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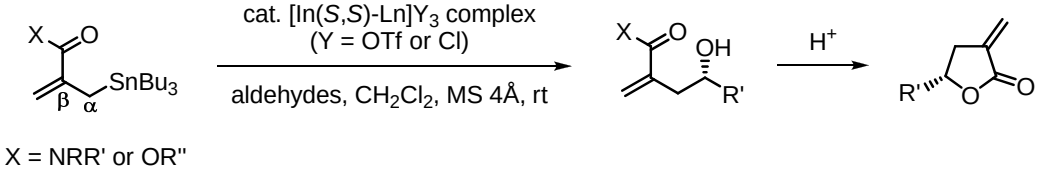


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# Indium-catalyzed enantioselective allylation of aldehydes with β-carbonyl allylstannanes: an efficient synthetic method for chiral α-methylene-γ-lactones

Takamasa Suzuki, Jun-ichi Atsumi, Tetsuya Sengoku, Masaki Takahashi and Hidemi Yoda*

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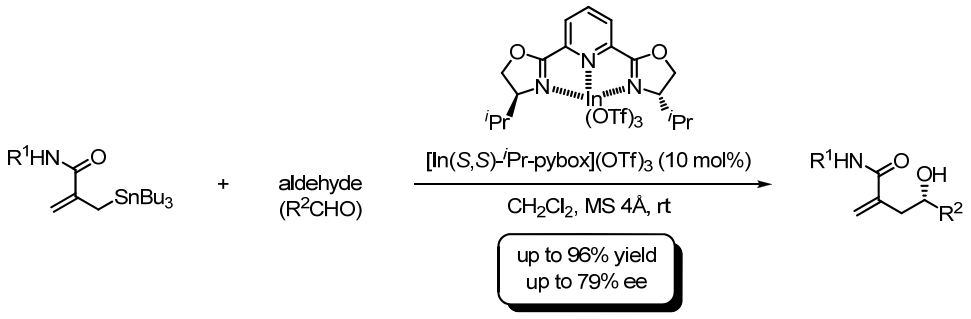
**Abstract—** The catalytic enantioselective allylation of aldehydes with β-carbonyl allyltributylstannanes in the presence of chiral indium complexes gave the optically active homoallylic alcohols, which can be converted to the corresponding optically active α-methylene-γ-butyrolactones.

## 1. Introduction

Asymmetric allylation of aldehydes is one of the most efficient methods to prepare the chiral homoallylic alcohols [1-3] which are the versatile building blocks for creating an abundant of biologically important compounds. Allylsilanes and allylstannanes have been used as potential reagents for allylation reactions due to their fascinating and excellent reactivity, effectively achieving catalytic asymmetric alkylation in the nucleophilic processes. Although a large number of these reactions employing reagents without functional groups have been reported to date, to the best of our knowledge, only few examples of allylation reactions with β-carbonyl allylstannanes have appeared in the literature [4]. Recently, we reported the first example of enantioselective allylation between β-amido allyltributylstannanes and aldehydes in the presence of [In(*S*,*S*)-$^{i}$Pr-pybox](OTf)$_3$, which afforded chiral γ-hydroxy amides in high chemical and enantiomeric yields (Scheme 1) [4a]. In this paper, we present the details of our studies on the catalytic enantioselective allylation with several types of β-carbonyl allyltributylstannanes, applying to the preparation of optically active α-methylene-γ-butyrolactones [5].




**Scheme 1.** Catalytic enantioselective allylation of aldehydes with β-amido allyltributylstannanes in the presence of [In(*S*,*S*)-$^{i}$Pr-pybox](OTf)$_3$.

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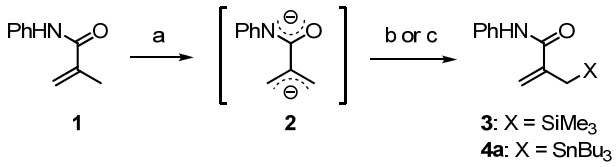
## 2. Results and discussion

### Preparation of allylating reagents

As shown in Scheme 2, β-substituted allylating reagents **3** and **4a** were generated by adding chlorotrimethylsilane or chlorotributyltin to the dianion solution of **2** prepared from *N*-phenyl methacrylamide (**1**) according to our preceding literature [4d].



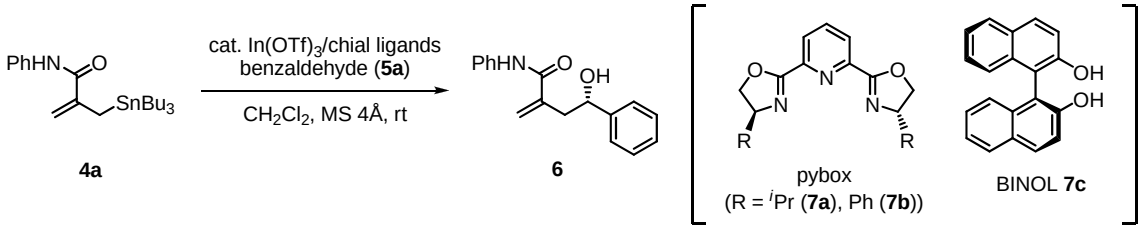

**Scheme 2**. *Reagents and conditions*: (a) *t*-BuOK, THF, -78 ºC, 1 h, then *n*-BuLi, -78 ºC, 13 min; (**2**); (b) $Me_3SiCl$, THF, -78 ºC, 1 h, -0 ºC, 3 h; 89% (**3**) (two steps); (b) *n*-$Bu_3SnCl$, THF, -78 ºC, 1 h; 77% (**4a**) (two steps).

### Enantioselective allylation of benzaldehyde (5a) with allyltrimethylsilane 3 and allyltributylstannane 4a

To examine whether allylating reagents work, we attempted the reactions of **3** and **4a** with benzaldehyde (**5a**) in the presence of $In(OTf)_3$ [6] (Table 1). Under the conditions employing catalytic and stoichiometric amounts of $In(OTf)_3$ in $CH_2Cl_2$ at ambient temperature, **3** failed to react with **5a** and was recovered intact. By contrast, **4a** reacted smoothly (8 h) in the presence of 30 mol% of $In(OTf)_3$ to afford γ-hydroxy amide **6** in 89% yield (entry 1). Having assured the sufficient reactivity of the β-carbonyl allyltributylstannane, we turned our attention to the development of catalytic asymmetric allylation with **4a**. As for the chiral source, we chose (*S*)-4-isopropyl-2,6-bis(oxazolin-2-yl)pyridine **7a** ([M(*S*,*S*)-$^i$Pr-pybox]$X_3$) because a number of examples that lead to high enantiomeric yields of products have recently been achieved, making this molecule an excellent candidate for the chiral ligand [6]. By use of 30 mol% of the chiral ligand, the optically active **6** was formed enantioselectively with 81% yield and 37% ee (Table 1, entry 2) [7]. With the catalyst loads from 10 to 30 mol% (Table 1, entries 2-4), this allylation reaction proceeded efficiently (72-96% yield and 37-63% ee) whereas in the presence of 5 mol% of catalyst, the reaction resulted in only 41% yield of the desired product with 53% ee. On the other hand, there are no significant effects of adding TMSCl [6a] in enantiomeric yields of products (entry 6), while the use of alternative ligands, neither **7b** nor **7c** [8] led to give further improvements in the enantiomeric excesses (entries 7 and 8).

Next, we further investigated the same catalytic asymmetric allylation with other *N*-substituted β-amido allyltributylstannanes **4b-h** prepared from the corresponding *N*-substituted methacrylamides as mentioned above (Table 2). Under the optimal reaction conditions for **4a**, *N*-aliphatic reagents **4b** and **4c** gave optically active adducts **8** and **9** with 26 and 39% ee, respectively (entries 2 and 3). It should be noted that the reactions of *N*-aromatic

**Table 1.** Enantioselective allylation of benzaldehyde (**5a**) with allyltributylstannane **4a** in the presence of chiral catalysts.[a]




| entry | $In(OTf)_3$ (mol%) | chiral ligands | TMSCl (equiv.) | % yield of **6**[b] | % ee[c] (config)[d] |
|---|---|---|---|---|---|
| 1 | 30 | -- | -- | 89 | -- |
| 2 | 30 | $^i$Pr-pybox (**7a**) | -- | 81 | 37 (*S*) |
| 3 | 20 | $^i$Pr-pybox (**7a**) | -- | 72 | 51 (*S*) |
| 4 | 10 | $^i$Pr-pybox (**7a**) | -- | 96 | 63 (*S*) |
| 5 | 5 | $^i$Pr-pybox (**7a**) | -- | 41 | 53 (*S*) |
| 6 | 10 | $^i$Pr-pybox (**7a**) | 1.2 | 85 | 32 (*S*) |
| 7 | 10 | Ph-pybox (**7b**) | -- | 96 | 49 (*S*) |
| 8 | 10 | BINOL (**7c**) | -- | 90 | 21 (*S*) |

[a]All reactions were carried out in the presence of activated MS 4Å (120 mg) in $CH_2Cl_2$ (0.2 mol/L) at ambient temperature.

