Low-valent cobalt-catalyzed C-C bond formation through imine-directed C-H activation

Xu, Wengang

2017

Xu, W. (2017). Low-valent cobalt-catalyzed C-C bond formation through imine-directed C-H activation. Doctoral thesis, Nanyang Technological University, Singapore.

<http://hdl.handle.net/10356/73039>

<https://doi.org/10.32657/10356/73039>

**NANYANG
TECHNOLOGICAL
UNIVERSITY**

SINGAPORE

**LOW-VALENT COBALT-CATALYZED C-C BOND
FORMATION THROUGH IMINE-DIRECTED C-H
ACTIVATION**

XU WENGANG

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

2017

**LOW-VALENT COBALT-CATALYZED C–C BOND
FORMATION THROUGH IMINE-DIRECTED C–H
ACTIVATION**

XU WENGANG

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

A thesis submitted to the Nanyang Technological University
in partial fulfillment of the requirement for the degree of
Doctor of Philosophy

2017

Acknowledgements

I would like to express the most important acknowledgement of gratitude to my supervisor, Associate Professor Naohiko Yoshikai for his patient guidance, enthusiastic encouragement and valuable critiques of my four years' research work, and his patience on the thesis revision. His attitude and dedication towards science will always inspire me in my future career.

I would like to thank my collaborator Dr. Rupankar Paira and my student Mr. Jie-Hui Pek for helping me finish some of my research projects.

I wish to extend my thanks to all of Dr. Yoshikai's group members for their help and friendship over the past four years, especially to Dr. Takeshi Yamakawa for the useful discussion in my first year.

I would like to thank Ms. Ee-Ling Goh in the NMR laboratory, Mrs. Wen-Wei Zhu in the Mass spectrometry laboratory, and all other support staffs at CBC.

I also would like to thank Nanyang Technological University for providing me the research scholarship.

Finally, I would like to extend my gratitude to my family for their unfailing support, especially my parents. As farmers, they are not rich, but have poured all their effort to support my education for more than 20 years and give me their endless love, understanding and encouragement.

TABLE OF CONTENTS

Acknowledgements	i
Table of contents	ii
List of abbreviations	iv
Abstract	vi
Chapter 1. Introduction	1
1.1 Transition Metal-Catalyzed Directed C–H Functionalization: A Brief Introduction	1
1.2 Low-Valent Cobalt-Catalyzed C–H Functionalization	3
1.3 Design and Summary of Thesis Research	12
1.4 References	17
Chapter 2. Cobalt-Catalyzed Linear-Selective ortho-Alkylation of Aromatic Imines with Styrenes	22
2.1 Introduction	22
2.2 Results and Discussion	27
2.3 Conclusion	38
2.4 Experimental Section	39
2.5 References	75
Chapter 3. Cobalt-Catalyzed, Imine-Directed Olefin Hydroarylation under Grignard-Free Conditions	79
3.1 Introduction	79
3.2 Results and Discussion	81
3.3 Conclusion	88
3.4 Experimental Section	89
3.5 References	100
Chapter 4. Cobalt-Catalyzed, N–H Imine-Directed Olefin Hydroarylation	104
4.1 Introduction	104

4.2	Results and Discussion.....	107
4.3	Conclusion.....	118
4.4	Experimental Section.....	119
4.5	References	153
Chapter 5. Cobalt-Catalyzed Regioselective Alkylation of N–H Imines with Styrene		
		158
5.1	Introduction	158
5.2	Results and Discussion.....	161
5.3	Conclusion.....	170
5.4	Experimental Section.....	170
5.5	References	192
Chapter 6. Cobalt-Catalyzed, Pivalophenone N–H Imine-Directed C–H Alkylation, Arylation and Alkenylation		
		196
6.1.	Introduction	196
6.2	Results and Discussion.....	199
6.3	Conclusion.....	219
6.4	Experimental Section.....	219
6.5	References	280
List of Publications		284

List of Abbreviations

δ	chemical shift (ppm)
$^{\circ}\text{C}$	degree centigrade
Ac	acetyl
acac	acetylacetonate
Ar	aryl (substituted aromatic ring)
BARF	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
Bn	benzyl
b	broad
brs	Broad singlet
<i>t</i> Bu	<i>tert</i> -butyl
Cy	cyclohexyl
COD	1,5-cyclooctadiene
d	doublet
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DMF	<i>N,N</i> -dimethylformamide
DMPU	3,4,5,6-tetrahydro-2-pyrimidinone
DMSO	dimethyl sulfoxide
Et	ethyl
h	hour
H	hydrogen
HRMS	High Resolution Mass Spectrometry
Hz	hertz
IMes	1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
IPr·HCl	1,3-Bis(2,6-diisopropylphenyl)imidazolium Chloride

<i>J</i>	coupling constants
LB	Lewis base
m	multiplet
M	concentration (mol/L)
M ⁺	parent ion peak (mass spectrum)
Me	methyl
mg	milligram
min	minute(s)
mL	milliliter
mmol	millimole
mol %	mole percent
m.p.	melting point
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
Ph	phenyl
PMP	<i>p</i> -methoxyphenyl
ppm	parts per million
<i>i</i> Pr	isopropyl
q	quartet
rt	room temperature
s	singlet
t	triplet
TBHP	tert-Butyl hydroperoxide
TBS	<i>tert</i> -butyldimethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidine-1-oxyl
THF	tetrahydrofuran

TLC	thin layer chromatography
TMEDA	Tetramethylethylenediamine
TMS	Trimethylsilyl

Abstract

Transition metal-catalyzed C–H activation has become a powerful approach for atom- and step-economical synthesis. From a sustainable point of view, the use of earth-abundant transition metals in C–H activation is highly desirable. In this context, cobalt-catalyzed C–H activation has received growing interest. The last several years of research has demonstrated that both low-valent and high-valent cobalt species can be engaged in a variety of C–H functionalization reactions, but still in its infancy.

This thesis describes low-valent cobalt-catalyzed C–C bond-forming reactions via directed C–H activation, with a particular focus on the development of novel catalytic systems and directing groups. Chapter 2 reports on a highly linear-selective hydroarylation reaction of styrenes via ketimine-directed C–H activation. The systematic development of a novel triarylphosphine ligand, in combination with fine tuning of other reaction conditions, enabled us to reverse the intrinsic branched selectivity of typical cobalt catalysts in this type of reaction. Chapter 3 describes the use of metallic magnesium as an effective reductant for the cobalt-catalyzed C–H functionalization. While air- and moisture-sensitive Grignard reagents have been typically employed as reductants, the present study has demonstrated that magnesium serves as a viable alternative in a series of imine-directed olefin hydroarylation reactions. Chapters 4–6 report on the utility of N–H imine as a directing group for cobalt-catalyzed C–H functionalization. As described in Chapter 4, this directing group was first identified as a powerful directing group for the hydroarylation of vinylsilane and alkyl olefins. A series of otherwise difficult hydroarylation reactions, including *ortho*-tetraalkylation of benzophenone imines have been achieved. Chapter 5 describes an extension of the N–H imine-directed hydroarylation to styrene derivatives, where intriguing substrate- or ligand-dependent regioselectivity of C–H activation and C–C bond formation was observed. Finally, Chapter 6 focuses on the use of pivaloyl N–H imine as a transformable directing group. This N–H imine not only efficiently promotes

cobalt-catalyzed *ortho* C–H functionalization reactions with alkyl, aryl, and alkenyl electrophiles, but also readily undergo fragmentation into a nitrile functional group, thus enabling facile preparation of *ortho*-substituted benzonitriles.

Chapter 1. Introduction

1.1 Transition Metal-Catalyzed Directed C–H Functionalization: A Brief Introduction

The direct conversion of ubiquitous carbon–hydrogen bonds, C–H functionalization, is among ideal approaches for the formation of new carbon–carbon and carbon–heteroatom, which would have significant impact on the synthesis of pharmaceuticals, natural products, agrochemicals, polymers, and feedstock commodity chemicals.¹ If the site selectivity among multiple C–H bonds in a starting material were guaranteed, such selective C–H functionalization would not only contribute to streamlining of synthetic plan but also enable late-stage functionalization/diversification of complex molecules. Over the past decades, transition metal-mediated C–H activation has been most extensively studied as a means to achieve selective and catalytic C–H functionalization, owing to the diversity of elementary reaction patterns in which transition metal complexes can be engaged.²

One of the most common and successful strategies to achieve efficiency and site-selectivity in transition metal-catalyzed C–H functionalization is the use of heteroatom directing groups. Coordination of the directing group to a transition metal complex helps the metal center to approach the proximal C–H bond, which not only lowers the activation barrier of C–H bond cleavage but also ensures its positional selectivity. Such an elementary process, typically called cyclometalation, can be combined with various elementary reactions, thus allowing for the introduction of carbon- or heteroatom-based functional groups (Scheme 1.1).

Scheme 1.1. Directing group-assisted C–H functionalization

While cyclometalation had been known for many decades for various transition metal elements, its great potential in the development of selective C–H functionalization came to attention much later, especially upon the seminal report of Murai and coworkers on Ru-catalyzed, ketone-directed aromatic C–H alkylation with olefins (Scheme 1.2).³ Since then, a number of transition metal catalysts, directing groups, reaction partners, and other conditions have been explored to develop myriad of directed C–H functionalization reactions.

Despite the significant progress made, until recently, most of directed C–H functionalization reactions have been developed using precious second- and third-row transition metals.⁴ Given the increasing awareness of sustainable aspects in chemical synthesis, considerable attention has been given to the use of earth-abundant first-row transition metals as catalysts for C–H functionalization as well as other synthetically important transformation.⁵ In this context, our group has explored the potential of low-valent cobalt species as catalysts for directed C–H functionalization, as discussed in the next section.

Scheme 1.2. Ruthenium-catalyzed addition of acetophenone to styrene³

1.2 Low-Valent Cobalt-Catalyzed C–H Functionalization

Historically, cobalt was the first metal used in catalytic directed C–H bond functionalization. In the early 1950s, Murahashi reported on $\text{Co}_2(\text{CO})_8$ -catalyzed *ortho*-carbonylation/cyclization of azobenzene and aldimines to afford heterocyclic products under harsh conditions (Scheme 1.3).⁶ These reactions likely involve the formation of five-membered cobaltacycle species via sp^2 nitrogen-assisted C–H activation. In retrospect, the discovery of these reactions might have evolved into the concept of the potential of cobalt complexes in this respect. Nevertheless, no significant follow-up study on cobalt-catalyzed directed C–H functionalization had been performed for a long time.

To achieve the C–H activation, chelation-assisted cyclometalation process was proposed, in which the C=N or N=N group was used as the directing group to promote the C–H cleavage and determined the *ortho* regioselectivity. This cobalt-catalyzed process suggested the potential of cobalt complexes for C–H functionalization with the assistance of a chelated directing group.

Scheme 1.3. Cobalt-catalyzed carbonylative cyclization of azobenzene⁶

Since the early 1990s, stoichiometric cyclometalation reactions of a well-defined cobalt complex have been extensively studied by Klein and coworkers.⁷ Thus, they have

demonstrated that a cobalt(I) complex, $\text{Co}(\text{CH}_3)(\text{PMe}_3)_4$ is capable of undergoing cyclometalation of substrates bearing various directing groups such as $\text{N}=\text{N}$,^{7a} $\text{C}=\text{X}$ ($\text{X} = \text{N}$,^{7b} O ,^{7c} S ^{7d}), and phosphine groups, thus affording four-, five-, six-membered cobaltacycle complexes (Scheme 1.4).^{7e} These cyclometalation reactions are generally assumed to proceed through chelation-assisted oxidative addition of the C–H bond followed by reductive elimination of methane.

Scheme 1.4. Stoichiometric cyclometalation reactions using $[\text{Co}(\text{CH}_3)(\text{PMe}_3)_4]$ ⁷

In 1994, Kisch and coworkers reported an isolated example of cobalt-catalyzed directed C–H functionalization (Scheme 1.5).⁸ In the presence of a catalytic amount of $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$ or $\text{CoH}(\text{H}_2)(\text{PMe}_3)_3$, an azobenzene derivative reacted with two equivalents of diphenylacetylene to afford *ortho*-dialkenylated azobenzene product with Z-

configuration. While this reaction may be regarded as directed alkyne hydroarylation, its mechanism and the origin of the stereochemical outcome remain unclear.

Scheme 1.5. Cobalt-catalyzed *ortho*-alkenylation of azobenzene derivative with diphenylacetylene⁸

Inspired by the above-discussed previous studies, several low-valent cobalt catalytic systems comprising cobalt salts, Grignard reagents, and phosphorus, nitrogen or carbene ligands have been developed by Yoshikai's group to promote the hydroarylation of alkenes and alkynes directed by electron-rich N-aryl groups.^{5a, c} Recently, Petit and coworkers used a simple and well-defined low-valent cobalt complex, Co(PMe₃)₄, to catalyze analogous directed hydroarylation reactions.⁹ The C–C bond formation with electrophiles through C–H bond functionalization have also been achieved by low-valent cobalt-based systems, as demonstrated by groups of Nakamura, Ackermann, and Yoshikai *et al.*^{5a, c}

Besides the above catalytic systems, Cp*Co(III) catalytic systems and cobalt-catalyzed oxidative C–H activation systems with specific directing groups such as 8-aminoquinoline-derived bidentate amide have been developed to achieve different types of C–H functionalization reactions.^{5a}

For C–H bond activation, there are four types of general mechanisms, including oxidative addition, σ -bond metathesis, electrophilic substitution, and 1,2-addition (Scheme 1.6).¹⁰ For low-valent cobalt catalytic system, oxidative addition and σ -bond metathesis commonly occur to activate the C–H bond. On the other hand, for high-valent cobalt catalytic system (Cp*Co(III)), σ -bond metathesis is the privileged pathway for C–H activation.

Scheme 1.6. Four general mechanisms for C–H activation.¹⁰

In this thesis research, we focused on further development of the low-valent cobalt-catalyzed C–H functionalization. In recent years, mainly two types of C–H functionalization reactions catalyzed by low-valent cobalt species have been developed, namely, hydroarylation reactions and coupling reactions with electrophiles.

As mentioned above, after the report on the first modern cobalt-catalyzed C–H functionalization reaction by Kisch in 1994,⁸ no significant progress was made on the low-valent cobalt-catalyzed C–H functionalization for more than a decade. In 2010, Yoshikai and co-workers devised a low-valent cobalt catalytic system consisting of CoBr₂, a phosphine ligand (PMePh₂), and a stoichiometric amount of Grignard reagent (MeMgCl) as the reductant to efficiently catalyze the addition of 2-arylpyridines to an internal alkyne to afford the hydroarylation products at high temperature (Scheme 1.7a).¹¹ The scope of the alkyne hydroarylation could be further expanded to N-2-pyrimidyl indole substrates by slightly change of the ligand and the Grignard reagent, which allowed the reaction to take place under mild conditions (Scheme 1.7b).¹² Furthermore, electron-rich N-aryl imines were also found as efficient directing groups for the alkyne hydroarylation. Thus, ketimines

(Scheme 1.7c),¹³ aldimines (Scheme 1.7d),¹⁴ and α,β -unsaturated imines (Scheme 1.7e)¹⁵ could all be used as viable substrates by fine tuning of the ligand and Grignard reagent.

Scheme 1.7. Low-valent cobalt-catalyzed directed alkyne hydroarylation¹¹⁻¹⁵

(a) Hydroarylation with 2-aryl pyridine

(b) Hydroarylation with N-pyrimidyl indoles

(c) Hydroarylation with ketimines

(d) Hydroarylation with aldimines

(e) Hydroarylation with α,β -unsaturated ketimines

A series of low-valent cobalt catalysts based on the combination of cobalt salts, ligands, and Grignard reagents have also been developed for directed hydroarylation of alkenes. Nakamura and co-workers achieved N-methyl amide-directed hydroarylation of alkyl olefins using a catalytic system comprised of Co(acac)_3 , CyMgCl , and 1,3-Dimethyl-

3,4,5,6-tetrahydro-2-pyrimidinone (DMPU) (Scheme 1.8a).¹⁶ Meanwhile, Yoshikai group established pyridyl-directed hydroarylations of styrenes that regioselectivity afforded linear or branched adducts by choosing either a phosphine or a N-heterocyclic carbene (NHC) ligand, respectively (Scheme 1.8b).^{17a} The branched selectivity for the Co-PR₃ systems was attributed to the additional stability caused by the η^3 -benzyl-type coordination after styrene insertion to cobalt hydride bond. On the other hand, the reason for the linear selectivity in the Co-IMes-catalytic system is considered to be the steric bulkiness of the IMes ligand, supported by a computational study by Fu and coworkers.^{17b}

Furthermore, for aryl ketimine (Scheme 1.8c),¹⁸ and aldimine substrates (Scheme 1.8d),¹⁹ branched-selective styrene hydroarylation was achieved using cobalt-phosphine systems. In addition, ketimine-directed linear selective hydroarylation of vinylsilane and alkyl olefins was achieved using cobalt-phenanthroline-type catalysts (Scheme 1.8e).²⁰

Scheme 1.8. Low-valent cobalt-catalyzed directed alkene hydroarylation¹⁶⁻²⁰

(a) Amide-directed alkene hydroarylation

(b) Pyridyl-directed styrene hydroarylation with divergent regioselectivity

(c) Ketimine-directed styrene hydroarylation

(d) Aldimine-directed styrene hydroarylation

(e) Ketimine-directed alkyl alkene hydroarylation

The C–C bond-formation reactions through directed C–H arylation, alkenylation, and alkylation with organic electrophiles have been achieved with low-valent catalysts for several specific types of substrates.^{5a, c} The first directed C–H arylation reactions with aryl electrophiles was reported by Song and Ackermann in 2012 (Scheme 1.9a).²¹ Thus, 2-arylpiperidines and N-pyrimidylindoles were arylated with aryl carbamates, sulfamates, or chlorides in the presence of a cobalt–NHC catalyst and a substoichiometric amount of

CyMgCl, which served as a reductant as well as a base. In the same year, Yoshikai's group independently reported an analogous cobalt–NHC catalyst for the C–H arylation of N-aryl ketimines with aryl chlorides (Scheme 1.9b).²² More recently, Ackermann expanded the scope of their C–H arylation system to N-methyl benzamides with a modification of the NHC ligand (Scheme 1.9c).²³

Scheme 1.9. Low-valent cobalt-catalyzed directed C–H arylation with aryl electrophiles^{21–}

23

(a) C–H arylation of 2-aryl pyridines and 2-pyrimidyl indoles

(b) C–H arylation of ketimines

(c) C–H arylation of amides

C–H alkenylation and alkylation could be achieved through low-valent cobalt-catalyzed hydroarylation of alkyne and alkene, respectively.^{5a, c} However, there are obvious limitations in these hydroarylation reactions. The alkyne hydroarylation does not allow for the introduction of cyclic alkenyl groups. In addition, the regioselectivity is primarily

determined by the relative steric hindrance of the alkyne substituents, which often leads to a mixture of regioisomeric products. For the alkene hydroarylation, most of internal alkene, especially cyclic alkenes, cannot be employed as substrates. Furthermore, the regioselectivity for 1-alkenes, except for styrenes, is always linear. As such, the reaction does not allow for the introduction of various secondary alkyl groups.

The above limitations of hydroarylation warrant the development of directed C–H alkenylation and alkylation reactions with alkenyl and alkyl electrophiles. Regarding the C–H alkenylation, viable reaction systems were reported by Ackermann's group in 2015. A $\text{CoI}_2\text{-IPr}\cdot\text{HCl}$ precatalyst, in combination with CyMgCl , promoted the C–H alkenylations of 2-phenylpyridine and N-pyrimidylindole with enol phosphates, carbamates, or carbonates at room temperature (Scheme 1.10).²⁴

Scheme 1.10. Low-valent cobalt-catalyzed directed C–H alkenylation²⁴

The first example of low-valent cobalt-catalyzed arene C–H alkylation was reported by Nakamura and coworkers in 2011. Thus, a catalytic system comprising $\text{Co}(\text{acac})_2$, CyMgCl and DMPU, promoted *ortho*-alkylation of N-methylbenzamide with alkyl chlorides (Scheme 1.11a).²⁵ In 2013, our group reported a cobalt-catalyzed directed C–H alkylation reaction of aryl ketimines with primary and secondary alkyl halides ($\text{X} = \text{Cl}$ or Br), where the use of NHC ligands featuring a N,N'-diisopropylimidazoli(ni)um backbone led to high efficiency (Scheme 1.11b).²⁶ Compared with Nakamura's C–H alkylation, the reaction is notable for the broad applicability to secondary alkyl chlorides

and bromides. At the same time, Ackermann's group extended their study on C–H arylation to achieve the C–H alkylation of 2-phenyl pyridine and N-pyrimidylindole derivatives with alkyl chlorides by a modification of the NHC ligand (Scheme 1.11c).^{21b}

Scheme 1.11. Low-valent cobalt-catalyzed directed C–H alkylation^{25, 26, 21b}

(a) C–H alkylation with amides

(b) C–H alkylation with ketimines

(c) C–H alkylation with 2-aryl pyridines and 2-pyrimidyl indoles

1.3 Design and Summary of Thesis Research

Given the aforementioned background, our attention was drawn to major limitations of previously developed low-valent cobalt-catalyzed C–H functionalization reactions with respect to several aspects, namely, (1) the control of regioselectivity, (2) the method for the generation of active catalyst, and (3) the scope of directing group. This thesis research aimed at addressing these limitations, and thereby significantly expanding the scope and

utility of low-valent cobalt-catalyzed directed C–H functionalization, as briefly summarized below.

Chapter 2 focuses on the control of regioselectivity. In this aspect, we became particularly interested in the branched/linear selectivity in directed hydroarylation of styrenes. For styrene hydroarylation reactions with 2-phenyl-pyridine derivatives, cobalt–NHC (IMes) and cobalt–PCy₃ catalysts displayed linear and branched selectivity, respectively.¹⁷ The reason for the linear selectivity in the Co–IMes-catalytic system is considered to be the steric bulkiness of the IMes ligand, which would disfavor the formation of a more congested η^3 -benzylcobalt intermediate.²⁷ The branched selectivity for the Co–PCy₃ system was attributed to the additional stability caused by the η^3 -benzyl coordination, which was also supported by a computational study from the group of Fu.²⁸ For both the catalytic systems, the reductive elimination would be the regioselectivity-determining step, while the branched pathway would be dominant in the absence of significant ligand effect, owing to the stabilizing η^3 -benzyl coordination. Indeed, the scope of the branched-selective hydroarylation could be readily extended to aryl ketimines and aldimines using simple triarylphosphine ligands. We conjectured that this intrinsic branched selectivity of cobalt catalysis might be reversed by an electronically or sterically modified ligand that functions in favor of the linear pathway or penalizes the branched pathway. Our study along this line has led to a new catalytic system featuring an elaborately optimized triarylphosphine, which promotes highly linear-selective addition of aryl ketimines to styrene (Scheme 1.12).

Scheme 1.12. Linear-selective addition of aryl ketimines to styrenes

Chapter 3 focused on the method for the generation of active cobalt catalysts. Most of low-valent cobalt-catalyzed hydroarylation reactions need a substoichiometric amount of a Grignard reagent, such as *t*-BuCH₂MgBr and TMSCH₂MgCl, as a reductant for the cobalt precatalyst,^{5c} which significantly reduces the practicality and the functional group compatibility. While Petit and coworkers recently reported the competence of Co(PMe₃)₄ as a catalyst for the imine-directed alkyne hydroarylation.⁹ The use of this specific complex prohibits us from enjoying the advantage of ligand-based electronic and steric tuning of cobalt catalysts. As such, a more convenient alternative reductant to Grignard reagents is desired. Our present study has demonstrated that magnesium metal serves as an effective reductant to generate low-valent cobalt species, which exhibit catalytic activity towards imine-directed hydroarylation reactions of styrene and vinylsilane (Scheme 1.13).

Scheme 1.13. Low-valent cobalt-catalyzed hydroarylation with Mg as the reductant

The rest of the thesis research described in chapters 4 to 6 revolves around exploration of a new and useful directing group, which continues to be an important topic in transition metal-catalyzed directed C–H functionalization. Effective directing groups

employed for the low-valent cobalt-catalyzed C–H functionalization have thus far been limited to N-heteroaryl group such as pyridyl and pyrimidyl groups, N-aryl aldimine/ketimine, and N-methylamide. In hope of extending the scope of directing groups for cobalt-catalyzed C–H functionalization, our attention was attracted to the potential utility of N–H imine functional group for several reasons. N–H imine substrates can be readily prepared by the addition of organolithium or Grignard reagents to organonitriles. This method, distinct from the ketone-amine condensation for N-substituted imines, allows for facile preparation of sterically hindered imines. With such advantages, other research groups have demonstrated the utility of aryl N–H imines as viable substrates for transition metal-catalyzed directed C–H functionalization/annulation reactions with unsaturated compounds such as alkynes and allenes. Last but not least, benzophenone N–H imine was reported to participate in a cyclometalation reaction with $\text{CoMe}(\text{PMe}_3)_4$.

Our present studies, promoted by the above consideration, have led to the development of a series of cobalt-catalyzed C–C bond-formation reactions via N–H imine-directed C–H activation. Chapter 4 reports on hydroarylation reactions of vinylsilanes and alkyl olefins (Scheme 1.14). A series of cobalt–phosphine catalytic systems were developed for efficient and selective alkylation of aryl alkyl imines and diaryl imines, where the superiority directing ability of N–H imine to N-aryl imine was amply demonstrated. Among notable transformations uniquely enabled by the N–H imine directing group is a fourfold *ortho*-alkylation of benzophenone imines at room temperature.

Scheme 1.14. Low-valent cobalt-catalyzed N–H imine directed alkyne hydroarylation

Chapter 5 describes an extension of the scope of alkenes for the N–H imine-directed hydroarylation to styrene (Scheme 1.15). Modified cobalt-phosphine catalytic systems were developed for the selective monoalkylation of various aryl alkyl and diaryl N–H imines with styrene. Like the N-aryl imine-directed styrene hydroarylation, intrinsic preference for branched selectivity was observed for most of imine substrates examined, while a switch of the regioselectivity also took place depending on the substituents on the arene and imine moieties.

Scheme 1.15. Low-valent cobalt-catalyzed N–H imine-directed styrene hydroarylation

Chapter 6 reports on the use of pivalophenone N–H imine as an excellent substrate for directed *ortho*-C–H bond alkylation, arylation, and alkenylation with the corresponding organic electrophiles (Scheme 1.16). The choice of appropriate cobalt–NHC catalyst and electrophile (i.e., alkyl bromide, aryl chloride, or alkenyl phosphate) allowed us to achieve the C–H alkylation, arylation, and alkenylation directed by *tert*-butyl N–H imine group at room temperature. Furthermore, the alkylation and arylation products readily underwent transformation of the *t*-butyl N–H imine into a cyano group under peroxide photolysis,²⁹ or aerobic copper catalysis.³⁰ Thus, the overall process would provide a complementary and convenient synthetic route to a variety of *ortho*-substituted benzonitriles.

Scheme 1.16. Pivalophenone imine as a substrate for C–H/electrophile coupling and a benzonitrile surrogate

Overall, this thesis has led to significant advancement of low-valent cobalt catalysis for directed C–H functionalization, especially in terms of the design of catalysts and substrates, which also have implications for further development in C–H functionalization catalyzed by cobalt and other transition metals. The successful development of linear-selective ligands in chapter 2 would hold promise for design and discovery of novel ligands that can not only control the selectivity but also enhance the catalytic activity in various cobalt-catalyzed C–H functionalization reactions. The demonstration of Mg-based catalytic systems, described in Chapter 3, would stimulate not only the use of this reductant in other hydroarylation reactions but also exploration of even more convenient and effective reductants. The power of N–H imine directing group amply demonstrated in Chapter 4–6, deserves further studies from practical and mechanistic points of view. For example, the development of new efficient *ortho* C–H functionalization reactions of pivalophenone imine, regardless of the catalyst used, would lead to valuable methods for the preparation of various *ortho*-functionalized benzonitriles.

1.4 References

- ¹ (a) Noisier, A. F. M.; Brimble, M. A. *Chem. Rev.* **2014**, *114*, 8775-8806; (b) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369-375; (c) Yamaguchi, J.; Yamaguchi, A. D.;

Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960-9009; (d) Schipper, D. J.; Fagnou, K. *Chem. Mater.* **2011**, *23*, 1594-1600; (e) Feng, Y.; Chen, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 958-961.

² Representative recent reviews on C–H activation: (a) Kuhl, N.; Schroder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443-1460; (b) Tani, S.; Uehara, T. N.; Yamaguchi, J.; Itami, K. *Chem. Sci.* **2014**, *5*, 123-135; (c) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74-80; (d) Thirunavukkarasu, V. S.; Kozhushkov, S. I.; Ackermann, L. *Chem. Commun.* **2014**, *50*, 29-39; (e) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726-11743; (f) Satoh, T.; Miura, M. *Chem. - Eur. J.* **2010**, *16*, 11212-11222; (g) Daugulis, O. *Top. Curr. Chem.* **2009**, *292*, 57-84; (h) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242-3272; (i) Ackermann, L.; Vicente, R.; Kapdi, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792-9826; (j) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094-5115.

³ Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M. Chatani, N. *Nature* **1993**, *366*, 529-531.

⁴ For selected reviews and accounts, see: (a) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308-1318; (b) Ackerman, L.; Li, J. *Nat. Chem.* **2015**, *7*, 686-687; (c) Zhang, X.-S.; Chen, K.; Shi, Z.-J. *Chem. Sci.* **2014**, *5*, 2146-2159; (d) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281-295; (e) Kuhl, N.; Hopkinson, M. N.; Wencel- Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236-10254; (f) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879-5918; (g) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936-946; (h) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826-839; (i) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788-802; (j) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; (k) Zhao, D.; You, J.; Hu, C. *Chem. - Eur. J.* **2011**, *17*, 5466-5492; (l) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780-1824; (m) Ackermann, L.; Vicente, R. *Top.*

Curr. Chem. **2009**, 292, 211-229; (n) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, 110, 624-655.

⁵ For selected reviews, see: (a) Shang, R.; Ilies, L.; Nakamura, E. *Chem. Rev.* **2017**, 117, 9086-9139; (b) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, 6, 498-525; (c) Su, B.; Cao, Z.-C.; Shi, Z.-J. *Acc. Chem. Res.* **2015**, 48, 886-896; (d) Ackermann, L. *J. Org. Chem.* **2014**, 79, 8948-8954; (e) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, 47, 1208-1219; (f) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19-30; (g) Yoshikai, N. *Synlett* **2011**, 1047-1051; (h) Nakao, Y. *Chem. Rec.* **2011**, 11, 242-251; (i) Nakamura, E.; Yoshikai, N. *J. Org. Chem.* **2010**, 75, 6061-6067; (j) Kulkarni, A. A.; Daugulis, O. *Synthesis* **2009**, 4087-4109.

⁶ (a) Murahashi, S.; Horiie, S. *J. Am. Chem. Soc.* **1956**, 78, 4816-4817; (b) Murahashi, S. *J. Am. Chem. Soc.* **1955**, 77, 6403-6404.

⁷ (a) Klein, H. F.; Helwig, M.; Koch, U.; Florke, U.; Haupt, H. J. *Z. Naturforsch., B: J. Chem. Sci.* **1993**, 48, 778-784; (b) Klein, H.-F.; Beck, R.; Flörke, U.; Haupt, H.-J. *Eur. J. Inorg. Chem.* **2003**, 1380-1387; (c) Klein, H.-F.; Camadanli, S.; Beck, R.; Leukel, D.; Flörke, U. *Angew. Chem., Int. Ed.* **2005**, 44, 975-977; (d) Camadanli, S.; Beck, R.; Florke, U.; Klein, H.-F. *Dalton. Trans.* **2008**, 5701-5704; (e) Klein, H.-F.; Schneider, S.; He, M.; Floerke, U.; Haupt, H.-J. *Eur. J. Inorg. Chem.* **2000**, 2295-2301.

⁸ Halbritter, G.; Knoch, F.; Wolski, A.; Kisch, H. *Angew. Chem. Int. Ed.* **1994**, 33, 1603-1605.

⁹ (a) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M. *J. Am. Chem. Soc.* **2015**, 137, 2448-2451; (b) Fallon, B. J.; Garsi, J. B.; Derat, E.; Amatore, M.; Aubert, C.; Petit, M. *ACS Catal.* **2015**, 5, 7493-7497; (c) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M. *Org. Lett.* **2016**, 18, 2292-2295

¹⁰ Balcells, D.; Clot, E.; Eisenstein, O. *Chem. Rev.* **2010**, 110, 749-823.

- ¹¹ Gao, K.; Lee, P.-S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2010**, *132*, 12249-12251
- ¹² Ding, Z.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 4698-4701.
- ¹³ Lee, P.-S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 17283-17295.
- ¹⁴ Yamakawa, T.; Yoshikai, N. *Tetrahedron* **2013**, *69*, 4459-465.
- ¹⁵ Yamakawa, T.; Yoshikai, N. *Org. Lett.* **2013**, *15*, 196-199.
- ¹⁶ Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221-5223.
- ¹⁷ (a) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 400-402; (b) Yang, Z.; Yu, H.; Fu, Y. *Chem. Eur. J.* **2013**, *19*, 12093-12103.
- ¹⁸ Dong, J.; Lee, P.-S.; Yoshikai, N. *Chem. Lett.* **2013**, *42*, 1140-1142.
- ¹⁹ Lee, P.-S.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 1240-1244.
- ²⁰ Gao, K.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 6888-6892.
- ²¹ (a) Song, W.; Ackermann, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 8251-8254. (b) Punji, B.; Song, W.; Shevchenko, G. A.; Ackermann, L. *Chem. -Eur. J.* **2013**, *19*, 10605-10610.
- ²² Gao, K.; Lee, P.-S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234-4237.
- ²³ Li, J.; Ackermann, L. *Chem. - Eur. J.* **2015**, *21*, 5718-5722.
- ²⁴ Moselage, M.; Sauermann, N.; Richter, S. C.; Ackermann, L. *Angew. Chem., Int. Ed.* **2015**, *54*, 6352-6355.
- ²⁵ Chen, Q.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 428-429.
- ²⁶ Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2013**, *135*, 9279-9282.
- ²⁷ Trost, B. M.; Czabaniuk, L. C. *Angew. Chem.* **2014**, *126*, 2868-2895; *Angew. Chem. Int. Ed.* **2014**, *53*, 2826-2851.
- ²⁸ Yang, Z.; Yu, H.; Fu, Y. *Chem. Eur. J.* **2013**, *19*, 12093-12103.
- ²⁹ Griller, D.; Mendenhall, G. D.; Van Hoof, W.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6068-6070.
- ³⁰ Zhang, L.; Ang, G. Y.; Chiba, S. *Org. Lett.* **2010**, *12*, 3682-3685.

Chapter 2. Cobalt-Catalyzed Linear-Selective *ortho*-Alkylation of Aromatic Imines with Styrenes

2.1 Introduction

Hydroarylation of alkenes through transition metal-catalyzed C–H activation has received significant attention as a straightforward and atomic economical approach for the alkylation of arenes.¹ This type of hydroarylation and the classical Friedel-Crafts-type arene alkylation using alkenes are generally known to show orthogonal substrate scope and regioselectivity. The former reaction typically employs a directing group appended arene or an electron-deficient heteroarene to facilitate the C–H activation, while the latter reaction is applicable to electron-rich arenes and heteroarenes. Furthermore, the former reaction using 1-alkene typically gives the linear alkylation product, while the latter reaction exhibits exclusive branched selectivity. This general regioselectivity trend is not withstanding. Interestingly, the transition metal-catalyzed hydroarylation of styrenes has been found to show variable linear/branched selectivity depending on the substrate and the catalytic system, as illustrated below.

Murai's seminal work on the ruthenium-catalyzed, ketone-directed hydroarylation demonstrated linear selectivity in the reaction of 2-methylstyrene, which afforded the 1,2-diarylethane product (Scheme 2.1a).² Following this report, several examples of linear-selective styrene hydroarylation,³ such as rhodium-catalyzed reactions of 2-phenylpyridine and benzimidazole, have been reported (Scheme 2.1b, c).^{3b, c} As a more recent example, a cobalt-catalyzed, amide-assisted styrene hydroarylation also afforded the linear adduct as the major product, albeit with modest regioselectivity (Scheme 2.1d).³ⁱ

While less common, branched-selective styrene hydroarylation reactions have also been reported.⁴ Uchimaru et al. observed exclusive branched selectivity in the ruthenium-

catalyzed addition of N-methylaniline to styrene (Scheme 2.2),^{4a} while Nakao and Hiyama achieved branched-selective addition of electron-deficient heteroarenes such as azoles and substituted indoles to styrenes under nickel/N-heterocyclic carbene catalysis, affording a series of 1,1-diarylethane derivatives (Scheme 2.3).^{4b, d}

Scheme 2.1. Typical chelation-assisted hydroarylation reactions of styrenes

a) Murai (1993)

b) Kim (1996)

c) Ellman (2002)

d) Nakamura (2010)

Scheme 2.2. Ruthenium-catalyzed addition of N-methylaniline to styrene **Scheme 2.3.** Nickel-catalyzed hydroheteroarylation of styrenes

Despite the interesting individual hydroarylation reactions discussed above, examples of catalyst-controlled regiodivergent styrene hydroarylation, leading to either of the 1,1- and 1,2-diarylethane products, have been rare.⁵ Ong and coworkers reported nickel-catalyzed linear- or branched-selective addition reactions of benzimidazole to styrene with or without AlMe_3 as the co-catalyst, respectively (Scheme 2.4a).^{5a} By the modification of the indole N-protecting group and the supporting diphosphine ligand, Shibata and coworkers achieved iridium-catalyzed regiodivergent addition reactions of indole derivatives to styrenes (Scheme 2.4b).^{5c}

Prior to the above reports, in 2011, our group reported linear- or branched-selective addition reactions of 2-phenylpyridine to styrene with cobalt–N-heterocyclic carbene (IMes) or cobalt–monophosphine (PCy_3) catalysts, respectively (Scheme 2.5a).^{6a} The scope of branched-selective styrene hydroarylation was further extended to aryl ketimines and aldimines by the modification of the phosphine ligand and other reaction conditions (Scheme 2.5b).^{6b, c}

Scheme 2.4. Typical regiodivergent addition of styrenes **Scheme 2.5** Cobalt-catalysed hydroarylation reactions of styrene

On the basis of deuterium-labeling experiments, the regiodivergence of the cobalt-catalyzed styrene hydroarylation was rationalized by a catalytic cycle involving reversible oxidative addition of C–H bond to low-valent cobalt species, reversible and competitive selective styrene insertion steps to give branched (A) or linear (B) intermediates, and irreversible reductive elimination steps that determined the regioselectivity (Scheme 2.6). The branched selectivity for the Co–PR₃ systems was attributed to the additional stability

caused by the η^3 -benzyl-type coordination in the intermediate A and its reductive elimination.⁷ On the other hand, the reason for the linear selectivity in the Co–IMes-catalytic system is considered to be the steric bulkiness of the IMes ligand, which would favor the less congested intermediate B and its reductive elimination. The mechanistic assumptions were also supported by a computational study by Fu and coworkers.⁸ Importantly, both of our experimental study and Fu's computational study implied that cobalt shows intrinsic preference for the branched selectivity in the absence of the significant steric bias in the ligand.

Scheme 2.6. Proposed catalytic cycle for the cobalt-catalyzed directed hydroarylation of styrene

Given the above mechanistic understanding, we became interested in changing the intrinsic branched selectivity of cobalt catalysts by supporting ligands, thus extending the scope of linear-selective styrene hydrarylation. Our attention was attracted to the addition reaction of an aryl ketimine to styrene, for which the Co–IMes catalytic system showed rather sluggish catalytic activity. In this study, we revisited this reaction by systematic

steric/electronic tuning of ligands to identify a novel triarylphosphine (bis(2,4-dimethoxyphenyl)(phenyl)phosphine) that, in combination with a Lewis base additive, allowed highly linear-selective hydroarylation with a variety of aryl ketimines and styrenes.

2.2 Results and Discussion

The present study started with a screening of ligands for the addition of the imine derived from acetophenone and *p*-anisidine (**1a**) to styrene (**2a**) as a model reaction, employing a catalytic system comprising CoBr₂ (5 mol%), ligand (10 mol%), and CyMgBr (50 mol%) (Table 2.1). As reported previously, the use of triphenylphosphine or *para*-substituted triarylphosphine in this reaction led to the branched product **3aa'** as the major product.^{6d} Somewhat unexpectedly, bulky triarylphosphines such as tris(2,6-diethylphenyl)phosphine (**L1**) and tris(2-ethylphenyl)phosphine (**L2**) did not change the branched selectivity (l/b = 6:94 to 12:88) affording **3aa'** in moderate yields. However, by contrast, triarylphosphines containing 2,6-dimethoxyphenyl groups (**L3-L5**) preferentially afforded the linear product **3aa** albeit in low yield and modest regioselectivity. Through screening several ligands bearing 2-methoxyaryl groups (**L6-L10**), a l/b ratio over 9/1 was achieved with **L8** and **L9** that bear 2,4-dimethoxyphenyl groups, while analogous ligands bearing 2,5-dimethoxyphenyl groups (**L11** and **L12**) exhibited branched selectivity. Analogues of **L9** bearing ethoxy or N,N-dimethylamino groups instead of the methoxy groups led to branched selectivity (**L13** and **L14**). Ligands adding electron-donating (methoxy) or withdrawing (fluoro) group on the non-substituted phenyl group of **L9** even led to the opposite selectivity (**L15** and **L16**). Among other ligands examined, only 2-dimethylaminophenyl(diphenyl)phosphine **L18** exhibited linear selectivity close to 9:1. IMes ligand, which was previously used in the linear selective addition of 2-phenylpyridine to styrene, also showed linear selectivity albeit in a very low yield. The reaction without a

ligand, led to a moderate yield with branched selectivity. Above all, **L9** gave the highest linear selectivity albeit with low efficiency.

Table 2.1. Screening of ligands for the addition of aryl ketimine to styrene. ^a

L1 : 44% (6/94)	L2 : 55% (12/88)	L3 (n = 0): 8% (61/39) L4 (n = 1): 2% (83/17) L5 (n = 2): 3% (66/33)	L6 (n = 0): 17% (68/32) L7 (n = 1): 3% (33/67)
L8 (n = 0): 14% (91/9) L9 (n = 1): 14% (92/8) L10 (n = 2): 32% (10/90)	L11 (n = 1): 5% (26/74) L12 (n = 2): 15% (1/99)	L13 : 10% (29/71)	L14 : 6% (34/66)
L15 (R = F): 14% (33/67) L16 (R = OMe): 13% (38/62)	L17 (n = 1): 20% (22/78) L18 (n = 2): 7% (88/12)	IMes•HCl : 4% (93:7)	no ligand 51% (11/89)

^a The reaction was performed on a 0.3 mmol scale and at the imine concentration of 0.4 M.

The yield was determined by GC using tridecane as the internal standard.

Having identified **L9** as a promising linear-selective ligand, we further screened the reaction conditions to improve the reaction efficiency (Table 2.2). the yield was improved

to 40% at the reaction temperature of 40 °C (entry 1). The addition of pyridine (80 mol%) to this reaction further improved the yield to 54% without affecting the linear selectivity (Table 2.2, entry 2). Further increase of the loading of pyridine (6 equiv.), led to a slightly improvement (entry 3). The addition of TMEDA instead of pyridine had no positive influence on the yield and the selectivity (entry 4), while the addition of DMPU (80 mol%) led to a certain degree of improvement (entry 5). Interestingly, the addition of DBU caused a dramatic enhancement of the reactivity, affording **3aa** in 91% yield with l/b ratio of 93/7 (entry 6). Among substituted pyridine as additives, 2-methoxypyridine was found to be superior to the parent pyridine (entry 7). The addition of 4 equiv. of 2-methoxypyridine resulted in an excellent yield (91%) and linear selectivity (97/3) (entry 8). Control experiments using DBU (entry 9) or 2-methoxyl-pyridine (entry 10) in the absence of **L9** led to a predominant formation of the branched product, which clearly illustrated the phosphine ligand played a crucial role in the linear-selective reaction.

Table 2.2. Screening of the additives

entry	Additives	yield% (l/b) ^a
1	-	40 (93/7)
2	pyridine	54 (93/7)
3 ^b	pyridine	64 (97/3)
4	TMEDA	38 (88/12)
5	DMPU	63 (97/3)
6	DBU	91 (93/7)
7	2-methoxyl-pyridine	70 (95/5)
8 ^c	2-methoxyl-pyridine	91 (97/3) ^d
9 ^e	DBU	67 (2/98)
10 ^e	2-methoxyl-pyridine	70 (4/96)

^a Determined by ¹H-NMR with 1,1,2,2-tetrachloroethane as the internal standard. ^b The amount of pyridine was 6 equiv. ^c The amount of 2-methoxypyridine was 4 equiv. ^d Isolate yield and the b/l was determined with ¹H-NMR. ^e No phosphine ligand (**L9**) was added.

With the optimized reaction conditions in hand, we examined the addition of ketimine derivatives to styrene (Table 2.3). Ketimines derived from *para*-substituted acetophenones gave the products **3aa–3fa** in moderate to good yields, with the linear/branched ratio higher than 90/10. The reaction of *meta*-methyl substituted ketimine took place exclusively at the less hindered *ortho* position with the regioselectivity of 91/9 (**3ga**). For the reaction of propiophenone-derived imine, DBU (80 mol%) proved to be an excellent additive to achieve much higher yield and selectivity (see **3ha**) than that achieved using 2-methoxypyridine (72% yield, l/b = 81/19). Tetralone derivatives and 4-chromanone derived ketimines also afforded the desired 1,2-diarylethanes (**3ia–3la**) in good yields with high regioselectivities. Excellent reactivity was achieved for 3-iminoindole albeit with poor regioselectivity (**3ma** and **3ma'**).

Table 2.3. Catalytic addition of various ketimines to styrene.

^a The reaction time was 48 h. ^b DBU (80 mol%) was used as additive.

Compared to the above discussed examples, ketimines bearing a *meta*-alkoxy or fluoro substituent (**1n–1p**) behaved very differently under the present reaction conditions (Figure 2.1). The C–H alkylation occurred at the position proximal to the alkoxy group or the fluorine atom presumably due to the secondary interaction between the O or F atom and the catalyst, as was also the case for related reaction reported by us⁹ and Ackermann et al.¹⁰ To our surprise, the 2-methoxypyridine system afforded the branched adducts as the major products with b/l ratios of 8/2 to 7/3. This observation may suggest that the secondary interaction also has a significant effect on the competition between the linear and branched

pathways. Interestingly, the DBU catalytic system improved the linear selectivity significantly affording **3na–3pa** as the major products with the regioselectivity of ca. 6:4–9:1.

additive	3na	3oa	3pa
2-methoxypyridine	28% (18/82) ^a	68% (27/73)	69% (30/70)
DBU	23% (67/33) ^a	74% (58/42)	72% (89/11)

Figure 2.1. 1,2-Diarylethanes obtained from *meta*-alkoxy or -fluoro imines and styrene. ^a The yield was determined by ¹H-NMR and the linear-to-branched ratio is shown in the parentheses.

The existence of the secondary interaction was further indicated by the reaction of ketimine derived from 3',4'-difluoroacetophenone (Figure 2.2). The reaction took place preferentially at the ortho C–H bond proximal to the fluorine atom, which was accompanied by a nonnegligible amount of the product **3ra** arising from C–H activation of the distal position. Interestingly, the latter product was obtained with much higher linear selectivity than the former, especially with 2-methoxypyridine as the additive. This observation may

also indicate that the presence of a Co-F secondary interaction influences the regiochemical outcome of the reaction.

Figure 2.2. Reaction of 3,4-difluoro-substituted imine with styrene. ^a The yield was determined by ^1H -NMR and the linear-to-branched ratio is shown in the parentheses.

Next, various styrene derivatives were examined to react with acetophenone imine. As summarized in Table 2.4, *para*-methyl (**3ab**), *t*-butyl (**3ac**), TMS (**3ad**), methoxy (**3ae**), and fluoro (**3af**) substituted styrenes afforded good yields with a ratio of the linear to branched product more than 90/10. However, for *para*-phenyl styrene, the selectivity became moderate around 3/1 (**3ag**). *Meta*- and *ortho*-substituted styrenes participated in the reaction with **1a** to afford the corresponding 1,2-diarylethanes **3ah–3al** in good yields with high regioselectivities (90:10 or greater), especially for the *ortho*-methoxy and fluoro substituted styrenes (**3ah** and **3ai**). Di- (**3am**, **3an**, **3ap**) and tri-substituted styrenes (**3ao**) also afforded good yields and high regioselectivities (91/9, or higher). The reaction of 2-vinylbenzofuran occurred sluggishly with poor regioselectivity (5%, l:b = 50:50; see **3aq**). The reason for such poor reactivity needs further investigation.

Table 2.4. Catalytic linear selective addition of ketimine to styrene derivatives.

^a DBU (80 mol%) was used as additive. ^b The yield was determined by ¹H-NMR and the linear-to-branched ratio is shown in the parentheses.

To gain insight into the mechanism, the reaction of pentadeuterated imine [D]₅-**1a** with 4-methoxystyrene was examined under various conditions. The distribution of the deuterium atoms in the product [D]_n-**3ae**, the recovered ketimine [D]_n-**1a** and styrene derivatives [D]_n-**2e** was analyzed (Table 2.5). After 6 h under the standard condition, the 1,2-diaryl ethane product, [D]_n-**3ae** was obtained in 79% yield with a substantial decrease

in the deuteration rate at the *ortho* position and significant deuterium incorporation into the C2 and C3 positions (entry 1). The degree of H-D scrambling between the recovered styrene and ketimine and the yield of **3ae** decreased significantly at 0 °C (entry 2), which would be explained by the deceleration of all the elementary steps. With DBU as the additive, the yield and H/D scrambling patterns were similar to the case for 2-methoxypyridine (entry 3). As expected, the reaction without the additive was sluggish, while substantial H/D scrambling between the recovered starting materials was observed (entry 4). Taken together these observations suggest that C–H activation and styrene insertion (both branched and linear) take place rapidly and reversibly, and that the styrene insertion steps have no influence on the regioselectivity. The rate- and regioselectivity-determining step is likely reductive elimination, and the primary role of the Lewis base additives is assumed to be the acceleration of this step.

Table 2.5. Deuterium-labeling experiments under different conditions

0.3 mmol	0.3 mmol								
D₅-1a	2e								
Entry	Deviation from standard conditions	Yield [%] ^a	1H intergrations						
			1	2	3	4	5	6	
1	none	79	0.41	0.93	0.96	1.26	1.47	0.54	
2	0 °C instead of 40 °C	10	0.48	1.14	0.96	0.62	1.50	0.85	
3	DBU (80 mol%) instead of 2-methoxypyridine	82	0.36	0.85	0.92	1.11	1.22	0.63	
4	2-methoxypyridine omitted	19	0.32	0.99	0.9	1.06	1.27	0.68	

^a Determined by ¹H-NMR with 1,1,2,2-tetrachloroethane as the internal standard.

Based on the above mechanistic argument, the regioselectivity should be determined by the relative stability of the transition states (TS) of linear- and branched reductive eliminations (REs). Thus, the ligand **L9** is considered to stabilize the linear RE-TS and/or destabilize the branched RE-TS. The results of the ligand screening suggest that the linear selectivity of **L9** cannot be simply explained by steric factors, because the much bulkier ligands such as **L1** and **L2** exhibited branched selectivity, like unhindered triarylphosphines. As such, we are tempted to propose that the methoxy group of **L9** serves as a hemilabile coordinating group to the cobalt center to influence the regioselectivity (Figure 2.3). Such coordination would afford extra stability to the linear TS (**TS B**), while the branched TS (**TS A**) may not be able to accept the hemilabile coordination due to the coordinative saturation.

Figure 2.3. Proposed transition state (TS) for branched and linear selectivity

The present alkylation products are amenable to a variety of synthetic transformations (Scheme 2.7). Jiao's copper-catalyzed system with sodium azide under aerobic conditions¹¹ allowed conversion of the acetyl group to a primary amide group, affording **5ac** with the potentially sensitive benzylic positions untouched. Selective conversion of the acetyl group to a formyl (**6ac**) or a carboxyl (**7ab**, **7af**) group was also achieved under aerobic conditions using a copper-catalyzed method developed by Bi and Liu¹² or a manganese-catalyzed method of Ishii,¹³ respectively. The carboxyl products were cyclized to afford 10,11-dihydro-5H-dibenzo[a,d]cycloheptan-5-ones **8ab** and **8af**, featuring a core structure of pharmaceutically useful compounds such as amitriptyline (antidepressant).

Scheme 2.7. Transformations of 1,2-diarylethane products.

Reaction conditions: (a) CuCl₂ (10 mol%), TEMPO (20 mol%), H₂O (30 mol%), NaN₃ (3 equiv), O₂ (1 atm), DMF, 120 °C; (b) CuI (30 mol%), O₂ (1 atm), DMSO, 120 °C; (c) Mn(OAc)₃ (1 mol%), AcOH, O₂ (1 atm), 100 °C; (d) polyphosphoric acid, 155 °C.

2.3 Conclusion

In summary, a highly linear-selective addition reaction of aryl ketimines to styrene derivatives was achieved with new cobalt-based catalytic systems. The intrinsic branched selectivity of cobalt in this type of reaction was successfully reversed by carefully tuned triarylphosphine ligand, bis(2,4-dimethoxyphenyl)phenylphosphine, while the enhancement of the catalytic efficiency was achieved by Lewis base additives such as 2-methoxypyridine and DBU. The ligand screening study and the mechanistic study on the deuterated substrates under different conditions shed light on the roles of the phosphine ligand and the Lewis base additives. The ability of the present phosphine ligand to serve as a hemilabile P,O-ligand is proposed to give rise to the linear selectivity, while this mechanistic proposal warrants further experimental and theoretical supports.

2.4 Experimental Section

Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. THF was distilled over Na/benzophenone. Anhydrous CoBr₂ (> 98%) was purchased from Alfa Aesar and used as received. Grignard reagents were prepared from the corresponding alkyl halides and magnesium turnings in THF, and titrated before use. Styrene derivatives were either purchased or prepared using Wittig reaction on the corresponding aryl aldehydes according to the literature procedure,²⁵ and purified by silica gel column chromatography. All the phosphine ligands were either purchased or prepared from the reaction of aryl magnesium halides or aryl lithiums with aryl phosphine chlorides according to the literature process,³² and purified by silica gel column chromatography or recrystallization.

