Development of Radical-Mediated Synthetic Methods via Single-Electron Transfer by Transition Metal Catalysts

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Contents

Chapter 1

General Introduction

■ Radical Chemistry

Radicals are highly reactive species with singly occupied orbitals. They are useful intermediates in synthetic chemistry due to their unique reactivity based on single-electron chemistry.[1] Radical reactions can be conducted with protic functional groups and solvents such as carboxylic acids, alcohols, and water, which generally disturb ionic reactions based on two-electron chemistry. Radical-specific processes are well-known, such as β-scission,[2] intramolecular cyclization,[3] and 1,5-hydrogen transfer (**Figure 1**, upper).[4] Unique stereoselectivity of radical reactions is also important for organic synthesis (**Figure 1**, lower). *anti*-Markovnikov addition to alkenes[5] and chemoselectivity depending on bond dissociation energy[6] are essential for fine organic synthesis.

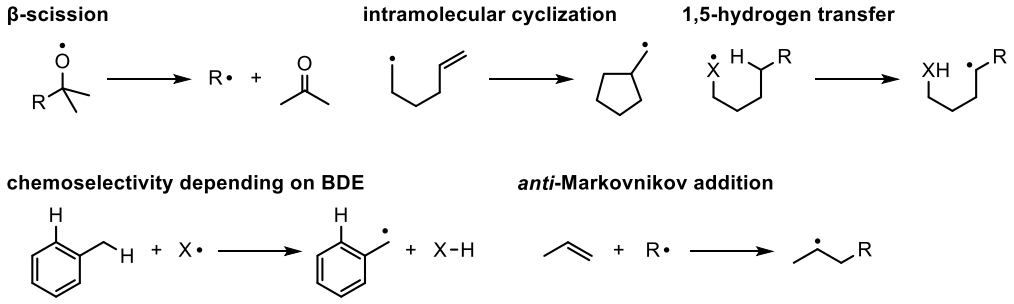

Figure 1. Representative examples of unique reactivity of radicals.

In order to develop radical reactions, it is crucial that how to generate radicals. A traditional approach is heating or photoirradiation of radical precursors (**Figure 2**). Peroxides[7] and azo compounds[8] are typical radical initiators. Barton esters[9] and dithiocarbamates[10] are also known as useful radical precursors to generate targeted radicals. With these methods, radical precursors are directly activated to generate radicals, so they are simple methods that do not require any additives. However, harsh conditions or using highly reactive radical precursors are often required.

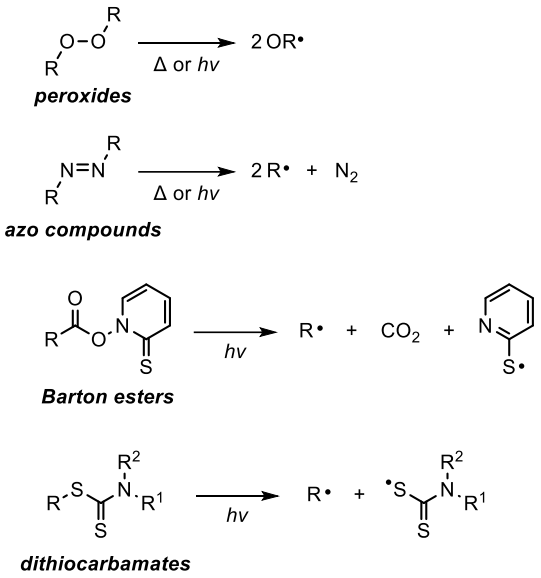

Figure 2. Direct generation of radicals from radical precursors.

■ Radical Generation *via* Thermal Single-Electron Transfer

On the other hand, single-electron transfer (SET) by transition metal catalysts, which is a main topic in this dissertation, is also a reliable method to generate radicals. Several name reactions are known as examples of the use of thermal SET (**Figure 3**). Kharasch addition[11] and Meerwein arylation[12] include single-electron reduction process and Scholl reaction[13] uses single-electron oxidation. Some of the latest studies are shown below.

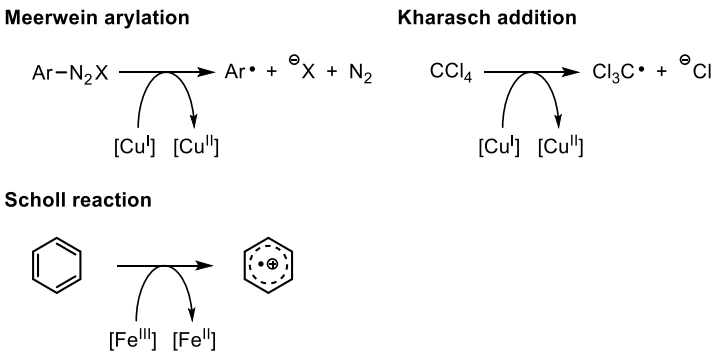

Figure 3. Representative name reactions using thermal SET.

Recently, a combination of copper catalysts and α-halocarbonyl compounds has been used to generate α-carbonyl radicals. Nishikata *et al.* reported a copper-catalyzed Heck-type reaction *via* a generation of tertiary alkyl radicals (**Figure 4**).[14] A single-electron transfer from the copper(I) catalyst to ethyl 2-bromoisobutyrate formed the tertiary alkyl radicals.

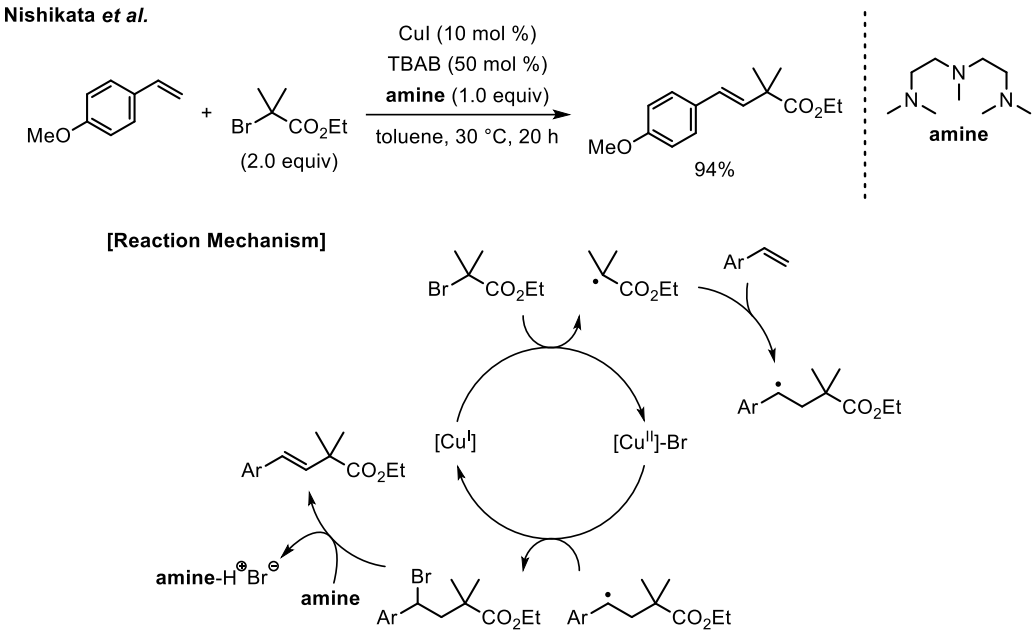

Figure 4. Copper-catalyzed Heck-type reaction *via* a radical pathway.

Fu *et al.* reported an enantioconvergent reaction of α-halocarbonyl compounds (**Figure 5**).[15] As with the Nishikata's work, a single-electron transfer from the copper(I) catalyst to alkyl bromides is crucial. The radicals generated from a racemic mixture of the alkyl bromides lost the stereochemistry at the α position. Then, the radicals were trapped by the chiral copper catalyst, which is the reason why the enantioconvergent reaction could occur.

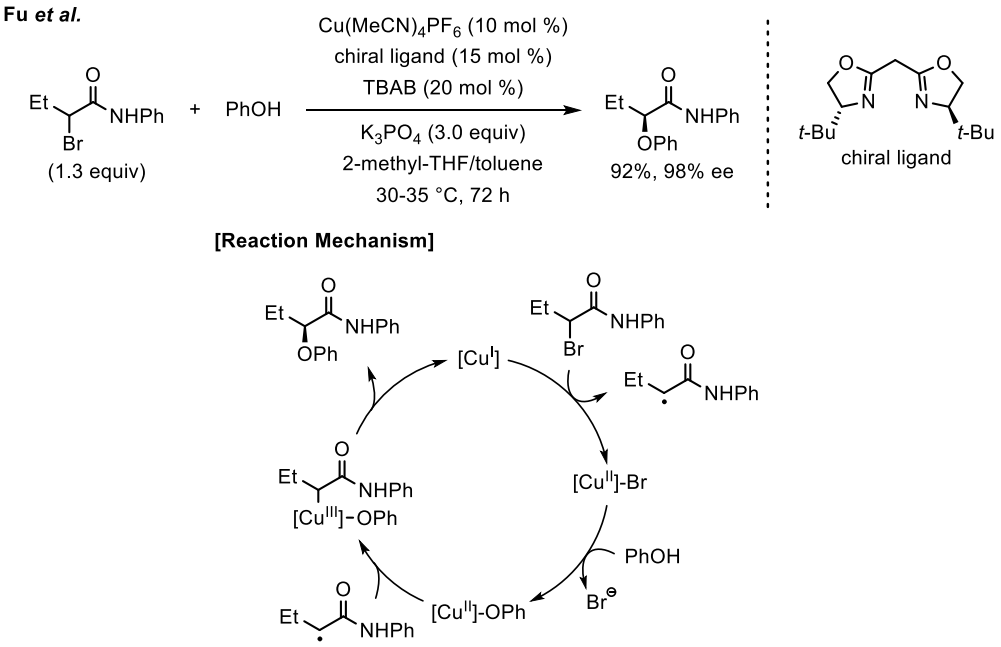

Figure 5. Copper-catalyzed enantioconvergent alkoxylation of α-halocarbonyl compounds.

■ Radical Generation *via* Photochemical Single-Electron Transfer

Not only thermal SET but also photochemical SET is a useful method to generate radicals. Particularly, visible-light photoredox catalysts have contributed to developing the field of modern organic chemistry. Photoexcited photoredox catalysts act as single-electron oxidants or reductants to generate various kinds of radicals. Since MacMillan *et al.* reported the first use of $[Ru(bpy)_3]^{2+}$ as the photoredox catalyst (**Figure 6**),[16] numerous studies have been conducted using polypyridyl complexes of ruthenium(II) or iridium(III).[17]

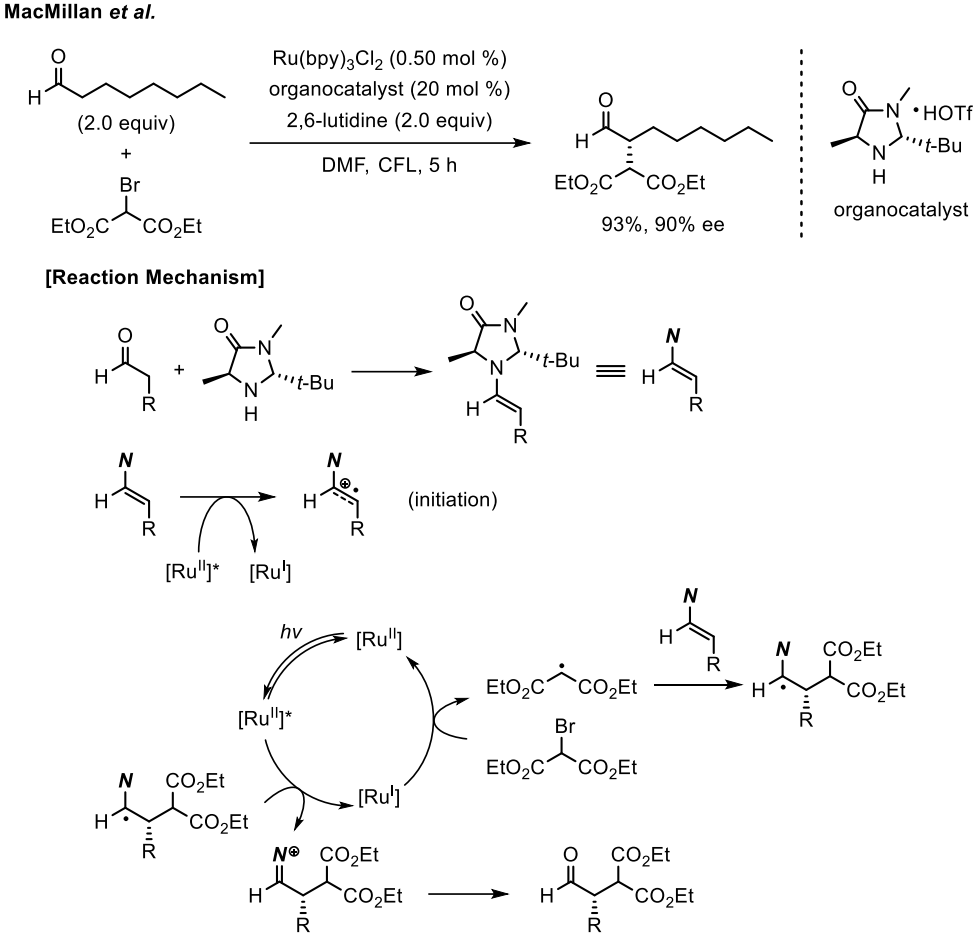

Figure 6. Asymmetric alkylation of aldehydes using a ruthenium photoredox catalyst.

The development of photoredox catalysis has provided a variety of bond-formation methods involving sp^3 carbons, further increasing the utility of synthetic organic chemistry with photoredox catalysts. However, iridium(III) or ruthenium(II) photoredox catalysts are very expensive. Therefore, the development of photoredox catalysts using cheap and earth-abundant metals, such as chromium, iron, cobalt, and copper, is an important research area.[18] Although photoexcited species of first-row transition metals are known to have short lifetimes due to their small ligand-field splitting,[19] several intensive works have been reported. The representative works in this area are shown below.

Shores and Ferreira *et al.* reported a [4+2] cycloaddition using a chromium(III) photoredox catalyst (**Figure 7**).[20] Mechanistic studies indicated that the photoexcited

chromium(III) complex converted electron-rich vinylarenes to their radical cations *via* single-electron oxidation.

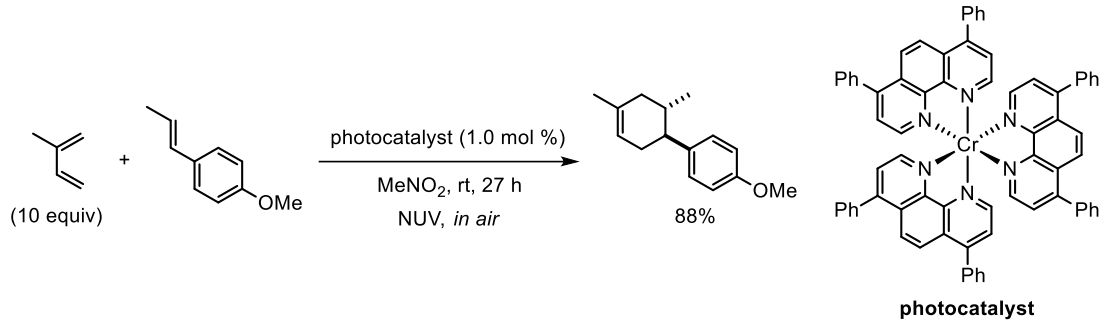

Figure 7. Diels-Alder reaction using a chromium(III) photoredox catalyst.

Recently, McCusker and MacMillan *et al.* developed a cobalt-based photoredox catalyst and applied it to a C(sp^2)–N cross-coupling reaction of arylboronic acids and aryl amides (**Figure 8**).[21] The oxidative cobalt(III) photocatalyst was strong enough to take away single-electrons from aryl amides.

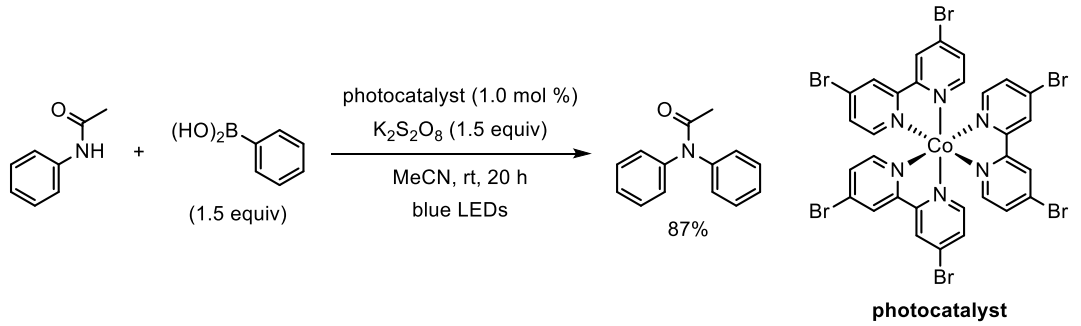

Figure 8. C(sp^2)–N cross-coupling reaction using a cobalt(III) photoredox catalyst.

Moreover, the combination of photoredox catalysts with transition metal catalysts, namely metallaphotoredox catalysis, has become mainstream in synthetic chemistry.[22] Transition metal catalysts have offered reliable methods to form new bonds, such as cross-coupling reactions. The concept of metallaphotoredox catalysis is to use photoredox-derived radicals for the transition metal-catalyzed reactions. The first reports of metallaphotoredox catalysis were carried out by Molander *et al.*[23] and MacMillan *et al.*[24], respectively (**Figure 9**). Benzylic radicals and α-amino

radicals generated *via* single-electron transfer by photoredox catalysts were incorporated into the catalytic cycle of nickel, forming $C(sp^3)$–$C(sp^2)$ bonds.

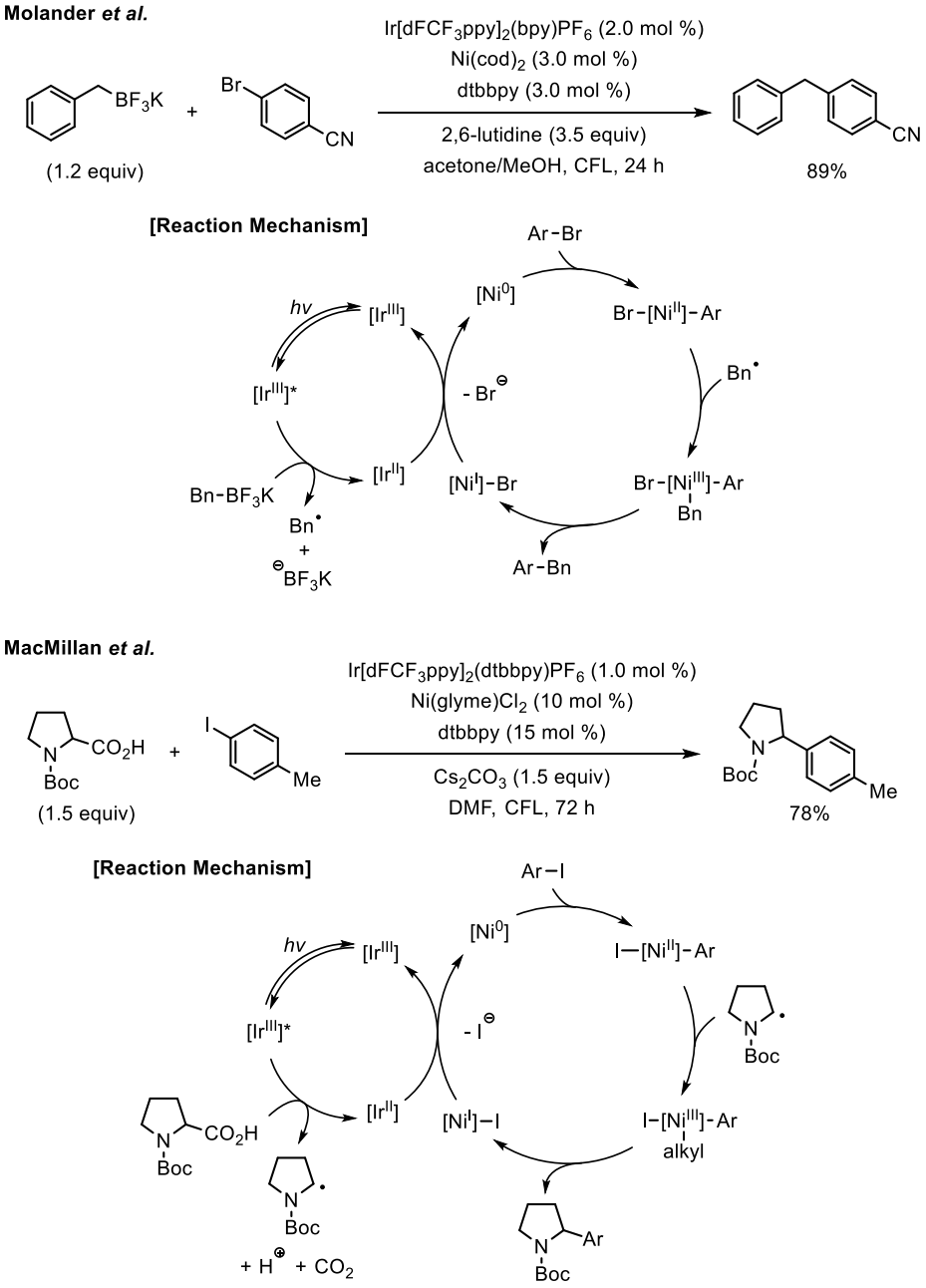

Figure 9. The first reports of metallaphotoredox catalysis.

On the other hand, studies on the generation of radicals and the formation of new bonds with a single transition metal catalyst have also attracted attention. If the single-electron reactivity

of transition metal catalysts, well-known for their two-electron reactivity, is revealed, it may be possible to achieve reactions similar to those using metallaphotoredox catalysis without external photoredox catalysts. In particular, research on photoexcited palladium catalysts has made great progress.[25] For example, it was reported that photoexcited palladium(0) complexes undergo single-electron transfer to generate palladium(I) complexes and radicals. Gevorgyan *et al.* reported a photoexcited palladium-catalyzed Heck reaction (**Figure 10**).[26] Single-electron transfer from the photoexcited palladium(0) catalyst to alkyl halides generated alkyl radicals. The palladium catalyst showed both single-electron and two-electron reactivities. Catalytic systems using other transition metals are also under development but will be mentioned in Chapter 5.

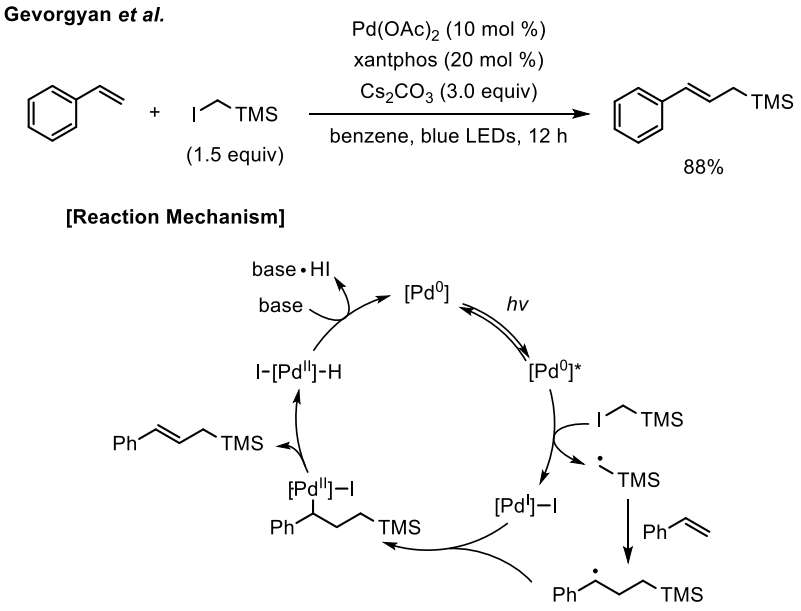

Figure 10. Photoexcited palladium-catalyzed Heck reaction.

■ Overview

As mentioned above, thermal and photochemical single-electron transfer by transition metal catalysts offer practical ways to generate various radicals. Inspired by previous excellent works, the author was led to develop useful transformations and new catalytic systems. In this

dissertation, some chemical transformations based on radical generation *via* SET by transition metal catalysts are described. The details are shown below.

In Chapter 2, the author reports a copper-catalyzed aminoalkoxylation of alkylarenes *via* formal double C(sp^3)–H functionalization (**Figure 11**). In this reaction, a single-electron transfer from a copper(I) catalyst to *N*-fluorobenzenesulfonimide generated an *N*-centered radical, which acted as a hydrogen-absorbing reagent and an amino group source. Biological active arylethanolamines could be synthesized with this method from readily available alkylarenes instead of vinylarenes.

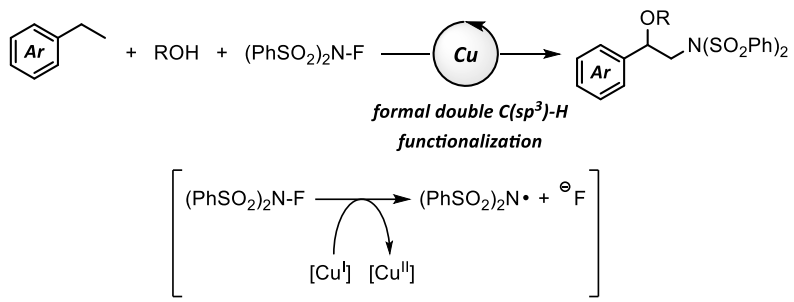

Figure 11. Chapter 2: copper-catalyzed aminoalkoxylation of ethylarenes.

In Chapter 3, the author reports a photoexcited copper-catalyzed *anti*-Markovnikov hydration of vinylarenes (**Figure 12**). A new copper(II) photoredox catalyst has been developed and the catalyst exhibited a strong oxidizing ability for single-electron oxidation of vinylarenes. A regioselective addition of H_2O to the resulting radical cations gave the desired alcohols. This is the first example of intermolecular quenching of photoexcited copper(II) complexes. Detailed studies revealed the photophysical properties of the catalyst.

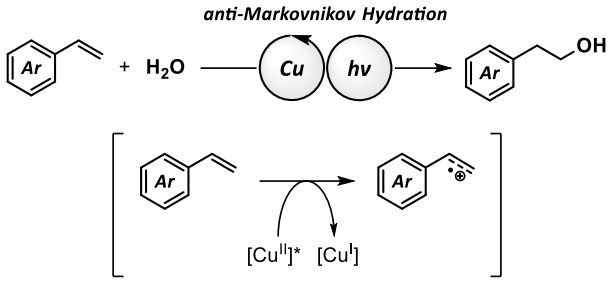

Figure 12. Chapter 3: photoexcited copper-catalyzed *anti*-Markovnikov hydration.

In Chapter 4, the author reports a photoexcited palladium-catalyzed cross-coupling reaction of α-chlorocarbonyl compounds with arylboronic acids (**Figure 13**). Although α-chlorocarbonyl compounds are less reactive than iodides and bromides, a single-electron reduction of α-chlorocarbonyl compounds by the photoexcited palladium(0) catalyst enabled a formal oxidative addition *via* a radical pathway.

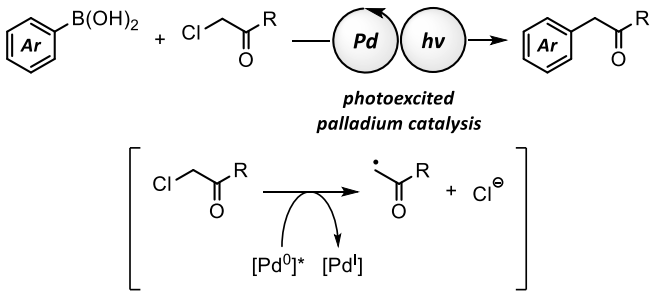

Figure 13. Chapter 4: photoexcited palladium-catalyzed cross-coupling reaction.

In Chapter 5, the author reports a photoexcited nickel-catalyzed acylcyanation of vinylarenes (**Figure 14**). The photoexcited nickel(0) catalyst undergoes a single-electron reduction of acyl fluorides to generate the corresponding acyl radicals. The nickel catalyst showed both a single-electron reactivity and a two-electron reactivity. The reaction proceeded under mild conditions, so the method could be applied to the late-stage functionalization of naturally derived molecules.

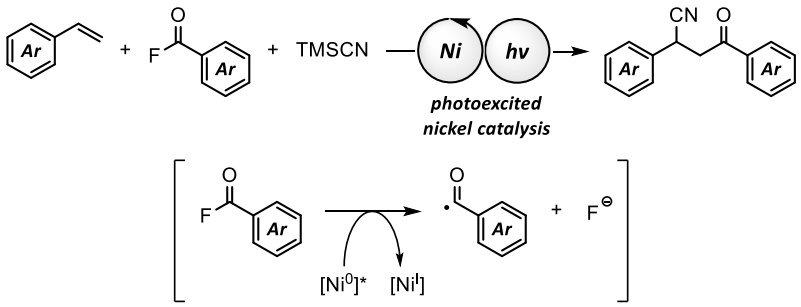

Figure 14. Chapter 5: photoexcited nickel-catalyzed acylcyanation of vinylarenes.

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Chapter 2

Copper Radical-Polar Crossover Catalysis: 1,2-Aminoalkoxylation of Alkylarenes *via* Formal Double C(sp^3)–H Functionalization

Abstract

A double C(sp^3)–H functionalization of ethylarenes with alcohols and *N*-fluorobenzenesulfonimide is reported. The reaction proceeds in three stages. (1) copper-catalyzed benzylic alkoxylation of ethylarenes gives 1-(1-alkoxyethyl)benzenes. (2) The resulting 1-(1-alkoxyethyl)benzenes are gradually converted into vinylarenes. (3) copper-catalyzed aminoalkoxylation of the intermediary vinylarenes yields arylethanolamines. Overall, the C–N and C–O bonds are formed regioselectively at the homobenzylic and benzylic positions of ethylarenes.

Introduction

Arylethanolamine derivatives are quite common in pharmaceuticals and natural products (**Figure 1**a).[1] They are also used as intermediates for the synthesis of chiral auxiliaries and ligands.[2] Numerous methods have been developed for their syntheses, particularly from vinylarenes as starting materials.[3] Typically, vinylarenes are oxidized to form the corresponding epoxides, which are subjected to the reaction with amines, and thus, two steps are required (**Figure 1**b).[4] On the contrary, the direct aminoalkoxylation of vinylarenes is an efficient way. Yoon reported a regio- and enantioselective iron(II)-catalyzed aminoalkoxylation of vinylarenes with *N*-sulfonyl oxaziridines to form oxazolidines that can be easily manipulated to produce the unprotected arylethanolamines.[5] Notably, unprotected arylethanolamines could be directly synthesized by using *O*-pivaloylhydroxylamine triflic acid ($PivONH_3OTf$) as a nitrogen source in an iron(II)-catalyzed reaction of vinylarenes.[6] A regioselective copper(I)-catalyzed aminoalkoxylation of vinylarenes with various alkoxy sources and *N*-fluorobenzenesulfonimide (NFSI) as a nitrogen sources was also demonstrated by the groups of Studer, Zhang, and Pérez.[7,8]

Considering the ease of storage and transportation, ethylarenes are more attractive as starting materials than vinylarenes, which are easily polymerized under radical and ionic conditions. Furthermore, vinylarenes are industrially prepared from ethylarenes by catalytic dehydrogenation.[9] However, there have been no reports on the use of ethylarenes as starting materials for the synthesis of arylethanolamines, although the direct conversion of chemical feedstocks into high-value-added products is becoming increasingly important in chemical research.[10]

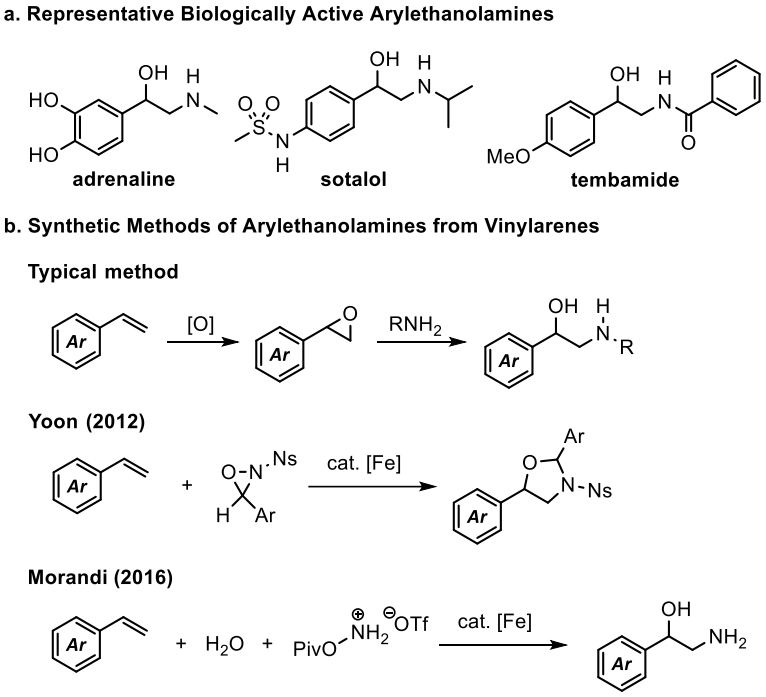


Figure 1. Background for the development of the reaction. (a) Examples of biologically active compounds that contain arylethanolamine motif. (b) Overview of methods for the synthesis of arylethanolamines from vinylarenes.

In order to achieve the transformation from ethylarenes to arylethanolamines, regioselective double C(sp^3)–H functionalization is required.[11] Generally, it is difficult to distinguish multiple C(sp^3)–H bonds and to convert each of them selectively in a single reaction, because strong reaction conditions or special designs of substrates such as directing groups are necessary for C(sp^3)–H functionalization due to their low reactivity. To solve this problem, the author focused on the Nicewicz's interesting study (**Figure 2**a).[12] They reported homobenzylic oxidation using a photoredox catalyst and a cobalt dehydrogenative catalyst. This reaction begins with a formal dehydrogenation of photoredox-generated benzylic radicals. Hydration of vinyl arenes generated *in situ* gives *anti*-Markovnikov Wacker-type oxidation products. Based on their study, the author envisaged copper-catalyzed double C(sp^3)–H functionalization with NFSI (**Figure 2**b). It is well-known that a single-electron transfer from copper(I) to NFSI generates an *N*-centered radical, which abstracts a hydrogen atom from ethylarenes to generate benzylic

radicals.[13] The author assumed that if a formal dehydrogenation of photoredox-generated benzylic radicals takes place with copper(II) to give the corresponding vinylarenes, formal double C(sp^3)–H functionalized products are obtained by difunctionalization of the vinylarenes.

In this chapter, the author reports a copper(I)-catalyzed double C(sp^3)−H functionalization of ethylarenes for the synthesis of arylethanolamines. C−N and C−O bonds are introduced regioselectively at the homobenzylic and benzylic positions of ethylarenes, respectively.

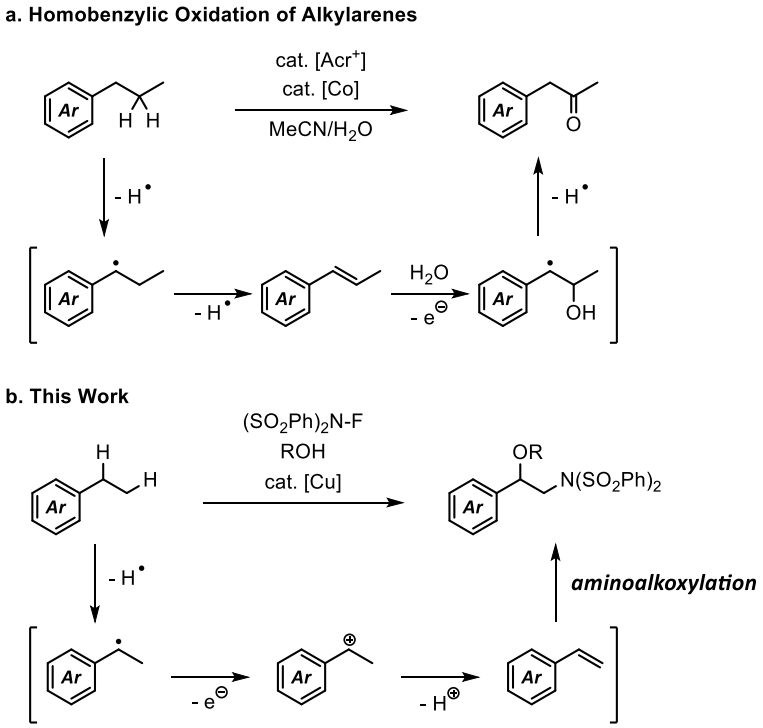


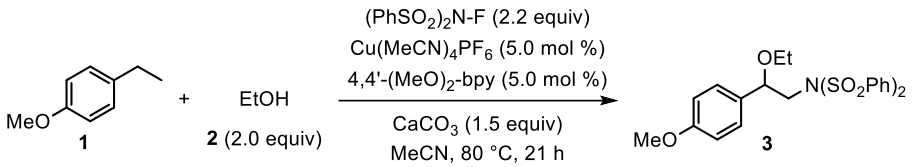
Figure 2. (a) Homobenzylic oxidation of alkylarenes *via in situ* generation of vinylarenes. (b) This work: regioselective 1,2-aminoalkoxylation of alkylarenes *via in situ* generation of vinylarenes.

Result and Discussions

■ Copper-Catalyzed 1,2-Aminoalkoxylation of Alkylarenes

A mixture of 4-methoxy-1-ethylbenzene (**1**, 0.20 mmol), ethanol (**2**, 2.0 equiv), and NFSI (2.2 equiv) in MeCN (2.0 mL) was stirred for 21 hours at 80 °C in the presence of $Cu(MeCN)_4PF_6$ (5.0 mol %), 4,4′-dimethoxy-2,2′-bipyridyl [4,4′-$(MeO)_2$-bpy, 5.0 mol %], and $CaCO_3$ (1.5 equiv). Doubly functionalized product **3** was formed in 95% NMR yield. After chromatographic purification, **3** was isolated in 81% yield (**Table 1**, entry 1). A larger scale experiment using 1.0 mmol of **1** gave a similar result (74% isolated yield). The copper catalyst was indispensable for the reaction (entry 2). Other copper sources such as $Cu(OAc)_2$ and CuCl gave inferior results (entries 3 and 4). In the absence of 4,4′-$(MeO)_2$-bpy, the NMR yield of **3** decreased to 35% (entry 5). When 4,4′-di-*tert*-butyl-2,2′-bipyridne (dtbbpy) and 4,7-dimethoxy-1,10-phenantholine [4,7-$(MeO)_2$-phen] were used as the ligands, **3** was obtained in moderate yields (entries 6 and 7). Solvent screening showed that MeCN was the optimal solvent (entries 8 and 9). The reaction scarcely occurred in the absence of $CaCO_3$ (entry 10). No desired product was detected when other carbonates such as K_2CO_3, Cs_2CO_3, and $AgCO_3$ were employed (entries 11−13). It is assumed that the added $CaCO_3$ plays an important role in the scavenging of fluoride anions. Thus, $CaCO_3$ is converted into CaF_2 and H_2CO_3.

