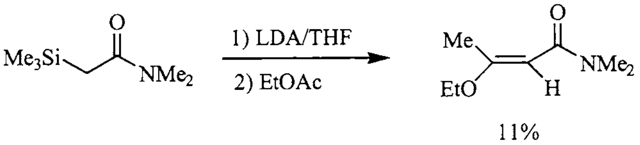
α-Silyl acetamides were shown to be reduced with lithium aluminum hydride to the corresponding β-aminosilanes.[405]

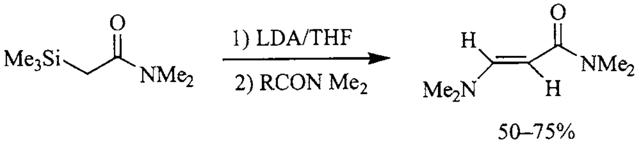


M = Si, Ge

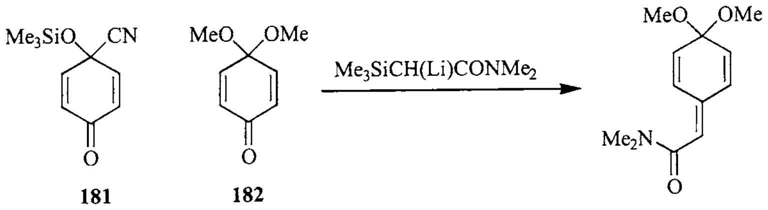
N,N-Dimethyltrimethylacetamide was deprotonated and the resulting lithium reagent reacted with acetyl chloride, but this gave a poor yield of the desired β-ketoamide. Included among the products was *N,N*-diisopropylacetamide resulting from reaction of the diisopropylamine present from the LDA.[406] The reaction of the enolate with ethyl acetate gave only a 11% yield of the α,β-unsaturated amide. On the other hand, reaction with amides gives β-enamino amides in moderate to good yields.

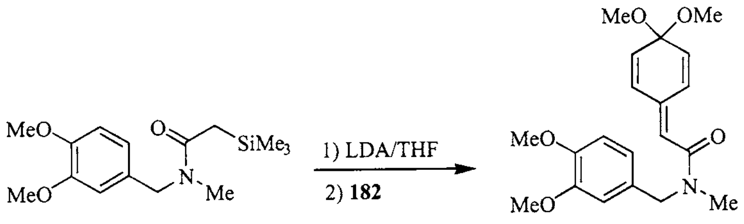




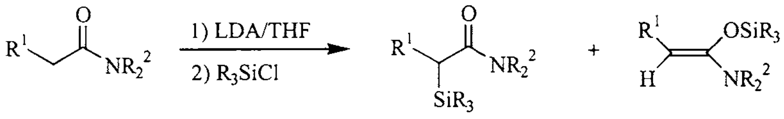


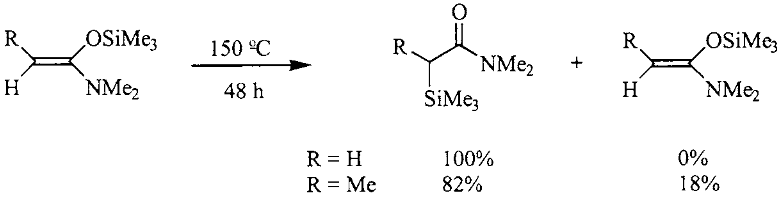
The reaction of the lithium reagent of *N*,*N*-dimethyl(trimethylsilyl)acetamide with **181** did not proceed as desired, but with **182** it reacted nicely.[407] In a similar vein the amide **183** was deprotonated and condensed with **182** to give the adduct **184** in good yield.


181 **182**

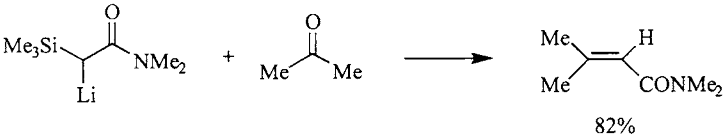

183 **184**

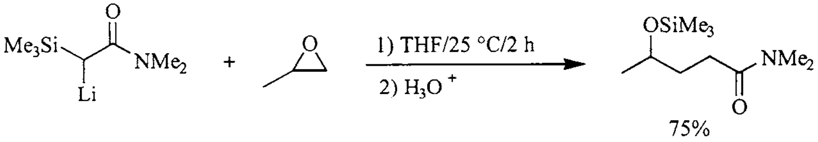
Rathke and Woodbury[408] studied the reaction of the enolate anions of several amides with trimethylchlorosilane. They found that a *tert*-butyldimethylchlorosilane quench favors O-silylation, smaller groups on the nitrogen atom favor C-silylation, larger groups on the α-carbon tend to favor O-silylation, and that thermal isomerization of the O-silylated to the C-silylated tautomer is possible.





Woodbury and Rathke[409] formed the lithium enolate of *N*,*N*-dimethyl(trimethylsilyl)acetamide with ketones, aldehydes, and epoxides. The reaction with carbonyl compounds provides the expected α,β-unsaturated amides in good yields and the reaction with epoxides produces the trimethylsilyl ethers of 4-hydroxyamides.

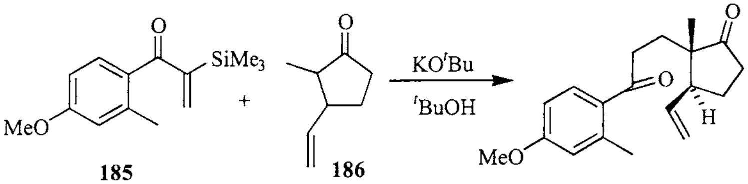




The reaction of the lithium enolates of *N*,*N*-dimethyltrimethylsilylacetamide and ethyl trimethylsilylacetate with nitrones gives a mixture of products with acyclic nitrones, including the α,β-unsaturated carbonyl compound and diazenes.[410] With cyclic nitrones, aziridines and their rearranged products are formed.

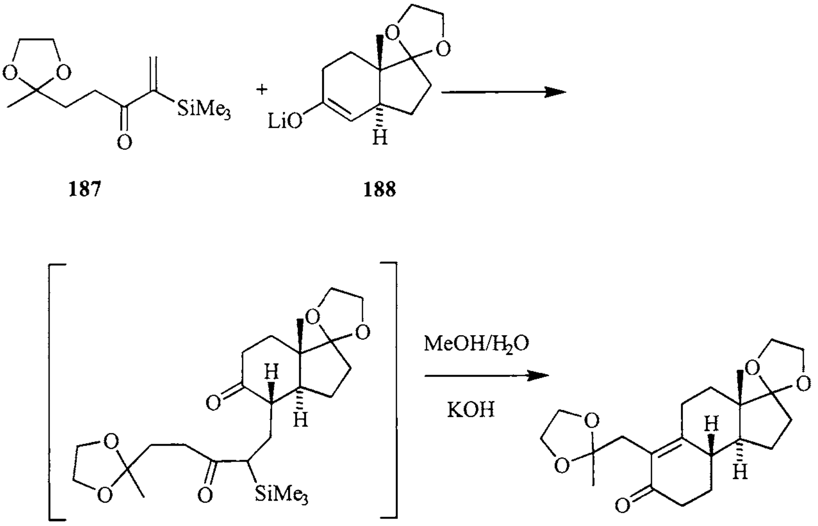
15. MICHAEL ADDITIONS TO α-SILYL-α,β-UNSATURATED CARBONYLS

The 2-trimethylsilyl enone **185** was reacted with the enolate of **186** in a synthesis of estrone.[411]



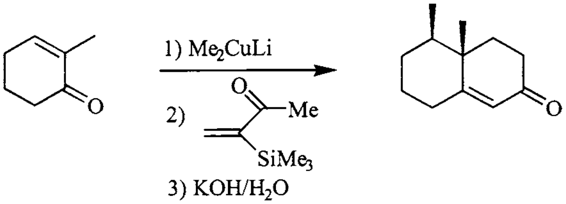
185 **186**

The α-trimethylsilyl enone **187** was reacted with enolate **188** as a key step into steroid systems.[412]

