Development of new carbon-carbon bond forming reactions through 1,4-migration of rhodium

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**NANYANG
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SINGAPORE

**DEVELOPMENT OF NEW CARBON-CARBON BOND
FORMING REACTIONS THROUGH 1,4-MIGRATION
OF RHODIUM**

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List of abbreviations

δ	chemical shift (ppm)
$^{\circ}\text{C}$	degree centigrade
Ac	acetyl
acac	acetylacetonate
Ar	aryl (substituted aromatic ring) or argon atmosphere
BBN	9-borabicyclo[3.3.1]nonane
binap	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
biphep	2,2'-bis(diphenylphosphino)-1,1'-biphenyl
Bn	benzyl
Boc	<i>tert</i> -butyloxycarbonyl
brs	broad singlet
Bu	butyl
Bz	benzoyl
cat.	catalytic
cod	1,5-cyclooctadiene
coe	cyclooctene
cm^{-1}	wave number
Cy	cyclohexyl
d	doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DFT	density functional theory
DME	1,2-dimethoxyethane

DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
dppf	1,1'-bis(diphenylphosphino)ferrocene
dr	diastereomeric ratio
EDG	electron donating group
ee	enantiomeric excess
Eq	equation
equiv	equivalent
Et	ethyl
EWG	electron withdrawing group
FTIR	Fourier Transform Infrared Spectroscopy
Fc	ferrocenyl
g	gram
h	hour
Hz	hertz
<i>J</i>	coupling constants
k	reaction rate
kcal	kilocalorie
LDA	lithium diisopropylamide
LG	leaving group
LHMDS	lithium bis(trimethylsilyl)amide

M	concentration (N, mol/dm ⁻³)
M ⁺	parent ion peak (mass spectrum)
m	multiplet
Me	methyl
mg	milligram
MHz	megahertz
min	minutes
mL	milliliters
mmol	millimole
MOP	2-(Diphenylphosphino)-2'-methoxy-1,1'-binaphthyl
Ms	methanesulfonyl
NBS	<i>N</i> -bromosuccinimide
NMR	nuclear magnetic resonance
Ns	4-nitrobenzenesulfonyl
OTf	trifluoromethanesulfonate
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
quient	quientet
Rh	rhodium
rt	room temperature
s	singlet
segphos	4,4'-Bi-1,3-benzodioxole-5,5'-diylbis(diphenylphosphane)

sept	septet
sext	sextet
t	triplet
Tf	trifluoromethanesulfonyl
tfb	tetrafluorobenzobarrelenes
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	<i>N,N,N',N'</i> -tetramethylethylenediamine
TMS	trimethylsilyl
Ts	<i>para</i> -toluenesulfonyl

Abstract

This thesis documents our attempts to advance the chemistry of C–C bond forming reactions via 1,4-Rh shift.

Chapter 1 is an introduction of rhodium-catalyzed C–C bond forming reactions and 1,4-migration of rhodium. In the first section of Chapter 1, catalytic reactions of rhodium with organometallics are discussed. This section has been further divided into three subsections: 1,4-additions to alkenes, 1,2-additions to carbonyl and imine compounds, and additions to alkynes. The second section is an introduction of 1,4-migration of rhodium and its applications to catalytic C–C bonds forming reactions.

Chapter 2 describes our discovery of a reaction of potassium aryloxymethyltrifluoroborates with α,β -unsaturated carbonyl compounds in the presence of a chiral diene–rhodium catalyst, which introduces 2-methoxyaryl groups at the β -position of the α,β -unsaturated carbonyl compounds with high enantioselectivity in high yields. It may be surprising that these alkylboron reagents gave the hydroarylation products. The reaction is assumed to proceed through 1,4-Rh shift from aryloxymethyl–Rh intermediate to 2-methoxyaryl–Rh. The wide availability of phenol derivatives makes this asymmetric conjugate arylation synthetically useful.

Chapter 3 describes the first example of catalytic arylstannylation of alkynes. The reaction of arylstannanes ArSnR_3 with unfunctionalized alkynes was found to proceed in the presence of a rhodium catalyst and a catalytic amount of zinc chloride to give *ortho*-alkenylarylstannanes with high selectivity in high yields. The catalytic cycle is very unique, consisting of three transmetalation steps, from Sn to Rh, Rh to

Zn, and Zn to Sn, in addition to arylrhodation of the alkyne followed by 1,4-migration of Rh from the 2-arylalkenyl carbon to the *ortho*-alkenylaryl carbon.

Chapter 4 describes the first example of carbozincation of unfunctionalized alkynes using Rh catalysis. The addition of arylzinc reagents ArZnCl to alkynes was found to be catalyzed by rhodium complexes in the presence of a catalytic amount of zinc chloride. The selectivity in giving 2-arylalkenylzinc species or *ortho*-alkenylarylzinc species, the latter of which is generated through 1,4-Rh migration from alkenyl to aryl in the catalytic cycle, is controlled by the ligand on rhodium. Ligands cod and binap gave 2-arylalkenylzinc species and *ortho*-alkenylarylzinc species, respectively, with high selectivity.

CHAPTER 1

Introduction of Rhodium-Catalyzed Carbon–Carbon Bond Forming Reactions and 1,4-Migration of Rhodium

1.1 Introduction of the rhodium-catalyzed carbon–carbon bond forming reactions

The carbon–carbon bond is viewed as the heart of organic chemistry, and considerable attention has been paid to develop new synthetic methods for forming new carbon–carbon bonds over the last several decades. The transition metal-catalyzed reactions in this regard have become fashionable since application of palladium complexes to catalytic cross-coupling reactions. Specifically, Kumada,^{1a} Stille,^{1b} Mirozoki-Heck,^{1c} Suzuki-Miyaura,^{1d} Sonogashira^{1e}, Hiyama,^{1f} and Tsuji-Trost^{1g} are the famous examples of Pd-catalyzed coupling reactions. Like these cross-coupling reactions, transition-metal catalysts have proved to be extremely powerful tools for C–C bond formation.

The rhodium complexes have also been frequently used in combination with the organometallic reagents to construct new carbon–carbon bonds. In this section, such addition reactions are discussed according to the following classification: 1,4-addition to electron-deficient olefins, 1,2-addition to carbonyl and imine compounds, and addition to alkynes.

1.1.1 Rhodium-catalyzed 1,4-addition to electron-deficient olefins

The copper-catalyzed conjugate addition reaction² was most commonly used before the discovery of the rhodium-catalyzed conjugate addition. Copper complexes can catalyze the 1,4-addition reaction in good yields with high chemoselectivities using Grignard reagents, organolithium reagents, or organozinc reagents as organometallics, at a very low temperature under anhydrous conditions. The strict reaction conditions have restricted its application.

As a milestone of rhodium catalysis, Miyaura reported in 1997 that a Rh(I) complex can catalyze the 1,4-addition of aryl/alkenylboronic acids to enones in high yields (Scheme 1.1).^{3a} In this report, a wide range of aromatic and vinylic groups can be introduced to enones at the β -position using $[\text{Rh}(\text{acac})(\text{CO})_2]/\text{dppb}$ as the catalyst in aqueous solvent at 50 °C. It is worth noting that bisphosphine ligands with a larger bite angle had better catalytic activity under the same reaction conditions. The absence of water led to low conversion of the substrate, since water in this reaction might accelerate the hydrolysis step. No 1,2-addition to the enone was observed, which is ascribed to the relatively low reactivity of organoboron reagents. Obviously, the mildness of the reaction conditions makes it more attractive than the copper-catalyzed 1,4-addition.

Scheme 1.1. First Example of Rhodium-Catalyzed Hydroarylation/Alkenylation of Enones

$\text{R}^1 = \text{H, Me, Ph}$; $\text{R}^2 = \text{H, Me, Bu, Ph}$; $\text{R}^3 = \text{aryl, alkenyl}$

aqueous solvent: DMF/ H_2O (6/1), cyclohexane/ H_2O (6/1), or MeOH/ H_2O (6/1)

Ligand effect on reactivity: $\text{dppb} > \text{dppp} > \text{TFP} > \text{dppe} > \text{PPh}_3$

Hayashi and Miyaura reported the first asymmetric arylation/alkenylation reaction of enones with arylboron reagents in 1998.^{3b} In this reaction, the β -arylated ketones were produced in high yields with excellent enantioselectivities by treating the enones with arylboronic acid in dioxane/ H_2O (10/1) at 100 °C under the catalysis of a Rh(I) complex generated in situ from (*S*)-binap and $[\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]$. Compared with the initial report by Miyaura in 1997,^{3a} the rhodium precursor was changed from $[\text{Rh}(\text{acac})(\text{CO})_2]$ to $[\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]$ due to the selective in situ generation of a Rh-(*S*)-binap species. For instance, 2-cyclohexenone (**1**) reacted with phenylboronic acid (**2**) to give the desired hydroarylation product **3** in only 43%

ee and 15% yield with $[\text{Rh}(\text{acac})(\text{CO})_2]$ as the rhodium source (entry 2, Scheme 1.2). On the contrary, the use of $[\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]$ led to a 64% yield and 97% ee (entry 1, Scheme 1.2). Consistently, the use of isolated $[\text{Rh}(\text{acac})((S)\text{-binap})]$ led to exactly the same results (64% yield and 97% ee) (entry 3, Scheme 1.2), suggesting that Rh–(*S*)-binap species is a key intermediate in the catalytic cycle. A main side reaction is hydrolysis of the arylboronic acids catalyzed by the rhodium complex, rather than 1,2-addition to the enone. The authors found that the yield was improved by using a large excess amount of $\text{PhB}(\text{OH})_2$ (**2**) (entry 4, Scheme 1.2).

Scheme 1.2. Rhodium-Catalyzed Asymmetric Hydroarylation of Enones

entry	Rh complex	equiv of $\text{PhB}(\text{OH})_2$	yield (%)	ee (%)
1	$[\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]$	1.4	64	97
2	$[\text{Rh}(\text{acac})(\text{CO})_2]$	1.4	15	43
3	$[\text{Rh}(\text{acac})((S)\text{-binap})]^a$	1.4	64	97
4	$[\text{Rh}(\text{acac})(\text{C}_2\text{H}_4)_2]$	2.5	93	97

^a without additional binap added

In 2002, Hayashi reported a mechanism generally accepted for the rhodium-catalyzed hydroarylation of enones under aqueous conditions.^{3c} Scheme 1.3 displays a catalytic cycle for the asymmetric arylation reaction of 2-cyclohexenone with phenylboronic acid catalyzed by Rh/(*S*)-binap complex. The reaction involves three steps, that is, transmetalation, phenylrhodation (π -coordination and insertion), and hydrolysis. It is interesting that rhodium in the catalytic cycle maintains the oxidation state of +1.

Scheme 1.3. A Catalytic Cycle for Rhodium-Catalyzed Hydrophenylation of 2-Cyclohexenone

Thus, phenylboronic acid (**2**) undergoes transmetalation with a HO-Rh species **A** to generate the Ph-Rh intermediate **B** and $\text{B}(\text{OH})_3$ (Scheme 1.3).^{3c} The carboryhodation of 2-cyclohexenone (**3**) with the Ph-Rh intermediate **B** provides the oxa- π -allylrhodium intermediate **D**, along with the generation of a new stereogenic carbon center. The intermediate **D** undergoes protonolysis to produce the 1,4-addition product and to regenerate the HO-Rh species in the presence of a protic solvent (usually water or alcohols). The Ph-Rh species **B** also undergoes hydrolysis with a proton source to give benzene as the side product. Thus, an excess amount of arylboron reagent is necessary to achieve acceptable yields of arylation products. Finding a more active catalyst is a way to minimize the amount of arylboron reagents.

$[\text{Rh}(\text{OH})((S)\text{-binap})]_2$, which is prepared from $[\text{RhCl}((S)\text{-binap})]_2$, was used as a more active catalyst for these arylation reactions in 2002.^{3c} For instance, the use of $[\text{Rh}(\text{OH})((S)\text{-binap})]_2$ instead of $[\text{Rh}(\text{acac})((S)\text{-binap})]$ realized the 1,4-addition reaction of phenylboron reagent **2** to 2-cyclohexenone (**1**) in the presence of 2.5 equiv of the boron reagent at a much lower temperature (35 °C) (Scheme 1.4a). At this low temperature, both the isolated yield and enantioselectivity of the product were increased. Some stoichiometric reactions were performed to explain the enhanced reactivity of $[\text{Rh}(\text{OH})((S)\text{-binap})]_2$. As is shown in Scheme 1.4b, the rhodium–hydroxide complex **4** is rapidly transmetalated with phenylboronic acid, which produces the phenylrhodium complex **5** in >99% conversion at ambient temperature within 30 min. In contrast, the conversion is <8% for the rhodium–acac complex **6** under the same conditions (Scheme 1.4b). A higher temperature (80 °C) is required for the transmetalation on $[\text{Rh}(\text{acac})((S)\text{-binap})]$. These experimental results indicate that the transmetalation of organoboronic acids takes place at a higher rate on $[\text{Rh}(\text{OH})((S)\text{-binap})]_2$ (**4**) than on the corresponding acac complex **6**. Since then, the rhodium–acac complexes have been rarely employed in the rhodium-catalyzed addition reactions.

Scheme 1.4. [Rh(OH)((S)-binap)]₂-Catalyzed Asymmetric Arylation Reaction

Undeniably, the choice of ligands is another fundamental issue for the Rh-catalyzed 1,4-addition reaction and is based on three criteria, namely, catalytic activity, enantioselectivity, and ease of synthesis. Recently, much attention has been paid to the design and synthesis of chiral ligands for enantioselective variant of Rh-catalyzed hydroarylation reactions. The chiral ligands in these reactions can be classified into two families, bidentate phosphorus and diene ligands. Some of these chiral ligands are compared for their enantioselectivity in the rhodium-catalyzed enantioselective 1,4-addition of phenylboron reagents to 2-cyclohexenone as a model system, which is illustrated in Schemes 1.5 and 1.6. Notably, this limited comparison is not sufficient enough to predict which ligand works better for the rhodium-catalyzed 1,4-addition of specific enones, since some ligands may show higher enantioselectivity for other substrates such as linear enones.

Scheme 1.5. Selected Bidentate Phosphorous Ligands

Hayashi and Miyauro reported the first example of Rh(I)-catalyzed asymmetric 1,4-addition of arylboronic acids to enones, where (S)-binap worked as the chiral ligand in 1998.^{3b} Similar to (S)-binap, many other bisphosphine ligands with an axially-chiral biaryl backbone, including (R)-P-Phos (**L₂**), MeO-biphep (**L_{3a}**, **L_{3b}**, and **L_{3c}**), difluorophos (**L₄**), and synphos (**L_{5a}**, **L_{5b}**, and **L_{5c}**) (Scheme 1.5), were successfully employed to the model reaction in >90% ee.⁴ The bisphosphine ligand

L₆⁵ with the planar-chiral cyrhetren and P-chiral bisphosphine ligand (*R,R*)-QuinoxP* **L**₇⁶ are reported to produce the hydroarylation product in high yield with high selectivity.

Notably, in 2003, Miyaura disclosed that [Rh(OH)(cod)]₂ (cod = 1,5-cyclooctadiene) can smoothly catalyze the hydroarylation reaction of PhB(OH)₂ (**2**) to methyl vinyl ketone (**7**) in DME/H₂O even at 0 °C (Eq 1.1).⁷

In 2003, Bn-nbd, a chiral diene ligand based on a *C*₂-symmetric norbornadiene, was firstly employed to the rhodium-catalyzed asymmetric 1,4-addition.^{8a} The model reaction gave rise to the arylation product in 87% yield and 96% ee, with [RhCl((*S,S*)-**L**_{8b})]₂ as the catalyst (Scheme 1.6). In 2006, Hayashi and his coworkers disclosed that the transmetalation of arylboron reagents took place at a faster rate on the Rh/cod complex than on the Rh/binap complex under the same conditions.⁹ The higher catalytic activity of the Rh/diene system for these reactions has encouraged organic chemists to develop diene ligands. Since then, the use of chiral diene ligands has been dramatically developed for rhodium-catalyzed asymmetric 1,4-addition during the past 16 years.¹⁰ A variety of bicyclic diene scaffolds have been successfully employed as ligands to generate the target arylation product in high yield and enantioselectivity. They are bicyclo[2,2,1]heptadiene variations (**L**_{8a}, **L**_{8b}, and **L**_{8c}),⁸ bicyclo[2,2,2]octadiene variations (**L**_{9a}, **L**_{9b}, **L**_{9c}, and **L**_{9d}),^{11a-11d} bicyclo[3,3,1]nonadiene variations (**L**_{10a} and **L**_{10b}),¹² and bicyclo[3,3,2]decadiene variation **L**₁₁.^{12b} Although many reported diene ligands have been applied to the transition metal-catalyzed reactions, they are still not as

popular as bisphosphines ligands. One of the reasons is that their synthetic methods have not been developed well. Therefore, searching for the novel enantioselective synthesis of chiral diene ligands is attractive and challenging. Another drawback of diene ligands is their relatively weak coordination ability towards the transition metals. However, diene ligands are undeniably the ‘rising stars’ thanks to their high catalytic activity and selectivity for the rhodium-catalyzed 1,4-addition reactions.

Scheme 1.6. Selected Examples of Chiral Diene Ligands

In addition to organoborons, organostannanes were successfully used for the rhodium-catalyzed 1,4-addition reactions in 1998 by Oi and his coworkers (Scheme 1.7a).^{13a} The addition products were formed in high yields by treating enones with a slight excess amount of ArSnMe_3 in the presence of a Rh/cod catalyst in THF at 60 °C. The yields were low with bulkier organostannanes ArSnBu_3 and Ar_4Sn . The authors also reported that the presence of water in the reaction system enhanced the yields of some difficult substrates.^{13c} Interestingly, the phosphorus ligands showed very low catalytic activity for this catalytic reaction, while the cod ligand showed very high catalytic ability. Hayashi successfully employed the Rh/chiral diene system to catalyze these reactions, which resulted in very high yields and enantioselectivities (Scheme 1.7b).^{13d} For instance, the reaction of PhSnMe_3 (**9**) with 2-cyclohexenone (**1**) in the presence of Rh/(*R,R*)-**L**_{8b} catalyst and 0.06 equiv of NaOMe in toluene at 60 °C gave a high yield of the arylation product **3** after acidic workup. The use of binap instead of Bn-nbd led to a yield of less than 10% for the arylation product **3**.

Scheme 1.7. Rh-Catalyzed Arylation of Enones/Enonates with Arylstannanes

Compared with organoborons and organostannanes, organozinc reagents are considered as more reactive organometallic reagents for the transition metal-

catalyzed C–C bond formation reactions. In 2004, arylzinc chlorides were used as nucleophiles in the rhodium-catalyzed 1,4-addition reactions, which produced the desired arylation products in good yields with high enantioselectivities.^{14a} For example, a high yield of zinc enolate **12** was generated by treating PhZnCl (**11**) with 2-cyclohexenone (**1**) in the presence of catalyst [RhCl((*R*)-binap)]₂ in tetrahydrofuran at ambient temperature for 1 h (Eq 1.2). Hydrolysis of **12** gave the β-chiral ketone **3** with 99% ee in a yield of 98%. Since then, arylzinc reagents have been successfully applied to the addition reactions to some other activated alkenes.¹⁴

Alkylmetal reagents have been widely used in the alkylation reactions in the presence of copper catalysts.² However, only a few examples of rhodium-catalyzed alkylation of α,β -unsaturated carbonyl compounds are available, which may be ascribed to the low reactivity of alkyl–Rh intermediates to α,β -unsaturated carbonyl compounds. In 2015, Nishimura found that the reaction of cyclopropylboronic acid (**12**) with electron-deficient alkenes **13** (such as enones, enoates, and alkenylsulfones) gave high yields of alkylation products **14** with good enantioselectivities in the presence of a chiral diene–rhodium catalyst (Scheme 1.8).¹⁵ It should be noted that the cyclopropyl group can avoid β -hydrogen elimination of the alkyl–Rh(I) intermediate since the formation of strained cyclopropene is relatively difficult.

Scheme 1.8. Rhodium-Catalyzed Cyclopropylation of Activated Alkenes.

In 2008, Hayashi reported the first example of rhodium-catalyzed conjugate alkynylation of enones.^{16a} New Csp–Csp³ bonds were formed in high yields by the 1,4-addition of (triisopropylsilyl)acetylene (**15**) to enones **16** in the presence of a Rh/DTBM-segphos catalyst in dioxane at 80 °C for 24 h (Scheme 1.9). A main side product **18** was formed by the rhodium-catalyzed dimerization of the acetylene, even though the bulky triisopropylsilyl group was used. Alkynylsilanol^{16b} and diphenyl[(triisopropylsilyl)ethynyl]methanol,^{16c} which were relatively unreactive toward the dimerization under the reaction conditions, were successfully applied as the alkynylation reagents for the rhodium-catalyzed conjugate alkynylation. However, all acetylenes for the alkynylation of enones must be substituted with bulky trialkylsilyl groups on one side. There are still some problems remaining to be solved.

Scheme 1.9. Rhodium-Catalyzed Alkynylation of α,β -Unsaturated Carbonyl Compounds.

Not only enones and enoates but many other alkenes activated by adjacent electron-withdrawing groups were successfully applied to the rhodium-catalyzed conjugate addition reactions.^{3d-31} For example, α,β -unsaturated aldehydes,¹⁷ α,β -unsaturated amides,¹⁸ nitroalkenes,¹⁹ alkenyl sulfones,²⁰ and alkenyl phosphonates,²¹ were successfully hydroarylated in good yields in the presence of the rhodium catalyst and proton source (Scheme 1.10).

Scheme 1.10. Selected Examples of Rhodium-Catalyzed Conjugate Addition

1.1.2 Rhodium-catalyzed 1,2-addition to carbonyl and imine compounds

The addition of organometallic reagents to carbon–oxygen or carbon–nitrogen double bonds is a commonly used method to form new carbon–carbon bonds in organic synthesis. For instance, the Barbier-Grignard type reactions can

give rise to products in moderate to high yields. Rhodium(I) complexes have also been extensively used as catalysts for the 1,2-addition to carbonyl and imine compounds.^{3d-3l}

In 1998, Miyaura first reported the Rh(I)-catalyzed addition of alkenyl/aryl boronic acids to aldehydes producing the corresponding secondary alcohols in high yields.²² The authors observed that electron-withdrawing groups on aldehydes and electron-donating groups on arylboronic acids accelerate the reaction, suggesting that the nucleophilic attack of aryl–Rh on the carbonyl group is involved in the catalytic cycle. In 2000, the authors reported the effects of phosphine ligands on the 1,2-addition of phenylboron reagent **2** to 4-MeOC₆H₄CHO (**19**) (Scheme 1.11).²³ Their results suggested that the Rh/bisphosphine complexes with a large P–Rh–P (such as dppf) accelerate the reaction and that the bulky and electron-donating ligands (like ^tBu₃P) show good catalytic activity when several monophosphines are employed. Typically, at the ligand-to-Rh ratio of 1:1, a quantitative yield of the alcohol **20** was obtained in the presence of a rhodium(I) catalyst generated in situ from ^tBu₃P and [Rh(acac)(coe)₂] in DME/H₂O at 25 °C for 16 h.

Scheme 1.11. Rhodium-Catalyzed Addition of PhB(OH)₂ (2**) to 4-MeOC₆H₄CHO (**19**)**

Effect of bite angle (at 80 °C):

dppe (6%) dppp (71%) dppf (85%) dppf at 50 °C (20%)

Effect of cone angle (at 50 °C):

Ph₃P (33%) Me₃P (24%) ⁱPr₃P (88%) ^tBu₃P at 20 °C (99%)

The addition to α,β -unsaturated aldehydes is special because it may proceed through either 1,2-addition or 1,4-addition. Particularly, Miyaura discovered that such competitive process is well controlled by the ligand on the rhodium catalyst.²³ In the addition reaction of phenylboronic acid (**2**) to cinnamaldehyde (**21**), the Rh/diene catalytic system gave the 1,4-addition product **23** in 88% yield without any 1,2-addition product **22**, whereas the Rh/^tBu₃P system gave rise to the 1,2-adduct **22** in 90% yield (Scheme 1.12).

Scheme 1.12. Ligand Control of 1,2-Addition or 1,4-Addition to Cinnamaldehyde

Compared with the dramatic growth of rhodium-catalyzed asymmetric 1,4-addition, the enantioselective arylation of aldehydes is still associated with some challenges. In 1998, Miyaura and his coworkers reported that the hydroarylation product **25** was obtained in 78% yield with only 41% ee by the reaction of aromatic aldehyde **24** with phenylboronic acid (**2**) under the catalysis of a rhodium complex generated in situ from $[\text{Rh}(\text{acac})(\text{CH}_2=\text{CH}_2)_2]$ and (*S*)-MeO-MOP in aqueous solvent at 60 °C (Scheme 1.13).²² Since then, various ligand systems have been developed for such reactions. For example, some selected chiral ligands shown in Scheme 1.13 were successfully applied to the Rh-catalyzed addition of phenylboronic acid (**2**) to aldehyde **24**.²⁴ Of these ligands, Ogasawara's planar

chiral P-olefin ligand **L**₁₅ is the best ligand in terms of enantioselectivity, although the yield of the arylation product is low.^{24c}

Scheme 1.13. Selected Ligands for Rhodium-Catalyzed Asymmetric Hydroarylation of Aldehydes

Before arylboron reagents, arylstannanes were employed in the rhodium-catalyzed arylation of aldehydes in 1997.²⁵ As shown in Scheme 1.14, the addition of phenyltrimethylstannane (**9**) to arylaldehydes **26** was catalyzed by Rh/cod complex in THF at 60 °C. The hydroarylation product **27** was isolated after hydrolysis in the yield of over 85%. When cyclohexanecarboxaldehyde (**28**) was used, the yield of the product **29** was much lower because of the byproduct **30**. The

authors proposed that the byproduct **30** was formed by the insertion of another aldehyde **28** into the rhodium–oxygen bond of intermediate **D**, which is shown in Scheme 1.20. Later, Li carried out these reactions in the degassed boiling water under the catalysis of $[\text{Rh}(\text{cod})_2]\text{BF}_4$.²⁶ Under these modified conditions, aromatic aldehydes gave the hydroarylation products in the yield of over 70%, and aliphatic aldehydes produced the 1,2-adducts in the yield of over 52%.

Scheme 1.14. First Example of Rhodium-Catalyzed Hydroarylation of Aldehydes with Arylstannanes

Ketones are less reactive than aldehydes in the rhodium-catalyzed 1,2-addition, which can be attributed to their steric hindrance. In 2006, Hayashi and his coworkers reported that the arylation products **33** were formed in high yields by treatment of isatins **31** with arylboronic acids **32** at 50 °C in the presence of a catalyst in situ generated from $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ and (*R*)-MeO-MOP ((*R*)-**L**₁₂), with THF/H₂O being used as the solvent, and the reaction showed moderate to high enantioselectivities (Scheme 1.15).^{27a} A key point for this reaction lies in that the carbonyl group of isatins **31** is activated by the adjacent electron-withdrawing group. Similarly, 2,2,2-trifluoroacetophenones^{27b} and α -ketoesters^{27c} are reactive toward Rh-catalyzed 1,2-addition with organoboron reagents. In 2016, Tang and his coworkers reported the rhodium-catalyzed enantioselective hydroarylation of simple

aryl ketones.^{27d} The high yield and enantioselectivity were achieved with (*R,R,R,R*)-WingPhos as the ligand.

Scheme 1.15. Rhodium-Catalyzed Hydroarylation of Isatins

In 2000, Miyaura reported that the addition of phenyltrimethylstannane (**9**) or sodium tetraphenylborate (**35**) to *N*-sulfonyl aldimines **34** is catalyzed by rhodium complex, $[\text{Rh(cod)(MeCN)}_2]\text{BF}_4$ or $[\text{Rh(cod)(MeCN)}_2]\text{BF}_4/\text{dppb}$, to give high yields of the corresponding 1,2-addition products (Scheme 1.16).²⁸

Scheme 1.16. Rhodium-Catalyzed Hydroarylation of Aldimines

In 2000, Hayashi reported the first example of enantioselective arylation of imines.²⁹ The reaction of *N*-(4-nitrobenzene)sulfonyl aldimines **37** with aryl/alkenylstannanes **38** in the presence of a catalyst generated in situ from $[\text{Rh(acac)(CH}_2\text{=CH}_2)_2]$ and **L16** in refluxed dioxane for 12 h produced the diarylmethylamines **39** in moderate to high yields and >92% ee (Scheme 1.17). The addition of 10 equiv of LiF was necessary for high reproducibility of these reactions.

Scheme 1.17. Rhodium-Catalyzed Asymmetric Hydroarylation of Imines

Ketimines are less reactive than aldimines, which could be ascribed to the steric hindrance. Hayashi successfully developed the Rh-catalyzed 1,2-addition reaction to *N*-tosyl ketimines **40** in 2010, with chiral diene–rhodium complex as a catalyst and sodium tetraarylborates **41** as organometallic reagents (Scheme 1.18).³⁰ High yields were achieved using methanolic dioxane as the solvent.

Scheme 1.18. Rhodium-Catalyzed Asymmetric Hydroarylation of Ketimines

In addition to the arylation of imines, the rhodium-catalyzed methylation of imines has been developed.³¹ The reaction was not applicable to the addition of the alkyl groups which possess β -hydrogen.

Von Zezschwitz and his coworkers developed the Rh-catalyzed 1,2-methylation of cyclic enones with AlMe_3 .³² For instance, the 1,2-methylation product **44** was produced in 84% yield by the addition reaction of AlMe_3 to

cyclohex-2-enone (**1**) using $[\text{RhCl}((S)\text{-binap})]_2$ prepared in situ as a catalyst in THF at ambient temperature (Scheme 1.19).^{32c} On the other hand, the 1,4-methylation product **43** was the main product when $[\text{RhCl}(\text{cod})]_2$ was used instead of $[\text{RhCl}((S)\text{-binap})]_2$. This is a typical example of ligand control of chemoselectivity of the reaction.

Scheme 1.19. Rhodium-Catalyzed Addition of AlMe_3 to Cyclohex-2-enone

The catalytic cycle for these Rh-catalyzed 1,2-addition reactions is almost the same as that for 1,4-addition reaction. For example, the addition of $\text{PhB}(\text{OH})_2$ to aromatic aldehydes can be illustrated with three steps – transmetalation, phenylrhodation (coordination and insertion), and hydrolysis (Scheme 1.20).^{22,23} Starting with the rhodium(I) complex **A**, the transmetalation generates the phenylrhodium species **B**. The next step is coordination of $\text{C}=\text{N}$ or $\text{C}=\text{O}$ to rhodium. Then, the $\text{C}=\text{N}$ or $\text{C}=\text{O}$ bond inserts into the rhodium–carbon bond, which generates a rhodium alkoxide/amide intermediate **D**. Hydrolysis of the rhodium alkoxide/amide **D** releases the hydroarylation product and regenerates $\text{HO-Rh}/[\text{Rh}]^+[\text{BF}_4]^-$. In the reaction of tetraphenylborate or arylboronic esters in an anhydrous environment, the direct transmetalation of rhodium alkoxide/amide **D** takes place to regenerate aryl/alkenyl rhodium **B**, not by way of $\text{HO-Rh}/[\text{Rh}]^+[\text{BF}_4]^-$ species **A**.

Scheme 1.20. Catalytic Cycle for Rh-Catalyzed 1,2-Addition

1.1.3 Rhodium-catalyzed addition to alkynes

Compared with carbonyl compounds, alkynes are unreactive toward some organometallic reagents like Grignard reagents and organozinc reagents. However, the transition metal-catalyzed addition of organometallic reagents to triple bonds has received much attention and evolved as a convenient and reliable approach to functionalized alkenes. Particularly, hydrocarbonation³³ and carbometalation³⁴ of alkynes are two major subjects in this research area (Scheme 1.21). Notably, a rhodium complex is one of the best metals to selectively produce the *cis*-addition product without E/Z isomerization.

Scheme 1.21. Transition Metal-Catalyzed Addition of Organometallic Reagents to Alkynes to Form C–C Bond

In 2002, Hayashi reported the first example of Rh-catalyzed hydroarylation reaction of internal acetylenes.³⁵ Trisubstituted alkenes **47** were produced in high yields with perfect *E* geometry by the addition of arylboron reagents **46** to internal alkynes **45** in dioxane/H₂O at 100 °C, using an in situ generated dppb–Rh complex as the catalyst (Scheme 1.22a). Although the regioselectivity was low in the addition to alkyl(aryl)alkynes, the alkynes substituted with electron-withdrawing groups (such as ester and phosphonate) produced the β-arylation products with high regioselectivities. Lautens and his coworkers found in 2002 that the addition of arylboronic acids to 2-alkynylpyridines **48** proceeded with high stereo- and regioselectivity to give the hydroarylation products **49** in 60–80% yield. They proposed that the pyridyl group coordinates to rhodium to control the regioselectivity as a directing group (Scheme 1.22b).³⁶

Scheme 1.22. Rhodium-Catalyzed Hydroarylation of Alkynes

Hayashi also found that the addition of phenylboroxine (**51**) to 4-octyne (**50**) with D₂O as a proton source gave the arylation product **52**, where the deuterium was incorporated into the *ortho*-position of the phenyl ring (Eq 1.3). The arylation product **54** formed by the reaction of C₆D₅B(OH)₂ (**53**) with 4-octyne (**50**) in H₂O was found to have one deuterium at the vinylic position (Eq 1.4). These deuterium labeling studies suggest that the 1,4-migration of rhodium from the alkenyl carbon to the phenyl carbon takes place in the catalytic cycle. After careful mechanistic studies, the authors proposed the mechanism of this reaction, which is presented in Scheme 1.23. Thus, the transmetalation of aryl group from B (boron) to Rh takes place in the reaction of the arylboronic acid with a HO–Rh species **A** to generate an Ar–Rh intermediate **B**, and the syn-addition of the aryl–Rh intermediate **B** to the alkyne gives a 2-arylalkenyl–Rh species **C**. The next step is 1,4-migration of Rh

from the alkenyl position to the aryl position to generate an *ortho*-alkenylphenyl–Rh intermediate **D**. Finally, the product is released by the hydrolysis of the *ortho*-alkenylphenyl–Rh intermediate **D**, and the HO–Rh species **A** is regenerated. In Section 1.2.2, the 1,4-migration process is discussed in detail.

Scheme 1.23. Catalytic Cycle of Rhodium-Catalyzed Hydroarylation of Alkynes

In 2002, Mori reported the use of organotin reagents for the rhodium-catalyzed addition to alkynes.³⁷ For instance, the reaction of 4-octyne (**50**) with *p*-MeOC₆H₄SnBu₃ (**55**) in the presence of a catalyst [Rh(OH)(cod)]₂ and 1 equiv of phenol in toluene/H₂O at 100 °C gave the hydroarylation product **56** in 72% yield (Scheme 1.24). The phenol is proposed to accelerate the hydrolysis step.

Scheme 1.24. Rhodium-Catalyzed Hydroarylation of 4-Octyne (50**) with Arylstannane **55****

Carbometalation of alkynes is one of the most efficient methods of generating substituted alkenyl–metals that are useful synthetic intermediates for multisubstituted alkenes.³⁴ Recently, Lam reported the carbozincation of ynamides **59** using alkyl- and arylzinc reagents **60** as nucleophiles in the presence of [Rh(acac)(cod)] under mild conditions, which produced the corresponding alkenylzincs **61** with high regioselectivities (Scheme 1.25).³⁹ However, the rhodium-catalyzed addition of arylmetals to simple unfunctionalized alkynes remains to be a challenging reaction because of their low reactivity. In Chapters 3 and 4, the rhodium-catalyzed arylstannylation and arylzincation of the unfunctionalized alkynes will be reported as new discoveries to fill in this blank.

Scheme 1.25. Rhodium-Catalyzed Carbozincation of Ynamides

1.2 Introduction of 1,4-migration of rhodium and its application to carbon–carbon bond forming reactions

The 1,4-metal shift is involved in several interesting metal-catalyzed reactions as a key step.⁴⁰ In most cases, the metal intramolecularly exchanges its position with a hydrogen. Thus, the 1,4-metal shift is also viewed as a unique way to functionalize the remote C–H bond. The 1,4-migration of rhodium is sometimes involved in the catalytic cycle of rhodium-catalyzed C–C bond forming reactions. Typically, the mechanism of 1,4-Rh(I) shift is proposed to be composed of two steps, oxidative addition and reductive elimination (Scheme 1.26). In the catalytic cycle, the five-membered ring metallacycle intermediate is formed by oxidative addition to the carbon–hydrogen bond, and then undergoes reductive elimination to yield the rearranged intermediate with higher thermodynamic stability. However, solid evidence proving the existence of such a five-membered ring metallacycle is still lacking. A more stable carbon–rhodium bond accounts for the major driving force for these shifts. Here, the reported studies on 1,4-migration of rhodium are introduced in the order of 1) 1,4-rhodium shift from alkyl to aryl carbon, 2) from alkenyl to aryl carbon, and 3) from alkyl to alkyl carbon.

Scheme 1.26. Proposed Pathway of 1,4-Migration of Rhodium(I)

1.2.1 1,4-Migration of rhodium from alkyl to aryl carbons and its application to carbon–carbon bond forming reactions

Migration of rhodium from alkyl to aryl carbon is a frequently used strategy to form an aryl–Rh intermediate, which subsequently undergoes the next reactions in the catalytic cycle.⁴¹ This 1,4-migration is reversible, while an aryl–Rh species is thermodynamically preferred to an alkyl–Rh species. Moreover, aryl–Rh species are more reactive than alkyl–Rh species in almost all rhodium-catalyzed reactions, which accounts for another important driving force for these reactions. In 2000, Miura reported the first example of 1,4-rhodium shift from alkyl to aryl carbon (Scheme 1.27).^{41a} The treatment of phenylboronic acid (**2**) with 7 equiv of norbornene (**62**) in the presence of a Rh/dppp catalyst in toluene at 100 °C gave the tetraalkylated benzene **63** as a main product. The key step in this reaction is the Rh shift from alkyl to aryl to form a new aryl–Rh intermediate, which undergoes addition to **62** again. It is noted that there is no β -hydrogen available for β -elimination in the alkyl–Rh intermediate and that the alkyl–Rh species is relatively unreactive towards the addition to the C=C bonds.

Scheme 1.27. 1,4-Migration of Rh from sp^3 Carbon to sp^2 Carbon (Miura)

Since Miura's report in 2000, the alkyl-to-aryl 1,4-Rh shift has been reported to be involved as a key step in the catalytic cycle of several types of rhodium-catalyzed reactions.⁴¹ Most of them are 1,4-hydrogen-rhodium shifts. In 2010, Cramer and his coworkers reported a rhodium-catalyzed isomerization/cyclization of a *tert*-cyclobutanol **63** through a 1,4-Rh/Si shift (Scheme 1.28).^{41g} As shown in the scheme, an alkyl-Rh intermediate **C** is generated by β -carbon elimination from a RO-Rh species **B**. Then, the alkylrhodium species **C** undergoes the 1,4-Rh/Si shift to generate an arylrhodium species **D**. The intramolecular addition of the arylrhodium species **D** to the carbonyl group generates another rhodium alkoxide **E**. The intramolecular Rh-catalyzed C-Si activation⁴² produces a tricyclic product **64** and releases a Me-Rh species **F**, while the latter can be further hydrolyzed into HO-Rh and CH_4 . The silicon/rhodium positional switch is the key step for the proposed pathway. It was also shown that the selectivity between 1,4-Rh/Si and 1,4-Rh/H shifts can be controlled mainly by the ligand on the rhodium complex. Notably, the 1,4-silicon shift, rather than the 1,4-hydrogen shift, is more synthetically useful in some cases.

Scheme 1.28. Rhodium-Catalyzed 1,4-Si Shift from sp^2 Carbon to sp^3 Carbon (Cramer)

The 1,4-rhodium shift was also employed in the polymerization of 3,3-diphenylcyclopropene (**65**) (Scheme 1.29).^{41j} The polymerization is initiated by the addition of a 3,5- $\text{Me}_2\text{C}_6\text{H}_3\text{-Rh}$ species to the alkene **65**. The continuous arylrhodation/1,4-Rh shift would generate the final polymer **66** at the molar mass of up to 9000 g/mol. Importantly, the choice of the initiator would also affect the molar mass of the polymer. Obviously, 3,5- $\text{Me}_2\text{C}_6\text{H}_3\text{B}(\text{OH})_2$ attained the best results, since the relatively bulky structure forced rhodium shift from alkyl group to the phenyl group rather than the 3,5- $\text{Me}_2\text{C}_6\text{H}_3$ group.

Scheme 1.29. Polymerization of 3,3-Diarylcyclopropenes through 1,4-Rh Shift

In 2009, Cramer reported the first example of enantioselective 1,4-migration of rhodium.^{41d} As shown in Scheme 1.30, treatment of a cyclobutanol **67** bearing two phenyl groups at the 3-position with a Rh/(*S*)-**L**₄ catalyst in refluxed toluene for 12 h gave the desired isomerization product **68** in 92% ee. This asymmetric reaction is unique in that the key step is enantioselective 1,4-shift of rhodium.