Table 1. Development of 1,2-Aminoalkoxylation of 4-Methoxy-1-ethylbenzene (1)[a]



entry	change from standard conditions	yields of **3** (%)
1	none	95 (81)[b]
2	without $Cu(MeCN)_4PF_6$	n.d.
3	$Cu(OAc)_2$ instead of $Cu(MeCN)_4PF_6$	88
4	CuCl instead of $Cu(MeCN)_4PF_6$	83
5	without 4,4'-$(MeO)_2$-bpy	35
6	dtbbpy instead of 4,4'-$(MeO)_2$-bpy	49
7	4,7-$(MeO)_2$-phen instead of 4,4'-$(MeO)_2$-bpy	50
8	1,2-dichloroethane instead of MeCN	68
9	benzene instead of MeCN	24
10	without $CaCO_3$	13
11	K_2CO_3 instead of $CaCO_3$	n.d.
12	Cs_2CO_3 instead of $CaCO_3$	n.d.
13	Ag_2CO_3 instead of $CaCO_3$	n.d.

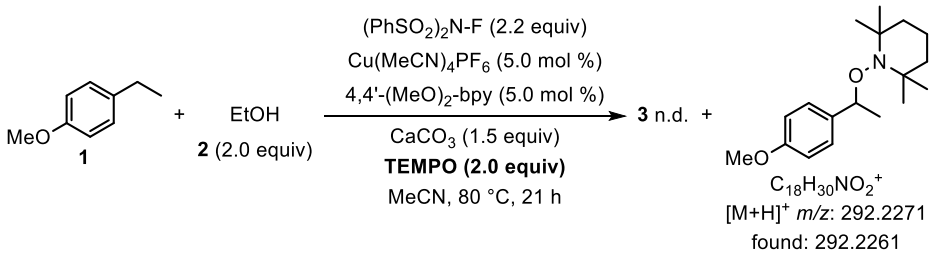
[a]On a 0.20 mmol scale. Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard. [b]Isolated yield after preparative thin-layer chromatographic purification. n.d. = not detected.

■ Reaction Mechanism

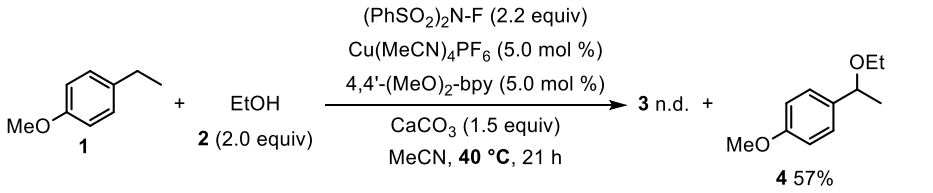
To gain mechanistic insight, some control experiments were carried out (**Scheme 1**). In the presence of 2.0 equiv of 2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPO), the formation of the desired product **3** was completely prevented. Starting material **1** remained almost unchanged, but the TEMPO adduct of **1** was detected by high-resolution mass spectrometry (HRMS: $DART^+$) analysis (**Scheme 1**a). When the reaction was conducted at a lower temperature (40 °C), product **3** was not observed, and instead, 1-(1-ethoxyethyl)-4-methoxybenzene (**4**) was formed in 57% yield (**Scheme 1**b). When **4** was subjected to the modified conditions using 1.1 equiv of

Scheme 1. Control Experiments[a]

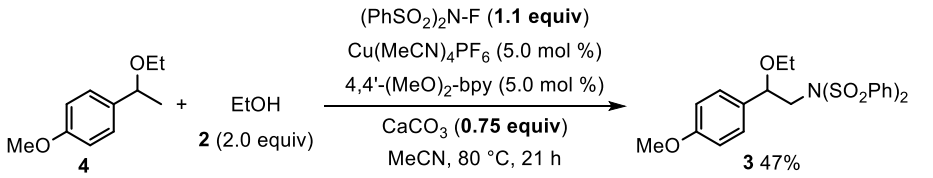
a. The Reaction in the Presence of Radical Scavenger



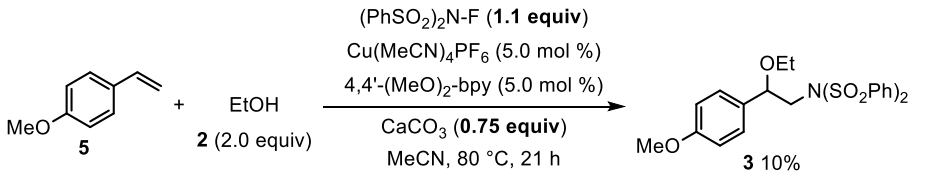
b. The Reaction at Lower Temperature



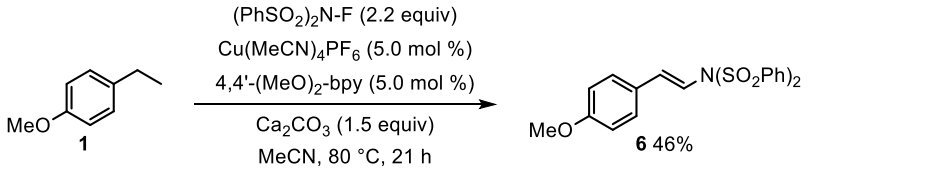
c. The Reaction Starting from Benzylic Ether 4



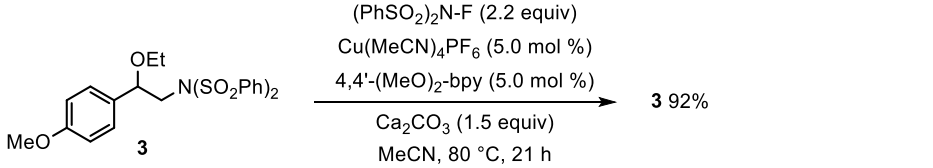
d. The Reaction Starting from 4-Methoxystyrene (5)



e. The Reaction in the Absence of Ethanol



f. The Stability of the Product

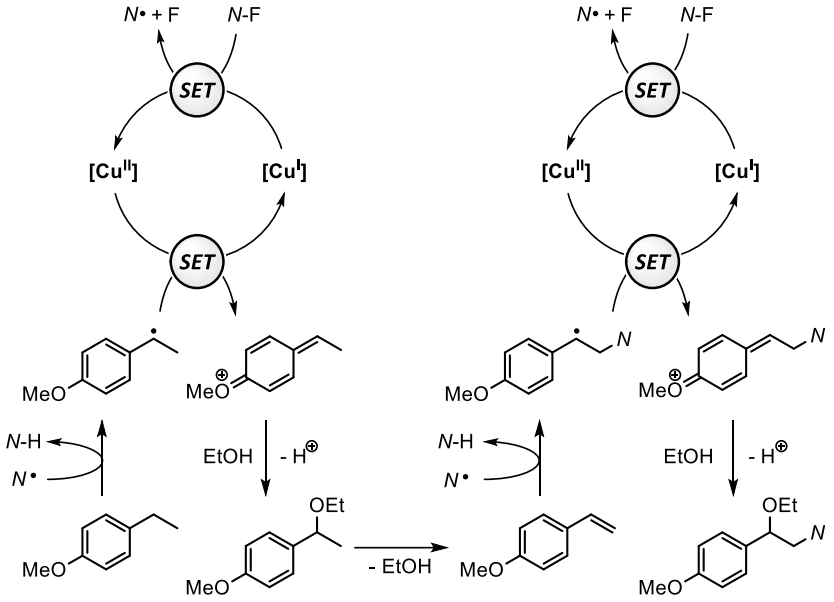


[a]On a 0.20 mmol scale. Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard.

NFSI and 0.75 equiv of $CaCO_3$, **3** was produced in 47% yield (**Scheme 1**c). Furthermore, when 4-methoxystyrene (**5**) was used as the starting material under the standard conditions, **3** was obtained albeit in a rather low yield (10%) and various byproducts were formed (**Scheme 1**d). These results suggest that 1-(1-alkoxyethyl)benzenes undergo the elimination of alkoxy groups to give the corresponding vinylarenes, which are the key intermediates in the reaction. The gradual formation of the vinylarene might be important in this reaction system. Additionally, enamine **6** was obtained in the absence of ethanol (**2**), so it is possible to generate vinylarenes without the formation of benzylic ether **4**. Interestingly, the elimination of the alkoxy group from **3** did not proceed under standard conditions (**Scheme 1**f).

On the basis of the control experiments and the previous reports, the author proposes the reaction mechanism shown in **Scheme 2**.[7c, 14] The reaction consists of two catalytic cycles by copper. The first catalytic cycle is initiated by single-electron transfer (SET) from copper(I) to NFSI, generating an *N*-centered radical. Then, a hydrogen atom at the benzylic position of ethylarene **1** is abstracted by the *N*-centered radical. The resulting benzyl radical is oxidized by a copper(II) species to form a quinone methide along with the regeneration of copper(I). The quinone methide reacts with ethanol (**2**) to give 1-(1-ethoxyethyl)-benzene (**4**). Then, the elimination of the ethoxy group affords 4-methoxystyrene (**5**). The direct pathway from the quinone methide to styrene derivative **5** cannot be ruled out. The second catalytic cycle is also initiated by SET from copper(I) to NFSI, generating *N*-centered radical, which adds to the C–C double bond of **5**. The resulting benzyl radical is oxidized by copper(II) to form a quinone methide along with the regeneration of copper(I). The quinone methide reacts with ethanol (**2**) to give the desired product **3**.

Scheme 2. Proposed Mechanism for the Formation of 3

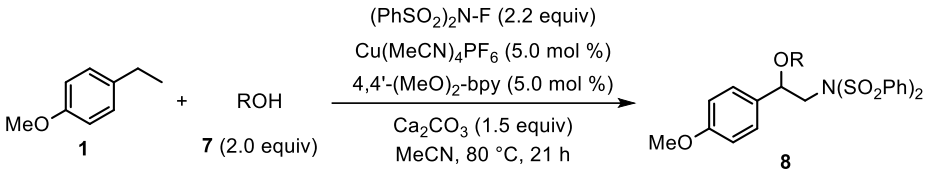


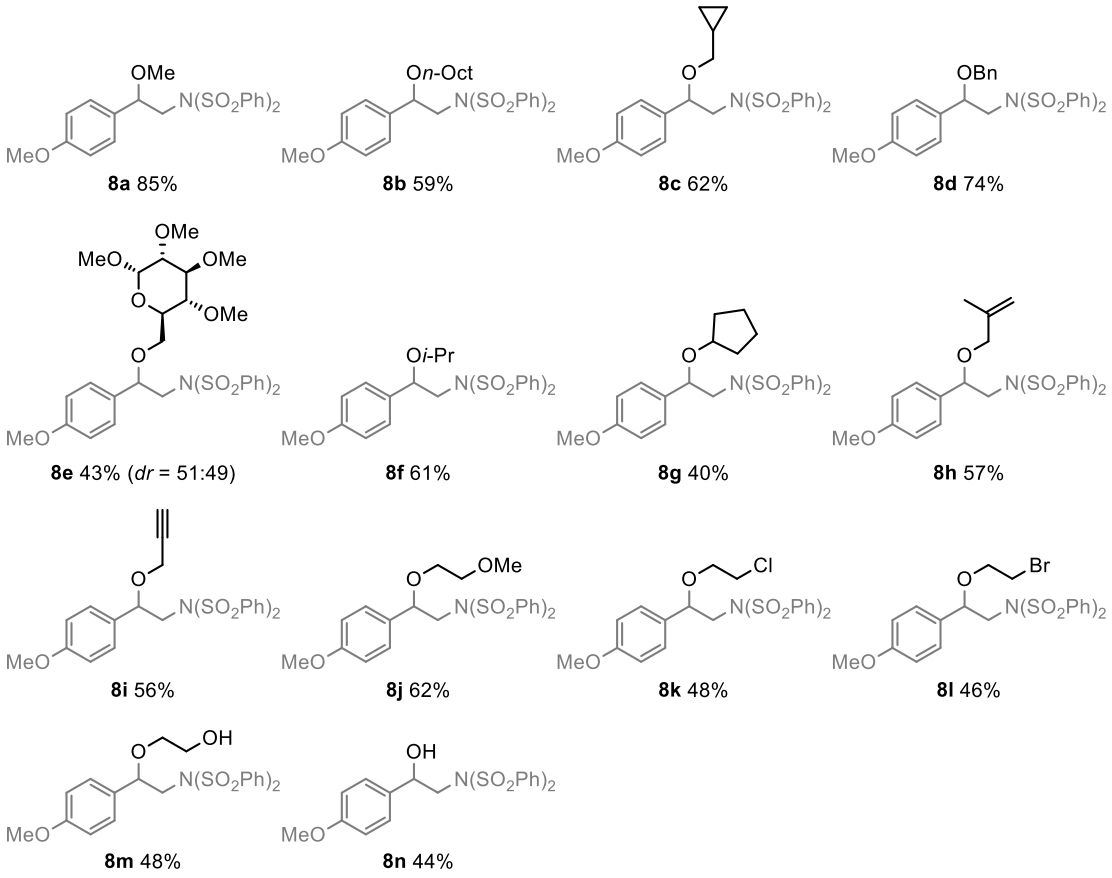
N = $(PhSO_2)_2N$.

■ Substrate Scope

The scope with respect to alcohols **7a**−**7m** was examined in the reaction of 4-methoxy-1-ethylbenzene (**1**) (**Table 2**). Primary and secondary alcohols such as methanol (**7a**), 1-octanol (**7b**), cyclopropylmethanol (**7c**), phenylmethanol (**7d**), 2-propanol (**7f**), and cyclopentanol (**7g**) smoothly reacted to furnish the corresponding products (**8a**−**8d**, **8f**, and **8g**) in yields ranging from 40% to 75%. Methyl 2,3,4-tri-*O*-methyl-glucopyranoside (**7e**) was also amenable to this reaction. On the contrary, tertiary alcohols such as 2-methyl-2-propanol and 2-methyl-2-butanol failed to give the desired products, likely due to steric hindrance. The reaction with 2-methyl-2-propen-1-ol (**7h**) and 2-propyn-1-ol (**7i**) bearing unsaturated C−C bonds provided products **8h** and **8i** in 57% and 56% yields, respectively. 2-Substituted ethanol derivatives **7j**−**7m** having methoxy, chloro, bromo, and hydroxyl groups, respectively, participated in this reaction (**8j**−**8m**). Notably, water (**7n**) was a suitable reactant to give unprotected benzyl alcohol derivative **8n**.[15]

Table 2. Reaction with Various Alcohols 7a–7m and Water (7n)[a]



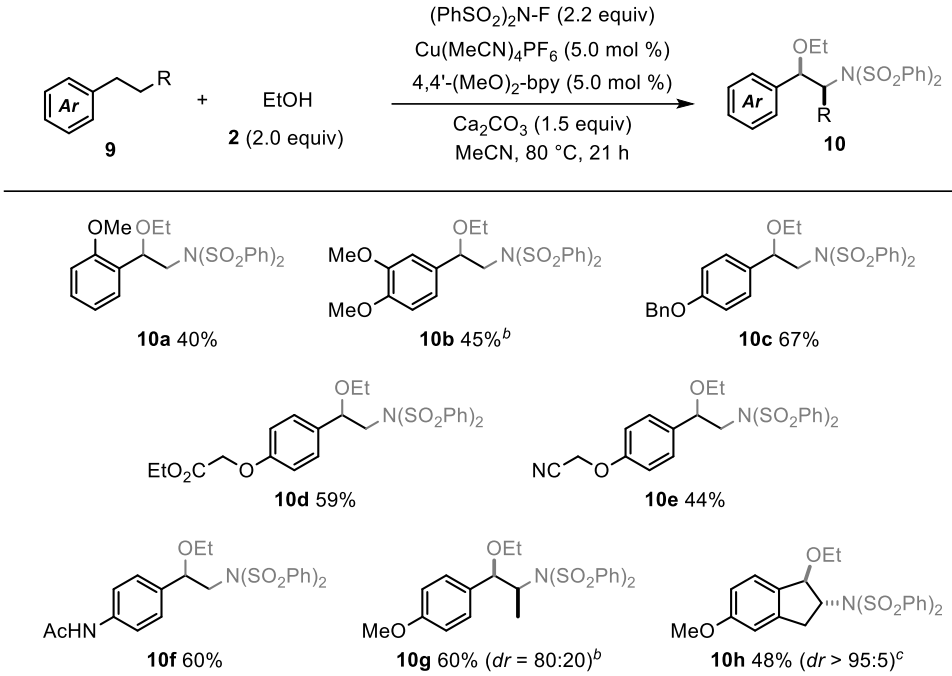


[a]On a 0.20 mmol scale. Isolated yields after preparative thin-layer chromatographic purification.

Ethylarenes **9a**–**9h** were subjected to the double C(sp^3)–H functionalization reaction with ethanol (**2**) and NFSI (Table 3). In this protocol, an electron-donating substituent on the benzene ring was essential for stabilizing the cationic intermediates and/or enhancing the elimination of the ethoxy group. When 1-*tert*-butyl-4-ethylbenzene was used as the substrate, 1-*tert*-butyl-4-(1-ethoxyethyl)benzene was formed along with a trace amount of the doubly functionalized product (see the Experimental Section). 2-Methoxy- and 3,4-dimethoxy-1-ethylbenzenes (**9a** and **9b**) proceeded smoothly to give products **10a** and **10b** in 40% and 45%

yields, respectively. Other 4-alkoxy-1-ethylbenzenes **9c**–**9e** were also transformed into products **10c**–**10e** respectively, in moderate yields. The acetamide group could be applied to an electron-donating substituent, furnishing product **10f** in 60% yield. The reaction of 4-methoxy-1-propylbenzene (**9g**) gave a mixture of diastereomers **10g** in 60% yield (*dr* = 80:20). The relative configuration of the minor diastereomer was unambiguously assigned as *syn* by a single-crystal X-ray analysis (CCDC 2245280). Therefore, *anti*-addition of ethanol (**2**) is preferable in this reaction. When 5-methoxyindan (**9h**) was used as the substrate, the single diastereomer **10h** was obtained in 48% yield.

Table 3. reaction with Various Alkylarenes 9a–9h[a]



[a]On a 0.20 mmol scale. Isolated yields after preparative thin-layer chromatographic purification. Diastereo ratios were determined by ^{1}H NMR analysis. [b]The reaction was performed at 70 °C. [c]The reaction was performed at 50 °C.

■ **Synthetic Applications**

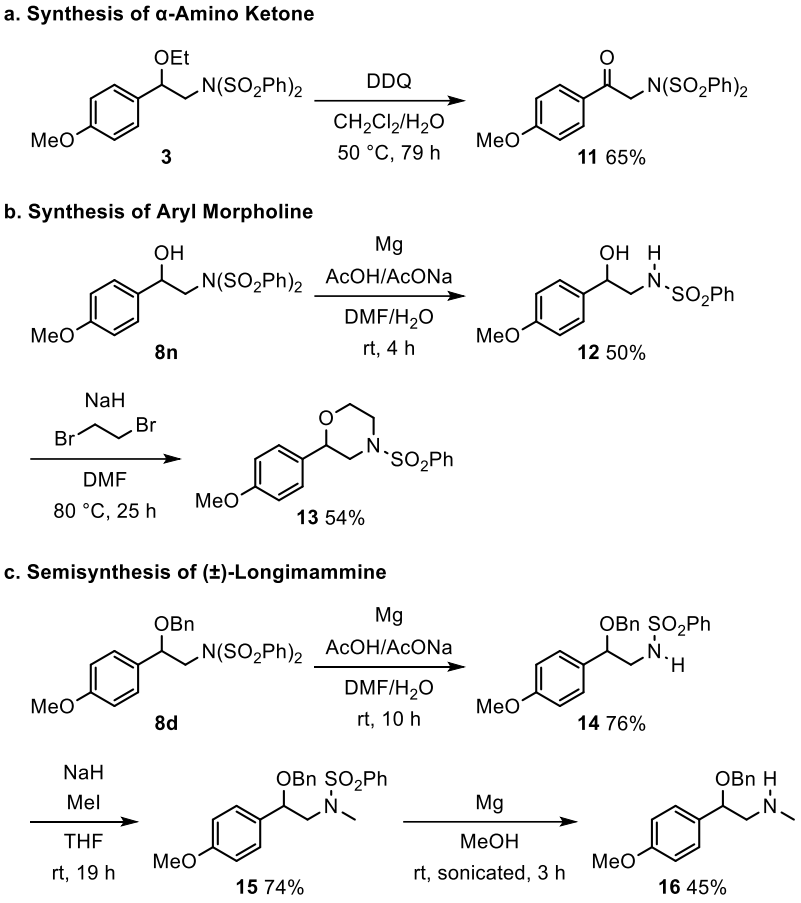
The synthetic utility of the doubly functionalized products was exemplified by further transformation (**Scheme 3**). The oxidation of **3** by using 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) afforded α-amino ketone **11** (**Scheme 3**a). The removal of the benzenesulfonyl group in **8n** was readily achieved on treatment with magnesium at room temperature. The resulting **12** underwent dialkylation to give morpholine derivative **13** in 54% yield (**Scheme 3**b).

Finally, our protocol was applied to the semisynthesis of (±)-longimammine, which is an alkaloid isolated from a Mexican cactus, Dolichothele longimamma (**Scheme 3**c).[16] The sequential desulfonylation of **8d** and the *N*-methylation of **14** afforded compound **15**. A modified desulfonylation procedure was utilized for the removal of the additional sulfonyl group,[17] and longimammine-*O*-benzylether **16** was obtained in 45% yield.

Conclusion

In summary, the direct use of ethylarenes as starting materials, underutilized chemical feedstocks, was described for the regioselective synthesis of arylethanolamines. The formal double C(sp^3)−H functionalization based on copper single-electron redox catalysis occurs at the homobenzylic and benzylic positions of ethylarenes.

Scheme 3. Further Transformation of Arylethanolamine Derivatives



Experimental Section.

■ **General Methods.**

All reactions were carried out under a nitrogen atmosphere unless otherwise noted. IR measurements were performed on an Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter and a JASCO FTIR-4X with ATR Pro 4X. ^{1}H and 13C{^{1}H} NMR spectra were recorded on a JEOL JNM-ECZ400S/L1 (^{1}H at 400.44 MHz and 13C{^{1}H} at 100.69 MHz) spectrometer. NMR data were obtained in $CDCl_3$ unless otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm ($CHCl_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm ($CDCl_3$). High-resolution mass spectra were recorded on JEOL JMS-SX102A (EI, a magnetic sector mass spectrometer with an electron ionization source) and Thermo Fisher Scientific Exactive Plus [ESI, a Fouriertransform (orbitrap) mass spectrometer with an electrospray ionization source]. Preparative thin-layer chromatography (PTLC) was performed on silica gel plates with PF254 indicator (Merck). Flash column chromatography was performed with silica gel 60N (Kanto).

■ **Materials.**

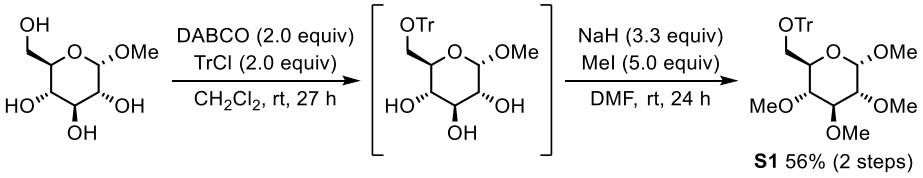
All chemicals and anhydrous solvents were obtained from commercial suppliers and used without further purification unless otherwise noted. Anhydrous MeCN (FUJIFILM Wako and Kanto) was degassed before use. $Cu(MeCN)_4PF_6$ (TCI), 4,4'-dimethoxy-2,2'-bipyridyl (TCI), *N*-fluorobenzenesulfonimide (TCI), and $CaCO_3$ (FUJIFILM Wako) were obtained from commercial suppliers.

Alcohols **2**, **7a**–**7d**, and **7f**–**7m** were obtained from commercial suppliers and used without further purification [EtOH (**2**, FUJIFILM Wako), MeOH (**7a**, FUJIFILM Wako), 1-

octanol (**7b**, FUJIFILM Wako), cyclopropanemethanol (**7c**, TCI), BnOH (**7d**, Nacalai), *i*-PrOH (**7f**, FUJIFILM Wako), cyclopentanol (**7g**, TCI), β-methallyl alcohol (**7h**, Nacalai), propargyl alcohol (**7i**, TCI), 2-methoxyethanol (**7j**, Nacalai), 2-chloroethanol (**7k**, Sigma-Aldrich), 2-bromoethanol (**7l**, TCI), ethylene glycol (**7m**, Nacalai), H_2O (**7n**, FUJIFILM Wako)]. Alcohol **7e** was prepared according to the procedure detailed later. Ethylarenes **1** and **9a** were obtained from commercial suppliers and used without further purification [4-ethylanisole (**1**, TCI) and 2-ethylanisole (**9a**, TCI)]. Ethylarenes **9b**–**9h** were prepared according to the procedure detailed later.

■ Substrate Preparatrion.

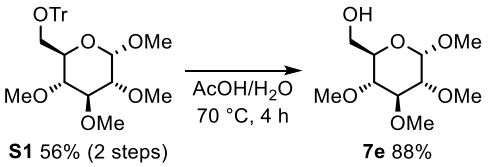
Methyl 2,3,4-tri-*O*-methyl-α-D-glucopyranoside (7e):



S1 56% (2 steps)

The tritylation of methyl α-D-glucopyranoside was carried out according to the literature procedure.[18] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added methyl α-D-glucopyranoside (2.9 g, 15 mmol, 1.0 equiv), TrCl (8.4 g, 30 mmol, 2.0 equiv), DABCO (3.4 g, 30 mmol, 2.0 equiv), and CH_2Cl_2 (60 mL, 0.25 M). The reaction mixture was stirred at room temperature. After 27 hours, the mixture was filtered and concentrated under reduced pressure. The crude mixture was used in the next reaction without further purification. Trimethylation of the tritylated product was carried out according to the following procedure. To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added the crude mixture, NaH (60% in liquid paraffin, 2.0 g, 50 mmol, 3.3 equiv), and DMF (45 mL, 0.33 M). Then, iodomethane (4.7 mL, 75 mmol, 5.0 equiv) was added slowly

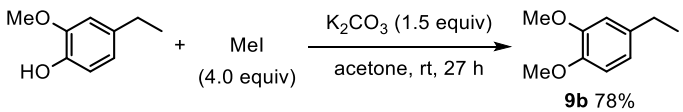
at 0 °C. The reaction mixture was stirred at room temperature. After 24 hours, saturated aqueous solution of NH_4Cl was added to the mixture, and extracted with AcOEt × 3 times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 2:1) to give **S1** (4.0 g, 8.5 mmol, 56% yield in 2 steps). The analytical data of **S1** matched well with the already reported one.[19]



S1 56% (2 steps) **7e** 88%

The detritylation of **S1** was carried out according to the literature procedure.[19] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added **S1** (4.0 g, 8.5 mmol, 1.0 equiv), AcOH (26 mL), and H_2O (6.5 mL). The reaction mixture was stirred at 70 °C in an oil bath. After 4 hours, the mixture was filtered, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (CH_2Cl_2/MeOH = 10:1) to give **7e** (1.8 g, 7.5 mmol, 88% yield). The analytical data of **7e** matched well with the already reported one.[19]

4-ethyl-1,2-dimethoxybenzene (9b):

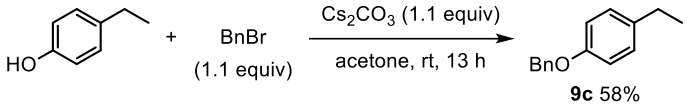


9b 78%

4-Ethyl-1,2-dimethoxybenzene (**9b**) was prepared according to the literature procedure.[20] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added K_2CO_3 (620 mg, 4.5 mmol, 1.5 equiv), acetone (30 mL, 0.10 M), 2-methoxy-4-

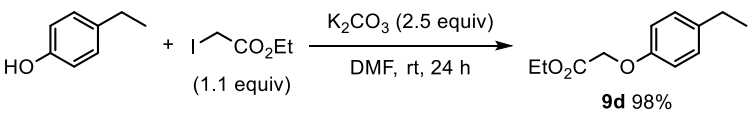
ethylphenol (430 μL, 3.0 mmol, 1.0 equiv), and methyl iodide (750 μL, 12 mmol, 4.0 equiv). The reaction mixture was stirred at room temperature. After 27 hours, the mixture was filtered and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography to give **9b** (390 mg, 2.3 mmol, 78% yield). The analytical data of **9b** matched well with the already reported one.[20]

1-(benzyloxy)-4-ethylbenzene (9c):



1-(Benzyloxy)-4-ethylbenzene (**9c**) was prepared according to the literature procedure.[21] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added 4-ethylphenol (610 mg, 5.0 mmol, 1.0 equiv), benzyl bromide (650 μL, 5.5 mmol, 1.1 equiv), Cs_2CO_3 (1.8 g, 5.5 mmol, 1.1 equiv), and MeCN (13 mL, 0.38 M). The reaction mixture was stirred at room temperature. After 13 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **9c** (620 mg, 2.9 mmol, 58% yield). The analytical data of **9c** matched well with the already reported one.[21]

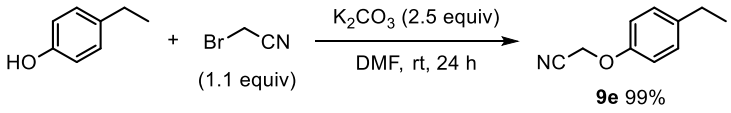
Ethyl 2-(4-ethylphenoxy)acetate (9d):



Ethyl 2-(4-ethylphenoxy)acetate (**9d**) was prepared according to the literature procedure.[22] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar

were added 4-ethylphenol (730 mg, 6.0 mmol, 1.0 equiv), ethyl iodoacetate (780 μL, 6.6 mmol, K_2CO_3 (2.1 g, 15 mmol, 2.5 equiv), and DMF (40 mL, 0.15 M). The reaction mixture was stirred at room temperature. After 24 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give **9d** (1.2 g, 5.9 mmol, 98% yield). The analytical data of **9d** matched well with the already reported one.[22]

2-(4-ethylphenoxy)acetonitrile (9e):



2-(4-Ethylphenoxy)acetonitrile (**9e**) was prepared with a similar procedure to the literature one.[23] To an oven-dried side-arm tube equipped with a stirrer bar were added 4-ethylphenol (610 mg, 5.0 mmol, 1.0 equiv), bromoacetonitrile (400 μL, 6.0 mmol, 1.2 equiv), K_2CO_3 (1.4 g, 10 mmol, 2.0 equiv), and acetone (5.0 mL, 1.0 M). The reaction mixture was stirred at room temperature. After 24 hours, the mixture was filtered and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give **9e** as a colorless oil (800 mg, 5.0 mmol, 99% yield).

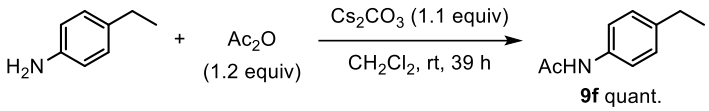
IR (ATR, cm^{-1}): 2966, 2868, 1508, 1211, 1046, 827.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.17 (d, 2H, J = 8.8 Hz), 6.91 (d, 2H, J = 8.8 Hz), 4.74 (s, 2H), 2.62 (q, 2H, J = 7.6 Hz), 1.22 (t, 3H, J = 7.6 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): 154.7, 139.1, 129.1, 115.3, 115.0, 53.9, 28.0, 15.7.

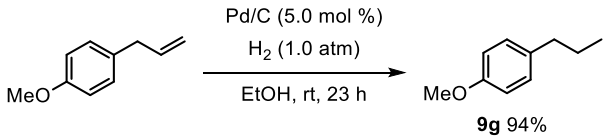
HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{10}H_{11}NO^+$ 161.0841; Found 161.0837.

***N*-(4-ethylphenyl)acetamide (9f):**



N-(4-ethylphenyl)acetamide (**9f**) was prepared according to the literature procedure.[24] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added 4-ethylaniline (380 µL, 3.0 mmol, 1.0 equiv), acetic anhydride (340 µL, 3.6 mmol, 1.2 equiv), and CH_2Cl_2 (12 mL, 0.25 M). The reaction mixture was stirred at room temperature. After 39 hours, saturated aqueous solution of Na_2CO_3 was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by recrystallization (CH_2Cl_2/hexane) to give **9f** (520 mg, 3.0 mmol, quant). The analytical data of **9f** matched well with the already reported one.[24]

1-methoxy-4-propylbenzene (9g):

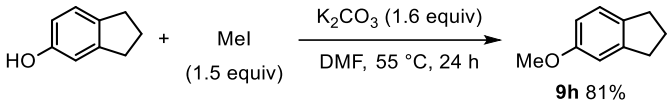


1-Methoxy-4-propylbenzene (**9g**) was prepared according to the following procedure. To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Pd/C (Pd 5% wetted with H_2O, 319.3 mg, 0.15 mmol, 5.0 mol %), 4-allylanisole (460 µL, 3.0 mmol, 1.0 equiv), and EtOH (30 mL, 0.10 M). The flask was connected to a hydrogen balloon and immersed in a dry ice/acetone bath. After 10 vacuum/H_2-filling cycles, the cooling bath was removed. The reaction mixture was stirred at room temperature. After 23 hours, the mixture was filtered through a pad of Celite with acetone. The filtrate was concentrated under reduced pressure.

The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **9g** (420 mg, 2.8 mmol, 94% yield). The analytical data of **9g** matched well with the already reported one.[25] Therefore, only the ^{1}H NMR data is presented here.

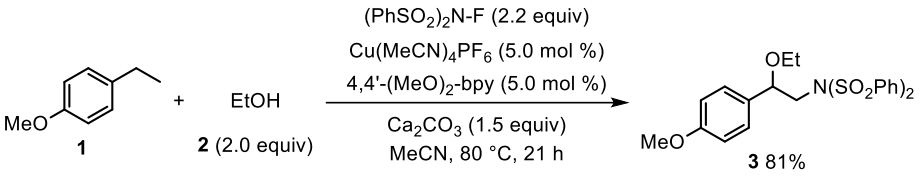
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.09 (d, 2H, *J* = 8.8 Hz), 6.83 (d, 2H, *J* = 8.8 Hz), 3.79 (s, 3H), 2.53 (t, 2H, *J* = 7.6 Hz), 1.61 (tq, 2H, *J* = 7.6, 7.6 Hz), 0.93 (t, 3H, *J* = 7.6 Hz).

5-methoxy-2,3-dihydro-1*H*-indene (9h):



5-Methoxy-2,3-dihydro-1*H*-indene (**9h**) was prepared according to the literature procedure.[26] To an oven-dried 4 mL vial equipped with a stirrer bar were added 5-hydroxyindan (404 mg, 3.0 mmol, 1.0 equiv), K_2CO_3 (663 mg, 4.8 mmol, 1.6 equiv), and DMF (2.5 mL). The mixture was stirred at room temperature for 10 minutes. Then, methyl iodide (280 μL, 4.5 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 55 °C in an oil bath. After 24 hours, H_2O was added to the mixture, and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **9h** (359 mg, 2.4 mmol, 81% yield). The analytical data of **9h** matched well with the already reported one.[26]

■ **Typical Procedure for the Copper-Catalyzed Aminoalkoxylation of Alkylarenes.**



In a nitrogen-filled glove-box, $Cu(MeCN)_4PF_6$ (3.73 mg, 0.010 mmol, 5.0 mol %), *N*-fluorobenzenesulfonimide (138.7 mg, 0.44 mmol, 2.2 equiv), EtOH (23.3 μL, 0.40 mmol, 2.0 equiv), and MeCN (2.0 mL, 0.10 M) were added to 4-ethylanisole (26.7 mg, 0.20 mmol, 1.0 equiv), 4,4'-$(MeO)_2$-bpy (2.16 mg, 0.010 mmol, 5.0 mol %), and $CaCO_3$ (30.0 mg, 0.30 mmol, 1.5 equiv) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred at 80 °C in an aluminum heating block. After 21 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **3** as a colorless oil (75.8 mg, 0.16 mmol, 81% yield).

IR (ATR, cm^{-1}): 3071, 2974, 2874, 1609, 1510, 1367, 1161.

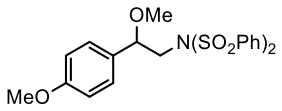
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.09 (d, 4H, *J* = 7.6 Hz), 7.63 (t, 2H, *J* = 7.6 Hz), 7.53 (t, 4H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 4.69 (dd, 1H, *J* = 9.2, 3.2 Hz), 4.16 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.81 (s, 3H), 3.57 (dd, 1H, *J* = 15.6, 3.2 Hz), 3.22 (dq, 1H, *J* = 9.6, 7.2 Hz), 3.05 (dq, 1H, *J* = 9.6, 6.8 Hz), 0.94 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 139.9, 133.6, 131.3, 128.8, 128.6, 128.2, 114.0, 79.9, 63.9, 55.3, 54.6, 14.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{25}NO_6S_2Na^+$ 498.1016; Found 498.1012.

■ **Characterization of the Aminoalkoxylation Products 8a–8m and 10a–10h.**

8a:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8a** as a pale yellow oil (68.3 mg, 0.15 mmol, 75% yield).

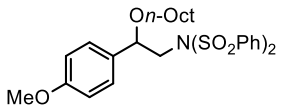
IR (ATR, cm^{-1}): 2938, 2833, 1609, 1508, 1449, 1350, 1163, 1028.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11 (d, 4H, *J* = 7.6 Hz), 7.63 (t, 2H, *J* = 7.6 Hz), 7.54 (t, 4H, *J* = 7.6 Hz), 7.27 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 4.51 (dd, 1H, *J* = 9.6, 2.8 Hz), 4.15 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.81 (s, 3H), 3.56 (dd, 1H, *J* = 15.6, 2.8 Hz), 2.89 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.7, 139.9, 133.6, 130.4, 128.7, 128.5, 128.1, 114.1, 82.6, 56.0, 55.3, 54.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{23}NO_6S_2Na^+$ 484.0859; Found 484.0860.

8b:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8b** as a white solid (65.6 mg, 0.12 mmol, 59% yield).

IR (ATR, cm^{-1}): 2928, 2857, 1510, 1371, 1250, 1169, 918.

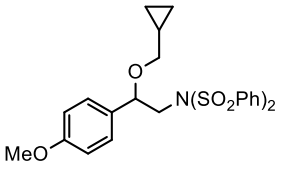
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10–8.04 (m, 4H), 7.63 (tt, 2H, *J* = 7.2, 1.2 Hz), 7.56–7.49 (m, 4H), 7.28 (d, 2H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 4.66 (dd, 1H, *J* = 9.2, 3.6 Hz), 4.14 (dd,

1H, *J* = 15.6, 9.2 Hz), 3.82 (s, 3H), 3.59 (dd, 1H, *J* = 15.6, 3.6 Hz), 3.12 (dt, 1H, *J* = 9.2, 7.2 Hz), 2.97 (dt, 1H, *J* = 9.2, 6.8 Hz,), 1.37–1.04 (m, 12H), 0.88 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 139.9, 133.6, 131.3, 128.8, 128.5, 128.2, 114.0, 79.9, 68.8, 55.2, 54.5, 31.8, 29.42, 29.36, 29.2, 25.9, 22.6, 14.1.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{29}H_{37}NO_6S_2Na^+$ 582.1955; Found 582.1955.

8c:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **8c** as a pale yellow oil (62.6 mg, 0.12 mmol, 62% yield).

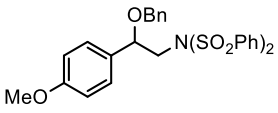
IR (ATR, cm^{-1}): 3071, 3005, 2859, 1512, 1377, 1250, 1167.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.02 (m, 4H), 7.67–7.58 (m, 2H), 7.55–7.48 (m, 4H), 7.27 (d, 2H, *J* = 8.8 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 4.79 (dd, 1H, *J* = 9.2, 3.6 Hz), 4.16 (dd, 1H, *J* = 16.0, 9.2 Hz), 3.80 (s, 3H), 3.59 (dd, 1H, *J* = 15.6, 3.6 Hz), 2.95 (dd, 1H, *J* = 10.4, 6.8 Hz), 2.90 (dd, 1H, *J* = 10.4, 6.8 Hz), 0.78–0.63 (m, 1H), 0.49–0.29 (m, 2H), 0.05–-0.04 (m, 1H), -0.04–-0.13 (m, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.5, 139.8, 133.6, 131.1, 128.7, 128.6, 128.3, 114.0, 79.4, 73.0, 55.2, 54.5, 10.3, 3.54, 2.72.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{27}NO_6S_2Na^+$ 524.1172; Found 524.1176.

