**Doctoral Dissertation**

# Studies on Synthesis of $CF_3$- and $SCF_3$-Substituted Compounds Using Fluorine-Containing Building Blocks

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# Preface and Acknowledgement

The studies in this thesis have been carried out under the guidance of Professor Masahiro Miura from April 2019 to March 2021 and Professor Koji Hirano from April 2021 to March 2025 at Department of Applied Chemistry, Graduate School of Engineering, Osaka University. This study focused on synthesis of $CF_3$- and $SCF_3$-substituted compounds using fluorine-containing building blocks.

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# Contents

# General Introduction

## 1. Organo-Fluorine Compounds

Owing to the unique steric and electronic characteristics of the fluorine atom, its incorporation into parent organic molecules often enhances their biological activities such as lipophilicity and metabolic stability.[1] Therefore, organo-fluorine compounds are frequently utilized in medicinal and agrochemical applications. To date, more than 20% of pharmaceuticals and 40% of agrochemicals contain fluorine atoms in their structures.[2] Among them, this discussion focuses on two representative fluorinated functional groups: a trifluoromethyl ($CF_3$) group and a trifluoromethylthio ($SCF_3$) group.

### Trifluoromethyl ($CF_3$) group

The trifluoromethyl ($CF_3$) group, which contains three fluorine atoms on a single carbon, is an attractive functional group that maximizes the beneficial effects of fluorine introduction. The $CF_3$ group exhibits strong electron-withdrawing properties (Hammett substituent constant $\sigma_p = 0.54$)[3] and high lipophilicity (Hansch parameter $\pi_R = 0.88$).[4] Thus, the introduction of $CF_3$ into a parent molecule can dramatically change its properties. As a result, the $CF_3$ group is widely found in biologically active compounds. For example, Alpelisib, an anticancer agent, exemplifies how introducing $CF_3$ group can significantly enhance pharmacological activity (Figure 1).[5] In addition, many pharmaceuticals, such as Efavirenz (an HIV-RT inhibitor) and Befloxatone (an antidepressant), have been developed with $CF_3$ group, highlighting their significance in medicinal chemistry.

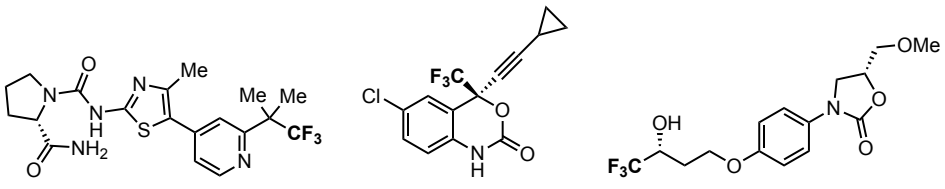



**Figure 1**. Examples of $CF_3$-containing bioactive molecules.

### Trifluoromethylthio ($SCF_3$) group

In addition to $CF_3$ group, recently, there has been growing interest in $XCF_3$ groups (X = O, S), where the $CF_3$ is attached to a chalcogen atom. Among them, the

trifluoromethylthio ($SCF_3$) group has received particular attention due to its electron-withdrawing capability (Hammett substituent constant $\sigma_p = 0.50$)[3] comparable to that of the $CF_3$ group, coupled with superior lipophilicity (Hansch parameter $\pi_R = 1.44$).[4] This unique properties has driven significant research into the synthesis of $SCF_3$-containing molecules. Biologically active molecules containing $SCF_3$ group, such as Cefazaflur (β-lactam antibiotic), Toltrazuril (antiprotozoal agent), and EP0396427 (pesticide), have also been developed (Figure 2).

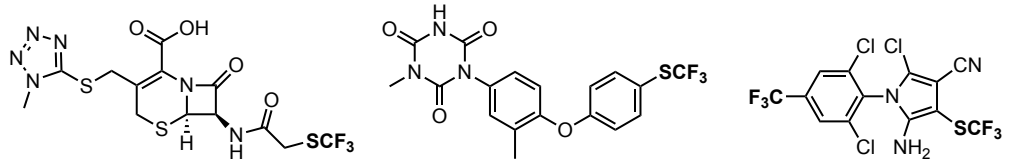



**Figure 2**. Examples of $SCF_3$-containing bioactive molecules.

## 2. Synthesis of $CF_3$- and $SCF_3$-Substituted Compounds

### Construction of C($sp^2$)–$CF_3$ motif by direct trifluoromethylation

As mentioned above, the $CF_3$ group is one of the most representative fluorinated substituents in biologically active compounds. Thus, the development of efficient synthetic protocols for the preparation of $CF_3$-containing molecules has been a long-standing research focus in the synthetic community.[6] Over the years, various nucleophilic and electrophilic trifluoromethylation reagents have been developed, including Ruppert-Prakash reagent,[7] Langlois reagent,[8] Togni reagent,[9] Umemoto reagent,[10] and Shibata reagent[11] (Figure 3). These reagents enable the trifluoromethylation reactions of aryl halides or simple (hetero)arenes to form the C($sp^2$)–$CF_3$ bond.

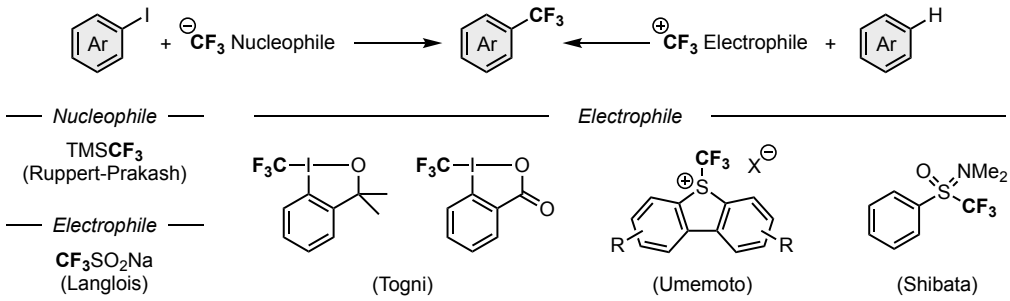



**Figure 3**. Representative nucleophilic and electrophilic trifluoromethylation reagents.

## Construction of C(sp²)–SCF₃ motif by direct trifluoromethylthiolation

Given the growing demands and expectations for $SCF_3$-substituted compounds in recent years, several trifluoromethylthiolation reagents have also been developed,[12] and selected examples are shown in Figure 4. Using $MSCF_3$ reagents (M = Cu or Ag), the trifluoromethylthiolation of aryl halides has been achieved. Additionally, the coupling reactions of electrophilic $SCF_3$ reagents with aryl boronic acids or (hetero)arenes have also been reported. These methods have enabled the formation of C(sp²)–$SCF_3$ bonds.

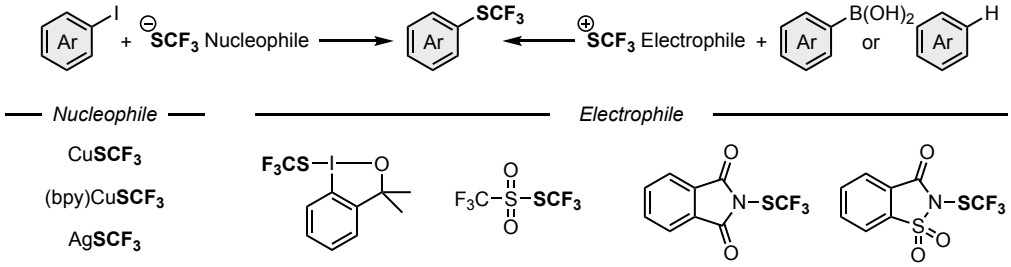
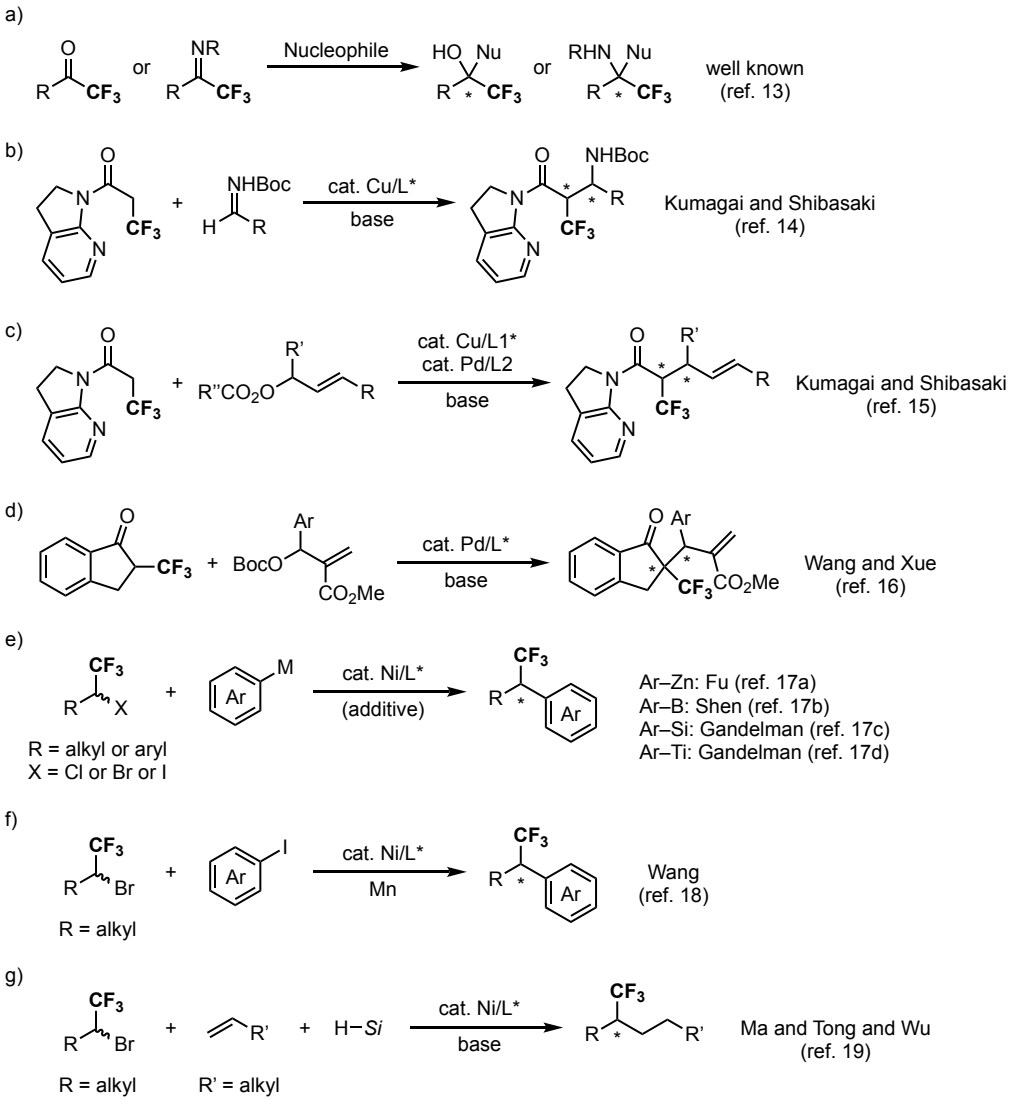



**Figure 4**. Representative nucleophilic and electrophilic trifluoromethylthiolation reagents.

## Building block strategy for the synthesis of $CF_3$- and $SCF_3$-substituted compounds

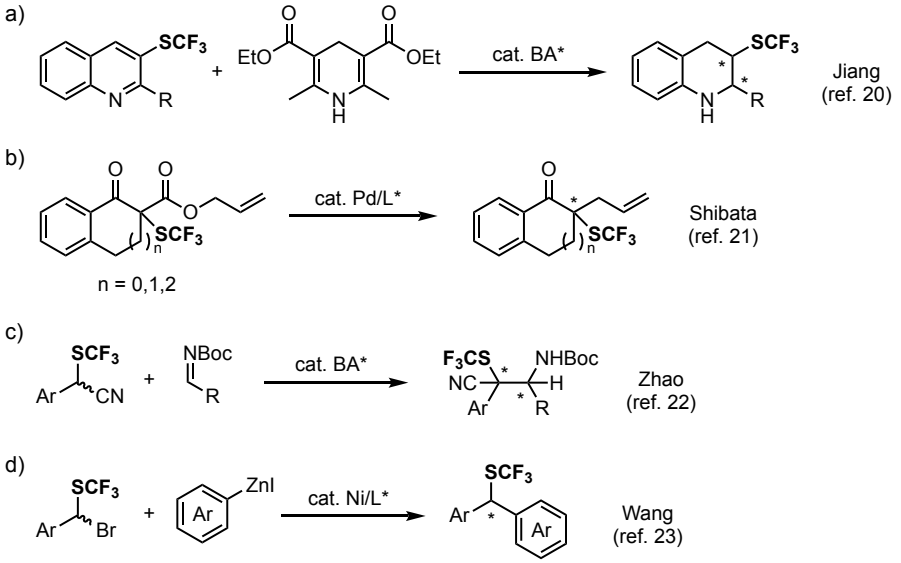
The direct trifluoromethylation/trifluoromethylthiolation methods are highly effective for C(sp²)–$CF_3$/$SCF_3$ bond formation. However, the construction of C(sp³)–$CF_3$/$SCF_3$ motifs, particularly their asymmetric synthesis, remains a challenging task. On the other hand, functionalization of small molecules pre-installed with $CF_3$ or $SCF_3$ substituents, known as building block strategy, is a powerful approach for the asymmetric construction of $CF_3$- and $SCF_3$-substituted $sp^3$ carbon center. Since $CF_3$-carbonyls, -imines, and their derivatives are readily available, enantioselective reductions and addition-type reactions toward optically active α-$CF_3$ alcohols and amines have been actively explored by many synthetic chemists (Scheme 1a).[13] An α-$CF_3$ carbonyl is also a good starting platform. Kumagai and Shibasaki elegantly designed the α-$CF_3$ amide bearing a 7-azaindoline directing group and successfully performed a Cu-catalyzed Mannich-type reaction with high diastereo- and enantioselectivity (Scheme 1b).[14] Subsequently, the same research group extended this strategy to asymmetric α-allylation with the allyl carbonates by using a Cu/Pd dual catalyst system (Scheme 1c).[15] In 2021, Wang and Xue reported the Pd-catalyzed asymmetric α-allylation of simple α-$CF_3$ cyclic ketones without any directing groups (Scheme 1d).[16] The metal-catalyzed enantioconvergent C–C cross-coupling reaction of racemic α-halo $CF_3$ compounds with

organometallic reagents has also emerged as a practical method to generate a chiral $CF_3$-substituted $sp^3$ carbon center without need for any proximal heteroatoms.[17] Fu reported seminal work on the Ni-catalyzed enantioconvergent cross-coupling of racemic α-Br and α-I $CF_3$ compounds with arylzinc reagents (Scheme 1e).[17a] Enantioconvergent cross-coupling reactions of racemic α-halo $CF_3$ compounds with arylborates,[17b] arylsilanes,[17c] and organotitanium-based nucleophiles[17d] have also been reported by other groups. In addition, in the presence of a reductant, electrophilic coupling of racemic α-Br $CF_3$ compounds with (hetero)aryl iodides has been successfully achieved (Scheme 1f).[18] Furthermore, a three-component coupling reaction involving α-Br $CF_3$ compounds, terminal alkenes, and hydrosilanes has also been developed (Scheme 1g).[19]




**Scheme 1**. Synthesis of $CF_3$-substituted compounds using fluorine-containing building blocks.

Several examples of the synthesis of chiral $SCF_3$ molecules using $SCF_3$-containing building blocks have also been reported. Jiang demonstrated a chiral Brønsted acid (BA)-catalyzed asymmetric transfer hydrogenation of 3-trifluoromethylthioquinolines with Hantzsch ester (Scheme 2a).[20] Also, Shibata achieved Pd-catalyzed decarboxylative asymmetric allylic alkylation, forming a tetrasubstituted stereogenic center (Scheme 2b).[21] Zhao's group has developed a BA-catalyzed enantioselective Mannich-type reaction using $SCF_3$-substituted benzylic cyanide as a starting building block (Scheme 2c).[22] More recently, Wang and co-workers reported Ni-catalyzed enantioconvergent cross-coupling of racemic α-Br compounds with arylzinc reagents (Scheme 2d).[23]




**Scheme 2**. Synthesis of $SCF_3$-substituted compounds using fluorine-containing building blocks.

The author aims to asymmetrically construct C($sp^3$)–$CF_3$/$SCF_3$ motifs using $CF_3$/$SCF_3$-substituted alkenes as building blocks, the details of which are discussed in the main text.

## 3. $CF_3$/$SCF_3$-Substituted Alkenes

### $CF_3$-substituted alkenes

$CF_3$-substituted alkenes can be relatively easily prepared by the direct trifluoromethylation of the corresponding alkenyl iodides. In the presence of transition metal catalyst, several functionalizations of $CF_3$-substituted alkenes have been reported (Figure 5). These reactions enable the introduction of various substituents at the β-

position relative to the $CF_3$ group by the regioselective addition of in situ generated organometallic nucleophile species to $CF_3$-alkenes. However, these reactions typically involve defluorination, yielding *gem*-difluoroalkenes as the major products. As the representative examples, aryl-,[24] alkyl-,[25] boryl-,[26] and silyldefluorination[26e,27] reactions of $CF_3$-substituted alkenes have been reported by several groups. The author has also previously reported a hydrodefluorination reaction of $CF_3$-substituted alkenes using hydrosilanes as nucleophile. [28] Despite these efforts, there has been no report of $CF_3$-remaining reactions for the asymmetric synthesis of $CF_3$-substituted compounds.

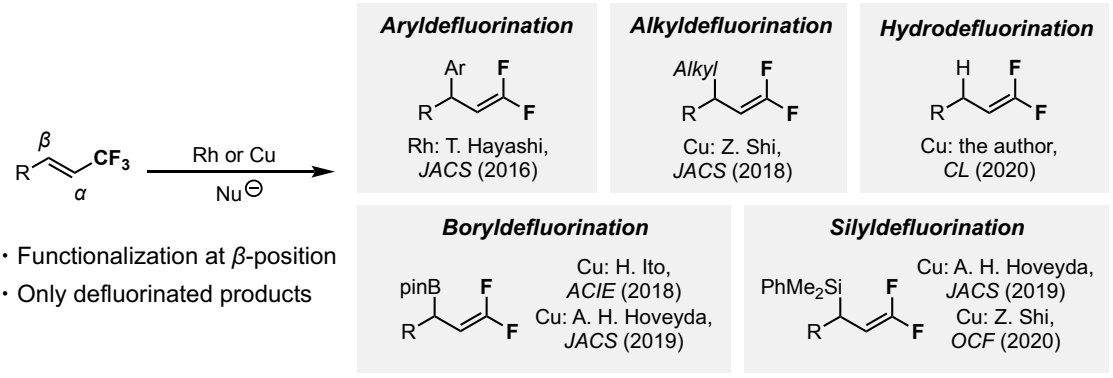
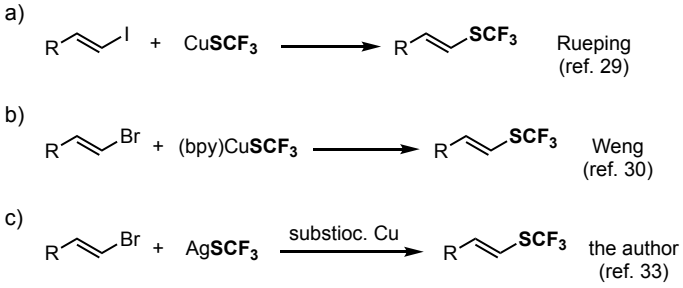



**Figure 5**. Transition metal-catalyzed defluorinative functionalizations of $CF_3$-substituted alkenes.

### $SCF_3$-substituted alkenes

Previously, numerous methods have been developed to directly introduce the $SCF_3$ group onto alkenes. Among them, a trifluoromethylthiolation using $CuSCF_3$ reagent is a powerful technique due to its high reactivity. For example, Rueping reported the synthesis of $SCF_3$-substituted alkenes using alkenyl iodides and $CuSCF_3$ (Scheme 3a).[29] Weng further developed the trifluoromethylthiolation of alkenyl bromides using modified (bpy)$CuSCF_3$ (Scheme 3b).[30] These reactions can prepare the $SCF_3$-substituteed alkenes from readily available alkenyl halides in a single step. However, a simple $CuSCF_3$ reagent is thermodynamically unstable and difficult to handle.[31] The stability of (bpy)$CuSCF_3$ is greatly improved by the bpy ancillary ligand, but it should be pre-synthesized from $TMSCF_3$, $CuF_2$, and $S_8$, and carefully purified before use.[32] Recently, the author also developed a modified reaction system: a copper-mediated trifluoromethylthiolation of alkenyl iodides with $AgSCF_3$ was reported (Scheme 3c).[33] This protocol employs $CuSCF_3$ generated in situ from commercially available CuI and $AgSCF_3$, which is convenient and synthetically advantageous. Our CuI/$AgSCF_3$ reaction system

demonstrated a broad substrate scope and high scalability, thus providing $SCF_3$ alkenes more readily accessible. The synthetic applications of the $SCF_3$-substituted alkenes have not been explored previously, and the transformations described in this thesis represent the first examples.




**Scheme 3**. Synthetic methods for $SCF_3$-substituted alkenes using $CuSCF_3$ reagents.

## 4. Aim of This Thesis

### Construction of C($sp^3$)–$CF_3$ motif by copper-catalyzed functionalizations of $CF_3$-substituted alkenes

Building on the background of $CF_3$ compounds discussed above, the author proposed a novel synthetic method for the C($sp^3$)–$CF_3$ construction using the $CF_3$-substituted alkene as a building block. The working hypothesis is illustrated in Figure 6. First, a nucleophilic copper(I) species is generated from a Cu salt, ligand (L), and nucleophile (Nu). The copper species undergoes *syn*-addition to the $CF_3$-alkene to form an α-$CF_3$ alkylcopper intermediate. Thanks to the strong electron-withdrawing nature of the $CF_3$ group, the insertion raction proceeds regioselectively. Subsequently, this intermediate

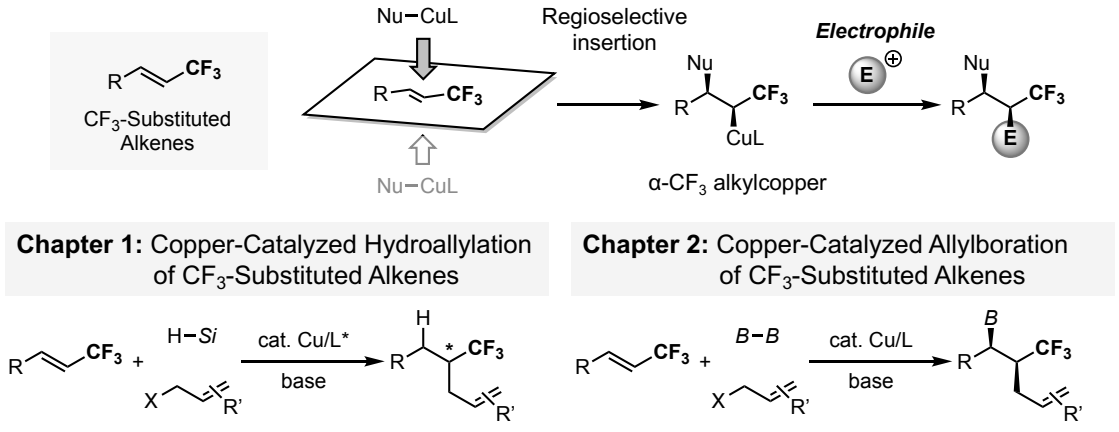



**Figure 6**. Synthesis of $CF_3$-substituted compounds using fluorine-containing building blocks.

reacts with electrophile (E) stereospecifically, allowing the introduction of various substituents at the α-position to $CF_3$ group. The author envisioned that this approach would enable the synthesis of aliphatic $CF_3$ molecules, which are challenging to prepare by other methods.

In Chapter 1, the author developed a copper-catalyzed hydroallylation of $CF_3$-substituted alkenes with hydrosilanes and allylic halides (Figure 6, left). Additionally, asymmetric induction is also possible by using the chiral bisphosphine ligand, and optically active $CF_3$ compounds are obtained with high enantiopurity.

Chapter 2 demonstrates that the replacement of hydrosilanes with diborons facilitates the allylboration of $CF_3$-alkenes, introducing the Bpin substituent at the β-position relative to the $CF_3$ group (Figure 6, right).

**Construction of C($sp^3$)–$SCF_3$ motif by copper-catalyzed functionalizations of $SCF_3$-substituted alkenes**

In the $CF_3$-substituted alkenes used in Chapters 1 and 2, the strong electron-withdrawing nature of the $CF_3$ group induces charge polarization on the alkene moiety and lowers its LUMO level, enabling a smooth reaction with nucleophilic copper species (Figure 7). This inspired the hypothesis that $SCF_3$-substituted alkenes, which possess comparable electron-withdrawing properties, could similarly function as a building block for the synthesis of corresponding $SCF_3$ compounds (Figure 8).

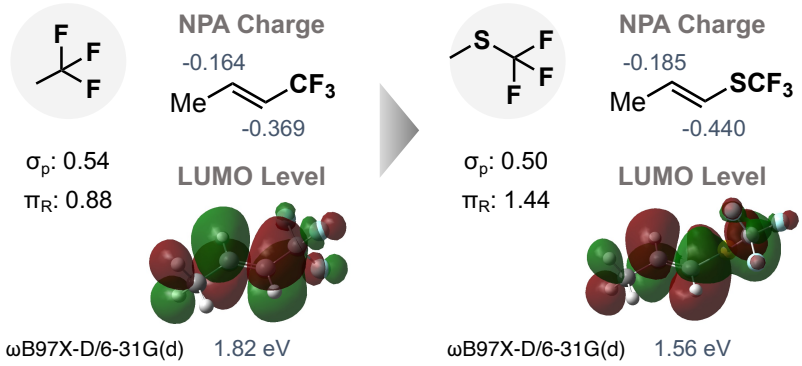



**Figure 7**. DFT-calculated charge density and LUMO levels of $CF_3$- and $SCF_3$-substituted alkenes.

In Chapter 3, the author developed a copper-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes with pinacolborane (Figure 8, left). The desired hydroborated products were obtained via σ-bond metathesis between an in situ

generated α-$SCF_3$ alkylcopper intermediate and pinacolborane. Moreover, the Bpin moiety in the products can be further transformed to provide various optically active trifluoromethylthio compounds.

In Chapter 4, using hydrosilanes and allylic electrophiles instead of pinacolborane, the author achieved three component coupling reactions involving $SCF_3$-substituted alkenes (Figure 8, right). The suitable choice of a chiral ligand facilitated carbon–carbon bond formation at the α-position to $SCF_3$, providing the corresponding hydroallylated products with high regio- and enantioselectivity.

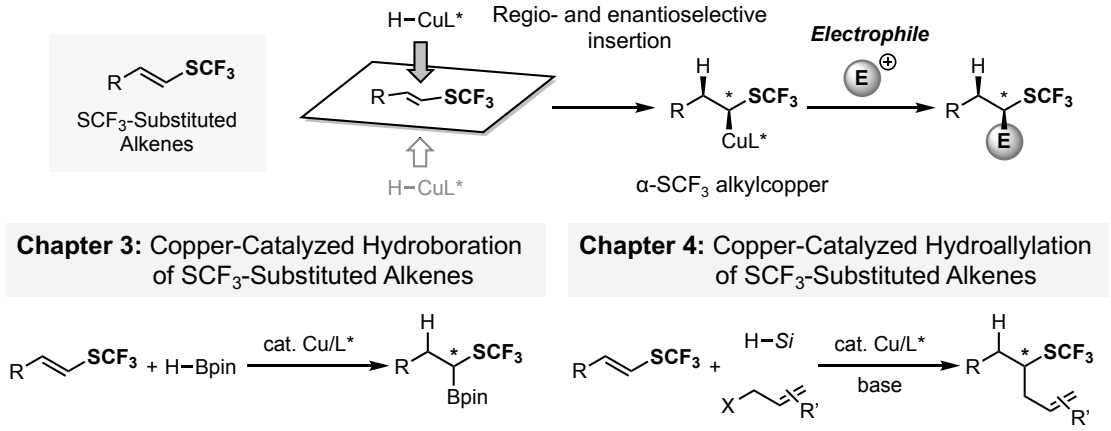



**Figure 8**. Synthesis of $SCF_3$-substituted compounds using fluorine-containing building blocks.

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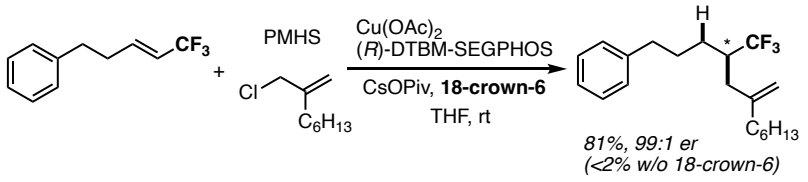
# Chapter 1

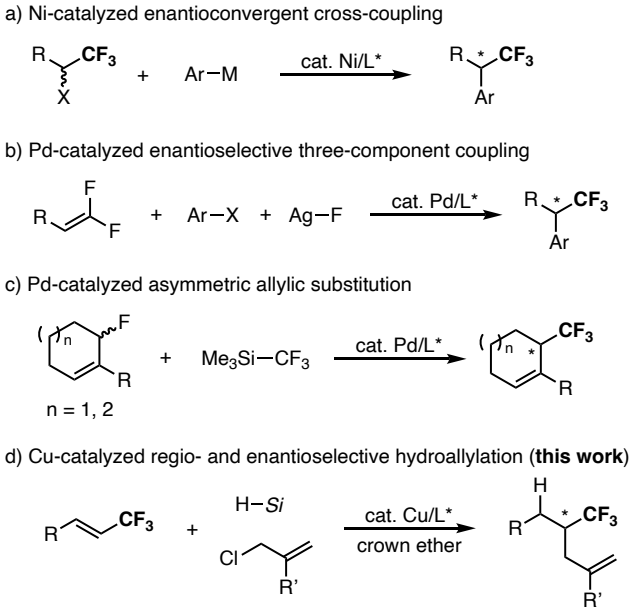
# Copper-Catalyzed Regio- and Enantioselective Hydroallylation of $CF_3$-Substituted Alkenes: Effect of Crown Ether

A Cu-catalyzed regio- and enantioselective hydroallylation of $CF_3$-substituted alkenes with hydrosilanes and allylic chlorides has been developed. An in situ generated CuH species undergoes the hydrocupration regio- and enantioselectively to form a chiral α-$CF_3$ alkylcopper intermediate, which then leads to the optically active hydroallylated product. The key to success is the use of not only an appropriate chiral bisphosphine ligand but also 18-crown-6 to suppress the otherwise predominant β-F elimination from the α-$CF_3$ alkylcopper intermediate. The asymmetric Cu catalysis successfully constructs the nonbenzylic and nonallylic $CF_3$-substituted $C_{sp3}$ chiral center, which is difficult to operate by other means.



## Introduction

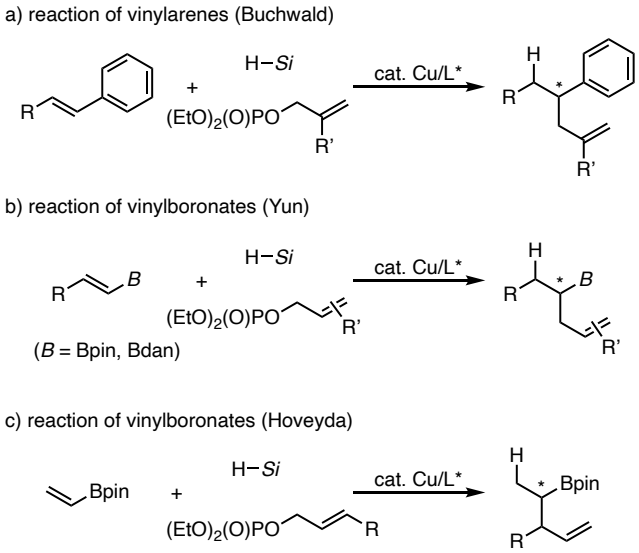
As described in the General Introduction, due to the high utility and demand for the $CF_3$ molecules in the design of pharmaceuticals and agrochemicals, synthetic chemists have developed numerous strategies for the preparation of $CF_3$-containing organic molecules. However, in comparison to Ar-$CF_3$ and alkenyl-$CF_3$, the synthesis of $C_{sp3}$–$CF_3$ molecules, in particular, their enantioenriched forms, still remains underdeveloped. While several chiral α-$CF_3$ alcohols[1]/amines[2] and related α-$CF_3$ carbonyls[3] are relatively easily prepared by the stereoselective trifluoromethylation of carbonyls/imines or reduction and addition reactions of trifluoromethylated carbonyl/imines, the construction of the point chirality at a position α to $CF_3$ without any proximal heteroatoms is a formidable challenge. Limited successful examples include the Ni-catalyzed enantioconvergent cross-coupling reaction of racemic $CF_3$-substituted secondary alkyl halides with organometallic reagents (Scheme 1.1a), the Pd-catalyzed enantioselective three-component coupling reaction of *gem*-difluoroalkenes, aryl halides, and AgF (Scheme 1.1b),[4] and the Pd-catalyzed asymmetric allylic substitution of allylic fluorides with trifluoromethylsilanes (Scheme 1.1c).[5]




**Scheme 1.1**. Catalytic asymmetric construction of $CF_3$-substituted stereocenters without any proximal heteroatoms.

Herein, the author reports a totally different approach to optically active $C_{sp3}$–$CF_3$ molecules using $CF_3$-subsituted alkene as the starting platform: a Cu-catalyzed regio- and

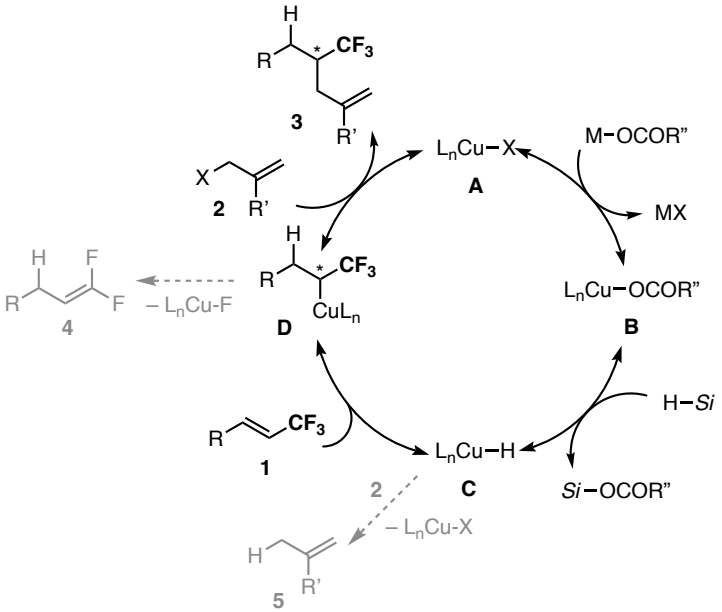
enantioselective hydroallylation of $CF_3$-subsituted alkene with hydrosilanes and allylic chlorides is described (Scheme 1.1d). The asymmetric Cu catalysis can construct the nonbenzylic and nonallylic $CF_3$-substituted chiral center, which is difficult to operate by other means. Although there are some examples of copper hydride catalyzed regio- and enantioselective hydroallylation of vinylarenes and vinylboronates, which were originally developed by Buchwald (Scheme 1.2a),[6] Yun (Scheme 1.2b),[7] and Hoveyda (Scheme 1.2c),[8] the application of $CF_3$-subsituted alkenes remains elusive. Related stereoselective hydrogenation[9] and Michael addition[10] have been reported, but the applicable substrates were restricted to highly electron deficient $CF_3$-substituted acrylic acids and nitroalkenes. Additionally, the critical effect of the crown ether is found to suppress the competitive β-F elimination from an α-$CF_3$ organocopper intermediate.




**Scheme 1.2**. Reported examples of copper hydride catalyzed regio- and enantioselective hydroallylation of alkenes.

The author's blueprint for the asymmetric synthesis of $C_{sp3}$–$CF_3$ molecules by an enantioselective Cu-catalyzed hydroallylation is shown in Scheme 1.3, the scenario of which is based on the recent progress of CuH-catalyzed[11] stereoselective hydrofunctionalization of alkenes developed by the author's group,[12] Yun,[7,13] Buchwald,[6,14] and others.[15] The *in situ* formed ligand-coordinated copper complex $L_nCu$-X (**A**) undergoes a salt metathesis with the acetate-type external base MOCOR" to form the copper acetate species $L_nCu$-OCOR" (**B**). Subsequent σ-bond metathesis with the hydrosilane generates the active copper hydride **C**. With guidance by the strong

electron-withdrawing nature of the $CF_3$ group, the double-bond moiety of $CF_3$-subsituted alkene **1** inserts the Cu–H bond regioselectively to furnish the α-$CF_3$ alkylcopper intermediate **D**. The desired hydroallylated product **3** and starting copper salt **A** then follow from electrophilic trapping with the allylic electrophile **2** to complete the catalytic cycle. If the enantioselectivity and the regioselectivity are successfully controlled in the insertion step by a judicious choice of the ancillary chiral ligand (**C** to **D**), the optically active α-$CF_3$ alkylcopper is formed, en route to the enantioenriched product via a stereospecific allylation. However, there are several issues to overcome in the aforementioned reaction design. First, the copper hydride **C** should react with the $CF_3$-subsituted alkene **1** in preference to the alkene moiety of allyl electrophile **2** to avoid the formation of the reduced byproduct **5**. Moreover, suitable conditions including the ligand and external base should be identified to suppress the formation of *gem*-difluoroalkene **4** through the conceivably competitive β-F elimination from the α-$CF_3$ alkylcopper **D**, which is frequently observed in the metal-catalyzed reactions of 1-trifluoromethylalkenes with some nucleophiles.

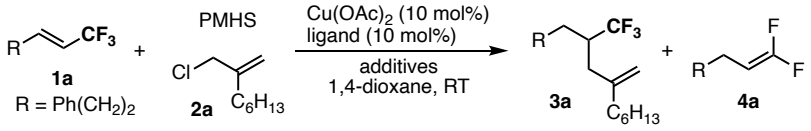



**Scheme 1.3**. Working hypothesis and conceivable side reactions in copper-catalyzed regio- and enantioselective hydroallylation of 1-trifluoromethylalkene 1 with hydrosilane and allylic electrophile 2.

**Results and discussion**

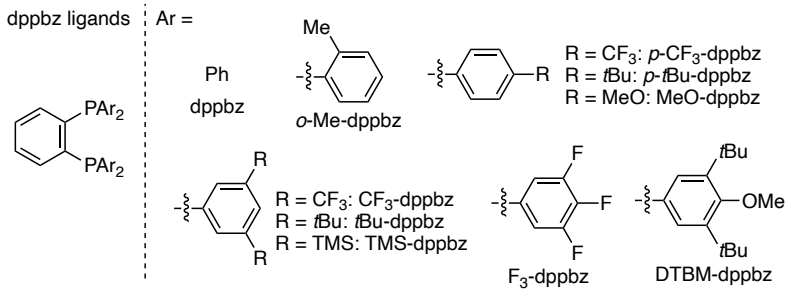
The author's optimization studies commenced with the $CF_3$-alkene **1a** and allylic chloride **2a** for the development of nonenantioselective hydroallylation conditions. In an early experiment, on the basis of previous work,[12c] treatment of **1a** with **2a** (2.0 equiv) and polymethylhydrosiloxane (PMHS; 3.0 equiv) in the presence of the $Cu(OAc)_2$ catalyst, the bis(diphenylphosphino)benzene (dppbz) ligand, and the cesium pivalate base in 1,4-dioxane at room temperature afforded the desired hydroallylated product **3a** regioselectively in 34% yield. However, as mentioned in Scheme 1.3, the *gem*-difluoroalkene **4a** was also observed in 30% yield (Table 1.1, entry 1). Inspired by the preliminary result and the previously observed positive effect of substituents at the remote position in the bisphosphine ligands to suppress the β-F elimination,[12c] we then tested several modified dppbz-type ligands. Although the electron-withdrawing substituents completely shut down the conversion of **1a** (entry 2), the introduction of electron-donating groups at the remote meta and/or para positions generally increased the hydroallylation selectivity over the hydrodefluorination except for the *t*Bu-dppbz ligand (entries 3–7). In particular, the MeO-dppbz ligand furnished the desired **3a** in 80% yield without any detection of **4a** (entry 6). On the other hand, the *o*-methyl-substituted *o*-Me-dppbz resulted in no reaction because of steric factors (entry 8). The judicious choice of external base was critical: the related CsOAc also promoted the reaction (entry 9), but the sluggish conversion was observed with the less basic KOAc and NaOAc (entry 10). Moreover, the more basic Li*O*t*B*u and Na*O*t*B*u, which are frequently employed in related Cu-catalyzed hydrofunctionalizations of alkenes,[11-15] mainly formed the *gem*-difluoroalkene **4a** (entries 11 and 12). This is probably because of the higher affinity of Li and Na cations to the fluorine atom[16] to accelerate the β-F elimination. Finally, an increase in the amount of PMHS to 4.0 equiv further improved the yield of **3a** to 94% (90% isolated yield; entry 13). As shown in entries 4 and 5, TMS-dppbz and *t*Bu-dppbz also gave a high conversion of **1a** but with a low product selectivity. To increase the selectivity for **3a**, we added 18-crown-6 because it can accommodate the Cs cation to suppress the undesired interaction between the Lewis acidic Cs cation and the Lewis basic fluorine atom in the α-$CF_3$ alkylcopper intermediate **D** for the β-F elimination (Figure 1.1)[17] Gratifyingly, the chemoselectivity was dramatically changed, and the desired **3a** was obtained in 85% and 99% yields (entries 14 and 15, respectively). However, the positive effect was somewhat unique, and 18-crown-6 was detrimental to the optimal

**Table 1.1**. Optimization studies for copper-catalyzed regioselective hydroallylation of 1-trifluoromethylalkene **1a** with PMHS and allyl chloride **2a**[a]




| entry | ligand | additives | yield of **3a** (%)[b] | yield of **4a** (%)[b] |
|---|---|---|---|---|
| 1 | dppbz | CsOPiv | 34 | 30 |
| 2 | $CF_3$-dppbz, *p*-$CF_3$-dppbz, or $F_3$-dppbz | CsOPiv | 0 | 0 |
| 3 | DTBM-dppbz | CsOPiv | 76 | 13 |
| 4 | TMS-dppbz | CsOPiv | 58 | 30 |
| 5 | *t*Bu-dppbz | CsOPiv | 0 | 78 |
| 6 | MeO-dppbz | CsOPiv | 80 | 0 |
| 7 | *p*-*t*Bu-dppbz | CsOPiv | 43 | 24 |
| 8 | *o*-Me-dppbz | CsOPiv | 0 | 0 |
| 9 | MeO-dppbz | CsOAc | 67 | 0 |
| 10 | MeO-dppbz | KOAc or NaOAc | ~10 | trace |
| 11 | MeO-dppbz | LiO*t*Bu | 4 | 34 |
| 12 | MeO-dppbz | NaO*t*Bu | 20 | 44 |
| 13[c] | MeO-dppbz | CsOPiv | 94 (90) | 0 |
| 14 | TMS-dppbz | CsOPiv, 18-crown-6 | 85 | 9 |
| 15 | *t*Bu-dppbz | CsOPiv, 18-crown-6 | 99 (93) | 0 |
| 16[c] | MeO-dppbz | CsOPiv, 18-crown-6 | 51 | 11 |

[a] Conditions unless specific otherwise: **1a** (0.25 mmol), PMHS (0.75 mmol based on Si–H), **2a** (0.50 mmol), $Cu(OAc)_2$ (0.025 mmol), ligand (0.025 mmol), additives (0.50 mmol), 1,4-dioxane (1.5 mL), rt, 6 h, $N_2$. [b] Estimated by $^1H$ NMR. Isolated yields are given in parentheses. [c] With 1.0 mmol of PMHS based on Si–H.



$Cu(OAc)_2$/MeO-dppbz-catalyzed conditions (entry 16). Additional observations in the optimization studies are to be noted. Other common monodentate and bidentate phosphine ligands showed much poorer performance; some other ethereal solvents and hydrosilanes also promoted the reaction, but the combination of 1,4-dioxane and PMHS proved to be best from the viewpoint of cost and performance. The chloride leaving group was the key to success, and the corresponding allylic bromide, acetate, carbonate, and phosphate did not form the hydroallylated product at all; the allylic bromide was too reactive and was rapidly consumed by a direct reduction with the copper hydride (reaction of **C** with **2** to **5** in Scheme 1.3), whereas other allylic alcohol derivatives only gave the *gem*-difluoroalkene **4** probably because of less reactivity with the α-$CF_3$ alkylcopper intermediate (reaction of **D** with **2** to give **3** in Scheme 1.3). Thus, the reactivity balance of the allylic electrophile is also of great importance.

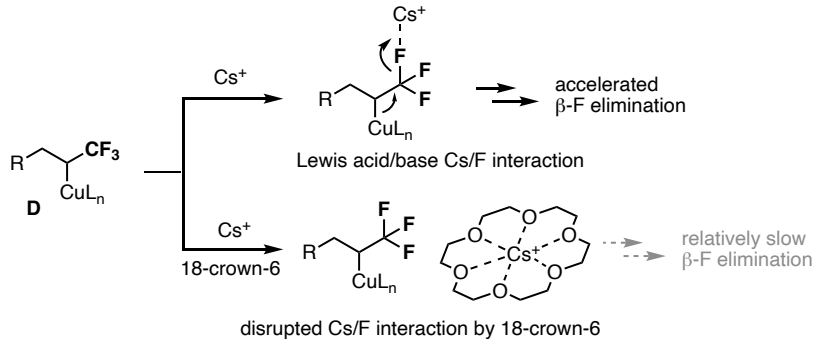
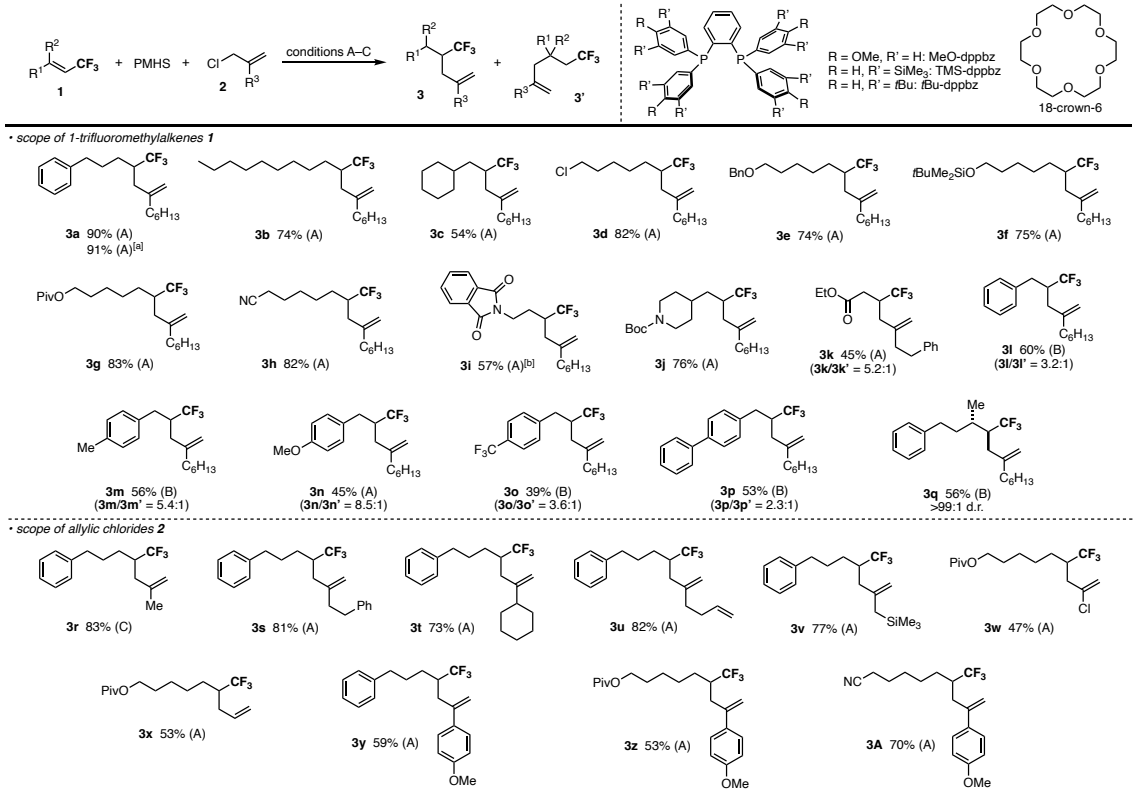



**Figure 1.1**. Possible mechanism of the undesired β-F elimination promoted by Cs cation and role of 18-crown-6.

The author then examined the substrate scope of the Cu-catalyzed hydroallylation (Scheme 1.4). The crown-ether-free, MeO-dppbz-promoted conditions (conditions A) were generally successfully applied, but in some specific cases the crown-ether-assisted, TMS-dppbz- and *t*Bu-dppbz-ligated Cu catalysis (conditions B and C, respectively) showed better performance. In addition to the model substrate (**1a**), the primary and secondary alkyl-substituted $CF_3$-subsituted alkenes were successfully coupled with **2a** to form the corresponding hydroallylated products **3b**, **c** in 74% and 54% yields, respectively. The reaction conditions were also compatible with several common functional groups, including the alkyl chloride, benzyl ether, silyl ether, ester, nitrile, phthalimide, and Boc-protected amine (**3d**-**j**). The ester-conjugated substrate **1k** also participated in the reaction to give **3k** as the major regioisomer. In the cases of styrenyl-type substances **1l**-**p**,

mixtures of regioisomers were generally formed, probably due to the aryl-vinyl conjugation[18] being competitive with the electron-withdrawing nature of the $CF_3$ group in the insertion step (**C** to **D** in Scheme 1.3), but the desired products could be isolated in synthetically useful yields by chromatographic purification (**3l**-**p**). As a general trend, the introduction of electron-donating groups increased the regioselectivity.[19] It is noteworthy that the trisubstituted alkene **1q** was selectively converted to **3q** with high regio- and diastereoselectivity.[20] The reaction could also be performed on a 1.0 mmol scale without any erosion of yield and selectivity (**3a**), thus indicating the good reproducibility.