Scheme 1.30. Enantioselective 1,4-Rhodium Shift from Alkyl to Aryl Carbon

1.2.2 1,4-Migration of rhodium from alkenyl to aryl carbons and its application to carbon–carbon bond forming reactions

Hayashi and his coworkers reported the first example of alkenyl to aryl rhodium migration in the rhodium-catalyzed reaction of arylboron reagents with alkynes under aqueous conditions (Scheme 1.22), which was supported by the deuterium-labeling experiments (Eq 1.3 and 1.4).³⁵ Thereafter, the 1,4-migration of rhodium from alkenyl to aryl carbon has been frequently used in tandem reactions, since the Ar–Rh species generated by 1,4-Rh shift is reactive enough towards addition to unsaturated bonds (such as carbonyl and vinyl groups).^{43a–f} For instance, in 2005, Murakami reported that the arylation of an internal alkyne **69** equipped with ester groups is catalyzed by a rhodium(I) complex to produce a cyclic ketone **70** as the main product, which results from the 1,4-Rh shift and the subsequent intramolecular 1,2-addition of the arylrhodium species to the ester (Scheme 1.31a).^{43a} Notably, the aprotic solvent is necessary for the high yield of the desirable cyclization product; otherwise, the aryl rhodium may undergo protonolysis in protic solvent. Using the same strategy, in 2007, Hayashi and his coworkers reported that the cyclic products **73** are obtained through the rhodium-catalyzed addition of aryl/methyl boronates **72** to aryl ethynyl ketones **71**, which was achieved through 1,4-Rh shift/1,4-addition sequence (Scheme 1.31b).^{43c}

Scheme 1.31. Catalytic Tandem Reaction via 1,4-Rh Shift from Alkenyl to Aryl

(a) Rhodium-catalyzed cyclization via addition/1,4-Rh shift/1,2-addition

(b) Rhodium-catalyzed cyclization via addition/1,4-Rh shift/intramolecular 1,4-addition

In 2012, Hayashi and his coworkers further reported the asymmetric hydroarylation of enone **2** with (E) -1,2-diphenylethenylboronic acid (**74**) in the presence of a Rh/diene complex, which produced a hydroarylation product **75** rather than an alkenylation product (Scheme 1.32).^{43e} They proposed a catalytic cycle involving the 1,4-migration of rhodium from the vinylic carbon to the aromatic carbon followed by 1,4-addition as the key steps. DFT calculations proved that five-membered ring rhoda(III)cycle **B** is an intermediate during the 1,4-shift of rhodium, and the *ortho*-alkenylphenyl–Rh intermediate **A** is more thermodynamically stable

than the 2-arylalkenyl–Rh species **C**. However, more experimental evidence still remains to be obtained for the detailed mechanism.

Scheme 1.32. Rhodium-Catalyzed Tandem Reaction via 1,4-Rh Shift/Intermolecular 1,4-Addition ([Rh] = Rh(bod))

In most cases, the 1,4-rhodium migration has been reported for Rh(I) complexes. By contrast, much little is known about 1,4-Rh(III) shift, even though $\text{Cp}^*\text{Rh(III)}$ complex is one of the best catalysts for C–H activation.⁴⁴ In 2013, Ishii and his coworkers reported the first example of 1,4-migration of Rh(III).^{43g,43h} Thus, treating $[\text{Cp}^*\text{Rh(III)Cl}(3\text{-MeC}_6\text{H}_4)(\text{PMe}_3)]$ (**76**) with 5 equiv of diphenylacetylene in the presence of 1.1 equiv of $\text{NaBAr}^{\text{F}}_4$ ($\text{Ar}^{\text{F}} = 3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$) in 1,2-dichloroethane at 25°C for 1 h gave a mixture of arylrhodium(III) complex **78** and alkenylrhodium(III) complex **77** in a ratio of 5:1 (Scheme 1.33). The reversibility of 1,4-Rh shift was proved through the isomerization of the arylrhodium(III) complex **78** to the more thermodynamically stable **79** at 50°C .

Scheme 1.33. 1,4-Metal Migration in a Cp*Rh(III) Complex and Its Reversibility

1.2.3 1,4-Migration of rhodium from alkyl to alkyl carbons and its application to carbon–carbon bond forming reactions

The 1,4-shift of rhodium from alkyl/alkenyl to aryl carbon is a well-known step, which has been found in many catalytic reactions. In contrast, much less is known regarding the 1,4-rhodium/hydrogen exchange between two alkyl carbons. In 2014, Lam and his coworkers found the isomerization of allylrhodium intermediates through 1,4-Rh shift during the allylation of cyclic imines (Scheme 1.34).⁴⁵ As shown in the scheme, the authors proposed that a more reactive allylrhodium **B** with less steric congestion at the γ -position was generated from the intermediate **A** through 1,4-Rh shift from the allylic carbon to another allylic carbon. The allylation of imine **80** with the allylrhodium **B** leads to the production of the main product **83**.

Scheme 1.34. 1,4-Rhodium Shift from an Allyl Carbon to Another Allyl Carbon

1.3 Conclusion and outlook

Ever since Miyaura made his inspirational report in the year of 1997, the research on carbon–carbon bond forming reactions involving rhodium complexes as catalysts has significantly progressed. Addition reactions of organoboron and related reagents to various unsaturated substrates have been developed, often with high enantioselectivity. Furthermore, the 1,4-Rh migration has offered a unique twist to the organorhodium chemistry. The combination of 1,4-Rh shift and other elementary steps has enabled a variety of mechanistically intriguing and synthetically attractive cascade transformations. It is desirable to extend the rhodium migration chemistry to some other reactions such as carbometalation and hydroarylation. Here, the project of mine is to focus on the development of new C–C bond forming reactions through 1,4-migration of rhodium.

1.4 Reference

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CHAPTER 2

Aryloxymethyltrifluoroborates for Rhodium-Catalyzed Asymmetric Arylation of Enones. 1,4-Rhodium Shift from sp^3 to sp^2 Carbons

2.1 Introduction

Rhodium-catalyzed asymmetric conjugate arylation of electron-deficient alkenes has attracted considerable attention as one of the most convenient and reliable methods of creating benzylic stereocenters with high enantioselectivity (Scheme 2.1).^{1,2} Among various arylating agents, arylboron compounds such as boronic acids, boronates, and trifluoroborates, are by far the most commonly used because of their easy handling in air and moisture.

Scheme 2.1. Rh-Catalyzed Asymmetric Arylation of Alkenes with Arylboron Reagents

The arylboron reagents³ are prepared by the borylation of aryllithium or aryl Grignard reagents at low temperature in most cases (Scheme 2.2).^{4a,4b} These reactive arylmetals are prepared from the corresponding halides or tin compounds, or arenes bearing appropriate directing groups. However, this method is incompatible with base-sensitive functional groups such as carbonyl groups and nitrile.

Scheme 2.2. Electrophilic Borate Trapping of Hard Arylmetal Reagents

Borylation of Ar-X (X = halides, triflate) and Ar-H by transition metal-catalyzed reaction with diboron reagents is another preparation method, which has been developed recently (Scheme 2.3).^{4a,4b} The relatively mild conditions allow us to prepare a wider scope of arylboron reagents, while the use of expensive transition metal (palladium, iridium, *et al.*) limits the application.

Scheme 2.3 Direct Boronylation By Transition Metal-Catalyzed Coupling or C-H Functionalization

On the other hand, Molander reported synthesis of alkoxymethyltrifluoroborates ($\text{ROCH}_2\text{BF}_3\text{K}$) from alcohols (ROH) and their use as alkoxymethyl nucleophiles in the palladium-catalyzed cross-coupling reactions^{6,7} (Scheme 2.4a). In this Chapter, we report that the reaction of aryloxymethyltrifluoroborates ($\text{ArOCH}_2\text{BF}_3\text{K}$) with α,β -unsaturated carbonyl compounds in the presence of a chiral diene-rhodium catalyst introduces *ortho*-methoxyaryl groups at the β -position in high yields with high enantioselectivity, where the reaction proceeds through the 1,4-shift of rhodium^{8,9} from aryloxymethyl to *ortho*-methoxyaryl intermediates (Scheme 2.4b). Considering the very wide availability of substituted phenols and their easy conversion into aryloxymethyltrifluoroborates,^{6,7} this 1,4-shift/arylation sequential reaction is of great advantage over the reaction of *ortho*-methoxyarylboron reagents. The 1,4-Rh

shift from alkyl–Rh to aryl–Rh intermediates⁸ has been reported to be involved as a key step in the catalytic cycle of several types of rhodium-catalyzed reactions, which have been developed since Miura's report in 2000.^{8a} As a reaction related to the present study, there has been a report where the Rh shift between aryloxymethyl and *ortho*-methoxyaryl is proposed to explain a methoxy-directed aryl-to-aryl 1,3-Rh migration.¹⁰

Scheme 2.4. Rh-Catalyzed Conjugate Arylation, Aryloxymethyl Intermediates, and 1,4-Rh Shift

(a) Alkoxyethyltrifluoroborates for Pd-catalyzed cross-coupling (Molander)

(b) Aryloxymethyltrifluoroborates for Rh-catalyzed asymmetric addition

2.2 Results and discussion

In the first set of experiments, benzalacetone (**2a**) was allowed to react with phenoxymethyltrifluoroborate **1a** (1.2 equiv to **2a**) in the presence of 5 mol% of a rhodium catalyst coordinated with (*R,R*)-Ph-bod,¹³ which is one of the most commonly used chiral diene ligands.¹² The reaction with Cs₂CO₃ (2.0 equiv) as a base in dioxane/H₂O (10/1) at 60 °C for 16 h, which is one of the standard conditions for rhodium-catalyzed asymmetric conjugate arylation,¹ did not give any addition products (Table 2.1, entry 1). This is expected because the rhodium-catalyzed conjugate addition of organoboron reagents is known to work well for the introduction of aryl and alkenyl groups but not for that of alkyl groups.¹ On heating the reaction to 100 °C, formation of the addition product **3aa**, where a 2-methoxyphenyl group rather than a phenoxymethyl group was introduced at the β-position, was observed albeit in a low yield (19%) (entry 3). The yield of **3aa** was improved with a higher ratio of water (entries 4 and 5), and the reaction in pure water¹³ gave the highest yield (86%) of **3aa**, which was an *R* isomer of 98% ee (entry 6). A more amount (2.0 equiv to **2a**) of the boron reagent **1a** increased the yield of **3aa** to 96% (entry 7). The use of 2-methoxyphenyltrifluoroborate **4a** in place of **1a** gave essentially the same result (91% yield, 98% ee) (entry 8), which may well suggest that the reaction proceeds through a 2-methoxyphenyl–Rh intermediate (*vide infra*). The yield of **3aa** was slightly lower with K₃PO₄ as a base (entry 9), and KOH was not an appropriate base for the present reaction (entry 10). Another choice of chiral diene ligand is Fc-tfb, whose enantioselectivity is higher than that of Ph-bod in most of the rhodium-catalyzed asymmetric arylation reactions.¹⁴ Although Fc-tfb ligand was not better than Ph-bod for the addition to enone **2a** due to the lower

yield (entry 11), Fc-tfb ligand showed higher performance for some other enone substrates (see Table 2.2). The yields were low with bisphosphine ligands such as binap and segphos (entries 12 and 13).

Table 2.1. Rhodium-Catalyzed Asymmetric Arylation of Benzalacetone (2a) with Phenoxyethylborate 1a^a

Reaction scheme: **1a** + **2a** $\xrightarrow[\text{solvent, additive, 16 h}]{\text{Rh/L}^* (5.0 \text{ mol\% Rh})}$ **3aa**

Ligands shown: **4a** (2-OMe-5-BF₃K-phenyl), **(R,R)-Ph-bod**, **(S,S)-Fc-tfb** (Fc = ferrocenyl), **(R)-segphos**, and **(R)-binap**.

entry	ligand on Rh	additive (equiv)	solvent (mL)	temp (°C)	yield (%) ^b 3aa	% ee ^c 3aa
1	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	dioxane/H ₂ O (1.0/0.1)	60	0	—
2	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	dioxane/H ₂ O (1.0/0.1)	80	3	—
3	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	dioxane/H ₂ O (1.0/0.1)	100	19	—
4	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	dioxane/H ₂ O (0.5/0.5)	100	57	98
5	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	toluene/H ₂ O (0.5/0.5)	100	70	98
6	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	H ₂ O (1.1)	100	84	98
7 ^e	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (4)	H ₂ O (1.1)	100	96	98
8 ^f	(<i>R,R</i>)-Ph-bod ^d	Cs ₂ CO ₃ (2)	H ₂ O (1.1)	100	91	98
9	(<i>R,R</i>)-Ph-bod ^d	K ₃ PO ₄ (2)	H ₂ O (1.1)	100	76	98
10	(<i>R,R</i>)-Ph-bod ^d	KOH (2)	H ₂ O (1.1)	100	<3	—
11	(<i>S,S</i>)-Fc-tfb ^g	Cs ₂ CO ₃ (2)	H ₂ O (1.1)	100	42	>99
12	(<i>R</i>)-binap ^h	Cs ₂ CO ₃ (2)	H ₂ O (1.1)	100	39	99
13	(<i>R</i>)-segphos ⁱ	Cs ₂ CO ₃ (2)	H ₂ O (1.1)	100	<3	—

^a Reaction conditions: **1a** (0.24 mmol), **2a** (0.20 mmol), Rh catalyst (5 mol% Rh), at 100 °C for 16 h. ^b Isolated yield. ^c The % ee was determined by HPLC on a chiral stationary phase column. ^d [RhCl((*R,R*)-Ph-bod)]₂. ^e With **1a** (0.40 mmol). ^f Reaction with **4a** (0.24 mmol) instead of **1a**. ^g [RhCl((*S,S*)-Fc-tfb)]₂. ^h [RhCl(coe)₂]₂/(*R*)-binap. ⁱ [RhCl(coe)₂]₂/(*R*)-segphos.

The results for the 1,4-shift/arylation reaction of **1a** with several other α,β -unsaturated carbonyl compounds are summarized in Table 2.2. The yields and enantioselectivities of the products are high for linear enones, such as chalcone (**2b**) and 3-nonen-2-one (**2c**), under the conditions using 1.2 equiv of **1a** in the presence of $[\text{RhCl}((R,R)\text{-Ph-bod})]_2$ (5 mol% Rh) catalyst (entries 2 and 3). For 2-cyclohexenone (**2d**), the yield and % ee were not satisfactory (67% yield, 87% ee) under the same conditions (entry 4). The yield was improved from 67% to 82% by the use of 2.0 equiv of boron reagent **1a** (entry 5), and % ee was increased to 94% ee by changing the diene ligand to (S,S) -Fc-tfb (entry 6). The reaction of 2-cycloheptenone (**2f**) was also improved by the use of (S,S) -Fc-tfb ligand and an excess amount of **1a** (entries 8 and 9). α,β -Unsaturated ester **2g** is also a suitable substrate for the 1,4-shift/arylation reaction (entry 10).

Table 2.2. Rhodium-Catalyzed Asymmetric Arylation of Enones **2 with Phenoxyethylborate **1a**^a**

entry	2	diene ligand	yield (%) ^b	ee (%) ^c
1	2a	(R,R) -Ph-bod	3aa : 84	98 (<i>R</i>)
2	2b	(R,R) -Ph-bod	3ab : 94	>99 (<i>R</i>)
3	2c	(R,R) -Ph-bod	3ac : 84	97 (<i>S</i>)
4	2d	(R,R) -Ph-bod	3ad : 67	87 (<i>R</i>)
5 ^d	2d	(R,R) -Ph-bod	3ad : 82	88 (<i>R</i>)
6 ^d	2d	(S,S) -Fc-tfb	3ad : 77	94 (<i>R</i>)
7	2e	(R,R) -Ph-bod	3ae : 76	96 (<i>R</i>)

8	2f	(<i>R,R</i>)-Ph-bod	3af : 75	88 (<i>R</i>)
9 ^d	2f	(<i>S,S</i>)-Fc-tfb	3af : 81	93 (<i>R</i>)
10 ^d	2g	(<i>R,R</i>)-Ph-bod	3ag : 87	97 (<i>R</i>)

^a Reaction conditions: **1a** (0.24 mmol), enone **2** (0.20 mmol), Cs₂CO₃ (0.40 mmol), [RhCl((*R,R*)-Ph-bod)]₂ (5 mol% of Rh), H₂O (1.1 mL) at 100 °C for 16 h. ^b Isolated yield. ^c The % ee was determined by HPLC on chiral stationary phase columns. The absolute configurations were estimated by stereochemical similarity to those reported for asymmetric arylation with Rh/(*R,R*)-Ph-bod catalyst. ^d With **1a** (0.40 mmol) and Cs₂CO₃ (0.80 mmol).

Aryloxymethylborates bearing substituents on the phenyl group, which were prepared from the corresponding phenol derivatives according to the Molander's procedures,⁶ were subjected to the present 1,4-shift/arylation reaction (Table 2.3). Those substituted with Me (**1b**), MeO (**1c**), F (**1d**), Cl (**1e**), Br (**1f**), CF₃ (**1g**), and COOEt (**1h**) at the *para*-position gave high yields of the arylation products **5** with high % ee in the reaction with **2a** and/or **2b** in the presence of [RhCl((*R,R*)-Ph-bod)]₂ (5 mol% Rh) catalyst (entries 1–8). The introduced aromatic groups in **5** are all substituted at the 5-position in addition to the MeO group at the 2-position, as expected from the 1,4-Rh shift mechanism. In the reaction of aryloxymethylborates with substituents at the *meta*-position, the regioselectivity of the 1,4-Rh shift in giving 2,4-disubstituted isomer **6** or 2,6-disubstituted isomer **7** is an interesting subject of study. With Me (**1i**), Cl (**1j**), and COOEt (**1k**) at the 3-position, the regioselectivity was very high to give the less hindered isomers **6** exclusively (entries 9–12). With OMe (**1l**) and Br (**1m**) as 3-substituents, the regiochemistry was not perfect, the **6/7** ratio ranging between 12/1 and 6/1 (entries 13–17). It is notable that the selectivity is not strongly dependent on the enone/enoate substrates. The regioselective 1,4-shift leading to less hindered isomers **6na** and **6oa** was also observed in the reaction of aryloxymethylborates where the aryl groups are 3,4-dimethylphenyl (**1n**) and 2-naphthyl (**1o**) (entries 18 and 19). The 1,4-shift/arylation reaction is also applicable to the ortho substituted borates **1p**, **1q**, and **1r**, which gave

the corresponding arylation products **8** although the yields are somewhat lower (entries 20–22).

Table 2.3. Rhodium-Catalyzed Asymmetric Arylation of Enones **2 with Substituted Aryloxymethylborates **1**^a**

entry	1	2	regioselectivity ^b	yield (%) ^c	ee (%) ^d
1	1b	2a	—	5ba : 90	99
2	1c	2a	—	5ca : 92	98
3	1d	2b	—	5db : 83	>99.5
4	1e	2b	—	5eb : 86	>99.5
5 ^e	1f	2a	—	5fa : 85	98
6	1f	2b	—	5fb : 84	99
7	1g	2b	—	5gb : 90	99
8	1h	2b	—	5hb : 87	>99.5
9	1i	2a	6/7 = >50/1	6ia : 89	99
10	1i	2b	6/7 = >50/1	6ib : 97	99
11 ^e	1j	2b	6/7 = >50/1	6jb : 91	99
12 ^e	1k	2b	6/7 = >50/1	6kb : 87	99
13	1l	2a	6/7 = 7/1	6la : 92 ^f	99
14	1l	2b	6/7 = 12/1	6lb : 94 ^f	>99.5
15	1l	2e	6/7 = 11/1	6le : 77 ^f	96
16	1l	2g	6/7 = 9/1	6lg : 92 ^f	98
17 ^e	1m	2b	6/7 = 6/1	6mb : 86 ^f	>99.5

18	1n	2a	6/7 = >50/1	6na : 91	99
19	1o	2a	6/7 = >50/1	6oa : 80	98
20 ^e	1p	2a	—	8pa : 72	99
21 ^e	1q	2a	—	8qa : 78	97
22 ^e	1r	2a	—	8ra : 74	97

^a Reaction conditions: **1** (0.24 mmol), enone **2** (0.20 mmol), Cs₂CO₃ (0.40 mmol), [RhCl((*R,R*)-Ph-bod)]₂ (5 mol% of Rh), H₂O (1.1 mL) at 100 °C for 16 h. ^b Determined by ¹H NMR. ^c Isolated yield. ^d The % ee was determined by HPLC on chiral columns. The absolute configuration of **5fb** was determined to be *R* by X-ray analysis (CCDC 1500570) and others are estimated by stereochemical similarity to those reported for asymmetric arylation with Rh/(*R,R*)-Ph-bod catalyst. ^e With **1** (0.40 mmol) and Cs₂CO₃ (0.80 mmol). ^f Yield of a mixture of **6** and **7**.

The 1,4-shift/arylation products **5–8** shown in Table 2.3 are expected to be also obtainable by use of the corresponding *ortho*-methoxyarylboronic acids (see, entry 8 in Table 2.1). However, the synthesis of aryloxymethylborates from phenol derivatives is generally much more straightforward than that of the *ortho*-methoxyarylboronic acids. As an example, the reported synthetic scheme for ester-substituted 2-methoxyphenylboronic acids **4h,k**¹⁵ is shown in Scheme 2.5, where an ester-substituted phenols were converted into the boronic acids by multiple step reactions including *ortho*-bromination and palladium-catalyzed borylation. To the contrary, the aryloxymethylborates **1h,k** are prepared by one step from the phenols by Molander's method.⁶ It should be noted that the present rhodium catalysis can skip the *ortho* C–H functionalization steps required for the synthesis of *ortho*-methoxyarylboron reagents.

Scheme 2.5. Comparison of Synthesis and Reaction of Aryloxymethylborates **1 with *ortho*-Methoxyphenylboronic Acids **4****

Deuterium labeling studies provided us with some information on the mechanism of 1,4-Rh shift from the phenoxymethyl carbon to the 2-methoxyphenyl carbon (Scheme 2.6). The product **3aa-d₅** formed by the reaction of pentadeuterio-phenoxymethylborate **1a-d₅** with benzalacetone (**2a**) was found to be a mixture of deuterium-regioisomers **3aa-d₅** (**9**) and **3aa-d₅** (**10**) in a ratio of 3 to 1. The reaction pathway to produce isomer **9**, which is substituted with OCH_2D group at 2-position and with D_4 at other positions, is simple. Transmetalation of the phenoxymethyl group from boron to rhodium generates alkyl-Rh intermediate **A**, which is not reactive towards the addition to enone¹⁶ but undergoes the 1,4-Rh shift by way of a Rh(III) species¹⁷ to form a 2-methoxyphenyl-Rh intermediate **B**. Addition of the aryl-Rh **B** to the enone **2a** produces the isomer **9**. The reversibility of 1,4-Rh shift between sp^3 carbon and sp^2 carbon is demonstrated by the formation of the isomer **10**, where the methoxy group at the 2-position is OCHD_2 and H is at the 3-position.

The reaction of *N*-sulfonylimine **13** with phenoxymethylborate **1a** proceeded in a different way (equation 2.1). It gave phenoxymethylation product **14** instead of 1,4-shift/arylation product. The yield is not high (40%) under the standard conditions used for α,β -unsaturated carbonyl compounds **2**. The addition of alkyl–Rh intermediate to imine **13** before the 1,4-shift is consistent with the report²⁰ that *N*-sulfonylimines undergoes methylation with a methylboron reagent in the presence of a diene/rhodium catalyst.

2.3 Conclusion

In summary, a new type of rhodium-catalyzed conjugate arylation using aryloxymethyltrifluoroborates as nucleophiles was developed. In the catalytic cycle, an aryloxymethyl–Rh intermediate generated by transmetallation from the boron reagent undergoes C–H activation by 1,4-Rh shift to form an *ortho*-methoxyaryl–Rh intermediate, which is reactive towards α,β -unsaturated carbonyl compounds. The asymmetric conjugate addition is efficiently catalyzed by a chiral diene–rhodium catalyst in H_2O with high enantioselectivity ($\geq 93\%$ ee).

2.4 Experimental section

2.4.1 Materials

The α,β -unsaturated carbonyl compounds, phenols, Cs_2CO_3 , dibromomethane, methanesulfonic acid, HPLC grade water, KHF_2 , potassium *t*-butoxide, and *n*-BuLi were purchased and used as received. 1,4-Dioxane, toluene, and THF were distilled over benzophenone ketyl under nitrogen. Rhodium complexes, $[\text{RhCl}(\text{coe})_2]_2$,²¹ $[\text{RhCl}((R,R)\text{-Ph-bod})]_2$,²² and $[\text{RhCl}((S,S)\text{-Fc-tfb})]_2$ ²³ were prepared according to the reported procedures. Potassium bromomethyltrifluoroborate^{6b} was prepared according to the reported procedure.

2.4.2 Preparation of Potassium Aryloxymethyltrifluoroborates 1a-r

They were prepared from phenols and potassium bromomethyltrifluoroborate ($\text{BrCH}_2\text{BF}_3\text{K}$) according to the procedure reported by Molander (equation 2.2).^{6a}

Preparation of Potassium Phenoxymethyltrifluoroborate (1a) [1027642-30-3]. It was synthesized according to the reported procedure.²⁵ To a 100 mL 2-neck round-bottom-flask was added potassium *tert*-butoxide (3.37 g, 30 mmol) and dry THF (50 mL). Phenol (2.82 g, 30 mmol) was added to the suspension via syringe at 0 °C under N_2 . The mixture was stirred at 0 °C for 15 min and allowed to warm to

room temperature over 30 min. Potassium bromomethyltrifluoroborate (2.00 g, 10 mmol) was added in one portion at 0 °C. The reaction mixture was stirred at room temperature for 1 day, and 4.5 M KHF₂ (4.5 mL) was added. The mixture was kept stirring at room temperature for 30 min, and the suspension was concentrated and dried overnight in vacuo. The crude solid was suspended in Et₂O (25 mL) and filtered to remove the organic impurities. The crude solid was purified by continuous Soxhlet extraction with acetonitrile (60 mL). The extract was concentrated and then cooled using an ice-water bath. The white precipitates were collected and dried to give 84% yield (1.80 g, 8.4 mmol) of the target compound **1a**. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.94 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 6.75 (tt, *J*_{H,H} = 7.3 Hz, 1.2 Hz, 1H), 6.83 (d, *J*_{H,H} = 7.7 Hz, 2H), 7.18 (dd, *J*_{H,H} = 8.5 Hz, 7.3 Hz, 2H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 113.8, 118.3, 128.9, 162.1. The OCH₂B carbon was not observed in ¹³C NMR of compounds **1**. The spectral data are in agreement with reported literature values.^{6a}

Preparation of Potassium (4-Methylphenoxy)methyltrifluoroborate (1b). Similarly to the preparation of **1a**, **1b** was prepared with 4-methylphenol (0.65 g, 6.0 mmol) and BrCH₂BF₃K (0.40 g, 2.0 mmol). The product was obtained in 70% yield (0.32 g, 1.4 mmol) as a white crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.19 (s, 3H), δ 2.90 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 6.72 (d, *J*_{H,H} = 8.5 Hz, 2H), 6.98 (d, *J*_{H,H} = 8.6 Hz, 2H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 20.0, 113.5, 126.6, 129.3, 160.0. **HRMS** (APCI) *m/z* calcd. For C₈H₉BF₃O (M-K) 189.0706; found, 189.0702.

Preparation of Potassium (4-Methoxyphenoxy)methyltrifluoroborate (1c) [1448675-13-5]. Similarly to the preparation of **1a**, **1c** was prepared with 4-methoxyphenol (0.74 g, 6.0 mmol) and BrCH₂BF₃K (0.40 g, 2.0 mmol). The product was obtained in 82% yield (0.40 g, 1.6 mmol) as a white crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.88 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 3.66 (s, 3H), 6.75 (d, *J*_{H,H} = 9.0 Hz, 2H), 6.77 (d, *J*_{H,H} = 9.2 Hz, 2H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 55.2, 114.1, 114.2, 151.8, 156.2. **HRMS** (APCI) *m/z* calcd. For C₈H₉BF₃O₂ (M-K) 205.0655; found, 205.0653. The spectral data are in agreement with reported literature values.^{6a}

Preparation of Potassium (4-Fluorophenoxy)methyltrifluoroborate (1d). The potassium aryloxide generated from 4-fluorophenol (0.67 g, 6.0 mmol) was treated with BrCH₂BF₃K (0.40 g, 2.0 mmol) at 45 °C for 1 day. The product was obtained in 87% yield (0.40 g, 1.7 mmol) as a light yellow crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.93 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 6.82 (dd, *J*_{H,H} = 9.2 Hz, *J*_{H,¹⁹F} = 4.6 Hz, 2H), 6.99 (t, *J*_{H,H} = *J*_{H,¹⁹F} = 8.9 Hz, 2H); **¹³C NMR** (100 MHz, DMSO-*d*₆) δ 114.5 (d, *J*_{C,¹⁹F} = 7.8 Hz), 115.2 (d, *J*_{C,¹⁹F} = 22.4 Hz), 155.3 (d, *J*_{C,¹⁹F} = 231.6 Hz), 158.4. **HRMS** (APCI) *m/z* calcd. For C₇H₆BF₄O (M-K) 193.0455; found, 193.0460.

Preparation of Potassium (4-Chlorophenoxy)methyltrifluoroborate (1e).

The potassium aryloxide generated from 4-chlorophenol (0.77 g, 6.0 mmol) was treated with $\text{BrCH}_2\text{BF}_3\text{K}$ (0.40 g, 2.0 mmol) at 45 °C for 1 day. The product was obtained in 91% yield (0.45 g, 1.8 mmol) as a white crystalline solid. **^1H NMR** (500 MHz, $\text{DMSO-}d_6$) δ 2.95 (q, $J_{\text{H},^{19}\text{F}} = 5.1$ Hz, 2H), 6.85 (d, $J_{\text{H,H}} = 9.0$ Hz, 2H), 6.99 (d, $J_{\text{H,H}} = 9.1$ Hz, 2H); **^{13}C NMR** (125 MHz, $\text{DMSO-}d_6$) δ 115.5, 121.9, 128.6, 160.9. **HRMS** (APCI) m/z calcd. For $\text{C}_7\text{H}_6\text{BClF}_3\text{O}$ (M-K) 209.0159; found, 209.0157.

Preparation of Potassium (4-Bromophenoxy)methyltrifluoroborate (1f).

The potassium aryloxide generated from 4-bromophenol (5.2 g, 30 mmol) was treated with $\text{BrCH}_2\text{BF}_3\text{K}$ (2.0 g, 10 mmol) at 45 °C for 1 day. The product was obtained in 85% yield (2.49 g, 8.5 mmol) as a white crystalline solid. **^1H NMR** (500 MHz, $\text{DMSO-}d_6$) δ 2.95 (q, $J_{\text{H},^{19}\text{F}} = 5.2$ Hz, 2H), 6.69 (d, $J_{\text{H,H}} = 9.0$ Hz, 2H), 7.47 (d, $J_{\text{H,H}} = 9.1$ Hz, 2H); **^{13}C NMR** (125 MHz, $\text{DMSO-}d_6$) δ 109.5, 116.1, 131.5, 161.4. **HRMS** (APCI) m/z calcd. For $\text{C}_7\text{H}_6\text{BBrF}_3\text{O}$ (M-K) 252.9654; found, 252.9651.

Preparation of Potassium (4-Trifluoromethylphenoxy)methyltrifluoro-

borate (1g). The potassium aryloxide generated from 4-trifluoromethylphenol (0.97 g, 6.0 mmol) was treated with $\text{BrCH}_2\text{BF}_3\text{K}$ (0.40 g, 2.0 mmol) at 45 C for 1 day. The product was obtained in 74% yield (0.42 g, 1.5 mmol) as a yellow crystalline solid. **^1H NMR** (500 MHz, $\text{DMSO-}d_6$) δ 3.01 (q, $J_{\text{H},^{19}\text{F}} = 5.0$ Hz, 2H), 7.03 (d, $J_{\text{H,H}} =$

8.6 Hz, 2H), 7.54 (d, $J_{\text{H,H}} = 8.6$ Hz, 2H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 114.4, 119.1 (q, $J_{\text{C},^{19}\text{F}} = 31.7$ Hz), 124.9 (q, $J_{\text{C},^{19}\text{F}} = 268.9$ Hz), 126.4 (q, $J_{\text{C},^{19}\text{F}} = 15.0$ Hz), 165.0. **HRMS** (APCI) m/z calcd. For $\text{C}_8\text{H}_6\text{BF}_6\text{O}$ (M-K) 243.0423; found, 243.0418.

Preparation of Potassium (4-Ethoxycarbonylphenoxy)methyltrifluoroborate (1h). The potassium aryloxide generated from 4-ethoxycarbonylphenol (5.0 g, 30 mmol) was treated with $\text{BrCH}_2\text{BF}_3\text{K}$ (2.0 g, 10 mmol) at 45 °C for 1 day. The product was obtained in 62% yield (1.77 g, 6.2 mmol) as a white crystalline solid. ^1H NMR (500 MHz, DMSO- d_6) δ 1.30 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 3.07 (q, $J_{\text{H},^{19}\text{F}} = 5.1$ Hz, 2H), 4.25 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 6.93 (d, $J_{\text{H,H}} = 8.9$ Hz, 2H), 7.82 (d, $J_{\text{H,H}} = 8.9$ Hz, 2H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 14.2, 59.9, 113.9, 120.0, 130.8, 165.6, 166.0. **HRMS** (APCI) m/z calcd. For $\text{C}_{10}\text{H}_{11}\text{BF}_3\text{O}_3$ (M-K) 247.0761; found, 247.0758.

Preparation of Potassium (3-Methylphenoxy)methyltrifluoroborate (1i). Similarly to the preparation of **1a**, **1i** was prepared with 3-methylphenol (0.65 g, 6.0 mmol) and $\text{BrCH}_2\text{BF}_3\text{K}$ (0.40 g, 2.0 mmol). The product was obtained in 80% yield (0.36 g, 1.6 mmol) as a white crystalline solid. ^1H NMR (500 MHz, DMSO- d_6) δ 2.23 (s, 3H), 2.92 (q, $J_{\text{H},^{19}\text{F}} = 5.0$ Hz, 2H), 6.57 (d, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.62 (d, $J_{\text{H,H}} = 7.9$ Hz, 1H), 6.65 (s, 1H), 7.05 (t, $J_{\text{H,H}} = 7.8$ Hz, 1H); ^{13}C NMR (75 MHz, DMSO-

d_6) δ 21.2, 110.9, 114.4, 119.2, 128.6, 138.1, 162.1. **HRMS** (APCI) m/z calcd. For $C_8H_9BF_3O$ (M-K) 189.0706; found, 189.0708.

Preparation of Potassium (3-Chlorophenoxy)methyltrifluoroborate (1j).

The potassium aryloxide generated from 3-chlorophenol (0.77 g, 6.0 mmol) was treated with $BrCH_2BF_3K$ (0.40 g, 2.0 mmol) at 45 °C for 1 day. The product was obtained in 89% yield (0.44 g, 1.8 mmol) as a white crystalline solid. **1H NMR** (500 MHz, $DMSO-d_6$) δ 2.98 (q, $J_{H,^{19}F}$ = 5.2 Hz, 2H), 6.81 (d, $J_{H,H}$ = 8.2 Hz, 2H), 6.86 (s, 1H), 7.20 (t, $J_{H,H}$ = 8.2 Hz, 1H); **^{13}C NMR** (125 MHz, $DMSO-d_6$) δ 113.2, 113.6, 118.3, 130.2, 133.2, 163.1. **HRMS** (APCI) m/z calcd. For $C_7H_6BClF_3O$ (M-K) 209.0159; found, 209.0158.

Preparation of Potassium (3-Ethoxycarbonylphenoxy)methyltrifluoroborate (1k). The potassium aryloxide generated from 3-ethoxycarbonylphenol (5.0 g, 30 mmol) was treated with $BrCH_2BF_3K$ (2.0 g, 10 mmol) at 45 °C for 2 days. The product was obtained in 87% yield (2.49 g, 8.7 mmol) as a white crystalline solid. **1H NMR** (500 MHz, $DMSO-d_6$) δ 1.31 (t, $J_{H,H}$ = 7.1 Hz, 3H), 3.01 (q, $J_{H,^{19}F}$ = 5.1 Hz, 2H), 4.29 (q, $J_{H,H}$ = 7.1 Hz, 2H), 7.12 (ddd, $J_{H,H}$ = 8.2 Hz, 2.6 Hz, 1.3 Hz, 1H), 7.33 (t, $J_{H,H}$ = 8.0 Hz, 1H), 7.40 (dt, $J_{H,H}$ = 8.1 Hz, 1.3 Hz, 1H), 7.41 (s, 1H); **^{13}C NMR** (125 MHz, $DMSO-d_6$) δ 14.1, 60.5, 113.8, 119.3, 119.4, 129.2, 130.8, 162.1,

165.9. **HRMS** (APCI) m/z calcd. For $C_{10}H_{11}BF_3O_3$ (M-K) 247.0761; found, 247.0760.

Preparation of Potassium (3-Methoxyphenoxy)methyltrifluoroborate

(1l). Similarly to the preparation of **1a**, **1l** was prepared with 3-methoxyphenol (3.7 g, 30 mmol) and $BrCH_2BF_3K$ (2.0 g, 10 mmol). The product was obtained in 84% yield (2.05 g, 8.4 mmol) as a white crystalline solid. **1H NMR** (300 MHz, $DMSO-d_6$) δ 2.92 (q, $J_{H,^{19}F}$ = 5.1 Hz, 2H), 3.70 (s, 3H), 6.35 (d, $J_{H,H}$ = 8.0 Hz, 1H), 6.39 (s, 1H), 6.42 (d, $J_{H,H}$ = 8.1 Hz, 1H), 7.07 (t, $J_{H,H}$ = 8.1 Hz, 1H); **^{13}C NMR** (75 MHz, $DMSO-d_6$) δ 54.7, 99.8, 104.2, 106.3, 129.3, 160.2, 163.5. **HRMS** (APCI) m/z calcd. For $C_8H_9BF_3O_2$ (M-K) 205.0655; found, 205.0653.

Preparation of Potassium (3-Bromophenoxy)methyltrifluoroborate

(1m). The potassium aryloxide generated from 3-bromophenol (2.6 g, 15 mmol) was treated with $BrCH_2BF_3K$ (1.0 g, 5.0 mmol) at 45 °C for 1 day. The product was obtained in 95% yield (1.39 g, 4.8 mmol) as a white crystalline solid. **1H NMR** (400 MHz, $DMSO-d_6$) δ 2.97 (q, $J_{H,^{19}F}$ = 5.1 Hz, 2H), 6.85 (dd, $J_{H,H}$ = 8.4 Hz, 2.3 Hz, 1H), 6.94 (d, $J_{H,H}$ = 8.0 Hz, 1H), 7.01 (s, 1H), 7.14 (t, $J_{H,H}$ = 8.1 Hz, 1H); **^{13}C NMR** (125 MHz, $DMSO-d_6$) δ 113.5, 116.5, 121.2, 121.7, 130.6, 163.2. **HRMS** (APCI) m/z calcd. For $C_7H_6BBBrF_3O$ (M-K) 252.9654; found, 252.9648.

Preparation of Potassium (3,4-Dimethoxy)methyltrifluoroborate

(1n). Similarly to the preparation of **1a**, **1n** was prepared with 3,4-dimethylphenol (3.7 g, 30 mmol) and BrCH₂BF₃K (2.0 g, 10 mmol). The product was obtained in 84% yield (2.03 g, 8.4 mmol) as a white crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.10 (s, 3H), 2.14 (s, 3H), 2.88 (q, *J*_{H,¹⁹F} = 5.1 Hz, 2H), 6.54 (dd, *J*_{H,H} = 8.2 Hz, 2.7Hz, 1H), 6.63 (d, *J*_{H,H} = 2.7 Hz, 1H), 6.91 (d, *J*_{H,H} = 8.2 Hz, 1H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 18.3, 19.7, 110.7, 115.2, 125.4, 129.7, 136.3, 160.2. **HRMS** (APCI) *m/z* calcd. For C₉H₁₁BF₃O (M-K) 203.0862; found, 203.0865.

Preparation of Potassium (2-Naphthoxy)methyltrifluoroborate (1o).

The potassium aryloxide generated from 2-naphthol (4.3 g, 30 mmol) was treated with BrCH₂BF₃K (2.0 g, 10 mmol) at 45 °C for 1 day. The product was obtained in 56% yield (1.48 g, 5.6 mmol) as a pink crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 3.09 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 7.08 (dd, *J*_{H,H} = 8.9 Hz, 2.5 Hz, 1H), 7.20 (d, *J*_{H,H} = 2.5 Hz, 1H), 7.25 (t, *J*_{H,H} = 7.7 Hz, 1H), 7.38 (t, *J*_{H,H} = 7.5 Hz, 1H), 7.71 (d, *J*_{H,H} = 8.8 Hz, 1H), 7.74 (d, *J*_{H,H} = 7.3 Hz, 1H), 7.75 (d, *J*_{H,H} = 7.6 Hz, 1H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 105.2, 119.5, 122.4, 125.7, 126.4, 127.2, 127.7, 128.4, 134.7, 160.2. **HRMS** (APCI) *m/z* calcd. For C₁₁H₉BF₃O (M-K) 225.0706; found, 225.0699.

Preparation of Potassium (2-Methylphenoxy)methyltrifluoroborate

(1p). Similarly to the preparation of **1a**, **1p** was prepared with 2-methylphenol (3.2 g, 30 mmol) and BrCH₂BF₃K (2.0 g, 10 mmol). The product was obtained in 72% yield (1.64 g, 7.2 mmol) as a white crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.09 (s, 3H), 2.96 (q, *J*_{H,¹⁹F} = 5.2 Hz, 2H), 6.65 (t, *J*_{H,H} = 7.3 Hz, 1H), 6.86 (d, *J*_{H,H} = 8.1 Hz, 1H), 7.00 (d, *J*_{H,H} = 7.3 Hz, 1H), 7.05 (t, *J*_{H,H} = 7.7 Hz, 1H); **¹³C NMR** (125 MHz, DMSO-*d*₆) δ 16.1, 110.2, 117.9, 125.1, 126.5, 129.5, 160.1. **HRMS** (APCI) *m/z* calcd. For C₈H₉BF₃O (M-K) 189.0706; found, 189.0703.

