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LETTERS

Chelation control through the coordination of an olefinic π-bond to Lewis acid[†]

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Abstract

The reaction of a 1:1 mixture of *ortho*-alkenylbenzaldehydes **3** and their *para*-isomers **4** with Bu_3SnH (1 equiv.) in the presence of Me_3Al (1 equiv.) resulted in very high (>10:1) to good (3.4:1) chemoselective reduction of **3**, giving the *ortho*-alkenyl benzyl alcohol **5** selectively. Similarly, the highly chemoselective allylation of **3d** in the presence of **4d** was observed when the mixture was treated with allyltributyltin/Me_3Al. The chemoselectivities are most probably due to the bidentate chelation of the Lewis acid to an olefinic π-bond and a lone pair of aldehydes. © 2000 Published by Elsevier Science Ltd.

Keywords: chelation; alkenes; Lewis acid; carbonyl compounds; reduction; allylation.

The Lewis acid mediated chelation control is one of the most fundamental and practically important concepts in modern organic chemistry.[1] It is well accepted that the chelating controlled reaction proceeds through the coordination of a *lone electron pair of heteroatoms*, such as an oxygen of an aldehyde or a nitrogen atom of an imine, to a Lewis acid. We recently reported that chemoselective reduction and allylation of certain acetylenic aldehydes proceeded through bidentate chelation of Lewis acids to *π-electrons of C–C triple bonds* and a lone pair from an oxygen atom of the aldehydes.[2] It was thought necessary to inspect whether the concept of the chelation control between π-electrons and n-electrons is applicable to systems other than the combination between C–C triple bonds and aldehydes. We wish to report here that chemoselective nucleophilic attack of the aldehyde **1** takes place in the Lewis acid mediated reaction of a 1:1 mixture of **1** and **2** (Eq. (1)); most probably the bidentate chelation of Lewis acids between π-electrons of an olefinic π-bond and n-electrons of aldehyde is a key for this chemoselective reaction.

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[†] This paper is dedicated to Professor Harry H. Wasserman on the occasion of his 80th birthday.

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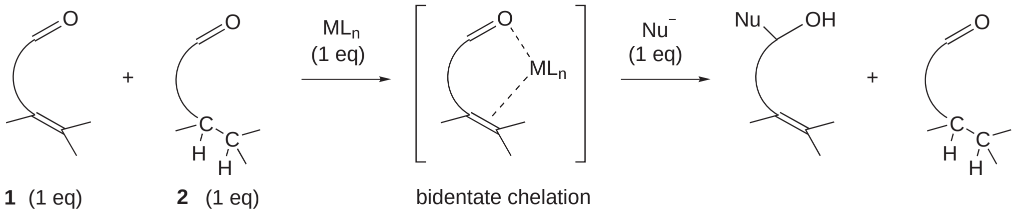
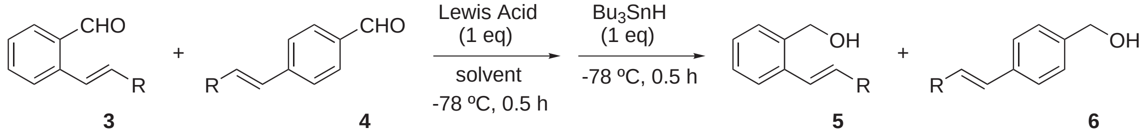


(1)

We examined the reaction of an equimolar mixture of the olefinic aldehyde **3** and its *para*-isomer **4** with Bu_3SnH (1 equiv.) in the presence of Lewis acids (1 equiv.) (Eq. (2)). The results are summarized in Table 1. When we used $BF_3{\cdot}OEt_2$ as a Lewis acid, no selectivity was obtained in the reaction of **3a** and **4a**, and the corresponding reduced products **5a** and **6a** were obtained in a ratio of 1:1 (entry 1). However, the reactions promoted by aluminum-based Lewis acids afforded **5a** as a major product (entries 2–4), and a good chemoselectivity was observed when we used Me_3Al in CH_2Cl_2; **5a** was obtained in 74% yield along with the recovered **3a** (12% yield), and **6a** was only obtained in 16% yield along with the recovered **4a** (59%) (entry 4).[3,4] Although higher chemoselectivity was obtained by using $GaCl_3$ as a Lewis acid in the analogous competitive reduction using *ortho*-alkynylbenzaldehydes and their *para*-isomers,[2] a low selectivity was observed in the present reaction (entry 5). While the better selectivity (6.9:1) was obtained with $CuOTf{\cdot}(C_6H_6)_{0.5}$, the reaction was heterogeneous due to the low solubility of $CuOTf{\cdot}(C_6H_6)_{0.5}$ in CH_2Cl_2, resulting in low chemical yield of **5a** (entry 7). The selectivity in the Me_3Al promoted reductions was improved to 5.3:1 by using toluene as a solvent (entry 8). The



(2)

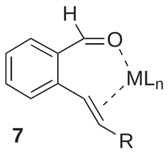
a: R = H **b:** R = Me3Si **c:** R = Me **d:** R = Ph

Table 1
Lewis acid mediated competitive reduction of **3** and **4** with Bu_3SnH[a]

