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Synthesis of Arylglycine and Mandelic Acid Derivatives through Carboxylations of α-Amido and α-Acetoxy Stannanes with Carbon Dioxide

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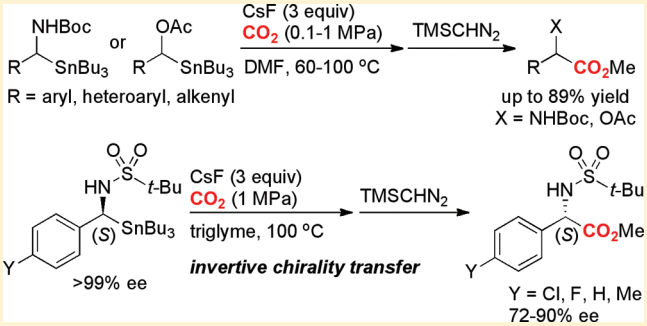
Supporting Information

ABSTRACT: Incorporation reactions of carbon dioxide (CO_2) with *N*-Boc-α-amido and α-acetoxy stannanes were developed using CsF as a mild tin activator. Monoprotected α-amido stannanes could be used, and the corresponding arylglycine derivatives were obtained in moderate-to-high yields under 1 MPa (10 atm) of CO_2 pressure. α-Acetoxy stannanes also underwent carboxylation to afford mandelic acid derivatives in excellent yields under ambient CO_2 pressure. Both transformations enabled the synthesis of α-tertiary and α-quaternary carboxylic acid derivatives. In addition, the chirality of (*S*)-*N*-*tert*-butylsulfonyl-α-amido stannanes was transferred with up to 90% inversion of configuration at 100 °C.

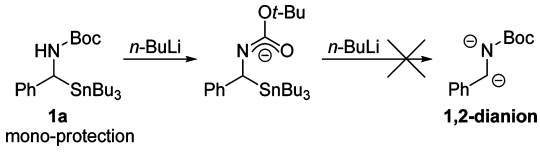


INTRODUCTION

α-Amino and α-hydroxy acid derivatives comprise an important class of molecules exhibiting various functions in both biochemistry and organic chemistry. In particular, the arylglycine class of nonproteogenic α-amino acids has recently received much attention because novel glycopeptide antibiotics such as vancomycin[1] contain arylglycine components in their structure. α-Hydroxy acid derivatives, e.g., mandelic acid, are used widely in cosmetics for skin care and as useful building blocks in organic synthesis.[2] Therefore, the development of an efficient process for their syntheses is an important goal in organic chemistry. One such synthetic strategy is carboxylation of an amine or alcohol derivative with CO_2 at the α-position of nitrogen and oxygen atoms; this route for generating α-amino and α-hydroxy acid derivatives would be more straightforward than existing methodologies[1−3] and, by using CO_2, would take advantage of an ubiquitous, inexpensive, nontoxic, and renewable C1 source.

Although considerable progress in the development of CO_2 fixation techniques has been made,[4] carboxylations of sp^3 carbon located at the α-position of heteroatoms have required the use of strongly basic organolithium reagents (e.g., *n*- or *sec*-BuLi with or without a ligand), which undergo either (a) deprotonation[5] or (b) Sn−Li exchange of α-stannanes[6,7] to generate a lithium carbanion, followed by carboxylation to provide α-amino and α-hydroxy acid derivatives. Therefore, these transformations require substrates without an acidic proton and must be operated under strictly anhydrous conditions in order to induce efficient carboxylation. In the context of amino acid synthesis, monoprotected α-amino acids, especially *N*-Boc derivatives, are more useful than bis-protected ones, because conventional peptide synthesis generally employs *N*-Boc- or *N*-Fmoc-amido acid derivatives due to the ease of protection and deprotection sequences (e.g., Merrifield peptide synthesis[8]). However, if *n*-BuLi is employed for monoprotected *N*-Boc-α-amido stannane **1a** in Sn−Li exchange reactions, deprotonation of the acidic amide N−H initially occurs to generate an amido anion; this species does not undergo further Sn−Li exchange to generate a 1,2-dianion, presumably owing to either a high kinetic barrier or the intrinsic thermodynamic instability of the resulting 1,2-dianion (Scheme 1).[9] Thus, we

Scheme 1. Unfavorable 1,2-Dianion Formation



considered the use of a milder base that would selectively activate tin atoms, and we have already reported that CsF is a suitable activator for **1a**, promoting carboxylation with CO_2 to afford the corresponding arylglycine derivatives in high yields under 1 MPa (10 atm) of CO_2.[10] Taking advantage of the easy accessibility of monoprotected α-amido stannanes from imine equivalents,[11,12] a novel one-pot process for α-amino acid synthesis from imine precursors using TMS-$SnBu_3$ and CsF was developed.[10] In this article, we report the substituent effects

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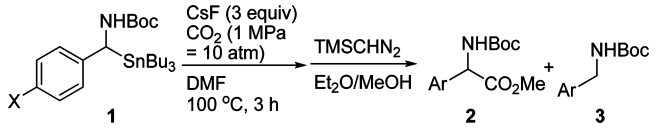
Table 1. Reactivities of *p*-Substituted α-Aryl Amido Stannanes



entry	R	Hammett σ	^{119}Sn NMR (ppm)	yield (%)[a] 2	3	1
1	H (**1a**)	0.00	−26.4	95 (83)	<1	–
2	CF_3 (**1b**)	0.53	−20.2	<1	>99	–
3	CO_2Me (**1c**)	0.45	−21.5	53	43	–
4	Cl (**1d**)	0.22	−24.6	81	12	–
5	F (**1e**)	0.06	−26.3 (J_{Sn-F} = 21.9 Hz)	88	6	–
6	Me (**1f**)	−0.14	−28.2	42	<1	43
7	OMe (**1g**)	−0.28	−29.2	15	<1	67

[a]Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The values in parentheses represent isolated yield.

on the aromatic ring of α-aryl α-amido stannanes as well as expansion of the substrate scope that includes a ketoimine-derived α-amido stannane and α-acetoxy stannanes. Results of chirality transfer transformations using chiral α-amido stannanes are also presented.

RESULTS AND DISCUSSION

Carboxylation of *N*-Boc-α-Amido Stannanes. First, various *para*-substituted α-aryl α-amido stannanes bearing both electron-donating and -withdrawing groups were synthesized using methods described in our recent report;[11] these were then applied to carboxylation under 1 MPa (10 atm) of CO_2 pressure at 100 °C in the presence of 3 equiv of CsF. This process yielded a mixture of the desired carboxylate, **2**, the yield of which was determined after esterification with $TMSCHN_2$, and protiodestannylation product **3** (Table 1). All of the substrates except **1b** underwent carboxylation; however, the yield of **2** depended on the electronic character of the substituent of the aromatic ring. Interestingly, Hammett σ-values[13] are useful in the prediction of each yield. When using electron-deficient substrates with positive σ-values such as those bearing trifluoromethyl, methoxy carbonyl, chloro, and fluoro substituents on their aromatic ring (**1b**−**1e**), the yield of **3** increased in response to Hammett σ-values, presumably because proton transfer from the amide N−H moiety was allowed to proceed.[10] In contrast, the reaction of electron-rich substrates with negative σ-values such as those having methoxy and methyl groups (**1f** and **1g**) reduced the yield of **2** owing to incomplete reaction of α-amido stannane **1**. In addition, ^{119}Sn NMR analysis of α-amido stannanes **1** in C_6D_6 correlated perfectly with Hammett σ-values (the chemical shift of tin atoms are moved to upfield in response to the increased electron density of aromatic rings) and are thus consistent with the trend outlined above. In addition, the NMR spectra of **1e** having a *p*-fluoro-phenyl group revealed nuclear coupling between ^{119}Sn and ^{19}F (J_{Sn-F} = 21.9 Hz). Based on the correlation between Hammett σ-values and the yield of each component, substrates with σ-values close to zero such as **1a** and **1e** provide the highest yields of carboxylation products. Carboxylations using these two α-amido stannanes prevented the generation of **3** at a maximum level without unreacted **1** remaining.

In order to obtain quantitative data on the reaction rates, the ratio of conversion (**2** + **3**/**2a** + **3a**)[14] at an early time point (15 min: <40% conversion) was used to approximate k_X/k_H (X = Cl, F, Me, OMe). Plotting $\log(k_X/k_H)$ versus Hammett σ-values indeed revealed a linear relationship with ρ = +1.83 (Figure 1),

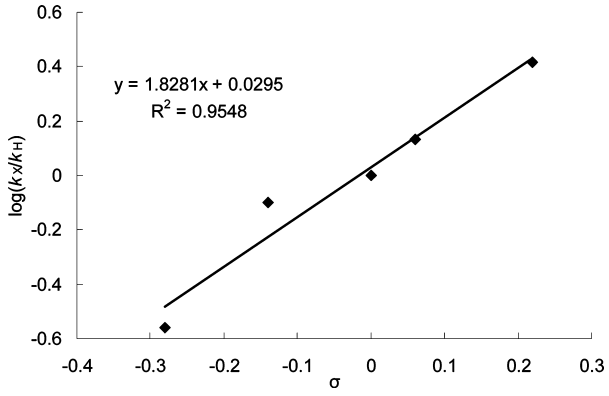


Figure 1. Hammett relationship between σ-values and $\log(k_X/k_H)$.

indicating that anion formation[10,15] is the rate-determining step and the negative charge at the benzylic position is stabilized by π-electrons of the aryl group in the transition state (Figure 1).

