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Stereospecific formation of deuterated homoallyl alcohols by Lewis acid-promoted reactions of allyltin and allylsilicon reagents toward aldehydes

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Abstract—Stereoselectively prepared (*Z*)-3-deuterioallyltin and (*E*)-3-deuterioallylsilicon were allowed to react with aldehydes in the presence of $BF_3{\cdot}OEt_2$. The stereospecifically afforded products were predominantly an *anti*-homoallyl alcohol from the (*Z*)-reagent and a *syn*-one from the (*E*)-reagent. These results strongly indicate both reactions proceed via a *syn*-synclinal transition state.

Allyltin and allylsilicon reagents occupy important positions in organic synthesis because of their useful reactivities and selectivities.[1] Among them, Lewis acid-promoted reaction[2] toward aldehydes is recognized as a widely applicable method due to the efficient nucleophilic introduction of an allyl group and its characteristic stereoselectivity. Innumerable reports on their application have appeared including successful asymmetric reactions.

It is known that 3,3-disubstituted allyltins predominantly afford stereospecific products under Lewis acid-promoted conditions; *syn*-homoallyl alcohols are selectively obtained from *E*-reagents and *anti*-ones from *Z*-reagents, as demonstrated recently.[3] On the other hand, 3-monosubstituted allyltins stereoselectively but not stereospecifically afford *syn*-homoallyl alcohols, i.e. both *E*- and *Z*-reagents preferentially gave *syn*-products regardless of the geometry and the substituents of the reagents.[1,2] Then, how about 3-unsubstituted allyltin? This issue has not been well addressed so far. It is taken for granted that there is no diastereomer for the unsubstituted homoallylic product. Thus, it is essential that one of the two terminal hydrogens of the allyltin should be labeled isotopically to distinguish the hydrogens and the diastereomeric products.

The steric environment at the reacting terminal position of the allyl moiety is very different between 3-substituted ones and 3-unsubstituted ones. Since the latter have no sterically demanding substituent, diastereoselectivity could not be expected, if the steric factor dominates the stereoselection. On the other hand, if the electronic and orbital factors dominate, diastereoselectivity would be observed. In other words, such stereochemical information would be very helpful to understand the most simple, fundamental and synthetically useful reaction. In addition, it would be also synthetically useful if deuterated homoallyl alcohols could be readily obtained as a regio- and stereoisomerically enriched form which would be otherwise difficult to achieve.

To undertake such investigation, the 3-deuterated allylic tin reagent was absolutely required as a stereo- and regio-defined form. In this regard, an excellent solution was reported recently by Orain and Guillemin[4] who applied the Schwartz reagent to propargyltin. Following their procedure, (*Z*)-(3-deuterioallyl)triphenyltin **1** (70% D) was successfully prepared. (*E*)-(3-Deuterioallyl)dimethyloctylsilicon **2** (93% D) was also prepared in a similar way for comparison of the metallic moieties and of the geometry of the reagents in the allylation reaction.

The reactions of these reagents toward aldehydes (**3**) were performed with the help of $BF_3{\cdot}OEt_2$ as a Lewis acid in dichloromethane.[5] Benzaldehyde (**3a**), heptanal (**3b**), and cyclohexanecarbaldehyde (**3c**), were employed

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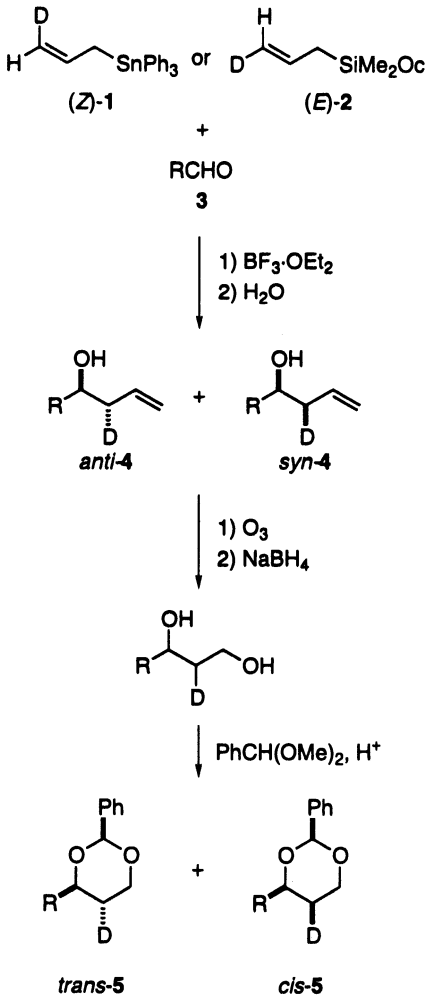
as typical aromatic, primary aliphatic, and secondary aliphatic aldehydes, respectively. The conformation and the isomeric ratio of the allylated products (**4**) could not be determined as they were except those of **4c**.[6] Accordingly, **4** were converted into cyclic benzylidene acetals (**5**)[7] via two steps (Scheme 1). Thus, the two diastereomers were undoubtedly identified and the ratios were determined by ^{1}H NMR.[8]