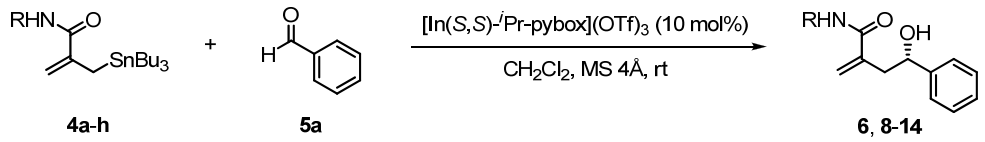
[b]Isolated yield.

[c]Determined by chiral HPLC analysis using Daicel Chiralpak IB and IC columns.

[d]Predicted configurations, see ref [5k] and [9].

analogues **4d** and **4e** proceeded with attractive enantiomeric yields (63 and 70% ee) under the identical conditions and 4-*tert*-butyl-substituted *N*-phenyl derivative **4f** gave the highest enantiomeric excess (77% ee) together with the satisfactory chemical yield (81%). In contrast, the reactions with methoxy-substituted *N*-phenyl derivatives **4g** and **4h** resulted in loss of the enantioselectivities with 9.1 and 0.2% ee, respectively.

**Table 2.** Enantioselective allylation of benzaldehyde (**5a**) with **4a-h** in the presence of 10 mol% of [In(*S*,*S*)-$^{i}$Pr-pybox](OTf)$_3$.[a]




**4a-h** **5a** **6**, **8-14**

| entry | R (**4**: allystannanes)[a] | % yield (adducts)[b] | % ee[c] (config)[d] |
|---|---|---|---|
| 1[e] | Phenyl (**4a**) | 96 (**6**) | 63 (*S*) |
| 2 | *tert*-Butyl (**4b**) | 88 (**8**) | 26 (*S*) |
| 3 | Cyclohexyl (**4c**) | 78 (**9**) | 39 (*S*) |
| 4 | 3-Biphenyl (**4d**) | 74 (**10**) | 63 (*S*) |
| 5 | 3,5-Di-*tert*-butylphenyl (**4e**) | 78 (**11**) | 70 (*S*) |
| 6 | 4-*tert*-Butylphenyl (**4f**) | 81 (**12**) | 77 (*S*) |
| 7 | 2-Methoxyphenyl (**4g**) | 78 (**13**) | 9.1 (*S*) |
| 8 | 4-Methoxyphenyl (**4h**) | 56 (**14**) | 0.2 (*S*) |

[a]All reactions were carried out in the presence of activated MS 4Å (120 mg) in $CH_2Cl_2$ (0.2 mol/L) at ambient temperature.

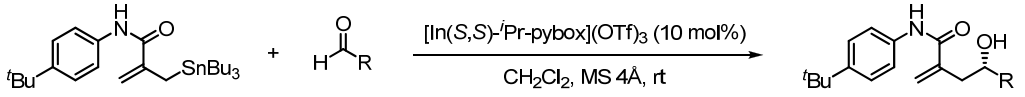
[b]Isolated yield.

[c]Determined by chiral HPLC analysis using Daicel Chiralpak IB and IC columns.

[d]Predicted configurations, see ref [5k] and [9].

[e]See Table 1.

**Table 3.** Enantioselective allylation of aldehyde **5** with **4f** in the presence of 10 mol% of [In(*S*,*S*)-$^{i}$Pr-pybox](OTf)$_3$.[a]




**4f** **5** **12**, **15-23**

| entry | R (**5**: aldehydes) | % yield (adducts)[b] | % ee[c] (config)[d] |
|---|---|---|---|
| 1[e] | Phenyl (**5a**) | 78 (**12**) | 77 (*S*) |
| 2 | Isobutyl (**5b**) | 45 (**15**) | 47 (*R*) |
| 3 | *tert*-Butyl (**5c**) | 45 (**16**) | 58 (*R*) |
| 4 | 4-Methoxyphenyl (**5d**) | 79 (**17**) | 59 (*S*) |
| 5 | 3-Chlorophenyl (**5e**) | 90 (**18**) | 61 (*S*) |
| 6 | 4-Nitrophenyl (**5f**) | 79 (**19**) | 58 (*S*) |
| 7 | 4-Isopropylphenyl (**5g**) | 94 (**20**) | 79 (*S*) |
| 8 | 4-*tert*-Butylphenyl (**5h**) | 81 (**21**) | 61 (*S*) |
| 9 | 1-Naphthyl (**5i**) | 94 (**22**) | 68 (*S*) |
| 10 | 2-Naphthyl (**5j**) | 94 (**23**) | 74 (*S*) |

[a]All reactions were carried out in the presence of activated MS 4Å (120 mg) in $CH_2Cl_2$ (0.2 mol/L) at ambient temperature.

[b]Isolated yield.

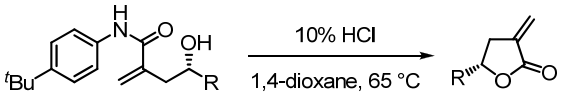
[c]Determined by chiral HPLC analysis using Daicel Chiralpak IB or IC columns.

[d]Predicted configurations, see ref [4d], [5k] and [9].

[e]See Table 2.

Using allylstannane **4f** that afforded the best enantiomeric yield, we investigated the allylation reaction with various aldehydes **5b-j** under the same reaction conditions as employed in Table 2. Table 3 shows that the reactions with the aliphatic aldehydes **5b** and **5c** gave moderate enantiomeric excesses and relatively low chemical yields (entries 2 and 3). A modest improvement in the asymmetric allylation was observed for aromatic aldehydes **5d-j**, which resulted in better yields of the desired products (entries 4-10). In particular, the reaction with isopropyl-subsituted *N*-phenyl derivative **5g** was found to give the highest enantiomeric excess (79% ee) and sufficiently high chemical yield (94%).

Through treatment with 10% HCl in 1,4-dioxane, the γ-hydroxy amides **12**, **15** and **20-23** underwent efficient formation of α-methylene-γ-butyrolactones **24-29** without loss of enantiomeric purity [4d] in the yields ranging from 79 to 99% yields, respectively (Scheme 3).



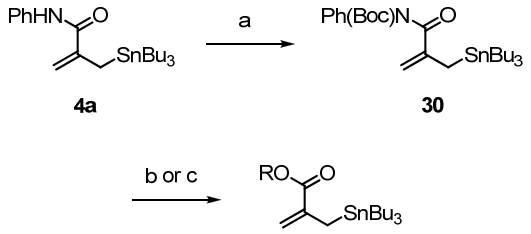

**12**: R = $C_6H_5$
**15**: R = $^i$Bu
**20**: R = (4-$^i$Pr)$C_6H_4$
**21**: R = (4-$^t$Bu)$C_6H_4$
**22**: R = 1-Naphthyl
**23**: R = 2-Naphthyl

**24**: R = $C_6H_5$ (99%)
**25**: R = $^i$Bu (83%)
**26**: R = (4-$^i$Pr)$C_6H_4$ (79%)
**27**: R = (4-$^t$Bu)$C_6H_4$ (88%)
**28**: R = 1-Naphthyl (92%)
**29**: R = 2-Naphthyl (91%)

**Scheme 3.** Synthesis of α-methylene-γ-butyrolactones **24-29** by acidic hydrolysis.

**Enantioselective allylation of benzaldehyde (5a) with β-alkoxycarbonyl allyltributylstannanes 31-35**

Having elucidated details of the enantioselective allylation with a series of β-amido allyltributylstannanes, we next focussed on the reaction with β-alkoxycarbonyl versions **31-35**. These substrates were obtained by the substitution reactions of **30** [10] with the corresponding alkoxides. **30** was prepared from **4a** via Boc-protection of the secondary amide group under basic conditions (Scheme 4).



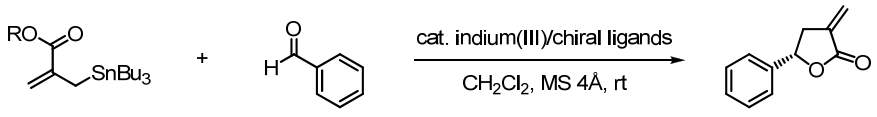

**4a** **30**

**31-35**
(R = Et, Me, $^i$Pr, Bn, Ph)

**Scheme 4** *Reagents and conditions*: (a) $Boc_2O$, $Et_3N$, DMAP, $CH_2Cl2$, rt, 18 h; 98% (**30**); (b) NaH, ROH, 0 ºC to rt; 92% (**31**; R = Et); 67% (**32**; R = Me); (c) NaH, ROH, THF, rt; 68% (**33**; R = $^i$Pr); 64% (**34**; R = Bn); 57% (**35**; R = Ph)

When the allylation reaction between **5a** and **31** was performed in the presence of [In(*S*,*S*)-$^i$Pr-pybox](OTf)$_3$, α-methylene-γ-butyrolactone **24** was directly obtained in 53% yield without isolation of the corresponding homoallylic alcohol (Table 4, entry 1). After purification by column chromatography, the product **24** proved to be almost racemic (2.1% ee, entry 1).

