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DIVERGENTLY STEREOCONTROLLED REACTION OF AN ALLYLIC SILANE BEARING AN ASYMMETRIC ETHEREAL CARBON TOWARD ALDEHYDES

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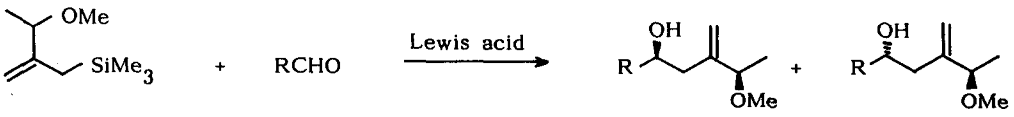
Summary: Lewis acid mediated allylation of aldehydes by an allylsilane bearing an asymmetric ethereal functionality proceeded in divergently stereocontrolled manners, i.e., $TiCl_4$ afforded the syn isomer, whereas $BF_3{\cdot}OEt_2$ afforded the anti isomer predominantly.

As one of the major problems in the field of organic chemistry, stereocontrolled bond-formation in acyclic systems has been attracting our attention. A promising approach to the solution is the reaction of allylic metal reagents.[1] Although many investigations have been made into various types of stereoselective reactions, most of them concerned the chirality and the metal coordination (reagent and/or Lewis acid) of the substrate (e.g. carbonyl compound).[2] There are a limited number of reports on the use of a coordinative functionality on the allylic metal reagent.[3] Under these circumstances, here we provide a divergently stereocontrolled reaction between aldehydes and an allylic silane bearing an asymmetric ethereal functionality, whose coordination to the Lewis acid was found to play a very important role.



(1)

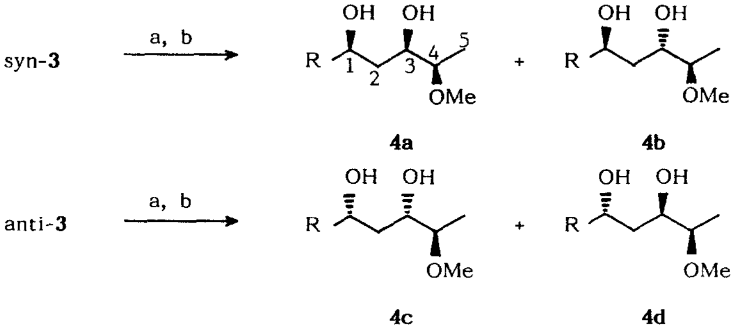
1 **2** syn-**3** anti-**3**

Racemic allylic silane **1** was employed as an asymmetric and coordinative reagent, which was readily prepared from 3-methyl-3-buten-2-ol.[4] Lewis acid mediated allylation[5] by **1** toward aldehydes **2** was expected to yield a couple of diastereomeric homoallylic alcohols, syn-**3** and anti-**3** (eq.1). Table 1 represents the results indicating a marked contrast between the product compositions given by the two Lewis acids, $TiCl_4$ and $BF_3{\cdot}OEt_2$. $TiCl_4$ afforded the syn isomer (syn-**3**) and $BF_3{\cdot}OEt_2$ afforded the anti isomer (anti-**3**) predominantly in the reaction with reactive aldehydes.

Table 1. Stereoselective reaction between **1** and **2**[a]

Entry	Aldehyde	Lewis acid	Product ratio[b]		Total yield[c]
	R		syn-**3**	anti-**3**	%
1	p-$O_2NC_6H_4$	$TiCl_4/Et_2O$[d](Ti)	100	0	98
2		$BF_3 \cdot OEt_2$ (B)	21	79	67
3	m-$O_2NC_6H_4$	Ti	100	0	88
4		B	23	77	(74)
5	o-$O_2NC_6H_4$	Ti	100	0	93
6		B	13	87	91
7	p-ClC_6H_4	Ti	100	0	70
8		B	44	56	(45)
9	o-ClC_6H_4	Ti	100	0	quant.
10		B	31	69	78
11	2,6-$Cl_2C_6H_3$	Ti	100	0	84
12		B	11	89	72
13	C_6H_5	Ti	100	0	(46)
14		B	54	46	(41)
15	p-MeC_6H_4	Ti	41	59	24
16		B	48	52	(35)
17	n-C_7H_{15}	Ti	100	0	94
18		B	29	71	(28)
19	c-C_6H_{11}	Ti	96	4	49
20		B	41	59	(25)

(a) To a mixture of **2** and Lewis acid (2 equiv.) in CH_2Cl_2 at -78° C was added **1** and the reacting solution was stirred for 3 h at -78 - 0° C. (b) The ratios were determined by ^1H NMR spectroscopy. (c) Isolated yield (NMR yield). (d) About 2 equiv. of Et_2O to $TiCl_4$ was added. Without Et_2O, the yield decreased but the ratio remained high.



