Highly *syn*-Selective Additions of Allylic Stannanes to Protected α-Amino Aldehydes

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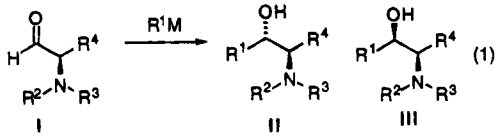
Summary: The γ-oxygenated allylic stannane (*R*)-**8b** adds to the threonine- and serine-derived *N*-BOC aldehydes **1** and **14** in the presence of $MgBr_2$ to afford the *syn* adducts **9b** and **15b** as the sole products.

The synthesis of biologically important β-amino alcohols by additions of organometallic reagents to *N*-protected α-amino aldehydes **I** (eq 1) has received wide-



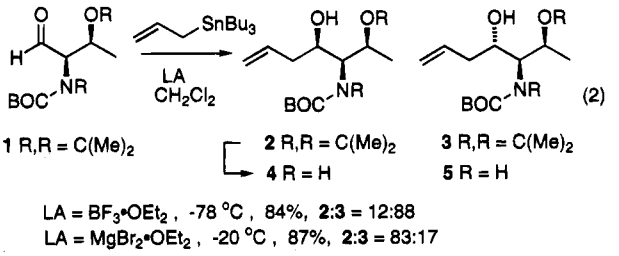
(1)

spread attention in recent years.[1] The approach is particularly appealing in view of the ready availability of various α-amino acid precursors in nonracemic form.[2] However, significant aldehyde epimerization and/or low diastereoselectivity is encountered in many cases. Furthermore, most additions lead mainly to the *anti* products **II** through nonchelated transition states.[3] The formation of *syn* adducts **III** (chelation control) is relatively uncommon.[4]

In connection with our development of nonracemic γ-alkoxy allylic stannanes as reagents for carbohydrate synthesis,[5] we decided to examine the stereochemical outcome of S_E2' additions to *N*-protected nonracemic α-amino aldehydes. The promising nature of our initial studies prompts this preliminary disclosure.

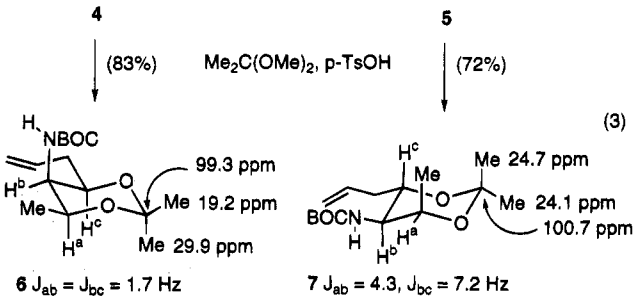
As a starting point, we selected the protected threonine aldehyde **1** described by Garner.[6] Addition of allyltributyltin in the presence of $BF_3{\cdot}OEt_2$ afforded the adducts **2** and **3** in 84% yield. Likewise, $MgBr_2{\cdot}OEt_2$-promoted addition afforded these two products in 87% yield (eq 2).

Because of slow conformational inversion, ^1H NMR analysis of **2** and **3** could not be employed to determine



(2)

diastereomeric ratios. However, the free amido alcohols **4** and **5**, secured by hydrolysis of the foregoing mixtures, showed well-defined peaks for the two diastereomers and revealed 12:88 and 83:17 ratios for the BF_3- and $MgBr_2$-derived products, respectively. The former was shown to be the *syn,syn* and the latter the *anti,syn* product upon ^1H and ^{13}C NMR analysis of the 6-membered acetonides **6** and **7** secured through treatment of the diols with 2,2-dimethoxypropane and *p*-TsOH (eq 3).[7]



(3)

Our studies on γ-oxygenated allylic stannane additions were carried out with the MOM and TBS derivatives **8a** and **8b**.[8] On the basis of earlier findings with α-alkoxy aldehydes, we expected the (*S*)-stannanes to be matched with aldehyde **1** in BF_3-promoted reactions.[5] However, both (*RS*)-**8a** and (*RS*)-**8b** (2.5 equiv) failed to give any useful products with aldehyde **1** in the presence of $BF_3{\cdot}OEt_2$ (Table 1, entries 1 and 2). Thus, neither of the stannane enantiomers appears to react under these conditions.

The $MgBr_2$-promoted reactions fared considerably better. Addition of 2.0 equiv of the racemic stannane (*RS*)-**8a** led to an 87:13 mixture of adducts **9a** and **10a** in 85% yield. In keeping with the preferences observed for α-alkoxy aldehydes, the recovered stannane was enriched in the (*S*) enantiomer (Table 1, entry 3).[5] Thus, the major product is most likely the *syn,syn,syn* adduct **9** arising from the matched pairing in a chelation-controlled addition.