Preparation of Potassium (2-Methoxyphenoxy)methyltrifluoroborate

(1q). Similarly to the preparation of **1a**, **1q** was prepared with 2-methoxyphenol (3.7 g, 30 mmol) and BrCH₂BF₃K (2.0 g, 10 mmol). The product was obtained in 70% yield (1.7 g, 7.0 mmol) as a white crystalline solid. **¹H NMR** (500 MHz, DMSO-*d*₆) δ 2.93 (q, *J*_{H,¹⁹F} = 5.1 Hz, 2H), 3.71 (s, 3H), 6.71 (t, *J*_{H,H} = 7.6 Hz, 1H), 6.81 (d, *J*_{H,H} = 7.8 Hz, 1H), 6.83 (d, *J*_{H,H} = 7.7 Hz, 1H), 6.90 (t, *J*_{H,H} = 7.9 Hz, 1H); **¹³C NMR** (75 MHz, DMSO-*d*₆) δ 55.2, 111.1, 111.4, 118.3, 120.7, 148.6, 151.8. **HRMS** (APCI) *m/z* calcd. For C₈H₉BF₃O₂ (M-K) 205.0655; found, 205.0654.

Preparation of Potassium (2-Fluorophenoxy)methyltrifluoroborate (**1r**).

The potassium aryloxy generated from 2-fluorophenol (3.4 g, 30 mmol) was treated with $\text{BrCH}_2\text{BF}_3\text{K}$ (2.0 g, 10 mmol) at 45 °C for 2 days. The product was obtained in 81% yield (1.87 g, 8.1 mmol) as a yellow crystalline solid. **^1H NMR** (300 MHz, $\text{DMSO}-d_6$) δ 3.03 (q, $J_{\text{H},^{19}\text{F}} = 5.0$ Hz, 2H), 6.68-6.82 (m, 1H), 6.94-7.14 (m, 3H); **^{13}C NMR** (75 MHz, $\text{DMSO}-d_6$) δ 113.5 (d, $J_{\text{C},^{19}\text{F}} = 1.4$ Hz), 114.9 (d, $J_{\text{C},^{19}\text{F}} = 17.9$ Hz), 118.3 (d, $J_{\text{C},^{19}\text{F}} = 6.7$ Hz), 124.4 (d, $J_{\text{C},^{19}\text{F}} = 3.5$ Hz), 150.0 (d, $J_{\text{C},^{19}\text{F}} = 10.3$ Hz), 151.7 (d, $J_{\text{C},^{19}\text{F}} = 240.7$ Hz). **HRMS** (APCI) m/z calcd. For $\text{C}_7\text{H}_6\text{BF}_4\text{O}$ (M-K) 193.0455; found, 193.0451.

Preparation of Potassium (2-Deuteriophenoxy)methyltrifluoroborate

(**1a-d₁**). The *o*-deuteriophenol was synthesized according to a known procedure.²⁴ Treatment of an ethereal solution of *o*-bromophenol with 2 equiv of *n*-butyllithium at 0 °C for 2-3 h afforded the dianionic lithium intermediate. Quenching the dianion with D_2O produced *o*-deuteriophenol in 90% isolated yield.

The procedure for preparation of phoxymethylborate **1a** was followed by employing *o*-deuteriophenol (3.4 g, 30 mmol). The product was obtained in 89% yield (1.91 g, 8.9 mmol) as a white crystalline solid. **^1H NMR** (500 MHz, $\text{DMSO}-d_6$) δ 2.94 (q, $J_{\text{H},^{19}\text{F}} = 5.3$ Hz, 2H), 6.76 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.83 (d, $J_{\text{H,H}} = 8.9$ Hz, 1H), 7.15–7.21 (m, 2H); **^{13}C NMR** (125 MHz, $\text{DMSO}-d_6$) δ 113.5 (t, $J_{\text{C},^2\text{H}} = 24.1$ Hz), 113.8, 118.4, 128.8, 128.9, 162.0. **HRMS** (APCI) m/z calcd. For $\text{C}_7\text{H}_5\text{BDF}_3\text{O}$ (M-K) 176.0612; found, 176.0614.

Preparation of Potassium (Pentadeuteriophenoxy)methyltrifluoroborate (1a-d₅). Similarly to the preparation of **1a**, **1a-d₅** was prepared with phenol-*d*₆ (0.60 g, 6.0 mmol) and BrCH₂BF₃K (0.40 g, 2.0 mmol). The product was obtained in 90% yield (0.39 g, 1.8 mmol) as a white crystalline solid. ¹H NMR (500 MHz, DMSO-*d*₆) δ 2.99 (q, *J*_{H,¹⁹F} = 5.4 Hz, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 113.5 (t, *J*_{C,²H} = 24.2 Hz), 118.1 (t, *J*_{C,²H} = 24.4 Hz), 128.5 (t, *J*_{C,²H} = 24.1 Hz), 161.9. HRMS (APCI) *m/z* calcd. For C₇H₂BD₅F₃O (M-K) 180.0863; found, 180.0866.

2.4.3 A Typical Procedure for Rhodium-Catalyzed Asymmetric Arylation of **2** with **1** (entry 6 in Table 2.1 and entry 1 in Table 2.2)

In an oven-dried Schlenk tube, were placed [RhCl((*R,R*)-Ph-bod)]₂ (3.97 mg, 0.005 mmol, 5 mol% of Rh), Cs₂CO₃ (130 mg, 0.40 mmol, 2.0 equiv), benzalacetone (**2a**) (29.2 mg, 0.20 mmol), and potassium phenoxymethyltrifluoroborate (**1a**) (51.4 mg, 0.24 mmol, 1.2 equiv) under argon. Degassed water (1.1 mL) was added, and the mixture was stirred at 100 °C for 16 h. The reaction mixture was passed through a short column of silica gel with EtOAc as eluent and the water stayed in silica gel. The solvent was removed on a rotary evaporator. After ¹H NMR analysis of the residue, the crude product was subjected to silica gel chromatography with EtOAc/hexane (1/10) to give **3aa** (43.6 mg, 0.17 mmol, 86% yield) as a colorless oil.

In entry 7 in Table 2.1, 2 equiv of potassium phenoxymethyltrifluoroborate (**1a**) (85.7 mg, 0.40 mmol) and Cs₂CO₃ (260 mg, 0.80 mmol, 4.0 equiv) were used.

In entries 11 and 12 in Table 2.1, $[\text{RhCl}((R)\text{-binap})]_2$ and $[\text{RhCl}((R)\text{-segphos})]_2$ were generated in situ from $[\text{RhCl}(\text{coe})_2]_2$ (3.59 mg, 0.010 mmol of Rh) and the corresponding bisphosphine ligands (0.011 mmol).

2.4.3 Characterization of the products

Compound 3aa [1005497-30-2]. (86% yield, 98% ee (*R*), Table 2.1, entry 6). The crude product was subjected to silica gel chromatography with EtOAc/hexane (1/10) to give **3aa** (43.6 mg, 0.17 mmol, 86% yield) as a colorless oil. The ee was measured by HPLC (Chiralpak IE column, 0.6 mL/min, hexane/2-propanol = 98/2, 230 nm, $t_{\text{major}} = 22.9$ min (*R*), $t_{\text{minor}} = 21.9$ min (*S*)); $[\alpha]_{\text{D}}^{25} +35.8$ (c 0.963, CHCl_3) for 98% ee. **^1H NMR** (500 MHz, CDCl_3) δ 2.10 (s, 3H), 3.14 (dd, $J_{\text{H,H}} = 16.5$ Hz, 7.3 Hz, 1H), 3.17 (dd, $J_{\text{H,H}} = 16.3$ Hz, 8.1 Hz, 1H), 3.80 (s, 3H), 4.99 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.85 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 6.89 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 7.11 (dd, $J_{\text{H,H}} = 7.6$ Hz, 1.7 Hz, 1H), 7.14–7.21 (m, 2H), 7.23–7.29 (m, 4H); **^{13}C NMR** (125 MHz, CDCl_3) δ 30.2, 39.5, 48.9, 55.4, 110.8, 120.5, 126.1, 127.5, 127.8, 127.9, 128.3, 132.1, 143.4, 156.7, 207.3. **HRMS** (ESI) calcd for $\text{C}_{17}\text{H}_{18}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 277.1199, found 277.1192. The spectral data are in agreement with reported literature values.²⁵

Compound 3ab [6402-59-5]. (94% yield, >99.5% ee (*R*), Table 2.2, entry 2). The crude product was subjected to silica gel chromatography to give **3ab** (59.4 mg, 0.19 mmol, 94% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IB column, 1.0 mL/min, hexane/2-propanol = 97/3, 280 nm, t_{major} = 8.1 min (*R*), t_{minor} = 9.2 min (*S*)); $[\alpha]_{\text{D}}^{25} +25.4$ (c 1.32, CHCl_3) for >99.5% ee. **^1H NMR** (300 MHz, CDCl_3) δ 3.72 (d, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 3.77 (s, 3H), 5.18 (t, $J_{\text{H,H}}$ = 7.4 Hz, 1H), 6.86 (t, $J_{\text{H,H}}$ = 7.8 Hz, 1H), 6.93 (d, $J_{\text{H,H}}$ = 7.5 Hz, 1H), 7.07–7.33 (m, 7H), 7.43 (t, $J_{\text{H,H}}$ = 7.2 Hz, 2H), 7.54 (tt, $J_{\text{H,H}}$ = 7.3 Hz, 2.5 Hz, 1H), 7.95 (d, $J_{\text{H,H}}$ = 7.1 Hz, 2H); **^{13}C NMR** (75 MHz, CDCl_3) δ 39.8, 43.8, 55.4, 110.9, 120.5, 126.1, 127.5, 128.06, 128.09, 128.12, 128.2, 128.5, 132.6, 132.8, 137.2, 143.6, 156.9, 198.4. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{20}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 339.1356, found 339.1359. The spectral data were in agreement with reported literature values.²⁶

Compound 3ac [603984-43-6]. (84% yield, 97% ee (*S*), Table 2.2, entry 3). The crude product was subjected to silica gel chromatography to give **3ac** (41.6 mg, 0.17 mmol, 84% yield) as a colorless oil. The ee was measured by HPLC (Chiralcel OJ-H column, 0.4 mL/min, hexane/2-propanol = 98/2, 280 nm, t_{major} = 18.7 min (*S*), t_{minor} = 20.1 min (*R*)); $[\alpha]_{\text{D}}^{25} +2.4$ (c 1.27, CHCl_3) for 97% ee. **^1H NMR** (400 MHz, CDCl_3) δ 0.83 (t, $J_{\text{H,H}}$ = 6.8 Hz, 3H), 1.05–1.30 (m, 6H), 1.51–1.70 (m, 2H), 2.04 (s, 3H), 2.68 (dd, $J_{\text{H,H}}$ = 15.6 Hz, 7.3 Hz, 1H), 2.72 (dd, $J_{\text{H,H}}$ = 15.6 Hz, 7.2 Hz, 1H), 3.56 (quint, $J_{\text{H,H}}$ = 7.2 Hz, 1H), 3.82 (s, 3H), 6.85 (d, $J_{\text{H,H}}$ = 8.2 Hz, 1H), 6.90 (td,

$J_{\text{H,H}} = 7.4 \text{ Hz}$, 1.0 Hz , 1H), $7.12 \text{ (dd, } J_{\text{H,H}} = 7.6 \text{ Hz, } 1.6 \text{ Hz, } 1\text{H})$, $7.16 \text{ (t, } J_{\text{H,H}} = 7.8 \text{ Hz, } 1\text{H})$; $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 14.0, 22.5, 27.0, 30.1, 31.8, 34.8, 34.9, 49.9, 55.3, 110.7, 120.6, 127.1, 127.9, 132.5, 157.3, 208.6. The spectral data are in agreement with reported literature values.²⁷

Compound 3ad [869540-81-8]. (77% yield, 94% ee (*R*), Table 2.2, entry 6).

The crude product was subjected to silica gel chromatography to give **3ad** (31.5 mg, 0.15 mmol, 77% yield) as a colorless oil. The ee was measured by HPLC (Chiralpak IA column, 0.7 mL/min, hexane/2-propanol = 97/3, 230 nm, $t_{\text{major}} = 11.2 \text{ min}$ (*R*), $t_{\text{minor}} = 10.7 \text{ min}$ (*S*)); $[\alpha]^{25}_{\text{D}} +37.6$ (c 1.31, CHCl_3) for 94% ee ($[\alpha]^{25}_{\text{D}} -36.3$ (c 1.02, CHCl_3) was reported for (*S*)-3-(2-methoxyphenyl)-cyclohexanone (94% ee)).²⁸ $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 1.79 (qdd, $J_{\text{H,H}} = 12.5 \text{ Hz, } 4.5 \text{ Hz, } 3.2 \text{ Hz, } 1\text{H}$), 1.87 (qd, $J_{\text{H,H}} = 12.3 \text{ Hz, } 2.9 \text{ Hz, } 1\text{H}$), 2.02 (br d, $J_{\text{H,H}} = 13.1 \text{ Hz, } 1\text{H}$), 2.13 (ddt, $J_{\text{H,H}} = 13.1 \text{ Hz, } 6.4 \text{ Hz, } 3.5 \text{ Hz, } 1\text{H}$), 2.38 (td, $J_{\text{H,H}} = 12.7 \text{ Hz, } 6.2 \text{ Hz, } 1\text{H}$), 2.46 (br d, $J_{\text{H,H}} = 14.3 \text{ Hz, } 1\text{H}$), 2.50 (t, $J_{\text{H,H}} = 13.0 \text{ Hz, } 1\text{H}$), 2.58 (ddt, $J_{\text{H,H}} = 14.0 \text{ Hz, } 4.4 \text{ Hz, } 2.0 \text{ Hz, } 1\text{H}$), 3.42 (tt, $J_{\text{H,H}} = 11.8 \text{ Hz, } 4.1 \text{ Hz, } 1\text{H}$), 3.82 (s, 3H), 6.87 (dd, $J_{\text{H,H}} = 8.2 \text{ Hz, } 1.1 \text{ Hz, } 1\text{H}$), 6.94 (td, $J_{\text{H,H}} = 7.6 \text{ Hz, } 1.3 \text{ Hz, } 1\text{H}$), 7.18 (dd, $J_{\text{H,H}} = 7.6 \text{ Hz, } 1.7 \text{ Hz, } 1\text{H}$), 7.22 (td, $J_{\text{H,H}} = 7.8 \text{ Hz, } 1.8 \text{ Hz, } 1\text{H}$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 25.6, 31.0, 37.9, 41.4, 47.5, 55.2, 110.5, 120.6, 126.5, 127.5, 132.5, 156.7, 211.6. The spectral data are in agreement with reported literature values.²⁹

Compound 3ae [155325-52-3]. (76% yield, 96% ee (*R*), Table 2.2, entry 7).

The crude product was subjected to silica gel chromatography to give **3ae** (28.9 mg, 0.15 mmol, 76% yield) as a colorless oil. The ee was measured by HPLC (Chiralpak IC column, 0.6 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 42.2$ min (*R*), $t_{\text{minor}} = 44.8$ min (*S*)); $[\alpha]_{\text{D}}^{25} +76.5$ (*c* 1.43, CHCl₃) for 96% ee. **¹H NMR** (500 MHz, CDCl₃) δ 2.00–2.10 (m, 1H), 2.25–2.49 (m, 4H), 2.64 (dd, $J_{\text{H,H}} = 18.3$ Hz, 7.8 Hz, 1H), 3.69 (tt, $J_{\text{H,H}} = 10.2$ Hz, 7.2 Hz, 1H), 3.84 (s, 3H), 6.89 (dd, $J_{\text{H,H}} = 8.2$ Hz, 1.1 Hz, 1H), 6.94 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.2 Hz, 1H), 7.18 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.8 Hz, 1H), 7.24 (td, $J_{\text{H,H}} = 7.8$ Hz, 1.7 Hz, 1H); **¹³C NMR** (125 MHz, CDCl₃) δ 29.1, 36.8, 38.7, 44.6, 55.2, 110.5, 120.6, 126.6, 127.7, 131.2, 157.4, 219.4. The spectral data are in agreement with reported literature values.³⁰

Compound 3af. (81% yield, 93% ee (*R*), Table 2.2, entry 9). The crude product was subjected to silica gel chromatography to give **3af** (35.3 mg, 0.16 mmol, 81% yield) as a colorless oil. The ee was measured by HPLC (Chiralpak IC column, 1.0 mL/min, hexane/2-propanol = 97/3, 254 nm, $t_{\text{major}} = 18.9$ min (*R*), $t_{\text{minor}} = 17.3$ min (*S*)); $[\alpha]_{\text{D}}^{25} +66.7$ (*c* 1.09, CHCl₃) for 93% ee. **¹H NMR** (500 MHz, CDCl₃) δ

1.54 (q, $J_{\text{H,H}} = 13.1$ Hz, 1H), 1.68 (qdt, $J_{\text{H,H}} = 12.2$ Hz, 3.6 Hz, 2.0 Hz, 1H), 1.72 (q, $J_{\text{H,H}} = 12.5$ Hz, 1H), 1.94–2.08 (m, 3H), 2.55–2.69 (m, 3H), 2.88 (dd, $J_{\text{H,H}} = 14.9$ Hz, 11.2 Hz, 1H), 3.36 (tt, $J_{\text{H,H}} = 11.6$ Hz, 2.4 Hz, 1H), 3.83 (s, 3H), 6.85 (dd, $J_{\text{H,H}} = 8.2$ Hz, 1.1 Hz, 1H), 6.91 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.4 Hz, 1H), 7.12 (dd, $J_{\text{H,H}} = 7.6$ Hz, 1.8 Hz, 1H), 7.18 (t, $J_{\text{H,H}} = 7.8$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 24.5, 29.7, 35.4, 37.5, 43.9, 50.2, 55.3, 110.5, 120.6, 126.5, 127.1, 135.1, 156.1, 214.2. **HRMS** (ESI) calcd for $\text{C}_{14}\text{H}_{18}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 241.1199, found 241.1194.

Compound 3ag. (87% yield, 97% ee (*R*), Table 2.2, entry 10). The crude product was subjected to silica gel chromatography to give **3ag** (49.4 mg, 0.17 mmol, 87% yield) as a colorless oil. The ee was measured by HPLC (Chiralpak IC column, 1.0 mL/min, hexane/2-propanol = 97/3, 230 nm, $t_{\text{major}} = 8.9$ min (*R*), $t_{\text{minor}} = 7.3$ min (*S*)); $[\alpha]_{\text{D}}^{25} +25.8$ (c 1.06, CHCl_3) for 97% ee. ^1H NMR (500 MHz, CDCl_3) δ 1.10 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 3.02 (dd, $J_{\text{H,H}} = 15.4$ Hz, 8.7 Hz, 1H), 3.06 (dd, $J_{\text{H,H}} = 15.4$ Hz, 7.5 Hz, 1H), 3.79 (s, 3H), 4.03 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 4.94 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.84 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H), 6.90 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.1 Hz, 1H), 7.13–7.21 (m, 3H), 7.23–7.29 (m, 4H); ^{13}C NMR (125 MHz, CDCl_3) δ 14.0, 39.7, 40.5, 55.4, 60.2, 110.8, 120.5, 126.1, 127.6, 127.8, 127.9, 128.2, 131.9, 143.3, 156.9, 172.1. **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{20}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 307.1305, found 307.1310.

Compound 5ba. (90% yield, 99% ee (*R*), Table 2.3, entry 1). The crude product was subjected to silica gel chromatography to give **5ba** (48.2 mg, 0.18 mmol, 90% yield) as a pale orange oil. The ee was measured by HPLC (Chiralpak IC column, 0.7 mL/min, hexane/2-propanol = 97/3, 280 nm, $t_{\text{major}} = 16.2$ min (*R*), $t_{\text{minor}} = 17.5$ min (*S*)); $[\alpha]_{\text{D}}^{25} +12.1$ (*c* 1.29, CHCl₃) for 99% ee. **¹H NMR** (500 MHz, CDCl₃) δ 2.08 (s, 3H), 2.24 (s, 3H), 3.11 (dd, $J_{\text{H,H}} = 16.2$ Hz, 7.2 Hz, 1H), 3.16 (dd, $J_{\text{H,H}} = 16.3$ Hz, 8.4 Hz, 1H), 3.76 (s, 3H), 4.94 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.73 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 6.90 (d, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.96 (d, $J_{\text{H,H}} = 8.3$ Hz, 1H), 7.12–7.18 (m, 1H), 7.20–7.28 (m, 4H); **¹³C NMR** (125 MHz, CDCl₃) δ 20.7, 30.1, 39.6, 48.9, 55.6, 110.9, 126.1, 127.8, 127.9, 128.3, 128.7, 129.6, 131.9, 143.5, 154.7, 207.4. **HRMS** (ESI) calcd for C₁₈H₂₀NaO₂ [M+Na]⁺ 291.1356, found 291.1362.

Compound 5ca. (92% yield, 98% ee (*R*), Table 2.3, entry 2). The crude product was subjected to silica gel chromatography to give **5ca** (52.3 mg, 0.18 mmol, 92% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IC column, 1.2 mL/min, hexane/2-propanol = 95/5, 230 nm, $t_{\text{major}} = 15.3$ min (*R*), $t_{\text{minor}} = 19.8$ min (*S*)); $[\alpha]_{\text{D}}^{25} +5.2$ (*c* 0.92, CHCl₃) for 98% ee. **¹H NMR** (500 MHz, CDCl₃)

δ 2.10 (s, 3H), 3.14 (d, $J_{\text{H,H}} = 7.5$ Hz, 2H), 3.72 (s, 3H), 3.74 (s, 3H), 4.96 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.69 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 6.70 (s, 1H), 6.77 (d, $J_{\text{H,H}} = 8.4$ Hz, 1H), 7.14–7.20 (m, 1H), 7.22–7.28 (m, 4H); ^{13}C NMR (125 MHz, CDCl_3) δ 30.2, 39.7, 48.9, 55.6, 56.1, 111.0, 111.9, 115.0, 126.2, 127.9, 128.3, 133.6, 143.2, 151.1, 153.6, 207.1. **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{20}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 307.1305, found 307.1311.

Compound 5db. (83% yield, >99.5% ee (*R*), Table 2.3, entry 3). The crude product was subjected to silica gel chromatography to give **5db** (55.5 mg, 0.17 mmol, 83% yield) as a white solid. The ee was measured by HPLC (Chiralpak IE column, 0.7 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 28.0$ min (*R*), $t_{\text{minor}} = 27.3$ min (*S*)); $[\alpha]_{\text{D}}^{25} +22.5$ (c 0.926, CHCl_3) for >99.5% ee. ^1H NMR (500 MHz, CDCl_3) δ 3.67 (dd, $J_{\text{H,H}} = 17.1$ Hz, 7.1 Hz, 1H), 3.70 (dd, $J_{\text{H,H}} = 17.1$ Hz, 7.7 Hz, 1H), 3.75 (s, 3H), 5.16 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.74–6.79 (m, 1H), 6.82–6.88 (m, 2H), 7.15–7.22 (m, 1H), 7.25–7.30 (m, 4H), 7.45 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.55 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.8$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 39.6, 43.6, 56.0, 111.7 (d, $J_{\text{C},^{19}\text{F}} = 8.2$ Hz), 113.1 (d, $J_{\text{C},^{19}\text{F}} = 22.6$ Hz), 115.0 (d, $J_{\text{C},^{19}\text{F}} = 23.6$ Hz), 126.4, 128.0, 128.1, 128.4, 128.6, 133.0, 134.5 (d, $J_{\text{C},^{19}\text{F}} = 6.4$ Hz), 137.0, 142.9, 153.0 (d, $J_{\text{C},^{19}\text{F}} = 2.2$ Hz), 157.1 (d, $J_{\text{C},^{19}\text{F}} = 236.1$ Hz), 197.9. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{FNaO}_2$ $[\text{M}+\text{Na}]^+$ 357.1261, found 357.1268.

Compound 5eb. (86% yield, >99.5% ee (*R*), Table 2.3, entry 4). The crude product was subjected to silica gel chromatography to give **5eb** (60.3 mg, 0.17 mmol, 86% yield) as a pale yellow solid. The ee was measured by HPLC (Chiralpak IC column, 0.6 mL/min, hexane/2-propanol = 98/2, 230 nm, $t_{\text{major}} = 17.3$ min (*R*), $t_{\text{minor}} = 18.7$ min (*S*)); $[\alpha]_{\text{D}}^{25} -8.0$ (c 0.94, CHCl_3) for >99.5% ee. **^1H NMR** (500 MHz, CDCl_3) δ 3.64 (dd, $J_{\text{H,H}} = 17.0$ Hz, 6.8 Hz, 1H), 3.70 (dd, $J_{\text{H,H}} = 17.0$ Hz, 8.0 Hz, 1H), 3.74 (s, 3H), 5.14 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.74 (d, $J_{\text{H,H}} = 8.6$ Hz, 1H), 7.08 (d, $J_{\text{H,H}} = 2.6$ Hz, 1H), 7.11 (dd, $J_{\text{H,H}} = 8.7$ Hz, 2.7 Hz, 1H), 7.14–7.19 (m, 1H), 7.23–7.28 (m, 4H), 7.43 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.50 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.93 (d, $J_{\text{H,H}} = 7.8$ Hz, 2H); **^{13}C NMR** (125 MHz, CDCl_3) δ 39.5, 43.5, 55.7, 112.1, 125.5, 126.3, 127.1, 127.99, 128.03, 128.1, 128.4, 128.5, 133.0, 134.6, 137.0, 142.9, 155.5, 197.9. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{ClNaO}_2$ $[\text{M}+\text{Na}]^+$ 373.0966, found 373.0973.

Compound 5fa. (85% yield, 98% ee (*R*), Table 2.3, entry 5). The crude product was subjected to silica gel chromatography to give **5fa** (56.5 mg, 0.17 mmol, 85% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IE column, 1.0 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 15.5$ min (*R*), $t_{\text{minor}} = 14.7$ min (*S*)); $[\alpha]_{\text{D}}^{25} -36.9$ (c 1.34, CHCl_3) for 98% ee. **^1H NMR** (500 MHz,

CDCl₃) δ 2.10 (s, 3H), 3.09 (dd, $J_{\text{H,H}} = 16.6$ Hz, 6.9 Hz, 1H), 3.16 (dd, $J_{\text{H,H}} = 16.6$ Hz, 8.5 Hz, 1H), 3.77 (s, 3H), 4.94 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.71 (d, $J_{\text{H,H}} = 8.6$ Hz, 1H), 7.16–7.30 (m, 7H); ¹³C NMR (125 MHz, CDCl₃) δ 30.3, 39.2, 48.5, 55.7, 112.6, 112.9, 126.4, 127.9, 128.4, 130.2, 130.6, 134.7, 142.6, 155.9, 206.6. **HRMS** (ESI) calcd for C₁₇H₁₇BrNaO₂ [M+Na]⁺ 355.0304, found 355.0301.

Compound 5fb. (84% yield, 99% ee (*R*), Table 2.3, entry 6). The crude product was subjected to silica gel chromatography to give **5fb** (66.3 mg, 0.17 mmol, 84% yield) as a pale orange solid. The ee was measured by HPLC (Chiralpak IE column, 0.6 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 35.1$ min (*R*), $t_{\text{minor}} = 33.2$ min (*S*)); $[\alpha]_{\text{D}}^{25} -11.6$ (c 1.04, CHCl₃) for 99% ee. ¹H NMR (500 MHz, CDCl₃) δ 3.65 (dd, $J_{\text{H,H}} = 17.1$ Hz, 6.7 Hz, 1H), 3.73 (dd, $J_{\text{H,H}} = 17.1$ Hz, 8.0 Hz, 1H), 3.76 (s, 3H), 5.15 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.71 (d, $J_{\text{H,H}} = 8.6$ Hz, 1H), 7.18 (t, $J_{\text{H,H}} = 8.8$ Hz, 1H), 7.23 (d, $J_{\text{H,H}} = 2.6$ Hz, 1H), 7.25–7.30 (m, 5H), 7.45 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 7.55 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 39.4, 43.5, 55.6, 112.5, 112.9, 126.3, 127.9, 128.0, 128.3, 128.5, 130.1, 130.8, 132.9, 135.0, 137.0, 142.8, 155.9, 197.8. **HRMS** (ESI) calcd for C₂₂H₁₉BrNaO₂ [M+Na]⁺ 417.0461, found 417.0456.

Compound 5gb. (90% yield, 99% ee (*R*), Table 2.3, entry 7). The crude product was subjected to silica gel chromatography to give **5gb** (69.3 mg, 0.18 mmol, 90% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IE column, 1.0 mL/min, hexane/2-propanol = 98/2, 254 nm, $t_{\text{major}} = 15.7$ min (*R*), $t_{\text{minor}} = 14.7$ min (*S*)); $[\alpha]^{25}_{\text{D}} -1.2$ (*c* 1.26, CHCl_3) for 99% ee. **^1H NMR** (500 MHz, CDCl_3) δ 3.69 (dd, $J_{\text{H,H}} = 17.0$ Hz, 6.9 Hz, 1H), 3.76 (dd, $J_{\text{H,H}} = 17.1$ Hz, 7.9 Hz, 1H), 3.82 (s, 3H), 5.21 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.89 (d, $J_{\text{H,H}} = 8.5$ Hz, 1H), 7.27 (t, $J_{\text{H,H}} = 8.8$ Hz, 1H), 7.25–7.30 (m, 4H), 7.40 (s, 1H), 7.45 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 7.47 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.55 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.94 (d, $J_{\text{H,H}} = 7.3$ Hz, 2H); **^{13}C NMR** (125 MHz, CDCl_3) δ 39.5, 43.5, 55.7, 110.5, 122.6 (q, $J_{\text{C},^{19}\text{F}} = 32.3$ Hz), 124.4 (q, $J_{\text{C},^{19}\text{F}} = 269.6$ Hz), 124.9 (q, $J_{\text{C},^{19}\text{F}} = 3.7$ Hz), 125.0 (q, $J_{\text{C},^{19}\text{F}} = 4.0$ Hz), 126.4, 127.95, 128.01, 128.4, 128.6, 133.0, 133.3, 137.0, 142.7, 159.3, 197.9. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{F}_3\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 407.1229, found 407.1234.

Compound 5hb. (87% yield, >99.5% ee (*R*), Table 2.3, entry 8). The crude product was subjected to silica gel chromatography to give **5hb** (67.5 mg, 0.18 mmol, 87% yield) as a pale yellow solid. The ee was measured by HPLC (Chiralpak ID column, 0.8 mL/min, hexane/2-propanol = 97/3, 254 nm, $t_{\text{major}} = 40.9$ min (*R*), $t_{\text{minor}} = 45.8$ min (*S*)); $[\alpha]^{25}_{\text{D}} -73.5$ (*c* 1.14, CHCl_3) for >99.5% ee. **^1H NMR** (500 MHz, CDCl_3) δ 1.34 (t, $J_{\text{H,H}} = 7.2$ Hz, 3H), 3.75 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H), 3.83 (s, 3H), 4.31 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 5.19 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.84 (d, $J_{\text{H,H}} = 8.5$ Hz, 1H), 7.16 (tt, $J_{\text{H,H}} = 7.2$ Hz, 1.4 Hz, 1H), 7.25 (t, $J_{\text{H,H}} = 7.9$ Hz, 2H), 7.29 (d, $J_{\text{H,H}} = 7.7$ Hz,

2H), 7.44 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.54 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.90 (dd, $J_{\text{H,H}} = 8.5$ Hz, 2.2 Hz, 1H), 7.93 (d, $J_{\text{H,H}} = 2.1$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.1$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 14.3, 39.3, 43.7, 55.6, 60.6, 110.2, 122.6, 126.2, 127.97, 128.04, 128.3, 128.5, 129.2, 129.8, 132.5, 133.0, 137.1, 143.3, 160.6, 166.5, 198.1. **HRMS** (ESI) calcd for $\text{C}_{25}\text{H}_{24}\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 411.1567, found 411.1575.

Compound 6ia. (89% yield, 99% ee (*R*), Table 2.3, entry 9). The crude product was subjected to silica gel chromatography to give 6ia (47.9 mg, 0.18 mmol, 89% yield) as a yellow oil. The ee was measured by HPLC (Chiralpak IE column, 0.6 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 33.0$ min (*R*), $t_{\text{minor}} = 30.5$ min (*S*)); $[\alpha]_{\text{D}}^{25} +29.4$ (c 1.47, CHCl_3) for 99% ee. ^1H NMR (500 MHz, CDCl_3) δ 2.09 (s, 3H), 2.31 (s, 3H), 3.13 (d, $J_{\text{H,H}} = 7.7$ Hz, 2H), 3.78 (s, 3H), 4.93 (t, $J_{\text{H,H}} = 7.8$ Hz, 1H), 6.66 (s, 1H), 6.70 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.98 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H), 7.13–7.18 (m, 1H), 7.22–7.27 (m, 4H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.4, 30.1, 39.3, 49.0, 55.4, 111.8, 121.1, 126.1, 127.7, 127.9, 128.3, 129.2, 137.4, 143.6, 156.6, 207.5. **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{20}\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 291.1356, found 291.1361.

Compound 6ib. (97% yield, 99% ee (*R*), Table 2.3, entry 10). The crude product was subjected to silica gel chromatography to give **6ib** (64.1 mg, 0.19 mmol, 97% yield) as a yellow solid. The ee was measured by HPLC (Chiralpak IE column, 0.8 mL/min, hexane/2-propanol = 98/2, 230 nm, $t_{\text{major}} = 21.4$ min (*R*), $t_{\text{minor}} = 20.1$ min (*S*)); $[\alpha]_{\text{D}}^{25} +24.6$ (*c* 1.19, CHCl₃) for 99% ee. **¹H NMR** (500 MHz, CDCl₃) δ 2.31 (s, 3H), 3.70 (d, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.75 (s, 3H), 5.13 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.67 (s, 1H), 6.69 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H), 7.00 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.15 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H), 7.25 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.28 (d, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.43 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 7.54 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.2$ Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 21.3, 39.5, 43.8, 55.3, 111.8, 121.0, 125.0, 127.8, 127.99, 128.03, 128.2, 128.4, 129.6, 132.8, 137.1, 137.3, 143.8, 156.6, 198.4. **HRMS** (ESI) calcd for C₂₃H₂₂NaO₂ [M+Na]⁺ 353.1512, found 353.1518.

Compound 6jb. (91% yield, 99% ee (*R*), Table 2.3, entry 11). The crude product was subjected to silica gel chromatography to give **6jb** (63.7 mg, 0.18 mmol, 91% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak ID

column, 0.6 mL/min, hexane/2-propanol = 98/2, 254 nm, $t_{\text{major}} = 20.0$ min (*R*), $t_{\text{minor}} = 19.1$ min (*S*); $[\alpha]_{\text{D}}^{25} +11.6$ (c 1.15, CHCl_3) for 99% ee. **¹H NMR** (500 MHz, CDCl_3) δ 3.69 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H), 3.77 (s, 3H), 5.12 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.83 (s, 1H), 6.87 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H), 7.05 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 7.15–7.20 (m, 1H), 7.24–7.28 (m, 4H), 7.45 (t, $J_{\text{H,H}} = 7.8$ Hz, 2H), 7.56 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H); **¹³C NMR** (125 MHz, CDCl_3) δ 39.4, 43.5, 55.6, 111.6, 120.5, 126.3, 127.94, 127.95, 128.02, 128.3, 128.5, 128.9, 131.2, 133.0, 137.0, 143.1, 157.4, 198.0. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{ClNaO}_2$ $[\text{M}+\text{Na}]^+$ 373.0966, found 373.0972.

Compound 6kb. (87% yield, 99% ee (*R*), Table 2.3, entry 12). The crude product was subjected to silica gel chromatography to give **6kb** (67.4 mg, 0.17 mmol, 87% yield) as a pale-yellow solid. The ee was measured by HPLC (Chiralpak IC column, 1.0 mL/min, hexane/2-propanol = 97/3, 254 nm, $t_{\text{major}} = 35.0$ min (*R*), $t_{\text{minor}} = 28.7$ min (*S*); $[\alpha]_{\text{D}}^{25} -9.3$ (c 0.910, CHCl_3) for 99% ee. **¹H NMR** (500 MHz, CDCl_3) δ 1.37 (t, $J_{\text{H,H}} = 7.2$ Hz, 3H), 3.72 (dd, $J_{\text{H,H}} = 17.1$ Hz, 7.7 Hz, 1H), 3.75 (dd, $J_{\text{H,H}} = 17.1$ Hz, 7.1 Hz, 1H), 3.83 (s, 3H), 4.36 (q, $J_{\text{H,H}} = 7.2$ Hz, 2H), 5.22 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.15–7.19 (m, 1H), 7.21 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H), 7.24–7.28 (m, 4H), 7.44 (t, $J_{\text{H,H}} = 8.1$ Hz, 2H), 7.52 (d, $J_{\text{H,H}} = 1.7$ Hz, 1H), 7.54 (tt, $J_{\text{H,H}} = 7.4$ Hz, 1.9 Hz, 1H), 7.59 (dd, $J_{\text{H,H}} = 8.0$ Hz, 1.6 Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.0$ Hz, 2H); **¹³C NMR** (125 MHz, CDCl_3) δ 14.3, 39.8, 43.4, 55.6, 60.9, 111.5, 122.0, 126.3, 127.8, 127.98,

128.00, 128.3, 128.5, 129.8, 133.0, 137.0, 137.8, 142.9, 156.7, 166.4, 197.9. **HRMS** (ESI) calcd for C₂₅H₂₄NaO₄ [M+Na]⁺ 411.1567, found 411.1574.

Compounds 6la and 7la (7:1). (92% yield, 99% ee (*R*), Table 2.3, entry 13). The crude product was subjected to silica gel chromatography to give the mixture (52.3 mg, 0.18 mmol, 92% yield) as a yellow oil. The ee for **compound 6la** was measured by HPLC (Chiralpak IE column, 1.0 mL/min, hexane/2-propanol = 95/5, 230 nm, *t*_{major} = 13.7 min (*R*), *t*_{minor} = 13.0 min (*S*) (**7la** *t*_{major} = 11.5 min (*R*), *t*_{minor} = 11.3 min (*S*)); [α]_D²⁵ +28.7 (*c* 0.942, CHCl₃) for this mixture. **¹H NMR** (500 MHz, CDCl₃) for **compound 6la** δ 2.08 (s, 3H), 3.11 (d, *J*_{H,H} = 7.8 Hz, 2H), 3.77 (s, 6H), 4.88 (t, *J*_{H,H} = 7.7 Hz, 1H), 6.41 (d, *J*_{H,H} = 8.1 Hz, 1H), 6.43 (s, 1H), 7.00 (d, *J*_{H,H} = 8.1 Hz, 1H), 7.10–7.18 (m, 1H), 7.20–7.30 (m, 4H); **¹H NMR** (500 MHz, CDCl₃) for **compound 7la** δ 2.09 (s, 3H), 3.32 (dd, *J*_{H,H} = 16.3, 7.7 Hz, 1H), 3.40 (dd, *J*_{H,H} = 16.3, 7.7 Hz, 1H), 3.80 (s, 6H), 5.29 (t, *J*_{H,H} = 7.7 Hz, 1H), 6.53 (d, *J*_{H,H} = 8.3 Hz, 2H), 7.10–7.18 (m, 2H), 7.20–7.30 (m, 4H); **¹³C NMR** (125 MHz, CDCl₃) for **compound 6la** δ 30.2, 39.2, 49.1, 55.3, 55.4, 98.9, 104.1, 124.7, 126.1, 127.8, 128.29, 128.32, 143.8, 157.7, 159.4, 207.6, (**7la** δ 55.7). **HRMS** (ESI) calcd for C₁₈H₂₀NaO₃ [M+Na]⁺ 307.1305, found 307.1309.

Compounds 6lb and 7lb (12:1). (94% yield, >99.5% ee (*R*), Table 2.3, entry 14). The crude product was subjected to silica gel chromatography to give the mixture (65.1 mg, 0.19 mmol, 94% yield) as a yellow oil. The ee for **Compound 6lb** was measured by HPLC (Chiralpak IE column, 0.5 mL/min, hexane/2-propanol = 98/2, 230 nm, $t_{\text{major}} = 57.7$ min (*R*), $t_{\text{minor}} = 54.6$ min (*S*) (**7lb** $t_{\text{major}} = 61.9$ min (*R*), $t_{\text{minor}} = 64.6$ min (*S*)); $[\alpha]_{\text{D}}^{25} +21.4$ (c 1.24, CHCl_3) for this mixture. **^1H NMR** (500 MHz, CDCl_3) for **compound 6lb** δ 3.70 (d, $J_{\text{H,H}} = 7.5$ Hz, 2H), 3.75 (s, 3H), 3.77 (s, 3H), 5.10 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.42 (dd, $J_{\text{H,H}} = 8.4$ Hz, 2.5 Hz, 1H), 6.44 (d, $J_{\text{H,H}} = 2.5$ Hz, 1H), 7.03 (d, $J_{\text{H,H}} = 8.3$ Hz, 1H), 7.10–7.18 (m, 1H), 7.20–7.30 (m, 4H), 7.44 (t, $J_{\text{H,H}} = 7.5$ Hz, 2H), 7.55 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.97 (d, $J_{\text{H,H}} = 7.1$ Hz, 2H); **^1H NMR** (500 MHz, CDCl_3) for **compound 7lb** δ 3.70 (d, $J_{\text{H,H}} = 7.5$ Hz, 2H), 3.73 (s, 6H), 5.51 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.53 (d, $J_{\text{H,H}} = 8.3$ Hz, 2H), 7.08–7.18 (m, 2H), 7.20–7.30 (m, 4H), 7.44 (t, $J_{\text{H,H}} = 7.5$ Hz, 2H), 7.55 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.97 (d, $J_{\text{H,H}} = 7.1$ Hz, 2H); **^{13}C NMR** (125 MHz, CDCl_3) for **compound 6lb** δ 38.4, 42.8, 54.2, 54.3, 97.8, 103.0, 124.1, 125.0, 126.95, 127.03, 127.2, 127.4, 127.5, 131.8, 136.1, 142.9, 156.7, 158.3, 197.5, (**7lb** δ 54.7). **HRMS** (ESI) calcd for $\text{C}_{23}\text{H}_{22}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 369.1461, found 369.1465.

