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THE REACTION OF α-STANNYLMETHYLLITHIUM WITH ESTERS

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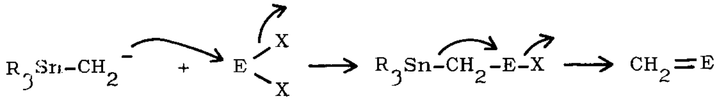
Ketonic compounds were prepared from esters using α-stannylmethyllithium as the reagent.

In our previous paper,1) we investigated the reaction of trialkylstannylmethyllithium with several electrophiles, and observed that the stannyl compound is a versatile reagent for the preparation of α-olefins from carbonyl compounds, cyclopropanes from oxiranes, allyl alcohols from α-chloro ketones, and cyclopropanols from α,β-epoxy ketones. In the present study, we investigated the reaction of this reagent with esters, and found that the reaction is useful as a preparative method of ketonic compounds from esters.

The reaction of conventional organometals with esters of simple alcohols usually produces tertiary alcohols because the primarily-produced ketones are more reactive than the starting esters. When appropriate precautions were adopted to stabilize the ketonic intermediate, as enolate for instance, the reaction could be stopped at the stage of ketone formation. The successful ketone preparations through the manipulation of alcohol moiety2) or solvent system3) are mostly designed on this concept. In all the reactions developed recently in our laboratory utilizing α-stannylmethyl carbanion 1, the reagent behaved as a methylene double anion equivalent 2, due to the carbanionic nature of the tin-bearing carbon (Scheme 1). In view of this reasoning, we envisioned that the reagent would give a stable enolate 3 when applied on an ester molecule. Actually the ketone formation was achieved using two equivalents of trimethyl (1a) or triphenylstannylmethyllithium (1b) as the reagent. The results are shown in Table 1. In case of octanoate, a minor amount of olefin 5 was formed as a byproduct when 1a was used as a reagent (run 1), while selective formation of ketone 4 was achieved with 1b (runs 2-3).

The reaction is assumed to proceed via an α-stannyl ketone 6 as the primary product, followed by the attack of the second molecule of the reagent either at



1 a: R = Me
b: R = Ph

$$\boxed{\begin{array}{c} CH_2^{=} \\ \\ \underline{2} \end{array}}$$

Scheme 1

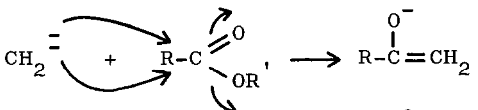


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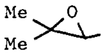
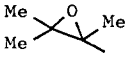
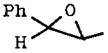
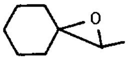
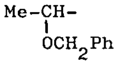
Table 1. Preparation of Ketones from Esters.

Run	Starting material R^1COOR^2		Reagent	Yield of product (%)	
	R^1	R^2		R^1COCH_3 4	R^1-C(=CH$_2$)CH$_3$ 5
1	Me(CH$_2$)$_6$-	Et	1a	58	21
2	"		1b	57	0
3	"	Me	1b	73	0
4	Ph	Et	1a	84	0
5	"		1b	21	0
6	c-C$_6$H$_{11}$-	Me	1a	48	0
7	"		1b	15	0
8	PhCH=CH-	Et	1b	80	0
9		Et	1a	80	0[a]
10		Me	1a	12	0
11		Me	1a	51	0
12		Et	1a	82	16
13	"		1b	10	0[a]
14	 Me-CH(OCH$_2$Ph)-	Et	1a	75	11[b]

a) Starting material (13% and 26%, respectively) was recovered.

b) Three-minute reaction.

the carbonyl carbon (path a) or at the tin atom (path b) of 6. The second step proceeded even when only one equivalent of the reagent was used (the starting ester was partly recovered in this case). This contrasts to the reaction of α-silyl carbanion, which terminates at the stage of α-silyl ketone formation[4)] with α-proton abstraction.[5)] While the path b gives the ketone 4 through an enolate, the path a gives a bisstannyl compound 7, which decomposes to the olefin 5 on a silica gel column. Since the tin atom is known to be more susceptible to the nucleophilic attack when the substituent is phenyl than when the substituent is methyl,[6)] it is predictable that the ketone formation is more selective with the triphenyl reagent 1b as compared with the trimethyl reagent 1a. The esters having bulky group at α-position are more likely to produce ketones (runs 4-7), probably because the path a is disfavored due to the steric effect. Notably, however, the reagent 1b gave inferior results in these cases.