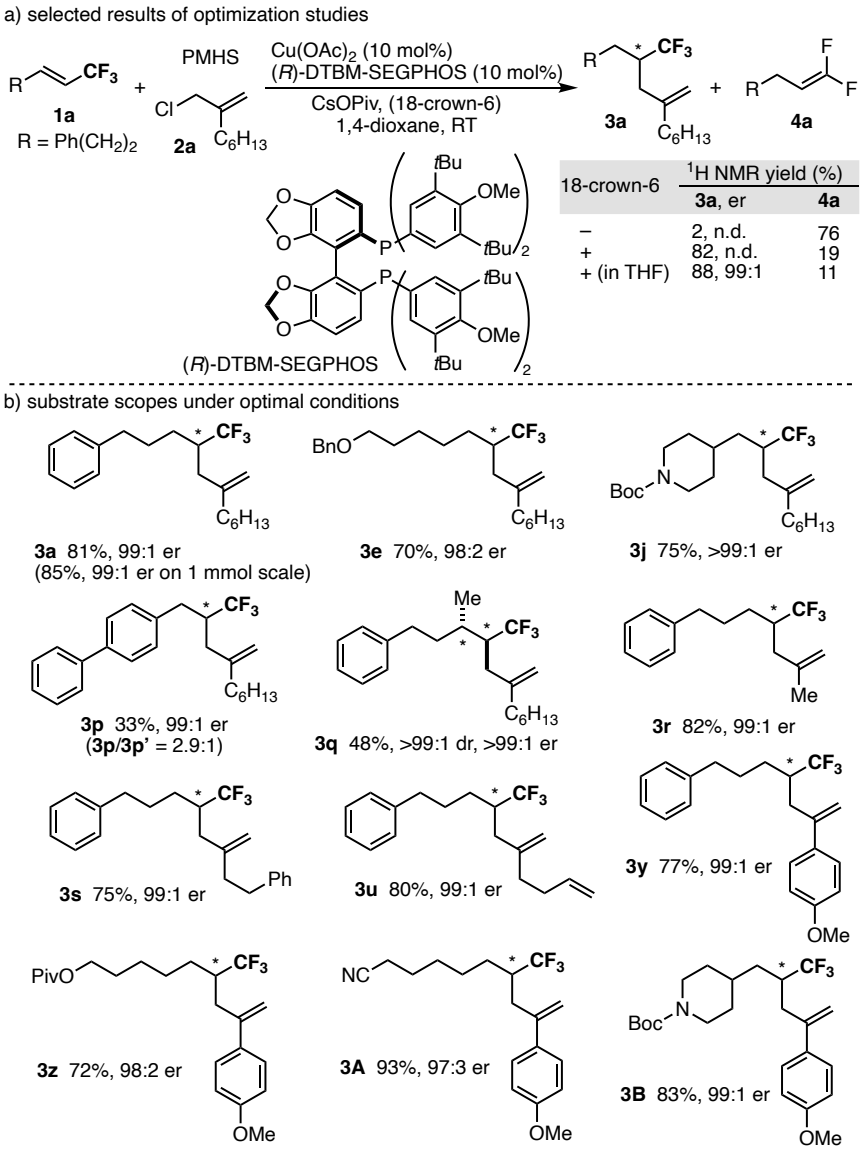
The scope of allylic chlorides **2** was also broad: the methyl-, phenethyl-, and cyclohexyl-substituted **2b-d** underwent the reaction smoothly to furnish **3r-t** in 73-81%




**Scheme 1.4**. Products of Cu-catalyzed regioselective hydroallylation of $CF_3$-substituted alkenes **1** with PMHS and allylic chlorides **2**. Conditions A: **1** (0.25 mmol), PMHS (1.0 mmol of PMHS based on Si–H), **2** (0.50 mmol), CsOPiv (0.50 mmol), $Cu(OAc)_2$ (0.025 mmol), MeO-dppbz (0.025 mmol), 1,4-dioxane (1.5 mL), RT, 6 h. Conditions B: **1** (0.25 mmol), PMHS (0.75 mmol of PMHS based on Si–H), **2** (0.50 mmol), CsOPiv (0.50 mmol), 18-crown-6 (0.50 mmol), $Cu(OAc)_2$ (0.025 mmol), TMS-dppbz (0.025 mmol), 1,4-dioxane (1.5 mL), RT, 6 h; Conditions C. **1** (0.25 mmol), PMHS (0.75 mmol of PMHS based on Si–H), **2** (0.50 mmol), CsOPiv (0.50 mmol), 18-crown-6 (0.50 mmol), $Cu(OAc)_2$ (0.025 mmol), *t*Bu-dppbz (0.025 mmol), 1,4-dioxane (1.5 mL), RT, 6 h. Isolated yields of pure regioisomers are shown. The conditions employed (A, B, or C) are given in parentheses. The dr was determined by $^1$H NMR in the crude product. [a] On a 1.0 mmol scale. [b] With $(EtO)_3SiH$ (0.75 mmol) instead of PMHS.

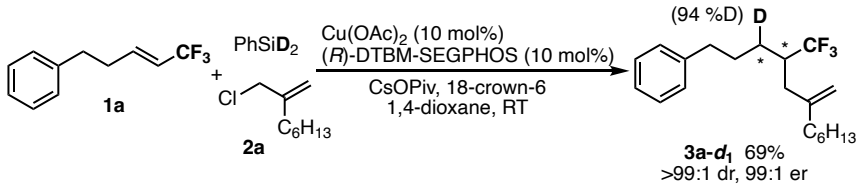
yields. The copper-catalyzed conditions tolerated the isolated terminal alkene and allylsilane functions (**3u**, **v**), which can be useful synthetic handles for further manipulations. Notably, the reaction with **2g** selectively occurred at the allyl position to afford **3w** with the vinyl chloride left intact. Additionally, the parent allyl chloride (**2h**) and aryl-substituted allyl chloride **2i** were accommodated under the standard conditions to deliver the corresponding **3x**-**z**, and **3A** in good yields.

The author next investigated the enantioselective conditions using asymmetric catalysis. Unfortunately, the simple replacement of the MeO-dppbz ligand with chiral




**Scheme 1.5**. Copper-catalyzed regio- and enantioselective hydroallylation of $CF_3$-substituted alkenes **1**. Optimal conditions: **1** (0.25 mmol), **2** (0.50 mmol), PMHS (0.75 mmol based on Si–H), 18-crown-6 (0.63 mmol), $Cu(OAc)_2$ (0.025 mmol), (*R*)-DTBM-SEGPHOS (0.025 mmol), CsOPiv (0.50 mmol), THF (1.5 mL), RT, 12 h, $N_2$. Isolated yields of pure regioisomers are shown. The enantiomeric ratio (er) was determined by HPLC analysis on a chiral stationary phase.

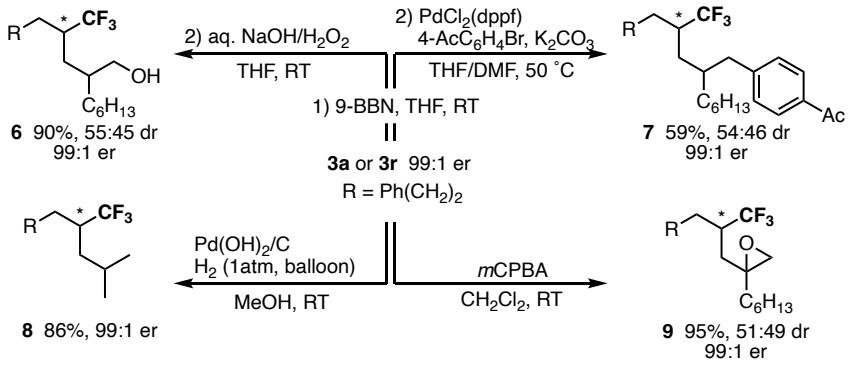
bisphosphine ligands was detrimental as far as we tested. For example, the reaction of **1a** with PMHS and **2a** in the presence of the $Cu(OAc)_2$/(*R*)-DTBM-SEGPHOS catalyst and CsOPiv base dominantly produced the *gem*-difluoroalkene **4a** in 76% yield. The targeted **3a** was formed only in 2% yield (Scheme 1.5a). However, similar to the cases of TMS- and *t*Bu-dppbz ligands (entries 14 and 15 in Table 1.1), the addition of 18-crown-6 dramatically improved the chemoselectivity to form **3a** in 82% yield. Additional fine tunings proved THF to be a somewhat better solvent, and the enantioenriched hydroallylated product was finally obtained in 88% yield with 99:1 enantiomeric ratio (er). Under the optimal 18-crown-6-assisted enantioselective conditions, various combinations of $CF_3$-substituted alkenes **1** and allylic chlorides **2** were successfully employed (Scheme 1.5b). A benzyl ether (**3e**), Boc-protected amine (**3j, 3B**), isolated terminal alkene (**3u**), ester (**3z**), and nitrile (**3A**) were equally tolerated to give the corresponding hydroallylated products with 97:3 to 99:1 er. As same under the nonenantioselective conditions in Scheme 1.4, the aryl-conjugated system **1p** afforded a mixture of regioisomers **3p** and **3p'**, but the desired isomer was successfully isolated with high enantiopurity (**3p**; 99:1 er). Particularly notable is the successful control of both diastereoselectivity and enantioselectivity in the production of **3q**. The enantioselective reaction could also be conducted on a 1.0 mmol scale without any drop in the yield and enantioselectivity (**3a**). Furthermore, an asymmetric catalysis with $Ph_2SiD_2$ successfully synthesized the deuterium-labeled chiral $CF_3$-substituted molecule **3a**-$d_1$ (Scheme 1.6), which has applications in biological labeling studies and drug discovery.[21] Additionally, the result can also support the mechanistic hypothesis in Scheme 1.3, in which the copper hydride species **A** is formed from the hydrosilane and the hydride is finally transferred to the product **3** via the alkyl copper intermediate **D**.




**Scheme 1.6**. Synthesis of deuterium-labeled chiral **3a**-$d_1$.

The allylic function in the optically active **3a**, **r** could be readily derivatized (Scheme 1.7). A regioselective hydroboration with 9-BBN was followed by an oxidation with aqueous $H_2O_2$ to form the chiral alcohol **6** in 90% yield. A Suzuki-Miyaura coupling of

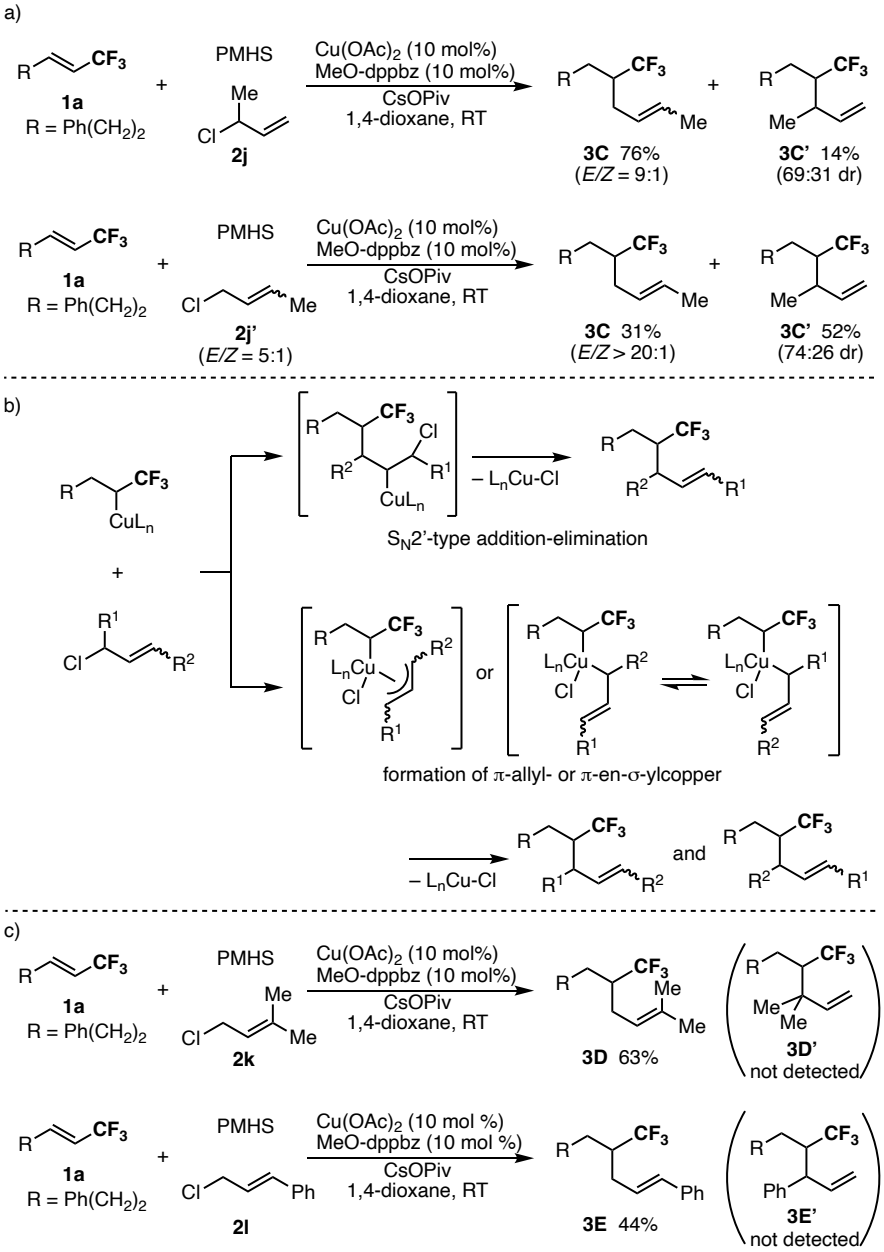
the same alkylborane intermediate was also possible, delivering **7** in 59% overall yield. Additionally, the chiral alkane **8** and epoxide **9** were obtained in high yields by the standard hydrogenation and epoxidation reactions, respectively. All transformations proceeded without any erosion of enantiomeric excess.




**Scheme 1.7**. Derivatizations of **3a, r**.

To get some insight into the allylation process (**D** and **2** to **A** and **3** in Scheme 1.3), the regioisomeric allyl chlorides 3-chlorobut-1-ene (**2j**) and 1-chlorobut-2-ene (**2j'**) were tested under the nonenantioselective conditions using MeO-dppbz (Scheme 1.8a). The branched **2j** reacted with **1a** to deliver a mixture of linear **3C** and branched **3C'** in favor of linear **3C**. On the other hand, the linear **2j'** also formed a regioisomeric mixture, but the **3C**/**3C'** ratio was reversed; the branched **3C'** was mainly observed. The replacement of MeO-dppbz with TMS-dppbz and *t*Bu-dppbz, in conjunction with 18-crown-6, also resulted in similar trends. These phenomena suggest that the $S_N2'$-type addition-elimination-type mechanism[22] is mainly operating, while the formation of π-allyl- or π-en-σ-yl copper species[23] is competitively involved, particularly in a case of sterically congested allylic chloride such as **2j'** (Scheme 1.8b). The different *E:Z* ratios of the starting **2j'** (*E:Z* = 5:1) and the linear product **3C** (*E:Z* > 20:1) can also support involvement of the π-allyl- or π-en-σ-yl copper intermediate and its rapid *E:Z* (*syn/anti*) isomerization. Actually, the more hindered prenyl chloride (**2k**) and cinnamyl chloride (**2l**) gave the corresponding liner hydroallylated products (**3D**, **E**, respectively) exclusively (Scheme 1.8c), probably via the formation of π-allyl- or π-en-σ-yl copper then reductive elimination at the more sterically accessible position.[24]

Finally, the author examined the effects of KOPiv and KOPiv/18-crown-6 on the initial reaction rate of hydrodefluorination of **1a** with $(MeO)_2MeSiH$ to **4a** under stoichiometric conditions using 1.0 equiv of $Cu(OAc)_2$ and TMS-dppbz (Figure 1.2).[25]




**Scheme 1.8**. Reactions with 1- or 3-Substituted Allyl Chlorides **2**.

In comparison to the parent conditions without any additives, the addition of KOPiv increased the initial rate by 1.57 times, thus indicating the alkali cation accelerated β-F elimination from the α-$CF_3$ alkylcopper (Figure 1.1, top). On the other hand, when the combination of KOPiv and 18-crown-6 was used, relatively moderate acceleration (1.22 times) was observed. The result is consistent with our assumption that 18-crown-6 disrupts the interaction of the alkali cation and fluorine atom to decrease the rate of the β-F elimination (Figure 1.1, bottom).

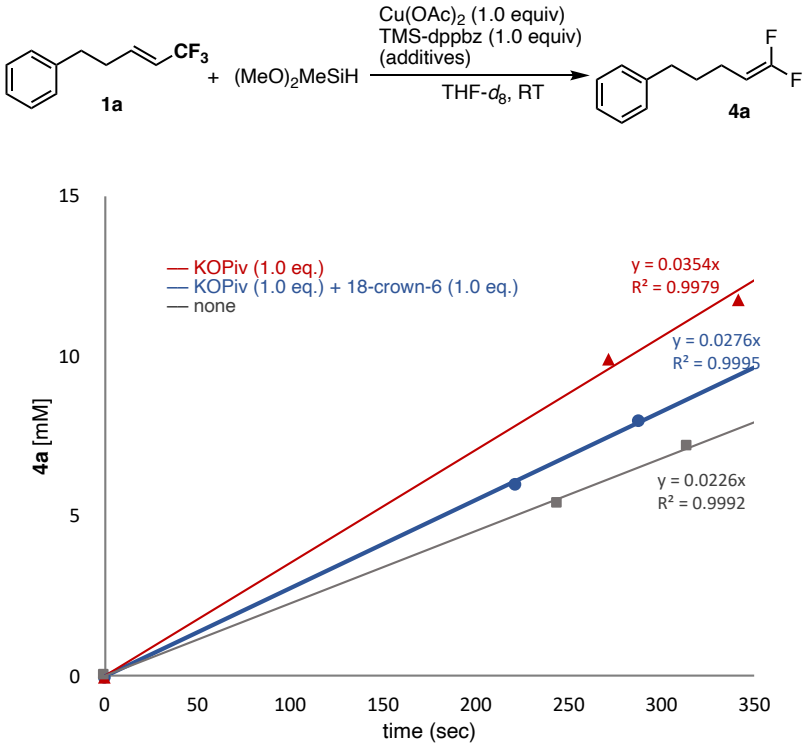



**Figure 1.2**. Effects of additives on the initial reaction rate in the hydrodefluorination of **1a** with $(MeO)_2MeSiH$.

## Summary

In conclusion, the author has developed a CuH-catalyzed regio- and enantioselective hydroallylation of $CF_3$-substituted alkenes. The key to success is the combined use of 18-crown-6-ether and CsOPiv base to suppress the otherwise predominant β-F elimination from an α-$CF_3$ organocopper intermediate. The asymmetric Cu catalysis successfully controls the point chirality at the position α to $CF_3$ even in the absence of any proximal directing heteroatoms. The present strategy can provide a new repertoire of $CF_3$-containing chiral molecules, which have high potential in medicinal and pharmaceutical chemistry.

## Experimental Section

### Instrumentation and Chemicals

$^1H$, $^{13}C\{^1H\}$, $^{19}F\{^1H\}$, and $^2H$ NMR spectra were recorded at 400 MHz, 100 MHz, 376 MHz, and 61 Hz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by

APCI or EI using TOF or a magnetic sector, respectively. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakosil C-200, Wako Pure Chemical Co.) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-20AR (pump, SHIMADZU, 7.5 mL/min $CHCl_3$ or ethyl acetate) and SPD-20A (UV detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. 1,4-Dioxane was dried on a Glass Contour Solvent dispensing system (Nikko Hansen & Co., Ltd.) prior to use. Anhydrous THF was available from Kanto Chemical Co. and used out of the bottle. $Cu(OAc)_2$ and (*R*)-DTBM-SEGPHOS were purchased from FUJIFILM Wako Pure Chemical Co. and TCI, respectively. CsOPiv was obtained from Aldrich but should be crushed to pieces with a mortar and a pestle in a glovebox filled with nitrogen and then dried at 100 ˚C under high vacuum overnight (note: this preactivation was essential for reproducibility. Without dryness, we often observed poor conversion of the starting $CF_3$-substituted alkenes albeit with the remaining high chemoselectivity). MeO-dppbz, TMS-dppbz, and *t*Bu-dppbz were prepared from 1,2-bis(dichlorophosphino)benzene and corresponding aryl Grignard reagents.[26] $CF_3$-substituted alkenes **1a-j**,[27] **1l-p**,[28] and **1q**[12c] were prepared according to the reported methods. The allyl chlorides **2a**, **c-f**, and **i** were synthesized according to the literature.[29] Ethyl (*E*)-4,4,4-trifluorobut-2-enoateand (**1k**) and allylic chlorides **2b**, **g**, **h**, and **j-l** are commercially available. Unless otherwise noted, all reactions were performed under nitrogen atmosphere.

**Experimental Procedures**

**Copper-catalyzed regioselective hydroallylation of $CF_3$-substituted alkenes (Conditions A; 0.25 mmol scale)**

Synthesis of **3a** (Table1, entry 13) is representative. $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), MeO-dppbz (14 mg, 0.025 mmol), and CsOPiv (117 mg, 0.50 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (1.5 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. PMHS (57 μL, 1.0 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 80 mg, 0.50 mmol) was added in one portion, and (*E*)-

(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**, 50 mg, 0.25 mmol) was finally added. The reaction solution was stirred at room temperature for 6 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane to give (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 75 mg, 0.23 mmol, 90%).

**Copper-catalyzed regioselective hydroallylation of $CF_3$-substituted alkenes (Conditions A; 1.0 mmol scale)**

Synthesis of **3a** (Scheme 3, 1.0 mmol scale) is representative. $Cu(OAc)_2$ (18 mg, 0.10 mmol), MeO-dppbz (57 mg, 0.10 mmol), and CsOPiv (468 mg, 2.0 mmol) were placed in a 50 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (6.0 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. PMHS (240 mg, 4.0 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 321 mg, 2.0 mmol) was added in one portion, and (*E*)-(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**, 200 mg, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 6 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane to give (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 299 mg, 0.92 mmol, 91%).

**Copper-catalyzed regioselective hydroallylation of $CF_3$-substituted alkenes (Conditions B; 0.25 mmol scale)**

Synthesis of **3p** (Scheme 3) is representative. $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), TMS-dppbz (26 mg, 0.025 mmol), CsOPiv (117 mg, 0.50 mmol), and 18-crown-6 (132 mg, 0.50 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (1.5 mL) was added to the tube, and the solution was stirred vigorously for 15 min at room temperature. PMHS (43 μL, 0.75 mmol) was then added dropwise via syringe, and the resulting solution was stirred vigorously at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 80 mg, 0.50 mmol) was added in one portion, and (*E*)-4-(3,3,3-trifluoroprop-1-en-1-yl)-1,1'-biphenyl (**1p**, 62 mg, 0.25 mmol) was finally added. The reaction solution was stirred at room temperature for 6 h. The resulting mixture was directly filtered through a short pad

of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) to give 4-(4-methylene-2-(trifluoromethyl)decyl)-1,1'-biphenyl (**3p**, 50 mg, 0.13 mmol, 53%).

**Copper-catalyzed regioselective hydroallylation of $CF_3$-substituted alkenes (Conditions C; 0.25 mmol scale)**

Synthesis of **3a** (Table1, entry 15) is representative. $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), *t*Bu-dppbz (22 mg, 0.025 mmol), CsOPiv (117 mg, 0.50 mmol), and 18-crown-6 (132 mg, 0.50 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (1.5 mL) was added to the tube, and the solution was stirred vigorously for 15 min at room temperature. PMHS (43 μL, 0.75 mmol) was then added dropwise via syringe, and the resulting solution was stirred vigorously at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 80 mg, 0.50 mmol) was added in one portion, and (*E*)-(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**, 50 mg, 0.25 mmol) was finally added. The reaction solution was stirred at room temperature for 6 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane to give (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 76 mg, 0.23 mmol, 93%).

**Copper-catalyzed regio- and enantioselective hydroallylation of of $CF_3$-substituted alkenes (Enantioselective conditions; 0.25 mmol scale)**

Synthesis of **3a** (Scheme 4) is representative. $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), (*R*)-DTBM-SEGPHOS (30 mg, 0.025 mmol), CsOPiv (117 mg, 0.50 mmol), and 18-crown-6 (165 mg, 0.63 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (1.5 mL) was added to the tube, and the solution was stirred vigorously for 15 min at room temperature. PMHS (43 μL, 0.75 mmol) was then added dropwise via syringe, and the resulting solution was stirred vigorously at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 80 mg, 0.50 mmol) was added in one portion, and (*E*)-(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**, 50 mg, 0.25 mmol) was finally added. The reaction solution was stirred at room temperature for 12 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica

gel column chromatography with hexane to give (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 67 mg, 0.20 mmol, 81%, 99:1 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 11.3 min, minor isomer: $t_R$ = 13.1 min, UV detection at 254 nm, 30 °C).

**Copper-catalyzed regio- and enantioselective hydroallylation of of $CF_3$-substituted alkenes (Enantioselective conditions; 1.0 mmol scale)**

Synthesis of **3a** (Scheme 4) is representative. $Cu(OAc)_2$ (18 mg, 0.10 mmol), (*R*)-DTBM-SEGPHOS (118 mg, 0.10 mmol), CsOPiv (468 mg, 2.0 mmol), and 18-crown-6 (661 mg, 2.5 mmol) were placed in a 50 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (6.0 mL) was added to the tube, and the solution was stirred vigorously for 15 min at room temperature. PMHS (180 mg, 3.0 mmol) was then added dropwise via syringe, and the resulting solution was stirred vigorously at the same temperature. After 15 min, 2-(chloromethyl)oct-1-ene (**2a**, 321 mg, 2.0 mmol) was added in one portion, and (*E*)-(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**, 200 mg, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 12 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane to furnish (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 289 mg, 0.89 mmol, 85%, 99:1 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 11.3 min, minor isomer: $t_R$ = 13.1 min, UV detection at 254 nm, 30 °C).

**Hydroboration/oxidation of 3a (Scheme 6)**

A 50 mL Schlenk tube equipped with a stir bar was charged with borabicyclo[3.3.1]nonane dimer (73 mg, 0.30 mmol) in a glovebox filled with nitrogen. The reaction tube was sealed with a septum and taken out of the glovebox. THF (5.0 mL) and (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 65 mg, 0.20 mmol, 99:1 er) was added to the tube, and the solution was stirred overnight at room temperature. Sodium hydroxide aqueous solution (1 M, 1.5 mL) and hydrogen peroxide (30 wt%, 0.5 mL) were added to the reaction mixture, and the solution was stirred for 20 min. The reaction was

quenched with saturated aqueous sodium thiosulfate and ammonium chloride aqueous solution. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) to give 2-(5-phenyl-2-(trifluoromethyl)pentyl)octan-1-ol (**6**, 62 mg, 0.18 mmol, 90%, 55:45 d.r., 99:1 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OD-H column, 98.5/1.5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 24.8, 27.4 min, minor isomer: $t_R$ = 26.3, 49.7 min, UV detection at 210 nm, 30 ºC).

**Hydroboration/Suzuki-Miyaura coupling of 3a (Scheme 6)**

A 50 mL Schlenk tube equipped with a stir bar was charged with borabicyclo[3.3.1]nonane dimer (73 mg, 0.30 mmol) in a glovebox filled with nitrogen. The reaction tube was sealed with a septum and taken out of the glovebox. THF (5.0 mL) and (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 65 mg, 0.20 mmol, 99:1 er) was added to the tube, and the solution was stirred overnight at room temperature. The reaction mixture was evaporated in vacuo. THF/DMF (0.4 mL/1.7 mL), $PdCl_2$(dppf) (4.4 mg, 0.006 mmol), 4-bromoacetophenone (60 mg, 0.30 mmol), and $K_2CO_3$ (55 mg, 0.40 mmol) were added the residue, and the mixture was stirred at 50 ℃ for 8 h. The reaction mixture was diluted with ethyl acetate (20 mL). The combined organic layer was washed with $H_2O$ and brine, and dried over $Na_2SO_4$. The organic layer was concentrated in vacuo, and the residue was purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) to give 1-(4-(2-(5-phenyl-2-(trifluoromethyl)pentyl)octyl)phenyl)ethan-1-one (**7**, 50 mg, 0.12 mmol, 59%, 54:46 d.r., 99:1 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (YMC CHIRAL ART Cellulose-SB column, 95/5 *n*-hexane/chloroform, 0.5 mL/min, major isomer: $t_R$ = 25.1, 26.9 min, minor isomer: $t_R$ = 34.1, 37.5 min, UV detection at 250 nm, 25 ºC).

**Hydrogenation of 3r (Scheme 6)**

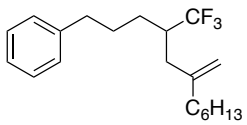
A 20 mL round bottom flask equipped with a stir bar was charged with (6-methyl-4-(trifluoromethyl)hept-6-en-1-yl)benzene (**3r**, 26 mg, 0.10 mmol, 99:1 er), $Pd(OH)_2$ on carbon (20 wt%, 5.1 mg), and MeOH (2.5 mL). The flask was evacuated and backfilled

with hydrogen (this process was repeated a total of 3 times), and the suspension was stirred at room temperature for 24 h under hydrogen atmosphere (1 atm, balloon). The reaction flask was then evacuated and backfilled with $N_2$. The mixture was diluted with ethyl acetate and filtered through a pad of Celite. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography with hexane to give (6-methyl-4-(trifluoromethyl)heptyl)benzene (**8**, 22 mg, 0.08 mmol, 86%, 99:1 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 99.9/0.1 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 12.5 min, minor isomer: $t_R$ = 13.9 min, UV detection at 220 nm, 30 °C).

**Epoxidation of 3a (Scheme 6)**

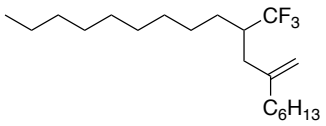
To a solution of *m*-chloroperoxybenzoic acid (74 mg as a 70 wt% solid, 0.30 mmol) in $CH_2Cl_2$ (1.5 mL) at 0 °C under air was added (6-methylene-4-(trifluoromethyl)dodecyl)benzene (**3a**, 65 mg, 0.20 mmol, 99:1 er). The suspension was stirred at room temperature overnight. The reaction was quenched with 1 M NaOH. Extraction was repeated a total of 3 times with $CHCl_3$. The solvent was removed under reduced pressure to give 2-hexyl-2-(5-phenyl-2-(trifluoromethyl)pentyl)oxirane (**9**, 65 mg, 0.19 mmol, 95%, 51:49 dr, 99:1 er) in an analytically pure form. The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 99.9/0.1 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 35.7, 45.5 min, minor isomer: $t_R$ = 29.0, 34.1 min, UV detection at 210 nm, 30 °C).

**Characterization Data of Products**

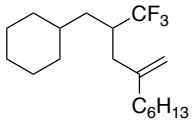



**(6-Methylene-4-(trifluoromethyl)dodecyl)benzene (3a):** Purified by silica gel column chromatography with hexane: 75 mg (90%, 0.25 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.20-7.15 (m, 3H), 4.81 (s, 1H), 4.75 (s, 1H), 2.58 (t, *J* = 7.6 Hz, 2H), 2.36 (dd, *J* = 14.3, 4.3 Hz, 1H), 2.31-2.18 (m, 1H), 2.03 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.96 (t, *J* = 7.5 Hz, 2H), 1.82-1.56 (m, 3H), 1.54-1.46 (m, 1H), 1.45-

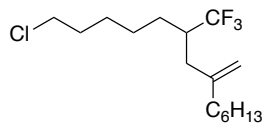
1.35 (m, 2H), 1.34-1.26 (m, 6H), 0.89 (t, $J$ = 6.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.7, 141.9, 128.5 (q, $J$ = 278.4 Hz), 128.3 (4C), 125.9, 112.0, 40.7 (q, $J$ = 24.6 Hz), 36.0, 35.3, 34.8 (q, $J$ = 2.5 Hz), 31.7, 29.0, 28.7, 27.52, 27.50, 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.25; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{30}F_3$: 327.2294, found: 327.2293. Chiralcel OJ-H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 11.3 min, minor isomer: $t_R$ = 13.1 min.



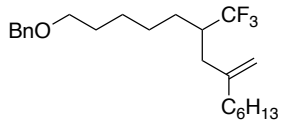

**7-Methylene-9-(trifluoromethyl)octadecane (3b):** Purified by silica gel column chromatography with hexane and GPC (ethyl acetate): 62 mg (74%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.78 (s, 1H), 2.36 (dd, $J$ = 14.3, 4.3 Hz, 1H), 2.28-2.14 (m, 1H), 2.04 (dd, $J$ = 14.3, 9.4 Hz, 1H), 1.99 (t, $J$ = 7.6 Hz, 2H), 1.54-1.50 (m, 1H), 1.46-1.36 (m, 4H), 1.35-1.26 (m, 19H), 0.91-0.86 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.9, 128.6 (q, $J$ = 278.6 Hz), 111.9, 40.7 (q, $J$ = 24.2 Hz), 35.3, 34.8 (q, $J$ = 2.7 Hz), 31.9, 31.7, 29.7, 29.5, 29.4, 29.3, 29.0, 27.8, 27.5, 26.9, 22.7, 22,6, 14.10, 14.08; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.33; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{38}F_3$: 335.2920, found: 335.2920.



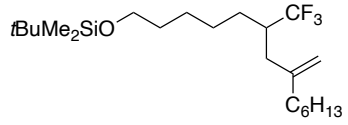

**(4-Methylene-2-(trifluoromethyl)decyl)cyclohexane (3c):** Purified by silica gel column chromatography with hexane: 41 mg (54%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 4.83 (d, $J$ = 1.2 Hz, 1H), 4.78 (s, 1H), 2.37 (dd, $J$ = 14.1, 4.7 Hz, 1H), 2.32-2.25 (m, 1H), 2.01-1.95 (m, 3H), 1.72-1.63 (m, 5H), 1.48-1.35 (m, 4H), 1.33-1.24 (m, 8H), 1.22-1.07 (m, 3H), 0.91-0.87 (m, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.9, 128.7 (q, $J$ = 278.6 Hz), 112.0, 37.7 (q, $J$ = 24.4 Hz), 35.9, 35.7 (q, $J$ = 2.8 Hz), 35.2, 34.9, 33.5, 33.0, 31.7, 29.0, 27.5, 26.5, 26.2 (2C), 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.77; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{32}F_3$: 305.2451, found: 305.2459.




**1-Chloro-8-methylene-6-(trifluoromethyl)tetradecane (3d):** Purified by silica gel column chromatography with hexane: 65 mg (82%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.85 (s, 1H), 4.78 (d, *J* = 0.6 Hz, 1H), 3.53 (t, *J* = 6.6 Hz, 2H), 2.38 (dd, *J* = 14.3, 4.2 Hz, 1H), 2.29-2.16 (m, 1H), 2.03 (dd, *J* = 14.4, 9.6 Hz, 1H), 1.98 (t, *J* = 7.7 Hz, 2H), 1.77 (quin, *J* = 6.8 Hz, 2H), 1.54-1.33 (m, 8H), 1.33-1.26 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.7, 128.5 (q, *J* = 278.5 Hz), 112.0, 44.9, 40.6 (q, *J* = 24.7 Hz), 35.3, 34.8 (q, *J* = 2.8 Hz), 32.3, 31.7, 29.0, 27.63 (q, *J* = 2.0 Hz), 27.5, 27.0, 26.2, 22.6, 14,1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.31; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{16}H_{29}ClF_3$: 313.1904, found: 313.1916.

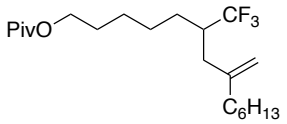



**(((8-Methylene-6-(trifluoromethyl)tetradecyl)oxy)methyl)benzene (3e):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 72 mg (74%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H), 7.31-7.27 (m, 1H), 4.83 (s, 1H), 4,77 (d, *J* = 0.6 Hz, 1H), 4.50 (s, 2H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.36 (dd, *J* = 14.3, 4.2 Hz, 1H), 2.27-2.15 (m, 1H), 2.03 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.98 (t, *J* = 7.6 Hz, 2H), 1.61 (quin, *J* = 6.7 Hz, 2H), 1.53-1.31 (m, 8H), 1.31-1.26 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.7, 138.5, 128.4 (q, *J* = 278.6 Hz), 128.2 (2C), 127.5 (2C), 127.4, 111.8, 72.8, 70.1, 40.6 (q, *J* = 24.6 Hz), 35.2, 34.7 (q, *J* = 2.7 Hz), 31.6, 29.4, 28.9, 27.7 (q, *J* = 1.9 Hz), 27.4, 26.7, 26.2, 22.5, 14.0; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.30; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{23}H_{35}F_3O$: 384.2635, found: 384.2634. Chiralcel OJ-H column, 99.7/0.3 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 10.6 min, minor isomer: $t_R$ = 12.3 min.

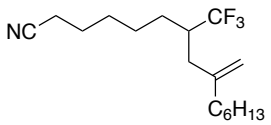



***tert*-Butyldimethyl((8-methylene-6-(trifluoromethyl)tetradecyl)oxy)silane (3f):**

Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v): 77 mg (75%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.77 (s, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.36 (dd, *J* = 14.3, 4.3 Hz, 1H), 2.28-2.14 (m, 1H), 2.03 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.98 (t, *J* = 8.3 Hz, 2H), 1.55-1.46 (m, 3H), 1.44-1.37 (m, 4H), 1.35-1.28 (m, 9H), 0.91-0.87 (m, 3H), 0.89 (s, 9H), 0.04 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.8, 128.6 (q, *J* = 278.6 Hz), 111.9, 63.1, 40.7 (q, *J* = 24.5 Hz), 35.3, 34.8 (q, *J* = 2.7 Hz), 32.5, 31.7, 29.0, 27.8 (q, *J* = 1.7 Hz), 27.5, 26.7, 26.0 (4C), 22.6, 18.4, 14.1, -5.3 (2C); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.32; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{22}H_{44}F_3OSi$: 409.3108, found: 409.3107.

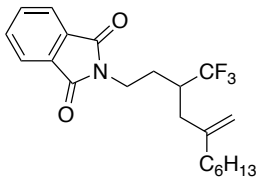



**8-Methylene-6-(trifluoromethyl)tetradecyl pivalate (3g):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v): 79 mg (83%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.84 (s, 1H), 4.78 (s, 1H), 4.04 (t, *J* = 6.6 Hz, 2H), 2.37 (dd, *J* = 14.3, 4.2 Hz, 1H), 2.28-2.15 (m, 1H), 2.03 (dd, *J* = 14.3, 9.6 Hz, 1H), 1.98 (t, *J* = 7.6 Hz, 2H), 1.62 (quin, *J* = 6.7 Hz, 2H), 1.56-1.33 (m, 8H), 1.31-1.29 (m, 6H), 1.19 (s, 9H), 0.88 (t, *J* = 6.6 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 178.6, 145.7, 128.5 (q, *J* = 278.9 Hz), 112.0, 64.2, 40.6 (q, *J* = 24.5 Hz), 38.7, 35.3, 34.8 (q, *J* = 2.7 Hz), 31.7, 29.0, 28.4, 27.7 (q, *J* = 1.9 Hz), 27.5, 27.2 (3C), 26.6, 26.1, 22.6, 14.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.31; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{21}H_{38}F_3O_2$: 379.2818, found: 379.2817.

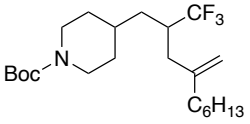



**9-Methylene-7-(trifluoromethyl)pentadecanenitrile (3h):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 62 mg (82%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.85 (s, 1H), 4.78 (d, *J* = 0.6 Hz, 1H), 2.39 (dd, *J* = 14.3, 4.0 Hz, 1H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.29-2.15 (m, 1H), 2.03 (dd, *J* = 14.2, 9.8 Hz, 1H), 1.98 (t, *J* = 7.8 Hz, 2H), 1.66 (quin, *J* = 7.2 Hz, 2H), 1.58-1.35 (m, 8H), 1.34-1.29 (m, 6H), 0.89 (t, *J* = 6.7 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.6,

128.4 (q, $J$ = 278.6 Hz), 119.6, 112.1, 40.6 (q, $J$ = 24.6 Hz), 35.3, 34.7 (q, $J$ = 2.7 Hz), 31.7, 29.0, 28.8, 27.5, 27.5 (q, $J$ = 2.0 Hz), 26.1, 25.1, 22.6, 17.1, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.28; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{17}H_{29}F_3N$: 304.2247, found: 304.2245.

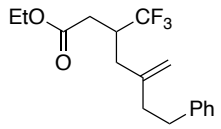



**2-(5-Methylene-3-(trifluoromethyl)undecyl)isoindoline-1,3-dione (3i):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 55 mg (57%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.88-7.82 (m, 2H), 7.75-7.70 (m, 2H), 4.84 (s, 1H), 4.82 (s, 1H), 3.83-3.72 (m, 2H), 2.43 (dd, $J$ = 14.5, 3.9 Hz, 1H), 2.40-2.29 (m, 1H), 2.07 (dd, $J$ = 14.1, 10.0 Hz, 1H), 1.99-1.90 (m, 3H), 1.88-1.79 (m, 1H), 1.52-1.31 (m, 2H), 1.29-1.20 (m, 6H), 0.87 (t, $J$ = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 168.2 (2C), 145.0 (2C), 134.0 (2C), 132.0, 128.1 (q, $J$ = 278.1 Hz), 123.3 (2C), 112.8, 39.1 (q, $J$ = 25.2 Hz), 36.1, 35.2, 34.9 (q, $J$ = 2.7 Hz), 31.7, 29.0, 27.5, 26.9, 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.71; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{27}F_3NO_2$: 382.1988, found: 382.1988.

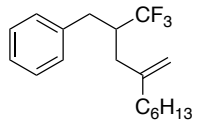



***tert*-Butyl 4-(4-methylene-2-(trifluoromethyl)decyl)piperidine-1-carboxylate (3j):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) and GPC (ethyl acetate): 77 mg (76%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 4.84 (s, 1H), 4.78 (s, 1H), 4.08 (br, 2H), 2.66 (br, 2H), 2.41 (dd, $J$ = 14.2, 4.1 Hz, 1H), 2.35-2.24 (m, 1H), 2.03-1.94 (m, 3H), 1.68-1.59 (m, 3H), 1.54-1.48 (m, 2H), 1.45 (s, 9H), 1.42-1.38 (m, 1H), 1.33-1.26 (m, 7H), 1.14-0.95 (m, 2H), 0.89 (t, $J$ = 6.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.8, 145.5, 128.5 (q, $J$ = 278.5 Hz), 112.4, 79.3, 44.0 (br, 2C), 37.6 (q, $J$ = 24.5 Hz), 35.6 (q, $J$ = 2.7 Hz), 35.2, 35.0, 33.5, 32.6, 31.7 (2C), 29.0, 28.4 (3C), 27.5, 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.74; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{39}F_3NO_2$: 406.2297, found: 406.2928. Chiralcel OJ-

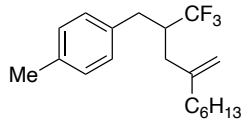
H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 14.0 min, minor isomer: $t_R$ = 20.0 min.



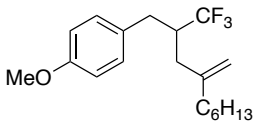

**Ethyl 5-methylene-7-phenyl-3-(trifluoromethyl)heptanoate (3k):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC ($CHCl_3$); 35 mg (45%, 0.25 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.21-7.17 (m, 3H), 4.92 (s, 1H), 4.87 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.05-2.92 (m, 1H), 2.82-2.69 (m, 2H), 2.55-2.46 (m, 2H), 2.43-2.28 (m, 3H), 2.09 (dd, *J* = 14.3, 10.5 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 171.0, 144.1, 141.6, 128.4 (2C), 128.3 (2C), 127.6 (q, *J* = 277.8 Hz), 126.0, 113.6, 61.0, 38.0 (q, *J* = 26.2 Hz), 36.7, 35.1 (q, *J* = 2.4 Hz), 34.1, 32.9 (q, *J* = 2.3 Hz), 14.1; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -71.92; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{17}H_{22}F_3O_2$: 315.1566, found: 315.1567.



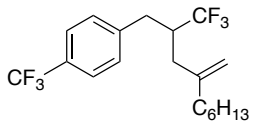

**(4-Methylene-2-(trifluoromethyl)decyl)benzene (3l):** Purified by silica gel column chromatography with hexane; 45 mg (60%, 0.25 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.23-7.16 (m, 3H), 4.82 (s, 1H), 4.79 (s, 1H), 2,91 (dd, *J* = 14.2, 6.2 Hz, 1H), 2.68 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.63-2.50 (m, 1H), 2.37 (dd, *J* = 14.7, 5.8 Hz, 1H), 2.10 (dd, *J* = 14.7, 7.8 Hz, 1H), 1.96-1.84 (m, 2H), 1.29-1.26 (m, 3H), 1.24-1.18 (m, 5H), 0.87 (t, *J* = 6.8 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 145.6, 138.6, 129.0 (2C), 128.3 (2C), 128.0 (q, *J* = 279.1 Hz), 126.4, 112.2, 43.1 (q, *J* = 22.0 Hz), 35.0, 34.4, 34.0, 31.5, 28.8, 27.2, 22.5, 14.0; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -70.20; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{18}H_{26}F_3$: 299.1981, found: 299.1982.



