This is to certify that the

dissertation entitled

A STUDY OF SILYL ENOL ETHERS

presented by

Paul David Weipert

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Michael William Rathke
Major professor

Date 8-15-90

A STUDY OF SILYL ENOL ETHERS

By

Paul David Weipert

A DISSERTATION

Submitted to
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ABSTRACT

A STUDY OF SILYL ENOL ETHERS

By

Paul David Weipert

An investigation of regioselection in silyl enol ether formation was conducted using trimethylsilyl iodide, tertiary amine bases, and 2-methylcyclohexanone. The effect of addition order, base, solvent, and temperature on the ratio of regioisomers was determined. The more substituted isomer predominated and the ratio of isomers was affected only slightly in all cases studied. These findings were shown not to be due to a rapid equilibration of isomers. The mechanism of silylation is discussed in light of these results.

The preparation of silicon functionalized silyl enol ethers was also investigated. Dialkylaminodimethylchlorosilanes were effective for this purpose and were used to prepare a series of dialkylaminodimethylsilyl enol ethers. These compounds could be converted into a variety of other functionalized silyl enol ethers including alkoxy, acetoxy, chloro, and vinyl derivatives. Symmetrical dimethylsilyl bis-enol ethers were prepared from dichlorodimethylsilane and mixed dimethylsilyl bis-enol ethers were prepared from dialkylaminodimethylsilyl enol ethers.

The coupling reaction of dimethylsilyl bis-enol ethers to produce 1,4-diketones was investigated. Using ceric ammonium nitrate to initiate the reaction led to diketones in variable yield, depending upon the substitution

pattern of the enol ether. A comparison was made to the other methods for the preparation of diketones.

Dedication

To My Mother, Father,

Sisters and Brothers

Acknowledgements

Knowledge has always been transmitted from teacher to student, from teacher to student, generation after generation. It has been my honor and privilege to have been the student of one of the finest teachers in this tradition, Dr. Micheal Rathke. Thanks Doc.

The author would like to thank Dr. William Reusch for serving both as a sagacious second reader and as a substitute dart team member. The contributions made by all the organic faculty members have been extensive and are deeply appreciated.

The author would like to thank the members of the Rathke group, Mike, Rick, Demetrius, Ezzeddine, Shau-Lin, and Leo, for their generous assistance and support.

One of the benefits of graduate school is having the opportunity to come in contact with the many other superb students in the department. You have enriched my work and life and are owed a debt of graditude. I wish you all the best.

I wish to thank from my heart, Lisa Dixon, without whose assistance this work may not have been possible.

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CHAPTER I

REGIOSELECTION IN SILYL ENOL ETHER FORMATION

INTRODUCTION

A silyl enol ether (Figure 1) was first prepared by Gilman and Clark[1] in 1947. They reacted ethyl sodioacetoacetate with triethylsilyl chloride to produce ethyl β-triethylsiloxycrotonate (Equation 1). Aside from a dispute about its structure[2,3] (C *vs.* O silylation), little research appeared concerning this class of compounds until 1964 when Kruger and Rochow [4] published a general method for silyl enol ether synthesis. These researchers sought to demonstrate the utility of sodium bis(trimethylsilyl)amide (NaHMDS) for the preparation of sodium enolates from ketones. To establish this, they reacted the resulting enolate solutions with alkylhalosilanes to produce silyl enol ethers in moderate yields (Equation 2).

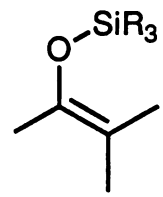
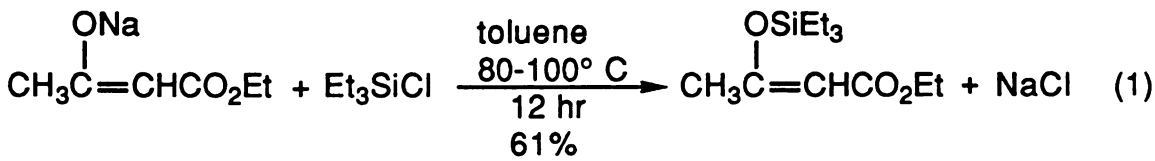
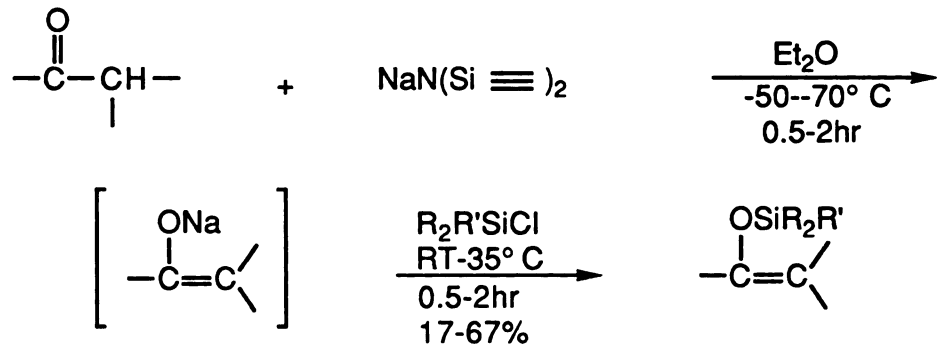


Figure 1 - Silyl Enol Ether



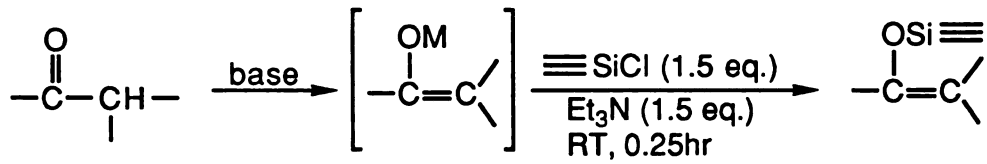
(1)



(2)

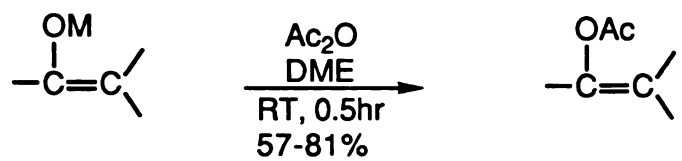
The next advance in the chemistry of silyl enol ethers came as an insightful communication from Stork and Hudrlik[5]. These researchers prepared silyl enol ethers by generating ketone enolates with sodium hydride, or with potassium triphenylmethide (kinetic and eqiulibrium conditions), or by conjugate addition of a cuprate reagent, followed by addition of trimethylsilyl chloride (Equation 3). Stork and Hudrlik envisioned silyl enol ethers not only as isolable derivates of metal enolate ions, but also as convenient presursors for them. It was known from the work of House and Kramer[6] and House and Trost[7] that enolates could be trapped and isolated as enol acetates (Equation 4), and that enol acetates could be used as precursors for enolates through the action of two equivalents of methyllithium (Equation 5). Unfortunately, the by-product of the regeneration is the strongly basic lithium *t* - butoxide which usually interfers with subsequent reactions of the lithium enolates. Stork anticipated that silyl enol ethers would react with one equivalent of methyllithium to produce a lithium enolate and the inert and volatile tetramethylsilane[8] (Equation 6). Stork and Hudrlik even used this by-product as an internal standard in NMR investigations that established the viability of this process. A second and equally valuable observation was that, when the

enolate could be prepared regioisomerically pure, the silyl enol ether would be formed as a single isomer. Further, they observed that regeneration of the metal enolate ion by reaction with organometallics produced (as with enol acetates[7]) the corresponding regioisomer as illustrated in Scheme 1.

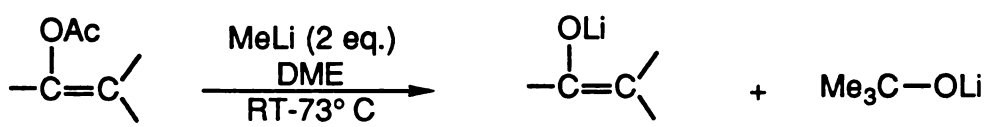


(3)

base=NaH, DME, reflux, 3hr
(Ph$_3$)CK (0.8 eq.), DME, RT, 0.5hr
(Ph$_3$)CK, DME, RT, 0.5hr
MeMgBr/CuI (cat.), Et$_2$O, 0° C, 5min



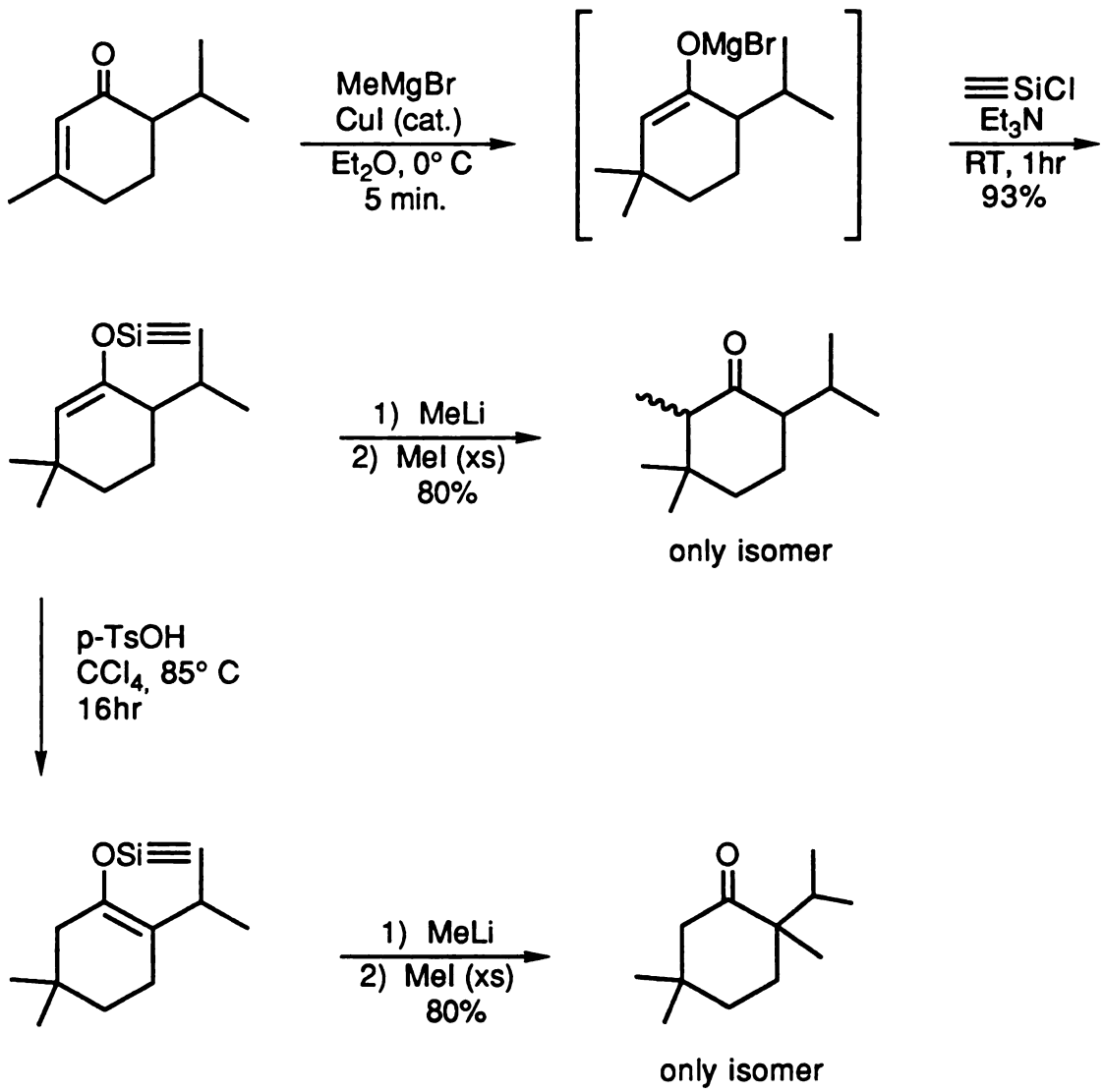
(4)



(5)

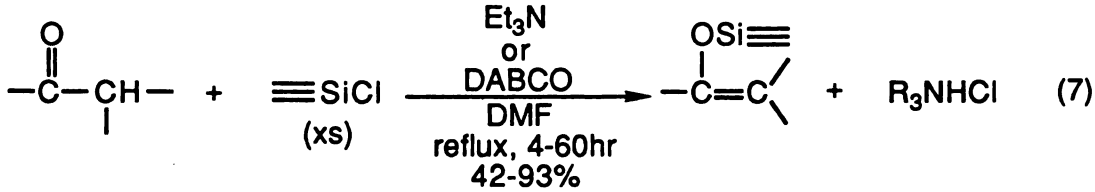
(6)

Scheme 1 - Study of Silyl Enol Ethers by Stork and Hudrlik

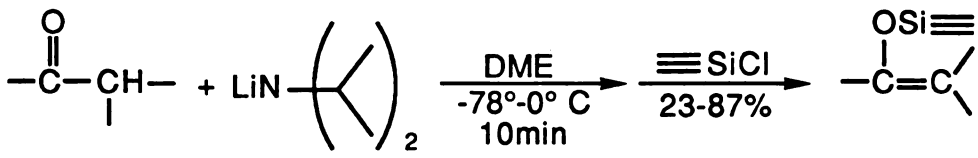


House and co-workers[9] soon added to this growing body of knowledge when they published an independent and highly detailed account of their research on the preparation of silyl enol ethers. House and co-workers developed two new procedures for the synthesis of silyl enol ethers. The first, which they applied to symmetrical ketones, to ketones capable of enolizing in

one direction only, and to aldehydes, involved heating the carbonyl compound in dimethylformamide (DMF) solvent in the presence of an excess of trimethylsilyl chloride using either triethylamine or 1,4-diazabicyclo[2.2.2]octane (DABCO) as the base (Equation 7). The second, which was similar to previous approaches, involved treating a carbonyl compound with the powerful base lithium diisopropylamide (LDA) followed by addition of trimethylsilyl chloride to the resulting enolate solution (Equation 8). Both of these procedures have since become standard for the preparation of silyl enol ethers. The first procedure, because of its simplicity and the low cost of triethylamine, has often been used for the large scale preparation of simple silyl enol ethers. This procedure was important in another respect; whereas previous preparations involved converting the carbonyl compound quantitatively to a metal enolate followed by addition of the silyl chloride in a second step, this one step procedure presumably relied on the ablility of silyl chlorides to trap equilibrium concentrations of enolate ions in the presence of weak tertiary amine bases. In the second procudure, House and co-workers introduced the use of LDA which has proven to be one of the most selective bases for the deprotonation of carbonyl compounds[10]. The use of LDA allowed the preparation of the less substituted (kinetic) enolate and, by silylation, the less substituted silyl enol ether.

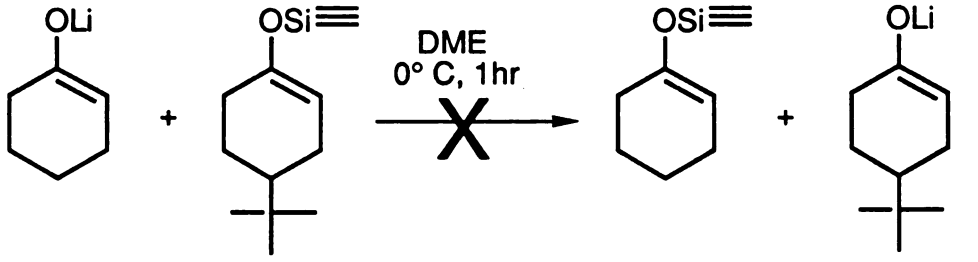


(7)



(8)

House and co-workers also examined the possibility that silyl enol ethers underwent equilibration with enolate anions by attack of the enolate oxygen at silicon. If this process occurred, their ratios of silyl enol ether products (where regioisomers are possible) would not necessarily reflect the ratio of enolate anions. To test this, they prepared a mixture of the silyl enol ether of 4-*t*-butylcyclohexanone and the lithium enolate of cyclohexanone; after standing one hour then quenching with water, they observed no silyl enol ether from cyclohexanone (Equation 9).

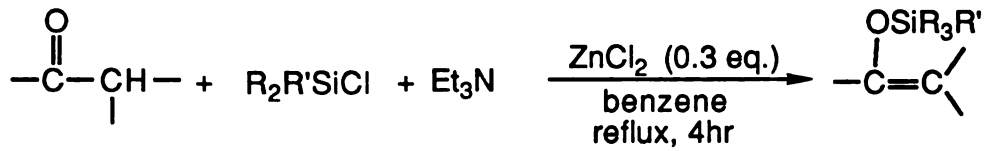


(9)

Since these early fundamental studies, many other preparations of silyl enol ethers have been developed. The preparations have typically been one step procedures and, as the reactions of silyl enol ethers developed, increasing attention was focused on regioisomeric purity. The different preparations are briefly reviewed in chronological order.

In a French patent, Bazouin and co-workers[11] at Rhone-Poulenc showed that addition of an alkyl halosilane to a solution of a ketone or

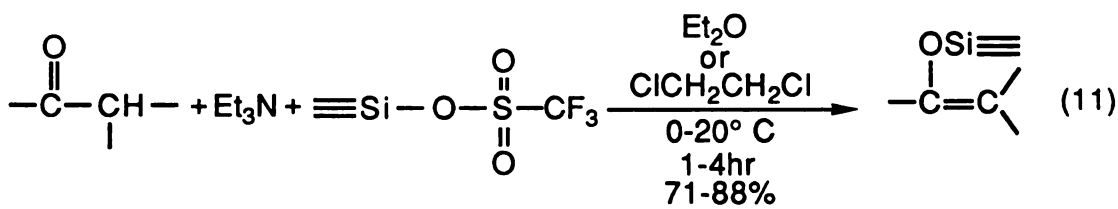
aldehyde with triethylamine and a catalytic amount of anhydrous zinc chloride led to silyl enol ethers (Equation 10). The zinc chloride reduces both the time and temperature necessary for silylation as compared to the House procedure in DMF. The mild conditions have made this procedure ideal for the preparation of reactive siloxydienes[12].



Increasing the acidity of carbonyl compounds by use of Lewis acid catalysts led naturally to the use of more reactive (more Lewis acidic) silylating agents. In 1976 Simchen and Kober[13] reported an extremely efficient, if somewhat costly, preparation of silyl enol ethers using trimethylsilyl trifluoromethansulfonate (trimethylsilyl triflate) and triethylamine. The silylation is typically performed in diethyl ether or 1,2-dichloroethane at temperatures of 0-20° C and is complete in several hours (Equation 11). Simchen and co-workers[14] later investigated this process in greater detail and published the relative rates for silylation of ketones using a variety of silyl reagents in the presence of triethylamine (Table 1). As can be seen from Table 1, trimethylsilyl triflate is second only to trimethylsilyl iodide in reactivity.

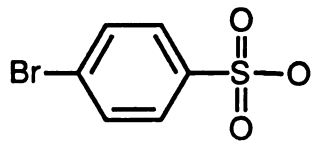
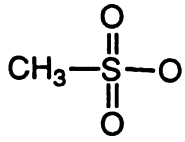
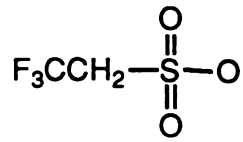
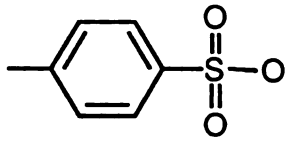
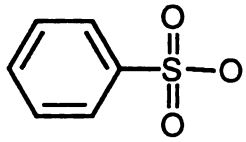
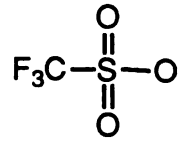
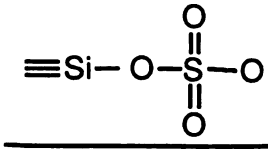
An interesting approach to the preparation of silyl enol ethers was developed by Kuwajima and co-workers[15] in 1976. They reported that a combination of ethyl trimethylsilylacetate[16] and tetra-n-butylammonium fluoride (ETSA-TBAF) would convert ketones and aldehydes to silyl enol ethers in high yields. Their procedure employs 0.01-0.003 equivalents of TBAF in THF solvent at ambient temperature for one to three hours (Equation 12). The

reaction pathway is believed to involve generation of an ester enolate by fluoride induced desilylation, deprotonation of the carbonyl compound by the ester enolate, and reaction of the resulting enolate with either trimethylsilyl fluoride or with ethyl trimethylsilyl acetate (Scheme 2). Tamura and co-workers[17] later reported a very similar procedure in which methylketene methyl trimethylsilylacetal is used in place of ethyl trimethylsilylacetate (Equation 13). Their procedure is believed to follow the same course as that of Kuwajima. The mechanism is especially interesting as it contrasts to the results of House (Equation 9). These procedures avoid large amounts of inorganic salt or HCl-amine salt by-products and do not require aqueous workup.

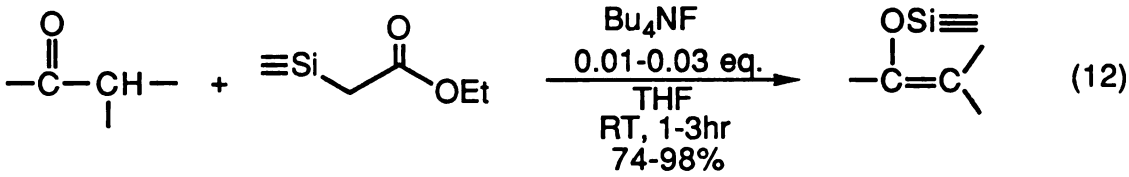


House and co-workers reported that, "attempts to obtain silyl (enol) ethers by reactions of ketones with sodium hydride in the presence of excess trimethylsilyl chloride to trap the enolate anions as formed were uniformly unsuccessful."[9] In 1978 Hudrlik and Takacs[18] reinvestigated this approach and found that while the reaction was highly solvent dependent, it would procede with either sodium or potassium hydride (only trace amounts of product observed with lithium hydride). The reaction was found to be most

Table 1 - Relative Rates for the Silylation of Ketones with Silyl Reagents and Triethylamine

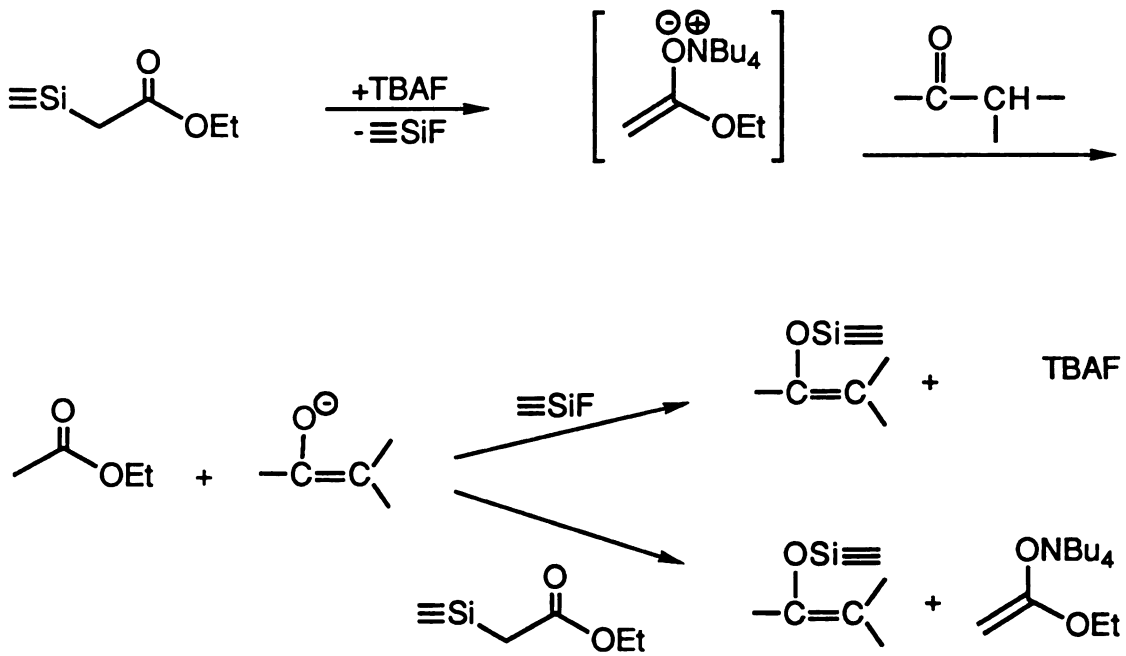
X	K_{rel}	X	K_{rel}
Cl	1		570
	40		$1.4x10^4$
	100	Br	$1x10^4$
	160		$6.7x10^8$
	270	I	$7x10^9$

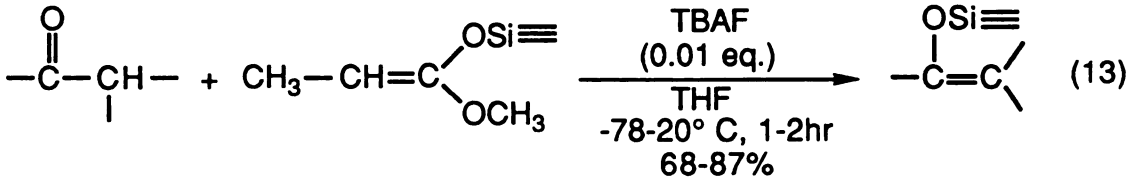
from reference 14



(12)

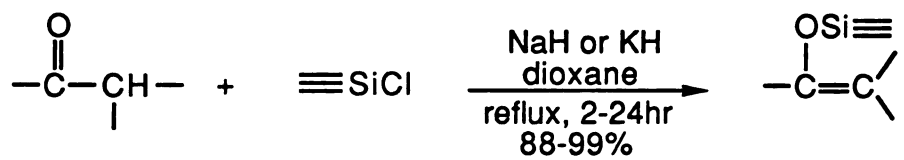
Scheme 2 - Synthesis of Silyl Enol Ethers Using Ethyl Trimethylsilylacetate and TBAF



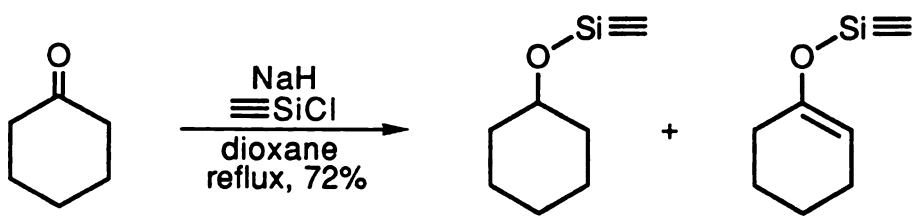


(13)

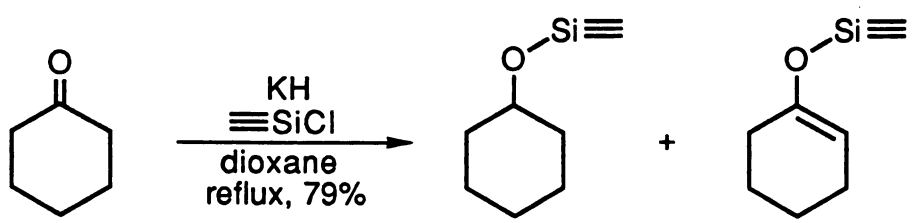
satisfactory when using sodium hydride in heptane, toluene or dioxane at reflux temperature, or when using potassium hydride in dioxane at reflux temperature (Equation 14). It is commonly believed that the reaction of alkali metal hydrides with carbonyl compounds is catalyzed by traces of alkoxides acting as proton transfer agents. These researchers were led by this observation to consider that, to the extent that reduction of the ketone by the metal hydride took place, silyl ethers would be formed by trapping the alkoxide with trimethylsilyl chloride; to the extent that direct enolization took place, silyl enol ethers would be formed. This is clearly shown by their results, two examples of which are given in Equations 15 and 16.



(14)

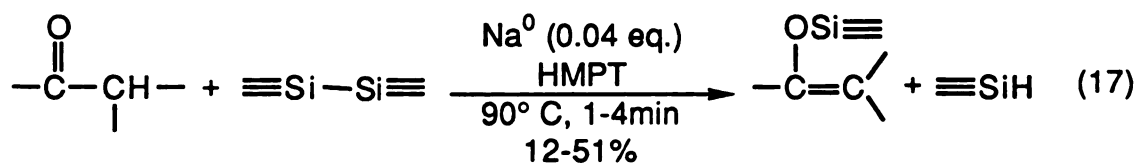


(15)

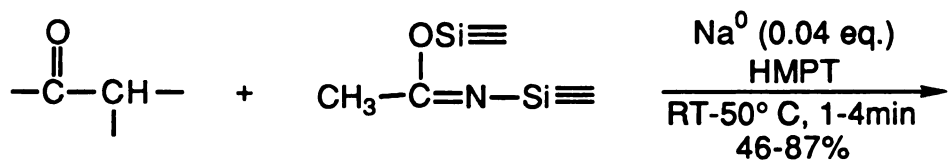


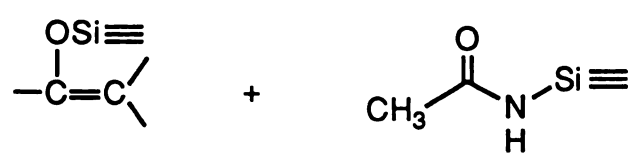
(16)

Another procedure which relies upon reductive conditions was developed by Geruad and Frainnet[19] in 1978. They discovered that silyl enol ethers could be prepared from ketones using hexamethyldisilane in the presence of a catalytic amount of sodium in HMPT solvent (Equation 17). The yields of product, unfortunately, were poor; but two years later they reported[20] a similar system in which bis(trimethylsilyl)acetamde[21] was used as the silylating agent with marked improvement in yields (Equation 18). For both systems they proposed that a trace amount of a ketone enolate was formed by the action of the sodium metal, and this then reacted with the silylating agent. The anion produced from this reaction would then deprotonate a ketone, allowing the system to operate catalytically (Scheme 3).



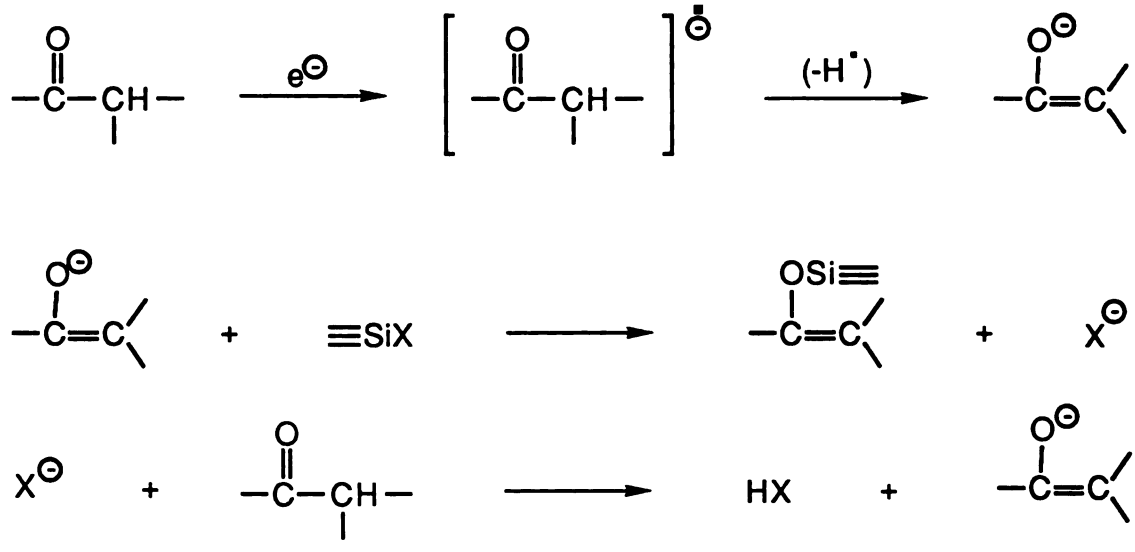
(17)



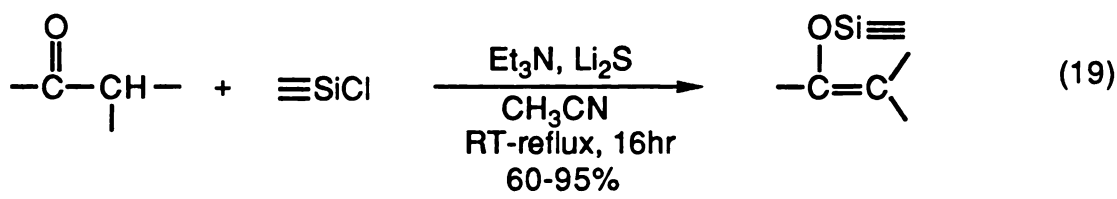


(18)

Scheme 3 - Synthesis of Silyl Enol Ethers Using Sodium Metal and Silylating Reagents

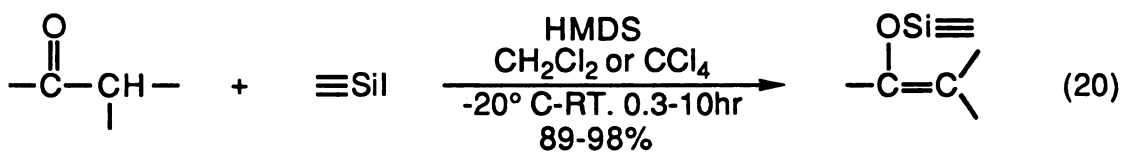


Olah and co-workers[22] introduced a reagent, lithium sulfide, which effectively mediates the reaction of ketones and aldehydes with trimethylsilyl chloride using triethylamine as base (Equation 19). While the mechanism of this procedure is not clear, it apparently does not involve the formation of hexamethyldisilathiane.



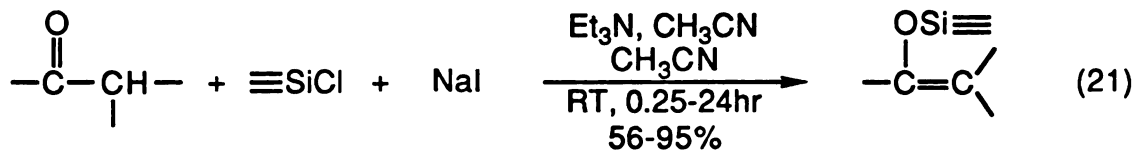
(19)

Use of the most reactive silylating reagent, trimethylsilyl iodide, for the preparation of silyl enol ethers was reported by Miller and McKean[23] in 1979. They obtained excellent yields of product from ketones and aldehydes, using trimethylsilyl iodide with hexamethyldisilazane as base in either di- or tetrachloromethane solvent at room temperature or below (Equation 20).



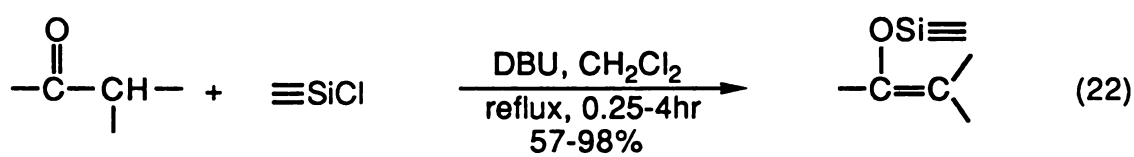
(20)

While the use of trimethylsilyl iodide for the preparation of silyl enol ethers has several advantages, the reagent also has several drawbacks: it should be freshly prepared and used under strictly anhydrous conditions, as it fumes in air and turns purple on standing, making prolonged storage undesirable. Also, although commercially available, it is relatively expensive. In 1979 Olah[24] reported an exceptionally simple and inexpensive method for the *in situ* generation of this reagent from trimethylsilyl chloride and sodium iodide in acetonitrile. This method was soon applied to silyl enol ether synthesis by Duboudin and co-workers[25] (Equation 21).