The OTBS stannane (*RS*)-**8b** showed even higher stereoselectivity. Addition of 2.3 equiv of this stannane to aldehyde **1** in the presence of $MgBr_2$ afforded the *all-syn* product **9b** as the only adduct, in 70% yield, along

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(1) For a recent survey of this area, see: Reetz, M. T.; Rölfing, K.; Griebenow, N. *Tetrahedron Lett.* **1994**, *35*, 1969.

(2) *Cf.* Jurczak, J.; Golebiowski, A. *Chem. Rev.* **1989**, *89*, 149.

(3) For recent examples, see: (a) Hormuth, S.; Reissig, H.-U.; Dorsch, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1449. (b) Heneghan, M.; Procter, G. *Synlett* **1992**, 489. (c) Golebiowski, A.; Jurczak, J. *Synlett* **1993**, 241.

(4) Recent examples include the following: (a) Ti(IV)-promoted addition of tributylallyltin and trimethylallylsilane to Cbz-protected α-amino aldehydes: Kiyooka, S.; Suzuki, K.; Shirouchi, M.; Kaneko, Y.; Tanimori, S. *Tetrahedron Lett.* **1993**, *34*, 5729. Kiyooka, S.; Nakano, M.; Shiota, F.; Fujiyama, R. *J. Org. Chem.* **1989**, *54*, 5409. (b) Pinacol cross-coupling of BOC- and Cbz-protected α-amino aldehydes: Konradi, A. W.; Pedersen, S. F. *J. Org. Chem.* **1990**, *55*, 4506. (c) Addition of organocopper and manganese reagents to BOC- and Cbz-protected α-amino aldehydes: ref 1. (d) Sn(IV)-promoted addition of trimethylallylsilane to *N*-Cbz-*O*-TBS-L-serinal: Jurczak, J.; Prokopowicz, P.; Golebiowski, A. *Tetrahedron Lett.* **1993**, *34*, 7107.

(5) (a) Marshall, J. A.; Luke, G. P. *J. Org. Chem.* **1991**, *56*, 483. (b) Marshall, J. A. *Chemtracts—Org. Chem.* **1992**, *5*, 75. (c) Marshall, J. A.; Beaudoin, S.; Lewinski, K. *J. Org. Chem.* **1993**, *58*, 5876. (d) Marshall. J. A.; Seletsky, B. M.; Luke, G. P. *J. Org. Chem.* **1994**, *59*, 3413.

(6) Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361. The *ee* of our aldehyde **14** was found to be 90% by ^{19}F NMR analysis of the Mosher MTPA ester of the derived alcohol.

(7) *Cf.* Rychnovsky. S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945.

(8) (a) Marshall, J. A.; Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *113*, 647. (b) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.

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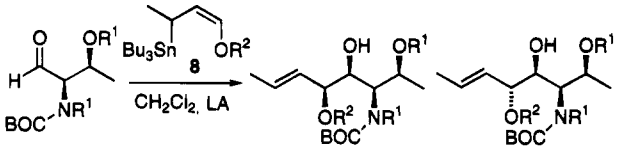
Table 1. Additions of γ-Oxygenated Allylic Stannanes 8a and 8b to the Threonine-Derived Aldehyde 1

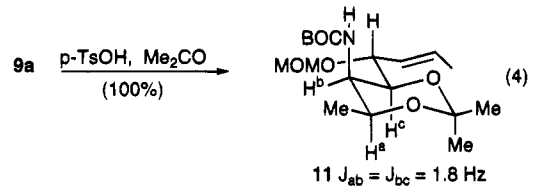


entry	R^2	stannane	LA	yield, %	product
1	MOM	(*RS*)-**8a**	BF_3·OEt_2	*a*	
2	TBS	(*RS*)-**8b**	BF_3·OEt_2	*a*	
3	MOM	(*RS*)-**8a**[b]	$MgBr_2$·OEt_2	85	**9a**, **10a**[c]
4	TBS	(*RS*)-**8b**[d]	$MgBr_2$·OEt_2	70	**9b**
5	TBS	(*R*)-**8b**	$MgBr_2$·OEt_2	84	**9b**

[a] Decomposition reaction run at −78 to −65 °C. [b] 2.0 equiv of (*RS*)-**8a**; recovered (*S*)-**8a** of 85% ee. [c] *Syn*:*anti* = 87:13. [d] 2.3 equiv of (*RS*)-**8b**; recovered (*S*)-**8b** of 55% ee.

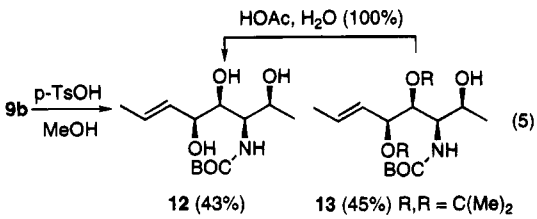
with recovered (*S*)-**8b** (Table 1, entry 4). Finally, with nonracemic stannane (*R*)-**8b**, adduct **9b** was secured in 84% yield (Table 1, entry 5).

