博士論文

論文題目　　Development of Transition Metal-Catalyzed Hydroarylation and Acyloxyalkylation of Unsaturated Molecules

(遷移金属触媒による不飽和分子のヒドロアリール化及びアシロキシアルキル化反応の開発)

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Development of Transition Metal-Catalyzed Hydroarylation and Acyloxyalkylation of Unsaturated Molecules

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Contents

Abbreviations

Ac	acetyl
acac	acetylacetonate
Ar	aryl
^{n}Bu	*normal*-butyl
^{t}Bu	*tert*-Butyl
Co	cobalt
cod	1,5-cyclooctadiene
cot	1,3,5,7-cyclooctatetraene
Cp*	pentamethylcyclopentadienyl
Cu	copper
DMF	*N*,*N*-dimethylformamide
DTBP	di-*tert*-butyl peroxide
Et	ethyl
Fe	iron
Ir	iridium
Me	methyl
NHPI	*N*-hydroxyphthalimide
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
Pd	palladium
Ph	phenyl
^{i}Pr	*iso*-propyl
R	alkyl or general substituent
Re	rhenium
Rh	rhodium
Ru	ruthenium
TBHP	*tert*-butyl hydroperoxide

Chapter 1

1.1 Introduction

Addition reaction is one of the most efficient and useful methods to introduce many functional groups and substituents to two atoms of unsaturated molecules. Useful organic molecules, such as drugs, bioactive molecules, agrochemicals and organic functional materials, can be synthesized by the addition reactions. Unfortunately, two regioisomers are often formed in the process of operation, if less-polarized and/or less sterically differentiated C–C multiple bonds are used as acceptors of the addition reactions. Therefore, the development of highly regioselective addition reactions is extremely desirable.

1.2 Hydroarylation of Unsaturated Molecules

Formation of C-C bonds is a core issue in synthetic organic chemistry. A useful method for the formation of aromatic C-C bonds is palladium- or nickel-catalyzed cross-coupling reactions between aryl halides (or pseudohalides) and various organometallic reagents, that is, Suzuki-Miyaura, Stille, Kumada-Tamao, Negishi, and Mizoroki-Heck cross-coupling reactions. However, these transition metal-catalyzed cross-coupling reactions can be realized by prefunctionalizations, such as halogenation and triflation of aromatic substrates. Therefore, several steps are required to synthesize the desired products.

A C-H bond is one of the most basic chemical bonds that constitute organic compounds. Because of its high bond energy, stability, and resistance, it is usually difficult to promote chemical reactions of C-H bonds (**Table 1.1**).[1] The C–H bond activations have recently been received much attention as ideal transformations. Compared to conventional methods involving cross-coupling reactions, C–H transformations require fewer reaction steps to obtain target molecules and can enhance the atom economy.[2] Therefore, effective activation of inert C-H bonds and

development of novel, efficient, and environmentally friendly methods to construct C-C bonds are hot topics in synthetic organic chemistry.

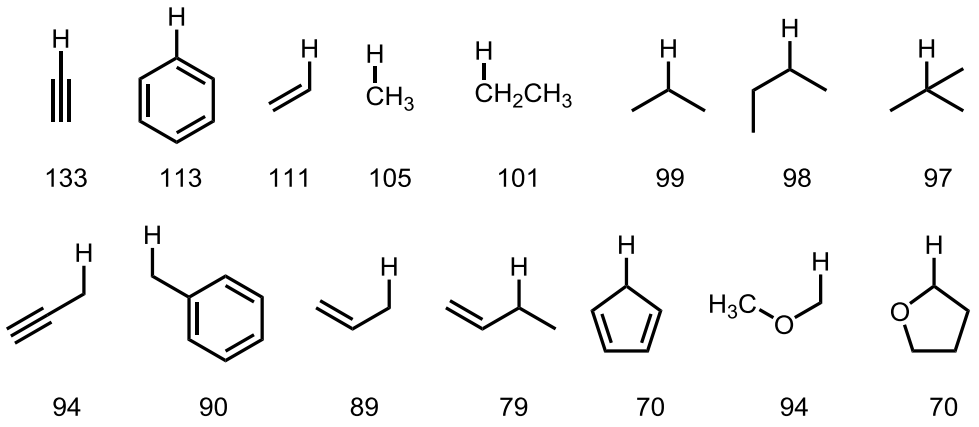
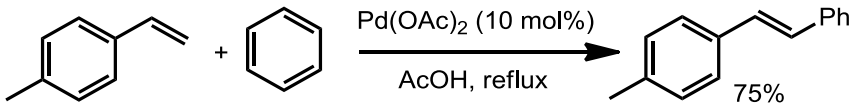


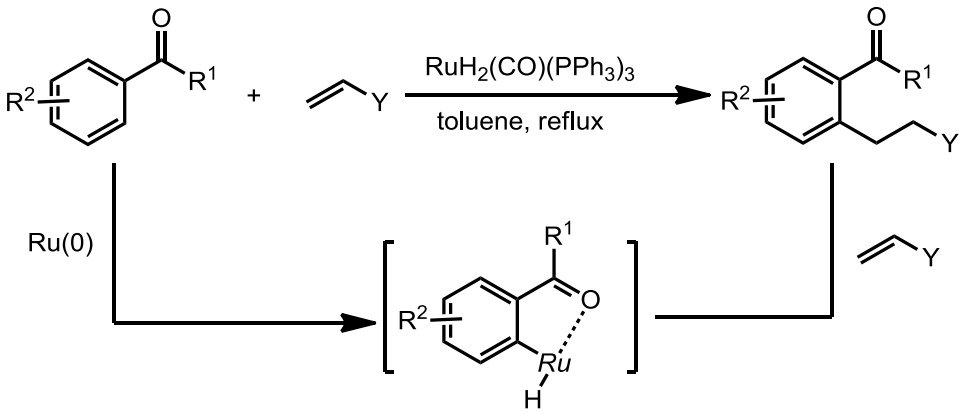
Table 1.1 Bond dissociation energies of C-H bonds (kcal mol^{-1})

A report from Fujiwara group is the earliest research in this area. In 1967, they reported that styrene reacted with benzene to yield stilbene in the presence of one equivalent of $PdCl_2$ (**Scheme 1.1**).[3] Then in 1969 they further found $Pd(OAc)_2$ to be a more efficient catalyst.[4]



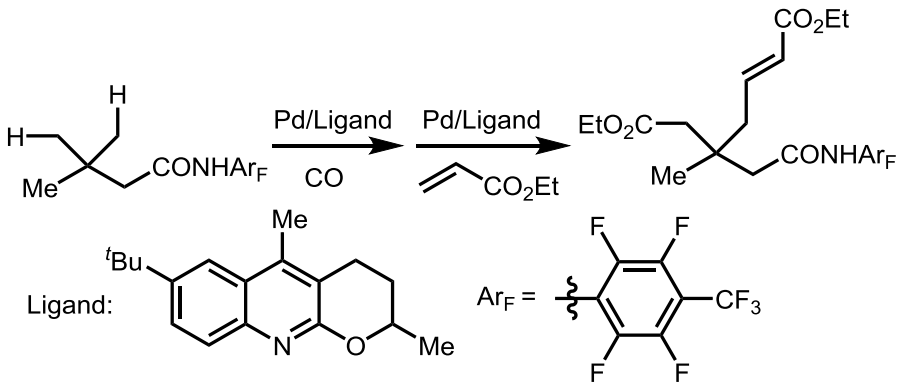
Scheme 1.1 Pd-catalyzed aromatization of olefins

The first practical hydroarylation of unsaturated molecules via C-H activation was reported by Murai in 1993 (**Scheme 1.2**).[5] The C-H bonds in aromatic groups are cleaved by a ruthenium complex to give the addition products. The reaction proceeded efficiently and selectively.



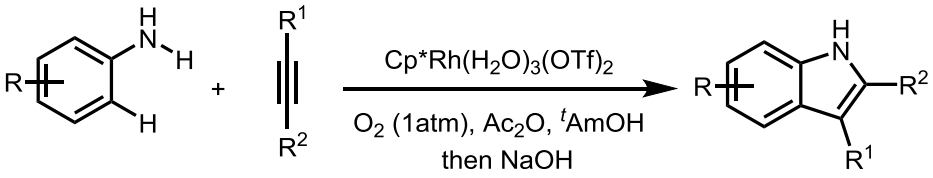
Scheme 1.2 Addition of aromatic C-H bond to olefins

The γ-C(sp^3)-H olefination of aliphatic amides has been achieved under palladium catalysis (**Scheme 1.3).**[6] The use of a combination of a quinoline-based ligand and a weakly coordinating amide directing group is important to promote the reaction. The reaction provided a new method for constructing highly functionalized quaternary carbon centers at the β-position of aliphatic acids.



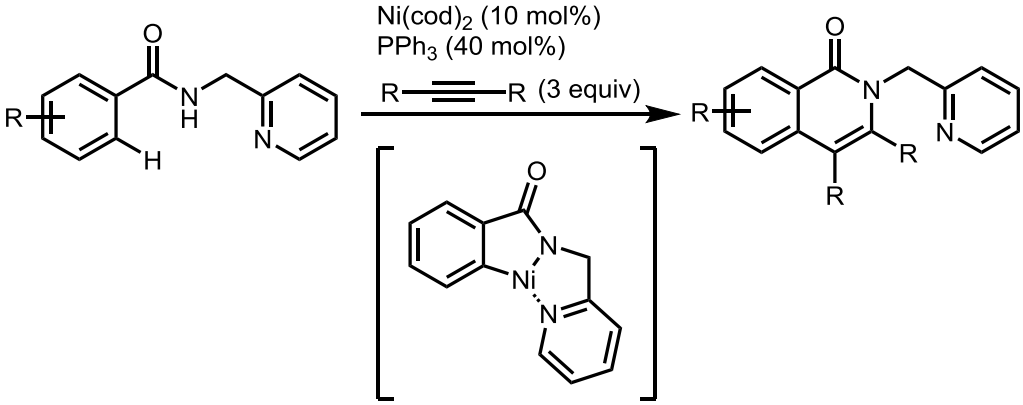
Scheme 1.3 Ligand-enabled C-H olefination and carbonylation

A practical and efficient rhodium-catalyzed aerobic C–H activation for the facile synthesis of a broad range of 2,3-disubstituted indoles from simple anilines and alkynes has been developed (**Scheme 1.4**).[7] Environmentally friendly oxygen was employed as the sole clear oxidant to oxidize the Rh(I) to Rh(III) species in the presence of an appropriate acid.



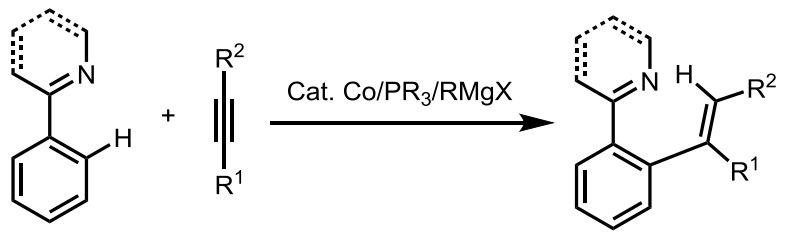
Scheme 1.4 Rh-catalyzed oxidative C-H activation/annulation

Although the pioneering synthesis of an *ortho*-nickelated complex[8] via C–H bonds activation has been reported, there was no example of a nickel-catalyzed C-H transformation. A nickel-catalyzed synthesis of isoquinoline derivatives through chelation assistance and oxidative cycloaddition between aromatic amides and alkynes was achieved (**Scheme 1.5**).[9]



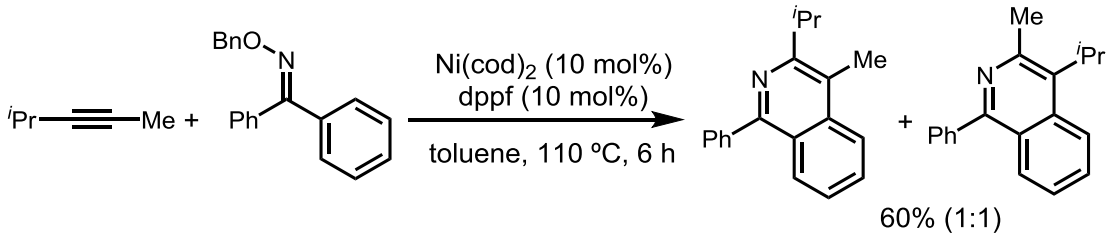
Scheme 1.5 Ni-catalyzed chelation-assisted transformation

In 2010, cobalt-catalyzed addition reactions of 2-arylpyridines and aromatic imines to unactivated internal alkynes to give trisubstituted alkenes with high regio- and stereoselectivities using a catalytic system consisting of a cobalt salt, phosphine ligand, and Grignard reagent (**Scheme 1.6**).[10]



Scheme 1.6 Co-catalyzed hydroarylation of alkynes

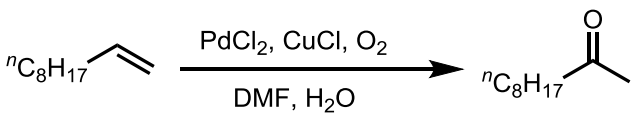
In the case of hydroarylation reactions using less polarized and/or less sterically differentiated C–C multiple bonds, two regioisomers are generally formed. For example, a nickel-catalyzed synthesis of 3,4-disubstituted isoquinolines between alkynes and aromatic imines afforded a mixture of isoquinolines (**Scheme 1.7**).[11]



Scheme 1.7 Ni-catalyzed synthesis of 3,4-disubstituted isoquinolines

1.3 Difunctionalization of Unsaturated Molecules

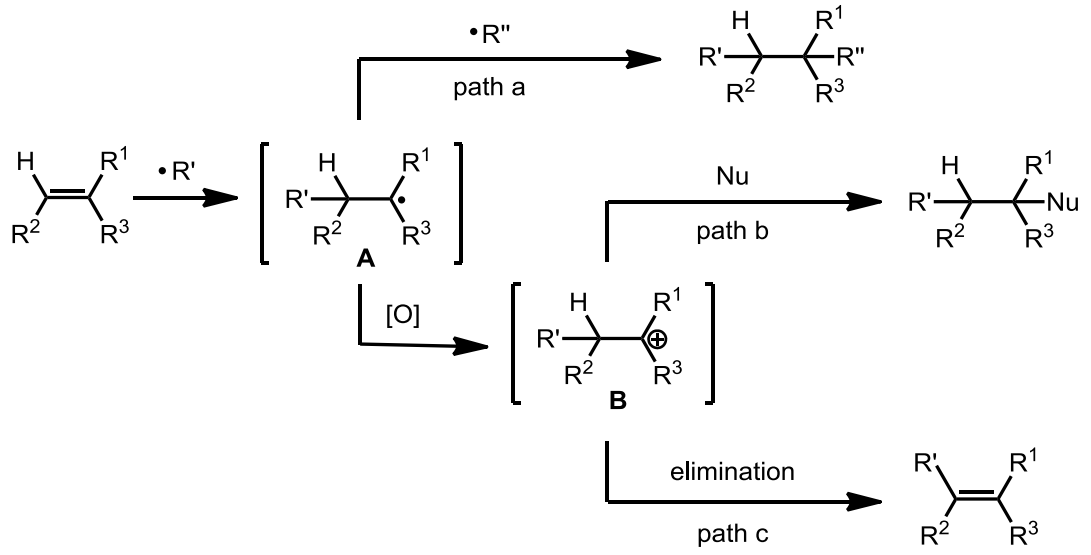
More than 50 years ago, researchers in Wacker Chemical Corporation found that alkenes were converted to aldehydes and ketones in the presence of palladium chloride as a catalyst and copper chloride as an oxidant in an aqueous phase (**Scheme 1.8**).[12] Nowadays, palladium-catalyzed Wacker reactions are successfully applied to the industrial manufacture of acetaldehyde. In addition, a silver-catalyzed epoxidation of ethylene is also an important commercial synthetic route for ethylene oxide, which is a chemical raw material. Transition metal-catalyzed functionalization of alkenes have sprung up like mushrooms after rain owing to painstaking research works.



Scheme 1.8 Wacker-Tsuji oxidation

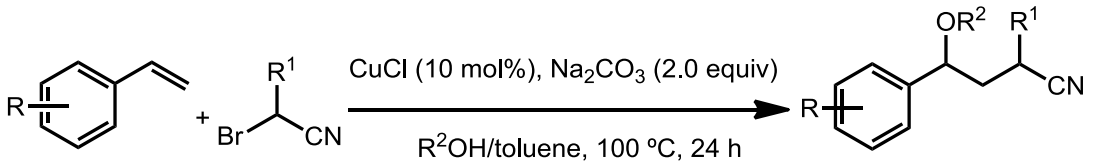
Transition metal-catalyzed difunctionalization of alkenes is also an important subject because two new functional groups can be brought into unsaturated molecules in only one step to efficiently construct highly functionalized structures of pharmaceuticals and natural products.[13]

Mechanistically, difunctionalization of alkenes can be divided into two categories: radical and metal-catalyzed nucleophilic difunctionalizations, respectively. The radical difunctionalization begins with the addition of a radical to a C-C double bond to give intermediate **A**, which is trapped by extrinsic radical species to provide the product or oxidized to carbocation **B (Scheme 1.9)**.[14] Subsequently, nucleophilic attack of the extrinsic nucleophile to generate difunctionalization product. By the way, carbocation **B** also undergoes *β*-H elimination to give alkylated alkene.



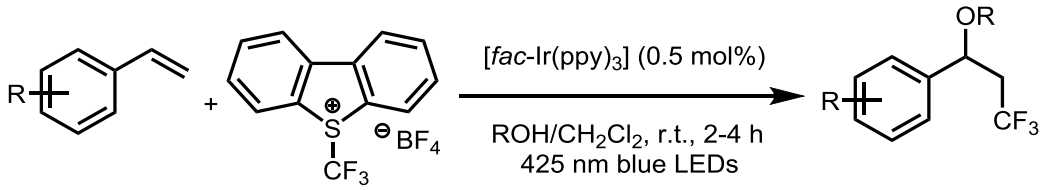
Scheme 1.9 Radical difunctionalization of simple alkenes

Lei developed a copper-catalyzed radical carboxygenation of styrenes with alkyl bromides as a radical resource (**Scheme 1.10**).[15] Both the alkylation and alkoxylation of styrenes occur under catalytic radical difunctionalization in one pot. A wide range of styrenes and alcohols are well compatible under the reaction conditions. The result of EPR experiment indicates that alkyl halides could oxidize Cu(I) to Cu(II) in this transformation.



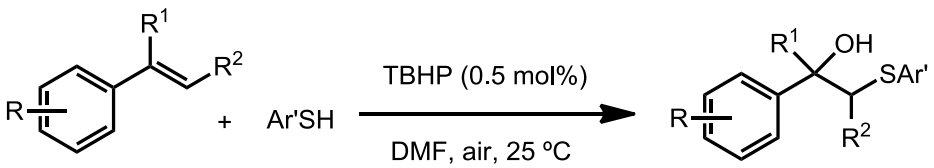
Scheme 1.10 Three-component alkoxycyanomethylation of alkenes

The first visible light-driven three-component oxytrifluoromethylation of alkenes was described by Akita using photoredox Ir catalysis (**Scheme 1.11**).[16] The choice of the Umemoto's reagent is a key to promote the reaction. Nucleophiles, such as water, alcohols, and carboxylic acids, are suitable to provide highly efficient and regioselective oxytrifluoromethylated products under the irradiation of a light-emitting diode (LED) lamp even on natural sunlight.



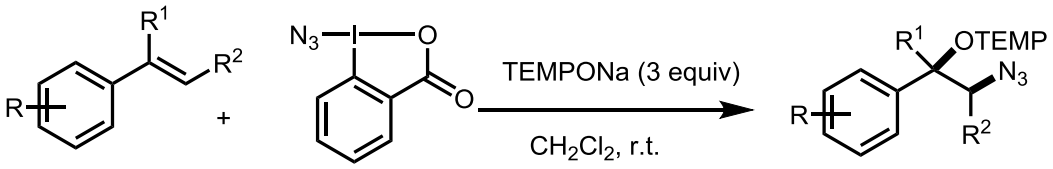
Scheme 1.11 Photocatalytic hydroxytrifluoromethylation of styrenes by electrophilic CF_3 reagents

Zou achieved a novel hydroxysulfurization of styrenes with arylthiols in the presence of 0.5 mol% TBHP as a catalyst and green air (O_2) as a sole oxidant (**Scheme 1.12**).[17] The various hydroxysulfurizated products can be obtained effectively, simply and conveniently, even on scaled up in a one-pot process without other additives.



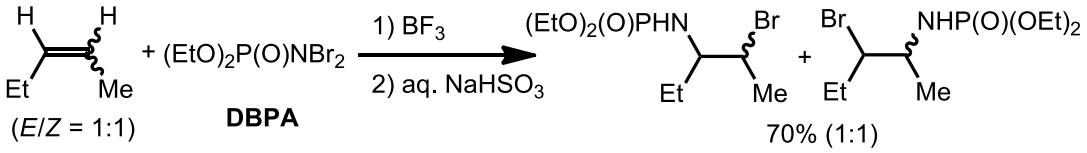
Scheme 1.12 Radical hydroxysulfurization of styrenes leading to hydroxysulfides

Radical azidooxygenation of various alkenes is described using an easily prepared N_3-iodine(III) reagent as N_3 source and mild organic reducing reagent, TEMPONa (**Scheme 1.13**).[18] The reaction proceeded to give azidated products in good to excellent yields. Furthermore, cyclic systems delivered azidooxygenated products with excellent diastereoselectivity.



Scheme 1.13 Stereoselective radical azidooxygenation of alkenes

In difunctionalization of non-polarized and/or less sterically differentiated alkenes, two regioisomers are sometimes formed. For example, the addition of **DBPA** to an alkene gave a 1:1 mixture of the corresponding adducts (**Scheme 1.14**).[19]



Scheme 1.14 Ionic addition of diethyl *N*,*N*-dibromophosphoroamidate to alkenes

As mentioned above, not only is hydroarylation faced with a regioselective problem but also difunctionalization of unsaturated molecules. For solving this problem, in the doctor course thesis, I developed rhenium-catalyzed synthesis of 1,3-diiminoisoindolines via C-H bond activation (**Chapter 2**) and iron-catalyzed acyloxyalkylation of styrenes via decarboxylation of hypervalent iodine(III) reagents (**Chapter 3**).