**Table 4.** Enantioselective allylation and cyclization sequence of benzaldehyde (**5a**) with **31-35** catalyzed by chiral indium(III) catalysts.




**31-35** **5a** **24**

| entry | R | indium | chiral ligand | mol% | % yield of **24**[a] | % ee[b] (confign)[c] |
|---|---|---|---|---|---|---|
| 1 | Et (**31**) | $In(OTf)_3$ | $^i$Pr-pybox (**7a**) | 30 | 53 | 2.1 (*S*) |
| 2 | Et (**31**) | $InCl_3$ | $^i$Pr-pybox (**7a**) | 30 | trace | ND[d] |
| 3 | Et (**31**) | $InCl_3$ | BINOL (**7c**) | 30 | 94 | 14 (*S*) |
| 4 | Et (**31**) | $InCl_3$ | BINOL (**7c**) | 15 | 93 | 58 (*S*) |
| 5 | Me (**32**) | $InCl_3$ | BINOL (**7c**) | 15 | 96 | 39 (*S*) |
| 6 | $^i$Pr (**33**) | $InCl_3$ | BINOL (**7c**) | 15 | 90 | 25 (*S*) |
| 7 | Bn (**34**) | $InCl_3$ | BINOL (**7c**) | 15 | 64 | 53 (*S*) |
| 8 | Ph (**35**) | $InCl_3$ | BINOL (**7c**) | 15 | 78 | 45 (*S*) |

[a]Isolated yield.

[b]Determined by chiral HPLC analysis using Daicel Chiralpak IC column.

[c] Predicted configurations, see ref [5k].

[d]Not determined.

Whereas replacement of $In(OTf)_3$ with $InCl_3$ [8] under same conditions led to production of only trace amount of **24** detected on TLC (entry 2), the use of the chiral ligand **7c** [8] instead of **7a** led to form the optically active **24** with 94% yield and 14% ee (entry 3). When reducing the amount of catalyst (15 mol%), enantioselectivity was significantly improved (58% ee, entry 4). Under identical conditions, the allylation reactions with other β-alkoxycarbonyl allyltributylstannanes **32**-**35** exhibited significant levels of enantioselectivity and afforded **24** with up to 53% ee (entries 5-8).

**Mechanistic interpretation for the asymmetric allylation**

The asymmetric allylation would be explained on the basis of chiral coordination environment created by the isopropyl groups of the rigid pybox ligand. Typically, three of the six available $In^{3+}$ octahedral coordination sites are bound by the chelation of three nitrogen atoms in the chiral ligand, leaving three sites available for the two carbonyl functions of β-amido allyltributylstanannes and aldehydes. Due to the fact that the aldehydes are less sterically congested than the β-amido allyltributylstanannes, the formers can coordinate the $In^{3+}$ complex at a less crowded disposition as illustrated in Figure 1, while destabilizing steric interactions between the tributylstannylmethyl groups and isopropyl moieties of the pybox ligand should be minimized. In such a case, the aldehyde molecules would adopt low-energy conformation that decreases steric hindrance created by the isopropyl moieties (Model A) rather than more sterically demanding conformation (Model B). Hence, the nucleophilic attack between the flexible allylic arms and the carbonyl carbons proceeded enantioselectively through the asymmetric transition state, leading to the observed absolute configurations of the products with the moderate enantiomeric yields.

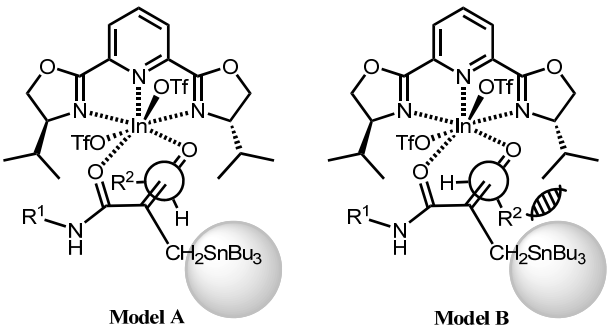



**Figure 1**. Plausible transition models of β-amido allyltributylstannanes **4**.

On the other hand, similar mechanistic rationale could explain the observed results for the use of the $In^{3+}$-binaphthol catalyst. For steric reasons, the catalyst-reactant chelates would prevent conformations with the aromatic ring of the aldehyde locating at closer disposition of the bulky binaphthyl moieties. Based on this consideration, two conformational models could be proposed to satisfy geometrical requirement for the occurrence of the allylation reactions (Models C and D in Figure 2). It was anticipated that the larger tributylstannylmethyl substituent should be oriented away from the steric crowding present at the molecular edges of the binaphthyl ligand, suggesting that the thermodynamically more favored conformation (Model C) should be formed in the reaction as the major transition state relative to the other (Model D). The experimental data concerning the product stereochemistry are in good agreement with the conformational model in which all the absolute stereocenters created at the hydroxy-bearing carbon atom proved to be *S*.

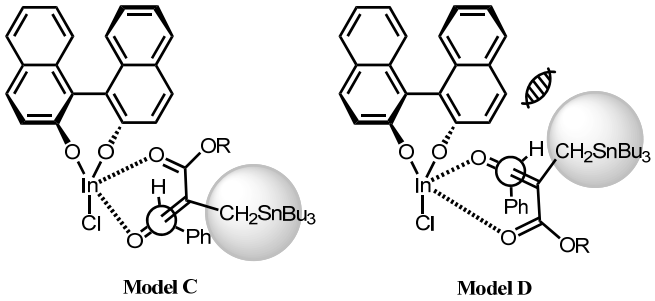



**Figure 2.** Plausible transition models of the β-alkoxycarbonyl allyltributylstannanes.

## 3. Conclusion

We have demonstrated the details of catalytic enantioselective allylation of various aldehydes with β-carbonyl allyltributylstannanes in the presence of 10 mol% of [In(*S*,*S*)-$^{i}$Pr-pybox](OTf)$_3$ or 15 mol% of [In(*S*)-BINOL]$Cl_3$ complexes, respectively. The reactions between *N*-aryl β-amido allyltributylstannanes and aromatic aldehydes were found to be effective, giving high enantioselectivity. On the other hands, the reaction of β-alkoxycarbonyl allyltributylstannanes and benzaldehyde provided directly the corresponding α-methylene-γ-butyrolactones. These methods possess desirable advantages of being not only *catalytic* and *enantioselective* in the allylation, but able to give optically active α-methylene-γ-butyrolactones without employing chiral allyltributylstannanes prepared through tedious elaboration [4c, 4d].

## 4. Experimental section

### 4.1. General

All solvents and reagents were of reagent grade quality from Aldrich Chemical Company, Fluka, Acros or Wako Pure Chemicals and used without any further purification. Melting points were measured on an automated melting point system (MPA 100, Stanford Research Systems). Fourier transform infrared (FT-IR) spectra were recorded

on a Shimadzu FTIR-8200A spectrometer. The $^{1}$H- and $^{13}$C-nuclear magnetic resonance (NMR) spectra operating at the frequencies of 300 and 75 MHz, respectively, were measured with a JEOL JNM-AL300 spectrometer in chloroform-*d* ($CDCl_3$) unless otherwise stated. Chemical shifts are reported in parts per million (ppm) relative to TMS as internal standard (δ = 0 ppm) for $^{1}$H NMR, and $CDCl_3$ was used as internal standard (δ = 77.0) for $^{13}$C NMR. The coupling constants are reported in hertz (Hz). Optical rotations were measured in 1 dm path length cell of 2 mL capacity using a JASCO Model DIP-1000 polarimeter at a wavelength of 589 nm. Reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm Merck silica gel 60-$F_{254}$ precoated silica gel plates by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in methanol followed by heating. Column chromatography was performed on Kanto Chemical silica gel 60N eluting with the indicated solvent system. The non-crystalline compounds were shown to be homogeneous by chromatographic methods and characterized by NMR, IR, high resolution mass spectra (HRMS) and microanalysis. High-pressure liquid chromatography (HPLC) was carried out using a Shimadzu Model LC-10AD or 10AT intelligent pump and SPD-10A UV detector. HRMS were recorded on a JEOL JMS-T100CS spectrometer. Microanalyses were performed with a JSL Model JM 10.

