Anomalous *threo*-Diastereoselectivity in Allylic Silane– or Stannane–Aldehyde Condensation Reactions: New Interpretation of the Antiperiplanar *vs.* Synclinal Problem on the Transition-state Conformations

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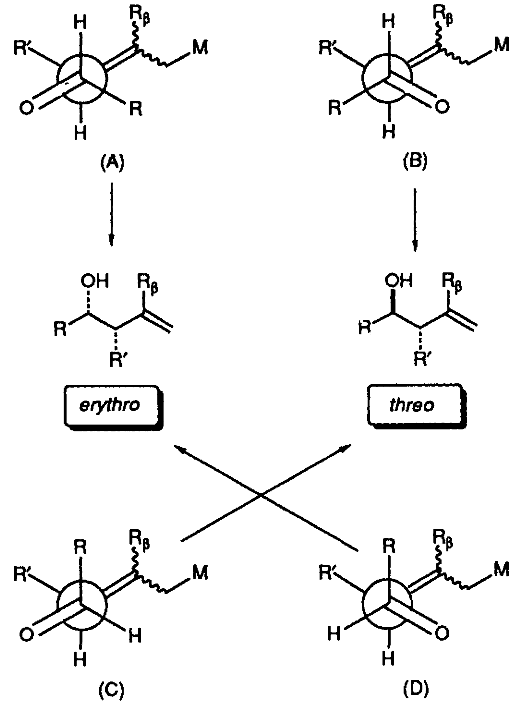
Unusual *threo*-diastereoselectivity has been observed in the intermolecular reactions of β-substituted crotyl-silane or -stannane with 2-benzyloxypropanal under chelation conditions, which implies preference for the synclinal over the antiperiplanar transition state.

The carbonyl addition reaction of allylic organometallic reagents is of current interest and of considerable synthetic utility for acyclic stereocontrol.[1] Among the various organometallic reagents that have been successfully employed, storable allylic silanes and stannanes comprise a unique group which undergo *erythro*-selective reaction with aldehydes regardless of the allylic geometry (in the presence of a Lewis acid).[1a,c,2] An antiperiplanar (ap) transition-state model (**A**) has been proposed to explain the characteristic *erythro*-diastereoselectivity (Scheme 1).[1a,2a] Recently, Denmark has reported the intramolecular reaction of allylic silanes or stannanes in which *erythro*-selectivity implies a preference for a synclinal (sc) (**D**) over the other ap transition state (**C**) (not **A**).[3] Herein, we report intermolecular reactions that show an

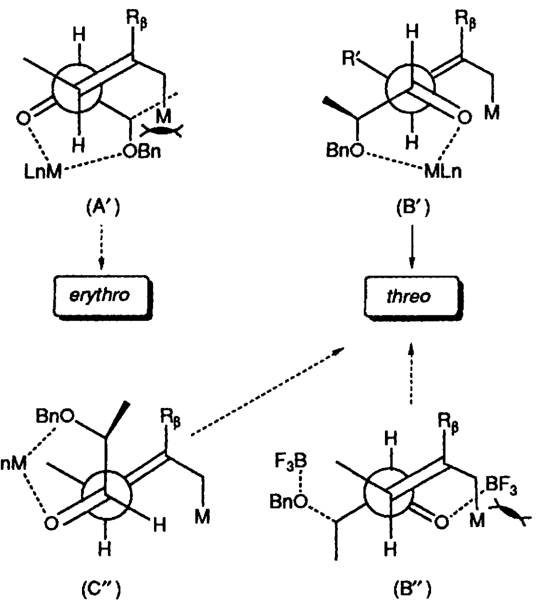
Table 1. Reaction of 2-benzyloxypropanal (**1**; R = Me) and crotylmetal (**2**).[a]

Run	(2) (M)	Lewis acid (MLn)	Yield (%)	(**3**)	(**4**)	(**5**)	(**6**)
1[b]	(**2a**) ($SnBu_3$)[c]	$MgBr_2$	—	93	7	0	0
2	(*E*)(**2a**)($SnBu_3$)[d]	$MgBr_2$[e]	80	90	10	0	0
3	(*E*)(**2b**)($SnBu_3$)[d]	$MgBr_2$[e]	85	24	76	0	0
4	(*E*)(**2b**)($SiMe_3$)[d]	$MgBr_2$[e]	80	11	89	0	0
5		$TiCl_4$	80	36	64	0	0
6		$ZnBr_2$	70	33	67	0	0
7		$SnCl_4$	90	3	97	0	0
8	(*Z*)(**2b**)($SiMe_3$)[f]	$SnCl_4$	85	6	94	0	0
9		$BF_3{\cdot}OEt_2$[g]	90	26	0	66	8
10[h]		$BF_3{\cdot}OEt_2$	90	8	1	88	3