Further studies of various α-amido stannanes with considerable electron density within the aromatic ring revealed that sterically demanding *ortho*-substituted α-aryl α-amido stannanes (**1h** and **1i**) and α- and β-naphthyl amido stannanes (**1j** and **1k**) were tolerated in this carboxylation yielding **2** together with trace amounts of protiodestannylation product **3** (<1%) (Table 2). In addition to heteroaromatic substrates (**1l**−**1n**), cyclic substrates (**1o**−**1p**) were also active in this process. Finally, considering the synthetic advantage of using this fluoride-mediated carboxylation, we attempted to prepare α-quaternary arylglycines. Under identical conditions (100 °C, 3 h), racemic α-amido stannane **1q** derived from *N*-sulfonyl ketoimine[16] was carboxylated to give α-disubstituted glycine derivative **2q** in moderate yield. There was a small difference between ^{1}H NMR and isolated yields for all compounds, indicating that some material loss occurred during the purification process by 10% K_2CO_3/silica gel column

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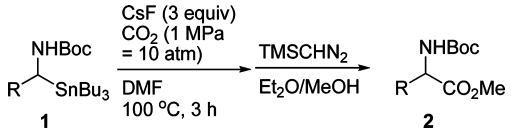
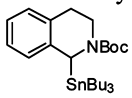
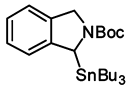
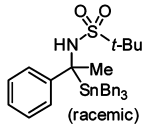
Table 2. Further Substrate Scope



entry	substrate		yield of **2** (%)[a]
1	R = *o*-OMe-C_6H_4	(**1h**)	100 (85)
2	R = *o*-F-C_6H_4	(**1i**)	91 (74)
3	R = 1-naphthyl	(**1j**)	84 (83)
4	R = 2-naphthyl	(**1k**)	86 (78)
5[b]	R = 2-furyl	(**1l**)	65 (60)
6[c]	R = 2-benzofuranyl	(**1m**)	74 (70)
7	R = 2-thienyl	(**1n**)	85 (89)
8		(**1o**)	83 (78)
9[b]		(**1p**)	81 (84)
10[d]		(**1q**)	42 (36)

[a]Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The values in parentheses represent isolated yield. [b]The reaction was performed at 120 °C. [c]15% of **3m** was observed. [d]17% of **3q** and 24% of acetophenone were observed.

chromatography[17] followed by preparative TLC in order to remove organotin residues and **3**.

Carboxylation of α-Acetoxy Stannanes. Next, we turned our attention to examine carboxylations of α-alkoxy stannanes **6** with CO_2. To our knowledge, there have been no reports on a general carboxylation of α-alkoxy stannanes with CO_2 promoted by a fluoride ion. First, several α-hydroxy stannanes having different protecting groups (PGs) were prepared from benzaldehyde[6l,m,18] and subjected to carboxylation (Table 3). Among potential candidates such as acetyl, ethyl carbonyl, MOM, and TMS, the use of acetyl protection was most effective, giving high conversion even at 60 °C within 3 h. Protection other than that with the TMS group is necessary; under the conditions examined, retro-stannylation occurs, affording benzaldehyde starting material exclusively. On the other hand, the α-oxygenated stannanes have no acidic protons, and the proton transfer reaction, which produces a protiodestannylation product, cannot proceed. Higher pressure was therefore not required to achieve the desired carboxylation,[10] giving **7** even under ambient CO_2 pressure using a gas balloon (1 atm).

Having decided on an optimal protecting group, various α-acetoxy stannanes **6** were prepared and tested in the fluoride-mediated carboxylation process (Table 4). High yields were achieved for all substrates with the exception of 2-furyl α-acetoxy stannane **6j**. Product yields were not influenced by the electronic character of substituents on the aromatic ring because carboxylation is only allowed to proceed in the absence of a proton source, a trend which is different from that of the carboxylation of *N*-Boc-α-amido stannanes **1**. As for electronically more deficient substrates (entries 1−4), a lower temperature (60 °C) was sufficient to achieve complete conversion. In addition to α-aryl substrates (entries 1−11), α-alkenyl and cyclic substrates were also active in this process (entries 12 and 13). It is notable that acetophenone-derived α-disubstituted α-alkoxy stannane also underwent smooth carboxylation (entry 14).

In order to demonstrate the synthetic utility of this process, we developed a one-pot protocol for the synthesis of acetyl mandelic acid **7aa**′ from benzaldehyde that does not require the isolation of α-acetoxy stannane intermediate **6aa** (Scheme 2). The stannylation in the first step could be mediated by the combination of CsF and TMS-$SnBu_3$ in CH_3CN.[11] After 3 h, simple solvent exchange was carried out by means of evaporation of CH_3CN and other volatile materials followed by introduction of DMF. Additional CsF was then added under CO_2 gas to promote the following carboxylation at 100 °C, affording the desired carboxylic acid, which was converted into its stable *t*-$BuNH_2$ salt. After the fine solids had been washed using hexane to completely remove organotin residues, carboxylic acid **7aa**′ was obtained in 52% yield by treatment with acid.

Chirality Transfer System. For the purpose of preparing chiral α-amino or α-hydroxy acids using this carboxylation, we then evaluated the extent of chirality transfer when starting from optically active substrates. According to the reported asymmetric syntheses, several potential chiral substrates were prepared. Unfortunately, carboxylations of (*S*)-**1a**[12c] (47% ee), (*S*)-*N*-Boc-*N*-(*p*-methoxyphenyl)-α-(tributylstannyl)-benzylamine (**1r**[5b]) (84% ee), and (*S*)-**6aa**[12c] (95% ee) in DMF gave only racemic products (Scheme 3).

By contrast, the use of (*S*)-*N*-*tert*-butylsulfonyl-α-amido stannane **8a** (>99% ee), which was prepared according to the procedure reported by Chong,[12b] afforded product with an ee of 47% in DMF (Table 5).[19] After the screening of several solvents such as DMSO, toluene, 1,4-dioxane, DME, diglyme, and triglyme (triethylene glycol dimethyl ether), triglyme was found to be superior, affording the corresponding α-amino acid

Table 3. Investigation of Protecting Groups (PGs) of Alcohols

entry	PG		temp (°C)	time (h)	yield (%)[a]
1	Ac	(**6aa**)	60	3	93
2	C(O)Et	(**6ab**)	60	6	84
3	MOM	(**6ac**)	100	8	66
4	TMS	(**6ad**)	100	1	–

[a]Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.

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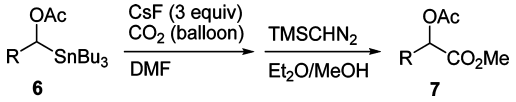
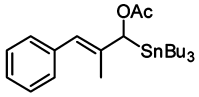
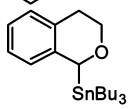
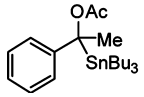
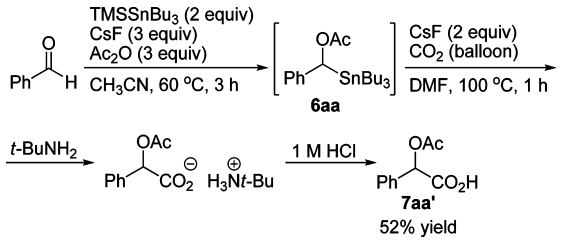
Table 4. Carboxylation of α-Acetoxy Stannanes



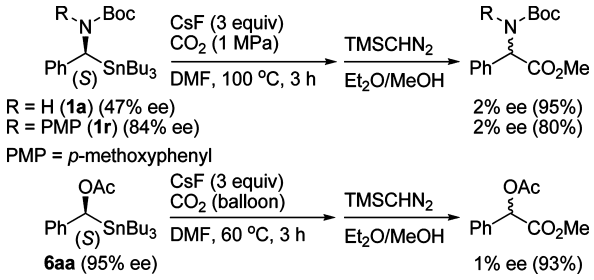
entry	substrate		temp (°C)	time (h)	yield (%)[a]
1	R = *p*-CF_3-C_6H_4	(**6b**)	60	1	87 (79)
2	R = *p*-Cl-C_6H_4	(**6c**)	60	1	93 (81)
3	R = *p*-F-C_6H_4	(**6d**)	60	2	89 (80)
4	R = Ph	(**6aa**)	60	3	93 (84)
5	R = *o*-Me-C_6H_4	(**6e**)	100	3	90 (82)
6	R = *p*-Me-C_6H_4	(**6f**)	100	3	86 (78)
7	R = *o*-OMe-C_6H_4	(**6g**)	100	3	95 (84)
8	R = 1-naphthyl	(**6h**)	60	3	93 (85)
9	R = 2-naphthyl	(**6i**)	60	3	94 (82)
10	R = 2-furyl	(**6j**)	100	3	55 (49)
11	R = 2-thienyl	(**6k**)	100	1	79 (71)
12		(**6l**)	100	1	93 (82)
13		(**6m**)	120	4	80 (73)
14		(**6n**)	100	3	91 (83)

[a]Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The values in parentheses represent isolated yield.

Scheme 2. One-Pot Synthesis of Acetyl Mandelic Acid 7aa′ from Benzaldehyde and CO_2



Scheme 3. Various Potential Substrates for Chirality Transfer Reactions



in 85% ee with inversion of the stereogenic center (entries 1–7).[5b,12b] Although the reaction caused erosion of the enantioselectivity to some degree, it is notable that chirality could be maintained at 100 °C, indicating that the carboxylation of *N*-sulfonyl-α-amido stannane does not proceed via a carbanion intermediate. When TBAT (tetrabutylammonium triphenyldifluorosilicate) was used as a fluoride source instead of CsF, chirality was maintained in 66% ee, albeit with decreased yield (entry 8). Other substitutions on the aromatic ring were screened, and it was revealed that an electron-deficient substituent such as fluoride or chloride slightly enhanced the racemization and protiodestannylation (entries 9 and 10). On the other hand, chirality was maintained in 90% ee when using α-tolyl amido stannane **8d** (entry 11). Although the mechanism for inversion of stereochemistry is not clear at this stage, we propose that carboxylation proceeds through a hypercoordinated fluorostannate and that a transition state such as structure **11** might be involved in the invertive carboxylation, where CO_2 undergoes back-side attack by fluorostannate (Figure 2). Electron-deficient substituents such as fluoride and chloride might result in the generation of small quantities of the dissociated benzylic anion, leading to a decrease in enantioselectivity and an increase in protiodestannylation. On the other hand, electron-donating tolyl substitution might suppress the formation of the benzylic anion, instead maintaining the coordinated stannane, leading to the higher level of chirality transfer. As discussed in Table 1, ^{119}Sn NMR spectroscopy of **8** in C_6D_6 also supported the order of electron density of substrates. These results would open a new window for the enantioselective synthesis of arylglycines from CO_2 and imines.

