



**NANYANG  
TECHNOLOGICAL  
UNIVERSITY**

**COBALT-CATALYZED ARYLZINCATION OF ALKYNES  
AND ALKENES INVOLVING 1,4-COBALT MIGRATION**

**TAN BOON HONG**

**SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES**

**2014**

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A thesis submitted to the Nanyang Technological University

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**2014**

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Boon Hong Tan

*Nanyang Technological University, 2014*

*“Nobody ever figures out what life is all about, and it doesn't matter. Explore the world.*

*Nearly everything is really interesting if you go into it deeply enough.”*

Richard P. Feynman

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## List of Abbreviations

|                    |                                      |
|--------------------|--------------------------------------|
| $\delta$           | chemical shift (ppm)                 |
| $^{\circ}\text{C}$ | degree centigrade                    |
| Ac                 | acetyl                               |
| Ar                 | aryl (substituted aromatic ring)     |
| app.               | apparent                             |
| aq                 | aqueous                              |
| br                 | broad                                |
| Bn                 | benzyl                               |
| Boc                | <i>Tert</i> -butyloxycarbonyl        |
| <i>n</i> Bu        | butyl                                |
| <i>t</i> Bu        | <i>tert</i> -butyl                   |
| cod                | 1,5-cyclooctadiene                   |
| coe                | cyclooctene                          |
| Cp*                | 1,2,3,4,5-pentamethylcyclopentadiene |
| Cy                 | cyclohexyl                           |
| d                  | doublet                              |
| dd                 | doublet of doublet                   |
| dt                 | doublet of triplet                   |
| dppb               | 1,4-Bis(diphenylphosphino)butane     |
| dppbz              | 1,2-Bis(diphenylphosphino)benzene    |
| dppe               | 1,2-Bis(diphenylphosphino)ethane     |
| dppf               | 1,1'-Bis(diphenylphosphino)ferrocene |
| dppp               | 1,3-Bis(diphenylphosphino)propane    |
| DMI                | 1,3-dimethyl-2-imidazolidinone       |

|                |                                   |
|----------------|-----------------------------------|
| ESI            | electrospray ionization           |
| eq /equiv.     | equivalent                        |
| EtOAc          | ethyl acetate                     |
| Et             | ethyl                             |
| EtCN           | propionitrile                     |
| g              | gram                              |
| h              | hour                              |
| H              | hydrogen                          |
| HOAc           | acetic acid                       |
| HRMS           | high resolution mass spectrometry |
| Hz             | hertz                             |
| <i>J</i>       | coupling constants                |
| LDA            | lithium diisopropylamide          |
| m              | multiple                          |
| m/z            | mass per charge ratio             |
| M              | concentration (mol/L)             |
| M <sup>+</sup> | parent ion peak (mass spectrum)   |
| Me             | methyl                            |
| mg             | milligram                         |
| MHz            | mega hertz                        |
| min            | minute                            |
| mL             | milliliter                        |
| mmol           | millimole                         |
| m.p.           | melting point                     |
| NMP            | <i>N</i> -Methylpyrrolidone       |
| NMR            | nuclear magnetic resonance        |

|                   |                                 |
|-------------------|---------------------------------|
| Ph                | phenyl                          |
| PMP/ <i>p</i> -An | <i>p</i> -methoxyphenyl         |
| ppm               | parts per million               |
| <i>i</i> Pr       | <i>iso</i> -propyl              |
| Py                | pyridine                        |
| q                 | quartet                         |
| s                 | singlet                         |
| sat               | saturated                       |
| rt/r.t.           | room temperature                |
| t                 | triplet                         |
| td                | triplet of doublet              |
| TBS               | <i>tert</i> -butyldimethylsilyl |
| TEA               | triethylamine                   |
| Temps             | temperature                     |
| Tf                | trifluoromethyl                 |
| THF/thf           | tetrahydrofuran                 |
| TLC               | thin layer chromatography       |
| TMS               | trimethylsilyl                  |
| <i>p</i> -Tol     | <i>p</i> -toluene               |
| Ts                | <i>p</i> -toluenesulfonyl       |
| <i>p</i> -TSA     | <i>p</i> -toluenesulfonic acid  |
| vol               | volume                          |

## Abstract

Development in the fields of organometallic chemistry and homogenous catalysis enables synthetic chemists to utilize seemingly unreactive C–H bonds as entry point for synthetic transformations to access more complex organic molecules. During the past decades, we have witnessed significant progress in the area of catalytic transition metal-catalyzed C–H functionalization. However, a careful perusal of the recent advancement in this area, we noticed that the focus is mainly placed on the development of chelation-assisted C–H bond functionalization. Recent progress in a new class of C–H bond activation via through-space metal migrations offers new opportunities in cascade bond forming reactions.

This thesis describes the development of cobalt-based catalyst for C–H bond functionalization reactions via 1,4-migration. Chapter 2 details the development of cobalt–Xantphos complex catalyzed addition of an arylzinc reagent to an alkyne to afford *ortho*-alkenylarylzinc species via vinyl-to-aryl 1,4-cobalt migration. Further synthetic manipulations of *ortho*-alkenylarylzinc species allow the access to various benzo-fused carbocycles.

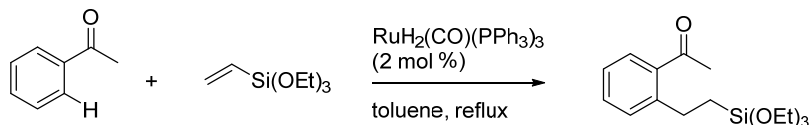
Chapter 3 describes a cobalt–diphosphine-catalyzed addition reaction of arylzinc to norbornene derivatives to afford *o*-(2-*exo*-norbornyl)arylzinc species, which involves an alkyl-to-aryl 1,4-cobalt migration. The key feature of this reaction is the suppression of “merry-go-round” adducts and therefore allowing further trapping of *ortho*-(2-*exo*-norbornyl)arylzinc species with common organic electrophiles under copper or palladium catalysis.

## Chapter 1. Introduction

The pursuit of atom economical reactions for efficient and selective synthesis of bulk and fine chemicals remains a fundamentally important challenge to synthetic organic chemists. In recent years, it has become clear that direct C–H functionalization presents an enormous impact on chemical synthesis and can potentially shorten synthetic routes of natural products by unprecedented retrosynthetic disconnection in both early and late stages. This has led to extensive investigation to understand how to cleave and functionalize inert C–H bonds with predictable regioselectivity using transition metals.<sup>1</sup>

The use of heteroatom-containing directing groups is one of the most direct and well-practiced approaches to resolve regioselectivity and reactivity issues in C–H bond functionalization. One of the earliest and most important examples of this class of C–H functionalization was reported by Murai and co-workers in 1993, on ruthenium-catalyzed *ortho*-alkylation reaction of aromatic ketones with olefins (Scheme 1.1).<sup>2</sup> This groundbreaking finding has driven the development of several other catalytic systems for chelation-assisted C–H bond functionalization reactions including alkylation,<sup>3 & 4</sup> alkenylation,<sup>5</sup> arylation<sup>6</sup> and many other carbon–carbon and carbon–heteroatom bond formations.<sup>7</sup>

### Scheme 1.1. Ruthenium-Catalyzed Hydroarylation to Olefins

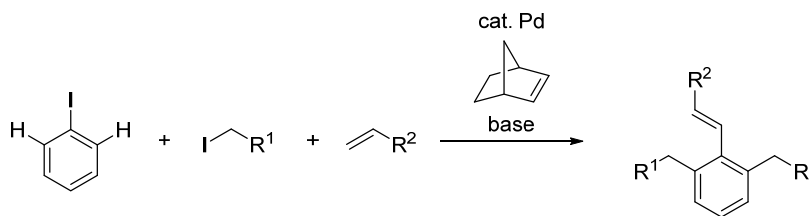


While the chelation-assistance approach offers a complete control over the regioselectivity of C–H activation, the need for a heteroatom-containing directing group sometimes limits their synthetic utility. Therefore, it presents an opportunity for synthetic chemists to develop a new class of regioselective remote through-space C–H functionalization without the need of a directing group.

## 1.1 Norbornene-Mediated *ortho* C–H Functionalization and Subsequent Developments to Palladium Migration.

The origin of through-space C–H activation dates back to 1985, Catellani and coworkers reported a palladium-catalyzed reaction of bromobenzene with norbornene to afford 1,2,3,4,4a,12b-hexahydro-1,4-methanotriphenylene.<sup>8</sup> This seminal study set the stage for the development of the well-known Catellani reaction (Scheme 1.2),<sup>9</sup> an elegant palladium-catalyzed domino reaction mediated by norbornene.

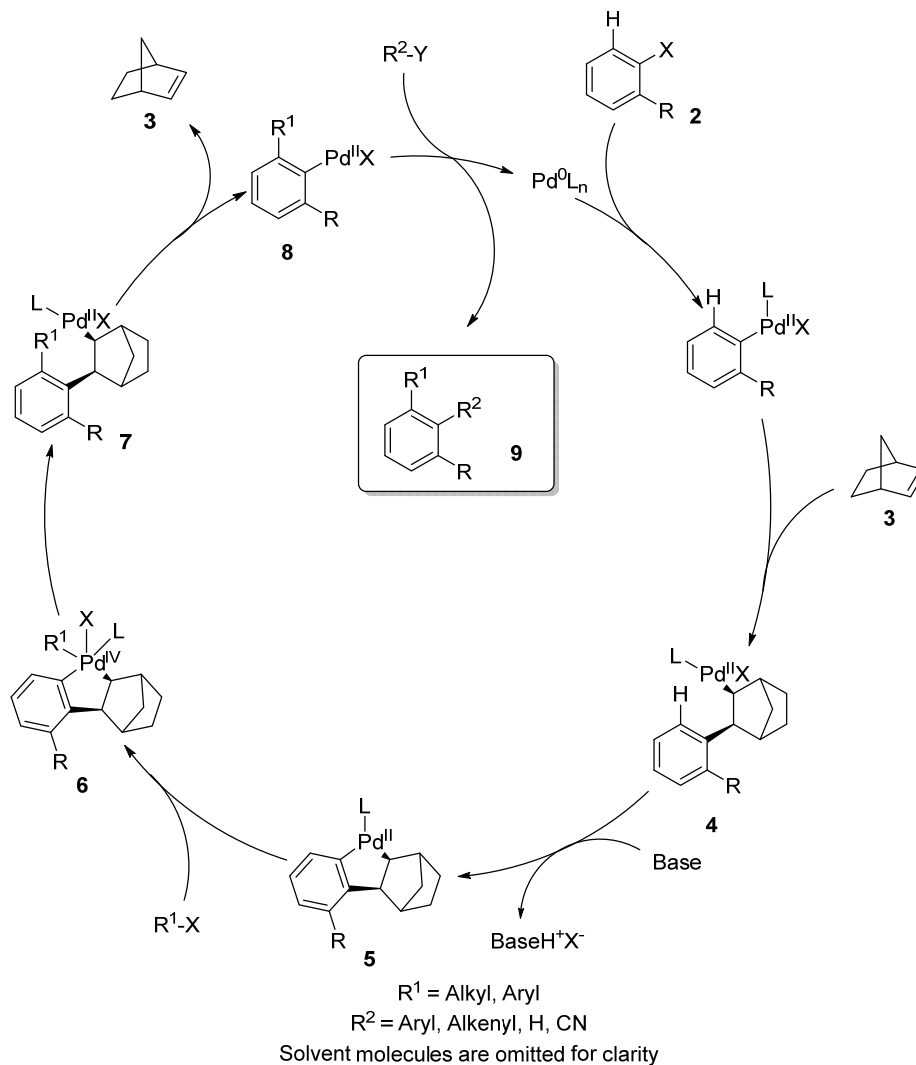
**Scheme 1.2.** Initial Report of the Catellani Reaction



Mechanistic details of the Catellani reaction pivots on the nature of norbornene to trigger a competitive reaction pathway and form a rigid catalyst scaffold which positions palladium atom in the proximity to a C–H bond. The proposed catalytic cycle for the Catellani reaction involves multiple oxidation state transitions of palladium between (0), (II), and potential (IV) (Scheme 1.3). Initial oxidative addition of mono-*ortho*-substituted aryl iodide **2** to Pd(0) is followed by insertion to norbornene **3** to give *syn*-norbornylpalladium(II) intermediate **4**. Electrophilic palladation of the *ortho* position of the aromatic ring and concomitant deprotonation lead to the formation of a palladacycle **5**. This palladium(II) intermediate **5** can then undergo oxidative addition with alkyl or aryl halides to give a palladium(IV) complex **6**. Formation of a new C–C bond at the *ortho* position through reductive elimination generates another norbornylpalladium(II) intermediate **7**. With no *ortho* position available for further functionalization, displacement of norbornene via  $\beta$ -carbon elimination is favored due to increased steric strain of **7** to form an

arylpalladium species **8**, which can further participate in a traditional palladium-catalyzed coupling reaction to yield the desired product **9** and regenerate Pd(0) catalyst.

**Scheme 1.3.** Mechanism of the Catellani Reaction

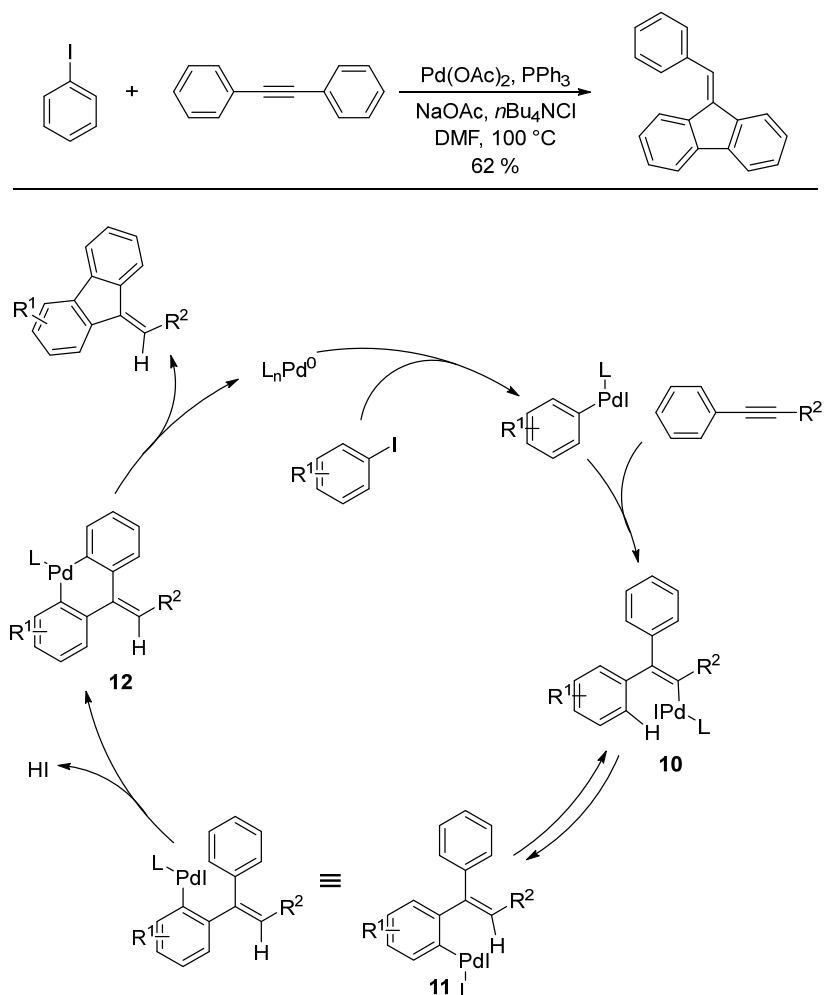


Catellani reaction shows that the rigid norbornene backbone allows the activation of the proximal C–H bond through-space. However, use of superstoichiometric quantity of norbornene is often required; the natural extension of such through-space C–H activation chemistry is to eliminate the use of norbornene. This can be achieved by careful design of an appropriate organopalladium intermediate accessible from common starting material (e.g., organic halides, alkynes, and alkenes) for palladium catalysis, where the palladium atom is located in the proximity of a specific C–H bond. The through-space interaction of

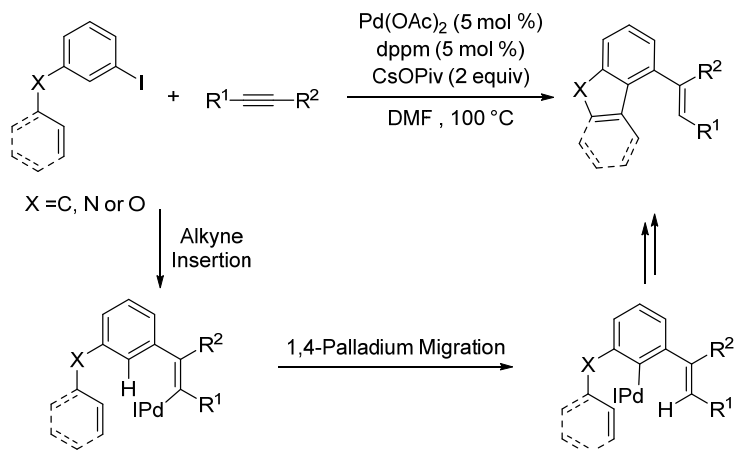
the palladium center with the nearby C–H bond would result in cleavage of the C–H bond, and then lead to complete relocation of the palladium atom from the original position to the remote carbon atom. This net process is called as “palladium migration”.

One-step 1,4-palladium migration is the most commonly seen among the other palladium migrations. This is probably due to the formation of relatively strain-free five-membered palladacycle. The earliest and most important example of 1,4-palladium migration was reported by Larock and co-workers in 2000, for a palladium-catalyzed synthesis of 9-alkylidene-9*H*-fluorenes (Scheme 1.4).<sup>10</sup> The mechanism involves oxidative addition of an aryl iodide to Pd(0) followed by migratory insertion of alkyne to afford an alkenylpalladium intermediate **10**. Due to the close proximity of the Pd atom and the neighbouring aromatic C–H bond in the intermediate **10**, the Pd center undergoes 1,4-migration to the *ortho* position of the aryl ring to form an *ortho*-alkenylaryl palladium intermediate **11**. Rotation of the aryl-alkenyl single bond of the intermediate **11** brings the palladium center to the proximity of another aryl ring, which results in the second C–H palladation to afford a palladacycle intermediate **12**. Subsequent reductive elimination affords the corresponding fluorene product and regenerates of the Pd(0) catalyst. A further survey led to the first well-studied example of palladium migration in terms of substrate scope, reaction conditions and mechanism.<sup>11</sup> It also illustrated the huge synthetic potential of this migration chemistry in cascade bond forming reactions. Following this groundbreaking work, this unique palladium migration chemistry has been employed in the synthesis of various heterocycles, such as carbazoles, indoles, xanthenes and fluoren-9-ones (Scheme 1.5).<sup>12</sup>

## Scheme 1.4. Palladium-Catalyzed Fluorene Synthesis and Proposed Catalytic Cycle

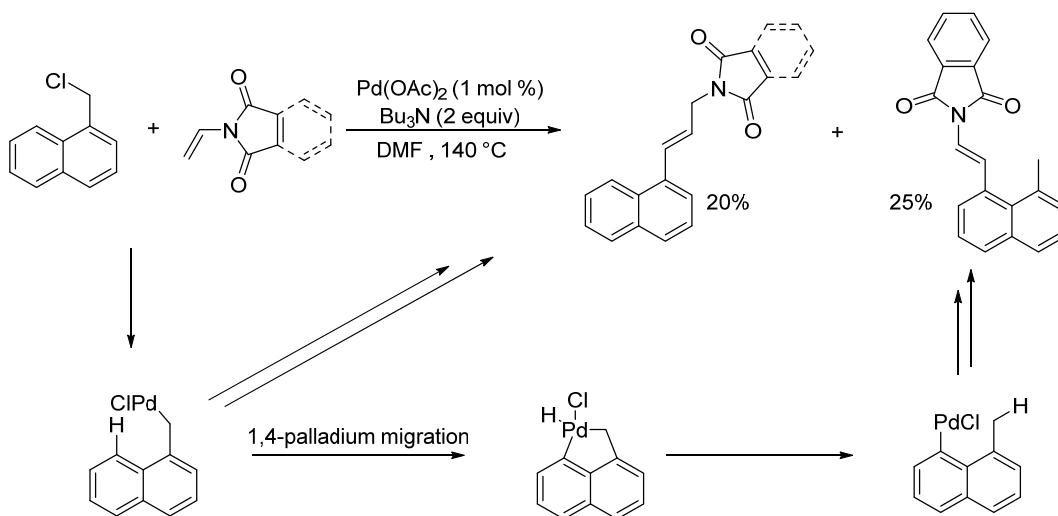


## Scheme 1.5. Palladium-Catalyzed Synthesis of Vinylic Carbazoles, Indoles and Dibenzofurans Involving 1,4-Palladium Migration



This unique palladium migration is not limited to vinyl-to-aryl migration. Alkyl-to-aryl palladium migration can also occur in two different ways. Palladium migration from a 1-naphthylmethyl position to the neighboring 8-naphthyl position was discovered as a side reaction in the Heck reaction of 1-(chloromethyl)naphthalene with an *N*-vinyl imide (Scheme 1.6).<sup>13</sup> The reaction gave a mixture of normal Heck product and another Heck product arising from palladium migration. The scope of this 1,4-migration–Heck process was rather limited, as other olefins, including vinyl esters, did not afford any of such products.

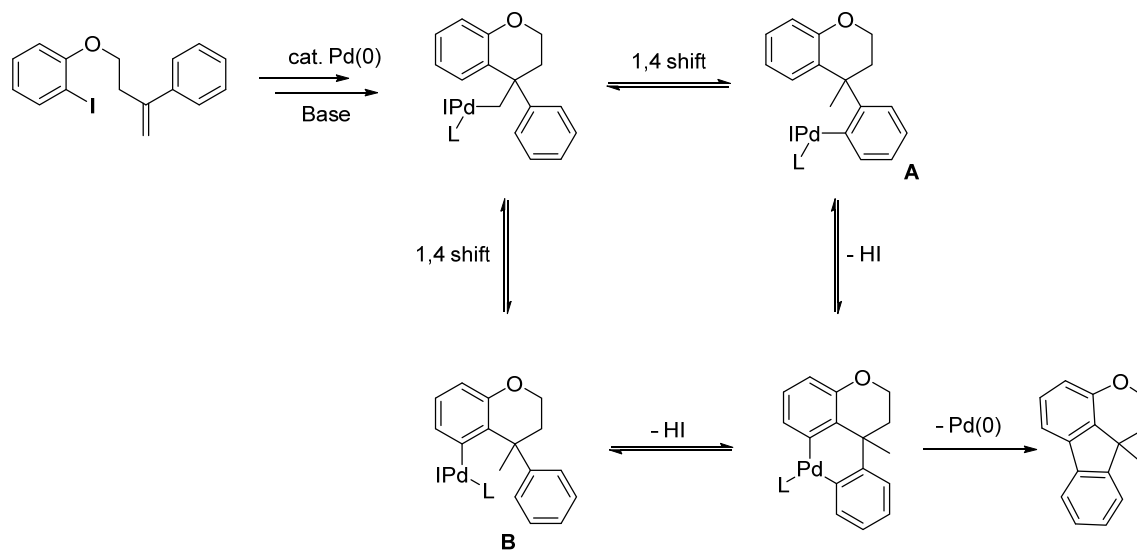
**Scheme 1.6.** Palladium-Catalyzed Reaction of  $\alpha$ -Chloromethylnaphthalene with Olefins Involving 1,4-Palladium Migration



In 2004, Larock and coworkers reported another example of an alkyl-to-aryl 1,4-palladium migration, which takes place between homobenzylic and aromatic carbon atoms (Scheme 1.7).<sup>14</sup> In the presence of a Pd(0) catalyst and a base, an aryl iodide with an ether side chain containing an  $\alpha$ -substituted styrenyl moiety undergoes a cascade reaction to afford a tetracyclic product. The reaction is likely initiated by the oxidative addition of the aryl iodide to Pd(0) followed by Heck cyclization to give a homobenzylpalladium species. This species has two aromatic C–H bond in the proximity of the Pd center, and thus is capable of undergoing 1,4-palladium migration to either of the aromatic positions to afford

an arylpalladium intermediate **A** or **B**. Both of these putative intermediates can undergo the second aromatic C–H palladation to give a common diarylpalladium intermediate, reductive elimination of which eventually affords the tetracyclic product.

**Scheme 1.7.** Palladium-Catalyzed Alkyl-to-Aryl 1,4-Palladium Migration and Cyclization



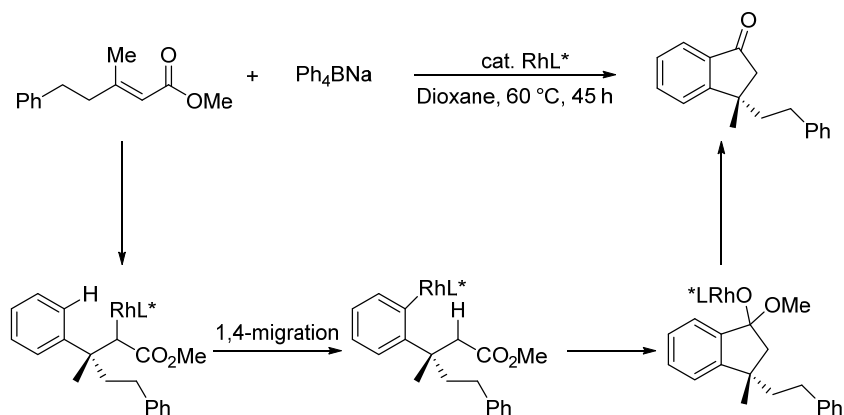
### 1,4-Rhodium Migration.

Given the diverse reactivities of *d*-block elements, it is not surprising that other transition metals are also known to undergo remote metal migrations. In addition to palladium migration, rhodium migration has also been studied extensively. To the best of our knowledge, the first example of alkyl-to-aryl 1,4-rhodium migration was reported in 2000 by Miura and coworkers. They found that rhodium-catalyzed reaction of phenylboronic acid with norbornene affords multiply norbornylated benzene derivatives in a “merry-go-round” fashion (Scheme 1.8).<sup>15</sup> A proposed mechanism for this reaction involves generation of an arylrhodium species via initial transmetalation, followed by the insertion to norbornene into the Rh–aryl bond in an *exo*-fashion to afford a norbornylrhodium intermediate **13**. The structure of the intermediate **13** greatly resembles the palladium in Catellani reaction (Scheme 1.3, intermediate **4**). The intermediate **13**



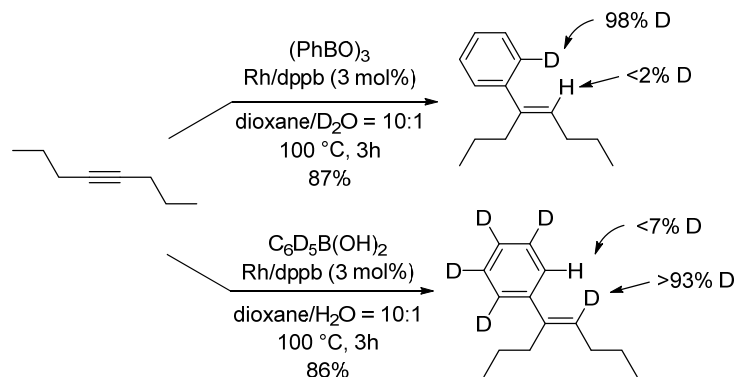
materials, alkyl-to-aryl 1,4-rhodium migration can be utilized in the synthesis of 3,4-dihydrocoumarins,<sup>17</sup> indanols<sup>18</sup> and spirocarbocycles<sup>19</sup>

**Scheme 1.9.** Rhodium-Catalyzed 1,4-Addition Involving 1,4-Rhodium Migration

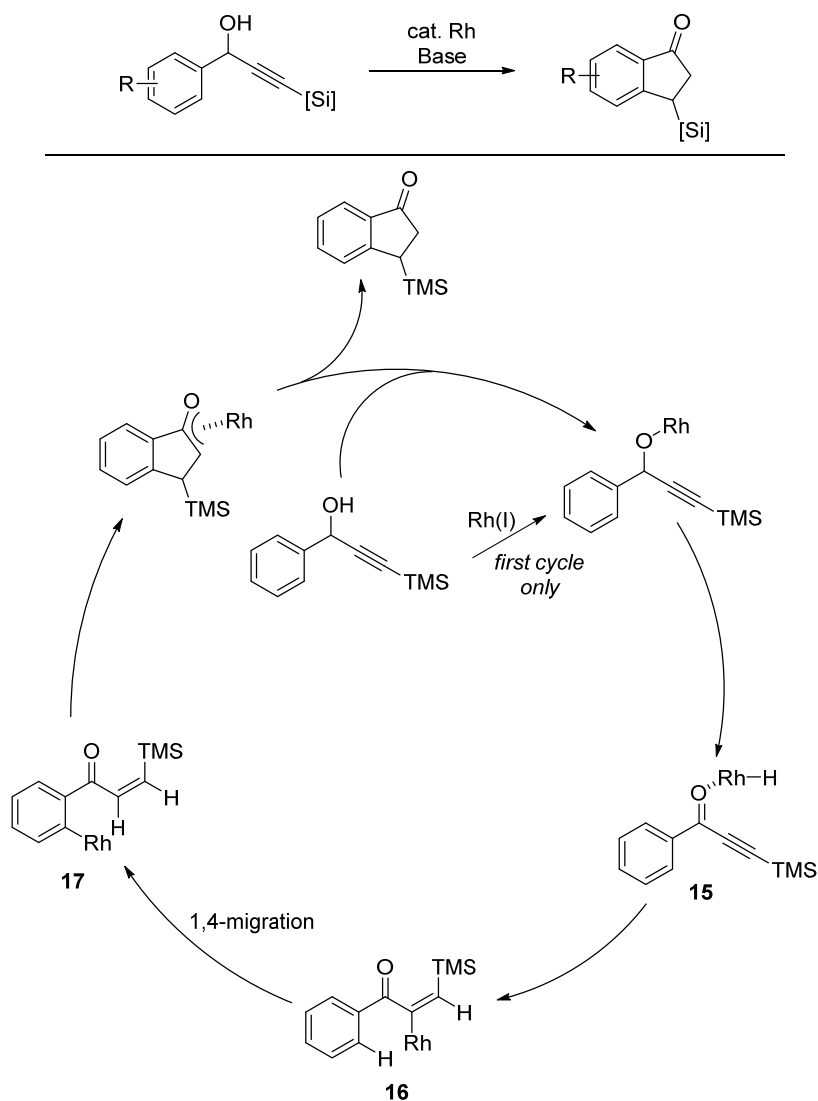


Vinyl-to-aryl 1,4-rhodium migration has also been observed. Hayashi and co-workers reported the first example of such migration in the hydroarylation of alkynes under protic conditions (Scheme 1.10).<sup>20</sup> The reaction conducted in a mixture of dioxane and D<sub>2</sub>O showed that protonolysis did not occur on the vinylic carbon, but rather on the *ortho*-position of the phenyl group. When pentadeuterated phenylboronic acid was used, near complete (93%) deuterium incorporation into vinylic carbon was observed. This set of experiments clearly supports the key 1,4-rhodium migration process, and also points to a mechanistic difference between palladium and rhodium migrations. While a rhodium migration involves unambiguous positional exchange between the rhodium and the remote hydrogen atoms, in a palladium migration, the original C–Pd bond is protonated not necessarily by the remote hydrogen atom.