Preparation of Aryl Imines

All imines were synthesized according to the literature procedures,¹⁴ and purified by recrystallization or distillation. Spectral data for the following known imines showed good agreement with the literature data:

(*E*)-4-Methoxy-*N*-(1-phenylethylidene)aniline (**1a**)¹⁵

(*E*)-4-Methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline (**1b**)¹⁶

(*E*)-*N*-(1-([1,1'-biphenyl]-4-yl)ethylidene)-4-methoxyaniline (**1c**)¹⁷

(*E*)-4-Methoxy-*N*-(1-(4-methoxyphenyl)ethylidene)aniline (**1d**)¹⁸

(*E*)-*N*-(1-(4-Fluorophenyl)ethylidene)-4-methoxyaniline (**1e**)¹⁸

(*E*)-4-Methoxy-*N*-(1-(*m*-tolyl)ethylidene)aniline (**1g**)¹⁹

(*E*)-*N*-(3,4-Dihydronaphthalen-1(2*H*)-ylidene)-4-methoxyaniline (**1h**)²⁰

(*E*)-*N*-(Chroman-4-ylidene)-4-methoxyaniline (**1k**)²¹

4-Methoxy-*N*-(1-phenylpropylidene)aniline (*E/Z* = 10/1) (**1l**)²⁰

(*E*)-4-Methoxy-*N*-((1-methyl-1*H*-indol-3-yl)methylene)aniline (**1m**)²²

(*E*)-*N*-(1-(Benzo[*d*][1,3]dioxol-5-yl)ethylidene)-4-methoxyaniline (**1n**)²³

(*E*)-4-Methoxy-*N*-(1-(3-methoxyphenyl)ethylidene)aniline (**1o**)¹⁹

(*E*)-*N*-(1-(3-Fluorophenyl)ethylidene)-4-methoxyaniline (**1p**)²⁴

(*E*)-4-Methoxy-*N*-(1-pentadeuteriophenylethylidene)aniline ([**D**]**5-1a**)¹⁷

(*E*)-4-Methoxy-*N*-(1-(4-(methylthio)phenyl)ethylidene)aniline (**1f**): Yellow solid; M.p. 129-130 °C; ¹H NMR (400 MHz, CDCl₃): δ 2.22 (s, 3H), 2.53 (s, 3H), 3.82 (s, 3H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.90 (m, 2H), 7.28 (m, 2H), 7.89 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 15.3, 17.1, 55.5, 114.2, 120.8, 125.6, 127.5, 136.3, 141.6, 144.8, 155.9, 164.9; HRMS (ESI) Calcd for C₁₆H₁₈NOS [M + H]⁺ 272.1109, found 272.1110.

(*E*)-4-Methoxy-*N*-(4-methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)aniline (**1i**): Yellow solid; M.p. 101-102 °C; ¹H NMR (400 MHz, CDCl₃): δ 1.36 (dd, *J* = 7.1, 0.7 Hz, 3H), 1.64-1.72 (m, 1H), 2.02 (qd, *J* = 9.0, 4.8 Hz, 1H), 2.46-2.53 (m, 1H), 2.64-2.71 (m, 1H), 2.99-3.07 (m, 1H), 3.81 (s, 3H), 6.73-6.78 (m, 2H), 6.87-6.92 (m, 2H), 7.27-7.30 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 8.28-8.31 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.0, 26.8, 30.3, 32.8, 55.4, 114.2, 120.8, 126.2, 127.3, 130.7, 133.4, 144.6, 145.7, 155.8, 166.0; HRMS (ESI) Calcd for C₁₈H₂₀NO [M + H]⁺ 266.1545, found 266.1543.

(*E*)-4-Methoxy-*N*-(6-methoxy-3,4-dihydronaphthalen-1(2*H*)-ylidene)aniline (1j):

Yellow solid; M.p. 114-115 °C; ^1H NMR (400 MHz, CDCl_3): δ 1.85-1.91 (m, 2H), 2.50-2.54 (m, 2H), 2.82 (t, $J = 6.2$ Hz, 2H), 3.81 (s, 3H), 3.86 (s, 3H), 6.73-6.77 (m, 2H), 6.87-6.92 (m, 3H), 7.22-7.26 (m, 1H), 7.92 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 22.4, 23.0, 29.2, 55.4-55.6 (m), 111.4, 114.2, 118.2, 12.09, 126.4, 130.3, 135.2, 144.6, 155.8, 156.8, 166.2; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 282.1494, found 282.1481.

(*E*)-*N*-(1-(3,4-Difluorophenyl)ethylidene)-4-methoxyaniline (1q): Yellow solid; M.p. 89-90 °C; ^1H NMR (400 MHz, CDCl_3): δ 2.22 (s, 3H), 3.81 (s, 3H), 6.71-6.75 (m, 2H), 6.90-6.93 (m, 2H), 7.16-7.25 (m, 1H), 7.66-7.69 (m, 1H), 7.85 (ddd, $J = 11.8, 7.8, 2.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 17.0, 55.4, 114.3, 116.2 (d, $J = 18.5$ Hz), 116.9 (d, $J = 17.5$ Hz), 120.7, 123.5 (dd, $J = 6.7, 3.4$ Hz), 136.9 (dd, $J = 5.1, 3.6$ Hz), 144.1, 150.0 (dd, $J = 249, 12.9$ Hz), 151.8 (dd, $J = 254, 12.9$ Hz), 156.2, 163.2; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{14}\text{F}_2\text{NO}$ $[\text{M} + \text{H}]^+$ 262.1043, found 262.1040.

Preparation of Styrene Derivatives

The following styrene derivatives were prepared by Wittig reaction of the corresponding aryl aldehydes according to the literature procedure,²⁵ and purified by silica gel column chromatography. Their spectral data showed good agreement with the literature data:

Trimethyl(4-vinylphenyl)silane (**2d**)²⁶

4-Vinyl-1,1'-biphenyl (**2g**)²⁷

1-Methoxy-2-vinylbenzene (**2k**)²⁷

1,4-Dimethyl-2-vinylbenzene (**2m**)²⁸

2,4-Dimethoxy-1-vinylbenzene (**2n**)²⁹

1,2,3-Trimethoxy-5-vinylbenzene (**2o**)³⁰

5-Vinylbenzo[*d*][1,3]dioxole (**2p**)³⁰

2-Vinylbenzofuran (**2q**)³¹

Preparation of Triarylphosphine Ligands

Except for a few commercially available derivatives, triarylphosphines were prepared by the reaction of aryl Grignard or aryllithium reagents with PCl_3 , PhPCl_2 , or Ph_2PCl according to the literature procedure,³² and purified by silica gel chromatography or recrystallization. Spectral data for the following known triarylphosphines showed good agreement with the literature data.

Tris(2,6-dimethoxyphenyl)phosphine (**L3**)³²

Bis(2,6-dimethoxyphenyl)(phenyl)phosphine (**L4**)³²

(2,6-Dimethoxyphenyl)diphenylphosphine (**L5**)³²

Bis(2-methoxyphenyl)(phenyl)phosphine (**L7**)³²

Bis(2,4-dimethoxyphenyl)(phenyl)phosphine (**L9**)³³

(2,4-Dimethoxyphenyl)diphenylphosphine (**L10**)³⁴

Bis(2,5-dimethoxyphenyl)(phenyl)phosphine (**L11**)³²

(2,5-Dimethoxyphenyl)diphenylphosphine (**L12**)³²

2,2'-(Phenylphosphinediyl)bis(*N,N*-dimethylaniline) (**L17**)³⁵

2-(Diphenylphosphino)-*N,N*-dimethylaniline (**L18**)³⁵

Tris(2,6-diethylphenyl)phosphine (L1): A three-necked, oven-dried flask was equipped with a dropping funnel and a reflux condenser. In this flask was added 0.24 g of magnesium turnings (10 mmol). A solution of 2-bromo-1,3-diethylbenzene (1.52 mL, 9 mmol) in 20 mL of dry THF was added dropwise. The reaction started after heating to reflux. After the addition was completed, the mixture was heated to reflux for 2 h, and cooled down to 0 °C.

A solution of phosphorus trichloride (0.18 mL, 2 mmol) in 10 mL of dry THF was added dropwise. Afterward, the resulting suspension was heated to reflux for 3 h. After it was cooled down to room temperature, water (10 mL) was added to quench the remaining Grignard reagents. The organic layer was separated. The aqueous layer was extracted twice with 20 mL portions of EtOAc. The combined organic phases were washed with brine (50 mL $\times$ 2) and dried with MgSO_4 . The solvent was evaporated under reduced pressure. The raw product was recrystallized from hot ethanol to give the desired product as white solid (0.48 g, 56%). M.p. 154-155 °C; ^1H NMR (400 MHz, CDCl_3): δ 0.86 (b, 18H), 2.84 (b, 12H), 6.90 (d, $J = 4.7$ Hz, 6H), 7.12 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.5, 27.9, 126.0, 128.2, 135.8, 149.4; ^{31}P NMR (162 MHz, CDCl_3): δ -30.1; HRMS (ESI) Calcd for $\text{C}_{30}\text{H}_{40}\text{P}$ $[\text{M} + \text{H}]^+$ 431.2859, found 431.2868.

Tris(2-ethylphenyl)phosphine (L2): Same procedure as used for **L1** was applied to 1-bromo-2-ethylbenzene (1.25 mL, 9 mmol), phosphorus trichloride (0.18 mL, 2 mmol) and Mg (0.24 g, 10 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a white solid (0.19 g, 27%). R_f 0.80 (hexane/EtOAc = 10/1); M.p. 96-97 °C; ^1H NMR (400 MHz, CDCl_3): δ 1.15 (t, $J = 7.4$ Hz, 9H), 2.84 (q, $J = 7.8$ Hz, 6H), 6.78-6.81 (m, 3H), 7.06 (t, $J = 6.8$ Hz, 3H), 7.22-7.32 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 15.1 (d, $^4J_{\text{C-P}} = 3.1$ Hz), 27.5 (d, $^3J_{\text{C-P}} = 22.4$ Hz), 126.0, 128.2 (d, $^3J_{\text{C-P}} = 5.0$ Hz), 128.8, 133.9, 134.9 (d, $^2J_{\text{C-P}} = 11.6$ Hz), 148.5 (d, $^1J_{\text{C-P}} = 25.5$ Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -24.0; HRMS (ESI) Calcd for $\text{C}_{24}\text{H}_{28}\text{P}$ $[\text{M} + \text{H}]^+$ 347.1929, found 347.1930.

Tris(2,4-dimethoxyphenyl)phosphine (L8): Same procedure as used for **L1** was applied to 1-bromo-2,4-dimethoxybenzene (2.1 mL, 14.4 mmol), phosphorus trichloride (0.36 mL, 4 mmol), and Mg (0.48 g, 20 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 5/1) of the crude product afforded the title compound as a white solid (0.72 g, 41%). R_f 0.42 (hexane/EtOAc = 1/1); M.p. 184-185 °C; ^1H NMR (400 MHz, CDCl_3): δ 3.72 (s, 9H), 3.80 (s, 9H), 6.39 (dd, J = 8.3, 2.3 Hz, 3H), 6.46 (dd, J = 4.4, 2.3 Hz, 3H), 6.61 (dd, J = 8.3, 4.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.2, 55.7, 98.2, 105.0, 116.6 (d, $^2J_{\text{C-P}}$ = 11.5 Hz), 134.6, 161.6, 162.6 (d, $^1J_{\text{C-P}}$ = 17.7 Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -43.9; HRMS (ESI) Calcd for $\text{C}_{24}\text{H}_{28}\text{O}_6\text{P}$ $[\text{M} + \text{H}]^+$ 443.1624, found 443.1621.

Bis(2,4-diethoxyphenyl)(phenyl)phosphine (L13): A three-necked, oven-dried flask was equipped with a dropping funnel and a reflux condenser. In this flask was added 0.24 g of magnesium turnings (10 mmol). A solution of 1-bromo-2,4-diethoxybenzene (2.1 g, 8.6 mmol) in 20 mL of dry THF was added dropwise. The reaction started after heating to reflux. After the addition was completed, the mixture was heated to reflux for 3 h, and cooled down to 0 °C. A solution of PPhCl_2 (0.47 mL, 3.44 mmol) in 10 mL of dry THF was added dropwise. Afterward, the resulting suspension was heated to reflux for 12 h. After it was cooled down to room temperature, water (10 mL) was added to quench the remaining Grignard reagents. The organic layer was separated. The aqueous layer was extracted twice with 20 mL portions of EtOAc. The combined organic phases were washed with brine (50 mL $\times$ 2) and dried with MgSO_4 . The solvent was evaporated under reduced pressure. Silica

gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as colorless viscous oil (0.62 g, 41%). R_f 0.38 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 1.12 (t, $J = 7.0$ Hz, 6H), 1.40 (t, $J = 7.0$ Hz, 6H), 3.88-3.97 (m, 4H), 4.00 (q, $J = 7.0$ Hz, 4H), 6.37 (dd, $J = 8.3, 2.2$ Hz, 2H), 6.44 (dd, $J = 3.7, 2.4$ Hz, 2H), 6.66 (dd, $J = 8.3, 4.9$ Hz, 2H), 7.26-7.34 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.3, 14.8, 63.3, 63.9 (d, $^4J_{\text{C-P}} = 0.8$ Hz), 99.5 (d, $^3J_{\text{C-P}} = 2.2$ Hz), 105.4 (d, $^3J_{\text{C-P}} = 2.2$ Hz), 117.0 (d, $^2J_{\text{C-P}} = 10.3$ Hz), 127.8 (two signals overlapped), 133.8 (d, $^1J_{\text{C-P}} = 20.9$ Hz), 134.6 (d, $^3J_{\text{C-P}} = 4.2$ Hz), 137.8 (d, $^2J_{\text{C-P}} = 11.0$ Hz), 161.0 (d, $^3J_{\text{C-P}} = 2.1$ Hz), 161.6 (d, $^1J_{\text{C-P}} = 15.6$ Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -26.9; HRMS (ESI) Calcd for $\text{C}_{26}\text{H}_{32}\text{O}_4\text{P}$ $[\text{M} + \text{H}]^+$ 439.2038, found 439.2033.

4,4'-(Phenylphosphinediyl)bis(3-methoxy-*N,N*-dimethylaniline) (L14): Same procedure as used for **L13** was applied to 4-bromo-3-methoxy-*N,N*-dimethylaniline (0.4 g, 1.74 mmol), PPhCl_2 (0.1 mL, 0.78 mmol) and Mg (0.1 g, 2.1 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 5/1) of the crude product afforded the title compound as a white solid (0.14 g, 44%). M.p. 164-165 °C; ^1H NMR (400 MHz, CDCl_3): δ 2.96 (s, 12H), 3.74 (s, 6H), 6.21-6.25 (m, 4H), 6.59 (dd, $J = 8.2, 4.9$ Hz, 2H), 7.24-7.26 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 40.4, 55.6, 95.5, 105.1, 111.4 (d, $^2J_{\text{C-P}} = 7.7$ Hz), 127.4, 127.7 (d, $^2J_{\text{C-P}} = 6.6$ Hz), 133.3 (d, $^1J_{\text{C-P}} = 19.9$ Hz), 134.9 (d, $^3J_{\text{C-P}} = 1.7$ Hz), 139.1 (d, $^2J_{\text{C-P}} = 11.2$ Hz), 152.5, 162.7 (d, $^2J_{\text{C-P}} = 17.0$ Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -32.0; HRMS (ESI) Calcd for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_2\text{P}$ $[\text{M} + \text{H}]^+$ 409.2045, found 409.2046.

Bis(2,4-dimethoxyphenyl)(4-methoxyphenyl)phosphine (L15): A three-necked, oven-dried flask was equipped with a dropping funnel and a reflux condenser. In this flask were added phosphorus trichloride (0.18 mL, 2 mmol) and THF (5 mL). The solution was cooled down to -78 °C. A solution of (4-methoxyphenyl)zinc(II) bromide in 10 mL of dry THF, which was prepared from a THF solution of (4-methoxyphenyl)magnesium bromide (2.1 mL, 0.95 M) and $\text{ZnCl}_2 \cdot \text{TMEDA}$ (0.51 g, 2 mmol) was added in 2 h. After it was warmed to room temperature, a THF solution of (2,4-dimethoxyphenyl)magnesium bromide (3.3 mL, 1.5 M) was added dropwise. After the addition was completed, the mixture was heated to reflux for 4 h, and cooled down to room temperature. Water (10 mL) was added to quench the remaining Grignard reagents. The organic layer was separated. The aqueous layer was extracted twice with 20 mL portions of EtOAc. The combined organic phases were washed with brine (50 mL $\times$ 2) and dried with MgSO_4 . The solvent was evaporated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 5/1) of the crude product afforded the title compound as white solid (0.30 g, 36%). R_f 0.30 (hexane/EtOAc = 2/1); M.p. 144-145 °C; ^1H NMR (400 MHz, CDCl_3): δ 3.72 (s, 6H), 3.80 (s, 6H), 3.81 (s, 3H), 6.39 (dd, J = 8.4, 2.3 Hz, 2H), 6.46 (dd, J = 4.2, 2.3 Hz, 2H), 6.59 (dd, J = 8.3, 4.5 Hz, 2H), 6.84-6.87 (m, 2H), 7.17-7.22 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.1, 55.3, 55.7, 98.2 (d, $^4J_{\text{C-P}}$ = 2.0 Hz), 105.0 (d, $^3J_{\text{C-P}}$ = 0.9 Hz), 113.9 (d, $^2J_{\text{C-P}}$ = 8.0 Hz), 117.2 (d, $^2J_{\text{C-P}}$ = 10.2 Hz), 127.9 (d, $^2J_{\text{C-P}}$ = 8.3 Hz), 134.5 (d, $^3J_{\text{C-P}}$ = 1.1 Hz), 135.2 (d, $^1J_{\text{C-P}}$ = 22.1 Hz), 105.0, 159.9, 161.8, 162.4 (d, $^1J_{\text{C-P}}$ = 16.9 Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -32.2; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{26}\text{O}_5\text{P}$ $[\text{M} + \text{H}]^+$ 413.1518, found 413.1515.

Bis(2,4-dimethoxyphenyl)(4-fluorophenyl)phosphine (L16): Same procedure as used for **L15** was applied to (2,4-dimethoxyphenyl)magnesium bromide (2.2 mL, 1.5 M), phosphorus trichloride (0.13 mL, 1.5 mmol), (4-fluorophenyl)magnesium bromide (1.3 mL, 1.2 M) and $\text{ZnCl}_2 \cdot \text{TMEDA}$ (0.38 g, 1.5 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 5/1) of the crude product afforded the title compound as white solid (0.21 g, 35%). R_f 0.45 (hexane/EtOAc = 2/1); M.p. 152-153 °C; ^1H NMR (400 MHz, CDCl_3): δ 3.71 (s, 6H), 3.79 (s, 6H), 6.40 (dd, J = 8.4, 2.3 Hz, 2H), 6.47 (dd, J = 4.3, 2.3 Hz, 2H), 6.59 (dd, J = 8.3, 4.7 Hz, 2H), 6.99 (t, J = 8.6 Hz, 2H), 7.21-7.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.3 (d, J = 1.0 Hz), 55.7 (t, J = 0.8 Hz), 98.3 (d, J = 2.0 Hz), 105.1 (d, J = 0.9 Hz), 115.2 (dd, J = 20.8, 7.6 Hz), 116.4 (d, J = 10.0 Hz), 132.8 (dd, J = 11.3, 3.4 Hz), 134.6 (d, J = 1.6 Hz), 135.4 (dd, J = 22.1, 7.8 Hz), 162.0, 162.4 (d, J = 16.8 Hz), 163.1 (d, J = 249 Hz); ^{31}P NMR (162 MHz, CDCl_3): δ -31.0 (d, J = 6.3 Hz); HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{23}\text{FO}_4\text{P}$ $[\text{M} + \text{H}]^+$ 401.1318, found 401.1317.

Cobalt-Catalyzed Linear-Selective Addition of Aryl Imines to Styrenes

Typical Procedure: 1-(2-Phenethylphenyl)ethanone (3aa). In a Schlenk tube were placed (*E*)-4-methoxy-*N*-(1-phenylethylidene)aniline (**1a**, 68 mg, 0.30 mmol), bis(2,4-dimethoxyphenyl)(phenyl)phosphine (**L9**, 11.5 mg, 0.060 mmol), a freshly prepared THF solution of CoBr₂ (0.30 M, 0.10 mL, 0.030 mmol), 2-methoxypyridine (126 μ L, 0.24 mmol) and THF (0.45 mL). The resulting solution was cooled in an ice bath, followed by the addition of CyMgBr (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, styrene (**2a**, 53 μ L, 0.45 mmol) was added. The resulting mixture was warmed to 40 °C and stirred for 24 h. The reaction was then allowed to cool to room temperature, quenched by the addition of HCl (3 N, 1.0 mL), and stirred for 1 h. The resulting mixture was extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO₄ and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (60 mg, 91%). The l/b ratio was determined to be 97/3 by ¹H NMR integrations of characteristic signals at 2.54 and 2.37 ppm. The ¹H and ¹³C NMR spectra showed good agreement with the literature data.³⁶

*R*_f 0.46 (hexane/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 2.54 (s, 3H), 2.88-2.92 (m, 2H), 3.16-3.20 (m, 2H), 7.12-7.33 (m, 7H), 7.40 (td, *J* = 7.5, 1.4 Hz, 2H), 7.68 (dd, *J* = 7.7, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.6, 36.3, 38.2, 125.8, 125.9, 128.2, 128.6, 129.2, 131.4, 131.5, 137.9, 141.9, 142.2, 201.9; HRMS (ESI) Calcd for C₁₆H₁₇O [M + H]⁺ 225.1279, found 225.1280.

1-(4-Methyl-2-phenethylphenyl)ethanone (3ba): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline (**1b**, 72 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (61 mg, 85%). The l/b ratio was determined to be 90/10 by ^1H NMR integrations of characteristic singlet signals at 2.51 and 2.37 ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{4d}

R_f 0.50 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.34 (s, 3H), 2.51 (s, 3H), 2.83-2.97 (m, 2H), 3.12-3.16 (m, 2H), 7.02-7.29 (m, 7H), 7.61 (d, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 29.4, 36.7, 38.2, 125.7, 126.6, 128.2, 128.6, 130.0, 132.4, 134.6, 142.1, 142.5, 201.1; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ $[\text{M} + \text{H}]^+$ 239.1436, found 239.1434.

1-(3-Phenethyl-[1,1'-biphenyl]-4-yl)ethanone (3ca): The typical procedure was applied to (*E*)-*N*-(1-([1,1'-biphenyl]-4-yl)ethylidene)-4-methoxyaniline (**1c**, 90 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow solid (71 mg, 79%). The l/b ratio was determined to be 93/7 by ^1H NMR integrations of characteristic singlet signals at 2.57 and 2.40 ppm.

M.p. 84-86 $^\circ\text{C}$; R_f 0.45 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.57 (s, 3H), 2.91-2.94 (m, 2H), 3.22-3.26 (m, 2H), 7.15-7.31 (m, 5H), 7.36-7.57 (m, 7H), 7.78 (d, J =

8.1 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.6, 36.7, 38.2, 124.5, 125.8, 127.2, 128.0, 128.3, 128.7, 128.8, 130.2, 130.4, 136.1, 139.9, 141.9, 142.8, 144.1, 201.2; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{21}\text{O}$ $[\text{M} + \text{H}]^+$ 301.1592, found 301.1602.

1-(4-Methoxy-2-phenethylphenyl)ethanone (3da): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(4-methoxyphenyl)ethylidene)aniline (**1d**, 77 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (66 mg, 87%). The l/b ratio was determined to be 94/6 by ^1H NMR integrations of characteristic singlet signals at 2.53 and 2.43 ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{Error! Bookmark not defined.}

R_f 0.44 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.53 (s, 3H), 2.85-2.89 (m, 2H), 3.18-3.22 (m, 2H), 3.79 (s, 3H), 6.68 (d, J = 2.6 Hz, 1H), 6.77 (dd, J = 8.7, 2.7 Hz, 1H), 7.16-7.20 (m, 1H), 7.23-7.33 (m, 4H), 7.75 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.2, 37.2, 37.9, 55.3, 111.0, 117.0, 125.8, 128.0, 128.2, 128.7, 129.8, 132.6, 142.1, 145.7, 161.9, 199.5; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}_2$ $[\text{M} + \text{H}]^+$ 255.1385, found 255.1394.

1-(4-Fluoro-2-phenethylphenyl)ethanone (3ea): The typical procedure was applied to (*E*)-*N*-(1-(4-fluorophenyl)ethylidene)-4-methoxyaniline (**1e**, 73 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude

product afforded a mixture of the title compound and its branched isomer as a light yellow oil (61 mg, 84%). The l/b ratio was determined to be 92/8 by ^1H NMR integrations of characteristic singlet signals at 2.51 and 2.37 ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{Error! Bookmark not defined.}

R_f 0.53 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.51 (s, 3H), 2.85-2.89 (m, 2H), 3.15-3.19 (m, 2H), 6.90-6.97 (m, 2H), 7.12-7.33 (m, 5H), 7.71 (dd, J = 8.7, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.5, 36.4, 37.7, 112.8 ($^2J_{\text{C-F}}$ = 21.0 Hz), 118.2 ($^2J_{\text{C-F}}$ = 21.0 Hz), 126.0, 128.3, 128.6, 132.0 ($^3J_{\text{C-F}}$ = 9.0 Hz), 133.8 ($^4J_{\text{C-F}}$ = 3.0 Hz), 141.4, 146.0 ($^3J_{\text{C-F}}$ = 8.0 Hz), 164.1 ($^1J_{\text{C-F}}$ = 253.0 Hz), 200.1; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{16}\text{FO}$ [$\text{M} + \text{H}$] $^+$ 243.1185, found 243.1182.

1-(4-(Methylthio)-2-phenethylphenyl)ethanone (3fa): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(4-(methylthio)phenyl)ethylidene)aniline (**1f**, 81 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow solid (33 mg, 41%). The l/b ratio was determined to be 92/8 by ^1H NMR integrations of characteristic singlet signals at 2.52 and 2.38 ppm.

R_f 0.59 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.43 (s, 3H), 2.52 (s, 3H), 2.85-2.89 (m, 2H), 3.11-3.21 (m, 2H), 6.97 (d, J = 2.0 Hz, 1H), 7.10 (dd, J = 8.3, 2.1 Hz, 1H), 7.14-7.31 (m, 5H), 7.65 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.7, 29.3, 36.7, 37.9, 122.6, 125.8, 128.2 (two signals overlapped), 128.7, 130.5, 133.4, 141.8, 143.1, 143.7, 200.2; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{OS}$ [$\text{M} + \text{H}$] $^+$ 271.1157, found 271.1158.

1-(5-Methyl-2-phenethylphenyl)ethanone (3ga): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(*m*-tolyl)ethylidene)aniline (**1g**, 72 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol) with an extended reaction time of 48 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (49 mg, 68%). The l/b ratio was determined to be 91/9 by ^1H NMR integrations of characteristic signals at 2.52 and 1.58 (d, $J = 7.2$ Hz, 3H) ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{Error!}

Bookmark not defined.

R_f 0.50 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.37 (s, 3H), 2.52 (s, 3H), 2.83-2.86 (m, 2H), 3.08-3.12 (m, 2H), 7.11-7.29 (m, 7H), 7.46 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.0, 29.7, 35.9, 38.3, 125.8, 128.2, 128.6, 129.8, 131.4, 132.2, 135.5, 137.8, 138.8, 142.0, 202.1; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ $[\text{M} + \text{H}]^+$ 239.1436, found 239.1431.

8-Phenethyl-3,4-dihydronaphthalen-1(2H)-one (3ha): The typical procedure was applied to (*E*)-*N*-(3,4-dihydronaphthalen-1(2H)-ylidene)-4-methoxyaniline (**1h**, 75 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (68 mg, 90%). The l/b ratio was determined to be 97/3 by ^1H NMR integrations of characteristic signals at 2.51 and 1.58 (d, $J = 7.1$ Hz, 3H) ppm.

R_f 0.48 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.04-2.10 (m, 2H), 2.64 (t, $J = 6.8$ Hz, 2H), 2.83-2.87 (m, 2H), 2.94 (t, $J = 6.0$ Hz, 2H), 3.28-3.32 (m, 2H), 7.05 (d, J

= 7.5 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.14-7.20 (m, 1H), 7.21-7.36 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 22.9, 31.1, 37.8, 37.9, 41.0, 125.6, 127.1, 128.2, 128.6, 130.1, 130.9, 132.3, 142.4, 144.9, 145.9, 200.0; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{O}$ $[\text{M} + \text{H}]^+$ 251.1436, found 251.1438.

4-Methyl-8-phenethyl-3,4-dihydronaphthalen-1(2H)-one (3ia): The typical procedure was applied to (*E*)-4-methoxy-*N*-(4-methyl-3,4-dihydronaphthalen-1(2H)-ylidene)aniline (**1i**, 80 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (70 mg, 88%). The l/b ratio was determined to be 94/6 by GC using *n*-tridecane as the internal standard.

R_f 0.51 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 1.37 (d, J = 7.0 Hz, 3H), 1.82-1.90 (m, 1H), 2.17-2.25 (m, 1H), 2.55-2.62 (m, 1H), 2.74-2.82 (m, 1H), 2.83-2.90 (m, 2H), 3.03-3.11 (m, 1H), 3.23-3.34 (m, 2H), 7.07-7.09 (m, 1H), 7.14-7.20 (m, 2H), 7.22-7.32 (m, 4H), 7.35 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.2, 29.6, 33.8, 37.6, 37.8, 38.0, 125.7, 125.8, 128.2, 128.6, 130.0, 130.5, 132.4, 142.4, 144.6, 150.4, 200.2; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{21}\text{O}$ $[\text{M} + \text{H}]^+$ 265.1592, found 265.1597.

6-Methoxy-8-phenethyl-3,4-dihydronaphthalen-1(2H)-one (3ja): The typical procedure was applied to (*E*)-4-methoxy-*N*-(6-methoxy-3,4-dihydronaphthalen-1(2H)-

ylidene)aniline (**1j**, 84 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (54 mg, 64%). The l/b ratio was determined to be 97/3 by ^1H NMR integrations of characteristic signals at 2.63 and 1.57 (d, J = 8.0 Hz, 3H) ppm.

R_f 0.33 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.02-2.10 (m, 2H), 2.63 (t, J = 6.8 Hz, 2H), 2.84-2.88 (m, 2H), 2.94 (t, J = 6.0, 2H), 3.29-3.33 (m, 2H), 3.80 (s, 3H), 6.58 (dd, J = 20.8, 2.7 Hz, 2H), 7.16-7.20 (m, 1H), 7.24-7.33 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 23.0, 31.8, 37.6, 38.4, 41.0, 55.2, 111.4, 115.9, 124.5, 125.7, 128.2, 128.7, 142.5, 148.0, 148.7, 161.9, 198.5; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{21}\text{O}_2$ $[\text{M} + \text{H}]^+$ 281.1542, found 281.1540.

5-Phenethylchroman-4-one (3ka): The typical procedure was applied to (*E*)-*N*-(chroman-4-ylidene)-4-methoxyaniline (**1k**, 76 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (61 mg, 81%). The l/b ratio was determined to be 92/8 by ^1H NMR integrations of characteristic signals at 3.32 and 1.57 ppm.

R_f 0.32 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.78-2.86 (m, 4H), 3.30-3.34 (m, 2H), 4.48 (t, J = 6.4 Hz, 2H), 6.76 (d, J = 7.5 Hz, 1H), 6.83-6.86 (m, 1H), 7.15-7.22 (m, 1H), 7.26-7.32 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 37.5, 37.6, 39.4, 66.4, 116.3, 119.4, 124.2, 125.7, 128.2, 128.6, 134.8, 142.2, 145.8, 163.2, 193.0; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{17}\text{O}_2$ $[\text{M} + \text{H}]^+$ 253.1229, found 253.1231.

1-(2-Phenethylphenyl)propan-1-one (3la): The reaction of 4-methoxy-*N*-(1-phenylpropylidene)aniline (*E/Z* = 10/1) (**11**, 72 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol) was performed according to the typical procedure except for the use of DBU (37 μ L, 0.24 mmol) instead of 2-methoxypyridine. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (66 mg, 92%). The l/b ratio was determined to be 98/2 by ^1H NMR integrations of characteristic signals at 3.08-3.12 (m, 2H) and 4.72 (q, J = 6.9 Hz) ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{4f}

R_f 0.74 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 1.17 (t, J = 7.3 Hz, 3H), 2.85- 2.81 (q, J = 7.3 Hz, 2H), 2.86-2.90 (m, 2H), 3.08-3.12 (m, 2H), 7.15-7.28 (m, 7H), 7.36 (td, J = 7.5, 1.4 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 8.7, 35.2, 36.3, 38.5, 126.1, 128.4, 128.5, 128.8, 131.2, 131.5, 138.7, 142.1, 205.6; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ [$\text{M} + \text{H}$]⁺ 239.1436, found 239.1432.

1-Methyl-2-phenethyl-1H-indole-3-carbaldehyde (3ma) and 1-methyl-2-(1-phenylethyl)-1H-indole-3-carbaldehyde (3ma'): The typical procedure was applied to (*E*)-4-methoxy-*N*-((1-methyl-1H-indol-3-yl)methylene)aniline (**1m**, 79 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 10/1) of the crude product afforded the title compounds **3ma** (32 mg, 41%) and **3ma'** (45 mg, 57%)

both as light yellow oil. Characterization data of **3ma'** were previously reported by us.^{6c}

3ma: R_f 0.33 (hexane/EtOAc = 3/1); ^1H NMR (400 MHz, CDCl_3): δ 3.00 (t, $J = 7.5$ Hz, 2H), 3.37 (t, $J = 7.5$ Hz, 2H), 3.45 (s, 3H), 7.08-7.09 (m, 2H), 7.20-7.30 (m, 6H), 8.23-8.26 (m, 1H), 10.10 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.9, 29.4, 36.6, 109.4, 113.7, 120.7, 122.8, 123.1, 125.8, 126.7, 128.4, 128.7, 136.9, 139.7, 150.2, 184.0; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{18}\text{NO}$ $[\text{M} + \text{H}]^+$ 264.1388, found 264.1386.

1-(3-Methoxy-2-phenethylphenyl)ethanone (3na) and 1-(3-methoxy-2-(1-phenylethyl)phenyl)ethanone (3na'): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(3-methoxyphenyl)ethylidene)aniline (**1n**, 77 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol). The crude product was analyzed by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard. The overall yield (28%) and the ratio (18/82) of the title compounds **3na** and **3na'** were determined by characteristic signals at 3.05 ppm (methylene of **3na**) and 4.64 ppm (methine of **3na'**).

1-(4-Phenethylbenzo[d][1,3]dioxol-5-yl)ethanone (3oa): The reaction of (*E*)-*N*-(1-(benzo[d][1,3]dioxol-5-yl)ethylidene)-4-methoxyaniline (**1o**, 81 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol) was performed according to the typical procedure except for the use of DBU (37 μL , 0.24 mmol) instead of 2-methoxypyridine. Silica gel chromatography (eluent:

hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (60 mg, 74%). The l/b ratio was determined to be 58/42 by ^1H NMR integrations of characteristic signals at 2.49 and 1.70 ppm. Note that characterization data of the branched isomer were previously reported by us.^{6d}

R_f 0.48 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.49 (s, 3H), 2.84-2.88 (m, 2H), 3.15-3.19 (m, 2H), 5.93 (s, 2H), 6.70 (d, J = 8.4 Hz, 1H), 7.14-7.32 (m, 5H), 7.37 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.4, 29.5, 36.2, 105.6, 124.9, 126.0, 126.2, 128.4, 128.9, 131.9, 142.4, 147.5, 150.0, 199.6; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{17}\text{O}_3$ $[\text{M} + \text{H}]^+$ 269.1178, found 269.1181.

1-(3-Fluoro-2-phenethylphenyl)ethanone (3pa): The reaction of (*E*)-*N*-(1-(3-fluorophenyl)ethylidene)-4-methoxyaniline (**1p**, 73 mg, 0.30 mmol) and **2a** (53 μL , 0.45 mmol) was performed according to the typical procedure except for the use of DBU (37 μL , 0.24 mmol) instead of 2-methoxypyridine. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (52 mg, 72%). The l/b ratio was determined to be 89/11 by ^1H NMR integrations of characteristic singlet signals at 2.44 and 2.38 ppm. The ^1H and ^{13}C NMR spectra showed good agreement with the literature data.^{4f}

R_f 0.48 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.44 (s, 3H), 2.84-2.88 (m, 2H), 3.12-3.17 (m, 2H), 7.14-7.29 (m, 7H), 7.39 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.0 (d, $^3J_{\text{C-F}}$ = 3.7 Hz), 29.8, 36.6, 118.2 (d, $^2J_{\text{C-F}}$ = 23.9 Hz), 124.3 (d, $^4J_{\text{C-F}}$ = 3.0 Hz), 125.9, 127.0 (d, $^3J_{\text{C-F}}$ = 8.7 Hz), 128.3, 128.7, 140.4, 141.7, 161.7 (d, $^1J_{\text{C-F}}$ = 246.1

Hz), 201.2; HRMS (ESI) Calcd for C₁₆H₁₆FO [M + H]⁺ 243.1185, found 243.1187.

1-(3,4-Difluoro-2-phenethylphenyl)ethanone (3qa) and 1-(4,5-difluoro-2-phenethylphenyl)ethanone (4qa): The typical procedure was applied to (*E*)-*N*-(1-(3,4-difluorophenyl)ethylidene)-4-methoxyaniline (**1q**, 78 mg, 0.30 mmol) and **2a** (53 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of **3qa** and its branched isomer (51 mg, 65%) and a mixture of **4qa** and its branched isomer (12 mg, 16%) both as light yellow oil. The l/b ratio of the former mixture was determined to be 68/32 by ¹H NMR integrations of characteristic signals at 2.45 and 2.41 ppm. The l/b ratio of the latter was determined to be 95/5 by ¹H NMR integrations of characteristic signals at 2.48 and 2.36 ppm.

3qa: *R*_f 0.34 (hexane/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 2.45 (s, 3H), 2.85-2.89 (m, 2H), 3.19-3.24 (m, 2H), 7.03-7.10 (m, 1H), 7.16-7.30 (m, 5H), 7.44 (ddd, *J* = 8.7, 4.9, 1.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.1, 29.5, 36.4, 114.2 (d, *J* = 18.2 Hz), 125.37 (dd, *J* = 7.7, 3.8 Hz), 126.1, 128.4, 128.6, 132.43 (d, *J* = 12.5 Hz), 134.9, 141.3, 149.5 (dd, *J* = 248.1, 12.5 Hz), 152.2 (dd, *J* = 255.8, 14.4 Hz), 199.6; HRMS (ESI) Calcd for C₁₆H₁₅F₂O [M + H]⁺ 261.1091, found 261.1087.

4qa: *R*_f 0.41 (hexane/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 2.48 (s, 3H), 2.83-2.87 (m, 2H), 3.11-3.15 (m, 2H), 7.00 (dd, *J* = 11.2, 7.7 Hz, 1H), 7.17-7.21 (m, 3H); 7.26-7.29 (m, 2H), 7.49 (dd, *J* = 10.8, 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.5, 35.6, 37.8, 118.6 (d, *J* = 17.2 Hz), 120.2 (d, *J* = 16.9 Hz), 126.1, 128.4, 128.6, 133.8-138.9 (m), 140.1-140.2 (m), 141.1, 147.8 (dd, *J* = 248.5, 12.8 Hz), 151.6 (dd, *J* = 255.1, 12.4 Hz), 199.0;

HRMS (ESI) Calcd for $C_{16}H_{15}F_2O$ $[M + H]^+$ 261.1091, found 261.1091.

1-(2-(4-Methylphenethyl)phenyl)ethanone (3ab): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-methyl-4-vinylbenzene (**2b**, 59 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (59 mg, 82%). The l/b ratio was determined to be 98/2 by 1H NMR integrations of characteristic signals at 2.38 and 2.53 ppm.

R_f 0.53 (hexane/EtOAc = 5/1); 1H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.53 (s, 3H), 2.82-2.86 (m, 2H), 3.11-3.15 (m, 2H), 7.07-7.13 (m, 4H), 7.23-7.28 (m, 2H), 7.40 (td, J = 7.5, 1.4 Hz, 1H), 7.67 (dd, J = 7.7, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 29.7, 36.5, 37.8, 125.9, 128.5, 129.0, 129.2, 131.4, 131.5, 135.2, 137.9, 138.8, 142.0, 202.0; HRMS (ESI) Calcd for $C_{17}H_{19}O$ $[M + H]^+$ 239.1436, found 239.1437.

1-(2-(4-(Tert-butyl)phenethyl)phenyl)ethanone (3ac): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-(*tert*-butyl)-4-vinylbenzene (**2c**, 52 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (76 mg, 90%). The l/b ratio was determined to be 96/4 by 1H NMR integrations of characteristic signals at

2.48 and 2.35 ppm.

R_f 0.57 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 1.31 (s, 9H), 2.48 (s, 3H), 2.82-2.86 (m, 2H), 3.12-3.17 (m, 2H), 7.15 (d, J = 8.1 Hz, 2H), 7.22-7.32 (m, 4H), 7.39 (td, J = 7.5, 1.3 Hz, 1H), 7.63 (dd, J = 8.0, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.6, 31.4, 34.3, 36.1, 37.7, 125.2, 125.9, 128.3, 129.0, 131.4, 131.4, 138.0, 138.8, 142.0, 148.6, 202.0; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{25}\text{O}$ $[\text{M} + \text{H}]^+$ 281.1905, found 281.1909.

1-(2-(4-(Trimethylsilyl)phenyl)phenyl)ethanone (3ad): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and trimethyl(4-vinylphenyl)silane (**2d**, 79 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (75 mg, 84%). The l/b ratio was determined to be 91/9 by ^1H NMR integrations of characteristic signals at 2.48 and 2.37 ppm.

R_f 0.77 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 0.25 (s, 9H), 2.48 (s, 3H), 2.82-2.86 (m, 2H), 3.12-3.17 (m, 2H), 7.22-7.29 (m, 4H), 7.37-7.39 (m, 1H), 7.43-7.47 (m, 2H), 7.63-7.66 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ -1.1, 29.6, 36.1, 38.2, 125.9, 128.1, 129.2, 131.4, 131.5, 133.4, 137.4, 137.9, 141.9, 142.5, 201.9; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{25}\text{OSi}$ $[\text{M} + \text{H}]^+$ 297.1675, found 297.1672.

1-(2-(4-Methoxyphenethyl)phenyl)ethanone (3ae): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-methoxy-4-vinylbenzene (**2e**, 61 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (61 mg, 80%). The l/b ratio was determined to be 98/2 by ^1H NMR integrations of characteristic signals at 2.52 and 2.36 (s, 3H) ppm.

R_f 0.40 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.52 (s, 3H), 2.80-2.84 (m, 2H), 3.09-3.13 (m, 2H), 3.77 (s, 3H), 6.82 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.3 Hz, 2H), 7.21-7.28 (m, 2H), 7.38 (td, J = 7.5, 1.3 Hz, 1H), 7.65 (dd, J = 7.7, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.7, 36.6, 37.3, 55.2, 113.7, 125.9, 129.2, 129.5, 131.4, 131.5, 134.0, 137.8, 141.9, 157.8, 201.9; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}_2$ $[\text{M} + \text{H}]^+$ 255.1385, found 255.1380.

1-(2-(4-Fluorophenethyl)phenyl)ethanone (3af): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-fluoro-4-vinylbenzene (**2f**, 54 μ L, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (61 mg, 84%). The l/b ratio was determined to be 96/4 by ^1H NMR integrations of characteristic signals at 2.55 and 2.39 (s, 3H) ppm.

R_f 0.49 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.55 (s, 3H), 2.83-2.87 (m, 2H), 3.11-3.14 (m, 2H), 6.93-6.97 (m, 2H), 7.15-7.20 (m, 3H), 7.29 (td, J = 7.6, 1.3 Hz, 1H), 7.39 (td, J = 7.5, 1.4 Hz, 1H), 7.70 (dd, J = 7.7, 1.3 Hz, 1H); ^{13}C NMR (100 MHz,

CDCl₃): δ 29.7, 36.7 ($^5J_{\text{C-F}} = 1.4$ Hz), 37.4, 115.1 ($^2J_{\text{C-F}} = 21.1$ Hz), 126.2, 129.6, 130.0, 130.1, 131.7 ($^4J_{\text{C-F}} = 1.0$ Hz), 137.7 ($^3J_{\text{C-F}} = 3.0$ Hz), 137.7, 141.90, 161.4 ($^1J_{\text{C-F}} = 243.2$ Hz), 201.9; HRMS (ESI) Calcd for C₁₆H₁₆FO [M + H]⁺ 243.1185, found 243.1194.

1-(2-(2-([1,1'-Biphenyl]-4-yl)ethyl)phenyl)ethanone (3ag): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 4-vinyl-1,1'-biphenyl (**2g**, 81 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compound and its branched isomer as a light yellow oil (65 mg, 72%). The l/b ratio was determined to be 75/25 by ¹H NMR integrations of characteristic signals at 2.53 and 2.40 (s, 3H) ppm.

R_f 0.41 (hexane/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 2.53 (s, 3H), 2.90-2.94 (m, 2H), 3.17-3.21 (m, 2H), 7.23-7.34 (m, 4H), 7.38-7.44 (m, 4H), 7.48-7.52 (m, 2H), 7.54-7.59 (m, 2H), 7.67-7.69 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.7, 36.3, 37.8, 126.0, 126.7, 127.0 (two signals overlapped), 128.4, 128.7, 129.1, 129.3, 131.5, 137.8, 138.8, 141.0, 141.1, 141.9, 201.9; HRMS (ESI) Calcd for C₂₂H₂₁O [M + H]⁺ 301.1592, found 301.1599.

1-(2-(3-Methylphenyl)phenyl)ethanone (3ah): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-methyl-3-vinylbenzene (**2h**, 59 μ L, 0.45 mmol). Silica gel

chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow oil (64 mg, 90%). The l/b ratio was determined to be 94/6 by ^1H NMR integrations of characteristic signals at 2.32 and 2.28 ppm.

R_f 0.54 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.32 (s, 3H), 2.52 (s, 3H), 2.81-2.85 (m, 2H), 3.11-3.15 (m, 2H), 6.98-7.05 (m, 3H), 7.16 (t, J = 7.5 Hz, 1H), 7.23-7.27 (m, 2H), 7.38 (td, J = 7.5, 1.4 Hz, 1H), 7.65 (dd, J = 7.7, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 29.8, 36.6, 38.3, 125.8, 126.1, 126.7, 128.3, 129.3, 129.5, 131.6, 131.6, 137.9, 138.0, 142.0, 142.2, 202.1; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ $[\text{M} + \text{H}]^+$ 239.1436, found 239.1432.

1-(2-(3-Fluorophenethyl)phenyl)ethanone (3ai): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-fluoro-3-vinylbenzene (**2i**, 55 μL , 0.45 mmol) except for the use of DBU (37 μL , 0.24 mmol) instead of 2-methoxypyridine and with an extended reaction time of 48 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow oil (58 mg, 80%). The l/b ratio was determined to be 95/5 by ^1H NMR integrations of characteristic signals at 2.55 and 2.42 ppm.

R_f 0.49 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.55 (s, 3H), 2.85-2.90 (m, 2H), 3.12-3.16 (m, 2H), 6.84-6.90 (m, 1H), 6.91-6.95 (m, 1H), 6.98-7.01 (m, 1H), 7.19-7.23 (m, 2H), 7.29 (td, J = 7.6, 1.4 Hz, 1H), 7.39 (td, J = 7.5, 1.4 Hz, 1H), 7.70 (dd, J = 7.7, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.6, 36.2, 37.8, 112.7 (d, $^2J_{\text{C-F}}$ = 21.0 Hz),

115.4 (d, $^2J_{\text{C-F}} = 20.7$ Hz), 124.2 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 126.1, 129.5, 129.6 (d, $^3J_{\text{C-F}} = 8.2$ Hz), 131.6 (d, $^3J_{\text{C-F}} = 8.0$ Hz), 137.5, 141.6, 144.5 (two signals overlapped), 162.8 (d, $^1J_{\text{C-F}} = 245.1$ Hz), 201.7; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{16}\text{FO}$ $[\text{M} + \text{H}]^+$ 243.1185, found 243.1182.

1-(2-(2-Methylphenethyl)phenyl)ethanone (3aj): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-methyl-2-vinylbenzene (**2j**, 53 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a white solid (58 mg, 81%). The l/b ratio was determined to be 94/6 by ^1H NMR integrations of characteristic signals at 2.30 and 2.15 ppm.

R_f 0.43 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.30 (s, 3H), 2.49 (s, 3H), 2.86-2.90 (m, 2H), 3.09-3.13 (m, 2H), 7.08-7.15 (m, 4H), 7.22-7.29 (m, 2H), 7.38 (td, $J = 7.5, 1.4$ Hz, 1H), 7.64 (dd, $J = 7.7, 1.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 19.2, 29.6, 34.8, 35.5, 125.9, 126.0, 129.0, 129.3, 130.1, 131.4, 131.5, 136.1, 138.1, 140.0, 141.9, 201.9; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ $[\text{M} + \text{H}]^+$ 239.1436, found 239.1434.

1-(2-(2-Methoxyphenethyl)phenyl)ethanone(3ak): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-methoxy-2-vinylbenzene (**2k**, 60 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title

compound as a white solid (54 mg, 71%).

M.p. 81-82 °C; R_f 0.37 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.50 (s, 3H), 2.88 (dd, J = 9.2, 6.5 Hz, 2H), 3.11 (dd, J = 9.4, 6.3 Hz, 2H), 3.79 (s, 3H), 6.82-6.87 (m, 2H), 7.09-7.11 (m, 1H), 7.14-7.19 (m, 1H), 7.22-7.26 (m, 2H), 7.34-7.38 (m, 1H), 7.57-7.59 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.8, 32.4, 34.0, 55.2, 99.9, 110.2, 120.3, 125.7, 127.1, 128.6, 130.1, 130.1, 131.4, 138.5, 141.9, 157.4, 202.3; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{O}_2$ $[\text{M} + \text{H}]^+$ 255.1385, found 255.1383.

1-(2-(2-Fluorophenethyl)phenyl)ethanone (3a): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1-fluoro-2-vinylbenzene (**2l**, 56 μL , 0.45 mmol) except for the use of DBU (37 μL , 0.24 mmol) instead of 2-methoxypyridine and with an extended reaction time of 48 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow solid (70 mg, 90%). The l/b ratio was determined to be 99/1 by ^1H NMR integrations of characteristic signals at 2.55 and 2.38 ppm.

M.p. 68-69 °C; R_f 0.56 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.54 (s, 3H), 2.91-2.95 (m, 2H), 3.13-3.17 (m, 2H), 6.96-7.05 (m, 2H), 7.12-7.23 (m, 3H), 7.27 (td, J = 7.6, 1.4 Hz, 1H), 7.37 (td, J = 7.5, 1.4 Hz, 1H), 7.67 (dd, J = 7.7, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.6, 31.0 (d, $^3J_{\text{C-F}}$ = 2.4 Hz), 34.7 (d, $^4J_{\text{C-F}}$ = 1.4 Hz), 115.0 (d, $^2J_{\text{C-F}}$ = 22.3 Hz), 123.9 (d, $^4J_{\text{C-F}}$ = 3.6 Hz), 126.0, 127.5 (d, $^3J_{\text{C-F}}$ = 8.1 Hz), 126.0, 128.6 (d, $^2J_{\text{C-F}}$ = 16.0 Hz), 129.2, 131.0 (d, $^3J_{\text{C-F}}$ = 5.2 Hz), 131.4, 131.5, 137.8, 141.6, 161.1 (d, $^1J_{\text{C-F}}$ = 244.7 Hz), 201.8; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{16}\text{FO}$ $[\text{M} + \text{H}]^+$ 243.1185, found 243.1189.

1-(2-(2,5-Dimethylphenethyl)phenyl)ethanone (3am): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1,4-dimethyl-2-vinylbenzene (**2m**, 59 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow oil (65 mg, 86%). The ratio of the products was determined to be 90/10 by ^1H NMR integrations of characteristic signals at 2.50 and 2.08 ppm.

R_f 0.62 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.27 (s, 6H), 2.50 (s, 3H), 2.82-2.86 (m, 2H), 3.07-3.11 (m, 2H), 6.91 (d, J = 7.6 Hz, 1H), 6.98-7.02 (m, 2H), 7.22-7.99 (m, 2H), 7.37-7.41 (m, 1H), 7.63-7.65 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 18.7, 20.9, 29.6, 34.9, 35.5, 125.9, 126.7, 129.0, 130.0 (two signals overlapped), 131.4, 131.5, 132.9, 135.2, 138.0, 139.8, 142.0, 202.0; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{21}\text{O}$ $[\text{M} + \text{H}]^+$ 253.1592, found 253.1595.

1-(2-(2,4-Dimethoxyphenethyl)phenyl)ethanone (3an): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 2,4-dimethoxy-1-vinylbenzene (**2n**, 74 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a white solid (67 mg, 78%).

R_f 0.27 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.51 (s, 3H), 2.79-2.83 (m,

2H), 3.05-3.09 (m, 2H), 3.77 (s, 3H), 3.78 (s, 3H), 6.38 (dd, $J = 8.2, 2.4$ Hz, 1H), 6.43 (d, $J = 2.4$ Hz, 1H), 6.99 (d, $J = 8.2$ Hz, 1H), 7.21-7.25 (m, 2H), 7.35 (td, $J = 7.3, 1.4$ Hz, 1H), 7.58 (dd, $J = 7.0, 1.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.8, 31.8, 34.2, 55.2, 55.3, 98.4, 103.8, 122.5, 125.6, 128.5, 130.3, 131.0, 131.4, 138.5, 142.0, 158.3, 159.2, 202.4; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{21}\text{O}_3$ $[\text{M} + \text{H}]^+$ 285.1491, found 285.1490.

1-(2-(3,4,5-Trimethoxyphenethyl)phenyl)ethanone (3ao): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 1,2,3-trimethoxy-5-vinylbenzene (**2o**, 87.4 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 10/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow oil (86 mg, 91%). The l/b ratio was determined to be 92/8 by ^1H NMR integrations of characteristic signals at 2.53 and 2.43 ppm.

R_f 0.15 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.53 (s, 3H), 2.80-2.84 (m, 2H), 3.14-3.17 (m, 2H), 3.83 (s, 9H), 6.41 (s, 2H), 7.23 (d, $J = 7.6$ Hz, 1H), 7.28 (t, $J = 7.5$ Hz, 1H), 7.39 (t, $J = 7.4$ Hz, 1H), 7.68 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.5, 36.2, 38.5, 55.9, 60.7, 105.5, 125.9, 129.2, 131.4, 131.5, 136.0, 137.6, 137.7, 141.7, 152.9, 201.8; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{23}\text{O}_4$ $[\text{M} + \text{H}]^+$ 315.1596, found 315.1596.

1-(2-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)phenyl)ethanone (3ap): The typical procedure was applied to **1a** (68 mg, 0.30 mmol) and 5-vinylbenzo[d][1,3]dioxole (**2ap**, 67 mg, 0.45 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture the title compound and its branched isomer as a light yellow oil (68 mg, 84%). The l/b ratio was determined to be 98/2 by ^1H NMR integrations of characteristic signals at 2.56 and 2.42 ppm.

R_f 0.42 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 2.56 (s, 3H), 2.78-2.82 (m, 2H), 3.09-3.13 (m, 2H), 5.90 (s, 2H), 6.65-6.68 (m, 1H), 6.70-6.73 (m, 2H), 7.21-7.23 (m, 1H), 7.28 (td, $J = 7.6, 1.4$ Hz, 1H), 7.39 (td, $J = 7.5, 1.4$ Hz, 1H), 7.68 (dd, $J = 7.7, 1.3$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 29.6, 36.7, 37.8, 100.6, 108.0, 109.1, 121.3, 125.9, 129.3, 131.5, 131.5, 135.8, 137.6, 141.8, 145.6, 147.4, 201.7; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{17}\text{O}_3$ $[\text{M} + \text{H}]^+$ 269.1178, found 269.1181.

Deuterium-Labeling Experiments

The reaction of [D]₅-**1a** (69.1 mg, 0.3 mmol) and 1-methoxy-4-vinylbenzene (41 μ L, 0.3 mmol) was performed under different conditions in Table 2 for 6 h. The reaction was quenched with water (1 mL), and extracted with EtOAc (10 $\times$ 2 mL). The solvent was removed under reduced pressure. The yield was determined using 1,1,2,2-tetrachloroethane as the internal standard. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 20/1/1) afforded the unreacted ketimine, the unreacted 1-methoxy-4-vinylbenzene, and the hydroarylation products. Each of them was analyzed by ¹H NMR to determine the distribution of the deuterium atoms.

