**Doctoral Dissertation**

# Development of Synthetic Methodologies Using Nitrogen- or Boron-Substituted Organostannanes

**Kensuke Suzuki**

**January 2021**

**Department of Applied Chemistry**

**Graduate School of Engineering**

**Osaka University**

## Preface and Acknowledgements

The study of this doctoral dissertation was carried out under the guidance of Prof. Dr. Makoto Yasuda at the Department of Applied Chemistry, Graduated School of Engineering, Osaka University from April 2015 to March 2021. The thesis describes the development of synthetic methodologies using nitrogen- or boron-substituted organostannanes.

I would like to express my deepest appreciation to Prof. Dr. Makoto Yasuda for his precise guidance, helpful suggestions and hearty encouragements throughout this work. His enthusiasm for chemistry has always motivated me. He also gave me a lot of invaluable experience. I really appreciate him for supervising me. I would also like to thank Professors Dr. Ikuya Shibata and Dr. Sensuke Ogoshi for their helpful advice and kind assistance. I gratefully express acknowledgement to Associate Prof. Dr. Yoshihiro Nishimoto for his great assistance, helpful suggestion and stimulating discussion. I really wish to make a grateful acknowledgement to Assistant Prof. Dr. Akihito Konishi for his sharp comments and kind encouragement.

I am deeply thankful to Ms. Yoshimi Shinomiya and Ms. Tomoko Shimizu for giving me her grateful support and heartwarming kindness.

I express my appreciation to the all members of the Yasuda Group. I am deeply indebted to my seniors since I joined Yasuda group in 2015. Particularly, I would like to express special thanks to my mentor Dr. Naoto Esumi for his kind encouragement and great suggestion. I would like to express my thanks to my juniors in Yasuda group. I gratefully wish to thank Mr. Sugihara Naoki for his helpful assistance and active working.

I have had the great support of Mr. Hiroshi Moriguchi, Dr. Nobuko Kanehisa, Dr. Kyoko Inoue, and Dr. Hiroaki Tanaka with analytic assistance at the analytical instrumentation facility.

Professor Yasuda also assisted me to visit Stanford University, USA. Prof. Dr. Noah Burns willingly accepted me to his group as a visiting student for three months from June 2019. Special thanks to him for his kind support and stimulating discussions. I am also grateful for his lab members.

I wish to thank Japan Chemical Industry Association for the financial support.

Finally, I would like to express my gratitude to my parents, Atsuhiko Suzuki and Mieko Suzuki, and my older sisters, Chiaki Suzuki and Erika Suzuki for their understanding to my work, constant assistance and financial support.

January, 2021

Kensuke Suzuki

## List of Publications

1) **Regio- and Stereo-Controlled Addition Reaction of Aminoallylic Stannanes to Aldehydes Mediated by Germanium Dichloride**
   K. Suzuki, Y. Nishimoto, H. Yunoki, K. Tsuruwa, N. Esumi, M. Yasuda
   *Chem. Lett.* **2018**, *47*, 821-824.

2) **Geometrically Selective Synthesis of (*E*)-Enamides via Radical Allylation of Alkyl Halides with *α*-Aminoallylic Stannanes**
   K. Suzuki, Y. Nishimoto, M. Yasuda
   *Org. Lett.* **2019**, *21*, 6589-6592.

3) **(*o*-Phenylenediamino)borylstannanes: Efficient Reagents for Borylation of Various Alkyl Radical Precursors**
   K. Suzuki, Y. Nishimoto, M. Yasuda
   *Chem. Eur. J.* DOI: 10.1002/chem.202004692

**<Supplementary Publications>**

1) **Synthesis of 1,4-Dicarbonyl Compounds from Silyl Enol Ethers and Bromocarbonyls, Catalyzed by an Organic Dye under Visible-Light Irradiation with Perfect Selectivity for the Halide Moiety over the Carbonyl Group**
   N. Esumi, K. Suzuki, Y. Nishimoto, M. Yasuda
   *Org. Lett*., **2016**, *18*, 5704-5707.

2) **Generation of α-Iminyl Radicals from α-Bromo Cyclic *N*-Sulfonylimines and Application to Coupling with Various Radical Acceptors Using a Photoredox Catalyst**
   N. Esumi, K. Suzuki, Y. Nishimoto, M. Yasuda
   *Chem. Eur. J.* **2017**, *24*, 312–316.

## Contents

## General Introduction

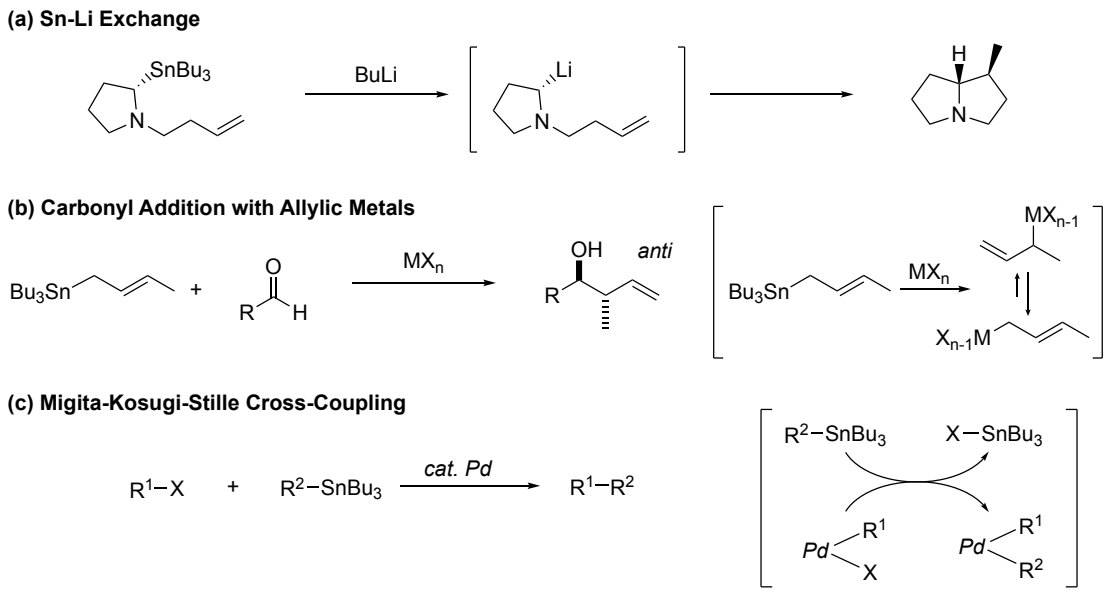
Productions of high-value-added chemicals from petrochemical feedstocks have contributed to human society and raised the level of life. Owing to the development of organic synthesis, great progress has been made in medicinal, agrochemical and material science. In order to access the highly designed and functionalized molecules, the invention of chemo-, stereo-, and regioselective chemical transformations is highly required.

Organometallic compounds have played an important role in the chemical transformation with chemo-, stereo-, and regioselectivity. For instance, the cross-coupling reactions using transition-metal catalysts are one of the biggest achievements in organic synthesis and enable the synthesis of highly functionalized compounds.[1] For the sake of the establishment of cost-effective synthetic methods, the reactions using typical element that are abundant in earth's crust is attractive. Organolithiums and -magnesiums have been widely used for constructing new carbon-carbon bonds, because they have strong nucleophilicity due to their highly polarized carbon–metal bonds. However, the high reactivity prevents the compatibility with functional groups, and their application to chemoselective reactions is a challenging issue. On the other hand, organoboron, -silicon, and -tin compounds are employed in chemoselective reactions because of their high functional compatibility and moderate reactivity.

In particular, organotin compounds are one of the most useful organometallic reagents. Since diethyltin diiodide was firstly synthesized as an organotin compound by E. Frankland,[2] the tin chemistry has been developed and their application has made a great progress in organic synthesis.[3] Organotin compounds exhibit different reactivity from other organometallic reagents and are employed for chemo-, stereo-, and regioselective reactions.

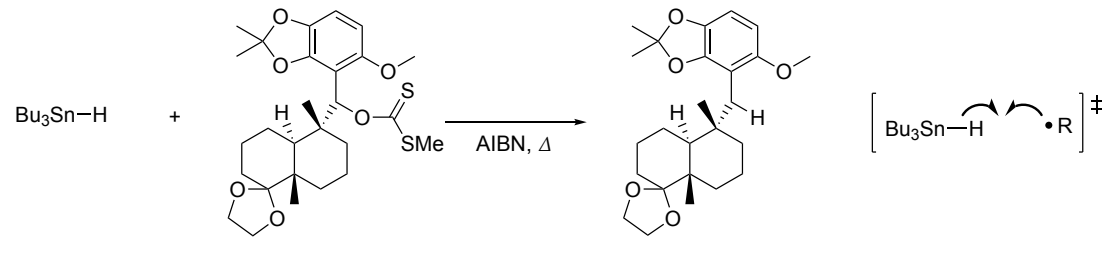
One of the most powerful methods for activation of organotin compounds is transmetalation. Transmetalation between organotin compounds and appropriate metal species readily affords active metal species, which act as useful reagents for various transformations (Scheme 1). For example, organolithium reagents are prepared by the unique Sn-Li exchange (Scheme 1a).[4] Transmetalation of allylstannanes with metal halides such as $SnCl_4$, $TiCl_4$, or $SnCl_2$ produces the allyl metal intermediates[5,6] to accomplish the regio- and stereoselective carbonyl addition (Scheme 1b). Migita-Kosugi-Stille cross-coupling is recognized as a useful cross-coupling and it proceeds also via transmetalation between a palladium species and an organotin compound (Scheme 1c).[7,8]

**Scheme 1.** Transmetalations with organotin compounds: (a) tin-lithium exchange (b) metal salt-mediated carbonyl addition (c) Migita-Kosugi-Stille cross-coupling

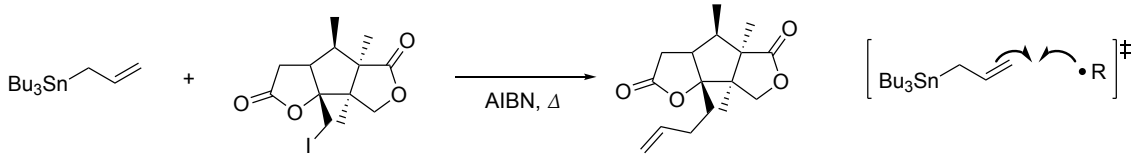



In addition, organotin compounds have a highly activity to radical intermediates.[9,10] The stannyl radical mediated reactions show excellent chemoselectivity, and are often applied in the late stage in the total synthesis of natural products (Scheme 2). In general, organotin hydrides have been widely employed as reductants under radical conditions by use of AIBN or UV irradiation.[11] Moreover, the carbon-carbon bond formations were achieved using allylstannane with high chemoselectivity.[12]

**Scheme 2.** Highly chemoselective radical reactions with organostannanes



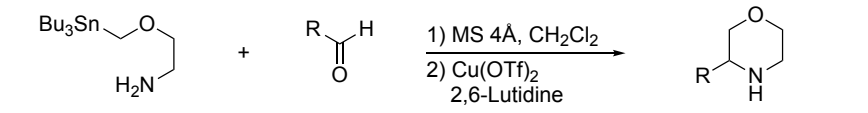

T. Kamishima, T. Kikuchi, T. Katoh, *Eur. J. Org. Chem.* **2013**, 4558.




S. J. Danishefsky, *J. Am. Chem. Soc.* **2002**, *124*, 2080.

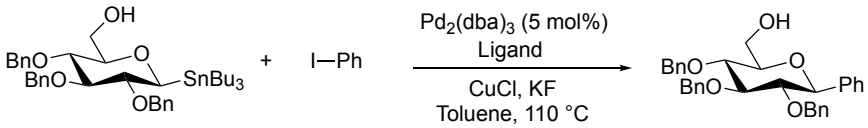
Recently, the development of synthetic methods using functionalized organotin compounds have a huge significance for the efficient synthesis of highly functionalized molecules. For example, Sn Amine Protocol (SnAP) reagents, which are commercially available reagents, are used for the synthesis of heterocyclic compounds.[13] Anomeric stannanes were applied to the synthesis of aryl glycosides via a glycosyl cross-coupling.[14] Thus, it is important to invent novel functionalized organotin reagents and establish their application for accessing functional compounds.

**Scheme 3.** Recent examples of organostannanes substituted with functional groups




**Sn Amine Protocol (SnAP) Reagent**

J. W. Bode, *Angew. Chem. Int. Ed.* **2013**, *52*, 1705.

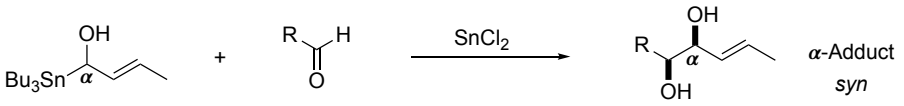



**Anomeric Stannane**

P. Liu, M. A. Walczak, *J. Am. Chem. Soc.* **2017**, *139*, 17908.

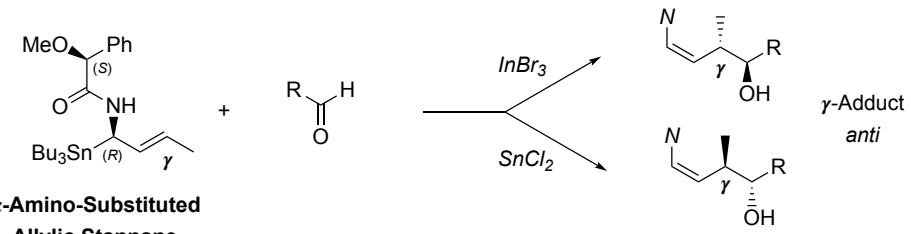
$\alpha$-Heteroatom-substituted allylic stannanes as functionalized organotin compounds have been focused on, and many regio- and stereoselective reactions were reported. For example, Marshall's and our groups reported that the carbonyl addition reaction of oxygen-atom-substituted allylic stannanes afforded 1,2-diol compounds with a high stereoselectivity.[15–17] Moreover, homochiral nitrogen-atom-substituted allylic stannanes were newly developed for the stereoselective synthesis of 1,4-aminoalcohols via transmetalation with $InBr_3$ or $SnCl_2$.[18]

**Scheme 4.** Regio- and stereoselective carbonyl addition with $\alpha$-heteroatom-substituted allylic stannanes




**α-Oxy-Substituted Allylic Stannane**

M. Yasuda, A. Baba, *Tetrahedron Lett.* **2009**, *50*, 3209.
M. Yasuda, A. Baba, *Tetrahedron* **2009**, *65*, 9569.



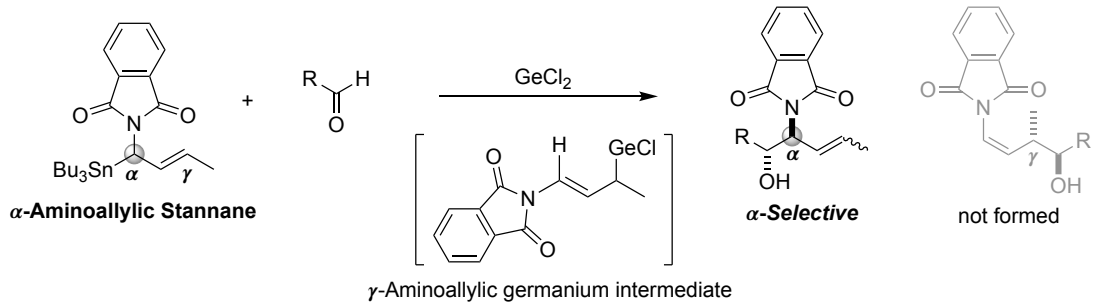

**α-Amino-Substituted Allylic Stannane**

M. Yasuda, A. Baba, *Organometallics* **2014**, *33*, 3924.

In this context, $\alpha$-heteroatom-substituted allylic stannanes have much potential for the efficient synthesis of highly functionalized compounds. Further investigation on the development of the synthetic methods using aminoallylic stannanes was carried out in this study.

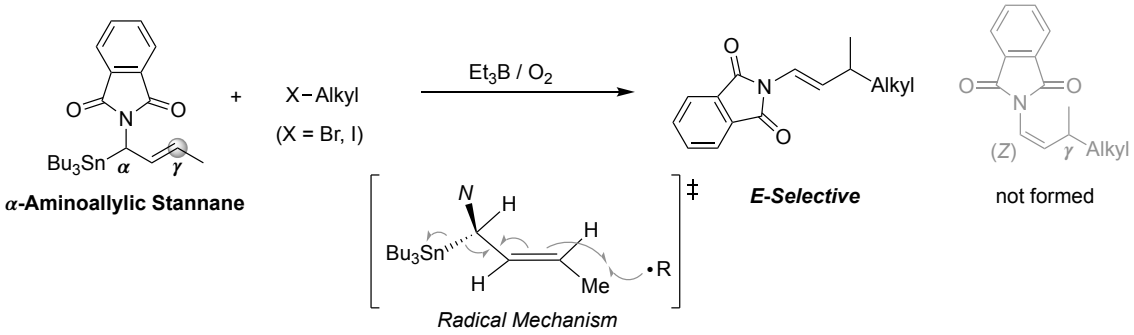
In Chapter 1, regio- and stereoselective addition reactions of α-(*N*-phthaloylamino)aminoallyllic stannanes to carbonyl compounds by $GeCl_2$ were accomplished to afford 1,2-amino alcohols (Scheme 5). In this reaction, a γ-aminoallylic germanium, which was generated by transmetalation between $GeCl_2$ and aminoallylic stannane, reacted with aldehydes to produce the 1,2-amino alcohol derivatives with a high stereoselectivity.

**Scheme 5.** Regio- and stereoselective addition with $\alpha$-aminoallylic stannane mediated by $GeCl_2$




In Chapter 2, the *E*-selective synthesis of enamides by the radical addition of α-(*N*-phthaloylamino)aminoallyllic stannanes with alkyl halides under radical conditions (Scheme 6) is described. The radical reaction system via the acyclic transition state is a key factor for *E*-selectivity.

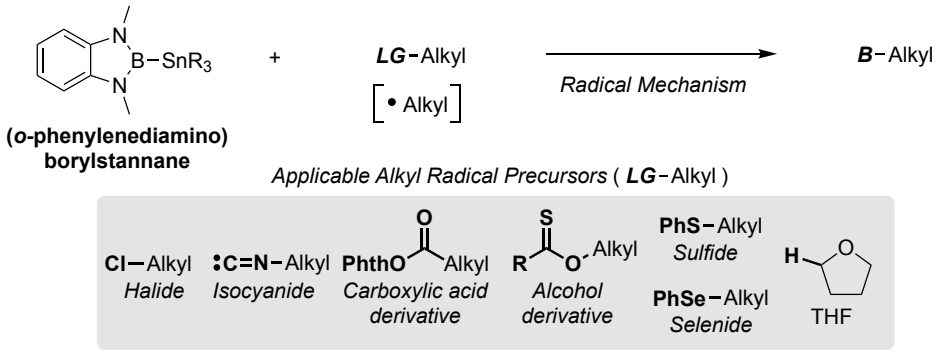
**Scheme 6.** *E*-selective synthesis of enamides by radical addition with $\alpha$-aminoallylic stannane




In Chapter 3, (*o*-phenylenediamino)borylstannanes possessing a high reactivity to alkyl radicals were invented to achieve a radical borylation. Typical stannyl radical mediated reactions are limited to reduction or carbon-carbon bond formation reactions. A heteroatom-carbon bond formation has never been achieved by organotin compounds. Therefore, I focused on borylstannanes that have a less

polar boron-tin bond, and investigated radical borylations. The reaction of borylstannanes with various alkyl radical precursors under radical conditions was found to proceed successfully to afford the borylated products (Scheme 7).

**Scheme 7.** Radical borylation of various alkyl radical precursors using borylstannanes





[1] J. F. Hartwig, *Organotransition Metal Chemistry: From Bonding to Catalysis*, University Science Books, CA, **2010**.

[2] E. Frankland, *Philos. Trans. R. Soc.* **1852**, *142*, 417.

[3] E. T. Alwyn G. Davies, Keith Pannell, *Tin Chemistry: Fundamentals, Frontiers, and Applications*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, **2008**.

[4] I. Coldham, R. Hufton, D. J. Snowden, *J. Am. Chem. Soc.* **1996**, *118*, 5322.

[5] G. E. Keck, D. E. Abbott, E. P. Boden, E. J. Enholm, *Tetrahedron Lett.* **1984**, *25*, 3927.

[6] M. Yasuda, K. Hirata, M. Nishino, A. Yamamoto, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 13442.

[7] M. Kosugi, Y. Shimizu, T. Migita, *Chem. Lett.* **1977**, *6*, 1423.

[8] D. Milstein, J. K. Stiile, *J. Am. Chem. Soc.* **1978**, *100*, 3636.

[9] C. G. Gutierrez, L. R. Summerhays, *J. Org. Chem.* **1984**, *49*, 5206.

[10] W. P. Neumann, *Synthesis* **1987**, 665.

[11] T. Kamishima, T. Kikuchi, T. Katoh, *Eur. J. Org. Chem.* **2013**, *2013*, 4558.

[12] V. B. Birman, S. J. Danishefsky, *J. Am. Chem. Soc.* **2002**, *124*, 2080.

[13] C.-V. T. Vo, G. Mikutis, J. W. Bode, *Angew. Chem. Int. Ed.* **2013**, *52*, 1705.

[14] F. Zhu, J. Rodriguez, T. Yang, I. Kevlishvili, E. Miller, D. Yi, S. O'Neill, M. J. Rourke, P. Liu, M. A. Walczak, *J. Am. Chem. Soc.* **2017**, *139*, 17908.

[15] J. A. Marshall, K. W. Hinkle, *J. Org. Chem.* **1995**, *60*, 1920.

[16] M. Yasuda, T. Azuma, K. Tsuruwa, S. A. Babu, A. Baba, *Tetrahedron Lett.* **2009**, *50*, 3209.

[17] M. Yasuda, K. Tsuruwa, T. Azuma, S. A. Babu, A. Baba, *Tetrahedron* **2009**, *65*, 9569.

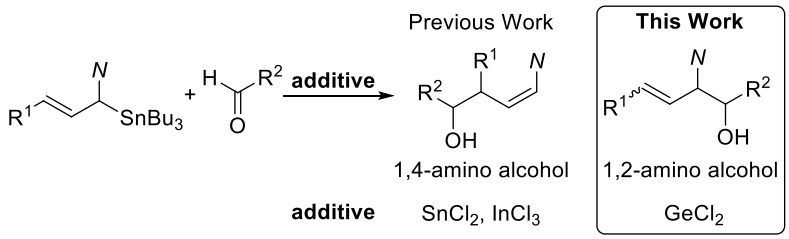
[18] M. Yasuda, Y. Nagano, H. Yunoki, K. Tsuruwa, A. Baba, *Organometallics* **2014**, *33*, 3924.

## Chapter 1. Regio- and Stereo-Controlled Addition Reaction of Aminoallylic Stannanes to Aldehydes Mediated by Germanium Dichloride

### 1-1. Introduction

Amino alcohol moieties are very important functional units that impart pharmacological and biological activity to molecules.[1] Compounds that contain such units are also useful building blocks[2] and are versatile ligands for numerous types of metal complexes.[3] Therefore, the development of a synthetic method for amino alcohols through carbon-carbon bond formation is one of the most important issues in organic synthesis. An amino-substituted allylmetal could be a powerful and practical tool, and the addition of an allylic metal to a carbonyl compound is part of a highly evolving field of study.[4] Actually, addition reactions to carbonyl compounds using amino-substituted allylboranes,[5] allyllithiums[6] or allylsilanes[7] have been reported. Recently, we reported that homochiral carbonylamino-substituted allylic stannanes reacted with aldehydes in the presence of $SnCl_2$ or $InCl_3$ to afford 1,4-aminoalcohols in a highly stereoselective manner.[8-10] While continuing the study, we found that the regioselectivity of the addition reaction of a carbonylamino-substituted allylic stannane depends on a used metal salt. Herein, we describe that $GeCl_2$ mediated the addition of an α-aminoallylic stannane to an aldehyde, and 1,2-amino alcohols were obtained in contrast to $SnCl_2$ and $InCl_3$ (Scheme 1).[8]

**Scheme 1.** Addition reaction of α-aminoallylic stannane to aldehyde

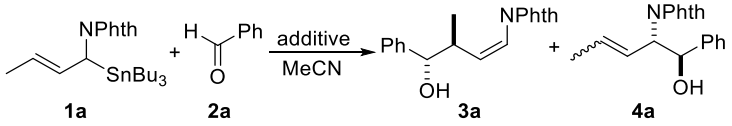



### 1-2. Results and Discussion

α-(*N*-Phthaloylamino)allylic stannane **1a** was chosen as an amino-substituted nucleophile because of its facile preparation,[11] stability in air,[12] and easy deprotection.[13] The reaction of **1a** with benzaldehyde **2a** under various conditions was investigated, and the results are summarized in Table 1. No reaction was observed without using additives (entry 1). The use of either $SnCl_2$ or $InCl_3$ as an additive[14] preferentially furnished 1,4-*N*-phthaloylamino alcohol **3a** in high diastereoselectivity without the formation of 1,2-*N*-phthaloylamino alcohol **4a** (entries 2 and 3).[15] This regioselectivity was consistent with our previous report.[8] $TiCl_4$ gave **3a** in a moderate yield with a low

diastereoselectivity (*syn*/*anti* = 29:71) (entry 4).[16] The use of $BF_3 \cdot OEt_2$ resulted in a low yield (entry 5).[17] Surprisingly, $GeCl_2$·dioxane afforded 1,2-*N*-phthaloylamino alcohol **4a** in high regio- and stereoselectivity (entry 6).[18] These results suggested that regio- and stereoselectivities were controlled by the loaded metal halide in the reaction of aminoallylic stannane **1a** with carbonyl compounds.

**Table 1.** Investigation of the reaction of phthaloylaminoallylic stannane **1a** with benzaldehyde **2a**[a]




**1a** **2a** **3a** **4a**

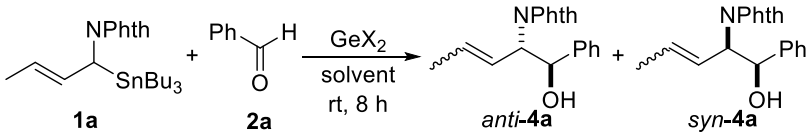
| Entry | Additive | Temp. | Yield [%][b] | | | |
|---|---|---|---|---|---|---|
| | | | **3a** | *syn*/*anti* | **4a** | *syn*/*anti* |
| 1 | none | rt | 0 | - | 0 | - |
| 2 | $SnCl_2$ | –10 ºC | 51 | 1:99 | 0 | - |
| 3 | $InCl_3$ | –10 ºC | 69 | 6:94 | 0 | - |
| 4[c] | $TiCl_4$ | –78 ºC | 58 | 29:71 | 0 | - |
| 5[c] | $BF_3$•$OEt_2$ | –78 ºC | 20 | 1:>99 | 0 | - |
| 6[d,e] | $GeCl_2$•dioxane | rt | <5 | - | 60 | 1:>99[f] |

[a]**1a** (1.3 equiv), **2a** (1.0 equiv), additive (1.3 equiv). [b]Yields were determined by $^1$H NMR using 1,1,2,2-tetrachloroethane or anisole as an internal standard. [c]$CH_2Cl_2$ was used instead of MeCN. [d]THF was used instead of MeCN. [e]**1a** (1 equiv), **2a** (5 equiv), additive (1 equiv). [f]*E*/*Z* = 67:33.

As shown in Table 1, $GeCl_2$ gave 1,2-*N*-phthaloylamino alcohol **4a** in the addition reaction of α-(*N*-phthaloylamino)allylic stannane **1a** to benzaldehyde **2a** in contrast to $SnCl_2$ and $InCl_3$. This interesting result prompted us to investigate $GeCl_2$-mediated reaction toward the selective synthesis of 1,2-amino alcohols **4**. We optimized the reaction conditions in the addition of **1a** to **2a**, and the results are summarized in Table 3. When the addition of $GeCl_2$ was carried out in THF solution, the *anti*-isomer **4a** was exclusively given in 60% yield (entry 1). The ratio of the *E*/*Z* isomer was 67:33, and their stereochemistries were determined by $^3J_{HH}$ value of vicinal protons. In fact, the *E*/*Z*-mixed *anti*-**4a** was hydrogenated by $H_2$/Pd-C to afford a single product **5a** (eq 1). $GeBr_2$ and $GeI_2$ as well as $GeCl_2$ afforded *anti*-**4a** in 45% and 47% yields, respectively, although the yields were slightly lower (entries 2 and 3). A survey showed highly polar solvents were effective in this reaction, and THF

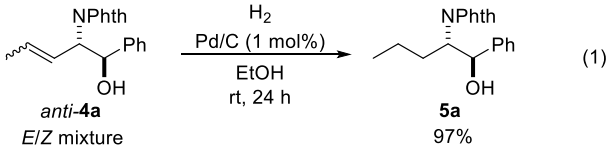
afforded the best results (entries 4-7). The recrystallization of the *E*/*Z*-isomer mixture of **4a** gave a single crystal of *anti*-*E*-**4a**, and then its relative stereochemistry was confirmed by X-ray diffraction analysis (Figure 1).[19]

**Table 2.** Optimization of $GeX_2$-mediated addition reaction of phthaloylaminoallylic stannane **1a** with benzaldehyde **2a**[a]




| Entry | $GeX_2$ | Solvent | Amino Alcohol **4a** | | |
|---|---|---|---|---|---|
| | | | Yield [%][b] | *anti*/*syn* | *E*/*Z*[c] |
| 1 | $GeCl_2$·dioxane | THF | 60 | >99:1 | 67:33 |
| 2 | $GeBr_2$·dioxane | THF | 45 | >99:1 | 56:44 |
| 3 | $GeI_2$ | THF | 47 | >99:1 | 64:36 |
| 4 | $GeCl_2$·dioxane | DMSO | 58 | >99:1 | 57:43 |
| 5 | $GeCl_2$·dioxane | acetone | 21 | >99:1 | 62:38 |
| 6 | $GeCl_2$·dioxane | EtOAc | 24 | >99:1 | 58:42 |
| 7 | $GeCl_2$·dioxane | dioxane | 29 | >99:1 | 59:41 |

[a]**1a** (0.5 mmol), **2a** (2.5 mmol), $GeCl_2$·dioxane (0.5 mmol) in solvent (1 mL) at room temperature for 8 h. [b]Yields were determined by $^1$H NMR using 1,1,2,2-tetrachloroethane or anisole as an internal standard. [c]*E*/*Z* ratio of *anti*-**4a**.



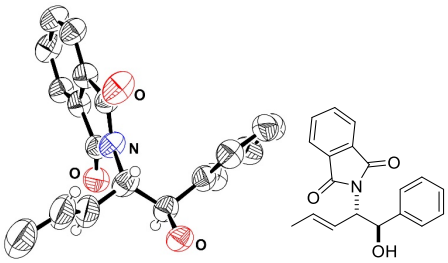
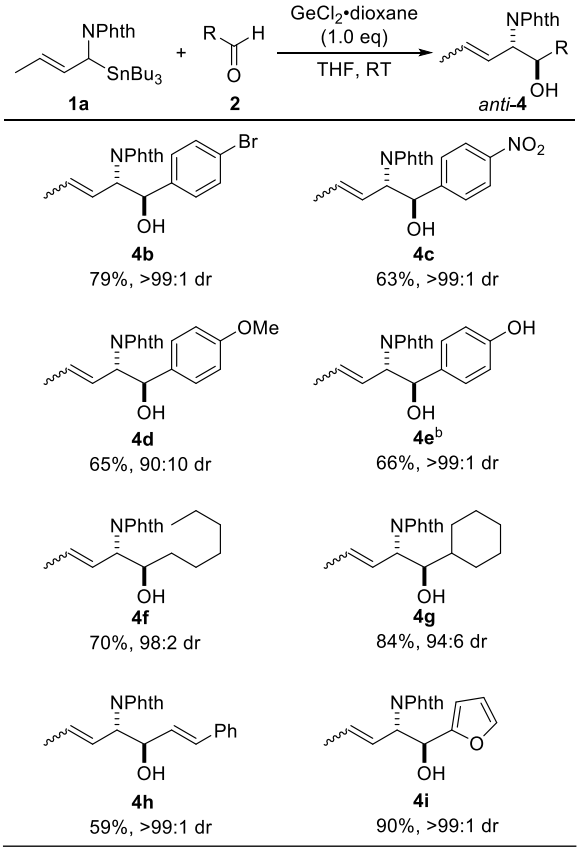




**Figure 1.** ORTEP drawing of *anti*-*E*-**4a** with 50% probability thermal ellipsoids. Some hydrogen atoms are omitted for clarity.

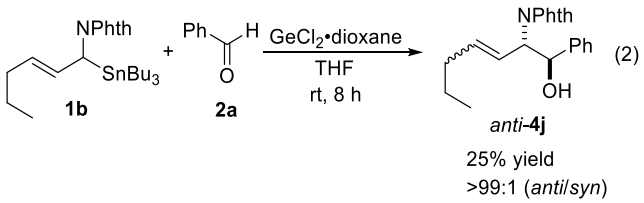
With the optimized conditions in hand, the scope of aldehydes **2** was investigated (Scheme 2). Aromatic aldehydes with electron-withdrawing and electron-donating groups gave the corresponding 1,2-phthaloylamino alcohols **4** in moderate to high yields (**4b**, **4c**, **4d**, and **4e**). Aliphatic aldehydes **2f** and **2g** were also applicable to this reaction system to afford **4f** and **4g**, respectively, in high yields and *anti*-selectivity. The α,β-unsaturated aldehyde **2h** and heteroaromatic aldehyde **2i** afforded the corresponding 1,2-phthaloylamino alcohols **4h** and **4i**, respectively.

**Scheme 2.** Scope of aldehyde 2 in the addition reaction using α-aminoallylic stannane **1a**.[a]



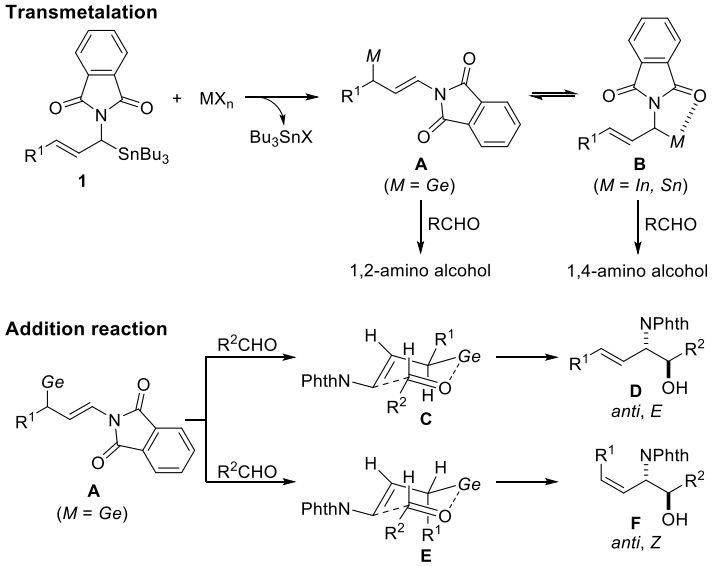

[a]The reactions were employed using **1a** (1 equiv), **2** (5 equiv), and $GeCl_2$·dioxane (1 equiv) in THF (0.5 M) at room temperature for 8 h. Yields were determined by $^1H$ NMR using 1,1,2,2-tetrachloroethane or anisole as an internal standard. A diastereo ratio (dr) shows *anti*/*syn*. In all cases, the geometry of the olefin moiety was non-selective. [b]**1a** (1.0 mmol), $GeCl_2$·dioxane (1.0 mmol). Slow addition of **2e** (0.5 mmol) in THF (2 mL) for 5 h and additional mixing for 4 h.

The addition reaction using (*N*-phthaloylamino)allylic stannane **1b**, which have a longer alkyl group than **1a**, also occurred to give the desired 1,2-amino alcohol *anti*-**4j** diastereoselectively although the yield was low (Eq 2). In all cases shown in Scheme 2 and Eq 2, the corresponding 1,2-phthaloylamino alcohols were exclusively obtained without 1,4-phthaloylamino alcohols.



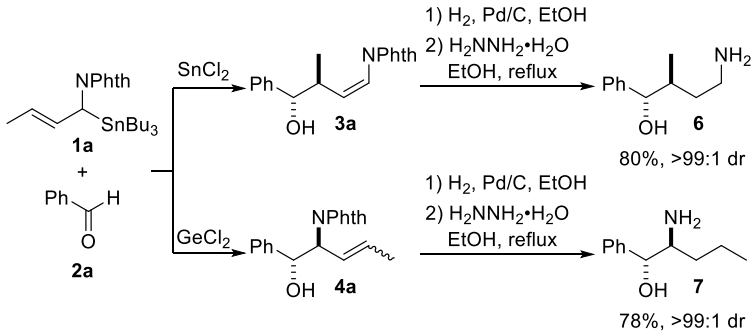

We investigated the active species in the $GeCl_2$-mediated addition reactions of aminoallylic stannane **1**. When the mixture of **1a** with $GeCl_2$ were monitored by $^{119}Sn$ NMR spectroscopy, the generated $Bu_3SnCl$ was confirmed by $^{119}Sn$ NMR,[20],[21] which indicated that transmetalation between **1a** and $GeCl_2$ proceeded to give the corresponding allylic germanium. However, unidentified decomposed species were observed via $^1H$ NMR due to the short lifespans of the active species. Plausible reaction mechanisms based on the experimental results are shown in Scheme 3. Transmetalation between aminoallylic stannane **1** and $GeCl_2$ through an *anti* $S_E2'$ process gives allylic germanium **A**. The species **A** has an *E*-geometry due to the bulky phthaloylamino group.[22] As the *anti*-form with *E*/*Z* mixed products **D** and **F** were obtained in the experiment, the species **A** (*Ge*) reacts with aldehyde via the cyclic transition states **C** and **E** to give the 1,2-aminoalcohols **D** and **F**, respectively.[23,24] The steric hindrance $R^1$ disturbs the transmetalation and the addition reaction via cyclic transition states so that **1b** gave lower yield than **1a** (Eq. 2). On the other hand, $InCl_3$ and $SnCl_2$ gave 1,4-amino alcohols via the allylic metal species **B** due to the chelation between oxygen and the metal center.[8] The Lewis acidity of germanium halide moiety is low so that the isomerization of **A** to **B** allylic metal species does not occur.[25]

**Scheme 3.** Plausible reaction mechanism



The synthesized *N*-phthaloylamino alcohols were effectively transformed to the stereo-controlled saturated aminoalcohols (Scheme 4).[2],[26] The product **3a**, which was produced by $SnCl_2$-mediated allylation, underwent hydrogenation catalyzed by Pd/C followed by deprotection of the phthalimido moiety by $H_2NNH_2 \cdot H_2O$ to give 1,4-aminoalcohol **6** without a loss of the stereochemistry. A similar procedure gave 1,2-aminoalcohol **7** from **4a** and maintained the high stereoisomeric ratio. In general, 1,2- and 1,4-amino alcohols represent significant building blocks in pharmaceutical synthesis. Therefore, this individual synthesis of the 1,4- and 1,2-amino alcohols from same starting materials with a simple change in the metal salts has an important significance.

**Scheme 4.** Individual synthesis of 1,4- and 1,2-amino alcohols from **1a** and **2a** by changing metal salts




## 1-3. Conclusion

The $GeCl_2$-mediated stereoselective allylation of aldehydes with α-(*N*-phthaloylamino)allylic stannane **1** was achieved. In this reaction, a γ-(*N*-phthaloylamino)allylic germanium, which is generated by transmetalation between $GeCl_2$ and allylic stannane **1**, reacted with aldehydes to produce the 1,2-amino alcohol derivatives with high diastereoselectivity. In contrast to our previously reported $SnCl_2$- or $InCl_3$-mediated allylation affording 1,4-amino alcohol derivatives, allylic germanium **A** added to an aldehyde without the isomerization of **A** to **B** to give 1,2-amino alcohol derivatives selectively because of the low Lewis acidity of germanium halide. Various types of carbonyl compounds such as aliphatic aldehydes and aromatic aldehydes were applicable. The diastereoselectively synthesized *N*-phthaloylaminoalcohol derivatives were successfully transformed to the corresponding stereo-controlled aminoalcohols via hydrogenation using Pd/C followed by deprotection of the phthalimido moiety with hydrazine.

## 1-4. Experimental Section

### General Information

NMR spectra were recorded on a JEOL JNM-400 (400 MHz for $^{1}$H NMR and 100 MHz for $^{13}$C NMR) spectrometer. Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 for $^{1}$H NMR) and residual $CHCl_3$ (δ = 77.0 for $^{13}$C NMR) as an internal reference. Infrared (IR) spectra were recorded on a HORIBA FT-720 Fourier transform infrared spectrophotometer. Column chromatography was performed with silica gel. Purification by recycle HPLC was performed using a SHIMADZU recycle HPLC system (SPD-20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) from the Japan Analytical Industry Co. (NEXT recycling preparative HPLC). Reactions were carried out in dry solvents under a nitrogen atmosphere, unless otherwise stated. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), Wako Pure Chemical Industries, Ltd., and used after purification by distillation or used without purification in the cases of solid substrates.

### Materials

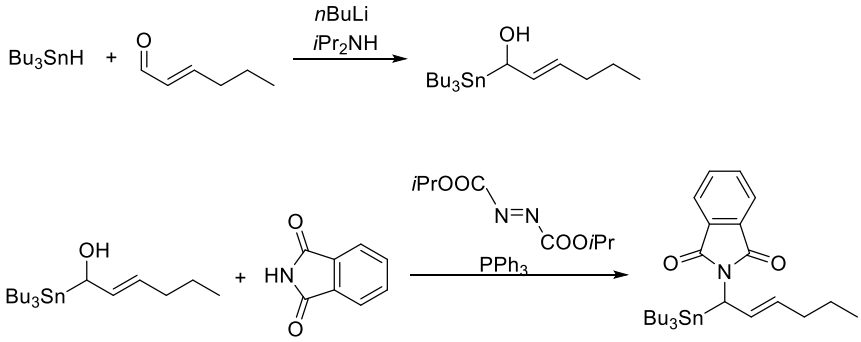
Aminoallylic stannane **1a** was prepared by known methods and these compounds were reported. Aminoallylic stannane **1b** is new compound, and the synthetic method and the characterization data is shown below.

**Tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1a)**

To a stirred solution of tributyl(1-hydroxy-(*E*)-2-butenyl)stannane (51.1 g 130 mmol, purity 92%), phthalimide (34.5 g, 234 mmol) and $Ph_3P$ (61.4 g, 234 mmol) in dry THF (270 mL) was slowly added DEAD (102.5 g, 235 mmol, 40% toluene solution) for 15 min at 0 °C. The mixture was stirred for 17 h at room temperature. The solvent was evaporated and hexane (200 mL) was poured with stirring. The formed solid was filtered off and the solvent was evaporated and the residue was purified by column chromatography (hexane/ethyl acetate = 97/3) to give the pure product as yellow liquid (15.0 g, 23%). IR: (neat) 1709 (C=O) cm$^{-1}$; $^{1}$H NMR: (600 MHz, $CDCl_3$) 7.87- 7.80 (m, 2H), 7.74-7.66 (m, 2H), 5.63 (ddd, $J$ = 14.7, 7.0, 1.7 Hz, 1H), 5.19 (dq, $J$ = 14.7, 6.5 Hz, 1H), 4.41 (d, $J$ = 7.0 Hz, $^{2}J_{Sn\text{-}H}$ = 52.4, 1H), 1.69-1.62 (m, 3H), 1.56-1.50 (m, 6H), 1.37-1.23 (m, 6H), 1.09-0.77 (m, 6H), 1.09-0.77 (m, 9H); $^{13}$C NMR: (151 MHz, $CDCl_3$) 168.9 (s), 133.8 (d), 132.0 (s), 129.6 (d, d, $^{2}J_{Sn\text{-}C}$ = 14.4 Hz), 123.0 (d), 119.8 (d, d, $^{3}J_{Sn\text{-}C}$ = 31.5 Hz), 39.5 (d, d, $^{1}J_{119Sn\text{-}C}$ = 268.4 Hz, $^{1}J_{117Sn\text{-}C}$ = 255.7 Hz), 28.9 (t, d, $^{2}J_{Sn\text{-}C}$ = 21.0 Hz), 27.3 (t, d, $^{3}J_{Sn\text{-}C}$ = 58.0), 17.4 (q), 13.6 (q), 11.1 (t, $^{1}J_{119Sn\text{-}C}$ = 330.3 Hz, $^{1}J_{117Sn\text{-}C}$ = 314.8 Hz); $^{119}$Sn NMR: (150 MHz, $CDCl_3$) -13.7; MS: (EI, 70 eV) *m*/*z* 491 (1.4, $M^+$), 435 (21), 434 (100, $M^+$ - Bu), 433 (40), 432 (74), 30 (431), 430 (42), 266 (20), 235 (33), 233 (26), 200 (76, $M^+$ -

$SnBu_3$), 179 (53), 177 (44), 175 (27); HRMS: (EI, 70 eV) Calculated: $C_{24}H_{37}NO_2Sn$ ($M^+$) 491.1846, Found: $C_{24}H_{37}NO_2Sn$ ($M^+$) 491.1853.