**Scheme 1.10.** Rhodium-Catalyzed Hydroarylation of Alkynes Involving 1,4-Rhodium Migration



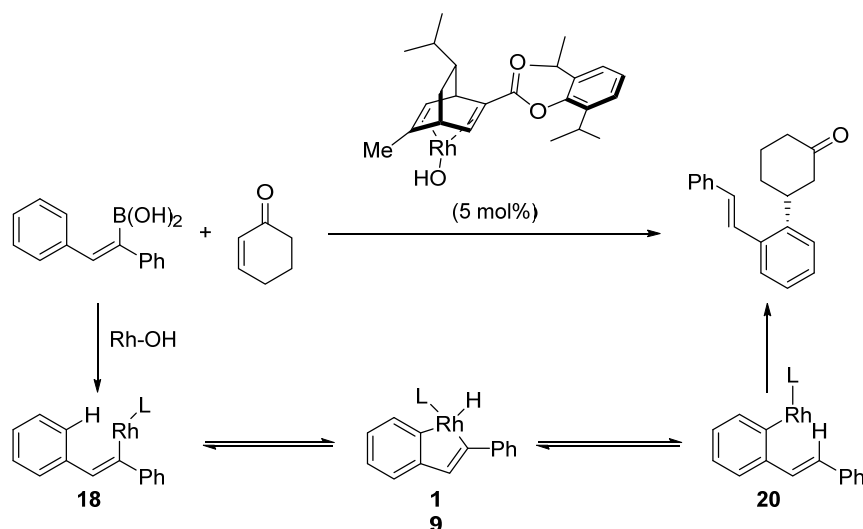
Another example of vinyl-to-aryl 1,4-rhodium migration was discovered independently by Hayashi and Iwasawa groups.<sup>21,22</sup> They found that an aryl propargyl alcohol undergoes isomerization under rhodium-catalyzed conditions, to furnish an indanone derivative. A proposed catalytic cycle for this transformation is shown in Scheme 1.11. Thus, an alkoxyrhodium species formed from the rhodium(I) catalyst and the alcohol, undergoes  $\beta$ -hydride elimination to afford a ketone-ligated rhodium hydride species **15**. Subsequent hydrorhodation of the C–C triple bond affords an alkenylrhodium intermediate **16**. A crossover experiment confirmed that this insertion is strictly an intramolecular process and no dissociation of rhodium hydride occurs from the intermediate **15**. The intermediate **16** then undergoes 1,4-rhodium migration to afford an arylrhodium intermediate **17**, followed by intramolecular 1,4-addition and subsequent protonolysis, thus furnishing the indanone product.

**Scheme 1.11.** Rhodium-Catalyzed Isomerization of Aryl Propargyl Alcohol to Indanone

1,4-Rhodium migration is generally proposed to proceed through a C–H oxidative addition/C–H reductive elimination sequence. This proposal was recently supported by experimental and theoretical studies of Hayashi and coworkers on a tandem 1,4-migration/1,4-addition reaction of a  $\beta$ -arylalkenylboronic acid to an enone (Scheme 1.12).<sup>23</sup> This reaction likely involves the following steps prior to 1,4-addition: (1) transmetalation of the alkenylboronic acid with the rhodium(I) catalyst to give an alkenylrhodium species **18**, (2) intramolecular oxidative addition of the *ortho* C–H bond to the rhodium center to afford a rhoda(III)cycle intermediate **19**, and (3) reductive elimination to give an

arylrhodium species **20** with concomitant formation of a new C–H bond at the vinylic position. This key process was corroborated by density functional theory (DFT) calculations.

**Scheme 1.12.** Rhodium-Catalyzed Tandem 1,4-Migration/1,4-Addition

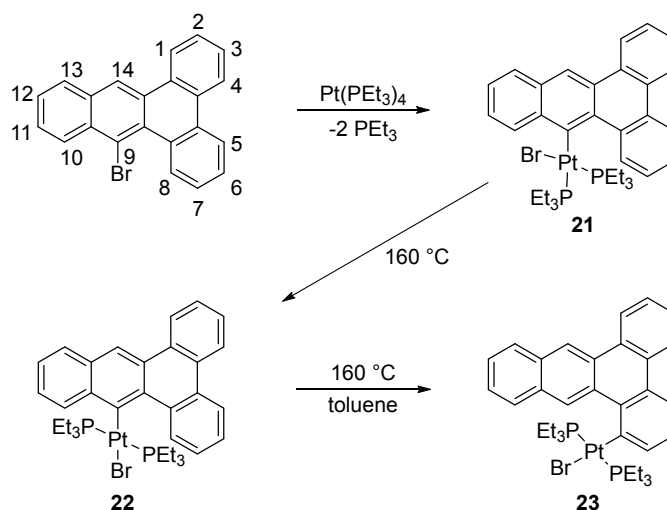


### 1.3 Nickel and Platinum 1,4-Migration.

The examples discussed above and many others have amply demonstrated the versatility of palladium and rhodium 1,4-migrations in tandem reactions to gain access to various fine chemicals. Other metals such as nickel and platinum have also been known to undergo similar 1,4-migration under very specific conditions. An example of aryl-to-aryl 1,4-platinum migration was found by Sharp and coworker in an stoichiometric reaction of 9-bromodibenz[*a,c*]anthracene with a platinum(0) complex (Scheme 1.13).<sup>24</sup> The reaction initially affords a *cis*-arylpalladium(II) complex **21** through oxidative addition of 9-bromodibenz[*a,c*]anthracene to Pt(0) as indicated by <sup>31</sup>P NMR analysis. When heated to 160 °C, the complex **21** will undergo thermal isomerization to the *trans* isomer **22**. This

isomerization process changes the complex conformation and forces the Pt center closer to the H8. This leads to an increase in agostic interaction between the platinum center and the 8-position, and eventually to 1,4-platinum migration to afford another arylplatinum complex **23**. It appears that complex **23** is thermodynamically more stable than complex **21** and **22** because of reduced steric repulsion between the aryl and other ligands on platinum.

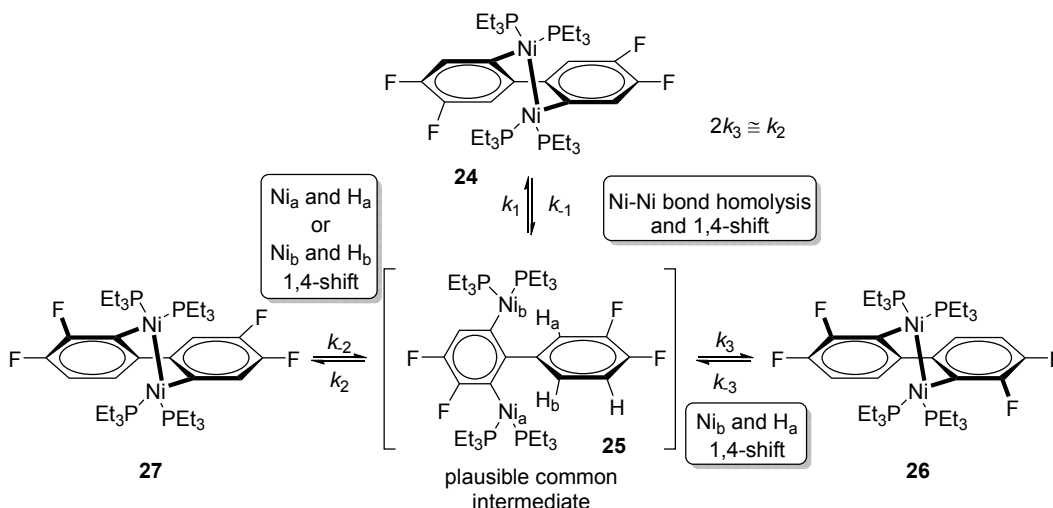
**Scheme 1.13.** 1,4-Platinum Migration at the Edge of Dibenz[*a,c*]anthracene



In a mechanistic study of C–H bond activation by monovalent nickel conducted by Johnson and coworkers, it was found that nickel can undergo 1,4-shift in a dinuclear Ni(I) biarylyl complex.<sup>25</sup> When allowed to stand at room temperature over 48 h, a bimetallic Ni(I) complex **24** isomerized to isomeric Ni(I) complexes **26** and **27** in 1:2 ratio (Scheme 1.14). This implies that a common intermediate exists that forms **27** twice as rapidly as it forms **26**. The isomerization process from complex **24** to **26** and **27**, requires the migration of the hydrogen substituents in the *ortho* (6 and 6') position of the biarylyl ligand. As a possible mechanism, the Ni–Ni bond of complex **24** may undergo reversible and homolytic cleavage to give a dinickel intermediate **25**. The agostic interaction of the Ni centers and *ortho* hydrogens allows C–H activation of the intermediate **25** to give thermodynamically more stable complexes **26** or **27**. This overall process of isomerization may be regarded as 1,4-

nickel migration. To the best of our knowledge, this report remains the only example of 1,4-nickel migration to date.

**Scheme 1.14.** 1,4-Nickel Migration in Isomerization of Ni(I) Biarylyl Complex



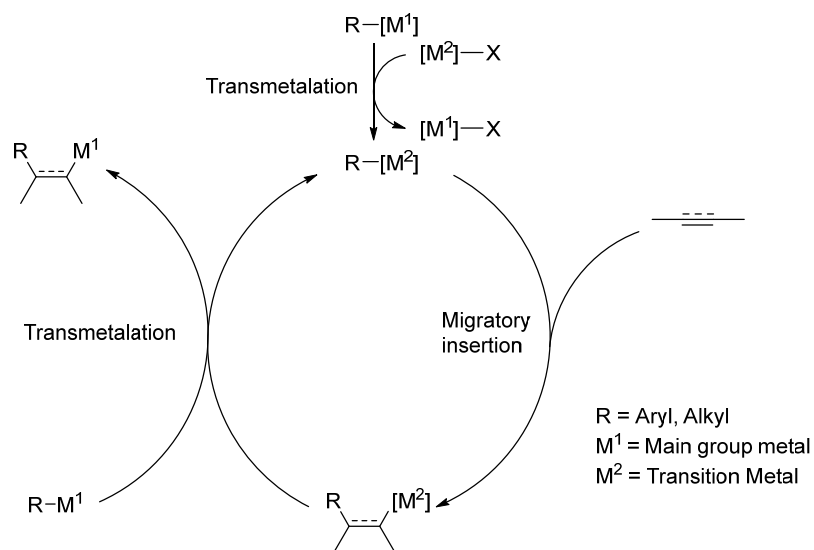
## 1.4 Recent Advances in Intermolecular Carbometalation Reactions.

Carbometalation is an important initiation step for some of 1,4 migrations discussed above. Examples like rhodium-catalyzed addition of a boronic acid to an alkyne or norbornene, followed by 1,4-rhodium migration, involve migratory insertion of an arylrhodium species into unsaturated C–C bond as key initial step. Therefore, pronounced reactivity of arylmetal species towards alkyne insertion and facile transmetalation between organometal species and classical organometallic (Mg, Li, Zn) reagents may serve as hints towards the development of new class of 1,4 migration reactions. In this section, we will discuss a few selected carbometalation reactions.

Classical organometallic reagents such as organomagnesium and organozinc reagents play an indispensable role in modern organic chemistry due to their versatile

reactivity and availability. In general, addition of organomagnesium and organozinc reagents to C–C multiple bonds are difficult but with the use of transition metals as catalyst, this process can be easily achieved. The general accepted mechanism of such carbometalation (Scheme 1.15) involves the following steps: 1) transmetalation of classical organometallic reagent, R–M<sup>1</sup> (M<sup>1</sup>: Main group metal) with transition metal catalyst (M<sup>2</sup>–X). 2) Migratory insertion of C–C multiple bond to R–M<sup>2</sup> species. 3) Transmetalation with R–M<sup>1</sup> as catalyst turnover step to afford corresponding alkenyl- or alkyl–M<sup>1</sup> species.

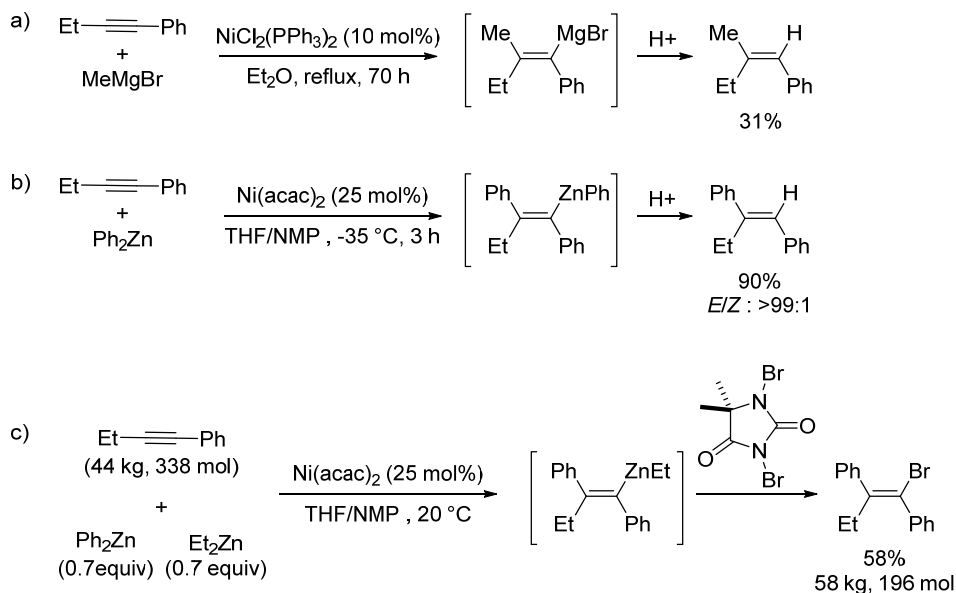
**Scheme 1.15.** General Mechanism for Carbometalation



In 1978, Duboudin and coworkers reported a nickel-catalyzed carbomagnesiation of unreactive alkynes, such as dialkylacetylenes and phenylacetylenes (Scheme 1.16, a).<sup>26</sup> Despite limited scope and low yields of this reaction, this reaction overcomes the longstanding challenge of carbometalation of simple alkynes. Following this work, Knochel reported a nickel-catalyzed carbozincation of arylacetylenes (Scheme 1.16, b).<sup>27</sup> The reaction proceeded smoothly at -35 °C with good to excellent regioselectivity, almost complete *syn* stereoselectivity and high yield. A modified Knochel's carbozincation procedure was deployed by chemists at the Bristol-Myers Squibb Company for the large

scale synthesis of (*Z*)-1-bromo-2-ethylstilbene (Scheme 1.16, c),<sup>28</sup> a key intermediate of a selective estrogen-receptor modulator.

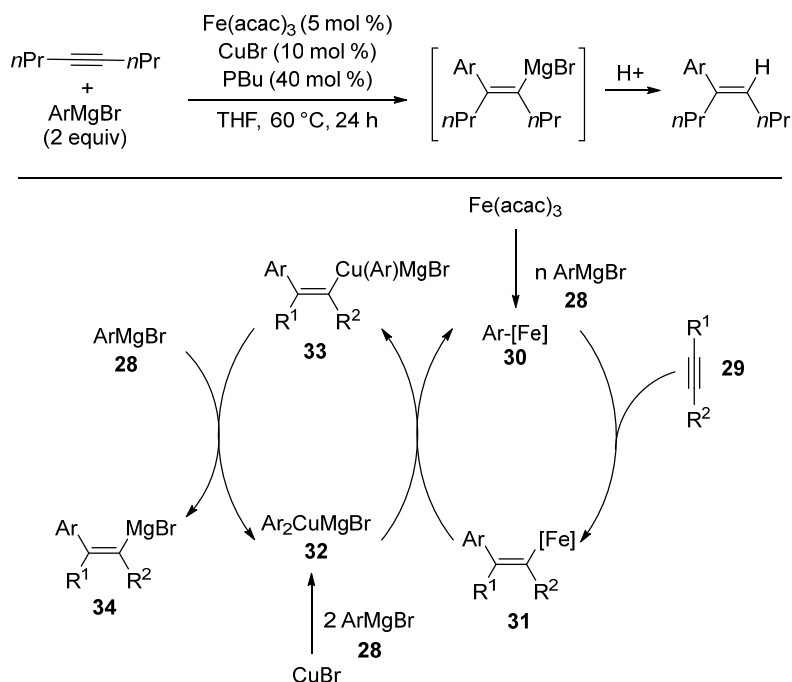
**Scheme 1.16.** Nickel-Catalyzed Carbometalation and Large Scale Synthesis of (*Z*)-1-bromo-2-ethylstilbene



Despite initial success by Duboudin, efficient catalytic carbomagnesiation of dialkylacetylenes remains a challenge to overcome. Very recently, Hayashi and coworkers reported arylmagnesiation of unactivated alkynes catalyzed cooperatively by iron and copper complexes (Scheme 1.17).<sup>29</sup> This also presents a rare example of efficient cooperative catalysis and most striking feature is that metals (Fe, Cu and Mg) present in the reaction are all inexpensive and easily available. The proposed mechanism involves the formation of aryliron species **30**<sup>30</sup> generated from Fe(acac)<sub>3</sub> and an excess amount of aryl Grignard reagent **28**. Migratory insertion of an alkyne **29** to aryliron species **30** affords arylalkenyliron species **31**. The likely role of copper catalyst is to assist the metal exchange between aryliron and aryl Grignard reagent. Thus, transmetalation of arylalkenyliron species **31** and diarylcuprate **32** (derived from CuBr and aryl Grignard reagent **28**)<sup>31</sup> affords arylalkenylcuprate species **33** and regeneration of aryliron species **30**. Transmetalation

between alkenylarylcuprate species **33** with aryl Grignard **28**<sup>32</sup> releases arylalkenylmagnesium bromide **34** to complete the catalytic cycle.

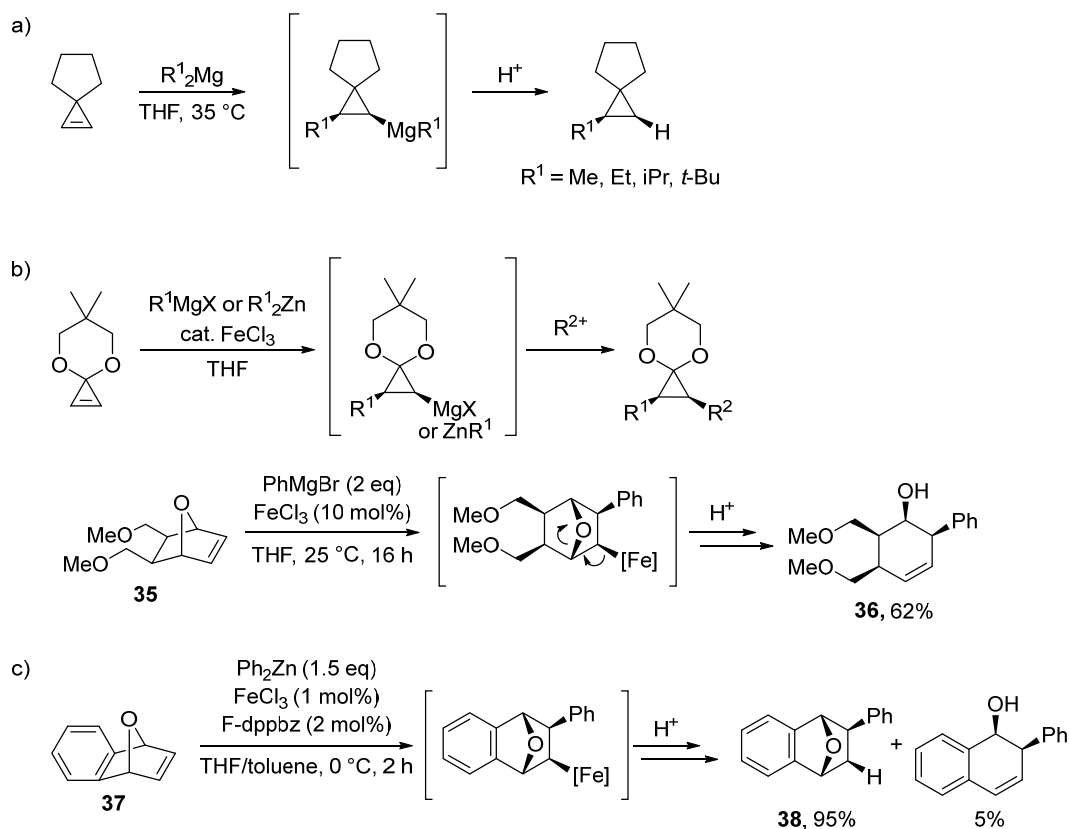
**Scheme 1.17.** Iron/Copper-Catalyzed Arylmagnesiation of Alkynes and Proposed Catalytic Cycle



One strategy to achieve intermolecular carbometalation reactions is employing the use of highly reactive alkynes and alkenes. For example, carbometalation of highly strained cyclopropenes, can occur without the aid of any metal catalyst despite the long reaction time required (Scheme 1.18, a).<sup>33</sup> Nakamura and co-workers reported that the addition of simple iron salt enhances carbometalation of cyclopropenone acetal with organomagnesium and -zinc reagents (Scheme 1.18, b).<sup>34</sup> When employing the use of oxabicyclic alkene **35**, the reaction gave proceed via  $\beta$ -oxygen elimination pathway to give ring-opening product **36** in 62% yield. Masahura and co-workers later reported that the use of 1,2-bis(diphenylphos- phino)benzene) ligands can efficiently suppressed the  $\beta$ -oxygen

elimination pathway to afford the corresponding carbozincation product **38** in high yield (Scheme 1.18, c).<sup>35</sup>

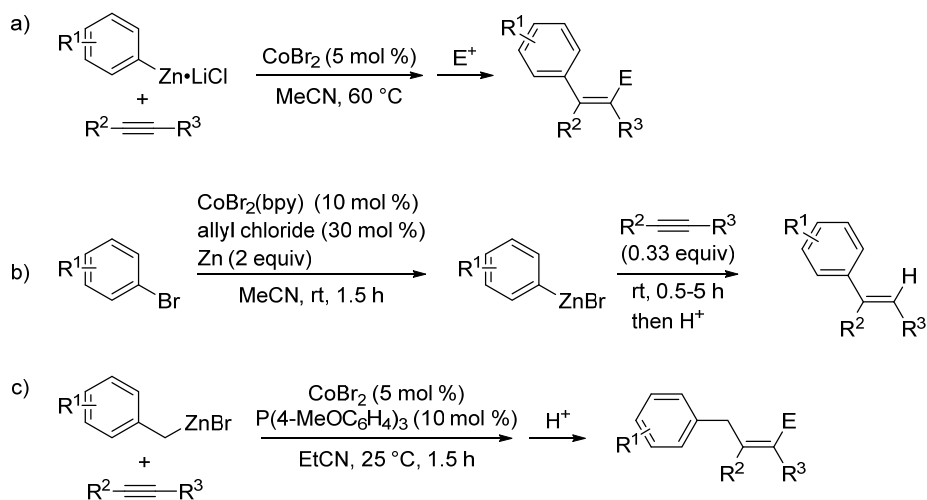
**Scheme 1.18.** Iron-Catalyzed Carbometalation of Strained Alkenes



Recently, cobalt also emerges as efficient catalysts for carbometalation of unactivated alkynes. Oshima and coworkers reported ligand free cobalt-catalyzed arylzincation of unactivated alkynes with high *E/Z* selectivity. Interestingly, the reaction only proceeds in acetonitrile and not in THF, hence arylzinc reagents prepared from direct zinc insertion to aryl iodides<sup>36</sup> cannot be used directly (Scheme 1.19, a). This limitation was later overcome by Gosmini's group,<sup>37</sup> who reported that a simple  $\text{CoBr}_2(\text{bpy})$  complex can catalyze the formation of arylzinc reagent as well as the subsequent arylzincation to simple alkyne (Scheme 1.19, b). Cobalt catalyst is also found to be effective for

benzylzincation of alkynes to provide allylbenzene derivatives in high yields (Scheme 1.19, c).<sup>38</sup>

**Scheme 1.19.** Cobalt-Catalyzed Carbometalation of Unactivated Alkynes



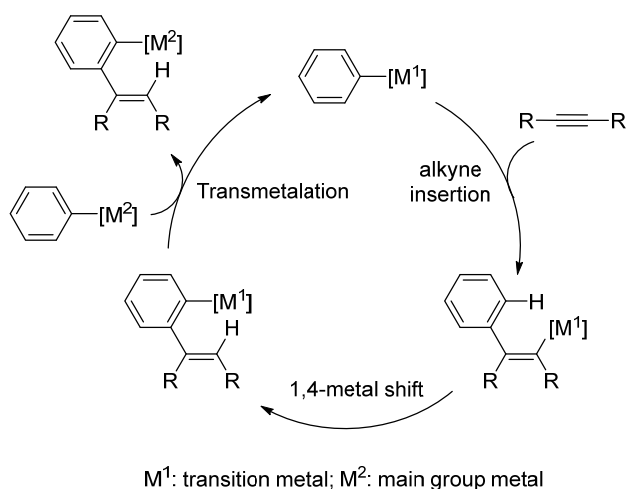
## 1.5 Design and Summary of Thesis Research.

As discussed above, migratory insertion of a C–C multiple bond into an arylmetal species represents a well-studied entry to alkyl-to-aryl and alkenyl-to-aryl 1,4-metal migrations. Catalyst turnover is achieved by protodemetalation (Rh), trapping of the arylmetal species with an internal electrophile (Rh), or C–H metalation/reductive elimination (Pd). The arylmetal species are typically generated by transmetalation with an arylmetal reagent (Rh) or by oxidative addition of an aryl halide (Pd). In light of the breadth of arylmetal reagents and carbometalation reactions using such reagents and transition metal catalysts, we wondered whether alternative transition metal/arylmatal combinations other than rhodium/arylboration could also promote 1,4-metal migration in the reaction with unsaturated hydrocarbons. In particular, we were intrigued by a new hypothetical catalytic cycle for the reaction of an arylmetal and an unsaturated hydrocarbon that features an

unprecedented termination step, that is, transmetalation (Scheme 1.20). The catalytic cycle involves alkyne insertion into an aryl- $M^1$  species ( $M^1$ : transition metal), 1,4-metal migration, and transmetalation between the resulting 2-alkenylaryl- $M^1$  species and an Ar- $M^2$  reagent ( $M^2$ : main group metal). Such a catalytic cycle is highly attractive, because interception of the resulting 2-alkenylaryl- $M^2$  product with a variety of electrophiles would significantly expand the synthetic scope of 1,4-metal migration.

For the implementation of this concept, an appropriate choice of the transition metal and main group metal should be crucial. For example, the combination of rhodium and boron would not be feasible, because smooth transmetalation between an organorhodium species and an organoboron reagent is unknown.

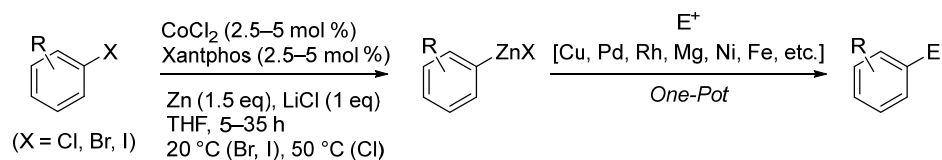
**Scheme 1.20.** Hypothetical Catalytic Cycle for Arylmatalation of Alkyne Involving 1,4-Migration.



Recently, our group reported that a cobalt-Xantphos complex efficiently catalyzes zinc insertion into aryl iodides, bromides, and chlorides (Scheme 1.21),<sup>39</sup> which was originally reported by Knochel and coworkers.<sup>40</sup> The resulting arylzinc reagents can participate in a variety of metal-mediated electrophilic trapping reactions (e.g., Negishi coupling) in one pot without apparent interference from the cobalt catalyst. A careful

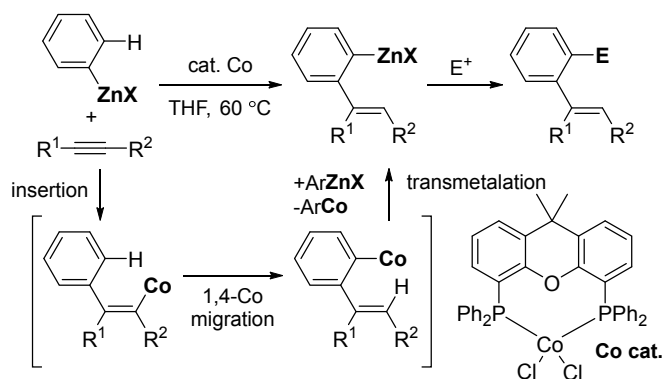
examination of this work, revealed the combination of arylzinc reagent and cobalt catalyst may be suitable for the hypothetical catalytic cycle.

**Scheme 1.21.** Cobalt-Catalyzed Zinc Insertion into Aryl Halides



With this proposed mechanism, we embarked on a series of research projects on cobalt-catalyzed arylzincation involving 1,4-cobalt migration, which will be discussed in detail in the following chapters. In Chapter 2, we describe the discovery, development, scope, and application of a cobalt-catalyzed reaction of an arylzinc reagent with an alkyne that involves vinyl-to-aryl 1,4-cobalt migration.<sup>41</sup> To our best knowledge, this represents the first example for 1,4-cobalt migration. The most differentiating feature of this reaction is the transmetalation with arylzinc reagent after 1,4-migration, affording *ortho*-alkenylarylzinc species that can be trapped by external electrophiles (Scheme 1.22).

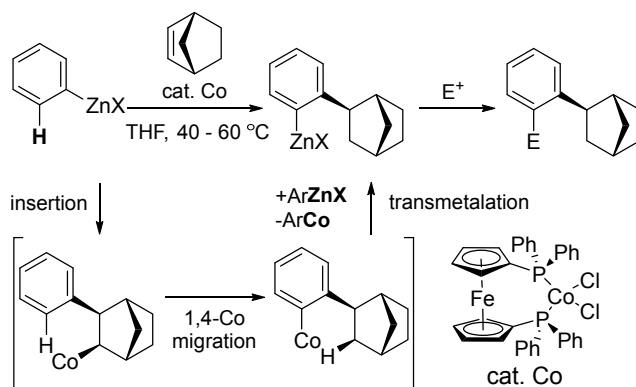
**Scheme 1.22.** Cobalt-Catalyzed Arylzincation to Alkynes Involving 1,4-Cobalt Migration



In Chapter 3, we describe the extension this 1,4-cobalt migration chemistry in the report of cobalt-catalyzed arylzincation to norbornene.<sup>42</sup> Unlike Miura and coworkers' work on rhodium-catalyzed hydroarylation of arylboronic acids to norbornene (Scheme

1.8), our present reaction allows the suppression of “merry-go-round” multi-norbornylation affording *o*-(2-*exo*-norbornyl)-arylzinc species that can be trapped with external electrophiles (Scheme 1.23).