### 4.2. Experimental procedures

*4.2.1. General procedure for the preparation of the chiral γ-hydroxy amides (Table 2). (S)-4-Hydroxy-2-methylene-N,4-diphenylbutanamide (**6**)*

Under argon atmosphere, to the suspension of $In(OTf)_3$ (13.2 mg, 0.0235 mmol) {predried at 120 °C for 1 h under reduced pressure (ca. 1.0 Torr)} and MS 4Å (120 mg) {also predried at 180 °C for 3 h under reduced pressure (ca. 1.0 Torr)} in $CH_2Cl_2$ (0.7 mL) was added (*S*)-$^{i}$Pr-pybox **7a** (14.2 mg, 0.0470 mmol) at room temperature and stirred for 0.5 h. A solution of benzaldehyde (**5a**) (30 mg, 0.282 mmol) in $CH_2Cl_2$ (0.2 mL) was added and stirred for 1h. The solution of **4a** (106 mg, 0.235 mmol) in $CH_2Cl_2$ (0.3 mL) was slowly added dropwise at the same temperature and stirred for 16 h. The reaction was quenched by the addition of aqueous $NaHCO_3$ (5.0 mL), then $CH_2Cl_2$ was removed in *vacuo*. The mixture was filtered through Celite and the resulting solution was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=2:1) to give **6** (60.0 mg, 96%) as a white solid. Mp 101.1-102.0 °C; $[\alpha]_D^{17}$ -46.7 (*c* 1.00, $CHCl_3$); IR (KBr) 3279 (N-H), 2868 (O-H), 1647 (C=O) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$): δ 8.65 (brs, 1H, N*H*), 7.54-7.08 (m, 10H, Ar*H*), 5.82 (s, 1H, C$H_2$), 5.30 (s, 1H, C$H_2$), 4.87 (ddd, *J* = 8.3, 3.4, 3.3 Hz, 1H, C*H*), 4.46 (d, *J* = 3.3 Hz, 1H, O*H*), 2.75 (dd, *J* = 14.2, 3.4 Hz, 1H, C$H_2$), 2.65 (dd, *J* = 14.2, 8.3 Hz, 1H, C$H_2$); $^{13}$C NMR ($CDCl_3$) δ 172.5 (*C*), 144.5 (*C*), 144.3 (*C*), 140.4 (*C*), 129.4 (*C*H), 128.2 (*C*H), 127.2 (*C*H), 127.1 (*C*H), 126.6 (*C*H), 125.7 (*C*$H_2$), 122.7 (*C*H), 74.1 (*C*H), 44.8 (*C*$H_2$). Anal. Calcd for $C_{28}H_{27}NO_4$: C, 76.17; H, 6.16; N, 3.17; Found: C, 76.43; H, 6.81; N, 5.30.

*4.2.1.1. (S)-N-tert-Butyl-4-hydroxy-2-methylene-4-phenylbutanamide (**8**)*. Mp 110.4-110.9 °C; $[\alpha]_D^{23}$ -13.3 (*c* 2.43, $CHCl_3$); IR (KBr) 3360 (N-H), 2970 (O-H), 1651 (C=O) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$): δ 7.35-7.19 (m, 5H, Ar*H*), 6.18 (brs, 1H, N*H*), 5.51 (s, 1H, C$H_2$), 5.38 (d, *J* = 3.4 Hz, 1H, O*H*), 5.16 (s, 1H, C$H_2$), 4.77 (dt, *J* = 8.3, 3.4 Hz, 1H, C*H*), 2.64 (dd, *J* = 13.9, 3.4 Hz, 1H, C$H_2$), 2.53 (dd, *J* = 13.9, 8.3 Hz, 1H, C$H_2$), 1.36 (s, 9H, C$H_3$); $^{13}$C NMR ($CDCl_3$): δ 170.0 (*C*) , 144.5 (*C*), 143.5 (*C*), 128.1 (*C*H), 127.0 (*C*H), 125.7 (*C*H), 120.0 (*C*$H_2$), 74.4 (*C*H), 51.5 (*C*), 43.4 (*C*$H_2$), 28.5 (*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{15}H_{21}NO_2$+Na: 270.1465, found 270.1446.

*4.2.1.2. (S)-N-Cyclohexyl-4-hydroxy-2-methylene-4-phenylbutanamide (**9**)*. Mp 95.8-96.6 °C; $[\alpha]_D^{19}$ -14.5 (*c* 1.00, $CHCl_3$); IR (KBr) 3279 (N-H), 2855 (O-H), 1645 (C=O) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$): δ 7.36-7.19 (m, 5H, Ar*H*), 6.29 (d, *J* = 7.5 Hz, 1H, N*H*), 5.55 (s, 1H, C$H_2$), 5.33 (d, *J* = 3.5 Hz, 1H, O*H*), 5.19 (s, 1H, C$H_2$), 4.81 (ddd, *J* = 8.1, 4.2, 3.5 Hz, 1H, C*H*), 3.77 (m, 1H, C*H*), 2.68 (dd, *J* = 13.9, 4.2 Hz, 1H, C*H*), 2.56 (dd, *J* = 13.9, 8.1 Hz, 1H, C$H_2$), 1.94-1.90 (m, 2H, C$H_2$), 1.74-1.59 (m, 3H, C$H_2$), 1.40-1.11 (m, 5H, C$H_2$); $^{13}$C NMR ($CDCl_3$): δ 169.5 (*C*), 144.4 (*C*), 142.7 (*C*), 128.1 (*C*H), 127.1 (*C*H), 125.7 (*C*H), 120.5 (*C*$H_2$), 74.3 (*C*H), 48.6 (*C*H), 43.4 (*C*$H_2$), 32.8 (*C*$H_2$), 25.4 (*C*$H_2$), 24.7 (*C*$H_2$). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.99; H, 8.60; N, 5.07.

*4.2.1.3. (S)-N-(3-Biphenyl)-4-hydroxy-2-methylene-4-phenylbutanamide (**10**)*. Mp 147.2-148.1 °C; $[\alpha]_D^{28}$ -19.7 (*c* 0.500, EtOH); IR (KBr) 3202 (N-H), 3088 (O-H), 1616 (C=O) $cm^{-1}$; $^{1}$H NMR (acetone-$d^6$): δ 9.61 (brs, 1H, N*H*), 8.08 (m, 1H, Ar*H*), 7.77-7.21 (m, 13H, Ar*H*), 5.93 (d, *J* = 0.8 Hz, 1H, C$H_2$), 5.46 (d, *J* = 0.9 Hz, 1H, C$H_2$), 5.04 (d, *J* = 3.9 Hz, 1H, O*H*), 4.92 (ddd, *J* = 8.3, 4.1, 3.9 Hz, 1H, C*H*), 2.82 (ddd, *J* = 13.9, 4.1, 0.9 Hz, 1H, C$H_2$), 2.72 (dd, *J* = 13.9, 8.3, 0.8 Hz, 1H, C$H_2$); $^{13}$C NMR (acetone-$d^6$) δ 168.6 (*C*), 146.6 (*C*), 144.2 (*C*), 142.7 (*C*), 142.1 (*C*), 141.0 (*C*), 130.4 (*C*H), 130.1 (*C*H), 129.2 (*C*H), 128.7 (*C*H), 128.1 (*C*H), 128.0 (*C*H), 127.0 (*C*H), 123.3 (*C*H), 122.7 (*C*$H_2$), 199.5 (*C*H), 119.9 (*C*H), 74.5 (*C*H), 44.2 (*C*$H_2$); HRMS ($ESI^+$) *m/z* calcd for $C_{23}H_{21}NO_2$+Na: 366.1465, found 366.1447.

*4.2.1.4. (S)-N-(3,5-Di-tert-butylphenyl)-4-hydroxy-2-methylene-4-phenylbutanamide (**11**)*. Mp 141.2-141.7 °C; $[\alpha]_D^{20}$ -41.2 (*c* 1.76, $CHCl_3$); IR (KBr) 3277 (N-H), 2870 (O-H), 1599 (C=O) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$): δ 8.16 (brs, 1H, N*H*), 7.41-7.20 (m, 8H, Ar*H*), 5.81 (s, 1H, C$H_2$), 5.34 (s, 1H, C$H_2$), 4.92 (dt, *J* = 8.3, 3.3 Hz, 1H, C*H*), 4.33 (d, *J* = 3.3 Hz, 1H, O*H*), 2.81 (dd, *J* = 14.0, 3.3 Hz, 1H, C$H_2$), 2.69 (dd, *J* = 14.0, 8.3 Hz, 1H, C$H_2$), 1.32 (s, 18H, C$H_3$); $^{13}$C NMR ($CDCl_3$) δ 168.1 (*C*), 151.7 (*C*), 144.0 (*C*), 143.0 (*C*), 137.0 (*C*), 128.3 (*C*H), 127.4 (*C*), 125.8 (*C*H), 121.8 (*C*$H_2$), 118.9 (*C*H), 114.8 (*C*H), 74.5 (*C*H), 43.1 (*C*$H_2$), 34.9 (*C*),

31.4 (2*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{25}H_{33}NO_2$+Na: 402.2404, found 402.2433.

