Synergistic Effect of Multichiral Centres. Chelation Control *vs.* Acetal Template in 1,3-Asymmetric Induction

Yoshinori Yamamoto* and Jun-ichi Yamada

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

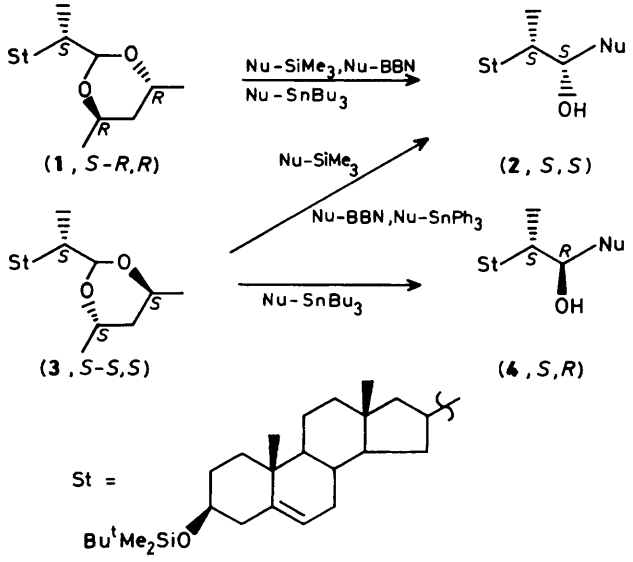
The allylation of the β-siloxyacetal (**5**), (*S–R,R* isomer) in the presence of $TiCl_4$ gave the chelation adduct (**6**) with very high selectivity, while the (*R–R,R*) isomer (**8**) also produced the chelation adduct (**9**), indicating that the 1,3-asymmetric induction is dictated by chelation rather than the acetal template.

We recently reported that (**1**) (*S–R,R* isomer) gave (**2**) upon treatment with nucleophiles, while (**3**) (*S–S,S* isomer) also produced (**2**) when treated with organometallic reagents with low nucleophilicity but afforded (**4**) with organometallic reagents with high nucleophilicity[1] (Scheme 1). The high asymmetric induction from (**1**) to (**2**) is a reflection of the synergistic effect of the 1,2- and 1,3-chiral centres. The conversion of (**3**) into (**2**) indicates loss of the effect of the 1,3-chiral centre. The question of whether multichiral centres in the same reactant exert a synergistic effect upon asymmetric induction or offset one another has not been investigated systematically.[2] We now report a synergistic effect of two 1,3-chiral centres.

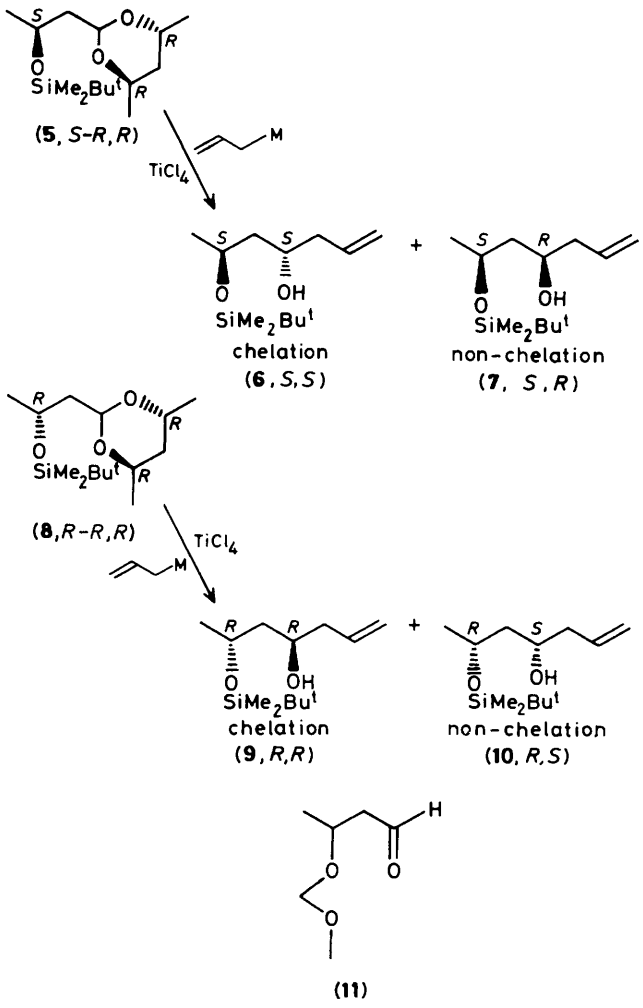
The cyclic acetal derivatives, (**5**) (*S–R,R*) and (**8**) (*R–R,R*), were prepared from the corresponding methyl (*S*)- and (*R*)-3-hydroxybutyrates, respectively.[3]† Allylation with several allylmetal reagents in the presence of $TiCl_4$, followed by the usual work-up,[4] gave the homoallyl alcohols in good yields (Scheme 2). The results are summarized in Table 1.‡