1.4 References

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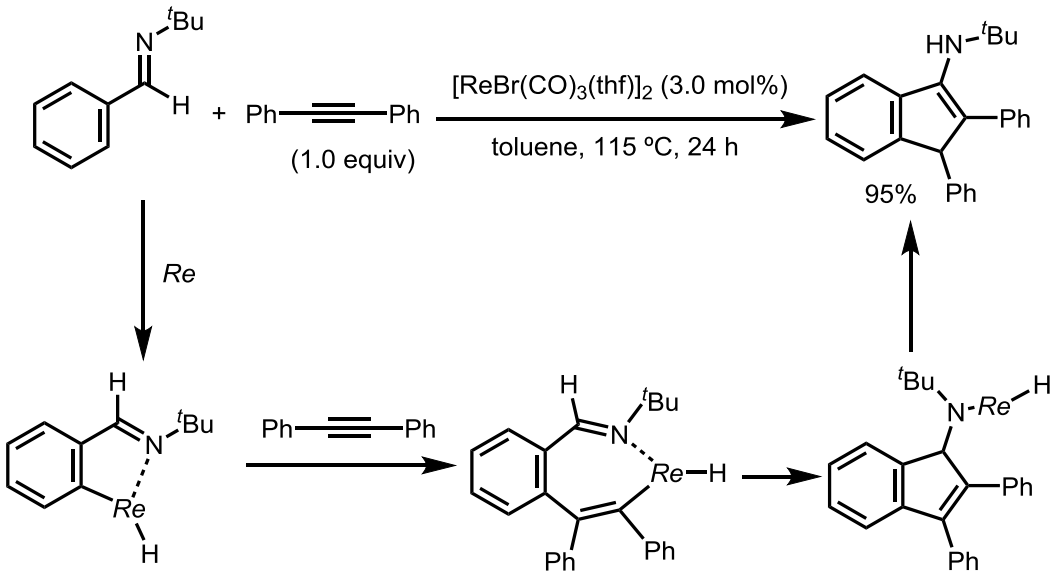
Chapter 2 Rhenium-Catalyzed Synthesis of 1,3-Diiminoisoindolines via Insertion of Carbodiimides into a C-H Bond of Aromatic and Heteroaromatic Imidates

2.1 Introduction

Rhenium is a manganese-group, sixth-period, transition metal (Group 7) in the same group with manganese, technetium, and bohrium in the periodic table. The electronegativity of rhenium is lower than late transition metals, such as ruthenium, rhodium, and palladium. Therefore, Re–X (X = C, N, O) bonds are more polarized than other M–X bonds of late transition metals. In other words, the Re–X bond in rhenium complexes or intermediates has relatively strong nucleophilicity, and the complexes or intermediates can react with polar unsaturated molecules.[1-2]

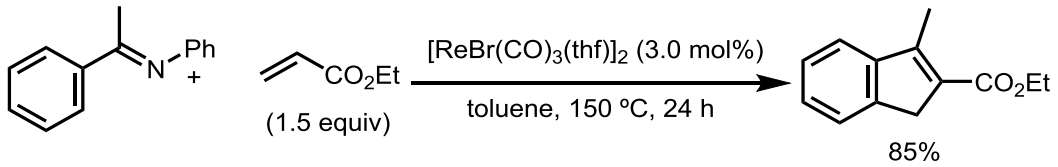
2.2 Precedents of Rhenium-Catalyzed C-H Bond Transformations

Rhenium(I) carbonyl complexes also catalyze C(sp^2)-H bond functionalization (**Scheme 2.1**).[3] In 2005, Kuninobu and Takai successfully reported synthesis of aminoindene derivatives from aromatic aldimines and alkynes using a rhenium complex $[ReBr(CO)_3(thf)]_2$ as a catalyst. It proceeds via the following steps: (1) coordination of a nitrogen atom of the imino group to a rhenium center; (2) C-H bond activation to form an *ortho*-metalated intermediate; (3) insertion of an alkyne into a rhenium-carbon bond to give an alkenyl-rhenium intermediate; (4) intramolecular nucleophilic attack to a carbon atom of the imino group; and (5) reductive elimination and 1,3-rearrangement of the hydrogen atom.



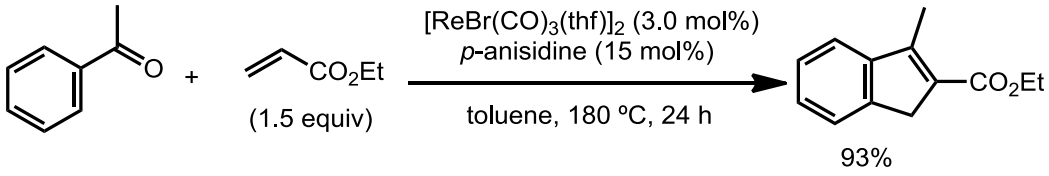
Scheme 2.1 Re-catalyzed synthesis of aminoindene derivatives

In 2006, Kuninobu and Takai group described a cyclization reaction from aromatic ketimines and acrylates, and indene derivative was obtained in 85% yield in the presence of catalytic amounts of $[ReBr(CO)_3(thf)]_2$ (**Scheme 2.2**).[4] In this reaction, a C=N double bond plays a role as both a directing group for C-H bond activation and an acceptor of the cyclization.



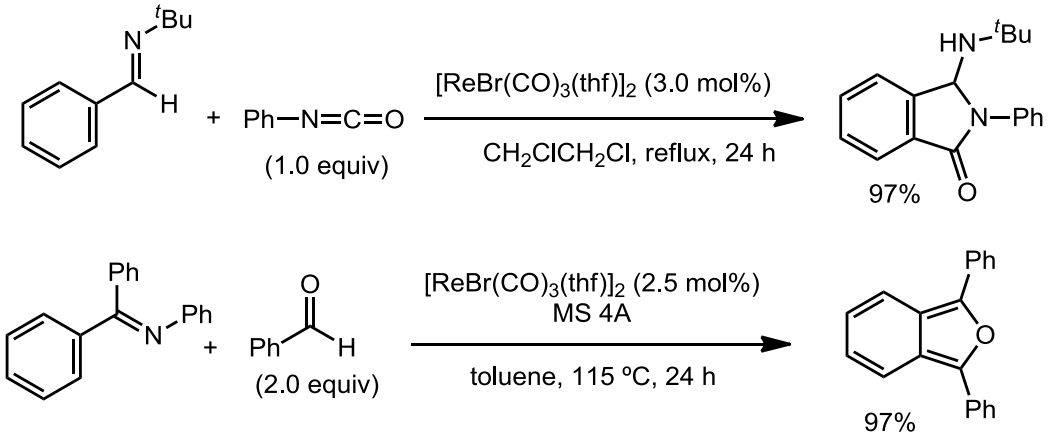
Scheme 2.2 Re-catalyzed synthesis of indenes from aromatic ketimines and acrylates

When acetophenone was used instead of the ketimine in the presence of a catalytic amount of $[ReBr(CO)_3(thf)]_2$/*p*-anisidine cocatalyst in toluene at 180 ℃ for 24 h gave the desired indene derivative in 93% yield (**Scheme 2.3**).



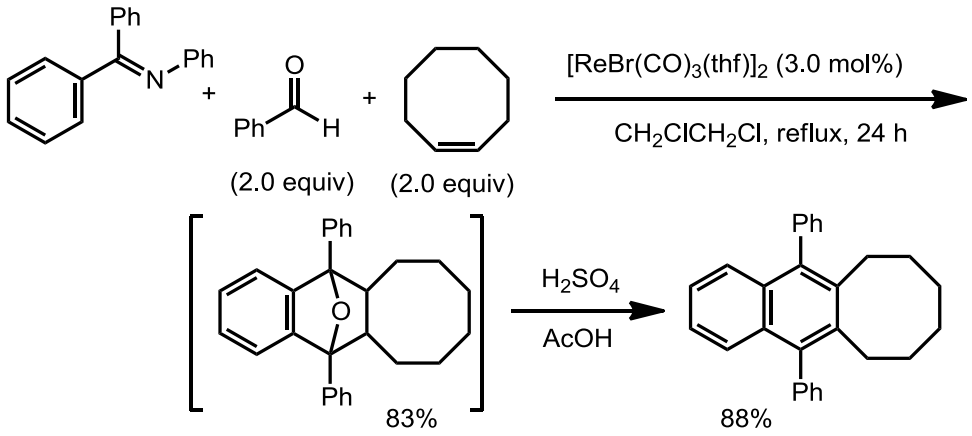
Scheme 2.3 One-pot annulation of ketones and α,β-unsaturated esters

The rhenium complex $[ReBr(CO)_3(thf)]_2$ can be employed as a catalyst to promote insertion of polar unsaturated molecules, such as isocyanates and aldehydes, into a C-H bond of aromatic compounds to form phthalimidine and isobenzofuran derivatives (**Scheme 2.4**).[5-6]



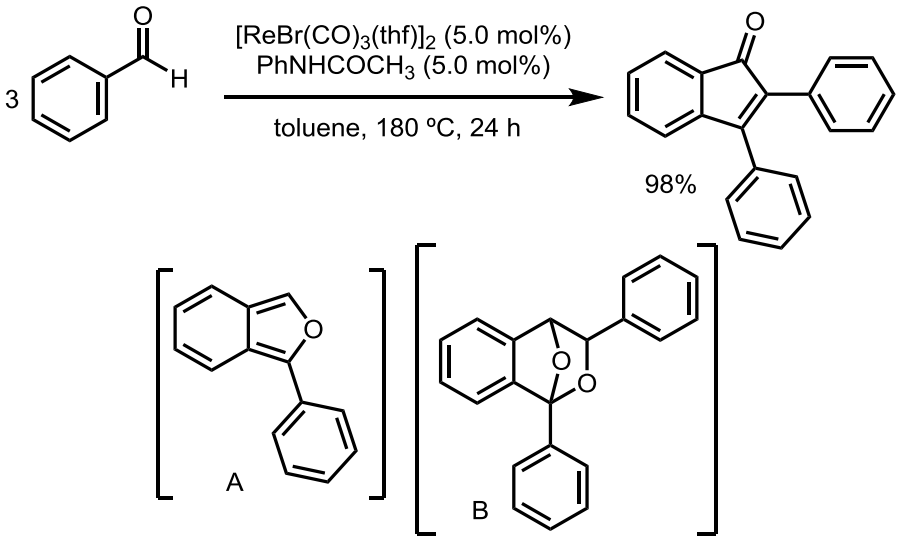
Scheme 2.4 Re-catalyzed insertion of polar unsaturated molecules

The formed isobenzofuran derivatives can be trapped easily by (*Z*)-cyclooctene via Diels–Alder reaction (**Scheme 2.5**).[7] Naphthalene derivatives were formed by dehydration under acidic conditions without isolation.[8]



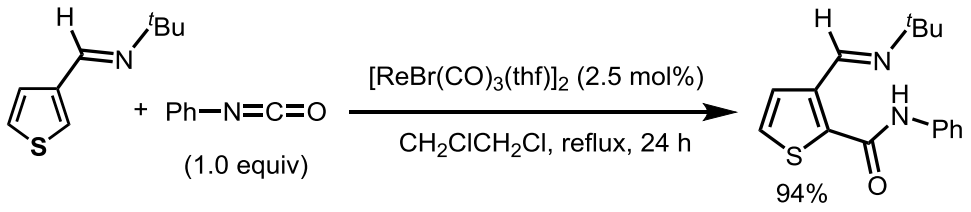
Scheme 2.5 Re-catalyzed synthesis of naphthalene derivatives

Synthesis of indenone derivatives was achieved using 3 equivalents of aryl aldehydes under rhenium/amide catalysis (**Scheme 2.6**).[9] This reaction is a new synthetic route to construct indenones via rhenium-catalyzed three-component annulation. The rhenium catalyst plays as both a catalyst for C-H bond transformation and a Lewis acid.



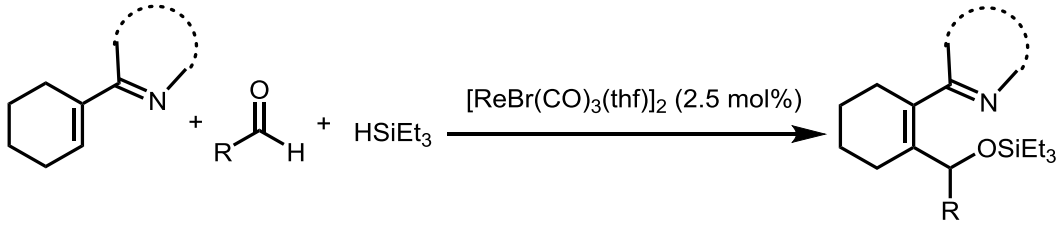
Scheme 2.6 Re-catalyzed dehydrative trimerization of aldehydes

The rhenium complex $[ReBr(CO)_3(thf)]_2$ also activates heteroaromatic C-H bonds. Notably, the insertion of isocyanates into a C-H bond of heteroaromatic compounds occurs regioselectively (**Scheme 2.7**).[10]



Scheme 2.7 Re-catalyzed heteroaromatic C-H bond transformation

Rhenium complexes also catalyze olefinic C-H bond functionalization. When $[ReBr(CO)_3(thf)]_2$ is used as a catalyst, insertion of polar unsaturated molecules into an olefinic C-H bond occurs to give *γ*,*δ*-unsaturated carbonyl compounds (**Scheme 2.8**).[11]



Scheme 2.8 Re-catalyzed olefinic C-H bond transformation

2.3 Precedents of Synthesis of 1,3-Diiminoisoindolines

A 1,3-diiminoisoindoline skeleton is a partial structure of phthalocyanines and their metal complexes, which are useful as organic functional materials, such as pigments, organic electroluminescence, and organic field effect transistors (**Figure 1.1**).[12] In addition, 1,3-diiminoisoindolines and their derivatives show biological activities as complement component antagonist[13] and antimalarial candidates.[14]

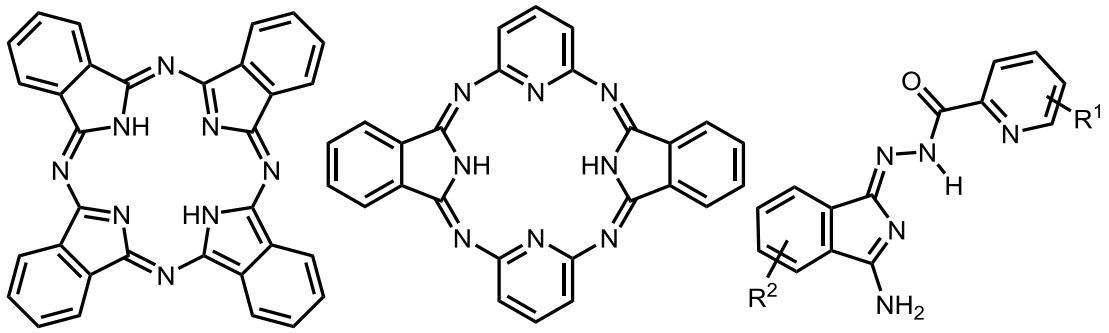
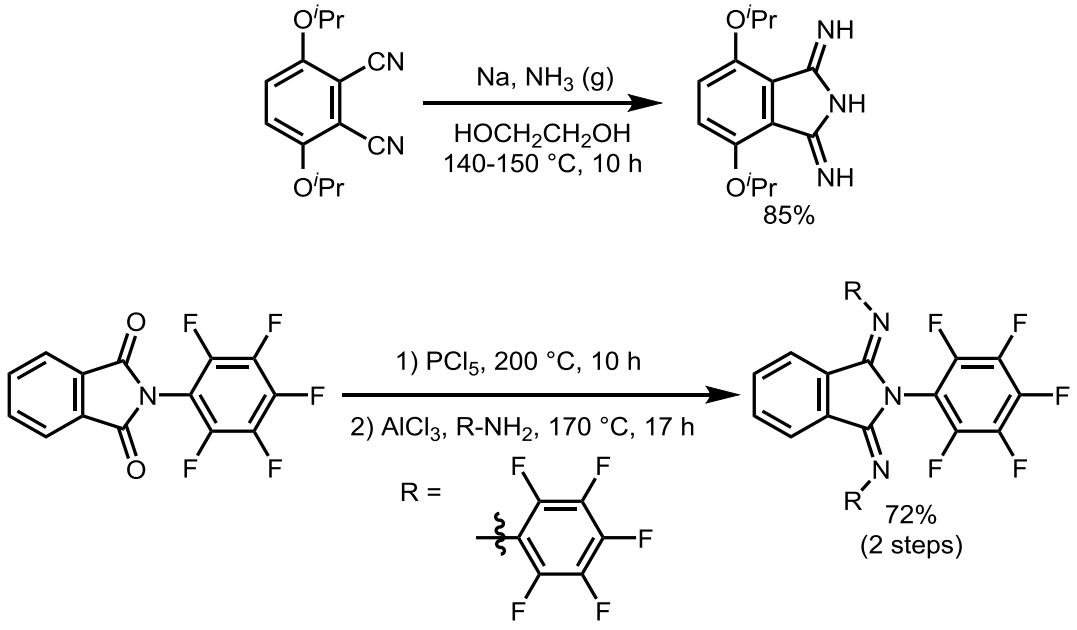


Figure 1.1 Phthalocyanines and related compounds

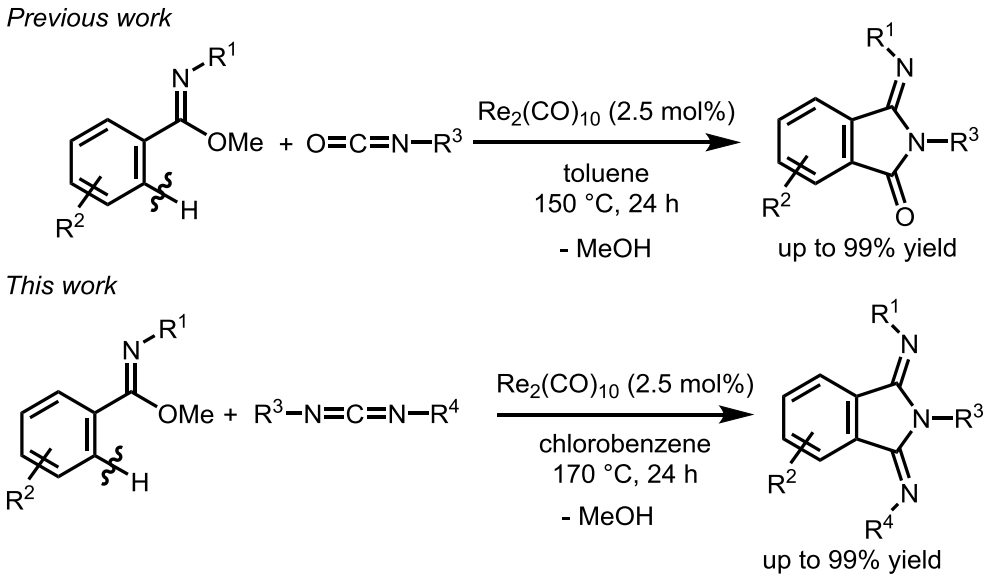
Several reactions to synthesize 1,3-diiminoisoindolines have been reported. These reactions, however, require harsh reaction conditions and only symmetrical 1,3-diiminoisoindolines are obtained (**Scheme 2.9**).[15-16] Therefore, it is necessary to develop a new method for the synthesis of 1,3-diiminoisioinolines. Synthetic reactions of 1,3-diiminoisoindolines are, however, still rare. In addition, synthesis of unsymmetrical 1,3-diiminoisoindolines is still difficult.



Scheme 2.9 Previous method for synthesis of diiminoisoindolines

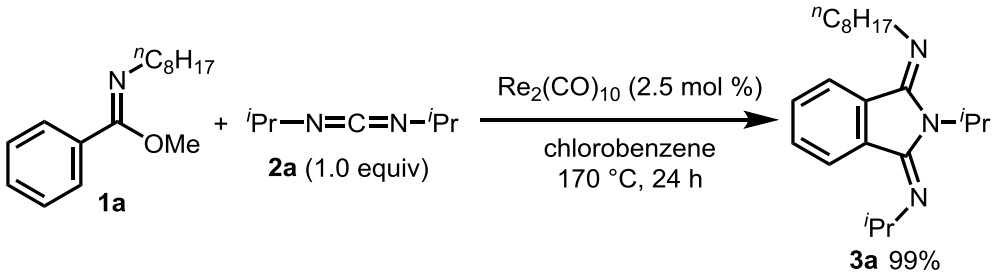
2.4 Research Purpose

Our group recently reported a rhenium-catalyzed synthesis of 3-iminoisoindolinones using aromatic imidates and isocyanates. Due to the methoxy leaving group, a C=N double bond of the directing groups remains after the reaction (**Scheme 2.10**).[17] I investigated several reactions of imidates with other unsaturated molecules, such as carbodiimides. As a result, I found that a rhenium complex catalyzed a reaction between aromatic imidates and carbodiimides to give 1,3-diiminoisoindolines efficiently.



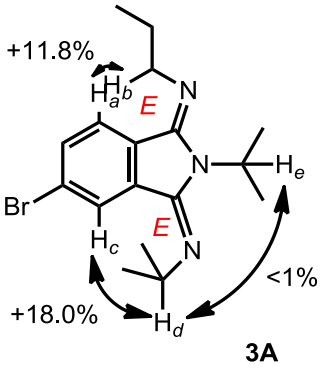
Scheme 2.10 C-H Insertion-cyclization sequence

I began my studies with several transition metal complexes and salts using aromatic imidate **1a** and *N,N′*-diisopropylcarbodiimide **2a** as model substrates. A rhenium complex, $Re_2(CO)_{10}$, exhibited high catalytic activity. Treatment of **1a** with **2a** in the presence of $Re_2(CO)_{10}$ catalyst in chlorobenzene at 170 ℃ for 24 h gave 1,3-diiminoisoindoline **3a** in 99% yield (**Scheme 2.11**). I also checked several other transition metal complexes for the annulation reaction, but their reactivity shows low efficiency.[18]



Scheme 2.11 Re-catalyzed synthesis of 1,3-diiminoisoindoline from aromatic imidate and carbodiimide

(*E*)-*N*-((*E*)-5-Bromo-2-isopropyl-3-(isopropylimino)-1-isoindolinylidene)-1-prop anamine **3A** was employed to investigate nuclear Overhauser effect experiments (see experimental section for details) for confirming the stereochemistry of the imino groups (**Scheme 2.12**). These protons, H_a and H_b, H_c and H_d, are positive correlation, so I confirmed that the configuration of these imino groups are *E*.



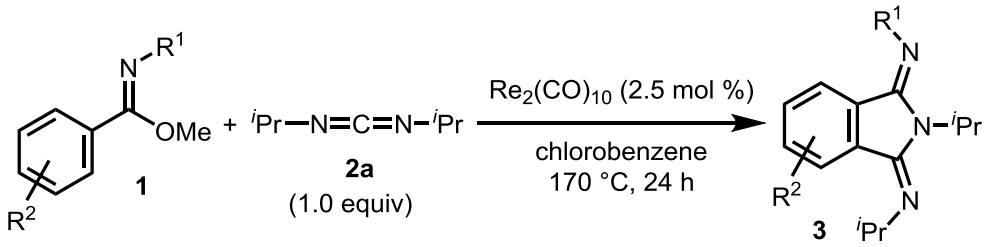
Scheme 2.12 nOe Experiment

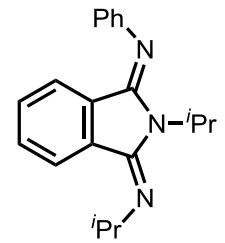
Interestingly, the by-product, methanol, fails to add to carbodiimide **2a**. Previous results show that methanol can add to carbodiimide.[19]

I then investigated the scope of aromatic imidates **1** in the rhenium-catalyzed annulation reaction with *N,N′*-diisopropylcarbodiimide **2a** (**Table 2.1**). A reaction of aromatic imidate with a phenyl group on the nitrogen, **1b**, proceeded well to give the expected 1,3-diiminoisoindoline **3b** in 85% yield. Functional groups, such as -OMe, -CF_3, -MeO_2C, -Br and -Ph, were tolerated and the desired products were obtained in excellent yield. Two regioisomers, **3h** and **3h′**, were observed when an aromatic

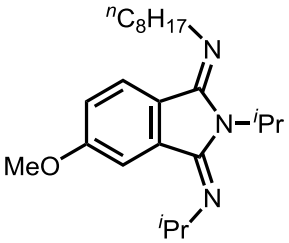
imidate with a methyl group at the *meta*-position **1h**. In this reaction, **3h** is the major product because of the sterically less hindered site. The desired reaction also proceeded regioselectively when naphthyl imidate **1i** and heteroaromatic imidates **1j** and **1k** were used as substrates.