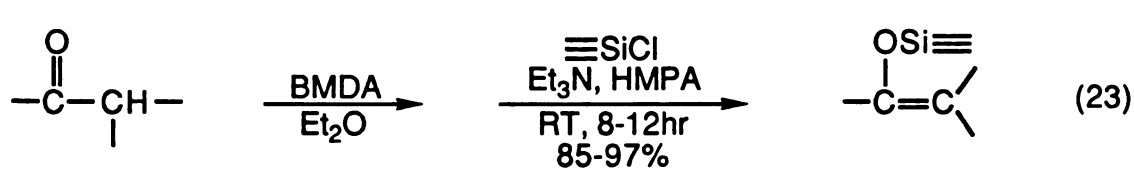
(21)

In 1981 Yamaguchi and co-workers[26] reported the use of 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) as an effective base for the preparation of silyl enol ethers from ketones and trimethylsilyl chloride either with or without silver salts in methylene chloride solvent (Equation 22). Use of triethylamine under the same conditions failed.



(22)

Another base found suitable for the preparation of silyl enol ethers was bromomagnesium diisopropylamide (BMDA) as reported by Krafft and Holton[27] (Equation 23). Their procedure involves addition of a ketone to an ethereal slurry of BMDA followed by addition of trimethylsilyl chloride, triethylamine and hexamethylphosphoramide (HMPA). This procedure was found to be effective only for highly hindered ketones, as other ketones gave substantial amounts of aldol products.



(23)

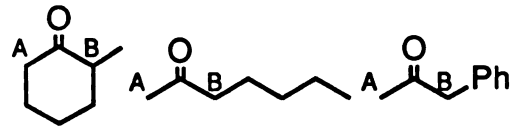
Corey[28] reported the suprising fact that trimethylsilyl chloride could be present during the deprotonation of ketones with LDA at -78° C. This internal quench procedure reduces losses due to self-condensation, and reduces the possibility of equilibration of the enolate anions.

The regioselectivity of the various silyl enol ether preparations for three representative unsymmetrical ketones can be seen in Table 2. The first six entries apparently represent the inherent selectivity of strong bases in the kinetic deprotonation of ketones. Of note are the ratios obtained for potassium triphenylmethide and for potassium hydride, since potassium enolates are believed to undergo rapid equilibration even under "kinetic" conditions. The other entries all tend to favor the more substituted silyl enol ether. The ratios obtained with trimethylsilyl chloride and triethylamine in DMF are in close agreement with the thermodynamic ratios obtained upon prolonged acid catalyzed (*p* -TsOH) equilibration published by Stork[5].

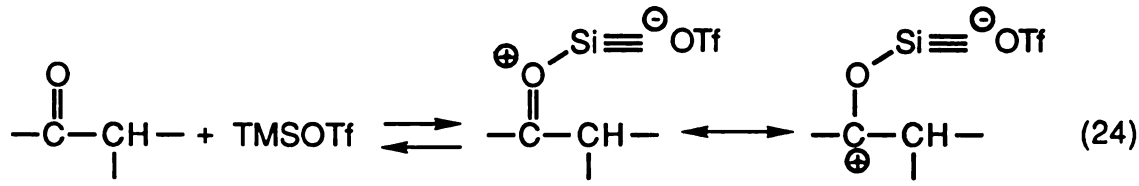
Indeed, while Stork and Hudrlik could equilibrate a mixture of regioisomers with acid in carbon tetrachloride at reflux for 16 hours. (Scheme 1), House and co-workers[9] found equilibraiton could be most satisfactorily performed with a mixture of triethylamine hydrochloride and trimethylsilyl chloride in DMF. The equilibration was faster and there was less loss of product due to desilylation and/or aldol condensation.

Simchen and co-workers[30] proposed an interesting mechanism for the equilibration of silyl enol ethers in the presence of trimethylsilyl triflate. They believe complexation of a ketone with trimethylsilyl triflate leads to an oxonium intemediate as shown in Equation 24. This intermediate, they speculate, is reactive enough to undergo proton exchange with a silyl enol ether; this process is repeated until the product ratio reflects the acid catalyzed

Table 2 - Regioselection in Silyl Enol Ether Preparations

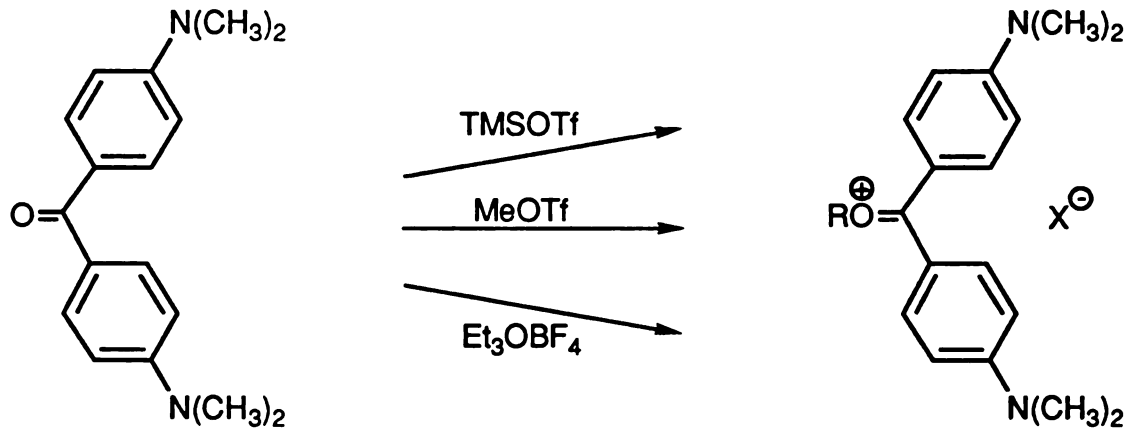
Entry	Procedure	Silyl Ether Ratio (A/B) 			Investigator[ref.]
1	LDA, internal quench	----	95:5	50:50	Corey[28]
2	LDA then ≡SiCl	99:1	84:16	0:100	House[9]
3	≡Si(CH$_2$)C(=O)OEt , Bu_4NF	70:30	86:14	62:38	Kuwajima[15]
4	Na^0 (cat.), BSA	75:25	60:40	15:85	Frainnet[20]
5	Ph_3CK (xs.)	67:33	50:50	----	Stork[5]
6	KH, internal quench	63:37	53:47	----	Hudrlik[18]
7	NaH then ≡SiCl	26:74	----	----	Stork[5]
8	≡SiOTf, Et_3N	26:74	----	60:40	Simchen[13]
9	≡SiCl, Et_3N, NaI	10:90	56:44	40:60	Duboudin[25]
10	≡SiI, HMDS	10:90	8:92	----	Miller[23]
11	≡SiCl, Et_3N, DMF	12:88	8:92	----	House[9]
12	BMDA, ≡SiCl, Et_3N	3:97	----	----	Krafft[27]

equilibration ratio. As evidence for the possibility of this oxonium intermediate they prepared and characterized, with UV and NMR, the salts formed from Michler's ketone and the three electrophilic reagents shown in Scheme 4.



(24)

Scheme 4 - Oxonium Ion Formation with Michler's Ketone

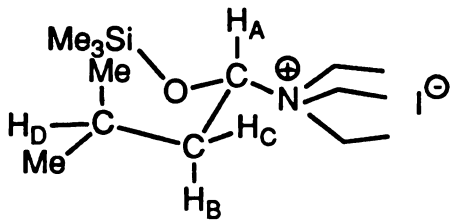


Duboudin and co-workers[25], using a similar silylating system (*in situ* generated trimethylsilyl iodide with Et_3N), have proposed a different explanation for the observed regiochemistry. They detected (by ^1H NMR) onium salts (Figure 2), formed by reaction of a carbonyl compound with trimethylsilyl iodide and triethylamine, which they claimed were the immediate precursors to silyl enol ethers. They further claimed that a unimolecular thermal elimination from these onium intermediates would account for the formation of silyl enol ethers. They propose that the regiochemistry is determined by

elimination from these onium intermediates would account from the formation of silyl enol ethers. They propose that the regiochemistry is determined by

> A transition state somewhat polarized depending on the steric hindrance of the amine and the carbonyl skeleton, with eventual assistance of the lone pair of either the nitrogen or I^- for the abstraction of the proton. This transition state could be stabilized by the mesomeric effect of the trimethylsiloxy group. The regiochemistry would be governed by the length and the strength of the nitrogen functional carbon bond which depends on the steric hindrance of the ketone and the amine in the transtion state.

Duboudin and co-workers provided a scheme (Scheme 5) to rationalize their results.

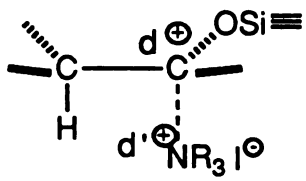


	d	Coupling Constants (J=Hz)
H_a	4.70, d	$J_{AB} = 9$, $J_{AC} \cong 0$
H_b	1.73	$J_{BC} = 13.5$, $J_{BD} = 2.5$
H_c	1.97	$J_{CD} = 11.5$
H_d	1.73	

Figure 2 - Onium Salt Characterized by Duboudin

Scheme 5 - Transition States Depicted by Duboudin

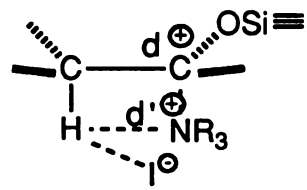
Strong steric hindrance



$d^{\oplus} >> d'^{\oplus}$

(formation of the more substituted enoxysilane)

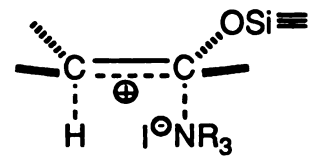
middle



$d^{\oplus} > d'^{\oplus}$

(formation of the less substituted enoxysilane)

weak



(formation of the more substituted enoxysilane)

trimethylsilyl iodide and a weak tertiary amine base, that would produce the less substituted silyl enol ether. Weak base routes to silyl enol ethers have proven to be efficient for a wide variety of carbonyl compounds, and when compared to strong base routes (requiring bases such as LDA, NaHMDS, Ph_3CK, or KH) are notably less expensive. Since the most common procedure used to produce the less substituted silyl enol ether requires the use of LDA, a weak base route to these regioisomers would likely be an attractive, low cost alternative. The effect on regioselection that the various reaction parameters (addition order, solvent, stoichiometry and temperature) might have, has not been reported. The second objective was to gain some mechanistic insight into silylation reactions that might resolve the conflicting proposals put forth by Simchen and co-workers[29], and by Duboudin and co-workers[25], to explain the observed regioselection.

RESULTS

To study regioselection in the formation of silyl enol ethers, 2-methylcyclohexanone was chosen as the model unsymmmetrical ketone. The trimethylsilyl iodide used in these studies was prepared by the method of Lissel and Drechsler[30] (Equation 25). By freshly preparing trimethylsilyl iodide as a pure compound, any secondary factors present in an in situ preparation, such as unreacted trimethylsilyl chloride and metal salts, are avoided. In addition, trimethylsilyl iodide is readily soluble in a wide range of solvents, whereas *in situ* preparations are often restricted by the solubility of the metal iodide.

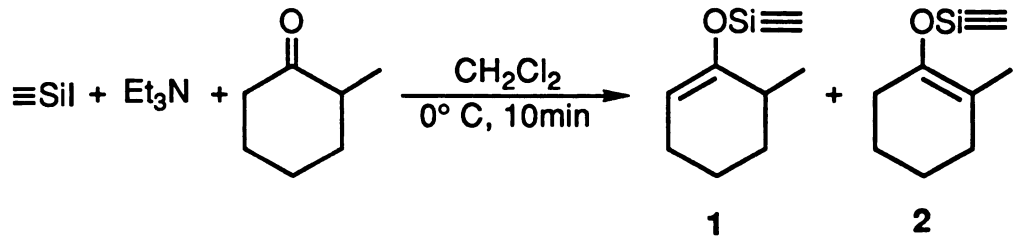
$$\equiv SiCl + LiI \xrightarrow[\text{RT, 4hr}]{\text{neat}} \equiv SiI + LiCl \qquad (25)$$

81-88%

As standard reaction conditions, 2-methylcyclohexanone was added to a mixture of trimethylsilyl iodide and triethylamine in methylene chloride at 0° C (Equation 26). After ten minutes, an internal standard was added and the reaction mixture was analyzed (by GLC) for the regioisomeric silyl enol ethers **1** and **2**. Changing the addition order of the three reactants had little effect on the ratio of products (Table 3). Use of excess triethylamine in the reaction shifted the ratio of products slightly and gave nearly the same conversion of ketone as the standard reaction.

A survey of a variety of solvents (Table 4) showed some effect on the regioselection in silyl enol ether formation. The greatest percentage of the less substituted isomer was obtained in pentane, but the ratio had only improved from approximately 9:1 to 4:1 in favor of the more substituted isomer.

Since the reaction appeared to be most selective in pentane, the effect of temperature on the reaction was examined using this solvent (Table 5). When the temperature was lowered to -78° C, the reaction showed a rapid initial conversion of the ketone to silyl enol ether, but failed to reach completion even after 1.5 hours at -78° C. The ratio of products also showed a marked change



(26)

1 **2**

Table 3 - Effect of Addition Order and Excess Amine of **1**:**2** Ratio

Entry	Equivalents[a]			Addition Order	Product[b] Ratio **1** : **2**
	≡SiI	Et_3N	Ketone		
1	1	1	1	Ketone last	9:91
2	1	1	1	≡ SiI last	7:93
3	1	1	1	Et_3N last	5:95
4	1	2	1	Ketone last	15:85

a) Reations conducted in CH_2Cl_2 (0.5 M) at 0° C for 10 minutes.
b) Ratio determined by GLC analysis

Table 4 - Effect of Solvent on **1**:**2** Ratio

Entry	Solvent[a]	Product Ratio (**1** : **2**)[b]
1	benzene	18:32
2	Et_2O	14:86
3	pentane	18:32
4	1,2-dichloroethane	10:90

a) Reactions conducted with 2-methylcyclohexanone (1 eq.), Et_3N (1 eq.), and trimethylsilyl iodide (1 eq.) at 0° C at 0.5 M concentration.
b) Ratio determined by GLC analysis.

as the reaction progressed; the ratio after 30 minutes was 33:67 (entry 3) but had changed to 14:86 (entry 4) at similar conversions of ketone to silyl enol ether.

Table 5 - Effect of Temperature on **1**:**2** Ratio

Entry	Temperature[a]	Time (min)	Ketone[b] (%)	Product[c] Ratio (**1** : **2**)
1	0° C	10	11	18:81
2	-78° C	10	41	30:70
3	-78° C	30	35	33:67
4	-78° C	60	38	14:86
5	-78° C	90	29	14:86

a) Reactions conducted with 2-methylcyclohexanone (1 eq.), Et_3N (1 eq.), and trimethylsilyl iodide (1 eq.) in pentane (0.5 M).
b) Determined by GLC analysis using decane as internal standard.
c) Ratio determined by GLC analysis.

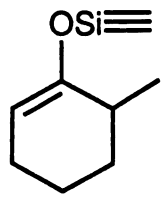
The effect of the steric demands of the base was briefly examined by using N,N-diisopropylethylamine (Hunig's base), either alone or in conjunction with triethylamine, in pentane at 0° C (Table 6). The isomer ratio in both of these reactions was in close agreement with the results obtained with triethylamine under the same reaction conditions.

Table 6 - Effect of Base on **1**:**2** Ratio

Entry	Base[a]	Time (min)	Ketone[b] (%)	Product[c] Ratio (**1** : **2**)
1	$(i\text{-}Pr)_2NEt$	5	23	16:84
2		30	16	16:84
3	$(i\text{-}Pr)_2NEt + Et_3N$	5	24	18:82
4		30	9	18:82

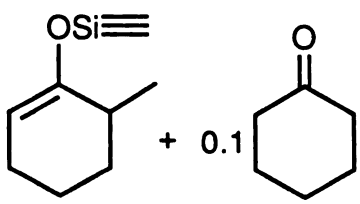
a) Reaction conducted with 2-methylcyclohexanone (1 eq.) and trimethylsilyl iodide (1 eq.) in pentane (0.5 M) at 0° C.
b) Determined by GLC analysis using decane as internal standard.
c) Ratio determined by GLC analysis.

A possible acid catalyzed equilibration of the isomers under the reaction conditions was also examined. The less substituted minor isomer **1** was prepared as a pure compound by the method of House[9]. When this compound was added to a mixture of trimethylsilyl iodide (0.1 equivalents) and triethylamine in CH_2Cl_2 at 0° C, no equilibration to the more substituted isomer **2** was observed by GLC analysis, even after 30 minutes (Equation 27). When compound **1** was submitted to the reaction conditions given by Equation 28, a small amount of the other regioisomer was observed. This was also true for the reaction given by Equation 29, despite the 10 fold increase in reactants *vs* compound **2.** Using Hunig's base in this reaction gave a 89:11 ratio of products (Equation 30).



1

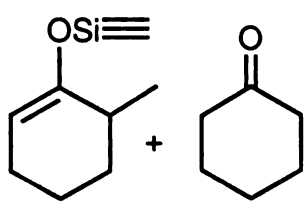
+ Et_3N + 0.1 ≡SiI $\xrightarrow[0°\ C,\ 30\ min]{CH_2Cl_2}$ no equilibration (27)



1

+ 0.1 + 0.1 Et_3N + 0.1 ≡SiI $\xrightarrow[0°\ C,\ 5\ min]{CH_2Cl_2}$ **1 : 2** (28)

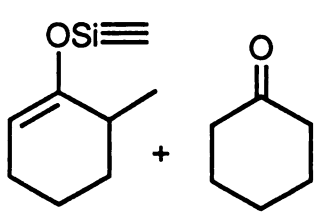
93:7



+ + Et_3N + ≡SiI $\xrightarrow[0°\ C]{CH_2Cl_2}$ **1 : 2** (29)

10 min 94:6

40 min 94:6



1

+ + $(i\text{-}Pr)_2NEt$ + ≡SiI $\xrightarrow[0°\ C]{CH_2Cl_2}$ **1 : 2** (30)

10 min 94:6

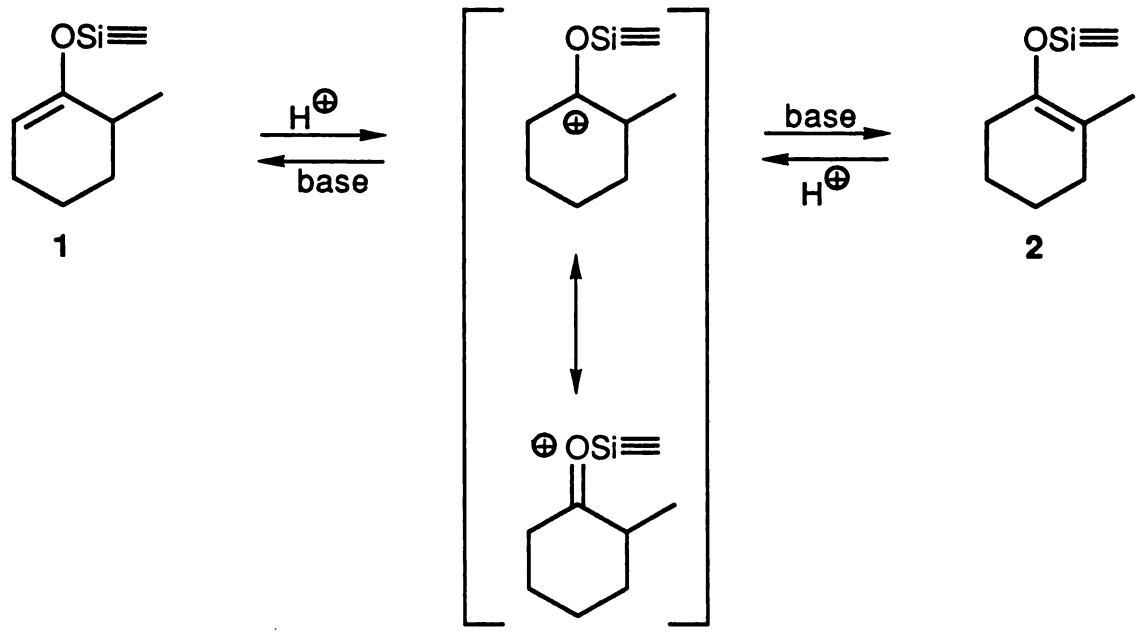
40 min 94:6

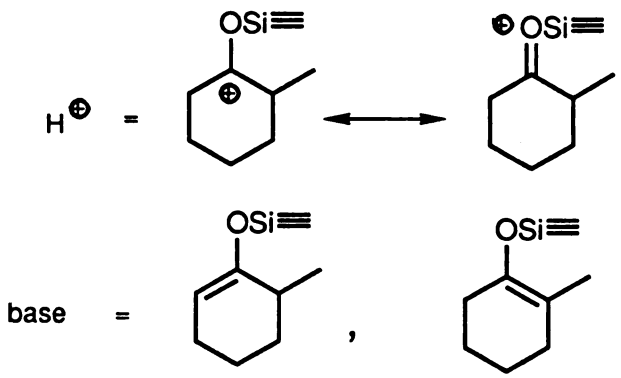
DISCUSSION

The lack of response to the changes made in the reaction conditions led us to consider the mechanistic proposals put forth by Simchen and co-workers[29] and by Duboudin and co-workers[25]. Since the ratio of isomers obtained in these experiments was similar to the ratios obtained by Stork and Hudrlik[5] and by House and co-workers[9] upon prolonged acid catalyzed equilibraion, it was possible that a rapid equilibrium was reponsible for the predominance of the more substituted isomer **3**. In support of this possibility, a slight change in the isomer ratio was observed at low temperature in pentane solvent (Table 5). Simchen proposes a rapid equilibrium and proposes that an oxonium intermediate serves as the proton donor for this process. For the reaction studied here, the equilibration would thus be given by Scheme 6.

We have tested this possible equilibration process by experiment. Compound **1** was prepared and as a control added to a mixture of trimethylsilyl iodide and triethylamine. As expected, no equilibration was observed. To generate an oxonium intermediate, cyclohexanone was silylated under the usual reaction conditions. Cyclohexanone should behave analogously to 2-methylhexanone and form an oxonium ion intermediate. If compound **1** reacted with this, the equilibration described by Scheme 6 should occur. It is noteworthy that isomerization took place only to the extent of 6-7%, under the standard reaction conditions, when silylating either 0.1 or 1.0 equivalent of the cyclohexanone. This small percentage of isomerization was far from the 10:90 **1**: **2** ratio observed for acid catalyzed equilibration of compound **2**. As the ratio did not change over time, the possibility of a

Scheme 6 - Oxonium Ion Catalyzed Equilibration of **1** and **2**



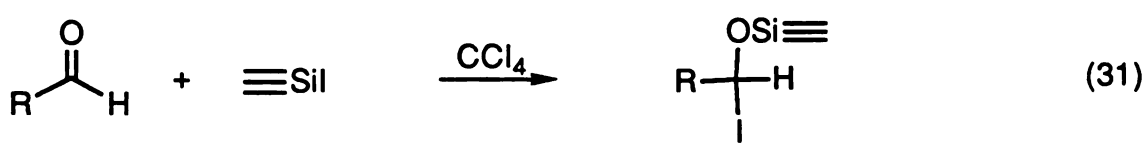


significant equilibration process here seems slight. The oxonium ion is not ruled out as a reactive intermediate in the reaction, but it appears not to influence the regiochemical outcome as a proton source. If the results presented here are accurate and not due to adventitious traces of acid, the equilibration would account for the differences in the ratios found for reactions

in other solvents. The non-polar solvent pentane would be expected to be least favorable for oxonium ion formation and might lead to greater selectivity for compound **1**.

It is useful here to review the possible pathways leading to the silyl enol ethers **1** and **2** (Scheme 7).

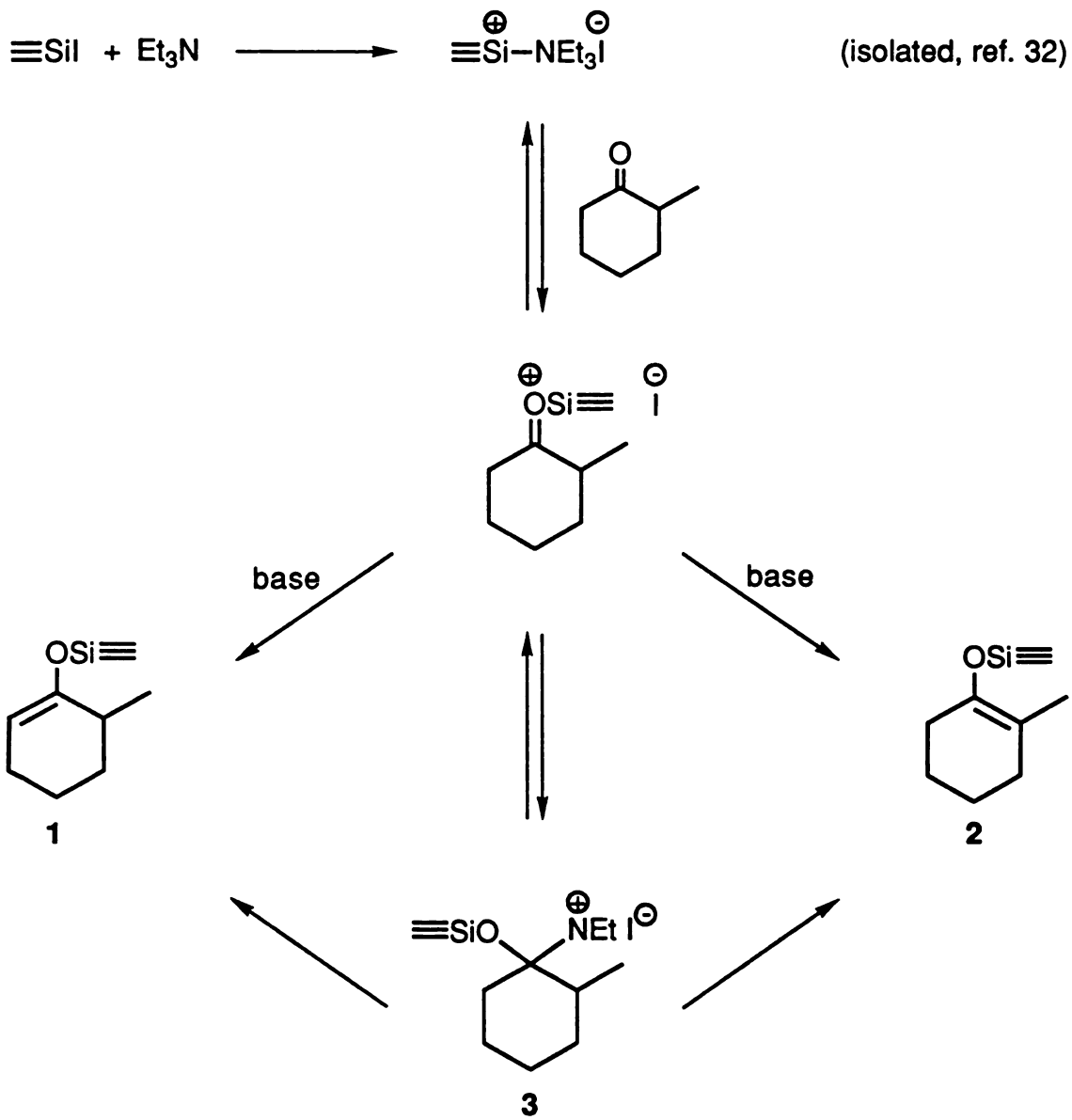
Doboudin and co-workers[25] have proposed that the onium salt **3** is the immediate precursor to the silyl enol ethers **1** and **2**, and that the product is formed by a thermal unimolecular elimination. Several other observations regarding onium intermediates are in order. Jung and co-workers[31] have observed (by ^1H NMR) products given by Equation 31. These products were unfortunately too unstable to be isolated. Duboudin and co-workers claim that the onium adducts of aldehydes could be isolated but provide no experimental procedure and incomplete spectral data. They were unable to isolate ketone onium adducts, such as **3**, since the elimination to silyl enol ethers was facile even at low temperatures.



(31)

The elimination process proposed by Duboudin is of course a variant of the well-known Hofmann elimination. The typical procedure for performing a Hofmann elimination involves heating an organoammonium hydroxide neat either at atmospheric or reduced pressure to distill the olefin as it is formed. Two general features of this reaction are that as substitution at the nitrogen bearing carbon is increased the process becomes more facile and the major

Scheme 7 - Proposed Mechanisms of Silyl Enol Ether Formation



(detected by ^{1}H NMR, reference 25)

isomer is usually the less substituted olefin ("Hofmann rule").

In the case of the intermediate **3** the elimination should be further facilitated by the anomeric effect of the oxygen substituent. The lack of a second organic substituent in the case of onium intermediates derived from aldehydes probably cannot account entirely for the higher temperatures required for their silyl enol ether formation. Finally, the description of the transition state put forth by Duboudin lacks in predictive power. Instead we suggest that the equilibrium between the onium intermediate **3** and the oxonium intermediate is shifted to favor **3**, leading to longer reaction times or higher temperatures necessary for conversion to product. The regioselectivity observed can be accounted for by suggesting that the transition state from the oxonium ion to product is late and simply reflects the difference in product stability.

EXPERIMENTAL

A. General

Methylene chloride, pentane and 1,2-dichloroethane were dried by distillation from CaH_2 under argon. Diethyl ether was used directly from a freshly opened can. Benzene was dried by distillation from sodium / benzophenone. Trimethylsilyl chloride was distilled from CaH_2 and stored over polyvinylpyridine under argon. Trimethylsilyl iodide was prepared by the method of Lissel and Drechsler[30] and stored over copper metal under argon. Trimethylsilyl iodide was prepared fresh weekly. Lithium iodide was purchased from Aldrich Chemical Company, used as received and stored in a dry dessicator. Triethylamine, diisopropylamine, and diisopropylethylamine were dried by distillation from CaH_2 under argon. Cyclohexanone (Fisher) and 2-methylcyclohexanone were dried by distillation from CaH_2 under argon. Decane (Aldrich Gold Label-99%) and n-BuLi 1.6 M in hexane (Aldrich) were used as received.

Gas chromatography was performed with a Hewlett-Packard 5880A instrument fitted with either a Foxboro 25 meter GB-1 column (I. D. 0.25 mm, 0.25 mm film). Infrared spectra were obtained from neat samples on KBr plates using a Nicolet FT-IR/42 instrument (absorptions reported in cm^{-1}). ^1H NMR spectra were obtained in $CDCl_3$ (Cambridge Isotopes Inc.) using either a Varian VXR-300 (s) at 300 MHz. ^{13}C NMR spectra were obtained using a Varian VXR-300 (s) at 75 MHz. Chemical shifts are reported in parts per million

(d scale). Data are reported as follows: chemical shift (multiplicity: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet; intregration; coupling constant in Hz). Mass spectra were obtained using a Finnigan 4000 EI GC/MS instrument at the ionizing energy (eV) indicated. Data are reported as m / e (relative intensity).

All glassware used in the following procedures was oven dried (120° C) and purged with argon. Typically, the reactions were conducted in round bottom flasks fitted with magnetic stirring, a gas takeoff valve (to Hg bubbler) and a septem inlet. Addition of reagents employed standard syringe techniques. Concentration of organic extracts was accomplished at reduced pressure (aspirator) using a rotory evaporator.

B. Optimization of **1**: **2** Isomer Ratio Using Trimethylsilyl Iodide

The following general procedure was used to obtain the results presented in Tables 3-6.

To a stirred solution of trimethylsilyl iodide (0.27 mL, 2 mmol) in the specified solvent (4 mL) was added the specified amine (2 or 4 mmol, as specified) and 2-methylcyclohexanone (243 µL, 2 mmol) at either 0° C (ice) or -78° C (dry ice-acetone) (as specified). After 10 minutes, decane (0.39 mL, 2 mmol) was added as an internal standard. An aliquot was removed via syringe and immediately analyzed by GLC for compounds **1** and **2**. All reactions showed satisfactory mass balance by GLC.

C. Preparation of 1-Trimethylsiloxy-6-methylcyclohexene **1**.

To a solution of diisopropylamine (14.7 mL, 105 mmol) in Et_2O (150 mL) cooled to 0° C with an ice bath, n-BuLi 1.6 M in hexanes (66 mL, 105 mmol) was added slowly and allowed to stir for 20 minutes. The LDA solution was

cooled to -78° C with an acetone-dry ice bath and 2-methylcyclohexanone (12.2 mL, 100 mmol) was added dropwise over 10 minutes. This mixture was allowed to stir for 1 hour at -78° C. A full vacuum was applied to remove the solvent and amine, leaving a white solid. Et_2O (200 mL) was added to dissolve the enolate and the clear solution cooled to -78° C. Trimethylsilyl chloride (12.7 mL, 100 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. Workup with 1:1 ice / $NaHCO_3$ (200 mL) and pentane (200 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material showed a 94:6 ratio of **1**: **2**; conversion of ketone to product >90%. Distillation at reduced pressure through a Nester-Faust annular spinning band column (60 cm length, I. D. 0.5 cm) at a reflux ratio of 20:1, gave pure material at 86-91° C (46 mm Hg).

IR (neat): 3024, 2961, 2936, 2858, 1663, 1458, 1252, 1192, 953, 903.
^1H NMR (300 MHz, $CDCl_3$): δ 0.15 (s, 9H, $SiCH_3$), 1.00 (d, 3H, 6.9 Hz, CH_3), 1.27-2.18 (m, 7H, CH_2, CH), 4.77 (td, 1H, 3.9, 1.2 Hz, enol).
^{13}C NMR (75 MHz, $CDCl_3$): δ 0.34, 18.68, 20.28, 24.36, 31.63, 33.61, 103.47, 154.19.
Spectral data is in agreement with reference 9.

D. Equilibration Studies of 1-Trimethylsiloxy-6-methylcyclohexene **1**

1. **1** / Et_3N / $(CH_3)_3SiI$ (1 : 1 : 0.1)

To a solution of **2** (0.1844 g, 1 mmol) in CH_2Cl_2 (2 mL) cooled to 0° C with an ice bath, Et_3N (0.14 mL, 1 mmol) and trimethylsilyl iodide (14 μL, 0.1 mmol) were added and allowed to stir for 30 minutes at 0° C. Decane (0.19 mL, 1 mmol) was added as an internal standard. An aliquot was removed and

immediately analyzed by GLC. Compound **1** was detected in 101% yield against the internal standard; compound **2** was not detected.

2. **1** / cyclohexanone / Et_3N / $(CH_3)_3SiI$ (1 : 0.1 : 0.1 : 0.1)

To a solution of **1** (0.1845 g, 1 mmol) in CH_2Cl_2 (2 mL) cooled to 0° C with an ice bath, Et_3N (0.14 mL, 1 mmol) and trimethylsilyl iodide (14 µL, 0.1 mmol) were added in that order and allowed to stir for 5 minutes at 0° C. Decane (0.19 mL, 1 mmol) was added as an internal standard. An aliquot was removed and immediately analyzed by GLC. Compound **1** was detected in 89.2% yield, compound **2** in 6.9% yield (ratio 93:7) and 2-methylcyclohexanone in 4.1% yield (balance 100%).

3. **1** / cyclohexanone / Et_3N/$(CH_3)_3SiI$ (1 : 1 : 1 : 1)

Using the procedure described above combined **1** (0.1844 g, 1 mmol) in CH_2Cl_2 (2 mL), Et_3N (0.14 mL, 1 mmol), cyclohexanone (0.1 mL, 1 mmol) and trimethylsilyl iodide (0.13 mL, 1 mmol) at 0° C. Decane (0.19 mL, 1 mmol) was added after 10 minutes. An aliquot at 10 minutes showed, by GLC, **1** in 91%, **2** in 6% (ratio 94:6, balance 97%). An aliquot at 40 minutes showed **1** in 90%, **2** in 6% (ratio 94:6, balance 96%). The conversion of cyclohexanone to silyl enol ether was ca. 80%.