[a] Unless otherwise noted, all reactions were run using 1.0 equiv. of Lewis acid and 2.2 equiv. of crotylmetal (**2**) in CH_2Cl_2 at −78 °C. [b] See ref. 2b (R = Bu^n). [c] *E*:*Z* = 56:44. [d] 90% *E*. [e] At −25 °C. [f] >95% *Z*. [g] 2 Equiv. of $BF_3{\cdot}OEt_2$ were used. [h] 2-Dimethyl-t-butylsiloxypropanal was used instead of 2-benzyloxypropanal (**1**; R = Me).



Scheme 1



Scheme 2. **a**; R_β = H
b; R_β = Me

unusual *threo*-selectivity implying a high preference for the sc (**B**) over the ap transition state (**A**).

In the synthesis of the brassinolide side chain,[4] we unexpectedly observed that the reaction of β-methylcrotyltri-n-butylstannane with steroidal 22-benzyloxy-23-aldehydes under chelation conditions[5] gave mainly the (chelation) *threo* (24-epibrassinolide type) product. Therefore, we examined the simple diastereoselectivity in the reactions of the β-methylcrotyl-stannane or -silane (**2b**) with 2-benzyloxypropanal (**1**; R = Me) (Scheme 2, Table 1). The reaction of the crotylstannane (**2a**) has been reported to provide predominantly the (chelation) *erythro*-adduct (**3a**) under chelation conditions ($MgBr_2$) (run 1).[2b] In sharp contrast, the β-methyl counterpart (**2b**) gave mainly the unusual (chelation) *threo*-product (**4b**) (runs 3—8).† It should be noted that $SnCl_4$ shows remarkably high *threo*-selectivity irrespective of the allylic geometry (runs 7 and 8).

The stereochemical assignments of the products deserve special comments. The *threo*-configuration of (**4b**) was confirmed, after conversion to the α-methyl ketone (**7**), by correlation with the authentic ketone which was derived from the *erythro*-major ester (**8**).[6] The most distinguishing feature is the α-methyl ^{13}C NMR signal.[7]

The unusual *threo*-selectivity prompted us to gain an insight into the transition-state conformation which could explain the anomaly in diastereoselectivity. The observed *threo*-selectivity implies a preference for the sc (**B'**) over the ap (**A'**) transition state (Scheme 3).‡ In the chelation controlled reactions, the Lewis acids are complexed to the alkoxyaldehydes (**1**) in a *syn*-fashion. Therefore, there remains an open space allowing the sc conformation (**B'**), which would be more

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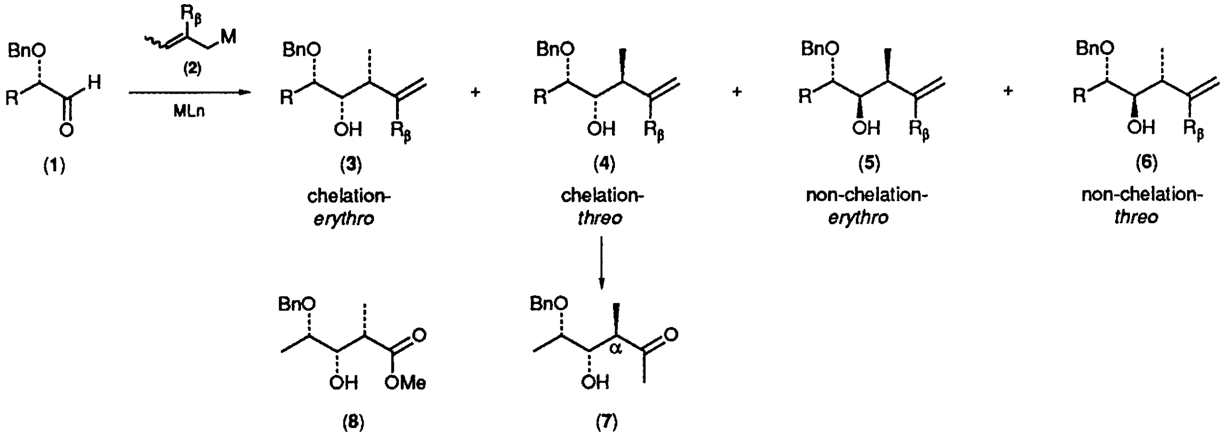
† We then focused our attention on the simple diastereoselection in the reaction with the achiral α-benzyloxyacetaldehyde (**1**; R = H). Here again unusual *threo*-selectivities were observed [$MgBr_2$: 70% *threo* (80% yield); $SnCl_4$: 83% *threo* (96% yield)].

