Notes

A Stereoselective, Two-Step Preparation of α-Alkyl-α,β-unsaturated Esters[1]

Gerald L. Larson,* Carmen Fernandez de Kaifer,[2] Rosa Seda, Luz E. Torres,[3] and J. Roberto Ramirez

Department of Chemistry, University of Puerto Rico, Rio Piedras, Puerto Rico 00931

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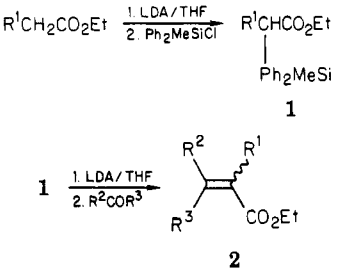
Although the use of α-silyl acetates in the preparation of α,β-unsaturated esters has been known and applied for nearly a decade,[4] the potentially very useful extension of this reaction to α-alkylated esters has not yet been reported.[5] Our finding that lithium ester enolates can be directly C-silylated with diphenylmethylchlorosilane[6] suggested the possibility that esters might be directly converted in two steps to α-alkylated-α,β-unsaturated esters **2** via the silylation–condensation–elimination sequence shown in Scheme I. We report herein that this is, in fact, the case, thereby adding an important dimension to the Yamamoto–Rathke[4a,c] application of the Peterson reaction. This approach has certain advantages over the Wittig transformation of aldehydes and ketones to α,β-unsaturated esters,[7] most notably the ability to employ a normal unfunctionalized ester as the starting material.

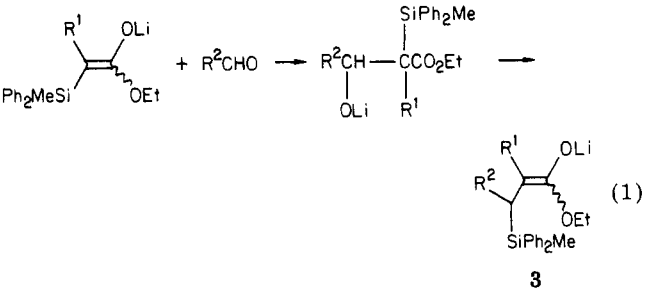
The results are shown in Table I. As can be noted, the yields are moderate to good and the reaction proceeds with both aldehydes and ketones. Acrolein reacts in the normal 1,2 fashion (entry 1) and the combination of two lengthy chains poses no problem (entry 11).

The reaction is moderately stereoselective, giving rise to predominantly the *Z* isomer, in contrast to the α-silyl acetates where the *E* isomer predominates.[4a] Although this

Scheme I



could be a result of the formation of a mixture of *Z* and *E* enolates and therefore a pref–parf[8] mixture of β-oxido silanes, which could undergo a syn elimination,[9] we feel that a more likely explanation is a stepwise elimination of the β-oxido silane. Strong evidence for such a stepwise elimination of certain β-oxido silanes has recently been reported by Yamamoto and co-workers[10] and supported by results from the Larcheveque laboratory.[11] This then dictates that the stereoselectivity of the reaction is not determined, to any great extent at least, by the geometry of the enolate or its mode of addition to the aldehyde (or ketone) to form the β-oxido silane but, in fact, by the relative stabilities of the β-silyloxy enolates **3a** and **3b** formed by a 1,3-migration of silicon from carbon to oxygen (eq 1). This is consistent with the results reported here



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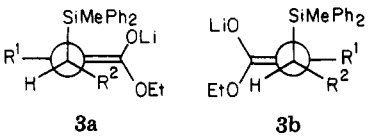
and those reported in previous work as well, in that where R = H conformation **3b** would be the more stable and the



3a **3b**

E isomer would predominate as observed. On the other hand, where R ≠ H, then conformation **3a** would be the more stable and the *Z* isomer would be the predominant product as is seen in the present study and in other cases where R is Cl[5a] and Me_3Si,[5b] as well as in a closely related system.[12]

(1) The Chemistry of α-Silyl Carbonyl Compounds. Part 6. Presented in part at the 185th National American Chemical Society Meeting, Seattle, WA, March 1983; Abstr. No. 229, and the XV Congreso Latinoamericano de Quimica, San Juan, P.R., Oct 1982.

(2) Summer research participant from Interamerican University supported by the Resource Center for Science and Engineering, University of Puerto Rico.

(3) MARC Honors Undergraduate Research Trainee 1981–82.

(4) (a) Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1974**, *96*, 1620–1621. (b) Taguchi, H.; Shimoji, K.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2529–2531. (c) Hartzell, S. L.; Sullivan, D. F.; Rathke, M. W. *Tetrahedron Lett.* **1974**, 1403–1406. (d) Larson, G. L.; Rosario Lopez, O. *Rev. Latinoamer. Quim.* **1975**, *6*, 116–118. (e) Larson, G. L.; Prieto, A.; Hernandez, A. *Tetrahedron Lett.* **1981**, *22*, 1575–1578. (f) Tulshian, D. B.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1981**, *103*, 474–475. (g) Larson, G. L.; Quiroz, F.; Suarez, J. *Synth. Commun.* **1983**, *13*, 833–845.