4. **1** / cyclohexanone / $(i\text{-}Pr)_2NEt$ / $(CH_3)_3SiI$ (1 : 1 : 1 : 1)

Using the procedure described above combined **1** (0.092 g, 0.5 mmol) in CH_2Cl_2 (1 mL), $(iPr)_2NEt$ (87 µL, 0.5 mmol), cyclohexanone (0.1 mL, 1 mmol) and trimethylsilyl iodide (68 µL, 0.5 mmol) at 0° C. Decane (97 µL, 0.5 mmol) was added after 10 minutes. An aliquot at 10 minutes showed, by GLC, a ratio of **1**: **2** of 89:11. An aliquot at 30 minutes showed **1** in 88%, **2** in 11.5%, and 2-

methylcyclohexanone in 1.5% (ratio 88: 12, balance 101%). The conversion of cyclohexanone to silyl enol ether was ca. 80%.

CHAPTER II

PREPARATION OF SILICON FUNCTIONALIZED SILYL ENOL ETHERS

INTRODUCTION

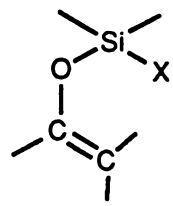
Silyl enol ethers are increasingly important reagents in organic synthesis, measured both by the number and by the diversity of their applications[33]. Applications of silyl enol ethers now surpass those of any other enol derivative and rival those of enolate anions. The chemistry of silyl enol ethers often complements that of enolates; whereas enolates are typically strong nucleophiles and bases, silyl enol ethers are not and often must be used in conjunction with Lewis acid catalysts. Other factors which have made silyl enol ethers ideal for a variety of synthetic endeavors are their low cost, ease of preparation, mild desilylation conditions, and clean reactions.

The development of the chemistry of silyl enol ethers can be divided into three stages. The first stage was their development as trapping agents and as precursors for enolate anions[5,8,9]. The second stage was the development of their reactions with electrophiles under neutral or Lewis acidic conditions. Examples of this include alkylation reactions[34] and the Mukaiyama aldol reaction[35]. The third and most recent stage was the development of reactions unique to silyl enol ethers. Examples of this include their oxidation by palladium to give enones[36], the Diels-Alder reactions of siloxydienes[12,37], cyclopropanation by reaction with carbenes[38], and [2+2] cycloadditions with ketenes[39].

In light of the tremendous expansion of the chemistry of silyl enol ethers, it was surprising to find relatively few examples of silicon functionalized silyl enol ethers. Commonly, simple trimethylsilyl enol ethers are used, though

occasionally, *t* - butyldimethylsilyl enol ethers are used in reactions requiring high temperatures (some Claisen rearrangements of silyl ketene acetals[40]) or strong Lewis acids (some Mukaiyama aldol reactions[41]).

Covalent attachment of groups to the silicon atom of silyl enol ethers is notable in contrast to alkali metal enolates. Functionalized silyl enol ethers (Figure 3) that have a non-alkyl group attached to silicon could offer several extensions to the properties and reactions of silyl enol ethers. The functional group could alter the reactivity of the silyl enol ether. An electron donating group should increase the electron density of the enol ether and cause the enol ether to be more nucleophilic. Alternatively, an electron withdrawing group should make the silicon more Lewis acidic and the silicon might serve as a catalyst for reaction with electrophiles. Additionally, a replaceable functional group could allow intramolecular attachment of an electrophile. The silicon would then act as a tethering atom for an intramolecular reaction of an electrophile and an enol ether. Finally, a functional group on silicon could offer the prospect of improved regioselection in the formation of silyl enol ethers.

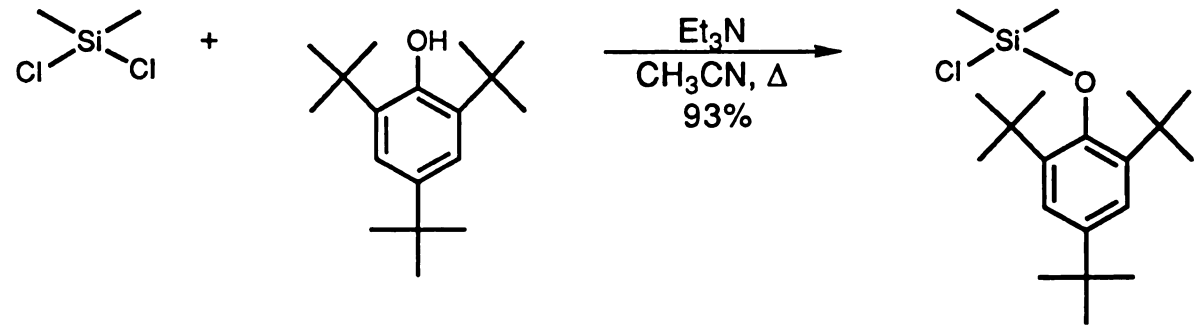


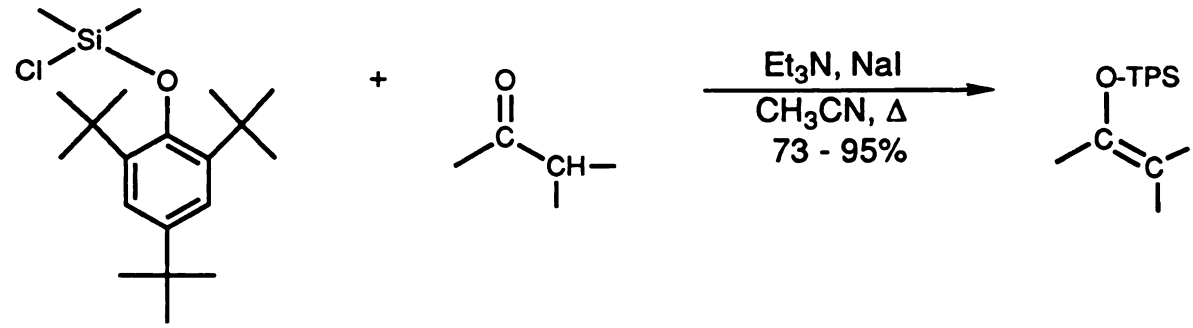
(X ≠ alkyl, aryl)

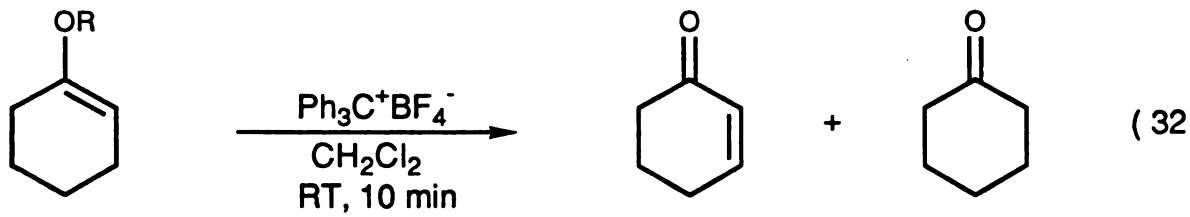
Figure 3 - Silicon Functionalized Silyl Enol Ether

There are some reports of silicon functionalized silyl enol ethers. In these laboratories, Manis and Rathke[42] have prepared (2,4,6-tri-butylphenoxy)dimethylsilyl enol ethers by the method given in Scheme 8. These compounds, in addition to their excellent hydrolytic stability, gave an improved yield in the trityl tetrafluoroborate oxidation of silyl enol ethers (Equation 32).

Scheme 8 - Synthesis of TPS Silyl Enol Ethers







(32)

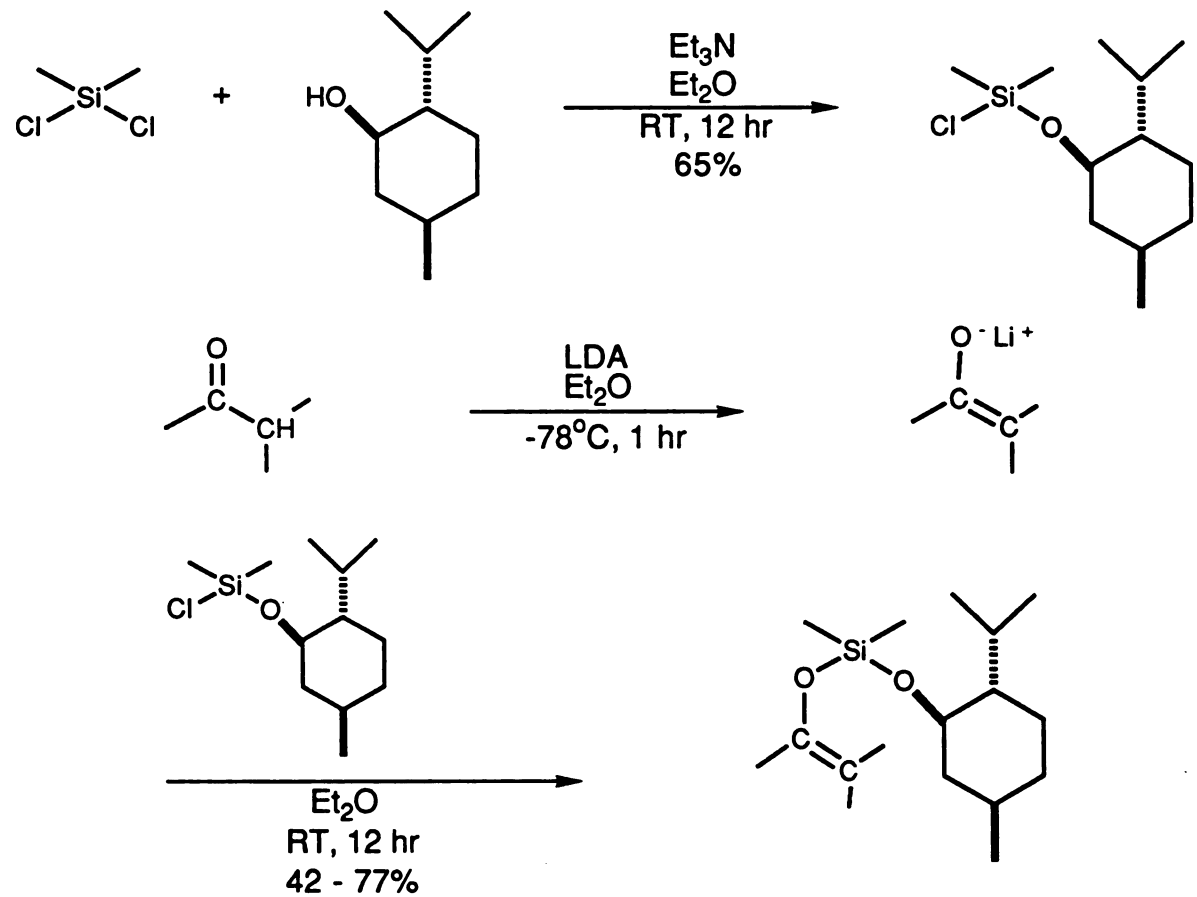
R = TPS	91%	6%
R = $Si(CH_3)_3$	64%	34%

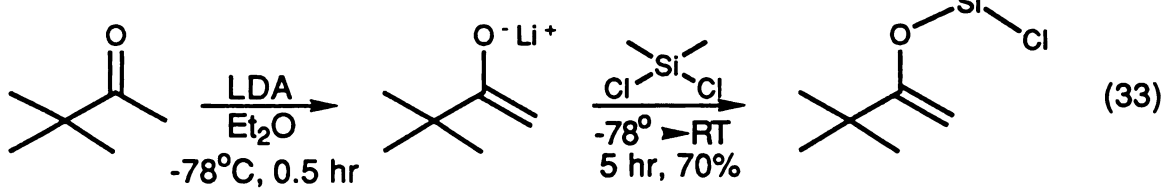
Kaye and Learminth[43] have prepared bornyloxy- and menthyloxy-dimethyl silyl enol ethers (Scheme 9) by a similar route. They anticipate that these chiral auxiliaries will display asymmetric induction in the reactions of the enol ether. These researchers demonstrated several examples of functionalized silyl enol ethers.

A more flexible approach to a wide variety of functionalized silyl enol ethers has been reported by Walkup[44]. After preparing a lithium enolate from pinacolone and LDA, Walkup added dichlorodimethylsilane at low temperature to produce a chlorodimethylsilyl enol ether in good yield (Equation 33). He then found, as expected, that the functionalized silyl enol ether could be substituted at silicon by a variety of protic nucleophiles, in the presence of triethylamine to produce new silyl enol ethers (Equation 34). The success of this approach, of course, depends on a reliable synthesis of chlorodimethylsilyl enol ethers. This requires that the enolate reacts faster with dichlorodimethylsilane than it reacts with the product chlorodimethylsilyl enol ether. That all enolates are able to meet this requirement has been questioned by Kaye and Learmonth[43].

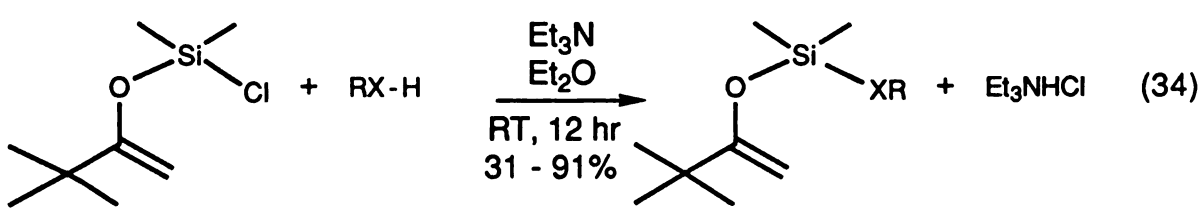
In two subsequent publications Walkup and coworkers described applications of functionalized silyl enol ethers. In the first, Walkup and Obeyesekere[45] prepared a series of silyl enol ethers with (S)-methyl mandelate functionality by the method outlined by Equations 33 and 34. They then epoxidized these silyl enol ethers with *m*-chloroperbenzoic acid (MCPBA) and after opening the epoxide and derivatization of the α-hydroxyketone, they examined the product for facial selectivity in the epoxidation (Scheme 10).

Scheme 9 - Synthesis of Menthyloxydimethylsilyl Enol Ethers





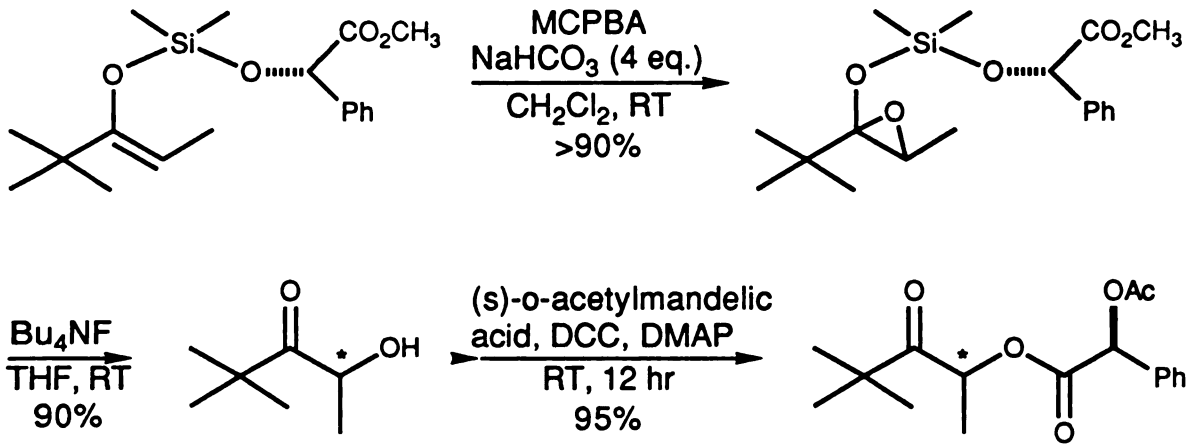
(33)



(34)

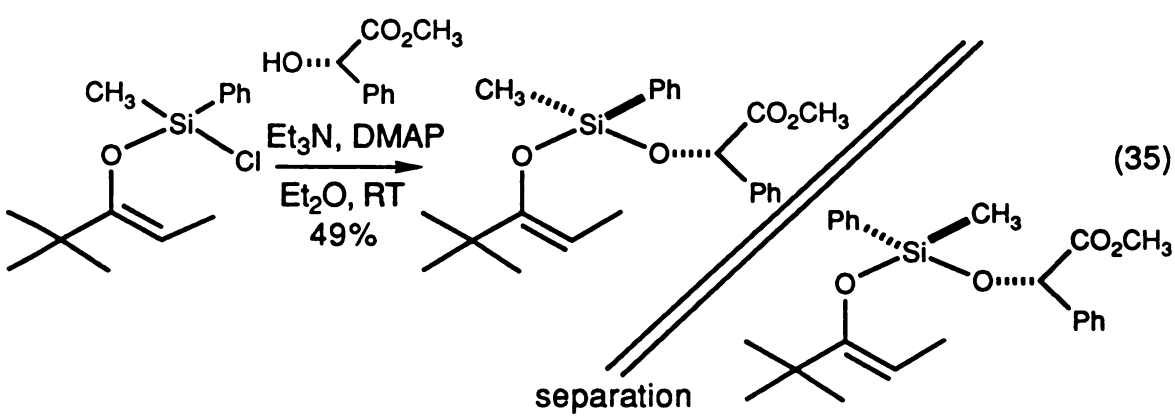
Unfortunately, the enantiomeric excess found for the mandelate-dimethylsilyl enol ether was only 10-14%. Walkup and Obeyesekere then attempted to increase the facial selectivity by preparing silyl enol ethers with the same chiral alkoxide but with a methyl and a phenyl group on silicon (Equation 35). After separation of the diastereomers, the epoxidation sequence was repeated with the individual stereoisomers. Again, the enantiomeric excess was only 10-14%. The major stereoisomer (absolute configuration not assigned) of the product was the same for either diastereomer leading to the conclusion that the diastereofacial selectivity for the epoxidation of an alkoxydimethylsilyl enol ether by MCPBA is affected by a chiral alkoxy group and not by a chiral silicon center[45,46].

Scheme 10 - Epoxidation of (S)-Methyl Mandelatedimethylsilyl Enol Ether

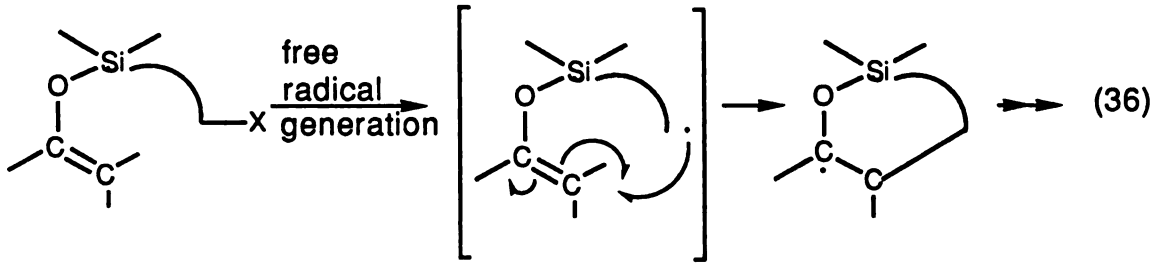


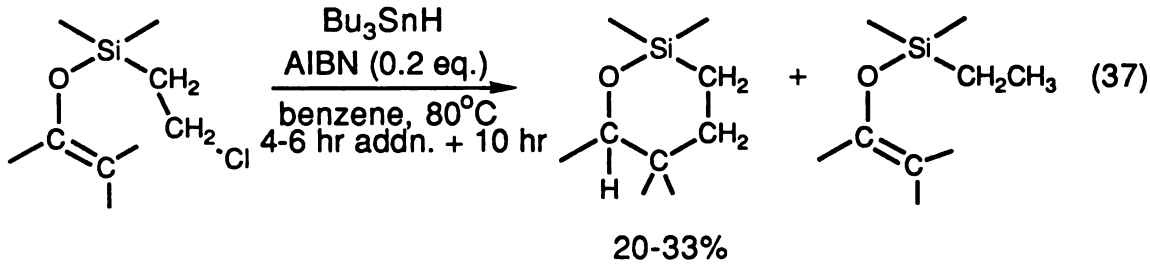
In their second publication on the applications of silicon functionalized silyl enol ethers, Walkup and coworkers[47] examined free radical reactions. They envisioned that a group with a latent radical center could be attached to silicon. Subjecting this functionalized silyl enol ether to radical generating

conditions would allow for an intramolecular radical addition to the enol ether (Equation 36). A series of (2-chloroethyl)dimethylsilyl enol ethers were prepared and tributylstannane in the presence of azobisisobutrylnitrile (AIBN) was added (Equation 37). These gave (by ^1H NMR analysis) a mixture of oxasilacyclohexane and simple reduction products. The oxasilacyclohexane product was difficult to isolate, so the crude mixture was either treated with excess methyllithium to give γ-(trimethylsilyl) alcohols or treated with the Tamao oxidation conditions[48] to give diols (Scheme 11). Overall the process constitutes a reductive α-alkylation of a silyl enol ether. Though the yields are consistently low, and the starting material, chloro(2-chloroethyl)dimethyl silane, is not commercially available[47], this process does demonstrate the use of a silicon group as a "template" for an intramolecular reaction of a silyl enol ether, one of the principle objectives of our research.



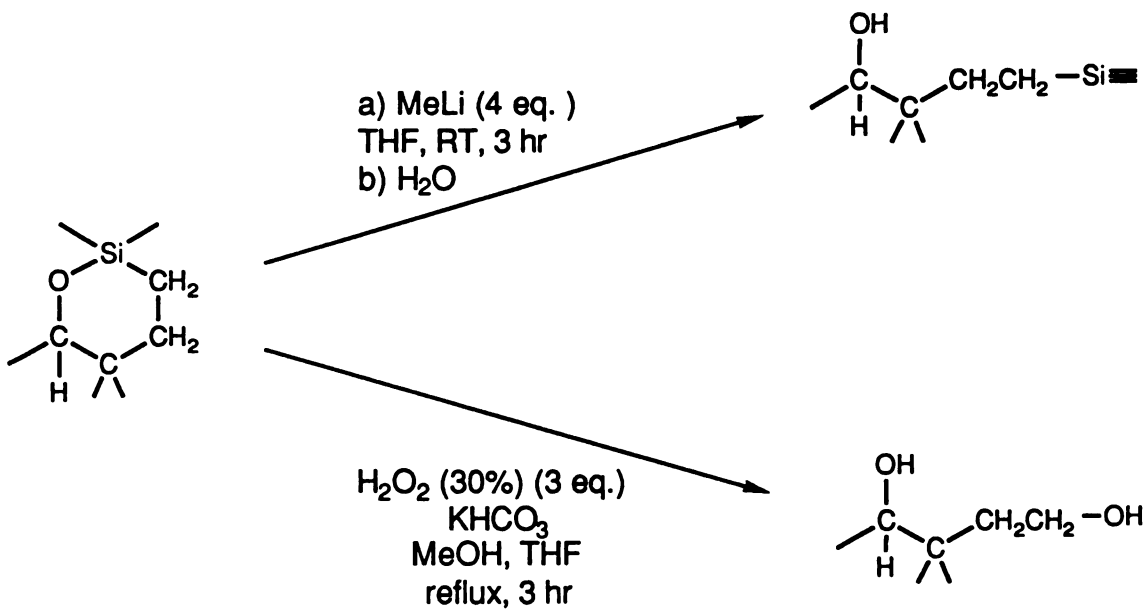
(35)





20-33%

Scheme 11 - Walkup's Radical Addition Products



Finally, one can consider dimethylsilyl bis-enol ethers (Figure 4) as an example of a functionalized silyl enol ether. Compounds of the class have been prepared by Kruger and Rochow[4], Bazouin and coworkers[11], Fataftah and coworkers[49], and by Walkup[44]. Using sodium bis(trimethylsilyl)amide, Kruger and Rochow prepared the sodium enolate of acetophenone and reacted the enolate with dichlorodimethylsilane to produce the bis-enol ether in 67% yield (Equation 38). Bazouin and coworkers prepared the same bis-enol ether in 112% (sic) yield by reacting acetophenone with dichlorodimethylsilane in the presence of a catalytic amount of zinc chloride and using triethylamine as the base (Equation 39). Fataftah and coworkers, presumably unaware of these earlier results, developed two new methods for preparing bis-enol ethers. In the first method, they deprotonated ketones with the highly hindered and expensive base, lithium tetramethylpiperidide (LiTMP), and then added dichlorodimethylsilane (Equation 40). The second method required refluxing a mixture of the ketone, dichlorodimethylsilane and three equivalents of triethylamine in THF (Equation 41). This method, which is similar to that of House and coworkers[9], requires reaction times ranging from two up to twenty days. Walkup also prepared a bis-enol ether, when he reacted the lithium enolate of pinacolone with dichlorodimethylsilane (Equation 42). A common feature of all these preparations is that both enol ethers are the same. A mixed bis-enol ether has never been prepared and the chemistry of bis-enol ethers has never been explored.

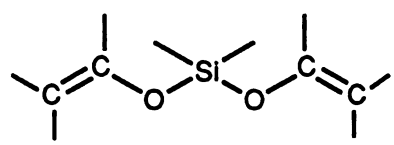
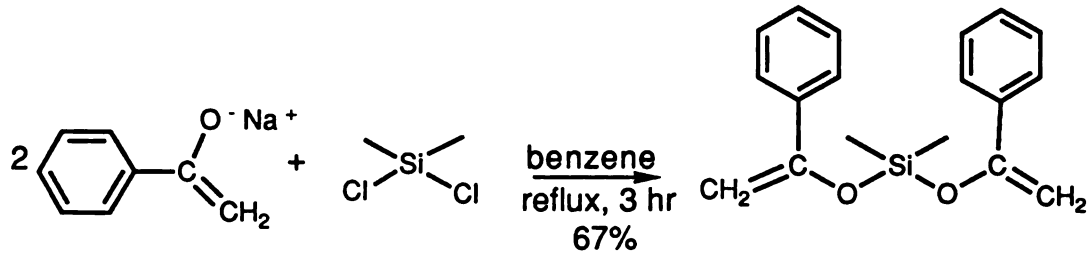
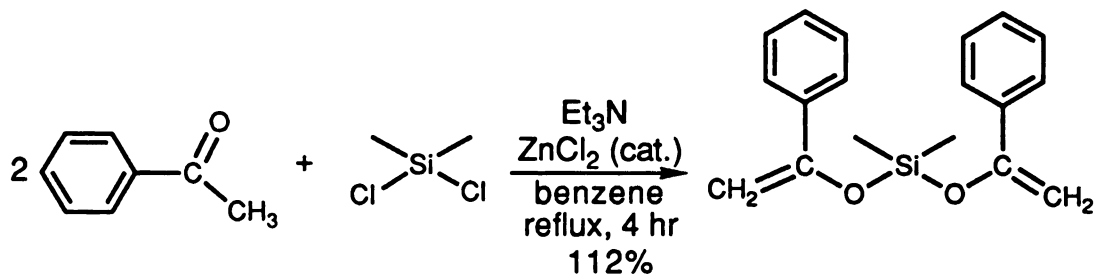


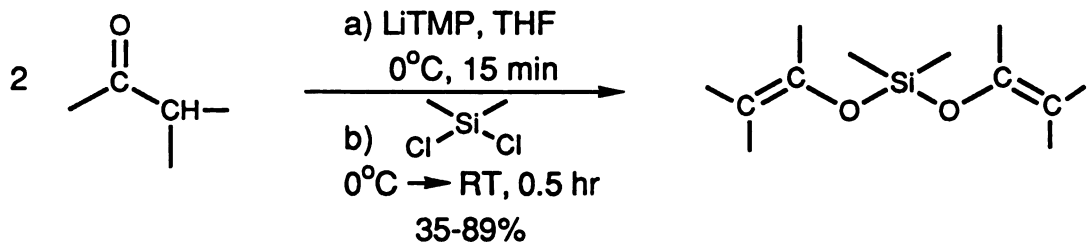
Figure 4 - Dimethylsilyl Bis-Enol Ether


2
O⁻ Na⁺
C
CH2
+
Cl
Si
Cl
benzene
reflux, 3 hr
67%
CH2
C
O
Si
O
C
CH2

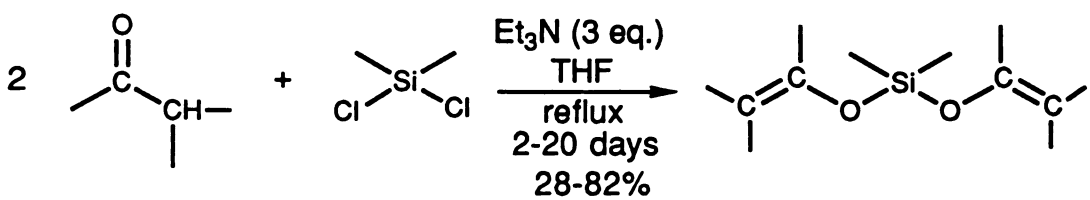
(38)


2
O
C
CH3
+
Cl
Si
Cl
Et3N
ZnCl2 (cat.)
benzene
reflux, 4 hr
112%
CH2
C
O
Si
O
C
CH2

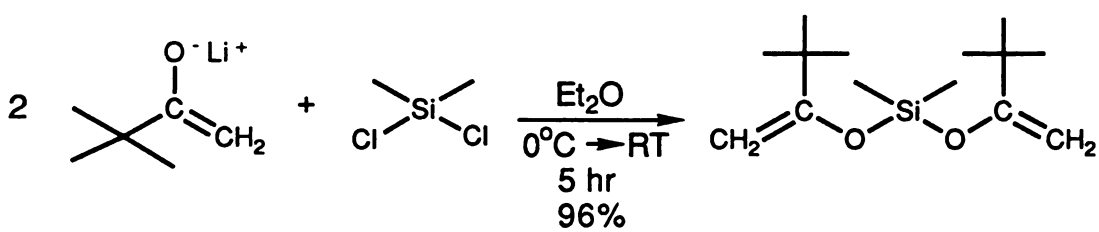
(39)


2
O
C
CH
a) LiTMP, THF
0°C, 15 min
b)
Cl
Si
Cl
0°C → RT, 0.5 hr
35-89%
C
O
Si
O
C

(40)


2
O
C
CH
+
Cl
Si
Cl
Et3N (3 eq.)
THF
reflux
2-20 days
28-82%
C
O
Si
O
C

(41)


2
O⁻ Li⁺
C
CH2
+
Cl
Si
Cl
Et2O
0°C → RT
5 hr
96%
CH2
C
O
Si
O
C
CH2

(42)

Trimethylsilyl enol ethers were initially prepared by reacting enolate anions with trimethylsilyl chloride. The preparation of trimethylsilyl enol ethers has since been improved by the use of silyl iodides and tertiary amine bases. With this in mind, we decided to extend the use of silyl iodides to the preparation of silicon functionalized silyl enol ethers. Our initial target was the synthesis of the silyl enol ether prepared by Walkup, 2-(chlorodimethylsiloxy)-3,3-dimethylbutene, or the iodo- analogue. We hoped that by generating the silyl iodide of dichlorodimethylsilane *in situ* with sodium iodide, and by using triethylamine as the base (the procedure of Duboudin and coworkers[25]), that we could adjust the reaction conditions to give a good yield of a halodimethylsilyl enol ether with minimum formation of the corresponding bis-enol ether. This approach proved unsuccessful. We were able, however, to use N,N-dimethylaminodimethylchlorosilane as the synthetic equivalent of dichlorodimethylsilane. A series of aminodimethylsilyl enol ethers was prepared using sodium iodide and triethylamine. These amino-functionalized silyl enol ethers could be converted to other functionalized silyl enol ethers, including the chloro- derivative.

We also planned to prepare bis-enol ethers using a silyl iodide approach. Bis-enol ethers having identical enol groups were readily obtained from the ketone, dichlorodimethylsilane, and sodium iodide using triethylamine as the base. Mixed bis-enol ethers were obtained by using N,N-diethylaminodimethylsilyl enol ethers as precursors.

RESULTS

We began our studies on the preparation of silicon functionalized silyl enol ethers with several experiments using ^1H NMR to monitor the reactions. Sodium iodide was dissolved in deuteroacetonitrile, then dichlorodimethylsilane, triethylamine and pinacolone were added to the NMR tube. After obtaining a ^1H NMR spectrum, chemical shift values given by Walkup[44] (Figure 5) were used to make assignments. Integration of the methyl groups on silicon provided the relative amounts of the three compounds in the reaction mixture (Table 7).

While these results were encouraging, we wanted a more flexible and accurate method of analysis. The chlorodimethylsilyl enol ether product could be converted to an alkoxydimethylsilyl enol ether as Walkup[44] had shown, and the alkoxy derivative could be detected and measured by GLC analysis. To this end, the methoxydimethylsilyl enol ether and the dimethylsilyl bis-enol ether of

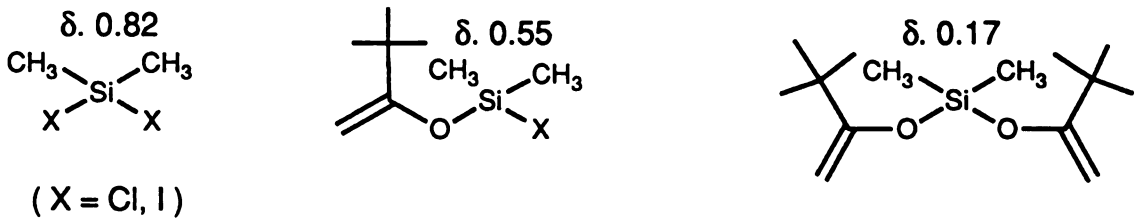
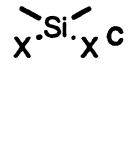
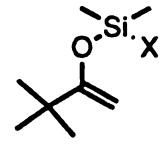
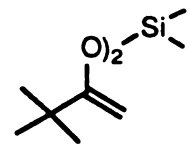


Figure 5 - ^1H NMR Chemical Shifts (Si-CH_3)

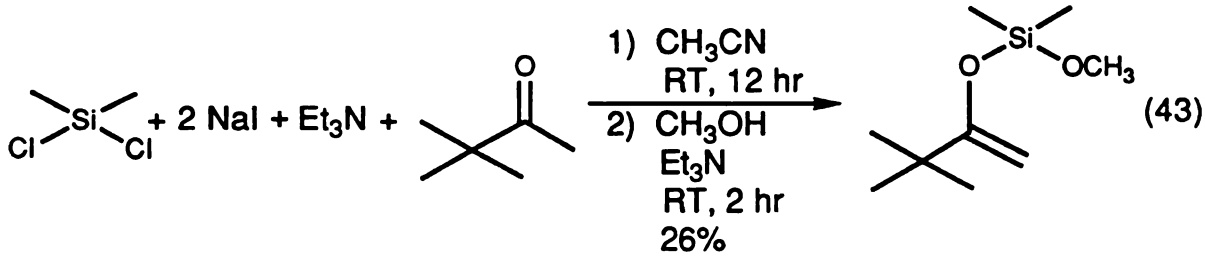
Table 7 - Preparation of Functionalized Silyl Enol Ethers - ^1H NMR Study

Entry	Equivalents [a] $(CH_3)_2SiCl_2$	NaI	Time (min)	Product Ratios [b] 		
1	1	1	8	50	35	15
			53	40	35	25
2	2	1	7	149	38	13
			45	128	50	22
3	2	4	6	125	53	22
			49	113	82	5

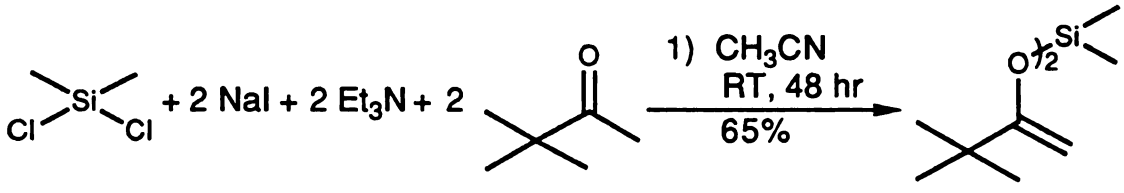
a) Reactions using Et_3N (1 eq.) and pinacolone (1 eq.) in CD_3CN at RT.

b) Ratios determined by integration of silicon methyl signals in ^1H NMR.

c) X = Cl, I.