■ CONCLUSION

We have developed novel carboxylation reactions of monoprotected *N*-Boc-α-amido stannanes and α-acetoxy stannanes using CO_2 as a C1 source. Both transformations enabled the synthesis of α-tertiary and α-quaternary carboxylic acid derivatives. In addition, chiral *N*-sulfonyl substrates underwent carboxylation with inversion of the stereogenic center providing

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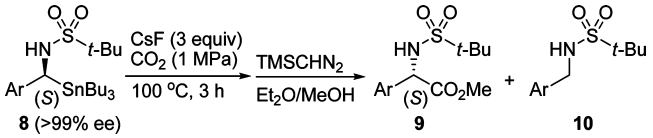
Table 5. Chirality Transfer Reactions



8 (>99% ee) **9** **10**

entry	Ar	^{119}Sn NMR (ppm)	solvent	yield (%)[a]	ee (%)[b]
1	Ph (**8a**)	−3.6	DMF	67 (<1)	47
2	Ph		DMSO	45 (10)	31
3[c]	Ph		toluene	13 (4)	80
4	Ph		1,4-dioxane	47 (3)	75
5[d]	Ph		DME	85 (7)	74
6	Ph		diglyme	71 (8)	79
7	Ph		triglyme	69 (7)	85
8[e]	Ph		triglyme	40 (7)	66
9	*p*-F-C_6H_4 (**8b**)	−3.6 (J_{Sn-F} = 17.6 Hz)	triglyme	50 (10)	80
10	*p*-Cl-C_6H_4 (**8c**)	−1.9	triglyme	70 (14)	72
11	*p*-Me-C_6H_4 (**8d**)	−6.1	triglyme	32 (5)	90

[a]Yields were determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The values in parentheses represent the yield of protiodestannylation product **10**. [b]Ee's were determined by chiral HPLC analysis. [c]39% of **8a** remained. [d]The reaction was performed at 80 °C. [e]TBAT (tetrabutylammonium triphenyldifluorosilicate) was used instead of CsF.

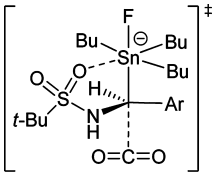


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Figure 2. Proposed transition state in carboxylation of **8** for invertive chirality transfer.

products with up to 90% ee. Examination of catalytic enantioselective synthesis of arylglycine derivatives from CO_2 as well as α-amino metal reagents other than stannanes are both currently underway.

EXPERIMENTAL SECTION

General. NMR spectra were recorded on a 500 MHz (^{1}H), 125 MHz (^{13}C), or 160 MHz (^{119}Sn) spectrometer. Chemical shifts in $CDCl_3$ were reported in the scale relative to $CHCl_3$ (7.26 ppm) for ^{1}H NMR and to $CDCl_3$ (77.0 ppm) for ^{13}C NMR as internal references. ^{119}Sn NMR was measured in C_6D_6 using $SnMe_4$ (0 ppm) as an internal reference. Column chromatography was performed with neutral silica gel (40−50 μm). In general, all manipulations were performed under an argon atmosphere unless otherwise stated. Dry solvents were purified under argon using a solvent purification system (THF, Et_2O, toluene, DMF, and MeCN). Triglyme was distilled from CaH. **Caution!** $TMSCHN_2$ is potentially explosive, especially when CH_2N_2 is generated after a long time in storage.

Synthesis of α-Amido Stannanes. *N*-Boc-α-amido stannanes (**1a**−**1n**) were prepared according to reported methods.[11] *N*-Boc-α-amido stannanes (**1o**−**1p**) were prepared according to a reported method.[5b] *rac*-*N*-(*tert*-Butylsulfonyl)-α-amido stannane (**1q**) was prepared according to the modified procedure of a reported one[12b] (reaction of $LiSnBu_3$ with *N*-*tert*-butylsulfoyl ketoimine[16] at −78 °C). Chiral **1r** was prepared following the reported method.[5b] *N*-Boc-α-amido stannanes (**1a**, **1c**, **1d**, **1g**, **1h**, **1j**, **1k**, **1l**, and **1n**) are known compounds.[11]

***N*-(*tert*-Butoxycarbonyl)-α-(tributylstannyl)-4-trifluoromethylbenzylamine (1b).** Colorless oil; IR (neat): 3416, 2957, 2872, 1699, 1503, 1417, 1367, 1265, 1165, 1067 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 5.18 (d, *J* = 5.0 Hz, 1H), 4.24 (d, *J* = 5.0 Hz, 1H), 1.47 (s, 9H), 1.39−1.33 (m, 6H), 1.26−1.19 (m, 6H), 0.87−0.80 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.2, 150.4, 126.6 (q, J_{CF} = 32.2 Hz), 125.5, 124.6 (q, J_{CF} = 270.3 Hz), 124.1, 79.8, 45.7, 29.0, 28.5, 27.5, 13.8, 11.3 ppm. HRMS (ESI): *m*/*z* calcd for $C_{21}H_{33}F_3O_2NSn$ [M−Bu]$^+$: 508.1480. Found: 508.1476.

***N*-(*tert*-Butoxycarbonyl)-α-(tributylstannyl)-4-fluorobenzylamine (1e).** Colorless oil; IR (neat): 3415, 2956, 2871, 1700, 1603, 1506, 1416, 1334, 1229, 1150 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.99−6.92 (m, 4H), 5.14 (d, *J* = 5.0 Hz, 1H), 4.14 (d, *J* = 5.0 Hz, 1H), 1.46 (s, 9H), 1.42−1.35 (m, 6H), 1.28−1.20 (m, 6H), 0.87−0.77 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.3 (d, J_{CF} = 239.6 Hz), 156.9, 141.4 (d, J_{CF} = 3.6 Hz), 125.5 (d, J_{CF} = 8.4 Hz), 115.1 (d, J_{CF} = 20.3 Hz), 79.4, 44.8, 28.9, 28.4, 27.4, 13.7, 10.9 ppm. HRMS (ESI): *m*/*z* calcd for $C_{20}H_{33}FO_2NSn$ [M − Bu]$^+$: 458.1512. Found: 458.1507.

***N*-(*tert*-Butoxycarbonyl)-α-(tributylstannyl)-4-methylbenzylamine (1f).** Colorless oil; IR (neat): 3379, 2955, 2871, 1670, 1611, 1509, 1417, 1336, 1248, 1169 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.04 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 5.12 (d, *J* = 5.0 Hz, 1H), 4.16 (d, *J* = 5.0 Hz, 1H), 2.29 (s, 3H), 1.45 (s, 9H), 1.41−1.30 (m, 6H), 1.27−1.19 (m. 6H), 0.86−0.72 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.8, 142.4, 133.8, 129.0, 124.3, 79.1, 45.4, 28.9, 28.4, 27.4, 20.9, 13.7, 10.9 ppm. HRMS (ESI): *m*/*z* calcd for $C_{21}H_{36}O_2NSn$ [M − Bu]$^+$: 454.1763. Found: 454.1759.

***N*-(*tert*-Butoxycarbonyl)-α-(tributylstannyl)-2-fluorobenzylamine (1i).** Colorless oil; IR (neat): 3416, 2956, 2853, 1699, 1505, 1418, 1366, 1226, 1141, 1036 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.13−7.09 (m, 1H), 7.06−7.01 (m, 2H), 6.97−6.93 (m, 1H), 5.10 (d, *J* = 6.3 Hz, 1H), 4.54 (d, *J* = 6.3 Hz, 1H), 1.45 (s, 9H), 1.42−1.34 (m, 6H), 1.30−1.20 (m, 6H), 0.88−0.77 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.7 (d, J_{CF} = 240.9 Hz), 156.4, 132.5 (d, J_{CF} = 13.1 Hz), 126.3 (d, J_{CF} = 4.8 Hz), 125.8 (d, J_{CF} = 7.1 Hz), 124.2 (d, J_{CF} = 3.6 Hz), 115.0 (d, J_{CF} = 21.5 Hz), 79.3, 39.2, 28.8, 28.4, 27.4, 13.7, 10.6 ppm. HRMS (ESI): *m*/*z* calcd for $C_{20}H_{33}FO_2NSn$ [M − Bu]$^+$: 458.1512. Found: 458.1509.

***N*-*tert*-Butyl (Benzofuran-2-yl(tributylstannyl)methyl)-carbamate (1m).** Colorless oil; IR (neat): 3392, 2956, 2871, 1702, 1499, 1418, 1366, 1251, 1167, 1075 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 (t, *J* = 4.5 Hz, 1H), 7.33 (t, *J* = 4.5 Hz, 1H), 7.15−

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7.13 (m, 2H), 6.23 (s, 1H), 5.10 (d, J = 6.0 Hz, 1H), 4.50 (d, J = 6.0 Hz, 1H), 1.47 (s, 9H), 1.45−1.42 (m, 6H), 1.28−1.21 (m, 6H), 0.94−0.82 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.5, 156.0, 154.4, 129.3, 122.5, 122.4, 119.8, 110.4, 98.2, 79.6, 39.2, 28.8, 28.4, 27.4, 13.6, 11.1 ppm; HRMS (ESI): m/z calcd for $C_{26}H_{44}O_3NSn$ $[M + H]^+$: 538.2343. Found: 538.2331.