Transformations of Hydroarylation Products

2-(4-(*tert*-Butyl)phenethyl)benzamide (5ac**):** The reaction was performed according to the procedure reported by Jiao and coworkers.¹¹ In a Schlenk tube equipped with a stirrer bar were placed 1-(2-(4-(*tert*-butyl)phenethyl)phenyl)ethanone (**3ac**, 112 mg, 0.40 mmol), NaN_3 (75.6 mg, 1.2 mmol), CuCl_2 (5.4 mg, 0.040 mmol), and TEMPO (12.8 mg, 0.080 mmol). To the mixture was added H_2O (216 μL , 12 mmol) and anhydrous DMF (2.0 mL). The resulting solution was heated at 120 °C for 12 h with vigorous stirring under O_2 (1 atm). After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with brine (20 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/1) to afford the title compound as a light yellow solid (79 mg, 70%).

M.p. 124-125 °C; R_f 0.3 (hexane/EtOAc = 1/1); ^1H NMR (400 MHz, CDCl_3): δ 1.29 (s, 9H), 2.89-2.93 (m, 2H), 3.08-3.12 (m, 2H), 5.51 (s, 1H), 6.12 (s, 1H), 7.09 (d, J = 8.1 Hz, 2H), 7.21 (dd, J = 13.6, 6.1 Hz, 1H), 7.27 (d, J = 8.0 Hz, 3H), 7.36 (dd, J = 13.6, 7.5 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 31.4, 34.3, 35.3, 37.5, 125.1, 125.9, 126.9, 128.3, 130.2, 130.3, 135.5, 138.6, 140.0, 148.8, 172.4; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{24}\text{NO}$ [$\text{M} + \text{H}$]⁺ 282.1858, found 282.1855.

2-(4-(*tert*-Butyl)phenethyl)benzaldehyde (6ac**):** The reaction was performed according to the procedure reported by Bi, Liu and coworkers.¹² In a Schlenk tube equipped with a stirrer bar were placed **3ac** (140 mg, 0.50 mmol), CuI (28.6 mg, 0.15 mmol), and DMSO (1.5 mL). The resulting solution was heated at 120 °C for 12 h with vigorous stirring under O₂ (1 atm). After cooling to room temperature, the reaction mixture was diluted with CH₂Cl₂ (50 mL) and washed with water (20 mL x 3). The organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: CH₂Cl₂/hexane = 1/2) to afford the title compound as a light yellow oil (71 mg, 54%).

R_f 0.36 (hexane/DCM = 1/1); ¹H NMR (400 MHz, CDCl₃): δ 1.32 (s, 9H), 2.85-2.89 (m, 2H), 3.30-3.34 (m, 2H), 7.14-7.17 (m, 2H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.30-7.33 (m, 2H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.50 (td, *J* = 7.5, 1.5 Hz, 1H), 7.83 (dd, *J* = 7.7, 1.5 Hz, 1H), 10.22 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 31.4, 34.4, 34.8, 37.8, 125.3, 126.6, 128.1, 131.1, 132.1, 133.75, 133.80, 138.2, 144.6, 149.0, 192.2; HRMS (ESI) Calcd for C₁₉H₂₃O [M + H]⁺ 267.1749, found 267.1740.

2-(4-Methylphenethyl)benzoic acid (7ab**):** The reaction was performed according to the procedure reported by Ishii and coworkers.¹³ In a Schlenk tube equipped with a stirrer bar were placed 1-(2-(4-methylphenethyl)phenyl)ethanone (**3ab**, 120 mg, 0.50 mmol),

Mn(OAc)₃•4H₂O (1.3 mg, 0.005 mmol), and AcOH (1 mL). The resulting mixture was heated at 100 °C under O₂ for 15 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc/hexane/AcOH = 1/10/1) to afford the title compound as a light yellow solid (82 mg, 68%).

M.p. 78-79 °C; *R_f* 0.30 (EtOAc/hexane/AcOH = 1/5/1); ¹H NMR (400 MHz, CDCl₃): δ 2.31 (s, 3H), 2.89-2.93 (m, 2H), 3.30-3.34 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.30 (td, *J* = 7.7, 1.1 Hz, 1H), 7.46 (td, *J* = 7.6, 1.4 Hz, 1H), 8.10 (dd, *J* = 7.9, 1.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.0, 37.2, 37.7, 126.2, 128.1, 128.4, 129.0, 131.5, 131.8, 133.0, 135.3, 138.8, 144.9, 173.5; HRMS (ESI) Calcd for C₁₆H₁₇O₂ [M + H]⁺ 241.1229, found 241.1230.

2-(4-Fluorophenethyl)benzoic acid (7af): The reaction of 1-(2-(4-fluorophenethyl)phenyl)ethanone (**3af**, 122 mg, 0.50 mmol) was performed by the same procedure as described above. Silica gel chromatography (EtOAc/hexane/AcOH = 1/10/1) of the crude product afforded the title compound as a light yellow solid (78 mg, 64%).

M.p. 126-127 °C; *R_f* 0.32 (EtOAc:hexane:AcOH = 1:5:1); ¹H NMR (400 MHz, CDCl₃): δ 2.88-2.92 (m, 2H), 3.28-3.32 (m, 2H), 6.91-6.95 (m, 2H), 7.13-7.16 (m, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.29-7.33 (m, 1H), 7.46 (td, *J* = 7.5, 1.3 Hz, 1H), 8.09 (dd, *J* = 7.8, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 37.2 (two signals overlapped), 115.0 (d, ²*J*_{C-F} = 21.1 Hz), 126.3, 128.0, 129.9 (d, ³*J*_{C-F} = 7.8 Hz), 131.5, 131.9, 133.1, 137.5, 144.5, 161.3 (d, ¹*J*_{C-F} = 243.4 Hz), 173.1; HRMS (ESI) Calcd for C₁₅H₁₄FO₂ [M + H]⁺ 245.0978, found

245.0976.

3-Methyl-10,11-dihydro-5H-dibenzo[*a,d*][7]annulen-5-one (8ab): A mixture of 2-(4-methylphenethyl)benzoic acid (**7ab**, 70 mg, 0.29 mmol) and polyphosphoric acid (2 mL) was heated at 155 °C with vigorous stirring for 15 h. After cooling to room temperature, the reaction mixture was directly subjected to purification by column chromatography on silica gel (eluent: EtOAc/hexane = 1/20) to afford the title compound as a light brown oil (57 mg, 90%).

R_f 0.43 (hexane/EtOAc = 5:1); ^1H NMR (400 MHz, CDCl_3): δ 2.37 (s, 3H), 3.11-3.20 (m, 4H), 7.11 (d, J = 7.7 Hz, 1H), 7.20-7.25 (m, 2H), 7.31 (td, J = 7.7, 1.2 Hz, 1H), 7.42 (td, J = 7.4, 1.4 Hz, 1H), 7.82 (d, J = 1.1 Hz, 1H), 7.98 (dd, J = 7.9, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 20.8, 34.5, 35.0, 126.6, 129.2, 129.4, 130.4, 130.8, 132.2, 133.2, 136.2, 138.3, 138.8, 139.1, 141.9, 195.9; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{15}\text{O}$ $[\text{M} + \text{H}]^+$ 223.1123, found 223.1124.

3-Fluoro-10,11-dihydro-5H-dibenzo[*a,d*][7]annulen-5-one (8af): The reaction of 2-(4-fluorophenethyl)benzoic acid (**7af**, 60 mg, 0.25 mmol) was performed by the same procedure as described above. Silica gel chromatography (eluent: EtOAc/hexane = 1/20) of the crude product afforded the title compound as a light brown oil (48 mg, 85%).

R_f 0.44 (hexane/ EtOAc = 5:1); ^1H NMR (400 MHz, CDCl_3): δ 3.19 (s, 4H), 7.10-7.15 (m,

1H), 7.19-7.26 (m, 2H), 7.32-7.36 (m, 1H), 7.45 (td, $J = 7.5, 1.4$ Hz, 1H), 7.73 (dd, $J = 9.9, 2.8$ Hz, 1H), 8.00 (dd, $J = 7.9, 1.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 34.2, 35.0, 117.0 (d, $^2J_{\text{C-F}} = 23.1$ Hz), 119.3 (d, $^2J_{\text{C-F}} = 21.6$ Hz), 126.8, 129.3, 130.8, 131.2 (d, $^3J_{\text{C-F}} = 7.3$ Hz), 132.7, 137.9, 137.9 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 140.0 (d, $^3J_{\text{C-F}} = 6.2$ Hz), 142.0, 161.5 (d, $^1J_{\text{C-F}} = 245.2$ Hz), 193.9; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{12}\text{FO}$ $[\text{M} + \text{H}]^+$ 227.0872, found 227.0870.

2.5 References

- ¹ Recent Reviews: a) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2011**, *45*, 814-825; b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev. (Washington, DC, U. S.)* **2012**, *112*, 5879-5918; c) Zhu, C.; Wang, R.; Falck, J. R. *Chem. Asian J.* **2012**, *7*, 1502-1514; d) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009.
- ² Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529-531.
- ³ For examples of linear-selective addition, see: a) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62-83; b) Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc. Perkin Trans. 1* **1996**, 2201-2206; c) Matsumoto, T.; Periana, R. A.; Taube, D. J.; Yoshida, H. *J. Mol. Catal. A* **2002**, *180*, 1-18; d) Jun, C.-H.; Moon, C. W.; Hong, J.-B.; Lim, S.-G.; Chung, K.-Y.; Kim, Y.-H. *Chem. Eur. J.* **2002**, *8*, 485-492; e) Tan, K. L.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 13964-13965; f) Martinez, R.; Genet, J.-P.; Darses, S. *Chem. Commun.* **2008**, 3855-3857; g) Martinez, R.; Simon, M.-O.; Chevalier, R.; Pautigny, C.; Genet, J.-P.; Darses, S. *J. Am. Chem. Soc.* **2009**, *131*, 7887-7895; h) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939-3942; i) Ilies, L.; Chen, Q.;

Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221-5223. j) Schinkel, M.; Marek, I.; Ackermann, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 3977-3980; *Angew. Chem.* **2013**, *125*, 4069-4072; k) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 5410-5413; *Angew. Chem.* **2014**, *126*, 5514-5517.

⁴ For examples of branched-selective addition, see: a) Uchimaru, Y.; *Chem. Commun.* **1999**, 1133-1134; b) Nakao, Y.; Kashiwara, N.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 16170-16171; c) Mukai, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 6410-6413; d) Nakao, Y.; Kashiwara, N.; Kanyiva, K. S.; Hiyama, T. *Angew. Chem.* **2010**, *122*, 4553-4556; *Angew. Chem. Int. Ed.* **2010**, *49*, 4451-4454; e) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258-10261; f) Crisenza, G. E. M.; Sokolova, O. O.; Bower, J. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 14866-14870; *Angew. Chem.* **2015**, *127*, 15079-15083; g) Ebe, Y.; Nishimura, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899-5902; h) Hatano, M.; Ebe, Y.; Nishimura, T.; Yorimitsu, H. *J. Am. Chem. Soc.* **2016**, *138*, 4010-4013.

⁵ a) Shih, W.-C.; Chen, W.-C.; Lai, Y.-C.; Yu, M.-S.; Ho, J.-J.; Yap, G. P. A.; Ong, T.-G. *Org. Lett.* **2012**, *14*, 2046-2049; b) Lee, W.-C.; Wang, C.-H.; Lin, Y.-H.; Shih, W.-C.; Ong, T.-G.; *Org. Lett.* **2013**, *15*, 5358-5361; c) Pan, S.; Ryu, N.; Shibata, T. *J. Am. Chem. Soc.* **2012**, *134*, 17474-17477.

⁶ a) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2010**, *133*, 400-402; b) Lee, P.-S.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 1240-1244; c) Dong, J.; Lee, P.-S.; Yoshikai, N. *Chem. Lett.* **2013**, *42*, 1140-1142.

⁷ Trost, B. M.; Czabaniuk, L. C. *Angew. Chem.* **2014**, *126*, 2868-2895; *Angew. Chem. Int. Ed.* **2014**, *53*, 2826-2851.

⁸ Yang, Z.; Yu, H.; Fu, Y. *Chem. Eur. J.* **2013**, *19*, 12093-12103.

⁹ Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208-1219.

- ¹⁰ a) Song, W.; Ackermann, L. *Angew. Chem.* **2012**, *124*, 8376-8379; *Angew. Chem. Int. Ed.* **2012**, *51*, 8251-8254; b) Punji, B.; Song, W.; Shevchenko, G. A.; Ackermann, L. *Chem. Eur. J.* **2013**, *19*, 10605-10610.
- ¹¹ Tang, C.; Jiao, N. *Angew. Chem.* **2014**, *126*, 6646-6650; *Angew. Chem. Int. Ed.* **2014**, *53*, 6528-6532.
- ¹² Zhang, L.; Bi, X.; Guan, X.; Li, X.; Liu, Q.; Barry, B.-D.; Liao, P. *Angew. Chem.* **2013**, *125*, 11513-11517; *Angew. Chem. Int. Ed.* **2013**, *52*, 11303-11307.
- ¹³ Nakamura, R.; Obora, Y.; Ishii, Y. *Adv. Synth. Catal.* **2009**, *351*, 1677.
- ¹⁴ (a) Mršić, N.; Minnaard, A. J.; Feringa, B. L.; Vries, J. G. d. *J. Am. Chem. Soc.* **2009**, *131*, 8358-8359; (b) Gautier, F. -M.; Jones, S.; Martin, S. J. *Org. Biomol. Chem.* **2009**, *7*, 229-231.
- ¹⁵ Samec, J. S. M.; Ell, A. H.; Bäckvall, J.-E. *Chem. Eur. J.* **2005**, *11*, 2327-2334.
- ¹⁶ Kutlescha, K.; Venkanna, G. T.; Kempe, R. *Chem. Commun.* **2011**, *47*, 4183-4185.
- ¹⁷ Gao, K.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 6888-6892.
- ¹⁸ Imamoto, T.; Iwadate, N.; Yoshida, K. *Org. Lett.* **2006**, *8*, 2289-2292.
- ¹⁹ Moessner, C.; Bolm, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 7564-7567.
- ²⁰ Yoshikai, N.; Matsumoto, A.; Norinder, J.; Nakamura, E. *Angew. Chem. Int. Ed.* **2009**, *48*, 2925-2928.
- ²¹ Zhou, X.; Bao, M.; Zhou, Y. *Adv. Synth. Catal.* **2011**, *353*, 84-88.
- ²² Tobisu, M.; Yamaguchi, S.; Chatani, N. *Org. Lett.* **2007**, *9*, 3351-3353.
- ²³ Gao, K.; Lee, P. -S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234-4237.
- ²⁴ Lee, P. -S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 17283-17295.
- ²⁵ Faler, C. A.; Joullie, M. *Org. Lett.* **2007**, *9*, 1987-1990.
- ²⁶ Qin, Y.; Cheng, G.; Sundararaman, A.; Jäkle, F. *J. Am. Chem. Soc.* **2002**, *124*, 12672-12673.

- ²⁷ Yamamoto, T.; Yamakawa, T. *J. Org. Chem.* **2009**, *74*, 3603-3605.
- ²⁸ Su, W.; Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2004**, *6*, 1421-1424.
- ²⁹ Zhao, L.-J.; Kwong, C. K.-W.; Shi, M.; Toy, P. H. *Tetrahedron* **2005**, *61*, 12026-12032.
- ³⁰ Faler, C. A.; Joullié, M. M. *Org. Lett.* **2007**, *9*, 1987-1990.
- ³¹ Aitken, R. A.; Burns, G. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2455-2460.
- ³² Horner, L.; Simons, G. *Phosphorous and Sulfur and the Related Elements* **1983**, *15*, 165-169.
- ³³ Muller, A.; Otto, S.; Roodt, A. *Dalton Trans.* **2008**, 650-657.
- ³⁴ Ivanov, V. V.; Yurchenko, A. A.; Chernega, A. N.; Pinchuk, A. M.; Tolmachev, A. A. *Heteroatom Chem.* **2002**, *13*, 84-92.
- ³⁵ Cairns, S. M.; McEwen, W. E. *Heteroatom Chem.* **1990**, *1*, 9-19.
- ³⁶ Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62-83.

Chapter 3. Cobalt-Catalyzed, Imine-Directed Olefin Hydroarylation under Grignard-Free Conditions

3.1 Introduction

Regioselective alkylation of arenes is among the most important transformation in organic chemistry. Besides conventional alkylation reactions such as the cross-coupling between aryl (or alkyl) halides and alkyl (or aryl) metal reagents and the Friedel-Crafts alkylation, the transition metal-catalyzed addition of arenes to alkenes (hydroarylation) through chelation-assisted C–H bond activation has drawn increasing attention as a step-economical approach for the regioselective arene alkylation reaction.¹ Following the seminal work of Lewis and Smith on ruthenium-catalyzed ortho-ethylation of phenol with ethylene² and the ground-breaking discovery of ruthenium-catalyzed ortho-alkylation of aryl ketones with olefins by Murai and co-workers,³ various late transition metals such as ruthenium,⁴ rhodium,⁵ rhenium,⁶ iridium,⁷ cobalt,⁸ and iron⁹ have been exploited to develop olefin hydroarylation reactions directed by oxygen- and nitrogen-based functional groups. In this context, our group has developed a series of cobalt-based catalytic systems for the hydroarylation of olefins with sp² nitrogen directing groups.^{10,11} For example, cobalt catalysts generated in situ from cobalt(II) salts, triarylphosphine ligands, and Grignard reagents promote the addition of aryl N–PMP ketimines or aldimines to styrene to regioselectively afford 1,1-diarylethane derivatives (Scheme 3.1a, b),^{8d, e} which represent notable examples of branched-selective hydroarylation.^{4b, 7b, d-f, 12} Aryl ketimines can also participate in the addition reaction to vinylsilane under a related catalytic system employing 1,10-phenanthroline as the supporting ligand (scheme 3.1c).^{8c}

Scheme 3.1. Cobalt-catalyzed N–PMP imine-directed hydroarylation of olefins

For all the catalytic systems shown in Scheme 3.1, Grignard reagents, such as *t*-BuCH₂MgBr and Me₃SiCH₂MgBr are used in substoichiometric quantity in order to reduce the cobalt(II) precatalysts, which significantly reduces the practicality and the functional group compatibility of the cobalt-catalyzed hydroarylation reactions. To solve this problem, the use of a more convenient reductant is apparently desired. Then the question is what kind of reductant is able to function as an alternative to Grignard reagent to generate catalytically active cobalt species. Based on our previous study on the imine-directed hydroarylation reaction of alkynes, alkyl Grignard reagents such as *t*-BuCH₂MgBr are assumed to reduce cobalt(II) salts to catalytically active Co(0) species.¹³ On the other hand, Mg metal has been known to be used as a reductant for the preparation a Co(0) complex such as Co(PMe₃)₄.¹⁴ Moreover, a recent work of Petit and co-workers demonstrated the competence of Co(PMe₃)₄ as a catalyst for the imine-directed hydroarylation of alkynes.¹⁵

Based on these empirical observations and literature knowledge, we envisioned that magnesium metal could be used as an alternative to Grignard reagents to generate a catalytically active cobalt species for the olefin hydroarylation. In this chapter, we report on the development of modified cobalt-based catalytic systems employing Mg metal as the reductant, which allowed us to achieve all the hydroarylation reactions shown in Scheme 3.1.

3.2 Results and Discussion

We initially explored the addition of acetophenone imine (**1a**) to styrene (**2a**), which was previously achieved with a catalytic system consisting of CoBr₂, P(4-FC₆H₄)₃, and CyMgBr at room temperature (Table 3.1). In the presence of CoBr₂ (10 mol%), P(4-FC₆H₄)₃ (20 mol%), and flamed-dried Mg turning (50 mol%), the reaction proceeded at 100 °C to afford the branched hydroarylation product **3** of styrene in a moderate yield of 56% (entry 1). Upon heating, the color of the reaction mixture turned dark brown in 5 min, which indicated that the cobalt pre-catalyst was reduced at the high temperature. The use of catalytic systems employing other triarylphosphine ligands, such as P(4-MeOC₆H₄)₃ and P(4-MeC₆H₄)₃ resulted in comparable yields (ca. 50%) and regioselectivities (entries 2 and 3), while a sterically hindered triarylphosphine ligand, P(2-MeOC₆H₄)₃, significantly retarded the reaction and exhibited moderate linear selectivity (entry 4). The use of PCy₃ gave a lower yield (35%) than that obtained with P(4-FC₆H₄)₃ (entry 5). A bi-dentate phosphine ligand performed very poorly to afford only a trace amount of the desired product (entry 6), while no reaction was observed under ligand-free conditions (entry 7).

Despite the moderate yields of the desired hydroarylation product achieved with the triarylphosphine ligands, we observed full conversion of the ketamine for the initial

screening experiments in THF. In fact, a nonnegligible amount of **3** was found to be reduced under such conditions, affording the corresponding amine (ca. 20%) as the byproduct. To our delight, the use of Et₂O as the solvent completely suppressed the reduction and further improved the yield to 81% (entry 8). Cyclopentylmethylether (CPME) also inhibited the reduction albeit without significantly improvement of the yield (60 %) (entry 9). The reaction in Et₂O was further improved by lowering the reaction temperature to 80 °C, affording **3** in a near quantitative (95%) yield (entry 10). A slightly lower yield (90%) was observed by reducing the loading of CoBr₂ and P(4-FC₆H₄)₃ to 5 mol% and 10 mol%, respectively (entry 11). A comparably yield was achieved using Bu₂O as a more practical and safer solvent instead of Et₂O (entry 12). Cobalt precatalysts were also found to be important for the catalytic efficiency. Diminished yields (ca. 20%) were obtained with CoCl₂ and CoI₂, while we did not observe the precatalyst reduction process using Co(OAc)₂ and Co(acac)₂. For unknown reasons, Reike Mg, failed to promote the present reaction.

Table 3.1. Addition of aryl imine **1a** to styrene **2a** using Mg as a reductant.^a

entry	Ligand	solvent	yield% (b/l) ^b
1	P(4-FC ₆ H ₄) ₃	THF	56 (>99/1)
2	P(4-MeOC ₆ H ₄) ₃	THF	55 (>99/1)
3	P(3-MeC ₆ H ₄) ₃	THF	52 (>99/1)
4	P(2-MeOC ₆ H ₄) ₃	THF	8 (45/55)
5	PCy ₃	THF	35 (>99/1)
6	dppp	THF	3 (>99/1)
7	none	THF	0
8	P(4-FC ₆ H ₄) ₃	Et ₂ O	81 (>99/1)
9	P(4-FC ₆ H ₄) ₃	CPME	60 (>99/1)
10 ^c	P(4-FC ₆ H ₄) ₃	Et ₂ O	95 (>99/1)
11 ^d	P(4-FC ₆ H ₄) ₃	Et ₂ O	90 (>99/1)
12 ^c	P(4-FC ₆ H ₄) ₃	Bu ₂ O	91 (>99/1)

^a The reaction was performed using **1a** (0.2 mmol) and **2a** (0.3 mmol). Determined by ¹H-NMR with 1,1,2,2-tetrachloroethane as the internal standard. ^b Yield and branched/linear (b/l) selectivity were determined by GC. ^c The reaction temperature was 80 °C. ^d CoBr₂ (5 mol%) and P(4-FC₆H₄)₃ (10 mol%) were used.

With the optimized reaction condition in hand, we explored the scope of ketimines and styrene derivatives (Table 3.2). Ketimines derived from *para*-phenyl and fluoroacetophenones afforded the branched adducts (**4b** and **4c**) in good yields. However, the reaction of the *para*-methoxy-substituted ketimine was sluggish and gave the adduct **4d** in a moderate yield of 50 %. For imines bearing *meta*-fluoro and 3,4-methylenedioxy groups, the alkylation took place at the proximal position of these groups in good yields (**4e** and **4f**) presumably due to the secondary directing effects of the fluorine and oxygen atoms. The

reactions of styrene derivatives substituted by *para*-methoxy, fluoro, boryl, silyl, and *meta*-methyl groups with **1a** took place smoothly to give the alkylation products **4g-4k** in good yields with excellent regioselectivity. Somewhat unexpectedly, the present catalytic system failed to promote the reaction of imines or styrenes bearing Grignard reagent-sensitive functional groups such as ester and cyano groups, although these functional groups were not affected.

Table 3.2. Addition of aryl ketimines to styrenes.^a

^a The reaction was performed using 0.3 mmol of ketimine and 0.45 mmol of styrene. The b/l ratio was greater than 99/1 unless otherwise indicated in the parentheses. ^b THF was used as the solvent.

Having demonstrated the feasibility of the styrene hydroarylation using aryl ketimines, we moved to examine the aldimine-directed styrene hydroarylation with Mg as the reductant. Without significant modification of the original reaction conditions (Scheme

3.1b), the addition of aldimine derived from 1-naphthaldehyde to styrene was achieved using magnesium instead of $\text{Me}_3\text{SiCH}_2\text{MgCl}$ at 80 °C, affording the adduct **6a** in 77% yield with exclusive branched selectivity (Table 3.3). Interestingly, no reduction of aldimine was observed, while ketimine-directed styrene hydroarylation was accompanied by reduction when performed in THF (via *supra*). Et_2O proved to be a much less effective solvent because of the poor solubility of the aldimine. Using this catalytic system, aldimines derived from *ortho*-methyl and phenyl benzaldehydes participated in the reaction with styrene, to afford the desired products, **6b** and **6c**, respectively, in good yields (Table 3.3). For *meta*-methyl substituted aldimines, the alkylation occurred at the less hindered position (see **6d**). The reaction of parent benzaldimine with excess styrene (3 equiv.) afforded the dialkylation product, **6e**, in a moderate yield. The C3-iminoindole substrate underwent C2-alkylation in a moderate yield (see **6f**). A variety of styrenes bearing *para*-, *meta*-, or *ortho*-substituents could also be employed as substrates for the present aldimine-directed hydroarylation (see **6g-6l**).

Table 3.3. Addition of aryl aldimines to styrenes.^a

^a The reaction was performed using 0.3 mmol of aldimine and 0.45 mmol of styrene. ^b

Styrene (3 equiv) was used. ^c $\text{P(4-FC}_6\text{H}_4)_3$ was used instead of $\text{P(4-MeC}_6\text{H}_4)_3$

As last, we extended the Mg-based method of catalyst generation to ketimine-directed vinylsilane hydroarylation. On the basis of the previously developed catalytic system (Scheme 3.1c), we were able to achieve the addition of 4-phenylacetophenone imine to vinyltrimethylsilane using a catalytic system comprising CoBr₂ (10 mol%), 1,10-phenanthroline (10 mol%), and Mg (50 mol%) in THF at 80 °C, which afforded the linear-selective hydroarylation product **8a** in 65% yield (Table 3.4). No desired product was observed in Et₂O as the solvent presumably because of the low solubility of the cobalt-phenanthroline complexes. The ketimines bearing *para*-methoxy and fluoro-substituents afforded the desired product **8b** and **8c**, respectively although the latter product was obtained as a mixture with a non-negligible amount of hydrodefluorination product. Again, the secondary directing effect of a 3,4-methelenedioxy group led to the regioselective alkylation at the proximal position (see **8d**). Rather unexpectedly, ketimines derived from *meta*-methylacetophenone and 2-acetonaphthone both afforded a mixture of regioisomers with only moderate regioselectivity, slightly favoring alkylation at the more hindered position (see **8e'** and **8f'**). These result are in stark contrast to the reaction of the same substrates under the original catalytic system, where exclusive alkylation of the less hindered position was observed. This regioselective difference may imply a difference in the electronic nature of catalytically active species generated under the Mg-based and the Grignard-based systems.

Table 3.4. Addition of aryl ketimines to vinylsilane.^a

^a The reaction was performed using 0.3 mmol of ketimine and 0.45 mmol of vinylsilane. ^b The product was obtained as a mixture (2:1) with an *ortho*-alkylation/defluorination product (overall yield is shown).

3.3 Conclusion

In summary, we have demonstrated that Mg can be used as a reductant instead of Grignard reagents to achieve cobalt-catalyzed, imine-directed hydroarylation reactions of alkenes. Through slight modification of the original conditions, i.e. temperature, solvent, and catalyst loading, the ketamine- and aldimine-directed styrene hydroarylation as well as

ketamine-directed vinylsilane hydroarylation have been achieved albeit with narrower substrate scopes. The higher temperature required for the present catalytic systems would be essential for the reduction of the cobalt precatalysts under heterogeneous conditions, and would also imply the lower reactivity of the catalytically active species. Observations such as C=N bond reduction and different regioselectivities also underscore the difference between the Mg-based and Grignard-based catalytic systems.

3.4 Experimental Section

Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. THF and Et₂O were distilled over Na/benzophenone. Anhydrous CoBr₂ (> 98%) was purchased from Alfa Aesar and used as received. Mg turnings (98%) were purchased from Sigma Aldrich and used as received.

Preparation of Starting Materials

Preparation of Aryl Imines

All imines shown below were synthesized according to the literature procedures,¹⁶ and purified by recrystallization or distillation. Their ¹H and ¹³C-NMR spectra showed good agreement with the literature data.¹⁷

Preparation of Styrene Derivatives

Among the following styrene derivatives, **2d**, **2e**, **2g**, and **2h** were prepared using Wittig reaction on the corresponding aryl aldehydes according to the literature procedure.¹⁸ Their ¹H and ¹³C NMR spectra showed good agreement with the literature data.¹⁹

Cobalt-Catalyzed Addition of Aryl Ketimines to Styrenes

Typical Procedure: In a Schlenk tube were placed Mg turning (3.6 mg, 0.15 mmol) and CoBr_2 (6.7 mg, 0.030 mmol). The solids were heated using a heat gun at around 300 °C under vacuum for 5 min. After cooling down under nitrogen atmosphere, $\text{P}(\text{4-FC}_6\text{H}_4)_3$ (19.2 mg, 0.060 mmol) and THF (0.20 mL) were added. The resulting mixture was heated at 80 °C for 5 min, during which the color of the mixture turned dark brown. The mixture was cooled to room temperature and THF was removed under reduced pressure. To the residue were added (*E*)-*N*-(4-methoxyphenyl)-1-phenylethan-1-imine (**1a**, 68 mg, 0.30 mmol), styrene (**2a**, 53 μL , 0.45 mmol), and Et_2O (0.75 mL), and then the resulting mixture was stirred at 80 °C for 12 h. The reaction mixture was allowed to cool to room temperature and filtered through a short pad of silica gel. The filtrate was hydrolyzed using 3N HCl (1.0 mL) for 1 h, and then extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified on silica gel (eluent: hexane/EtOAc = 20/1) to afford 1-(2-(1-phenylethyl)phenyl)ethanone (**4a**) (59 mg, 87% yield).

^1H and ^{13}C NMR spectra of the following known compounds showed good agreement with the literature data.^{8c}

1-(2-(1-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)phenyl)ethan-1-one (4i): The typical procedure was applied to (E)-4-methoxy-N-(1-phenylethylidene)aniline (68 mg, 0.3 mmol), and 4,4,5,5-tetramethyl-2-(4-vinylphenyl)-1,3,2-dioxaborolane (104 mg, 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow solid (93 mg, 89%).

M.p = 101-102 °C; R_f 0.21 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 7.71 (d, J = 8.2 Hz, 2H), 7.49 (dd, J = 7.7, 1.1 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.31 (dd, J = 7.9, 1.3 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.18 (d, J = 7.7 Hz, 2H), 4.91 (q, J = 7.2 Hz, 1H), 2.39 (s, 3H), 1.61 (d, J = 7.2 Hz, 3H), 1.33 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.9, 149.7, 145.2, 139.4, 135.0, 131.2, 128.7, 128.0, 127.7, 126.0, 83.9, 39.9, 30.6, 25.1, 22.1. HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_3\text{B}$ $[\text{M} + \text{H}]^+$ 351.2132, found 351.2142.

Cobalt-Catalyzed Addition of Aryl Aldimines to Styrenes

Typical Procedure: In a Schlenk tube were placed Mg turning (3.6 mg, 0.15 mmol) and CoBr_2 (6.7 mg, 0.030 mmol). The solids were heated using a heat gun at around 300 °C under vacuum for 5 min. After cooling down under nitrogen atmosphere, $\text{P}(\text{4-MeC}_6\text{H}_4)_3$ (19 mg, 0.06 mmol), (E)-N-(4-methoxyphenyl)-1-(naphthalene-1-yl)methanimine (78 mg,

0.30 mmol), styrene (53 μ L, 0.45 mmol) and THF (0.75 mL) were added. The resulting mixture was heated at 80 $^{\circ}$ C for 12 h. The reaction mixture was allowed to cool to room temperature and filtered through a short pad of silica gel. The filtrate was hydrolyzed using 3N HCl (1.0 mL) for 1 h, and then extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified on silica gel (eluent: hexane/EtOAc = 20/1) to afford 2-(1-phenylethyl)-1-naphthaldehyde (**6a**) (60 mg, 77% yield).

^1H and ^{13}C NMR spectra of the following known compounds showed good agreement with the literature data.^{8d}

5-Methyl-2-(1-phenylethyl)benzaldehyde (6d): The typical procedure was applied to (E)-N-(3-methylbenzylidene)-4-methoxyaniline (69 mg, 0.30 mmol) and styrene (53 μ L, 0.45

mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow oil (52 mg, 76%).

R_f 0.45 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 10.28 (s, 1H), 7.63 (s, 1H), 7.36 – 7.33 (m, 1H), 7.29 – 7.24 (m, 3H), 7.20 – 7.15 (m, 3H), 5.18 (q, J = 7.1 Hz, 1H), 2.38 (s, 3H), 1.65 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 192.8, 146.1, 146.0, 136.6, 135.0, 133.39, 132.42, 128.7, 128.6, 128.0, 126.4, 38.8, 22.5, 21.0; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{14}\text{O}$ $[\text{M} + \text{H}]^+$ 224.1201, found 224.1203.

2-(1-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)-1-

naphthaldehyde (6h): The typical procedure was applied to (*E*)-4-methoxy-*N*-(naphthalene-1-ylmethylene)aniline (78 mg, 0.30 mmol) and 4,4,5,5-tetramethyl-2-(4-vinylphenyl)-1,3,2-dioxaborolane (104 mg, 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow solid (84 mg, 73%).

M.p = 140-141 °C; R_f 0.20 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 11.1 (s, 1H), 8.77 (d, J = 8.7 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.4 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.52 – 7.48 (m, 1H), 7.34 (d, J = 8.7 Hz, 1H), 7.26 (d, J = 7.6 Hz, 2H), 5.20 (q, J = 7.1 Hz, 1H), 1.76 (d, J = 7.1 Hz, 3H), 1.32 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3): δ 194.2, 149.2, 148.4, 135.3, 134.3, 132.4, 131.4, 129.0, 128.8, 128.6, 127.5, 126.5, 126.1, 124.7, 83.9, 39.4, 25.09, 25.07, 22.0. HRMS (ESI) Calcd for $\text{C}_{25}\text{H}_{28}\text{O}_3\text{B}$ $[\text{M} + \text{H}]^+$ 387.2132, found 387.2140.

2-(1-(m-Tolyl)ethyl)-1-naphthaldehyde (6j): The typical procedure was applied to (*E*)-4-methoxy-*N*-(naphthalene-1-ylmethylene)aniline (78 mg, 0.30 mmol) and 1-methyl-3-vinylbenzene (59 μ L, 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow oil (57 mg, 69%).

*R*_f 0.54 (hexane/EtOAc = 5/1); ¹H NMR (400 MHz, CDCl₃): δ 11.09 (s, 1H), 8.84 – 8.81 (m, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.65 – 7.60 (m, 1H), 7.55 – 7.51 (m, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.09 – 7.03 (m, 3H), 5.17 (q, *J* = 7.2 Hz, 1H), 2.32 (s, 3H), 1.77 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 194.3, 149.6, 145.1, 138.4, 134.3, 132.4, 131.3, 128.9, 128.85, 128.77, 128.7, 128.6, 127.4, 126.4, 126.1, 125.0, 124.8, 39.2, 22.2, 21.7. HRMS (ESI) Calcd for C₂₀H₁₉O [M + H]⁺ 275.1436, found 275.1433.

2-(1-(2,4-Dimethoxyphenyl)ethyl)-1-naphthaldehyde (6l): The typical procedure was applied to (*E*)-4 methoxy-*N*-(naphthalene-1-ylmethylene)aniline (78 mg, 0.30 mmol) and 2,4-dimethoxy-1-vinylbenzene (74 mg, 0.45 mmol) for 12 h. Silica gel chromatography

(eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow oil (62 mg, 65%).

R_f 0.27 (hexane/EtOAc = 5/1); ^1H NMR (400 MHz, CDCl_3): δ 11.11 (s, 1H), 8.88 (d, J = 8.7 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.58 (dd, J = 8.6, 6.9, 1H), 7.47 (dd, J = 8.1, 6.9 Hz, 1H), 7.36 (d, J = 8.7 Hz, 1H), 7.26 – 7.24 (m, 1H), 6.50 (dd, J = 8.4, 2.5 Hz, 1H), 6.37 (d, J = 2.5 Hz, 1H), 5.30 (q, J = 7.2 Hz, 1H), 3.78 (s, 3H), 3.63 (s, 3H), 1.67 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 194.9, 160.0, 157.9, 150.4, 133.9, 132.2, 130.9, 128.6, 128.4, 127.9, 126.2, 126.1, 125.5, 125.4, 104.2, 98.8, 55.6, 55.4, 32.5, 21.60. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3$ $[\text{M} + \text{H}]^+$ 321.1491, found 321.1494.

Cobalt-Catalyzed Addition of Aryl Ketimines to Vinylsilane

In a Schlenk tube were placed Mg turning (3.6 mg, 0.15 mmol) and CoBr_2 (6.7 mg, 0.030 mmol). The solids were heated using a heat gun at around 300 °C under vacuum for 5 min. After cooling down under nitrogen atmosphere, 1,10-phenanthroline (5.4 mg, 0.030 mmol), (*E*)-1-([1,1'-biphenyl]-4-yl)-*N*-(4-methoxyphenyl)ethan-1-imine (90 mg, 0.30 mmol), trimethylvinylsilane (67 μL , 0.45 mmol) and THF (0.75 mL) were added. The resulting mixture was heated at 80 °C for 12 h. The reaction mixture was allowed to cool to room temperature and filtered through a short pad of silica gel. The filtrate was hydrolyzed using 3N HCl (1.0 mL) for 1 h, and then extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified on silica gel (eluent: hexane/EtOAc = 30/1) to afford 1-(3-(2-(trimethylsilyl)ethyl)-[1,1'-biphenyl]-4-yl)ethan-1-one (**8a**) (58 mg, 65% yield).

^1H and ^{13}C NMR spectra of the following known compounds showed good agreement with the literature data.^{8c}

1-(4-Fluoro-2-(2-(trimethylsilyl)ethyl)phenyl)ethanone (8c): The typical procedure was applied to (*E*)-*N*-(1-(4-fluorophenyl)ethylidene)-4-methoxyaniline (73 mg, 0.30 mmol) and trimethyl(vinyl)silane (67 μL , 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 30/1) of the crude product afforded a 2:1 mixture of the title compound and its defluorination product as a light yellow oil (46 mg, 67%).

R_f 0.48 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.76 (dd, J = 8.6, 5.8 Hz, 1H), 7.06 (dd, J = 10.1, 2.6 Hz, 1H), 6.99 (td, J = 8.2, 2.6 Hz, 1H), 2.97 – 2.88 (m, 2H), 2.64 (s, 3H), 0.92 – 0.84 (m, 2H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 200.4, 164.6 (d, $^1J_{\text{C-F}}$ = 252.7 Hz), 150.3 (d, $^3J_{\text{C-F}}$ = 7.9 Hz), 133.6 (d, $^4J_{\text{C-F}}$ = 3.0 Hz), 132.2 (d, $^3J_{\text{C-F}}$ = 9.2 Hz), 117.4 (d, $^2J_{\text{C-F}}$ = 21.0 Hz), 112.5 (d, $^3J_{\text{C-F}}$ = 21.5 Hz), 30.0, 28.8, 19.2, 1.6. HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{20}\text{OSiP}$ $[\text{M} + \text{H}]^+$ 239.1267, found 239.1267.

1-(4-(2-(Trimethylsilyl)ethyl)benzo[d][1,3]dioxol-5-yl)ethanone (8d): The typical procedure was applied to (*E*)-*N*-(1-(benzo[d][1,3]dioxol-5-yl)ethylidene)-4-methoxyaniline (81 mg, 0.30 mmol) and trimethyl(vinyl)silane (67 μ L, 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded the title compound as a light yellow oil (55 mg, 70%).

R_f 0.32 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.35 (d, J = 8.2 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.01 (s, 2H), 2.88 – 2.82 (m, 2H), 2.53 (s, 3H), 0.83 – 0.78 (m, 2H), 0.05 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 199.6, 149.9, 146.8, 131.5, 129.1, 126.2, 105.2, 101.6, 29.6, 21.4, 17.6, -1.6. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{21}\text{O}_3\text{Si}$ $[\text{M} + \text{H}]^+$ 265.1260, found 265.1257.

1-(5-Methyl-2-(2-(trimethylsilyl)ethyl)phenyl)ethanone (8e) and 1-(3-methyl-2-(2-(trimethylsilyl)ethyl)phenyl)ethanone (major) (8e'): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(*m*-tolyl)ethylidene)aniline (72 mg, 0.30 mmol) and trimethyl(vinyl)silane (67 μ L, 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 20/1) of the crude product afforded a mixture of the title compounds as a light yellow oil (52 mg, 72%). The ratio of **8e** and **8e'** was determined to be 44:56 by ^1H -NMR integrations of characteristic singlet signals at 2.33 and 2.36 ppm. ^1H and ^{13}C NMR spectra of pure **8e** were previously reported.^{8c}

R_f 0.52 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.41 (s, 1H, **8e**), 7.22 – 7.13 (m, 2H, **8e** + **8e'**), 2.81 – 2.75 (m, 2H, **8e** + **8e'**), 2.56 (s, 3H, **8e**), 2.36 (s, 3H, **8e**), 2.33

(s, 3H, **8e'**), 2.17 (s, 3H, **8e'**), 0.84 – 0.77 (m, 2H, **8e** + **8e'**), 0.04 (s, 9H, **8e**), 0.01 (s, 9H, **8e'**); ^{13}C NMR (100 MHz, CDCl_3 , **8e'**): δ 193.2, 188.9, 141.9, 135.4, 135.3, 131.7, 130.1, 129.1, 27.7, 25.9, 21.1, 20.1, -1.6.

1-(3-(2-(Trimethylsilyl)ethyl)naphthalen-2-yl)ethanone (8f) and 1-(1-(2-(Trimethylsilyl)ethyl)naphthalen-2-yl)ethanone (8f'): The typical procedure was applied to (*E*)-4-methoxy-*N*-(1-(naphthalene-2-yl)ethylidene)aniline (83 mg, 0.30 mmol) and trimethyl(vinyl)silane (67 μL , 0.45 mmol) for 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 30/1) of the crude product afforded a mixture of the title compounds as a light yellow oil (55 mg, 70%). The ratio of **8f** and **8f'** was determined to be 37:63 by ^1H NMR integrations of characteristic singlet signals at 2.65 and 2.72 ppm. ^1H and ^{13}C NMR spectra of pure **8f** were previously reported.^{8c}

R_f 0.41 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 8.17 (s, 1H, **8f**), 8.11 (d, J = 8.1 Hz, 1H, **8f'**), 7.87 – 7.84 (m, 1H, **8f** + **8f'**), 7.78 (d, J = 8.1 Hz, 1H, **8f**), 7.72 (d, J = 8.6 Hz, 1H, **8f'**), 7.69 (s, 1H, **8f**), 7.60 – 7.50 (m, 3H, **8f'**; 1H, **8f**), 7.50 – 7.44 (m, 1H, **8f**), 3.21 – 3.15 (m, 2H, **8f'**), 3.05 – 3.00 (m, 2H, **8f**), 2.72 (s, 3H, **8f**), 2.65 (s, 3H, **8f'**), 1.01 – 0.96 (m, 2H, **8f'**), 0.90 – 0.84 (m, 2H, **8f**), 0.15 (s, 9H, **8f'**), 0.07 (s, 9H, **8f**); ^{13}C NMR (100 MHz, CDCl_3 , **8f'**): δ 203.9, 142.0, 135.6, 134.9, 131.9, 120.0, 127.2, 126.9, 126.4, 125.4, 124.6, 31.2, 23.7, 19.9, -1.5. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{23}\text{OSi}$ $[\text{M} + \text{H}]^+$ 271.1518, found 271.1512.

3.5 References

¹ a) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826-834; b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624-655; c) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013-3039; d) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704-712.

² Lewis, L. N.; Smith, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 2728-2735.

³ Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529-531.

⁴ a) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62-83; b) Uchimaru, Y.; *Chem. Commun.* **1999**, 1133-1134; c) Martinez, R.; Simon, M. O.; Chevalier, R.; Pautigny, C.; Genet, J.P.; Darses, S. *J. Am. Chem. Soc.* **2009**, *131*, 7887-7895; d) Kakiuchi, F.; Kochi, T.; Mizushima, E.; Murai, S. *J. Am. Chem. Soc.* **2010**, *132*, 17741-17750; e) Rouquet, G.; Chatani, N.; *Chem. Sci.* **2013**, *4*, 2201-2208; f) Schinkel, M.; Marek, I.; Ackermann, L. *Angew. Chem.* **2013**, *125*, 4069-4072; *Angew. Chem. Int. Ed.* **2013**, *52*, 3977-3980.

⁵ a) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 6616-6623; b) Jun, C.-H.; Lee, D.-Y.; Lee, H.; Hong, J. -B. *Angew. Chem.* **2000**, *112*, 3214-3216; *Angew. Chem. Int. Ed.* **2000**, *39*, 3070-3072; c) Lim, Y. -G.; Han, J. -S.; Yang, S. -S.; Chun, J. H. *Tetrahedron Lett.* **2001**, *42*, 4853-4856; d) Lim, S. -G.; Ahn, J. -A.; Jun, C.-H. *Org. Lett.* **2004**, *6*, 4687-4690.

⁶ Kuninobu, Y.; Nishina, Y.; Okaguchi, K.; Shouho, M.; Takai, K. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1393-1401.

⁷ a) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y. K.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939-3942; b) Pan, S.; Ryu, N.; Shibata, T. *J. Am. Chem. Soc.* **2012**, *134*,

17474-17477; c) Shibata, T.; Shizuno, T. *Angew. Chem.* **2014**, *126*, 5514-5517; *Angew. Chem. Int. Ed.* **2014**, *53*, 5410-5413; d) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258-10261; e) Crisenza, G. E. M.; Sokolova, O. O.; Bower, J. F. *Angew. Chem.* **2015**, *127*, 15079-15083; *Angew. Chem. Int. Ed.* **2015**, *54*, 14866-14870; f) Ebe, Y.; Nishimura, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899-5902.

⁸ a) Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221-5223; b) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 400-402; c) Gao, K.; Yoshikai, N. *Angew. Chem.* **2011**, *123*, 7020-7024; *Angew. Chem. Int. Ed.* **2011**, *50*, 6888-6892; d) Lee, P. -S.; Yoshikai, N. *Angew. Chem.* **2013**, *125*, 1278-1282; *Angew. Chem. Int. Ed.* **2013**, *52*, 1240-1244; e) Dong, J.; Lee, P. -S.; Yoshikai, N. *Chem. Lett.* **2013**, *42*, 1140-1142; f) Xu, W.; Yoshikai, N. *Angew. Chem.* **2014**, *126*, 14390-14394; *Angew. Chem. Int. Ed.* **2014**, *53*, 14166-14170.

⁹ Wong, M. Y.; Yamakawa, T.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 442-445.

¹⁰ a) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208-1219; b) Yoshikai, N.; *Bull. Chem. Soc. Jpn.* **2014**, *87*, 843-857.

¹¹ a) Ackermann, L. *J. Org. Chem.* **2014**, *79*, 8948-8954; b) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498-525.

¹² Crisenza, G. E. M.; Bower, J. F. *Chem. Lett.* **2016**, *45*, 2-9.

¹³ Lee, P. -S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 17283-17295.

¹⁴ Klein, H. -F. H. H. Karsch, *Chem. Ber.* **1975**, *108*, 944-955.

¹⁵ a) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M. *J. Am. Chem. Soc.* **2015**, *137*, 2448-2451; b) Fallon, B. J.; Garsi, J. B.; Derat, E.; Amatore, M.; Aubert, C.; Petit, M. *ACS Catal.* **2015**, *5*, 7493-7497.

- ¹⁶ a) Mrcic, N.; Minnaard, A. J.; Feringa, B. L.; de Vries, J. G. *J. Am. Chem. Soc.* **2009**, *131*, 8358; b) Gautier, F. M.; Jones, S.; Martin, S. J. *Org. Biomol. Chem.* **2009**, *7*, 229.
- ¹⁷ **1a**, Samec, J. S. M.; Ell, A. H.; Bäckvall, J. E. *Chem. Eur. J.* **2005**, *11*, 2327; **1b**, see ref. 8c; **1c** and **1e**, see ref. 13, 17283; **1d**, Imamoto, T.; Iwadate, N.; Yoshida, K. *Org. Lett.* **2006**, *8*, 2289; **1f**, Gao, K.; Lee, P.-S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234; **5a** and **5e**, Denmark, S. E.; Nakajima, N.; Stiff, C. M.; Nicaise, O. J. C.; Kranz, M. *Adv. Synth. Catal.* **2008**, *350*, 1023; **5b**, Yamada, K. I.; Konishi, T.; Nakano, M.; Fujii, S.; Cadou, R.; Yamamoto, Y.; Tomioka, K. *J. Org. Chem.* **2012**, *77*, 1547; **5c**: Yu, X.; Lu, X. *Adv. Synth. Catal.* **2011**, *353*, 569; **5d**, Jiang, Q.; Wang, J. Y.; Guo, C.; *J. Org. Chem.* **2014**, *79*, 8768; **5f**, Tobisu, M.; Yamaguchi, S.; Chatani, N. *Org. Lett.* **2007**, *9*, 3351.
- ¹⁸ Cho, S. J.; Jensen, N. H.; Kurome, T.; Kadar, S.; Manzano, M. L.; Malberg, J. E.; Caldarone, B.; Roth, B. L.; Kozikowski, A. P. *J. Med. Chem.* **2009**, *52*, 1885.
- ¹⁹ **2d**, Hu, J.; Gao, B.; Li, L.; Ni, C.; Hu, J. *Org. Lett.* **2015**, *17*, 3086; **2e**, Qin, Y.; Cheng, G.; Sundararaman, A.; Jäkle, F. *J. Am. Chem. Soc.* **2002**, *124*, 12672; **2g**, Wipf, P.; Hopkins, C. R. *J. Org. Chem.* **2001**, *66*, 3133; **2h**, Zhao, L. Kwong, M. J. C. K. W.; P. Shi.; Toy, H. *Tetrahedron* **2005**, *61*, 12026.

Chapter 4. Cobalt-Catalyzed, N-H Imine-Directed Olefin Hydroarylation

4.1 Introduction

The addition of arenes to alkenes through transition metal-catalyzed directed C–H activation has attracted significant attention as an atom- and step-economical approach to achieve regioselective alkylation of aromatic compounds. This type of transformation has been extensively developed using precious transition-metals, such as Ru, Rh, and Ir.^{1,2} On the other hand, increasing effort has been devoted to the development of alternative catalysts based on cost-effective first-row transition-metals such as cobalt,³ iron,⁴ and manganese.⁵ In this context, we and Petit et al. have shown the competence of low-valent cobalt species as catalysts for hydroarylation reactions directed by electron-rich N-aryl groups.^{3b-i, 6} For instance, *ortho*-alkylation of aryl N–PMP (*para*-methoxyphenyl) imine was achieved with a cobalt-phenanthroline-type catalyst under mild conditions (Scheme 4.2a).^{3b}

Despite the progress in the cobalt-catalyzed C–H functionalization using the N–PMP imine directing group, its limitations have also become apparent.⁷ First, only imines derived from sterically less hindered aryl ketones such as acetophenone, propiophenone, and tetralone, can be readily employed for these transformations, because the imine preparation becomes increasingly less efficient and difficult with bulky aryl ketones. This is a common limitation in the other N-aryl and N-alkyl-imine-directed C–H functionalization reactions regardless of transition metals used.^{8, 9, 10, 11, 12} Second, the N-aryl imine directing group is generally incapable of promoting twofold *ortho*-C–H functionalization, because its steric repulsion with the initially installed alkyl group prevents the second C–H activation. For the same reason, *ortho*-substituted substrates are

typically unable to participate in the reaction.

To overcome the limitations mentioned above, we proposed to utilize N–H imine instead of N-aryl imine as the directing group for C–H activation. Recently, N–H imine directed C–H activation reactions have been reported.^{13, 14, 15} Zhao *et al.* reported rhodium- and ruthenium-catalyzed annulations of N–H imines with either alkynes to give indene derivatives (Scheme 4.1a),^{13a, e} while Miura and Wang achieved isoquinolines through rhodium- and manganese-catalyzed dehydrogenative annulations of N–H imines with alkynes, respectively (Scheme 4.1b).¹⁴ A recent example of rhodium-catalyzed annulations of N–H imines with allenes also afforded indenenes (Scheme 4.1c).^{13b}

Scheme 4.1. Examples of N–H imine-directed C–H functionalization

a) Zhao *et al.* (ref 13a, e)

b) Miura and Wang *et al.* (ref 14)

c) Cramer *et al.* (ref 13b)

Scheme 4.2. Cobalt-catalyzed imine-directed olefin hydroarylation

a) Previous work (Ref. 3b)

b) This work

In this chapter, we report that the N–H imine acts as a viable directing group for cobalt-catalyzed hydroarylation reactions of vinylsilanes and alkyl olefins. The use of this directing group allows us to overcome the above-mentioned limitations of N-aryl imines (Scheme 4.2b). Unlike the N-aryl imines prepared by ketone-amine condensation, bulky N–H imines can be readily prepared by the addition of appropriate organolithium or Grignard reagents to aryl nitriles. The thus-prepared N–H imines display prominent reactivity in the cobalt-catalyzed directed hydroarylation. Notably, even fourfold *ortho*-alkylation of benzophenone imines can be achieved with high efficiency at room temperature, owing to the minimal steric size,¹⁶ and the strong coordination ability of N–H imine.¹⁷

4.2 Results and Discussion

Our initial effort focused on the screening of reaction conditions for the addition of phenyl butyl imine (**1a**) to vinyltrimethylsilane (1.5 equiv) (Table 4.1). After a brief screening of the triarylphosphine ligands using CoBr₂ (10 mol%) as the precatalyst and *t*-BuCH₂MgBr (50 mol%) as the reductant, P(3-MeOC₆H₄)₃ was identified as the best ligand, exclusively affording the monoalkylation product **2a** in 96% yield (entries 1–3). The use of 1,10-phenanthroline, previously used for the N–PMP imine-directed hydroarylation of vinylsilane,^{3b} resulted in a much lower catalytic reactivity (entry 4). The high efficiency of the reaction could be retained with a lower amount of CoBr₂ (5 mol%) and P(3-MeOC₆H₄)₃ (10 mol%) (entry 5). Interestingly, we observed that the cobalt source had a dramatic influence on the catalytic activity. Whereas CoCl₂ exhibited somewhat lower catalytic activity (entry 6), other cobalt salts, such as CoI₂, Co(acac)₂, and Co(acac)₃, promoted the second C–H activation to afford a mixture of **2a** and the dialkylation product **2b** (entries 7–9). It was particularly notable that Co(acac)₂ and Co(acac)₃ afforded the product **2b** as the major product (ca. 50% yield) regardless of the limited amount of vinylsilane (1.5 equiv). Under the Co(acac)₃/P(3-MeOC₆H₄)₃ system, the yield of **2b** could be further improved to 83% by increasing the amount of vinylsilane to 2.5 equivalents, which was accompanied by only a small trace amount of **2a** (entry 10).