**1-Methyl-4-(4-methylene-2-(trifluoromethyl)decyl)benzene (3m):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate); 43 mg (56%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 4.82 (s, 1H), 4.79 (s, 1H), 2.88 (dd, *J* = 14.2, 6.1 Hz, 1H), 2.63 (dd, *J* = 14.2, 6.9 Hz, 1H), 2.59-2.47 (m, 1H), 2.35 (dd, *J* = 14.7, 5.8 Hz, 1H), 2.32 (s, 3H), 2.09 (dd, *J* = 14.7, 7.6 Hz, 1H), 1.94-1.84 (m, 2H), 1.32-1.25 (m, 3H), 1.24-1.18 (m, 5H), 0.87 (t, *J* = 6.8 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.7, 135.9, 135.4, 129.0 (2C), 128.9 (2C), 128.1 (q, *J* = 279.2 Hz), 112.1, 43.1 (q, *J* = 24.1 Hz), 35.0, 34.4 (q, *J* = 2.2 Hz), 33.6 (q, *J* = 2.3 Hz), 31.6, 28.8, 27.2, 22.5, 20.9, 14.0; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.16; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{19}H_{28}F_3$: 313.2138, found: 313.2138.

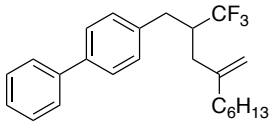



**1-Methoxy-4-(4-methylene-2-(trifluoromethyl)decyl)benzene (3n):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v), GPC ($CHCl_3$), and GPC (ethyl acetate); 36 mg (45%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.10-7.06 (m, 2H), 6.84-6.81 (m, 2H), 4.82 (d, *J* = 1.4 Hz, 1H), 4.79 (s, 1H), 3.79 (s, 3H), 2.86 (dd, *J* = 14.3, 6.1 Hz, 1H), 2.62 (dd, *J* = 14.3, 6.9 Hz, 1H), 2.56-2.44 (m, 1H), 2.35 (dd, *J* = 14.6, 5.8 Hz, 1H), 2.09 (dd, *J* = 14.6, 7.6 Hz, 1H), 1.94-1.84 (m, 2H), 1.30-1.22 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 158.3, 145.8, 130.6, 130.1 (2C), 128.2 (q, *J* = 279.1 Hz), 113.8 (2C), 112.1, 55.2, 43.3 (q, *J* = 24.1 Hz), 35.2, 34.5 (q, *J* = 2.5 Hz), 33.3 (q, *J* = 2.4 Hz), 31.7, 28.9, 27.4, 22.6, 14.0; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.13; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{19}H_{28}F_3O$: 329.2087, found: 329.2087.

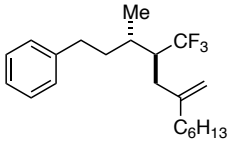



**1-(4-Methylene-2-(trifluoromethyl)decyl)-4-(trifluoromethyl)benzene (3o):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate); 36 mg (39%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$)

δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.86 (s, 1H), 4.82 (s, 1H), 2.93 (dd, *J* = 14.4, 6.8 Hz, 1H), 2.78 (dd, *J* = 14.4, 6.1 Hz, 1H), 2.65-2.52 (m, 1H), 2.43 (dd, *J* = 14.6, 5.2 Hz, 1H), 2.08 (dd, *J* = 14.6, 8.7 Hz, 1H), 1.95-1.85 (m, 2H), 1.33-1.26 (m, 3H), 1.25-1.21 (m, 5H), 0.87 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.2, 142.9, 129.4 (2C), 129.0 (q, *J* = 32.1 Hz), 127.9 (q, *J* = 278.8 Hz), 125.3 (q, *J* = 3.7 Hz, 2C), 124.2 (q, *J* = 270.2 Hz), 112.7, 43.0 (q, *J* = 24.7 Hz), 35.2, 34.7 (q, *J* = 2.3 Hz), 33.9 (q, *J* = 2.2 Hz), 31.6, 28.9, 27.4, 22.5, 14.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -62.47, -70.19; HRMS (EI) m/z ($[M]^+$) calcd for $C_{19}H_{24}F_6$: 366.1777, found: 366.1779.

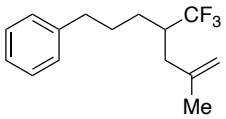



**4-(4-Methylene-2-(trifluoromethyl)decyl)-1,1'-biphenyl (3p):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v); 50 mg (53%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.59-7.56 (m, 2H), 7.54-7.51 (m, 2H), 7.45-7.41 (m, 2H), 7.36-7.31 (m, 1H), 7.25-7.23 (m, 2H), 4.84 (d, *J* = 1.2 Hz, 1H), 4.82 (s, 1H), 2.96 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.73 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.67-2.54 (m, 1H), 2.40 (dd, *J* = 14.6, 5.7 Hz, 1H), 2.13 (dd, *J* = 14.6, 7.9 Hz, 1H), 1.98-1.86 (m, 2H), 1.31-1.25 (m, 3H), 1.24-1.18 (m, 5H), 0.84 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.7, 140.8, 139.5, 137.8, 129.6 (2C), 128.8 (2C), 128.2 (q, *J* = 279.1 Hz), 127.2, 127.1 (2C), 127.0 (2C), 112.4, 43.2 (q, *J* = 24.4 Hz), 35.2, 34.6 (q, *J* = 2.4 Hz), 33.8 (q, *J* = 2.5 Hz), 31.7, 29.0, 27.4, 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.15; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{24}H_{30}F_3$: 375.2294, found: 375.2291. Chiralcel OJ-H column, 99.5/0.5 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 16.6 min, minor isomer: $t_R$ = 14.9 min.

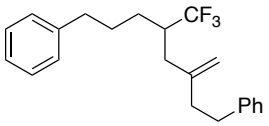



**((3*S**,4*S**)-3-Methyl-6-methylene-4-(trifluoromethyl)dodecyl)benzene (3q):** Purified by silica gel column chromatography with hexane and GPC (ethyl acetate): 47 mg (56%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.20-7.16 (m, 3H), 4.80 (d, *J* = 0.3 Hz, 1H), 4.75 (s, 1H), 2.70-2.63 (m, 1H), 2.58-2.51 (m,

1H), 2.37-2.25 (m, 2H), 2.20-2.13 (m, 1H), 1.92 (t, *J* = 7.4 Hz, 2H), 1.83-1.75 (m, 2H), 1.72-1.62 (m, 1H), 1.45-1.34 (m, 2H), 1.34-1.26 (m, 6H), 1.03 (dd, *J* = 7.0, 1.2 Hz, 3H), 0.89 (t, *J* = 6.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.9, 142.1, 128.6 (q, *J* = 280.4 Hz), 128.4 (2C), 128.3 (2C), 125.8, 112.2, 44.8 (q, *J* = 23.0 Hz), 36.7, 35.0, 34.1, 32.7 (q, *J* = 2.8 Hz), 31.7, 31.5, 29.0, 27.5, 22.6, 15.1, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -65.08; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{32}F_3$: 341.2451, found: 341.2449. Chiralcel OJ-H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 9.8 min, minor isomer: $t_R$ = 12.4 min.

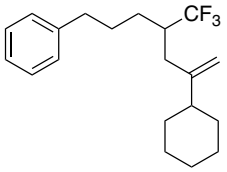



**(6-Methyl-4-(trifluoromethyl)hept-6-en-1-yl)benzene (3r):** Purified by silica gel column chromatography with pentane; 53mg (83%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.15 (m, 3H), 4.82 (s, 1H), 4.74 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.34 (dd, *J* = 13.8, 4.5 Hz, 1H), 2.30-2.19 (m, 1H), 2.07 (dd, *J* = 13.8, 9.1 Hz, 1H), 1.82-1.72 (m, 1H), 1.70 (s, 3H), 1.68-1.55 (m, 2H), 1.53-1.45 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.9, 141.6, 128.43 (q, *J* = 278.6 Hz), 128.35 (4C), 125.9, 113.4, 40.6 (q, *J* = 24.7 Hz), 36.5 (q, *J* = 2.8 Hz), 36.0, 28.6, 27.5 (q, *J* = 1.9 Hz), 21.8; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.28; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{20}F_3$: 257.1512, found: 257.1510. Chiralcel OJ-H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 16.1 min, minor isomer: $t_R$ = 18.2 min.

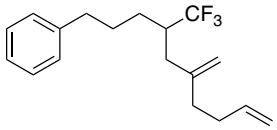



**(3-Methylene-5-(trifluoromethyl)octane-1,8-diyl)dibenzene (3s):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v): 70 mg (81%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 4H), 7.21-7.14 (m, 6H), 4.88 (s, 1H), 4.81 (s, 1H), 2.82-2.67 (m, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 2.40 (dd, *J* = 14.4, 4.4 Hz, 1H), 2.28 (t, *J* = 7.8 Hz, 2H), 2.25-2.18 (m, 1H), 2.07 (dd, *J* = 14.3, 9.2 Hz, 1H), 1.81-1.56 (m, 3H), 1.53-1.43 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 144.9, 141.8, 141.7, 128.43 (q, *J* = 278.8 Hz), 128.41 (2C), 128.36 (4C), 128.3 (2C), 126.0, 125.9,

112.7, 40.8 (q, $J$ = 24.7 Hz), 37.1, 36.0, 35.08 (q, $J$ = 2.7 Hz), 34.1, 28.7, 27.5 (q, $J$ = 1.8 Hz); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.21; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{26}F_3$: 347.1981, found: 347.1985. Chiralcel OD-H column, 99.7/0.3 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 15.6 min, minor isomer: $t_R$ = 25.9 min.

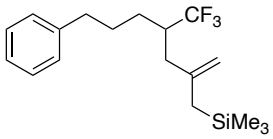



**(6-Cyclohexyl-4-(trifluoromethyl)hept-6-en-1-yl)benzene (3t):** Purified by silica gel column chromatography with hexane: 59 mg (73%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.28 (m, 2H), 7.20-7.15 (m, 3H), 4.82 (s, 1H), 4.71 (d, $J$ = 1.0 Hz, 1H), 2.58 (t, $J$ = 7.4 Hz, 2H), 2.41 (dd, $J$ = 14.7, 4.2 Hz, 1H), 2.32-2.19 (m, 1H), 2.01 (dd, $J$ = 14.7, 9.7 Hz, 1H), 1.79-1.66 (m, 8H), 1.31-1.24 (m, 3H), 1.21-1.13 (m, 2H), 1.12-1.01 (m, 1H), 0.88 (t, $J$ = 6.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 141.9, 128.6 (q, $J$ = 279.0 Hz), 128.3 (4C), 125.8, 109.9, 43.3, 41.0 (q, $J$ = 24.4 Hz), 36.0, 33.8 (q, $J$ = 2.7 Hz), 32.6, 32.2, 28.7, 27.5 (q, $J$ = 1.9 Hz), 26.8, 26.7, 26.3; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.16; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{28}F_3$: 325.2138, found: 325.2138.

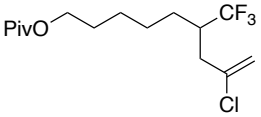



**(6-Methylene-4-(trifluoromethyl)dec-9-en-1-yl)benzene (3うう):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v); 61 mg (82%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.15 (m, 3H), 5.80 (ddt, $J$ = 17.0, 10.3, 6.4 Hz, 1H), 5.03 (ddt, $J$ = 17.1, 1.8, 1.6 Hz, 1H), 4.97 (ddt, $J$ = 10.2, 1.9, 1.2 Hz, 1H), 4.84 (s, 1H), 4.79 (d, $J$ = 0.6 Hz, 1H), 2.59 (t, $J$ = 7.5 Hz, 2H), 2.37 (dd, $J$ = 14.4, 4.4 Hz, 1H), 2.32-2.14 (m, 3H), 2.08-2.02 (m, 3H), 1.82-1.66 (m, 2H), 1.64-1.55 (m, 1H), 1.53-1.45 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 144.8, 141.8, 137.9, 128.5 (q, $J$ = 278.9 Hz), 128.4 (4C), 125.9, 114.9, 112.5, 40.7 (q, $J$ = 24.7 Hz), 36.0, 34.9 (q, $J$ = 2.6 Hz), 34.6, 31.8, 28.7, 27.5 (q, $J$ = 1.9 Hz); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.24; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{24}F_3$: 297.1825, found:

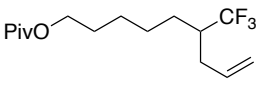
297.1825. Chiralcel OJ-H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 15.7 min, minor isomer: $t_R$ = 22.1 min.




**Trimethyl(2-methylene-7-phenyl-4-(trifluoromethyl)heptyl)silane (3v):** Purified by silica gel column chromatography with hexane: 63 mg (77%, 0.25 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.20-7.15 (m, 3H), 4.62-4.61 (m, 2H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.31-2.19 (m, 2H), 1.98 (dd, *J* = 14.4, 9.8 Hz, 1H), 1.83-1.66 (m, 2H), 1.65-1.55 (m, 2H), 1.53-1.41 (m, 2H), 0.02 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 144.7, 143.3, 129.9 (q, *J* = 278.6 Hz), 129.74 (2C), 129.73 (2C), 127.2, 111.7, 42.2 (q, *J* = 24.7 Hz), 38.2 (q, *J* = 2.7 Hz), 37.4, 30.1, 28.9 (q, *J* = 2.0 Hz), 27.4, -1.4 (3C); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -70.20; HRMS (EI) m/z ([M]$^+$) calcd for $C_{18}H_{27}F_3Si$: 328.1829, found: 328.1841.

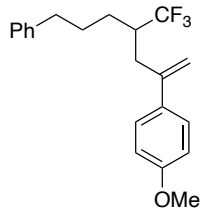



**8-Chloro-6-(trifluoromethyl)non-8-en-1-yl pivalate (3w):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v) and GPC ($CHCl_3$); 38 mg (47%, 0.25 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.28 (d, *J* = 0.9 Hz, 1H), 5.25 (d, *J* = 0.5 Hz, 1H), 4.05 (t, *J* = 6.6 Hz, 2H), 2.66 (dd, *J* = 14.2, 4.8 Hz, 1H), 2.58-2.45 (m, 1H), 2.39 (dd, *J* = 14.1, 8.6 Hz, 1H), 1.67-1.58 (m, 3H), 1.51-1.42 (m, 3H), 1.40-1.32 (m, 2H), 1.20 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 178.6, 139.0, 127.9 (q, *J* = 278.6 Hz), 115.3, 64.2, 40.3 (q, *J* = 25.2 Hz), 38.7, 38.1 (q, *J* = 2.9 Hz), 28.4, 27.3 (q, *J* = 1.6 Hz), 27.2 (3C), 26.3, 26.0; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -70.20; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{15}H_{25}ClF_3O_2$: 329.1490, found: 329.1493.

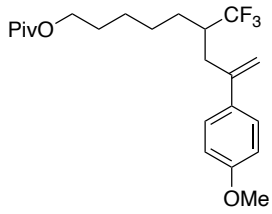



**6-(Trifluoromethyl)non-8-en-1-yl pivalate (3x):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v) and GPC ($CHCl_3$); 39 mg (53%,

0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.76 (ddt, *J* = 17.0, 7.6, 6.7 Hz, 1H), 5.13-5.07 (m, 2H), 4.05 (t, *J* = 6.6 Hz, 2H), 2.42-2.35 (m, 1H), 2.24-2.05 (m, 2H), 1.67-1.56 (m, 3H), 1.49-1.33 (m, 5H), 1.20 (s, 9H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 178.6, 134.5, 128.3 (q, *J* = 278.8 Hz), 117.6, 64.2, 42.5 (q, *J* = 24.7 Hz), 38.7, 32.2 (q, *J* = 2.7 Hz), 28.4, 27.2 (4C), 26.4, 26.0; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.04; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{15}H_{26}F_3O_2$: 295.1879, found: 295.1886.

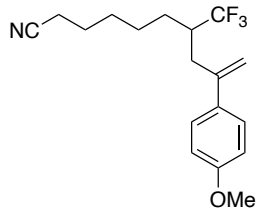



**1-Methoxy-4-(7-phenyl-4-(trifluoromethyl)hept-1-en-2-yl)benzene (3y):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v) and GPC (ethyl acetate); 51 mg (59%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.28-7.24 (m, 4H), 7.20-7.16 (m, 1H), 7.11-7.09 (m, 2H), 6.89-6.85 (m, 2H), 5.22 (d, *J* = 0.6 Hz, 1H), 5.01 (d, *J* = 0.7 Hz, 1H), 3.82 (s, 3H), 2.94 (dd, *J* = 14.3, 4.0 Hz, 1H), 2.49 (t, *J* = 7.3 Hz, 2H), 2.43 (dd, *J* = 14.5, 9.8 Hz, 1H), 2.22-2.09 (m, 1H), 1.74-1.63 (m, 1H), 1.57-1.47 (m, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 159.3, 144.3, 141.8, 132.2, 128.5 (q, *J* = 278.8 Hz), 128.4 (2C), 128.3 (2C), 127.4 (2C), 125.8, 114.2, 113.9 (2C), 55.3, 40.7 (q, *J* = 24.7 Hz), 35.8, 34.3 (q, *J* = 2.6 Hz), 28.3, 27.1 (q, *J* = 1.9 Hz), ; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -70.11; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{21}H_{24}F_3O$: 349.1774, found: 349.1774. Chiralcel OJ-H column, 97/3 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 19.5 min, minor isomer: $t_R$ = 31.9 min.

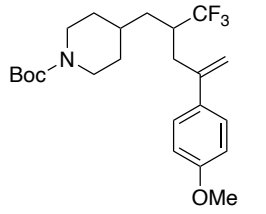



**8-(4-Methoxyphenyl)-6-(trifluoromethyl)non-8-en-1-yl pivalate (3z):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 53 mg (53%, 0.25 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 6.90-6.86 (m, 2H), 5.27 (d, *J* = 0.6 Hz, 1H), 5.06 (d, *J* = 0.6 Hz, 1H), 3.99 (t, *J* = 6.6 Hz, 2H), 3.82 (s, 3H), 2.96 (dd, *J* = 14.3, 3.9 Hz, 1H), 2.43 (dd, *J* = 14.4, 9.8 Hz, 1H), 2.20-2.07

(m, 1H), 1.59-1.50 (m, 3H), 1.49-1.30 (m, 3H), 1.27-1.22 (m, 2H), 1.18 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 178.6, 159.4, 144.4, 132.1, 128.5 (q, $J$ = 278.7 Hz), 127.4 (2C), 114.1, 113.9 (2C), 64.2, 55.2, 40.7 (q, $J$ = 24.7 Hz), 38.7, 34.4 (q, $J$ = 2.7 Hz), 28.3, 27.4 (q, $J$ = 1.8 Hz), 27.2 (3C), 26.2, 26.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.21; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{32}F_3O_3$: 401.2298, found: 401.2298. Chiralcel OJ-H column, 95/5 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 9.3 min, minor isomer: $t_R$ = 10.0 min.

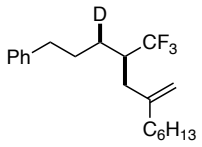



**9-(4-Methoxyphenyl)-7-(trifluoromethyl)dec-9-enenitrile (3A):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 58 mg (70%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 6.91-6.87 (m, 2H), 5.28 (d, $J$ = 0.4 Hz, 1H), 5.06 (d, $J$ = 0.5 Hz, 1H), 3.82 (s, 3H), 2.98 (dd, $J$ = 14.3, 3.8 Hz, 1H), 2.41 (dd, $J$ = 14.4, 10.2 Hz, 1H), 2.27 (t, $J$ = 7.2 Hz, 2H), 2.19-2.08 (m, 1H), 1.61-1.51 (m, 3H), 1.49-1.38 (m, 2H), 1.35-1.28 (m, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 144.2, 132.0, 128.4 (q, $J$ = 278.6 Hz), 127.4 (2C), 119.6, 114.2, 114.0 (2C), 55.3, 40.6 (q, $J$ = 24.7 Hz), 34.3 (q, $J$ = 2.8 Hz), 28.6, 27.1 (q, $J$ = 1.6 Hz), 25.8, 25.0, 17.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.23; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{23}F_3NO$: 326.1726, found: 326.1729. Chiralcel OJ-H column, 95/5 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 27.6 min, minor isomer: $t_R$ = 33.3 min.

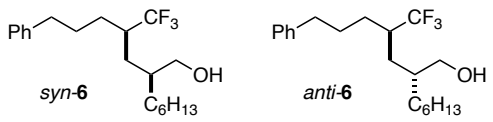



***tert*-Butyl 4-(4-(4-methoxyphenyl)-2-(trifluoromethyl)pent-4-en-1-yl)piperidine-1-carboxylate (3B):** Purified by silica gel column chromatography with hexane/ethyl acetate (10/1, v/v) and GPC (ethyl acetate): 88 mg (83%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 6.90-6.87 (m, 2H), 5.27 (s, 1H), 5.06 (s, 1H), 3.97 (br, 2H), 3.83 (s, 3H), 3.02 (dd, $J$ = 14.3, 3.3 Hz, 1H), 2.56 (br, 1H), 2.54

(br, 1H), 2.34 (dd, *J* = 14.1, 9.9 Hz, 1H), 2.21-2.12 (m, 1H), 1.53-1.46 (m, 2H), 1.44 (s, 9H), 1.40-1.24 (m, 3H), 0.95 (qd, *J* = 12.0, 4.2 Hz, 1H), 0.79 (qd, *J* = 12.5, 4.3 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 154.8, 144.2, 131.9, 128.5 (q, *J* = 278.6 Hz), 127.4 (2C), 114.4, 114.0 (2C), 79.28, 55.3, 43.7 (br, 2C), 37.9 (q, *J* = 24.8 Hz), 35.3 (q, *J* = 2.4 Hz), 34.8, 33.5, 32.4, 31.5, 28.5 (3C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.96; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{33}F_3NO_3$: 428.2407, found: 428.2404. Chiralcel OJ-H column, 97/3 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 21.1 min, minor isomer: $t_R$ = 15.7 min.

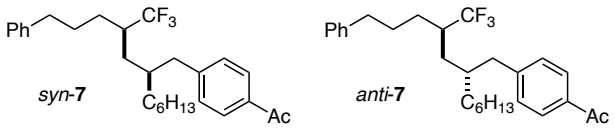



**(3*R**,4*R**)-(3-Deuterio-6-methylene-4-(trifluoromethyl)dodecyl)benzene (3a-*d*):** Purified by silica gel column chromatography with hexane: 58 mg (69%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.28 (m, 2H), 7.20-7.15 (m, 3H), 4.81 (s, 1H), 4.75 (d, *J* = 0.6 Hz, 1H), 2.58 (t, *J* = 7.6 Hz, 2H), 2.36 (dd, *J* = 14.3, 4.3 Hz, 1H), 2.30-2.18 (m, 1H), 2.03 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.96 (t, *J* = 7.6 Hz, 2H), 1.80-1.62 (m, 2H), 1.59-1.55 (m, 1H), 1.46-1.35 (m, 2H), 1.33-1.26 (m, 6H), 0.89 (t, 6.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.7, 141.9, 128.5 (q, *J* = 278.5 Hz), 128.3 (4C), 125.8, 112.0, 40.6 (q, *J* = 24.4 Hz), 35.9, 35.3, 34.7 (q, *J* = 2.6 Hz), 31.7, 29.0, 28.6, 27.5, 27.1 (t, *J* = 19.7 Hz), 22.6, 14.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.26; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{29}DF_3$: 328.2357, found: 328.2358. Chiralcel OJ-H column, hexane, 0.5 mL/min, major isomer: $t_R$ = 11.8 min, minor isomer: $t_R$ = 13.7 min.



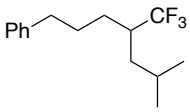

**A 55:45 diastereomixture of (*S**)-2-((*R**)-5-Phenyl-2-(trifluoromethyl)pentyl)octan-1-ol (*syn*-6) and (*R**)-2-((*R**)-5-Phenyl-2-(trifluoromethyl)pentyl)octan-1-ol (*anti*-6) (relative stereochemistry was tentatively assigned):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 62 mg (90%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 7.21-7.16 (m, 0.55 × 3H for *syn*-**6** and 0.45 × 3H for *anti*-**6**), 3.60-3.47

(0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 2.62 (t, *J* = 7.2 Hz, 0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 2.25-2.12 (m, 0.55 × 1H for *syn*-**6** and 0.45 × 1H for *anti*-**6**), 1.77-1.60 (m, 0.55 × 4H for *syn*-**6** and 0.45 × 4H for *anti*-**6**), 1.51-1.47 (m, 0.55 × 1H for *syn*-**6** and 0.45 × 1H for *anti*-**6**), 1.47-1.40 (m, 0.55 × 1H for *syn*-**6** and 0.45 × 1H for *anti*-**6**), 1.35-1.26 (m, 0.55 × 11H for *syn*-**6** and 0.45 × 11H for *anti*-**6**), 1.17-1.13 (m, 0.55 × 1H for *syn*-**6** and 0.45 × 1H for *anti*-**6**), 0.88 (t, *J* = 6.7 Hz, 0.55 × 3H for *syn*-**6** and 0.45 × 3H for *anti*-**6**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.84, 141.78, 128.8 (q, *J* = 278.4 Hz), 128.7 (q, *J* = 278.6 Hz), 128.4 (8C), 125.91, 125.90, 65.29 (2C), 40.4 (q, *J* = 24.6 Hz), 40.3 (q, *J* = 24.4 Hz), 38.0 (2C), 36.0, 35.9, 31.81, 31.79, 31.3, 30.9, 30.1 (q, *J* = 2.5 Hz), 30.0 (q, *J* = 1.9 Hz), 29.6 (2C), 28.53, 28.50, 28.28 (q, *J* = 2.8 Hz), 28.25 (q, *J* = 2.3 Hz), 26.8, 26.6, 22.6 (2C), 14.1 (2C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.26 (*anti*-**5**), -70.32 (*syn*-**5**); HRMS (EI) m/z ($[M]^+$) calcd for $C_{20}H_{31}F_3O$: 344.2322, found: 344.2326. Chiralcel OD-H column, 98.5/1.5 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 24.8, 27.4 min, minor isomer: $t_R$ = 26.3, 49.7 min.

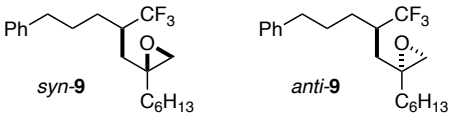



**A 54:46 diastereomixture of 1-(4-((*S**)-2-((*R**)-5-Phenyl-2-(trifluoromethyl)pentyl)octyl)phenyl)ethan-1-one (*syn*-7) and 1-(4-((*R**)-2-((*R**)-5-Phenyl-2-(trifluoromethyl)pentyl)octyl)phenyl)ethan-1-one (*anti*-7) (relative stereochemistry was tentatively assigned):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 50 mg (59%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.88-7.85 (m, 0.54 × 2H for *syn*-**7** and 0.46 × 2H for *anti*-**7**), 7.31-7.27 (m, 0.54 × 2H for *syn*-**7** and 0.46 × 2H for *anti*-**7**), 7.22-7.15 (m, 0.54 × 4H for *syn*-**7** and 0.46 × 4H for *anti*-**7**), 7.11-7.09 (m, 0.54 × 1H for *syn*-**7** and 0.46 × 1H for *anti*-**7**), 2.68-2.44 (m, 0.54 × 4H for *syn*-**7** and 0.46 × 4H for *anti*-**7**), 2.58 (s, 0.54 × 3H for *syn*-**7**), 2.57 (s, 0.46 × 3H for *anti*-**7**), 2.17-2.05 (m, 0.54 × 1H for *syn*-**7** and 0.46 × 1H for *anti*-**7**), 1.75-1.63 (m, 0.54 × 2H for *syn*-**7** and 0.46 × 2H for *anti*-**7**), 1.61-1.35 (m, 0.54 × 5H for *syn*-**7** and 0.46 × 5H for *anti*-**7**), 1.33-1.21 (m, 0.54 × 10H for *syn*-**7** and 0.46 × 10H for *anti*-**7**), 0.88 (t, *J* = 6.8 Hz, 0.46 × 3H for *anti*-**7**), 0.87 (t, *J* = 7.1 Hz, 0.54 × 3H for *syn*-**7**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 197.84, 197.79, 146.7, 146.5, 141.7, 141.6, 135.20, 135.18, 129.31 (2C), 129.27 (2C), 128.62 (q, *J* = 278.8 Hz),

128.59 (q, $J$ = 278.1 Hz), 128.5 (2C), 128.43 (2C), 128.42 (2C), 128.38 (2C), 128.36 (2C), 128.3 (2C), 126.0, 125.9, 40.7, 40.4, 40.2 (q, $J$ = 24.7 Hz), 40.3 (q, $J$ = 24.2 Hz), 37.2, 36.9, 35.9 (2C), 33.4, 33.1, 32.5 (q, $J$ = 2.4 Hz), 31.9 (q, $J$ = 1.4 Hz), 31.8 (2C), 29.49, 29.47, 28.4, 28.14, 28.06 (q, $J$ = 1.6 Hz), 27.9 (q, $J$ = 1.4 Hz), 26.5 (2C), 26.3, 26.0, 22.6 (2C), 14.1 (2C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.11, -70.15; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{28}H_{38}F_3O$: 447.2869, found: 447.2874. YMC CHIRAL ART Cellulose-SB column, 95/5 n-hexane/chloroform, 0.5 mL/min, major isomer: $t_R$ = 25.1, 26.9 min, minor isomer: $t_R$ = 34.1, 37.5 min.

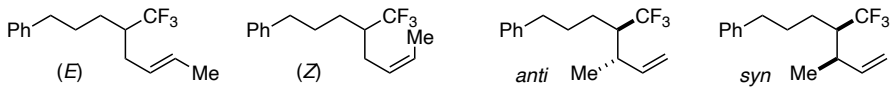



**(6-Methyl-4-(trifluoromethyl)heptyl)benzene (8):** Purified by silica gel column chromatography with hexane: 22 mg (86%, 0.10 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.21-7.16 (m, 3H), 2.61 (t, $J$ = 7.4 Hz, 2H), 2.16-2.02 (m, 1H), 1.75-1.66 (m, 3H), 1.44 (quin, $J$ = 5.6 Hz, 2H), 1.27-1.20 (m, 2H), 0.90 (d, $J$ = 6.6 Hz, 3H), 0.87 (d, $J$ = 6.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.9, 128.8 (q, $J$ = 278.4 Hz), 128.4 (2C), 128.3 (2C), 125.9, 40.4 (q, $J$ = 24.7 Hz), 37.2 (q, $J$ = 2.1 Hz), 36.0, 28.6, 28.2 (q, $J$ = 2.5 Hz), 25.5, 22.8, 22.2; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.41; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{22}F_3$: 259.1668, found: 259.1657. Chiralcel OJ-H column, 99.9/0.1 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 12.5 min, minor isomer: $t_R$ = 13.9 min.




**A 49:51 diastereomixture of (*S**)-2-Hexyl-2-((*R**)-5-phenyl-2-(trifluoromethyl)pentyl)oxirane (*syn*-9) and (*R**)-2-Hexyl-2-((*R**)-5-phenyl-2-(trifluoromethyl)pentyl)oxirane (*anti*-9) (relative stereochemistry was tentatively assigned):** 65 mg (95%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 0.49 × 2H for *syn*-**9** and 0.51 × 2H for *anti*-**9**), 7.21-7.16 (m, 0.49 × 3H for *syn*-**9** and 0.51 × 3H for *anti*-**9**), 2.65 (m, 0.49 × 3H for *syn*-**9** and 0.51 × 2H for *anti*-**9**), 2.56-2.52 (m, 0.49 × 2H for *syn*-**9** and 0.51 × 1H for *anti*-**9**), 2.30-2.17 (m, 0.49 × 1H for

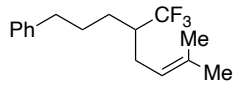
*syn*-**9**), 2.12 (dd, *J* = 14.7, 4.4 Hz, 0.51 × 1H for *anti*-**9**), 2.08-1.96 (m, 0.51 × 1H for *anti*-**9**), 1.82-1.67 (m, 0.49 × 3H for *syn*-**9** and 0.51 × 4H for *anti*-**9**), 1.62-1.44 (m, 0.49 × 4H for *syn*-**9** and 0.51 × 4H for *anti*-**9**), 1.35-1.27 (m, 0.49 × 8H for *syn*-**9** and 0.51 × 8H for *anti*-**9**), 0.88 (t, *J* = 6.8 Hz, 0.49 × 3H for *syn*-**9** and 0.51 × 3H for *anti*-**9**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.69, 140.65, 127.4 (6C), 127.2 (2C), 127.2 (q, *J* = 278.5 Hz, 2C), 124.9 (2C), 56.5, 56.2, 51.7, 50.7, 38.3 (q, *J* = 25.3 Hz), 37.6 (q, *J* = 25.5 Hz), 34.9, 34.8, 33.9, 32.5, 32.2 (q, *J* = 2.2 Hz), 31.1 (q, *J* = 2.3 Hz), 30.7 (2C), 28.3 (2C), 27.5 (2C), 27.44, 27.41, 23.6, 23.4, 21.5 (2C), 13.0 (2C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.07, -70.58; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{30}F_3O$: 343.2243, found: 343.2243. Chiralcel OJ-H column, 95/5 hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 35.7, 45.5 min, minor isomer: $t_R$ = 29.0. 34.1 min.



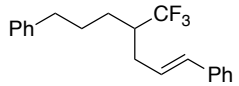
**3C** (*E*/*Z* = 9:1) **3C'** (69:31 d.r.)

**A 85:15 regiomixture of (4-(Trifluoromethyl)oct-6-en-1-yl)benzene (3C) and (5-Methyl-4-(trifluoromethyl)hept-6-en-1-yl)benzene (3C') (relative stereochemistry of 3C' was tentatively assigned):** Purified by silica gel column chromatography with hexane and GPC ($CHCl_3$): 48 mg (74%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 0.85 × 2H for **3C** and 0.15 × 2H for **3C'**), 7.20-7.16 (m, 0.85 × 3H for **3C** and 0.15 × 3H for **3C'**), 5.81-5.71 (m, 0.15 × 1H for **3C'**), 5.55 (dqt, *J* = 10.8, 7.1, 1.4 Hz, 0.85 × 0.1 × 1H for (*Z*)-**3C**), 5.47 (dq, *J* = 15.1, 6.4 Hz, 0.85 × 0.9 × 1H for (*E*)-**3C**), 5.32 (dt, *J* = 15.2, 6.8 Hz, 0.85 × 1H for **3C**), 5.04-5.00 (m, 0.15 × 2H for **3C'**), 2.60 (t, *J* = 7.5 Hz, 0.85 × 2H for **3C** and 0.15 × 2H for **3C'**), 2.34-2.26 (m, 0.85 × 1H for **3C**), 2.26-2.19 (m, 0.15 × 1H for **3C'**), 2.16-2.02 (m, 0.85 × 1H for **3C**), 2.10 (dt, *J* = 16.7, 7.6 Hz, 0.85 × 1H for **3C** and 0.15 × 1H for **3C'**), 1.71 (quin, *J* = 7.9 Hz, 0.85 × 2H for **3C** and 0.15 × 2H for **3C'**), 1.64 (dd, *J* = 6.4, 0.8 Hz, 0.85 × 3H for **3C**), 1.61-1.55 (m, 0.85 × 1H for **3C** and 0.15 × 1H for **3C'**), 1.52-1.44 (m, 0.85 × 1H for **3C** and 0.15 × 1H for **3C'**), 1.07 (dd, *J* = 7.1, 1.0 Hz, 0.15 × 0.31 × 3H for *syn*-**3C'**), 1.05 (dd, *J* = 7.0, 0.9 Hz, 0.15 × 0.69 × 3H for *anti*-**3C'**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.9, 141.8, 140.8, 140.1, 128.38 (q, *J* = 278.8 Hz), 128.36, 128.35, 128.2, 127.0, 126.9, 126.4, 126.2, 125.9, 115.0, 114.8, 42.8 (q, *J* = 24.5 Hz), 36.1 (q, *J* = 1.8 Hz), 35.94, 35.90, 35.8, 30.9 (q, *J* = 2.8 Hz), 29.7, 28.7, 28.4, 27.2, 26.8 (q, *J* = 2.1 Hz), 25.2 (q, *J* = 2.6 Hz),

24.4 (q, $J$ = 2.2 Hz), 17.9, 15.3, 12.7 (All observed signals are shown because of complexity associated with regio- and stereoisomers.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -66.07, -66.12, -69.95, -70.15; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{20}F_3$: 257.1512, found: 257.1514.




**(7-Methyl-4-(trifluoromethyl)oct-6-en-1-yl)benzene (3D):** Purified by silica gel column chromatography with hexane, GPC ($CHCl_3$), and GPC (ethyl acetate): 33 mg (48%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 7.21-7.15 (m, 3H), 5.06 (t, $J$ = 6.3 Hz, 1H), 2.60 (t, $J$ = 7.3 Hz, 2H), 2.29-2.25 (m, 1H), 2.16-2.01 (m, 2H), 1.75-1.65 (m, 2H), 1.69 (s, 3H), 1.64-1.56 (m, 1H), 1.59 (s, 3H), 1.52-1.43 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.9, 134.1, 128.5 (q, $J$ = 278.6 Hz), 128.4 (2C), 128.3 (2C), 125.9, 120.3, 43.1 (q, $J$ = 24.2 Hz), 35.9, 28.7, 27.1 (q, $J$ = 2.1 Hz), 26.4 (q, $J$ = 2.7 Hz), 25.8, 17.7; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -70.12; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{22}F_3$: 271.1668, found: 271.1658.




**(*E*)-(4-(Trifluoromethyl)hept-1-ene-1,7-diyl)dibenzene (3E):** Purified by silica gel column chromatography with hexane and GPC (ethyl acetate): 14 mg (17%, 0.25 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.33-7.30 (m, 4H), 7.27-7.23 (m, 3H), 7.19-7.14 (m, 3H), 6.42 (dt, $J$ = 15.7, 1.3 Hz, 1H), 6.10 (dt, $J$ = 15.8, 6.9 Hz, 1H), 2.61 (t, $J$ = 7.4 Hz, 2H), 2.53 (dddd, $J$ = 14.5, 7.0, 5.4, 1.6 Hz, 1H), 2.36 (dtd, $J$ = 14.4, 7.5, 1.2 Hz, 1H), 2.27-2.17 (m, 1H), 1.79-1.71 (m, 2H), 1.70-1.63 (m, 1H), 1.60-1.56 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.7, 137.1, 132.8, 128.6 (2C), 128.39 (2C), 128.36 (2C), 128.27 (q, $J$ = 278.9 Hz), 127.4, 126.2 (2C), 126.0, 125.9, 42.9 (q, $J$ = 24.7 Hz), 35.8, 31.4 (q, $J$ = 2.6 Hz), 28.5, 26.9 (q, $J$ = 2.0 Hz); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -69.85; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{22}F_3$: 319.1668, found: 319.1666.

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[25] In the kinetic experiments, we chose $(MeO)_2MeSiH$, TMS-dppbz, and KOPiv as the optimal hydrosilane, ligand, and base, respectively, because other combinations provided a heterogeneous system and thus irreproducible results. See the Supporting Information for details.

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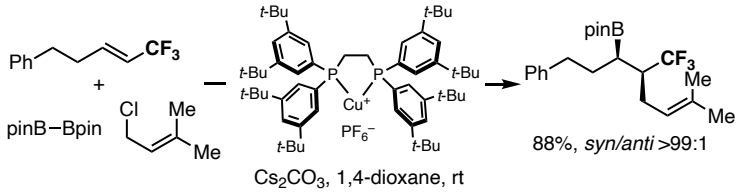
# Chapter 2

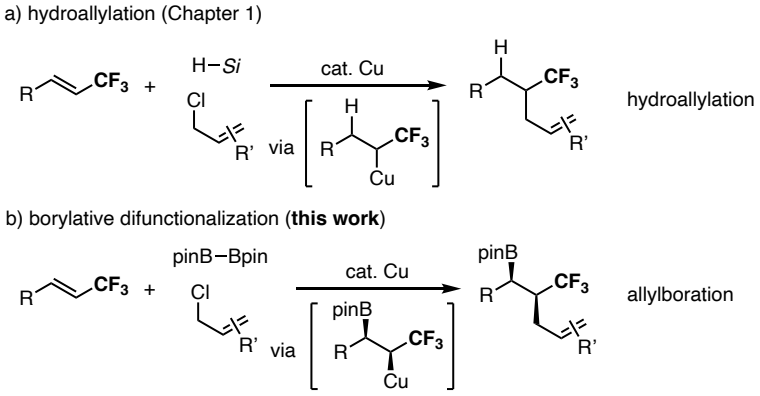
## Ligand-Enabled Copper-Catalyzed Regio- and Stereoselective Allylboration of $CF_3$-Substituted Alkenes

A copper-catalyzed regio- and stereoselective allylboration of $CF_3$-substituted alkenes with bis(pinacolato)diboron (pinB–Bpin) and allylic chlorides has been developed to form functionalized trifluoromethylated products with high diastereoselectivity. The key to success is the judicious choice of $Cs_2CO_3$ base and *t*-Bu-modified dppe-type ligand, which enables the otherwise challenging high catalyst turnover and suppression of the competing defluorination side reaction from an alkylcopper intermediate. The product derivatization of the resulting Bpin moiety can deliver diverse $CF_3$-containing molecules with high stereochemical fidelity.



## Introduction

In Chapter 1, the author succeeded in developing of copper-catalyzed hydroallylation of $CF_3$-substituted alkenes with hydrosilane nucleophiles and allylic electrophiles (Scheme 2.1a), in which the $CF_3$ group was successfully retained by the judicious choice of supporting ligands and basic additives.[1] Building on a continuing interest in this chemistry, the author envisioned that replacement of the hydrosilane with bis(pinacolato)diboron (pinB–Bpin) enabled the borylative difunctionalization of the $CF_3$-substituted alkene. Herein, the author reports a copper-catalyzed regio- and stereoselective allylboration with pinB–Bpin and allylic chlorides (Scheme 2.1b).[2] The combination of modified dppe-type ancillary ligands and $Cs_2CO_3$ base successfully promotes the otherwise challenging difunctionalization over the defluorination side reaction. The related deuterioboration using pinB–Bpin and $D_2O$ was reported by Hoveyda,[3] but the application of other electrophiles is not trivial, to the best of the author's knowledge.



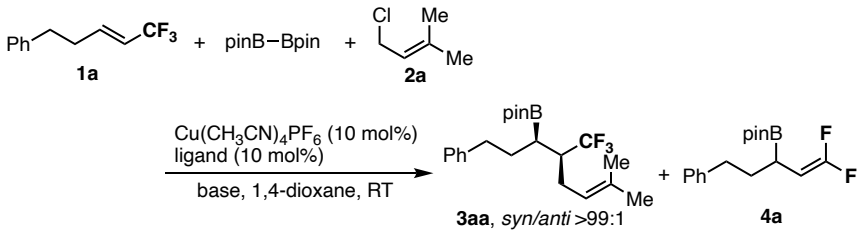

**Scheme 2.1**. $CF_3$-compatible catalytic functionalizations of 1-trifluoromethylalkenes.

## Results and discussion

On the basis of previous hydroallylation reaction,[1] the author's initial trial was performed with the $CF_3$-substituted alkene **1a**, pinB–Bpin (3.0 equiv), and prenyl chloride (**2a**; 2.0 equiv) in the presence of $Cu(CH_3CN)_4PF_6$/MeO-dppbz catalyst and $Cs_2CO_3$ base at room temperature (Table 2.1, entry 1). The desired allylborated product **3aa** was obtained in 40% $^1$H NMR yield with high regioselectivity and >99:1 *syn/anti* ratio, but the conversion was moderate and the possible *gem*-difluoroalkene byproduct **4a** was also formed in 10 % yield. The parent dppbz and related substituted dppbz ligands such as *t*Bu-dppbz and DTBM-dppbz were then tested, but no significant improvement was

observed (entries 2–4). Thus, the author moved attention to structurally relevant but more electron-donating ethylene-bridged analogues, dppe ligands.[4] While the MeO-dppe ligand showed performance and selectivity similar to MeO-dppbz (entry 5), *t*Bu-dppe and DTBM-dppe dramatically increased the yield of **3aa** to 94 and 80% yields, respectively (entries 6 and 7). Several other para- and meta-substituted dppe derivatives as well as the parent dppe were also examined, but moderate conversion and chemoselectivity were observed regardless of their electronic nature of substituents (entries 8–14). The choice of base was also critical: less basic CsOPiv, $K_2CO_3$, and KOPiv resulted in lower conversion (entries 15–17), whereas NaO*t*Bu and LiO*t*Bu mainly afforded the *gem*-difluoroalkene **4a** (entries 18 and 19) by the β-F elimination from an a-$CF_3$ alkylcopper intermediate, which is accelerated by strong interaction between F and Na or Li alkali metal.[3,5] The suitable basicity of $Cs_2CO_3$ promotes regeneration of the catalytically active Cu–Bpin species while its lower affinity to F and B atoms[3] effectively suppresses the undesired β-F elimination. The author also tested pinB–Bdan and neoB–Bneo instead of pinB–Bpin, but the targeted allylborated products **3aa-Bdan** and **3aa-Bneo** were not obtained at all (entries 20 and 21). Additional observations are noted: no conversion occurred in the absence of Cu, ligand, or base. Other Cu salts and solvents were also evaluated, but the combination of $Cu(CH_3CN)_4PF_6$ and 1,4-dioxane was optimal. The Cl leaving group was important for the successful three-component-coupling, and other common leaving groups such as Br and OAc gave only a negligible amount of **3aa**. Different from the previous hydroallylation,[1] any positive effects of crown ethers were not detected.

