Catalytic Asymmetric Allylation Reactions. 3. Extension to Methallylstannane, Comparison of Procedures, and Observation of a Nonlinear Effect

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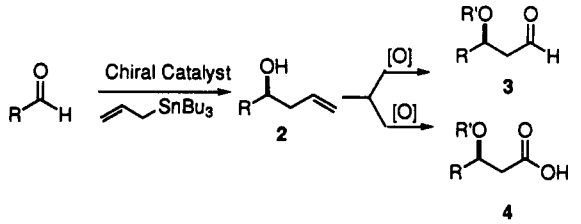
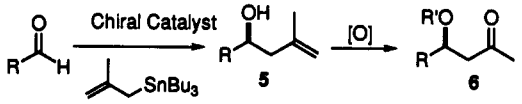
Summary: Enantioselective additions of methallylstannanes to representative aldehydes with four chiral Lewis acid systems afford ee's of 84–99% using 10 mol % of catalyst. In one case, use of (*R*)-BINOL of 50% ee gave product with 88% ee.

In two recent reports[1,2] we have disclosed efficient protocols for the enantioselective Lewis acid catalyzed reaction of allyltri-*n*-butylstannane with aldehydes, using chiral Lewis acid *catalysts* derived from (*R*)- or (*S*)-BINOL.[3] These remarkably effective[1,3] and simple[2] procedures yield products of structure **2**, which are easily convertible, by simple ozonolysis of the terminal vinyl moiety, to either β-hydroxy (alkoxy[4]) aldehydes **3** or β-hydroxy (alkoxy[4]) carboxylic acids **4**, products which correspond to asymmetric aldol additions of enolate derivatives of acetaldehyde or acetic acid.



We record herein the results of an investigation using methallyltri-*n*-butylstannane in such CAA reactions. Thus, in this case, oxidative cleavage of the vinyl moiety yields products equivalent to those of an asymmetric crossed aldol reaction between aldehydes and the enolate of acetone. Although the structural change from allylstannane to methallylstannane may seem somewhat trivial (replacement of H by CH_3 at a position which remains sp^2 hybridized throughout the reaction) the asymmetric synthesis of products such as **5** or **6** is quite difficult.[5–7] In



fact, the only other report of catalytic asymmetric methodology for the preparation of methallyl addition products of structure **5** is that of Yamamoto,[5a] who has described the addition of methallyltrimethylsilane to benzaldehyde and (*E*)-hexenal (in 68 and 50% yield, respectively, with 82 and 80% ee) using a chiral (acyloxy)borane catalyst. Stoichiometric "reagent based" procedures for methallyl addition products **5** have been reported by Corey[5b] and by Brown.[5c] Catalytic asymmetric methodology for products similar to **6** have been reported (ee's 80–85%), again by Yamamoto,[6] using CAB catalysis with trimethylsilyl enol

Table I

entry	R	method	*T*, °C (time, h)	yield[h] (%)	ee[i,j] (%)
1	Ph	A[a]	−20 (60)	75	91
2		B[b]	−20 (14)	**95**	**96**
3		C[c]	−20 (12)	92	93
4		D[d]	−20 (20)	95	85
5			0 (0.75)	96	91
6			23 (0.5)	99	92
7	furyl	A	−20 (12)	**99**	**99**
8		B		90	99
9		C		80	95
10		D	0 (1.5)	99	93
11			23 (0.5)	98	93
12	$PhCH_2CH_2$	A	−20 (40)	**97**	**98**
13		B	−20 (14)	90	98
14		C	−20 (12)	95	95
15		D	0 (1)	90	90
16			23 (2)	80	90
17	c-C_6H_{11}	A	−20 (48)	**50**	**84**
18		B	−20 (14)	65	75
19		C	−20 (12)	45	83
20		D	0 (23)	70	50
21			23 (15)	63	54
22	p-$OCH_3C_6H_4$	A	−20 (48)	61	93
23		C	−20 (12)	65	86
24		D	0 (4)	**80**	**93**
25	$C_6H_5CH{=}CH$	A	−20 (12)	68	87
26		C	−20 (12)	35	86
27		D	0 (23)	**83**	**86**
28	Ph	D[e]	23 (30)	80	83
29		D[f]		66	20
30	furyl	A[g]	−20 (12)	99	88
31		D[g]	23 (17)	56	50

[a] Catalyst prepared from (*R*)-BINOL and $Ti(O\text{-}i\text{-}Pr)_4$ at 1:1 stoichiometry in the presence of 4-Å MS as previously described.[1] [b] Catalyst prepared from (*R*)-BINOL and $Ti(O\text{-}i\text{-}Pr)_4$ at 2:1 stoichiometry in the presence of 4-Å MS and CF_3CO_2H (0.030 equiv relative to Ti) as previously described.[1] [c] Catalyst prepared identically to method B but without CF_3CO_2H. [d] Catalyst prepared from (*R*)-BINOL and $Ti(O\text{-}i\text{-}Pr)_4$ in dichloromethane solution at 23 °C for 1 h as previously described.[2] [e] This entry was conducted using 5 mol % of catalyst. [f] This entry was conducted using 2 mol % of catalyst. [g] These reactions were conducted using BINOL of 50% ee. [h] All yields are isolated yields. [i] In all cases enantiomeric excess was determined using the chiral shift reagent $Eu(hfc)_3$. [j] With benzaldehyde and cyclohexanecarboxaldehyde, (*R*)-BINOL gave (*R*) product. We assume the same sense of addition (to *re* face of substrate) for the other cases.