(43)



(44)

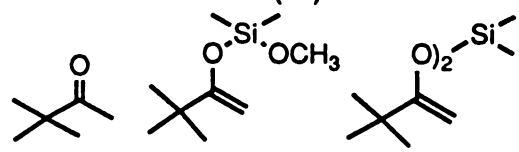
pinacolone were prepared for use as standards by the reactions of Equations 43 and 44.

Next, attempts were made to optimize the reaction for the methoxydimethyl-silyl enol ether. Product distributions, were determined (Table 8) when 2,4,6,-trimethylpyridine (collidine) or N-ethyl-N,N-diisopropylamine (Hunig's base) were substituted for triethylamine (Entries 2 and 3), when the reaction time was shortened from 6 hours to 2 hours. (Entry 4), and when the stoichiometry of the sodium iodide and dichlorodimethylsilane was changed (Entries 5 and 6). No reaction took place when the acetonitrile solvent was replaced with pentane, methylene chloride, dimethylformamide, or triethylamine.

Lithium iodide was also substituted for sodium iodide for the in situ generation of the silyl iodide. These experiments, Table 9, were based on a communication by Lissel and Drechsler[30], who reported that trimethylsilyl iodide could be prepared by reacting lithium iodide with neat trimethylsilyl chloride (Equation 45).

From the reactions performed thus far, several general features can be noted. The best results required a 100% excess of diiododimethylsilane, and even under these conditions the formation of the bis-enol ether was not suppressed completely. Clearly the difference in reactivity between diiododimethylsilane and the iododimethyl silyl enol ether is small. Similarly, addition of only one equivalent of sodium iodide to one equivalent of dichlorodimethylsilane seems to lead to a mixture of mono-and diiodosilanes. We also found acetonitrile to be the only effective solvent, and reactions in that

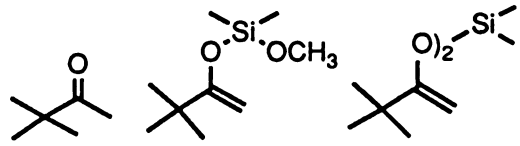
Table 8 - Preparation of the Methoxydimethylsilyl Enol Ether of Pinacolone

Entry	Equivalents[a] $(CH_3)_2SiCl_2$ / NaI		Base	Time (hr)	Product[b] (%) 			Balance[c] (%)
1	1	2	Et_3N	6	2	36	28	94
2	1	2	collidine	6	8	35	24	91
3	1	2	$(i\text{-}Pr)_2NEt$	6	41	28	10	89
4	1	2	Et_3N	2	3	41	27	98
5	1	4	Et_3N	6	0	61	17	95
6	1.2	2.4	Et_3N	6	0	41	26	93

a) Reactions using base (1 eq.) and pinacolone in CH_3CN at room temperature followed by addition of Et_3N and CH_3OH at room temperature for 2 hr.
b) Product percentages determined by GLC analysis using decane as internal standard
c) Mass balance for pinacolone

solvent were complete within two hours. Bulky amines such a Hunig's base or collidine do not improve the product distribution, and lithium iodide was a poor substitute for sodium iodide. Another issue that was examined was whether the results were due to kinetic or equilibrium control. To test for this, the bis-enol ether of pinacolone was reacted with diiododimethylsilane (generated with sodium iodide and dichloromethylsilane). The results given in Equation 46 indicate that equilibrium was achieved.

Table 9 - Preparation of the Methoxydimethylsilyl Enol Ether of Pinacolone Using LiI

Entry	Solvent	Products[a] (%) 			Balance[b] (%)
1	CH_3CN	59	10	6	81
2	CH_2Cl_2	51	0	2	53[c]
3	n-C_5H_{12}	41	29	8	87
4	Et_3N	only[d]	0	0	--[d]

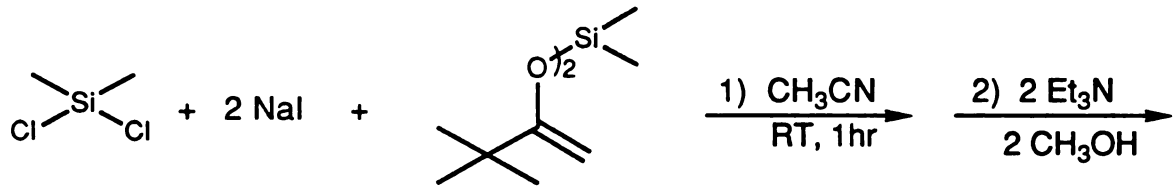
a) Reactions using LiI (2 eq.), Et_3N (1 eq.), silane (1 eq.) and pinacolone (1 eq.) at room temperature ofr 2 hr followed by Et_3N and CH_3OH at room temperature for 2 hr. Product percentages determined by GLC analysis using decane as internal standard.
b) Mass balance for pinacolone.
c) An unidentified peak appears in the GLC chromatograph.
d) Percentage not determined.

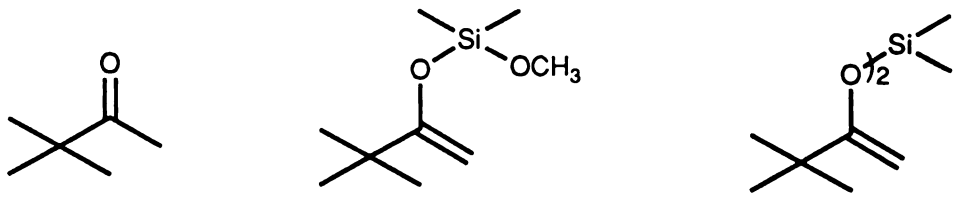
$$\equiv\text{Si-Cl} + \text{LiI} \xrightarrow[81\text{-}88\%]{\text{RT, 4 hr}} \equiv\text{Si-I} + \text{LiCl} \qquad (45)$$

Though the use of diiododimethylsilane seemed to provide the most direct approach to functionalized silyl enol ethers, the degree of specificity in the reactions is unsatisfactory. Therefore, we decided to investigate the use of N,N-dimethylaminodimethylchlorosilane, which can be considered a synthetic equivalent of dichlorodimethylsilane.

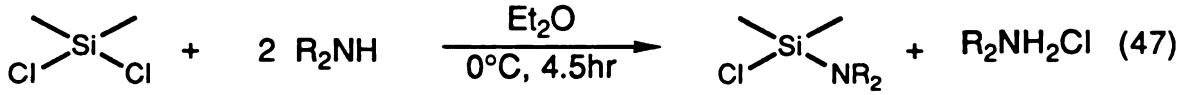
N,N-dimethylaminodimethylchlorosilane is commercially available or can be easily prepared using the procedure of Washburne and Peterson[50]. The yield of this procedure can be increased to 76% (from 67%) by conducting

the reaction at 0° C for 4.5 hours and by using a more efficient distillation column. The N,N-diethylamino-derivative has been prepared by the same procedure in 88% yield (Equation 47).





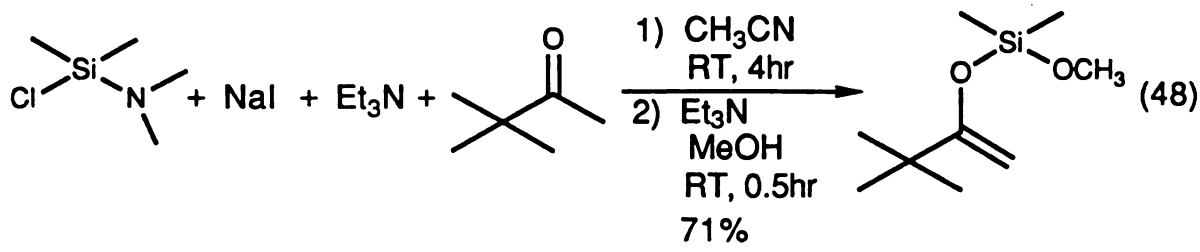
4% 50% 23% (46)



(47)

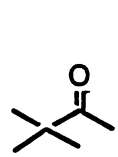
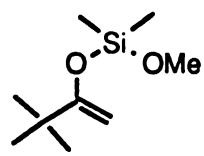
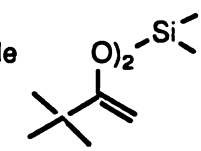
R = CH_3 76%
= CH_2CH_3 88%

Subjecting N,N-dimethylaminodimethylchlorosilane to the usual reaction conditions resulted in a good yield of the methoxydimethylsilyl enol ether of pinacolone (Equation 48). Several control experiments were performed, with the results given in Table 10.



(48)

Table 10 - Preparation of the Methoxydimethylsilyl Enol Ether of Pinacolone Using N,N-Dimethylamino dimethylchlorosilane

	Equivalents[a]		Product[b] (%)			Balance[c] (%)
	NaI	Et_3N				
1	1	1	11	97	0	108
2	0	1	98	0	0	98
3	1	0	32	17	22	93
4	0	0	96	0	0	96

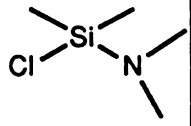
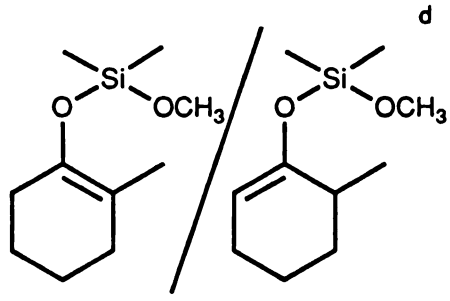
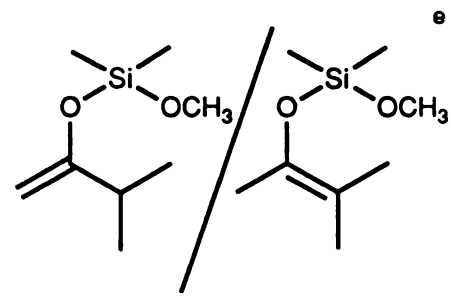
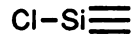
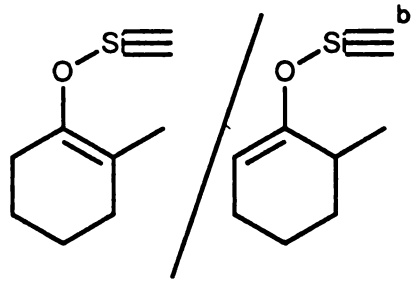
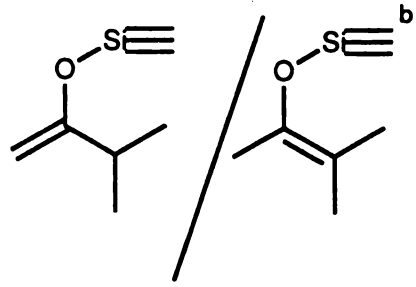
a) Reactions using silane (1 eq.) and pinacolone in CH_3CN at room temperature for 2.5hr followed by addition of Et_3N and CH_3OH at room temperature for 0.5hr.
b) Product percentages determined by GLC analysis using decane as internal standard.
c) Mass balance for pinacolone.

The rates of silyl enol ether formation for the aminochlorosilane and for trimethylsilyl chloride were compared using sodium iodide, triethylamine and pinacolone in acetonitrile were comparable; both silanes showed a $t_{1/2} < 15$ minutes.

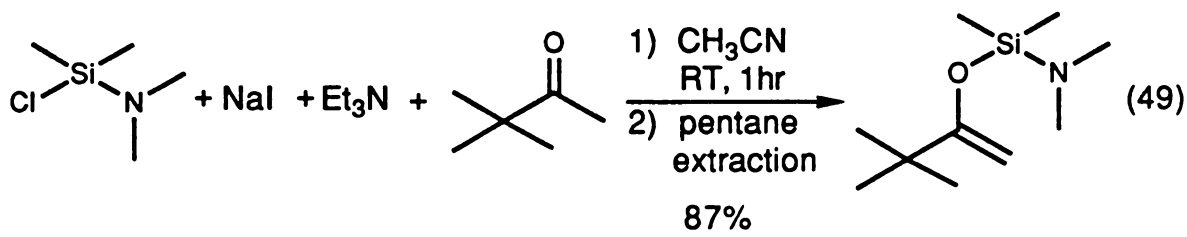
The regioselectivity of silyl enol ether formation for the aminochlorosilane and for trimethylsilyl chloride was also determined. Examination of the product ratio for two unsymmetrical ketones, 2-methylcyclohexanone and 3-methyl-2-butanone, again showed the two silanes to be comparable, Table 11. Aminodimethylsilyl enol ethers can be obtained in good yields provided a non-aqueous isolation procedure is used. For instance, an 87% yield of the N,N-dimethylaminosilyl enol ether of pinacolone was obtained by extracting the crude reaction mixture in acetonitrile with dry pentane (Equation 49). We prepared a series of N,N-diethylaminosilyl enol ethers using this isolation technique, Table 12.

As another example of functionalized silyl enol ethers, the acetoxydimethylsilyl enol ether of pinacolone was prepared in 73% yield by the method given by Equation 50. It was hoped that exposure of this compound to Lewis acid catalysts would induce an intramolecular acylation reaction to give a 1,3-diketone. Unfortunately, treatment with a variety of Lewis acids ($ZnCl_2$, $MgCl_2$, $BF_3{\cdot}OEt_2$, $Ti(OiPr)_4$) in CCl_4 or CD_3CN gave either no reaction, or decomposition of the starting material.

Table 11 - Comparison of Regioselection in Silyl Enol Ether Formation

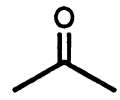
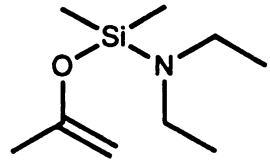
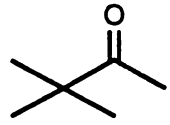
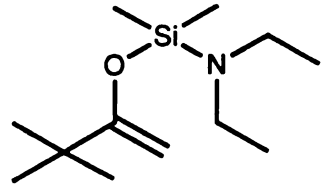
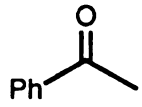
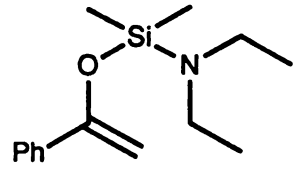
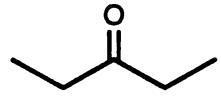
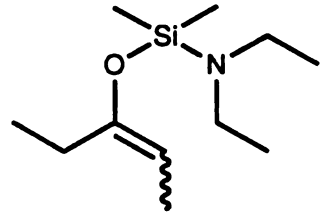
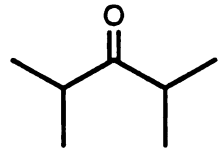
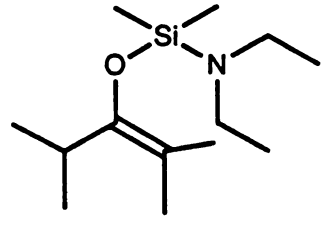
Silane	Product Ratios[a,c]	
	 [d] 85 : 15	 [e] 86 : 14
	 [b] 90 : 10	 [b] 80 : 20

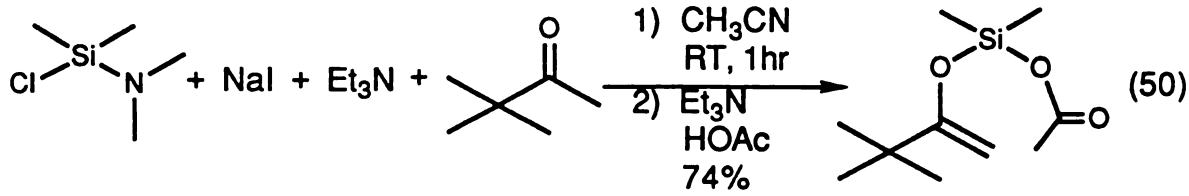
a) Reactions using silane, sodium iodide, triethylamine and ketone in CH_3CN at room temperature for 15 minutes, followed by addition of Et_3N and CH_3OH at room temperature for 30 minutes.
b) Reference 25.
c) Determined by GLC analysis
d) Isolated yield 64%.
e) Tentative assignment.



(49)

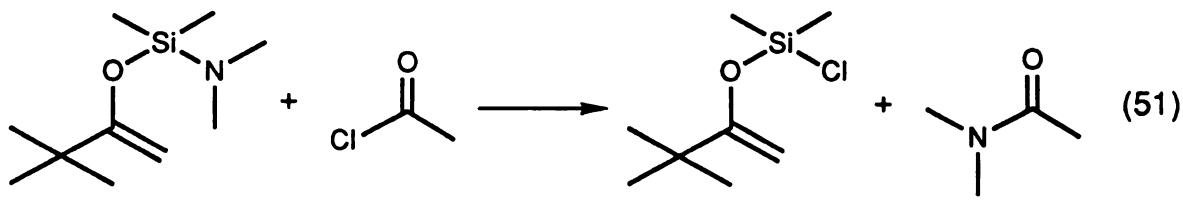
Table 12 - Preparation of N,N-Diethylaminodimethylsilyl Enol Ethers

Entry	Ketone	Product	Yield (%)
1			79
2			84
3			66
4			87
5			63

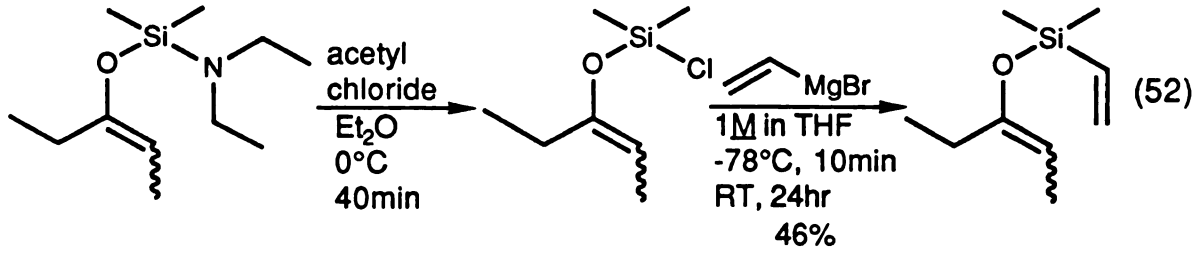


(50)

We discovered that treating the N,N-dimethylaminodimethylsilyl enol ether of pinacolone with acetyl chloride at ambient temperature would convert (by ^1H NMR) and GLC analysis the aminosilyl enol ether quantitatively into the chlorodimethylsilyl enol ether (Equation 51). The amino group thus allows for the circumvention of the problems encountered when using dichlorodimethylsilane to prepare functionalized silyl enol ethers. The conversion of an aminosilyl enol ether to a chlorosilyl enol ether also allows for substitution reactions at silicon with nucleophiles other than the protic nucleophiles (CH_3OH, CH_3CO_2H) used for direct substitution reactions of aminosilyl enol ethers. As an example of this strategy, a dimethylvinylsilyl enol ether was prepared by conversion of a diethylaminodimethylsilyl enol ether to the chloro compound followed by addition of the Grignard reagent (Equation 52).



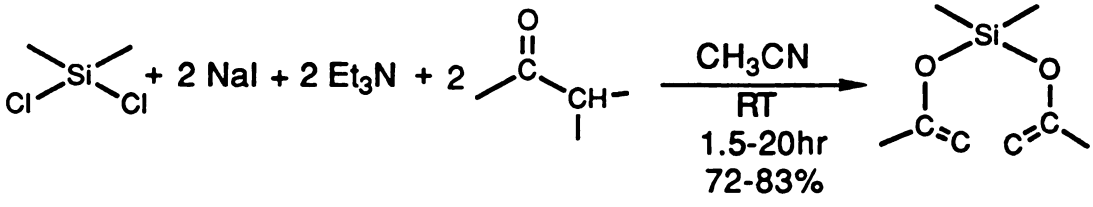
(51)



(52)

Symmetrical dimethylsilyl bis-enol ethers were easily prepared from dichlorodimethylsilane using the general reaction given by Equation 53. A series of these compounds was prepared in good yield, as shown in Table 13.

To prepare mixed dimethylsilyl bis-enol ethers it was necessary to attach each enol ether in separate, controlable steps. N,N-diethylaminodimethylsilyl enol ethers were found to be well suited for this purpose. From these compounds mixed dimethylsilyl bis-enol ethers could be prepared in moderate yields (Table 14) by conversion of the amino group to chloro, followed by the usual silylation conditions (NaI, Et_3N, CH_3CN) with a second carbonyl conpound (Equation 54).



(53)

Table 13 - Preparation of Symmetrical Bis-Enol Ethers

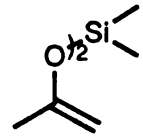
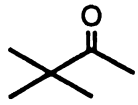
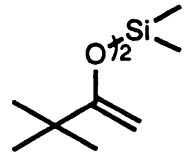
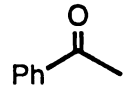
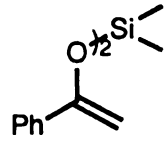
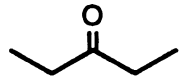
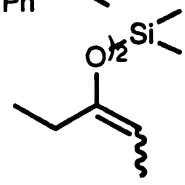
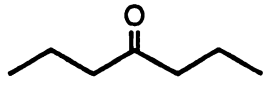
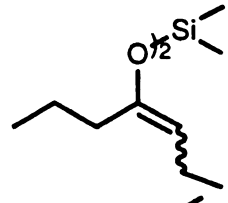
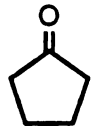
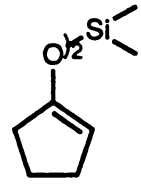
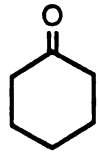
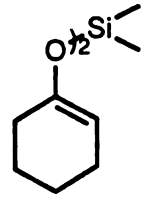
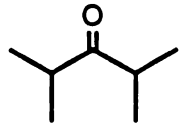
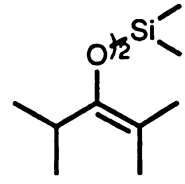
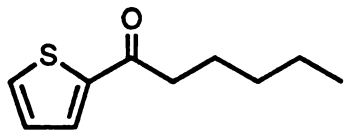
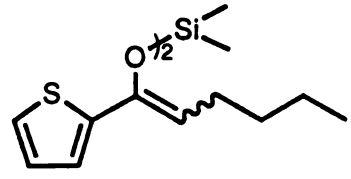
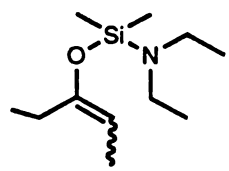
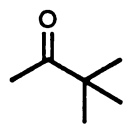
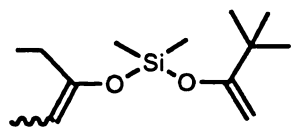
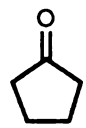
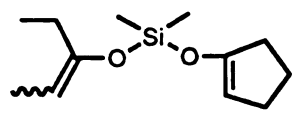
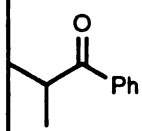
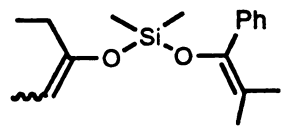
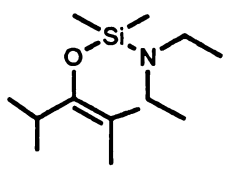
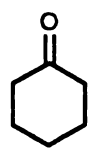
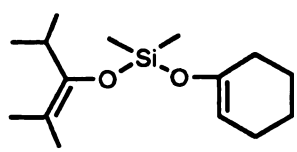
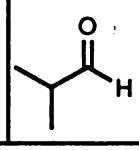
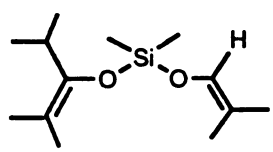
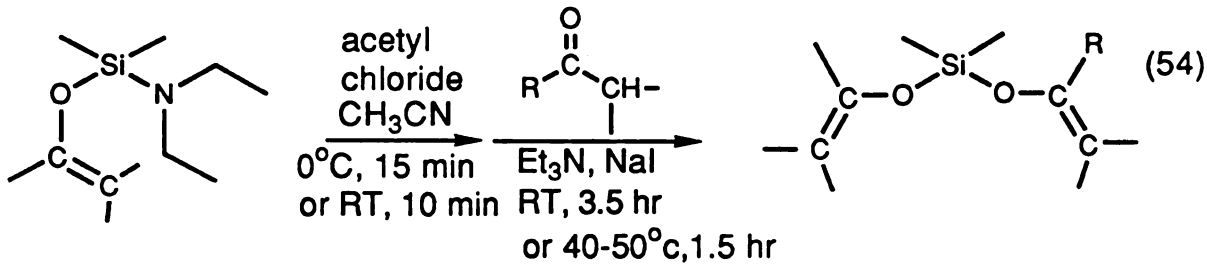
Entry	Ketone	Product	Time (hr)	Yield (%)
1			2	73
2			1.5	73
3			1.75	83
4			1.5	76
5			5	76
6			1.5	76
7			2	72
8			20	72
9			18.5	75

Table 14 - Preparation of Mixed Bis-enol Ethers

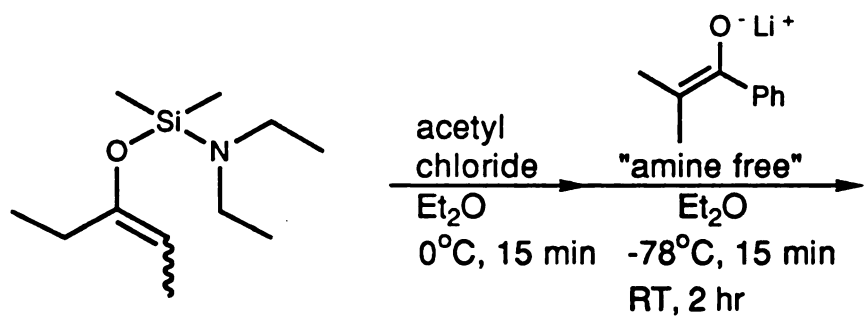
Entry	Aminosilyl Enol Ether	Ketone	Product	Yield (%)	Procedure
1				45	A
2				52	A
3				28	B
4				75	B
5				63	B

Procedure A: The aminosilyl enol ether was reacted with acetyl chloride at 0° C for 15 min in CH_3CN. The ketone, amine, NaI and pentane were added and allowed to stir at 0° C for 30min. The reaction was allowed to stir at RT fo r 3.5hr.

Procedure B: The aminosilyl enol ether was reacted with acetyl chloride at RT for 10 min in CH_3CN. The ketone and amine were added and the mixture heated to 40-50° C. NaI in CH_3CN was added dropwise and allowed to stir for 1.5hr.



(54)

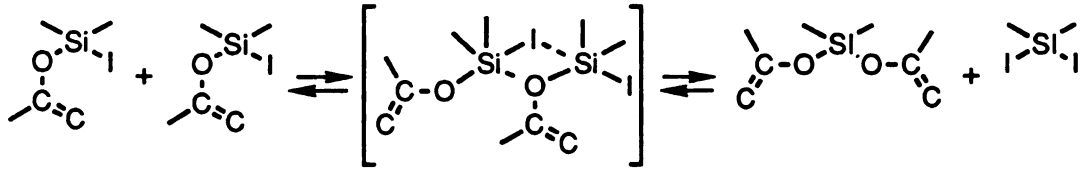


(55)

One other attempt to prepare a dimethylsilyl bis-enol ether from a aminosilyl enol ether was made. Conversion of the amino group to chloro followed by addition of a "amine-free" lithium enolate solution did produce a mixed bis-enol ether (by GLC analysis). Unforunately, the product mixture was exceedingly complex and no attempt at product isolation was made (Equation 55).

DISCUSSION

Our attempts to prepare functionalized silyl enol ethers directly from dichlorodimethylsilane were based on the thoughts that either chloroiododimethylsilane could be prepared selectively, or that diiododimethylsilane would be significantly faster in its silylation reactions with carbonyl compounds than an iododimethylsilyl enol ether. In neither case did a high degree of selectivity exist. The dimethylsilyl bis-enol ether product was formed in a 1: 2 ratio with the dimethylsilyl mono-enol ether product, when a 1:2 ratio of sodium iodide to dichlorodimethylsilane was used. Even when the reaction was conducted with a 100% excess of diiododimethylsilane, formation of the bis-enol ether product was not suppressed completely. The equilibration of diiododimethylsilane with a dimethylsilyl bis-enol ether (Equation 46) suggests that even if an iododimethylsilyl enol ether could be prepared and isolated, given sufficient time, the compound would disproportionate (Equation 56).

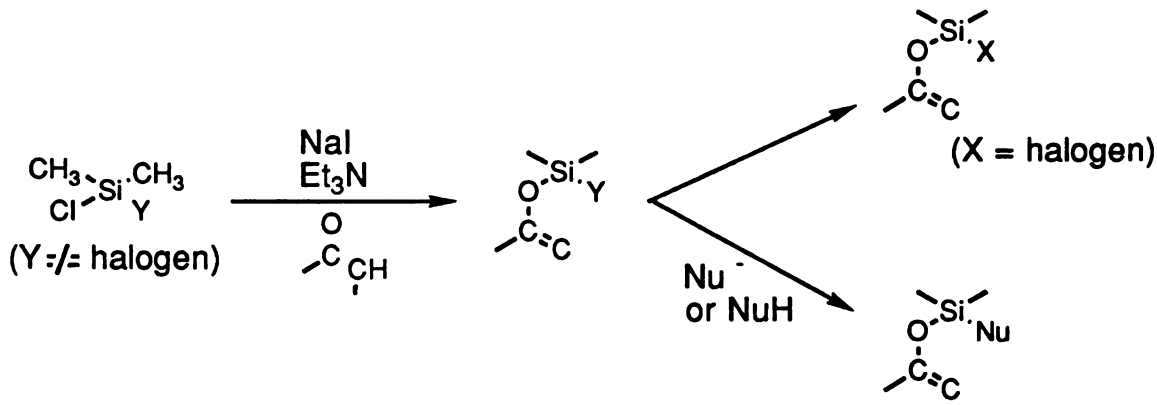


(56)

After these experiments, it was clearly necessary to find and develop a chlorodimethylsilane derivative which had a functional group which could either be converted to a halogen after formation of the enol ether, or which had

a reactivity similar to that of a halosilane after formation of the enol ether (Scheme 12).

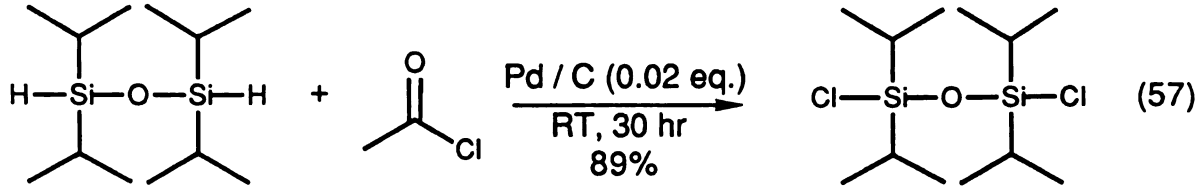
Scheme 12 - Second Approach to Functionalized Silyl Enol Ethers



Alkoxydimethylsilyl enol ethers, such as those developed by Rathke and Manis[42] and by Kaye and Learmonth[43], were not promising prospects. Changing the alkoxy group into any other group, especially a halogen, seemed unlikely. Silyl ethers are relatively stable and are usually cleaved under strongly acidic or fluoride ion conditions; under these condtions the enol ether would be unlikely to remain intact.

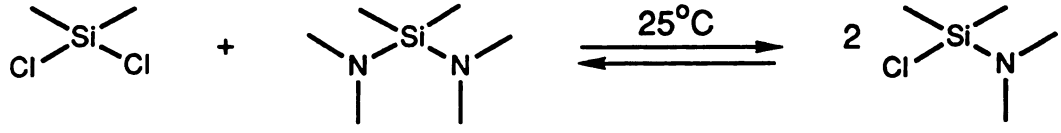
Another possibility centered on chlorodimethylsilane. This compound is commercially available, and Guibe and coworkers[51] have shown that silyl hydrides can be converted to silyl chlorides. They recommended that the silyl hydride compound, in their example 1,1,3,3-tetraisopropyldisiloxane, be treated with an excess of acetyl chloride in the presence of palladium on charcoal (Equation 57). While the synthesis of a dimethylsilyl enol ether might well be feasible, there were however, concerns that the enol ether might be

reduced or chlorinated during the convertion of the silyl hydride to a silyl chloride, using the conditions specified by Guibe.



(57)

Alternatively, the use of N,N-dimethylaminodimtheylchlorosilane seemed more practical. This compound is commercially available or can be easily prepared using the procedure of Washburne and Peterson[50] or the procedure of Ito and coworkers[52]. The success of these procedures is due to a favorable equilibrium between dichlorodimethylsilane and bis(dimethylamino)-dimethylsilane (Equation 58). Van Wazer and Moedritzer[53] have studied this process using ^1H NMR and have determined the equilibrium constant, Keq = 6000.



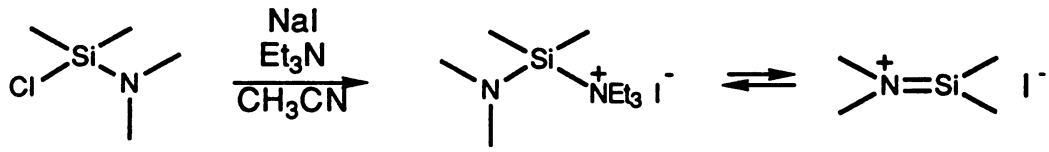
(58)

A favorable equilibrium also exists when the N,N-dimethylaminodimethylchlorosilane is converted to the iodo compound. Silylation of carbonyl compounds in the presence of triethylamine leads cleanly to the desired N,N-dimthylaminodiethylsilyl enol ether, with no bis-enol ether

product formed. One other interesting aspect of silylations with aminosilanes is that in the absence of triethylamine, the amino group of the silane will act as a base. The protonated amino group is then a reactive species for silylation and bis-enol ether products are formed.

It was surprising to find little difference in the rate and regiochemistry of silylations with the N,N-dimethylaminodimethylchlorosilane and trimethylsilyl chloride. The reactive species for the trimethylsilyl chloride, sodium iodide, triethylamine system is given by Equation 59. The aminosilane however, may exist as a pair of reactive species in equilibrium (Equation 60). Both the rate and regiochemistry of silylation are apparently governed by the extreme reactivity of these intermediates.

$$\equiv\text{Si-Cl} + \text{NaI} + \text{Et}_3\text{N} \xrightarrow{\text{CH}_3\text{CN}} \equiv\text{Si-}\overset{+}{\text{N}}\text{Et}_3\ \overset{-}{\text{I}} \qquad (59)$$



(60)

All of the objectives given by Scheme 12 were met when we found that aminodimethylsilyl enol ethers could be iaolated in good yield (Table 12), that they could be reacted with protic nucleophiles to give new functionalized silyl enol ethers (Equations 48 and 50), and that they could be reacted with acetyl chloride to give chlorosilyl enol ethers (equation 51). The use of aminodimethylchlorosilane to prepare functionalized silyl enol ethers

compares favorably with the approach developed by Walkup[44] in that it seems to be viable for a wider range of ketones, gives similar yields, and is both more convient and more economical.

