Tetrahedron Letters,Vol.25,No.16,pp 1673-1676,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

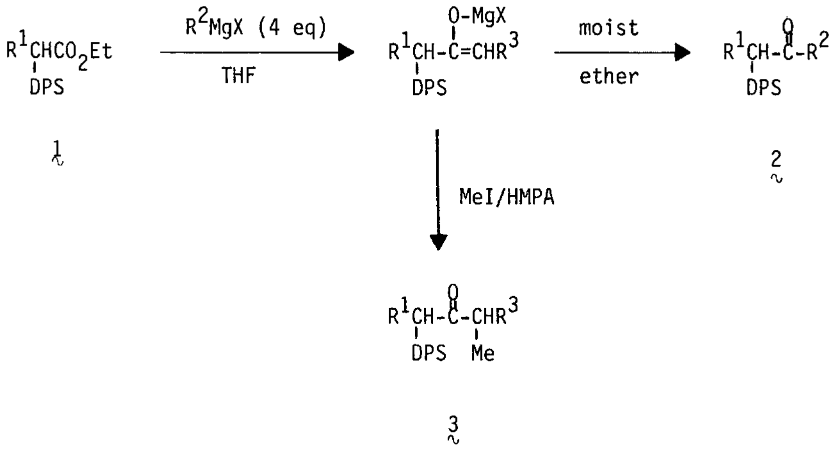
AN EFFICIENT SYNTHESIS OF β-KETOSILANES[1]

Gerald L. Larson*, Ingrid Montes de López-Cepero[2] and Luz E. Torres[3]
Department of Chemistry, University of Puerto Rico, Río Piedras, P.R. 00931 (USA)

Summary: The reaction of α-silyl esters with an excess of a Grignard reagent leads to β-ketosilanes in good yield.

In our continuing interest in the synthetic utility of α-silyl carbonyl compounds we sought a convenient synthesis of β-ketosilanes, the previous syntheses of which have been either lengthy or non-general[4]. Demuth has described a preparation of trimethylsilylmethyl ketones via the reaction of trimethylsilylmethyllithium and secondary or tertiary esters, primary esters leading to lower yields[5]. We have now found that the Demuth approach can be carried out in an inverse manner wherein the ester contains the silicon moiety.

Treatment of α-silyl esters **1**[6] with an excess (> 4 equivalents) of a Grignard reagent in THF at reflux for 48 h followed by hydrolysis with moist ether and chromatographic purification on silica gel eluting with triethylamine:ethyl acetate:hexane (0.5:1.0:98.5) at 0°[7] gave the β-ketosilanes shown in the Table. The reaction is best when R^1 is larger than methyl, where the major product is in fact the olefin resulting from double addition followed by elimination. Moreover, vinyl, 1-pentynyl and allylmagnesium bromide all add twice to the carbonyl of **1c**. Methylation of the reaction mixture resulting from the reaction of **1c** with n-propylmagnesium bromide (MeI/HMPA-THF) gave **3** in 87% yield indicating that the excess of Grignard reagent forms the enolate of the β-ketosilane in high yield and in a regiospecific manner. Treatment of the dimethylated α-silyl ester 4 with vinylmagnesium bromide leads to enolate 5, which was hydrolyzed to 6 and methylated to 7, which in turn was thermolyzed to enol silyl ether 8[8]. This opens the possibility of employing α-silyl esters as precursors to regiospecifically generated enol silyl ethers[9].

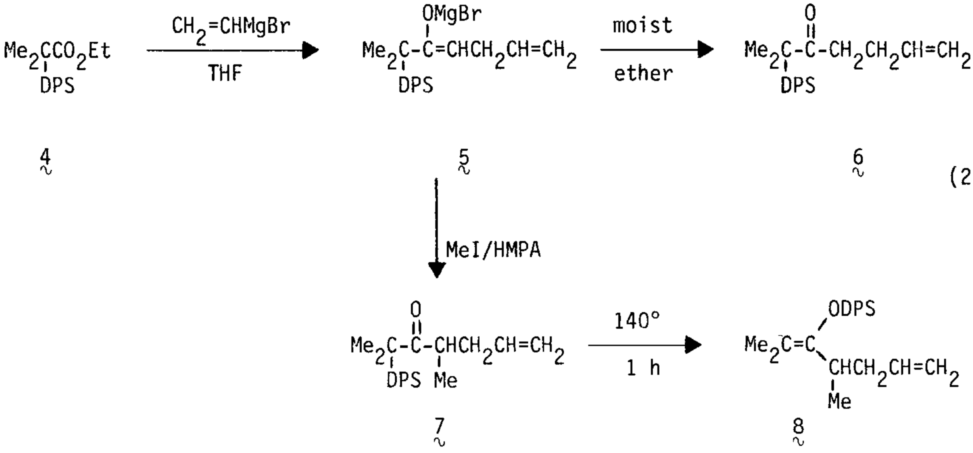


$$R^1\underset{DPS}{CH}CO_2Et \xrightarrow[THF]{R^2MgX\ (4\ eq)} R^1\underset{DPS}{CH}-\overset{O-MgX}{C}=CHR^3 \xrightarrow[ether]{moist} R^1\underset{DPS}{CH}-\overset{O}{\overset{\|}{C}}-R^2 \qquad (1)$$

$$R^1\underset{DPS}{CH}-\overset{O-MgX}{C}=CHR^3 \xrightarrow{MeI/HMPA} R^1\underset{DPS}{CH}-\overset{O}{\overset{\|}{C}}-\underset{Me}{C}HR^3$$

