299. Efficient Conversion of Esters to α-Trimethylsilylketones

Preliminary communication

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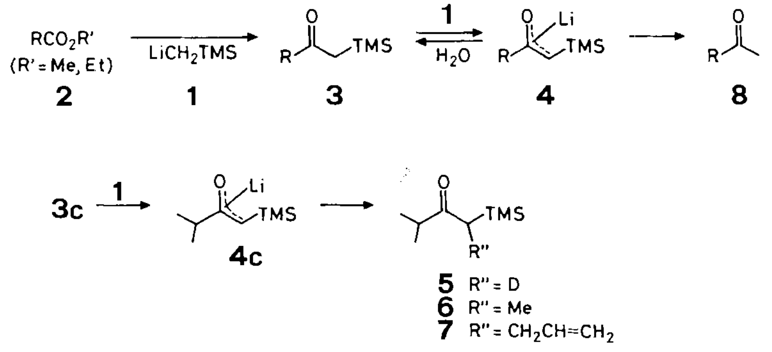
Summary

Secondary and tertiary carboxylic methyl or ethyl esters (**2a–c**) were converted with trimethylsilylmethyllithium (**1**) to *α*-trimethylsilylketones (**3a–c**) in high yields. Under identical reaction conditions the primary esters **2d,e** gave **3d,e** in lower yields. Since the trimethylsilyl (TMS) group *α* to a ketone is known to undergo facile elimination under a variety of reaction conditions, the method also constitutes a highly versatile ester to methylketone sequence.

Trimethylsilylmethyllithium (**1**)1) should have the potential to react with esters **2** to give *α*-silylketones **3** as represented in the *Scheme*. A prerequisite to the successful outcome of this sequence is a protection of the ketone function in **3** from further nucleophilic attack. The work of *Stork et al.* [2] suggests that competitive enolate formation on the *α*-trimethylsilylketone **3** should provide effective blocking of the ketone.

Scheme



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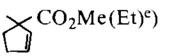
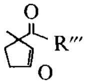
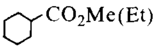
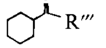
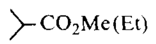
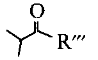
1) The readily available reagent **1** was prepared in pentane as described in [1] for ether solutions.

In fact the reaction of methyl or ethyl esters (**2**) with **1** at 0° in pentane gave, after work-up with water[2]), the *a*-trimethylsilylketones **3** (see *Table*). The secondary and tertiary esters **2a–c** underwent smooth conversion to the desired *a*-trimethylsilylketones **3a–c**. A lower yield (of **3d, e**) was observed for the primary esters **2d** and **2e** under the same experimental conditions. In each of these runs a single by-product was formed, but its structure has not yet been investigated. Most notably, all runs listed in the *Table* consumed 2 equivalents of the lithium reagent, indicating effective competition of lithiation (→**4**) with the primary addition step (→**3**). Direct proof for the consecutive lithiation steps involved was obtained upon treatment of isolated **3b** and **3c** with 1 equivalent of **1** at 0° in pentane. The reactions were subsequently quenched with D_2O. Deuteriation was localized in both cases as depicted in the *Scheme* for **5**. Inverse addition (kinetic lithiation) led to identical results. Furthermore, electrophiles such as methyl iodide and allyl chloride reacted with **4c** in boiling pentane solutions regioselectively to give **6** and **7** in yields of 65–75%. Spectral data conclusively ruled out the occurrence of *O*-alkylation. Since *a*-silylketones[3]) offer important synthetic potential [1] [5–7], they have been prepared in particular cases from acids [8], acid chlorides [9] or anhydrides [10][4]). These functional groups are often undesirable in synthetic schemes, and therefore, the title method (**2**→**3**) is a highly convenient alternative.