Scheme 1. a $NaIO_4$, OsO_4; b $NaBH_4$.

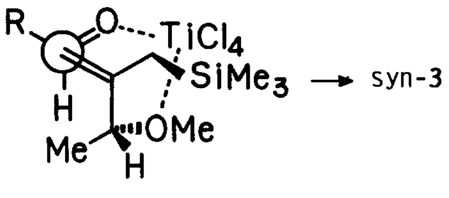
As an extreme, $TiCl_4$ and $BF_3 \cdot OEt_2$ exhibited 100% syn-selectivity and 89% anti-selectivity respectively in the case of 2,6-dichlorobenzaldehyde (entries 11 and 12). However, both the efficiency and the selectivity of the reaction decreased for less reactive aldehydes (especially entries 15 and 16).

The stereochemistry of the produced homoallylic alcohols **3** was determined by the NMR analysis of the derivatives of **3**. Both homoallylic alcohols, *syn*-**3** and *anti*-**3** (R=p-$O_2NC_6H_4$), were induced to the corresponding diastereomeric mixtures of diols **4** by applying oxidative cleavage and reduction method (Scheme 1). From the ^{13}C NMR spectra of **4**, the both 1,3- and 3,4-relative stereochemistries[6] were confirmed to be *syn*, *syn* and *anti*, *anti* for **4a** and **4b**, and *syn*, *anti* and *anti*, *syn* for **4c** and **4d**, respectively, as shown in Scheme 1. Thus, the major products from the $TiCl_4$- mediated reaction were determined to be 1,4-*syn* and those from the BF_3-mediated reaction were to be 1,4-*anti*.

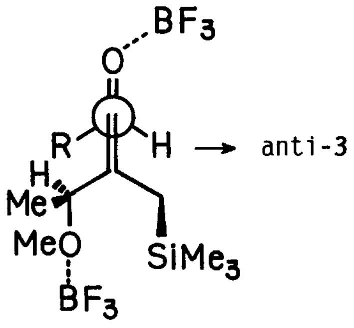
Though the reason for this divergent selectivity is not certain now, it should concern the mode of the reagent coordination to the Lewis acid. $TiCl_4$ has two acceptor sites,[2d,7] so it can complex with both the reagent **1** and the substrate **2** tightly by bridging at the transition state,[8] which is thought conformationally restricted cyclic one (like **A**).[9]

On the contrary, BF_3 has only one acceptor site[2d,7] and can hardly bind the two reactants **1** and **2** together. Therefore, the transition state will be acyclic one (like **B**), which induces the opposite stereoselection.

From the present success of the divergent 1,4-stereoinduction, to utilize the coordination of the metallic reagent to an appropriate Lewis acid can be a new way to control stereoselectivity in acyclic reaction systems. Further application and improvement of the reactions are now in progress as well as mechanistic details.



A



B

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6. Selected ^{13}C NMR data of **4** are collected in Table 2 below. The relative shift of the each value can be explained by the hydrogen-bond and the conformational congestion. For details, see, Kiyooka, S.; Kuroda, H.; Shimasaki, Y. Tetrahedron Lett. **1986**, 27, 3009; Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. J. Org. Chem. **1979**, 44, 4294.

Table 2. tb} 6,8,2

Diol	Chemical Shift/ppm					assignment	
	C_1	C_2	C_3	C_4	C_5	1,3	3,4
4a	76.0	41.6	73.6	80.2	14.6	syn	syn
4b	70.9	39.5	70.2	79.2	13.3	anti	anti
4c	73.9	40.5	73.6	79.3	13.2	syn	anti
4d	72.3	40.6	70.5	79.9	14.5	anti	syn

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