

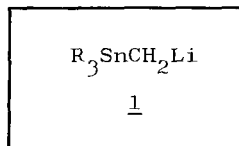
THE REACTION OF TRIALKYLSTANNYLMETHYLLITHIUM WITH α, β -EPOXY KETONES.
A PREPARATIVE METHOD OF β, γ -UNSATURATED KETONES BY HOMOLOGATION
OF α, β -UNSATURATED KETONES

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α, β -Epoxy ketones 2, upon treatment with two equivalents of trialkylstannylmethyllithium 1, afforded cyclopropanols 3 as a single product in acyclic system, and a mixture of cyclopropanols 3 and methylene 1,2-diols 4 in cyclic system. Under acidic conditions, the cyclopropanols gave β, γ -unsaturated ketones 5 in good yields.

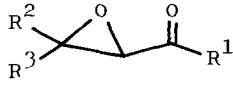
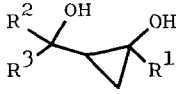
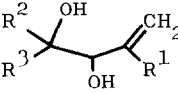
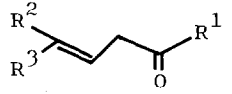
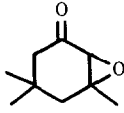
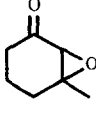
In our previous paper,¹⁾ we reported on the reaction of trialkylstannylmethyllithium (1) with several electrophiles, and its versatile use for the preparation of α -olefins from carbonyl compounds,^{1a)} methyl ketones from esters,^{1b)} cyclopropanes from oxiranes,^{1a)} and allyl alcohols from α -chloro ketones.^{1a)} In the present paper, we describe the reaction of 1 with α, β -epoxy ketones 2, which could be a useful synthetic method for the preparation of β, γ -unsaturated ketones 5.

One equivalent of an epoxy ketone 2 was added to a THF solution containing two equivalents of 1¹⁾ at -78°C , and the reaction mixture was allowed to warm up to room temperature in 1 h. After stirred for another 2 h, the products were extracted with ethyl acetate. Acyclic substrates 2a - 2c produced cyclopropanols 3 as single product, while cyclic substrates 2d - 2e produced mixtures of 3 and 4. The results are shown in Table 1. The low yield of 3c reflects the trend that the phenyl substituted oxiranes generally undergoes complicated reaction with the reagent 1.¹⁾ When the reaction of 2a was carried out using one equivalent of the reagent, the product was a stannyl compound 6, which gave a vinyl oxirane 7 upon the treatment with silica gel.