Table 2.1 Reactions between several aromatic or heteroaromatic imidates **1** and *N*,*N*'-diisopropylcarbodiimide **2a**

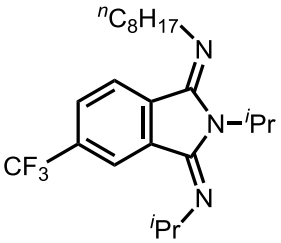




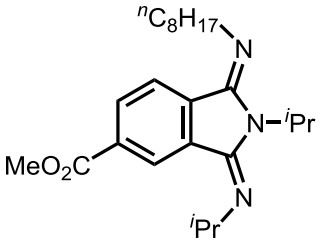
3b 85%



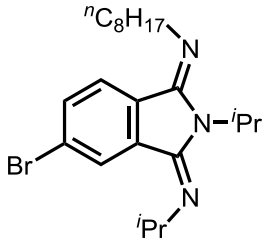
3c 99%



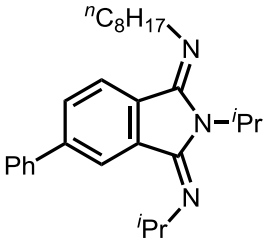
3d 99%



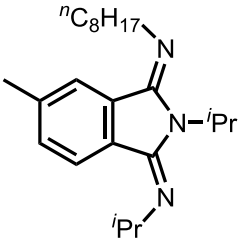
3e 97%



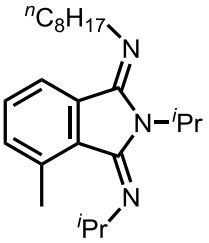
3f 96%



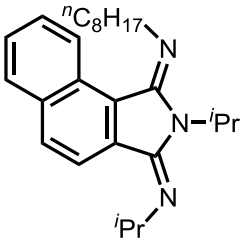
3g 99%



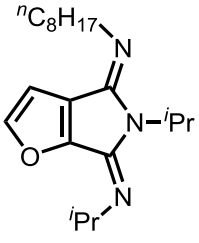
3h 70%



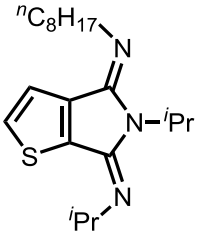
3h' 28%



3i 94%



3j 63%



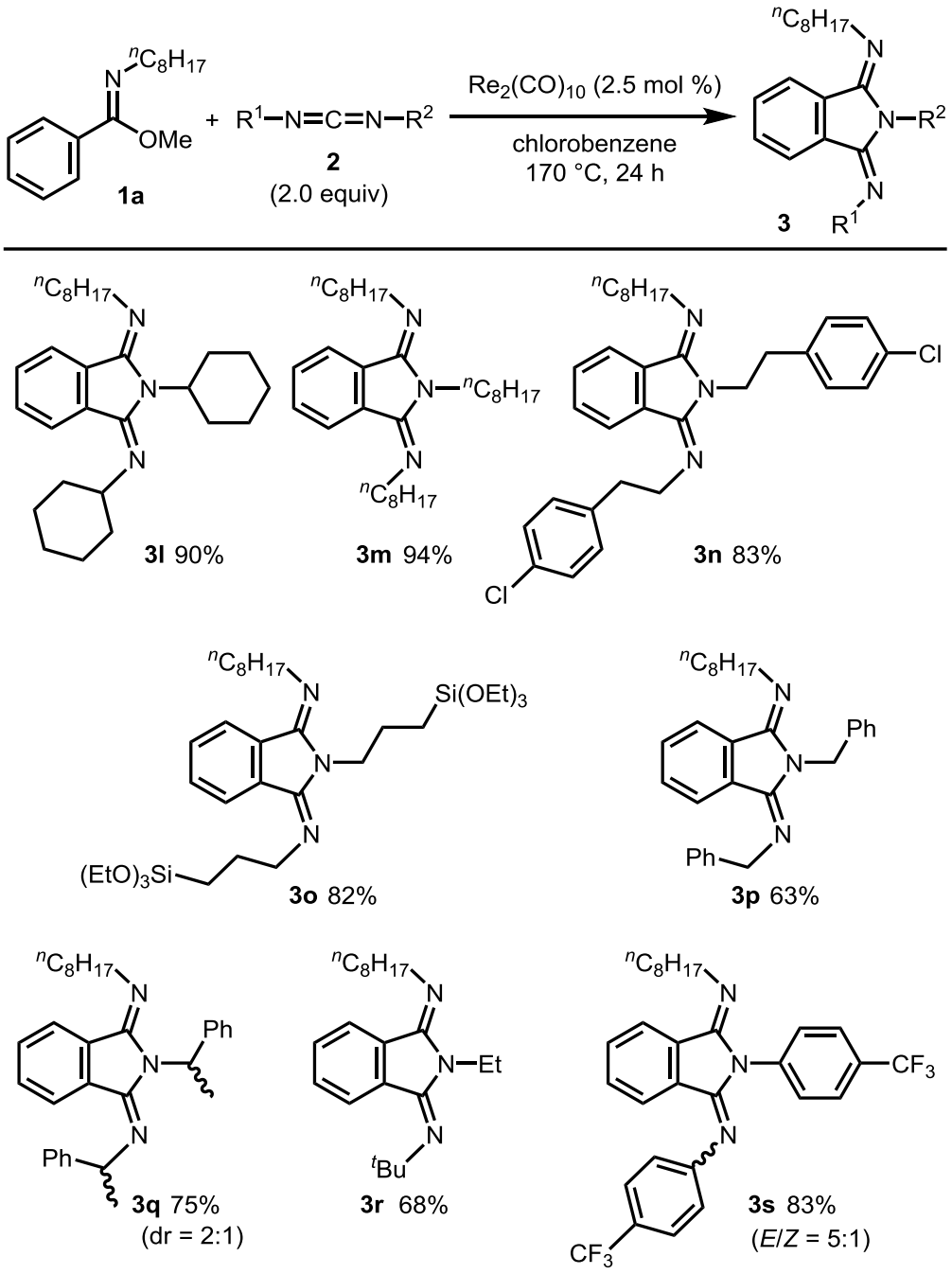
3k 68%

Next, I examined the substrate scope of carbodiimides (**Table 2.2**). Under the optimized reaction conditions, a reaction of dicyclohexylcarbodiimide (**2b**) with **1a** afforded the corresponding 1,3-diiminoisoindoline **3l** in 90% yield. Better results were

obtained for carbodiimides bearing primary alkyl groups, **2c**-**2e** to afford 1,3-diiminoisoindolines **3m**-**3o** in 82%-94% yields without loss of the functional groups. Gratifyingly, reactions of dibenzylic carbodiimides proceeded smoothly and provided desired 1,3-diiminoisoindolines **3p** and **3q** in good yields. Interestingly, the regioselectivity was completely controlled in the reaction between **1a** and unsymmetric carbodiimide **2h**, and a single product **3r** was produced. Diaryl carbodiimide **2i** gave the corresponding 1,3-diiminoisoindoline **3s** in 83% yield (*E*/*Z* = 5:1).

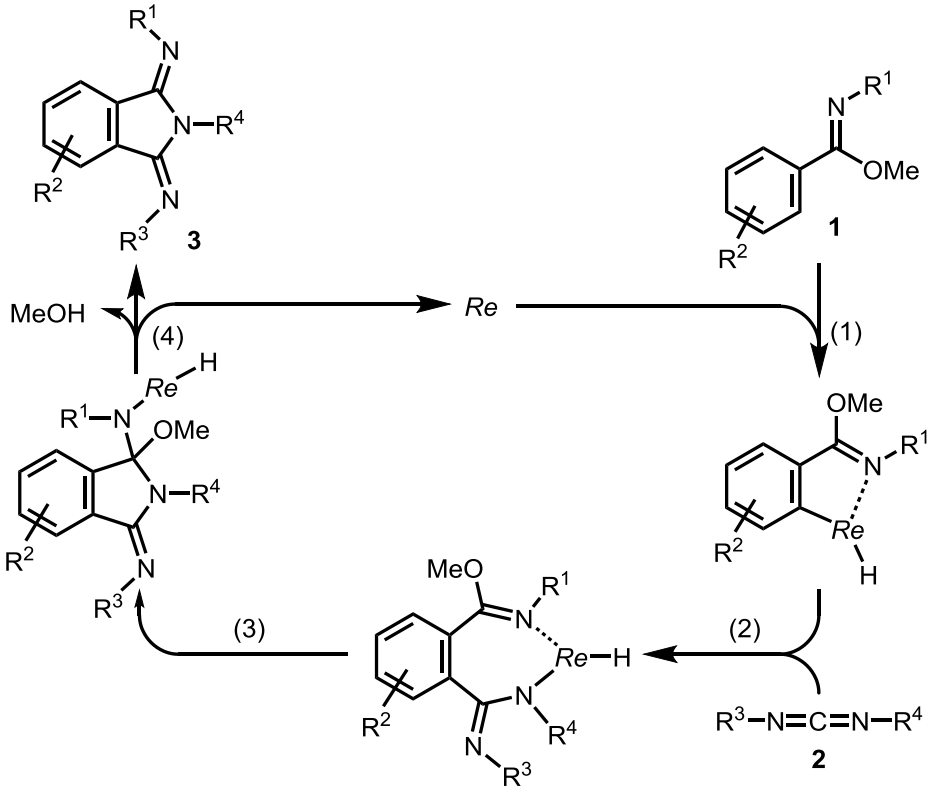
This reaction is the first example of transition metal-catalyzed insertion of a carbodiimide into a C-H bond of aromatic and heteroaromatic compounds and a novel example of the synthesis of an unsymmetric 1,3-diiminoisoindoline derivative.

Table 2.2 Reactions between aromatic imidate **1a** and several carbodiimides **2**



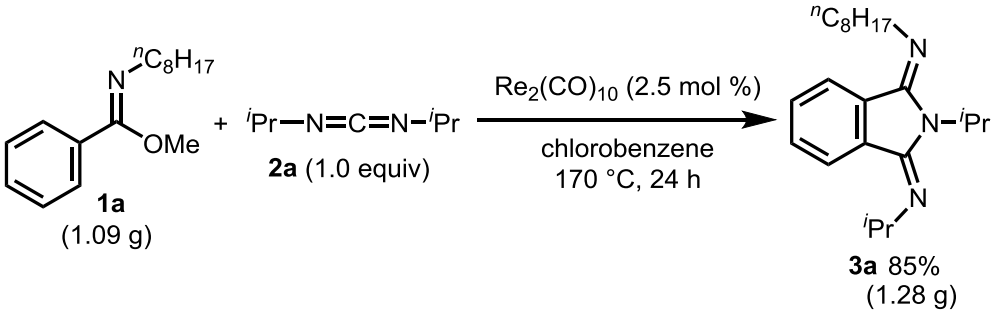
A proposed mechanism for the formation of 1,3-diiminoisoindolines **3** is shown in **Scheme 2.13**: (1) oxidative addition of aromatic imidate **1** to a rhenium catalyst (C-H bond activation); (2) insertion of carbodiimide **2** into the formed rhenium-carbon bond; (3) stereoinversion of a C=N double bond to avoid the steric repulsion between substituents R^3 and R^4, and intramolecular nucleophilic cyclization; and (4) reductive elimination and elimination of methanol to give

1,3-diiminoisoindoline **3** and regenerate the rhenium catalyst. As described above, the stereochemistry of product **3** was determined by nuclear Overhauser effect experiments. In addition, the formation of methanol was detected by ^{1}H NMR of the crude mixture.



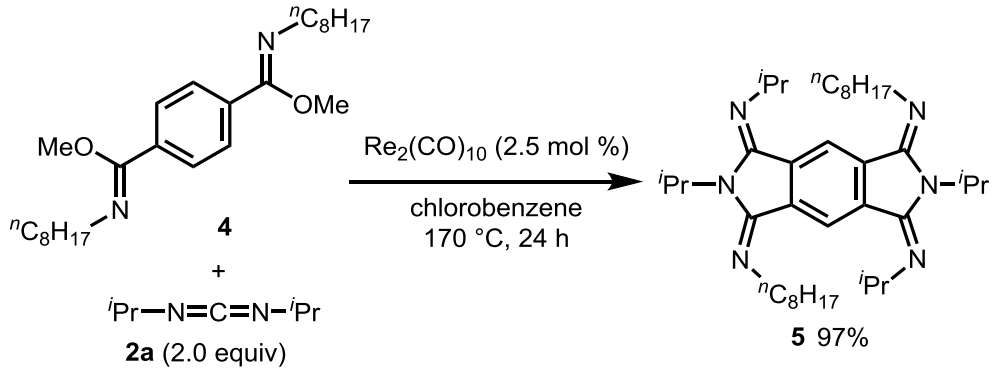
Scheme 2.13 Proposed mechanism for the formation of 1,3-diiminoisoindolines **3**

The imidate **1a** was employed to conduct a gram-scale reaction, demonstrating the practicability of this method (**Scheme 2.14**). An annulation reaction of 1.09 g of aromatic imidate **1a** with carbodiimide **2a** gave 1.28 g of the desired product **3a** in 85% yield.



Scheme 2.14 Gram-scale synthesis of 1,3-diiminoisoindoline

A double annulation reaction also proceeded in excellent yield (**Scheme 2.15**). Treatment of aromatic diimidate **4** with *N*,*N*-diisopropylcarbodiimide (**2a**) in the presence of $Re_2(CO)_{10}$ catalyst in chlorobenzene at 170 ℃ for 24 h gave 1,3-diiminoisoindoline **5** in 97% yield as a single product. The reaction proceeded highly regioselectively and only single product **5** was obtained, whereas a regioisomer could be formed.



Scheme 2.15 Double annulation reaction

2.5 Summary

I established a novel, facile and efficient method for the synthesis of 1,3-diiminoisoindolines and their related compounds from aromatic or heteroaromatic imidates and carbodiimides via C-H bond activation. The desired reaction proceeded in advance of the consumption of carbodiimides by the addition of methanol (byproduct) to carbodiimides. To the best of my knowledge, this is the first example of a transition metal-catalyzed C-H insertion of carbodiimides.

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[18] $ReBr(CO)_5$, 26%; $[ReBr(CO)_3(thf)]_2$, 30%; $Re_2(CO)_{10}$, 33%; $[Rh(OH)(cod)]_2$/*rac*-BINAP, 8%; $[Cp^*IrCl_2]_2$, 16%. The desired reaction did not proceed using the following transition metal complexes and salts: $Mn_2(CO)_{10}$, $MnBr(CO)_5$, $Ru_3(CO)_{12}$, $RuH_2(CO)(PPh_3)_3$, $[RuCl_2(p\text{-cymene})]_2$, $RhCl(PPh_3)_3$, $[Cp^*RhCl_2]_2$, $[Ir(OMe)(cod)]_2$/dtbpy, $Pd(OAc)_2$, and $Cu(OAc)_2$.

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Chapter 3 Iron-Catalyzed Acyloxyalkylation of Styrenes via Decarboxylation of Hypervalent Iodine(III) Reagents

3.1 Introduction

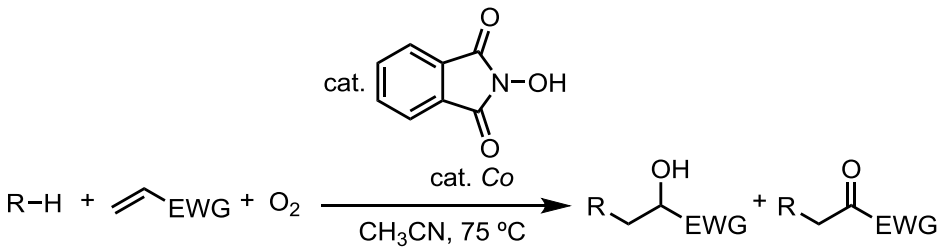
Organic reactions involving olefins play a very important role in the development of organic synthesis. Olefin compounds are readily available at low cost and allow for more conversion of functional groups. Therefore, it is necessary to develop new and efficient ways to realize olefin functionalization. Recently, transition metal-catalyzed difunctionalizations of alkenes are important topic because these reactions can synthesize highly functionalized backbones of pharmaceuticals and natural products.[1-4] In traditional oxyalkylation of alkenes, the osmium-catalyzed Sharpless epoxidation play an important role, but the toxic osmium catalyst and two steps (epoxidation and alkylation) are necessary, which hasn't meet the requirements of modern organic reactions. Oxyalkylation of alkenes is still challenging and the examples are quite rare.

3.2 Precedents of Metal-Catalyzed Oxyalkylation of Alkenes

As a representative method for oxyalkylation of alkenes, epoxidation of alkenes is well known. However, the reaction requires two steps, epoxidation and alkylation, which is not ideal considering the requirements of modern organic reactions, such as environmentally benign, eased handling, low cost, and ready availability. Along this line, transition metal-catalyzed oxyalkylation of alkenes has received gradual attention.

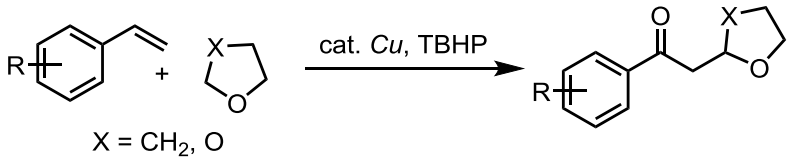
Ishii described a novel cobalt/*N*-hydroxyphthalimide co-catalytic method for a free radical addition of cycloalkanes and molecular oxygen to electron-deficient alkenes (**Scheme 2.1**).[5] A reaction between 1,3-dimethyladamantane and methyl acrylate under oxygen atmosphere in the presence of catalytic amounts of NHPI and

$Co(acac)_3$ at 75 ℃ for 16 h gave oxyalkylated product in 91% yield.



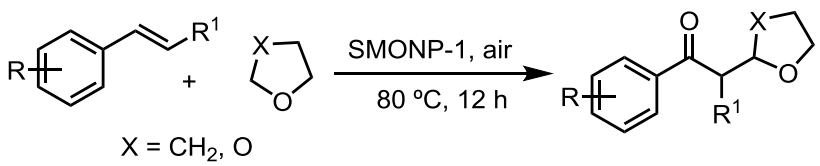
Scheme 2.1 Co-catalyzed oxyalkylation of alkenes using *N*-hydroxyphthalimide

Zhang reported Cu-catalyzed difunctionalization of vinylarenes with cyclic ethers and oxygen in the presence of 1-1.2 equivalents of TBHP under aerobic conditions (**Scheme 2.2**).[6] The various oxyalkylated products of vinylarenes were obtained with excellent regioselectivity and good functional group tolerance.



Scheme 2.2 Cu-mediated oxyalkylation of vinylarenes

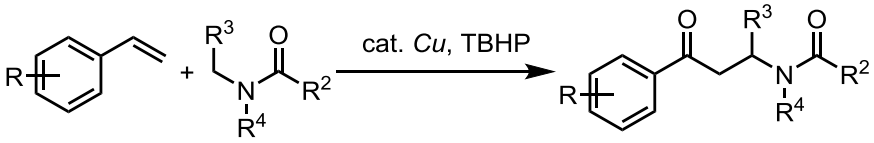
A similar result of regioselective oxyalkylation of vinylarenes catalyzed by diatomite supported manganese oxide nanoparticles was developed by Wang (**Scheme 2.3**).[7] α-Carbonyl β-alkylated aryl derivatives can be obtained in good yields with high regioselectivity at 80 ℃ for 12 h under air atmosphere using a new heterogeneous catalyst SMONP-1.



SMONP-1: diatomite supported Mn_3O_4 nanoparticles

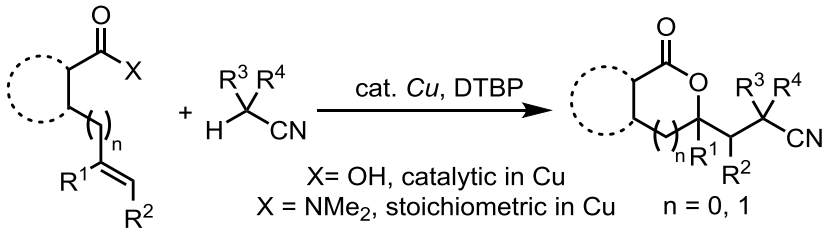
Scheme 2.3 SMONP-1-catalyzed regioselective oxyalkylation of vinylarenes

A simple, practical, inexpensive and new strategy for synthesis of *N*-(3-oxo-3-phenylpropyl)-acetamide derivatives via a copper-catalyzed oxidative coupling between styrenes and *N*,*N*-disubstituted amides was reported by Mao (**Scheme 2.4**).[8] The reaction of various styrenes with *N*,*N*-disubstituted acetamides give the corresponding products in moderate yields. Furthermore, some amides products could be changed into *β*-amino carbonyls by successive hydrolysis.



Scheme 2.4 Functionalization of amides via Cu-catalyzed oxyalkylation of vinylarenes

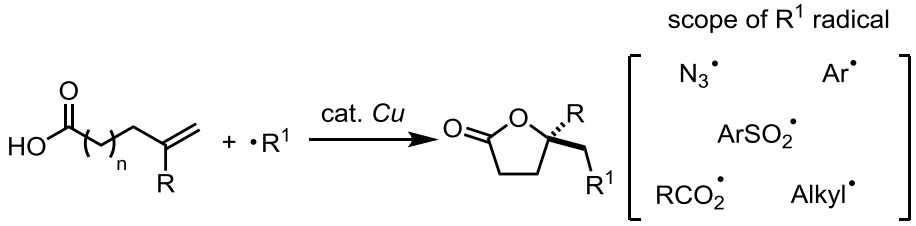
Zhu achieved copper-catalyzed intramolecular oxyalkylation of alkenes with alkylnitriles (**Scheme 2.5**).[9] Formation of C(sp^3)-C(sp^3) and C(sp^3)-O bonds can be achieved from alkylnitriles by using copper salt in situ generated the alkylative lactonization products to generate two quaternary carbon atoms simultaneously. The addition of a cyanomethyl radical was not dependent on di-*tert*-butylperoxide (DTBP), which initiated the present domino process.



Scheme 2.5 Cu-mediated/catalyzed oxyalkylation of alkenes

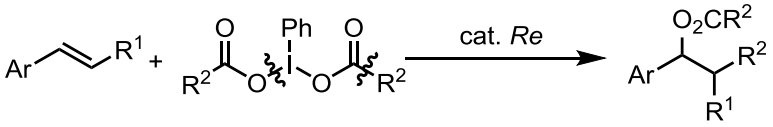
Buchwald recently realized a rapid synthesis of enantiomerically enriched lactones by copper-catalyzed enantioselective radical oxyalkylation of alkenes (**Scheme 2.6**).[10] Enantioselective difunctionalization reactions including

oxyazidation, oxysulfonylation, oxyarylation, diacyloxylation, and oxyalkylation are applicable to the synthesis of various useful chiral lactones, which contains a tetrasubstituted stereocenter.



Scheme 2.6 Cu-catalyzed enantioselective radical oxyalkylation of alkenes

Wang reported the first example which both of oxygenation and alkylation sources come from hypervalent iodine(III) reagents in the difunctionalizations of alkenes (**Scheme 2.7**).[11] This reaction proceeded via decarboxylative acyloxyalkylation of alkenes in the presence of a rhenium catalyst and hypervalent iodine(III) reagents. Visible light irradiation is, however, necessary to promote the reaction in some cases.