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(1) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467.

(2) Keck, G. E.; Geraci, L. S. *Tetrahedron Lett.*, in press.

(3) For recent examples of a very similar procedure using a catalyst prepared from BINOL, $TiCl_2(O\text{-}i\text{-}Pr)_2$, and 4-Å MS, see: (a) Keck, G. E.; Geraci, L. S.; Tarbet, K. H. *Abstracts of Papers*, 205th National Meeting of the American Chemical Society, Denver, CO, March, 1993; American Chemical Society: Washington, DC, 1993; ORGN 294. (b) Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001.

(4) The free hydroxyl in structures **2** and **5** can, of course, be easily protected if desired.

(5) (a) Furuta, K.; Mouri, M.; Yamamoto, H. *Syn-lett.* **1991**, 561. (b) Corey, E. J.; Yu, C.-M., Kim, S.-S. *J. Am. Chem. Soc.* **1989**, *111*, 5495. (c) Brown, H. C.; Vara Prasad, J. V. N.; Zee, S.-H. *J. Org. Chem.* **1986**, *51*, 432.

(6) Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc*, **1991**, *113*, 1041.

(7) For example, see: (a) Paterson, I.; Goodman, M. J. *Tetrahedron Lett.* **1989**, *30*, 997. (b) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

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ethers. Finally, although stoichiometric asymmetric aldol methodology can be used for the preparation of products of structure **6**, the ee's are often low with the requisite unsubstituted enolates.[7]

Four procedures for the CAA reaction were examined, and the results are summarized in Table I. All reactions (except as noted) were performed using 10 mol % of catalyst (Ti to RCHO).

The first, and obvious, point to notice is that the additional methyl substituent is tolerated in the reaction. Thus, in all but one case (cyclohexanecarboxaldehyde) the yields (80–99%) and ee's (86–99%) are similar to, or better than, those obtained with the parent allyltri-*n*-butylstannane. In three cases (benzaldehyde, furaldehyde, and 3-phenylpropionaldehyde), employment of the original[1] procedures gives optimal results, while for two substrates (cinnamaldehyde and *p*-methoxybenzaldehyde), the simplified protocol[2] (procedure D) with the 2:1 catalyst is optimal.

The "best" procedures in each case are given in bold type in Table I. However, it should be noted that the simplified procedure (method D) using the 2:1 catalyst is competitive with methods A and B for the first three aldehydes. Thus, with benzaldehyde, this procedure gives a 99% yield of product with 92% ee in a reaction conducted at rt for 30 min, while the optimal procedure B (with a somewhat less convenient catalyst preparation) gives 95% yield of product with 96% ee, but in a −20 °C reaction conducted for 14 h. In general, it can be anticipated that some experimentation will be necessary to determine the optimum procedure for a given substrate and that the "optimum" protocol for a given application may well sacrifice a small increase in ee for the extreme simplicity and practicality of procedure D.

Attempts to decrease the amount of catalyst required using method D gave two unexpected and puzzling results. Thus, in the run corresponding to entry 28, the amount of catalyst was decreased from 10 to 5 mol %. Not only did the required reaction time increase much more dramatically than anticipated (from 99% yield in 0.5 h to 80% yield in 30 h), but the enantiomeric excess was also decreased. Further decrease in the amount of catalyst (to 2%, entry 29) not only further eroded the conversion *but also resulted in a precipitous drop in ee*, to only 20%. Although the reasons for this result remain obscure, it does not appear likely that catalyst can be employed at much below the 10% level using this procedure.

Another interesting observation was made when potential nonlinear behavior[8] was examined (entries 30 and 31). Using (*R*)-BINOL of 50% ee and method A at a reaction temperature of −20 °C gave a positive nonlinear effect, yielding product with 88% ee. However, when the reaction was conducted at 23 °C using method D, no nonlinear effect was observed; the product was obtained in 50% ee.

Such observations are intriguing with respect to the molecular structure(s) of the catalyst(s) responsible for the very high levels of asymmetric induction achievable using these CAA procedures.[9] Unfortunately, the experimental techniques most appropriate for direct investigations of such questions would appear to be hopelessly slow relative to the time scale of important chemical events in these systems.

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Supplementary Material Available: ^1H and ^{13}C NMR spectra for methallyl addition products and ^1H NMR spectral data for racemates and enantiomerically enriched products in the presence of $Eu(hfc)_3$ (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(8) (a) Komatsu N.; Hashizume, M.; Sugim, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 4529. (b) Kiramura, M.; Okada, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.

(9) For complete experimental descriptions for these reactions, see refs 1 and 2.