***N*-*tert*-Butyl 1-(Tributylstannyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (1o).** Colorless oil; IR (neat): 2956, 2871, 1690, 1603, 1456, 1364, 1294, 1234, 1173, 1039 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.09−6.86 (m, 3H), 6.85 (6.81 for rotamer) (d, J = 7.5 Hz, 1H), 5.32 (5.27) (s, 1H), 4.29−4.26 (3.85−3.30) (m, 1H), 3.35−3.30 (2.93−2.89) (m, 1H), 3.01−2.94 (2.73−2.66) (m, 2H), 1.50 (1.48) (s, 9H), 1.40−1.34 (m, 6H), 1.28−1.19 (m, 6H), 0.86−0.76 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.7 (153.4), 139.9 (139.5), 131.5 (131.4), 128.9 (128.1), 126.3 (126.2), 123.94 (123.87), 123.7 (123.6), 79.8 (79.1), 49.8 (49.5), 41.9. 40.8, 28.90 (28.85), 28.6 (28.5), 27.44 (27.38), 13.59 (13.57), 10.5 (10.3) ppm. HRMS (ESI): m/z calcd for $C_{22}H_{36}O_2NSn$ $[M - Bu]^+$: 466.1768. Found: 466.1766.

***N*-*tert*-Butyl 1-(Tributylstannyl)isoindoline-2-carboxylate (1p).** Colorless oil; IR (neat): 2956, 2853, 1688, 1463, 1365, 1257, 1220, 1119, 1023, 879 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20−7.06 (m, 3H), 7.00 (6.95 for rotamer) (d, J = 7.3 Hz, 1H), 5.10 (5.02) (s, 1H), 4.97 (4.81) (d, J = 14.9 Hz, 1H), 4.54 (4.47) (d, J = 14.9 Hz, 1H), 1.52 (1.50) (s, 9H), 1.43−1.36 (m, 6H), 1.28−1.20 (m, 6H), 0.90−0.83 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.5 (153.2), 143.4 (143.1), 134.9 (134.4), 127.1 (127.0), 124.9 (124.8), 122.5 (122.3), 120.9 (120.1), 79.8 (79.0), 55.2 (55.1), 52.4 (52.1), 28.90 (28.86), 28.63 (28.56), 27.44 (27.38), 13.7 (13.6), 10.3 (10.1) ppm. HRMS (ESI): m/z calcd for $C_{21}H_{34}O_2NSn$ $[M - Bu]^+$: 452.1606. Found: 452.1602.

***N*-(1-Tributylstannyl-1-methylbenzyl)-*tert*-butanesulfonamide (1q).** Pale yellow oil; IR (neat): 3267, 2955, 1597, 1493, 1375, 1293, 1129, 1080, 1023, 939 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31 (d, J = 4.0 Hz, 4H), 7.13−7.11 (m, 1H), 3.99 (s, 1H), 1.92 (s, 3H), 1.44 (s, 9H), 1.38−1.19 (m, 12H), 0.90−0.77 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.5, 128.4, 125.0, 124.4, 59.7, 55.2, 28.8, 27.5, 26.2, 24.5, 13.6, 11.2 ppm. HRMS (ESI): m/z calcd for $C_{24}H_{45}O_2NSSnNa$ $[M + Na]^+$: 554.2091. Found: 554.2079.

Synthesis of α-Acetoxy Stannanes. α-Acetoxy stannanes (**6aa** and **6b**−**6l**) were prepared according to a reported method.[6l] α-Acetoxy stannane **6m** was prepared according to a reported method.[20] α-Acetoxy stannane **6n** was prepared by the reaction of $LiSnBu_3$ and acetophenone at −78 °C. **6aa**,[12c] **6b**,[12c] **6e**,[12c] and **6j**[21] are known compounds.

4-Chlorophenyl(tributylstannyl)methyl Acetate (6c). Colorless oil; IR (neat): 2956, 2926, 2871, 2853, 1726, 1594, 1489, 1370, 1246, 1091 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, J = 7.3 Hz, 2H), 7.04 (d, J = 7.3 Hz, 2H), 5.87 (s, 1H), 2.14 (s, 3H), 1.43−1.37 (m, 6H), 1.28−1.21 (m, 6H), 0.88−0.82 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 139.6, 134.6, 129.0, 123.9, 73,4, 28.8, 27.3, 21.0, 13.6, 9.9 ppm. HRMS (EI): m/z calcd for $C_{17}H_{26}ClO_2Sn$ $[M - Bu^+]$: 417.0643 Found: 417.0632.

4-Fluorophenyl(tributylstannyl)methyl Acetate (6d). Colorless oil; IR (neat): 2956, 2926, 2871, 2853, 1725, 1604, 1508, 1418, 1370, 1227 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09−6.96 (m, 4H), 5.86 (s, 1H), 2.13 (s, 3H), 1.43−1.35 (m, 6H), 1.28−1.19 (m, 6H), 0.89−0.80 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 160.6 (d, J_{CF} = 242.0 Hz), 138.6 (d, J_{CF} = 3.6 Hz), 125.3 (d, J_{CF} = 7.3 Hz), 115.2 (d, J_{CF} = 21.4 Hz), 72.7, 28.8, 27.3, 21.0, 13.6, 9.9 ppm. HRMS (EI): m/z calcd for $C_{17}H_{26}FO_2Sn$ $[M - Bu^+]$: 401.0939. Found: 401.0939.

4-Tolyl(tributylstannyl)methyl Acetate (6f). Colorless oil; IR (neat): 2956, 2925, 2871, 2853, 1723, 1512, 1463, 1369, 1339, 1250 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.08 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H), 5.86 (s, 1H), 2.30 (s, 3H), 2.12 (s, 3H), 1.42−1.36 (m, 6H), 1.27−1.20 (m, 6H), 0.86−0.80 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 139.6, 134.6, 129.0, 123.9, 73.4, 28.8, 27.3, 21.0, 13.6, 9.9 ppm. HRMS (EI): m/z calcd for $C_{18}H_{29}O_2Sn$ $[M - Bu^+]$: 397.1190. Found: 397.1186.

2-Methoxyphenyl(tributylstannyl)methyl Acetate (6g). Colorless oil; IR (neat): 2955, 2928, 2870, 2853, 1726, 1599, 1585, 1490, 1370, 1332 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (d, J = 7.1 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.95 (t, J = 7.1 Hz, 1H), 6.79 (d, J = 7.5 Hz, 1H), 6.06 (s, 1H), 3.80 (s, 3H), 2.17 (s, 3H), 1.47−1.31 (m, 6H), 1.29−1.21 (m, 6H), 0.87−0.72 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 153.0, 131.0, 125.4, 125.3, 120.6, 109.0, 69.4, 54.7, 28.7, 27.3, 20.9, 13.6, 10.1 ppm. HRMS (EI): m/z calcd for $C_{18}H_{29}O_3Sn$ $[M - Bu^+]$: 413.1139. Found: 413.1126.

1-Naphthyl(tributylstannyl)methyl Acetate (6h). Colorless oil; IR (neat): 3058, 2955, 2926, 2871, 2852, 1721, 1593, 1509, 1463, 1397 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.86−7.84 (m, 2H), 7.66−7.62 (m, 1H), 7.49−7.43 (m, 4H), 7.00 (s, 1H), 2.14 (s, 3H), 1.34−1.26 (m, 6H), 1.19−1.12 (m, 6H), 0.83−0.70 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 138.3, 133.6, 129.0, 128.5, 125.6, 125.58, 125.55, 125.50, 122.8, 120.6, 71.9, 28.6, 27.3, 21.1, 13.5, 10.6 ppm. HRMS (EI): m/z calcd for $C_{21}H_{29}O_2Sn$ $[M - Bu^+]$: 433.1190. Found: 433.1180.

2-Naphthyl(tributylstannyl)methyl Acetate (6i). Colorless oil; IR (neat): 3056, 2955, 2926, 2871, 2852, 1725, 1631, 1600, 1507, 1463 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (t, J = 7.2 Hz, 3H), 7.53 (s, 1H), 7.46−7.36 (m, 2H), 7.24−7.21 (m, 1H), 6.08 (s, 1H), 2.19 (s, 3H), 1.45−1.31 (m, 6H), 1.26−1.19 (m, 6H), 0.92−0.75 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 140.4, 133.7, 131.6, 128.1, 127.7, 127.4, 126.1, 124.9, 123.1, 120.9, 73.6, 28.8, 27.3, 21.1, 13.6, 10.1 ppm. HRMS (EI): m/z calcd for $C_{21}H_{29}O_2Sn$ $[M - Bu^+]$: 433.1190. Found: 433.1183.

2-Thienyl(tributylstannyl)methyl Acetate (6k). Pale yellow oil; IR (neat): 2956, 2925, 2871, 2853, 1725, 1464, 1371, 1295, 1245, 1074 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 (d, J = 4.6 Hz, 1H), 6.91 (dd, J = 3.4, 4.6 Hz, 1H), 6.74 (d, J = 3.4 Hz, 1H), 6.07 (s, 1H), 2.10 (s, 3H), 1.47−1.41 (m, 6H), 1.30−1.23 (m, 6H), 0.92−0.85 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 146.1, 126.7, 123.1, 122.0, 68.5, 28.8, 27.3, 20.9, 13.6, 10.3 ppm. HRMS (EI): m/z calcd for $C_{15}H_{25}O_2SSn$ $[M - Bu^+]$: 389.0597. Found: 389.0585.

(*E*)-1-(Tributylstannyl)-2-methyl-3-phenylallyl Acetate (6l). Colorless oil; IR (neat): 2956, 2926, 2871, 2853, 1724, 1643, 1598, 1492, 1463, 1370 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (dd, J = 5.3, 7.3 Hz, 2H), 7.25 (d, J = 5.3 Hz, 2H), 7.18 (t, J = 7.3 Hz, 1H), 6.30 (s, 1H), 5.42 (s, 1H), 2.14 (s, 3H), 1.86 (s, 3H), 1.58−1.50 (m, 6H), 1.36−1.27 (m, 6H), 1.04−0.86 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 138.1, 128.81, 128.78, 128.0, 125.7, 119.5, 76.3, 28.9, 27.4, 21.0, 16.1, 13.7, 10.3 ppm. HRMS (EI): m/z calcd for $C_{20}H_{31}O_2Sn$ $[M - Bu^+]$: 423.1346. Found: 423.1348.