Entry	Substrate			Lewis acid	Solvent	Yield[b]		Yield[b]		Ratio
	R	3	4			5	%	6	%	5:6
1	H	**3a**	**4a**	$BF_3{\cdot}OEt_2$	CH_2Cl_2	**5a**	41	**6a**	42	1.0:1
2	H	**3a**	**4a**	$EtAlCl_2$	CH_2Cl_2	**5a**	56	**6a**	22	2.5:1
3	H	**3a**	**4a**	Et_2AlCl	CH_2Cl_2	**5a**	45	**6a**	15	3.0:1
4	H	**3a**	**4a**	Me_3Al	CH_2Cl_2	**5a**	74	**6a**	16	4.6:1
5	H	**3a**	**4a**	$GaCl_3$	CH_2Cl_2	**5a**	49	**6a**	17	2.9:1
6	H	**3a**	**4a**	$Sc(OTf)_3$	CH_2Cl_2	**5a**	59	**6a**	18	3.3:1
7	H	**3a**	**4a**	$CuOTf{\cdot}(C_6H_6)_{0.5}$	CH_2Cl_2	**5a**	26	**6a**	4	6.9:1
8	H	**3a**	**4a**	Me_3Al	Toluene	**5a**	84	**6a**	16	5.3:1
9	H	**3a**	**4a**	Me_3Al	Hexane	**5a**	70	**6a**	21	3.3:1
10	Me_3Si	**3b**	**4b**	Me_3Al	Toluene	**5b**	62	**6b**	18	3.4:1
11	CH_3	**3c**	**4c**	Me_3Al	Toluene	**5c**	72	**6c**	9	8.0:1
12	Ph	**3d**	**4d**	Me_3Al	Toluene	**5d**	69	**6d**	5	13.8:1

[a] The reaction was performed in the molar ratio of **3**:**4**:Lewis acid:Bu_3SnH = 1:1:1:1 at −78°C.
[b] Isolated yield.

selective reductions were also observed with the starting materials having other alkenyl groups and the best selectivity was obtained in the reaction of **3d** bearing a phenyl group at the terminal olefinic carbon (entries 10–12). In all the above reactions, the material balance of substrates was high. Accordingly, the selective activation of **3** is ascribed most probably to the preferred formation of the bidentate chelation **7** rather than the monodentate coordination **8**. In fact, the competitive reaction with $BF_3{\cdot}OEt_2$ (entry 1), which is believed to be a monodentate Lewis acid, produced a 1:1 mixture of the reduced alcohols. On the other hand, the use of aluminum Lewis acids which are able to act as a pentacoordinate Lewis acid predominantly gave, in general, **5**.[3–5]



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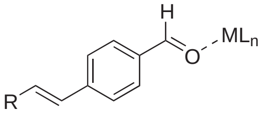

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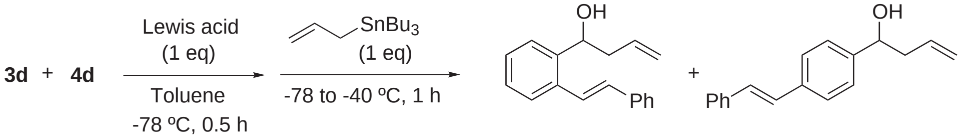
The strong chelation effect of Me_3Al upon olefinic π-bond was found also in the allylation with allyltributyltin. A 1:1 mixture of **3d** and **4d** was treated with 1 equiv. of allyltin in the presence of 1 equiv. of Lewis acid under similar reaction conditions as above. The reaction mediated by Me_3Al gave the allylation product **9** exclusively, however, the chemical yield of **9** was quite low. The use of $EtAlCl_2$, instead of Me_3Al, gave **9** in higher chemical yield with high chemoselectivity (Eq. (3)).[6]



(3)

	9	**10**	ratio **9**:**10**
Me_3Al	12%	trace	
$EtAlCl_2$	53%	4%	13.3:1

The good to high chemoselectivities observed here are most probably due to the effective bidentate chelation of alkenyl groups to Lewis acids. It is now clear that chelation between the n- and π-electrons with certain Lewis acids is operative not only in the alkyne–aldehyde system[2] but also in the alkene–aldehyde analogue. Further studies on this new type of chelation control are ongoing in our laboratory.

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6. One of the referees pointed out that the styrene double bond and the carbonyl group competed to be coplanar with the aromatic ring when they were *ortho* but not *para*. If the aldehyde rotates so that its π-system is perpendicular to the aromatic ring, then it will be more reactive. Alternatively, if the C–C double bond rotates to be perpendicular, its inductive effect would also increase the reactivity of the *ortho* situated aldehyde. Thus, as the strength of the Lewis decreases and its steric size increases, one would expect the **5**:**6** ratio to increase — just as observed. The referee suggested carrying out an IR study. Accordingly, we measured the IR spectra of substrates **3** and **4**, but no noticeable differences in the wavenumbers of the stretching vibrational absorptions for either the carbonyl groups or alkenyl groups for both compounds were obtained; for example, **3a**: 1695 cm^{-1} (C=O), 1626 cm^{-1} (C=C); **4a**: 1703 cm^{-1} (C=O), 1628 cm^{-1} (C=C); **3c**: 1697 cm^{-1} (C=O), 1650 cm^{-1} (C=C); **4c**: 1693 cm^{-1} (C=O), 1655 cm^{-1} (C=C). Consequently, we performed additional experiments in response to the referee's query. A 1:1 mixture of **3a** and **4a** with $LiAlH_4$ (0.25 equiv.) gave the reduction products **5a** and **6a** in 37% and 36% yield, respectively. This result strongly supports that the chemoselectivities observed in the reactions using Me_3Al/ Bu_3SnH or allyl$SnBu_3$ are most probably due to the chelation effect of Me_3Al.