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PREPARATION OF DIMETHYLSILYL BIS-ENOL ETHERS

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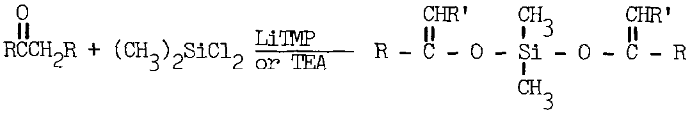
Abstract:

Dichlorodimethylsilane is reacted with two equivalents of ketone enolates to give dimethylsilyl bis-enol ethers in good yields. Lithium tetramethylpiperidide (LiTMP) as well as triethylamine (TEA) are used in deprotonation of ketones. An intramolecular aldol type of coupling has been achieved in an excellent yield on treatment of the dimethylsilyl bis-enol ether, derived from cyclohexanone, with $TiCl_4$.

Trimethylsilyl enol ethers were originally introduced as precursors for specific enolates(1,2), and much of their chemistry is like that of enols. Their usefulness surpasses that of all other enol derivatives(3), because of their ease of preparation, clean reactions, and the mildness of desilylation processes: they also combine a reasonable reactivity with a high selectivity. A large number of reactions of silyl enol ethers have been used as part of synthetic routes to natural products and other complex molecules(4) as well as simple coupling reactions(5-7). Silyl enol ethers as synthetic reagents have been noted in the regeneration of the enolates to react with electrophiles under basic conditions or direct reaction with electrophiles under neutral or acidic (Lewis acid) conditions. Although a great deal of attention has been paid to silyl enol ethers(4,8), nothing has been mentioned about the formation of dimethylsilyl bis-enol ethers. The presence of two enolates trapped on one silicon atom raises the question of whether these enolates could affect each other and to what degree this type of effect will be of value in organic synthesis, especially in the coupling reactions. We report here two simple and efficient methods for the synthesis of some dimethylsilyl bis-enol ethers as shown in equation 1.



$$R\overset{O}{\overset{\|}{C}}CH_2R + (CH_3)_2SiCl_2 \xrightarrow[\text{or TEA}]{\text{LiTMP}} R-\overset{CHR'}{\overset{\|}{C}}-O-\underset{CH_3}{\overset{CH_3}{Si}}-O-\overset{CHR'}{\overset{\|}{C}}-R$$

The following procedure for the synthesis of 1 ($R=C_2H_5$, $R'=CH_3$) is representative for the first method (kinetic conditions): to a solution of LiTMP (4 mmole) in THF (4 ml), generated from tetramethylpiperidine and n-butyllithium at 0°C under nitrogen, was added 3.9 mmole of 3-pentanone dropwise over three minutes, followed by the subsequent stirring at 0°C for 15 minutes and then the reaction mixture was quenched with dichlorodimethylsilane (1 mmole), all added at once. The reaction mixture was removed from the ice bath and stirred for 30 min and worked up(9) to give bis (2-penten-3-oxy) dimethylsilane (87%). In a similar way, other dimethylsilyl bis-enol ethers were prepared (Table 1) .

Table 1

	Product 1			NMR Spectrum δ($CDCl_3$)	Elemental Analysis[d]
Entry	R	R'	% a(b)	Vinyl CH	(C,H)Found (Calcd)%
1	CH_3	H	81(69)	4.17(d,4H)	55.86(55.76),9.23(9.36)
2	C_2H_5	CH_3	89(57)	4.54,4.80(9,2H)[c]	62.94(63.09);10.40(10.59)
3	$-(CH_2)_4-$		83(56)	5.00(t , 2H)	66.43(66.61);9.73(9.58)
4	$-(CH_2)_3-$		87(82)	4.75(bs,2H)	64.09(64.23);8.88(8.98)
5	Ph	H	35(-)[e]	4.66,4.99(d,2H)	72.79(72.93);6.87(6.80)
6	$PhCH_2$	Ph	41(28)[f]	5.43,5.93(s,2H)[c]	80.86(80.63);6.77(6.77)

a. LiTMP method b. TEA method c. The two peaks are for Z and E vinylic protons , respectively d. Elemental analysis for silicon and oxygen not done e. No detectable product has been observed f. isolated yield

These results show that symmetrical ketones or which can enolize in only one direction are reacted with dichlorodimethylsilane to afford dimethylsilyl bis-enol ethers in good yields. It is also noted that the stabilized enolates derived from acetophenone and dibenzyl ketone are slower in their reaction with dichlorodimethylsilane(10).

Lithium diisopropylamide (LDA) is the reagent of choice for deprotonation reactions of ketones, esters and other carbon acids. In synthesis of trimethylsilyl enol ethers, diisopropylamine , resulted from the reaction of LDA and the carbon acid, does not react with the quenching reagent trimethylchlorosilane. In synthesis of dimethylsilyl bis-enol ethers using LDA, the yields are always less then 35%. The reason for the low yields is the reaction of diisopropylamine with dichlorodimethylsilane(11). It has been tried to remove the resulted amine after deprotonation of the ketones by vacuum, but again poor yields were obtained. The problem of the low yields has been solved by the use of the more hindered base LiTMP.

The synthesis of dimethylsilyl bis-enol ethers were also found to be achieved by refluxing the mixture of the ketone, dichlorodimethylsilane and three fold excess triethylamine (TEA) in tetrahydrofuran or the ketone itself(thermodynamic conditions). The yields are good but the draw back in this method is the reaction time which was ranging from two up to twenty days.

The dimethylsily bis-enol ethers derived from 3-pentanone and dibenzyl ketone, show geometrical isomers. NMR analysis for the vinylic protons of the crude products shows the predominance of the Z-protons (>90 %) in both derivatives under thermodynamic conditions , while it shows the predominance of the E-protons (~ 60 % with the dibenzyl and 80 % with 3-pentanone derivatives) under kinetic conditions .

We report here a preliminary investigation on the use of dimethylsilyl bis-enol ethers in synthesis. The silyl bis-enol ether derived from cyclohexanone has been treated with titanium tetrachloride in methylene chloride at - 15°C and it resulted in the formation of β-hydroxy ketone (aldol reaction) in a very high yield (91%). Although the aldol condensation is an important reaction , its synthetic utility is severely curtailed due to several problems , such as di - and poly-condensation and the unfavorable equilibria of condensation, that usually accompany this type of reaction. In order to avoid such common side reactions and to displace the equilibrium which would otherwise be unfavorable , the principle of metal chelate formation was used[12-14] .

It seems that with silyl bis-enol ethers,the intramolecular coupling enhanced by titanium tetrachloride with the silicon atom serving as chelating reagent offers a simple procedure and gives a high yield. However , further investigation into this problem as well as similar applications is in progress .

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9. The work-up is as described in reference 1.
10. Overnight stirring for acetophenone and over 24 hours for dibenzyl ketone.
11. Mixing diisopropylamine with dichlorodimethylsilane in THF resulted in the formation of white precipitate , also mixing them in $CDCl_3$ showed two types of doublet and two types of septet in addition to an - $^{+}\overset{|}{\underset{|}{N}}H$ peak at δ 9.0 ppm.
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