Tributyl(3,4-dihydro-1*H*-isochromen-1-yl)stannane (6m). Colorless oil; IR (neat): 2955, 2851, 1601, 1488, 1457, 1418, 1376, 1339, 1291, 1270 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ = 7.05−7.03 (m, 1H), 6.93−6.92 (m, 2H), 6.84 (d, J = 8.0 Hz, 1H), 5.52 (s, 1H), 3.84−3.80 (m, 1H), 3.61−3.57 (m, 1H), 2.73−2.67 (m, 1H), 2.56−2.51 (m, 1H), 1.59−1.53 (m, 6H), 1.37−1.53 (m, 6H), 1.04−0.89 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.2, 130.8, 129.0, 125.9, 123.7, 122.1, 75.1, 65.4, 29.2, 29.0, 27.3, 13.6, 10.0 ppm. HRMS (EI): m/z calcd for $C_{17}H_{27}OSn$ $[M - Bu^+]$: 367.1084. Found: 367.1077.

1-Phenyl-1-(tributylstannyl)ethyl Acetate (6n). Colorless oil; IR (neat): 2955, 2871, 1717, 1493, 1369, 1266, 1230, 1070, 1033, 953 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31−7.28 (m, 2H), 7.14−7.11 (m, 3H), 2.16 (s, 3H), 1.83 (s, 3H), 1.39−1.19 (m, 12H), 0.92−0.69 (m, 15H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.9, 147.1, 128.2, 125.1, 123.4, 81.7, 28.8, 27.5, 24.7, 21.5, 13.6, 11.6 ppm. HRMS (EI): m/z calcd for $C_{18}H_{29}O_2Sn$ $[M - Bu]^+$: 397.1190. Found: 397.1193.

Synthesis of Optically Active 8. (*S*)-*N*-(*tert*-Butylsulfonyl)-α-(tributylstannyl)benzylamines (**8a**, **8b**, **8c**, and **8d**) were prepared according to a previously reported method.[12b] α-Amido stannanes (**8a**, **8c**, and **8d**) are known compounds.[12b]

(*S*)-*N*-(*tert*-Butylsulfonyl)-α-(tributylstannyl)-4-fluorobenzylamine (8b). Colorless oil; IR (neat): 3280, 2956, 2926, 2871, 2853, 1603, 1507, 1458, 1303, 1125 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.03−6.95 (m, 4 H), 4.53 (d, J = 9.0 Hz, 1 H), 4.43 (d, J = 9.0 Hz, 1

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H), 1.45−1.31 (m, 6 H), 1.29−1.22 (m, 15 H), 0.95−0.82 (m, 15 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.4 (J_{CF} = 242.0 Hz), 141.2 (J_{CF} = 3.5 Hz), 125.4 (J_{CF} = 7.1 Hz), 115.4 (J_{CF} = 21.5 Hz), 59.7, 47.1, 28.8, 27.3, 24.2, 13.6, 9.6 ppm. HRMS (ESI): m/z calcd for $C_{19}H_{33}FNO_2SSn$ [M − Bu$^+$]: 478.1233. Found: 478.1230. $[\alpha]^{24}_D$ +45.6 (c = 0.98, $CHCl_3$, >99% ee).

General Procedure for Carboxylations of *N*-Boc-α-Amido Stannanes. Dry CsF (22.8 mg, 0.15 mol, 3 equiv), which was preheated for 10 min by a heat gun under vacuum before use (<5 mmHg at ca. 400 °C), was quickly mixed with *N*-Boc-α-amido stannane **1a** (26.2 mg, 0.053 mmol). After addition of dry DMF (1.5 mL), the mixture was put inside an autoclave and sealed tightly. CO_2 gas was introduced into the autoclave (1 MPa), which was heated at 100 °C for 3 h. After the mixture cooled to 0 °C, water and Et_2O were added, and the pH of the mixture was adjusted to 2 by 1 M HCl. The organic layer was extracted with Et_2O, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was diluted with MeOH (ca. 2 mL) followed by treatment with $TMSCHN_2$ (2 M in Et_2O). After 1 h, AcOH was added until N_2 bubbling ceased, and the mixture was directly concentrated under high vacuum to afford the crude product. Yields of **2a** and **3a** were determined at this stage using 1,1,2,2-tetrachloroethane (δ = 5.9 ppm in $CDCl_3$, 2H) as an internal standard (**2a**: 95%, **3a**: <1%). The crude product was then purified by 10% K_2CO_3−SiO_2 column chromatography[17] (hexane−AcOEt, 1:1) to remove organotin residues, followed by preparative PTLC (hexane−AcOEt, 7:1) for separation from **3a**, affording methyl 2-(*tert*-butoxycarbonylamino)-2-phenylacetate (**2a**) (11.7 mg, 0.044 mmol) in 83% yield as a colorless amorphous solid.

α-Amino acid derivatives (**2a**, **2d**, **2e**, **2f**, **2i**, **2j**, **2k**, **2l**, **2n**, and **2r**) are known compounds.[10]

Methyl 2-(*N*-*tert*-Butoxycarbonylamino)-2-(4-methoxycarbonylphenyl)acetate (2c). Colorless oil; IR (neat): 3366, 2979, 2954, 1722, 1613, 1578, 1417, 1367, 1282, 1166 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.3 Hz, 2H), 5.67 (d, J = 6.6 Hz, 1H), 5.38 (d, J = 6.6 Hz, 1H), 3.91 (s, 3H), 3.72 (s, 3H), 1.43 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 166.6, 154.7, 141.9, 130.2, 130.1, 127.1, 80.4, 57.3, 53.0, 52.2, 28.3 ppm. HRMS (ESI): m/z calcd for $C_{16}H_{21}O_6NNa$ [M + Na]$^+$: 346.1261. Found: 346.1256.

Methyl 2-(*N*-*tert*-Butoxycarbonylamino)-2-(2-methoxylphenyl)acetate (2h). White solid; mp 79−81 °C; IR (neat): 3448, 2977, 1749, 1603, 1465, 1367, 1252, 1166, 1053, 913 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32−7.29 (m, 2H), 6.95 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 5.65 (d, J = 8.9 Hz, 1H), 5.47 (d, J = 8.9 Hz, 1H), 3.82 (s, 3H), 3.68 (s, 3H), 1.44 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.0, 156.9, 155.3, 130.3, 129.7, 125.8, 120.9, 111.0, 79.9, 55.5, 54.6, 52.5, 28.3 ppm. HRMS (ESI): m/z calcd for $C_{15}H_{21}O_5NNa$ [M + Na]$^+$: 318.1307. Found: 318.1312.

Methyl 2-(*N*-*tert*-Butoxycarbonylamino)-2-(benzofuran-2-yl)acetate (2m). Pale yellow solid; mp 74−76 °C; IR (neat): 3429, 3057, 2979, 1752, 1586, 1438, 1368, 1266, 1161, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.31−7.21 (m, 2H), 6.75 (s, 1H), 5.65 (d, J = 7.8 Hz, 1H), 5.61 (d, J = 7.8 Hz, 1H), 3.78 (s, 3H), 1.45 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.4, 155.0, 154.1, 151.8, 128.0, 124.9, 123.2, 121.5, 111.6, 105.5, 80.8, 53.3, 52.2, 28.4 ppm. HRMS (ESI): m/z calcd for $C_{16}H_{19}O_5NNa$ [M + Na]$^+$: 328.1155. Found: 328.1151.

2-*N*-*tert*-Butyl 1-Methyl 3,4-Dihydroisoquinoline-1,2(1*H*)-dicarboxylate (2o). Colorless oil; mp 74−76 °C; IR (neat): 3056, 2979, 1745, 1698, 1393, 1265, 1166, 1098, 1001, 934 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49−7.46 (m, 1H), 7.23−7.22 (m, 2H), 7.17−7.15 (m, 1H), 5.60 (5.43 for rotamer) (s, 1H), 3.80−3.76 (m, 2H), 3.71 (s, 3H), 2.99−2.92 (m, 1H), 2.89−2.80 (m, 1H), 1.50 (1.47) (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.5 (172.2), 154.7 (154.6), 135.7 (135.4), 132.5 (132.0), 128.6 (128.3), 128.2 (127.8), 127.72 (127.69), 126.5, 80.7 (80.5), 58.7 (57.6), 52.5 (52.3), 40.8 (39.7), 28.4 (28.3), 21.2 ppm. HRMS (ESI): m/z calcd for $C_{16}H_{21}O_4NNa$ [M + Na]$^+$: 314.1363. Found: 314.1358.

***N*-*tert*-Butyl Methyl Isoindoline-1,2-dicarboxylate (2p).** Colorless amorphous solid; IR (neat): 3055, 2929, 1755, 1703, 1398, 1266, 1201, 1122, 1017, 899 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21−7.10 (m, 1H), 6.90−6.86 (m, 2H), 6.71 (6.62) (d, J = 6.5 Hz, 1H), 5.58 (5.33 for rotamer) (d, J = 2.9 Hz, 1H), 4.79 (4.63) (dd, J = 2.9, 14.3 Hz, 1H), 4.56 (4.34) (d, J = 14.3 Hz, 1H), 3.22 (s, 3H), 1.45 (1.43) (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2 (170.8), 154.2 (153.7), 137.8 (137.3), 135.3 (135.1), 128.7 (128.6), 127.7 (127.6), 123.1 (123.0), 122.84 (122.82), 80.49 (80.45), 65.9−65.0, 52.5 (52.3), 52.2 (52.0), 28.4 (28.3) ppm. HRMS (ESI): m/z calcd for $C_{15}H_{19}O_4NNa$ [M + Na]$^+$: 300.1206. Found: 300.1206.