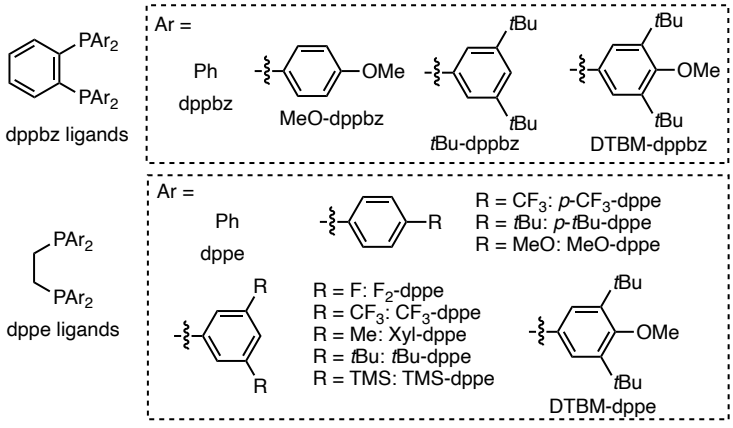
**Table 1.1**. Optimization studies for copper-catalyzed regio- and stereoselective allylboration of **1a** with $B_2pin_2$ and allyl chloride **2a**[a]



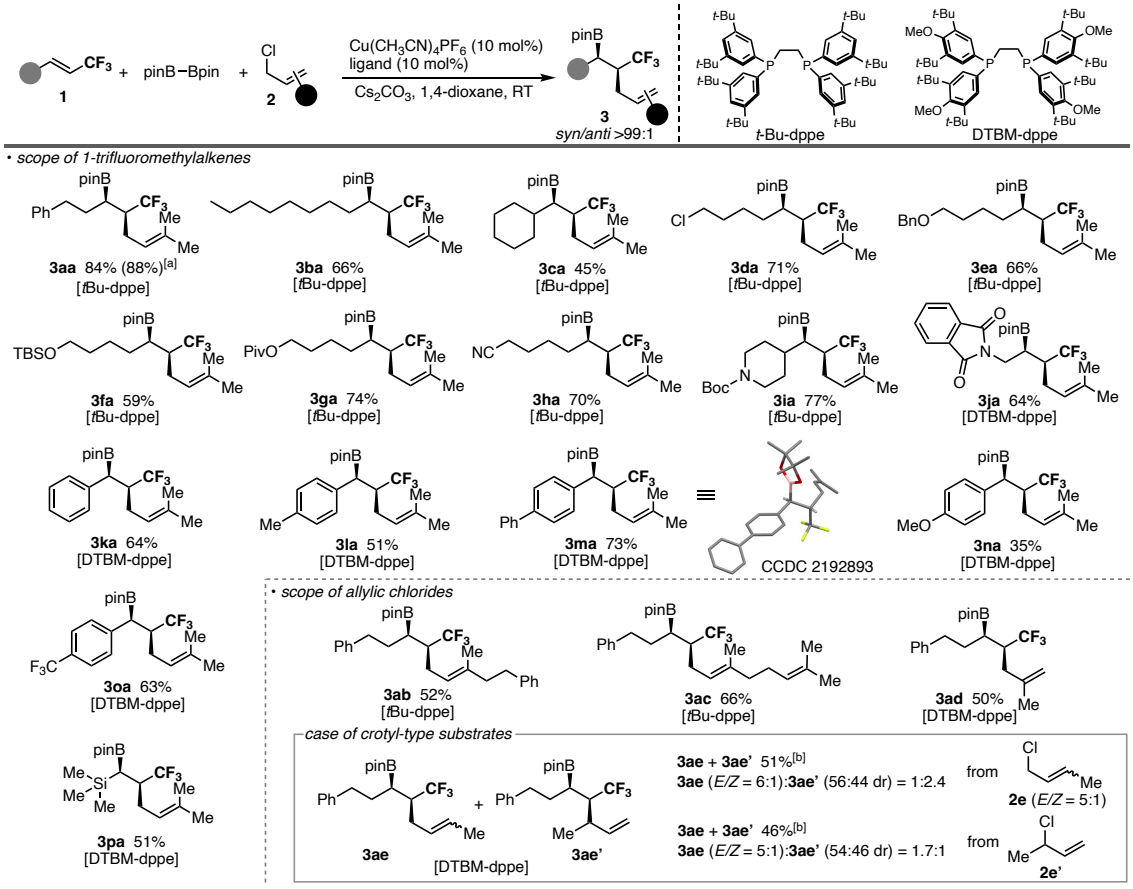

| entry | ligand | base | yield of **3a** (%)[b] | yield of **4a** (%)[b] |
|---|---|---|---|---|
| 1 | MeO-dppbz | $Cs_2CO_3$ | 40 | 10 |
| 2 | dppbz | $Cs_2CO_3$ | 23 | 7 |

| | | | | |
|---|---|---|---|---|
| 3 | *t*Budppbz | $Cs_2CO_3$ | 13 | 19 |
| 4 | DTBM-dppbz | $Cs_2CO_3$ | 36 | 7 |
| 5 | MeO-dppe | $Cs_2CO_3$ | 34 | 4 |
| 6 | *t*Bu-dppe | $Cs_2CO_3$ | 94 (84) | 3 |
| 7 | DTBM-dppe | $Cs_2CO_3$ | 80 | 3 |
| 8 | dppe | $Cs_2CO_3$ | 30 | 5 |
| 9 | *p*-$CF_3$-dppe | $Cs_2CO_3$ | 22 | 19 |
| 10 | *p*-*t*Bu-dppe | $Cs_2CO_3$ | 21 | 0 |
| 11 | $F_2$-dppe | $Cs_2CO_3$ | 24 | 17 |
| 12 | $CF_3$-dppe | $Cs_2CO_3$ | 9 | 17 |
| 13 | Xyl-dppe | $Cs_2CO_3$ | 22 | 1 |
| 14 | TMS-dppe | $Cs_2CO_3$ | 39 | 4 |
| 15 | *t*Bu-dppe | CsOPiv | 19 | 4 |
| 16 | *t*Bu-dppe | $K_2CO_3$ | 31 | 0 |
| 17 | *t*Bu-dppe | KOPiv | 17 | 4 |
| 18 | *t*Bu-dppe | NaO*t*Bu | 6 | 51 |
| 19 | *t*Bu-dppe | LiO*t*Bu | 0 | 34 |
| 20[c] | *t*Bu-dppe | $Cs_2CO_3$ | trace | 15 |
| 21[d] | *t*Bu-dppe | $Cs_2CO_3$ | 0 | 0 |

[a] Conditions: **1a** (0.20 mmol), pinB–Bpin (0.60 mmol), **2a** (0.40 mmol), $Cu(CH_3CN)_4PF_6$ (0.020 mmol), ligand (0.020 mmol), base (0.40 mmol), 1,4-dioxane (1.0 mL), RT, 18 h, $N_2$. [b] Estimated by $^1H$ NMR. Isolated yields are given in parentheses. [c] With pinB–Bdan instead of pinB–Bpin. The desired product and byproduct were Bdan-derived **3aa-Bdan** and **4a-Bdan**, respectively. [d] With neoB–Bneo instead of pinB–Bpin. The desired product and byproduct were Bneo-derived **3aa-Bneo** and **4a-Bneo**, respectively.



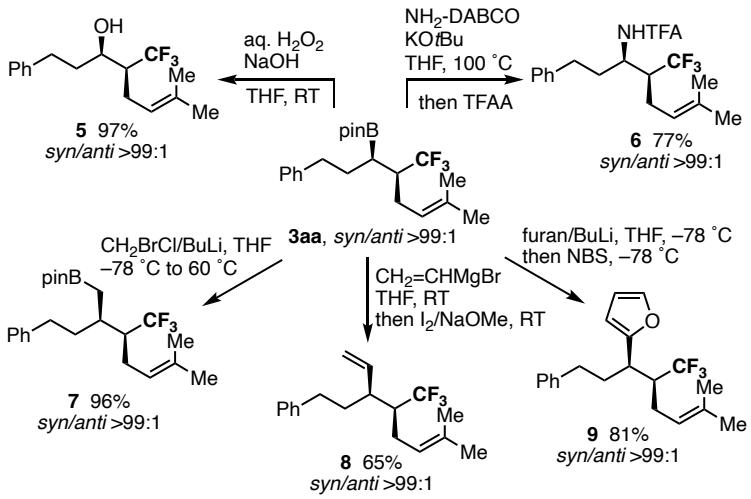
With optimal conditions in hand, the author examined the generality of the reaction (Scheme 2.2). The copper catalysis accommodated primary and secondary alkyl substituents at the β-position of $CF_3$-alkene (**3aa**-**3ca**). The reaction conditions were compatible with several functional groups, including the alkyl chloride (**3da**), benzyl ether (**3ea**), silyl ether (**3fa**), pivalate ester (**3ga**), and nitrile (**3ha**). The amine-based functions such as Boc-protected amine (**3ia**) and phthalimide (**3ja**) were also tolerated. Notably, aryl-conjugated $CF_3$-alkenes also underwent the regioselective allylboration (**3ka**-**3oa**): the boryl group and allyl group selectively introduced at the β- and α-position, respectively, to the $CF_3$ probably because the regioselectivity in the insertion step of $CF_3$-substituted alkene into the Cu–Bpin bond is predominantly controlled by strong electron-withdrawing nature of the $CF_3$ group over the aryl-vinyl conjugation.[6] Furthermore, the $Me_3Si$-substituted substrate was converted to the desired **3pa** with the *gem*-borylsilyl




**Scheme 2.2**. Cu-Catalyzed regio- and diastereoselective allylboration of $CF_3$-substituted alkenes **1** with pinB–Bpin and allylic chlorides **2**. Conditions: $Cu(CH_3CN)_4PF_6$ (0.020 mmol), ligand (0.020 mmol), **1** (0.20 mmol), pinB–Bpin (0.60 mmol)**, 2** (0.40 mmol), $Cs_2CO_3$ (0.40 mmol), 1,4-dioxane (1.0 mL), RT, 18–48 h. Isolated yields are shown. The ligand employed is shown in square bracket. [a] On a 1.0 mmol scale. [b] $^1$H NMR yields.

carbon center. Regardless of steric and electronic nature of the substituent, both regioselectivity and diastereoselectivity were uniformly high. The regioselectivity and relative stereochemistry were confirmed by the X-ray analysis of **3ma** (CCDC 2192893), and those of other compounds were assigned by analogy. As a general trend, in cases of aryl-conjugated substrates DTBM-dppe showed better performance than *t*Bu-dppe. The scope and limitation of allylic chlorides **2** were also investigated. Other prenyl-type electrophiles **2b** and **2c** could be employed with maintenance of the starting (*E*)-geometry (**3ab** and **3ac**). The methally chloride (**2d**) also participated in the reaction (**3ad**). In the case of crotyl chloride (**2e**; *E/Z* = 5/1), a 1:2.4 mixture of **3ae** and **3ae'** was observed. On the other hand, the regioisomeric **2e'** also afforded a mixture of **3ae** and **3ae'** but with the opposite selectivity (**3ae**:**3ae'** = 1.7:1). These phenomena suggest that the electrophilic allylation step involves both the $S_N2'$-type addition-elimination-type mechanism and the formation of π-allyl- (or π-en-σ-yl) copper species and that the major pathway is dependent on the substitution pattern of allylic electrophile.

The resulting Bpin moiety in the allylborated product **3aa** could be readily transformed with high stereochemical fidelity (Scheme 2.3). The oxidation and amination were possible with aq. $H_2O_2$ and $NH_2$-DABCO,[7] respectively, and the corresponding $CF_3$-containing alcohol **5** and amine **6** were obtained in good yields without any erosion of the diastereomeric ratio. One-carbon homologation was also feasible (**7**).[8] Moreover, the stereospecific oxidative cross-couplings[9] with the vinyl Grignard reagent and 2-furyllithium proceeded smoothly to form the corresponding C–C coupled products **8** and **9** in 65 and 81% yields, respectively.




**Scheme 2.3**. Stereospecific transformations of Bpin moiety in **3aa**.

Finally, to investigate the origin of higher catalytic performance of the *t*Bu-dppe ligand than that of the parent dppe, several experiments were implemented. One possibility is the attractive London dispersion between the *t*Bu substituents and $CF_3$-substituted alkene to accelerate the insertion step.[10] However, in the author's preliminary computational studies based on DFT calculations, the activation barrier was small enough to promote the insertion smoothly for both *t*Bu-dppe- and parent dppe-ligated Cu–Bpin species. Thus, the London dispersion cannot be a pivotal factor for the observed higher activity of *t*Bu-dppe. Another possibility is the smooth generation of a catalytically competent monomeric Cu–Bpin species, which is generally unfavored with (bis)phosphine ligands and in equilibrium with the corresponding dimer and/or its higher aggregate.[11] Actually, in the stoichiometric reaction of $Cu(CH_3CN)_4PF_6$/*t*Bu-dppe, pinB–Bpin, $Cs_2CO_3$, and **1a**, the conversion of **1a** started just upon mixing and completed within 35 min (Figure 2.1). In contrast, a ca. 1 h induction period was observed with the dppe ligand, and full conversion was achieved after 2.5 h. These distinct reaction profiles support the rapid generation of monomeric *t*Bu-dppe-ligated Cu–Bpin, which is promoted by the bulky *t*Bu groups at the remote meta-position of ligand to increase the overall reaction efficiency. However, the author cannot completely exclude the possibility that the *t*-Bu substituent accelerates the allylation step with the allylic chloride electrophile.

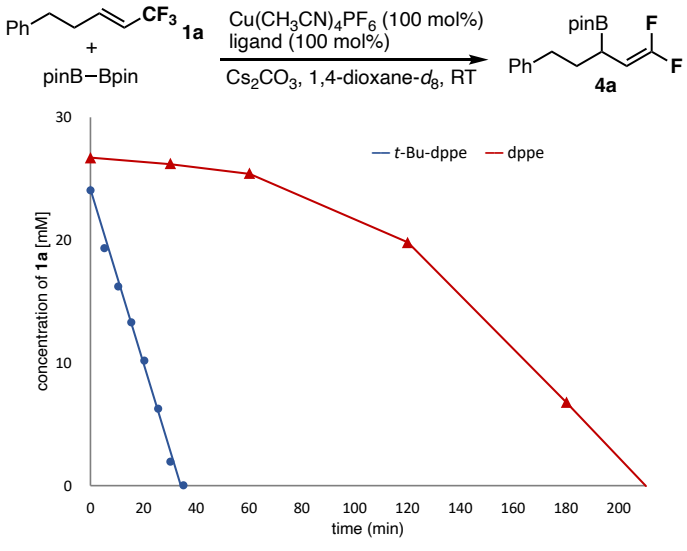



**Figure 2.1**. Reaction progresses of stoichiometric reactions of Cu/ligand, **1a**, and pinB–Bpin.

## Summary

In conclusion, the author has developed a copper-catalyzed regio- and

diastereoselective allylboration of $CF_3$-substituted alkenes with pinB–Bpin and allylic chlorides. The judicious choice of Cs-based base and ancillary bisphosphine ligands with the remote steric bulkiness enables suppression of the otherwise competitive defluorination process and high reaction efficiency. The boryl group in the obtained product is readily transformed to versatile functional groups with high stereochemical fidelity. Thus, the present Cu catalysis can provide stereoselective access to $CF_3$-containing molecules of potent interest in pharmaceutical chemistry.

## Experimental Section

### Instrumentation and Chemicals

$^{1}H$, $^{13}C\{^{1}H\}$, $^{19}F\{^{1}H\}$, $^{31}P\{^{1}H\}$, and $^{11}B$ NMR spectra were recorded at 400 MHz, 100 MHz, 376 MHz, 162 MHz, and 128 MHz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by APCI using TOF. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakosil C-200, Wako Pure Chemical Co.) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-20AR (pump, SHIMADZU, 7.5 mL/min $CHCl_3$ or ethyl acetate) and SPD-20A (UV detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC). The crystal measurement was performed with XtaLAB Synergy-S/Cu (Rigaku). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. 1,4-Dioxane was dried on a Glass Contour Solvent dispensing system (Nikko Hansen & Co., Ltd.) prior to use. $Cu(CH_3CN)_4PF_6$ and pinB–Bpin were purchased from TCI. $Cs_2CO_3$ was obtained from FUJIFILM Wako Pure Chemical Co. Modified dppe ligands, except for DTBM-dppe and Xyl-dppe, were prepared according to the literature methods.[12] $CF_3$-substituted alkene **1p** was a commercial source (TCI) and others **1a-j**[13] and **1k-o**[14] were synthesized by the reported methods. The allyl chlorides **2a**, **2c**, and **2d** were commercially available whereas **2b**[15] was synthesized from the corresponding allylic alcohols. Unless otherwise noted, all reactions were performed under nitrogen atmosphere.

### Experimental Procedures

### Preparation of Modified Dppe-Type Ligands

Synthesis of Xyl-dppe: To a solution of 1,2-bis(dichlorophosphino)ethane (1.0 g, 4.3 mmol) in THF (20 mL) was added a THF solution of 3,5-dimethylphenylmagnesium bromide (1 M, 34.4 mL, 34.4 mmol) at –78 °C. After stirred for 1 h, the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with a saturated aqueous $NH_4Cl$. Extraction was repeated a total of 3 times with chloroform, and combined organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. Methanol was added, and the residue was sonicated for several minutes. After collected by filtration, the titled compound (60%, 1.3 g) was obtained as a white solid.

Synthesis of DTBM-dppe: To a solution of 1,2-bis(dichlorophosphino)ethane (1.0 g, 4.3 mmol) in THF (20 mL) was added a THF solution of 3,5-di-*tert*-butyl-4-methoxyphenylmagnesium bromide (1 M, 34.4 mL, 34.4 mmol) at –78 °C. After stirred for 1 h, the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with a saturated aqueous $NH_4Cl$. Extraction was repeated a total of 3 times with chloroform, and combined organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. Methanol was added, and the residue was sonicated for several minutes. After collected by filtration, the titled compound (91%, 3.8 g) was obtained as a white solid.

**General procedure for the copper-catalyzed regio- and diastereoselective allylboration of $CF_3$-substituted alkenes 1 with pinB–Bpin and allylic chlorides 2**

$Cu(CH_3CN)_4PF_6$ (7.5 mg, 0.020 mmol, 10 mol %), *t*Bu-dppe (17 mg, 0.020 mmol, 10 mol %), and $Cs_2CO_3$ (130 mg, 0.40 mmol, 2.0 equiv) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (1.0 mL) was added to the tube, and the solution was stirred at room temperature. After 15 min, $B_2pin_2$ (152 mg, 0.60 mmol, 3.0 equiv) and allylic chlorides (**2**; 0.40 mmol, 2.0 equiv) were added, and $CF_3$-substituted alkenes (**1**; 0.20 mmol, 1.0 equiv) was finally added. The reaction solution was stirred at room temperature for 18 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane/ethyl acetate as an eluent to give the allylborated products **3** with >99:1 *syn/anti* ratio. In some cases, additional purifications by GPC was performed.

Synthesis of **3aa** (Scheme 3, 1.0 mmol scale): $Cu(CH_3CN)_4PF_6$ (38 mg, 0.10 mmol), *t*Bu-dppe (85 mg, 0.10 mmol), and $Cs_2CO_3$ (652 mg, 2.0 mmol) were placed in a 50 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. 1,4-Dioxane (5.0 mL) was added to the tube, and the solution was stirred at room temperature. After 15 min, $B_2pin_2$ (762 mg, 3.0 mmol) and 1-chloro-3-methylbut-2-ene (**2a**; 209 mg, 2.0 mmol) were added, and (*E*)-(5,5,5-trifluoropent-3-en-1-yl)benzene (**1a**; 200 mg, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 18 h. The resulting mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate) to give 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**, 339 mg, 0.85 mmol, 88%) with >99:1 *syn/anti* ratio.

**Oxidation of 3aa (Scheme 2.3)**

A 20 mL Schlenk tube equipped with a stir bar was charged with 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**; 59 mg, 0.15 mmol, >99:1 *syn/anti*) and THF (1.0 mL). Sodium hydroxide aqueous solution (1 M, 1.5 mL) and hydrogen peroxide (30 wt%, 0.5 mL) were added to the reaction mixture, and the solution was stirred for 20 min. The reaction was quenched with saturated aqueous sodium thiosulfate and ammonium chloride aqueous solution. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) to give (3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-ol (**5**; 39 mg, 0.14 mmol, 97%) with >99:1 *syn/anti* ratio.

**Amination of 3aa (Scheme 2.3)**

$NH_2$-DABCO (58 mg, 0.15 mmol) and KO*t*Bu (41 mg, 0.36 mmol) were placed in a 10 mL microwave reaction vessel in a glovebox filled with nitrogen. 4,4,5,5-Tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**; 59 mg, 0.15 mmol, >99:1 *syn/anti*) and THF (1.8 mL) were added to the reaction tube. The reaction tube was sealed with a cap and taken out of the glovebox, and the

resulting mixture was stirred for 3 h at 100 °C. TFAA (42 μL, 0.30 mmol) was then added, and the reaction mixture was heated at 100 °C (oil bath) for additional 1 h. The reaction was quenched with ethyl acetate and $H_2O$. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) to give 2,2,2-trifluoro-*N*-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)acetamide (**6**; 44 mg, 0.12 mmol, 77%) with >99:1 *syn/anti* ratio.

**Homologation of 3aa (Scheme 2.3)**

To a solution of 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**; 59 mg, 0.15 mmol, >99:1 *syn/anti*) and bromochloromethane (39 mg, 0.30 mmol) in THF (1.5 mL) at -78 °C was added *n*-BuLi (1.56 M hexane solution, 0.16 mL, 0.25 mmol), and the solution was stirred at the same temperature for 30 min. The mixture was allowed to warm to room temperature over 30 min and then heated at 60 °C (oil bath) for additional 3 h. The resulting mixture was quenched with $NH_4Cl$ and extracted with ethyl acetate. The combined organic layer was dried over $Na_2SO_4$, and the solvent was removed under reduced pressure to give 4,4,5,5-tetramethyl-2-((2*R**,3*S**)-6-methyl-2-phenethyl-3-(trifluoromethyl)hept-5-en-1-yl)-1,3,2-dioxaborolane (**7**; 59 mg, 0.14 mmol, 96%) with >99:1 *syn/anti* ratio in an analytically pure form.

**Vinylation of 3aa (Scheme 2.3)**

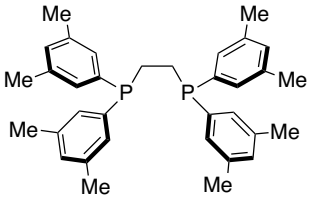
To a solution of 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**; 59 mg, 0.15 mmol, >99:1 *syn/anti*) in THF (1.5 mL) at room temperature was added vinylmagnesium bromide (1.0 M in THF, 0.60 mmol) dropwise. The resulting mixture was stirred at room temperature for 30 min and cooled down to -78 °C. A solution of iodine (152 mg, 0.60 mmol) in MeOH (2.0 mL) was added dropwise to the reaction mixture, followed 30 min later by a solution of NaOMe (65 mg, 1.2 mmol) in MeOH (2.5 mL). The reaction mixture was then allowed to warm to room temperature and stirred for an additional 18 h, and the reaction was quenched with saturated aqueous sodium thiosulfate. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane to give

((3*R**,4*R**)-7-methyl-4-(trifluoromethyl)-3-vinyloct-6-en-1-yl)benzene (**8**; 29 mg, 0.10 mmol, 65%) with >99:1 *syn/anti* ratio.

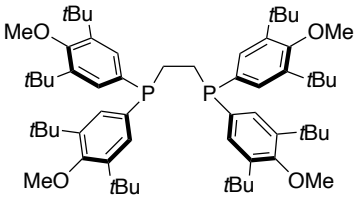
**Arylation of 3aa (Scheme 2.3)**

A solution of furan (12 mg, 0.18 mmol) in THF (0.6 mL) was cooled to -78 °C and treated with *n*-BuLi (1.56 M hexane solution, 0.12 mL, 0.18 mmol). The cooling bath was removed and the mixture was stirred at room temperature for 1 h. The mixture was again cooled to -78 °C, and 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (**3aa**; 59 mg, 0.15 mmol, >99:1 *syn/anti*) was added dropwise as a solution in THF (0.3 mL). The mixture was stirred at -78 °C for 1 h. A solution of NBS (32 mg, 0.18 mmol) in THF (0.6 mL) was added dropwise. After 1 h at –78 °C, the reaction was quenched with saturated aqueous sodium thiosulfate. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane to give 2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)furan (**9**; 39 mg, 0.12 mmol, 81%) with >99:1 *syn/anti* ratio.

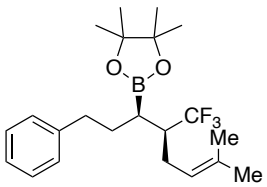
**Characterization Data of Products**



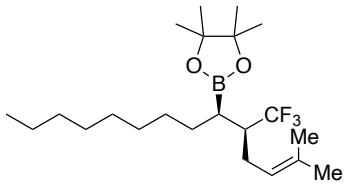

**1,2-Bis(bis(3,5-dimethylphenyl)phosphanyl)ethane (Xyl-dppe):** 1.3 g (60%, 4.3 mmol scale); White solid; m.p. 142.1–144.7 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 4H), 6.92 (s, 8H), 2.25 (s, 24H), 2.07 (t, $J$ = 3.7 Hz, 4H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 137.8 (d, $J$ = 3.5 Hz), 137.7 (d, $J$ = 3.6 Hz), 130.5 (d, $J$ = 9.3 Hz), 130.4, 130.3 (d, $J$ = 9.4 Hz), 23.9 (d, $J$ = 4.2 Hz), 21.3; $^{31}$P{$^{1}$H} NMR (162 MHz, $CDCl_3$) δ -12.12; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{34}H_{41}P_2$: 511.2678, found: 511.2672.



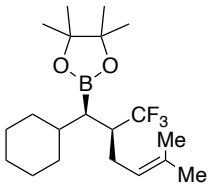

**1,2-Bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphanyl)ethane (DTBM-dppe):** 3.8 g (91%, 4.3 mmol scale); White solid; m.p. 232.3–233.0 ℃; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, $J$ = 3.8 Hz, 4H), 7.23 (d, $J$ = 3.9 Hz, 4H), 3.65 (s, 12H), 2.09 (t, $J$ = 3.7 Hz, 4H), 1.35 (s, 72H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 160.1, 143.5 (d, $J$ = 3.5 Hz), 143.4 (d, $J$ = 3.3 Hz), 131.2 (d, $J$ = 9.9 Hz), 131.1 (d, $J$ = 10.1 Hz), 64.2, 35.8, 32.1, 25.3; $^{31}$P{$^{1}$H} NMR (162 MHz, $CDCl_3$) δ -12.15; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{62}H_{97}O_4P_2$: 967.6857, found: 967.6857.



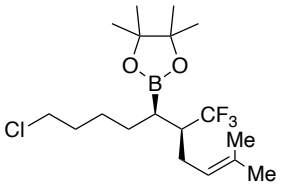

**4,4,5,5-Tetramethyl-2-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (3aa):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 67 mg (84%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.19-7.16 (m, 3H), 4.99 (t, $J$ = 7.0 Hz, 1H), 2.77 (ddd, $J$ = 13.4, 10.4, 4.8 Hz, 1H), 2.48 (ddd, $J$ = 16.9, 9.9, 7.0 Hz, 1H), 2.42-2.31 (m, 1H), 2.29-2.21 (m, 2H), 1.88-1.78 (m, 1H), 1.72-1.67 (m, 1H), 1.66 (s, 3H), 1.59 (s, 3H), 1.31-1.29 (m, 1H), 1.27 (s, 6H), 1.26 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 142.5, 133.5, 128.6 (q, $J$ = 280.0 Hz), 128.5 (2C), 128.3(2C), 125.8, 121.3, 83.4 (2C), 44.9 (q, $J$ = 23.6 Hz), 36.0, 28.6, 25.8, 25.2 (q, $J$ = 2.2 Hz), 25.0 (2C), 24.6 (2C), 21.9 (the boron-bound carbon, very weak), 17.7; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.31; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 33.35; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{22}H_{33}BF_3O_2$: 397.2530, found: 397.2530.



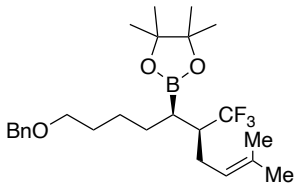
**4,4,5,5-Tetramethyl-2-((5*S**,6*R**)-2-methyl-5-(trifluoromethyl)tetradec-2-en-6-yl)-1,3,2-dioxaborolane (3ba):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 53 mg (66%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.12 (t, *J* = 7.4 Hz, 1H), 2.36-2.21 (m, 3H), 1.70 (s, 3H), 1.62 (s, 3H), 1.56-1.47 (m, 1H), 1.40-1.34 (m, 2H), 1.31-1.30 (m, 2H), 1.28-1.26 (m, 10H), 1.24 (s, 6H), 1.23 (s, 6H), 0.88 (t, *J* = 6.7 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 133.1, 128.7 (q, *J* = 280.0 Hz), 121.7, 83.2 (2C), 45.2 (q, *J* = 23.4 Hz), 31.9, 29.7 (2C), 29.5, 29.3, 27.2, 25.8, 25.4 (q, *J* = 2.2 Hz), 24.8 (2C), 24.6 (2C), 22.7, 17.7, 14.1 (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.58; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 34.14; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{22}H_{41}BF_3O_2$: 405.3150, found: 405.3139.



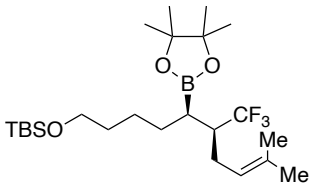

**2-((1*R**,2*S**)-1-Cyclohexyl-5-methyl-2-(trifluoromethyl)hex-4-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3ca):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 33 mg (45%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.17 (tq, *J* = 7.4, 1.2 Hz, 1H), 2.42-2.21 (m, 3H), 1.80-1.66 (m, 5H), 1.69 (s, 3H), 1.62 (s, 3H), 1.59-1.51 (m, 1H), 1.25 (s, 12H), 1.22-1.09 (m, 4H), 1.00 (qd, *J* = 12.2, 3.2 Hz, 1H), 0.84 (qd, *J* = 12.5, 3.5 Hz, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 132.3, 129.0 (q, *J* = 279.5 Hz), 122.5, 83.2 (2C), 42.4 (q, *J* = 23.3 Hz), 36.2, 33.3, 32.2, 29.7 (the boron-bound carbon, very weak), 26.53, 26.50, 26.3, 25.8, 25.4 (q, *J* = 1.8 Hz), 25.1 (2C), 24.8 (2C), 17.6; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -68.15; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 32.95; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{20}H_{35}BF_3O_2$: 375.2680, found: 375.2679.



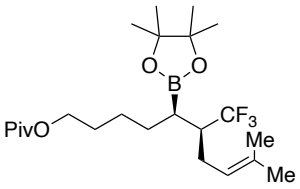
**2-((5*R**,6*S**)-1-Chloro-9-methyl-6-(trifluoromethyl)dec-8-en-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3da):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 54 mg (71%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, *J* = 6.3 Hz, 1H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.40-2.24 (m, 3H), 1.81-1.74 (m, 2H), 1.71 (s, 3H), 1.62 (s, 3H), 1.56-1.49 (m, 2H), 1.42-1.32 (m, 2H), 1.28-1.26 (m, 1H), 1.24 (s, 6H), 1.23 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 133.5, 128.6 (q, *J* = 279.8 Hz), 121.4, 83.4 (2C), 45.02, 44.97 (q, *J* = 23.7 Hz), 32.7, 27.1, 26.1, 25.8, 25.4 (q, *J* = 2.4 Hz), 24.9 (2C), 24.6 (2C), 22.4 (the boron-bound carbon, very weak), 17.7; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.40; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 34.08; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{18}H_{32}BClF_3O_2$: 383.2134, found: 383.2134.



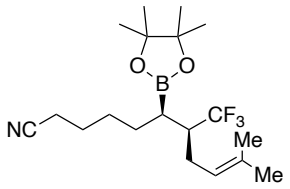

**2-((5*R**,6*S**)-1-(Benzyloxy)-9-methyl-6-(trifluoromethyl)dec-8-en-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3ea):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 60 mg (66%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 4H), 7.30-7.25 (m, 1H), 5.11 (t, *J* = 6.7 Hz, 1H), 4.49 (s, 2H), 3.46 (t, *J* = 6.6 Hz, 2H), 2.38-2.21 (m, 3H), 1.69 (s, 3H), 1.66-1.59 (m, 2H), 1.61 (s, 3H), 1.50-1.43 (m, 1H), 1.43-1.35 (m, 1H), 1.33-1.24 (m, 3H), 1.23 (s, 6H), 1.22 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 138.7, 133.3, 128.6 (q, *J* = 280.0 Hz), 128.3 (2C), 127.6 (2C), 127.4, 121.6, 83.3 (2C), 72.8, 70.3, 45.1 (q, *J* = 23.6 Hz), 29.9, 27.0, 26.4, 25.8, 25.4 (q, *J* = 2.4 Hz), 24.8 (2C), 24.6 (2C), 17.7 (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.49; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 33.61; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{25}H_{39}BF_3O_3$: 455.2949, found: 455.2938.



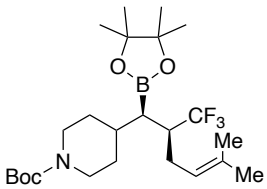

***tert*-Butyldimethyl(((5*R**,6*S**)-9-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-(trifluoromethyl)dec-8-en-1-yl)oxy)silane (3fa):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 57 mg (59%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.11 (t, *J* = 7.0 Hz, 1H), 3.59 (t, *J* = 6.3 Hz, 2H), 2.35-2.23 (m, 3H), 1.70 (s, 3H), 1.62 (s, 3H), 1.54-1.48 (m, 3H), 1.46-1.35 (m, 2H), 1.26-1.18 (m, 2H), 1.23 (s, 6H), 1.22 (s, 6H), 0.89 (s, 9H), 0.04 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 133.2, 128.6 (q, *J* = 279.8 Hz), 121.6, 83.2 (2C), 63.2, 45.1 (q, *J* = 23.5 Hz), 33.1, 27.0, 26.2, 26.0 (3C), 25.8, 25.3 (q, *J* = 2.0 Hz), 24.8 (2C), 24.6 (2C), 22.5 (the boron-bound carbon, very weak), 18.4, 17.7, -5.3 (2C); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.52; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 33.02; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{24}H_{47}BF_3O_3Si$: 479.3339, found: 479.3339.




**(5*R**,6*S**)-9-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-(trifluoromethyl)dec-8-en-1-yl pivalate (3ga):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 66 mg (74%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, *J* = 6.8 Hz, 1H), 4.03 (t, *J* = 6.5 Hz, 2H), 2.38-2.24 (m, 3H), 1.70 (s, 3H), 1.63 (quin, *J* = 7.0 Hz, 2H), 1.62 (s, 3H), 1.57-1.45 (m, 2H), 1.44-1.35 (m, 1H), 1.29-1.21 (m, 2H), 1.24 (s, 6H), 1.22 (s, 6H), 1.19 (s, 9H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 178.6, 133.4, 128.6 (q, *J* = 279.9 Hz), 121.5, 83.3 (2C), 64.4, 45.0 (q, *J* = 23.6 Hz), 38.7, 28.9, 27.2 (3C), 26.6, 26.3, 25.8, 25.3 (q, *J* = 2.1 Hz), 24.8 (2C), 24.6 (2C), 22.5 (the boron-bound carbon, very weak), 17.7; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.41; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 33.44; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{23}H_{41}BF_3O_4$: 449.3049, found: 449.3045.

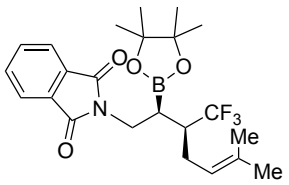


**(6*R**,7*S**)-10-Methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-(trifluoromethyl)undec-9-enenitrile (3ha):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 52 mg (70%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.09 (t, *J* = 7.2 Hz, 1H), 2.41-2.32 (m, 1H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.32-2.24 (m, 2H), 1.71 (s, 3H), 1.69-1.64 (m, 2H), 1.62 (s, 3H), 1.60-1.56 (m, 1H), 1.54-1.47 (m, 1H), 1.43-1.32 (m, 2H), 1.24 (s, 6H), 1.23 (s, 6H), 1.22-1.18 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 133.8, 128.5 (q, *J* = 280.0 Hz), 121.2, 119.7, 83.5 (2C), 44.9 (q, *J* = 23.6 Hz), 28.9, 25.8, 25.7, 25.5, 25.3 (q, *J* = 2.3 Hz), 24.9 (2C), 24.6 (2C), 22.2 (the boron-bound carbon, very weak), 17.8, 17.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.26; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 33.42; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{19}H_{32}BF_3NO_2$: 374.2482, found: 374.2487.

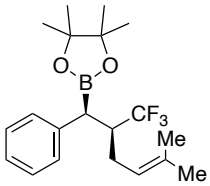


***tert*-Butyl 4-((1*R**,2*S**)-5-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)hex-4-en-1-yl)piperidine-1-carboxylate (3ia):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 73 mg (77%, 0.20 mmol scale); White solid; m.p. 68.4–70.5 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.16 (t, *J* = 6.2 Hz, 1H), 4.10 (br, 2H), 2.67-2.63 (m, 2H), 2.41-2.23 (m, 3H), 1.74-1.66 (m, 2H), 1.69 (s, 3H), 1.65-1.61 (m, 2H), 1.62 (s, 3H), 1.45 (s, 9H), 1.25 (s, 12H), 1.23-1.16 (m, 1H), 1.07 (qd, *J* = 13.6, 4.2 Hz, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 154.8, 132.7, 128.7 (q, *J* = 279.6 Hz), 122.0, 83.5 (2C), 79.3, 44.1 (br, 2C), 42.3 (q, *J* = 23.5 Hz), 34.9, 31.9, 31.4, 29.1 (the boron-bound carbon, very weak), 28.4 (3C), 25.7, 25.6, 25.1 (2C), 24.8 (2C), 17.6; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -68.14; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.83; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{24}H_{42}BF_3NO_4$: 476.3158,

found: 476.3160.

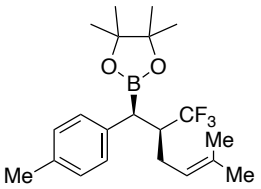


**2-((2*S**,3*S**)-6-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(trifluoromethyl)hept-5-en-1-yl)isoindoline-1,3-dione (3ja):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (10/1, v/v): 58 mg (64%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (m, 2H), 7.73-7.68 (m, 2H), 5.17 (t, *J* = 6.3 Hz, 1H), 3.95 (dd, *J* = 13.7, 9.2 Hz, 1H), 3.73 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.42-2.36 (m, 3H), 2.15 (td, *J* = 9.1, 2.8 Hz, 1H), 1.72 (s, 3H), 1.65 (s, 3H), 1.14 (s, 6H), 1.12 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 168.3 (2C), 134.0, 133.8 (2C), 132.2 (2C), 128.2 (q, *J* = 279.8 Hz), 123.1 (2C), 120.8, 83.6 (2C), 43.5 (q, *J* = 24.3 Hz), 36.5, 25.8, 25.6, 24.8 (2C), 24.5 (2C), 21.6 (the boron-bound carbon, very weak), 17.8; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -67.44; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 32.25; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{23}H_{30}BF_3NO_4$: 452.2219, found: 452.2206.

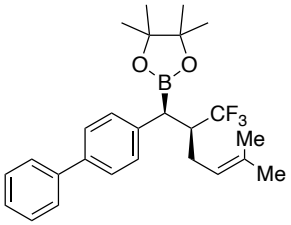


**4,4,5,5-Tetramethyl-2-((1*S**,2*S**)-5-methyl-1-phenyl-2-(trifluoromethyl)hex-4-en-1-yl)-1,3,2-dioxaborolane (3ka):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 47 mg (64%, 0.20 mmol scale); White solid; m.p. 57.7–59.5 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.21 (m, 4H), 7.20-7.14 (m, 1H), 5.17 (t, *J* = 7.0 Hz, 1H), 2.74-2.65 (m, 2H), 2.43-2.28 (m, 2H), 1.70 (s, 3H), 1.56 (s, 3H), 1.21 (s, 6H), 1.18 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 139.1, 133.5, 129.7 (2C), 128.3 (q, *J* = 281.0 Hz), 128.2 (2C), 126.0, 120.9, 83.8 (2C), 46.4 (q, *J* = 23.0 Hz), 31.8 (the boron-bound carbon, very weak), 26.8 (q, *J* = 2.2 Hz), 25.8, 24.6 (2C), 24.5 (2C), 17.7; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -66.43; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.57; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for

$C_{20}H_{29}BF_3O_2$: 369.2211, found: 369.2198.

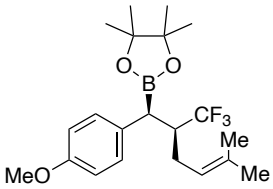


**4,4,5,5-Tetramethyl-2-((1*S**,2*S**)-5-methyl-1-(*p*-tolyl)-2-(trifluoromethyl)hex-4-en-1-yl)-1,3,2-dioxaborolane (3la):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 39 mg (51%, 0.20 mmol scale); White solid; m.p. 49.3–51.6 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.16 (t, *J* = 7.0 Hz, 1H), 2.70-2.62 (m, 2H), 2.41-2.26 (m, 2H), 2.30 (s, 3H), 1.70 (s, 3H), 1.56 (s, 3H), 1.21 (s, 6H), 1.18 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 135.8, 135.4, 133.5, 129.6 (2C), 128.9 (2C), 128.4 (q, *J* = 280.9 Hz), 121.0, 83.7 (2C), 46.4 (q, *J* = 22.8 Hz), 31.2 (the boron-bound carbon, very weak), 26.8 (q, *J* = 2.2 Hz), 25.8, 24.6 (2C), 24.5 (2C), 21.0, 17.7; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -66.33; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.11; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{21}H_{31}BF_3O_2$: 383.2367, found: 383.2367.

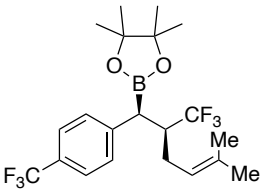


**2-((1*S**,2*S**)-1-([1,1'-Biphenyl]-4-yl)-5-methyl-2-(trifluoromethyl)hex-4-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3ma):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 64 mg (73%, 0.20 mmol scale); White solid; m.p. 79.5–80.8 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 7.52-7.49 (m, 2H), 7.43-7.40 (m, 2H), 7.33-7.29 (m, 3H), 5.19 (t, *J* = 7.0 Hz, 1H), 2.80-2.67 (m, 2H), 2.45-2.30 (m, 2H), 1.71 (s, 3H), 1.58 (s, 3H), 1.23 (s, 6H), 1.20 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 141.0, 138.8, 138.1, 133.6, 130.1 (2C), 128.7 (2C), 128.4 (q, *J* = 280.9 Hz), 127.0, 126.9 (2C), 126.8 (2C), 120.9, 83.8 (2C), 46.4 (q, *J* = 23.0 Hz), 31.2 (the boron-bound carbon, very weak), 26.8 (q, *J* = 2.0 Hz), 25.9, 24.64 (2C), 24.57 (2C), 17.8; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -

66.31; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.57; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{26}H_{33}BF_3O_2$: 445.2525, found: 445.2510.

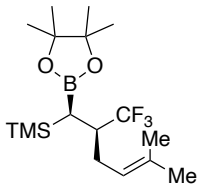



**2-((1*S**,2*S**)-1-(4-Methoxyphenyl)-5-methyl-2-(trifluoromethyl)hex-4-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3na):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v): 27 mg (35%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.18-7.15 (m, 2H), 6.82-6.78 (m, 2H), 5.16 (t, *J* = 6.1 Hz, 1H), 3.78 (s, 3H), 2.68-2.58 (m, 2H), 2.40-2.25 (m, 2H), 1.70 (s, 3H), 1.56 (s, 3H), 1.21 (s, 6H), 1.19 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 157.9, 133.5, 130.8, 130.7 (2C), 128.4 (q, *J* = 280.9 Hz), 121.0, 113.6 (2C), 83.7 (2C), 55.1, 46.4 (q, *J* = 22.6 Hz), 26.7 (q, *J* = 1.6 Hz), 25.8, 24.61 (2C), 24.57 (2C), 17.8 (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -66.31; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 32.98; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{21}H_{31}BF_3O_3$: 399.2317, found:399.2317.

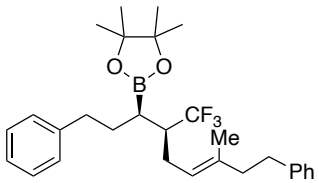



**4,4,5,5-Tetramethyl-2-((1*S**,2*S**)-5-methyl-2-(trifluoromethyl)-1-(4-(trifluoromethyl)phenyl)hex-4-en-1-yl)-1,3,2-dioxaborolane (3oa):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v), GPC (ethyl acetate) and GPC (chloroform): 55 mg (63%, 0.20 mmol scale); White solid; m.p. 51.1–52.3 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.17 (t, *J* = 6.6 Hz, 1H), 2.81-2.72 (m, 2H), 2.42-2.25 (m, 2H), 1.72 (s, 3H), 1.59 (s, 3H), 1.20 (s, 6H), 1.19 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 143.3, 134.1, 130.0 (2C), 128.3 (q, *J* = 32.1 Hz), 128.1 (q, *J* = 280.8 Hz), 125.0 (q, *J* = 3.6 Hz, 2C), 124.4 (q, *J* = 270.1 Hz), 120.3, 84.1 (2C), 46.0 (q, *J* = 23.4 Hz), 31.7 (the boron-bound carbon, very weak), 26.9 (q, *J* = 2.1 Hz), 25.8, 24.6 (2C), 24.5 (2C), 17.8; $^{19}$F{$^1$H} NMR

(376 MHz, $CDCl_3$) δ -62.34, -66.15; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.92; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{21}H_{28}BF_6O_2$: 437.2085, found: 437.2074.

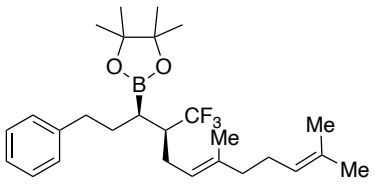



**Trimethyl((1*S**,2*R**)-5-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)hex-4-en-1-yl)silane (3pa):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 37 mg (51%, 0.20 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.0 Hz, 1H), 2.59-2.51 (m, 1H), 2.34-2.26 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.24 (s, 6H), 1.22 (s, 6H), 0.81 (d, *J* = 2.5 Hz, 1H), 0.11 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 132.2, 129.0 (q, *J* = 280.0 Hz), 122.6, 82.8 (2C), 42.3 (q, *J* = 24.5 Hz), 27.5 (q, *J* = 1.4 Hz), 25.6, 25.1 (2C), 24.5 (2C), 17.6, 13.7 (the boron-bound carbon, very weak), -0.6 (3C); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -70.48; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 33.21; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{17}H_{33}BF_3O_2Si$: 365.2293, found: 365.2304.

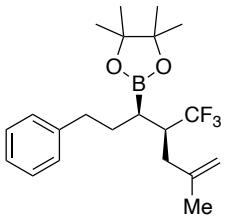



**4,4,5,5-Tetramethyl-2-((3*R**,4*S**,*E*)-7-methyl-1,9-diphenyl-4-(trifluoromethyl)non-6-en-3-yl)-1,3,2-dioxaborolane (3ab):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 51 mg (52%, 0.20 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 4H), 7.18-7.15 (m, 6H), 5.03 (t, *J* = 6.9 Hz, 1H), 2.75 (dd, *J* = 10.4, 4.5 Hz, 1H), 2.66 (dd, *J* = 10.1, 5.9 Hz, 2H), 2.44 (ddd, *J* = 16.9, 10.0, 6.9 Hz, 1H), 2.39-2.33 (m, 1H), 2.30-2.23 (m, 3H), 1.90-1.78 (m, 1H), 1.70-1.61 (m, 1H), 1.63 (s, 3H), 1.275 (s, 6H), 1.266 (s, 6H), 1.25-1.22 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 142.5, 142.2, 136.6, 128.54 (q, *J* = 280.9 Hz), 128.49 (2C), 128.4 (2C), 128.32 (2C), 128.27 (2C), 125.8, 125.7, 121.8, 83.4 (2C), 44.9 (q, *J* = 23.4 Hz), 41.5, 36.0, 34.5, 28.7, 25.1 (q, *J* = 3.2 Hz), 25.0 (2C),

24.7 (2C), 16.2 (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -67.33; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 33.90; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{29}H_{39}BF_3O_2$: 487.2995, found: 487.2995.

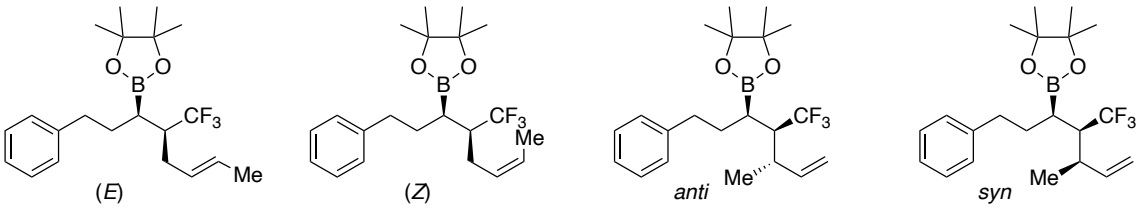



**2-((3*R**,4*S**,*E*)-7,11-Dimethyl-1-phenyl-4-(trifluoromethyl)dodeca-6,10-dien-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3ac):** Reaction time was 48 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 62 mg (66%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.19-7.16 (m, 3H), 5.07 (tq, *J* = 6.8, 1.4 Hz, 1H), 5.02 (t, *J* = 7.0 Hz, 1H), 2.77 (ddd, *J* = 15.0, 10.5, 4.8 Hz, 1H), 2.46 (ddd, *J* = 16.8, 10.0, 6.8 Hz, 1H), 2.41-2.35 (m, 1H), 2.33-2.23 (m, 2H), 2.07-2.02 (m, 2H), 1.98-1.95 (m, 2H), 1.83 (qd, *J* = 10.8, 4.2 Hz, 1H), 1.72-1.63 (m, 1H), 1.67 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.31-1.29 (m, 1H), 1.27 (s, 6H), 1.26 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.5, 137.1, 131.4, 128.6 (q, *J* = 280.0 Hz), 128.5 (2C), 128.3 (2C), 125.6, 124.2, 121.3, 83.4 (2C), 45.0 (q, *J* = 23.4 Hz), 39.7, 36.0, 28.7, 26.5, 25.7, 25.2 (q, *J* = 2.5 Hz), 25.0 (2C), 24.6 (2C), 22.0 (the boron-bound carbon, very weak), 17.7, 16.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -67.26; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 34.31; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{27}H_{41}BF_3O_2$: 465.3151, found: 465.3131.