Compounds 6le and 7le (11:1). (77% yield, 96% ee (*R*), Table 2.3, entry 15). The crude product was subjected to silica gel chromatography to give the mixture (34.0 mg, 0.15 mmol, 77% yield) as a pale yellow oil. The ee for **Compound 6le** was measured by HPLC (Chiralpak IB column, 1.0 mL/min, hexane/2-propanol = 98/2, 280 nm, $t_{\text{major}} = 17.5$ min (*R*), $t_{\text{minor}} = 19.9$ min (*S*) (**7le** $t_{\text{major}} = 14.7$ min (*R*), $t_{\text{minor}} = 16.3$ min (*S*)). $[\alpha]_{\text{D}}^{25} +64.5$ (c 1.56, CHCl_3) for this mixture. $^1\text{H NMR}$ (400 MHz, CDCl_3) for **compound 6le** δ 1.95–2.10 (m, 1H), 2.20–2.50 (m, 4H), 2.60 (dd, $J_{\text{H,H}} = 18.2$ Hz, 7.6 Hz, 1H), 3.59 (tt, $J_{\text{H,H}} = 10.0$ Hz, 7.2 Hz, 1H), 3.80 (s, 3H), 3.81 (s, 3H), 6.46 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.47 (s, 1H), 7.06 (d, $J_{\text{H,H}} = 8.0$ Hz, 1H), (**7le** δ 3.76 (s, 6H), 6.56 (d, $J_{\text{H,H}} = 7.3$ Hz, 2H), 7.16 (t, $J_{\text{H,H}} = 8.2$ Hz, 1H)); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) for **compound 6le** δ 28.3, 35.4, 37.7, 43.7, 54.2, 54.4, 97.8, 102.8, 122.6, 126.0, 157.4, 158.5, 218.7, (**7le** δ 54.0). **HRMS** (ESI) calcd for $\text{C}_{19}\text{H}_{22}\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 243.0997, found 243.0995.

Compounds 6lg and 7lg (9:1). (92% yield, 98% ee (*R*), Table 2.3, entry 16).

The crude product was subjected to silica gel chromatography to give the mixture (57.8 mg, 0.18 mmol, 92% yield) as a pale yellow oil. The ee for **Compound 6lg** was measured by HPLC (Chiralpak IE column, 0.7 mL/min, hexane/2-propanol = 98.5/1.5, 230 nm, $t_{\text{major}} = 34.0$ min (*R*), $t_{\text{minor}} = 32.0$ min (*S*) (**7lg** $t_{\text{major}} = 25.8$ min (*R*), $t_{\text{minor}} = 24.7$ min (*S*)). $[\alpha]_{\text{D}}^{25} +17.6$ (*c* 0.936, CHCl₃) for this mixture. **¹H NMR** (400 MHz, CDCl₃) for **compound 6lg** δ 1.09 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 2.97 (dd, $J_{\text{H,H}} = 15.3$ Hz, 8.6 Hz, 1H), 3.03 (dd, $J_{\text{H,H}} = 15.3$ Hz, 7.6 Hz, 1H), 3.74 (s, 3H), 3.76 (s, 3H), 4.01 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 4.84 (t, $J_{\text{H,H}} = 8.0$ Hz, 1H), 6.38–6.44 (m, 1H), 6.40 (s, 1H), 7.04 (d, $J_{\text{H,H}} = 8.7$ Hz, 1H), 7.10–7.25 (m, 5H); **¹H NMR** (400 MHz, CDCl₃) for **compound 7lg** δ 1.09 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 3.19 (dd, $J_{\text{H,H}} = 15.5$ Hz, 7.8 Hz, 1H), 3.31 (dd, $J_{\text{H,H}} = 15.5$ Hz, 8.1 Hz, 1H), 3.76 (s, 6H), 4.01 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 5.26 (t, $J_{\text{H,H}} = 8.0$ Hz, 1H), 6.51 (d, $J_{\text{H,H}} = 8.3$ Hz, 2H), 7.10–7.25 (m, 5H); **¹³C NMR** (100 MHz, CDCl₃) for **compound 6lg** δ 14.0, 39.8, 40.0, 55.2, 55.4, 60.2, 98.8, 103.9, 124.5, 126.0, 127.8, 128.1, 128.2, 143.6, 157.8, 159.4, 172.1, (**7lg** δ 55.7, 127.7, 104.5). **HRMS** (ESI) calcd for C₁₉H₂₂NaO₄ [M+Na]⁺ 337.1416, found 337.1414.

Compounds 6mb and 7mb (6:1). (86% yield, >99.5% ee (*R*), Table 2.3, entry 17). The crude product was subjected to silica gel chromatography to give the mixture (67.9 mg, 0.19 mmol, 86% yield) as a pale yellow oil. The ee for **Compound 6mb** was measured by HPLC (Chiralpak ID column, 0.8 mL/min, hexane/2-propanol = 97/3, 230 nm, $t_{\text{major}} = 14.7$ min (*R*), $t_{\text{minor}} = 13.3$ min (*S*) (**7mb** $t_{\text{major}} = 29.2$ min (*R*), $t_{\text{minor}} = 28.6$ min (*S*)); $[\alpha]_{\text{D}}^{25} +9.49$ (c 1.09, CHCl_3) for this mixture. $^1\text{H NMR}$ (500 MHz, CDCl_3) for **compound 6mb** δ 3.69 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H), 3.76 (s, 3H), 5.11 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.96 (d, $J_{\text{H,H}} = 1.6$ Hz, 1H), 6.98 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 7.01 (dd, $J_{\text{H,H}} = 8.3$ Hz, 1.5 Hz, 1H), 7.15–7.22 (m, 1H), 7.25–7.30 (m, 4H), 7.44 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 7.56 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H); $^1\text{H NMR}$ (500 MHz, CDCl_3) for **compound 7mb** δ 3.72 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H), 3.77 (s, 3H), 5.19 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H), 6.85 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H), 6.88 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 7.12 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.15–7.22 (m, 1H), 7.25–7.30 (m, 4H), 7.44 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 7.56 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H), 7.95 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) for **compound 6mb** δ 39.4, 43.4, 55.6, 114.4, 120.6, 123.4, 126.2, 127.9, 128.0, 128.3, 128.5, 129.2, 131.7, 132.9, 137.0, 143.0, 157.5, 197.9, (**7mb** δ 55.5). **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{BrNaO}_3$ $[\text{M}+\text{Na}]^+$ 417.0461, found 417.0469.

Compound 6na. (91% yield, 99% ee (*R*), Table 2.3, entry 18). The crude product was subjected to silica gel chromatography to give **6na** (51.5 mg, 0.18 mmol, 91% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IE column, 1.0 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 16.8$ min (*R*), $t_{\text{minor}} = 16.0$ min (*S*)); $[\alpha]_{\text{D}}^{25} +12.1$ (c 0.901, CHCl₃) for 99% ee. **¹H NMR** (500 MHz, CDCl₃) δ 2.10 (s, 3H), 2.15 (s, 3H), 2.22 (s, 3H), 3.11 (dd, $J_{\text{H,H}} = 16.2$ Hz, 7.3 Hz, 1H), 3.16 (dd, $J_{\text{H,H}} = 16.2$ Hz, 8.2 Hz, 1H), 3.77 (s, 3H), 4.92 (t, $J_{\text{H,H}} = 7.9$ Hz, 1H), 6.65 (s, 1H), 6.85 (s, 1H), 7.14–7.17 (m, 1H), 7.24–7.28 (m, 4H); **¹³C NMR** (125 MHz, CDCl₃) δ 18.9, 19.8, 30.1, 39.3, 49.0, 55.6, 112.7, 126.0, 127.8, 128.1, 128.2, 129.2, 129.3, 135.5, 143.7, 154.7, 207.5. **HRMS** (ESI) calcd for C₁₉H₂₂NaO₂ [M+Na]⁺ 305.1512, found 305.1514.

Compound 6oa. (80% yield, 98% ee (*R*), Table 2.3, entry 19). The crude product was subjected to silica gel chromatography to give **6oa** (48.7 mg, 0.16 mmol, 80% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IB column, 1.0 mL/min, hexane/2-propanol = 97/3, 230 nm, $t_{\text{major}} = 14.6$ min (*R*), t_{minor}

= 17.7 min (*S*)); $[\alpha]^{25}_{\text{D}} -91.1$ (*c* 0.921, CHCl_3) for 98% ee. **^1H NMR** (500 MHz, CDCl_3) δ 2.12 (s, 3H), 3.21 (dd, $J_{\text{H,H}} = 16.3$ Hz, 7.4 Hz, 1H), 3.26 (dd, $J_{\text{H,H}} = 16.2$ Hz, 8.0 Hz, 1H), 3.89 (s, 3H), 5.09 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.09 (s, 1H), 7.18 (t, $J_{\text{H,H}} = 6.7$ Hz, 1H), 7.25–7.33 (m, 5H), 7.39 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.53 (s, 1H), 7.69 (d, $J_{\text{H,H}} = 7.9$ Hz, 1H), 7.70 (d, $J_{\text{H,H}} = 8.0$ Hz, 1H); **^{13}C NMR** (125 MHz, CDCl_3) δ 30.3, 40.0, 49.1, 55.4, 105.5, 123.7, 125.9, 126.18, 126.23, 126.8, 127.4, 128.1, 128.3, 128.6, 133.4, 133.9, 143.2, 155.7, 207.1 **HRMS** (ESI) calcd for $\text{C}_{21}\text{H}_{20}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 327.1356, found 327.1358.

Compound 8pa. (72% yield, 99% ee (*R*), Table 2.3, entry 20). The crude product was subjected to silica gel chromatography to give 8pa (38.6 mg, 0.14 mmol, 72% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak ID column, 0.8 mL/min, hexane/2-propanol = 98/2, 230 nm, $t_{\text{major}} = 8.1$ min (*R*), $t_{\text{minor}} = 8.8$ min (*S*)); $[\alpha]^{25}_{\text{D}} +23.5$ (*c* 0.994, CHCl_3) for 99% ee. **^1H NMR** (500 MHz, CDCl_3) δ 2.09 (s, 3H), 2.28 (s, 3H), 3.14 (d, $J_{\text{H,H}} = 7.7$ Hz, 2H), 3.63 (s, 3H), 4.98 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.98 (t, $J_{\text{H,H}} = 7.5$, 1H), 7.04 (d, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.05 (d, $J_{\text{H,H}} = 7.5$ Hz, 1H), 7.13–7.18 (m, 1H), 7.22–7.28 (m, 4H); **^{13}C NMR** (125 MHz, CDCl_3) δ 16.4, 30.4, 39.5, 49.7, 60.4, 123.9, 125.5, 126.2, 127.8, 128.4, 129.8, 131.4, 136.6, 143.9, 156.4, 206.9. **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{20}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 291.1356, found 291.1361.

Compound 8qa. (78% yield, 97% ee (*R*), Table 2.3, entry 21). The crude product was subjected to silica gel chromatography to give **8qa** (44.4 mg, 0.16 mmol, 78% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IC column, 0.8 mL/min, hexane/2-propanol = 95/5, 230 nm, $t_{\text{major}} = 27.2$ min (*R*), $t_{\text{minor}} = 23.9$ min (*S*)); $[\alpha]_{\text{D}}^{25} +40.2$ (*c* 1.01, CHCl₃) for 97% ee. **¹H NMR** (500 MHz, CDCl₃) δ 2.10 (s, 3H), 3.16 (d, $J_{\text{H,H}} = 7.7$ Hz, 2H), 3.67 (s, 3H), 3.83 (s, 3H), 4.98 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.76 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 6.80 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H), 7.00 (t, $J_{\text{H,H}} = 7.9$ Hz, 1H), 7.12–7.18 (m, 1H), 7.22–7.28 (m, 4H); **¹³C NMR** (125 MHz, CDCl₃) δ 30.3, 39.7, 49.1, 55.6, 60.3, 110.8, 119.7, 123.8, 126.2, 127.8, 128.3, 137.6, 143.7, 146.7, 152.9, 207.0. **HRMS** (ESI) calcd for C₁₈H₂₀NaO₂ [M+Na]⁺ 307.1305, found 307.1309.

Compound 8ra. (74 % yield, 97% ee (*R*), Table 2.3, entry 22). The crude product was subjected to silica gel chromatography to give **8ra** (40.4 mg, 0.15 mmol, 74% yield) as a pale yellow oil. The ee was measured by HPLC (Chiralpak IC column, 0.7 mL/min, hexane/2-propanol = 99/1, 230 nm, $t_{\text{major}} = 23.7$ min (*R*), $t_{\text{minor}} = 22.4$ min (*S*)); $[\alpha]_{\text{D}}^{25} +10.7$ (*c* 0.935, CHCl₃) for 97% ee. **¹H NMR** (500 MHz,

CDCl₃) δ 2.10 (s, 3H), 3.17 (d, $J_{\text{H,H}} = 7.7$ Hz, 2H), 3.74 (s, 3H), 4.95 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.91–6.98 (m, 3H), 7.17 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.22 (d, $J_{\text{H,H}} = 6.8$ Hz, 2H), 7.26 (t, $J_{\text{H,H}} = 7.0$ Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 30.3, 39.7, 48.8, 61.0, 115.1 (d, $J_{\text{C},^{19}\text{F}} = 19.2$ Hz), 122.9 (d, $J_{\text{C},^{19}\text{F}} = 3.1$ Hz), 123.4 (d, $J_{\text{C},^{19}\text{F}} = 7.8$ Hz), 126.4, 127.7, 128.4, 138.5 (d, $J_{\text{C},^{19}\text{F}} = 2.1$ Hz), 143.3, 145.3 (d, $J_{\text{C},^{19}\text{F}} = 10.3$ Hz), 155.8 (d, $J_{\text{C},^{19}\text{F}} = 245.8$ Hz), 206.6. **HRMS** (ESI) calcd for C₁₇H₁₇FN₂O₂ [M+Na]⁺ 295.1105, found 295.1109.

Compound 3aa-d₅. (82%, Scheme 2.6). The crude product was subjected to silica gel chromatography to give **3aa-d₅** (43.2 mg, 0.16 mmol, 82% yield) as a colorless oil. The ratio is determined by ¹H and ²H NMR. **¹H NMR** (500 MHz, CDCl₃) δ 2.07 (s, 3H), 3.14 (dd, $J_{\text{H,H}} = 16.5$ Hz, 7.3 Hz, 1H), 3.17 (dd, $J_{\text{H,H}} = 16.3$ Hz, 8.1 Hz, 1H), 3.70–3.80 (m, 1.75H), 4.99 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.85 (s, 0.25H), 7.14–7.21 (m, 1H), 7.23–7.29 (m, 4H); **²H NMR** (77 MHz, acetone) δ 3.79 (br s, 1.2H), 6.5–7.5 (m, 3.8H); **HRMS** (ESI) calcd for C₁₇H₁₃D₅NaO₂ [M+Na]⁺ 286.1513, found 286.1516.

Compound 3aa-*d*₅ (9). ¹³C NMR (125 MHz, CDCl₃) δ 30.1, 39.6, 48.9, 55.1 (t, $J_{\text{C},^2\text{H}} = 21.9$ Hz), 110.5 (t, $J_{\text{C},^2\text{H}} = 23.4$ Hz), 120.0 (t, $J_{\text{C},^2\text{H}} = 24.6$ Hz), 126.1, 127.0 (t, $J_{\text{C},^2\text{H}} = 24.2$ Hz), 127.5 (t, $J_{\text{C},^2\text{H}} = 23.5$ Hz), 127.9, 128.2, 132.2, 143.5, 156.6, 207.1.

Compound 3aa-*d*₅ (10). ¹³C NMR (125 MHz, CDCl₃) δ 30.1, 39.6, 48.9, 54.8 (quint, $J_{\text{C},^2\text{H}} = 21.7$ Hz), 110.8, 120.0 (t, $J_{\text{C},^2\text{H}} = 24.6$ Hz), 126.1, 127.0 (t, $J_{\text{C},^2\text{H}} = 24.2$ Hz), 127.5 (t, $J_{\text{C},^2\text{H}} = 23.5$ Hz), 127.9, 128.2, 132.2, 143.5, 156.6, 207.1.

Compound 3aa-*d*₁. (87%, Scheme 2.6). The crude product was subjected to silica gel chromatography to give **3aa-*d*₁** (44.4 mg, 0.17 mmol, 87% yield) as a colorless oil. The ratio is determined by ¹H and ²H NMR. ¹H NMR (500 MHz, acetone-*d*₆) δ 2.06 (s, 3H), 3.17 (dd, $J_{\text{H,H}} = 16.5$ Hz, 7.3 Hz, 1H), 3.20 (dd, $J_{\text{H,H}} =$

16.3 Hz, 8.1 Hz, 1H), 3.78 (t, $J_{\text{H,H}} = 1.5$ Hz, 0.98H), 3.80 (s, 1.68H), 4.97 (t, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.88 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H), 6.92 (d, $J_{\text{H,H}} = 8.2$ Hz, 0.46H), 7.08–7.14 (m, 2H), 7.16–7.22 (m, 3H), 7.28 (d, $J_{\text{H,H}} = 7.9$ Hz, 2H); **^2H NMR** (77 MHz, acetone) δ 3.79 (s, 0.47H), 6.95 (s, 0.53H); **HRMS** (ESI) calcd for $\text{C}_{17}\text{H}_{17}\text{D}_1\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 278.1262, found 278.1260.

Compound 3aa- d_1 (11). **^{13}C NMR** (75 MHz, CDCl_3) δ 30.1, 39.5, 48.9, 55.4, 110.6 (t, $J_{\text{C},^2\text{H}} = 23.8$ Hz), 120.5, 126.1, 127.5, 127.8, 127.9, 128.2, 132.2, 143.5, 156.7, 207.2.

Compound 3aa- d_1 (12). **^{13}C NMR** (75 MHz, CDCl_3) δ 30.1, 39.5, 48.9, 55.1 (t, $J_{\text{C},^2\text{H}} = 21.9$ Hz), 110.8, 120.5, 126.1, 127.4, 127.8, 127.9, 128.2, 132.2, 143.5, 156.7, 207.2.

Compound 14. $^1\text{H NMR}$ (500 MHz, acetone- d_6) δ 4.00 (dd, $J_{\text{H,H}} = 10.0$ Hz, 8.3 Hz, 1H), 4.22 (dd, $J_{\text{H,H}} = 10.0$ Hz, 3.1 Hz, 1H), 5.03 (d, $J_{\text{H,H}} = 4.1$ Hz, 1H), 5.39 (dt, $J_{\text{H,H}} = 8.2$ Hz, 3.4 Hz, 1H), 6.86 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 6.87 (t, $J_{\text{H,H}} = 7.7$ Hz, 1H), 6.91 (tt, $J_{\text{H,H}} = 7.4$ Hz, 1.0 Hz, 1H), 6.98 (d, $J_{\text{H,H}} = 7.8$ Hz, 2H), 7.13 (td, $J_{\text{H,H}} = 7.7$ Hz, 1.7 Hz, 1H), 7.26 (t, $J_{\text{H,H}} = 8.1$ Hz, 1.0 Hz, 2H), 7.43 (d, $J_{\text{H,H}} = 7.3$ Hz, 1H); $^{13}\text{C NMR}$ (500 MHz, CDCl_3) δ 70.3, 73.2, 113.7, 116.6, 119.1, 120.7, 121.1, 126.7, 128.66, 128.71, 155.2, 157.0. **HRMS** (ESI) calcd for $\text{C}_{14}\text{H}_{12}\text{NO}_4\text{S}$ $[\text{M}+\text{H}]^+$ 290.0493, found 290.0494.

2.4.5 Single crystal X-ray diffraction data for **5fb**

Figure 2.6.1. ORTEP illustration of compound **5fb**.

Table 2.4. Crystal Data and Structure Refinement for Compound **5fb**

Empirical formula	$\text{C}_{22}\text{H}_{19}\text{BrO}_2$	
Formula weight	395.28 g/mol	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal size	0.086 × 0.146 × 0.376 mm	
Crystal habit	clear pale yellow plate	
Crystal system	Monoclinic	
Space group	P 1 2(1) 1	
Unit cell dimensions	$a = 11.8971(6)$ Å	$\alpha = 90^\circ$
	$b = 5.9845(3)$ Å	$\beta =$
		$95.961(2)^\circ$
	$c = 12.3079(7)$ Å	$\gamma = 90^\circ$
Volume	$871.56(8)$ Å ³	
Z	2	
Density (calculated)	1.506 g/cm ³	
Absorption coefficient	3.304 mm ⁻¹	
F(000)	404	
Theta range for data collection	3.61 to 72.43°	

Index ranges	$-14 \leq h \leq 14, -7 \leq k \leq 7, -15 \leq l \leq 15$
Reflections collected	13071
Independent reflections	3380 [R(int) = 0.0365]
Coverage of independent reflections	99.8%
Absorption correction	Multi-Scan
Max. and min. transmission	0.764 and 0.370
Structure solution technique	direct methods
Structure solution program	SHELXT, Acta Cryst., Sect. A 2015, A71, 3-8.
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)
Function minimized	$\sum w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	3380 / 1 / 227
Goodness-of-fit on F^2	1.090
Final R indices	3347 data; $I > 2\sigma(I)$ R1 = 0.0264, wR2 = 0.0694
Weighting scheme	all data R1 = 0.0267, wR2 = 0.0696 $w = 1 / [\sigma^2(F_o^2) + (0.0685P)^2]$ where $P = (F_o^2 + 2F_c^2) / 3$
Largest diff. peak and hole	0.326 and $-0.658 \text{ e}\text{\AA}^{-3}$
R.M.S. deviation from mean	$0.068 \text{ e}\text{\AA}^{-3}$

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Chapter 3

Migratory Arylstannylation of Alkynes Catalyzed Cooperatively by a Rhodium Complex and Zinc Chloride

3.1 Introduction

Organostannanes are the organometallic reagents that have been extensively used for organic synthesis.¹ They can be easily handled, which can be ascribed to their inertness towards oxygen and moisture due to the low polarity of the C–Sn bonds. In addition, organostannanes are reactive with various electrophiles in the presence of appropriate activators (Scheme 3.1). The palladium-catalyzed cross-coupling reaction (Stille coupling) is a classical example.² Compared with the more popular organoboron reagents for Suzuki coupling, organostannanes can generally be more easily transmetalated with the transition metal catalyst. The tin-lithium exchange is an invaluable method to prepare organolithium reagents, which will not produce lithium halides as byproduct.³ The Chan-Lam-Evans-type coupling⁴ is also a useful reaction to convert C–Sn bonds to C–N or C–O bonds in a chemoselective manner. Moreover, halodemetalation and protonolysis of organotin reagents are the conventional methods to form carbon–heteroatom and carbon–hydrogen bonds.⁵

Scheme 3.1. Selected Examples of Transformations of Organostannanes

The organostannanes have been most commonly prepared by the reaction of highly reactive organometallic reagents (RLi, RMgX) with tin electrophiles.

Meanwhile, considerable attention has been paid to the development of their new synthetic methods due to the synthetic utility of organotin reagents (Scheme 3.2). Palladium- or nickel-catalyzed stannylation of organic electrophiles with distannanes is one of such examples.⁶

Scheme 3.2. Typical Method to Prepare Arylstannanes

Here, we show our new findings that migratory arylstannylation of unfunctionalized alkynes is catalyzed by Rh complexes in the presence of a catalytic amount of ZnCl_2 to give *ortho*-alkenylarylstannanes in high yields. The reaction is proposed to proceed through 1,4-migration of Rh from the alkenyl carbon to the aryl carbon⁷⁻⁹ (Scheme 3.3a). The detailed discussion of 1,4-migration of Rh is shown in Chapter 1. Carbostannylation of alkynes with allyl- and alkynylstannanes has been achieved using transition metals such as Pd and Ni.^{10,11} However, the addition of arylstannanes has not been reported, to the best of our knowledge (Scheme 3.3b). In addition, the rhodium-catalyzed carbometalation of unfunctionalized alkynes has also not been reported. This type of arylmetalation reaction that is accompanied by the 1,4-migration of the metal has been reported by Yoshikai for arylzincation catalyzed by a cobalt complex (Scheme 3.3c).¹²

Scheme 3.3. Arylstannylation of Alkynes and 1,4-Migration

(a) Rhodium-catalyzed migratory arylstannylation of alkynes (This Work)

(b) Catalytic carbostannylation of alkynes

(c) Cobalt-catalyzed migratory arylzincation of alkynes (Yoshikai)

3.2 Results and discussion

The results obtained for the reaction of 4-octyne (**2a**) with PhSnBu₃ (**1a**, 2.0 equiv to **2a**) under various conditions are summarized in Table 3.1. The migratory arylstannylation was found to proceed in the presence of ZnCl₂ (1.0 equiv to **2a**) and a rhodium catalyst generated from [RhCl(coe)₂]₂ (5.0 mol % of Rh) and binap¹³ (5.5 mol%) in dioxane at 130 °C for 16 h to give 4-(2-stannylphenyl)-4-octene (**3aa**) in 85% yield with perfect *E* geometry¹⁴ (entry 1). The direct arylstannylation product **4aa** was not formed in a detectable amount under these reaction conditions. The yield of **3aa** was dependent on the amount of ZnCl₂ to some extent. With 2.0 equiv of ZnCl₂, the yield was slightly increased (89%) (entry 2). The yields were lower

with less amount of ZnCl_2 , being 73%, 71%, and 27%, with 0.50, 0.25, and 0.10 equiv of ZnCl_2 , respectively (entries 3–5). It is noted that ZnCl_2 is working as a catalyst though a substoichiometric amount is necessary for a high yield of **3aa**. The presence of ZnCl_2 is essential for the present arylstannylation, **3aa** being not formed at all in its absence (entry 6). At a lower reaction temperature (100 °C), the yield of **3aa** was lower by 10% (entry 7). Other zinc halides such as ZnBr_2 and ZnI_2 were less catalytically active than ZnCl_2 (entries 8 and 9). It was difficult to find a substitute of ZnCl_2 from other metal salts. For example, CuCl ¹⁵ gave a trace amount of **3aa** (entry 10). The binap ligand on Rh can be replaced by other biaryldiphosphine such as segphos or biphep. The yields with segphos¹⁶ and biphep were slightly lower (73% and 71%, respectively) than that with binap for the reaction of PhSnBu_3 (**1a**) (entries 11 and 12), while segphos performed better for the reactions of some other arylstannanes (see Table 3.2). The catalytic activity of other phosphine–Rh complexes were much lower. While dppf ligand gave a low yield (16%) of **3aa** (entry 13), the reaction did not take place with dppe, dppp, xantphos, or PPh_3 (entries 14–17). Rh complex with cyclooctadiene (cod) ligand or Ir/binap complex did not catalyze the reaction either (entries 18 and 19). The cobalt complex, $\text{CoCl}_2(\text{xantphos})$, which has been reported to be an effective catalyst for the migratory arylzincation,¹² is not a catalyst of choice for the present arylstannylation (entry 20).

Table 3.1. Rhodium-Catalyzed Phenylstannylation of 4-Octyne (2a) with PhSnBu₃ (1a)^a

Entry	Rh catalyst ^b (5 mol%)	Additive (equiv to 2a)	Yield (%) ^c of 3aa
1	Rh/binap	ZnCl ₂ (1.0)	85
2	Rh/binap	ZnCl ₂ (2.0)	89
3	Rh/binap	ZnCl ₂ (0.50)	73
4	Rh/binap	ZnCl ₂ (0.25)	71
5	Rh/binap	ZnCl ₂ (0.10)	27
6	Rh/binap	—	0
7 ^d	Rh/binap	ZnCl ₂ (1.0)	75
8	Rh/binap	ZnBr ₂ (1.0)	43
9	Rh/binap	ZnI ₂ (1.0)	18
10	Rh/binap	CuCl (1.0)	<3
11	Rh/segphos	ZnCl ₂ (1.0)	73
12	Rh/biphep	ZnCl ₂ (1.0)	71
13	Rh/dppf	ZnCl ₂ (1.0)	16
14	Rh/dppe	ZnCl ₂ (1.0)	0
15	Rh/dppp	ZnCl ₂ (1.0)	0
16	Rh/xantphos	ZnCl ₂ (1.0)	0
17	Rh/PPh ₃ ^e	ZnCl ₂ (1.0)	<3
18	Rh/cod ^f	ZnCl ₂ (1.0)	0
19	Ir/binap ^g	ZnCl ₂ (1.0)	0
20	Co/xantphos ^h	ZnCl ₂ (1.0)	7

^a Reaction conditions: 4-Octyne (**2a**) (0.20 mmol), PhSnBu₃ (**1a**) (0.40 mmol), and ZnCl₂ (0.20 mmol) in dioxane (1.0 mL) at 130 °C (bath temp) for 16 h. ^b Rh catalyst (5 mol% of Rh) was generated in situ from [RhCl(coe)₂]₂ (10 μmol of Rh) and bisphosphine (11 μmol). ^c Isolated yield. ^d At 100 °C. ^e RhCl(PPh₃)₃ (10 μmol). ^f [RhCl(cod)]₂ (10 μmol of Rh). ^g [IrCl(coe)₂]₂ (10 μmol of Ir) + binap (11 μmol). ^h CoCl₂(xantphos) (10 μmol).

The reaction conditions optimized for the phenylstannylation with PhSnBu₃ (**1a**), that is, Rh/binap (5 mol%) and ZnCl₂ (1.0 equiv) at 130 °C (entry 1 in Table 3.1), were successfully applied to the reaction of several other aryltin reagents

ArSnR₃ with 4-octyne (**2a**) (Table 3.2). The phenyltin reagents PhSnR₃, where R is methyl (**1b**), propyl (**1c**), or octyl (**1d**), all gave the corresponding phenylstannylation products **3ba–3da** in high yields (entries 2–4). It should be noted that trioctylarylstannanes are almost non-toxic. The yields are generally high for *para*-substituted aryltin reagents, those substituted with Me, Ph, Me₃Si, and CF₃O groups giving the corresponding products in 83–91% yields (entries 5–8). The lower yield (65%) for MeO-substituted one **1i** is mainly due to the instability of the product **3ia** under the reaction conditions (entry 9). For the reaction of aryltin reagents substituted with electron-withdrawing groups at the *para*-position, Cl (**1k**), Br (**1l**), CN (**1m**), and COOMe (**1n**), the Rh/binap catalyst was not very effective resulting in lower yields of the corresponding arylstannylation products. The use of Rh/segphos as a catalyst instead of Rh/binap improved the reaction for these aryltin reagents (entries 11–18). A typical example is the reaction of 4-BrC₆H₄SnBu₃, where the yields of the product **3la** are 47% and 78% with binap and segphos ligands, respectively (entries 13 and 14). In the arylstannylation with *meta*-substituted aryltin reagents, perfect regioselectivity of the 1,4-migration was observed. Thus, the reaction of those substituted with Me (**1p**), Me₃Si (**1q**), and CF₃ (**1r**) exclusively gave the corresponding 2,4-disubstituted aryltins **3pa–3ra**, which are the less hindered isomers (entries 20–22). The regioselectivity was also high for the reaction of 2-naphthyltin **1s**, where the 1,4-migration took place to the less hindered 3-position selectively (entry 23). Unfortunately, the migratory arylstannylation did not take place for *ortho*-substituted tin reagent **1t** under the present conditions (entry 24).

Table 3.2. Rhodium-Catalyzed Arylstannylation of 4-Octyne (2a) with ArSnR₃ 1^a

Entry	ArSnR ₃ 1	L on Rh ^b	yield (%) ^c of 3
1	PhSnBu ₃ (1a)	binap	85 (3aa)
2	PhSnMe ₃ (1b)	binap ^d	77 (3ba)
3	PhSnPr ₃ (1c)	binap	89 (3ca)
4	PhSnOct ₃ (1d)	binap	78 (3da)
5	4-MeC ₆ H ₄ SnBu ₃ (1e)	binap	87 (3ea)
6	4-PhC ₆ H ₄ SnBu ₃ (1f)	binap	91 (3fa)
7	4-Me ₃ SiC ₆ H ₄ SnBu ₃ (1g)	binap	83 (3ga)
8	4-CF ₃ OC ₆ H ₄ SnBu ₃ (1h)	binap	83 (3ha)
9	4-MeOC ₆ H ₄ SnBu ₃ (1i)	binap ^d	65 (3ia)
10	4-FC ₆ H ₄ SnBu ₃ (1j)	binap	77 (3ja)
11	4-ClC ₆ H ₄ SnBu ₃ (1k)	binap	73 (3ka)
12	4-ClC ₆ H ₄ SnBu ₃ (1k)	segphos	84 (3ka)
13	4-BrC ₆ H ₄ SnBu ₃ (1l)	binap	47 (3la)
14	4-BrC ₆ H ₄ SnBu ₃ (1l)	segphos	78 (3la)
15	4-NCC ₆ H ₄ SnBu ₃ (1m)	binap	51 (3ma)
16	4-NCC ₆ H ₄ SnBu ₃ (1m)	segphos	67 (3ma)
17	4-MeOOCCH ₂ CH ₂ SnBu ₃ (1n)	binap	61 (3na)
18	4-MeOOCCH ₂ CH ₂ SnBu ₃ (1n)	segphos	82 (3na)
19	4-CF ₃ C ₆ H ₄ SnBu ₃ (1o)	segphos	69 (3oa)
20	3-MeC ₆ H ₄ SnBu ₃ (1p)	binap	77 (3pa) ^e
21	3-Me ₃ SiC ₆ H ₄ SnBu ₃ (1q)	binap	84 (3qa) ^e
22	3-CF ₃ C ₆ H ₄ SnBu ₃ (1r)	binap	67 (3ra) ^e
23	2-naphthylSnBu ₃ (1s)	binap	83 (3sa) ^e
24	2-MeC ₆ H ₄ SnBu ₃ (1t)	binap	<3 (3ta)

^a Reaction conditions: 4-Octyne (**2a**) (0.20 mmol), ArSnR₃ **1** (0.40 mmol), ZnCl₂ (0.20 mmol), and Rh catalyst (5 mol% of Rh) in dioxane (1.0 mL) at 130 °C (bath temp) for 16 h. ^b Rh catalyst (5 mol% of Rh) was generated in situ from [RhCl(coe)₂]₂ (10 μmol of Rh) and binap or segphos (11 μmol). ^c Isolated yield. ^d In THF at 90 °C. ^e Regioselective 1,4-shift giving the products **3** shown below.

The results obtained for the reaction of PhSnBu_3 (**1a**) with several unfunctionalized alkynes substituted with alkyl and aryl groups are summarized in Table 3.3. The migratory arylstannylation proceeded well for longer-chain dialkylacetylenes, 5-decyne (**2b**) and 8-hexadecyne (**2c**), to give high yields of the corresponding products, **3ab** and **3ac**, respectively. In the reaction of unsymmetrically substituted dialkylacetylene **2d**, the regioselectivity was low, resulting in the formation of a mixture of **3ad** and its regioisomer in a ratio of 1.2/1.0. Diarylacetylenes also underwent the migratory arylstannylation, although the yields are generally lower than those for dialkylacetylenes.¹⁷ The reaction of alkyl(aryl)alkynes **2h–2l**, proceeded with high regioselectivity for the bond formation between the phenyl group of phenyltin **1a** and the alkyl-substituted alkyne carbon. This selectivity is as expected from the reported regiochemistry of carbometalation of alkyl(aryl)alkynes.¹⁸

Table 3.3. Rhodium-Catalyzed Arylstannylation of Alkynes **2 with PhSnBu₃ (**1a**)^a**

^a Reaction conditions: Alkyne **2** (0.20 mmol), PhSnBu₃ **1a** (0.40 mmol), ZnCl₂ (0.20 mmol), and Rh catalyst (5 mol% of Rh), generated in situ from [RhCl(coe)₂]₂ (10 μmol of Rh) and binap (11 μmol), in dioxane (1.0 mL) at 130 °C (bath temp) for 16 h. The structures of main regioisomers are shown for the products from unsymmetrically substituted alkynes.

The reaction pathway of the present migratory arylstannylation of alkynes, which is catalyzed cooperatively by Rh complex and ZnCl₂, is proposed as shown in Scheme 3.4. Thus, the transmetalation of the aryl group from Sn to Rh takes place in the reaction of PhSnR₃ **1** with a Cl–Rh species **A** to generate a Ph–Rh intermediate **B** and ClSnR₃,¹⁹ the latter being to be involved in the final step leading to the stannylation product **3**. The syn-addition of the Ph–Rh **B** to the alkyne **2** generates a 2-arylalkenyl–Rh **C**, and 1,4-migration of Rh from alkenyl to aryl^{7,8} gives an *ortho*-alkenylphenyl–Rh intermediate **D**, which has been reported to be thermodynamically more stable than **C**.^{8e} Transmetalation between the *ortho*-alkenylphenyl–Rh **D** and ZnCl₂ takes place to give an arylzinc chloride **E** and the Cl–Rh species **A**. Finally, the reaction of the arylzinc chloride **E** with ClSnR₃,²⁰ which was formed in the initial step, leads to the *ortho*-alkenylphenylstannane **3**,

with regeneration of ZnCl_2 . Direct transmetalation between the aryl–Rh intermediate **D** and ArSnR_3 **1** giving Ar–Rh **B** and the product **3** is less likely because a catalytic amount of ZnCl_2 is essential for the present arylstannylation (see entries 1–6 in Table 3.1).

Scheme 3.4. A Catalytic Cycle Proposed for Migratory Arylstannylation of Alkynes Catalyzed by Rh Complex and ZnCl_2

The reactions shown in Scheme 3.5 gave us further information on the catalytic cycle. Stoichiometric reactions of a Ph–Rh complex, $\text{RhPh}(\text{PPh}_3)(\text{binap})$ (**5**),²¹ with ClSnBu_3 (2.0 eq) in the presence of ZnCl_2 (1.2 eq) in dioxane at 130 °C gave 93% yield of PhSnBu_3 (**1a**), while the yield of **1a** is very low (12%) in the absence of ZnCl_2 under otherwise the same conditions (Scheme 3.5a). These reactions are related to the last transmetalation step producing the *ortho*-alkenylphenylstannane **3** from the Ar–Rh intermediate **D** in the catalytic cycle. The results show that the direct transmetalation between the intermediate **D** and ClSnR_3 is slow and that ZnCl_2 greatly accelerates the transmetalation. The fast transmetalation in the presence of ZnCl_2 is probably because of a lower energy caused by the double transmetalations from Rh to Zn and from Zn to Sn by the way

of the arylzinc species **E**. Rhodium-catalyzed 1,4-migration of Sn from an alkenylstannane **4ae** to an arylstannane **3ae** was observed in the presence of ZnCl₂, albeit in a low yield (16%).²² The 1,4-migration of Sn did not take place in the absence of ZnCl₂ (Scheme 3.5b). The catalytic cycle involving the 1,4-Rh shift from the intermediates **C** to **D** is supported by these results. The deuterium-labeling study using C₆D₅SnBu₃ (**1a-d₅**) (Scheme 3.5c), where the deuterium is incorporated at olefinic carbon in **3aa-d₅**, further supports this catalytic cycle involving the 1,4-Rh shift.

Scheme 3.5. Reactions to Support the Catalytic Cycle

The synthetic utility of arylstannanes has been well established.¹ According to the reported procedures,^{23–25} tributylstannyl group in **3aa** was converted into deuterio (**8**), iodo (**9**), and fluoro (**10**) successfully (Scheme 3.6). The palladium-catalyzed cross-coupling with an aryl iodide² and the rhodium-catalyzed conjugate addition to 2-cyclohexenone¹⁹ gave high yields of the corresponding products, **11** and **12**, respectively, as expected.

Scheme 3.6. Transformation of *ortho*-Alkenylarylstannane **3aa**

(a) $(\text{CF}_3\text{CO})_2\text{O}$, D_2O . (b) I_2 , CH_2Cl_2 . (c) selectfluor, AgOTf , acetone. (d) 4- $\text{IC}_6\text{H}_4\text{COOMe}$, $\text{PdCl}_2(\text{PPh}_3)_2$ (10 mol%), CuI , DMF. (e) 2-cyclohexenone, $[\text{RhCl}(\text{cod})]_2$ (5 mol% Rh), KOH , dioxane/ H_2O .

3.3 Conclusion

To summarize, migratory arylstannylation was found to take place in the reaction of arylstannanes ArSnR_3 with unfunctionalized alkynes in the presence of a bisphosphine–rhodium catalyst and a catalytic amount of zinc chloride to produce *ortho*-alkenylarylstannanes in high yields. A catalytic cycle involving three transmetalation steps, that is, transmetalation of aryl groups from Sn to Rh, Rh to Zn, and Zn to Sn, is proposed.

3.4 Experimental section

3.4.1 Materials

Alkynes (**2a–2c**, **2e–2h**, **2k**, and **2l**), aryl halides, bisphosphine ligands, *n*-BuLi, D₂O, CuI, CuCl, AgOTf, KOH, Mg, ZnCl₂, ZnBr₂, ZnI₂, cyclohex-2-enone, trifluoroacetic anhydride, tributyltin chloride, PhSnCl₃, PhSnBu₃ (**1a**), PhSnMe₃ (**1b**), 4-MeOC₆H₄SnBu₃ (**1i**), 4-FC₆H₄SnBu₃ (**1j**), 4-ClC₆H₄SnBu₃ (**1k**), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate), 1-bromooctane, 1-bromopropane, [IrCl(cod)₂]₂, CoCl₂(xantphos), PdCl₂(PPh₃)₂, RhCl(PPh₃)₃ and iodine were purchased and used as received. Dioxane and THF were distilled over benzophenone ketyl under N₂.

