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THE REACTION OF β-STANNYL CARBONYL COMPOUNDS WITH LEWIS ACIDS

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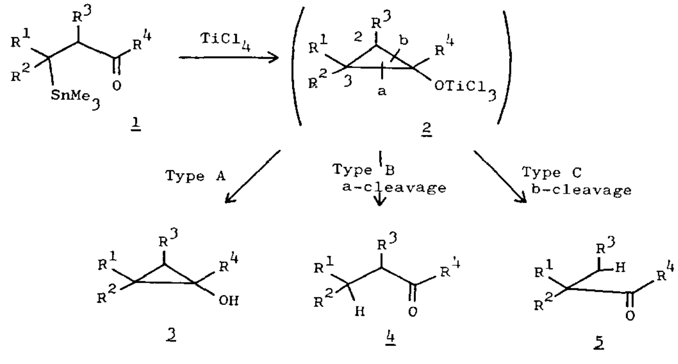
β-Stannyl carbonyl compounds, when treated with Lewis acids, afforded cyclopropane derivatives or ketones, and the reaction was applied to the synthesis of β,γ-enones from α,β-enones.

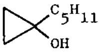
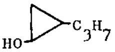
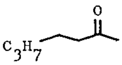
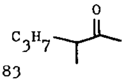
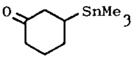
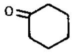
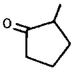
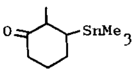
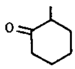
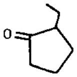
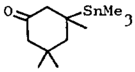
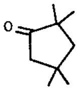
Tin compounds having an electron-deficient center at the γ-position usually undergo the cyclization to produce cyclopropanes.1) As part of our study of using cyclopropane ring system as a three-carbon building block, we studied the reaction of several types of tin compounds capable of developing cationic center at the γ-position, and found that diverse types of reaction occurred depending upon the mode of formation of the cationic center as well as upon the substitution pattern of the tin compounds.2) In the present study, we investigated the reaction of β-stannyl carbonyl compounds, induced by $TiCl_4$ or $TiCl_4/Me_3SiSPh$.

When the β-stannyl carbonyl compounds 1 were treated with $TiCl_4$, cyclopropanols 3 or ketones 4 or 5 were obtained depending upon the substitution pattern of the substrate. The results are shown in Table 1. All the reactions seem to proceed through a common intermediate 2, shown in Scheme 1. If the tin-bearing carbon was primary (R^1, R^2=H), or, if the carbonyl group was aldehyde (R^4=H), the reaction terminated at this stage, producing 3 as final product (Type A). However, if these requirements were not met, C-C bond fission at either a (Type B) or b (Type C) position proceeded producing ketones 4 or 5. The acid or base-induced ring opening of



Scheme 1

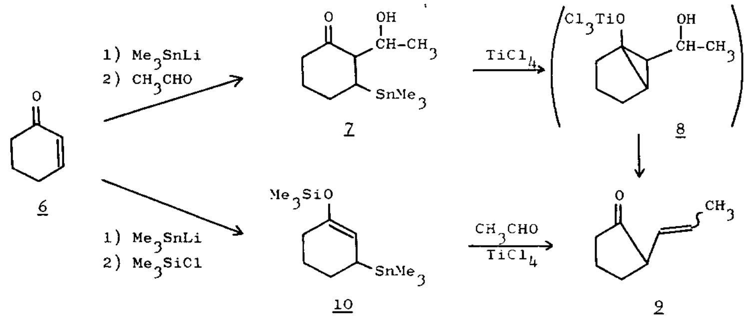
Table 1. Reaction of 1 with $TiCl_4$.[a]

Starting material (1)				Product			Yield (%)
R^1	R^2	R^3	R^4	Type A (3)	Type B (4)	Type C (5)	
H	H	H	C_5H_{11}				70[b,c]
C_3H_7	H	H	H				100[b,d]
C_3H_7	H	H	CH_3		 17 :	 83	46[e]
					 25 :	 75	65[e]
					 87 :	 13	45
							54

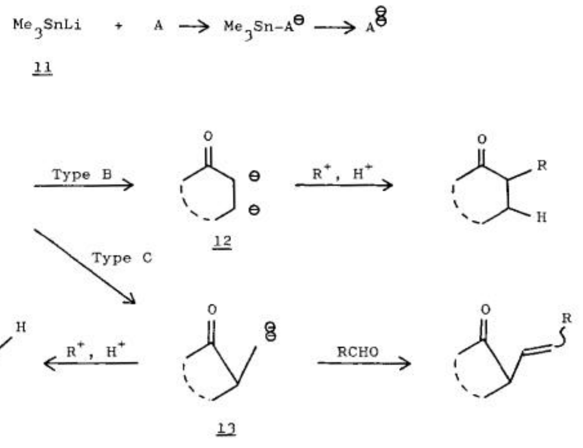
a) To a 0.1 M CH_2Cl_2 solution of 1 was added an equivalent of a 0.5 M CH_2Cl_2 solution of $TiCl_4$ at -78 °C. The mixture was stirred for 15 min, poured onto a $NaHCO_3$aq, and extracted with CH_2Cl_2. The products were purified on a silica gel column ($CHCl_3$). b) The structure was speculated from the NMR data of the crude product. c) Tributylstannyl compound was used. d) Cis-trans mixture. e) Reaction at 0 °C.

cyclopropanols or their derivatives has been well documented,[3] and the ring opening usually proceeds with proton attack predominantly on the less substituted carbon (C2 or C3 in 2). The present results are in accord with the general trend.