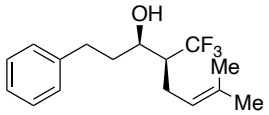

**4,4,5,5-Tetramethyl-2-((3*R**,4*S**)-6-methyl-1-phenyl-4-(trifluoromethyl)hept-6-en-3-yl)-1,3,2-dioxaborolane (3ad):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v) and GPC (ethyl acetate): 38 mg (50%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.19-7.15 (m, 3H), 4.75 (s, 1H), 4.63 (s, 1H), 2.79 (ddd, *J* = 13.4, 10.2, 4.8 Hz, 1H), 2.70-

2.53 (m, 1H), 2.47 (ddd, $J$ = 16.8, 9.8, 7.0 Hz, 1H), 2.27 (d, $J$ = 7.1 Hz, 2H), 1.90-1.77 (m, 1H), 1.71-1.63 (m, 1H), 1.69 (s, 3H), 1.262 (s, 6H), 1.258 (s, 6H), 1.23-1.22 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.5, 142.2, 128.5 (q, $J$ = 280.0 Hz), 128.5 (2C), 128.3 (2C), 125.8, 113.5, 83.4 (2C), 42.2 (q, $J$ = 24.0 Hz), 36.0, 34.8 (q, $J$ = 2.1 Hz), 28.1, 24.9 (2C), 24.6 (2C), 21.8 (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -67.24; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 34.26; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{31}BF_3O_2$: 383.2373, found: 383.2367.

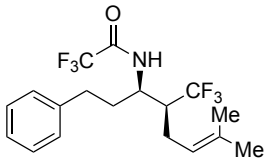



**A 27:73 regiomixture of 4,4,5,5-tetramethyl-2-((3*R**,4*S**)-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)-1,3,2-dioxaborolane (3ae) and 4,4,5,5-tetramethyl-2-((3*R**,4*R**)-5-methyl-1-phenyl-4-(trifluoromethyl)hept-6-en-3-yl)-1,3,2-dioxaborolane (3ae') (relative stereochemistry of 3ae' was tentatively assigned):** Reaction time was 18 h. Purified by silica gel column chromatography with hexane/ethyl acetate (40/1, v/v), GPC (ethyl acetate), and GPC ($CHCl_3$): 20 mg (26%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.24 (m, 0.27 × 2H for **3ae** and 0.73 × 2H for **3ae'**), 7.19-7.14 (m, 0.27 × 3H for **3ae** and 0.73 × 3H for **3ae'**), 5.78-5.68 (m, 0.27 × 1H for **3ae**), 5.58 (ddd, $J$ = 17.0, 10.2, 9.1 Hz, 0.73 × 0.54 × 1H for *anti*-**3ae'**), 5.39-5.22 (m, 0.27 × 1H for **3ae** and 0.73 × 0.46 × 1H for *syn*-**3ae'**), 4.95 (dd, $J$ = 10.2, 1.6 Hz, 0.73 × 0.46 × 1H for *syn*-**3ae'**), 5.00 (ddd, $J$ = 17.0, 1.6, 0.9 Hz, 0.73 × 0.46 × 1H for *syn*-**3ae'**), 4.87 (dd, $J$ = 10.2, 1.6 Hz, 0.73 × 0.54 × 1H for *anti*-**3ae'**), 4.85 (ddd, $J$ = 17.0, 1.6, 0.8 Hz, 0.73 × 0.54 × 1H for *anti*-**3ae'**), 2.89-2.73 (m, 0.27 × 1H for **3ae** and 0.73 × 1H for **3ae'**), 2.54-2.49 (m, 0.73 × 1H for **3ae'**), 2.47-2.31 (m, 0.27 × 2H for **3ae** and 0.73 × 2H for **3ae'**), 2.29-2.16 (m, 0.27 × 2H for **3ae**), 1.87-1.64 (m, 0.27 × 2H for **3ae** and 0.73 × 2H for **3ae'**), 1.58 (dd, $J$ = 6.0, 0.9 Hz, 0.27 × 3H for **3ae**), 1.33-1.30 (m, 0.27 × 1H for **3ae** and 0.73 × 1H for **3ae'**), 1.28 (s, 0.73 × 6H for **3ae'**), 1.27 (s, 0.27 × 6H for **3ae** and 0.73 × 6H for **3ae'**), 1.26 (s, 0.27 × 6H for **3ae**), 1.09 (dq, $J$ = 6.7, 1.7 Hz, 0.73 × 0.46 × 3H for *syn*-**3ae'**), 0.91 (d, $J$ = 6.8 Hz, 0.73 × 0.54 × 3H for *anti*-**3ae'**);

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.8, 142.5, 142.4, 142.1, 141.2, 128.59, 128.56, 128.50 (q, *J* = 277.6 Hz), 128.29, 128.28 (q, *J* = 281.0 Hz), 128.22, 127.9, 127.7, 125.8, 125.6, 114.8, 114.3, 83.5, 83.42, 83.39, 49.3 (q, *J* = 23.2 Hz), 48.8 (q, *J* = 22.3 Hz), 44.8, 44.6, 37.2, 37.1, 36.0, 35.7, 29.8, 28.3, 27.5, 27.1, 25.02, 24.97, 24.62, 24.59, 24.54, 19.1, 18.7, 17.9 (All observed signals are shown because of complexity associated with regio- and stereoisomers.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -60.56, -60.67, -67.07, -67.42; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 34.21; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{31}BF_3O_2$: 383.2367, found: 383.2377.

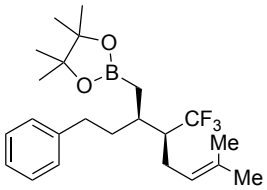



**(3*R**,4*S**)-7-Methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-ol (5):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 40 mg (97%, 0.15 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.22-7.18 (m, 3H), 5.11 (t, *J* = 7.0 Hz, 1H), 4.00-3.94 (m, 1H), 2.86 (ddd, *J* = 14.2, 9.6, 5.4 Hz, 1H), 2.65 (ddd, *J* = 16.3, 9.2, 7.0 Hz, 1H), 2.38-2.28 (m, 2H), 2.27-2.16 (m, 1H), 1.96-1.86 (m, 1H), 1.85-1.76 (m, 1H), 1.68 (s, 3H), 1.67 (s, 1H), 1.60 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.4, 134.0, 128.52 (2C), 128.46 (2C), 128.0 (q, *J* = 279.9 Hz), 126.1, 121.0, 68.8 (q, *J* = 2.2 Hz), 48.8 (q, *J* = 22.5 Hz), 36.1, 32.5, 25.8, 22.2 (q, *J* = 2.2 Hz), 17.7; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -67.28; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{22}F_3O$: 287.1617, found: 287.1629.

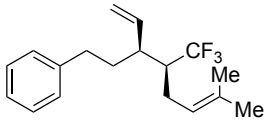



**2,2,2-Trifluoro-*N*-((3*R**,4*S**)-7-methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)acetamide (6):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 44 mg (77%, 0.15 mmol scale); White solid; m.p. 58.1–60.9 °C; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.24-7.20 (m, 1H), 7.15-7.13 (m, 2H), 6.36 (d, *J* = 8.6 Hz, 1H), 5.04 (t, *J* = 7.0 Hz, 1H), 4.27 (t, *J* = 10.3 Hz, 1H), 2.72 (ddd, *J* = 14.1, 8.7, 5.6 Hz, 1H), 2.57 (dt, *J* = 14.0, 7.9 Hz, 1H), 2.51-2.39 (m, 1H), 2.39-2.32 (m,

1H), 2.17 (dt, *J* = 15.1, 8.7 Hz, 1H), 2.05-1.97 (m, 1H), 1.90-1.80 (m, 1H), 1.69 (s, 3H), 1.56 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 156.7 (q, *J* = 36.7 Hz), 140.1, 136.0, 128.7 (2C), 128.4 (2C), 127.5 (q, *J* = 280.0 Hz), 126.5, 118.7, 115.7 (q, *J* = 286.4 Hz), 48.3, 46.7 (q, *J* = 23.4 Hz), 32.7, 31.7, 25.7, 24.0 (q, *J* = 2.2 Hz), 17.7; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -66.04, -76.04; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{22}F_6NO$: 382.1600, found: 382.1600.

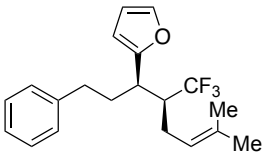



**4,4,5,5-Tetramethyl-2-((2*R**,3*S**)-6-methyl-2-phenethyl-3-(trifluoromethyl)hept-5-en-1-yl)-1,3,2-dioxaborolane (7):** 59 mg (96%, 0.15 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.20-7.15 (m, 3H), 5.11 (t, *J* = 6.7 Hz, 1H), 2.66 (ddd, *J* = 13.5, 10.8, 5.7 Hz, 1H), 2.54 (ddd, *J* = 13.5, 10.7, 5.7 Hz, 1H), 2.34-2.27 (m, 1H), 2.23-2.15 (m, 2H), 2.13-2.05 (m, 1H), 1.77-1.71 (m, 1H), 1.69 (s, 3H), 1.63-1.59 (m, 1H), 1.60 (s, 3H), 1.24 (s, 6H), 1.23 (s, 6H), 1.02 (dd, *J* = 16.0, 6.3 Hz, 1H), 0.89 (dd, *J* = 16.0, 8.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.3, 133.0, 128.8 (q, *J* = 280.6 Hz), 128.4 (4C), 125.8, 121.7, 83.1 (2C), 46.3 (q, *J* = 22.6 Hz), 35.8, 34.3, 32.9 (q, *J* = 1.2 Hz), 25.8, 24.9 (2C), 24.8 (2C), 23.6 (q, *J* = 2.6 Hz), 17.7, 14.0 (the boron-bound carbon, very weak); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -65.99; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 33.64; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{35}BF_3O_2$: 411.2681, found: 411.2676.




**((3*S**,4*S**)-7-Methyl-4-(trifluoromethyl)-3-vinyloct-6-en-1-yl)benzene (8):** Purified by silica gel column chromatography with hexane: 29 mg (65%, 0.15 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.15 (m, 3H), 5.75 (ddd, *J* = 17.1, 9.8, 9.4 Hz, 1H), 5.16 (dd, *J* = 9.8, 1.6 Hz, 1H), 5.09 (d, *J* = 17.1 Hz, 1H), 5.06 (t, *J* = 6.7 Hz, 1H), 2.68 (ddd, *J* = 13.8, 10.0, 5.3 Hz, 1H), 2.50-2.40 (m, 2H), 2.25-2.14 (m, 3H), 1.84-1.71 (m, 2H), 1.68 (s, 3H), 1.58 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz,

$CDCl_3$) δ 141.9, 138.6, 133.5, 128.42 (2C), 128.39 (2C), 128.2 (q, $J$ = 280.2 Hz), 125.9, 121.2, 117.4, 48.0 (q, $J$ = 22.9 Hz), 42.1 (q, $J$ = 1.8 Hz), 33.8, 33.2, 25.8, 24.0 (q, $J$ = 6.9 Hz), 17.7; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -66.32; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{24}F_3$: 297.1825, found: 297.1822.




**2-((3*R**,4*S**)-7-Methyl-1-phenyl-4-(trifluoromethyl)oct-6-en-3-yl)furan (9):** Purified by silica gel column chromatography with hexane: 39 mg (81%, 0.15 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, $J$ = 1.8, 0.8 Hz, 1H), 7.29-7.25 (m, 2H), 7.20-7.16 (m, 1H), 7.13-7.11 (m, 2H), 6.33 (dd, $J$ = 3.2, 1.8 Hz, 1H), 6.12 (d, $J$ = 3.2 Hz, 1H), 5.04 (t, $J$ = 6.8 Hz, 1H), 3.11 (dt, $J$ = 10.9, 4.6 Hz, 1H), 2.55 (ddd, $J$ = 13.8, 9.9, 5.0 Hz, 1H), 2.48-2.37 (m, 2H), 2.25 (dt, $J$ = 15.3, 6.9 Hz, 1H), 2.19-2.09 (m, 2H), 2.03-1.95 (m, 1H), 1.67 (s, 3H), 1.52 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.6, 141.6, 141.4, 133.7, 128.40 (2C), 128.39 (2C), 127.9 (q, $J$ = 280.2 Hz), 126.0, 120.8, 110.1, 107.7, 47.5 (q, $J$ = 23.1 Hz), 37.3 (q, $J$ = 1.8 Hz), 33.9, 32.7, 25.8, 24.9 (q, $J$ = 2.4 Hz), 17.6; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -66.43; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{24}F_3O$: 337.1774, found: 337.1773.

## References and Notes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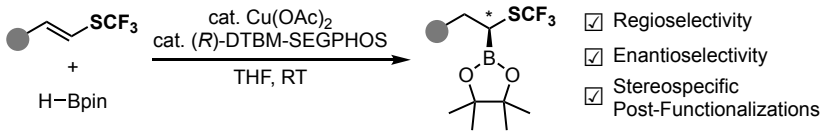
# Chapter 3

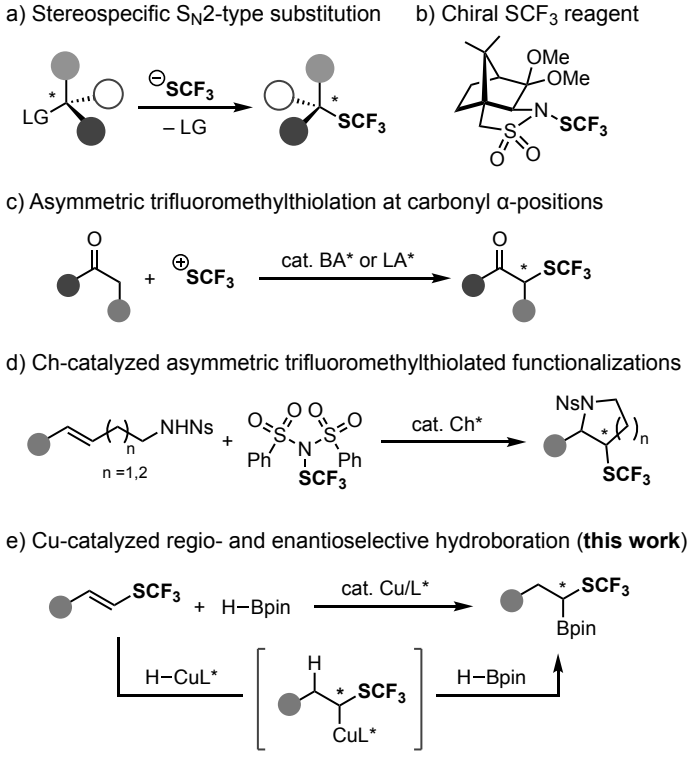
# Asymmetric Synthesis of $SCF_3$-Substituted Alkylboronates by Copper-Catalyzed Regio- and Enantioselective Hydroboration of $SCF_3$-Substituted Alkenes

A synthetic method for preparation of optically active trifluoromethylthio ($SCF_3$) compounds by a copper-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes with H–Bpin has been developed. The enantioselective hydrocupration of an *in situ* generated CuH species and subsequent boration reaction generate a chiral $SCF_3$-contaning alkylboronate, of which Bpin moiety can be further transformed to deliver various optically active $SCF_3$ molecules. Computational studies suggest that the $SCF_3$ group successfully controls the regioselectivity in the reaction.



## Introduction

In Chapters 1 and 2, the author achieved the synthesis of alkyl $CF_3$ compounds using $CF_3$-substituted alkenes. Building on this chemistry, this chapter focuses on the synthesis of alkyl $SCF_3$ compounds using the corresponding $SCF_3$-substituted alkenes. As mentioned in the General Introduction, the $SCF_3$ group is a representative fluorinated substituent and is anticipated to be a valuable functional group in drug discovery. Although various synthetic methods for $C(sp^2)$–$SCF_3$ compounds have been synthesized in the past decade, the synthesis of $C(sp^3)$–$SCF_3$ molecules, especially catalytic asymmetric version, is still underdeveloped.[1] For the synthesis of optically active $SCF_3$ compounds, stereospecific $S_N2$-type trifluoromethylthiolation on chiral carbon center was reported (Scheme 3.1a).[2] Also, a chiral trifluoromethylthiolation reagent was developed by Shen to achieve the asymmetric trifluoromethylthiolation of cyclic β-ketoesters (Scheme 3.1b).[3] However, in these cases, preparation of a stoichiometric amount of chiral starting materials or reagents was basically required. Recently, catalytic $S_N2$-type substitution of racemic propargyl substrates using chiral Cu catalysts has also been reported.[4] On the other hand, catalytic asymmetric trifluoromethylthiolation reactions at the α-position of carbonyl or nitrile compounds were successfully explored using chiral




**Scheme 3.1**. Stoichiometric or catalytic asymmetric construction of $SCF_3$-substituted stereocenters.

Brønsted or Lewis acids (BA or LA; Scheme 3.1c).[1a,5] In addition, several asymmetric trifluoromethylthiolated functionalizations have been achieved using optically active chalcogenide (Ch) catalysts (Scheme 3.1d).[6] Despite the aforementioned certain efforts, there still remains structural limitations in the synthesis of chiral $SCF_3$-contaning compounds, and expansion of their chemical space is highly desired.

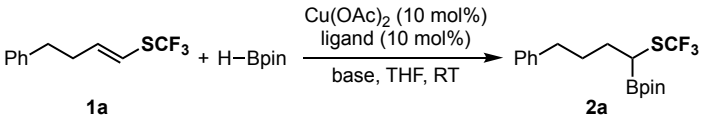
Herein, the author reports a copper-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes with pinacolborane (H–Bpin; Scheme 3.1e). The alkene moiety undergoes the regio- and enantioselective insertion into in-situ generated CuH species[7] to form an optically active α-$SCF_3$ alkylcopper intermediate. Subsequent boration reaction with H–Bpin provides the Bpin-substituted $SCF_3$ compound in an enantioenriched form. Moreover, the Bpin moiety in the product could be easily transformed to various useful functional groups. To the best of our knowledge, such a chiral platform containing $SCF_3$ and Bpin functions in the *gem*-relationship is disclosed for the first time. More recently, Liu and co-workers reported an enantioconvergent coupling reaction of benzyl halides and $[Me_4N][SCF_3]$ in the presence of copper catalyst with N,N,P-type tridentate ligand.[8] However, the carbon radical-based strategy still required the use of benzyl halides to only construct the aryl- and $SCF_3$-substituted chiral carbon center. Thus, it is complementary to the author's method, which gives an alkyl-substituted chiral center.

**Results and discussion**

The author commenced optimization studies for nonenantioselective conditions using $SCF_3$-substituted alkene **1a** as a model substrate with achiral biphosphine ligands (Table 3.1). In the presence of $Cu(OAc)_2$ catalyst and bis(diphenylphosphino)benzene (dppbz) ligand, treatment of **1a** with H–Bpin in THF solvent at room temperature afforded the desired hydroborated product **2a** in 9% $^1$H NMR yield. The yield was poor, but the high regioselectivity was observed. Inspired by the previously reported positive effects of substituents at remote positions in the biphosphine ligand to improve reaction efficiency,[9] the author then tested several modified dppbz ligands (entries 2-8). As expected, bulky substituents at meta-positions on phenyl ring accelerated the desired hydroboration reaction. In particular, *t*Bu-dppbz showed high performance to yield **2a** in 99% yield (entry 5). On the other hand, other common bidentate and monodentate phosphine ligands showed relatively poor activity. Although the desired product was

obtained in only 37% with DTBM-dppbz (entry 8), an improvement of the reaction efficiency by the addition of some bases was observed. For example, LiOAc could accelerate the reaction (entry 9), while an alkoxide base diminished the yield (entry 10). Acetate-type bases bearing other alkali metal cations were also effective (entries 11-13). Among them, CsOAc was best and increased the yield to 91% (entry 13). In cases of cesium carbonate and fluoride bases, the reaction yields were slightly decreased (entries 14 and 15). On the other hand, under the *t*Bu-dppbz-mediated conditions, CsOAc gave the negligible impact on the yield of **2a** (entry 16). CsOAc may play an important role in the initial formation step of the active CuH species. Actually, the acceleration of the initial reaction rate was observed in detailed kinetic studies.

**Table 3.1**. Optimization studies for copper-catalyzed regioselective hydroboration of $SCF_3$-substituted alkene **1a** with H–Bpin.[a]

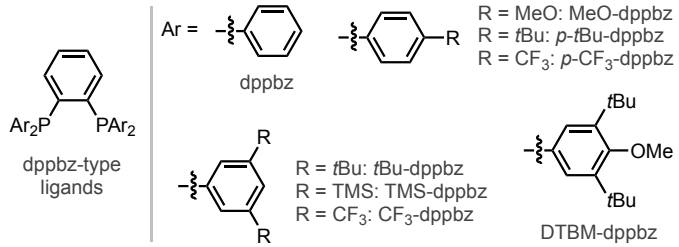



**1a** **2a**

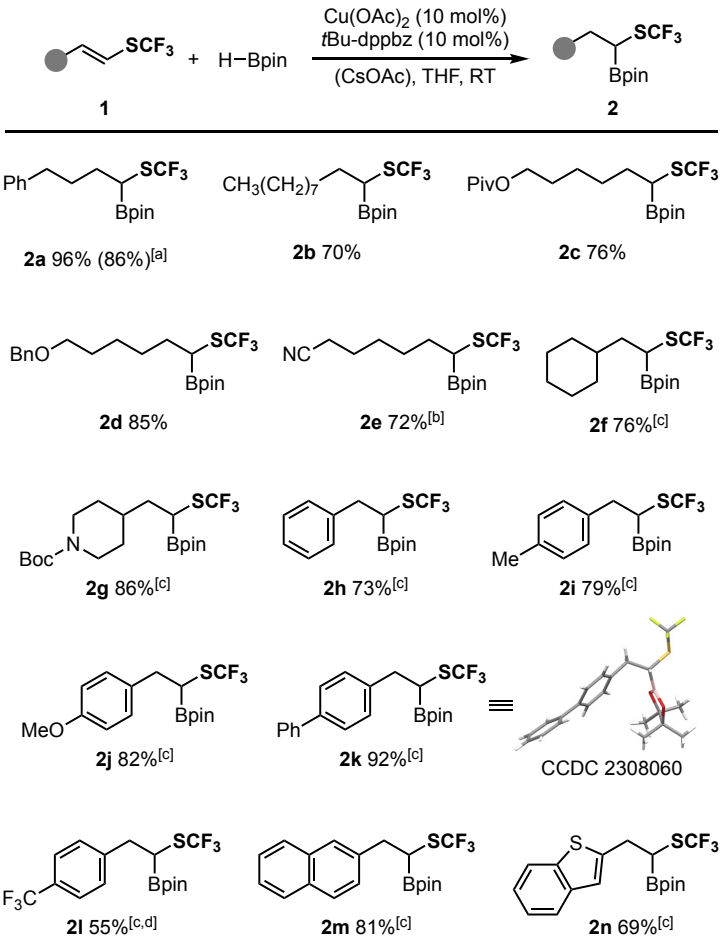
| entry | ligand | base | yield (%)[b] |
|---|---|---|---|
| 1 | dppbz | | 9 |
| 2 | MeO-dppbz | | trace |
| 3 | *p*-*t*Bu-dppbz | | 8 |
| 4 | *p*-$CF_3$-dppbz | | 0 |
| 5 | *t*Bu-dppbz | | 99 (96) |
| 6 | TMS-dppbz | | 73 |
| 7 | $CF_3$-dppbz | | 49 |
| 8 | DTBM-dppbz | | 37 |
| 9 | DTBM-dppbz | LiOAc | 83 |
| 10 | DTBM-dppbz | LiO*t*Bu | 15 |
| 11 | DTBM-dppbz | NaOAc | 57 |
| 12 | DTBM-dppbz | KOAc | 89 |
| 13 | DTBM-dppbz | CsOAc | 91 |
| 14 | DTBM-dppbz | $Cs_2CO_3$ | 67 |
| 15 | DTBM-dppbz | CsF | 69 |

| | | | |
|---|---|---|---|
| 16 | *t*Bu-dppbz | CsOAc | 97 |

[a] Conditions: **1a** (0.20 mmol), H–Bpin (0.70 mmol), $Cu(OAc)_2$ (0.020 mmol), ligand (0.020 mmol), base (0.40 mmol), THF (0.30 mL), RT, 4 h, $N_2$. [b] Estimated by $^1H$ NMR. Isolated yield is given in parentheses.



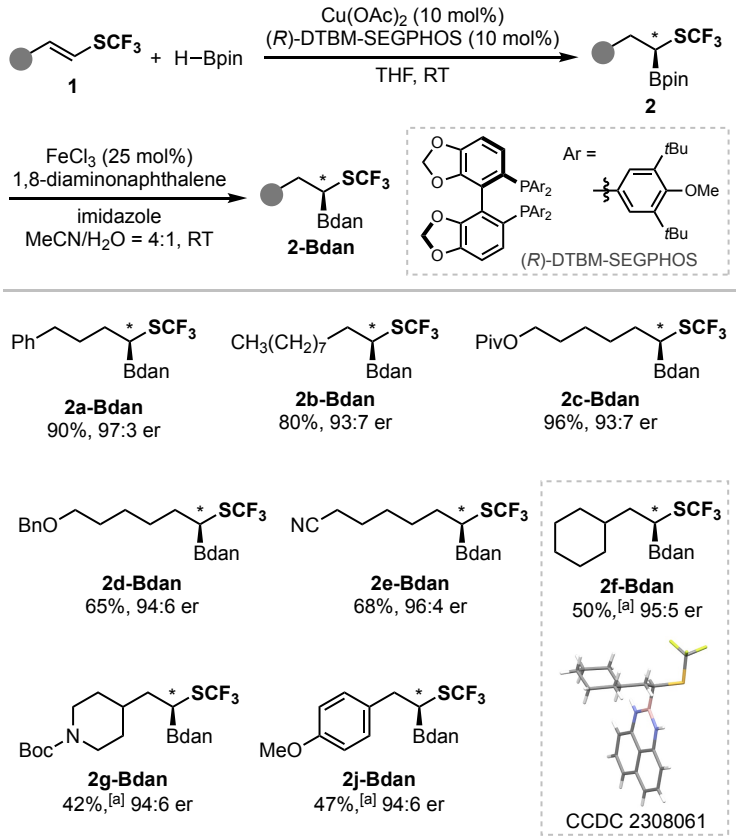

Under the optimal reaction conditions (entry 5 in Table 3.1), the generality of the reaction was examined (Scheme 3.2). The primary alkyl-substituted $SCF_3$-alkene **1b** also reacted with H–Bpin efficiently to afford the corresponding hydroborated product **2b** in




**Scheme 3.2**. Products of Cu-catalyzed regioselective hydroboration of $SCF_3$-substituted alkenes **1** with H–Bpin. Conditions: **1** (0.20 mmol), H–Bpin (0.70 mmol), $Cu(OAc)_2$ (0.020 mmol), *t*Bu-dppbz (0.020 mmol), THF (0.30 mL), RT, 4-18 h. Isolated yields are shown. [a] On a 1.0 mmol scale. [b] In toluene (0.30 mL). [c] With CsOAc (0.40 mmol). [d] The regioisomeric ratio (rr) was 2.8:1. The regioisomer was detected as the simple $CF_3$-substituted styrene by the elimination process of $SCF_3$ group.

70% yield. The reaction conditions were tolerant of various functional groups, including ester (**2c**), ether (**2d**), and nitrile (**2e**). In cases of secondary alkyl substituted $SCF_3$-alkene **1f** and **1g**, the addition of CsOAc was necessary to obtain the satisfactory conversion probably due to their steric bulkiness. In addition, aryl-conjugated substrates could be successfully employed in the presence of CsOAc base. Both electron-rich and -neutral substrates were coupled with H–Bpin in good yields (**2h**-**2k**). Although the substrate with an electron-deficient aromatic ring gave a mixture of regioisomers, the target product was isolated in an acceptable yield (**2l**). The reaction with naphthalene- and benzothiophen-conjugated substrates was also possible (**2m** and **2n**). The hydroboration of **1a** could also be scaled up to form **2a** in 86 % yield even on a 1.0 mmol scale. The regioselectivity of the hydroboration reaction was confirmed by the X-ray analysis of **2k** (CCDC 2308060).

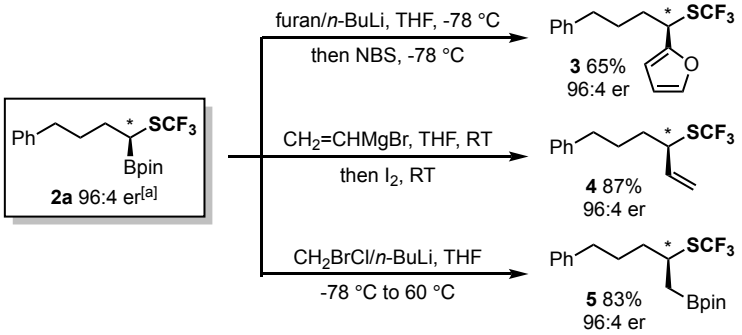
Encouraged by the successful results mentioned above, the author then examined the enantioselective conditions using a chiral biphosphine ligand (Scheme 3.3). After intensive ligand screening, the author found that the replacement of *t*Bu-dppbz with (*R*)-DTBM-SEGPHOS gave the hydroborated product **2a** in a high yield with high




**Scheme 3.3**. Cu-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes **1**. Conditions: **1** (0.20 mmol), H–Bpin (0.70 mmol), $Cu(OAc)_2$ (0.020 mmol), (*R*)-DTBM-SEGPHOS (0.020 mmol), THF (0.30 mL), RT, 4-18 h. Isolated yields are shown. [a] With CsOAc (0.40 mmol).

enantioselectivity. The enantiomeric ratio was estimated by HPLC analysis of **2a-Bdan** after derivatization using the reported Bpin to Bdan transesterification.[10] The enantioselective reaction conditions were also compatible with aliphatic $SCF_3$-substituted alkenes bearing some common functional groups (**2b-Bdan**-**2e-Bdan**). Similar to nonenantioselective conditions, the addition of CsOAc as an external base was necessary for the secondary alkyl-substituted (**2f-Bdan** and **2g-Bdan**) and aryl-conjugated (**2j-Bdan**) $SCF_3$-alkenes. However, the yields still remained only moderate even in the presence of CsOAc likely due to steric repulsions between the bulky DTBM-SEGPHOS ligand and the substituent at the β-position of $SCF_3$ group. The author confirmed that CsOAc gave no effect on the enantioselectivity. The absolute configuration of **2f-Bdan** was confirmed to be *S* by the X-ray analysis (CCDC 2308061), and those of other compounds were assigned by analogy.

The Bpin moiety of the product obtained in the enantioselective reaction easily underwent various chemical transformations to produce the functionalized $SCF_3$-contaninig molecules with high stereochemical fidelity (Scheme 3.4). For example, the hydroborated product **2a** successfully reacted with furanyllithium and vinyl Grignard reagent to furnish the corresponding furanylation[11] and vinylation[12] products, respectively, without any erosion of enantiomeric ratio. In addition, a homologation reaction of **2a** was also possible to yield the one carbon elongated product **5** with high enantiospecificity.[13] Thus, the chiral α-$SCF_3$ alkylboronates **2** would be valuable platforms for versatile optically active $SCF_3$ molecules. Unfortunately, attempts to apply cross-coupling-type transformations remained unsuccessful.

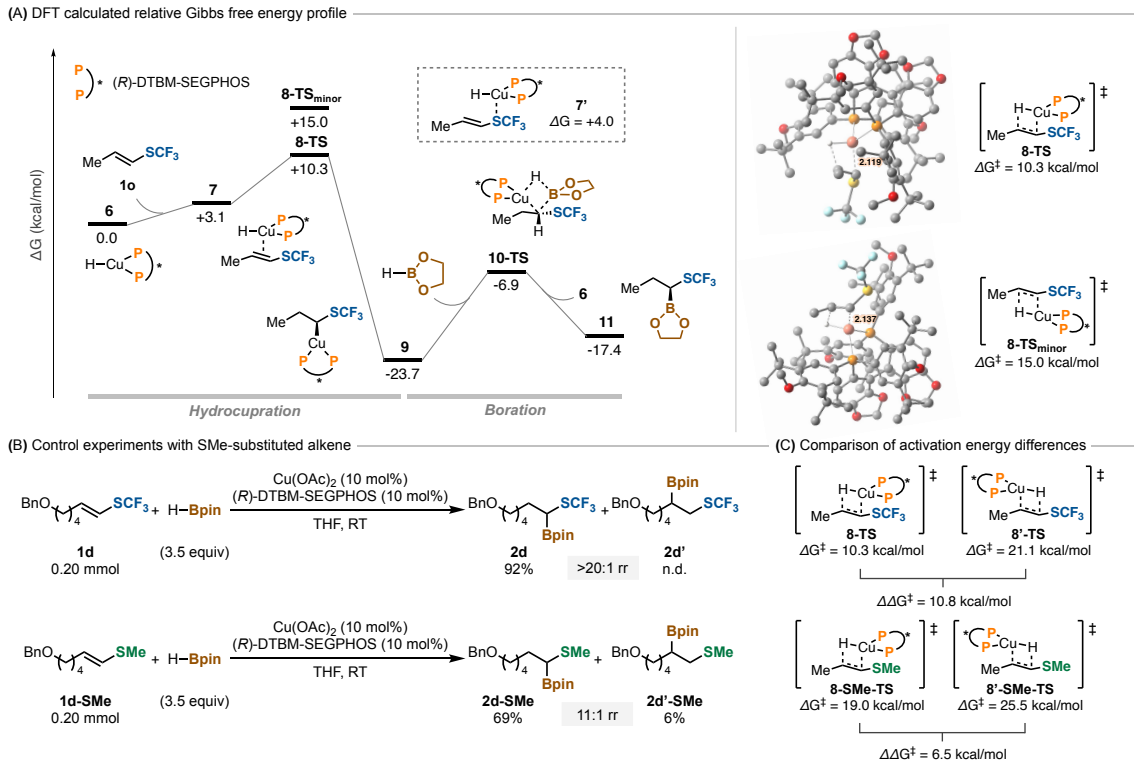



**Scheme 3.4**. Stereospecific transformations of Bpin moiety in **2a**. See the Experimental Procedures for more detailed conditions. [a] Estimated by HPLC analysis of **2a-Bdan** after derivatization.

Finally, the author investigated the mechanism of hydroboration reaction through a combination of control experiments and density functional theory (DFT) calculations

(Scheme 3.5). All calculations were carried out using Gaussian 16 program.[14] The long-range and dispersion corrected ωB97X-D function[15] was employed for geometry optimizations and single-point energy calculations. Geometries of intermediates and transition states were optimized with a standard 6-31G(d) basis set (LanL2DZ basis set for Cu). Single-point energy calculations were performed using the 6-311+G(d,p) basis set (SDD basis set for Cu) in THF using the SMD solvation model.[16] In the case of *t*Bu-dppbz ligand, an activation energy of the hydrocupration transition was lower than that of simple dppbz ligand ($\Delta G^{\ddagger}$ = 12.0 and 16.0 kcal/mol, respectively, with respect to the monomeric CuH). The results indicate some favorable dispersion interaction[17] between *t*Bu substituents of ligand and substrate, including a C-H/C-F interaction with $SCF_3$ group. However, since both activation barriers are relatively small, the possibility that *t*Bu substituent promotes other steps, such as the generation of active CuH species, cannot be excluded. The author also calculated the relative Gibbs free energies of each intermediate and transition state, giving (*S*)- or (*R*)-enantiomer, respectively, in the asymmetric hydroboration of 1-trifluoromethylthioalkene **1o** with the (*R*)-DTBM-SEGPHOS ligand (Scheme 3.5A). The dimeric CuH species is generally thermodynamically stable than monomeric CuH **6**,[17d,18] expecting that the reaction was initiated by the coordination of substrate **1o** to the active **6** in equilibrium. Actually, a clear linear effect of enantiomer excess (ee) between ligand and product was observed, supporting the identification of monomeric CuH as the real active species. The relative Gibbs energy of Cu($\eta^2$-alkene) complex **7** was +3.1 kcal/mol with respect to **6**, and it is more favorable than the other possible Cu complex **7'**, in which the $SCF_3$ group of **1o** coordinates to the Cu center. As reported by Hartwig and co-workers in their computational study of the copper-catalyzed hydroboration of simple olefin substrates, the boration step is stereospecific with retention of configuration.[18b] Therefore, the enantioselectivity of the reaction is considered to be determined in the hydrocupration of alkene moiety. In the transition state **8-TS**, the distance between Cu and C at α-position of the $SCF_3$ group was 2.119 Å. In contrast, the longer atomic distance (2.137 Å) was observed in **8-TS$_{minor}$** that leads to the minor enantiomer. Also, the activation energy of **8-TS** was 4.7 kcal/mol lower than **8-TS$_{minor}$**. The enantioselective hydrocupration forms α-$SCF_3$ alkylcopper intermediate **9**, which then undergoes the stereoretentive boration reaction through transition state **10-TS**. In the boration step, monomeric CuH **6** is regenerated and the desired product **11** is obtained. The stereochemistry of **11** is consistent with the absolute configuration

confirmed by X-ray analysis. The overall Gibbs energy change of the reaction is -17.4 kcal/mol, indicating an exergonic process, which is the driving force of the reaction. In addition, the effect of fluorine atom on regioselectivity was evaluated by the reaction with the corresponding SMe-alkene (Scheme 3.5B). While the hydroboration reaction of **1d** proceeded with excellent regioselectivity, the reaction with the corresponding SMe-substituted alkene **1d-SMe** under otherwise identical conditions gave an 11:1 mixture of regioisomers.[19] As shown in Scheme 3.5C, these results can also be explained by DFT calculations. The energy difference between the regioisomeric transition states **8-TS** and **8'-TS** was 10.8 kcal/mol. On the other hand, in the case of SMe-alkene **1o-SMe**, the energy difference between the corresponding transition states (**8-SMe-TS** and **8'-SMe-TS**) is smaller ($\Delta\Delta G^{\ddagger}$ = 6.5 kcal/mol). These results suggest that the high electronegativity of the fluorine atom in **1** effectively decreases the activation barrier in the α-insertion process to deliver the α-$SCF_3$ alkylboronate with high regioselectivity.




**Scheme 3.5**. Mechanistic investigations; (A) DFT calculated relative Gibbs free energy profile of the asymmetric hydroboration of $SCF_3$-substituted alkene **1o** with Cu–H catalyst at ωB97X-D/6-311+G(d,p)&SDD/SMD(THF)//ωB97X-D/6-31G(d)&LanL2DZ, (B) control experiments with corresponding SMe-substituted alkene, (C) comparison of activation free energy differences between transition states leading to regioisomers.

## Summary

In Chapter 3, the author has developed a Cu-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes. Appropriate chiral copper catalysts can successfully construct the *gem*-Bpin- and $SCF_3$-substituted chiral carbon center. Several stereospecific transformations of Bpin moiety in the product demonstrate the high synthetic potential that successfully expands the chemical space of chiral $SCF_3$-containing molecules. Furthermore, the author investigated the regioselectivity and enantioselectivity of the reaction by using theoretical calculation analysis and obtained some important findings that $SCF_3$ successfully controls the regioselectivity.

## Experimental Section

### Instrumentation and Chemicals

$^1H$, $^{13}C\{^1H\}$, $^{19}F\{^1H\}$, and $^{11}B$ NMR spectra were recorded at 400 MHz, 100 MHz, 376 MHz, and 128 Hz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by APCI or EI using TOF or a magnetic sector, respectively. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakosil C-200, Wako Pure Chemical Co.) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-20AR (pump, SHIMADZU, 7.5 mL/min $CHCl_3$ or ethyl acetate) and SPD-20A (UV detector, SHIMADZU, 254 nm) or by LC-20AR (pump, SHIMADZU, 7.5 mL/min $CHCl_3$ or ethyl acetate) and RID-20A (refractive index detector, SHIMADZU) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC). The crystal measurement was performed with XatLAB Synergy-S/Cu (Rigaku). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Anhydrous THF was available from Kanto Chemical Co. and used out of the bottle. $Cu(OAc)_2$ and (*R*)-DTBM-SEGPHOS were purchased from FUJIFILM Wako Pure Chemical Co. and TCI, respectively. CsOAc was obtained from TCI but should be crushed to pieces with a mortar and a pestle in a glovebox filled with nitrogen and then dried at 100 ˚C under high vacuum overnight. H–Bpin was purchased from TCI and stocked in a glovebox (note: The freshness of H–Bpin was essential for reproducibility.). *t*Bu-dppbz was prepared from 1,2-bis(dichlorophosphino)benzene and corresponding aryl Grignard reagent.[20]

$SCF_3$-substituted alkenes **1a**–**n**[21] were prepared according to the reported methods. Unless otherwise noted, all reactions were performed under nitrogen atmosphere.

**Experimental Procedures**

**General procedure for the copper-catalyzed regioselective hydroboration of $SCF_3$-substituted alkenes (0.20 mmol scale)**

Synthesis of **2a** (Table 3.1, entry 5) is representative. $Cu(OAc)_2$ (3.6 mg, 0.020 mmol) and *t*Bu-dppbz (18 mg, 0.020 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (0.30 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. H–Bpin (101 μL, 0.70 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 5 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 47 mg, 0.20 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (ethyl acetate) to give 4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**, 69 mg, 0.19 mmol, 96%).

**Copper-catalyzed regioselective hydroboration of $SCF_3$-substituted alkene 1a (Scheme 3.3; 1.0 mmol scale)**

$Cu(OAc)_2$ (18 mg, 0.10 mmol) and *t*Bu-dppbz (90 mg, 0.10 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (1.5 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. H–Bpin (0.50 mL, 3.5 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 5 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 232 mg, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (ethyl acetate) to give 4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**, 313 mg, 0.87 mmol, 86%).

**Copper-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes followed by Fe-catalyzed ligand exchange with 1,8-diaminonaphthalene**

Synthesis of **2a** (Scheme 3.3; 0.20 mmol scale) is representative. $Cu(OAc)_2$ (3.6 mg, 0.020 mmol) and (*R*)-DTBM-SEGPHOS (24 mg, 0.020 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (0.30 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. H–Bpin (101 μL, 0.70 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 5 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 47 mg, 0.20 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting mixture was directly filtered through a short pad of silica gel, and the filtrate was evaporated in vacuo. The residue was used for the next step without purification.

Imidazole (41 mg, 0.60 mmol) and 1,8-diaminonaphthalene (48 mg, 0.30 mmol) were placed in another 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. A solution of $FeCl_3$ (8.1 mg, 0.050 mmol) in $H_2O$ (0.20 mL) and MeCN (0.80 mL) solution of the crude hydroborated product obtained above were sequentially added to the tube. The solution was stirred at ambient temperature for 12 h. The resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layer was dried over sodium sulfate. The filtrate was evaporated in vacuo and purified by silica gel column chromatography with hexane/ethyl acetate (10/1, v/v) to give 2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (**2a-Bdan**, 71 mg, 0.18 mmol, 90%). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 17.9 min, minor isomer: $t_R$ = 19.8 min, UV detection at 254 nm, 30 °C).

**Copper-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkene 1a (1.0 mmol scale)**

$Cu(OAc)_2$ (18 mg, 0.10 mmol) and (*R*)-DTBM-SEGPHOS (118 mg, 0.10 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (1.5 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. H–Bpin (0.50 mL, 3.5 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 5 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 232 mg, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting

mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (ethyl acetate) to give 4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**, 343 mg, 0.95 mmol, 94%). The enantiomeric ratio was determined by HPLC analysis after derivatization of Bpin to Bdan (CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 17.9 min, minor isomer: $t_R$ = 19.8 min, UV detection at 254 nm, 30 ºC). A portion of the product was converted to **2a-Bdan** using the aforementioned method, and the enantiomeric ratio was confirmed to be 96:4.

**Furanylation of 2a (Scheme 3.4)**

A solution of furan (12 mg, 0.18 mmol) in THF (0.6 mL) was cooled to -78 °C and treated with *n*-BuLi (1.56 M hexane solution, 0.12 mL, 0.18 mmol). The cooling bath was removed, and the mixture was stirred at room temperature for 1 h. The mixture was again cooled to -78 °C, and (*S*)-4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**; 54 mg, 0.15 mmol) was added dropwise as a solution in THF (0.3 mL). The mixture was stirred at -78 °C for 1 h. A solution of NBS (32 mg, 0.18 mmol) in THF (0.6 mL) was added dropwise. After 1 h at –78 °C, the reaction was quenched with saturated aqueous sodium thiosulfate. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane to give (*R*)-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)furan (**3**; 29 mg, 0.10 mmol, 65%, 96:4 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 31.2 min, minor isomer: $t_R$ = 21.5 min, UV detection at 254 nm, 30 ºC).

**Vinylation of 2a (Scheme 3.4)**

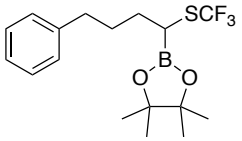
To a solution of (*S*)-4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**; 54 mg, 0.15 mmol) in THF (1.5 mL) at room temperature was added vinylmagnesium bromide (1.0 M in THF, 0.60 mmol) dropwise. The resulting mixture was stirred at room temperature for 30 min and cooled down to -78 °C. A solution of iodine (152 mg, 0.60 mmol) in MeOH (2.0 mL) was added dropwise to the reaction mixture. The reaction mixture was then allowed to warm to room temperature and stirred

for an additional 18 h. The reaction was quenched with saturated aqueous sodium thiosulfate. Extraction was repeated a total of 3 times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane to give (*R*)-(6-phenylhex-1-en-3-yl)(trifluoromethyl)sulfane (**4**; 34 mg, 0.13 mmol, 87%, 96:4 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 10.8 min, minor isomer: $t_R$ = 9.8 min, UV detection at 254 nm, 30 °C).

**Homologation of 3aa (Scheme 3.4)**

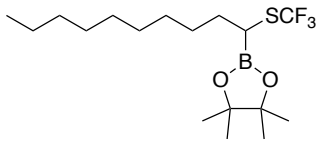
To a solution of (*S*)-4,4,5,5-tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (**2a**; 54 mg, 0.15 mmol) and bromochloromethane (39 mg, 0.30 mmol) in THF (1.5 mL) at -78 °C was added *n*-BuLi (1.56 M hexane solution, 0.16 mL, 0.25 mmol), and the solution was stirred at the same temperature for 30 min. The mixture was allowed to warm to room temperature over 30 min and then heated at 60 °C for additional 3 h. The resulting mixture was quenched with saturated aq. $NH_4Cl$ and extracted with ethyl acetate. The combined organic layer was dried over $Na_2SO_4$, and the solvent was removed under reduced pressure to give (*S*)-4,4,5,5-tetramethyl-2-(5-phenyl-2-((trifluoromethyl)thio)pentyl)-1,3,2-dioxaborolane (**5**; 46 mg, 0.12 mmol, 83%, 96:4 er) in an analytically pure form.

**Characterization Data of Products**

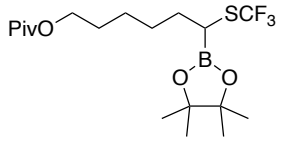



**4,4,5,5-Tetramethyl-2-(4-phenyl-1-((trifluoromethyl)thio)butyl)-1,3,2-dioxaborolane (2a):** Purified by GPC (ethyl acetate): 69 mg (96%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 2.74 (t, *J* = 6.6 Hz, 1H), 2.64 (t, *J* = 7.3 Hz, 2H), 1.85-1.76 (m, 3H), 1.74-1.64 (m, 1H), 1.26 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 141.9, 131.3 (q, *J* = 305.1 Hz), 128.4 (4C), 125.8, 84.5 (2C), 35.5, 31.1, 29.8, 26.4 (the boron-bound carbon, very weak), 24.6 (4C); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -40.17; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.78; HRMS

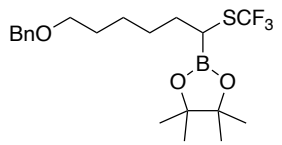
(APCI) m/z ([M+H]$^+$) calcd for $C_{17}H_{25}BF_3O_2S$: 361.1618, found: 361.1600.



