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STEREOCHEMICAL CONSEQUENCES FOR THE LEWIS ACID MEDIATED ADDITIONS OF ALLYL AND CROTYLTRI-n-BUTYLSTANNANE TO CHIRAL β-HYDROXYALDEHYDE DERIVATIVES

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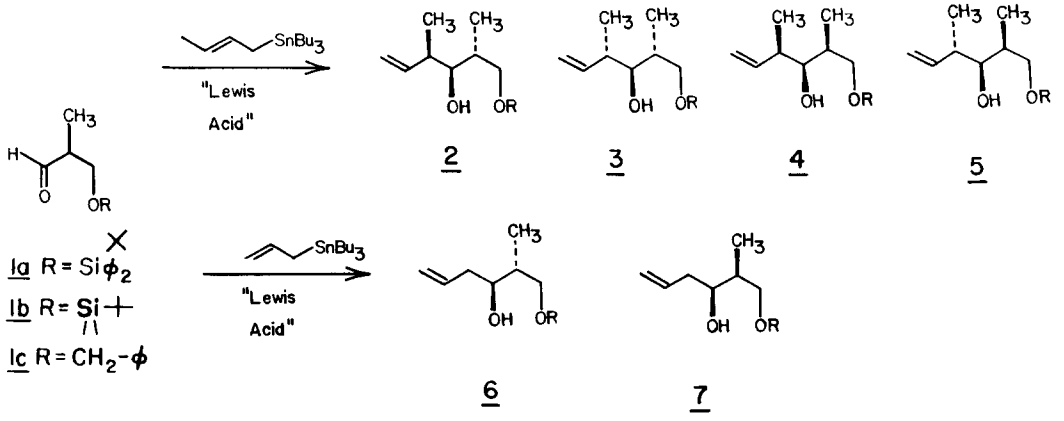
Summary: Proper choice of Lewis acid and hydroxyl protecting group allows for selective addition of crotyltri-n-butylstannane to either face of the aldehyde carbonyl in derivatives of 2-methyl-3-hydroxypropanal with preservation of erythro selectivity for the bond construction; allyl additions are limited to diastereofacial selectivity consistent with "chelation control."

In two previous reports[2a,b] we have defined protocols for highly selective addition reactions of allyl and crotyltri-n-butylstannanes to chiral α-hydroxyaldehyde derivatives. In this, our third report on a "two electron" organostannane approach to acyclic stereoselection,[3] we consider the viability of such an approach to at least a partial solution of the "hydroxyl, methyl, hydroxyl..." problem which is crucial to synthetic reconstruction of many important naturally occurring materials.

The processes investigated are summarized in equations (1) and (2) below. Thus, reaction of crotyltri-n-butylstannane with a chiral β-hydroxyaldehyde derivative of general structure 1 can lead to the production of diastereomers 2-5, while allyltri-n-butylstannane additions are conceptually less complex, since only diastereofacial selectivity in the addition process must be controlled.



With respect to the process embodied in equation 1, our first task was to define conditions which led to the production of a mixture of all possible products 2-5, to develop a precise analytical method for such mixtures, and to unambiguously establish product structures, including stereochemistry. This proved possible by using $ZnBr_2$ as catalyst with substrate 1a, to afford a capillary vpc separable mixture of 2a-5a, followed by oxidative olefin cleavage and reduction to afford a mixture of four diols, each of which was correlated with materials independently synthesized via the "chain extension" approach of Kishi.[4,5] Results obtained for the Lewis acid mediated addition of crotyltri-n-butylstannane to substrate 1a are summarized below.[6,7]

Table I

Substrate	Lewis Acid	2(C,E)	3(C,T)	4(F,E)	5(F,T)	Ratio(4/2)
1a	$ZnBr_2$ (-78° → 0°)	27	4	67	2	2.5:1
1a	$ZnBr_2$ (0° → 23°)	19	18	50	13	2.6:1
1a	$BF_3 \cdot Et_2O$	10	--	90	--	9:1 (90%)
1a	$BF_3 \cdot Et_2O$ (2.1 eq.)	12	--	88	--	7:1 (87%)
1a	$TiCl_4$	33	--	67	--	2:1
1a	Et_2AlCl	17	--	83	--	5:1
1a	$ZrCl_4$	2	--	78	--	3.5:1
1b	$BF_3 \cdot Et_2O$ (2.1 eq.)	5	--	95	--	18:1 (92%)

Thus, a relatively high preference for Felkin-Anh[6] diastereofacial selectivity with the characteristic erythro selectivity for the bond construction[8] was observed with $BF_3 \cdot Et_2O$ as catalyst and substrate 1a. Systematic study with respect to silyl function and temperature yielded the optimal protocol for obtention of the stereochemistry embodied in 4: reaction of 1b with crotyltri-n-butylstannane and 2.1 eq. of $BF_3 \cdot Et_2O$ at ca. -90°C, to yield 4b and 2b in a ratio of 95:5, with only traces of 3b and 5b detectable by capillary vpc analysis. Thus, remarkably high diastereofacial selectivity (18:1) for the "Cram" or "Felkin-Anh" product can be realized with essentially complete control in the bond construction.