**Scheme 1.23.** Cobalt-Catalyzed Arylzincation to Norbornene Involving 1,4-Cobalt Migration



Throughout our research in the last four years, cobalt has emerged as a promising metal catalyst for 1,4-migration chemistry. More importantly, the combination of arylzinc reagents and cobalt catalysts allow the generation of stable *ortho*-substituted arylzinc reagents that can be trapped by external electrophiles leading to more diverse classes of fine chemicals that are not easily available by existing methods.<sup>43</sup>

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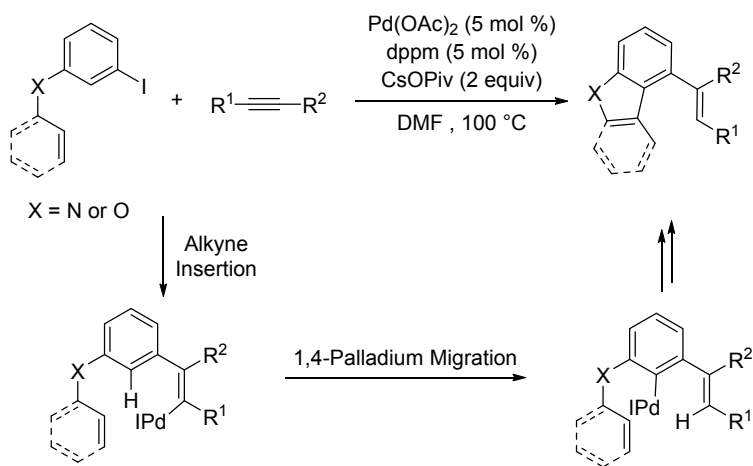
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## Chapter 2. Cobalt-Catalyzed Arylzincation of Unactivated Alkynes through 1,4-Cobalt Migration

### 2.1 Introduction

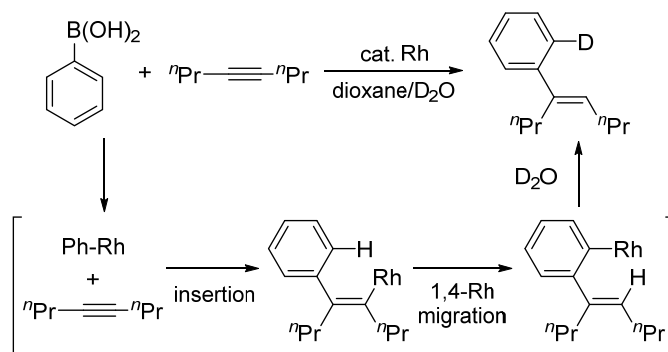
1,4-Metal migrations,<sup>1</sup> particularly in organorhodium-<sup>2</sup> and organopalladium-mediated<sup>3</sup> reactions, have gained significant attention as a novel class of C–H functionalizations reaction. These metal migration processes are not only mechanistically important but also synthetically useful. As an early example of 1,4-palladium migration, Larock and co-workers reported a novel annulation process involving iodobenzene and diphenylacetylene under palladium-catalyzed conditions affording 9-benzylidene-9*H*-fluorene involving 1,4-palladium migration.<sup>4</sup> The vinyl-to-aryl 1,4-palladium migration was later exploited in the synthesis of vinylic carbazoles, indoles, and dibenzofurans from appropriately designed aryl iodides and internal alkynes through alkyne insertion, 1,4-migration, and intramolecular C–C coupling (Scheme 2.1).<sup>5</sup>

**Scheme 2.1.** Palladium-Catalyzed Synthesis of Vinylic Carbazoles, Indoles and Dibenzofurans Involving 1,4-Palladium Migration

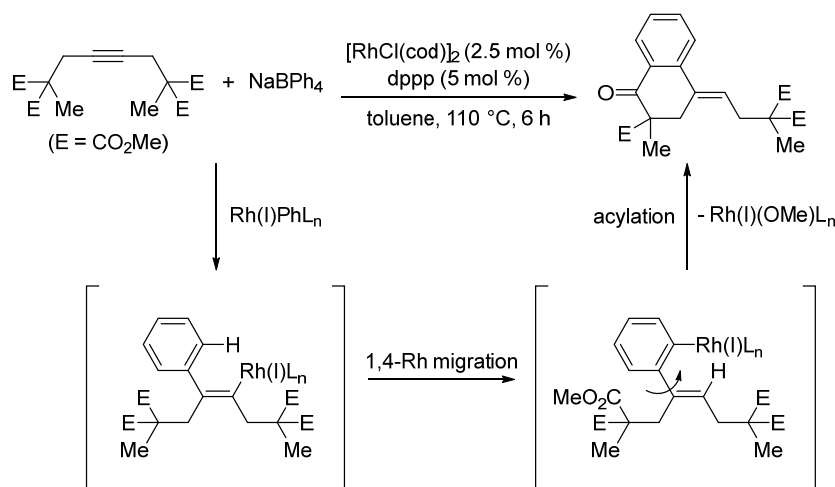


After the first observation of 1,4-rhodium migration in the reaction of an arylboronic acid with norbornene by Miura et al.,<sup>6</sup> Hayashi and coworkers reported that a rhodium-catalyzed hydroarylation reaction of an alkyne with an arylboronic acid involves insertion of the alkyne into an arylrhodium species, vinyl-to-aryl 1,4-rhodium migration, and protonation of the resulting *ortho*-alkenylarylrhodium species (Scheme 2.2).<sup>7</sup> These early studies set the stage for subsequent development of a variety of domino cyclization reactions involving 1,4-rhodium migration followed by trapping of the arylrhodium species with an internal electrophile (e.g., carbonyl group).<sup>8</sup> As an early example of such domino reactions, Murakami and coworkers demonstrated that an arylrhodium species generated through alkyne insertion–1,4-migration sequence can be intercepted by an ester moiety in an intramolecular manner, thus affording a cyclic ketone product (Scheme 2.3).<sup>9</sup>

**Scheme 2.2.** Rhodium-Catalyzed Alkyne Hydroarylation Involving 1,4-Rhodium Migration

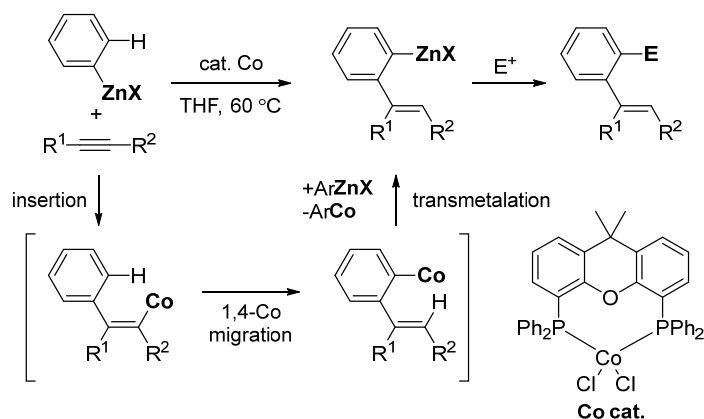


**Scheme 2.3.** Intramolecular Acylation Of Organorhodium(I) With Ester Involving 1,4-Rhodium Migration



We report here, a cobalt-catalyzed reaction of an arylzinc reagent with an alkyne that involves a similar vinyl-to-aryl 1,4-cobalt migration. Importantly, the reaction is distinct from rhodium-catalyzed hydroarylation reaction (Scheme 2.2) in that the 1,4-migration is followed by transmetalation with the arylzinc reagent (Scheme 2.4).<sup>10</sup> The resulting *ortho*-alkenylarylzinc species can be trapped by external electrophiles, thus allowing access to a variety of 1-alkenyl-arenes functionalized in the 2-position, many of which are not readily accessible using current synthetic methods.

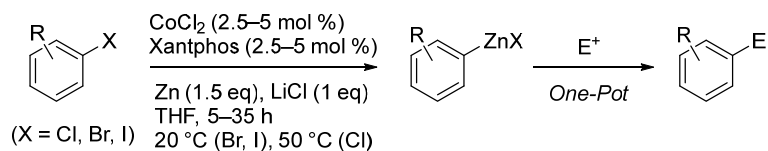
**Scheme 2.4.** Cobalt-Catalyzed Alkyne Arylzincation Involving 1,4-Cobalt Migration



## 2.2 Results and discussion

Recently, our group reported that a  $\text{CoCl}_2$ -Xantphos catalyst significantly accelerates insertion of  $\text{Zn}\cdot\text{LiCl}$  into aryl halides (Scheme 2.5),<sup>11</sup> which was originally reported by Knochel and coworkers.<sup>12</sup> While the original method is applicable to aryl iodides and highly activated aryl bromides, the cobalt-catalyzed protocol allows efficient conversion of aryl iodides, bromides, and even some chlorides into the corresponding arylzinc reagents. The resulting arylzinc reagents can participate in a variety of metal-mediated electrophilic trapping reactions (e.g., Negishi coupling) in one pot without apparent interference from cobalt catalyst.

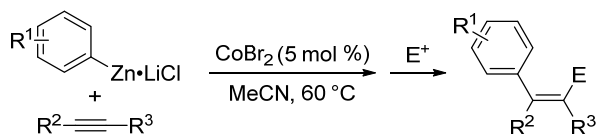
**Scheme 2.5.** Cobalt–Xantphos-Catalyzed, LiCl-Mediated Preparation of Arylzinc Reagents from Aryl Halides



In the course of extension of such electrophilic trapping reactions, we became interested in the addition of our arylzinc reagent to an alkyne. Upon a few initial experiments, we came across an observation that the addition of a 4-methoxyphenylzinc reagent **1a** prepared from 4-iodoanisole and  $\text{Zn}\cdot\text{LiCl}$  with the cobalt catalyst in THF (denoted as type **A** reagent) reacted with 4-octyne (**2a**), at 60 °C, and on quenching with water afforded the *syn*-addition product **3aa** in 70% yield (Table 2.1, entry 1). This observation indicated that cobalt–Xantphos catalyst not only accelerated the zinc insertion step but also catalyzed the addition of **1a** to **2a**. At a glance, this result did not appear extremely surprising in light of the report of Oshima and coworkers on an arylzincation reaction of an unactivated alkyne catalyzed by  $\text{CoBr}_2$  alone (Scheme 2.6).<sup>13</sup> However, the

solvent effect on this reaction attracted our attention. Thus, the  $\text{CoBr}_2$ -catalyzed reaction worked only in a solvent containing acetonitrile but does not take place at all in pure THF, which was used in our experiment.

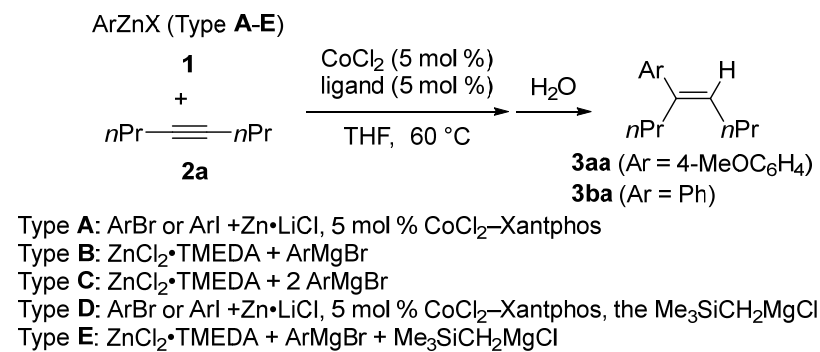
**Scheme 2.6.** Cobalt-Catalyzed Arylzincation of Alkynes



We performed a systematic study on the ligand effect on the cobalt-catalyzed addition of phenylzinc reagent (prepared from equimolar amounts of  $\text{PhMgBr}$  and  $\text{ZnCl}_2 \cdot \text{TMEDA}$ ; type **B** reagent) to 4-octyne **2a** in THF. Expectedly, the  $\text{CoCl}_2$ -Xantphos catalyst promoted the reaction to afford the *syn*-adduct **3ba** in 90% yield (Table 1, entry 2). It is noteworthy that a preformed [ $\text{CoCl}_2$ - (Xantphos)] complex exhibited equally high catalytic activity as the catalyst generated in situ. Other common phosphine ligands, such as, DPEphos, dppe, dppp, and  $\text{PPh}_3$ , or performing the reaction under ligand-free conditions did not display any measurable catalytic activity (entries 3-7). While it is well known that a low-valent cobalt complex catalyzes cyclotrimerization of alkynes,<sup>14</sup> only a trace amount (1-3 %) of a cyclotrimerization product of **2a** was detected under the standard conditions. Solvent effects play significant role in the reactivity. It was observed that the reaction was slightly slower in THF/toluene solvent mixture and was significantly retarded by the use of MeCN as a co-solvent. From atom efficiency, it is noteworthy that a diphenylzinc reagent (0.55 equiv) prepared from a 1:2 mixture of  $\text{ZnCl}_2 \cdot \text{TMEDA}$  and  $\text{PhMgBr}$  (type **C** reagent) afforded **3ba** in 74% yield (entry 10), thus indicating transfer of both of the phenyl group on the zinc atom. In addition, the reactivity of the type **A** arylzinc reagent was enhanced upon transmetalation with one equivalent of  $\text{Me}_3\text{SiCH}_2\text{MgCl}$  (type **D** reagent), resulting in the formation of **3aa** a near quantitative yield (entry, 11). Consistent with our observation,

a mixed arylzinc reagent prepared from  $\text{ZnCl}_2 \cdot \text{TMEDA}$ ,  $\text{PhMgBr}$  and  $\text{Me}_3\text{SiCH}_2\text{MgCl}$  (type **E** reagent) was also reactive (entry 12). The use of  $\text{PhMgBr}$  instead of phenylzinc reagents afforded only a trace amount of the desired product **3ba**, although alkyne **2a** was consumed by unidentified side reactions.

**Table 2.1.** Screening of Reaction Conditions<sup>[a]</sup>

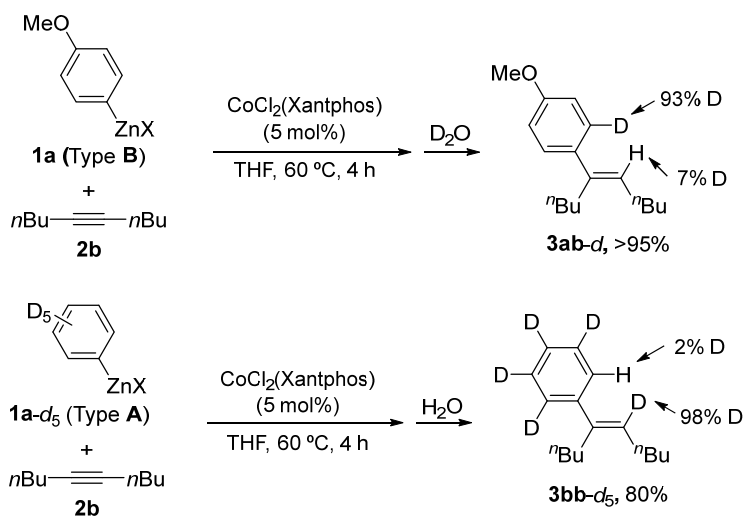


| Entry             | Ar, reagent type (equiv)                      | Ligand           | Yield [%] <sup>[b]</sup> |
|-------------------|---|------------------|--------------------------|
| 1 <sup>[c]</sup>  | 4-MeOCH <sub>6</sub> H <sub>4</sub> , A (3)   | Xantphos         | 70                       |
| 2                 | Ph, B (1.1)                                   | Xantphos         | 90 (90)                  |
| 3                 | Ph, B (1.4)                                   | DPEphos          | 3                        |
| 4                 | Ph, B (1.4)                                   | dppe             | 0                        |
| 5                 | Ph, B (1.4)                                   | dppp             | 2                        |
| 6 <sup>[d]</sup>  | Ph, B (1.4)                                   | PPh <sub>3</sub> | 1                        |
| 7                 | Ph, B (1.4)                                   | None             | 1                        |
| 8 <sup>[e]</sup>  | Ph, B (1.1)                                   | Xantphos         | 69                       |
| 9 <sup>[f]</sup>  | Ph, B (1.1)                                   | Xantphos         | 7                        |
| 10                | Ph, C (0.55)                                  | Xantphos         | 74                       |
| 11 <sup>[c]</sup> | 4-MeOCH <sub>6</sub> H <sub>4</sub> , D (1.5) | Xantphos         | 99 (94)                  |
| 12                | Ph, E (1.5)                                   | Xantphos         | 77                       |

<sup>[a]</sup>Reactions Conditions: CoCl<sub>2</sub> (5 mol %), ligand (5 mol %), **2a** (0.3 or 0.6 mmol), ArZnX, THF, 60 °C, 4 h. <sup>[b]</sup>Determined by GC using *n*-tridecane as an internal standard. The *E/Z* ratio was > 50:1 as determined by <sup>1</sup>H NMR spectroscopy as well as GC analysis. The yield of isolated product is shown in parentheses. <sup>[c]</sup>CoCl<sub>2</sub>–Xantphos catalyst was used for both the zinc insertion and addition reactions. <sup>[d]</sup>PPh<sub>3</sub> (10 mol %) was used. <sup>[e]</sup>Performed in THF/toluene (1:1). <sup>[f]</sup> Performed in THF/MeCN (1:1).

Results of deuterium-labeling-experiments (Scheme 2.7) revealed a key critical difference between our present reaction and the  $\text{CoBr}_2$ -catalyzed arylzincation reported by Oshima and coworkers. The reaction of 4-methoxyphenylzinc reagent with 5-decyne, upon quenching with  $\text{D}_2\text{O}$ , afford the adduct **3ab-d**, with predominantly deuteration of the *ortho* position of aryl group (93%) rather than the vinyl position (7%). Moreover, when the reaction of pentadeuteriophenylzinc reagent with 5-decyne was quenched with  $\text{H}_2\text{O}$ , almost complete transfer of one of the *ortho*-deuterium atom of the arylzinc reagent to the vinylic position was observed in the product **3bb-d<sub>5</sub>**.

**Scheme 2.7.** Deuterium-Labeling Experiments<sup>[a]</sup>

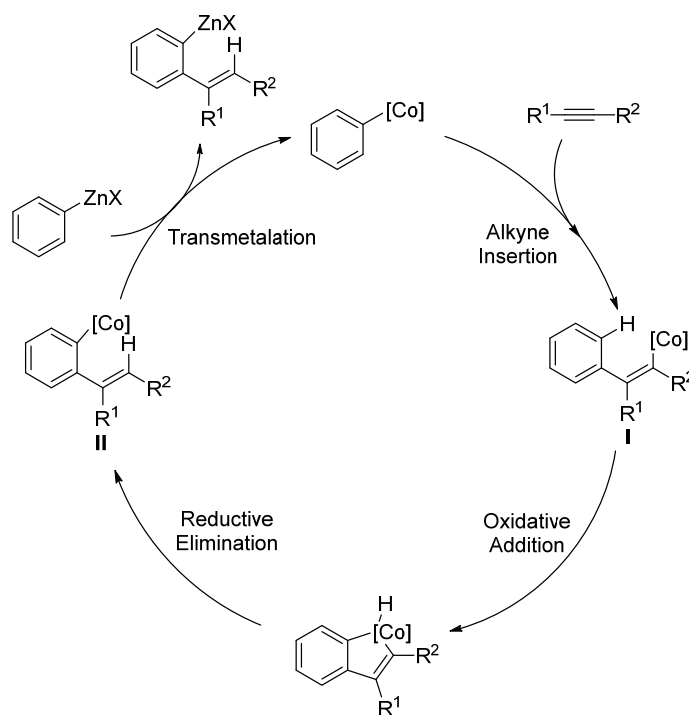


<sup>[a]</sup>The proton content on each carbon atom was estimated by  $^1\text{H}$  NMR analysis.

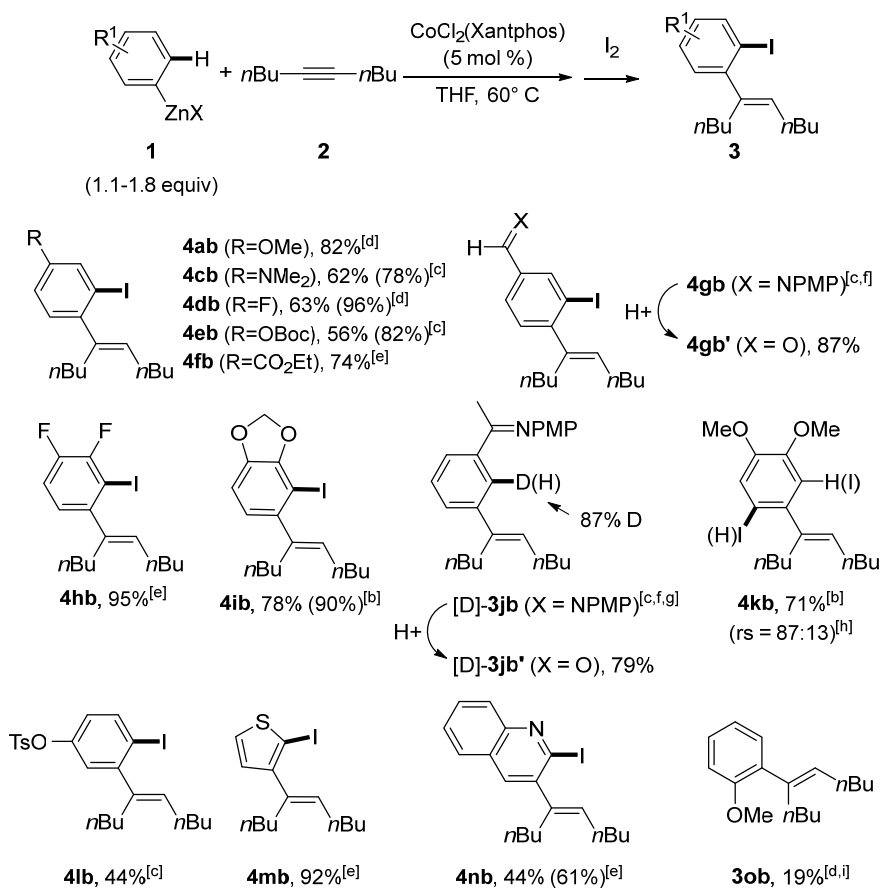
The above results reminded us of Hayashi's work on the rhodium-catalyzed alkyne hydroarylation reaction (Scheme 2.2), in which the same type of deuterium-labeling experiments were performed to support the proposed 1,4-migration mechanism. Thus, in analogy to the rhodium catalysis, we propose a catalytic cycle consisting of the following steps: 1) insertion of the alkyne into an arylcobalt species generated from the cobalt precatalyst and the arylzinc reagent, 2) 1,4-cobalt migration of the resulting alkenylcobalt

species **I** to generate an *ortho*-alkenylarylcobalt species **II**, and 3) transmetalation between **II** and the arylzinc reagent to afford an *ortho*-alkenylarylzinc species and regenerate the active arylcobalt species. While at this stage we are unable to confirm the mechanistic nature of the migration, in light of the computational studies done by Hayashi and co-workers on the rhodium migration,<sup>15</sup> we speculate that the bulky backbone of Xantphos forces cobalt center to be in close proximity to the *ortho*-hydrogen of the aryl group. Thus, an increased agostic interaction between the cobalt center and the *ortho*-hydrogen causes alkenylcobalt species **I** to undergo oxidative addition, which is followed by reductive elimination of the resulting Co(III) intermediate to afford the thermodynamically more stable *ortho*-alkenylarylcobalt species **II** (Scheme 2.8). It is also noteworthy that from the deuterium-labeling experiment results, we can conclude that 1,4-cobalt migration occurs much faster than cobalt-to-zinc transmetalation step under our present conditions.

**Scheme 2.8.** Putative Catalytic Cycle for 1,4-Cobalt Migration



The differentiating feature of this “migratory arylzincation” reaction compared with the rhodium-catalyzed hydroarylation reaction is that the product bears a reactive aryl-zinc bond, which allows trapping of external electrophiles. Thus, we explored the generality of the addition-migration process using  $I_2$  as the electrophile (Scheme 2.9). A variety of arylzinc reagents participated in the reaction with 5-decyne to afford the corresponding 1-iodo-2-alkenylarenes in moderate to good yields (**4ab–4nb**). Owing to the versatility of  $CoCl_2$ -Xantphos system, arylzinc reagent bearing potentially sensitive functional groups including dimethylamino (**4cb**), carbonate (**4eb**), ester (**4fb**), aldimine (**4gb**), and tosyloxy (**4lb**) groups as well as heterocycles, such as thienyl (**4mb**) and quinolinyl (**4nb**) groups can be prepared by zinc insertion and directly used for the reaction with 5-decyne. Arylzinc reagents with less sensitive substituents such as alkoxy and fluoro groups, can be generated directly by transmetalation of  $ZnCl_2 \cdot TMEDA$  with the corresponding Grignard reagents, and then subjected to the reaction with 5-decyne, affording the desired products in modest to good yields. The reaction of *ortho*-methoxyphenylzinc reagent was rather sluggish (**3ob**), presumably due to steric hindrance. The poor reactivity of the *ortho*-substituted arylzinc reagents explains the observation that the present reaction does not afford any twofold addition product. Thus, the *ortho*-alkenylarylzinc reagent would be too sterically hindered to enter the catalytic cycle of migratory arylzincation (cf. Scheme 2.8). Note that, the yield of the iodinated products were generally lower than those of the corresponding hydroarylation products obtained by quenching with  $H_2O$  (see parenthesis) due to partial decomposition during isolation.

Scheme 2.9. Scope of Migratory Arylzincation – Arylzinc Reagents<sup>[a]</sup>

<sup>[a]</sup> Scope of the migratory arylzincation (0.6–1 mmol scale unless otherwise noted). The yields in the parenthesis refer to the yields of hydroarylation products obtained by quenching with H<sub>2</sub>O. Ts = toluene-sulfonyl, Boc = *tert*-butyloxycarbonyl. <sup>[b]</sup> Reagent type = **B**. <sup>[c]</sup> Reagent type = **A**. <sup>[d]</sup> Reagent type = **C**. <sup>[e]</sup> Reagent type = **D**. <sup>[f]</sup> PMP = *p*-methoxyphenyl. The product was isolated after hydrolysis of the imine. <sup>[g]</sup> The reaction was quenched with D<sub>2</sub>O. <sup>[h]</sup> rs = regioselectivity. <sup>[i]</sup> The reaction was quenched with H<sub>2</sub>O.

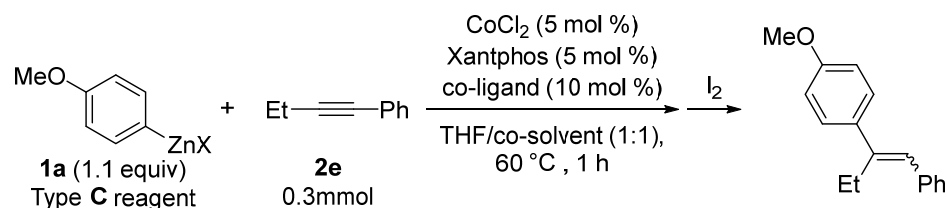
Cobalt 1,4-migration was also feasible for different alkynes including dialkyl-, arylalkyl-, and silylalkylalkynes, while the catalytic system required minor modifications for arylalkylalkynes (Scheme 2.10, **4ac–4ah**, **4ii**, and **3me**). When we subject **1a** (type **C** reagent) to 1-phenyl-1-butyne **2e** under standard conditions, the reaction afforded the

desired product **4ae** in 84% yield with substantial degree of *E/Z* isomerization (ca. 6:4; Table 2.2, entry 1). In order to reduce the degree of *E/Z* isomerization, we screened some co-solvents and co-ligands. The use of pyridine as co-solvent severely retarded the reaction, presumably due to strong coordination of pyridine to the cobalt catalyst (entry 2). DMI or NMP improved the *E/Z* ratio to ca. 9:1 but substantially lowered the catalytic activity (entries 3 and 4). Interestingly, acetonitrile which was found to inhibit the reaction (Table 2.1, entry 9), was compatible with type **C** reagent to afford the desired product in a moderate yield with a good *E/Z* ratio (90:10; Table 2.1, entry 4). The addition of PPh<sub>3</sub> or P(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> (10 mol%) as a co-ligand did not display any significant influence on the reactivity and selectivity (entries 5 and 6), while P(OPh)<sub>3</sub> improved the *E/Z* ratio of ca. 9:1 while maintaining the catalytic activity (entry 7). It is also noteworthy that the use of NiXantphos instead of Xantphos, without modification of any other conditions, also improved the *E/Z* ratio to 85:15 with a similar level of catalytic activity (entry 8).

As summarized in Scheme 2.10, the reaction of dialkyl- and silylalkylalkynes took place smoothly under the original conditions (see **4ac**, **4ad**, and **4ah**). With the P(OPh)<sub>3</sub> modified catalytic system, a series of arylalkylalkynes also participated in the reaction with high stereoselectivity (See **4ae-4ag**, **4ii** and **3me**). While no regioselectivity was observed for 4-methylpent-2-yne (see corresponding adduct **4ad**), silylalkyl-, and arylalkylalkynes underwent regioselective arylation on the acetylenic carbon atom proximal to the alkyl group (**4ae-4ah**, **4ii**, and **3me**); this is consistent with regioselectivity commonly observed for carbometalation of alkynes.<sup>16</sup> Unfortunately, the reaction of diphenylacetylene afforded, upon protonation, the adduct **3aj** with only a modest *E/Z* ratio (60:40). In this case, no improvement of *E/Z* ratio was achieved by addition of P(OPh)<sub>3</sub>. Terminal alkynes such as

phenylacetylene and 1-octyne and sterically hindered alkynes such as bis(trimethylsilyl)acetylene were unreactive and did not participate in the reaction.<sup>17</sup>

**Table 2.2.** Screening of Solvent and Ligand Effects on *E/Z* Isomerization<sup>[a]</sup>



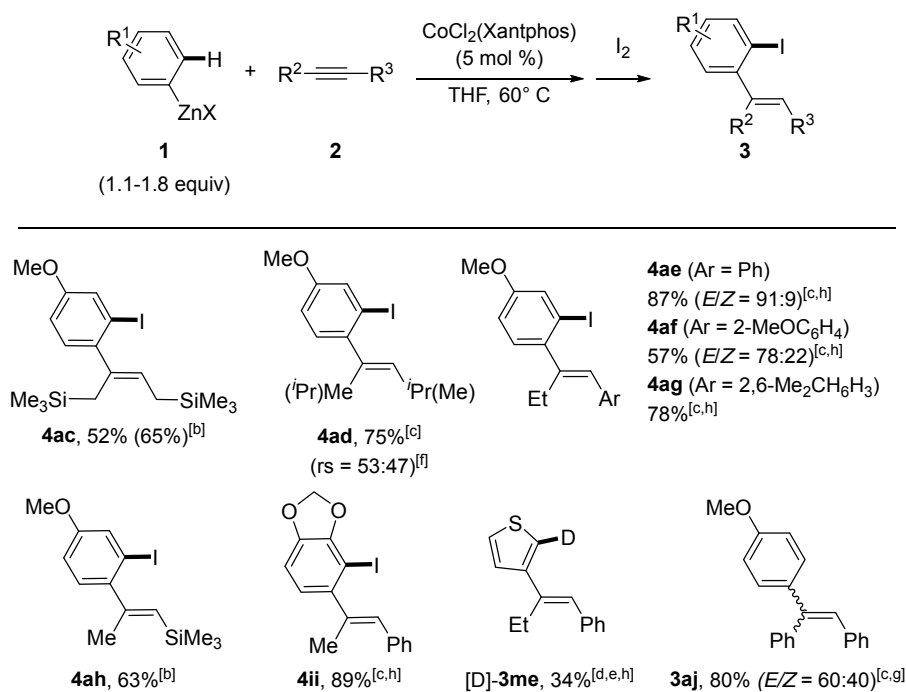
| Entry            | Co-solvent | Co-ligand                                      | Yield % <sup>[b]</sup>   |
|------------------|------------|--|--------------------------|
| 1 <sup>[c]</sup> | -          | -  | 84 ( <i>E/Z</i> : 62/38) |
| 2                | pyridine   | -  | trace                    |
| 3                | DMI        | -  | 12 ( <i>E/Z</i> : 91/9)  |
| 4                | NMP        | -  | 11 ( <i>E/Z</i> : 92/8)  |
| 5                | MeCN       | -  | 62 ( <i>E/Z</i> : 90/10) |
| 6                | -          | PPh <sub>3</sub>                               | 88 ( <i>E/Z</i> : 63/37) |
| 7                | -          | P(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> | 81 ( <i>E/Z</i> : 66/34) |
| 8                | -          | P(OPh) <sub>3</sub>                            | 75 ( <i>E/Z</i> : 89/11) |
| 9 <sup>[d]</sup> | -          | -  | 80 ( <i>E/Z</i> : 85:15) |

<sup>[a]</sup> Reactions Conditions: CoCl<sub>2</sub> (5 mol %), ligand (5 mol %), co-ligand (10 mol %), **2e** (0.3 mmol), **1a** (type C reagent), THF (volume is determined by concentration of Grignard reagent. When co-solvent is used, its volume corresponds to the volume of THF used), 60 °C, 1 h. DMI = 1,3-Dimethyl-2-imidazolidinone, NMP = *N*-Methyl-2-pyrrolidone. <sup>[b]</sup> Determined by GC using *n*-tridecane as an internal standard. The *E/Z* ratio was determined by <sup>1</sup>H NMR spectroscopy as well as GC analysis. <sup>[c]</sup> Reactions Conditions: CoCl<sub>2</sub> (5 mol %), ligand (5 mol %), **2e** (0.3 mmol), **1a** (type C reagent), THF, 60 °C, 1 h. <sup>[d]</sup> NiXantphos (5 mol %) was used instead of Xantphos.

