Pergamon

Tetrahedron Letters, Vol. 35, No. 12, pp. 1913-1916, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0207-E

A Practical Synthetic Method for Enantio-enriched α-Hydroxystannanes

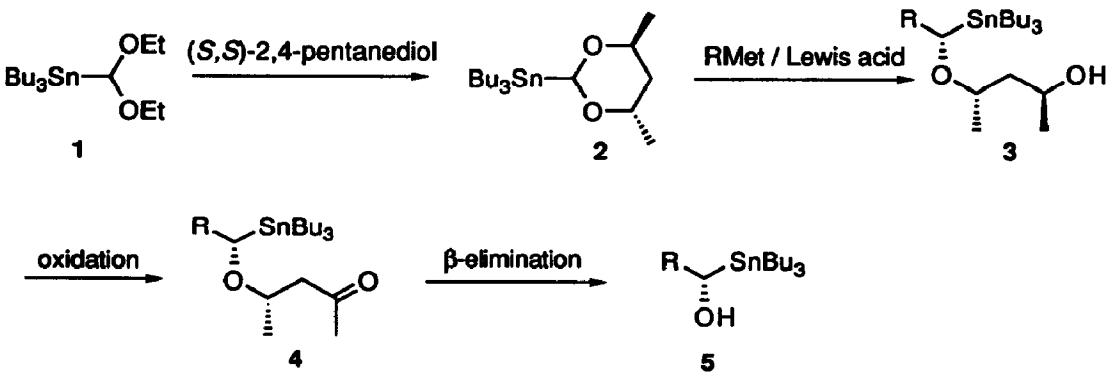
Katsuhiko Tomooka, Tatsuya Igarashi, and Takeshi Nakai*

Department of Chemical Technology, Tokyo Institute of Technology
Meguro-ku, Tokyo 152, Japan

Abstract: *The $TiCl_4$-promoted reaction of (4S, 6S)-(4,6-dimethyl-1,3-dioxan-2-yl)tributylstannane with Grignard reagents is shown to afford, after oxidation followed by base treatment, the (S)-α-hydroxystannanes in >95~20% ee.*

Chiral α-alkoxystannanes are valuable precursor of configurationally defined α-alkoxy organolithiums, since the Sn/Li transmetalation occurs with complete retention of configuration.[1] In particular, *enantio-enriched* α-alkoxystannanes have currently received much interest as precursors of enantio-defined α-alkoxylithiums in mechanistic and synthetic studies.[2] Three synthetic methods for enantio-enriched α-hydroxystannanes have been reported so far, including ones based on the kinetic resolution of α-acetoxystannanes *via* lipase-catalyzed hydrolysis[3] and the chromatographic resolution of their MTPA-esters.[1a] More attractive is the method developed independently by Chong's and Marshall's groups, which involves the asymmetric reduction of acylstannanes with (*R*)- or (*S*)-binaphthol-modified lithium aluminum hydride to provide high enantiomeric excesses.[4, 5] However, this procedure requires severe precautions due to the extremely high air-sensitivity of the acylstannanes,[6] and hence its reproductivity was often poor in our hands. We now report a new, practical method for asymmetric synthesis of α-hydroxystannanes which relies upon application of Johnson's chiral acetal protocol (Scheme 1).[7, 8]

Scheme 1



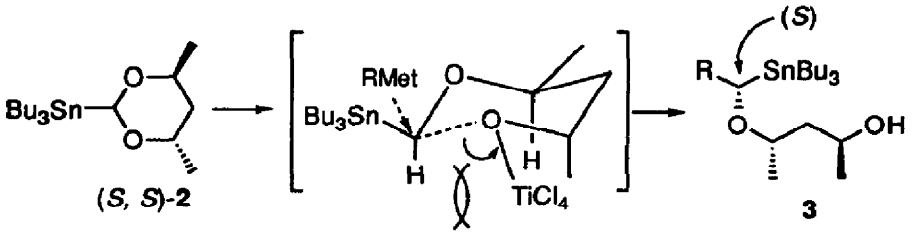
First, the requisite chiral acetal **2** was prepared in 74% yield from the known stannyl acetal **1**[9] and (*S, S*)-2,4-pentanediol (99% ee).[10] Next, we examined the reactions of **2** with various organometallic reagents in the presence of Lewis acids (Table 1).[11]

