# Stereoselective Synthesis of α,β-Unsaturated Esters

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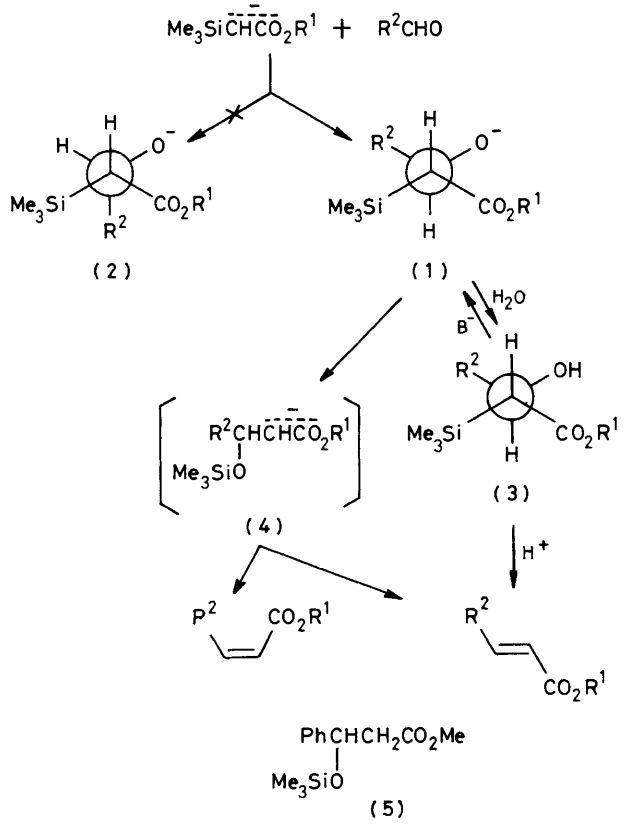
*Summary* Reaction of α-silylated ester magnesium enolates with aldehydes affords exclusively one diastereoisomer of the two possible β-hydroxy silanes which give pure *E*-unsaturated esters on acid work-up.

THE formation of α,β-unsaturated esters from α-silylated ester enolates is an interesting synthetic reaction,[1] but its stereoselectivity depends on the reaction conditions.[2] In connection with other work,[3] we were interested in controlling this stereochemistry.

The reaction is thought to occur *via* the formation of the very unstable stereoisomeric β-silyl alkoxides (**1**) and (**2**) which undergo spontaneous elimination even at low temperature (−78 °C). We report here that it is possible by operating at −110 °C with lithium as counter-ion to stabilize these alkoxides and to isolate the corresponding hydroxy silyl esters in *ca.* 40% yield after hydrolysis. However best results are obtained by changing the counter-ion. The addition of 1 equiv. of magnesium bromide to the preformed enolate before addition of the electrophile (an aldehyde) leads to the formation of the silylated alkoxide (**1**) which is stable in tetrahydrofuran (THF) even at room temperature,† and may be hydrolysed to the hydroxy-silane (**3**) in good to excellent yields. Unexpectedly, in all cases, we isolated only one of the two possible diastereoisomers, irrespective of the substituents $R^1$ and $R^2$ ($R^1$ = Me, $Pr^i$, and $Bu^t$; $R^2$ = $Pr^n$, $Pr^i$, and Ph). Changes in reaction time or temperature did not lead to detection of the other diastereosisomer.‡

† Isopropylmagnesium chloride is not basic enough in THF to abstract a proton from silylated esters.

‡ β-Hydroxy-α-silyl-esters are relatively stable and their purity was verified by $^1H$ and $^{13}C$ n.m.r. spectroscopy and g.l.c.




These results allowed us to control the stereochemistry of the formation of the α,β-unsaturated esters. It is well known that the acid-catalysed elimination of β-hydroxy silanes takes place by an *anti*-pathway.[4] The reaction of (**3**) with $BF_3$–$OEt_2$ in methylene dichloride for 1 h afforded the *E*-unsaturated esters quantitatively (Table).

However, we did not succeed in preparing *Z*-unsaturated esters by using basic work-up conditions; the reaction of (**3**) with sodium bis(trimethylsilyl)amide (NaHMDS) in THF for 1 h at 0 °C afforded mainly the *E*-unsaturated esters, the *E*:*Z* ratio depending on R²§ (< 10% of products resulting from retroaldolisation were observed). However, the addition of 1 equiv. of hexamethylphosphoric triamide (HMPT) to the solution of the magnesium enolate at 0 °C caused elimination and allowed mainly the *Z*-unsaturated esters to be obtained (Table). This result may be explained in terms of a *syn*-elimination followed by partial isomerisation of the *Z*-unsaturated ester to the more stable *E*-ester, or by a transfer of silicon from carbon to oxygen to give the β-substituted enolate (**4**) followed by a β-elimination.

TABLE. Synthesis of α,β-unsaturated esters.[a]

| Conditions[b] | R¹ | R² | % Yield of (**3**) | % Yield of ester | *E*:*Z* |
|---|---|---|---|---|---|
| (A) | Me | $Bu^n$ | 76 | 97 | 98:2 |
| (A) | $Pr^i$ | $Pr^i$ | 75 | 100 | >99:1 |
| (A) | Me | Ph | 78 | 100 | >99:1 |
| (B) | Me | $Bu^n$ | — | 75 | 15:85 |
| (B) | Me | Ph | — | 73 | 20:80 |
| (B) | Et | $C_5H_{11}$ | — | 65 | 29:71 |

[a] All reactions were carried out by adding 1 equivalent of $MgBr_2$ at −65 °C to the lithium ester enolate (lithium diisopropylamide; −80 °C, 30 min). After 1 hour, the aldehyde was added at −80 °C. [b] (A): After hydrolysis, the hydroxy-ester (**3**) was stirred for 1 h with 1 equiv. of $BF_3$–$OEt_2$ (in $CH_2Cl_2$); (B): before hydrolysis, HMPT was added at 0 °C and the mixture was stirred for 30 min.

As the reaction of (**3**; R¹ = Me, R² = Ph) with NaHMDS leads to a *Z*:*E* ratio of 10:90 while the same reaction of the β-silyloxy-ester (**5**) synthesized by an independent pathway gives the *E*-isomer exclusively, we assume that the base-induced elimination does not proceed by a pure *syn*-elimination; it appears, as previously suggested,[5] that the 1,3-migration of the silyl group has a predominant role in the elimination pathway.

However, the results observed after the addition of HMPT to the magnesium enolate clearly indicate that the relative importance of the two processes is closely dependent on the nature of the counter-ion and the solvent.

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§ With R¹ = Me, the *E*:*Z* ratios are the following: 70:30 (R² = $Pr^n$); 75:25 (R² = $Pr^i$); 90:10 (R² = Ph). It is worth noting that the reaction of the lithium enolate with R¹ = Me in THF with butanal affords the same *E*:*Z* ratio of 70:30.

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