[RhCl(cod)₂]₂,²⁶ [RhCl(cod)₂]₂,²⁷ 4-BrC₆H₄SnBu₃ (**1l**) [17151-49-4],²⁸ 4-NCC₆H₄SnBu₃ (**1m**) [79048-30-9],²⁸ 4-MeOCC₆H₄SnBu₃ (**1n**) [91734-76-8],²⁹ and but-2-yn-1-ylcyclohexane (**2d**) [57497-07-1]³⁰ were prepared according to the reported procedures.

3.4.2 Preparation of trioctyl(phenyl)stannane (**1d**) [143363-50-2]

To a solution of octylmagnesium bromide in THF (25.0 mL), prepared from magnesium turnings (593 mg, 24 mmol) and 1-bromooctane (3.86 g, 20.0 mmol), PhSnCl₃ (1.51 g, 5.0 mmol) was added dropwise over 15 min at room temperature. The mixture was stirred at 65 °C for 10 h before H₂O (10.0 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was subjected to

chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give trioctyl(phenyl)stannane (**1d**) [143363-50-2] (70%, 1.87 g, 3.5 mmol) as colorless oil. The spectral data are in agreement with reported literature values.³¹

PhSnPr₃ (**1c**) [55335-05-2] was prepared in the same manner as above using propylmagnesium bromide, and the spectral data are in agreement with reported literature values.³²

3.4.3 Preparation of tributyl(4-(trifluoromethoxy)phenyl)stannane (**1h**) and tributyl(pentadeuterophenyl)stannane (**1a-d₅**)

To a solution of 4-(trifluoromethoxy)phenylmagnesium bromide in THF (10.0 mL), prepared from magnesium turnings (288 mg, 12 mmol) and 4-bromotrifluoromethoxybenzene (2.41 g, 10.0 mmol), Bu₃SnCl (3.26 g, 10.0 mmol) was added dropwise over 15 min at room temperature. The mixture was stirred at 65 °C for 10 h before H₂O (5.0 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give tributyl(4-(trifluoromethoxy)phenyl)stannane (**1h**) (84%, 3.79 g, 8.4 mmol) as colorless oil. **¹H NMR** (400 MHz, CDCl₃) δ 0.92 (t, *J*_{H,H} = 7.3 Hz, 9H), 1.09 (t, *J*_{H,H} = 8.1 Hz, *J*_{H,¹¹⁹Sn} = 51.2 Hz, 6H), 1.36 (sext, *J*_{H,H} = 7.3 Hz, 6H), 1.45–1.65 (m, 6H), 7.19 (d, *J*_{H,H} = 7.6 Hz, 2H), 7.50 (d, *J*_{H,H} = 8.1 Hz, *J*_{H,¹¹⁹Sn} = 35.7 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 9.7 (*J*_{C,¹¹⁹Sn} = 343.4 Hz, *J*_{C,¹¹⁷Sn} = 328.2 Hz), 13.6, 27.4 (*J*_{C,¹¹⁹Sn} =

55.9 Hz), 29.0 ($J_{\text{C},^{119}\text{Sn}} = 20.3$ Hz), 120.3 ($J_{\text{C},^{119}\text{Sn}} = 41.7$ Hz), 120.6 (q, $J_{\text{C},^{19}\text{F}} = 256.8$ Hz), 137.6 ($J_{\text{C},^{119}\text{Sn}} = 33.5$ Hz), 140.6 ($J_{\text{C},^{119}\text{Sn}} = 368.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 352.7$ Hz), 149.5 (q, $J_{\text{C},^{19}\text{F}} = 1.4$ Hz). **HRMS** (ESI) calcd for $\text{C}_{19}\text{H}_{31}\text{OF}_3\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 475.1247, found 475.1272.

$\text{C}_6\text{D}_5\text{SnBu}_3$ (**1a-d₅**) was prepared in the same manner as above using pentadeuterophenylmagnesium bromide and Bu_3SnCl . Thus, the reaction of a solution of pentadeuterophenylmagnesium bromides in THF (10.0 mL), prepared from magnesium turnings (299 mg, 12 mmol) and pentadeuterophenyl bromide (1.62 g, 10.0 mmol), with Bu_3SnCl (3.26 g, 10.0 mmol) at 65 °C for 10 h gave tributyl(pentadeuterophenyl)stannane (**1a-d₅**) (83% yield, 3.09 g, 8.3 mmol) as colorless oil. **¹H NMR** (300 MHz, CDCl_3) δ 0.93 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 1.10 (t, $J_{\text{H,H}} = 8.1$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.1$ Hz, 6H), 1.37 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.44–1.75 (m, 6H); **¹³C NMR** (75 MHz, CDCl_3) δ 9.5 ($J_{\text{C},^{119}\text{Sn}} = 339.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.6$ Hz), 13.7, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 56.6$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 20.1$ Hz), 127.4 (t, $J_{\text{C},^2\text{H}} = 24.1$ Hz), 136.0 (t, $J_{\text{C},^2\text{H}} = 24.0$ Hz), 141.7. **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{27}\text{D}_5\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 396.1738, found 396.1733.

4-MeC₆H₄SnBu₃ (**1e**) [31614-66-1],³¹ 4-PhC₆H₄SnBu₃ (**1f**) [51533-89-2],³² 4-Me₃SiC₆H₄SnBu₃ (**1g**) [38860-01-4],³³ 4-CF₃C₆H₄SnBu₃ (**1o**) [86487-19-6],²⁹ 3-MeC₆H₄SnBu₃ (**1p**) [68971-88-0],³⁰ 3-Me₃SiC₆H₄SnBu₃ (**1q**) [1026787-60-9],³⁴ 3-CF₃C₆H₄SnBu₃ (**1r**) [53566-38-4],²⁴ 2-naphthylSnBu₃ (**1s**) [972-11-2],²⁴ and 2-MeC₆H₄SnBu₃ (**1t**) [68971-87-9]²⁹ were prepared in the same manner as above from the corresponding arylmagnesium bromides and Bu_3SnCl . Their spectral data are in agreement with reported literature values.

3.4.4 Preparation of 1-(4-trimethylsilylphenyl)but-1-yne (**2i**) and 1-(3,4,5-trimethoxyphenyl)but-1-yne (**2j**)

$\text{PdCl}_2(\text{PPh}_3)_2$ (351.0 mg, 0.50 mmol, 5.0 mol%) and 1,4-bis(diphenylphosphino)butane (426.5 mg, 1.0 mmol, 10.0 mol%) were placed in a 100 mL flask under nitrogen. DMSO (25 mL) was added and the mixture was stirred at room temperature for 10 min. To the mixture, 1-bromo-4-(trimethylsilyl)benzene (2.29 g, 10.0 mmol), 2-pentynoic acid (1.18 g, 12.0 mmol), and DBU (4.58 g, 30.0 mmol) were added. The mixture was heated at 110 °C for 12 h. The mixture was diluted with 20.0 mL of diethyl ether, and it was passed through a short pad of silica gel with ethyl acetate as an eluent. The solution was washed with H_2O and brine, dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel to give 1-(4-trimethylsilylphenyl)but-1-yne (**2i**) (86%, 1.74 g, 8.6 mmol) as pale yellow oil. **^1H NMR** (400 MHz, CDCl_3) δ 0.25 (s, 9H), 1.24 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 2.42 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 7.36 (d, $J_{\text{H,H}} = 8.1$ Hz, 2H), 7.43 (d, $J_{\text{H,H}} = 8.1$ Hz, 2H); **^{13}C NMR** (100 MHz, CDCl_3) δ -1.2, 13.1, 13.9, 80.0, 92.1, 124.3, 130.6, 133.1, 139.9. **HRMS** (ESI) calcd for $\text{C}_{13}\text{H}_{19}\text{Si}$ $[\text{M}+\text{H}]^+$ 203.1256, found 203.1218.

The alkyne, 1-(3,4,5-trimethoxyphenyl)but-1-yne (**2j**), was prepared in the same manner as above using 5-bromo-1,2,3-trimethoxybenzene. Thus, the reaction of PdCl₂(PPh₃)₂ (351.0 mg, 0.50 mmol, 5.0 mol%), 1,4-bis(diphenylphosphino)butane (426.5 mg, 1.0 mmol, 10.0 mol%), 5-bromo-1,2,3-trimethoxybenzene (2.47 g, 10.0 mmol), 2-pentynoic acid (1.18 g, 12.0 mmol), and DBU (4.58 g, 30.0 mmol) at 110 °C for 12 h gave **2j** (72% yield, 1.59 g, 7.2 mmol) as colorless solid. **¹H NMR** (400 MHz, CDCl₃) δ 1.24 (t, *J*_{H,H} = 7.5 Hz, 3H), 2.41 (q, *J*_{H,H} = 7.5 Hz, 2H), 3.83 (s, 3H), 3.84 (s, 6H), 6.63 (s, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 12.9, 13.8, 55.9, 60.8, 79.7, 90.6, 108.6, 119.0, 138.1, 152.8. **HRMS** (ESI) calcd for C₁₃H₁₇O₃ [M+H]⁺ 221.1178, found 221.1190.

3.4.5 A typical procedure for migratory arylstannylation of alkynes catalyzed by rhodium complex and zinc chloride (Table 3.1, entry 1)

[RhCl(coe)₂]₂ (3.58 mg, 0.0050 mmol, 5.0 mol% of Rh), binap (6.85 mg, 0.0055 mmol, 5.5 mol%), ZnCl₂ (27.3 mg, 0.20 mmol), and PhSnBu₃ (**1a**) (146.9 mg, 0.40 mmol) were placed in a 10 mL Schlenk tube under nitrogen. Dioxane (1.0 mL) was added and the mixture was stirred at room temperature for 10 min. Before the tube was sealed, 4-octyne (**2a**) (22.0 mg, 0.20 mmol) was added. The tube was placed in a preheated oil bath at 130 °C and the mixture was stirred for 16 h. The reaction mixture was passed through a short pad of basic aluminum oxide with ethyl acetate as the eluent. The solvent was removed on a rotary

evaporator. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give (*E*)-4-(2-tributylstannylphenyl)oct-4-ene (**3aa**) (85%, 81.2 mg, 0.17 mmol) as colorless oil.

The procedures shown above in Section 3.4.5 for the reaction of PhSnBu₃ (**1a**) with 4-octyne (**2a**) (Table 3.1, entry 1) were used for the reaction of ArSnR₃ (**1c–1h**, **1j–1n**, and **1p–1t**) with 4-octyne (**2a**) (Table 3.2, entries 3–8, 10, 11, 13, 15, 17, and 20–24), and that of PhSnBu₃ (**1a**) with unfunctionalized alkynes (**2b–2l**) (Table 3.3).

In the reaction of ArSnR₃ (**1k–1o**) with 4-octyne (**2a**) (Table 3.2, entries 12, 14, 16, 18, and 19), the procedures shown in Section 3.4.5 were modified by use of segphos instead of binap.

In Table 3.2 entry 2, the procedures shown in Section 3.4.5 were modified by using THF as solvent and decreasing the reaction temperature to 90 °C. Thus, the reaction of [RhCl(coe)₂]₂ (3.58 mg, 0.0050 mmol, 5.0 mol% of Rh), binap (6.85 mg, 0.0055 mmol, 5.5 mol%), ZnCl₂ (27.3 mg, 0.20 mmol), PhSnMe₃ (**1b**) (96.4 mg, 0.40 mmol), and 4-octyne (**2a**, 22.0 mg, 0.20 mmol) in THF (1.0 mL) at 90 °C for 16 h gave (*E*)-4-(2-trimethylstannylphenyl)oct-4-ene (**3ba**) (77% yield, 54.1 mg, 0.15 mmol) as colorless oil. The same procedures for the reaction of PhSnMe₃ (**1b**) with 4-octyne (**2a**) were also applied to the reaction of 4-MeOC₆H₄SnBu₃ (**1i**) with 4-octyne (**2a**) (Table 3.2, entry 9).

3.4.6 Reactions to support the catalytic cycle (Scheme 3.5)

Scheme 3.5a

Scheme 3.5a, entry 1: In an oven-dried Schlenk tube, $\text{RhPh}(\text{PPh}_3)(\text{binap})$ (**5**)²¹ (106.0 mg, 0.10 mmol) and ZnCl_2 (16.4 mg, 0.12 mmol) were placed under nitrogen. Dioxane (1.0 mL) and Bu_3SnCl (65.3 mg, 0.20 mmol) were added and the mixture was heated at 130°C for 30 min. The reaction was quenched with saturated aqueous solution of Na_2CO_3 (1.0 mL). The mixture was extracted with diethyl ether, and the combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was subjected to short chromatography on silica gel (pre-treated with 1% Et_3N in hexanes) to give tributyl(phenyl)stannane (**1a**) (93%, 34.5 mg, 0.09 mmol) as colorless oil. $R_f = 0.9$ (hexanes). The spectral data are in agreement with reported literature values.²⁵

Scheme 3.5a, entry 2: The procedures for entry 1 in Scheme 3.5a were modified by removing ZnCl_2 . The reaction of $\text{RhPh}(\text{PPh}_3)(\text{binap})$ (107.1 mg, 0.10 mmol) and Bu_3SnCl (66.0 mg, 0.20 mmol) in dioxane (1.0 mL) at 130°C for 30 min gave tributyl(phenyl)stannane (**1a**) (12%, 4.5 mg, 0.01 mmol) as colorless oil.

Scheme 3.5b

Preparation of compound 4ae: To a solution of 2-bromo-1,1,2-triphenylethylene (3.35 g, 10.0 mmol) in diethyl ether (20.0 mL), n-BuLi (5.0 mL, 10.0 mmol, 2.0 M in cyclohexane) was added dropwise at $-78\text{ }^{\circ}\text{C}$ over 30 min. The mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$ and stirred for 2 h. Bu_3SnCl (3.30 g, 10.1 mmol) was added to the mixture at $0\text{ }^{\circ}\text{C}$. The mixture was stirred at room temperature for 12 h before H_2O (5.0 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et_3N in hexanes) to give **4ae** (88%, 4.78 g, 8.8 mmol) as pale yellow oil. $R_f = 0.8$ (hexanes). **^1H NMR** (400 MHz, CDCl_3) δ 0.53 (t, $J_{\text{H,H}} = 8.2\text{ Hz}$, $J_{\text{H},^{119}\text{Sn}} = 50.8\text{ Hz}$, 6H), 0.80 (t, $J_{\text{H,H}} = 7.2\text{ Hz}$, 9H), 1.16 (sext, $J_{\text{H,H}} = 7.2\text{ Hz}$, 6H), 1.21–1.32 (m, 6H), 6.87–7.03 (m, 8H), 7.12 (t, $J_{\text{H,H}} = 7.6\text{ Hz}$, 2H), 7.28–7.35 (m, 5H); **^{13}C NMR** (100 MHz, CDCl_3) δ 11.6 ($J_{\text{C},^{119}\text{Sn}} = 334.2\text{ Hz}$, $J_{\text{C},^{117}\text{Sn}} = 319.6\text{ Hz}$), 13.6, 27.3 ($J_{\text{C},^{119}\text{Sn}} = 61.6\text{ Hz}$), 29.0 ($J_{\text{C},^{119}\text{Sn}} = 19.3\text{ Hz}$), 124.4, 125.9, 127.1, 127.2, 127.6, 128.0 ($J_{\text{C},^{119}\text{Sn}} = 15.6\text{ Hz}$), 128.1, 129.4, 130.0, 142.5 ($J_{\text{C},^{119}\text{Sn}} = 49.2\text{ Hz}$), 145.9 ($J_{\text{C},^{119}\text{Sn}} = 26.0\text{ Hz}$), 146.2 ($J_{\text{C},^{119}\text{Sn}} = 25.4\text{ Hz}$), 148.3, 152.7 ($J_{\text{C},^{119}\text{Sn}} = 24.7\text{ Hz}$). **HRMS** (ESI) calcd for $\text{C}_{32}\text{H}_{42}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 569.2206, found 569.2206.

Scheme 3.5b, entry 1: In an oven-dried Schlenk tube, $[\text{RhCl}(\text{coe})_2]_2$ (10.9 mg, 0.015 mmol, 15 mol% of Rh), binap (19.9 mg, 0.032 mmol, 16 mol%), ZnCl_2

(81.5 mg, 0.60 mmol) and compound **4ae** (110.2 mg, 0.20 mmol) were placed under nitrogen. Before the tube was sealed, dioxane (1.0 mL) was added. The reaction mixture was heated at 130 °C for 16 h. The reaction mixture was passed through a short pad of basic aluminum oxide with ethyl acetate as the eluent. The solvent was removed on a rotary evaporator. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give **3ae** (16%, 17.6 mg, 0.32 mmol) as colorless oil.

Scheme 3.5b, entry 2: The procedures for entry 1 in Scheme 3.5b were modified by removing ZnCl₂. The reaction of compound **4ae** (112.2 mg, 0.21 mmol), [RhCl(coe)₂]₂ (10.5 mg, 0.015 mmol, 15 mol% of Rh) and binap (19.5 mg, 0.032 mmol, 16 mol%) in dioxane (1.0 mL) at 130 °C for 16 h did not give **3ae**. Compound **3ae** was not detected by ¹H NMR or GC.

Scheme 3.5c

Scheme 3.5c: The procedures for the reaction of PhSnBu₃ (**1a**) with 4-octyne (**2a**) (Table 3.1, entry 1) were used for the reaction of C₆D₅SnBu₃ (**1a-d₅**) with 4-octyne (**2a**). Thus, the reaction of [RhCl(coe)₂]₂ (3.61 mg, 0.0050 mmol, 5.0 mol% of Rh), binap (6.92 mg, 0.0110 mmol, 5.5 mol%), ZnCl₂ (27.6 mg, 0.20 mmol), C₆D₅SnBu₃ (**1a-d₅**) (148.9 mg, 0.40 mmol) and 4-octyne (**2a**) (22.3 mg, 0.20 mmol) in dioxane (1.0 mL) at 130 °C for 16 h gave **3aa-d₅** (87% yield, 83.9 mg, 0.17 mmol) as colorless oil.

Scheme 3.5d

Preparation of PhZnCl (6a**):** An oven-dried Schlenk flask equipped with a stir bar was charged with a solution of bromobenzene (3.39 g, 22.0 mmol) in THF (12.0 mL). The solution was cooled down to -80°C and n-BuLi (7.4 mL, 20.0 mmol, 2.69 M in hexanes) was added dropwise over 30 min. Precipitates were formed immediately. The reaction mixture was stirred at -80°C for 90 min. To the THF solution of phenyllithium thus generated, the THF solution of ZnCl_2 (30.0 mL, 30 mmol, 1.0 M) was added dropwise at -80°C . The reaction mixture was allowed to warm to room temperature to give a solution of phenylzinc chloride (**6a**) (0.4 M) and ZnCl_2 (0.2 M) in THF.

Scheme 3.5d: In an oven-dried Schlenk tube, $[\text{RhCl}(\text{coe})_2]_2$ (3.58 mg, 0.0050 mmol, 5.0 mol% of Rh) and binap (6.85 mg, 0.0110 mmol, 5.5 mol%) were placed under nitrogen. Dioxane (1.2 mL) was added and the mixture was stirred at room temperature for 10 min. To the mixture, 4-octyne (**2a**) (22.3 mg, 0.20 mmol) and 1.0 mL of the THF solution containing phenylzinc chloride (**6a**) (0.40 mmol, 0.4 M) and ZnCl_2 (0.4 mmol, 0.2 M), whose preparation is shown above, were added at room temperature. After the mixture was concentrated to *ca.* 1.0 mL under the flow of dry N_2 , the reaction mixture was heated at 130°C for 5 h. Bu_3SnCl (163.1 mg, 0.50 mmol) was added to the mixture at room temperature and the mixture was heated at 130°C for another 5 h. The reaction mixture was passed through a short pad of basic aluminum oxide with ethyl acetate as the eluent. The solvent was

removed on a rotary evaporator. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give (*E*)-4-(2-tributylstannylphenyl)oct-4-ene (**3aa**) (78%, 74.6 mg, 0.16 mmol) as colorless oil.

3.4.7 Transformations of (*E*)-4-(2-tributylstannylphenyl)oct-4-ene (**3aa**) (Scheme 3.6)

Deuterodestannylation of **3aa** was carried out according to a reported procedure.²³ To a mixture of trifluoroacetic anhydride (3.02g, 14.4 mmol) and **3aa** (85.9 mg, 0.18 mmol) in THF (1.0 mL) at 0 °C was added deuterium oxide (0.27 g, 13.5 mmol). The mixture was stirred at 0 °C for 10 min and was neutralized by addition of 6 N aqueous sodium hydroxide. The mixture was extracted with Et₂O, and the combined organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel to give (*E*)-4-(2-deuteriophenyl)oct-4-ene (**8**) (98%, 33.5 mg, 0.18 mmol) as colorless oil.

Iododestannylation of **3aa** was carried out according to a reported procedure²⁴ with minor modifications. An oven-dried flask was charged with **3aa** (114.7 mg, 0.24 mmol), I₂ (91.4 mg, 0.36 mmol), and CH₂Cl₂ (5.0 mL). The

mixture was stirred at room temperature for 2 h before saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (3.0 mL) was added. The mixture was extracted with Et_2O , and the combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel (pre-treated with 1% Et_3N in hexanes) to give (*E*)-4-(2-iodophenyl)oct-4-ene (**9**) (87%, 65.5 mg, 0.21 mmol) as colorless oil.

Fluorodestannylation of **3aa** was carried out according to a reported procedure.²⁵ Under nitrogen at room temperature, to a solution of **3aa** (90.6 mg, 0.19 mmol) in dry acetone (2.0 mL) was added silver triflate (97.6 mg, 0.38 mmol) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (80.9 mg, 0.23 mmol). The mixture was stirred at room temperature for 20 min, and it was passed through a short pad of silica gel with ethyl acetate as the eluent. The solvent was removed on a rotary evaporator. The residue was subjected to chromatography on silica gel to give (*E*)-4-(2-fluorophenyl)oct-4-ene (**10**) (69%, 27.1 mg, 0.13 mmol) as colorless oil.

The cross-coupling of **3aa** was performed according to a reported procedure³⁵ with some modifications. Under nitrogen, **3aa** (95.5 mg, 0.20 mmol), methyl 4-iodobenzoate (78.6 mg, 0.30 mmol), PdCl₂(PPh₃)₂ (14.0 mg, 0.020 mmol, 10 mol%), and CuI (28.6 mg, 0.15 mmol) were placed in a 10 mL Schlenk tube. DMF (4.0 mL) was added by syringe and the mixture was allowed to stir at 60 °C for 12 h. The mixture was passed through a short pad of silica gel with ethyl acetate as the eluent. The solvent was removed on a rotary evaporator. The residue was subjected to chromatography on silica gel to give (*E*)-4-(2-(4-methoxycarbonylphenyl)phenyl)oct-4-ene (**11**) (83%, 53.5 mg, 0.17 mmol) as pale yellow oil.

[RhCl(cod)]₂ (2.46 mg, 0.0050 mmol, 5 mol% of Rh), **3aa** (190.9 mg, 0.40 mmol), 2-cyclohexenone (19.2 mg, 0.20 mmol), and KOH (5.61 mg, 0.10 mmol) were placed in a 10 mL Schlenk tube under nitrogen. Dioxane (1.0 mL) and water (0.1 mL) were added by syringe, and the mixture was heated at 100 °C for 16 h. The mixture was passed through a short pad of silica gel with ethyl acetate as the eluent. The solvent was removed on a rotary evaporator. The residue was subjected to chromatography on silica gel to give the product **12** (87%, 49.5 mg, 0.17 mmol) as colorless oil.

3.4.8 Characterization of the products

Compound 3aa. (Table 3.2, entry 1, 85% yield, colorless oil). The *E* geometry was assigned by NOESY NMR study. **¹H NMR** (400 MHz, CDCl₃) δ 0.88 (t, *J*_{H,H} = 7.3 Hz, 9H), 0.90 (t, *J*_{H,H} = 7.2 Hz, 3H), 0.97 (t, *J*_{H,H} = 7.3 Hz, 3H), 0.99 (t, *J*_{H,H} = 8.0 Hz, *J*_H, ¹¹⁹Sn = 51.4 Hz, 6H), 1.32 (sext, *J*_{H,H} = 7.2 Hz, 6H+2H), 1.42–1.54 (m, 8H), 2.14 (q, *J*_{H,H} = 7.5 Hz, 2H), 2.32 (t, *J*_{H,H} = 8.0 Hz, 2H), 5.27 (t, *J*_{H,H} = 7.0 Hz, 1H), 7.15 (d, *J*_{H,H} = 7.4 Hz, 1H), 7.18 (td, *J*_{H,H} = 7.1 Hz, 1.5 Hz, 1H), 7.23 (td, *J*_{H,H} = 7.3 Hz, 1.6 Hz, 1H), 7.42 (dd, *J*_{H,H} = 7.0 Hz, 1.2 Hz, *J*_H, ¹¹⁹Sn = 42.9 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 10.9 (*J*_C, ¹¹⁹Sn = 339.7 Hz, *J*_C, ¹¹⁷Sn = 324.5 Hz), 13.6, 14.1, 14.4, 21.6, 22.9, 27.5 (*J*_C, ¹¹⁹Sn = 60.9 Hz), 29.2 (*J*_C, ¹¹⁹Sn = 18.9 Hz), 30.6, 34.9, 125.6 (*J*_C, ¹¹⁹Sn = 42.4 Hz), 127.4 (*J*_C, ¹¹⁹Sn = 9.6 Hz), 127.9 (*J*_C, ¹¹⁹Sn = 35.0 Hz), 129.5, 136.9 (*J*_C, ¹¹⁹Sn = 32.7 Hz), 140.7 (*J*_C, ¹¹⁹Sn = 412.3 Hz, *J*_C, ¹¹⁷Sn = 393.8 Hz), 144.3 (*J*_C, ¹¹⁹Sn = 14.6 Hz), 152.7 (*J*_C, ¹¹⁹Sn = 28.4 Hz). **HRMS** (ESI) calcd for C₂₆H₄₆Na¹²⁰Sn [M+Na]⁺ 501.2519, found 501.2537.

Compound 3ba. (Table 3.2, entry 2, 77% yield, colorless oil). ¹H NMR (400 MHz, CDCl₃) δ 0.24 (t, $J_{\text{H},^{119}\text{Sn}} = 53.0$ Hz, 9H), 0.91 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H),

0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.8$ Hz, 2H), 1.46 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.15 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.34 (t, $J_{\text{H,H}} = 8.1$ Hz, 2H), 5.31 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.19 (d, $J_{\text{H,H}} = 7.5$ Hz, 1H), 7.22 (t, $J_{\text{H,H}} = 6.9$ Hz, 1H), 7.24–7.28 (m, 1H), 7.47 (d, $J_{\text{H,H}} = 6.9$ Hz, $J_{\text{H},^{119}\text{Sn}} = 49.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ – 7.4 ($J_{\text{C},^{119}\text{Sn}} = 350.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 334.8$ Hz), 14.1, 14.5, 21.6, 22.9, 30.5, 34.8, 125.9 ($J_{\text{C},^{119}\text{Sn}} = 47.8$ Hz), 127.6 ($J_{\text{C},^{119}\text{Sn}} = 38.2$ Hz), 127.8 ($J_{\text{C},^{119}\text{Sn}} = 9.5$ Hz), 130.0, 136.3 ($J_{\text{C},^{119}\text{Sn}} = 38.6$ Hz), 141.0 ($J_{\text{C},^{119}\text{Sn}} = 497.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 475.1$ Hz), 144.2 ($J_{\text{C},^{119}\text{Sn}} = 16.4$ Hz), 152.4 ($J_{\text{C},^{119}\text{Sn}} = 31.1$ Hz). **HRMS** (ESI) calcd for $\text{C}_{17}\text{H}_{28}\text{Na}^{120}\text{Sn}$ [$\text{M}+\text{Na}$] $^{+}$ 375.1111, found 375.1118.

Compound 3ca. (Table 3.2, entry 3, 89% yield, colorless oil). ^1H NMR (400 MHz, CDCl_3) δ 0.90 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.96 (t, $J_{\text{H,H}} = 7.2$ Hz, 9H), 0.98 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.00 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.8$ Hz, 6H), 1.36 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.5$ Hz, 2H), 1.55 (sext, $J_{\text{H,H}} = 7.7$ Hz, 6H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.32 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.27 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.16 (dd, $J_{\text{H,H}} = 7.6$ Hz, 1.3 Hz, 1H), 7.18 (td, $J_{\text{H,H}} = 7.1$ Hz, 1.6 Hz, 1H), 7.23 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.6 Hz, 1H), 7.43 (dd, $J_{\text{H,H}} = 7.0$ Hz, 1.4 Hz, $J_{\text{H},^{119}\text{Sn}} = 43.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9 ($J_{\text{C},^{119}\text{Sn}} = 339.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 323.8$ Hz), 14.1, 14.4, 19.1 ($J_{\text{C},^{119}\text{Sn}} = 62.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 59.2$ Hz), 20.4 ($J_{\text{C},^{119}\text{Sn}} = 18.6$ Hz), 21.6, 22.9, 30.6, 34.9, 125.6 ($J_{\text{C},^{119}\text{Sn}} = 41.0$ Hz), 127.5 ($J_{\text{C},^{119}\text{Sn}} = 9.5$ Hz), 128.0 ($J_{\text{C},^{119}\text{Sn}} = 35.1$ Hz), 129.5, 136.9 ($J_{\text{C},^{119}\text{Sn}} = 32.4$ Hz), 140.7 ($J_{\text{C},^{119}\text{Sn}} = 412.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 394.1$ Hz), 144.3 ($J_{\text{C},^{119}\text{Sn}} = 14.7$ Hz), 152.7 ($J_{\text{C},^{119}\text{Sn}} = 27.7$ Hz). **HRMS** (ESI)

calcd for $C_{23}H_{40}Na^{120}Sn$ $[M+Na]^+$ 459.2059, found 459.2050.

Compound 3da. (Table 3.2, entry 4, 78% yield, colorless oil). **1H NMR** (400 MHz, $CDCl_3$) δ 0.88 (t, $J_{H,H} = 7.0$ Hz, 9H), 0.90 (t, $J_{H,H} = 7.2$ Hz, 3H), 0.97 (t, $J_{H,H} = 7.2$ Hz, 3H), 0.98 (t, $J_{H,H} = 8.3$ Hz, $J_{H,^{119}Sn} = 50.7$ Hz, 6H), 1.20–1.40 (br m, 32H), 1.41–1.60 (m, 8H), 2.14 (q, $J_{H,H} = 7.4$ Hz, 2H), 2.31 (t, $J_{H,H} = 8.0$ Hz, 2H), 5.26 (t, $J_{H,H} = 7.0$ Hz, 1H), 7.15 (d, $J_{H,H} = 7.6$ Hz, 1H), 7.17 (td, $J_{H,H} = 7.1$ Hz, 1.5 Hz, 1H), 7.22 (td, $J_{H,H} = 7.3$ Hz, 1.6 Hz, 1H), 7.41 (dd, $J_{H,H} = 7.0$ Hz, 1.3 Hz, $J_{H,^{119}Sn} = 42.8$ Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 11.2 ($J_{C,^{119}Sn} = 339.2$ Hz, $J_{C,^{117}Sn} = 323.0$ Hz), 14.09, 14.13, 14.4, 21.6, 22.7, 23.0, 26.9 ($J_{C,^{119}Sn} = 18.6$ Hz), 29.2, 29.3, 30.6, 31.9, 34.5 ($J_{C,^{119}Sn} = 58.1$ Hz), 34.9, 125.6 ($J_{C,^{119}Sn} = 41.7$ Hz), 127.4, 127.9, 129.5, 136.9 ($J_{C,^{119}Sn} = 32.9$ Hz), 140.8, 144.3, 152.7. **HRMS** (ESI) calcd for $C_{38}H_{71}^{120}Sn$ $[M+H]^+$ 647.4578, found 647.4565.

Compound 3ea. (Table 3.2, entry 5, 87% yield, colorless oil). **1H NMR** (400 MHz, $CDCl_3$) δ 0.88 (t, $J_{H,H} = 7.3$ Hz, 9H), 0.89 (t, $J_{H,H} = 7.3$ Hz, 3H), 0.96 (t, $J_{H,H} = 7.3$ Hz, 3H), 0.98 (t, $J_{H,H} = 7.8$ Hz, $J_{H,^{119}Sn} = 49.6$ Hz, 6H), 1.32 (sext, $J_{H,H} = 7.3$ Hz, 6H), 1.28–1.40 (m, 2H), 1.41–1.54 (m, 8H), 2.12 (q, $J_{H,H} = 7.4$ Hz, 2H), 2.30 (t, $J_{H,H} = 8.2$ Hz, 2H), 2.32 (s, 3H), 5.25 (t, $J_{H,H} = 7.0$ Hz, 1H), 7.02–7.08

(m, 2H), 7.21 (s, $J_{\text{H},^{119}\text{Sn}} = 44.3$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.8 ($J_{\text{C},^{119}\text{Sn}} = 338.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 323.7$ Hz), 13.6, 14.1, 14.4, 21.1, 21.6, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 62.3$ Hz, $J_{\text{C},^{117}\text{Sn}} = 59.4$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.7$ Hz), 30.6, 35.0, 127.7 ($J_{\text{C},^{119}\text{Sn}} = 37.0$ Hz), 128.3, 129.4, 134.8, 137.6, 140.5, 144.1, 149.8. **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{48}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 515.2676, found 515.2684.

Compound 3fa. (Table 3.2, entry 6, 91% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.92 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.98 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.02 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 47.2$ Hz, 6H), 1.33 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.32–1.42 (m, 2H), 1.44–1.55 (m, 8H), 2.16 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.35 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.32 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.23 (d, $J_{\text{H,H}} = 8.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 16.0$ Hz, 1H), 7.32 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.43 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 7.45 (d, $J_{\text{H,H}} = 8.0$ Hz, 1H), 7.58 (d, $J_{\text{H,H}} = 7.1$ Hz, 2H), 7.63 (d, $J_{\text{H,H}} = 1.9$ Hz, $J_{\text{H},^{119}\text{Sn}} = 43.6$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 339.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.9$ Hz), 13.7, 14.1, 14.5, 21.7, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 61.4$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.7$ Hz), 30.6, 34.9, 126.4 ($J_{\text{C},^{119}\text{Sn}} = 9.7$ Hz), 126.9, 127.1, 128.1 ($J_{\text{C},^{119}\text{Sn}} = 36.1$ Hz), 128.7, 129.7, 135.6 ($J_{\text{C},^{119}\text{Sn}} = 32.9$ Hz), 138.2, 141.3, 141.5, 144.0 ($J_{\text{C},^{119}\text{Sn}} = 13.9$ Hz), 151.8. **HRMS** (ESI) calcd for $\text{C}_{32}\text{H}_{50}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 577.2832, found 577.2823.

Compound 3ga. (Table 3.2, entry 7, 83% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.26 (s, 9H), 0.89 (t, $J_{\text{H,H}} = 7.2$ Hz, 9H+3H), 0.96 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.99 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 48.8$ Hz, 6H), 1.33 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H+2H), 1.43–1.53 (m, 8H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.32 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.27 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.15 (d, $J_{\text{H,H}} = 7.5$ Hz, $J_{\text{H},^{119}\text{Sn}} = 15.0$ Hz, 1H), 7.39 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.4 Hz, 1H), 7.58 (s, $J_{\text{H},^{119}\text{Sn}} = 42.3$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ −1.0, 11.0 ($J_{\text{C},^{119}\text{Sn}} = 337.9$ Hz, $J_{\text{C},^{117}\text{Sn}} = 322.1$ Hz), 13.7, 14.1, 14.4, 21.7, 22.9, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 60.1$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 19.5$ Hz), 30.6, 34.8, 127.2, 129.7, 132.6, 136.7, 139.7, 142.2, 144.3, 153.1. **HRMS** (ESI) calcd for C₂₉H₅₄NaSi¹²⁰Sn [M+Na]⁺ 573.2914, found 573.2903.

Compound 3ha. (Table 3.2, entry 8, 83% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}} = 7.2$ Hz, 9H), 0.90 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.01 (t, $J_{\text{H,H}} = 8.2$ Hz, $J_{\text{H},^{119}\text{Sn}} = 49.9$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.2$ Hz, 6H+2H), 1.43–1.54 (m, 8H), 2.13 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.30 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.27 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.04 (dd, $J_{\text{H,H}} = 8.4$ Hz, 1.4 Hz, 1H), 7.14 (d, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 16.5$ Hz, 1H), 7.23 (d, $J_{\text{H,H}} = 1.5$ Hz, $J_{\text{H},^{119}\text{Sn}} = 43.4$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 343.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 328.4$ Hz, 1H).

Hz), 13.6, 14.1, 14.3, 21.5, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 59.2$ Hz), 29.0 ($J_{\text{C},^{119}\text{Sn}} = 19.2$ Hz), 30.6, 34.9, 119.7, 120.6 (q, $J_{\text{C},^{19}\text{F}} = 256.5$ Hz), 128.6 ($J_{\text{C},^{119}\text{Sn}} = 34.4$ Hz), 128.9 ($J_{\text{C},^{119}\text{Sn}} = 37.0$ Hz), 130.2, 143.3 ($J_{\text{C},^{119}\text{Sn}} = 13.1$ Hz), 143.4 ($J_{\text{C},^{119}\text{Sn}} = 380.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 343.7$ Hz), 147.3, 151.2 ($J_{\text{C},^{119}\text{Sn}} = 25.0$ Hz). **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{45}\text{F}_3\text{ONa}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 585.2342, found 585.2335.

Compound 3ia. (Table 3.2, entry 9, 65% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.96 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.98 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.5$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H+2H), 1.42–1.52 (m, 8H), 2.11 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.29 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 3.80 (s, 3H), 5.24 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 6.76 (dd, $J_{\text{H,H}} = 8.4$ Hz, 2.8 Hz, 1H), 6.97 (d, $J_{\text{H,H}} = 2.8$ Hz, $J_{\text{H},^{119}\text{Sn}} = 46.6$ Hz, 1H), 7.09 (d, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 17.6$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 340.5$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.5$ Hz), 13.6, 14.1, 14.4, 21.6, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 60.6$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 30.6, 35.0, 55.1, 112.2, 122.4, 128.6, 129.3, 142.2, 143.8, 145.2, 157.2. **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{48}\text{ONa}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 531.2625, found 531.2617.

Compound 3ja. (Table 3.2, entry 10, 77% yield, colorless oil). **^1H NMR**

(400 MHz, CDCl₃) δ 0.886 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.894 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.99 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.9$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.27–1.37 (m, 2H), 1.41–1.53 (m, 8H), 2.12 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.28 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.24 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 6.88 (td, $J_{\text{H,H}} = J_{\text{H},^{19}\text{F}} = 8.6$ Hz, 2.8 Hz, 1H), 7.09 (dd, $J_{\text{H,H}} = 2.0$ Hz, $J_{\text{H},^{19}\text{F}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 43.6$ Hz, 1H), 7.10 (d, $J_{\text{H,H}} = 8.3$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 343.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 327.7$ Hz), 13.6, 14.1, 14.4, 21.5, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.7$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.1$ Hz), 30.6, 35.0, 114.0 (d, $J_{\text{C},^{19}\text{F}} = 20.9$ Hz, $J_{\text{C},^{119}\text{Sn}} = 8.7$ Hz), 122.7 (d, $J_{\text{C},^{19}\text{F}} = 17.5$ Hz, $J_{\text{C},^{119}\text{Sn}} = 34.1$ Hz), 129.2 (d, $J_{\text{C},^{19}\text{F}} = 6.5$ Hz, $J_{\text{C},^{119}\text{Sn}} = 39.4$ Hz), 129.9, 143.4 ($J_{\text{C},^{119}\text{Sn}} = 13.2$ Hz), 143.6 (d, $J_{\text{C},^{19}\text{F}} = 2.1$ Hz), 148.4 (d, $J_{\text{C},^{19}\text{F}} = 3.1$ Hz, $J_{\text{C},^{119}\text{Sn}} = 25.8$ Hz), 161.1 (d, $J_{\text{C},^{19}\text{F}} = 248.6$ Hz). **HRMS** (ESI) calcd for C₂₆H₄₅FNa¹²⁰Sn [M+Na]⁺ 519.2425, found 519.2407.

Compound 3ka. (Table 3.2, entry 12, 84% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H+3H), 0.96 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.00 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.7$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H+2H), 1.42–1.51 (m, 8H), 2.12 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.28 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.25 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.06 (d, $J_{\text{H,H}} = 8.2$ Hz, $J_{\text{H},^{119}\text{Sn}} = 16.2$ Hz, 1H), 7.18 (dd, $J_{\text{H,H}} = 8.2$ Hz, 2.3 Hz, 1H), 7.34 (d, $J_{\text{H,H}} = 2.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 42.1$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 342.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 327.6$ Hz), 13.6, 14.1, 14.4, 21.5, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.1$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.0$ Hz), 30.5, 34.8, 127.4 ($J_{\text{C},^{119}\text{Sn}} = 8.5$ Hz), 129.2 ($J_{\text{C},^{119}\text{Sn}} = 35.7$ Hz), 130.0, 132.0 ($J_{\text{C},^{119}\text{Sn}} = 53.4$ Hz),

136.1 ($J_{\text{C},^{119}\text{Sn}} = 34.6$ Hz), 143.3 ($J_{\text{C},^{119}\text{Sn}} = 13.0$ Hz), 143.4, 150.8 ($J_{\text{C},^{119}\text{Sn}} = 25.4$ Hz). **HRMS** (ESI) calcd for $\text{C}_{26}\text{H}_{45}\text{NaCl}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 535.2129, found 535.2140.

