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3-STANNYL-1-SILYLOXYCYCLOHEX-1-ENES: SYNTHETIC EQUIVALENTS FOR KETONE α,β-DIANIONS

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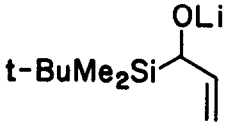
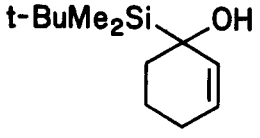
Summary: The preparation of 3-stannyl-1-silyloxycyclohex-1-enes and their use as synthons for α,β-dianions for cyclohexanone are described.

The use of umpolung has become a standard practice in organic synthesis.[2] Among the molecular substructures for which charge reversal has received considerable attention is the carbonyl homoenolate anion. Indeed a number of creative approaches have been described in the literature[3] although in general the new methodology has been limited to acyclic systems.[4] Recently Kuwajima described a procedure which utilizes the Brooke rearrangement of an α-silyl alcohol anion (1) to generate a homoenolate equivalent.[5] This procedure has a further advantage in that the products from trapping the anion possess a silyl enol ether which may be subsequently alkylated adjacent to the initial alkylation site (ketone α,β-dianion synthon). This sequence however is also limited to acyclic systems because the starting material 2 is not easily accessible.



1



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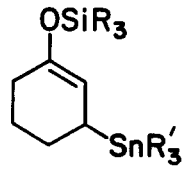
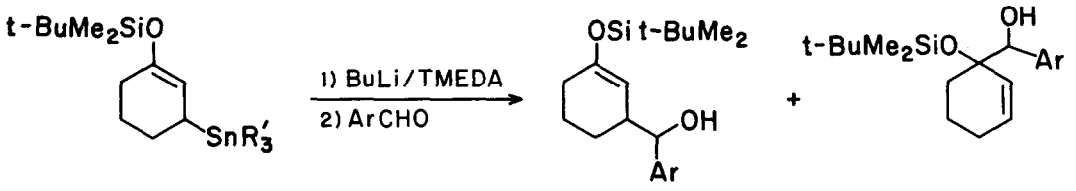


3

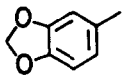
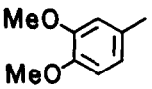
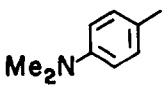
We have been exploring the chemistry of silylstannanes and found that they would readily undergo conjugate addition to enones to give 3 in a reaction catalyzed by cyanide.[6] If transmetallation of 3 could be efficiently effected, the cyclic equivalent of Kuwajima's homoenolate anion would be generated. We report here the success of this approach and the use of 3 as a synthetic equivalent for the α,β-dianion of cyclohexanone.



3a R = Me
b R = Bu

4

5

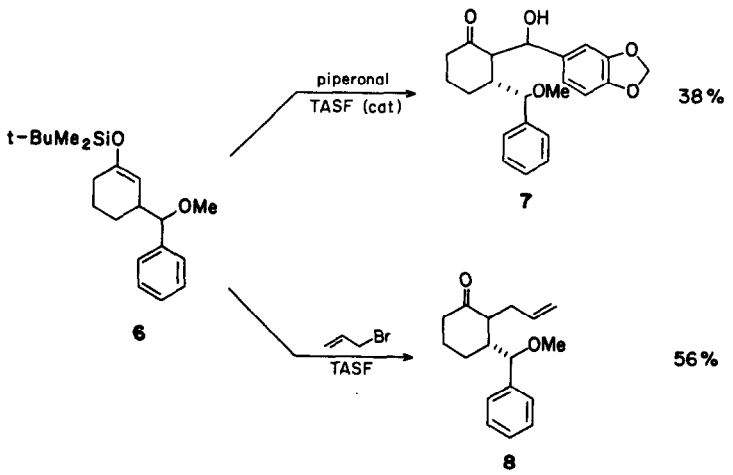
Ar	Isolated % Yield of 4	5	γ:α Ratio
	68	3	25:1
	66	10	6.6:1
	63	13	5:1
	42	21	2:1

Since it was reported that only the tert-butyldimethylsilyl reagents 1 were useful as homoenolates,[5,7] we were forced to abandon our silylstannane route to 3.[8] Fortunately an alternative synthesis of 3 (a R = t-BuMe$_2$, R' = Me; b R = t-BuMe$_2$, R' = Bu) was possible by conjugate addition of R'$_3$SnLi to cyclohexenone (THF, -78 °C) and trapping with tert-butyldimethylsilyl chloride.[9]

Compound 3 was essentially inert to methyl-, butyl-, and sec-butyllithium in THF at -78 °C and it was largely decomposed (probably due to secondary reactions of the transmetallated material) at temperatures above -20 °C. However, if 1.1 equivalent of TMEDA was present, transmetallation was easily effected with butyllithium (1 h, -78 °C for 3a; 5 h, -78 °C for 3b).

The anion was nicely quenched with aromatic aldehydes to give 50-75% yields of the silyl protected homoaldol products 4.[10,11] In all cases the gamma product was preferred, however the γ,α ratio was sensitive to the particular aldehyde used. For example, with benzaldehyde the γ,α ratio was 25/1 but with 4-dimethylaminobenzaldehyde it was 2/1. The yields quoted here are for pure products after isolation by flash chromatography on silica gel (0-25% ethyl acetate/hexane gradient).

The ketone α,β dianion equivalence of 3 was ultimately demonstrated by first methylating 4 (R = Ph; NaH/THF/MeI/RT). The clear colorless oil 6 (75%) was further reacted with piperonal in the presence of a catalytic amount of tris(dimethylamino)sulfonium difluorotrimethylsiliconate (TASF; THF/ACN/-78 °C to RT).[12] Standard workup and chromatography gave 7 (38%) as a mixture of diastereomers.[13] Alternatively, stoichiometric TASF induced allylation of 6 gave 8 in 56% yield.



Thus 3 can be viewed as a synthon for the α,β dianion of a ketone. The overall procedure is complementary to conventional methods for effecting α,β-bis-functionalization of ketones.[14] For example the sequence we have described allows homoaldol products to be easily prepared. An apparently unknown α-oxygenated cuprate reagent would be required to directly effect the same transformation.[15]

References

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