Electronic and steric effects on the regioselectivity of 1,4-cobalt migration are worth further discussion. The presence of difluoro- or methylenedioxy moiety at the *meta* and *para* positions resulted in exclusive migration to the *ortho* positions proximal to the functional group (**4hb** and **4ib**); this selectivity may be attributed to the stabilizing effect of the fluorine atom on the *ortho* aryl-metal bond (for **4hb**)<sup>18</sup> and/or coordination of *meta*-

fluorine/oxygen atom to the cobalt center during the migration process.<sup>19</sup> An *N*-aryl imine group at the *meta* position also served as the directing group (**3jc-d**), reminiscence of chelated assisted C-H activation reactions.<sup>20</sup> In contrast, *meta* position bearing bulky substrates such as 3,4-dimethoxy- and 3-tosyloxyphenylzinc reagents resulted in preferential metal migration to the less sterically hindered *ortho* position (**4kb** and **4lb**),<sup>15</sup> presumably the coordination of the *meta*-oxygen atom to cobalt center is not feasible owing to the free rotation of the methoxy group and/or the reduced basicity (for **4lb**). Regioselective migration to the C2-position of 3-thienyl- and 3-quinolinylyl zinc reagents (see corresponding product **4mb** and **4nb**), while ascribing regioselectivity to specific parameters such as acidity of the C2-proton remains unclear to date.<sup>21</sup>

**Scheme 2.10.** Scope of Migratory Arylzincation - Alkynes<sup>[a]</sup>

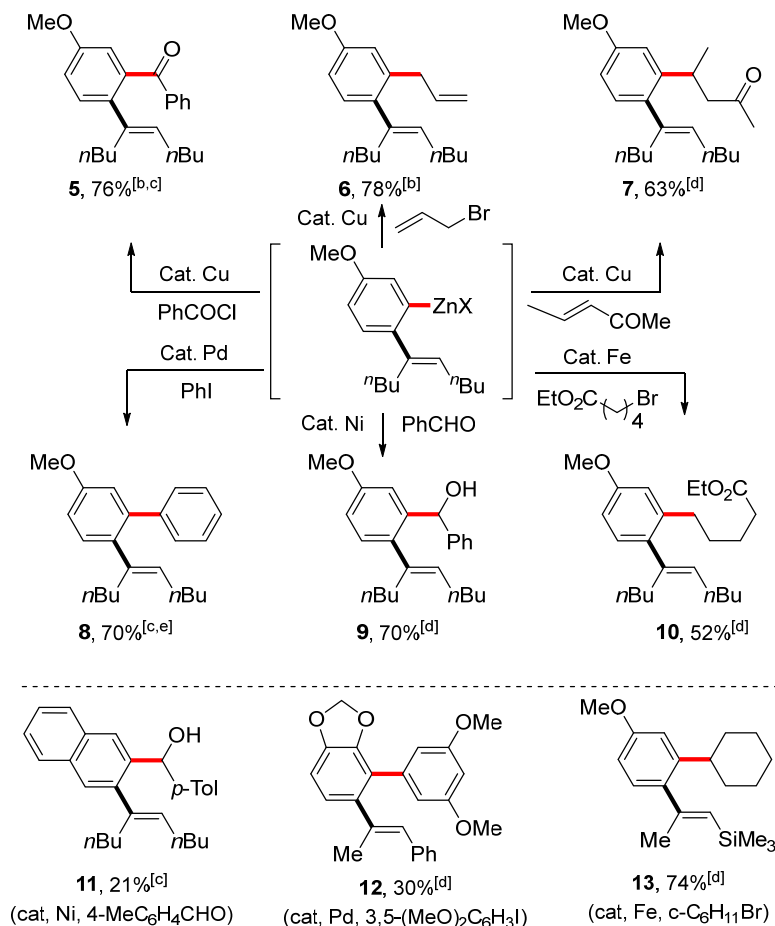


<sup>[a]</sup> Scope of the migratory arylzincation (0.6–1 mmol scale unless otherwise noted). The yields in the parenthesis refer to the yields of hydroarylation products obtained by quenching with  $\text{H}_2\text{O}$ . <sup>[b]</sup>

Reagent type = **B**. <sup>[c]</sup>Reagent type = **C**. <sup>[d]</sup>Reagent type = **D**. <sup>[e]</sup>The reaction was quenched with D<sub>2</sub>O. <sup>[f]</sup>rs = regioselectivity. <sup>[g]</sup>The reaction was quenched with H<sub>2</sub>O. <sup>[h]</sup>P(OPh)<sub>3</sub> (10 mol %) was added.

The *ortho*-alkenylarylzinc reagent generated from 4-methoxyphenylzinc reagent with 5-decyne was amenable to a variety of transition-metal-catalyzed C-C bond forming reactions (Scheme 2.11). Thus, copper-catalyzed acylation, allylation and conjugate addition, palladium-catalyzed Negishi coupling, nickel-catalyzed cross-coupling addition to an aldehyde, and iron-catalyzed cross-coupling with an alkyl halide, without obvious interference from the cobalt catalyst, afforded 1-alkenyl-2-functionalized arenes **5-10** respectively, in moderate to good yields. The feasibility of external electrophilic trapping was further demonstrated by three additional examples (see products, **11-13**), albeit with modest yield for the first two cases, which could be improved on by optimizing the trapping conditions (compare yields of **4ii** and **12**). Note that the regioselectivity of cobalt-migration starting with 2-naphthylzinc reagent took place exclusively at the less hindered aromatic carbon (see **11**).<sup>2e</sup>

**Scheme 2.11.** Transition-Metal-Catalyzed Transformation of *ortho*-Alkenylarylzinc Species<sup>[a]</sup>

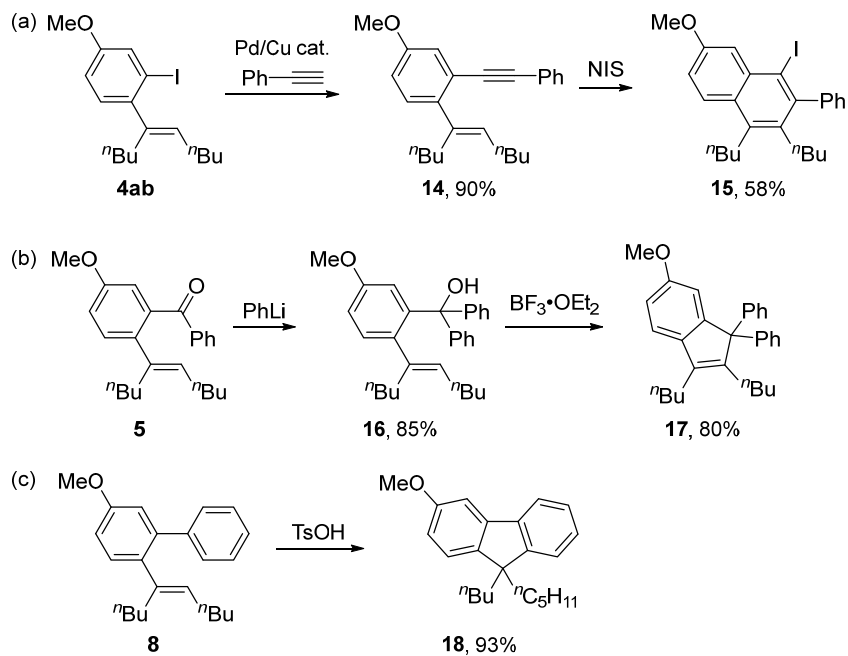


<sup>[a]</sup>Reaction was carried out in 1 mmol scale unless otherwise noted. See Experimental Section for details of the reaction conditions. <sup>[b]</sup>Reaction was carried out in 5 mmol scale. <sup>[c]</sup>Reagent type = **B**. <sup>[d]</sup>Reagent type = **E**. <sup>[e]</sup>Reaction was carried out in 3 mmol scale.

The 1-alkenyl-2-functionalized arenes obtained by the present reaction serve as starting materials for the synthesis of benzo-fused carbocycles. This idea was readily demonstrated by three set of transformations: 1) naphthalene synthesis (**15**) from 1-iodo-2-alkenylarene **4ab** through Sonogashira coupling followed by NIS-mediated iodocarbocyclization (Scheme 2.12, a),<sup>22</sup> 2) indene synthesis (**17**) from 1-benzoyl-2-

alkenylarene **5** through phenyllithium addition followed by  $\text{BF}_3$ -mediated cyclization (Scheme 2.12, b), and fluorene synthesis (**18**) from 1-phenyl-2-alkenylarene **8** through Friedel-Crafts cyclization (Scheme 2.12, c).

**Scheme 2.12.** Transformation of 1-Alkenyl-arenes Functionalized in the 2-Position



See Experimental Section for details of the reaction conditions. NIS = N-iodosuccinimide. TsOH = *p*-toluenesulfonic acid.

## 2.3 Conclusion

In summary, we have developed a cobalt-catalyzed addition reaction of an arylzinc reagent to an unactivated internal alkyne that follows a subsequent 1,4-cobalt migration and cobalt-to-zinc transmetalation to afford an *ortho*-alkenylaryl-zinc species, which can be further functionalized. While Co-Xantphos catalyst performs best for zinc insertion and as well as migratory arylzincation reactions, the origin of this catalytic activity remains unclear at the present moment. To our best knowledge, the present 1,4-cobalt migration in

cobalt-catalyzed C–C bond forming reactions is the first example and it provides an entry to a new example of C–H bond functionalization using cobalt catalysts.<sup>10a</sup>

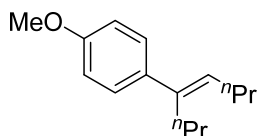
## 2.4 Experimental section

**General.** All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed as described by Still et al., using 40–63 m silica gel (Si 60, Merck).  $^1\text{H}$  and  $^{13}\text{C}$  nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) NMR spectrometers.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and  $\text{CHCl}_3$  (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25  $\mu\text{m}$  film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-ToF Premier LC HR mass spectrometer.

**Materials.** Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Zinc powder (-100 mesh, 99.9%) was purchased from Alfa Aesar, and preactivated by the treatment with aq. HCl. Anhydrous  $\text{CoCl}_2$  (97%) was purchased from Alfa Aesar and was used as received.  $\text{CoCl}_2(\text{Xantphos})$  was prepared according to the literature procedure. THF was distilled over Na/benzophenone. Grignard reagents were prepared from the corresponding halides and magnesium turnings in anhydrous THF and titrated before use. The following compounds were prepared according to the literature procedures, and their  $^1\text{H}$  and  $^{13}\text{C}$  spectra showed good agreement with the literature data.

- 4-Bromophenyl *tert*-butylcarbonate

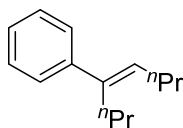
- (*E*)-*N*-(1-(3-Bromophenyl)ethylidene)-4-methoxyaniline
- (*E*)-*N*-(4-Bromobenzylidene)-4-methoxyaniline
- 3-Bromophenyl 4-methylbenzenesulfonate



**(*E*)-1-methoxy-4-(oct-4-en-4-yl)benzene (Scheme 2, 3aa): Type D Reagent (1.5 equiv),**

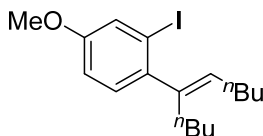
Zinc Reagent was prepared in 2.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 14 h). Zinc Reagent (1.1 mL, 0.9 mmol) was transferred to a freshly dried Schlenk tube and cooled to 0 °C. (CH<sub>3</sub>)<sub>3</sub>SiCH<sub>2</sub>MgBr (1 mL, 0.9 M, 0.9 mmol) was added dropwise and the reaction mixture was allowed to stir for 1 h before 4-octyne (66.1 mg, 0.6 mmol) was added. The reaction was then heated to 60 °C and stirred for 4 h. The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (123.1 mg, 94%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 5.58 (t, *J* = 7.2 Hz, 1H), 3.79 (s, 3H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.15 (q, *J* = 7.3 Hz, 2H), 1.45 (sextet, *J* = 7.4 Hz, 2H), 1.35 (sextet, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.3, 139.3, 136.0, 127.8, 127.3 (2 x C), 113.5 (2 x C), 55.2, 31.7, 30.6, 23.1, 21.8, 13.94, 13.90; HRMS (ESI) Calcd for C<sub>15</sub>H<sub>23</sub>O [M + H]<sup>+</sup> 219.1749, found 219.1754.



**(E)-1-(dec-5-en-4-yl)benzene (Scheme 2, 3ba): Type B Reagent (1.4 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 4 h). The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (101.7 mg, 90%).

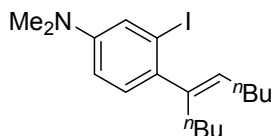
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 – 7.27 (m, 4H), 7.22 – 7.18 (m, 1H), 5.65 (t, *J* = 7.2 Hz, 1H), 2.47 (t, *J* = 7.6 Hz, 2H), 2.17 (q, *J* = 7.3 Hz, 2H), 1.52 – 1.42 (m, 2H), 1.36 (sextet, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 143.5, 140.0, 129.2, 128.1 (2 x C), 126.3 (3 x C), 31.7, 30.7, 23.1, 21.8, 14.0 (2 x C); HRMS (ESI) Calcd for C<sub>14</sub>H<sub>21</sub> [M + H]<sup>+</sup> 189.1634, found 189.1651.



**(E)-1-(dec-5-en-5-yl)-2-iodo-4-methoxybenzene (Scheme 4, 4ab): Type B Reagent (1.1 equiv)**, reaction was carried out in 5.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, overnight). The reaction was cooled to 0 °C before addition of I<sub>2</sub> (1.40g, 5.5 mmol) and resulting mixture was allowed to stirred for 1 h. The reaction was then quenched with saturated aqueous solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (10 mL), and dilute with ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced

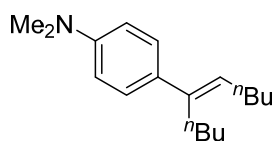
pressure. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (1.53 g, 82 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 (d,  $J = 2.4$  Hz, 1H), 7.00 (d,  $J = 8.4$  Hz, 1H), 6.83 (dd,  $J = 8.4, 2.5$  Hz, 1H), 5.25 (t,  $J = 7.2$  Hz, 1H), 3.78 (s, 3H), 2.36 (t,  $J = 7.4$  Hz, 2H), 2.19 – 2.14 (m, 2H), 1.48 – 1.39 (m, 4H), 1.34 – 1.21 (m, 4H), 0.94 (t,  $J = 6.4$  Hz, 3H), 0.87 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.1, 142.7, 141.7, 131.5, 129.7, 124.0, 113.8, 99.9, 55.5, 31.7, 31.5, 30.2, 27.7, 22.8, 22.5, 14.05, 14.00; HRMS (ESI) Calcd for  $\text{C}_{17}\text{H}_{26}\text{IO}$   $[\text{M} + \text{H}]^+$  373.1028, found 373.1044.



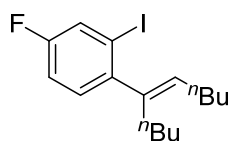
**(E)-4-(dec-5-en-5-yl)-3-iodo-N,N-dimethylaniline (Scheme 4, 4cb): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (138.1 mg, 1.0 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 6 h. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (238.9 mg, 62 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.11 (d,  $J = 2.4$  Hz, 1H), 6.86 (d,  $J = 8.1$  Hz, 1H), 6.59 (d,  $J = 8.4, 2.0$  Hz, 1H), 5.16 (t,  $J = 7.2$  Hz, 1H), 2.84 (s, 6H), 2.27 (t,  $J = 7.4$  Hz, 2H), 2.08 (q,  $J = 7.0$  Hz, 2H), 1.36 – 1.30 (m, 4H), 1.29 – 1.11 (m, 4H), 0.85 (t,  $J = 7.0$  Hz, 3H), 0.79 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  149.5, 142.8, 137.6, 131.2, 129.5, 122.8, 112.2, 100.5, 40.7 (2 x C), 31.8, 31.6, 30.3, 27.7, 22.8, 22.5, 14.04, 14.02; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{29}\text{NI}$   $[\text{M} + \text{H}]^+$  386.1345, found 386.1344.



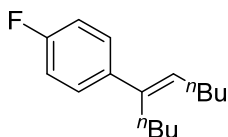
**(E)-4-(dec-5-en-5-yl)-N,N-dimethylaniline (Scheme 4, 4cb-H): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (82.9 mg, 0.6 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 6 h. The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (121.4 mg, 78 %).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.24 (d, *J* = 8.9 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 5.56 (t, *J* = 7.2 Hz, 1H), 2.93 (s, 3H), 2.45 (t, *J* = 7.1 Hz, 2H), 2.16 (q, *J* = 7.1 Hz, 2H), 1.43 – 1.36 (m, 4H), 1.34 – 1.31 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 149.4, 139.4, 131.8, 126.8 (2 x C), 126.3, 112.4 (2 x C), 40.7 (2 x C), 32.3, 31.1, 29.3, 28.2, 22.8, 22.5, 14.1, 14.0; HRMS (ESI) Calcd for C<sub>18</sub>H<sub>30</sub>N [M + H]<sup>+</sup> 260.2378, found 260.2376.



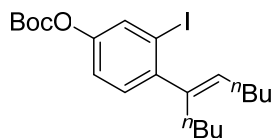
**(E)-1-(dec-5-en-5-yl)-4-fluoro-2-iodobenzene (Scheme 4, 4db): Type C Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (226.8 mg, 63 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (dd,  $J = 8.3, 2.6$  Hz, 1H), 7.06 – 7.02 (m, 1H), 7.01 – 6.96 (m, 1H), 5.25 (t,  $J = 7.2$  Hz, 1H), 2.35 (t,  $J = 7.6$  Hz, 2H), 2.17 (q,  $J = 7.1$  Hz, 2H), 1.45 – 1.37 (m, 4H), 1.33 – 1.19 (m, 4H), 0.93 (t,  $J = 7.0$  Hz, 3H), 0.86 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  160.5 (d,  $^1J_{\text{C-F}} = 249.7$  Hz), 145.2 (d,  $^4J_{\text{C-F}} = 3.4$  Hz), 142.3, 131.9, 130.0 (d,  $^3J_{\text{C-F}} = 7.7$  Hz), 125.8 (d,  $^2J_{\text{C-F}} = 23.4$  Hz), 114.6 (d,  $^2J_{\text{C-F}} = 20.6$  Hz), 98.5 (d,  $^3J_{\text{C-F}} = 7.9$  Hz), 31.7, 31.3, 30.2, 27.7, 22.8, 22.5, 14.02, 13.96; HRMS (ESI) Calcd for  $\text{C}_{16}\text{H}_{23}\text{F}$   $[\text{M} + \text{H}]^+$  361.0829, found 361.0845.



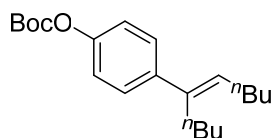
**(E)-1-(dec-5-en-5-yl)-4-fluorobenzene (Scheme 4, 4db-H): Type C Reagent (1.1 equiv),** reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, 4 h). The reaction was allowed to cool to room temperature before quenching with saturated aqueous  $\text{NH}_4\text{Cl}$  solution. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (135.0 mg, 96 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 – 7.25 (m, 2H), 6.99 – 6.95 (m, 2H), 5.57 (t,  $J = 7.3$  Hz, 1H), 2.45 (t,  $J = 7.2$  Hz, 2H), 2.17 (q,  $J = 7.2$  Hz, 2H), 1.44 – 1.34 (m, 4H), 1.30 – 1.27 (m, 3H), 0.93 (t,  $J = 7.1$  Hz, 3H), 0.86 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.7 (d,  $^2J_{\text{C-F}} = 244.6$  Hz), 139.5 (d,  $^5J_{\text{C-F}} = 3.3$  Hz), 139.1, 129.1, 127.7 (d,  $^4J_{\text{C-F}} = 7.7$  Hz), 114.8 (d,  $^3J_{\text{C-F}} = 21.1$  Hz), 32.1, 30.8, 29.6, 28.2, 22.6, 22.5, 14.03, 13.95; HRMS (ESI) Calcd for  $\text{C}_{16}\text{H}_{24}\text{F}$   $[\text{M} + \text{H}]^+$  235.1862, found 235.1865.



**(*E*)-tert-butyl (4-(dec-5-en-5-yl)-3-iodophenyl) carbonate (Scheme 4, 4eb): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (138.2 mg, 1.0 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 6 h. Silica gel chromatography (eluent: hexane/ether = 150/1 – 50/1) of the crude product afforded the title compound as a yellow oil (256.6 mg, 56 %).

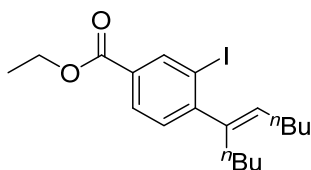
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.64 (d, *J* = 1.9 Hz, 1H), 7.11 – 7.06 (m, 2H), 5.26 (t, *J* = 7.3 Hz, 1H), 2.35 (t, *J* = 7.2 Hz, 2H), 2.16 (q, *J* = 7.1 Hz, 2H), 1.56 (s, 9H), 1.45 – 1.38 (m, 4H), 1.33 – 1.20 (m, 4H), 0.93(t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 151.6, 149.1, 146.8, 142.5, 131.8, 131.5, 129.6, 120.6, 98.4, 83.9, 3.6, 31.3, 30.2, 27.7 (3 x C), 27.6, 22.8, 22.4, 14.01, 13.96; HRMS (ESI) Calcd for C<sub>21</sub>H<sub>32</sub>O<sub>3</sub>I [M + H]<sup>+</sup> 459.1396, found 459.1389.



**(*E*)-tert-butyl (4-(dec-5-en-5-yl)phenyl) carbonate (Scheme 4, 4eb-H): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (82.9 mg, 0.6 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 4 h. The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 150/1

– 50/1) of the crude product afforded the title compound as a colourless oil (163.6 mg, 82 %).

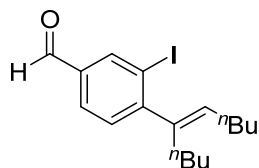
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 (d,  $J = 8.5$  Hz, 2H), 7.08 (d,  $J = 8.5$  Hz, 2H), 5.60 (t,  $J = 7.3$  Hz, 1H), 2.46 (t,  $J = 7.1$  Hz, 2H), 2.17 (q,  $J = 7.1$  Hz, 2H), 1.56 (s, 9H), 1.43 – 1.37 (m, 3H), 1.35 – 1.28 (m, 4H), 0.92 (t,  $J = 7.0$  Hz, 3H), 0.86 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.0, 149.6, 141.2, 139.2, 129.4, 127.2, 120.8, 83.4, 32.0, 30.8, 29.5, 28.2, 27.7, 22.6, 22.4, 14.0, 13.9; HRMS (ESI) Calcd for  $\text{C}_{21}\text{H}_{33}\text{O}_3$   $[\text{M} + \text{H}]^+$  333.2430, found 333.2421.



**(*E*)-ethyl 4-(dec-5-en-5-yl)-3-iodobenzoate (Scheme 4, 4fb): Type D Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 10 mol % Xantphos, 20 °C, 5 h). Reaction mixture was cooled to 0 °C.  $(\text{CH}_3)_3\text{SiCH}_2\text{MgBr}$  (1.67 mL, 0.9 M, 1.5 mmol) was added dropwise and the reaction mixture was allowed to stir for 1 h before 5-decyne (138.2 mg, 1.0 mmol) was added. The reaction was then heated to 60 °C and stirred for 6 h. Silica gel chromatography (eluent: hexane/ether = 150/1 – 50/1) of the crude product afforded the title compound as a light yellow oil (306.6 mg, 74 %).

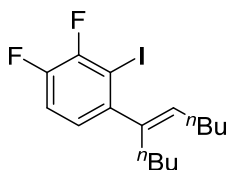
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.49 (d,  $J = 1.7$  Hz, 1H), 7.93 (dd,  $J = 7.9, 1.7$  Hz, 1H), 7.15 (d,  $J = 7.9$  Hz, 1H), 5.29 (t,  $J = 7.3$  Hz, 1H), 4.37 (q,  $J = 7.1$  Hz, 2H), 2.39 (t,  $J = 7.7$  Hz, 2H), 2.19 (q,  $J = 6.7$  Hz, 1H), 1.46 – 1.40 (m, 4H), 1.39 (t,  $J = 7.1$  Hz, 3H), 1.33 – 1.19 (m, 4H), 0.94 (t,  $J = 7.1$  Hz, 3H), 0.85 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1,

153.7, 142.7, 140.2, 131.9, 130.0, 129.4, 128.8, 98.8, 61.2, 31.6, 31.0, 30.2, 27.7, 22.8, 22.5, 14.3, 14.0, 13.9; HRMS (ESI) Calcd for  $C_{19}H_{28}IO_2$   $[M + H]^+$  415.1134, found 415.1149.



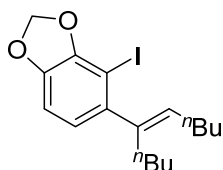
**(E)-4-(dec-5-en-5-yl)-3-iodobenzaldehyde (Scheme 4, 4gb): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol %  $CoCl_2$ , 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (138.2 mg, 1.0 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 6 h. The reaction mixture was cooled to room temperature before addition of  $I_2$  (3 equiv) and allowed to stir for 1 h. Aqueous HCl (1.5 mL, 1 M) was then added and stirred for 1 hr. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (321.9 mg, 87 %).

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  9.91 (s, 1H), 8.33 (d,  $J = 1.6$  Hz, 1H), 7.78 (dd,  $J = 7.8, 1.7$  Hz, 1H), 7.25 (d,  $J = 7.3$  Hz, 1H), 5.32 (t,  $J = 7.3$  Hz, 1H), 2.41 (t,  $J = 7.6$  Hz, 2H), 2.20 (q,  $J = 7.1$  Hz, 2H), 1.47 – 1.39 (m, 4H), 1.34 – 1.20 (m, 4H), 0.94 (t,  $J = 7.0$  Hz, 3H), 0.86 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  190.4, 155.5, 142.6, 140.7, 135.9, 132.2, 130.1, 128.7, 99.6, 31.5, 31.0, 30.3, 27.7, 22.8, 22.5, 14.0, 13.9; HRMS (ESI) Calcd for  $C_{17}H_{24}IO$   $[M + H]^+$  371.0872, found 371.0867.



**(E)-1-(dec-5-en-5-yl)-3,4-difluoro-2-iodobenzene (Scheme 4, 4hb): Type D Reagent (1.1 equiv)**, Zinc Reagent was prepared in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 5 h). The reaction mixture was cooled to 0 °C. (CH<sub>3</sub>)<sub>3</sub>SiCH<sub>2</sub>MgBr (1 mL, 0.9 M, 0.9 mmol) was added dropwise and the reaction mixture was allowed to stir for 1 h before 5-decyne (110.5 mg, 0.8 mmol) was added. The reaction was then heated to 60 °C and stirred for 6 h. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a colourless oil (287.5 mg, 95 %).

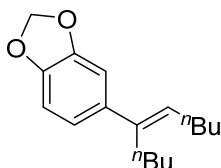
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.06 (dt, <sup>2</sup>J<sub>H-F</sub> = 9.6, <sup>2</sup>J<sub>H-H</sub> = 8.1 Hz, 1H), 6.86 (ddd, <sup>2</sup>J<sub>H-H</sub> = 8.5, <sup>3</sup>J<sub>H-F</sub> = 5.1, <sup>4</sup>J<sub>H-F</sub> = 1.9 Hz, 1H), 5.27 (t, *J* = 7.3 Hz, 1H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.18 (q, *J* = 7.1 Hz, 2H), 1.46-1.38 (m, 4H), 1.32 – 1.19 (m, 4H), 0.93 (t, *J* = 7.1 Hz, 2H), 0.86 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 149.78 (dd, <sup>1</sup>J<sub>C-F</sub> = 245.1, 13.7 Hz), 148.16 (dd, <sup>1</sup>J<sub>C-F</sub> = 251.0, 15.6 Hz), 146.35 (d, <sup>3</sup>J<sub>C-F</sub> = 4.0 Hz), 141.62 (d, <sup>4</sup>J<sub>C-F</sub> = 1.3 Hz), 132.37 (d, <sup>5</sup>J<sub>C-F</sub> = 0.7 Hz), 124.49 (dd, <sup>3</sup>J<sub>C-F</sub> = 6.1, 3.3 Hz), 116.23 (dd, <sup>2</sup>J<sub>C-F</sub> = 17.2, 1.4 Hz), 88.15 (d, <sup>2</sup>J<sub>C-F</sub> = 20.2 Hz), 31.6, 31.2, 30.2, 27.6, 22.8, 22.4, 14.0, 13.9; HRMS (ESI) Calcd for C<sub>16</sub>H<sub>22</sub>F<sub>2</sub>I [M + H]<sup>+</sup> 379.0734, found 379.0750.



**(E)-5-(dec-5-en-5-yl)-4-iodobenzo[d][1,3]dioxole (Scheme 4, 4ib): Type B Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %

CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (301.3 mg, 78%).

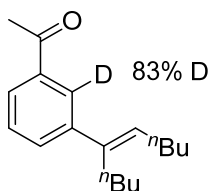
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.69 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 1H), 6.02 (s, 2H), 5.25 (t, *J* = 7.3 Hz, 1H), 2.34 (t, *J* = 7.3 Hz, 2H), 2.16 (q, *J* = 7.1 Hz, 2H), 1.46 – 1.37 (m, 4H), 1.33 – 1.20 (m, 4H), 0.93 (t, *J* = 7.0 Hz, 3H), 0.86 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 149.2, 144.3, 142.5, 141.7, 131.7, 122.3, 107.5 (2 x C), 100.4, 31.8, 31.5, 30.3, 27.7, 22.8, 22.4, 14.03, 13.98; C<sub>17</sub>H<sub>23</sub>O<sub>2</sub>INa [M + Na]<sup>+</sup> 409.0641, found 409.0660.



**(*E*)-5-(dec-5-en-5-yl)benzo[*d*][1,3]dioxole (Scheme 4, 4ib-H): Type B Reagent (1.1 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (140.6 mg, 90%).

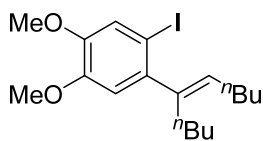
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.83 (d, *J* = 1.7 Hz, 1H), 6.80 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 5.93 (s, 2H), 5.54 (t, *J* = 7.2 Hz, 1H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.40 – 1.38 (m, 4H), 1.31 – 1.28 (m, 4H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 147.4, 146.1, 139.6, 138.0, 128.3, 119.5,

107.9, 107.0, 100.8, 32.1, 30.9, 29.7, 28.2, 22.7, 22.4, 14.03, 13.98; HRMS (ESI) Calcd for  $C_{17}H_{25}O_2$   $[M + H]^+$  261.1855, found 261.1861.

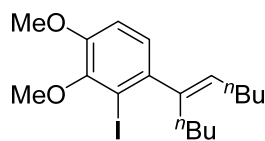


**(E)-1-(3-(dec-5-en-5-yl)phenyl)-2-deuterium-ethanone (Scheme 4, 3jb-d): Type A Reagent (1.67 equiv)**, Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol %  $CoCl_2$ , 5 mol % Xantphos, 20 °C, Overnight). 5-decyne (138.2 mg, 1.0 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and stirred for 6 h. The reaction was cooled to room temperature before quenching with  $D_2O$  (0.5 mL, 25 mmol). Aqueous HCl (1.5 mL, 1 M) was then added and stirred for 1 hr. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (204.1 mg, 79 %).

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.79 (d,  $J = 7.7$  Hz, 1H), 7.52 (d,  $J = 7.8$  Hz, 1H), 7.37 (t,  $J = 7.7$  Hz, 1H), 5.69 (t,  $J = 7.4$  Hz, 1H), 2.60 (s, 3H), 2.52 (t,  $J = 6.9$  Hz, 3H), 2.21 (q,  $J = 7.2$  Hz, 2H), 1.44 – 1.37 (m, 4H), 1.35 – 1.26 (m, 4H), 0.93 (t,  $J = 7.1$  Hz, 3H), 0.87 (d,  $J = 6.9$  Hz, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  198.1, 143.8, 139.2, 136.9, 130.9, 130.2, 128.2, 126.3, 31.9, 30.7, 29.2, 28.2, 26.5, 22.5, 22.4, 13.9, 13.8 (Unable to identify C-D coupling); HRMS (ESI) Calcd for  $C_{18}H_{26}OD$   $[M + H]^+$  260.2125, found 260.2136.



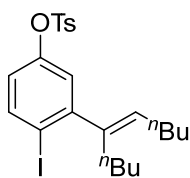
4kb



4kb'

**(E)-1-(dec-5-en-5-yl)-2-iodo-4,5-dimethoxybenzene (major) (Scheme 4, 4kb): Type B Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (285.6 mg, 71% regioselectivity **4kb**:**4kb'** = 87:13, isolated).

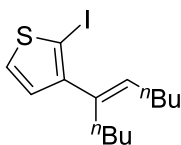
**(4kb)** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.23 (s, 1H), 6.63 (s, 1H), 5.27 (t, *J* = 7.3 Hz, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.17 (q, *J* = 7.0 Hz, 2H), 1.46 – 1.40 (m, 4H), 1.33 – 1.24 (m, 4H), 0.94 (t, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 148.6, 147.8, 141.82, 141.76, 131.5, 121.3, 112.4, 87.1, 56.0, 55.8, 31.6, 31.4, 30.2, 27.6, 22.8, 22.4, 13.98, 13.95; **(4kb')** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.81 (s, 2H), 5.24 (t, *J* = 7.3 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.35 (t, *J* = 7.6 Hz, 2H), 2.16 (q, *J* = 6.9 Hz, 2H), 1.44 – 1.38 (m, 4H), 1.33 – 1.22 (m, 4H), 0.93 (t, *J* = 6.5 Hz, 3H), 0.86 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 150.7, 148.5, 143.0, 142.7, 131.2, 124.9, 111.7, 98.2, 60.2, 56.0, 31.7, 31.4, 30.3, 27.6, 22.8, 22.4, 14.0, 13.99; HRMS (ESI) Calcd for C<sub>18</sub>H<sub>28</sub>OI [M + H]<sup>+</sup> 403.113, found 403.1146.