*4.2.1.5. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-2-methylene-4-phenylbutanamide (**12**)*. Mp 164.0-165.0 °C; $[\alpha]_D^{24}$ -55.9 (*c* 1.00, $CHCl_3$); IR (KBr) 2957 (N-H), 2868 (O-H), 1649 (C=O) $cm^{-1}$; $^1H$ NMR (acetone-$d^6$): δ 9.46 (brs, 1H, N*H*), 7.67-7.65 (m, 2H, Ar*H*), 7.43-7.18 (m, 6H, Ar*H*), 7.21 (m, 1H, Ar*H*), 5.86 (d, *J* = 0.9 Hz, 1H, C$H_2$), 5.41 (d, *J* = 0.9 Hz, 1H, C$H_2$), 5.10 (brs, 1H, O*H*), 4.89 (dt, *J* = 8.3, 4.0 Hz, 1H, C*H*), 2.79 (ddd, *J* = 13.9, 4.0, 0.9 Hz, 1H, C$H_2$), 2.68 (ddd, *J* = 13.9, 8.3, 0.9 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$); $^{13}C$ NMR (acetone-$d^6$): δ 168.5 (*C*), 147.5 (*C*), 146.6 (*C*), 144.2 (*C*), 137.8 (*C*), 129.2 (*C*H), 128.1 (*C*H), 127.0 (*C*H), 126.5 (*C*H), 122.4 (*C*$H_2$), 120.8 (*C*H), 74.5 (*C*H), 44.3 (*C*$H_2$), 35.2 (*C*), 32.0 (*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{21}H_{25}NO_2$+Na: 346.1778, found 346.1764.

*4.2.1.6. (S)-4-Hydroxy-N-(2-methoxyphenyl)-2-methylene-4-phenylbutanamide (**13**)*. $[\alpha]_D^{22}$ -2.07 (*c* 1.05, $CHCl_3$); IR (NaCl) 3354 (N-H), 3005 (O-H), 1649 (C=O), 1226 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 8.54 (brs, 1H, N*H*), 8.34 (dd, *J* = 9.3, 1.4 Hz, 1H, Ar*H*), 7.37-7.18 (m, 5H, Ar*H*), 7.08-6.84 (m, 3H, Ar*H*), 5.75 (s, 1H, C$H_2$), 5.33 (s, 1H, C$H_2$), 4.86 (ddd, *J* = 8.4, 3.7, 3.5 Hz, 1H, C*H*), 4.65 (d, *J* = 3.5 Hz, 1H, O*H*), 3.83 (s, 3H, C$H_3$), 2.77 (dd, *J* = 14.1, 3.7 Hz, 1H, C$H_2$), 2.65 (dd, *J* = 14.1, 8.4 Hz, 1H, C$H_2$); $^{13}C$ NMR ($CDCl_3$): δ 167.9 (*C*), 148.2 (*C*), 144.2 (*C*), 142.9 (*C*), 128.2 (*C*H), 127.2 (*C*H), 125.7 (*C*H), 124.2 (*C*H), 124.2 (*C*H), 121.5 (*C*$H_2$), 121.0 (*C*H), 120.0 (*C*H), 110.0 (*C*H) 74.0 (*C*H), 55.7 (*C*$H_3$), 43.2 (*C*$H_2$). Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 73.04; H, 6.55; N, 4.98.

*4.2.1.7. (S)-4-Hydroxy-N-(4-methoxyphenyl)-2-methylene-4-phenylbutanamide (**14**)*. Mp 121.6-122.2 °C; $[\alpha]_D^{23}$ -0.06 (*c* 2.03, $CHCl_3$); IR (KBr) 3568 (N-H), 3279 (O-H), 1603 (C=O), 1250 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 8.40 (brs, 1H, N*H*), 7.43 (d, *J* = 9.0 Hz, 2H, Ar*H*), 7.36-7.23 (m, 5H, Ar*H*), 6.85 (d, *J* = 9.0 Hz, 2H, Ar*H*), 5.80 (s, 1H, C$H_2$), 5.31 (s, 1H, C$H_2$), 4.88 (dt, *J* = 8.3, 3.1 Hz, 1H, C*H*), 4.56 (d, *J* = 3.1 Hz, 1H, O*H*), 3.78 (s, 3H, C$H_3$), 2.76 (dd, *J* = 14.1, 3.1 Hz, 1H, C$H_2$), 2.65 (dd, *J* = 14.1, 8.3 Hz, 1H, C$H_2$); $^{13}C$ NMR ($CDCl_3$) δ 168.0 (*C*), 156.6 (*C*), 143.9 (*C*), 142.6 (*C*), 130.7 (*C*), 128.3 (*C*H), 127.4 (*C*H), 125.6 (*C*H), 122.3 (*C*$H_2$), 122.0 (*C*H), 114.1 (*C*H), 74.7 (*C*H), 55.4 (*C*$H_3$), 43.0 (*C*$H_2$); HRMS ($ESI^+$) *m/z* calcd for $C_{18}H_{19}NO_3$+Na: 320.1257, found 320.1234.

*4.2.1.8. (R)-N-(4-tert-Butylphenyl)-4-hydroxy-6-methyl-2-methyleneheptanamide (**15**)*. Mp 107.2-107.7 °C; $[\alpha]_D^{24}$ +3.62 (*c* 1.00, $CHCl_3$); IR (KBr) 3267 (N-H), 2957 (O-H), 1647 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.46 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.30 (d, *J* = 8.6 Hz, 2H, Ar*H*), 5.89 (s, 1H, C$H_2$), 5.41 (s, 1H, C$H_2$), 3.89-3.82 (m, 1H, C*H*), 3.73 (brs, 1H, O*H*), 2.57 (dd, *J* = 14.1, 2.6 Hz, 1H, C$H_2$), 2.35 (dd, *J* = 14.1, 8.3 Hz, 1H, C$H_2$), 1.84-1.71 (m, 1H, C*H*), 1.50-1.41 (m, 1H, C$H_2$), 1.30-1.21 (m, 1H, C$H_2$), 1.29 (s, 9H, C$H_3$), 0.92 (d, *J* = 6.6 Hz, 3H, C$H_3$), 0.90 (d, *J* = 6.6 Hz, 3H, C$H_3$); $^{13}C$ NMR ($CDCl_3$) δ 167.8 (*C*), 147.3 (*C*), 143.4 (*C*), 135.3 (*C*), 125.7 (*C*H), 122.2 (*C*$H_2$), 119.9 (*C*H), 70.1 (*C*H), 46.5 (*C*$H_2$), 41.0 (*C*$H_2$), 34.3 (*C*), 31.3 (*C*$H_3$), 24.6 (*C*H), 23.2 (*C*$H_3$), 22.1 (*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{19}H_{29}NO_2$+Na: 326.2091, found 326.2069.

*4.2.1.9. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-5,5-dimethyl-2-methylenehexanamide (**16**)*. Mp 155.2-156.6 °C; $[\alpha]_D^{20}$ +3.51 (*c* 0.41, $CHCl_3$); IR (KBr) 3568 (N-H), 2957 (O-H), 1597 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 8.39 (brs, 1H, N*H*), 7.47 (d, *J* = 6.7 Hz, 2H, Ar*H*), 7.34 (d, *J* = 6.7 Hz, 2H, Ar*H*), 5.88 (s, 1H, C$H_2$), 5.46 (s, 1H, C$H_2$), 3.39 (ddd, *J* =10.2, 4.1, 2.0 Hz, 1H, C*H*), 3.06 (d, *J* = 4.1 Hz, 1H, O*H*), 2.61 (dd, *J* = 13.9, 2.0 Hz, 1H, C$H_2$), 2.29 (dd, *J* = 13.9, 10.2 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$), 0.96 (s, 9H, C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 167.8 (*C*), 147.4 (*C*), 144.8 (*C*), 135.2 (*C*), 125.8 (*C*H), 121.2 (*C*$H_2$), 119.8 (*C*H), 81.0 (*C*H), 35.3 (*C*$H_2$), 35.2 (*C*), 34.4 (*C*), 31.3 (*C*$H_3$), 25.5 (*C*$H_3$). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.20; H, 9.63; N, 4.62. Found: C, 75.13; H, 9.24; N, 4.57.

*4.2.1.10. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-4-(4-methoxyphenyl)-2-methylenebutanamide (**17**)*. Mp 137.0-138.0 °C; $[\alpha]_D^{23}$ -32.1 (*c* 1.00, $CHCl_3$); IR (KBr) 3568 (N-H), 2964 (O-H), 1655 (C=O), 1248 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 8.17 (brs, 1H, N*H*), 7.46 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.36 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.30 (d, *J* = 8.8 Hz, 2H, Ar*H*), 6.87 (d, *J* = 8.8 Hz, 2H, Ar*H*), 5.83 (s, 1H, C$H_2$), 5.36 (s, 1H, C$H_2$), 4.89 (dt, *J* = 8.1, 3.0 Hz, 1H, C*H*), 3.85 (d, *J* = 3.0 Hz, 1H, O*H*), 3.79 (s, 3H, C$H_3$), 2.79 (dd, *J* = 14.1, 3.0 Hz, 1H, C$H_2$), 2.70 (dd, *J* = 14.1, 8.1 Hz, 1H, C$H_2$), 1.31 (s, 9H, C$H_3$); $^{13}C$ NMR ($CDCl_3$) δ 167.9 (*C*), 159.0 (*C*), 147.7 (*C*), 143.0 (*C*), 136.1 (*C*), 135.0 (*C*), 127.0 (*C*H), 125.8 (*C*H), 122.0 (*C*$H_2$), 120.0 (*C*H), 113.8 (*C*H), 74.3 (*C*H), 55.3 (*C*$H_3$), 43.0 (*C*$H_2$), 34.4 (*C*), 31.3 (*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{22}H_{27}NO_3$+Na: 376.1883, found 376.1871.