Methyl 2-(1,1-Dimethylethylsulfonamido)-2-phenyl-2-methylacetate (2q). White solid; mp 102−103 °C; IR (neat): 3274, 2953, 1742, 1447, 1309, 1258, 1125, 1077, 1029, 993 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45−7.43 (m, 2H), 7.39−7.36 (m, 2H), 7.33−7.32 (m, 1H), 5.03 (s, 1H), 3.78 (s, 3H), 2.03 (s, 3H), 1.40 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.7, 141.1, 128.7, 128.4, 125.6, 65.2, 60.2, 53.2, 42.3, 24.2 ppm; HRMS (ESI): m/z calcd for $C_{14}H_{21}O_4NSNa$ [M + Na]$^+$: 322.1084. Found: 322.1080.

General Procedure for Carboxylations of α-Acetoxy Stannanes. Dry CsF (31.4 mg, 0.21 mol, 3 equiv), which was preheated for 10 min by a heat gun under vacuum before use (<5 mmHg at ca. 400 °C), was quickly mixed with α-acetoxy stannane **6aa** (30.1 mg, 0.069 mmol). After addition of dry DMF (1.5 mL), the mixture was filled with CO_2 gas (0.1 MPa = 1 atm: balloon), which was heated at 60 °C for 3 h. After the mixture cooled to 0 °C, water and Et_2O were added, and the pH of the mixture was adjusted to 2 by 1 M HCl. The organic layer was extracted with Et_2O, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was diluted with MeOH (ca. 2 mL) followed by treatment with $TMSCHN_2$ (2 M in Et_2O). After 1 h, AcOH was added until N_2 bubbling ceased, and the mixture was directly concentrated under high vacuum to afford the crude product. The yield was determined at this stage using 1,1,2,2-tetrachloroethane (δ = 5.9 ppm in $CDCl_3$, 2H) as an internal standard (93%). The crude product was then purified by 10% K_2CO_3−SiO_2 column chromatography[17] (hexane−AcOEt, 15:1) to remove organotin residues, followed by preparative PTLC (hexane−Et_2O, 6:1) to afford methyl acetoxy(phenyl)acetate (**7aa**) (12.0 mg, 0.058 mmol) in 84% yield as a colorless oil.

Methyl Acetoxy(4-trifluoromethylphenyl)acetate (7b). Colorless oil; IR (neat): 3057, 2957, 1748, 1623, 1438, 1420, 1374, 1327, 1266, 1232 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 5.99 (s, 1H), 3.74 (s, 3H), 2.22 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.0, 168.6, 137.6, 131.4 (d, J_{CF} = 32.6 Hz), 127.9, 125.8 (d, J_{CF} = 3.6 Hz), 123.8 (d, J_{CF} = 270.6 Hz), 73.7, 52.9, 20.7 ppm. HRMS (EI): m/z calcd for $C_{10}H_8F_3O_2$ [M − OAc$^+$]: 217.0476 Found: 217.0470.

Methyl Acetoxy(4-chlorophenyl)acetate (7c).[22] Colorless oil; IR (neat): 2955, 2926, 2852, 1747, 1652, 1598, 1493, 1373, 1269, 1176 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42−7.36 (m, 4H), 5.90 (s, 1H), 3.73 (s, 3H), 2.20 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 169.0, 135.3, 132.2, 129.0, 129.0, 73.7, 52.8, 20.7 ppm. LRMS (EI): m/z calcd for $C_{11}H_{11}ClO_4$ [M$^+$]: 242. Found: 242.

Methyl Acetoxy(4-fluorophenyl)acetate (7d). Colorless oil; IR (neat): 2957, 2925, 2851, 1749, 1607, 1512, 1438, 1373, 1349, 1228 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (dd, J = 5.2, 8.7 Hz, 2H), 7.08 (t, J = 8.7 Hz, 2H), 5.91 (s, 1H), 3.73 (s, 3H), 2.20 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 169.17, 163.17 (d, J_{CF} = 246.1 Hz), 129.7 (d, J_{CF} = 3.9 Hz), 129.5 (d, J_{CF} = 8.8 Hz), 115.8 (d, J_{CF} = 21.4 Hz), 73.7, 52.7, 20.7 ppm. HRMS (EI): m/z calcd for $C_{11}H_{11}FO_4$ [M$^+$]: 226.0641. Found: 226.0642.

Methyl Acetoxy(phenyl)acetate (7aa).[23] Colorless oil; IR (neat): 3035, 2955, 1749, 1496, 1456, 1437, 1373, 1277, 1234, 1083 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48−7.46 (m, 2H), 7.41−7.39 (m, 3H), 5.93 (s, 1H), 3.73 (s, 3H), 2.20 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 160.3, 133.7, 129.2, 128.8, 127.6, 74.4, 52.6, 20.7 ppm. LRMS (EI): m/z calcd for $C_{11}H_{12}O_4$ [M$^+$]: 208. Found: 208.

Methyl Acetoxy(2-tolyl)acetate (7e). Colorless oil; IR (neat): 3056, 2955, 1747, 1496, 1437, 1373, 1266, 1237, 1173, 1110 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, J = 8.0 Hz, 1H), 7.27−7.21

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(m, 3H), 6.22 (s, 1H), 3.73 (s, 3H), 2.45 (s, 3H), 2.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 169.6, 136.8, 132.4, 130.8, 129.2, 128.0, 126.4, 71.5, 52.6, 20.7, 19.3 ppm. HRMS (EI): m/z calcd for $C_{12}H_{14}O_4$ [M − AcOH$^+$]: 162.0681. Found: 162.0680.

Methyl Acetoxy(4-tolyl)acetate (7f).[23] Colorless oil; IR (neat): 3055, 2955, 1747, 1517, 1438, 1373, 1266, 1236, 1180, 1056 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.90 (s, 1H), 3.72 (s, 3H), 2.36 (s, 3H), 2.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 169.5, 139.3, 130.8, 129.5, 127.6, 74.3, 52.6, 21.2, 20.7 ppm. LRMS (EI): m/z calcd for $C_{12}H_{14}O_4$ [M$^+$]: 222. Found: 222.

Methyl Acetoxy(2-methoxyphenyl)acetate (7g).[24] Colorless oil; IR (neat): 2956, 2844, 1747, 1604, 1497, 1465, 1372, 1351, 1256, 1231 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39−7.35 (m, 2H), 7.00−6.92 (m, 2H), 6.44 (s, 1H), 3.86 (s, 3H), 3.73 (s, 3H), 2.17 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 169.8, 157.2, 130.8, 129.4, 122.6, 120.8, 111.2, 68.7, 55.8, 52.5, 20.8 ppm. LRMS (EI): m/z calcd for $C_{12}H_{14}O_5$ [M$^+$]: 238. Found: 238.

Methyl Acetoxy(1-naphthyl)acetate (7h).[25] Colorless oil; IR (neat): 3055, 2986, 1748, 1513, 1437, 1372, 1340, 1265, 1229, 1055 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 2H), 7.63−7.47 (m, 4H), 6.68 (s, 1H), 3.71 (s, 3H), 2.21 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 169.7, 133.9, 131.0, 130.1, 129.9, 128.8, 127.5, 127.0, 126.1, 125.2, 123.7, 72.4, 52.7, 20.8 ppm. LRMS (EI): m/z calcd for $C_{12}H_{14}O_5$ [M$^+$]: 258. Found: 258.

Methyl Acetoxy(2-naphthyl)acetate (7i).[26] Colorless oil; IR (neat): 3055, 2986, 1747, 1437, 1372, 1341, 1265, 1231, 1126, 1058 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1H), 7.89−7.84 (m, 3H), 7.58−7.51 (m, 3H), 6.10 (s, 1H), 3.73 (s, 3H), 2.24 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 169.3, 133.5, 133.0, 131.0, 128.7, 128.2, 127.7, 127.4, 126.8, 126.6, 124.6, 74.6, 52.7, 20.8 ppm. LRMS (EI): m/z calcd for $C_{12}H_{14}O_5$ [M$^+$]: 258. Found: 258.

Methyl Acetoxy(2-furyl)acetate (7j). Colorless oil; IR (neat): 3055, 2987, 1758, 1438, 1421, 1372, 1265, 1217, 1152, 1050 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, J = 1.6 Hz, 1H), 6.49 (d, J = 3.2 Hz, 1H), 6.41 (dd, J = 1.6, 3.2 Hz, 1H), 6.09 (s, 1H), 3.79 (s, 3H), 2.18 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 167.2, 146.6, 143.9, 111.1, 110.8, 67.5, 53.0, 20.6 ppm. HRMS (EI): m/z calcd for $C_9H_{10}O_5$ [M$^+$]: 198.0528. Found: 198.0528.

Methyl Acetoxy(2-thienyl)acetate (7k). Colorless oil; IR (neat): 3056, 2956, 1751, 1438, 1373, 1339, 1266, 1230, 1127, 1044 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, J = 5.1 Hz, 1H), 7.18 (d, J = 3.5 Hz, 1H), 7.02 (dd, J = 3.5, 5.1 Hz, 1H), 6.20 (s, 1H), 3.78 (s, 3H), 2.20 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 168.5, 135.2, 127.9, 127.2, 127.0, 70.0, 52.9, 20.6 ppm. HRMS (EI): m/z calcd for $C_9H_{10}O_4S$ [M$^+$]: 214.0300. Found: 214.0300.

(*E*)-Methyl 2-Acetoxy-3-methyl-4-phenylbut-3-enoate (7l). Colorless oil; IR (neat): 3057, 2955, 1744, 1541, 1492, 1372, 1339, 1266, 1235, 1175 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37−7.34 (m, 2H), 7.31−7.25 (m, 3H), 6.69 (s, 1H), 5.52 (s, 1H), 3.79 (s, 3H), 2.20 (s, 3H), 1.94 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 169.2, 136.3, 131.9, 130.6, 129.0, 128.2, 127.3, 78.1, 52.6, 20.8, 14.3 ppm. HRMS (EI): m/z calcd for $C_{14}H_{16}O_4$ [M$^+$]: 248.1049. Found: 248.1048.