**(E)-3-(dec-5-en-5-yl)-4-iodophenyl 4-methylbenzenesulfonate (Scheme 4, 4lb): Type A Reagent (1.5 equiv)**, Zinc Reagent was prepared in 1.2 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 7 h). 5-decyne (138.2 mg, 1.0 mmol) was added to the reaction mixture. The reaction mixture was then heated to 60 °C and

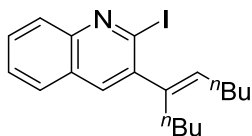
stirred for 6 h. (Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (225.5 mg, 44 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.74 – 7.69 (m, 3H), 7.31 (d,  $J = 8.1$  Hz, 2H), 6.65 – 6.62 (m, 2H), 5.15 (t,  $J = 7.3$  Hz, 1H), 2.44 (s, 3H), 2.27 (t,  $J = 7.8$  Hz, 2H), 2.12 (q,  $J = 7.1$  Hz, 2H), 1.40 – 1.37 (m, 4H), 1.30 – 1.20 (m, 2H), 1.13–1.06 (m, 2H), 0.92 (t,  $J = 7.2$  Hz, 3H), 0.85 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  150.7, 149.4, 145.4, 142.2, 140.0, 132.2, 132.1, 129.8 (2 x C), 128.6 (2 x C), 123.5, 122.0, 96.8, 31.6, 30.8, 30.0, 27.6, 22.7, 22.4, 21.7, 14.0, 13.9; HRMS (ESI) Calcd for  $\text{C}_{23}\text{H}_{30}\text{O}_3\text{SI}$   $[\text{M} + \text{H}]^+$  513.0960, found 513.0958.



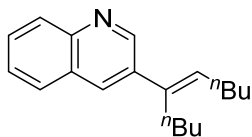
**(E)-3-(dec-5-en-5-yl)-2-iodothiophene (Scheme 4, 4mb): Type A Reagent (1.5 equiv),** Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 20 °C, 8 h). 5-decyne (138.5 mg, 1.0 mmol) was added. The reaction was then heated to 60 °C and stirred for 6 h. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (320.4 mg, 92 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 (d,  $J = 5.6$  Hz, 1H), 6.72 (d,  $J = 5.5$  Hz, 1H), 5.47 (t,  $J = 7.3$  Hz, 1H), 2.35 (t,  $J = 7.4$  Hz, 2H), 2.18 (q,  $J = 7.3$  Hz, 2H), 1.46 – 1.40 (m, 4H), 1.33 – 1.18 (m, 4H), 0.93 (t,  $J = 7.1$  Hz, 3H), 0.86 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  149.6, 135.5, 132.7, 130.2, 127.6, 73.6, 31.8, 30.7, 30.4, 27.9, 22.53, 22.47, 14.04, 13.97; HRMS (ESI) Calcd for  $\text{C}_{14}\text{H}_{22}\text{SI}$   $[\text{M} + \text{H}]^+$  349.0487, found 349.0461.



**(E)-3-(dec-5-en-5-yl)-2-iodoquinoline (Scheme 4, 4nb): Type D Reagent (1.67 equiv),** Zinc Reagent was prepared in 1.67 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 20 h). The reaction mixture was cooled to 0 °C. (CH<sub>3</sub>)<sub>3</sub>SiCH<sub>2</sub>MgBr (1.56 mL, 0.9 M, 1.4 mmol) was added dropwise and the reaction mixture was allowed to stir for 1 h before 5-decyne (138.2 mg, 1.0 mmol) was added. The reaction was then heated to 60 °C and stirred for 4 h. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (161.3 mg, 41 %).

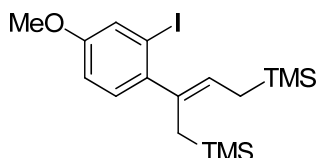
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.04 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.70 (s, 1H), 7.65 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.53 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 5.44 (t, *J* = 7.3 Hz, 1H), 2.49 (t, *J* = 7.4 Hz, 2H), 2.23 (q, *J* = 7.1 Hz, 2H), 1.49 – 1.38 (m, 4H), 1.34 – 1.26 (m, 4H), 0.96 (t, *J* = 7.1 Hz, 2H), 0.87 (t, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 147.9, 143.0, 141.0, 134.7, 133.6, 129.5, 128.5, 127.4, 127.1, 127.0, 125.6, 31.5, 31.4, 30.3, 27.8, 22.7, 22.5, 14.0, 13.9; HRMS (ESI) Calcd for C<sub>19</sub>H<sub>25</sub>NI [M + H]<sup>+</sup> 394.1032, found 394.1028.



**(E)-3-(dec-5-en-5-yl)quinoline (Scheme 4, 4nb-H): Type D Reagent (1.5 equiv),** Zinc Reagent was prepared in 2.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 20 h). Zinc Reagent (1.1 mL, 0.9 mmol) was transferred to a freshly dried Schlenk tube and cooled to 0 °C. (CH<sub>3</sub>)<sub>3</sub>SiCH<sub>2</sub>MgBr (1.1 mL, 0.9 M, 0.9 mmol)

was added dropwise and the reaction mixture was allowed to stir for 1 h before 5-decyne (82.9 mg, 0.6 mmol) was added. The reaction was then heated to 60 °C and stirred for 4 h. The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (97.9 mg, 61 %).

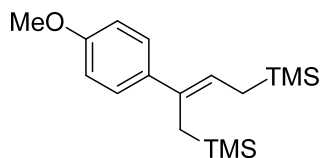
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.95 (d, *J* = 2.3 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 2.0 Hz, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 5.83 (t, *J* = 7.3 Hz, 1H), 2.61 (t, *J* = 7.3 Hz, 2H), 2.27 (q, *J* = 7.2 Hz, 2H), 1.48 – 1.40 (m, 4H), 1.38 – 1.34 (m, 4H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 150.0, 147.0, 137.2, 136.0, 131.8, 131.7, 129.0, 128.7, 128.0, 127.7, 126.6, 32.0, 30.8, 29.2, 28.4, 22.6, 22.5, 14.0, 13.9.; HRMS (ESI) Calcd for C<sub>19</sub>H<sub>26</sub>N [M + H]<sup>+</sup> 268.2065, found 268.2064.



**(Z)-2-(2-iodo-4-methoxyphenyl)but-2-ene-1,4-diylbis(trimethylsilane) (Scheme 4, 4ac): Type B Reagent (1.2 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a colourless oil (224.9 mg, 52%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 (d, *J* = 2.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.81 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.23 (t, *J* = 8.5 Hz, 1H), 3.77 (s, 3H), 1.89 (s, 2H), 1.49 (d, *J* = 8.5 Hz, 2H), 0.07 (s, 9H), -0.10 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.0, 143.2, 138.1, 130.2,

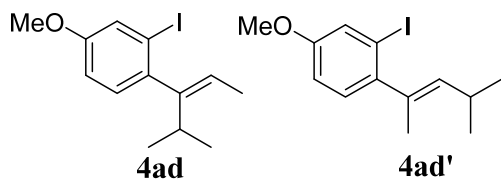
124.8, 124.2, 113.7, 98.9, 55.4, 22.9, 19.5, -0.6 (3 x C), -1.2 (3 x C); HRMS (ESI) Calcd for C<sub>17</sub>H<sub>29</sub>IOSi<sub>2</sub> [M + H]<sup>+</sup> 455.0699, found 455.0700.



**(Z)-2-(4-methoxyphenyl)but-2-ene-1,4-diylbis(trimethylsilane) (Scheme 4, 4ac-H):**

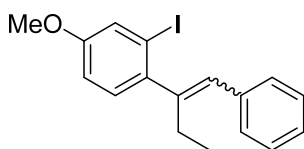
**Type B Reagent (1.2 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). The reaction was allowed to cool to room temperature before quenching with saturated aqueous NH<sub>4</sub>Cl solution. Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (119.6 mg, 65%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.23 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.49 (t, *J* = 8.4 Hz, 1H), 3.80 (s, 3H), 1.90 (s, 2H), 1.51 (d, *J* = 8.4 Hz, 2H), 0.03 (s, 9H), -0.14 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.0, 138.0, 135.1, 127.4, 120.4, 113.3, 55.2, 20.5, 20.0, -0.8, -1.5; HRMS (ESI) Calcd for C<sub>17</sub>H<sub>31</sub>OSi<sub>2</sub> [M + H]<sup>+</sup> 307.1913, found 307.1926.



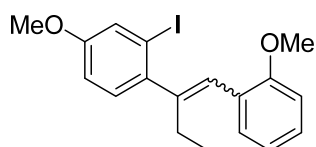
**(E)-2-iodo-4-methoxy-1-(4-methylpent-2-en-3-yl)benzene (Scheme 4, 4ad): Type C Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 6 h). Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a yellow oil (101.6 mg, 75 %, regioselectivity **4ad:4ad'** = 53:47, determined by <sup>1</sup>H NMR after isolation).

**(4ad)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 (d,  $J = 2.7$  Hz, 1H), 7.01 (d,  $J = 8.5$  Hz, 1H), 6.84 (dd,  $J = 8.5, 2.7$  Hz, 1H), 5.23 (q,  $J = 6.9$  Hz, 1H), 3.78 (s, 3H), 3.02 (septet,  $J = 7.0$  Hz, 1H), 1.80 (d,  $J = 6.9$  Hz, 3H), 1.03-0.94 (m, 6H); **(4ad')**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 (d,  $J = 2.6$  Hz, 1H), 7.04 (d,  $J = 8.4$  Hz, 1H), 6.82 (dd,  $J = 8.5, 2.7$  Hz, 1H), 5.10 (dd,  $J = 9.3, 1.4$  Hz, 1H), 3.78 (s, 3H), 2.70 – 2.61 (m, 1H), 1.90 (d,  $J = 1.4$  Hz, 3H), 1.05 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.1, 158.0, 147.8, 142.8, 139.9, 138.5, 135.8, 129.3, 128.9, 125.6, 124.0, 123.9, 114.1, 113.3, 102.1, 98.4, 55.5, 55.4, 29.4, 27.6, 22.6, 21.8 (broad peak), 18.0, 13.2 ( $^{13}\text{C}$  NMR of 2 isomers are indistinguishable); HRMS (ESI) Calcd for  $\text{C}_{13}\text{H}_{18}\text{OI}$   $[\text{M} + \text{H}]^+$  317.0402, found 317.0393.



**(E)-2-iodo-4-methoxy-1-(1-phenylbut-1-en-2-yl)benzene (Scheme 4, 4ae): Type C Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 10 mol %  $\text{P}(\text{OPh})_3$ , 60 °C, 12 h). Silica gel chromatography (eluent: hexane) of the crude product afforded the title compound as a light yellow oil (316.9 mg, 87%,  $E:Z = 91:9$  - Determined with  $^1\text{H}$  NMR after isolation).

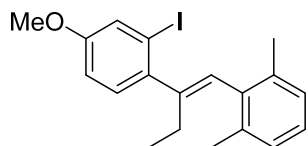
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (d,  $J = 2.6$  Hz, 1H), 7.38 – 7.34 (m, 4H), 7.28 – 7.24 (m, 1H), 7.12 (d,  $J = 8.5$  Hz, 1H), 6.90 (dd,  $J = 8.4, 2.5$  Hz, 1H), 6.32 (s, 1H), 3.80 (s, 3H), 2.61 (q,  $J = 7.6$  Hz, 2H), 0.97 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.5, 146.7, 140.6, 137.6, 130.4, 129.5, 128.7 (2 x C), 128.2 (2 x C), 126.7, 124.1, 113.9, 99.2, 55.5, 25.5, 12.5; HRMS (ESI) Calcd for  $\text{C}_{17}\text{H}_{18}\text{OI}$   $[\text{M} + \text{H}]^+$  365.0402, found 365.0417.



**(E)-2-iodo-4-methoxy-1-(1-(2-methoxyphenyl)but-1-en-2-yl)benzene (Scheme 4, 4af):**

**Type C Reagent (1.1 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 10 mol % P(OPh)<sub>3</sub>, 60 °C, 12 h). Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (134.8 mg, 57%, *E:Z* = 78:22 - Determined with <sup>1</sup>H NMR after isolation).

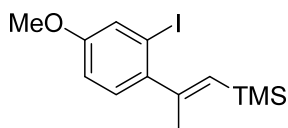
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.42 (d, *J* = 2.6 Hz, 1H), 7.39 – 7.37 (m, 1H), 7.26 – 7.24 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.98 (td, *J* = 7.4, 1.2 Hz, 1H), 6.89 (dd, *J* = 8.5, 2.6 Hz, 2H), 6.38 (s, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 2.57 (qd, *J* = 7.5, 1.0 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.4, 157.4, 146.2, 140.6, 129.8, 129.6, 128.2, 126.6, 126.3, 124.1, 120.1, 113.9, 110.6, 99.4, 55.48, 55.46, 25.7, 12.6; HRMS (ESI) Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>I [M + H]<sup>+</sup> 395.0508, found 395.0515.



**(E)-2-(2-(2-iodo-4-methoxyphenyl)but-1-en-1-yl)-1,3-dimethylbenzene (Scheme 4,**

**4ag): Type C Reagent (1.1 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 10 mol % P(OPh)<sub>3</sub>, 60 °C, 12 h). Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a yellow solid (183.6 mg, 78 %). m.p. 63.8–64.9 °C.

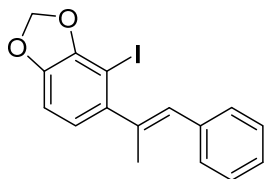
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (d,  $J = 2.6$  Hz, 1H), 7.16 – 7.06 (m, 4H), 6.91 (dd,  $J = 8.4, 2.6$  Hz, 1H), 6.19 (s, 1H), 3.81 (s, 3H), 2.37 (s, 6H), 2.22 (q,  $J = 7.4$  Hz, 2H), 0.74 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.5, 147.1, 140.2, 136.5 (2 x C), 136.4, 130.6, 128.7, 127.1 (2 x C), 126.6, 124.2, 113.9, 97.6, 55.5, 25.1, 21.0 (2 x C), 11.9; HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{22}\text{OI}$   $[\text{M} + \text{H}]^+$  393.0715, found 393.0746.



**(E)-2-(2-iodo-4-methoxyphenyl)prop-1-en-1-yl)trimethylsilane (Scheme 4, 4ah):**

**Type B Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, 12 h). Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a light yellow oil (218.2 mg, 63%).

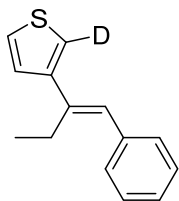
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 (d,  $J = 2.6$  Hz, 1H), 7.05 (d,  $J = 8.4$  Hz, 1H), 6.84 (dd,  $J = 8.4, 2.6$  Hz, 1H), 5.37 (d,  $J = 1.1$  Hz, 1H), 3.78 (s, 3H), 2.07 (d,  $J = 1.1$  Hz, 3H), 0.21 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.1, 155.9, 144.7, 139.8, 127.7, 123.9, 114.1, 96.5, 55.4, 23.2, -0.2 (3 x C); HRMS (ESI) Calcd for  $\text{C}_{13}\text{H}_{20}\text{OSi}_2\text{I}$   $[\text{M} + \text{H}]^+$  347.0328, found 347.0328.



**(E)-4-iodo-5-(1-phenylprop-1-en-2-yl)benzo[d][1,3]dioxole (Scheme 4, 4ii): Type C Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos

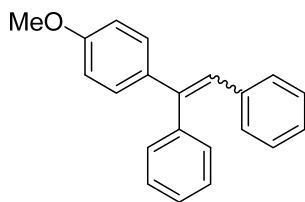
catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 10 mol % P(OPh)<sub>3</sub>, 60 °C, 12 h). Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a yellow solid (324.1 mg, 89 %). m.p. 58.3-59.5 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38 (d, *J* = 4.5 Hz, 1H), 7.28 – 7.39 (m, 1H), 6.79 – 6.74 (m, 2H), 6.37 (q, *J* = 1.5 Hz, 1H), 6.05 (s, 2H), 2.16 (d, *J* = 1.5 Hz, 1H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 149.5, 144.7, 143.7, 140.1, 137.6, 130.8, 128.9, 128.2, 126.7, 121.4, 107.9, 100.6, 20.1; HRMS (ESI) Calcd for C<sub>25</sub>H<sub>30</sub>IO [M + H]<sup>+</sup> 473.1341, found 473.1346.



**(*E*)-3-(1-phenylbut-1-en-2-yl)-2-deuterium-thiophene (Scheme 4, 3me-*d*): Type D Reagent (1.5 equiv)**, Zinc Reagent was prepared in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 20 °C, 8 h). The reaction mixture was cooled to 0 °C. (CH<sub>3</sub>)<sub>3</sub>SiCH<sub>2</sub>MgBr (1.0 mL, 0.9 M, 0.92 mmol) was added dropwise and the reaction mixture was allowed to stir for 1 h before but-1-yn-1-ylbenzene (87.2 mg, 0.67 mmol) was added. The reaction was then heated to 60 °C and stirred for 6 h. The reaction was cooled to room temperature before quenching with D<sub>2</sub>O (0.5 mL, 25 mmol). Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (49.1 mg, 34 %).

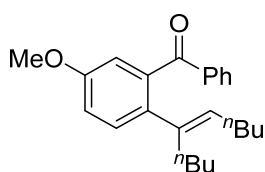
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37 – 7.18 (m, 7H), 6.86 (s, 1H), 2.67 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 143.5, 138.7, 137.9, 128.7 (2 x C), 128.2 (2 x C), 126.5, 126.1, 125.8, 125.4, 120.0 (t, *J*<sub>C-D</sub> = 28.1 Hz), 23.5, 14.0; HRMS (ESI) Calcd for C<sub>14</sub>H<sub>14</sub>SD [M + H]<sup>+</sup> 216.0957, found 216.0956.



**(1-(4-methoxyphenyl)ethene-1,2-diyl)dibenzene (Scheme 4, 3aj): Type C Reagent (1.5 equiv)**, reaction was carried out in 0.6 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 80 °C, 4 h). Silica gel chromatography (eluent: hexane) of the crude product afforded the title compound as a light yellow oil (137.5 mg, 80%, *E:Z* = 60:40 – Determined Using <sup>1</sup>H NMR after isolation).<sup>23</sup>

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34 – 7.24 (m, 5H), 7.21 – 7.19 (m, 1H), 7.16 – 7.05 (m, 5H), 7.01 – 6.99 (m, 1H), 6.90 – 6.89 (m, 1H), 6.87 – 6.83 (m, 2H), 3.82 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 159.2, 142.1, 140.5, 137.6, 136.0, 130.4, 129.4, 128.7, 128.5, 128.0, 127.3, 126.5, 126.4, 113.6, 55.3; HRMS (ESI) Calcd for C<sub>21</sub>H<sub>19</sub>O [M + H]<sup>+</sup> 287.1436, found 287.1432.

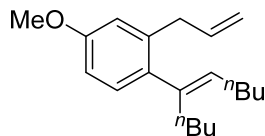
### Transition-Metal Catalyzed Transformation of 2-Alkenylarylzinc Species



**(*E*)-(2-(dec-5-en-5-yl)-5-methoxyphenyl)(phenyl)methanone (Scheme 5, 5): Type B Reagent (1.1 equiv)**, reaction was carried out in 5.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, overnight). To the reaction was added a THF solution of CuCN·LiCl (1 mL of 1 M solution, 1 mmol) at -20 °C followed by the addition of benzoyl chloride (0.63 g, 4.5 mmol). The reaction was then stirred at 0 °C for 4

h. The reaction was then quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (10 mL), and dilute with ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (1.20 g, 76 %).

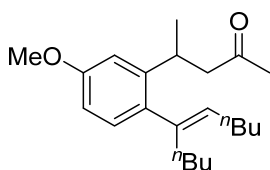
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 (dd,  $J = 8.3, 1.3$  Hz, 2H), 7.51 (ddd,  $J = 7.0, 2.5, 1.3$  Hz, 1H), 7.40–7.36 (m, 2H), 7.22 (d,  $J = 8.5$  Hz, 1H), 6.98 (dd,  $J = 8.5, 2.8$  Hz, 1H), 6.89 (d,  $J = 2.7$  Hz, 1H), 5.25 (t,  $J = 7.3$  Hz, 1H), 3.81 (s, 3H), 2.13 (t,  $J = 7.3$  Hz, 2H), 1.88 (q,  $J = 7.1$  Hz, 2H), 1.18–1.11 (m, 8H), 0.80 (t,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1, 157.8, 139.5, 138.6, 137.8, 136.2, 132.8, 132.6, 130.0 (2 x C), 128.1 (2 x C), 115.8, 113.1, 55.4, 31.49, 31.47, 30.7, 28.1, 22.8, 22.3, 14.0, 13.9; HRMS (ESI) Calcd for  $\text{C}_{24}\text{H}_{31}\text{O}_2$   $[\text{M} + \text{H}]^+$  351.2324, found 351.2316.



**(*E*)-2-allyl-1-(dec-5-en-5-yl)-4-methoxybenzene (Scheme 5, 6): Type B Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a THF solution of  $\text{CuCN}\cdot\text{LiCl}$  (0.2 mL of 1 M solution, 0.2 mmol) at -20 °C followed by the addition of allyl bromide (96.8 mg, 0.8 mmol). The reaction was then warmed to room temperature and stirred for 4 h. The reaction was then quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (10 mL), and dilute with ethyl acetate (5 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated

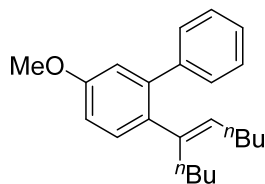
under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (178.7 mg, 78 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.98 (d,  $J = 8.3$  Hz, 1H), 6.74 (d,  $J = 2.7$  Hz, 1H), 6.69 (dd,  $J = 8.3, 2.8$  Hz, 1H), 5.97 – 5.87 (m, 1H), 5.20 (t,  $J = 7.3$  Hz, 1H), 5.06 (q,  $J = 1.6$  Hz, 1H), 5.04 – 5.01 (m, 1H), 3.78 (s, 3H), 3.34 (dt,  $J = 6.6, 1.5$  Hz, 2H), 2.29 (t,  $J = 7.4$  Hz, 2H), 2.15 (q,  $J = 7.1$  Hz, 2H), 1.41 – 1.35 (m, 4H), 1.28 – 1.21 (m, 4H), 0.922 (t,  $J = 7.4$  Hz, 3H), 0.85 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.0, 139.5, 138.6, 138.0, 137.0, 130.3, 130.2, 115.6, 114.5, 110.9, 55.1, 37.4, 32.2, 32.1, 30.4, 27.8, 22.9, 22.5, 14.04, 13.99; HRMS (ESI) Calcd for  $\text{C}_{20}\text{H}_{31}\text{O}$   $[\text{M} + \text{H}]^+$  287.2375, found 287.2377.



**(*E*)-4-(2-(dec-5-en-5-yl)-5-methoxyphenyl)pentan-2-one (Scheme 5, 7): Type E Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a THF solution of  $\text{CuCN}\cdot 2\text{LiCl}$  (0.2 mL of 1 M solution, 0.2 mmol) at -20 °C, followed by the addition of (*E*)-pent-3-en-2-one (67.3 mg, 0.8 mmol) and chlorotrimethylsilane (173.8 mg, 1.6 mmol). The reaction was then warmed to room temperature and stirred for 5 h. The reaction was then quenched by aqueous solution of HCl (3 mL, 1 M) and allowed to stir for 1 h before diluted with ethyl acetate (5 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (166.4 mg, 63 %).

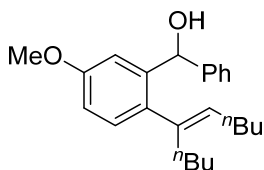
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.95 (d,  $J = 7.9$  Hz, 1H), 6.74 (d,  $J = 2.6$  Hz, 1H), 6.68 (dd,  $J = 8.3, 2.7$  Hz, 1H), 5.19 (t,  $J = 7.2$  Hz, 1H), 3.80 (s, 3H), 3.52 – 3.44 (m, 1H), 2.68 – 2.55 (m, 2H), 2.39 – 2.23 (m, 2H), 2.16 (q,  $J = 7.1$  Hz, 2H), 2.08 (s, 3H), 1.43 – 1.34 (m, 4H), 1.30 – 1.23 (m, 4H), 1.18 (d,  $J = 6.7$  Hz, 3H), 0.92 (t,  $J = 6.9$  Hz, 3H), 0.85 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  207.7, 158.3, 145.1, 139.7, 136.3, 130.5, 111.6, 110.2 (2 x C), 55.1, 52.2, 32.5, 32.1, 31.1, 30.4, 30.1, 27.8, 22.8, 22.41, 21.9, 13.99, 13.96; HRMS (ESI) Calcd for  $\text{C}_{22}\text{H}_{35}\text{O}_2$   $[\text{M} + \text{H}]^+$  331.2637, found 331.2637.



**(*E*)-2-(dec-5-en-5-yl)-5-methoxy-1,1'-biphenyl (Scheme 5, 8): Type B Reagent (1.1 equiv)**, reaction was carried out in 3.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, overnight). To the reaction was added a THF solution of  $\text{Pd}_2(\text{dba})_3/\text{SPhos}$  (0.5 mL of 0.12 M solution, 0.06 mmol) at 20 °C followed by the addition of iodobenzene (0.55 g, 2.7 mmol). The reaction was then stirred for 4 h. The reaction was then quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (10 mL), and dilute with ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a colourless oil (0.61 g, 70 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.39 (m, 2H), 7.35 – 7.28 (m, 3H), 7.13 – 7.11 (m, 1H), 6.83 – 6.81 (m, 2H), 5.39 (t,  $J = 7.3$  Hz, 1H), 3.82 (s, 3H), 2.09 – 2.03 (m, 2H), 1.80 – 1.76 (m, 2H), 1.35 – 1.29 (m, 4H), 1.10 – 1.02 (m, 4H), 0.90 (t,  $J = 7.0$  Hz, 3H), 0.72 (t,

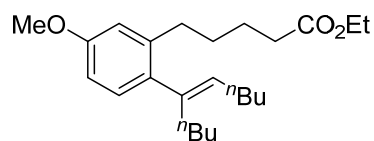
$J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.2, 142.3, 141.1, 140.7, 136.2, 131.33, 131.2, 129.0 (2 x C), 127.8 (2 x C), 126.7, 115.2, 112.2, 55.3, 31.9, 30.5, 30.4, 27.8, 22.6, 22.4, 14.0, 13.9; HRMS (ESI) Calcd for  $\text{C}_{23}\text{H}_{31}\text{O}$   $[\text{M} + \text{H}]^+$  323.2375, found 323.2377.



**(E)-2-(2-(dec-5-en-5-yl)-5-methoxyphenyl)(phenyl)ethanol (Scheme 5, 9): Type E**

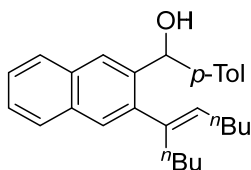
**Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol %  $\text{CoCl}_2$ , 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a  $\text{Ni}(\text{acac})_2$  (25.7 mg, 0.1 mmol, 10 mol %) at 20 °C, followed by benzaldehyde (95.5 mg, 0.9 mmol). The reaction was stirred for 5 h. The reaction was then quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (2 mL), and dilute with ethyl acetate (3 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (222.1 mg, 70 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 – 7.28 (m, 4H), 7.26 – 7.22 (m, 1H), 7.01 (d,  $J = 8.5$  Hz, 1H), 6.93 (d,  $J = 2.5$  Hz, 1H), 6.77 (dd,  $J = 8.2, 2.6$  Hz, 1H), 6.01 (d,  $J = 3.7$  Hz, 1H), 5.19 (t,  $J = 7.2$  Hz, 1H), 3.75 (s, 3H), 2.36 – 2.26 (m, 2H), 2.15 – 2.10 (m, 3H), 1.33–1.31 (m, 4H), 1.28 – 1.26 (m, 4H), 0.89 (t,  $J = 6.8$  Hz, 3H), 0.84 (t,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.4, 143.9, 142.3, 139.0, 136.4, 131.4, 130.4, 128.2 (2 x C), 127.1, 126.7 (2 x C), 112.9, 112.3, 72.5, 55.2 32.5, 31.9, 30.4, 27.8, 22.8, 22.4, 14.0, 13.9; HRMS (ESI) Calcd for  $\text{C}_{24}\text{H}_{33}\text{O}_2$   $[\text{M} + \text{H}]^+$  353.2481, found 353.2479.



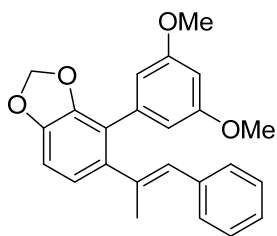
**((E)-ethyl-5-(2-(dec-5-en-5-yl)-5-methoxyphenyl)pentanoate (Scheme 5, 10): Type E Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a FeCl<sub>3</sub> (8.1 mg, 0.05 mmol, 5 mol %) at 20 °C, followed by ethyl 5-bromopentanoate (125.4 mg, 0.6 mmol). The reaction was stirred at room temperature for 20 h. The reaction was then quenched by saturated aqueous solution of NH<sub>4</sub>Cl (2 mL), and dilute with ethyl acetate (3 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a light yellow oil (116.9 mg, 52 %).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.94 (d, *J* = 8.3 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 6.66 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.19 (t, *J* = 7.2 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.57-2.53 (m, 2H), 2.32 – 2.26 (m, 4H), 2.15 (q, *J* = 7.0 Hz, 2H), 1.71 – 1.56 (m, 4H), 1.41-1.36 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 7H), 0.93 (t, *J* = 7.2 Hz 3H), 0.85 (t, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 173.60 158.0, 140.8, 139.9, 137.0, 130.3, 130.1, 114.1, 110.3, 60.2, 55.1, 34.3, 32.8, 32.3, 32.1, 31.1, 30.4, 27.8, 25.1, 22.8, 22.4, 14.2, 13.99, 13.96; HRMS (ESI) Calcd for C<sub>24</sub>H<sub>39</sub>O<sub>3</sub> [M + H]<sup>+</sup> 375.2899, found 375.2902.



**(E)-3-(3-(dec-5-en-5-yl)naphthalen-2-yl)(phenyl)methanol (Scheme 5, 11): Type E Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a Ni(acac)<sub>2</sub> (25.7 mg, 0.1 mmol, 10 mol %) at 20 °C, followed by 4-methylbenzaldehyde (96.1 mg, 0.8 mmol). The reaction was stirred for 5 h. The reaction was then quenched by saturated aqueous solution of NH<sub>4</sub>Cl (2 mL), and dilute with ethyl acetate (3 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (92.8 mg, 30%).

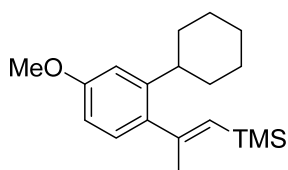
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.80 – 7.73 (m, 3H), 7.53 (s, 1H), 7.46 – 7.38 (m, 3H), 7.20 – 7.18 (m, 2H), 7.15 – 7.12 (m, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 5.25 (t, *J* = 7.2 Hz, 1H), 2.51 – 2.43 (m, 1H), 2.35 – 2.28 (m, 2H), 2.23 (s, 3H), 2.16 (q, *J* = 6.7 Hz, 2H), 1.35 – 1.26 (m, 8H), 0.92 (t, *J* = 6.7 Hz, 3H), 0.83 (t, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 142.2, 141.4, 140.1, 139.1, 135.6, 132.6, 132.2, 131.5, 130.3, 128.3, 127.9, 127.4, 127.3, 126.7, 126.1, 126.0, 125.9, 125.5, 70.3, 31.9, 31.8, 30.6, 27.8, 22.8, 22.4, 19.3, 14.0, 13.9; HRMS (ESI) Calcd for C<sub>28</sub>H<sub>35</sub>O [M + H]<sup>+</sup> 387.2688, found 387.2674.