Table. *Conversions of esters* **2** *to a-silylketones* **3** *and methylketones* **8**

	Starting esters **2**	Products	Yields of **3**[a])[b])[c]) $R''' = CH_2TMS$	Yields of **8**[a])[b]) $R''' = Me$
a	 $CO_2Me(Et)$[e])		96 (92)	95[d])
b	 $CO_2Me(Et)$		84 (77)	(80)[c])
c	 $CO_2Me(Et)$		82 (74)	83[c])
d	$CH_3CH_2CO_2Me(Et)$	CH_3CH_2COR'''	44 (35)	45[c])
e	$CH_3(CH_2)_6CO_2Me(Et)$	$CH_3(CH_2)_6COR'''$	45 (40)	(41)[c])

[a]) The yields did not differ significantly for methyl and ethyl esters.

[b]) All compounds exhibited satisfactory analytical data (IR., 270 MHz-^{1}H-NMR., MS., and GC.).

[c]) Yields according to GC.-analysis of the crude reaction products (glass capillary column OV 101). In parentheses, isolated yields after distillations at reduced pressure. Rearrangement of the *a*-silylketones **3** to silylenolethers was avoided by temperatures below 100° [3].

[d]) Purification was achieved on *Merck* plates, silica gel 2 mm.

[e]) Notably, treatment of this neopentyl system with methyllithium at −78° afforded mainly carbinol product.

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[2]) A round-bottomed flask with septum inlet was flushed with argon (dried on a column packed with *Oxisorb* G) and immersed into an ice-water bath. 1 mmol of ester **2**, dissolved in 5 ml of dry pentane, was stirred in the reaction vessel for 2 min and then 3 ml of a 0.67 molar (2 mmol) solution of **1** in pentane[1]) was added all at once. The reaction was allowed to proceed at 0° for 2 h. Addition of water and drying the rapidly separated organic layer ($MgSO_4$) afforded the *a*-silylketones **3**.

[3]) Direct access to *a*-trimethylsilylketones is not possible by silylation of ketones [4].

[4]) For preparations by routes not involving acid derivatives see [6] [11] [12].

We took advantage of the well-known facile elimination of the TMS group *α* to a ketone group under a variety of reaction conditions[5]) and converted the lithiated *α*-silylketones **4** *in situ* to methylketones **8**[6]). Thus the method is expanded to a novel and versatile ester to methylketone sequence under extremely mild conditions.

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REFERENCES

[1] *R.A. Ruden & B.L. Gaffney,* Synth. Commun. *5,* 15 (1975).

[2] *G. Stork & B. Ganem,* J. Amer. chem. Soc. *95,* 6152 (1973); *G. Stork & J. Singh,* ibid. *96,* 6181 (1974).

[3] *A.G. Brook, D.M. MacRae & A.R. Bassindale,* J. organomet. Chemistry *86,* 185 (1975).

[4] *H.O. House, M. Gall & H.D. Olmstead,* J. org. Chemistry *36,* 2361 (1971).

[5] *P.F. Hudrlik & D. Peterson,* Tetrahedron Letters *1974,* 1133.

[6] *P.F. Hudrlik & D. Peterson,* J. Amer. chem. Soc. *97,* 1464 (1975).

[7] *K. Utimoto, M. Obayashi & H. Nozaki,* J. org. Chemistry *41,* 2940 (1976).

[8] *M.J. Jorgenson,* in Organic Reactions J. Wiley & Sons, vol. *18,* p. 1 (1970).

[9] *T.H. Chan, E. Chang & E. Vinokur,* Tetrahedron Letters *1970,* 1137.

[10] *C.R. Hauser & C.R. Hance,* J. Amer. chem. Soc. *74,* 5091 (1952).

[11] *M. Obayashi, K. Utimoto & H. Nozaki,* Tetrahedron Letters *1978,* 1383.

[12] *T. Sato, T. Abe & I. Kuwajima,* Tetrahedron Letters *1978,* 259.

[13] *F.C. Whitmore, L.H. Sommer, J. Gold & R.E. Van Strien,* J. Amer. chem. Soc. *69,* 1551 (1947).

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[5]) For example see [2] [9] [10] [13].

[6]) Instead of rapid work-up with water[2]), methanol was added to the reaction mixture. The homogeneous solutions thus formed were stirred at RT. for 1 h. Extraction with additional water and pentane led to the isolation of the crude methylketones **8**.