8d:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8d** as a colorless oil (80.4 mg, 0.15 mmol, 74% yield).

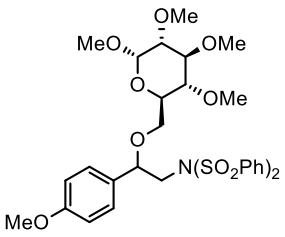
IR (ATR, cm^{-1}): 2976, 2864, 1614, 1512, 1377, 1250, 1167.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08–7.96 (m, 4H), 7.61–7.50 (m, 2H), 7.43–7.23 (m, 9H), 7.17–7.09 (m, 2H), 6.91 (d, 2H, *J* = 8.4 Hz), 4.79 (dd, 1H, *J* = 10.0, 3.2 Hz), 4.35 (d, 1H, *J* = 12.0 Hz), 4.27 (dd, 1H, *J* = 16.0, 9.6 Hz), 4.04 (d, 1H, *J* = 12.0 Hz), 3.82 (s, 3H), 3.61 (dd, 1H, *J* = 16.0, 3.6 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.8, 139.6, 138.0, 133.6, 130.5, 128.7, 128.6, 128.4, 128.2, 127.4, 114.2, 79.7, 70.0, 55.3, 54.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{28}H_{27}NO_6S_2Na^+$ 560.1172; Found 560.1176.

8e:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8e** as a colorless oil (57.0 mg, 0.086 mmol, 43% yield, *dr* = 51:49).

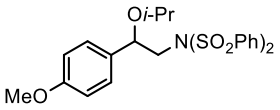
IR (ATR, cm^{-1}): 2934, 2837, 1373, 1167, 1032, 719.

^{1}H NMR (diastereo mixture, *dr* = 51:49, $CDCl_3$, 400 MHz): δ 8.05–7.95 (m, 8H), 7.66–7.58 (m, 4H), 7.56–7.45 (m, 8H), 7.33–7.27 (m, 4H), 6.88 (d, 4H, *J* = 8.8 Hz), 4.85 (dd, 1H, *J* = 8.4, 4.4 Hz), 4.78–4.69 (m, 3H), 4.12 (dd, 1H, *J* = 11.2, 8.8 Hz), 4.08 (dd, 1H, *J* = 11.2, 8.8 Hz), 3.82 (s, 3H), 3.81 (s, 3H), 3.71 (dd, 1H, *J* = 13.6, 4.4 Hz), 3.67 (dd, 1H, *J* = 13.6, 4.4 Hz), 3.61 (s, 3H), 3.60 (s, 3H), 3.56–3.35 (m, 6H), 3.49 (s, 3H), 3.48 (s, 3H), 3.42 (s, 6H), 3.38 (s, 3H), 3.34–3.23 (m, 2H), 3.28 (s, 3H), 3.16 (dd, 1H, *J* = 9.6, 3.6 Hz), 3.05 (dd, 1H, *J* = 9.6, 3.6 Hz), 2.97 (dd, 1H, *J* = 10.0, 8.8 Hz), 2.94 (dd, 1H, *J* = 10.0, 8.8 Hz).

^{13}C{^{1}H} NMR (diastereo mixture, *dr* = 51:49, $CDCl_3$, 101 MHz): δ 159.71, 159.66, 139.7, 139.5, 133.70, 133.65, 130.7, 130.5, 128.90, 128.85, 128.7, 128.6, 128.4, 114.0, 97.1, 83.8, 83.4, 81.7, 81.6, 80.9, 80.2, 79.9, 79.8, 70.6, 69.9, 68.0, 67.9, 60.8, 60.7, 60.4, 60.3, 58.92, 58.88, 55.2, 55.1, 54.2, 53.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{31}H_{39}NO_{11}S_2Na^+$ 688.1857; Found 688.1855.

8f:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8f** as a white solid (60.5 mg, 0.12 mmol, 61% yield).

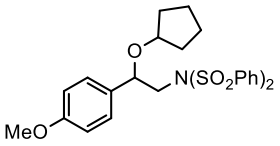
IR (ATR, cm^{-1}): 2968, 1510, 1373, 1250, 1163, 756.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07 (d, 4H, J = 7.6 Hz), 7.63 (t, 2H, *J* = 7.6 Hz), 7.53 (t, 4H, *J* = 7.6 Hz), 7.30 (d, 2H, *J* = 8.8 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 4.85 (dd, 1H, *J* = 9.2, 3.6 Hz), 4.12 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.82 (s, 3H), 3.56 (dd, 1H, *J* = 16.0, 4.0 Hz), 3.32 (hept, 1H, *J* = 6.0 Hz), 0.96 (d, 3H, *J* = 6.4 Hz), 0.80 (d, 3H, *J* = 6.0 Hz).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 159.5, 139.7, 133.6, 131.9, 128.79, 128.77, 128.3, 113.9, 68.9, 55.2, 54.7, 23.2, 20.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{27}NO_6S_2Na^+$ 512.1172; Found 512.1173.

8g:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8g** as a colorless oil (41.8 mg, 0.081 mmol, 40% yield).

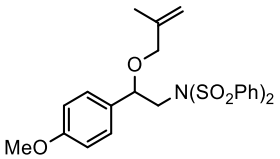
IR (ATR, cm^{-1}): 3069, 2957, 2258, 1612, 1516, 1447, 1381, 1243, 1171.

^1H NMR ($CDCl_3$, 400 MHz): δ 8.01 (d, 4H, *J* = 8.0 Hz), 7.63 (t, 2H, *J* = 7.6 Hz), 7.51 (t, 4H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.8 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 4.78 (dd, 1H, *J* = 9.2, 4.0 Hz), 4.07 (dd, 1H, *J* = 15.6, 8.8 Hz), 3.82 (s, 3H), 3.70–3.63 (m, 1H), 3.62 (dd, 1H, *J* = 15.6, 4.0 Hz), 1.64–1.44 (m, 4H), 1.43–1.23 (m, 4H).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 159.5, 139.7, 133.6, 131.9, 128.8, 128.6, 128.4, 114.0, 79.2, 78.0, 55.3, 54.5, 32.7, 31.2, 23.4.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{26}H_{29}NO_6S_2Na^+$ 538.1329; Found 538.1314.

8h:



The reaction was carried out according to the typical procedure. The crude mixture was

purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8h** as a colorless oil (57.2 mg, 0.11 mmol, 57% yield).

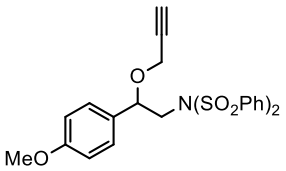
IR (ATR, cm^{-1}): 3073, 3005, 2918, 2859, 1609, 1512, 1368, 1254, 1165.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13–8.04 (m, 4H), 7.67–7.58 (m, 2H), 7.55–7.47 (m, 4H), 7.29 (d, 2H, *J* = 8.4 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 4.89 (s, 1H), 4.84 (s, 1H), 4.72 (dd, 1H, *J* = 9.6, 3.6 Hz), 4.21 (dd, 1H, *J* = 16.0, 9.6 Hz), 3.82 (s, 3H), 3.65 (d, 1H, *J* = 12.8 Hz), 3.58 (dd, 1H, *J* = 15.6, 3.2 Hz), 3.44 (d, 1H, *J* = 12.8 Hz), 1.52 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.7, 141.7, 139.7, 133.6, 130.5, 128.8, 128.7, 128.4, 114.0, 112.3, 79.0, 71.7, 55.3, 54.2, 19.4.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{27}NO_6S_2Na^+$ 524.1172; Found 524.1173.

8i:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8i** as a pale yellow solid (54.6 mg, 0.11 mmol, 56% yield).

IR (ATR, cm^{-1}): 3285, 3067, 2918, 2839, 2120, 1611, 1512, 1371, 1165.

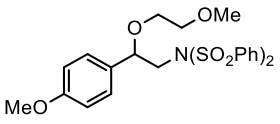
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.08 (m, 4H), 7.67–7.59 (m, 2H), 7.57–7.49 (m, 4H), 7.30 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 4.95 (dd, 1H, *J* = 9.2, 3.2 Hz), 4.22 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.86 (dd, 1H, *J* = 15.6, 2.4 Hz), 3.82 (s, 3H), 3.66 (dd, 1H, *J* = 15.6, 6.4 Hz), 3.58 (dd, 1H, *J* = 15.6, 2.8 Hz), 2.32 (t, 1H, *J* = 2.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.9, 139.7, 133.7, 129.4, 128.8, 128.7, 128.5, 114.2, 79.6,

79.1, 74.6, 55.33, 55.29, 54.1.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{23}NO_6S_2Na^+$ 508.0859; Found 508.0861.

8j:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8j** as a pale yellow solid (63.8 mg, 0.13 mmol, 62% yield).

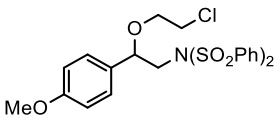
IR (ATR, cm^{-1}): 3082, 2880, 2808, 1614, 1512, 1342, 1253, 1167.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.09–8.02 (m, 4H), 7.66–7.60 (m, 2H), 7.55–7.48 (m, 4H), 7.29 (d, 2H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 4.75 (dd, 1H, *J* = 8.8, 3.6 Hz), 4.16 (dd, 1H, *J* = 15.6, 8.8 Hz), 3.81 (s, 3H), 3.64 (dd, 1H, *J* = 15.6, 4.0 Hz), 3.35–3.25 (m, 3H), 3.28 (s, 3H), 3.25–3.17 (m, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.7, 139.7, 133.6, 130.8, 128.8, 128.6, 128.4, 114.0, 80.6, 71.5, 67.7, 58.9, 55.2, 54.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{27}NO_7S_2Na^+$ 528.1121; Found 528.1120.

8k:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8k** as a pale yellow oil (48.7 mg, 0.095 mmol, 48% yield).

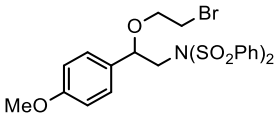
IR (ATR, cm^{-1}): 2967, 1512, 1377, 1250, 1167, 824.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10–8.03 (m, 4H), 7.65 (t, 2H, *J* = 7.2 Hz), 7.54 (t, 4H, *J* = 7.6 Hz), 7.29 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 8.4 Hz), 4.74 (dd, 1H, *J* = 9.2, 3.6 Hz), 4.18 (dd, 1H, *J* = 16.0, 9.6 Hz), 3.82 (s, 3H), 3.62 (dd, 1H, *J* = 16.0, 3.6 Hz), 3.42–3.32 (m, 1H), 3.30–3.12 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.9, 139.7, 133.7, 130.2, 128.8, 128.5, 128.3, 114.2, 80.7, 68.6, 55.3, 54.4, 42.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{24}ClNO_6S_2Na^+$ 532.0626; Found 532.0630.

8l:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8l** as a pale yellow oil (51.2 mg, 0.092 mmol, 46% yield).

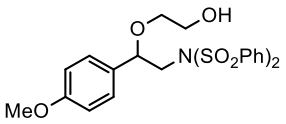
IR (ATR, cm^{-1}): 2965, 2843, 1614, 1512, 1377, 1250, 1167.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13–8.00 (m, 4H), 7.71–7.60 (m, 2H), 7.59–7.49 (m, 4H), 7.29 (d, 2H, *J* = 8.4 Hz), 6.90 (d, 2H, *J* = 8.4 Hz), 4.73 (dd, 1H, *J* = 9.6, 3.6 Hz), 4.17 (dd, 1H, *J* = 16.0, 9.6 Hz), 3.82 (s, 3H), 3.62 (dd, 1H, *J* = 16.0, 3.6 Hz), 3.40 (td, 1H, *J* = 10.8, 7.2 Hz), 3.26 (ddd, 1H, *J* = 10.8, 7.6, 5.2 Hz), 3.08 (ddd, 1H, *J* = 10.0, 7.6, 5.2 Hz), 2.95 (td, 1H, *J* = 10.0, 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.9, 139.8, 133.8, 130.1, 128.8, 128.5, 128.3, 114.2, 80.6, 68.5, 55.3, 54.5, 29.5.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{24}BrNO_6S_2Na^+$ 576.0121; Found 576.0123.

8m:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8m** as a pale yellow oil (47.5 mg, 0.097 mmol, 48% yield).

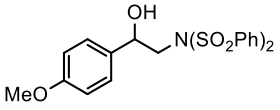
IR (ATR, cm^{-1}): 3545, 2965, 2866, 1614, 1512, 1377, 1250, 1167.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05–7.95 (m, 4H), 7.70–7.60 (m, 2H), 7.58–7.49 (m, 4H), 7.26 (d, 2H, *J* = 8.4 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 4.62 (dd, 1H, *J* = 9.6, 3.2 Hz), 4.12 (dd, 1H, *J* = 15.6, 9.6 Hz), 3.81 (s, 3H), 3.54 (ddd, 1H, *J* = 9.0, 6.8, 2.8 Hz), 3.47 (ddd, 1H, *J* = 9.0, 5.6, 2.8 Hz), 3.31 (ddd, 1H, *J* = 9.6, 5.2, 2.8 Hz), 3.03 (ddd, 1H, *J* = 10.0, 6.8, 2.8 Hz), 2.16 (br, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.8, 139.7, 133.8, 130.3, 129.0, 128.4, 128.1, 114.2, 79.6, 69.9, 61.6, 55.3, 54.4.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{25}NO_7S_2Na^+$ 514.0965; Found 514.0968.

8n:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **8n** as a pale yellow oil (39.7 mg, 0.089 mmol, 44% yield).

IR (ATR, cm^{-1}): 3545, 2976, 2843, 1514, 1377, 1252, 1167.

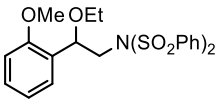
^{1}H NMR (CDCl3, 400 MHz): δ 8.13–8.03 (m. 4H), 7.66 (t, 2H, *J* = 7.6 Hz), 7.56 (t, 4H, *J* = 8.0 Hz), 7.33 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 8.4 Hz), 5.09 (br, 1H), 3.84 (d, 2H, *J* = 6.4 Hz),

3.81 (s, 3H), 2.73 (br, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 139.4, 134.0, 132.8, 129.1, 128.5, 127.1, 114.1, 72.4, 55.6, 55.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{21}NO_6S_2Na^+$ 470.0702; Found 470.0702.

10a:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10a** as a white solid (37.7 mg, 0.079 mmol, 40% yield).

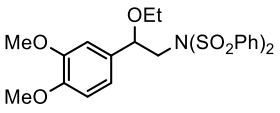
IR (ATR, cm^{-1}): 2967, 2897, 1450, 1373, 1163, 1088, 1024.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15 (d, 4H, *J* = 7.6 Hz), 7.64 (t, 2H, *J* = 7.6 Hz), 7.54 (t, 4H, *J* = 8.0 Hz), 7.44 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.30–7.24 (m, 1H), 6.99 (t, 1H, *J* = 7.6 Hz), 6.87 (d, 1H, *J* = 8.0 Hz), 5.14 (dd, 1H, *J* = 10.0, 2.8 Hz), 4.10 (dd, 1H, *J* = 15.2, 10.0 Hz), 3.89 (s, 3H), 3.61 (dd, 1H, *J* = 15.6, 3.2 Hz), 3.29 (dq, 1H, *J* = 9.6, 7.2 Hz), 3.06 (dq, 1H, *J* = 9.6, 6.8 Hz), 0.98 (t, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 157.1, 140.0, 133.6, 128.9, 128.69, 128.67, 127.4, 127.1, 120.9, 110.3, 74.1, 64.4, 55.3, 52.5, 15.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{25}NO_6S_2Na^+$ 498.1016; Found 498.1011.

10b:



The reaction was carried out at 70 °C in an aluminum heating block. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10b** as a colorless oil (44.8 mg, 0.089 mmol, 45% yield).

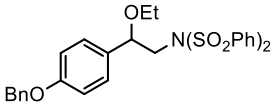
IR (ATR, cm^{-1}): 3071, 2928, 2839, 1516, 1373, 1163, 1024, 862.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10–8.04 (m, 4H), 7.64 (t, 2H, *J* = 7.6 Hz), 7.53 (t, 4H, *J* = 8.0 Hz), 6.94– 6.80 (m, 3H), 4.68 (dd, 1H, *J* = 9.2, 3.6 Hz), 4.16 (dd, 1H, *J* = 15.6, 8.8 Hz), 3.89 (s, 3H), 3.88 (s, 3H), 3.61 (dd, 1H, *J* = 16.0, 3.6 Hz), 3.25 (dq, 1H, *J* = 9.6, 7.2 Hz), 3.08 (dq, 1H, *J* = 9.6, 7.2 Hz), 0.97 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 149.2, 148.9, 139.8, 133.7, 131.7, 128.8, 128.5, 119.4, 111.0, 109.4, 80.3, 64.0, 55.93, 55.87, 54.6, 15.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{27}NO_7S_2Na^+$ 528.1121; Found 528.1124.

10c:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10c** as a colorless oil (75.0 mg, 0.14 mmol, 67% yield).

IR (ATR, cm^{-1}): 3067, 2972, 2872, 1508, 1371, 1167, 1086.

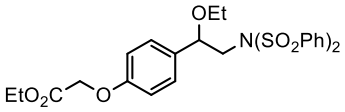
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14–8.04 (m, 4H), 7.69–7.59 (m, 2H), 7.58–7.49 (m, 4H), 7.48–7.38 (m, 4H), 7.38–7.32 (m, 1H), 7.29 (d, 2H, *J* = 8.4 Hz), 6.97 (d, 2H, *J* = 8.8 Hz), 5.07 (s, 2H),

4.69 (dd, 1H, *J* = 9.2, 3.2 Hz), 4.17 (dd, 1H, *J* = 15.6, 9.6 Hz), 3.57 (dd, 1H, *J* = 16.0, 3.2 Hz), 3.23 (dq, 1H, *J* = 9.2, 6.8 Hz), 3.05 (dq, 1H, *J* = 9.2, 6.8 Hz), 0.95 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 158.8, 139.8, 136.8, 133.6, 131.5, 128.8, 128.59, 128.56, 128.2, 128.0, 127.5, 114.9, 79.9, 70.0, 63.9, 54.6, 14.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{29}H_{29}NO_6S_2Na^+$ 574.1329; Found 574.1331.

10d:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10d** as a colorless oil (64.8 mg, 0.12 mmol, 59% yield).

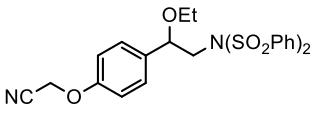
IR (ATR, cm^{-1}): 3067, 2976, 2872, 1755, 1371, 1167, 1084.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12–8.05 (m, 4H), 7.67–7.60 (m, 2H), 7.58–7.49 (m, 4H), 7.29 (d, 2H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 4.68 (dd, 1H, *J* = 9.6, 3.2 Hz), 4.62 (s, 2H), 4.28 (q, 2H, *J* = 7.2 Hz), 4.14 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.55 (dd, 1H, *J* = 15.6, 3.2 Hz), 3.20 (dq, 1H, *J* = 9.6, 7.2 Hz), 3.04 (dq, 1H, *J* = 9.6, 6.8 Hz), 1.31 (t, 3H, *J* = 7.2 Hz), 0.93 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 168.8, 157.8, 139.8, 133.7, 132.4, 128.8, 128.6, 128.2, 114.8, 79.9, 65.3, 63.9, 61.4, 54.6, 14.9, 14.1.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{26}H_{29}NO_8S_2Na^+$ 570.1227; Found 570.1229.

10e:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10e** as a colorless oil (44.0 mg, 0.088 mmol, 44% yield).

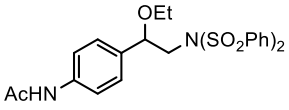
IR (ATR, cm^{-1}): 3067, 2976, 2872, 2263, 1508, 1369, 1165, 1084.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12–8.06 (m, 4H), 7.68–7.61 (m, 2H), 7.57–7.51 (m, 4H), 7.35 (d, 2H, *J* = 8.8 Hz), 6.97 (d, 2H, *J* = 8.8 Hz), 4.78 (s, 2H), 4.71 (dd, 1H, *J* = 9.6, 3.2 Hz), 4.15 (dd, 1H, *J* = 15.6, 9.2 Hz), 3.55 (dd, 1H, *J* = 15.6, 3.2 Hz), 3.21 (dq, 1H, *J* = 9.6, 7.2 Hz), 3.05 (dq, 1H, *J* = 9.6, 6.8 Hz), 0.94 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 156.4, 139.8, 134.1, 133.7, 128.8, 128.6, 128.5, 115.2, 115.0, 79.9, 64.1, 54.6, 53.6, 14.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{24}N_2O_6S_2Na^+$ 523.0968; Found 523.0967.

10f:



The reaction was carried out according to the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 1:1) to give **10f** as a colorless oil (60.6 mg, 0.12 mmol, 60% yield).

IR (ATR, cm^{-1}): 3300, 3065, 2976, 1668, 1514, 1368, 1165, 1084.

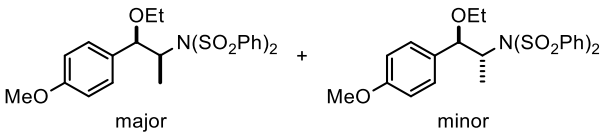
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.02 (m, 4H), 7.63 (t, 2H, *J* = 7.2 Hz), 7.53 (t, 4H, *J* = 8.0 Hz), 7.49 (d, 2H, *J* = 8.4 Hz), 7.39 (br, 1H), 7.30 (d, 2H, *J* = 8.4 Hz), 4.69 (dd, 1H, *J* = 9.6, 3.2

Hz), 4.15 (dd, 1H, *J* = 15.6, 9.6 Hz), 3.54 (dd, 1H, *J* = 15.6, 2.8 Hz), 3.21 (dq, 1H, *J* = 9.6, 6.8 Hz), 3.04 (dq, 1H, *J* = 9.6, 6.8 Hz), 2.16 (s, 3H), 0.93 (t, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 168.4, 139.7, 137.9, 135.1, 133.7, 128.8, 128.5, 127.5, 120.1, 80.0, 64.1, 54.5, 24.5, 14.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{26}N_2O_6S_2Na^+$ 525.1124; Found 525.1127.

10g:



The reaction was carried out at 70 °C in an aluminum heating block. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **10g** as a colorless oil (56.9 mg, 0.12 mmol, 60% yield, *dr* = 80:20). Recrystallization of **10g** from CH_2Cl_2/pentane gave a single crystal of the minor diastereomer, and its structure was confirmed by an X-ray structural analysis.

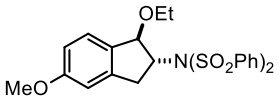
IR (ATR, cm^{-1}): 3064, 2974, 1350, 1242, 1165, 1082, 827.

^{1}H NMR (the major diastereomer, *dr* = 80:20, $CDCl_3$, 400 MHz): major: δ 7.69 (d, 4H, *J* = 7.2 Hz), 7.60– 7.54 (m, 2H), 7.40 (t, 4H, *J* = 7.6 Hz), 7.22 (d, 2H, *J* = 8.8 Hz), 6.68 (d, 2H, *J* = 8.8 Hz), 4.78 (d, 1H, *J* = 9.2 Hz), 4.31 (dq, 1H, *J* = 9.2, 6.8 Hz), 3.82 (s, 3H), 3.25 (q, 2H, *J* = 6.8 Hz), 1.56 (d, 3H, *J* = 6.8 Hz), 1.09 (t, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR (the major diastereomer, *dr* = 80:20, $CDCl_3$, 101 MHz): δ 159.2, 133.4, 130.5, 129.8, 129.3, 128.7, 128.5, 113.4, 83.5, 64.2, 63.1, 55.1, 18.0, 15.2.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{27}NO_6S_2Na^+$ 512.1172; Found 512.1169.

10h:



The reaction was carried out at 50 °C in an aluminum heating block. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **10h** as a colorless oil (45.9 mg, 0.094 mmol, 48% yield).

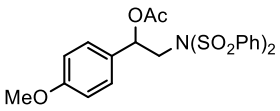
IR (ATR, cm^{-1}): 2970, 2928, 1449, 1368, 1165, 1082.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10 (d, 4H, *J* = 6.8 Hz), 7.72–7.65 (m, 2H), 7.63–7.55 (m, 4H), 7.22 (d, 1H, *J* = 8.0 Hz), 6.79 (dd, 1H, *J* = 8.4, 2.4 Hz), 6.60 (d, 1H, *J* = 2.4 Hz), 5.61 (d, 1H, *J* = 6.0 Hz), 4.80 (td, 1H, *J* = 8.8, 6.4 Hz), 3.76 (s, 3H), 3.61–3.44 (m, 2H), 3.30 (dd, 1H, *J* = 15.6, 8.4 Hz), 2.91 (dd, 1H, *J* = 15.6, 9.2 Hz), 1.09 (t, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 160.2, 140.0, 133.9, 132.5, 129.1, 128.5, 125.6, 113.9, 109.2, 85.0, 68.4, 65.0, 55.3, 35.5, 15.6.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{25}NO_6S_2Na^+$ 510.1016; Found 510.1012.

■ Copper-Catalyzed Aminoacetoxylation of Ethylarene 1.



The reaction was carried out with 5.0 equiv of AcOH instead of EtOH. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give an aminoacetoxylated product as a colorless oil (35.7 mg, 0.073 mmol, 37%).

IR (ATR, cm^{-1}): 3067, 2934, 2839, 1740, 1369, 1229, 1165, 1030.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (d, 4H, *J* = 7.6 Hz), 7.65 (t, 2H, *J* = 7.6 Hz), 7.53 (t, 4H, *J* = 7.6 Hz), 7.31 (d, 2H, *J* = 8.8 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 6.05 (dd, 1H, *J* = 9.2, 4.4 Hz), 4.10

(dd, 1H, *J* = 15.6, 9.2 Hz), 3.92 (dd, 1H, *J* = 15.6, 4.4 Hz), 3.81 (s, 3H), 1.89 (s, 3H).

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 101 MHz): δ 169.8, 159.9, 139.4, 133.9, 129.3, 129.0, 128.4, 128.2, 114.1, 73.4, 55.3, 52.2, 20.9.

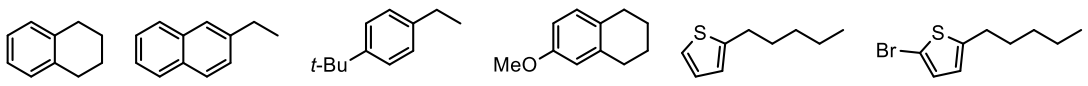
HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{23}NO_7S_2Na^+$ 512.0808; Found 512.0806.

■ Substrate Scope (Limitation).

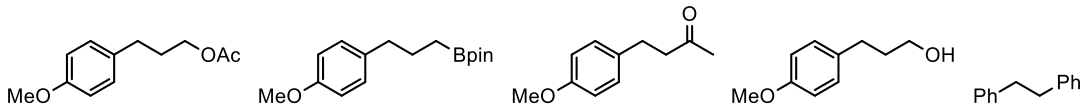
Nucleophiles

n.d. n.d. < 15% n.d. n.d.

Alkylarenes



n.d. n.d. < 15% n.d. n.d. n.d.



n.d. < 15% n.d. n.d. n.d.

■ X-Ray Crystallography of the Minor Diastereomer of 10g.

A single crystal of the minor diastereomer of **10g** was placed on the end of a micro-mount coated with NVH oil. The X-ray intensity data collection was carried out on a Rigaku HyPix-6000 CCD area detector using graphitemonochromated Mo-Kα radiation (l = 0.71075 Å) at 100(2) K. Preliminary indexing was performed from a set of twelve frames. Equivalent reflections were merged, and the collected images were processed by a Rigaku CrysAlisPro program. The initial structures were determined by the direct or Patterson method on SHELXS.[27] The further structure determination was performed by Fourier transform method and refined by least squares method on SHELXL[27,28] operated by Yadokari-XG software package.[29] All reflections were used during refinement with the exception of affected reflections by the beam-

stopper. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using riding models, except for the hydroxy hydrogen in the hydrolysis product. The thermal ellipsoids of the disorders were fixed by SHELXL restraints. These results were checked by the IUCR's CheckCIF routine.

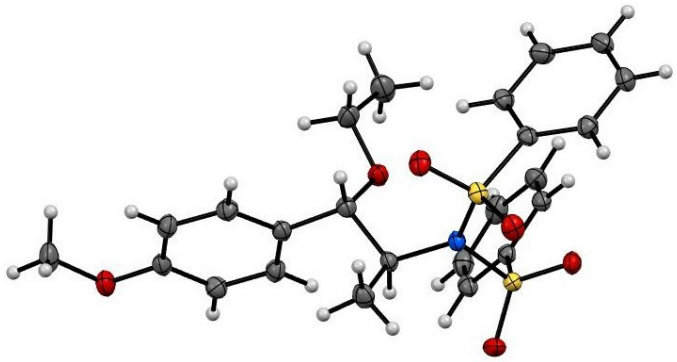


Figure 3. ORTEP drawing of the minor diastereomer of **10g** (CCDC 2245280). Thermal ellipsoids are shown at 50% probability.

Table 4. Crystal Data and Structure Refinement for the Minor Diastereomer of 10g.

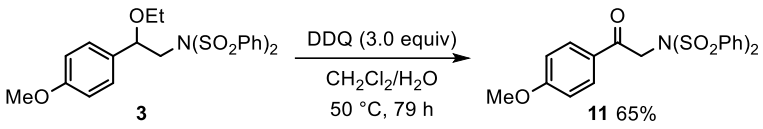
Empirical formula	$C_{24}H_{27}NO_6S_2$
Formula weight	489.58
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system	*triclinic*
Space group	P –1
Cell constants:	a = 10.0431(5) Å, α = 108.143(4)°
	b = 11.2263(5) Å, β = 96.635(4)°
	c = 11.2900(4) Å, γ = 101.380(4)°
Volume	1164.25(9) $Å^3$
Z	2

Absorption coefficient	0.270 mm^{-1}
F(000)	516
Crystal size	0.47 x 0.48 x 0.83 mm^3
Theta range for data collection	3.8810 to 29.8050°
Index ranges	–12<=h<=13, –14<=k<=14, –14<=l<=14
Reflections collected	13944
Independent reflections	5184 [*R* (int) = 0.0300]
Completeness to theta	25.242° 99.5%
Data / restraints / parameters	5184 / 0 / 301
Goodness-of-fit on F^2	1.073
Final R indices [I>2σ(I)]	R_1 = 0.0373, wR_2 = 0.1015
R indices (all data)	R_1 = 0.0422, wR_2 = 0.1049

■ **A 1.0 mmol Scale Reaction.**

In a nitrogen-filled glove-box, $Cu(MeCN)_4PF_6$ (18.6 mg, 0.050 mmol, 5.0 mol %), *N*-fluorobenzenesulfonimide (693.7 mg, 2.2 mmol, 2.2 equiv), EtOH (117 μL, 2.0 mmol, 2.0 equiv), and MeCN (10 mL, 0.10 M) were added to 4-ethylanisole (136 mg, 1.0 mmol, 1.0 equiv), 4,4'-$(MeO)_2$-bpy (10.8 mg, 0.050 mmol, 5.0 mol %), and $CaCO_3$ (150 mg, 1.5 mmol, 1.5 equiv) in an oven-dried Schlenk tube equipped with a stirrer bar. The vessel was taken outside the glove-box. The reaction mixture was stirred at 80 °C in an oil bath. After 21 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **3** as a colorless oil (352.4 mg, 0.74 mmol, 74% yield).

■ **The Synthesis of α-Aminoketone 11.**



The α-aminoketone **11** was synthesized according to the following procedure. To an oven-dried 4 mL vial equipped with a stirrer bar were added **3** (94.0 mg, 0.20 mmol, 1.0 equiv), DDQ (140 mg, 0.60 mmol, 3.0 equiv), CH_2Cl_2 (2.0 mL), and H_2O (100 μL). The reaction mixture was stirred at 50 °C in an aluminum heating block. After 79 hours, the mixture was filtered and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **11** as a pale yellow solid (57.0 mg, 0.13 mmol, 65% yield).

IR (ATR, cm^{-1}): 3064, 2937, 2842, 1694, 1599, 1369, 1237, 1163.

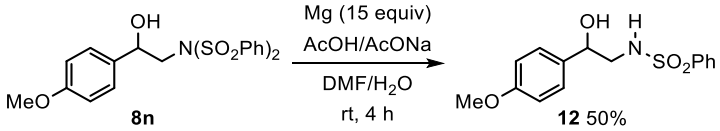
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.03 (m, 4H), 7.85 (d, 2H, *J* = 8.4 Hz), 7.66 (t, 2H, *J* = 7.2 Hz), 7.55 (t, 4H, *J* = 8.0 Hz), 6.94 (d, 2H, *J* = 8.8 Hz), 5.14 (s, 2H), 3.87 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 189.2, 164.1, 139.3, 134.0, 130.3, 128.9, 128.8, 127.3, 114.1, 55.5, 53.2.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{19}NO_6S_2Na^+$ 468.0546; Found 468.0547.

■ **The Synthesis of *N*-Protected Morpholine 13.**

12:



The mono-desulfonylated product **12** was synthesized according to the literature procedure.[30] To an oven-dried 10 mL two-necked round-bottom flask equipped with a stirrer bar were added **8n** (140 mg, 0.32 mmol, 1.0 equiv), AcOH/AcONa buffer (1:1, 8.0 M, 1.6 mL), and

DMF (4.8 mL, 0.067 M). Then magnesium turnings (120 mg, 4.8 mmol, 15 equiv) were added in one portion. The reaction mixture was stirred at room temperature. After 4 hours, H_2O was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 1:1) to give **12** as a white solid (49.7 mg, 0.16 mmol, 50% yield).

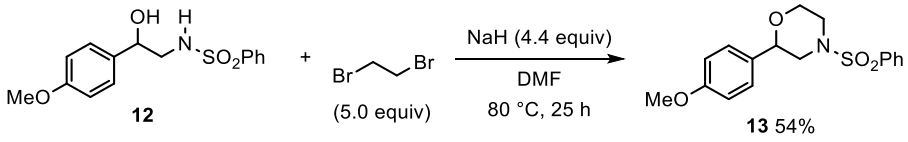
IR (ATR, cm^{-1}): 3431, 3139, 2837, 1511, 1249, 1148, 1026.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84 (d, 2H, *J* = 8.0 Hz), 7.57 (t, 1H, *J* = 7.6 Hz), 7.49 (t, 2H, *J* = 7.6 Hz), 7.18 (d, 2H, *J* = 8.8 Hz), 6.84 (d, 2H, *J* = 8.8 Hz), 5.21 (br, 1H), 4.73 (dd, 1H, *J* = 8.4, 3.6 Hz), 3.78 (s, 3H), 3.27–3.14 (m, 1H), 3.04 (ddd, 1H, *J* = 13.6, 8.8, 4.8 Hz), 2.63 (br, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 139.8, 132.9, 132.7, 129.1, 127.1, 127.0, 114.1, 72.4, 55.3, 50.2.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{17}NO_4SNa^+$ 330.0770; Found 330.0775.

13:



N-Protected morpholine **13** was synthesized according to the following procedure. To an oven-dried 4 mL vial equipped with a stirrer bar were added **12** (13.7 mg, 0.045 mmol, 1.0 equiv), NaH (60% in liquid paraffin, 7.9 mg, 0.20 mmol, 4.4 equiv), and DMF (450 μL, 0.10 M). Then, 1,2-dibromoethane (17 μL, 0.20 mmol, 4.4 equiv) was added at 0 °C. The reaction mixture was stirred at 80 °C in an aluminum heating block. After 25 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried

over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13** as a white solid (8.0 mg, 0.024 mmol, 54% yield).

IR (ATR, cm^{-1}): 2913, 2853, 1515, 1246, 1166, 1089, 962.

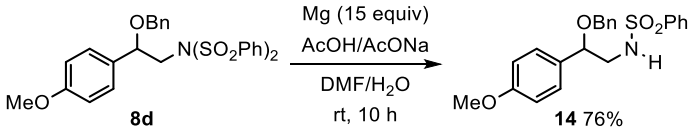
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91–7.77 (m, 2H), 7.63–7.55 (m, 1H), 7.54–7.45 (m, 2H), 7.19 (d, 2H, *J* = 8.8 Hz), 6.85 (d, 2H, *J* = 8.8 Hz), 4.99 (br, 1H), 4.79–4.68 (m, 1H), 3.79 (s, 3H), 3.23 (ddd, 1H, *J* = 13.2, 8.4, 4.0 Hz), 3.05 (ddd, 1H, *J* = 13.2, 8.8, 4.4 Hz), 2.35 (br, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 135.3, 133.1, 130.8, 129.2, 127.8, 127.3, 113.9, 66.2, 55.3, 51.9, 45.4.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{19}NO_4SNa^+$ 356.0927; Found 356.0931.

■ Semisynthesis of (±)-Longimammine.

14:



Compound **14** was synthesized according to the literature procedure.[30] To an oven-dried Schlenk tube equipped with a stirrer bar were added **8d** (470 mg, 0.87 mmol, 1.0 equiv), AcOH/AcONa buffer (1:1, 8.0 M, 4.4 mL), and DMF (13 mL, 0.067 M). Then magnesium turnings (319 mg, 13 mmol, 15 equiv) were added in one portion. The reaction mixture was stirred at room temperature. After 10 hours, H_2O was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 1:1) to give **14** as a white solid (264 mg, 0.66 mmol, 76% yield).

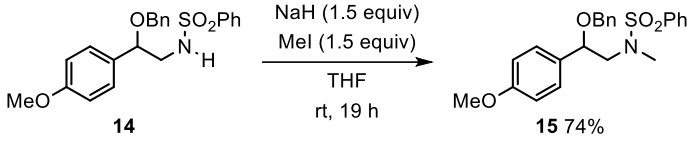
IR (KBr, cm^{-1}): 3295, 2869, 1609, 1512, 1325, 1248, 1164, 1075, 1028.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82–7.76 (m, 2H), 7.60–7.52 (m, 1H), 7.51–7.44 (m, 2H), 7.39–7.28 (m, 3H), 7.26–7.21 (m, 2H), 7.17 (d, 2H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 4.92 (d, 1H, *J* = 8.8 Hz), 4.38 (d, 1H, *J* = 11.2 Hz), 4.34 (dd, 1H, *J* = 9.2, 4.0 Hz), 4.16 (d, 1H, *J* = 11.6 Hz), 3.81 (s, 3H), 3.22 (ddd, 1H, *J* = 12.8, 9.2, 4.0 Hz), 3.08 (ddd, 1H, *J* = 12.8, 9.2, 4.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.8, 140.0, 137.6, 132.6, 130.2, 129.1, 128.5, 128.1, 128.0, 127.9, 127.0, 114.2, 79.3, 70.5, 55.3, 49.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{23}NO_4SNa^+$ 420.1240; Found 420.1240.

15:



Compound **15** was synthesized according to the following procedure. To an oven-dried 4 mL vial equipped with a stirrer bar were added **14** (218.6 mg, 0.55 mmol, 1.0 equiv), NaH (60% in liquid paraffin, 33.0 mg, 0.83 mmol, 1.5 equiv), and THF (1.1 mL, 0.50 M). Then, methyl iodide (51.4 μL, 0.83 mmol, 1.5 equiv) was added at 0 °C. The reaction mixture was stirred at room temperature. After 19 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 4:1) to give **15** as a colorless oil (166.7 mg, 0.41 mmol, 74% yield).