Compound 3la. (Table 3.2, entry 14, 78% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H+3H), 0.96 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.00 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.2$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H+2H), 1.42–1.51 (m, 8H), 2.12 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.28 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.26 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.00 (d, $J_{\text{H,H}} = 8.1$ Hz, $J_{\text{H},^{119}\text{Sn}} = 16.1$ Hz, 1H), 7.32 (dd, $J_{\text{H,H}} = 8.2$ Hz, 2.2 Hz, 1H), 7.48 (d, $J_{\text{H,H}} = 2.1$ Hz, $J_{\text{H},^{119}\text{Sn}} = 41.4$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 343.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 327.1$ Hz), 13.6, 14.1, 14.4, 21.5, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.5$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.2$ Hz), 30.5, 34.8, 120.7, 129.7, 130.0, 130.3, 139.0, 143.3, 144.1, 151.2. **HRMS** (ESI) calcd for $\text{C}_{26}\text{H}_{45}\text{NaBr}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 579.1624, found 579.1625.

Compound 3ma. (Table 3.2, entry 16, 67% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.886 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.892 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.01 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.2$ Hz, 6H), 1.31 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.25–1.36 (m, 2H), 1.41–1.50 (m, 8H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz,

2H), 2.31 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.28 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.20 (d, $J_{\text{H,H}} = 7.9$ Hz, $J_{\text{H},^{119}\text{Sn}} = 14.4$ Hz, 1H), 7.50 (dd, $J_{\text{H,H}} = 7.9$ Hz, 1.8 Hz, 1H), 7.66 (d, $J_{\text{H,H}} = 1.7$ Hz, $J_{\text{H},^{119}\text{Sn}} = 39.2$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 345.3$ Hz, $J_{\text{C},^{117}\text{Sn}} = 329.8$ Hz), 13.6, 14.1, 14.3, 21.6, 22.8, 27.3 ($J_{\text{C},^{119}\text{Sn}} = 62.3$ Hz), 29.0 ($J_{\text{C},^{119}\text{Sn}} = 19.3$ Hz), 30.5, 34.5, 109.6 ($J_{\text{C},^{119}\text{Sn}} = 44.8$ Hz), 119.8, 128.2 ($J_{\text{C},^{119}\text{Sn}} = 30.9$ Hz), 131.0, 131.1 ($J_{\text{C},^{119}\text{Sn}} = 8.5$ Hz), 140.3 ($J_{\text{C},^{119}\text{Sn}} = 35.6$ Hz), 142.9, 143.5 ($J_{\text{C},^{119}\text{Sn}} = 12.2$ Hz), 157.2 ($J_{\text{C},^{119}\text{Sn}} = 24.8$ Hz). **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{45}\text{NNa}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 526.2472, found 526.2480.

Compound 3na. (Table 3.2, entry 18, 82% yield, colorless oil). The *E* geometry was assigned by NOESY NMR study. **^1H NMR** (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.02 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 49.9$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H+2H), 1.42–1.53 (m, 8H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.33 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 3.90 (s, 3H), 5.30 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.20 (d, $J_{\text{H,H}} = 8.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 15.0$ Hz, 1H), 7.87 (dd, $J_{\text{H,H}} = 8.0$ Hz, 1.8 Hz, 1H), 8.09 (d, $J_{\text{H,H}} = 1.8$ Hz, $J_{\text{H},^{119}\text{Sn}} = 43.2$ Hz, 1H); **^{13}C NMR** (75 MHz, CDCl_3) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 342.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 327.3$ Hz), 13.6, 14.1, 14.3, 21.6, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.3$ Hz, $J_{\text{C},^{117}\text{Sn}} = 59.6$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.1$ Hz), 30.6, 34.6, 51.9, 127.1 ($J_{\text{C},^{119}\text{Sn}} = 41.3$ Hz), 127.8 ($J_{\text{C},^{119}\text{Sn}} = 32.9$ Hz), 128.8 ($J_{\text{C},^{119}\text{Sn}} = 8.8$ Hz), 130.3, 138.1 ($J_{\text{C},^{119}\text{Sn}} = 35.4$ Hz), 141.2, 143.9 ($J_{\text{C},^{119}\text{Sn}} = 13.1$ Hz), 157.5 ($J_{\text{C},^{119}\text{Sn}} = 27.5$ Hz), 167.6. **HRMS** (ESI) calcd for

$\text{C}_{28}\text{H}_{48}\text{O}_2\text{Na}^{120}\text{Sn} [\text{M}+\text{Na}]^+ 559.2574$, found 559.2605.

Compound 3oa. (Table 3.2, entry 19, 69% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.90 (t, $J_{\text{H,H}} = 7.2$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.02 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 52.2$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.27–1.37 (m, 2H), 1.42–1.52 (m, 8H), 2.15 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.32 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.29 (t, $J_{\text{H,H}} = 7.1$ Hz, 1H), 7.23 (d, $J_{\text{H,H}} = 7.9$ Hz, $J_{\text{H},^{119}\text{Sn}} = 14.5$ Hz, 1H), 7.46 (dd, $J_{\text{H,H}} = 8.0$ Hz, 1.5 Hz, 1H), 7.63 (s, $J_{\text{H},^{119}\text{Sn}} = 42.4$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 343.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 328.7$ Hz), 13.6, 14.1, 14.4, 21.6, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.0$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.2$ Hz), 30.5, 34.7, 124.4 (q, $J_{\text{C},^{19}\text{F}} = 3.8$ Hz), 124.7 (q, $J_{\text{C},^{19}\text{F}} = 272.2$ Hz), 127.5 (q, $J_{\text{C},^{19}\text{F}} = 31.6$ Hz), 127.9, 130.5, 133.2 (q, $J_{\text{C},^{19}\text{F}} = 3.4$ Hz), 142.0, 143.6, 156.2. **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{45}\text{F}_3\text{Na}^{120}\text{Sn} [\text{M}+\text{Na}]^+ 569.2393$, found 569.2371.

Compound 3pa. (Table 3.2, entry 20, 77% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H+3H), 0.97 (t, $J_{\text{H,H}} = 8.2$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.2$ Hz, 6H), 0.97 (t, $J_{\text{H,H}} = 8.2$ Hz, 3H), 1.32 (sext, $J_{\text{H,H}} = 7.4$ Hz, 6H), 1.29–1.38 (m, 2H) 1.43–1.53 (m, 8H), 2.13 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.31 (t, $J_{\text{H,H}} = 8.2$ Hz, 2H), 2.32 (s, 3H), 5.26 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 6.99 (s, 1H), 7.02 (d, $J_{\text{H,H}} = 7.5$ Hz,

1H), 7.31 (d, $J_{\text{H,H}} = 7.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 42.9$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.8 ($J_{\text{C},^{119}\text{Sn}} = 339.9$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.5$ Hz), 13.6, 14.1, 14.4, 21.3, 21.7, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 61.0$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.6$ Hz), 30.6, 34.9, 126.6 ($J_{\text{C},^{119}\text{Sn}} = 44.5$ Hz), 128.8 ($J_{\text{C},^{119}\text{Sn}} = 36.6$ Hz), 129.4, 136.7, 136.9, 137.1, 144.4 ($J_{\text{C},^{119}\text{Sn}} = 14.5$ Hz), 152.7 ($J_{\text{C},^{119}\text{Sn}} = 29.1$ Hz). **HRMS** (ESI) calcd for $\text{C}_{27}\text{H}_{48}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 515.2676, found 515.2698.

Compound 3qa. (Table 3.2, entry 21, 84% yield, colorless oil). **^1H NMR** (500 MHz, CDCl_3) δ 0.27 (s, 9H), 0.90 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.92 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.987 (t, $J_{\text{H,H}} = 7.2$ Hz, 3H), 0.993 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.7$ Hz, 6H), 1.33 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.33–1.41 (m, 2H), 1.44–1.52 (m, 8H), 2.15 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.33 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.28 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.28 (s, $J_{\text{H},^{119}\text{Sn}} = 16.4$ Hz, 1H), 7.34 (d, $J_{\text{H,H}} = 7.2$ Hz, 1H), 7.43 (d, $J_{\text{H,H}} = 7.1$ Hz, $J_{\text{H},^{119}\text{Sn}} = 43.0$ Hz, 1H); **^{13}C NMR** (125 MHz, CDCl_3) δ -1.1, 10.8 ($J_{\text{C},^{119}\text{Sn}} = 339.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 323.9$ Hz), 13.6, 14.2, 14.4, 21.6, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 60.4$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.5$ Hz), 30.6, 35.0, 129.5, 130.5, 132.6, 136.3, 139.1, 141.6, 144.5, 151.8. **HRMS** (ESI) calcd for $\text{C}_{29}\text{H}_{54}\text{NaSi}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 573.2914, found 573.2917.

Compound 3ra. (Table 3.2, entry 22, 67% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.91 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.98 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.02 (t, $J_{\text{H,H}} = 8.2$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.0$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.26–1.42 (m, 2H), 1.42–1.51 (m, 8H), 2.15 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.32 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H), 5.29 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.34 (s, 1H), 7.40 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H), 7.53 (d, $J_{\text{H,H}} = 7.6$ Hz, $J_{\text{H},^{119}\text{Sn}} = 40.0$ Hz, 1H); **¹³C NMR** (125 MHz, CDCl₃) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 343.1$ Hz, $J_{\text{C},^{117}\text{Sn}} = 328.1$ Hz), 13.6, 14.1, 14.4, 21.6, 22.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.7$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.2$ Hz), 30.6, 34.8, 121.8 (q, $J_{\text{C},^{19}\text{F}} = 3.7$ Hz, $J_{\text{C},^{119}\text{Sn}} = 41.0$ Hz), 124.1 (q, $J_{\text{C},^{19}\text{F}} = 3.6$ Hz, $J_{\text{C},^{119}\text{Sn}} = 34.0$ Hz), 124.4 (q, $J_{\text{C},^{19}\text{F}} = 272.2$ Hz), 129.6 (q, $J_{\text{C},^{19}\text{F}} = 31.8$ Hz), 130.6, 137.1 ($J_{\text{C},^{119}\text{Sn}} = 33.0$ Hz), 143.4 ($J_{\text{C},^{119}\text{Sn}} = 13.0$ Hz), 146.3, 153.2 ($J_{\text{C},^{119}\text{Sn}} = 28.2$ Hz). **HRMS** (ESI) calcd for C₂₇H₄₅F₃Na¹²⁰Sn [M+Na]⁺ 569.2393, found 569.2393.

Compound 3sa. (Table 3.2, entry 23, 83% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H+3H), 1.00 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.06 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.8$ Hz, 6H), 1.34 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.25–1.41 (m, 2H), 1.47–1.54 (m, 8H), 2.19 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.39 (t, $J_{\text{H,H}} = 7.9$ Hz, 2H), 5.38 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.40–7.45 (m, 2H), 7.56 (s, $J_{\text{H},^{119}\text{Sn}} = 14.3$ Hz, 1H), 7.73–7.80 (m, 2H), 7.89 (s, $J_{\text{H},^{119}\text{Sn}} = 48.3$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 340.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.2$ Hz), 13.7, 14.2, 14.3, 21.6, 23.0, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 62.1$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 19.0$ Hz), 30.6, 34.8, 125.2, 125.7, 125.9, 127.3, 127.5, 129.9, 131.7, 133.0, 137.1 ($J_{\text{C},^{119}\text{Sn}} = 30.6$ Hz), 140.0,

144.1 ($J_{\text{C},^{119}\text{Sn}} = 11.6$ Hz), 149.3. **HRMS** (ESI) calcd for $\text{C}_{30}\text{H}_{48}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 551.2676, found 551.2660.

Compound 3ab. (Table 3.3, 84% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.0$ Hz, 3H), 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.94 (t, $J_{\text{H,H}} = 7.1$ Hz, 3H), 0.99 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.6$ Hz, 6H), 1.28–1.52 (m, 20H), 2.16 (q, $J_{\text{H,H}} = 7.1$ Hz, 2H), 2.34 (t, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.25 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.16 (d, $J_{\text{H,H}} = 7.4$ Hz, 1.3 Hz, 1H), 7.19 (td, $J_{\text{H,H}} = 7.1$ Hz, 1.6 Hz, 1H), 7.24 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.7 Hz, 1H), 7.42 (dd, $J_{\text{H,H}} = 7.0$ Hz, 1.3 Hz, $J_{\text{H},^{119}\text{Sn}} = 43.0$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 339.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.5$ Hz), 13.6, 13.9, 14.0, 22.6, 23.1, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 61.0$ Hz), 28.1, 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 30.6, 32.0, 32.5, 125.6 ($J_{\text{C},^{119}\text{Sn}} = 42.6$ Hz), 127.5 ($J_{\text{C},^{119}\text{Sn}} = 9.5$ Hz), 127.9 ($J_{\text{C},^{119}\text{Sn}} = 34.8$ Hz), 129.6, 136.9 ($J_{\text{C},^{119}\text{Sn}} = 30.5$ Hz), 140.7 ($J_{\text{C},^{119}\text{Sn}} = 413.7$ Hz, $J_{\text{C},^{117}\text{Sn}} = 395.4$ Hz), 144.4 ($J_{\text{C},^{119}\text{Sn}} = 14.4$ Hz), 152.7 ($J_{\text{C},^{119}\text{Sn}} = 28.3$ Hz). **HRMS** (ESI) calcd for $\text{C}_{28}\text{H}_{50}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 529.2832, found 529.2819.

Compound 3ac. (Table 3.3, 83% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.2$ Hz, 9H), 0.85–0.92 (m, 6H), 0.99 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.8$ Hz, 6H), 1.18–1.40 (m, 24H), 1.42–1.54 (m, 8H), 2.15 (q, $J_{\text{H,H}} = 7.2$

Hz, 2H), 2.33 (t, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.25 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.16 (d, $J_{\text{H,H}} = 7.4$ Hz, 1H), 7.19 (td, $J_{\text{H,H}} = 7.1$ Hz, 1.5 Hz, 1H), 7.24 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.6 Hz, 1H), 7.42 (dd, $J_{\text{H,H}} = 7.0$ Hz, 1.5 Hz, $J_{\text{H},^{119}\text{Sn}} = 42.8$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 10.9 ($J_{\text{C},^{119}\text{Sn}} = 339.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.6$ Hz), 13.7, 14.06, 14.09, 22.6, 22.7, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 62.1$ Hz), 28.5, 29.16, 29.17, 29.3, 29.6, 29.8, 30.0, 31.9, 32.8, 125.6 ($J_{\text{C},^{119}\text{Sn}} = 42.3$ Hz), 127.4 ($J_{\text{C},^{119}\text{Sn}} = 9.4$ Hz), 127.9 ($J_{\text{C},^{119}\text{Sn}} = 34.9$ Hz), 129.6, 136.9 ($J_{\text{C},^{119}\text{Sn}} = 32.4$ Hz), 140.7 ($J_{\text{C},^{119}\text{Sn}} = 414.0$ Hz, $J_{\text{C},^{117}\text{Sn}} = 395.7$ Hz), 144.4 ($J_{\text{C},^{119}\text{Sn}} = 14.5$ Hz), 152.7 ($J_{\text{C},^{119}\text{Sn}} = 28.1$ Hz). **HRMS** (ESI) calcd for $\text{C}_{34}\text{H}_{62}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 613.3771, found 613.3762.

Compound 3ad:3ad' (1.2:1). (Table 3.3, 84% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) for **3ad** δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.83–0.91 (m, 2H), 0.98 (t, $J_{\text{H,H}} = 8.3$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.10–1.41 (m, 4H), 1.43–1.60 (m, 6H), 1.73 (d, $J_{\text{H,H}} = 6.8$ Hz, 3H), 1.60–1.83 (m, 5H), 2.22 (d, $J_{\text{H,H}} = 7.1$ Hz, 2H), 5.39 (q, $J_{\text{H,H}} = 6.8$ Hz, 1H), 7.10 (dd, $J_{\text{H,H}} = 7.4$ Hz, 1.3 Hz, 1H), 7.16–7.29 (m, 2H), 7.41 (dd, $J_{\text{H,H}} = 6.9$ Hz, 1.6 Hz, 1H); **3ad'** δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.83–0.91 (m, 2H), 0.97 (t, $J_{\text{H,H}} = 8.3$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.10–1.40 (m, 4H), 1.43–1.60 (m, 6H), 1.60–1.83 (m, 5H), 1.96 (s, 3H), 2.03 (t, $J_{\text{H,H}} = 7.0$ Hz, 2H), 5.31 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.4 Hz, 1H), 7.16–7.29 (m, 3H), 7.43 (dd, $J_{\text{H,H}} = 7.0$ Hz, 1.4 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) for **3ad** δ 10.7 ($J_{\text{C},^{119}\text{Sn}} = 339.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 323.9$ Hz), 13.6, 14.1, 26.3, 26.6, 27.5 ($J_{\text{C},^{119}\text{Sn}} =$

60.7 Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 19.0$ Hz), 33.6, 36.4, 38.4, 125.5, 127.0, 127.5 ($J_{\text{C},^{119}\text{Sn}} = 10.0$ Hz), 128.2, 136.8, 140.5, 143.7, 153.2; **3ad'** δ 10.8 ($J_{\text{C},^{119}\text{Sn}} = 340.9$ Hz, $J_{\text{C},^{117}\text{Sn}} = 326.5$ Hz), 13.6, 18.9, 26.4, 26.6, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 60.7$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 19.0$ Hz), 33.4, 36.6, 40.1, 124.6, 125.8, 127.6 ($J_{\text{C},^{119}\text{Sn}} = 10.0$ Hz), 128.3, 137.0, 140.4, 140.7, 154.0. **HRMS** (ESI) calcd for $\text{C}_{28}\text{H}_{48}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 527.2676, found 527.2703.

Compound 3ae. (Table 3.3, 72% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) δ 0.83 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.98 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.6$ Hz, 6H), 1.27 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.4–1.5 (m, 6H), 6.58 (s, 1H), 7.01 (dd, $J_{\text{H,H}} = 7.6$ Hz, 1.0 Hz, 1H), 7.05–7.30 (m, 12H), 7.54 (dd, $J_{\text{H,H}} = 7.2$ Hz, 1.1 Hz, $J_{\text{H},^{119}\text{Sn}} = 41.6$ Hz, 1H); **^{13}C NMR** (100 MHz, CDCl_3) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 342.2$ Hz, $J_{\text{C},^{117}\text{Sn}} = 327.0$ Hz), 13.6, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.6$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 126.7, 126.8, 127.5, 127.6 ($J_{\text{C},^{119}\text{Sn}} = 9.3$ Hz), 128.0, 128.2, 129.4, 129.5, 129.6, 130.6, 137.2, 137.4, 140.8, 142.0, 146.3 ($J_{\text{C},^{119}\text{Sn}} = 14.3$ Hz), 152.4 ($J_{\text{C},^{119}\text{Sn}} = 25.1$ Hz). **HRMS** (ESI) calcd for $\text{C}_{32}\text{H}_{42}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 569.2206, found 569.2222.

Compound 3af. (Table 3.3, 78% yield, colorless oil). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 0.83 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.96 (t, $J_{\text{H,H}} = 7.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.6$ Hz, 6H), 1.26 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.40–1.48 (m, 6H), 3.78 (s, 3H), 3.81 (s, 3H), 6.43 (s, 1H), 6.72 (d, $J_{\text{H,H}} = 8.8$ Hz, 2H), 6.78 (d, $J_{\text{H,H}} = 8.8$ Hz, 2H), 7.00 (dd, $J_{\text{H,H}} = 7.6$ Hz, 1.1 Hz, 1H), 7.06 (d, $J_{\text{H,H}} = 8.6$ Hz, 2H), 7.11 (d, $J_{\text{H,H}} = 8.8$ Hz, 2H), 7.19 (td, $J_{\text{H,H}} = 7.4$ Hz, 1.5 Hz, 1H), 7.24 (td, $J_{\text{H,H}} = 7.2$ Hz, 1.4 Hz, 1H), 7.52 (dd, $J_{\text{H,H}} = 7.2$ Hz, 1.1 Hz, $J_{\text{H},^{119}\text{Sn}} = 41.7$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 341.9$ Hz, $J_{\text{C},^{117}\text{Sn}} = 326.7$ Hz), 13.6, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 61.7$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 55.1, 55.2, 113.4, 113.6, 126.5, 127.5 ($J_{\text{C},^{119}\text{Sn}} = 9.4$ Hz), 128.3, 129.5, 130.2, 130.6, 131.8, 133.3, 137.3 ($J_{\text{C},^{119}\text{Sn}} = 32.1$ Hz), 142.0, 144.1 ($J_{\text{C},^{119}\text{Sn}} = 14.6$ Hz), 152.8, 158.3, 158.9. **HRMS** (ESI) calcd for $\text{C}_{34}\text{H}_{46}\text{O}_2\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 629.2417, found 629.2411.

Compound 3ag. (Table 3.3, 74% yield, colorless solid). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 0.83 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.96 (t, $J_{\text{H,H}} = 8.3$ Hz, $J_{\text{H},^{119}\text{Sn}} = 52.1$ Hz, 6H), 1.26 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.40–1.48 (m, 6H), 6.51 (s, 1H), 6.88 (t, $J_{\text{H,H}} = J_{\text{H},^{19}\text{F}} = 8.7$ Hz, 2H), 6.94 (t, $J_{\text{H,H}} = J_{\text{H},^{19}\text{F}} = 8.7$ Hz, 2H), 6.97 (dd, $J_{\text{H,H}} = 7.1$ Hz, 1.0 Hz, 1H), 7.06 (dd, $J_{\text{H,H}} = 8.6$ Hz, $J_{\text{H},^{19}\text{F}} = 5.5$ Hz, 2H), 7.13 (dd, $J_{\text{H,H}} = 8.7$ Hz, $J_{\text{H},^{19}\text{F}} = 5.5$ Hz, 2H), 7.20 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.5 Hz, 1H), 7.27 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.4 Hz, 1H), 7.54 (dd, $J_{\text{H,H}} = 7.2$ Hz, 1.2 Hz, $J_{\text{H},^{119}\text{Sn}} = 41.5$ Hz, 1H); $^{13}\text{C NMR}$

(100 MHz, CDCl₃) δ 11.1 ($J_{\text{C},^{119}\text{Sn}} = 343.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 326.9$ Hz), 13.6, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.8$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 115.2 (d, $J_{\text{C},^{19}\text{F}} = 21.3$ Hz), 115.4 (d, $J_{\text{C},^{19}\text{F}} = 21.4$ Hz), 126.9, 127.7, 128.4, 129.5, 130.9 (d, $J_{\text{C},^{19}\text{F}} = 7.9$ Hz), 132.3 (d, $J_{\text{C},^{19}\text{F}} = 7.9$ Hz), 133.2 (d, $J_{\text{C},^{19}\text{F}} = 3.2$ Hz), 136.4 (d, $J_{\text{C},^{19}\text{F}} = 2.6$ Hz), 137.5, 142.0, 145.1, 151.9, 161.6 (d, $J_{\text{C},^{19}\text{F}} = 247.4$ Hz), 162.3 (d, $J_{\text{C},^{19}\text{F}} = 247.7$ Hz). **HRMS** (ESI) calcd for C₃₂H₄₀F₂Na¹²⁰Sn [M+Na]⁺ 605.2018, found 605.2023. The structure of compound **3ag** was confirmed by single crystal X-ray diffraction (Section 3.4.9).

Compound 3ah:3ah' (9:1). (Table 3.3, 73% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) for **3ah** δ 0.83 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 1.00 (t, $J_{\text{H,H}} = 8.4$ Hz, 6H), 1.04 (t, $J_{\text{H,H}} = 7.8$ Hz, 3H), 1.26 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.40–1.50 (m, 6H), 2.68 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 6.33 (s, 1H), 7.15–7.38 (m, 8H), 7.49 (d, $J_{\text{H,H}} = 7.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 42.7$ Hz, 1H), (**3ah'** δ 1.12 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 2.31 (quint, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.63 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H)); **¹³C NMR** (100 MHz, CDCl₃) for **3ah** δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 338.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 323.7$ Hz), 12.9, 13.6, 25.9, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.2$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 18.8$ Hz), 126.2, 126.5, 127.4, 127.6, 128.2, 128.7, 129.9, 137.3, 137.8, 141.1, 148.4, 151.7. **HRMS** (ESI) calcd for C₂₆H₄₆Na¹²⁰Sn [M+Na]⁺ 521.2206, found 521.2206.

Compound 3ai:3ai' (10:1). (Table 3.3, 77% yield, colorless oil). ^1H NMR (400 MHz, CDCl_3) for **3ai** δ 0.29 (s, 9H), 0.83 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 1.01 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 50.3$ Hz, 6H), 1.05 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 1.28 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.41–1.50 (m, 6H), 2.70 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 6.33 (s, 1H), 7.23–7.30 (m, 3H), 7.32 (d, $J_{\text{H,H}} = 7.8$ Hz, 2H), 7.50 (d, $J_{\text{H,H}} = 7.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 41.6$ Hz, 1H), 7.53 (d, $J_{\text{H,H}} = 8.0$ Hz, 2H), (**3ai'** δ 0.26 (s, 9H), 1.13 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 2.34 (quint, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.63 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H)); ^{13}C NMR (100 MHz, CDCl_3) for **3ai** δ -1.1, 11.1 ($J_{\text{C},^{119}\text{Sn}} = 339.9$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.0$ Hz), 12.9, 13.6, 26.0, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 61.9$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.0$ Hz), 126.2 ($J_{\text{C},^{119}\text{Sn}} = 40.5$ Hz), 127.4, 127.6 ($J_{\text{C},^{119}\text{Sn}} = 9.5$ Hz), 128.0, 128.7, 133.3, 137.3 ($J_{\text{C},^{119}\text{Sn}} = 31.6$ Hz), 138.2, 138.5, 141.1, 148.6 ($J_{\text{C},^{119}\text{Sn}} = 13.9$ Hz), 151.7. **HRMS** (ESI) calcd for $\text{C}_{31}\text{H}_{50}\text{NaSi}^{120}\text{Sn}$ [$\text{M}+\text{Na}$] $^+$ 593.2601, found 593.2617.

Compound 3aj:3aj' (17:1). (Table 3.3, 76% yield, colorless oil). ^1H NMR (400 MHz, CDCl_3) for **3aj** δ 0.84 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 1.02 (t, $J_{\text{H,H}} = 8.4$

Hz, 6H), 1.07 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 1.29 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.43–1.51 (m, 6H), 2.71 (q, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.87 (s, 6H), 3.88 (s, 3H), 6.27 (s, 1H), 6.57 (s, 2H), 7.20–7.37 (m, 3H), 7.49 (d, $J_{\text{H,H}} = 7.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 42.5$ Hz, 1H), (**3aj'** δ 1.34 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 2.33 (quint, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.60 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H)); **^{13}C NMR** (100 MHz, CDCl_3) for **3aj** δ 11.1 ($J_{\text{C},^{119}\text{Sn}} = 340.4$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.2$ Hz), 12.9, 13.6, 26.1, 27.5, 29.1 ($J_{\text{C},^{119}\text{Sn}} = 18.7$ Hz), 56.0, 60.9, 105.9, 126.3, 127.4, 127.6, 128.7, 133.5, 136.9, 137.3, 141.1, 148.1, 151.6, 153.0. **HRMS** (ESI) calcd for $\text{C}_{31}\text{H}_{48}\text{O}_3\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 611.2523, found 611.2550.

Compound 3ak:3ak' (8:1). (Table 3.3, 71% yield, colorless oil). **^1H NMR** (400 MHz, CDCl_3) for **3ak** δ 0.84 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.91 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.01 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.4$ Hz, 6H), 1.28 (sext, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.41–1.50 (m, 8H), 2.61 (deformed t, $J_{\text{H,H}} = 8.2$ Hz, 2H), 6.35 (s, 1H), 7.18–7.39 (m, 8H), 7.49 (d, $J_{\text{H,H}} = 7.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 41.8$ Hz, 1H), (**3ak'** δ 2.28 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.68 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H)); **^{13}C NMR** (100 MHz, CDCl_3) for **3ak** δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 340.1$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.1$ Hz), 13.6, 14.5, 21.7, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.1$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.1$ Hz), 35.3, 126.1, 126.5, 127.5, 127.6, 128.2, 128.7, 129.0, 137.2, 137.9, 140.8, 147.3, 152.2. **HRMS** (ESI) calcd for $\text{C}_{29}\text{H}_{44}\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 535.2363, found 535.2394.

Compound 3al:3al' (7:1). (Table 3.3, 73% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) for **3al** δ 0.84 (t, $J_{\text{H,H}} = 7.3$ Hz, 9H), 0.87 (t, $J_{\text{H,H}} = 7.2$ Hz, 3H), 1.01 (t, $J_{\text{H,H}} = 8.4$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.2$ Hz, 6H), 1.24 (t, $J_{\text{H,H}} = 7.3$ Hz, 6H), 1.27–1.35 (m, 2H), 1.39–1.51 (m, 8H), 2.64 (deformed t, $J_{\text{H,H}} = 8.1$ Hz, 2H), 6.34 (s, 1H), 7.16–7.39 (m, 8H), 7.50 (d, $J_{\text{H,H}} = 7.0$ Hz, $J_{\text{H},^{119}\text{Sn}} = 41.9$ Hz, 1H), (**3al'** δ 2.30 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 5.67 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H)); **¹³C NMR** (100 MHz, CDCl₃) for **3al** δ 11.0 ($J_{\text{C},^{119}\text{Sn}} = 340.3$ Hz, $J_{\text{C},^{117}\text{Sn}} = 325.1$ Hz), 13.6, 13.9, 23.1, 27.4 ($J_{\text{C},^{119}\text{Sn}} = 62.0$ Hz), 29.1 ($J_{\text{C},^{119}\text{Sn}} = 19.7$ Hz), 30.6, 32.9, 126.2, 126.5, 127.5, 127.6, 128.2, 128.7, 128.9, 137.3, 137.9, 140.9, 147.4, 152.2. **HRMS** (ESI) calcd for C₂₆H₄₆Na¹²⁰Sn [M+Na]⁺ 549.2519, found 549.2546.

Compound 3aa-d₅. (Scheme 3.5c, 87% yield, colorless oil). **¹H NMR** (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}} = 7.1$ Hz, 9H+3H), 0.96 (t, $J_{\text{H,H}} = 6.7$ Hz, 3H), 0.99 (t, $J_{\text{H,H}} = 8.1$ Hz, $J_{\text{H},^{119}\text{Sn}} = 51.0$ Hz, 6H), 1.32 (sext, $J_{\text{H,H}} = 7.1$ Hz, 6H+2H), 1.42–1.51 (m, 8H), 2.14 (t, $J_{\text{H,H}} = 7.5$ Hz, 2H), 2.32 (t, $J_{\text{H,H}} = 8.0$ Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 10.8 ($J_{\text{C},^{119}\text{Sn}} = 339.6$ Hz, $J_{\text{C},^{117}\text{Sn}} = 324.7$ Hz), 13.6, 14.1, 14.4, 21.6, 22.9, 27.5 ($J_{\text{C},^{119}\text{Sn}} = 61.0$ Hz), 29.2 ($J_{\text{C},^{119}\text{Sn}} = 18.9$ Hz), 30.5, 34.9, 125.1 (t, $J_{\text{C},^2\text{H}} = 23.8$

Hz), 126.9 (t, $J_{C,H} = 23.9$ Hz), 127.5 (t, $J_{C,H} = 23.2$ Hz), 129.2 (t, $J_{C,H} = 22.8$ Hz), 136.5 (t, $J_{C,H} = 23.9$ Hz), 140.5, 144.2 ($J_{C,^{119}\text{Sn}} = 14.6$ Hz), 152.6 ($J_{C,^{119}\text{Sn}} = 28.6$ Hz); $^2\text{H}\{^1\text{H}\}$ NMR (61 MHz, acetone) δ 5.26 (s, 1H), 7.19 (s, 2H), 7.32 (s, 1H), 7.43 (s, 1H). **HRMS** (ESI) calcd for $\text{C}_{26}\text{H}_{41}\text{D}_5\text{Na}^{120}\text{Sn}$ $[\text{M}+\text{Na}]^+$ 506.2833, found 506.2838.

Compound 8 [374107-00-3]. (Scheme 3.6, 98% yield, colorless oil). ^1H NMR (500 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.48 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.18 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.48 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 5.67 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.21 (td, $J_{\text{H,H}} = 7.4$ Hz, 1.3 Hz, 1H), 7.30 (t, $J_{\text{H,H}} = 6.9$ Hz, 1H), 7.30 (d, $J_{\text{H,H}} = 6.7$ Hz, 1H), 7.34 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.8, 23.1, 30.6, 31.7, 126.0 (t, $J_{C,H} = 24.1$ Hz), 126.3, 128.0, 128.1, 129.2, 140.0, 143.5. The spectral data are in agreement with reported literature values.^{8a}

Compound 9. (Scheme 3.6, 96% yield, colorless oil). ^1H NMR (400 MHz, CDCl_3) δ 0.98 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.07 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.39 (sext, $J_{\text{H,H}} = 7.8$ Hz, 2H), 1.57 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.25 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.46 (t, $J_{\text{H,H}} = 7.8$ Hz, 2H), 5.37 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.95 (td, $J_{\text{H,H}} = 7.7$ Hz, 1.7 Hz, 1H), 7.17 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.7 Hz, 1H), 7.31 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.2 Hz, 1H), 7.89 (dd,

$J_{\text{H,H}} = 7.9 \text{ Hz}$, 1.1 Hz , 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 14.0, 14.2, 21.2, 22.7, 30.0, 33.5, 99.4, 127.5, 127.8, 129.6, 131.3, 139.0, 143.3, 149.1. **HRMS** (ESI) calcd for $\text{C}_{14}\text{H}_{20}\text{I}$ $[\text{M}+\text{H}]^+$ 315.0610, found 315.0613.

Compound 10 [1092526-15-2]. (Scheme 3.6, 69% yield, colorless oil).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 0.86 (t, $J_{\text{H,H}} = 7.3 \text{ Hz}$, 3H), 0.96 (t, $J_{\text{H,H}} = 7.4 \text{ Hz}$, 3H), 1.30 (sext, $J_{\text{H,H}} = 7.4 \text{ Hz}$, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4 \text{ Hz}$, 2H), 2.18 (q, $J_{\text{H,H}} = 7.3 \text{ Hz}$, 2H), 2.44 (t, $J_{\text{H,H}} = 7.6 \text{ Hz}$, 2H), 5.50 (t, $J_{\text{H,H}} = 7.2 \text{ Hz}$, 1H), 6.99 (dd, $J_{\text{H,H}} = 8.4 \text{ Hz}$, $J_{\text{H},^{19}\text{F}} = 10.6 \text{ Hz}$, 1H), 7.06 (dd, $J_{\text{H,H}} = 7.4 \text{ Hz}$, 1.2 Hz , 1H), 7.17 (d, $J_{\text{H,H}} = 7.2 \text{ Hz}$, 1H), 7.19–7.23 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 13.8, 21.5, 22.9, 30.3, 32.5, 115.4 (d, $J_{\text{C},^{19}\text{F}} = 23.1 \text{ Hz}$), 123.7 (d, $J_{\text{C},^{19}\text{F}} = 3.2 \text{ Hz}$), 126.4, 127.9 (d, $J_{\text{C},^{19}\text{F}} = 8.0 \text{ Hz}$), 130.6 (d, $J_{\text{C},^{19}\text{F}} = 4.6 \text{ Hz}$), 131.9 (d, $J_{\text{C},^{19}\text{F}} = 14.6 \text{ Hz}$), 136.1, 160.0 (d, $J_{\text{C},^{19}\text{F}} = 245.8 \text{ Hz}$). The spectral data are in agreement with reported literature values.³⁶

Compound 11. (Scheme 3.6, 83% yield, pale yellow oil). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 0.69 (t, $J_{\text{H,H}} = 7.3 \text{ Hz}$, 3H), 0.91 (t, $J_{\text{H,H}} = 7.4 \text{ Hz}$, 3H), 1.10 (sext, $J_{\text{H,H}} = 7.5 \text{ Hz}$, 2H), 1.40 (sext, $J_{\text{H,H}} = 7.3 \text{ Hz}$, 2H), 1.79 (t, $J_{\text{H,H}} = 7.7 \text{ Hz}$, 2H), 2.06

(q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 3.93 (s, 3H), 5.48 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.20–7.33 (m, 4H), 7.50 (d, $J_{\text{H,H}} = 8.3$ Hz, 2H), 8.01 (d, $J_{\text{H,H}} = 8.3$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 21.5, 22.8, 30.3, 32.9, 52.0, 126.8, 127.6, 128.3, 129.1, 129.2, 129.7, 130.4, 132.2, 138.6, 141.2, 143.6, 147.2, 167.2. **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{27}\text{O}_2$ $[\text{M}+\text{H}]^+$ 323.2011, found 323.1995.

Compound 12. (Scheme 3.6, 87% yield, colorless oil). ^1H NMR (400 MHz, CDCl_3) δ 0.87 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.94 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.27 (sext d, $J_{\text{H,H}} = 7.8$ Hz, 2.2 Hz, 2H), 1.43 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 1.69 (qt, $J_{\text{H,H}} = 12.8$ Hz, 4.5 Hz, 1H), 1.82 (qd, $J_{\text{H,H}} = 12.3$ Hz, 3.2 Hz, 1H), 1.91 (br d, $J_{\text{H,H}} = 13.2$ Hz, 1H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.11–2.20 (m, 1H), 2.22–2.31 (m, 2H), 2.38 (td, $J_{\text{H,H}} = 14.5$ Hz, 6.6 Hz, 1H), 2.4–2.5 (m, 1H), 2.45 (br d, $J_{\text{H,H}} = 14.1$ Hz, 1H), 2.53 (t, $J_{\text{H,H}} = 13.8$ Hz, 1H), 3.23 (tt, $J_{\text{H,H}} = 12.2$ Hz, 3.9 Hz, 1H), 5.21 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.05 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.0 Hz, 1H), 7.15 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.6 Hz, 1H), 7.25 (td, $J_{\text{H,H}} = 7.8$ Hz, 1.2 Hz, 1H), 7.29 (dd, $J_{\text{H,H}} = 7.7$ Hz, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.2, 21.3, 23.0, 25.9, 30.1, 33.4, 34.9, 40.6, 41.2, 49.3, 125.6, 125.8, 126.8, 129.5, 130.4, 139.6, 141.7, 143.8, 211.1. **HRMS** (ESI) calcd for $\text{C}_{20}\text{H}_{29}\text{O}$ $[\text{M}+\text{H}]^+$ 285.2218, found 285.2221.

3.4.9 Single crystal X-ray diffraction data for compound 3ag (CCDC 1841177)

Table 3.4. Crystal data and structure refinement for compound 3ag

Empirical formula	$\text{C}_{32}\text{H}_{40}\text{F}_2\text{Sn}$	
Formula weight	581.33 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.020 x 0.040 x 0.320 mm	
Crystal habit	colorless needle	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	$a = 17.1715(13)$ Å	$\alpha = 90^\circ$.
	$b = 17.8894(14)$ Å	$\beta =$
	$101.309(3)^\circ$.	
	$c = 9.4518(7)$ Å	$\gamma = 90^\circ$.
Volume	$2847.1(4)$ Å ³	
Z	4	
Density (calculated)	1.356 g/cm ³	
Absorption coefficient	0.928 mm ⁻¹	
F(000)	1200	
Theta range for data collection	2.48 to 27.94°.	

Index ranges	$-22 \leq h \leq 20$, $-22 \leq k \leq 23$, $-12 \leq l \leq 11$
Reflections collected	16876
Independent reflections	6610 [R(int) = 0.0945]
Coverage of independent reflections	96.5%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9820 and 0.7560
Structure solution technique	direct methods
Structure solution program	XT, VERSION 2014/5
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2016/6 (Sheldrick, 2016)
Function minimized	$\sum w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	6610 / 0 / 319
Goodness-of-fit on F^2	1.014
Final R indices	3523 data; $I > 2\sigma(I)$ R1 = 0.0663, wR2 = 0.1362 all data R1 = 0.1468, wR2 = 0.1726
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0685P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Largest diff. peak and hole	1.424 and $-1.680 \text{ e}\text{\AA}^{-3}$
R.M.S. deviation from mean	$0.155 \text{ e}\text{\AA}^{-3}$

3.5 Refernece

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3.6 NMR spectra

CHAPTER 4

Rhodium-Catalyzed Arylzincation of Alkynes. Ligand Control of 1,4-Migration Selectivity

4.1 Introduction

Carbometalation of alkynes is one of the most efficient methods of generating substituted alkenyl–metals which are useful synthetic intermediates for the multisubstituted alkenes. The addition of arylmetals to simple unfunctionalized alkynes has been a reaction of challenge because of their low reactivity.¹ The first-row transition metals including Ni, Co, Fe, Mn, and Cr have been reported to catalyze the addition of arylmagnesium² and –zinc³ reagents to the unfunctionalized alkynes (Scheme 4.1). The detailed discussion on rhodium catalyzed addition of organometals to alkynes is shown in Section 1.1.3.

Scheme 4.1. Catalytic Carbometalation of Alkynes

In 2009, Yorimitsu and Oshima reported ligand-free catalytic arylzincation of alkynes in presence of 5 mol% of CoBr₂ (Scheme 4.2).^{3c} In 2014, Yoshikai reported a new type of Co-catalyzed arylzincation of alkynes where *ortho*-alkenylarylzinc species are formed through 1,4-migration of cobalt from the alkenyl carbon to the aryl carbon.⁴ The use of Xantphos as a ligand totally changed the products.

Scheme 4.2. Cobalt-Catalyzed Arylzincation of Alkynes.

In this chapter, we introduce our findings that arylzincation of alkynes is catalyzed by Rh complexes in the presence of a catalytic amount of ZnCl_2 and the arylzincation with or without 1,4-migration is controlled with high selectivity by the ligands on rhodium (Scheme 4.3). The 1,4-shift of rhodium from alkenyl to aryl carbons has been known as a key step in several Rh-catalyzed multiple carbon–carbon bond forming reactions including asymmetric reactions.^{5–7} To the best of our knowledge, it is the first example of the carbozincation of unfunctionalized alkynes using Rh catalysis.