The structure of adduct **9a** was surmised through acid treatment, whereupon acetonide **11** was obtained quantitatively (eq 4). Analysis of the ^1H NMR spectrum



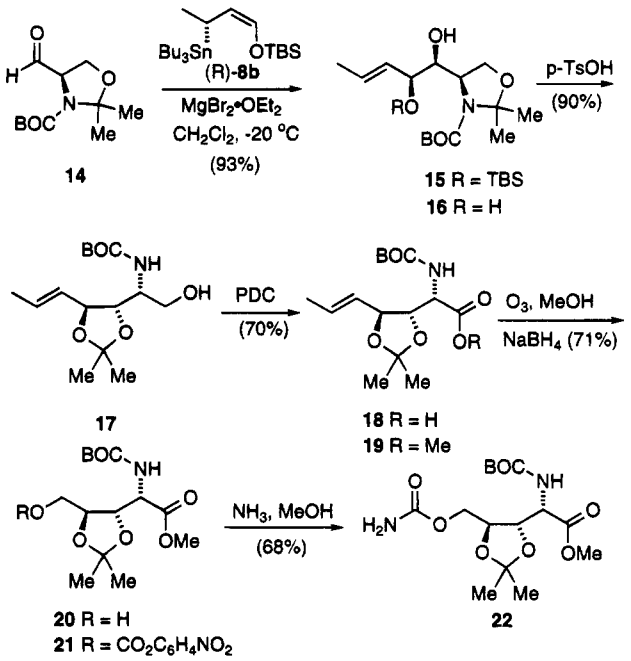
confirmed the *syn* relationship of the adjacent carbinyl and α-amino protons. The configuration of the remaining center follows from transition state considerations for the S_E2' addition.[5]

Unequivocal confirmation of adduct **9b** was secured through brief exposure to acid, which yielded a 1:1 mixture of crystalline triol **12** and rearranged acetonide **13** (eq 5). The latter proved suitable for single crystal X-ray analysis, which verified the structure assignment.[9]



In a second application of the foregoing methodology, we examined the addition of stannane (*R*)-**8b** to the serine-derived aldehyde **14**[6] in the presence of $MgBr_2$. As before, a single product was produced in high yield. This was presumed to be the *syn,syn* product **15** by analogy with the previous addition to aldehyde **1** (see Table 1). In order to confirm this point, we converted adduct **15** to the 5-*O*-carbamoyl polyoxamic acid derivative **22**, previously synthesized by a nonselective sequence starting from L-tartaric acid.[10]

Accordingly, treatment of **15** with TBAF followed by acid afforded the desilylated rearranged acetonide **17**.



Oxidation of the primary alcohol with PDC[11] gave the acid **18**, which was esterified with CH_2N_2. Ozonolysis of the resulting unsaturated ester **19** and *in situ* reduction with $NaBH_4$ yielded the alcohol **20**. The *p*-nitrophenyl carbonate derivative **21** gave rise to the desired carbamate **22** upon ammonolysis.[12] The spectral properties of **22** were in close agreement with the reported values.[10]

Thus, we have found that allylic stannanes undergo highly *syn*-selective additions to protected α-amino aldehydes such as **1** and **14** in the presence of $MgBr_2$. The γ-(silyloxy) stannane **8b** is particularly effective. Also noteworthy is the remarkable enantiomeric preference of aldehyde **1** for stannane (*R*)-**8b** (see Table 1, entry 4). Presumably, these additions proceed under chelation control involving the aldehyde and *N*-BOC grouping. Interestingly, the addition of vinylmagnesium bromide to aldehyde **14** is reported to give mainly the *anti* adduct (6:1).[13] Further studies on additions of oxygenated allylic stannanes to various *N*-protected α-amino aldehydes as a route to amino sugars and related natural products are in progress.

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Supplementary Material Available: Experimental procedures and spectral data for key intermediates (21 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.

(9) The authors have deposited atomic coordinates for **13** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(10) Saksena, A. K.; Lovey, R. G.; Girijavallabhan, V. M.; Ganguly, A. K.; McPhail, A. T. *J. Org. Chem.* **1986**, *51*, 5024. For recent alternative approaches to related polyoxamic acid derivatives, see: (a) Banik, B. K.; Manhas, M. S.; Bose, A. K. *J. Org. Chem.* **1993**, *58*, 307. (b) Ikota, N. *Chem. Pharm. Bull.* **1989**, *37*, 3399. (c) Matsuura, F.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett.* **1994**, *35*, 733.
(11) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.
(12) Millar, A.; Kim, K. H.; Minster, D. K.; Ohgi, T.; Hecht, S. M. *J. Org. Chem.* **1986**, *51*, 189.
(13) Garner, P.; Park, J. M. *J. Org. Chem.* **1988**, *53*, 2979.