Since the direction of the bond cleavage was not always selective, we attempted to introduce a leaving group into 2, in order to attain the selectivity. When the β-stannyl enolate, prepared by the conjugate addition of Me_3SnLi to α,β-enone 6, was reacted with acetaldehyde, an aldol product 7 was obtained as a diastereomeric mixture in 75% yield. Treatment of 7 with $TiCl_4$ afforded β,γ-enone 9 in 74% yield as a mixture of cis : trans = 1 : 3.[4] The reaction could reasonably be schemed as involving hydroxy cyclopropanol 8. Evidently the tin-carbon bond attacked the carbonyl carbon rather than the alcohol carbon, both at the γ-position from the stannyl group, and the presence of the hydroxyl leaving group induced the selective bond cleavage. The same product was obtained when a silyl enol ether 10 was reacted with acetaldehyde in the presence of $TiCl_4$. The formation of the product 9 as a cis-trans mixture might be ascribable to the poor diastereoselectivity in the aldol condensation.[5]



Since the tin-bearing carbon behaves as a carbanion, Me_3SnLi (11) could be regarded as a reagent capable of



Scheme 2

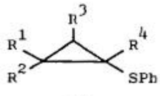
imparting double anion character to a substrate A as illustrated in Scheme 2. Thus, the α,β-enone is equivalent to α,β-dianion 12 in the Type B reaction, while it is equivalent to β,β-dianion 13 in the Type C reaction. The present reaction could be contrasted to the conventional method of cyclopropanol preparation through the Simmons-Smith cyclopropanation of enol derivatives.$^{6)}$ The reaction is synthetically attractive because the β-stannyl carbonyl compounds are easily available by the conjugate addition of a stannyl anion to α,β-enones, and more importantly, the net reaction is the introduction of two nucleophiles into an α,β-enone, sometimes with carbon skeleton rearrangement.

Although the cyclopropane intermediate was not always isolable in the TiCl$_4$-induced reaction, it was isolated as cyclopropyl phenyl sulfide 14, irrespective of the substitution pattern of the substrate, when the reaction was induced by TiCl$_4$/Me$_3$SiSPh. The results are shown in Table 2. Notably the major product from the secondary tin compound 1c was confirmed to be cis, by comparing with the authentic samples of cis and trans structure prepared by the known method.$^{7)}$ The NMR signal of the proton on the sulfur-bearing carbon of 14c appeared at lower field in cis isomer at δ 2.0 - 2.5, as compared with that of trans isomer which appeared at δ 1.75 - 2.1. In view of the NMR signals of 14d in these regions, the product was also concluded as cis-predominant. The reaction of 1g gave a stereochemically homogeneous product 14g, for which we assigned the cis structure in accordance with the previous results. Presumably the reaction proceeded through a thionium ion 15. Despite the previous report$^{1)}$ that the nucleophilic attack by the

Table 2. Reaction of 1 with Me$_3$SiSPh/TiCl$_4$.$^{a)}$

	Starting material 1				Yield of product 14 (%)	Cis/trans
	R^1	R^2	R^3	R^4		
a	H	H	H	H	78$^{b)}$	
b	H	H	H	CH$_3$	92$^{b)}$	
c	CH$_3$	H	H	H	84	98/2
d	C$_3$H$_7$	H	H	H	76	94/6
e	H	H	CH$_3$	H	52	71/29
f	CH$_3$	CH$_3$	H	CH$_3$	54	
g	C$_3$H$_7$	H	H	CH$_3$	56$^{c)}$	

a) To a 0.1 M CH$_2$Cl$_2$ solution of 1 and Me$_3$SiSPh (1 eq) was added an equivalent of a 0.5 M CH$_2$Cl$_2$ solution of TiCl$_4$ at -78 °C. The mixture was stirred for 15 min, and worked up in the same way as described in Table 1, footnote a).
b) Tributylstannyl compound was used.
c) Reaction at 0 °C.



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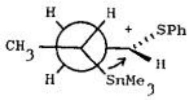

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tin-carbon bond to form cyclopropane ring proceeds with inversion at the attacking carbon, the predominant formation of the less stable isomer of cis structure could not be rationalized by this reaction scheme. As a possible alternative, we assumed a reaction scheme proceeding with retention of the tin-bearing carbon as shown in 15. In an intermediate with methyl and thionium moiety in anti conformation, the attack by the front lobe of the tin-carbon bond could lead to the cis product. An example of the reaction proceeding with retention of the tin-bearing carbon has recently been reported in the cyclization to five-membered ring system.⁸⁾ Further manipulation of the product as a synthetic synthon is currently under way.

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