The present reaction was then applied on esters having oxygen substituent at α-position (runs 9-14). Probably because of the chelating effect of lithium cation with oxygen functions as shown in 8, the path a was retarded effectively

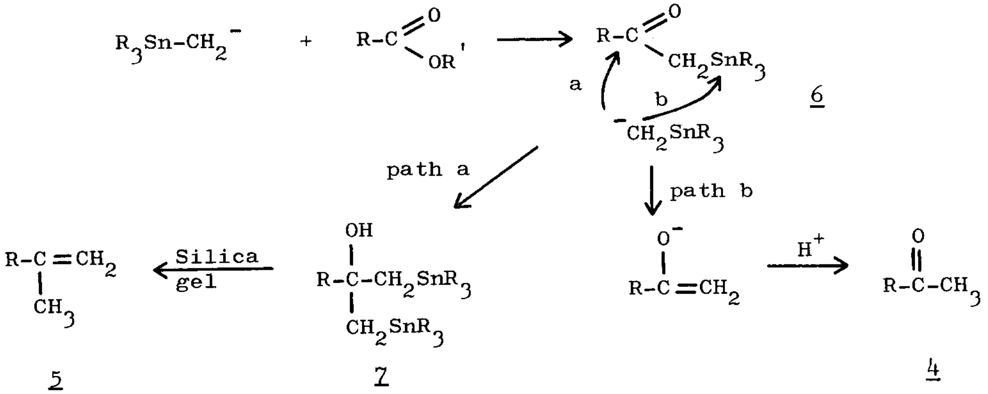
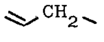
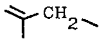
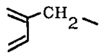


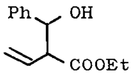
Table 2. Preparation of Aldols from Esters.

Run	Starting material				Reagent	Yield of product	Diastereomer[a] ratio
	R^1COOR^2		R^3COR^4			$R^1COCH_2\underset{OH}{C}{<}^{R^3}_{R^4}$ 9	
	R^1	R^2	R^3	R^4			
15	Ph	Et	Ph	H	1a	71	
16	"		Et	H	1a	86	
17	n-C_7H_{15}-	Me	Ph	H	1b	98	
18	"		Et	H	1b	66	
19	"		Me	Me	1b	61	
20	Me-CH- OCH$_2$Ph	Et	Ph	H	1a	60	2 : 1
21	"		Me	H	1a	60	3.2 : 1
22	"		Et	H	1a	66	4.5 : 1
23	"		H	H	1a	51[b]	
24		Et	Ph	H	1a	c)	
25		"	"		1a	69	
26		"	Me	Me	1a	64	

a) Determined by NMR with a shift reagent Eu(fod)$_3$.

b) $[\alpha]_D = -13.6°$.

c) Product 10.



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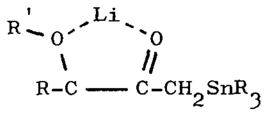

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even with the trimethyl reagent, and the ketones were obtained selectively. The general trend that the triphenyl reagent induces the selective formation of ketone, despite with lower yield, was also observed in run 13. The reaction from the optically active lactate derivative gave an optically active benzyloxy ketone (run 14). It was found that the reaction was very fast: the three-minute reaction gave no less yield than the three-hour reaction. Remarkably the optical activity of the product was independent upon the reaction time ($[\alpha]_D \approx -19.5^o$), thus indicating that no racemization took place during the reaction. The HPLC analysis on a chiral column⁷⁾ indicated that the product was 100% optically pure.

When the reaction mixture of 1 with esters was treated with carbonyl compounds in the same pot, aldol products 9 were obtained (Table 2). In contrast to the conventional aldol reaction starting from ketones, no problem concerning with the regiochemistry arises, and no alternative regioisomer was identified even in aliphatic system (runs 17-19).

The β,γ-unsaturated esters having a substituent on β-position also underwent the same type reaction (runs 25-26). With a β-unsubstituted ester (run 24), however, the reagent abstracted an α-proton, producing an aldol 10 in 82% yield.

General Procedures: To a solution of 1a(1) or 1b(8) (2 eq) was added an ester (1 eq) at -78°C, and the solution was stirred for 0.5-3 h at this temperature. For ketone preparation, the solution was quenched by NH_4Cl_{aq}, and worked up. For aldol preparation, a carbonyl compound (1 eq) was added to the solution at -78°C, and stirred for another 1 h before workup.

References and Footnotes

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5) M. Demuth, Helv. Chim. Acta, 61, 3136 (1978).
6) J. L. Wardell, J. Organomet. Chem., 9, 89 (1967).
7) Chiralcel OB (Daicel Chemical Industries, Ltd), 25 x 0.46 cm, with hexane-2-propanol (9 : 1). The authors are indebted to Dr. H. Ohnishi, Daicel Chemical Industries, Ltd., for the analysis.
8) Prepared from triphenylstannylmethyl iodide and n-butyllithium at -50°C in diethyl ether.

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