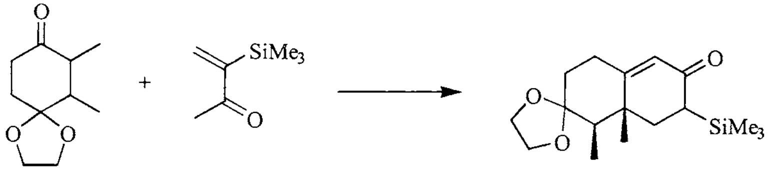


187 **188**

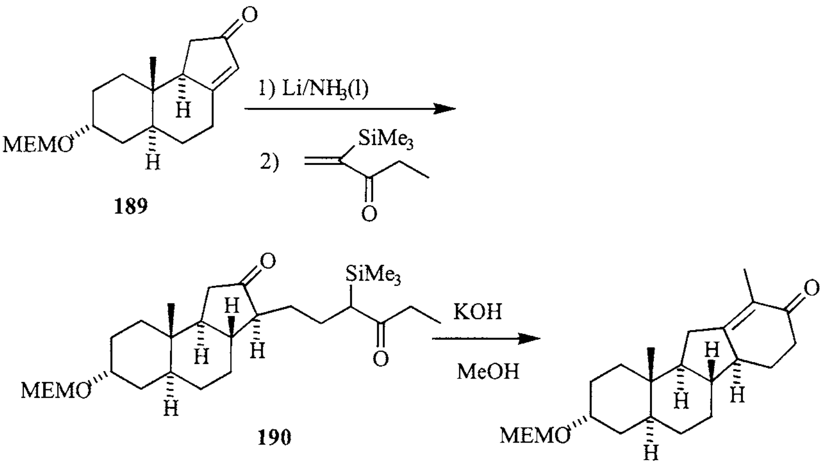
The utility of 3-(trimethylsilyl)-3-buten-2-one as a Michael acceptor was demonstrated by the following example.[413]



3-Trimethylsilylbut-3-en-2-one was used as the Michael acceptor in a synthesis of 4,4-ethylenedioxy-2,3-dimethylcyclohexanone, a key intermediate in the synthesis of sesquiterpenes of the eremophilane–valencane family, after desilylation.[414]



Trapping of the enolate of **189**, generated by lithium reduction of the enone, with ethyl α-trimethylsilylvinyl ketone gave the Michael adduct **190**, which was not isolated, but directly desilylated to **191**.[415]



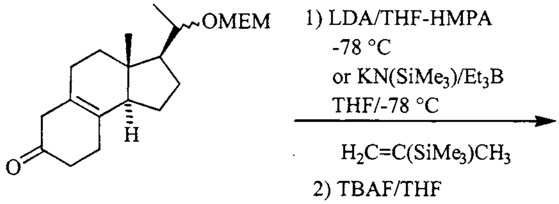
189

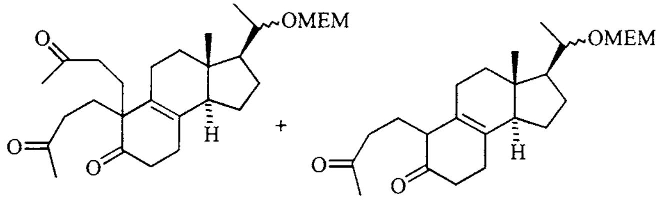
190

191

not isolated, identified by IR

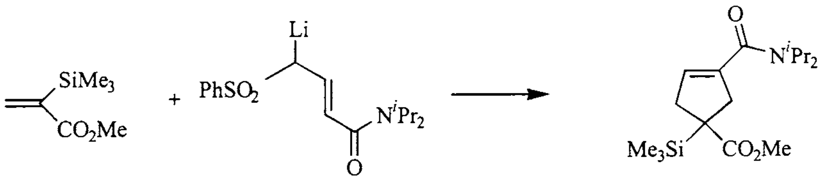
The use of 3-trimethylsilylbuten-2-one as a Michael acceptor was employed in a synthesis of Δ^9-progesterone.[416]



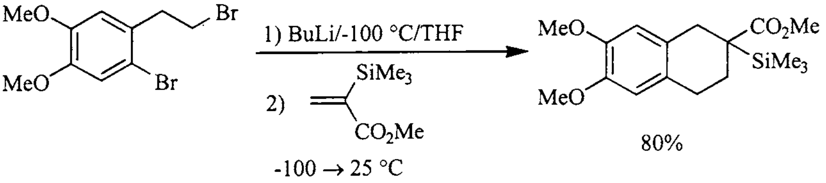


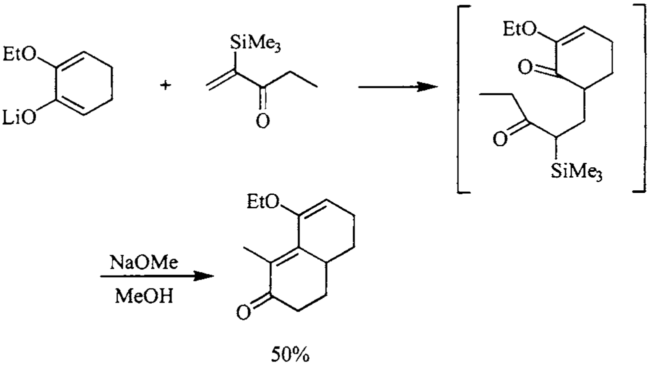
LDA 50% yield 3:2 ratio
$KN(SiMe_3)_2$ 63% yield 1:1 ratio

Methyl 2-trimethylsilylacrylate was reacted with 1-benzenesulfonyl-2-(*N*,*N*-diisopropyl)carboxamidoallyllithium to give the cyclization product, which is also an α-silyl ester, in 57% yield.[417]

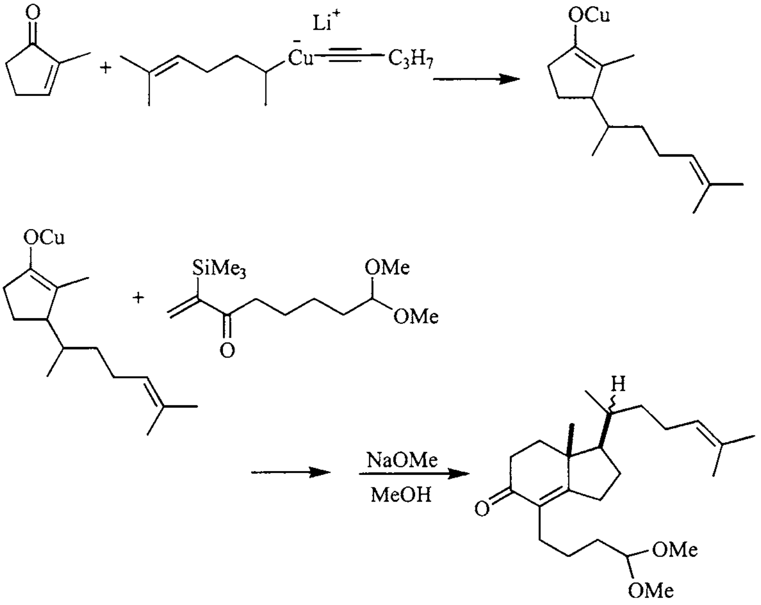


Methyl-2-trimethylsilylacrylate was employed as the acceptor and nucleophile in a new annulation sequence as illustrated.[418] The α-silyl ester produced was readily desilylated with aqueous base. Ene diones were synthesized using the Michael acceptor ability of an α-trimethylsilylenone.[419]

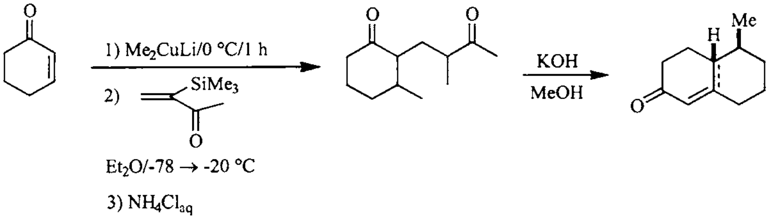




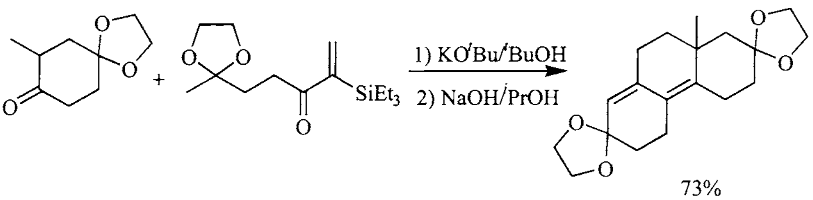
The α-trimethylsilyl enone concept was utilized by Boeckman and co-workers[420] in a Michael addition of a regiospecifically generated enolate in a synthesis of gascardic acid.



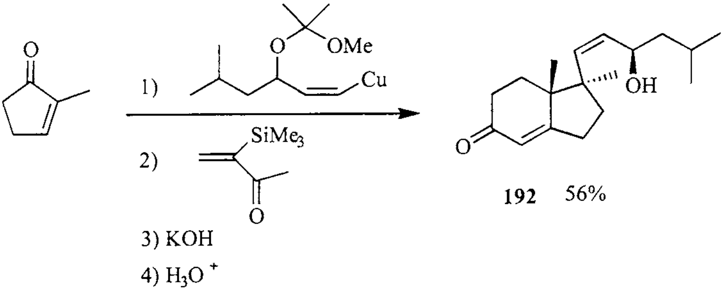
Boeckman, Jr.[421] was the first to show the reactivity of α-trimethylsilyl enones with a regiospecifically generated copper enolate.