**Tributhyl{(*E*)-1-phthaloylamino-2-hexenyl}stannane (1b)**




*n*-BuLi (1.6 M/hexane solution 14 ml, 22 mmol) was added to the solution of diisopropylamine (2.25 g, 22 mmol) in THF (20 mL). The solution was stirred for 10 min at 0 °C. $Bu_3SnH$ (5.90 g, 20 mmol) was dropwised to the solution and stirred for 1 h at -78 °C. Then, *trans*-2-hexenal (1.98 g, 20 mmol) was dropwised slowly and stirred for 4 h. The reaction mixture was quenched by 15% $NH_4F$ aq. (30 mL). The organic layer was extracted with ethyl acetate (3 x 30 mL) and the collected organic layer was dried over $MgSO_4$. Then the solvent was removed with vacuum. Tributhyl {(*E*)-1-hydroxy-2-hexenyl}stannane was obtained as a yellow oil in ca. 86% purity (7.04 g, 78%). To a solution of {(*E*)-1-hydroxy-2-hexenyl}tributhylstannane (6.72 g, 14.8 mmol, ca. 86% purity), phthalimide (2.99 g, 20.3 mmol), and $PPh_3$ (5.24 g, 20.0 mmol) in dry THF (30 mL) was slowly added diisopropyl azodicarboxylate (10.5 mL, 20 mmol, 1.9 M toluene solution) over 15 min at 0 °C. The mixture was stirred for 12 h at room temperature. The solvent was evaporated, and hexane (100 mL) was poured with stirring. The generated solid was filtered off and the solvent was evaporated and the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 90/10) to give the pure product as a yellow liquid (3.44 g, 45%).

IR (neat): 1702 $cm^{-1}$ (C=O); $^1H$ NMR: (400 MHz, $CDCl_3$) 7.85-7.82 (m, 2H), 7.71-7.69 (m, 2H), 5.60 (dd, $J$ = 15,2, 7.6 Hz, 1H), 5.18 (td, $J$ = 15.2, 7.4, 1H), 4.42 (dd, $J$ = 26.6, 7.4 , 1H), 2.02-1.87 (m, 2H), 1.59-1.24 (m, 14H), 1.06-0.83 (m, 18H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 168.9 (s), 133.8 (d), 132.0 (s), 128.6 (d, d by $J_{Sn\text{-}C}$ = 8.2 Hz), 125.3 (d, d by $J_{Sn\text{-}C}$ = 16.4 Hz), 123.0 (d), 39.6 (d, d by $J_{119Sn\text{-}C}$ = 133.5 Hz, d by $J_{117Sn\text{-}C}$ = 127.8 Hz), 34.3 (t, d by $J_{Sn\text{-}C}$ = 24.6 Hz), 28.9 (t, d by $J_{Sn\text{-}C}$ = 9.9 Hz), 27.4 (t, d by $J_{Sn\text{-}C}$ = 28.7 Hz), 22.7 (t), 13.7 (q), 11.1 (t, d by $J_{119Sn\text{-}C}$ = 165.5 Hz, d by $J_{117Sn\text{-}C}$ = 158.1 Hz); $^{119}Sn$ NMR: (100 MHz, $CDCl_3$) -13.4; HRMS: (EI, 70 eV) Calculated ($C_{26}H_{41}NO_2Sn$): 519.2159 ($M^+$) Found: 519.2155.

**General Procedure**

To a stirred solution of $GeCl_2$-dioxane (1.0 mmol) and carbonyl compound (5.0 mmol) in dry THF (2 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.0 mmol). The mixture was stirred at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The generated white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried over $MgSO_4$. The residue was purified by flash-chromatography (hexane/EtOAc) and/or recrystallization.

**Products**

**(*Z*)-(1*R**,2*R**)-2-Methyl-1-phenyl-4-*N*-phthaloyl-3-buten-1-ol (3a)**

To a suspended solution of $InCl_3$ (1.3 mmol, 0.24 g) and benzaldehyde (1.0 mmol, 0.11 g) in dry MeCN (4 mL) was added tributyl(1-*N*-phthaloyl-2-butenyl)stannane (1.3 mmol, 0.2 M MeCN solution 6.5 mL). The mixture was stirred for 8 h at -10 °C and then quenched by aqueous $NH_4F$ (30%; 20 mL). The obtained white precipitate was filtered off by Celite and the filtrate was extracted with diethyl ether (3 x 40 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated to afford the crude product (yield 69%, *anti*/*syn* = 96:4). The residue was purified by flash-chromatography (hexane/EtOAc = 75:25) and recrystallization to give the pure product as a colorless solid (0.071 g, 23%). mp: 105-108 °C; IR (KBr): 3433 (OH), 1712 (C=O) $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) 7.93 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.42-7.21 (m, 5H), 6.23 (d, *J* = 8.9 Hz, 1H), 5.75 (dd, *J* = 11.4, 8.9 Hz, 1H), 4.35 (dd, *J* = 9.2, 7.0 Hz, 1H), 4.06 (d, *J* = 7.0 Hz, 1H, OH, $D_2O$ exchangeable), 2.77-2.66 (m, 1H), 0.85 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR: (100 MHz, $CDCl_3$) 167.5 (s), 143.2 (s), 135.2 (d), 134.6 (d), 131.9 (s), 128.2 (d), 127.5 (d), 126.9 (d), 123.9 (d), 117.3 (d), 78.3 (d) , 41.4 (d), 17.4 (q); MS: (CI, 200 eV) 306 (M - 1, 2), 290 (9), 148 (100), 143 (41); HRMS: (CI, 200 eV) Calcd: $C_{19}H_{18}NO_3$ (M + H) 308.1287; Found: $C_{19}H_{18}NO_3$ (M + H) 308.1279; Analysis: $C_{19}H_{17}NO_3$ (307.34) Calcd: C, 74.25; H, 5.58; N, 4.56, Found: C, 74.00; H, 5.78; N, 4.37.

**(1*R**, 2*S**)-1-Phenyl-2-(*N*-phthaloylamino)-3-penten-1-ol (4a)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and benzaldehyde (1.06 g, 10.0 mmol) in dry THF (4 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was

extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 80:20, 0.343 g, 56%, *E*/*Z* = 52:48). mp: 123.9-124.6 ºC; IR: (KBr) 3525 (OH), 1770, 1708 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) *E*-form; 7.80-7.72 (m, 2H), 7.72-7.63 (m, 2), 7.43-7.35 (m, 2H), 7.30-7.17 (m, 3H), 6.07 (ddq, *J* = 16.1, 9.0, 1.8 Hz, 1H), 5.89-5.71 (m, 1H) , 5.25 (dd, *J* = 7.1, 2.0 Hz, 1H), 4.89 (ddd, *J* = 9.0, 7.1, 4.3 Hz, 1H), 3.22 (d, *J* = 2.0 Hz, 1H, OH, $D_2O$ exchangeable), 1.73 (dd, *J* = 7.3, 1.8 Hz, 3H), *Z*-form; 7.80-7.72 (m, 2H), 7.72-7.63 (m, 2H), 7.43-7.35 (m, 2H), 7.30-7.17 (m, 3H), 6.20-5.97 (m, 1H), 5.89-5.71 (m, 1H), 5.33-5.27 (m, 2H), 3.31 (d, *J* = 1.7 Hz, 1H, OH, $D_2O$ exchangeable), 1.58 (dd, *J* = 7.7, 2.0 Hz, 3H);$^{13}C$ NMR: (100 MHz, $CDCl_3$) *E*-form; 168.0 (s), 140.3 (s), 133.9 (d), 132.5 (d), 131.5 (s), 128.2 (d), 127.9 (d), 126.6 (d), 124.4 (d), 123.2 (d), 73.9 (d), 59.9 (d), 17.8 (q), *Z*-form; 168.1 (s), 140.3 (s), 133.9 (d), 132.5 (d), 131.5 (s), 131.3 (d), 128.2 (d), 127.9 (d), 126.5 (d), 123.7 (d), 123.2 (d), 74.7 (d), 53.9 (d), 13.2 (q); MS: (CI, 200 eV) *m*/*z* 308 ($M^+$ + H, 1.6), 291 (23), 290 (100); HRMS: (CI, 200 eV) Calculated: $C_{19}H_{18}NO_3$ ($M^+$ + H) 308.1287, Found: $C_{19}H_{18}NO_3$ ($M^+$ + H) 308.1286; Analysis: $C_{19}H_{17}NO_3$ (307.34) Calcd: C, 74.25; H, 5.58; N, 4.56, Found: C, 74.14; H, 5.59; N, 4.53.

**(1*R**, 2*S**)-1-(4-Bromophenyl)-2-(*N*-phthaloylamino)-3-penten-1-ol (4b)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and *p*-bromobenzaldehyde (1.85 g, 10.0 mmol) in dry THF (4 mL) was added tributyl {1-(*N*-phthaloylamino)-(*E*)--2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4Faq$ (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 80/20) to give the pure product as a viscous liquid (0.139 g, 18%, *E*/*Z* = 63:37). IR: (neat) 3421 (OH), 1709 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) *E*-form; 7.83-7.75 (m, 2H), 7.75-7.65 (m, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 5.99 (ddq, *J* = 16.1, 7.4, 1.2 Hz, 1H), 5.75 (dq, *J* = 6.6, 1.2 Hz, 1H), 5.21 (dd, *J* = 7.4, 1.9 Hz, 1H), 4.83 (dd, *J* = 7.4, 7.4 Hz, 1H), 3.35 (d, *J* = 1.9 Hz, 1H, OH, $D_2O$ exchangeable), 1.72 (dd, *J* = 6.6, 1.2 Hz, 3H) *Z*-form; 7.83-7.75 (m, 2H), 7.75-7.65 (m, 2H), 7.40 (d, *J* = 10.4 Hz, 2H), 7.29 (d, *J* = 10.4 Hz, 2H), 6.06 (ddq, *J* = 11.0, 11.0, 1.9 Hz, 1H), 5.83 (dq, *J* = 7.0, 1.9 Hz, 1H), 5.27-5.18 (m, 1H), 5.27-5.18 (m, 1H), 3.45 (d, *J* = 1.4 Hz, 1H, OH, $D_2O$ exchangeable), 1.58 (dd, *J* = 7.0, 1.9 Hz, 3H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) *E*-form; 168.1 (s), 139.4 (s), 134.2 (d), 133.1 (d), 131.5 (s), 131.4 (d), 128.4 (d), 123.8 (d), 123.4 (d), 121.9 (s), 74.3

(d), 59.9 (d), 17.9 (q), *E*-form; 168.2 (s), 139.4 (s), 134.2 (d), 131.8 (d), 131.5 (s), 131.4 (d), 128.3 (d), 123.4 (d), 123.0 (d), 121.9 (s), 73.5 (d), 53.9 (d), 13.3 (q); MS: (CI, 200 eV) *m*/*z* 388 (M + H + 2, 1.1), 386 (M + H, 1.8), 370 (96), 368 (100); HRMS: (CI, 200 eV) Calculated ($C_{19}H_{17}BrNO_3$) 386.0392 (M + H), Found: 386.0307; Analysis: $C_{19}H_{16}BrNO_3$ (386.24) Calcd: C, 59.08; H, 4.18; N, 3.63; Br, 20.69, Found: C, 58.95; H, 4.16; N, 3.57; Br, 20.53.

**(1*R**, 2*S**)-1-(4-Nitrophenyl)-2-(*N*-phthaloylamino)-3-penten-1-ol (4c)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and *p*-nitrobenzaldehyde (1.51 g, 10.0 mmol) in dry THF (4 mL) was added tributyl {1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 75:25) to give the product (0.275 g, 35%, *E*/*Z* = 31:69). mp: 143.5-145.2 ºC; IR: (KBr) 3448 (OH), 1697 (C=O), 1520 ($NO_2$), 1346 $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) *E*-form 8.13 (d, *J* = 8.8 Hz, 2H), 7.87-7.78 (m, 2H), 7.78-7.69 (m, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 6.00 (ddq, *J* = 15.1, 8.1, 2.3 Hz, 1H), 5.72 (dq, *J* = 15.1, 6.7 Hz, 1H), 5.33 (d, *J* = 5.9 Hz, 1H), 4.86 (dd, *J* = 8.1, 5.9 Hz, 1H), 3.78 (d, *J* = 1.5 Hz, 1H, OH, $D_2O$ exchangeable), 1.72 (d, *J* = 6.9 Hz, 3H); *Z*-form 8.16 (d, *J* = 8.8 Hz, 2H), 7.87-7.78 (m, 2H), 7.78-7.69 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 6.08 (ddq, *J* = 10.5, 9.4, 1.8 Hz, 1H), 5.83 (dq, *J* = 10.5, 6.9 Hz, 1H), 5.38 (d, *J* = 5.3 Hz, 1H), 5.27 (dd, *J* = 9.4, 5.3 Hz, 1H), 3.89 (d, *J* = 1.5 Hz, 1H, OH, $D_2O$ exchangeable), 1.52 (dd, *J* = 6.1, 2.7 Hz, 3H); $^{13}$C NMR: (100 MHz, $CDCl_3$) 168.3 (s), 168.1 (s), 147.7 (s), 147.6 (s), 147.4 (s), 134. 3 (d), 133.5 (d), 131.9 (d), 131.3 (s), 131.3 (s), 127.6 (d), 127.4 (d), 123.6 (d), 123.3 (d), 123.0 (d), 122.3 (d), 74.2 (d), 73.5 (d), 59.9 (d), 53.8 (d), 17.8 (q), 13.2 (q); MS: (CI, 200 eV) *m*/*z* 353 (96, M + H), 336 (22), 335 (100), 200 (21); HRMS: (CI, 200 eV) Calculated $C_{19}H_{17}N_2O_5$ (M + H) 353.1137, Found: $C_{19}H_{17}N_2O_5$ (M + H) 353.1152; Analysis: $C_{19}H_{16}N_2O_5$ (352.34) Calcd: C, 64.77; H, 4.58; N, 7.95, Found: C, 64.66; H, 4.51; N, 7.92.

**(1*R**, 2*S**)-1-(4-Methoxyphenyl)-2-(*N*-phthaloylamino)-3-penten-1-ol (4d)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and *p*-methoxybenzaldehyde (1.36 g, 10.0 mmol) in dry THF (4 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl

(1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4Faq$ (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 80:20, 0.310 g, 43%, *E*/*Z* = 55:45). IR: (neat) 3444 (OH), 1709 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) *E*-form 7.80-7.72 (m, 2H), 7.72-7.63 (m, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 6.06 (ddq, *J* = 15.3, 6.8, 1.7 Hz, 1H), 5.79 (dq, *J* = 15.3, 6.3 Hz, 1H), 5.23 (dd, *J* = 6.8, 2.0 Hz, 1H), 4.86 (dd, *J* = 6.8, 6.8 Hz, 1H), 3.73 (s, 3H), 3.01 (d, *J* = 2.0 Hz, 1H, OH, $D_2O$ exchangeable), 1.74 (d, *J* = 6.3 Hz, 3H), *Z*-form 7.80-7.72 (m, 2H), 7.72-7.63 (m, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.16-5.99 (m, 1H), 5.91-5.73 (m, 1H), 5.31-5.15 (m, 1H), 5.31-5.15 (m, 1H), 3.74 (s, 3H), 3.09 (s, 1H, OH, $D_2O$ exchangeable), 1.64 (dd, *J* = 6.6, 1.9 Hz, 3H) $^{13}C$ NMR: (100 MHz, $CDCl_3$) *E*-form 167.9 (s), 159.1 (s), 133.9 (d), 132.4 (s), 132.2 (d), 131.4 (s), 127.8 (d), 124.8 (d), 123.1 (d), 113.5 (d), 73.2 (d), 59.6 (d), 55.0 (q), 17.8 (q), *Z*-form; 167.9 (s), 159.1 (s), 133.9 (d), 132.4 (s), 131.4 (s), 131.1 (d), 127.7 (d), 124.3 (d), 123.1 (d), 113.5 (d), 74.0 (d), 55.0 (q), 53.6 (d), 13.3 (q) MS: (EI, 70 eV) *m*/*z* 337 (0.67, $M^+$), 201 (43), 186 (33), 137 (100); HRMS: (EI, 70 eV) Calculated: $C_{20}H_{19}NO_4$ 337.1314 ($M^+$), Found: $C_{20}H_{19}NO_4$ 337.1310.

**(1*R**, 2*S**)-1-(4-Hydroxyphenyl)-2-(*N*-phthaloylamino)-3-penten-1-ol (4e)**

To a stirred solution of $GeCl_2$-dioxane (0.93 g, 4.0 mmol) and tributyl{1-(*N*-phthaloylamino)- (*E*)-2-butenyl}stannane (1.99 g, 4.0 mmol) in dry THF (4 mL) was slowly added 4-hydroxybenzaldehyde (0.25 g, 2.0 mmol, 1M of THF solution) with a syringe pump for 5 h at room temperature. The mixture was further stirred for 4 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4Faq$ (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 50:50), and recrystallization from hexane/ethyl acetate (9/1) to give the pure product as white solid (0.181 g, 29%, *E*/*Z* = 67:33). mp: 190.2-191.3 ºC; IR: (KBr) 3417 (OH), 1712 (C=O) $cm^{-1}$; $^1H$ NMR: (600 MHz, DMSO-$d_6$) *E*-form 9.11 (s, 1H, OH, $D_2O$ exchangeable), 7.83-7.71 (m, 2H), 7.83-7.71 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.50 (d, *J* = 8.5 Hz, 2H), 5.92 (ddq, *J* = 15.2, 8.5, 1.7 Hz, 1H), 5.55 (dq, *J* = 15.2, 6.3 Hz, 1H), 5.48 (s, 1H, OH, $D_2O$ exchangeable), 4.88 (d, *J* = 8.5 Hz, 1H), 4.56 (dd, *J* = 8.5, 8.5 Hz, 1H), 1.59 (dd, *J* = 6.3, 1.7 Hz, 3H), *Z*-form 9.11 (s, 1H, OH, $D_2O$ exchangeable), 7.83-7.71 (m, 2H), 7.83-7.71 (m, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.52 (d, *J* = 8.4 Hz, 2H), 5.96-5.89 (m, 1H), 5.62

(dq, $J$ = 10.9, 7.0 Hz, 1H), 5.47 (s, 1H, OH, $D_2O$ exchangeable), 4.94-4.85 (m, 1H), 4.94-4.85 (m, 1H), 1.55 (dd, $J$ = 7.0, 1.2 Hz, 3H); $^{13}$C NMR: (151 MHz, DMSO-$d_6$) 167.5 (s), 167.4 (s), 156.9 (s), 156.9 (s), 135.0 (d), 135.0 (d), 133.0 (s), 133.0 (s), 131.1 (s), 131.1 (s), 129.2 (d), 129.0 (d), 128.0 (d), 127.9 (d), 127.9 (d), 127.6 (d), 123.4 (d), 123.4 (d), 115.0 (d), 115.0 (d), 72.7 (d), 72.1 (d), 58.6 (d), 53.1 (d), 18.1 (q), 13.6 (q); MS: (EI, 70 eV) $m/z$ 323 (0.58, $M^+$), 201 (100), 186 (54), 160 (23), 123 (40); HRMS: (EI, 70 eV) Calculated: $C_{19}H_{17}NO_4$ 323.1158 ($M^+$), Found: $C_{19}H_{17}NO_4$ 323.1156.

**(4*R**, 5*S**)-4-(*N*-Phthaloylamino)-2-undecene-5-ol (4f)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and heptanal (1.14 g, 10.0 mmol) in dry THF (4 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 85/15) to give the pure product as a viscous liquid (0.130 g, 21%, $E/Z$ = 50:50). IR: (neat) 3467 (OH), 1712 (C=O) cm$^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) *E*-form 7.91-7.79 (m, 2H), 7.79-7.67 (m, 2H), 5.95 (ddq, $J$ = 15.4, 8.5, 1.5 Hz, 1H), 5.77 (dq, $J$ = 15.4, 6.5 Hz, 1H), 4.64 (dq, $J$ = 8.5, 4.2 Hz, 1H), 4.06-3.98 (m, 1H), 3.59 (s, 1H, OH, $D_2O$ exchangeable), 1.72 (dd, $J$ = 6.5, 1.5 Hz, 3H), 1.58-1.42 (m, 2H), 1.42-1.17 (m, 16H), 0.86 (t, $J$ = 6.8 Hz, 3H), *Z*-form 7.91-7.79 (m, 2H), 7.79-7.67 (m, 2H), 6.01 (ddq, $J$ = 10.7, 9.9, 1.5 Hz, 1H), 5.83 (dq, $J$ = 10.7, 7.0 Hz, 1H), 5.06 (dd, $J$ = 9.9, 4.3 Hz, 1H), 4.13-4.06 (m, 1H), 3.41 (s, 1H, OH, $D_2O$ exchangeable), 1.77 (dd, $J$ = 7.0, 1.5 Hz, 3H), 1.58-1.42 (m, 2H), 1.42-1.167 (m, 16H), 0.86 (t, $J$ = 6.8 Hz, 3H) $^{13}$C NMR: (100 MHz, $CDCl_3$) 168.7 (s), 168.7 (s), 134.2 (d), 134.2 (s), 132.1 (d), 131.7 (s), 131.7 (s), 130.8 (d), 123.9 (d), 123.4 (d), 123.4 (d), 123.4 (d), 72.8 (d), 72.3 (d), 58.9 (d), 52.6 (d), 34.1 (t), 33.9 (t), 31.7 (t), 31.7 (t), 29.2 (t), 29.2 (t), 25.6 (t), 25.6 (t), 22.5 (t), 22.5 (t), 17.9 (q), 14.0 (q), 14.0 (q), 13.5 (q); MS: (CI, 200 eV) $m/z$ 316 (100, M + H), 298 (20); HRMS: (CI, 200 eV) Calculated: $C_{19}H_{26}NO_3$ 316.1913 (M + H), Found: $C_{19}H_{26}NO_3$ 316.1909.

**(1*R**, 2*S**)-1-Cyclohexyl-2-(*N*-phthaloylamino)-3-penten-1-ol (4g)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and cyclohexanecarboxaldehyde (1.12 g, 10.0 mmol) in dry THF (4 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%;

20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 85:15) to give the pure product as a viscous liquid (0.225 g, 36%, *E*/*Z* = 45:55). IR: (neat) 3456 (OH), 1709 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) *E*–form 7.89-7.79 (m, 2H), 7.79-7.67 (m, 2H), 6.07-5.94 (m, 1H), 5.81-5.68 (m, 1H), 5.27 (dd, *J* = 9.7, 5.3 Hz, 1H), 3.88 (t, *J* = 5.3 Hz, 1H), 3.19 (s, 1H, OH, $D_2O$ exchangeable), 1.72 (d, *J* = 7.3 Hz, 3H), 2.01-1.02 (m, 10H); *Z*–form 7.89-7.79 (m, 2H), 7.79-7.67 (m, 2H), 6.07-5.94 (m, 1H), 5.81-5.68 (m, 1H), 4.87 (dd, *J* = 8.2, 5.5 Hz, 1H, 2-H), 3.81 (t, *J* =5.5 Hz, 1H, 1-H), 3.32 (s, 1H, OH', $D_2O$ exchangeable), 1.68 (d, *J* = 7.3 Hz, 3H), 2.01-1.02 (m, 10H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 168.6 (s), 168.5 (s), 134.1 (d), 134.1 (d), 131.7 (s), 131.7 (s), 131.6 (d), 130.5 (d), 124.6 (d) , 124.0 (d), 123.4 (d), 123.3 (d), 76.5 (d), 76.0 (d), 55.9 (d), 49.7 (d), 40.1 (d), 40.1 (d), 30.0 (t), 29.9 (t), 27.1 (t), 27.0 (t), 26.3 (t), 26.3 (t), 26.2 (t), 26.2 (t), 25.9 (t), 25.9 (t), 17.9 (q), 13.51 (q) MS: (CI, 200 eV) *m*/*z* 314 (100, $M^+ + H$), 296 (55, M - OH), 201 (20, $CH_3CH$=CHPhthNCH); HRMS: (CI, 200 eV) Calculated: $C_{19}H_{24}NO_3$ 314.1756 ($M^+ + H$) Found: $C_{19}H_{24}NO_3$ 314.1765.

**(3*R**, 4*S**)-1-Phenyl-4-(*N*-phthaloylamino)-hepta-1,5-dien-3-ol (4h)**

To a stirred solution of $GeCl_2$-dioxane (0.928 g, 4.01 mmol) and tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.990 g, 4.02 mmol) in dry THF (8 mL) was slowly added cinnamaldehyde (0.266 g 2.0 mmol, 1M of THF solution) with a syringe pump for 7 h at room temperature. The mixture was further stirred for 4 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 75/25), and recrystallization to give the pure product as a white solid (0.181 g, 27%, *E*/*Z* = 62:38). mp: 83.9-85.6 ºC; IR: (KBr) 3537 (OH), 1701 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) *E*-form 7.91-7.76 (m, 2H), 7.76-7.63 (m, 2H), 7.35-7.14 (m, 5H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 15.9, 6.1 Hz, 1H), 6.03 (dd, *J* = 15.9, 7.5 Hz, 1H), 5.83 (dq, *J* = 15.9, 6.3 Hz, 1H), 4.91-4.73 (m, 1H), 4.91-4.73 (m, 1H), 3.21 (s, 1H, OH, $D_2O$ exchangeable), 1.74 (d, *J* = 6.3 Hz, 3H), *Z*-form 7.91-7.76 (m, 2H), 7.76-7.63 (m, 2H), 7.35-7.14 (m, 5H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.19 (dd, *J* = 15.9, 7.0 Hz, 1H), 6.09 (ddq, *J* = 11.1, 9.6, 1.7 Hz, 1H), 5.87 (dq, *J* = 11.1, 7.0 Hz, 1H), 5.20 (dd, *J* = 9.6, 6.5 Hz, 1H), 4.86 (dd, *J* = 7.0, 6.5 Hz, 1H), 3.06 (s, 1H, OH, $D_2O$ exchangeable), 1.77 (dd, *J* = 7.0, 1.7 Hz, 3H), $^{13}C$ NMR:

(100 MHz, $CDCl_3$) 168.3 (s), 168.3 (s), 136.3 (s), 136.3 (s), 134.1 (d), 134.0 (d),133.0 (d) 132.9 (d), 132.4 (d), 131.5 (d), 131.5 (d), 131.2 (d), 128.4 (d), 128.4 (d), 128.1 (d), 128.0 (d), 127.7 (d), 126.5 (d), 126.5 (d), 124.1 (d), 123.7 (d), 123.3 (d), 123.3 (d), 73.7 (d), 73.0 (d), 58.6 (d), 52.4 (d), 17.9 (q), 13.5 (q); MS: (EI, 70 eV) *m*/*z* 333 (0.43, $M^+$), 201 (69), 200 (100) 186 (30), 133 (34); HRMS: (EI, 70 eV) Calculated: $C_{21}H_{19}NO_3$ 333.1365 ($M^+$), Found: $C_{21}H_{19}NO_3$ 333.1364.

**(1*R**, 2*S**)-1-Furyl-2-(*N*-phthaloylamino)-3-penten-1-ol (4i)**

To a stirred solution of $GeCl_2$-dioxane (0.46 g, 2.0 mmol) and 2-furaldehyde (0.68 g, 10.0 mmol) in dry THF (4 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-butenyl}stannane (1.04 g, 2.0 mmol). The mixture was stirred for 8 h at room temperature and then quenched by aqueous HCl (1 M; 10 mL). The reaction mixture was extracted with diethyl ether (3 x 20 mL). $NH_4$Faq (30%; 20 mL) was added to the collected organic layers. The formed white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 20 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography (hexane/ethyl acetate = 75:25, 0.361 g, 61%, *E*/*Z* = 52:48) and recrystallization from hexane/ethyl acetate (9/1) to give the pure product as a white solid (0.230 g, 39%). mp: 86.2-87.9 ºC; IR: (KBr) 3521 (OH), 1705 (C=O) $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) *E*-form 7.83-7.75 (m, 2H), 7.75-7.65 (m, 2H), 7.35-7.30 (m, 1H), 6.30 (d, *J* = 2.9 Hz, 1H), 6.23 (dd, *J* = 2.9, 1.7 Hz, 1H), 6.02 (ddq, *J* = 15.7, 7.5, 1.7 Hz, 1H), 5.83 (dq, *J* = 15.7, 7.2 Hz, 1H), 5.33 (dd, *J* = 7.5, 3.4 Hz, 1H), 5.08 (dd, *J* = 7.5, 7.5 Hz, 1H), 3.22 (d, *J* = 3.4 Hz, 1H, OH, $D_2O$ exchangeable), 1.71 (dd, *J* = 7.2, 1.7 Hz), *Z*-form 7.83-7.75 (m, 2H), 7.75-7.65 (m, 2H), 7.35-7.30 (m, 1H), 6.31 (d, *J* = 3.1 Hz, 1H), 6.24 (dd, *J* = 3.1, 1.9 Hz, 1H), 6.05 (ddq, *J* = 11.0, 9.4, 1.0 Hz, 1H), 5.86 (dq, *J* = 11.0, 6.8 Hz, 1H), 5.48 (dd, *J* = 9.4, 7.2 Hz, 1H), 5.37 (dd, *J* = 7.2, 3.2 Hz, 1H), 3.21 (d, *J* = 3.2 Hz, 1H, OH, $D_2O$ exchangeable), 1.73 (dd, *J* = 6.8, 1.0 Hz, 3H), $^{13}$C NMR: (100 MHz, $CDCl_3$) *E*-form 167.9 (s), 152.9 (s), 142.3 (d), 134.0 (d), 132.4 (d), 121.5 (s), 124.4 (d), 123.3 (d), 110.2 (d), 107.6 (d), 67.7 (d), 57.3 (d), 17.8 (q), *Z*-form 167.9 (s), 152.9 (s), 142.3 (d), 134.0 (d), 131.5 (d), 131.5 (s), 123.8 (d), 123.3 (d), 110.1 (d), 107.6 (d), 68.3 (d), 51.4 (d), 13.3 (q); MS: (EI, 70 eV) *m*/*z* 297 (0.29, $M^+$), 201 (100), 200 (41), 186 (42), 160 (21); HRMS: (EI, 70 eV) Calculated: $C_{17}H_{15}NO_4$ 297.1001 ($M^+$), Found: $C_{17}H_{15}NO_4$ 297.1003; Analysis: $C_{17}H_{15}NO_4$ (297.31) Calcd: C, 68.68; H, 5.09; N, 4.71, Found: C, 68.46; H, 4.99; N, 4.70.

**(1*R**, 2*S**)-1-Phenyl-2-(*N*-phthaloylamino)-3-hepnten-1-ol (4j)**

To a solution of $GeCl_2$-dioxane (0.125 g, 0.54 mmol) and benzaldehyde (0.267 g, 2.5 mmol) in dry THF (2 mL) was added tributyl{1-(*N*-phthaloylamino)-(*E*)-2-hexenyl} stannane (0.261 g, 0.5 mmol).

The mixture was stirred for 8 h at room temperature, and then quenched by aqueous HCl (1 M; 5 mL). The reaction mixture was extracted with diethyl ether (3 x 10 mL). $NH_4F$ aq (30%; 10 mL) was added to the collected organic layers. The generated white precipitate was filtered off and the filtrate was extracted with diethyl ether (3 x 10 mL). The collected organic layers were dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash column chromatography to give the pure product as a viscous liquid (hexane/ethyl acetate = 80:20, 0.035 g, 21%, *E*/*Z* = 58:42).

IR (neat): 3412 $cm^{-1}$ (OH), 1741 $cm^{-1}$ (C=O); $^1H$ NMR: *E*-form; 7.78-7.74 (m, 2H), 7.70-7.67 (m, 2H), 7.38-7.36 (m, 2H), 7.27-7.18 (m, 3H), 6.04 (ddt, *J* = 15.5, 8.5, 1.2 Hz, 1H), 5.73 (dt, *J* = 15.5, 6.8 Hz, 1H) , 5.24 (dd, *J* = 6.5, 1.7 Hz, 1H), 4.79 (t, *J* = 8.5 Hz, 1H), 3.29 (d, *J* = 1.7 Hz, 1H), 2.03 (m, 2H), 1.37 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H); *Z*-form; 7.78-7.75 (m, 2H), 7.70-7.66 (m, 2H), 7.41-7.36 (m, 2H), 7.29-7.19 (m, 3H), 6.12-6.06 (m, 1H), 5.77-5.71 (m, 1H), 5.30-5.24 (m, 2H), 3.35 (s, 1H), 2.06-1.91 (m, 2H), 1.28-1.19 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); $^{13}C$ NMR: *E*-form; 168.1 (s), 140.3 (s), 137.9 (d), 134.1 (d), 131.5 (s), 128.2 (d), 128.0 (d), 126.6 (d), 123.3 (d), 122.8 (d), 74.1 (d), 60.2 (d), 34.4 (t), 22.0 (t), 13.6 (q), *Z*-form; 168.1 (s), 140.2 (s), 137.3 (d), 134.1 (d), 131.5 (s), 128.3 (d), 128.0 (d), 126.5 (d), 123.3 (d), 122.3 (d), 74.8 (d), 54.4 (d), 29.6 (t), 22.3 (t), 13.6 (q); HRMS: (EI, 70 eV) Calculated ($C_{21}H_{21}NO_3$): 335.1521 ($M^+$) Found: 335.1516.

**(1*R**, 2*S**)-2-Methyl-1-phenyl-4-aminobutan-1-ol (6)**

To a stirred solution of 5 wt% Pd/C (0.022 g, 1.0 mol%) in EtOH (16 mL) was added (1*R**,2*R**)-2-Methyl-1-phenyl-4-(*N*-phthaloylamino)-(*Z*)-3-buten-1-ol (0.312 g, 1.02 mmol), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 24 h. The catalyst was removed by filtration, and the filtrate was evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate = 78:22) to give (1*R**, 2*S**)-2-methyl-1-phenyl-4-(*N*-phthaloylamino)butan-1-ol as a viscous liquid (0.281 g, 90%).

IR: (neat) 3471 (OH), 1709 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.87-7.81 (m, 2H), 7.75-7.69 (m, 2H), 7.35-7.22 (m, 5H), 4.48 (dd, *J* = 7.0, 3.8 Hz, 1H), 3.86-3.73 (m, 2H), 2.08 (dddd, *J* = 13.3, 8.2, 7.5, 4.3 Hz, 1H), 2.04 (d, *J* = 3.8 Hz, 1H, OH, $D_2O$ exchangeable), 1.98-1.85 (m, 1H), 1.58-1.45 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 168.4 (s), 143.0 (s), 133.8 (d), 132.1 (s), 128.2 (d), 127.5 (d), 126.6 (d), 123.1 (d), 78.7 (d), 37.9 (d), 36.3 (t), 31.7 (t), 15.9 (q); MS: (EI, 70 eV) *m*/*z* 309 (0.37, $M^+$), 203 (100), 202 (22), 174 (39), 160 (71); HRMS: (EI, 70 eV) Calculated: $C_{19}H_{19}NO_3$ 309.1365 ($M^+$), Found: $C_{19}H_{19}NO_3$ 309.1366; Analysis: $C_{19}H_{19}NO_3$ (309.36) Calcd: C, 73.77; H, 6.19; N, 4.53, Found: C, 73.49; H, 6.17; N, 4.51.

To a stirred solution of (1*R**, 2*S**)-2-methyl-1-phenyl-4-(*N*-phthaloylamino)butan-1-ol (0.800 g, 2.59 mmol) in EtOH (16 mL) was added $N_2H_4/H_2O$ (1.30 g, 25.9 mmol) and the solution was heated to reflux for 6 h. After being cooled to room temperature and the formed white precipitate was filtered off with EtOAc. The filtrate was evaporated and purified by column chromatography (ethyl acetate/methanol/triethylamine = 18:77:5) to give the pure product as a white solid (0.397 g, 85%). mp: 62.4-62.9 ºC; IR: (KBr) 3344, 3000 (br) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.40-7.28 (m, 2H), 7.40-7.28 (m, 2H), 7.28-7.17 (m, 1H), 4.36 (d, *J* = 7.0 Hz, 1H), 3.30 (brs, 3H, $NH_2$ and OH, $D_2O$ exchangeable), 3.00-2.82 (m, 1H), 2.82-2.58 (m, 1H), 2.09-1.91 (m, 1H), 1.65-1.43 (m, 2H), 0.81 (d, *J* = 7.0 Hz, 3H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 144.7 (s), 127.9 (d), 126.8 (d), 126.6 (d), 78.2 (d), 39.7 (d), 38.8 (t), 35.8 (t), 17.4 (q); HRMS: (CI, 70 eV) Calculated: $C_{11}H_{18}NO$ 180.1388 ($M^+$), Found: $C_{11}H_{17}NO$ 180.1389.

**(1*R**, 2*S**)-1-Phenyl-2-(*N*-phthaloylamino)-3-pentan-1-ol (5a)**

To a stirred solution of 5 wt% Pd/C (0.024 g, 1.0 mol%) in EtOH (16 mL) was added *E*/*Z*-mixture of (1*R**, 2*S**)-1-phenyl-2-(*N*-phthaloylamino)-3-penten-1-ol (0.346 g, 1.13 mmol), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 24 h. The catalyst was removed by filtration, and the filtrate was evaporated. The residue was purified by flash column chromatography (hexane/ethyl acetate = 82:18) to give (1*R**, 2*S**)-1-Phenyl-2-(*N*-phthaloylamino)-3-pentan-1-ol (**5**) as a viscous liquid (0.313 g, 90%). IR: (neat) 3521 (OH), 1705 (C=O) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.82-7.74 (m, 2H), 7.74-7.66 (m, 2H), 7.40 (d, *J* = 7.0 Hz, 2H), 7.28 (dd, *J* = 7.3, 7.0 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 5.19 (d, *J* = 5.6 Hz, 1H), 4.49 (ddd, *J* = 11.8, 5.6, 3.4 Hz, 1H), 3.50 (s, 1H, OH, $D_2O$ exchangeable), 2.22 (dddd, *J* = 14.0, 11.8, 9.2, 5.5 Hz, 1H), 1.85 (dddd, *J* = 14.0, 9.1, 7.0, 3.4 Hz, 1H), 1.27-1.10 (m, 2H), 0.85 (t, *J* = 7.5 Hz, 3H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 168.7 (s), 141.3 (s), 133.9 (d), 131.2 (s), 128.1 (d), 127.7 (d), 126.2 (d), 123.1 (d), 75.0 (d), 57.7 (d), 28.7 (t), 19.5 (t), 13.6 (q); MS: (EI, 70 eV) *m*/*z* 309 (0.36, $M^+$), 203 (100), 202 (21), 174 (37), 160 (69); HRMS: (EI, 70 eV) Calculated: $C_{19}H_{19}NO_3$ 309.1365 ($M^+$), Found: $C_{19}H_{19}NO_3$ 309.1364; Analysis: $C_{19}H_{19}NO_3$ (309.36) Calcd: C, 73.77; H, 6.19; N, 4.53, Found: C, 73.65; H, 6.11; N, 4.49.

**(1*R**, 2*S**)-1-Phenyl-2-aminopentan-1-ol (7)**

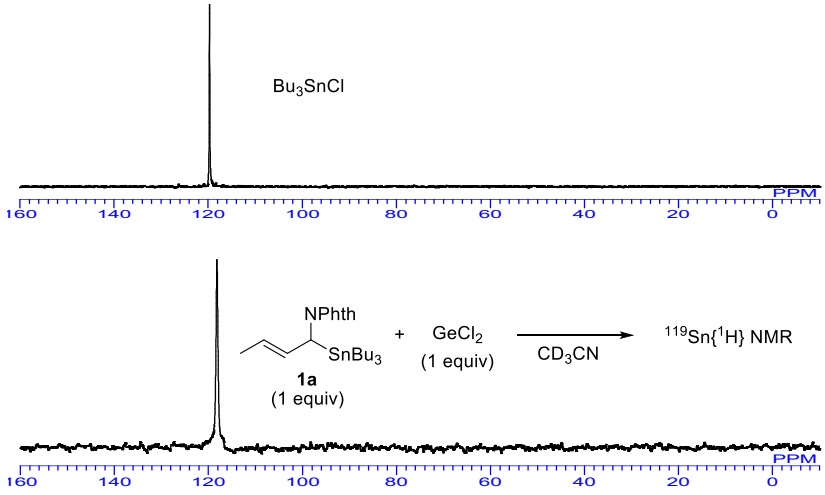
To a stirred solution of (1*R**, 2*S**)-1-phenyl-2-(*N*-phthaloylamino)-3-pentan-1-ol (**5**) (0.670 g, 2.17 mmol) in EtOH (16 mL) was added $N_2H_4/H_2O$ (1.09 g, 21.7 mmol) and the solution was heated to reflux for 6 h. After being cooled to room temperature and the formed white precipitate was filtered off with EtOAc. The filtrate was evaporated and purified by column chromatography (ethyl

acetate/methanol/triethylamine = 77:18:5) to give the pure product as a viscous liquid (0.343 g, 88%). IR: (neat) 3433-3028 (br) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.40-7.21 (m, 5H), 4.56 (d, $J$ = 5.1 Hz, 1H), 3.00 (ddd, $J$ = 9.4, 5.1, 3.3 Hz, 1H), 1.93 (brs, 3H, $NH_2$ and OH, $D_2O$ exchangeable), 1.52-1.34 (m, 2H), 1.30-1.19 (m, 1H), 1.14-1.01 (m, 1H), 0.88 (dd, $J$ = 7.0, 7.0 Hz, 3H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 141.6 (s), 127.6 (d), 126.8 (d), 126.3 (d), 76.0 (d), 55.9 (d), 34.0 (t), 19.0 (t), 13.7 (q); HRMS: (EI, 70 eV) Calculated: $C_{11}H_{17}NO$ 179.1310 ($M^+$), Found: $C_{11}H_{17}NO$ 179.1308.

**Observation of $Bu_3SnCl$ in Transmetalation between Allylic Stannane 1a and $GeCl_2$**

Allylic stannane **1a** (0.5 mmol) was added to $GeCl_2$ (0.5 mmol) in $CD_3CN$ (2 mL), and the reaction mixture was stirred for 10 min at room temperature. Then, the solution was monitored by $^{119}Sn$ NMR.

$^{119}Sn\{^1H\}$ NMR (150 MHz, $CD_3CN$, vs $Me_4Sn/CDCl_3$ as an external standard)




**X-ray Structure Data**

See CIF files

*anti*/*E*-**4a: 1567194 (CCDC)**

**1-5. Reference**


[1] a) E. J. Corey, J. O. Link, *J. Org. Chem*. **1991**, *56*, 442. b) T. Fujita, M. Yoneta, R. Hirose, S. Sasaki, K. Inoue, M. Kiuchi, S. Hirose, K. Adachi, M. Arita, K. Chiba, *Bioorg. Med. Chem. Lett*. **1995**, *5*, 847. c) T. Laïb, J. Chastanet, J. Zhu, *J. Org. Chem*. **1998**, *63*, 1709. (d) C. W. Johannes, M. S. Visser, G. S. Weatherhead, A. H. Hoveyda, *J. Am. Chem. Soc.* **1998**, 120, 8340. e) E. J. Corey, F. Zhang, *Angew. Chem. Int. Ed.* **1999**, *38*, 1931. f) M. T. Barros, M. A. J. Charmier, C. D. Maycock, T. Michaud, *Tetrahedron* **2005**, *61*, 7960. g) S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561. h) B. M. Teresa, J. C. M. Adilia, C. D. Maycockd, T. Michaud, T. *Tetrahedron* **2005**, *61*, 7960

[2] a) G. Li, H. T. Chang, K. B. Sharpless, *Angew. Chem. Int. Ed.* **1996**, *35*, 451. b) A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymmetry* **1998**, *9*, 1. c) D. Rechavi, M. Lemaire, *Chem. Rev*. **2002**, *102*, 3467. d) P. O'Brien, *Angew. Chem. Int. Ed.* **1999**, *38*, 326. (e) R. S. C. Kumar, G. V. Reddy, G. Shankaraiah, K. S. Babu, J. M. Rao, *Tetrahetron Lett*. **2010**, *51*, 1114.