**(*E*)-4-(3,5-dimethoxyphenyl)-5-(1-phenylprop-1-en-2-yl)benzo[*d*][1,3]dioxole**

**(Scheme 5, 12): Type B Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 10 mol % P(OPh)<sub>3</sub>, 60 °C, 6 h). To the reaction was added a THF solution of Pd<sub>2</sub>(dba)<sub>3</sub>/SPhos (0.2 mL of 0.1 M solution, 0.02 mmol) at 20 °C followed by the addition of 1-iodo-3,5-dimethoxybenzene (264.1 mg, 1.0 mmol). The reaction was then stirred for 20 h. The reaction was then quenched by saturated aqueous solution of NH<sub>4</sub>Cl (5 mL), and dilute with ethyl acetate (5 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 200/1 – 150/1) of the crude product afforded the title compound as a yellow oil (78.6 mg, 21%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.18 (m, 3H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.68 (d, *J* = 2.3 Hz, 2H), 6.53 (s, 1H), 6.43 (t, *J* = 2.3 Hz, 1H), 5.97 (s, 2H), 3.74 (s, 6H), 1.77 (d, *J* = 1.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 160.4 (2 x C), 146.5, 145.2, 139.4, 139.3, 138.2, 137.01, 130.00, 128.7 (2 x C), 128.1 (2 x C), 126.3, 122.2, 121.6, 107.7 (2 x C), 107.2, 101.1, 99.9, 55.3 (2 x C), 19.7; HRMS (ESI) Calcd for C<sub>24</sub>H<sub>23</sub>O<sub>4</sub> [M + H]<sup>+</sup> 375.1596, found 375.1606.

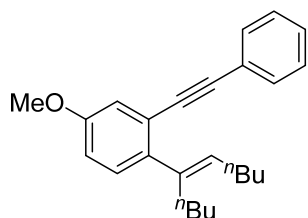


**(E)-2-(2-(2-cyclohexyl-4-methoxyphenyl)prop-1-en-1-yl)trimethylsilane (Scheme 5, 13):**

**Type E Reagent (1.1 equiv)**, reaction was carried out in 1.0 mmol scale with Co–Xantphos catalysis (5 mol % CoCl<sub>2</sub>, 5 mol % Xantphos, 60 °C, 4 h). To the reaction was added a FeCl<sub>3</sub> (8.1 mg, 0.05 mmol, 5 mol %) at 20 °C, followed by bromocyclohexane (97.8 mg, 0.6 mmol). The reaction was stirred at room temperature for 20 h. The reaction was then quenched by saturated aqueous solution of NH<sub>4</sub>Cl (2 mL), and dilute with ethyl acetate (3 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 250/1 – 150/1) of the crude product afforded the title compound as a yellow oil (145.9 mg, 74 %).

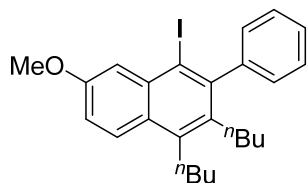
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.99 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 2.7 Hz, 1H), 6.67 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.30 (s, 1H), 3.80 (s, 3H), 2.76 – 2.65 (m, 1H), 2.06 (s, 3H), 1.84 – 1.73 (m, 5H), 1.46 – 1.24 (m, 5H), 0.19 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.2, 154.1, 145.3, 139.7, 129.4, 127.9, 112.1, 110.1, 55.1, 40.7, 34.7 (2 x C), 27.1 (2 x C), 26.2, 24.7, 0.0 (3 x C); HRMS (ESI) Calcd for C<sub>19</sub>H<sub>31</sub>OSi [M + H]<sup>+</sup> 303.2144, found 303.2132.

### Transformations of 2-Alkenylarylzinc Intermediate



**(E)-1-(dec-5-en-5-yl)-4-methoxy-2-(phenylethynyl)benzene (Scheme 6, 14):** A mixture of **3** (1.0 mmol), phenylacetylene (1.2 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (21.0 mg, 0.03 mmol), and TBAF·3H<sub>2</sub>O (0.78 g, 3mmol) was stirred under N<sub>2</sub> at 80 °C for 5 h. The mixture was washed by water, extracted with ether (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a yellow oil (0.33 g, 90 %).<sup>24</sup>

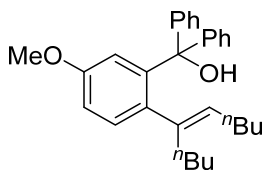
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.48 – 7.46 (m, 2H), 7.35 – 7.31 (m, 3H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 2.7 Hz, 1H), 6.83 (dd, *J* = 8.5, 2.8 Hz, 1H), 5.46 (t, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.20 (q, *J* = 7.1 Hz, 2H), 1.43 – 1.35 (m, 4H), 1.32 – 1.25 (m, 4H), 0.87 (t, *J* = 6.1 Hz, 3H), 0.84 (t, *J* = 6.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.6, 140.2, 139.6, 131.4 (2 x C), 130.9, 129.9, 128.3 (2 x C), 128.0, 123.7, 122.4, 116.6, 114.8, 91.8, 89.5, 55.4, 32.1, 30.9, 30.6, 28.0, 22.6, 22.4, 14.0 (2 x C); HRMS (ESI) Calcd for C<sub>25</sub>H<sub>31</sub>O [M + H]<sup>+</sup> 347.2375, found 347.2368.



**1,2-dibutyl-4-iodo-6-methoxy-3-phenylnaphthalene (Scheme 6, 15):** *N*-Iodosuccinimide (202.0 mg, 0.9 mmol,) was added to a solution of **3a** (104.0 mg, 0.3 mmol)

in CH<sub>2</sub>Cl<sub>2</sub> (1 mL). The reaction vial was sealed and protected from light. The resulting slightly red solution was heated to 50 °C and stirred under an air atmosphere for 5 h. The mixture was quenched by addition of saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (10 mL). The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 15 mL). The combined organic layers were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a yellow oil (82.1 mg, 58 %).<sup>25</sup>

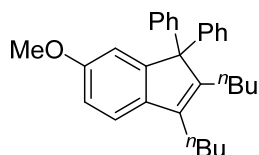
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.94 (d, *J* = 9.4 Hz, 1H), 7.43 – 7.33 (m, 5H), 7.15 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.06 (d, *J* = 2.6 Hz, 1H), 3.90 (s, 3H), 3.10 – 3.06 (m, 2H), 2.68 – 2.64 (m, 2H), 1.68 (tt, *J* = 7.9, 5.9 Hz, 2H), 1.61 – 1.54 (m, 3H), 1.35 (tt, *J* = 7.9, 6.0 Hz, 2H), 1.17 (h, *J* = 7.3 Hz, 2H), 1.02 (t, *J* = 7.2 Hz, 3H), 0.73 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.8, 143.1, 142.0, 136.4, 134.2, 133.0, 129.4 (2 x C), 127.7 (2 x C), 127.1, 126.6, 126.3, 125.7, 118.2, 106.3, 55.3, 33.6, 33.5, 29.7, 28.7, 23.5, 23.0, 14.0, 13.6; HRMS (ESI) Calcd for C<sub>25</sub>H<sub>30</sub>IO [M + H]<sup>+</sup> 473.1341, found 473.1346.



**(*E*)-2-(2-(dec-5-en-5-yl)-5-methoxyphenyl)diphenylmethanol (Scheme 6, 16):** To a THF solution of **5** (0.35 g, 1.0 mmol) was added dropwise a THF solution of phenyllithium (0.8 mL of 1.6M solution, 1.3 mmol) at -78 °C. The result reaction mixture was stirred for 2 h before quenching with saturated NH<sub>4</sub>Cl (2 mL), and dilute with ethyl acetate (4 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel

chromatography (eluent: hexane/ether = 150/1 – 100/1) of the crude product afforded the title compound as a yellow oil (0.36 g, 85 %).

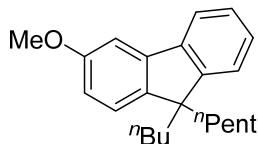
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 – 7.20 (m, 10H), 6.95 (d,  $J = 8.4$  Hz, 1H), 6.75 (dd,  $J = 8.3, 2.7$  Hz, 1H), 6.23 (d,  $J = 2.7$  Hz, 1H), 5.08 (t,  $J = 7.2$  Hz, 1H), 4.79 (s, 1H), 3.62 (s, 3H), 2.00 (q,  $J = 7.0$  Hz, 2H), 1.29 – 1.20 (m, 4H), 1.18 – 1.14 (m, 4H), 0.85 (t,  $J = 6.8$  Hz, 3H), 0.80 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.9, 147.7, 145.4 (2 x C), 142.3, 134.8, 133.1, 132.3, 128.1 (4 x C), 127.7 (4 x C), 127.1 (2 x C), 117.2, 110.9, 83.7, 55.0, 32.0, 31.5, 30.4, 27.7, 23.0, 22.4, 13.94, 13.90.; HRMS (ESI) Calcd for  $\text{C}_{30}\text{H}_{37}\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  429.2794, Found 429.2806.



**2,3-dibutyl-6-methoxy-1,1-diphenyl-1H-indene (Scheme 6, 17):** To a  $\text{CH}_2\text{Cl}_2$  solution of **5a** (129.0 mg, 0.3 mmol) was added dropwise  $\text{BF}_3 \cdot \text{OEt}_2$  (51.0 mg, 0.36 mmol) at 0 °C. The result reaction mixture was allowed to warm to 20 °C stirred for 1 h before quenching with saturated  $\text{NH}_4\text{Cl}$  (2 mL), and dilute with ethyl acetate (4 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a yellow oil (96.1 mg, 80 %).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24 – 7.13 (m, 11H), 6.79 (d,  $J = 2.3$  Hz, 1H), 6.75 (dd,  $J = 8.2, 2.4$  Hz, 1H), 3.70 (s, 3H), 2.55 – 2.51 (m, 2H), 2.28 – 2.24 (m, 2H), 1.63 (tt,  $J = 8.1, 6.3$  Hz, 2H), 1.47 (sextet,  $J = 7.2$  Hz, 2H), 1.06 (sextet,  $J = 7.3$  Hz, 2H), 0.98 (t,  $J = 7.3$  Hz, 3H), 0.66 (t,  $J = 7.4$  Hz, 3H), 0.63 – 0.56 (m, 2H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.8, 153.8, 147.7, 143.9 (2 x C), 138.0, 137.5, 128.4 (4 x C), 128.1 (4 x C), 126.4 (2 x C), 119.2,

111.5, 111.2, 68.6, 55.4, 31.7, 31.1, 27.1, 25.8, 23.2 (2 x C), 14.1, 13.6; HRMS (ESI) Calcd for C<sub>30</sub>H<sub>37</sub>O<sub>2</sub> [M + H]<sup>+</sup> 429.2794, Found 429.2806.



**9-butyl-3-methoxy-9-pentyl-9H-fluorene (Scheme 6, 8):** To a CH<sub>2</sub>Cl<sub>2</sub> solution of **7** (0.32 g, 1.0 mmol) at 20 °C was added *p*-TsOH·H<sub>2</sub>O (0.57 g, 3.0 mmol). The resulting mixture was heated to 60 °C and stirred for 6 h before it was quenched with saturated NaHCO<sub>3</sub> (10 mL). The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colourless oil (0.30 g, 93 %).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.67 – 7.65 (m, 1H), 7.31 – 7.28 (m, 3H), 7.23 – 7.20 (m, 2H), 6.86 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.89 (s, 3H), 1.95 – 1.90 (m, 4H), 1.10 – 1.02 (m, 6H), 0.72 – 0.59 (m, 10H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 159.0, 151.6, 142.8, 142.3, 140.9, 127.0, 126.6, 123.4, 122.8, 119.5, 113.2, 104.6, 55.4, 54.3, 40.4, 40.2, 32.3, 26.0, 23.4, 23.1, 22.38, 14.0, 13.8; HRMS (ESI) Calcd for C<sub>23</sub>H<sub>31</sub>O [M + H]<sup>+</sup> 323.2375, found 323.2373.

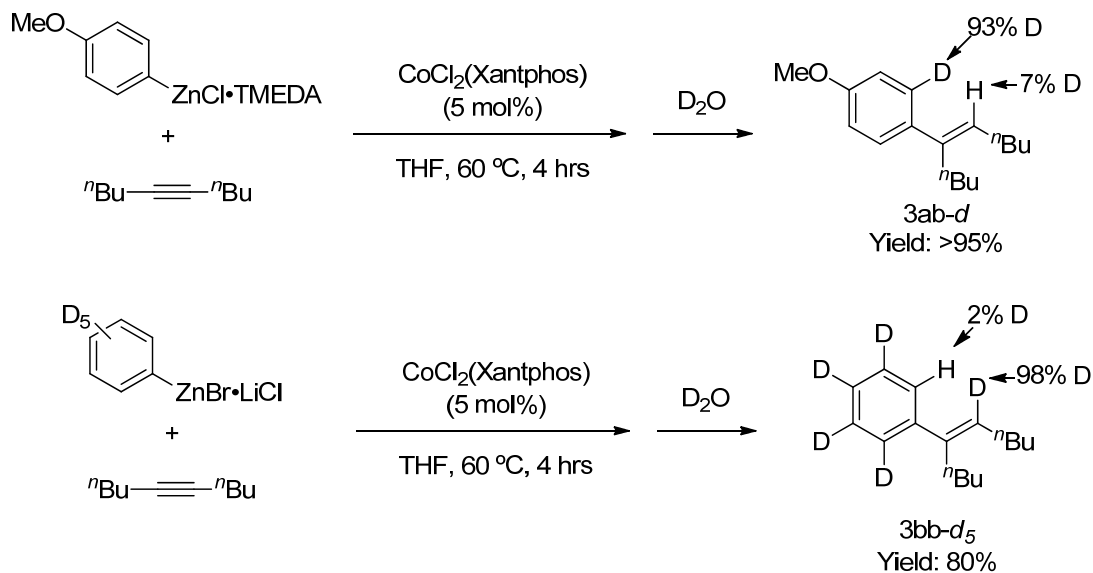
### Deuterium-Labeling Experiments:

**(3ab-d) Type A reagent:** In a 10 mL Schlenk tube was placed ZnCl<sub>2</sub>·TMEDA (167 mg, 0.66 mmol). The Schlenk tube was submerged in an ice bath for 15 mins prior to the addition of Grignard reagents. To the ZnCl<sub>2</sub>·TMEDA was added a THF solution of (4-methoxyphenyl)magnesium bromide (0.66 mmol) dropwise at 0 °C. THF was then added to the solution to obtain 0.6 M reaction concentration. After stirring for 1 hr at 0 °C, the

Schlenk tube was placed at room temperature condition and  $\text{CoCl}_2$ -Xantphos complex (21.3 mg, 0.03 mmol) was added. After stirring for 5 mins, 5-decyne (82.9 mg, 0.6 mmol) was added. The resulting solution was stirred at 60 °C for 4 h, and then allowed to cool to room temperature, quenched by  $\text{D}_2\text{O}$  (1 mL), and dilute with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Purification of the crude mixture by silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) afforded carbometalation product, which were analyzed by  $^1\text{H}$  NMR (see attached spectra).

**(3bb-*d*<sub>5</sub>) Type D reagent:** Anhydrous LiCl (84.8 mg, 2 mmol) was placed in a 10 mL Schlenk tube, dried under vacuum (1 mbar) at 150 °C for 20 min, and cooled down to room temperature (20 °C) under  $\text{N}_2$ . To the Schlenk tube was added zinc powder (196 mg, 3 mmol), and the heterogeneous mixture of Zn and LiCl was dried under vacuum (1 mbar) at 150 °C for 15 min. While cooling to room temperature, the reaction tube was evacuated and backfilled with  $\text{N}_2$  for three times. The mixture was suspended with THF (2 mL), followed by the activation of Zn with  $\text{BrCH}_2\text{CH}_2\text{Br}$  (10  $\mu\text{L}$ , 0.1 mmol) and  $\text{Me}_3\text{SiCl}$  (3  $\mu\text{L}$ , 0.02 mmol) and stirring for 5 min. Then Xantphos (57.8 mg, 0.10 mmol) and  $\text{CoCl}_2$  (13.0 mg, 0.10 mmol) were added sequentially. After stirring for additional 5 min, and bromobenzene-*d*<sub>5</sub> (2 mmol) was added in one portion. The reaction was stirred at room temperature. To the arylzinc reagent was added 5-decyne (82.9 mg, 0.6 mmol). The resulting solution was stirred at 60 °C for 4 h, and then allowed to cool to room temperature, quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (1 mL), and dilute with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Purification

of the crude mixture by silica gel chromatography (eluent: hexane/ether = 150/1 – 100/1) afforded carbometalation product, which were analyzed by  $^1\text{H}$  NMR (see attached spectra).



## 2.5 References

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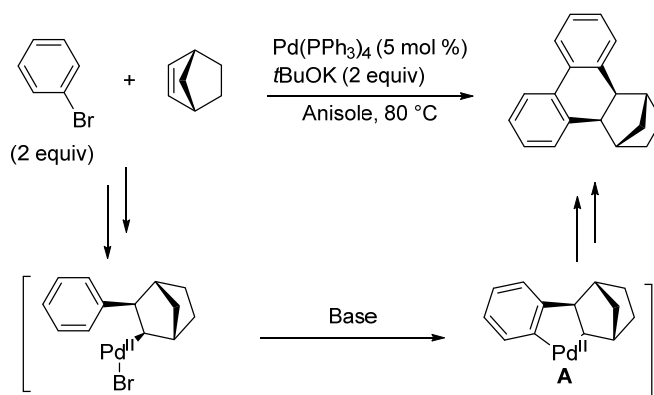
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## Chapter 3. : Cobalt-Catalyzed Arylzincation of Norbornene Derivatives through 1,4-Cobalt Migration

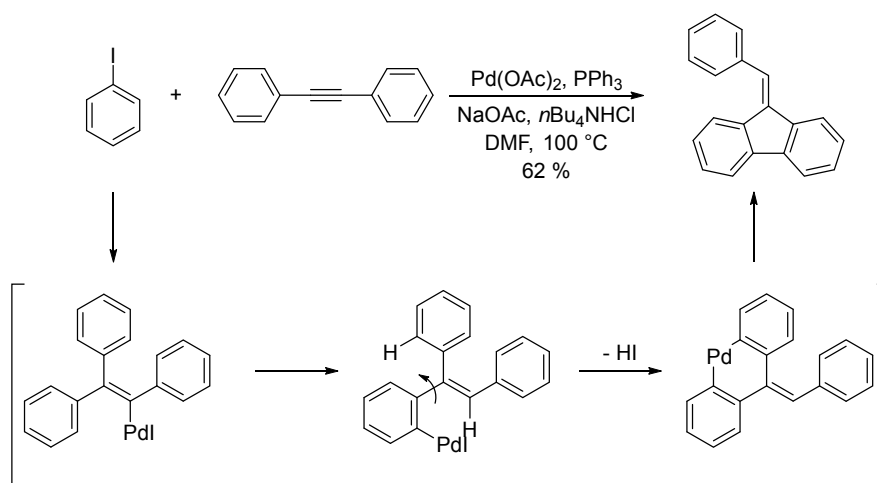
### 3.1 Introduction

Remote 1,4-metal migration of organorhodium and -palladium species, offers unique opportunities for the development of novel catalytic transformations involving C–H functionalization and cascade bond formation.<sup>1,2,3</sup> Such 1,4-metal migration reactions are often preceded by insertion of an unsaturated C=C bond into an aryl metal species. In 1985, Catellani and co-workers reported a palladium-catalyzed reaction of bromobenzene with norbornene to afford 1,2,3,4,4a,12b-hexahydro-1,4-methanotriphenylene (Scheme 3.1).<sup>4</sup> The reaction was proposed to involve insertion of norbornene into a phenylpalladium species followed by intramolecular aromatic C–H activation, forming a palladacycle **A** as a key intermediate. While the reaction does not involve complete migration of the palladium atom, this work is notable for the demonstration of the feasibility of intramolecular C–H activation in a 1,4-manner. In 2000, Larock and co-workers reported palladium-catalyzed synthesis of 9-alkylidene-9*H*-fluorene from iodobenzene and diphenylacetylene, which involves a complete 1,4-vinyl-to-aryl migration of the palladium atom (Scheme 3.2).<sup>5</sup>

**Scheme 3.1.** Palladium-Catalyzed Synthesis of 1,2,3,4,4a,12b-Hexahydro-1,4-methanotriphenylene



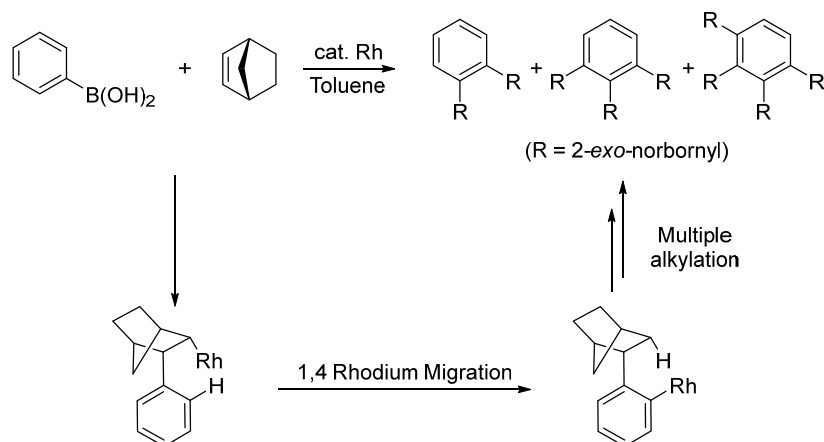
**Scheme 3.2.** Palladium-Catalyzed Synthesis of 9-Alkylidene-9H-fluorene



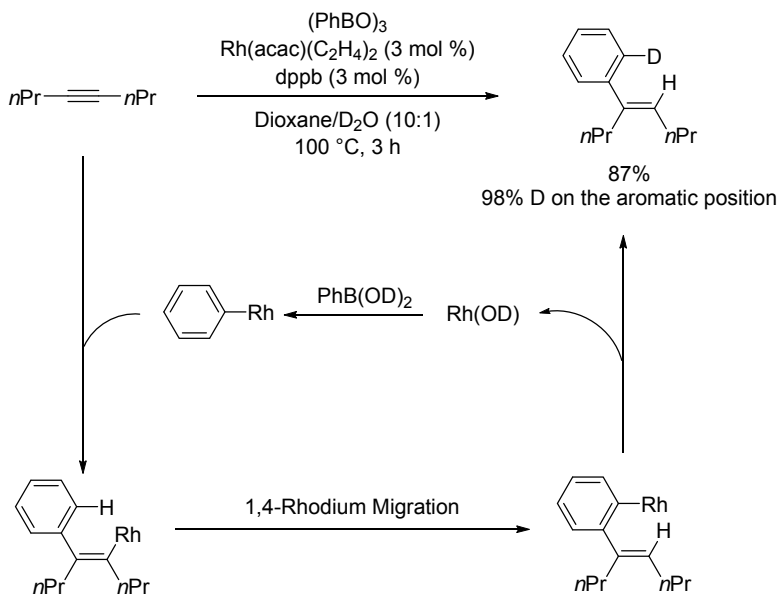
In 2000, Miura and coworkers reported on a rhodium-catalyzed merry-go-round addition reaction of an arylboronic acid to norbornene, affording multi-norbornylated arenes through repetition of a sequence consisting of insertion of norbornene into arylrhodium species and alkyl-to-aryl 1,4-rhodium migration (Scheme 3.3).<sup>6</sup> The reaction is reminiscent of Catellani reaction but is distinct in that the metal center is completely migrated from the C(sp<sup>3</sup>) carbon to the C(sp<sup>2</sup>) carbon.<sup>7</sup> One year later, Hayashi and coworkers reported on rhodium-catalyzed hydroarylation of an internal alkyne with an

arylboronic acid, revealing its mechanism involving 1,4-rhodium migration (Scheme 3.4).<sup>8</sup> Thus, this apparently simple reaction likely involves insertion of the alkyne into an arylrhodium species, vinyl-to-aryl 1,4-rhodium migration, and protoderhodation of the resulting *o*-alkenylaryl rhodium species.

**Scheme 3.3.** Rhodium-Catalyzed Addition of Arylboronic Acid to Norbornene Involving 1,4-Rhodium Migration

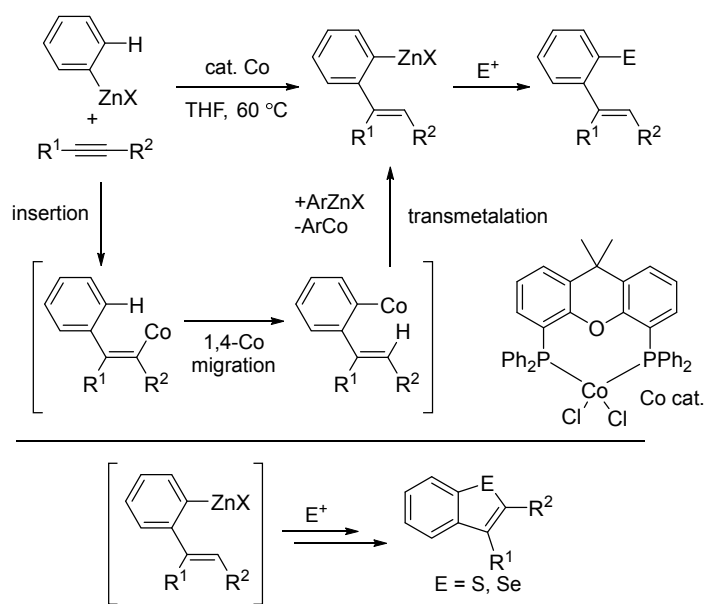


**Scheme 3.4.** Rhodium-Catalyzed Addition of Arylboronic Acid to Alkyne Involving 1,4-Rhodium Migration



Recently, we disclosed the first example of 1,4-cobalt migration in an addition reaction of an arylzinc reagent to an internal alkyne catalyzed by a cobalt-diphosphine complex (Scheme 3.5).<sup>9</sup> A unique feature of this reaction is that it produces an *o*-alkenylarylzinc species, which can be intercepted by an external electrophile. This “migratory arylzincation” can be exploited in the synthesis of benzoheteroles derivatives.<sup>10</sup>

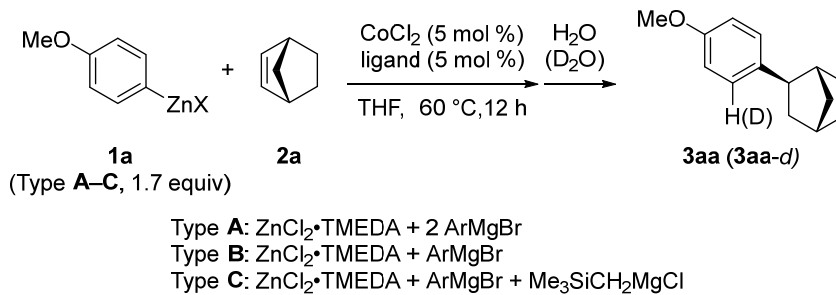
**Scheme 3.5.** Cobalt-Catalyzed Addition of Arylzinc Reagent to Alkyne Involving 1,4-Cobalt Migration



With this previous study as well as the above discussed palladium and rhodium catalysis of norbornene, it was natural for us to explore the feasibility of addition of an arylzinc reagent to norbornene. Here we report that a cobalt-diphosphine complex can also catalyze migratory arylzincation of norbornene derivatives. Thus, unlike the rhodium-catalyzed merry-go-round addition, the present reaction affords *o*-(2-*exo*-norbornyl)-arylzinc species presumably through insertion of norbornene into an arylcobalt species, alkyl-to-aryl cobalt migration, and subsequent cobalt-to-zinc transmetalation.<sup>11</sup>

## 3.2 Results and Discussion

The present study began with a screening of cobalt catalysts for the addition of 4-methoxyphenylzinc reagent (**1a**, 1.7 equiv; prepared from a 1:2 mixture of  $\text{ZnCl}_2 \cdot \text{TMEDA}$  and  $4\text{-MeOC}_6\text{H}_4\text{MgBr}$  and denoted as type **A** reagent) to norbornene **2a**, which was conducted at 60 °C for 12 h (Table 3.1). Naturally, the  $\text{CoCl}_2\text{-Xantphos}$  catalyst, which is the optimum catalyst for the migratory arylzincation to an internal alkyne,<sup>9a</sup> was examined first. However it exhibited poor catalytic activity, affording the arylation product **3aa** only in a low yield of 2% (entry 1). Upon subsequent screening of common diphosphine ligands (entries 2–8), *dppf* was identified to be the most effective ligand, which promoted the addition reaction to afford **3aa** in 69% yield (entry 3). Among all other diphosphine ligands that were screened, *dppp*, *dppb*, BISBI (2,2'-bis(diphenylphosphinomethyl)-1,1'-biphenyl) displayed moderate performances, affording **3aa** in ca. 40% yield (entries 5, 6 and 8), while *DPEphos* was inadequate. Curiously, the reaction using *dppe* or *dppbz* as the ligand afforded, a 1,2-dinorbornylated product in ca. 30–55% yield as revealed by GC and GCMS analysis of the reaction mixture (entries 4 and 7), which was reminiscent of Miura's merry-go-round reaction (Scheme 3.3) Monodentate phosphines such as  $\text{PPh}_3$  as well as ligand-free system were not effective (entries 9 and 10).

**Table 3.1.** Screening of Reaction Conditions<sup>[a]</sup>

| Entry             | ArZnX type | Ligand           | Yield [%] <sup>[b]</sup> |
|-------------------|------------|------------------|--------------------------|
| 1                 | A          | Xantphos         | 2                        |
| 2                 | A          | DPEphos          | 6                        |
| 3                 | A          | dppf             | 69                       |
| 4                 | A          | dppe             | 18 <sup>[c]</sup>        |
| 5                 | A          | dppp             | 38                       |
| 6                 | A          | dppb             | 35                       |
| 7                 | A          | dppbz            | 3 <sup>[c]</sup>         |
| 8                 | A          | BISBI            | 42                       |
| 9 <sup>[d]</sup>  | A          | PPh <sub>3</sub> | 7                        |
| 10                | A          | None             | 1                        |
| 11 <sup>[e]</sup> | A          | dppf             | 76                       |
| 12 <sup>[e]</sup> | B          | dppf             | <1                       |
| 13 <sup>[f]</sup> | C          | dppf             | 82                       |

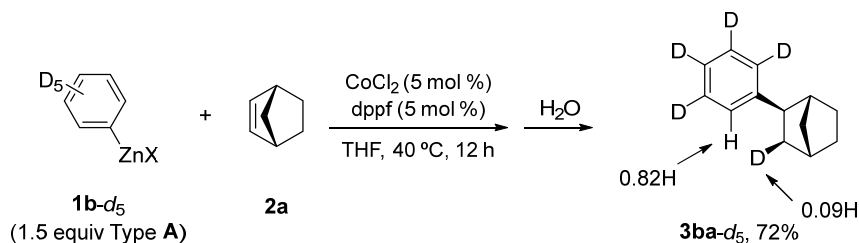
<sup>[a]</sup>Unless otherwise noted, the reaction was performed on a 0.3 mmol scale and was quenched with H<sub>2</sub>O. <sup>[b]</sup> Determined by GC using *n*-tridecane as an internal standard. <sup>[c]</sup>1,2-di-2-nobonylated product was obtained (55% and 34% for entries 4, and 7, respectively). <sup>[d]</sup>10 mol % of PPh<sub>3</sub> was used. <sup>[e]</sup>The reaction was performed with 1.2 equiv of arylzinc reagent at 40 °C for 18 h. <sup>[f]</sup>The reaction was performed with 1.5 equiv of arylzinc reagent at 40 °C for 12 h and quenched with D<sub>2</sub>O. The yield was determined by <sup>1</sup>H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Further examination of the reaction parameters revealed that the reaction could be achieved without problem using a reduced amount of type **A** arylzinc reagent (1.2–1.5 equiv) at lower temperature of 40 °C (entry 11). However, unlike our previous studies on migratory arylation reaction to internal alkynes<sup>9a</sup>, a monoarylzinc reagent prepared from a 1:1 mixture of 4-MeOC<sub>6</sub>H<sub>4</sub>MgBr and ZnCl<sub>2</sub>•TMEDA (type **B** reagent) as well as

the one prepared from 4-MeOC<sub>6</sub>H<sub>4</sub>I and Zn•LiCl<sup>12</sup> were unreactive, indicative of only one of the two aryl groups on the type **A** reagent is transferable in the present reaction. Addition of a “dummy” Grignard reagent, i.e., Me<sub>3</sub>SiCH<sub>2</sub>MgCl, to this unreactive reagent could reestablish its reactivity. Thus, the mixed diorganozinc reagent (type **C**) undergoes addition to **2a**, and upon quenching with D<sub>2</sub>O, afforded deuterated adduct **3aa-d** in 82% yield (entry 13).<sup>13</sup> Analysis of the <sup>1</sup>H NMR spectrum of **3aa-d** showed that the integration of 1.12 for the position *ortho* to the 2-norbornyl group, which suggests significant deuterium incorporation into this position and hence formation of an *o*-(2-*exo*-norbornyl)-arylzinc species via 1,4-cobalt migration. To further substantiate the claim, all of the norbornyl carbon atoms of **3aa-d** appeared as clear singlet signals in <sup>13</sup>C NMR spectrum, demonstrating that the 3-*exo*-position of the norbornyl group was virtually not deuterated.