Table 4.1. Effect of reaction conditions on addition of N–H imine **1a** to vinyltrimethylsilane

Reaction scheme: **1a** (N-phenyl-N-butyl imine) + vinyltrimethylsilane $\xrightarrow[\text{THF, rt, 12 h}]{\text{CoX}_n (10 \text{ mol\%}), \text{L} (20 \text{ mol\%}), t\text{-BuCH}_2\text{MgBr} (50 \text{ mol\%})}$ **2a** (monoalkylated product) + **2b** (bisalkylated product).

entry	CoX _n	L	yield(%) (A) ^a	yield(%) (B) ^a
1	CoBr ₂	P(4-ClC ₆ H ₄) ₃	79	0
2	CoBr ₂	P(3-FC ₆ H ₄) ₃	82	0
3	CoBr ₂	P(3-MeOC ₆ H ₄) ₃	96	0
4 ^b	CoBr ₂	1,10-phenanthroline	9	0
5 ^c	CoBr ₂	P(3-MeOC ₆ H ₄) ₃	92	0
6	CoCl ₂	P(3-MeOC ₆ H ₄) ₃	71	0
7	CoI ₂	P(3-MeOC ₆ H ₄) ₃	66	13
8	Co(acac) ₂	P(3-MeOC ₆ H ₄) ₃	26	53
9	Co(acac) ₃	P(3-MeOC ₆ H ₄) ₃	31	46
10 ^d	Co(acac) ₃	P(3-MeOC ₆ H ₄) ₃	4	83

^a The data was determined with GC using tridecane as the internal standard. ^b The loading of the ligand was 10 mol%. ^c CoBr₂ (5 mol%) and P(3-MeOC₆H₄)₃ (10 mol%) was used. ^d Vinylsilane (2.5 equiv) was used.

With the optimized conditions in hand, the scope of aryl-alkyl imines in the alkylation reactions with vinylsilane was studied (Table 4.2). With CoBr₂ (5 mol%) as the catalyst precursor (conditions A), monoalkylation of *para*- and *meta*-substituted phenyl butyl N–H imine took place smoothly to afford the ketone products **2c–f** in good yields after hydrolysis. For the 4-methoxy- and 3,4-methylenedioxy-substituted imines, attenuation of the catalytic activity by using less effective ligand P(4-ClC₆H₄)₃ instead of P(3-MeOC₆H₄)₃ was necessary to achieve the selective monoalkylation while suppressing the second alkylation (**2d** and **2e**). As was the cases in the previous chapters, the 3,4-methylenedioxy

group exhibited secondary directing effect, thus assisting exclusive alkylation of the proximal *ortho* C–H bond (**2e**). The present catalytic system was also applicable to the more hindered aryl isopropyl and *t*-butyl N–H imines with different substituents such as methylthio, methoxy, and dimethylamino groups, affording the products **2g–k** in high yields. Besides vinyltrimethylsilane, vinylsilanes bearing phenyldimethylsilyl groups could also be used as the alkylation agents (see **2l** and **2m**).

Table 4.2. Addition of aryl alkyl N–H imines to vinylsilane^a

Condition A: CoBr ₂ (5 mol%) P(3-MeOC ₆ H ₄) ₃ (10 mol%) <i>t</i> -BuCH ₂ MgBr (50 mol%) THF, rt, 12 h	(H ⁺)	Condition B: Co(acac) ₃ (10 mol%) P(3-MeOC ₆ H ₄) ₃ (20 mol%) <i>t</i> -BuCH ₂ MgBr (50 mol%) THF, rt, 12 h	2 (X = NH or O)
	1			

Condition A

2a' (R = H), 89% 2c (R = Me), 92% 2d (R = OMe), 70% ^[b]		2e , 82% ^b		2f , 83%
2g , 94%		2h (R = H), 95% 2i (R = SMe), 87%		2j (R = OMe), 85% 2k (R = NMe ₂), 87%
				2l (R = Me), 68% 2m (R = Ph), 65%

Condition B

2b (R = H), 78% ^c 2n (R = Ph), 75% ^c 2o (R = F), 83% ^c 2p (R = OMe), 85% ^c 2q (R = NMe ₂), 71% ^c 2r (R = OCF ₃), 81% ^c		2s , 80%
2t , 95%		2u , 81%
		2v , 56%

^a Unless otherwise noted, the reaction was performed using 0.3 mmol of imine and 0.45 mmol (1.5 equiv) of vinylsilane, followed by acidic hydrolysis (for the ketone products) or

direct purification (for the imine products).^b CoBr₂ (10 mol%) and P(4-ClC₆H₄)₃ (20 mol%) were used as the precatalysts. ^c Vinylsilane (0.75 mmol, 2.5 equiv) was used.

By changing the cobalt salt to Co(acac)₃ (conditions B) and using 2.5 equivalents of vinylsilane, the dialkylation of aryl butyl imines bearing various *para*-substituents was achieved, affording the desired products **2n-r** in good yields. On the other hand, the more hindered aryl isopropyl and *t*-butyl N-H imines did not undergo the dialkylation under conditions B but only affording the monoalkylation products, presumably due to the steric repulsion between the initially installed alkyl group and the bulky alkyl groups of the N-H imine. As expected, the alkylation of *ortho*-monosubstituted aryl butyl imines, which were inert under conditions A, was efficiently promoted with Co(acac)₃ as the cobalt precatalyst (see **2s** and **2t**). Furthermore, *meta*-tolyl- and 2-naphthyl butyl imines, which reacted rather sluggishly under conditions A, underwent regioselective alkylation at the less hinder position under conditions B, thus affording the products **2u** and **2v** in moderate to good yields.

We next focused our attention to the reaction of benzophenone N-H imine **3a** (Table 4.3). Under catalytic systems comprising Co(acac)₂ (10 mol%) and P(3-MeOC₆H₄)₃ (20 mol%) or P(3-FC₆H₄)₃ (20 mol%), the reaction of **3a** with excess vinylsilane (6 equiv) took place at room temperature to afford the trialkylation product **4a** in good yield along with a small amount of the tetraalkylation product **4b** after 12 h (entries 1 and 2). Strikingly, the reaction under the Co(acac)₂/P(3-FC₆H₄)₃ system was dramatically accelerated by the addition of pyridine (80 mol%), resulting in the full consumption of the starting material within 5 minutes (entry 3). After 10 minutes, the major products were a mixture of **4a** and **4b**, along with a trace amount of the dialkylation product (entry 4). The tetraalkylation product **4b** was obtained predominantly after 15–20 minutes in high yield (entries 5 and 6).

The rapid tetraalkylation is particularly noteworthy when compared previously reported directed hydroarylation with benzophenone,¹⁸ which gave mono- or di-alkylation products at elevated temperature.

Table 4.3. Addition of benzophenone N–H imine to vinyltrimethylsilane^a

entry	L	additives	yield(%) ^b				
			3a	mono	di	4a	4b
1	P(3-MeOC ₆ H ₄) ₃	-	0	0	0	60	9
2	P(3-FC ₆ H ₄) ₃	-	0	0	0	71	10
3 ^c	P(3-FC ₆ H ₄) ₃	pyridine (80 mol%)	0	0	45	39	<1
4 ^d	P(3-FC ₆ H ₄) ₃	pyridine (80 mol%)	0	0	3	50	38
5 ^e	P(3-FC ₆ H ₄) ₃	pyridine (80 mol%)	0	0	1	1	91
6 ^f	P(3-FC ₆ H ₄) ₃	pyridine (80 mol%)	0	0	<1	<1	91

^a Reaction conditions: **3a** (0.2 mmol), vinyltrimethylsilane (1.2 mmol, 6 equiv), $[\text{Co}(\text{acac})_2]$ (10 mol%), ligand (20 mol%), $t\text{-BuCH}_2\text{MgBr}$ (50 mol%), THF at room temperature for 12 h. ^b Estimated by GC analysis. ^c Reaction time = 5 min. ^d Reaction time = 10 min. ^e Reaction time = 15 min. ^f Reaction time = 20 min.

Using the pyridine-modified catalytic system (conditions C), benzophenone imines bearing a variety of substituents efficiently afforded multi-alkylation products (Table 4.4).

Various *para*-substituted benzophenone imines participated in the tetraalkylation reaction with vinyltrimethylsilane, affording the highly hindered products **4b-j** in excellent yields. Benzophenone imine bearing a 3,4-methylenedioxy group, also afforded the tetraalkylation product **4k** in a good yield. Dimethylphenylvinylsilane could be used as the alkylation reagent in place of vinyltrimethylsilane, affording the tetraalkylation product **4l**. As expected, *ortho*-methyl benzophenone imines with or without other *para*-substituents all smoothly participated in the alkylation reaction, giving the trialkylation products **4m-o** in excellent yields. Because of the steric hindrance of the *meta*-substituents, *meta*-methyl-substituted imine underwent di- or trialkylation at less hindered positions (see **4p** and **4q**). For the same reason, 2-naphthyl phenyl N-H imine afforded the trialkylation product **4r**.

Table 4.4. Addition of diarylketone N–H imines to vinylsilane^a

^a Unless otherwise noted, the reaction was performed using 0.3 mmol of imine and 1.8 mmol (6 equiv) of vinylsilane. ^b 1.05 mmol (3.5 equiv) of vinylsilane was used. ^c 0.90 mmol (3 equiv) of vinylsilane was used.

By modification of the $\text{Co}(\text{acac})_3/\text{P}(\text{3-MeOC}_6\text{H}_4)_3$ catalytic system with the addition of pyridine (80 mol%), the N–H imine-directed alkylation with alkyl olefins was achieved using phenyl *t*-butyl N–H imine as the model substrate (Table 4.5). Alkyl alkenes bearing primary, secondary or tertiary alkyl groups all afforded the hydroarylation products

in moderate to good yields (see **5a-h**), while a part of the unreacted alkene was found to undergo isomerization to the internal isomers. Methylene cyclohexane, norbornene, and vinyl carbazole could also be used as alkylating agents, affording the corresponding products **5i-k** in moderate to good yields. A mixture of branched products **5l** and its linear isomer was obtained with styrene as the alkylation agent, which was in contrast to the branched selectivity typically observed for the cobalt-catalyzed, N-PMP imine-directed styrene hydroarylation.^{3d, e} Unstrained internal alkenes such as cyclohexene failed to participate in the reaction.

Table 4.5. Addition of N-H imine to alkyl olefins.^a

^a The reaction was performed using 0.3 mmol of imine and 0.45 mmol (1.5 equiv) of olefin.

^b The reaction mixture was hydrolyzed with 3N HCl. ^c The ratio of branched and linear isomers determined by ¹H NMR spectroscopy.

To compare the directing ability of the N–H imine with that of N–PMP imine, two competition experiments using sterically hindered *t*-butyl phenyl imine and acetophenone N–PMP imine were performed. First, the competition experiment under the optimized conditions for the N–H imine-directed hydroarylation resulted in fast and predominant alkylation of the N–H imine within 20 minutes (Scheme 4.3a). Notably, the second competition under the cobalt/phenanthroline catalytic system, optimized for the N–PMP imine-directed hydroarylation, also resulted in the preferential alkylation of the N–H imine, despite low yields after longer reaction time (Scheme 4.3b). It should be pointed out that the cobalt/phenanthroline system promotes the reaction of the N–PMP imine alone efficiently at room temperature. As such, in this competition, the N–H imine is assumed to prevent the reaction of the N–PMP imine by strongly coordinating to the catalyst. Overall, the stronger directing ability of the N–H imine in these competition experiments may be rationalized by the superior coordination ability of the N–H imine to the low-valent cobalt center compared with that of the N–PMP imine.

Scheme 4.3. Competition experiments using N–H and N–PMP imines^a

^a Yields were determined by GC using *n*-tridecane as an internal standard.

Besides the competition experiment, alkylation reactions of deuterated aryl imine were performed to probe the deuterium distribution in the products (Scheme 4.4). The reaction of deuterated pivalophenone imine with phenyldimethylvinylsilane afforded the monoalkylation product with a moderate degree of deuterium incorporation into both of the methylene positions and a substantial decrease in the deuterium content at the remaining *ortho* position. Likewise, the reaction of deuterated benzophenone imine resulted in a tetraalkylation product with deuterium incorporation into both of the methylene groups. To rationalize these results, we propose a catalytic cycle involving C–H oxidative addition, alkene insertion, and reductive elimination (Scheme 4.5). The C–H oxidative addition and alkene insertion steps would take place reversibly, resulting in the formation of branched and linear alkylcobalt intermediates. Then the reductive elimination would occur exclusively from the linear alkylcobalt intermediate (A) to afford the linear alkylation product. While nonproductive, the branched alkylcobalt intermediate (B) accounts for the deuterium incorporation into the methylene group bonded to the aryl group.

Scheme 4.4. Deuterium-labeling experiments

Scheme 4.5. Proposed catalytic cycle

4.3 Conclusion

To summarize, we have shown that N-H imine can be used as a highly efficient directing group for the cobalt-catalyzed olefin hydroarylation. Owing to the ready

accessibility, the strong coordinating ability, and the minimal steric size, this directing group was found to promote a series of hydroarylation reaction that have not been achieved using N-PMP imine directing group. Of particular note, the fourfold *ortho*-alkylation of benzophenone N-H imines was achieved with remarkable high efficiency at room temperature. The present study would hold promise for further extension of the scope of N-H imine as a directing group for directed C-H bond functionalization reactions.

4.4 Experimental Section

Preparation of Starting Materials

Preparation of Aryl Imines

All the imines **1a–1r** and **3a–3p** shown below were synthesized according to the literature procedures,¹⁹ and purified by recrystallization or distillation. Spectral data of the known imines **1b**,¹⁹ **1d**,¹⁹ **1e**,¹⁹ **1i**,¹⁹ **1j**,²⁰ **1n**,²¹ **1o**,²² **1q**,¹⁹ **1r**,¹⁹ **3a**,²³ **3g**,²⁴ **3h**,¹⁹ and **3i**²⁵ showed good agreement with the literature data.

1-Phenylpentan-1-imine (1a): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.32 (brs, 1H), 7.70 (s, 2H), 7.42-7.36 (m, 3H), 2.72 (t, $J = 7.6$ Hz, 2H), 1.64-1.56 (m, 2H), 1.45-1.35 (m, 2H), 0.93 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 179.2, 139.2, 130.3, 128.6, 126.5, 37.5, 28.5, 22.5, 14.0; HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 162.1283, found 162.1284.

1-(4-Methoxyphenyl)pentan-1-imine (1c): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.06 (brs, 1H), 7.70 (d, $J = 7.8$ Hz, 2H), 6.89 (d, $J = 8.9$ Hz, 2H), 3.81 (s, 3H), 2.68 (t, $J = 8.0$ Hz, 2H), 1.62-1.54 (m, 2H), 1.43-1.34 (m, 2H), 0.92 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.1, 161.4, 131.4, 128.2, 113.8, 55.4, 37.5, 28.6, 22.5, 14.0; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$ $[\text{M} + \text{H}]^+$ 192.1388, found 192.1383.

4-(1-Iminopentyl)-N,N-dimethylaniline (1f): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.67 (brs, 1H), 7.65 (d, $J = 8.6$ Hz, 2H), 6.69-6.64 (m, 2H), 2.97 (s, 6H), 2.68 (t, $J = 7.8$ Hz, 2H), 1.65-1.56 (m, 2H), 1.45-1.35 (m, 2H), 0.93 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.0, 151.8, 127.9, 126.0, 111.4, 40.2, 37.2, 29.0, 22.6, 14.0; HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{21}\text{N}_2$ $[\text{M} + \text{H}]^+$ 205.1706, found 205.1702.

1-(4-(Trifluoromethoxy)phenyl)pentan-1-imine (1g): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.51 (brs, 1H), 7.81 (brs, 2H), 7.22 (d, $J = 8.6$ Hz, 2H), 2.69 (t, $J = 8.0$ Hz, 2H), 1.63-1.53 (m, 2H), 1.44-1.34 (m, 2H), 0.93 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.2, 150.8, 128.5, 126.9, 120.8 (q, $J = 256.6$ Hz), 120.6, 37.58, 28.3, 22.5, 14.0; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NOF}_3$ $[\text{M} + \text{H}]^+$ 246.1106, found 246.1102.

1-(Benzo[d][1,3]dioxol-5-yl)pentan-1-imine (1h): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.16 (brs, 1H), 7.32-7.22 (m, 2H), 6.80 (d, $J = 8.2$ Hz, 1H), 5.99 (s, 2H), 2.66 (t, $J = 7.2$ Hz, 2H), 1.63-1.54 (m, 2H), 1.44-1.34 (m, 2H), 0.93 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.0, 149.6, 148.2, 121.4, 108.1, 107.1, 101.6, 37.7, 28.7, 22.6, 14.1; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{16}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 206.1181, found 206.1185.

1-(Naphthalen-2-yl)pentan-1-imine (1k): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.52 (brs, 1H), 8.17 (s, 1H), 7.95-7.82 (m, 4H), 7.55-7.48 (m, 2H), 2.86 (t, $J = 8.0$ Hz, 2H), 1.72-1.62 (m, 2H), 1.50-1.41 (m, 2H), 0.97 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 179.1, 136.5, 134.4, 133.1, 129.0, 128.4, 127.9, 127.3, 126.8, 126.7, 124.0, 37.7, 28.6, 22.6, 14.2; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 212.1439, found 212.1442.

1-(o-Tolyl)pentan-1-imine (1l): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.30 (brs, 1H), 7.25-7.13 (m, 3H), 7.10 (d, $J = 7.3$ Hz, 1H), 2.61-2.56 (m, 2H), 2.31 (s, 3H), 1.61-1.53 (m, 2H), 1.43-1.33 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 183.7, 142.4, 133.7, 130.8, 128.4, 126.2, 125.8, 40.4, 28.1, 22.6, 19.8, 14.0; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 176.1439, found 176.1443.

1-(2-(Trifluoromethyl)phenyl)pentan-1-imine (1m): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.44 (brs, 1H), 7.64 (d, $J = 7.8$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.43 (t, $J = 7.7$ Hz, 1H), 7.24 (d, $J = 7.7$ Hz, 1H), 2.59 (t, $J = 8.4$ Hz, 2H), 1.64-1.56 (m, 2H), 1.43-1.33 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 181.3, 141.5 (q, $^3J_{\text{C-F}} = 2.1$ Hz), 132.0 (q, $^4J_{\text{C-F}} = 1.0$ Hz), 128.6, 127.9, 126.64 (q, $^2J_{\text{C-F}} = 30.9$ Hz), 126.56 (q, $^3J_{\text{C-F}} = 5.0$ Hz), 124.1 (q, $^1J_{\text{C-F}} = 273.8$ Hz), 40.5, 27.6, 22.4, 14.0; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NF}_3$ $[\text{M} + \text{H}]^+$ 230.1157, found 230.1158.

2,2-Dimethyl-1-(4-(methylthio)phenyl)propan-1-imine (1p): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.10 (brs, 1H), 7.20-7.06 (m, 4H), 2.43 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.8, 138.7, 127.0, 125.8 (two peaks overlapped), 40.2, 28.5, 15.6; HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{18}\text{NS}$ $[\text{M} + \text{H}]^+$ 208.1160, found 208.1160.]

(4-Methoxyphenyl)(phenyl)methanimine (3b): white solid; M.p. = 41 – 42 °C; ^1H NMR (400 MHz, CDCl_3): δ 9.46 (brs, 1H), 7.58-7.38 (m, 7H), 6.93-6.90 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.8, 161.6, 140.2, 131.7, 130.4, 130.2, 128.5 (two peaks overlapped), 113.8, 55.6; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}$ $[\text{M} + \text{H}]^+$ 212.1075, found 212.1078.

(4-Fluorophenyl)(phenyl)methanimine (3c): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.67 (brs, 1H), 7.59-7.39 (m, 7H), 7.08-7.04 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.1, 164.1 (d, $^1J_{\text{C-F}} = 252.0$ Hz), 139.5, 135.3, 130.8, 130.3, 128.5, 128.2, 115.3 (d, $^2J_{\text{C-F}} = 22.0$ Hz); HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{11}\text{FN}$ $[\text{M} + \text{H}]^+$ 200.0876, found 200.0879.

(4-(Methylthio)phenyl)(phenyl)methanimine (3d): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.54 (brs, 1H), 7.56-7.35 (m, 7H), 7.28-7.21 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.6, 142.0, 130.7, 130.2, 129.9, 129.0, 128.4, 128.3, 125.5, 15.2; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{NS}$ $[\text{M} + \text{H}]^+$ 228.0847, found 228.0849.

4-(Imino(phenyl)methyl)-N,N-dimethylaniline (3e): Light yellow solid; M.p. = 66-67 °C; ^1H NMR (400 MHz, CDCl_3): δ 9.23 (brs, 1H), 7.57-7.50 (m, 4H), 7.45-7.37 (m, 3H), 6.71-6.66 (m, 2H), 3.02 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.0, 152.1, 141.0, 130.3, 129.8, 128.6, 128.4, 126.4, 111.4, 40.4; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2$ $[\text{M} + \text{H}]^+$ 225.1392, found 225.1390.

Phenyl(4-(trifluoromethoxy)phenyl)methanimine (3f): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.78 (brs, 1H), 7.65 (s, 2H), 7.54-7.39 (m, 5H), 7.25 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.1, 150.9, 139.3, 137.8, 130.6, 130.5, 128.7, 128.3, 120.7, 120.6 (q, $^1J_{\text{C-F}} = 258.0$ Hz); HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{11}\text{NF}_3\text{O}$ $[\text{M} + \text{H}]^+$ 266.0793, found 266.0797.

Benzo[d][1,3]dioxol-5-yl(phenyl)methanimine (3j): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.32 (brs, 1H), 7.50-7.32 (m, 5H), 7.17-7.14 (m, 1H), 7.03 (d, $J = 7.8$ Hz, 1H), 6.75 (d, $J = 8.1$ Hz, 1H), 5.93 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.3, 149.5, 147.7, 130.0, 128.3, 128.2, 128.1, 127.0, 123.8, 108.5, 107.8, 101.5; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{12}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 226.0868, found 226.0871.

Phenyl(o-tolyl)methanimine (3k): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.76 (brs, 1H), 7.66 (d, $J = 6.6$ Hz, 2H), 7.42-7.35 (m, 3H), 7.24-7.15 (m, 2H), 7.02-6.95 (m, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.0, 156.9, 139.2, 130.8, 130.5, 129.7, 129.1, 128.3, 128.1, 120.8, 111.5, 55.7; HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{14}\text{N}$ $[\text{M} + \text{H}]^+$ 196.1126, found 196.1124.

(4-Methoxyphenyl)(o-tolyl)methanimine (3l): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.22 (brs, 1H), 7.61 (d, $J = 7.3$ Hz, 2H), 7.33-7.15 (m, 4H), 6.88-6.84 (m, 2H), 3.81 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.0, 161.9, 141.3, 134.7, 131.0, 130.5, 129.9, 128.8, 127.6, 126.0, 113.8, 55.5, 19.8; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{16}\text{NO}$ $[\text{M} + \text{H}]^+$ 226.1232, found 226.1231.

(4-Fluorophenyl)(o-tolyl)methanimine (3m): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.46 (brs, 1H), 7.68 (d, $J = 6.0$ Hz, 2H), 7.31 (t, $J = 7.3$ Hz, 1H), 7.24 (t, $J = 6.8$ Hz, 2H), 7.16 (d, $J = 7.8$ Hz, 1H), 7.03 (t, $J = 8.7$ Hz, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.6, 164.7 (d, $^1J_{\text{C-F}} = 251.2$ Hz), 140.8, 134.6, 130.7 (two peaks overlapped), 130.4 (d, $^3J_{\text{C-F}} = 7.8$ Hz), 129.1, 127.6, 126.2, 115.6 (d, $^2J_{\text{C-F}} = 21.8$ Hz), 19.8. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{13}\text{NF}$ $[\text{M} + \text{H}]^+$ 214.1032, found 214.1028.

Naphthalen-2-yl(phenyl)methanimine (3n): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.83 (brs, 1H), 8.01 (s, 1H), 7.92-7.75 (m, 4H), 7.66-7.43 (m, 7H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.5, 134.4, 132.9, 130.5, 129.0, 128.6, 128.4, 127.9, 127.5, 126.8, 125.4; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{14}\text{N}$ $[\text{M} + \text{H}]^+$ 232.1126, found 232.1131.

Di-m-tolylmethanimine (3o): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.64 (brs, 1H), 7.28-7.20 (m, 8H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.5, 139.3, 138.0, 131.1, 128.9, 128.1, 125.8, 21.4; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 210.1283, found 210.1287.

(3,5-Dimethylphenyl)(phenyl)methanimine (3p): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.65 (brs, 1H), 7.58 (s, 2H), 7.50-7.39 (m, 3H), 7.17 (s, 2H), 7.11 (s, 1H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.9, 139.6, 138.1, 132.1, 130.4, 128.4, 126.3, 125.3, 113.6, 21.4; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 210.1283, found 210.1289.

Cobalt-Catalyzed N–H Imine-Directed Olefin Hydroarylation

Typical Procedure: 1-(2-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-one (**2a'**). In a Schlenk tube were placed 1-phenylpentan-1-imine (**1a**, 49 mg, 0.30 mmol), tris(3-methoxyphenyl)phosphine (10.1 mg, 0.030 mmol), a freshly prepared THF solution of CoBr_2 (0.15 M, 0.10 mL, 0.015 mmol), and THF (0.45 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t\text{-BuCH}_2\text{MgBr}$ (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, trimethyl(vinyl)silane (67 μL , 0.45 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 12 h. The reaction was then quenched by the addition of HCl (3 N, 1.0 mL), and stirred for 1 h. The resulting mixture was extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 30/1) of the crude product afforded the title compound as a light yellow oil (70 mg, 89%).

R_f 0.65 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.62 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 2.98 (t, J = 7.3 Hz, 2H), 2.91-2.86 (m, 2H), 1.85-1.76 (m, 2H), 1.57-1.46 (m, 2H), 1.06 (t, J = 7.3 Hz, 3H), 0.95-0.91 (m, 2H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.81, 145.19, 138.72, 131.06, 130.42, 128.09, 125.59, 42.21, 28.20, 26.81, 22.69, 19.84, 14.15, -1.58; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{27}\text{OSi}$ $[\text{M} + \text{H}]^+$ 263.1831, found 263.1826.

1-(4-Methyl-2-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-one (2c): Light yellow oil (76 mg, 92%; eluent: hexane/EtOAc = 30/1). R_f 0.67 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.48 (d, J = 7.9 Hz, 1H), 7.08 (s, 1H), 7.02 (d, J = 7.9 Hz, 1H), 2.85 (t, J = 7.9 Hz, 2H), 2.80-2.75 (m, 2H), 2.35 (s, 3H), 1.72-1.64 (m, 2H), 1.44-1.35 (m, 2H), 0.96-0.92 (m, 3H), 0.83-0.79 (m, 2H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.0, 145.9, 141.6, 135.5, 131.3, 128.8, 126.2, 41.9, 28.3, 27.0, 22.7, 21.6, 19.8, 14.2, -1.6; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{29}\text{OSi}$ $[\text{M} + \text{H}]^+$ 277.1988, found 277.1987.

1-(4-Methoxy-2-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-one (2d): The typical procedure was modified using CoBr_2 (10 mol%) and tris(4-chlorophenyl)phosphine (20 mol%) as the precatalyst. Light yellow oil (61 mg, 70%; eluent: hexane/EtOAc = 30/1). R_f 0.45 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.63 (d, J = 8.6 Hz, 1H), 6.78 (d, J = 2.6 Hz, 1H), 6.72 (dd, J = 8.6, 2.6 Hz, 1H), 3.84 (s, 3H), 2.87-2.83 (m, 4H), 1.72-1.63 (m, 2H), 1.44-1.34 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H), 0.84-0.78 (m, 2H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.3, 161.9, 149.3, 131.5, 130.4, 116.1, 110.4, 55.5, 41.4, 29.0, 27.3, 22.8, 19.5, 14.2, -1.5; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{29}\text{O}_2\text{Si}$ $[\text{M} + \text{H}]^+$ 293.1937, found 293.1939.

1-(4-(2-(Trimethylsilyl)ethyl)benzo[d][1,3]dioxol-5-yl)pentan-1-one (2e): The typical

procedure was modified using CoBr_2 (10 mol%) and tris(4-chlorophenyl)phosphine (20 mol%) as the precatalyst. Light yellow oil (75 mg, 82%; eluent: hexane/EtOAc = 30/1) R_f 0.42 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.22 (d, J = 8.2 Hz, 1H), 6.63 (d, J = 8.2 Hz, 1H), 5.97 (s, 2H), 2.82-2.73 (m, 4H), 1.67-1.59 (m, 2H), 1.40-1.30 (m, 2H), 0.92-0.87 (m, 3H), 0.80-0.74 (m, 2H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.0, 149.5, 146.7, 132.3, 128.6, 124.6, 105.2, 101.5, 41.5, 27.4, 22.7, 21.3, 17.8, 14.2, -1.6; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{27}\text{O}_3\text{Si}$ $[\text{M} + \text{H}]^+$ 307.1729, found 307.1725.

1-(5-(Trifluoromethyl)-2-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-one (2f): Light yellow oil (82 mg, 83%; eluent: hexane/EtOAc/ NEt_3 = 30/1/1); R_f 0.65 (hexane/EtOAc/ NEt_3 = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.71 (s, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 2.88 (t, J = 7.2 Hz, 2H), 2.81-2.76 (m, 2H), 1.73-1.66 (m, 2H), 1.45-1.36 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H), 0.82-0.77 (m, 2H), 0.04 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 204.6, 149.2 (q, $^4J_{\text{C-F}}$ = 1.3 Hz), 139.2, 131.0, 128.1 (q, $^2J_{\text{C-F}}$ = 33.0 Hz), 127.5 (q, $^3J_{\text{C-F}}$ = 3.7 Hz), 124.7 (q, $^3J_{\text{C-F}}$ = 3.9 Hz), 124.2 (q, $^1J_{\text{C-F}}$ = 273.2 Hz), 42.3, 30.0, 28.2, 26.6, 22.6, 14.1, -1.62; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{26}\text{F}_3\text{OSi}$ $[\text{M} + \text{H}]^+$ 331.1705, found 331.1709.

2-Methyl-1-(2-(2-(trimethylsilyl)ethyl)phenyl)propan-1-one (2g): Light yellow oil (69.8 mg, 94%; eluent: hexane/EtOAc = 30/1); R_f 0.67 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, J = 7.8 Hz, 1H), 7.36 (td, J = 7.8, 1.4 Hz, 1H), 7.28 (d, J = 7.8 Hz, 1H), 7.21 (td, J = 7.3, 0.9 Hz, 1H), 3.32-3.21 (m, 1H), 2.72-2.65 (m, 2H), 1.17 (d, J = 6.9 Hz, 6H), 0.84-0.78 (m, 2H), 0.28 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 210.0, 145.0, 138.8, 130.7, 130.2, 127.4, 125.5, 39.5, 28.0, 19.9, 18.9, -1.59; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{25}\text{SiO}$ $[\text{M} + \text{H}]^+$ 249.1675, found 249.1679.

2,2-Dimethyl-1-(2-(2-(trimethylsilyl)ethyl)phenyl)propan-1-imine (2h): The typical procedure for **2a** was applied to 2,2-dimethyl-1-phenylpropan-1-imine (**1g**, 44 mg, 0.30 mmol) and trimethyl(vinyl)silane (67 μL , 0.45 mmol) without hydrolysis. Silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 30/1/1) of the crude product afforded the title compound as a light yellow oil (75 mg, 95%). R_f 0.70 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 8.59 (brs, 1H), 7.42-7.35 (m, 2H), 7.27-7.23 (m, 1H), 7.12 (d, J = 7.5 Hz, 1H), 2.61-2.57 (m, 2H), 1.35 (s, 9H), 0.96-0.91 (m, 2H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.5, 141.0, 128.9, 128.0, 126.1, 125.0, 40.5, 29.0, 28.0, 19.6, -1.6; HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{28}\text{NSi}$ $[\text{M} + \text{H}]^+$ 262.1991, found 262.1989.

2,2-Dimethyl-1-(4-(methylthio)-2-(2-(trimethylsilyl)ethyl)phenyl)propan-1-imine (2i):

The reaction mixture was quenched with water and then subjected to workup and purification; Light yellow oil (78 mg, 87%; eluent: hexane/EtOAc/NEt₃ = 30/1/1); *R_f* 0.54 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.22 (brs, 1H), 7.15 (d, *J* = 1.8 Hz, 1H), 6.99 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 2.47 (s, 3H), 2.44-2.39 (m, 2H), 1.19 (s, 9H), 0.81-0.76 (m, 2H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.3, 142.2, 138.0, 137.9, 127.0, 126.6, 123.0, 40.5, 28.9, 27.9, 19.4, 15.9, -1.7; HRMS (ESI) Calcd for C₁₇H₃₀NSiS [M + H]⁺ 308.1868, found 308.1867.

1-(4-Methoxy-2-(2-(trimethylsilyl)ethyl)phenyl)-2,2-dimethylpropan-1-one (2j): Light yellow oil (74 mg, 85%; eluent: hexane/EtOAc = 30/1); *R_f* 0.55 (hexane/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 7.10 (d, *J* = 8.5 Hz, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 6.68 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.81 (s, 3H), 2.47-2.42 (m, 2H), 1.24 (s, 9H), 0.85-0.80 (m, 2H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 214.7, 160.0, 144.6, 133.0, 126.4, 114.8, 110.1, 100.2, 55.4, 45.1, 28.3, 28.0, 19.5, -1.6; HRMS (ESI) Calcd for C₁₇H₂₉O₂Si [M + H]⁺ 293.1937, found 293.1937.

1-(4-(Dimethylamino)-2-(2-(trimethylsilyl)ethyl)phenyl)-2,2-dimethylpropan-1-one (2k): *R_f* 0.50 (hexane/EtOAc/NEt₃ = 10/1/1); light yellow oil (78 mg, 87%; eluent: hexane/EtOAc = 30/1); ¹H NMR (400 MHz, CDCl₃): δ 7.16 (d, *J* = 8.6 Hz, 1H), 6.56 (d, *J*

= 2.3 Hz, 1H), 6.47 (dd, J = 8.6, 2.3 Hz, 1H), 2.97 (s, 6H), 2.52-2.46 (m, 2H), 1.26 (s, 9H), 0.86-0.79 (m, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 214.0, 151.0, 144.9, 128.2, 127.0, 113.0, 108.3, 45.0, 40.5, 28.7, 28.4, 20.0, -1.6; HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{32}\text{NOSi}$ $[\text{M} + \text{H}]^+$ 306.2253, found 306.2258.

1-(2-(2-(Dimethyl(phenyl)silyl)ethyl)phenyl)pentan-1-one (2l): Light yellow oil (66 mg, 68%; eluent: hexane/EtOAc = 30/1); R_f 0.60 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.56-7.48 (m, 3H), 7.37-7.34 (m, 4H), 7.23-7.19 (m, 2H), 2.82 (t, J = 7.3 Hz, 2H), 2.80-2.75 (m, 2H), 1.70-1.61 (m, 2H), 1.42-1.32 (m, 2H), 1.10-1.05 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H), 0.32 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.8, 144.9, 139.4, 138.8, 133.9, 131.1, 130.5, 129.1, 128.1, 128.0, 125.7, 42.2, 28.2, 26.8, 22.7, 18.8, 14.2, -2.9; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{29}\text{OSi}$ $[\text{M} + \text{H}]^+$ 325.1988, found 325.1989.

1-(2-(2-(Dimethyl(phenyl)silyl)ethyl)phenyl)pentan-1-one (2m): R_f 0.55 (hexane/EtOAc = 5/1); light yellow oil (87.5 mg, 65%; eluent: hexane/EtOAc = 30/1); ^1H NMR (400 MHz, CDCl_3): δ 7.61-7.59 (m, 6H), 7.48 (dd, J = 7.6 Hz, 1H), 7.44-7.31 (m, 10H), 7.24-7.19 (m, 2H), 2.91-2.87 (m, 2H), 2.78 (t, J = 7.3 Hz, 2H), 1.75-1.70 (m, 2H), 1.65-1.58 (m, 2H), 1.37-1.27 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.8, 144.4, 139.1, 136.0, 135.2, 131.1, 130.5, 129.7, 128.1, 127.9, 125.8, 42.2,

28.6, 26.7, 22.6, 16.6, 14.2; HRMS (ESI) Calcd for $C_{31}H_{33}OSi$ $[M + H]^+$ 449.2301, found 449.2301.

Typical Procedure under conditions B: 1-(2,6-bis(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2b): In a Schlenk tube were placed tris(3-methoxyphenyl)phosphine (21.2 mg, 0.060 mmol), $Co(acac)_3$ (10.8 mg, 0.030 mmol), and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of *t*-BuCH₂MgBr (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, trimethyl(vinyl)silane (114 μ L, 0.75 mmol) and 1-phenylpentan-1-imine (**1a**, 49 mg, 0.30 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through celite and washed with EtOAc (5 mL x 3). The solution was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 100/1/1) of the crude product afforded the title compound as a light yellow oil (85 mg, 78%).

R_f 0.80 (hexane/EtOAc = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.20 (brs, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.6 Hz, 2H), 2.53-2.41 (m, 6H), 1.75-1.67 (m, 2H), 1.49-1.39 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H), 0.87-0.72 (m, 4H), 0.02 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.8, 141.2, 140.8, 128.2, 126.0, 40.9, 27.5, 27.4, 22.8, 20.0, 14.2, -1.6; HRMS (ESI) Calcd for $C_{21}H_{40}NSi_2$ $[M + H]^+$ 362.2699, found 362.2704.

1-(3,5-Bis(2-(trimethylsilyl)ethyl)-[1,1'-biphenyl]-4-yl)pentan-1-imine (2n): Light yellow oil (98.5 mg, 64%; eluent: hexane/EtOAc/NEt₃ = 100/1/1), *R_f* 0.75 (hexane/EtOAc = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.20 (brs, 1H), 7.61-7.57 (m, 2H), 7.46-7.41 (m, 2H), 7.37-7.32 (m, 1H), 7.29 (s, 2H), 2.56-2.45 (m, 6H), 1.78-1.67 (m, 2H), 1.51-1.39 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.92-0.77 (m, 4H), 0.03 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 183.8, 141.45, 141.40, 141.2, 140.3, 128.9, 127.5, 127.4, 125.0, 41.0, 27.6, 27.5, 22.8, 20.1, 14.3, -1.6; HRMS (ESI) Calcd for C₂₇H₄₄NSi₂ [M + H]⁺ 438.3012, found 438.3018.

1-(4-Fluoro-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2o): Light yellow oil (94.5 mg, 83%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.80 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.23 (brs, 1H), 6.77 (d, *J* = 9.8 Hz, 2H), 2.47-2.40 (m, 6H), 1.72-1.62 (m, 2H), 1.48-1.37 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.85-0.73 (m, 4H), 0.02 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 183.2, 162.7 (d, ¹*J*_{C-F} = 245.1 Hz), 143.5 (d, ³*J*_{C-F} = 6.7 Hz), 137.13, 112.59 (d, ²*J*_{C-F} = 21.2 Hz), 41.1, 27.5, 27.4, 22.7, 19.5, 14.2, -1.7; HRMS (ESI) Calcd for C₂₁H₃₉NOFSi [M + H]⁺ 368.2785, found 368.2784.

1-(4-Methoxy-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2p): Light yellow oil (100 mg, 83%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.75 (hexane/EtOAc = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.17 (brs, 1H), 6.61 (s, 2H), 3.79 (s, 3H), 2.48-2.40 (m, 6H), 1.72-1.64 (m, 2H), 1.47-1.38 (m, 2H), 0.95 (t, J = 7.3 Hz, 2H), 0.83-0.76 (m, 4H), 0.02 (s, 19H); ^{13}C NMR (100 MHz, CDCl_3): δ 183.9, 159.4, 142.6, 134.2, 111.4, 55.3, 41.2, 27.7, 27.6, 22.8, 19.8, 14.2, -1.7; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{42}\text{NOSi}_2$ $[\text{M} + \text{H}]^+$ 392.2805, found 392.2808.

4-(1-Iminopentyl)-N,N-dimethyl-3,5-bis(2-(trimethylsilyl)ethyl)aniline (2q): Light yellow oil (86mg, 71%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.77 (hexane/EtOAc = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 8.69 (brs, 1H), 6.45 (s, 2H), 2.96 (s, 6H), 2.49-2.41 (m, 6H), 1.74-1.66 (m, 2H), 1.48-1.40 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H), 0.83 (dd, J = 14.5, 5.8 Hz, 4H), 0.035 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3): δ 184.4, 150.4, 141.8, 130.6, 110.2, 41.3, 40.8, 27.9, 27.7, 22.8, 20.1, 14.2, -1.6; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{45}\text{N}_2\text{Si}_2$ $[\text{M} + \text{H}]^+$ 405.3121, found 405.3120.

1-(4-(Trifluoromethoxy)-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2r):

Light yellow oil (97mg, 81%; eluent: hexane/EtOAc/NEt₃ = 50/1/1); *R_f* 0.76 (hexane/EtOAc = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.16 (brs, 1H), 6.92 (s, 2H), 2.47-2.43 (m, 6H), 1.75-1.63 (m, 2H), 1.48-1.38 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.86-0.70 (m, 4H), 0.02 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 182.8, 149.2, 143.2, 130.3, 120.7 (q, ¹*J*_{C-F} = 255 Hz), 118.3, 40.9, 27.5, 27.3, 22.7, 19.5, 14.2, -1.7.; HRMS (ESI) Calcd for C₂₂H₃₉NOF₃Si₂ [M + H]⁺ 446.2522, found 446.2517.

1-(2-Methyl-6-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2s): Light yellow oil (67 mg, 80%; eluent: hexane/EtOAc = 50/1); *R_f* 0.75 (hexane/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 9.15 (brs, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 2.51-2.43 (m, 4H), 2.22 (s, 3H), 1.73-1.65 (m, 2H), 1.48-1.38 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.84-0.74 (m, 2H), 0.02 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 184.2, 142.1, 140.9, 133.0, 128.0, 127.7, 126.2, 40.4, 27.5, 27.4, 22.8, 20.0, 19.7, 14.2, -1.7; HRMS (ESI) Calcd for C₁₇H₃₀NSi [M + H]⁺ 276.2148, found 276.2151.

1-(2-(Trifluoromethyl)-6-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (2t): The reaction was performed using 0.45 mmol of trimethyl(vinyl)silane; Light yellow oil (94 mg, 95%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.71 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.31 (brs, 1H), 7.49-7.44 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 2.66-2.39 (m, 4H), 1.81-1.63 (m, 2H), 1.48-1.37 (m, 2H), 0.97-0.94 (m, 3H), 0.85-0.76 (m, 2H), 0.02 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 180.9, 142.9, 141.0, 132.7 (q, ⁴*J*_{C-F} = 1.0 Hz), 128.3, 126.7 (q, ²*J*_{C-F} = 30.3 Hz), 124.3 (q, ¹*J*_{C-F} = 274.0 Hz), 123.8 (q, ³*J*_{C-F} = 5.2 Hz), 40.3, 27.2, 26.9, 22.5, 20.0, 14.2, -1.7; HRMS (ESI) Calcd for C₁₇H₂₇F₃NSi [M + H]⁺ 330.1865, found 330.1872.

1-(5-Methyl-2-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-one (2u): The reaction was performed using 0.45 mmol of trimethyl(vinyl)silane. The resulting mixture was hydrolyzed with HCl (3N, 1 mL) for 1 h and then subjected to workup and purification; Light yellow oil (67 mg, 81%; eluent: hexane/EtOAc = 50/1). *R_f* 0.70 (hexane/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 7.29 (s, 1H), 7.17-7.15 (m, 2H), 2.88-2.83 (m, 2H), 2.74-2.69 (m, 2H), 2.35 (s, 3H), 1.73-1.64 (m, 2H), 1.45-1.35 (m, 2H), 0.97-0.92 (m, 3H), 0.82-0.76 (m, 2H), 0.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 206.1, 142.0, 138.8, 135.1, 131.8, 130.3, 128.6, 42.2, 27.7, 26.8, 22.7, 21.2, 19.9, 14.2, -1.6; HRMS (ESI) Calcd for C₁₇H₂₉OSi [M + H]⁺ 277.1988, found 277.1986.

1-(3-(2-(trimethylsilyl)ethyl)naphthalen-2-yl)pentan-1-one (2v): The reaction was performed using 0.45 mmol of trimethyl(vinyl)silane. The resulting mixture was hydrolyzed with HCl (3N, 1 mL) for 1 h and then subjected to workup and purification; Light yellow oil (53 mg, 56%; eluent: hexane/EtOAc = 50/1); R_f 0.60 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 8.04 (s, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.69 (s, 1H), 7.54 – 7.50 (m, 1H), 7.48 – 7.44 (m, 1H), 3.05 – 2.99 (m, 2H), 2.98 – 2.93 (m, 2H), 1.79 – 1.71 (m, 2H), 1.50 – 1.39 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.89 – 0.84 (m, 2H), 0.06 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.6, 141.9, 137.7, 134.8, 131.2, 128.9, 128.6, 128.4, 127.9, 127.4, 126.1, 42.2, 28.4, 27.0, 22.8, 19.6, 14.2, -1.50; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{29}\text{OSi}$ $[\text{M} + \text{H}]^+$ 313.1988, found 313.1989.

Typical procedure for multiple alkylation of benzophenone N–H imine under conditions C: bis(2,6-bis(2-(trimethylsilyl)ethyl)phenyl)methanimine (4b): In a Schlenk tube were placed tris(3-fluorophenyl)phosphine (19.2 mg, 0.060 mmol), $\text{Co}(\text{acac})_2$ (7.7 mg, 0.030 mmol), pyridine (19 μL , 0.24 mmol), and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t\text{-BuCH}_2\text{MgBr}$ (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, diphenylmethanimine (**3a**, 55 mg, 0.30 mmol) and trimethyl(vinyl)silane (268 μL , 1.8 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through silica gel and washed with EtOAc (5 mL x 3). The filtrate was concentrated

under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 100/1/1) of the crude product afforded the title compound as a light yellow oil (148 mg, 85%).

R_f 0.90 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 10.03 (brs, 1H), 7.25 (t, J = 8.0 Hz, 2H), 7.11 (d, J = 7.7 Hz, 4H), 2.60-2.50 (m, 8H), 0.80-0.60 (m, 8H), -0.03 (s, 36H); ¹³C NMR (100 MHz, CDCl₃): δ 178.0, 143.8, 129.0, 127.2, 126.2, 28.4, 19.4, -1.6; HRMS (ESI) Calcd for C₃₃H₆₀NSi₄ [M + H]⁺ 582.3803, found 582.3802.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(4-methoxy-2,6-bis(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4c): Light yellow oil (178 mg, 97%; eluent: hexane/EtOAc/NEt₃ = 100/1/1). R_f 0.87 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.90 (brs, 1H), 7.22 (d, J = 7.7 Hz, 1H), 7.08 (d, J = 7.7 Hz, 2H), 6.64 (s, 2H), 3.81 (s, 3H), 2.49 – 2.44 (m, 8H), 0.72 – 0.65 (m, 8H), -0.05 (s, 36H); ¹³C NMR (100 MHz, CDCl₃): δ 177.7, 159.9, 146.0, 143.7, 140.6, 133.4, 128.9, 127.1, 112.5, 55.4, 28.7, 28.4, 19.4, 19.1, -1.5, -1.6; HRMS (ESI) Calcd for C₃₄H₆₂NOSi₄ [M + H]⁺ 612.3909, found 612.3907.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(4-fluoro-2,6-bis(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4d): Light yellow oil (176 mg, 98%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); R_f 0.89 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400

MHz, CDCl_3): δ 9.99 (brs, 1H), 7.24 (t, $J = 7.7$ Hz, 1H), 7.10 (d, $J = 7.7$ Hz, 2H), 6.82 (d, $J = 9.8$ Hz, 2H), 2.52-2.40 (m, 8H), 0.72-0.64 (m, 8H), -0.04 (s, 36H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.2, 163.2 (d, $J = 247.0$ Hz), 147.0, 143.6, 140.2, 136.1, 129.2, 127.3, 113.5 (d, $J = 21.5$ Hz), 28.6, 28.4, 19.5, 18.8, -1.56, -1.60; HRMS (ESI) Calcd for $\text{C}_{33}\text{H}_{59}\text{FNSi}_4$ $[\text{M} + \text{H}]^+$ 600.3709, found 600.3712.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(4-(methylthio)-2,6-bis(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4e): Light yellow oil (173 mg, 92%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.87 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.96 (brs, 1H), 7.23 (t, $J = 7.7$ Hz, 1H), 7.09 (d, $J = 7.7$ Hz, 2H), 6.99 (s, 2H), 2.52-2.40 (m, 11H), 0.72-0.64 (m, 8H), -0.04 (s, 36H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.5, 158.8, 144.6, 143.7, 139.1, 129.0, 127.2, 125.3, 116.5, 28.5, 28.4, 19.5, 19.2, 16.0, -1.6; HRMS (ESI) Calcd for $\text{C}_{34}\text{H}_{62}\text{NSi}_4\text{S}$ $[\text{M} + \text{H}]^+$ 628.3680, found 628.3682.

4-((2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(imino)methyl)-N,N-dimethyl-3,5-bis(2-

(trimethylsilyl)ethyl)aniline (4f): Light yellow oil (178 mg, 95%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.85 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.78 (b, 1H), 7.19 (t, $J = 7.6$ Hz, 1H), 7.06 (d, $J = 7.6$ Hz, 2H), 6.43 (s, 2H), 2.94 (s, 6H), 2.49-2.41 (m, 8H), 0.70-0.66 (m, 8H), -0.062 (s, 18H), -0.064 (s, 18H);

^{13}C NMR (100 MHz, CDCl_3): δ 178.0, 150.9, 145.0, 143.8, 141.0, 129.7, 128.6, 126.9, 111.5, 40.7, 28.8, 28.4, 19.4, 19.3, -1.5 (two peaks overlapped); HRMS (ESI) Calcd for $\text{C}_{35}\text{H}_{65}\text{N}_2\text{Si}_4$ $[\text{M} + \text{H}]^+$ 625.4225, found 625.4218.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(4-(trifluoromethoxy)-2,6-bis(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4g): Light yellow oil (200 mg, 100%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.87 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 10.05 (b, 1H), 7.27 (t, J = 7.7 Hz, 1H), 7.12 (d, J = 7.7 Hz, 2H), 6.99 (s, 2H), 2.55-2.45 (m, 8H), 0.74-0.66 (m, 8H), -0.02 (s, 18H), -0.03 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.1, 149.7, 146.6, 143.6, 140.1, 131.1 (q, $^3J_{\text{C-F}}$ = 7.7 Hz), 129.3, 127.4, 120.8 (q, $^1J_{\text{C-F}}$ = 258 Hz), 119.0, 28.6, 28.4, 19.5, 18.7, -1.60, -1.65; HRMS (ESI) Calcd for $\text{C}_{34}\text{H}_{59}\text{F}_3\text{NOSi}_4$ $[\text{M} + \text{H}]^+$ 666.3626, found 666.3629.

Bis(4-methoxy-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)methanimine (4h): Light yellow oil (183 mg, 95%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.85 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.76 (brs, 1H), 6.63 (s, 4H), 3.81 (s, 6H), 2.48-2.41 (m, 8H), 0.72-0.66 (m, 8H), -0.05 (s, 36H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.4, 159.8, 145.8, 112.4, 100.2, 55.4, 28.6, 19.2, -1.5; HRMS (ESI) Calcd for $\text{C}_{35}\text{H}_{64}\text{NO}_2\text{Si}_4$ $[\text{M} + \text{H}]^+$ 642.4014, found 642.4017.

Bis(4-fluoro-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)methanimine (4i): Light yellow oil (184 mg, 99%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.90 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.92 (brs, 1H), 6.85 (d, J = 9.7 Hz, 4H), 2.50-2.46 (m, 8H), 0.74-0.68 (m, 8H), -0.02 (s, 36H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.4, 163.2 (d, $^1J_{\text{C-F}}$ = 247.6 Hz), 146.8 (d, $^3J_{\text{C-F}}$ = 6.7 Hz), 136.2, 113.6 (d, $^2J_{\text{C-F}}$ = 21.3 Hz), 28.5, 18.9, -1.6; HRMS (ESI) Calcd for $\text{C}_{33}\text{H}_{58}\text{NF}_2\text{Si}_4$ $[\text{M} + \text{H}]^+$ 618.3614, found 618.3610.

(4-Fluoro-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)(4-methoxy-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)methanimine (4j): light yellow oil (160 mg, 85%; eluent: hexane/EtOAc/ NEt_3 = 100/1/1); R_f 0.87 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.54 (brs, 1H), 6.81 (d, J = 9.8 Hz, 2H), 6.64 (s, 2H), 3.81 (s, 3H), 2.50-2.39 (m, 8H), 0.73-0.64 (m, 8H), -0.04 (s, 18H), -0.05 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.9, 163.1 (d, $^1J_{\text{C-F}}$ = 246.9 Hz), 160.0, 146.8 (d, $^3J_{\text{C-F}}$ = 8.2 Hz), 145.7, 136.6, 133.3, 113.4 (d, $^2J_{\text{C-F}}$ = 21.2 Hz), 112.5, 55.4, 28.6, 28.5, 19.2, 18.8, -1.56, -1.59; HRMS (ESI) Calcd for $\text{C}_{34}\text{H}_{61}\text{FNOSi}_4$ $[\text{M} + \text{H}]^+$ 630.3814, found 630.3817.

(4,6-Bis(2-(trimethylsilyl)ethyl)benzo[d][1,3]dioxol-5-yl)(2,6-bis(2-(trimethylsilyl)ethyl)phenyl)methanimine (4l): Light yellow oil (156 mg, 83%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.79 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.90 (brs, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.7 Hz, 2H), 6.58 (s, 1H), 5.92 (s, 2H), 2.55-2.28 (m, 8H), 0.79-0.49 (m, 8H), -0.02 (s, 9H), -0.03 (s, 18H), -0.10 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 177.2, 147.5, 144.7, 143.7, 140.5, 138.5, 133.9, 128.9, 127.1, 126.5, 107.0, 101.0, 28.4, 28.3, 23.4, 19.4, 19.0, 17.7, -1.6; HRMS (ESI) Calcd for C₃₄H₆₀NO₂Si₄ [M + H]⁺ 626.3701, found 626.3705.