[3] a) E. J. Corey, F. J. Hannon, *Tetrahedron Lett*. **1987**, *28*, 5237. b) D. J. Ager, I. Prakash, S. R. Schaad, *Chem. Rev.* **1996**, *96*, 835. c) C. Tanyeli, S. Odabas, M. Erdem, E. Çakır, E. Keskin, *Tetrahedron: Asymmetry* **2007**, *18*, 2349.

[4] See, selected reviews; a) *Main Group Metals in Organic Synthesis*, Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004. b) *Comprehensive Organometallic Chemistry*, 3rd ed.; Crabtree, R. H., Mingos, D. M. P., Eds.; Elsevier: Amsterdam, 2007.

[5] a) A. Schlapbach, R. W. Hoffmann, *Eur. J. Org. Chem.* **2001**, 323. b) F. Berrée, N. Gernigon, A. Hercouet, C. H. Lin, B. Carboni, *Eur. J. Org. Chem.* **2009**, 329.

[6] D. J. Pippel, G. A. Weisenburger, S. R. Wilson, P. Beak, *Angew. Chem. Int. Ed*. **1998**, *37*, 2522.

[7] R. J. P. Corriu, V. Huynh, J. J. E. Moreau, *J. Organometal. Chem.* **1983**, *259*, 283G.

[8] M. Yasuda, Y. Nagano, H. Yunoki, K. Tsuruwa, A. Baba, *Organometallics* **2014**, *33*, 3924.

[9] See, selected reviews for allylic stannanes in organic synthesis; a) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207. b) A. Baba, I. Shibata, M. Yasuda, in *Comprehensive Organometallic Chemistry*, 3rd ed.; Crabtree, R. H., Mingos, D. M. P., Eds.; Elsevier: Amsterdam, 2007; Vol. 9, pp 341–379.

[10] See, reports for reactions using heteroatom-substituted allylic stannanes; a) A. J. Pratt, E. J. Thomas, *J. Chem. Soc., Chem. Commun.* **1982**, 1115. b) M. Shibasaki, H. Suzuki, Y. Torisawa, S. Ikegami, *Chem. Lett.* **1983**, *12*, 1303. c) J. A. Marshall, K. W. Hinkle, *J. Org. Chem.* **1996**, *61*, 105. d) J. A. Marshall, J. A. Jablonowski, G. S. Welmaker, *J. Org. Chem.* **1996**, *61*, 2904. e) G. A. Weisenburger, P. Beak, *J. Am. Chem. Soc.* **1996**, *118*, 12218. f) C. Serino, N. Stehle,

Y. S. Park, S. Florio, P. Beak, *J. Org. Chem.* **1999**, *64*, 1160. g) W. H. Pearson, Y. Ren, *J. Org. Chem.* **1999**, *64*, 688. h) M. Yasuda, T. Azuma, K. Tsuruwa, S. A. Babu, A. Babu, *Tetrahedron Lett.* **2009**, *50*, 3209.

[11] W. H. Pearson, N. S. Barta, J. W. Kampf, *Tetrahedron Lett*. **1997**, *38*, 3369.

[12] The allylic stannane **1a** can be isolated by column chromatography and stored in air for months.

[13] P. G. M. Wuts, T. W. Greene, Protection for the amino group. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; John Wiley & Sons, Inc.: Hoboken, 2015; p 696.

[14] a) M. Yasuda, M. Tsuchida, A. Baba, *Chem. Commun.* **1998**, 563. b) M. Yasuda, Y. Matsukawa, K. Okamoto, T. Sako, N. Kitahara, A. Baba, *Chem. Commun.* **2000**, 2149. c) M. Yasuda, K. Okamoto, T. Sako, A. Baba, *Chem. Commun.* **2001**, 157. d) M. Yasuda, K. Hirata, M. Nishino, A. Yamamoto, A. Baba, *J. Am. Chem. Soc*. **2002**, *124*, 13442.

[15] M. Yasuda, T. Miyai, I. Shibata, A. Baba, R. Nomura, H. Matsuda, *Tetrahedron Lett*. **1995**, *36*, 9497.

[16] a) Y. Yamamoto, T. Komatsu, K. Maruyama, *J. Organomet. Chem.* **1985**, 285, 31. b) J. Fujiwara, M. Watanabe, T. Sato, *J. Chem. Soc., Chem. Commun.* **1994**, 349. c) M. Nakada, Y. Urano, S. Kobayashi, M. Ohno, *Tetrahedron Lett.* **1994**, *35*, 741.

[17] a) A. Hosomi, H. Iguchi, M. Endo, H. Sakurai, H. *Chem. Lett.* **1979**, *8*, 977. b) Y. Yamamoto, H. Yatagai, Y. Naruta, K. Maruyama, *J. Am. Chem. Soc.* **1980**, *102*, 7107. c) S. E. Denmark, E. J. Weber, T. M. Wilson, T. M. Willson, *Tetrahedron* **1989**, *45*, 1053. d) A. Takuwa, Y. Nishigaichi, K. Yamashita, H. Iwamoto, *Chem. Lett.* **1990**, *19*, 1761. e) T. N. Mitchell, U. Schneider, K. Heesche-Wagner, *J. Organomet. Chem.* **1991**, *411*, 107. f) B. Ghosh, M. D. R. I. Amado-Sierra, D. Holmes, R. E. Maleczka, *Org. Lett.* **2014**, *16*, 2318. g) S. Raghavan, S. Rajendar, *Org. Biomol. Chem.* **2015**, *13*, 5044.

[18] a) J. Yamaguchi, Y. Tamada, T. Takeda, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 607. b) Y. Hashimoto, H. Kagoshima, K. Saigo, *Tetrahedron Lett.* **1994**, *35*, 4805.

[19] CCDC number of *anti-E*-**4a**: 1567194

[20] See Supporting Information about the observation of $Bu_3SnCl$ by $^{119}Sn$ NMR.

[21] We synthesized, isolated, and characterized some allylic indium compounds. a) M. Yasuda, M. Haga, A. Baba, *Organometallics* **2009**, *28*, 1998. b) M. Yasuda, M. Haga, A. Baba, *Eur. J. Org. Chem.* **2009**, 5513. (c) M. Yasuda, M. Haga, Y. Nagaoka, A. Baba, *Eur. J. Org. Chem.* **2010**, *28*, 5359.

[22] When transmetalation between hydroxyallylic stannane and $SnCl_2$, *Z*-form is generated because of coordination of oxygen to metal center. See ref. 10h.

[23] H. E. Zimmerman, M. D. Traxler, *J. Am. Chem. Soc.* **1957**, *79*, 1920.

[24] In general, the reaction of allylic stannanes with electrophiles, which includes the transmetalation between allylic stannanes and metal halides, proceeds via $S_E2'$ like other allylic metals. In fact, we previously reported that an α-aminoallylic stannane transmetalates with $InBr_3$ or $SnCl_2$ via $S_E2'$. See ref. 8, 9, and 10.

[25] a) M. Yasuda, S. Tanaka, A. Baba, *Org. Lett.* **2005**, *7*, 1845. b) S. Tanaka, N. Tagashira, K. Chiba, M. Yasuda, A. Baba, *J. Org. Chem.* **2008**, *73*, 6312.

[26] E. A. Hallinan, T. J. Hagen, R. K. Husa, S. Tsymbalov, S. N. Rao, J. vanHoeck, M. F. Rafferty, A. Stapelfeld, M. A. Savage, M. Reichman, *J. Med. Chem*. **1993**, *36*, 3293.

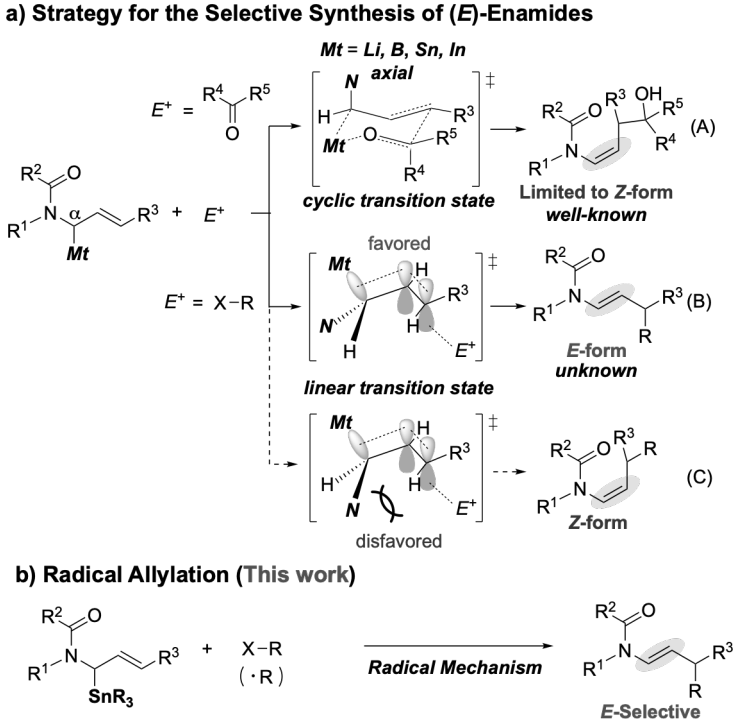
## Chapter 2. Geometrically Selective Synthesis of (*E*)-Enamides via Radical Allylation of Alkyl Halides with α-Aminoallylic Stannanes

### 2-1. Introduction

Enamides are valuable synthetic intermediates in the preparation of heterocycles[1] and amino acids,[2] and serve as useful substrates in reactions such as polymerization,[3] cycloaddition,[4] and addition.[5] In particular, the (*E*)-enamide framework appears in a broad range of natural products and biologically active compounds.[6] There are two conventional approaches to the synthesis of enamides: an addition reaction of amides to alkynes[7] and an addition reaction of amides to carbonyl compounds followed either by the dehydration or acylation of imines.[8] These methods lack regioselectivity and/or *E*/*Z* stereoselectivity, and often require harsh reaction conditions, but a transition-metal catalyzed synthesis of enamides was recently developed with examples that include the isomerization of *N*-allylamides,[9] the addition of amides to alkynes,[10] and a cross-coupling reaction of amides with vinyl compounds.[11] In these cases, (*E*)-enamides are selectively obtained under mild conditions, but problems with functional group tolerance have persisted.

An allylation reaction with electrophiles at the γ-position when using α-(carbonylamino)allylic metals has shown promise as a method for the synthesis of enamides (Scheme 1a). When using carbonyl compounds as electrophiles, allylation with α-(carbonylamino)allylic metals (Mt = Li, B, SnX, $InX_2$) leads only to (*Z*)-enamides[12-14] via a six-membered cyclic transition state with an amino substituent in the axial position due to an anomeric effect[15] (Scheme 1a-A). On the other hand, the reaction with alkyl halides via linear transition state would achieve (*E*)-selectivity (Scheme 1a-B) because steric hindrance of amino group and hydrogen atom prevent affording *Z*-form in the transition states (Scheme 1a-C), in which a C-Mt bond and a $\pi$ orbital of the C=C bond are conjugated.[16] The reported allylation using forms of allyl lithium, however, gives (*Z*)-enamides due to an *anti-syn* form of the π-allyl lithium that is fixed by the intramolecular coordination of a Boc group to a high-Lewis acidic lithium center.[12] Therefore, we decided that the use of low-Lewis acidic allylic stannanes could enable the formation of (*E*)-enamides via a linear transition state (Scheme 1a-B). Because low-nucleophilic allylic stannanes are generally inert to organic halides, we adopted an activation of organic halides via a radical mechanism. Herein, we report the stereoselective synthesis of (*E*)-enamides via radical allylation with alkyl halides using α-(carbonylamino)allylic stannanes with $Et_3B$ serving as a radical initiator (Scheme 1b).

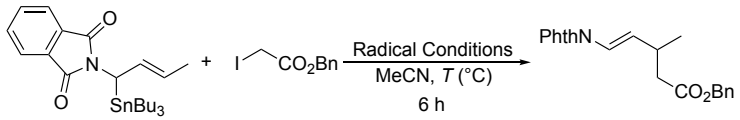
**Scheme 1.** Stereoselective Synthesis of Enamides by Use of α-(Carbonylamino)allylic Stannanes




## 2-2. Results and Discussion

The reaction conditions for an allylation of α-phthaloylallylstannane **1a** were investigated using α-iodoester **2a** (Table 1). No reaction was observed without the use of radical initiators (entry 1). In the presence of AIBN, *E*-isomer product **3aa** was selectively obtained, although the yield was low (entry 2). Reactions using either benzoyl peroxide or lauroyl peroxide gave no target product (entries 3 and 4), and UV irradiation was ineffective (entry 5). To our delight, the $Et_3B$/air system[17] gave the *E*-isomer product **3aa** in a 67% yield with high stereoselectivity (entry 6). When the reaction temperature was set at -20 °C, **3aa** was formed in a 93% yield (entry 7). The reaction under a nitrogen atmosphere (air-free conditions) hardly proceeded, which indicated a radical-based mechanism (entry 8). A catalytic amount of $Et_3B$ (0.1 equiv) afforded a lower yield of **3aa** (57%) (entry 9). Therefore, this reaction system involves a radical chain mechanism, although it was necessary to use a stoichiometric amount of $Et_3B$ to complete the reaction.

**Table 1.** Optimization of the Reaction Conditions[a]



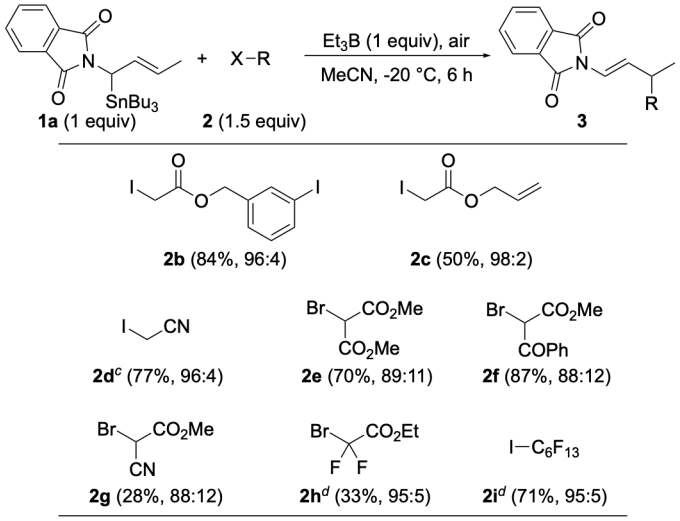

**1a** **2a** **3aa**

| Entry | Radical Conditions | *T* (°C) | Yield (%) | *E*/*Z* |
|---|---|---|---|---|
| 1 | no radical initiator | 80 | 0 | - |
| 2 | AIBN (0.2 equiv) | 80 | 7 | - |
| 3 | lauroyl peroxide (1 equiv) | 80 | 0 | - |
| 4 | benzoyl peroxide (1 equiv) | 80 | 0 | - |
| 5 | UV irradiation | rt | 9 | - |
| 6 | $Et_3B$ (1 equiv), air | rt | 67 | 97:3 |
| 7[b] | $Et_3B$ (1 equiv), air | -20 | 93(83) | 96:4 |
| 8[c] | $Et_3B$ (1 equiv) | rt | 2 | - |
| 9 | $Et_3B$ (0.1 equiv), air | -20 | 57 | 96:4 |

[a]**1a** (0.50 mmol), **2a** (0.75 mmol), and MeCN (1 mL). Air (3 mL) was introduced. Yields and *E*/*Z* ratios were determined by $^1$H NMR analysis. [b]**1a** (1.0 mmol), **2a** (1.5 mmol). An isolated yield in parentheses are shown. [c]In a nitrogen-filled glove box.

With the optimized reaction conditions in hand, the scope of alkyl halides was evaluated (Scheme 2). Various types of electro-deficient alkyl halides were applied to the present radical allylation. Iodoesters **2b** and **2c** stereoselectively provided *E*-isomer products in high yields. Aryl iodide and terminal olefin moieties, which do not tolerate the process of transition-metal catalyzed synthesis,[9],[11a-c] were nonetheless suitable in this reaction system. The allylation of iodo acetonitrile **2d** proceeded in a high yield. Bromo dimethylmalonate **2e**, bromo ketoester **2f**, and bromo cyanoacetate **2g** afforded the corresponding enamides in moderate to high yields with a high level of *E*-selectivity. Moreover, perfluoro alkyl halides such as ethyl bromodifluoroacetate **2h** and perfluorohexyl iodide **2i** were feasible substrates.

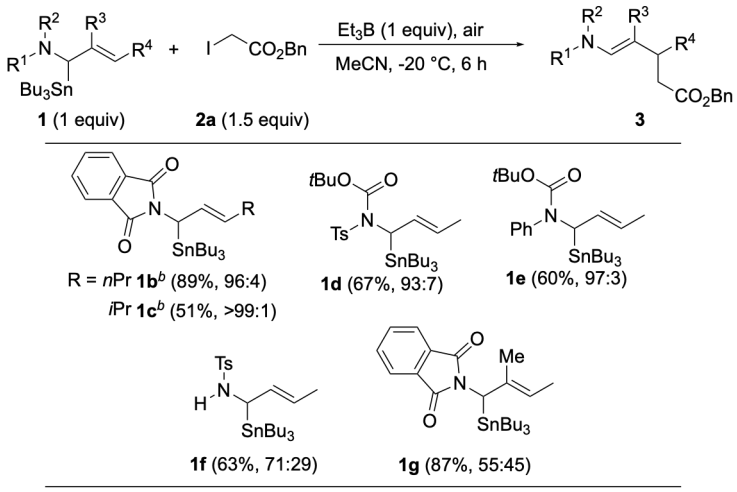
**Scheme 2.** Substrate Scope of Alkyl Halides[a]




[a]**1a** (0.50 mmol), **2** (0.75 mmol), 1 M $Et_3B$ in hexane (0.5 mL), and MeCN (1 mL) at -20 °C for 6 h. Air (3 mL) was added. An isolated yield and an *E*/*Z* ratio in parentheses are shown. *E*/*Z* ratios were determined by $^1H$ NMR analysis. [b]The reaction was conducted in $CH_2Cl_2$ at 0 °C. [c]**1a** (0.50 mmol), **2d** (1.0 mmol). [d]**1a** (0.50 mmol), **2** (1.5 mmol).

The scope of the aminoallylic stannanes is shown in Scheme 3. Aminoallylic stannanes with *n*-Pr and *i*-Pr groups (**1b** and **1c**) at the α-position stereoselectively afforded (*E*)-enamides in 72 and 27% yields, respectively. Allylic stannanes bearing two substituents on the nitrogen atom (**1d** and **1e**) gave excellent *E*-selectivity. On the other hand, monosubstituted aminoallylic stannane (**1f**) led to a product with lower *E*-selectivity. Unfortunately, reactions with aminoallylic stannane bearing a Me group at the β-position (**1g**) resulted in low stereoselectivity.

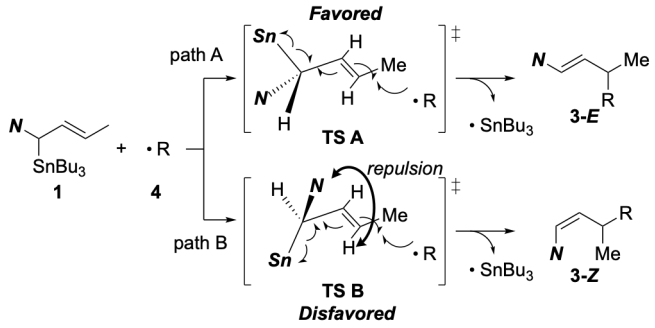
**Scheme 3.** Substrate Scope of α-Aminoallylic Stannanes[a]



[a]**1** (0.50 mmol), **2a** (0.75 mmol), 1 M $Et_3B$ in hexane (0.5 mL), and MeCN (1 mL) at -20 °C for 6 h. Air (3 mL) was added. An isolated yield and an *E*/*Z* ratio in parentheses are shown. *E*/*Z* ratios were determined by $^1H$ NMR analysis. [b]**1** (0.50 mmol), **2a** (1.5 mmol).

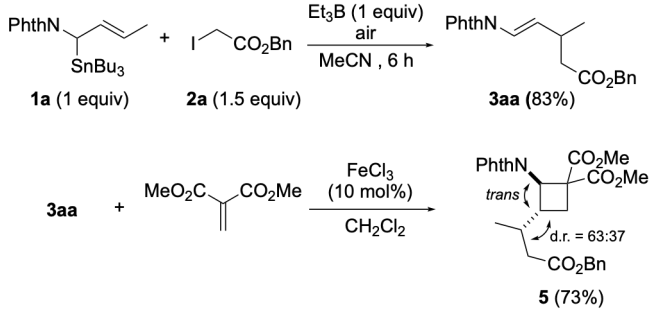
A plausible mechanism is shown in Scheme 4. Alkyl radical **4** is generated from alkyl halide **2** by $Et_3B$ and $O_2$. Radical **4** adds to the carbon-carbon double bond of allylic stannane **1** with elimination of a stannyl radical via two possible transition states, in which a C-Sn bond and a $\pi$ orbital of the C=C bond are conjugated (paths A and B). In path B to form the *Z* product (**3-*Z***), the large steric hindrance between the amino group and the hydrogen atom creates an unstable transition state, **TS B**. Therefore, preferential elimination occurs through **TS A** to give *E*-enamide (**3-*E***). It is noteworthy that the radical reaction system involving an acyclic transition state accomplished the (*E*)-selective synthesis of enamides.

**Scheme 4.** Proposed Reaction Mechanism




The utility of the present synthetic method of (*E*)-enamides was demonstrated (Scheme 5). Many natural products contain *trans*-Aminocyclobutanes.[18] (*E*)-Enamide **3aa**, which was synthesized by the allylation of alkyl halide **2a** with allylic stannane **1a**, underwent stereoselective [2+2] cyclization[19] with a methylene malonate to selectively give *trans*-aminocyclobutane **5**.

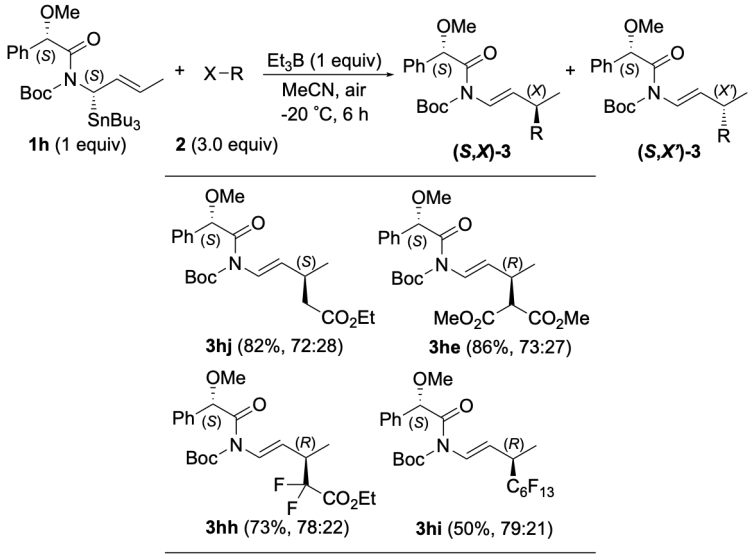
**Scheme 5.** Synthesis of *trans*-Aminocyclobutane Derivative by use of this method



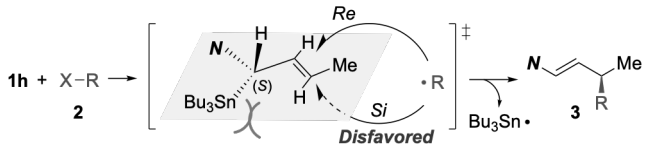
A radical allylation of homochiral aminoallylic stannane **1h**[20] was performed (Scheme 6A). The reaction of **1h** with iodo ethylacetate **2j** diastereoselectively gave enamide (*S*,*S*)-(*E*)-**3hj**,[21] which suggests that an alkyl radical preferentially approaches the *Re* face of the carbon-carbon double bond of **1h**. Moreover, the reaction using bulkier alkyl halides **2e**, **2h**, and **2i** resulted in a higher level of stereoselectivity. These results agree well with the proposed mechanism wherein steric repulsion between an approaching alkyl radical (R·) and a bulky $Bu_3Sn$ group prevents an approach from the *Si* face (Scheme 6B).

**Scheme 6.** Chiral Transfer by Use of optically active aminoallyl stannane[a]

**(A)**




**(B)**




[a]**1h** (0.50 mmol), **2** (1.5 mmol), 1 M $Et_3B$ in hexane (0.5 mL), and MeCN (1 mL) at -20 °C for 6 h. Air (3 mL) was added. An isolated yield and diastereo ratio in parentheses are shown.

## 2-3. Conclusion

The (*E*)-selective synthesis of enamides was achieved via the radical reaction of α-(carbonylamino)allyl stannanes with alkyl halides. This reaction showed good functional group tolerance. The radical reaction system via the acyclic transition state is a key factor to (*E*)-selectivity. The use of a homochiral aminoallylic stannane revealed the preference for an alkyl radical in the radical addition step.

## 2-4. Experimental Section

### General

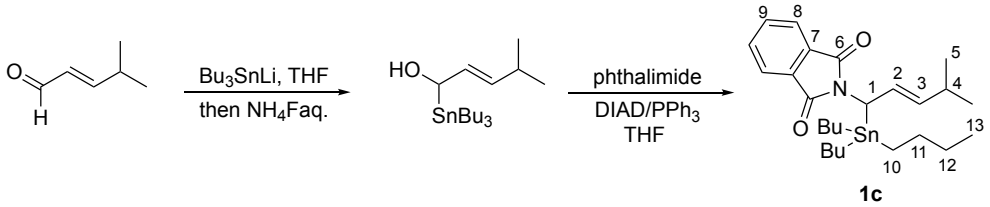
NMR spectra were recorded on JEOL JNM-400 (400 MHz for $^{1}$H NMR, 100 MHz for $^{13}$C NMR, and 150 MHz for $^{119}$Sn NMR) spectrometer. Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 for $^{1}$H NMR), residual $CHCl_3$ (δ = 77.0 for $^{13}$C NMR) as an internal reference, and $Me_4Sn$ (δ = 0 for $^{119}$Sn NMR) as an external reference. New compounds were characterized by $^{1}$H, $^{13}$C, $^{13}$C off-resonance techniques, COSY, HMQC, and HMBC. Infrared (IR) spectra were recorded on a JASCO FT/IR-6200 Fourier transform infrared spectrophotometer. Column chromatographies were performed with silica gel. Purification by recycle HPLC was performed on SHIMADZU recycle HPLC system (SPD- 20A, RID-10A, DGU-20A, LC-6AD, and FCV-20H2) and Japan Analytical Industry Co. (NEXT recycling preparative HPLC). Reactions were carried out in dry solvents under nitrogen atmosphere, unless otherwise stated. UV irradiation was carried out using a 300 W high-pressure mercury lamp through a pyrex filter. Reagents were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI), FUJIFILM Wako Pure Chemical Corporation, Ltd., and used without purification. X-ray diffraction analysis was carried out by Rigaku XtaLAB Synergy with Hypix-6000HE.

### Materials

Dehydrated solvents were purchased from FUJIFILM Wako Pure Chemical Corporation and used as obtained. Alkyl halides **2d**, **2e**, **2h**, and **2i** were purchased. Alkyl halides **2b**,[22] **2c**,[23] **2f**,[24] **2g**[25] and **2j**,[26] α-aminoallylic stannane **1a**[27] and **1b**,[27] and methylene malonate[28] were prepared by known methods and these compounds were reported. The preparation and characterization of new α-aminoallylic stannanes **1c**, **1d**, **1e**, **1f**, **1g**, and **1h** were described below. $Et_3B$ (1 M in Hexane) and lauroyl peroxide were purchased from Sigma-Aldrich and used as obtained. AIBN and benzoyl peroxide were purchased from FUJIFILM Wako Pure Chemical Corporation and used as obtained. All other reagents were commercially available.

**Synthesis of Substrates**

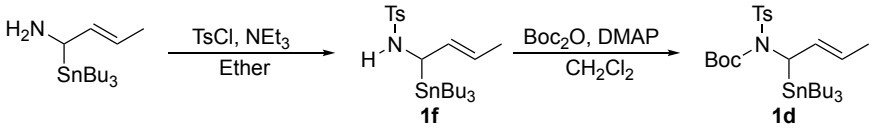
**Tributhyl{(*E*)-1-phthaloylamino-4-methylpent-2-en-1-yl}stannane (1c)**



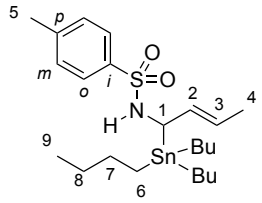

**1c**

To a solution of naphthalene (0.624 mmol, 0.0800 g) in THF (72 mL), were added lithium clippings (35.8 mmol, 0.249 g). The mixture started turning dark green and was stirred at room temperature for 1 h under nitrogen atmosphere. Then tributyltin chloride (12.7 mmol, 2.53 g) was added dropwise and the mixture was stirred at room temperature for 3 h, to give the solution of $Bu_3SnLi$. The resulting mixture was transferred via cannula to another reaction vessel in order to remove unreacted Li, and then the mixture was cooled to -78 °C. Isobutyraldehyde (11.8 mmol, 1.18 g) in THF (5 mL) was added dropwise. The reaction mixture was stirred at -78 °C for 4 h, and then was quenched by 15% $NH_4F$ aq. (50 mL). The organic layer was extracted with ethyl acetate (3 x 100 mL) and the collected organic layers were dried over $MgSO_4$. Then, the solvent was removed with vacuum. {(*E*)-1-hydroxy-4-methylpent-2-en-1-yl}tributhylstannane was obtained as a yellow oil in ca. 73% purity (1.97 g, 43% yield). To a solution of {(*E*)-1-hydroxy-4-methylpent-2-en-1-yl}tributhylstannane (1.97 g, 5.07 mmol), phthalimide (10.1 mmol 1.48 g), and $PPh_3$ (10.2 mmol, 2.68 g) in THF (15 mL) was slowly added diisopropyl azodicarboxylate (10 mmol, 5.3 mL, 1.9 M toluene solution) at 0 °C. The mixture was stirred for 12 h at room temperature. The solvent was evaporated, and the residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 90/10) to give the pure product **1c** as a yellow liquid (0.936 g, 36% yield). $^1$H NMR: (400 MHz, $CDCl_3$) 7.85-7.82 (m, 2H, 8-H x 2), 7.73-7.70 (m, 2H, 9-H x 2), 5.59-5.54 (m, 1H, 2-H), 5.20-5.14 (m, 1H, 3-H), 4.51-4.36 (m, d by $^3J_{H\text{-}H}$ = 8.2 Hz, d by $^2J_{Sn\text{-}H}$ = 52.2 Hz, 1H, 1-H), 2.23 (oct, $J$ = 7.8 Hz, 1H, 4-H), 1.60-1.40 (m, 6H, 11-$H_2$ x 3), 1.33-1.24 (m, 6H, 12-$H_2$ x 3), 1.05-0.84 (m, 21H, 10-$H_2$ x 3, 13-$H_2$ x 3 and 4-Me x 2); $^{13}$C NMR: (100 MHz, $CDCl_3$) 168.9 (s, C-6), 133.8 (d, C-9), 132.4 (d, C-3, d by $^3J_{Sn\text{-}C}$ = 31.1 Hz), 132.0 (s, C-7), 125.5 (d, C-2, d by $^2J_{Sn\text{-}C}$ = 13.9 Hz), 123.0 (d, C-8), 39.6 (d, C-1, d by $^1J_{119Sn\text{-}C}$ = 276 Hz, d by $^1J_{117Sn\text{-}C}$ = 256 Hz), 30.7 (d, C-4), 29.0 (t, C-11, d by $^2J_{Sn\text{-}C}$ = 19.6 Hz), 27.4 (t, C-12, d by $^3J_{Sn\text{-}C}$ = 58.2 Hz), 22.6 (q, 4-Me), 22.5 (q, 4-Me), 13.7 (q, C-13), 11.1 (t, C-10, d by $^1J_{119Sn\text{-}C}$ = 330 Hz, d by $^1J_{117Sn\text{-}C}$ = 316 Hz); HRMS: (CI, 70 eV) Calculated ($C_{26}H_{42}NO_2Sn$) 520.2238 ($[M + H]^+$) Found: 520.2245

**Preparation of Tributhyl{(*E*)-1-(*N*-tosylamino) but-2-en-1-yl }stannane (1f) and Tributhyl {(*E*)-1-(*N*-*tert*-Butoxycarbonyl-*N*-tosylamino) but-2-en-1-yl}stannane (1d)**

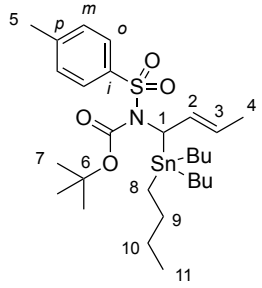



**(1) Tributhyl{(*E*)-1-(*N*-tosylamino)but-2-en-1-yl}stannane (1f)**




To a solution of tosyl chloride (10.2 mmol, 1.94 g) and triethyl amine (10.9 mmol, 1.10 g) in $Et_2O$ (20 mL) was added {(*E*)-1-aminobut-2-en-1-yl}tributylstannane (8.63 mmol, 3.11 g) at 0 °C. The mixture was warmed to room temperature and stirred for 6 h. After water (20 mL) was poured into the solution, the aqueous phase was extracted by $CH_2Cl_2$ (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the target product **1f** as a colorless oil (2.84 mmol, 1.46 g, 33% yield). $^1$H NMR: (400 MHz, $CDCl_3$) 7.74 (d, $J$ = 8.5 Hz, 2H, *m*-H x 2), 7.26 (d, $J$ = 8.5 Hz, 2H, *o*-H x 2), 5.26-5.18 (m, 1H, 2-H), 5.12-5.03 (m, 1H, 3-H), 4.97-4.90 (m, 1H, NH), 3.88-3.70 (m, t by $^3J_{H\text{-}H}$ = 7.7 Hz and d by $^2J_{Sn\text{-}H}$ = 54.0 Hz, 1H, 1-H), 2.41 (s, 3H, 5-$H_3$), 1.53-1.38 (m, 9H, 4-$H_3$ and 7-$H_2$ x 3), 1.37-1.20 (m, 6H, 8-$H_2$ x 3), 0.96-0.84 (m, 15H, 6-$H_2$ x 3 and 9-$H_3$ x 3); $^{13}$C NMR: (100 MHz, $CDCl_3$) 142.9 (s, C-*i*), 138.0 (s, C-*p*), 131.7 (d, C-2), 129.2 (d, C-*o*), 127.5 (d, C-*m*), 119.3 (d, C-3), 44.5 (d, C-1), 28.8 (t, C-7, d by $^2J_{Sn\text{-}C}$ = 20.5 Hz), 27.3 (t, C-8, d by $^3J_{Sn\text{-}C}$ = 55.7 Hz), 21.5 (q, C-5), 17.4 (q, C-4), 13.6 (q, C-9), 9.33 (t, C-6, d by $^1J_{119Sn\text{-}C}$ = 317 Hz, d by $^1J_{117Sn\text{-}C}$ = 303 Hz); HRMS: (CI, 70 eV) Calculated ($C_{23}H_{42}NO_2SSn$) 516.1958 ([M + $H^+$]) Found: 516.1971

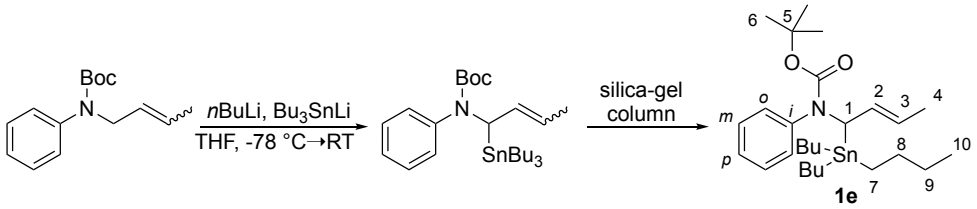
**(2) Tributyl{(*E*)-1-(*N*-*tert*-Butoxycarbonyl-*N*-tosylamino)but-2-en-1-yl}stannane (1d)**




To a solution of tributhyl{(*E*)-1-(*N*-tosylamino)but-2-en-1-yl}stannane **1f** (1.54 mmol, 0.792 g) and

di-*tert*-butyl dicarbonate (4.62 mmol, 1.01 g) was added 4-dimethylaminopyridine (0.31 mmol, 0.0379 g). After the mixture was stirred for 6 h, the solvent was evaporated. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the target product **1d** as a colorless oil (0.87 mmol, 0.535 g, 57% yield). IR: (neat) 1704 (CO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.74 (d, *J* = 8.4 Hz, 2H, *o*-H x 2), 7.25 (d, *J* = 8.4 Hz, 2H, *m*-H x 2), 5.64-5.58 (m, 1H, 2-H), 5.39-5.31 (m, 1H, 3-H), 4.77-4.60 (d, $^3J_{H\text{-}H}$ = 8.2 Hz, d, $^2J_{Sn\text{-}H}$ = 59.4 Hz, 1H, 1-H), 2.42 (s, 3H, 5-$H_3$), 1.72-1.67 (m, 3H, 4-$H_3$), 1.57-1.39 (m, 6H, 9-$H_2$ x 3), 1.35-1.21 (m, 16H, 10-$H_2$ x 3, 7-$H_3$ x 3), 0.97-0.80 (m, 15H, 8-$H_2$ x 3, 11-$H_3$ x 3); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 152.2 (s, CO), 143.6 (s, C-*p*), 138.0 (s, C-*i*), 131.0 (d, C-2), 128.8 (d, C-*m*), 128.0 (d, C-*o*), 120.9 (d, C-3), 84.1 (s, C-6), 48.9 (d, C-1), 28.9 (t, C-9, d by $^2J_{Sn\text{-}C}$ = 19.7 Hz), 27.8 (q, C-7), 27.4 (t, C-10, d by $^3J_{Sn\text{-}C}$= 59.0 Hz), 21.5 (q, C-5), 17.5 (q, C-4), 13.6 (q, C-11), 11.4 (t, C-8, d by $^1J_{119Sn\text{-}C}$ = 333 Hz, d by $^1J_{117Sn\text{-}C}$ = 321 Hz); HRMS: (CI, 70 eV) Calculated ($C_{28}H_{50}NO_4SSn$) 616.2483 ($[M + H]^+$) Found: 616.2475

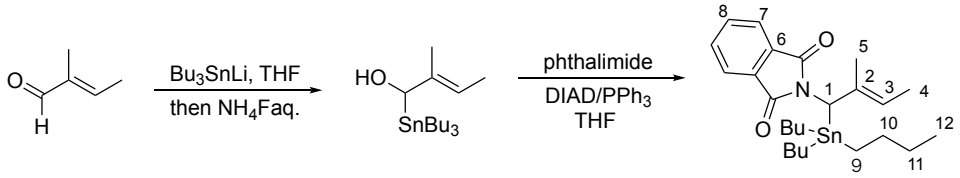
**Tributhyl{(*E*)-1- (*N*-*tert*-Butoxycarbonyl-*N*-phenylamino-but-2-en-1-yl}stannane (1e)**




To a solution of *N*-*tert*-butoxycarboyl-*N*-phenyl-but-2-ene (10.0 mmol, 2.49 g) and THF (20 mL) was added *n*-BuLi (12 mmol, 7.5 mL, 1.6 M in Hexane) dropwise at -78 °C. The yellow solution was stirred for 1.5 h at -78 °C, and then the solution of tributyltin chloride (13.0 mmol, 4.24 g) in THF (5 mL) was added dropwise at -78 °C. The mixture was warmed to room temperature and was stirred for 6 h. After water (10 mL) was poured into the solution, the aqueous phase was extracted by EtOAc (30 mL x 3). The combined organic phase was dried over $MgSO_4$, and evaporated. The residue (*E*/*Z* = 50:50) was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the target (*E*)-isomer **1e** as a colorless oil (1.33 g, 2.48 mmol, 25%). IR: (neat) 1678 (OCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.26 (t, *J* = 7.3 Hz, 2H, *o*-H x 2), 7.18 (d, *J* = 7.3 Hz, 2H, *m*-H x 2), 7.12 (t, *J* = 7.3 Hz, 1H, *p*-H), 5.76-5.66 (m, 1H, 2-H), 5.29-5.16 (m, 1H, 3-H), 3.77-3.51 (br, 1H, 1-H), 1.73-1.67 (m, 3H, 4-$H_3$), 1.60-1.44 (m, 6H, 8-$H_2$ x 3), 1.42-1.26 (m, 15H, 9-$H_2$ x 3, 6-$H_3$ x 3), 0.98-0.81 (m, 15H, 7-$H_2$ x 3, 10-$H_3$ x 3); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 154.9 (s, CO), 145.1 (s, C-*i*, d by $^3J_{Sn\text{-}C}$ = 18.0), 132.2 (d, C-2, d by $^2J_{Sn\text{-}C}$ = 16.3 Hz), 128.2 (d, C-*o*), 125.9 (d), 125.2 (d), 118.3 (d, C-3), 79.7 (s, C-5), 56.0 (d, C-1, d by $^1J_{119Sn\text{-}C}$ = 327 Hz, d by $^1J_{117Sn\text{-}C}$ = 312 Hz), 29.1 (t, C-8, d by $^2J_{Sn\text{-}C}$ = 19.6 Hz), 28.2 (q, C-6), 27.5 (t, d by $^3J_{Sn\text{-}C}$ = 58.2 Hz, C-9), 17.7 (q, C-4, d by $^4J_{Sn\text{-}C}$ = 9.0 Hz,), 13.0 (q, C-

10), 11.4 (t, C-7, d by $^{1}J_{119Sn-C}$ = 327 Hz, d by $^{1}J_{117Sn-C}$ = 312 Hz); HRMS: (CI, 70 eV) Calculated ($C_{27}H_{48}NO_2Sn$) 538.2707 ($[M + H]^+$) Found: 538.2694

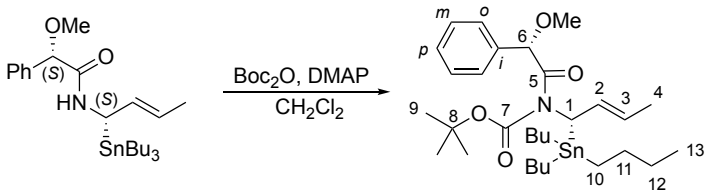
**Tributhyl{(*E*)-1-phthaloylamino-2-methyl-but-2-en-1-yl}stannane (1g)**




**1g**

*n*-BuLi (1.6 M/hexane solution 14 ml, 22 mmol) was added to the solution of diisopropylamine (2.45 g, 24 mmol) in THF (20 mL) at 0 °C. The solution was stirred for 10 min at 0 °C. $Bu_3SnH$ (5.92 g, 20 mmol) was dropwised to the solution at -78 °C and stirred for 1 h at -78 °C. Then, *trans*-2-methyl-2-butenal (1.85 g, 20 mmol) was dropwised slowly to the solution of the prepared $Bu_3SnLi$ and stirred for 4 h at -78 °C. The reaction mixture was quenched by 15% $NH_4F$ aq (30 mL). The organic layer was extracted with ethyl acetate (3 x 30 mL) and the collected organic layer was dried over $MgSO_4$. Then the solvent was removed under reduced pressure. {(*E*)-1-Hydroxy-2-methyl-2-butenyl}tributhylstannane was obtained as a yellow oil in ca. 86% purity (6.32 g, 16.8 mmol, 83% yield). To a solution of {(*E*)-1-hydroxy-2-methyl-2-butenyl} tributhylstannane (6.32 g, 16.8 mmol), phthalimide (2.94 g, 20.0 mmol), and $PPh_3$ (5.25 g, 20.0 mmol) in dry THF (30 mL) was slowly added diethyl azodicarboxylate (10.5 mL, 20 mmol, 1.9 M toluene solution) over 15 min at 0 °C. The mixture was stirred for 12 h at room temperature. The solvent was evaporated, and hexane (100 mL) was poured with stirring. The generated solid was filtered off and the solvent was evaporated and the residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the pure product **1g** as a yellow liquid (2.29 g, 27%). IR: (neat) 1706 (NCO) $cm^{-1}$; $^{1}H$ NMR: (400 MHz, $CDCl_3$) 7.87-7.82 (m, 2H, 7-H x 2), 7.74-7.69 (m, 2H, 8-H x 2), 4.93 (q, $J$ = 7.8 Hz, 1H, 3-H), 4.30 (m, $^{2}J_{Sn-H}$ = 55.1 Hz, 1H, 1-H) , 1.62 (s, 3H, 5-$H_3$), 1.58-1.40 (m, 9H, 4-$H_3$, 10-$H_2$ x 3), 1.33-1.24 (m, 6H, 11-$H_2$ x 3), 0.98-0.81 (m, 15H, 9-$H_2$ x 3, 12-$H_3$ x 3); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 169.2 (s, CO), 134.3 (s, C-2), 133.8 (d, C-8), 131.9 (s, C-6), 123.0 (d, C-7), 113.7 (d, C-3), 44.3 (d, C-1, d by $^{1}J_{119Sn-C}$ = 270 Hz, d by $^{1}J_{117Sn-C}$ = 258 Hz), 28.9 (t, C-10, d by $^{3}J_{Sn-C}$ = 19.7 Hz), 27.3 (t, C-11, d by $^{2}J_{Sn-C}$ = 58.8 Hz), 15.1 (q, C-5), 13.3 (q, C-12), 11.7 (q, C-4), 10.1 (t, C-9, d by $^{1}J_{119Sn-C}$ = 331 Hz, d by $^{1}J_{117Sn-C}$ = 316 Hz); HRMS: (CI, 70 eV) Calculated ($C_{25}H_{40}NO_2Sn$) 506.2080 ($[M + H]^+$) Found: 506.2081

**(1*S*,2*E*)-1-{*N*-(*S*)-2-methoxy-2-phenylacetyl-*N*-*tert*-butoxycarbonylamino}but-2-en-1-yl tributhylstannane (1h)**




**1h**

To a solution of (1*S*,2*E*)-1-*N*-{(*S*)-2-methoxy-2-phenylacetylamino-but-2-en-1-yl}tributhyl stannane (2.90 mmol, 1.48 g) and di-*tert*-butyl dicarbonate (8.52 mmol, 1.86 g) in dichloromethane (3 mL) was added 4-dimethylaminopyridine (0.64 mmol, 0.0786 g) at room temperature. After the mixture was stirred for 6 h at room temperature, the solvent was evaporated. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9:1) to give the target product **1h** as a colorless oil (1.68 g, 2.76 mmol, 95% yield). IR: (neat) 1731 (NCOC), 1678 (NCOO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.46 (dd, $J$ = 7.7, 1.9 Hz, 2H, *o*-H x 2), 7.34-7.28 (m, 3H, *m*-H x 2, *p*-H), 5.91 (s, 1H, 6-H), 5.59-5.53 (m, 1H, 2-H), 5.21-5.14 (m, 1H, 3-H), 4.10 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, d, $^2J_{Sn\text{-}H}$ = 55.2 Hz, 1H, 1-H), 3.36 (s, 3H, OMe), 1.67-1.61 (m, 3H, 4-$H_3$), 1.45 (s, 9H, O*t*Bu), 1.42-1.33 (m, 6H, 11-$H_2$ x 3), 1.26-1.16 (m, 6H, 12-$H_2$ x 3), 0.90-0.72 (m, 15H, 10-$H_2$ x 3, 13-$H_3$ x 3); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 173.8 (s, C-5), 154.1 (s, C-7), 136.7 (s, C-*i*), 130.7 (d, C-2, d by $^2J_{Sn\text{-}C}$ = 19.6 Hz), 128.3 (d), 128.2 (d), 128.1 (d), 119.8 (d, C-3, d by $^3J_{Sn\text{-}C}$ = 34.4 Hz), 83.2 (s, C-8), 82.5 (d, C-6), 57.1 (q, OMe), 49.1 (d, C-1), 29.0 (t, C-11, d by $^2J_{Sn\text{-}C}$ = 19.6 Hz), 27.8 (q, O*t*Bu), 27.4 (t, C-12, d by $^3J_{Sn\text{-}C}$ = 58.2 Hz), 17.5 (q, C-4), 12.7 (q, C-13), 11.1 (t, C-10, d by $^1J_{119Sn\text{-}C}$ = 335.1 Hz, d by $^1J_{117Sn\text{-}C}$ = 320.3 Hz); HRMS: (CI, 70 eV) Calculated ($C_{30}H_{52}NO_4Sn$) 610.2918 ($[M + H]^+$) Found: 610.2920

**Optimization of Radical Conditions**

**Entries 1-4**;

To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.5 mmol) and benzyl 2-iodoacetate **2a** (0.75 mmol) in acetonitrile (1 mL) was added radical initiator. The reaction mixture was stirred at 80 °C for 6 hours, and then quenched by water. The solution was extracted with EtOAc (3 x 15 mL). The collected organic layers were dried over $MgSO_4$ and evaporated to give a crude product **3aa** which was analyzed by $^1H$ NMR.