Methyl 3,4-Dihydro-1*H*-isochromene-1-carboxylate (7m).[27] Colorless oil; IR (neat): 3055, 2954, 1747, 1492, 1454, 1436, 1376, 1344, 1266, 1216 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 (d, J = 6.9 Hz, 1H), 7.25−7.19 (m, 2H), 7.14 (d, J = 7.4 Hz, 1H), 5.38 (s, 1H), 4.34−4.29 (m, 1H), 4.04−3.99 (m, 1H), 3.79 (s, 3H), 2.91−2.87 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6, 133.7, 131.0, 129.1, 127.5, 126.3, 126.1, 74.8, 62.9, 52.4, 28.0 ppm. LRMS (EI): m/z calcd for $C_{11}H_{12}O_3$ [M$^+$]: 192. Found: 192.

Methyl 2-Acetoxy-2-phenylpropanoate (7n). Colorless oil; IR (neat): 2952, 2851, 1747, 1449, 1373, 1266, 1225, 1125, 1073, 983 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (dd, J = 7.2, 1.4 Hz, 2H), 7.40−7.32 (m, 3H), 3.70 (s, 3H), 2.21 (s, 3H), 1.95 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.4, 169.9, 139.7, 128.5, 128.2, 124.7, 81.6, 52.7, 24.0, 21.4 ppm. HRMS (EI): m/z calcd for $C_{12}H_{14}O_4$ [M$^+$]: 222.0892. Found: 222.0890.

One-Pot Synthesis of Acetyl Mandelic Acid. Dry CsF (91.6 mg, 0.6 mmol, 3 equiv) was preheated for 10 min by a heat gun under vacuum before use (<5 mmHg at ca. 400 °C), to which dry CH_3CN (1.5 mL), benzaldehyde (d = 1.045 g/mL, 20 μL, 0.2 mmol), Ac_2O (d = 1.08 g/mL, 57 μL, 0.6 mmol, 3 equiv), and TMS-$SnBu_3$ (d = 1.04 g/mL, 134 μL, 0.4 mmol, 2 equiv) were added in this order, and then the mixture was heated at 60 °C for 3 h. After cooling to 0 °C, the solvent was evaporated and dried under reduced pressure (<5 mmHg) for 1 h. After the addition of preheated CsF (60.8 mg, 0.4 mmol, 2 equiv), the mixture was filled with CO_2 gas (0.1 MPa = 1 atm: balloon), followed by addition of dry DMF (1.5 mL), and then heated at 100 °C for 1 h. After the mixture cooled to 0 °C, water and Et_2O were added and the pH of the mixture was adjusted to 2 by 1 M HCl. The organic layer was extracted with Et_2O, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was diluted with Et_2O (ca. 2 mL). As t-$BuNH_2$ (d = 0.696 g/mL, 21 μL, 0.2 mmol, 1 equiv) was added slowly, white precipitates appeared. After 1 h, Et_2O was removed under reduced pressure followed by the addition of hexane (ca. 2 mL). The solids were collected by filtration and washed with hexane, which were dissolved in water with the pH adjusted to 2 by 1 M HCl. The product was extracted with CH_2Cl_2, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure to give 2-acetoxy-2-phenelacetic acid (**7aa′**) (20.2 mg, 0.104 mmol) as a colorless oil in 52% yield.

2-Acetoxy-2-phenylacetic acid (7aa′). Colorless oil; IR (neat): 3036, 1740, 1497, 1456, 1374, 1233, 1183, 1082, 1053, 1004 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49−7.47 (m, 2H), 7.41−7.34 (m, 2H), 5.93 (s, 1H), 2.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.1, 170.4, 133.1, 129.5, 128.9, 127.6, 74.1, 20.6 ppm. LRMS (EI): m/z calcd for $C_{10}H_{10}O_4$ [M$^+$]: 194. Found: 194 ((*R*) and (*S*) products are commercially available from a chemical supplier).

General Procedure of Chirality Transfer Reactions. Dry CsF (22.8 mg, 0.15 mol, 3 equiv), which was preheated for 10 min by a heat gun under vacuum before use (<5 mmHg at ca. 400 °C), was quickly mixed with (*S*)-*N*-(*tert*-butylsulfonyl)-α-(tributylstannyl)-benzylamine (**8a**) (26.2 mg, 0.051 mmol). After addition of dry triglyme (1.5 mL), the mixture was put inside an autoclave and sealed tightly. CO_2 gas was introduced into the autoclave (1 MPa), which was heated at 100 °C for 3 h. After the mixture cooled to 0 °C, water and Et_2O were added, and the pH of the mixture was adjusted to 2 by 1 M HCl. The organic layer was extracted with Et_2O, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was diluted with MeOH (ca. 2 mL) followed by treatment with $TMSCHN_2$ (2 M in Et_2O). After 1 h, AcOH was added until N_2 bubbling ceased, and the mixture was directly concentrated under high vacuum to afford the crude product, to which Et_2O was added and the mixture was washed with H_2O to remove most of triglyme. Yields of **9a** and protiodestannylation product were determined at this stage using 1,1,2,2-tetrachloroethane (δ = 5.9 ppm in $CDCl_3$, 2H) as an internal standard (**9a**: 69%, protiodestannylation product: 7%). The crude product was then purified by 10% K_2CO_3−SiO_2 column chromatography[17] (AcOEt only) to remove organotin residues, followed by preparative PTLC (hexane−AcOEt, 7:1) for separation from **10a**, affording methyl (*S*)-2-(1,1-dimethylethylsulfonamido)-2-phenylacetate (**9a**) (6.1 mg, 0.021 mmol) in 42% yield as white solids with 85% ee.

Methyl (*S*)-2-(1,1-Dimethylethylsulfonamido)-2-phenylacetate (9a).[28] White solid; mp 151−153 °C; IR (neat): 3287, 3056, 2981, 1745, 1479, 1366, 1266, 1175, 1074, 1021 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38−7.34 (m, 5H), 5.20 (d, J = 8.3 Hz, 1H), 5.15 (d, J = 8.3 Hz, 1H), 3.75 (s, 3H), 1.30 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6, 136.7, 129.1, 128.7, 127.1, 60.1, 60.0, 53.2, 24.0 ppm. LRMS (EI): m/z calcd for $C_{13}H_{19}NO_4S$ [M]$^+$: 285. Found: 285. $[\alpha]^{24}_D$ +94.8 (c = 0.55, $CHCl_3$, 85% ee). HPLC (Chiralpak AD-H, 2-propanol/hexane 3/97, flow 1.0 mL/min, detection at 220 nm): t_R 48.1 min (major) and 27.9 min (minor). The absolute configuration was determined to be (*S*) by comparison of specific rotation with literature data. {Lit. (>99% ee) $[\alpha]^{25}_D$ = −102.6 (c = 0.50, $CHCl_3$) for *R* isomer.[28]}

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Methyl 2-(1,1-Dimethylethylsulfonamido)-2-(4-fluorophenyl)acetate (9b). Colorless amorphous solid; IR (neat): 3288, 2984, 2957, 2924, 1752, 1606, 1512, 1452, 1305, 1132 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35−7.32 (m, 2 H), 7.09−7.05 (m, 2 H), 5.20 (d, J = 8.0 Hz, 1 H), 5.14 (d, J = 8.0 Hz, 1 H), 3.76 (s, 3 H), 1.30 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.4, 162.8 (J_{CF} = 245.6 Hz), 132.7 (J_{CF} = 3.5 Hz), 128.9 (J_{CF} = 8.4 Hz), 116.6 (J_{CF} = 21.5 Hz), 60.1, 59.3, 53.3, 24.0 ppm. HRMS (EI): m/z calcd for $C_{11}H_{15}FNO_2S$ [M − CO_2Me]$^+$: 244.0802. Found: 244.0801. $[\alpha]^{24}_D$ +71.8 (c = 0.54, $CHCl_3$, 82% ee). HPLC (Chiralpak AD-H, 2-propanol/hexane 3/97, flow 1.0 mL/min, detection at 230 nm.): t_R 39.3 min (major) and 23.9 min (minor).

Methyl 2-(1,1-Dimethylethylsulfonamido)-2-(4-chlorophenyl)acetate (9c). White solid; mp 103−105 °C; IR (neat): 3284, 2985, 1740, 1492, 1440, 1313, 1220, 1132, 1016, 977 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37−7.34 (m, 2H), 7.31−7.29 (m, 2H), 5.20−5.16 (m, 2H), 3.75 (s, 3H), 1.30 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 135.3, 134.7, 129.3, 128.5, 60.2, 59.3, 53.3, 24.0 ppm. HRMS (EI): m/z calcd for $C_{11}H_{15}NO_2ClS$ [M − CO_2Me]$^+$: 260.0512. Found: 260.0505. $[\alpha]^{24}_D$ +80.2 (c = 0.40, $CHCl_3$, 72% ee). HPLC (Chiralpak AD-H, 2-propanol/hexane 5/95, flow 1.0 mL/min, detection at 230 nm.): t_R 23.0 min (major) and 17.9 min (minor).

Methyl 2-(1,1-Dimethylethylsulfonamido)-2-(4-methylphenyl)acetate (9d). White solid; mp 126−127 °C; IR (neat): 3282, 2981, 1738, 1440, 1336, 1223, 1172, 1105, 1026, 977 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.23 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.16 (d, J = 8.6 Hz, 1H), 5.09 (d, J = 8.6 Hz, 1H), 3.74 (s, 3H), 2.35 (s, 3H), 1.30 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.8, 138.6, 133.7, 129.7, 127.0, 60.1, 59.8, 53.1, 24.0, 21.2 ppm. HRMS (EI): m/z calcd for $C_{12}H_{18}O_2NS$ [M − CO_2Me]$^+$: 240.1058. Found: 240.1054. $[\alpha]^{24}_D$ +57.3 (c = 0.33, $CHCl_3$, 90% ee). HPLC (Chiralcel OD-H, 2-propanol/hexane 1/99, flow 1.0 mL/min, detection at 220 nm.): t_R 22.9 min (major) and 26.7 min (minor).