Bis(2,6-bis(2-(dimethyl(phenyl)silyl)ethyl)phenyl)methanimine (4m): Light yellow oil (227 mg, 91%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.80 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.93 (brs, 1H), 7.52 – 7.47 (m, 8H), 7.40 – 7.33 (m, 12H), 7.25 – 7.20 (m, 2H), 7.05 – 7.02 (m, 4H), 2.46 – 2.42 (m, 8H), 0.99 – 0.83 (m, 8H), 0.24 (m, 24H); ¹³C NMR (100 MHz, CDCl₃): δ 177.6, 143.6, 139.3, 133.8, 130.6, 129.1 (two signals overlapped), 128.0, 127.4, 28.4, 18.6, -2.9; HRMS (ESI) Calcd for C₅₃H₆₈NSi₄ [M + H]⁺ 830.4429, found 830.4428.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(2-methyl-6-(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4n): Light yellow oil (141 mg, 95%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.79 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 10.07 (s, 1H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 3H), 7.06 (d, *J* = 7.3 Hz, 1H), 2.60-2.38 (m, 6H), 2.31 (s, 3H), 0.78-0.58 (m, 6H), -0.02 (s, 18H), -0.04 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 178.2, 144.0, 143.7, 140.6, 140.1, 136.3, 129.3, 129.0, 128.9, 127.4, 127.0, 28.3, 28.2, 22.1, 19.4, 19.0, -1.6; HRMS (ESI) Calcd for C₂₉H₅₀NSi₃ [M + H]⁺ 496.3251, found 496.3257.

(4-Fluoro-2,6-bis(2-(trimethylsilyl)ethyl)phenyl)(2-methyl-6-(2-

(trimethylsilyl)ethyl)phenyl)methanimine (4o): Light yellow oil (151 mg, 98%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.79 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 10.05 (s, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 9.8 Hz, 2H), 2.59-2.37 (m, 6H), 2.28 (s, 3H), 0.72-0.63 (m, 6H), -0.03 (s, 27H); ¹³C NMR (100 MHz, CDCl₃): δ 177.4, 163.2 (d, ¹*J*_{C-F} = 247.1 Hz), 146.9 (d, ³*J*_{C-F} = 7.2 Hz), 143.8, 140.5, 136.1, 129.3, 129.0, 127.6, 116.7, 113.4 (d, ²*J*_{C-F} = 21.1 Hz), 28.4, 28.2, 22.0, 19.2, 18.8, -1.60, -1.64. HRMS (ESI) Calcd for C₂₉H₄₉FNSi₃ [M + H]⁺ 514.3157, found 514.3159.

Bis(5-methyl-2-(2-(trimethylsilyl)ethyl)phenyl)methanimine (4p): The reaction was performed using 0.90 mmol (3 equiv) of trimethyl(vinyl)silane; Light yellow oil (92 mg, 75% yield; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.75 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.71 (brs, 1H), 7.16-7.11 (m, 6H), 2.44-2.39 (m, 4H), 2.32 (s, 6H), 0.69-0.64 (m, 4H), -0.09 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 181.6, 140.4, 135.4, 132.1, 130.5, 130.0, 129.5, 27.6, 21.1, 19.2, -1.7; HRMS (ESI) Calcd for C₂₅H₄₀NSi₂ [M + H]⁺ 410.2699, found 410.2702.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(3,5-dimethylphenyl)methanimine (4q): The reaction was performed using 0.90 mmol (3 equiv) of trimethyl(vinyl)silane; Light yellow oil (87 mg, 71% yield; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.75 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.42 (brs, 1H), 7.30-7.25 (m, 3H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.07 (s, 1H), 2.41-2.35 (m, 4H), 2.29 (s, 6H), 0.82-0.57 (m, 4H), -0.13 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 178.6, 142.2, 138.8, 138.1, 132.8, 128.6, 128.1, 126.1, 125.8, 27.7, 21.4, 19.7, -1.8; HRMS (ESI) Calcd for C₂₅H₄₀NSi₂ [M + H]⁺ 410.2699, found 410.2703.

(2,6-Bis(2-(trimethylsilyl)ethyl)phenyl)(3-(2-(trimethylsilyl)ethyl)naphthalen-2-

yl)methanimine (4r): Light yellow oil (115 mg, 72%; eluent: hexane/EtOAc/NEt₃ = 100/1/1); *R_f* 0.78 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.89 (brs, 1H), 7.83-7.76 (m, 2H), 7.66-7.45 (m, 3H), 7.39-7.28 (m, 2H), 7.17-7.10 (m, 2H), 3.24 (brs, 2H), 2.46 (t, *J* = 8.8 Hz, 4H), 1.10-1.06 (m, 2H), 0.75 (brs, 4H), 0.10 (s, 9H), -0.13 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ 179.2, 143.2, 142.1, 141.1, 136.4, 134.3, 131.9, 131.3, 128.6, 128.5, 127.4, 127.1, 126.3 (two peaks overlapped), 125.5, 29.2, 27.8, 19.5, 19.1, -1.35, -1.67; HRMS (ESI) Calcd for C₃₂H₅₀NSi₃ [*M* + *H*]⁺ 532.3251, found 532.3254.

Typical procedure for N–H imine-directed hydroarylation of alkyl olefins: 1-(2-(3,3-

Dimethylbutyl)phenyl)-2,2-dimethylpropan-1-imine (5a). In a Schlenk tube were placed tris(3-methoxyphenyl)phosphine (21.2 mg, 0.060 mmol), Co(acac)₃ (10.8 mg, 0.030 mmol), pyridine (19 μL, 0.24 mmol) and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of *t*-BuCH₂MgBr (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, 2,2-dimethyl-1-phenylpropan-1-imine (**1g**, 48mg, 0.30 mmol) and 3,3-dimethylbut-1-ene (58 μL, 0.45 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through silica gel and washed with EtOAc (5 mL x 3). Silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 50/1/1) of the crude product afforded the title compound as a light

yellow oil (60 mg, 81%).

R_f 0.64 (hexane/EtOAc = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.19 (brs, 1H), 7.24-7.21 (m, 2H), 7.14-7.10 (m, 1H), 7.00 (d, J = 7.4 Hz, 1H), 2.47-2.41 (m, 2H), 1.48-1.42 (m, 2H), 1.23 (s, 9H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 141.6, 139.4, 129.6, 128.0, 126.2, 125.1, 46.7, 40.5, 30.9, 29.5, 29.2, 29.0; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{28}\text{O}$ $[\text{M} + \text{H}]^+$ 246.2222, found 246.2226.

1-(2-Hexylphenyl)-2,2-dimethylpropan-1-imine (5b): Light yellow oil (48 mg, 65%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.67 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.18 (brs, 1H), 7.25-7.23 (m, 2H), 7.15-7.10 (m, 1H), 7.00 (d, J = 7.6 Hz, 1H), 2.46 (d, J = 8.0 Hz, 2H), 1.60-1.52 (m, 2H), 1.38-1.25 (m, 6H), 1.22 (s, 9H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.6, 138.9, 129.4, 127.9, 126.2, 125.1, 40.6, 33.9, 31.9, 31.9, 29.7, 28.9, 22.8, 14.3; HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 246.2222, found 246.2224.

1-(2-Decylphenyl)-2,2-dimethylpropan-1-imine (5c): light yellow oil (51 mg, 54%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.70 (hexane/EtOAc = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.15 (brs, 1H), 7.24 (d, J = 4.8 Hz, 2H), 7.15-7.11 (m, 1H), 7.01 (d, J = 7.5 Hz, 1H), 2.48-2.44 (m, 2H), 1.62-1.51 (m, 2H), 1.32-1.21 (m, 23H), 0.88 (t, J = 6.9 Hz,

3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 139.0, 131.0, 129.4, 127.9, 126.2, 125.1, 40.6, 33.9, 32.1, 32.0, 30.0, 29.80, 29.7, 29.6, 28.9, 28.2, 22.9, 14.3; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{36}\text{N}$ $[\text{M} + \text{H}]^+$ 302.2848, found 302.2844.

1-(2-(2-Cyclohexylethyl)phenyl)-2,2-dimethylpropan-1-imine (5d): Light yellow oil (58.6 mg, 72%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.67 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.18 (brs, 1H), 7.23 (d, J = 3.8 Hz, 2H), 7.14-7.09 (m, 1H), 7.00 (d, J = 7.5 Hz, 1H), 2.49-2.44 (m, 2H), 1.75-1.62 (m, 5H), 1.48-1.42 (m, 2H), 1.31-1.11 (m, 13H), 0.97-0.86 (m, 2H).; ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.5, 139.2, 129.4, 127.9, 126.2, 125.0, 40.5, 40.0, 38.2, 33.5, 31.3, 29.0, 26.8, 26.5; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{30}\text{N}$ $[\text{M} + \text{H}]^+$ 272.2378, found 272.2380.

2,2-Dimethyl-1-(2-(4-phenylbutyl)phenyl)propan-1-imine (5e): Light yellow oil (60 mg, 68%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.64 (hexane/EtOAc = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.19 (brs, 1H), 7.30-7.23 (m, 4H), 7.20-7.12 (m, 4H), 7.02 (d, J = 7.4 Hz, 1H), 2.63 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 7.2 Hz, 2H), 1.71-1.61 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 142.6, 142.1, 138.6, 129.4, 128.6, 128.5, 128.0,

126.2, 125.9, 125.2, 40.6, 36.0, 33.8, 31.7, 31.5, 28.9; HRMS (ESI) Calcd for $C_{21}H_{28}N$ $[M + H]^+$ 294.2222, found 294.2227.

1-(2-(3-Cyclohexylpropyl)phenyl)-2,2-dimethylpropan-1-imine (5f): Light yellow oil (62 mg, 70%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.68 (hexane/EtOAc = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.12 (brs, 1H), 7.27-7.23 (m, 2H), 7.15-7.10 (m, 1H), 7.01 (d, J = 7.6 Hz, 1H), 2.47-2.41 (m, 2H), 1.72-1.54 (m, 7H), 1.26-1.10 (m, 15H), 0.91-0.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 141.5, 138.9, 129.3, 127.9, 126.1, 125.0, 40.5, 37.74, 37.68, 34.1, 33.5, 29.2, 28.9, 26.9, 26.6; HRMS (ESI) Calcd for $C_{20}H_{32}N$ $[M + H]^+$ 286.2535, found 286.2543.

2,2-Dimethyl-1-(2-(3-(trimethylsilyl)propyl)phenyl)propan-1-imine (5g): Light yellow oil (45 mg, 54%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1); R_f 0.69 (hexane/EtOAc = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.36 (brs, 1H), 7.44-7.41 (m, 2H), 7.34-7.29 (m, 1H), 7.20 (d, J = 7.6 Hz, 1H), 2.70-2.65 (m, 2H), 1.80-1.71 (m, 2H), 1.40 (s, 9H), 0.74-0.69 (m, 2H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 141.6, 138.8, 129.4, 127.9, 126.2, 125.1, 40.6, 37.8, 28.9, 26.5, 17.3, -1.5; HRMS (ESI) Calcd for $C_{17}H_{30}NSi$ $[M + H]^+$ 276.2148, found 276.2152.

1-(2-(2-(Cyclohex-3-en-1-yl)ethyl)phenyl)-2,2-dimethylpropan-1-imine (5h): Light yellow oil (58.2 mg, 72%; eluent: hexane/EtOAc/NEt₃ = 50/1/1); *R_f* 0.65 (hexane/EtOAc = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.19 (brs, 1H), 7.25-7.24 (m, 2H), 7.15-7.11 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 5.65 (s, 2H), 2.53-2.48 (m, 2H), 2.17-2.09 (m, 1H), 2.07-2.01 (m, 2H), 1.79-1.50 (m, 4H), 1.31-1.19 (m, 11H); ¹³C NMR (100 MHz, CDCl₃): δ 190.8, 141.6, 139.0, 129.4, 128.0, 127.3, 126.6, 126.2, 125.1, 40.6, 39.1, 34.0, 32.0, 31.4, 29.0, 29.0, 25.4; HRMS (ESI) Calcd for C₁₉H₂₈N [M + H]⁺ 270.2222, found 270.2222.

1-(2-(Cyclohexylmethyl)phenyl)-2,2-dimethylpropan-1-imine (5i): The resulting mixture was hydrolyzed with HCl (3N, 1 mL) for 1 h and then subjected to workup and purification; Light yellow oil (47.9 mg, 62%; eluent: hexane/EtOAc = 50/1); *R_f* 0.63 (hexane/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 7.39 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 2.44 (d, *J* = 7.0 Hz, 2H), 1.69-1.62 (m, 5H), 1.45 (s, 9H), 1.25-1.08 (m, 4H), 0.93-0.87 (m, 8H); ¹³C NMR (100 MHz, CDCl₃): δ 201.8, 137.6, 132.6, 130.9, 130.4, 126.0, 125.5, 42.1, 41.6, 38.8, 33.6, 29.2, 26.6, 26.4; HRMS (ESI) Calcd for C₁₈H₂₈N [M + H]⁺ 258.2222, found 258.2226.

1-(2-(((2R)-bicyclo[2.2.1]heptan-2-yl)phenyl)-2,2-dimethylpropan-1-imine (5j): light yellow oil (62 mg, 81%; eluent: hexane/EtOAc/NEt₃ = 30/1/1); *R_f* 0.60 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.15 (brs, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.28-7.23 (m, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 2.50 (t, *J* = 7.4 Hz, 1H), 2.35 (s, 1H), 1.81-1.44 (m, 5H), 1.33-1.16 (m, 13H); ¹³C NMR (100 MHz, CDCl₃): δ 191.4, 144.3, 141.6, 128.1, 126.4, 125.8, 124.9, 47.4, 45.1, 40.4, 36.7, 32.8, 31.6, 30.3, 29.1, 28.4; HRMS (ESI) Calcd for C₁₈H₂₆N [M + H]⁺ 256.2065, found 256.2071.

1-(2-(2-(9H-carbazol-9-yl)ethyl)phenyl)-2,2-dimethylpropan-1-imine (5k): Light yellow solid (81 mg, 76%; eluent: hexane/EtOAc/NEt₃ = 30/1/1); M.p. = 111 – 112 °C; *R_f* 0.51 (hexane/EtOAc = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 8.12 (d, *J* = 7.7 Hz, 2H), 7.51-7.46 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.33-7.22 (m, 5H), 7.15 (d, *J* = 8.0 Hz, 1H), 4.50-4.46 (m, 2H), 3.00-2.95 (m, 2H), 1.21 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.7, 141.7, 140.2, 134.9, 130.2, 128.4, 126.9, 126.4, 126.0, 123.1, 120.6, 119.2, 108.9, 45.2, 40.9, 33.6, 28.7; HRMS (ESI) Calcd for C₂₅H₂₇N₂ [M + H]⁺ 355.2174, found 355.2173.

2,2-Dimethyl-1-(2-(1-phenylethyl)phenyl)propan-1-imine (5I) and **2,2-dimethyl-1-(2-phenethylphenyl)propan-1-imine (5I')**: Light yellow oil (68 mg, 85% yield; eluent: hexane/EtOAc/NEt₃ = 50/1/1, **5I**:**5I'** = 55:45 as determined by ¹H NMR); *R_f* 0.60 (hexane/EtOAc = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 8.91 (brs, 1H, **5I** + **5I'**), 7.33–7.12 (m, 8H, **5I** + **5I'**), 7.04–6.96 (m, 1H, **5I** + **5I'**), 4.05 (brs, 1H, **5I**), 2.91–2.86 (m, 2H, **5I'**), 2.80–2.76 (m, 2H, **5I'**), 1.61 (d, *J* = 7.2 Hz, 3H, **5I**), 1.26 (s, 9H, **5I**), 1.20 (s, 9H, **5I'**); ¹³C NMR (100 MHz, CDCl₃, **5I** + **5I'**): δ 190.4, 146.3, 141.7, 141.3, 137.7, 130.9, 129.5, 128.7, 128.6, 128.2, 128.0, 127.6, 127.1, 126.4, 126.3, 125.7, 125.5, 47.4, 42.0, 40.64, 40.60, 38.3, 36.0, 32.8, 30.3, 29.2, 28.9, 23.0 (the number of the ¹³C NMR peaks are greater than expected from the molecular formulae presumably due to the presence of rotamers of **5I**); HRMS (ESI) Calcd for C₁₉H₂₄N [M + H]⁺ 266.1909, found 266.1906.

Deuterium-Labeling Experiments

The reaction of [D]₁₀-**3a** (58 mg, 0.3 mmol) and trimethyl(vinyl)silane (258 μ L, 0.3 mmol) was performed according to the typical procedure for **4b**. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 50/1/1) afforded the hydroarylation products. The product was analyzed by ¹H NMR to determine the distribution of the deuterium atoms.

The reaction of [D]₅-**1o** (58 mg, 0.3 mmol) and dimethyl(phenyl)(vinyl)silane (73 μ L, 0.3 mmol) was performed according to the typical procedure for **2h**. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 100/1/1) afforded the hydroarylation products. The product was analyzed by ¹H NMR to determine the distribution of the deuterium atoms.

4.5 References

¹ a) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826-834; b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624-655; c) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704-712; d) Crisenza, G. E. M.; Bower, J. F. *Chem. Lett.* **2016**, *45*, 2-9.

² a) Schinkel, M.; Marek, I.; Ackermann, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 3977-3980; *Angew. Chem.* **2013**, *125*, 4069-4072; b) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258-10261; c) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 5410-5413; *Angew. Chem.* **2014**, *126*, 5514-5517; d) Crisenza, G. E. M.; Sokolova, O. O.; Bower, J. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 14866-14870; *Angew. Chem.* **2015**, *127*, 15079-15083; e) Ebe, Y.; Nishimura, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899-5902; f) Hatano, M.; Ebe, Y.; Nishimura, T.; Yorimitsu, H. *J. Am. Chem. Soc.* **2016**, *138*, 4010-4013.

³ a) Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221-5223; b) Gao, K.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 6888-6892; *Angew. Chem.* **2011**, *123*, 7020-7024; c) Lee, P.-S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 17283-17295; d) Lee, P.-S.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 1240-1244; *Angew. Chem.* **2013**, *125*, 1278-1282; e) Dong, J.; Lee, P.-S.; Yoshikai, N. *Chem. Lett.* **2013**, *42*, 1140-1142; f) Xu, W.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2014**, *53*, 14166-14170; *Angew. Chem.* **2014**, *126*, 14390-14394; g) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M. *J. Am. Chem. Soc.* **2015**, *137*, 2448-2451; h) Fallon, B. J.; Garsi, J. B.; Derat, E.; Amatore, M.; Aubert, C.; Petit, M. *ACS Catal.* **2015**, *5*, 7493-7497; i) Fallon, B. J.; Derat, E.; Amatore, M.; Aubert, C.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Petit, M. *Org. Lett.* **2016**, *18*, 2292-2295; j) Yoshino, T.; Ikemoto, H.; Matsunaga, S.; Kanai, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 2207-2211; *Angew. Chem.* **2013**, *125*, 2263-2267.

⁴ Wong, M. Y.; Yamakawa, T. Yoshikai, N. *Org. Lett.* **2015**, *17*, 442-445.

- ⁵ a) Zhou, B.; Chen, H.; Wang, C. *J. Am. Chem. Soc.* **2013**, *135*, 1264-1267; b) Zhou, B.; Ma, P.; Chen, H.; Wang, C. *Chem. Commun.* **2014**, *50*, 14558-14561.
- ⁶ For reviews on cobalt-catalyzed C–H functionalization, see: a) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208-1219; b) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498-525.
- ⁷ a) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2013**, *135*, 9279-9282; b) Gao, K.; Lee, P.-S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234-4237.
- ⁸ a) Yoshikai, N.; Matsumoto, A.; Norinder, J.; Nakamura, E. *Angew. Chem. Int. Ed.* **2009**, *48*, 2925-2928; *Angew. Chem.* **2009**, *121*, 2969-2972; b) Yoshikai, N.; Asako, S.; Yamakawa, T.; Ilies, L.; Nakamura, E. *Chem. Asian J.* **2011**, *6*, 3059-3065.
- ⁹ a) Lim, S.-G.; Ahn, J.-A.; Jun, C.-H. *Org. Lett.* **2004**, *6*, 4687-4690; b) Jun, C.-H.; Hong, J.-B.; Kim, Y.-H.; Chung, K.-Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 3440-3442; *Angew. Chem.* **2000**, *112*, 3582-3584; c) Jun, C.-H.; Moon, C. W.; Hong, J.-B.; Lim, S.-G.; Chung, K.-Y.; Kim, Y.-H. *Chem. Eur. J.* **2002**, *8*, 485-492; d) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2005**, *70*, 6775-6781; e) Harada, H.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2008**, *73*, 6772-6779.
- ¹⁰ a) Oi, S.; Ogino, Y.; Fukita, S.; Inoue, Y. *Org. Lett.* **2002**, *4*, 1783-1785; b) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875-1877; c) Ackermann, L. *Org. Lett.* **2005**, *7*, 3123-3125.
- ¹¹ Kuninobu, Y.; Yu, P.; Takai, K. *Org. Lett.* **2010**, *12*, 4274-4276.
- ¹² a) Liu, W.; Zell, D.; John, M.; Ackermann, L. *Angew. Chem. Int. Ed.* **2015**, *54*, 4092-4096; *Angew. Chem.* **2015**, *127*, 4165-4169; b) Liu, W.; Richter, S. C.; Zhang, Y.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, *55*, 7747-7750; *Angew. Chem.* **2016**, *128*, 7878-7881.

- ¹³ a) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun.* **2009**, 5141-5143; b) He, R.; Huang, Z.-T.; Zheng, Q.-Y.; Wang, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 4950-4953; *Angew. Chem.* **2014**, *126*, 5050-5053.
- ¹⁴ a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2005**, *7*, 2229-2231; b) Jia, T.; Zhao, C.; He, R.; Chen, H.; Wang, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 5268-5271; *Angew. Chem.* **2016**, *128*, 5354-5357; c) Kim, J. H.; Gressies, S.; Glorius, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 5577-5581; *Angew. Chem.* **2016**, *128*, 5667-5671.
- ¹⁵ a) Sun, Z.-M.; Chen, S.-P.; Zhao, P. *Chem. Eur. J.* **2010**, *16*, 2619-2627; b) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 8181-8184; *Angew. Chem.* **2010**, *122*, 8357-8360; c) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 11098-11102; *Angew. Chem.* **2011**, *123*, 11294-11298; d) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 10630-10634; *Angew. Chem.* **2013**, *125*, 10824-10828; e) Zhang, J.; Ugrinov, A.; Zhao, P. *Angew. Chem. Int. Ed.* **2013**, *52*, 6681-6684; *Angew. Chem.* **2013**, *125*, 6813-6816.
- ¹⁶ a) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740-4761; b) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900-2936.
- ¹⁷ Klein, H.-F.; Camadanli, S.; Beck, R.; Leukel, D.; Flörke, U. *Angew. Chem. Int. Ed.* **2005**, *44*, 975-977; *Angew. Chem.* **2005**, *117*, 997-999.
- ¹⁸ Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M. Chatani, N. *Nature* **1993**, *366*, 529-531
- ¹⁹ He, R.; Huang, Z.-T.; Zheng, Q.-Y.; Wang, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 4950-4953.
- ²⁰ Sun, Z.-M.; Chen, S.-P.; Zhao, P. *Chem. Eur. J.* **2010**, *16*, 2619-2627.
- ²¹ Barbota, F.; Miginiaca, L. *Synth. Commun.* **1997**, *27*, 2601-2614.

- ²² Port, A.; Sanchez-Aris, M.; Cervelló, E.; Jaime, C.; Virgili, A.; Farriol, M.; Gallardo, I.; *Polycyclic Aromat. Compd.* **2003**, *23*, 457-470.
- ²³ Lee, J. H.; Gupta, S.; Jeong, W.; Rhee, Y. H.; Park, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 10851-10855.
- ²⁴ Keyaria, C. M.; Polta, R. *J. Carbohydr. Chem.* **2010**, *29*, 181-206.
- ²⁵ Zheng, G.; Ma, X.; Li, J.; Zhu, D.; Wang, M. *J. Org. Chem.* **2015**, *80*, 8910-8915.

Chapter 5. Cobalt-Catalyzed Regioselective Alkylation of N–H Imines with Styrene

5.1 Introduction

Alkene hydroarylation (addition of arenes to alkenes) through transition metal-catalyzed directed C–H activation has drawn significant attention as an atom- and step-economical synthetic approach to alkylated arenes. From the viewpoints of practicality and scope, this type of transformation has two major issues among others. First, catalysts used in such transformations are typically based on precious second and third row transition-metals, such as ruthenium, rhodium, and iridium,^{1, 2} and the use of earth-abundant first-row transition metals remains rare. Second, the reaction typically exhibits linear selectivity with 1-alkenes.^{2a, c, 3} It is not trivial to achieve the opposite, branched selectivity or to switch the regioselectivity at will, while notable progress has been made for branched-selective hydroarylation of styrenes and other alkenes.^{2b, d-f, 4}

Over the past several years, we have developed a series of cobalt-based catalytic systems for nitrogen-directed, branched- or linear-selective hydroarylation of styrenes. Cobalt-tricyclohexylphosphine or –triarylphosphine systems allow for the branched-selective styrene hydroarylation using 2-arylpyridines,⁵ aryl aldimines,⁶ and ketimines.⁷ On the other hand, the use of a bulky N-heterocyclic carbene (NHC) or a unique triarylphosphine featuring 2,4-dimethoxyphenyl groups enables the linear-selective styrene hydroarylation using 2-arylpyridines,⁵ or ketimines,⁸ respectively (Scheme 5.1). While these catalytic systems are considered to share the same, mutually competing reaction pathways leading to the branched or linear product, the generally preferred branched selectivity was ascribed to η^3 -benzyl coordination in the branched pathway. Meanwhile,

the linear selectivity observed with the specific ligands, i.e. 1,3-bis(2,4,6-trimethylphenyl)-imidazolium (IMes) and $\text{PPh}[2,4-(\text{MeO})_2\text{C}_6\text{H}_3]_2$ was rationalized by the large steric shielding of IMes ligand,^{5,9} and hemilabile coordination of *ortho*-methoxy substituent,⁸ respectively, which were assumed to work favorably for the linear alkylcobalt intermediate.

Scheme 5.1. Cobalt-catalyzed N-PMP imine directed styrene hydroarylation

The aromatic substrates thus far used for the cobalt-catalyzed styrene hydroarylation are rather limited, when synthetic utility is concerned. 2-Arylpyridines are not considered versatile substrates because of the difficulty with removal and modification of pyridine ring. Furthermore, aryl N-PMP ketimines are limited to those derived from less sterically unhindered aryl ketones such as acetophenone, propiophenone, and tetralone. Bulkier variants such as benzophenone and pivalophenone imines are nontrivial to use because of their difficult preparation, which is a common limitation for the other N-aryl and N-alkyl imine-directed C–H functionalizations regardless of the transition metal used.^{10,11,12,13,14}

As described in the previous chapter, we have demonstrated that N–H imine serves as a highly efficient directing group for cobalt-catalyzed hydroarylations of olefins,¹⁵ which also represents a notable example in the recent progress in the use of N–H imine as the directing group for C–H functionalization.¹⁶ While vinylsilanes and alkyl olefins were mainly explored as olefin substrates, we observed that the reaction of pivalophenone N–H

imine and styrene proceeded with equally good efficiency under a cobalt-triarylphosphine catalytic system, but produced a mixture of the branched and linear products in an almost 1:1 ratio (Scheme 5.2). In light of the intrinsic branched selectivity of cobalt-phosphine catalytic systems, which was broadly observed for N-PMP imine substrates, the lack of regioselectivity in this particular reaction appeared to originate from the nature of N-H imine substrate.^{7, 8}

Scheme 5.2. Pivalophenone N-H imine-directed styrene hydroarylation

Intrigued by the above regioselectivity, we have explored the scope and regioselectivity of N-H imine-directed olefin hydroarylation under cobalt catalysis, which is reported in this chapter (Scheme 5.3). Exploration of a series of N-H imines derived from benzophenone derivatives and aryl alkyl ketones led to lines of intriguing observation regarding the linear/branched selectivity and the regioselectivity of C-H activation, which shed light on factors influencing these selectivities. Among the most notable observations is the reaction of an unsymmetrical benzophenone imines, which resulted in selective and exclusive monoalkylation of one of the aryl rings, regardless of their subtle electronic/steric difference.¹⁵

Scheme 5.3 Cobalt-catalyzed N–H imine-directed styrene hydroarylation

5.2 Results and Discussion

The present study commenced with screening of reaction conditions for the addition of benzophenone N–H imine (**1a**) to styrene (**2a**, 1.5 equiv) (Table 5.1). Various triarylphosphine ligands (20 mol%) were screened using CoBr_2 (10 mol%) as the cobalt source and $t\text{-BuCH}_2\text{MgBr}$ (50 mol%) as the reductant. The reaction using triphenylphosphine afforded the mono-alkylation product **3aa** in moderate yield with exclusively branched selectivity, accompanied by a trace amount of the dialkylation product **3aa'** (entry 1). $\text{P}(\text{4-FC}_6\text{H}_4)_3$, previously used for the N-aryl imine-directed hydroarylation of styrene,⁷ gave rise to a higher efficiency albeit with lower selectivity for the monoalkylation product **3aa**. Though highly effective for the N–H imine-directed hydroarylation of vinylsilane and alkyl alkene (*cf.* Chapter 4),¹⁵ $\text{P}(\text{3-MeOC}_6\text{H}_4)_3$ and $\text{P}(\text{3-FC}_6\text{H}_4)_3$ did not improve the present reaction (entries 3 and 4). Eventually, $\text{P}(\text{3-ClC}_6\text{H}_4)_3$ was identified as the optimum ligand for the mono-selective alkylation, affording **3aa** and **3aa'** in 45% and 3% yields, respectively (entry 6). The cobalt source was found to have dramatic influence on the catalytic activity, as was the case for vinylsilane hydroarylation.¹⁵ While the reaction became sluggish using CoCl_2 or CoI_2 (entries 7 and 8), the use of cobalt acetylacetonate salts, $\text{Co}(\text{acac})_2$, and $\text{Co}(\text{acac})_3$, led to apparently higher catalytic activity

with an increased amount of the dialkylation product **3aa'** (entries 9 and 10). In terms of the selectivity toward monoalkylation, Co(acac)₂ was designated as the optimal cobalt source for the present reaction, affording **3aa** in an isolated yield of 76%.

Table 5.1. Effect of reaction conditions on addition of benzophenone N–H imine (**1a**) to styrene (**2a**).

<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;"> <p>1a</p> </div> <div style="text-align: center;"> <p>CoX_n (10 mol%) L (10-20 mol%) <i>t</i>-BuCH₂MgBr (50 mol%) styrene (2a) (1.5 equiv)</p> <hr style="width: 50%; margin: 0 auto;"/> <p>THF, rt, 12 h</p> </div> <div style="text-align: center;"> <p>3aa</p> </div> <div style="text-align: center;"> <p>3aa'</p> </div> </div>				
entry	CoX _n	L	yield% ^a (3aa)	yield% ^a (3aa')
1	CoBr ₂	PPh ₃	38	5
2	CoBr ₂	P(4-FC ₆ H ₄) ₃	23	14
3	CoBr ₂	P(3-MeOC ₆ H ₄) ₃	20	-
4	CoBr ₂	P(3-FC ₆ H ₄) ₃	33	8
5	CoBr ₂	P(4-ClC ₆ H ₄) ₃	15	-
6	CoBr ₂	P(3-ClC ₆ H ₄) ₃	45	3
7	CoCl ₂	P(3-ClC ₆ H ₄) ₃	8	-
8	CoI ₂	P(3-ClC ₆ H ₄) ₃	26	-
9	Co(acac) ₃	P(3-ClC ₆ H ₄) ₃	54	21
10	Co(acac) ₂	P(3-ClC ₆ H ₄) ₃	76 ^b	9

^a The data was determined with GC using tridecane as the internal standard. ^b Isolated yield.

With the optimized conditions in hand, the scope of diaryl- and aryl-alkyl imines for the styrene hydroarylation was studied (Table 5.2). Various *para*-substituted benzophenone imines participated in the alkylation reaction with styrene, affording the branched products **3ba-3fa** in good yields. Notably, unsymmetrical diaryl imines bearing phenyl and *para*-substituted (OMe, F, or SMe) phenyl groups underwent selective alkylation on the latter benzene ring (see **3ba-3da**). Furthermore, diaryl imine bearing *para*-

methoxyphenyl- and *para*-tolyl groups was selectively alkylated on the former aryl group in good yield (see **3ea**). Such high regioselectivity observed for unsymmetrical diaryl N–H imines with moderate electronic bias is remarkable when compared to other reported C–H functionalization reactions of diaryl N–H imine, where aryl groups of substantial electronic difference (e.g., phenyl and *para*-nitrophenyl) is necessary to achieve high regioselectivity. For diaryl imines bearing phenyl and *meta*-substituted (Me or CF₃) phenyl groups, the alkylation took place exclusively at the *ortho* position of the phenyl group regardless of the *meta*-substituent, affording the branched products **3ga** and **3ha** in good yields. The reaction of di(*meta*-tolyl) imine occurred at the less hindered *ortho* position to afford the branched product **3ia** in somewhat lower yield. Interestingly, the presence of a 3,4-methylenedioxy group on one of the aryl groups of diaryl imine led the exclusive alkylation at the proximity of the ether functionality.^{15, 17} with a moderate preference (4:1) for the linear alkylation product **3ja'**.

Monoalkylation of *para*-substituted phenyl butyl N–H imines took place smoothly to afford, upon hydrolysis, the ketone products **3ka–3na** in good yields with moderate to high branched selectivity (b/l = 4/1 to 12/1). As expected from the case for **3ja'**, the reaction of 3,4-methylenedioxyphenyl butyl N–H imine proceeded with the same sense of regioselectivity of C–H activation and hydroarylation, thus affording the product **3qa'** with high linear selectivity. The fluorine atom of *meta*-fluorophenyl butyl N–H imine exhibited the same effect as the 3,4-methylenedioxy group did (see **3oa'**). Thus, the secondary directing effect of the *meta*-oxygen and -fluorine would have not only controlled the site of C–H activation but also played a major role in reversing the intrinsic branched selectivity. On the other hand, the reaction of *meta*-trifluoromethylphenyl butyl N–H imine occurred at the less hindered *ortho* position, selectively affording the branched product **3pa** in good yield. While our preliminary experiment showed poor linear/branched selectivity for

pivalophenone imine (Scheme 5.2), the regioselectivity for such substrates could be dramatically changed by bis(2,5-dimethoxyphenyl)(phenyl)phosphane (**L1**). By using this ligand exclusively linear-selective addition was achieved to afford the products **3ra'** and **3sa'** in high yield. was the case of **3ja'**, phenyl *n*-butyl N-H imine bearing a 3,4-methylenedioxy group took part in the alkylation at the proximal *ortho* position in better linear-selectivity (see **3qa'**).

Table 5.2. Addition of N-H imines to styrene.^a

^a Unless otherwise noted, the reaction was performed using 0.3 mmol of imine and 0.45 mmol (1.5 equiv) of styrene, followed by acidic hydrolysis (for the ketone products) or

direct purification (for the imine products). ^b Bis(2,5-dimethoxyphenyl)(phenyl)phosphine (**L1**) (20 mol%) was used as the ligand.

Next, various styrene derivatives were examined to react with the unsymmetrical benzophenone N–H imine **1b**. As summarized in Table 5.3, styrenes bearing *para*-methyl, *t*-butyl, methoxy, fluoro, chloro, methylthio, and trimethylsilyl groups afforded the branched hydroarylation products **3bb–3bh** in good yields. The present catalytic system was also applicable to *meta*-methyl, fluoro, methoxy, and chloro-substituted styrenes, which afforded the corresponding adducts **3bi–3bl** in good yields. *ortho*-Substituted styrenes also participated in the reaction with **1b** (see **3bm** to **3bo**). Note that all these reactions again took place exclusively at the *ortho* position of *para*-methoxyphenyl group.

Table 5.3. Addition of styrene derivatives to benzophenone imine^a

^a Reaction conditions: **1b** (0.3 mmol), styrene (0.45 mmol, 1.5 equiv), $[\text{Co}(\text{acac})_2]$ (10 mol%), $\text{P}(\text{3-ClC}_6\text{H}_4)_3$ (20 mol%), $t\text{-BuCH}_2\text{MgBr}$ (50 mol%), THF at room temperature for 12 h.

To gain insight into the mechanism, the reaction of deuterated benzophenone imine $[\text{D}_{10}]$ -**1a** and 4-methoxystyrene (**2d**) was examined under the standard conditions (Scheme 5.4). The desired product was afforded in good yield with significant H/D scrambling. Substantial deuterium incorporation was observed at the methyl and methine position, with ^1H NMR integrations of 1.10H and 0.47H, respectively. Meanwhile, the deuterium contents at the remaining three *ortho*-positions decreased significantly, as indicated by ^1H NMR

integrations of 0.43H for the *ortho* position of the alkylated benzene ring and 1.38H for the *ortho* positions of the non-alkylated benzene ring.

A plausible catalytic cycle involves reversible oxidative addition of C–H bond to low-valent cobalt species, reversible and competitive selective styrene insertion steps to give branched (**A**) or linear (**B**) intermediates, and irreversible reductive elimination steps (Scheme 5.5). The reversibility of the first two steps as well as the competitiveness of the two insertion pathways would account for H/D scrambling observed in the labeling experiment. At least for parent benzophenone imine and sterically and electronically unbiased aryl alkyl imines, it would be reasonable to assume that the rate- and the linear/branched selectivity are determined in the reductive elimination.⁸

Scheme 5.4. Deuterium-labeling experiments

Scheme 5.5. Proposed catalytic cycle

Besides the above general mechanistic picture, we are tempted to comment on the regioselectivity of C–H functionalization and/or hydroarylation observed for some specific cases. First, the reactions of *meta*-oxygen or fluorine-substituted imines could be rationalized in terms of secondary directing effect. Thus, Co–O (or Co–F) interaction would not only favor cyclometalation at its proximity but also stabilize the linear alkylcobalt intermediate **A'**, while interfering the η^3 -benzyl coordination in the branched intermediate **B'**, which would lead to preferential formation of the linear product, such as **3ja'**, **3oa'**, and **3qa'** (Figure 5.1). Second, the highly linear selective reaction of pivalophenone imines (**3ra'** and **3sa'**) could be attributed to the bulky imine and the nature of **L1**. The bulkiness of the imine group would destabilize the more congested branched intermediate, while the *ortho*-methoxy group of **L1** would serve as a hemilabile ligand to Co to stabilize the linear intermediate. Lastly, the striking regioselectivity of C–H alkylation for unsymmetrical diaryl imines **1b–1e** is not trivial to rationalize. The methoxy, fluoro, and methylthio groups

in these substrates, located in the *meta* position of the C–H bond to be cleaved, would act as moderately electron-withdrawing groups to accelerate the C–H oxidative addition, while their possible role to accelerate other elementary steps could not be excluded.

Figure 5.1. Proposed intermediates for branched and linear selectivity (X = O or F)

The present alkylation products are amenable to further alkylation on the remaining *ortho*-C–H bond using our previously reported methods (*cf.* Chapter 4; Scheme 5.6).¹⁵ The reaction of alkylated benzophenone imine **3ba** with vinylsilane under the catalytic system developed for benzophenone imine resulted in monoalkylation of unhindered phenyl group, affording the product **4** in good yield and regioselectivity (5/1). Likewise, the reaction of alkylated aryl butyl imine **3ma** with vinylsilane under appropriate conditions furnished unsymmetrically dialkylation product **5** in good yield.

Scheme 5.6. Further alkylation of the mono-alkylation products with vinylsilane.

5.3 Conclusion

In summary, we have demonstrated that N–H imine is an effective directing group for the hydroarylation of styrenes under cobalt-phosphine catalysis. For a variety of diaryl and aryl alkyl N–H imines, the reaction proceeded smoothly to afford the corresponding branched adducts in good yield and regioselectivity. Strikingly, exclusive positional selectivity of C–H alkylation was observed for some unsymmetrical diaryl imines with modest electronic and no steric biases. Furthermore, the intrinsic branched selectivity was reserved by several factors such as the presence of a secondary directing group, the bulkiness of the imine directing group, and the nature of the phosphine ligand. The mechanistic origins of the observed regioselectivities and their synthetic implications would deserve further exploration.

5.4 Experimental Section

Preparation of Starting Materials

Preparation of Aryl Imines

All the imines **1a–1s** shown below were synthesized according to the literature procedures^{16c, h} and purified by recrystallization or distillation. ¹H and ¹³C-NMR spectra of the known imines showed good agreement with the literature data.^{16c, h, 15}

Cobalt-Catalyzed N–H Imine-Directed Styrene Hydroarylation

Typical Procedure: phenyl(2-(1-phenylethyl)phenyl)methanimine (3aa). In a Schlenk tube were placed tris(3-chlorophenyl)phosphine (22 mg, 0.060 mmol), $\text{Co}(\text{acac})_2$ (7.7 mg, 0.030 mmol), and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t\text{-BuCH}_2\text{MgBr}$ (1.0 M in THF, 0.15 mL, 0.15 mmol). After

stirring for 30 min, diphenylmethanimine (**1a**, 55 mg, 0.30 mmol) and styrene (**2a**, 52 μ L, 0.45 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through silica gel and washed with EtOAc (5 mL x 3). The filtrate was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 50/1/1) of the crude product afforded the title compound as a light yellow oil (65 mg, 76%).

R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.45 (brs, 1H), 7.68 (d, J = 6.5 Hz, 2H), 7.49 – 7.42 (m, 1H), 7.41 – 7.35 (m, 4H), 7.23 – 7.16 (m, 4H), 7.15 (s, 1H), 7.07 (d, J = 7.8 Hz, 2H), 4.12 (q, J = 6.7 Hz, 1H), 1.52 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.8, 145.8, 143.4, 140.5, 138.8, 131.2, 129.9, 129.3, 128.6, 128.5, 128.4, 127.9, 127.7, 126.4, 126.3, 41.2, 22.5; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{20}\text{N}$ $[\text{M} + \text{H}]^+$ 286.1596, found 286.1598.

(4-Methoxy-2-(1-phenylethyl)phenyl)(phenyl)methanimine (3ba): Light yellow oil (88 mg, 92%; eluent: hexane/EtOAc/ NEt_3 = 30/1/1). R_f 0.42 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 8.74 (brs, 1H), 7.69 – 7.63 (m, 2H), 7.48 – 7.42 (m, 1H), 7.40 – 7.34 (m, 2H), 7.24 – 7.17 (m, 2H), 7.16 – 7.07 (m, 4H), 6.91 (d, J = 2.6 Hz, 1H), 6.80 (dd, J = 8.4, 2.6 Hz, 1H), 4.15 (q, J = 7.1 Hz, 1H), 3.82 (s, 3H), 1.52 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.6, 160.3, 145.7, 145.4, 139.3, 133.3, 131.0, 129.5, 128.51, 128.49, 128.4, 127.6, 126.3, 114.0, 111.0, 55.4, 41.2, 22.4; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{22}\text{NO}$ $[\text{M} + \text{H}]^+$ 316.1701, found 316.1704.

(4-Fluoro-2-(1-phenylethyl)phenyl)(phenyl)methanimine (3ca): Light yellow oil (61 mg, 77%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.51 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.41 (brs, 1H), 7.75 – 7.60 (m, 2H), 7.50 – 7.43 (m, 1H), 7.40 – 7.36 (m, 2H), 7.25 – 7.20 (m, 2H), 7.17 – 7.11 (m, 2H), 7.11 – 7.03 (m, 3H), 6.96 (td, J = 8.3, 2.7 Hz, 1H), 4.34 – 4.03 (m, 1H), 1.51 (d, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 177.88, 163.3 (d, $^1J_{\text{C-F}}$ = 248.1 Hz), 155.2, 147.1, 145.0, 137.46 (d, $^3J_{\text{C-F}}$ = 3.3 Hz), 131.8 (two signals overlapped), 128.64 (two signals overlapped), 128.56 (d, $^3J_{\text{C-F}}$ = 1.9 Hz), 127.57, 126.54, 114.83 (d, $^2J_{\text{C-F}}$ = 21.7 Hz), 113.46 (d, $^2J_{\text{C-F}}$ = 21.7 Hz), 41.3, 22.3; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{19}\text{FN}$ $[\text{M} + \text{H}]^+$ 304.1502, found 304.1502.

(4-(Methylthio)-2-(1-phenylethyl)phenyl)(phenyl)methanone (3da): Typical procedure for 3aa was applied to (4-(methylthio)phenyl)(phenyl)methanimine (**1d**) and styrene. After 12 h, The reaction mixture was then quenched by the addition of HCl (3 N, 1.0 mL), and stirred for 1 h. The resulting mixture was extracted with EtOAc (5 mL x 3). The organic layer was dried over MgSO_4 and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 30/1) of the crude product afforded the title compound as a light yellow oil (72 mg, 72%, b/l = 13/1 as determined by ^1H NMR).

R_f 0.49 (hexane/EtOAc/ NEt_3 = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.72 – 7.67 (m, 2H), 7.57 – 7.51 (m, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.21 (d, J = 1.8 Hz, 1H), 7.19 – 7.11 (m, 5H),

7.11 – 7.05 (m, 2H), 4.55 (q, $J = 7.2$ Hz, 1H), 2.47 (s, 3H), 1.60 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.5, 146.6, 145.4, 141.9, 138.2, 135.4, 133.3, 130.4, 129.4, 128.4, 128.5, 128.1, 126.3, 125.7, 122.5, 40.4, 22.1, 15.4; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{21}\text{OS}$ $[\text{M} + \text{H}]^+$ 333.1313, found 333.1316.

(4-Fluoro-2-(1-phenylethyl)phenyl)(phenyl)methanimine (3ea): Light yellow oil (76 mg, 77%; eluent: hexane/EtOAc/ $\text{NEt}_3 = 50/1/1$). R_f 0.45 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.23 (brs, 1H), 7.70 – 7.42 (m, 2H), 7.24 – 7.05 (m, 8H), 6.90 – 6.86 (m, 1H), 6.78 (dd, $J = 8.4, 2.6$ Hz, 1H), 4.27 – 4.00 (m, 1H), 3.81 (s, 3H), 2.40 (s, 3H), 1.51 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.4, 160.2, 145.7, 141.4, 136.5, 129.2, 128.5 (two signals overlapped), 127.7, 127.6, 127.1, 126.2, 114.0, 113.8, 111.0, 55.4, 41.2, 22.4, 21.6; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{24}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 330.1858, found 330.1861.

(4-Fluoro-2-(1-phenylethyl)phenyl)(phenyl)methanimine (3fa): Light yellow oil (76 mg, 77%; eluent: hexane/EtOAc/ $\text{NEt}_3 = 50/1/1$). R_f 0.31 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.05 (brs, 1H), 7.61 (d, $J = 8.7$ Hz, 2H), 7.23 – 7.16 (m, 2H), 7.15 – 7.05 (m, 4H), 6.90 – 6.82 (m, 3H), 6.77 (dd, $J = 8.4, 2.6$ Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 1.50 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3):

δ 177.8, 162.0, 160.2, 145.8, 133.6, 131.9, 130.2, 129.3, 128.5 (two signals overlapped), 127.6, 126.3, 114.0, 113.8, 111.0, 55.5, 41.3, 22.5; HRMS (ESI) Calcd for $C_{23}H_{24}NO_2$ [$M + H$] $^+$ 346.1807, found 346.1809.

(2-(1-Phenylethyl)phenyl)(m-tolyl)methanimine (3ga): Light yellow oil (57 mg, 63%; eluent: hexane/EtOAc/ NEt_3 = 20/1/1). R_f 0.51 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.35 (brs, 1H), 7.70 – 7.49 (m, 1H), 7.44 – 7.35 (m, 3H), 7.27 – 7.24 (m, 3H), 7.18 (d, J = 7.6 Hz, 3H), 7.17 – 7.08 (m, 1H), 7.10 – 7.07 (m, 2H), 4.26 – 3.94 (m, 1H), 2.35 (s, 3H), 1.52 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.0, 145.9, 138.6, 138.3, 132.0, 130.0, 129.2, 128.6, 128.5 (two signals overlapped), 128.4, 127.9, 127.8, 127.7, 127.6, 126.3, 126.2, 41.2, 22.6, 21.6; HRMS (ESI) Calcd for $C_{22}H_{22}N$ [$M + H$] $^+$ 300.1752, found 300.1756.

(2-(1-Phenylethyl)phenyl)(3-(trifluoromethyl)phenyl)methanimine (3ha): Light yellow oil (88 mg, 83%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.51 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.49 (brs, 1H), 7.77 – 7.59 (m, 3H), 7.52 – 7.45 (m, 3H), 7.40 (t, J = 7.4 Hz, 2H), 7.22 (t, J = 7.3 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.08 – 7.04 (m, 2H), 4.41 – 3.96 (m, 1H), 1.54 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 147.7, 144.8, 140.8, 138.1, 131.6, 130.6, 130.4, 128.8, 128.7,

128.6 (two signals overlapped), 128.2 (br), 127.6, 126.7, 126.1 (q, $^2J_{C-F} = 3.7$ Hz), 125.5, 124.9, 124.1 (q, $^1J_{C-F} = 272.2$ Hz), 41.2, 22.3; HRMS (ESI) Calcd for $C_{22}H_{19}F_3N$ $[M + H]^+$ 354.1470, found 354.1472.

(5-Methyl-2-(1-phenylethyl)phenyl)(m-tolyl)methanimine (3ia): Light yellow oil (53 mg, 56%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.55 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.40 (brs, 1H), 7.53 (s, 1H), 7.47 – 7.36 (m, 1H), 7.29 – 7.22 (m, 3H), 7.22 – 7.17 (m, 3H), 7.14 – 7.05 (m, 3H), 6.99 (s, 1H), 4.08 (q, $J = 7.0$ Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 1.50 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 146.2, 138.8, 138.3, 136.0, 131.9, 130.0, 128.8, 128.6, 128.5, 128.4, 128.4, 127.8, 127.6 (two signals overlapped), 126.2, 125.8, 40.9, 22.6, 21.6, 21.1; HRMS (ESI) Calcd for $C_{23}H_{24}N$ $[M + H]^+$ 314.1909, found 314.1907.

(5-Methyl-2-(1-phenylethyl)phenyl)(m-tolyl)methanimine (3ja): Light yellow oil (73 mg, 74%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1; l/b = 4/1 as determined by 1H NMR). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.33 (brs, 1H), 7.73 – 7.57 (m, 2H), 7.51 – 7.42 (m, 1H), 7.42 – 7.32 (m, 3H), 7.23 – 7.17 (m, 2H), 7.19 – 7.11 (m, 1H), 6.96 (d, $J = 7.0$ Hz, 2H), 6.75 (s, 2H), 6.01 (s, 2H), 2.91 – 2.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 147.7, 146.6, 141.6, 139.4, 135.2, 132.2, 131.0, 128.6, 128.6,

128.4, 128.3, 126.2, 122.2, 106.6, 101.4, 35.7, 30.1; HRMS (ESI) Calcd for $C_{22}H_{20}NO_2$ $[M + H]^+$ 330.1494, found 330.1497.

1-(2-(1-Phenylethyl)phenyl)pentan-1-one (3ka): 1-(2-(1-Phenylethyl)phenyl)pentan-1-one (3ka): Light yellow oil (61 mg, 76%; eluent: hexane/EtOAc = 50/1; b/l = 8/1 as determined by 1H NMR). R_f 0.58 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.32 (m, 3H), 7.29 – 7.20 (m, 3H), 7.17 – 7.12 (m, 3H), 4.73 (q, J = 7.1 Hz, 1H), 2.78 – 2.65 (m, 1H), 2.54 – 2.39 (m, 1H), 1.61 (d, J = 7.2 Hz, 3H), 1.55 – 1.45 (m, 2H), 1.27 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.2, 146.4, 144.8, 140.4, 130.6, 128.5, 128.4, 128.3, 127.1, 126.2, 125.9, 42.8, 39.9, 26.3, 22.5, 22.3, 14.1; HRMS (ESI) Calcd for $C_{19}H_{23}O$ $[M + H]^+$ 267.1749, found 267.1746.

1-(4-Fluoro-2-(1-phenylethyl)phenyl)pentan-1-one (3la): Light yellow oil (72 mg, 82%; eluent: hexane/EtOAc = 50/1; b/l = 4/1 as determined by 1H NMR). R_f 0.58 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.45 (dd, J = 8.6, 5.8 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.20 – 7.12 (m, 3H), 7.03 (dd, J = 10.6, 2.6 Hz, 1H), 6.95 – 6.89 (m, 1H), 4.85 (q, J = 7.1 Hz, 1H), 2.77 – 2.68 (m, 1H), 2.53 – 2.44 (m, 1H), 1.59 (d, J = 7.1 Hz, 3H), 1.56 – 1.46 (m, 2H), 1.34 – 1.21 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.4, 164.1 (d, $^1J_{C-F}$ = 250.9 Hz), 149.0 (d, $^3J_{C-F}$ = 7.3 Hz), 145.7, 136.0 (d, $^4J_{C-F}$ = 3.2 Hz), 129.8

(d, $^3J_{C-F}$ = 8.9 Hz), 128.6, 128.2, 126.4, 115.7 (d, $^2J_{C-F}$ = 22.0 Hz), 112.8 (d, $^2J_{C-F}$ = 21.6 Hz), 42.6, 39.8, 26.4, 22.5, 22.1, 14.1; HRMS (ESI) Calcd for $C_{19}H_{22}FO$ $[M + H]^+$ 285.1655, found 285.1656.

1-(4-Methoxy-2-(1-phenylethyl)phenyl)pentan-1-one (3ma): Light yellow oil (75 mg, 84%; eluent: hexane/EtOAc = 50/1; b/l = 8/1 as determined by 1H NMR). R_f 0.45 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 8.6 Hz, 1H), 7.28 – 7.21 (m, 2H), 7.20 – 7.12 (m, 3H), 6.85 (d, J = 2.5 Hz, 1H), 6.73 (dd, J = 8.6, 2.5 Hz, 1H), 5.01 (q, J = 7.1 Hz, 1H), 3.79 (s, 3H), 2.81 – 2.72 (m, 1H), 2.65 – 2.56 (m, 1H), 1.59 (d, J = 7.0 Hz, 3H), 1.57 – 1.48 (m, 2H), 1.34 – 1.22 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.9, 161.6, 148.9, 146.4, 132.0, 130.4, 128.4, 128.2, 126.1, 115.2, 110.1, 55.4, 42.0, 39.7, 26.8, 22.6, 22.2, 14.1; HRMS (ESI) Calcd for $C_{20}H_{25}O_2$ $[M + H]^+$ 297.1855, found 297.1856.

1-(4-(Methylthio)-2-(1-phenylethyl)phenyl)pentan-1-one (3na): Light yellow oil (58 mg, 62%; eluent: hexane/EtOAc = 50/1; b/l = 12/1 as determined by 1H NMR). R_f 0.50 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.2 Hz, 1H), 7.32 – 7.21 (m, 2H), 7.18 – 7.12 (m, 4H), 7.07 (dd, J = 8.2, 1.9 Hz, 1H), 4.88 (q, J = 7.2 Hz, 1H), 2.77 – 2.67 (m, 1H), 2.57 – 2.47 (m, 1H), 2.45 (s, 3H), 1.60 (d, J = 7.2 Hz, 3H), 1.55 – 1.45

(m, 2H), 1.32 – 1.21 (m, 2H), 0.87 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.7, 146.3, 146.1, 142.5, 136.1, 128.5, 128.4, 128.2, 126.2, 126.0, 122.70, 42.3, 39.7, 26.6, 22.5, 22.2, 15.3, 14.1; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{25}\text{OS}$ $[\text{M} + \text{H}]^+$ 313.1626, found 313.1621.