Table 1. Lewis-acid Promoted Reactions of Acetal **2** with Organometallic Reagents[a]

entries	RMet	Lewis acid	isolated yield of **3** (%)	de (%)[b]
1	EtMgBr	BF_3•Et_2O	85	88
2	EtMgBr	$TiCl_4$	85	>95
3	n-BuMgBr	$TiCl_4$	54	92
4	n-BuLi[c]	$TiCl_4$	84	45
5	CH_2=$CHCH_2$MgBr	$TiCl_4$	30	>95
6	PhMgBr	$TiCl_4$	67	20
7	MeMgBr	$TiCl_4$	71	30

(a) Unless otherwise noted, the reaction was run in dichloromethane at -78 °C using 5 equiv. of RMet in THF and 2 equiv. of Lewis acid (ref. 11). (b) Determined by ^{1}H NMR and HPLC analysis. (c) Two equivalents of n-BuLi in hexane solution was used.

As seen in the table, the yield and diastereoselectivity of this reaction vary with the natures of organometallic reagent and Lewis acid used.[12] Of special interest is that the use of a Grignard reagent provides a significantly higher % de than that of an organolithium (entries 3 *vs.* 4). The best results were obtained with the combination of alkyl-Grignard reagents with $TiCl_4$ (entries 2 and 3). Finally, the resulting alcohols **3** were converted to the corresponding α-hydroxystannanes **5** *via* the conventional oxidation / β-elimination sequence. For example, α-hydroxystannane **5a** (R=Et) was obtained in 90% yield *via* Swern oxidation[13] of **3a** (R=Et) followed by treatment of the resulting ketone **4a**[14] with potassium carbonate in methanol.[15] The enantiomeric purity of **5a** was determined as >95% ee by ^{1}H NMR and HPLC analysis of its MTPA ester. The absolute configuration of **5a** was established as (*S*) by comparison of the optical rotation of its MOM derivative with the reported value: $[\alpha]_D^{28}$ +38.8° (*c* 0.63, $CHCl_3$); lit.[4] $[\alpha]_D$ +34.8° (*c* 1.1, $CHCl_3$) for 96% ee (*S*). The stereochemical outcome, *i.e.*, (*S,S*)-**2** → (*S*)-**5**, is consistent with the sense of asymmetric induction originally reported by Johnson et al.[7] The steric course of the present acetal cleavage can be visualized as depicted below, thus imparting high stereo-predictability to the present methodology.

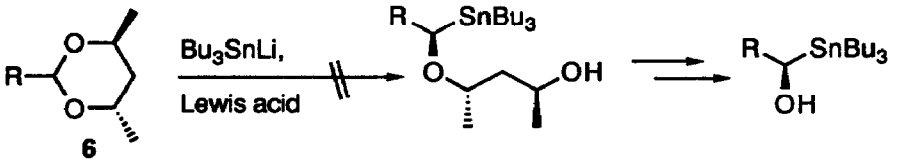


In summary, we have developed a practical and stereo-predictable method for asymmetric synthesis of α-hydroxystannanes. Further improvement of the present method and new applications of enantio-defined α-hydroxystannane derivatives are in progress in our laboratory.

Acknowledgment: We thank Professor Toshiyuki Ito (Okayama University) for providing the spectral data of α-hydroxystannanes. This work was supported by the Grant-in-Aid for Scientific Research, Ministry of Education, Science, and Culture, Japan.

References and Notes

1. (a) Still, W. C.; Streekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201. (b) Sawyer, J. S.; Kucerovy, A.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 842.
2. (a) Chong, J. M.; Mar, E. K. *Tetrahedron Lett.* **1990**, *31*, 1981. (b) Chan, C.-M. P.; Chong, J. M. *Tetrahedron Lett.* **1990**, *31*, 1985. (c) Tomooka, K.; Igarashi, T.; Watanabe, M.; Nakai, T. *Tetrahedron Lett.* **1992**, *33*, 5795. (d) Brickmann, K.; Bruckner, R. *Chem. Ber.* **1993**, *126*, 1227. (c) Tomooka, K.; Igarashi, T.; Nakai, T. *Tetrahedron Lett.*, in press.
3. Ito, T.; Ohta, T. *Tetrahedron Lett.* **1990**, *31*, 6407.
4. Chan, C. M.; Chong, J. M. *J. Org. Chem.* **1988**, *53*, 5584.
5. Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1988**, *29*, 1657. Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043.
6. It has been known that acylstannanes are quantitatively converted to the corresponding crystalline tributyltin carboxylates by air within minutes at room temperature; see ref. 4.
7. Lindell, S. D.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 3947. For a review on the chiral acetal protocol for asymmetric synthesis of alcohols; see: Alexakis, A.; Mangeney, P. *Tetrahedron Asymmetry* **1990**, *1*, 477.
8. More conveniently, an alternative route is possible which involves the Lewis acid-promoted reaction of the chiral acetal **6** with Bu_3SnLi. Unfortunately, attempted reactions of **6** (R=Et) with Bu_3SnLi using various Lewis acids failed.