The (*S–R,R*) isomer (**5**) gave the chelation adduct (**6**) (*S,S* isomer) with very high stereoselectivity regardless of the nucleophilicity of the reagent (entries 1—3). This is reasonable, since the effects of both the chelation and the acetal template operate in the same direction to enhance the 1,3-asymmetric induction. The reaction of (**8**) (*R–R,R* isomer) also produced the chelation adduct (**9**) (*R,R* isomer) predominantly (entries 4 and 5). If the acetal template had dictated chiral induction, the non-chelation isomer (**10**) (*R,S*) would have predominated. Therefore, it is clear that 1,3-asymmetric induction is dictated primarily by the chelation, rather than the acetal template.

The relatively low selectivity of allyltributyltin compared with that of allyl-9-BBN (70:30 *vs.* 90:10) reflects the high nucleophilicity of the tin reagent.[1] The boron reagent reacts after bond breaking in the acetal template, thus the chiral induction is completely dictated by the chelation (entry 5 *vs.*



Scheme 1. Nu = nucleophile



Scheme 2

† (*R*)- and (*S*)-3-(methoxy)-methoxybutanals were converted into the corresponding acetals, which were partially hydrolysed to give the corresponding 3-hydroxyacetals. Silyl protection of the resulting hydroxyacetals gave (**5**) and (**8**).

‡ Structures were determined as described previously (ref. 3). The adducts were hydrolysed to the 1,3-diols with Bu_4NF. These diols were converted into the corresponding 1,3-dioxane derivatives with *p*-nitrobenzaldehyde.

Table 1. $TiCl_4$ mediated allylation of β-siloxyacetals.[a]

Entry	β-Siloxyacetal	M in allylmetal reagent	Product ratio[b] Chelation : Non-chelation	Total yield /%	Chirality of the major isomer[c] Template	Chirality of the major isomer[c] Chelation
			(**6**) : (**7**)			
1	(**5**)	$SnBu_3$	94 : 6	88	+	+
2	(**5**)	$SiMe_3$	94 : 6	82	+	+
3	(**5**)	BBN[d]	90 : 10	90	+	+
			(**9**) : (**10**)			
4	(**8**)	$SnBu_3$	70 : 30	88	−	+
5	(**8**)	BBN[d]	90 : 10	92	−	+
6	(**11**)	$SnBu_3$	79 : 21	93		

[a] All reactions were carried out on a 1 mmol scale as described previously.[1,3] [b] Determined by 400 MHz ^1H n.m.r. spectroscopy. [c] The chirality of the major isomer was (+) consistent with or (−) opposite to the chirality predicted either by the template or by the chelation concept. [d] 9-Borabicyclo[3.3.1]nonan-9-yl.

3). The related β-alkoxyaldehyde (**11**) produced moderate selectivity (entry 6).[5] It is thus clear that high 1,3-asymmetric induction (entry 1) is realized with the synergistic effect of the chelation and acetal template.

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References

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2 S. Masamune, W. Choy, J. S. Petersen, and L. R. Sita, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 1, investigated double asymmetric induction in reactions between a chiral reagent and a chiral substrate, whereas our system involves the asymmetric induction between an achiral reagent and a chiral substrate which has multi-chiral centres.

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5 M. T. Reetz and A. Jung, *J. Am. Chem. Soc.*, 1983, **105**, 4833. Although the benzyloxy protected aldehyde produced high selectivity, the selectivity decreased with the methoxymethyl protected derivatives (**11**).