1-(3-Fluoro-2-phenethylphenyl)pentan-1-one (3oa): Light yellow oil (70 mg, 82%; eluent: hexane/EtOAc = 50/1; $b/l = 1/13$ as determined by ^1H NMR). R_f 0.55 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.35 – 7.12 (m, 8H), 3.11 – 3.05 (m, 2H), 2.92 – 2.84 (m, 2H), 2.75 – 2.69 (m, 2H), 1.69 – 1.58 (m, 2H), 1.42 – 1.32 (m, 2H), 0.94 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 204.5, 162.0 (d, $^1J_{\text{C-F}} = 246.3$ Hz), 145.8 (d, $^2J_{\text{C-F}} = 19.0$ Hz), 142.0, 141.5 (d, $^3J_{\text{C-F}} = 3.9$ Hz), 128.9, 128.6, 127.3 (d, $^3J_{\text{C-F}} = 8.7$ Hz), 126.2, 123.6 (d, $^3J_{\text{C-F}} = 3.4$ Hz), 118.0 (d, $^2J_{\text{C-F}} = 23.5$ Hz), 42.2, 37.0, 28.4 (d, $^3J_{\text{C-F}} = 3.6$ Hz), 26.6, 22.6, 14.2; HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{22}\text{FO}$ $[\text{M} + \text{H}]^+$ 285.1655, found 285.1657.

1-(2-(1-Phenylethyl)-5-(trifluoromethyl)phenyl)pentan-1-one (3pa): Light yellow oil (81 mg, 81%; eluent: hexane/EtOAc = 50/1; $b/l = 7/1$ as determined by ^1H NMR). R_f 0.55 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.65 – 7.57 (m, 2H), 7.46 (d, $J =$

8.1 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.20 – 7.09 (m, 3H), 4.74 (q, $J = 7.0$ Hz, 1H), 2.78 – 2.67 (m, 1H), 2.48 – 2.39 (m, 1H), 1.62 (d, $J = 7.2$ Hz, 3H), 1.58 – 1.46 (m, 2H), 1.35 – 1.20 (m, 2H), 0.87 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.7, 148.9, 145.3, 141.0, 129.6 (d, $^2J_{\text{C-F}} = 28.0$ Hz), 129.1, 128.7, 128.3, 127.1 (q, $^3J_{\text{C-F}} = 3.6$ Hz), 126.6, 124.0 (d, $^1J_{\text{C-F}} = 271.9$ Hz), 123.7 (q, $^3J_{\text{C-F}} = 3.8$ Hz), 42.7, 40.1, 26.0, 22.4, 22.0, 14.0; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{22}\text{F}_3\text{O}$ $[\text{M} + \text{H}]^+$ 335.1623, found 335.1628.

1-(4-phenethylbenzo[d][1,3]dioxol-5-yl)pentan-1-one (3qa'): Light yellow oil (77 mg, 83%; eluent: hexane/EtOAc = 50/1; b/l = 1/17 as determined by ^1H NMR). R_f 0.50 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.30 (d, $J = 8.2$ Hz, 1H), 7.27 – 7.22 (m, 4H), 7.19 – 7.13 (m, 1H), 6.69 (d, $J = 8.2$ Hz, 1H), 5.93 (s, 2H), 3.17 – 3.08 (m, 2H), 2.91 – 2.84 (m, 2H), 2.82 – 2.75 (m, 2H), 1.76 – 1.58 (m, 2H), 1.45 – 1.29 (m, 2H), 0.94 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 202.8, 149.6, 147.5, 142.4, 132.6, 128.9, 128.4, 126.0, 124.8, 124.5, 105.7, 101.6, 41.2, 36.4, 29.5, 27.2, 22.7, 14.2; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{23}\text{O}_3$ $[\text{M} + \text{H}]^+$ 311.1647, found 311.1650.

1-(4-(Dimethylamino)-2-phenethylphenyl)-2,2-dimethylpropan-1-one (3ra'): General procedure for **3da** was applied using bis(2,5-dimethoxyphenyl)(phenyl)phosphane as the

ligand. Light yellow oil (83 mg, 90%; eluent: hexane/EtOAc = 50/1). R_f 0.50 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.31 – 7.25 (m, 3H), 7.24 – 7.15 (m, 3H), 6.51 (dd, J = 8.5, 2.6 Hz, 1H), 6.47 (d, J = 2.5 Hz, 1H), 2.95 (s, 6H), 2.93 – 2.87 (m, 2H), 2.86 – 2.78 (m, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 213.3, 150.9, 142.5, 141.5, 128.8, 128.5, 128.3, 127.5, 126.0, 114.0, 108.6, 45.0, 40.4, 38.8, 37.0, 28.5; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{28}\text{NO}$ $[\text{M} + \text{H}]^+$ 310.2171, found 310.2175.

1-(4-Methoxy-2-phenethylphenyl)-2,2-dimethylpropan-1-one (3sa'): General procedure for **3pa** was applied. Light yellow oil (82 mg, 92%; eluent: hexane/EtOAc = 50/1). R_f 0.50 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.31 – 7.21 (m, 3H), 7.14 (d, J = 7.1 Hz, 2H), 6.95 (d, J = 8.5 Hz, 1H), 6.81 (d, J = 2.6 Hz, 1H), 6.71 (dd, J = 8.5, 2.6 Hz, 1H), 3.79 (s, 3H), 2.94 – 2.83 (m, 2H), 2.81 – 2.72 (m, 2H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.2, 159.2, 159.1, 128.7, 128.6, 127.5, 126.3, 126.3, 114.8, 110.9, 110.5, 55.4, 40.7, 38.2, 36.1, 28.9; HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{28}\text{NO}$ $[\text{M} + \text{H}]^+$ 297.1855, found 297.1857.

(4-Methoxy-2-(1-(p-tolyl)ethyl)phenyl)(phenyl)methanimine (3bb): Light yellow oil (88 mg, 89%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.45 (hexane/EtOAc/ NEt_3 =

10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.36 (brs, 1H), 7.65 (d, $J = 7.3$ Hz, 2H), 7.47 – 7.41 (m, 1H), 7.39 – 7.33 (m, 2H), 7.11 (d, $J = 8.4$ Hz, 1H), 7.03 – 6.94 (m, 4H), 6.89 (d, $J = 2.5$ Hz, 1H), 6.77 (dd, $J = 8.4, 2.6$ Hz, 1H), 4.08 (q, $J = 6.8$ Hz, 1H), 3.81 (s, 3H), 2.27 (s, 3H), 1.48 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.7, 160.3, 145.7, 142.8, 139.4, 135.8, 133.3, 131.0, 130.4, 129.5, 129.2, 128.5, 127.5, 114.0, 111.0, 55.5, 40.9, 22.5, 21.2; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{24}\text{NO}$ $[\text{M} + \text{H}]^+$ 330.1858, found 330.1858.

(2-(1-(4-(Tert-butyl)phenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3bc):

Light yellow oil (100 mg, 90%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.48 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.25 (brs, 1H), 7.64 (d, $J = 7.3$ Hz, 2H), 7.43 (t, $J = 7.0$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 2H), 7.25 – 7.17 (m, 2H), 7.11 (d, $J = 8.4$ Hz, 1H), 7.04 – 6.97 (m, 2H), 6.92 (d, $J = 2.3$ Hz, 1H), 6.78 (dd, $J = 8.4, 2.4$ Hz, 1H), 4.11 (q, $J = 6.9$ Hz, 1H), 3.82 (s, 3H), 1.50 (d, $J = 7.2$ Hz, 3H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.7, 160.3, 149.0, 145.8, 142.6, 139.4, 133.3, 131.0, 129.5, 128.5 (two signals overlapped), 127.3, 125.4, 114.1, 110.9, 55.5, 40.8, 34.5, 31.6, 22.5; HRMS (ESI) Calcd for $\text{C}_{26}\text{H}_{30}\text{NO}$ $[\text{M} + \text{H}]^+$ 372.2327, found 372.2330.

(4-Methoxy-2-(1-(4-methoxyphenyl)ethyl)phenyl)(phenyl)methanimine (3bd): Light yellow oil (95 mg, 92%; eluent: hexane/EtOAc/NEt₃ = 30/1/1). R_f 0.40 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.26 (brs, 1H), 7.65 (d, J = 7.1 Hz, 2H), 7.47 – 7.41 (m, 1H), 7.37 (q, J = 6.8 Hz, 2H), 7.11 (d, J = 8.4 Hz, 1H), 7.03 – 6.95 (m, 2H), 6.88 (d, J = 2.5 Hz, 1H), 6.80 – 6.71 (m, 3H), 4.08 (q, J = 6.9 Hz, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 1.48 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.7, 160.3, 158.0, 145.8, 139.3, 137.9, 131.0, 130.3, 129.5, 129.0, 128.6, 128.5, 128.4, 113.9, 110.9, 55.4 (two signals overlapped), 40.5, 22.6; HRMS (ESI) Calcd for C₂₃H₂₄NO₂ [M + H]⁺ 346.1807, found 346.1802.

(2-(1-(4-Fluorophenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3be): Light yellow oil (93 mg, 93%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). R_f 0.45 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.39 (brs, 1H), 7.61 (d, J = 6.9 Hz, 2H), 7.47 – 7.40 (m, 1H), 7.40 – 7.32 (m, 2H), 7.12 (d, J = 8.3 Hz, 1H), 7.04 – 6.96 (m, 2H), 6.89 – 6.83 (m, 3H), 6.79 (dd, J = 8.4, 2.6 Hz, 1H), 4.11 (q, J = 6.8 Hz, 1H), 3.82 (s, 3H), 1.47 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.6, 161.5 (d, $^1J_{C-F}$ = 244.2 Hz), 160.4, 141.4 (d, $^4J_{C-F}$ = 3.2 Hz), 133.0, 131.4, 131.1, 130.3, 129.7, 129.1 (d, $^3J_{C-F}$ = 7.8 Hz), 128.6, 128.4, 115.2 (d, $^2J_{C-F}$ = 21.1 Hz), 114.0, 111.1, 55.5, 40.6, 22.6; HRMS (ESI) Calcd for C₂₂H₂₁FNO [M + H]⁺ 334.1607, found 334.1607.

(2-(1-(4-Chlorophenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3bf): Light yellow oil (82 mg, 78%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.45 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.31 (brs, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.47 – 7.39 (m, 1H), 7.39 – 7.32 (m, 2H), 7.16 – 7.10 (m, 3H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.84 (q, *J* = 3.9, 3.0 Hz, 1H), 6.79 (dd, *J* = 8.4, 2.5 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 1H), 3.82 (s, 3H), 1.47 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.60, 160.4, 144.2, 133.1, 132.1, 131.5, 131.1, 130.3, 129.4, 129.0, 128.6 (two signals overlapped), 128.4, 114.0, 111.1, 55.5, 40.7, 22.4; HRMS (ESI) Calcd for C₂₂H₂₁ClNO [M + H]⁺ 350.1312, found 350.1314.

(4-Methoxy-2-(1-(4-(methylthio)phenyl)ethyl)phenyl)(phenyl)methanimine (3bg): Light yellow oil (95 mg, 88%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.43 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.34 (brs, 1H), 7.62 (d, *J* = 9.8 Hz, 2H), 7.49 – 7.39 (m, 1H), 7.38 – 7.32 (m, 2H), 7.14 – 7.06 (m, 3H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.90 – 6.81 (m, 1H), 6.78 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.08 (d, *J* = 6.9 Hz, 1H), 3.81 (s, 3H), 2.42 (s, 3H), 1.47 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.6, 164.1, 160.3, 146.0, 142.8, 139.1, 136.0, 131.0, 128.2, 127.6, 127.2, 126.4, 114.0, 113.8, 111.0, 55.5, 40.7, 22.4, 16.3; HRMS (ESI) Calcd for C₂₃H₂₄NOS [M + H]⁺ 362.1579, found

362.1576.

(4-Methoxy-2-(1-(4-(trimethylsilyl)phenyl)ethyl)phenyl)(phenyl)methanimine (3bh):

Light yellow oil (105 mg, 90%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.50 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.34 (brs, 1H), 7.65 (d, *J* = 6.3 Hz, 2H), 7.47 – 7.39 (m, 1H), 7.39 – 7.35 (m, 4H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 2H), 6.94 (d, *J* = 2.5 Hz, 1H), 6.80 (ddd, *J* = 8.4, 2.5, 1.1 Hz, 1H), 4.23 – 4.07 (m, 1H), 3.83 (s, 3H), 1.53 (d, *J* = 7.1 Hz, 3H), 0.24 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 178.6, 160.2, 146.2, 139.3, 137.9, 133.6, 133.3, 131.0, 129.5, 128.5, 128.4, 127.0, 114.1, 113.8, 110.9, 55.4, 41.2, 22.3, -0.9; HRMS (ESI) Calcd for C₂₅H₃₀NOSi [M + H]⁺ 388.2097, found 388.2099.

(4-Methoxy-2-(1-(m-tolyl)ethyl)phenyl)(phenyl)methanimine (3bi): Light yellow oil (80 mg, 81%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.50 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.39 (brs, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.48 – 7.41 (m, 1H), 7.39 – 7.33 (m, 2H), 7.14 – 7.06 (m, 2H), 6.95 – 6.87 (m, 3H), 6.83 (s, 1H), 6.78 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.08 (q, *J* = 6.4 Hz, 1H), 3.82 (s, 3H), 2.23 (s, 3H), 1.49 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.7, 160.3, 145.6, 138.0, 131.0, 130.3, 129.0,

128.5 (two signals overlapped), 128.4 (two signals overlapped), 128.3, 127.1, 124.6, 114.7, 114.1, 110.9, 55.5, 41.2, 22.5, 21.7; HRMS (ESI) Calcd for $C_{23}H_{24}NO$ $[M + H]^+$ 330.1858, found 330.1862.

(2-(1-(3-Fluorophenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3bj): Light yellow oil (85 mg, 85%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.25 (brs, 1H), 7.62 (d, J = 7.4 Hz, 2H), 7.47 – 7.41 (m, 1H), 7.38 – 7.33 (m, 2H), 7.19 – 7.10 (m, 2H), 6.84 – 6.72 (m, 5H), 4.12 (q, J = 7.3 Hz, 1H), 3.82 (s, 3H), 1.48 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 163.0 (d, $^1J_{C-F}$ = 245.4 Hz), 160.4, 148.4 (d, $^3J_{C-F}$ = 6.5 Hz), 139.2, 131.1, 130.1 (d, $^2J_{C-F}$ = 21.2 Hz), 129.8 (d, $^3J_{C-F}$ = 13.0 Hz), 128.6, 128.4, 123.4 (d, $^4J_{C-F}$ = 2.5 Hz), 114.5 (d, $^2J_{C-F}$ = 21.6 Hz), 114.1, 113.9, 113.3, 113.1, 111.2, 55.5, 41.0, 22.3; HRMS (ESI) Calcd for $C_{22}H_{21}FNO$ $[M + H]^+$ 334.1607, found 334.1609.

(4-Methoxy-2-(1-(3-methoxyphenyl)ethyl)phenyl)(phenyl)methanimine (3bk): Light yellow oil (86 mg, 83%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.40 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.30 (brs, 1H), 7.66 (d, J = 8.1 Hz, 2H), 7.47 – 7.41 (m, 1H), 7.37 (d, J = 7.8 Hz, 2H), 7.15 – 7.09 (m, 2H), 6.89 (d, J

= 2.5 Hz, 1H), 6.78 (dd, J = 8.4, 2.6 Hz, 1H), 6.70 – 6.64 (m, 2H), 6.61 – 6.59 (m, 1H), 4.10 (q, J = 7.0 Hz, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 1.49 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.6, 160.3, 159.7, 147.3, 131.0, 130.1, 129.5, 128.5, 127.4, 120.0, 114.3, 114.0, 113.8 (two signals overlapped), 112.7, 111.4, 111.1, 55.4, 55.3, 41.2, 22.4; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{24}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 346.1807, found 346.1802.

(4-Methoxy-2-(1-(3-methoxyphenyl)ethyl)phenyl)(phenyl)methanimine (3bl): Light yellow oil (76 mg, 72%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.31 (brs, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.46 – 7.39 (m, 1H), 7.35 (t, J = 7.8 Hz, 2H), 7.16 – 7.07 (m, 3H), 7.00 (s, 1H), 6.95 – 6.90 (m, 1H), 6.85 (q, J = 3.0 Hz, 1H), 6.80 (dd, J = 8.4, 2.5 Hz, 1H), 4.10 (q, J = 6.8 Hz, 1H), 3.83 (s, 3H), 1.47 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 178.6, 160.4, 147.8, 139.2, 134.3, 131.1, 129.7, 129.3, 128.6, 128.4, 127.8, 126.5, 126.0, 114.1 (two signals overlapped), 113.9, 111.2, 55.5, 41.0, 22.3; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{21}\text{ClNO}$ $[\text{M} + \text{H}]^+$ 350.1312, found 350.1315.

(4-Methoxy-2-(1-(2-methoxyphenyl)ethyl)phenyl)(phenyl)methanimine (3bm): Light yellow oil (78 mg, 75%; eluent: hexane/EtOAc/ NEt_3 = 50/1/1). R_f 0.40

(hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.51 (brs, 1H), 7.70 (d, J = 7.3 Hz, 2H), 7.45 – 7.39 (m, 1H), 7.38 – 7.32 (m, 2H), 7.24 (d, J = 1.7 Hz, 1H), 7.15 (td, J = 7.8, 1.7 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 2.6 Hz, 1H), 6.76 – 6.71 (m, 2H), 4.53 (q, J = 7.1 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 1.42 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.3, 160.0, 156.8, 146.0, 133.8, 130.7, 128.7, 128.2, 127.5, 125.8, 120.5, 114.1, 113.8 (two signals overlapped), 113.5, 110.5, 110.4, 55.4, 55.2, 34.6, 21.8; HRMS (ESI) Calcd for C₂₃H₂₄NO₂ [M + H]⁺ 346.1807, found 346.1805.

(2-(1-(2-Fluorophenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3bn): Light yellow oil (71 mg, 71%; eluent: hexane/EtOAc/NEt₃ = 50/1/1). *R_f* 0.50 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.36 (brs, 1H), 7.63 (d, J = 7.5 Hz, 2H), 7.44 – 7.38 (m, 1H), 7.36 – 7.30 (m, 2H), 7.22 – 7.08 (m, 3H), 7.03 (td, J = 7.5, 1.3 Hz, 1H), 6.92 – 6.82 (m, 2H), 6.79 (dt, J = 8.4, 2.1 Hz, 1H), 4.43 (q, J = 6.5 Hz, 1H), 3.80 (s, 3H), 1.48 (d, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.4, 160.7 (d, ¹*J*_{C-F} = 246.3 Hz), 160.2, 144.3, 139.2, 133.3, 132.5 (d, ²*J*_{C-F} = 14.3 Hz), 130.9, 129.8, 128.6 (d, ³*J*_{C-F} = 4.6 Hz), 128.4, 128.4, 128.1 (d, ³*J*_{C-F} = 8.3 Hz), 124.1 (d, ⁴*J*_{C-F} = 3.2 Hz), 115.6 (d, ²*J*_{C-F} = 22.3 Hz), 114.2, 110.9, 55.4, 35.0, 21.4; HRMS (ESI) Calcd for C₂₂H₂₁FNO [M + H]⁺ 334.1607, found 334.1609.

(2-(1-(2,4-Dimethoxyphenyl)ethyl)-4-methoxyphenyl)(phenyl)methanimine (3bo):

Light yellow oil (88 mg, 78%; eluent: hexane/EtOAc/NEt₃ = 30/1/1). *R_f* 0.30 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.44 (brs, 1H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.46 – 7.39 (m, 1H), 7.38 – 7.30 (m, 2H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 2.5 Hz, 1H), 6.73 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.43 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.31 (d, *J* = 2.5 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.56 (s, 3H), 1.39 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.4, 160.0, 159.5, 157.7, 146.4, 139.5, 133.1, 130.7, 129.4, 128.7, 128.2, 127.9, 126.4, 114.0, 110.3, 104.0, 98.7, 55.5, 55.4, 55.2, 34.2, 21.9; HRMS (ESI) Calcd for C₂₄H₂₆NO₃ [*M* + *H*]⁺ 376.1913, found 376.1916.

Deuterium-Labeling Experiments

The reaction of [D]₁₀-**3a** (58 mg, 0.3 mmol) and 1-methoxy-4-vinylbenzene (60 mg, 0.45 mmol) was performed according to the typical procedure for **4b**. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 50/1/1) afforded the hydroarylation products. The product was analyzed by ¹H NMR to determine the distribution of the deuterium atoms.

Transformation of the Alkylation Products

(4-Methoxy-2-(1-phenylethyl)phenyl)(2-(2-(trimethylsilyl)ethyl)phenyl)methanimine

(4): In a Schlenk tube were placed tris(3-fluorophenyl)phosphine (19.2 mg, 0.060 mmol), $\text{Co}(\text{acac})_2$ (7.7 mg, 0.030 mmol), pyridine (19 μL , 0.24 mmol), and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t\text{-BuCH}_2\text{MgBr}$ (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, (4-methoxy-2-(1-phenylethyl)phenyl)(phenyl)methanimine (**3ba**, 95 mg, 0.30 mmol) and trimethyl(vinyl)silane (156 μL , 1.05 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through silica gel and washed with EtOAc (5 mL x 3). The filtrate was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 100/1/1) of the crude product afforded the title compound as a light yellow oil (88 mg, 71%). The product was obtained as two regioisomers. The ratio of the two isomers (1:1) was determined with ^1H -NMR.

R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.69 (brs, 1H), 7.31 – 7.20 (m, 5H), 7.17 – 7.05 (m, 5H), 6.80 – 6.77 (m, 1H), 6.73 (dt, J = 8.5, 1.9 Hz, 1H), 4.59 (br, 1H), 3.77 (s, 3H), 2.77 – 2.52 (m, 2H), 1.48 (d, J = 7.0 Hz, 2H), 0.87 – 0.76 (m, 3H), -0.04 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 180.2, 160.7, 146.0, 129.7, 129.6, 129.5, 128.5 (two signals overlapped), 128.3, 127.8 (two signals overlapped), 126.4, 126.2, 126.1,

125.7, 114.7, 111.0, 55.42, 40.3, 27.7, 22.4, 19.3, -1.6; HRMS (ESI) Calcd for $C_{27}H_{34}NOSi$ $[M + H]^+$ 416.2410, found 416.2413.

1-(4-methoxy-2-(1-phenylethyl)-6-(2-(trimethylsilyl)ethyl)phenyl)pentan-1-imine (5):

In a Schlenk tube were placed tris(3-methoxyphenyl)phosphine (21.2 mg, 0.060 mmol), $Co(acac)_3$ (10.8 mg, 0.030 mmol), and THF (0.55 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t-BuCH_2MgBr$ (1.0 M in THF, 0.15 mL, 0.15 mmol). After stirring for 30 min, trimethyl(vinyl)silane (114 μ L, 0.75 mmol) and 1-(4-methoxy-2-(1-phenylethyl)phenyl)pentan-1-imine (**3ma**, 89 mg, 0.30 mmol) were added. The resulting mixture was warmed to room temperature and stirred for 12 h. The resulting mixture was filtered through silica gel and washed with EtOAc (5 mL x 3). The solution was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc = 100/1/1) of the crude product afforded the title compound as a light yellow oil (81 mg, 68%). The product was obtained as a mixture of two rotamers. The ratio of the rotamer (53:47) was determined with 1H -NMR.

R_f 0.65 (hexane/EtOAc = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.10 (brs, 1H, major + minor), 7.29 – 7.12 (m, 5H, major + minor), 6.73 – 6.60 (m, 2H, major + minor), 4.17 (q, J = 7.0 Hz, 1H, major), 4.03 (q, J = 6.9 Hz, 1H, minor), 3.81 – 3.75 (m, 3H, major + minor), 2.59 – 1.95 (m, 4H, major + minor), 1.66 – 1.52 (m, 4H, major + minor), 1.51 – 1.19 (m, 2H, major + minor), 1.02 – 0.72 (m, 6H, major + minor), 0.02 (s, 9H, major + minor); ^{13}C

NMR (100 MHz, CDCl₃): δ 184.3, 183.5, 159.4, 159.3, 146.3, 146.1, 143.3, 142.6, 128.7, 128.6 (two signals overlapped), 127.9, 127.4, 126.3, 126.2, 111.6, 111.4, 111.3, 110.9, 55.4, 41.5, 41.2, 41.0, 27.8 (two signals overlapped), 27.7, 27.2, 23.4, 22.8, 22.6, 19.8, 19.7, 14.3, 14.2, -1.6; HRMS (ESI) Calcd for C₂₅H₂₈NOSi [M + H]⁺ 396.2723, found 396.2727.

5.5 References

¹ Recent Reviews: a) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2011**, *45*, 814-825; b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev. (Washington, DC, U. S.)* **2012**, *112*, 5879-5918; c) Zhu, C.; Wang, R.; Falck, J. R. *Chem. Asian J.* **2012**, *7*, 1502-1514; d) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009. c) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704-712; d) Crisenza, G. E. M.; Bower, J. F. *Chem. Lett.* **2016**, *45*, 2-9.

² Recent examples: a) Schinkel, M.; Marek, I.; Ackermann, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 3977-3980; *Angew. Chem.* **2013**, *125*, 4069-4072; b) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258-10261; c) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 5410-5413; *Angew. Chem.* **2014**, *126*, 5514-5517; d) Crisenza, G. E. M.; Sokolova, O. O.; Bower, J. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 14866-14870; *Angew. Chem.* **2015**, *127*, 15079-15083; e) Ebe, Y.; Nishimura, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899-5902; f) Hatano, M.; Ebe, Y.; Nishimura, T.; Yorimitsu, H. *J. Am. Chem. Soc.* **2016**, *138*, 4010-4013.

³ For examples of linear-selective addition, see: a) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62-83; b) Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc. Perkin Trans. I* **1996**, 2201-2206; c) Matsumoto, T.; Periana, R. A.; Taube, D. J.; Yoshida, H. *J. Mol. Catal. A* **2002**, *180*, 1-18;

d) Jun, C.-H.; Moon, C. W.; Hong, J.-B.; Lim, S.-G.; Chung, K.-Y.; Kim, Y.-H. *Chem. Eur. J.* **2002**, *8*, 485-492; e) Tan, K. L.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 13964-13965; f) Martinez, R.; Genet, J.-P.; Darses, S. *Chem. Commun.* **2008**, 3855-3857; g) Martinez, R.; Simon, M.-O.; Chevalier, R.; Pautigny, C.; Genet, J.-P.; Darses, S. *J. Am. Chem. Soc.* **2009**, *131*, 7887-7895; h) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939-3942; i) Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221-5223.

⁴ For examples of branched-selective addition, see: a) Uchimaru, Y.; *Chem. Commun.* **1999**, 1133-1134; b) Nakao, Y.; Kashihara, N.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 16170-16171; c) Mukai, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 6410-6413; d) Nakao, Y.; Kashihara, N.; Kanyiva, K. S.; Hiyama, T. *Angew. Chem.* **2010**, *122*, 4553-4556; *Angew. Chem. Int. Ed.* **2010**, *49*, 4451-4454.

⁵ Gao, K.; Lee, P.-S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2010**, *132*, 12249-12251.

⁶ Lee, P.-S.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 1240-1244.

⁷ Dong, J.; Lee, P.-S.; Yoshikai, N. *Chem. Lett.* **2013**, *42*, 1140-1142.

⁸ Xu, W.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2014**, *53*, 14166-14170; *Angew. Chem.* **2014**, *126*, 14390-14394.

⁹ Yang, Z.; Yu, H.; Fu, Y. *Chem. Eur. J.* **2013**, *19*, 12093-12103.

¹⁰ a) Yoshikai, N.; Matsumoto, A.; Norinder, J.; Nakamura, E. *Angew. Chem. Int. Ed.* **2009**, *48*, 2925-2928; *Angew. Chem.* **2009**, *121*, 2969-2972; b) Yoshikai, N.; Asako, S.; Yamakawa, T.; Ilies, L.; Nakamura, E. *Chem. Asian J.* **2011**, *6*, 3059-3065.

¹¹ a) Lim, S.-G.; Ahn, J.-A.; Jun, C.-H. *Org. Lett.* **2004**, *6*, 4687-4690; b) Jun, C.-H.; Hong, J.-B.; Kim, Y.-H.; Chung, K.-Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 3440-3442; *Angew. Chem.* **2000**, *112*, 3582-3584; c) Jun, C.-H.; Moon, C. W.; Hong, J.-B.; Lim, S.-G.; Chung, K.-Y.;

Kim, Y.-H. *Chem. Eur. J.* **2002**, *8*, 485-492; d) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2005**, *70*, 6775-6781; e) Harada, H.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2008**, *73*, 6772-6779.

¹² a) Oi, S.; Ogino, Y.; Fukita, S.; Inoue, Y. *Org. Lett.* **2002**, *4*, 1783-1785; b) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875-1877; c) Ackermann, L. *Org. Lett.* **2005**, *7*, 3123-3125.

¹³ Kuninobu, Y.; Yu, P.; Takai, K. *Org. Lett.* **2010**, *12*, 4274-4276.

¹⁴ a) Liu, W.; Zell, D.; John, M.; Ackermann, L. *Angew. Chem. Int. Ed.* **2015**, *54*, 4092-4096; *Angew. Chem.* **2015**, *127*, 4165-4169; b) Liu, W.; Richter, S. C.; Zhang, Y.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, *55*, 7747-7750; *Angew. Chem.* **2016**, *128*, 7878-7881.

¹⁵ Xu, W.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2016**, *55*, 12731-12735.

¹⁶ a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2005**, *7*, 2229-2231; b) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun.* **2009**, 5141-5143; c) Sun, Z.-M.; Chen, S.-P.; Zhao, P. *Chem. Eur. J.* **2010**, *16*, 2619-2627; d) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 8181-8184; *Angew. Chem.* **2010**, *122*, 8357-8360; e) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 11098-11102; *Angew. Chem.* **2011**, *123*, 11294-11298; f) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 10630-10634; *Angew. Chem.* **2013**, *125*, 10824-10828; g) Zhang, J.; Ugrinov, A.; Zhao, P. *Angew. Chem. Int. Ed.* **2013**, *52*, 6681-6684; *Angew. Chem.* **2013**, *125*, 6813-6816. h) He, R.; Huang, Z.-T.; Zheng, Q.-Y.; Wang, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 4950-4953; *Angew. Chem.* **2014**, *126*, 5050-5053. i) Jia, T.; Zhao, C.; He, R.; Chen, H.; Wang, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 5268-5271; *Angew. Chem.* **2016**, *128*, 5354-5357; j) Kim, J. H.; Gressies, S.; Glorius, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 5577-5581; *Angew. Chem.* **2016**, *128*, 5667-5671.

- ¹⁷ Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208-1219.

Chapter 6. Cobalt-Catalyzed, Pivalophenone N–H Imine-Directed C–H Alkylation, Arylation and Alkenylation

6.1 Introduction

Transition metal-catalyzed directed C–H bond functionalization to form C–C and C-heteroatom bond with specific regioselectivity has found diverse applications in synthetic chemistry.¹ The versatility of the directing group is among the most important factors defining the utility of such transformations. From this point of view, the use of a cyano group as a directing group could be highly attractive in light of a large number of commercially available nitriles as well as the wide applicability of the cyano group in conventional and modern synthetic transformations. The initial breakthrough in this respect was made by Murai and coworkers on the ruthenium-catalyzed addition of benzonitrile to vinylsilane.² Following this work, several reports on cyano-directed *ortho* C–H bond functionalization have been reported (Scheme 6.1a).³ Regardless of the progress made, the nature of the cyano group poses intrinsic difficulty in its use as a directing group for *ortho* C–H functionalization. Thus, the cyano group can coordinate to a transition metal competitively through π - or σ -coordination modes, while only the former mode would be suitable for directed *ortho* C–H activation (Scheme 6.1b).⁴ Furthermore, the σ -coordination is often, if not always, preferred to the π - coordination. As such, it would be desirable to develop a readily accessible, broadly applicable, and easily transformable directing group that functions as a cyano group equivalent, a notable recent example being Wang's use of an imidate group for manganese-catalyzed *ortho*-alkenylation with terminal alkynes (Scheme 6.2).⁵ Such efforts would provide an attractive and practical approach for the synthesis of *ortho*-functionalized benzonitriles. In particular, arene C–H alkylation using

alkyl electrophiles would be an attractive target of such reaction development, because, in comparison with arene C–H arylation,⁶ directing groups available for this reaction manifold are still limited regardless of the recent progress made by palladium,⁷ ruthenium,⁸ nickel,⁹ cobalt,¹⁰ and iron catalysts.^{11, 12}

Scheme 6.1. Cyano group-directed arene C–H bond functionalization: Examples and intrinsic difficulty

Scheme 6.2. Manganese-catalyzed imidate-directed *ortho*-alkenylation

In the previous chapters, we presented cobalt-catalyzed olefin hydroarylation using N–H imine as a powerful directing group,¹³ which represents a rare example of N–H imine-directed C–H functionalization that results in the retention of the imine directing group (Scheme 6.3a).¹⁴ In order to broaden the application of N–H imine as the directing group for cobalt-catalyzed C–H functionalization as well as to address the above mentioned challenge, we envisioned the use of *t*-BuC=NH group of pivalophenone N–H imine as a directing group for the cobalt-catalyzed C–H functionalization with organic electrophiles.^{10,15} This study was inspired by the study of Ingold et al. on the reactivity of N–H imines. They showed that *t*-Bu₂C=NH decomposed into pivalonitrile (*t*-BuCN) and *tert*-butyl radical under peroxide photolysis conditions, while sterically less hindered N–H imines underwent dimerization to afford azine derivatives (Scheme 6.3b).¹⁶ Thus, we conjectured that the resulting *tert*-butyl N–H imine would undergo homolytic fragmentation to afford an *ortho*-functionalized benzonitrile.

In this chapter, we report on cobalt-catalyzed *ortho* C–H functionalization reaction of pivalophenone N–H imines with alkyl, aryl, and alkenyl electrophiles and the use of the pivaloyl imine as a nitrile surrogate. The desired alkylation, arylation, and alkenylation reactions are achieved under mild conditions using appropriate cobalt–N-heterocyclic carbene catalysts. For the alkylation and arylation, the products can be readily transformed into the corresponding *ortho*-substituted benzonitrile derivatives via peroxide photolysis or aerobic copper catalysis was performed (Scheme 6.3c). Overall, the present method would provide a complementary and convenient synthetic route to a variety of *ortho*-substituted benzonitriles.

Scheme 6.3. N–H imine as directing and transformable functional group for cobalt-catalyzed C–H activation

a) previous work

b) Ingold *et al*

c) this work

6.2 Results and Discussion

The feasibility of the C–H alkylation was initially explored for the coupling between pivalophenone N–H imine (**1a**) and *n*-octyl bromide (**2a**, 1.5 equiv) (Table 6.1). Through screening of different types of ligands (see entries 1–10) such as phosphines and different types of N-heterocyclic carbenes (NHC), *N,N'*-diisopropylimidazolium tetrafluoroborate (**L1**•HBF₄) was found to afford the monoalkylation product **3aa** in the highest yield (90%), when combined with CoBr₂ (10 mol%) and *t*-BuCH₂MgBr (2 equiv) as the cobalt precatalyst and the reductant, respectively. Note that **L1** was also one of the optimum

ligands for the previously reported cobalt-catalyzed N–PMP imine-directed C–H alkylation reaction.^{10b-e} Other alkyl sources, such as *n*-octyl tosylate and *n*-octyl chloride also afforded **3aa** albeit in modest yields (entries 11 and 12). It is also worthwhile to note that valerophenone N–H imine reacted rather sluggishly with **2a** under the present conditions, indicating the superior directing ability of the *tert*-butyl N–H imine.

Table 6.1. Optimization of cobalt-catalyzed C–H alkylation

entry	L	yield% ^a (3aa)
1	PPh ₃	26
2	PCy ₃	5
3	dppe	6
4	IMes•HCl	4
5	SIMes•HCl	3
6	IPr•HCl	6
7	SIPr•HCl	4
8	L1 •HBF ₄	90 ^b
9	L3 •HBF ₄	35
10	L4 •HCl	76
11 ^c	L1 •HBF ₄	22
12 ^d	L1 •HBF ₄	55

^a The data was determined with GC using tridecane as the internal standard. ^b The yield was isolated yield. ^c *n*-Octyl-OTs (1.5 equiv) was used. ^d *n*-Octyl-Cl (1.5 equiv) was used.

With the optimized condition in hand, the scope of the mono C–H alkylation reaction of *tert*-butyl N–H imine derivatives was explored. First, various primary alkyl bromides were examined to react with the parent imine **1a**, which exclusively afforded the corresponding monoalkylation products **3aa–3al** in good yields (Table 6.2). A variety of functional groups and steric factors could be tolerated including alkyl chloride (**3ad**), alkyl fluoride (**3ae**), olefin moieties (**3af–3ah**), and bulky substituents at the α -position (**3ai–3al**). When 6-bromo-1-hexene (**2g**) was used, it should be noted that the simple alkylation product **3ag** was the exclusively product, while the analogous reaction using acetophenone N-aryl imine was accompanied by a notable amount of a ring-closing alkylation (cyclopentylmethylation) product.^{10d} Secondary alkyl groups could also be installed under the present condition. A series of cycloalkyl bromides participated in the reaction with **1a** to afford the corresponding alkylation products **3am–3ao** in good yields. However, for acyclic secondary alkyl bromides, the reaction was somewhat sluggishly, afforded the desired products **3ap** and **3aq** without any isomerized, primary alkylation products.

Table 6.2. C–H alkylation of pivalophenone imine (**1a**) with alkyl bromides ^a

3aa , 90%	3ab , 83%
3ac , 91%	3ad (X = Cl), 75% 3ae (X = F), 80%
3af (n = 1), 82% 3ag (n = 2), 70%	3ah , 75%
3ai (R = <i>i</i> -Pr), 81% 3aj (R = <i>c</i> -C ₄ H ₉), 90% 3ak (R = <i>c</i> -C ₆ H ₁₁), 87% 3al (R = <i>t</i> -Bu), 91%	3am , 85%
3an , 87%	3ao , 84%
3ap , 51%	3aq , 54%

^a Reaction conditions: Imine **1** (0.3 mmol), alkyl bromide **2** (1.5 equiv), CoBr₂ (10 mol%), L1•HBF₄ (10 mol%), *t*-BuCH₂MgBr (2 equiv), THF, rt, 12 h.

Afterwards, various of substituted pivalophenone imines proved amenable to the present C–H alkylation reaction using *n*-octyl bromide (Table 6.3). *Para*- and *meta*-substituents such as methyl, phenyl, methoxy, trifluoromethoxy, methylthio, dimethylamino, fluoro, and trifluoromethyl groups (see **3ba–3ha** and **3ja**) could be tolerated. For imines bearing *meta*-methyl, trifluoromethyl, or methoxy groups as well as 2-naphthyl imine, the alkylation underwent exclusively or selectively at the less hindered position (see **3ia–3ka** and **3na**), while a 3,4-methylenedioxy group led the alkylation

reaction taking place preferentially at the proximal *ortho*-position albeit with modest regioselectivity (see **3ma**). Besides these *n*-octylation reactions, cyclohexylation reactions also proceeded smoothly with several substituted imines (see **3bn**, **3fn**, **3in**, and **3nn**).

Table 6.3. C–H alkylation of pivalophenone imines with alkyl bromides ^a

^a Reaction conditions: Imine **1** (0.3 mmol), alkyl bromide **2** (1.5 equiv), CoBr₂ (10 mol%), **L1**·HBF₄ (10 mol%), *t*-BuCH₂MgBr (2 equiv), THF, rt, 12 h. ^b The major regioisomer is shown (r.r. = regioisomer ratio). The yield refers to the overall yield.

Given the success of the C–H alkylation reaction, we turned our attention to the feasibility of cobalt-catalyzed directed *ortho* C–H arylation of pivalophenone N–H imines.^{10c, e, 17} First, ligand screening for the coupling of imine **1a** with 4-chloroanisole (**4a**) was conducted (Table 6.4). When **L1** was used, which is the best ligand for C–H alkylation, only trace amount of arylation product **5aa** was obtained. Then other types of NHC ligands were examined (entry 2 to 5), which showed that the substituent on nitrogen was crucial for the efficiency. Changing the cobalt source to Co(acac)₂ and Co(acac)₃, the yield was slightly improved (entry 6 and 7). Increasing the equivalent of *t*-BuCH₂MgBr to 2.5 equivalent and adding TMEDA (80 mol%) could further improve the yield (entry 8 to 10). Finally, a combined use of imidazolium salt **L2**•HBr featuring N-2,6-diethylphenyl groups and cyclohexane-based backbone as NHC precursor and TMEDA (80 mol%) as additive, respectively, was found to be effective. Thus, a catalytic system comprised of these key components, Co(acac)₃, and *t*-BuCH₂MgBr efficiently promoted the arylation reaction at room temperature, affording the desired biaryl product **5aa** in 84% yield without any trace of the diarylation product (entry 11). Note that the use of 4-bromoanisole in place of **4a** failed to give the product **5aa** but resulted in the direct cross-coupling between 4-bromoanisole and *t*-BuCH₂MgBr.

Table 6.4. Screening of Reaction Conditions for C–H Arylation

entry	CoXn	L	yield% ^a (A)
1	CoBr ₂	L1 •HBF ₄	trace
2	CoBr ₂	IMes•HCl	22
3	CoBr ₂	IPr•HCl	16
4	CoBr ₂	IEt•HCl	24
5	CoBr ₂	L2 •HBr	22
6	Co(acac) ₂	IEt•HCl	32
7	Co(acac) ₃	IEt•HCl	37
8 ^b	Co(acac) ₃	IEt•HCl	42
9 ^{b,c}	Co(acac) ₃	IEt•HCl	55
10 ^{b,c}	Co(acac) ₃	IMes•HCl	50
11 ^{b,c}	Co(acac) ₃	L2 •HBr	84 ^d

L1•HBF₄

IEt•HCl

L2•HBr

^a The data was determined with GC using tridecane as the internal standard. ^b *t*-

BuCH₂MgBr (2.5 equiv) was used. ^c TMEDA (80 mol%) was used as the additive. ^d The

yield was isolated yield.

Under the optimized condition, our subsequent exploration demonstrated its applicability to various aryl chlorides, which reacted with **1a** to afford the corresponding biaryls **5ab–5at** in moderate to good yields (Table 6.5). A variety of *para*-, *meta*-, and *ortho*-substituted aryl chlorides were tolerated with electron-donating substituents such as

methoxy, dimethylamino, and siloxy groups and electron-withdrawing substituents such as fluoro and trifluoromethyl groups. For the *ortho*-substituted aryl chlorides and 1-naphthyl chloride, the arylation reaction took place somewhat sluggishly (see **5am–5ap** and **5at**) presumably due to the steric effect. Arylation of a series of substituted pivalophenone imines with 4-chloroanisole also occurred smoothly affording the desired biaryl products **5ba–5ma** in good yields. In contrast to the modest regioselectivity observed for the alkylation of the same imine (see **3ma** in Table 6.3), the imine bearing a 3,4-methylenedioxy group underwent arylation exclusively at the proximal *ortho* position (see **5ma**). 2-Naphthyl N–H imine afforded the arylation product **5na** as a regioisomeric mixture while alkylation occurred exclusive at the less hindered position (see **3na** and **3nn**).

Table 6.5. C–H arylation of pivalophenone imines with aryl chlorides ^a **Scope of aryl chloride** **Scope of imines**

^a Reaction conditions: Imine **1** (0.3 mmol), aryl chloride **4** (1.5 equiv), CoBr₂ (10 mol%), **L2**•HBr (10 mol%), *t*-BuCH₂MgBr (2.5 equiv), TMEDA (80 mol%), THF, rt, 12 h. ^b The major regioisomer is shown (r.r. = regioisomer ratio). The yield refers to the overall yield.

After the success on N–H imine directed C–H alkylation and arylation, the feasibility of alkenylation was also explored. Ligand screening was performed for the coupling of N–H imine **1a** with cyclohexenyl enol phosphate (**6a**) (Table 6.6). Phosphine ligands, such as PPh₃ and PCy₃ gave no alkenylation product (entries 1 and 2), while NHC ligands led to the desired product in moderate to good yield, especially for the ligands with N-2,6-diisopropylphenyl substituents (entries 3–8). The imidazolium salt, **L5**•HCl featuring 2,6-diisopropylphenyl groups and benzo-based backbone as NHC precursor was found to be the most effective. Thus, a catalytic system comprised of CoBr₂, **L5**•HCl and *t*-BuCH₂MgBr efficiently promoted the alkenylation reaction at room temperature, affording the desired product **7aa** in 88% yield (entry 9).

Table 6.6. Screening of Reaction Conditions for C–H alkenylation

entry	Ligand	yield% ^a (A)
1	PPh ₃	-
2	PCy ₃	-
3	IMes•HCl	29
4	IPr•HCl	53
5	SIMes•HCl	40
6	SIPr•HCl	46
7	IEt•HCl	38
8	L2 •HBr	37
9	L5 •HCl	88 ^b

^a The data was determined with GC using tridecane as the internal standard. ^b The yield was isolated yield.

With the optimized condition in hand, our subsequent exploration demonstrated on the scope of alkenyl phosphates, which reacted with **1a** to afford the corresponding alkenylation products **7ab–7ai** in moderate to good yields (Table 6.7). Different numbered cyclic alkenyl phosphates from cyclopentenyl to cyclodecenyl (**7ab–7ae**), and cyclododecenyl (**7af**) were tolerated. For the cyclodecenyl and cyclododecenyl phosphates, the alkenylation products were obtained as E/Z isomer with moderate to good selectivity. Various substituents on the 2- and 4-position of the cyclohexenyl phosphate such as 4-*t*-butyl (**7ag**), phenyl (**7ah**) and 2-methyl cyclohexenyl phosphates (**7ai**) exhibited no significant impact on the reactivity. Linear alkenyl phosphate was also tolerated, albeit with moderate E/Z selectivity (see **7aj**). The scope of pivalophenone N–H imines was then

explored. Alkenylation of *para*-substituted aryl N–H imines with cyclohexenyl phosphate (**6a**) took place smoothly affording the desired alkenylation products **7ba–7ha** in good yields. For methylene-3,4-dioxyl substituted aryl N–H imine, the regioselectivity observed at the proximal *ortho* position (see **5ma**), as was the case for *meta*-fluoro, and methoxy pivalophenone N–H imines (**7ka** and **7la**). For *meta*-methyl pivalophenone N–H imine, the reaction produced the alkenylation product **7ia**, undergoing alkenylation at the less hindered position (see **3na**). For the alkenylation of 2-naphthyl imine, the regioselectivity was opposite to alkylation and arylation (see **3na** and **5na**), occurring at the hinder position with good regioselectivity (see **7na**).

Table 6.7. C–H arylation of pivalophenone imines with alkenyl phosphates^a

		<p>CoBr₂ (10 mol%) L5•HCl (10 mol%) <i>t</i>-BuCH₂MgBr (2 equiv) THF, rt, 12 h</p>	
1	6		7
scope of alkenyl phosphates			
7ab , 85%	7ac , 79%	7ad , 86%	7ae , 82% (E/Z = 10/1)
7af , 78% (E/Z = 4/1)	7ag (R = <i>t</i> -Bu), 84% 7ah (R = Ph), 85%	7ai , 88%	7aj , 90% (E/Z = 4/1)
scope of imines			
7ba (R = Me), 85% 7ca (R = Ph), 86% 7da (R = OMe), 83% 7ea (R = OCF ₃), 79% 7ga (R = NMe ₂), 82% 7ha (R = F), 81%	7ia/7ia' (3/1), 76%	7ka (R = OMe), 81% 7la (R = F), 79%	
7ma , 84%	7na/7na' (4/1), 82%		

^a Reaction conditions: Imine **1** (0.3 mmol), alkenyl phosphates **6** (1.5 equiv), CoBr₂ (10 mol%), **L5**•HCl (10 mol%), *t*-BuCH₂MgBr (2.0 equiv), THF, rt, 12 h.

To test the feasibility of the conversion of the *t*-BuC=NH group into a cyano group, we initially subjected a solution of the simple pivalophenone N–H imine **1a** in di-*tert*-butyl peroxide to UV (254 nm) irradiation. The reaction afforded a substantial amount (40%) of azine **8**, which was accompanied by only a small amount (4%) of benzonitrile (Scheme 6.4a). This result was not totally unexpected, which suggested the formation of the iminyl radical. In a sharp contrast, *ortho*-alkylated product **3aa** under the same conditions furnished the benzonitrile derivative **9a** quantitatively (Scheme 6.4b). This might be caused by the steric of the *ortho*-substituents. Likewise, the imine-to-nitrile conversion of the *ortho*-arylated product **5aa** proceeded smoothly to afford the 2-cyanobiaryl **9b** in somewhat lower yield (79%), which was due to the formation of 6-(*tert*-butyl)-3-methoxyphenanthridine as a byproduct as a result of intramolecular cyclization of the iminyl radical.¹⁸ Furthermore, a copper-catalyzed protocol employing Cu(OAc)₂ (10 mol%) and O₂ (1 atm) in DMF, originally developed by Chiba for the conversion of 2-biaryl N–H imines to phenanthridines,¹⁹ provided similarly efficiency for the conversion of **3aa** and **5aa** to **9a** and **9b**, respectively, presumably via homolytic fragmentation of a putative iminyl-copper species (Scheme 6.4c). However, when we subjected the alkenylation product **7aa** in di-*tert*-butyl peroxide to UV (254 nm) irradiation, the spirocyclization product **10** was obtained with good yield (Scheme 6.4d).

Scheme 6.4. Contrasting decomposition pathways of pivalophenone imines

With these two protocols in hand, we explored two-step synthesis of *ortho*-alkylated or -arylated benzonitriles (Table 6.8) containing C–H alkylation or arylation and the imine-to-nitrile conversion. Alkylation or arylation reactions of pivalophenone N–H imines were performed under the respective optimized conditions, followed by submission of the crude products to the peroxide photolysis (A) or the aerobic copper catalysis (B) conditions. To our satisfactory, these protocols worked particularly well for the preparation of *ortho*-alkylated benzonitriles. The desired products **9c–9p** were obtained in yields close to the yields of the corresponding C–H alkylation products (cf. Table 6.2 and Table 6.3), resulted from the high efficiency of the second step. The yields of the *ortho*-arylated benzonitrile

derivatives **9q–9v** (ca. 60%) were apparently lower than that of the corresponding C–H arylation products (ca. 80%; cf. Table 6.5), reflecting the imperfect chemoselectivity of the second step.

Table 6.8. Two-step synthesis of *ortho*-substituted benzonitriles^a

^a The first step was performed under optimized conditions for the alkylation or arylation, and the crude product was directly subjected to the second step. The yields refer to overall yields based on **1**.

Several experiments were performed to gain insight into the mechanism of the C–H alkylation and arylation reactions (Scheme 6.5). Upon a treatment of imine **1i** in [D₈]-THF with *t*-BuCH₂MgBr (1.5 equiv) at room temperature, the N–H proton signal was near completely disappeared, and a sizable chemical shift change of the C=N carbon and some other corresponding protons and carbons were observed in ¹H/¹³C NMR. This control experiment clearly showed the deprotonation of N–H imine with the formation of a magnesium alkylideneamide species (Scheme 6.5a), which would suggest that the imine N–H proton is also readily deprotonated under the alkylation/arylation conditions, and that the alkylideneamide anion serves as the actual directing group for the cobalt-mediated C–H activation. The competition experiments demonstrated the superiority of this anionic directing group to an N-aryl imine directing group, for both the alkylation and the arylation reactions (Scheme 6.5b). We also probed the orthogonality of the Co–**L1** and Co–**L2** systems by competition experiments (Scheme 6.5c). As a result, the Co–**L1** system selectively promoted the C–H alkylation of **1a** with *n*-octyl bromide without significant influence of 4-chloroanisole. By contrast, an analogous competition under the Co–**L2** system either the C–H alkylation or the C–H arylation product was not achieved, which suggested that the present of *n*-octyl bromide interfered the C–H activation. Finally, to probe the effect of TEMPO on the reaction efficiency, TEMPO was added to the standard conditions for C–H alkylation and arylation, respectively (Scheme 6.5d). The C–H alkylation with *n*-octyl bromide was not apparently interfered. In contract, significant inhibitory effects were observed in the alkylation reactions with cyclohexyl bromide and

arylation with 4-chloroanisole. These observations suggest that, a single electron transfer event is involved presumably in the carbon–halogen bond cleavage at least for the latter two cases.¹⁶ A catalytic cycle was proposed based on the above mechanistic study (**Error! Reference source not found.**).

Scheme 6.5. Mechanistic experiments^a

^a Yields for Scheme 6.5b-d were determined by GC using *n*-tridecane as an internal standard. (PMP = *p*-methoxyphenyl)

Scheme 6.6. Proposed catalytic cycle

6.3 Conclusion

In summary, we have developed facile two-step protocols for the synthesis of *ortho*-alkylated, and -arylated benzonitriles via cobalt-catalyzed directed C–H alkylation, and arylation of pivalophenone N–H imines and subsequent fragmentation of the *t*-butyl N–H imine moiety under peroxide photolysis or aerobic copper catalysis. *Ortho*-alkenylation of pivalophenone N–H imine was also achieved with alkenyl phosphate with a new low valent cobalt-catalyzed system. Mechanistic study shows the N–H imine is deprotonated by Grignard reagent and act as the real directing group.

6.4 Experimental Section

Preparation of Starting Materials

Preparation of Aryl Imines

All imines shown below were synthesized according to the literature procedures,²⁰ and purified by recrystallization or distillation. Spectral data for **1a**,²¹ **1d**,²⁰ **1f**,¹³ and **1g**²⁰ showed good agreement with the literature data:

1a (R = H)
1b (R = Me)
1c (R = Ph)
1d (R = OMe)
1e (R = OCF₃)
1f (R = SMe)
1g (R = NMe₂)
1h (R = F)

1i (R = Me)
1j (R = CF₃)
1k (R = OMe)
1l (R = F)

1m **1n** **1o**

2,2-Dimethyl-1-(p-tolyl)propan-1-imine (1b): Light yellow liquid; ¹H NMR (400 MHz, CDCl₃): δ 9.13 (brs, 1H), 7.14 – 7.08 (m, 4H), 2.35 (s, 3H), 1.23 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.5, 139.7, 137.8, 128.7, 126.5, 40.2, 28.7, 21.3; HRMS (ESI) Calcd for C₁₂H₁₈N [M + H]⁺ 176.1439, found 176.1435.

1-([1,1'-Biphenyl]-4-yl)-2,2-dimethylpropan-1-imine (1c): white solid; M.p. 92-93 °C. ¹H NMR (400 MHz, CDCl₃): δ 9.27 (brs, 1H), 7.62 – 7.56 (m, 4H), 7.48 – 7.42 (m, 2H), 7.39 – 7.34 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 1.30 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.2, 141.0, 140.6, 129.0 (two signals overlapped), 127.7, 127.2, 127.1, 126.8, 28.6. HRMS (ESI) Calcd for C₁₇H₂₀N [M + H]⁺ 238.1596, found 238.1586.

2,2-Dimethyl-1-(4-(trifluoromethoxy)phenyl)propan-1-imine (1e): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.16 (brs, 1H), 7.28 – 7.17 (m, 4H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.1, 149.1, 141.0, 128.3, 120.7, 120.6 (q, $^1J_{\text{C-F}} = 257.5$ Hz), 40.5, 28.5. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NOF}_3$ $[\text{M} + \text{H}]^+$ 246.1106, found 246.1105.