Scheme 2.7 Re-cactalyzed oxyalkylations of alkenes

3.3 Research Purpose

Second and third row transition metal catalysts, such as rhenium, palladium, and gold exhibit powerful catalytic activities. However, the relatively high price and considerable toxicity limit their applications and improvements. Iron is the most abundant transition metal and has recently received much attention in synthetic organic chemistry.[12]

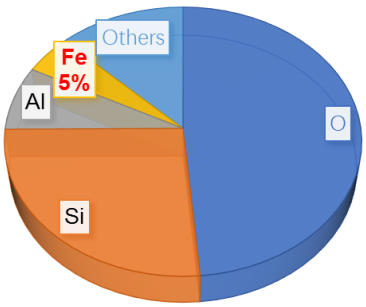
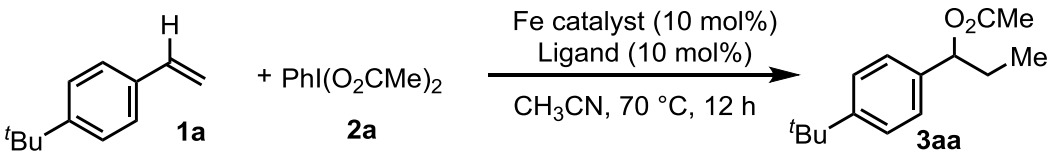


Figure 3.1 Elemental abundance

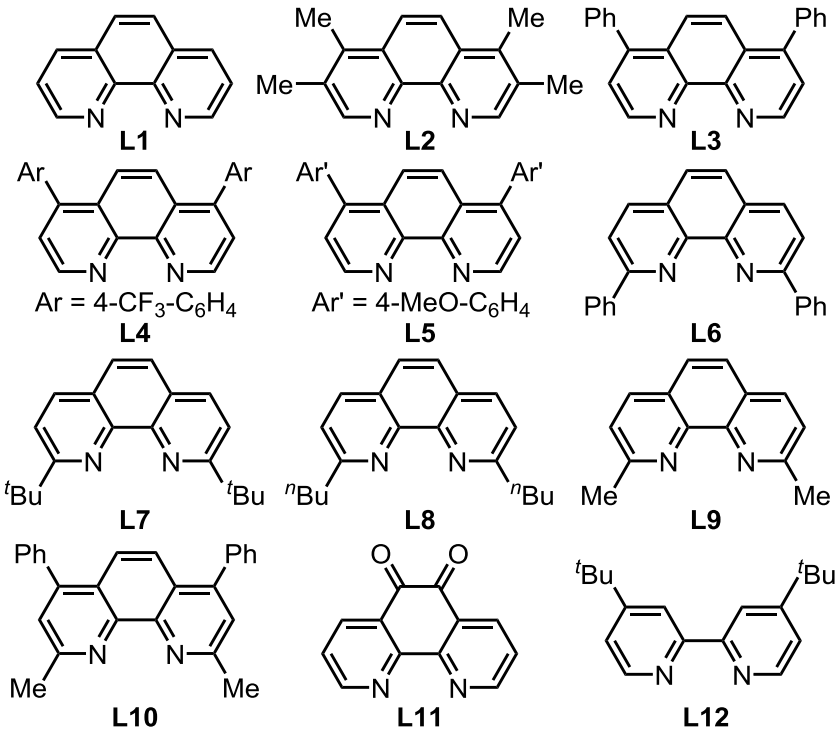
I successfully replaced the rhenium catalyst in the reaction (**Scheme 2.7)** with an iron catalyst. Iron-catalyzed acyloxyalkylation is economical and environmentally benign, and the reaction requires no visible light irradiation.

I chose 1-(*tert*-butyl)-4-vinylbenzene (**1a**) and iodobenzene diacetate (**2a**) as model substrates for optimizing the reaction conditions (**Table 3.1**). Formation of the desired product was not observed in the presence of catalytic amounts of $Fe(CO)_3$(cot) and phenanthroline (**L1**) (entry 1). Acyloxyalkylated product **3aa** was obtained employing ligand **L2** or **L3** (entries 2 and 3). The desired product **3aa** was not formed when electron-withdrawing or electron-donating groups were introduced into the phenyl groups of phenanthroline derivatives (entries 4 and 5). The results of phenanthrolines **L6**-**L9** with substituents, Ph, ^{t}Bu, ^{n}Bu or Me groups, at the 2- and 9-positions suggest that the two methyl groups on 2,9-position of phenanthroline are indispensable (entries 6-9). A combination of 4,7-diphenylphenanthroline and 2,9-dimethylphenanthroline, 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (bathocuproine, **L10**) gave the best result and **3aa** was isolated in 53% yield (entry 10). 9,10-Phenanthrenedione **(L11**) or 4,7-di(*tert*-butyl)bipyridine (**L12**) did not provide the desired product **3aa** (entries 11 and 12). Acyloxyalkylated product **3aa** was also delivered in 50% yield using $Fe(OAc)_2$ as a catalyst (entry 13). Other iron complexes and salts gave **3aa** the lower yields.[13]

Table 3.1 Oxyalkylation of alkenes: optimization of reaction conditions.[a]



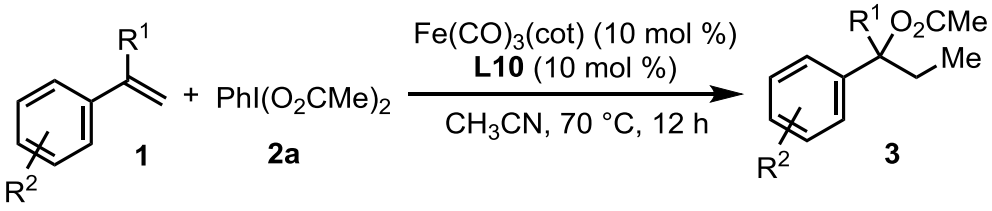
entry[a]	cat. iron	ligand	3aa (%)[b]
1	$Fe(CO)_3(cot)$	**L1**	0
2	$Fe(CO)_3(cot)$	**L2**	23
3	$Fe(CO)_3(cot)$	**L3**	12
4	$Fe(CO)_3(cot)$	**L4**	0
5	$Fe(CO)_3(cot)$	**L5**	0
6	$Fe(CO)_3(cot)$	**L6**	7
7	$Fe(CO)_3(cot)$	**L7**	20
8	$Fe(CO)_3(cot)$	**L8**	15
9	$Fe(CO)_3(cot)$	**L9**	20
10	$Fe(CO)_3(cot)$	**L10**	53[c]
11	$Fe(CO)_3(cot)$	**L11**	0
12	$Fe(CO)_3(cot)$	**L12**	3
13	$Fe(OAc)_2$	**L10**	50

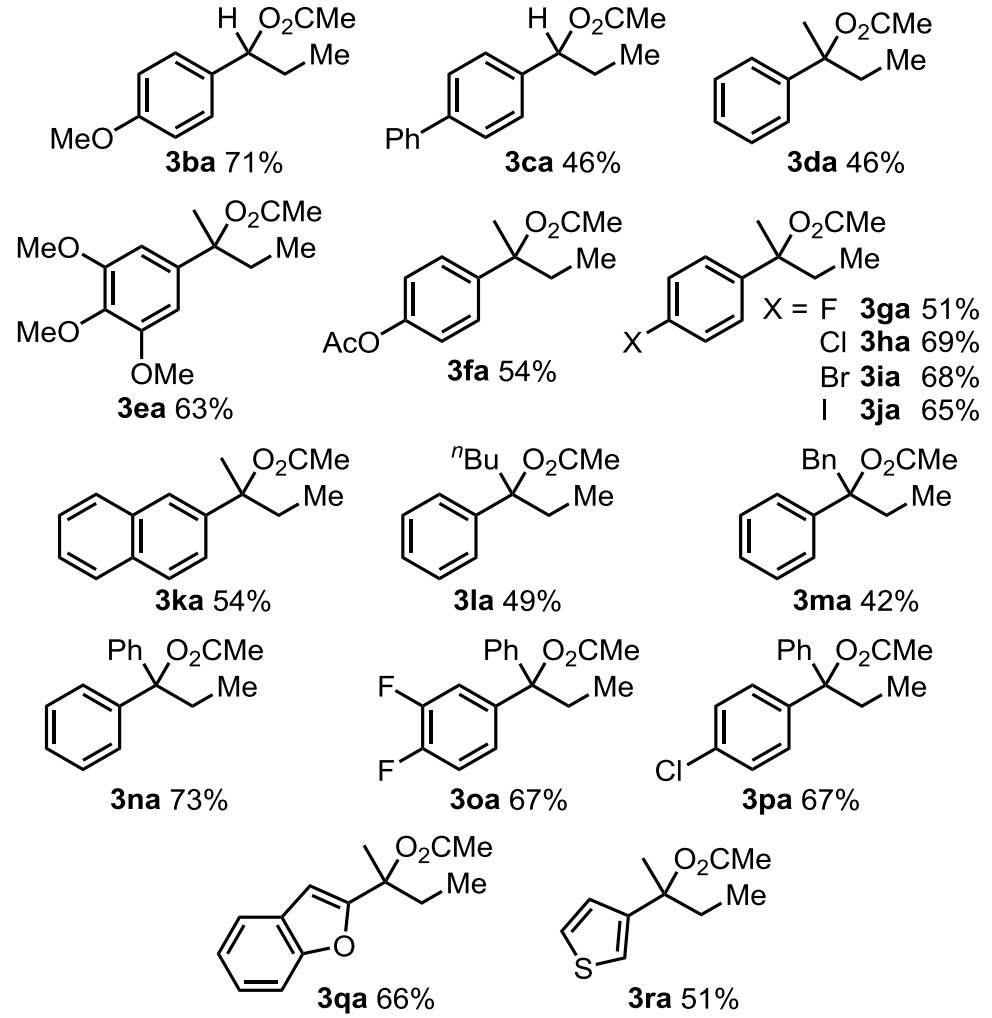


[a]Reaction conditions: **1a** (0.25 mmol, 1.0 equiv.), **2a** (0.325 mmol, 1.3 equiv.), iron catalyst (0.05 mmol, 10 mol%), ligand (0.05 mmol, 10 mol%), CH_3CN (1 mL), 70 °C, 12 h. [b]Yield determined by ^1H NMR analysis using $Cl_2CH_2CH_2Cl_2$ as an internal standard. [c]Isolated yield. cot = cyclooctatetraene.

Next, the substrate scope of styrenes was investigated (**Table 3.2**). Styrenes bearing a methoxy group ,**1b**, or phenyl group, **1c**, gave target products **3ba** and **3ca** without loss of the functional groups. α-Methylstyrenes **1d-1k** bearing a strong electron-donating group, ester, halogens including iodine or naphthalenyl group, also reacted smoothly with iodobenzene diacetate. Styrenes **1l-1p** with other α-substituent, such as benzyl, butyl, phenyl, or a substituted aromatic group, delivered the acyloxyalkylated products in moderate yields. The corresponding. five-membered heteroaromatic compounds with a vinyl group, **1q** and **1r**, were well compatible with the reaction conditions to form the corresponding acetoxyalkylated products **3qa** and **3ra** in 66% and 51% yields, respectively.

Table 3.2 Reactions between several styrenes **1** and (diacetoxyiodo)benzene (**2a**).[a]



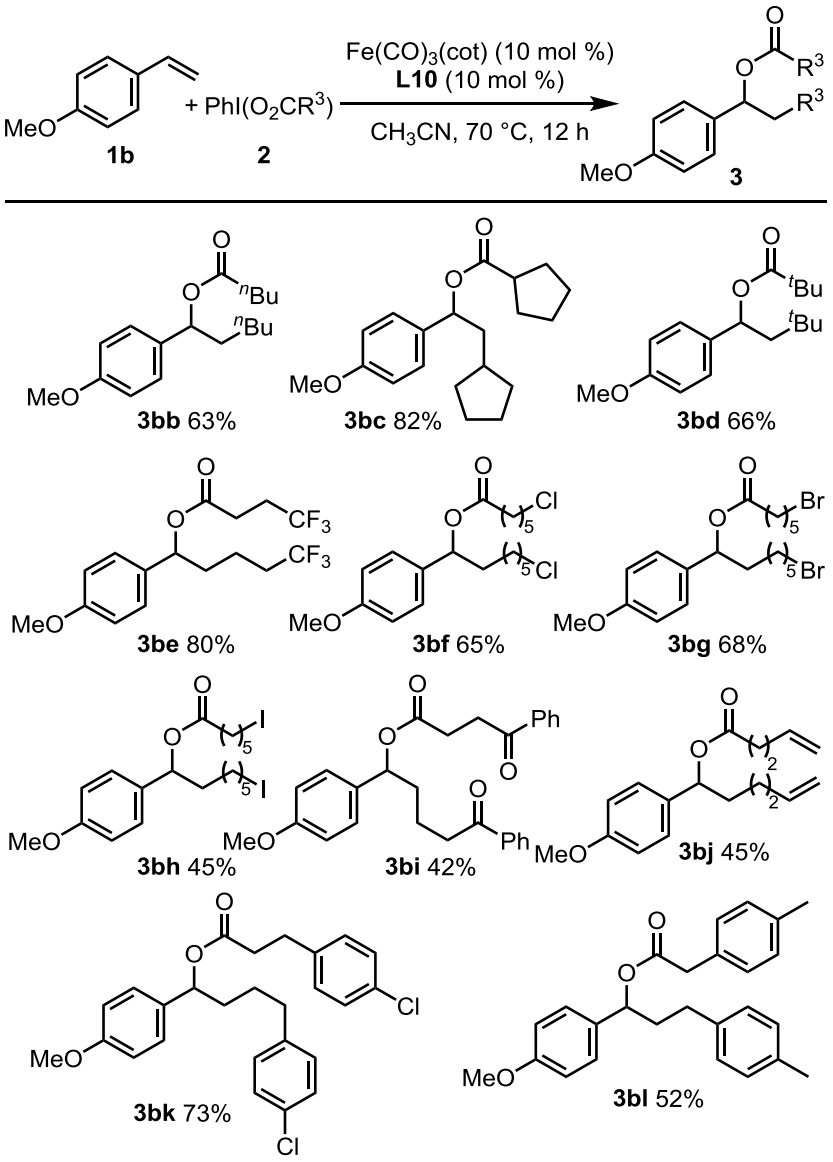


[a]Reaction conditions: **1** (0.250 mmol, 1.0 equiv), **2a** (0.3250 mmol, 1.3 equiv), $Fe(CO)_3(cot)$ (0.0500 mmol, 10 mol%), **L10** (0.0500 mmol, 10 mol%), CH_3CN (1.0 mL), 70 °C, 12 h.

Next, several hypervalent iodine(III) reagents were investigated as shown (**Table 3.3**). In all entries, no visible light irradiation was necessary to produce radical species derived from the hypervalent iodine(III) reagents. Hypervalent iodine(III) reagents **2b**-**2d** attached primary, secondary, and tertiary aliphatic carboxylate provided the

desired acyloxyalkylated products **3bb**-**3bd** in 63%-82% yields. In a previous study by Wang, no results of the using any hypervalent iodine(III) reagents containing functional groups were reported (Scheme 2.7).[11] I therefore screened hypervalent iodine(III) reagents **2e**-**2j** bearing functional groups, such as trifluoromethyl, chlorine, bromine, or iodine atoms, carbonyl groups and inactive alkene moieties. As a result, the acyloxyalkylation reactions took place to give products **3be**-**3bj** in moderate to good yields. The reaction of styrene **1b** with hypervalent iodine(III) reagent **2k** or **2l** bearing 4-chlorophenyl or 4-methylbenzyl groups afforded the corresponding products in 73% and 52% yields, respectively.

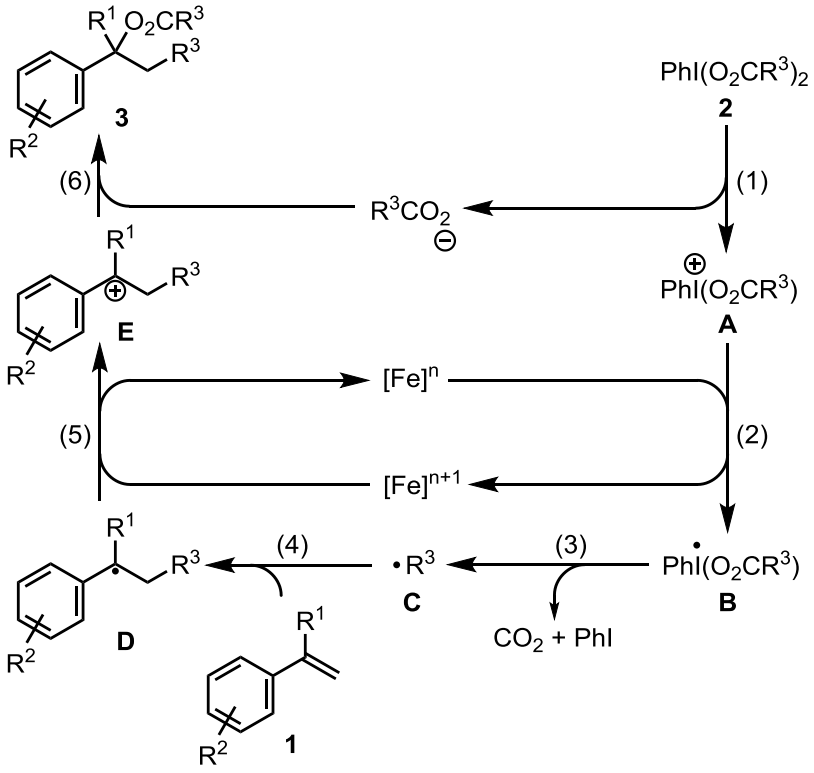
Table 3.3 Reactions between styrene **1b** and (diacyloxyiodo)benzene **2**.[a]



[a]Reaction conditions: **1b** (0.250 mmol, 1.0 equiv), **2** (0.325 mmol, 1.3 equiv), $Fe(CO)_3$(cot) (0.0500 mmol, 10 mol %), **L10** (0.0500 mmol, 10 mol %), CH_3CN (1.0 mL), 70 °C, 12 h.

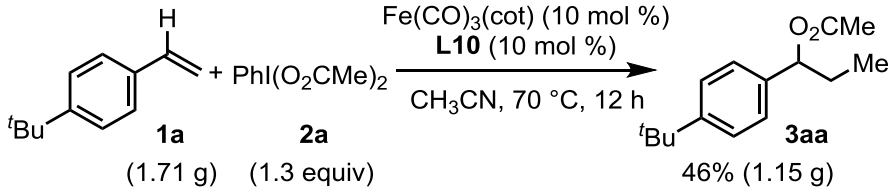
To elucidate the reaction mechanism, we carried out a reaction in the presence of 1.0 equivalent of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as a radical scavenger under the standard reaction conditions to check whether the reation involve redical species or not. As a result, the acyloxyalkylation reaction was inhibited completely. This result indicated that the mechanism of the acyloxyalkylation reaction processes a radical pathway. The plausible reaction mechanism for the iron-catalyzed acyloxyalkylation of styrene derivatives using hypervalent iodine(III) reagents is

shown in **Scheme 2.8**, based on the previous report:[14] (1) Generation of cationic specie **A** through heterolysis of iodobenzene diacetate; (2) oxidation of **A** by Fe^n to give radical iodine intermediate **B**; (3) homolysis of **B** to provide radical species **C** with the formation of iodobenzene and release carbon dioxide; (4) addition of **C** radical to styrene derivative **1** to convey benzylic radical **D**; (5) oxidation of **D** by $[Fe]^{n+1}$ to deliver benzylic cation **E**; and (6) nucleophilic attack of the carboxylate to **E** to give the desired product **3**.



Scheme 2.8 Proposed reaction mechanism.

For demonstrating the practicability of this method, gram scale reaction was conducted by treatment of 1.71 g of **1a** with **2a** in the presence of catalytic amounts of $Fe(CO)_3$(cot) and **L4** gave 1.15 g of **3aa** in 46% yield (**Scheme 2.9**).



Scheme 2.9 Gram-scale reaction.

3.4 Summary

I succeeded in the development of an iron-catalyzed acyloxyalkylation of styrene derivatives using hypervalent iodine(III) reagents. A variety of styrenes and hypervalent iodine(III) reagents were well compatible with the reaction conditions to give acyloxyalkylated products in moderate to good yields, even in gram scale, without loss of the functional groups. The phenanthroline ligands are very important in the reaction system even though the role of phenanthroline ligands is unclear. In a similar previously reported rhenium-catalyzed oxyalkylation, some cases needed visible light irradiation to promote reaction. The present reaction, however, required no irradiation. Furthermore, compared with Wang's result, I expanded the scope of hypervalent iodine(III) reagents with functional.

3.5 References

[1] For examples of copper catalysis, see: (a) Miller, Y.; Miao, L.; Hosseini, A. S.; Chemler, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 12149. (b) Kaneko, K.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Org. Lett.* **2013**, *15*, 2502. (c) Shimizu, Y.; Kanai, M. *Tetrahedron Lett.* **2014**, *55*, 3727.

[2] For examples of silver catalysis, see: (a) Li, Z.; Song, L.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 4640. (b) Yuan, Y.; Shen, Y.; Wang, K.; Jiao, N. *Chem. Asian J.* **2013**, *8*, 2932. (c) Wu, X.; Chu, L.; Qing, F.-L. *Angew. Chem. Int. Ed.* **2013**, *52*, 2198. (d) Wu, K.; Liang, Y.; Jiao, N. *Molecules* **2016**, *21*, 352.

[3] For examples of palladium catalysis, see: (a) Minatti, A.; Muñiz, K. *Chem. Soc. Rev.* **2007**, *36*, 1142. (b) Desai, L. V.; Sanford, M. S. *Angew. Chem. Int. Ed.* **2007**, *46*, 5737. (c) Urkalan, K. B.; Sigman, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 18042. (d) McDonald, R. I.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981. (e) Matsura, B. S.; Condie, A. G.; Buff, R. C.; Karahalis, G. J.; J. Stephenson, C. R. *Org. Lett.* **2011**, *13*, 6320. (f) Li, Z.; García-Domínguez, A.; Nevado, C. *J. Am. Chem. Soc.* **2015**, *137*, 11610.

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[8] Yan, H.; Lu, L.; Rong, G.; Liu, D.; Zheng, Y.; Chen, J.; Mao, J. *J. Org. Chem.* **2014**, *79*, 7103.

[9] Bunescu, A.; Wang, Q.; Zhu, J. *Chem. Eur. J.* **2014**, *20*, 14633.

[10] Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2015**, *137*, 8069.

[11] Wang, Y.; Zhang, L.; Yang, Y.; Zhang, P.; Du, Z.; Wang, C. *J. Am. Chem. Soc.* **2013**, *135*, 18048.

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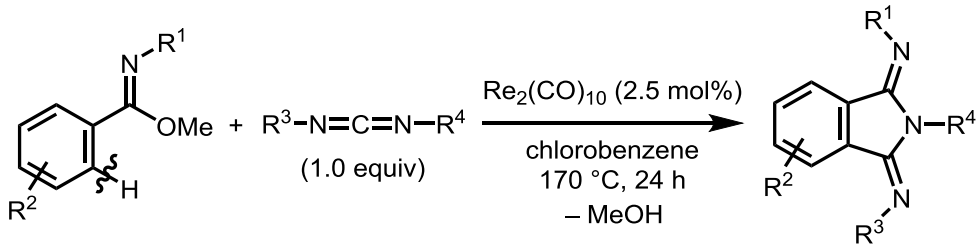
M.; Gianino, J. B.; Schindler, C. S. *Nature* **2016**, *533*, 374. (j) Jia, T.; Zhao, C.; He, R.; Chen, H.; Wang, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 5268.

[13] Fe(0) powder, 41%; $[FeCp^*(CO)_2]_2$, 30%; $Fe(acac)_2$, 38%; $Fe(OTf)_2$, 0%;$Fe(ClO_4)_2$, 12%; FeS, 34%; FeF_2, 24%; $FeCl_2$, 19%; $FeBr_2$, 25%; Fe_3O_4, 0%; $Fe(OEt)_3$, 26%; $Fe(OTf)_3$, 0%.

[14] For several reviews and papers of organic reactions using hypervalent iodine(III) reagents, see: (a) Boye, A. C.; Meyer, D.; Ingison, C. K.; French, A. N.; Wirth, T. *Org. Lett.* **2003**, *5*, 2157. (b) Correa, A.; Tellitu, I.; Dom ńguez, E.; SanMartin, R. *J. Org. Chem.* **2006**, *71*, 8316. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (d) Wardrop, D. J.; Bowen, E. G.; Forslund, R. E.; Sussman, A. D.; Weerasekera, S. L. *J. Am. Chem. Soc.* **2009**, *132*, 1188. (e) Lovick, H. M.; Michael, F. E. *J. Am. Chem. Soc.* **2010**, *132*, 1249. (f) Brand, J. P.; Gonz ález, D. F.; Nicolai, S.; Waser, J. *Chem. Commun.* **2011**, *47*, 102. (g) Liu, L.; Lu, H.; Wang, H.; Yang, C.; Zhang, X.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. *Org. Lett.* **2013**, *15*, 2906.