**4,4,5,5-Tetramethyl-2-(1-((trifluoromethyl)thio)decyl)-1,3,2-dioxaborolane (2b):** Purified by GPC (ethyl acetate): 52 mg (70%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 2.71 (t, $J$ = 7.2 Hz, 1H), 1.76 (dt, $J$ = 7.6, 7.2 Hz, 2H), 1.46-1.35 (m, 2H), 1.31-1.26 (m, 12H), 1.28 (s, 12H), 0.88 (t, $J$ = 6.7 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 131.3 (q, $J$ = 305.0 Hz), 84.4 (2C), 31.9, 31.4, 29.5, 29.4, 29.29, 29.27, 28.1, 26.8 (the boron-bound carbon, very weak), 24.63 (2C), 24.60 (2C), 22.7, 14.1; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -40.19; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.68; HRMS (EI) m/z ([M]$^+$) calcd for $C_{17}H_{32}BF_3O_2S$: 368.2172, found: 368.2162.

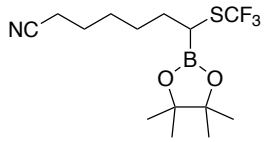


**6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-6-((trifluoromethyl)thio)hexyl pivalate (2c):** Purified by GPC (ethyl acetate): 63 mg (76%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.04 (t, $J$ = 6.6 Hz, 2H), 2.71 (t, $J$ = 7.1 Hz, 1H), 1.78 (dt, $J$ = 7.4, 6.6 Hz, 2H), 1.67-1.59 (m, 2H), 1.52-1.33 (m, 4H), 1.27 (s, 12H), 1.19 (s, 9H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 178.6, 131.3 (q, $J$ = 305.1 Hz), 84.5 (2C), 64.1, 38.7, 31.3, 28.4, 27.7, 27.2 (3C), 26.6 (the boron-bound carbon, very weak), 25.6, 24.62 (2C), 24.60 (2C); $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -40.16; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.71; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{18}H_{33}BF_3O_4S$: 413.2142, found: 413.2151.

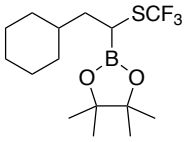


**2-(6-(Benzyloxy)-1-((trifluoromethyl)thio)hexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2d):** Purified by GPC (ethyl acetate): 71 mg (85%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H), 7.30-7.26 (m, 1H), 4.50

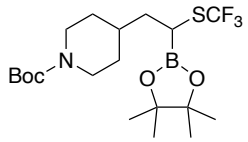
(s, 2H), 3.46 (t, $J$ = 6.5 Hz, 2H), 2.70 (t, $J$ = 7.1 Hz, 1H), 1.78 (dt, $J$ = 7.1, 6.9 Hz, 2H), 1.66-1.57 (m, 2H), 1.49-1.36 (m, 4H), 1.26 (s, 12H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 138.6, 131.3 (q, $J$ = 305.1 Hz), 128.4 (2C), 127.6 (2C), 127.5, 84.5 (2C), 72.9, 70.3, 31.4, 29.6, 28.0, 26.5 (the boron-bound carbon, very weak), 25.9, 24.63 (2C), 24.61 (2C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -40.16; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.66; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{31}BF_3O_3S$: 419.2037, found: 419.2033.



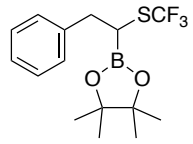

**7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-7-((trifluoromethyl)thio)heptanenitrile (2e):** Purified by GPC (ethyl acetate): 48 mg (72%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 2.72 (t, $J$ = 6.9 Hz, 1H), 2.35 (t, $J$ = 7.1 Hz, 2H), 1.82-1.76 (m, 2H), 1.71-1.64 (m, 2H), 1.53-1.39 (m, 4H), 1.27 (s, 12H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 131.3 (q, $J$ = 305.0 Hz), 119.6, 84.6 (2C), 31.0, 28.3, 27.1, 26.7 (the boron-bound carbon, very weak), 25.1, 24.62 (2C), 24.61 (2C), 17.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -40.15; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.80; HRMS (EI) m/z ($[M]^+$) calcd for $C_{14}H_{23}BF_3NO_2S$: 337.1497, found: 337.1486.



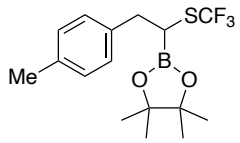

**2-(2-Cyclohexyl-1-((trifluoromethyl)thio)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2f):** Purified by GPC (ethyl acetate): 51 mg (76%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 2.73 (dd, $J$ = 9.0, 7.2 Hz, 1H), 1.74-1.58 (m, 7H), 1.45-1.33 (m, 1H), 1.27 (s, 12H), 1.25-1.11 (m, 3H), 0.95-0.84 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 131.3 (q, $J$ = 305.0 Hz), 84.3 (2C), 38.8, 36.5, 33.1, 32.7, 26.4, 26.2, 26.1, 24.6 (2C), 24.5 (2C) (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -40.12; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.90; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{27}BF_3O_2S$: 339.1774, found: 339.1770.



***tert*-Butyl 4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-((trifluoromethyl)thio)ethyl)piperidine-1-carboxylate (2g):** Purified by GPC (ethyl acetate): 76 mg (86%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.08 (br, 2H), 2.73-2.64 (m, 3H), 1.77-1.64 (m, 4H), 1.62-1.54 (m, 1H), 1.45 (s, 9H), 1.27 (s, 12H), 1.17-1.04 (m, 2H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 154.8, 131.2 (q, $J$ = 305.1 Hz), 84.5 (2C), 79.3, 43.7 (2C), 37.8, 34.7, 31.8, 31.6, 28.4 (3C), 24.62 (2C), 24.56 (2C), 23.8 (the boron-bound carbon, very weak); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -40.06; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.48; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{19}H_{34}BF_3NO_4S$: 440.2252, found: 440.2249.

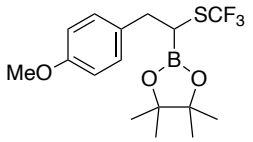


**4,4,5,5-Tetramethyl-2-(2-phenyl-1-((trifluoromethyl)thio)ethyl)-1,3,2-dioxaborolane (2h):** Purified by GPC (ethyl acetate): 48 mg (73%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.19 (m, 5H), 3.15 (dd, $J$ = 13.1, 5.7 Hz, 1H), 3.03 (dd, $J$ = 13.1, 9.8 Hz, 1H), 2.96 (dd, $J$ = 9.8, 5.7 Hz, 1H), 1.16 (s, 6H), 1.13 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 138.9, 131.3 (q, $J$ = 305.5 Hz), 129.1 (2C), 128.4 (2C), 126.8, 84.5 (2C), 38.0, 27.2 (the boron-bound carbon, very weak), 24.6 (2C), 24.5 (2C); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -40.07; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.50; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{15}H_{20}BF_3O_2S$: 332.1232, found: 332.1226.

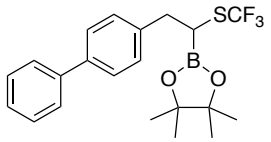


**4,4,5,5-Tetramethyl-2-(2-(*p*-tolyl)-1-((trifluoromethyl)thio)ethyl)-1,3,2-dioxaborolane (2i):** Purified by GPC (ethyl acetate): 54 mg (79%, 0.20 mmol scale); Pale yellow oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, $J$ = 8.1 Hz, 2H), 7.08 (d, $J$ = 8.1 Hz, 2H), 3.10 (dd, $J$ = 13.2, 5.9 Hz, 1H), 3.00 (dd, $J$ = 13.2, 9.7 Hz, 1H), 2.93 (dd, $J$ = 9.7, 5.9 Hz, 1H), 2.31 (s, 3H), 1.18 (s, 6H), 1.15 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz,

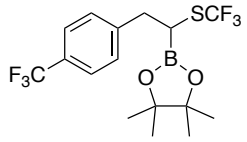
$CDCl_3$) δ 136.3, 135.8, 131.3 (q, $J$ = 305.4 Hz), 129.05 (2C), 129.00 (2C), 84.5 (2C), 37.5, 27.7 (the boron-bound carbon, very weak), 24.6 (2C), 24.5 (2C), 21.1; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -40.02; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.54; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{23}BF_3O_2S$: 347.1461, found: 347.1462.



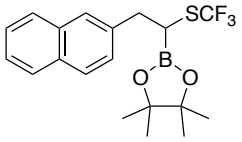

**2-(2-(4-Methoxyphenyl)-1-((trifluoromethyl)thio)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2j):** Purified by GPC (ethyl acetate): 59 mg (82%, 0.20 mmol scale); White solid; m.p. 48.5-49.2 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.18-7.14 (m, 2H), 6.84-6.80 (m, 2H), 3.78 (s, 3H), 3.09 (dd, $J$ = 12.7, 5.2 Hz, 1H), 2.98 (dd, $J$ = 12.7, 9.7 Hz, 1H), 2.92 (dd, $J$ = 9.7, 5.2 Hz, 1H), 1.18 (s, 6H), 1.15 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 131.3 (q, $J$ = 305.2 Hz), 131.0, 130.2 (2C), 113.7 (2C), 84.5 (2C), 55.3, 37.0, 27.8 (the boron-bound carbon, very weak), 24.60 (2C), 24.57 (2C); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -40.02; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.11; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{23}BF_3O_3S$: 363.1410, found: 363.1406.



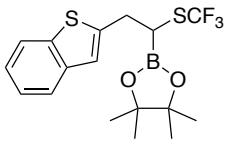

**2-(2-([1,1'-Biphenyl]-4-yl)-1-((trifluoromethyl)thio)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2k):** Purified by GPC (ethyl acetate): 75 mg (92%, 0.20 mmol scale); White solid; m.p. 102.7-103.1 °C (decomposed); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.58-7.55 (m, 2H), 7.54-7.51 (m, 2H), 7.45-7.41 (m, 2H), 7.36-7.31 (m, 3H), 3.20 (dd, $J$ = 13.2, 5.8 Hz, 1H), 3.08 (dd, $J$ = 13.2, 9.8 Hz, 1H), 3.00 (dd, $J$ = 9.8, 5.8 Hz, 1H), 1.18 (s, 6H), 1.14 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.9, 139.7, 138.0, 131.3 (q, $J$ = 305.5 Hz), 129.6 (2C), 128.8 (2C), 127.2, 127.1 (2C), 127.0 (2C), 84.6 (2C), 37.6, 27.4 (the boron-bound carbon, very weak), 24.61 (2C), 24.56 (2C); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -40.02; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 31.28; HRMS (APCI) m/z ($[M]^+$) calcd for $C_{21}H_{24}BF_3O_2S$: 408.1540, found: 408.1542.



**4,4,5,5-Tetramethyl-2-(2-(4-(trifluoromethyl)phenyl)-1-((trifluoromethyl)thio)ethyl)-1,3,2-dioxaborolane (2l):** Purified by GPC (ethyl acetate): 44 mg (55%, 0.20 mmol scale); Pale yellow solid; m.p. 45.1-46.2 ℃; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 3.20 (dd, *J* = 13.8, 6.3 Hz, 1H), 3.11 (dd, *J* = 13.8, 9.3 Hz, 1H), 2.96 (dd, *J* = 9.3, 6.3 Hz, 1H), 1.17 (s, 6H), 1.15 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 143.0, 131.2 (q, *J* = 306.0 Hz), 129.6 (2C), 129.2 (q, *J* = 32.3 Hz), 125.3 (q, *J* = 3.7 Hz, 2C), 124.2 (q, *J* = 270.0 Hz), 84.7 (2C), 37.7, 27.3 (the boron-bound carbon, very weak), 24.5 (4C); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -40.05, -62.48; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.92; HRMS (EI) m/z ($[M]^+$) calcd for $C_{16}H_{19}BF_6O_2S$: 400.1106, found: 400.1094.

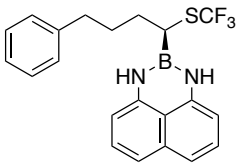


**4,4,5,5-Tetramethyl-2-(2-(naphthalen-2-yl)-1-((trifluoromethyl)thio)ethyl)-1,3,2-dioxaborolane (2m):** Purified by GPC (ethyl acetate): 62 mg (81%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.81-7.76 (m, 3H), 7.69 (s, 1H), 7.48-7.41 (m, 2H), 7.37 (dd, *J* = 8.4, 1.7 Hz, 1H), 3.31 (dd, *J* = 13.6, 6.0 Hz, 1H), 3.22 (dd, *J* = 13.6, 9.8 Hz, 1H), 3.06 (dd, *J* = 9.8, 6.0 Hz, 1H), 1.14 (s, 6H), 1.10 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 136.5, 133.4, 132.4, 131.3 (q, *J* = 305.3 Hz), 128.1, 127.7 (2C), 127.54, 127.47, 126.1, 125.6, 84.5 (2C), 38.1, 27.5 (the boron-bound carbon, very weak), 24.6 (2C), 24.5 (2C); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -40.00; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 31.55; HRMS (APCI) m/z ($[M]^+$) calcd for $C_{19}H_{22}BF_3O_2S$: 382.1384, found: 382.1387.

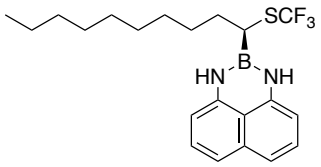


**2-(2-(Benzo[*b*]thiophen-2-yl)-1-((trifluoromethyl)thio)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2n):** Purified by GPC (ethyl acetate): 54 mg (69%, 0.20 mmol scale); Pale yellow oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.68

(dd, $J$ = 7.4, 1.4 Hz, 1H), 7.31 (ddd, $J$ = 7.4, 7.2, 1.2 Hz, 1H), 7.27 (ddd, $J$ = 7.8, 7.2, 1.4 Hz, 1H), 7.11 (d, $J$ = 0.6 Hz, 1H), 3.42 (dd, $J$ = 15.0, 6.7 Hz, 1H), 3.38 (dd, $J$ = 15.0, 8.0 Hz, 1H), 3.07 (dd, $J$ = 8.0, 6.7 Hz, 1H), 1.19 (s, 6H), 1.18 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.1, 139.7, 139.6, 131.2 (q, $J$ = 305.7 Hz), 124.2, 123.9, 123.0, 122.8, 122.2, 84.8 (2C), 33.0, 24.64 (2C), 24.56 (2C) (The carbon signal bound to boron was not observed due to quadrupolar relaxation.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -40.00; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 32.13; HRMS (APCI) m/z ($[M]^+$) calcd for $C_{17}H_{20}BF_3O_2S_2$: 388.0948, found: 388.0961.

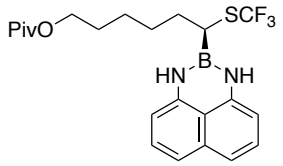



**(*S*)-2-(4-Phenyl-1-((trifluoromethyl)thio)butyl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (2a-Bdan):** Purified by silica gel column chromatography with hexane/ethyl acetate (10/1, v/v): 71 mg (90%, 0.20 mmol scale); Pale yellow oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.24-7.21 (m, 1H), 7.20-7.16 (m, 2H), 7.12-7.08 (m, 2H), 7.05-7.03 (m, 2H), 6.29 (dd, $J$ = 7.1, 0.9 Hz, 2H), 5.61 (br, 2H), 2.78-2.75 (m, 1H), 2.72-2.62 (m, 2H), 1.85-1.77 (m, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.6, 140.2 (2C), 136.2, 131.2 (q, $J$ = 305.5 Hz), 128.6 (2C), 128.5 (2C), 127.6 (2C), 126.1, 119.8, 118.4 (2C), 106.4 (2C), 35.5, 31.2, 30.3 (the boron-bound carbon, very weak), 29.8; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -40.03; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 29.74; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{21}BF_3N_2S$: 401.1469, found: 401.1469. CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 17.9 min, minor isomer: $t_R$ = 19.8 min.

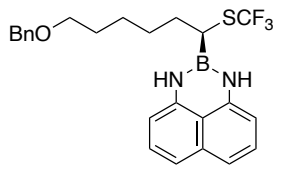



**(*S*)-2-(1-((Trifluoromethyl)thio)decyl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (2b-Bdan):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 65 mg (80%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR

(400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.05 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.36 (dd, *J* = 7.2, 1.0 Hz, 2H), 5.73 (br, 2H), 2.76 (t, *J* = 7.3 Hz, 1H), 1.82-1.77 (m, 2H), 1.49-1.42 (m, 2H), 1.36-1.29 (m, 4H), 1.27-1.23 (m, 8H), 0.87 (t, *J* = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.3 (2C), 136.2, 131.2 (q, *J* = 305.3 Hz), 127.6 (2C), 119.8, 118.3 (2C), 106.3 (2C), 32.1, 31.9, 30.5 (the boron-bound carbon, very weak), 29.5, 29.44, 29.41, 29.3, 28.3, 22.7, 14.1; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -39.98; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 30.24; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{21}H_{29}BF_3N_2S$: 409.2095, found: 409.2096. CHIRALCEL OD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 28.7 min, minor isomer: $t_R$ = 34.4 min.

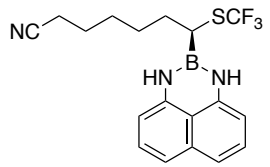



**(*S*)-6-(1*H*-Naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-6-((trifluoromethyl)thio)hexyl pivalate (2c-Bdan):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 87 mg (96%, 0.20 mmol scale); Pale red oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.06 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.37 (dd, *J* = 7.2, 1.0 Hz, 2H), 5.79 (br, 2H), 4.06 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 7.2 Hz, 1H), 1.85-1.79 (m, 2H), 1.68-1.61 (m, 2H), 1.55-1.47 (m, 2H), 1.44-1.38 (m, 2H), 1.19 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.7, 140.2 (2C), 136.2, 131.1 (q, *J* = 305.4 Hz), 127.6 (2C), 119.8, 118.3 (2C), 106.3 (2C), 64.0, 38.8, 32.0, 30.4 (the boron-bound carbon, very weak), 28.4, 27.8, 27.2 (3C), 25.7; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -40.00; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 30.03; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{29}BF_3N_2O_2S$: 453.1993, found: 453.1987. CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 19.1 min, minor isomer: $t_R$ = 17.8 min.

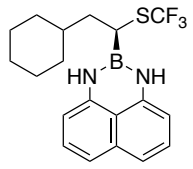



**(*S*)-2-(6-(Benzyloxy)-1-((trifluoromethyl)thio)hexyl)-2,3-dihydro-1*H*-naphtho[1,8-**

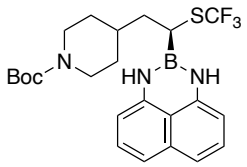
***de*][1,3,2]diazaborinine (2d-Bdan):** Purified by GPC (ethyl acetate): 59 mg (65%, 0.20 mmol scale); Pale red oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.30 (m, 4H), 7.28-7.27 (m, 1H), 7.12 (dd, *J* = 8.2, 7.3 Hz, 2H), 7.05 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.35 (dd, *J* = 7.3, 1.0 Hz, 2H), 5.73 (br, 2H), 4.49 (s, 2H), 3.46 (t, *J* = 6.4 Hz, 2H), 2.76 (t, *J* = 7.2 Hz, 1H), 1.81 (dt, *J* = 7.6, 6.8 Hz, 2H), 1.62 (tt, *J* = 7.2, 6.6 Hz, 2H), 1.52-1.39 (m, 4H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 140.23, 138.6, 136.2, 131.1 (q, *J* = 305.3 Hz), 128.4 (2C), 127.7 (2C), 127.6 (4C), 119.8, 118.3 (2C), 106.3 (2C), 72.9, 70.1, 32.0, 30.3 (the boron-bound carbon, very weak), 29.5, 28.1, 26.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.96; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 29.97; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{24}H_{27}BF_3N_2OS$: 459.1888, found: 459.1883. CHIRALCEL OJ-H column, 85/15 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 29.1 min, minor isomer: $t_R$ = 36.1 min.



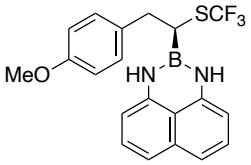

**(*S*)-7-(1*H*-Naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-7-((trifluoromethyl)thio)heptanenitrile (2e-Bdan):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) and GPC (ethyl acetate): 51 mg (68%, 0.20 mmol scale); Pale red oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.06 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.38 (dd, *J* = 7.2, 1.0 Hz, 2H), 5.75 (br, 2H), 2.78 (t, *J* = 7.2 Hz, 1H), 2.36 (t, *J* = 7.0 Hz, 2H), 1.87-1.81 (m, 2H), 1.71-1.65 (m, 2H), 1.54-1.50 (m, 4H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 140.1 (2C), 136.2, 131.0 (q, *J* = 305.6 Hz), 127.6 (2C), 119.8, 119.6, 118.4 (2C), 106.4 (2C), 31.8, 30.2 (the boron-bound carbon, very weak), 28.4, 27.4, 25.1, 17.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.95; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 30.66; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{18}H_{20}BF_3N_3S$: 378.1421, found: 378.1415. CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 39.7 min, minor isomer: $t_R$ = 38.0 min.



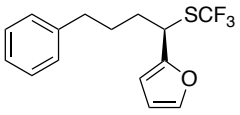
**(*S*)-2-(2-cyclohexyl-1-((trifluoromethyl)thio)ethyl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (2f-Bdan):** Purified by silica gel column chromatography with hexane and GPC (ethyl acetate): 37 mg (50%, 0.20 mmol scale); White solid; m.p. 65.1-67.2 ℃; $[\alpha]_D^{20}$ = +53.0 (c = 0.30, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 8.2, 7.3 Hz, 2H), 7.06 (dd, *J* = 8.2, 1.0 Hz, 2H), 6.37 (dd, *J* = 7.3, 1.0 Hz, 2H), 5.73 (br, 2H), 2.82 (t, *J* = 8.0 Hz, 1H), 1.78-1.62 (m, 7H), 1.53-1.43 (m, 1H), 1.28-1.09 (m, 3H), 1.00-0.87 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.3 (2C), 136.2, 131.1 (q, *J* = 305.5 Hz), 127.6 (2C), 119.8, 118.3 (2C), 106.3 (2C), 39.5, 36.1, 33.2, 33.1, 27.9 (the boron-bound carbon, very weak), 26.4, 26.1, 26.0; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -39.85; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 29.96; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{19}H_{23}BF_3N_2S$: 379.1625, found: 379.1604. CHIRALCEL OD-H column, 94/6 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 32.9 min, minor isomer: $t_R$ = 46.5 min.



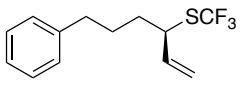

***tert*-Butyl (*S*)-4-(2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-2-((trifluoromethyl)thio)ethyl)piperidine-1-carboxylate (2g-Bdan):** Purified by GPC (ethyl acetate): 40 mg (42%, 0.20 mmol scale); White solid; m.p. 182.6-184.0 ℃; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.07 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.37 (dd, *J* = 7.2, 1.0 Hz, 2H), 5.74 (br, 2H), 4.10 (br, 2H), 2.80 (t, *J* = 7.5 Hz, 1H), 2.69 (t, *J* = 10.7 Hz, 2H), 1.76-1.66 (m, 5H), 1.45 (s, 9H), 1.21-1.08 (m, 2H), ; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.8, 140.2 (2C), 136.2, 131.0 (q, *J* = 305.6 Hz), 127.6 (2C), 120.0, 118.4 (2C), 106.4 (2C), 79.5, 43.5 (br, 2C), 38.6, 34.4, 32.1, 31.7, 28.5 (3C), 27.5 (the boron-bound carbon, very weak); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -39.81; $^{11}B$ NMR (128 MHz, $CDCl_3$) δ 30.82; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{30}BF_3N_3O_2S$: 480.2102, found: 480.2103. CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 44.1 min, minor isomer: $t_R$ = 32.0 min.




**(*S*)-2-(2-(4-Methoxyphenyl)-1-((trifluoromethyl)thio)ethyl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (2j-Bdan):** Purified by GPC (ethyl acetate): 38 mg (47%, 0.20 mmol scale); Yellow oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.18-7.15 (m, 2H), 7.09 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.04 (dd, *J* = 8.3, 1.0 Hz, 2H), 6.86-6,82 (m, 2H), 6.26 (dd, *J* = 7.2, 1.0 Hz, 2H), 5.61 (br, 2H), 3.78 (s, 3H), 3.22-3.14 (m, 1H), 3.06-2.99 (m, 2H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 158.6, 140.1 (2C), 136.2, 131.1 (q, *J* = 305.8 Hz), 130.5, 130.0 (2C), 127.6 (2C), 119.8, 118.3 (2C), 114.1 (2C), 106.3 (2C), 55.3, 38.0, 31.9 (the boron-bound carbon, very weak); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.90; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 29.83; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{20}H_{19}BF_3N_2OS$: 403.1261, found: 403.1250. CHIRALPAK AD-H column, 95/5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 33.3 min, minor isomer: $t_R$ = 41.7 min.

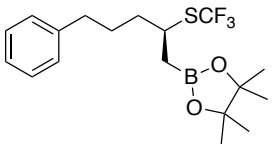



**(*R*)-2-(4-Phenyl-1-((trifluoromethyl)thio)butyl)furan (3):** Purified by silica gel column chromatography with hexane: 29 mg (65%, 0.15 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.29-7.28 (m, 2H), 7.20-7.13 (m, 3H), 6.31 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.21 (d, *J* = 3.2 Hz, 1H), 4.38 (dd, *J* = 8.8, 6.5 Hz, 1H), 2.68-2.57 (m, 2H), 2.14-2.04 (m, 1H), 2.04-1.95 (m, 1H), 1.78-1.59 (m, 2H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 152.3, 142.5, 141.5, 130.5 (q, *J* = 305.4 Hz), 128.4 (2C), 128.3 (2C), 126.0, 110.4, 107.8, 42.3 (q, *J* = 1.9 Hz), 35.2, 33.5, 28.8; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -40.14; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{15}H_{16}F_3OS$: 301.0868, found: 301.0859. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 31.2 min, minor isomer: $t_R$ = 21.5 min.




**(*R*)-(6-Phenylhex-1-en-3-yl)(trifluoromethyl)sulfane (4):** Purified by GPC

(chloroform): 34 mg (87%, 0.15 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 7.21-7.15 (m, 3H), 5.76 (ddd, *J* = 17.0, 10.1, 9.6 Hz, 1H), 5.19 (d, *J* = 17.0 Hz, 1H), 5.14 (d, *J* = 10.1 Hz, 1H), 3.80-3.74 (m, 1H), 2.68-2.59 (m, 2H), 1.78-1.64 (m, 4H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.6, 137.7, 130.5 (q, *J* = 304.9 Hz), 128.43 (2C), 128.37 (2C), 126.0, 117.1, 48.4 (q, *J* = 1.2 Hz), 35.3, 33.6, 28.6; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.93; HRMS (APCI) m/z ([M]$^{+}$) calcd for $C_{13}H_{15}F_3S$: 260.0847, found: 260.0839. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 10.8 min, minor isomer: $t_R$ = 9.8 min.




**(*S*)-4,4,5,5-Tetramethyl-2-(5-phenyl-2-((trifluoromethyl)thio)pentyl)-1,3,2-dioxaborolane (5):** Purified by GPC (chloroform): 46 mg (83%, 0.15 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.19-7.16 (m, 3H), 3.47 (tt, *J* = 7.1, 6.4 Hz, 1H), 2.62 (t, *J* = 6.7 Hz, 2H), 1.83-1.69 (m, 4H), 1.30 (d, *J* = 7.1 Hz, 2H), 1.21 (s, 6H), 1.20 (s, 6H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.9, 131.3 (q, *J* = 304.4 Hz), 128.4 (2C), 128.3 (2C), 125.8, 83.6 (2C), 43.0, 36.7, 35.5, 28.2, 24.8 (2C) 24.7 (2C), 19.4 (the boron-bound carbon, very weak); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.13; $^{11}$B NMR (128 MHz, $CDCl_3$) δ 32.61; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{18}H_{27}BF_3O_2S$: 375.1780, found: 375.1782. CHIRALCEL OD-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 12.3 min, minor isomer: $t_R$ = 11.8 min.

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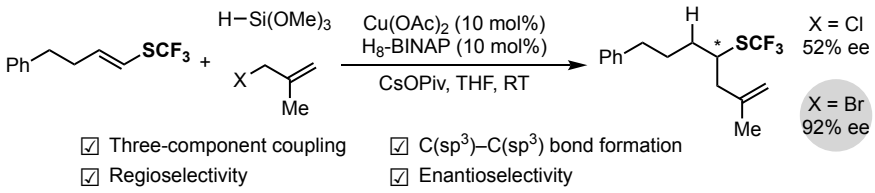
# Chapter 4

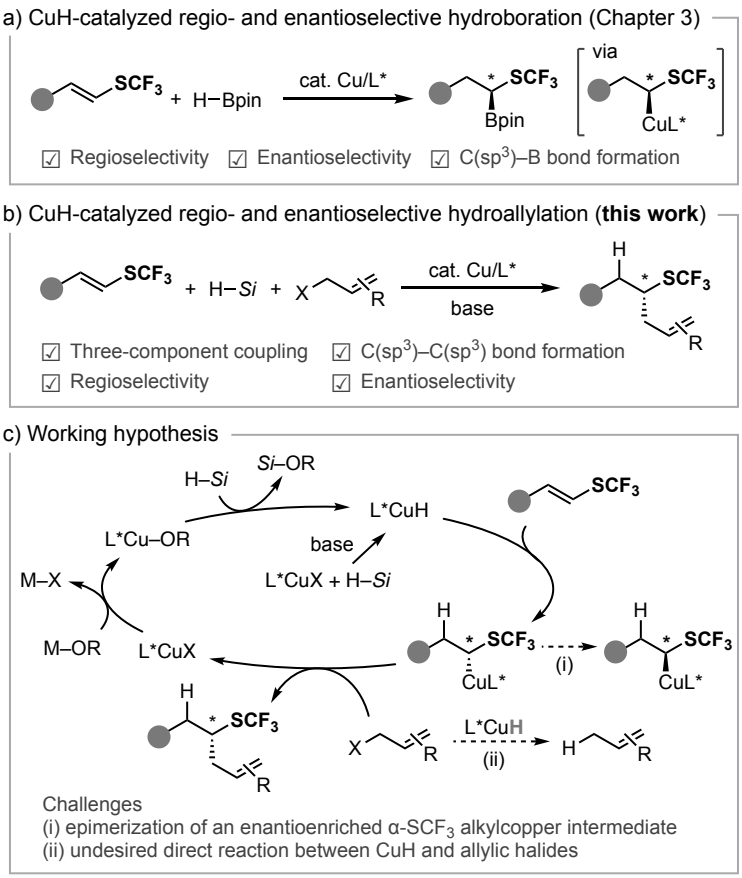
# Copper-Catalyzed Regio- and Enantioselective Hydroallylation of $SCF_3$- Substituted Alkenes: Leaving Group-Dependent Stereochemistry

A copper-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes with hydrosilanes and allylic electrophiles has been developed. The judicious choice of chiral ligands successfully promotes the enantioselective $C(sp^3)$–$C(sp^3)$ bond formation at the α-position of trifluoromethylthio ($SCF_3$) group, which is otherwise difficult to perform by other means. Experimental and computational mechanistic studies reveal that leaving groups of allylic electrophiles significantly influence the enantioselectivity as well as chemoselectivity.



## Introduction

In Chapter 3, the author has acheived the synthesis of optically active $SCF_3$-substituted alkylboronates by a copper hydride (CuH)-catalyzed regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes (Scheme 4.1a).[1] In this reaction, the high electronegativity of fluorine atoms in the $SCF_3$ group enabled the regioselective α-insertion. In addition, the suitable choice of chiral ligand gave an enantioenriched α-$SCF_3$ alkylcopper intermediate that leads to the Bpin-substituted chiral $SCF_3$ compound. The starting $SCF_3$-substituted alkenes can be easily prepared from the corresponding alkenyl halides according to the literature methods. Therefore, the CuH-based hydrofunctionalization[2] of $SCF_3$-alkenes would be a groundbreaking strategy for the synthesis of versatile optically active $SCF_3$ molecules. During continuing interest in this chemistry, the author attempted to develop a three-component coupling reaction with higher modularity: a CuH-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes with hydrosilanes and allylic electrophiles is described (Scheme 4.1b). The author's working hypothesis is shown in Scheme 4.1c. A monomeric CuH species[3] is initially generated from a copper pre-catalyst and hydrosilane and then undergoes regio- and enantioselective hydrocupration to the $SCF_3$-substituted alkene. The formed enantioenriched alkylcopper intermediate can be trapped with allylic electrophiles to produce the desired hydroallylated product. The CuH species is regenerated through successive salt metathesis/σ-bond metathesis involving the resulting CuX species, base, and hydrosilane. The related CuH-catalyzed hydroallylation reactions of electronically activated styrenes and other active alkenes have been studied,[4] but there are several challenges unique to the $SCF_3$-alkenes; (i) stereochemical lability of the α-$SCF_3$ alkylcopper intermediate: less reactive allylic electrophiles compared to the H–Bpin in Scheme 4.1a can lead to undesired epimerization (racemization) at the carbon center α to $SCF_3$; (ii) moderate reactivity of the $SCF_3$-alkene toward CuH species:[5] an undesired direct reaction between CuH and allylic electrophiles can form the simply reduced byproduct. The author reveals that the suitable choice of leaving group of allylic electrophiles prevents the epimerization to dramatically increase the enantioselectivity. Moreover, slow addition of allylic electrophiles avoids the direct reduction of allylic electrophiles, resulting in improved chemoselectivity. Detailed optimization studies, substrate scope, and experimental/computational mechanistic investigations are reported herein.



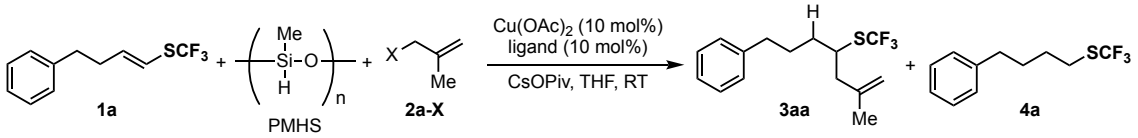

**Scheme 4.1**. CuH-catalyzed functionalizations of $SCF_3$-substituted alkenes.

## Results and discussion

The author initially performed optimization studies for the nonenantioselective hydroallylation of $SCF_3$-alkene **1a** with polymethylhydrosiloxane (PMHS) and methallyl chloride **2a-Cl** (Table 4.1). Inspired by the hydroallylation of $CF_3$-substituted alkenes (Chapter 1),[6] the author first chose a combination of $Cu(OAc)_2$ pre-catalyst and MeO-modified bis(diphenylphosphino)benzene (dppbz) ligand. In the presence of CsOPiv base, the desired hydroallylation reaction of **1a** with PMHS and **2a-Cl** in THF solvent proceeded at room temperature to afford the hydroallylated product **3aa** in 83% $^1$H NMR yield (entry 1). As expected from the author's proposal in Scheme 4.1c, the regioselectivity of the reaction was fully controlled to form $C(sp^3)$–$C(sp^3)$ bond at the α-position of $SCF_3$ group exclusively. In Chapter 3, the positive effects of substituents at the *meta* positions in dppbz ligands were observed to improve reaction efficiency probably due to some favorable dispersion interactions between ligand and substrate. However, in the hydroallylation, the use of *t*Bu- or TMS-dppbz resulted in a lower yield

of **3aa** and a higher amount of the reductive byproduct **4a** (entries 2 and 3). In control experiments, the author found that *t*Bu-dppbz accelerated the undesired direct reaction between **2a-Cl** and CuH catalysts ((ii) in Scheme 4.1c) in comparison with MeO-dppbz ligand. Thus, the use of *t*Bu-dppbz ligand rapidly consumed **2a-Cl** to interfere with the formation of **3aa** and preferentially produce **4a**. Other modified dppbz-type ligands, such as $CF_3$-, *p*-*t*Bu-, and *p*-$CF_3$-dppbzs, diminished the yield of **3aa** (entries 4-6). On the other hand, DTBM-dppbz and simple dppbz provided **3aa** in comparable yields (entries 7 and 8). Also, with $(MeO)_3SiH$ instead of PMHS, the yield of **3aa** was slightly increased (entry 9). The leaving groups of allylic electrophiles significantly influenced the chemoselectivity whether CuH reacts with **1a** or **2a-X**. When using more reactive methallyl bromide **2a-Br** instead of **2a-Cl**, the yield of **3aa** was largely dropped (entry 10), indicating that the CuH species reacted with **2a-Br** over **1a**. Indeed, the calculated LUMO levels of **1o** (model of **1a**), **2a-Cl**, and **2a-Br** suggest the much higher electrophilicity of **2a-Br** than **1o** and **2a-Cl** (Figure 4.1). In the case of methallyl phosphate **2a-OP(O)(OEt)$_2$**, the yield was slightly decreased to give **3aa** in 73% (entry 11). Since the LUMO level of **2a-OP(O)(OEt)$_2$** is higher than that of **2a-Cl** (2.36 eV, Figure 4.1), the reactivity as an allylic electrophile is simply lower. Meanwhile, methallyl alcohol and its acetate derivatives failed to deliver the desired product (entries 12 and 13). Finally, **3aa** was obtained in 93% yield by increasing the amount of **2a-Cl** to 2.5 equiv (entry 14). Additional investigations of base and solvent revealed that the combination of CsOPiv and THF was optimal.

**Table 4.1**. Optimization studies for CuH-catalyzed regioselective hydroallylation of $SCF_3$-substituted alkene **1a** with hydrosilanes and allylic electrophiles **2a-X**.[a]




| entry | ligand | -X | yield of **3aa** (%)[b] | yield of **4a** (%)[b] |
|---|---|---|---|---|
| 1 | MeO-dppbz | –Cl | 83 | 11 |
| 2 | *t*Bu-dppbz | –Cl | 23 | 58 |
| 3 | TMS-dppbz | –Cl | 22 | 67 |
| 4 | $CF_3$-dppbz | –Cl | 61 | 36 |
| 5 | *p*-*t*Bu-dppbz | –Cl | 69 | 27 |

| | | | | |
|---|---|---|---|---|
| 6 | *p*-$CF_3$-dppbz | –Cl | 26 | 35 |
| 7 | DTBM-dppbz | –Cl | 80 | 17 |
| 8 | dppbz | –Cl | 84 | 11 |
| 9[c] | MeO-dppbz | –Cl | 84 | 11 |
| 10[c] | MeO-dppbz | –Br | 46 | 17 |
| 11[c] | MeO-dppbz | –OP(O)$(OEt)_2$ | 73 | 16 |
| 12[c] | MeO-dppbz | –OH | 0 | 74 |
| 13[c] | MeO-dppbz | –OAc | 0 | 46 |
| 14[c,d] | MeO-dppbz | –Cl | 93 (83) | 7 |

[a] Conditions: **1a** (0.20 mmol), PMHS (0.60 mmol based on Si–H), **2a-X** (0.40 mmol), $Cu(OAc)_2$ (0.020 mmol), ligand (0.020 mmol), CsOPiv (0.40 mmol), THF (1.0 mL), RT, 4 h, $N_2$. [b] Estimated by $^1$H NMR. Isolated yield is given in parentheses. [c] With $(MeO)_3SiH$ instead of PMHS. [d] With **2a-Cl** (0.50 mmol).

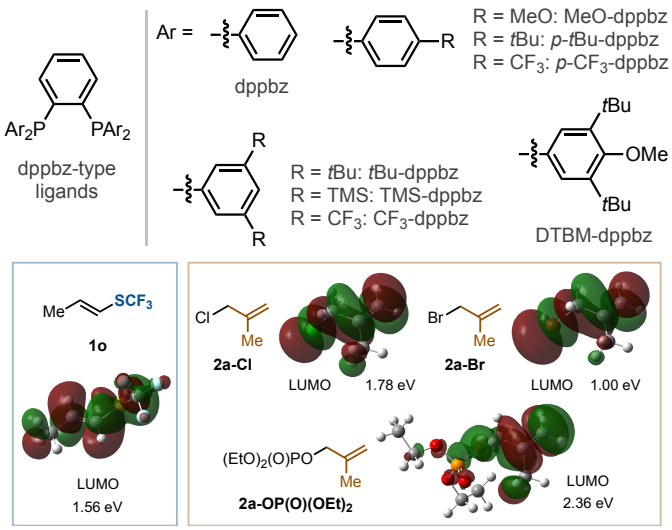
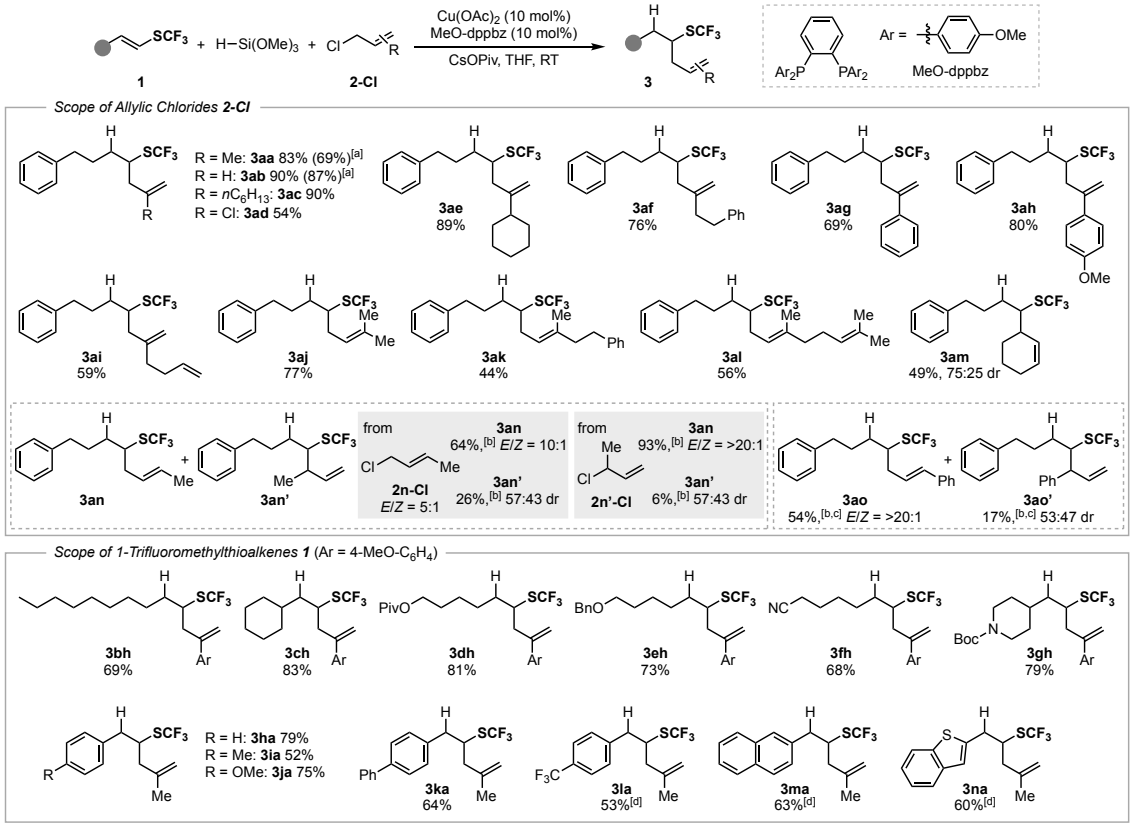



**Figure 4.1**. DFT calculated LUMO levels of **1o**, **2a-Cl**, **2a-Br**, and **2a-OP(O)$(OEt)_2$** at ωB97X-D/6-31G(d) level of theory.

After establishing the optimal reaction conditions (entry 14 in Table 4.1), the author investigated the scope of the reaction with various functionalized allylic chlorides and $SCF_3$-substituted alkenes (Scheme 4.2). In addition to **2a-Cl**, the reaction with simple allyl chloride **2b-Cl** successfully proceeded to yield the corresponding hydroallylated product **3ab** in 90% yield. In this case, MeO-dppbz showed better performance than DTBM-dppbz and dppbz. Other allylic chlorides bearing various functional groups at the 2-position, including longer alkyl (**3ac**), chloro (**3ad**), cyclohexyl (**3ae**), phenethyl (**3af**), and aryl (**3ag** and **3ah**) groups, could also be employed. Even when using allyllic chloride

with an additional terminal alkene moiety (**3ai**), which is potentially competitive in the reaction, the C($sp^3$)–C($sp^3$) bond formation occurred selectively at α-position of $SCF_3$ group and the terminal alkene was left intact. The reaction with prenyl-type electrophiles dominantly gave the corresponding linear products (**3aj-3al**). With 3-chlorocyclohexene as a coupling partner, **3am** was obtained in 49% yield with 75:25 diastereomeric ratio (dr). In the case of crotyl chloride **2n-Cl**, a mixture of regioisomers (**3an** and **3an'**) was obtained. In contrast, the reaction with its branched isomer **2n'-Cl** proceeded with relatively high regioselectivity at the γ-position of Cl, indicating that the allylation process competes at the α- and γ-positions of Cl but with the regioselectivity dependent on neighboring steric environment. Similarly, the reaction with cinnamyl chloride **2o-Cl** yielded a mixture of **3ao** and **3ao'**. On the other hand, the reaction with other functionalized $SCF_3$-alkenes was also possible. For example, the primary- and secondary-alkyl substituted $SCF_3$-alkenes were successfully coupled with **2h** to give **3bh** and **3ch** in 69% and 83%, respectively. Common functional groups, including pivalic ester (**3dh**),

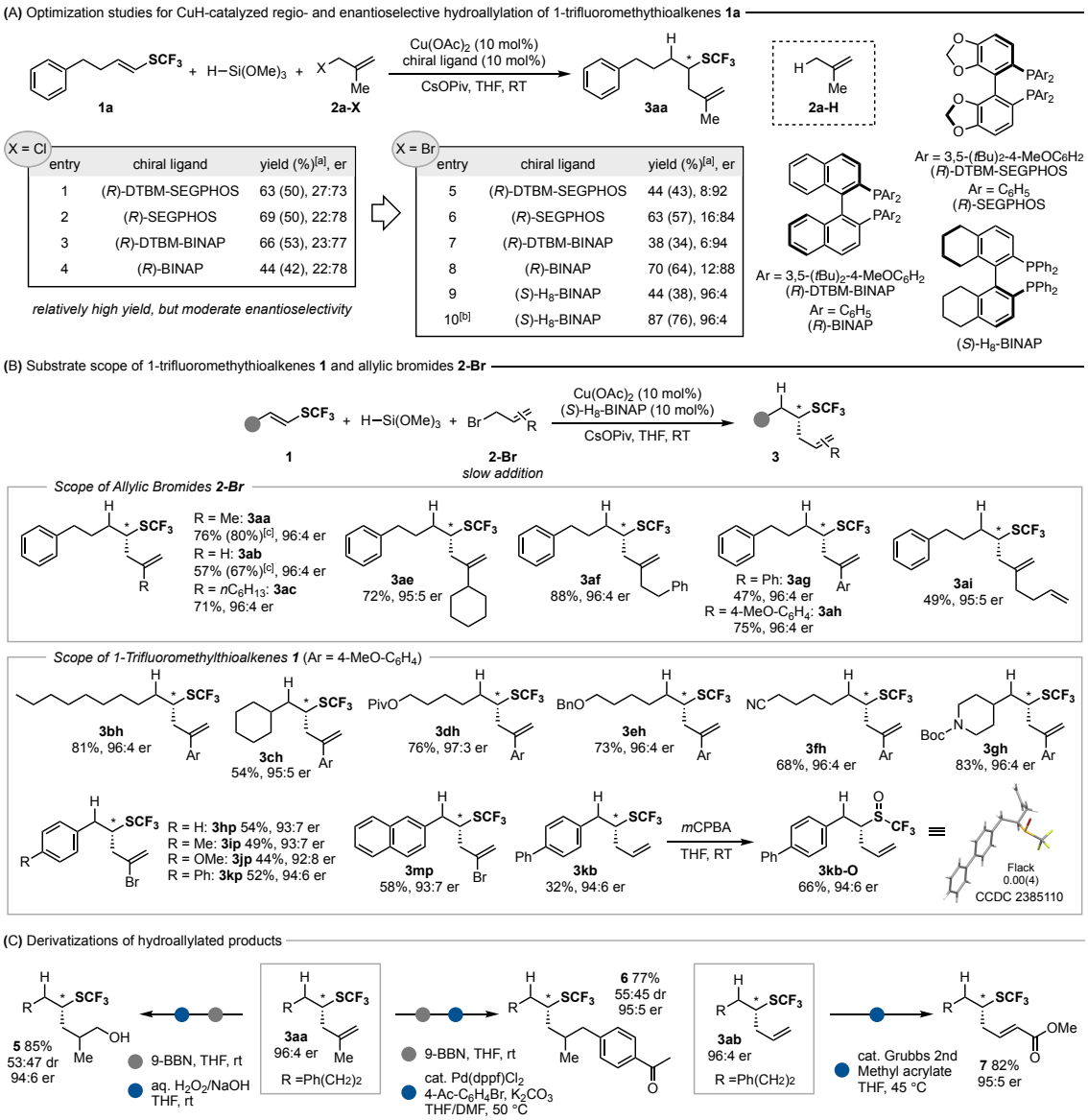



**Scheme 4.2**. Products of CuH-catalyzed regioselective hydroallylation of $SCF_3$-substituted alkenes **1** with hydrosilanes and allylic chlorides **2-Cl**. Conditions: **1** (0.20 mmol), $(MeO)_3SiH$ (0.60 mmol), **2-Cl** (0.50 mmol), $Cu(OAc)_2$ (0.020 mmol), *p*-MeO-dppbz (0.020 mmol), CsOPiv (0.40 mmol), THF (1.0 mL), RT, 4-18 h. Isolated yields are shown. [a] On a 1.0 mmol scale. [b] $^1H$ NMR yields. [c] From cinnamyl chloride **2o-Cl** (*E*/*Z* = >20:1). [d] With DTBM-dppbz instead of MeO-dppbz.

benzyl ether (**3eh**), nitrile (**3fh**), and Boc-protected amine (**3gh**) were compatible to yield the corresponding hydroallylated products. In cases of aryl-conjugated substrates with electron-neutral and -rich aromatic rings, the corresponding hydroallylated products were given with high regioselectivity (**3ha**-**3ka**). However, substrates with electron-deficient (**3la**) or condensed (**3ma** and **3na**) aromatic ring gave a mixture of regioisomers. The author found that the yield and regioselectivity with those substrates were improved by using DTBM-dppbz ligand instead of MeO-dppbz (see the Supporting Information for details). In addition, the hydroallylation reaction was scalable, and **3aa** and **3ab** were obtained in acceptable yields even on a 1.0 mmol scale, suggesting the high practicality of the CuH-based strategy.