The use of this silane has also recently been extended to other areas; Stork and Keitz[54] have prepared alkynyl and alkenyl silyl ethers by means similar to the ones used here to prepare a dimethylvinylsilyl enol ether.

The synthesis of symmetrical dimethylsilyl bis-enol ethers proceded in good yields and is an attractive alterative to the strong base routes developed by other researchers[4,11,44,49]. Through the use of aminodimethylsilyl enol ethers, mixed bis-enol ethers were synthesized for the first time. One aspect of the preparation of these compounds that deserves comment is the addition order used when attaching a second enol ether to the silane. It is necessary to add the sodium iodide (preferably as a solution) last to the mixture of the chlorosilyl enol ether, ketone and triethylamine. This minimizes loss of yield to disproportionation and the formation of the symmetrical bis-enol ethers. Our principle objective in synthesizing bis-enol ethers was the hope that the enol ethers could be coupled at the α-carbon to produce 1,4-diketones. The results of an investigation of this process is presented in Chapter 3 of this work.

EXPERIMENTAL

A. General

Acetonitrile, methylene chloride and pentane were dried by distillation from CaH_2 under argon. Diethyl ether was used directly from a freshly opened can. Methanol was dried by distillation from sodium metal under argon. Acetic acid was prepared from glacial acetic acid and 1.5 mol% acetic anhydride. Acetyl chloride was freshly distilled before use. Dimethylformamide (DMF-anhydrous), decane (Gold Label-99%), n-BuLi (1.6 M in hexane), and vinylmagnesium bromide (1.0 M in THF) were purchased from Aldrich Chemical Company and used as received. Trimethylsilyl chloride and dichlorodimethylsilane were distilled from CaH_2 and stored over polyvinylpyridine under argon. Lithium iodide (Aldrich) was used as received. Sodium iodide was dried in an abderhalden apparatus with 0.1 mmHg vacuum and refluxing toluene for 8 hours. Both salts were stored in a dry desiccator. Triethylamine, diethylamine, diisopropylamine, diisopropylethylamine and collidine were dried by distillation from CaH_2 under argon. Dimethylamine was purchased from Eastman-Kodak Chemical Company in sealed ampules and used as received. Pinacolone, 3-pentanone, cyclopentanone, 2-methylcyclohexanone, 2,4-dimethyl-3-pentanone and isobutyrophenone (Aldrich) and cyclohexanone (Fisher) and 3-methylbutanone (Eastman) were all dried by distillation from CaH_2 under argon. Acetone (J. T. Baker "Photrex"

grade) was distilled from Na_2CO_3. Acetophenone (Baker) was distilled from P_2O_5. Isobutyraldehyde (Aldrich) was distilled immediately before use and 4-heptanone (Aldrich) was used as received. The 2-hexanoylthiophene was generously provided by Mike Benz and Dr. E. LeGoff.

Gas chromatography was performed with a Hewlett-Packard 5880A instrument fitted with either a Foxboro 25 meter GB-1 column (I. D. 0.25 mm, 0.25 mm film), or a Restek 30 meter Rtx-1 column (I. D. 0.32 mm, 0.25 mm film). Infrared spectra were obtained from neat samples on KBr plates using a Nicolet FT-IR/42 instrument (absorptions reported in cm^{-1}). ^1H NMR spectra were obtained in $CDCl_3$ or CD_3CN (Cambridge Isotopes Inc.) using either a Varian T-60 at 60 MHz or a Varian VXR-300 (s) at 300 MHz as indicated. ^{13}C NMR spectra were obtained using a Varian VXR-300 (s) at 75 MHz. Chemical shifts are reported in parts per million (δ. scale). Data are reported as follows: chemical shift (multiplicity: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet; intregration; coupling constant in Hz). Mass spectra were obtained using a Finnigan 4000 EI GC/MS instrument at the ionizing energy (eV) indicated. Data are reported as m/e (relative intensity).

Unless noted, all glassware used in the following procedures was oven dried (120° C) and purged with argon. Typically, the reactions were conducted in round bottom flasks fitted with magnetic stirring, a gas takeoff valve (to Hg bubbler) and a septem inlet. Addition of reagents employed standard syringe or cannula transfer techniques. Concentration of organic extracts was accomplished at reduced pressure (aspirator) using a rotory evaporator.

B. NMR Experiments to Study the Formation of 2-halodimethylsiloxy-3,3-dimethyl-1-butene.

The following experiments employed a Varian T-60 NMR operated at ambient temperature. The results of these experiments appear in Table 1. The following procedure is representative.

1. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1:1:1:1)

To a 5mm NMR tube which was oven dried, flushed with argon, and fitted with a septum, NaI (0.0852 g, 0.57 mmol) and CD_3CN (0.4ml) were charged to produce a clear, colorless solution. The dichlorodimethylsilane (69 µl, 0.57 mmol) was added to produce a clear, yellow solution. The Et_3N (79 µl, 0.57 mmol) was added to produce an opaque, white mixture. Tetramethylsilane (TMS) (1 µl) was added as the internal standard. Pinacolone (71 µl, 0.57 mmol) was added and the time marked as zero. After every addition the reaction was shaken vigorously by hand. Spectra were obtained from δ. 6 to δ. -0.2 and the regions of interest were integrated. Time was marked at the completion of the integration. Integration of the methyl groups on silicon was used to determine the relative ratios of products. Periodically the NMR tube was withdrawn from the spectrometer and inspected; it appeared as a slightly opaque yellow solution with white solid settled at the bottom. The observed chemical shifts and multiplicities agreed with literature values and are given below (referenced to TMS). Silyl enol ether products were observed in 60% yield after 1 hour (85% conversion of ketone).

2. $(CH_3)_2SiCl_2$ / Na I / Et_3N / $(CH_3)_3CCOCH_3$ (2:1:1:1)

Using the procedure described above combined NaI (0.0555 g, 0.37 mmol), CD_3CN (0.35 mL), $(CH_3)_2SiCl_2$ (90 µL, 0.74 mmol), Et_3N (52 µl, 0.37 mmol), and $(CH_3)_3CCOCH_3$ (46 µl, 0.37 mmol). Silyl enol ether products were observed in 72% yield after 1 hour. (94% conversion of ketone).

3. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (2:4:1:1)

Using the procedure described above combined NaI (0.1130 g, 0.75 mmol), CD_3CN (0.38 mL), $(CH_3)_2SiCl_2$ (46 µl, 0.37 mmol), Et_3N (26 µl, 0.19 mmol), and $(CH_3)_3CCOCH_3$ (24 µl, 0.19 mmol). Silyl enol ether products were observed in 87% yield after 1 hour (92% conversion of ketone).

4. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1:0:1:1)

In the absence of NaI no silyl enol ether products were observed by NMR.

C. Preparation of 2-(methoxydimethylsiloxy)-3,3-dimethyl-1-butene and Bis(3,3-dimethyl-1-buten-1-oxy)dimethylsilane.

1. Preparation of 2-(methoxydimethylsiloxy)-3,3-dimethyl-1-butene

A solution of NaI (24.0 g, 160 mmol) in CH_3CN (100 mL) was prepared and dichlorodimethylsilane (9.7 mL, 80 mmol) was added and allowed to stir for 15 minutes at room temperature. Et_3N (11.2 mL, 80 mmol) was added to produce an opaque white mixture. A solution of pinacolone (10 mL, 80 mmol) in CH_3CN (10 mL) was added dropwise via a pressure equalized addition funnel over 1 hour. The reaction was allowed to stir for 12 hours then cooled to 0° C with an ice bath. A mixture of Et_3N (11.2 mL, 80 mmol) and CH_3OH (3.3

mL, 80 mmol) was added dropwise over 30 minutes. The reaction was allowed to stir for 2 hours after the completion of the addition. Workup in 200 mL 1:1 ice / saturated aqueous $NaHCO_3$ and 100 mL pentane. The aqueous layer was extracted 2 x 50 mL pentane and the combined organic layers dried over Na_2SO_4. Filtered and concentrated to give 12.9 g crude. Distillation of reduced pressure gave 3.9 g (26%) b.p. 80-82° C (55 mm Hg).

IR (neat):3125,2967,2913,2872,1624,1464,1296,1260,1186,1092,1015,839.
^1H NMR (300 MHz, CDCl3): δ 0.17 (s, 6H, $SiCH_3$), 1.05 (s, 9H, $(CH_3)_3$), 3.51 (s, 3H, OCH_3), 4.07 (d, 1H, 1.2Hz, enol), 4.11 (d, 1H, 1.2Hz, enol)
^{13}C NMR (75 MHz, $CDCl_3$): δ -3.40, 28.01, 36.42, 50.13, 86.67, 66.25.
MSEI (25 eV): 189 (M+1, 38), 173 (9.7), 131 (3.8), 75 (base), 83 (6.2).

2. Preparation of Bis(3,3-dimethyl-1-buten-1-oxy)dimethylsilane.

A solution of NaI (19.2 g, 128 mmol) in CH_3CN (80 mL) was prepared and dichlorodimethylsilane (8.1 mL, 64 mmol) was added and allowed to stir for 15 minutes at room temperature. Et_3N (17.9 mL, 128 mmol) was added followed by a solution of pinacolone (16.0 mL, 128 mmol) in CH_3CN (10 mL) via a pressure equalized addition funnel over 30 minutes. The reaction was allowed to stir for 48 hours at room temperature. Workup as above afforded 16.2 g crude. Distillation at reduced pressure gave 10.67 g (65%) b.p. 47-53° C (0.6 mm Hg)

IR (neat): 3125, 2969, 2913. 2872, 1626, 1464, 1254, 1015, 885.
^1H NMR (300 MHz, $CDCl_3$): δ 0.24 (s, 6H, $SiCH_3$), 1.05 (s, 9H, $(CH_3)_3C$), 4.12 (s, 2H, enol).
^{13}C NMR (75 MHz, CDCl3): δ -2.92, 27.99, 36.34, 87.04, 165.92.

MS-EI (70 eV): 241 (M-15, 1.5), 199 (16), 157 (7), 75 (base), 57 (14).

D Preparation of 2-(methoxydimethylsiloxy)-3,3-dimethyl-1-butene from Dichlorodimethylsilane GLC Study.

The results of these experiments appear in Tables 2 and 3. The following procedure is representative.

1. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

To a solution of NaI (0.30 g, 2 mmol) in CH_3CN (2 mL) dichlorodimethylsilane (0.13 mL, 1 mmol) and pinacolone (125 µl, 1 mmol) were added and allowed to stir for 6 hours at room temperature. EtN_3 (0.14 mL, 1 mmol) and CH_3OH (41 µl, 1 mmol) were added and allowed to stir for 1 hour at room temperature. Workup in 20 mL 1:1 ice / saturated aqueous $NaHCO_3$ and 10 mL pentane and the combined organic layers dired over Na_2SO_4. Decane (97 µL, 0.5 mmol) was added to the solution as an internal standard and the solution was analyzed by GLC. Ketone (2%), product (36%), bis-enol ether (28%).

2. $(CH_3)_2SiCl_2$ / NaI / Collidine / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined NaI (0.30 g, 2 mmol), CH_3CN (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), collidine (0.13 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 6 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41µl,1mmol) were added and workup as above. Ketone (8%), product (35%), bis-enol ether (24%).

3. $(CH_3)_2SiCl_2$ / NaI / i-Pr_2NEt / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined NaI (0.30 g, 2 mmol), CH3CN (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), i-Pr_2NEt (0.17 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 6 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 µL, 1 mmol) were added and workup as above. Ketone (41%), product (28%), bis-enol ether (10%).

4. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined NaI (0.30 g, 2 mmol), CH_3CN (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 2 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 µL, 1 mmol) were added and workup as above. Ketone (3%), product (41%), bis-enol ether (27%).

5. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 4 : 1 : 1)

Using the procedure described above combined NaI (0.60 g, 4 mmol), CH_3CN (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 6 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 µL, 1 mmol) were added and workup as above. Ketone (0%), product (61%), bis-enol ether (17%).

6. $(CH_3)_2SiCl_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1.2 : 2.4 : 1 : 1)

Using the procedure described above combined NaI (0.36 g, 2.4 mmol), CH_3CN (2.4 mL), $(CH_3)_2SiCl_2$ (0.15 mL, 1.2 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 6 hours at room temperature. Et_3N (0.17 mL, 1.4 mmol) and CH_3OH (57 µL, 1.4 mmol) were added and workup as above. Ketone (0%), product (41%), bis-enol ether (26%).

7. $(CH_3)_2SiCl_2$ / LiI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined LiI (0.27 g, 2 mmol), CH_3CN (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 μL, 1 mmol). Reaction time 2 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 μL, 1 mmol) were added and workup as above. Ketone (59%), product (10%), bis-enol ether (6%).

8. $(CH_3)_2SiCl_2$ / LiI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined LiI (0.27 g, 2 mmol), CH_2Cl_2 (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 μL, 1 mmol). Reaction time 2 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 μL, 1 mmol) were added and workup as above. Ketone (51%), product (0%), bis-enol ether (2%).

9. $(CH_3)_2SiCl_2$ / LiI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : 1 : 1)

Using the procedure described above combined LiI (0.27 g, 2 mmol), pentane (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 μl, 1 mmol). Reaction time 2 hours at room temperature. Et_3N (0.14 mL, 1 mmol) and CH_3OH (41 μL, 1 mmol) were added and workup as above. Ketone (41%), product (29%), bis-enol ether (8%).

10. $(CH_3)_2SiCl_2$ / LiI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 2 : ∞ : 1)

Using the procedure described above combined LiI (0.27 g, 2 mmol), Et_3N (2 mL), $(CH_3)_2SiCl_2$ (0.13 mL, 1 mmol), and pinacolone (125 μL, 1 mmol). Reaction time 2 hours at room temperature. CH_3OH (41 μL, 1 mmol) was added and workup as above. GLC analysis showed ketone only.

E. Equilibration of Bis(3,3-dimethyl-1-buten-1-oxy)dimethylsilane.

To a solution of NaI (0.30 g, 2 mmol) in CH_3CN (1 mL) dichlorodimethylsilane (0.14 mL, 1 mmol) was added and allowed to stir 15 min at room temperature. Bis(3,3-dimethyl-1-buten-2-oxy) dimethylsilane (0.26 g, 1 mmol) was added and allowed to stir for 1 hour at room temperature. Et_3N (0.27 mL, 2 mmol) and CH_3OH (82 μL, 2 mmol) were added and allowed to stir 1 hour at room temperature. Workup and analysis as described above. Ketone (4%), product (50%), bis-enol ether (23%).

F. Preparation of N,N-dimethylamino- and N,N-diethylaminodimethyl-chlorosilane.

1. N,N-dimethylaminodimethylchlorosilane.

To a 2L 3-neck round bottom flask fitted with mechanical stirring, gas takeoff (to Hg bubbler) and a septum inlet Et_2O (600 mL) and dichlorodimthylsilane (67.2 mL, 0.554 mol) were charged and cooled to 0° C with an ice bath. Dimethylamine (50 g, 1.109 mol) was added via canula over 30 minutes with rapid stirring. The thick, white mixture was allowed to stir for an additional 4 hours at 0° C then brought to room temperature. The amine-hydrochloride salt was filtered out with a Buchner funnel as rapidly as possible and the salt washed 2 x 150 mL with Et_2O. The Et_2O was distilled at atmospheric pressure through a 15 cm Vigreux column to give 58.36 g (76%) at 107-109° C (literature[50] bp 108-109°C).

2. N,N-diethylaminodimethylchlorosilane.

Using the procedure described above combined Et_2O (1.2 L), $(CH_3)_2SiCl_2$ (116 mL, 0.96 mol) and diethylamine (200 mL, 1.93 mol) added via addition funnel over 70 min. After removal of the salt by filtration and Et_2O by distillation at atmospheric pressure, distilled the product at reduced pressure through a 30 cm Widmar column to give 128.9 g (88%) at 82-84° C (68 mm Hg) (literature[55] bp 84-87° C, 90 mm Hg).

^1H NMR (60 MHz, CCl_4) δ 0.55 (s, 6H, $SiCH_3$), 1.0 (t, 6H, 7 Hz, $NCH_2\underline{CH_3}$), 2.9 (q, 4H, 7 Hz, $N\underline{CH_2}CH_3$).

G. Preparation of Methoxydimethylsilyl Enol Ethers from N,N-Dimethylaminodimethylchlorosilane

1. Preparation of 2-(methoxydimethylsiloxy)-3,3-dimethyl-1-butene

A solution of NaI (7.5 g, 50 mmol) in CH_3CN (100 mL) was prepared and N,N-dimethylaminodimethylchlorosilane (7.3 mL, 50 mmol) was added and allowed to stir for 15 minutes at room temperature. Et_3N (7.0 mL, 50 mmol) followed by pinacolone (6.3 mL, 50 mmol) were added and allowed to stir for 4 hours at room temperature. The mixture was cooled to 0° C with an ice bath and Et_3N (7.0 mL, 50 mmol) followed by CH_3OH (2.0 mL, 50 mmol) were added and allowed to stir for 30 minutes. Workup with 150 mL 1:1 ice / saturated aqueous $NaHCO_3$ and 150 mL pentane. The aqueous layer was extracted 1 x 100 mL with pentane and the combined organic layers dried over Na_2SO_4. Filtered and concentrated to give 9.52 g crude material as a clear, yellow liquid. Distilled at reduced pressure to give 6.72 g (71%) at 93-95° C (53 mm Hg). Spectral data identical to that given previously.

The following control experiments were conducted and analyzed by GLC using decane as an internal standard. The results appear in Table 4.

2. $(CH_3)_2Si(Cl)N(CH_3)_2$ / NaI / Et_3N / $(CH_3)_3CCOCH_3$ (1 : 1 : 1 : 1)

Using the procedure described above combined NaI (0.15 g, 1 mmol), CH_3CN (2 mL), $(CH_3Si(Cl)N(CH_3)_2$ (0.15 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 µL, 1 mmol). Reaction time 2.5 hours at room temperature. Mixture was cooled to 0° C and Et_3N (0.14 mL, 1 mmol) and CH_3OH (43 µL, 1 mmol) were added. Workup with 20 mL 1 : 1 ice / $NaHCO_3$ and 15 mL pentane. The aqueous layer was extracted 1 x 8 mL with pentane and the combined organic layers dried over Na_2SO_4. Decane (97 µL, 0.5 mmol) was added and the solution analyzed by GLC. Ketone (11%), product (97%), bis-enol ether (0%).

3. $(CH_3)_2Si(Cl)N(CH_3)_2$ / NaI / Et_3N/$(CH_3)_3CCOCH_3$ (1 : 0 : 1 : 1)

Using the procedure described above combined CH_3CN (2 mL), $(CH_3Si(Cl)N(CH_3)_2$ (0.15 mL, 1 mmol), Et_3N (0.14 mL, 1 mmol), and pinacolone (125 µl, 1 mmol). Quench and workup as above. Ketone (98%), product (0%), bis-enol ether (0%).

4. $(CH_3)_2Si(Cl)N(CH_3)_2$ / NaI / Et_3N/$(CH_3)_3CCOCH_3$ (1 : 1 : 0 : 1)

Using the procedure described above combined NaI (0.15 g, 1 mmol), CH_3CN (2 mL), $(CH_3Si(Cl)N(CH_3)_2$ (0.15 mL, 1 mmol), and pinacolone (125 µl, 1 mmol). Quench and workup as above. Ketone (32%), product (17%), bis-enol ether (22%).

5. $(CH_3)_2Si(Cl)N(CH_3)_2$ / NaI / Et_3N/$(CH_3)_3CCOCH_3$ (1 : 0 : 0 : 1)

Using the procedure described above combined CH_3CN (2 mL), $(CH_3Si(Cl)N(CH_3)_2$ (0.15 mL, 1 mmol), and pinacolone (125 µl, 1 mmol). Quench and workup as above. Ketone (96%), product (0%), bis-enol ether (0%).

6. Preparation of 1-(methoxydimethylsiloxy)-2-methylcyclohexene and 1-(methoxydimethylsiloxy)-6-methylcyclohexene.

To a solution of NaI (5.25 g, 35 mmol) in CH_3CN (70 mL) $(CH_3)_2Si(Cl)N(CH_3)_2$ (4.82 g, 35 mmol) was added and allowed to stir for 15 minutes at room temperature. Et_3N (4.9 mL, 25 mmol) followed by 2-methylcyclohexanone (4.2 mL, 35 mmol) were added and allowed to stir for 30 minutes at room temperature. The mixture was cooled to 0° C with an ice bath and Et_3N (4.9 mL, 35 mmol) followed by CH_3OH (1.4 mL, 35 mmol) were added and allowed to stir for 30 minutes. Workup with 150 mL 1 : 1 ice / $NaHCO_3$ and 150 mL pentane. The aqueous layer was extracted 2 x 50 mL pentane and the combined organic layers dried over Na_2SO_4. Filtered and concentrated to give 7.33 g crude material. Distilled at reduced pressure to give 4.47 g (64%) at 52-56° C (0.3 mm Hg). as 85 / 15 mixture of isomers (more substituted / less substituted).

IR (neat): 2963, 2932, 2859, 2838, 1692, 1447, 1258, 1184, 1094, 947, 831.
^1H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 6H, $SiCH_3$), 1.03 (d, 0.45H, 6.9 Hz, 6-Me minor), 1.68-1.46 (m, 6.4 H), 1.96-1.88 (m, 2H), 2.09-2.01 (m, 2H), 3.50 (s, 3H, OCH_3), 4.89 (td, 0.15H, 4.0, 1.2 Hz, enol minor).
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.90, -2.89, 16.13, 18.62, 20.13, 22.94, 23.76, 30.00, 30.11, 30.12, 31.56, 33.41, 50.13, 103.98, 111.96, 142.35
MS-EI (70 eV): 200 (M^+, 2.3), 185 (29), 112 (28), 75 (10), 73 (base)

H. Preparation of Dialkylaminodimethylsilyl Enol Ethers

The following procedure is representative. The results appear in Table 6.

1. 2-(N,N-diethylaminodimethylsiloxy)propene

To a solution of NaI (30 g, 200 mmol) in CH_3CN (200 mL) N,N-diethylaminodimethylchlorosilane (29.8 g, 196 mmol) was added and allowed to stir for 10 minutes at room temperature. Et_3N (28 mL, 200 mmol) followed by acetone (14.7 mL, 200 mmol) were added and allowed to stir for 2 hours at room temperature. The mixture was extracted 4 x 50 mL with pentane via syringe. Concentration and distillation at reduced pressure through a 7 cm Vigreux column gave 29.2 g (79%) at 82-84° C (10 mm Hg).

IR (neat): 3115, 2967, 2932, 2869, 1636, 1449, 1373, 1279, 1256, 1173, 1044, 934.

^1H NMR (300 MHz, $CDCl_3$): δ 0.16 (s, 6H, $SiCH_3$), 0.99 (t, 6H, 7 Hz, NCH_2CH_3), 1.75 (d, 3H, 0.6 Hz), 2.85 (q, 4H, 7 Hz, NCH_2CH_3), 4.03 (d, 1H, 0.6 Hz, enol), 4.05 (s, 1H, enol).

^{13}C NMR (75 MHz, $CDCl_3$): δ -2.13, 15.64, 22.77, 39.59, 91.45, 155.82.

MS-EI (70 eV): 172 (M-15, 26); 130 (4); 115 (59); 75 (16); 58 (88); 40 (base).

2. 2-(N,N-diethylaminodimethylsiloxy)-3,3-dimethyl-1-butene

Using the procedure described above combined NaI (30 g, 200 mmol) CH_3CN (200 mL), $(CH_3)_2Si(Cl)N(CH_2CH_3)_2$ (30.3 g, 200 mmol), Et_3N (28 mL, 200 mmol), and pinacolone (25 mL, 200 mmol). Reaction time 1.5 hours at

room temperature. Distillation at reduced pressure through a 15 cm Vigreux column gave 38.38 g (84%) at 55° C (0.65 mm Hg). (literature[44] bp. 101-105° C, 25 mm Hg).

IR (neat): 3127, 2967, 2932, 2913, 2890, 1617, 1483, 1375, 1298, 1258, 1186, 1032, 934, 791, 693.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (s,6H, $SiCH_3$), 0.99 (t, 6H, 7 Hz, $NCH_2\underline{CH_3}$) 1.02 (s, 9H, $(CH_3)_3$, 2.86 (q, 4H, 7 Hz, $N\underline{CH_2}CH3$), 3.92 (d, 1H, 1Hz, enol) 4.02 (d, 1H, 1 Hz, enol).

^{13}C NMR (75 MHZ, $CDCl_3$): δ -1.85, 15.64, 28.15, 36.55, 39.65, 85.25, 167.05.

MS-EI (70 eV): 229 (M+, 3); 214 (30); 172 (7); 157 (26); 130 (26); 75 (base).

3. 2-(N,N-dimethylaminodimethylsiloxy)-3,3-dimethyl-1-butene

Using the procedure described above combined NaI (2.25 g, 15 mmol) CH_3CN (15 mL), $(CH_3)_2Si(Cl)N(CH_3)_2$ (2.07 g, 15 mmol), Et_3N (2.1 mL, 15 mmol), and pinacolone (1.9 mL, 15 mmol). Reaction time 1 hour at room temperature. Extraction 5 x 10 mL with pentane. Distillation at reduced pressure bulb to bulb gave 2.60 g (87%) at 80° C (oven, 25 mm Hg).

IR (neat): 2967, 2897, 2869, 2849, 1618, 1483, 1464, 1298, 1258, 1184, 1032, 1009, 995, 833.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (s, 6H, $SiCH_3$), 1.03 (s, 9H, $(CH_3)_3C$), 2.50 (s, 6H, $N(CH_3)_2$), 3.87 (d, 1H, 1.2 Hz, enol), 4.04 (d, 1H, 1.2 Hz, enol)

^{13}C NMR (75 MHz, $CDCl_3$): δ -3.00, 28.13, 36.56, 37.51, 85.36, 167.01.

MS-EI (70 eV): 202 (M+1, 96), 201 (base), 187 (81), 186 (35), 119 (81), 100 (65), 75 (40).

4. α-(N,N-diethylaminodimethylsiloxy)styrene

Using the procedure described above combined NaI (30 g, 200 mmol), CH_3CN (200 mL), $(CH_3)_2Si(Cl)N(CH_2CH_3)_2$ (30.3 g, 200 mmol), Et_3N (28 mL, 200 mmol), and acetophenone (23.3 mL, 200 mmol). Reaction time 2 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 33.02 g (66%) at 89-91° C (0.45 mm Hg).

IR (neat): 3059, 3027, 2968, 2930, 2869, 1617, 1574, 1493, 1466, 1447, 1318, 1304, 1288, 1258, 1173, 1030, 936, 831.

^{11}H NMR (300 MHz, CDCN): δ 0.22 (s, 6H, $SiCH_3$), 0.98 (t, 6H, 7 Hz, NCH_2CH_3), 2.89 (q, 4H, 7 Hz, NCH_2CH_3), d 4.46 (d, 1H, 1.5 Hz, enol) 4.94 (d, 1H, 1.5 Hz, enol), 7.4-7.2 (m, 3H, Ar), 7.65-7.55 (m, 2H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ -2.27, 15.65, 39.64, 91.14, 125.22, 127.96, 127.99, 137.88, 155.52.

MS-EI (70 eV): 249 (M+, 12); 234 (25); 177 (base); 101 (22); 77 (12); 75 (84); 58 (20).

5. 3-(N,N-diethylaminodimethylsiloxy)-2-pentene.

Using the procedure described above combined NaI (22.5 g, 150 mmol), CH_3CN (150 mL), $(CH_3)_2Si(Cl)N(CH_2CH_3)_2$ (22.8 g, 150 mmol), Et_3N (21 mL, 150 mmol), and 3-pentanone (15.9 mL, 150 mmol). Reaction time 2.5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 26.37 g (92%) at 45-46° C (0.4 mm Hg) as a mixture of isomers, Z / E 88 : 12.

IR (neat): 3042, 2969, 2934, 2867, 1678, 1466, 1375, 1256, 1208, 1194, 1175, 1030, 934.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (s, 6H, $SiCH_3$), 0.99 (t, 6H, 6.9 Hz, NCH_2CH_3), 1.00 (t, 3H, 7.5 Hz, CH_3CH_2-), 1.50 (dt, 3H, 6.6, 1.5 Hz, $=CHCH_3$), 2.02 (qt, 2H, 7.5, 1.5 Hz, CH_3CH_2-), 2.86 (q, 4H, 6.9 Hz, NCH_2CH_3), 4.45 (q, H, 6.6 Hz, enol (Z)), 4.60 (q, H, 6.6 Hz, enol (E)).

^{13}C NMR (75 MHz, $CDCl_3$): δ -1.71, 10.63, 11.77, 15.68, 24.00 (E), 29.34 (Z), 39.56, 100.35, 152.74.

MS-EI (70 eV): 216 (M+1, base), 200 (6), 130 (11), 86 (9), 75 (37), 73 (69), 69 (27).

6. 3-(N,N-diethylaminodimethylsiloxy)-2,4-dimethyl-2-pentene

Using the procedure described above combined NaI (9.0 g, 60 mmol), CH_3CN (60 mL), $(CH_3)_2Si(Cl)N(CH_2CH_3)_2$ (9.1 g, 60 mmol), Et_3N (8.4 mL, 60 mmol), and 2,4-dimethyl-3-pentanone (8.5 mL, 60 mmol). Reaction time 2.5 hours at room temperature. Extraction 1 x 20 mL, 3 x 15 mL with pentane. Distillation at reduced pressure through a 7 cm Vigreux column gave 9.15 g (63%) at 54-56° C (0.4 mm Hg).

IR (neat): 2967, 2930, 2867, 1672, 1468, 1375, 1264, 1204, 1169, 1073, 1030, 932.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.15 (s, 6H, $SiCH_3$), 0.96 (d, 6H, 6.6 Hz, $(CH_3)_2CH$), 0.99 (t, 6H, 6.9 Hz, $N(CH_2CH_3)_2$) 1.57 (s, 3H, $=C(CH_3)_2$), 1.58 (s, 3H, $=C(CH_3)_2$), 2.77 (septet, 1H, 6.6 Hz, $(CH_3)_2CH$), 2.88 (q, 4H, 6.9 Hz, $N(CH_2CH_3)_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ -1.50, 15.54, 18.55, 18.81, 20.06, 29.38, 39.67, 106.59, 149.15.

MS-EI: (70 eV): 244 (M+1, base), 229 (12), 201 (10), 149 (31), 133 (25), 97 (30), 75 (4), 73 (5).

I. Preparation of 2-(acetoxydimethylsiloxy)-3,-dimethyl-1-butene

To a solution of NaI (7.5 g, 50 mmol) in CH_3CN (50 mL) N,N-dimethylaminodimethylchlorosilane (6.89 g, 50 mmol) was added and allowed to stir for 15 minutes at room temperature, Et_3N (7.0 mL, 50 mmol) followed by pinacolone (6.3 mL, 50 mmol) were added and allowed to stir for 1 hour at room temperature. Et_3N (7.0 mL, 50 mmol) followed by acetic acid (2.9 mL, 50 mmol) were added and allowed to stir for 0.5 hour at room temperature. The reaction mixture was extracted 5 x 50 mL pentane via syringe. The combined pentane extracts were concentrated to give 14.64 g crude yellow liquid. Distillation ot reduced pressure gave 8.01 g (74%) at 86-92° C (32 mm Hg).

IR (neat): 3127, 2969, 2915, 2872, 1728, 1630, 1483, 1464, 1267, 1042, 1019, 885.

^1H NMR (300 MHz, $CDCl_3$): δ 0.39 (s, 6H, $SiCH_3$), 1.06 (s, 9H, $(CH_3)_3$), 2.09 (s, 3H, $COCH_3$), 4.13 (d, 1H, 1.5Hz, enol), 4.18 (d, 1H, 1.5Hz, enol)

^{13}C NMR (75 MHz, $CDCl_3$): δ -2.10, 22.75, 27.92, 36.30, 87.98, 132.15, 165.76.

MS-EI (70 eV): 216 (M+, 2), 201 (0.6), 157 (0.3), 117 (base), 75 (70), 43 (16).

J. Preparation of 3-(dimethylvinylsiloxy)-2-pentene

To a solution of 3-(N,N-dimethylaminodimethylsiloxy)-2-pentene (6.5 g, 35 mmol) in Et_2O (35 mL) at 0° C acetyl chloride (2.49 mL, 35 mmol) was added dropwise and allowed to stir for 40 minutes. The mixture was cooled to -78° C with an acetone-dry ice bath and vinylmagnesium bromide 1.0 M in THF

(35 mL, 35 mmol) was added slowly over 10 minutes. The cooling bath was removed and the reaction was allowed to reach room temperature and stir for 24 hours. Workup in 200 mL saturated aqueous $NaHCO_3$ and 70 mL pentane. The aqueous layer was extracted 2 x 35 mL pentane and the combined organic layers dried over Na_2SO_4. Filtered and concentrated to give 7.16 g crude material. Distillation at reduced pressure gave 2.73 g (46%) at 46-51° C (60 mm Hg) as a 10 : 1 Z / E mixture of isomers.

IR (neat): 3052, 2969, 2942, 2921, 2882, 1680, 1653, 1464, 1408, 1254, 1051, 957, 787.

^1H NMR (300 MHz, $CDCl_3$): δ 0.21 (minor), 0.23 (major) (s, 6H, $SiCH_3$), 0.98 (t, 3H, 7.5 Hz, CH_2CH_3), 4.49 (major), 4.70 (minor) (q, 1H, 6.6Hz, enol) 5.78 (dd, 1H, 20 Hz, 4.2 Hz, vinyl), 5.98 (dd, 1H, 15Hz, 4.2Hz, vinyl) 6.17 (dd, 1H, 20 Hz, 15 Hz, vinyl)

^{13}C NMR (75MHz, $CDCl_3$,): δ -1.20 (minor), 0.38 (major), 7.88, 10.67, 11.65, 14.14, 24.00, 29.39, 35.43, 42.83, 100.60 (minor), 100.99 (major), 131.59 (minor), 132.86 (major), 137.71 (major), 139.49 (minor), 152.59.

MS-EI (70eV): 171 (M+1, 83), 170 (24), 159 (base), 155 (52), 143 (34), 141 (52), 87 (93), 86 (21), 75 (50), 73 (34).

K. Preparation of Symmetrical Dimethylsilyl Bis-Enol Ethers

The following procedure is representative. The results apprear in Table 7.

1. Bis (1-propenyl-2-oxy)dimethylsilane

To a solution of NaI (45 g, 300 mmol) in CH_3CN (300 mL) dichlorodimethylsilane (18.2 mL, 150 mmol) was added and allowed to stir for 10 minutes at room temperature. Et_3N (42 mL, 300 mmol) followed by acetone (22 mL, 300 mmol) were added and allowed to stir for 1 hour and 50 minutes at room temperature. Workup in 400 mL 1:1 ice / saturated aqueous $NaHCO_3$ and 200 mL pentane. The aqueous layer was extracted 2 x 50 mL pentane and the combined organic layers dried over Na_2SO_4. Filtered, concentrated and distilled through a 15 cm Vigreux column gave 18.73 (73%) at 87° C (70 mm Hg).

IR (neat): 3115, 2990, 2968, 2957, 2922, 1642, 1443, 1260, 1051, 907.
^1H NMR (300 Mz, $CDCl_3$): δ 0.26 (s, 6H, $SiCH_3$) 1.79 (d, 6H, 1Hz, CH_3), 4.10 (bs, 2H, enol), 4.2 (s, 2H, enol)
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.50, 22.30, 92.17, 154.77.
MS-EI (70 eV): 157 (M-15, 9), 144 (49), 115 (46), 77 (41), 75 (base).