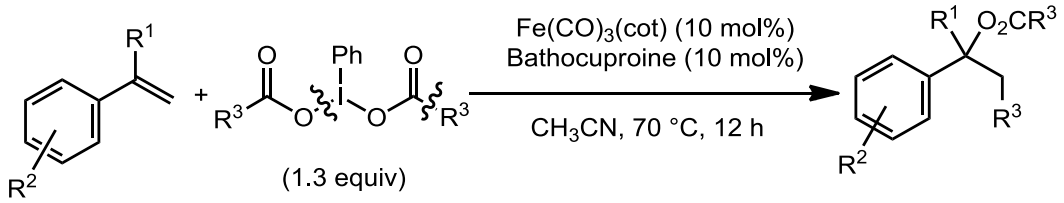
Chapter 4 Summary

I developed a rhenium-catalyzed synthesis of 1,3-diiminoisoindolines from aromatic imidates and carbodiimides via C-H bond activation (**Scheme 4.1**). Various unsymmetrical 1,3-diiminoisoindolines were obtained in good to excellent yields with good functional group tolerance. This reaction could be applicable for the gram-scale synthesis. To the best of my knowledge, this is the first example of a transition metal-catalyzed C-H insertion of carbodiimides, and this reaction is a novel method for synthesizing 1,3-diiminoisoindolines. Especially, it can be applied to synthesis of unsymmetrical 1,3-diiminoisoindolines.



Scheme 4.1 Re-catalyzed synthesis of 1,3-diiminoisoindolines via C-H bond activation

I also succeeded in the development of iron-catalyzed oxyalkylation of styrene derivatives using hypervalent iodine(III) reagents (**Scheme 4.2**). The choice of bathocuproine ligand was important to promote the reaction. Visible light irradiation was not necessary in this reaction. The reaction proceeded in moderate to good yields, even on gram scale, using a variety of styrenes and hypervalent iodine(III) reagents without loss of the functional groups. Compared with a previously reported similar rhenium-catalyzed oxyalkylation, the scope of hypervalent iodine(III) reagents with functional groups was expanded, and the iron-catalyzed reaction is expected to be used for the synthesis of medicines and nature products.



Scheme 4.2 Fe-catalyzed acyloxyalkylation of styrenes

The following is a summary of the above: I have achieved to develop transition metal-catalyzed regioselective hydroarylation and acyloxyalkylation of unsaturated molecules. Both of reactions proceeded in good yields with high regioselectivity even in gram scale under low catalyst loadings. I hope that these results will give a useful insight into synthetic organic chemistry.

Experimental Section

Rhenium-Catalyzed Synthesis of 1,3-Diiminoisoindolines via Insertion of Carbodiimides into a C-H Bond of Aromatic and Heteroaromatic Imidates

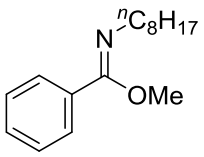
General. All reactions were carried out in a dry solvent under an argon atmosphere. Chlorobenzene was purchased from Aldrich Co. and were dried and degassed before use. $Re_2(CO)_{10}$ was purchased from Aldrich Co. Aromatic imidates (**1a**-**1k** and **4**) and carbodiimides (**2c**-**2h**) were prepared according to the literature methods.[1,2] Carbodiimides (**2a**, **2b,** and **2h**) were purchased from Tokyo Kasei Kogyo Co. NMR spectra were recorded on JEOL ECX500 (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) and JEOL ECS400 (400 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR, 78 MHz for ^{29}Si, 376 MHz for ^{19}F NMR) spectrometers. Proton chemical shifts are reported relative to Me_4Si ($CDCl_3$) at 0.00 ppm or residual solvent peak ($CDCl_3$ at 7.26 ppm). Carbon chemical shifts are reported relative to $CDCl_3$ at 77.26 ppm. Fluorine chemical shifts are reported relative to TFA ($CDCl_3$) at -76.55 ppm as an external standard. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. ESI-mass spectra were measured on a JEOL JMS-T100LC AccuTOF spectrometer for HRMS.

Typical procedure for the preparation of (*Z*)-methyl *N*-octylbenzimidate (1a). A mixture of *N*-octylbenzamide (9.32 g, 40.0 mmol) and $SOCl_2$ (40 mL) was refluxed for 24 h in a 100 mL round-bottom flask under an argon atmosphere. Then, the remained $SOCl_2$ was removed in vacuo to give *N*-octylbenzimidoyl chloride.

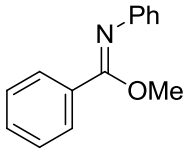
To a 100 mL round-bottom flask was added MeONa (60.0 mmol in 5M Methanol solution) and remove MeOH by vacuum pump. Then, THF (40 mL) and the prepared (*Z*)-*N*-octylbenzimidoyl chloride in THF (20 mL) was added to the mixture and stirred at room temperature for 24 h. The resulting mixture was quenched with water and extracted with ethyl acetate (3 x 20 mL). And the combined organic layer was dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 19/1) to give (*Z*)-methyl *N*-octylbenzimidate as a yellow oil (**1a**, 7.71 g, 78% yield).

Typical procedure for the preparation of *N*,*N*'-Methanediylidenebis(1-octanamine) (2c). A dry 100 mL round-bottom flask was charged with 80 mL of dichloromethane, 4.23 g of triphenylphosphine (16.1

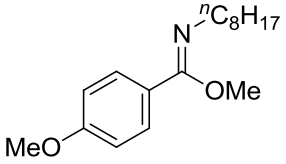
mmol, 1.25 equiv), and a magnetic stir bar. A dry pressure-equalizing dropping funnel was charged with 6 mL of dichloromethane and 0.83 mL of bromine (16.1 mmol, 1.25 equiv) and was then placed on the 100 mL round-bottom flask. The whole apparatus was placed under a nitrogen atmosphere, and the triphenylphosphine solution was cooled to 0 ℃. The bromine solution was added dropwise over the course of 30 min, and the resulting solution was allowed to stir for an additional 10 min. To the resulting suspension of dibromotriphenylphosphorane, 4.5 mL of triethylamine (32.3 mmol, 2.26 equiv) was added. In a similar fashion, 3.67 g of *N,N′*-di-*n*-octylurea (12.9 mmol) was added in five equivalent portions to the suspension at 0 ℃ over 1 h. One hour after the last addition of the urea, the reaction mixture was stirred at room temperature for overnight. Water was poured to the round-bottom flask in order to extract the triethylammonium hydrobromide, and organic and aqueous phases were separated using a separatory funnel. The organic phases were combined and dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by short column chromatography on silica gel with hexane as the eluent to give the pure product **2c** as a colorless oil. Yield: 2.75g (80%)



(*Z*)-Methyl *N*-octylbenzimidate (1a). 7.71 g, 78%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.24 (m, 3H), 7.24-7.17 (m, 2H), 3.69 (s, 3H), 3.17 (t, *J* = 6.9 Hz, 2H), 1.45 (tt, *J* = 7.4, 6.9 Hz, 2H), 1.25-1.01 (m, 10H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 132.7, 129.3, 128.3, 128.0, 52.9, 50.1, 32.2, 32.0, 29.5, 29.4, 27.4, 22.8, 14.2.; IR (neat, ν/ cm^{-1}) 2926, 2855, 1728, 1674, 1275, 1115, 699; HRMS (ESI$^+$) Calcd for $C_{16}H_{26}NO$ $[M+H]^+$ 248.2014, Found 248.2025.



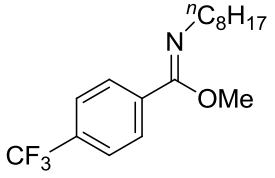
(*Z*)-Methyl *N*-phenylbenzimidate (1b). 6.92 g, 91%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.27 (m, 3H), 7.22 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.17 (dd, *J* = 8.0, 8.0 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.4 Hz, 2H), 3.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 148.6, 131.5, 130.1, 129.5, 129.1, 128.1, 122.8, 121.9, 54.2. The analytical data match those reported in the literature.[3]



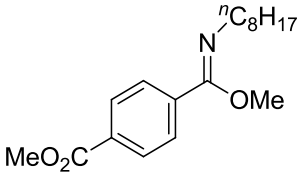
(*Z*)-Methyl 4-methoxy-*N*-octylbenzimidate (1c). 3.24 g, 62%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.29 (t, *J* = 7.1 Hz, 2H), 1.54-1.48 (m, 2H), 1.51-1.21 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 160.4, 129.8, 125.0, 113.7, 55.4, 53.0, 50.3, 32.3, 32.1, 29.6, 29.5, 27.4, 22.9, 14.3.; IR (neat, ν/ cm^{-1}) 2927, 2854, 1670, 1609, 1511, 133, 1273, 1249, 1175, 836; HRMS (ESI$^+$) Calcd for $C_{17}H_{28}NO_2$ $[M+H]^+$ 278.2120, Found 278.2122

(*Z*)-Methyl *N*-octyl-4-(trifluoromethyl)benzimidate (1d). 5.45 g, 80%; Yellow oil;

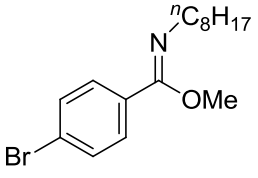
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 3.80 (s, 3H), 3.22 (t, *J* = 7.1 Hz, 2H), 1.57-1.46 (m, 2H), 1.37-1.14 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 136.3, 131.5 (q, $^2J_{CF}$ = 37.4 Hz), 128.6, 125.5 (q, $^3J_{CF}$ = 3.8 Hz), 124.1 (q, $^1J_{CF}$ = 271 Hz), 53.3, 50.2, 32.13, 32.08, 29.6, 29.5, 27.4, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 2928, 2856, 1676, 1620, 1326, 846; HRMS (ESI$^+$) Calcd for $C_{17}H_{25}F_3NO$ $[M+H]^+$ 316.1888, Found 316.1877.



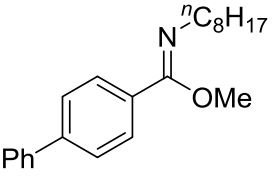
(*Z*)-Methyl 4-(methoxy(octylimino)methyl)benzoate (1e). 3.55 g, 50%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 3.92 (s, 3H), 3.79 (s, 3H), 3.21 (t, *J* = 7.1 Hz, 2H), 1.57-1.42 (m, 2H), 1.42-1.12 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 159.87, 137.047, 131.0, 129.8, 128.2, 53.2, 52.5, 50.1, 32.1, 32.0, 29.6, 29.5, 27.4, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 2927, 2855, 1730, 1672, 1435, 1277, 1117, 1020, 714; HRMS (ESI$^+$) Calcd for $C_{18}H_{28}NO_3$ $[M+H]^+$ 306.2069, Found 306.2057.



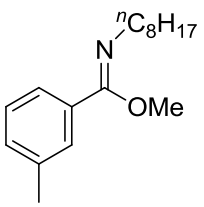
(*Z*)-Methyl 4-bromo-*N*-octylbenzimidate (1f). 4.40 g, 78%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 3.77 (s, 3H), 3.23 (t, *J* = 7.1 Hz, 2H), 1.55-1.47 (m, 2H), 1.30-1.15 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 131.7, 131.5, 129.8, 123.8, 53.2, 50.2, 32.2, 32.1, 29.6, 29.5, 27.4, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 2926, 2854, 1671, 1282, 1282, 1013, 829, 667; HRMS (ESI$^+$) Calcd for $C_{16}H_{25}BrNO$ $[M+H]^+$ 326.1120, Found 326.1128.



(*Z*)-Methyl *N*-octyl-[1,1'-biphenyl]-4-carbimidate (1g). 6.44 g, 66%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.58 (m, 4H), 7.52-7.42 (m, 4H), 7.39 (t, *J* = 7.3 Hz, 1H), 3.85 (s, 3H), 3.36 (t, *J* = 7.1 Hz, 2H), 1.66-1.52 (m, 2H), 1.43-1.18 (m, 10H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 142.3, 140.6, 131.6, 129.1, 128.6, 127.9, 127.4, 127.2, 53.1, 50.3, 32.3, 32.1, 29.6, 29.5, 27.5, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 2926, 2854, 1668, 1277, 1113, 768, 738, 697; HRMS (ESI$^+$) Calcd for $C_{22}H_{30}NO$ $[M+H]^+$ 324.2327, Found 324.2325.

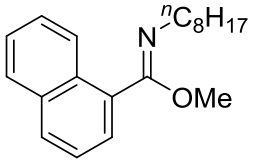


(*Z*)-Methyl 3-methyl-*N*-octylbenzimidate (1h). 4.52 g, 65%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 7.5, 7.3 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.13-7.06 (m, 2H), 3.76 (s, 3H), 3.22 (t, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.57-1.43 (m, 2H), 1.32-1.13 (m, 10H), 0.84 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 138.3, 132.8, 130.2, 128.6, 128.3, 125.1, 53.1, 50.2, 32.2, 32.1, 29.6, 29.5, 27.4, 22.9, 21.6, 14.4; IR (neat, ν/ cm^{-1}) 2926, 2855, 1730, 1671, 1639, 1278,

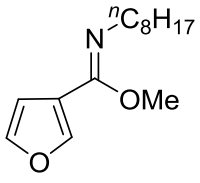


1116, 713; HRMS (ESI$^+$) Calcd for $C_{17}H_{28}NO$ $[M+H]^+$ 262.2171, Found 262.2166.

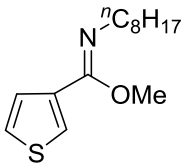
(*Z*)-Methyl *N*-octyl-1-naphthimidate (1i). 5.28 g, 67%; Reddish brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91-7.84 (m, 2H), 7.72-7.68 (m, 1H), 7.50-7.46 (m, 3H), 7.35 (d, *J* = 6.9, 1H), 3.93 (s, 3H), 3.03 (t, *J* = 7.1 Hz, 2H), 1.51-1.46 (m, 2H), 1.30-1.09 (m, 10H), 0.85 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 133.6, 131.8, 130.3, 129.4, 128.6, 127.0, 126.5, 125.6, 125.5, 125.3, 53.3, 50.3, 32.1, 31.9, 29.6, 29.5, 27.4, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 3058, 2927, 2854, 1672, 1458, 1284, 1105, 820, 750; HRMS (ESI$^+$) Calcd for $C_{20}H_{28}NO$ $[M+H]^+$ 298.2171, Found 298.2166.



(*Z*)-Methyl *N*-octylfuran-3-carbimidate (1j). 4.38 g, 67%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 1.1 Hz, 1H), 7.43 (dd, *J* = 2.0, 1.5 Hz, 1H), 6.65-6.58 (m, 1H), 3.73 (s, 3H), 3.40 (t, *J* = 7.1 Hz, 2H), 1.65-1.57 (m, 2H), 1.40-1.25 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.1, 143.9, 142.8, 117.5, 110.4, 52.7, 50.0, 32.3, 32.1, 29.7, 29.6, 27.6, 22.9, 14.4; IR (neat, ν/ cm^{-1}) 2927, 2854, 1671, 1296, 1162; HRMS (ESI$^+$) Calcd for $C_{14}H_{24}NO_2$ $[M+H]^+$ 238.1807, Found 238.1801.

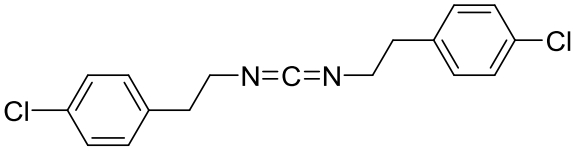


(*Z*)-Methyl *N*-octylthiophene-3-carbimidate (1k). 5.48 g, 60%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 2.9, 1.1 Hz, 1H), 7.24 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.13 (dd, *J* = 5.0, 1.1 Hz, 1H), 3.68 (s, 3H), 3.31 (t, *J* = 7.1 Hz, 2H), 1.50-1.45 (m, 2H), 1.30-1.10 (m, 10H), 0.80 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 132.7, 127.7, 127.0, 125.4, 52.9, 50.2, 32.3, 32.1, 29.7, 29.5, 27.5, 22.9, 14.3; IR (neat, ν/ cm^{-1}) 2926, 2854, 1671, 1264, 1198, 795, 705; HRMS (ESI$^+$) Calcd for $C_{14}H_{24}NOS$ $[M+H]^+$ 254.1579, Found 254.1577.

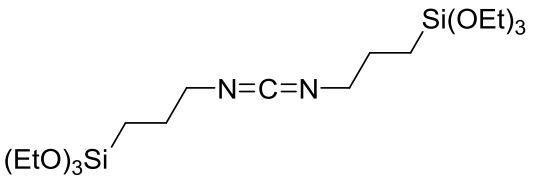


***N,N'*-Methanediylidenebis(1-octanamine) (2c).** 5.03 g, 80%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.16 (t, *J* = 6.8 Hz, 4H), 1.57-1.50 (m, 4H), 1.35-1.23 (m, 20H), 0.86 (t, *J* = 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 47.0, 32.0, 31.5, 29.44, 29.39, 27.1, 22.9, 14.3; HRMS (ESI$^+$) Calcd for $C_{17}H_{35}N_2$ $[M+H]^+$ 267.2800, Found 267.2789

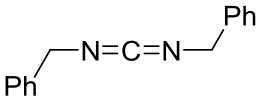
***N,N'*-Methanediylidenebis(2-(4-chlorophenyl)ethanamine) (2d).** 2.24 g, 62%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.2 Hz, 4H), 7.03 (d, *J* = 8.2 Hz, 4H), 3.22 (t, *J* = 7.0 Hz, 4H), 2.64 (t, *J* = 7.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 137.5, 132.5, 130.4, 128.8, 47.7, 36.9; IR (KBr, ν/ cm^{-1}) 3329, 2932, 2126, 1638, 1492, 1342, 1015, 812; HRMS (ESI$^+$) Calcd for $C_{17}H_{16}Cl_2N_2Na$ $[M+Na]^+$ 341.0588, Found 341.0594.



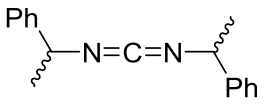
***N,N′*-Methanediylidenebis(3-(triethoxysilyl)propan-1-amine) (2e).** 3.73 g, 80%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84-3.67 (m, 12H), 3.22-3.10 (m, 4H), 1.73-1.55 (m, 4H), 1.24-1.10 (m, 18H), 0.67-0.56 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 58.5, 49.5, 25.1, 18.4, 7.9; IR (neat, ν/ cm^{-1}) 2973, 2927, 2129, 1637, 1369, 1080, 956, 793; HRMS (ESI$^+$) Calcd for $C_{19}H_{42}N_2O_6Si_2Na$ [M+Na]$^+$ 473.2479, Found 473.2501.



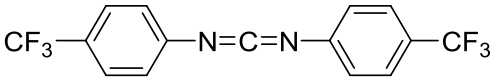
***N,N′*-Methanediylidenebis(1-phenylmethanamine) (2f).** 1.29 g, 44%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.26 (m, 6H), 7.20 (d, *J* = 7.1 Hz, 4H), 4.30 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 138.5 128.7, 127.7, 127.6, 50.5; IR (KBr, ν/ cm^{-1}) 1685, 1654, 1559, 1457, 1026, 696; HRMS (ESI$^+$) Calcd for $C_{15}H_{14}N_2Na$ [M+Na]$^+$ 245.1055, Found 245.1052.



Bis(1-phenylethyl)methanediimine (2g). 2.23g, 38%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (m, 5H), 7.29-7.23 (m, 5H), 4.62-4.52 (m, 2H), 1.50-1.44 (m, 6H);^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 128.7, 127.53, 127.51, 126.2, 56.9, 24.9; IR (neat, ν/ cm^{-1}) 2973, 2124, 1684, 1453, 1072, 759, 699; HRMS (ESI$^+$) Calcd for $C_{17}H_{19}N_2$ [M+H]$^+$ 251.1548, Found 251.1548.

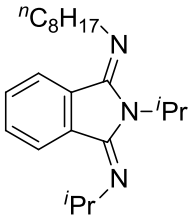


***N,N′*-Methanediylidenebis(4-(trifluoromethyl)aniline) (2i).** 1.47 g, 70%; Reddish brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 4H), 7.27 (d, *J* = 7.8 Hz, 4H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 133.6, 129.3 (q, $^1J_{CF}$ = 273 Hz), 127.1 (q, $^3J_{CF}$ = 4.0 Hz), 124.8 (q, $^2J_{CF}$ = 30.1 Hz), 123.1; IR (KBr, ν/ cm^{-1}) 2163, 1664, 1468, 928, 893, 703, HRMS (ESI$^+$) Calcd for $C_{15}H_9F_6N_3$ [M+H]$^+$ 331.0670, Found 331.0672.

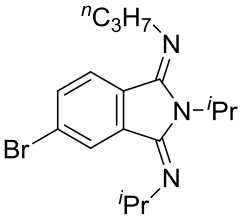


Typical procedure for rhenium-catalyzed synthesis of (*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-1-isoindolinylidene)-1-octanamine 3a by a C-H bond activation and successive dealkoxylative annulation. A mixture of (*Z*)-methyl *N*-octylbenzimidate (**1a**, 61.8 mg, 0.250 mmol), *N*,*N*′-methanediylidenebis(propan-2-amine) (**2a**, 31.5 mg, 0.250 mmol), $Re_2(CO)_{10}$ (4.1 mg, 6.3 mol), and chlorobenzene (1.0 mL) was stirred at 170 ℃ for 24 h in a sealed tube. Then, the solvent was removed in vacuo and the product was isolated by column chromatography on silica gel (*n*-hexane/EtOAc = 10:1) to give (*E*)-*N*-((*E*)-2-isopropyl-3-(isopropylimino)-1-isoindolinylidene)-1-octanamine (**3a**, 84.8 mg, 99% yield).

(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-1-isoindolinylidene)-1-octanamine (3a). 84.8 mg, 99%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.94 (m, 2H),

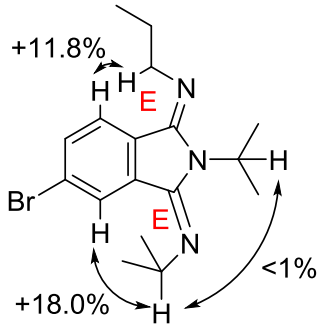


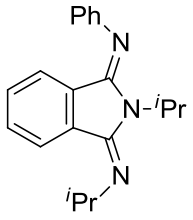
7.50-7.39 (m, 2H), 4.89 (hept, *J* = 5.7 Hz, 1H), 4.54 (hept, *J* = 5.7 Hz, 1H), 3.87 (t, *J* = 6.9 Hz, 2H), 1.78-1.69 (m, 2H), 1.46 (m, 8H), 1.38-1.20 (m, 14H), 0.86 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 149.3, 131.9, 131.4, 130.3, 130.1, 126.2, 126.1, 50.2, 48.6, 43.1, 32.8, 32.1, 29.8, 29.6, 27.8, 25.3, 23.0, 19.6, 14.4; IR (neat, ν/ cm^{-1}) 2963, 2926, 2855, 1637, 1362, 1239, 1096, 767, 674; HRMS (ESI$^+$) Calcd for $C_{22}H_{36}N_3$ [M+H]$^+$ 342.2909, Found 342.2899.



(*E*)-*N*-((*E*)-5-Bromo-2-isopropyl-3-(isopropylimino)isoindolin -1-ylidene) -1-propanamine (3A). 71.8 mg, 82%; Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 4.89 (hept, *J* = 7.5 Hz, 1H), 4.48 (hept, *J* = 7.1 Hz, 1H), 3.81 (t, *J* = 6.7 Hz, 2H), 1.83-1.69 (m, 2H), 1.45 (d, *J* = 7.5 Hz, 6H), 1.30 (d, *J* = 7.1 Hz, 6H), 1.05 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 147.9, 133.0, 130.6, 130.0, 129.2, 127.4, 124.6, 52.0, 48.7, 43.3, 26.0, 25.3, 19.5, 12.3; IR (KBr, ν/ cm^{-1}) 2966, 2929, 1634, 1376, 1313, 806; HRMS (ESI$^+$) Calcd for $C_{17}H_{25}BrN_3$ [M+H]$^+$ 350.1232, Found 350.1241.

