THE 1,3 0→C SILYL REARRANGEMENT OF SILYL ENOL ETHER ANIONS -

SYNTHESIS OF & -SILYL KETONES

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Summary: Silyl enol ethers with sterically hindered silyl groups are transformed into the corresponding α-silyl ketones by treatment with n-butyllithium/ potassium tert-butylate.

The thermal rearrangement of α -silyl ketones 3 to silyl enol ethers 2 is well-known¹⁾. It is of little preparative value, however, since the silyl enol ethers 2 are easily prepared from the parent ketones 1, while there is no general synthetic route from 1 to 3: Although certain derivatives of ketones can be α -silylated (e.g. dimethylhydrazones²⁾), the ketones themselves cannot. Even a silylation reagent especially suited for the C-silylation of ester enolates leads to exclusive O-silylation in the case of ketone enolates^{3,4)}. Therefore α -silyl ketones which are valuable intermediates⁵⁾ had to be prepared by CC bond forming reactions⁶⁾, by a two-step isomerization of silyl epoxides^{3,5a)}, from α -seleno silyl enol ethers⁷⁾ or by isomerization of β -silyl allyl alcohols⁸⁾.



In the course of an earlier study on the triisopropylsilyl (TIPS) group⁹⁾ we discovered the first examples of transformation $2 \rightarrow 3$ via the anions of 2, rendering compounds 3 available in two steps from the parent ketones 1. Relevant findings by Kuwajima (involving reductive cleavage of a C-Se bond followed by Si migration⁷⁾), by Weber¹⁰⁾ and recent interest in α -silyl ketones^{8,11,18)} prompt us to present our results here.

When the TIPS enol ether 2a of 4-tert-butylcyclohexanone 1a is treated in hexane with 2 eq n-butyllithium and 2.5 eq potassium tert-butylate¹²⁾ at ambient temperature for 24 hr, two products are isolated after aqueous workup (ratio 5:1, 98 % isolated) which can be separated by chromatography. The structures 3ac and 3at are in agreement with spectral data (¹H-NMR, MS, IR), with the interconversion to a mixture of the original 5:1 ratio when the

entry	ketone	silyl enol ether ^{a,b}	products ^b	conditions ^C	yield ^d
1			$ \bigoplus_{\underline{3ac}}^{0} + \bigoplus_{\underline{3at}}^{0} \bigoplus_{\underline{3at}}^{0} $	24 hr r.t.	98
2	<u>1a</u>		$\bigcup_{\underline{3bc}}^{0} \bigcup_{\underline{3bc}}^{\text{DIMS}} + \bigcup_{\underline{3bt}}^{0} \bigcup_{\underline{3bt}}^{\text{DIMS}}$	3 hr 0°	80
3	<u>1a</u>	OTMS $\frac{2c}{2c}$		24 hr r.t.	71
4				10 hr r.t.	77
5	<u>1d</u>			6 hr r.t.	54
6	$\overset{\circ=}{\checkmark}$			24 hr r.t.	60 ^e
7				5 hr r.t.	50 ^e
8	$\stackrel{\texttt{ll}}{\checkmark}$	the second secon	$\begin{array}{c} 0\\ \downarrow\\ \downarrow\\$	¹⁾ 20 hr r.t.	63 ^e
9	$\stackrel{\mathbb{i}}{\searrow}$		-	48 hr r.t.	_f
10	K=			48 hr r.t.	_f
11 12		$\frac{2b}{2a} + \frac{2d}{2e}$	$\frac{3bc}{3ac} + \frac{3bt}{3at} + \frac{3d}{3ac}$		

Table. Metallation and 1,3 $0 \rightarrow C$ Si migration of silyl enol ethers

TIPS = triisopropylsilyl DIMS = diisopropylmethylsilyl TMS = trimethylsilyl
a All silyl ethers 2 were prepared in nearly quantitative yield from the ketone, Et₃N and the silyl triflate^{9a)} in benzene at 0°, except the camphor derivative which was formed from the pregenerated enolate (THF, LDA, -78°, 5 min, then TIPS triflate, -78°-r.t., 99%, cp.¹³⁾.
b Satisfactory IR and NMR spectra were obtained for all new compounds.

- c All reactions were carried out by stirring with 2 eq nBuLi and 2.5 eq KO^tBu in hexane under an inert atmosphere, the conditions are not optimized.
- d Isolated yields after chromatography.
- e Several minor products, one of them TIPS-OH, were formed.
- f No reaction.

individual isomers are treated with KOH or HCl at ambient temperature (in the latter case there is a concomitant slower desilylation to give <u>1a</u>) and with the re-isomerization to <u>2a</u> observed when the major isomer of 3a is distilled.



Similar results with various silyl enol ethers are compiled in the table. Several conclusions can be drawn:

- Although the reaction clearly does not work in the case of TMS enol ethers (entry 3, the cleavage of TMS enol ethers by methyllithium being a standard method for generation of enolate anions¹⁴⁾), it can be used with sterically hindered silyl groups other than TIPS (entries 2 and 5).
- (2) The rearrangement seems to be triggered by allylic rather than vinylic metallation (via <u>i</u> rather than via <u>ii</u>), since enol ethers without an allylic α-proton are inert under the reaction conditions (entries 9 and 10). (An anion corresponding to <u>ii</u> is postulated as intermediate by Kuwajima⁷⁾.)
- (3) The silyl group migrates preferentially to the less hindered terminus of the allyl anion (entries 7 and 8).
- (4) The reaction is less useful in the case of open chain sterically unhindered silyl enol ethers. Byproducts are formed probably by Si-O cleavage and/or condensation reactions, as evidenced by the formation of TIPS-OH and the appearance of olefinic signals in the crude product ¹H-NMR spectrum (entries 6,7,8).
- (5) The rearrangement is strictly intramolecular within the analytical limits (crossover experiments, entries 11 and 12). Thus when an equimolar mixture of <u>2b</u> and <u>2d</u> was treated with nBuLi/KO^tBu, the only products were <u>3bc</u>, <u>3bt</u> and <u>3d</u> (2 % of <u>3a</u> and <u>3e</u> would have been detected by 250 MHz ¹H-NMR).

Because of the high Si-O bond energy silyl migrations in electroneutral molecules usually occur in the direction from other atoms to $oxygen^{1}$. In the present case of migration in the opposite direction this factor is obviously outweighed by the formation of an enolate from an allyl anion. Anionic 1,3 Si migrations between 0 and C are observable only if the normally fast elimination of silyloxide (Peterson olefination^{1b,14)}) is retarded, e.g. when the C

atoms are part of an aryl nucleus¹⁵⁾ or when one of them is replaced by a Si atom^{10,16)}. In the present case elimination would yield an allene, which does not even occur in open chain systems¹⁷⁾.

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