1 2 3

R^1 = Me, 1a; Et, 1b; $^nC_8H_{17}$, 1c



$$Me_2\underset{DPS}{C}CO_2Et \xrightarrow[THF]{CH_2=CHMgBr} Me_2\underset{DPS}{C}-\overset{OMgBr}{C}=CHCH_2CH=CH_2 \xrightarrow[ether]{moist} Me_2\underset{DPS}{C}-\overset{O}{\overset{\|}{C}}-CH_2CH_2CH=CH_2 \qquad (2)$$

$$\xrightarrow{MeI/HMPA} Me_2\underset{DPS}{C}-\overset{O}{\overset{\|}{C}}-\underset{Me}{C}HCH_2CH=CH_2 \xrightarrow[1\ h]{140°} Me_2C=C\begin{matrix} ODPS \\ \underset{Me}{C}HCH_2CH=CH_2 \end{matrix}$$

4 5 6 7 8

(DPS=Ph_2MeSi)

PREPARATION OF β-KETOSILANES

Entry	Ester	Grignard	Product	% Yield[a]
1	**1a**	$^{n}C_{6}H_{13}MgBr$	$CH_{3}CH(DPS)CO^{n}C_{6}H_{13}$	trace[b]
2	**1b**	$^{n}C_{3}H_{7}MgBr$	$CH_{3}CH_{2}CH_{2}CO^{n}C_{3}H_{7}$[c]	42[c]
3	**1c**	$^{n}C_{3}H_{7}MgBr$	$^{n}C_{8}H_{17}CH(DPS)CO^{n}C_{3}H_{7}$	69
4	**1c**	PhMgBr	$^{n}C_{8}H_{17}CH(DPS)COPh$	82
5	**1c**	$CH_{3}MgBr$	$^{n}C_{8}H_{17}CH(DPS)COCH_{3}$	71
6	**1c**	$^{n}C_{3}H_{7}MgBr$	$^{n}C_{8}H_{17}CH(DPS)COCH(CH_{3})Et$[d]	87
7	**4**	$CH_{2}{=}CHMgBr$	$Me_{2}C(DPS)COCH_{2}CH_{2}CH{=}CH_{2}$	78
8	**4**	$CH_{2}{=}CHMgBr$	$Me_{2}C(DPS)COCH(CH_{3})CH_{2}CH{=}CH_{2}$[d]	75

a. Isolated yields. b. 3-n-hexyl-2-nonene formed in 66% yield. c. Product of protodesilylation of crude β-ketosilane. d. Reaction mixture treated with MeI/HMPA before work up.

ACKNOWLEDGEMENTS: We wish to thank the NIH-MBRS program (RR-8102-10), Pfizer Pharmaceuticals of P.R. and the UPR department of chemistry for support of our work and the NSF for a grant to help purchase the Jeol FX90Q NMR spectrometer. We thank Professor John Soderquist for helpful discussions.

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1. The chemistry of α-silyl carbonyl compounds 7.
2. Graduate student funded by NIH-MBRS program.

3. Recipient of a National Science Foundation predoctoral fellowship administered by the department of chemistry.
4. The most general preparation of β-ketosilanes is via the oxidation of β-hydroxysilanes, usually prepared from α,β-epoxysilanes. See, for example, R. A. Ruden and B. L. Gaffney, Synthetic Commun., 5, 15 (1975); P. F. Hudrlik and D. Peterson, J. Am. Chem. Soc., 97, 1464 (1975); K. Yamamoto, Y. Tomo and S. Suzuki, Tetrahedron Lett., 2861 (1980); W. E. Fristad, T. R. Bailey and L. A. Paquette, J. Org. Chem., 45, 3028 (1980). These latter authors used chromic acid-sulfuric acid to oxidize and protodesilylate the β-hydroxysilanes in a single step, but mention that pyridinium chlorochromate oxidation of β-hydroxysilanes leads to β-ketosilanes in good yield. The Lewis acid catalyzed rearrangement of α,β-epoxysilanes gives β-ketosilanes; J. J. Eisch and J. E. Galle, Ibid, 41, 2615 (1976); M. Obayashi, K. Utimoto and H. Nozaki, Tetrahedron Lett., 1807 (1977), 1383 (1978); P. F. Hudrlik, Ibid, 1453 (1976). For another route to β-ketosilanes see C. J. Kowalski, M. L. O'Dowd, C. M. Burke and K. W. Fields, J. Am. Chem. Soc., 102, 5411 (1980).
5. M. Demuth, Helv. Chim. Acta., 61, 3136 (1978).
6. Prepared by direct silylation of the ester enolate. G. L. Larson and L. M. Fuentes, J. Am. Chem. Soc., 103, 2418 (1981).
7. Although some of the β-ketosilanes are more resistant to hydrolysis than others, we found these conditions to be best for general isolation of the desired product with a minimum of desilylation.
8. The thermal rearrangement of β-ketosilanes to enol silyl ethers is well known. A. G. Brook, D. M. MacRae and W. W. Limburg, Ibid, 89, 5493 (1967).
9. For reviews on the synthetic importance of enol silyl ethers see E. Colvin, "Silicon in Organic Synthesis", Butterworths, Boston, Mass., 1981, chapter 17. W. P. Weber, "Silicon Reagents for Organic Synthesis", Springer-Verlag, New York, N. Y. 1983, Chapters 12-16.

(Received in USA 23 January 1984)