In order to circumvent the problem of polymerization encountered with the Michael addition of enolates with methyl vinyl ketone and similar substrates, Stork and Ganem[422] turned to the α-silyl-α,β-unsaturated ketones as Michael acceptors. This turned out to be an excellent solution to the problem, due most likely to the ability of the silyl group to stabilize an α-anion and to its greater steric bulk, which would discourage polymerization. This concept has now been employed by several workers in Michael additions.

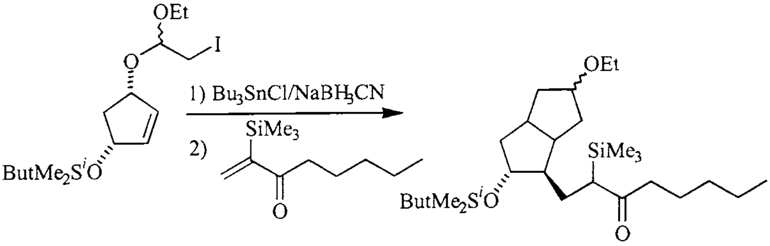


The selectively generated enolate of a cyclopentanone was trapped with 3-trimethylsilyl 2-butenone. Concomitant annulation and desilylation gives the AB ring system **192.**[423]

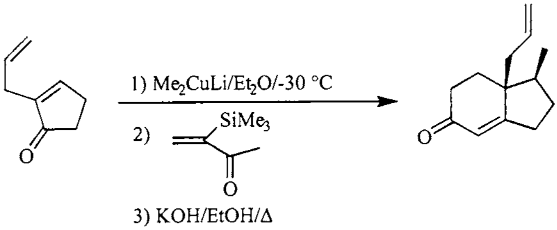


192 56%

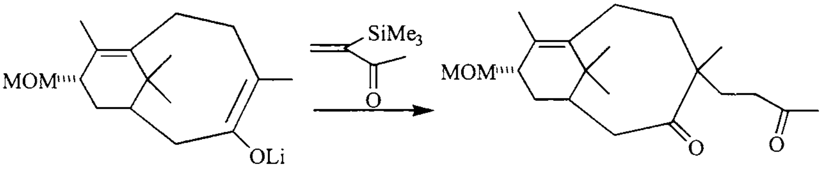
An α-trimethylsilylenone trapping of a radical formed by radical cyclization was illustrated by Stork and co-workers.[424]



Kende and Chen[425] used the α-trimethylsilylenone Michael reaction in a synthesis of (±)-8-deoxyanistatin.

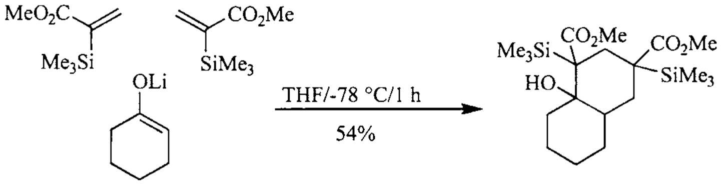


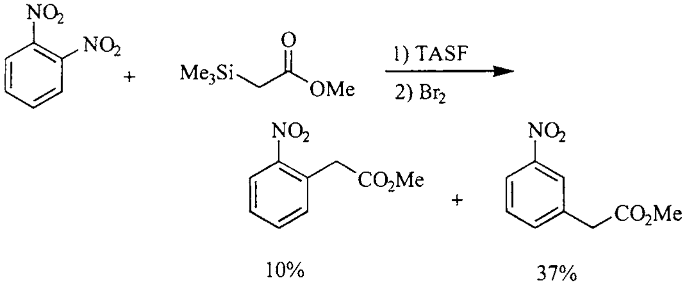
Michael addition of 3-trimethylsilyl 2-butenone on enolate **193** was used by Holton in a synthesis of the taxane ring system. The trimethylsilyl group is lost upon workup.[426] The Michael acceptor ability of α-trimethylsilylenones was also used in the trapping of a lithium enolate generated from an enone and lithium in liquid ammonia.[427]



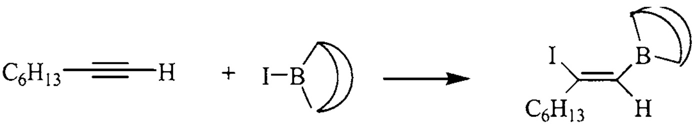
193

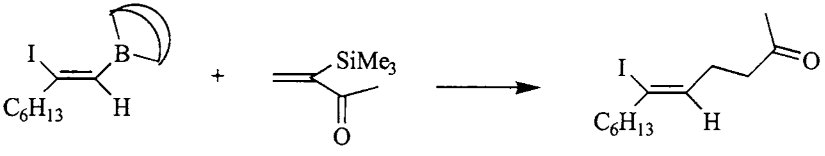
Methyl 2-trimethylsilylacrylate was used in a sequential Michael–Michael–aldol cyclization procedure introduced by Posner and co-workers for the formation of polyfunctionalized cyclohexanols.[428]





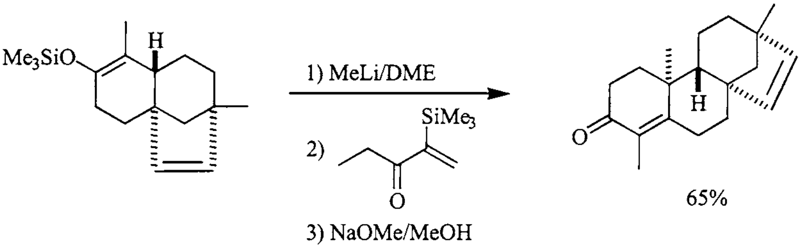
The vinylborane resulting from the iodoboration of terminal alkynes with B-iodo-9-BBN can be stereospecifically Michael-added to 3-trimethylsilyl 2-butenone.[429]





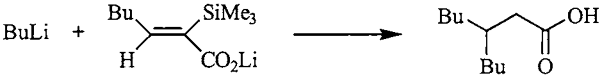
52% yield 99% *Z*

The Michael addition of a ketone lithium enolate with an α-trimethylsilyl enone was used in the synthesis of adrenosterone by Stork and co-workers.[430] The Michael acceptor ability of 3-trimethylsilyl-2-butenone was used in the synthesis of glycinoeclepin A.[431] The enhanced Michael acceptor ability of the α-trimethylsilyl α,β-unsaturated ketones was employed by Monti and Yang[432] in the synthesis of stachenone.



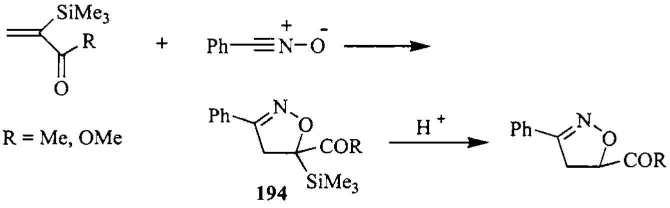
65%

Cooke, Jr.[433] showed that not only α-silyl-α,β-unsaturated ketones are good Michael acceptors, but that this concept can be used in the conjugate addition to α,β-unsaturated acids as well.

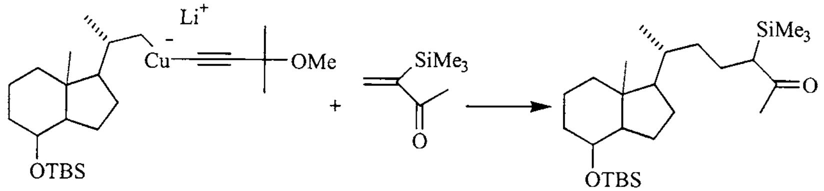


87%

The reaction of 2-(trimethylsilyl)enones or acrylates with nitrile oxides has been reported to give good yields of the cycloadducts **194** in an improvement on the reaction with the protiodesilylated derivatives.[434] The reaction of organocuprate **195** with the Michael acceptor, 3-trimethylsilyl 2-butenone, gave α-trimethylsilyl ketone **196**.[435]

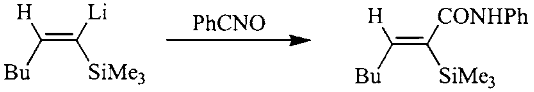


194



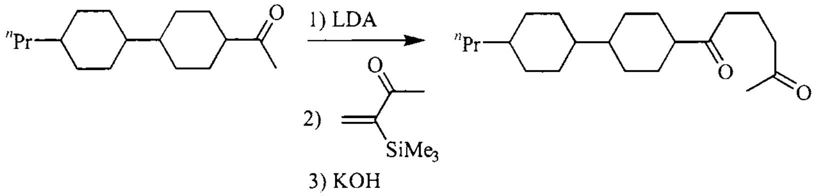
195 **196**

The reaction of 1-trimethylsilylvinylmagnesium halides with isocyanates produces *N*-substituted α-trimethylsilyl-α,β-unsaturated amidate anions, which have been found to be excellent Michael acceptors with organolithium and Grignard reagents.[436]