IR (KBr, cm^{-1}): 2931, 2888, 2863, 1610, 1516, 1340, 1247, 1163.

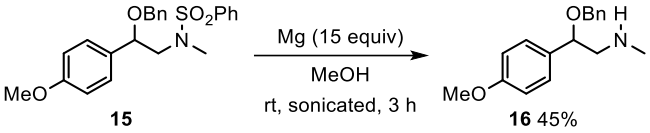
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79–7.72 (m, 2H), 7.58–7.51 (m, 1H), 7.51–7.43 (m, 2H), 7.38–7.23 (m, 7H), 6.91 (d, 2H, *J* = 8.8 Hz), 4.60 (dd, 1H, *J* = 8.4, 4.8 Hz), 4.43 (d, 1H, *J* = 11.6 Hz), 4.26 (d, 1H, *J* = 11.6 Hz), 3.82 (s, 3H), 3.30 (dd, 1H, *J* = 14.8, 5.2 Hz), 3.23 (dd, 1H, *J* = 14.4,

8.0 Hz), 2.80 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.6, 138.4, 138.1, 132.4, 131.2, 129.0, 128.3, 128.1, 127.7, 127.6, 127.2, 114.1, 80.9, 70.5, 56.6, 55.3, 37.1.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{25}NO_4SNa^+$ 434.1397; Found 434.1397.

16:



(±)-Longimammine-*O*-benzylether **16** was synthesized according to the literature procedure.[17] To an oven-dried Schlenk tube equipped with a stirrer bar were added **15** (104.3 mg, 0.25 mmol, 1.0 equiv), magnesium turnings (91.2 mg, 3.0 mmol, 15 equiv), and MeOH (5.0 mL, 0.050 M). The reaction mixture was stirred at room temperature under sonication. After 3 hours, brine was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (CH_2Cl_2/MeOH = 15:1) to give **16** as a white solid (30.7 mg, 0.11 mmol, 45% yield).

IR (KBr, cm^{-1}): 3338, 2919, 2850, 1611, 1513, 1248, 1029.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.24 (m, 7H), 6.92 (d, 2H, *J* = 8.8 Hz), 4.53 (dd, 1H, *J* = 8.4, 3.6 Hz), 4.46 (d, 1H, *J* = 11.6 Hz), 4.28 (d, 1H, *J* = 11.2 Hz), 3.82 (s, 3H), 2.93 (dd, 1H, *J* = 12.4, 9.2 Hz), 2.68 (dd, 1H, *J* = 12.4, 4.4 Hz), 2.42 (s, 3H), 2.16 (br, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 159.4, 138.3, 132.3, 128.4, 128.1, 127.9, 127.6, 114.0, 79.9, 70.5, 58.6, 55.3, 36.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{21}NO_2Na^+$ 294.1465; Found 294.1445.

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Chapter 3

Copper Photoredox Catalysis: *anti*-Markovnikov Hydration *via* Single-Electron Oxidation of Vinylarenes

Abstract

The author reports that a combination of copper(II) chloride and bathophenanthroline works as a photoredox catalyst under visible light irradiation. The copper(II) photocatalyst shows a strong oxidation ability enough to oxidize vinylarenes. Using this catalytic system, *anti*-Markovnikov hydration of vinylarenes proceeded efficiently. Detailed studies revealed a reaction mechanism and a property of the catalyst.

Introduction

Photoredox catalysts are currently an attractive tool in organic synthesis based on radical chemistry.[1] The rapid progress in this field has depended on the development of visible light photoredox catalysts. The photoexcited photoredox catalysts act as either single electron oxidants or reductants to generate various kinds of organic radicals (**Figure 1**a). However, photoredox catalysts exhibiting highly oxidative ability are rare (**Figure 1**b).[1b,2] Polypyridyl complexes of ruthenium(II) or iridium(III) are the most well-known photoredox catalyst, but these transition metals are too expensive and scares in nature. Although some organic photocatalysts showing high reduction potentials have been developed, they tend to suffer from poor thermal and photostability.[3] Furthermore, tuning their redox potential often requires the separate synthesis of independent catalyst structures. Therefore, the development of highly oxidative photoredox catalysts using earth-abundant transition metals is an important research area.[4]

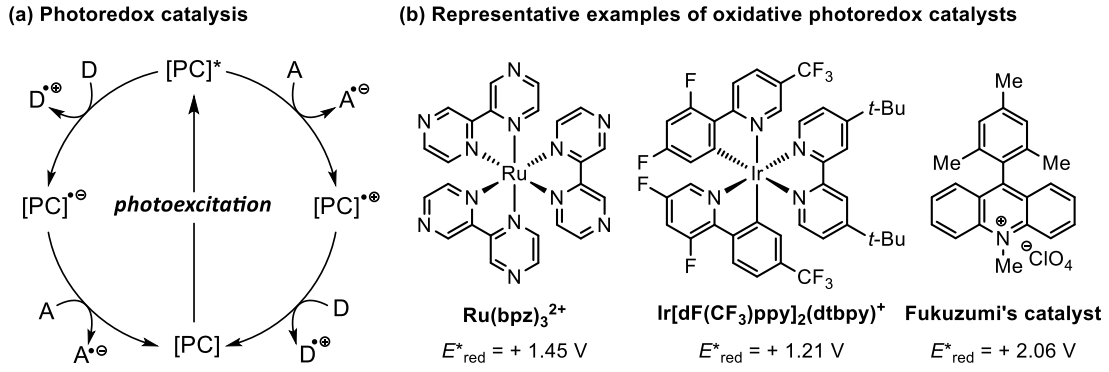
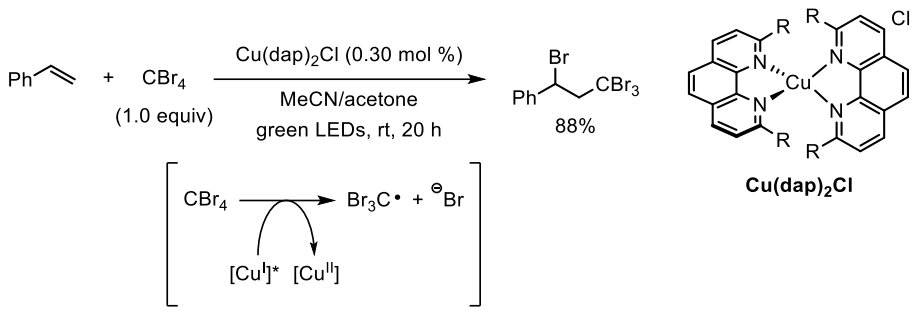


Figure 1. Photoredox catalysts.

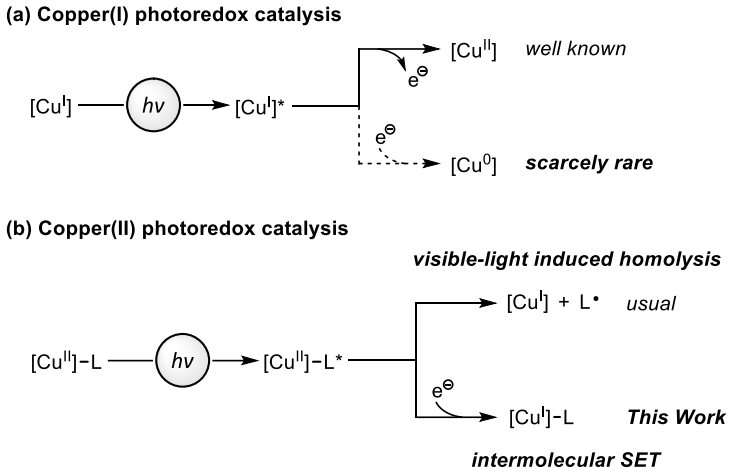
Copper is one of the most attractive options due to their abundance and low cost. Recently, based on the early work of Sauvage[5] and McMillin,[6] it emerged that homoleptic bis-diimine copper(I) or heteroleptic diamine-diphosphine copper(I) complexes work as photoredox catalysts and have strong reduction abilities.[7] Additionally, inspired by Reiser's pioneering work (**Scheme 1**),[8] various reactions using copper(I) photoredox catalysts have been reported.[9]

Scheme 1. An Early Example of Copper(I) Photoredox Catalysts



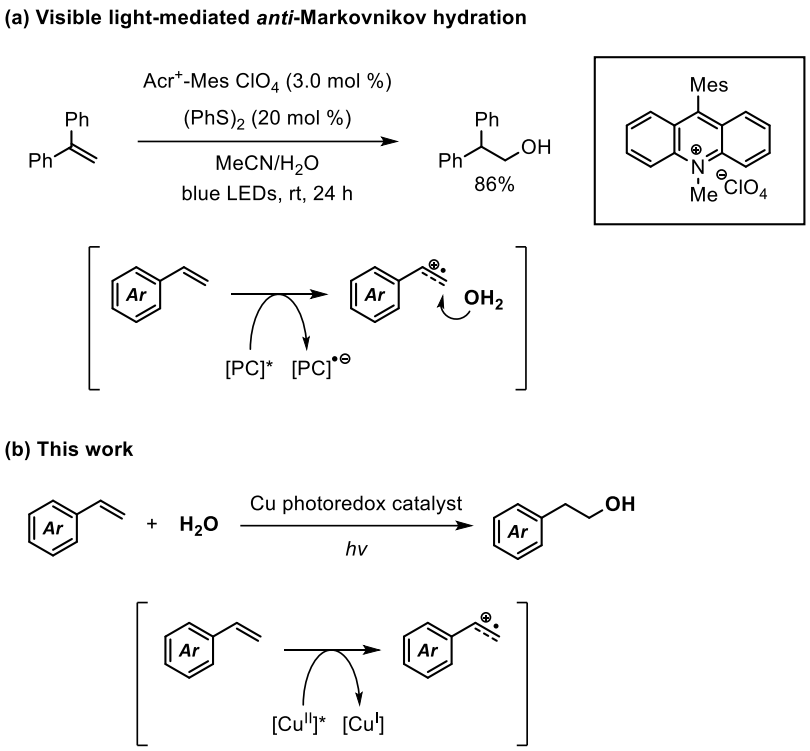
On the other hand, there are scarcely rare reports that photoexcited copper(I) complexes receive a single electron from organic molecules (**Scheme 2**a).[10] We then envisaged the use of more electron-poor copper(II) complexes for single-electron oxidation (**Scheme 2**b). It is well-known that copper(II) complexes undergo homolytic ligand dissociation *via* ligand-to-metal charge transfer (LMCT) process under photoirradiation.[11] The generation of various radicals, such as benzylic,[12] chlorine,[13] and azide[14] radicals, have been reported by different groups.[15] In contrast, there is no report of intermolecular single-electron transfer events using copper(II) catalysts. In this work, the author disclosed that a copper(II) bathophenanthroline (bphen) complex acts as a photoredox catalyst for single-electron transfer *via* bimolecular quenching. The copper(II) catalyst exhibits a strong oxidizing power enough to receive a single electron from vinylarenes, so we applied this catalytic system to the *anti*-Markovnikov hydration of vinylarenes.

Scheme 2. The Development of Copper Photocatalysis



Hydration of alkenes is an important transformation to give alcohols from readily available starting materials. Although the Markovnikov hydration is well established, *anti*-Markovnikov hydration is more challenging.[16] Despite extensive work to develop catalytic reactions, most of them are formal hydration reactions.[17] In 2017, Lei and co-workers reported *anti*-Markovnikov hydration of vinylarenes using an organic photoredox catalyst (Acr^+-Mes ClO_4^-: Fukuzumi's catalyst) (**Scheme 3**a).[18] In this reaction, a generation of radical cations *via* single-electron oxidation of vinylarenes by the photoexcited acridinium catalyst is crucial. The direct addition of H_2O to the radical cations gave the desired products. Lei's report is the first example of *anti*-Markovnikov hydration and a great breakthrough in hydration chemistry. However, as mentioned above, organic photocatalysts have some problems, so it is meaningful to develop a better catalytic system for *anti*-Markovnikov hydration. Herein, the author reports photoinduced *anti*-Markovnikov hydration of vinylarenes using a new class of copper(II) photoredox catalysts (**Scheme 3**b).

Scheme 3. Photoinduced *anti*-Markovnikov Hydration

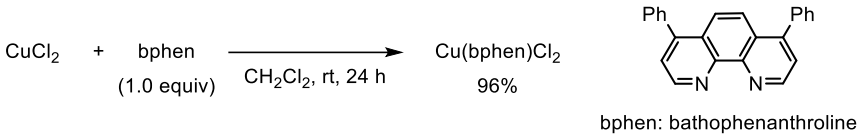


Result and Discussion

■ Initial studies

$Cu(bphen)Cl_2$ was prepared by simply mixing $CuCl_2 \cdot 2H_2O$ and bphen in CH_2Cl_2 at room temperature (**Scheme 4**). The structure of the complex was confirmed by a single-crystal X-ray analysis (**Figure 2**). The complex has a planar geometry, and two molecules interact to form a dimer in the crystalline state.

Scheme 4. Preparation of $Cu(bphen)Cl_2$



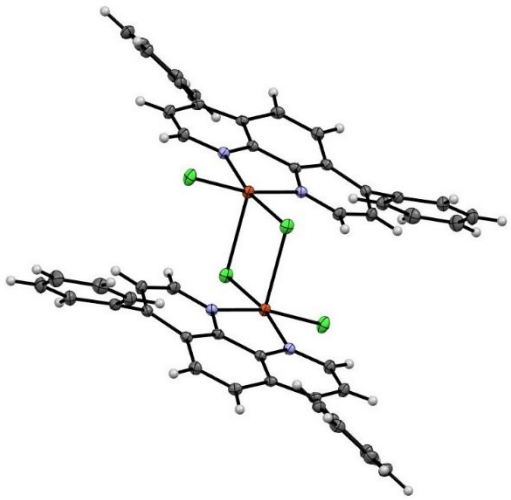


Figure 2. X-ray crystal structure of Cu(bphen)Cl_2.

Then, the photophysical properties of Cu(bphen)Cl_2 was investigated. A solution of Cu(bphen)Cl_2 in MeCN/acetone/H_2O displayed an absorption tailing to 450 nm and a broad absorption from the visible region to the infrared region, which is characteristic for copper(II) complexes (**Figure 3**a). Upon excitation at 445 nm, an emission centered at 512 nm was detected (**Figure 3**b).

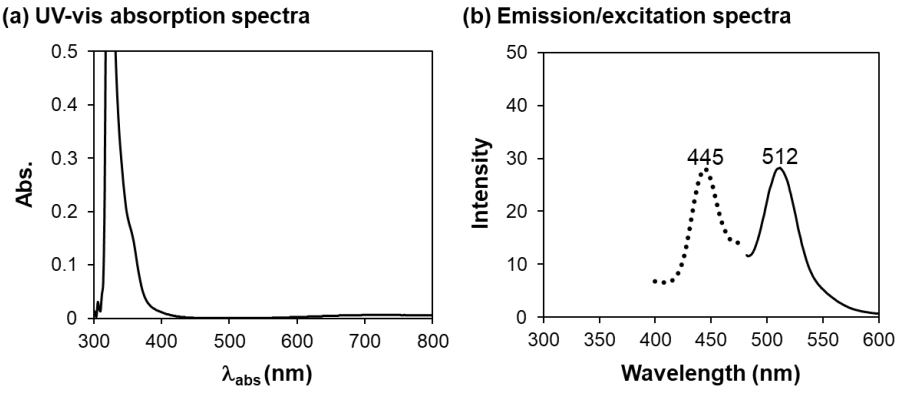


Figure 3. Absorption spectra and emission spectra of Cu(bphen)Cl_2 in MeCN/acetone/H_2O (5:5:1). (a) UV-vis absorption spectra. (b) emission spectra (solid line) and excitation spectra (dashed line).

Next, the lifetime of the emission was measured and determined as 18.3 ns (**Figure 4**), so the emission of Cu(bphen)Cl_2 was attributed to fluorescence. Although photoexcited species

of first-row transition metals are known to have short lifetimes,[19] the fluorescence lifetime of Cu(bphen)Cl_2 is long enough for an intermolecular quenching.

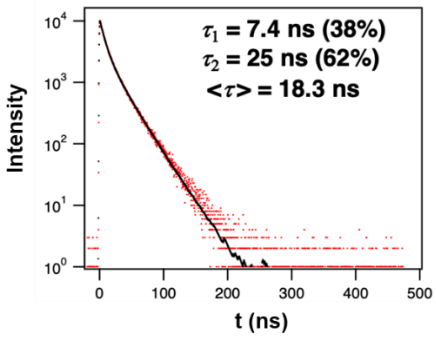


Figure 4. Fluorescence decay profile of Cu(bphen)Cl_2 in MeCN/acetone/H_2O (5:5:1).

A cyclic voltammogram (CV) of Cu(bphen)Cl_2 showed a reversible Cu(II)/Cu(I) reduction wave at $E_{1/2}$ = –0.47 V (vs Fc/Fc^+) (**Figure 5**a). Using $E^{0\text{-}0}$ value (2.60 eV) estimated from the fluorescence and the excitation spectra (see the Experimental Section) and this ground state reduction potential, the excited state of Cu(bphen)Cl_2 was predicted to have a reduction potential of +2.51 V (vs SCE). This is the highest potential among transition metal-based photoredox catalysts and is capable of single-electron oxidation of vinylarenes.[20] Actually, a linear quenching depending on the concentration of the quencher was observed in a quenching experiment with styrene ($E_{p/2}$ = +1.97 V vs SCE) (**Figure 5**b), and the kinetic constant of the quenching was determined as 5.8×10^8 $M^{-1}s^{-1}$. On the basis of the estimated reduction potential of Cu(bphen)Cl_2, this quenching was considered to be due to a single-electron transfer from the alkene to the photoexcited Cu(bphen)Cl_2. Encouraged by the high excited reduction potential and the efficiency of a single-electron transfer, the author tried the application of the copper(II) complex to the *anti*-Markovnikov hydration.

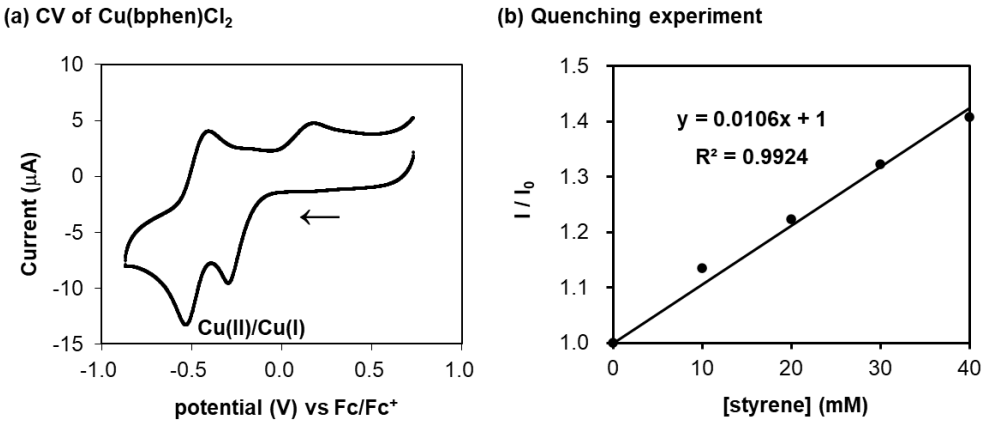
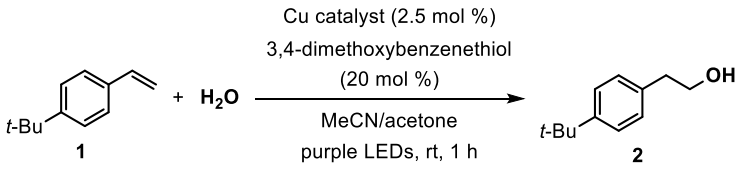


Figure 5. (a) Cyclic voltammogram of Cu(bphen)Cl_2 in MeCN (100 mV/s scan late, 0.10 M in $TBAPF_6$). (b) Quenching of the fluorescence with styrene at 510 nm (λ_{ex} = 430 nm) in MeCN/acetone/H_2O (5:5:1).

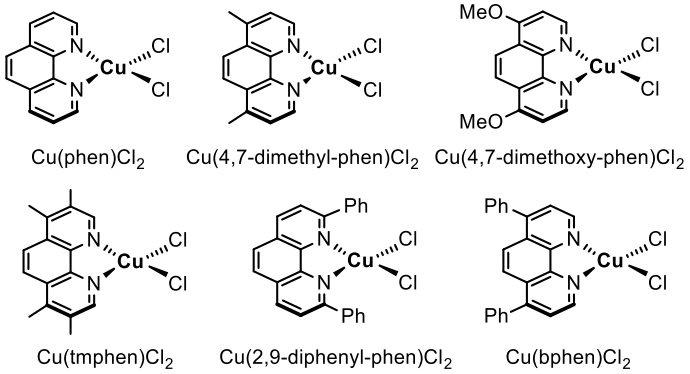
■ Reaction development

The study was started with 4-*t*-butyl-styrene (**1**) as a model substrate. As a result of ligand screening, the author found that bphen was the best ligand (**Table 1**). Substituents on 1,10-phenanthroline scaffold are essential for the reaction (entries 1–6). Next, the author investigated other copper sources by using an *in situ* complexation method. The author found that $Cu(OAc)_2$ and $Cu(OTf)_2$ gave inferior results to $CuCl_2 \cdot 2H_2O$ (entries 7–9). When the *in situ* complexation method was used, the reaction rate was slower than that of the isolated complex, but the author chose the *in situ* method for simple experimental manipulation. Finally, the author established the standard conditions for *anti*-Markovnikov hydration of vinylarenes as described in **Table 1**, entry 10. A mixture of **1** (0 30 mmol), H_2O (0.45 mL), $CuCl_2 \cdot 2H_2O$ (2.5 mol %), bphen (2.5 mol %), and 3,4-dimethoxybenzenethiol (20 mol %) in MeCN/acetone (1:1, 4.5 mL) was irradiated with purple LEDs (λ_{max} = 390 nm) at ambient temperature. After 5 hours, the primary alcohol **2** was formed in 60% NMR yield. Purification by preparative thin-layer chromatography gave **2** in 54% isolated yield.

Table 1. Screening of Copper(II) Catalysts[a]



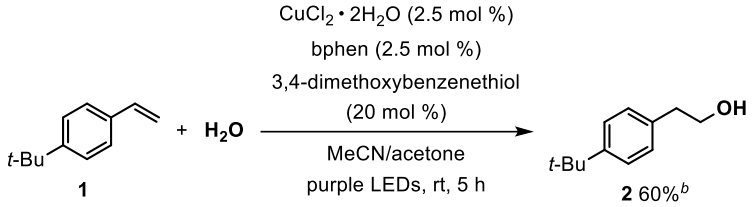
entry	Cu Catalyst	yield of 2 (%)[b]
1	$Cu(phen)Cl_2$	n.d.
2	$Cu(4,7\text{-dimethyl-phen})Cl_2$	n.d.
3	$Cu(4,7\text{-dimethoxy-phen})Cl_2$	12
4	$Cu(tmphen)Cl_2$	13
5	$Cu(2,9\text{-diphenyl-phen})Cl_2$	46
6	$Cu(bphen)Cl_2$	60
7	$CuCl_2 \cdot 2H_2O$ + bphen	48
8	$Cu(OTf)_2$ + bphen	37
9	$Cu(OAc)_2$ + bphen	16
10[c]	$CuCl_2 \cdot 2H_2O$ + bphen	60 (54)[d]



[a]On a 0.30 mmol scale. [b]Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard. [c]The reaction time was 5 hours. [d]Isolated yield after preparative thin-layer chromatographic purification. n.d. = not detected. phen = 1,10-phenanthroline. tmphen = 3,4,7,8-tetramethyl-1,10-phenanthroline.

Some control experiments were carried out, and all of the copper salt, ligand, thiol, and photoirradiation were indispensable for the reaction (**Table 2**, entries 1–4). The reaction didn't proceed at all without light even if the reaction temperature was raised to 60 °C (**Table 2**, entry 5). These results strongly suggested that the copper complex acted as a photocatalyst.

Table 2. Control Experiments[a]



1 **2** 60%[b]

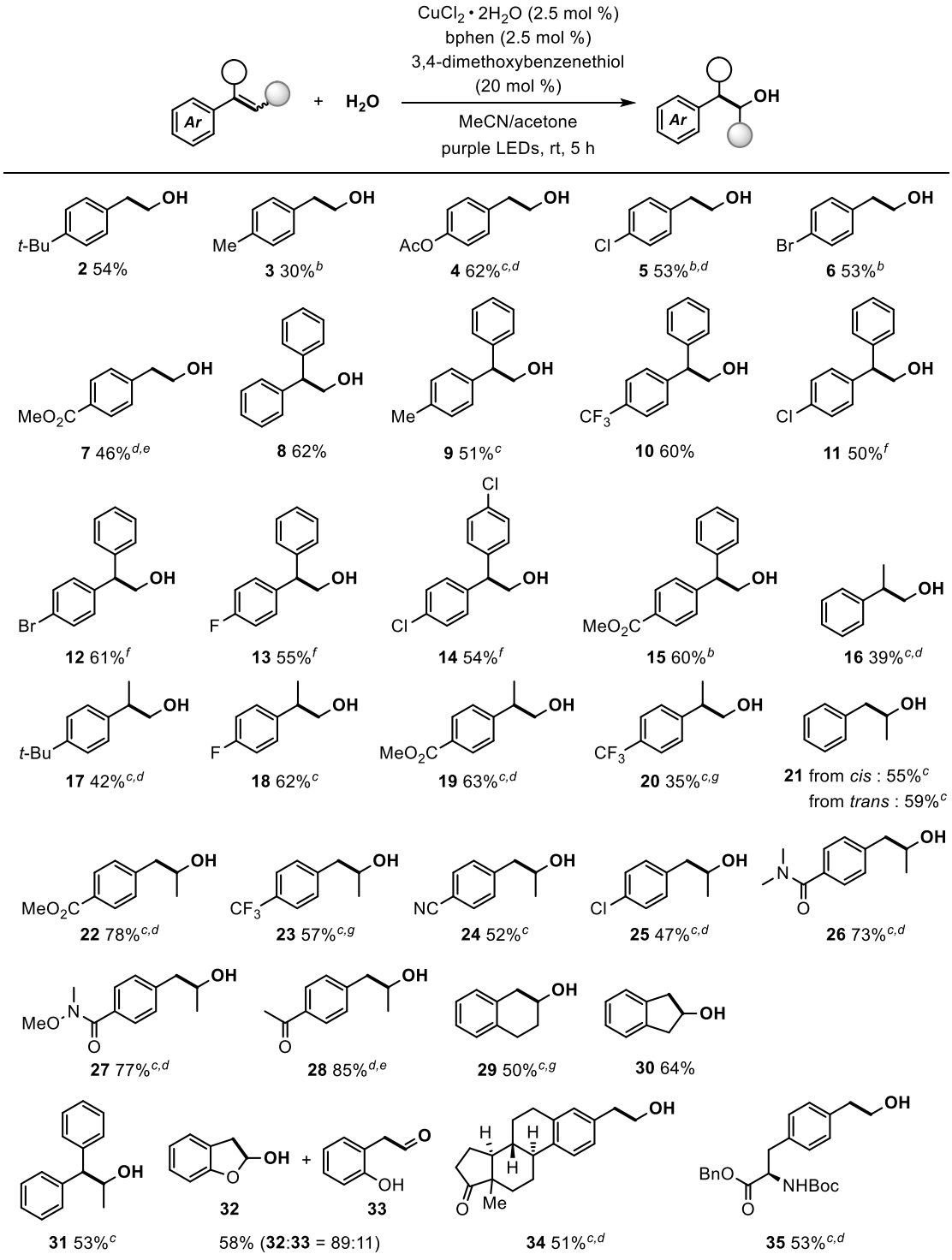
entry	Deviation from Standard Conditions	yield of 2
1	without $CuCl_2 \cdot 2H_2O$	n.d.
2	without bphen	n.d.
3	without 3,4-dimethoxybenzenethiol	n.d.
4	without light (rt)	n.d.
5	without light (60 °C)	n.d.

[a]On a 0.30 mmol scale. [b]Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard.

■ Substrate Scope

The scope of vinylarenes was examined in the hydration reaction (**Table 3**). An electronically diverse array of *para*-substituted styrenes reacted well to give the corresponding primary alcohols **2**–**7**. Various α-substituted styrenes were also applicable to the reaction. Although β-Alkyl styrenes gave the corresponding products **21**–**28**, β-aryl styrenes such as stilbene didn't react at all. The reaction proceeded regardless of the geometry of alkenes on prop-1-en-1-ylbenzene. Cyclic and trisubstituted vinylarenes could be hydrated. Interestingly, when 2,3-benzofuran was used as a substrate, regioselective hydration occurred to give 2-hydroxy-2,3-dihydrobenzofuran (**32**) as a mixture with hydrolyzed form **33**. This protocol showed a high functional group tolerance, so it could be applied to the late-stage functionalization of naturally occurring compounds. An estrone derivative and an L-phenylalanine derivative were converted to the primary alcohols **34** and **35**, respectively.

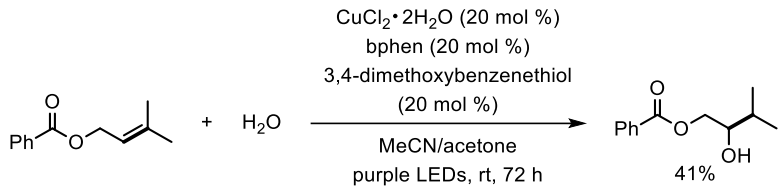
Table 3. *anti*-Markovnikov Hydration with Various Vinylarenes[a]



[a]On a 0.30 mmol scale. Isolated yields after preparative thin-layer chromatographic purification. [b]The reaction time was 7 hours. [c]The reaction time was 15 hours. [d]10 mol % of Cu salt and bphen were used. [e]The reaction time was 30 hours. [f]The reaction time was 8 hours. [g]5.0 mol % of Cu salt and bphen were used.

The hydration reaction using an aliphatic tri-substituted alkene was also examined, and the desired product was obtained in 41% yield (**Scheme 5**).

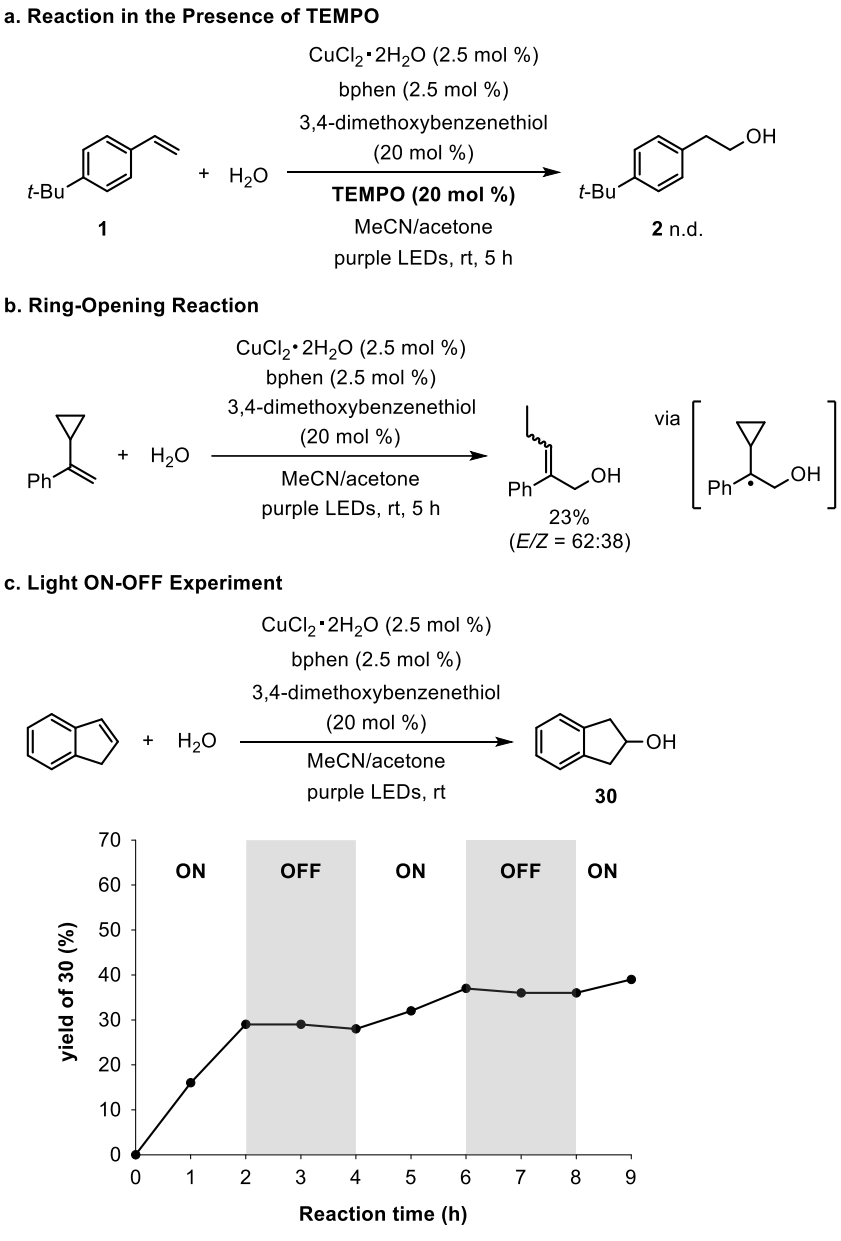
Scheme 5. *anti*-Markovnikov Hydration of the Aliphatic Alkene



■ Mechanistic Studies

To gain detailed mechanistic insight, a series of mechanistic studies were conducted. In the presence of 20 mol % of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), the reaction was completely inhibited (**Scheme 6**a). This result offered the possibility that the reaction was mediated by radical species. A radical probe experiment with (1-cyclopropylvinyl)benzene gave a ring-opening product in 23% yield, which indicated the generation of benzylic radical intermediates (**Scheme 6**b). Light ON-OFF experiment using indene as a substrate showed that the hydration reaction proceeded only under photoirradiation (**Scheme 6**c). This demonstrates that light is required to sustain the catalytic cycle.

Scheme 6. Mechanistic Studies



Interestingly, spectroscopic analysis of the mixture of Cu(bphen)Cl_2 and 3,4-dimethoxybenzenethiol (1:8) indicated the formation of a different copper(II) complex (**Figure 6**). A ligand exchange between the chloride and the thiolate could occur, but the exact structure of the generated copper(II) species has not been determined.

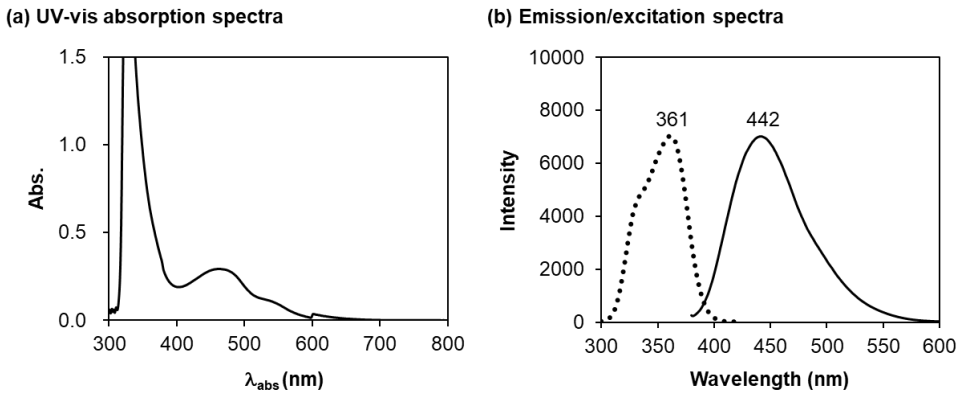


Figure 6. Spectroscopic analysis of the mixture of Cu(bphen)Cl_2 and 3,4-dimethoxybenzenethiol (1:8). The experiment was carried out in MeCN/acetone/H_2O (5:5:1).

A quenching experiment of the *in situ* generated copper(II) catalyst was carried out (**Figure 7**). The linear quenching of photoexcited copper(II) catalyst by 4-*tert*-butylstyrene (+ 1.72 V vs SCE) was observed, and the Stern-Volmer constant was determined as 29 M^{-1}. Therefore, the author concluded that the catalytically active species in the hydration reaction is the copper(II) complex generated *in situ*. Quenching experiments with various alkenes suggested that the redox potential of the photoexcited state of the *in situ* generated copper(II) species was over +2.10 V vs SCE (see the Experimental Section).

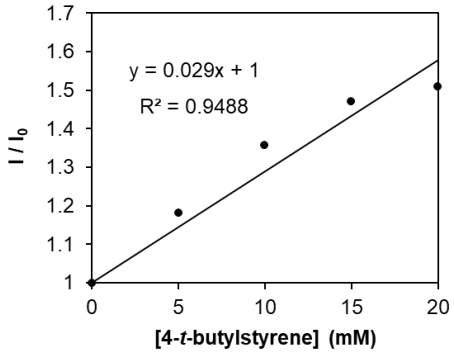
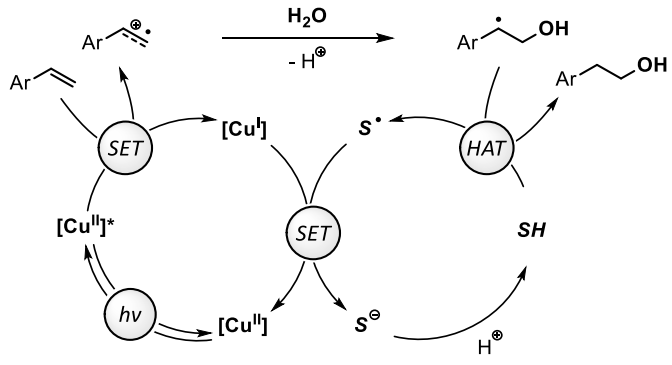


Figure 7. Stern-Volmer plot of the mixture of Cu(bphen)Cl_2 and 3,4-dimethoxybenzenethiol (1:8). The experiment was carried out in MeCN/acetone/H_2O (5:5:1).

■ Proposed Mechanism

Based on the previous report and mechanistic studies, the author proposed the reaction mechanism shown in **Scheme 7**. Initially, the copper(II) complex is excited to copper(II)* under photoirradiation. A single electron transfer from a vinylarene to copper(II)* generates a radical cation of vinylarenes and copper(I), respectively. Then, the addition of H_2O and the subsequent deprotonation occurs to give a benzylic radical intermediate. A hydrogen atom transfer from the thiol catalyst provides the desired primary alcohol. The copper(I) was oxidized by the thiyl radical to regenerate the copper(II). The resulting thiolate is immediately protonated, and the thiol catalyst is regenerated.

Scheme 7. Proposed Mechanism

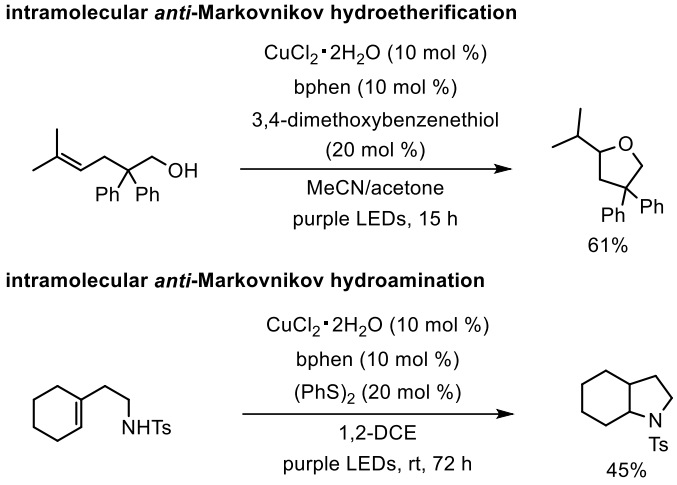


SH = 3,4-dimethoxybenzenethiol.