‡ The allylic stannane or silane reactions, even in an intermolecular fashion, do not necessarily arise from the antiperiplanar transition state as has been suggested. The antiperiplanar transition state **C'** leading to the *threo*-product will be destabilized by the steric repulsion of the γ-methyl group and the chelated ring.



Scheme 3

favourable than the ap conformation (**A**′). The sc preference might also be due to a 'pinwheel' shape[8] for the ground-state conformer of (**2b**) (see **A**′) because of the 1,2-repulsion[9] between R_β (H) and MCH_2. Thus, the ap transition state (**A**′) would be destabilized by the steric repulsion of the MCH_2 group [or R_β of *Z*-(**2b**)] and the chelated ring.

These arguments on the *threo*-selectivity based on the chelation sc conformation (**B**′) lead us to predict *erythro*-selectivity in the non-chelation (*anti*-complexation) conditions *via* the ap transition state (**A**) because of the steric repulsion in the non-chelation sc conformation (**B**″). This is found to be correct. In the presence of $BF_3{\cdot}OEt_2$ (2 equiv.), the (non-chelation) *erythro*-product (**5b**) was obtained predominantly (Table 1, run 9).§ Furthermore, 2-dimethyl-t-butylsiloxypropanal gave high level of (non-chelation) *erythro*-selectivity (run 10).

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References

1 Reviews, (a) Y. Yamamoto, *Acc. Chem. Res.*, 1987, **20**, 243; (b) R. W. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 555; (c) A. Hosomi, *Acc. Chem. Res.*, 1988, **21**, 200; (d) T. Hiyama, *J. Synth. Org. Chem. Jpn.*, 1981, **39**, 81; (e) H. Sakurai, *Synlett.*, 1989, 1.

2 (a) T. Hayashi, M. Konishi, and M. Kumada, *J. Am. Chem. Soc.*, 1982, **104**, 4963; (b) G. E. Keck and E. P. Boden, *Tetrahedron Lett.*, 1984, **25**, 1879.

3 S. E. Denmark and E. J. Weber, *Helv. Chim. Acta.*, 1983, **66**, 1655; *J. Am. Chem. Soc.*, 1984, **106**, 7970. Also see, K. Mikami, T. Maeda, N. Kishi, and T. Nakai, *Tetrahedron Lett.*, 1984, **25**, 5151. The problem is the relative preference of the antiperiplanar **A** *vs.* the other synclinal conformation **B**.

4 Reviews, K. Mori, *J. Synth. Org. Chem. Jpn.*, 1985, **43**, 849; N. B. Mandava, *Annu. Rev. Plant Physiol. Plant Mol. Biol.*, 1988, **39**, 23.

5 Review, M. T. Reetz, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 556.

6 M. T. Reetz, K. Kesseler, and A. Jung, *Tetrahedron*, 1984, **40**, 4327. Also see: K. Mikami, T.-P. Loh, and T. Nakai, *Tetrahedron Asymmetry*, 1990, **1**, 13.

7 C. H. Heathcock, in 'Asymmetric Synthesis,' ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3.

8 C. S. Wilcox and R. E. Babston, *J. Org. Chem.*, 1984, **49**, 1451; C. Gennari, M. Beretta, A. Bernardi, G. Moro, C. Scolastico, and R. Todeschini, *Tetrahedron*, 1986, **42**, 893.

9 F. Johnson, *Chem. Rev.*, 1968, **68**, 375; R. W. Hoffmann, *Chem. Rev.*, 1989, **89**, 1841.

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§ Furthermore, *erythro*-selectivity (85%) was also observed with α-benzyloxyacetaldehyde (**1**; R = H) under non-chelation conditions [$BF_3{\cdot}OEt_2$ (2 equiv.)] (97% yield).