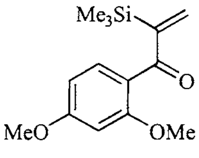


10 examples 49–83% 69%

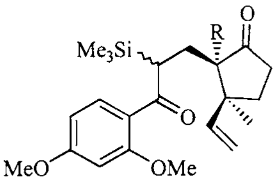
Some mesogenic tercyclohexyl derivatives were prepared employing the Michael addition of the enolate of a methylcyclohexyl ketone with 2-trimethylsilyl-3-butenone.[437]



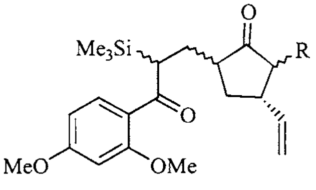
Structures **198** and **199** were prepared by the reaction of the corresponding lithium enolate of the cyclopentanone with the α-trimethylsilyl-α,β-unsaturated ketone **197**, where the presence of the



197



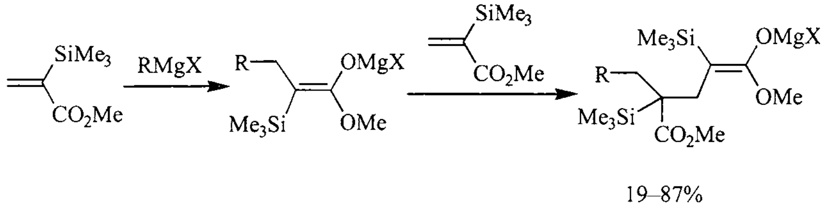
198

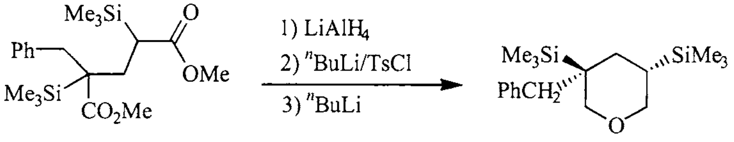


199

trimethylsilyl group aids in the Michael addition.[438] This chemistry was used in a total synthesis of (–)-Norgestrel, an important oral contraceptive.

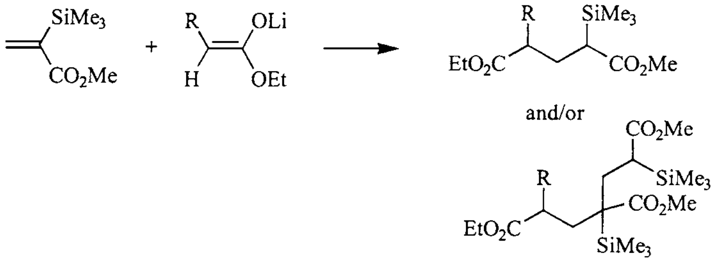
The reaction of methyl 2-trimethylsilylacrylate with Grignard reagents results in the formation of Michael addition of the Grignard to the acrylate followed by addition of the resulting anion to another acrylate molecule.[439] The sequence was shown to occur with high stereoselectivity. Reduction and cyclization gives the tetrahydropyran, **200**.



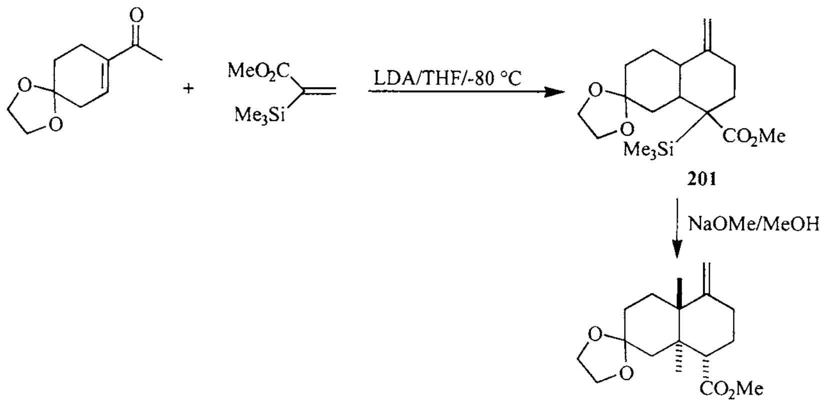


200

Methyl 2-trimethylsilylacrylate reacts with organolithium or Grignard reagents to give 1:1 and/or 1:2 adducts. The reaction with enolates proceeds in a like manner.[440]

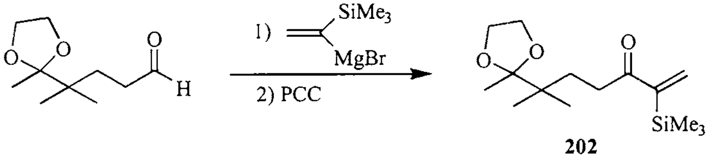


Methyl 2-trimethylsilylacrylate was shown to nicely react with the ketone enolate of an acyl cyclohexene to give annulation providing **201**, desilylation of which was carried out with sodium methoxide in methanol.[441]

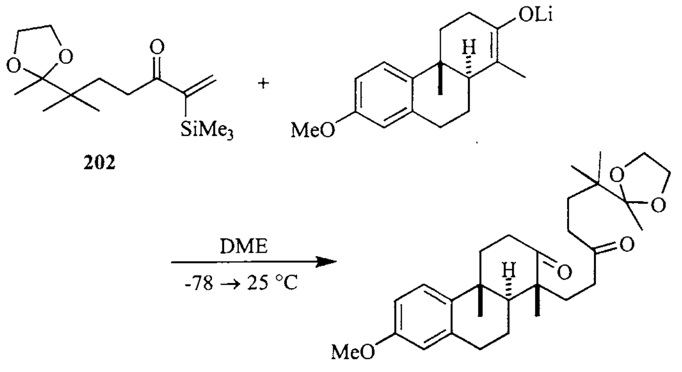


201

α-Trimethylsilyl enone **202** was used as a Michael acceptor to show the validity of a route to pentacyclic triterpenes.[442] Enolate **204** was added to enone **203** in good yield.[443]

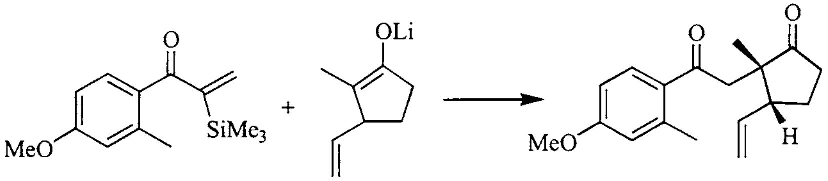


202



202

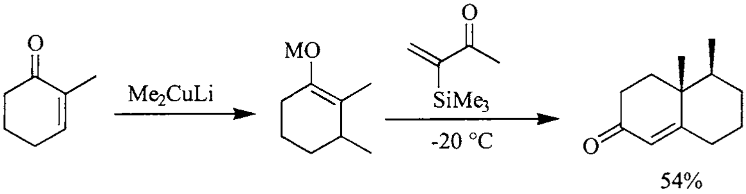
42%



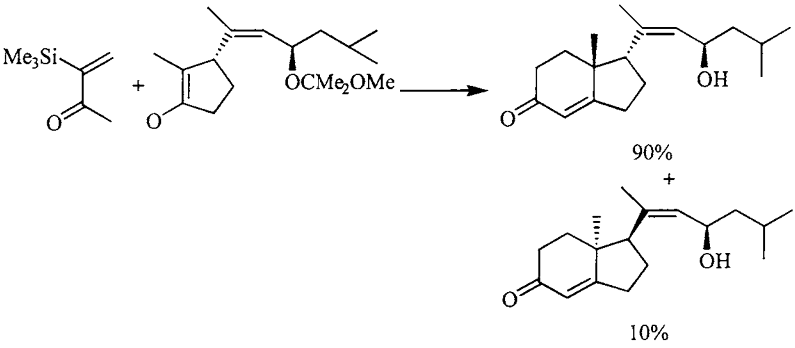
203 **204**

Another use of the Michael acceptor ability of 3-trimethylsilyl-2-butenone is to be found in the annulation of a cyclopentanone derivative used in the synthesis of a chiral steroid CΔ-ring system.[444]

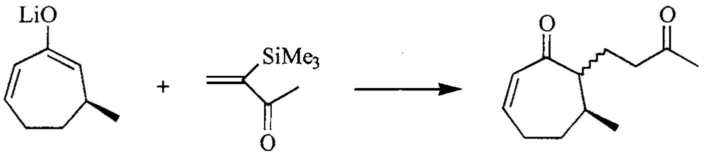
A new annulation methodology which involved the addition of diorganocuprate to an α,β-unsaturated ketone and then reacting the resulting enolate with α-trimethylsilylvinyl ketones was first presented by Boeckman.[445]