Attention was then turned to the task of obtaining "chelation controlled" diastereofacial selectivity in such reactions, which has proven to be a formidable challenge. In addition to examining three Lewis acids previously shown[2] to be highly effective with α-alkoxyaldehydes (ZnI_2, $TiCl_4$, and $MgBr_2$) a large number of other Lewis acids were investigated with both substrates 1a and 1c. As expected, no conditions leading to good selectivity for the formation of 2 could be found using siloxy substrate 1a. Results obtained with the benzyl substrate 1c are summarized in Table II below.

Table II

Lewis Acid	2(C,E)	4(C,T)	5(F,E)	3(F,T)
ZnI_2[8]	40	48	7	5
$ZnBr_2$[8]	36	46	8	10
$TiCl_4$	59	41	--	--
$SnCl_4$[9]	39	61	--	--
$SnCl_4$[10]	58	42	--	--
$MgBr_2$	81	7	10	2
MgI_2	78	22	--	-- (88%)

The results above clearly reveal that diastereofacial selectivity is high for all catalysts examined, however, erythro selectivity in the bond construction is low or non-existant in most cases.[12] Best results to date are obtained with $MgBr_2$, which gives 91:9 diastereofacial selectivity and 89:11 erythro selectivity.

It would seem, therefore, that allylstannane additions in the "chelation controlled" sense should be a relatively simple proposition since diastereofacial selectivity is the only stereochemical feature of such reactions, and all Lewis acids in Table II provided excellent diastereoface selection with crotyltri-n-butylstannane. This is not, however, the case. Results for allyl additions to 1c are summarized in Table III below.

Table III

Entry	Lewis Acid	6 (Chelation)	7 (Felkin)	Ratio (Chelation/Felkin)
1	$BF_3 \cdot Et_2O$	52	48	1.1:1
2	ZnI_2	64	36	1.8:1
3	$MgBr_2$	72	28	2.6:1
4	MgI_2	70	30	2.3:1
5	$TiCl_4$[10]	82	18	4.6:1
6	$TiCl_4$[11]	53	47	1.1:1
7	$SnCl_4$[10]	90	10	9:1 (90%)
8	$SnCl_4$[11]	98	2	60:1 (88%)

The lower diastereofacial selectivities observed for the allyl additions are in accord with our previous observations for additions to α-alkoxyaldehydes.[2b] In the present case, only $TiCl_4$ and $SnCl_4$ show useful diastereofacial selectivity. It should also be noted that "normal" addition versus "inverse" addition with $TiCl_4$ and $SnCl_4$ show opposite behaviour (entries 5 and 6 versus 7 and 8), leading to excellent (60:1) diastereofacial selectivity

for the case of inverse addition of $SnCl_4$. In this instance, the actual organotin species undergoing reaction with the aldehyde is allyltrichlorostannane, which is formed very rapidly by redistribution[13] between allyltri-n-butylstannane and $SnCl_4$.[14]

References and Notes

1. Fellow of the Alfred P. Sloan Foundation, 1981-1985.

2. (a) G. E. Keck and E. P. Boden, Tetrahedron Lett., **25**, 265 (1984).
   (b) G. E. Keck and E. P. Boden, preceding paper in this issue.

3. For "one electron" carbon-carbon bond forming reactions using organostannanes, note G. E. Keck and J. B. Yates, J. Am. Chem. Soc., **104**, 5829 (1982).

4. (a) M. R. Johnson and Y. Kishi, Tetrahedron Lett., 4347 (1979); H. Nagaoka and Y. Kishi,
   (b) Tetrahedron, **37**, 3873 (1981).

5. Full experimental details and a complete discussion of the results described herein will be given in our full paper.

6. (a) In this and previous[2] papers, we use "chelation" and "Felkin-Anh[6b] to describe diastereofacial selectivity (c.f. structures 2 and 3 versus 4 and 5) consistent with this description, but without mechanistic implication.
   (b) N. T. Anh & O. Eisenstein, Nouv. J. Chim., **1**, 61 (1977) and references therein.
   (c) In both this and the preceding paper,[2b] we use erythro and threo in the sense advanced by Heathcock.[6d]
   (d) C. H. Heathcock, M. C. Pirrung, J. Lampe, C. T. Buse, and S. D. Young, J. Org. Chem., **46**, 2290 (1981).
   (e) For convenience, abbreviations for diastereofacial selectivity (C or F) and bond formation stereochemistry (E or T) follow the structure numbers in Tables I and II.

7. All organostannane reactions were performed in methylene chloride and, unless otherwise indicated, at the following temperatures: -78° ($BF_3{\cdot}Et_2O$, $TiCl_4$, Et_2AlCl, $ZrCl_4$), -22° ($MgBr_2$, MgI_2) or 0° (ZnI_2, $ZnBr_2$).

8. Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, J. Am. Chem. Soc., **102**, 7107 (1980).

9. Other products (corresponding to reverse crotyl addition) are also produced in this case.

10. This experiment was performed utilizing "normal" addition, i.e. addition of organostannane to a stirring solution of aldehyde and Lewis acid at -78°.

11. This experiment was performed utilizing "inverse" addition, i.e. addition of aldehyde to a stirring solution of organostannane and Lewis acid.

12. Similar effects are also noted with α-alkoxyaldehydes.[2a]

13. See A. Gambaro, V. Peruzzu, G. Plazzogna, and G. Tagliavini, J. Organometal. Chem., **197**, 45 (1980) and references therein.

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