**Entry 5**;

A solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.5 mmol) and benzyl 2-

iodoacetate **2a** (0.75 mmol) in acetonitrile (1 mL) was stirred and irradiated by UV lamp for 6 h at room temperature, and then quenched by water. The solution was extracted with EtOAc (3 x 15 mL). The collected organic layers were dried over $MgSO_4$ and evaporated to give a crude product **3aa** which was analyzed by $^1H$ NMR.

**Entries 6-9**;

To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (1 equiv) and benzyl 2-iodoacetate **2a** (1.5 equiv) in acetonitrile was added triethylborane (1 M/hexane solution). Air was bubbled with a syringe. The reaction mixture was stirred for 6 hours, and then quenched by water. The solution was extracted with EtOAc (3 x 15 mL). The collected organic layers were dried over $MgSO_4$ and evaporated to give a crude product **3aa** which was analyzed by $^1H$ NMR.

**Experimental Procedure**

General Procedure

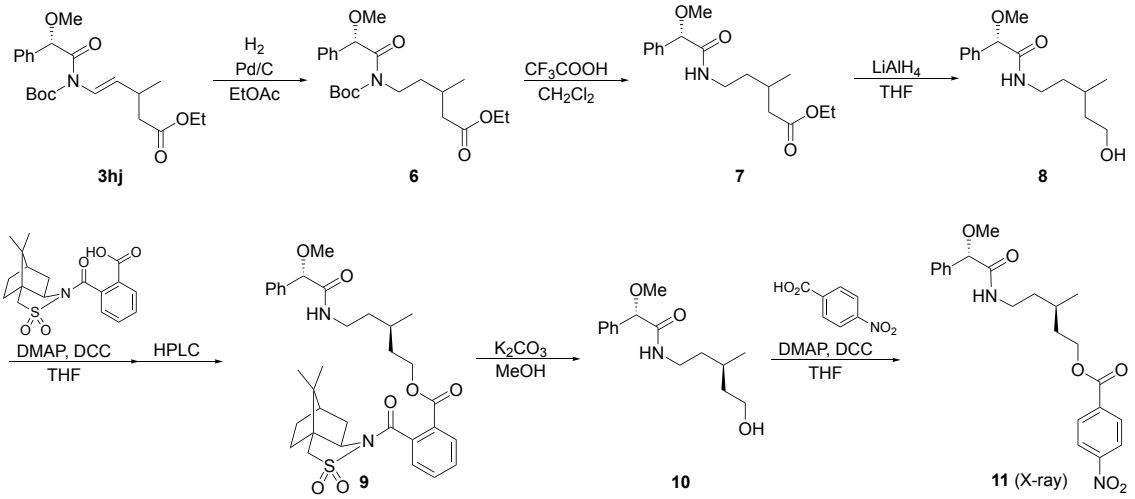
To a solution of aminoallylic stannane **1** (0.5 mmol) and alkyl halide **2** (0.75 mmol) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by silica-gel column chromatography to give the target product **3**.

**Mechanism of the Allylation Using Aminoallylic Lithium**

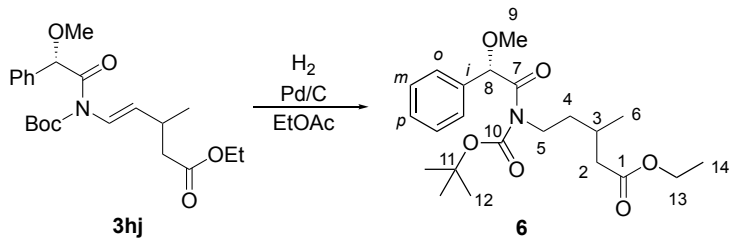
The structure of π-allyl lithium is fixed to the anti-syn form by the coordination of Boc group in the allylation of methyl iodide.

**Detemination of Absolute Configuration**

The absolute configuration of the major isomer in chiral transfer reaction was determined by transforming into the compound **11**. The structure was determined by X-ray diffraction analysis.



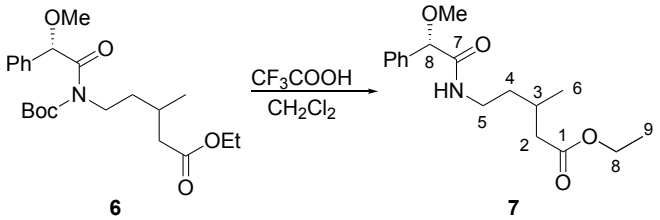

**Ethyl 5-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido}-3-methyl pentanoate (6)**




To a stirred solution of palladium on carbon (0.213 g) in EtOAc (20 mL) was added ethyl (*E*)-5-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido}-3-methylpent-4-enoate **3hj** (4.93 mmol, 2.00 g), and the resulting solution was hydrogenated under hydrogen atmosphere (1 atm) for 3 h. The catalyst was removed by filtration through celite, and the filtrate was evaporated. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the pure product **6** as colorless viscous liquid (1.36 g, 68%). The diastereo ratio was 72:28, which was estimated by the ratio of the starting material **3hj** because $^{1}$H and $^{13}$C NMR spectra of major and minor isomers overlap almost perfectly. Therefore, Combined spectrum data of major and minor isomers are listed below. $^{1}$H NMR: (400 MHz, $CDCl_3$) 7.41-7.29 (m, 5H, Ph), 5.96 (s, 1H, 8-H), 4.11 (q, $J$ = 7.0 Hz, 2H, 13-$H_2$), 3.73-3.56 (m, 2H, 5-$H_2$), 3.37 (s, 3H, OMe), 2.33-2.25 (m, 1H, 2-$H^a$), 2.12-2.06 (m, 1H, 2-$H^b$), 1.93-1.86 (m, 1H, 3-H), 1.50-1.30 (m, 11H, 4-$H_2$ and O*t*Bu), 1.24 (t, $J$ = 7.0 Hz, 3H, 14-$H_3$), 0.94 (d, $J$ = 6.5 Hz, 3H, 6-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 173.4 (s), 172.6 (s), 152.6 (s), 136.5 (s), 128.3

(d), 128.2 (d), 128.2 (d), 83.0 (s), 82.9 (d), 60.0 (q), 57.2 (q), 43.0 (t), 41.4 (t), 34.9 (t), 28.1 (d), 27.7 (q), 19.5 (q), 14.1 (q); HRMS: (CI, 70 eV) Calculated ($C_{22}H_{34}NO_6$) 408.2386 ($[M + H]^+$) Found: 408.2379

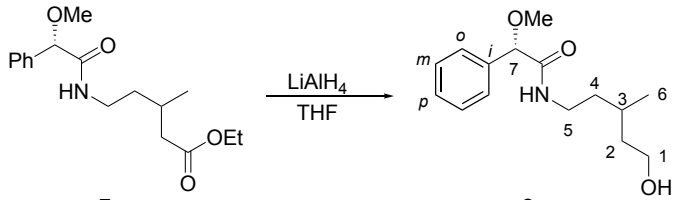
**Ethyl 5-{(*S*)-2-methoxy-2-phenylacetamido}-3-methylpentanoate (7)**




6 7

To a solution of ethyl 5-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido}-3-methylpentanoate **6** (3.33 mmol, 1.36 g) in $CH_2Cl_2$ (13 mL) was added trifluoroacetic acid (6.5 mL) and the resulting solution was stirred for 30 min at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was extracted with dichloromethane. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5:5) to give the pure product **7** as a colorless viscous liquid (0.845 g, 83% yield). The diastereo ratio was 72:28, which was estimated by the ratio of the starting material **3hj** because $^1H$ and $^{13}C$ NMR spectra of major and minor isomers overlap almost perfectly. Therefore, Combined spectrum data of major and minor isomers are listed below. IR: (neat) 1730 (NCOC), 1657 (COO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.42-7.31 (m, 5H, Ph), 6.93 (br, 1H, NH), 4.67 (s, 1H, 8-H), 4.17-4.11 (m, 2H, 9-$H_2$), 3.37 (s, 3H, OMe), 3.31 (q, $J$ = 6.5 Hz, 2H, 5-H), 2.33-2.26 (m, 1H, 2-$H^a$), 2.17 (m, 1H, 2-$H^b$), 2.05-1.97 (m, 1H, 3-H), 1.62-1.52 (m, 1H, 4-$H^a$), 1.48-1.38 (m, 1H, 4-$H^b$), 1.28-1.24 (m, 3H, 10-$H_3$), 0.96 (m, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.9 (s), 170.9 (s), 136.4 (s), 128.4 (d), 128.3 (d), 126.9 (d), 83.3 (d), 60.2 (t), 57.0 (q), 41.3 (t), 36.8 (t), 35.8 (t), 27.8 (d), 19.5 (q), 14.1 (q); HRMS: (CI, 70 eV) Calculated ($C_{17}H_{26}NO_4$) 308.1862 ($[M + H]^+$) Found: 308.1865

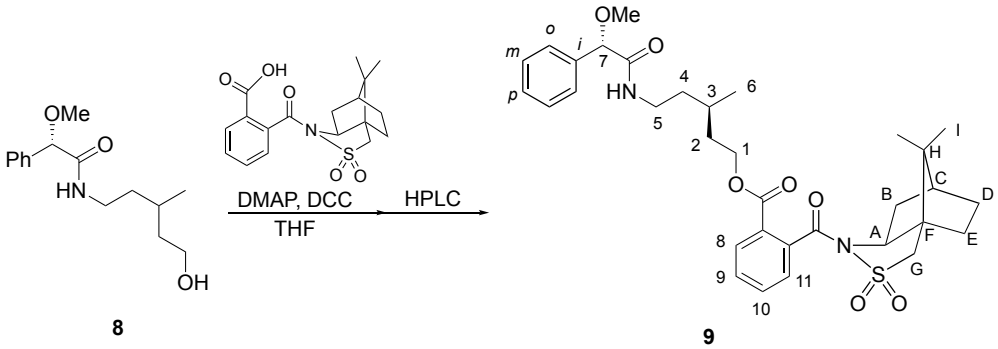
**5-{(*S*)-2-methoxy-2-phenylacetylamino}-3-methyl-1-pentanol (8)**




**7** **8**

To a solution of ethyl 5-{(*S*)-2-methoxy-2-phenylacetamido}-3-methylpentanoate **7** (0.115 mmol, 0.0355 g) of in THF (0.5 mL) was added $LiAlH_4$ (0.3 mmol, 0.0114 g) at 0 °C and the resulting solution was warmed to room temperature, and stirred for 1 h. The reaction was quenched by water and the mixture was extracted with EtOAc. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the crude product. The residue was purified by GPC to give the pure product **8** as a colorless highly viscous liquid (0.0211 g, 69%). The diastereo ratio was 72:28, which was estimated by the ratio of the starting material **3hj** because $^1H$ and $^{13}C$ NMR spectra of major and minor isomers overlap almost perfectly. Therefore, Combined spectrum data of major and minor isomers are listed below. IR: (neat) 1714 (NCOC), 1653 (COO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.40-7.31 (m, 5H, Ph), 6.83 (br, 1H, NH), 4.60 (s, 1H, 7-H), 3.71-3.53 (m, 2H, 1-H), 3.35 (s, 3H, OMe), 3.43-3.04 (m, 2H, 5-H), 1.95 (br, 1H, OH), 1.68-1.49 (m, 3H), 1.45-1.33 (m, 2H), 0.91 (d, $J$ = 6.8 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 170.6 (s), 137.0 (s), 128.5 (d), 128.4 (d), 126.9 (d), 83.7 (d), 60.5 (t), 57.1 (q), 39.3 (t), 39.2 (t), 36.9 (t), 36.7 (t), 36.6 (t), 27.0 (d), 26.9 (d), 19.6 (q); HRMS: (CI, 70 eV) Calculated ($C_{15}H_{24}NO_3$) 266.1756 ($[M + H]^+$) Found: 266.1755

**(*R*)-5-{(*S*)-2-methoxy-2-phenylacetamido}-3-methylpentyl-2-{(6*S*,7a*S*)-8,8-dimethyl-2,2-dioxidohexahydro-3H-3a,6-methanobenzo[c]isothiazole-1-carbonyl} benzoate (9)**

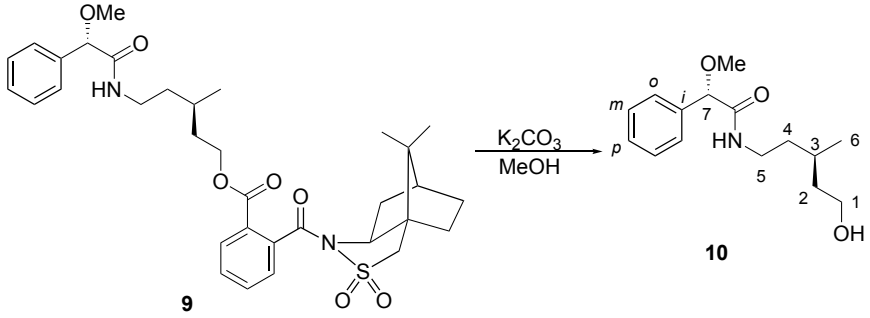



**8** **9**

To a stirred solution of *N*-(2-carboxybenzoyl)-(+)-10,2-camphorsultam (0.276 g, 0.505 mmol), dicyclohexylcarbodiimide **8** (3.47 g, 0.758 mmol) and 4-dimethylaminopyridine (0.112 g, 0.917 mmol) in $CH_2Cl_2$ (2 mL) was added 5-{(*S*)-2-methoxy-2-phenylacetylamino}-3-methyl-1-pentanol

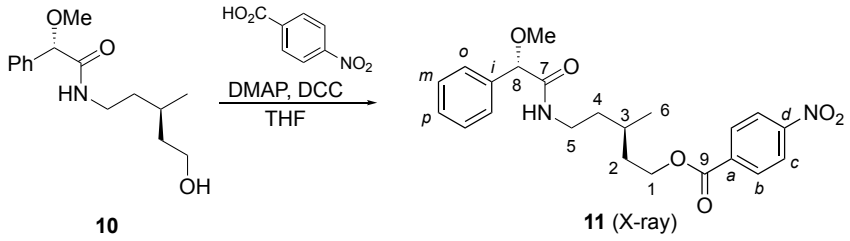
(0.134 g, 0.505 mmol) at 0 °C. The mixture was allowed to warm to room temperature. After stirring at room temperature for 24 h, the filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 55:45) yielding the mixture of diastereomers (dr = 61:39). The mixture was purified by HPLC to give the major product **9** as a white sticky solid (0.121 g, 39%) and the minor product as a viscous liquid (0.0776 g, 25%). $[\alpha]_D^{20}$ +12.5 ($c$ = 0.0012 g/mL, $CHCl_3$), IR: (KBr) 1716 (HNCOC), 1685 (NCOC), 1655 (COO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.98 (d, $J$ = 7.5 Hz, 1H), 7.60 (t, $J$ = 7.5 Hz, 1H), 7.52 (t, $J$ = 7.5 Hz, 1H), 7.47 (d, $J$ = 7.5 Hz, 1H), 7.39-7.30 (m, 5H), 6.78 (br, 1H), 4.59 (s, 1H), 4.38-4.23 (m, 2H), 4.08 (br, 1H), 3.41 (m, 7H), 2.47 (br, 1H), 2.15 (br, 1H), 1.95-1.87 (m, 3H), 1.83-1.55 (m, 4H), 1.47-1.35 (m, 3H), 1.24 (s, 3H), 0.98-0.97 (m, 6H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 170.2, 167.2, 165.0, 137.0, 135.4, 131.7, 130.1, 129.3, 128.9, 128.3, 128.2, 126.8, 83.6, 65.5, 63.3, 57.1, 52.8, 48.2, 47.5, 44.6, 37.5, 36.7, 36.2, 35.0, 32.9, 27.5, 26.3, 20.6, 19.9, 19.1; HRMS: (CI, 70 eV) Calculated ($C_{33}H_{43}N_2O_7S$) 611.2791 ($[M + H]^+$) Found: 611.2793

**(*R*)-5-{(*S*)-2-methoxy-2-phenylacetylamino}-3-methyl-1-pentanol (10)**




$K_2CO_3$ (2.02 mmol, 0.279 g) was added to a solution of **9** (0.198 mmol, 0.121 g) in methanol (5 mL) at rt. After stirring for 2 h, the reaction mixture was concentrated under reduced pressure and purified by GPC to give **10** (0.147 mmol, 74%). $[\alpha]_D^{20}$ +9.37 ($c$ = 0.0196 g/mL, $CHCl_3$), IR: (neat) 1714 (NCOC), 1653 (COO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.39-7.30 (m, 5H), 6.80 (br, 1H), 4.60 (s, 1H), 3.71-3.59 (m, 2H), 3.43-3.32 (m, 4H), 3.28-3.17 (m, 1H), 1.84 (br, 1H), 1.69-1.50 (m, 3H), 1.45-1.35 (m, 2H), 0.92 (d, $J$ = 6.8 Hz, 3H), 3.15-3.04 (m, 1H, 3-H), 1.95 (br, 1H, OH), 1.37 (d, 3H, $J$ = 6.8, 4-H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 170.6 (s), 137.0 (s), 128.5 (d), 128.4 (d), 126.9 (d), 83.7 (d), 60.5 (t), 57.1 (q), 39.2 (t), 36.9 (t), 36.6 (t), 27.0 (d), 19.6 (q); HRMS: (CI, 70 eV) Calculated ($C_{15}H_{24}NO_3$) 266.1756 ($[M + H]^+$) Found: 266.1757

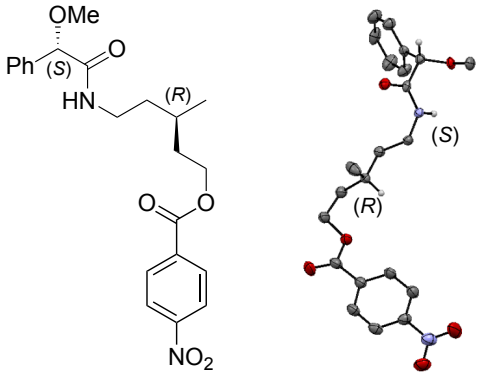
**(*R*)-5-{(*S*)-2-methoxy-2-phenylacetamido}-3-methylpentyl 4-nitrobenzoate (11)**




**10** **11** (X-ray)

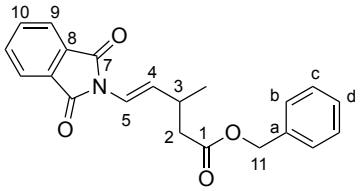
To a stirred solution of *p*-nitrobenzoic acid (0.279 mmol, 0.0466 g), *N*,*N*-dimethyl-4-aminopyridine (0.436 mmol, 0.0532 g) and *N*,*N*-Dicyclohexylcarbodiimide (0.262 mmol, 0.0540 g) in $CH_2Cl_2$ (1.5 mL) was added (*R*)-5-{(*S*)-2-methoxy-2-phenylacetylamino}-3-methyl-1-pentanol **10** (0.0579 g, 0.218 mmol) at 0 °C. The mixture was allowed to warm to room temperature. After stirring at room temperature for 12 h, the filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 50/50) to give the product **11** as a colorless solid (0.0642 g, 71% yield). The structure was identified by X-ray diffraction analysis (CCDC: 1915886). $[\alpha]_D^{20}$ +15.0 (*c* = 0.0044 g/mL, $CHCl_3$), IR: (neat) 1724 (NCOC), 1672 (COO) cm $^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) 8.28 (dt, *J* = 8.7, 1.8 Hz, 2H, *c*-H x 2), 8.19 (dt, *J* = 8.7, 1.8 Hz, 2H, *b*-H x 2), 7.39-7.30 (m, 5H, Ph), 6.78 (br, 1H, NH), 4.61 (s, 1H, 8-H), 4.45-4.33 (m, 2H, 1-$H_2$), 3.43-3.27 (m, 5H, OMe and 5-$H_2$), 1.90 (m, 1H), 1.75-1.59 (m, 3H), 1.49-1.41 (m, 1H), 1.02 (d, *J* = 6.3 Hz, 3H, 6-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 170.4 (s, C-7), 164.7 (s, C-9), 150.4 (s), 136.9 (s), 135.6 (s), 130.6 (d, C-*b*), 128.5 (d), 128.4 (d), 126.9 (d), 123.5 (d, C-*c*), 83.7 (d, C-8), 64.1 (t, C-1), 57.1 (q, OMe), 36.8 (t), 36.6 (t), 35.2 (t), 27.8 (d, C-3), 19.3 (q, C-6); HRMS: (CI, 70 eV) Calculated ($C_{22}H_{27}N_2O_6$) 415.1869 ($[M + H]^+$) Found: 415.1873

The ORTEP drawing of **11** was shown below.



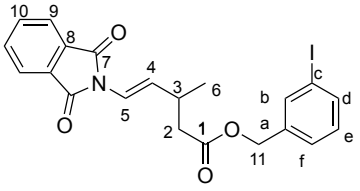
**Product Data**

**Benzyl (*E*)-3-methyl-5-phthaloylamino-4-pentenoate (3aa)**




To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (1.03 mmol, 0.504 g) and benzyl 2-iodoacetate **2a** (1.57 mmol, 0.442 g) in MeCN (2 mL) was added 1 M triethylborane in hexane (1.0 mmol, 1.0 mL) at -20 °C. Then 6 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (10 mL) was added and the mixture was extracted with AcOEt (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the target product **3aa** as a white solid (0.300 g, 83%). mp: 58-60 °C; IR: (KBr) 1778 (OCO), 1719 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.88-7.84 (m, 2H, 9-H x 2), 7.77-7.72 (m, 2H, 10-H x 2), 7.38-7.22 (m, 5H, Ph), 6.66 (d, $J$ = 14.7 Hz, 1H, 5-H), 6.58 (dd, $J$ = 14.7, 7.3 Hz, 1H, 4-H), 5.16 (d, $J$ = 12.3 Hz, 1H, 11-$H^a$), 5.12 (d, $J$ = 12.3, 1H, 11-$H^b$), 2.84 (sept, $J$ = 7.3 Hz, 1H, 3-H), 2.51(dd, $J$ = 14.8, 7.3 Hz, 1H, 2-$H^a$), 2.45 (dd, $J$ =14.8, 7.3 Hz, 2-$H^b$), 1.17 (d, $J$ = 6.8 Hz, 3H, $CH_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.9 (s, C-1), 166.5 (s, C-7), 135.9 (s, C-a), 134.3 (d, C-9), 131.7 (s, C-8), 128.5 (d), 128.4 (d), 128.1 (d), 125.3 (d, C-5), 123.5 (d, C-10) 117.4 (d, C-4), 66.2 (t, C-11), 41.8 (t, C-2), 33.0 (d, C-3), 20.4 (q, $CH_3$); HRMS: (EI, 70 eV) Calculated ($C_{21}H_{19}NO_4$) 349.1314 ($M^+$) Found: 349.1312

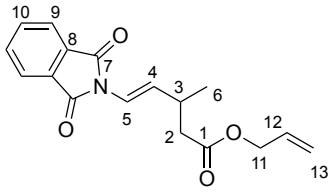
**3-Iodobenzyl (*E*)-3-methyl-5-phthaloylamino-4-pentenoate (3ab)**




To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.533 mmol, 0.261 g) and 3-iodobenzyl 2-iodoacetate **2b** (0.737 mmol, 0.311 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the target product **3ab** as

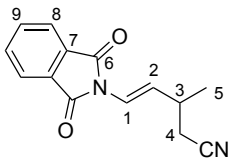
a colorless oil (0.213 g, 84%). IR: (neat) 1778 (OCO), 1716 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.86-7.83 (m, 2H, 9-H x 2), 7.74-7.72 (m, 2H, 10-H x 2), 7.69 (s, 1H, b-H), 7.55 (d, 1H, d-H), 7.31 (d, 1H, f-H), 7.04 (t, 1H, e-H), 6.65 (d, $J$ = 15.0 Hz, 1H, 5-H), 6.55 (dd, $J$ = 15.0, 7.7 Hz, 1H, 4-H), 5.08 (d, $J$ = 12.1 Hz, 1H, 11-$H^a$), 5.03 (d, $J$ = 12.1 Hz, 1H, 11-$H^b$), 2.82 (sept, $J$ = 7.1 Hz, 1H, 3-H), 2.50 (dd, $J$ = 15.0, 7.3 Hz, 1H, 2-$H^a$), 2.45 (dd, $J$ =15.0, 7.3 Hz, 1H, 2-$H^b$), 1.17 (d, $J$ = 7.1 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.7 (s, C-1), 166.3 (s, C-7), 138.1 (s, C-a), 137.0 (d, C-b), 137.0 (d, C-d), 134.3 (d, C-10), 131.5 (s, C-8), 130.1 (d, C-e), 127.4 (d, C-f), 125.0 (d, C-4), 123.4 (d, C-9), 117.4 (d, C-5), 94.2 (s, C-c), 65.0 (t, C-11), 41.6 (t, C-2), 32.9 (d, C-3), 20.4 (q, C-6); HRMS: (EI, 70 eV) Calculated ($C_{21}H_{18}NO_4I$) 475.0281 ($M^+$) Found: 475.0274

**Allyl (*E*)-3-methyl-5-phthaloylamino-4-pentenoate (3ac)**



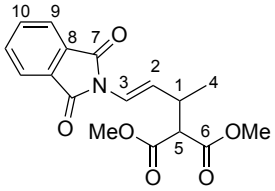

To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.493 mmol, 0.242 g) and allyl iodoacetate **2c** (0.754 mmol, 0.171 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ac** as colorless viscous liquid (0.0745 g, 50%). IR: (neat) 1779 (OCO), 1717 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.87-7.83 (m, 2H, 9-H x 2), 7.76-7.72 (m, 2H, 10-H x2), 6.71 (d, $J$ = 15.0, 1H, 5-H), 6.58 (dd, $J$ = 15.0, 8.2 Hz, 1H, 4-H), 5.93 (m, 1H, 12-H), 5.32 (dd, $J$ = 17.4, 2.0, 1H, 13-$H^a$), 5.23 (dd, $J$ = 10.7, 2.0 Hz, 1H, 13-$H^b$), 4.60 (d, $J$ = 5.8, 2H, 11-$H_2$), 2.83 (sept, $J$ = 7.2 Hz, 1H, 3-H), 2.49 (dd, $J$ = 15.0, 7.2 Hz, 1H, 2-$H^a$), 2.41 (dd, $J$ = 15.0, 7.2 Hz, 2-$H^b$), 1.18 (d, $J$ = 6.8, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.7 (s, C-1), 166.4 (s, C-7), 134.3 (d, C-10), 132.1 (d, C-12), 131.6 (s, C-8), 125.3 (d, C-4), 123.4 (d, C-9), 118.3 (t, C-13), 117.3 (d, C-5), 65.0 (t, C-11), 41.7 (t, C-2), 32.8 (d, C-3), 20.3 (q, C-6); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{17}NO_4$) 299.1158 ($M^+$) Found: 299.1157

***trans*-*N*-(4-cyano-3-methylbut-1-enyl)phthalimide (3ad)**




To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.489 mmol, 0.240 g) and iodoacetonitrile **2d** (1.02 mmol, 0.171 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ad** as a white solid (0.0908 g, 77%). 4% of a *cis*-isomer was included. mp: 68-72 °C; IR: (KBr) 2242 (CN), 1718 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.89-7.85 (m, 2H, 9-H x 2), 7.78-7.75 (m, 2H, 8-H x 2), 6.78 (d, $J$ = 14.6 Hz, 1H, 1-H), 6.61 (dd, $J$ = 14.6, 8.0 Hz, 1H, 2-H), 2.72 (m, 1H, 3-H), 2.51 (dd, $J$ = 16.7, 6.7 Hz, 1H, 4-H$^a$), 2.45 (dd, $J$ = 16.7, 6.7 Hz, 4-H$^b$), 1.30 (d, $J$ = 6.7, 3H, 5-H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 166.2 (s, C-6), 134.4 (d, C-9), 131.3 (s, C-7), 123.5 (d, C-8), 122.3 (d, C-2), 118.6 (d, C-1), 118.1 (s, CN), 33.1 (d, C-3), 25.1 (t, C-4), 19.8 (q, C-5); HRMS: (EI, 70 eV) Calculated ($C_{14}H_{12}N_2O_2$) 240.0899 ($M^+$) Found: 240.0895

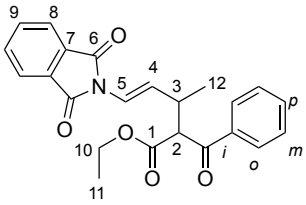
**Dimethyl {(*E*)-4-phthaloylamino-2-buten-2-yl)}malonate (3ae)**




To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.479 mmol, 0.235 g) and dimethyl bromomalonate **2e** (0.732 mmol, 0.154 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ae** as a white solid (0.111g, 70%). 5% of a *cis*-isomer was included. mp: 133-135 °C; IR: (KBr) 1760 (OCO), 1715 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.78-7.74 (m, 2H, 9-H x 2), 7.68-7.64 (m, 2H, 10-H x 2), 6.64 (d, $J$ =

14.5 Hz, 1H, 3-H), 6.66 (dd, *J* = 14.5, 8.7 Hz, 1H, 2-H), 3.68 (s, 3H, OMe), 3.64 (s, 3H, OMe), 3.33 (d, *J* = 9.2 Hz, 1H, 5-H), 2.99 (m, 1H, 1-H), 1.12 (d, *J* = 6.9 Hz, 3H, 4-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 168.3 (s, C-6), 168.2 (s, C-6), 166.2 (s, C-7), 134.3 (d, C-9), 131.3 (s, C-8), 123.4 (d, C-10), 122.3 (d, C-2), 118.6 (d, C-3), 57.6 (d, C-5), 52.34 (q, OMe), 52.27 (q, OMe), 36.2 (d, C-1), 18.5 (q, C-4); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{17}NO_6$) 331.1056 ($M^+$) Found: 331.1052

**Ethyl (*E*)-2-benzoyl-3-methyl-5-phthaloylamino-2-pentenoate (3af)**




To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.493 mmol, 0.242 g) and α-bromo ethyl benzoylacetate **2f** (0.749 mmol, 0.182 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3af** as a white solid (0.162g, 87%) as the mixture of diastereomers (d.r. = 50:50). Each diastereomer was separated by HPLC.

<u>one diastereomer</u>

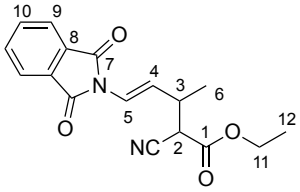
mp: 81-83 °C; IR: (KBr) 1729 (OCO), 1718 (NCO), 1679 (CO) $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) 8.07 (d, *J* = 7.5 Hz, 1H, *o*-H x 2), 7.88-7.84 (m, 2H, 8-H x 2), 7.77-7.74 (m, 2H, 9-H x 2), 7.61 (t, *J* = 7.5 Hz, 1H, *p*-H), 7.50 (t, *J* = 7.5 Hz, 2H, *m*-H x 2), 6.78 (d, *J* = 15.5 Hz, 1H, 5-H), 6.64 (dd, *J* = 15.5, 9.2 Hz, 1H, 4-H), 4.37 (d, *J* = 9.7 Hz, 1H, 2-H), 4.17-4.04 (m, 2H, 10-$H_2$), 3.40-3.30 (m, 1H, 3-H), 1.17 (t, *J* = 7.0 Hz, 3H, 11-$H_3$), 1.15 (d, *J* = 5.1 Hz, 3H, 12-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 193.6 (s, C-13), 168.2 (s, C-1), 166.4 (s,C-6), 136.7 (s, C-*i*), 134.4 (d, C-9), 133.7 (d, C-*p*), 131.6 (s, C-7), 128.8 (d), 128.7 (d), 123.5 (d, C-8), 122.8 (d, C-4), 118.7 (d, C-5), 61.5 (t, C-10), 60.5 (d, C-2), 36.6 (d, C-3), 19.2 (q, C-12), 14.0 (q, C-11); HRMS: (EI, 70 eV) Calculated ($C_{23}H_{21}NO_5$) 391.1420 ($M^+$) Found: 391.1416

<u>another diastereomer</u>

mp: 107-111 °C; IR: (KBr) 1780 (OCO), 1720 (NCO), 1685 (CO) $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) 7.99 (d, *J* = 7.5 Hz, 1H, *o*-H x 2), 7.81-7.77 (m, 2H, 8-H x 2), 7.71-7.67 (m, 2H, 9-H x 2), 7.55 (t, *J* =

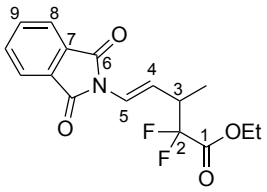
7.5 Hz, 1H, *p*-H), 7.45 (t, *J* = 7.5 Hz, 2H, *m*-H x 2), 6.74 (d, *J* = 15.5 Hz, 1H, 5-H), 6.51 (dd, *J* = 15.5, 9.2 Hz, 1H, 4-H), 4.39 (d, *J* = 9.7 Hz, 1H, 2-H), 4.17 (q, *J* = 7.3 Hz, 2H, 10-$H_2$), 3.38-3.29 (m, 1H, 3-H) , 1.25 (d, *J* = 7.3 Hz, 3H, 12-$H_3$), 1.21 (t, *J* = 7.0 Hz, 3H, 11-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 193.7 (s, C-13), 168.4 (s, C-1), 166.2 (s,C-6), 136.6 (s, C-*i*), 134.3 (d, C-9), 133.4 (d, C-*p*), 131.4 (s, C-7), 128.6 (d), 128.5 (d), 123.4 (d, C-8), 122.8 (d, C-4), 118.9 (d, C-5), 61.5 (t, C-10), 60.0 (d, C-2), 36.1 (d, C-3), 18.5 (q, C-12), 14.0 (q, C-11); HRMS: (EI, 70 eV) Calculated ($C_{23}H_{21}NO_5$) 391.1420 ($M^+$) Found: 391.1418

**Ethyl (*E*)-2-cyano-3-methyl-5-phthaloylamino-4-pentenoate (3ag)**



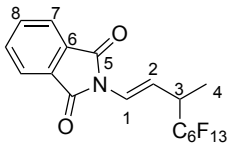

To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.473 mmol, 0.232 g) and ethyl bromocyanoacetate **2g** (0.746 mmol, 0.1432 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ag** as a colorless viscous liquid (0.0417 g, 28%). IR: (neat) 2120 (CN), 1750 (COO), 1720 (NCO) $cm^{-1}$; $^1$H NMR: (400 MHz, $CDCl_3$) 7.89-7.86 (m, 2H, 9-H), 7.78-7.75 (m, 2H, 9-H), 6.81 (d, *J* = 14.8 Hz, 1H, 5-H), 6.64 (dd, *J* = 14.8, 8.7 Hz, 1H, 4-H), 4.29 (q, *J* = 6.8, 2H, C-11), 3.58 (d, *J* = 5.3, 1H, 2-H), 3.09 (sept, *J* = 7.7, 1H, 3-H), 1.36 (d, *J* = 7.3 Hz, 3H,6-H), 1.33 (t, *J* = 7.2, 3H, 12-C); $^{13}$C NMR: (100 MHz, $CDCl_3$) 166.2 (s, C-8), 165.1 (s, C-1), 134.6 (d, C-10), 131.5 (s, C-8), 123.7 (d, C-9), 120.2 (d, C-4), 119.0 (d, C-5), 115.0 (s, CN), 62.9 (t, C-4), 44.8 (d, C-2), 37.5 (d, 3-C), 18.8 (q, C-6), 14.1 (q, C-12); HRMS: (EI, 70 eV) Calculated ($C_{17}H_{16}N_2O_4$) 312.1110 ($M^+$) Found: 312.1112

**Ethyl (*E*)-2,2-difluoro-3-methyl-5-phthaloylamino-4-pentenoate (3ah)**



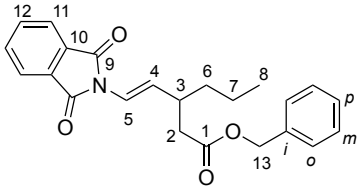
To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.529 mmol, 0.260 g) and 2-bromo-2,2-difluoro ethylacetate **2h** (1.52 mmol, 0.309 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (1.5 mmol, 1.5 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ah** as a colorless viscous liquid (0.0555 g, 33%). 5% of a *cis*-isomer was included. IR: (neat) 1765 (OCO), 1724 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.90-7.86 (m, 2H, 8-H x 2), 7.77-7.74 (m, 2H, 9-H x 2), 6.80 (d, $J$ = 15.0 Hz, 1H, 5-H), 6.56 (dd, $J$ = 15.0, 9.2 Hz, 1H, 4-H), 4.38-4.30 (m, 2H, $OCH_2CH_3$), 3.11-2.96 (m, 1H, 3-H), 1.36 (t, $J$ = 7.2 Hz, 3H, $OCH_2CH_3$), 1.28 (d, $J$ = 7.2, 3H, 3-Me); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 166.1 (s, C-6), 163.8 (t, $^2J_{F\text{-}C}$ = 33.2 Hz, C-1), 134.6 (d, C-8), 131.4 (s, C-7), 123.7 (d, C-9), 121.2 (d, C-5), 116.2 (t, $^1J_{F\text{-}C}$ = 254.4 Hz, C-2), 116.0 (d, C-4), 62.8 (t, $OCH_2CH_3$), 41.1 (t, $^2J_{F\text{-}C}$ = 22.9 Hz, C-3), 14.0 (q, $OCH_2CH_3$), 13.1 (q, $CHCH_3$); HRMS: (CI, 70 eV) Calculated ($C_{16}H_{16}F_2NO_4$) 324.1042 ($[M + H]^+$) Found: 324.1042

***N*-(*E*)-(3-perfluorohexyl-but-1-enyl)phthalimide (3ai)**



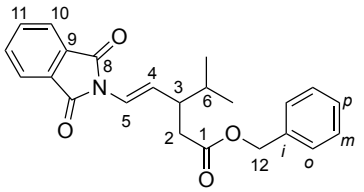

To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1a** (0.516 mmol, 0.253 g) and perfluorohexyl iodide **2i** (1.48 mmol, 0.661 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.50 mmol, 0.50 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ai** as a white solid (0.191 g, 71%). 5% of a *cis*-isomer was included. mp: 70-75 °C; IR: (KBr) 1722 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.90-7.86 (m, 2H, 7-H x 2), 7.78-7.74 (m, 2H, 8-H x 2), 6.84 (d, $J$ = 14.6 Hz, 1H, 1-H), 6.65 (dd, $J$ = 14.6, 9.2 Hz, 1H, 2-H), 3.15-3.04 (m, 1H, 3-H), 1.37 (d, $J$ = 6.8 Hz, 3H, 4-H); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 166.2 (C-5), 134.6 (C-7), 131.5 (C-6), 123.7 (C-8), 121.1 (C-1), 115.2 (C-2), 39.7 (t, $^2J_{F\text{-}C}$ = 22.0, C-3); HRMS: (EI, 70 eV) Calculated ($C_{18}H_{10}F_{13}NO_2$) 519.0504 ($M^+$) Found: 519.0504

