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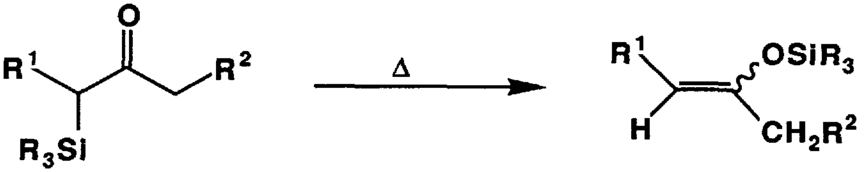
A REGIO- AND STEREOSELECTIVE SYNTHESIS OF (Z) ENOL METHYLDIPHENYLSILYL ETHERS[1]

Gerald L. Larson,[3*] Reyes Berrios[3a] and Jose A. Prieto[3b]
Department of Chemistry, University of Puerto Rico, Rio Piedras, P.R. 00931
and Huls America, Inc. Petrarch Systems, Bartram Road, Bristol, PA 19007

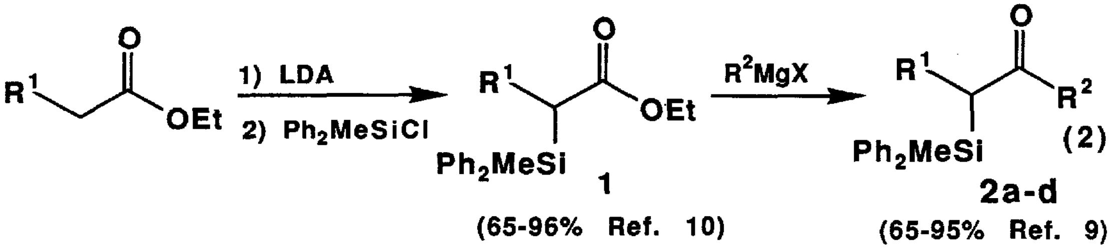
Summary: *The thermal rearrangement of α-(methyldiphenylsilyl) ketones in an apolar solvent or in the absence of a solvent provides Z:E mixtures of the corresponding enol silyl ethers. This same rearrangement in acetonitrile, however, gives the Z isomer cleanly, thus providing a regio- and stereoselective entry into (Z) enol silyl ethers.*

The synthetic utility of enol silyl ethers is now well established.[4] Although a variety of methods exist for the preparation of these highly useful materials there are few that are truly regioselective[5] and even fewer that are stereoselective.[6] Such processes would add greatly to the synthetic potential of these already highly utilized systems. One potential general entry for the regioselective preparation of enol silyl ethers is to make use of the thermal rearrangement of β-ketosilanes, which quantitatively produces the thermodynamically more stable enol ethers[7] as shown in eq. 1. This rearrangement, which can be carried out with various catalysts as well, has been shown to be stereoselective.

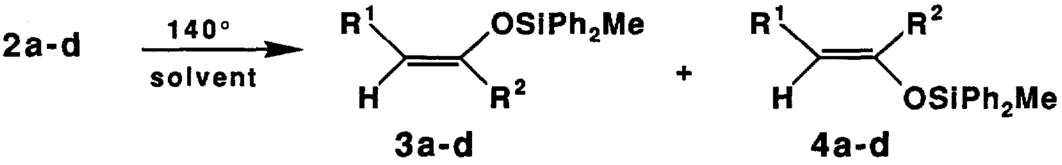


(1)

It has been reported that the thermal rearrangement of α-silyl ketones shown in eq. 1 has little ionic character and shows essentially no solvent effect.[7] These conclusions were later shown to be the result of kinetic experiments carried out at or near the isokinetic temperature[8]. We felt that the possibility of a solvent effect on the stereoselectivity of the reaction might exist. This, in fact, is the case. We chose to look at the α-(methyldiphenylsilyl) ketones, readily prepared in two steps from esters.[9,10] (eq. 2) Thermolysis of **2** (R^1 = $^nC_8H_{17}$, R^2 = Me) in benzene-d_6 at 140°C for 1 h showed complete conversion to the corresponding enol silyl ethers with low stereoselectivity. The thermolysis carried out in the absence of solvent also produced mixtures of Z and E enol ethers. Remarkably, however, the rearrangement in acetonitrile-d_3 provided the enol silyl ethers exclusively as the Z isomers **3**.[11]