In a nice application of the advantage of employing an α-trimethylsilyl-α,β-enone in the Michael addition of enolates to the enone is shown in the construction of the C and D rings of the steroid skeleton.[446]

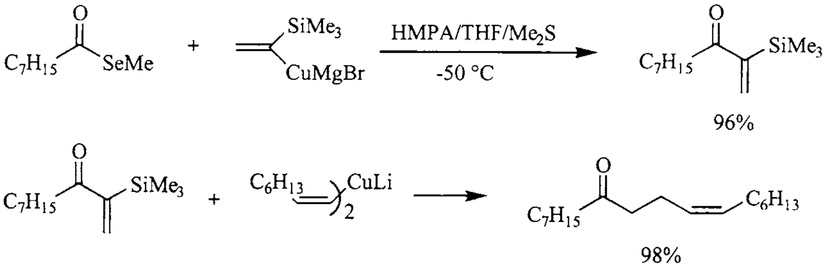


The use of the Michael addition of an enolate to 3-trimethylsilylbut-3-en-2-one was utilized in a key step in the synthesis of clavularin B, which is the *trans*-isomer of **205**.[447]



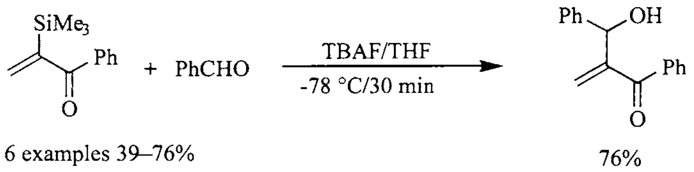
205

Acyl selenides can be reacted with 1-trimethylsilylvinyl copper reagents to give α-silyl-α,β-unsaturated ketones, which in turn can be reacted with lithium vinylcuprates to give addition and loss of the trimethylsilyl group leading to γ,δ-unsaturated ketones with the stereochemistry of the vinylcuprate reagent.[448]

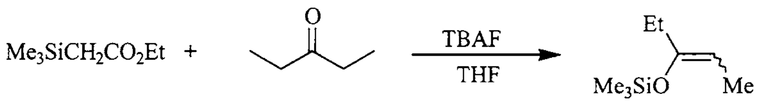


16. REACTION OF α-SILYL CARBONYL SYSTEMS WITH FLUORIDE ION

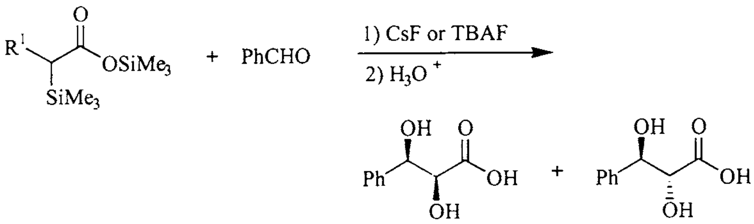
The reaction of α-trimethylsilyl enones represent a 1-acylethenyl anion equivalent when reacted with aldehydes under the influence of fluoride ion.[449]



Ethyl trimethylsilylacetate in conjunction with fluoride ion reacts with ketones to give (*Z*)-silyl enol ethers in good yields.[450]



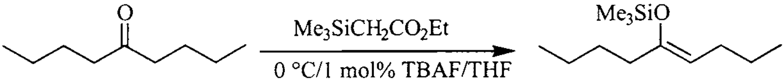
Treatment of trimethylsilyl α-trimethylsilyl esters with fluoride ion and benzaldehyde was shown to give the β-hydroxyacids with a preference for the *erythro*-diastereomer.[451]

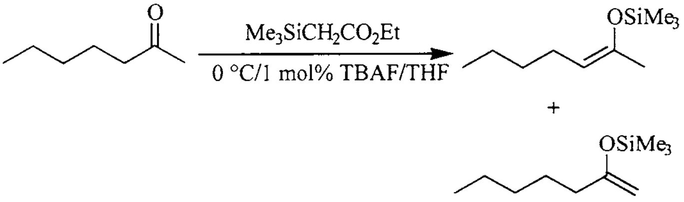


erythro *threo*

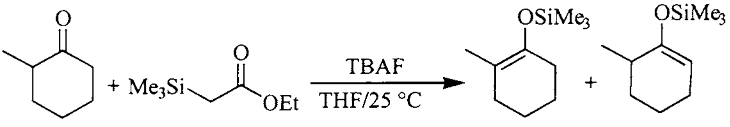
erythro:*threo* = 70:30 → 81:19

Kuwajima and co-workers[452] have shown that treatment of ethyl trimethylsilylacetate with tetrabutylammonium fluoride in THF in the presence of a ketone leads to both regio- and stereoselective formation of trimethylsilyl enol ethers. This is a very important transformation due to the tremendous synthetic utility of the trimethylsilyl enol ethers. Kinetic control is argued to account for the results.

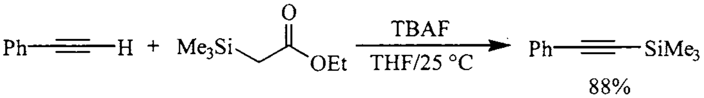




Ethyl trimethylsilylacetate was shown by Kuwajima and co-workers[453] to be an excellent silylating agent for alcohols and ketones to form the silyl ethers and enol silyl ethers, respectively. The regioselectivity in the formation of the enol silyl ethers favors the kinetic isomers. This reagent will also silylate terminal acetylenes.

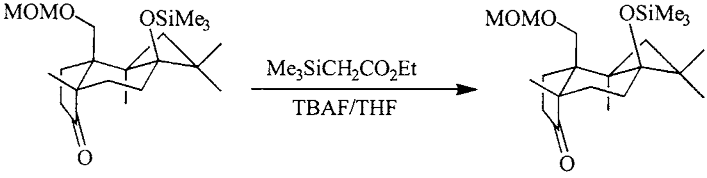


20% 80%

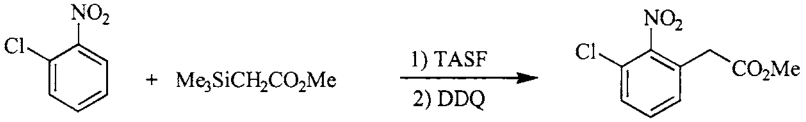


88%

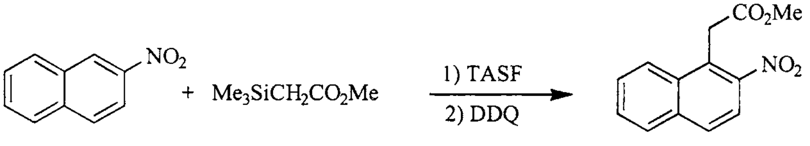
The use of ethyl trimethylsilylacetate to trimethylsilylate a tertiary alcohol in the presence of an enolizable ketone was accomplished.[454]



Methyl trimethylsilylacetate was used as the source of the enolate of methylacetate in the reaction with *o*-dinitrobenzene.[455] Methyl trimethylsilylacetate was reacted with *o*-chloronitrobenzene under the influence of fluoride ion to give the ester **206** after oxidation. A similar reaction with β-nitronaphthalene provided **207**.[456,457]

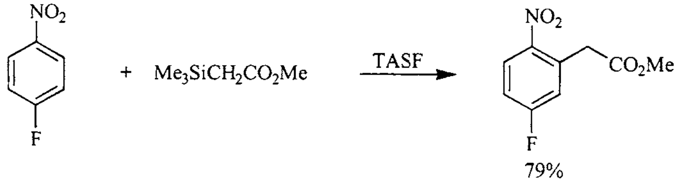


206

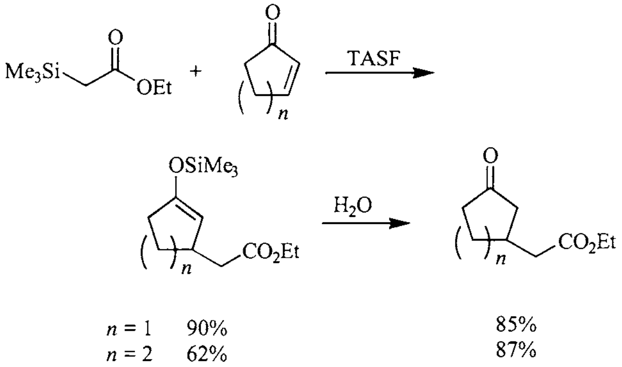


207

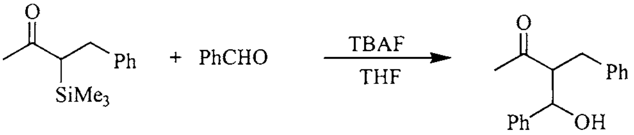
The nucleophilic addition of the enolate of methyl acetate was accomplished by the reaction of methyl trimethylsilylacetate with fluoride ion in the presence of nitroaromatic substrates.[458] In the example shown the trimethylsilyl ketene acetal of methyl trimethylsilylacetate gave the same product in 77% percent yield. This approach was utilized in an approach to indoles, 2-indolinones, and arylacetic acids.