(5) Some α-substituted-α-silyl esters have been deprotonated and condensed with aldehydes and ketones. These are (a) α-chloro (Chan, T. H.; Moreland, M. *Tetrahedron Lett.* **1978**, 515–518), (b) α-trimethylsilyl (Hartzell, S. L.; Rathke, M. W. *Ibid.* **1976**, 2737–2740), and (c) α-thiophenoxy (Agawa, T.; Ishikawa, M.; Komatsu, M.; Oshiro, Y. *Bull. Soc. Chem. Jpn.* **1982**, *55*, 1205–1208).

(6) Larson, G. L.; Fuentes, L. M. *J. Am. Chem. Soc.* **1981**, *103*, 2418–2419.

(7) Gosney, I.; Rowley, A. G. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G., Ed.; Academic Press: New York, 1979; pp 27ff. Recently a modification of the Horner–Emmons olefination has been reported to give α-methyl-α,β-unsaturated esters with high *Z* stereoselectivity: Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408.

(8) Carey, F. A.; Kuehne, M. E. *J. Org. Chem.* **1982**, *47*, 3811–3815.

(9) Hudrlik, P. F.; Peterson, D. *J. Am. Chem. Soc.* **1975**, *97*, 1464–1468.

(10) Yamamoto, K.; Tomo, Y.; Suzuki, S. *Tetrahedron Lett.* **1980**, *21*, 2861–2864.

(11) Larcheveque, M.; Debal, A. *J. Chem. Soc., Chem. Commun.* **1981**, 877–878.

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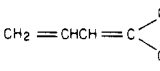
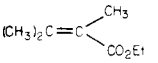
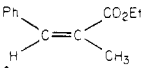
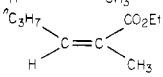
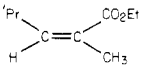
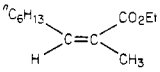
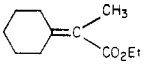
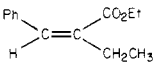
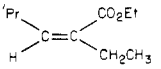
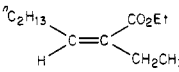
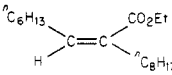
Table I

entry	ester	carbonyl compd	product	% yield[b] (Z:E ratio)
1	CH_3CHCO_2Et | $SiMePh_2$[a]	acrolein		65 (77:23)
2		acetone		54
3		benz-aldehyde		65 (78:22)
4		1-butanal		57 (75:25)
5		2-methyl-propanal		60 (90:10)
6		1-heptanal		69 (75:25)
7		cyclo-hexanone		77
8	$CH_3CH_2CHCO_2Et$ | $SiMePh_2$	benz-aldehyde		73 (80:20)
9		2-methyl-propanal		55 (82:18)
10		1-heptanal		67 (78:22)
11	$^nC_8H_{17}CHCO_2Et$ | $SiMePh_2$[a]	1-heptanal		62 (71:29)

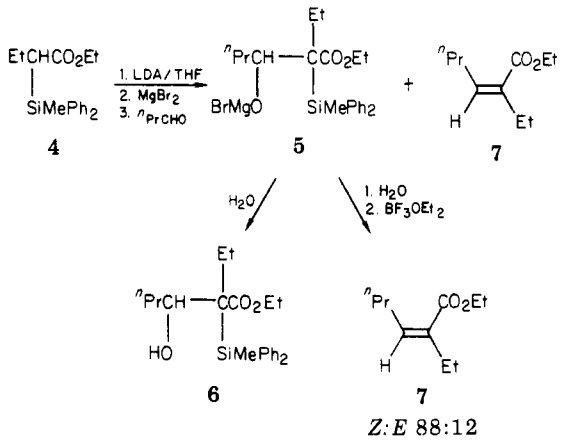
[a] $SiMePh_2$ = diphenylmethylsilyl. [b] Isolated yields, Z:E ratios determined by ^1H NMR.[13]

In order to more thoroughly understand the stereoselectivity of the condensation–elimination steps we attempted to prepare and isolate the β-hydroxy-α-silyl esters via the use of the magnesium enolates as was done with trimethylsilyl acetates in the Larcheveque study. Thus, ethyl α-(diphenylmethylsilyl)butanonate (4) was treated sequentially with LDA, magnesium bromide, and 1-butanal (Scheme II) in the hopes of generating a stable β-oxido silane (5). Treatment of the product of this reaction with water gave no evidence for the presence of a β-hydroxy silane (6). Furthermore, treatment of the mixture after the condensation but before any hydrolysis with HMPA, conditions reported to give predominant syn elimination,[11] gave 7 in a Z:E ratio of 67:33. Hydrolytic workup followed by treatment of the crude reaction product with boron trifluoride etherate gave 7 in a Z:E ratio of 88:12. Clearly the reaction is not cleanly stereoselective under any of these conditions, due in part at least to the fact that the reaction must be warmed to room temperature and above to achieve reasonable chemical yields.