2. Bis-(3,3-dimethyl-1-butenyl-2-oxy)dimethylsilane

Using the procedure described above combine NaI (24 g, 160 mmol), CH_3CN (160 mL), dichlorodimethylsilane (9.7 mL, 80 mmol), Et_3N (22.3 mL, 160 mmol), and pinacolone (22.3 mL, 160 mmol). Reaction time 1.5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 15.05 g (73%) at 115-118° C (3 mm Hg).

IR (neat): 3125, 1969, 2913, 2872, 1626, 1464, 1254, 1015, 885.
^1H NMR (300 MHz, $CDCl_3$): δ 0.24 (s, 6H, $SiCH_3$), 1.05 (s, 18H, t-Bu), 4.12 (s, 4H, enol)
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.92, 27.99, 36.34, 87.04, 165.92.

MS-EI (70 eV): 241 (M-15, 1.5), 199 (16), 157 (7), 155 (10), 75 (base), 57 (14).

3. Bis (α-styryloxy)dimethylsilane

Using the procedure described above combine NaI (12.9 g, 86 mmol), CH_3CN (170 mL), dichlorodimethylsilane (5.2 mL, 43 mmol), Et_3N (12 mL, 86 mmol), and acetophenone (10 mL, 86 mmol). Reaction time 1.75 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 10.63 g (83%) at 112-113° C (0.008 mm Hg).

IR (neat): 3119, 3108, 3085, 3059, 3036, 3029, 2967, 2907, 1688,, 1624, 1576, 1445, 1262, 1015, 853.

^1H NMR (300 MHz, CD_3CN): δ 0.40 (s, 6H, $SiCH_3$), 4.65 (d, 2H, 2 Hz, enol), 5.06 (d, 2H, 2 Hz, enol), 7.3-7.4 (m, 6H, Ar), 7.65-7.8 (m, 4H, Ar).

^{13}C NMR (75 MHz, CD_3CN): δ -3.04, 92.59, 125.54, 128.73, 129.02, 137.16, 155.04.

MS-EI (70 eV): 297 (M+1, 9), 296 (35), 281 (17), 268 (base), 219 (3), 205 (57),, 176 (25), 103 (9), 75 (49).

4. Bis-(2-pentenyl-3-oxy)dimethylsilane

Using the procedure described above combine NaI (27 g, 180 mmol), CH_3CN (180 mL), dichlorodimethylsilane (10.9 mL, 90 mmol), Et_3N (25 mL, 180 mmol), and 3-pentanone (19 mL, 90 mmol). Reaction time 1.5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 15.55 g (76%) at 117-120° C (10 mm Hg) as a mixture of isomers: 66 ZZ : 30ZE : 4EE.

IR (neat): 3046, 2971, 2940, 2921, 2882, 1682, 1464, 1260, 1040, 909.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (minor) 0.23 (major) (s, 6H, $SiCH_3$), 1.01 (t, 6H, 7.5 Hz, $\underline{CH_3}CH_3$), 1.51 (dt, 6H, 6.6 Hz, 1.5 Hz, $=CHCH_3$), 2.08 (m, 4H, $CH_3\underline{CH_3}$), 4.52 (qt, 1.4H, 6.6 Hz, 1.2 Hz, enol (major)), 4.73 (q, 0.7H, 6.6 Hz, enol (minor)).

^{13}C NMR (75 MHz, $CDCl_3$): δ -1.95 (minor), -1.56 (major), 10.59, 11.56, 11.66, 11.68, 23.94 (EE), 29.28 (ZE), 29.35 (ZZ), 101.02 (major), 101.07 (minor), 152.12.

MS-EI (70 eV): 229 (M+1, 1.3), 228 (1), 159 (25), 147 (41), 133 (19), 75 (base), 73 (72), 69 (3).

5. Bis(3-heptenyl-4-oxy)dimethylsilane

Using the procedure described above combine NaI (15 g, 100 mmol), CH_3CN (100ml), dichlorodimethylsilane (6 mL, 50 mmol), Et_3N (14 mL, 100 mmol), and 4-heptanone (14 mL, 100 mmol). Reaction time 5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 10.85 g (76%) at 88-93° C (1.2 mm Hg) as a mixture of isomers: ZZ / ZE 53 : 47.

IR (neat): 3048, 2956, 2934, 2874, 1676, 1458, 1260, 1046, 970.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.20 (minor) 0.21 (major) (s, 6H, $SiCH_3$), 0.84-0.96 (m, 12H, CH_3, 1.47 (sextet, 4H, 7.5 Hz, $CH_3\underline{CH_2}CH_3$), 1.87-2.07 (m, 8H, CH_2), 4.43 (t, 0.6H, 7.5 Hz, enol (major)), 4.74 (t, 0.4H, 7.5Hz, enol (minor)).

^{13}C NMR (75 MHz, $CDCl_3$): δ -1.96 (minor), -1.59 (major), 13.63, 13.65, 13.71, 14.42, 15.26, 18.58, 18.63, 20.20, 20.21, 20.27, 32.98 (EE), 38.45 (ZE), 38.51 (ZZ), 110.15 (minor) 110.31 (major), 110.37 (minor), 148.89.

MS-EI (70 eV): 285 (M+1, 3), 284 (12), 241 (4), 171 (36), 170 (base), 113 (3), 75 (64).

6. Bis(cyclopentenyl-1-oxy)dimethylsilane

Using the procedure described above combine NaI (30 g, 200 mmol), CH_3CN (200ml), dichlorodimethylsilane (12.1 mL, 100 mmol), Et_3N (28 mL, 200 mmol), and cyclopentanone (17.7 mL, 100 mmol). Reaction time 1.5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 16.95 g (76%) at 74° C (0.55 mm Hg).

IR (neat): 3071, 2959, 2903, 2853, 1649, 1441, 1264, 1032, 938.
^1H NMR (300 MHz, $CDCl_3$): δ 0.26 (s, 6H, $SiCH_3$), 1.84 (quintet, 4H, 7.5H, CH_2 C-4), 2.20-2.32 (m, 8H, CH_2), 4.74 (quintet, 2H, 1.8 Hz, enol).
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.46, 21.32, 28.64, 33.11, 103.58, 153.71.
MS-EI (70 eV): 225 (M+1, 8), 224 (33), 195 (19), 75 (base), 67 (75).

7. Bis(cyclohexenyl-1-oxy)dimethylsilane

Using the procedure described above combine NaI (30 g, 200 mmol), CH_3CN (200ml), dichlorodimethylsilane (12.1 mL, 100 mmol), Et_3N (28 mL, 200 mmol), and cyclohexanone (17.7 mL, 100 mmol). Reaction time 1.5 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 16.95 g (76%) at 74° C (0.55 mm Hg).

IR (neat): 3071, 2959, 2903, 2853, 1649, 1441, 1264, 1032, 938.
^1H NMR (300 MHz, $CDCl_3$): δ 0.26 (s, 6H, $SiCH_3$), 1.84 (quintet, 4H, 7.5Hz, CH_2 C-4), 2.20-2.32 (m, 8H, CH_2), 4.74 (quintet, 2H, 1.8 Hz, enol).
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.46, 21.32, 28.64, 33.11, 103.58, 153.71.
MS-EI (70 eV): 225 (M+1, 8), 224 (33), 195 (19), 75 (base), 67 (75).
Spectral data is in agreement with reference 43.

8. Bis(1-[α-thienyl]-1-hexenyl-1-oxy)dimethylsilane

Using the procedure described above combine NaI (7.5 g, 50 mmol), CH_3CN (100 ml), dichlorodimethylsilane (3.0 mL, 2.5 mmol), Et_3N (7 mL, 50 mmol), and 2-hexanoylthiophene (9.11 mL, 50 mmol). Reaction time 18.5 hours at room temperature. Workup gave 9.9 g crude material which showed 75% conversion of ketone by ^1H NMR. Isomer ratio ZZ / ZE 83 : 17 by ^1H NMR.

^1H NMR (300 MHz, $CDCl_3$): δ 0.25(major), 0.28 (minor) (s, 6H, $SiCH_3$), 0.80-0.95 (m, 6H, CH_2), 1.20-1.50 (m, 9H, CH_2), 1.7-1.8 (m, 1H, CH_2), 2.10-2.35 (m, 3H, CH_2), 2.88 (t, 1H, 7.5Hz, CH_2, ketone), 5.18 (minor), 5.30 (major) (t, 1.5H, 7.5 Hz, enol), 6.91 (dd, 4.8Hz, 3.6Hz, Th), 6.95-7.18 (m, 4.5H, Th), 7.65 (dd, 1H, Th)

9. Bis(2,4-dimethyl-2-pentenyl-3-oxy)dimethylsilane

Using the procedure described above combine NaI (17.25 g, 115 mmol), CH_3CN (150 mL), dichlorodimethylsilane (7 mL, 57.5 mmol), Et_3N (16 mL, 115 mmol), and 2,4-dimethyl-3-pentanone (16.3 mL, 115 mmol). Reaction time 20 hours at room temperature. Distillation at reduced pressure through a 7 cm Vigreux column gave 12.34 g (75%) at 85-88° C (0.85 mm Hg).

IR (neat): 2967, 2930, 2903, 2870, 1749, 1470, 1560, 1252, 1074, 959.
^1H NMR (300 MHz, $CDCl_3$): δ 0.19 (s, 6H, $SiCH_3$), 0.99 (d, 12H, 6.9 Hz, $CH(\underline{C}H_3)_2$), 1.61 (s, 12H, $=C(CH_3)_2$), 2.82 (septet, 2H, 6.9 Hz, $\underline{C}H(CH_3)_2$).
^{13}C NMR (75 MHz, $CDCl_3$): δ -1.86, 18.52, 18.70, 20.00, 29.18, 107.14, 149.80.

MS-EI (70 eV): 285 (M+1, 0.2), 284 (0.4), 269 (0.3), 170 (85), 155 (27), 75 (base).

L. Preparation of Mixed Dimethylsilyl Bis-Enol Ethers

The results appear in Table 8.

1. 3-(3',3'-dimethyl-1'-butenyl-2'-oxydimethylsiloxy)-2-pentene

To a solution of 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (6.7 g, 35 mmol) in CH_3CN (70 mL) cooled to 0° C, acetyl chloride (2.49 mL, 35 mmol) was added and allowed to stir for 15 minutes ot 0° C. Pinacolone (4.4 mL, 35 mmol), Et_3N (4.9 mL, 35 mmol), NaI (5.25 g, 35 mmol) and pentane (70 mL) were added in that order and allowed to stir for 30 minutes at 0° C. The cooling bath was removed and the reaction mixture was allowed to stir for 3.5 hours at room temperature. The supernatent pentane layer wa removed via syringe and the reaction mixture extracted 4 x 20 mL with pentane via syringe. The combined pentane layers were concentrated and distilled at reduced pressure to give 3.81 g (45%) at 50-53 ° C (0.2 mmHg), as a mixture of isomers 88:12 Z/E.

IR (neat): 3125, 3046, 2969, 2940, 2917, 2870, 1682, 1626, 1464, 1296, 1260, 1036, 839.

^1H NMR (300 MHz, $CDCl_3$): δ 0.23 (minor), 0.26 (major) (s, 6H, $SiCH_3$), 1.03 (t, 3H, 7.5 Hz, CH_2CH_3), 1.05 (s, 9H, $(CH_3)_3C$), 1.53 (dt, 3H, 6.6 Hz, 1.2 Hz, $=CHCH_3$), 2.09 (m, 2H, CH_2CH_3), 4.11 (d, 1H, 1.2 Hz, enol), 4.14 (d, 1H, 1.2 Hz, enol), 4.54 (major), 4.75 (minor) (q, 1H, 6.6 Hz, enol)).

^{13}C NMR (75 MHz, $CDCl_3$): δ -2.59 (minor), -2.27 (major), 10.52, 11.57, 11.71, 23.90 (minor), 28.02, 29.23 (major), 36.35, 87.03, 101.12, 152.21, 166.00.
MS-EI (70 eV): 243 (M+1, 7), 242 (2), 227 (5), 185 (38), 157 (20), 142 (base), 113 (25), 75 (25).

2. 3-(cyclopentenyl-1'-oxydimethylsiloxy)-2-pentene

Using the procedure described above combined 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (6.7 g, 35 mmol) in CH_3CN (70 mL), acetyl chloride (2.49 mL, 35 mmol), cyclopentanone (3.1 mL, 35 mmol), Et_3N (4.9 mL, 35 mmol), NaI (5.25 g, 35 mmol) and pentane (70 mL). Distillation at reduced pressure gave 4.11 g (52%) at 68-71° C (0.75 mmHg), as a mixture of isomers 88 : 12 Z / E.

IR (neat): 3069, 3046, 2969, 2940, 2921, 2853, 1682, 1648, 1456, 1262, 1040, 909.
^1H NMR (300 MHz, $CDCl_3$): δ 0.22 (minor), 0.24 (major) (s, 6H, $SiCH_3$), 0.95-1.10 (m, 3H, 7.5 Hz, $CH_2\underline{C}H_3$), 1.49 (dt, 3H, 6.6 Hz, 1.2 Hz, $=CH\underline{C}H_3$), 1.80-2.40 (m, 8H, CH_2), 4.52 (qt, 0.9H, 6.6 Hz, 1.2 Hz, enol, major), 4.73 (quintet, 1H, 1.8 Hz, enol), 4.75 (q, 0.1H, 6.6 Hz, enol,.minor).
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.02 (major), 7.90, 10.48, 11.65, 21.35, 23.21 (minor), 28.64, 29.22 (major), 33.24, 35.43, 101.15, 103.44, 152, 154.

3. 3-(β,β-dimethyl)-α-styryloxydimethylsiloxy)-2-pentene

To a solution of 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (4.79 g, 25 mmol) in CH_3CN (25 mL), acetyl chloride (1.78 mL 25 mmol) was added and allowed to stir for 10 minutes at room temperature. Isobutyrophenone (3.75 mL, 25 mmol), and Et_3N (3.5 mL, 25 mmol) were added and the mixture

was heated to 40-50° C in an oil bath. NaI (4.5 g, 30 mmol) in CH_3CN (30 mL) was added dropwise with a pressure equalized addition funnel over 35 minutes. The mixture was maintained at 40-50° C for an additional 55 minutes. Workup in 200 mL 1:1 ice / saturated aqueous $NaHCO_3$ and 100 mL pentane. The aqueous layer was extraced 2 x 50 mL pentane and the combined organic layers dried over Na_2SO_4. Concentration and distillation (bulb to bulb) at reduced pressure gave 2.04 g (28%) at 67-71° C (oven) (1.1 mm Hg) as a mixture of isomers Z / E 88 : 12.

IR (neat): 3058, 3025, 2968, 2919, 2880, 2863, 1682, 1653, 1260, 1154, 1047, 907, 866, 801.

^1H NMR (300 MHz, $CDCl_3$): δ 0.005 (minor), 0.01 (major) (s, 6H, $SiCH_3$), 0.92 (minor), 0.97 (major) (t, 3H, 7.5 Hz, $\underline{C}H_3CH_2$), 1.46 (dt, 3H, 6.6 Hz, 1.2 Hz, $=CH\underline{C}H_3$) 1.66 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 1.97 (m, 2H, $CH_3\underline{C}H_2$), 4.45 (major) (qt, 0.9H, 6.6 Hz, 1.2 Hz, enol), 4.62 (minor) (q, 0.1H, 6.6 Hz, enol), 7.18-7.38 (m, 5H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ -1.68 (minor), -1.34 (major), 10.52, 11.63, 18.19, 19.81, 23.85 (minor), 29.25 (major), 100.87, 113.40, 127.62, 127.70, 129.10, 138.55, 142.70, 152.09,

MS-EI (70 eV): 159 (2), 148 (2), 131 (1), 105 (base), 77 (79), 75 (11), 73 (8).

4. 3-(cyclohexenyl-1'-oxydimethylsiloxy)-2,4-dimethyl-2-pentene

Using the procedure described above combined 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (6.09 g, 25 mmol) in CH_3CN (25 mL), acetyl chloride (1.78 mL, 25 mmol), cyclohexanone (2.6 mL, 25 mmol), Et_3N (3.5 mL, 25 mmol), NaI (4.12 g, 27.5 mmol) in CH_3CN (25 mL). Distillation at

reduced pressure through a 7 cm Vigreux column gave 5.06 g (75%) at 81-84° C (0.50 mmHg), as a mixture of isomers Z / E 88 : 12.

IR (neat): 2965, 2932, 2886, 2863, 1672, 1458, 1368, 1258, 1190, 1074, 901.
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (s, 6H, $SiCH_3$), 0.98 (d, 6H, 6.9 Hz, iPr), 1.45-1.54 (m, 2H, CH_2), 1.58 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.61-1.69 (m, 2H, CH_2), 1.95-2.07 (m, 4H, CH_2), 2.80 (septet, 1H, 6.9 Hz, iPr), 4.98 (tt, 1H, 4 Hz, 1.2 Hz, enol).
^{13}C NMR (75 MHz, $CDCl_3$): δ -1.85, 18.48, 18.54, 19.92, 22.28, 23.12, 23.79, 29.04, 29.65, 104.64, 107.55, 148.58, 149.56.
MS-EI (70 eV): 269 (M+1, 2), 268 (6), 267 (1), 187 (10), 171 (25), 170 (base), 155 (18), 97 (1), 75 (3).

5. 3-(2'-methylpropenyl-1'-oxydimethylsiloxy)-2,4-dimethyl-2-pentene

Using the procedure described above combined 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (6.09 g, 25 mmol) in CH_3CN (25 mL), acetyl chloride (1.78 mL, 25 mmol), isobutyraldehyde (2.27 mL, 25 mmol), Et_3N (43.5 mL, 25 mmol), NaI (4.12 g, 27.5 mmol) in CH_3CN (25 mL). Distillation at reduced pressure through a 7 cm Vigreux column gave 3.84 g (63%) at 63-65° C (0.8 mmHg).

IR (neat): 2967, 2926, 2872, 1686, 1676, 1456, 1260, 1163, 1076, 957, 884.
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.20 (s, 6H, $SiCH_3$), 0.97 (d, 6H, 6.9 Hz, iPr), 1.53 (d, 3H, 1.5 Hz, CH_3), 1.57 (s, 3H, CH_3), 1.59 (d, 3H, 1.5 Hz, CH_3), 1.60 (s, 3H, CH_3), 2.80 (septet, 1H, 6.9 Hz, iPr), 6.12 (septet, 1H, 1.5 Hz, enol).
^{13}C NMR (75 MHz, $CDCl_3$): δ -2.46, 14.85, 18.45, 19.30, 19.86, 28.99, 107.69, 114.04, 132.18, 148.42.

MS-EI (70 eV): 243 (M+1, 2), 242 (1), 241(3), 227 (1), 187 (40), 129 (10), 113 (6), 75 (35), 73 (78), 71 (58), 59 (base), 55 (12).

6. 3-(β,β-dimethyl-α-styryloxydimethylsiloxy)-2-pentene

To a solution of i-Pr_2NH (4.9 mL, 35 mmol) in pentane (35 mL) cooled to 0° C, n-BuLi 1.6 M in hexanes (22 mL, 35 mmol) was added slowly and alllowed to stir for 15 minutes at 0 ° C. Isobutyrophenone (5.25 mL, 35 mmol) was added dropwise to produce a bright yellow enolate solution and was allowed to stir for 15 minutes at 0° C. The solvents and amine were removed under full vacuum to give a viscous yellow residue. Et_2O was added to give a clear, yellow "amine-free" enolate solution. In a second flask, to a solution of 3-(N,N-diethylaminodimethylsiloxy)-2-pentene (6.7 g, 35 mmol) in Et_2O (35 mL), acetyl chloride (2.5 mL, 35 mmol) was added and allowed to stir for 15 minutes at 0° C. This mixture was cooled to -78° C with an acetone-dry ice bath. The enolate solution was added slowly over 15 minutes via canula transfer. The cooling bath was removed and the reaction mixture allowed to reach room temperature over 2 hours. Workup in 100 mL $NaHCO_3$ and 100 mL Et_2O. Aqueous layer was extracted 2 x 50 mL Et_2O; combined organic layer 1 x 20 mL NaCl, dried over $MgSO_4$. GLC analysis indicated some product in a very complex mixture.

CHAPTER III

COUPLING REACTIONS OF DIMETHYLSILYL BIS-ENOL ETHERS

INTRODUCTION

The synthesis of 1,4-dicarbonyl compounds (Figure 6) has attracted the efforts of organic chemists for some time. Primarily because these compounds are the immediate precursors to a variety of other systems including cyclopentenones, furans, pyrroles, and thiophenes.

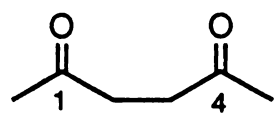
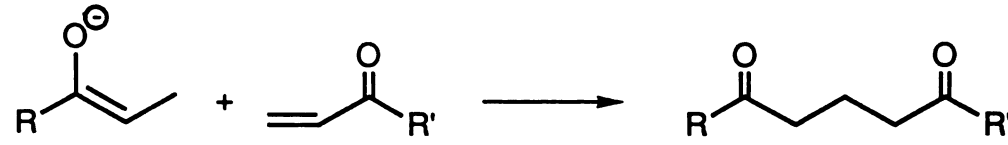


Figure 6 - 1,4-Dicarbonyl Compounds

Dicarbonyl compounds are usually formed by condensation reactions. For instance, 1,3-dicarbonyl compounds can be easily prepared by the reaction of an enolate with an acylating agent (Equation 61) and 1,5-dicarbonyl compounds can be prepared by conjugate addition of an enolate to an α,β-unsaturated carbonyl compound (Equation 62). 1,4-Dicarbonyl compounds, however, are not amenable to such simple approaches.

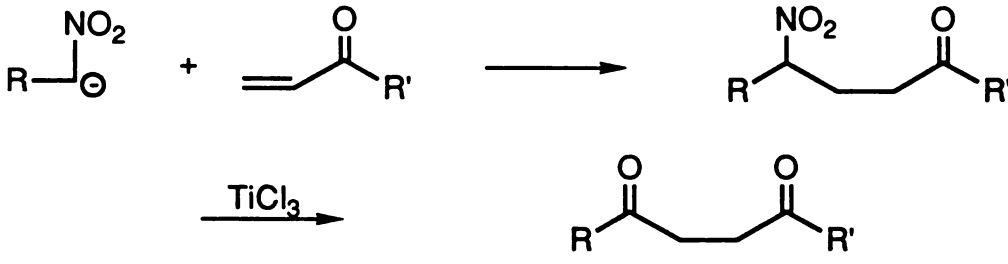
(61)



(62)

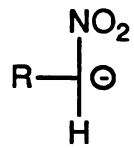
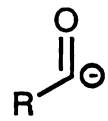
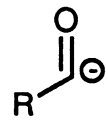
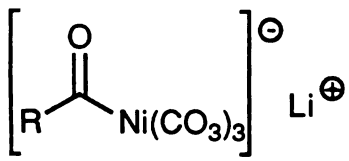
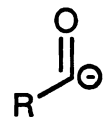
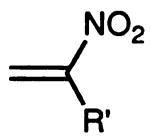
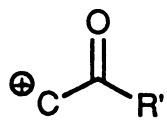
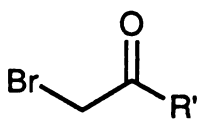
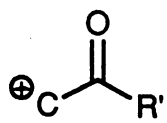
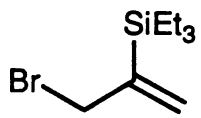
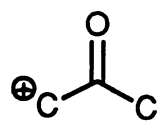
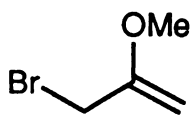
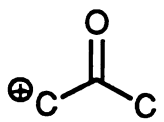
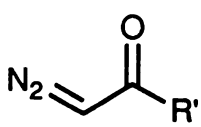
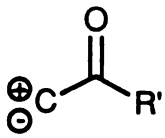
This is especially true when one narrows down the problem to the synthesis of 1,4-diketones. These compounds have typically been made by either a "charge inversion"[56] approach or by a radical coupling approach. Some of the reagents used to prepare 1,4-diketones which have charge inversion are given in Table 15 together with their synthetic equivalents. Seebach[56] has described these reagents as having "reactivity umpolung" and his notation (a=accepter, d=donor) is included.

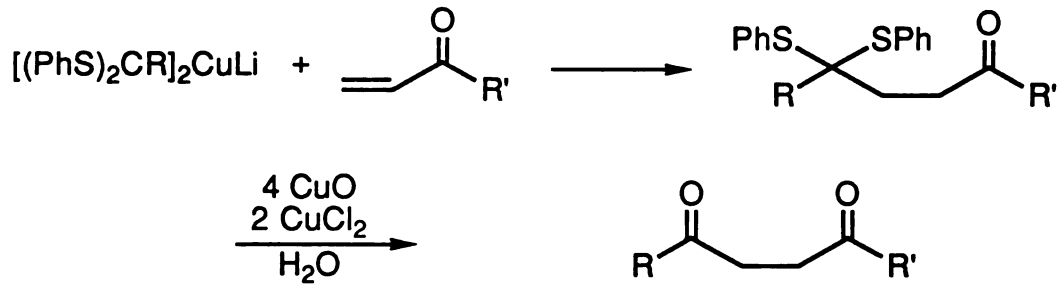
1,4-diketones have been synthesized by the addition of acyl anion equivalents, such as nitro-stabilized carbanions[57] (Equation 63), lithium di[bis(phenylthio)methyl]cuprate[58] (Equation 64), and acyl carbonylnickelate[59] (Equation 65), to α,β-unsaturated ketones.



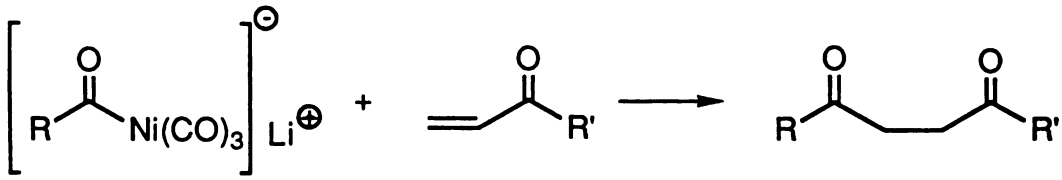
(63)

Table 15 - Summary of "Charge Inversion" Approaches to 1,4-Diketones

Reagent	Synthetic Equivalent	Equation
	 : d^1	(63)
$[(PhS)_2CR]_2CuLi$	 : d^1	(64)
	 : d^1	(65)
	 : a^2	(66)
	 : a^2	(67)(73)
	 : a^2	(71)
	 : a^2	(72)
	 : a^2, d^2	(Scheme13)

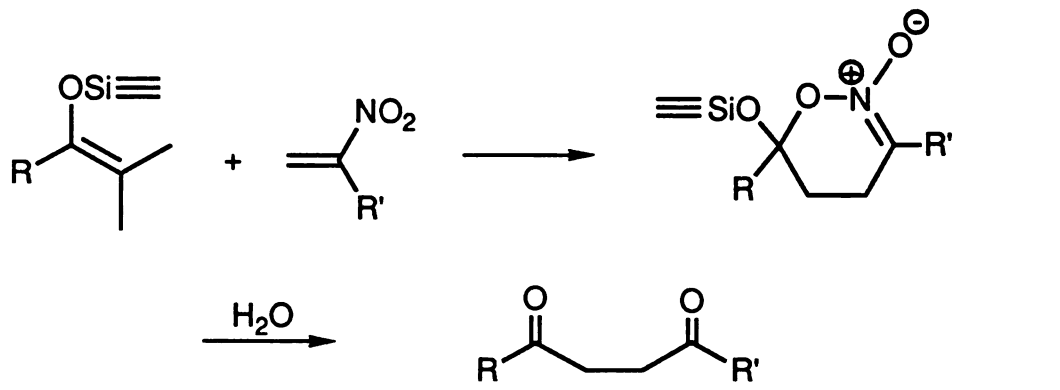


(64)



(65)

Yoshikoshi and co-workers[60] used a tin(IV) chloride catalyzed addition of silyl enol ethers to α,β-unsaturated nitroalkenes (Equation 66) to form 1,4-diketones. The nitroalkene in this procedure functions as an α-acyl cation equivalent.

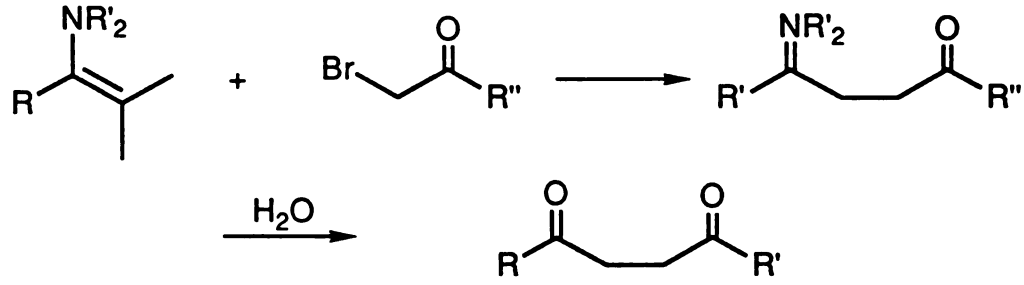


(66)

A particularly attractive approach, at least conceptually, to 1,4-diketones is the direct alkylation of enolates with α-haloketones. Though this reaction has

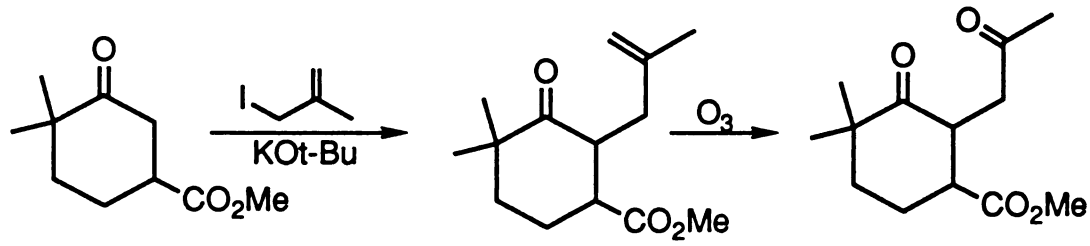
been accomplished with the enolates of diethyl malonate[61] and barbituric acid[62], a successful reaction of an enolate of a simple ketone with an α-haloketone has never been reported.

It is possible, however, as several groups have shown[63], to alkylate enamines with α-bromoketones (Equation 67). This appears to be a general method which allows access to a wide variety of 1,4-diketones. The only inconvenient aspects of the method seem to be the preparation of the lachrymatory α-haloketone and the general problem of regiocontrol in the preparation of both the α-haloketone and the enamine.



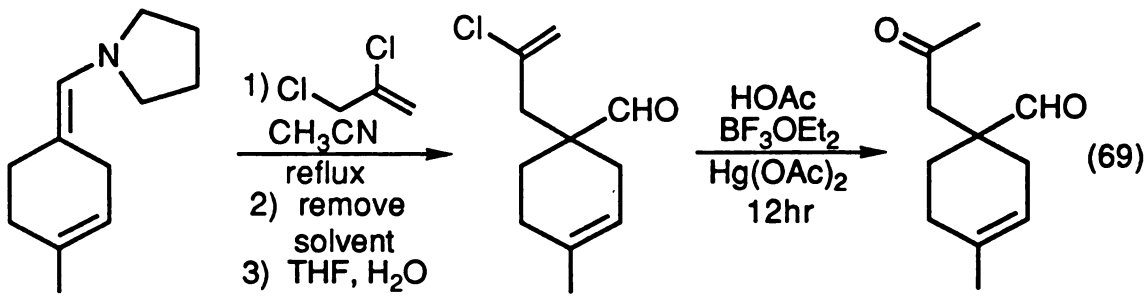
(67)

An alternative approach to 1,4-diketones is the alkylation of ketone enolates with masked α-haloketones. Miyano and Dorn[64] reacted methallyl iodide with a ketone enolate to obtain the corresponding alkylation product which was converted with ozone to a 1,4-diketone (Equation 68).



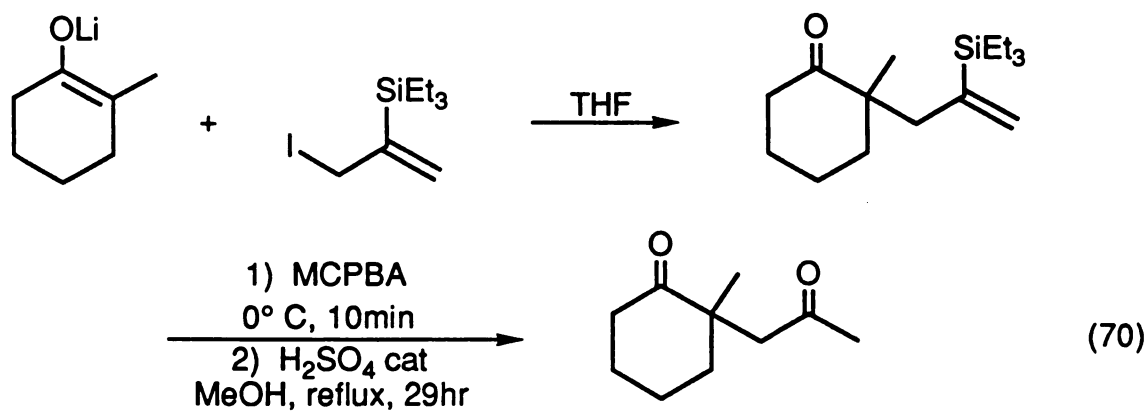
(68)

A similar reagent, 2,3-dichloro-1-propene, was studied extensively by Lansbury[65]. This reagent and the bromo- analogue have the advantage over methallyl iodide in that as masked α-haloketones they are at the proper oxidation level. An example of their use is provided by Martin and Chou[66] (Equation 69). The most common problem of halo-olefins as ketone equivalents is unwanted furan formation during the strongly acidic hydrolysis.



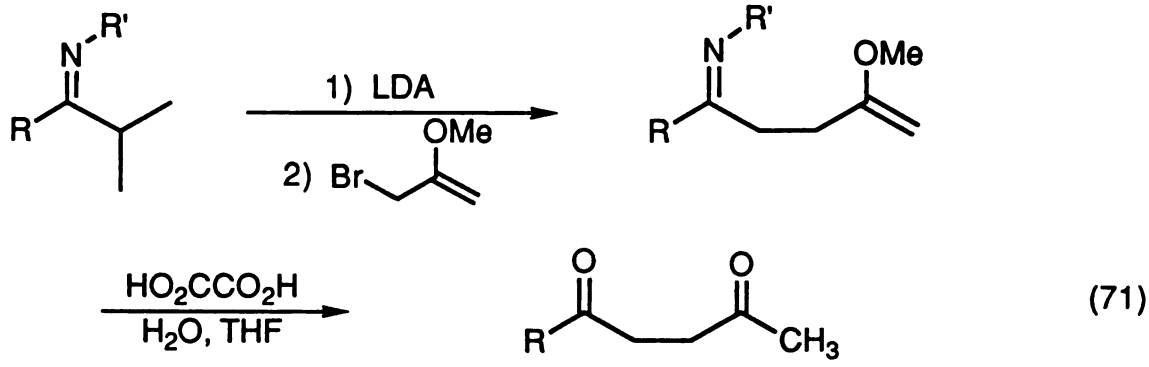
(69)

Stork and Jung[67] developed a milder procedure using vinyl silanes as carbonyl equivalents. They reacted ketone enolates with 3-iodo-2-trimethylsilyl-1-propene to give the corresponding alkylation product which was converted to a 1,4-diketone (Equation 70).