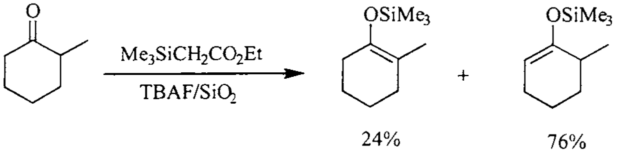
Ethyl trimethylsilylacetate was successfully conjugate-added to cycloalkenones under the influence of fluoride ion in a methodology based on earlier work by Kuwajima and co-workers.[457] The initial adduct was trapped as the enol silyl ether.



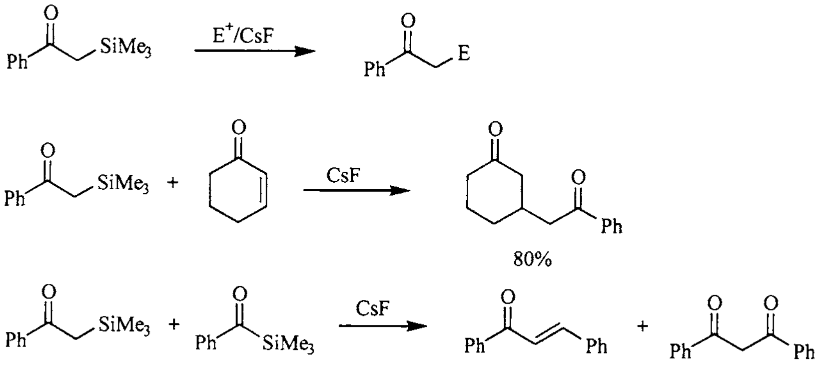
It was shown that α-trimethylsilyl ketones react, as do their isomeric enol silyl ether counterparts, with aldehydes under the influence of fluoride ion.[459] It is unclear whether isomerization of the α-silyl ketone to the enol silyl ether takes place prior to reaction.



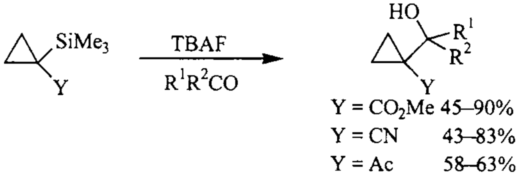
Silica supported tetrabutylammonium fluoride was shown to be an effective catalyst for the reaction of ethyl trimethylsilylacetate with ketones.[460]

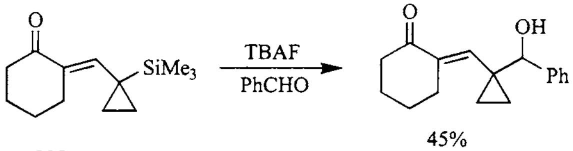


α-trimethylsilyl ketones were shown to react with various electrophiles in the presence of fluoride ion to give direct electrophilic replacement of the trimethylsilyl group.[461]



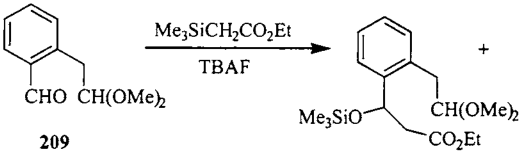
Cyclopropyl anions were generated "in situ" in the presence of carbonyl compounds by treatment of 1-trimethylsilylcyclopropyl esters, nitriles, and ketones with fluoride ion. This entry into aldol condensations of cyclopropyl systems was even carried out with a vinylogous system **208**.[462]



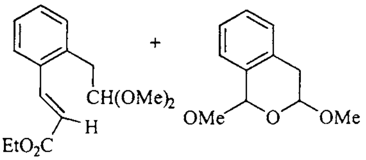


208

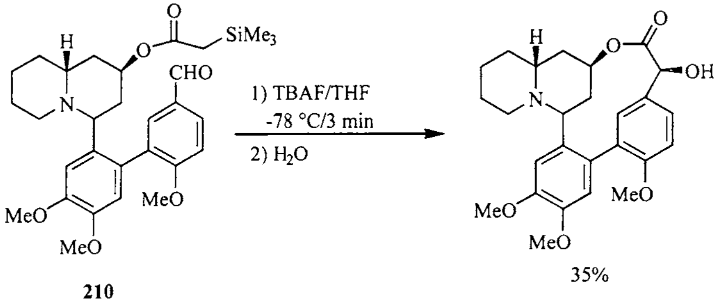
The reaction of the monoprotected dialdehyde **209** with ethyl trimethylsilylacetate and fluoride ion gives three products derived from the enolate of ethyl acetate.[463]



209

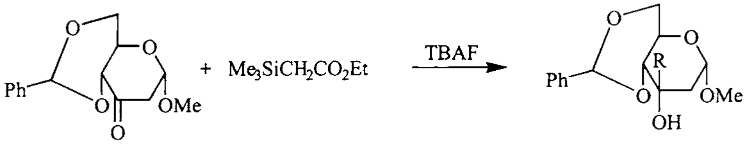


α-Silyl ester **210**, prepared by the reaction of trimethylsilylketene on the alcohol, was used as an "in situ" source of the ester enolate for intramolecular reaction with the aldehyde group by treatment with fluoride ion.[464]



210

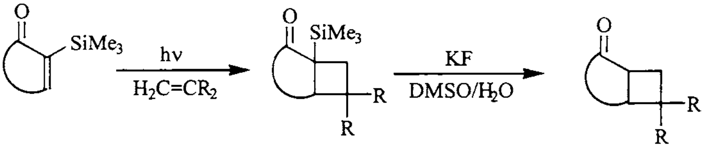
Ethyl trimethylsilylacetate was used to bring about the condensation of ethyl acetate with the carbonyl of the sugar **211**.[465]



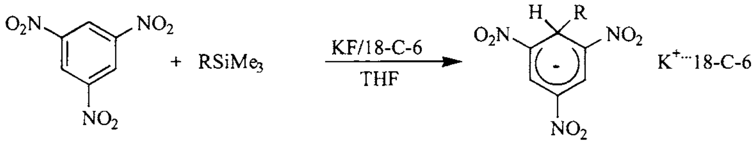
211

$R = CH_2CO_2Et$

α-Silylcycloalkenones were photoadded to olefins to give β-ketosilanes, which could be protiodesilylated with fluoride ion in DMSO containing a small amount of water.[466]

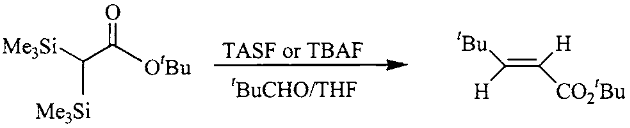


α-Silyl esters and ketones were reacted with 1,3,5-trinitrobenzene under the influence of fluoride ion to give attack of the enolate on the benzene ring to form the potassium salt.[467] A similar reaction occurs with acyl-, benzyl-, allyl-, or ethynylsilanes as well.



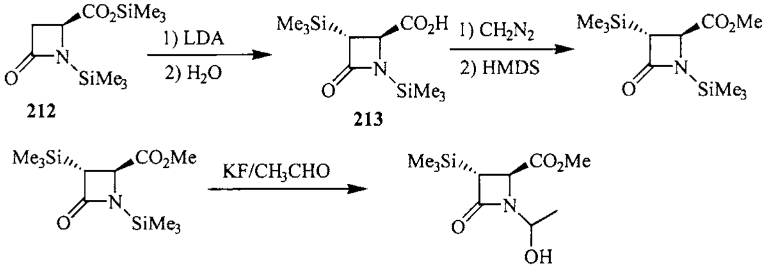
R = CH_2CO_2Me, CH_2CO_2Et, CH_2COEt

The reaction of *tert*-butyl α,α-bis(trimethylsilyl)acetate with fluoride ion in the presence of an aldehyde gives the Peterson reaction corresponding to that of the enolate of *tert*-butyl trimethylsilylacetate.[468]



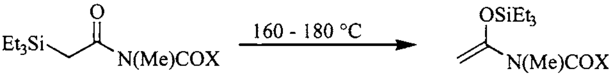
65%; 100% (*E*)

The bis(trimethylsilylated)acetidinone **212** gives a 1,4-C to O migration upon deprotonation to provide the C-trimethylsilylated material **213**.[469] The ester of this material reacts with acetaldehyde under the influence of fluoride ion to give reaction at the nitrogen.