**Benzyl (*E*)-3-propyl-5-phthaloylamino-4-pentenoate (3ba)**



To a solution of tributyl{(*E*)-1-phthaloylamino-2-butenyl}stannane **1b** (0.486 mmol, 0.252 g) and benzyl 2-iodoacetate **2a** (1.49 mmol, 0.412 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ba** as colorless viscous liquid (0.164 g, 89%). $^1$H NMR: (400 MHz, $CDCl_3$) 7.86-7.82 (m, 2H, 11-H x 2), 7.74-7.71 (m, 2H, 12-H x 2), 7.34 (d, *J* = 7.6 Hz, 2H, *o*-H x 2), 7.27 (t, *J* = 7.6 Hz, 2H, *m*-H x 2), 7.18 (t, *J* = 7.6 Hz, 1H, *p*-H), 6.62 (d, *J* = 14.7 Hz, 1H, 5-H), 6.41 (dd, , *J* = 14.7, 9.4 Hz, 1H, 4-H), 5.12 (d, , *J* = 13.7 Hz, 1H, 13-H$^a$), 5.07 (d, *J* = 13.7 Hz, 1H, 13-H$^b$), 2.67-2.58 (m, 1H, 3-H), 2.54-2.39 (m, 2H, 2-$H_2$), 1.48 (m, 4H, 6-$H_2$ and 7-$H_2$), 0.88 (t, , *J* = 7.0 Hz, 3H, 8-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 171.9 (s, C-1), 166.3 (s, C-9), 135.8 (s, C-*i*), 134.2 (d, C-12), 131.5 (s, C-10), 128.3 (d). 128.3 (d), 127.9 (d), 123.7 (d, C-4), 123.3 (d, C-11), 118.1 (d, C-5), 66.0 (t, C-13), 40.6 (t, C-2), 38.6 (d, C-3), 37.1 (t, C-6), 20.2 (t, C-7), 13.8 (q, C-8); HRMS: (EI, 70 eV) Calculated ($C_{23}H_{23}NO_4$) 377.1627 ($M^+$) Found: 377.1623

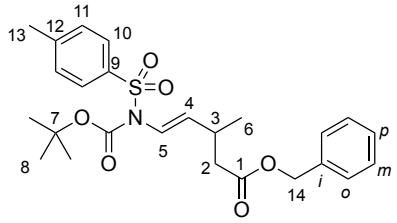
**Benzyl (*E*)-3-*iso*-propyl-5-phthaloylamino-4-pentenoate (3ca)**



To a solution of tributhyl{(*E*)-1-phthaloylamino-4-methylpent-2-en-1-yl}stannane **1c** (0.484 mmol, 0.251 g) and iodo benzylacetate **2a** (1.47 mmol, 0.408 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at -20 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product

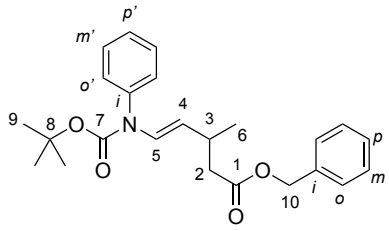
**3ca** as a colorless oil (0.0937 g, 51%). IR: (neat) 1779 (COO), 1720 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.86-7.82 (m, 2H, 10-H x 2), 7.75-7.71 (m, 2H, 11-H x 2), 7.34 (d, *J* = 7.1 Hz, 2H, *o*-H x 2), 7.26 (t, *J* = 7.1 Hz, 2H, *m*-H x 2), 7.15 (t, *J* = 7.1 Hz, 1H, *p*-H), 6.59 (d, *J* = 14.7 Hz, 1H, 5-H), 6.44 (dd, *J* = 14.7, 9.4 Hz, 1H, 4-H), 5.13 (d, *J* = 12.1 Hz, 1H, 12-$H^a$), 5.06 (d, *J* = 12.1 Hz, 1H, 12-$H^b$), 2.61-2.39 (m, 3H, 3-H and 2-$H_2$), 1.77-1.68 (m, 1H, 6-H), 0.93 (d, *J* = 6.8 Hz, 3H, 6-Me), 0.91 (d, *J* = 6.8 Hz, 3H, 6-Me); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.3 (s, C-1), 166.3 (s, C-8), 135.8 (s, *i*-C), 134.2 (d, C-11), 131.6 (s, C-9), 128.4 (d), 128.3 (d), 127.9 (d), 123.3 (d, C-10), 121.5 (d, C-4), 118.7 (d, C-5), 66.0 (t, C-12), 45.0 (d, C-3), 38.1 (t, C-2), 31.8 (d, C-6), 20.5 (q, 6-Me), 18.8 (q, 6-Me); HRMS: (CI, 70 eV) Calculated ($C_{23}H_{24}NO_4$) 378.1705 ($[M + H]^+$) Found: 378.1707

**Benzyl (*E*)-5-[{*N*-(*tert*-butoxycarbonyl)-4-methylphenyl}sulfonamido]**
**-3-methylpent-4-enoate (3da)**



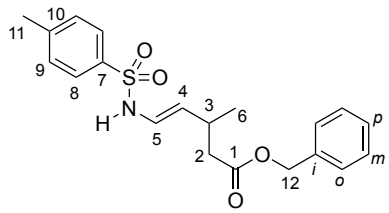

To a solution of tributyl {(*E*)-1-(*N*-*tert*-Butoxycarbonyl-*N*-tosylamino)but-2-en-1-yl}stannane **1d** (0.464 mmol, 0.285 g) and iodo benzylacetate **2a** (0.730 mmol, 0.202 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3da** as colorless viscous liquid (0.146 g, 67%). 7% of a *cis*-isomer was included. $^1H$ NMR: (400 MHz, $CDCl_3$) 7.79 (d, *J* = 7.7 Hz, 2H, 10-H x 2), 7.36-7.29 (m, 7H, 11-H x 2 and Ph), 6.15 (d, *J* = 13.5 Hz, 1H, 5-H), 5.73 (dd, *J* = 13.5, 8.2 Hz, 1H, 4-H), 5.14 (s, 2H, 14-$H_2$), 2.88 (sept, *J* = 8.2 Hz, 1H, 3-H), 2.50-2.39 (m, 5H, 13-$H_3$ and 2-$H_2$), 1.35 (s, 9H, O*t*Bu), 1.14 (d, *J* = 8.2 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.7 (s, C-1), 150.4 (s, C-15), 144.3 (s, C-12), 137.5 (d, C-4), 136.7 (s, C-9), 135.8 (s, C-*i*), 129.2 (d), 128.5 (d), 128.2 (d), 128.1 (d), 127.9 (d), 122.0 (d, C-5), 84.2 (s, C-7), 66.3 (t, C-14), 41.1 (t, C-2), 31.8 (d, C-3), 27.7 (q, C-8), 21.6 (q, C-13), 19.7 (q, C-6); HRMS: (FAB, 70 eV) Calculated ($C_{25}H_{31}NO_6SNa$) 496.1770 ($[M + Na]^+$) Found: 496.1777

**Benzyl (*E*)-5-{(*tert*-butoxycarbonyl)(phenyl)amino}-3-methylpent-4-enoate (3ea)**



To a solution of tributhyl{(*E*)-1-(*N*-*tert*-butoxycarbonyl-*N*-phenylamino-2-butenyl}stannane **1e** (0.489 mmol, 0.262 g) and iodo benzylacetate **2a** (0.759 mmol, 0.210 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3ea** as colorless viscous liquid (0.116 g, 60% yield). 9% of a *cis*-isomer was included. IR: (neat) 1710 (NCO), 1661 (OCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.38-7.27 (m, 8H), 7.10 (d, $J$ = 14.0 Hz, 1H, 5-H), 7.05 (d, $J$ = 7.6 Hz, 2H), 5.11 (d, $J$ = 12.4 Hz, 1H, 10-$H^a$), 5.07 (d, $J$ = 12.4 Hz, 1H, 10-$H^b$), 4.27 (dd, $J$ = 14.0, 8.2 Hz, 1H, 4-H), 2.68 (sept, $J$ = 7.8 Hz, 1H, 3-H), 2.25 (d, $J$ = 7.8 Hz, 2H, 2-$H_2$), 1.41 (s, 9H, O*t*Bu), 0.98 (d, $J$ = 7.8 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.2 (s, C-1), 152.6 (s, C-7), 138.9 (s, C-*i*'), 136.0 (s, C-*i*), 129.1, 129.0, 128.6, 128.5, 128.2, 128.1, 127.3, 115.1 (d, C-4), 81.2 (C-8), 66.1 (t, C-10), 42.4 (t, C-2), 32.0 (d, C-3), 28.1 (q, O*t*Bu), 20.8 (q, C-6); HRMS: (CI, 70 eV) Calculated ($C_{24}H_{30}NO_4$) 396.2175 ($[M + H]^+$) Found: 396.2167

**Benzyl (*E*)-3-methyl-5-{(4-methylphenyl)sulfonamide}pent-4-enoate (3fa)**



To a solution of tributhyl{(*E*)-1-(*N*-tosylamino)but-2-en-1-yl}stannane (0.495 mmol, 0.255 g) and iodo benzylacetate (0.776 mmol, 0.214 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column

chromatography (hexane/ethyl acetate = 7:3) to give the target *trans*-isomer **3fa-*E*** as a colorless oil (0.076 g, 45%) and the *cis*-isomer **3fa-*Z*** as a colorless oil (0.033 g, 18%).

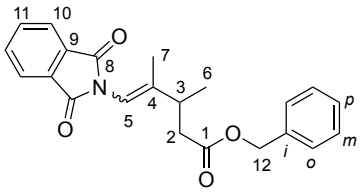
*trans*-isomer:

$^1$H NMR: (400 MHz, $CDCl_3$) 7.79 (d, $J$ = 7.2 Hz, 2H, 8-H x 2), 7.39-7.28 (m, 7H, 9-H x 2 and Ph), 6.16-6.05 (m, 2H, 5-H and NH), 5.02 (s, 2H, 12-$H_2$), 4.93 (dd, $J$ = 13.5, 8.7 Hz, 1H, 4-H), 2.66-2.59 (m, 1H, 3-H), 2.40 (s, 3H, 11-$H_3$), 2.28 (m, 2H, 2-$H_2$), 0.99 (d, $J$ = 6.8 Hz, 3H, 6-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 171.9 (s, C-1), 143.7 (s, C-10), 136.7 (s, C-7), 135.8 (s, C-*i*), 129.7 (d), 128.6 (d), 128.3 (d), 128.2 (d), 126.8 (d, C-8), 122.6 (d, C-5), 118.6 (d, C-4), 66.2 (t, C-12), 42.0 (t, C-2), 31.4 (d, C-3), 21.5 (q, C-11), 20.4 (q, C-6); HRMS: (CI, 70 eV) Calculated ($C_{20}H_{24}NO_4S$) 374.1426 ($M^+$) Found: 374.1431

*cis*-isomer:

$^1$H NMR: (400 MHz, $CDCl_3$) 7.77 (d, $J$ = 8.2 Hz, 2H, 8-H x 2), 7.52 (d, $J$ = 9.7 Hz, 1H, NH), 7.36-7.25 (m, 7H, 9-H x 2 and Ph), 6.00 (t, $J$ = 9.7 Hz, 1H, 5-H), 4.99 (d, $J$ = 12.1 Hz, 1H, 12-H$^a$), 4.90 (d, $J$ = 12.1 Hz, 1H, 12-H$^b$), 4.45 (t, $J$ = 9.7 Hz, 1H, 4-H), 2.79-2.72 (m, 1H, 3-H), 2.42-2.37 (m, 4H, 2-H$^a$ and 11-$H_3$), 2.22 (dd, $J$ = 16.9, 10.6 Hz, 1H, 2-H$^b$), 0.93 (d, $J$ = 6.8 Hz, 3H, 6-$H_3$); $^{13}$C NMR: (100 MHz, $CDCl_3$) 173.6 (s, C-1), 143.4 (s, C-10), 137.3 (s, C-7), 135.4 (s, C-*i*), 129.5 (d), 128.6 (d), 128.4 (d), 128.2 (d), 126.9 (d, C-8), 122.3 (d, C-5), 117.4 (d, C-4), 66.5 (t, C-12), 41.4 (t, C-2), 26.9 (d, C-3), 21.5 (q, C-11), 21.0 (q, C-6); HRMS: (CI, 70 eV) Calculated ($C_{20}H_{24}NO_4S$) 374.1426 ($M^+$) Found: 374.1428

**Benzyl (*E*)-3,4-dimethyl-5-phthaloylamino-4-pentenoate (3ga)**



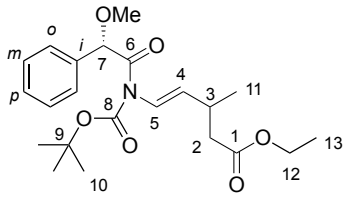

To a solution of tributhyl{(*E*)-1-phthaloylamino-2-methyl-but-2-en-1-yl}stannane **1g** (0.533 mmol, 0.270 g) and iodo benzylacetate **2a** (0.786 mmol, 0.217 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product as a viscous liquid. The mixture was purified by HPLC to give the *E*-isomer **3ga-*E*** as a viscous liquid (0.0932 g,

48%) and *Z*-isomer **3ga-*Z*** as a viscous liquid (0.0756 g, 39%).

*E*-isomer: IR: (neat) 1768(COO), 1725 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.88-7.83 (m, 2H, 10-H x 2), 7.75-7.71 (m, 2H, 11-H x 2), 7.40-7.28 (m, 5H, Ph), 5.99 (s, 1H, 5-H), 5.19 (d, *J* = 12.3 Hz, 1H, 12-$H^a$), 5.15 (d, *J* = 12.3 Hz, 1H, 12-$H^b$), 2.97 (sext, *J* = 7.0 Hz, 1H, 3-H), 2.60 (dd, *J* = 14.7, 7.0 Hz, 1H, 2-$H^a$), 2.47 (dd, *J* = 14.7, 7.0 Hz, 1H, 2-$H^b$), 1.63 (s, 3H, 7-$H_3$), 1.20 (d, *J* = 7.0 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.8 (s, C-1), 166.8 (s, C-8), 143.9 (s, C-4), 135.8 (s, C-*i*), 134.0 (d, C-11), 131.9 (s, C-5), 128.4 (d), 128.3 (d), 128.1 (d), 123.3 (d, C-10), 112.8 (d, C-5), 66.3 (t, C-12), 40.1 (t, C-2), 37.0 (d, C-3), 18.9 (q, C-6), 13.8 (q, C-7); HRMS: (CI, 70 eV) Calculated ($C_{22}H_{22}NO_4$) 364.1549 ($[M + H]^+$) Found: 364.1554

*Z*-isomer: IR: (neat) 1767(COO), 1725 (NCO) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.87-7.82 (m, 2H, 10-H x 2), 7.75-7.25 (m, 2H, 11-H x 2), 7.30-7.25 (m, 5H, Ph), 5.84 (q, *J* = 1.5 Hz, 1H, 5-H), 5.11 (d, *J* = 12.3 Hz, 1H, 12-$H^a$), 5.02 (d, *J* = 12.3 Hz, 1H, 12-$H^b$), 3.01 (sext, *J* = 7.2 Hz, 1H, 3-H), 2.55 (dd, *J* = 14.8, 7.2 Hz, 1H, 2-$H^a$), 2.36 (dd, *J* = 14.8, 7.2 Hz, 1H, 2-$H^b$), 1.84 (d, *J* = 1.5 Hz, 3H, 7-$H_3$), 1.13 (d, *J* = 7.2 Hz, 3H, 6-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.7 (s, C-1), 167.4 (s, C-8), 144.7 (s, C-4), 135.8 (s, C-*i*), 134.0 (d, C-11), 131.9 (s, C-5), 128.3 (d), 127.9 (d), 127.9 (d), 123.4 (d, C-10), 112.4 (d, C-5), 66.2 (t, C-12), 39.2 (t, C-2), 31.8 (d, C-3), 17.9 (q, C-6), 15.4 (q, C-7); HRMS: (CI, 70 eV) Calculated ($C_{22}H_{22}NO_4$) 364.1549 ($[M + H]^+$) Found: 364.1547

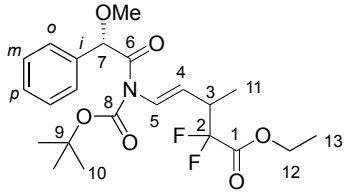
**Ethyl (*E*)-5-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido}-3-methyl pent-4-enoate (3hj)**




To a solution of (1*S*,2*E*)-1-{*N*-(*S*)-2-methoxy-2-phenylacetyl-*N*-*tert*-butoxycarbonylamino}but-2-en-1-yl tributhylstannane **1h** (0.489 mmol, 0.298 g) and iodo ethylacetate **2j** (1.54 mmol, 0.330 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3hj** as colorless viscous liquid (0.163 g, 82%) as the mixture of diastereomers (d.r. = 72:28). Only spectrum data of a major isomer is listed below. IR: (neat) 1734 (NCO), 1650 (COOEt)

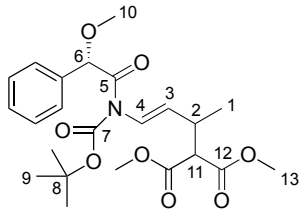
$cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.40-7.31 (m, 5H, Ph), 6.23 (d, $J$ = 14.0 Hz, 1H, 5-H), 5.65 (s, 1H, 7-H), 5.37 (m, 1H, 4-H), 4.16-4.07 (m, 2H, 12-$H_2$), 3.39 (s, 3H, OMe), 2.75 (sept, $J$ = 7.3 Hz, 1H, 3-H), 2.34 (dd, $J$ = 15.0, 7.3 Hz, 1H, 2-$H^a$), 2.27 (dd, $J$ = 15.0, 7.3 Hz, 1H, 2-$H^b$), 1.43 (s, 9H, O*t*Bu), 1.24 (t, $J$ = 7.3 Hz, 13-$H_3$), 1.08 (d, $J$ = 7.3 Hz, 3H, 11-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.2 (s), 171.9 (s), 152.1 (s, C-8), 135.9 (s, C-*i*), 129.9 (s, C-4), 128.5 (d), 128.4 (d), 128.2 (d), 123.6 (d, C-5), 83.6 (s, C-9), 83.0 (d, C-7), 60.3 (t, C-12), 57.5 (q, OMe), 41.4 (t, C-2), 31.7 (d, C-3), 27.6 (q, C-10), 19.9 (q, C-11), 14.1 (q, C-13); HRMS: ($FAB^+$, 70 eV) Calculated ($C_{22}H_{32}NO_6$) 406.2230 ($[M + H]^+$) Found: 406.2231

**Ethyl (*E*)-5-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido}-3-methyl pent-4-enoate (3he)**



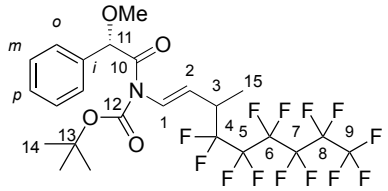

To a solution of (1*S*,2*E*)-1-{*N*-(*S*)-2-methoxy-2-phenylacetyl-*N*-*tert*-butoxycarbonylamino}but-2-en-1-yl tributhylstannane **1h** (0.501 mmol, 0.305 g) and perfluorohexyl iodide **2e** (1.58 mmol, 0.320 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3he** as colorless viscous liquid (0.161 g, 73%) as the mixture of diastereomers (d.r. = 78:22). Only spectrum data of a major isomer is listed below. IR: (neat) 1758 (NCOO), 1665 (COOEt) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.38-7.32 (m, 5H, Ph), 6.44 (d, $J$ = 14.2 Hz, 5-H), 5.61 (s, 1H, 7-H), 5.31 (dd, $J$ = 14.2, 9.2 Hz, 1H, 4-H), 4.35-4.26 (m, 2H, 12-$H_2$), 3.38 (s, 3H, OMe), 3.03-2.92 (m, 1H, 3-H), 1.44 (s, 9H, O*t*Bu), 1.29 (t, $J$ = 7.2 Hz, 3H, 13-$H_3$), 1.16 (d, $J$ = 7.0 Hz, 3H, 11-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 171.9 (s, C-6), 163.5 (s, C-1, t by $^2J_{19F\text{-}C}$ = 22.8 Hz), 151.7 (s, C-8), 135.6 (s, C-*i*), 128.6 (d), 128.4 (d), 128.1 (d), 127.6 (d), 119.1 (d, C-4), 116.1 (s, C-2, t by $^1J_{19F\text{-}C}$ = 254 Hz), 84.2 (s, C-9), 82.9 (d, C-7), 62.7 (t, C-12), 57.4 (q, OMe), 40.0 (d, C-3, t by $^2J_{19F\text{-}C}$ = 22.9 Hz), 27.4 (q, C-10), 13.8 (q, C-13), 12.8 (q, C-11); HRMS: ($FAB^+$, 70 eV) Calculated ($C_{22}H_{30}F_2NO_6$) 442.2041 ($[M + H]^+$) Found: 442.2038

**Dimethyl 2-[4-{(*S*)-*N*-(*tert*-butoxycarbonyl)-2-methoxy-2-phenylacetamido} butan-2-yl]malonate (3hh)**



To a solution of (1*S*,2*E*)-1-{*N*-(*S*)-2-methoxy-2-phenylacetyl-*N*-*tert*-butoxycarbonylamino}but-2-en-1-yl tributhylstannane **1h** (0.489 mmol, 0.298 g) and dimethyl bromomalonate **2h** (1.49 mmol, 0.314 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air (not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3hh** as colorless viscous liquid (0.189 g, 86%) as the mixture of diastereomers (d.r. = 73:27). Only spectrum data of a major isomer is listed below. IR: (neat) 1745 (NCO), 1663 (COOMe) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.39-7.31 (m, 5H, Ph), 6.30 (d, $J$ = 14.4 Hz, 1H, 4-H), 5.62 (s, 1H, 6-H), 5.38 (dd, $J$ = 14.4 , 9.2 Hz, 1H, 3-H), 3.72 (s, 3H, 13-$H^a_3$), 3.71 (s, 3H, 13-$H^b_3$), 3.37 (s, 3H, 10-$H_3$), 3.31 (d, $J$ = 7.7 Hz, 1H, 11-H), 3.00 (sext, $J$ = 7.7 Hz, 1H, 2-H), 1.44 (s, 9H, O*t*Bu), 1.10 (d, $J$ = 7.7 Hz, 3H, 1-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.1 (s, C-5), 168.3 (s, C-12), 168.2 (s, C-12), 151.9 (s, C-7), 135.8 (s, C-*i*), 128.5 (d), 128.3 (d), 128.1 (d), 126.1 (d, C-4), 125.2 (d, C-3), 83.8 (s, C-8), 82.9 (d, C-6), 57.4 (q, C-10), 57.3 (d, C-11), 52.4 (q, C-13), 35.4 (d, C-2), 27.6 (q, O*t*Bu), 18.3 (q, C-1); HRMS: ($FAB^+$, 70 eV) Calculated ($C_{23}H_{32}NO_8$) 450.2128 ($[M + H]^+$) Found: 450.2124

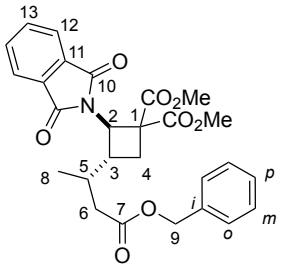
***tert*-Butyl {(*S*)-2-methoxy-2-phenylacetyl}{(*E*)-4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-3-methylnon-1-en-1-yl}carbamate (3hi)**



To a solution of (1*S*,2*E*)-1-{*N*-(*S*)-2-methoxy-2-phenylacetyl-*N*-*tert*-butoxycarbonylamino}but-2-en-1-yl tributhylstannane **1h** (0.5 mmol, 0.305 g) and perfluorohexyl iodide **2i** (1.48 mmol, 0.662 g) in MeCN (1 mL) was added 1 M triethylborane in hexane (0.5 mmol, 0.5 mL) at 0 °C. Then 3 mL of air

(not dried) was introduced via syringe, and the mixture was stirred at -20 °C for 6 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **3hi** as colorless viscous liquid (0.159 g, 50%) as the mixture of diastereomers (d.r. = 79:21). Only spectrum data of a major isomer is listed below. IR: (neat) 1743 (NCOO), 1669 (NCOC) $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) 7.40-7.31 (m, 5H, Ph), 6.43 (d, $J$ = 14.5 Hz, 1H, 1-H), 5.64 (s, 3H, 11-H), 5.39 (dd, $J$ = 14.5, 9.5, 1H, 2-H), 3.39 (s, 3H, OMe), 3.09-2.98 (m, 1H, 3-H), 1.43 (s, 9H, O*t*Bu), 1.27 (d, $J$ = 6.7 Hz, 3H, 15-$H_3$); $^{13}C$ NMR: (100 MHz, $CDCl_3$) 172.2 (s, C-10), 151.7 (s, C-12), 135.7 (s, C-*i*), 128.7 (d), 128.5 (d), 128.2 (d), 127.6 (d, C-1), 119.0 (d, C-2), 84.4 (s, C-13), 83.1 (d, C-11), 57.5 (q, OMe), 38.6 (td, $^2J_{19F\text{-}C}$ = 23.0), 27.5 (q, C-14), 13.5 (q, C-15); HRMS: ($FAB^+$, 70 eV) Calculated ($C_{24}H_{25}F_{13}NO_4$) 638.1576 ($[M + H]^+$) Found: 638.1566

**Dimethyl 3-{4-(benzyloxy)-4-oxobutan-2-yl}-2-(phthaloylamino)cyclobutane-1,1-dicarboxylate (5)**




Iron trichloride (0.069 mmol, 0.0112 g) was dissolved in $CH_2Cl_2$ (0.5 mL) and the yellow solution was cooled to 0 °C. To the solution was added the mixture of methylene malonate and **3aa** in $CH_2Cl_2$ (2 mL) dropwise. The reaction mixture was stirred at room temperature for 3 h. Then water (5 mL) was added and the mixture was extracted with AcOEt (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7:3) to give the product **5** as colorless viscous liquid (0.177 g, 73% yield) as the mixture of diastereomers (d.r. = 63:37). $^1H$ NMR: (400 MHz, $CDCl_3$) a major isomer: 7.85-7.81 (m, 2H, 12-H x 2), 7.75-7.71 (m, 2H, 13-H x 2), 7.38-7.22 (m, 5H, Ph), 5.18 (d, 1H, 2-H), 5.13-5.06 (m, 2H, 9-$H_2$), 3.74 (s, 3H, OMe), 3.60 (s, 3H, OMe), 3.60-3.43 (m, 1H, 3-H), 3.03-2.94 (m, 1H, 4-$H^a$), 2.37-2.28 (m, 1H, 6-$H^a$), 2.16-2.06 (m, 2H, 5-H and 6-$H^b$), 1.83-1.76 (m, 1H, 4-$H^a$), 0.84 (d, $J$ = 6.0 Hz, 3H, 8-$H_3$); a minor isomer: 7.85-7.81 (m, 2H), 7.75-7.71 (m, 2H), 7.38-7.22 (m, 5H), 5.18 (d, 1H), 4.97 (s, 2H), 3.75 (s, 3H), 3.60 (s,

3H), 3.60-3.43 (m, 1H), 3.03-2.94 (m, 1H), 2.37-2.28 (m, 1H), 2.16-2.06 (m, 2H), 1.83-1.76 (m, 1H), 0.93 (d, $J$ = 6.0 Hz, 3H); $^{13}$C NMR: (100 MHz, $CDCl_3$) a major isomer: 172.1 (s, C-7), 170.0 (s, $C$O$_2$Me), 168.2 (s, $C$O$_2$Me), 168.0 (s, C-10), 135.7 (s, C-*i*), 134.2 (d, C-13), 131.5 (s, C-11), 128.5 (d), 128.2 (d), 128.1 (d), 123.4 (d, C-12), 66.2 (t, C-9), 55.2 (s, C-1), 53.0 (q, OMe), 52.9 (q, OMe), 51.7 (d, C-2), 39.5 (d, C-3), 39.0 (t, C-4), 35.6 (d, C-5), 29.0 (t, C-6), 16.6 (q, C-8); a minor isomer: 171.8 (s), 170.1 (s), 168.3 (s), 168.0 (s), 135.6 (s), 134.2 (d), 131.5 (s), 128.4 (d), 128.2 (d), 128.1 (d), 123.3 (d), 66.1 (t), 55.0 (s), 53.0 (q), 52.9 (q), 51.9 (d), 39.4 (d), 38.5 (t), 35.3 (d), 28.9 (t), 16.6 (q); HRMS: (EI, 70 eV) Calculated ($C_{18}H_{10}NO_2$) 493.1737 ($M^+$) Found: 493.1744

## 2-5. Reference


[1] a) A. G.Schultz, P. R. Guzzo, D. M. J. Nowak, *Org. Chem.* **1995**, *60*, 8044. b) M. A. Brodney, A. *J.* Padwa, *Org. Chem.* **1999**, *64*, 556. c) A. Fürstner, T. Dierkes, O. R. Thiel, G. Blanda, *Chem. Eur. J.* **2001**, *7*, 5286. d) D. T. Davies, N. Kapur, Parsons, A. F. *Tetrahedron* **2000**, *56*, 3941.

[2] For recent reviews, see: a) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029. b) J.-A. Ma, *Angew. Chem. Int. Ed.* **2003**, *42*, 4290.

[3] D. H. Lorenz, *Encycl. Polym. Sci. Technol.* **1971**, *14*, 239.

[4] a) L. E. Overman, L. A. Clizbe, *J. Am. Chem. Soc.* **1976**, *98*, 2352. b) A. Charles, M. B. Smith, *J. Org. Chem.* **1988**, *53*, 1161. c) A. R. Katritzky, B. Rachwal, S. Rachwal, *J. Org. Chem.* **1995**, *60*, 3993. (d) C. Gaulon, R. Dhal, T. Chapin, V. Maisonneuve, G. Dujardin, *J. Org. Chem.* **2004**, *69*, 4192.

[5] R. Matsubara, Y. Nakamura, S. Kobayashi, *Angew. Chem. Int. Ed.* **2004**, *43*, 1679.

[6] a) D. L. Galinis, T. C. McKee, L. K. Pannell, J. H. Cardellina, M. R. Boyd, *J. Org. Chem.* **1997**, *62*, 8968. b) K. Suzumura, I. Takahashi, H. Matsumoto, K. Nagai, B. Setiawan, R. M. Rantiamodjo, K. Suzuki, N. Nagano, *Tetrahedron Lett.* **1997**, *38*, 7573. c) K. L. Erickson, J. Beutler, J. H. Cardellina, M. R. Boyd, *J. Org. Chem.* **1997**, *62*, 8188. d) K. A. Dekker, Aiello, J. R. H. Hirai, T. Inagaki, T. Sakakibara, Y. Suzuki, J. F. Thompson, Y. Yamauchi, N. Kojima, *J. Antibiot.* **1998**, *51*, 14. e) B. Kunze, R. Jansen, F. Sasse, G. Hofle, H. Reichenbach, *J. Antibiot.* **1998**, *51*, 1075. f) T. C. McKee, D. L. Galinis, L. K. Pannell, J. H. Cardellina, J. Laasko, C. M. Ireland, L. Murray, R. J. Capon, M. R. Boyd, *J. Org. Chem.* **1998**, *63*, 7805. g) L. Yet, *Chem. Rev.* **2003**, *103*, 4283. h) R. Shen, C. Lin, T. E. J. Bowman, B. J. Bowman, Jr, J. A. Porco, *J. Am. Chem. Soc.* **2003**, *125*, 7889.

[7] (a) H. Mohre, R. Kilian, *Tetrahedron* **1969**, *25*, 5745. (b) T. Kondo, A. Tanaka, S. Kotachi, Y. Watanabe, *J. Chem. Soc., Chem. Commun.* **1995**, 413.

[8] a) C. A. Zuzza, M. B. Smith, *Synth. Commun.* **1987**, *17*, 729. b) A. L. Cambell, G. R. Lenz, *Synthesis*, **1987**, 421. c) R. K. Boeckmann, S. W. Goldstein, M. A. Walters, *J. Am. Chem. Soc.* **1988**, *110*, 8250. d) Lenz, G. R.; Costanza, C.; Lessor, R. A.; Ezell, E. F. *J. Org. Chem.* **1990**, *55*, 1753. e) M. B. Smith, C. J. Wang, P. F. Keusenkothen, B. T. Dembofsky, J. Cl. Fay, C. A. Zezza, T. W. Kwon, J. Sheu, Y. C. Son, R. F. Menezes, *Chem. Lett.* **1992**, 247.

[9] a) J. K. Stille, Y. Becker, *J. Org. Chem.* **1980**, *45*, 2139. b) S. Krompiec, M. Pigulla, M. Krompiec, S. Baj, J. Mrowiec-Białoń, J. Kasperczyk, *Tetrahedron Lett.* **2004**, *45*, 5257. c) B. Neugnot, J.-C. Cintrat, B. Rousseau, *Tetrahedron* **2004**, *60*, 3575.

[10] a) T. Kondo, A. Tanaka, S. Kotachi, Y. Watanabe, *J. Chem. Soc. Chem. Commun.* **1995,** 413. b) L. J. Gooßen, J. E. Rauhaus, G. Deng, *Angew. Chem. Int. Ed.* **2005**, *44*, 4042.

[11] Recent reports: a) T. Ogawa, T. Kiji, K. Hayami, H. Suzuki, *Chem. Lett.* **1991**, 1443. b) T. Hosokawa, M. Takano, Y. Kuroki, S. Murahashi, *Tetrahedron Lett.* **1992**, *33*, 6643. c) L. Jiang, G. E. Job, A. Klapars, S. L. Buchwald, *Org. Lett.* **2003**, *5*, 3667. d) P. Y. S. Lam, G. Vincent, D. Bonne, C. G. Clark, *Tetrahdron Lett.* **2003**, *44*, 4927. e) X. Pan, Q. Cai, D. Ma, *Org. Lett.* **2004**, *6*, 1809. f) V. I. Timokhin, S. S. Stahl, *J. Am. Chem. Soc.* **2005**, *127*, 17888. g) H. Tsujita, Y. Ura, S. Matsuki, K. Wada, T. Mitsudo, T. Kondo, *Angew. Chem. Int. Ed.* **2007**, *46*, 5160. h) Y. Bolshan, R. A. Batey, *Angew. Chem. Int. Ed.* **2008**, *47*, 2109.

[12] a) G. A. Weisenburger, P. *J.* Beak, *Am. Chem. Soc.* **1996**, *118*, 12218. b) D. J. Pippel, G. A. Weisenburger, N. C. Faibish, P. Beak, *J. Am. Chem. Soc.* **2001**, *123*, 4919. The structure of π-allyl lithium is fixed to the anti-syn form by the coordination of Boc group in the allylation of methyl iodide. (See the Supporting Information)

[13] A. Schlapbach, R. W. Hoffmann, *Eur. J. Org. Chem.* **2001**, 323.

[14] a) M. Yasuda, Y. Nagano, H. Yunoki, K. Tsuruwa, A. Baba*Organometallics* **2014**, *33*, 3924. b) K. Suzuki, Y. Nishimoto, H. Yunoki, K. Tsuruwa, N. Esumi, M. Yasuda *Chem. Lett.* **2018**, *47*, 821.

[15] E. Juaristi, G. Cuevas, *Tetrahedron*, **1992**, *48*, 5019.

[16] C. Csuletti, D. Furlani, D. Marton, G. T agliavini, G. Valle, *J. Organomet. Chem.* **1986**, *315*, 287.

[17] Y. Takeyama, Y. Ichinose, K. Oshima K. Utimoto, *Tetrahedron Lett.* **1989**, *30*, 3159.

[18] a) The Chemistry of Cyclobutanes (Eds.: Z. Rappoport, J. F. Liebman), Wiley, Chichester, 2005. b) G. JimØnez-OsØs, F. Corzana, J. H. Busto, M. PØrez-Fernµndez, J. M. Peregrina, A. Avenoza, *J. Org. Chem.* **2006**, *71*, 1869. c) A. Fernµndez-Tejada, F. Corzana, J. H. Busto, G. JimØnez-OsØs, J. M. Peregrina, A. Avenoza, *Chem. Eur. J.* **2008**, *14*, 7042

[19] F. Nanteuil, J. Waser, *Angew. Chem. Int. Ed.* **2013**, *52*, 9009.

[20] Aminoallyl stannane **1h** was prepared from Boc protection of [Tributyl{(1*S*,2*E*)-1-[(*S*)-2-

methoxy-2-phenylacetylamino]-2-butenyl}stannane which was prepared by separation of diastereomers with our previous method (ref 14b). (See Supporting Information)

[21] The absolute configuration of the product was determined by X-ray analysis of the substrate X which was derived from the product.

[22] I. Suzuki, N. Esumi, M. Yasuda, A. Baba, *Chem. Lett.* **2015**, *44*, 38.

[23] D. P. Curran, J. Tamine, *J. Org. Chem.* **1991**, *56*, 2746.

[24] M. M. Lakouraj, M. Tajbakhsh, M. Mokhtary, *J. Chem. Res.* **2005**, *8*, 481.

[25] A. Chandra, K. N. Par ida, J. N. Moorthy, *Tetrahedron* **2017**, *73*, 5827.

[26] D. Meyer, P. Renaud, *Angew. Chem. In. Ed.* **2017**, *56*, 10858.

[27] K. Suzuki, Y. Nishimoto, H. Yunoki, K. Tsuruwa, N. E sumi, M. Yasuda, *Chem. Lett.* **2018**, *47*, 821.

[28] F. Nanteuil, J. Waser, *Angew. Chem. Int. Ed.* **2013**, *52*, 9009.

## Chapter 3. (*o*-Phenylenediamino)borylstannanes: Efficient Reagents for Borylation of Various Alkyl Radical Precursors

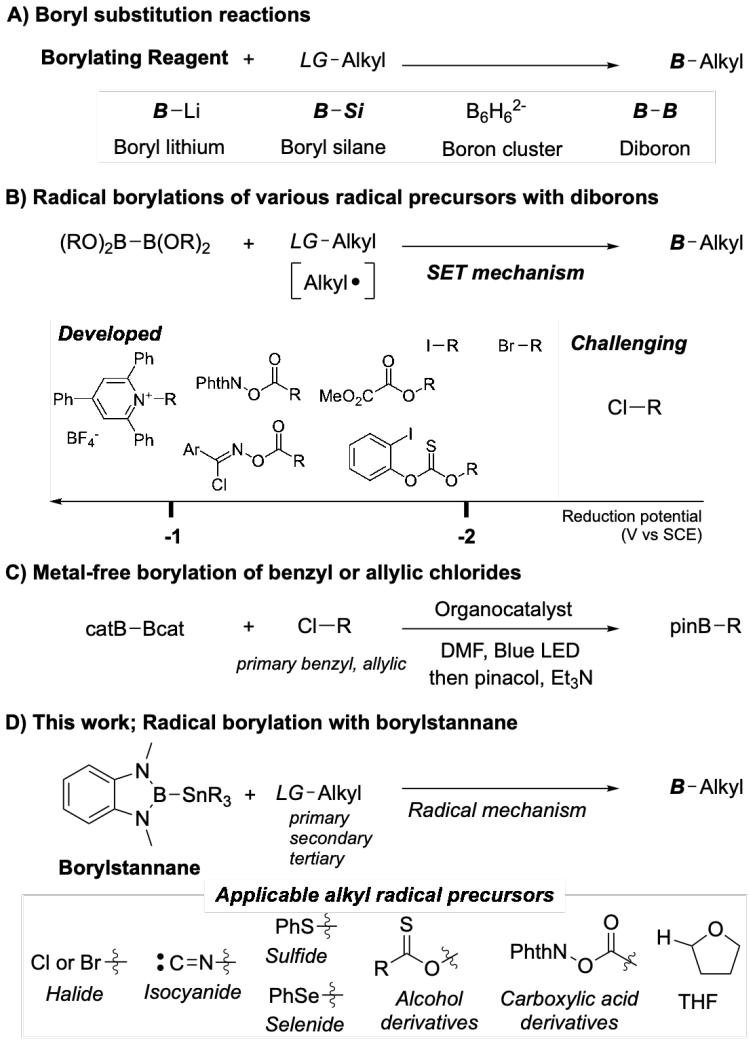
### 3-1. Introduction

Alkyl boronates represent valuable synthetic intermediates that are readily transformed into various functional compounds.[1–6] Therefore, much effort has been spent into the development of efficient synthetic methods. Amazing progress has been made in transition-metal-catalyzed borylations.[7–10] On the other hand, protocols mediated by main-group-element reagents without transition metal catalysts have also been promising. Electrophilic borylation of organometallic compounds[11] and hydroboration of alkenes[12] are recognized as practical methods, but these methods suffer from incompatibility with functional groups and poor regioselectivity, respectively. Several borylating reagents have been used to accomplish boryl substitution reactions leading to alkyl boronates without transition metal catalysts (Figure 1A). Boryllithium has been employed in the borylation of alkyl chlorides,[13] but their high level of reactivity narrows both the substrate scope and the functional group tolerance. Although borylsilanes act as borylating reagents, applicable substrates are limited to primary alkyl bromides and silylation proceeds as an unavoidable side-reaction.[14] Boron dianion cluster ($B_6H_6^{2-}$) reacts with primary and secondary sulfonates as well as primary alkyl bromides and iodides to give alkylboronic esters,[15] but only one boron atom in the cluster is consumed for C-B bond formation and other boron atoms become waste. Recently, trapping alkyl radical intermediates by diboron compounds has opened a new avenue for the access to various aliphatic boronic esters (Figure 1B).[16] To date, various radical precursors including alkyl halides,[17–21] carboxylic acid,[22–26] amine,[27–29] and alcohol derivatives[30–32] have been revealed as applicable substrates for radical borylations. Available substrates are restricted, however, by their own reduction potentials because the generation of alkyl radical intermediates from the substrates relies on single electron transfer (SET) in almost all cases. Therefore, the use of alkyl chlorides as substrates remains challenging due to their lower reduction potentials (Table S1) regardless of the ready availability. Melchiorre has reported the borylation of alkyl chlorides using an organocatalyst (Figure 1C), but the applicable substrates are limited to primary benzylic and allylic chlorides.[19]

Herein, we report that (*o*-phenylenedamino)borylstannanes were newly synthesized and employed as borylating reagents to access aliphatic boronates from various alkyl chlorides including secondary and tertiary ones (Figure 1D). Borylstannanes were used for radical reactions for the first time. The present method allows the borylation of isocyanides, selenides, sulfides, and alcohol or carboxylic acid derivatives. In particular, this is the first report of radical borylative desulfurization and deselenation.

In addition, radical C($sp^3$)-H borylation of THF was achieved using photoexcited aryl ketone via the process of hydrogen atom transfer (HAT).

**Figure 1.** (A) Borylating reagents giving aliphatic boron compounds in boryl substitutions. (B) Radical borylations using diborons and the chart of reduction potentials of each radical precursor. (C) Borylation of alkyl chlorides using a nucleophilic organocatalyst. (D) This work; Radical borylation with borylstannane.