Based on the aforementioned results, the author next explored the enantioselective conditions by suitable choice of optically active ligands (Scheme 4.3A). However, simple replacement of MeO-dppbz with chiral biphosphine ligands induced only moderate enantioselectivity: even SEGPHOS- (entries 1 and 2) or BINAP-type ligands (entries 3 and 4), which were effective for previous hydroboration reaction,[1] showed 27:73-22:78 enantiomeric ratio (er). After intensive optimization studies, the author found that switching leaving group of the allylic electrophile from chloride to bromide resulted in an improvement of enantioselectivity, albeit in lower yields (entries 5-8). Thus, the author performed further ligand screening with **2a-Br**. As a result, when using (*S*)-$H_8$-BINAP as a chiral ligand, **3aa** was obtained with 96:4 er but still in 44% yield (entry 9). Considering higher electrophilicity of **2a-Br** (Figure 4.1), the lower yield is attributed to generation of the reductive byproduct **2a-H** by the direct reaction between CuH and **2a-Br**. Therefore, the author attempted slow addition of **2a-Br** to avoid the undesired direct reaction. As a result, by adding 0.4 equivalent at 20 minutes intervals for five times, **3aa** was obtained in 87% yield with maintenance of high enantioselectivity (entry 10). In the case of **2a-OP(O)(OEt)$_2$**, poorer enantioselectivity was observed compared to **2a-Cl**.

Under optimal reaction conditions, various functionalized allylic bromides **2-Br** and $SCF_3$-substituted alkenes **1** proved to be applicable (Scheme 4.3B). Similar to nonenantioselective conditions, several allylic bromides with useful functional groups at the 2-position could be used (**3aa**-**3ac** and **3ae**-**3ai**). In addition, both alkyl- and aryl-substituted $SCF_3$-alkenes provided the corresponding hydroallylated products in good to high yields with high enantioselectivity (**3bh**-**3gh**, **3hp**-**3kp**, and **3mp**). The absolute configuration of **3kb-O** was confirmed to be *R* by the X-ray analysis after oxidation of




**Scheme 4.3**. Enantioselective hydroallylation; (A) Optimization studies for CuH-catalyzed regio- and enantioselective hydroallylation of **1a**. Conditions: **1a** (0.20 mmol), $(MeO)_3SiH$ (0.60 mmol), **2a-X** (0.50 mmol), $Cu(OAc)_2$ (0.020 mmol), chiral ligand (0.020 mmol), CsOPiv (0.40 mmol), THF (1.0 mL), RT, 4 h, $N_2$. [a] Estimated by $^1H$ NMR. Isolated yields are given in parentheses. [b] Slow addition of **2a-Br** (0.4 equiv × 5, 20 minutes intervals). (B) Products of CuH-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes **1** with hydrosilanes and allylic bromides **2-Br**. Conditions: **1** (0.20 mmol), $(MeO)_3SiH$ (0.60 mmol), **2-Br** (0.40 mmol; slow addition), $Cu(OAc)_2$ (0.020 mmol), (*S*)-$H_8$-BINAP (0.020 mmol), CsOPiv (0.40 mmol), THF (1.0 mL), RT, 4-18 h. Isolated yields are shown. [c] On a 1.0 mmol scale. (C) Derivatization of hydroallylated products **3aa** and **3ab**.

**3kb** (CCDC 2385110), and those of other compounds were assigned by analogy. Furthermore, the reaction gave **3aa** and **3ab** in 80% and 67% yields, respectively, even on a 1.0 mmol scale.

The resulting olefin moiety of the enantioenriched product could be further transformed to deliver chiral $SCF_3$-containing compounds with additional functionality

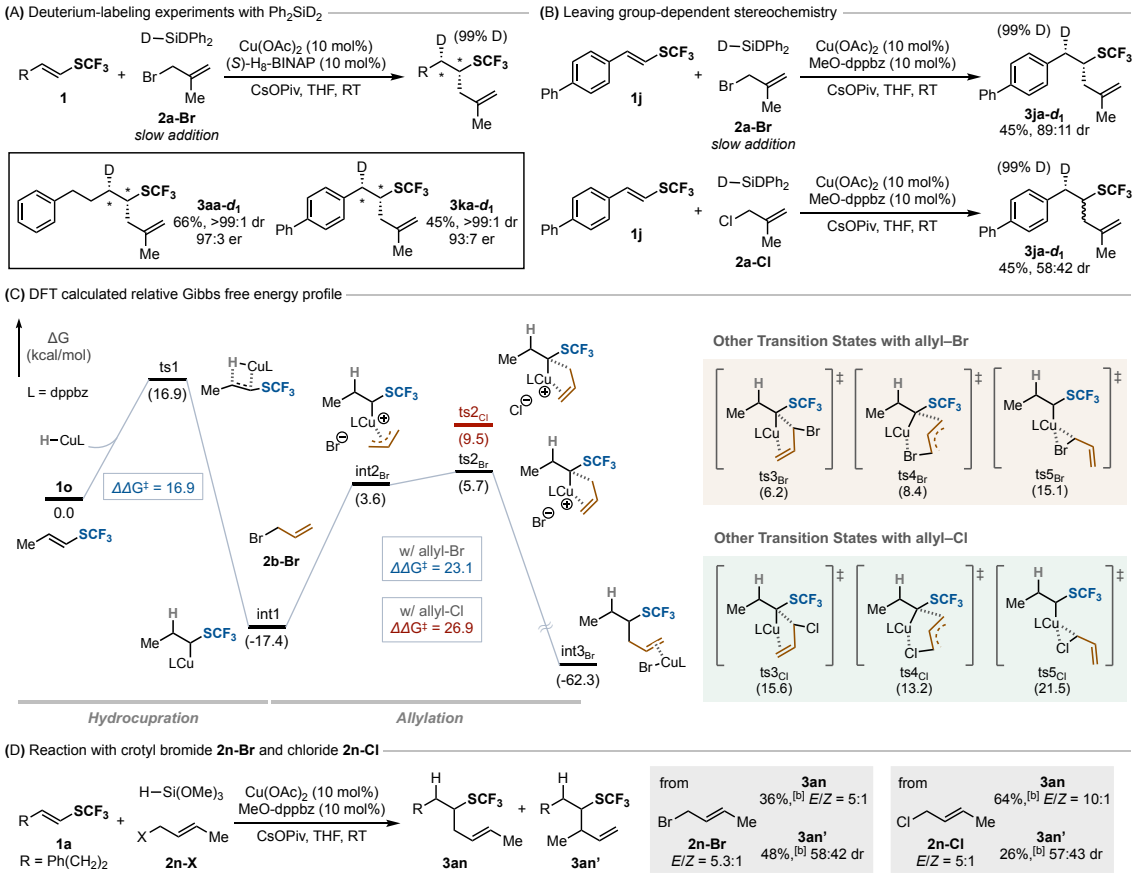
(Scheme 4.3C). A regioselective hydroboration of **3aa** with 9-BBN followed by an oxidation with $H_2O_2$ aq. yielded the $SCF_3$-containing chiral alcohol **5** in an overall 85% yield with 94:6 er. Moreover, the Suzuki-Miyaura cross-coupling of the same alkylborane intermediate with 4-bromoacetophenone effectively produced **6** in 77% without any erosion of enantiomeric ratio. Furthermore, an olefin metathesis reaction between **3ab** and methyl acrylate was also possible to afford **7** in 82% yield with 95:5 er.

The author then investigated the mechanism of hydroallylation reaction by several control experiments (Scheme 4.4). First, the author performed the deuterium-labeling experiments using $Ph_2SiD_2$ instead of $(MeO)_3SiH$ (Scheme 4.4A). Under the enantioselective conditions, the reaction of **1a** and **1j** with $Ph_2SiD_2$ efficiently gave the deuterium-labeled chiral $SCF_3$-substituted products **3aa**-$d_1$ and **3ka**-$d_1$ with 99% D. These results prove the author's hypothesis that CuH species is generated *in situ* from the copper salt and hydrosilane. Furthermore, the high *syn* diastereoselectivity of **3aa**-$d_1$ and **3ka**-$d_1$ was observed, indicating that the hydrocupration is *syn*-selective and the electrophilic allylation process of alkylcopper intermediate with allylic bromide basically occurs with retention of configuration (Scheme 4.1c). To get more information about the leaving group-dependent stereochemistry of the reaction (Scheme 4.3A), the author next performed the deuterium-labeling experiments with methallyl bromide **2a-Br** and chloride **2a-Cl** using $Cu(OAc)_2$/MeO-dppbz catalyst (Scheme 4.4B). The reaction with **2a-Br** mainly gave the *syn*-isomer with relatively high diastereoselectivity (89:11 dr). However, surprisingly, the reaction with **2a-Cl** gave an almost 1:1 mixture of *syn*- and *anti*-diastereomers (58:42 dr). These results suggest the possibility of epimerization of the α-$SCF_3$ alkyl copper intermediate prior to allylation process ((i) in Scheme 4.1c).[7] The allylic chloride is less reactive, and allylation process is thus relatively slow. Accordingly, the epimerization of α-$SCF_3$ alkylcopper species competitively occurs, leading to the erosion of dr.[8] The hypothesis is also consistent with the results using sterically demanding prenyl-type electrophile; even with the Br leaving group, the enantioselectivity was much lower. Thus, the allylation kinetics gave significant impact on the enantiomeric ratio of finally observed hydroallylated product.

Finally, the author further investigated the allylation process using density functional theory (DFT) calculations (Scheme 4.4C). The structures of each intermediate and transition state were optimized using Gaussian 16 program[9] supported by the artificial force induced reaction (AFIR) method implemented in the Global Reaction Route

Mapping (GRRM) program.[10] The long-range and dispersion corrected ωB97X-D function[11] was employed for geometry optimizations and single-point energy calculations. Geometries of intermediates and transition states were optimized with a standard 6-31G(d) basis set (LanL2DZ basis set for Cu, Br) in THF using the SMD solvation model.[12] Single-point energy calculations were performed using the 6-311+G(d,p) basis set (SDD basis set for Cu, Br) in THF. First, the author investigated hydrocupration step between computational model substrate **1o** and CuH with simple dppbz ligand. Similar to previous hydroboration,[1] hydrocupration of **1o** proceeded through four-membered transition state (ts1), and its activation energy was 16.9 kcal/mol. The author then explored the allylation reaction pathway between the generated alkylcopper intermediate int1 and allyl bromide **2b-Br**. The author's investigation revealed that the most favorable pathway proceeds via the formation of a π-allyl copper intermediate ($int2_{Br}$).[13] Subsequent carbon–carbon bond formation occurs through transition state $ts2_{Br}$ with an activation barrier of 23.1 kcal/mol. The reaction with allyl chloride **2b-Cl** was also examined, and it was found to proceed through a similar reaction mechanism to allyl bromide. However, the activation barrier was 26.9 kcal/mol, indicating a significantly slower reaction rate compared to allyl bromide. These results support the hypothesis that the epimerization of the alkylcopper intermediate competitively occurs in reactions with allylic chlorides. Moreover, unique ionic nature of α-$SCF_3$ alkylcopper species is suggested by natural population analysis (NPA). Other possible pathways for allylation with **2b-Br** include $S_N2$- and $S_N2'$-type mechanisms ($ts3_{Br}$ and $ts4_{Br}$),[14] with activation energies of 23.6 and 25.8 kcal/mol, respectively. The author considers that these two pathways can compete under standard conditions and that the optimal pathway may shift depending on the steric environment of the substrates. Indeed, the product regioselectivity was highly dependent on the structure of starting allylic electrophile as shown in the crotylation and prenylation (Scheme 4.2). On the other hand, an oxidative addition mechanism, proceeding through a three-centered transition state $ts5_{Br}$, was found to be energetically unfavorable. Similarly, stereoinvertive pathway was also disfavored. For the reaction with allyl chloride, the author's computational studies revealed no plausible alternatives to the optimal π-allyl pathway ($ts2_{Cl}$), as the corresponding $ts3_{Cl}$, $ts4_{Cl}$, and $ts5_{Cl}$ all exhibited higher activation barriers. Such differences in potentially competitive pathways depending on the leaving group also influenced the regioselectivity of the reaction: In the reaction with crotyl-type

electrophiles, the bromide **2n-Br** gave a 1:1.3 mixture of the linear (**3an**) and branched (**3an'**) isomers, while the regioselectivity was reversed in the case of chloride **2n-Cl** (Scheme 4.4D).




**Scheme 4.4**. Mechanistic studies; (A) Deuterium-labeling experiments. Conditions: **1** (0.20 mmol), $Ph_2SiD_2$ (0.40 mmol), **2a-Br** (0.40 mmol; slow addition), $Cu(OAc)_2$ (0.020 mmol), (*S*)-$H_8$-BINAP (0.020 mmol), CsOPiv (0.40 mmol), THF (1.0 mL), RT, 4 h. (B) Leaving group-dependent stereochemistry. (C) DFT calculated relative Gibbs energy profile at ωB97X-D/6-311+G(d,p)&SDD/SMD(THF)//ωB97X-D/6-31G(d)&LanL2DZ/SMD(THF) level of theory. (D) Reaction with crotyl bromide **2n-Br** and chloride **2n-Cl**.

## Summary

In conclusion, the author has developed a Cu-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes with hydrosilanes and allylic electrophiles. A chiral CuH catalyst enables the asymmetric construction of carbon stereocenter α to the $SCF_3$ group via $C(sp^3)$–$C(sp^3)$ bond formation. Detailed mechanistic studies, including theoretical calculations, reveal the possibility for epimerization of the α-$SCF_3$ alkylcopper intermediate and the crucial choice of the leaving group of allylic electrophiles for the acceptable enantioselectivity of the hydroallylated product. Post functionalizations of the

introduced allyl moiety can access versatile chiral $SCF_3$-containing compounds of potent interest in fields of pharmaceutical and medicinal chemistry.

## Experimental Section

### Instrumentation and Chemicals

$^1H$, $^{13}C\{^1H\}$, $^{19}F\{^1H\}$, and $^2H$ NMR spectra were recorded at 400 MHz, 100 MHz, 376 MHz, and 61 Hz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by APCI or EI using TOF or a magnetic sector, respectively. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakosil C-200, Wako Pure Chemical Co.) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-20AR (pump, SHIMADZU, 7.5 mL/min $CHCl_3$ or ethyl acetate) and SPD-20A (UV detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC). The crystal measurement was performed with XatLAB Synergy-S/Cu (Rigaku).

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Anhydrous THF was available from Kanto Chemical Co. and used out of the bottle. $Cu(OAc)_2$ and (*S*)-$H_8$-BINAP were purchased from FUJIFILM Wako Pure Chemical Co. and Ardrich, respectively. CsOPiv was obtained from Aldrich but should be crushed to pieces with a mortar and a pestle in a glovebox filled with nitrogen and then dried at 100 ˚C under high vacuum overnight. MeO-dppbz was prepared from 1,2-bis(dichlorophosphino)benzene and corresponding aryl Grignard reagent.[15] $SCF_3$-substituted alkenes **1a**–**n**[16] were prepared according to the reported methods. The allylic chlorides/bromides **2c**, **e**-**i**, and **k** were synthesized according to the literature.[17] Allylic chlorides/bromides **2a**, **b**, **d**, **j**, **l**, **m**, **n**, allyl chloride **2n', o**, and allylic bromide **2p** are commercially available. Unless otherwise noted, all reactions were performed under nitrogen atmosphere.

### Experimental Procedures

#### Copper-catalyzed regioselective hydroallylation of $SCF_3$-substituted alkenes (0.20 mmol scale)

Synthesis of **3aa** (Table1, entry 14) is representative. $Cu(OAc)_2$ (3.6 mg, 0.020 mmol),

MeO-dppbz (11 mg, 0.020 mmol), and CsOPiv (94 mg, 0.40 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (1.0 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. $(MeO)_3SiH$ (76 μL, 0.60 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, methallyl chloride (**2a-Cl**, 45 mg, 0.50 mmol) was added in one portion, and (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 47 mg, 0.20 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (chloroform) to give (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 48 mg, 0.17 mmol, 83%).

**Copper-catalyzed regioselective hydroboration of $SCF_3$-substituted alkenes (1.0 mmol scale)**

Synthesis of **3aa** (Scheme 4) is representative. $Cu(OAc)_2$ (18 mg, 0.10 mmol), MeO-dppbz (57 mg, 0.10 mmol), and CsOPiv (0.47 g, 2.0 mmol) were placed in a 50 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (5.0 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. $(MeO)_3SiH$ (0.37 g, 3.0 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, methallyl chloride (**2a-Cl**, 0.23 g, 2.5 mmol) was added in one portion, and (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 0.23 g, 1.0 mmol) was finally added. The reaction solution was stirred at room temperature for 4 h. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (chloroform) to give (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 0.20 g, 0.68 mmol, 69%).

**Copper-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes (enantioselective conditions; 0.20 mmol scale)**

Synthesis of **3aa** (Scheme5A, entry 10) is representative. $Cu(OAc)_2$ (3.6 mg, 0.020 mmol), (*S*)-$H_8$-BINAP (13 mg, 0.020 mmol), and CsOPiv (94 mg, 0.40 mmol) were placed in a 20 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (1.0 mL) was added to the tube, and the solution was stirred for

15 min at room temperature. $(MeO)_3SiH$ (76 μL, 0.60 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 47 mg, 0.20 mmol) was added. Finally, methallyl bromide (**2a-Br**, 11 mg × 5, 0.08 mmol × 5) was added at 20 min intervals for five times. The reaction solution was stirred at room temperature for 4 h from the first addition of **2a-Br**. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (chloroform) to give (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 44 mg, 0.15 mmol, 76%, 96:4 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 10.1 min, minor isomer: $t_R$ = 8.0 min, UV detection at 260 nm, 25 °C).

**Copper-catalyzed regio- and enantioselective hydroallylation of $SCF_3$-substituted alkenes (enantioselective conditions; 1.0 mmol scale)**

Synthesis of **3aa** (Scheme5B) is representative. $Cu(OAc)_2$ (18 mg, 0.10 mmol), (*S*)-$H_8$-BINAP (63 mg, 0.10 mmol), and CsOPiv (0.47 g, 2.0 mmol) were placed in a 50 mL Schlenk tube, which was then filled with nitrogen by using the standard Schlenk technique. THF (5.0 mL) was added to the tube, and the solution was stirred for 15 min at room temperature. $(MeO)_3SiH$ (0.37 g, 3.0 mmol) was then added dropwise via syringe, and the resulting solution was stirred at the same temperature. After 15 min, (*E*)-(4-phenylbut-1-en-1-yl)(trifluoromethyl)sulfane (**1a**, 0.23 g, 1.0 mmol) was added. Finally, methallyl bromide (**2a-Br**, 54 mg × 5, 0.40 mmol × 5) was added at 20 min intervals for five times. The reaction solution was stirred at room temperature for 4 h from the first addition of **2a-Br**. The resulting mixture was directly filtered through a short pad of silica gel. The filtrate was evaporated in vacuo and purified by GPC (chloroform) to give (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 0.23 g, 0.80 mmol, 80%, 96:4 er).

**Hydroboration/oxidation of 3aa (Scheme 4.3C)**

A 50 mL Schlenk tube equipped with a stir bar was charged with borabicyclo[3.3.1]nonane dimer (55 mg, 0.225 mmol) in a glovebox filled with nitrogen. The reaction tube was sealed with a septum and taken out of the glovebox. THF (4.0 mL)

and (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 43 mg, 0.15 mmol, 96:4 er) was added to the tube, and the solution was stirred overnight at room temperature. Sodium hydroxide aqueous solution (2 M, 0.6 mL) and hydrogen peroxide (30 wt%, 0.4 mL) were added to the reaction mixture, and the solution was stirred for 20 min. The reaction was quenched with saturated aqueous sodium thiosulfate and ammonium chloride aqueous solution. Extraction was repeated a total of three times with ethyl acetate, and combined organic phase was then evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v) to give 2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptan-1-ol (**5**, 39 mg, 0.13 mmol, 85%, 53:47 dr, 94:6 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OD-H column, 98.5/1.5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 27.4, 31.0 min, minor isomer: $t_R$ = 25.3, 34.9 min, UV detection at 210 nm, 25 °C).

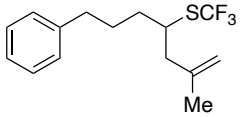
**Hydroboration/Suzuki-Miyaura coupling of 3aa (Scheme 4.3C)**

A 50 mL Schlenk tube equipped with a stir bar was charged with borabicyclo[3.3.1]nonane dimer (55 mg, 0.225 mmol) in a glovebox filled with nitrogen. The reaction tube was sealed with a septum and taken out of the glovebox. THF (4.0 mL) and (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 43 mg, 0.15 mmol, 96:4 er) was added to the tube, and the solution was stirred overnight at room temperature. The reaction mixture was evaporated in vacuo. THF/DMF (0.4 mL/1.7 mL), $PdCl_2$(dppf) (3.3 mg, 0.0045 mmol), 4-bromoacetophenone (45 mg, 0.225 mmol), and $K_2CO_3$ (42 mg, 0.30 mmol) were added the residue, and the mixture was stirred at 50 ℃ for 8 h. The reaction mixture was diluted with ethyl acetate (20 mL). The combined organic layer was washed with $H_2O$ and brine, and dried over $Na_2SO_4$. The organic layer was concentrated in vacuo, and the residue was purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v) to give 1-(4-(2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptyl)phenyl)ethan-1-one (**6**, 47 mg, 0.12 mmol, 77%, 55:45 dr, 95:5 er). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALPAK AD-H column, 99.5/0.5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 19.4, 24.8 min, minor isomer: $t_R$ = 18.4, 24.0 min, UV detection at 217 nm, 25 °C).

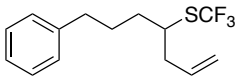
**Olefin metathesis of 3ab and methyl acrylate (Scheme 4.3C)**

A 20 mL round bottom flask equipped with a stir bar and a balloon was charged with Grubbs 2nd catlyst (6.4 mg, 0.0075 mmol), which was then filled with nitrogen by using the standard Schlenk technique. THF (1.5 mL) and (2-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (**3aa**, 43 mg, 0.15 mmol, 96:4 er) was added to the flask, and methyl acrylate (65 mg, 0.75 mmol) was finally added dropwise via syringe. The solution was then allowed to warm to 45 °C and stirred for 22 h. The reaction mixture was directly filtered through a short pad of neutral alumina and $Na_2SO_4$. The filtrate was evaporated in vacuo, and the residue was purified by silica gel column chromatography with hexane/ethyl acetate (40/1 → 5/1, v/v) to give methyl (*E*)-8-phenyl-5-((trifluoromethyl)thio)oct-2-enoate (**7**, 41 mg, 0.12 mmol, 82%, 95:5 e.r.). The enantiomeric ratio was determined by HPLC analysis in comparison with authentic racemic sample (CHIRALCEL OD-H column, 98/2 *n*-hexane/chloroform, 0.5 mL/min, major isomer: $t_R$ = 28.0 min, minor isomer: $t_R$ = 31.2 min, UV detection at 225 nm, 25 $^oC$).

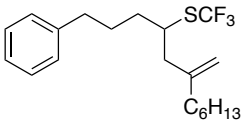
**Characterization Data of Products**



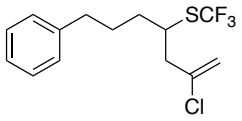

**(2-Methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3aa):** Purified by GPC (chloroform): 48 mg (83%, 0.20 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 4.85-4.84 (m, 1H), 4.73 (d, *J* = 0.8 Hz, 1H), 3.36-3.29 (m, 1H), 2.69-2.55 (m, 2H), 2.42 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.35 (dd, *J* = 14.3, 8.2 Hz, 1H), 1.88-1.74 (m, 3H), 1.71 (s, 3H), 1.66-1.57 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.8, 141.5, 131.3 (q, *J* = 304.4 Hz), 128.4 (2C), 128.3 (2C), 125.9, 114.0, 44.1, 44.0, 35.5, 33.8, 27.9, 21.8; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -39.07; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{20}F_3S$: 289.1232, found: 289.1207. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 10.1 min, minor isomer: $t_R$ = 8.0 min.




**(7-Phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ab):** Purified by GPC (chloroform): 50 mg (90%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 7.21-7.16 (m, 3H), 5.77 (ddt, *J* = 16.6, 10.5, 7.1 Hz, 1H), 5.12 (ddt, *J* = 10.5, 1.7, 1.1 Hz, 1H), 5.11 (ddt, *J* = 16.6, 1.7, 1.4 Hz, 1H), 3.24 (tt, *J* = 6.3, 6.0 Hz, 1H), 2.68-2.57 (m, 2H), 2.50-2.39 (m, 2H), 1.88-1.70 (m, 3H), 1.69-1.58 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.8, 133.7, 131.2 (q, *J* = 304.2 Hz), 128.41 (2C), 128.38 (2C), 126.0, 118.5, 45.6, 39.6, 35.4, 33.7, 28.2; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.14; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{14}H_{17}F_3S$: 274.1003, found: 274.0993. CHIRALCEL OD-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 13.1 min, minor isomer: $t_R$ = 12.7 min.

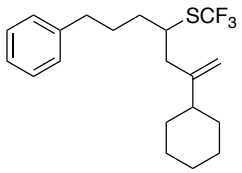



**(6-Methylene-1-phenyldodecan-4-yl)(trifluoromethyl)sulfane (3ac):** Purified by GPC (chloroform): 64 mg (90%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.21-7.15 (m, 3H), 4.84 (d, *J* = 1.3 Hz, 1H), 4.75 (s, 1H), 3.35-3.28 (m, 1H), 2.68-2.55 (m, 2H), 2.44 (dd, *J* = 14.4, 6.5 Hz, 1H), 2.33 (dd, *J* = 14.4, 8.6 Hz, 1H), 1.97 (t, *J* = 7.4 Hz, 2H), 1.88-1.69 (m, 3H), 1.65-1.55 (m, 1H), 1.46-1.36 (m, 2H), 1.34-1.26 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 145.7, 141.8, 131.3 (q, *J* = 304.5 Hz), 128.38 (2C), 128.37 (2C), 125.9, 112.7, 44.2, 42.5, 35.5, 35.3, 33.7, 31.7, 29.0, 27.9, 27.5, 22.6, 14.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.05; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{20}H_{30}F_3S$: 359.2015, found: 359.2013. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 16.8 min, minor isomer: $t_R$ = 10.7 min.

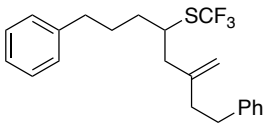



**(2-Chloro-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ad):** Purified by GPC (chloroform): 33 mg (54%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$)

δ 7.31-7.27 (m, 2H), 7.21-7.17 (m, 3H), 5.28 (d, *J* = 1.4 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 3.53-3.47 (m, 1H), 2.74 (dd, *J* = 14.6, 6.7 Hz, 1H), 2.70-2.57 (m, 3H), 1.89-1.72 (m, 3H), 1.70-1.57 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.6, 138.4, 131.0 (q, *J* = 304.6 Hz), 128.42 (2C), 128.38 (2C), 126.0, 115.7, 45.4, 43.3, 35.3, 33.3, 28.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.83; HRMS (EI) m/z ($[M]^+$) calcd for $C_{14}H_{16}ClF_3S$: 308.0613, found: 308.0610.

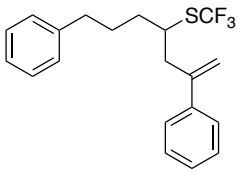



**(2-Cyclohexyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ae):** Purified by GPC (chloroform): 63 mg (89%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 4.85 (s, 1H), 4.73 (s, 1H), 3.35-3.28 (m, 1H), 2.68-2.55 (m, 2H), 2.48 (dd, *J* = 14.7, 6.4 Hz, 1H), 2.33 (dd, *J* = 14.7, 8.7 Hz, 1H), 1.86-1.69 (m, 9H), 1.63-1.54 (m, 1H), 1.31-1.21 (m, 2H), 1.19-1.04 (m, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 141.8, 131.3 (q, *J* = 304.3 Hz), 128.4 (4C), 125.9, 110.6, 44.6, 43.3, 41.6, 35.5, 33.6, 32.5, 32.3, 27.9, 26.8, 26.7, 26.3; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.98; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{28}F_3S$: 357.1858, found: 357.1869. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 5.9 min, minor isomer: $t_R$ = 5.2 min.

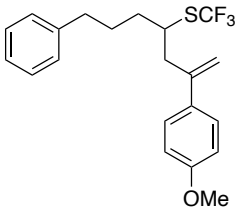



**(6-Methylene-1,8-diphenyloctan-4-yl)(trifluoromethyl)sulfane (3af):** Purified by GPC (chloroform): 57 mg (76%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 4H), 7.21-7.15 (m, 6H), 4.91 (s, 1H), 4.81 (s, 1H), 3.35-3.28 (m, 1H), 2.80-2.69 (m, 2H), 2.67-2.54 (m, 2H), 2.48 (dd, *J* = 14.5, 6.6 Hz, 1H), 2.36 (dd, *J* = 14.5, 8.4 Hz, 1H), 2.29 (t, *J* = 8.0 Hz, 2H), 1.89-1.67 (m, 3H), 1.65-1.56 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 144.9, 141.8, 141.7, 131.3 (q, *J* = 304.3 Hz), 128.43 (2C), 128.41 (2C), 128.38 (2C), 128.3 (2C), 126.0, 125.9, 113.4, 44.2, 42.8, 37.1, 35.5, 34.2, 33.7, 27.9; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.99; HRMS (APCI) m/z ($[M+H]^+$)

calcd for $C_{22}H_{26}F_3S$: 379.1702, found: 379.1700. CHIRALCEL OD-H column, 99.8/0.2 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 15.7 min, minor isomer: $t_R$ = 14.3 min.

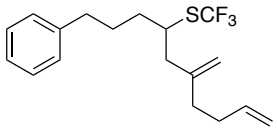



**(2,7-Diphenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ag):** Purified by GPC (chloroform): 48 mg (69%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 7.26-7.25 (m, 2H), 7.20-7.16 (m, 1H), 7.11-7.09 (m, 2H), 5.32 (d, *J* = 1.2 Hz, 1H), 5.09 (d, *J* = 0.9 Hz, 1H), 3.23-3.16 (m, 1H), 3.04 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.77 (dd, *J* = 14.4, 9.0 Hz, 1H), 2.58-2.44 (m, 2H), 1.83-1.70 (m, 2H), 1.67-1.59 (m, 1H), 1.57-1.49 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 145.0, 141.8, 139.8, 131.2 (q, *J* = 304.6 Hz), 128.6 (2C), 128.38 (2C), 128.36 (2C), 127.9, 126.3 (2C), 125.9, 116.0, 44.2, 42.0, 35.3, 33.1, 27.7; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -38.80; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{20}H_{22}F_3S$: 351.1389, found: 351.1390. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 25.9 min, minor isomer: $t_R$ = 17.7 min.

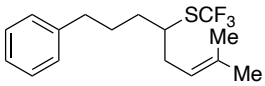



**(2-(4-Methoxyphenyl)-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ah):** Purified by GPC (chloroform): 61 mg (80%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.28-7.25 (m, 4H), 7.20-7.16 (m, 1H), 7.11 (d, *J* = 7.0 Hz, 2H), 6.89-6.85 (m, 2H), 5.24 (d, *J* = 1.0 Hz, 1H), 5.00 (s, 1H), 3.82 (s, 3H), 3.24-3.17 (m, 1H), 3.02 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.73 (dd, *J* = 14.4, 9.2 Hz, 1H), 2.59-2.45 (m, 2H), 1.84-1.69 (m, 2H), 1.67-1.60 (m, 1H), 1.58-1.48 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 159.4, 144.3, 141.8, 132.1, 131.3 (q, *J* = 304.5 Hz), 128.4 (2C), 128.3 (2C), 127.4 (2C), 125.9, 114.5, 113.9 (2C), 55.3, 44.2, 42.2, 35.4, 33.1, 27.7; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -38.79; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{21}H_{24}F_3OS$: 381.1494, found: 381.1485.

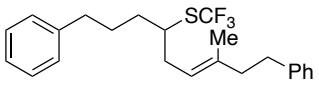
CHIRALCEL OJ-H column, 97/3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 13.9 min, minor isomer: $t_R$ = 12.2 min.




**(6-Methylene-1-phenyldec-9-en-4-yl)(trifluoromethyl)sulfane (3ai):** Purified by GPC (chloroform): 39 mg (59%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.21-7.16 (m, 3H), 5.80 (ddt, *J* = 17.0, 10.3, 6.3 Hz, 1H), 5.03 (ddt, *J* = 17.0, 1.9, 1.6 Hz, 1H), 4.97 (ddt, *J* = 10.3, 1.9, 1.2 Hz, 1H), 4.87 (d, *J* = 1.3 Hz, 1H), 4.79 (s, 1H), 3.35-3.28 (m, 1H), 2.69-2.55 (m, 2H), 2.45 (dd, *J* = 14.5, 6.6 Hz, 1H), 2.34 (dd, *J* = 14.5, 8.5 Hz, 1H), 2.22-2.15 (m, 2H), 2.07 (t, *J* = 7.4 Hz, 2H), 1.90-1.70 (m, 3H), 1.67-1.55 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 144.7, 141.8, 137.9, 131.2 (q, *J* = 304.3 Hz), 128.39 (2C), 128.36 (2C), 125.9, 114.9, 113.2, 44.1, 42.6, 35.5, 34.6, 33.7, 31.7, 27.9; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -39.04; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{18}H_{24}F_3S$: 329.1545, found: 329.1545. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 12.6 min, minor isomer: $t_R$ = 7.2 min.

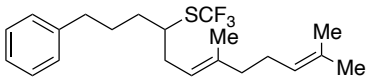



**(7-Methyl-1-phenyloct-6-en-4-yl)(trifluoromethyl)sulfane (3aj):** Purified by GPC (chloroform): 46 mg (77%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 7.21-7.16 (m, 3H), 5.13-5.08 (m, 1H), 3.20 (tt, *J* = 7.0, 5.8 Hz, 1H), 2.66 (ddd, *J* = 13.8, 8.4, 6.2 Hz, 1H), 2.59 (dd, *J* = 13.8, 6.3 Hz, 1H), 2.41 (dd, *J* = 14.8, 6.5 Hz, 1H), 2.34 (dd, *J* = 14.8, 6.9 Hz, 1H), 1.87-1.69 (m, 3H), 1.71 (s, 3H), 1.64-1.57 (m, 1H), 1.60 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 141.9, 135.1, 131.4 (q, *J* = 304.1 Hz), 128.39 (2C), 128.38 (2C), 125.9, 119.7, 46.6, 35.5, 34.0, 33.6, 28.3, 25.8, 18.0; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -39.13; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{16}H_{22}F_3S$: 303.1389, found: 303.1390.

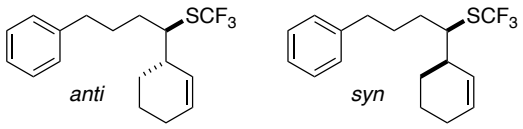



**(*E*)-(7-Methyl-1,9-diphenylnon-6-en-4-yl)(trifluoromethyl)sulfane (3ak) (*E*-**

**geometry was assigned by analogy with previous work[18l]):** Purified by GPC (chloroform): 35 mg (44%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 4H), 7.20-7.16 (m, 6H), 5.10 (t, *J* = 7.0 Hz, 1H), 3.16 (tt, *J* = 7.2, 5.8 Hz, 1H), 2.70 (dd, *J* = 9.6, 7.2 Hz, 2H), 2.65-2.53 (m, 2H), 2.43-2.35 (m, 2H), 2.30 (t, *J* = 8.6 Hz, 2H), 1.83-1.74 (m, 1H), 1.72-1.59 (m, 2H), 1.64 (s, 3H), 1.55-1.47 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 142.0, 141.9, 138.0, 131.4 (q, *J* = 304.2 Hz), 128.4 (6C), 128.3 (2C), 125.9, 125.8, 120.3, 46.5, 41.5, 35.4, 34.4, 33.9, 33.5, 28.2, 16.5; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -39.14; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{23}H_{28}F_3S$: 393.1858, found: 393.1866.



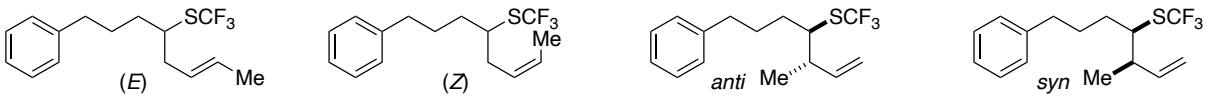

**(*E*)-(7,11-Dimethyl-1-phenyldodeca-6,10-dien-4-yl)(trifluoromethyl)sulfane (3al):** Purified by GPC (chloroform): 41 mg (56%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 5.12 (t, *J* = 7.2 Hz, 1H), 5.07 (td, *J* = 6.8, 1.3 Hz, 1H), 3.21 (tt, *J* = 6.9, 5.6 Hz, 1H), 2.68-2.56 (m, 2H), 2.45-2.33 (m, 2H), 2.10-2.04 (m, 2H), 2.02-1.99 (m, 2H), 1.87-1.71 (m, 3H), 1.68 (s, 3H), 1.65-1.57 (m, 1H), 1.604 (s, 3H), 1.595 (s, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 141.9, 138.6, 131.6, 131.4 (q, *J* = 304.1 Hz), 128.4 (4C), 125.9, 124.1, 119.7, 46.6, 39.8, 35.5, 33.8, 33.7, 28.3, 26.5, 25.7, 17.7, 16.3; $^{19}$F{$^1$H} NMR (376 MHz, $CDCl_3$) δ -39.14; HRMS (APCI) m/z ([M+H]$^+$) calcd for $C_{21}H_{30}F_3S$: 371.2015, found: 371.2027.




**3am** (75:25 dr)

**A 75:25 diastereomixture of ((*R**)-1-((*S**)-cyclohex-2-en-1-yl)-4-phenylbutyl)(trifluoromethyl)sulfane (*anti*-3am) and ((*R**)-1-((*R**)-cyclohex-2-en-1-yl)-4-phenylbutyl)(trifluoromethyl)sulfane (*syn*-3am) (relative stereochemistry was tentatively assigned):** Purified by GPC (chloroform): 31 mg (49%, 0.20 mmol scale); Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 0.75 × 2H for *anti*-**3am** and 0.25 × 2H for *syn*-**3am**), 7.21-7.17 (m, 0.75 × 3H for *anti*-**3am** and 0.25 × 3H for *syn*-**3am**), 5.86-5.79 (m, 0.75 × 1H for *anti*-**3am** and 0.25 × 1H for *syn*-**3am**), 5.53-5.47 (m, 0.75 × 1H for *anti*-**3am** and 0.25 × 1H for *syn*-**3am**), 3.16 (dt, *J* = 8.4, 4.7 Hz, 0.25 × 1H

for *syn*-**3am**), 3.09 (dt, *J* = 8.6, 4.2 Hz, 0.75 × 1H for *anti*-**3am**), 2.70-2.59 (m, 0.75 × 2H for *anti*-**3am** and 0.25 × 2H for *syn*-**3am**), 2.57-2.50 (m, 0.75 × 1H for *anti*-**3am** and 0.25 × 1H for *syn*-**3am**), 2.02-1.97 (m, 0.75 × 2H for *anti*-**3am** and 0.25 × 2H for *syn*-**3am**), 1.92-1.85 (m, 0.75 × 1H for *anti*-**3am** and 0.25 × 1H for *syn*-**3am**), 1.83-1.72 (m, 0.75 × 4H for *anti*-**3am** and 0.25 × 4H for *syn*-**3am**), 1.70-1.61 (m, 0.75 × 1H for *anti*-**3am** and 0.25 × 1H for *syn*-**3am**), 1.58-1.43 (m, 0.75 × 2H for *anti*-**3am**), 1.30-1.21 (m, 0.25 × 2H for *syn*-**3am**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.88 (*anti*-**3am**), 141.86 (*syn*-**3am**), 131.49 (q, *J* = 304.0 Hz, *anti*-**3am**), 131.45 (q, *J* = 303.5 Hz, *syn*-**3am**), 130.9 (*anti*-**3am**), 129.7 (*syn*-**3am**), 128.39 (0.75 × 2C for *anti*-**3am** and 0.25 × 2C for *syn*-**3am**), 128.36 (0.75 × 2C for *anti*-**3am** and 0.25 × 2C for *syn*-**3am**), 128.31 (*syn*-**3am**), 126.9 (*anti*-**3am**), 125.9 (0.75 × 1C for *anti*-**3am** and 0.25 × 1C for *syn*-**3am**), 51.3 (*syn*-**3am**), 51.2 (*anti*-**3am**), 40.0 (*anti*-**3am**), 39.7 (*syn*-**3am**), 35.5 (0.75 × 1C for *anti*-**3am** and 0.25 × 1C for *syn*-**3am**), 32.6 (*anti*-**3am**), 32.5 (*syn*-**3am**), 29.0 (*anti*-**3am**), 28.8 (*syn*-**3am**), 26.1 (*anti*-**3am**), 25.6 (*syn*-**3am**), 25.2 (*anti*-**3am**), 25.0 (*syn*-**3am**), 21.9 (*anti*-**3am**), 21.7 (*syn*-**3am**); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -39.18 (*syn*-**3am**), -39.48 (*anti*-**3am**); HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{17}H_{22}F_3S$: 315.1389, found: 315.1393.



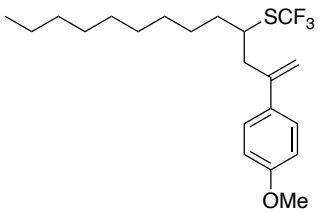

**3an** (*E*/*Z* = 19:1) **3an'** (55:45 dr)

**A 96:4 regiomixture of (1-phenyloct-6-en-4-yl)(trifluoromethyl)sulfane (3an) and (3-methyl-7-phenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3an') (relative stereochemistry of 3an' was tentatively assigned):** Purified by GPC (chloroform): 48 mg (83%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 0.96 × 2H for **3an** and 0.04 × 2H for **3an'**), 7.21-7.16 (m, 0.96 × 3H for **3an** and 0.04 × 3H for **3an'**), 5.81-5.67 (m, 0.04 × 1H for **3an'**), 5.66-5.57 (m, 0.96 × 0.05 × 1H for (*Z*)-**3an**), 5.55-5.47 (m, 0.96 × 0.95 × 1H for (*E*)-**3an**), 5.41-5.33 (m, 0.96 × 1H for **3an**), 5.10-5.04 (m, 0.04 × 2H for **3an'**), 3.20 (tt, *J* = 6.3, 6.0 Hz, 0.96 × 1H for **3an**), 3.13-3.05 (m, 0.04 × 1H for **3an'**), 2.68-2.56 (m, 0.96 × 2H for **3an** and 0.04 × 2H for **3an'**), 2.46-2.31 (m, 0.96 × 2H for **3an** and 0.04 × 1H for **3an'**), 1.80-1.70 (m, 0.96 × 3H for **3an** and 0.04 × 3H for **3an'**), 1.68-1.64 (m, 0.04 × 3H for **3an'**), 1.66 (dd, *J* = 6.2, 1.0 Hz, 0.96 × 3H for **3an**), 1.63-1.58 (m, 0.96 × 1H for **3an** and 0.04 × 1H for **3an'**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.8, 131.3 (q, *J* = 304.2 Hz), 129.2, 128.4 (4C), 126.2, 125.9, 46.2,

38.4, 35.4, 33.5, 28.1, 18.0 (Only the peaks of **3an** are shown due to the very weak peak of **3an'**.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -39.11, -39.16, -39.26, -39.52; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{20}F_3S$: 289.1232, found: 289.1241.

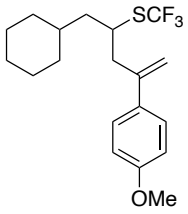

**3ao** (*E*/*Z* = >20:1) **3ao'** (71:29 dr)

**A 86:14 regiomixture of (1,7-diphenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ao) and (3,7-diphenylhept-1-en-4-yl)(trifluoromethyl)sulfane (3ao') (relative stereochemistry of 3ao' was tentatively assigned):** Purified by GPC (chloroform): 30 mg (43%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.314 (m, 0.14 × 2H for **3ao'**), 7.33-7.30 (m, 0.86 × 3H for **3ao** and 0.14 × 3H for **3ao'**), 7.30-7.26 (m, 0.86 × 2H for **3ao**), 7.25-7.21 (m, 0.86 × 2H for **3ao**), 7.20-7.16 (m, 0.86 × 3H for **3ao** and 0.14 × 3H for **3ao'**), 7.12-7.09 (m, 0.14 × 2H for **3ao'**), 6.44 (d, *J* = 15.8 Hz, 0.86 × 1H for **3ao**), 6.15 (dt, *J* = 15.8, 7.2 Hz, 0.86 × 1H for **3ao**), 6.10-6.01 (m, 0.14 × 1H for **3ao'**), 5.22-5.07 (m, 0.14 × 2H for **3ao'**), 3.67 (dd, *J* = 8.6, 5.6 Hz, 0.14 × 0.71 × 1H for *anti*-**3ao'**), 3.54 (t, *J* = 8.0 Hz, 0.14 × 0.29 × 1H for *syn*-**3ao'**), 3.48-3.42 (m, 0.14 × 1H for **3ao'**), 3.32 (tt, *J* = 6.3, 5.6 Hz, 0.86 × 1H for **3ao**), 2.71-2.57 (m, 0.86 × 4H for **3ao**), 2.57-2.48 (m, 0.14 × 2H for **3ao'**), 1.90-1.72 (m, 0.86 × 3H for **3ao** and 0.14 × 3H for **3ao'**), 1.72-1.61 (m, 0.86 × 1H for **3ao** and 0.14 × 1H for **3ao'**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.7, 138.0, 137.0, 133.5, 131.2 (q, *J* = 304.5 Hz), 128.62, 128.57, 128.42, 128.38, 128.3, 128.2, 128.1, 127.5, 127.10, 127.05, 126.2, 126.0, 125.9, 125.3, 118.3, 117.8, 54.2, 51.3, 46.1, 38.9, 35.4, 33.7, 28.2, 28.1, 27.8 (All observed signals are just shown because of complexity associated with regio- and stereoisomers.); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -39.06, -39.14, -39.40; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{22}F_3S$: 351.1389, found: 351.1397.