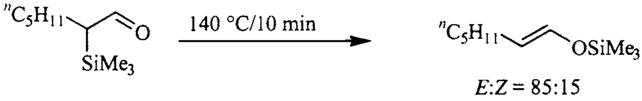
17. REARRANGEMENTS OF α-SILYL CARBONYL SYSTEMS

The thermal rearrangement of triethylsilyl urea derivatives was observed.[470]

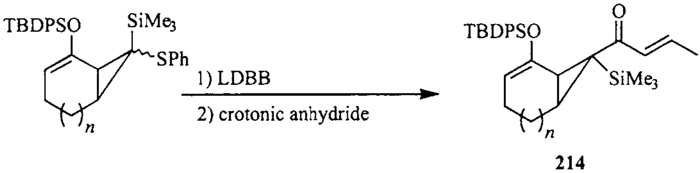


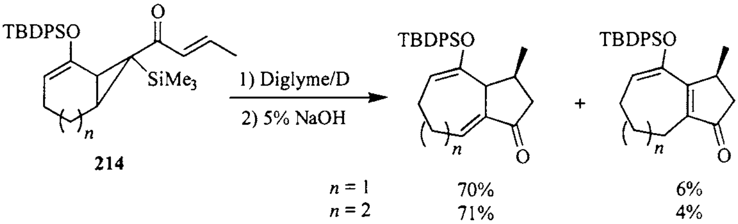
X = H, OMe, OEt

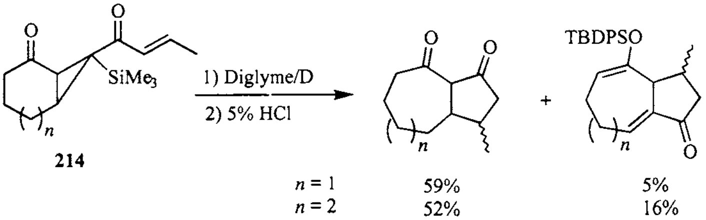
The thermolysis of α-trimethylsilyl aldehydes requires only 10 minutes at 140 °C for completion.[17a]



The thermolysis of α-trimethylsilylcyclopropyl ketones such as **214** was employed in the preparation of fused bicyclic systems including hydroazulenes.[471]

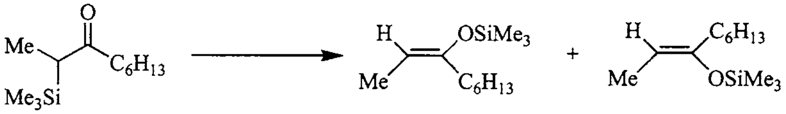






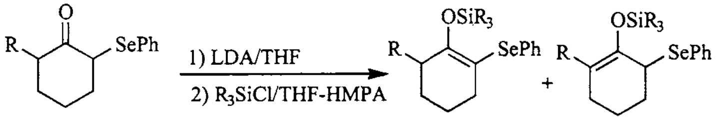
Kwart and Barnett[472] studied the thermal rearrangement of α-silyl ketones to silyl enol ethers using ^{29}Si-enriched material and determined that Si–O bond formation is very important and that the reaction occurs with initial attack of the oxygen on silicon to form a pentacoordinate intermediate, which then rearranges. This is in contrast to the mechanism put forth by Brook and co-workers[473] and Larson and Fernandez[474] who felt that the reaction was basically concerted based on the absence of a strong solvent effect.

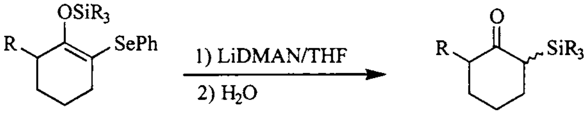
Matsuda and co-workers[475] have shown that the isomerization of α-trimethylsilyl ketones to silyl enol ethers can be accomplished in a stereoselective fashion with thermolysis and Wilkinson's catalyst both leading to the *E*-isomer as the major component and trimethylsilyl triflate and trimethyliodosilane both leading to the *Z*-isomer and the major component. The stereoselectivity of these processes, however, do not approach that of the thermolysis in acetonitrile employed by Larson and co-workers.[476]



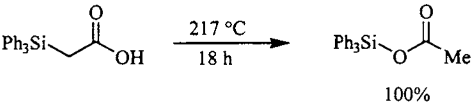
Conditions		
175 °C/15 min\neat	93	7
$HRh(CO)(PPh_3)_3/C_6H_6$/105 °C/12 h	75	25
Me_3SiOTf/HMDS/DCM/0 °C/5 min	28	72
Me_3SiI/HgI_2/HMDS/DCM/25 °C/15 h	18	82

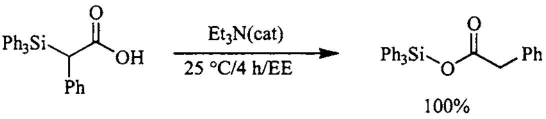
The trimethylsilyl enol ether of α-phenylseleno ketones can be converted to the vinyllithium reagent by way of metal–metal exchange. The resulting lithium reagent can then be trimethylsilylated and hydrolyzed to produce α-trimethylsilyl ketones in good yields.[477]



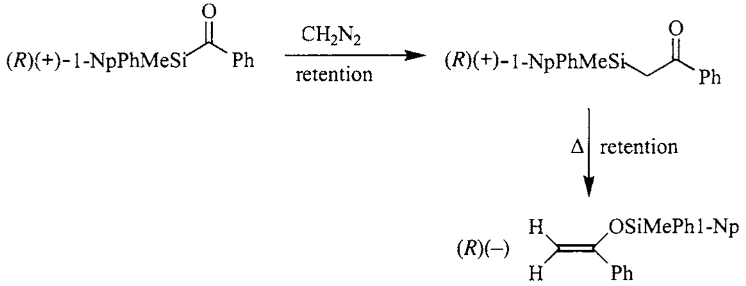


The thermal and base-catalyzed rearrangement of silylacetic acids was reported by Brook and co-workers.[478] As expected based on the α-silylketone to silyl enol ether rearrangement, the products are the corresponding acetoxysilanes.

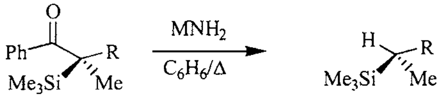




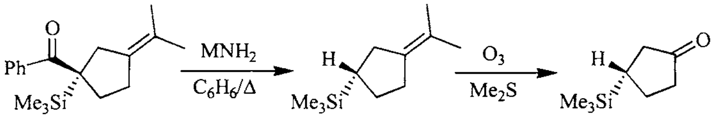
Brook and co-workers[479] showed that the insertion of diazomethane generated carbene into the silicon–acyl bond occurs with retention of configuration at silicon to give the α-silyl ketone and, furthermore, that the α-silyl ketone to silyl enol ether rearrangement occurs with retention at silicon in a four-centered, intramolecular process.



Paquette and co-workers[480] prepared optically active α-trimethylsilyl ketones and used them to study the Haller–Bauer cleavage. This was shown to be with retention of configuration at carbon. This was turned into an asymmetric synthesis of chiral C-centered α-trimethylsilyl ketones.[481] The approach was also applied to cyclic systems to prepare chiral substituted trimethylsilylcyclopentanes.[482]



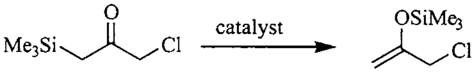
(M = Na, K; R = $PhCH_2$, $Me_2C{=}CHCH_2$, $PhCH_2CH_2$, C_5H_{11})



The reaction of ethyl(phenylmercuri)fluorochloroacetate with triethylsilane provides the α-triethylsilyl-α-fluoroester.[483]

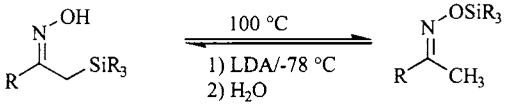
$$PhHgCFClCO_2Et + Et_3SiH \xrightarrow[50\ h]{110\ ^\circ C} \underset{71\%}{Et_3SiCH_2CHFCO_2Et}$$

Certain iridium, rhodium, palladium, and platinum catalysts were found to bring about the rearrangement of 3-chloro-1-(trimethylsilyl)propan-2-one.[484]

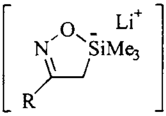


catalyst = $IrH(CO)(PPh_3)_3$, *trans*-$[IrCl(CO)(PPh_3)]_2$, $RhH(PPh_3)_4$, $Pd(PPh_3)_4$, Pt(*trans*-stilbene)$(PPh_3)_2$, $Pt(\eta^3\text{-}CH_2COCH_2)(PPh_3)_2$

The ketoxime of trimethylsilylmethyl ketones shows a reversible 1,4-migration of the silyl group from oxygen to carbon. An intermediate of *syn* geometry, **215**, is postulated to account for the migrations.[485]