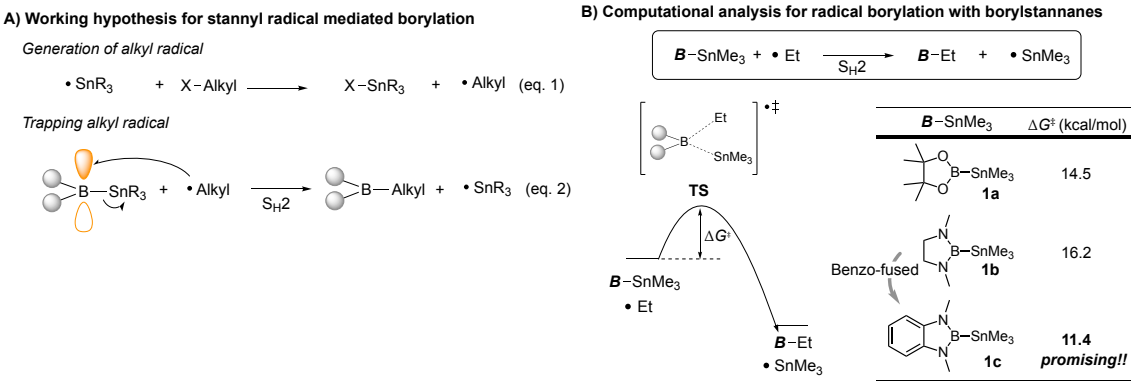



## 3-2. Results and Discussion

A working hypothesis for radical borylation with borylstannanes is depicted in Figure 2A. First, trialkylstannyl radicals react with alkyl radical precursors (X-Alkyl) to afford alkyl radicals (eq. 1).[33,34] Next, the reaction of borylstannanes with the alkyl radicals proceeds via an $S_H2$ mechanism (eq. 2).[35–37] To examine candidates that could be efficient borylstannanes, we estimated the activation

energy of the reaction of alkyl radicals with borylstannanes via DFT calculation (Figure 2B). The reaction of pinacolateborylstannane **1a** with an ethyl radical proceeded via the $S_H2$ mechanism, and its activation energy is a feasible value. A synthetic method for **1a**, however, has unfortunately not been developed, which likely is because of its unstable nature.[38] A higher activation barrier was estimated for reaction of the known isolable borylstannane **1b**, which possesses an ethylenediamino group.[39,40] The present radical borylation would proceed via the interaction of a vacant *p*-orbital at the boron atom with the SOMO of the alkyl radical (eq. 2). Therefore, we expected phenylenediaminoborylstannane **1c** to improve the efficiency of radical borylation, because the energy level of the LUMO, which includes the vacant *p*-orbital of the boron atom, is lowered by the benzo-fusion on the ethylenediaminoboryl group to allow a more feasible interaction with the SOMO of alkyl radicals. In fact, the activation energy of the borylation using **1c** is lower than that of either **1a** or **1b**.

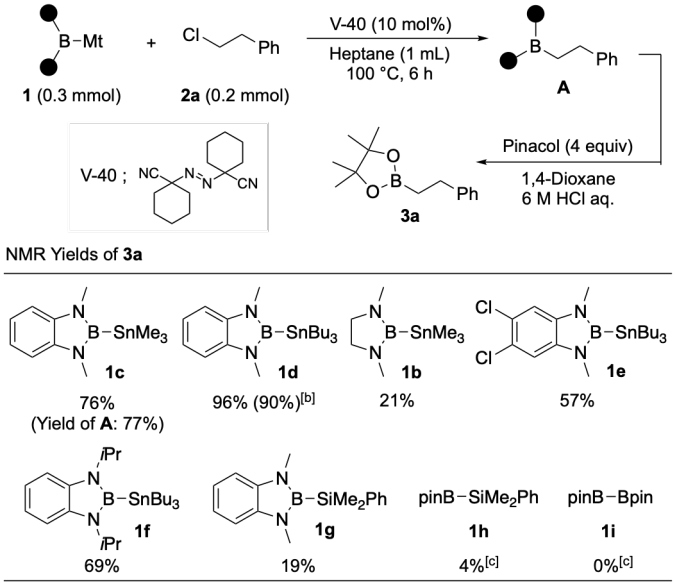
**Figure 2.** (A) Working hypothesis for borylation using borylstannanes. (B) Computational studies of the radical borylation step using borylstannane **1a-1c** ((U)M062X/6-31+G(d,p) for H, B, C, N, O and LANL2DZ for Sn).




We started screening borylating reagents in the borylation of alkyl chloride **2a** based on our calculation results (Table 1). The synthesis of borylstannanes **1c-1f** was successfully achieved via electrophilic substitution of (*o*-phenylenediamino)borylbromides with stannyllithium. They were isolated using silica gel column chromatography and kept at room temperature under a nitrogen atmosphere. In particular, borylstannane **1c** was characterized by X-ray crystallographic analysis, which revealed a trigonal planar structure for the boron center and a tetrahedral structure for the tin center. The bond length of B-Sn (2.249(4) Å) is longer than the reported B-Si (2.03 Å) bond of (pin)B-$SiPhMe_2$.[41] By using (phenylenediamino)borylstannane **1c,** the reaction of **2a** in the presence of V-

40 as a radical initiator at 100 °C successfully gave the borylated product **A**. Because the formed diamonoboryl product **A** was too air-sensitive for storage, it was treated with pinacol under acidic conditions to quantitatively form the alkylboronate **3a** as an isolable compound. Tributylstannyl-substituted one **1d** proved to be the best borylating reagent. In contrast, the reaction of **1b** resulted in a low yield as expected from the calculated result discussed in Figure 2. Dichloro-substituted borylstannane **1e** gave a lower yield than **1d**. *N*,*N*'-di-isopropyl-substituted borylstannane **1f** afforded a moderate yield probably owing to the steric hindrance. Borylsilanes (**1g** and **1h**) and diboron **1i** both failed in reactions that were either sluggish or non-existent, respectively. These results underscore the advantage of a stannyl radical over either silyl or boryl radicals in terms of the proposed radical chain mechanism (Figure 2A). Our extensive screening of radical initiators, solvents and reaction temperatures is described in the Supporting Information (Tables S2-3).

**Table 1**. Comparison of Reactivities Between Borylating Reagents in the Reaction of Phenethyl Chloride **2a**[a]

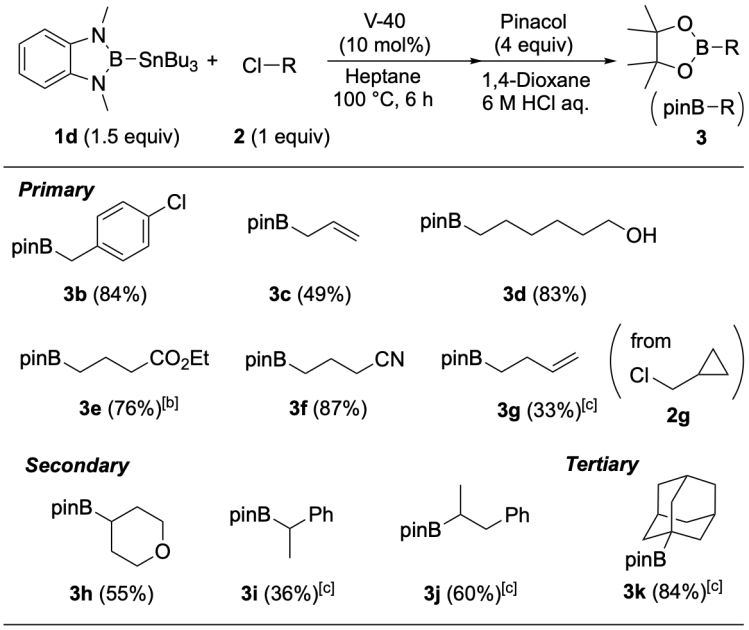



[a] Borylating reagent **1** (0.3 mmol), 2-phenethyl chloride **2a** (0.2 mmol), V-40 (0.02 mmol), and heptane (1 mL) at 100 °C for 6 h; pinacol (0.8 mmol), 1,4-dioxane (1 mL), 6 M HCl aq (1 mL), rt, 2 h. Yields were determined by $^1$H NMR analysis. [b] The yield of isolated product **3a** is shown. [c] Without pinacol treatment.

With the optimized conditions in hand, the scope of alkyl chlorides was evaluated (Table 2). *p*-Chlorobenzyl chloride successfully underwent borylation to give boronate **3b** with an intact aryl chloride moiety.[42] Allyl chloride also gave the allyl boronate **3c**, which shows the alkene moiety is tolerated, but the yield was moderate because the stability and less reactivity of the allyl radical

disturbs the borylation. Primary alkyl chlorides bearing hydroxy, ethoxycarbonyl, and cyano groups were converted into the corresponding boronates (**3d**-**3f**) in high yields. The reaction of cyclopropylmethyl chloride **2g** gave the ring-opening product **3g** exclusively,[43] which supported the radical mechanism. It is noteworthy that secondary and tertiary alkyl chlorides were applicable to the present borylation in contrast to the previous reactions.[19] 4-Chlorotetrahydropyran and 1-phenethyl chloride worked well to afford the target products (**3h** and **3i**). 2-Chloro-1-phenylpropane turned out to be a suitable substrate for this reaction, giving boronate **3j**. 1-Chloroadamane smoothly provided the corresponding boronate **3k**.

**Table 2.** Substrate Scope of Alkyl Chlorides[a]

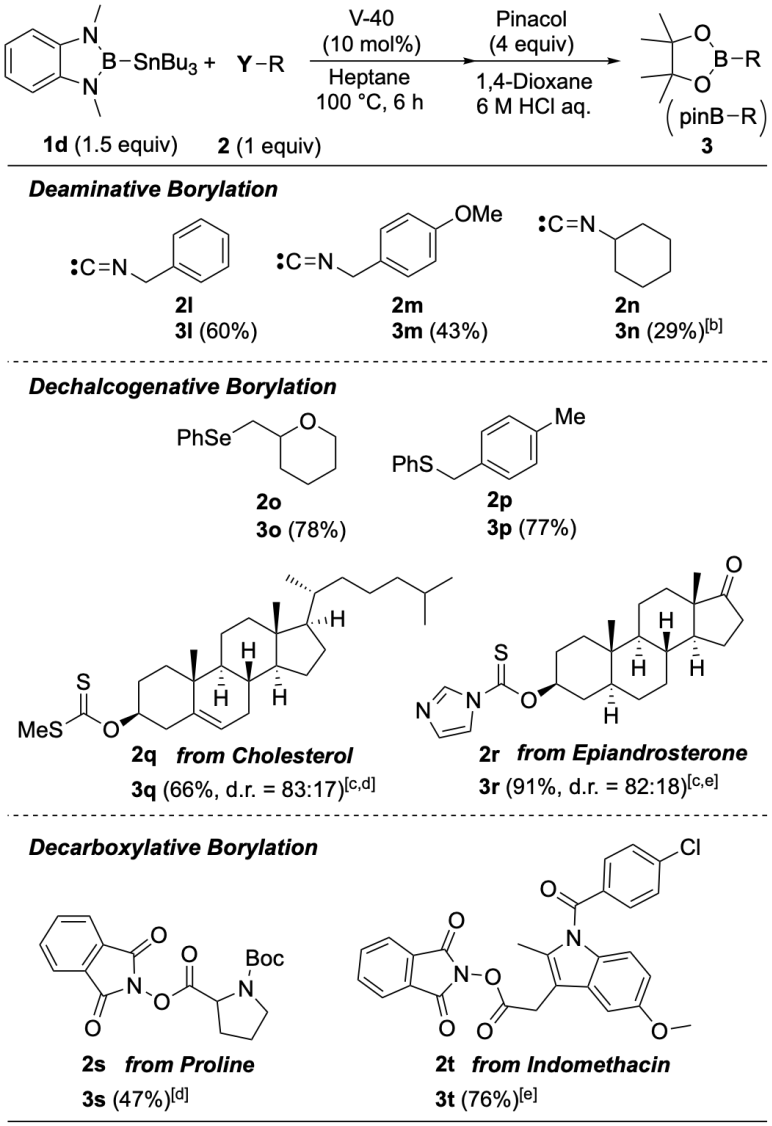



[a] Borylstannane **1d** (0.6 mmol), alkyl chloride **2** (0.4 mmol), V-40 (0.04 mmol), and heptane (2 mL) at 100 °C for 6 h; pinacol (1.6 mmol), 1,4-dioxane (2 mL), 6 M HCl aq (2 mL), rt, 2 h. Yields of isolated products are shown. [b] TsOH•$H_2O$ (4 equiv) was used instead of HCl. [c] Borylstannane **1d** (0.6 mmol), alkyl chloride **2** (0.2 mmol), V-40 (0.1 mmol).

Borylstannane **1d** was applied to the reaction with other alkyl radical sources instead of alkyl chlorides (Table 3). Deaminative borylation of isocyanides, which are readily prepared from amines, was accomplished under the same conditions as the borylation of alkyl chlorides. Benzylic isocyanides (**2l**, **2m**) and cyclohexyl isocyanide **2n** were transformed into the corresponding boronic esters.[44] Deselenative borylation of phenyl selenide **2o** proceeded to give β-oxyboronic esters. *p*-Methylbenzyl phenyl sulfide **2p** was used as a radical precursor and the radical borylative desulfurization proceeded in a good yield.[45] Xanthate **2q** from cholesterol and thionocarbamate **2r** from epiandrosterone reacted

with the retention of stereochemistry and good diastereoselectivity. Decarboxylative borylation of phthalimide esters (**2s**, **2t**) from proline and indomethacin successfully afforded the corresponding products.

**Table 3**. A Series of Radical Boprylations Using Various Radical Sources[a]

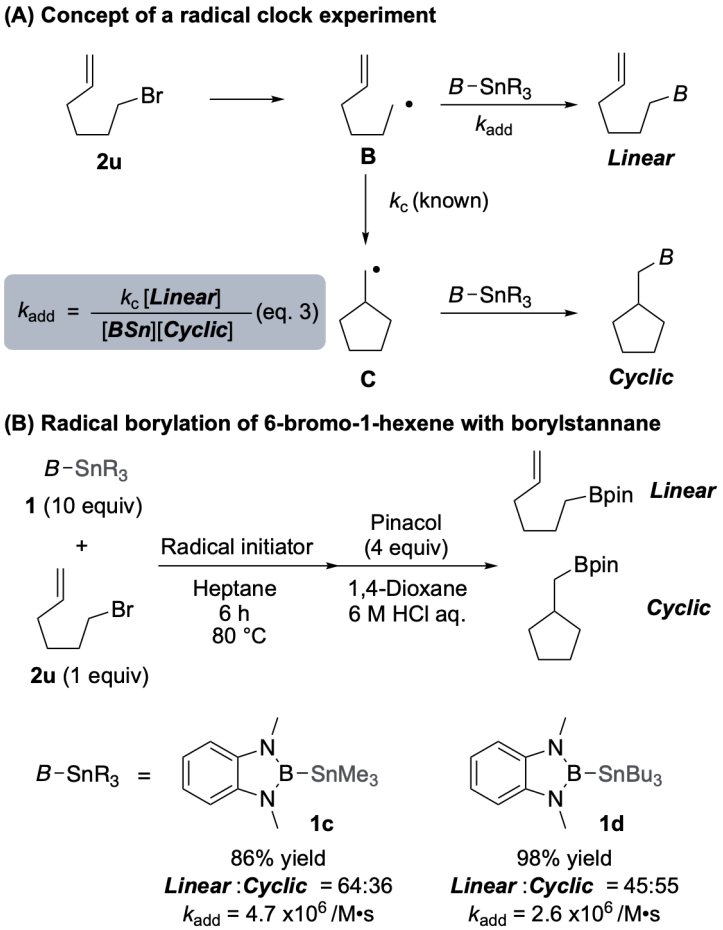



[a] Borylstannane **1d** (0.3 mmol), alkyl radical precursor **2** (0.2 mmol), V-40 (0.02 mmol), and heptane (1 mL) at 100 °C for 6 h; pinacol (0.8 mmol), 1,4-dioxane (1 mL), 6 M HCl aq (1 mL), rt, 2 h. Yields of isolated products are shown. [b] Reaction temperature: 120 °C. [c] Borylstannane **1d** (0.6 mmol), alkyl radical precursor **2** (0.2 mmol), V-40 (0.1 mmol). [d] $TsOH \cdot H_2O$ (4 equiv) was used instead of HCl. [e] 1,4-Dioxane was used instead of heptane.

We performed radical clock experiments[46–48] to evaluate the reaction rate for the $S_H2$ step. 6-Bromo-1-hexene **2u** was reacted with an excess amount of borylstannane **1** (Figure 3). The pseudo-

first-order rate constant for the homolytic substitution reaction of the borylstannane with 5-hexen-1-yl radical **B** was estimated from the product ratio (***Linear***/***Cyclic***), the concentration of borylstannane, and the known cyclization rate constant (Figure 3A, eq. 3). Then, the rate constants for radical borylations of 5-hexen-1-yl radical **B** using **1c** and **1d** at 80 °C were estimated to be 4.7 x $10^6$ /M·s and 2.6 x $10^6$ /M·s, respectively (Figure 3B). These rate constants for the borylation of 5-hexen-1-yl radical **B** were found to be slightly larger than that for the reduction with $Bu_3SnH$ (1.1 x $10^6$ /M·s at 80 °C).[48] In addition, the radical clock experiment was performed at different reaction temperatures and an Eyring plot gave the activation parameters: $\Delta H^{\ddagger}$ (2.68 kcal/mol), $\Delta S^{\ddagger}$ (22.0 cal/mol·K), and the activation energy $\Delta G^{\ddagger}$ (9.23 kcal/mol) (Figure S4). The experimental value of $\Delta G^{\ddagger}$ almost matched the calculations (11.4 kcal/mol in Figure 2B).

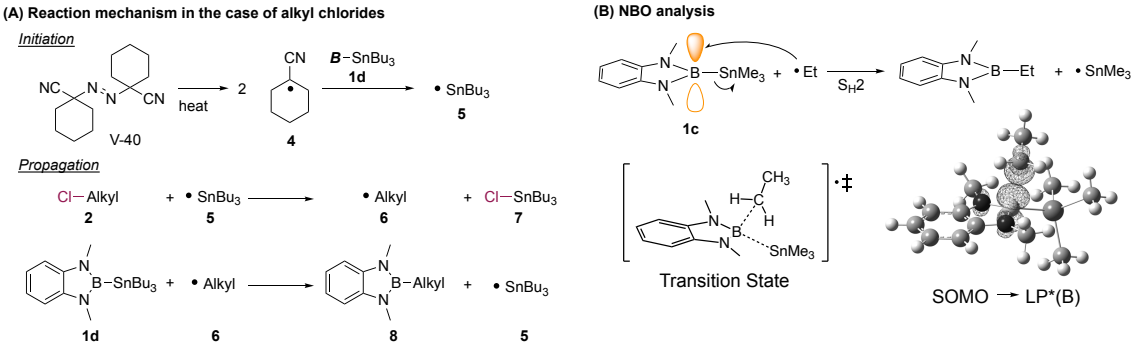
**Figure 3.** (A) Concept of the radical clock experiment using borylstannane. (B) Radical borylation of 6-bromo-1-hexene with borylstannane **1c** and **1d**.




The reaction mechanism for borylation of alkyl chlorides is presented in Figure 4A. In this reaction, alkyl radical **4** generated from the decomposition of V-40 reacts with borylstannane **1d** to form

tributylstannyl radical **5**. The generated stannyl radical **5** reacts with alkyl chloride **2**, which leads to alkyl radical **6** and stannyl chloride **7**. The radical **6** is trapped by borylstannane **1d** to give the corresponding borylated product **8**, and stannyl radical **5** is regenerated. NBO analysis for the transition state of the $S_H2$ reaction between the ethyl radical and borylstannane **1c** revealed a significant interaction between SOMO (ethyl radical) and LP* (boron) (Figure 4B). This interaction is evident in the α spin-set and is estimated to amount to 49.8 kcal/mol. Considering the fact that the vacant *p*-orbital of the boron plays a vital role in the $S_H2$ mechanism, we evaluated the LUMOs of **1b** and **1c** (Figure 4C). In the case of **1c**, the vacant *p*-orbital of the boron effectively conjugates with the orbital on the phenylenediamine structure to delocalize the LUMO. On the other hand, the vacant *p*-orbital of the boron in **1b** is isolated. Therefore, the lower energy level of the LUMO of **1c** allows a larger interaction with the SOMO of the alkyl radical, which enables efficient borylation.

**Figure 4.** (A) Reaction mechanism when using alkyl chlorides. (B) Gauss View representation of key orbitals for the transition state. (SOMO --> LP*(boron) (49.8 kcal/mol) (UM062X/6-31+G(d,p) for H, B, C, N and LANL2DZ for Sn). (C) Unoccupied molecular orbitals of **1b** and **1c** (M062X/6-31+G(d,p) for H, B, C, N and LANL2DZ for Sn)



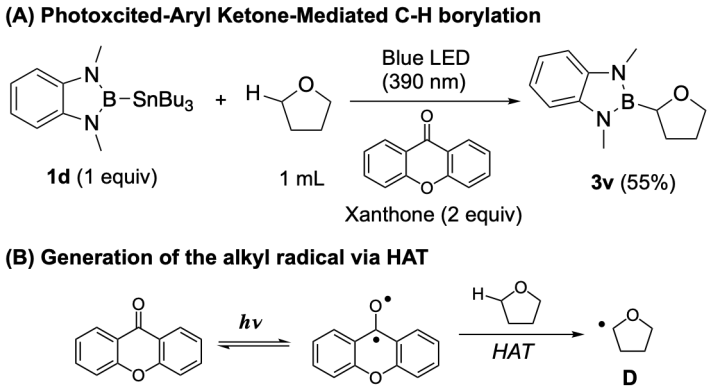

**(C) Comparison of unocupied MOs of 1b with 1c**

| Boryl stannane | Picture of MO | Energy level |
|---|---|---|
| B–SnMe3 (**1b**) | LUMO+1 | 0.26 eV |
| B–SnMe3 (**1c**) | LUMO | 0.023 eV |

Instead of a borylation of the carbon-heteroatom bond using a radical initiator, we tackled C-H borylation with borylstannane via a radical pathway. Aggarwal reported the attractive C($sp^3$)-H

borylation of alkanes via HAT.[49] In our strategy, the HAT process undergoes by using the triplet state of aryl ketone to access alkyl radicals.[50–52] Therefore, via the use of xanthone under light irradiation, a radical C-H borylation of THF with borylstannane **1d** was carried out. Gratifyingly, the mono-borylated product **3v** was obtained (Scheme 1-A). The key for this reaction was the generation of a nucleophilic radical **D** via the HAT of a photoexcited aryl ketone (Scheme 1-B and Figure S7).

**Scheme 1.** (A) Radical C-H borylation of THF with borylstannane. Borylstannane **1d** (0.1 mmol), THF (1 mL), and xanthone (0.2 mmol) at room temperature under visible light irradiation for 12 h. An NMR yield of the product **3v** is shown. (B) The key step for generating an alkyl radical.




## 3-3. Conclusion

We have developed novel borylstannanes for borylating reagents. Various types of alkyl radical precursors were successfully applied toward dehalogenative-, deaminative-, dechalgenative-, decarboxylative-, and C($sp^3$)-H borylation. The *o*-phenylenediamino structure in borylstannanes enables high efficiency for trapping alkyl radicals via $S_H2$ reactions. The present method provides a useful approach for syntheses of alkyl boronates, which are widely used in organic synthesis. Further investigations into the utility of borylstannanes in radical reactions are now under way.

## 3-4. Experimental Section

### General Information

Commercial reagents were purchased from Aldrich, Tokyo Chemical Industry Co., Ltd. (TCI), Nacalai Tesque, Inc. or FUJIFILM Wako Pure Chemical Corporation, Ltd., and were used without prior purification. Reactions were carried out in dried solvents under a nitrogen atmosphere. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Column chromatography was conducted with silica gel. Purification by GPC was conducted using

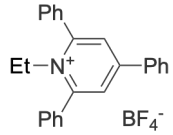
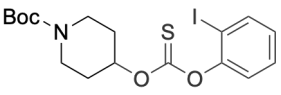
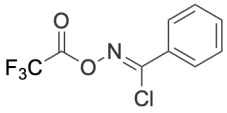
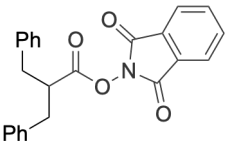
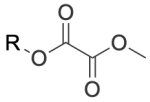
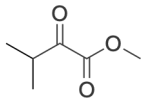
Japan Analytical Industry Co. (NEXT recycling preparative HPLC). NMR spectra were recorded on JEOL JNM-400 (400 MHz for $^{1}H$ NMR, 100 MHz for $^{13}C$ NMR, 127 MHz for $^{11}B$ NMR, and 150 MHz for $^{119}Sn$ NMR) spectrometer. Chemical shifts were reported in ppm on the δ scale relative to tetramethylsilane (δ = 0 for $^{1}H$ NMR) and residual $CHCl_3$ (δ = 77.0 for $^{13}C$ NMR) as an internal reference, and boron trifluoride diethyl etherate (δ = 0 for $^{11}B$ NMR) and $Me_4Sn$ (δ = 0 for $^{119}Sn$ NMR) as an external reference. New compounds were characterized by $^{1}H$, $^{13}C$, $^{13}C$ off-resonance techniques, COSY, HMQC, and HMBC. Positive EI and CI high-resolution mass spectra were recorded on a magnetic sector type mass spectrometer (JEOL JMS-700). Data collection for X-ray crystal analysis was performed on a Rigaku/XtaLAB Synergy-S/Cu diffractometer.

**Materials**

Dehydrated solvents including hexane, heptane, benzene, toluene, 1,4-dioxane, tetrahydrofurane, acetonitrile, dimethyl sulfioxide were purchased from FUJIFILM Wako Pure Chemical Industries, Ltd.. Borylstannane **1b** was synthesized by a known method.[53] The preparation and characterization of new borylstannanes (**1c**-**1f**) and borylsilane **1g** are described below. Borylsilanes **1h** and bis(pinacolato)diboron **1i** were purchased from TCI. Alkyl chlorides (**2a**-**2i**, **2k**) and isocyanides (**2l**, **2n**) were purchased. The preparation and characterization of isocyanide **2m**, selenide **2o**, and sulfide **2p** are described below. Alkyl chloride **2j**,[54] xanthate (**2q**, **2r**),[55] and phthalimide esters (**2s**,[56] **2t**[57]) were prepared from known methods.

**Reduction Potentials of Radical Precursors**

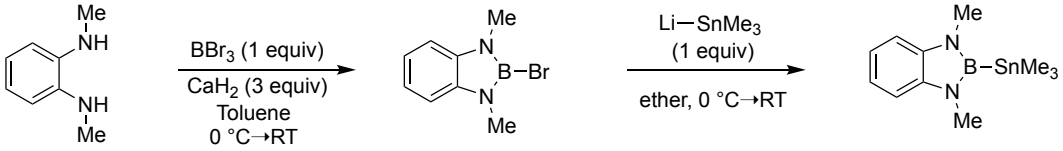
**Table S1**. Reduction Potentials of Radical Precursors.

| Substrate | Reduction potential (V vs SCE) | Substrate | Reduction potential (V vs SCE) |
|---|---|---|---|
|  Katrizky's pyridium salt | -0.93[58] |  2-iodophenyl thionocarbonate | -1.90[59] -2.35 (V vs $Fc/Fc^+$) |
|  *N*-hydroxy-benzimidoyl chloride | -1.09[60] | Et—I Iodo ethane | -1.90[61] |
|  Phthalimide ester | -1.34[62] | Et—Br Bromo ethane | -2.13[63] |
|  Alkyl mehtly oxalate | no report[a] | Et—Cl Chloro ethane | -2.79[65] |
|  (similar compound as alkyl mehtyl oxalate) | -1.75[54] | | |

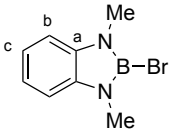
[a]There is no report on the reduction potential of the alkyl mehtyl oxalates, but they are reported to be one-electron reduced by the excited $Ir(ppy)_3$ ($E$ (Ir(Ⅲ)*/Ir(Ⅳ)) = -1.73 V vs SCE)[55].

**Synthesis and Characterization of Borylating Reagents**

**1,3-Dimethyl-2-(trimethylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1c)**



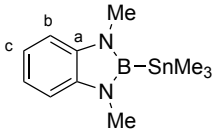

**1) 2-Bromo-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole**




The borylbromide was synthesized using the reported protocol.[66] To a slurry of calcium hydride (4.41 g, 105 mmol) in toluene (105 mL) precooled at 0 °C were added a solution of boron tribromide (8.76 g, 34.9 mmol) in toluene (70 mL) and a solution of *N*,*N*'-dimethyl-*o*-phenylene diamine (4.76 g, 34.9 mmol) in toluene (70 mL) slowly at the same time at 0 °C. Then, the slurry was stirred for 4 h at room temperature. The reaction mixture was filtered under nitrogen atmosphere. The filtrate was concentrated under nitrogen atmosphere. The residue was purified by distillation under reduced pressure (0.16 Torr) to afford the target product as a white solid (5.74 g, 25.5 mmol, 73% yield).

**bp:** 88 °C (0.16 Torr); **mp:** 45-48 °C; **$^1$H NMR: (400 MHz, $CDCl_3$)** 7.04-6.95 (m, 4H, b-H x 2 and c-H x 2), 3.29 (s, 6H, Me x 2); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 137.4 (s, C-a), 119.4 (d), 108.5 (d), 29.5 (q, Me); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 24.1 ; **HRMS: (EI, 70 eV)** Calculated ($C_8H_{10}BrN_2B$) 224.0120 ($M^+$) Found: 224.0119

**2) 1,3-Dimethyl-2-(trimethylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1c)**




Trimethyltin lithium was prepared with Uchiyama's method.[67] To a solution of naphthalene (0.0641 g, 0.5 mmol) in THF (20 mL) were added lithium clippings (0.0208 g, 30 mmol). The resulting mixture started turning dark green and was stirred at room temperature for 1 h under nitrogen atmosphere. Then, trimethyltin chloride (1.99 g, 10 mmol) was added dropwise and the mixture was stirred at room temperature for 4 h. The mixture was concentrated under reduced pressure in a nitrogen-filled glove box. After the residue was diluted with ether, the precipitated white solid and the unreacted lithium clippings was filtered off. The resulting solution of trimethyltin lithium in ether was added to a solution of 2-bromo-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (2.25 g, 10 mmol) in ether (10 mL) at 0 °C. Then, the mixture was stirred for 1 h at room temperature. The mixture was filtered through short silica gel pad with hexane. The filtrate was concentrated and the residue was purified by silica gel column chromatography (hexane, column length 20 cm, diameter 26 mm silica gel) to give the pure product as a white solid (1.48 g, 4.79 mmol, 48% yield).

**mp:** 40-43 °C; **$^{1}$H NMR: (400 MHz, $CDCl_3$)** 7.11 (s, 4H, b-H x 2 and c-H x 2), 3.51 (s, 6H, NMe x 2), 0.30 (m, 9H, $SnMe_3$, d by $^{2}J_{119Sn-H}$ = 49.7 Hz, d by $^{2}J_{117Sn-H}$ = 47.6 Hz); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 138.9 (s, C-a), 118.9 (d), 108.2 (d), 31.7 (q, NMe), -11.1 (q, $SnMe_3$); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 33.8; **$^{119}$Sn NMR: (150 MHz, $CDCl_3$)** -149 (q, $^{1}J_{Sn-B}$ = 928 Hz); **HRMS: (EI, 70 eV)** Calculated ($C_{11}H_{19}N_2BSn$) 310.0663 ($M^+$) Found: 310.0669

X-ray crystallographic data of 1,3-Dimethyl-2-(trimethylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (**1c**) CCDC 2038341

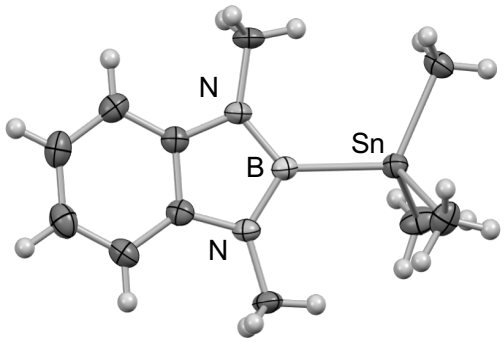
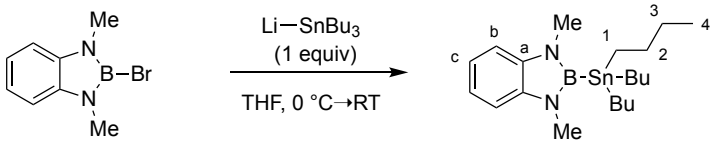



**Figure S1.** ORTEP drawing of 1,3-Dimethyl-2-(trimethylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole **1c** at the 50% probability level.

Empirical formula = $C_{11}H_{19}BN_2Sn$
Formula weight = 308.78
Crystal system = triclinic
Space group = P-1
a/Å = 7.2659(4)
b/Å = 8.3393(4)
c/Å = 11.6883(7)
$\alpha$ /° = 77.594(4)
$\beta$ /° = 88.776(4)
$\gamma$ /° = 80.211(4)
Volume/Å$^3$ = 681.53(7)
Z value = 2
F(000) = 308.0
Radiation CuKα (λ = 1.54184)
Data/restraints/parameters = 2757/0/141
Goodness-of-fit on $F^2$ = 1.041
Temperature = -150 ℃
$R_1$ [I>=2σ(I)] = 0.0414
$wR_2$ [all data] = 0.1088

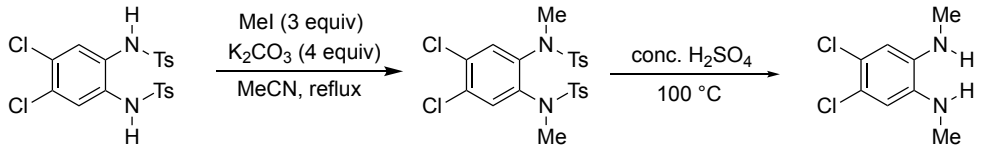
**Synthesis of 1,3-dimethyl-2-(tributylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1d)**



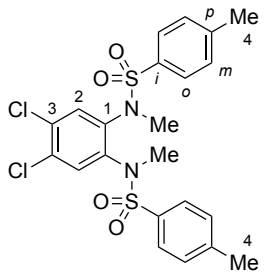

Tri-*n*-butyltin lithium was prepared with Uchiyama's method.[67] To a solution of naphthalene (0.0886 g, 0.692 mmol) in THF (28 mL), were added lithium clippings (0.288 g, 41.5 mmol). The resulting mixture started turning dark green and was stirred at room temperature for 1 h under nitrogen atmosphere. Then, tri-*n*-butyltin chloride (4.50 g, 13.8 mmol) was added dropwise and the mixture was stirred at room temperature for 4 h. The resulting solution of tri-*n*-butyltin lithium was added to a solution of 2-bromo-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2] diazaborole (3.11g 13.8 mmol) in THF (14 mL) at 0 °C. Then, the mixture was stirred for 1 h at room temperature. The mixture was filtered through short silica gel pad with hexane. The filtrate was concentrated and the residue was purified by silica gel column chromatography (hexane, column length 20 cm, diameter 26 mm silica gel) to give the pure product as a colorless liquid (3.33 g, 7.65 mmol, 55% yield).

**$^{1}$H NMR: (400 MHz, $CDCl_3$)** 7.05 (s, 4H, b-H x 2 and c-H x 2), 3.45 (s, 6H, NMe x 2), 1.66-1.44 (m, 6H, 2-$H_2$ x 3), 1.40-1.25 (m, 6H, 3-$H_2$ x 3), 1.09-0.81 (m, 15H, 1-$H_2$ x 3 and 4-$H_3$ x 3); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 139.2 (s, C-a), 118.7 (d), 108.1 (d), 31.9 (q, NMe), 30.2 (t, C-2, d by $^{2}J_{Sn\text{-}C}$ = 18.0 Hz), 27.6 (t, C-3, d by $^{3}J_{Sn\text{-}C}$ = 54.1 Hz), 13.7 (q, C-4), 7.83 (t, C-1, d by $^{1}J_{119Sn\text{-}C}$ = 294 Hz, d by $^{1}J_{117Sn\text{-}C}$ = 283 Hz); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 34.6 ; **$^{119}$Sn NMR: (150 MHz, $CDCl_3$)** -135 (q, $^{1}J_{Sn\text{-}B}$ = 747 Hz); **HRMS: (EI, 70 eV)** Calculated ($C_{20}H_{37}N_2BSn$) 436.2072 ($M^+$) Found: 436.2065

**Synthesis of 4,5-dichloro-*N*,*N*'-dimethylbenzene-1,2-diamine**




**1) *N*,*N*'-(4,5-Dichloro-1,2-phenylene)bis(*N*,4-dimethylbenzenesulfonamide)**

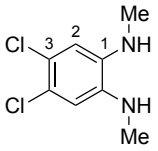



To a solution of *N*,*N*'-(4,5-dichloro-1,2-phenylene)bis(4-methyl benzenesulfonamide) (11.9 g, 24.5 mmol) and $K_2CO_3$ (10.4 g, 73.5 mmol) was added iodomethane (13.6 g, 98.1 mmol). The reaction mixture was heated to reflux overnight. After the mixture was cooled to room temperature, the solvent was evaporated under reduced pressure. To the resulting white precipitate was added water (150 ml) and $CHCl_3$ (150 ml). The layers were separated, and the aqueous layer was extracted three times with $CHCl_3$. The combined organic layer

was dried over $MgSO_4$ and the volatiles were evaporated under reduced pressure. The residue was recrystallized from $CHCl_3$ and hexane to give the target product as a white solid (10.6 g, 20.6 mmol, 84 % yield).

**mp:** 215-220 °C; **$^1$H NMR: (400 MHz, $CDCl_3$)** 7.71 (d, $J$ = 8.5 Hz, 4H, *o*-H x 4), 7.38 (d, $J$ = 8.5 Hz, 4H, *m*-H x 4), 6.95 (s, 2H, 2-H x 2), 3.16 (s, 6H, NMe x 2), 2.48 (s, 6H, 4-$H_3$ x 2); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 144.2 (s, C-*p*), 140.6 (s, C-1), 133.9 (s, C-*i*), 132.6 (s, C-3), 129.9 (d), 129.7 (d), 128.2 (d, C-*o*), 38.5 (q, NMe), 21.6 (q, C-4); **HRMS: (EI, 70 eV)** Calculated ($C_{22}H_{22}Cl_2N_2O_4S_2$) 512.0398 ($M^+$) Found: 512.0389

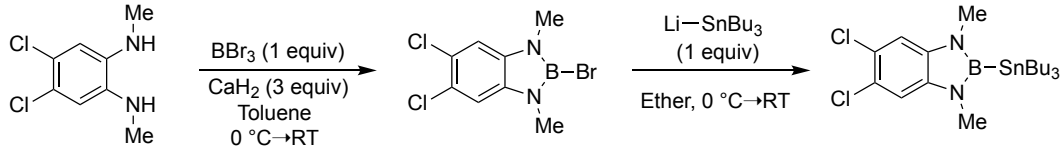
**2) 4,5-Dichloro-*N*,*N*'-dimethylbenzene-1,2-diamine**



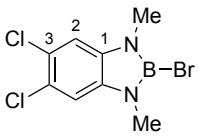

*N*,*N*'-(4,5-Dichloro-1,2-phenylene)bis(*N*,4-dimethylbenzenesulfonamide) (10.6 g, 20.6 mmol) was dissolved in 98% aq. $H_2SO_4$ (50 mL). The mixture was heated to 90 °C and was stirred for 4 h. After the mixture was cooled to room temperature, the reaction mixture was poured into ice and the pH was adjusted to ~11 using NaOH aq. The generated purple solid was filtered and the residue was dissolved in $CHCl_3$. The solution was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The solid was recrystallized from $CHCl_3$ and hexane at 0 °C to give colorless needles (4.02 g, 16.8 mmol, 82% yield).

**mp:** 117-118 °C; **$^1$H NMR: (400 MHz, $CDCl_3$)** 6.61 (s, 2H, 2-H x 2), 3.25 (br, 2H, N*H*Me x 2), 2.80 (s, 6H, NH*Me* x 2); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 138.0 (s, C-1), 121.4 (s, C-3), 111.4 (d, C-2), 30.9 (q, NHMe); **HRMS: (EI, 70 eV)** Calculated ($C_8H_{10}Cl_2N_2$) 204.0221 ($M^+$) Found: 204.0216

**Synthesis of 5,6-dichloro-1,3-dimethyl-2-(tributylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2] diazaborole (1e)**




**1) 2-Bromo-5,6-dichloro-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole**

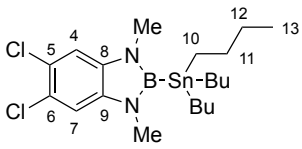



The borylbromide was synthesized using the reported protocol.[66] To a slurry of calcium hydride (2.36 g, 56.0 mmol) in toluene (56 mL) precooled at 0 °C were added a solution of boron tribromide (4.86 g, 18.7 mmol) in toluene (37 mL) and a solution of 4,5-dichloro-*N*,*N*'-dimethylbenzene-1,2-diamine (3.83 g, 18.7 mmol) in toluene (37 mL) slowly at the same time at 0 °C. Then, the slurry was stirred for 4 h at room temperature. After the reaction mixture was filtered in a nitrogen-filled glove box, the filtrate was concentrated under reduced

pressure. The resulting solid was recrystallized from $CHCl_3$ and hexane at 0 °C to form a purple solid (2.72 g, 9.35 mmol, 50% yield).

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.01 (s, 2H, 2-H x 2), 3.27 (s, 6H, NMe x 2); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 136.9 (s, C-1), 122.9 (s, C-3), 109.8 (d, C-2), 29.7 (q, NMe); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 24.8

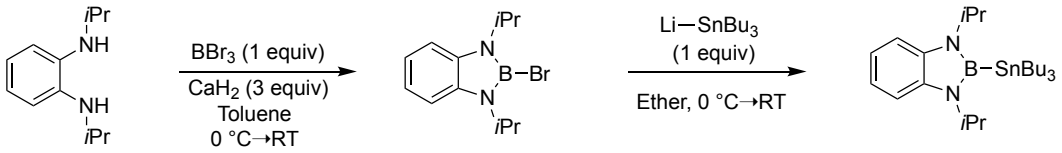
**2) 5,6-Dichloro-1,3-dimethyl-2-(tributylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1e)**



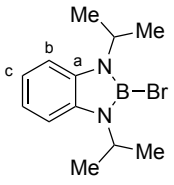

Tri-*n*-butyltin lithium was prepared with Uchiyama's method.[67] To a solution of naphthalene (0.0160 g, 0.125 mmol) in THF (5 mL), were added lithium clippings (0.0520 g, 7.50 mmol). The resulting mixture started turning dark green and was stirred at room temperature for 1 h under nitrogen atmosphere. Then, tri-*n*-butyltin chloride (0.814 g, 2.50 mmol) was added dropwise and the mixture was stirred at room temperature for 4 h. The mixture was concentrated under reduced pressure in a nitrogen-filled glove box. After the residue was diluted with ether, the precipitated white solid and the unreacted lithium clippings was filtered off. The resulting solution of tri-*n*-butyltin lithium in ether was added to a solution of 2-bromo-5,6-dichloro-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (0.734 g, 2.50 mmol) in THF (2.5 mL) and ether (2.5 mL) at 0 °C. Then, the mixture was stirred for 1 h at room temperature. The mixture was filtered through short silica gel pad with hexane. The filtrate was concentrated and the residue was purified by silica gel column chromatography (hexane, column length 20 cm, diameter 26 mm silica gel) to give the pure product as colorless liquid (0.540 g, 1.07 mmol, 43% yield).