■ Further Applications

Further studies were carried out to reveal the reactivity of the copper(II) photocatalyst. Some known reactions were carried out with the copper photoredox catalyst instead of Fukuzumi's catalyst (**Scheme 8**).[21] Intramolecular hydroetherification and hydroamination proceeded efficiently under slightly modified conditions. These results demonstrated the potential of the copper(II) bathophenanthroline complex not only for the hydration reaction but also for various oxidative functionalization of alkenes.

Scheme 8. Intramolecular Reactions



Conclusion

In summary, the author has developed the highly oxidative copper(II) photocatalyst and applied the catalyst to *anti*-Markovnikov hydration of vinylarenes. The reaction can be performed on a variety of substrates. Furthermore, the photophysical properties of the copper(II) catalyst were investigated. These studies provide deep insights into the design of copper(II) photocatalysts.

Experimental Section.

■ **General Methods.**

All reactions were carried out under a nitrogen atmosphere unless otherwise noted. IR measurements were performed on a JASCO FTIR-4X with ATR Pro 4X. UV-vis absorption spectra were recorded on a HITACHI U-1900 Spectrophotometer. Emission spectra were recorded on HITACHI F-2700 fluorescence spectrophotometer. FL decay profiles were measured by using HORIBA Jobin Yvon FluoroCube lifetime spectrofluorometer equipped with HORIBA Nano-LED-370 and analyzed using DAS6 FL decay analysis software. Cyclic Voltammetry (CV) was recorded on Electronic Analyzer CHI-600B. Irradiation of photoreactions was carried out using a Kessil lamp (PR160L-390 nm). ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a JEOL ECS 400 MHz spectrometer. NMR data were obtained in $CDCl_3$ unless otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm ($CHCl_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm ($CDCl_3$). High-resolution mass spectra were recorded on ESI-TOF mass spectrometers, Bruker Daltonics microTOF II. Preparative thin-layer chromatography (PTLC) was performed on silica gel plates with silica gel 60 PF254 indicator (Sigma-Aldrich). Flash silica gel column chromatography was performed with silica gel 60N (Kanto). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9210 (JAIGEL-H) using $CHCl_3$ as an eluent.

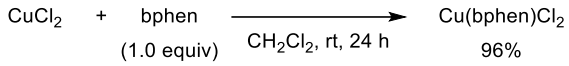
■ **Materials.**

All chemicals and anhydrous solvents were obtained from commercial suppliers and used without further purification unless otherwise noted. MeCN (Kanto) and acetone (FUJIFILM Wako and Kanto) were degassed before use. $CuCl_2 \cdot 2H_2O$ (Kanto), bathophenanthroline (Sigma-Aldrich and Kanto), and 3,4-dimethoxybenzenethiol (Sigma-Aldrich and Nacalai) were obtained

from commercial suppliers.

Alkenes were obtained from commercial suppliers and used without further purification [4-*tert*-butylstyrene (TCI), 4-methylstyrene (TCI), 4-chlorostyrene (TCI), 4-bromostyrene (TCI), 1,1-diphenylethylene (Sigma-Aldrich), *α*-methylstyrene (TCI), *cis*-*β*-methylstyrene (FUJIFILM Wako), *trans*-*β*-methylstyrene (Sigma-Aldrich), 1,2-dihydronaphthalene (TCI), indene (Kanto), 2,3-benzofuran (Sigma-Aldrich)].

■ **Preparation of Cu(bphen)Cl_2.**



Cu(bphen)Cl_2 was prepared according to the following procedure. To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added $CuCl_2$ (270 mg, 2.0 mmol, 1.0 equiv), bathophenanthroline (660 mg, 2.0 mmol, 1.0 equiv), and CH_2Cl_2 (30 mL, 0.067 M). The reaction mixture was stirred at room temperature. After 24 hours, the mixture was filtered out to give the copper(II) complex as a green solid (900 mg, 2.0 mmol, 96% yield). The complex was pure enough without further purification, recrystallization from acetone gave the purer complex.

■ **X-Ray Crystallography of Cu(bphen)Cl_2.**

A Crystal suitable for single-crystal X-ray diffraction was grown by slow volatilization of a concentrated sample in acetone at room temperature. A single crystal of Cu(bphen)Cl_2 was placed on the end of a micro-mount coated with NVH oil. The X-ray intensity data collection was carried out on a Rigaku HyPix-6000 CCD area detector using graphitemonochromated Mo-Kα radiation (l = 0.71075 Å) at 100(2) K. Preliminary indexing was performed from a set of twelve frames. Equivalent reflections were merged, and the collected images were processed by a Rigaku

CrysAlisPro program. The initial structures were determined by the direct or Patterson method on SHELXS.[22] The further structure determination was performed by Fourier transform method and refined by least squares method on SHELXL[22,23] operated by Yadokari-XG software package.[24] All reflections were used during refinement with the exception of affected reflections by the beam-stopper. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using riding models, except for the hydroxy hydrogen in the hydrolysis product. The thermal ellipsoids of the disorders were fixed by SHELXL restraints. These results were checked by the IUCR's CheckCIF routine.

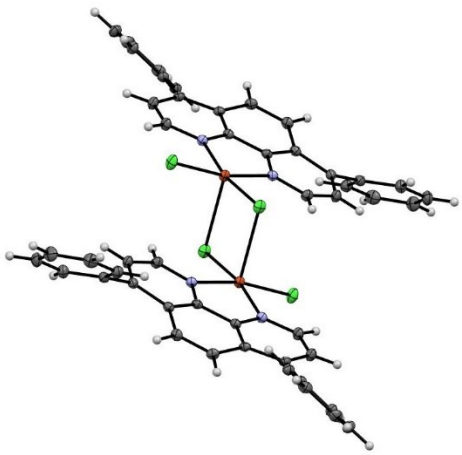
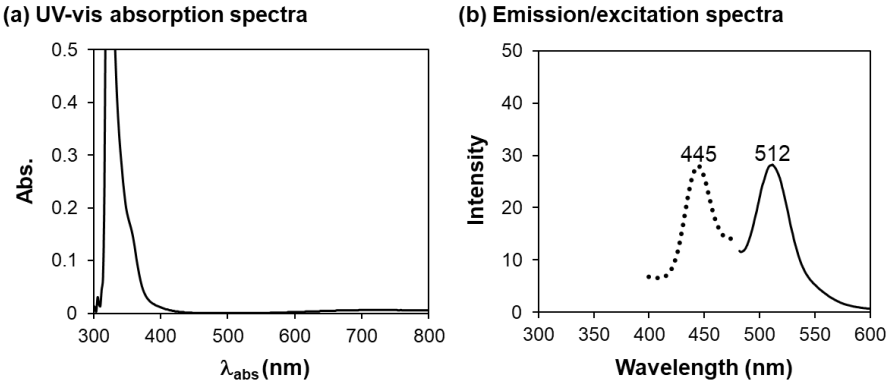


Figure 8. ORTEP drawing of $Cu(bphen)Cl_2$. Thermal ellipsoids are shown in 50% probability.

Empirical formula	$C_{48}H_{32}C_{14}Cu_2N_2$
Formula weight	933.65
Temperature	120 K
Wavelength	0.71073 Å
Crystal system	*triclinic*
Space group	P –1
Cell constants:	a = 10.1260(3) Å, α = 69.797(3)°

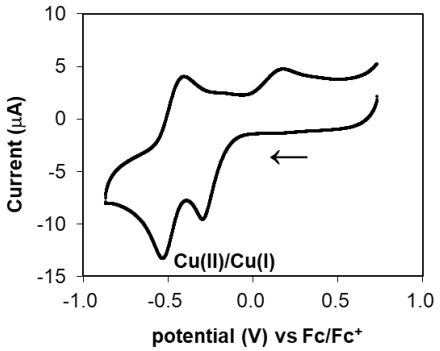
	b = 10.1367(3) Å, β = 66.634(3)°
	c = 11.0128(4) Å, γ = 88.359(3)°
Volume	966.12(6) Å^3
Z	1
Absorption coefficient	1.420 mm^{-1}
F(000)	474.00
Crystal size	0.0015 x 0.21 x 0.59 mm^3
Theta range for data collection	3.6760 to 29.6490°
Index ranges	–13<=h<=13, –13<=k<=13, –15<=l<=15
Reflections collected	12400
Independent reflections	4640 [R (int) = 0.0218]
Completeness to theta	25.242° 99.7%
Data / restraints / parameters	4640 / 0 / 262
Goodness-of-fit on F^2	1.063
Final R indices [I>2σ(I)]	R_1 = 0.0244, wR_2 = 0.0658
R indices (all data)	R_1 = 0.0270, wR_2 = 0.0668

■ **Spectroscopic Analysis of Cu(bphen)Cl$_2$.**



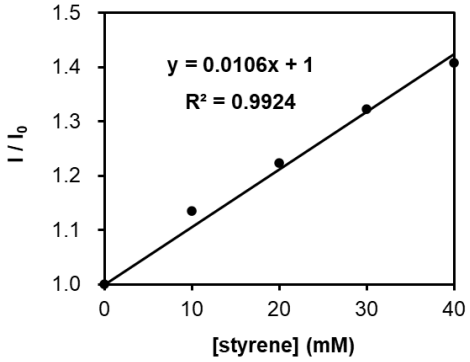
(a) UV-vis absorption spectra of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1). (b) Emission and excitation spectra of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1) The measurement was carried out after degassing by Ar bubbling. (c) Fluorescence decay profile of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1). The measurement was carried out after degassing by Ar bubbling. λ_{EX} = 404 nm. λ_{FL} = 490 nm. The lifetime of the excited state of $Cu(bphen)Cl_2$ was determined as 18.3 ns.

■ **Cyclic Voltammetry of $Cu(bphen)Cl_2$.**



The cyclic voltammetry experiment was performed using the conditions as follows. solvent: MeCN, supporting electrolyte: $TABPF_6$ (0.10 M), substrate concentration: 1.0 mM, working electrode: Pt, counter electrode: Pt coil, reference electrode: Ag/Ag^+ (MeCN), standard: Fc/Fc^+, scan rate: 100 mV/s, temperature: room temperature.

■ **Fluorescence Quenching of $Cu(bphen)Cl_2$.**



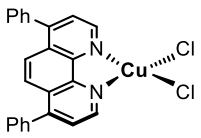
In each experiment, Cu(bphen)Cl_2 (1.0×10^{-4} M) and variable concentrations of styrene were combined in MeCN/acetone/H_2O (5:5:1) degassed by sparging with N_2 gas for 10 min. The solution in quartz cuvettes was irradiated at 430 nm and the emission intensity was observed at 510 nm. Stern-Volmer plot for the quenching is shown above. Stern-Volmer constant was determined as 11 M^{-1}. With the value of the lifetime of the excited state of Cu(bphen)Cl_2, the kinetic constant of the quenching was determined as 5.8×10^8 $M^{-1}s^{-1}$.

■ **Determination of the Excited State Reduction Potential of Cu(bphen)Cl_2.**

Excited state reduction potential is estimated using the Rehm-Weller equation.[25]

Rehem-Weller equation: $E^*_{red} = E_{red} + E^{0\text{-}0}$

E^*_{red} represents the excited state reduction potential, E_{red} represents the ground state reduction potential, and $E^{0\text{-}0}$ refers to the energy gap between the zeroeth vibration level of the ground and excited states. E_{red} refers to the Cu(II)/Cu(I) couple. $E^{0\text{-}0}$ is estimated by taking half the difference between excitation and emission peaks. Conversion Fc/Fc^+ to SCE was done by adding 0.38 V to the Fc/Fc^+ potential.

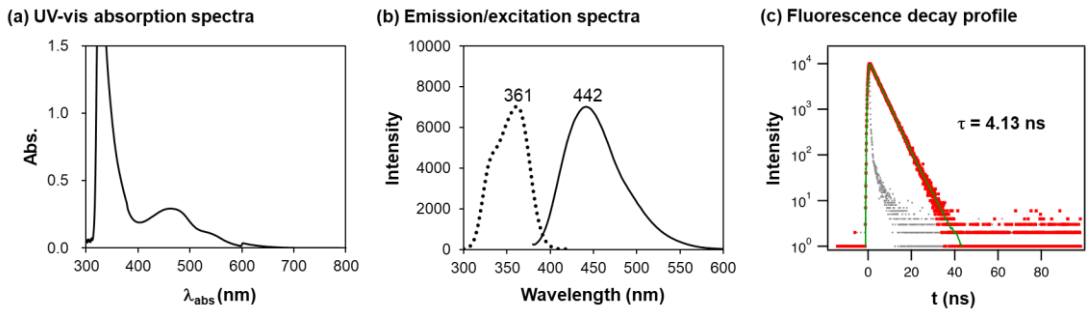


λ_{EX} = 445 nm
λ_{FL} = 512 nm
$E^{0\text{-}0} = h\nu$
= 2.60 eV

Cu(II)/Cu(I)
E_{red} = –0.47 V (vs Fc/Fc+)
E_{red} = –0.09 V (vs SCE)

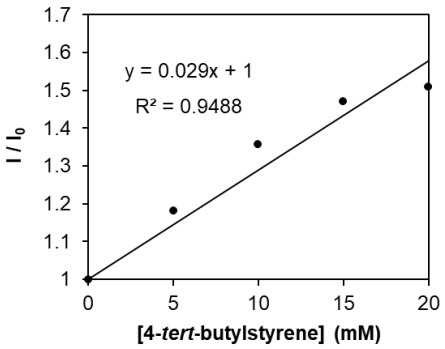
Cu(II)*/Cu(I)
E^*_{red} = +2.13 V (vs Fc/Fc^+)
E^*_{red} = +2.51 V (vs SCE)

■ **Photophysical Analysis of the *in situ* Generated Copper(II) Species.**



(a) UV-vis absorption spectra of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O =5:5:1) in the presence of 3,4-dimethoxybenzenethiol (8.0×10^{-4} M). (b) Emission/excitation spectra of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1) in the presence of 3,4-dimethoxybenzenethiol (8.0×10^{-4} M). The measurement was carried out after degassing by Ar bubbling. (c) Fluorescence decay profile of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1) in the presence of 3,4-dimethoxybenzenthiol (8.0×10^{-4} M). The measurement was carried out after degassing by Ar bubbling. λ_{EX} = 371 nm. λ_{FL} = 437 nm. The lifetime of the excited state of the *in situ* generated copper(II) species in MeCN/acetone/H_2O (5:5:1) was determined as 4.13 ns.

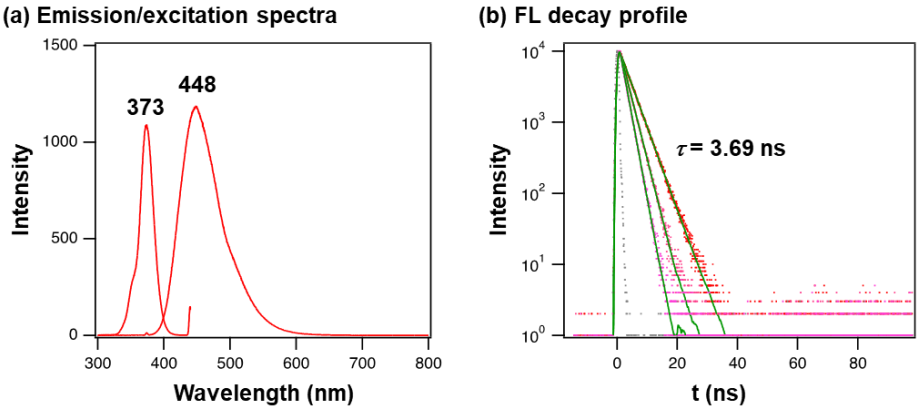
■ **Fluorescence Quenching of the *in situ* Generated Copper(II) Species.**



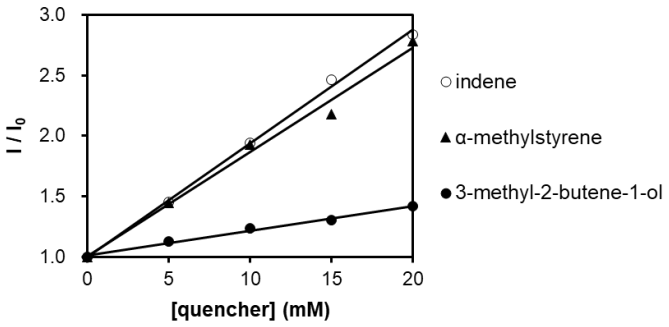
In each experiment, $Cu(bphen)Cl_2$ (1.0×10^{-4} M), 3,4-dimethoxybenzenethiol (8.0×10^{-4} M) and variable concentrations of 4-*tert*-butylstyrene were combined in MeCN/acetone/H_2O

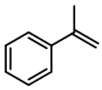
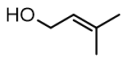
(5:5:1) degassed by sparging with N_2 gas for 10 min. The solution in quartz cuvettes was irradiated at 390 nm and the emission intensity was observed at 440 nm. Stern-Volmer plot for the quenching is shown above. Stern-Volmer constant was determined as 29 M^{-1}. With the value of the lifetime of the excited state, the kinetic constant of the quenching was determined as 7.1×10^9 $M^{-1}s^{-1}$.

■ The Excited State Reduction Potential of the *in situ* Generated Copper(II) Species.



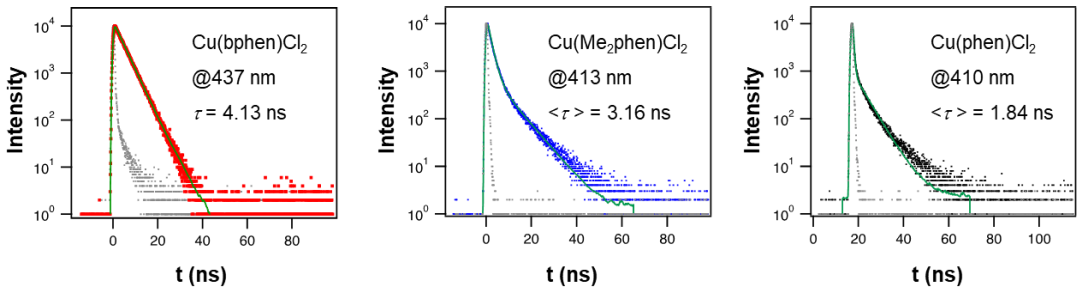
In order to estimate the excited reduction potential of the *in situ* generated copper(II) species, some experiments were carried out. The emission spectra, the excitation spectra, and the fluorescence decal profile are shown above. (a) Emission/excitation spectra of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone = 1:1) in the presence of 3,4-dimethoxybenzenethiol (8.0×10^{-4} M). The measurement was carried out after degassing by Ar bubbling. (b) Fluorescence decay profile of $Cu(bphen)Cl_2$ (1.0×10^{-4} M in MeCN/acetone = 1:1) in the presence of 3,4-dimethoxybenzenthiol (8.0×10^{-4} M). The measurement was carried out after degassing by Ar bubbling. λ_{EX} = 371 nm. λ_{FL} = 448 nm. The lifetime of the excited state of the copper(II) species was determined as 3.69 ns.

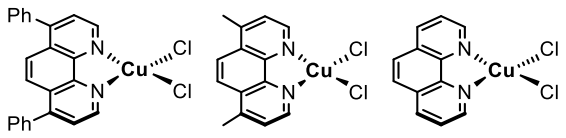


	E_{red} (vs SCE)	K_{SV}	k_q
 indene	+ 1.66 V	94 M^{-1}	2.5 × 10^{10} $M^{-1}s^{-1}$
 α-methylstyrene	+ 1.91 V	86 M^{-1}	2.3 × 10^{10} $M^{-1}s^{-1}$
 3-methyl-2-buten-1-ol	+ 2.10 V	20 M^{-1}	5.7 × 10^{9} $M^{-1}s^{-1}$

Next, a fluorescence quenching with various alkenes was carried out. In each experiment, $Cu(bphen)Cl_2$ (1.0×10^{-4} M), 3,4-dimethoxybenzenethiol (8.0×10^{-4} M) and variable concentrations of alkenes were combined in MeCN/acetone (1:1) degassed by sparging with N_2 gas for 10 min. The solution in quartz cuvettes was irradiated at 390 nm and the emission intensity was observed at 440 nm. Based on the result shown above, the excited reduction potential of the *in situ* generated copper(II) species is estimated over +2.10 V (vs SCE).

■ FL Decay Profiles of various copper(II) species.



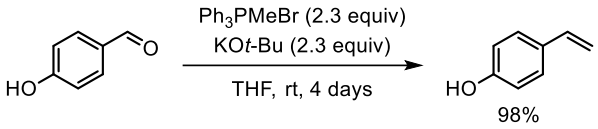


$Cu(bphen)Cl_2$ $Cu(Me_2phen)Cl_2$ $Cu(phen)Cl_2$

In order to investigate the effect of the ligands, the fluorescence lifetimes of various copper(II) complexes in the presence of 3,4-dimethoxybenzenthiol. Fluorescence decay profiles of copper(II) complexes (1.0×10^{-4} M in MeCN/acetone/H_2O = 5:5:1) in the presence of 3,4-dimethoxybenzenthiol (8.0×10^{-4} M). The measurement was carried out after degassing by Ar bubbling. λ_{EX} = 371 nm. λ_{FL} are shown above. $Cu(bphen)Cl_2$ showed the longest lifetime of the fluorescence. Substituents on the 1,10-phenanthroline backbone might prevent the formation of undesired excimer due to their steric effects.

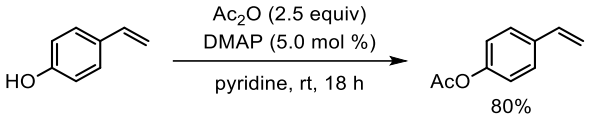
■ Substrate Preparation.

4-acetoxystyrene:



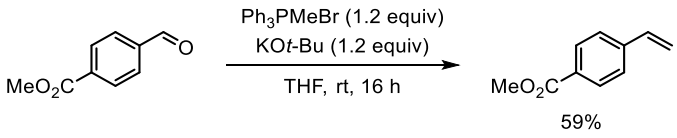
4-Hydroxystyrene was prepared according to the literature procedure.[26] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (13.2 g, 37 mmol, 2.3 equiv), KO*t*-Bu (4.1 g, 37 mmol, 2.3 equiv), and THF (120 mL, 0.13 M). The mixture was stirred at 0 °C for 15 minutes. Then, 4-hydroxybenzaldehyde (2.1 g, 16 mmol, 1.0 equiv) was added to the mixture and warmed to room temperature. After 4 days, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (CH_2Cl_2) to give the desired product (2.0 g, 16 mmol, 98% yield). The analytical data of the product matched well with the

reported one.



4-Acetoxystyrene was prepared according to the literature procedure.[27] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ac_2O (1.2 mL, 13 mmol, 2.5 equiv), DMAP (31 mg, 0.25 mmol, 5.0 mol %), 4-hydroxybenzaldehyde (610 mg, 5.0 mmol, 1.0 equiv), and pyridine (25 mL, 0.20 M). The reaction mixture was stirred at room temperature. After 18 hours, saturated aqueous solution of $CuSO_4$ was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with H_2O, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give the desired product (660 mg, 4.1 mmol, 80% yield). The analytical data of the product matched well with the reported one.

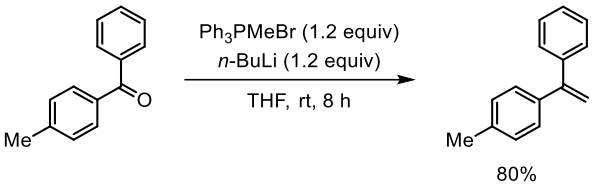
methyl 4-vinylbenzoate:



Methyl 4-vinylbenzoate was prepared according to the literature procedure.[28] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (4.3 g, 12 mmol, 1.2 equiv), KO*t*-Bu (1.4 g, 12 mmol, 1.2 equiv), and THF (50 mL, 0.20 M). The mixture was stirred at 0 °C for 1 hour. Then, methyl 4-formylbenzoate (1.6 g, 10 mmol, 1.0 equiv) was added to the mixture and warmed to room temperature. After 16 hours, brine was added to the mixture and extracted with hexane × 3 times. The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified

by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give the desired product (950 mg, 5.9 mmol, 59% yield). The analytical data of the product matched well with the reported one.

1-methyl-4-(1-phenylvinyl)benzene:

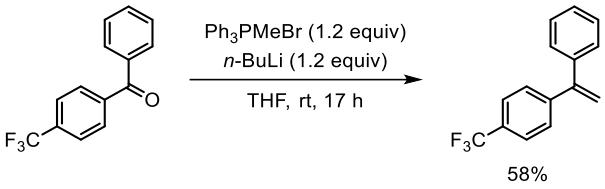


80%

1-Methyl-4-(1-phenylvinyl)benzene was prepared according to the literature procedure.[29] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (2.6 g, 7.2 mmol, 1.2 equiv) and THF (24 mL). Next, *n*-BuLi (1.6 M in hexane, 7.2 mmol, 1.2 equiv) was slowly added to the mixture at 0 °C. The reaction mixture was stirred at room temperature for 1 hour. Then, the mixture was cooled to 0 °C, and 4-methylbenzophenone (1.2 g, 6.0 mmol, 1.0 equiv) was added to the mixture and warmed to room temperature. After 8 hours, brine was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (930 mg, 4.8 mmol, 80% yield). The analytical data of the product matched well with the already reported one.[30] Therefore, only the ^{1}H NMR data is presented here.

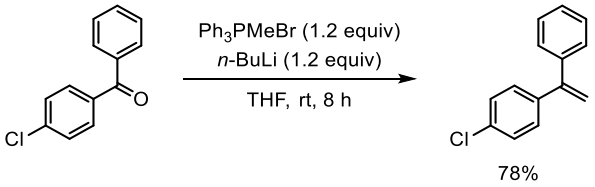
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.37–7.30 (m, 5H), 7.24 (d, 2H, *J* = 8.4 Hz), 7.14 (d, 2H, *J* = 8.4 Hz), 5.44 (s, 1H), 5.41 (s, 1H), 2.37 (s, 3H).

1-(1-phenylethenyl)-4-(trifluoromethyl)benzene:



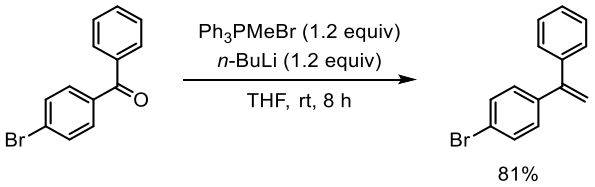
1-(1-Phenylethenyl)-4-(trifluoromethyl)benzene was prepared according to the literature procedure.[29] The reaction was carried out on an 8.3 mmol scale and the reaction time was 17 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (1.2 g, 4.8 mmol, 58% yield). The analytical data of the product matched well with the reported one.

1-chloro-4-(1-phenylvinyl)benzene:



1-Chloro-4-(1-phenylvinyl)benzene was prepared according to the literature procedure.[29] The reaction was carried out on a 6.0 mmol scale and the reaction time was 8 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (1.0 g, 4.7 mmol, 78% yield). The analytical data of the product matched well with the reported one.

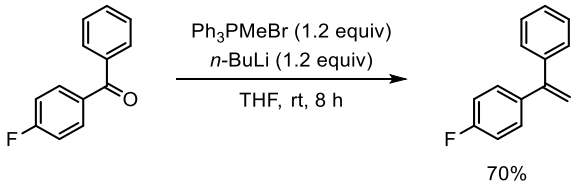
1-bromo-4-(1-phenylvinyl)benzene:



1-Bromo-4-(1-phenylvinyl)benzene was prepared according to the literature procedure.[29] The reaction was carried out on a 6.0 mmol scale and the reaction time was 8 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (1.3 g, 4.9 mmol, 81% yield). The analytical data of the product matched well with the already reported one.[30] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.46 (d, 2H, *J* = 8.8 Hz), 7.38–7.28 (m, 5H), 7.21 (d, 2H, *J* = 8.0 Hz), 5.47 (d, 1H, *J* = 0.8 Hz), 5.45 (s, 1H).

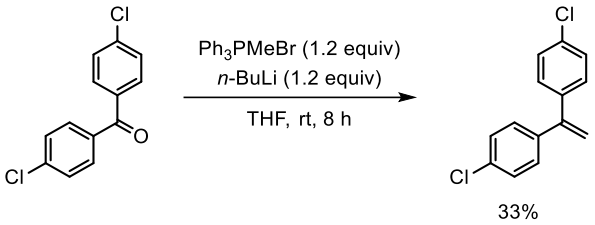
1-fluoro-4-(1-phenylvinyl)benzene:



1-Fluoro-4-(1-phenylvinyl)benzene was prepared according to the literature procedure.[29] The reaction was carried out on a 6.0 mmol scale and the reaction time was 8 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (830 mg, 4.2 mmol, 70% yield). The analytical data of the product matched well with the reported one.[30] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.38–7.28 (m, 7H), 7.02 (t, 2H, *J* = 8.4 Hz), 5.44 (s, 1H), 5.42 (s, 1H).

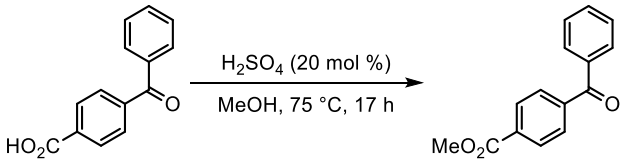
1,1-bis(4-chlorophenyl)ethene:



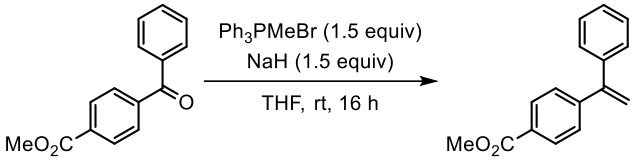
1,1-Bis(4-chlorophenyl)ethene was prepared according to the literature procedure.[29] The reaction was carried out on a 6.0 mmol scale and the reaction time was 8 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (490 mg, 2.0 mmol, 33% yield). The analytical data of the product matched well with the reported one.[30] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.31 (d, 4H, *J* = 8.8 Hz), 7.24 (d, 4H, *J* = 8.8 Hz), 5.45 (s, 2H).

methyl 4-(1-phenylvinyl)benzoate:



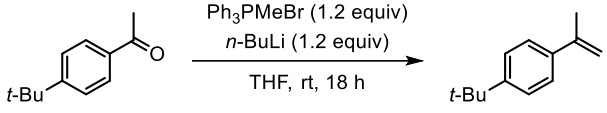
Methyl 4-benzoylbenzoate was prepared according to the literature procedure.[31] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar and a Dimroth condenser were added 4-benzoylbenzoic acid (2.3 g, 10 mmol, 1.0 equiv), sulfuric acid (0.10 mL, 2.0 mmol, 20 mol %), and MeOH (70 mL, 0.14 M). The reaction mixture was stirred at 75 °C in an oil bath. After 17 hours, the solvent was removed under reduced pressure. The residue was dissolved with CH_2Cl_2, washed with saturated aqueous solution of $NaHCO_3$, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was used in the next reaction without further purification.



37% (2 steps)

Methyl 4-(1-phenylvinyl)benzoate was prepared according to the literature procedure.[32] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (5.3 g, 15 mmol, 1.5 equiv) and THF (50 mL, 0.20 M). Next, NaH (60% in oil, 15 mmol, 1.5 equiv) was slowly added at 0 °C. The reaction mixture was stirred at room temperature for 1 hour. Then, the crude mixture of methyl 4-benzoylbenzoate (2.4 g, 10 mmol, 1.0 equiv) was added at 0 °C. the mixture was stirred at room temperature. After 16 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 40:1) to give the desired product (870 mg, 3.7 mmol, 37% yield in 2 steps). The analytical data of the product matched well with the reported one.

1-(*tert*-butyl)-4-(prop-1-en-2-yl)benzene:

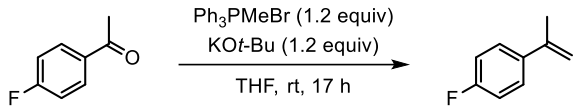


67%

1-(*tert*-Butyl)-4-(prop-1-en-2-yl)benzene was prepared according to the literature procedure.[33] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (2.2 g, 12 mmol, 1.2 equiv) and THF (10 mL, 0.50 M). Next, *n*-BuLi (1.6 M in hexane, 3.8 mL, 12 mmol, 1.2 equiv) was slowly added at 0 °C. The reaction mixture was stirred at 0 °C for 1 hour. Then, 4'-*tert*-butylacetophenone (1.8 g, 10 mmol, 1.0 equiv) was added

to the mixture and warmed to room temperature. After 18 hours, brine was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (580 mg, 3.3 mmol, 67% yield).The analytical data of the product matched well with the reported one.

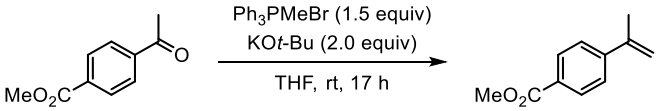
1-fluoro-4-(1-methylethenyl)benzene:



68%

1-Fluoro-4-(1-methylethenyl)benzene was prepared according to the literature procedure.[28] The reaction was carried out on an 8.0 mmol scale and the reaction time was 17 hours. The crude mixture was purified by flash silica gel column chromatography (pentane) to give the desired product (737 mg, 5.4 mmol, 68% yield). The analytical data of the product matched well with the reported one.

methyl 4-(prop-1-en-2-yl)benzoate:

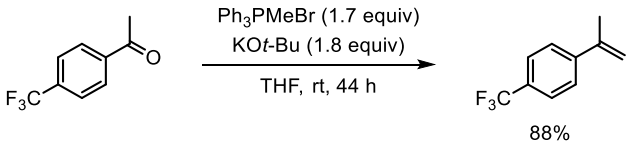


29%

Methyl 4-(prop-1-en-2-yl)benzoate was prepared according to the literature procedure.[34] The reaction was carried out on a 10 mmol scale and the reaction time was 17 hours. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 50:1) to give the desired product (510 mg, 2.9 mmol, 29% yield). The analytical data of the product matched well with the already reported one.[35] Therefore, only the ^1H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, 2H, *J* = 8.4 Hz), 7.52 (d, 2H, *J* = 8.8 Hz), 5.47 (s, 1H), 5.19 (quin, 1H, *J* = 1.6 Hz), 3.92 (s, 3H), 2.17 (s, 3H).

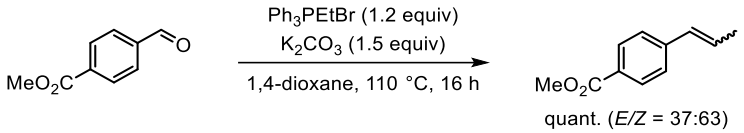
1-(1-methylethenyl)-4-(trifluoromethyl)benzene:



1-(1-Methylethenyl)-4-(trifluoromethyl)benzene was prepared according to the following procedure. To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (2.3 g, 6.4 mmol, 1.7 equiv), THF (15 mL, 0.30 M), KO*t*-Bu (790 mg, 7.0 mmol, 1.8 equiv). Then, 4-(Trifluoromethyl)acetophenone (730 mg, 3.9 mmol, 1.0 equiv) was added to the mixture. The reaction mixture was stirred at room temperature. After 44 hours, the solvent was removed under reduced pressure, and extracted with hexane × 5 times. The crude mixture was purified by flash silica gel column chromatography (pentane) to give the desired product (630 mg, 3.4 mmol, 88% yield). The analytical data matched well with the reported one.[28] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (d, 2H, *J* = 8.8 Hz), 7.55 (d, 2H, *J* = 8.8 Hz), 5.44 (s, 1H), 5.20 (t, 1H, *J* = 1.6 Hz), 2.20–2.14 (m, 3H).

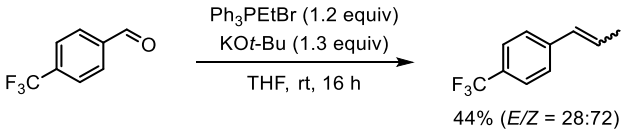
methyl 4-(1-propen-1-yl)benzoate:



Methyl 4-(1-propen-1-yl)benzoate was prepared according to the literature procedure.[36] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar and a

Dimroth condenser were added Ph_3PEtBr (3.3 g, 9.0 mmol, 1.2 equiv), K_2CO_3 (1.6 g, 11mmol, 1.5 equiv), methyl 4-formylbenzoate (1.2 g, 7.5 mmol, 1.0 equiv), and 1,4-dioxane (12 mL, 0.60 M). The reaction mixture was stirred at 110 °C in an oil bath. After 16 hours, the mixture was extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give the desired product (1.4 g, 7.8 mmol, quant.). The analytical data of the product matched well with the reported one.

1-(prop-1-en-1-yl)-4-(trifluoromethyl)benzene:

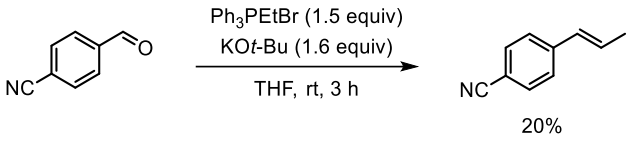


1-(Prop-1-en-1-yl)-4-(trifluoromethyl)benzene was prepared according to the following procedure. To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PEtBr (3.6 g, 9.8 mmol, 1.2 equiv), KO*t*-Bu (1.2 g, 10 mmol, 1.3 equiv), and THF (19 mL, 0.40 M). The mixture was stirred at room temperature for 1 hour, and 4-(trifluoromethyl)benzaldehyde (1.4 g, 8.0 mmol, 1.0 equiv) was added. Then the mixture was stirred at room temperature. After 16 hours, H_2O was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. After extraction with pentane × 3 times, the crude mixture was purified by flash silica gel column chromatography (pentane) to give the desired product (659 mg, 3.5 mmol, 44% yield). The analytical data of the product matched well with the reported one.[37] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.58 (d, 2H, *J* = 8.4 Hz), 7.53 (d, 2H, *J* = 8.4 Hz), 7.41 (d, 2H, *J* = 8.8 Hz), 7.38 (d, 2H, *J* = 8.0 Hz), 6.49–6.40 (m, 2H), 6.34 (dq, 1H, *J* = 15.6, 6.0 Hz), 5.91

(dq, 1H, *J* = 11.6, 6.8 Hz), 1.94–1.88 (m, 6H).

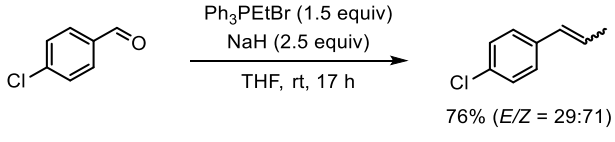
4-(prop-1-en-1-yl)benzonitrile:



4-(Prop-1-en-1-yl)benzonitrile was prepared according to the following procedure. To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PEtBr (5.6 g, 15 mmol, 1.5 equiv), KO*t*-Bu (1.8 g, 16 mmol, 1.6 equiv), and THF (24 mL, 0.40 M). The mixture was stirred at room temperature. After 30 minutes, 4-cyanobenzaldehyde (1.3 g, 10 mmol, 1.0 equiv) was added at 0 ℃. Then, the mixture was stirred at room temperature. After 3 hours, H_2O was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ AcOEt = 50:1) to give the desired product (273 mg, 1.9 mmol, 20% yield). The analytical data of the product matched well with the reported one.[38] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (d, 2H, *J* = 8.0 Hz), 7.39 (d, 2H, *J* = 8.4 Hz), 6.42–6.37 (m, 2H), 1.95–1.90 (m, 3H).