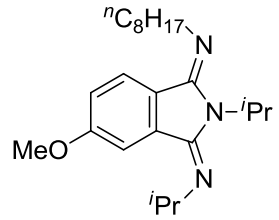
nOe correlation of 3A



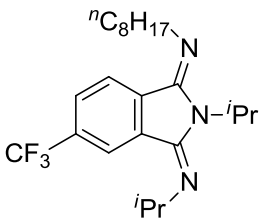


(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-1-isoindolinylidene)an iline (3b). 65.4 mg, 85%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 1H), 7.40 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.36-7.29 (m, 2H), 7.14-7.10 (m, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 7.7 Hz, 1H), 4.99 (hept, *J* = 6.9 Hz, 1H), 4.60 (hept, *J* = 6.1 Hz, 1H), 1.56 (d, *J* = 6.9 Hz, 6H), 1.33 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 148.8, 131.1, 131.0, 130.8, 130.5, 129.6, 129.2, 125.8, 125.6, 122.6, 120.6, 48.7, 43.5, 24.9, 19.4; IR (neat, ν/ cm^{-1}) 3293, 2969, 1855, 1633, 1360, 1028, 774; HRMS (ESI$^+$) Calcd for $C_{20}H_{24}N_3$ [M+H]$^+$ 306.1970, Found 306.1984.

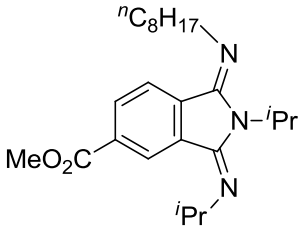
(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-5-methoxy-1-isoindolinylidene)-1-octanamine (3c). 89.3 mg, 99%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 6.98 (dd, *J* = 8.6, 2.4 Hz, 1H), 4.88 (hept, *J* = 7.5 Hz, 1H), 4.52 (hept, *J* = 6.3 Hz, 1H), 3.87 (s, 3H), 3.84 (t, *J* = 7.0 Hz, 2H), 1.81-1.69 (m, 2H), 1.52-1.41 (m, 8H), 1.41-1.22 (m, 14H), 0.91-0.86 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 151.1, 149.1, 133.2, 127.3, 124.9, 114.6, 112.5, 55.9, 50.2, 48.5, 43.1, 32.8, 32.1, 29.8, 29.6, 27.8, 25.1, 22.9, 19.6, 14.4; IR (neat, ν/ cm^{-1}) 2962, 2926, 2855, 1635, 1361, 1290, 1234, 1109; HRMS (ESI^+) Calcd for $C_{23}H_{38}N_3O$ $[M+H]^+$ 372.3015, Found 372.3029.

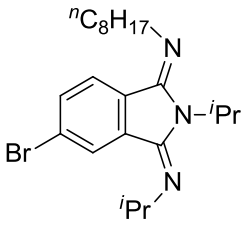


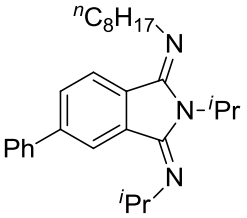
(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-5-(trifluoromethyl)-1-isoindolinylidene)-1-octanamine (3d). 101 mg, 99%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 5.93 (hept, *J* = 7.4 Hz, 1H), 4.55 (hept, *J* = 6.3 Hz, 1H), 3.91 (t, *J* = 6.8 Hz, 2H), 1.82-1.71 (m, 2H), 1.56-1.43 (m, 8H), 1.42-1.18 (m, 14H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 147.8, 134.5, 132.2 (q, $^{2}J_{CF}$ = 33.1 Hz), 131.7, 127.1 (q, $^{3}J_{CF}$ = 3.0 Hz), 126.5, 123.9 (q, $^{1}J_{CF}$ = 272 Hz), 122.9 (q, $^{3}J_{CF}$ = 3.8 Hz), 50.3, 48.8, 43.4, 32.8, 32.1, 29.7, 29.6, 27.8, 25.3, 23.0, 19.5, 14.4; IR (neat, ν/ cm^{-1}) 1965, 2927, 2856, 1638, 1325, 1134, 839, 666; HRMS (ESI^+) Calcd for $C_{23}H_{35}F_3N_3$ $[M+H]^+$ 410.2783, Found 410.2795.

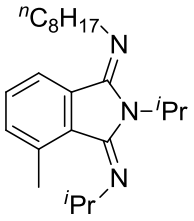


(1*E*,3*E*)-Methyl 2-isopropyl-3-(isopropylimino)-1-(octylimino)isoindoline-5-carboxylate (3e). 97.7 mg, 97%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 4.92 (hept, *J* = 10.1Hz, 1H), 4.62 (hept, *J* = 5.3 Hz, 1H), 3.97 (s, 3H), 3.90 (t, *J* = 6.4 Hz, 2H), 1.82-1.70 (m, 2H), 1.49-1.43 (m, 8H), 1.41-1.21 (m, 14H), 0.88 (t, *J* = 5.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 150.2, 148.2, 135.2, 131.7, 131.5, 131.4, 127.2, 126.0, 52.8, 50.4, 48.7, 43.3, 32.8, 32.1, 29.7, 29.6, 27.8, 25.3, 22.9, 19.6, 14.4; IR (neat, ν/ cm-1) 3398, 2928, 1636, 1259, 1031; HRMS (ESI^+) Calcd for $C_{24}H_{38}N_3O_2$ $[M+H]^+$ 400.2964, Found 400.2956.



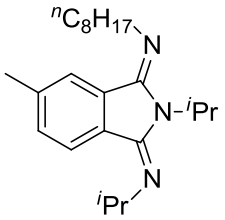
(*E*)-*N*-((*E*)-5-Bromo-2-isopropyl-3-(isopropylimino)-1-isoindolinylidene)-1-octanamine (3f).  101 mg, 96%; reddish brown solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 4.89 (hept, *J* = 6.3 Hz, 1H), 4.85 (hept, *J* = 5.7 Hz, 1H), 3.84 (t, *J* = 6.7 Hz, 2H), 1.80-1.68 (m, 2H), 1.45-1.35 (m, 8H), 1.33-1.26 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.0, 147.7, 132.8, 132.7, 130.2, 129.0, 127.1, 124.4, 49.8, 48.7, 43.2, 32.4, 31.9, 29.5, 29.4, 27.5, 25.0, 22.7, 19.2, 14.1; IR (KBr, ν/ cm^{-1}) 2929, 2832, 1658, 1378, 1030, 717, 700; HRMS (ESI^+) Calcd for $C_{22}H_{35}BrN_3$ $[M+H]^+$ 420.2014, Found 420.2015.

(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-5-phenylisoindolin-1-ylidene)octan-1-amine (3g).  104 mg, 99%; Yellow solid;^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.64-7.58 (m, 2H), 7.50 (m, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 4.92 (hept, *J* = 5.0 Hz, 1H), 4.65 (hept, *J* = 7.5 Hz, 1H), 3.93 (t, *J* = 6.9 Hz, 2H), 1.85-1.70 (m, 2H), 1.57-1.41 (m, 8H), 1.44-1.18 (m, 14H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 149.2, 143.5, 140.6, 132.2, 130.7, 129.3, 129.1, 128.3, 127.6, 126.5, 125.0, 50.3, 48.7, 43.2, 32.8, 32.2, 29.8, 29.7, 27.8, 25.4, 23.0, 19.6, 14.4; IR (neat, ν/ cm^{-1}) 2963, 2926, 1635, 1360; HRMS (ESI^+) Calcd for $C_{28}H_{40}N_3$ $[M+H]^+$ 418.3222, Found 418.3235.

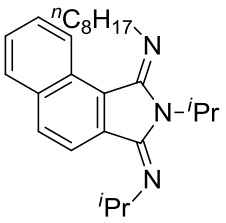
(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-4-methyl-1-isoindolinylidene)-1-octanamine (3h).  25.2 mg, 28%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.30 (dd, *J* = 7.6, 5.3 Hz, 1H), 7.25 (d, *J* = 5.3 Hz, 2H), 4.56 (hept, *J* = 6.3 Hz, 1H), 4.30 (hept, *J* = 6.3 Hz, 1H), 3.95-3.87 (m, 2H), 2.74 (s, 3H), 1.64-1.55 (m, 2H), 1.39-1.15 (m, 22H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6, 146.9, 137.3, 134.9, 133.6, 129.6, 129.1, 122.7, 48.4, 47.4, 42.3, 32.1, 29.5, 29.44, 29.43, 27.1, 26.1, 25.2, 22.9, 20.5, 14.4; IR (neat, ν/ cm^{-1}) 2964, 2925, 1636, 1360; HRMS (ESI+) Calcd for $C_{23}H_{38}N_3$ $[M+H]^+$ 356.3066, Found 356.3076.

(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-5-methylisoindolin-1-ylidene)octan-1-amine (3h'). 65.1 mg, 70%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* =

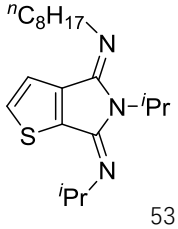
8.0 Hz, 1H), 7.81 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 4.89 (hept, *J* = 7.5 Hz, 1H), 4.53 (hept, *J* = 6.0 Hz, 1H), 3.89 (t, *J* = 6.9 Hz, 2H), 2.46 (s, 3H), 1.83-1.72 (m, 2H), 1.54-1.42 (m, 8H), 1.41-1.18 (m, 14H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 149.5, 140.4, 132.3, 131.0, 128.9, 126.9, 125.9, 50.2, 48.6, 43.1, 32.8, 32.1, 29.9, 29.7, 27.8, 25.3, 23.0, 22.1, 19.6, 14.4; IR (neat, ν/ cm^{-1}) 2964, 2925, 2856, 1635, 1362; HRMS (ESI^+) Calcd for $C_{23}H_{38}N_3$ $[M+H]^+$ 356.3066, Found 356.3053.



(*E*)-*N*-((*E*)-2-Isopropyl-3-(isopropylimino)-2,3-dihydro-1H-benzo[e]isoindol-1-ylidene)octan-1-amine (3i). 91.8 mg, 94%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.89-7.79 (m, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* =7.5 Hz, 1H), 4.78-4.62 (m, 2H), 3.88 (t, *J* = 6.7 Hz, 2H), 1.89-1.75 (m, 2H), 1.60 (t, *J* = 8.3 Hz, 5H), 1.57-1.45 (m, 3H), 1.44-1.21 (m, 14H), 0.89 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 152.3, 151.8, 134.8, 133.0, 131.1, 129.1, 128.4, 128.1, 128.0, 127.3, 127.2, 121.7, 50.6, 48.9, 48.3, 33.5, 32.1, 29.8, 29.6, 27.8, 25.4, 23.0, 21.0, 14.4.; IR (neat, ν/ cm^{-1}) 2962, 2925, 2855, 1638, 1360, 1238; HRMS (ESI^+) Calcd for $C_{26}H_{38}N_3$ $[M+H]^+$ 392.3066, Found 392.3042.

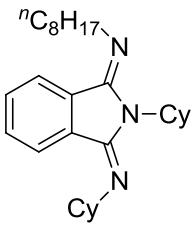


(*E*)-*N*-((*E*)-5-Isopropyl-6-(isopropylimino)-5,6-dihydro-4*H*-furo[2,3-c]pyrrol-4-ylidene)octan-1-amine (3j). 52.3 mg, 63%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* =1.3 Hz, 1H), 6.62 (d, *J* = 1.3 Hz, 1H), 4.70 (hept, *J* = 6.9 Hz, 1H), 4.31 (hept, *J* = 6.3 Hz, 1H), 3.62 (t, *J* = 7.1 Hz, 2H), 1.74-1.52 (m, 2H), 1.44 (d, *J* = 6.9 Hz, 6H), 1.42-1.24 (m, 10H), 1.23 (d, *J* = 6.2 Hz, 6H), 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 149.0, 148.4, 143.5, 122.4, 108.1, 52.1, 51.9, 44.0, 32.14, 32.10, 29.8, 29.6, 27.7, 25.4, 22.9, 20.1, 14.4; IR (neat, ν/ cm^{-1}) 2963, 2927, 1651, 1378, 1070; HRMS (ESI^+) Calcd for $C_{20}H_{34}N_3O$ $[M+H]^+$ 332.2702, Found 332.2697.

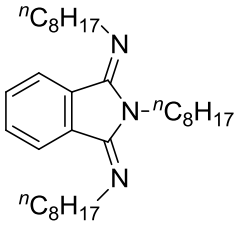


(*E*)-*N*-((*E*)-5-Isopropyl-6-(isopropylimino)-5,6-dihydro-4*H*-thieno[2,3-*c*]-4-pyrrolylidene)-1-octanamine (3k). 59.0 mg, 68%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 4.9 Hz, 1H), 7.35 (d, *J*

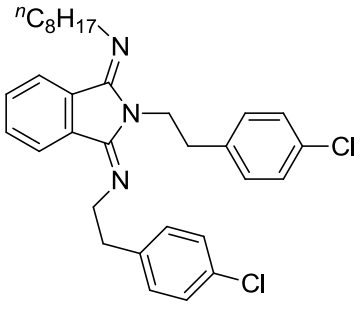
= 4.9 Hz, 1H), 4.79 (hept, *J* = 6.9 Hz, 1H), 3.91 (hept, *J* = 6.3 Hz, 1H), 3.73 (t, *J* = 7.1 Hz, 2H), 1.73-1.64 (m, 2H), 1.49-1.38 (m, 8H), 1.32-1.24 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 147.8, 138.9, 134.4, 132.9, 122.6, 53.2, 51.1, 43.9, 32.3, 32.1, 29.8, 29.6, 27.8, 25.0, 22.9, 20.0, 14.4.; IR (neat, ν/ cm^{-1}) 2964, 2926, 1637, 1378, 698; HRMS (ESI^+) Calcd for $C_{20}H_{34}N_3S$ $[M+H]^+$ 348.2473, Found 348.2479.



(*E*)-*N*-((*E*)-2-Cyclohexyl-3-(octylimino)isoindolin-1-ylidene)cyclohexanamine (3l). 95.0 mg, 90%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 5.8, 2.7 Hz, 1H), 7.89 (dd, *J* = 5.8, 2.5 Hz, 1H), 7.50-7.45 (m, 2H), 4.60-4.45 (m, 1H), 4.27-4.15 (m, 1H), 3.89 (t, *J* = 6.9 Hz, 2H), 2.71-2.59 (m, 2H), 2.05-1.70 (m, 8H), 1.69-1.09 (m, 22H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 149.2, 131.8, 131.3, 130.3, 130.0, 126.2, 126.0, 56.2, 51.5, 50.1, 35.2, 32.7, 32.1, 29.7, 29.7, 28.8, 27.7, 26.9, 26.3, 26.2, 24.7, 23.0, 14.4; IR (KBr, ν/ cm^{-1}) 3361, 2920, 2849, 1651, 1469, 1371, 1101, 771, 698, 673; HRMS (ESI^+) Calcd for $C_{28}H_{44}N_3$ $[M+H]^+$ 422.3535, Found 422.3518.

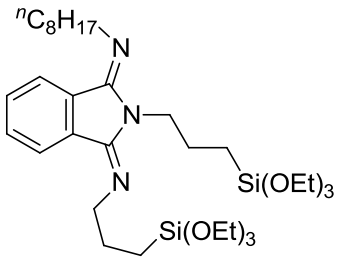


(*N*,*N*'*E*,*N*,*N*'*E*)-*N*,*N*'-(2-Octylisoindoline-1,3-diylidene)bis(1-octanamine) (3m). 114 mg, 94%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 5.7, 3.1 Hz, 2H), 7.53-7.50 (m, 2H), 3.91 (t, *J* = 7.0 Hz, 4H), 3.80 (t, *J* = 7.0 Hz, 2H), 1.93-1.73 (m, 4H), 1.53-1.43 (m, 4H), 1.35-1.27 (m, 28H), 0.93-0.84 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 131.8, 130.3, 126.2, 50.0, 39.0, 32.6, 32.2, 32.1, 29.8, 29.7, 29.66 (2C), 29.57, 27.9, 27.8, 27.3, 23.0 (2C), 14.4; IR (KBr, ν/ cm^{-1}) 2921, 1635, 1397, 1100, 676; HRMS (ESI^+) Calcd for $C_3H_{25}N_3$ $[M+H]^+$ 482.4474, Found 482.4491.

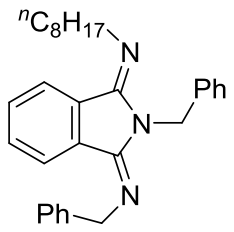


(*E*)-*N*-((*E*)-2-(4-Chlorophenethyl)-3-((4-chlorophenethyl)imino)isoindolin-1-ylidene)octan-1-amine (3n). 110 mg, 83%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.1 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 1H), 7.56-7.47 (m, 2H), 7.33-7.24 (m, 4H), 7.24-7.18 (m, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 4.12 (t, *J* = 7.0 Hz, 2H), 4.01 (t, *J* = 6.9 Hz, 2H), 3.88 (t,

J = 6.8 Hz, 2H), 3.03 (t, *J* = 7.0 Hz, 2H), 2.94 (t, *J* = 6.9 Hz, 2H), 1.81-1.68 (m, 2H), 1.55-1.45 (m, 2H), 1.43-1.23 (m, 8H), 0.89 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 150.8, 139.6, 138.9, 132.0, 131.8, 131.60, 131.56 (2C), 130.7, 130.6, 130.5, 128.6, 128.4, 126.3, 126.1, 51.4, 50.0, 40.3, 38.6, 33.4, 32.6, 32.2, 29.8, 29.7, 27.8, 23.0, 14.4; IR (KBr, ν/ cm^{-1}) 2923, 2850, 1644, 1490, 1428, 1396, 1338, 1093, 1014, 820, 667; HRMS (ESI^+) Calcd for $C_{32}H_{38}Cl_2N_3$ $[M+H]^+$ 534.2443, Found 534.2446.



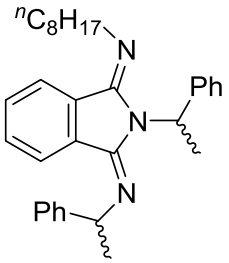
(*E*)-*N*-((*E*)-2-(3-(Triethoxysilyl)propyl)-3-((3-(triethoxysilyl)propyl)imino)isoindolin-1-ylidene)octan-1-amine (3o). 139 mg, 83%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05-7.96 (m, 2H), 7.54-7.47 (m, 2H), 3.95-3.73 (m, 16H), 1.92-1.80 (m, 2H), 1.79-1.67 (m, 6H), 1.50-1.41 (m, 2H), 1.38-1.26 (m, 10H), 1.26-1.15 (m, 16H), 0.91-0.78 (m, 5H), 0.66 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 151.3, 131.8, 131.7, 130.40, 130.37, 126.3, 126.2, 58.6, 58.5, 52.7, 50.7, 50.1, 41.7, 32.7, 32.2, 29.8, 29.6, 27.8, 25.9, 25.8, 22.9, 21.1, 18.6, 18.5, 14.4; ^{29}Si NMR (78 MHz, $CDCl_3$) δ -44.3, -44.4; IR (KBr, ν/ cm^{-1}) 2128, 1647, 1079, 956, 792; HRMS (ESI^+) Calcd for $C_{34}H_{64}N_3O_6Si_2$ $[M+H]^+$ 666.4334, Found 666.4330.



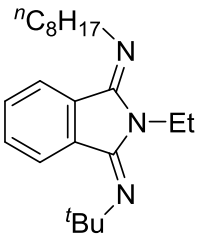
(*E*)-*N*-((*E*)-2-Benzyl-3-(benzylimino)isoindolin-1-ylidene)octan-1-amine (3p). 69.0 mg, 63%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 6.9 Hz, 2H), 7.58-7.51 (m, 2H), 7.49 (d, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 7.3 Hz, 2H), 7.36-7.31 (m, 2H), 7.30-7.22 (m, 3H), 7.23-7.16 (m, 1H), 5.21 (s, 2H), 5.15 (s, 2H), 3.95 (t, *J* = 6.9 Hz, 2H), 1.84-1.74 (m, 2H), 1.53-1.43 (m, 2H), 1.41-1.21 (m, 8H), 0.90 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 151.0, 141.8, 139.7, 131.7 (2C), 130.8, 130.7, 128.9, 128.5, 128.2, 127.4, 126.7, 126.6, 126.4, 125.3, 53.3, 50.0, 42.6, 32.6, 32.2, 29.8, 29.7, 27.7, 23.0, 14.4; IR (KBr, ν/ cm^{-1}) 2923, 1646, 1396, 1100, 720, 694; HRMS (ESI^+) Calcd for $C_{30}H_{36}N_3$ $[M+H]^+$ 438.2909, Found 438.2927.

(*E*)-*N*-((*E*)-2-(1-Phenylethyl)-3-(1-phenylethyl)imino)isoindolin-1-ylidene)octan-1-amine (dr = 2:1) (3q). 79.4 mg, 68%; Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08-7.96 (m, 1H), 7.93 (dd, *J* = 10.3, 9.0 Hz, 1H), 7.59-7.30 (m, 6H), 7.30-6.99 (m,

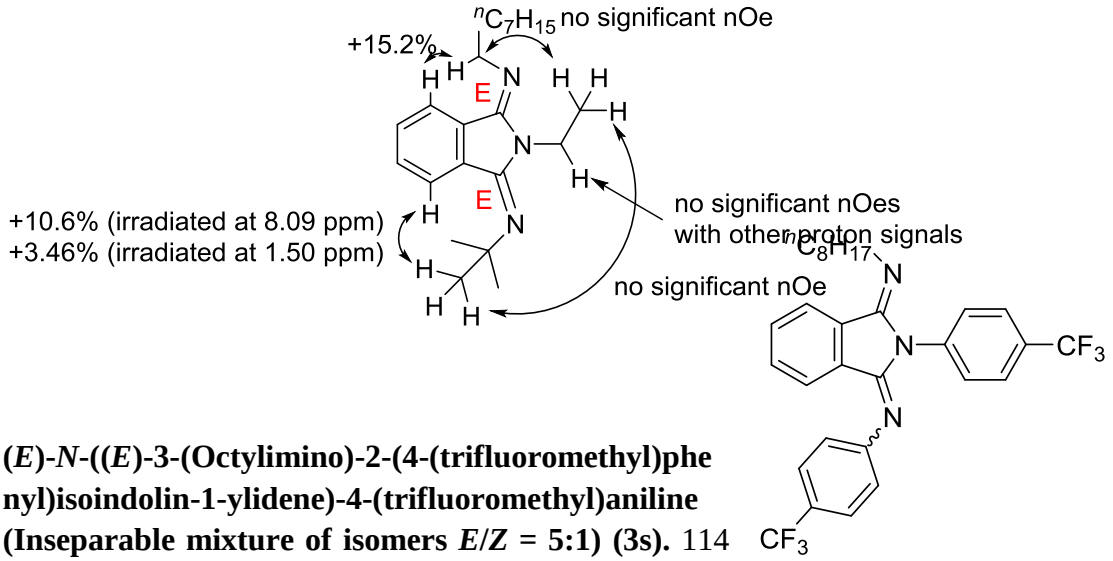
6H), 6.21 (q, *J* = 6.5 Hz, 1H), 5.49 (q, *J* = 6.4 Hz, 1H), 4.05 (q, *J* = 6.4 Hz, 2H), 1.96 (dd, *J* = 7.1, 1.9 Hz, 2H), 1.74 (td, *J* = 14.0, 7.0 Hz, 2H), 1.57 (d, *J* = 6.5 Hz, 2H), 1.51-1.40 (m, 3H), 1.40-1.23 (m, 8H), 0.95-0.81 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 150.7, 150.4, 149.7, 149.5, 147.7, 147.4, 143.41, 143.35, 131.7, 131.6, 131.2, 130.5 (2C), 130.43, 130.41, 128.5, 128.3, 128.0, 127.9, 127.8, 127.6, 126.6, 126.51, 126.45, 126.34, 126.30, 126.26 (2C), 126.13, 126.12, 126.0, 57.3, 57.0, 56.9, 50.0, 48.6, 48.3, 32.7 32.2, 29.8, 29.7, 27.7, 27.3, 27.2, 23.0, 16.9, 16.5, 14.4; IR (neat, ν/ cm^{-1}) 2925, 2124, 1637, 1368, 1102, 698; HRMS (ESI$^+$) Calcd for $C_{32}H_{40}N_3$ [M+H]$^+$ 466.3222, Found 466.3203.