*4.2.1.11. (S)-N-(4-tert-Butylphenyl)-4-(3-chlorophenyl)-4-hydroxy-2-methylenebutanamide (**18**)*. Mp 147.2-148.2 °C; $[\alpha]_D^{24}$ -47.2 (*c* 1.00, $CHCl_3$); IR (KBr) 3277 (N-H), 2959 (O-H), 1599 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 8.37 (brs, 1H, N*H*), 7.46-7.17 (m, 8H, Ar*H*), 5.85 (s, 1H, C$H_2$), 5.30 (s, 1H, C$H_2$), 5.09 (d, *J* = 3.3 Hz, 1H, O*H*), 4.83 (dt, *J* = 8.3, 3.3 Hz, 1H, C*H*), 2.74 (dd, *J* = 14.1, 3.3 Hz, 1H, C$H_2$), 2.59 (dd, *J* = 14.1, 8.3 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$); $^{13}C$ NMR ($CDCl_3$) δ 168.2 (*C*), 148.0 (*C*), 146.2 (*C*), 142.4 (*C*), 134.7 (*C*), 134.2 (*C*), 129.6 (*C*H), 127.5 (*C*H), 125.94 (*C*H), 125.88 (*C*H), 123.9 (*C*H), 122.2 (*C*$H_2$), 120.1 (*C*H), 73.8 (*C*H), 43.1 (*C*$H_2$), 34.4 (*C*), 31.3 (*C*$H_3$); HRMS ($ESI^+$) *m/z* calcd for $C_{21}H_{24}ClNO_2$+Na: 380.1388, found 380.1407.

*4.2.1.12. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-2-methylene-4-(4-nitrophenyl)butanamide (**19**)*. Mp 161.6-162.5 °C; $[\alpha]_D^{24}$ -58.2 (*c* 1.00, $CHCl_3$); IR (KBr) 2959 (N-H), 2868 (O-H), 1597 (C=O) $cm^{-1}$; $^1H$ NMR (acetone-$d^6$): δ 9.36 (brs, 1H, N*H*), 8.18 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.69 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.63 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.35 (d, *J* = 8.8 Hz, 2H, Ar*H*), 5.87 (s, 1H, C$H_2$), 5.46 (d, *J* = 4.0 Hz, 1H, O*H*), 5.33 (s, 1H, C$H_2$), 5.08 (ddd, *J* = 7.9, 4.2, 4.0 Hz, 1H, C*H*), 2.86 (dd, *J* = 13.7, 4.2 Hz, 1H, C$H_2$), 2.73 (dd, *J* = 13.7, 7.9 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$); $^{13}C$ NMR (acetone-$d^6$) δ 168.7 (*C*), 154.2 (*C*), 148.3 (*C*), 147.7 (*C*),

143.4 (*C*), 137.7 (*C*), 128.2 (*C*H), 126.6 (*C*H), 124.3 (*C*H), 122.7 (*C*$H_2$), 121.0 (*C*H), 73.7 (*C*H), 44.0 (*C*$H_2$), 35.2 (*C*), 32.0 (*C*$H_3$); HRMS (ESI$^+$) *m/z* calcd for $C_{21}H_{24}N_2O_4$+Na: 391.1628, found 391.1647.

*4.2.1.13. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-4-(4-isopropylphenyl)-2-methylenebutanamide (**20**).* Mp 189.9-190.8 °C; $[\alpha]_D^{23}$ -38.0 (*c* 1.00, $CHCl_3$); IR (KBr) 3184 (N-H), 2962 (O-H), 1600 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$): δ 8.35 (brs, 1H, N*H*), 7.46 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.34 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.29 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.19 (d, *J* = 8.2 Hz, 2H, Ar*H*), 5.84 (s, 1H, C$H_2$), 5.37 (s, 1H, C$H_2$), 4.87 (ddd, *J* = 8.3, 3.5, 3.1 Hz, 1H, C*H*), 3.94 (d, *J* = 3.1 Hz, 1H, O*H*), 2.90 (sept, *J* = 7.0 Hz, 1H, C*H*), 2.78 (dd, *J* = 14.3, 3.5 Hz, 1H, C$H_2$), 2.69 (dd, *J* = 14.3, 8.3 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$), 1.23 (d, *J* = 7.0 Hz, 6H, 2C$H_3$); $^{13}$C NMR ($CDCl_3$) δ 167.8 (*C*), 148.3 (*C*), 147.5 (*C*), 143.0 (*C*), 141.3 (*C*), 135.1 (*C*), 126.4 (*C*H), 125.8 (*C*H), 125.7 (*C*H), 122.2 (*C*$H_2$), 119.9 (*C*H), 74.7 (*C*H), 42.9 (*C*$H_2$), 34.4 (*C*), 33.8 (*C*H), 31.3 (*C*$H_3$), 23.9 (*C*$H_3$). Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83; Found: C, 79.12; H, 8.64; N, 3.87.

*4.2.1.14. (S)-N,4-Bis(4-tert-butylphenyl)-4-hydroxy-2-methylenebutanamide (**21**).* Mp 199.7-201.1 °C; $[\alpha]_D^{23}$ -34.1 (*c* 1.00, $CHCl_3$); IR (KBr) 2959 (N-H), 2866 (O-H), 1599 (C=O) cm$^{-1}$; $^1$H-NMR (acetone-d$^6$): δ 9.40 (brs, 1H, N*H*), 7.63 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.36-7.35 (m, 6H, Ar*H*), 5.87 (s, 1H, C$H_2$), 5.45 (s, 1H, C$H_2$), 4.92 (d, *J* = 3.9 Hz, 1H, O*H*), 4.85 (ddd, *J* = 8.4, 4.1, 3.9 Hz, 1H, C*H*), 2.78 (dd, *J* = 13.7, 4.1 Hz, 1H, C$H_2$), 2.67 (dd, *J* = 13.7, 8.4 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$), 1.28 (s, 9H, C$H_3$); $^{13}$C NMR (acetone-d$^6$) δ 168.6 (*C*), 150.8 (*C*), 147.5 (*C*), 144.6 (*C*), 143.7 (*C*), 138.0 (*C*), 126.9 (*C*H), 126.6 (*C*H), 126.1 (*C*H), 122.2 (*C*$H_2$), 120.8 (*C*H), 74.7 (*C*H), 44.3 (*C*$H_2$), 35.3 (*C*), 35.2 (*C*), 32.1 (2*C*$H_3$). Anal. Calcd for $C_{25}H_{33}NO$: C, 79.11; H, 8.76; N, 3.69; Found: C, 79.34; H, 9.12; N, 3.81.

*4.2.1.15. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-2-methylene-4-(naphthalen-1-yl)butanamide (**22**).* Mp 155.6-156.6 °C; $[\alpha]_D^{24}$ -94.2 (*c* 1.00, $CHCl_3$); IR (KBr) 3568 (N-H), 2961 (O-H), 1597 (C=O) cm$^{-1}$; $^1$H NMR ($CD_3OD$): δ 8.24 (d, *J* = 8.3 Hz, 1H, N*H*), 7.87-7.33 (m, 11H, Ar*H*), 5.85 (s, 1H, C$H_2$), 5.68 (dd, *J* = 8.7, 3.7 Hz, 1H, C*H*), 5.45 (s, 1H, C$H_2$), 3.07 (dd, *J* = 14.2, 8.7 Hz, 1H, C$H_2$), 2.74 (dd, *J* = 14.2, 3.7 Hz, 1H, C$H_2$), 1.32 (s, 9H, C$H_3$); $^{13}$C NMR ($CD_3OD$) δ 169.9 (*C*), 148.6 (*C*), 144.0 (*C*), 141.6 (*C*), 137.0 (*C*), 135.3 (*C*), 131.7 (*C*), 129.8 (*C*H), 128.8 (*C*H), 127.0 (*C*H), 126.7 (*C*H), 126.6 (*C*H), 126.5 (*C*H) 124.3 (*C*H), 123.9 (*C*H), 122.7 (*C*$H_2$), 121.8 (*C*H), 70.8 (*C*H), 43.4 (*C*$H_2$), 35.2 (*C*), 31.8 (*C*$H_3$). Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75. Found: C, 80.66; H, 7.35; N, 3.80.