The results are summarized in Table 1. When (*Z*)-**1** was applied to **3a**, *anti*-**4a**[9] was successfully obtained in 80% selectivity. Aliphatic aldehydes **3b** and **3c** also exhibited



Scheme 1.

Table 1. Reaction between deuterated allyl reagents and aldehydes

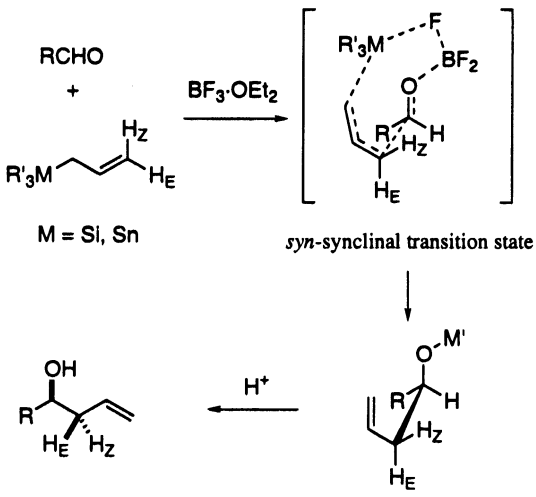
Allyl reagent	Aldehyde, R	Product, *anti*/*syn* ratio (yield, %)
(*Z*)-**1**	**3a**, Ph	**4a**, 80/20[a] (quant.)
	3b, *n*-hex	**4b**, 90/10[a] (86)
	3c, *c*-hex	**4c**, 92/8 (73)
(*E*)-**2**	**3a**, Ph	**4a**, 25/75[a] (45)
	3b, *n*-hex	**4b**, 12/88[a] (33)
	3c, *c*-hex	**4c**, 4/96 (67)

[a] Determined as a 1,3-dioxane derivative.

anti-selectivity with a little higher level than **3a**. Under similar conditions, (*E*)-**2** preferentially gave the opposite diastereoisomers. For **3a**, *syn*-**4a** was afforded in 75% selectivity,[10] and for aliphatic aldehydes **3b** and **3c**, higher *syn*-selectivities were again observed. These results unambiguously mean the Lewis acid-promoted reactions of the deuterated allyl-tin and -silicon reagents are not only stereoselective but also *stereospecific* like the reaction of 3,3-disubstituted allyltins.

It is interesting that the stereospecificity for the deuterated allyltin and allylsilicon reagents is very similar to that for 3,3-disubstituted allyltin reagents[3] in spite of their large difference in steric demand at the reacting 3-position of the allylic moiety. As mentioned above, the present good selectivity means that the major factor controlling the stereoselectivity is proven not to be the steric requirement of the substituent, but is apparently the electronic and orbital interactions. Thus, the reported antiperiplanar acyclic transition state model[11] is very improbable in these cases. In addition, the observed stereospecificity of the *syn*-homoallyl alcohol from the *E*-reagent and the *anti*-one from the *Z*-reagent is completely opposite to that expected from the six-membered cyclic transition state model. The most reasonable explanation for the present selectivity is, therefore, again a *syn*-synclinal acyclic transition state[12,13] (Scheme 2).

This feature is parallel to the computational result,[14] eight-membered cyclic transition states elicited for the mechanism of the BF_3-promoted reaction of allylsilane ($H_2C{=}CHCH_2SiH_3$) with acetaldehyde, where the most important factors determining the transition conformation were attributed to the interaction between the silicon and fluorine atoms and the *anti*-S_E2' manner[15] of the leaving silyl group. The present experiments have revealed that the most preferred approach of the allyl reagent is from the opposite direction to the coordinating BF_3, that corresponds to one of the proposed transition states in the literature.[14] Though there is no such computational result for the allyltin reagents, the present chemical results indicate that similar discussion can be applied to the reaction of allyltins.



Scheme 2.