An additional deuterium-labeling experiment further supported this putative 1,4-cobalt migration process (Scheme 3.6). Thus, the addition of pentadeuteriophenylzinc reagent **1b-d<sub>5</sub>** (type **A**) to **2a** under cobalt–dppf catalysis occurred with associated migration of one of the *o*-deuterium atoms to the *exo*-2-norbornyl position, as demonstrated by the analysis of the <sup>1</sup>H NMR spectrum of **3ba-d<sub>5</sub>**.

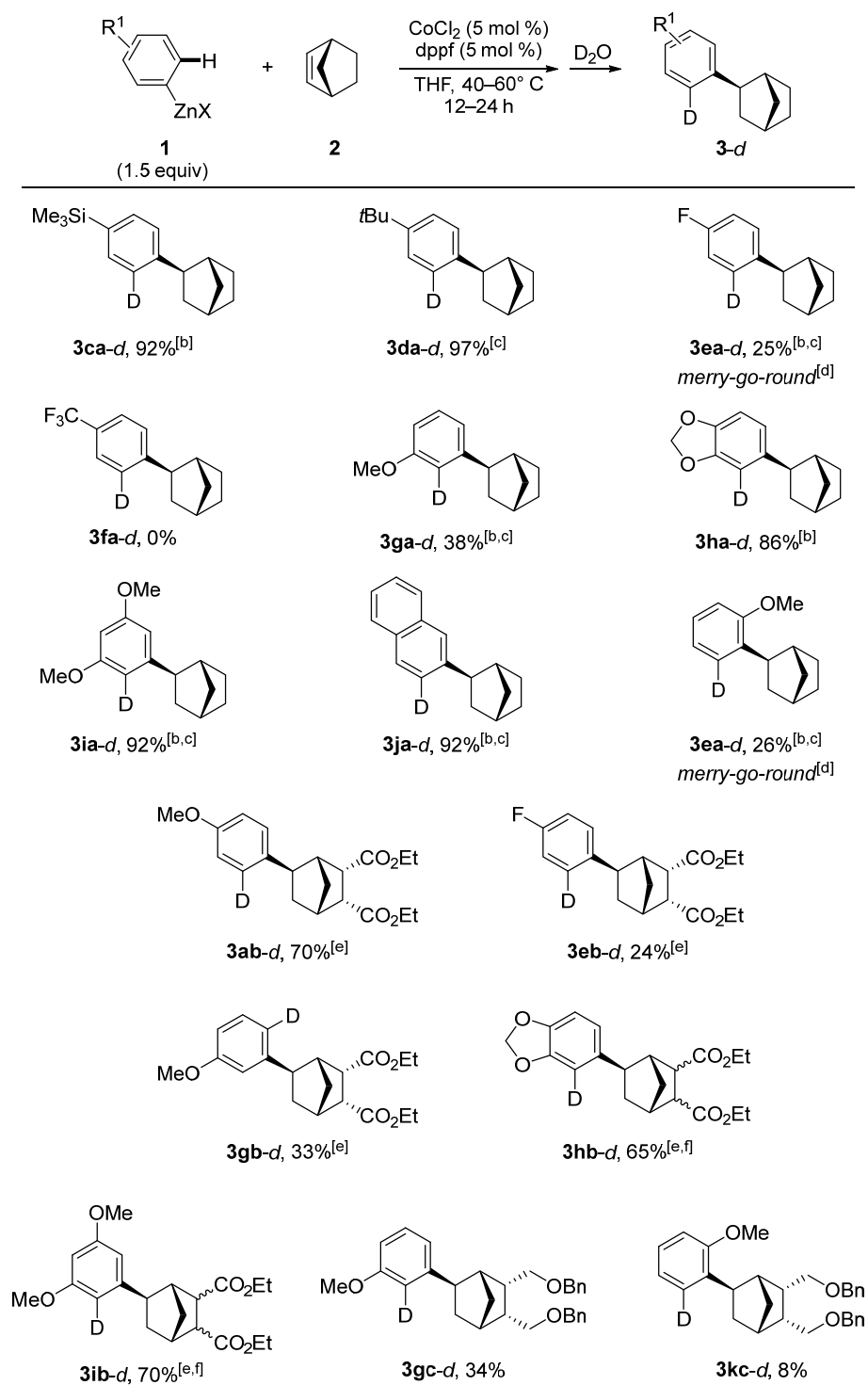
**Scheme 3.6.** Reaction of Pentadeuteriophenylzinc Reagent<sup>[a]</sup>



<sup>[a]</sup>The proton content on each carbon atom was estimated by <sup>1</sup>H NMR analysis.

With the optimized reaction conditions at hand, we explored the scope of the present migratory arylzincation reaction using different arylzinc reagents and norbornene derivatives (Scheme 3.7). Note that each reaction was quenched with D<sub>2</sub>O in order to

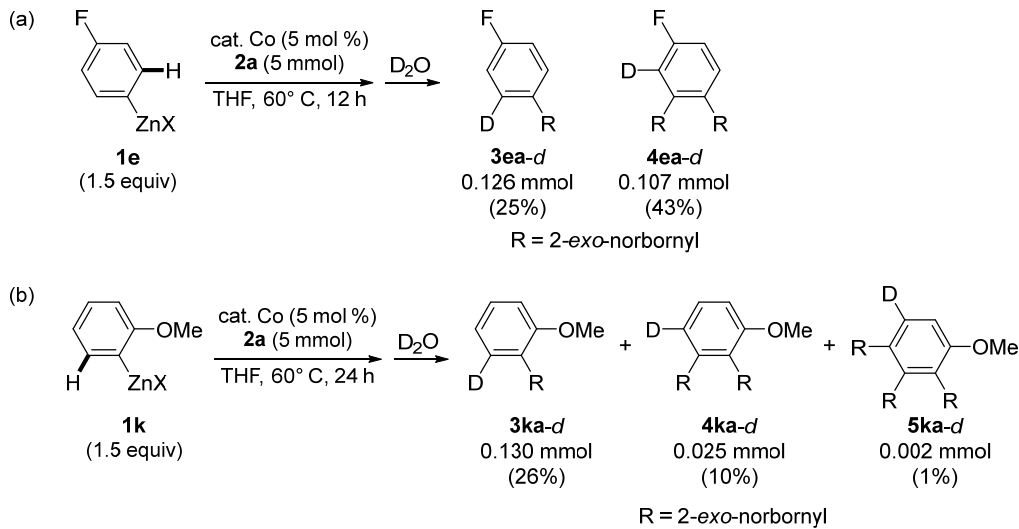
confirm 1,4-cobalt migration process as well as to gain insight into its regioselectivity. First, we explored the reactions of a series of arylzinc reagent with norbornene **2a**. 4-(Trimethylsilyl)phenylzinc and 4-*tert*-butyl-phenylzinc reagents afforded the desired product **3ca-d** and **3da-d** in excellent yields. On the other hand, no desired product was observed with electron-poor 4-(trifluoromethyl)phenylzinc reagent. Interestingly, 4-fluorophenylzinc reagent resulted in the formation of a mixture of mono- and di-addition products **3ea-d** and **4ea-d** in an approximate ratio of 1:1 (Scheme 3.8a). As mentioned earlier (Table 3.1, entries 4 and 7), the latter product appears to originate from the merry-go-round process reminiscent of Miura's rhodium-catalyzed reaction. Similar to the migratory arylzincation of alkynes, the *meta*-oxygen atom of 3-methoxy- and 3,4-methylenedioxyphenylzinc reagents caused secondary directing effect to induce regioselective 1,4-metal migration to its proximity (**3ga-d** and **3ha-d**). 3,5-Dimethoxyphenylzinc reagent also afforded the desired product **3ia-d** in an excellent yield. The reaction of 2-naphthylzinc reagent took place cleanly with complete regioselectivity of 1,4-metal migration to the less hindered 3-position, thus affording the adduct **3ja-d**. Merry-go-round process was also observed on the reaction of 2-methoxyphenyl reagent which afforded a mixture of mono-, di- and tri-addition adducts **3ka-d**, **4ka-d** and **5ka-d** respectively (Scheme 3.8b). Note that mesitylzinc reagent failed to partake in the reaction.

Scheme 3.7. Scope of Migratory Arylzincation<sup>[a]</sup>

<sup>[a]</sup>The reaction was performed on a 0.5 mmol scale. Unless otherwise stated, type **A** arylzinc reagent was used, and the isolation yield is shown. <sup>[b]</sup>Type **C** arylzinc reagent was used. <sup>[c]</sup>The yield was

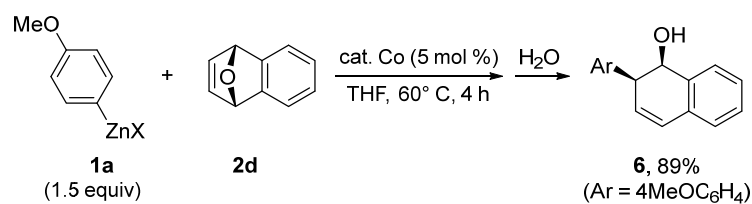
determined by  $^1\text{H}$  NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. <sup>[d]</sup>Merry-go-round addition was observed (see Scheme 3.8). <sup>[e]</sup>Dppe was used instead of dppf. <sup>[f]</sup>Obtained as a diastereomeric mixture.

Next we explored different norbornene derivatives. Norbornene bearing an *endo*-diester moiety **2b** failed to partake in the reaction with 4-methoxyphenylzinc reagent under Co–dppf catalysis. Interestingly, the use of dppe instead of dppf promoted the reaction to afford the desired product **3ab-d** in 70% yield. While the Co-dppe catalyst produced a di-addition product with parent norbornene (Table 3.1, entry 4), no such product was observed in this case. 4-Fluoro-, 3-methoxy-, 3,4-methylenedioxy-, and 3,5-dimethoxyphenylzinc reagents underwent the reaction smoothly to afford the corresponding adducts **3eb-d**, **3gb-d**, **3hb-d**, and **3ib-d**, respectively, albeit in modest yields. Curiously, the reaction of 3-methoxyphenylzinc reagent and **2b** exhibited the opposite regioselectivity to that observed in the reaction of the same reagent with **2a** (see **3ga-d**), thus resulting in deuteration of the position distal to the methoxy group (see **3gb-d**), while the regioselectivity remained consistent for 3,4-methylenedioxyphenylzinc reagent (see **3ha-d** and **3hb-d**). Unfortunately, some of these reactions produced a mixture of diastereomers, presumably due to epimerization of the  $\alpha$ -positions of the diester moiety. The reactions of 3-methoxy- and 2-methoxyphenylzinc reagents with an *endo*-diether **2c** took place under Co–dppf catalysis to afford the corresponding adducts **3gc-d** and **3kc-d**, albeit in low yields. In the former case, deuteration took place at the position proximal to the methoxy group. In the latter case, no merry-go-round adducts was observed unlike the reaction with norbornene (see Scheme 3.3). Also note that in these low-yielding cases, the norbornene derivative was largely recovered without affording any by-products.

Scheme 3.8. Merry-Go-Round Addition to Norbornene<sup>[a]</sup>

<sup>[a]</sup>cat. Co = CoCl<sub>2</sub> (5 mol %), dppf (5 mol %). The identities and quantities of norbornylated products were estimated by <sup>1</sup>H NMR, GC, and GCMS analysis of the product mixture. The yields in parentheses are based on 2a.

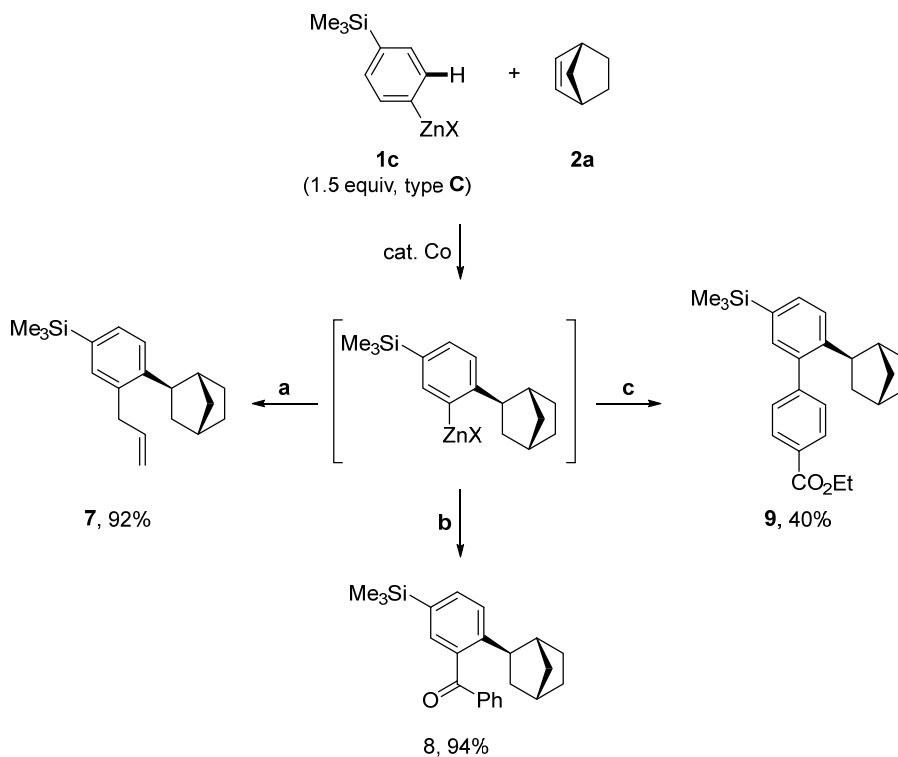
The reaction of 4-methoxyphenylzinc reagent **1a** with oxabicyclic alkene **2d** did not afford a migratory arylzincation product, but resulted in a ring-opening arylation product **6** (Scheme 3.9).<sup>14</sup> Efforts to suppress the  $\beta$ -oxygen elimination process by using less reactive arylzinc reagent (i.e., type **B** reagent) or by lowering the reaction temperature were futile to change the course of reaction.<sup>15</sup>

Scheme 3.9. Ring-Opening arylation of Oxabicyclic Alkene<sup>[a]</sup>

<sup>[a]</sup>cat. Co = CoCl<sub>2</sub> (5 mol %), dppf (5 mol %).

To further demonstrate the utility of this reaction, *o*-(2-*exo*-norbornyl)-arylzinc species formed by the present reaction was subjected to transition-metal-catalyzed cross-coupling reaction with organic electrophiles (Scheme 3.10).<sup>16</sup> The reaction of 4-(trimethylsilyl)phenylzinc reagent **1c** and **2a** was followed by copper-catalyzed allylation with allyl bromide and acylation with benzoyl chloride to afford the desired products **7** and **8**, respectively, in excellent yield.<sup>17</sup> The same *o*-(2-*exo*-norbornyl)-arylzinc intermediate also participated in the Negishi coupling with ethyl 4-iodobenzoate under Pd/Sphos catalysis, affording the biaryl product **9** in a moderate yield. The said transformations demonstrated that there was no interference by the Co catalyst present in the system.

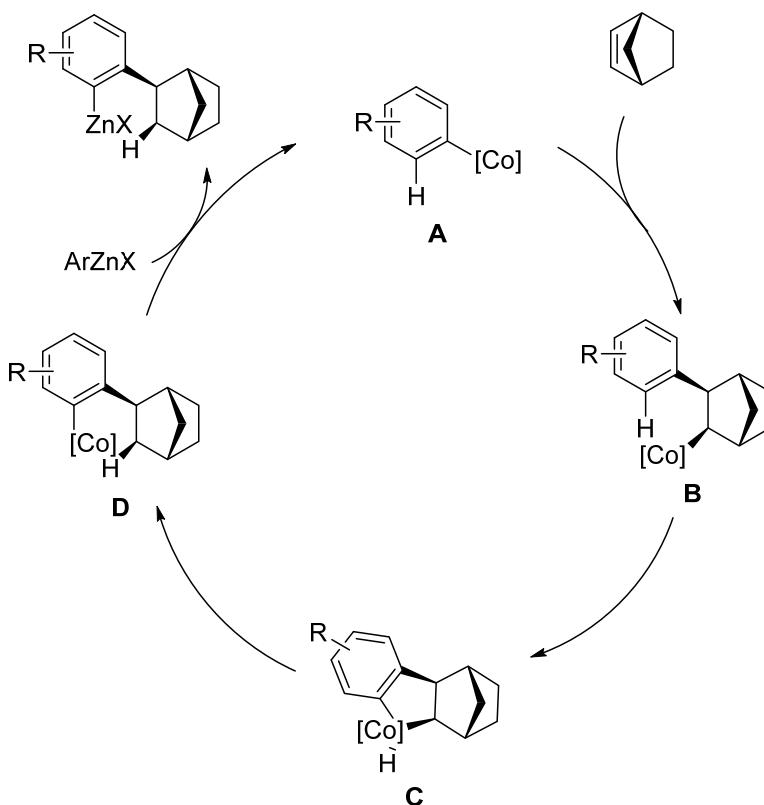
**Scheme 3.10.** Electrophile Trapping of *o*-Norbornylarylzinc Species



<sup>[a]</sup>CuCN·2LiCl (20 mol %), allyl bromide (3 equiv), 60 °C, 8 h. <sup>[b]</sup>CuCN·2LiCl (20 mol %), benzoyl chloride (3 equiv), 60 °C, 8 h. <sup>[c]</sup>Pd(OAc)<sub>2</sub> (4 mol %), Sphos (4 mol %), ethyl 4-iodobenzoate (3 equiv), 60 °C, 8 h.

A proposed catalytic cycle for the present migratory arylzincation is shown in Scheme 3.11. An arylcobalt species **A** generated from the cobalt precatalyst and the arylzinc reagent undergoes addition to norbornene to afford a norbornylcobalt species **B**. This species undergoes alkyl-to-aryl 1,4-cobalt migration presumably through a C–H oxidative addition intermediate **C**, thus affording *o*-(2-*exo*-norbornyl)arylcobalt species **D**. Subsequent transmetalation between **D** and the arylzinc reagent furnishes the *o*-(2-*exo*-norbornyl)-arylzinc species and regenerates the arylcobalt species **A**.

**Scheme 3.11.** Proposed Catalytic Cycle



### 3.3 Conclusion

In conclusion, we have reported on a cobalt–diphosphine-catalyzed addition reaction of arylzinc to norbornene derivatives, which involves an alkyl-to-aryl 1,4-cobalt migration and cobalt-to-zinc transmetalation as key step, thus generating *o*-(2-*exo*-norbornyl)-arylzinc species. The arylzinc product can be subject to various common electrophilic trapping reactions under copper or palladium catalysis.

### 3.4 Experimental section

**General.** All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed as described by Still et al.,<sup>18</sup> using 40–63 m silica gel (Si 60, Merck). <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) NMR spectrometers. <sup>1</sup>H and <sup>13</sup>C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and CHCl<sub>3</sub> (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-ToF Premier LC HR mass spectrometer.

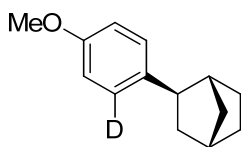
**Materials.** Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Zinc powder (-100 mesh, 99.9%) was purchased from Alfa Aesar, and preactivated by the treatment with aq. HCl. Anhydrous CoCl<sub>2</sub> (97%) was purchased from Alfa Aesar and was used as received. CoCl<sub>2</sub>(Xantphos) was prepared according to the literature procedure. THF was distilled over Na/benzophenone. Grignard reagents were prepared from the corresponding halides and magnesium turnings in anhydrous THF and titrated before use. Diethyl *endo*, *endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate and *endo*, *endo*-5,6-bis((benzyloxy)methyl)bicyclo[2.2.1]hept-2-ene was prepared according to literature procedures.<sup>19,20</sup>

**A Typical Procedure (Type A Reagent):** In a 10 mL Schlenk tube was placed  $\text{ZnCl}_2 \cdot \text{TMEDA}$  (189 mg, 0.75 mmol). The Schlenk tube was submerged in an ice bath for 15 mins prior to the addition of Grignard reagents. To the  $\text{ZnCl}_2 \cdot \text{TMEDA}$  was added a THF solution of ArylGrignard (1.50 mmol) dropwise at 0 °C. After stirring for 1 h at 0 °C, the Schlenk tube was placed at room temperature condition and dppf (13.9 mg, 0.025 mmol) and  $\text{CoCl}_2$  (3.3 mg, 0.025 mmol) was added. After stirring for 5 mins, norbornene (0.5 mmol) was added. The resulting solution was stirred at 40 °C for 16 h, and then allowed to cool to room temperature, quenched with  $\text{D}_2\text{O}$  (1 mL) and subsequently with saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (1 mL), and diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford desire product. For the reaction of parent norbornene, the desired product was typically obtained as a mixture with ArD/ArH (deuterated/protonated arylzinc reagent) and Ar–Ar homocoupling product of the arylzinc reagent).

**A Typical Procedure (Type B Reagent):** In a 10 mL Schlenk tube was placed  $\text{ZnCl}_2 \cdot \text{TMEDA}$  (189 mg, 0.75 mmol). The Schlenk tube was submerged in an ice bath for 15 mins prior to the addition of Grignard reagents. To the  $\text{ZnCl}_2 \cdot \text{TMEDA}$  was added a THF solution of arylGrignard (0.75 mmol) dropwise at 0 °C. After stirring for 1 h at 0 °C, the Schlenk tube was placed at room temperature condition and dppf (13.9 mg, 0.025 mmol) and  $\text{CoCl}_2$  (3.3 mg, 0.025 mmol) was added. After stirring for 5 mins, norbornene (0.5 mmol) was added. The resulting solution was stirred at 40 °C for 16 h, and then allowed to cool to room temperature, quenched with  $\text{D}_2\text{O}$  (1 mL) and subsequently with saturated

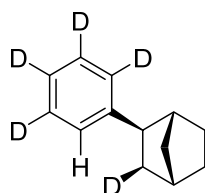
aqueous solution of  $\text{NH}_4\text{Cl}$  (1 mL), and diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford desire product.

**A Typical Procedure (Type C Reagent):** In a 10 mL Schlenk tube was placed  $\text{ZnCl}_2 \cdot \text{TMEDA}$  (189 mg, 0.75 mmol). The Schlenk tube was submerged in an ice bath for 15 mins prior to the addition of Grignard reagents. To the  $\text{ZnCl}_2 \cdot \text{TMEDA}$  was added a THF solution of arylGrignard (0.75 mmol) dropwise at  $0^\circ\text{C}$ . After stirring for 1 h at  $0^\circ\text{C}$ , a THF solution of  $(\text{CH}_3)_3\text{SiCH}_2\text{MgBr}$  (0.75 mmol) was added dropwise. The resulting solution was allowed to warm to room temperature and stirred for 30 mins before dppf (13.9 mg, 0.025 mmol) and  $\text{CoCl}_2$  (3.3 mg, 0.025 mmol) was added. After stirring for 5 mins, norbornene (0.5 mmol) was added. The resulting solution was stirred at  $40^\circ\text{C}$  for 12 h. The workup and purification procedures are the same as described above.



**exo-2-(4-methoxyphenyl)bicyclo[2.2.1]heptane (3aa-d):** The reaction of 4-methoxyphenylzinc reagent (type C) and norbornene was performed according to typical procedure at  $40^\circ\text{C}$  for 12 h. Short Silica gel chromatography (eluent: hexane) of the crude product afforded the title compound as a colourless oil mixture. The yield of the title compound was determined to be 82% by  $^1\text{H}$  NMR integration of the characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.13 (d,  $J = 9.2$  Hz, 2H), 6.84 – 6.81 (m, 2H), 3.77 (s, 3H), 2.68 (dd,  $J =$

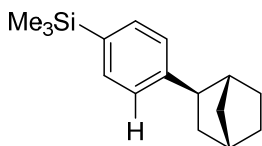
8.6, 5.8 Hz, 1H), 2.34 – 2.29 (m, 1H), 1.74 (ddd,  $J = 11.6, 8.9, 2.3$  Hz, 1H), 1.64 – 1.56 (m, 2H), 1.54 – 1.49 (m, 1H), 1.37 – 1.31 (m, 1H), 1.27 – 1.22 (m, 1H), 1.17 – 1.14 (m, 1H). Comparison with reported  $^1\text{H}$  NMR spectrum of non-deuterated derivative<sup>21</sup> and the integration (1.12) of the signal at 7.13 ppm (corresponding to the protons on the 2,6-positions) supported predominant deuteration of the 2-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.36, 139.70, 127.9, 113.5, 113.4, 55.2, 46.5, 43.2, 39.2, 36.8, 35.9, 30.5, 28.9. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{14}\text{H}_{18}\text{OD}$   $[\text{M} + \text{H}]^+$  204.1499, found 204.1498.



***exo,exo*-2-Deuterio-3-(2,3,4,5-tetradeuteriophenyl)bicyclo[2.2.1]heptane (3ba-*d*<sub>5</sub>):**

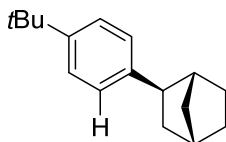
Magnesium turnings (37.7 mg, 1.55 mmol) suspended in THF (1.25 mL) in a 10 mL Schlenk tube was added bromobenzene-*d*<sub>5</sub> (1.50 mmol). The Schlenk tube was sealed and heated to 80 °C. After stirring at 80 °C for 2 h, the resulting Grignard was cooled to 0 °C and  $\text{ZnCl}_2 \cdot \text{TMEDA}$  (189 mg, 0.75 mmol) was added in one portion. After stirring for 1 h, the Schlenk tube was allowed to room temperature, and then dppf (13.9 mg, 0.025 mmol) and  $\text{CoCl}_2$  (3.2 mg, 0.025 mmol) was added. After stirring for 5 mins, norbornene (47.1 mg, 0.5 mmol) was added. The resulting mixture was stirred at 40 °C for 12 h, allowed to cool to room temperature, quenched by saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (1 mL), and dilute with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL).

The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford desired product as light yellow oil. The yield of the title compound was determined to be 72% by characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 (s, 1H), 2.73 (d,  $J = 9.1$  Hz, 1H), 2.38 – 2.32 (m, 2H), 1.79 – 1.71 (m, 1H), 1.61 – 1.52 (m, 3H), 1.39 – 1.33 (m, 1H), 1.30 – 1.23 (m, 1H), 1.18 (ddd,  $J = 9.7, 2.5, 1.4$  Hz, 1H). The proton contents at the 6-position of the aryl group and the 2-position of the norbornyl group were estimated to be 0.82 and 0.91 by NMR integrations, supporting the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{13}\text{H}_{12}\text{D}_5$   $[\text{M} + \text{H}]^+$  178.1644, found 178.1641.

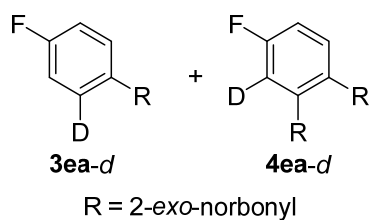


**exo-4-(Bicyclo[2.2.1]heptan-2-yl)-3-deuteriophenyl)trimethylsilane (3ca-d):** The reaction of 4-trimethylsilylphenylzinc reagent (type C) and was performed according to typical procedure at 40 °C for 12 h. Silica gel chromatography (eluent: hexane/ether = 150/1 – 50/1) of the crude product afforded the title compound as a colourless oil (112.9 mg, 92 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) 7.45 – 7.43 (m, 2H), 7.21 (dd,  $J = 8.1, 1.4$  Hz, 1H), 2.73 (dd,  $J = 8.8, 5.8$  Hz, 1H), 2.38 – 2.33 (m, 2H), 1.71– 1.63 (m, 1H), 1.61 – 1.50 (m, 3H), 1.39 – 1.32 (m, 1H), 1.29 – 1.24 (m, 1H), 1.20 – 1.15 (m, 1H), 0.25 (s, 9H). The integration (1.18) of the signal at 7.21 ppm (corresponding to the protons on the 3,5-positions) supported predominant deuteration of the 3-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  148.2, 136.8, 133.3, 133.2, 126.6, 126.3 (t,  $^1J_{\text{C-D}} = 24.1$  Hz), 47.3, 42.9, 39.0, 36.8, 36.1, 30.6, 28.9, -1.1 (3 x C). All of the norbornyl carbon atoms were observed as

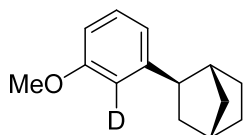
singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $C_{16}H_{24}SiD$   $[M + H]^+$  246.1788, found 246.1787.



**exo-2-(4-(tert-Butyl)-2-deuteriophenyl)bicyclo[2.2.1]heptane (3da-d):** The reaction of *tert*-butylphenylzinc reagent (type A) and was performed according to typical procedure at 40 °C for 12 h. Short Silica gel chromatography (eluent: hexane) of the crude product afforded the title compound as a colourless oil mixture. The yield of the title compound was determined to be 97% by characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.31 – 7.28 (m, 2H), 7.15 (d,  $J$  = 8.8 Hz, 1H), 2.71 (dd,  $J$  = 8.9, 5.7 Hz, 1H), 2.35 – 2.32 (m, 2H), 1.74 (ddd,  $J$  = 11.1, 8.9, 2.3 Hz, 1H), 1.70 – 1.51 (m, 4H), 1.33 – 1.32 (m, 2H), 1.31 (s, 9H), 1.16 (ddt,  $J$  = 9.7, 2.5, 1.2 Hz, 1H). The integration (1.11) of the signal at 7.15 ppm (corresponding to the protons on the 2,6-positions) supported predominant deuteration of the 2-position;  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  148.1, 144.5, 126.8, 125.1, 125.0, 46.9, 43.1, 39.1, 36.9, 36.1, 34.3, 31.5 (3 x C), 30.7, 29.0; The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $C_{17}H_{24}D$   $[M + H]^+$  230.2019, found 230.2026.

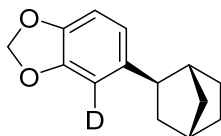


**3ea-d and 4ea-d:** The reaction of 4-fluorophenylzinc reagent (type C) and norbornene was performed according to the typical procedure at 60 °C for 12 h. Short-path silica gel column chromatography (eluent: hexane) of the crude product afforded a mixture containing the mono- and di-adducts **3ea-d** and **4ea-d** as a colorless oil. The identities of **3ea-d** and **4ea-d** were supported by GC, GCMS and HRMS analysis. We speculate that the diadduct **4ea-d** was obtained as a mixture of diastereomers, while no resolution was observed in the GC chromatogram. The quantities of these products (**3a-d**, 0.126 mmol; **4a-d**, 0.107 mmol) were estimated based on <sup>1</sup>H NMR (integrations of signals of characteristic benzylic protons as internal standard, 1,1,2,2-tetrachloroethane) and GC analysis (peak area divided by the number of carbon atoms). HRMS (ESI) Calcd for C<sub>13</sub>H<sub>15</sub>FD [M + H]<sup>+</sup> 192.1299, found 192.1296, C<sub>20</sub>H<sub>25</sub>FD [M + H]<sup>+</sup> 286.2081, found 286.2075.