(*E*)-*N*-((*E*)-3-(tert-Butylimino)-2-ethylisoindolin-1-ylidene)octan-1-amine (3r). 41.7 mg, 53%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.55-7.45 (m, 2H), 3.92 (t, *J* = 7.1 Hz, 2H), 3.86 (q, *J* = 8.6 Hz, 2H), 1.91-1.71 (m, 2H), 1.57-1.42 (m, 2H), 1.51 (s, 9H), 1.43-1.19 (m, 8H), 1.11 (t, *J* = 8.6 Hz, 3H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 147.1, 133.1, 130.9, 130.0, 129.6, 127.8, 126.1, 52.8, 50.1, 34.0, 32.7, 32.1, 31.7, 29.8, 29.6, 27.8, 23.0, 14.4, 13.0; IR (KBr, ν/ cm^{-1}) 2965, 2927, 2855, 1725, 1633, 1398, 1201, 1097, 678; HRMS (ESI$^+$) Calcd for $C_{22}H_{36}N_3$ [M+H]$^+$ 342.2909, Found 342.2906.



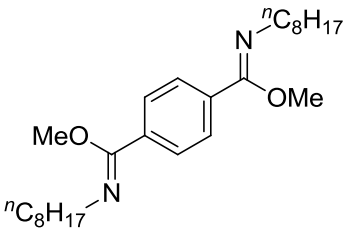
nOe correlation of 3r



(*E*)-*N*-((*E*)-3-(Octylimino)-2-(4-(trifluoromethyl)phenyl)isoindolin-1-ylidene)-4-(trifluoromethyl)aniline (Inseparable mixture of isomers *E*/*Z* = 5:1) (3s). 114 mg, 83%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.7 Hz, 0.8H), 7.97 (d, *J* = 7.7 Hz, 0.2H), 7.76-7.54 (m, 6H), 7.35-7.32 (m, 1H), 7.06-6.60 (m, 4H), 3.96 (t, *J* = 6.7 Hz, 1.7H), 2.99 (t, *J* = 6.7 Hz, 0.3H),

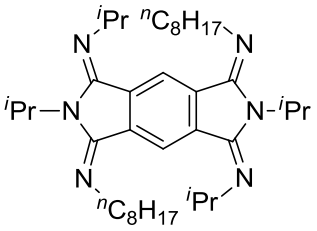
1.76-1.70 (m, 2H), 1.51-1.39 (m, 2H), 1.37-1.10 (m, 8H), 0.93-0.81 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 151.5, 151.0, 138.9, 132.3, 132.2, 131.2, 130.9, 130.6, 130.2, 130.0, 129.9, 129.3, 129.0, 126.8, 126.6, 126.3, 125.8, 125.5, 125.2, 123.6, 122.9, 120.8, 100.1, 50.3, 45.0, 32.1, 32.0, 31.9, 31.8, 30.0, 29.9, 29.6, 29.5, 29.5, 29.5, 27.7, 27.5, 22.9, 14.4 [The coupling patterns derived from ^{19}F atoms could not be analyzed because of the complexity of the signals.]; ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.91, -61.97, -62.76, -62.80; IR (KBr, ν/ cm^{-1}) 2927, 1651, 1322, 1120, 1066; HRMS (ESI$^+$) Calcd for $C_{30}H_{30}F_6N_3$ $[M+H]^+$ 546.2344, Found 546.2317.

(1*Z*,4*Z*)-Dimethyl *N*′1,*N*′4-dioctylterephthalimidate (4)



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 4H), 3.80 (s, 6H), 3.24 (t, *J* = 7.1 Hz, 4H), 0.99-0.77 (m, 4H), 1.24 (s, 20H), 0.86 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 133.6, 128.1, 53.1, 50.2, 32.2, 32.1, 31.8, 29.6, 27.4, 22.9, 14.3; IR (KBr, ν/ cm^{-1}) 3075, 2916, 1509, 1468, 1378, 1299, 1036; HRMS (ESI$^+$) Calcd for $C_{26}H_{45}N_2O_2$ $[M+H]^+$ 416.3403, Found 416.3406.

(*N*,*N*′*E*,*N*,*N*′*E*)-*N*,*N*′-((3*E*,7*E*)-2,6-Diisopropyl-3,7-bis(isopropylimino)-2,3,6,7-tetrahydropyrrolo[3,4-*f*]isoindole-1,5-diylidene)bis(octan-1-amine) (5).



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 2H), 4.90 (hept, *J* = 6.7 Hz, 2H), 4.51 (hept, *J* = 5.6 Hz, 2H), 3.92 (t, *J* = 3.9 Hz, 4H), 1.84-1.69 (m, 4H), 1.48 (d, *J* = 6.7 Hz, 12H), 1.37 (d, *J* = 5.6 Hz, 12H), 1.52-1.43 (m, 4H), 1.39-1.24 (m, 16H), 0.89 (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 148.3, 132.9, 132.2, 123.4, 50.3, 49.0, 43.5, 32.7, 32.2, 29.8, 29.7, 27.9, 25.3, 22.9, 19.5, 14.4; IR (KBr, ν/ cm^{-1}) 2972, 2915, 1685, 1370, 1215, 1078; HRMS (ESI$^+$) Calcd for $C_{38}H_{65}N_6$ $[M+H]^+$ 605.5271, Found 605.5247.

References

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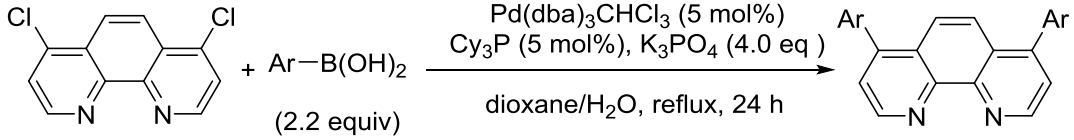
[3] Sueki, S.; Guo, Y.; Kanai, M.; Kuninobu, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 11879.

Iron-Catalyzed Acyloxyalkylation of Styrenes Using Hypervalent Iodine (III) Reagents

General. All reactions were carried out in a dry solvent under an argon atmosphere. CH_3CN was purchased from Kanto Co. and was dried and degassed before use. $Fe(CO)_3(cot)$ was purchased from Tokyo Kasei Kogyo Co. Styrenes (**1d-1g**, **1i-1m**, and **1o-1r**), iodobenzene carboxylates (**2b** and **2d-2k**), and ligands (**L6-L8**) were prepared according to the literature methods.[[1]] Ligands (**L4** and **L5**) were prepared according to general procedure. Iodobenzene carboxylates (**2a** and **2c**) and ligands **(L1-L3** and **L9-L12)** were purchased from Wako Co. and Sigma Aldrich Co. NMR spectra were recorded on JEOL ECX500 (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) and JEOL ECS400 (400 MHz for ^1H NMR, 100 MHz for ^{13}C NMR, 376 MHz for ^{19}F NMR) spectrometers. Proton chemical shifts are reported relative to Me_4Si ($CDCl_3$) at δ 0.00 ppm or residual solvent peak ($CDCl_3$ at δ 7.26 ppm). Carbon chemical shifts are reported relative to $CDCl_3$ at 77.26 ppm. Fluorine chemical shifts are reported relative to TFA ($CDCl_3$) at -76.55 ppm as an external standard. Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. ESI-mass spectra were measured on a JEOL JMS-T100LC AccuTOF spectrometer for HRMS.

General Procedure for Preparation of Ligand (L4 and L5).

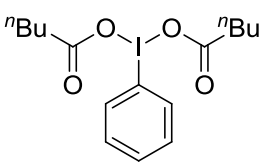


To a Schlenk tube equipped with a stir bar was added 4,7-dichloro-1,10-phenanthroline (49.8 mg, 0.200 mmol), arylboronic acid (0.440 mmol, 2.2 equiv), $Pd(dba)_3 \cdot CHCl_3$ (10.4 mg, 0.0100 mmol, 5.0 mol%), tricyclohexylphosphine (2.8 mg, 0.010 mmol, 5.0 mol%), K_3PO_4 (170 mg, 4.0 equiv in water (1.0 mL)), and dioxane (1.0 mL). After the reaction mixture was allowed to stir at reflux for 24 h, the mixture was purified by column chromatography on silica gel to give a ligand in 70%-75% yield.

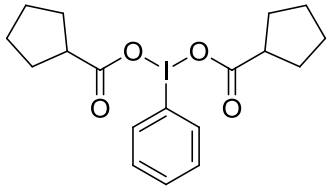
General Procedure for Preparation of Styrenes.[1] To a 100 mL two-necked, round-bottomed flask charged a solution of Ph_3MePBr (4.29 g, 12.0 mmol, 1.20 equiv) in THF (40.0 mL) was added ^{n}BuLi (2.69 M, 4.46 mL, 12.0 mmol, 1.20 equiv) at 0 ℃, and the mixture was stirred at 0 ℃ for 15 min. A solution of a ketone (10 mmol, 1.0 equiv) was added at 0 ℃. The reaction mixture was stirred at r.t. for 48 h. The resulting solution was quenched with aq. NH_4Cl and the mixture was extracted with ethyl acetate (3 x 40 mL). The combined organic phases were dried over $MgSO_4$,

concentrated in vacuo, and the residue was purified by column chromatography on silica gel to give styrene.

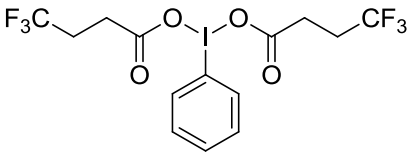
General Procedure for Preparation of Iodobenzene Pentanoate 2b.[2] To a 100 mL round-bottom flask, $PhI(OAc)_2$ (**2a**, 3.22 g, 10.0 mmol, 1.0 equiv) and pentanoic acid (1.63 g, 22.0 mmol, 2.2 equiv), and xylenes (50 mL) were added and the flask was operated on rotary evaporator at 65 ℃ under reduced pressure (ca. 30-50 Torr or 4-6 kPa). After xylenes was removed, the crude product was purified by recrystallization from hexane/dichloromethane to give product **2b** as a white solid (3.05 g, 75%).



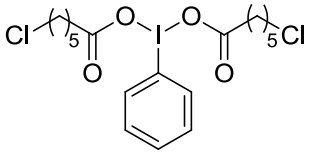
Iodobenzene divalerate (2b). 3.05 g, 75%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.8 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (dd, *J* = 7.8, 7.8 Hz, 2H), 2.35-2.12 (m, 4H), 1.52 (tt, *J* = 7.6, 7.6 Hz, 4H), 1.26 (qt, *J* = 7.3, 7.3 Hz, 4H), 0.85 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.2, 135.1, 131.8, 131.1, 122.0, 34.0, 27.9, 22.5, 13.9; IR (neat, ν/ cm^{-1}) 3410, 2926, 1539, 1412, 1105, 994, 727; HRMS (ESI^+) Calcd for $C_{16}H_{23}IO_4$ $[M + Na]^+$ 429.0533 Found 429.0530.



Iodobenzene dicyclopentanecarboxylate (2c). 2.58 g, 60%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.9 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (dd, *J* = 7.9, 7.9 Hz, 2H), 2.66 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.87-1.36 (m, 16H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.0, 134.9, 131.7, 131.0, 122.2, 43.9, 30.8, 26.0; IR (neat, ν/ cm^{-1}) 2927, 1650, 1508, 1110, 980, 830, 750; HRMS (ESI^+) Calcd for $C_{18}H_{23}IO_4$ $[M + Na]^+$ 453.0533, Found 453.0517.

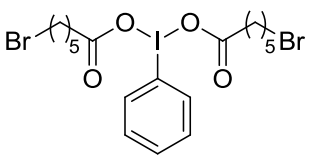


Iodobenzene di(4,4,4-trifluorobutanoate) (2e). 2.53 g, 52%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.67-7.59 (m, 1H), 7.57-7.46 (m, 2H), 2.54-7.47 (m, 4H), 2.46-2.29 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 135.1, 132.4 131.4, 126.7 (q, *J* = 274 Hz), 122.0, 30.2 (q, *J* = 28.8 Hz), 26.8 (q, *J* = 6.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.8 (d, *J* = 11.7 Hz); IR (neat, ν/ cm^{-1}) 2980, 2855, 1730, 1672, 1435, 1238, 1117, 1020, 784; HRMS (ESI^+) Calcd for $C_{14}H_{13}F_6IO_4$ $[M + Na]^+$ 508.9655, Found 508.9560.

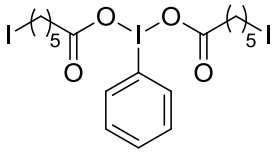


Iodobenzene di(6-bromohexanoate) (2f). 754.8 mg, 15%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (dd, *J* = 7.4, 7.4 Hz, 2H), 3.47 (t, *J* = 6.6 Hz, 4H), 2.25 (t, *J* = 7.3 Hz, 4H), 1.71 (tt, *J* = 7.2, 6.6 Hz, 4H), 1.55 (tt, *J* = 7.2, 7.7Hz, 4H), 1.37 (tt, *J* = 7.7, 7.3 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 135.0, 131.9, 131.1, 121.9, 45.0, 33.9,

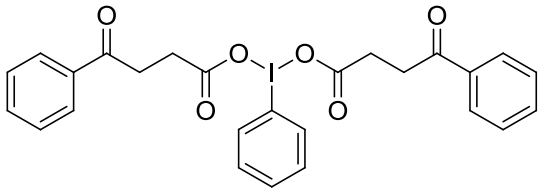
32.3, 26.6, 25.0; IR (neat, ν/ cm^{-1}) 3515, 3081, 2957, 1729, 1629, 1148, 1127, 1072, 763; HRMS (ESI^+) Calcd for $C_{18}H_{25}Cl_2IO_4$ $[M + Na]^+$ 525.0067, Found 525.0052.



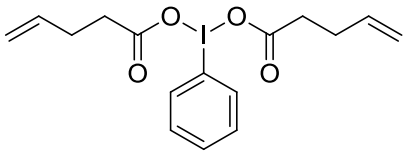
Iodobenzene di(6-chlorohexanoate) (2g). 592.3 mg, 10%; Colorless soil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.49 (t, *J* = , 7.9 Hz, 2H), 3.35 (t, *J* = 6.8 Hz, 4H), 2.26 (t, *J* = 7.4 Hz, 4H), 1.82-1.64 (m,, 4H), 1.64-1.47 (m, 4H), 1.1.46-1.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.7, 135.2, 132.0, 131.2, 122.0, 34.0, 33.8, 32.6, 27.9, 25.0; IR (neat, ν/ cm^{-1}) 2936, 2861, 1698, 1570, 1260, 1014, 733; MS (ESI^+) Calcd for $C_{18}H_{25}Br_2IO_4$ $[M + Na]^+$ 612.9057, Found 612.9057.



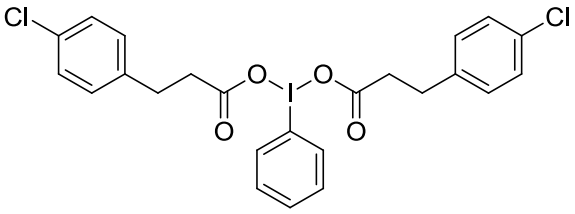
Iodobenzene di(6-iodohexanoate) (2h). 2.31 g, 60%; Colorless soil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.4 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 3.14 (t, *J* = 6.9 Hz, 4H), 2.27 (t, *J* = 7.4 Hz, 4H), 1.84-1.68 (m, 4H), 1.61-1.51 (m, 4H), 1.42-1.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.7, 135.2, 132.0, 131.2, 33.9, 33.3, 30.3, 24.8, 7.0; IR (neat, ν/ cm^{-1}) 3729, 1637, 1236, 992, 748, 632; HRMS (ESI^+) Calcd for $C_{18}H_{25}I_3O_4$ $[M + Na]^+$ 708.8779, Found 708.8790.

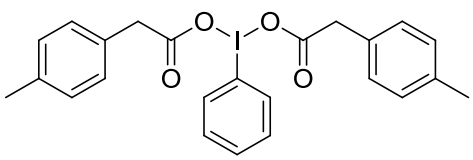


Iodobenzene di(4-oxo-4-phenylbutanoate) (2i). 3.28 g, 59%; Colorless soil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06-7.90 (m, 5H), 7.64-7.37 (m, 10H), 3.33 (t, *J* = 6.6 Hz, 2H), 3.23 (t, *J* = 6.6 Hz, 2H), 2.82 (t, *J* = 6.6 Hz, 2H), 2.71 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.6, 177.8, 136.9, 135.0, 133.3, 131.8, 131.1, 128.8, 128.3, 121.8, 34.3, 28.1; IR (neat, ν/ cm^{-1}) 3354, 3058, 2927, 1684, 1333, 1190, 994, 747; HRMS (ESI^+) Calcd for $C_{26}H_{23}IO_6$ $[M + H]^+$ 559.0612, Found 559.0584.

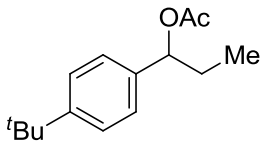


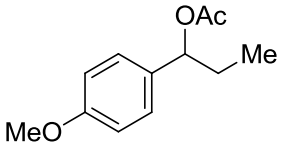
Iodobenzene di(pent-4-enoate) (2j). 421.0 mg, 10%; Colorless soil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.76 (td, *J* = 16.8, 6.3 Hz, 2H), 5.05-4.88 (m, 4H), 2.36 (dd, *J* = 10.7, 4.3 Hz, 4H), 2.33-2.22 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 137.2, 135.1, 131.9, 131.1, 122.0, 115.5, 33.4, 29.8; IR (neat, ν/ cm^{-1}) 2970, 2958, 1635, 1420, 1390, 1230, 1138, 782; HRMS (ESI^+) Calcd for $C_{16}H_{19}IO_4$ $[M + Na]^+$ 425.0220, Found 425.0218.

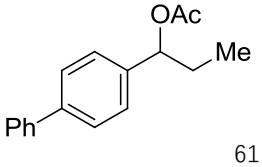
Iodobenzene di(3-(4-chlorophenyl)propanoate) (2k).  3.54 g, 62%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.1 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.45 (dd, *J* = 8.1, 7.0 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 4H), 7.05 (d, *J* = 8.2 Hz, 4H), 2.83 (t, *J* = 7.5 Hz, 4H), 2.55 (t, *J* = 7.5 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 139.4, 135.0, 132.1, 132.0, 131.1, 129.9, 128.7, 121.8, 35.5, 31.2; IR (neat, ν/ cm^{-1}) 2934, 1648, 1490, 1473, 1370, 1190, 1088, 740; HRMS (ESI$^+$) Calcd for $C_{24}H_{21}Cl_2IO_4$ [M + Na]$^+$ 592.9754, Found 592.9758.

Iodobenzene di(2-(*p*-tolyl)acetate) (2l).  3.68 g, 73%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.43 (dd, *J* = 8.2, 7.4 Hz, 2H), 7.20-7.30 (m, 8H), 3.54 (s, 4H), 2.32 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 136.6, 134.8, 131.9, 131.8, 131.0, 129.3, 129.2, 122.2, 40.8, 21.3; IR (neat, ν/ cm^{-1}) 2990, 2873, 1447, 1730, 1583, 1057, 960, 796; HRMS (ESI$^+$) Calcd for $C_{24}H_{23}IO_4$ [M + Na]$^+$ 525.0533, Found 525.0538.

Typical Procedure for Oxyalkylation of Styrene 1a. A mixture of 1-(*tert*-butyl)-4-vinylbenzene (**1a**, 40.1 mg, 0.250 mmol), Iodobenzene diacetate (**2a**, 104.7 mg, 0.325 mmol, 1.3 equiv), $Fe(CO)_3$(cot) (6.1 mg, 0.025 mmol, 10 mol%), **L4** (bathocuproine, 9.0 mg, 0.025 mmol, 10 mol%), and CH_3CN (1.0 mL) was stirred at 70 ℃ for 12 h in a sealed tube. Then, the solvent was removed in vacuo and the product was isolated by column chromatography on silica gel (*n*-hexane/EtOAc = 20:1) to give 1-(4-(*tert*-butyl)phenyl)propyl acetate (**3aa**, 31.0 mg, 53% yield).

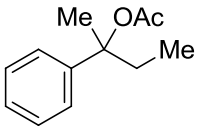
1-(4-(*tert*-Butyl)phenyl)propyl acetate (3aa).[4]  31.0 mg, 53%; Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 5.58 (t, *J* = 6.7 Hz, 1H), 1.99 (s, 3H), 1.90-1.68 (m, 2H), 1.23 (s, 9H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 151.0, 137.7, 126.5, 125.5, 77.5, 34.8, 31.6, 29.4, 21.6, 10.3.

1-(4-Methoxyphenyl)propyl acetate (3ba).[4]  40.0 mg, 71%; Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.61 (t, *J* = 7.0 Hz, 1H), 3.80 (s, 3H), 2.05 (s, 3H), 1.96-1.74 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 159.4, 132.8, 128.3, 114.0 ,77.4, 55.5, 29.3, 21.6, 10.2.

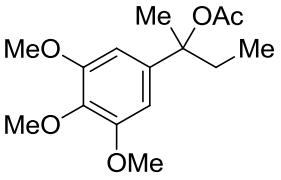
1-([1,1'-Biphenyl]-4-yl)propyl acetate (3ca).[4]  29.2 mg, 46%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.56 (m, 4H),

7.48-7.38 (m, 4H), 7.38-7.32 (m, 1H), 5.72 (t, *J* = 6.9 Hz, 1H), 2.09 (s, 3H), 2.2-1.81 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 141.0, 139.8, 129.0, 127.5, 127.4, 127.3, 127.3, 77.4, 29.5, 21.5, 10.2.

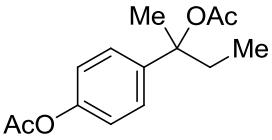
2-Phenylbutan-2-yl acetate (3da).[5] 22.1 mg, 46%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.28 (m, 4H), 7.25-7.20 (m, 1H), 2.07 (s, 3H), 1.85-1.75 (m, 2H), 1.82 (s, 3H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 145.1, 128.4, 127.0, 124.9, 84.6, 35.4, 24.6, 22.5, 8.4.



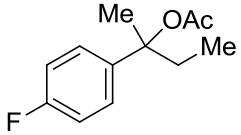
2-(3,4,5-Timethoxyphenyl)butan-2-yl acetate (3ea). 44.4 mg, 63%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.50 (s, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 2.07 (s, 3H), 2.04-1.94 (m, 2H), 1.79 (s, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 153.1, 141.1, 137.0, 102.4, 84.6, 61.0 56.3, 35.4, 24.5 22.5 8.5; IR (neat, ν/ cm^{-1}) 2974, 1736, 1589, 1413, 1244, 1126, 1012829, 772; HRMS (ESI$^+$) Calcd for $C_{15}H_{22}O_5$ $[M + Na]^+$ 305.1359, Found 305.1347.



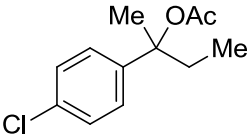
4-(2-Aetoxybutan-2-yl)phenyl acetate (3fa). 33.9 mg, 54%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 8.6 Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H), 2.10-1.95 (m, 2H), 1.80 (s, 3H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 169.6, 149.6, 142.6, 126.0, 121.3, 84.2, 35.2, 24.7, 22.4, 21.4, 8.3; IR (neat, ν/ cm^{-1}) 2980, 1375, 1508, 1369, 1202, 1016, 912; HRMS (ESI$^+$) Calcd for $C_{14}H_{18}O_4$ $[M + Na]^+$ 273.1097, Found 273.1103.



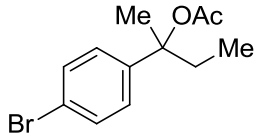
2-(4-Fluorophenyl)butan-2-yl acetate (3ga). 26.8 mg, 51%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.7 Hz, 2H), 7.00 (dd, *J* = 8.7, 8.7 Hz, 2H), 2.05 (s, 3H), 2.00 (q, *J* = 7.3 Hz, 2H), 1.80 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 161.8 (d, *J* = 244 Hz), 140.9 (d, *J* = 2.5 Hz), 126.6 (d, *J* = 7.5 Hz), 115.2 (d, *J* = 21.3 Hz), 84.1, 35.4, 24.5, 22.4, 8.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.2; IR (neat, ν/ cm^{-1}) 2973, 1733, 1487, 1105, 1245, 1090, 717; HRMS (ESI$^+$) Calcd for $C_{12}H_{15}FO_2$ $[M + Na]^+$ 233.09483, Found 233.0947.