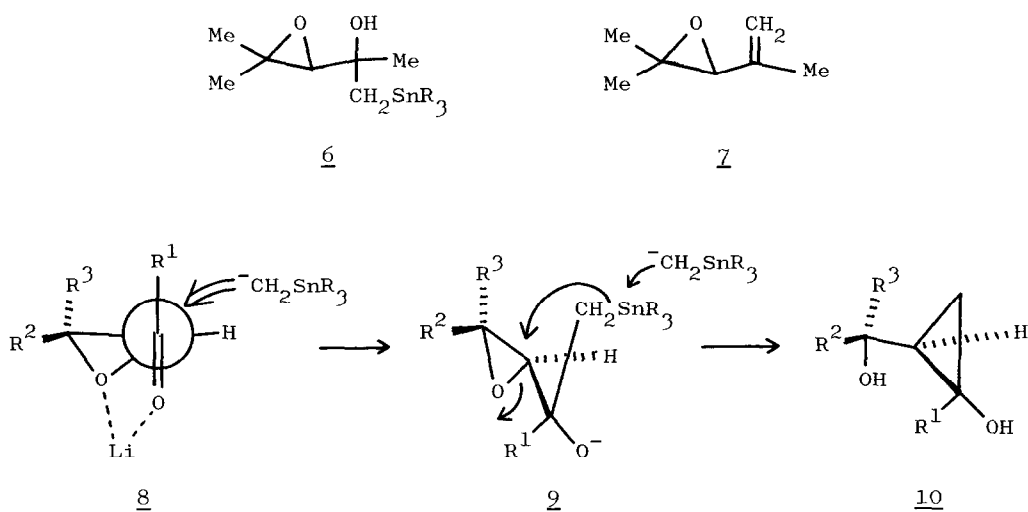


When the cyclopropanols 3a - 3c were treated with BF_3 -etherate or HCl, β, γ -unsaturated ketones 5a - 5c were obtained in good yields. It was also found that the HCl-treatment of the reaction mixture of 1 and 2a or 2b gave 5a or 5b, respectively, in fair yields in one pot. The results are included in the Table 1. The trans geometry was assigned for 5b by comparison with the authentic sample prepared by the known method.²⁾ The trans geometry was also speculated for 5c in view of the IR absorption at 965 cm^{-1} .³⁾ The $^1\text{H-NMR}$

Table 1. Products and Yields of the Reaction of α,β -Epoxy Ketones with Trialkylstannylmethyl lithium

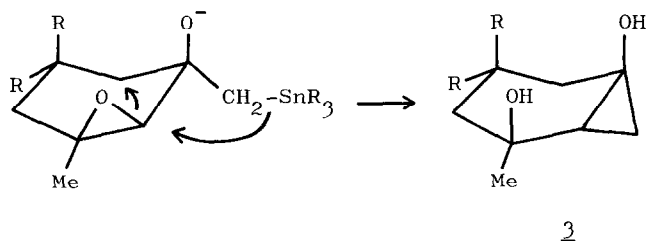
Starting materials				Products			
 $\underline{2}$				 $\underline{3}$		 $\underline{4}$	 $\underline{5}$
R ¹	R ²	R ³	Yields (%)	Yields (%)	Yields (%) from $\underline{3}$ from $\underline{2}$		
a Me	Me	Me	51	0	98	78	
b Me	H	n-Pr	75	0	~ 80	76	
c Me	H	Ph	17	0	91	-	
d			40	22	-	-	
e			42	n.d. a)	-	-	

a) Not determined.

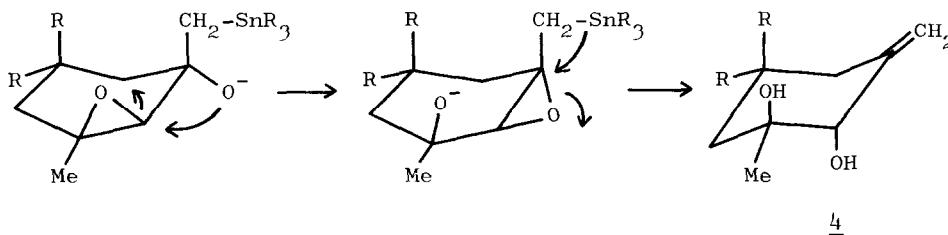


Scheme 1

Side A attack



Side B attack



Scheme 2

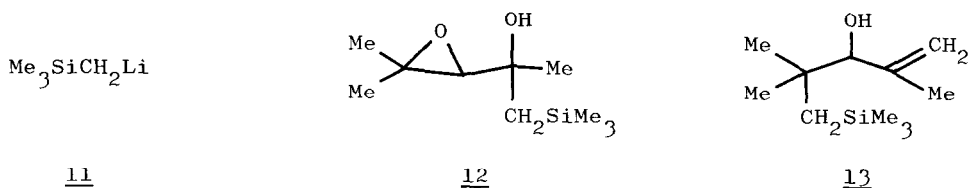
(400 MHz) and ^{13}C -NMR spectra of 3a were completely consistent with the assigned structure and indicated that this crystalline compound was stereochemically pure.⁵⁾ All the other products 3 and 4 were also stereochemically pure in view of NMR (60 or 100 MHz), TLC, and sharp melting points (except 3b, which did not crystallize), and no other isomers were identified in the reaction mixture. Although we could not confirm the stereochemistry of the products experimentally, it was predicted by assuming the reaction scheme as follows. In acyclic system, the carbanion 1 attacks the carbonyl group of the substrate presumably via a cyclic model as shown in Scheme 1, $\underline{8} \rightarrow \underline{9}$.⁶⁾ Although the reaction stops at this stage when only one equivalent of the reagent was used, affording 6 as final product, the use of two equivalents of the reagent induced a further reaction by the second molecule of the reagent attacking the tin atom of 9 and provoking the oxirane ring opening. Thus we assigned the structure 10 as the most probable structure of the cyclopropanols. In cyclic system, on the other hand, the reagent 1 could attack the carbonyl group from the side either opposite (A) or same (B) to the oxirane ring. Apparently from the stereochemical requirement as shown in Scheme 2, the side-A attack would give cyclopropanols 3, while the side-B attack give methylene 1,2-diols 4, thus providing the most plausible structures of the products as shown.