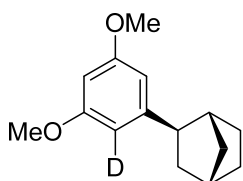
**exo-2-(3-Methoxy-2-deuteriophenyl)bicyclo[2.2.1]heptane (3ga-d):** The reaction of 3-methoxyphenylzinc reagent (type C) and norbornene was performed according to the typical procedure at 60 °C for 12 h. Short-path silica gel column chromatography (eluent: hexane) of the crude product afforded a mixture containing the title compound as a colorless oil. The yield of the title compound was determined to be 38% by <sup>1</sup>H NMR integration of the characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal

standard.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.19 (t,  $J = 8.0$  Hz, 1H), 6.81 (d,  $J = 7.7$  Hz, 1H), 6.70 (d,  $J = 8.1$  Hz, 1H), 3.79 (s, 3H), 2.71 (dd,  $J = 8.6, 5.9$  Hz, 1H), 2.37 – 2.33 (m, 2H), 1.76 (ddd,  $J = 11.6, 9.0, 2.3$  Hz, 1H), 1.67 – 1.61 (m, 2H), 1.56 – 1.51 (m, 2H), 1.37 – 1.32 (m, 1H), 1.29 – 1.23 (m, 1H), 1.20 – 1.16 (m, 1H). Comparison with reported  $^1\text{H}$  NMR spectrum of non-deuterated derivative<sup>22</sup> and the integration (0.22) of the signal around 6.77 ppm (which may correspond to the proton at the 2-position) supported predominant deuteration of the 2-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  159.5, 149.3, 129.1, 119.5, 113.2, 55.1, 47.3, 42.9, 39.2, 36.8, 36.2, 30.6, 28.9. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{14}\text{H}_{18}\text{OD}$   $[\text{M} + \text{H}]^+$  204.1499, found 204.1496.



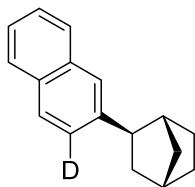
***exo*-5-(Bicyclo[2.2.1]heptan-2-yl)-4-deuteriobenzo[*d*][1,3]dioxole (3ha-*d*):** The reaction of 3,4-methylenedioxyphenylzinc reagent (type A) and norbornene was performed according to the typical procedure. Silica gel chromatography (eluent: hexane/ether = 100/1 – 20/1) of the crude product afforded the title compound as a colorless oil containing a small amount of benzo[*d*][1,3]dioxole (93.4 mg, 86 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.72 (d,  $J = 8.0$  Hz, 1H), 6.65 (d,  $J = 8.0$  Hz, 1H), 5.90 (s, 2H), 2.65 (dd,  $J = 9.5, 5.8$  Hz, 1H), 2.32 (s, 1H), 2.29 – 2.28 (m, 1H), 1.73 (ddd,  $J = 11.8, 9.0, 2.4$  Hz, 1H), 1.60 – 1.53 (m, 3H), 1.52 – 1.48 (m, 1H), 1.35 – 1.29 (m, 1H), 1.26 – 1.21 (m, 1H), 1.16 (ddt,  $J = 9.8, 3.0, 1.5$  Hz, 1H). The regioselective deuteration of the 4-position of the aryl group was supported by the absence of a singlet (or weak doublet) signal in the aromatic region;  $^{13}\text{C}$  NMR (101

MHz, CDCl<sub>3</sub>)  $\delta$  147.4, 145.1, 141.7, 119.6, 107.8, 100.7, 47.0, 43.1, 39.5, 36.7, 36.0, 30.5, 28.8. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>D [M + H]<sup>+</sup> 218.1291, found 218.1299.

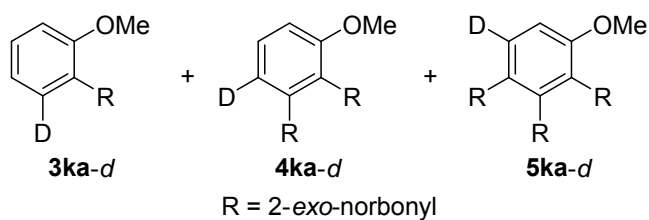


***exo*-2-(3,5-Dimethoxy-2-deuteriophenyl)bicyclo[2.2.1]heptane (3ia-d):** The reaction of 3,5-dimethoxyphenylzinc reagent (type C) and norbornene was performed according to the typical procedure at 60 °C for 12 h. Short-path silica gel column chromatography (eluent: hexane) of the crude product afforded a mixture containing the title compound as a colorless oil. The yield of the title compound was determined to be 97% by <sup>1</sup>H NMR integration of the characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.38 (d, *J* = 2.2 Hz, 1H), 6.27 (d, *J* = 2.2 Hz, 1H), 3.77 (s, 6H), 2.67 (dd, *J* = 9.2, 5.5 Hz, 1H), 2.35 – 2.32 (m, 2H), 1.74 (ddd, *J* = 11.6, 9.0, 2.3 Hz, 1H), 1.65 – 1.52 (m, 4H), 1.36 – 1.30 (m, 1H), 1.27 – 1.22 (m, 1H), 1.18 (m, 1H). Comparison with reported <sup>1</sup>H NMR spectrum of non-deuterated derivative<sup>23</sup> and the integration (1.03) of the signal at 6.38 ppm (corresponding to the proton at the 2,6-positions) supported predominant deuteration of the 2-position; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  160.6, 160.5, 150.1, 105.3, 100.4, 97.1, 55.2, 47.5, 42.8, 39.2, 36.7, 36.3, 30.5, 28.8. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support

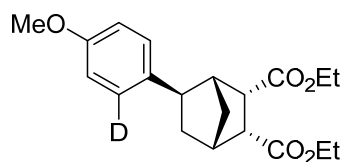
the structural assignment; HRMS (ESI) Calcd for  $C_{15}H_{20}O_2D$   $[M + H]^+$  234.1604, found 234.1602.



***exo*-2-(Bicyclo[2.2.1]heptan-2-yl)-3-deuterionaphthalene (3ja-d):** The reaction of 2-naphthylzinc reagent (type C) and norbornene was performed according to the typical procedure. Short-path silica gel column chromatography (eluent: hexane) of the crude product afforded a mixture containing the title compound as a colourless oil. The yield of the title compound was determined to be 97% by  $^1H$  NMR integration of the characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.79 – 7.75 (m, 3H), 7.62 (s, 1H), 7.46 – 7.37 (m, 2H), 2.90 (dd,  $J = 8.7, 5.8$  Hz, 1H), 2.50 – 2.47 (m, 1H), 2.42 – 2.39 (m, 1H), 1.87 – 1.74 (m, 2H), 1.70 – 1.58 (m, 3H), 1.46 – 1.39 (m, 1H), 1.35 – 1.29 (m, 1H), 1.26 – 1.20 (m, 1H). Comparison with reported  $^1H$  NMR spectrum of the non-deuterated derivative<sup>18</sup> and the integration (1.03) of the signal at 6.38 ppm (corresponding to the proton at the 1-position) supported predominant deuteration of the 3-position;  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  144.8, 133.47, 131.8, 127.8, 127.6, 127.4, 125.8, 125.0, 124.1, 47.4, 42.8, 38.9, 36.9, 36.1, 30.6, 29.0. The signal of the 3-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $C_{17}H_{18}D$   $[M + H]^+$  224.1550, found 224.1542.



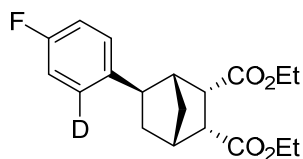
**3ka-d, 4ka-d and 5ka-d:** The reaction of 2-methoxyphenylzinc reagent (type C) and norbornene was performed according to the typical procedure at 60 °C for 24 h. Short-path silica gel column chromatography (eluent: hexane) of the crude product afforded a mixture containing mono-, di-, and tri-adducts **3ka-d**, **4ka-d**, and **5ka-d**. The identities of these products were supported by GC, GCMS, and HRMS analysis. Their quantities (**3ka-d**, 0.130 mmol; **4ka-d**, 0.025 mmol; **5ka-d**, 0.002 mmol) were estimated by  $^1\text{H}$  NMR (integration of the characteristic signal of benzylic proton using 1,1,2,2-tetrachloroethane as an internal standard) and GC analysis (peak area divided by the number of carbon atoms). HRMS (ESI) Calcd for  $\text{C}_{14}\text{H}_{18}\text{OD}$   $[\text{M} + \text{H}]^+$  204.1499, found 204.1500,  $\text{C}_{21}\text{H}_{28}\text{OD}$   $[\text{M} + \text{H}]^+$  298.2281, found 298.2284,  $\text{C}_{28}\text{H}_{38}\text{OD}$   $[\text{M} + \text{H}]^+$  392.3064, found 392.3062.



**Diethyl *exo*-5-(4-methoxy-2-deuteriophenyl)bicyclo[2.2.1]heptane-2,3-*endo*,*endo*-**

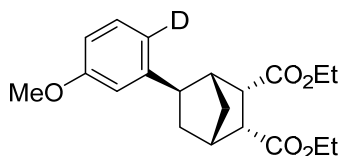
**dicarboxylate (3ab-d):** The reaction of 4-methoxyphenylzinc reagent (type A) and diethyl *endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate was performed according to the typical procedure using dppe instead of dppf. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (121.6 mg, 70 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.20 (d,  $J$  = 9.4 Hz, 1H), 6.85 – 6.82 (m, 2H), 4.21 – 4.11 (m, 4H), 3.78 (s, 3H), 3.49 (app. t,  $J$  = 8.3, 7.5 Hz, 1H), 3.12 (ddd,  $J$

= 11.7, 4.5, 1.7 Hz, 1H), 2.95 (dd,  $J = 11.7, 3.8$  Hz, 1H), 2.69 (t,  $J = 2.8$  Hz, 2H), 2.57 (dd,  $J = 3.7, 1.6$  Hz, 1H), 2.14 (ddd,  $J = 12.7, 8.9, 2.5$  Hz, 1H), 1.72 (dt,  $J = 10.1, 1.7$  Hz, 1H), 1.66 (dddd,  $J = 13.0, 6.0, 4.1, 1.7$  Hz, 1H), 1.27 (t,  $J = 7.1$  Hz, 1H), 1.26 (t,  $J = 7.2$  Hz, 1H). The integration (1.16) of the signal at 7.20 ppm (corresponding to the protons at the 2,6-positions) supported predominant deuteration of the 2-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.5, 172.2, 157.6, 138.3, 128.2, 128.2, 113.5, 60.3, 60.1, 55.2, 47.8, 46.8, 46.1, 41.4, 39.2, 37.2, 33.0, 14.2 (2C). The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{20}\text{H}_{26}\text{O}_5\text{D}$   $[\text{M} + \text{H}]^+$  348.1921, found 348.1925.



**Diethyl *exo*-5-(4-fluoro-2-deuteriophenyl)bicyclo[2.2.1]heptane-2,3-*endo,endo*-dicarboxylate (3eb-*d*):** The reaction of 4-fluorophenylzinc reagent (type A) and diethyl *endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate was performed according to the typical procedure using dppe instead of dppf at 60 °C for 12 h. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (40.2 mg, 24 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23 (dd,  $J = 9.3, 5.3$  Hz, 1H), 6.99 – 6.95 (m, 2H), 4.21 – 4.09 (m, 4H), 3.55 (dd,  $J = 8.6, 6.6$  Hz, 1H), 3.14 (ddd,  $J = 11.7, 4.6, 1.6$  Hz, 1H), 2.94 (dd,  $J = 11.7, 3.8$  Hz, 1H), 2.72 – 2.69 (m, 1H), 2.57 (dd,  $J = 3.7, 1.6$  Hz, 1H), 2.13 (ddd,  $J = 11.7, 8.9, 2.5$  Hz, 1H), 1.70 (dt,  $J = 10.2, 1.8$  Hz, 1H), 1.67 – 1.62 (m, 1H), 1.37 (ddd,  $J = 10.3, 2.9, 1.4$  Hz, 1H), 1.27 (t,  $J = 7.1$  Hz, 3H), 1.26 (t,  $J = 7.1$  Hz, 3H). The integration (1.14) of the signal at 7.23 ppm (corresponding to the protons at the

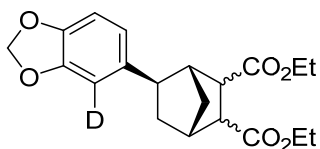
2,6-positions) supported predominant deuteration of the 2-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  174.5, 172.2, 161.1 (d,  $^2J_{\text{C-F}} = 243.4$  Hz), 141.6 (d,  $^5J_{\text{C-F}} = 3.1$  Hz), 128.6 (d,  $^4J_{\text{C-F}} = 7.9$  Hz), 114.9 (d,  $^3J_{\text{C-F}} = 20.9$  Hz), 114.8 (d,  $^3J_{\text{C-F}} = 20.9$  Hz) 60.4, 60.2, 47.9, 46.7, 46.0, 41.5, 39.3, 37.3, 33.3, 14.27, 14.24. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{23}\text{O}_4\text{FD}$   $[\text{M} + \text{H}]^+$  336.1721, found 336.1721.



**Diethyl *exo*-5-(5-methoxy-2-deuteriophenyl)bicyclo[2.2.1]heptane-2,3-*endo,endo*-**

**dicarboxylate (3gb-d):** The reaction of 3-methoxyphenylzinc reagent (type A) and diethyl *endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate was performed according to the typical procedure using dppe instead of dppf at 60 °C for 12 h. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (57.3 mg, 33 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 (app. dd,  $J = 8.1$ , 1H), 6.76 (d,  $J = 2.6$  Hz, 1H), 6.72 (dd,  $J = 8.3$ , 2.5 Hz, 1H), 4.20 (q,  $J = 7.1$  Hz, 2H), 4.14 (q,  $J = 7.1$  Hz, 2H), 3.80 (s, 3H), 3.28 (td,  $J = 4.8$ , 2.0 Hz, 1H), 3.01 (dd,  $J = 5.1$ , 1.7 Hz, 1H), 2.91 (dd,  $J = 8.6$ , 5.5 Hz, 1H), 2.80 – 2.73 (m, 2H), 1.84 (ddd,  $J = 13.3$ , 9.0, 2.4 Hz, 1H), 1.66 – 1.59 (m, 2H), 1.55 – 1.51 (m, 1H), 1.29 (t,  $J = 7.1$  Hz, 3H), 1.25 (t,  $J = 7.2$  Hz, 3H). The position of the deuterium atom (C2) was determined by comparison with compounds (**3ga**<sup>5</sup> and **3ga-d**) and characteristic signals such as apparent doublet at 7.21 ppm (C3–CH) and weakly coupled doublet at 6.76 ppm (C6–CH);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  174.2, 173.5, 159.6, 147.4, 129.2, 113.1, 110.8, 60.8, 60.7, 55.2, 49.7, 48.7, 47.7, 46.2, 40.6, 36.0,

33.7, 14.3, 14.2. The signal of the 2-position of the aryl group (expected to appear around 119 ppm as judged from  $^{13}\text{C}$  NMR spectra of **3ga**<sup>5</sup> and **3ga-d**) was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{20}\text{H}_{26}\text{O}_5\text{D}$   $[\text{M} + \text{H}]^+$  348.1921, found 348.1921.



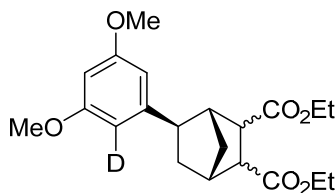
**Diethyl 5-(4-deuteriobenzo[d][1,3]dioxol-5-yl)bicyclo[2.2.1]heptane-2,3-dicarboxylate**

**(3hb-d):** The reaction of 3,4-methylenedioxyphenylzinc reagent (type A) and diethyl *endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate was performed according to the typical procedure using dppe instead of dppf at 60 °C for 12 h. Silica gel chromatography (eluent:hexane/ether = 50/1 – 15/1) of the crude product afforded two sets of fractions containing different diastereomers.

**Fraction 1:** Colorless oil containing two major diastereomers in ca. 1:1 ratio (27.2 mg, 15%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.74 – 6.61 (m, 2H), 5.92 (s, 2H), 4.24 – 4.11 (m, 4H), 3.30 – 3.26 (m, 1H), 2.99 – 2.84 (m, 1H), 2.76 – 2.65 (m, 2H), 1.93 – 1.75 (m, 2H), 1.62 – 1.50 (m, 3H), 1.32 – 1.24 (m, 6H). Pairs of doublet signals in 6.74–6.61 ppm indicated that the position proximal to the oxygen atom was deuterated;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  174.58, 174.57, 174.2, 173.2, 147.7, 147.6, 145.6, 139.8, 139.5, 139.4, 119.65, 119.64, 119.63, 108.0, 107.9, 107.73, 107.66, 100.84, 100.82, 60.81, 60.80, 60.78, 60.73, 60.67, 49.8, 49.7, 49.6, 48.7, 48.6, 48.1, 48.01, 47.95, 46.9, 46.0, 45.9, 42.24, 41.21, 41.16, 40.6, 37.7, 37.6, 35.9, 35.4, 33.9, 21.0, 14.4, 14.3, 14.20, 14.18, 14.16; The clear singlet signals

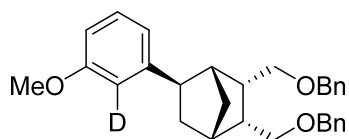
around 119 ppm (corresponding to the C6 position) are in accordance with the structural assignment; HRMS (ESI) Calcd for C<sub>20</sub>H<sub>24</sub>O<sub>6</sub>D [M + H]<sup>+</sup> 362.1714, found 362.1712.

**Fraction 2:** Colorless oil consisting of single diastereomer (90.2 mg, 50%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.73 (s, 2H), 5.91 (s, 2H), 4.25 – 4.07 (m, 4H), 3.52 – 3.44 (m, 1H), 3.12 (ddd, *J* = 11.7, 4.5, 1.6 Hz, 1H), 2.93 (dd, *J* = 11.7, 3.8 Hz, 1H), 2.68 (d, *J* = 4.5 Hz, 1H), 2.56 (dd, *J* = 3.7, 1.6 Hz, 1H), 2.12 (ddd, *J* = 12.3, 8.8, 2.6 Hz, 1H), 1.75 – 1.67 (m, 1H), 1.67 – 1.57 (m, 1H), 1.39 – 1.31 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) 172.5, 172.2, 147.6, 147.5, 145.4, 140.2, 119.9, 108.0, 107.9, 100.7, 60.3, 60.2, 47.9, 46.8, 46.0, 41.4, 39.8, 37.3, 33.3, 14.2. While the singlet signal (integration = 1.94) at 6.73 ppm in the <sup>1</sup>H NMR spectrum does not allow unambiguous determination of the position of deuteration, the singlet signal at 119.9 ppm (corresponding to the position distal to the methylenedioxy group) in the <sup>13</sup>C NMR spectrum confirms the regiochemical assignment; HRMS (ESI) Calcd for C<sub>20</sub>H<sub>24</sub>O<sub>6</sub>D [M + H]<sup>+</sup> 362.1714, found 362.1712.



**Diethyl 5-(3,5-dimethoxy-2-deuteriophenyl)bicyclo[2.2.1]heptane-2,3-dicarboxylate (3ib-d):** The reaction of 3,5-dimethoxyphenylzinc reagent (type A) and diethyl *endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate was performed according to the typical

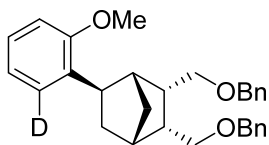
procedure using dppe instead of dppf at 60 ° C for 12 h. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded a diastereoisomeric mixture of the title compound as a colorless oil (132.1 mg, 70 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, major diastereomers) δ 6.37 (d, *J* = 2.3 Hz, 1H), 6.29 (d, *J* = 2.2 Hz, 1H), 4.22 – 4.11 (m, 4H), 3.78 (s, 6H), 3.31 – 3.26 (m, 1H), 2.99 (dd, *J* = 5.0, 1.6 Hz, 1H), 2.91 – 2.85 (m, 1H), 2.79 – 2.72 (m, 2H), 1.94 – 1.76 (m, 1H), 1.66 – 1.51 (m, 3H), 1.31 – 1.24 (m, 6H). The integration (0.85) of the signal at 6.37 ppm (corresponding to the protons at the 2,6-positions) supported predominant deuteration of the 2-position; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>, major diastereomer) δ 174.3, 173.6, 160.84, 160.82, 148.4, 105.4, 97.6, 60.9, 60.8, 55.40, 55.35, 49.8, 48.8, 47.7, 46.5, 40.7, 36.3, 33.9, 14.4, 14.3. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for C<sub>21</sub>H<sub>28</sub>O<sub>6</sub>D [M + H]<sup>+</sup> 378.2027, found 378.2032.



***endo,endo*-2,3-Bis((benzyloxy)methyl)-*exo*-5-(3-methoxy-2-**

**deuteriophenyl)bicyclo[2.2.1]heptane (3gc-d):** The reaction of 3-methoxyphenylzinc reagent (type A) and *endo,endo*-5,6-bis((benzyloxy)methyl)bicyclo[2.2.1]hept-2-ene was performed according to the typical procedure. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (75.4 mg, 34 %). <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.34 – 7.26 (m, 10H), 7.17 (dd, *J* = 8.3, 7.5 Hz, 1H), 6.79 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.68 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.48 (d, *J* = 3.1 Hz, 2H), 4.46 (d, *J* = 2.6 Hz, 2H), 3.74 (s, 3H), 3.67 (dd, *J* = 9.4, 6.3 Hz, 1H), 3.64 –

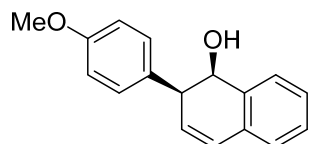
3.55 (m, 1H), 3.57 (dd,  $J = 5.8, 3.3$  Hz, 1H), 3.47 (dd,  $J = 9.4, 7.9$  Hz, 1H), 2.92 (dd,  $J = 8.5, 6.3$  Hz, 1H), 2.46 – 2.43 (m, 2H), 2.44 – 2.23 (m, 2H), 1.94 (ddd,  $J = 13.1, 8.9, 2.5$  Hz, 1H), 1.63 (dt,  $J = 9.9, 1.8$  Hz, 1H), 1.54 (dddd,  $J = 13.1, 5.8, 4.2, 1.3$  Hz, 1H), 1.36 (ddd,  $J = 9.9, 2.7, 1.4$  Hz, 1H). Comparison with reported  $^1\text{H}$  NMR spectrum of related compounds (**3ga**<sup>22</sup> and **3ga-d**) supported predominant deuteration of the 2-position;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  160.2, 149.4, 139.5, 129.6, 128.8 (4 x C), 128.21 (2 x C), 128.16 (2 x C), 127.99, 127.95, 120.1, 113.8, 111.1, 73.62, 73.61, 69.2, 68.4, 55.6, 47.2, 42.0, 41.1, 40.1, 39.4, 37.7, 32.1. The signal of the 2-position of the aryl group was too weak to be identified. All of the norbornyl carbon atoms were observed as singlet signals. These observations also support the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{30}\text{H}_{34}\text{O}_3\text{D}$   $[\text{M} + \text{H}]^+$  444.2649, found 444.2646.



**endo,endo-2,3-Bis((benzyloxy)methyl)-exo-5-(2-methoxy-6-**

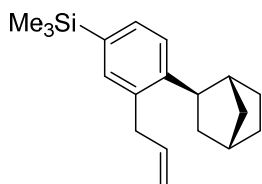
**deuteriophenyl)bicyclo[2.2.1]heptane (3kc-d):** The reaction of 2-methoxyphenylzinc reagent (type A) and *endo,endo*-5,6-bis((benzyloxy)methyl)bicyclo[2.2.1]hept-2-ene was performed according to the typical procedure. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (17.7 mg, 8 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  7.37 – 7.27 (m, 5H), 7.33 – 7.21 (m, 5H), 7.14 (dd,  $J = 8.1, 7.4$  Hz, 1H), 6.88 (m, 1H), 6.82 (dd,  $J = 8.1, 1.2$  Hz, 1H), 4.52 – 4.44 (m, 4H), 3.75 (s, 3H), 3.70 – 3.61 (m, 3H), 3.53 (t,  $J = 9.0$  Hz, 1H), 3.16 (ddd,  $J = 8.2, 6.1, 1.4$  Hz, 1H), 2.44 – 2.42 (m, 1H), 2.40 – 2.39 (m, 1H), 2.37 – 2.30 (m, 2H), 2.00 (ddd,  $J = 13.2, 8.9, 2.5$  Hz, 1H), 1.63 (dt,  $J = 9.8, 1.7$  Hz, 1H), 1.40 – 1.35 (m, 2H). The

deuteration of the 6-position was supported by comparison with  $^1\text{H}$  NMR spectrum of a related compound **3ka** reported in the literature<sup>24</sup>;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.0, 135.9, 135.8, 128.80 (2 x C), 128.76 (2 x C), 128.2 (2 x C), 128.1 (2 x C), 127.9, 127.86, 126.88, 120.5, 120.4, 110.6, 73.56, 73.55, 69.3, 68.8, 55.7, 45.6, 42.6, 41.1, 40.1, 37.8, 33.1, 31.7. The clear singlet signals of all the norbornyl carbons are in accordance with the structural assignment; HRMS (ESI) Calcd for  $\text{C}_{30}\text{H}_{34}\text{O}_3\text{D}$   $[\text{M} + \text{H}]^+$  444.2649, found 444.2646.

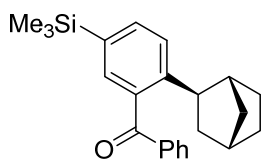


**cis-2-(4-Methoxyphenyl)-1,2-dihydronaphthalen-1-ol (6):** The reaction of 4-methoxyphenylzinc reagent (type A) and 1,4-dihydro-1,4-epoxynaphthalene was performed according to the typical procedure at 60 °C for 4 h. Silica gel chromatography (eluent: hexane/ether = 50/1 – 15/1) of the crude product afforded the title compound as a colorless oil (112.3 mg, 89 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (ddd,  $J = 6.9, 1.8, 0.8$  Hz, 1H), 7.30 – 7.21 (m, 2H), 7.17 – 7.14 (m, 3H), 6.85 – 6.84 (m, 1H), 6.83 – 6.81 (m, 1H), 6.67 (dd,  $J = 9.6, 1.9$  Hz, 1H), 6.10 (dd,  $J = 9.6, 4.3$  Hz, 1H), 4.92 (dd,  $J = 8.1, 6.2$  Hz, 1H), 3.81 (ddd,  $J = 6.3, 4.4, 2.0$  Hz, 1H), 3.77 (s, 3H), 1.48 (d,  $J = 8.2$  Hz, 1H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  159.1, 136.4, 132.8, 130.4 (2 x C), 130.2, 129.2, 128.3, 128.12, 128.09, 126.6, 126.4, 114.2 (2C), 71.4, 55.3, 46.5; HRMS (ESI) Calcd for  $\text{C}_{17}\text{H}_{17}\text{O}_2$   $[\text{M} + \text{H}]^+$  253.1229, found 253.1234. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra showed good agreement with the literature data.<sup>25</sup>

### Transformations of *ortho*-(2-*exo*-Norbornyl)arylzinc Species

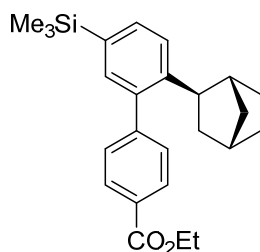


**exo-(3-Allyl-4-(bicyclo[2.2.1]heptan-2-yl)phenyl)trimethylsilane (7):** To the reaction mixture of 4-trimethylsilylphenylzinc reagent and norbornene (vide supra) were added a THF solution of  $\text{CuCN}\cdot 2\text{LiCl}$  (1 mL of 1 M solution, 0.1 mmol) and allyl bromide (181 mg, 1.5 mmol) at 0 °C. The resulting mixture was warmed to 60 °C and stirred for 8 h. The reaction was allowed to room temperature, quenched with saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (10 mL), and diluted with ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 100/1 – 20/1) of the crude product afforded the title compound as a yellow oil (130.9 mg, 92 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (dd,  $J = 7.7, 1.5$  Hz, 1H), 7.28 (d,  $J = 1.4$  Hz, 1H), 7.27 (d,  $J = 1.4$  Hz, 1H), 6.03 – 5.93 (m, 1H), 5.08 – 5.00 (m, 2H), 3.49 – 3.38 (m, 2H), 2.87 (dd,  $J = 9.1, 5.6$  Hz, 1H), 2.35 – 2.34 (m, 2H), 1.77 (ddd,  $J = 11.4, 9.1, 2.3$  Hz, 1H), 1.65 – 1.54 (m, 4H), 1.38 – 1.21 (m, 3H), 0.24 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  146.1, 137.5, 137.0, 136.9, 134.7, 131.3, 124.7, 115.6, 43.1, 42.1, 39.3, 37.5, 36.9, 36.5, 30.7, 29.0, -1.1 (3 x C); HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{29}\text{Si}$   $[\text{M} + \text{H}]^+$  285.2039, found 285.2037.



***exo*-(2-(Bicyclo[2.2.1]heptan-2-yl)-5-(trimethylsilyl)phenyl)(phenyl)methanone (8):**

To the reaction mixture of 4-trimethylsilylphenylzinc reagent and norbornene (vide supra) were added a THF solution of CuCN•2LiCl (1 mL of 1 M solution, 0.1 mmol) and benzoyl chloride (211 mg, 1.5 mmol) at 0 °C. The resulting mixture was warmed to 60 °C and stirred for 8 h. The reaction was allowed to room temperature, quenched with saturated aqueous solution of NH<sub>4</sub>Cl (10 mL), and diluted with ethyl acetate (10 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was dried over MgSO<sub>4</sub> concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 100/1 – 20/1) of the crude product afforded the title compound as a light yellow solid (163.8 mg, 94 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (d, *J* = 1.1 Hz, 1H), 7.82 (d, *J* = 1.4 Hz, 1H), 7.64 – 7.55 (m, 1H), 7.57 (dd, *J* = 2.4, 1.4 Hz, 1H), 7.51 – 7.39 (m, 3H), 7.35 (d, *J* = 1.4 Hz, 1H), 2.83 (dd, *J* = 8.5, 6.4 Hz, 1H), 2.37 – 2.35 (m, 1H), 2.29 – 2.27 (m, 1H), 1.64 – 1.60 (m, 1H), 1.58 – 1.54 (m, 2H), 1.48 – 1.44 (m, 2H), 1.21 (dt, *J* = 9.7, 1.7 Hz, 1H), 1.17 – 1.02 (m, 2H), 0.24 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 199.8, 146.4, 138.4, 137.9, 136.6, 134.9, 133.2, 132.4, 130.2 (2 x C), 128.4 (2 x C), 125.2, 43.7, 42.6, 40.2, 36.8, 36.7, 30.4, 28.4, -1.2 (3 x C); HRMS (ESI) Calcd for C<sub>23</sub>H<sub>29</sub>OSi [M + H]<sup>+</sup> 349.1988, found 349.1991.



**Ethyl *exo*-2'-(bicyclo[2.2.1]heptan-2-yl)-5'-(trimethylsilyl)-[1,1'-biphenyl]-4-carboxylate (9):** To the reaction mixture of 4-trimethylsilylphenylzinc reagent and

norbornene (vide supra) were a THF solution of Pd<sub>2</sub>(dba)<sub>3</sub>/SPhos (0.2 mL of 0.1 M solution, 0.02 mmol) and ethyl 4-iodobenzoate (414.1 mg, 1.5 mmol) at 20 °C. The resulting mixture was heated to 60 °C and stirred for 8 h. The reaction was allowed to room temperature, quenched with saturated aqueous solution of NH<sub>4</sub>Cl (10 mL), and diluted with ethyl acetate (2 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ether = 50/1 – 10/1) of the crude product afforded the title compound as a light yellow solid (78.5 mg, 40 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.22 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.29 (t, *J* = 4.7 Hz, 1H), 3.02 (dd, *J* = 5.0, 1.7 Hz, 1H), 2.94 (dd, *J* = 9.1, 1.3 Hz, 1H), 2.77 – 2.74 (m, 2H), 1.83 (dd, *J* = 9.0, 2.3 Hz, 1H), 1.64 (dq, *J* = 10.6, 1.6 Hz, 1H), 1.53 (ddd, *J* = 10.5, 2.6, 1.4 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 174.2, 173.4, 145.6, 126.9, 49.7, 48.7, 47.7, 46.1, 40.6, 35.9, 14.3, 14.2; HRMS (ESI) Calcd for C<sub>19</sub>H<sub>20</sub>O<sub>4</sub>D<sub>5</sub> [M + H]<sup>+</sup> 322.2067, found 322.2065.

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## List of Publications

1. Cobalt-Catalyzed Addition of Arylzinc Reagents to Alkynes to Form *Ortho*-Alkenylarylzinc Species Through 1,4-Cobalt Migration, Tan, B.-H.; Dong, J.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 9610.
2. Cobalt-Catalyzed Addition of Arylzinc Reagents to Norbornene Derivatives Through 1,4-Cobalt Migration, Tan, B.-H.; Yoshikai, N. *Org. Lett.* **2014**, *16*, 3392.