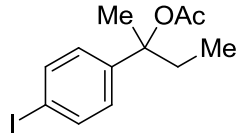
2-(4-Chlorophenyl)butan-2-yl acetate (3ha). 39.1 mg, 69%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 2.06 (s, 3H), 2.03-1.95 (m, 2H), 1.79 (s, 3H), 0.78 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 143.7, 132.8, 128.5, 126.4, 84.0, 35.3, 24.4, 22.4, 8.3; IR (neat, ν/ cm^{-1}) 2976, 1736, 1367, 1243, 1008, 816.; HRMS (ESI$^+$) Calcd for $C_{12}H_{15}ClO_2$ $[M + Na]^+$ 249.0653, Found 249.0639.



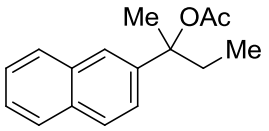
2-(4-Bromophenyl)butan-2-yl acetate (3ia). 46.3 mg, 68%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 2.06 (s, 3H), 2.01-1.95 (m, 2H), 1.78 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 169.9, 144.2, 131.5, 126.8, 121.0, 84.0, 35.3, 24.4, 22.4, 8.3; IR (neat, ν/ cm^{-1}) 2975, 2938, 1737, 1492, 1368, 1243, 1012, 820; HRMS (ESI^+) Calcd for $C_{12}H_{15}BrO_2$ $[M + Na]^+$ 293.0148 Found 293.0149.



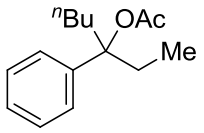
2-(4-Iodophenyl)butan-2-yl acetate (3ja). 51.6 mg, 65%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.0 Hz, 2H), 7.05 (d, *J* = 7.0 Hz, 2H), 2.06 (s, 3H), 1.98 (q, *J* = 7.4 Hz, 2H), 1.77 (s, 3H), 0.78 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 144.9, 137.5, 127.0, 92.6, 84.1, 35.3, 24.3, 22.4, 8.3; IR (neat, ν/ cm^{-1}) 2973, 1735, 1366, 1243, 1003, 942, 814; HRMS (ESI^+) Calcd for $C_{12}H_{15}IO_2$ $[M + Na]^+$ 341.0009, Found 341.0024.



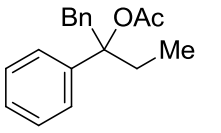
2-(Naphthalen-2-yl)butan-2-yl acetate (3ka).[6] 32.7 mg, 54%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89-7.80 (m, 3H), 7.78 (s, 1H), 7.53-7.41 (m, 3H), 2.20-2.14 (m, 2H), 2.13 (s, 3H), 1.95 (s, 3H), 0.83 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 142.4, 133.3, 132.6, 128.4, 128.2, 127.7, 126.2, 126.0, 123.7, 123.3, 84.7, 35.2, 24.5, 22.5, 8.4.



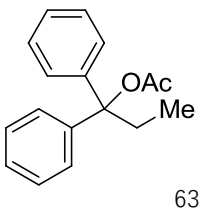
3-Phenylheptan-3-yl acetate (3la). 28.6 mg, 49%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.22 (m, 4H), 7.22-7.11 (m, 1H), 2.41-2.24 (m, 2H), 2.06 (s, 3H), 2.04-1.89 (m, 2H), 1.22-1.10 (m, 2H), 1.10-0.84 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H), 0.62 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 143.9, 128.2, 126.8, 125.3, 87.9, 37.6, 30.9, 25.6, 23.0, 22.3, 14.2, 7.9; IR (neat, ν/ cm^{-1}) 2934, 1735, 1366, 1245, 1016, 700; HRMS (ESI^+) Calcd for $C_{15}H_{22}O_2$ $[M + Na]^+$ 257.1512, Found 257.1518.



1,2-Diphenylbutan-2-yl acetate (3ma). 28.4 mg, 42%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.17 (m, 5H), 7.17-7.07 (m, 3H), 6.75 (d, *J* = 6.8 Hz, 2H), 3.58 (d, *J* = 13.6 Hz, 1H), 3.37 (d, *J* = 13.6 Hz, 1H), 2.49 (dq, *J* = 14.7, 7.4 Hz, 1H), 2.21 (dq, *J* = 14.7, 7.4 Hz, 1H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 143.1, 136.4, 130.6, 128.2, 127.9, 127.1, 126.6, 125.7, 87.5, 44.2, 29.9, 22.5, 8.0; IR (neat, ν/ cm^{-1}) 2970, 1735, 1366, 1231, 1021, 700; HRMS (ESI^+) Calcd for $C_{18}H_{20}O_2$ $[M + Na]^+$ 291.1356, Found 291.1352.

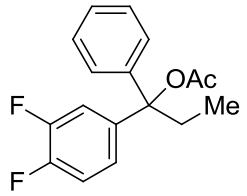


1,1-Diphenylpropyl acetate (3na). 46.4 mg, 73%; Colorless soil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.28 (m, 4H), 7.28-7.22 (m, 4H), 7.22-7.14 (m, 2H), 2.75 (q, *J* = 7.3 Hz, 2H), 2.11 (s, 3H), 0.72 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 145.0, 128.2,

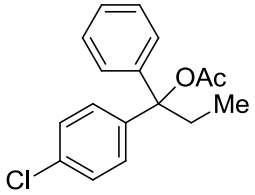


127.1, 126.2, 87.0, 29.8, 22.3 7.7; IR (neat, ν/ m^{-1}) 3512, 3059, 2974, 1953, 1717, 1448, 1252, 970, 763, 763; HRMS (ESI^+) Calcd for $C_{17}H_{18}O_2$ $[M + H]^+$ 277.1199, Found 277.1209.

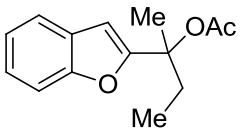
1-(3,4-Difluorophenyl)-1-phenylpropyl acetate (3oa). 48.2 mg, 67%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.23 (m, 4H), 7.23-7.17 (m, 1H), 7.13 (ddd, *J* = 11.7, 7.6, 2.0 Hz, 1H), 7.07-6.96 (m, 2H), 2.69 (q, *J* = 7.3 Hz, 2H), 2.11 (s, 3H), 0.70 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 149.8 (dd, *J* = 248, 99.5 Hz), 149.7 (dd, *J* = 248, 99.5 Hz), 144.2, 142.3 (dd, *J* = 5.0, 3.8 Hz,), 128.5, 127.5, 126.1, 122.4 (dd, *J* = 6.3, 3.8 Hz), 117.0 (d, *J* = 17.2 Hz), 115.8 (d, *J* = 18.6 Hz), 86.1, 29.8, 22.2, 7.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -138.4, -141.0; IR (neat, ν/ cm^{-1}) 3445, 2976, 1738, 1608, 1517, 1370, 1253, 1018, 867, 775; HRMS (ESI^+) Calcd for $C_{17}H_{16}F_2O_2$ $[M + Na]^+$ 313.1011, Found 313.1024.



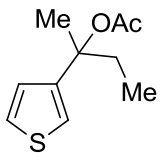
1-(4-Chlorophenyl)-1-phenylpropyl acetate (3pa). 48.2 mg, 67%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.11 (m, 9H), 2.72 (q, *J* = 7.3 Hz, 2H), 2.11 (s, 3H), 0.71 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 144.5, 143.7, 133.0, 128.43, 128.35, 127.8, 127.3, 126.2, 86.6, 29.8, 22.3, 7.7; IR (neat, ν/ cm^{-1}) 3081, 1983, 1598, 1372, 970, 639; HRMS (ESI^+) Calcd for $C_{17}H_{17}ClO_2$ $[M + Na]^+$ 311.0809, Found 311.0804.



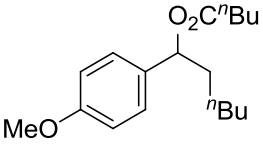
2-(Benzofuran-2-yl)butan-2-yl acetate (3qa). 38.1 mg, 66%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.31-7.45 (m, 2H), 6.62 (s, 1H), 2.28-2.08 (m, 2H), 2.06 (s, 3H), 1.86 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 158.8, 154.7, 128.4, 124.1, 122.9, 121.3, 111.4, 103.2, 80.5, 32.3, 22.6, 22.2, 8.3; IR (neat, ν/ cm^{-1}) 3471, 2972, 1740, 1455, 1242, 1017, 941, 751; HRMS (ESI^+) Calcd for $C_{14}H_{16}O_3$ $[M + Na]^+$ 255.0992, Found 255.0980.



2-(Thiophen-3-yl)butan-2-yl acetate (3ra). 25.5 mg, 51%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21-7.16 (m, 1H), 7.05-7.01 (m, 1H), 6.92 (d, *J* = 4.8 Hz, 1H), 2.07-1.97 (m, 2H), 1.96 (s, 3H), 1.73 (s, 3H), 0.72 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 146.4, 125.6, 120.2, 83.2, 34.5, 25.0, 22.5, 8.38; IR (neat, ν/ cm^{-1}) 3446, 2968, 1731, 1675, 1456, 1258, 1082, 791, 663; HRMS (ESI^+) Calcd for $C_{10}H_{17}O_2S$ $[M + Na]^+$ 221.0607, Found 221.0603.

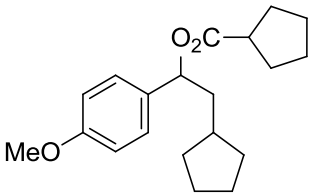


1-(4-Methoxyphenyl)hexyl pentanoate (3bb). 46.2 mg, 63%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.22 (m, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.70 (t, *J* = 7.1 Hz, 1H), 3.81 (s, 3H), 2.38-2.23 (m, 2H), 1.96-1.84 (m, 1H), 1.80-1.68 (m, 1H), 1.60

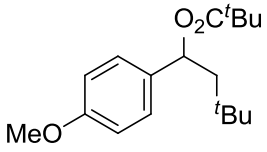


(tt, *J* = 7.4 Hz, 2H), 1.41-1.12 (m, 8H), 0.97-0.80 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 159.4, 133.4, 128.2, 113.9, 75.8, 55.5, 36.4, 34.6, 31.7, 27.3, 25.5, 22.7, 22.5, 14.2, 14.0; IR (neat, ν/ cm^{-1}) 2957, 2932, 1733. 1613, 1514, 1248, 1171, 830, 730; HRMS (ESI$^+$) Calcd for $C_{18}H_{28}O_3$ [M + Na]$^+$ 315.1931, Found 315.1942.

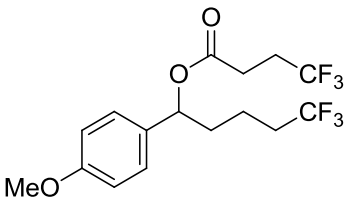
Procedure for gram scale. A mixture of 1-(tert-butyl)-4-vinylbenzene (**1a**, 1.71 g, 10.7 mmol), iodobenzene diacetate (**2a**, 4.47 g, 13.9 mmol), $Fe(CO)_3$(cot) (0.260 g, 1.07 mmol), L10 (bathocuproine, 0.385 g, 1.07 mmol), and CH_3CN (46.0 mL) was stirred at 70 ℃ for 12 h in a sealed tube. Then, the solvent was removed in vacuo and the product was isolated by column chromatography on silica gel (n-hexane/EtOAc = 20:1) to give 1-(4-(tert-butyl)phenyl)propyl acetate (**3aa**, 1.15 g, 46% yield).

2-Cyclopentyl-1-(4-methoxyphenyl)ethyl cyclopentanecarboxylate (3bc). 64.7 mg, 82%; Yellow oil; 

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 8.7, 2.1 Hz, 2H), 6.78 (dd, *J* = 8.7, 2.1 Hz, 2H), 5.62 (t, *J* = 7.1 Hz, 1H), 3.71 (s, 3H), 2.72-2.58 (m, 1H), 1.95-1.25 (m, 17H), 1.15-0.93 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 159.3, 133.6, 128.1, 113.9, 75.3, 55.4, 44.3, 42.8, 36.8, 33.0, 32.8, 30.1, 30.0, 26.01, 25.97, 25.3, 25.2; IR (neat, ν/ cm^{-1}) 2951, 2868, 1729, 1613, 1453, 1248, 1173, 1037, 830; HRMS (ESI$^+$) Calcd for $C_{20}H_{28}O_3$ [M + Na]$^+$ 339.1931, Found 339.1941.

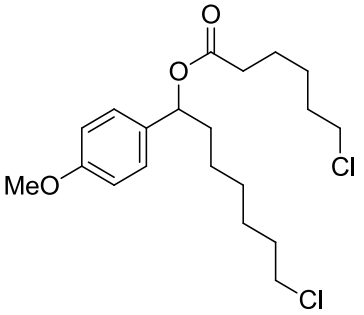
1-(4-Methoxyphenyl)-3,3-dimethylbutyl pivalate (3bd). 48.5 mg, 66%; Yellow oil; 

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.77 (dd, *J* = 8.9, 3.2 Hz, 1H), 3.78 (s, 3H), 2.02-1.91 (m, 1H), 1.57 (dd, *J* = 14.8, 3.3 Hz, 1H), 1.15 (s, 9H), 0.94 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8, 159.1, 135.4, 127.6, 114.0, 73.8, 55.4, 50.4, 38.8, 30.6, 30.2, 27.3; IR (neat, ν/ cm^{-1}) 3401, 2935, 1733, 1589, 1508, 1246, 1126, 831, 643; HRMS (ESI$^+$) Calcd for $C_{18}H_{28}O_3$ [M + Na]$^+$ 315.1931, Found 315.1942.

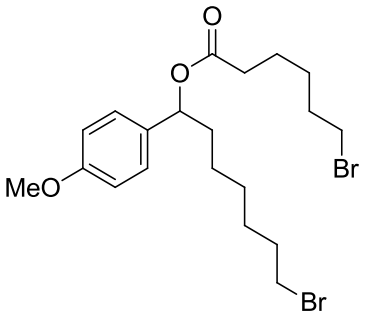
1-Methoxy-4-(5,5,5-trifluoro-3-methylene-1-((4,4,4-tri fluorobut-1-en-2-yl)peroxy)pentyl)benzene (3be). 74.5 mg, 80%; Yellow oil; 

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.71 (t, *J* = 7.1 Hz, 1H), 3.81 (s, 3H), 2.70-2.51 (m, 2H), 2.51-2.36 (m, 2H), 2.15-2.03 (m, 2H), 2.03-1.95 (m, 1H), 1.78-1.90 (m, 1H), 1.68-1.55 (m, 1H), 1.55-1.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 159.9, 131.7, 128.1, 127.0 (q, *J* = 253 Hz), 126.7 (q, *J* = 276 Hz), 114.3, 76.2, 55.5, 35.1, 33.5 (q, *J* = 29.0 Hz), 29.5 (q, *J* = 30.2 Hz), 27.6, 18.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.2 (t, *J* = 10.9 Hz, 3F), -67.8 (t, *J* = 10.4 Hz, 3F), IR (neat, ν/ cm^{-1}) 2959, 1740, 1613, 1515, 1331, 1251, 1109, 831, 626; HRMS (ESI$^+$) Calcd for $C_{16}H_{18}F_6O_3$ [M + Na]$^+$ 395.1052, Found 395.1043.

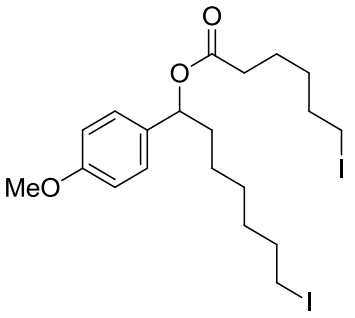
7-Chloro-1-(4-methoxyphenyl)heptyl 6-chlorohexanoate (3bf). 63.3 mg, 65% Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.70 (t, *J* = 7.0 Hz, 1H), 3.81 (s, 3H), 3.57-3.45 (m, 4H), 2.39-2.25 (m, 2H), 1.98-1.86 (m, 1H), 1.82-1.69 (m, 5H), 1.6-1.56 (m, 2H), 1.52-1.14 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 159.4, 133.0, 128.1, 114.0, 75.8, 55.4, 45.2, 45.0, 36.1, 34.5, 32.7, 32.4, 28.7, 26.9, 26.5, 25.6, 24.4; IR (neat, ν/ cm^{-1}) 2935, 2859, 1731, 1612, 1514, 1248, 1035, 831, 729, 649; HRMS (ESI^+) Calcd for $C_{20}H_{30}Cl_2O_3$[M + Na]$^+$ 411.1464, Found 411.1472.



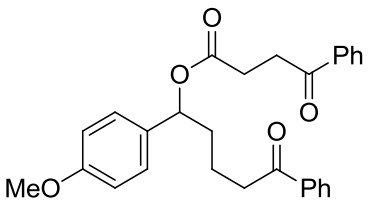
7-Bromo-1-(4-methoxyphenyl)heptyl 6-bromohexanoate (3bg). 81.0 mg, 68% Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.68 (t, *J* = 7.0 Hz, 1H), 3.80 (s, 3H), 3.46-3.27 (m, 4H), 2.42-2.16 (m, 2H), 2.04-1.71 (m, 6H), 1.71-1.52 (m, 2H), 1.52-1.09 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 159.4, 133.0, 128.2, 114.0, 75.9, 55.5, 36.2, 34.6, 34.1, 33.7, 32.9, 32.6, 28.6, 28.2, 27.8, 25.6, 24.3; IR (neat, ν/ cm^{-1}) 2935, 2857, 1731, 1513, 1461, 1248, 1174, 1034, 831, 732; HRMS (ESI^+) Calcd for $C_{20}H_{30}Br_2O_3$[M + Na]$^+$ 499.0454, Found 499.0451.



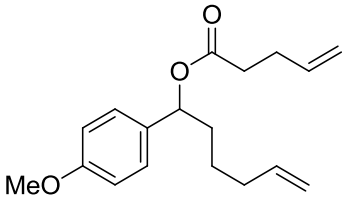
7-Iodo-1-(4-methoxyphenyl)heptyl 6-iodohexanoate (3bh). 64.4 mg, 45% Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.70 (t, *J* = 7.0 Hz, 1H), 3.81 (s, 3H), 3.24-307(m, 4H), 2.39-2.25 (m, 2H), 1.99-1.87 (m, 1H), 1.87-1.72 (m, 5H), 1.69-1.56 (m, 2H), 1.47-1.28 (m, 7H), 1.28-1.18 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 159.4, 132.9, 128.1, 114.0, 75.8, 55.4, 36.1, 34.5, 33.5, 33.3, 30.5, 30.1, 28.4, 25.6, 24.1, 7.4, 6.8; IR (neat, ν/ cm^{-1}) 2938, 2870, 1671, 1370, 1302, 922, 830 HRMS (ESI^+) Calcd for $C_{20}H_{30}I_2O_3$[M + Na]$^+$ 595.0177, Found 595.0187.



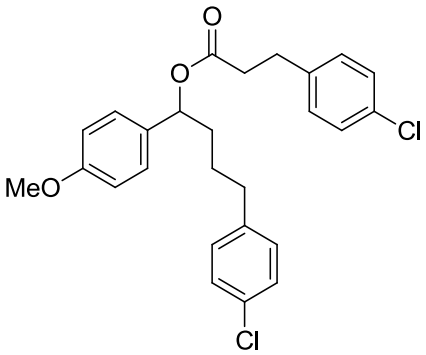
5-(4-Methoxyphenyl)-5-((4-oxo-4-phenylbut-1-en-2-yl)peroxy)-1-phenylpentan-1-one (3bi). 46.3 mg, 42%; Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01-7.87 (m, 4H), 7.62-7.51 (m, 2H), 7.45 (dd, *J* = 7.6, 7.6 Hz, 4H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 5.76 (t, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 3.41-3.20 (m, 2H), 2.98 (t, *J* = 7.1 Hz, 2H), 2.90-2.79 (m, 1H), 2.79-2.67 (m, 1H), 2.11-1.96 (m, 1H), 1.94-1.75 (m, 2H), 1.75-1.64 (m, 1H); ^{13}C NMR (125 MHz,



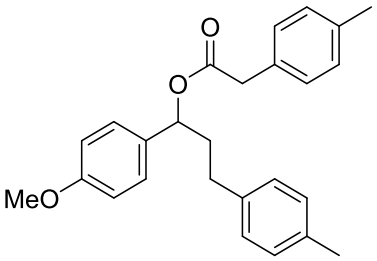
$CDCl_3$) δ 200.0, 198.3, 172.5, 159.5, 137.1, 136.8, 133.4, 133.2, 132.6, 128.82, 128.80, 128.3, 128.24, 128.18 114.1, 76.0, 55.5, 38.2, 35.7, 33.6, 28.8, 20.4; IR (neat, ν/ cm^{-1}) 2932, 1731, 1684, 1514, 1248, 1167, 1033, 831, 691; HRMS (ESI^+) Calcd for $C_{28}H_{28}O_5$ $[M + Na]^+$ 467.1829, Found 467.1828.

1-(4-methoxyphenyl)hex-5-en-1-yl pent-4-enoate (3bj). 

432.8 45; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.89-5.68 (m, 3H), 5.07-4.92 (m, 4H), 3.79 (s, 3H), 2.47-2.30 (m, 4H), 2.11-2.01 (m, 2H), 1.99-1.87 (m, 1H), 1.86-1.71 (m, 1H), 1.51-1.37 (m, 1H), 1.37-1.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 159.4, 138.5, 136.8, 133.0, 128.1, 115.6, 115.0, 114.0, 75.8, 55.4, 35.7, 34.0, 33.5, 29.1, 25.0; IR (neat, ν/ cm^{-1}) 2938, 2842 1780, 1520, 1090, 718, 700; HRMS (ESI^+) Calcd for $C_{16}H_{24}O_3$ $[M + Na]^+$ 311.3762, Found 311.3775.

4-(4-Chlorophenyl)-1-(4-methoxyphenyl)butyl 3-(4-chlorophenyl)propanoate (3bk). 

83.5 mg, 73%; Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.21 (m, 6H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 5.78 (t, *J* = 7.0 Hz, 1H), 3.87 (s, 3H), 2.96 (t, *J* = 7.7 Hz, 2H), 2.72-2.59 (m, 4H), 2.02-1.89 (m, 1H), 1.89-1.77 (m, 1H), 1.71-1.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 159.5, 140.5, 139.0, 132.5, 132.1, 131.7, 129.91, 129.87, 128.7, 128.6, 128.1, 114.0, 75.9, 55.4, 36.1, 35.6, 35.0, 30.4, 27.4; IR (neat, ν/ cm^{-1}) 3445, 2935, 1731, 1612, 1514, 1302, 1248, 1035, 831, 729, 649; HRMS (ESI^+) Calcd for $C_{26}H_{26}Cl_2O_3$ $[M + Na]^+$ 479.1151, Found 479.1529.

1-(4-Methoxyphenyl)-3-(*p*-tolyl)propyl 2-(*p*-tolyl)acetate (3bl). 

50.3 mg, 52% Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30-7.21 (m, 2H), 7.21-7.11 (m, 4H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.87 (dd, *J* = 8.8, 2.4 Hz, 2H), 5.71 (t, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 3.59 (s, 3H), 2.59-2.40 (m, 2H), 2.35 (s, 3H), 2.32 (s, 3H); 2.27-2.16 (m, 1H), 2.08-1.98 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 159.5, 138.3, 136.8, 135.6, 132.7, 131.3, 129.42, 129.36, 129.3, 128.4, 128.2, 114.0, 75.8, 55.5, 41.5, 38.1, 31.5, 21.3, 21.2; IR (neat, ν/ cm^{-1}) 2923, 1733, 1514, 1248, 1033, 808; HRMS (ESI^+) Calcd for $C_{26}H_{28}O_3$ $[M + Na]^+$ 411.4962, Found 411.4970.

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Publicaition List

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Manganese- and Borane-Mediated Synthesis of Isobenzofuranones from Aromatic Esters and Oxiranes via C–H Bond Activation

Org. Lett. **2016**, *18*, 304.

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