Scheme 4.3. Rhodium-Catalyzed Arylzincation of Alkynes.

4.2 Results and discussion

In our present studies, arylzinc reagents ArZnCl were prepared by lithiation of ArBr with BuLi in THF at $-80\text{ }^{\circ}\text{C}$ followed by addition of an excess amount (1.3 equiv) of ZnCl_2 to the THF solution of ArLi.^{8,9} The results obtained for the reaction of 3,5-(MeO)₂C₆H₃ZnCl (**1a**) with 4-octyne (**2a**) in the presence of several rhodium catalysts are summarized in Table 4.1. The reaction mixture containing 2-arylalkenylzinc **3aa** and/or *ortho*-alkenylarylzinc **4aa** was hydrolyzed with D₂O and the location of D (**5aa:6aa**) was analyzed by ¹H and ²H NMR spectra. The yield of the arylzincation and the selectivity with or without 1,4-migration are heavily dependent on the ligand on rhodium. The THF solution of ArZnCl (**1a**, 0.60 mmol, 3.0 equiv to **2a**) containing ZnCl_2 (0.18 mmol, 0.9 equiv to **2a**) was added to the alkyne (**2a**, 0.20 mmol) in the presence of a rhodium catalyst generated from [RhCl(coe)₂]₂ (3 mol% of Rh) and binap¹⁰ (3.3 mol%) in THF, and the mixture was heated at $50\text{ }^{\circ}\text{C}$ for 5 h. The arylzincation accompanied by the 1,4-migration proceeded selectively to give, after the D₂O quenching, 91% yield of **6aa**, where the deuterium is incorporated into the *ortho*-position of the phenyl ring (entry 1). On the other hand, the reaction in the presence of a rhodium catalyst coordinated with cod¹⁰ under otherwise the same conditions gave 82% yield of the arylation product where the deuterium is found mainly at the alkenyl carbon (**5aa:6aa** = 92:8) (entry 2). In the Rh/binap-catalyzed reaction, the amounts of ArZnCl **1a** and ZnCl_2 were reduced to 1.5 and 0.45 equiv, respectively, without loss of the arylzincation yield or 1,4-migration selectivity (entry 3). The presence of ZnCl_2 as a catalyst, which was added in an excess amount (1.3 equiv to ArLi) during the preparation of ArZnCl from ArLi, is essential for the present arylzincation. The yield of arylzincation was much lower

(22%) in the reaction with ArZnCl generated with 1.0 equiv of ZnCl₂ (entry 4). Diarylzinc Ar₂Zn generated from ArLi and 0.50 equiv of ZnCl₂ did not give the arylzincation products (entry 5). Other zinc salts, ZnX₂ (X = Br and I), which were used in an excess amount during the preparation of ArZnX¹¹ from ArLi, also catalyzed the reaction, but the yields and the migration selectivity were somewhat lower (entries 6 and 7). The lower yield and selectivity were observed with other phosphine ligands such as dppe, dppp, dppf, biphep, and PPh₃ (entries 8–12). The arylzincation did not proceed with xantphos ligand (entry 13), which has been reported to be the best ligand in the cobalt-catalyzed migratory arylzincation.⁴ Interestingly, the high selectivity in giving **3aa** without the 1,4-migration was observed only with 1,5-cyclooctadiene (cod). Other diene ligands including norbornadiene (nbd) promoted the migratory arylzincation giving **4aa** preferentially (entry 14).

Table 4.1. Rhodium-Catalyzed Arylzincation of 4-Octyne (2a) with 3,5-(MeO)₂C₆H₃ZnCl (1a)^a

entry	ligand on Rh ^b	additive (mmol) ^c	yield (%) ^d 5aa + 6aa	ratio ^e of 5aa : 6aa
1	binap	ZnCl ₂ (0.18)	91	<1:99
2	cod	ZnCl ₂ (0.18)	82	92:8
3 ^f	binap	ZnCl ₂ (0.09)	90	<1:99
4	binap	—	22	4:96
5 ^g	binap	—	<3	—
6 ^h	binap	ZnBr ₂ (0.18)	81	5:95
7 ^h	binap	ZnI ₂ (0.18)	87	3:97
8	dppe	ZnCl ₂ (0.18)	23	37:63

9	dppp	ZnCl ₂ (0.18)	52	48:52
10	dppf	ZnCl ₂ (0.18)	27	19:81
11	biphep	ZnCl ₂ (0.18)	83	12:88
12	PPh ₃	ZnCl ₂ (0.18)	78	6:94
13	xantphos	ZnCl ₂ (0.18)	<3	—
14	nbd	ZnCl ₂ (0.18)	83	5:95

^a Reaction conditions: 4-Octyne (**2a**) (0.20 mmol), ArZnCl (**1a**) (0.60 mmol), ZnCl₂ (0.18 mmol), and Rh catalyst (3 mol% of Rh) in THF (2.0 mL) at 50 °C for 5 h. The reaction was quenched with D₂O (0.2 mL). ^b [RhCl(coe)₂]₂ (6.0 μmol of Rh) + bisphosphine (6.6 μmol), RhCl(PPh₃)₃ (6.0 μmol), or ([RhCl(diene)]₂ (diene = cod or nbd, 6 μmol of Rh). ^c The excess amount of ZnX₂ used at the generation of ArZnX. ^d Isolated yield. ^e Determined by ¹H and ²H NMR spectra. ^f ArZnCl (**1a**) (0.30 mmol), ZnCl₂ (0.09 mmol), THF (1.0 mL) for 1 h. ^g Reaction of Ar₂Zn generated from ArLi (0.60 mmol) and ZnCl₂ (0.30 mmol). ^h ArZnX was generated from ArLi (0.60 mmol) and ZnX₂ (0.78 mmol, X = Br or I).

The rhodium-catalyzed arylzincation was also successful with several other arylzinc reagents ArZnCl and similar selectivity control in giving arylzincation products with or without 1,4-migration was observed in the arylzincation of 4-octyne (**2a**), whose results are summarized in Table 4.2. The selectivity of the addition/1,4-migration sequence giving *ortho*-alkenylphenylzinc **4** with binap as the ligand is very high for all the arylzinc reagents shown in Table 4.2, including unsubstituted phenylzinc (entry 2) and *para*-substituted ones with both electron-donating and -withdrawing groups (entries 3-8). The ratio of **5**:**6** ranges between <1:99 and 6:94. The 1,4-shift was regioselective in the reaction of *meta*-substituted phenylzinc reagents with Me, NMe₂, and SiMe₃, deuterium being exclusively incorporated into the less hindered position (entries 9, 11, 12). The regioselectivity was low with 3-MeOC₆H₄ZnCl (entry 10). Considering that the size of Me and MeO groups is not so different, it is probably because of the coordination of MeO group to Rh, which promotes the Rh 1,4-shift to the MeO side. Interestingly, the 1,4-migration took place selectively to the position next to MeO group in the reaction of 3-Me-5-MeOC₆H₃ZnCl (entry 13). The selective formation of 2-arylethenylzincs **3** without

1,4-migration was also realized using cod as the ligand of the rhodium catalyst for most of the arylzinc reagents examined, although the selectivity is generally not as high as that for the reaction with migration. The ratio of **5**:**6** after D₂O quenching is higher than 7:3 except for the arylzinc reagents substituted with electron-withdrawing groups. Zinc reagents 4-FC₆H₄ZnCl and 4-CF₃C₆H₄ZnCl gave the corresponding arylation products with **5**:**6** = 49:51 and <1:99, respectively¹² (entries 7 and 8).

Table 4.2. Rhodium-Catalyzed Arylzincation of 4-Octyne (2a) with Arylzinc Reagents 1^a

entry	1: Ar in ArZnCl	L on Rh ^b (A) or yield (%) ^c of 5 + ratio ^d of 5 : 6
1	1a : 3,5-(MeO) ₂ C ₆ H ₃	binap (B) 90 <1:99
		cod (A) 82 92:8
2	1b : Ph	binap (A) 87 2:98
		cod (A) 80 80:20
3	1c : 4-MeC ₆ H ₄	binap (B) 91 1:99
		cod (A) 68 77:23
4	1d : 4-MeOC ₆ H ₄	binap (A) 94 1:99
		cod (A) 84 74:26
5	1e : 4-Me ₂ NC ₆ H ₄	binap (B) 87 1:99
		cod (A) 71 94:6
6	1f : 4-Me ₃ SiC ₆ H ₄	binap (B) 85 6:94
		cod (A) 86 81:19
7	1g : 4-FC ₆ H ₄	binap (B) 83 <1:99
		cod (A) 52 49:51
8	1h : 4-CF ₃ C ₆ H ₄	binap (B) 93 <1:99
		cod (A) 87 <1:99
9	1i : 3-MeC ₆ H ₄	binap (B) 87 1:99 ^e
		cod (A) 72 86:14 ^e
10	1j : 3-MeOC ₆ H ₄	binap (A) 93 1:99 ^f
		cod (A) 82 80:20 ^f

11	1k : 3-Me ₂ NC ₆ H ₄	binap (B)	95	1:99 ^e
		cod (A)	72	95:5 ^e
12	1l : 3-Me ₃ SiC ₆ H ₄	binap (B)	87	1:99 ^e
		cod (A)	79	83:17 ^e
13	1m : 3-Me-5-MeOC ₆ H ₃	binap (B)	97	1:99 ^e
		cod (A)	79	>99:1
14	1n : 2-MeOC ₆ H ₄	binap (A)	88	13:87
		cod (A)	64	94:6

^a Reaction condition (A): ArZnCl **1** (0.60 mmol), ZnCl₂ (0.18 mmol), 4-octyne (**2a**) (0.20 mmol), and Rh catalyst (3 mol% of Rh), THF (total 2.0 mL) at 50 °C for 5 h. The reaction was quenched with D₂O (0.2 mL). (B): ArZnCl **1** (0.30 mmol), ZnCl₂ (0.09 mmol), 4-octyne (**2a**) (0.20 mmol), and Rh catalyst (3 mol% of Rh), THF (total 1.0 mL) at 50 °C for 1 h. ^b [RhCl(coe)₂]₂ (6 μmol of Rh) + binap (6.6 μmol) or [RhCl(cod)]₂ (6 μmol of Rh). ^c Isolated yield. ^d Determined by ¹H and ²H NMR. ^e Regioselective 1,4-shift giving the products **6** shown below. ^f A mixture of **6ja** and **6ja'** in a ratio of 2:1 and 4:1 with binap and cod, respectively.

The reaction conditions used for the arylzincation of 4-octyne are applicable to other unfunctionalized alkynes. The results are summarized in Table 4.3, which also contains examples where the generated zinc reagents were used for a few transformations other than the deuteration.¹³ The arylzincation with **1a** took place for symmetrically substituted dialkylalkynes **2b–2c** and diphenylacetylene (**2d**) to give the corresponding *ortho*-alkenylarylzinc or 2-arylalkenylzinc products with high selectivity using binap or cod (entries 1–4). In the reactions of alkyl(aryl)alkynes **2e–2f**, high regioselectivity was observed for the bond formation between the aryl group of the arylzinc and the alkyl-substituted alkyne carbon (entries 5 and 6). This selectivity is expected from the reported regiochemistry of carbometalation of alkyl(aryl)alkynes.¹ A high regioselectivity was also observed in the arylzincation of methyl(alkyl)alkyne **2g**, where the alkyl group is much larger than methyl (entry 7). The iodination of arylzinc reagents, 2-arylalkenylzinc **3** and

ortho-alkenylarylzinc **4**, with I₂ proceeded smoothly to give the corresponding alkenyl- and aryl iodides in high yields (entries 8–11). As another example of transformation of the resulting zinc reagents, Rh-catalyzed conjugate addition of the arylzinc species¹⁴ generated from 4-octyne (**2a**) and PhZnCl (**1b**) is shown in entry 12.¹⁵

Table 4.3. Rhodium-Catalyzed Arylzincation of Alkynes **2 with Arylzinc Reagents **1**^a**

entry 1) 1a with 2b (R ¹ = R ² = <i>n</i> -C ₅ H ₁₁) binap (A): 91%, 5ab:6ab = 1:99 cod (A): 78%, 5ab:6ab = 90:10	entry 2) 1a with 2c (R ¹ = R ² = <i>n</i> -C ₇ H ₁₅) binap (A): 97%, 5ac:6ac = 4:96 cod (A): 74%, 5ac:6ac = 93:7
entry 3) 1a with 2d (R ¹ = R ² = Ph) binap (B): 98%, 5ad:6ad = 13:87 cod (A): 86%, 5ad:6ad = 97:3	entry 4) 1b with 2d (R ¹ = R ² = Ph) binap (B): 97%, 5bd:6bd = 10:90 cod (A): ^b 61%, 5bd:6bd = 92:8
entry 5) 1a with 2e (R ¹ = Et, R ² = Ph) binap (B): 93%, 5ae:6ae = 10:90 cod (A): ^c 72%, 5ae:6ae = 94:6	entry 6) 1a with 2f (R ¹ = <i>i</i> -Pr, R ² = <i>p</i> -Tol) binap (B): 93%, 5af:6af = 10:90 cod (A): 89%, 5af:6af = 95:5 ^d
entry 7) 1a with 2g (R ¹ = Me, R ² = CH ₂ CMe(COOEt) ₂) cod (A): 87%, 5ag:6ag = 97:3	entry 8) 1b with 2a , cod (A) then I ₂ : ^e 63% 7ba
entry 9) 1b with 2a , binap (A) then I ₂ : ^f 77% 8ba 	entry 10) 1h with 2a , binap (B) then I ₂ : 87% 8ha
entry 11) 1a with 2h (R ¹ = Me, R ² = CH ₂ SiMe ₃) cod (A), then I ₂ : 73% 7ah 	entry 12) 67% 9 1b with 2a , binap (B) then cyclohex-2-enone: ^g 67% 9

^a For reaction conditions (A) and (B), see footnote *a* in Table 4.2. For iodination, I₂ (0.60 mmol) was added after the Rh-catalyzed arylzincation. ^b THF solutions of [RhCl(cod)]₂ and alkyne **2d** were added dropwise to PhZnCl (**1b**) and ZnCl₂ in THF over 40 min. ^c 1.5 mol% of Rh catalyst. ^d Containing 5% of its regioisomer. ^e 5 mmol scale. ^f 20 mmol scale, 1 mol% of Rh catalyst. ^g Cyclohex-2-enone (0.36 mmol) and [RhCl(cod)]₂ (15

The catalytic cycle of the present arylzincation of alkynes with/without 1,4-migratory is proposed in Scheme 4.4. Thus, the syn-addition of an aryl–Rh intermediated **A** to the alkyne generates a 2-arylalkenyl–Rh species **B**. Transmetalation of the alkenyl group from Rh to ZnCl₂ takes place to produce the

alkenylzinc product **3** and a Cl–Rh species **C**. Arylation of **C** with ArZnCl regenerates the aryl–Rh **A**.¹⁴ Direct transmetalation between the alkenyl–Rh **B** and ArZnCl **2** giving the aryl–Rh **A** and the alkenylzinc **3** is less likely because a catalytic amount of ZnCl₂ is necessary for the present arylzincation (see entries 4 and 5 in Table 4.1). When the transmetalation of the alkenyl–Rh intermediate **B** with ZnCl₂ is relatively slow, it undergoes 1,4-migration of Rh giving an *ortho*-alkenylphenyl–Rh intermediate **D**, which is thermodynamically more stable than **B**.^{6e} Transmetalation with ZnCl₂ finally leads to the *ortho*-alkenylarylzinc **4**. The selectivity in producing **3** or **4** is dependent on the reactivity of the alkenyl–Rh intermediate **B** towards transmetalation with ZnCl₂. It is our understanding that the transmetalation, which is an intermolecular reaction, is faster with a cod ligand and the Rh 1,4-migration which is an intramolecular event is not strongly affected by the ligands on rhodium. The faster transmetalation with cod ligand than binap ligand has been reported by Hayashi in 2006.¹⁶

Scheme 4.4. A Catalytic Cycle Proposed for Arylzincation of Alkynes Catalyzed by Rh Complexes and ZnCl₂

The reactions starting with alkenylzinc **3ba** and *ortho*-alkenylarylzinc **4ba** (equation 4.1) gave us further insight into the reaction mechanism. The isomerization of **3ba** into **4ba** was observed in the presence of ZnCl₂ with both Rh/binap and Rh/cod catalysts, while the isomerization is very slow without ZnCl₂. The isomerization from **4ba** to **3ba** was not observed under the same conditions with binap or cod ligand. These results demonstrate that ZnCl₂ plays a key role in the transmetalation steps in the catalytic cycle and that the *ortho*-alkenylarylzinc **4ba** is thermodynamically more stable than the alkenylzinc **3ba**. It is remarkable that the ratio of the 2-arylalkenylzinc **3** to the *ortho*-alkenylarylzinc **4** is not dependent on the reaction time or conversion. Thus, D₂O quench of the reaction of **1a** with **2a** at 15 min reaction time gave 47% yield of **5aa/6aa** (1/99) and 29% yield of **5aa/6aa** (93/7) with binap and cod ligands, respectively. The **5aa/6aa** ratios are essentially the same as those observed in entries 1 and 2 in Table 4.1. The 1,4-migration selectivity did not change when lower amount of **1a** was used. The organozincs **3**

and **4** generated by the reaction of alkyne **2** with an excess amount of ArZnCl **1** do not go back to the catalytic cycle shown in Scheme 4.4 in the presence of excess **1**, although both Rh/binap and Rh/cod catalyze the isomerization of **3** to **4** in the absence of ArZnCl **1** (equation 4.1).

4.3 Conclusion

In summary, we have disclosed that the addition of arylzinc reagents ArZnCl to unfunctionalized alkynes is efficiently catalyzed by rhodium complexes in the presence of a catalytic amount of zinc chloride. The selectivity between the 2-aryllkenylzincs and the *ortho*-alkenylarylzinc products, the latter of which is generated through 1,4-Rh migration from alkenyl to aryl, is controlled by the use of the appropriate ligands on rhodium.

4.4 Experimental section

4.4.1 Materials

Alkynes, aryl bromides, bisphosphine ligands, n-BuLi, D₂O, ZnCl₂, ZnBr₂, ZnI₂, 3-methyl-1-butyne, 4-iodotoluene, cyclohex-2-enone, and iodine were purchased and used as received. Et₂O and THF were distilled over benzophenone ketyl under N₂. [RhCl(coe)₂]₂,¹⁷ [RhCl(cod)]₂,¹⁸ Diethyl (2-butynyl)(methyl)malonate (**2g**) [182809-41-2],¹⁹ and but-2-yn-1-yltrimethylsilane (**2h**) [18825-29-1]²⁰ were prepared according to the reported procedures. 1-(4-Methylphenyl)-3-methyl-1-butyne (**2f**) [79756-94-8]²¹ was prepared from 3-methyl-1-butyne and 4-iodotoluene according to the reported procedure.²²

4.4.2 Preparation of arylzinc chlorides **1** in THF²³

Preparation of ZnCl₂ Solution (0.87 M in THF): A Schlenk flask equipped with a stir bar was flame-dried under vacuum and allowed to cool down to room temperature. Under nitrogen, ZnCl₂ (3.54 g, 26.0 mmol) was charged, and the flask was heated under vacuum in an oil-bath at 150 °C for 12 h. Then, the flask was cooled to room temperature and THF (anhydrous, 30.0 mL) was added. The mixture was vigorously stirred until all ZnCl₂ was dissolved.

Preparation of 3,5-(MeO)₂C₆H₃ZnCl (1a**, 0.40 M in THF):** An oven-dried Schlenk flask equipped with a stir bar was charged with a solution of 1-bromo-3,5-dimethoxybenzene (4.78 g, 22.0 mmol) in THF (12.0 mL). The solution was cooled down to -80 °C and n-BuLi (7.4 mL, 20.0 mmol, 2.69 M in hexanes) was added dropwise over 30 min. Precipitates were formed immediately. The reaction mixture

was stirred at $-80\text{ }^{\circ}\text{C}$ for 90 min. To the THF solution of aryllithium thus generated, the THF solution of ZnCl_2 (30.0 mL, 26.0 mmol, 0.87 M) prepared above was added dropwise at $-80\text{ }^{\circ}\text{C}$. The reaction mixture was allowed to warm to room temperature to give a solution of 3,5-(MeO) $_2$ C $_6$ H $_3$ ZnCl (**1a**, 0.40 M) and ZnCl_2 (0.12 M) in THF.

All other arylzinc reagents ArZnCl **1** were prepared in the same manner as above from the corresponding aryl bromides.

ArZnX (Ar = 3,5-(MeO) $_2$ C $_6$ H $_3$, X = Br and I) were prepared using ZnX_2 (X = Br and I), and Ar $_2$ Zn was prepared with 0.5 equiv of ZnCl_2 .

4.4.3 A typical procedure for Table 4.1 (entry 1)

In an oven-dried Schlenk tube, $[\text{RhCl}(\text{coe})_2]_2$ (2.15 mg, 0.0030 mmol, 3.0 mol% of Rh) and binap (4.11 mg, 0.0066 mmol, 3.3 mol%) were placed under nitrogen. THF (0.50 mL) was added and the mixture was stirred at room temperature for 10 min. 4-Octyne (**2a**) (22.0 mg, 0.20 mmol) was added at room temperature. To the mixture, 1.5 mL of the THF solution containing 3,5-(MeO) $_2$ C $_6$ H $_3$ ZnCl (**1a**) (0.60 mmol, 0.40 M) and ZnCl_2 (0.18 mmol, 0.12 M), whose preparation was shown in Section 4.4.2, was added at room temperature. The reaction mixture was heated at $50\text{ }^{\circ}\text{C}$ for 5 h before D $_2$ O (0.2 mL) was added. The reaction mixture was passed through a short silica gel pad with EtOAc as eluent. The solvent was removed on a rotary evaporator. After ^1H NMR analysis of the residue, the crude product was subjected to silica gel chromatography with hexane to give **6aa** (91% yield, 45.4 mg, 0.18 mmol) as colorless oil. ^2H NMR showed that **6aa** was produced selectively.

4.4.4 Typical procedures for Table 4.2 and Table 4.3 (entries 1-7)

4.4.4-1. Entry 2 in Table 4.2, condition (A) with binap ligand:

According to the procedures shown in Section 4.4.2, THF solution of PhZnCl (**1b**, 0.40 M) and ZnCl_2 (0.12 M) was prepared from bromobenzene (3.45 g, 22.0 mmol), *n*-BuLi (7.4 mL, 20.0 mmol, 2.69 M in hexane), and ZnCl_2 (3.54 g, 26.0 mmol). A part of this stock solution was used for the rhodium-catalyzed phenylzincation.

The procedures in Section 4.4.3 for the reaction of entry 1 in Table 4.1 were followed with $[\text{RhCl}(\text{coe})_2]_2$ (2.15 mg, 0.0030 mmol, 3.0 mol% of Rh), binap (4.11 mg, 0.0066 mmol, 3.3 mol%), 4-octyne (**2a**, 22.0 mg, 0.20 mmol), and THF solution containing PhZnCl (**1b**) (0.60 mmol, 0.40 M) and ZnCl_2 (0.18 mmol, 0.12 M) at 50 °C for 5 h. A mixture of **5ba** and **6ba** (87% yield, 32.9 mg, 0.17 mmol) was obtained as colorless oil. ^2H NMR showed that the ratio of **5ba**:**6ba** is 2:98.

4.4.4-2. Entry 3 in Table 4.2, condition (B) with binap ligand:

A THF solution of 4- $\text{MeC}_6\text{H}_4\text{ZnCl}$ (**1c**, 0.4 M) and ZnCl_2 (0.12 M) was prepared starting with 4-bromotoluene (3.76 g, 22.0 mmol) by otherwise the same procedures described in Section 4.4.2.

The procedures shown in Section 4.4.4-1 were modified by reducing the amount of THF, 4- $\text{MeC}_6\text{H}_4\text{ZnCl}$ (**1c**), and ZnCl_2 to (0.25 mL), (0.30 mmol, 0.40 M),

and (0.09 mmol, 0.12 M), respectively, and by shortening the reaction time to 1 h. A mixture of **5ca** and **6ca** (91% yield, 37.0 mg, 0.18 mmol) was obtained as colorless oil. ^2H NMR showed that the ratio of **5ca**:**6ca** is 1:99.

4.4.4-3. Entry 1 in Table 4.3, condition (A) with cod ligand:

The catalyst used for condition (A) with binap ligand (Section 4.4.4-1) was replaced by $[\text{RhCl}(\text{cod})]_2$. Thus, the reaction of $[\text{RhCl}(\text{cod})]_2$ (1.48 mg, 0.0030 mmol, 3.0 mol% of Rh), 6-dodecyne (**2b**, 33.3 mg, 0.20 mmol), 3,5-(MeO) $_2\text{C}_6\text{H}_3\text{ZnCl}$ (**1a**) (0.60 mmol, 0.40 M), and ZnCl_2 (0.18 mmol, 0.12 M) at 50 °C for 5 h gave a mixture of **5ab** and **6ab** (78% yield, 47.8 mg, 0.16 mmol) as colorless oil. ^2H NMR showed that the ratio of **5ab**:**6ab** is 90:10.

4.4.4-4. Entry 4 in Table 4.3, modified condition (A) with cod ligand:

Under nitrogen, an oven-dried Schlenk tube equipped with a stir bar was charged with THF solution (1.5 mL) containing PhZnCl (0.60 mmol) and ZnCl_2 (0.18 mmol) at room temperature (see Section 4.4.4-1 for the preparation of PhZnCl solution). A solution of $[\text{RhCl}(\text{cod})]_2$ (1.48 mg, 0.0030 mmol, 3.0 mol% of Rh) in THF (1.0 mL) and a solution of diphenylacetylene (**2d**) (35.6 mg, 0.20 mmol) in THF (1.0 mL) were added simultaneously into reaction mixture by syringe at room temperature over 40 min. Then, the mixture was heated at 50 °C for 5 h before D_2O

(0.2 mL) was added. The reaction mixture was passed through a short column of silica gel with EtOAc as eluent. The solvent was removed on a rotary evaporator. After ^1H NMR analysis of the residue, it was subjected to silica gel chromatography with pentane to give a mixture of **5bd** and **6bd** (61% yield, 31.5 mg, 0.12 mmol) as a colorless oil. ^2H NMR showed that the ratio of **5bd**:**6bd** is 92:8.

4.4.5 Procedures for the syntheses of alkenyl iodides **7** and aryl iodides **8** (Table 4.3, entries 8-11)

4.4.5-1. **7ba**, entry 8 in Table 4.3

In an oven-dried Schlenk flask, $[\text{RhCl}(\text{cod})]_2$ (37.0 mg, 0.075 mmol, 3 mol% of Rh) was placed under nitrogen, and it was dissolved in dry THF (12.5 mL). A THF solution (37.5 mL) containing phenylzinc chloride (**1b**) (15 mmol) and ZnCl_2 (4.5 mmol), which was prepared from bromobenzene (2.59 g, 16.5 mmol), *n*-BuLi (15.0 mmol), and ZnCl_2 (2.66 g, 19.5 mmol) according to the procedures shown in Section 4.4.4-1, was added at room temperature. Subsequently, 4-octyne (**2a**) (551 mg, 5.0 mmol) was added slowly to the solution over 10 min at 0 °C. The mixture was heated at 50 °C for 5 h, and I_2 (7.61 g, 30.0 mmol) was subsequently added at 0 °C. The mixture was stirred at room temperature for 30 min before saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (15 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The crude mixture was subjected to

chromatography on silica gel (pre-treated with 1% Et₃N in hexane) to give the product **7ba** (63%, 0.99 g, 3.2 mmol) as colorless oil.

4.4.5-2. **8ba**, entry 9 in Table 4.3

In an oven-dried Schlenk flask, [RhCl(coe)₂]₂ (71.8 mg, 0.10 mmol, 1 mol% of Rh) and binap (137.0 mg, 0.22 mmol, 1.1 mol%) were placed under nitrogen. Dry THF (5.0 mL) was added and the solution was stirred at room temperature for 10 min. A THF solution (45.0 mL) containing phenylzinc chloride (**1b**) (30.0 mmol) and ZnCl₂ (9.0 mmol), which was prepared from bromobenzene (5.18 g, 33.0 mmol), n-BuLi (30.0 mmol), and ZnCl₂ (5.32 g, 39.0 mmol) according to the procedures shown in Section 4.4.2, was added at room temperature. Then, 4-octyne (**2a**) (2.20 g, 20.0 mmol) was added slowly to the solution over 10 min at 0 °C. The mixture was heated at 50 °C for 1 h, and I₂ (15.2 g, 60.0 mmol, 3.0 equiv) was added at 0 °C. The resulting mixture was stirred at room temperature for 30 min before saturated aqueous solution of Na₂S₂O₃ (30 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO₄ and concentrated under reduced pressure. The crude mixture was subjected to chromatography on silica gel (pre-treated with 1% Et₃N in hexanes) to give the product **8ba** (77%, 4.82 g, 15.4 mmol) as colorless oil.

4.4.6 Procedures for the Rh-catalyzed arylzincation followed by conjugate addition (Table 4.3, entry 12)

In an oven-dried Schlenk tube, $[\text{RhCl}(\text{coe})_2]_2$ (2.15 mg, 0.0030 mmol, 3.0 mol% of Rh) and binap (4.11 mg, 0.0066 mmol, 3.3 mol%) were placed under nitrogen. THF (0.25 mL) was added and the mixture was stirred at room temperature for 10 min. 4-Octyne (**2a**) (22.0 mg, 0.20 mmol) was added at room temperature. To the mixture, 0.75 mL of the THF solution containing PhZnCl (0.30 mmol) and ZnCl_2 (0.09 mmol) (see Section 4.4.4-1 for the preparation of PhZnCl solution) was added at room temperature, and the mixture was heated at 50 °C for 1 h. Cyclohex-2-enone (34.6 mg, 0.36 mmol) and $[\text{RhCl}(\text{cod})]_2$ (7.40 mg, 0.015 mmol, 15 mol% of Rh) were added. The mixture was refluxed for 12 h before H_2O (2.0 mL) was added. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was subjected to chromatography on silica gel to give the product **9** (67%, 38.0 mg, 0.13 mmol) as colorless oil.

4.4.7 Preparation of alkenylzinc chloride **3ba** and arylzinc chloride **4ba** in THF

4.4.7-1. Preparation of alkenylzinc chloride **3ba** in THF

To a solution of compound **7ba** (0.99 g, 3.2 mmol) in Et_2O (3.0 mL), $n\text{-BuLi}$ in hexane (1.2 mL, 3.2 mmol, 2.69 M) was added dropwise over 30 min at $-80\text{ }^\circ\text{C}$. The mixture was allowed to warm to $0\text{ }^\circ\text{C}$ and stirred for 90 min before it was cooled back to $-80\text{ }^\circ\text{C}$. Dry ZnCl_2 (436.2 mg, 3.2 mmol) in THF (12.0 mL) was subsequently added and the mixture was allowed to warm to room temperature to give a solution of alkenylzinc chloride **3ba** (0.20 M) in THF.

4.4.7-2. Preparation of alkenylzinc chloride **4ba** in THF

To a solution of compound **8ba** (3.46 g, 11.0 mmol) in THF (10.0 mL), $n\text{-BuLi}$ in hexane (3.7 mL, 10.0 mmol, 2.69 M) was added dropwise over 30 min at $-80\text{ }^\circ\text{C}$. The mixture was stirred at $-80\text{ }^\circ\text{C}$ for 90 min before ZnCl_2 (1.36 g, 10 mmol) in THF (36.0 mL) was added. The mixture was allowed to warm to room temperature to give a solution of arylzinc chloride **4ba** (0.20 M) in THF.

4.4.8 Isomerization between alkenylzinc **3ba** and arylzinc **4ba** (equation 4.1)

Entry 1 in equation 4.2: In an oven-dried Schlenk flask, [RhCl(coe)₂]₂ (2.15 mg, 0.0030 mmol, 3.0 mol% of Rh), binap (4.11 mg, 0.0066 mmol, 3.3 mol%) were placed under nitrogen. Anhydrous THF (1.0 mL) was added and the mixture was stirred at room temperature for 10 min. The THF solution of **3ba** (1.0 mL, 0.20 mmol, 0.2 M), which was prepared in Section 4.4.7-1, was added. The mixture was heated at 50 °C for 5 h, and it was quenched with D₂O (0.2 mL). The reaction mixture was passed through a short column of silica gel with EtOAc as eluent. The solvent was removed on a rotary evaporator. After ¹H NMR analysis of the residue, the crude product was subjected to silica gel chromatography with pentane.

Entry 2: Anhydrous ZnCl₂ powder (54.5 mg, 0.40 mmol) and THF (1.0 mL) were added before **3ba** in THF was added.

Entry 3: [RhCl(cod)]₂ (1.48 mg, 0.0030 mmol, 3 mol% of Rh) was used as catalyst instead of [RhCl(coe)₂]₂ and binap. Anhydrous ZnCl₂ powder (54.5 mg, 0.40 mmol) and THF (1.0 mL) were added before **3ba** in THF was added.

The same procedures as those for equation 4.2 were followed by using a THF solution of **4ba** prepared in Section 4.4.7-2.

4.4.9 Characterization of the products

The ratios of **5** to **6** were determined by ^2H NMR analysis except for **5ae/6ae**, **5af/6af**, and **5ag/6ag**.

Compound 5aa. (Table 4.2, entry 1, cod (A), 82% yield, **5aa:6aa** = 92:8).

^1H NMR (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.96 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.16 (t, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.43 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.80 (s, 6H), 6.35 (t, $J_{\text{H,H}} = 2.1$ Hz, 1H), 6.50 (d, $J_{\text{H,H}} = 2.2$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.11, 14.15, 22.0, 23.1, 30.6, 32.0, 55.4, 98.4, 105.0, 129.1 (t, $J_{\text{C},^2\text{H}} = 23.0$ Hz), 140.1, 146.0, 160.7; ^2H NMR (61 MHz, acetone) δ 5.68 (s). **HRMS** (ESI) calcd for $\text{C}_{16}\text{H}_{24}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 250.1917, found 250.1898.

Compound 6aa. (Table 4.2, entry 1, binap (B), 90% yield, **5aa:6aa** = <1:99).

^1H NMR (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.96 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.16 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.43 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.80 (s, 6H), 5.67 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.35 (s, 1H), 6.50 (d, $J_{\text{H,H}} = 1.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.09, 14.14, 22.0, 23.2, 30.7, 32.0, 55.4, 98.4, 104.7 (t, $J_{\text{C},^2\text{H}} = 24.1$ Hz), 105.0, 129.4, 140.2 (t,

$J_{\text{C},^2\text{H}} = 4.1$ Hz), 146.0 (t, $J_{\text{C},^2\text{H}} = 8.8$ Hz), 160.6, 160.7; $^2\text{H NMR}$ (61 MHz, acetone) δ 6.50 (s). **HRMS** (ESI) calcd for $\text{C}_{16}\text{H}_{24}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 250.1917, found 250.1940.

Compound 5ba [819047-73-9]. (Table 4.2, entry 2, cod (A), 80% yield, **5ba:6ba** = 80:20). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.48 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.17 (t, $J_{\text{H,H}} = 7.1$ Hz, 2H), 2.48 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 7.21 (t, $J_{\text{H,H}} = 6.9$ Hz, 1H), 7.29 (t, $J_{\text{H,H}} = 7.2$ Hz, 2H), 7.34 (d, $J_{\text{H,H}} = 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 14.10, 14.11, 22.0, 23.2, 30.7, 31.8, 126.5, 128.1, 128.2, 129.0 (t, $J_{\text{C},^2\text{H}} = 22.8$ Hz), 140.1, 143.7; $^2\text{H NMR}$ (61 MHz, acetone) δ 5.66 (s). The spectral data are in agreement with reported literature values.²⁴

Compound 6ba [374107-00-3]. (Table 4.2, entry 2, binap (A), 87% yield, **5ba:6ba** = 2:98). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.48 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.18 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.48 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 5.67 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.21 (td, $J_{\text{H,H}} = 7.4$ Hz, 1.3 Hz, 1H), 7.30 (t, $J_{\text{H,H}} = 6.9$ Hz, 1H), 7.30 (d, $J_{\text{H,H}} = 6.7$ Hz, 1H), 7.34 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 14.10, 14.11, 22.0, 23.2, 30.8, 31.9, 126.2 (t, $J_{\text{C},^2\text{H}} = 24.1$ Hz), 126.5, 128.1, 128.2, 129.3, 140.2,

143.6; ^2H NMR (61 MHz, acetone) δ 7.35 (s). The spectral data are in agreement with reported literature values.^{6b}

Compound 5ca. (Table 4.2, entry 3, cod (A), 68% yield, **5ca:6ca** = 77:23).

^1H NMR (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.96 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.35 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.16 (t, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.34 (s, 3H), 2.46 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 7.11 (d, $J_{\text{H,H}} = 7.9$ Hz, 2H), 7.24 (d, $J_{\text{H,H}} = 8.1$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.94, 13.96, 21.0, 21.8, 23.1, 30.6, 31.6, 126.2, 128.1 (t, $J_{\text{C},^2\text{H}} = 22.8$ Hz), 128.8, 135.9, 139.7, 140.6; ^2H NMR (61 MHz, acetone) δ 5.63 (s). **HRMS** (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{D}$ $[\text{M}+\text{H}]^+$ 204.1863, found 204.1858.

Compound 6ca. (Table 4.2, entry 3, binap (B), 91% yield, **5ca:6ca** = 1:99).

^1H NMR (400 MHz, CDCl_3) δ 0.88 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.48 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.17 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.34 (s, 3H), 2.47 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 5.64 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H), 7.06–7.14 (br m, 2H), 7.25 (d, $J_{\text{H,H}} = 8.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.0, 21.8, 23.1, 30.6, 31.7, 125.9 (t, $J_{\text{C},^2\text{H}} = 23.9$ Hz), 126.2, 128.4, 128.7, 128.8, 135.9, 139.8, 140.5; ^2H NMR (61 MHz, acetone) δ 7.24 (s). **HRMS** (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{D}$ $[\text{M}+\text{H}]^+$ 204.1863, found 204.1864.

Compound 5da. (Table 4.2, entry 4, cod (A), 84% yield, **5da:6da** = 74:26).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.36 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.46 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.16 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.44 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 3.80 (s, 3H), 6.84 (d, $J_{\text{H,H}}$ = 8.7 Hz, 2H), 7.27 (d, $J_{\text{H,H}}$ = 8.6 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 14.0, 21.8, 23.1, 30.5, 31.7, 55.2, 113.5, 127.3, 127.5 (t, $J_{\text{C},^2\text{H}}$ = 22.5 Hz), 136.0, 139.2, 158.3; **²H NMR** (61 MHz, acetone) δ 5.58 (s). **HRMS** (ESI) calcd for C₁₅H₂₂DO [M+H]⁺ 220.1812, found 220.1818.

Compound 6da. (Table 4.2, entry 4, binap (A), 94% yield, **5da:6da** = 1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.37 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.16 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.45 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 3.81 (s, 3H), 5.60 (t, $J_{\text{H,H}}$ = 7.2 Hz, 1H), 6.84–6.86 (br m, 2H), 7.28 (d, $J_{\text{H,H}}$ = 9.3 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.94, 13.95, 21.8, 23.1, 30.6, 31.7, 55.2, 113.4, 113.5, 127.0 (t, $J_{\text{C},^2\text{H}}$ = 23.8 Hz), 127.3, 127.8, 135.9, 139.3, 158.3; **²H NMR** (61 MHz, acetone) δ 7.29 (s). **HRMS** (ESI) calcd for C₁₅H₂₂DO [M+H]⁺ 220.1812, found 220.1809.

Compound 5ea. (Table 4.2, entry 5, cod (A), 71% yield, **5ea:6ea** = 94:6).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.95 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.38 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.46 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.15 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.44 (t, $J_{\text{H,H}}$ = 7.7 Hz, 2H), 2.94 (s, 6H), 6.71 (d, $J_{\text{H,H}}$ = 8.6 Hz, 2H), 7.25 (d, $J_{\text{H,H}}$ = 8.8 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.95, 14.02, 21.9, 23.2, 30.5, 31.5, 40.8, 112.6, 126.1 (t, $J_{\text{C},^2\text{H}}$ = 23.0 Hz), 126.9, 131.9 (br s), 139.3, 149.3; **²H NMR** (61 MHz, acetone) δ 5.55 (s). **HRMS** (ESI) calcd for C₁₆H₂₅DN [M+H]⁺ 233.2128, found 233.2135.

Compound 6ea. (Table 4.2, entry 5, binap (B), 87% yield, **5ea:6ea** = 1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.39 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.16 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.45 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 2.95 (s, 6H), 5.60 (t, $J_{\text{H,H}}$ = 7.2 Hz, 1H), 6.70–6.76 (br m, 2H), 7.27 (d, $J_{\text{H,H}}$ = 9.3 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.9, 14.0, 21.9, 23.2, 30.6, 31.6, 40.9, 112.6, 112.7, 126.5, 126.6 (t, $J_{\text{C},^2\text{H}}$ = 23.9 Hz), 126.9, 132.1 (br s), 139.3, 149.1; **²H NMR** (61 MHz, acetone) δ 7.22 (s). **HRMS** (ESI) calcd for C₁₆H₂₅DN [M+H]⁺ 233.2128, found 233.2128.

Compound 5fa. (Table 4.2, entry 6, cod (A), 86% yield, **5fa:6fa** = 81:19).