Hammett Analysis. Dry CsF (22.8 mg, 0.15 mol, 3 equiv), which was preheated for 10 min by a heat gun under vacuum before use (<5 mmHg at ca. 400 °C), was quickly added to a mixture of *N*-Boc-α-amido stannane **1a** (26.2 mg, 0.025 mmol) and substituted **1** (0.025 mmol). After addition of dry DMF (1.5 mL), the solution was put inside an autoclave and sealed tightly. CO_2 gas was introduced into the autoclave (1 MPa), which was heated at 100 °C for 15 min (<40% conversion). After cooling to 0 °C, water and Et_2O were added, and the pH of the mixture was adjusted to 2 by 1 M HCl. The organic layer was extracted with Et_2O, washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure to afford the crude mixture. The amounts of remaining **1a** and substituted **1** were determined at this stage using 1,3,5-trimethoxybenzene (δ = 6.1 ppm in $CDCl_3$, 3H) in ^1H NMR as an internal standard. The peak of methine proton of C*H*$SnBu_3$ was used for calculation. If clean separation could not be observed in ^1H NMR, the molar ratio of **1a** and **1** was determined by ^{119}Sn NMR in *d*-benzene. The ratio of total conversion (**2** + **3**/**2a** + **3a**) was determined as [0.025 mmol (initial amounts of **1**) − (remaining amounts of **1**)]/[0.025 mmol (initial amounts of **1a**) − (remaining amounts of **1a**)]. Plotting of log [0.025 mmol (initial amounts of **1**) − (remaining amounts of **1**)]/[0.025 mmol (initial amounts of **1a**) − (remaining amounts of **1a**)] versus σ-values indeed revealed a linear relationship with ρ = +1.83.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopic data (^1H and ^{13}C NMR) of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For a special review on glycopeptide antibiotics, see: Nicolaou, K. C.; Boddy, C. N. C.; Bräse, S.; Winssinger, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 2096 and references cited therein.

(2) For a book and a review: (a) Coppola, G. M.; Schuster, H. F. *α-Hydroxy Acids in Enantioselective Syntheses*; Wiley-VCH: Weinheim, 1997. (b) Gröger, H. *Adv. Synth. Catal.* **2001**, *343*, 547.

(3) For representative reviews, see: (a) Williams, R. M.; Hendrix, J. A. *Chem. Rev.* **1992**, *92*, 889. (b) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539. (c) Seebach, D.; Sting, A. R.; Hoffmann, M. *Angew. Chem., Int. Ed.* **1996**, *35*, 2708. (d) Cativiela, C.; Díaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3517. (e) Maruoka, K.; Ooi, T. *Chem. Rev.* **2003**, *103*, 3013.

(4) For recent reviews, see: (a) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365. (b) Mori, M. *Eur. J. Org. Chem.* **2007**, 4981. (c) Correa, A.; Martín, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 6201. (d) Riduan, S. N.; Zhang, Y. *Dalton Trans.* **2010**, *39*, 3347. (e) Boogaerts, I. I. F.; Nolan, S. P. *Chem. Commun.* **2011**, *47*, 3021. (f) Ackermann, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 3842.

(5) (a) Katsoulos, G.; Schlosser, M. *Tetrahedron Lett.* **1993**, *34*, 6263. (b) Park, Y. S.; Beak, P. *J. Org. Chem.* **1997**, *62*, 1574. (c) Faibish, N. C.; Park, Y. S.; Lee, S.; Beak, P. *J. Am. Chem. Soc.* **1997**, *119*, 11561. (d) Tomooka, K.; Wang, L.-F.; Okazaki, F.; Nakai, T. *Tetrahedron Lett.* **2000**, *41*, 6121. (e) Barberis, C.; Voyer, N.; Roby, J.; Chénard, S.; Tremblay, M.; Labrie, P. *Tetrahedron* **2001**, *57*, 2965. (f) Stead, D.; Carbone, G.; O'Brien, P.; Campos, K. R.; Coldham, I.; Sanderson, A. *J. Am. Chem. Soc.* **2010**, *132*, 7260.

(6) For selected examples of tin−lithium exchange of α-amino and α-alkoxy stannanes followed by their functionalizations other than carboxylations, see: (a) Pearson, W. H.; Lindbeck, A. C. *J. Org. Chem.* **1989**, *54*, 5651. (b) Pearson, W. H.; Lindbeck, A. C. *J. Am. Chem. Soc.* **1991**, *113*, 8546. (c) Pearson, W. H.; Lindbeck, A. C.; Kampf, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 2622. (d) Wu, S.; Lee, S.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 715. (e) Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 12218. (f) Iula, D. M.; Gawley, R. E. *J. Org. Chem.* **2000**, *65*, 6196. (g) Ncube, A.; Park, S. B.; Chong, J. M. *J. Org. Chem.* **2002**, *67*, 3625. (h) Fraser, D. S.; Park, S. B.; Chong, J. M. *Can. J. Chem.* **2004**, *82*, 87. For α-alkoxy stannanes: (i) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (j) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201. (k) Chong, J. M.; Mar, E. K. *Tetrahedron Lett.* **1990**, *31*, 1981. (l) Ye, J.; Bhatt, R. K.; Falck, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 1. (m) Falck, J. R.; Bhatt, R. K.; Ye, J. *J. Am. Chem. Soc.* **1995**, *117*, 5973.

(7) For carboxylations through tin−lithium exchange, see: (a) Chan, P. C. -M.; Chong, M. *Tetrahedron Lett.* **1990**, *31*, 1985. (b) Chong, J. M.; Park, S. B. *J. Org. Chem.* **1992**, *57*, 2220. (c) Frey, O.; Hoffmann, M. H.; Kessler, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2026. (d) Hoffmann, M.; Burkhart, F.; Hessler, G.; Kessler, H. *Helv. Chim. Acta* **1996**, *79*, 1519. (e) Coeffard, V.; Beaudet, I.; Evain, M.; Grognec, E. L.; Quintard, J. -P. *Eur. J. Org. Chem.* **2008**, 3344.

(8) (a) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149. (b) Merrifield, R. B. *Science* **1986**, *232*, 341. (c) O'Donnell, M. J.; Zhou, C.; Scott, W. L. *J. Am. Chem. Soc.* **1996**, *118*, 6070.

(9) The reaction of **1a** with CO_2 in the presence of 2.5 equiv of *n*-BuLi in THF gave no desired amino acid. **1a** was recovered in 91% yield.

(10) Mita, T.; Chen, J.; Sugawara, M.; Sato, Y. *Angew. Chem., Int. Ed.* **2011**, *50*, 1393.
(11) (a) Mita, T.; Higuchi, Y.; Sato, Y. *Org. Lett.* **2011**, *13*, 2354. (b) Mita, T.; Higuchi, Y.; Sato, Y. *Synthesis* **2012**, *44*, 194.
(12) (a) Kells, K. W.; Chong, J. M. *Org. Lett.* **2003**, *5*, 4215. (b) Kells, K. W.; Chong, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 15666. (c) He, A.; Falck, J. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 6586.
(13) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96.
(14) Peaks of **2a** and substituted **2** in the crude mixture were sometimes overlapped in ^{1}H NMR as well as GC analyses partly due to the existence of rotamers of Boc-amino acid derivatives. Therefore, total conversion (**2a** + **3a** and **2** + **3**) was selected to determine the ρ-value, each of which was estimated based on the amount of unreacted **1a** and **1** by NMR calculation: See Experimental Section for details.
(15) The carboxylation of **1a** proceeded with an identical yield (90%) in the presence of 1 equiv of a radical scavenger BHT (3,5-di-*tert*-butyl-4-hydroxytoluene), indicating the exclusion of the radical mechanism.
(16) Ruano, J. L. G.; Alemán, J.; Cid, M. B.; Parra, A. *Org. Lett.* **2005**, *7*, 179.
(17) Harrowven, D. C.; Curran, D. P.; Kostiuk, S. L.; Wallis-Guy, I. L.; Whiting, S.; Stenning, K. J.; Tang, B.; Packard, E.; Nanson, L. *Chem. Commun.* **2010**, *46*, 6335.
(18) (a) Bhatt, R. K.; Ye, J.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 4081. (b) Busch-Petersen, J.; Bo, Y.; Corey, E. J. *Tetrahedron Lett.* **1999**, *40*, 2065. (c) Blanc, R.; Commeiras, L.; Parrain, J. -L. *Adv. Synth. Catal.* **2010**, *352*, 661.
(19) When (*S,R*)-*N*-*tert*-butylsulfinyl-α-amido stannane (ref 12b: >99de, >99% ee) was used, imine was only produced via retro-stannylation.
(20) Fort, Y.; Gros, P.; Rodriguez, A. L. *Tetrahedron Lett.* **2002**, *43*, 4045.
(21) Dussault, P. H.; Eary, C. T.; Lee, R. J.; Zope, U. R. *J. Chem. Soc., Perkin Trans. 1* **1999**, *15*, 2189.
(22) Yao, W.; Liao, M.; Zhang, X.; Xu, H.; Wang, J. *Eur. J. Org. Chem.* **2003**, *9*, 1784.
(23) Nemoto, H.; Kawamura, T.; Kitasaki, K.; Yatsuzuka, K.; Kamiya, M.; Yoshioka, Y. *Synthesis* **2009**, 1694.
(24) Basavaiah, D.; Krishna, P. R. *Tetrahedron* **1995**, *51*, 2403.
(25) Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 1080.
(26) Kimura, M.; Kuboki, A.; Sugai, T. *Tetrahedron: Asymmetry* **2002**, *13*, 1059.
(27) Semeyn, C.; Blaauw, R. H.; Hiemstra, H.; Speckamp, W. N. *J. Org. Chem.* **1997**, *62*, 3426.
(28) Hodgson, D. M.; Kloesges, J.; Evans, B. *Synthesis* **2009**, 1923.