In conclusion, diastereomerically deuterated homoallyl alcohols of both *syn*- and *anti*-forms were prepared in good to high stereoselectivity via the Lewis acid-promoted reaction of geometrically pure 3-deuterio-allyltin and allylsilicon reagents, and their stereochemistry was unambiguously determined. In addition, experimental evidence for the *syn*-synclinal transition state in the Lewis acid-promoted reaction of both unsubstituted allyltin and allylsilicon reagents toward aldehydes was obtained for the first time. The information on the transition structure is very valuable for understanding and designing stereoselective reaction systems including enantioselective ones. These results also indicate the *syn*-synclinal transition state is rather general for the Lewis acid-promoted reactions of various allylic metal reagents.

Acknowledgements

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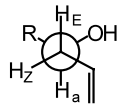
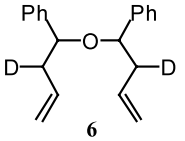
References

1. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
2. (a) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395–7426; (b) Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC Press: Boca Raton, 1996; pp. 91–184.
3. Nishigaichi, Y.; Takuwa, A. *Tetrahedron Lett.* **1999**, *40*, 109–112.
4. Orain, D.; Guillemin, J.-C. *J. Org. Chem.* **1999**, *64*, 3563–3566.
5. Typical experimental procedure: To a CH_2Cl_2 solution (1 mL) of an aldehyde (0.2 mmol) was added $BF_3{\cdot}OEt_2$ (0.4 mmol) at −78°C. After 5 min, (*Z*)-**1** (0.3 mmol) in dry CH_2Cl_2 (1 mL) was added and the mixture was stirred for 2 h at the same temperature. The mixture was poured into water and stirred vigorously. The products were extracted with ether. The ethereal solution was washed with 10% aqueous KF solution, dried over anhydrous Na_2SO_4, and condensed under reduced pressure. Homoallyl alcohol **3** was isolated by preparative TLC with hexane/diethyl ether (4/1) as eluent.
6. In the case of **4c**, as the allylic methylene protons were well separated in the NMR measurement, the configuration and the ratio of the major isomer could be determined at this stage. The coupling constant (*J*) between the methylene proton (H_E or H_Z) and the carbinol methine proton (H_a) is very helpful to determine the stereochemistry. The *anti*-isomers have larger *J* values than the *syn*-isomers; *anti*-**4a**: $J=7.3$ Hz, *syn*-**4a**: $J=5.4$ Hz; *anti*-**4b**: $J=7.6$ Hz, *syn*-**4b**: $J=4.2$ Hz; *anti*-**4c**: $J=8.8$ Hz, *syn*-**4c**: $J=3.4$ Hz.



7. ^{1}H NMR data for 1,3-dioxane derivatives **5a**.
trans-Form 2.10 (1H, dt, $J=4.9$, 12.1 Hz), 4.11 (1H, t, $J=11.5$ Hz), 4.35 (1H, dd, $J=4.9$, 11.5 Hz), 4.90 (1H, d, $J=11.2$ Hz), 5.71 (1H, s), 7.36 (6H, m), 7.43 (2H, d, $J=7.1$ Hz), 7.57 (2H, dd, $J=7.1$, 2.0 Hz).
cis-Form 1.76 (1H, br), 4.11 (1H, d, $J=11.5$ Hz), 4.35 (1H, d, $J=11.5$ Hz), 4.90 (1H, br), 5.71 (1H, s), 7.36 (6H, m), 7.43 (2H, d, $J=7.1$ Hz), 7.57 (2H, dd, $J=7.1$, 2.0 Hz).
8. From *anti*-**4**, *trans*-**5** was obtained, and *syn*-**4** was converted to *cis*-**5**.
9. The stereochemistry of **4a** was misassigned as *syn* from the analogy to the reaction of crotyltin in the previous report.[4]
10. Considerable amount of bis-homoallyl ether **6** was also obtained.



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11. Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Naruta, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7107–7109.
12. (a) Mikami, K.; Maeda, T.; Kishi, N.; Nakai, T. *Tetrahedron Lett.* **1984**, *25*, 5151–5154; (b) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970–7971; (c) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1994**, *59*, 5130–5132.
13. (a) Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, E. M. *Tetrahedron* **1989**, *45*, 1053–1065; (b) Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313–1316; (c) Denmark, S. E.; Hosoi, S. *J. Org. Chem.* **1994**, *59*, 5133–5135; (d) Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889–7896; (e) Keck, G. E.; Dougherty, S. M.; Savin, K. A. *J. Am. Chem. Soc.* **1995**, *117*, 6210–6223.
14. For the reaction of the allylsilicon reagent, a computational experiment showed the *syn*-synclinal transition state was possible: Bottoni, A.; Costa, A. L.; Tommaso, D. D.; Rossi, I.; Tagliavini, E. *J. Am. Chem. Soc.* **1997**, *119*, 12131–12135.
15. (a) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962; (b) Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865–2868.