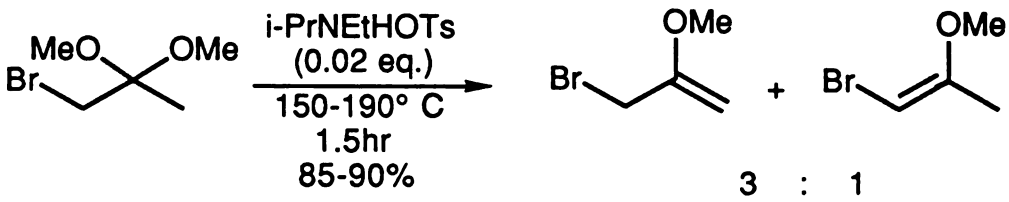


(70)

Jacobson and co-workers[68] have developed a procedure to synthesize 1,4-diketones from 2-methoxyallyl bromide and lithio-enamines (Equation 71). Unfortunately, the synthesis of 2-methoxyallyl bromide is inconvenient. Conventional methods of preparing enol ethers from bromoketones gave only minute amounts of the desired regioisomer. A pyrolytic cracking procedure was employed to synthesize the desired regioisomer (Equation 72). This time consuming procedure restricts the preparation of 2-methoxyallyl bromide to relatively small scale.

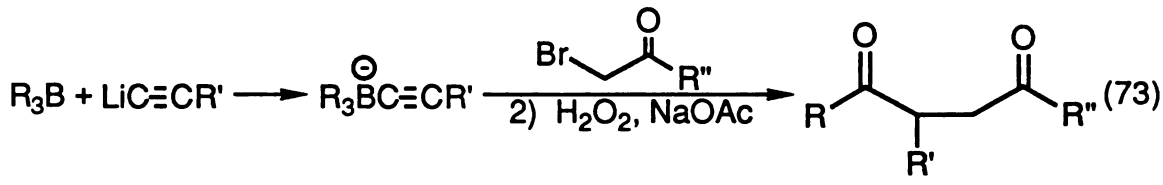


(71)



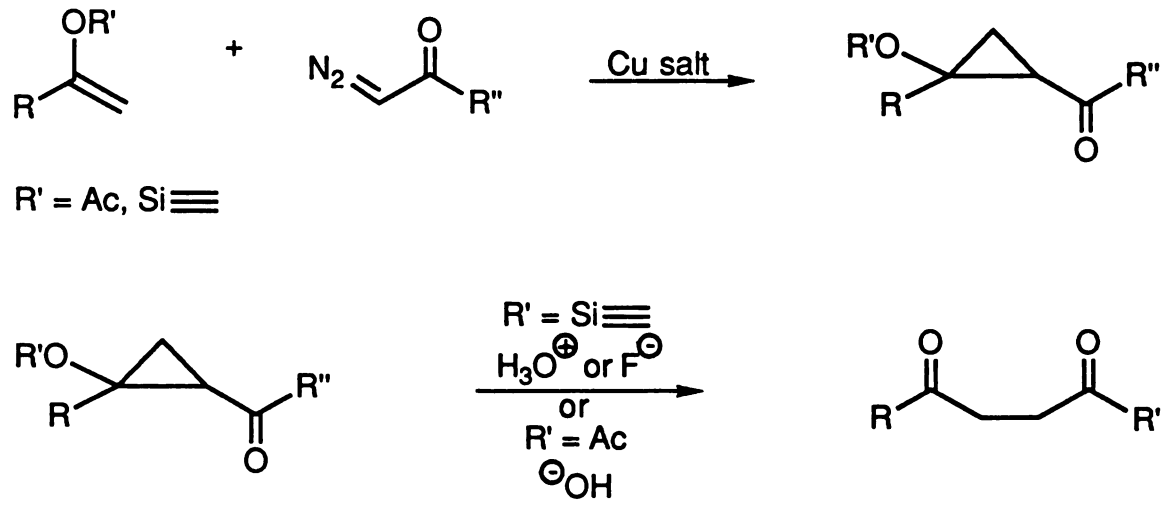
(72)

Pelter and coworkers[69] combine a trialkylborane, a lithium acetylide, and an α-halocarbonyl compound to form both the bonds between the α and β carbons and the γ and δ carbons (Equation 73). This remarkable "one-pot" procedure was used for the preparation of either 1,4-diketones or γ-ketoesters. It is efficient for 1,4-diketones which are not highly substituted. The only common limitation to this technique is access to the requisite trialkylborane



Another approach, which has had notable success in natural product synthesis, is the "cyclopropane trick"[70]. Based on pioneering studies by Wenkert[71] and others[72], the simplest form of this approach involves first, formation of a cyclopropane ring by reacting an α-diazocarbonyl compound with a silyl enol ether in the presence of a metal catalyst (typically copper salts), and second, ring opening of the cyclopropane to give a 1,4-dicarbonyl compound (Scheme 13). While newer preparations of α-diazocarbonyl compounds[73] have made this approach even more practical, many of these compounds are explosive and most (if not all) are carcinogens.

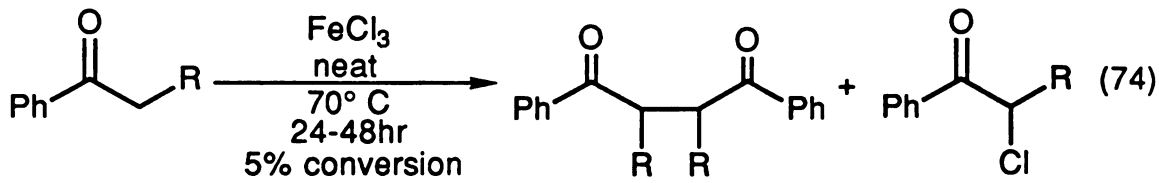
Scheme 13 - Synthesis of 1,4-Diketones via Cyclopropanes



These methods are all useful for the synthesis of particular compounds, however, they all have limitations. Some require multistep procedures; others require starting materials not readily available from the carbonyl compound itself. Several methods place limitations on the degree of substitution at the α- or β-carbon.

From the standpoint of simplicity, one of the most attractive synthetic routes to 1,4-diketones is formation of a bond between the α-carbons of two ketones. One possibility is hydrogen abstraction to give radical species capable of coupling or capable of being trapped by a ketone equivalent.

This line of thinking was put into practice by Inoue and co-workers[74]; they heated ketones with anhydrous ferric chloride using the ketones as solvent (Equation 74). They obtained fair amounts of coupled product mixed with α-chloroketone. Their procedure was limited to ketones which do not readily self-aldol.

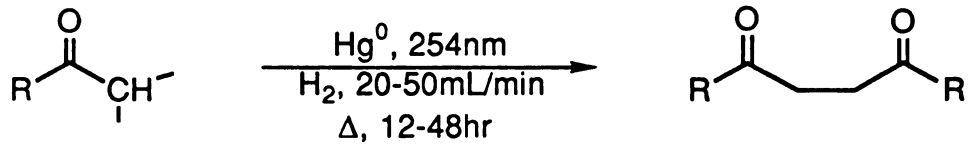


R = Me
Et

10 : 1

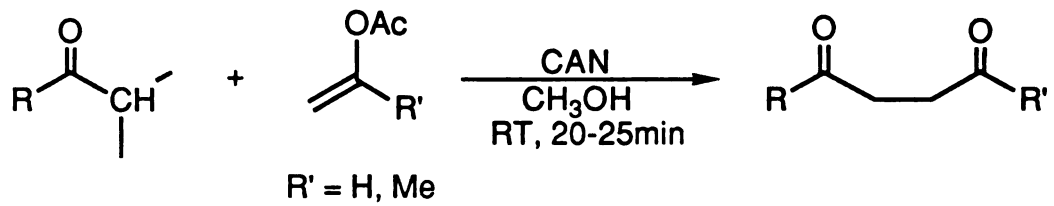
Crabtree and co-workers[75] have reexamined dehydrodimerizations and have developed an efficient system based on mercury-photosensitization. In this ingenious system, photo-excited mercury atoms, Hg*, are allowed to react with hydrogen gas (present in large excess) to produce hydrogen atoms. The hydrogens atoms thus generated abstract hydrogen from the organic substrate

present in the vapor phase (Equation 75). The dehydrodimer is protected because the low vapor pressure of the dimer prevents it from evaporating and reacting further. The obvious limitations of this procedure are a need for a volatile, symmetrical ketone, since hydrogen abstraction is not selective for unsymmetrical ketones, and an inability to cross couple ketones.



(75)

A system which does allow for cross coupling has been developed by Baciocchi and coworkers[76]. They found ceric ammonium nitrate (CAN) could abstract a hydrogen from a ketone and that the resulting radical could be trapped with either vinyl acetate or isopropenyl acetate (Equation 76). Attempts to extend this reaction to 2-alkyl substituted vinyl acetates failed when a ketone was used as the carbonyl reactant.

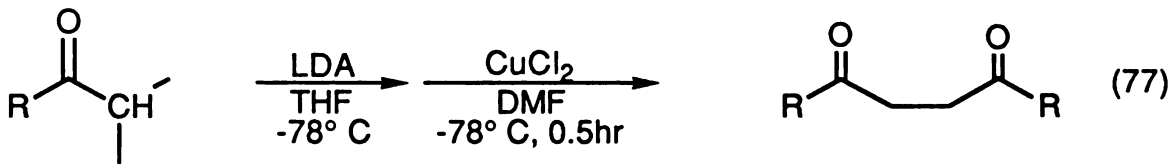


(76)

One can also approach coupling of ketone fragments in a slightly different way-by oxidizing enolate anions. Transition metal promoted dimerization of carbanions has been a convenient method for the formation of

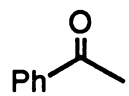
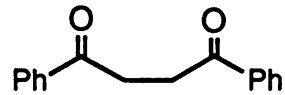
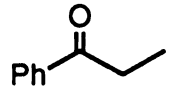
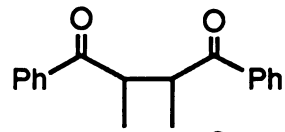
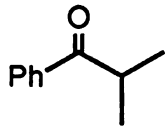
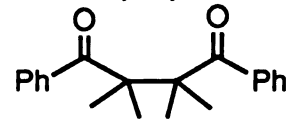
carbon-carbon bonds in organic synthesis. Copper (II) dimerizations of carbanions stabilized by sulfonyl, phosphoryl, and imidoyl groups are known[77].

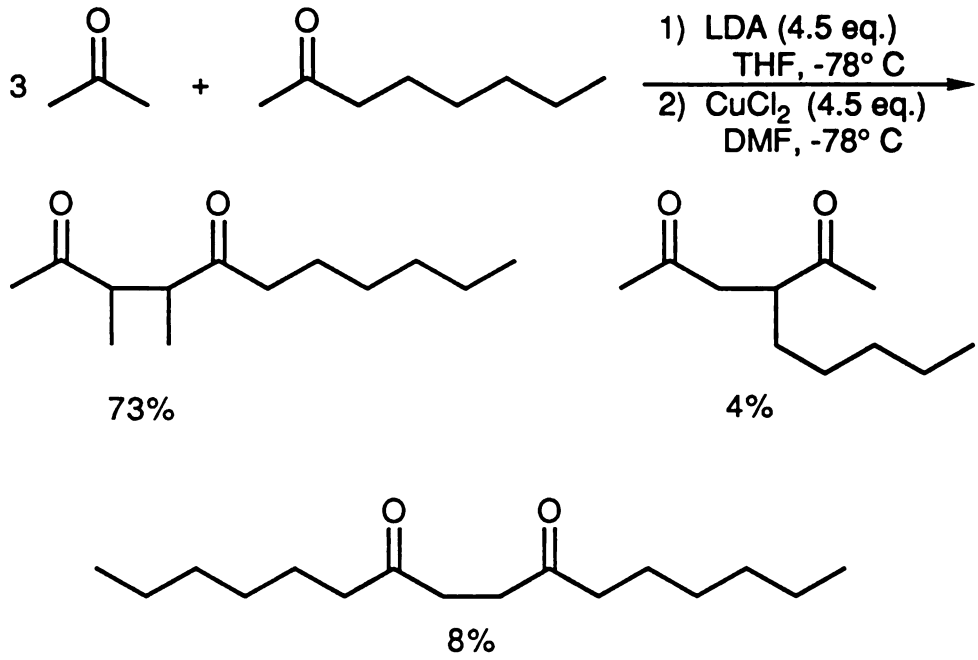
Saegusa and coworkers[78] applied this approach to ketone enolates. They prepared enolates with LDA at low temperature, then added a solution of cupric chloride in DMF to produce 1,4-diketones in variable yields (Equation 77). As can be seen in Table 16, there are good yields from enolates derived from methyl ketones. The yield of diketone drops sharply as the α-carbon of the ketone is increasingly substituted. Equation (78) shows the results from a cross coupling attempt.



(77)

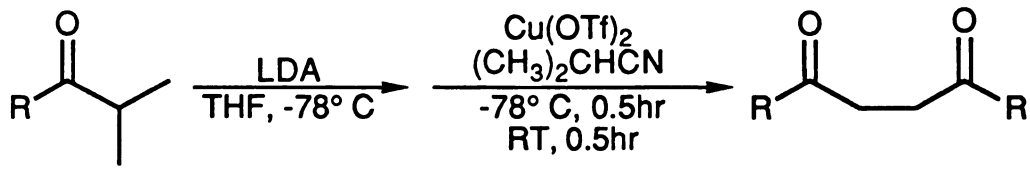
Table 16 - $CuCl_2$ Coupling of Lithium Enolates

Entry	Ketone	Diketone	Yield (%)
1			95
2			28
3			2



(78)

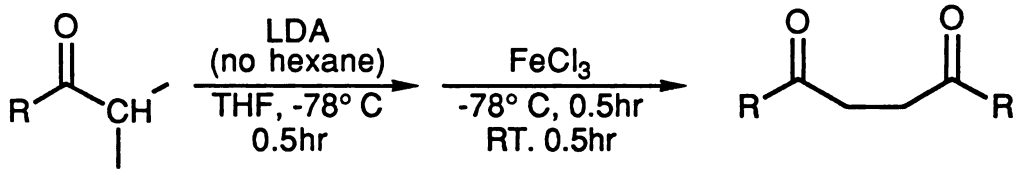
Kobayashi and coworkers[79] published an improvement, in yields, in this process using copper(II) triflate ($Cu(OTf)_2$) as the oxidant in isobutyronitrile solvent (Equation 79). The high cost of $Cu(OTf)_2$ detracts greatly from this procedure[80].



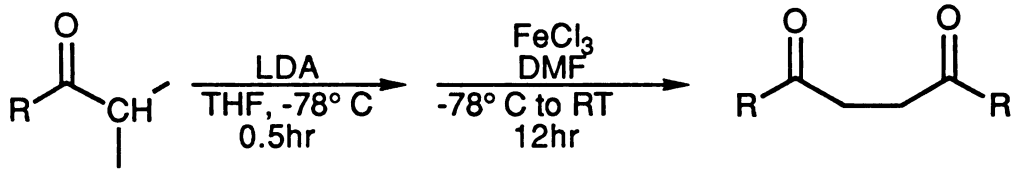
(79)

Independently, two groups, Nygren and Rathke[81], and Frazier and Harlow[82], discovered that anhydrous ferric chloride would dimerize ketone enolates (Equations 80, 81). The yields appear to be slightly greater for the procedure developed by Nygren and Rathke. This is possibly due to the removal of hexane (from the n-BuLi solution) and diisopropylamine, which allowed for the introduction of the metal oxidant without DMF as a co-solvent.

Interestingly, Nygren and Rathke found silver acetate to be the optimum oxidant for dimerization of cyclohexanone enolates[83]. The reaction seems to give higher yields when substitution at the α-carbon is increased.



(80)

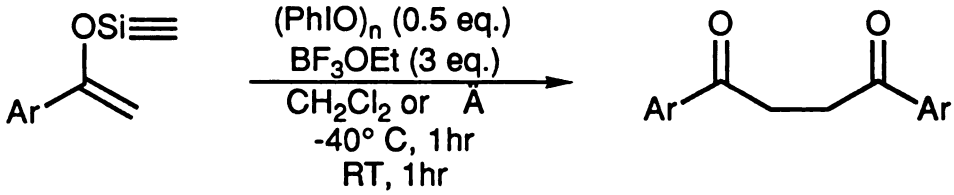


(81)

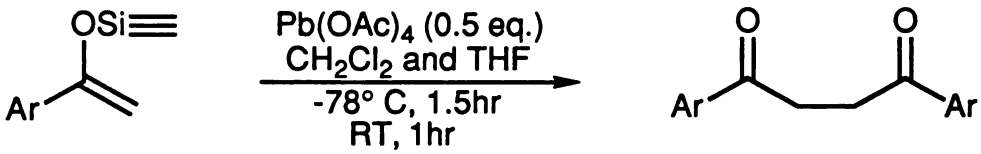
It is not necessary to have lithium enolates for this approach to be viable. Silyl enol ethers have also been employed in a similar fashion. Silyl enol ethers can be dimerized through the action of silver (I) oxide in DMSO as published by Saegusa and co-workers[84] (Equation 82). Again the dimerization appears to be sensitive to substitution at the α-carbon; the less substituted silyl enol ether from 2-butanone was dimerized in 76% yield while the more substituted isomer was dimerized in only 23% yield.

(82)

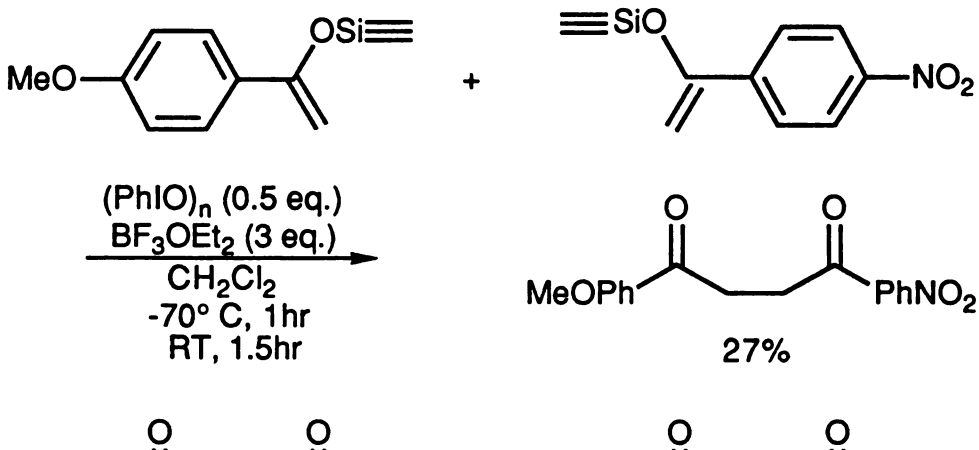
Recently, Moriarty and co-workers[85] have introduced two new procedures for the dimerization of silyl enol ethers to produce 1,4-diketones. One is based on the use of a hypervalent iodine oxidant (Equation 83) and the other is based on the more common oxidant lead tetraacetate (Equation 84). While the scope of these procedures was not fully defined, they appear to be effective for silyl enol ethers derived from aryl methyl ketones. The results of an attempt at cross coupling is given in Equation 85. Some of the mechanistic possibilities were offered by Moriarty and are shown in Scheme 14



(83)

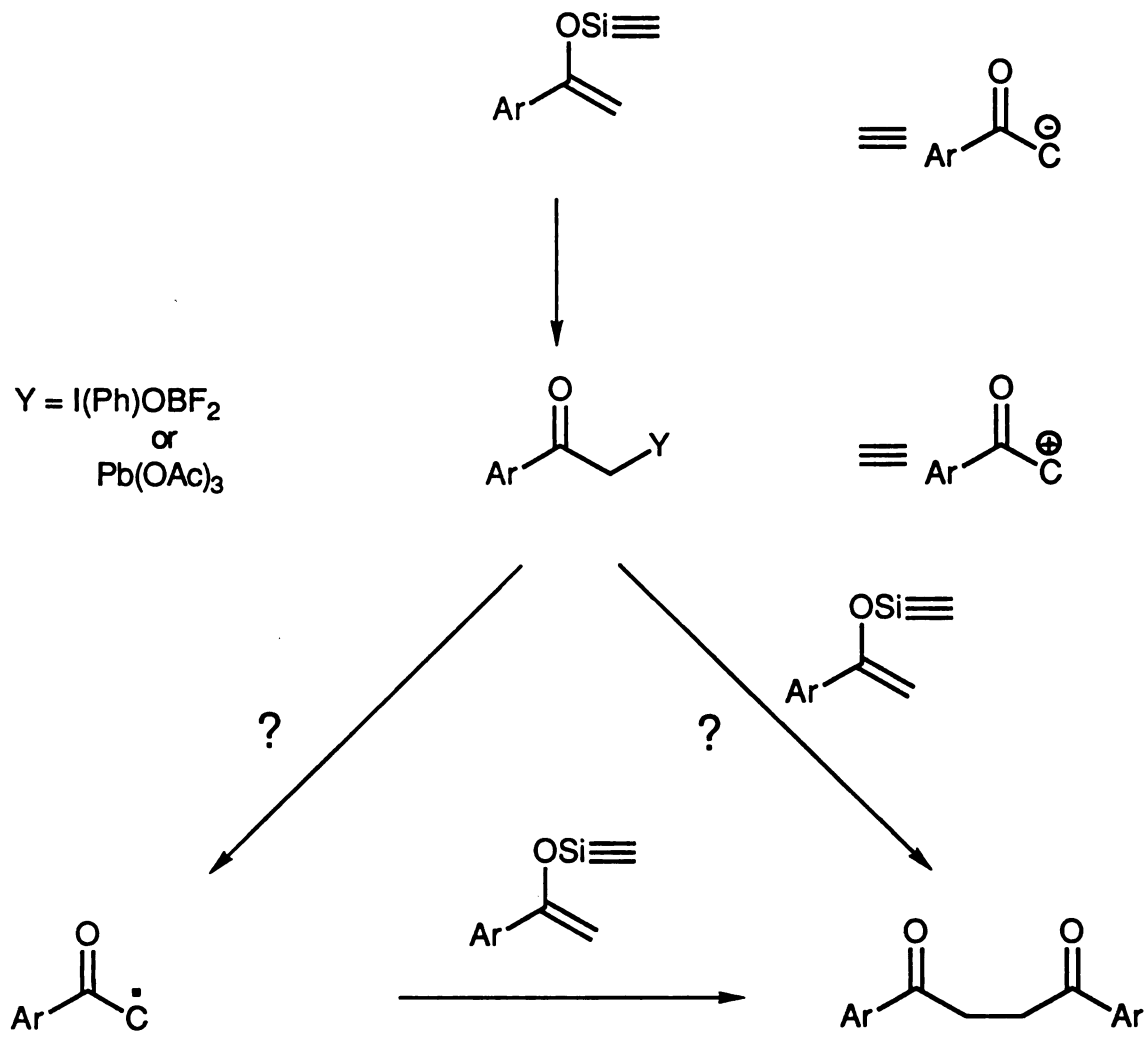


(84)

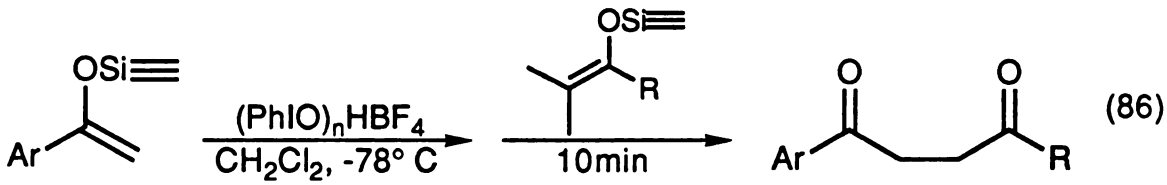


(85)

Scheme 14 - Synthesis of 1,4-Diketones Using $(PhIO)_n$-BF_3•OEt_2 or $Pb(OAc)_4$

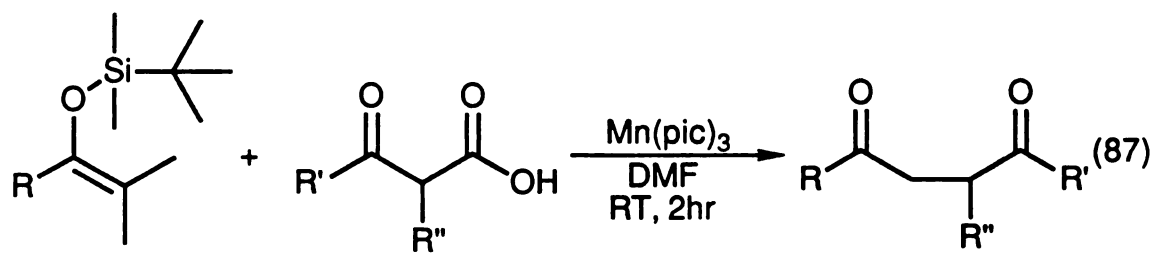


Caple and co-workers[86] have extended the use of hypervalent iodine for cross coupling through the development of a modified iodine oxidant (Equation 86). For instance, the use of the iodosobenzene-tetrafluoroboric acid complex allowed the cross coupling attempt given by Equation 85 to proceed in 61% yield with less than 10% self coupled products present.



(86)

The use of manganese (III) tris(2-pyridine carboxylate) $Mn(pic)_3$ as an oxidant has been suggested by Narasaka and co-workers[87]. They found β-ketocarboxylic acids would react with silyl enol ethers in the presence of this reagent (Equation 87). Narasaka proposes that an "α-ketoradical may be generated with $Mn(pic)_3$ via the decarboxylation reaction of the keto acids." As evidence for this, they find no products which incorporate the carboxylate group while use of the similar oxidant, manganese (III) acetate, leads to small amounts of products with the carboxylate group present. While this procedure provides access to unsymmetrical 1,4-diketones, the generality of this procedure is not known and more significantly requires β-ketoacids which are occasionally difficult to prepare[88].



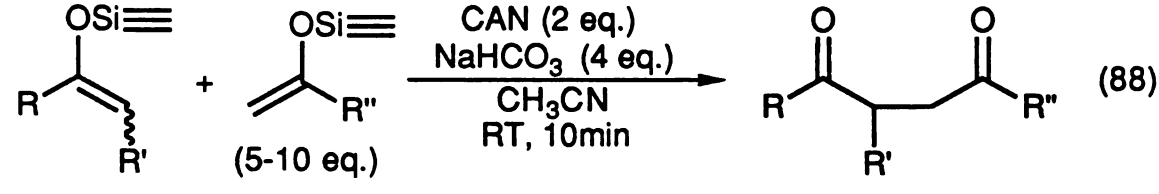
(87)

R = Ph, i-Pr

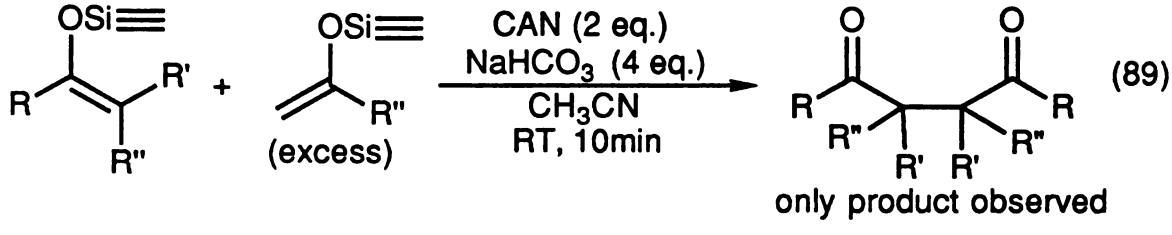
R' = Ph, i-Pr
R" = H, CH_3

The procedure which most attracted our attention was recently published by Baciocchi and co-workers[89]. They reported that two different silyl enol ethers could be coupled by use of two equivalents of ceric ammonium nitrate

(CAN) and four equivalents of sodium bicarbonate in acetonitrile solvent (Equation 88). In their procedure an α-alkyl substituted silyl enol ether coupled with an unsubstituted silyl enol ether in good yield provided the unsubstituted silyl enol ether was present in five to ten-fold excess. Otherwise, substantial amounts of self coupling of the α-substituted silyl enol ether were obtained. Under these conditions, unsubstituted silyl enol ethers did not couple. When they attempted to extend this procedure to the cross coupling of α,α-disubstituted silyl enol ethers with unsubstituted silyl enol ethers only self coupling of the disubstituted silyl enol ether was observed, even in the presence of a large excess of the unsubstituted silyl enol ether (Equation 89). Ceric ammonium nitrate is a well known one-electron oxidant and these researchers propose a mechanism based on this fact (Scheme 15).

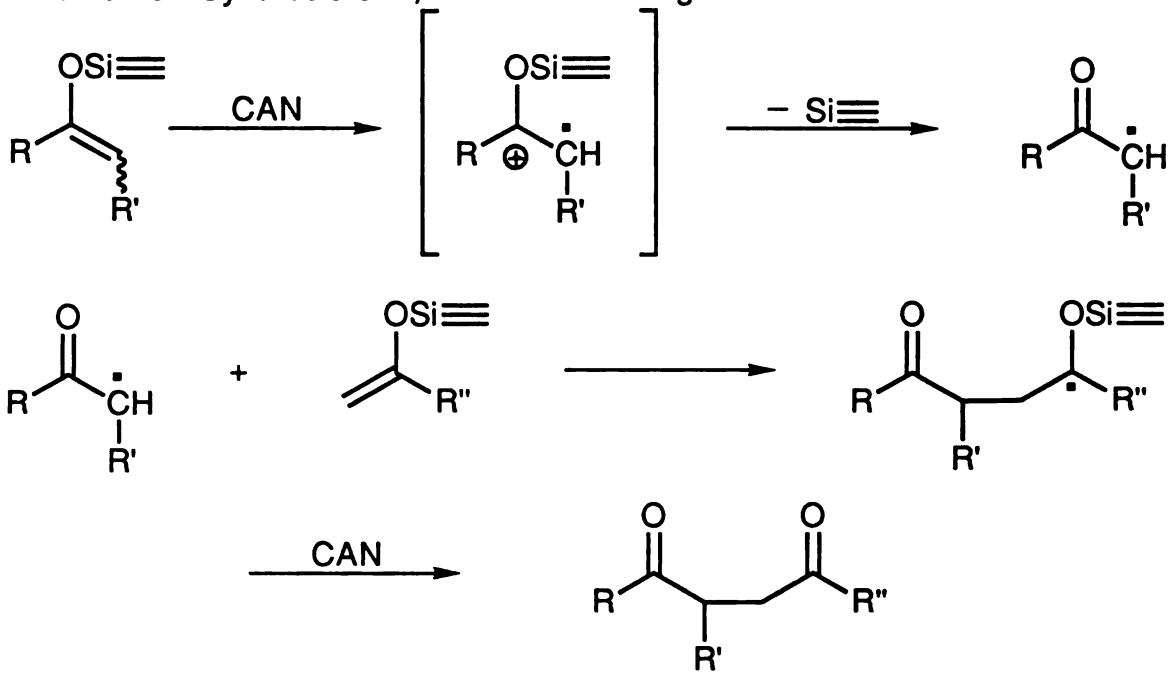


(88)

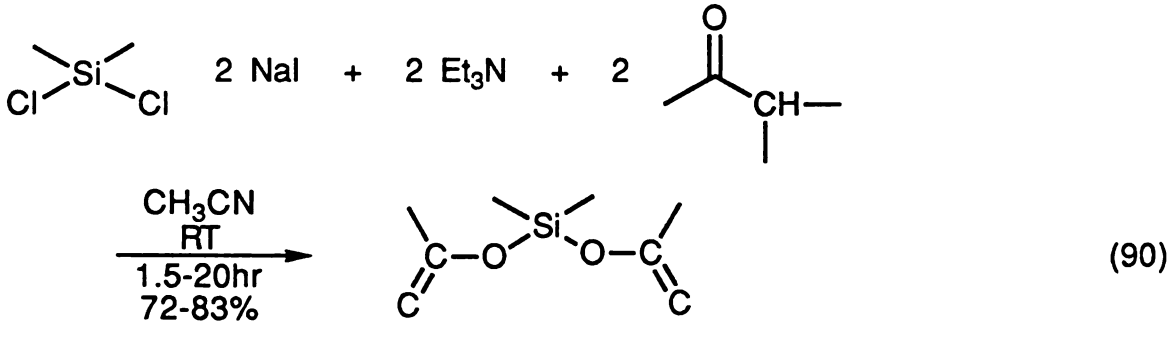


(89)

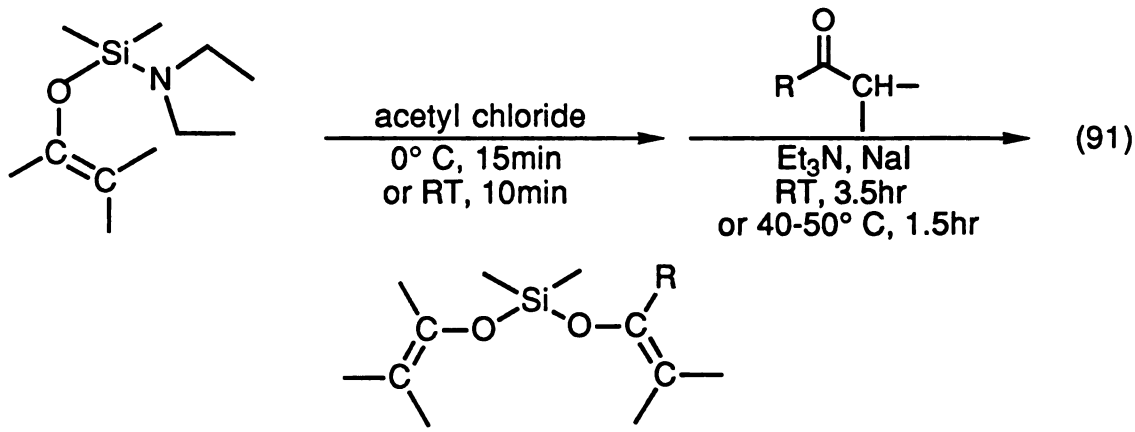
Scheme 15 - Synthesis of 1,4-Diketones Using CAN



This survey of 1,4-diketone synthesis was made, of course, with a particular purpose in mind; since we had developed convenient routes to both symmetrical dimethylsilyl bis-enol ethers (equation 90) and to mixed dimethylsilyl bis-enol ethers (equation 91), we had hoped that one of the coupling procedures described above could be applied to these compounds to produce 1,4-diketones. Bis-enol ethers might have a decided advantage in coupling reactions if the reaction took place intramolecularly or showed a significant cage effect. The mixed bis-enol ethers, if either of these effects were pronounced, would hopefully lead to unsymmetrical 1,4-diketones.



(90)



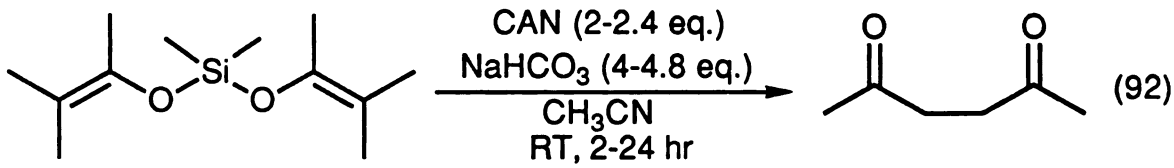
(91)

Of the procedures described for coupling silyl enol ethers, the one based on ceric ammonium nitrate (CAN) developed by Baciocchi and co-workers[89] appeared to be promising. Their procedure required mild conditions and used an inexpensive, commercially available oxidant. Other possible oxidants ($Pb(OAc)_4$, Ag_2O, $(PhIO)_nBF_3OEt_2$, $Cu(OTf)_2$) are notably more expensive. Our investigation of coupling dimethylsilyl bis-enol ethers with CAN is presented here.

RESULTS

The self-coupling of symmetrical dimethylsilyl bis-enol ethers was examined using the procedure of Baciocchi and co-workers[89] (equation 92).

The yields of 1,4-diketones are shown in Table 17. Qualitatively, several observations can be made. The color of ceric ammonium nitrate (CAN) is bright orange; as the reaction proceeds and the Ce^{4+} is reduced to Ce^{3+}, the color of the CAN solution is discharged and a white solid forms. With the unsubstituted dimethylsilyl bis-enol ether (entry 1) this occurs over 24 hours, with the α-monosubstituted bis-enol ethers (entries 2-5) this occurs within 3 hours typically, and with the α,α-disubstituted bis-enol ether (entry 6) this occurs within 1 hour.

