# 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*

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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.

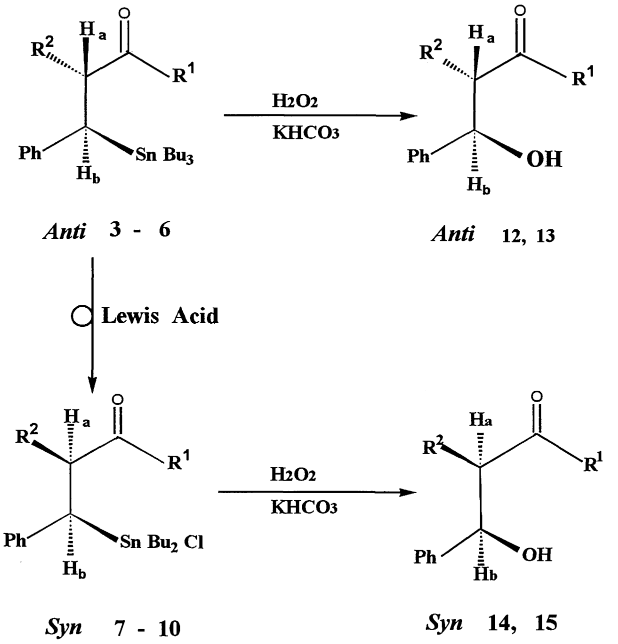
Enantio- and diastereoselective introductions of functional groups in the molecule are quite important for the synthesis of natural products. Many attempts for the enantio- and diastereoselective synthesis of α -substituted β -hydroxy compounds also have been appeared in the literature.[1] Among this 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 $\beta$-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]

**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.

We have successfully investigated diastereoselective synthesis of $\beta$-hydroxy-$\alpha$-substituted carbonyl compounds. This must be applicable for the diastereoselective organic synthesis.

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