

HIGHLY STEREOSELECTIVE REACTION OF α -METHYLTHIO ALDEHYDES WITH ALLYL-
TRIPHENYLSTANNANE : SYNTHESIS OF anti- β -METHYLTHIO ALCOHOLS

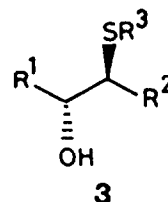
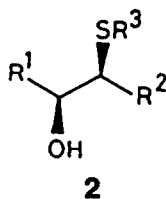
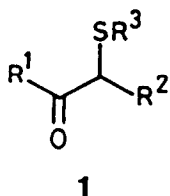
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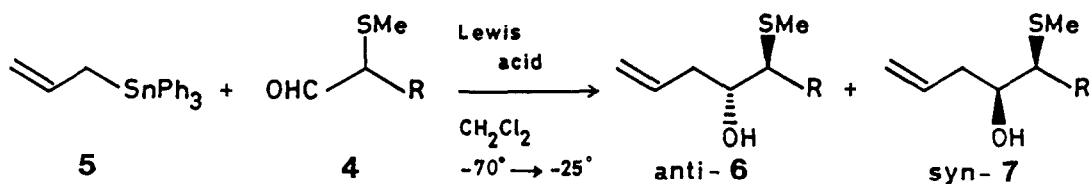
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Summary: The reaction of α -methylthio aldehydes **4** ($R=1^\circ$, 2°) with allyltriphenylstannane **5** in the presence of SnCl_4 gave anti- β -methylthio alcohols **6** in excellent selectivity.

In connection with the recent findings that conversion of β -alkylthio alcohols **2** and **3** into olefins¹ or epoxides² proceeds with complete stereospecificity, we examined the synthesis of the stereochemically pure **2** and **3** by reduction of the corresponding α -methylthio or α -phenylthio ketones **1** and found that $\text{Zn}(\text{BH}_4)_2$ reduction gave the expected anti-**3** (chelation-controlled products) only in limited cases, while L-Selectride reduction afforded syn-**2** (non-chelation-controlled Felkin-Anh products) with remarkably high stereoselectivity in every case, except when R^1 was secondary.³ These results are in sharp contrast with those obtained in the reduction of α -alkoxy ketones.⁴ The poor anti-selectivity observed in $\text{Zn}(\text{BH}_4)_2$ reaction could be ascribed to weaker affinity of sulfur than oxygen to Zn^{2+} and excellent syn-selectivity observed in L-Selectride reduction to a large contribution of a methylthio group in stabilizing a Felkin-Anh model.⁵



Taking into accounts of the unique characteristics of sulfur function in alkylthio ketones **1** observed above, we then focused our attention to the alkylation of α -methylthio aldehydes **4**⁶ with allyltriphenylstannane **5** in the presence of SnCl_4 . These reagents were chosen since they have a strong

Table I. Allylation of α -Methylthio Aldehyde 4 with Allyltriphenylstannane 5

R	Entry	SnCl ₄ (2 eq.) ^{*1}		Entry	BF ₃ ·Et ₂ O (2 eq.)	
		6	7 (Yield %)		6	7 (Yield %)
n-Bu	1	97	3 (88)	7	82	18 (51)
CH ₂ CH ₂ Ph	2	94	6 (80)	8	79	21 (62)
i-Pr	3	96	4 (94)	9	16	84 (75)
i-Pr	4	97	3 (82) ^{*2}		—	
c-Hexyl	5	95	5 (99)	10	13	87 (65)
Ph	6	59	41 (70)	11	20	80 (97)

*1 After the reaction had been completed, the mixture was treated with 10% HCl to decompose Sn-complex.

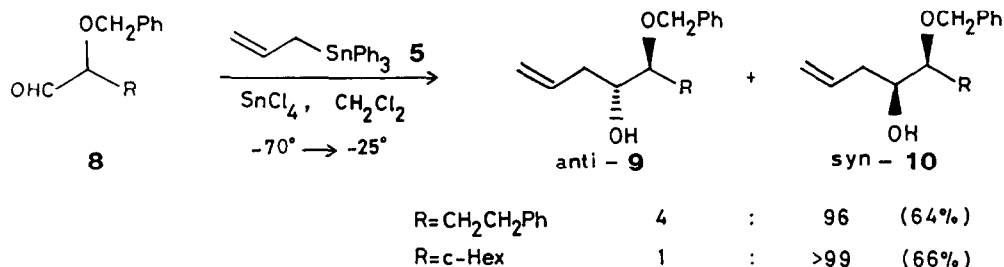
*2 One eq. of SnCl₄ was used.

affinity to sulfur.⁷ Alkylation using BF₃·Et₂O/CH₂Cl₂ incapable of bis-allylation⁸ was also carried out for comparison. The results were shown in Table I.

