A Highly Diastereoselective Synthesis of α-Substituted-β-hydroxy Compounds from Corresponding β-Stannyl Compounds

Makoto Yamamoto,* Kiyoshi Itoh, Keiki Kishikawa, and Shigeo Kohmoto
Department of Materials Science, Faculty of Engineering, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263

(Received June 26, 1997; CL-970487)

Anti- β -stannyl- α -substituted carbonyl compounds were completely converted to its syn-analogues, and each diastereomer was oxidized to its β -hydroxylated analogues with retention of the stereochemistry.

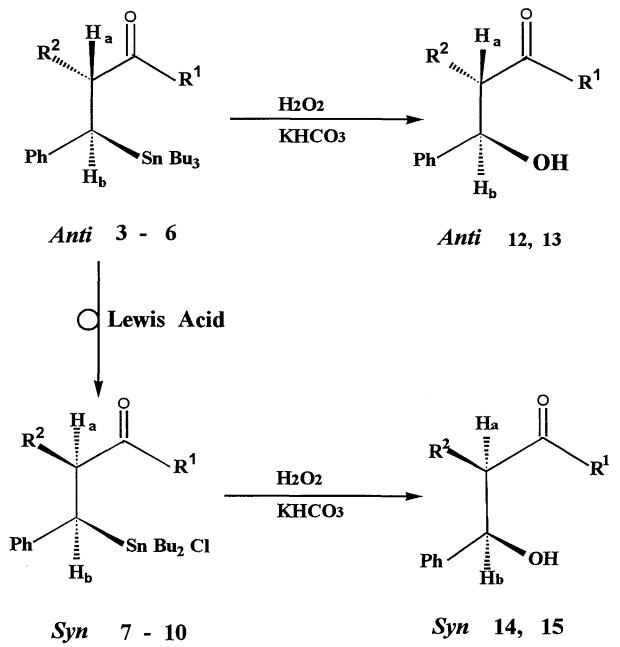
Enantio- and diastereoselective introductions of functional groups in the molecule are quite important for the synthesis of natural products. Many attempts for the enantio- and diastereoselective synthesis of α -substituted β -hydroxy compounds also have been appeared in the literature.[1] Among this field stereoselective aldol addition and Michael addition reactions are well studied since 1970's.[2]

On the other hand, it has been known that α , β -unsaturated carbonyl compounds gave α -substituted- β -stannyl compounds with high diastereoselectivity.[3]

In the course of our continuous studies of organostannyl compounds,[4] we have investigated a complete synthesis of *syn*- and *anti*- α -substituted- β -hydroxy carbonyl compounds from corresponding α , β -unsaturated carbonyl ones.

Ethyl cinnamate **1** was treated with tri-n-butyltin lithium,[5] which was prepared from hexa-n-butylditin with n-butyl lithium, followed by methylation to give the product which was purified by silica gel column chromatography to afford pure *anti*-isomer, ethyl 3-tri(n-butyl)stannyl-2-methyl-3-phenylpropanoate **3**. By the same procedure, various *anti*-tin compounds **4-6** were synthesized(Table 2).[6] In the stannylation reaction of **2** both cis and trans starting materials were used respectively, each main product was *anti*-one.

Although Lewis acid mediated conversion of the stereochemistry of the compounds is well known in the literature,[7] it is not so easy that tin compounds are usually unstable for a Lewis acid.



Scheme 1.

Table 1. Lewis acid promoted conversion of **3** to **7**

entry	Lewis acid	Conversion ratio[a] (*Syn* : *Anti*)	Yield of **7** (%)[b]
a	$SnCl_4$	100 : 0	78
b	$TiCl_4$	100 : 0	75
c	$AlCl_3$	12 : 88	10
d	$ZrCl_4$	9 : 91	7
e	$ZnCl_2$	0 : 100	0

[a] Determined by NMR. $BF_3 \cdot Et_2O$ was also used for the conversion. Corresponding ratio was 16 : 84 (12%).
[b] Isolated yield.

Table 2. Coupling constants of *anti* and *syn* tin-compounds

R^1	R^2	Comp. No	Yield(%) *	Jab(Hz)
		Anti		
OEt	Me	**3**	68	9.5
OEt	Allyl	**4**	56	11.1
Ph	Me	**5**	51	9.8
Ph	Allyl	**6**	72	9.1
		Syn		
OEt	Me	**7**	78	2.2
OEt	Allyl	**8**	99	1.8
Ph	Me	**9**	80	1.6
Ph	Allyl	**10**	68	1.9

* Isolated yield.