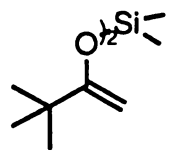
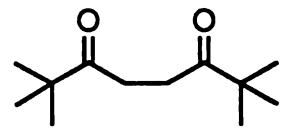
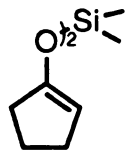
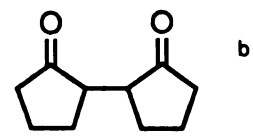
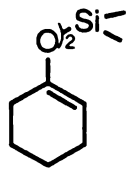
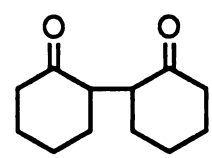
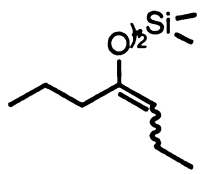
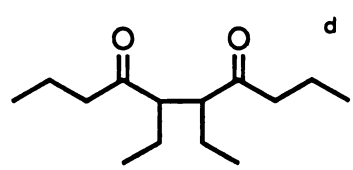
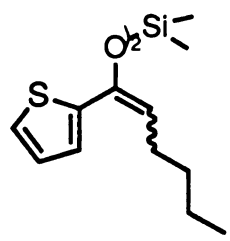
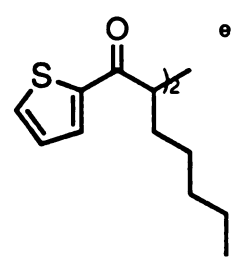
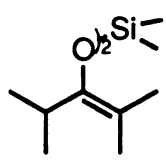
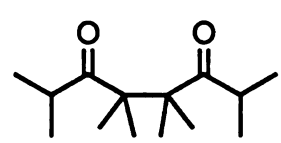


(92)

For the α,α-disubstituted bis-enol ether inversing the addition order, adding the CAN to the bis-enol ether, produced a negligible effect on the yield of diketone. The role of sodium bicarbonate was also briefly investigated. When this reagent was omitted from the reaction, only a trace of product was detected (by GLC analysis). If other bases, sodium carbonate or sodium acetate, were substituted, the product was observed in only slightly attenuated amounts (by GLC analysis). These observations are consistent with the view that sodium bicarbonate behaves as an acid scavenger in the reaction.

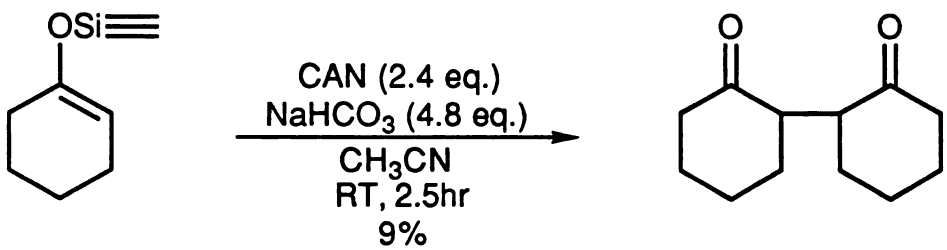
Use of CAN which was carefully purified by the method of Perrin[90] lead to identical yields (by GLC analysis) as CAN which was used as received.

Table 17 - CAN Coupling of Symmetrical Dimethylsilyl Bis-Enol Ethers

Entry	Bis-Enol Ether	1,4-Diketone	Time (hr)	Yield (%)
1			17	4
2		 b	2	55
3		 c	2.5	42
4		 d	3	55
5		 e	24	48
6			6	23 (21)

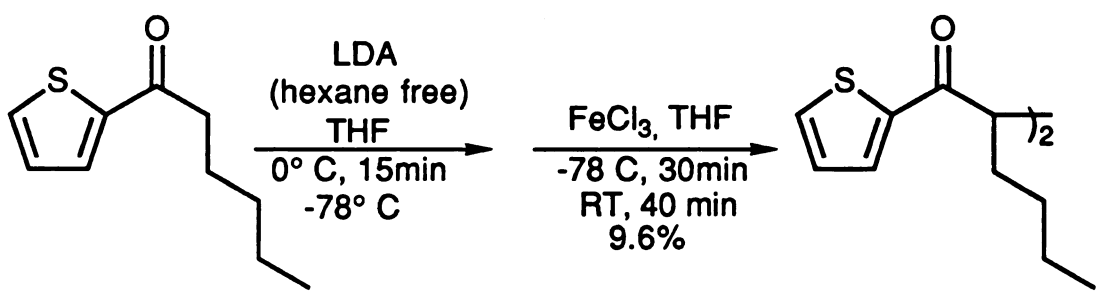
a) Procedure: A solution of the bis-enol ether 0.2 M in CH_3CN was added to a mixture of CAN (2-2.4 eq.) and $NaHCO_3$ (4-4.8 eq.) 0.2 M in CH_3CN at RT over 1-2hr. Time listed is the total reaction time at RT.
b) Crude product was a 3:1 mixture of diastereomers.
c) Crude product was a 1:1 mixture of diastereomers.
d) Crude product was a 4:5 mixture of diastereomers.
e) Mixture of diastereomers not determined.
f) A solution of CAN (2.4 eq.) 0.2 M in CH_3CN was added to a mixture of the bis-enol ether and $NaHCO_3$ (4.8eq.) 0.2 M in CH_3CN

The efficiency of coupling a bis-enol ether was compared in one example to that of a trimethylsilyl enol ether under the same reaction conditions (equation 93).



(93)

The CAN induced coupling was compared to the method of Rathke and Nygren[81] for preparing 1,4-diketones. A lithium enolate was prepared under the specified conditions and oxidatively coupled using anhydrous $FeCl_3$ in THF (equation 94).

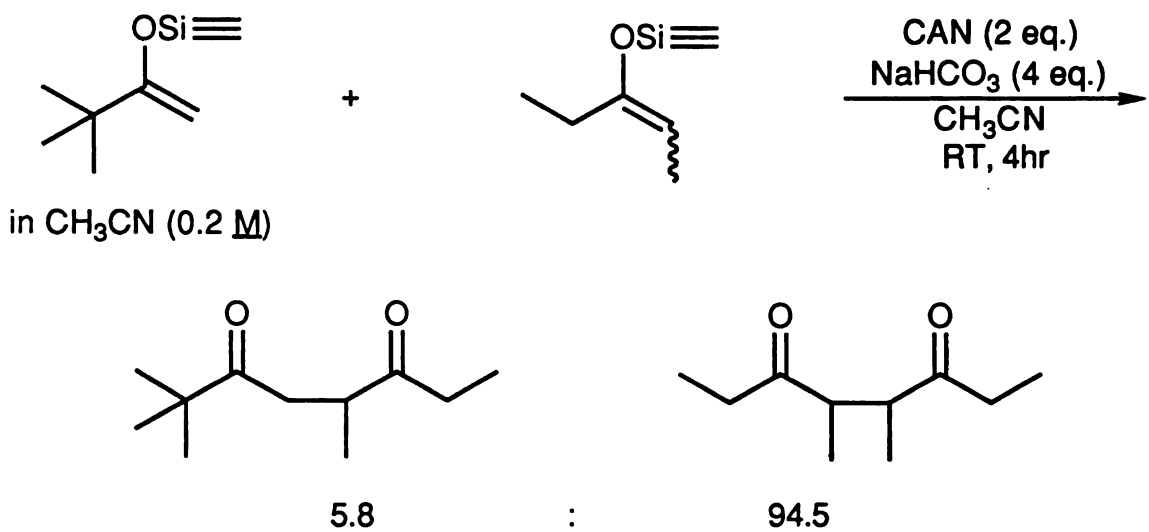


(94)

The crossed coupling of mixed dimethylsilyl bis-enol ethers was studied briefly. The initial experiment compared a mixed bis-enol ether to a simple mixture of two trimethylsilyl enol ethers (Scheme 16). When the two trimethylsilyl enol ethers were mixed together and added to the CAN and $NaHCO_3$ in CH_3CN, products were detected in a 5.8 : 94.2 ratio of cross-

coupled to self-coupled diketones. When the bis-enol ether was submitted to the same reaction conditions, products were detected in a 72 : 28 ratio of cross-coupled to self-coupled diketones. With these encouraging results, several other mixed bis-enol ethers were also submitted to the CAN coupling procedure (Table 18) with variable results.

Scheme 16 - Cross Coupling Silyl Enol Ethers with CAN



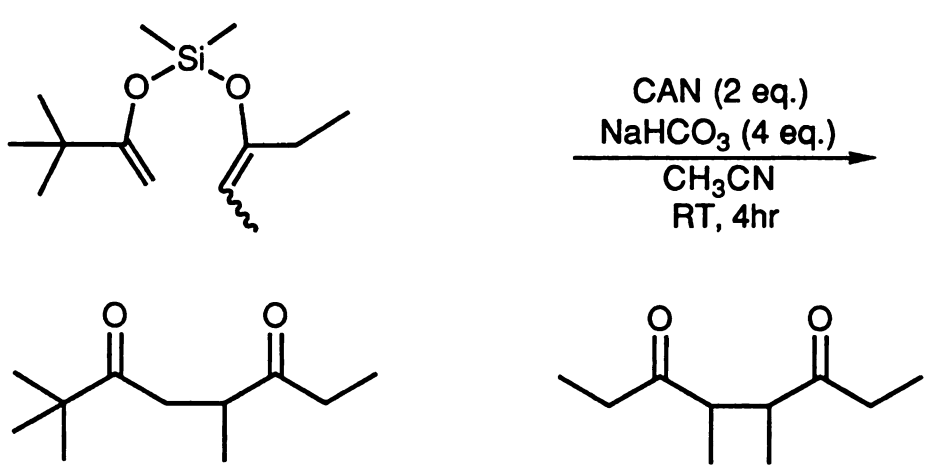
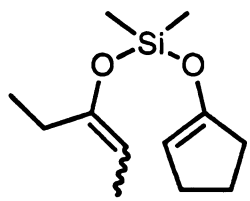
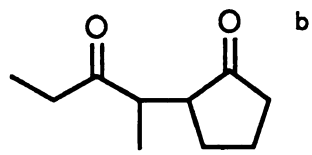
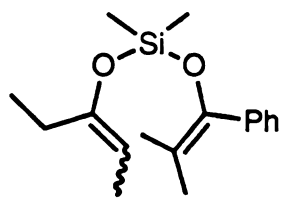
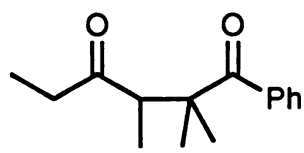
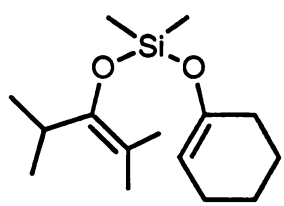
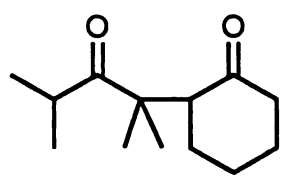
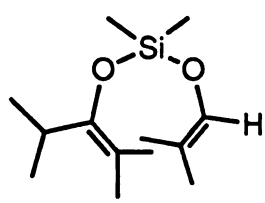
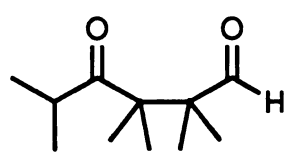


Table 18 - CAN Coupling of Mixed Dimethylsilyl Bis-Enol Ethers

Entry	Bis-Enol Ether	1,4-Diketone	Time[a] (hr)	Yield (%)
1		 [b]	4	55
2			3	0
3			5	0[c]
4			6.5	5.1[d]

a) Procedure: A solution of the bis-enol ether 0.2 M in CH_3CN was added to a mixture of CAN (2.4eq.) and $NaHCO_3$ (4.8 eq.) 0.2 M in CH_3CN at RT over 1-2 hours. Time listed is the total reaction time at RT.
b) Crude product was a 3:1 mixture of diastereomers.
c) Isolated 19% (adjusted for scale) of 2,4,4,5,5,7-hexa methyl-3,6-octadione.
d) Isolated ca. 17% (adjusted for scale) of 2,4,4,5,5,7-hexamethyl-3,6-octadione.

DISCUSSION

In keeping with the observations made by Baciocchi, the least effective substrate for the coupling was the unsubstituted dimethylsilyl bis-enol ether. It was suprising to obtain poor yields for the α,α-disubstituted dimethylsilyl bis-enol ether despite its apparent rapid reaction with CAN. We speculated that the substrate was oxidized by CAN at both enol ethers and the tertiary radicals produced undergo radical-radical coupling at a slow rate relative to other possible pathways, such as disproportionation or hydrogen abstraction. We thought that this result could be improved to favor the 1,4-diketone by slow addition of the oxidant to the substrate. The effect of this change was not evident in the yield of product which went from 23% to 21% upon inversing the addition order.

Coupling dimethylsilyl bis-enol ethers seems to have a decided advantage over coupling trimethylsilyl enol ethers for producing both symmetrical and unsymmetrical 1,4-diketones. Though the conditions were probably not optimum for the trimethylsilyl enol ethers (Equation 93 and Scheme 17) under the reaction conditions employed, the bis-enol ethers provided a higher yield in the self-coupling example and was more selective for the unsymmetrical diketone in the cross-coupling example. This finding may be due to cage effects in the reaction or possibly, may be indicative of an intramolecular reaction.

The comparison of the CAN coupling procedure to the $FeCl_3$ coupling of enolates demonstrates some of the variability in coupling procedures. In the example studied here, coupling of 2-hexanoylthiophene, the CAN procedure lead to a 48% yield of diketone while the $FeCl_3$-enolate procedure provided

only a 9% yield of diketone. However, Nygren and Rathke[81] found that the enolate of 2,4-dimethyl-3-pentanone could be coupled by $FeCl_3$ in 91% yield while the CAN procedure acheived only a 23% yield. Both of these procedures rely on oxidations of the substrates and, not suprisingly, are sensitive to changes in the substitution patterns.

The results obtained in the coupling reactions of mixed bis-enol ethers are perhaps the more difficult to rationalize. That an unsymmetrical 1, 4-dicarbonyl compound was obtained when two α-mono-substituted enol ethers or two α,α-disubtituted enol ethes comprise the mixed bis-enol ether puts the simple mechanistic scheme offered by Baciocchi (Scheme 15) in some doubt. To explain the failure of entries 2 and 3 in Table 18 to give unsymmetrical diketones requires that the disubstituted radical formed (since the more substituted enol ether is apparently oxidized first) is not efficiently trapped by the mono-substituted enol ether, despite the high yields obtained from the coupling reactions of symmetrical bis-enol ethers. An alternative explanation for the observed selectivity may be that the diketones are produced from radical-radical coupling. To acieve high yields of unsymmetrical diketones would require that the two radical intermediates are produced at similar rates.

EXPERIMENTAL

A. General

Acetonitrile was dried by distillation from CaH_2 under argon. Diethyl ether was used directly from a freshly opened can. Tetrahydrofuran (THF) was dried by distillation from sodium / benzophenone under argon. Hexane and ethyl acetate were reagent grade and were used as received. Diisopropylamine was dried by distillation from CaH_2 under argon. The n-butyl lithium 1.6 M in hexanes (Aldrich) was used as received. Ceric ammonium nitrate (CAN) (Fisher) and ferric chloride (anhydrous) (EM Science) were used as received.

Gas chromatography was performed with a Hewlett-Packard 5880A instrument fitted with a Restek 30 meter Rtx-1 column (I. D. 0.32 mm, 0.25 μm film). Thin layer chromatography was performed with Davisil 62 (Davison Chem., 60-200 mesh). Infrared spectra were obtained from neat samples on KBr plates or as solutions in CCl_4 using a Nicolet FT-IR/42 instrument (absorptions reported in cm^{-1}). ^1H NMR spectra were obtained in $CDCl_3$ or CD_3CN (Cambridge Isotopes Inc.) using either a Varian T-60 at 60 MHz or a Varian VXR-300 (s) at 300 MHz as indicated. ^{13}C NMR spectra were obtained using a Varian VXR-300 (s) at 75 MHz. Chemical shifts are reported in parts per million (δ. scale). Data are reported as follows: chemical shift (multiplicity: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet; integration; coupling constant in Hz). Mass spectra were obtained using a

Finnigan 4000 EI GC/MS instrument at the ionizing energy (eV) indicated. Data are reported as m/e (relative intensity). Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.

All glassware used in the following procedures was oven dried (120° C) and purged with argon. Typically, the reactions were conducted in round bottom flasks fitted with magnetic stirring, a gas takeoff valve (to Hg bubbler) and a septum inlet. Addition of reagents employed standard syringe or cannula transfer techniques. Concentration of organic extracts was accomplished at reduced pressure (aspirator) using a rotory evaporator. Column chromatography was performed according to the method of Still, et. al.[91]

B. Preparation of Symmetrical 1,4-Diketones

1. 2,2,7,7-Tetramethyl-3,6-octadione

To a mixture of CAN (10.96 g, 20 mmol) and $NaHCO_3$ (3.36 g, 40 mmol) in CH_3CN (100 mL) bis-(3,3-dimethyl-1-butenyl-2-oxy)dimethylsilane (2.56 g, 10 mmol) was added dropwise via syringe at room temperature. The reaction mixture was allowed to stir for 17 hours. Workup in saturated aqueous $NaHCO_3$ (200 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL) and the combined organic layer was washed with brine (1 x 50 mL) Dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (50 mm column, 60 g silica gel, 19:1 hexanes / ethyl acetate eluent, 30 mL fractions). Fractions 10-14 provided 0.21 g crude material. By ^1H NMR analysis yield ca. 4%.

^1H NMR (300 MHz, $CDCl_3$): δ 1.15 (s, 9H, $(CH_3)_3$), 2.74 (s, 4H, CH_2).

MS-EI (70 eV): 199 (M+1, 41), 198 (8), 141 (81), 113 (base), 85 (22), 57 (71).

2. [1.1'-bicyclopentyl]-2,2'-dione

To a mixture of CAN (7.67 g, 14 mmol) and $NaHCO_3$ (2.35 g, 28 mmol) in CH_3CN (70 mL) bis (cyclopentenyl-1-oxy)-dimethylsilane (1.57 g, 7 mmol) was added dropwise at room temperature. The reaction mixture was allowed to stir for 1 hour. Workup as above. The crude reaction product was a 3.5 : 1 mixture of diastereomers by GLC. Purified by column chromatography (50 mm column, 60 g silica gel, 9:1 hexanes / ethyl acetate eluent, 30 mL fractions). Fractions 11-28 provided 0.618 g of the major isomer as a white solid, m.p. 68-69° C (lit. m.p.[75] 67-69° C) and fractions 31-34 provided 0.024 g of the minor isomer mixed with a small amount of the major isomer as a light tan oil which solidified upon standing. Yield 0.624 g (55%).

IR (CCl4): 2965, 2880, 1744, 1455, 1405, 1150.
^1H NMR (300 MHz, $CDCl_3$): δ 1.5-1.7 (m, 2H, CH_2), 1.7-1.85 (m, 1H, CH_2), 1.95-2.1 (m, 6H, CH_2), 2.25-2.4 (m, 2H, CH_2), 2.55-2.7 (m, 2H, CH).
MS-EI (70 eV): 168 (M+2, 1.1), 167 (12), 166 (64), 138 (11), 84 (base), 83 (94), 67 (38).

3. [1,1'-Bicyclohexyl]-2,2'-dione from bis(cyclohexenyl-1-oxy)dimethylsilane

To a mixture of CAN (9.21 g, 16.8 mmol) and $NaHCO_3$ (2.82 g, 33.6 mmol) in CH_3CN (35 mL) a solution of bis(cyclohexenyl-1-oxy)dimethylsilane (1.77 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via a pressure equalized addition funnel over 2 hours at room temperature. The reaction

mixture was allowed to stir for 2 hours. Workup in $NaHCO_3$ (200 ml) and Et_2O (70 ml). The aqueous layer was extracted with Et_2O (2 x 35 mL) and the combined organic layer was washed with brine (1 x 10 ml). The crude reaction product was a 1:1 mixture of diastereomers by GLC. Dried over Na_2SO4, filtered, concentrated, and purified by column chromatography (50 mm column, 20 g silica gel, 19:1 hexanes / ethyl acetate eluent, 30 ml fractions). Fractions 18-42 gave 0.575 g (42%) of product as a mixture of diastereomers. By trituration, a small amount of pale yellow solid could be isolated m.p. 68-69.5° C (lit. m.p.[82] (meso isomer) 74-75° C)

IR (CCl4): 2940, 2867, 1709, 1559, 1449, 1256, 1215, 1132..

^1H NMR (300 MHz, $CDCl_3$): δ 1.2-1.4 (m, 2H, CH_2), 1.5-1.8 (m, 4H, CH_2), 1.8-1.95 (m, 2H, CH_2), 1.97-2.15 (m, 4H, CH_2), 2.3-2.45 (m, 4H, CH_2), 2.8-2.95 (m, 2H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ 25.38, 28.01, 30.06, 42.28, 48.92, 211.72.

MS-EI (70 eV): 195 (M+1, 15), 195 (47), 166 (4), 98 (base), 97 (74), 67 (26).

4. [1,1'-Bicyclohexyl]-2,2'-dione from 1-trimethylsiloxycyclohexene

Using the procedure described above combined CAN (18.42 g, 33.6 mmol), $NaHCO_3$ (5.65 g, 67.2 mmol), in CH_3CN (35 ml), and 1-trimethylsiloxycyclohexene (2.38 g, 14 mmol) in CH_3CN (35 mL). Workup and isolation as above. Fractions 24-30 gave 0.123 g (9%) of product as a mixture of diastereomers. Spectral data identical to that given above.

5. 5,6-diethyl-4,7-decadione

To a mixture of CAN (33 g, 60 mmol) and $NaHCO_3$ (10.1 g, 120 mmol) in CH_3CN (120 mL) bis(3-heptenyl-4-oxy)dimethylsilane (7.11 g, 25 mmol) in

CH_3CN (80 mL) was added via a pressure equalized addition funnel over 1 hour at room temperature. The reaction mixture was allowed to stir for 2 hours. Workup on $NaHCO_3$ (20 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (2 x 75 mL) and the combined organic layer dried over Na_2SO_4. The crude reaction product was a 4 : 5 mixture of diastereomers by GLC. Filtered, concentrated, and distilled at reduced pressure bulb-to-bulb gave 3.10 g (55%) at 100° C (oven) (0.15 mm Hg).

IR (CCl_4): 2967, 2936, 2878, 1705, 1464, 1406, 1383, 1260, 1034, 804..
^1H NMR (300 MHz, $CDCl_3$): δ 0.7-0.93 (m, 12H, CH_3), 1.23-1.7 (m, 8H, CH_2), 2.3-2.55 (m, 4H, CH_2), 2.65-2.75 (m, 1.14 H, CH major), 2.86-2.95 (m, 0.86 H, CH minor).
MS-EI (70 eV): 227 (M+1, 4.4), 226 (14), 225 (2), 183 (37), 155 (11), 113 (25), 71 (base).

6. 5,6-di(2'-thienoyl)decane using CAN

To a mixture of CAN (27.41 g, 50 mmol) and $NaHCO_3$ (8.4 g, 100 mmol) in CH_3CN (100 ml) bis(1-[α-thienyl]-1-hexenyl-1-oxy)dimethylsilane (9.84 g crude, ca. 19 mmol) in CH_3CN (150 mL) was added via a pressure equalized addition funnel over 2.5 hours at room temperature. The reaction mixture was allowed to stir for 24 hours. Workup in $NaHCO_3$ (500 mL) and Et_2O (200 mL). The aqueous layer was extracted with Et_2O (2 x 100 mL) and the combined organic layer washed with brine (1 x 150 mL). Dried over Na_2SO_4, filtered, and concentrated to give 8.65 g crude material, as a mixture of diastereomers, ratio not determined. Purified by column chromatography (60 mm column, 180 g silica gel, 9:1 hexanes / diethyl ether eluent, 40 ml fractions). Obtained 5.47 g crude product as a mixture of diastereomers which darkened upon standing

and 3.0 g of 2-hexanoylthiophene (33% recovery of starting ketone). The crude product was further purified by column chromatography as above and gave 0.975 g of product as white needles (single diastereomer) m.p. 162-162° C and 3.35 g of product as a oil (mixtue of diastereomers); yield 4.325 g (48%).

IR (CCl_4): 2970, 2930, 2880, 2850, 1654, 1410.

^1H NMR (300 MHz, $CDCl_3$): δ 0.60-0.75 (m, 6H, CH_3), 0.98-1.15 (m, 8H, CH_2), 1.3-1.42 (m, 2H, CH_2), 1.58-1.78 (m, 2H, CH_2), 3.64-3.75 (m, 2H, CH), 7.16 (dd, 2H, 5.0, 3.6 Hz, Th (5)), 7.68 (dd, 2H, 5.0, 1.2Hz, Th(3)), 7.82 (dd, 2H, 3.9, 1.2Hz, Th (4)).

^{13}C NMR (75 MHz, $CDCl_3$): δ 13.67, 22.66, 29.71, 32.21, 50.69, 128.41, 132.52, 134.68, 146.45, 196.57.

MS-EI (70 eV): 364 (M+2, 8), 363 (13), 362 (51), 361 (4), 319 (17), 307 (23), 306 (base), 250 (65), 208 (99), 83 (9).

7. 5,6-di(2'-thienoyl)decane using FeCl3

Following the procedure of Nygren and Rathke[81] a solution of n-BuLi (1.6M in hexanes)(15.6 mL, 25 mmol) was added to diisopropylamine (3.5 mL, 25 mmol) in pentane (10 ml) cooled to 0° C with an ice bath and allowed to stir for 15 minutes. The solvent was removed under full vacuum to give LDA as a white solid. The LDA was dissolved in THF (25 mL) and cooled to 0° C. The 2-hexanoylthiophene (4.52 g, 25 mmol) was added dropwise via syringe and allowed to stir for 15 minutes to give a bright yellow solution of the enolate. This was cooled to -78° C with a dry ice / acetone bath and $FeCl_3$ (4.06 g, 25 mmol) in THF (50 mL) was added via canula over 10 minutes. The reaction mixture was allowed to stir for 20 minutes then quenched into 1:1 ice / saturated KH_2PO_4 (200 mL) and Et_2O (100 mL). THe aqueous layer was

extracted with Et_2O (2 x 75 mL) and the combined organic layer washed with brine (1x50 ml). Dried over Na_2SO_4, filtered and concentrated to give 4.80 g crude material. Purified by column chromatography as described above to give 0.4344 g (9.6%) of product identical by TLC and ^1H NMR to that above.

8. 2,4,4,5,5,7-hexamethyl-3,6-octadione - silane added to CAN

To a mixture of CAN (16.45 g, 30 mmol) and $NaHCO_3$ (5.04 g, 60 mmol) in CH_3CN (100 mL) bis(2,4-dimethyl-2-penenyl-3-oxy)dimethylsilane (2.85 g, 10 mmol) in CH_3CN (70 mL) was added dropwise via pressure equalized addition funnel over 1.5 hours at room temperature. The mixture was allowed to stir for 4.5 hours. Workup in $NaHCO_3$ (200 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (2x60 mL) and the combined organic extracts dried over Na_2SO_4. Filtered, concentrated, and purified by column chromatography (50 mm column, 75 g silica gel, 450 mL hexanes, 200 mL 30:1 hexanes / diethyl ether 500 mL 20:1 hexanes diethyl ether eluent, 25 mL fractions). Fractions 28-37 gave 0.5112 g (23%) of product.

IR (CCl_4): 2978, 2936, 2874, 1696, 1636, 1472, 1395, 1092, 1013, 995.

^1H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, 12H, 6.6Hz, CH_3), 1.20 (s, 12H, CH_3), 3.12 (septet, 2H, 6.6Hz, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ 20.02. 22.22, 35.56, 53.22, 219.62.

MS-EI (70 eV): 227 (M+1, 19), 226 (30), 183 (base), 155 (7), 113 (13), 71 (99).

9. 2,4,4,5,5,7-hexamethyl-3,6-octadione CAN added to silane

To a mixture of bis-(2,4-dimethyl-2-pentenyl-3-oxy)dimethylsilane (2.85 g, 10 mmol) and $NaHCO_3$ (5.04 g, 60 mmol) in CH_3CN (100 mL), CAN (16.45 g, 30 mmol) in CH_3CN (70 mL) was added dropwise via pressure

equalized addition funnel over 1.5 hours at room temperature. The mixture was allowed to stir for 4.5 hours. Workup and isolation as described above gave 0.475 g (21%) of product identical to above by GLC, TLC and ^1H NMR analysis.

C. Preparation of Unsymmetrical 1,4-Diketones

1. 2,25-trimethyl-3,6-octadione from bis-enol ether

To a mixture of CAN (7.67 g, 14 mmol) and $NaHCO_3$ (2.35 g, 28 mmol) in CH_3CN (35 mL)3-(3', 3'-dimethyl-1'butenyl-2'oxydimethylsiloxy)-2-pentene (1.7 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via pressure equalized addition funnel over 2 hours at room temperature. The reaction mixture was allowed to stir for 2 hours. Workup in $NaHCO_3$ (200 mL) and Et_2O (150 mL). The aqueous layer was extracted with Et_2O (2 x 75 mL) and the combined organic extracts dried over Na_2SO_4. GLC anaylsis showed the title compound in a 72 : 28 ratio with the self coupled product, 4,5-dimethyl-3,6-octadione. No 2,2,7,7-tetramethyl-3,6-octadione was detected.

2. 2,2,5-trimethyl-3,6-octadione from trimethylsilyl enol ethers

To a mixture of CAN (7.67 g, 14 mmol) and $NaHCO_3$ (2.35 g, 28 mmol) in CH_3CN (35 mL) 3,3-dimethyl-2-trimethylsiloxy-1-butene (1.21 g, 7 mmol) and 3-trimethylsiloxy-2-pentene (1.11 g, 7 mmol) and 3-trimethylsiloxy-2-pentene (1.11 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via pressure equalized addition funnel over 2 hours at room temperature. The reaction mixture was allowed to stir for 2 hours. Workup as above. GLC anaylsis showed the title compound in a 5.8 : 94.2 ratio with the self coupled product,

4,5-dimethyl-3,6-octadione. No 2,2,7,7-tetramethyl-3,6-octadione was detected.

3. 2-(1'-methyl-2'-oxybutyl)cyclopentanone

To a mixture of CAN (9.21 g, 14 mmol) and $NaHCO_3$ (2.82 g, 33.6 mmol) in CH_3CN (35 mL)3-(cyclopentenyl-1'oxydimethyl)siloxy)-2-pentene (1.59 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via pressure equalized addition funnel over 2 hours at room temperature. The reaction mixture was allowed to stir for 2 hours. Workup in $NaHCO_3$ (200 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL) and the combined organic extracts dried over Na_2SO_4. The crude reaction product was a 3 : 1 mixture of diastereomers by GLC and 4,5-dimethyl-3,6-octadione appeared to be present in small amounts (<5%). Filtered, concentrated, and purified by column chromatography (50 mm column, 58 g silica gel, 19:1 hexanes / ethylacetate eluent, fractions 30 mL). Fractions 16-32 provided 0.652 g (55%) of product as a mixture of diastereomers.

IR (CCl_4): 2975, 2942, 2882, 1736, 1460, 1406, 1157, 1109, 978.

^1H NMR (300 MHz, $CDCl_3$): δ 0.93-1.06 (m, 3H, CH_3), 1.21 (d, 3H, 7.5Hz, CH_3), 1.6-2.6 (m, 9H, CH_2, CH), 2.75 (pentet, 0.25H, 7.6Hz, CH(C1')), 3.01 (dq, 0.75H, 7.6 Hz, 7.2Hz, CH (C1')).

^{13}C NMR (75 MHz, $CDCl_3$): δ 7.51, 14.03 (minor), 14.95 (major), 20.63 (major), 22.58 (minor), 25.81 (major), 26.23 (minor), 34.03 (major), 34.64 (minor), 37.65 (minor) 38.11 (major), 45.22 (minor), 45.73 (major), 51.57 (major), 51.72 (minor), 212.5, 220..

MS-EI (70 eV): 169 (M+1, 19), 168 (44), 139 (14), 111 (58), 83 (57), 57 (base).

4. 1-phenyl-2,2,3-trimethyl-1,4-hexadione attempt

To a mixture of CAN (2.63 g, 4.8 mmol) and $NaHCO_3$ (0.81 g, 9.6 mmol) in CH_3CN (10 mL)3-(β,β-dimethyl-α-styryloxydimethylsiloxy)-2-pentene (1.59 g, 7 mmol) in CH_3CN (10 mL) was added dropwise via pressure equalized addition funnel over 1 hours at room temperature. The reaction mixture was allowed to stir for 2 hours. Workup in $NaHCO_3$ (60 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (2 x 10 mL) and the combined organic layer was washed with brine (1x10 mL). Dried over Na_2SO_4, filtered, and concentrated. We were unable to detect any of the title compound both by GLC and by analysis of the fractions from column chromatography.

5. 2-(1',1'3'-trimethyl-2'oxybutyl)cyclohexanone attempt

To a mixture of CAN (9.21 g, 16.8 mmol) and $NaHCO_3$ (2.82 g, 33.6 mmol) in CH_3CN (35 mL)3-(cyclohexenyl-1'oxydimethyl)siloxy)-2,4-dimethyl-2-pentene (1.88 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via pressure equalized addition funnel over 2 hours. The reaction mixture was allowed to stir for 3 hours. Workup in $NaHCO_3$ (200 mL) and Et_2O (70 mL). The aqueous layer was extracted with Et_2O (2 x 35 mL) and the combined organic extracts layer was washed with brine (1x20 mL). Dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography (50 mm column, 100 g silica gel, 800 ml 10:1 hexanes / ethyl acetate, 300 mL 8:1 hexanes ethyl acetate eluent, 3o mL fractions). We were unable to isolate any of the title compound. Fractions 8-10 provided 0.15 g (19%) adjusted for scale) of 2,4,4,5,5,7-hexamethyl-3,6-octadione (> 90% purity). Amounts of cyclohexanone and [1,1'-Bicyclohexyl]-2,2'-dione were not determined.

6. 2,2,3,3,5-pentamethyl-4-oxohexanal

To a mixture of CAN (9.21 g, 16.8 mmol) and $NaHCO_3$ (2.82 g, 33.6 mmol) in CH_3CN (35 mL) 3-(2'-methylpropenyl-1'-oxydimethylsiloxy)-2,4-dimethyl-2-pentene (1.70 g, 7 mmol) in CH_3CN (35 mL) was added dropwise via pressure equalized addition funnel over 1 hour at room temperature. The reaction mixture was allowed to stir for 5.5 hours. Workup in $NaHCO_3$ (200 mL) and Et_2O (70 mL). The aqueous layer was extracted with Et_2O (2 x 35 mL) and the combined organic extracts layer was washed with brine (1x20 mL). Dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography (50 mm column, 70 g silica gel, 19:1 hexanes / ethyl acetate eluent, 30 mL fractions). Fractions 10-14 provided 0.066 g (5.1%) of product. Fractions 4-6 provided 0.206 g of crude 2,4,4,5,5,7-hexamethyl-3,6-octadione (adjusting for scale and purity ca. 17% yield).

IR (neat): 2977, 2936, 2876, 2730, 1719, 1701, 1636, 1470, 1381, 1011, 912, 735.

^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (s, 6H, CH_3), 1.02 (d, 3H, 6.9Hz, CH_3), 1.26 (s, 6H, CH_3), 3.02 (heptet, 1H, 6.9Hz, CH), 9.76 (s, 1H, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ 19.22, 19.83, 20.79, 35.07, 48.30, 55.15, 204.36, 219.29.

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