(2)

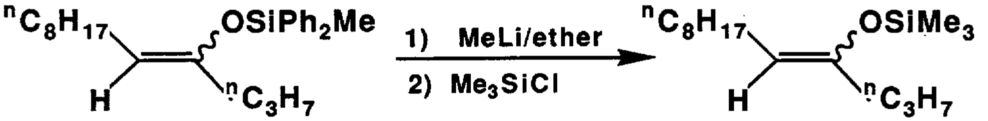


(3)

TABLE: Stereoselectivity of the Thermal Rearrangement of **2**.

R^1	R^2		**Solvent and Ratio of 3:4**		
			C_6D_6	neat	CD_3CN
Me	Et	**2a**	75:25	67:33	>99:1
$^nC_8H_{17}$	Ph	**2b**	60:40	>99:1	>99:1
$^nC_8H_{17}$	^iBu	**2c**	62:38	69:31	>99:1
$^nC_8H_{17}$	$^nC_3H_7$	**2d**	61:39	70:30	>99:1

It has long been known that enol silyl ethers are precursors to lithium enolates *via* their reaction with alkyllithium reagents, making enol silyl ethers of high isomeric purity an attractive entry into regio- and stereodefined lithium enolates.[12] In order to show that these enol silyl ethers are viable precursors to stereodefined lithium enolates a 69:31 mixture of **3d** and **4d** was treated with methyllithium in ether[13] at -10°C for one hour and then the resulting lithium enolate quenched with an excess of trimethylchlorosilane. This provided a 69:31 mixture of the enol trimethylsilyl ethers **5** and **6** in nearly quantitative yield. More importantly, identical treatment of pure **3d** gave only **5**, showing that the enol methyldiphenylsilyl ethers are readily converted to the synthetically strategic (Z) lithium enolates[14] in a stereospecific manner. (eq. 4)



3d:4d

5 = Z and 6 = E isomer

(4)

Experimental:

Enol Ethers: The enol silyl ethers were prepared by placing the β-ketosilane **2** in a reactivial neat or with the appropriate solvent and sealing this tightly with a screw top lid. The reaction mixture was then heated to 140-145°C in an oil bath for 2 - 3 h, after which time the reaction mixture was directly subjected to ^{1}H-NMR analysis.[11] For preparative purposes it is only necessary to remove the product in those cases where no solvent was used or to remove the solvent at reduced pressure. In both cases the resulting enol silyl ethers are produced essentially quantitatively and in high purity.

Compound 5: Into a 10 mL flask was placed 0.80 mL of a 1.40 M solution of methyllithium in ether and the temperature lowered to -10°C by means of a methanol-ice bath. After allowing this mixture to cool for 15 min 0.041 g (1.03 mmol) of **3d** in 2 mL of THF was added and this reaction mixture stirred for 1 h after which time 0.35 mL (23.58 mmol) of trimethylchlorosilane in 2 mL of THF containing a small amount of triethylamine was added. The solvent was removed at reduced pressure, the residue triturated with hexane and filtered and the hexane removed at reduced pressure. ^{1}H-NMR analysis of the product indicated a clean conversion to (Z)-4-(trimethylsilyloxy)-4-tridecene along with diphenyldimethylsilane.

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11. As is the case with the enol trimethylsilyl ethers, the vinyl protons of the (E) enol methyldiphenylsilyl ethers resonate at lower field than the (Z) isomers. The δ values (CDCl3) are as follows: **3a**,**4a** (5.17, 5.00); **3b**,**4b** (6.07, coincident with aryl protons); **3c**,**4c** (4.59, 4.53); **3d**,**4d** (4.62, 4.45).

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