1-(4-Fluorophenyl)-2,2-dimethylpropan-1-imine (1h): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.12 (brs, 1H), 7.14 (brs, 2H), 6.99 – 6.94 (m, 2H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.4, 162.4 (d, $^1J_{\text{C-F}} = 247.2$ Hz), 138.4, 128.3, 115.0 (d, $^2J_{\text{C-F}} = 21.4$ Hz), 40.5, 28.4. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{15}\text{NF}$ $[\text{M} + \text{H}]^+$ 180.1189, found 180.1196.

2,2-Dimethyl-1-(m-tolyl)propan-1-imine (1i): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.13 (brs, 1H), 7.19 (t, $J = 7.9$ Hz, 1H), 7.12 (d, $J = 7.3$ Hz, 1H), 6.99 – 6.95 (m, 2H), 2.34 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 142.4, 137.7, 128.7, 127.8, 127.1, 123.5, 40.1, 28.6, 21.5. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 176.1439, found 176.1437.

2,2-Dimethyl-1-(3-(trifluoromethyl)phenyl)propan-1-imine (1j): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.20 (brs, 1H), 7.57 (d, $J = 7.7$ Hz, 1H), 7.52 – 7.33 (m, 3H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.8, 143.0, 130.6 (q, $^2J_{\text{C-F}} = 32.1$ Hz), 129.9, 128.7, 124.9 (q, $^3J_{\text{C-F}} = 3.8$ Hz), 124.0 (q, $^1J_{\text{C-F}} = 272.2$ Hz), 123.3, 40.4, 28.3. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NF}_3$ $[\text{M} + \text{H}]^+$ 230.1157, found 230.1161.

1-(3-Methoxyphenyl)-2,2-dimethylpropan-1-imine (1k): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.18 (brs, 1H), 7.25 (t, $J = 8.3$ Hz, 1H), 6.87 (dd, $J = 8.3, 2.3$ Hz, 1H), 6.78 (d, $J = 7.5$ Hz, 1H), 6.73 (s, 1H), 3.81 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.2, 159.2, 143.7, 129.3, 119.0, 113.4, 112.6, 55.4, 40.9, 28.7. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$ $[\text{M} + \text{H}]^+$ 192.1389, found 192.1388.

1-(3-Fluorophenyl)-2,2-dimethylpropan-1-imine (1l): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.11 (brs, 1H), 7.29 – 7.22 (m, 1H), 7.01 – 6.86 (m, 3H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.9, 162.16 (d, $^1J_{\text{C-F}} = 247.2$ Hz), 144.4, 129.8 (d, $^3J_{\text{C-F}} = 7.5$ Hz), 122.2, 115.0 (d, $^2J_{\text{C-F}} = 21.0$ Hz), 113.7, 39.5, 28.4. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NF}$ $[\text{M} + \text{H}]^+$ 192.1189, found 192.1186.

1-(Benzo[d][1,3]dioxol-5-yl)-2,2-dimethylpropan-1-imine (1m): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.13 (brs, 1H), 6.75 – 6.71 (m, 1H), 6.68 (s, 1H), 6.65 (d, J = 7.8 Hz, 1H), 5.92 (s, 2H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.5, 147.4, 147.1, 136.2, 120.3, 108.0, 107.5, 101.2, 40.3, 28.7. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{16}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 206.1181, found 206.1182.

2,2-Dimethyl-1-(naphthalen-2-yl)propan-1-imine (1n): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.35 (brs, 1H), 7.86 – 7.80 (m, 3H), 7.68 (s, 1H), 7.54 – 7.48 (m, 2H), 7.35 (d, J = 8.1 Hz, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.3, 145.8, 139.9, 132.8, 128.3, 127.8, 127.7, 126.6, 126.5, 125.4, 124.8, 40.4, 28.7. HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 212.1439, found 212.1447.

1-(3,5-Difluorophenyl)-2,2-dimethylpropan-1-imine (1o): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 9.17 (brs, 1H), 6.89 – 6.58 (m, 3H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.0, 162.6 (dd, $^1J_{\text{C-F}}$ = 250.1 Hz, $^3J_{\text{C-F}}$ = 12.5 Hz), 145.3 (d, $^3J_{\text{C-F}}$ = 15.4 Hz), 110.3, 103.6 (t, $^2J_{\text{C-F}}$ = 25.0 Hz), 40.2, 28.4. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{14}\text{NF}_2$ $[\text{M} +$

$\text{H}]^+$ 198.1094, found 198.1096.

Preparation of Alkenyl Enol Phosphates

Enol phosphate esters (**6a-6k**) were prepared according to the procedure described by Kumada and coworkers.²² Spectral data for **6a**,²² **6b**,²² **6c**,²³ **6f**,²² and **6g**²² showed good agreement with the literature data:

(E)-cyclooct-1-en-1-yl diethyl phosphate (6d): Colorless liquid; ^1H NMR (400 MHz, CDCl_3): δ 5.37 (tt, $J = 8.6, 2.2$ Hz, 1H), 4.14 – 4.04 (m, 4H), 2.32 – 2.26 (dd, $J = 8.2, 4.2$ Hz, 2H), 2.06 – 1.97 (m, 2H), 1.64 – 1.55 (m, 2H), 1.54 – 1.43 (m, 6H), 1.33 – 1.25 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 149.7 (d, $J_{\text{C-P}} = 9.3$ Hz), 112.7 (d, $J_{\text{C-P}} = 4.9$ Hz), 64.1 (d, $J_{\text{C-P}} = 6.0$ Hz), 30.1, 29.4 (d, $J_{\text{C-P}} = 4.4$ Hz), 27.6, 26.2, 26.0, 25.2, 16.2 (d, $J_{\text{C-P}} = 6.9$ Hz). HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{24}\text{O}_4\text{P}$ $[\text{M} + \text{H}]^+$ 263.1412, found 263.1408.

Cyclodec-1-en-1-yl diethyl phosphate (E/Z = ca. 1:1) (6e): Light yellow liquid; major + minor component: ^1H NMR (400 MHz, CDCl_3): δ 5.21 (td, $J = 8.7, 2.1$ Hz, 1H) (minor), 4.99 (td, $J = 7.8, 0.9$ Hz, 1H) (major), 4.14 – 4.04 (m, 4H) (major + minor), 2.38 – 2.09 (m, 4H) (major + minor), 1.57 – 1.25 (m, 18H) (major + minor); ^{13}C NMR (100 MHz, CDCl_3): δ 148.1 (d, $J = 9.3$ Hz), 147.0 (d, $J = 7.6$ Hz), 117.4 (d, $J = 6.9$ Hz), 114.9 (d, $J = 4.5$ Hz), 64.13 (t, $J = 6.2$ Hz), 64.06 (d, $J = 6.2$ Hz), 34.8, 27.4 (d, $J = 4.3$ Hz), 27.1, 26.9, 26.1 (two signals overlapped), 25.5, 25.4, 25.2, 25.0, 24.6 (two signals overlapped), 24.2, 23.9, 20.9, 20.6, 16.22 (d, $J = 6.6$ Hz), 16.18 (d, $J = 6.6$ Hz). HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{28}\text{O}_4\text{P}$ [$\text{M} + \text{H}$] $^+$ 291.1725, found 291.1728.

4-(Tert-butyl)cyclohex-1-en-1-yl diethyl phosphate (6g): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 5.41 (dd, $J = 5.1, 1.7$ Hz, 1H), 4.11 (p, $J = 7.3$ Hz, 4H), 2.28 – 2.00 (m, 3H), 1.86 – 1.76 (m, 2H), 1.34 – 1.21 (m, 8H), 0.83 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 147.8 (d, $J_{\text{C-P}} = 8.6$ Hz), 110.6 (d, $J_{\text{C-P}} = 5.4$ Hz), 64.2 (d, $J_{\text{C-P}} = 6.0$ Hz), 43.5, 32.2, 28.9 (d, $J_{\text{C-P}} = 3.8$ Hz), 27.4, 25.1, 24.1, 16.3 (d, $J_{\text{C-P}} = 6.8$ Hz). HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{28}\text{O}_4\text{P}$ [$\text{M} + \text{H}$] $^+$ 291.1725, found 291.1729.

Diethyl (1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl) phosphate (6h): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 7.29 (t, $J = 7.5$ Hz, 2H), 7.22 – 7.17 (m, 3H), 5.59 – 5.55 (m, 1H), 4.21 – 4.12 (m, 4H), 2.83 – 2.75 (m, 1H), 2.49 – 2.19 (m, 4H), 2.03 – 1.83 (m, 2H), 1.36 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 147.5 (d, $J_{\text{C-P}} = 9.0$ Hz), 145.7, 128.4, 126.8, 126.2, 110.1 (d, $J_{\text{C-P}} = 5.4$ Hz), 64.1 (d, $J_{\text{C-P}} = 6.0$ Hz), 39.3, 31.5, 29.6, 28.1 (d, $J_{\text{C-P}} = 4.1$ Hz), 16.1 (d, $J_{\text{C-P}} = 6.7$ Hz). HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{24}\text{O}_4\text{P}$ $[\text{M} + \text{H}]^+$ 311.1412, found 311.1413.

E-diethyl hept-3-en-4-yl phosphate (6j): Light yellow liquid; ^1H NMR (400 MHz, CDCl_3): δ 5.45 – 5.41 (m, 1H), 4.14 – 4.06 (m, 4H), 2.34 (dd, $J = 12.8, 6.0$ Hz, 1H), 2.04 – 1.98 (m, 2H), 1.82 – 1.74 (m, 1H), 1.63 – 1.32 (m, 4H), 1.30 (t, $J = 7.0$ Hz, 6H), 1.05 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 151.6 (d, $J_{\text{C-P}} = 9.6$ Hz), 110.1 (d, $J_{\text{C-P}} = 4.0$ Hz), 64.2 (d, $J_{\text{C-P}} = 5.4$ Hz), 32.2 (d, $J_{\text{C-P}} = 4.7$ Hz), 31.4, 24.2, 19.6, 18.4, 16.2 (d, $J_{\text{C-P}} = 6.8$ Hz); $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, CDCl_3): δ -5.5. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{24}\text{O}_4\text{P}$ $[\text{M} + \text{H}]^+$ 251.1412, found 251.1416.

Experiment Detail for Cobalt-Catalyzed C-H Alkylation of Pivalophenone Imines with Alkyl Bromides

Typical Procedure: 2,2-dimethyl-1-(2-octylphenyl)propan-1-imine (3aa). In a Schlenk tube were placed **L1**•HBF₄ (4.9 mg, 0.020 mmol), a freshly prepared THF solution of CoBr₂ (0.20 M, 0.10 mL, 0.020 mmol), and THF (0.3 mL). The resulting solution was cooled in an ice bath, followed by the addition of *t*-BuCH₂MgBr (2.0 M in THF, 0.2 mL, 0.40 mmol). After stirring for 30 min, 2,2-dimethyl-1-phenylpropan-1-imine (**1a**, 33 mg, 0.20 mmol), and 1-bromooctane (**2a**, 52 μ L, 0.3 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 12 h, and then filtered through a short silica-gel column, which was washed with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 100/1/1) of the crude product afforded the title compound as a colorless oil (49 mg, 90%).

R_f 0.60 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.19 (brs, 1H), 7.26 – 7.23 (m, 2H), 7.15 – 7.10 (m, 1H), 7.01 (d, J = 7.5 Hz, 1H), 2.48 – 2.44 (m, 2H), 1.60 – 1.52 (m, 2H), 1.37 – 1.20 (m, 19H), 0.87 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 190.9, 141.6, 139.0, 129.4, 127.9, 126.2, 125.1, 40.6, 33.9, 32.1, 32.0, 30.0, 29.7, 29.5, 28.9, 22.9, 14.3. HRMS (ESI) Calcd for C₁₉H₃₂N [M + H]⁺ 274.2535, found 274.2535.

2,2-Dimethyl-1-(2-phenethylphenyl)propan-1-imine (3ab): Light yellow oil (44 mg, 83%). R_f 0.51 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 8.96 (s, 1H), 7.35 – 7.25 (m, 4H), 7.22 – 7.11 (m, 4H), 7.02 (d, J = 7.6 Hz, 1H), 2.91 – 2.87 (m, 2H), 2.80 – 2.76 (m, 2H), 1.21 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.4, 141.7, 137.7, 136.1, 129.5, 128.7 (two signals overlapped), 128.0, 126.4, 126.3, 125.5, 40.6, 38.3, 36.1, 28.9; HRMS (ESI) Calcd for C₁₉H₂₄N [M + H]⁺ 266.1909, found 266.1908.

2,2-Dimethyl-1-(2-(3-phenylpropyl)phenyl)propan-1-imine (3ac): Light yellow oil (51 mg, 91%).

R_f 0.50 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.20 (brs, 1H), 7.31 – 7.23 (m, 4H), 7.20 – 7.11 (m, 4H), 7.01 (d, $J = 7.5$ Hz, 1H), 2.67 (t, $J = 7.6$ Hz, 2H), 2.53 – 2.49 (m, 2H), 1.97 – 1.87 (m, 2H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 142.1, 141.6, 138.4, 129.3, 128.7, 128.6, 128.0, 126.3, 126.0, 125.3, 40.6, 36.2, 33.44 (two signals overlapped), 28.8; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 280.2065, found 280.2065.

1-(2-(4-Chlorobutyl)phenyl)-2,2-dimethylpropan-1-imine (3ad): Light yellow oil (38 mg, 75%). R_f 0.49 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.07 (brs, 1H), 7.27 – 7.23 (m, 2H), 7.19 – 7.12 (m, 1H), 7.03 (d, $J = 7.6$ Hz, 1H), 3.54 (t, $J = 6.4$ Hz, 2H), 2.54 – 2.48 (m, 2H), 1.86 – 1.65 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.5, 137.95, 129.3, 128.1, 126.4, 125.4, 45.0, 40.7, 33.0, 32.7, 29.0, 28.9; HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{23}\text{NCl}$ $[\text{M} + \text{H}]^+$ 252.1519, found 252.1517.

1-(2-(4-Fluorobutyl)phenyl)-2,2-dimethylpropan-1-imine (3ae): Light yellow oil (38 mg, 80%). R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.09 (brs, 1H), 7.26 – 7.25 (m, 2H), 7.19 – 7.12 (m, 1H), 7.03 (d, J = 7.7 Hz, 1H), 4.53 – 4.49 (m, 1H), 4.40 – 4.38 (m, 1H), 2.55 – 2.51 (m, 2H), 1.80 – 1.65 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.4, 138.1, 129.3, 128.1, 126.4, 125.4, 84.1 (d, $^1J_{\text{C-F}}$ = 167.7 Hz), 40.7, 33.4, 30.6 (d, $^2J_{\text{C-F}}$ = 19.6 Hz), 28.9, 27.5 (d, $^3J_{\text{C-F}}$ = 4.7 Hz); HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{23}\text{NF}$ $[\text{M} + \text{H}]^+$ 236.1815, found 236.1811.

2,2-Dimethyl-1-(2-(pent-4-en-1-yl)phenyl)propan-1-imine (3af): Light yellow oil (38 mg, 82%). R_f 0.62 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.18 (brs, 1H), 7.28 – 7.21 (m, 2H), 7.16 – 7.11 (m, 1H), 7.02 (d, J = 7.6 Hz, 1H), 5.86 – 5.75 (m, 1H), 5.06 – 4.94 (m, 2H), 2.51 – 2.46 (m, 2H), 2.12 – 2.07 (m, 2H), 1.72– 1.64 (m, 2H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.6, 138.5 (two signals overlapped), 129.4, 128.0, 126.3, 125.2, 115.2, 40.6, 34.0, 33.3, 31.0, 28.9. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{24}\text{N}$ $[\text{M} + \text{H}]^+$ 230.1909, found 230.1911.

1-(2-(hex-5-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (3ag): Light yellow oil (34 mg,

70%). R_f 0.65 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.10 (brs, 1H), 7.27 – 7.22 (m, 2H), 7.17 – 7.17 (m, 1H), 7.01 (d, J = 7.7 Hz, 1H), 5.85 – 5.74 (m, 1H), 5.03 – 4.91 (m, 2H), 2.52 – 2.43 (m, 2H), 2.10 – 2.03 (m, 2H), 1.65 – 1.55 (m, 2H), 1.47 – 1.39 (m, 2H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 141.6, 138.9, 138.7, 129.4, 128.0, 126.2, 125.2, 114.8, 40.6, 39.9, 33.8 (two signals overlapped), 31.4, 28.9. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 244.2065, found 244.2067.

2,2-Dimethyl-1-(2-(4-methylpent-3-en-1-yl)phenyl)propan-1-imine (3ah): Light yellow oil (37 mg, 75%). R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.14 (brs, 1H), 7.30 – 7.22 (m, 2H), 7.17 – 7.11 (m, 1H), 7.01 (d, J = 7.3 Hz, 1H), 5.17 – 5.10 (m, 1H), 2.52 – 2.48 (m, 2H), 2.28 – 2.22 (m, 2H), 1.68 (s, 3H), 1.55 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 141.6, 138.4, 132.8, 129.5, 127.9, 126.2, 125.2, 123.8, 40.6, 34.0, 30.4, 28.9, 25.9, 17.9. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 244.2065, found 244.2070.

1-(2-Isobutylphenyl)-2,2-dimethylpropan-1-imine (3ai): Light yellow oil (35 mg, 81%). R_f 0.62 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.16 (brs, 1H), 7.26 – 7.20 (m, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.01 (d, J = 7.6 Hz, 1H), 2.36 (d, J = 7.3 Hz, 2H), 1.95 – 1.87 (m, 1H), 1.21 (s, 9H), 0.88 (d, J = 6.5 Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 142.1, 137.6, 129.8, 127.8, 126.3, 125.2, 43.0, 40.6, 30.0, 29.0, 22.7. HRMS (ESI)

Calcd for $C_{15}H_{24}N$ $[M + H]^+$ 218.1909, found 218.1914.

1-(2-(Cyclobutylmethyl)phenyl)-2,2-dimethylpropan-1-imine (3aj): Light yellow oil (41 mg, 90%). R_f 0.63 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.12 (brs, 1H), 7.25 – 7.17 (m, 2H), 7.13 (td, J = 7.3, 1.8 Hz, 1H), 7.00 (d, J = 7.4 Hz, 1H), 2.62 – 2.50 (m, 3H), 2.09 – 2.00 (m, 2H), 1.89 – 1.64 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.9, 141.7, 137.3, 129.1, 127.8, 126.2, 125.2, 40.6 (two signals overlapped), 37.1, 28.9 (two signals overlapped), 18.6. HRMS (ESI) Calcd for $C_{16}H_{24}N$ $[M + H]^+$ 230.1909, found 230.1915.

1-(2-(cyclohexylmethyl)phenyl)-2,2-dimethylpropan-1-imine (3ak)¹³: Light yellow oil (45 mg, 87%). R_f 0.64 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.13 (brs, 1H), 7.25 – 7.19 (m, 2H), 7.13 (td, J = 7.2, 2.0 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 2.36 (d, J = 7.1 Hz, 2H), 1.72 – 1.49 (m, 6H), 1.26 – 1.10 (m, 12H), 0.98 – 0.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 142.1, 137.2, 129.9, 127.6, 126.2, 125.1, 41.7, 40.6, 39.6, 33.5, 29.0, 26.7, 26.6. HRMS (ESI) Calcd for $C_{18}H_{28}N$ $[M + H]^+$ 258.2222, found 258.2222.

2,2-Dimethyl-1-(2-neopentylphenyl)propan-1-imine (3al): Light yellow oil (42 mg, 91%). R_f 0.67 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.26 (brs, 1H), 7.28 – 7.20 (m, 2H), 7.16 (td, J = 7.3, 1.7 Hz, 1H), 6.97 (d, J = 7.3 Hz, 1H), 2.43 (s, 2H), 1.17 (s, 9H), 0.92 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.9, 142.6, 135.8, 130.9, 127.1, 126.7, 125.7, 47.4, 40.7, 32.8, 30.3, 29.2. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 232.2065, found 232.2058.

1-(2-Cyclopentylphenyl)-2,2-dimethylpropan-1-imine (3am): Light yellow oil (39 mg, 85%). R_f 0.56 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.11 (s, 1H), 7.34 – 7.25 (m, 2H), 7.11 (td, J = 7.5, 1.4 Hz, 1H), 6.99 (dd, J = 7.6, 1.2 Hz, 1H), 2.85 – 2.73 (m, 1H), 2.03 – 1.92 (m, 2H), 1.87 – 1.76 (m, 2H), 1.70 – 1.50 (m, 4H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.1, 143.5, 141.6, 128.3, 126.9, 125.9, 124.9, 43.4, 40.6, 28.9 (two signals overlapped), 26.4. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{24}\text{N}$ $[\text{M} + \text{H}]^+$ 230.1909, found 230.1901.

1-(2-Cyclohexylphenyl)-2,2-dimethylpropan-1-imine (3an): Light yellow oil (42 mg,

87%). R_f 0.56 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.13 (brs, 1H), 7.32 – 7.24 (m, 2H), 7.14 – 7.10 (m, 1H), 7.00 – 6.96 (m, 1H), 2.36 (tt, J = 11.7, 3.1 Hz, 1H), 1.86 – 1.65 (m, 6H), 1.37 – 1.19 (m, 13H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.1, 144.0, 141.0, 128.1, 127.0, 126.2, 125.2, 42.3, 40.6, 29.0, 27.1 (two signals overlapped), 26.3. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 244.2065, found 244.2070.

1-(2-Cycloheptylphenyl)-2,2-dimethylpropan-1-imine (3ao): Light yellow oil (43 mg, 84%). R_f 0.56 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.14 (brs, 1H), 7.27 – 7.26 (m, 2H), 7.14 – 7.07 (m, 1H), 6.97 (d, J = 7.7 Hz, 1H), 2.52 (t, J = 10.1 Hz, 1H), 1.85 – 1.41 (m, 12H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.2, 146.3, 142.6, 128.3, 127.0, 126.0, 124.9, 43.7, 40.6, 29.0, 28.0 (two signals overlapped), 27.7. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 258.2222, found 258.2228.

1-(2-Isopropylphenyl)-2,2-dimethylpropan-1-imine (3ap): Light yellow oil (21 mg, 51%). R_f 0.62 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.17 (brs, 1H), 7.34 – 7.27 (m, 2H), 7.13 (td, J = 7.6, 1.5 Hz, 1H), 6.99 (dd, J = 7.6, 0.8 Hz, 1H), 2.78 (hept, J = 6.9 Hz, 1H), 1.27 – 1.18 (m, 15H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 145.2, 140.7, 128.3, 126.2 (two signals overlapped), 125.2, 47.4, 40.7, 31.4, 28.9. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{22}\text{N}$ $[\text{M} + \text{H}]^+$ 204.1752, found 204.1757.

1-(2-(Sec-butyl)phenyl)-2,2-dimethylpropan-1-imine (3aq): Light yellow oil (24 mg, 53%). R_f 0.59 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.14 (brs, 1H), 7.31 – 7.25 (m, 2H), 7.16 – 7.10 (m, 1H), 6.99 (d, J = 7.6 Hz, 1H), 2.56 – 2.43 (m, 1H), 1.58 (d, J = 6.5 Hz, 2H), 1.23 (s, 9H), 1.19 (d, J = 7.0 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 144.3, 141.3, 128.2, 126.4, 126.2, 125.1, 40.6, 38.2, 30.4, 29.2, 29.1, 22.2, 12.6. HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{24}\text{N}$ $[\text{M} + \text{H}]^+$ 218.1909, found 218.1904.

2,2-dimethyl-1-(4-methyl-2-octylphenyl)propan-1-imine (3ba): Light yellow oil (50 mg, 87%). R_f 0.62 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.09 (brs, 1H), 7.05 (s, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 2.45 – 2.38 (m, 2H), 2.32 (s, 3H), 1.60 – 1.50 (m, 2H), 1.38 – 1.18 (m, 19H), 0.89–0.86 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 138.9 (two signals overlapped), 137.5, 130.0, 126.1, 125.8, 40.6, 33.9, 32.1, 30.1, 29.7, 29.5, 28.97, 22.9, 21.4, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{34}\text{N}$ $[\text{M} + \text{H}]^+$ 288.2691, found 288.2700.

2,2-Dimethyl-1-(3-octyl-[1,1'-biphenyl]-4-yl)propan-1-imine (3ca): Light yellow oil (60 mg, 87%). R_f 0.57 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.27 (brs, 1H), 7.62 – 7.58 (m, 2H), 7.50 – 7.42 (m, 3H), 7.39 – 7.33 (m, 2H), 7.10 (d, J = 7.9 Hz, 1H), 2.57 – 2.51 (m, 2H), 1.69 – 1.59 (m, 2H), 1.42 – 1.22 (m, 19H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 141.0 (two signals overlapped), 140.8, 139.5, 129.0, 128.1, 127.6, 127.3, 126.7, 123.9, 40.7, 34.1, 32.1, 30.1, 29.7, 29.4, 29.0, 22.9 (two signals overlapped), 14.3. HRMS (ESI) Calcd for $\text{C}_{25}\text{H}_{36}\text{N}$ $[\text{M} + \text{H}]^+$ 350.2848, found 350.2856.

2,2-Dimethyl-1-(3-octyl-[1,1'-biphenyl]-4-yl)propan-1-imine (3da): Light yellow oil (60 mg, 87%). R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.05 (brs, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 2.5 Hz, 1H), 6.67 (dd, J = 8.4, 2.6 Hz, 1H), 3.79 (s, 3H), 2.46 – 2.39 (m, 2H), 1.61 – 1.51 (m, 2H), 1.34 – 1.18 (m, 19H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 159.1, 140.8, 131.2, 127.3, 114.7, 110.4, 55.4, 40.7, 34.1, 32.1, 31.9, 30.0, 29.7, 29.4, 28.9, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{34}\text{NO}$ $[\text{M} + \text{H}]^+$ 304.2640, found 304.2640.

2,2-Dimethyl-1-(2-octyl-4-(trifluoromethoxy)phenyl)propan-1-imine (3ea): Light yellow oil (63 mg, 88%). R_f 0.52 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.20 (brs, 1H), 7.09 (s, 1H), 7.05 – 6.97 (m, 2H), 2.50 – 2.43 (m, 2H), 1.62 –

1.51 (m, 2H), 1.37 – 1.15 (m, 19H), 0.87 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.7, 148.9, 141.7, 140.0, 127.6, 121.6, 120.7 (q, $^1J_{\text{C-F}} = 241.4$ Hz), 117.6, 40.7, 33.8, 32.1, 31.6, 29.9, 29.6, 29.4, 28.8, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{31}\text{NOF}_3$ $[\text{M} + \text{H}]^+$ 358.2358, found 358.2355.

2,2-Dimethyl-1-(4-(methylthio)-2-octylphenyl)propan-1-imine (3fa): Light yellow oil (51 mg, 88%). R_f 0.60 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.15 (brs, 1H), 7.13 (d, $J = 1.6$ Hz, 1H), 7.02 (dd, $J = 8.0, 1.8$ Hz, 1H), 6.93 (d, $J = 8.0$ Hz, 1H), 2.48 (s, 3H), 2.45 – 2.39 (m, 2H), 1.59 – 1.51 (m, 2H), 1.37 – 1.18 (m, 19H), 0.87 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 139.8, 138.5, 138.0, 127.4, 126.7, 123.1, 40.7, 33.9, 32.1, 31.9, 30.0, 29.6, 29.4, 28.9, 22.9, 15.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{34}\text{NS}$ $[\text{M} + \text{H}]^+$ 320.2412, found 320.2411.

1-(4-(Dimethylamino)-2-octylphenyl)-2,2-dimethylpropan-1-one (3ga): The crude product was hydrolyzed with HCl (3M, 1 mL). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded the title compound as a light yellow oil (52 mg, 82%). R_f 0.55 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.20 (d, $J = 8.6$ Hz, 1H), 6.54 (d, $J = 2.6$ Hz, 1H), 6.48 (dd, $J = 8.6, 2.6$ Hz, 1H), 2.97 (s, 6H), 2.53 – 2.47 (m, 2H), 1.61 – 1.51 (m, 2H), 1.37 – 1.22 (m, 19H), 0.91 – 0.85 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 213.8, 150.9, 142.4, 128.5, 127.2, 113.6, 108.4, 45.0, 40.5, 34.6, 32.4,

32.2, 30.1, 29.8, 29.5, 28.4, 22.9, 14.4, 1.3. HRMS (ESI) Calcd for $C_{21}H_{36}NO$ $[M + H]^+$ 318.2797, found 318.2797.

1-(4-Fluoro-2-octylphenyl)-2,2-dimethylpropan-1-imine (3ha): Light yellow oil (50 mg, 85%). R_f 0.58 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 8.96 (brs, 1H), 7.01 – 6.91 (m, 2H), 6.86 – 6.79 (m, 1H), 2.48 – 2.41 (m, 2H), 1.60 – 1.51 (m, 2H), 1.36 – 1.17 (m, 19H), 0.89 – 0.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.0, 162.4 (d, $^1J_{C-F}$ = 246.0 Hz), 141.9, 137.4, 127.8 (d, $^3J_{C-F}$ = 8.0 Hz), 115.8 (d, $^2J_{C-F}$ = 21.0 Hz), 112.2 (d, $^2J_{C-F}$ = 21.5 Hz), 40.7, 33.9, 32.1, 31.5, 29.9, 29.6, 29.4, 28.8, 22.9, 14.3. HRMS (ESI) Calcd for $C_{19}H_{31}NF$ $[M + H]^+$ 292.2441, found 292.2444.

2,2-Dimethyl-1-(5-methyl-2-octylphenyl)propan-1-imine (3ia): Light yellow oil (50 mg, 86%). R_f 0.61 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 8.89 (brs, 1H), 7.13 (d, J = 7.9 Hz, 1H), 7.05 (dd, J = 8.1, 1.2 Hz, 1H), 6.81 (s, 1H), 2.45 – 2.38 (m, 2H), 2.30 (s, 3H), 1.58 – 1.49 (m, 2H), 1.36 – 1.18 (m, 19H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 135.9, 134.5, 129.2 (two signals overlapped), 128.7, 126.7, 40.5, 33.5, 32.1, 32.7, 30.0, 29.7, 29.5, 29.0, 22.9, 21.2, 14.3. HRMS (ESI) Calcd for $C_{20}H_{34}N$ $[M + H]^+$ 288.2691, found 288.2690.

2,2-dimethyl-1-(2-octyl-5-(trifluoromethyl)phenyl)propan-1-imine (3ja): Light yellow oil (53 mg, 77%). R_f 0.60 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.22 (brs, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.27 – 7.26 (m, 1H), 2.55 – 2.48 (m, 2H), 1.63 – 1.53 (m, 2H), 1.39 – 1.19 (m, 19H), 0.91 – 0.83 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.3, 143.5, 141.8, 129.9, 127.6 (q, $^2J_{\text{C-F}}$ = 32.7 Hz), 124.75 (q, $^3J_{\text{C-F}}$ = 3.5 Hz), 124.3 (d, $^1J_{\text{C-F}}$ = 274.0 Hz), 123.19 (d, $^3J_{\text{C-F}}$ = 5.8 Hz), 40.7, 33.9, 32.1, 31.7, 30.0, 29.6, 29.4, 28.8, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{31}\text{NF}_3$ $[\text{M} + \text{H}]^+$ 342.2409, found 342.2407.

2,2-Dimethyl-1-(5-methyl-2-octylphenyl)propan-1-imine (3ka) and 1-(3-methoxy-2-octylphenyl)-2,2-dimethylpropan-1-imine (3ka'): Light yellow oil (52 mg, 85%) with the ratio of 4:1. R_f 0.50 (hexane/EtOAc/ NEt_3 = 10/1/1); major component: ^1H NMR (400 MHz, CDCl_3): δ 7.15 (d, J = 8.6 Hz, 1H), 6.80 (dd, J = 8.6, 2.7 Hz, 1H), 6.54 (d, J = 2.7 Hz, 1H), 3.77 (s, 3H), 2.42 – 2.35 (m, 2H), 1.58 – 1.47 (m, 2H), 1.34 – 1.19 (m, 19H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 156.8, 142.4, 131.1, 130.4, 113.4, 111.9, 55.5, 40.5, 33.1, 32.2, 32.1, 30.0, 29.7, 29.0, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{34}\text{NO}$ $[\text{M} + \text{H}]^+$ 304.2640, found 304.2645.

2,2-dimethyl-1-(4-octylbenzo[d][1,3]dioxol-5-yl)propan-1-imine (3ma) and 1-(3-methoxy-2-octylphenyl)-2,2-dimethylpropan-1-imine (3ma'): Light yellow oil (52 mg, 82%) with the ratio of 3:2. R_f 0.50 (hexane/EtOAc/NEt₃ = 10/1/1); major and minor components: ¹H NMR (400 MHz, CDCl₃): δ 9.16 (brs, 1H) (major + minor), 6.70 (s, 1H) (minor), 6.62 (d, J = 8.0 Hz, 1H) (major), 6.50 (d, J = 8.1 Hz, 1H) (major + minor), 5.94 (s, 2H) (major), 5.92 (s, 2H) (minor), 2.44 – 2.32 (m, 2H) (major + minor), 1.56 – 1.47 (m, 2H) (major + minor), 1.37 – 1.17 (m, 19H) (major + minor), 0.86 (t, J = 6.6 Hz, 3H) (major + minor); ¹³C NMR (100 MHz, CDCl₃): δ 190.4, 190.0, 147.3, 146.5, 146.3, 144.9, 136.0, 132.9, 121.8, 119.4, 109.2, 106.5, 105.6, 101.2, 101.0, 40.6, 33.8, 32.2, 32.1, 30.6, 30.2, 29.9, 29.7, 29.6, 29.4, 29.1, 29.0, 22.9, 14.3. HRMS (ESI) Calcd for C₂₀H₃₂NO₂ [M + H]⁺ 318.2433, found 318.2435.

2,2-Dimethyl-1-(3-octylnaphthalen-2-yl)propan-1-imine (3na): Light yellow oil (55 mg, 85%) R_f 0.58 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 8.89 (brs, 1H), 7.78 (dd, J = 7.5, 1.9 Hz, 2H), 7.71 (s, 1H), 7.49 (s, 1H), 7.48 – 7.41 (m, 2H), 2.67 – 2.60 (m, 2H), 1.74 – 1.62 (m, 2H), 1.46 – 1.21 (m, 19H), 0.89 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 190.9, 140.5, 137.3, 133.1, 131.2, 127.9, 127.6, 127.4, 126.4, 125.9, 124.8, 40.8, 34.0, 32.1, 31.8, 30.0, 29.7, 29.5, 29.0, 22.9, 14.3. HRMS (ESI) Calcd for C₂₃H₃₄N [M + H]⁺ 324.2691, found 324.2686.

1-(3,5-Difluoro-2-octylphenyl)-2,2-dimethylpropan-1-imine (3oa): Light yellow oil (48 mg, 78%) R_f 0.58 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.23 (brs, 1H), 6.76 – 6.71 (m, 1H), 6.58 (d, $J = 8.4$ Hz, 1H), 2.48 – 2.33 (s, 2H), 1.54 – 1.42 (m, 2H), 1.36 – 1.17 (m, 19H), 0.87 (t, $J = 6.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 188.4, 161.9 (dd, $^1J_{\text{C-F}} = 248.8$ Hz, $^3J_{\text{C-F}} = 12.2$ Hz), 160.4 (dd, $^1J_{\text{C-F}} = 247.3$ Hz, $^2J_{\text{C-F}} = 12.8$ Hz), 144.0, 122.9, 109.2 (d, $^2J_{\text{C-F}} = 23.0$ Hz), 103.3 (t, $^2J_{\text{C-F}} = 25.9$ Hz), 40.6, 32.1, 30.9, 30.2, 29.5, 29.4, 28.9, 28.1, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{30}\text{NF}_2$ $[\text{M} + \text{H}]^+$ 310.2346, found 310.2343.

1-(2-Cyclohexyl-4-methylphenyl)-2,2-dimethylpropan-1-imine (3bn): Light yellow oil (43 mg, 83%). R_f 0.57 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.09 (brs, 1H), 7.10 (s, 1H), 6.94 (d, $J = 7.7$ Hz, 1H), 6.88 (d, $J = 7.8$ Hz, 1H), 2.38 – 2.28 (m, 4H), 1.83 – 1.66 (m, 4H), 1.56 – 1.18 (m, 15H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.2, 144.0, 138.4, 137.6, 127.6, 126.1, 125.9, 42.2, 40.6, 29.0, 27.1 (two signals overlapped), 26.3, 21.6. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 258.2222, found 258.2224.

1-(2-Cyclohexyl-4-(methylthio)phenyl)-2,2-dimethylpropan-1-imine (3fn): Light yellow oil (39 mg, 68%). R_f 0.53 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.16 (brs, 1H), 7.18 (d, J = 1.9 Hz, 1H), 7.01 (dd, J = 8.1, 1.9 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H), 2.49 (s, 3H), 2.38 – 2.30 (m, 1H), 1.83 – 1.69 (m, 4H), 1.46 – 1.24 (m, 6H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.6, 144.8, 138.1 (two signals overlapped), 126.8, 125.3, 123.2, 42.3, 40.7, 28.9, 27.0 (two signals overlapped), 26.3, 16.0. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{28}\text{NS}$ $[\text{M} + \text{H}]^+$ 290.1942, found 290.1938.

1-(2-Cyclohexyl-5-methylphenyl)-2,2-dimethylpropan-1-imine (3in): Light yellow oil (37 mg, 71%). R_f 0.61 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.10 (brs, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.09 (dd, J = 7.8, 1.6 Hz, 1H), 6.79 (d, J = 1.0 Hz, 1H), 2.37 – 2.27 (m, 4H), 1.79 – 1.70 (m, 4H), 1.51 – 1.19 (m, 15H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.2, 141.1, 134.6, 128.9 (two signals overlapped), 126.8, 126.6, 41.9, 40.5, 29.0, 27.2 (two signals overlapped), 26.35, 21.21. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 258.2222, found 258.2224.

1-(3-Cyclohexylnaphthalen-2-yl)-2,2-dimethylpropan-1-imine (3nn): Light yellow oil (48 mg, 81%). R_f 0.58 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.24 (brs, 1H), 7.78 (t, J = 7.0 Hz, 2H), 7.75 (s, 1H), 7.49 – 7.40 (m, 3H), 2.46 (t, J = 11.5 Hz, 1H), 1.95 – 1.73 (m, 6H), 1.46 – 1.24 (m, 13H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 142.6, 140.3, 133.1, 131.1, 127.7, 127.4, 126.2, 125.8, 125.4, 124.6, 42.3, 40.7, 28.9, 27.2 (two signals overlapped), 26.2. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 294.2222, found 294.2224.

Experiment Detail for Cobalt-Catalyzed C–H Arylation of Pivalophenone Imines with Aryl Chlorides

Typical Procedure: 1-(4'-methoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (**5aa**). In a Schlenk tube were placed **L2**•HBr (7.5 mg, 0.020 mmol), $\text{Co}(\text{acac})_3$ (6.8 mg, 0.020 mmol), and THF (0.3 mL). The resulting solution was cooled in an ice bath, followed by the addition of $t\text{-BuCH}_2\text{MgBr}$ (2.0 M in THF, 0.2 mL, 0.40 mmol). After stirring for 30 min, TMEDA (24 μL , 0.16 mmol), 2,2-dimethyl-1-phenylpropan-1-imine (**1a**, 33 mg, 0.20 mmol), and 1-bromo-4-methoxybenzene (**4a**, 37 μL , 0.3 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 12 h, and then filtered through a

short silica-gel column, which was washed with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/NEt₃ = 30/1/1) of the crude product afforded the title compound as a colorless oil (45 mg, 84%).

R_f 0.24 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.63 (brs, 1H), 7.44 – 7.25 (m, 5H), 7.16 – 7.08 (m, 1H), 6.96 – 6.86 (m, 2H), 3.82 (s, 3H), 0.89 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.8, 159.1, 141.2, 138.2, 134.2, 131.2, 130.2, 128.2, 127.8, 126.6, 113.7, 55.4, 40.6, 28.8. HRMS (ESI) Calcd for C₁₈H₂₂NO [M + H]⁺ 268.1701, found 268.1704.

1-([1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ab): Light yellow oil (39 mg, 81%). R_f 0.45 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.04 (brs, 1H), 7.43 – 7.28 (m, 8H), 7.13 (d, J = 7.7 Hz, 1H), 0.87 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.6, 141.7, 141.2, 138.6, 130.4, 130.2, 128.4, 128.3, 127.9, 127.5, 127.0, 40.6, 28.9. HRMS (ESI) Calcd for C₁₇H₂₀N [M + H]⁺ 238.1596, found 238.1600.

2,2-Dimethyl-1-(4'-methyl-[1,1'-biphenyl]-2-yl)propan-1-imine (5ac): Light yellow oil (42 mg, 83%). R_f 0.46 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.27

(brs, 1H), 7.41 – 7.24 (m, 5H), 7.16 (d, $J = 7.8$ Hz, 2H), 7.12 (d, $J = 7.4$ Hz, 1H), 2.37 (s, 3H), 0.89 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.7, 141.2, 138.8, 138.6, 137.2, 130.4, 130.0, 129.1, 128.2, 127.8, 126.8, 40.6, 28.9, 21.4. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{22}\text{N}$ [$\text{M} + \text{H}$] $^+$ 252.1752, found 252.1754.

1-(4'-Fluoro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ad): Light yellow oil (40 mg, 79%). R_f 0.41 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.61 (brs, 1H), 7.41 – 7.30 (m, 5H), 7.13 (d, $J = 7.7$ Hz, 1H), 7.08 – 7.01 (m, 2H), 0.88 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.4, 162.4 (d, $^1J_{\text{C-F}} = 246.9$ Hz), 141.2, 137.7 (d, $^4J_{\text{C-F}} = 3.3$ Hz), 137.6, 131.8 (d, $^3J_{\text{C-F}} = 7.9$ Hz), 130.3, 128.3, 128.0, 127.1, 115.3 (d, $^2J_{\text{C-F}} = 21.4$ Hz), 40.7, 28.8. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{NF}$ [$\text{M} + \text{H}$] $^+$ 256.1502, found 256.1507.

2,2-Dimethyl-1-(4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)propan-1-imine (5ae): Light yellow oil (42 mg, 68%). R_f 0.40 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.69 (brs, 1H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.51 (d, $J = 7.9$ Hz, 2H), 7.43 – 7.33 (m, 3H), 7.20 – 7.16 (m, 1H), 0.88 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 145.4, 141.0, 137.3, 130.6, 130.31, 129.7 (q, $^2J_{\text{C-F}} = 32.5$ Hz), 128.5, 128.1, 127.8, 125.3 (q, $^3J_{\text{C-F}} = 3.4$ Hz), 124.4 (q, $^1J_{\text{C-F}} = 272.0$ Hz), 40.8, 28.8. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NF}_3$ [$\text{M} + \text{H}$] $^+$

306.1470, found 306.1472.

2'-(1-Imino-2,2-dimethylpropyl)-N,N-dimethyl-[1,1'-biphenyl]-4-amine (5af): Light yellow oil (45 mg, 81%). R_f 0.35 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.28 (brs, 1H), 7.39 – 7.31 (m, 2H), 7.28 – 7.23 (m, 3H), 7.09 (d, J = 7.4 Hz, 1H), 6.74 – 6.69 (m, 2H), 2.97 (s, 6H), 0.91 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 192.4, 149.9, 141.2, 138.8, 130.8, 130.2, 129.8, 128.2, 127.9, 126.0, 112.3, 40.7, 40.6, 29.0. HRMS (ESI) Calcd for C₁₉H₂₅N₂ [M + H]⁺ 281.2018, found 281.2016.

1-(4'-((Tert-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ag): Light yellow oil (57 mg, 78%). R_f 0.34 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.25 (brs, 1H), 7.39 – 7.27 (m, 3H), 7.23 (d, J = 8.5 Hz, 2H), 7.11 – 7.08 (m, 1H), 6.85 – 6.81 (m, 2H), 0.99 (s, 9H), 0.87 (s, 9H), 0.20 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 192.0, 155.4, 138.3, 134.9, 131.3, 130.2, 128.2, 127.9, 126.9, 126.6, 120.1, 40.6, 28.9, 28.1, 26.0, -4.2. HRMS (ESI) Calcd for C₂₃H₃₄NOSi [M + H]⁺ 368.2410, found 368.2409.

2,2-Dimethyl-1-(4'-(trimethylsilyl)-[1,1'-biphenyl]-2-yl)propan-1-imine (5ah): Light yellow oil (50 mg, 81%). R_f 0.46 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.57 (brs, 1H), 7.53 – 7.48 (m, 2H), 7.43 – 7.29 (m, 1H), 7.14 (d, J = 7.3 Hz, 5H), 0.88 (s, 9H), 0.28 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.5, 142.0, 141.3, 139.5, 138.6, 133.3, 130.4, 129.5, 128.2, 127.8, 127.0, 40.6, 28.9, -0.9. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{28}\text{NSi}$ $[\text{M} + \text{H}]^+$ 310.1991, found 310.1997.

2,2-dimethyl-1-(3'-methyl-[1,1'-biphenyl]-2-yl)propan-1-imine (5ai): Light yellow oil (41 mg, 82%). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.57 (brs, 1H), 7.40 – 7.29 (m, 3H), 7.26 – 7.21 (m, 1H), 7.20 – 7.14 (m, 2H), 7.12 (d, J = 7.4 Hz, 2H), 2.36 (s, 3H), 0.88 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.7, 141.6, 141.3, 138.6, 137.9, 130.9, 130.3, 128.2, 128.2, 128.2, 127.8, 127.3, 126.9, 40.6, 29.0, 21.7. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{22}\text{N}$ $[\text{M} + \text{H}]^+$ 252.1752, found 252.1756.

1-(3'-Fluoro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5aj): Light yellow oil

(38 mg, 75%). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.65 (brs, 1H), 7.43 – 7.29 (m, 4H), 7.18 – 7.09 (m, 3H), 7.05 – 6.98 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.0, 162.6 (d, $^1J_{\text{C-F}} = 246.1$ Hz), 143.7 (d, $^4J_{\text{C-F}} = 8.1$ Hz), 137.2, 130.1, 129.7 (d, $^3J_{\text{C-F}} = 8.3$ Hz), 128.2, 128.0 (d, $^3J_{\text{C-F}} = 8.5$ Hz), 127.3, 126.7, 125.9 (d, $^4J_{\text{C-F}} = 2.4$ Hz), 117.0 (d, $^2J_{\text{C-F}} = 21.8$ Hz), 114.2 (d, $^2J_{\text{C-F}} = 21.0$ Hz), 40.6, 28.7. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{19}\text{NF}$ $[\text{M} + \text{H}]^+$ 256.1502, found 256.1498.

1-(3'-Methoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ak): Light yellow oil (45 mg, 84%). R_f 0.30 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.58 (brs, 1H), 7.41 – 7.30 (m, 3H), 7.27 (t, $J = 7.9$ Hz, 1H), 7.13 (d, $J = 7.4$ Hz, 1H), 6.99 – 6.93 (m, 2H), 6.88 – 6.84 (m, 1H), 3.80 (s, 3H), 0.90 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.7, 159.5, 143.1, 141.2, 138.4, 130.2, 129.4, 128.2, 128.0, 127.1, 122.7, 115.6, 113.3, 55.5, 40.7, 28.9. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}$ $[\text{M} + \text{H}]^+$ 268.1701, found 268.1702.

2,2-Dimethyl-1-(3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)propan-1-imine (5al): Light yellow oil (37 mg, 61%). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.69 (brs, 1H), 7.67 (s, 1H), 7.58 (d, $J = 7.7$ Hz, 2H), 7.51 – 7.34 (m, 4H), 7.18 (d, $J = 7.4$ Hz, 1H), 0.87 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.9, 142.4, 137.2, 133.6,

130.8 (q, $^2J_{C-F} = 32.2$ Hz), 130.6, 130.3, 128.8, 128.5, 128.1, 127.7, 127.0 (q, $^3J_{C-F} = 3.2$ Hz), 124.3 (q, $^1J_{C-F} = 272.4$ Hz), 124.2 (q, $^3J_{C-F} = 3.6$ Hz), 40.8, 28.8. HRMS (ESI) Calcd for $C_{18}H_{19}NF_3$ $[M + H]^+$ 306.1470, found 306.1471.

2,2-Dimethyl-1-(2'-methyl-[1,1'-biphenyl]-2-yl)propan-1-imine (5am): Light yellow oil (34 mg, 61%). R_f 0.45 (hexane/EtOAc/ $NEt_3 = 10/1/1$); 1H NMR (400 MHz, $CDCl_3$): δ 9.14 (brs, 1H), 7.38 – 7.30 (m, 2H), 7.25 – 7.21 (m, 3H), 7.18 – 7.14 (m, 3H), 2.21 (s, 3H), 0.91 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 142.1, 140.4, 137.7, 136.1, 131.4, 131.1, 130.5, 127.8, 127.6, 127.5, 126.9, 125.3, 40.3, 29.1, 20.8. HRMS (ESI) Calcd for $C_{18}H_{22}N$ $[M + H]^+$ 252.1752, found 252.1749.

1-(2'-Fluoro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5an): Light yellow oil (33 mg, 61%). R_f 0.46 (hexane/EtOAc/ $NEt_3 = 10/1/1$); 1H NMR (400 MHz, $CDCl_3$): δ 9.54 (brs, 1H), 7.41 – 7.24 (m, 5H), 7.20 – 7.16 (m, 1H), 7.15 – 7.07 (m, 2H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 159.8 (d, $^1J_{C-F} = 246.0$ Hz), 142.0, 132.9, 132.4, 131.2, 129.8 (d, $^3J_{C-F} = 8.0$ Hz), 128.9 (d, $^2J_{C-F} = 15.6$ Hz), 127.8, 127.6, 127.4, 123.8 (d, $^3J_{C-F} = 3.3$ Hz), 115.9 (d, $^2J_{C-F} = 22.8$ Hz), 40.4, 28.9. HRMS (ESI) Calcd for $C_{17}H_{19}NF$ $[M + H]^+$ 256.1502, found 256.1500.

1-(2'-Methoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ao): Light yellow oil (38 mg, 71%). R_f 0.35 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.29 (brs, 1H), 7.38 – 7.26 (m, 4H), 7.15 – 7.13 (m, 2H), 6.94 (tt, J = 7.5, 0.9 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 3.75 (s, 3H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 156.7, 135.4, 132.2, 131.2, 130.3, 129.3, 127.6, 126.9 (two signals overlapped), 126.7, 120.2, 110.8, 55.4, 40.0, 29.2. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}$ $[\text{M} + \text{H}]^+$ 268.1701, found 268.1700.

2,2-dimethyl-1-(2'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)propan-1-imine (5ap): Light yellow oil (28 mg, 45%). R_f 0.45 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.42 (brs, 1H), 7.74 – 7.71 (m, 1H), 7.52 – 7.42 (m, 2H), 7.38 – 7.29 (m, 4H), 7.24 – 7.20 (m, 1H), 1.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 189.8, 141.5, 139.4, 135.8, 132.9, 131.1, 131.0, 129.2 (q, $^2J_{\text{C-F}}$ = 29.4 Hz), 128.0, 127.5, 127.3, 127.2, 127.0 (q, $^3J_{\text{C-F}}$ = 5.2 Hz), 124.4 (q, $^1J_{\text{C-F}}$ = 274.1 Hz), 40.2, 29.4. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NF}_3$ $[\text{M} + \text{H}]^+$ 306.1470, found 306.1469.

2,2-Dimethyl-1-(2'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)propan-1-imine (5aq): Light yellow oil (47 mg, 84%). R_f 0.33 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.58 (brs, 1H), 7.39 – 7.27 (m, 3H), 7.13 – 7.08 (m, 1H), 6.89 – 6.78 (m, 3H), 5.98 (s, 2H), 0.92 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.7, 147.7, 147.1, 141.2, 138.2, 135.7, 130.3, 128.3, 128.0, 126.8, 123.9, 110.6, 108.2, 101.3, 40.7, 29.0. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 282.1494, found 282.1499.

1-(2',5'-Dimethoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ar): Light yellow oil (47 mg, 79%). R_f 0.31 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.40 (brs, 1H), 7.38 – 7.25 (m, 3H), 7.14 (dd, J = 7.1, 1.2 Hz, 1H), 6.86 – 6.79 (m, 2H), 6.74 (d, J = 2.6 Hz, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 0.96 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.2, 153.1, 151.0, 135.7, 131.1, 131.0, 127.6, 127.0, 126.8, 118.1, 114.1, 111.7 (two signals overlapped), 56.1, 55.8, 40.0, 29.2. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 298.1807, found 298.1805.

2,2-Dimethyl-1-(2-(naphthalen-2-yl)phenyl)propan-1-imine (5as): Light yellow oil (41 mg, 72%). R_f 0.41 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.71 (brs, 1H), 7.88 – 7.81 (m, 4H), 7.57 – 7.41 (m, 5H), 7.37 (td, J = 7.3, 1.9 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 0.86 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.6, 141.4, 139.2, 138.5, 133.3, 132.6, 130.7, 129.2, 128.4, 128.3 (two signals overlapped), 128.0, 128.0, 127.8, 127.1, 126.5, 126.4, 40.7, 29.0. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{22}\text{N}$ $[\text{M} + \text{H}]^+$ 288.1752, found 288.1755.

2,2-Dimethyl-1-(2-(naphthalen-1-yl)phenyl)propan-1-imine (5at): Light yellow oil (29 mg, 52%). R_f 0.41 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.44 (s, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.49 – 7.34 (m, 7H), 7.28 – 7.24 (m, 1H), 0.82 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.6, 142.7, 138.4, 136.6, 133.9, 132.6, 132.0, 129.0, 128.6, 128.2, 127.7, 127.4, 127.2, 126.4, 126.3, 125.9, 125.0, 40.3, 29.2. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{22}\text{N}$ $[\text{M} + \text{H}]^+$ 288.1752, found 288.1748.

1-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ba): Light yellow oil (45 mg, 80%). R_f 0.36 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz,

CDCl₃): δ 9.50 (brs, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.14 (s, 1H), 7.12 – 7.08 (m, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.91 – 6.86 (m, 2H), 3.82 (s, 3H), 2.39 (s, 3H), 0.89 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 192.0, 159.1, 138.1, 137.9, 134.4, 131.2, 131.0 (two signals overlapped), 127.8, 127.2, 113.7, 55.5, 40.6, 28.9, 21.4. HRMS (ESI) Calcd for C₁₉H₂₄NO [M + H]⁺ 282.1858, found 282.1859.

1-(4''-Methoxy-[1,1':3',1''-terphenyl]-4'-yl)-2,2-dimethylpropan-1-imine (5ca): Light yellow oil (53 mg, 78%). R_f 0.35 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.57 (brs, 1H), 7.65 – 7.61 (m, 2H), 7.56 (d, J = 1.8 Hz, 1H), 7.53 (dd, J = 7.8, 1.8 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.39 – 7.32 (m, 3H), 7.19 (d, J = 7.9 Hz, 1H), 6.94 – 6.90 (m, 2H), 3.84 (s, 3H), 0.93 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.8, 159.2, 141.1, 140.6, 140.1, 138.8, 134.2, 131.3, 129.1 (two signals overlapped), 128.5, 127.8, 127.3, 125.2, 113.9, 55.5, 40.8, 28.9. HRMS (ESI) Calcd for C₂₄H₂₆NO [M + H]⁺ 344.2014, found 344.2019.

1-(4',5-Dimethoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5da): Light yellow oil (48 mg, 81%). R_f 0.25 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.50 (brs, 1H), 7.29 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 8.1 Hz, 1H), 6.92 – 6.81 (m,

4H), 3.83 (s, 3H), 3.82 (s, 3H), 0.88 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.8, 159.2, 139.8, 134.2, 134.0, 131.1, 129.1 (two signals overlapped), 115.5, 113.8, 112.1, 55.5, 55.5, 40.7, 28.9. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 298.1807, found 298.1805.