¹H NMR (400 MHz, CDCl₃) δ 0.26 (s, 9H), 0.89 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.38 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.17 (t, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.48 (t, $J_{\text{H,H}}$ = 7.7 Hz, 2H), 7.33 (d, $J_{\text{H,H}}$ = 8.2 Hz, 2H), 7.46 (d, $J_{\text{H,H}}$ = 8.2 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ -1.1, 13.9, 14.0, 21.9, 23.0, 30.6, 31.6, 125.6, 129.0 (t, $J_{\text{C},^2\text{H}}$ = 22.6 Hz), 133.2, 138.1, 139.8, 143.9; **²H NMR** (61 MHz, acetone) δ 5.69 (s). **HRMS** (ESI) calcd for C₁₇H₂₈DSi [M+H]⁺ 262.2101, found 262.2100.

Compound 6fa. (Table 4.2, entry 6, binap (B), 85% yield, **5fa:6fa** = 6:94).

¹H NMR (400 MHz, CDCl₃) δ 0.26 (s, 9H), 0.89 (t, $J_{\text{H,H}}$ = 7.3 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.37 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.18 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.47 (t, $J_{\text{H,H}}$ = 7.7 Hz, 2H), 5.68 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 7.33 (d, $J_{\text{H,H}}$ = 8.0 Hz, 1H), 7.43–7.48 (br m, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ -1.1, 13.9, 14.0, 21.9, 23.0, 30.7, 31.6, 125.3 (t, $J_{\text{C},^2\text{H}}$ = 24.3 Hz), 125.6, 129.3, 133.1, 133.2, 138.1, 139.9, 143.8; **²H NMR** (61 MHz, acetone) δ 7.35 (s). **HRMS** (ESI) calcd for C₁₇H₂₈DSi [M+H]⁺ 262.2101, found 262.2113.

Compound 5ga. (Table 4.2, entry 7, cod (A), 52% yield, **5ga:6ga** = 49:51).

¹H NMR (400 MHz, CDCl₃) δ 0.86 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.94 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.33 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.45 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.14 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.43 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 6.92–6.99 (m, 2H), 7.22–7.30 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.90, 13.93, 21.7, 23.0, 30.5, 31.8, 114.8 (d, $J_{\text{C},^{19}\text{F}}$ = 21.2 Hz), 127.8 (d, $J_{\text{C},^{19}\text{F}}$ = 7.7 Hz), 128.8 (t, $J_{\text{C},^2\text{H}}$ = 23.0 Hz), 139.0, 139.5 (d, $J_{\text{C},^{19}\text{F}}$ = 2.9 Hz), 161.7 (d, $J_{\text{C},^{19}\text{F}}$ = 245.9 Hz); **²H NMR** (61 MHz, acetone) δ 5.63 (s). **HRMS** (ESI) calcd for C₁₄H₁₉DF [M+H]⁺ 208.1612, found 208.1616.

Compound 6ga. (Table 4.2, entry 7, binap (B), 83% yield, **5ga:6ga** = <1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.86 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.94 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.33 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.45 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.14 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.43 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 5.58 (t, $J_{\text{H,H}}$ = 7.2 Hz, 1H), 6.92–6.99 (m, 2H), 7.23–7.29 (m, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.90, 13.93, 21.7, 23.0, 30.6, 31.8, 114.7 (d, $J_{\text{C},^{19}\text{F}}$ = 21.2 Hz), 114.8 (d, $J_{\text{C-F}}$ = 21.2 Hz), 127.5 (td, $J_{\text{C},^2\text{H}}$ = 24.3 Hz, $J_{\text{C},^{19}\text{F}}$ = 7.9 Hz), 127.8 (d, $J_{\text{C},^{19}\text{F}}$ = 7.7 Hz), 129.2, 139.1, 139.4 (d, $J_{\text{C},^{19}\text{F}}$ = 3.1 Hz), 161.7 (d, $J_{\text{C},^{19}\text{F}}$ = 245.7 Hz); **²H NMR** (61 MHz, acetone) δ 7.38 (s). **HRMS** (ESI) calcd for C₁₄H₁₉DF [M+H]⁺ 208.1612, found 208.1618.

Compound 6ha. (Table 4.2, entry 8, binap (B), 93% yield, **5ha:6ha** = <1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.97 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.35 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.49 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.20 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.49 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 5.72 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 7.43 (d, $J_{\text{H,H}}$ = 8.8 Hz, 1H), 7.52–7.56 (br m, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.87, 13.92, 21.7, 22.9, 30.7, 31.5, 124.4 (q, $J_{\text{C},^{19}\text{F}}$ = 273.0 Hz), 124.9 (q, $J_{\text{C},^{19}\text{F}}$ = 3.8 Hz), 125.1 (q, $J_{\text{C},^{19}\text{F}}$ = 3.8 Hz), 126.0 (t, $J_{\text{C},^2\text{H}}$ = 25.1 Hz), 126.5, 128.4 (q, $J_{\text{C},^{19}\text{F}}$ = 32.4 Hz), 131.2, 139.1, 147.0; **²H NMR** (61 MHz, acetone) δ 7.58 (s). **HRMS** (ESI) calcd for C₁₅H₁₉DF₃ [M+H]⁺ 258.1580, found 258.1575.

Compound 5ia. (Table 4.2, entry 9, cod (A), 72% yield, **5ia:6ia** = 86:14).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.36 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.17 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.35 (s, 3H), 2.46 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 7.03 (dd, $J_{\text{H,H}}$ = 7.1 Hz, 0.4 Hz, 1H), 7.15 (s, 1H), 7.10–7.22 (m, 2H); **¹³C NMR** δ 13.9, 14.0, 21.5, 21.8, 23.1, 30.5, 31.7, 123.5, 127.1, 127.9, 128.0, 128.6 (t, $J_{\text{C},^2\text{H}}$ = 22.8 Hz), 137.5, 140.0, 143.5; **²H NMR** (61 MHz, acetone) δ 5.63 (s). **HRMS** (ESI) calcd for C₁₅H₂₁DNa [M+Na]⁺ 226.1682, found 226.1684.

Compound 6ia. (Table 4.2, entry 9, binap (B), 87% yield, **5ia:6ia** = 1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.36 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.17 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.35 (s, 3H), 2.46 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 5.64 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 7.03 (d, $J_{\text{H,H}}$ = 6.8 Hz, 1H), 7.15 (s, 1H), 7.10–7.22 (m, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.9, 14.0, 21.5, 21.8, 23.1, 30.6, 31.8, 123.2 (t, $J_{\text{C},^2\text{H}}$ = 24.0 Hz), 127.1, 127.9, 128.0, 129.0, 137.5, 140.1, 143.5; **²H NMR** (61 MHz, acetone) δ 7.13 (s). **HRMS** (ESI) calcd for C₁₅H₂₁DNa [M+Na]⁺ 226.1682, found 226.1662.

Compound 5ja. (Table 4.2, entry 10, cod (A), 82% yield, **5ja:(6ja+6ja')** = 80:20). **¹H NMR** (400 MHz, CDCl₃) δ 0.88 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.37 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.17 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.46 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 3.82 (s, 3H), 6.77 (dd, $J_{\text{H,H}}$ = 8.2 Hz, 2.5 Hz, 1H), 6.89 (t, $J_{\text{H,H}}$ = 2.4 Hz, 1H), 6.94 (dt, $J_{\text{H,H}}$ = 8.1 Hz, 1.0 Hz, 1H), 7.21 (t, $J_{\text{H,H}}$ = 7.9 Hz, 1H); **¹³C NMR** δ 13.9, 14.0, 21.8, 23.0, 30.5, 31.7, 55.2, 111.4, 112.4, 119.0, 128.9 (t, $J_{\text{C},^2\text{H}}$ = 22.9 Hz), 129.0, 139.8, 145.1, 159.5; **²H NMR** (61 MHz, acetone) δ 5.68 (s). **HRMS** (ESI) calcd for C₁₅H₂₁DONa [M+Na]⁺ 242.1631, found 242.1642.

Compound 6ja:6ja' (2:1). (Table 4.2, entry 10, binap (A), 93% yield, **5ja:(6ja+6ja')** = 1:99). The ratio of **6ja:6ja'** was determined by ^1H NMR of crude sample. **Compound 6ja:** ^1H NMR (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.17 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.46 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.82 (s, 3H), 5.68 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.77 (dd, $J_{\text{H,H}} = 8.2$ Hz, 2.2 Hz, 1H), 6.89 (d, $J_{\text{H,H}} = 2.5$ Hz, 1H), 7.21 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.8, 23.0, 30.6, 31.8, 55.2, 111.4, 112.4, 118.7 (t, $J_{\text{C},^2\text{H}} = 24.1$ Hz), 128.9, 129.3, 139.9, 145.1, 159.5; ^2H NMR (61 MHz, acetone) δ 6.93 (s). **Compound 6ja':** ^1H NMR (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.17 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.46 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.82 (s, 3H), 5.68 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.77 (dd, $J_{\text{H,H}} = 8.2$ Hz, 2.2 Hz, 1H), 6.94 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H), 7.22 (t, $J_{\text{H,H}} = 7.9$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.8, 23.0, 30.6, 31.8, 55.2, 111.5, 112.1 (t, $J_{\text{C},^2\text{H}} = 23.8$ Hz), 118.9, 129.0, 129.3, 139.9, 145.1, 159.4; ^2H NMR (61 MHz, acetone) δ 6.90 (s). **HRMS** (ESI) calcd for $\text{C}_{15}\text{H}_{21}\text{DONa}$ $[\text{M}+\text{Na}]^+$ 242.1631, found 242.1633.

Compound 5ka. (Table 4.2, entry 11, cod (A), 72% yield, **5ka:6ka** = 95:5).

¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.96 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.38 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.47 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.16 (t, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.46 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 2.96 (s, 6H), 6.66 (dd, $J_{\text{H,H}}$ = 6.9 Hz, 2.4 Hz, 1H), 6.73 (d, $J_{\text{H,H}}$ = 6.7 Hz, 1H), 6.75 (s, 1H), 7.18 (t, $J_{\text{H,H}}$ = 8.1 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.96, 14.04, 21.9, 23.1, 30.5, 32.0, 40.9, 111.2 (br s), 115.6 (br s), 128.3 (t, $J_{\text{C},^2\text{H}}$ = 23.5 Hz), 128.7, 140.7, 144.7, 150.5 (br s); **²H NMR** (61 MHz, acetone) δ 5.63 (s). **HRMS** (ESI) calcd for C₁₆H₂₅DN [M+H]⁺ 233.2128, found 233.2110.

Compound 6ka. (Table 4.2, entry 11, binap (B), 95% yield, **5ka:6ka** = 1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.90 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.97 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.39 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.48 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.18 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.47 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 2.97 (s, 6H), 5.66 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 6.68 (dd, $J_{\text{H,H}}$ = 6.8 Hz, 2.4 Hz, 1H), 6.76 (d, $J_{\text{H,H}}$ = 2.0 Hz, 1H), 7.19 (d, $J_{\text{H,H}}$ = 8.2 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.95, 14.03, 21.9, 23.1, 30.6, 32.0, 41.0, 111.3, 111.4, 115.5 (br t, $J_{\text{C},^2\text{H}}$ = 23.0 Hz), 128.6, 128.7, 140.8, 144.6, 150.3; **²H NMR** (61 MHz, acetone) δ 6.69 (s). **HRMS** (ESI) calcd for C₁₆H₂₅DN [M+H]⁺ 233.2128, found 233.2150.

Compound 5la. (Table 4.2, entry 12, cod (A), 79% yield, **5la:6la** = 83:17).

¹H NMR (400 MHz, CDCl₃) δ 0.28 (s, 9H), 0.89 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 0.97 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.38 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.48 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.18 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.48 (t, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 7.29 (td, $J_{\text{H,H}}$ = 6.8 Hz, 2.9 Hz, 1H), 7.32 (dt, $J_{\text{H,H}}$ = 7.8 Hz, 0.9 Hz, 1H), 7.38 (dt, $J_{\text{H,H}}$ = 8.0 Hz, 1.4 Hz, 1H), 7.47 (s, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ -1.1, 13.96, 14.00, 21.8, 23.1, 30.6, 31.8, 126.9, 127.5, 128.8 (t, $J_{\text{C},^2\text{H}}$ = 22.9 Hz), 131.1, 131.4, 140.0, 140.2, 142.7; **²H NMR** (61 MHz, acetone) δ 5.66 (s). **HRMS** (ESI) calcd for C₁₇H₂₈DSi [M+H]⁺ 262.2101, found 262.2107.

Compound 6la. (Table 4.2, entry 12, binap (B), 87% yield, **5la:6la** = 1:99).

¹H NMR (400 MHz, CDCl₃) δ 0.30 (s, 9H), 0.92 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.00 (t, $J_{\text{H,H}}$ = 7.4 Hz, 3H), 1.41 (sext, $J_{\text{H,H}}$ = 7.6 Hz, 2H), 1.51 (sext, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 2.21 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.51 (t, $J_{\text{H,H}}$ = 7.7 Hz, 2H), 5.68 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 7.31 (d, $J_{\text{H,H}}$ = 7.2 Hz, 1H), 7.41 (dd, $J_{\text{H,H}}$ = 7.3 Hz, 1.1 Hz, 1H), 7.50 (s, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ -1.1, 13.96, 14.00, 21.9, 23.1, 30.7, 31.9, 126.6 (t, $J_{\text{C},^2\text{H}}$ = 23.7 Hz), 127.4, 129.1, 131.1, 131.4, 140.0, 140.3, 142.7; **²H NMR** (61 MHz, acetone) δ 7.34 (s). **HRMS** (ESI) calcd for C₁₇H₂₈DSi [M+H]⁺ 262.2101, found 262.2104.

Compound S1ma. (Table 4.2, entry 13, quenched with H₂O). The E geometry and all aromatic protons were assigned by NOESY NMR study. **¹H NMR** (400 MHz, CDCl₃) δ 0.88 (t, *J*_{H,H} = 7.3 Hz, 3H), 0.96 (t, *J*_{H,H} = 7.4 Hz, 3H), 1.37 (sext, *J*_{H,H} = 7.6 Hz, 2H), 1.47 (sext, *J*_{H,H} = 7.4 Hz, 2H), 2.16 (q, *J*_{H,H} = 7.3 Hz, 2H), 2.33 (s, 3H), 2.48 (t, *J*_{H,H} = 7.6 Hz, 2H), 3.80 (s, 3H), 5.65 (t, *J*_{H,H} = 7.2 Hz, 1H), 6.60 (s, *H*_b, 1H), 6.69 (s, *H*_c, 1H), 6.76 (s, *H*_a, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.9, 14.0, 21.7, 21.9, 23.0, 30.6, 31.8, 55.1, 109.5, 112.4, 119.9, 129.1, 138.9, 140.1, 145.0, 159.5. **HRMS** (ESI) calcd for C₁₆H₂₅O [M+H]⁺ 233.1905, found 233.1913.

Compound 5ma. (Table 4.2, entry 13, cod (A), 79% yield, **5ma:6ma** = >99:1). **¹H NMR** (400 MHz, CDCl₃) δ 0.89 (t, *J*_{H,H} = 7.3 Hz, 3H), 0.97 (t, *J*_{H,H} = 7.3 Hz, 3H), 1.38 (sext, *J*_{H,H} = 7.6 Hz, 2H), 1.47 (sext, *J*_{H,H} = 7.4 Hz, 2H), 2.16 (t, *J*_{H,H} = 7.4 Hz, 2H), 2.33 (s, 3H), 2.44 (t, *J*_{H,H} = 7.6 Hz, 2H), 3.80 (s, 3H), 6.60 (s, 1H), 6.69 (s, 1H), 6.76 (s, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.9, 14.0, 21.7, 21.8, 23.0, 30.5, 31.8, 55.1, 109.5, 112.4, 119.8, 128.7 (t, *J*_{C,²H} = 22.8 Hz), 138.9, 140.0,

145.0, 159.5; ^2H NMR (61 MHz, acetone) δ 5.65 (s). HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{24}\text{DO}$ $[\text{M}+\text{H}]^+$ 234.1968, found 234.1965.

Compound 6ma. (Table 4.2, entry 13, binap (B), 97% yield, **5ma:6ma** = 1:99). ^1H NMR (400 MHz, CDCl_3) δ 0.89 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.37 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.47 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.17 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.33 (s, 3H), 2.44 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H), 3.80 (s, 3H), 5.66 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.60 (s, 1H), 6.76 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.7, 21.9, 23.0, 30.6, 31.8, 55.1, 109.2 (t, $J_{\text{C},^2\text{H}} = 23.9$ Hz), 112.4, 119.8, 129.1, 138.8, 140.0, 144.9, 159.4; ^2H NMR (61 MHz, acetone) δ 6.68 (s). HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{24}\text{DO}$ $[\text{M}+\text{H}]^+$ 234.1968, found 234.1965.

Compound 5na. (Table 4.2, entry 14, cod (A), 64% yield, **5na:6na** = 94:6). ^1H NMR (400 MHz, CDCl_3) δ 0.84 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.97 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.25 (sext, $J_{\text{H,H}} = 7.6$ Hz, 2H), 1.46 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.17 (t, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.44 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 3.81 (s, 3H), 6.85 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H), 6.89 (td, $J_{\text{H,H}} = 7.4$ Hz, 0.7 Hz, 1H), 7.09 (dd, $J_{\text{H,H}} = 7.4$ Hz, 1.7 Hz, 1H), 7.21 (td, $J_{\text{H,H}} = 7.8$ Hz, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.0, 21.6, 23.0, 30.1, 32.3, 55.4, 110.6, 120.3, 127.6, 129.8 (t, $J_{\text{C},^2\text{H}} = 23.2$ Hz), 130.7, 134.0, 139.7, 156.7; ^2H

NMR (61 MHz, acetone) δ 5.31 (s). HRMS (ESI) calcd for $C_{15}H_{22}DO$ $[M+H]^+$ 220.1812, found 220.1804.

Compound 6na. (Table 4.2, entry 14, binap (A), 88% yield, **5na:6na** = 13:87). 1H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, $J_{H,H}$ = 7.3 Hz, 3H), 0.97 (t, $J_{H,H}$ = 7.4 Hz, 3H), 1.25 (sext, $J_{H,H}$ = 7.6 Hz, 2H), 1.46 (sext, $J_{H,H}$ = 7.4 Hz, 2H), 2.17 (q, $J_{H,H}$ = 7.3 Hz, 2H), 2.44 (t, $J_{H,H}$ = 7.7 Hz, 2H), 3.81 (s, 3H), 5.39 (t, $J_{H,H}$ = 7.2 Hz, 1H), 6.85 (d, $J_{H,H}$ = 8.2 Hz, 1H), 6.89 (d, $J_{H,H}$ = 7.4 Hz, 1H), 7.21 (t, $J_{H,H}$ = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 21.6, 23.0, 30.2, 32.3, 55.4, 110.6, 120.2, 127.6, 130.1, 130.4 (t, $J_{C,H}$ = 24.1 Hz), 133.9, 139.7, 156.7; 2H NMR (61 MHz, acetone) δ 7.05 (s). HRMS (ESI) calcd for $C_{15}H_{22}DO$ $[M+H]^+$ 220.1812, found 220.1811.

Compound 5ab. (Table 4.3, entry 1, cod (A), 78% yield, **5ab:6ab** = 90:10). 1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, $J_{H,H}$ = 6.8 Hz, 3H), 0.90 (t, $J_{H,H}$ = 6.9 Hz, 3H), 1.20–1.40 (m, 10H), 1.44 (quint, $J_{H,H}$ = 7.0 Hz, 2H), 2.16 (t, $J_{H,H}$ = 7.3 Hz, 2H), 2.43 (t, $J_{H,H}$ = 7.5 Hz, 2H), 3.80 (s, 6H), 6.35 (t, $J_{H,H}$ = 2.2 Hz, 1H), 6.49 (d, $J_{H,H}$ = 2.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.5, 22.6, 28.37, 28.43, 29.5, 29.8, 31.6, 31.9, 55.3, 98.3, 104.8, 128.9 (t, $J_{C,H}$ = 22.6 Hz), 140.0, 145.9, 160.5;

^2H NMR (61 MHz, acetone) δ 5.67 (s). HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{32}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 306.2543, found 306.2543.

Compound 6ab. (Table 4.3, entry 1, binap (A), 91% yield, **5ab:6ab** = 1:99).

^1H NMR (400 MHz, CDCl_3) δ 0.86 (t, $J_{\text{H,H}}$ = 6.8 Hz, 3H), 0.91 (t, $J_{\text{H,H}}$ = 6.9 Hz, 3H), 1.20–1.40 (m, 10H), 1.44 (quint, $J_{\text{H,H}}$ = 7.0 Hz, 2H), 2.17 (q, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.43 (t, $J_{\text{H,H}}$ = 7.5 Hz, 2H), 3.80 (s, 6H), 5.66 (t, $J_{\text{H,H}}$ = 7.3 Hz, 1H), 6.35 (d, $J_{\text{H,H}}$ = 2.2 Hz, 1H), 6.50 (d, $J_{\text{H,H}}$ = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.5, 22.6, 28.4, 28.5, 29.5, 29.8, 31.6, 31.8, 55.3, 98.3, 104.5 (t, $J_{\text{C},^2\text{H}}$ = 24.0 Hz), 104.8, 129.2, 140.1, 145.8, 160.47, 160.50; ^2H NMR (61 MHz, acetone) δ 6.51 (s). HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{32}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 306.2543, found 306.2545.

Compound 5ac. (Table 4.3, entry 2, cod (A), 74% yield, **5ac:6ac** = 93:7).

^1H NMR (400 MHz, CDCl_3) δ 0.87 (t, $J_{\text{H,H}}$ = 6.9 Hz, 3H), 0.89 (t, $J_{\text{H,H}}$ = 6.7 Hz, 3H), 1.10–1.50 (m, 20H), 2.16 (t, $J_{\text{H,H}}$ = 7.3 Hz, 2H), 2.43 (t, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 3.80 (s, 6H), 6.35 (t, $J_{\text{H,H}}$ = 2.3 Hz, 1H), 6.49 (d, $J_{\text{H,H}}$ = 2.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.07, 14.09, 22.6, 22.7, 28.4, 28.7, 29.1, 29.2, 29.4, 29.6, 29.8, 31.8, 31.9, 55.3, 98.2, 104.8, 128.9 (t, $J_{\text{C},^2\text{H}}$ = 22.6 Hz), 140.0, 145.9, 160.5; ^2H NMR (61

MHz, acetone) δ 5.67 (s). **HRMS** (ESI) calcd for $C_{24}H_{40}DO_2$ $[M+H]^+$ 362.3169, found 362.3163.

Compound 6ac. (Table 4.3, entry 2, binap (A), 97% yield, **5ac:6ac** = 4:96).

1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, $J_{H,H}$ = 6.9 Hz, 3H), 0.91 (t, $J_{H,H}$ = 6.7 Hz, 3H), 1.20–1.50 (m, 20H), 2.18 (q, $J_{H,H}$ = 7.3 Hz, 2H), 2.45 (t, $J_{H,H}$ = 7.4 Hz, 2H), 3.81 (s, 6H), 5.67 (t, $J_{H,H}$ = 7.3 Hz, 1H), 6.36 (d, $J_{H,H}$ = 2.2 Hz, 1H), 6.51 (d, $J_{H,H}$ = 2.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 14.0, 14.1, 22.6, 22.7, 28.5, 28.7, 29.1, 29.2, 29.4, 29.6, 29.9, 31.8, 31.9, 55.2, 98.3, 104.5 (t, $J_{C,H} = 23.8$ Hz), 104.8, 129.2, 140.1, 145.8, 160.47, 160.49; **2H NMR** (61 MHz, acetone) δ 6.50 (s). **HRMS** (ESI) calcd for $C_{24}H_{40}DO_2$ $[M+H]^+$ 362.3172, found 362.3163.

Compound 5ad. (Table 4.3, entry 3, cod (A), 86% yield, **5ad:6ad** = 97:3).

1H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 6H), 6.43 (t, $J_{H,H}$ = 2.3 Hz, 1H), 6.50 (d, $J_{H,H}$ = 2.3 Hz, 2H), 7.03 (dd, $J_{H,H}$ = 7.8 Hz, 2.2 Hz, 2H), 7.05–7.16 (m, 3H), 7.21 (dd, $J_{H,H}$ = 7.6 Hz, 2.3 Hz, 2H), 7.28–7.36 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 55.3, 99.5, 106.1, 126.8, 127.4, 127.9, 128.0 (t, $J_{C,H} = 22.8$ Hz), 128.6, 129.5, 130.3,

137.1, 140.1, 142.4, 145.6, 160.5; ^2H NMR (61 MHz, acetone) δ 7.07 (s). **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{20}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 318.1604, found 318.1623.

Compound 6ad. (Table 4.3, entry 3, binap (B), 98% yield, **5ad:6ad** = 13:87).

^1H NMR (400 MHz, CDCl_3) δ 3.77 (s, 6H), 6.43 (d, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.50 (d, $J_{\text{H,H}} = 2.3$ Hz, 1H), 6.99 (s, 1H), 7.03 (dd, $J_{\text{H,H}} = 7.8$ Hz, 2.2 Hz, 2H), 7.05–7.16 (m, 3H), 7.21 (dd, $J_{\text{H,H}} = 7.6$ Hz, 2.3 Hz, 2H), 7.28–7.36 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 55.3, 99.6, 105.8 (t, $J_{\text{C},^2\text{H}} = 24.4$ Hz), 106.1, 126.8, 127.4, 127.9, 128.3, 128.6, 129.6, 130.3, 137.2, 140.1, 142.5, 145.6, 160.49, 160.52; ^2H NMR (61 MHz, acetone) δ 6.49 (s). **HRMS** (ESI) calcd for $\text{C}_{22}\text{H}_{20}\text{DO}_2$ $[\text{M}+\text{H}]^+$ 318.1604, found 318.1606.

Compound 5bd [42353-76-4]. (Table 4.3, entry 4, modified cod (A), 61% yield, **5bd:6bd** = 92:8). ^1H NMR (400 MHz, CDCl_3) δ 7.06 (br d, $J_{\text{H,H}} = 7.8$ Hz, 2H), 7.10–7.16 (m 3H), 7.20–7.25 (m, 2H), 7.26–7.38 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) δ 126.7, 127.4, 127.5, 127.6, 127.92 (t, $J_{\text{C},^2\text{H}} = 27.0$ Hz), 127.93, 128.2, 128.6, 129.5, 130.3, 137.3, 140.3, 142.5, 143.4; ^2H NMR (61 MHz, acetone) δ 7.04 (s). The spectral data are in agreement with reported literature values.^{2b}

Compound 6bd. (Table 4.3, entry 4, binap (B), 97% yield, **5bd:6bd** = 10:90).

¹H NMR (400 MHz, CDCl₃) δ 6.98 (s, 1H), 7.06 (dd, $J_{\text{H,H}} = 7.8$ Hz, 2.0 Hz, 2H), 7.10–7.16 (m, 3H), 7.20–7.25 (m, 2H), 7.26–7.38 (m, 7H); **¹³C NMR** (100 MHz, CDCl₃) δ 126.7, 127.3 (t, $J_{\text{C},^2\text{H}} = 24.3$ Hz), 127.4, 127.5, 127.6, 127.9, 128.07, 128.13, 128.2, 128.6, 129.5, 130.4, 137.4, 140.3, 142.5, 143.3; **²H NMR** (61 MHz, acetone) δ 7.33 (s). **HRMS** (ESI) calcd for C₂₀H₁₆D [M+H]⁺ 258.1393, found 258.1397.

The ratio of **5ae:6ae** was determined by ¹H NMR because ²H NMR peaks are overlapping.

Compound 5ae. (Table 4.3, entry 5, cod (A), 72% yield, **5ae:6ae** = 94:6).

¹H NMR (400 MHz, CDCl₃) δ 1.08 (t, $J_{\text{H,H}} = 7.5$ Hz, 3H), 2.71 (q, $J_{\text{H,H}} = 7.5$ Hz, 2H), 3.83 (s, 6H), 6.43 (t, $J_{\text{H,H}} = 2.0$ Hz, 1H), 6.63 (d, $J_{\text{H,H}} = 2.3$ Hz, 2H), 7.25 (t, $J_{\text{H,H}} = 7.0$ Hz, 1H), 7.34 (d, $J_{\text{H,H}} = 7.4$ Hz, 2H), 7.38 (t, $J_{\text{H,H}} = 7.1$ Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.5, 23.4, 55.3, 99.1, 105.1, 126.6, 127.3 (t, $J_{\text{C},^2\text{H}} = 23.4$ Hz), 128.2, 128.7, 138.0, 144.4, 145.1, 160.7; **²H NMR** (61 MHz, acetone) δ 6.74 (s). **HRMS** (ESI) calcd for C₁₈H₂₀DO₂ [M+H]⁺ 270.1604, found 270.1582.

Compound 6ae. (Table 4.3, entry 5, binap (B), 93% yield, **5ae:6ae** = 10:90).

¹H NMR (400 MHz, CDCl₃) δ 1.09 (t, $J_{\text{H,H}}$ = 7.5 Hz, 3H), 2.71 (q, $J_{\text{H,H}}$ = 7.5 Hz, 2H), 3.84 (s, 6H), 6.44 (d, $J_{\text{H,H}}$ = 2.0 Hz, 1H), 6.64 (d, $J_{\text{H,H}}$ = 2.1 Hz, 1H), 6.72 (s, 1H), 7.26 (t, $J_{\text{H,H}}$ = 7.0 Hz, 1H), 7.34 (d, $J_{\text{H,H}}$ = 7.4 Hz, 2H), 7.38 (t, $J_{\text{H,H}}$ = 7.1 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.5, 23.4, 55.3, 99.1, 104.7 (t, $J_{\text{C},^2\text{H}}$ = 24.4 Hz), 105.0, 126.6, 127.6, 128.2, 128.7, 138.1, 144.5, 145.0, 160.66, 160.69; **²H NMR** (61 MHz, acetone) δ 6.67 (s). **HRMS (ESI)** calcd for C₁₈H₂₀DO₂ [M+H]⁺ 270.1604, found 270.1592.

The ratio of **5af:6af** was determined by ¹H NMR because ²H NMR peaks are overlapping.

Compound 5af and 5af'. (Table 4.3, entry 6, cod (A), 89% yield, **5af:6af** = 95:5). The ratio of **5af:5af'** was determined by ¹H NMR. **Compound 5af:** **¹H NMR** (400 MHz, CDCl₃) δ 1.08 (d, $J_{\text{H,H}}$ = 6.9 Hz, 6H), 2.37 (s, 3H), 3.28 (sept, $J_{\text{H,H}}$ = 6.9 Hz, 1H), 3.82 (s, 6H), 6.42 (t, $J_{\text{H,H}}$ = 2.2 Hz, 1H), 6.44 (d, $J_{\text{H,H}}$ = 2.2 Hz, 2H), 7.17 (d, $J_{\text{H,H}}$ = 8.0 Hz, 2H), 7.22 (d, $J_{\text{H,H}}$ = 8.2 Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 21.2, 22.0, 29.2, 55.3, 98.4, 107.4, 127.6 (t, $J_{\text{C},^2\text{H}}$ = 23.2 Hz), 128.7, 128.9, 134.8, 136.1, 144.7, 149.0, 160.0; **²H NMR** (61 MHz, acetone) δ 6.31 (s). **Compound 5af':**

¹H NMR (400 MHz, CDCl₃) δ 1.00 (d, $J_{\text{H,H}} = 6.6$ Hz, 6H), 2.17 (s, 3H), 3.28 (sept, $J_{\text{H,H}} = 6.9$ Hz, 1H), 3.74 (s, 6H), 6.33 (t, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.38 (d, $J_{\text{H,H}} = 2.3$ Hz, 1H), 7.06 (d, $J_{\text{H,H}} = 8.0$ Hz, 2H), 7.22 (d, $J_{\text{H,H}} = 8.2$ Hz, 2H). **HRMS** (ESI) calcd for C₂₀H₂₄DO₂ [M+H]⁺ 298.1917, found 298.1942.

Compound 6af. (Table 4.3, entry 6, binap (B), 93% yield, **5af:6af** = 10:90).

¹H NMR (400 MHz, CDCl₃) δ 1.09 (d, $J_{\text{H,H}} = 6.9$ Hz, 6H), 2.37 (s, 3H), 3.28 (sept, $J_{\text{H,H}} = 6.9$ Hz, 1H), 3.83 (s, 6H), 6.35 (s, 1H), 6.42 (d, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.45 (d, $J_{\text{H,H}} = 2.3$ Hz, 1H), 7.18 (d, $J_{\text{H,H}} = 8.1$ Hz, 2H), 7.22 (d, $J_{\text{H,H}} = 8.1$ Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 21.1, 22.0, 29.2, 55.3, 98.4, 107.1 (t, $J_{\text{C},^2\text{H}} = 24.6$ Hz), 107.4, 127.9, 128.7, 128.9, 134.9, 136.1, 144.6, 149.0, 159.9, 160.0; **²H NMR** (61 MHz, acetone) δ 6.43 (s). **HRMS** (ESI) calcd for C₂₀H₂₄DO₂ [M+H]⁺ 298.1917, found 298.1888.

The ratio of **5ag:6ag** was determined by ¹H NMR because of some impurities in ²H NMR.

Compound 5ag. (Table 4.3, entry 7, cod (A), 87% yield, **5ag:6ag** = 97:3).

¹H NMR (400 MHz, CDCl₃) δ 1.25 (t, $J_{\text{H,H}} = 7.1$ Hz, 6H), 1.44 (s, 3H), 2.01 (s, 3H), 2.77 (s, 2H), 3.79 (s, 6H), 4.19 (q, $J_{\text{H,H}} = 7.1$ Hz, 4H), 6.36 (t, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.48 (d, $J_{\text{H,H}} = 2.3$ Hz, 2H); **¹³C NMR** (100 MHz, CDCl₃) δ 14.1, 16.3, 19.9, 34.6,

53.9, 55.3, 61.3, 98.7, 104.4, 121.9 (t, $J_{C,H} = 23.1$ Hz), 138.3, 146.1, 160.5, 172.0; ^2H NMR (61 MHz, acetone) δ 5.67 (s). **HRMS** (ESI) calcd for $\text{C}_{20}\text{H}_{28}\text{DO}_6$ $[\text{M}+\text{H}]^+$ 366.2027, found 366.2026.

Compound 7ba. (Table 4.3, entry 8, 63% yield). ^1H NMR (400 MHz, CDCl_3): δ 0.87 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.00 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.33 (sext, $J_{\text{H,H}} = 7.7$ Hz, 2H), 1.66 (sext, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.45 (t, $J_{\text{H,H}} = 7.7$ Hz, 2H), 2.66 (t, $J_{\text{H,H}} = 7.4$ Hz, 2H), 7.07 (d, $J_{\text{H,H}} = 8.4$ Hz, 2H), 7.27 (t, $J_{\text{H,H}} = 8.4$ Hz, 1H), 7.34 (t, $J_{\text{H,H}} = 7.6$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.0, 13.7, 21.4, 23.0, 36.7, 42.9, 106.3, 126.8, 128.0, 128.2, 147.3, 147.6. **HRMS** (ESI) calcd for $\text{C}_{14}\text{H}_{20}\text{I}$ $[\text{M}+\text{H}]^+$ 315.0610, found 315.0609.

Compound 8ba. (Table 4.3, entry 9, 77% yield). ^1H NMR (400 MHz, CDCl_3) δ 0.98 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.07 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.39 (sext, $J_{\text{H,H}} = 7.8$ Hz, 2H), 1.57 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.25 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.46 (t, $J_{\text{H,H}} = 7.8$ Hz, 2H), 5.37 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 6.95 (td, $J_{\text{H,H}} = 7.7$ Hz, 1.7 Hz, 1H), 7.17 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.7 Hz, 1H), 7.31 (td, $J_{\text{H,H}} = 7.5$ Hz, 1.2 Hz, 1H), 7.89 (dd, $J_{\text{H,H}} = 7.9$ Hz, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 14.2, 21.2, 22.7, 30.0, 33.5, 99.4, 127.5, 127.8, 129.6, 131.3, 139.0, 143.3, 149.1. **HRMS** (ESI) calcd for $\text{C}_{14}\text{H}_{20}\text{I}$ $[\text{M}+\text{H}]^+$ 315.0610, found 315.0613.

Compound 8ha. (Table 4.3, entry 10, 87% yield). **¹H NMR** (400 MHz, CDCl₃) 0.90 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 1.00 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.30 (sext, $J_{\text{H,H}} = 7.8$ Hz, 2H), 1.50 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.18 (q, $J_{\text{H,H}} = 7.3$ Hz, 2H), 2.38 (t, $J_{\text{H,H}} = 7.8$ Hz, 2H), 5.32 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.20 (d, $J_{\text{H,H}} = 8.0$ Hz, 1H), 7.52 (dd, $J_{\text{H,H}} = 7.9$ Hz, 1.0 Hz, 1H), 8.07 (d, $J_{\text{H,H}} = 0.8$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 14.0, 14.2, 21.2, 22.6, 30.0, 33.3, 98.9, 123.0 (q, $J_{\text{C},^{19}\text{F}} = 270.8$ Hz), 124.4 (q, $J_{\text{C},^{19}\text{F}} = 3.6$ Hz), 129.7, 129.9 (q, $J_{\text{C},^{19}\text{F}} = 32.6$ Hz), 132.3, 135.9 (q, $J_{\text{C},^{19}\text{F}} = 3.8$ Hz), 142.5, 152.9. **HRMS** (ESI) calcd for C₁₅H₁₉F₃I [M+H]⁺ 383.0484, found 383.0484.

Compound 7ah. (Table 4.3, entry 11, 73% yield). The regiochemistry and *Z* geometry was determined by NOESY NMR study. **¹H NMR** (400 MHz, CDCl₃) 0.19 (s, 9H), 2.00 (s, 3H), 2.58 (s, 2H), 3.80 (s, 6H), 6.26 (d, $J_{\text{H,H}} = 2.3$ Hz, 2H), 6.37 (d, $J_{\text{H,H}} = 2.2$ Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ -0.6, 20.9, 34.5, 55.3, 97.2, 98.5, 106.2, 138.4, 151.0, 160.5. **HRMS** (ESI) calcd for C₁₅H₂₄IO₂Si [M+H]⁺ 391.0590, found 391.0578.

Compound 9. (Table 4.3, entry 12, 67% yield). **¹H NMR** (400 MHz, CDCl₃) δ 0.87 (t, $J_{\text{H,H}} = 7.3$ Hz, 3H), 0.94 (t, $J_{\text{H,H}} = 7.4$ Hz, 3H), 1.27 (sext d, $J_{\text{H,H}} = 7.8$ Hz, 2.2 Hz, 2H), 1.43 (sext, $J_{\text{H,H}} = 7.3$ Hz, 2H), 1.69 (qt, $J_{\text{H,H}} = 12.8$ Hz, 4.5 Hz, 1H), 1.82 (qd, $J_{\text{H,H}} = 12.3$ Hz, 3.2 Hz, 1H), 1.91 (br d, $J_{\text{H,H}} = 13.2$ Hz, 1H), 2.14 (q, $J_{\text{H,H}} = 7.4$ Hz, 2H), 2.10–2.20 (m, 1H), 2.22–2.31 (m, 2H), 2.38 (td, $J_{\text{H,H}} = 14.5$ Hz, 6.6 Hz, 1H), 2.4–2.5 (m, 1H), 2.45 (br d, $J_{\text{H,H}} = 14.1$ Hz, 1H), 2.53 (t, $J_{\text{H,H}} = 13.8$ Hz, 1H), 3.23 (tt, $J_{\text{H,H}} = 12.2$ Hz, 3.9 Hz, 1H), 5.21 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H), 7.05 (dd, $J_{\text{H,H}} = 7.5$ Hz, 1.0 Hz, 1H), 7.15 (td, $J_{\text{H,H}} = 7.3$ Hz, 1.6 Hz, 1H), 7.25 (td, $J_{\text{H,H}} = 7.8$ Hz, 1.2 Hz, 1H), 7.29 (dd, $J_{\text{H,H}} = 7.7$ Hz, 1.4 Hz, 1H); **¹³C NMR** (100 MHz, CDCl₃) δ 13.9, 14.2, 21.3, 23.0, 25.9, 30.1, 33.4, 34.9, 40.6, 41.2, 49.3, 125.6, 125.8, 126.8, 129.5, 130.4, 139.6, 141.7, 143.8, 211.1. **HRMS** (ESI) calcd for C₂₀H₂₉O [M+H]⁺ 285.2218, found 285.2221.

4.5 Reference

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4.6 NMR spectra

c

Conclusions

This thesis presents the development of new Rh-catalyzed reactions that proceed through 1,4-migration of rhodium. Chapter 1 is an introduction of rhodium-catalyzed C–C bond forming reactions and 1,4-migration of rhodium. In Chapter 2, a new type of rhodium-catalyzed conjugate arylation using aryloxymethyltrifluoroborates as nucleophiles was developed. The 1,4-Rh shift from alkyl to aryl is the key step to generate an arylrhodium intermediate. The asymmetric conjugate addition is efficiently catalyzed by a chiral diene–rhodium catalyst in H₂O with high enantioselectivity ($\geq 93\%$ ee). In Chapter 3, migratory arylstannylation was found to take place in the reaction of arylstannanes ArSnR₃ with unfunctionalized alkynes in the presence of a bisphosphine–rhodium catalyst and a catalytic amount of zinc chloride to produce *ortho*-alkenylarylstannanes in high yields. A catalytic cycle involving three transmetalation steps, that is, transmetalation of aryl groups from Sn to Rh, Rh to Zn, and Zn to Sn is proposed. In Chapter 4, the thesis discloses that the addition of arylzinc reagents ArZnCl to unfunctionalized alkynes is efficiently catalyzed by rhodium complexes in the presence of a catalytic amount of zinc chloride. The selectivity between the 2-arylalkenylzincs and the *ortho*-alkenylarylzinc products, the latter of which is generated through 1,4-Rh migration from alkenyl to aryl, is controlled by the use of appropriate ligands on rhodium.

List of Publications related to this Thesis

1. **Ming, J.**; Hayashi, T. *Org. Lett.* **2016**, *18*, 6452.