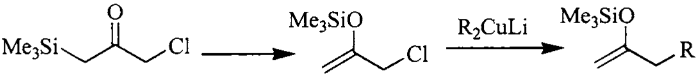


$R_3Si = Me_3Si$, ${}^tBuMe_2Si$

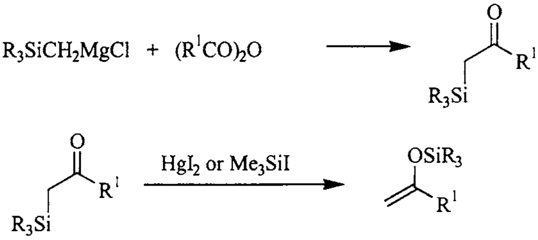


215

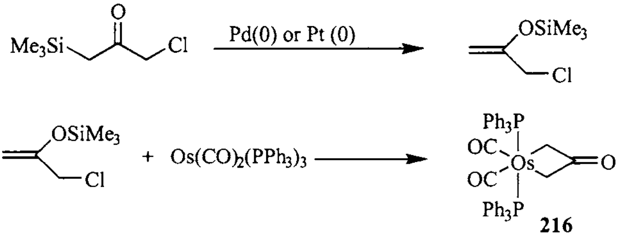
1-Trimethylsilyl-3-chloro-2-propanone, prepared from the Grignard procedure, was thermally isomerized to give the regiospecifically generated enol ether, which as an allyl chloride was reacted with lithium dialkylcuprates to give substituted silyl enol ethers.[486]



Silylmethyl ketones were prepared from silylmethylmagnesium chloride reaction on acid anhydrides as per the Hauser procedure,[487] which showed them to rearrange upon treatment with either mercuric iodide or trimethylsilyl iodide in an intermolecular reaction.

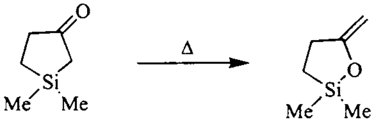


1-Trimethylsilyl-3-chloropropanone was shown to isomerize to the enol silyl ether upon treatment with palladium or platinum(0).[488] This enol ether was reacted with tris(triphenylphosphine)osmium dicarbonyl to give complex **216**. Similar complexes were obtained from the reaction of the enol ether with tetrakis(triphenylphosphine)platinum(0) and tetrakis(triphenylphosphine)iridium dicarbonyl.



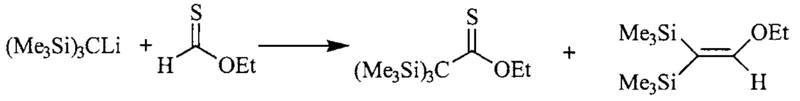
216

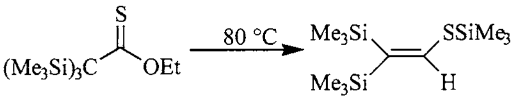
The silacyclopentane, 1,1-dimethyl-1-silacyclopent-3-one, was shown to thermally rearrange to the enol silyl ether **217**.[489]

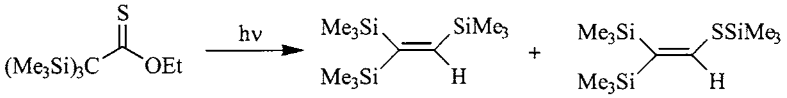


217

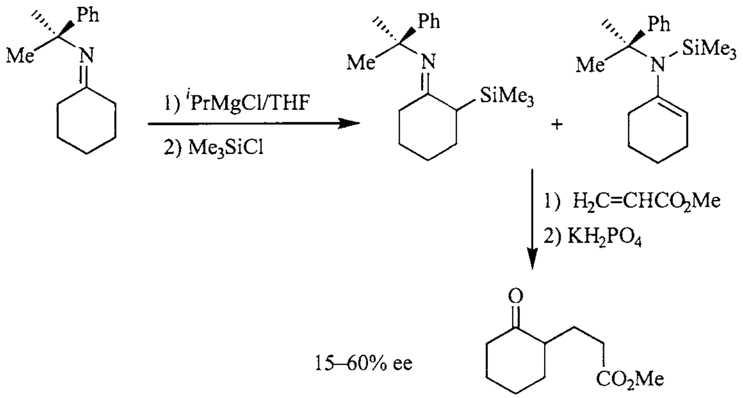
The reaction of tris(trimethylsilylmethyllithium with O-ethylthioformate gives tris(trimethylsilyl)ethanethial as pink-red crystals.[490] Thermolysis of this material at 80 °C gives the thioenol ether whereas photolysis results in the formation of tris(trimethylsilyl)ethylene in addition to the thioenol ether. This contrasts with the photochemistry of tris(trimethylsilyl)ethanal, which eliminated carbon monoxide and gives tris(trimethylsilyl)methane.



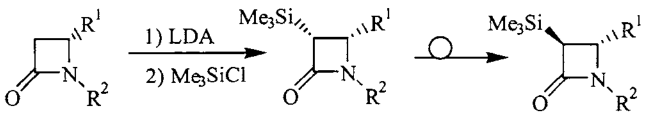




N-Trimethylsilyl enamines, which are slow to equilibrate with their isomeric α-trimethylsilyl imines, react with acrylonitrile or methyl acrylate to give an adduct of the α-trimethylsilyl imine which reacts faster than the silylated enamine.[491] This reaction was carried out in an enantioselective fashion as well.

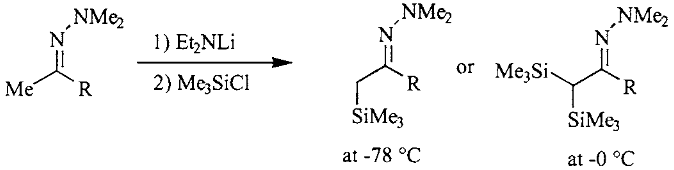


The deprotonation-trimethylsilylation of 1,4-disubstituted β-lactams occurs to place the trimethylsilyl group on carbon *cis* to the 4-substituent. The *cis*-isomer converts to the *trans*-isomer, however.[492] The C-trimethylsilylated β-lactam was reacted with acyl chlorides and aldehydes.

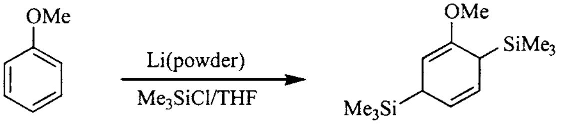


18. MISCELLANEOUS α-SILYL CARBONYL CHEMISTRY

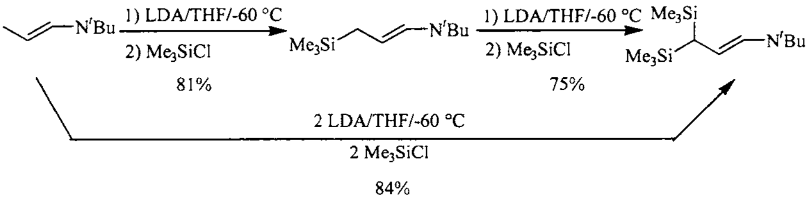
Deprotonation–trimethylsilylation of dimethylhydrazones at −78 °C provides the mono-α-trimethylsilylhydrazone.[493] The reaction at 0 °C, however, gives the bis-trimethylsilylated derivative.

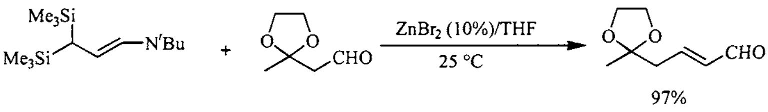


The reaction of anisole with lithium and trimethylchlorosilane in THF provides the methyl enol ether of an α-trimethylsilyl ketone.[494]

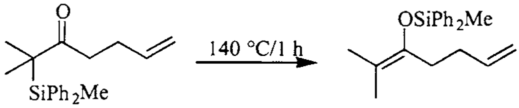


tert-Butylacetaldimine was converted to α,α-bis(trimethylsilyl)-*tert*-butylacetalimine by either two sequences of deprotonation–trimethylsilylation or by reaction of the aldimine with 2 equivalents each of lithium diisopropylamide and trimethylchlorosilane.[495] This silylated aldimine reacts with aldehydes in the presence of zinc bromide to give α,β-unsaturated aldimines and, upon hydrolysis, α,β-unsaturated aldehydes.

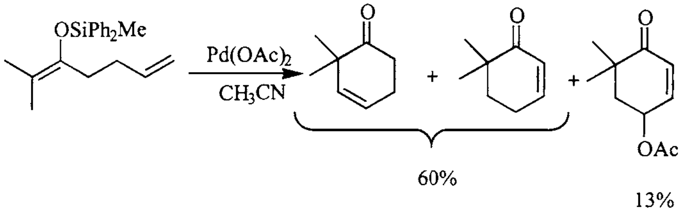




The thermal rearrangement of α-silyl ketones to the regiospecifically generated silyl enol ethers was utilized in the 6-*endo*-trig cyclizations of the unsaturated α-silyl ketones, **218**, as shown.[496]



218



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