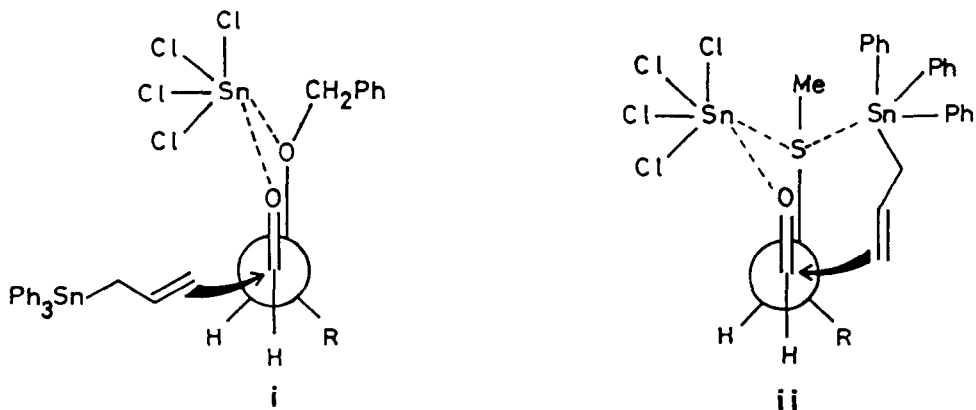
When R was primary or secondary alkyl group, all the reactions examined in the presence of SnCl₄ gave anti β -methylthio alcohols 6 with excellent stereoselectivity in good yield, except when R was a phenyl group (entry 6). It should be noted that anti-6 was obtained stereoselectively even when one equivalent of SnCl₄ was used (entry 4). The relative stereochemistry of the products 6 and 7 was determined after conversion into the corresponding epoxides (Me₃O⁺BF₄⁻; 2.5-5% aq. NaOH. J value of epoxide protons: trans 2.2-2.3 Hz; cis 4.1-4.4 Hz), because the reaction was known to proceed essentially in S_N2 fashion^{2c,3}.

The observed high anti-directing selectivity (Lewis acid: SnCl₄) is quite remarkable since an opposite selectivity giving syn-products has been observed in alkylation of the oxygen analogue of 4. Namely, reactions of α -benzyloxy aldehydes 8 with allyltrimethylsilane in the presence of SnCl₄⁹ or with allyltributylstannane in the presence of MgBr₂ or TiCl₄¹⁰ have been reported to afford syn- β -benzyloxy alcohols 10 with high stereoselectivity. Alkylation of 8 having the same R-group with 4 under the same reaction conditions

($\text{SnCl}_4/\text{CH}_2\text{Cl}_2$) used in the reaction of **4** was undertaken. Here again, syn-10 were obtained, which clearly demonstrated that syn-selectivity observed in **8** was not affected by a small difference in alkylating agent, R group or reaction conditions.



It is quite reasonable to consider a SnCl_4 -mediated cyclic transition state **i** for syn-directing reaction of **8**.⁹ However, further elaboration should be necessary to account for anti-selective additions observed in **4**. A model **ii** involving a unique four co-ordinated sulfur is considered to be a plausible candidate. Initially, the sulfur and oxygen functions in **4** may co-ordinate with the more reactive SnCl_4 than **5** forming the same type of a transition state as was considered in the reaction of **8** (see **i**), which should be more rigid and stable than **i** due to a strong affinity between sulfur and tin. In this chelated model, SnCl_4 would be located on the opposite side of an R group. Here, the lone pair remaining on the sulfur atom is highly expected to attack allylstannane **5** forming **ii**. The fact that one equivalent of SnCl_4 is enough for completion of the reaction may eliminate a contribution of SnCl_4 bis-adducts of any kind, which supports the intermediacy of **ii**. Once **ii** is formed, internal alkylation should take place irreversibly producing anti-**6** even if R is a bulky secondary alkyl group.



Alkylation using $\text{BF}_3 \cdot \text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$ incapable of bis-ligation presumed to proceed through a Felkin-Anh model⁵ giving anti-products, since as is

apparent from our previous work³ even a methylthio group contributes significantly in stabilizing the Felkin-Anh model. In fact, when R were primary, the expected anti-6 were obtained although the selectivity was not so satisfactory(Entry 7, 8). However, to our surprise, when R were i-propyl, cyclohexyl and phenyl groups, syn-7 were obtained as main products(Entry 9-11). The reason is remained unknown.

REFERENCES AND NOTES

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