1-(4'-Methoxy-5-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-

imine (5ea): Light yellow oil (55 mg, 78%). R_f 0.27 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.68 (brs, 1H), 7.30 (d, J = 7.5 Hz, 2H), 7.18 (s, 1H), 7.14 (s, 2H), 6.90 (dd, J = 8.5, 1.6 Hz, 2H), 3.83 (s, 3H), 0.87 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 159.6, 148.9, 140.0 (d, $^2J_{\text{C-F}}$ = 87.9 Hz), 132.8, 131.2, 129.5, 122.5, 120.7 (d, $^1J_{\text{C-F}}$ = 257.6 Hz), 118.8, 114.0, 55.5, 40.8, 28.8. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{F}_3$ $[\text{M} + \text{H}]^+$ 352.1524, found 352.1530.

1-(5-Fluoro-4'-methoxy-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ha):

Light yellow oil (45 mg, 79%). R_f 0.35 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.62 (brs, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.10 – 6.96 (m, 3H), 6.92 – 6.87 (m, 2H), 3.82 (s, 3H), 0.87 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.1, 162.3 (d, $^1J_{\text{C-F}}$ = 247.1 Hz), 159.5, 140.6, 137.2, 133.1, 131.1, 129.6 (d, $^3J_{\text{C-F}}$ = 8.1 Hz), 116.9 (d, $^2J_{\text{C-F}}$ = 21.3 Hz), 113.9, 113.4 (d, $^2J_{\text{C-F}}$ = 21.1 Hz), 55.5, 40.8, 28.8. HRMS (ESI) Calcd for

$C_{18}H_{21}NO$ $[M + H]^+$ 286.1607, found 286.1613.

1-(4'-Methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (5ia):

Light yellow oil (41 mg, 73%). R_f 0.37 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.57 (brs, 1H), 7.30 – 7.25 (m, 2H), 7.22 – 7.16 (m, 2H), 6.91 – 6.86 (m, 3H), 3.82 (s, 3H), 2.38 (s, 3H), 0.88 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.1, 159.0, 141.1, 136.3, 135.4, 134.3, 131.2, 130.2, 129.0, 128.5, 113.8, 55.5, 40.6, 29.0, 21.3. HRMS (ESI) Calcd for $C_{19}H_{24}NO$ $[M + H]^+$ 282.1858, found 282.1861.

1-(4-(4-Methoxyphenyl)benzo[d][1,3]dioxol-5-yl)-2,2-dimethylpropan-1-imine (5ma):

Light yellow oil (51 mg, 82%). R_f 0.31 (hexane/EtOAc/ NEt_3 = 10/1/1); 1H NMR (400 MHz, $CDCl_3$): δ 9.52 (brs, 1H), 7.33 (d, J = 8.7 Hz, 2H), 6.94 – 6.88 (m, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 5.96 (s, 2H), 3.82 (s, 3H), 0.89 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 159.4, 147.0, 145.3, 136.0, 131.9, 127.3, 121.2, 120.8, 113.9, 107.0, 101.2, 55.5, 40.6, 29.0. HRMS (ESI) Calcd for $C_{19}H_{22}NO_3$ $[M + H]^+$ 312.1600, found 312.1596.

1-(3-(4-Methoxyphenyl)naphthalen-2-yl)-2,2-dimethylpropan-1-imine (5na) and 1-(1-(4-methoxyphenyl)naphthalen-2-yl)-2,2-dimethylpropan-1-imine (5na'): Light yellow oil (48 mg, 75%) with a ratio of 3:2. R_f 0.35 (hexane/EtOAc/ NEt_3 = 10/1/1); major and minor components: ^1H NMR (400 MHz, CDCl_3): δ 9.62 (s, 1H, major + minor), 7.90 – 7.80 (m, 4H) (major + minor), 7.79 (s, 1H) (major), 7.65 (d, J = 8.5 Hz, 1H) (minor), 7.59 (s, 1H) (major), 7.54 – 7.46 (m, 4H) (major + minor), 7.43 – 7.37 (m, 3H) (major + minor), 7.29 – 7.24 (m, 2H) (major + minor), 7.00 – 6.92 (m, 4H) (major + minor), 3.87 (s, 3H) (minor), 3.85 (s, 3H) (major), 0.97 (s, 9H) (minor), 0.95 – 0.89 (m, 9H) (major); ^{13}C NMR (100 MHz, CDCl_3): δ 192.1, 191.3, 159.2, 159.2, 140.2, 139.8, 136.7, 135.1, 134.2, 133.16, 133.15, 133.13, 133.12, 133.11, 131.8, 131.6, 130.5, 129.0, 128.1, 127.9, 127.2, 127.1, 126.8, 126.7, 126.6, 126.6, 126.2, 124.8, 113.9, 113.5, 55.53, 55.51, 40.7, 40.2, 29.4, 29.0. HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{24}\text{NO}$ $[\text{M} + \text{H}]^+$ 318.1858, found 318.1860.

Experiment Detail for Cobalt-Catalyzed C–H Alkenylation of Pivalophenone Imines with Alkenyl Enol Phosphates

Typical Procedure: 2,2-dimethyl-1-(2',3',4',5'-tetrahydro-[1,1'-biphenyl])-2-

yl)propan-1-imine (7aa). In a Schlenk tube were placed **L5•HCl** (9.5 mg, 0.020 mmol), CoBr_2 (4.4 mg, 0.020 mmol), and THF (0.3 mL). The resulting solution was cooled in an ice bath, followed by the addition of *t*-BuCH₂MgBr (2.0 M in THF, 0.2 mL, 0.40 mmol). After stirring for 30 min, 2,2-dimethyl-1-phenylpropan-1-imine (**1a**, 33 mg, 0.20 mmol), and cyclohex-1-en-1-yl diethyl phosphate (**6a**, 70 mg, 0.3 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 12 h, and then filtered through a short silica-gel column, which was washed with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 50/1/1) of the crude product afforded the title compound as a colorless oil (43 mg, 88%).

R_f 0.54 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.33 (brs, 1H), 7.28 – 7.23 (m, 1H), 7.20 – 7.15 (m, 2H), 7.03 – 6.99 (m, 1H), 5.70 (brs, 1H), 2.32 – 2.25 (m, 2H), 2.15 – 2.09 (m, 2H), 1.75 – 1.67 (m, 2H), 1.65 – 1.58 (m, 2H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.9, 141.0, 140.5, 137.6, 129.4, 128.1, 127.8, 127.4, 126.0, 40.4, 30.3, 29.4, 25.8, 23.2, 22.0. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{24}\text{N}$ $[\text{M} + \text{H}]^+$ 242.1909, found 242.1910.

1-(2-(Cyclopent-1-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (7ab): Light yellow oil (39 mg, 85%). R_f 0.48 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.40 (brs, 1H), 7.27 – 7.25 (m, 2H), 7.20 – 7.16 (m, 1H), 7.01 (d, J = 7.7 Hz, 1H), 5.85 – 5.82 (m, 1H), 2.68 – 2.63 (m, 2H), 2.50 – 2.41 (m, 2H), 1.99 – 1.89 (m, 2H), 1.15 (s, 9H); ^{13}C

NMR (100 MHz, CDCl₃): δ 192.2, 142.6, 135.1, 134.8, 131.8, 127.8, 127.7, 127.5, 126.4, 47.4, 36.6, 34.0, 29.0, 23.7. HRMS (ESI) Calcd for C₁₆H₂₂N [M + H]⁺ 228.1752, found 228.1757.

1-(2-(Cyclohept-1-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (7ac): Light yellow oil (40 mg, 79%). *R_f* 0.52 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.32 (brs, 1H), 7.23 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.18 – 7.14 (m, 2H), 7.02 (dd, *J* = 7.3, 1.9 Hz, 1H), 5.80 (t, *J* = 6.5 Hz, 1H), 2.45 – 2.41 (m, 2H), 2.22 – 2.17 (m, 2H), 1.82 – 1.76 (m, 2H), 1.67 – 1.61 (m, 2H), 1.57 – 1.51 (m, 2H), 1.18 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.5, 144.7, 143.3, 134.1, 128.6, 128.2, 127.8, 127.1, 125.9, 43.7, 35.9, 32.7, 29.7, 29.2, 27.4, 26.8. HRMS (ESI) Calcd for C₁₈H₂₆N [M + H]⁺ 256.2065, found 256.2065.

1-(2-(Cyclooct-1-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (7ad): Light yellow oil (46 mg, 86%). *R_f* 0.54 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.24 (brs, 1H), 7.26 – 7.23 (m, 1H), 7.21 – 7.17 (m, 2H), 7.05 (d, *J* = 7.3 Hz, 1H), 5.64 (t, *J* = 8.3 Hz, 1H), 2.45 – 2.40 (m, 2H), 2.24 – 2.17 (m, 2H), 1.64 – 1.51 (m, 8H), 1.18 (s, 9H);

^{13}C NMR (100 MHz, CDCl_3): δ 191.8, 142.0, 140.9, 140.7, 132.4, 129.2, 127.8, 127.0, 126.1, 40.3, 31.4, 29.8 (two signals overlapped), 29.5, 27.2, 27.0, 26.5. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 270.2222, found 270.2226.

(E)-1-(2-(cyclodec-1-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (7ae): Light yellow oil (49 mg, 82%). R_f 0.54 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.24 (brs, 1H), 7.26 – 7.23 (m, 1H), 7.21 – 7.17 (m, 2H), 7.05 (d, J = 7.3 Hz, 1H), 5.64 (t, J = 8.3 Hz, 1H), 2.45 – 2.40 (m, 2H), 2.24 – 2.17 (m, 2H), 1.64 – 1.51 (m, 8H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.8, 142.0, 140.9, 140.7, 132.4, 129.2, 127.8, 127.0, 126.1, 40.3, 31.4, 29.8 (two signals overlapped), 29.5, 27.2, 27.0, 26.5. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{32}\text{N}$ $[\text{M} + \text{H}]^+$ 298.2535, found 298.2531.

1-(2-(Cyclododec-1-en-1-yl)phenyl)-2,2-dimethylpropan-1-imine (E/Z = 4/1) (7af): Light yellow oil (51 mg, 82%). R_f 0.56 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): major and minor components: δ 9.32 (brs, 1H) (major + minor), 7.35 – 7.09 (m, 3H) (major + minor), 7.04 (dd, J = 7.4, 1.4 Hz, 1H) (major), 6.97 (dd, J = 7.5, 0.9 Hz, 1H)

(minor), 5.78 (t, $J = 7.9$ Hz, 1H) (minor), 5.34 (t, $J = 7.9$ Hz, 1H) (major), 2.46 – 2.16 (m, 4H) (major + minor), 1.60 – 1.19 (m, 25H) (major + minor); ^{13}C NMR (100 MHz, CDCl_3): (major component) δ 191.3, 141.7, 141.4, 140.7, 133.3, 131.3, 127.8, 126.4, 126.1, 47.4, 40.3, 29.9, 27.6, 27.3, 25.7, 25.2, 24.9, 24.8, 24.7, 22.62, 22.56. HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{37}\text{N}$ $[\text{M} + \text{H}]^+$ 326.2848, found 326.2846.

2,2-Dimethyl-1-(4'-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine

(7ag): Light yellow oil (50 mg, 84%). R_f 0.64 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.24 (brs, 1H), 7.28 – 7.23 (m, 1H), 7.20 – 7.15 (m, 2H), 7.01 (d, $J = 7.2$ Hz, 1H), 5.72 – 5.68 (m, 1H), 2.45 – 2.11 (m, 3H), 1.94 – 1.82 (m, 2H), 1.32 – 1.14 (m, 11H), 0.89 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.9, 140.7, 140.5, 137.5, 129.7, 128.2, 127.8, 127.4, 126.1, 43.7, 40.4, 32.4, 31.9, 29.5, 27.4, 24.7. HRMS (ESI) Calcd for $\text{C}_{21}\text{H}_{32}\text{N}$ $[\text{M} + \text{H}]^+$ 298.2535, found 298.2534.

2,2-Dimethyl-1-(4'-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine

(7ah): Light yellow oil (54 mg, 85%). R_f 0.48 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.30 (brs, 1H), 7.34 – 7.18 (m, 8H), 7.05 (d, J = 7.3 Hz, 1H), 5.82 – 5.78 (m, 1H), 2.88 – 2.80 (m, 1H), 2.59 – 2.35 (m, 3H), 2.30 – 2.20 (m, 1H), 2.08 – 2.02 (m, 1H), 1.90 – 1.79 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.8, 146.9 (two signals overlapped), 140.5, 137.7, 128.9, 128.7, 128.3, 128.0, 127.5, 127.1, 126.4, 126.3, 40.5, 39.6, 34.1, 31.1, 30.4, 29.5. HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 318.2222, found 318.2222.

2,2-Dimethyl-1-(2'-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine

(7ai): Light yellow oil (45 mg, 88%). R_f 0.52 (hexane/EtOAc/ NEt_3 = 10/1/1); ^1H NMR (400 MHz, CDCl_3): δ 9.34 (brs, 1H), 7.26 – 7.17 (m, 2H), 7.11 (d, J = 7.3 Hz, 1H), 7.03 (d, J = 7.3 Hz, 1H), 5.68 – 5.58 (m, 1H), 2.58 – 2.42 (m, 1H), 2.22 – 2.06 (m, 2H), 1.89 – 1.64 (m, 2H), 1.44 – 1.19 (m, 11H), 0.84 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.6, 144.1, 140.8, 140.5, 130.6, 128.7, 127.7, 126.4, 126.0, 40.3, 33.0, 31.5, 30.0, 26.2, 20.3, 19.8. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{26}\text{NO}$ $[\text{M} + \text{H}]^+$ 256.2065, found 256.2061.

1-(2-(Hept-3-en-4-yl)phenyl)-2,2-dimethylpropan-1-imine (E/Z = 4/1) (7aj): Light yellow oil (46 mg, 90%). R_f 0.52 (hexane/EtOAc/NEt₃ = 10/1/1); major component: ¹H NMR (400 MHz, CDCl₃): δ 9.30 (brs, 1H), 7.26 – 7.13 (m, 3H), 7.05 – 7.02 (m, 1H), 5.37 (t, J = 7.2 Hz, 1H), 2.29 – 2.24 (m, 2H), 2.14 (p, J = 7.5 Hz, 2H), 1.30 (q, J = 7.5 Hz, 2H), 1.21 (s, 9H), 1.01 (t, J = 7.6 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 191.4, 141.6, 140.7, 140.5, 134.4, 130.5, 127.8, 126.6, 126.1, 40.3, 34.2, 29.9, 22.1, 21.8, 14.4, 14.2. HRMS (ESI) Calcd for C₁₈H₂₈N [M + H]⁺ 258.2222, found 258.2224.

2,2-Dimethyl-1-(5-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine (7ba): Light yellow oil (43 mg, 85%). R_f 0.53 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.25 (brs, 1H), 7.01 – 6.97 (m, 2H), 6.90 (d, J = 7.6 Hz, 1H), 5.67 (t, J = 3.4 Hz, 1H), 2.33 (s, 3H), 2.30 – 2.24 (m, 2H), 2.14 – 2.08 (m, 2H), 1.74 – 1.57 (m, 2H), 1.17 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 192.1, 141.0, 137.8, 137.5, 129.2, 128.9 (two signals overlapped), 127.4, 126.8, 40.4, 30.4, 29.5, 25.9, 23.3, 22.1, 21.4. HRMS (ESI) Calcd for C₁₈H₂₆N [M + H]⁺ 256.2065, found 256.2062.

2,2-Dimethyl-1-(2'',3'',4'',5''-tetrahydro-[1,1':3,1''-terphenyl]-4'-yl)propan-1-imine (7ca): Light yellow oil (55 mg, 86%). R_f 0.48 (hexane/EtOAc/NEt₃ = 10/1/1); major component: ¹H NMR (400 MHz, CDCl₃): δ 8.91 (brs, 1H), 7.60 (d, J = 7.1 Hz, 2H), 7.46 –

7.40 (m, 4H), 7.38 – 7.32 (m, 1H), 7.09 (d, $J = 8.6$ Hz, 1H), 5.77 – 5.74 (m, 1H), 2.36 – 2.30 (m, 2H), 2.17 – 2.11 (td, $J = 6.1, 2.6$ Hz, 2H), 1.76 – 1.70 (m, 2H), 1.67 – 1.61 (m, 2H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.8, 141.6, 140.9, 140.8, 139.5, 137.8, 129.6, 129.0, 128.0, 127.7, 127.3, 127.1, 124.8, 40.5, 30.5, 29.5, 25.9, 23.3, 22.1. HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{28}\text{N}$ $[\text{M} + \text{H}]^+$ 318.2222, found 318.2223.

1-(5-Methoxy-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine

(7da): Light yellow oil (46 mg, 83%). R_f 0.37 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 8.85 (brs, 1H), 6.94 (d, $J = 9.2$ Hz, 1H), 6.73 – 6.69 (m, 2H), 5.71 – 5.68 (m, 1H), 3.79 (s, 3H), 2.28 – 2.23 (m, 2H), 2.13 – 2.08 (m, 2H), 1.73 – 1.65 (m, 2H), 1.64 – 1.57 (m, 2H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.9, 159.0, 142.7, 137.7, 133.3, 129.4, 128.6, 113.5, 111.4, 55.4, 40.5, 30.2, 29.5, 25.8, 23.2, 22.0. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{26}\text{NO}$ $[\text{M} + \text{H}]^+$ 272.2014, found 272.2015.

2,2-Dimethyl-1-(5-(trifluoromethoxy)-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine (7ea):

Light yellow oil (51 mg, 79%). R_f 0.52 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.45 (brs, 1H), 7.04 (s, 3H), 5.75 (s, 1H), 2.30 –

2.23 (m, 2H), 2.29 – 2.24 (m, 2H), 1.74 – 1.59 (m, 4H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 190.9, 148.7, 143.2, 136.7, 130.8 (two signals overlapped), 129.0, 120.7 (d, $^1J_{\text{C-F}} = 257.2$ Hz), 120.6, 118.4, 40.6, 30.1, 29.3, 25.8, 23.1, 21.9. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{23}\text{NOF}_3$ $[\text{M} + \text{H}]^+$ 326.1732, found 326.1732.

6-(1-Imino-2,2-dimethylpropyl)-N,N-dimethyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-3-amine (7ga): Light yellow oil (47 mg, 82%). R_f 0.45 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 8.49 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 1H), 6.54 (dd, $J = 8.5, 2.6$ Hz, 1H), 6.51 (d, $J = 2.5$ Hz, 1H), 5.70 – 5.66 (m, 1H), 2.95 (s, 6H), 2.28 – 2.24 (m, 2H), 2.14 – 2.08 (m, 2H), 1.73 – 1.58 (m, 4H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 192.2, 150.0, 142.3, 138.7, 129.3, 128.6, 128.3, 112.0, 110.0, 40.7, 30.4, 29.7, 25.8, 23.3, 22.1. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{29}\text{N}_2$ $[\text{M} + \text{H}]^+$ 285.2331, found 285.2333.

1-(5-Fluoro-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (7ha): Light yellow oil (42 mg, 81%). R_f 0.52 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR (400 MHz, CDCl_3): δ 9.39 (brs, 1H), 6.98 (dd, $J = 8.2, 5.9$ Hz, 1H), 6.92 – 6.85 (m, 2H), 5.76 – 5.72 (m, 1H), 2.28 – 2.23 (m, 2H), 2.14 – 2.09 (m, 2H), 1.74 – 1.67 (m, 2H), 1.65 –

1.57 (m, 2H), 1.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.2, 162.2 (d, $^1J_{\text{C-F}} = 246.4$ Hz), 143.4 (d, $^3J_{\text{C-F}} = 8.0$ Hz), 136.8, 130.4, 129.2 (d, $^3J_{\text{C-F}} = 7.7$ Hz), 114.8 (d, $^2J_{\text{C-F}} = 21.1$ Hz), 113.0 (d, $^2J_{\text{C-F}} = 21.3$ Hz), 40.6, 30.1, 29.4, 25.8, 23.2, 21.9. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{23}\text{NF}$ $[\text{M} + \text{H}]^+$ 260.1815, found 260.1815.

2,2-Dimethyl-1-(4-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine (7ia) and 2,2-dimethyl-1-(6-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)propan-1-imine (7ia') (7ia:7ia' = 3:1): Light yellow oil (39 mg, 76%). R_f 0.54 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); major component: ^1H NMR (400 MHz, CDCl_3): δ 9.28 (s, 1H), 7.07 (d, $J = 0.6$ Hz, 2H), 6.81 (s, 1H), 5.66 (s, 1H), 2.31 (s, 3H), 2.28 – 2.22 (m, 2H), 2.13 – 2.07 (m, 2H), 1.73 – 1.66 (m, 2H), 1.64 – 1.57 (m, 2H), 1.17 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 192.2, 138.2, 137.5, 135.7, 129.1, 128.6, 128.0, 125.8, 123.4, 40.4, 30.4, 29.5, 25.9, 23.3, 22.1, 21.2. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{26}\text{N}$ $[\text{M} + \text{H}]^+$ 256.2065, found 256.2065.

1-(6-Methoxy-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine (7ka): Light yellow oil (48 mg, 79%). R_f 0.46 (hexane/EtOAc/ $\text{NEt}_3 = 10/1/1$); ^1H NMR

(400 MHz, CDCl₃): δ 9.25 (brs, 1H), 7.15 (dd, J = 8.3, 7.7 Hz, 1H), 6.81 (dd, J = 8.4, 1.3 Hz, 1H), 6.66 (dd, J = 7.7, 1.2 Hz, 1H), 5.55 – 5.50 (m, 1H), 3.80 (s, 3H), 2.29 – 2.09 (m, 4H), 1.76 – 1.58 (m, 4H), 1.20 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.9, 157.4, 143.2, 135.0, 130.0, 129.3, 127.1, 119.1, 110.2, 56.0, 39.9, 30.0, 29.9, 25.7, 23.1, 22.2. HRMS (ESI) Calcd for C₁₈H₂₆NO [M + H]⁺ 272.2014, found 272.2017.

1-(6-Fluoro-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)-2,2-dimethylpropan-1-imine

(7la): Light yellow oil (48 mg, 79%). R_f 0.52 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR (400 MHz, CDCl₃): δ 9.26 (brs, 1H), 7.18 – 7.12 (m, 1H), 7.00 – 6.95 (m, 1H), 6.83 (d, J = 7.6 Hz, 1H), 5.66 – 5.62 (m, 1H), 2.21 – 2.17 (m, 2H), 2.16 – 2.09 (m, 2H), 1.74 – 1.60 (m, 4H), 1.18 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 190.0, 160.3 (d, ¹ J_{C-F} = 245.8 Hz), 143.5, 132.1, 131.3, 128.8 (d, ² J_{C-F} = 17.1 Hz), 127.6 (d, ³ J_{C-F} = 8.9 Hz), 122.6, 115.1 (d, ² J_{C-F} = 23.5 Hz), 40.2, 30.1, 29.6, 25.7, 23.0, 22.0. HRMS (ESI) Calcd for C₁₇H₂₃NF [M + H]⁺ 260.1815, found 260.1817.

1-(4-(Cyclohex-1-en-1-yl)benzo[d][1,3]dioxol-5-yl)-2,2-dimethylpropan-1-imine

(7ma): Light yellow oil (48 mg, 84%). R_f 0.45 (hexane/EtOAc/NEt₃ = 10/1/1); ¹H NMR

(400 MHz, CDCl₃): δ 8.87 (s, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 5.94 (s, 2H), 5.73 – 5.69 (m, 1H), 2.33 – 2.27 (m, 2H), 2.16 – 2.10 (m, 2H), 1.73 – 1.59 (m, 4H), 1.16 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.0, 146.8, 144.8, 132.6, 131.2, 123.4, 120.8, 106.4, 101.0, 100.2, 40.4, 29.5, 29.0, 25.8, 23.0, 22.0. HRMS (ESI) Calcd for C₁₇H₂₄N [M + H]⁺ 242.1909, found 242.1912.

1-(1-(Cyclohex-1-en-1-yl)naphthalen-2-yl)-2,2-dimethylpropan-1-imine (7na) and 1-(3-(cyclohex-1-en-1-yl)naphthalen-2-yl)-2,2-dimethylpropan-1-imine (7na') (7na:7na' = 4:1): Light yellow oil (48 mg, 82%). R_f 0.52 (hexane/EtOAc/NEt₃ = 10/1/1); major component: ¹H NMR (400 MHz, CDCl₃): δ 9.30 (s, 1H), 7.97 – 7.93 (m, 1H), 7.84 – 7.77 (m, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.20 (d, J = 8.5 Hz, 1H), 5.72 – 5.68 (m, 1H), 2.31 – 2.15 (m, 4H), 1.82 – 1.63 (m, 4H), 1.28 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 191.3, 138.8, 138.1, 136.1, 133.1, 132.4, 129.7, 128.2, 126.6, 126.5, 126.4, 126.1, 124.1, 39.9, 32.3, 30.4, 25.7, 23.2, 22.3. HRMS (ESI) Calcd for C₂₁H₂₆N [M + H]⁺ 292.2065, found 292.2068.

Experiment Detail for the Synthesis of *ortho*-Substituted Benzonitriles

Conditions A: **3aa** or **5aa** (0.20 mmol) was weighed in a 10 mL vial containing a stir bar, and then dissolved in $t\text{-BuOO}t\text{-Bu}$ (0.5 mL). The vial was placed in Luzchem LZC-4V photoreactor and irradiated at 254 nm for 12 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/EtOAc = 100/1 for *ortho*alkylbenzonitrile, 30/1 for *ortho*-arylbenzonitrile) to afford the desired benzonitrile derivative.

Conditions B: In a 10 mL Schlenk tube containing a stir bar were placed **3aa** or **5aa** (0.2 mmol) and $\text{Cu}(\text{OAc})_2$ (3.6 mg, 0.020 mmol), followed by the addition of DMF (2 mL). An oxygen balloon was attached to the Schlenk tube, and the reaction mixture was stirred at 80 °C for 12 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/EtOAc = 100/1 for *ortho*-alkylbenzonitrile, 30/1 for *ortho*arylbenzonitrile) to afford the desired benzonitrile derivative.

2-Octylbenzonitrile (9a)²⁴: R_f 0.65 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H), 7.32 – 7.24 (m, 2H), 2.86 – 2.80 (m, 2H), 1.70 – 1.63 (m, 2H), 1.40 – 1.21 (m, 10H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100

MHz, CDCl₃): δ 147.1, 133.0, 132.9, 129.7, 126.5, 118.4, 112.6, 34.9, 32.1, 31.2, 29.6, 29.5, 29.4, 22.9, 14.3. HRMS (ESI) Calcd for C₁₅H₂₂N [M + H]⁺ 216.1752, found 216.1760.

4'-Methoxy-[1,1'-biphenyl]-2-carbonitrile (9b)²⁵: R_f 0.32 (hexane/EtOAc = 10/1); ¹H NMR (400 MHz, CDCl₃): δ 7.74 (dd, J = 7.8, 1.2 Hz, 1H), 7.62 (td, J = 7.8, 1.3 Hz, 1H), 7.53 – 7.47 (m, 3H), 7.40 (td, J = 7.6, 1.0 Hz, 1H), 7.04 – 7.00 (m, 2H), 3.87 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 160.3, 145.4, 134.0, 133.0, 130.8, 130.2, 130.1, 127.3, 119.2, 114.4, 111.3, 55.6. HRMS (ESI) Calcd for C₁₄H₁₂NO [M + H]⁺ 210.0919, found 210.0915.

Experiment Detail for Two-step synthesis of *ortho*-substituted bezonnitriles

Typical Procedure A: 2-(pent-4-en-1-yl)benzonitrile (9d). The reaction of 2,2-dimethyl-1-phenylpropan-1-imine (**1a**, 33 mg, 0.20 mmol) and 5-bromopent-1-ene (**2g**, 36 μ L, 0.30 mmol) was performed according to the typical procedure described above. The reaction

mixture was filtered through a short pad of silica gel, washing with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. The residue was eventually transferred into a 10 mL vial containing a stir bar, followed by the addition of *t*-BuOO*t*-Bu (0.5 mL). The vial was placed in Luzchem LZC-4V photoreactor and irradiated at 254 nm for 12 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/EtOAc = 100/1) to afford the title compound as a colorless oil (27 mg, 78%).

R_f 0.62 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (d, J = 7.7 Hz, 1H), 7.50 (td, J = 7.7, 1.2 Hz, 1H), 7.33 – 7.28 (m, 2H), 5.88 – 5.78 (m, 1H), 5.09 – 4.97 (m, 2H), 2.85 (t, J = 14.3 Hz, 2H), 2.14 (dd, J = 14.3, 7.1 Hz, 2H), 1.82 – 1.74 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 146.6, 138.1, 133.0, 132.9, 129.8, 126.6, 118.3, 115.5, 112.6, 34.2, 33.4, 30.2. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{14}\text{N}$ $[\text{M} + \text{H}]^+$ 172.1126, found 172.1124.

Typical Procedure B: 2-(3-phenylpropyl)benzonitrile (9c). The reaction of 2,2-dimethyl-1-phenylpropan-1-imine (**1a**, 33 mg, 0.20 mmol) and (3-bromopropyl)benzene (**2c**, 46 μL , 0.30 mmol) was performed according to the typical procedure described above. The reaction mixture was filtered through a short pad of silica gel, washing with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. The residue was eventually transferred into a 10 mL vial containing a stir bar, followed by the addition of $\text{Cu}(\text{OAc})_2$ (3.6 mg, 0.020 mmol) and DMF (2 mL). The reaction mixture was stirred under oxygen atmosphere (using a balloon) at 80 $^\circ\text{C}$ for 12 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/EtOAc = 100/1) to afford the title compound as a colorless oil (36 mg, 81%).

Spectral data for **9c**²⁶ showed good agreement with the literature data.

R_f 0.60 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.62 (d, J = 7.7 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.33 – 7.27 (m, 4H), 7.21 (d, J = 7.3 Hz, 3H), 2.90 (t, J = 7.6 Hz, 2H), 2.72 (t, J = 7.7 Hz, 2H), 2.07 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 146.5, 141.8, 133.1, 133.0, 129.70, 128.6 (two signals overlapped), 126.7, 126.2, 118.3, 112.6, 35.7, 34.4, 32.6. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 222.1283, found 222.1288.

2-(Cyclobutylmethyl)benzonitrile (9e): Light yellow oil (28 mg, 82%, procedure A).

R_f 0.60 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (dd, J = 8.0, 1.4 Hz, 1H), 7.48 (td, J = 7.7, 1.4 Hz, 1H), 7.29 – 7.24 (m, 2H), 2.93 (d, J = 7.6 Hz, 2H), 2.71 – 2.60 (m, 1H), 2.09 – 1.98 (m, 2H), 1.91 – 1.73 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 145.4, 133.0, 132.8, 129.7, 126.6, 118.6, 112.6, 41.3, 36.9, 28.3, 18.5. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{14}\text{N}$ $[\text{M} + \text{H}]^+$ 172.1126, found 172.1126.

2-(Cyclohexylmethyl)benzonitrile (9f): Light yellow oil (32 mg, 81%, procedure A). R_f 0.61 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (dd, J = 8.0, 1.4 Hz, 1H), 7.49 (td, J = 7.7, 1.4 Hz, 1H), 7.29 – 7.25 (m, 2H), 2.72 (d, J = 6.9 Hz, 2H), 1.74 – 1.60 (m, 5H), 1.23 – 1.13 (m, 4H), 1.08 – 0.98 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 145.7, 132.9, 132.6, 130.6, 126.5, 118.7, 113.1, 42.6, 39.8, 33.2, 26.6, 26.4. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 200.1439, found 200.1436.

2-Neopentylbenzonitrile (9g): Light yellow oil (29 mg, 85%, procedure A). R_f 0.61 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.62 (dd, $J = 7.7, 1.2$ Hz, 1H), 7.49 (td, $J = 7.8, 1.4$ Hz, 1H), 7.32 – 7.26 (m, 2H), 2.78 (s, 2H), 0.98 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 143.9, 133.0, 132.1, 131.8, 126.7, 119.3, 114.2, 48.0, 33.4, 29.6. HRMS (ESI) Calcd for $\text{C}_{12}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 174.1283, found 174.1286.

2-Cyclohexylbenzonitrile (9h)²⁷: Light yellow oil (30 mg, 82%, procedure A). R_f 0.57 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (dd, $J = 7.7, 1.5$ Hz, 1H), 7.55 – 7.50 (m, 1H), 7.36 (dd, $J = 8.0, 0.5$ Hz, 1H), 7.28 – 7.24 (m, 1H), 3.03 – 2.92 (m, 1H), 1.93 – 1.84 (m, 4H), 1.83 – 1.73 (m, 2H), 1.51 – 1.41 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 151.8, 133.2, 133.1, 126.8, 126.5, 118.5, 112.1, 43.0, 33.9, 26.8, 26.2. HRMS (ESI) Calcd for $\text{C}_{13}\text{H}_{16}\text{N}$ $[\text{M} + \text{H}]^+$ 186.1283, found 186.1283.

4-Methyl-2-octylbenzonitrile (9i): Light yellow oil (35 mg, 77%, procedure B). R_f 0.62 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.48 (d, $J = 7.9$ Hz, 1H), 7.11 (s, 1H), 7.07 (d, $J = 8.1$ Hz, 1H), 2.81 – 2.74 (m, 2H), 2.38 (s, 3H), 1.69 – 1.60 (m, 2H), 1.40 – 1.20 (m, 10H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 147.0, 143.7, 132.9, 130.4, 127.4, 118.8, 109.5, 34.8, 32.1, 31.2, 29.6, 29.5, 29.4, 22.9, 22.0, 14.3. HRMS

(ESI) Calcd for $C_{16}H_{24}N$ $[M + H]^+$ 230.1909, found 230.1911.

3-Octyl-[1,1'-biphenyl]-4-carbonitrile (9j): Light yellow oil (46 mg, 79%, procedure A).

R_f 0.55 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.52 – 7.49 (m, 2H), 7.48 – 7.45 (m, 2H), 7.44 – 7.41 (m, 1H), 2.92 – 2.86 (m, 2H), 1.76 – 1.67 (m, 2H), 1.44 – 1.24 (m, 10H), 0.90 – 0.86 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 145.8, 139.8, 133.4, 129.3, 128.7, 128.4, 127.5, 125.3, 118.6, 111.2, 35.0, 32.1, 31.3, 29.6 (two signals overlapped), 29.4, 22.9, 14.3. HRMS (ESI) Calcd for $C_{21}H_{26}N$ $[M + H]^+$ 292.2065, found 292.2070.

2-Octyl-4-(trifluoromethoxy)benzonitrile (9k): Light yellow oil (48 mg, 81%, procedure

A). R_f 0.50 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.4 Hz, 1H), 7.15 – 7.11 (m, 2H), 2.88 – 2.82 (m, 2H), 1.71 – 1.64 (m, 2H), 1.42 – 1.22 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 150.0, 134.8, 122.2 (d, $^1J_{C-F}$ = 238.5 Hz), 121.6, 118.6, 117.3, 111.0, 34.9, 32.0, 30.9, 30.8, 29.5, 29.4, 22.9, 14.3. HRMS (ESI) Calcd for $C_{16}H_{21}NOF_3$ $[M + H]^+$ 300.1575, found 300.1577.

4-(Methylthio)-2-octylbenzonitrile (9l): Light yellow oil (37 mg, 71%, procedure A). R_f

0.60 (hexane/EtOAc = 10/1); 1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.2 Hz, 1H), 7.10

(d, $J = 1.6$ Hz, 1H), 7.07 (dd, $J = 8.2, 1.9$ Hz, 1H), 2.81 – 2.75 (m, 2H), 2.50 (s, 3H), 1.69 – 1.61 (m, 2H), 1.40 – 1.23 (m, 10H), 0.88 (t, $J = 6.8$ Hz, 3H).; ^{13}C NMR (100 MHz, CDCl_3): δ 147.3, 145.9, 133.0, 126.1, 123.1, 118.6, 108.2, 34.9, 32.8, 31.1, 29.6, 29.5, 29.4, 22.9, 15.0, 14.3. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{24}\text{NS}$ $[\text{M} + \text{H}]^+$ 262.1629, found 262.1633.

4-Fluoro-2-octylbenzonitrile (9m): Light yellow oil (37 mg, 79%, procedure B). R_f 0.58 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.60 (dd, $J = 8.5, 5.5$ Hz, 1H), 7.04 – 6.95 (m, 2H), 2.86 – 2.80 (m, 2H), 1.70 – 1.62 (m, 2H), 1.40 – 1.23 (m, 10H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 165.2 (d, $^1J_{\text{C-F}} = 256.0$ Hz), 150.6 (d, $^3J_{\text{C-F}} = 8.8$ Hz), 135.2 (d, $^3J_{\text{C-F}} = 9.6$ Hz), 117.7, 117.0 (d, $^2J_{\text{C-F}} = 22.3$ Hz), 114.3 (d, $^2J_{\text{C-F}} = 22.8$ Hz), 108.7, 34.8, 32.0, 30.8, 29.5, 29.4, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{21}\text{NF}$ $[\text{M} + \text{H}]^+$ 234.1658, found 234.1665.

5-Methyl-2-octylbenzonitrile (9n): Light yellow oil (35 mg, 77%, procedure B). R_f 0.61 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, $J = 0.6$ Hz, 1H), 7.30 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.19 (d, $J = 7.9$ Hz, 1H), 2.81 – 2.75 (m, 2H), 2.34 (s, 3H), 1.67 – 1.60 (m, 2H), 1.38 – 1.23 (m, 10H), 0.87 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 144.1, 136.3, 133.8, 133.2, 129.6, 118.6, 112.3, 34.4, 32.1, 31.2, 29.6, 29.5, 22.9, 20.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{24}\text{N}$ $[\text{M} + \text{H}]^+$ 230.1909, found 230.1916.

2-Octyl-5-(trifluoromethyl)benzonitrile (9o): Light yellow oil (34 mg, 61%, procedure A). R_f 0.60 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.86 (d, J = 1.5 Hz, 1H), 7.75 (dd, J = 8.3, 1.5 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 2.93 – 2.87 (m, 2H), 1.73 – 1.64 (m, 2H), 1.30 – 1.26 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 151.1, 130.4, 129.9 (q, $^3J_{\text{C-F}}$ = 3.7 Hz), 129.5 (q, $^3J_{\text{C-F}}$ = 3.2 Hz), 128.8 (q, $^2J_{\text{C-F}}$ = 111.8 Hz), 123.4 (q, $^1J_{\text{C-F}}$ = 272.3 Hz), 117.0, 113.5, 34.9, 32.0, 30.9, 29.5, 29.4, 29.4, 22.9, 14.3. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{21}\text{NF}_3$ $[\text{M} + \text{H}]^+$ 284.1626, found 284.1629.

4'-(Trimethylsilyl)-[1,1'-biphenyl]-2-carbonitrile (9q): Light yellow oil (31 mg, 61%, procedure A). R_f 0.46 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.79 – 7.76 (m, 1H), 7.67 – 7.62 (m, 3H), 7.57 – 7.51 (m, 3H), 7.47 – 7.42 (m, 1H), 0.32 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 145.7, 141.5, 138.6, 134.1, 134.0, 133.1, 130.3, 128.2, 127.8, 119.0, 111.5, -0.9. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{18}\text{NSi}$ $[\text{M} + \text{H}]^+$ 252.1209, found 252.1213.

3'-Methyl-[1,1'-biphenyl]-2-carbonitrile (9r)²⁸: Light yellow oil (24 mg, 61%, procedure B). R_f 0.45 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.77 – 7.74 (m, 1H), 7.66 – 7.61 (m, 1H), 7.52 – 7.50 (m, 1H), 7.45 – 7.40 (m, 1H), 7.39 – 7.35 (m, 3H), 7.28 –

7.25 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 145.9, 138.6, 138.4, 133.9, 133.0, 130.3, 129.7 (two signals overlapped), 128.8, 127.6, 126.1, 119.0, 111.5, 21.7. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{12}\text{N}$ $[\text{M} + \text{H}]^+$ 194.0970, found 194.0972.

3'-Methoxy-[1,1'-biphenyl]-2-carbonitrile (9s)²⁹: Light yellow oil (24 mg, 58%, procedure B). R_f 0.31 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.78 – 7.74 (m, 1H), 7.67 – 7.61 (m, 1H), 7.54 – 7.51 (m, 1H), 7.47 – 7.37 (m, 2H), 7.15 – 7.12 (m, 1H), 7.10 – 7.08 (m, 1H), 7.01 – 6.97 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.9, 145.6, 139.7, 138.4, 134.0, 133.0, 130.3, 130.0, 127.8, 121.4, 114.7, 114.5, 111.6, 55.6. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{12}\text{NO}$ $[\text{M} + \text{H}]^+$ 210.0919, found 210.0920.

4'-Methoxy-5-methyl-[1,1'-biphenyl]-2-carbonitrile (9t): Light yellow oil (27 mg, 60%, procedure B). R_f 0.36 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.62 (d, J = 7.9 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.29 (s, 1H), 7.22 – 7.18 (m, 1H), 7.03 – 6.98 (m, 2H), 3.86 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.2, 145.3, 143.8, 133.9, 130.9, 130.8, 130.2, 128.1, 119.5, 114.4, 108.3, 55.6, 22.1. HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{14}\text{NO}$ $[\text{M} + \text{H}]^+$ 224.1075, found 224.1077.

4',5-Dimethoxy-[1,1'-biphenyl]-2-carbonitrile (9u): Light yellow oil (27 mg, 57%, procedure A). R_f 0.23 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.66 (d, J = 8.6 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.04 – 6.98 (m, 2H), 6.96 (d, J = 2.6 Hz, 1H), 6.90 (dd, J = 8.6, 2.5 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.9, 160.4, 147.5, 135.7, 130.8, 130.1, 119.6, 115.5, 114.4, 113.3, 103.2, 55.8, 55.6. HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 240.1025, found 240.1015.

5-Fluoro-4'-methoxy-[1,1'-biphenyl]-2-carbonitrile (9v): White solid (24 mg, 54%, procedure A). R_f 0.34 (hexane/EtOAc = 10/1); M.p. 146-147 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.74 (dd, J = 8.6, 5.6 Hz, 1H), 7.53 – 7.49 (m, 2H), 7.19 (dd, J = 9.5, 2.5 Hz, 1H), 7.10 (td, J = 8.2, 2.5 Hz, 1H), 7.05 – 7.00 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 165.1 (d, $^1J_{\text{C-F}}$ = 249.0 Hz), 160.7, 148.5 (d, $^3J_{\text{C-F}}$ = 7.6 Hz), 136.3 (d, $^3J_{\text{C-F}}$ = 4.6 Hz), 130.1, 129.6, 118.6, 117.3 (d, $^2J_{\text{C-F}}$ = 22.9 Hz), 114.9 (d, $^2J_{\text{C-F}}$ = 22.9 Hz), 114.6, 107.4, 55.6. HRMS (ESI) Calcd for $\text{C}_{14}\text{H}_{11}\text{NOF}$ $[\text{M} + \text{H}]^+$ 228.0825, found 228.0822.

Photolysis of the Alkenylation Product of N–H Imine (7aa)

3'-(Tert-butyl)spiro[cyclohexane-1,1'-isoindole] (10): **7aa** (48 mg, 0.20 mmol) was weighed in a 10 mL vial containing a stir bar, and then dissolved in *t*-BuOO*t*-Bu (0.5 mL). The vial was placed in Luzchem LZC-4V photoreactor and irradiated at 254 nm for 12 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/EtOAc = 100/1) and the title product was afforded as yellow oil (39 mg, 81%).

R_f 0.41 (hexane/EtOAc = 10/1); ^1H NMR (400 MHz, CDCl_3): δ 7.72 – 7.69 (m, 1H), 7.55 – 7.51 (m, 1H), 7.33 – 7.29 (m, 2H), 2.05 – 1.93 (m, 2H), 1.82 – 1.72 (m, 2H), 1.71 – 1.56 (m, 4H), 1.49 – 1.40 (m, 11H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.4, 160.8, 137.1, 127.2, 126.7, 123.9, 122.0, 75.6, 36.3, 35.5, 28.9, 26.2, 23.6. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{24}\text{N}$ [$\text{M} + \text{H}$] $^+$ 242.1909, found 242.1912.

Deuterium-Labeling Experiments

The reaction of $[D]_5\text{-1a}$ (33 mg, 0.2 mmol) and $n\text{-octyl}$ bromide (52 μL , 0.3 mmol) was performed according to the typical procedure for **3aa**. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 100/1/1) afforded the alkylation products. The product was analyzed by ^1H NMR to determine the distribution of the deuterium atoms.

The reaction of $[D]_5\text{-1a}$ (33 mg, 0.2 mmol) and 1-chloro-4-methoxybenzene (37 μL , 0.3 mmol) was performed according to the typical procedure for **5aa**. Purification of the crude product with silica gel chromatography (eluent: hexane/EtOAc/ NEt_3 = 100/1/1) afforded the alkylation products. The product was analyzed by ^1H NMR to determine the distribution of the deuterium atoms.

The reaction of $[\text{D}]_5\text{-1a}$ (33 mg, 0.2 mmol), **1a** (32 mg, 0.2 mmol) and *n*-octyl bromide (52 μL , 0.3 mmol) was performed according to the typical procedure for **3aa**. The yield was determined with GC using tridecane as the internal standard. The ratio of $[\text{D}]_4\text{-3aa}$ to **3aa** was determined with GC-MS.

The reaction of $[\text{D}]_5\text{-1a}$ (33 mg, 0.2 mmol), **1a** (32 mg, 0.2 mmol) and 1-chloro-4-methoxybenzene (37 μL , 0.3 mmol) was performed according to the typical procedure for **5aa**. The yield was determined with GC using tridecane as the internal standard. The ratio of $[\text{D}]_4\text{-3aa}$ to **3aa** was determined with GC-MS.

6.5 References

¹ For selected reviews, see: a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624-655; b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147-1169; c) Engle, K. M.; Mei, T. S.; Wasa, M.; Yu, J. Q. *Acc. Chem. Res.* **2012**, *45*, 788-802; d) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315-1345; e) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879-5918; f) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281-295; g) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814-825.

² Kakiuchi, F.; Sonoda, M.; Tsujimoto, T.; Chatani, N.; Murai, S. *Chem Lett* **1999**, 1083-1084.

³ a) Li, W.; Xu, Z.; Sun, P.; Jiang, X.; Fang, M. *Org. Lett.* **2011**, *13*, 1286-1289; b) Li, W.; Sun, P. *J. Org. Chem.* **2012**, *77*, 8362-8366; c) Du, B.; Jiang, X.; Sun, P. *J. Org. Chem.* **2013**, *78*, 12280-12280; d) Wan, J.-C.; Huang, J.-M.; Jhan, Y.-H.; Hsieh, J.-C. *Org. Lett.* **2013**, *15*, 2742-2745; e) Reddy, M. C.; Jeganmohan, M. *Chem. Commun.* **2015**, *51*, 10738-10741.

⁴ For the use of a cyano group as an end-on directing group for *meta*-selective C–H activation, see: a) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518-522; b) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature* **2014**, *507*, 215-220; c) Yang, G.; Lindovska, P.; Zhu, D.; Kim, J.; Wang, P.; Tang, R.-Y.; Movassaghi, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 10807-10813; d) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* **2015**, *137*, 11888-11891; e) Li, S.; Cai, L.; Ji, H.; Yang, L.; Li, G. *Nat Commun* **2016**, *7*; f) Patra, T.; Bag, S.; Kancherla, R.; Mondal, A.; Dey, A.; Pimparkar, S.; Agasti, S.; Modak, A.; Maiti, D. *Angew. Chem. Int. Ed.* **2016**, *55*, 7751-7755.

- ⁵ Yang, X.; Jin, X.; Wang, C. *Adv. Synth. Catal.* **2016**, 358, 2436-2442.
- ⁶ For selected reviews, see: a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, 107, 174-238; b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, 48, 9792-9826; c) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, 111, 1170-1214; d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, 111, 1215-1292; e) Liu, C.; Yuan, J.; Gao, M.; Tang, S.; Li, W.; Shi, R.; Lei, A. *Chem. Rev.* **2015**, 115, 12138-12204; f) Segawa, Y.; Maekawa, T.; Itami, K. *Angew. Chem. Int. Ed.* **2015**, 54, 66-81; g) Yang, Y.; Lan, J.; You, J. *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00567.
- ⁷ a) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, 48, 6097-6100; b) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, 132, 3965-3972; c) Zhao, Y.; Chen, G. *Org. Lett.* **2011**, 13, 4850-4853; d) Nadres, E. T.; Santos, G. I. F.; Shabashov, D.; Daugulis, O. *J. Org. Chem.* **2013**, 78, 9689-9714; e) Xiao, B.; Liu, Z.-J.; Liu, L.; Fu, Y. *J. Am. Chem. Soc.* **2013**, 135, 616-619; f) Zhang, S.-Y.; Li, Q.; He, G.; Nack, W. A.; Chen, G. *J. Am. Chem. Soc.* **2015**, 137, 531-539; g) Zhu, R.-Y.; He, J.; Wang, X.-C.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, 136, 13194-13197.
- ⁸ a) Ackermann, L.; Novak, P.; Vicente, R.; Hofmann, N. *Angew. Chem. Int. Ed.* **2009**, 48, 6045-6048; b) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, 13, 1875-1877.
- ⁹ a) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, 135, 5308-5311; b) Song, W.; Lackner, S.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, 53, 2477-2480; c) Ruan, Z.; Lackner, S.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, 55, 3153-3157.
- ¹⁰ a) Chen, Q. A.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, 133, 428-429; b) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2013**, 135, 9279-9282; c) Punji, B.; Song, W.; Shevchenko, G. A.; Ackermann, L. *Chem. Eur. J.* **2013**, 19, 10605-10610; d) Gao, K.; Yamakawa, T.; Yoshikai, N. *Synthesis* **2014**, 46, 2024-2039; e) Moselage, M.; Sauermann,

N.; Richter, S. C.; Ackermann, L. *Angew. Chem., Int. Ed.* **2015**, *54*, 6352–6355; f) Mei, R.; Ackermann, L. *Adv. Synth. Catal.* **2016**, *358*, 2443–2448.

¹¹ a) Monks, B. M.; Fruchey, E. R.; Cook, S. P. *Angew. Chem. Int. Ed.* **2014**, *53*, 11065–11069; b) Ilies, L.; Matsubara, T.; Ichikawa, S.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 13126–13129; c) Fruchey, E. R.; Monks, B. M.; Cook, S. P. *J. Am. Chem. Soc.* **2014**, *136*, 13130–13133; d) Cera, G.; Haven, T.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, *55*, 1484–1488.

¹² For C–H alkylation using olefins as alkylating agents, see: Dong, Z.; Ren, Z.; Thompson, S. J.; Xu, Y.; Dong, G. *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00574.

¹³ Xu, W.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2016**, *55*, 12731–12735.

¹⁴ For other C–H functionalization reactions employing N–H imine as a directing group, see: a) Fukutani, T.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Commun.* **2009**, 5141–5143; b) Sun, Z.-M.; Chen, S.-P.; Zhao, P. *Chem. Eur. J.* **2010**, *16*, 2619–2627; c) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 8181–8184; d) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 11098–11102; e) Tran, D. N.; Cramer, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 10630–10634; f) Zhang, J.; Ugrinov, A.; Zhao, P. *Angew. Chem. Int. Ed.* **2013**, *52*, 6681–6684; g) He, R.; Huang, Z.-T.; Zheng, Q.-Y.; Wang, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 4950–4953; h) Jia, T.; Zhao, C.; He, R.; Chen, H.; Wang, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 5268–5271; i) Kim, J. H.; Gressies, S.; Glorius, F. *Angew. Chem. Int. Ed.* **2016**, *55*, 5577–5581.

¹⁵ a) Ackermann, L. *J. Org. Chem.* **2014**, *79*, 8948–8954; b) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208–1219; c) Yoshikai, N. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 843–857; d) Moselage, M. Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498–525.

¹⁶ Griller, D.; Mendenhall, G. D.; Van Hoof, W.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6068–6070.

- ¹⁷ a) Gao, K.; Lee, P.-S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234-4237; b) Song, W.; Ackermann, L. *Angew. Chem. Int. Ed.* **2012**, *51*, 8251-8254.
- ¹⁸ McBurney, R. T.; Slawin, A. M. Z.; Smart, L. A.; Yu, Y.; Walton, J. C. *Chem. Commun.* **2011**, *47*, 7974-7976.
- ¹⁹ Zhang, L.; Ang, G. Y.; Chiba, S. *Org. Lett.* **2010**, *12*, 3682-3685.
- ²⁰ He, R.; Huang, Z.-T.; Zheng, Q.-Y.; Wang, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 4950-4953.
- ²¹ Port, A.; Sanchez-Aris, M.; Cervelló, E.; Jaime, C.; Virgili, A.; Farriol, M.; Gallardo, I. *Polycyclic Aromat. Compd.* **2003**, *23*, 457-470.
- ²² Hayashi, T.; Fujiwa, T.; Okamoto, Y.; Katsuro, Y.; Kumada, M. *Synthesis* **1981**, *12*, 1001-1003.
- ²³ Emmett, E. J.; Hayter, R. B.; Willis, C. M. *Angew. Chem. Int. Ed.* **2014**, *53*, 10204-10208.
- ²⁴ Panteleeva, E. V.; Vaganova, T. A.; Luk'yanets, E. A.; Shteingarts, V. D. *Russ. J. Org. Chem.* **2006**, *42*, 1280-1288.
- ²⁵ Piller, F. M.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 6802-6806.
- ²⁶ Amatore, M.; Gosmini, C. *Chem. Eur. J.* **2010**, *16*, 5848-5852.
- ²⁷ Itou, T.; Yoshimi, Y.; Morita, T.; Tokunaga, Y.; Hatanaka, M. *Tetrahedron* **2009**, *65*, 263-269.
- ²⁸ Li, W.; Xu, Z.; Sun, P.; Jiang, X.; Fang, M. *Org. Lett.* **2011**, *6*, 1286-1289.
- ²⁹ Mo, F.; Qiu, D.; Jiang, Y.; Zhang, Y.; Wang, J. *Tetrahedron Lett.* **2011**, *52*, 518-522.

List of Publications

1. Highly Linear Selective Cobalt-Catalyzed Addition of Aryl Imines to Styrenes: Reversing Intrinsic Regioselectivity by Ligand Elaboration, W. Xu, N. Yoshikai, *Angew. Chem. Int. Ed.* **2014**, 53, 14166-14170.
2. Ortho-C–H Benzylation of Aryl Imines with Benzyl Phosphates under Cobalt–Pyphos Catalysis, W. Xu, R. Paira, N. Yoshikai, *Org. Lett.* **2015**, 17, 4192-4195.
3. Cobalt-Catalyzed, Imine-Directed Olefin Hydroarylation under Grignard-Free Conditions, W. Xu, J. Pek, N. Yoshikai, *Adv. Synth. Catal.* **2016**, 358, 2564-2568.
4. N–H Imine as Powerful Directing Group for Cobalt-Catalyzed Olefin Hydroarylation, W. Xu, N. Yoshikai, *Angew. Chem. Int. Ed.* **2016**, 55, 12731-12735.
5. Pivalophenone imine as a benzonitrile surrogate for directed C–H bond functionalization, W. Xu, N. Yoshikai, *Chem. Sci.* **2017**, 8, 5299-5304.