*4.2.1.16. (S)-N-(4-tert-Butylphenyl)-4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanamide (**23**).* Mp 157.0-158.0 °C; $[\alpha]_D^{25}$ -60.1 (*c* 1.00, $CHCl_3$); IR (KBr) 3568 (N-H), 3223 (O-H), 1655 (C=O) cm$^{-1}$; $^1$H NMR (acetone-d$^6$): δ 9.47 (brs, 1H, N*H*), 7.89-7.84 (m, 4H, Ar*H*), 7.69-7.57 (m, 3H, Ar*H*), 7.50-7.34 (m, 4H, Ar*H*), 5.85 (d, *J* = 0.8 Hz, 1H, C$H_2$), 5.43 (d, *J* = 0.6 Hz, 1H, C$H_2$), 5.25 (d, *J* = 3.9 Hz, 1H, O*H*), 5.08 (ddd, *J* = 8.2, 4.3, 3.9 Hz, 1H, C*H*), 2.90 (ddd, *J* = 13.9, 4.3, 0.8 Hz, 1H, C$H_2$), 2.79 (ddd, *J* = 13.9, 8.2, 0.6 Hz, 1H, C$H_2$), 1.30 (s, 9H, C$H_3$); $^{13}$C NMR (acetone-d$^6$): δ 168.6 (*C*), 147.5 (*C*), 144.2 (*C*), 144.1 (*C*), 137.8 (*C*), 134.6 (*C*), 134.1 (*C*), 129.1 (*C*H), 128.9 (*C*H), 128.8 (*C*H), 127.1 (*C*H), 126.7 (*C*H), 126.5 (*C*H), 125.7 (*C*H), 125.5 (*C*H), 122.4 (*C*$H_2$), 120.8 (*C*H), 74.6 (*C*H), 44.2 (*C*$H_2$), 35.2 (*C*), 32.0 (*C*$H_3$). Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75; Found: C, 80.53; H, 7.62; N, 3.92.

*4.2.2. General procedure for the preparation of α-methylene-γ-butyrolactones from γ-hydroxy amides (Scheme 3). (S)-3-Methylene-5-phenyldihydrofuran-2(3H)-one (**24**)*

To a solution of **12** (121 mg, 0.453 mmol) in 1,4-dioxane (1.3 mL) was added 10% HCl (1.0 mL) and warmed up to 65 °C. After the mixture was stirred for 2 h, cooled to room temperature, quenched by the addition of water (5.0 mL) and extracted with ethyl acetate (30 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=4:1) to give **24** (76.0 mg, 96%) as a colorless oil. $[\alpha]_D^{23}$ +12.7 (*c* 1.00, $CHCl_3$); IR (NaCl) 1757 (C=O), 1279 (C-O) cm$^{-1}$; $^1$H NMR ($CDCl_3$): δ 7.42 (m, 5H, Ar*H*), 6.30 (t, *J* = 2.7 Hz, 1H, C$H_2$), 5.69 (t, *J* = 2.4 Hz, 1H, C$H_2$), 5.52 (dd, *J* = 8.0, 3.6 Hz, 1H, C*H*), 3.40 (ddt, *J* = 16.8, 8.0, 2.4 Hz, 1H, C$H_2$), 2.90 (ddt, *J* = 16.8, 3.6, 2.4 Hz, 1H, C$H_2$); $^{13}$C NMR ($CDCl_3$) δ 170.1 (*C*), 139.8 (*C*), 134.2 (*C*), 128.8 (*C*H), 128.5 (*C*H), 125.3 (*C*H), 122.4 (*C*$H_2$), 77.9 (*C*H), 36.2 (*C*$H_2$). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.86; H, 6.07.

*4.2.2.1. (R)-5-Isobutyl-3-methylenedihydrofuran-2(3H)-one (**25**).* $[\alpha]_D^{21}$ +26.1 (*c* 0.96, EtOH); IR (NaCl) 1762 (C=O), 1274 (C-O) cm$^{-1}$; $^1$H NMR ($CDCl_3$): δ 6.22 (t, *J* = 2.8 Hz, 1H, C$H_2$), 5.62 (t, *J* = 2.5 Hz, 1H, C$H_2$), 4.64-4.55 (m, 1H, C*H*), 3.07 (ddt, *J* = 16.9, 7.7, 2.5 Hz, 1H, C$H_2$), 2.54 (ddt, *J* = 16.9, 6.2, 2.8 Hz, 1H, C$H_2$), 1.92-1.79 (m, 1H, C*H*), 1.69 (ddd, *J* = 14.0, 8.7, 6.2 Hz, 1H, C$H_2$), 1.41 (ddd, *J* = 14.0, 8.1, 5.1 Hz, 1H, C$H_2$), 0.97 (d, *J* = 6.6 Hz, 3H, C$H_3$), 0.95 (d, *J* = 6.6 Hz, 3H, C$H_3$); $^{13}$C NMR ($CDCl_3$) δ 170.4 (*C*), 134.7 (*C*), 121.9 (*C*), 76.1 (*C*H), 45.5 (*C*$H_2$), 34.1 (*C*$H_2$), 24.7 (*C*H), 22.9 (*C*$H_3$), 22.1 (*C*$H_3$). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 7.46. Found: C, 69.77; H, 8.77.

*4.2.2.2. (S)-5-(4-Isopropylphenyl)-3-methylenedihydrofuran-2(3H)-one (**26**).* $[\alpha]_D^{23}$ +17.0 (*c* 1.46, $CHCl_3$); IR (NaCl) 1767 (C=O), 1277 (C-O) cm$^{-1}$; $^1$H NMR ($CDCl_3$): δ 7.26-7.25 (m, 4H, Ar*H*), 6.30 (t, *J* = 2.8 Hz, 1H, C$H_2$), 5.68 (t, *J* = 2.5 Hz, 1H, C$H_2$), 5.50 (dd, *J* = 7.7, 6.6 Hz, 1H, C*H*), 3.37 (ddt, *J* = 17.0, 7.7, 2.5 Hz, 1H, C$H_2$), 2.95-2.87 (m, 2H, C*H* and C$H_2$), 1.25 (d, *J* = 7.0 Hz, 6H, C$H_3$); $^{13}$C NMR ($CDCl_3$) δ 170.2 (*C*), 149.4 (*C*), 137.1 (*C*), 134.4 (*C*), 126.9 (*C*H), 125.5 (*C*H), 122.2 (*C*$H_2$), 78.0 (*C*H), 36.2 (*C*$H_2$), 33.8 (*C*H), 23.9 (*C*$H_3$). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.08; H, 7.42.

*4.2.2.3. (S)-5-(4-tert-Butylphenyl)-3-methylenedihydrofuran-2(3H)-one (**27**).* Mp 79.1-80.4 °C;

$[\alpha]_D^{23}$ +16.5 (*c* 1.22, $CHCl_3$); IR (KBr) 1766 (C=O), 1279 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.41 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.25 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.30 (s, 1H, C$H_2$), 5.68 (s, 1H, C$H_2$), 5.51 (t, *J* = 7.2 Hz, 1H, C*H*), 3.41-3.35 (m, 1H, C$H_2$), 2.98-2.88 (m, 1H, C$H_2$), 1.32 (s, 9H, C$H_3$); $^{13}C$ NMR ($CDCl_3$) δ 170.2 (*C*), 151.7 (*C*), 136.7 (*C*), 134.4 (*C*), 125.7 (*C*H), 125.2 (*C*H), 122.2 (*C*$H_2$), 77.9 (*C*H), 36.1 (*C*$H_2$), 34.6 (*C*), 31.2 (*C*$H_3$). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.53; H, 7.65.

*4.2.2.4. (S)-3-Methylene-5-(naphthalen-1-yl)dihydrofuran-2(3H)-one (**28**).* $[\alpha]_D^{22}$ -75.0 (*c* 2.45, $CHCl_3$); IR (NaCl) 1764 (C=O), 1281 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.87-7.81 (m, 3H, Ar*H*), 7.58-7.43 (m, 4H, Ar*H*), 6.34 (t, *J* = 2.8 Hz, 1H, C$H_2$), 6.25 (dd, *J* = 8.3, 5.7 Hz, 1H, C*H*), 5.66 (t, *J* = 2.5 Hz, 1H, C$H_2$), 3.62 (ddt, *J* = 17.0, 8.3, 2.8 Hz, 1H, C$H_2$), 2.95 (ddt, *J* = 17.0, 5.7, 2.5 Hz, 1H, C$H_2$); $^{13}C$ NMR ($CDCl_3$) δ 170.3 (*C*), 135.6 (*C*), 133.8 (*C*), 133.7 (*C*), 129.3 (*C*), 129.2 (*C*H), 128.7 (*C*H), 126.6 (*C*H), 125.9 (*C*H), 125.4 (*C*H), 123.0 (*C*$H_2$), 122.3 (*C*H). 121.7 (*C*H), 75.4 (*C*H), 35.8 (*C*$H_2$). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.45; H, 5.51.