Experimental Section

Spectra were recorded in the normal manner. All esters, aldehydes, and ketones were distilled prior to use. The α-silyl esters were prepared according to our published procedure in greater than 80% isolated yields. Glassware was dried in an oven or in a flame and cooled under an atmosphere of nitrogen prior to use.

Scheme II



Z:E 88:12

Preparation of (Z)- and (E)-Ethyl 2-Ethyl-2-pentenoate (Representative Procedure). Lithium diisopropylamide was prepared in the usual way from diisopropyl amine (3.3 mmol) and n-butyllithium (3.3 mmol) in THF at 0 °C, and this solution was cooled to −78 °C after which time ethyl (diphenylmethylsilyl)-butanoate in THF was added via syringe. This solution was stirred for 30 min and then 3.1 mmol of 1-butanal added. This solution was stirred at −78 °C (1 h), warmed to room temperature, and finally refluxed for 1.5 h. At this time 4 mmol of trimethylchlorosilane was added to fully silylate the diphenylmethylsiloxide produced and thereby facilitate ultimate product purification. The reaction mixture was added to hexane (25 mL) and washed with water (2 × 25 mL), dried, and concentrated. The ratio of isomers was determined at this stage. Purification was accomplished by silica gel chromatography, eluting with ethyl acetate:hexane (5:95).

Determination of the Z:E Ratio. The ratio of isomers was determined on the crude concentrated product before purification by ^1H NMR spectroscopy by observing the β-vinyl protons cis to the carbethoxy group in the E isomer (ca. 6.8 ppm) and those trans to the carbethoxy group in the Z isomer (ca. 5.7 ppm) as the probe.[13]

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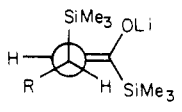
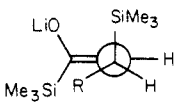
Registry No. 1 (R^1 = CH_3), 77772-22-6; 1 (R^1 = n-C_8H_{17}), 89638-16-4; 2 (R^1R^2 = $(CH_2)_5$), 63963-01-9; 4, 89638-15-3; (Z)-7, 72653-60-2; (E)-7, 72653-59-9; (Z)-CH_2=CHCH=C(CH_3)CO_2Et, 75088-95-8; (E)-CH_2=CHCH=C(CH_3)CO_2Et, 75088-96-9; $(CH_3)_2$C=C(CH_3)CO_2Et, 13979-28-7; (Z)-PhCH=C(CH_3)CO_2Et, 7042-34-4; (E)-PhCH=C(CH_3)CO_2Et, 7042-33-3; (Z)-n-C_3H_7CH=C(CH_3)CO_2Et, 66102-13-4; (E)-n-C_3H_7CH=C(CH_3)-CO_2Et, 22210-20-4; (Z)-i-PrCH=C(CH_3)CO_2Et, 21016-47-7; (E)-i-PrCH=C(CH_3)CO_2Et, 21016-46-6; (Z)-n-C_6H_{13}CH=C-(CH_3)CO_2Et, 73232-05-0; (E)-n-C_6H_{13}CH=C(CH_3)CO_2Et, 69303-47-5; (Z)-PhCH=C(CH_2CH_3)CO_2Et, 60754-34-9; (E)-PhCH=C(CH_2CH_3)CO_2Et, 60754-33-8; (Z)-i-PrCH=C-(CH_2CH_3)CO_2Et, 22147-76-8; (E)-i-PrCH=C(CH_2CH_3)CO_2Et, 22147-75-7; (Z)-n-C_6H_{13}CH=C(CH_2CH_3)CO_2Et, 89638-17-5; (E)-n-C_6H_{13}CH=C(CH_2CH_3)CO_2Et, 89638-18-6; (Z)-n-C_6H_{13}CH=C(n-C_8H_{17})CO_2Et, 89638-19-7; (E)-n-C_6H_{13}CH=C(n-C_8H_{17})CO_2Et, 89638-20-0; CH_2=CHCHO, 107-02-8; $(CH_3)_2$CO, 67-64-1; PhCHO, 100-52-7; n-C_3H_7CHO, 123-72-8; i-PrCHO, 78-84-2; n-C_6H_{13}CHO, 111-71-7; $ClSiMe_2Ph$, 144-79-6; cyclohexanone, 108-94-1.

(12) Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc.* **1981**, *103*, 6217–6219. These authors argue that the high stereoselectivity in the condensation of the lithium enolate of $Me_3SiCH_2COSiMe_3$ is due to the selective formation of the Z enolate. However, these results could also be interpreted in terms of a stepwise elimination in which a stereoselective elimination occurs via conformation i, which should be considerably more stable than its counterpart ii.



i



ii

(13) Katzenellenbogen, J. A.; Utawanit, T. *J. Am. Chem. Soc.* **1974**, *96*, 6153–6158.