6

9. Shiner, C. S.; Tsunoda, T.; Goodman, B. A.; Ingham, S.; Lee, S.; Vorndam, P. E. *J. Am. Chem. Soc.* **1989**, *111*, 1381.
10. **2**: To a solution of **1** (5 g, 12.7 mmol) in benzene (80 mL) were added (*S*, *S*)-2,4-pentanediol (2 g, 19.2 mmol) and *p*-toluenesulfonic acid monohydrate (250 mg). After being stirred for 1 h at room temperature, the solution was heated under reflux and the ethanol-benzene azeotrope (40 mL) was collected with a Dean-Stark apparatus. The resulting mixture was poured into aqueous pH 7 buffer and extracted with ether. The combined extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. Purification by flash chromatography gave 3.7 g of **2** (74% yield) as a colorless oil: ^{1}H NMR: 0.86-0.96 (m, 15H), 1.11 (d, *J*=6.2 Hz, 3H), 1.24-1.37 (m, 9H), 1.47-1.60 (m, 7H), 1.91 (ddd, *J*=6.0, 11.6, 13.0

Hz, 1H), 3.73 (ddq, *J*=2.5, 6.2, 12.2 Hz, 1H), 4.17 (dq, *J*=6.7 Hz, 1H), 5.66 (s, 1H). ^{13}C NMR: 8.91, 13.87, 16.39, 22.34, 27.33, 29.05, 38.20, 67.71, 68.96, 97.81. $[\alpha]_D^{25}$ +14.73° (*c* 1.11, $CHCl_3$).

11. **3a** (R=Et): A 1.0 M solution of $TiCl_4$ in CH_2Cl_2 (0.2 mmol) was added to a solution of acetal **2** (40 mg, 0.1 mmol) in CH_2Cl_2 (5 mL) at -78°C under nitrogen. After 5 min, EtMgBr (0.94 M in THF, 0.54 mL, 0.5 mmol) was slowly added to the mixture. After an additional 5 min, hydrochloric acid (0.5 N) was added, and the mixture was warmed to room temperature. The resulting mixture was extracted with ether. The combined extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated. Purification by flash chromatography gave 45 mg of **3a** (85% yield) as a colorless oil: ^1H NMR (major isomer): 0.88-1.00 (m, 18H), 1.17 (d, *J*=6.3 Hz, 3H), 1.23 (d, *J*=6.2 Hz, 3H), 1.32 (tq, *J*=7.7, 7.7Hz, 6H), 1.44-1.56 (m, 7H), 1.68-1.90 (m, 3H), 3.52 (brs, 1H), 3.62-3.74 (m, 1H), 3.90 (dd, *J*=5.5, 7.1 Hz, 1H), 4.10-4.22 (m, 1H). ^{13}C NMR (major isomer): 9.25, 12.63, 13.70, 18.57, 23.67, 27.53, 2 8.69, 29.28, 44.18, 64.22, 74.08, 76.76. HPLC: ODS-M, MeOH / H_2O = 9 / 1, 1.0 mL / min; 16.9 min for (*S*)-epimer, 19.3 min for (*R*)-epimer.
12. We have also examined the alkylation of acetal **2** using organocopper, organoaluminum, and organosilane reagents. However, these reactions gave poor results.
13. PDC and TPAP oxidation of **3a** gave a lower yield of ketone **4a**.
14. **4a** (R=Et): ^1H NMR (major isomer): 0.82-0.98 (m, 18H), 1.17 (d, *J*=5.8 Hz, 3H), 1.24-1.54 (m, 12H), 1.70-1.94 (m, 2H), 2.16 (s, 3H), 2.43 (dd, *J*=6.9, 15.4 Hz, 1H), 2.69 (dd, *J*=5.7, 15.4 Hz, 1H), 3.72-3.85 (m, 2H). IR: 1719 cm^{-1}.
15. However, treatment of **4d** (R=Ph) with potassium carbonate gave a complex mixture.

(*Received in Japan* 9 *November* 1993; *accepted* 11 *January* 1994)