1-chloro-4-(1-propen-1-yl)benzene:

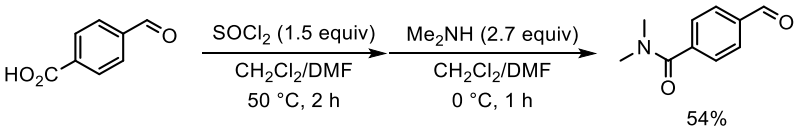


1-Chloro-4-(1-propen-1-yl)benzene was prepared according to the literature

procedure.[39] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PEtBr (4.5 g, 12 mmol, 1.5 equiv) and THF (28 mL, 0.30 M). Next, NaH (60% in oil, 820 mg, 20 mmol, 2.5 equiv) was slowly added at 0 °C. The reaction mixture was stirred at room temperature for 30 minutes. Then, the mixture was cooled to 0 °C and 4-chlorobenzaldehyde (1.1 g, 8.0 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature. After 17 hours, H_2O was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. After extraction with pentane × 3 times, the crude mixture was purified by flash silica gel column chromatography (pentane) to give the desired product (930 mg, 6.1 mmol, 76% yield).The analytical data of the product matched well with the reported one.[37] Therefore, only the ^{1}H NMR data is presented here.

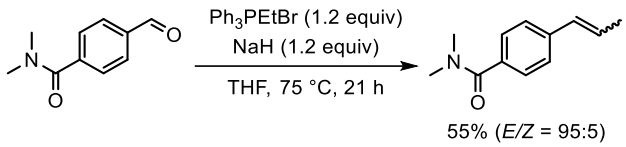
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.32 (d, 2H, *J* = 8.4 Hz), 7.28–7.20 (m, 6H), 6.43–6.32 (m, 2H), 6.23 (dq, 1H, *J* = 15.6, 6.4 Hz), 5.83 (dq, 1H, *J* = 12.0, 7.6 Hz), 1.92–1.86 (m, 6H).

***N*,*N*-dimethyl-4-(1-propenyl)-benzamide:**



4-Formyl-*N*,*N*-dimethylbenzamide was prepared according to the literature procedure.[40] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar and a Dimroth condenser were added terephthalaldehydic acid (1.5 g, 10 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL, 3.3 M). Then, thionyl chloride (1.1 ml, 15 mmol, 1.5 equiv) and DMF (0.25 mL) was slowly added. The reaction mixture was stirred at 50 ℃ in an oil bath. After 2 hours, the reaction mixture was added to 40% aqueous solution of dimethylamine (3.1 mL, 27 mmol, 2.7 equiv) at 0 ℃. The reaction mixture was stirred at 0 ℃. After 1 hour, the mixture was diluted with CH_2Cl_2, extracted

with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 1:1) to give the desired product (952 mg, 5.4 mmol, 54% yield). The analytical data of the product matched well with the reported one.



N,*N*-dimethyl-4-(1-propenyl)-benzamide was prepared in 55% yield (*E*/*Z* = 95:5) according to the literature procedure.[41] To an oven-dried 100 mL three-necked round-bottom flask equipped with a stirrer bar and a Dimroth condenser were added Ph_3PEtBr (3.8 g, 10 mmol, 1.2 equiv), NaH (60% in oil, 430 mg, 11 mmol, 1.2 equiv), and THF (20 mL, 0.40 M). The reaction mixture was stirred at 75 ˚C in an oil bath. After 1 hour, 4-formyl-*N*,*N*-dimethylbenzamide (1.5 g, 8.7 mmol, 1.0 equiv) was slowly added at 0 °C. The reaction mixture was stirred again at 75 ℃ in an oil bath. After 21 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. After extraction with hexane/AcOEt (10:1) × 5 times, the crude mixture was purified by flash silica gel column chromatography (hexane/ AcOEt = 2:1) to give the desired product (953 mg, 5.0 mmol, 55% yield).

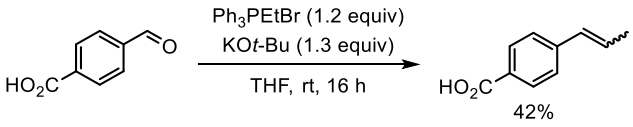
IR (ATR, cm^{-1}): 2930, 2911, 1620, 1489, 1390, 1263, 1082, 987, 860, 753.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.28 (m, 4H), 6.45–6.35 (m, 0.98H), 6.34–6.23 (m, 0.95H), 5.89–5.79 (m, 0.07H), 3.09 (s, 3H), 3.00 (s, 3H), 1.89 (dd, 3H, *J* = 6.4, 1.6 Hz).

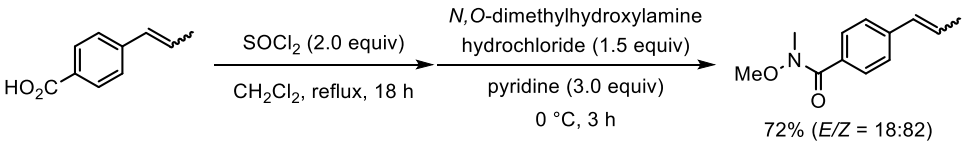
^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.3, 139.0, 138.7, 134.2, 134.0, 130.2, 129.0, 128.5, 127.8, 127.3, 127.0, 126.9, 125.4, 39.4, 35.23, 35.19, 18.4, 14.5.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{15}NONa^+$ 212.1046; Found 212.1046.

***N*-methoxy-*N*-methyl-4-(1-propenyl)-benzamide:**



4-(Prop-1-en-1-yl)benzoic acid was prepared according to the literature procedure.[42] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PEtBr (4.5 g, 12 mmol, 1.2 equiv), KO*t*-Bu (1.5 g, 13 mmol, 1.3 equiv), and THF (30 mL, 0.30 M). The reaction mixture was stirred at room temperature. After 1.5 hours, terephthalaldehydic acid (1.5 g, 10 mmol, 1.0 equiv) was added. Then, the mixture was stirred at room temperature. After 16 hours, saturated aqueous solution of $NaHCO_3$ was added to the mixture and extracted with H_2O × 3 times. The aqueous layer was neutralized with aqueous solution of HCl and extracted with Et_2O × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 2:1) to give the desired product (677 mg, 4.2 mmol, 42% yield). The analytical data of the product matched well with the reported one.



N-Methoxy-*N*-methyl-4-(1-propenyl)-benzamide was prepared according to the literature procedure.[43] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar and a Dimroth condenser were added 4-(1-propen-1-yl)benzoic acid (1.4 g, 8.3 mmol, 1.0 equiv), thionyl chloride (1.2 mL, 17 mmol, 2.0 equiv), CH_2Cl_2 (17 mL, 0.50 M). The reaction

mixture was stirred at 55 ℃ in an oil bath. After 18 hours, the solvent was removed under reduced pressure. The residue was diluted with CH_2Cl_2 (17 mL, 0.50 M) and *N*, *O*-dimethylhydroxylamine hydrochloride (1.2 g, 13 mmol, 1.5 equiv) was added. Then, pyridine (2.0 g, 25 mmol, 3.0 equiv) was slowly added at 0 ℃. The reaction mixture was stirred at 0 ℃. After 3 hours, aqueous solution of HCl was added to the mixture. The aqueous layer was extracted with AcOEt × 3 times. The combined organic phase was washed with aqueous solution of HCl and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give the desired product (1.2 g, 5.8 mmol, 72% yield).

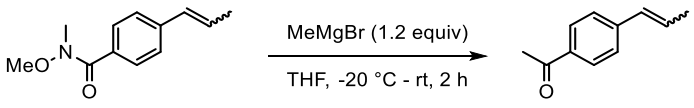
IR (ATR, cm^{-1}): 3020, 2965, 2933, 1635, 1414, 1366, 1215, 1179, 976, 855.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, 1.68H, *J* = 8.0 Hz), 7.63 (d, 0.32H, *J* = 8.0 Hz), 7.37–7.30 (m, 2H), 6.48–6.38 (m, 1H), 6.38–6.27 (m, 0.18H), 5.92–5.81 (m, 0.82H), 3.58 (s, 2.46H), 3.56 (s, 0.54H), 3.37 (d, 2.46H, *J* = 1.2 Hz), 3.36 (d, 0.54H, *J* = 2.0 Hz), 1.95–1.88 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.7, 140.2, 140.0, 131.8, 130. 4, 129.1, 128.6, 128.33, 128.29, 128.2, 127.7, 125.3, 61.0, 33.8, 18.5, 14.7.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{15}NO_2Na^+$ 228.0995; Found 228.0995.

1-[4-(prop-1-enyl)phenyl]ethenone:



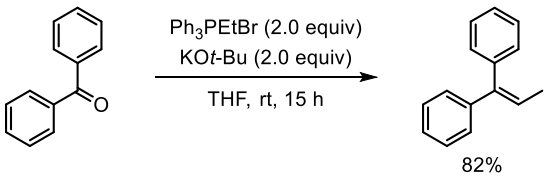
90% (*E*/*Z* = 31:69)

1-[4-(Prop-1-enyl)phenyl]ethenone was prepared according to the literature procedure.[44] To an oven-dried 100 mL three-necked round-bottom flask equipped with a stirrer bar were added *N*-methoxy-*N*-methyl-4-(1-propenyl)-benzamide (1.0 g, 5.1 mmol, 1.0 equiv) and THF (30 mL, 0.20 M). Then, MeMgBr (1.0 M in THF, 6.5 mL, 6.1 mmol, 1.2 equiv) was added

dropwise at -20 °C. The reaction mixture was stirred at- 20°C for 1 hour. Then, the reaction mixture was stirred at room temperature. After 1 hour, saturated aqueous solution of NH_4Cl was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give the desired product (739 g, 4.6 mmol, 90% yield). The analytical data of the product matched well with the reported one.[45] Therefore, only the ^{1}H NMR data is presented here.

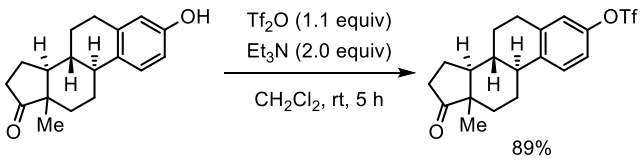
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.93 (d, 2H, *J* = 8.0 Hz), 7.89 (d, 2H, *J* = 8.8 Hz), 6.50–6.34 (m, 3H), 5.92 (dq, 1H, *J* = 11.2, 7.2 Hz), 2.60 (s, 3H), 2.58 (s, 3H), 1.95–1.90 (m, 6H).

prop-1-ene-1,1-diyldibenzene:



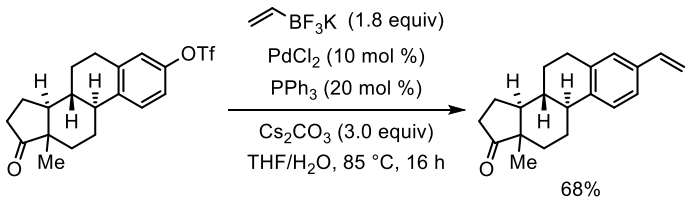
Prop-1-ene-1,1-diyldibenzene was prepared according to the literature procedure.[30] The reaction was carried out on a 5.0 mmol scale and the reaction time was 15 hours. The crude mixture was purified by flash silica gel column chromatography (hexane) to give the desired product (800 mg, 4.1 mmol, 82% yield). The analytical data of the product matched well with the reported one.

Estrone derivative:



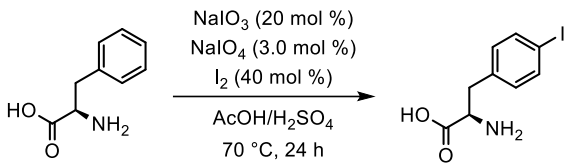
The Estrone derivative was prepared according to the literature procedure.[46] To an oven-

dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added estrone (1.7 g, 6.0 mmol, 1.0 equiv) and CH_2Cl_2 (40 mL, 0.20 M). Then, Et_3N (1.2 g, 12 mmol, 2.0 equiv) and Tf_2O (1.1 mL, 6.6 mmol, 1.1 equiv) were added dropwise at 0 °C. The reaction mixture was stirred at room temperature. After 5 hours, saturated aqueous solution of $NaHCO_3$ was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give the product (2.2 g, 5.4 mmol, 89% yield). The analytical data matched well with the reported one.

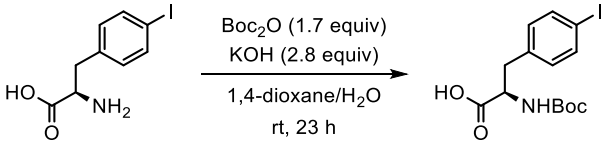


To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added triflated-estrone (2.1 g, 5.3 mmol, 1.0 equiv), potassium vinyl trifluoroborate (1.3 g, 9.5 mmol, 1.8 equiv), Cs_2CO_3 (5.1 g, 16 mmol, 3.0 equiv), $PdCl_2$ (94 mg, 0.53 mmol, 10 mol %), PPh_3 (170 mg, 0.64 mmol, 12 mol %), and THF/H_2O (10 + 1.4 mL, 0.45 M). The reaction mixture was stirred at 85 °C in an oil bath. After 16 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give the desired product (1.0 g, 3.6 mmol, 68% yield). The analytical data of the product matched well with the reported one.

L-phenylalanine derivative:

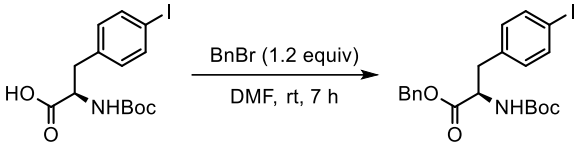


4-iodo-L-phenylalanine was prepared according to the literature procedure.[47] To an oven-dried 100 mL three-necked round-bottom flask equipped with a stirrer bar were added L-phenylalanine (6.6 g, 40 mmol, 1.0 equiv), $NaIO_3$ (1.6 g, 8.0 mmol, 20 mol %), I_2 (4.2 g, 16 mmol, 40 mol %), gracial AcOH (40 mL), and conc. H_2SO_4 (5.0 ml). The reaction mixture was stirred at 70 ℃ in an oil bath for 24 hours. Then, $NaIO_4$ (260 mg, 1.6 mmol, 3.0 mol %) was added, and the mixture was stirred at 70 ℃ in an oil bath. After 5 hours, AcOH was removed under reduced pressure. The orange-colored residue was dissolved with H_2O and washed with Et_2O × 2 times and CH_2Cl_2 × 2 times. The aqueous phase was transferred to an Erlenmeyer flask and cooled to 0 °C. The pH was adjusted to 7 by slow addition of cold aqueous solution of KOH with vigorous stirring. The cold, white, turbid mixture was filtered through a Buchner funnel, to give a white solid. The crude mixture was used in the next reaction without further purification.



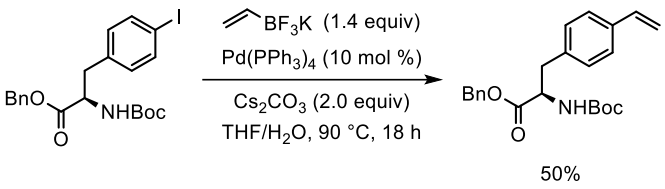
N-Boc-4-iodo-L-phenylalanine was prepared according to the literature procedure.[48] To an oven-dried 250 mL three-necked round-bottom flask equipped with a stirrer bar were added the crude mixture of 4-iodo-L-phenylalanine, Boc_2O (11 g, 50 mmol, 1.7 equiv), KOH (4.7 g, 84 mmol, 2.8 equiv), H_2O (70 mL) and 1,4-dioxane (70 mL). The reaction mixture was stirred at room temperature. After 23 hours, the solvent was removed under reduced pressure and extracted with Et_2O. By addition of aqueous solution of HCl, the aqueous phase was adjusted to pH value

of 7. Then AcOEt was added to the aqueous phase and the pH was adjusted to 2–2.5 with aqueous solution of HCl under vigorous stirring. The aqueous phase was extracted AcOEt × 3 times, and the combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was used in the next reaction without further purification.



56% (3 sreps)

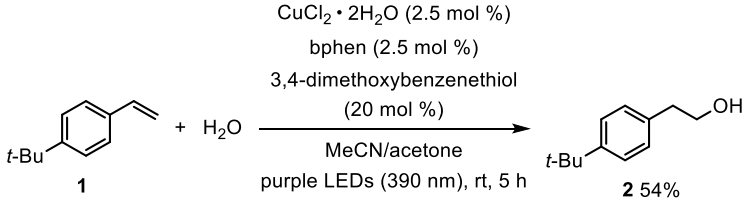
N-Boc-4-iodo-L-phenylalanine benzyl ester was prepared according to the literature procedure.[49] The crude mixture of *N*-Boc-4-iodo-L-phenylalanine was dissolved in 90% methanol in water and neutralized by addition of Cs_2CO_3 until it was weakly alkaline. The solvent was removed under reduced pressure, and any remaining water in the cesium salt of *N*-Boc-4-iodo-L-phenylalanine was further removed by repeated azeotropic distillation with toluene. The resulting dry salt was dissolved in DMF (30 mL), and benzyl bromide (3.6 mL, 30 mmol, 1.2 equiv) was added. The reaction mixture was stirred at room temperature. After 7 hours, the solvent was removed under reduced pressure. The residue was dissolved AcOEt and aqueous solution of AcOH (15% v/v), and the organic phase was washed with aqueous solution of citric acid (5% v/v), saturated aqueous solution of $NaHCO_3$, and brine. After the removal of the solvent under reduced pressure, the crude mixture was purified by flash silica gel column chromatography (CH_2Cl_2/AcOEt = 95:5) to give the desired product (11 g, 22 mmol, 56% yield in 3 steps). The analytical data of the product matched well with the reported one.[49]



The desired L-phenylalanine derivative was prepared according to the literature procedure.[50] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added *N*-Boc-4-iodo-L-phenylalanine benzyl ester (1.4 g, 3.0 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (340 mg, 0.30 mmol, 10 mol %), potassium vinyltrifluoroborate (560 mg, 4.2 mmol, 1.4 equiv), Cs_2CO_3 (2.0 g, 6.0 mmol, 2.0 equiv), THF (12 mL), and H_2O (1.3 mL). The reaction mixture was stirred at 90 ℃ in an oil bath. After 18 hours, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 9:1) and GPC (570 mg, 1.5 mmol, 50% yield). The analytical data of the product matched well with the already reported one.[51] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.39–7.31 (m, 3H), 7.31–7.23 (m, 4H), 7.00 (d, 2H, *J* = 7.6 Hz), 6.67 (dd, 1H, *J* = 17.6, 10.4 Hz), 5.71 (dd, 1H, *J* = 17.6, 0.8 Hz), 5.22 (d, 1H, *J* = 11.6 Hz), 5.19–5.05 (m, 3H), 4.97 (d, 1H, *J* = 8.0 Hz), 4.61 (q, 1H, *J* = 8.0 Hz), 3.07 (br, 2H), 1.4 (s, 9H).

- **Typical Procedure for the Copper-Catalyzed *anti*-Markovnikov Hydration of Vinylarenes.**

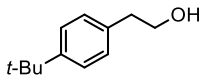


$CuCl_2 \cdot 2H_2O$ (1.3 mg, 7.6×10^{-3} mmol, 2.5 mol %), bathophenanthroline (2.6 mg,

7.8×10^{-3} mmol, 2.5 mol %) were added to a 25 mL test tube equipped with a stir bar. The vial was flushed with N_2 gas and quickly capped with a Teflon septum. 4-*tert*-Butylstyrene (48.2 mg, 0.30 mmol, 1.0 equiv), 3,4-dimethoxybenzenethiol (11.8 mg, 0.070 mmol, 20 mol %) were added to a 4.0 mL vial. In the glove box, the mixture was transferred to the test tube using MeCN (2.25 mL) and acetone (2.25 mL). H_2O (0.45 ml; degassed with argon gas for 30 min) was added *via* syringe. The mixture was stirred vigorously under purple LEDs (390 nm, 23 W) irradiation with a fan. After 5 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **2** as a colorless oil (29.0 mg, 0.16 mmol, 54% yield).

■ Characterization of the Products.

2:

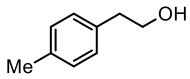


The analytical data of **2** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (d, 2H, *J* = 7.6 Hz), 7.17 (d, 2H, *J* = 8.4 Hz), 3.86 (t, 2H, *J* = 6.4 Hz), 2.85 (t, 2H, *J* = 6.4 Hz), 1.32 (s, 9H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 149.3, 135.3, 128.7, 125.5, 63.6, 38.6, 34.4, 31.3.

3:



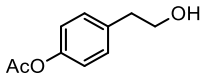
The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 7 hours. The crude mixture was purified by preparative thin-layer chromatography

(hexane/AcOEt = 3:1) to give **3** as a colorless oil (12.2 mg, 0.090 mmol, 30% yield). The analytical data of **3** matched well with the already reported one.[52] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.13 (s, 4H), 3.84 (t, 2H, *J* = 6.6 Hz), 2.84, (t, 2H, *J* = 6.6 Hz), 2.34 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 136.0, 135.3, 129.2, 128.9, 63.7, 38.7, 21.0.

4:

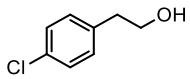


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 1:1) to give **4** as a pale yellow oil (33.5 mg, 0.19 mmol, 62% yield). The analytical data of **4** matched well with the already reported one.[53] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24 (d, 2H, *J* = 8.0 Hz), 7.05–7.00 (m, 2H), 3.86 (t, 2H, *J* = 6.2 Hz), 2.86 (t, 2H, *J* = 6.4 Hz), 2.29 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.7, 149.2, 136.2, 130.0, 121.5, 63.4, 38.5, 21.1.

5:



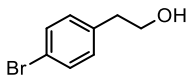
The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 7 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **5** as a pale yellow oil (25.0 mg, 0.16 mmol, 53% yield). The analytical data of **5** matched well with the already reported one.[18] Therefore, only the NMR data

are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.26 (m, 2H), 7.19–7.14 (m, 2H), 3.85 (t, 2H, *J* = 6.8 Hz), 2.84 (t, 2H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 137.0, 132.3, 130.3, 128.6, 63.4, 38.5.

6:

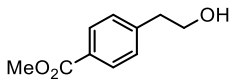


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 7 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **6** as a pale yellow oil (31.8 mg, 0.16 mmol, 53% yield). The analytical data of **6** matched well with the already reported one.[53] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.41 (m, 2H), 7.14–7.08 (m, 2H), 3.85 (t, 2H, *J* = 6.4 Hz), 2.83 (t, 2H, *J* = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 137.5, 131.6, 130.7, 120.3, 63.3, 38.5.

7:



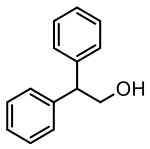
The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 30 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **7** as a beige solid (25.0 mg, 0.14 mmol, 46% yield). The analytical data of **7** matched well with the already reported one.[53] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 3.91 (s, 3H),

3.90 (t, 2H, J = 6.4 Hz), 2.93 (t, 2H, J = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 167.0, 144.1, 129.9, 129.0, 128.4, 63.3, 52.0, 39.1.

8:

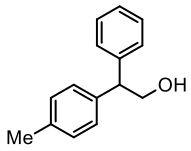


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 5 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **8** as a pale yellow solid (36.8 mg, 0.19 mmol, 62% yield). The analytical data of **8** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.18 (m, 10H), 4.26–4.14 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 141.3, 128.7, 128.3, 126.8, 66.1, 53.6.

9:



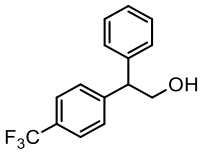
The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **9** as a beige solid (32.5 mg, 0.15 mmol, 51% yield). The analytical data of **9** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.19 (m, 5H), 7.18–7.10 (m, 4H), 4.22–4.12 (m, 3H), 2.32

(s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 141.6, 138.3, 136.4, 129.4, 128.7, 128.23, 128.15, 126.7, 66.2, 53.2, 21.0.

10:

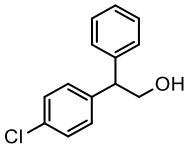


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 5 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **10** as a colorless oil (47.9 mg, 0.18 mmol, 60% yield). The analytical data of **10** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (d, 2H, *J* = 8.4 Hz), 7.43–7.30 (m, 4H), 7.29–7.21 (m, 3H), 4.31–4.17 (m. 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 145.7, 140.5, 129.0 (q, *J* = 32.4 Hz), 128.9, 128.7, 128.3, 127.2, 125.5 (q, *J* = 3.8 Hz), 122.8, 65.8, 53.3.

11:



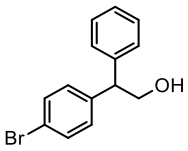
The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 8 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **11** as a pale yellow oil (35.0 mg, 0.15 mmol, 50% yield). The

analytical data of **11** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.17 (m, 9H), 4.22–4.10 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 140.9, 140.0, 132.6, 129.6, 128.79, 128.77, 128.2, 127.0, 65.9, 52.9.

12:

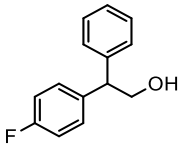


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 8 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **12** as a colorless oil (50.5 mg, 0.18 mmol, 61% yield). The analytical data of **12** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44 (d, 2H, J = 8.8 Hz), 7.36–7.30 (m, 2H), 7.28–7.20 (m, 3H), 7.15 (d, 2H, J = 8.4 Hz), 4.21–4.10 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 140.8, 140.5, 131.7, 130.0, 128.8, 128.2, 127.0, 120.6, 65.8, 52.9.

13:



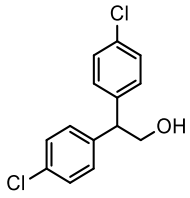
The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time

was 8 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **13** as a pale yellow oil (35.4 mg, 0.16 mmol, 55% yield). The analytical data of **13** matched well with the already reported one.[54] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.30 (m, 2H), 7.28–7.20 (m, 5H), 7.05–6.97 (m, 2H), 4.23–4.09 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 161.7 (d, J = 243.1 Hz), 141.2, 137.2 (d, J = 1.9 Hz), 129.7 (d, J = 7.6 Hz), 128.8, 128.2, 126.9, 115.5 (d, J = 21.0 Hz), 66.1, 52.8.

14:

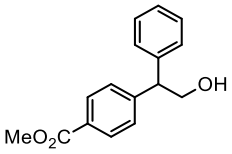


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 8 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **14** as a white solid (43.0 mg, 0.16 mmol, 54% yield). The analytical data of **14** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 (d, 4H, J = 8.4 Hz), 7.17 (d, 4H, J = 8.4 Hz), 4.19–4.10 (m, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 139.5, 132.8, 129.6, 128.9, 65.7, 52.2.

15:

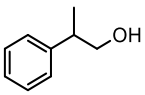


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 7 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **15** as a beige solid (46.1 mg, 0.18 mmol, 60% yield). The analytical data of **15** matched well with the already reported one.[55] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02–7.96 (m, 2H), 7.37–7.30 (m, 4H), 7.28–7.2 (m, 3H), 4.30–4.25 (m, 1H), 4.22–4.18 (m, 2H), 3.90 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.9, 146.8, 140.6, 129.9, 128.8, 128.7, 128.34, 128.29, 127.1, 65.8, 53.5, 52.1.

16:

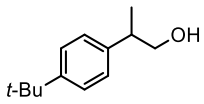


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **16** as a colorless oil (15.8 mg, 0.12 mmol, 39% yield). The analytical data of **16** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.30 (m, 2H), 7.27–7.21 (m, 3H), 3.49 (d, 2H, J = 8.8 Hz), 2.96 (dq, 1H, J = 13.6, 6.9 Hz), 1.29 (d, 3H, J = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 143.6, 128.6, 127.5, 126.7, 68.7, 42.4, 17.6.

17:

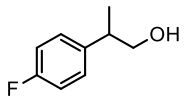


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 5 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **17** as a white solid (24.4 mg, 0.13 mmol, 42% yield). The analytical data of **17** matched well with the already reported one.[56] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 3.70 (d, 2H, *J* = 6.8 Hz), 2.93 (dq, 1H, *J* = 14.0, 6.9 Hz), 1.32 (s, 9H), 1.27 (d, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 149.4, 140.4, 127.1, 125.5, 68.7, 41.9, 34.4, 31.3, 17.5.

18:

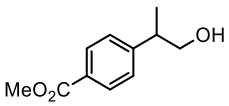


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **18** as a pale yellow oil (28.6 mg, 0.19 mmol, 62% yield). The analytical data of **18** matched well with the already reported one.[56] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24–7.17 (m, 2H), 7.05–6.97 (m, 2H), 3.69 (dd, 2H, *J* = 6.4, 3.2 Hz), 2.95 (dq, 1H, *J* = 13.6, 6.8 Hz), 1.26 (d, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 161.6 (d, *J* = 243.1 Hz), 139.3 (d, *J* = 2.9 Hz), 128.8 (d, *J* = 7.6 Hz), 115.4 (d, *J* = 20.9 Hz), 68.7, 41.7, 17.7.

19:

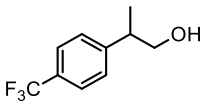


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **19** as a pale yellow oil (37.0 mg, 0.19 mmol, 63% yield). The analytical data of **19** matched well with the already reported one.[57] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (d, 2H, *J* = 8.4 Hz), 7.32 (d, 2H, *J* = 8.4 Hz), 3.91 (s, 3H), 3.74 (d, 2H, *J* = 6.8 Hz), 3.03 (dq, 1H, *J* = 13.6, 6.8 Hz), 1.30 (d, 3H, *J* = 7.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 167.0, 149.3, 129.9, 128.6, 127.5, 68.3, 52.0, 42.5, 17.4.

20:

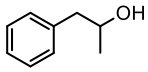


The reaction was carried out with 5.0 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **20** as a pale yellow oil (21.3 mg, 0.10 mmol, 35% yield). The analytical data of **20** matched well with the already reported one.[53] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59 (d, 2H, *J* = 7.6 Hz), 7.36 (d, 2H, *J* = 8.4 Hz), 3.74 (d, 2H, *J* = 6.4 Hz), 3.03 (dq, 1H, *J* = 14.4, 7.1 Hz), 1.30 (d, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 148.0, 128.9 (q, *J* = 32.1 Hz), 127.8, 125.5 (q, *J* = 3.5 Hz) 124.1 (q, *J* = 270.1 Hz), 68.3, 42.3, 17.4.

21:

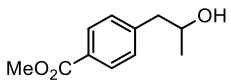


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **21** as a pale yellow oil (from *cis*-β-methylstyrene: 22.3 mg, 0.16 mmol, 55% yield. from *trans*-β-methylstyrene: 24.2 mg, 0.18 mmol, 59% yield). The analytical data of **21** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.29 (m, 2H), 7.27–7.18 (m, 3H), 4.08–3.98 (m, 1H), 2.80 (dd, 1H, *J* = 13.6, 4.8 Hz), 2.70 (dd, 1H, *J* = 13.2, 8.0 Hz), 1.25 (d, 3H, *J* = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 138.5, 129.4, 128.5, 126.5, 68.9, 45.8, 22.8.

22:

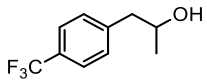


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **22** as a colorless oil (45.3 mg, 0.23 mmol, 78% yield). The analytical data of **22** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, 2H, *J* = 8.4 Hz), 7.30 (d, 2H, *J* = 7.6 Hz), 4.11–4.02 (m, 1H), 3.91 (s, 3H), 2.84 (dd, 1H, *J* = 13.4, 5.0 Hz), 2.77 (dd, 1H, *J* = 13.2, 8.0 Hz), 1.25 (d, 3H, *J* = 6.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 167.0, 144.1, 129.8, 129.4, 128.4, 68.6, 52.0, 45.7, 23.0.

23:

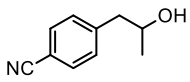


The reaction was carried out with 5.0 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **23** as a colorless oil (35.1 mg, 0.17 mmol, 57% yield). The analytical data of **23** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (d, 2H, *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 7.6 Hz), 4.11–4.02 (m, 1H), 2.84 (dd, 1H, *J* = 13.8, 5.0 Hz), 2.78 (dd, 1H, *J* = 13.6, 7.6 Hz), 1.26 (d, 3H, *J* = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 142.8, 129.7, 128.8 (q, *J* = 33.0 Hz), 125.4 (q, *J* = 3.9 Hz), 124.3 (q, *J* = 269.8 Hz), 68.6, 45.4, 23.0.

24:

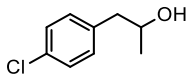


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **24** as a pale yellow oil (22.5 mg, 0.14 mmol, 47% yield). The analytical data of **24** matched well with the already reported one.[57] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60 (d, 2H, *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 8.4 Hz), 4.11–4.01 (m, 1H), 2.84 (dd, 1H, *J* = 13.8, 5.0 Hz), 2.78 (dd, 1H, *J* = 13.4, 7.4 Hz), 1.26 (d, 3H, *J* = 5.6 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 144.4, 132.1, 130.2, 118.9, 110.2, 68.4, 45.6, 23.2.

25:

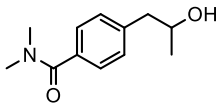


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **25** as a pale yellow oil (26.6 mg, 0.16 mmol, 52% yield). The analytical data of **25** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.25 (m, 2H), 7.15 (d, 2H, *J* = 8.8 Hz), 4.05–3.95 (m, 1H), 2.75 (dd, 1H, *J* = 13.4, 5.0 Hz), 2.67 (dd, 1H, *J* = 13.6, 7.6 Hz), 1.24 (d, 3H, *J* = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 137.0, 132.3, 130.7, 128.6, 68.7, 45.0, 22.9.

26:



The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (AcOEt) to give **26** as a colorless oil (45.2 mg, 0.22 mmol, 73% yield).

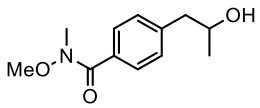
IR (ATR, cm^{-1}): 3396, 2966, 2925, 1608, 1491, 1392, 1265, 1080, 938, 759.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (d, 2H, *J* = 8.0 Hz), 7.25 (d, 2H, *J* = 8.4 Hz), 4.08–3.98 (m, 1H), 3.05 (s, 6H), 2.80 (dd, 1H, *J* = 13.6, 4.8 Hz), 2.73 (dd, 1H, *J* = 13.2, 8.0 Hz), 1.25 (d, 3H, *J* = 6.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 167.0, 144.1, 129.8, 129.4, 128.4, 68.6, 52.0, 45.7, 23.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{17}NO_2Na^+$ 230.1151; Found 230.1151.

27:



The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (AcOEt) to give **27** as a colorless oil (51.7 mg, 0.23 mmol, 77% yield).

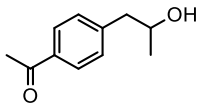
IR (ATR, cm^{-1}): 3408, 2966, 2930, 1625, 1611, 1418, 1373, 1112, 977, 938, 751, 563.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (d, 2H, *J* = 8.4 Hz), 7.27–7.23 (m, 2H), 4.09–4.00 (m, 1H), 3.56 (s, 3H), 3.36 (s, 3H), 2.81 (dd, 1H, *J* = 13.4, 5.0 Hz), 2.75 (dd, 1H, *J* = 13.6, 7.6 Hz), 1.25 (d, 3H, *J* = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.7, 141.5, 132.1, 129.0, 128.4, 68.6, 61.0, 45.5, 33.8, 22.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{17}NO_3Na^+$ 246.1101; Found 246.1081.

28:



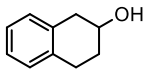
The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 30 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **28** as a colorless oil (45.6 mg, 0.26 mmol, 85% yield). The analytical data of **28** matched well with the already reported one.[57] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94–7.89 (m, 2H), 7.32 (d, 2H, *J* = 8.4 Hz), 4.12–4.01 (m, 1H), 2.84 (dd, 1H, *J* = 13.8, 5.0 Hz), 2.78 (dd, 1H, *J* = 13.8, 7.8 Hz), 2.59 (s, 3H), 1.26 (d, 3H, *J* = 6.4

Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.8, 144.4, 135.5, 129.6, 128.6, 68.6, 45.6, 26.6, 23.1.

29:

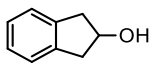


The reaction was carried out with 5.0 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **29** as a pale yellow oil (22.1 mg, 0.15 mmol, 50% yield). The analytical data of **29** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.15–7.06 (m, 4H), 4.21–4.13 (m, 1H), 3.10 (dd, 1H, *J* = 15.6, 4.4 Hz), 2.97 (dt, 1H, *J* = 17.2, 5.8 Hz), 2.90–2.73 (m, 2H), 2.11–2.02 (m, 1H), 1.88–1.77 (m, 1H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 135.6, 134.2, 129.5, 128.6, 126.0, 125.8, 67.2, 38.4, 31.5, 26.9.

30:



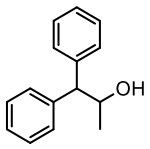
The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 5 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **30** as a white solid (25.8 mg, 0.19 mmol, 64% yield). The analytical data of **30** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27–7.22 (m, 2H), 7.20–7.15 (m, 2H), 4.74–4.68 (m, 1H), 3.22

(dd, 2H, J = 16.0, 6.0 Hz), 2.92 (dd, 2H, J = 16.4, 3.2 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 140.8, 126.6, 125.0, 73.1, 42.6.

31:

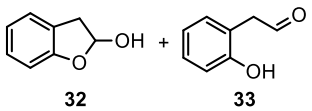


The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **31** as a white solid (33.6 mg, 0.16 mmol, 53% yield). The analytical data of **31** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.12 (m, 10H), 4.57–4.48 (m, 1H), 3.78 (d, 1H, J = 8.8 Hz), 1.17 (d, 3H, J = 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 142.5, 141.5, 128.9, 128.62, 128.59, 128.2, 126.9, 126.5, 70.0, 60.6, 21.4.

32 and 33:



32 **33**

The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 5 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **32** and **33** as a pale yellow oil (**32**:**33** = 89:11, 23.7 mg, 0.17 mmol, 58% yield). The analytical data of **32** and **33** matched well with the already reported one.[58]

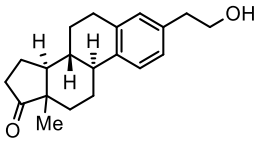
Therefore, only the NMR data are presented here.

^{1}H NMR of 32 ($CDCl_3$, 400 MHz): δ 7.24–7.09 (m, 2H), 6.96–6.80 (m, 2H), 6.07 (dd, 1H, *J* = 6.6, 2.2 Hz), 3.40 (dd, 1H, *J* = 16.6, 6.6 Hz), 3.04 (dd, 1H, *J* = 16.6, 1.8 Hz).

^{13}C{^{1}H} NMR of 32 ($CDCl_3$, 101 MHz): δ 157.6, 128.1, 125.0, 124.7, 121.2, 109.8, 100.7, 37.7.

Selected ^{1}H NMR signals of 33 ($CDCl_3$, 400 MHz): 9.79 (t, 1H, J = 2.2 Hz), 3.73 (d, 2H, J = 2.0 Hz).

34:

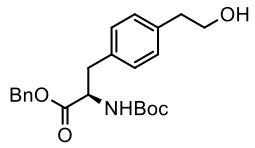


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **34** as a white solid (46.0 mg, 0.15 mmol, 51% yield). The analytical data of **34** matched well with the already reported one.[59] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.21 (m, 1H), 7.03 (d, 1H, *J* = 8.0 Hz), 6.98 (s, 1H), 3.86 (t, 2H, *J* = 6.6 Hz), 2.95–2.85 (m, 2H), 2.82 (t, 2H, *J* = 6.6 Hz), 2.51 (dd, 1H, *J* = 18.8, 8.8 Hz), 2.46–2.38 (m, 1H), 2.34–2.23 (m, 1H), 2.21–1.35 (m, 10H), 0.91 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 220.9, 137.9, 136.6, 135.8, 129.6, 126.4, 125.6, 63.6, 50.4, 47.9, 44.2, 38.6, 38.1, 35.8, 31.5, 29.3, 26.5, 25.7, 21.5, 13.8.