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.05 (s, 2H, b-H x 2), 3.40 (s, 6H, NMe x 2), 1.68-1.47 (m, 6H, 2-$H_2$ x 3), 1.40-1.29 (m, 6H, 3-$H_2$ x 3), 1.12-0.89 (m, 15H, 1-$H_2$ x 3 and 4-$H_3$ x 3); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 138.7 (s, C-a), 122.3 (s, C-c), 109 (d, C-b), 32.0 (q, NMe), 30.2 (t, C-2, d by $^2J_{Sn\text{-}C}$ = 18.8 Hz), 27.5 (t, C-3, d by $^3J_{Sn\text{-}C}$ = 54.9 Hz), 13.7 (q, C-4), 7.78 (t, C-1, d by $^1J_{119Sn\text{-}C}$ = 300 Hz, d by $^1J_{117Sn\text{-}C}$ = 287 Hz); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 35.8 ; **$^{119}$Sn NMR: (150 MHz, $CDCl_3$)** -137 (q, $^1J_{Sn\text{-}B}$ = 785 Hz); **HRMS: (EI, 70 eV)** Calculated ($C_{20}H_{35}N_2Cl_2BSn$) 504.1292 ($M^+$) Found: 504.1292

**Synthesis of 1,3-diisopropyl-2-(tributylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1f)**



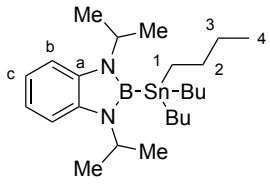

**1) 2-Bromo-1,3-diisopropyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole**




The borylbromide was synthesized using the reported protocol.[66] To a slurry of calcium hydride (5.49 g, 130 mmol) in toluene (130 mL) precooled at 0 °C were added a solution of boron tribromide (10.9 g, 43.5 mmol) in toluene (85 mL) and a solution of *N*,*N*'-diisopropylbenzene-1,2-diamine (8.36 g, 43.5 mmol) in toluene (85 mL) slowly at the same time at 0 °C. (*N*,*N*'-diisopropylbenzene-1,2-diamine was prepared with the known method.[68]) Then, the slurry was stirred for 4 h at room temperature. The reaction mixture was filtered under nitrogen atmosphere. The filtrate was concentrated under nitrogen atmosphere. The residue was purified by distillation under reduced pressure (0.12 Torr) to afford the target product as colorless oil (4.61 g, 16.4 mmol, 38% yield). The NMR spectra are in agreement with the literature report.[69]

**bp:** 88 °C (0.12 Torr); **$^{1}$H NMR: (400 MHz, $CDCl_3$)** 7.22-7.20 (m, 2H), 6.99-6.97 (m, 2H), 4.45 (sept, *J* = 7.0 Hz, 2H, NC*H*Me$_2$ x 2), 1.53 (d, *J* = 7.0 Hz, 12H, NCH*Me*$_2$ x 2); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 135.9 (s, C-a), 118.5 (d), 110.5 (d), 46.2 (d, N*C*HMe$_2$), 22.0 (q, NCH*Me*$_2$); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 22.2

**2) 1,3-Diisopropyl-2-(tributylstannyl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1f)**

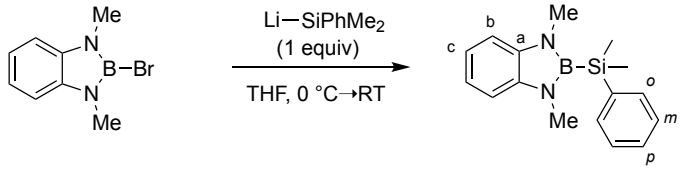



Tributyltin lithium was prepared with Uchiyama's method. To a solution of naphthalene (0.0942 g, 0.0735 mmol) in THF (30 mL) were added lithium clippings (0.306 g, 44.1 mmol). The resulting mixture started turning dark green and was stirred at room temperature for 1 h under nitrogen atmosphere. Then tri-*n*-butyltin chloride (4.78 g, 14.7 mmol) was added dropwise and the mixture was stirred at room temperature for 4 h. The resulting solution was added dropwise to a solution of 2-bromo-1,3-diisopropyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (4.13 g, 14.7 mmol) in THF (30 mL) at 0 °C. Then, the mixture was stirred for 1 h at room temperature. The mixture was filtered through short silica gel pad with hexane. The filtrate was concentrated and the residue was purified by silica gel column chromatography (hexane, column length 20 cm, diameter 26 mm silica gel) to give the pure product as a colorless liquid (5.20 g, 10.6 mmol, 72% yield).

**$^{1}$H NMR: (400 MHz, $CDCl_3$)** 7.30-7.26 (m, 2H), 6.96-6.92 (m, 2H), 4.31 (sept, *J* = 6.8 Hz, 2H, NC*H*Me$_2$ x 2), 1.55-1.43 (m, 18H, 2-H$_2$ x3 and NCH*Me*$_2$ x 2), 1.36-1.25 (m, 6H, 3-H$_2$ x 3), 1.02-0.84 (m, 15H, 1-H$_2$ x 3 and 4-H$_3$ x 3); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 137.5 (s, C-a), 117.8 (d), 111.7 (d), 49.0 (d, N*C*HMe$_2$), 30.2 (t, C-2, d by $^{2}J_{Sn\text{-}C}$ = 18.0 Hz), 27.6 (t, C-3, d by $^{3}J_{Sn\text{-}C}$ = 54.9 Hz), 22.4 (q, NCH*Me*$_2$), 13.7 (q, C-4), 8.48 (t, C-1, d by $^{1}J_{119Sn\text{-}C}$ = 293 Hz, d by $^{1}J_{117Sn\text{-}C}$ = 280 Hz); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 33.6; **$^{119}$Sn NMR: (150 MHz, $CDCl_3$)** -132 (q, $^{1}J_{Sn\text{-}B}$ = 834 Hz); **HRMS: (EI, 70**

**eV)** Calculated ($C_{24}H_{45}N_2BSn$) 492.2698 ($M^+$) Found: 492.2704

**2-{Dimethyl(phenyl)silyl}-1,3-dimethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1g)**




Lithium clippings (0.104 g, 15.0 mmol) were added to THF (5 mL). After the mixture was cooled to 0 °C, phenyldimethylsilyl chloride (0.862 g, 5.05 mmol) was added dropwise. The resulting mixture was stirred at 0 °C for 12 h. The resulting dark-red solution was added dropwise to a solution of 2-bromo-1,3-diisopropyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (1.12 g, 5.00 mmol) in THF (10 mL) at 0 °C. After the addition, the slurry was stirred for 1 h at room temperature. The mixture was filtered through short silica gel column with hexane. The filtrate was concentrated and the residue was purified by column chromatography (hexane, column length 20 cm, diameter 26 mm silica gel) to give the pure product as a white solid (0.540 g, 1.94 mmol, 39% yield).

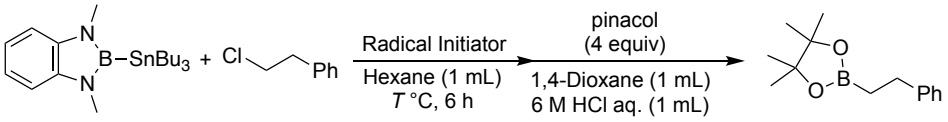
**mp:** 68-69 °C; **$^1$H NMR: (400 MHz, $CDCl_3$)** 7.56-7.54 (m, 2H), 7.33-7.31 (m, 3H), 7.04 (s, 4H), 3.35 (s, 6H, NMe x 2), 0.54 (s, 6H, SiPh*Me*$_2$); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 140.4 (s, C-*i*), 139.0 (s, C-a), 134.2 (d), 128.5 (d), 127.9 (d), 118.9 (d), 108.2 (d), 31.2 (q, NMe), -1.11 (q, SiPh*Me*$_2$); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 30.1; **$^{29}$Si NMR: (78.7 MHz, $CDCl_3$)** -115.9; **HRMS: (EI, 70 eV)** Calculated ($C_{16}H_{21}N_2SiB$) 280.1567 ($M^+$) Found: 280.1572

**Optimization of Reaction Conditions**

**(Table 1)** To an oven-dried 10 mL vial with a magnetic stir bar was added V-40 (0.0049 g, 0.02 mmol), heptane (1 mL), a borylating reagent **1** (0.3 mmol) and 2-phenetyl chloride **2a** (0.0282 g, 0.2 mmol) in a nitrogen-filled glove box. The vial was sealed with a screw cap and heated at 100 °C for 6 h by using a Thermo Mighty Stirrer (HHE-19G-US V). After cooled to room temperature, the solution of 0.8 M pinacol in 1,4-dioxane (1 mL) and 6 M HCl aq. (1 mL) was added and the mixture was stirred at room temperature for 2 h. (When using **1h** and **1i**, this treatment with pinacol was not carried out.) The organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure. 1,1,2,2-tetrachloroethane was added as an internal standard to the crude reaction mixture, and an aliquot was taken for $^1H$ NMR analysis in $CDCl_3$. Formation of the desired product was confirmed by comparing the NMR spectra with those of the reported compound **3a**.


**Figure S2.** The screw vial and the heating system.

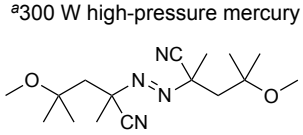
**Table S2.** Screening of radical initiators.



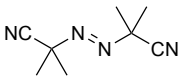

**1d** (1.5 equiv) **2a** (0.2 mmol) **3a**

| Entry | Radical Initiator | *T* °C | NMR Yield (%) |
|---|---|---|---|
| 1 | none | 100 | 0 |
| 2 | AIBN (20 mol%) | 70 | 0 |
| 3 | AIBN (100 mol%) | 70 | 4 |
| 4 | V-70 (20 mol%) | 40 | 0 |
| 5 | V-70 (20 mol%) | 100 | 27 |
| 6 | AIBN (20 mol%) | 100 | 55 |
| 7 | V-40 (20 mol%) | 100 | 95 |
| 8 | V-40 (10 mol%) | 100 | 96 |
| 9 | V-40 (1 mol%) | 100 | 94 |
| 10 | UV Irradiation[a] | RT | 18 |
| 11 | 1 M $Et_3B$ in Hex (1 eq.) / air bubbling | RT | 0 |
| 12 | Benzoyl Peroxide (20 mol%) | 70 | 0 |
| 13 | Lauroyl Peroxide (20 mol%) | 70 | 0 |
| 14 | $NaO_3SOOSO_3Na$ (20 mol%) | 70 | 0 |
| 15 | *t*BuOO*t*Bu (20 mol%) | 70 | 0 |

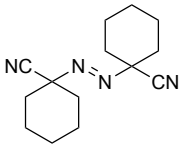
[a]300 W high-pressure mercury lamp through a Pyrex filter.




V-70

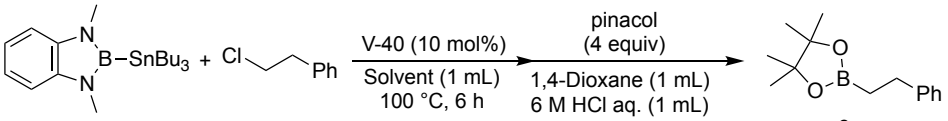



AIBN




V-40

**Table S3.** Screening of solvents.

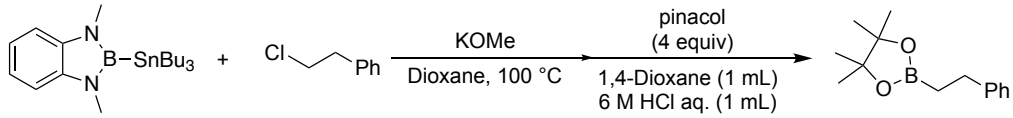



**1d** (1.5 equiv) **2a** (0.2 mmol) **3a**

| Entry | Solvent | Yield (%) |
|---|---|---|
| 1 | Hexane | 96 |
| 2 | Heptane | 96 |
| 3 | Benzene | 95 |
| 4 | Toluene | 70 |
| 5 | 1,4-Dioxane | 87 |
| 6 | THF | 85 |
| 7 | MeCN | 78 |
| 8 | DMSO | 54 |

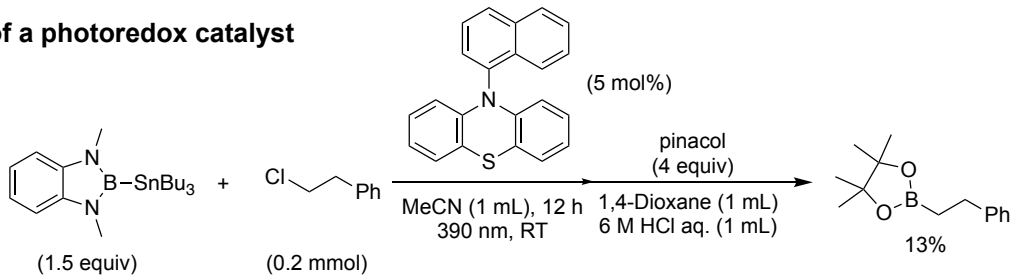
**Scheme S1.** Other reaction systems.

**Use of a strong base**



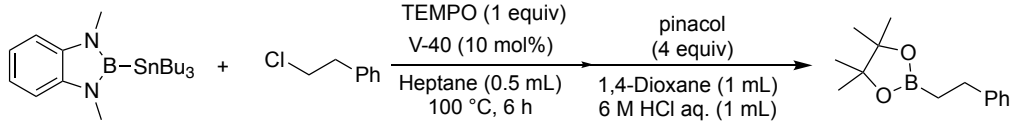

(1.5 equiv) (0.2 mmol) 8%

**Use of a photoredox catalyst**




(1.5 equiv) (0.2 mmol) 13%

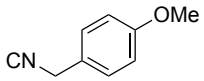
**Addition of TMPO**




(1.5 equiv) (0.1 mmol) 0%

**Synthesis and Characterization of Alkyl Radical Precursors**

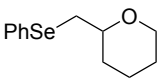
**1-(Isocyanomethyl)-4-methoxybenzene (2m)**




Neat 4-methoxybenzylamine (1.37 g, 10 mmol) was added to methyl formate (1.5 mL) and then the reaction was stirred at 60 °C for 12 h. The solution was concentrated by rotary evaporation. The resulting crude formamide was dissolved in $CH_2Cl_2$ (35 mL), and then *i*-$Pr_2NH$ (2.73 g, 27 mmol) was added. The solution was cooled to -30 °C, and then phosphorous oxychloride (1.69 g, 11 mmol) was added dropwise. After the mixture was stirred at -30 °C for 2 h, the reaction mixture was poured into a saturated aqueous solution of sodium carbonate. The organic layer was separated, and then the aqueous phase was extracted with $CH_2Cl_2$. The combined organic fractions were washed with water, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure, and the crude isonitrile was purified by flash column chromatography on a short pad of silica gel (hexane/ethyl acetate = 50:50) to afford the pure product (1.32 g, 8.97 mmol, 90% yield). The NMR spectra are in agreement with the literature report.[70]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.27 (d, *J* = 8.7 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 4.57 (s, 2H), 3.82 (s, 3H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 159.6, 157.0, 128.0, 124.4, 114.2, 55.3, 45.0; **HRMS: (EI, 70 eV)** Calculated ($C_9H_9NO$) 147.0684 ($M^+$) Found: 147.0685

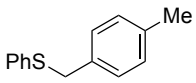
**2-{(Phenylselanyl)methyl}tetrahydro-2*H*-pyran (2o)**




To the solution of 5-hexen-1-ol (0.300 g, 3 mmol) in MeCN (25 mL), diphenyl diselenide (1.56 g, 3 mmol) and then DDQ (1.14 g, 3 mmol) were added and the mixture was stirred at 30 °C for 12 h. The reaction mixture was poured into 10% $Na_2CO_3$ solution to eliminate the formed hydroquinone and extracted with EtOAc. The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude was purified by flash column chromatography on a short pad of silica gel (hexane/ethyl acetate = 90:10) to afford the pure product (1.28 g, 68% yield). The NMR spectra are in agreement with the literature report.[71]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.52-7.50 (m, 2H), 7.28-7.20 (m, 3H), 4.03-3.99 (m, 1H), 3.51-3.37 (m, 2H), 3.08 (dd, *J* =7.0, 12.3 Hz, 1H), 2.93 (dd, *J* =7.0, 12.3 Hz, 1H), 1.86-1.76 (m, 2H), 1.60-1.42 (m, 3H), 1.37-1.27 (m, 1H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 132.3, 130.7, 128.9, 126.6, 77.0, 68.6, 33.6, 31.7, 25.7, 23.2; **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{16}OSe$) 256.0366 ($M^+$) Found: 256.0370

**(4-Methylbenzyl)(phenyl)sulfane (2p)**




To the solution of 4-methylbenzylbromide (1.11 g, 6 mmol) and benzenethiol (0.551 g, 5 mmol) in acetone (5 mL) was added potassium carbonate (1.38 g, 10 mmol). The mixture was refluxed for 24 h and was diluted with water and EtOAc. The organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography to give the pure product (1.07 g, quant.). The NMR spectra are in agreement with the literature report.[72]

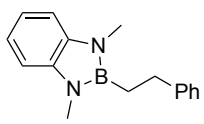
**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.35-7.16 (m, 7H), 7.12-7.07 (m, 2H), 4.11 (s, 2H), 2.34 (s, 3H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 136.7, 136.6, 134.2, 129.5, 129.1, 128.7, 128.6, 126.1, 38.6, 21.0; **HRMS: (EI, 70 eV)** Calculated ($C_{14}H_{14}S$) 214.0816 ($M^+$) Found: 214.0818

**Radical Borylation Using Borylstannane 1d**

**General Procedure 1**

To an oven-dried 10 mL vial with a magnetic stir bar was added V-40, solvent, borylstannane **1d** and alkyl radical precursor in a nitrogen-filled glove box. The vial was sealed with a screw cap and heated at 100 °C for 6 h by using a Thermo Mighty Stirrer (HHE-19G-US V ). After cooled to room temperature, 0.8 M pinacol in 1,4-dioxane (1 mL) and 6 M HCl aq. (2 mL) was added and the mixture was stirred at room temperature for 2 h. The organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by column chromatography to give the pure product.

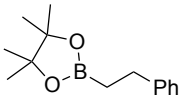
**1,3-Dimethyl-2-phenethyl-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (A)**




To a mixture of **1d** (0.218 g, 0.5 mmol) and 2-phenetyl chloride **2a** (0.141 g, 1 mmol) in heptane (2 mL) was added V-40 (0.0122 g, 0.1 mmol). The reaction mixture was stirred at 100 °C for 6 h. The solvent was removed under reduced pressure and the residue was purified by GPC with chloroform to give the pure product as a white solid (0.0795 g, 64% yield).

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.25-7.14 (m, 5H), 7.00-6.92 (m, 4H), 3.17 (s, 6H, NMe x 2), 2.81 (t, $J$ = 8.0 Hz, 2H, PhC$H_2$), 1.56 (t, $J$ = 8.0 Hz, 2H, BC$H_2$); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 144.2 (s) , 138.3 (s), 128.3 (d), 128.0 (d), 125.6 (d), 118.3 (d), 107.5 (d), 32.2 (t, Ph$C$H$_2$), 29.0 (q, NMe), 12.4 (br, $BCH_2$); **$^{11}$B NMR: (127 MHz, $CDCl_3$)** 31.0; **HRMS: (EI, 70 eV)** Calculated ($C_{16}H_{19}BN_2$) 250.1641 ($M^+$) Found: 250.1646

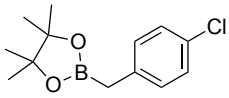
**4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (3a)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2a** (0.0281 g, 0.2 mmol) and V-40 (0.0049 g, 0.02 mmol) in heptane (2 mL) to give the product as colorless oil (0.0416 g, 90% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[73]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.29-7.12 (m, 5H), 2.74 (t, *J* = 8.2 Hz, 2H), 1.21 (s, 12H), 1.14 (t, *J* = 8.2 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 144.4, 128.2, 128.0, 125.5, 83.1, 29.9, 24.8 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{14}H_{21}BO_2$) 232.1635 ($M^+$) Found: 232.1638

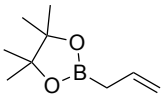
**2-(4-Chlorobenzyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3b)**



According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2b** (0.0644 g, 0.4 mmol) and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0852 g, 84% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[74]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.20 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 2.25 (s, 2H), 1.23 (s, 12H).; **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 137.1, 130.3, 128.3, 83.5, 24.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{13}H_{18}ClBO_2$) 252.1088 ($M^+$) Found: 252.1085

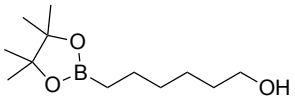
**2-Allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3c)**



According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2c** (0.0306 g, 0.4 mmol) and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0331 g, 49% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[74]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 5.92-5.82 (m, 1H), 5.03-4.92 (m, 2H), 1.73 (d, *J* = 7.2 Hz, 2H), 1.25 (s, 12 H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 134.0, 114.9, 83.2, 24.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_9H_{17}BO_2$) 168.1322 ($M^+$) Found: 168.1321

**6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-1-ol (3d)**

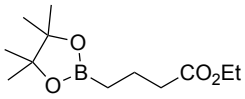


According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2d** (0.0546 g, 0.4 mmol) and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0758 g, 83% yield) after column

chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[75]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 3.63 (quin, *J* = 6.5 Hz, 2H), 1.60-1.53 (m, 2H), 1.46-1.39 (m, 2H), 1.37-1.30 (m, 4H), 1.24 (s, 12H), 0.78 (t, *J* = 7.5 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 82.9, 63.0, 32.7, 32.0, 25.4, 24.8, 23.9 (The signal of the α-B-carbon was not observed.); **HRMS: (CI, 70 eV)** Calculated ($C_{12}H_{26}BO_3$) 228.1975 ($[M+H]^+$) Found: 228.1976

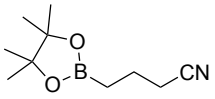
**Ethyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (3e)**




According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol) and alkyl chloride **2e** (0.0602 g, 0.4 mmol), and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL). After the reaction, the solution of pinacol (1.6 mmol) in 1,4-dioxane (2 mL) and $TsOH\cdot H_2O$ (0.152 g, 0.8 mmol) was added and the mixture was stirred for 2 h. Water was added to the reaction mixture and the organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate = 85:15) to give the product as colorless oil (0.0739 g, 76% yield). The NMR spectra are in agreement with the literature report.[75]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 4.09 (q, *J* = 7.0 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.72 (quin, *J* = 7.5 Hz, 2H), 1.24-1.22 (m, 15H), 0.79 (t, *J* = 7.5 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 173.6, 83.0, 60.0, 36.5, 24.8, 19.6, 14.2 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{24}BO_4$) 243.1768 ($M^+$) Found: 243.1767

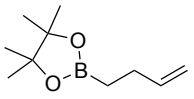
**4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)butanenitrile (3f)**




According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2f** (0.0414 g, 0.4 mmol) and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0680 g, 87% yield) after column chromatography (hexane/ethyl acetate = 80:20). The NMR spectra are in agreement with the literature report.[76]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 2.34 (t, *J* = 7.2 Hz, 2H), 1.79-1.71 (m, 2H), 1.22 (s, 12H), 0.91 (t, *J* = 7.7 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 119.8, 83.3, 24.8, 20.3, 19.1 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{10}H_{18}BNO_2$) 195.1431 ($M^+$) Found: 195.1432

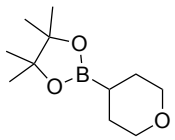
**2-(But-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3g)**



According to the general procedure 1, this compound was prepared from **1d** (0.262 g, 0.6 mmol), **2g** (0.0362 g, 0.4 mmol), and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0273 g, 33% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[77]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 5.94-5.84 (m, 1H), 5.02-4.88 (m, 2H), 2.20-2.14 (m, 2H), 1.24 (s, 12H), 0.89 (t, *J* = 7.7 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 140.6, 113.1, 83.0, 27.9, 24.8 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{10}H_{19}BO_2$) 182.1478 ($M^+$) Found: 182.1481

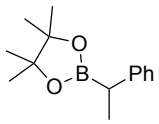
**4,4,5,5-Tetramethyl-2-(tetrahydro-2*H*-pyran-4-yl)-1,3,2-dioxaborolane (3h)**



According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2h** (0.0482 g, 0.4 mmol) and V-40 (0.0098 g, 0.04 mmol) in heptane (2 mL) to give the product as colorless oil (0.0464 g, 55% yield) after column chromatography (hexane/ethyl acetate = 80:20). The NMR spectra are in agreement with the literature report.[78]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 3.83 (td, *J* = 4.0, 8.0 Hz, 2H), 3.50-3.44 (m, 2H), 1.65-1.60 (m, 4H), 1.26-1.25 (m, 13H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 83.1, 68.8, 27.6, 24.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{11}H_{21}BO_3$) 212.1584 ($M^+$) Found: 212.1585

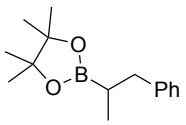
**4,4,5,5-Tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane (3i)**



According to the general procedure 1, this compound was prepared from **1d** (0.262 g, 0.6 mmol), **2i** (0.0281 g, 0.2 mmol), and V-40 (0.0244 g, 0.1 mmol) in heptane (1 mL) to give the product as colorless oil (0.0167 g, 36% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[79]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.27-7.20 (m, 4H), 7.14-7.10 (m, 1H), 2.43 (q, *J* = 7.5 Hz, 1H), 1.33 (d, *J* = 7.5 Hz, 3H), 1.21 (s, 6H), 1.19 (s, 6H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 144.9, 128.2, 127.7, 125.0, 83.2, 24.59, 24.56, 17.0 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{14}H_{21}BO_2$) 232.1635 ($M^+$) Found: 232.1638

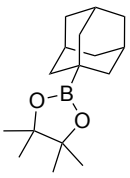
**4,4,5,5-Tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane (3j)**



According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2j** (0.0309 g, 0.2 mmol) and V-40 (0.0244 g, 0.1 mmol) in heptane (1 mL) to give the product as colorless oil (0.0297 g, 60% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[78]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.27-7.13 (m, 5H), 2.81 (dd, *J* = 7.6, 13.6 Hz, 1H), 2.54 (dd, *J* = 8.4, 13.6 Hz, 1H), 1.42-1.32 (m, 1H), 1.19 (s, 6H), 1.18 (s, 6H), 0.97 (d, *J* = 7.2 Hz, 3H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 128.9, 128.0, 125.5, 83.0, 38.9, 24.7, 15.2 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{15}H_{23}BO_2$) 246.1791 ($M^+$) Found: 246.1794

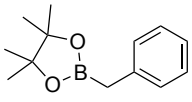
**2-((3*r*,5*r*,7*r*)-Adamantan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3k)**



According to the general procedure 1, this compound was prepared from **1d** (0.263 g, 0.6 mmol), **2k** (0.0341 g, 0.2 mmol), V-40 (0.0244 g, 0.1 mmol) in heptane (1 mL). After the reaction, the solution of pinacol (1.6 mmol) in 1,4-dioxane (2 mL) and TsOH · $H_2O$ (0.152 g, 0.8 mmol) was added and the mixture was stirred at room temperature for 2 h. Water was added to the reaction mixture and the organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate = 95:5) to give the product as a white solid (0.0445 g, 84% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[79]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 1.84 (br s, 3H), 1.75 (br t, *J* = 3.1 Hz, 12H), 1.21 (s, 12H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 82.6, 37.9, 37.5, 27.5, 24.6 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{16}H_{27}BO_2$) 262.2104 ($M^+$) Found: 262.2106

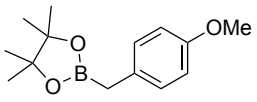
**2-Benzyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3l)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2l** (0.0234 g, 0.2 mmol), and V-40 (0.0049 g, 0.02 mmol) in heptane (1 mL) to give the product as colorless oil (0.0260 g, 60% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[80]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.25-7.10 (m, 5H), 2.29 (s, 2H), 1.23 (s, 12H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 138.6, 129.0, 128.2, 124.8, 83.4, 24.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{13}H_{19}BO_2$) 218.1478 ($M^+$) Found: 218.1475

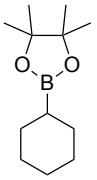
**2-(4-Methoxybenzyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3m)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2m** (0.0294 g, 0.2 mmol) and V-40 (0.0049 g, 0.02 mmol) in heptane (1 mL) to give the product as colorless oil (0.0215 g, 43% yield) after column chromatography (hexane/ethyl acetate = 80:20). The NMR spectra are in agreement with the literature report.[81]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.10 (d, *J* = 8.2 Hz, 2H), 6.79 (d, *J* = 8.2 Hz, 2H), 3.77 (s, 3H), 2.23 (s, 2H), 1.23 (s, 12H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 157.1, 130.5, 129.8, 113.7, 83.3, 55.2, 24.7; **HRMS: (EI, 70 eV)** Calculated ($C_{14}H_{21}BO_3$) 248.1584 ($M^+$) Found: 248.1586

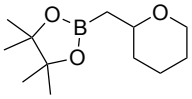
**2-Cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3n)**



According to the general procedure 1, the reaction was carried out at 120 °C. This compound was prepared from **1d** (0.262 g, 0.6 mmol), **2n** (0.0218 g, 0.2 mmol), and V-40 (0.0122 g, 0.1 mmol) in heptane (1 mL) to give the product as colorless oil (0.0120 g, 29% yield) after column chromatography (hexane/ethyl acetate = 90:10). The NMR spectra are in agreement with the literature report.[82]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 1.67-1.56 (m, 5H), 1.38-1.20 (m, 17H), 1.01-0.94 (m, 1H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 82.7, 27.9, 27.1, 26.7, 24.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{23}BO_2$) 210.1791 ($M^+$) Found: 210.1789

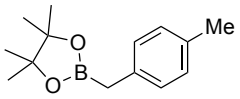
**4,4,5,5-Tetramethyl-2-{(tetrahydro-2*H*-pyran-2-yl)methyl}-1,3,2-dioxaborolane (3o)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2o** (0.0510 g, 0.2 mmol), and V-40 (0.0049 g, 0.02 mmol) in heptane (1 mL) to give the product as colorless oil (0.0351 g, 78% yield) after column chromatography (hexane/ethyl acetate = 80:20).[83]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 3.95-3.92 (m, 1H), 3.54-3.40 (m, 2H), 1.83-1.65 (m, 2H), 1.57-1.40 (m, 3H), 1.25-1.00 (m, 15H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 83.0, 75.5, 68.4, 33.8, 25.8, 24.73, 24.66, 23.72, 20.6; **HRMS: (CI, 70 eV)** Calculated ($C_{12}H_{24}BO_3$) 227.1819 ($[M+H]^+$) Found: 227.1817

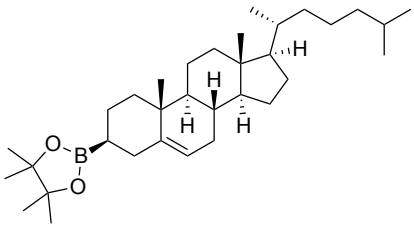
**2-(4-Methylbenzyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2p)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2p** (0.0429 g, 0.2 mmol), and V-40 (0.0049 g, 0.02 mmol) in heptane (1 mL) to give the product as colorless oil (0.0358 g, 77% yield) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[80]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.08 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 2.30 (s, 3H), 2.26 (s, 2H), 1.24 (s, 12H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 135.4, 134.1, 129.0, 128.8, 83.4, 24.7, 21.0 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{14}H_{21}BO_2$) 232.1635 ($M^+$) Found: 232.1637

**3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)cholest-5-ene (3q)**

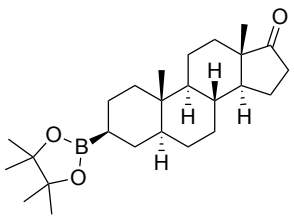


According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.6 mmol), **2r** (0.0954 g, 0.2 mmol), and V-40 (0.0244 g, 0.1 mmol) in heptane (1 mL). After the reaction, the solvent was evaporated and the solution of pinacol (0.0944 g, 0.8 mmol) in $CHCl_3$ (1 mL) and TsOH・$H_2O$ (0.0760 g, 0.4 mmol) was added. The mixture was stirred at room temperature for 2 h. Water was added to the reaction mixture and the organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate = 95:5) to give the product as a white solid (0.0660 g, 66% yield, dr = 83:17) after column chromatography (hexane/ethyl acetate = 95:5). The NMR spectra are in agreement with the literature report.[55]

**$^1$H NMR: (400 MHz, $CDCl_3$)** (Spectrum data of two isomers are listed.) 5.33-5.25 (m, 1H), 2.24-2.15 (m, 1H), 2.04-0.85 (m, 52H), 0.67 (s, 3H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** (Spectrum data of a major isomer is only listed.) 143.8, 118.5, 82.8, 56.9, 56.2, 50.6, 42.3, 40.9, 39.9, 39.5, 37.3, 36.2, 35.8, 33.8, 31.9, 31.8, 28.2, 28.0, 24.72, 24.72, 24.3, 24.0, 23.8, 22.8, 22.5, 20.7, 19.5, 18.7, 11.8 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{33}H_{57}BO_2$) 469.4452 ($M^+$) Found: 469.4445

**(3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-Dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (3r)**

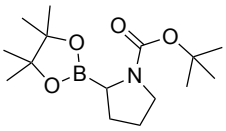
According to the general procedure 1, this compound was prepared from **1d** (0.262 g, 0.6 mmol), **2r**



(0.0801 g, 0.2 mmol) in 1,4-dioxane (1 mL) was added V-40 (0.0244 g, 0.1 mmol) to give the product as a white solid (0.0726 g, 91% yield, dr = 82:18) after column chromatography (hexane/ethyl acetate = 85:15). The ratio of diastereomers was assigned according to Aggawal's method. The NMR spectra are in agreement with the literature report.[59] Spectrum data of a major isomer is only listed below.

**$^1$H NMR: (400 MHz, $CDCl_3$)** (Spectrum data of two isomers are listed.) 2.48-2.35 (m, 1H), 2.11-1.84 (m, 2H), 1.83-1.15 (m, 27H), 1.12-0.66 (m, 11H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** (Spectrum data of a major isomer is only listed.) 221.6, 82.7, 54.7, 51.5, 47.81, 47.81, 39.3, 36.2, 35.8, 35.0, 31.5, 30.9, 30.0, 28.5, 24.7, 23.3, 21.7, 20.0, 13.8, 12.3 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{25}H_{41}BO_3$) 400.3149 ($M^+$) Found: 400.3152

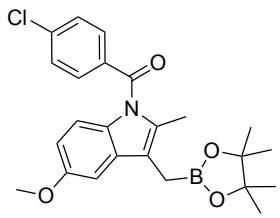
***tert*-Butyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolidine-1-carboxylate (3s)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2s** (0.0721 g, 0.2 mmol), and V-40 (0.0049 g, 0.02 mmol) in heptane (1 mL). After the reaction, the solution of pinacol (0.0944 g, 0.8 mmol) in 1,4-dioxane (1 mL) and $TsOH\cdot H_2O$ (0.0760 g, 0.4 mmol) was added. The mixture was stirred at room temperature for 2 h. Water was added to the reaction mixture and the organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/ethyl acetate = 50:50) to give the product as colorless oil (0.0277 g, 47% yield) after column chromatography (hexane/ethyl acetate = 50:50). The NMR spectra are in agreement with the literature report.[84]

**$^1$H NMR: (400 MHz, toluene-$d_8$, 80°C)** 3.33-3.03 (m, 3H), 1.75-1.61 (m, 3H), 1.48-1.41 (m, 10H), 1.16 (s, 12H); **$^{13}$C NMR: (100 MHz, toluene-$d_8$, 80°C)** 83.6, 78.7, 46.7, 29.1, 25.5, 25.1 (The signals of C=O and the α-B-carbon were not observed.); **HRMS: (CI, 70 eV)** Calculated ($C_{15}H_{29}NBO_4$) 298.2190 ($[M+H]^+$) Found: 298.2185

**(4-Chlorophenyl)[5-methoxy-2-methyl-3-{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}-1*H*-indol-1-yl]methanone (3t)**



According to the general procedure 1, this compound was prepared from **1d** (0.131 g, 0.3 mmol), **2t** (0.101 g, 0.2 mmol), and V-40 (0.0049 g, 0.02 mmol) in 1,4-dioxane (1 mL) to give the product as colorless oil (0.0646 g, 76% yield) after column chromatography (hexane/ethyl acetate = 85:15). The NMR spectra are in agreement with the literature report.[57]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 7.64 (d, $J$ = 8.0 Hz, 2H), 7.46 (d, $J$ = 8.0 Hz, 2H), 6.93 (d, $J$ = 9.0 Hz, 2H), 6.65 (dd, $J$ = 9.0, 2.5 Hz, 1H), 3.84 (s, 3H), 2.29 (s, 3H), 2.18 (s, 2H), 1.23 (s, 12H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 168.1, 155.7, 138.6, 134.5, 133.0, 131.8, 131.0, 130.8, 128.9, 116.5, 114.8, 111.1, 101.4, 83.5, 55.6, 24.7, 13.7 (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{24}H_{27}BNO_4Cl$) 439.1722 ($M^+$) Found: 439.1726

**Radical Clock Experiments**

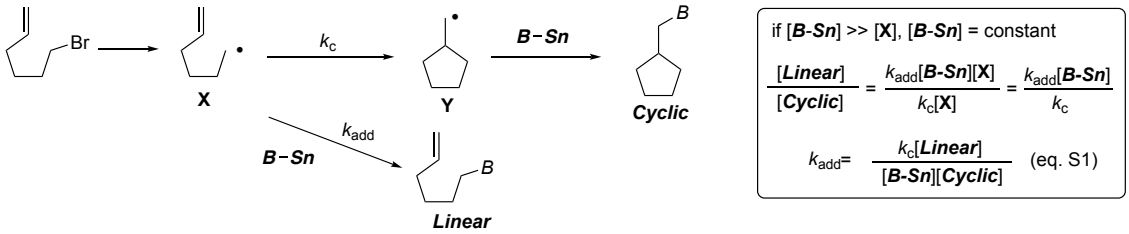
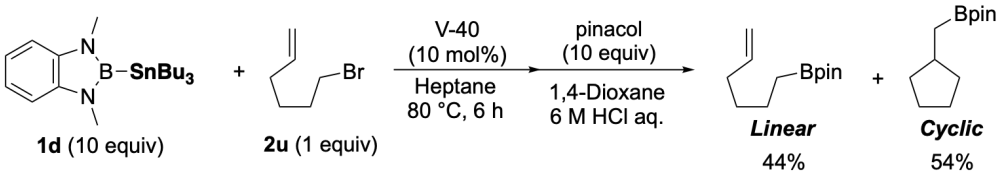



**Figure S3.** Reactions in a competition kinetic study.

The reaction of the 5-hexenyl radical **X** with the trapping reagent ***B-Sn*** leading to the borylated product ***Linear*** (second-order rate constant $k_{add}$) is considered to compete only with the irreversible unimolecular reaction leading to the cyclopentyl methyl radical **Y** (first-order rate constant $k_c$). If the variation of the concentration in trapping reagent is negligible (i.e., [***B-Sn***] is considered to be constant), the kinetic model can be simplified to pseudo-first-order and then integrated to give eq. S1. The cyclization to the cyclopentylmethyl radical with a known rate constant ($k_c$), and the rate constant of interest ($k_{add}$) is calculated from that ratio, the concentration of the trapping agent ***B-Sn***, and the known cyclization rate constant ($k_c$). The rate constant ($k_c$) is represented by the previously determined expression:[85]

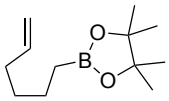
$$\log k_c / s^{-1} = (10.13 \pm 0.42) - (6.59 \pm 0.61)/2.3RT \qquad \text{(eq. S2)}$$

**Radical Clock Experiment by Use of 1d**




To a mixture of boryl stannane **1d** (0.870 g, 2 mmol) and 6-bromohex-1-ene **2u** (0.0326 g, 0.2 mmol) in heptane (5 mL) was added V-40 (0.0049 g, 0.02 mmol). The reaction mixture was stirred at 80 °C for 6 h. After cooled to room temperature, the solution of pinacol (0.236 g, 2 mmol) in 1,4-dioxane (2 mL) and 6 M HCl aq. (2 mL) was added and the mixture was stirred at room temperature for 2 h. The organic phase was extracted with EtOAc and dried over $MgSO_4$. The solvent was removed under reduced pressure. Internal standard (tetradecane) was added to the crude reaction mixture and an aliquot was taken for GC. Formation of the desired product was confirmed by comparing the retention time and HRMS with those of independently prepared authentic products **3u-linear** and **3u-cyclic**. The products were obtained as a mixture of **3u-linear** and **3u-cyclic** (98% yield, **3u-linear**:**3u-cyclic** = 45:55).

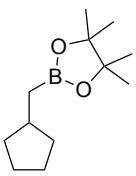
**2-(Hex-5-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3u-linear)**



The NMR spectra are in agreement with the literature report.[82]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 5.86-5.76 (m, 1H), 5.02-4.90 (m, 2H), 2.07- 2.01 (m, 2H), 1.47-1.35 (m, 4H), 1.24 (s, 12H), 0.78 (t, *J* = 7.7 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 139.2, 114.0, 82.8, 33.6, 31.6, 24.8, 23.5; **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{23}BO_2$) 210.1791 ($M^+$) Found: 210.1790

**2-(Cyclopentylmethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3u-cyclic)**



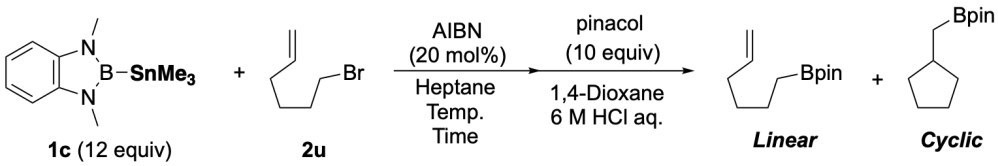
The NMR spectra are in agreement with the literature report.[82]

**$^1$H NMR: (400 MHz, $CDCl_3$)** 1.99-1.90 (m, 1H), 1.82-1.74 (m, 2H), 1.66-1.46 (m, 4H), 1.25 (s, 12H), 1.10-1.01 (m, 2H), 0.84 (d, *J* = 7.5 Hz, 2H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 82.8, 36.1, 35.0, 25.1, 24.8; **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{23}BO_2$) 210.1791 ($M^+$) Found: 210.1795

**Radical Clock Experiment by Use of 1c**

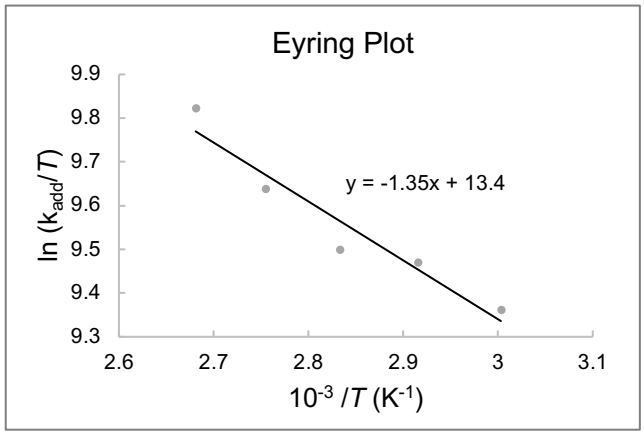
The reaction of borylstannane **1c** (0.256 g, 0.83 mmol) with 6-bromohex-1-ene **2u** (0.0113 g, 0.069 mmol) in heptane (5 mL) in the presence of AIBN (0.0023 g, 0.014 mmol) was conducted at different temperatures according to the procedure using borylstannane **1d**.

**Table S4.** Results of radical clock experiments using borylstannane **1c** at different temperatures.




| T (°C) | Time (h) | GC Yield (%) | | Ratio | $k_c$ (x $10^6$ $s^{-1}$) | $k_{add}$ (x $10^6$ $M^{-1}$ $s^{-1}$) |
|---|---|---|---|---|---|---|
| | | ***Linear*** | ***Cyclic*** | (***Linear***/***Cyclic***) | | |
| 60 | 1 | 59 | 23 | 2.5 | 0.63 | 3.9 |
| 70 | 1 | 53 | 25 | 2.2 | 0.84 | 4.4 |
| 80 | 1 | 55 | 31 | 1.8 | 1.1 | 4.7 |
| 90 | 1 | 53 | 33 | 1.6 | 1.4 | 5.6 |
| 100 | 2 | 54 | 35 | 1.5 | 1.8 | 6.9 |

The rate constant $k_c$ at each temperature is calculated from eq. S2 and the equation (eq. S1) leads the rate constant $k_{add}$.




***Activation Parameters***

$\Delta H^{\ddagger}$ (298 K) = 2.68 kcal/mol

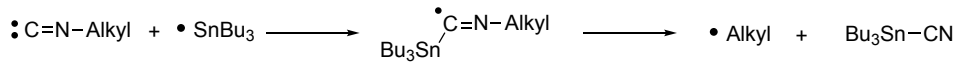
$\Delta S^{\ddagger}$ (298 K) = -22.0 cal/mol·K

$\Delta G^{\ddagger}$ (298 K) = 9.23 kcal/mol

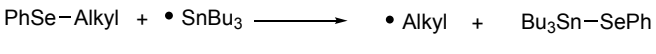
**Fugure S4.** Eyring plot of ln($k_{add}/T$) and 1/$T$ and the activation parameters.