*4.2.2.5. (S)-3-Methylene-5-(naphthalen-2-yl)dihydrofuran-2(3H)-one (**29**).* Mp 70.0-71.0 °C; $[\alpha]_D^{23}$ +34.9 (*c* 1.23, $CHCl_3$); IR (KBr) 1757 (C=O), 1273 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.85-7.81 (m, 4H, Ar*H*), 7.51-7.48 (m, 2H, Ar*H*), 7.37 (dd, *J* = 8.4, 1.8 Hz, 1H, Ar*H*), 6.33 (t, *J* = 2.7 Hz, 1H, C$H_2$), 5.70 (t, *J* = 2.5 Hz, 1H, C$H_2$), 5.66 (dd, *J* = 8.0, 7.3 Hz, 1H, C*H*), 3.45 (ddt, *J* = 17.1, 8.0, 2.5 Hz, 1H, C$H_2$), 2.97 (ddt, *J* = 17.1, 7.3, 2.7 Hz, 1H, C$H_2$); $^{13}C$ NMR ($CDCl_3$) δ 170.2 (*C*), 137.0 (*C*), 134.1 (*C*), 133.2 (*C*), 133.0 (*C*), 128.9 (*C*H), 128.0 (*C*H), 127.7 (*C*H), 126.6 (*C*H), 126.5 (*C*H), 124.5 (*C*H), 122.7 (*C*$H_2$), 122.6 (*C*H), 76.6 (*C*H), 36.2 (*C*$H_2$). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.03; H, 5.28.

*tert-Butyl phenyl{2-[(tributylstannyl)methyl]acryloyl}carbamate (**30**)*

To a solution of **4a** (150 mg, 0.333 mmol), $Et_3N$ (51.0 mg, 0.500 mmol), $Boc_2O$ (80.0 mg, 0.366 mmol) and DMAP (41.0 mg, 0.333 mmol) in $CH_2Cl_2$ (0.7 mL) was stirred for 35 h at room temperature. The reaction mixutre was filtered through Celite, then $CH_2Cl_2$ was removed in *vacuo*. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=20/1) to give **30** (180 mg, 98%) as a colorless oil. IR (NaCl) 2957 (C-H), 1737 (C=O), 1689 (C=O), 1153 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.40-7.12 (m, 5H, Ar*H*), 5.31 (s, 1H, C$H_2$), 5.14 (s, 1H, C$H_2$), 1.96 (s, 3H, C$H_2$), 1.55-1.23 (m, 12H, C$H_2$), 1.45 (s, 9H, C$H_3$), 1.00-0.78 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 174.7, 153.5, 148.2, 138.9, 129.0, 127.42, 127.38, 112.9, 83.2, 29.0, 27.8, 27.3, 15.9, 13.7, 10.2; HRMS ($ESI^+$) *m/z* calcd for $C_{27}H_{45}NO_3Sn$+Na: 574.2314, found 574.2278.

*4.2.3. General procedure for the preparation of β-alkoxycarbonyl allyltributylstannanes **31** and **32** (Scheme 4). Ethyl 2-[(tributylstannyl)methyl]acrylate (**31**)*

To a solution of NaH (192 mg, 8.34 mmol) and ethanol (5.0 mL) was added a solution of **30** (1.53 g, 2.78 mmol) in ethanol (3.3 mL) at 0 °C and warmed up to room temperature. After stirred for 1 h, the reaction was quenched by the addition of saturated aquous $NH_4Cl$ (5.0 mL) and the resulting solution was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=60:1) to give **31** (1.02 g, 92%) as a colorless oil. IR (NaCl) 2926 (C-H), 1713 (C=O), 1178 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 5.81 (s, 1H, C$H_2$), 5.27 (s, 1H, C$H_2$), 4.18 (q, *J* = 7.1 Hz, 2H, C$H_2$), 1.97 (s, 2H, C$H_2$), 1.59-1.23 (m, 12H, C$H_2$), 1.30 (t, *J* = 7.1 Hz, 3H, C$H_3$), 0.97-0.75 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 167.8, 141.3, 118.4, 60.6, 29.0, 27.3, 14.9, 14.2, 13.7, 9.7; HRMS ($ESI^+$) *m/z* calcd for $C_{18}H_{36}O_2Sn$+Na: 427.1629, found 427.1679.

*4.2.3.1. Methyl 2-[(tributylstannyl)methyl]acrylate (**32**).* IR (NaCl) 2926 (C-H), 1720 (C=O), 1169 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 5.81 (s, 1H, C$H_2$), 5.29 (s, 1H, C$H_2$), 3.73 (s, 3H, C$H_3$), 1.97 (s, 2H, C$H_2$), 1.56-1.23 (m, 12H, C$H_2$), 0.96-0.77 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 168.2, 141.0, 118.7, 51.7, 29.0, 27.3, 15.0, 13.7, 9.7; HRMS ($ESI^+$) *m/z* calcd for $C_{17}H_{34}O_2Sn$+Na: 413.1473, found 413.1519.

*4.2.3.2. General procedure for the preparation of β-alkoxycarbonyl allyltributylstannanes **33-35** (Scheme 4); Isopropyl 2-[(tributylstannyl)methyl]acrylate (**33**)*

To a solution of NaH (66.0 mg, 2.725 mmol) and 2-propanol (164 mg, 2.725 mmol) in THF (1.0 mL) was added a solution of **30** (500 mg, 0.908 mmol) in THF (1.0 mL) at 0 °C and warmed up to room temperature. After stirred for 30 min, the reaction was quenched by the addition of saturated aqueous $NH_4Cl$ (5.0 mL) and the resulting solution was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=50:1) to give **33** (257 mg, 68%) as a colorless oil. IR (NaCl) 2926 (C-H), 1709 (C=O), 1182 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 5.78 (s, 1H, C$H_2$), 5.26 (s, 1H, C$H_2$), 5.04 (sept, *J* = 6.2 Hz, 1H, C*H*), 1.96 (s, 2H, C$H_2$), 1.59-1.20 (m, 12H, C$H_2$), 1.27 (d, *J* = 6.2 Hz, 6H, C$H_3$), 0.97-0.75 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 167.3, 141.7, 118.0, 67.8, 29.0, 27.3, 21.8, 14.8, 13.6, 9.7. Anal. Calcd for $C_{19}H_{38}O_2Sn$: C, 54.70; H, 9.18. Found: C, 54.61; H, 8.81.

*4.2.3.3. Benzyl 2-[(tributylstannyl)methyl]acrylate (**34**)*. IR (NaCl) 2926 (C-H), 1717 (C=O), 1165 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.28-7.20 (m, 5H, Ar*H*), 5.79 (s, 1H, C$H_2$), 5.23 (s, 1H, C$H_2$), 5.08 (s, 2H, C$H_2$), 1.91 (s, 2H, C$H_2$), 1.47-1.12 (m, 12H, C$H_2$), 0.81-0.71 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 167.8, 141.1, 136.1, 128.4, 128.1, 128.0, 118.9, 66.4, 28.9, 27.3, 14.9, 13.7, 9.7; HRMS ($ESI^+$) *m/z* calcd for $C_{23}H_{38}O_2Sn$+Na: 489.1786, found 489.1835.

*4.2.3.4. Phenyl 2-[(tributylstannyl)methyl]acrylate (**35**)*. IR (NaCl) 2926 (C-H), 1732 (C=O), 1200 (C-O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.42-7.35 (m, 2H, Ar*H*), 7.25-7.19 (m, 1H, Ar*H*), 7.11-7.06 (m, 2H, Ar*H*), 6.06 (s, 1H, C$H_2$), 5.48 (s, 1H, C$H_2$), 2.07 (s, 2H, C$H_2$), 1.60-1.23 (m, 12H, C$H_2$), 1.01-0.79 (m, 15H, C$H_2$ and C$H_3$); $^{13}C$ NMR ($CDCl_3$): δ 166.3, 151.1, 140.8, 129.4, 125.6, 121.6, 120.3, 29.0, 27.3, 15.0, 13.7, 9.8; HRMS ($ESI^+$) *m/z* calcd for $C_{22}H_{36}O_2Sn$+Na: 475.1629, found 475.1650.

*4.2.4. General procedure for the preparation of chiral α-methylene-γ-butyrolactone **24** from β-alkoxycarbonyl allyltributylstannanes (Table 4, entry 4).*

Under argon atmosphere, to the suspension of $InCl_3$ (9.4 mg, 0.0425 mmol) {predried at 140 °C for 2 h under reduced pressure (ca, 1.0 Torr)} and MS 4Å (120 mg) {also predried at 180 °C for 3 h under reduced pressure (ca, 1.0 Torr)} in $CH_2Cl_2$ (0.9 mL) was added (*S*)-BINOL **7c** (16.2 mg, 0.0566 mmol) at room temperature and stirred for 2 h. A solution of benzaldehyde (**5a**) (36.0 mg, 0.340 mmol) in $CH_2Cl_2$ (0.2 mL) was added and stirred for 1h. Then, **31** (114 mg, 0.283 mmol) in $CH_2Cl_2$ (0.2 mL) was slowly added dropwise at the same temperature and stirred for 7 days. The reaction was quenched by the addition of aqueous $NaHCO_3$ (5.0 mL), then $CH_2Cl_2$ was removed in *vacuo*. The mixture was filtered through Celite and the resulting solution was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The residue was purified by column chlomatography (silica gel, hexane/EtOAc=6:1) to give **24** (46.0 mg, 93%) as a colorless oil.

## 5. Acknowledgements

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[10] The same allylation reaction of benzaldehyde (**5a**) with **30** containing the electron-withdrawing Boc group on the nitrogen atom afforded the corresponding adduct in satisfactory chemical yield (81%), albeit in low enantiomeric excess (12% ee).