35:

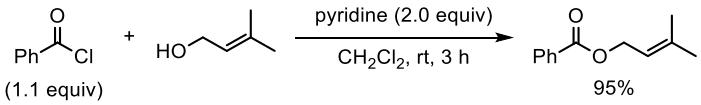


The reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **35** as a colorless oil (63.9 mg, 0.16 mmol, 53% yield). The analytical data of **35** matched well with the already reported one.[51] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.23 (m, 5H), (d, 2H, *J* = 16.0 Hz), (d, 2H, *J* = 16.0 Hz), 5.22–5.06 (m, 2H), (d, 1H, *J* = 16.0 Hz), 4.70–4.54 (m, 1H), 3.83 (t, 2H, *J* = 16.0 Hz), 3.13–2.96 (m, 2H), 2.82 (t, 2H, *J* = 16.0 Hz), 1.41 (s, 9H).

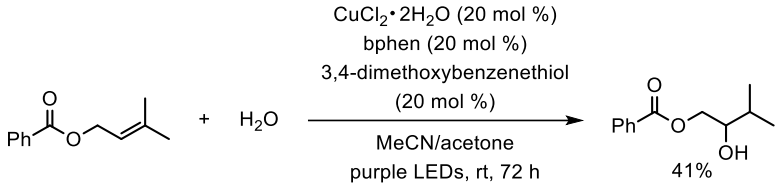
^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.7, 155.0, 137.1, 135.1, 133.9, 129.5, 129.1, 128.5, 128.4, 79.9, 67.0, 63.5, 54.4, 38.7, 37.8, 28.2.

■ *Anti*-Markovnikov Hydration of the Tri-Substituted Aliphatic Alkene.



The substrate of the reaction was prepared according to the literature procedure.[60] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added prenol (430 mg, 5.0 mmol, 1.0 equiv), pyridine (0.8 mL, 10 mmol, 2.0 equiv), CH_2Cl_2 (6.0 ml, 0.80 M). Then, benzoyl chloride (0.60 mL, 5.5 mmol, 1.1 equiv) was added at 0 ℃. The reaction mixture was stirred at room temperature. After 3 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and

concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ AcOEt = 20:1) to give the desired product (908 mg, 4.8 mmol, 95% yield). The analytical data matched well with the reported one.

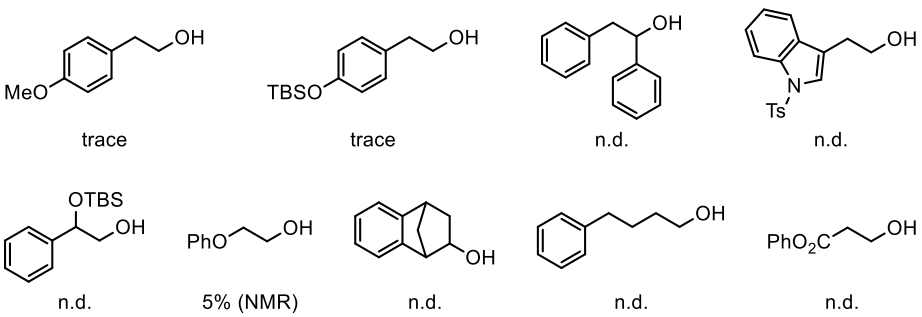


The reaction was carried out with 20 mol % of copper salt and bphen. The reaction time was 72 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give the desired product as a colorless oil (25.3 mg, 0.12 mmol, 41% yield). The analytical data matched well with the already reported one.[61] Therefore, only the NMR data are presented here.

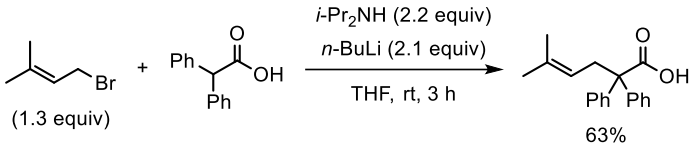
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08–8.03 (m, 2H), 7.61–7.55 (m, 1H), 7.45 (t, 2H, *J* = 7.8 Hz), 4.47 (dd, 1H, *J* = 11.6, 2.8 Hz), 4.31 (dd, 1H, *J* = 11.8, 7.4 Hz), 3.78–3.70 (m, 1H), 2.10 (d, 1H, *J* = 4.8 Hz), 1.94–1.80 (m, 1H), 1.04 (d, 3H, *J* = 6.4 Hz), 1.02 (d, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.8, 133.1, 129.9, 129.6, 128.4, 74.8, 67.8, 31.2, 18.7, 17.8.

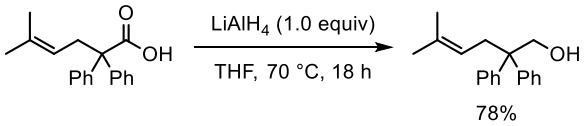
■ **Unsuccessful Substrates.**



■ **Intramolecular Hydrortherification.**

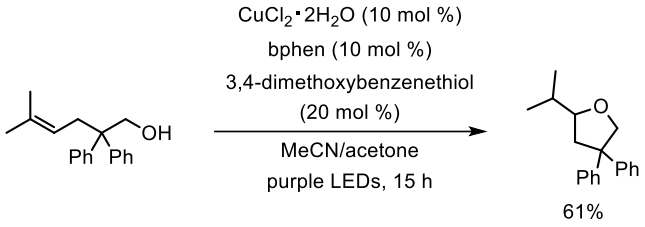


The substrate for intramolecular hydroetherification was prepared according to the literature procedure.[21a] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added diisopropylamine (3.1 mL, 22 mmol, 2.2 equiv) and THF (60 mL). *n*-BuLi (1.6 M in hexane, 14 mL, 21 mmol, 2.1 equiv) was added to the mixture at 0 °C. The mixture was stirred at 0 °C for 30 minutes. Then, diphenylacetic acid (2.1 g, 10 mmol, 1.0 equiv) in THF (10 mL) was added dropwise at -78 °C. After 1 hour. 1-bromo-3-methyl-2-butene (1.9 g, 13 mmol, 1.3 equiv) was added. The reaction mixture was stirred at room temperature. After 3 hours, saturated aqueous solution of NH_4Cl was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with 1.0 M aqueous solution of HCl, H_2O, and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give the desired product (1.8 g, 6.3 mmol, 63% yield). The analytical data of the product matched well with the reported one.



To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added lithium aluminium hydride (240 mg, 6.3 mmol, 1.0 equiv) and THF (10 mL). Then, the carboxylic acid (1.7 g, 6.3 mmol, 1.0 equiv) in THF (5.0 mL) was slowly added at 0 °C. The reaction mixture was stirred at 70 °C in an oil bath. After 18 hours, H_2O and 1.0 M aqueous solution of NaOH were added at 0°C. The mixture was extracted with Et_2O × 3 times. The

combined organic phase was passed through a pad of Celite and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give the desired product (1.3 g, 4.9 mmol, 78% yield). The analytical data of the product matched well with the reported one.

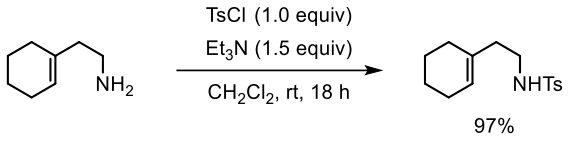


The intramolecular reaction was carried out with 10 mol % of copper salt and bphen. The reaction time was 15 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 20:1) to give the desired product as a colorless oil (48.8 mg, 0.18 mmol, 61% yield). The analytical data matched well with the already reported one.[21a] Therefore, only the NMR data are presented here.

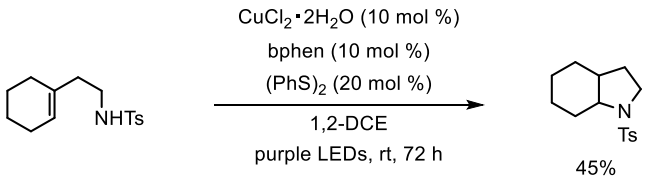
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.14 (m, 10H), 4.65 (dd, 1H, *J* = 8.6, 1.0 Hz), 4.05 (d, 1H, *J* = 8.8 Hz), 3.70 (ddd, 1H, *J* = 10.0, 7.2, 6.0 Hz), 2.53 (ddd, 1H, *J* = 12.0, 5.7, 1.2 Hz), 2.33 (dd, 1H, *J* = 11.8, 10.2 Hz), 1.83–1.68 (m, 1H), 0.98 (d, 3H, *J* = 6.4 Hz), 0.88 (d, 3H, *J* = 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): 146.4, 146.0, 128.3, 128.2, 127.12, 127.09, 126.3, 126.1, 84.1, 76.8, 55.9, 42.4, 33.5, 19.2, 18.3.

■ **Intramolecular Hydroamination.**



The substrate of intramolecular hydroamination was prepared according to the literature procedure.[21b] To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added 2-(1-cyclohexenyl)ethylamine (620 mg, 5.0 mmol, 1.0 equiv), TsCl (960 mg, 5.0 mmol, 1.0 equiv), Et_3N (1.1 mL, 7.5 mmol, 1.5 equiv), and CH_2Cl_2 (25 mL, 0.20 M). The reaction mixture was stirred at room temperature. After 18 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 7:1) to give the desired product (1.4 g, 4.8 mmol, 97% yield). The analytical data matched well with the reported one.

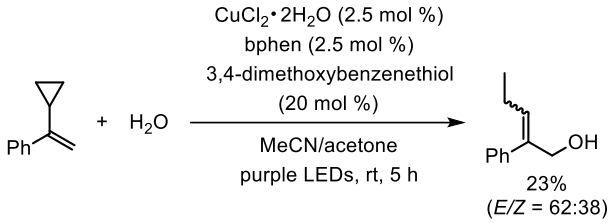


In a nitrogen-filled glove-box, 1,2-dichloroethane (0.60 mL, 0.50 M) was added to *N*-tosyl-2-(1-cyclohexenyl)ethylamine (84.2 mg, 0.30 mmol, 1.0 equiv), $CuCl_2 \cdot 2H_2O$ (5.5 mg, 0.030 mmol, 10 mol %), bphen (10.1 mg, 0.030 mmol, 10 mol %), and $(PhS)_2$ (12.9 mg, 0.060 mmol, 20 mol %) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred at room temperature under purple LEDs irradiation. After 72 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give the desired product (37.6 mg, 0.13 mmol, 45% yield). The analytical data matched well with the already reported one.[21b] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72 (d, 2H, *J* = 8.4 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 3.58–3.47 (m,

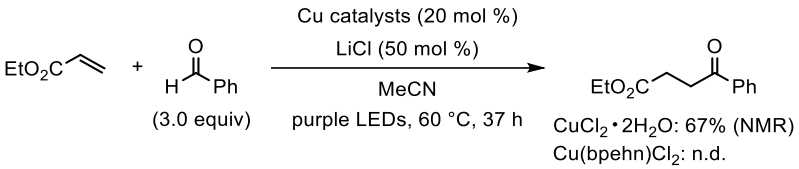
2H), 3.22–3.13 (m, 1H), 2.42 (s, 3H), 1.93–1.74 (m, 3H), 1.67–1.47 (m, 5H), 1.43–1.14 (m, 3H). **$^{13}C\{^{1}H\}$ NMR** ($CDCl_3$, 101 MHz): 143.0, 135.3, 129.5, 127.3, 59.5, 47.2, 37.7, 29.8, 27.6, 26.2, 23.1, 21.5, 21.3.

■ **Ring-Opening Reaction.**



The reaction was carried out with 2.5 mol % of copper salt and bphen. The reaction time was 7 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give the ring-opening product as a pale yellow oil (11.3 mg, 0.070 mmol, 23% yield). The analytical data of the product matched well with the already reported one.[62]

■ **Chlorine Radical Probe Experiments.**



In order to investigate the possibility that the generation of chlorine radicals *via* LMCT, the n reaction was carried out according to the literature procedure.[13d] In a nitrogen-filled glove-box, MeCN (1.0 mL, 0.30 M) was added to copper catalyst (0.060 mmol, 2.5 mol %), LiCl (0.15 mmol, 50 mol %), ethyl acrylate (0.30 mmol, 1.0 equiv), and benzaldehyde (0.90 mmol, 3.0 equiv) in an oven-dried 4 mL vial equipped with a stir bar. The vial was taken outside the glove-box. The reaction mixture was stirred under purple LEDs (390 nm, 23 W) irradiation at 60 °C in an oil bath. After 37 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was

concentrated under reduced pressure. The crude mixture was analyzed by ^{1}H NMR using 1,1,2,2-tetrabromoethane as an internal standard.

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Chapter 4

Photoexcited Palladium Catalysis: Cross-Coupling Reaction of α-Chlorocarbonyl Compounds with Arylboronic Acids

Abstract

A Suzuki-Miyaura cross-coupling reaction of α-chloroacetates or α-chloroacetamides with arylboronic acids proceeded under mild conditions by visible-light irradiation. The photoexcited palladium catalyst undergoes an oxidative addition with α-chlorocarbonyl compounds, which are less reactive than iodides and bromides. This reaction provides a useful method for the synthesis of bioactive α-arylacetates and α-arylacetamides.

Introduction

α-Arylacetates and α-arylacetamides are important synthetic intermediates and are often observed in the core structures of naturally deriving alkaloids and nonsteroidal anti-inflammatory drugs (**Figure 1**a).[1] Therefore, numerous methods for their preparation have long been developed. A transition metal-catalyzed cross-coupling reaction is one of the most straightforward and reliable approaches. There are two types of cross-coupling reactions. One is a cross-coupling reaction between metal enolates and aryl electrophiles,[2] and the other is between α-halocarbonyl compounds and aryl nucleophiles such as aryl-boron[3] or aryl-zinc[4] reagents (**Figure 1**b).

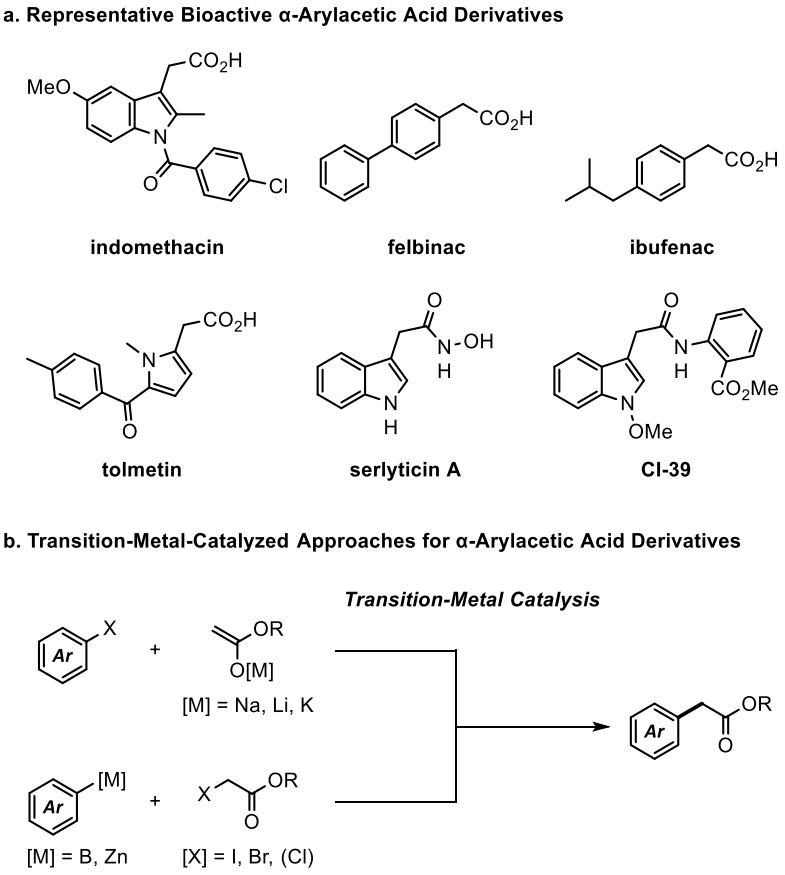


Figure 1. (a) Examples of natural products that contain the α-arylacetic acid or α-arylacetamide motif. (b) Overview of methods for the synthesis of α-arylacetic acid derivatives.

The first method requires strong bases to generate metal enolates and suffers from a low functional group tolerance. On the other hand, the second method has a high functional group tolerance, and the starting materials are readily available from commercial sources. As for α-halocarbonyl electrophiles, α-iodo and α-bromocarbonyl compounds are generally used due to their high reactivity.

In contrast, α-chlorocarbonyl compounds, although less expensive than iodides and bromides, are used in only a few cases (**Scheme 1**).[5,6] Molander reported a palladium-catalyzed cross-coupling reaction of α-chlorocarbonyl compounds with potassium aryltrifluoroborates under harsh reaction conditions (100 °C, a sealed microwave vial).[5a] A similar nickel-catalyzed reaction of arylboronic acids reported by Yang also requires heating at 80 °C.[5b] The only example of the cross-coupling reaction of α-chlorocarbonyl compounds which proceeded at or below room temperature was reported by Fu.[5c] They used aryl-(9-BBN) (9-BBN = 9-borabicyclo-[3.3.1]nonane), which is highly reactive and moisture sensitive. Thus, room temperature cross-coupling reactions of α-chlorocarbonyl compounds with arylboronic acids are yet to be developed.

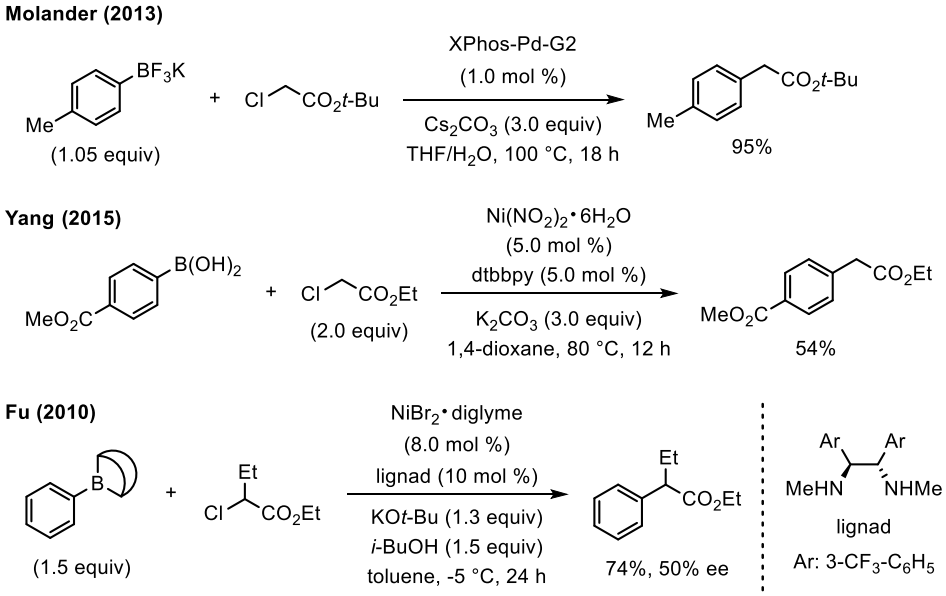
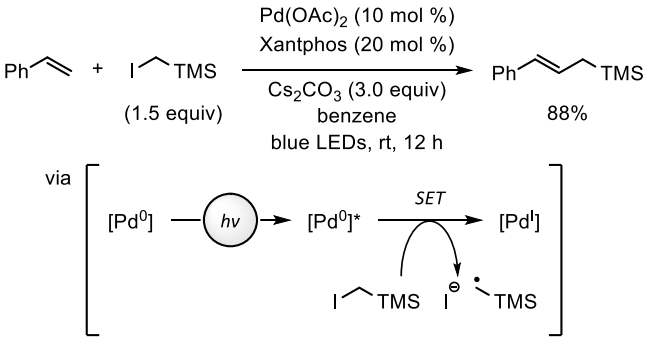


Figure 2. Examples of cross-coupling reactions of α-chlorocarbonyl compounds.

Recently, as mentioned in Chapter 1, photoexcited palladium catalysis has emerged as a new synthetic tool.[7] For example, Gevorgyan showed that single-electron transfer (SET) from photoexcited palladium(0) complexes to alkyl halides occurred to generate the corresponding alkyl radicals under visible-light irradiation, which allowed to use of less reactive electrophiles in cross-coupling reactions (**Scheme 1**).[8] This led the author to study the cross-coupling reaction of α-chlorocarbonyl compounds with arylboronic acids under photoirradiation. In this chapter, the author reports that the reaction proceeded smoothly at room temperature.

Scheme 1. Generation of Alkyl Radicals by Photoexcited Palladium Catalysis

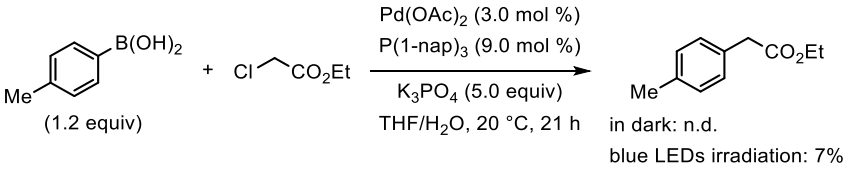


Results and Discussion

■ Photoexcited Palladium-Catalyzed Cross-Coupling Reaction

Gooßen reported that the palladium-catalyzed cross-coupling reaction of ethyl bromoacetate with arylboronic acids proceeds at room temperature.[3a] Although the author applied their reaction conditions [$Pd(OAc)_2$ (3.0 mol %), P(1-Nap)$_3$ (9.0 mol %), K_3PO_4 (5.0 equiv), THF/H_2O, rt, 21 hours] to the reaction of ethyl chloroacetate (**1**) with *p*-tolylboronic acid (**2a**), no formation of the desired cross-coupling product **3a** was observed. Next, the author conducted the same reaction under blue LED irradiation (470 nm, 23 W), and **3a** was obtained albeit in 7% yield (**Scheme 2**).

Scheme 2. Initial Results.

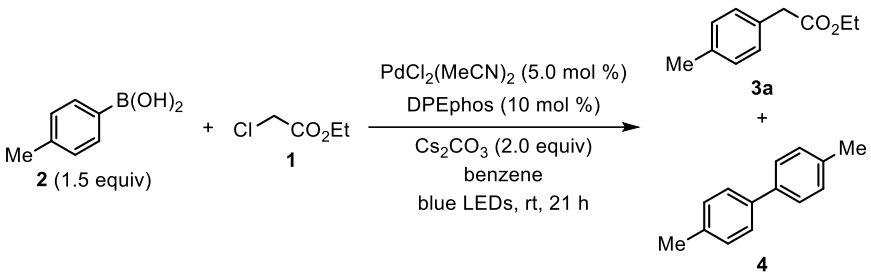


The preliminary result prompted the author to examine various kinds of palladium catalysts, ligands, and bases (see the Experimental Section). When a benzene solution of **1** (0.20 mmol) and **2a** (1.5 equiv) was stirred for 21 hours in the presence of $PdCl_2(MeCN)_2$ (5.0 mol %), DPEphos (10 mol %), and Cs_2CO_3 (2.0 equiv), the cross-coupling product **3a** was formed in 90% NMR yield along with the homocoupling product **4** (12% GC yield based on **2a**) (**Table 1**, entry 1).[9] The crude mixture was purified by preparative thin-layer chromatography (PTLC), and **3a** was isolated in 87% yield. The reaction scarcely occurred in the absence of light (entry 2). The palladium catalyst was indispensable for the reaction (entry 3). The homocoupling product **4** was formed in as much as 34% yield when ethyl iodoacetate was used in place of the α-chloro ester **1** (entry 4). This result shows that it is a reasonable choice to use α-chlorocarbonyl compounds for cross-selective coupling.[10]

■ Reaction Mechanism

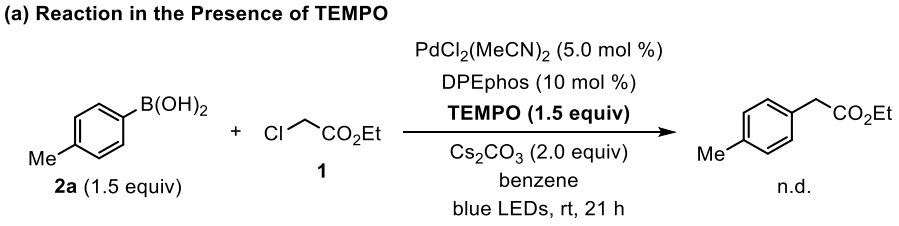
In the presence of 1.5 equiv of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), the reaction did not proceed at all (**Figure 3**a). Thus, it was likely that the reaction was mediated by radical species. UV−vis absorption spectra were measured to identify the light-absorbing species (**Figure 3**b). Ethyl chloroacetate (**1**) and *p*-tolylboronic acid (**2a**) had no absorption in the visible region. The palladium(0) complex showed an absorption centered at 350 nm tailing into the visible region. Thus, we considered that the palladium(0) complex absorbed light of blue LEDs, although the intensity was very weak.

Table 1. Photo-Assisted Suzuki-Miyaura Cross-Coupling Reaction of Ethyl Chloroacetate (1) and *p*-Tolylboronic Acid (2a)[a]



entry	deviation from standard conditions	yields of **3a** (%)	yields of **4** (%)
1	none	90 (87)	12
2	without light	<5	24
3	without $PdCl_2(MeCN)_2$/DPEphos	n.d.	<5
4	ethyl iodoacetate instead of **1**	49	34

[a]On a 0.20 mmol scale. The internal temperature under the photoirradiation is ca. 20–30 °C. [b]Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard. [c]Yields determined by GC analysis using 1,1,2,2-tetrabromoethane as an internal standard. [d]Isolated yield after preparative thin-layer chromatographic purification.



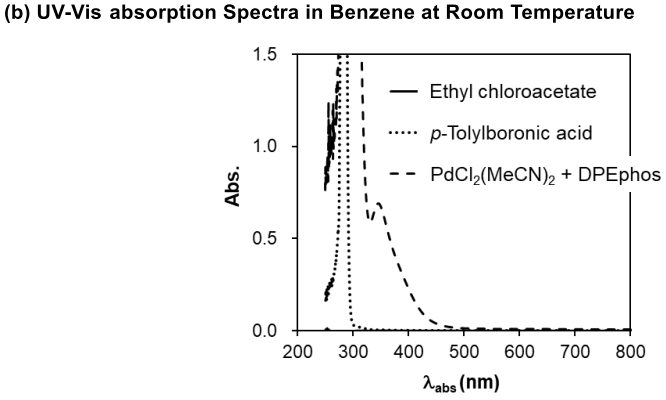
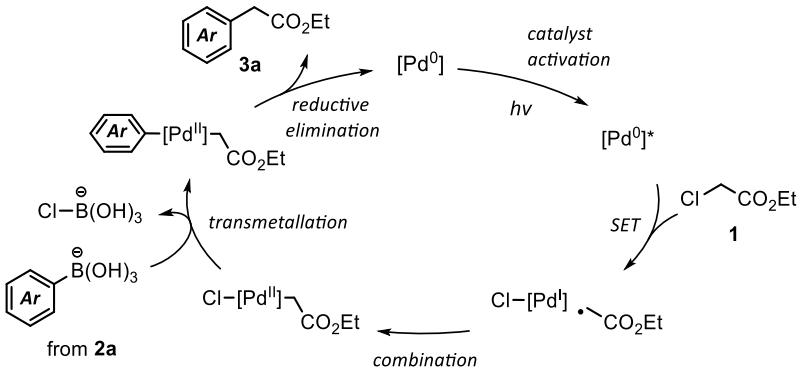


Figure 3. Mechanistic studies.

The author assumes a mechanism shown in **Scheme 3** for the formation of **3a** from **1** and **2a** based on the previous reports and the results of mechanistic studies. Initially, the

palladium(0) complex is excited under visible-light irradiation. A single electron transfers from the excited palladium(0) to **1**, generating (ethoxycarbonyl)methyl radical species and chloro palladium(I) complex. They combine to form an alkyl palladium(II) complex. Then, the transmetalation of the palladium(II) complex with **2a** provides an aryl alkyl palladium(II) complex. Finally, reductive elimination produces **3a** with the regeneration of the palladium(0) complex.

Scheme 3. Proposed Mechanism for the Formation of 3a



Ar = *p*-Tolyl.

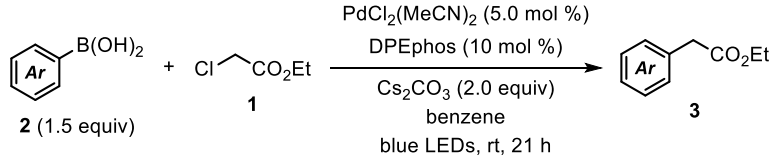
■ Substrate Scope

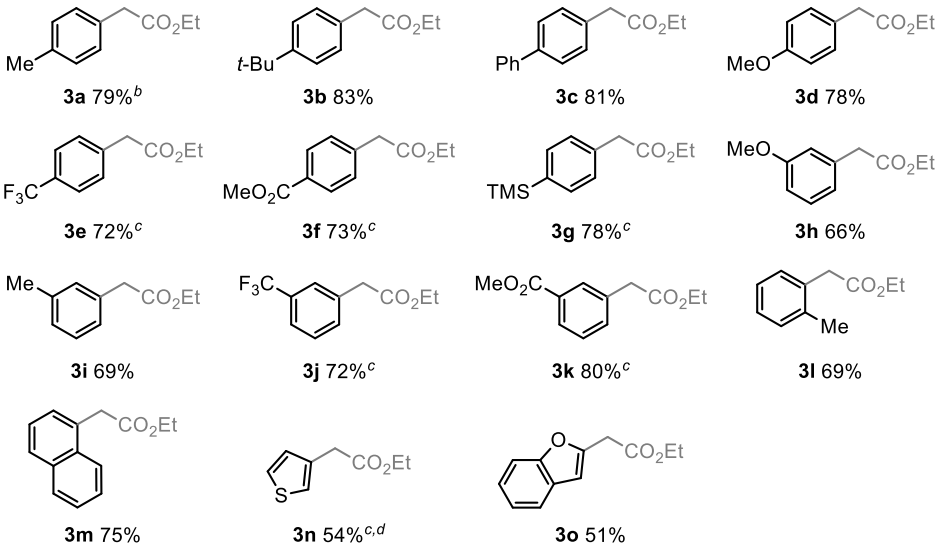
The scope of arylboronic acids **2** was examined in the cross-coupling reaction of ethyl chloroacetate (**1**) (**Table 2**). A slightly larger scale experiment using 122 mg of **1** (1.0 mmol) gave a similar result. An electronically diverse array of *para*-substituted arylboronic acids **2b**–**2g** reacted well to give the corresponding products **3b**–**3g** in yields ranging from 72% to 83%. *Meta*- and *ortho*-substituted arylboronic acids **2h**–**2m** were also applicable to the reaction. However, sterically very bulky arylboronic acid, such as 2,6-dimethylphenylboronic acid, failed to participate in the reaction. Heteroarylboronic acids **2n** and **2o** could be coupled with **1**, albeit in lower yields.

Next, the scope of α-chlorocarbonyl compounds **5** was investigated in the reaction with

p-tolylboronic acid (**2a**) (**Table 3**). Benzyl and *tert*-butyl esters **5a** and **5b** were successfully converted into the corresponding products in high yields. α-Chloroacetamides also participated in the reaction. Tertiary amides (**5c**−**5e**) gave the products in good yields (entries 3−5). The reaction of secondary amides **5f** was sluggish to give the product in 35% yield after 42 hours. α-Chloro ketones, α-chloro nitriles, and α-substituted acetates were unsuitable in the reaction.

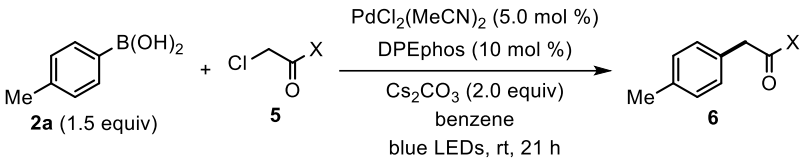
Table 2. Reaction with Various Arylboronic Acids 2[a]

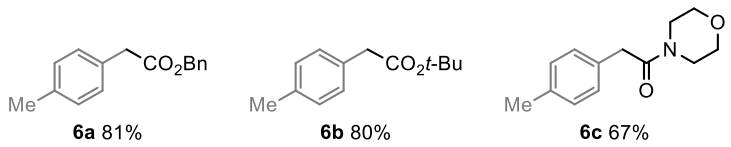




[a]On a 0.20 mmol scale. Isolated yields after preparative thin-layer chromatographic purification. [b]On a 1.0 mmol scale. [c]The reaction time was 42 hours. [d]On a 0.30 mmol scale.

Table 3. Reaction with Various α-Chlorocarbonyl Compounds 5[a]

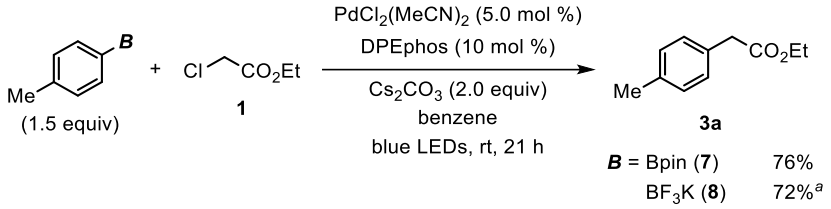




[a]On a 0.20 mmol scale. Isolated yields after preparative thin-layer chromatographic purification. [b]The reaction time was 42 hours.

p-Tolylboronic acid pinacol ester (**7**) and potassium *p*-tolyltrifluoroborate (**8**) were subjected to the reaction of ethyl chloroacetate (**1**) under the standard conditions (**Scheme 4**). The reactions proceeded as smoothly as in the case with *p*-tolylboronic acid (**2a**). The cross-coupling product **3a** was obtained in good yields, respectively.

Scheme 4. Other Arylboronic Acid Derivatives



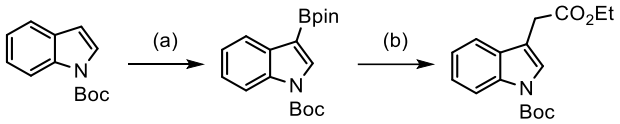
[a]H_2O (0.20 mL) was added. pin = pinacolato.

■ Synthetic Applications

Indole-3-acetic acid (IAA) is one of the most common plant hormones in the auxin.[11] It is well-known that IAA has a lot of biological effects inducing plant growth induction. The author synthesized the IAA derivative **10** from 1-Boc-indole in two steps (**Scheme 5**).[12] Initially, an

iridium-catalyzed C–H borylation of 1-Boc-indole was conducted to give 3-indollylboronic acid ester **9** in 73% yield. Subsequently, a photoassisted cross-coupling reaction afforded **10** in 64% yield.

Scheme 5. Synthesis of Indole-3-Acetic Acid Derivative 10[a]



9 73% **10** 64%

[a]Conditions: (a) bis(pinacolato)diboron, $[Ir(OMe)(cod)]_2$, dtbbpy, *n*-hexane, 80 °C, 61 h; (b) ethyl chloroacetate, $PdCl_2(MeCN)_2$, DPEphos, Cs_2CO_3, benzene, rt, blue LEDs, 42 h.

Conclusion

In conclusion, the author has demonstrated that α-chlorocarbonyl compounds are suitable electrophiles for the cross-coupling reaction with arylboronic acids under visible light irradiation. The key step is the single-electron reduction of α-chlorocarbonyl compounds by photoexcited palladium(0) complex. The reaction provides an efficient method for the synthesis of α-arylacetic acid derivatives due to mild reaction conditions at room temperature, broad substrate scope, and high functional-group compatibility.

Experimental Section

■ General Methods.

All reactions were carried out under a nitrogen atmosphere unless otherwise noted. IR measurements were performed on an Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter. UV-vis spectra were recorded on a JASCO V-750 spectrometer equipped with a JASCO ETC-505T temperature/stirring controller at 20 ℃. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a JEOL JNM-ECZ400S/L1 (^{1}H at 400.44 MHz and $^{13}C\{^{1}H\}$ at 100.69 MHz) spectrometer. NMR data were obtained in $CDCl_3$ unless otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm ($CHCl_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm ($CDCl_3$). High-resolution mass spectra were recorded on JEOL JMS-SX102A (EI). Preparative thin-layer chromatography (PTLC) was performed on silica gel plates with PF254 indicator (Merck). Flash column chromatography was performed with silica gel 60N (Kanto). Irradiation of photoreactions was carried out using an LEDs lamp (Controller: PD3-5024-4-PI, Head: LDL2-14630BL2, λ_{max} = 470 nm) purchased from CCS Inc (https://www.ccs-grp.com).

■ Materials.

All chemicals and anhydrous solvents were obtained from commercial suppliers and used without further purification unless otherwise noted. Anhydrous benzene (FUJIFILM Wako) was degassed before use. $PdCl_2(MeCN)_2$ (FUJIFILM Wako), Cs_2CO_3 (Nacalai), and DPEphos (TCI) were obtained from commercial suppliers.

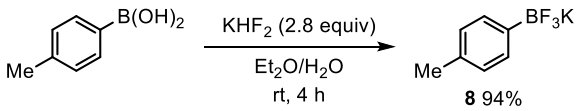
Arylboronic acids **2a**–**2o** were obtained from commercial suppliers and used without further purification [4-methylphenylboronic acid (TCI), 4-*tert*-butylphenylboronic acid (TCI), 4-biphenylboronic acid (TCI), 4-methoxyphenylboronic acid (FUJIFILM Wako), 4-

trifuluoromethylphenylboronic acid (TCI), 4-methoxycarbonylphenylboronic acid (FUJIFILM Wako), 4-trimethylsilylphenylboronic acid (TCI), 3-methoxyphenylboronic acid (TCI), 3-methylphenylboronic acid (TCI), 3-trifluoromethylphenylboronic acid (TCI), 3-methoxycarbonylphenylboronic acid (FUJIFILM Wako), 2-methylphenylboronic acid (FUJIFILM Wako), 1-naphthaleneboronic acid (FUJIFILM Wako), 3-thiopheneboronic acid (TCI), and 2-benzofuranylboronic acid (TCI)]. 4,4,5,5-Tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane (**7**, TCI) was used without further purification. Potassium (4-methylphenyl)trifluoroborate (**8**) was prepared according to the literature procedure.[13]

α-Chloroacetates and α-choroacetamides **1**, **5a**, **5b**, and **5d** were obtained from commercial suppliers and used without further purification [ethyl chloroacetate (Nacalai), /\benzyl chloroacetate (TCI), *tert*-butyl chloroacetate (FUJIFILM Wako), 1-(chloroacetyl)pyrrolidine (FUJIFILM Wako)]. 4-(Chloroacetyl)morpholine (**5c**) was prepared according to the literature procedure.[14] 1-(Chloroacetyl)indoline (**5e**) was prepared according to the literature procedure.[15] 2-Chloro-*N*-phenylacetamide (**5f**) was prepared according to the literature procedure.[15]

■ Substrate Preparation.

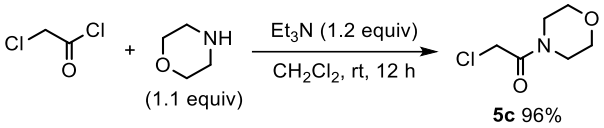
Potassium (4-methylphenyl)trifluoroborate (8):



Potassium (4-methylphenyl)trifluoroborate (**8**) was prepared according to the literature procedure.[13] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added 4-methylphenylboronic acid (270 mg, 2.0 mmol, 1.0 equiv) and Et_2O (2.0 mL). Then, potassium hydrogen difluoride (440 mg, 5.6 mmol, 2.8 equiv) and H_2O (1.8 mL) were added to

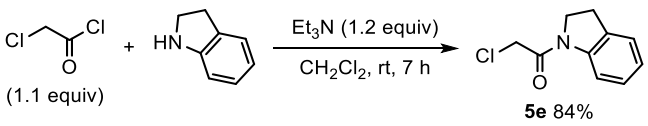
the white suspension. The reaction mixture was stirred at room temperature. After 4 hours, the mixture was concentrated under reduced pressure and the residue was dissolved in acetone (10 mL). The solution was filtered and concentrated under reduced pressure to obtain **8** (370 mg, 1.9 mmol, 94% yield). The analytical data of **8** matched well with the reported one.