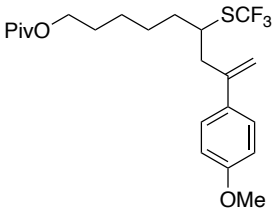



**(2-(4-Methoxyphenyl)tridec-1-en-4-yl)(trifluoromethyl)sulfane (3bh):** Purified by

GPC (chloroform): 54 mg (69%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 6.90-6.86 (m, 2H), 5.27 (d, *J* = 1.2 Hz, 1H), 5.04 (d, *J* = 0.9 Hz, 1H), 3.82 (s, 3H), 3.21-3.14 (m, 1H), 3.02 (dd, *J* = 14.4, 5.9 Hz, 1H), 2.75 (dd, *J* = 14.4, 9.1 Hz, 1H), 1.72-1.64 (m, 1H), 1.53-1.40 (m, 2H), 1.34-1.27 (m, 3H), 1.25-1.17 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 159.3, 144.5, 132.2, 131.3 (q, *J* = 304.5 Hz), 127.4 (2C), 114.3, 113.9 (2C), 55.3, 44.4, 42.2, 33.5, 31.9, 29.5, 29.33, 29.27, 29.1, 25.8, 22.7, 14.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.77; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{21}H_{32}F_3OS$: 389.2120, found: 389.2120. CHIRALCEL OD-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 14.3 min, minor isomer: $t_R$ = 16.2 min.

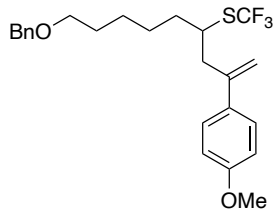



**(1-Cyclohexyl-4-(4-methoxyphenyl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3ch):** Purified by GPC (chloroform): 60 mg (83%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 6.89-6.86 (m, 2H), 5.25 (d, *J* = 1.2 Hz, 1H), 5.03 (d, *J* = 0.9 Hz, 1H), 3.82 (s, 3H), 3.22-3.15 (m, 1H), 3.08 (dd, *J* = 14.4, 5.5 Hz, 1H), 2.71 (dd, *J* = 14.4, 9.1 Hz, 1H), 1.67-1.40 (m, 7H), 1.35-1.03 (m, 4H), 0.91-0.81 (m, 1H), 0.64-0.54 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 159.3, 144.7, 132.3, 131.3 (q, *J* = 304.7 Hz), 127.4 (2C), 114.4, 113.8 (2C), 55.3, 43.4, 41.8, 41.4, 34.6, 33.7, 32.1, 26.4, 26.1, 25.9; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.49; HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{19}H_{26}F_3OS$: 359.1651, found: 359.1655. CHIRALCEL OD-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 14.9 min, minor isomer: $t_R$ = 17.1 min.

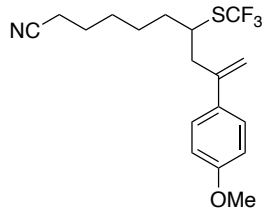



**8-(4-Methoxyphenyl)-6-((trifluoromethyl)thio)non-8-en-1-yl pivalate (3dh):** Purified by GPC (chloroform): 54 mg (69%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 6.90-6.86 (m, 2H), 5.28 (d, *J* = 1.2 Hz, 1H), 5.04 (d, *J* = 0.8

Hz, 1H), 4.00 (t, $J$ = 6.6 Hz, 2H), 3.82 (s, 3H), 3.21-3.14 (m, 1H), 3.04 (dd, $J$ = 14.4, 5.8 Hz, 1H), 2.74 (dd, $J$ = 14.4, 9.2 Hz, 1H), 1.73-1.66 (m, 1H), 1.60-1.53 (m, 2H), 1.52-1.43 (m, 2H), 1.40-1.21 (m, 3H), 1.18 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 178.6, 159.4, 144.4, 132.0, 131.3 (q, $J$ = 304.3 Hz), 127.4 (2C), 114.4, 113.9 (2C), 64.2, 55.3, 44.2, 42.2, 38.7, 33.3, 28.4, 27.2 (3C), 25.5 (2C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.79; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{22}H_{32}F_3O_3S$: 433.2019, found: 433.2019. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 43.2 min, minor isomer: $t_R$ = 53.7 min.

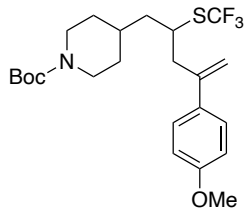



**(9-(Benzyloxy)-2-(4-methoxyphenyl)non-1-en-4-yl)(trifluoromethyl)sulfane (3eh):** Purified by GPC (chloroform): 63 mg (73%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 4H), 7.32-7.26 (m, 3H), 6.89-6.85 (m, 2H), 5.27 (d, $J$ = 1.2 Hz, 1H), 5.03 (d, $J$ = 0.8 Hz, 1H), 4.48 (s, 2H), 3.81 (s, 3H), 3.42 (t, $J$ = 6.5 Hz, 2H), 3.21-3.14 (m, 1H), 3.02 (dd, $J$ = 14.4, 5.8 Hz, 1H), 2.74 (dd, $J$ = 14.4, 9.2 Hz, 1H), 1.73-1.65 (m, 1H), 1.60-1.53 (m, 2H), 1.50-1.43 (m, 2H), 1.36-1.24 (m, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 144.4, 138.6, 132.1, 131.3 (q, $J$ = 304.6 Hz), 128.4 (2C), 127.6 (2C), 127.5, 127.4 (2C), 114.4, 113.9 (2C), 72.9, 70.2, 55.3, 44.4, 42.2, 33.4, 29.5, 25.8, 25.7; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.74; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{24}H_{30}F_3O_2S$: 439.1913, found: 439.1913. CHIRALCEL OJ-H column, 98/2 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 21.3 min, minor isomer: $t_R$ = 24.5 min.

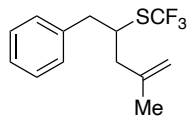



**9-(4-Methoxyphenyl)-7-((trifluoromethyl)thio)dec-9-enenitrile (3fh):** Purified by GPC (chloroform): 48 mg (68%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 6.91-6.87 (m, 2H), 5.29 (d, $J$ = 1.1 Hz, 1H), 5.04 (d, $J$ = 0.8

Hz, 1H), 3.83 (s, 3H), 3.20-3.13 (m, 1H), 3.07 (dd, $J$ = 14.3, 5.7 Hz, 1H), 2.73 (dd, $J$ = 14.3, 9.4 Hz, 1H), 2.29 (t, $J$ = 7.3 Hz, 2H), 1.74-1.67 (m, 1H), 1.65-1.56 (m, 2H), 1.54-1.44 (m, 2H), 1.40-1.29 (m, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 144.3, 131.9, 131.2 (q, $J$ = 304.3 Hz), 127.4 (2C), 119.6, 114.5, 114.0 (2C), 55.3, 44.1, 42.3, 32.9, 28.1, 25.08, 25.06, 17.0; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.77; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{23}F_3NOS$: 358.1447, found: 358.1444. CHIRALCEL OJ-H column, 97/3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 25.1 min, minor isomer: $t_R$ = 24.0 min.

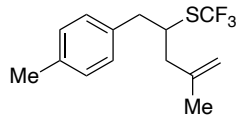



***tert*-Butyl 4-(4-(4-methoxyphenyl)-2-((trifluoromethyl)thio)pent-4-en-1-yl)piperidine-1-carboxylate (3gh):** Purified by GPC (chloroform): 73 mg (79%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 6.90-6.86 (m, 2H), 5.26 (d, $J$ = 1.1 Hz, 1H), 5.03 (s, 1H), 3.99 (br, 2H), 3.83 (s, 3H), 3.18-3.12 (m, 2H), 2.72-2.55 (m, 3H), 1.66-1.48 (m, 3H), 1.44 (s, 9H), 1.41-1.33 (m, 2H), 1.12-1.02 (m, 1H), 0.81-0.71 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 154.8, 144.4, 132.0, 131.2 (q, $J$ = 304.8 Hz), 127.4 (2C), 114.6, 113.9 (2C), 79.3, 55.3, 43.7 (br, 2C), 43.6, 41.4, 40.2, 33.0, 32.5, 30.8, 28.5 (3C); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.50; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{23}H_{33}F_3NO_3S$: 460.2128, found: 460.2106. CHIRALPAK AD-H column, 99.2/0.8 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 17.7 min, minor isomer: $t_R$ = 17.0 min.

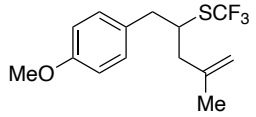



**(4-Methyl-1-phenylpent-4-en-2-yl)(trifluoromethyl)sulfane (3ha):** Purified by GPC (chloroform): 34 mg (65%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.27-7.23 (m, 1H), 7.21-7.18 (m, 2H), 4.89 (s, 1H), 4.79 (d, $J$ = 0.9 Hz, 1H), 3.59-3.50 (m, 1H), 3.03 (dd, $J$ = 14.2, 6.5 Hz, 1H), 2.98 (dd, $J$ = 14.2, 7.2 Hz, 1H), 2.41 (dd, $J$ = 14.6, 6.9 Hz, 1H), 2.31 (dd, $J$ = 14.6, 8.1 Hz, 1H), 1.71 (s, 3H); $^{13}C\{^{1}H\}$

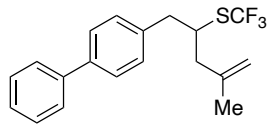
NMR (100 MHz, $CDCl_3$) δ 141.4, 137.8, 131.2 (q, $J$ = 304.6 Hz), 129.4 (2C), 128.5 (2C), 126.9, 114.2, 45.1, 42.8, 41.5, 21.8; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -38.92; HRMS (EI) m/z ($[M]^+$) calcd for $C_{13}H_{15}F_3S$: 260.0847, found: 260.0840.




**(4-Methyl-1-(*p*-tolyl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3ia):** Purified by GPC (chloroform): 29 mg (52%, 0.20 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12 (d, $J$ = 8.1 Hz, 2H), 7.08 (d, $J$ = 8.1 Hz, 2H), 4.89 (s, 1H), 4.79 (d, $J$ = 0.9 Hz, 1H), 3.53 (tt, $J$ = 7.1, 7.0 Hz, 1H), 2.99 (dd, $J$ = 14.2, 6.4 Hz, 1H), 2.94 (dd, $J$ = 14.2, 7.2 Hz, 1H), 2.41 (dd, $J$ = 14.6, 6.9 Hz, 1H), 2.33 (s, 3H), 2.30 (dd, $J$ = 14.6, 8.2 Hz, 1H), 1.71 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.4, 136.4, 134.7, 131.2 (q, $J$ = 304.5 Hz), 129.3 (2C), 129.2 (2C), 114.1, 45.2, 42.7, 41.0, 21.8, 21.1; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -38.85; HRMS (EI) m/z ($[M]^+$) calcd for $C_{14}H_{17}F_3S$: 274.1003, found: 274.1013.

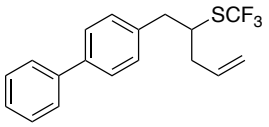



**(1-(4-Methoxyphenyl)-4-methylpent-4-en-2-yl)(trifluoromethyl)sulfane (3ja):** Purified by GPC (chloroform): 43 mg (75%, 0.20 mmol scale); Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.13-7.09 (m, 2H), 6.87-6.83 (m, 2H), 4.89 (s, 1H), 4.79 (d, $J$ = 0.9 Hz, 1H), 3.80 (s, 3H), 3.51 (tt, $J$ = 8.0, 7.0 Hz, 1H), 2.97 (dd, $J$ = 14.2, 6.3 Hz, 1H), 2.92 (dd, $J$ = 14.2, 7.1 Hz, 1H), 2.41 (dd, $J$ = 14.6, 6.9 Hz, 1H), 2.29 (dd, $J$ = 14.6, 8.1 Hz, 1H), 1.71 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 141.4, 131.2 (q, $J$ = 304.7 Hz), 130.4 (2C), 129.8, 114.1, 113.8 (2C), 55.2, 45.3, 42.6, 40.5, 21.8; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -38.87; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{18}F_3OS$: 291.1025, found: 291.1011.

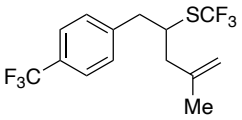



**(1-([1,1'-Biphenyl]-4-yl)-4-methylpent-4-en-2-yl)(trifluoromethyl)sulfane (3ka):**

Purified by GPC (chloroform): 43 mg (64%, 0.20 mmol scale); White solid; m.p. 37.4-38.5 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.46-7.42 (m, 2H), 7.36-7.32 (m, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 4.91 (s, 1H), 4.81 (s, 1H), 3.59 (tt, *J* = 7.0, 6.9 Hz, 1H), 3.07 (dd, *J* = 14.2, 6.5 Hz, 1H), 3.02 (dd, *J* = 14.2, 7.2 Hz, 1H), 2.45 (dd, *J* = 14.6, 6.9 Hz, 1H), 2.34 (dd, *J* = 14.6, 8.2 Hz, 1H), 1.73 (s, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.4, 140.7, 139.8, 136.8, 131.2 (q, *J* = 304.7 Hz), 129.9 (2C), 128.8 (2C), 127.3, 127.2 (2C), 127.0 (2C), 114.3, 45.1, 42.8, 41.1, 21.8; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.83; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{19}H_{19}F_3S$: 336.1160, found: 336.1161.

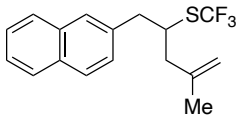



**(1-([1,1'-Biphenyl]-4-yl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3kb):** Purified by GPC (chloroform): 23 mg (35%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 7.56-7.54 (m, 2H), 7.46-7.42 (m, 2H), 7.36-7.32 (m, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.85 (ddt, *J* = 17.0, 11.1, 7.0 Hz, 1H), 5.19 (d, *J* = 11.1 Hz, 1H), 5.15 (d, *J* = 17.0 Hz, 1H), 3.54 (tt, *J* = 8.0, 6.2 Hz, 1H), 3.08 (dd, *J* = 14.1, 6.1 Hz, 1H), 2.99 (dd, *J* = 14.1, 8.2 Hz, 1H), 2.54-2.47 (m, 1H), 2.43-2.36 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 140.8, 139.9, 136.8, 133.6, 131.3 (q, *J* = 304.4 Hz), 129.8 (2C), 128.9 (2C), 127.4, 127.3 (2C), 127.1 (2C), 119.0, 46.8, 40.6, 38.0; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.03; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{18}H_{17}F_3S$: 322.1003, found: 322.1007. CHIRALCEL OJ-H column, 99.7/0.3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 34.9 min, minor isomer: $t_R$ = 43.5 min.

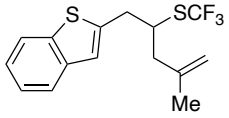



**(4-Methyl-1-(4-(trifluoromethyl)phenyl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3la):** Purified by GPC (chloroform): 35 mg (53%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.92 (s, 1H), 4.80 (d, *J* = 0.8 Hz, 1H), 3.55 (tt, *J* = 7.3, 7.1 Hz, 1H), 3.08 (dd, *J* = 14.2, 6.6 Hz, 1H), 3.02 (dd, *J* = 14.2, 7.0 Hz, 1H), 2.39 (dd, *J* = 14.6, 7.5 Hz, 1H), 2.35 (dd, *J* = 14.6,

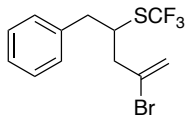
7.8 Hz, 1H), 1.73 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.8, 141.0, 131.0 (q, *J* = 305.2 Hz), 129.3 (q, *J* = 32.6 Hz), 129.8 (2C), 125.4 (q, *J* = 3.7 Hz, 2C), 124.2 (q, *J* = 270.4 Hz), 114.5, 44.7, 43.1, 40.9, 21.8; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -39.00, -62.47; HRMS (EI) m/z ($[M]^+$) calcd for $C_{14}H_{14}F_6S$: 328.0720, found: 328.0716.



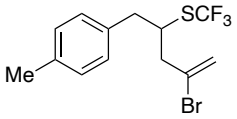

**(4-Methyl-1-(naphthalen-2-yl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3ma):** Purified by GPC (chloroform): 39 mg (63%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.84-7.79 (m, 3H), 7.64 (s, 1H), 7.50-7.44 (m, 2H), 7.33 (dd, *J* = 8.4, 1.6 Hz, 1H), 4.90 (s, 1H), 4.81 (s, 1H), 3.66 (tt, *J* = 7.3, 7.0 Hz, 1H), 3.20 (dd, *J* = 14.1, 6.4 Hz, 1H), 3.14 (dd, *J* = 14.1, 7.3 Hz, 1H), 2.45 (dd, *J* = 14.7, 6.8 Hz, 1H), 2.34 (dd, *J* = 14.7, 8.2 Hz, 1H), 1.72 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.4, 135.3, 133.4, 132.4, 131.2 (q, *J* = 304.7 Hz), 128.21, 128.16, 127.7, 127.6, 127.4, 126.2, 125.7, 114.3, 45.1, 42.8, 41.7, 21.8; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.82; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{17}H_{18}F_3S$: 311.1076, found: 311.1076.



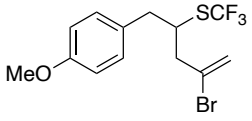

**2-(4-Methyl-2-((trifluoromethyl)thio)pent-4-en-1-yl)benzo[*b*]thiophene (3na):** Purified by GPC (chloroform): 38 mg (60%, 0.20 mmol scale); White solid; m.p. 33.4-36.2 °C; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.80-7.77 (m, 1H), 7.71 (dd, *J* = 6.9, 1.1 Hz, 1H), 7.34 (ddd, *J* = 7.7, 7.2, 1.3 Hz, 1H), 7.29 (ddd, *J* = 7.5, 7.2, 1.4 Hz, 1H), 7.11 (d, *J* = 0.7 Hz, 1H), 4.93 (s, 1H), 4.83 (s, 1H), 3.66 (tt, *J* = 7.2, 6.6 Hz, 1H), 3.32 (d, *J* = 6.2 Hz, 2H), 2.52 (dd, *J* = 14.6, 7.0 Hz, 1H), 2.37 (dd, *J* = 14.6, 7.8 Hz, 1H), 1.76 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.0, 140.5, 139.7 (2C), 131.1 (q, *J* = 304.8 Hz), 124.4, 124.1, 123.5, 123.1, 122.2, 114.5, 44.3, 42.6, 36.3, 21.8; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -39.01; HRMS (EI) m/z ($[M]^+$) calcd for $C_{15}H_{15}F_3S_2$: 316.0567, found: 316.0575.




**(4-Bromo-1-phenylpent-4-en-2-yl)(trifluoromethyl)sulfane (3hp):** Purified by GPC (chloroform): 35 mg (54%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.29-7.25 (m, 1H), 7.23-7.21 (m, 2H), 5.70 (dt, *J* = 1.8, 1.0 Hz, 1H), 5.58 (d, *J* = 1.8 Hz, 1H), 3.75 (tt, *J* = 7.3, 7.2 Hz, 1H), 3.07 (dd, *J* = 14.3, 6.7 Hz, 1H), 2.97 (dd, *J* = 14.3, 7.2 Hz, 1H), 2.77 (dd, *J* = 14.9, 7.2 Hz, 1H), 2.73 (dd, *J* = 14.9, 7.6 Hz, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 137.2, 130.9 (q, *J* = 304.9 Hz), 129.8, 129.4 (2C), 128.6 (2C), 127.1, 120.5, 46.2, 45.2, 40.5; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.56; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{12}H_{12}BrF_3S$: 323.9795, found: 323.9790. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 14.2 min, minor isomer: $t_R$ = 13.8 min.

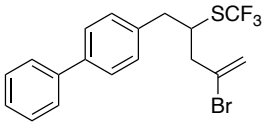



**(4-Bromo-1-(*p*-tolyl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3ip):** Purified by GPC (chloroform): 33 mg (49%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.15-7.09 (m, 4H), 5.70-5.69 (m, 1H), 5.58 (d, *J* = 1.8 Hz, 1H), 3.73 (tt, *J* = 7.3, 7.0 Hz, 1H), 3.02 (dd, *J* = 14.3, 6.7 Hz, 1H), 2.94 (dd, *J* = 14.3, 7.0 Hz, 1H), 2.77 (dd, *J* = 14.9, 7.0 Hz, 1H), 2.71 (dd, *J* = 14.9, 7.6 Hz, 1H), 2.34 (s, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 136.7, 134.0, 130.9 (q, *J* = 305.3 Hz), 129.9, 129.3 (4C), 120.4, 46.1, 45.3, 40.0, 21.1; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.51; HRMS (EI) m/z ([M]$^{+}$) calcd for $C_{13}H_{14}BrF_3S$: 337.9952, found: 337.9942. CHIRALCEL OJ-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 13.9 min, minor isomer: $t_R$ = 16.0 min.

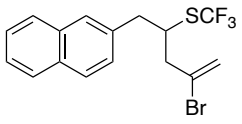



**(4-Bromo-1-(4-methoxyphenyl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3jp):** Purified by GPC (chloroform): 31 mg (44%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.15-7.12 (m, 2H), 6.88-6.84 (m, 2H), 5.70 (dt, *J* = 1.8, 1.0 Hz, 1H),

5.58 (d, $J$ = 1.8 Hz, 1H), 3.81 (s, 3H), 3.71 (tt, $J$ = 7.2, 7.0 Hz, 1H), 3.01 (dd, $J$ = 14.4, 6.6 Hz, 1H), 2.92 (dd, $J$ = 14.4, 7.1 Hz, 1H), 2.76 (dd, $J$ = 14.9, 7.1 Hz, 1H), 2.71 (dd, $J$ = 14.9, 7.7 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 130.9 (q, $J$ = 304.9 Hz), 130.5 (2C), 129.9, 129.1, 120.4, 113.9 (2C), 55.3, 46.0, 45.4, 39.6; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.54; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{13}H_{15}BrF_3OS$: 354.9974, found: 354.9989. CHIRALCEL OD-H column, 100/0 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 35.1 min, minor isomer: $t_R$ = 26.0 min.

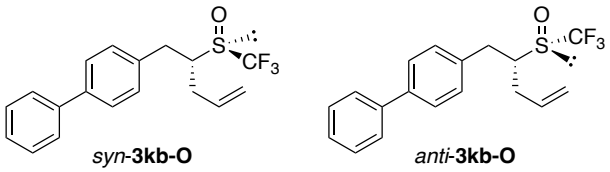



**(1-([1,1'-Biphenyl]-4-yl)-4-bromopent-4-en-2-yl)(trifluoromethyl)sulfane (3kp):** Purified by GPC (chloroform): 42 mg (52%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.61-7.54 (m, 4H), 7.46-7.42 (m, 2H), 7.36-7.32 (m, 1H), 7.30-7.28 (m, 2H), 5.72 (dt, $J$ = 1.8, 0.9 Hz, 1H), 5.59 (d, $J$ = 1.8 Hz, 1H), 3.80 (tt, $J$ = 7.2, 7.1 Hz, 1H), 3.11 (dd, $J$ = 14.4, 6.6 Hz, 1H), 3.01 (dd, $J$ = 14.4, 7.2 Hz, 1H), 2.81 (dd, $J$ = 14.9, 7.1 Hz, 1H), 2.75 (dd, $J$ = 14.9, 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.7, 140.0, 136.2, 130.9 (q, $J$ = 305.0 Hz), 129.9 (2C), 129.8, 128.8 (2C), 127.34, 127.29 (2C), 127.1 (2C), 120.6, 46.2, 45.2, 40.1; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.47; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{17}BrF_3S$: 401.0181, found: 401.0187. CHIRALCEL OJ-H column, 99.5/0.5 *n*-hexane/2-propanol, 1.0 mL/min, major isomer: $t_R$ = 23.6 min, minor isomer: $t_R$ = 35.7 min.




**(4-Bromo-1-(naphthalen-2-yl)pent-4-en-2-yl)(trifluoromethyl)sulfane (3mp):** Purified by GPC (chloroform): 43 mg (58%, 0.20 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.84-7.80 (m, 3H), 7.65 (s, 1H), 7.51-7.44 (m, 2H), 7.35 (dd, $J$ = 8.4, 1.7 Hz, 1H), 5.71 (dt, $J$ = 1.8, 0.9 Hz, 1H), 5.58 (d, $J$ = 1.8 Hz, 1H), 3.86 (tt, $J$ = 7.4, 7.2 Hz, 1H), 3.22 (dd, $J$ = 14.3, 6.8 Hz, 1H), 3.14 (dd, $J$ = 14.3, 7.2 Hz, 1H), 2.80 (dd, $J$ = 14.9, 7.0 Hz, 1H), 2.75 (dd, $J$ = 14.9, 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 134.7, 133.4, 132.5, 130.9 (q, $J$ = 305.1 Hz), 129.8, 128.4, 128.3, 127.73, 127.68, 127.3,

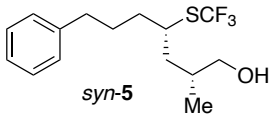
126.3, 125.9, 120.6, 46.2, 45.2, 40.7; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.45; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{15}BrF_3S$: 375.0024, found: 375.0021. CHIRALCEL OJ-H column, 99.7/0.3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 33.8 min, minor isomer: $t_R$ = 29.7 min.



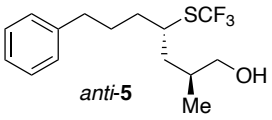

*syn*-**3kb-O** *anti*-**3kb-O**

**A 50:50 diastereomixture of 4-((*R*)-2-((*R*)-(trifluoromethyl)sulfinyl)pent-4-en-1-yl)-1,1'-biphenyl (*syn*-3kb-O) and 4-((*R*)-2-((*S*)-(trifluoromethyl)sulfinyl)pent-4-en-1-yl)-1,1'-biphenyl (*anti*-3kb-O) (relative stereochemistry was tentatively assigned):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 33 mg (66%, 0.15 mmol scale); White solid; m.p. 54.8-56.2 ℃; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.59-7.56 (m, 0.50 × 4H for *syn*-**3kb-O** and 0.50 × 4H for *anti*-**3kb-O**), 7.47-7.43 (m, 0.50 × 2H for *syn*-**3kb-O** and 0.50 × 2H for *anti*-**3kb-O**), 7.38-7.34 (m, 0.50 × 1H for *syn*-**3kb-O** and 0.50 × 1H for *anti*-**3kb-O**), 7.31-7.26 (m, 0.50 × 2H for *syn*-**3kb-O** and 0.50 × 2H for *anti*-**3kb-O**), 5.87 (ddt, *J* = 16.3, 9.3, 7.3 Hz, 0.50 × 1H for *syn*-**3kb-O**), 5.76 (ddt, *J* = 17.0, 10.4, 7.2 Hz, 0.50 × 1H for *anti*-**3kb-O**), 5.264 (d, *J* = 9.3 Hz, 0.50 × 1H for *syn*-**3kb-O**), 5.263 (d, *J* = 10.4 Hz, 0.50 × 1H for *anti*-**3kb-O**), 5.206 (d, *J* = 16.3 Hz, 0.50 × 1H for *syn*-**3kb-O**), 5.203 (d, *J* = 17.0 Hz, 0.50 × 1H for *anti*-**3kb-O**), 3.44-3.34 (m, 0.50 × 2H for *syn*-**3kb-O** and 0.50 × 1H for *anti*-**3kb-O**), 3.14-3.05 (m, 0.50 × 1H for *syn*-**3kb-O** and 0.50 × 1H for *anti*-**3kb-O**), 2.96 (dd, *J* = 15.0, 11.0 Hz, 0.50 × 1H for *anti*-**3kb-O**), 2.72-2.67 (m, 0.50 × 1H for *syn*-**3kb-O**), 2.62-2.50 (m, 0.50 × 1H for *syn*-**3kb-O** and 0.50 × 2H for *anti*-**3kb-O**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.5 (*syn*-**3kb-O**), 140.4 (*anti*-**3kb-O**), 140.3 (*syn*-**3kb-O**), 140.2 (*anti*-**3kb-O**), 135.4 (*syn*-**3kb-O**), 135.3 (*anti*-**3kb-O**), 132.3 (*syn*-**3kb-O**), 132.1 (*anti*-**3kb-O**), 129.9 (0.50 × 2C for *syn*-**3kb-O**), 129.6 (0.50 × 2C for *anti*-**3kb-O**), 128.8 (0.50 × 2C for *syn*-**3kb-O** and 0.50 × 2C for *anti*-**3kb-O**), 127.64 (0.50 × 2C for *syn*-**3kb-O**), 127.61 (0.50 × 2C for *anti*-**3kb-O**), 127.5 (*syn*-**3kb-O**), 127.4 (*anti*-**3kb-O**), 127.0 (0.50 × 2C for *syn*-**3kb-O** and 0.50 × 2C for *anti*-**3kb-O**), 125.9 (q, *J* = 333.4 Hz, 0.50 × 1C for *syn*-**3kb-O** and 0.50 × 1C for *anti*-**3kb-O**), 120.2 (*syn*-**3kb-O**), 120.1 (*anti*-**3kb-O**), 60.4 (*syn*-**3kb-O**), 59.7 (*anti*-**3kb-O**), 33.2 (*syn*-**3kb-O**), 32.0 (*anti*-**3kb-O**), 31.0 (*syn*-**3kb-O**), 30.1 (*anti*-**3kb-**

**O**); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -68.87 (*syn*-**3kb-O**), -69.44 (*anti*-**3kb-O**); HRMS (EI) m/z ($[M]^+$) calcd for $C_{18}H_{17}F_3OS$: 338.0952, found: 338.0942. CHIRALCEL OJ-H column, 98/2 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 33.4, 39.3 min, minor isomer: $t_R$ = 37.4, 64.0 min.

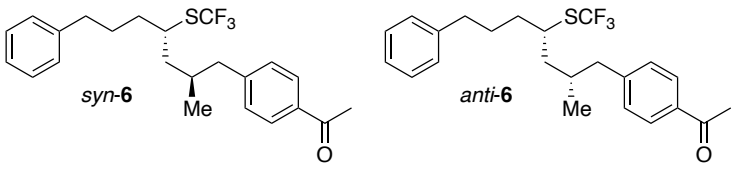


*syn*-**5**

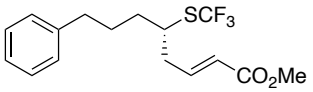


*anti*-**5**

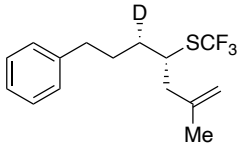
**A 53:47 diastereomixture of (2*R*,4*S*)-2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptan-1-ol (*syn*-5) and (2*S*,4*S*)-2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptan-1-ol (*anti*-5) (relative stereochemistry was tentatively assigned):** Purified by silica gel column chromatography with hexane/ethyl acetate (5/1, v/v): 39 mg (85%, 0.15 mmol scale); Colorless oil; $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 0.53 × 2H for *syn*-**5** and 0.47 × 2H for *anti*-**5**), 7.21-7.17 (m, 0.53 × 3H for *syn*-**5** and 0.47 × 3H for *anti*-**5**), 3.49-3.43 (m, 0.53 × 2H for *syn*-**5** and 0.47 × 2H for *anti*-**5**), 3.32-3.26 (m, 0.53 × 1H for *syn*-**5**), 3.24-3.19 (m, 0.47 × 1H for *anti*-**5**), 2.69-2.57 (m, 0.53 × 2H for *syn*-**5** and 0.47 × 2H for *anti*-**5**), 1.98-1.88 (m, 0.53 × 1H for *syn*-**5**), 1.86-1.73 (m, 0.53 × 4H for *syn*-**5** and 0.47 × 5H for *anti*-**5**), 1.72-1.63 (m, 0.53 × 1H for *syn*-**5** and 0.47 × 1H for *anti*-**5**), 1.50-1.37 (m, 0.53 × 1H for *syn*-**5** and 0.47 × 1H for *anti*-**5**), 1.30 (br, 0.53 × 1H for *syn*-**5** and 0.47 × 1H for *anti*-**5**), 0.933 (d, $J$ = 6.6 Hz, 0.53 × 3H for *syn*-**5**), 0.929 (d, $J$ = 6.7 Hz, 0.47 × 3H for *anti*-**5**); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.83 (*anti*-**5**), 141.81 (*syn*-**5**), 131.3 (q, $J$ = 304.4 Hz, 0.53 × 1C for *syn*-**5** and 0.47 × 1C for *anti*-**5**), 128.4 (0.53 × 4C for *syn*-**5** and 0.47 × 4C for *anti*-**5**), 125.9 (0.53 × 1C for *syn*-**5** and 0.47 × 1C for *anti*-**5**), 68.1 (*anti*-**5**), 67.4 (*syn*-**5**), 44.5 (*anti*-**5**), 44.4 (*syn*-**5**), 39.1 (*syn*-**5**), 38.7 (*anti*-**5**), 36.3 (*anti*-**5**), 35.6 (*anti*-**5**), 35.5 (*syn*-**5**), 34.5 (*syn*-**5**), 33.2 (*anti*-**5**), 33.0 (*syn*-**5**), 28.0 (*anti*-**5**), 27.8 (*syn*-**5**), 16.7 (*syn*-**5**), 16.0 (*anti*-**5**); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ -38.74 (*anti*-**5**), -38.88 (*syn*-**5**); HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{22}F_3OS$: 307.1338, found: 307.1322. CHIRALCEL OD-H column, 98.5/1.5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 27.4, 31.0 min, minor isomer: $t_R$ = 25.3, 34.9 min.



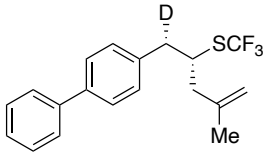

**A 55:45 diastereomixture of 1-(4-((2*R*,4*S*)-2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptyl)phenyl)ethan-1-one (*syn*-6) and 1-(4-((2*S*,4*S*)-2-methyl-7-phenyl-4-((trifluoromethyl)thio)heptyl)phenyl)ethan-1-one (*anti*-6) (relative stereochemistry was tentatively assigned):** Purified by silica gel column chromatography with hexane/ethyl acetate (20/1, v/v): 47 mg (77%, 0.15 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 7.31-7.27 (m, 0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 7.22-7.19 (m, 0.55 × 3H for *syn*-**6** and 0.45 × 3H for *anti*-**6**), 7.18-7.14 (m, 0.55 × 2H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 3.30-3.22 (m, 0.55 × 1H for *syn*-**6**), 3.22-3.15 (m, 0.45 × 1H for *anti*-**6**), 2.70 (dd, *J* = 13.2, 6.0 Hz, 0.55 × 1H for *syn*-**6**), 2.65-2.62 (m, 0.55 × 1H for *syn*-**6** and 0.45 × 1H for *anti*-**6**), 2.60-2.57 (m, 0.45 × 1H for *anti*-**6**), 2.59 (s, 0.45 × 3H for *anti*-**6**), 2.58 (s, 0.55 × 3H for *syn*-**6**), 2.50 (dd, *J* = 13.2, 7.8 Hz, 0.45 × 1H for *anti*-**6**), 2.40 (dd, *J* = 13.2, 8.3 Hz, 0.55 × 1H for *syn*-**6**), 2.12-2.03 (m, 0.45 × 1H for *anti*-**6**), 1.97-1.88 (m, 0.55 × 1H for *syn*-**6**), 1.80-1.66 (m, 0.55 × 4H for *syn*-**6** and 0.45 × 4H for *anti*-**6**), 1.60-1.55 (m, 0.55 × 3H for *syn*-**6** and 0.45 × 2H for *anti*-**6**), 1.45-1.38 (m, 0.45 × 1H for *anti*-**6**), 0.87 (t, *J* = 6.8 Hz, 0.55 × 3H for *syn*-**6** and 0.45 × 3H for *anti*-**6**); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.9 (*anti*-**6**), 197.8 (*syn*-**6**), 146.4 (*syn*-**6**), 146.3 (*anti*-**6**), 141.8 (*anti*-**6**), 141.7 (*syn*-**6**), 135.2 (0.55 × 1C for *syn*-**6** and 0.45 × 1C for *anti*-**6**), 131.3 (q, *J* = 304.1 Hz, *syn*-**6**), 131.2 (q, *J* = 304.2 Hz, *anti*-**6**), 129.33 (2C for *syn*-**6**), 129.31 (2C for *anti*-**6**), 128.5 (4C for *syn*-**6**), 128.42 (4C for *anti*-**6**), 128.37 (2C for *anti*-**6**), 128.3 (2C for *syn*-**6**), 126.0 (0.55 × 1C for *syn*-**6** and 0.45 × 1C for *anti*-**6**), 44.5 (*anti*-**6**), 44.1 (*syn*-**6**), 43.6 (*anti*-**6**), 43.1 (*syn*-**6**), 42.4 (*syn*-**6**), 41.8 (*anti*-**6**), 36.1 (*anti*-**6**), 35.49 (*anti*-**6**), 35.45 (*syn*-**6**), 34.3 (*syn*-**6**), 32.4 (*syn*-**6**), 31.9 (*anti*-**6**), 28.0 (*anti*-**6**), 27.5 (*syn*-**6**), 26.6 (0.55 × 1C for *syn*-**6** and 0.45 × 1C for *anti*-**6**), 19.4 (*syn*-**6**), 19.0 (*anti*-**6**); $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.64 (*anti*-**6**), -38.90 (*syn*-**6**); HRMS (APCI) m/z ([M+H]$^{+}$) calcd for $C_{23}H_{28}F_3OS$: 409.1807, found: 409.1798. CHIRALPAK AD-H column, 99.5/0.5 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 19.4, 24.8 min, minor isomer: $t_R$ = 18.4, 24.0 min.




**Methyl (*S*,*E*)-8-phenyl-5-((trifluoromethyl)thio)oct-2-enoate (7):** Purified by silica gel column chromatography with hexane/ethyl acetate (40/1 → 5/1, v/v): 41 mg (82%, 0.15 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.22-7.16 (m, 3H), 6.89 (dt, *J* = 15.6, 7.4 Hz, 1H), 5.89 (dt, *J* = 15.6, 1.4 Hz, 1H), 3.75 (s, 3H), 3.34-3.27 (m, 1H), 2.69-2.57 (m, 4H), 1.90-1.79 (m, 1H), 1.78-1.69 (m, 2H), 1.68-1.60 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 166.4, 143.7, 141.5, 130.9 (q, *J* = 304.6 Hz), 128.5 (2C), 128.3 (2C), 126.0, 124.3, 51.7, 44.8, 38.1, 35.3, 33.7, 28.2; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.14; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{16}H_{20}F_3O_2S$: 333.1131, found: 333.1137. CHIRALCEL OD-H column, 98/2 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 28.0 min, minor isomer: $t_R$ = 31.2 min.




**((4*S*,5*S*)-2-Methyl-7-phenylhept-1-en-4-yl-5-*d*)(trifluoromethyl)sulfane (3aa-$d_1$):** Purified by GPC (chloroform): 38 mg (66%, 0.20 mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H), 7.21-7.16 (m, 3H), 4.85-4.84 (m, 1H), 4.74-4.73 (m, 1H), 3.32 (dt, *J* = 7.7, 7.5 Hz, 1H), 2.65 (ddd, *J* = 13.8, 8.9, 6.4 Hz, 1H), 2.59 (ddd, *J* = 13.8, 8.8, 6.6 Hz, 1H), 2.42 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.34 (dd, *J* = 14.2, 5.9 Hz, 1H), 1.87-1.79 (m, 1H), 1.77-1.69 (m, 1H), 1.71 (s, 3H), 1.61-1.56 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.8, 141.5, 131.3 (q, *J* = 304.3 Hz), 128.39 (2C), 128.36 (2C), 125.9, 114.0, 44.1, 43.9, 35.5, 33.4 (t, *J* = 19.4 Hz), 27.8, 21.8; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -39.08; HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{19}DF_3S$: 290.1295, found: 290.1276. CHIRALCEL OJ-H column, 99.7/0.3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 26.2 min, minor isomer: $t_R$ = 30.5 min.




**((1*S*,2*R*)-1-([1,1'-Biphenyl]-4-yl)-4-methylpent-4-en-2-yl-1-*d*)(trifluoromethyl)sulfane (3ja-$d_1$):** Purified by GPC (chloroform): 30 mg (45%, 0.20

mmol scale); Colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.60-7.57 (m, 2H), 7.56-7.53 (m, 2H), 7.45-7.41 (m, 2H), 7.36-7.31 (m, 1H), 7.28-7/25 (m, 2H), 4.91 (s, 1H), 4.81 (s, 1H), 3.59 (dt, *J* = 7.7, 6.8 Hz, 1H), 3.05 (d, *J* = 6.2 Hz, 1H), 2.45 (dd, *J* = 14.6, 6.9 Hz, 1H), 2.34 (dd, *J* = 14.6, 8.1 Hz, 1H), 1.73 (s, 3H); $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 141.4, 140.8, 139.8, 136.8, 131.2 (q, *J* = 304.7 Hz), 129.8 (2C), 128.8 (2C), 127.3, 127.2 (2C), 127.0 (2C), 114.2, 45.0, 42.7, 40.7 (t, *J* = 19.6 Hz), 21.8; $^{19}$F{$^{1}$H} NMR (376 MHz, $CDCl_3$) δ -38.85; HRMS (EI) m/z ($[M]^+$) calcd for $C_{19}H_{18}DF_3S$: 337.1217, found: 337.1217. CHIRALCEL OJ-H column, 99.7/0.3 *n*-hexane/2-propanol, 0.5 mL/min, major isomer: $t_R$ = 26.2 min, minor isomer: $t_R$ = 30.5 min.

## References and Notes


[1] Y. Kojima, Y. Nishii, K. Hirano, *Angew. Chem. Int. Ed.* **2024**, *63*, e20240337.

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[7] The author consider that epimerization of the α-$SCF_3$ alkyl copper intermediate proceeds via stereoinvertive transmetalation with another copper complex. Related reactions via stereoinvertive Cu/Pd transmetalation: a) K. M. Logan, K. B. Smith, M. K. Brown, *Angew. Chem. Int. Ed.* **2015**, *54*, 5228-5231; b) K. Semba, K. Akiyama, H. Zheng, R. Kameyama,

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# Conclusion

This thesis describes the synthesis of $CF_3$- and $SCF_3$-substituted compounds using fluorine-containing building blocks. A variety of $C(sp^3)$–$CF_3$ and $C(sp^3)$–$SCF_3$ compounds, which are difficult to prepare by other means, are now easily accessible from simple and readily available starting substrates.

In Chapter 1, the author achieved the copper-catalyzed regio- and enantioselective hydroallylation of $CF_3$-substituted alkenes with hydrosilanes and allylic chlorides. The judicious choice of biphosphine ligands and CsOPiv base facilitated the otherwise challenging α-functionalization relative to the $CF_3$ group, avoiding an undesired β-F elimination successfully. The asymmetric induction was also achieved using the optically active DTBM-SEGPHOS ligand in a combination with CsOPiv and 18-crown-6.

In Chapter 2, with diborons instead of hydrosilanes, the allylboration of $CF_3$-substituted alkenes proceeded to introduce Bpin substituent at β-position to $CF_3$. Also in this case, the choice of Cs base was crucial, enabling the difunctionalization of $CF_3$-alkenes over the β-F elimination. Furthermore, subsequent transformations of the Bpin moiety in the allylborated products allowed the successful synthesis of $CF_3$-substituted compounds with various functional groups at the β-position.

In Chapter 3, a similar Cu-catalyzed alkene functionalization was applied for the synthesis of $SCF_3$-substituted compounds, which are also promising fluorinated molecules due to the high lipophilicity and electron-withdrawing nature of $SCF_3$ comparable to those of $CF_3$. In the presence of copper catalyst, the regio- and enantioselective hydroboration of $SCF_3$-substituted alkenes with pinacolborane efficiently provided optically active $SCF_3$-substituted alkylboronates. In this case, the choice of biphosphine ligands with bulky substituents at remote positions was critically important. The Bpin substituent in the product could be further transformed, enabling the introduction of various functional groups at the α-position to $SCF_3$.

In Chapter 4, the corresponding hydroallylation reaction was achieved using hydrosilanes and allylic electrophiles instead of pinacolborane. In the three-component coupling reaction involving $SCF_3$-alkenes, the electrophilicity of the coupling partner significantly influenced both chemo- and enantioselectivity of the reaction. The author uncovered that the α-$SCF_3$ alkyl copper intermediate undergoes epimerization in the reaction system, and experimentally and computationally demonstrated that the leaving group of allylic electrophiles greatly affects the enantiopurity of the product.

As mentioned above, the author successfully developed modular synthetic approaches

to the $CF_3$- and $SCF_3$-substituted compounds. The author is confident that these significant discoveries will pave the way for further advancements in the synthesis and application of alkyl $CF_3$/$SCF_3$ compounds. Unlike functionalizations of nonfluorinated reactive alkenes such as styrene derivatives or α,β-unsaturated esters, attempts to functionalize $CF_3$- and $SCF_3$-substituted alkenes often presents challenges in controlling chemoselectivity and encounters poor nucleophilicity of the alkylcopper intermediates. The accomplishments described herein are believed to not only facilitate the synthesis of $CF_3$/$SCF_3$-substituted compounds but also hold great potential for stereoselective synthesis of still inaccessible chiral fluorinated molecules.

# List of Publications

**1.** Copper-Catalyzed Regio- and Enantioselective Hydroallylation of 1-Trifluoromethylalkenes: Effect of Crown Ether
Yuki Kojima, Masahiro Miura, Koji Hirano
*ACS Catal.* **2021**, *11*, 11663-11670.

**2.** Ligand-Enabled Copper-Catalyzed Regio- and Stereoselective Allylboration of 1-Trifluoromethylalkenes
Yuki Kojima, Yuji Nishii, Koji Hirano
*Org. Lett.* **2022**, *24*, 7450-7454.

**3.** Asymmetric Synthesis of $SCF_3$-Substituted Alkylboronates by Copper-Catalyzed Hydroboration of 1-Trifluoromethylthioalkenes
Yuki Kojima, Yuji Nishii, Koji Hirano
*Angew. Chem. Int. Ed.* **2024**, *63*, e202403337.

**4.** Copper-Catalyzed Regio- and Enantioselective Hydroallylation of 1-Trifluoromethylthioalkenes: Leaving Group-Dependent Stereochemistry
Yuki Kojima, Shinichi Suda, Wataru Kanna, Yuji Nishii, Satoshi Maeda, Koji Hirano
*Manuscript in preparation*

# Supplementary List of Publications

**1.** Synthesis of highly condensed phospholes by the Lewis acid-assisted dehydrogenative Mallory reaction under visible light irradiation
Ikki Kamiyoshi, Yuki Kojima, Shibo Xu, Kosuke Yasui, Yuji Nishii, Koji Hirano
*Chem. Sci.* **2024**, *15*, 20413-20420.

**2.** Facile Preparation of $SeCF_3$-substituted Alkenes from Alkenyl Iodides and Selenium Powder
Haruka Matsui, Yuki Kojima, Koji Hirano

*Chem. Lett.* **2024**, *53*, upae076.

**3.** Direct Synthesis of Benzoselenophene and Benzothiophene Derivatives from 1,1-Diarylethelenes and Biaryls by Chalcogen Cation-Mediated Successive Bond Formation
Hiroki Iwamoto, Yuki Kojima, Kazutoshi Nishimura, Kosuke Yasui, Koji Hirano
*Org. Lett.* **2024**, *26*, 1006-1010.

**4.** Copper-mediated Trifluoromethylthiolation of Alkenyl Iodides with $AgSCF_3$
Yuki Kojima, Koji Hirano
*Chem. Lett*. **2023**, *52*, 791-793.

**5.** Pd-catalysed, Ag-assisted C2-H alkenylation of benzophospholes
Yu Tokura, Shibo Xu, Yuki Kojima, Masahiro Miura, Koji Hirano
*Chem. Commun*. **2022**, *58*, 12208-12211.

**6.** Synthesis of *gem*-Difluoroalkenes by Copper-catalyzed Regioselective Hydrodefluorination of 1-Trifluoromethylalkenes
Yuki Kojima, Tatsuaki Takata, Koji Hirano, Masahiro Miura
*Chem. Lett*. **2020**, *49*, 637-640.

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