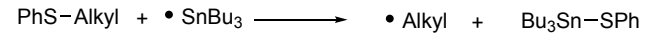
**Mechanisms for Generation of Alkyl Radicals from Other Radical Precursors than Chlorides**

**(1) Isocyanide**[86,87]

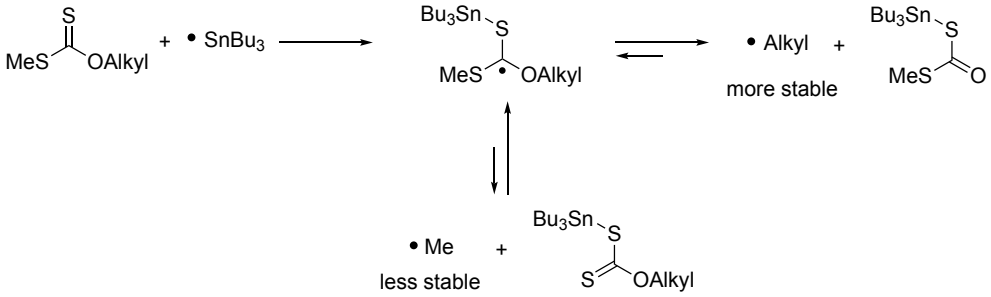



**(2) Selenide**[88,89] / **Sulfide**[90]




**(3) Xanthate**[91]




**(4) Phthalimide Ester**[92]

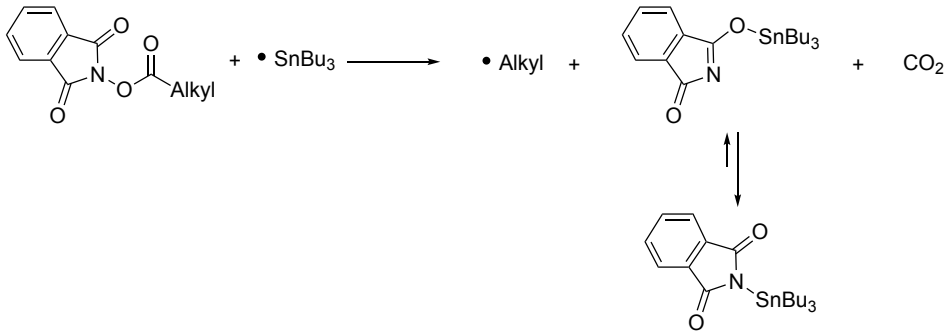
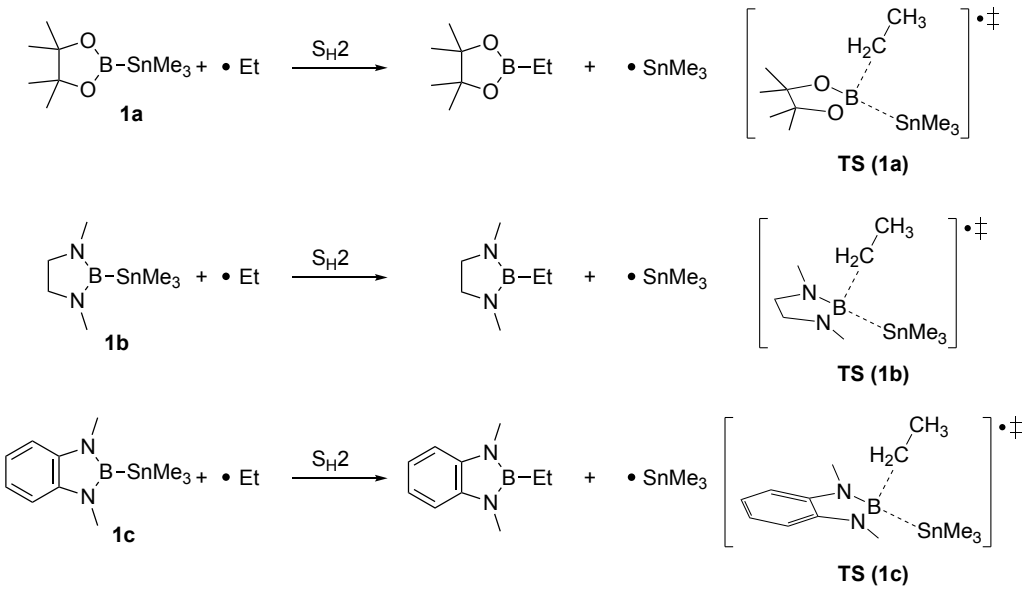


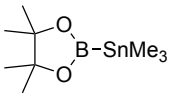

**Figure S5.** Mechanisms for the generation of alkyl radicals from (1) isocyanide, (2) selenide, sulfide, (3) xanthate, and (4) phthalimide ester.

**Computational Studies**

Geometries of all stationary points in the reaction profiles were optimized at the (U)M06-2X level with Lanl2dZ method for Sn and with 6-31G+(d,p) for H, B, C, N, O under vacuum at 298 K and 1 bar by using Gaussian 09 rev.C.01. Stationary points, minima, and transition states on the potential energy surface were identified by vibrational analysis. It was confirmed that the transition state had only one imaginary frequency. Gibbs free energies were calculated as a sum of the single-point electronic energy and thermal correction to the Gibbs free energy. Natural bond orbital analysis was performed under the optimized geometries using the NBO version 3.1 program as including in Gaussian.

(Gaussian 09 rev.C.01: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian 09 (Gaussian, Inc., Wallingford CT, 2009).)

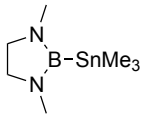




**1a**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | 2.53642 | -0.78024 | -0.05082 | H | -2.24732 | -1.89125 | -1.92737 |
| O | 1.16353 | -1.05554 | -0.42723 | C | 2.80833 | 1.4619 | -1.29067 |
| C | 2.5432 | 0.77831 | 0.04923 | H | 2.59591 | 2.52902 | -1.1872 |
| O | 1.16649 | 1.06755 | 0.40039 | H | 3.85035 | 1.34041 | -1.60097 |
| B | 0.39873 | 0.00874 | -0.0171 | H | 2.15883 | 1.05678 | -2.07237 |
| Sn(Iso=117.902) | -1.8653 | 0.00438 | -0.00319 | C | 3.4557 | 1.34631 | 1.12374 |
| C | -2.6283 | 1.9966 | 0.16474 | H | 4.49715 | 1.06962 | 0.92673 |
| H | -2.34344 | 2.60035 | -0.70103 | H | 3.38452 | 2.43716 | 1.12162 |
| H | -3.71989 | 1.98848 | 0.22966 | H | 3.176 | 0.98743 | 2.11569 |
| H | -2.23635 | 2.48713 | 1.05966 | C | 2.76942 | -1.4664 | 1.29383 |
| C | -2.59728 | -1.13657 | 1.65736 | H | 2.54988 | -2.53164 | 1.18585 |
| H | -3.69088 | -1.14327 | 1.66021 | H | 3.80611 | -1.35431 | 1.62474 |
| H | -2.25109 | -2.17212 | 1.60271 | H | 2.10789 | -1.05648 | 2.06294 |
| H | -2.25845 | -0.71455 | 2.6073 | C | 3.46316 | -1.35734 | -1.10812 |
| C | -2.64026 | -0.88003 | -1.79309 | H | 4.5033 | -1.09011 | -0.89216 |
| H | -3.73124 | -0.94036 | -1.74728 | H | 3.38199 | -2.44748 | -1.10688 |
| H | -2.36956 | -0.29246 | -2.67441 | H | 3.20502 | -0.99649 | -2.1052 |

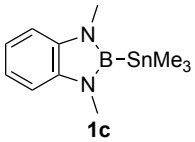
Sum of electronic and zero-point Energies= -533.857897
Sum of electronic and thermal Energies= -533.838785
Sum of electronic and thermal Enthalpies= -533.837841
Sum of electronic and thermal Free Energies= -533.907220



**1b**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | -3.32934 | 0.70304 | 0.09842 | H | 3.02346 | -1.10232 | -1.67966 |
| C | -3.27003 | -0.81785 | -0.10918 | H | 1.59603 | -2.14635 | -1.62448 |
| N | -1.86763 | -1.15011 | 0.13066 | H | 1.5809 | -0.68328 | -2.61709 |
| N | -1.94793 | 1.13898 | -0.09609 | C | 1.99384 | -0.90335 | 1.76443 |
| C | -1.49073 | -2.53461 | 0.00675 | H | 1.72305 | -0.34238 | 2.66299 |
| H | -0.42119 | -2.65066 | 0.20342 | H | 1.61927 | -1.92433 | 1.88124 |
| C | -1.68398 | 2.55175 | 0.0013 | H | 3.08524 | -0.94839 | 1.70683 |
| H | -0.61355 | 2.73805 | -0.11273 | H | -2.21391 | 3.10717 | -0.78323 |
| B | -1.06903 | 0.02621 | 0.02261 | H | -2.0027 | 2.95795 | 0.97345 |
| Sn | 1.19149 | 0.02217 | 0.00159 | H | -2.0345 | -3.15663 | 0.72901 |
| C | 2.06627 | 1.97764 | -0.13227 | H | -1.6975 | -2.92737 | -1.00086 |
| H | 3.15698 | 1.89436 | -0.15209 | H | -4.01081 | 1.19344 | -0.60734 |
| H | 1.75413 | 2.49555 | -1.04391 | H | -3.66388 | 0.95333 | 1.11818 |
| H | 1.79406 | 2.6002 | 0.72501 | H | -3.55221 | -1.08837 | -1.13975 |
| C | 1.92963 | -1.10548 | -1.67062 | H | -3.9371 | -1.35831 | 0.57347 |

Sum of electronic and zero-point Energies= -415.518713
Sum of electronic and thermal Energies= -415.501385
Sum of electronic and thermal Enthalpies= -415.500441
Sum of electronic and thermal Free Energies= -415.565452




**1c**

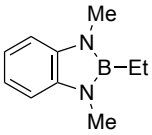
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | -2.42859 | 0.70862 | 0.00073 | Sn | 2.02881 | 0.00834 | 0.00026 |
| C | -2.40483 | -0.70151 | 0.00042 | C | 2.90112 | 1.96369 | -0.12198 |
| C | -3.58534 | -1.43711 | 0.00001 | H | 3.99154 | 1.87956 | -0.1467 |
| C | -4.79435 | -0.73644 | -0.00025 | H | 2.58643 | 2.4894 | -1.02811 |
| C | -4.81818 | 0.66102 | 0.00005 | H | 2.63429 | 2.57868 | 0.7424 |
| C | -3.63379 | 1.40293 | 0.0006 | C | 2.77215 | -1.12868 | -1.66025 |
| H | -3.56976 | -2.52265 | 0.00001 | H | 3.86542 | -1.10146 | -1.68058 |
| H | -5.7288 | -1.28805 | -0.0006 | H | 2.46401 | -2.1762 | -1.59413 |
| H | -5.77097 | 1.1804 | -0.00007 | H | 2.40415 | -0.73005 | -2.60938 |
| H | -3.65573 | 2.48832 | 0.00099 | C | 2.78764 | -0.92068 | 1.77853 |
| N | -1.07865 | -1.11882 | 0.00031 | H | 2.51192 | -0.35015 | 2.66943 |
| N | -1.11742 | 1.17226 | 0.00082 | H | 2.39371 | -1.9345 | 1.89462 |
| C | -0.74428 | -2.52523 | -0.00004 | H | 3.87876 | -0.98514 | 1.739 |
| H | 0.34187 | -2.63984 | -0.00911 | H | -1.26319 | 3.07341 | -0.88694 |
| C | -0.83701 | 2.59116 | 0.00037 | H | -1.2555 | 3.07283 | 0.89166 |
| H | 0.2431 | 2.74539 | -0.00483 | H | -1.13816 | -3.02314 | 0.89345 |
| B | -0.22743 | 0.04214 | 0.00103 | H | -1.15136 | -3.02512 | -0.88646 |

Sum of electronic and zero-point Energies= -567.899023
Sum of electronic and thermal Energies= -567.879958
Sum of electronic and thermal Enthalpies= -567.879014
Sum of electronic and thermal Free Energies= -567.947481

•Et

| | | | |
|---|---|---|---|
| C | 0.79448 | 0. | -0.02539 |
| H | 1.3493 | 0.92657 | 0.05525 |
| H | 1.3493 | -0.92658 | 0.05525 |
| C | -0.69452 | 0. | -0.00008 |
| H | -1.10541 | -0.88603 | -0.49316 |
| H | -1.08754 | -0.00005 | 1.02853 |
| H | -1.10541 | 0.88609 | -0.49307 |

Sum of electronic and zero-point Energies= -79.050720
Sum of electronic and thermal Energies= -79.046735
Sum of electronic and thermal Enthalpies= -79.045791
Sum of electronic and thermal Free Energies= -79.074870




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | 0.8333 | 0.70614 | -0.05823 | H | 2.01961 | -2.50525 | 0.08358 |
| C | 0.8333 | -0.70615 | -0.05825 | H | 4.14438 | -1.23356 | 0.33526 |
| C | 2.01662 | -1.41949 | 0.0823 | H | 4.14439 | 1.23353 | 0.33528 |
| C | 3.20731 | -0.69779 | 0.22337 | H | 2.01963 | 2.50524 | 0.08364 |
| C | 3.20732 | 0.69777 | 0.22339 | N | -0.47655 | -1.14746 | -0.21192 |
| C | 2.01662 | 1.41948 | 0.08235 | N | -0.47654 | 1.14747 | -0.21192 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | -0.79438 | -2.55633 | -0.22819 | H | -0.28968 | 3.0655 | -1.0576 |
| H | -1.8721 | -2.68128 | -0.34821 | H | -0.28972 | -3.0655 | -1.05758 |
| C | -0.79435 | 2.55634 | -0.2282 | H | -0.49106 | -3.0379 | 0.70901 |
| H | -1.87208 | 2.6813 | -0.34824 | C | -3.59297 | -0.00001 | 0.93985 |
| B | -1.3399 | 0.00001 | -0.31536 | H | -3.30303 | 0.88105 | 1.52181 |
| C | -2.91086 | 0.00001 | -0.44065 | H | -4.68381 | -0.00001 | 0.85408 |
| H | -3.24636 | 0.87406 | -1.01225 | H | -3.30303 | -0.88109 | 1.52178 |
| H | -3.24636 | -0.87402 | -1.01228 | | | | |
| H | -0.49104 | 3.03792 | 0.70899 | | | | |

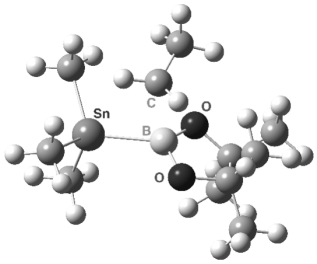
Sum of electronic and zero-point Energies= -524.104854
Sum of electronic and thermal Energies= -524.092164
Sum of electronic and thermal Enthalpies= -524.091220
Sum of electronic and thermal Free Energies= -524.143622

• $SnMe_3$

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Sn(Iso=117.902) | 0.00008 | -0.00023 | -0.29069 | H | 2.22515 | -1.54024 | 0.17522 |
| C | -0.50584 | 1.94508 | 0.48873 | H | 2.70511 | 0.16599 | 0.15198 |
| H | -0.47166 | 1.91548 | 1.58317 | C | -1.43213 | -1.40979 | 0.48924 |
| H | 0.19861 | 2.70482 | 0.14282 | H | -2.44411 | -1.16875 | 0.15624 |
| H | -1.51175 | 2.24163 | 0.18297 | H | -1.19657 | -2.42788 | 0.17096 |
| C | 1.93765 | -0.53422 | 0.48926 | H | -1.41182 | -1.37613 | 1.5839 |
| H | 1.90472 | -0.50984 | 1.58388 | | | | |

Sum of electronic and zero-point Energies= -122.884487
Sum of electronic and thermal Energies= -122.876757
Sum of electronic and thermal Enthalpies= -122.875813
Sum of electronic and thermal Free Energies= -122.918083

**TS (1a)**

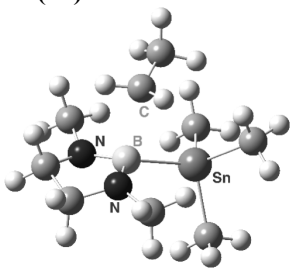



| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | 2.42454 | -0.3607 | -0.78 | H | -3.83157 | 0.68462 | -1.57607 |
| O | 1.15617 | 0.28411 | -1.01894 | H | -2.89326 | 2.04984 | -0.95718 |
| C | 2.54704 | -0.28536 | 0.7741 | H | -2.27176 | 1.0876 | -2.30889 |
| O | 1.16338 | -0.32213 | 1.18871 | C | 3.14506 | 1.03625 | 1.25607 |
| B | 0.39133 | 0.14208 | 0.13321 | H | 2.97798 | 1.12582 | 2.33317 |
| Sn(Iso=117.902) | -1.84144 | -0.28392 | 0.01406 | H | 4.22168 | 1.0767 | 1.06451 |
| C | -2.79407 | -0.09413 | 1.92252 | H | 2.67477 | 1.89021 | 0.75994 |
| H | -2.84926 | 0.95191 | 2.23728 | C | 3.2791 | -1.45431 | 1.4141 |
| H | -3.81366 | -0.48832 | 1.88647 | H | 4.30287 | -1.52321 | 1.03013 |
| H | -2.2413 | -0.64633 | 2.68701 | H | 3.32721 | -1.30692 | 2.49645 |
| C | -2.10951 | -2.29663 | -0.68761 | H | 2.76448 | -2.39704 | 1.22039 |
| H | -3.17284 | -2.52261 | -0.80994 | C | 2.29562 | -1.79527 | -1.29386 |
| H | -1.61665 | -2.4386 | -1.65327 | H | 2.0112 | -1.76416 | -2.34893 |
| H | -1.68691 | -3.01462 | 0.02052 | H | 3.23855 | -2.3426 | -1.2013 |
| C | -2.81804 | 1.0363 | -1.3628 | H | 1.51743 | -2.33661 | -0.74612 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | 3.51088 | 0.37941 | -1.54418 | H | -0.43317 | 2.78502 | -1.42106 |
| H | 4.4965 | -0.0409 | -1.3158 | H | 0.05411 | 4.1669 | -0.4312 |
| H | 3.33467 | 0.27651 | -2.61828 | H | 1.24113 | 2.92598 | -0.88516 |
| H | 3.51689 | 1.44356 | -1.29966 | H | -1.17225 | 2.36578 | 0.99351 |
| C | -0.13734 | 2.32754 | 0.65911 | H | 0.58132 | 2.29292 | 1.47381 |
| C | 0.20353 | 3.08825 | -0.58373 | | | | |

Sum of electronic and zero-point Energies= -612.907430
Sum of electronic and thermal Energies= -612.884934
Sum of electronic and thermal Enthalpies= -612.883989
Sum of electronic and thermal Free Energies= -612.959052

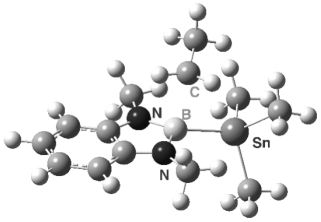
**TS (1b)**




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| C | -3.26018 | 0.15929 | -0.70752 | H | 1.67416 | -0.05862 | 2.51953 |
| C | -3.07159 | -1.2562 | -0.15437 | H | 2.43268 | -1.51118 | 1.85316 |
| N | -1.78577 | -1.18021 | 0.52651 | H | 3.219 | 0.06015 | 1.66636 |
| N | -1.89571 | 0.63269 | -0.90901 | H | -2.23137 | 2.1273 | -2.34387 |
| C | -1.29697 | -2.37842 | 1.15664 | H | -2.20193 | 2.71383 | -0.66725 |
| H | -0.33513 | -2.17926 | 1.64104 | H | -1.99288 | -2.73145 | 1.92855 |
| C | -1.75004 | 1.98907 | -1.368 | H | -1.1524 | -3.19891 | 0.43447 |
| H | -0.68895 | 2.23364 | -1.47376 | H | -3.84155 | 0.17901 | -1.63683 |
| B | -1.02527 | -0.07015 | 0.00796 | H | -3.78258 | 0.79683 | 0.03045 |
| Sn(Iso=117.902) | 1.23659 | -0.17673 | -0.20678 | H | -3.03014 | -1.99485 | -0.97335 |
| C | 2.10415 | 1.52598 | -1.18903 | H | -3.88106 | -1.5512 | 0.52543 |
| H | 3.18991 | 1.40413 | -1.25242 | C | -0.94071 | 1.30413 | 1.79474 |
| H | 1.71885 | 1.62387 | -2.20832 | H | -0.73132 | 0.5417 | 2.54185 |
| H | 1.90036 | 2.45883 | -0.65616 | H | -2.0014 | 1.51346 | 1.66785 |
| C | 1.73384 | -1.89411 | -1.40043 | C | -0.00189 | 2.4708 | 1.7133 |
| H | 2.81643 | -1.96779 | -1.54059 | H | -0.15133 | 3.05244 | 0.798 |
| H | 1.39096 | -2.81423 | -0.91784 | H | -0.16055 | 3.15746 | 2.55761 |
| H | 1.26388 | -1.83429 | -2.38586 | H | 1.04723 | 2.1592 | 1.75234 |
| C | 2.24943 | -0.44721 | 1.67408 | | | | |

Sum of electronic and zero-point Energies= -494.566447
Sum of electronic and thermal Energies= -494.546744
Sum of electronic and thermal Enthalpies= -494.545800
Sum of electronic and thermal Free Energies= -494.614505

**TS (1c)**

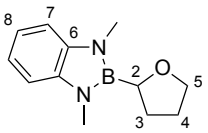



| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| C | -2.44041 | 0.58109 | -0.39405 | H | 2.70125 | 2.48164 | -0.12333 |
| C | -2.4331 | -0.76736 | 0.03475 | C | 2.42197 | -1.56199 | -1.88797 |
| C | -3.62322 | -1.47355 | 0.18898 | H | 3.50303 | -1.6652 | -2.02057 |
| C | -4.82135 | -0.81545 | -0.10208 | H | 2.01217 | -2.55146 | -1.66483 |
| C | -4.82824 | 0.51382 | -0.53356 | H | 1.99215 | -1.22773 | -2.83615 |
| C | -3.63752 | 1.23029 | -0.68392 | C | 3.00925 | -0.89869 | 1.43134 |
| H | -3.62153 | -2.5067 | 0.52262 | H | 2.94969 | -0.1923 | 2.26455 |
| H | -5.76117 | -1.34647 | 0.00912 | H | 2.59118 | -1.85179 | 1.77067 |
| H | -5.77312 | 1.00038 | -0.75281 | H | 4.06701 | -1.06264 | 1.20539 |
| H | -3.64777 | 2.26386 | -1.01611 | H | -1.20406 | 2.56866 | -1.88859 |
| N | -1.1221 | -1.15932 | 0.23719 | H | -1.30593 | 3.12086 | -0.20241 |
| N | -1.13387 | 1.03598 | -0.45134 | H | -1.238 | -2.62043 | 1.74909 |
| C | -0.80562 | -2.46967 | 0.75115 | H | -1.18379 | -3.25567 | 0.08717 |
| H | 0.27926 | -2.57619 | 0.82715 | C | -0.06512 | 0.60224 | 2.26618 |
| C | -0.83862 | 2.3858 | -0.87077 | H | 0.42712 | -0.27984 | 2.67184 |
| H | 0.24207 | 2.5406 | -0.8557 | H | -1.14964 | 0.60245 | 2.35064 |
| B | -0.24719 | -0.01544 | 0.02351 | C | 0.64298 | 1.9156 | 2.38662 |
| Sn | 1.98536 | -0.17094 | -0.31218 | H | 0.17881 | 2.67982 | 1.75527 |
| C | 2.89744 | 1.69527 | -0.85797 | H | 0.61363 | 2.29241 | 3.41953 |
| H | 3.98178 | 1.56933 | -0.93203 | H | 1.7001 | 1.84016 | 2.10872 |
| H | 2.53465 | 2.03939 | -1.831 | | | | |

| | |
|---|---|
| Sum of electronic and zero-point Energies= | -646.950516 |
| Sum of electronic and thermal Energies= | -646.927700 |
| Sum of electronic and thermal Enthalpies= | -646.926756 |
| Sum of electronic and thermal Free Energies= | -647.004174 |

**C-H Borylation of THF by The Triplet State of Xanthone**

**Procedure for synthesis of 1,3-dimethyl-2-(tetrahydrofuran-2-yl)-2,3-dihydro-1*H*-benzo[*d*][1,3,2]diazaborole (3v)**




To an oven-dried 5 mL vial with a magnetic stir bar was added xanthone (0.0392 g, 0.2 mmol), THF (1 mL), and **1d** (0.0435 g, 0.1 mmol) under nitrogen atmosphere in a nitrogen-filled glove box. The vial was then positioned 3 cm from two 40 W blue LEDs (Kessil PR160L-390 nm) at maximum brightness, and irradiated for 12 h with continuous fan cooling. The mixture was concentrated under reduced pressure. Internal standard (1,1,2,2-tetrachloroethane) was added to the crude reaction mixture and an aliquot was taken for $^{1}H$ analysis in $CDCl_3$. Formation of the desired product was confirmed by comparing the NMR spectra

(55% yield). The target product was purified by column chromatography (hexane/ethyl acetate = 80:20) and GPC with chloroform to give the pure product as a colorless oil (0.0026 g, 11% yield). **$^1$H NMR: (400 MHz, $CDCl_3$)** 7.04-6.98 (m, 4H, 7-H x 2 and 8-H x 2), 4.04 (dd, *J* = 15.0, 6.8 Hz, 1H, 5-H$^a$), 3.99 (dd, *J* = 11.5, 6.7 Hz, 1H, 2-H), 3.77 (dd, *J* = 14.5, 7.9 Hz, 1H, 5-H$^b$), 3.37 (s, 6H, NMe x 2), 2.25-2.19 (m, 1H), 2.04 (m, 2H), 1.85-1.75 (m, 1H); **$^{13}$C NMR: (100 MHz, $CDCl_3$)** 138.4 (s, C-6), 118.6 (d), 107.8 (d), 68.9 (t, C-5), 30.5 (t), 29.3 (q, NMe), 26.9 (t) (The signal of the α-B-carbon was not observed.); **HRMS: (EI, 70 eV)** Calculated ($C_{12}H_{17}BN_2O$) 216.1434 ($M^+$) Found: 216.1431

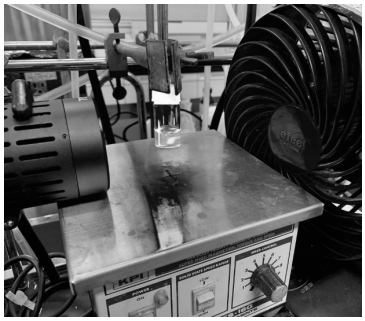
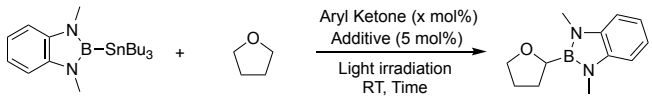


**Figure S6.** Photoreaction Setup.

**Optimization of C-H Borylation**

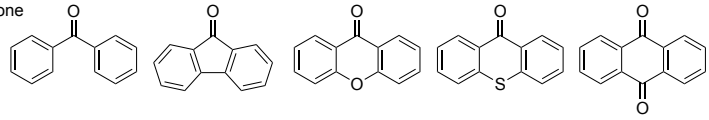
**Table. S3** Screening of aryl ketones, light source, and equivalents.




**1d** (1 equiv) (1 mL) **3u**

| Entry | Aryl Ketone | mol% | Light | Time | Yield (%) |
|---|---|---|---|---|---|
| 1 | **A** | 100 | 370 nm (40 W) | 18 | 24 |
| 2 | **B** | 100 | 370 nm (40 W) | 18 | 0 |
| 3 | **C** | 100 | 370 nm (40 W) | 18 | 28 |
| 4 | **D** | 100 | 370 nm (40 W) | 18 | 0 |
| 5 | **E** | 100 | 370 nm (40 W) | 18 | 0 |
| 6 | **A** | 100 | Kessil LED (40 W) x 2 | 15 | 12 |
| 7 | **A** | 100 | 390 nm (40 W) | 15 | 17 |
| 8 | **A** | 100 | 370 nm (40 W) | 15 | 18 |
| 9 | **C** | 100 | Kessil LED (40 W) x 2 | 15 | 14 |
| 10 | **C** | 100 | 390 nm (40 W) | 15 | 33 |
| 11 | **C** | 100 | 370 nm (40 W) | 15 | 24 |
| 12 | **C** | 50 | 390 nm (40 W) | 12 | 12 |
| **13** | **C** | **200** | **390 nm (40 W)** | **12** | **51** |

Aryl Ketone



**A** **B** **C** **D** **E**

**Plausible Mechanism for C-H Borylation**

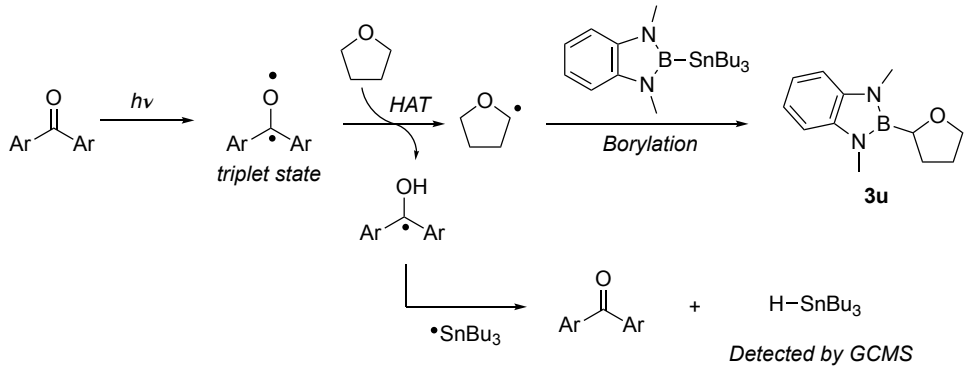



**Figure S7.** Mechanism for C-H borylation of THF.

## 3-5. Reference


[1] A. Suzuki, *Acc. Chem. Res.* **1982**, *15*, 178.

[2] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457.

[3] S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angew. Chem. Int. Ed.* **2001**, *40*, 4544.

[4] H. Doucet, *Eur. J. Org. Chem.* **2008**, *2008*, 2013.

[5] D. G. Hall, *Boronic Acids: Preparation and Applications in Organic Synthesis Medicine and Materials*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2011**.

[6] C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, *53*, 5481.

[7] M. Wang, Z. Shi, *Chem. Rev.* **2020**, *120*, 7348.

[8] K. Kubota, H. Iwamoto, H. Ito, *Org. Biomol. Chem.* **2017**, *15*, 285.

[9] J. F. Hartwig, *Acc. Chem. Res.* **2012**, *45*, 864.

[10] I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890.

[11] H. C. Brown, T. E. Cole, *Organometallics* **1983**, *2*, 1316.

[12] H. C. Brown, B. C. Subba Rao, *J. Am. Chem. Soc.* **1956**, *78*, 5694.

[13] Y. Segawa, M. Yamashita, K. Nozaki, *Science* **2006**, *314*, 113.

[14] E. Yamamoto, K. Izumi, Y. Horita, H. Ito, *J. Am. Chem. Soc.* **2012**, *134*, 19997.

[15] X. Mu, J. C. Axtell, N. A. Bernier, K. O. Kirlikovali, D. Jung, A. Umanzor, K. Qian, X. Chen, K. L. Bay, M. Kirollos, A. L. Rheingold, K. N. Houk, A. M. Spokoyny, *Chem* **2019**, *5*, 2461.

[16] F. W. Friese, A. Studer, *Chem. Sci.* **2019**, *10*, 8503.

[17] L. Zhang, Z. Q. Wu, L. Jiao, *Angew. Chem. Int. Ed.* **2020**, *59*, 2095.

[18] Q. Liu, J. Hong, B. Sun, G. Bai, F. Li, G. Liu, Y. Yang, F. Mo, *Org. Lett.* **2019**, *21*, 6597.

[19] D. Mazzarella, G. Magagnano, B. Schweitzer-Chaput, P. Melchiorre, *ACS Catal.* **2019**, *9*, 5876.

[20] Y. Cheng, C. Mück-Lichtenfeld, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 16832.

[21] M. Jiang, H. Yang, H. Fu, *Org. Lett.* **2016**, *18*, 5248.

[22] A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* **2017**, *357*, 283.

[23] D. Hu, L. Wang, P. Li, *Org. Lett.* **2017**, *19*, 2770.

[24] Q. Zhang, X. Li, W. Zhang, S. Ni, Y. Wang, Y. Pan, *Angew. Chem. Int. Ed.* **2020**, *59*, 1.

[25] D. Wei, T. M. Liu, B. Zhou, B. Han, *Org. Lett.* **2020**, *22*, 234.

[26] C. Shu, R. Madhavachary, A. Noble, V. K. Aggarwal, *Org. Lett.* **2020**, *22*, 7213.

[27] J. Wu, L. He, A. Noble, V. K. Aggarwal, *J. Am. Chem. Soc.* **2018**, *140*, 10700.

[28] J. Hu, G. Wang, S. Li, Z. Shi, *Angew. Chem. Int. Ed.* **2018**, *57*, 15227.

[29] F. Sandfort, F. Strieth-Kalthoff, F. J. R. Klauck, M. J. James, F. Glorius, *Chem. Eur. J.* **2018**, *24*, 17210.

[30] J. Wu, R. M. Bär, L. Guo, A. Noble, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2019**, *58*, 18830.

[31] F. W. Friese, A. Studer, *Angew. Chem. Int. Ed.* **2019**, *58*, 9561.

[32] G. Ma, C. Chen, S. Talukdar, X. Zhao, C. Lei, H. Gong, *Chem. Commun.* **2020**, 10219.

[33] C. G. Gutierrez, L. R. Summerhays, *J. Org. Chem.* **1984**, *49*, 5206.

[34] W. P. Neumann, *Synthesis* **1987**, *8*.

[35] C. Ollivier, P. Renaud, *Chem. Rev.* **2001**, *101*, 3415.

[36] C. Carra, J. C. Scaiano, *Eur. J. Org. Chem.* **2008**, 4454.

[37] R. Uematsu, C. Saka, Y. Sumiya, T. Ichino, T. Taketsugu, S. Maeda, *Chem. Commun.* **2017**, *53*, 7302.

[38] M. Suginome, *Organometallics* **2000**, *19*, 4647.

[39] S. Y. Onozawa, Y. Hatanaka, T. Sakakura, S. Shimada, M. Tanaka, *Organometallics* **1996**, *15*, 5450.

[40] S. Y. Onozawa, Y. Hatanaka, N. Choi, M. Tanaka, *Organometallics* **1997**, *16*, 5389.

[41] C. Kleeberg, J. Plotzitzka, *Z. Anorg. Allg. Chem.* **2018**, *644*, 1280.

[42] When 4-chlorotoluene was used for the present radical borylation, no borylation product was observed and the starting material was recovered.

[43] The yield of **3g** in the crude product determined by $^{1}$H NMR was moderate (53%). However, the isolated yield was decreased during the purification by silica gel column chromatography.

[44] The generation of the radical would be very slow and the isocyanide **2n** is decomposed under heating conditions. Thus, the yield of **3n** was low. In fact, isocyanide **2n** was not recovered and

the complicated by-products were observed.

[45] When 2-phenylethyl phenyl sulfide was employed as a radical precursor, the yield of the desired product was very low (11% yield). The simple alkyl radicals are hardly generated from alkylsulfides because C-S bonds are stronger than C-Cl bonds. Thus, the generation of the stabilized radical such as benzyl radical is necessary for the desulfurizative borylation.

[46] D. Lai, D. Griller, S. Husband, *J. Am. Chem. Soc.* **1972**, *98*, 1224.

[47] T. F. Jeffress, K. M. Jeffress, C. Chatgilialoglu, J. Dickhaut, B. Giese, *J. Org. Chem.* **1991**, *56*, 6399.

[48] D. Dakternieks, D. J. Henry, C. H. Schiesser, *J. Phys. Org. Chem.* **1999**, *12*, 233.

[49] C. Shu, A. Noble, V. K. Aggarwal, *Nature* **2020**, *586*, 714.

[50] M. Fagnoni, D. Dondi, D. Ravelli, A. Albini, *Chem. Rev.* **2007**, *107*, 2725.

[51] H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A. K. Singh, A. Lei, *Chem. Rev.* **2017**, *117*, 9016.

[52] L. Capaldo, D. Ravelli, *Eur. J. Org. Chem.* **2017**, *2017*, 2056.

[53] R. R. Singidi, A. M. Kutney, J. C. Gallucci, T. V. Rajanbabu, *J. Am. Chem. Soc.* **2010**, *132*, 13078.

[54] F. Mohanazadeh, A. R. Momeni, *Org. Prep. Proced. Int.* **1996**, *28*, 492.

[55] F. W. Friese, A. Studer, *Angew. Chem. Int. Ed.* **2019**, *58*, 9561.

[56] W. Xue, M. Oestreich, *Angew. Chem. Int. Ed.* **2017**, *56*, 11649.

[57] A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* **2017**, *357*, 283.

[58] F. J. R. Klauck, M. J. James, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 12336.

[59] J. Wu, R. M. Bär, L. Guo, A. Noble, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2019**, *58*, 18830.

[60] Q. Zhang, X. Li, W. Zhang, S. Ni, Y. Wang, Y. Pan, *Angew. Chem. Int. Ed.* **2020**, 59, 21875.

[61] D. Vasudevan, *Russ. J. Electrochem.* **2005**, *41*, 310.

[62] K. Okada, K. Okamoto, N. Morita, K. Okubo, M. Oda, *J. Am. Chem. Soc.* **1991**, *113*, 9401.

[63] F. L. Lambert, K. Kobayashi, *J. Am. Chem. Soc.* **1960**, *82*, 5324.

[64] J. Zhu, Y. Yuan, S. Wang, Z. J. Yao, *ACS Omega* **2017**, *2*, 4665.

[65] F. L. Lambert, G. B. Ingall, *Tetrahedron Lett.* **1974**, *15*, 3231.

[66] L. Weber, J. Halama, V. Werner, K. Hanke, L. Böhling, A. Chrostowska, A. Dargelos, M. MacIejczyk, A. L. Raza, H. G. Stammler, B. Neumann, *Eur. J. Inorg. Chem.* **2010**, 5416.

[67] D. Y. Wang, C. Wang, M. Uchiyama, *J. Am. Chem. Soc.* **2015**, *137*, 10488.

[68] D. M. C. Ould, A. C. Rigby, L. C. Wilkins, S. J. Adams, J. A. Platts, S. J. A. Pope, E. Richards, R. L. Melen, *Organometallics* **2018**, *37*, 712.

[69] L. Weber, J. Kahlert, L. Böhling, A. Brockhinke, H. G. Stammler, B. Neumann, R. A. Harder, P. J. Low, M. A. Fox, *J. Chem. Soc. Dalt. Trans.* **2013**, *42*, 2266.

[70] T. Yurino, Y. Tange, R. Tani, T. Ohkuma, *Org. Chem. Front.* **2020**, *7*, 1308.

[71] M. Tiecco, L. Testaferri, M. Tingoli, D. Bartoli, R. Balducci, *J. Org. Chem.* **1990**, *55*, 429.

[72] T. Garnier, M. Danel, V. Magné, A. Pujol, V. Bénéteau, P. Pale, S. Chassaing, *J. Org. Chem.* **2018**, *83*, 6408.

[73] E. Yamamoto, K. Izumi, Y. Horita, H. Ito, *J. Am. Chem. Soc.* **2012**, *134*, 19997.

[74] L. Mao, K. J. Szabó, T. B. Marder, *Org. Lett.* **2017**, *19*, 1204.

[75] A. Joshi-Pangu, X. Ma, M. Diane, S. Iqbal, R. J. Kribs, R. Huang, C. Y. Wang, M. R. Biscoe, *J. Org. Chem.* **2012**, *77*, 6629.

[76] D. Anand, Y. He, L. Li, L. Zhou, *Org. Biomol. Chem.* **2019**, *17*, 533.

[77] S. K. Bose, K. Fucke, L. Liu, P. G. Steel, T. B. Marder, *Angew. Chem. Int. Ed.* **2014**, *53*, 1799.

[78] D. Wei, T. M. Liu, B. Zhou, B. Han, *Org. Lett.* **2020**, *22*, 234.

[79] A. S. Dudnik, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 10693.

[80] T. C. Atack, R. M. Lecker, S. P. Cook, *J. Am. Chem. Soc.* **2014**, *136*, 9521.

[81] H. Kinuta, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2015**, *137*, 1593.

[82] Y. Cheng, C. Mück-Lichtenfeld, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 16832.

[83] X. Mu, J. C. Axtell, N. A. Bernier, K. O. Kirlikovali, D. Jung, A. Umanzor, K. Qian, X. Chen, K. L. Bay, M. Kirollos, A. L. Rheingold, K. N. Houk, A. M. Spokoyny, *Chem* **2019**, *5*, 2461.

[84] M. Wollenburg, D. Moock, F. Glorius, *Angew. Chem. Int. Ed.* **2019**, *58*, 6549.

[85] D. Dakternieks, D. J. Henry, C. H. Schiesser, *J. Phys. Org. Chem.* **1999**, *12*, 233.

[86] S. Z. Zard, *Radical Reactions in Organic Synthesis*, Oxford University Press, **2003**.

[87] D. H. R. Barton, G. Bringmann, G. Lamotte, W. B. Motherwell, R. S. H. Motherwell, A. E. A. Porter, *J. Chem. Soc. Perkin Trans. 1* **1980**, 2657.

[88] D. L. J. Clive, G. J. Chittattu, V. Farina, W. A. Kiel, S. M. Menchen, C. G. Russell, A. Singh, C. K. Wong, N. J. Curtis, *J. Am. Chem. Soc.* **1980**, *102*, 4438.

[89] P. Renaud, *Radical Reactions Using Selenium Precursors. In Organoselenium Chemistry Modern Developments in Organic Synthesis*, Springer, **2000**.

[90] C. G. Gutierrez, L. R. Summerhays, *J. Org. Chem.* **1984**, *49*, 5206.

[91] D. H. R. Barton, D. Crich, A. Löbberding, S. Z. Zard, *Tetrahedron* **1986**, *42*, 2329.

[92] D. H. R. Barton, P. Blundell, J. C. Jaszberenyi, *Tetrahedron Lett.* **1989**, *30*, 2341.

# Conclusion

In this study, the synthetic methodologies with nitrogen- or boron-atom-substittuted tin compounds have been developed for the chemo-, regio-, and stereoselective synthesis of highly functionalized compounds.

Firstly, regio- and stereo-controlled addition of $\alpha$-(*N*-phthaloylamino)allylic stannane to aldehydes by $GeCl_2$ was described in Chapter 1. Whereas the methods using $InBr_3$ or $SnCl_2$ led to $\gamma$-addition product, $GeCl_2$ afforded 1,2-amino alcohol derivatives with a high anti-selectivity through transmetalation between aminoallylic stannane and $GeCl_2$. The regioselectivity could be controlled by using different metal salts in the reaction with various carbonyl compounds.

Secondly, *E*-selective synthesis of enamide derivatives from $\alpha$-(*N*-phthaloylamino)allylic stannane was mentioned in Chapter 2. The radical addition of aminoallylic stannanes with alkyl halides proceeds via linear transition state to realize the *E*-selectivity. Asymmetric induction with an optically active aminoallylic stannane provided one enantiomer of *E*-enamides preferably and the mechanism of the radical addition was revealed from the stereoselectivity.

In Chapter 3, (*o*-phenylenediamino)borylstannanes were found to have the high ability to accept alkyl radicals from various alkyl radical precursors. DFT calculation disclosed that the interaction between the *p*-orbital on the boron atom with the SOMO of the alkyl radical was a key to this reaction, which enables efficient borylation. The strategy of the benzo-fusion on borylstannanes was significantly effective for lowering the LUMO level, which realized the radical borylation with borylstannanes for the first time.

A knowledge obtained from Chanpter 1 and 2 is that each ionic reaction and radical reaction system shows different reactivities in the reaction with $\alpha$-heteroatom-substituted allylic stannanes. The knowledge helps us to synthesize functional molecules with controlling high chemoselectivity. Chapter 3 gives us an important idea that the stannyl radical-mediated reactions potentially has the high compatibility with various functional groups and shows the broad substrate scope. Conventional stannyl radical-mediated reactions have included reduction or carbon-carbon bond formation, but the present method using borylstannanes achieves the carbon-heteroatom bond formation at the first time. This knowledge gives us the idea that the chemistry of stannyl radical-mediated reactions have further potential for development.

In conclusion, the synthetic methods using nitrogen- or boron-atom-substituted tin compounds have been established in this doctoral dissertation. The insights obtained from the present works are expected to contribute to organic synthesis of highly functionalized compounds.