In order to avoid the elimination of tin group from **3**, we have selected the conditions carefully: stannylated *anti* compound **3** was treated with various Lewis acids in dichloromethane at -20° C for 45 min. The reaction mixture was quenched with water, extracted with benzene and concentrated to give the product which was checked its *syn/anti* ratio by NMR spectra. Although tin group in **3** was changed to chloro-di-n-butyltin,[8] the conversion using $SnCl_4$ and $TiCl_4$ proceeded excellently. In the cases of entry c and d large amount of starting **3** has still remained in the reaction mixture. Using $ZnCl_2$ none of the *syn*-compound was detected(Table 1).

Syn-compounds **8-10** were also synthesized in good yields from corresponding *anti* compounds **4-6** by using $SnCl_4$ or $TiCl_4$ (Table 2). Tri-n-alkylstannyl group can be easily eliminated by oxidative treatment. We have chosen following two oxidative substitution method: with lead tetraacetate (LTA)[4] and hydrogen peroxide/ $KHCO_3$.[9] LTA oxidative substitution of **3** gave low yield(18%) of corresponding β-acetoxylated product **11** with retention of the stereochemistry. The hydrogen peroxide method gave good yield of **12** with retention of the stereochemistry. *Anti*-stereochemistry in **12** was proved in this stage by comparison of the data of coupling constant J_{ab} = 8.2 Hz with those of the authentic sample(Me ester) J_{ab} = 8.6 Hz. [10]

By treating with hydrogen peroxide/$KHCO_3$ *anti*-compounds **4**, *syn* compounds **8** and **9** also gave hydroxylated products **13**, **14** and **15** with retention of the stereochemistry, respectively (Table 3).[11]

We have successfully investigated diastereoselective synthesis of β-hydroxy-α-substituted carbonyl compounds. This must be applicable for the diastereoselective organic synthesis.

Table 3. Synthesis of diastereoselective hydroxy compounds

Comp. No	R^1	R^2	Yield(%)	Diastereomer	J_{ab} (Hz)
12	OEt	Me	61	*Anti*	8.2
13	OEt	Allyl	57	*Anti*	9.7
14	OEt	Allyl	69	*Syn*	6.4
15 *	Ph	Me	63	*Syn*	2.4

* Cf. Reference 12.

References and Notes

1 J. D. Morrison, "Asymmetric Synthesis," Vol. 3, Academic Press, Orlando (1984) P. 111. S. Masamune, G. Bates, and J.W. Corcoran, *Angew. Chem. Intern. Ed. Engl.*, **16,** 585 (1977) and references cited therein.

2 For example, M. Nogradi,"Stereoselective Synthesis," VCH, New York (1986) P193.

3 I. Fleming and M. Rowley, *Tetrahedron Lett.*, **26**, 3857 (1985). I. Fleming and M. Rowley, *Tetrahedron,* **42,** 3181(1986) and references cited therein.

4 M. Yamamoto, S. Irie, T. Arase, S. Kohmoto, and K. Yamada, *J. Chem. Chem. Commun.*, **1990**, 1492. M. Yoshitake, M. Yamamoto, S. Kohmoto, and K. Yamada, *J. Chem. Soc., Perkin Trans., 1*, **1990**, 1226. M. Yamamoto, H. Izukawa, M. Saiki and K. Yamada, *J. Chem. Soc. Chem. Commun.*, **1988,** 560, and references cited therein.

5 W. C. Still, *J. Am. Chem. Soc.*, **100**, 1481(1978).

6 I. Fleming and C. J. Urch, *Tetrahedron Lett.*, **24**, 4591 (1983). G. J. McGarvey and J. M. Williams, *J. Am. Chem. Soc.*, **107,** 1435(1985).

7 For example, D. Schinzer, "Stereoselectivities in Lewis Acid Promoted Reactions,"Klumer Academic Publishers, Dordrecht(1989).

8 It is reported that infra red absorption band of a carbonyl group in β-(chlorodialkyl)stannyl carbonyl compound shifted about 50 cm^{-1} lower. ^{1}H-NMR and its infra red spectral data showed satisfactory results. H. Nakahira, I. Ryu, M. Ikebe, Y. Oku, A. Ogawa, N. Kambe, N. Sonoda, and S. Murai, *J. Org. Chem.*, **57**, 17(1992).

9 M. Ochiai, S. Iwaki, T. Ukita, Y. Matsuura, M. Shiro, and Y. Nagao, *J. Am. Chem. Soc.*, **110**, 4060(1988).

10 J. Canceill, J. J. Basselier, and J. Jacqes, *Bull. Soc. Chim. Fr.*, **1967,** 1024.

11 All compounds gave satisfactory spectral data.

12 C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirru , J. E. Sohn, and J. Lampe, *J Org. Chem.*, **45**, 106 (1980).