Although cis and trans cyclopropanols such as 3 have been prepared by carbene addition to vinyl compounds, and converted to β,γ -unsaturated aldehydes, no stereochemical pathway has been mentioned.⁷⁾

With a view to compare the reactivities of the stannyl reagent with those of the corresponding silyl compound, the reaction of trimethylsilylmethyl lithium 11 with 2a was investigated next. When the reaction was carried out at -78°C ,

the product was a silyl compound 12, while a silyl compound 13 was obtained, along with a fair amount of 12, when the reaction was carried out at room temperature for 2 h. It has been reported that silyl or phosphoryl carbanions having ethoxycarbonyl group react with α,β -epoxy ketones to afford vinyl oxiranes, which might be produced through an intermediate corresponding to 12.⁸⁾ Evidently, the second molecule of the reagent attacked the oxirane ring rather than silicone atom of 12, in contrast with the reaction of the stannyl counterpart. Further, the silyl compound 12 resisted to the reaction by potassium hydroxide, while it produced an unidentifiable product upon treatment with BF_3 -etherate.

Since α,β -epoxy ketones can be prepared easily from the corresponding α,β -unsaturated ketones, the present reaction could be a convenient method for the preparation of β,γ -unsaturated ketones by inserting methylene group between olefinic and carbonyl groups of α,β -unsaturated ketones.



References and Footnotes

- 1) (a) E. Murayama, T. Kikuchi, K. Sasaki, N. Sootome, and T. Sato, *Chem. Lett.*, 1984, 1897; E. Murayama, T. Kikuchi, H. Nishio, M. Uematsu, K. Sasaki, N. Sootome, and T. Sato, *J. Chem. Soc. Jpn.*, 1985, in press. (b) H. Matsuoka and T. Sato, 31st Symposium on Organometallic Chemistry Japan, Tsukuba, October 1984, p. 178, Abstr. No., B117.
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- 3) Although the NMR datum was consistent with the proposed structure, it was not completely identical with those reported for either cis or trans structure.⁴⁾
- 4) J. Fayos, J. Clardy, L. J. Dolby, and T. Farnham, *J. Org. Chem.*, 42, 1349 (1977); L. S. Hegedus and R. K. Stiverson, *J. Amer. Chem. Soc.*, 96, 3250 (1974).
- 5) ¹H-NMR (400 MHz, CDCl_3 -TMS), δ 0.57 (dd, 1H, $J = 7.3$ and 5.2 Hz), 0.79 (dd, 1H, $J = 5.2$ and 10.7 Hz), 0.95 (bs, 1H), 1.16 (dd, 1H, $J = 7.3$ and 10.7 Hz), 1.31 (s, 3H), 1.36 (s, 3H), 1.62 (s, 3H), and 1.79 (bs, 1H). ¹³C-NMR (CDCl_3 -TMS), δ 14.6 (t), 18.6 (q), 26.9 (q), 28.6 (q), 32.7 (d), 49.9 (s), and 62.5 (s). dd: doublet of doublet.
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- 7) E. J. Corey and P. Ulrich, *Tetrahedron Lett.*, 1975, 3685.
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