4-(Chloroacetyl)morpholine (5c):



4-(Chloroacetyl)morpholine (**5c**) was prepared according to the literature procedure.[14] To an oven-dried side-arm tube equipped with a stirrer bar were added morpholine (290 μL, 3.3 mmol, 1.1 equiv), triethylamine (510 μL, 3.6 mmol, 1.2 equiv), and CH_2Cl_2 (5.2 mL). Then, chloroacetyl chloride (240 μL, 3.0 mmol, 1.0 equiv) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature. After 12 hours, saturated aqueous solution of $NaHCO_3$ was added to the mixture, and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 1:3) to give **5c** (470 mg, 2.9 mmol, 96% yield). The analytical data of **5c** matched well with the reported one.

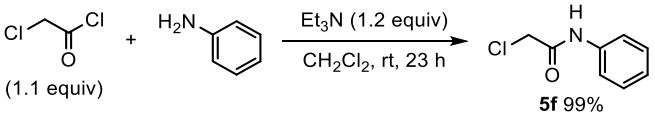
1-(Chloroacetyl)indoline (5e):



1-(Chloroacetyl)indoline (**5e**) was prepared according to the literature procedure.[15] To an oven-dried side-arm tube equipped with a stirrer bar were added indoline (470 μL, 4.2 mmol,

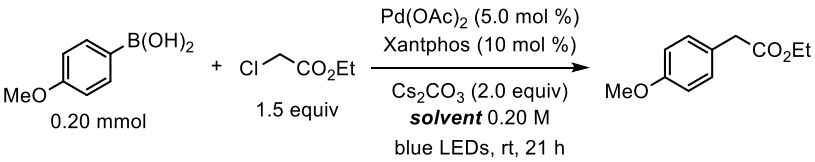
1.0 equiv), triethylamine (700 μL, 5.0 mmol, 1.2 equiv), and CH_2Cl_2 (15 mL). Then, chloroacetyl chloride (370 μL, 4.6 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at room temperature. After 7 hours, H_2O was added to the mixture, and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 3:1) to give **5e** (690 mg, 3.5 mmol, 84% yield). The analytical data of **5e** matched well with the reported one.

2-Chloro-*N*-phenylacetamide (5f):

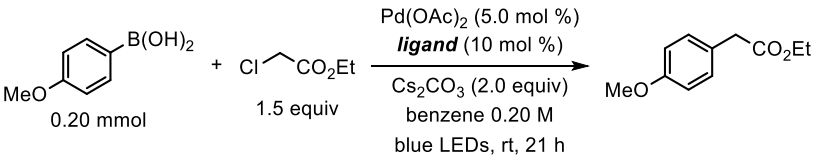


2-Chloro-*N*-phenylacetamide (**5f**) was prepared with a similar procedure to the literature one.[15] To an oven-dried side-arm tube equipped with a stirrer bar were added aniline (460 μL, 5.0 mmol, 1.0 equiv), triethylamine (830 μL, 6.0 mmol, 1.2 equiv), and CH_2Cl_2 (10 mL). Then, chloroacetyl chloride (440 μL, 5.5 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at room temperature. After 7 hours, H_2O was added to the mixture, and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by recrystallization (CH_2Cl_2/hexane) to give **5f** in 99% yield. The analytical data of **5f** matched well with the reported one.

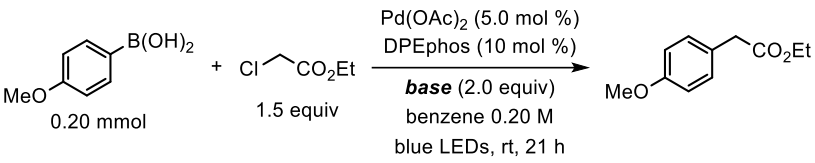
■ Optimization of Reaction Conditions.



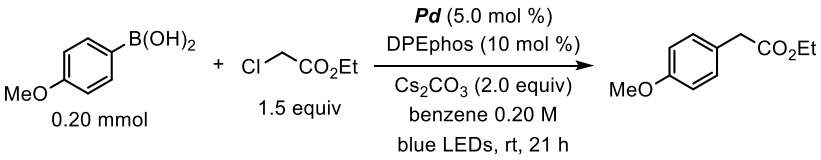
solvent	yield (NMR)	***solvent***	yield (NMR)
hexane	<1%	DCE	43%
toluene	n.d.	acetone	5%
THF	2%	DMA	n.d.
DMF	n.d.	benzene	43% (isolated)



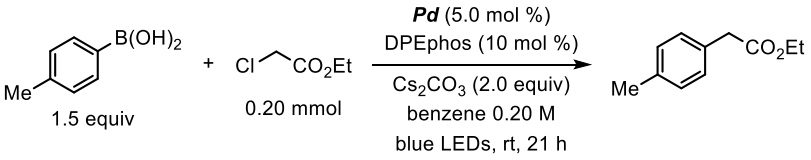
ligand	yield (NMR)	***ligand***	yield (NMR)
PPh_3	49%	DPEphos	93% (58% isolated)
JohnPhos	66%		
PCy_3	53%	(*rac*)-BINAP	< 1%
IPr·HCl	22%	dppf	n.d.
$P(otol)_3$	25%	dppm	n.d.
dppe	n.d.	dppp	n.d.



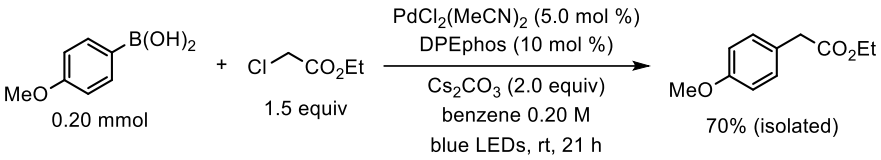
base	yield (NMR)	***base***	yield (NMR)
K_3PO_4	50%	NaOAc	1%
K_2CO_3	42%	KOAc	9%
KOH	27%	NaOEt	42%
CsF	80%	$Ba(OH)_2 \cdot 8\,H_2O$	< 1%
KF	58%		



Pd	yield (NMR)	*Pd*	yield (NMR)
$Pd_2(dba)_3$	< 1%	$PdCl_2(MeCN)_2$	70% (isolated)

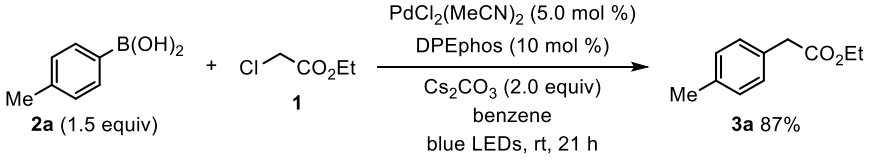


Pd	yield (NMR)	*Pd*	yield (NMR)
$Pd(OAc)_2$	94%	$PdCl_2(MeCN)_2$	90%
$Pd(PPh_3)_4$	55%		



Ar-B(OH)$_2$	**halide**	**base**	**conc.**	**time**	**yield** (isolated)
		1.5 eq.			63%
		3.0 eq.			63%
				10 h	69%
				36 h	74%
			0.40 M		62%
			0.10 M		66%
	2.0 eq.				69%
1.5 eq.					78%
2.0 eq.					69%

■ Typical Procedure for the Photo-Assisted Cross-Coupling Reaction.

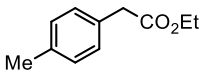


In a nitrogen-filled glove-box, benzene (2.0 mL, 0.10 M) was added to **1** (24.7 mg, 0.20 mmol, 1.0 equiv), **2a** (40.8 mg, 1.5 equiv), $PdCl_2(MeCN)_2$ (2.6 mg, 5.0 mol %), DPEphos (10.8 mg, 10 mol %), and Cs_2CO_3 (130.3 mg, 2.0 equiv) in an oven-dried 4 mL vial equipped with a

stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred under blue LEDs irradiation with a fan. After 21 hours, the mixture was passed through a pad of Florisil® with Et_2O. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3a** as a colorless oil (31.3 mg, 0.18 mmol, 87% yield).

■ Characterization of the Coupling Products 3a–3o and 6a–6f.

3a:

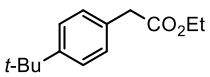


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1). The analytical data of **3a** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.57 (s, 2H), 2.33 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 171.8. 136.6, 131.1, 129.2, 129.1, 60.8, 41.0, 21.0, 14.2.

3b:

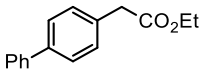


The reaction was carried out on a 0.20 mmol scale in benzene (0.20 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3b** as a colorless oil (36.8 mg, 83% yield). The analytical data of **3b** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.33 (m, 2H), 7.24–7.20 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.59 (s, 2H), 1.32 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.8. 149.9, 131.1, 128.9, 125.5, 60.8, 40.9, 34.4, 31.3, 14.2.

3c:

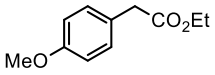


The reaction was carried out on a 0.20 mmol scale in benzene (0.20 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3c** as a white solid (38.5 mg, 81% yield). The analytical data of **3c** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61–7.54 (m, 4H), 7.47–7.41 (m, 2H), 7.39–7.31 (m, 3H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.66 (s, 2H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.6, 140.8, 140.0, 133.2, 129.6, 128.7, 127.3, 127.2, 127.1, 60.9, 41.0, 14.2.

3d:



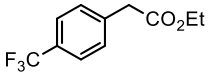
The reaction was carried out on a 0.20 mmol scale in benzene (0.20 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **3d** as a colorless oil (30.3 mg, 78% yield). The analytical data of **3d** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23–7.17 (m, 2H), 6.89–6.83 (m, 2H), 4.14 (q, *J* = 7.2 Hz, 2H),

3.79 (s, 3H), 1.55 (s, 2H), 1.25 (t, J = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.9, 158.7, 130.2, 126.2, 114.0, 60.8, 55.2, 40.5, 14.2.

3e:

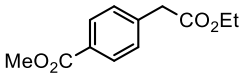


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3e** as a white solid (33.3 mg, 72% yield). The analytical data of **3e** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 4.17 (q, J = 7.2 Hz, 2H), 3.67 (s, 2H), 1.26 (t, J = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 170.7, 138.1, 129.6, 129.5 (q, 32.6 Hz), 124.1 (q, J = 271.2 Hz), 122.5 (q, J = 3.8 Hz), 61.1, 41.1, 14.1.

3f:

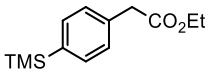


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **3f** as a colorless oil (32.0 mg, 73% yield). The analytical data of **3f** matched well with the already reported one.[18] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.04–7.95 (m, 2H), 7.39–7.32 (m, 2H), 4.16 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 3.67 (s, 2H), 1.25 (t, J = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 170.8, 166.9, 139.3, 129.8, 129.3, 129.0, 61.1, 52.1, 41.4, 14.1.

3g:

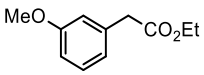


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3g** as a colorless oil (37.1 mg, 78% yield). The analytical data of **3g** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.46 (m, 2H), 7.30–7.26 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.61 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.26 (s, 9H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.5, 139.0, 134.7, 133.6, 128.6, 60.8, 41.4, 14.2, –1.1.

3h:

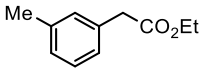


The reaction was carried out on a 0.20 mmol scale in benzene (0.20 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3h** as a colorless oil (25.7 mg, 66% yield). The analytical data of **3h** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23 (t, *J* = 8.0 Hz, 1H) 6.89–6.78 (m, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.58 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.4, 159.7, 135.6, 129.5, 121.6, 114.9, 112.6, 60.8, 55.2, 41.5, 14.1.

3i:

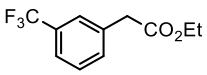


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3i** as a colorless oil (24.3 mg, 69% yield). The analytical data of **3i** matched well with the already reported one.[19] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (t, *J* = 7.6 Hz, 1H) 7.13–7.03 (m, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.57 (s, 2H), 2.34 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.7, 138.2, 134.0, 130.0, 128.4, 127.8, 126.2, 60.8, 41.3, 21.3, 14.2.

3j:

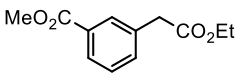


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3j** as a colorless oil (33.3 mg, 72% yield). The analytical data of **3j** matched well with the already reported one.[20] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58–7.40 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.67 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 170.8, 135.0, 132.7, 130.9 (q, *J* = 32.6 Hz), 129.0, 126.1 (q, *J* = 3.8 Hz), 124.03 (q, *J* = 270.2 Hz), 123.97 (q, *J* = 3.9 Hz), 61.1, 41.1, 14.1.

3k:

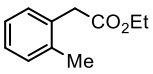


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **3k** as a colorless oil (35.6 mg, 80% yield). The analytical data of **3k** matched well with the already reported one.[21] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, *J* = 8.8 Hz), 7.49 (d, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.92 (s, 3H), 3.67 (s, 2H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.1, 166.9, 134.5, 133.8, 131.5, 130.5, 128.6, 128.3, 61.0, 52.1, 41.1, 14.1.

3l:

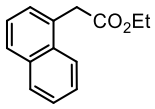


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3l** as a white solid (24.1 mg, 69% yield). The analytical data of **3l** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23–7.10 (m, 4H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.63 (s, 2H), 2.32 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.5, 136.8, 132.9, 130.3, 130.1, 127.3, 126.1, 60.8, 39.3, 19.6, 14.2.

3m:

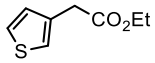


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3m** as a colorless oil (32.3 mg, 75% yield). The analytical data of **3m** matched well with the already reported one.[17] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.04–7.99 (m, 1H), 7.90–7.84 (m, 1H), 7.83–7.77 (m, 1H), 7.57–7.40 (m, 4H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.07 (s, 2H), 1.22 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.6, 133.8, 132.1, 130.7, 128.7, 128.0, 127.9, 126.3, 125.7, 125.5, 123.8, 60.9, 39.2, 14.1.

3n:

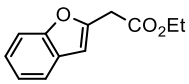


The reaction was carried out on a 0.30 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3n** as a colorless oil (27.4 mg, 54% yield). The analytical data of **3n** matched well with the already reported one.[22] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29 (dd, *J* = 4.8, 3.2 Hz, 1H), 7.17–7.13 (m, 1H), 7.05 (dd, *J* = 5.2, 1.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.65 (s, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.1, 133.7, 128.5, 125.7, 122.8, 60.9, 35.9, 14.2.

3o:

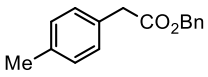


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **3o** as a colorless oil (21.4 mg, 51% yield). The analytical data of **3o** matched well with the already reported one.[23] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.29–7.17 (m, 2H), 6.63 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 168.9, 154.9, 150.7, 128.5, 123.9, 122.7, 120.7, 111.0, 105.0, 61.4, 34.7, 14.1.

6a:

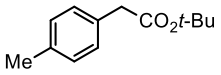


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **6a** as a colorless oil (38.8 mg, 81% yield). The analytical data of **6a** matched well with the already reported one.[24] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.40–7.28 (m, 5H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 5.13 (s, 2H), 3.64 (s, 2H), 2.34 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.6, 136.7, 135.9, 130.8, 129.2, 129.1, 128.5, 128.2, 128.1, 66.5, 40.9, 21.0.

6b:

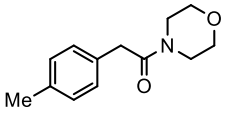


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **3b** as a colorless oil (32.5 mg, 80% yield). The analytical data of **6b** matched well with the already reported one.[25] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.16 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.49 (s, 2H), 2.33 (s, 3H),1.44 (s, 9H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.2, 136.3, 131.6, 129.1, 129.0, 80.6, 42.2, 28.0, 21.0.

6c:

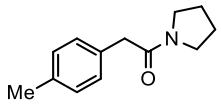


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 1:1) to give **6c** as a white solid (28.9 mg, 67% yield). The analytical data of **6c** matched well with the already reported one.[5a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.13 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 3.69 (s, 2H), 3.66–3.61 (m, 4H), 3.50–3.45 (m, 2H), 3.44–3.39 (m, 2H), 2.32 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.8, 136.5, 131.6, 129.4, 128.3, 66.7, 66.4, 46.5, 42.1, 40.4, 21.0.

6d:

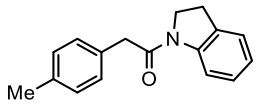


The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 1:1) to give **6d** as a white solid (27.4 mg, 66% yield). The analytical data of **6d** matched well with the already reported one.[25] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.61 (s, 2H), 3.48 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.32 (s, 3H), 1.95–1.77 (m, 4H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.7, 136.2, 131.8, 129.2, 128.8, 46.8, 45.9, 41.9, 26.1, 24.3, 21.0.

6e:



The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 21 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **6e** as a white solid (38.1 mg, 76% yield).

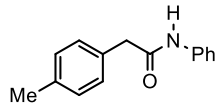
IR (ATR, cm^{-1}): 3048, 3003, 2916, 1659, 1481, 1395, 1277, 760.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.24–7.08 (m, 6H), 7.00 (t, *J* = 7.6 Hz, 1H), 4.06 (t, *J* = 8.4 Hz, 2H), 3.77 (s, 2H), 3.15 (t, *J* = 8.8 Hz, 2H), 2.34 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 169.3, 143.1, 136.6, 131.1, 129.4, 128.9, 127.5, 124.4, 123.7, 117.1, 48.1, 43.2, 28.0, 21.0.

HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{17}H_{17}NO^+$ 251.1305; Found 251.1309.

6f:



The reaction was carried out on a 0.20 mmol scale in benzene (0.10 M) for 42 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5:1) to give **6f** as a white solid (15.9 mg, 35% yield). The analytical data of **6f** matched well with the already reported one.[25] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.31–7.24 (m, 2H), 7.23 (d, *J* = 9.2 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.10 (br, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 3.70 (s, 2H), 2.37 (s, 3H).

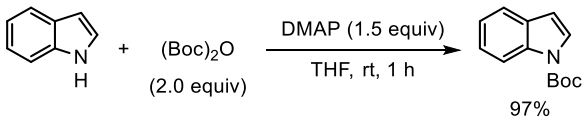
^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ = 169.3, 137.6, 137.4, 131.2, 129.9, 129.4, 128.9, 124.4, 119.7, 44.4, 21.1.

■ A 1.0 mmol Scale Reaction

In a nitrogen-filled glove-box, benzene (10 mL, 0.10 M) was added to **1** (122 mg, 1.0 mmol, 1.0 equiv), **2a** (204 mg, 1.5 equiv), $PdCl_2(MeCN)_2$ (13 mg, 5.0 mol %), DPEphos (54 mg, 10 mol %), and Cs_2CO_3 (650 mg, 2.0 equiv) in an oven-dried 50 mL round-bottom flask equipped with a stirrer bar. The flask was taken outside the glove-box. The reaction mixture was stirred under blue LEDs irradiation with a fan. After 21 hours, the mixture was passed through a pad of Florisil® with Et_2O. The filtrate was concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10:1) to give **3a** (139 mg, 0.78 mmol, 79% yield).

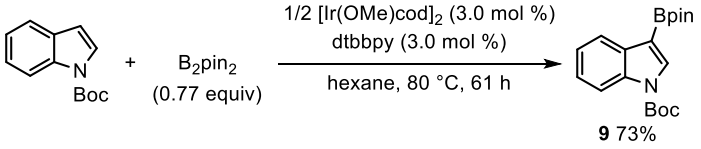
■ **Synthesis of Indole-3-Acetic Acid Derivative 10.**

***N*-Boc-indole:**



N-Boc-indole was prepared according to the literature procedure.[26] To an oven-dried 50 mL round-bottom flask equipped with a stirrer bar were added indole (360 mg, 3.0 mmol, 1.0 equiv), 4-dimethylaminopyridine (550 mg, 1.5 equiv), $(Boc)_2O$ (1.3 g, 2.0 equiv), and THF (30 mL, 0.10 M). The reaction mixture was stirred at room temperature. After 17 hours, saturated aqueous solution of $NaHCO_3$ was added to the mixture, and extracted with ethyl acetate × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10:1) to give *N*-Boc-indole (650 mg, 3.0 mmol, 97% yield). The analytical data of the product matched well with the reported one.

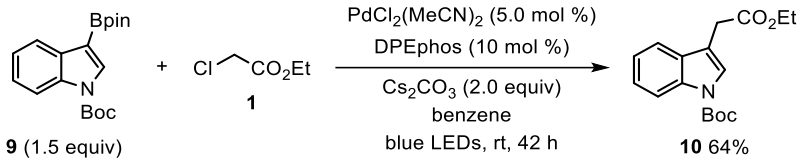
***N*-Boc-indole-3-boronic acid pinacol ester (9):**



N-Boc-indole-3-boronic acid pinacol ester (**9**) was prepared according to the literature procedure.[27] In a nitrogen-filled glove-box, hexane (3.4 mL, 0.50 M) was added to *N*-Boc-indole (370 mg, 1.7 mmol, 1.0 equiv), B_2pin_2 (330 mg, 0.77 equiv), $[Ir(OMe)cod]_2$ (17 mg, 3.0 mol %), and dtbbpy (14 mg, 3.0 mol %) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred at 80 ℃. After 61 hours, H_2O was added to the mixture, and extracted with CH_2Cl_2 × 3 times. The combined organic phase was

washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10:1) to give **9** (420 mg, 1.2 mmol, 73% yield). The analytical data of **9** matched well with the reported one.

Indole-3-acetic acid derivative 10:



In a nitrogen-filled glove-box, benzene (2.0 mL, 0.10 M) was added to **1** (24.5 mg, 0.20 mmol, 1.0 equiv), **9** (103.0 mg, 1.5 equiv), $PdCl_2(MeCN)_2$ (2.6 mg, 5.0 mol %), DPEphos (10.8 mg, 10 mol %), and Cs_2CO_3 (130.3 mg, 2.0 equiv) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred under blue LEDs irradiation with a fan. After 42 hours, the mixture was passed through a pad of Florisil® with Et_2O. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 10:1) to give **10** as a colorless oil (39.0 mg, 0.13 mmol, 64% yield). The analytical data of **10** was already reported.[28] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15 (d, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.36–7.29 (m, 1H), 7.28–7.21 (m, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.71 (d, *J* = 0.8 Hz, 2H), 1.67 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 171.0, 149.6, 135.4, 130.1, 124.5, 124.4, 122.5, 119.0, 115.2, 113.2, 83.6, 61.0, 31.2, 28.2, 14.2.

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Chapter 5

Photoexcited Nickel Catalysis: Acylcyanation of Vinylarenes *via* Acyl Radical Generation from Acyl Fluorides

Abstract

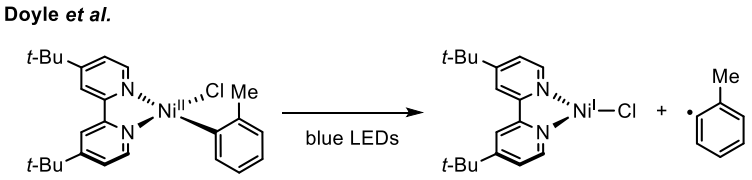
Photoinduced nickel-catalyzed acylcyanation of vinylarenes is reported. Single-electron reduction of acyl fluorides was triggered by a photoexcited nickel(0) catalyst, leading to the formation of the acyl radicals. The reaction didn't proceed at all without photoirradiation. The resulting acyl radicals added to vinylarenes to generate benzylic radicals, which were captured by a nickel(I) cyanide species. Reductive elimination of a nickel(II) acyl cyanide complex occurred to form C–CN bonds. Thus, the nickel catalyst shows both single-electron and two-electron reactivities.

Introduction

Photoexcited transition metal catalysis has emerged as an attractive strategy for replacing or complementing metallaphotoredox catalysis.[1] As mentioned in Chapters 1 and 4, photoexcited palladium catalysis is one of the most studied ones. Recently, photocatalysis using other transition metals, such as cobalt, copper, rhodium, iridium, and so on, has also been getting more attention.[2]

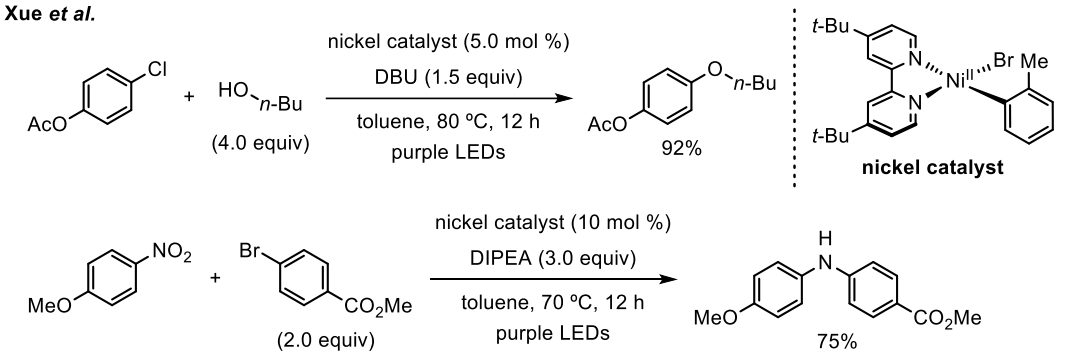
Photoexcited nickel catalysis is also an attractive research area, because nickel is earth-abundant and cheap transition metal. Although nickel catalysts have been frequently used together with photoredox catalysts, the photoreactivity of nickel catalysts themselves has been less studied.[3] In 2018, Doyle *et al.* reported the first example of visible-light active nickel complexes (**Scheme 1**).[4] They demonstrated that nickel(II) aryl halide complexes undergo the cleavage of the Ni–C(sp^2) bond *via* LMCT process to give nickel(I) complexes and aryl radicals.

Scheme 1. Photoinduced Homolysis of Ni–C(sp^2) Bonds



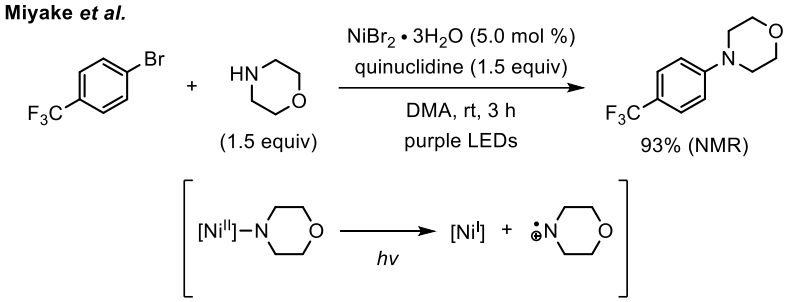
With the Doyle group's discoveries, Xue *et al.* reported C–O and C–N coupling reactions using a nickel(II) aryl bromide complex as a precursor of catalytically active nickel(I) species (**Scheme 2**).[5] Photoinduced elimination of the ligands is a practical way to generate nickel(I) species from nickel(II) complex.[6]

Scheme 2. Photoinduced C–O and C–N Coupling Reactions



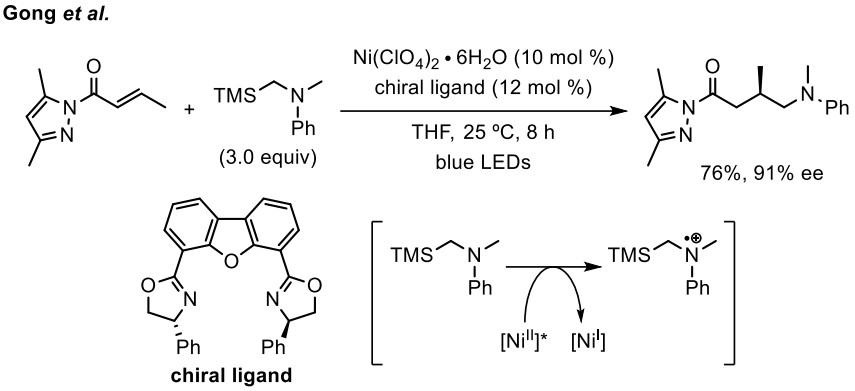
Miyake reported another use of LMCT process of photoexcited nickel(II) complexes (**Scheme 3**).[7] A cross-coupling reaction of aryl halides with amines proceeded efficiently under photoirradiation. A photoinduced LMCT of nickel(II) amine complexes gave reactive aminium radicals and nickel(I) complexes.

Scheme 3. C–N Cross-Coupling Reaction *via* Photoexcitation of Nickel Amine Complexes



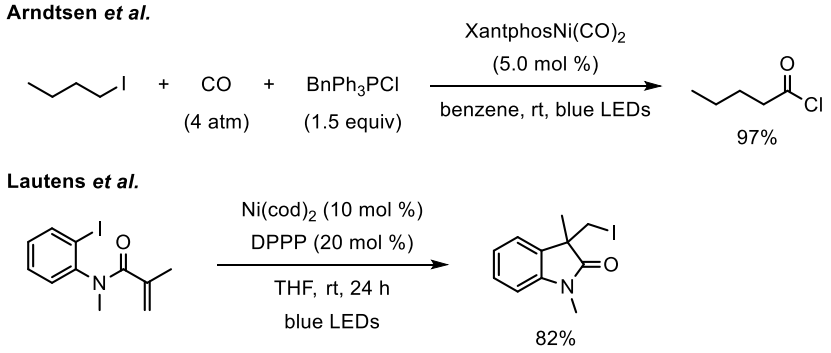
About single-electron transfer of photoexcited nickel complexes, intermolecular single-electron oxidation by photoexcited nickel(II) complexes was reported in 2018 (**Scheme 4**).[8] Gong *et al.* reported bifunctional nickel catalysis for an asymmetric 1,4-addition of radicals. Chiral nickel(II) complexes acted as Lewis acid to activate the substrates and photoredox catalysts to generate α-amino radicals *via* single-electron oxidation of α-silylamines.

Scheme 4. Asymmetric β-Aminomethylation of Enones



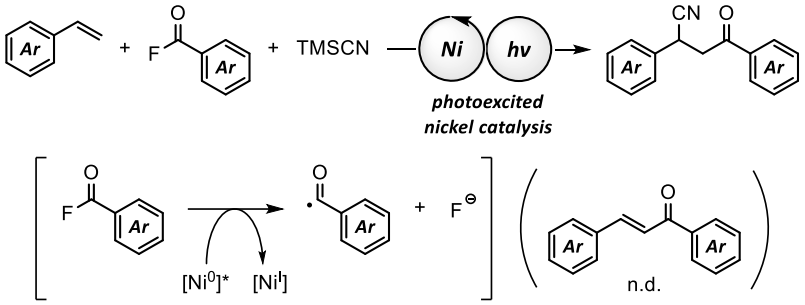
Furthermore, there are some reports that photoexcitation of nickel catalysts promotes oxidative addition and reductive elimination (**Scheme 5**).[9] However, studies on photoexcited nickel catalysis are still in progress.

Scheme 5. Promotion of Oxidative Addition and Reductive Elimination



Herein, the author reports photoinduced nickel-catalyzed acylcyanation of vinylarenes (**Scheme 6**).[10,11] This reaction proceeded without exogenous photosensitizers. A single-electron reduction of acyl fluorides to furnish acyl radicals is key to the progress of the reaction. Notably, although photoexcited palladium-catalyzed Heck-type reactions of vinylarenes with alkyl halide are well known,[11] the enones, proposed Heck-type products, were not observed in this reaction.

Scheme 6. This Work: Photoexcited Nickel-Catalyzed Acylcyanation of Vinylarenes

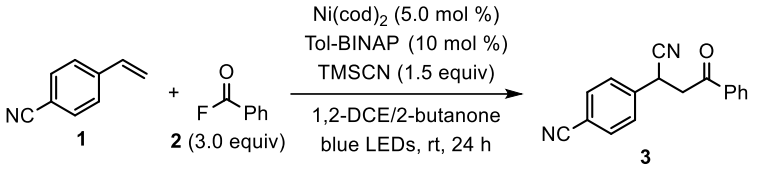


Result and Discussion

■ **Nickel-Catalyzed Acylcyanation of Vinylarenes**

A mixture of 4-cyanostyrene (**1**, 0.30 mmol), benzoyl fluoride (**2**, 3.0 equiv), and TMSCN (1.5 equiv), $Ni(cod)_2$ (5.0 mol %), and Tol-BINAP (10 mol %) in 1,2-dichloroethane (1,2-DCE)/2-butanone (1:1, 0.20 M) was stirred for 24 hours under visible-light irradiation (λ_{max} = 425 nm). The desired product **3** was obtained in 66% NMR yield (**Table 1**, entry 1). When the reaction time was extended up to 48 hours, the product **3** was isolated in 70% yield after preparative thin-layer chromatographic purification (entry 2). The reaction scarcely occurred in the absence of $Ni(cod)_2$ (entry 3). Nickel(II) precatalyst gave **3** in lower yield (entry 4). Although a photoexcited palladium catalyst is well-known, the palladium(0) catalyst was unsuitable for this reaction (entry 5). An appropriate ligand is critical for the reaction (entries 6–9). The product **3** was formed without ligands albeit in low yield (entry 6). In contrast, no desired product was observed when 4,4'-di-*t*-butyl-2,2'-bipyridyl (dtbbpy) was used (entry 7). Monodentate or bidentate aryl phosphine ligands gave inferior results (entries 8 and 9). Despite a higher reactivity of benzoyl chloride than benzoyl fluoride, the reaction didn't proceed well (entry 10). Photoirradiation was indispensable for the reaction (entry 11). The reaction didn't proceed at all without light, even if the reaction temperature was raised to 70 °C (entry 12).

Table 1. Development of 1,2-Acylcyanation of 4-Cyanostyrene (1)[a]



entry	change from standard conditions	yields of **3** (%)[b]
1	none	66
2	48 h	70[c]
3	without $Ni(cod)_2$	n.d.
4	$NiCl_2$(glyme) instead of $Ni(cod)_2$	15
5	$Pd(PPh_3)_4$ instead of $Ni(cod)_2$	n.d.
6	without Tol-BINAP	14
7	dtbbpy instead of Tol-BINAP	n.d.
8	PPh_3 (20 mol %) instead of Tol-BINAP	30
9	BINAP instead of Tol-BINAP	41
10	benzoyl chloride instead of **2**	4
11	without light	n.d.
12	without light (70 °C)	n.d.

[a]On a 0.30 mmol scale. [b]Yields determined by ^{1}H NMR analysis using 1,1,2,2-tetrabromoethane as an internal standard. [c]Isolated yield after preparative thin-layer chromatographic purification. n.d. = not detected.

■ Mechanistic Studies

Mechanistic studies were carried out in order to reveal the detailed reaction mechanism. This reaction didn't occur without light, so UV-vis absorption spectra were measured to identify what is a light-absorbing species (**Figure 1**). 4-Cyanostyrene (**1**) and benzoyl fluoride (**2**) didn't have absorption in the visible region, whereas the nickel(0) catalyst showed an absorption tailing into the visible region. Thus, the author considered that photoexcited nickel(0) catalyst is essential for the reaction.

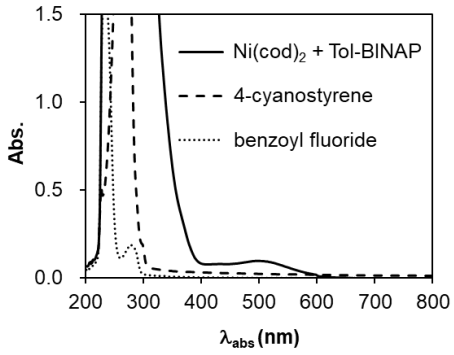
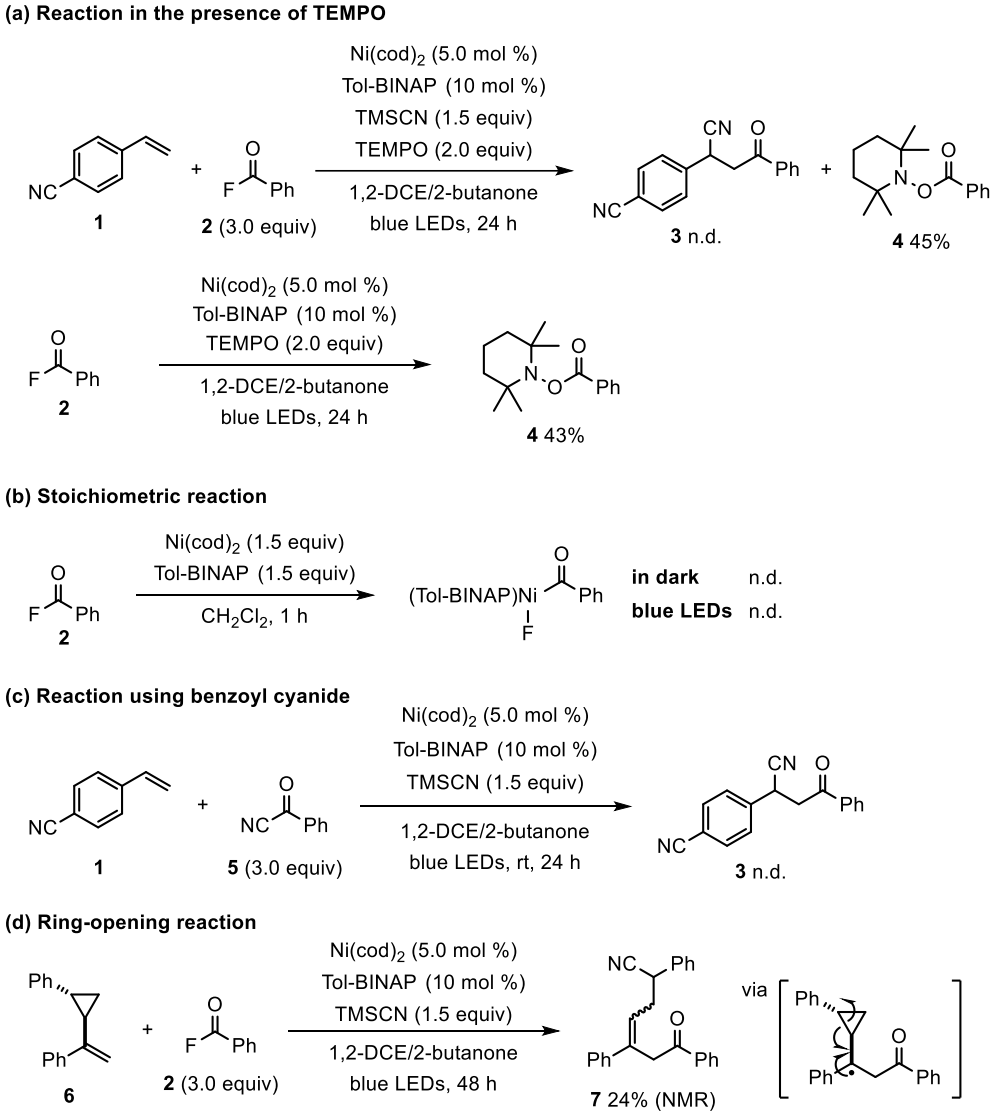


Figure 1. UV-vis spectra in CH_2Cl_2 at room temperature.

When the reaction was conducted in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), the desired product was not obtained at all (**Scheme 7**a, upper). Instead, the TEMPO adduct **4** was isolated in 45% yield, suggesting the intermediacy of acyl radicals. The TEMPO adduct **4** was also formed without 4-cyanostyrene (**1**) and TMSCN (**Scheme 7**a, lower), which indicated that acyl radicals were generated from benzoyl fluoride (**2**). The results of stoichiometric reaction meant that an oxidative addition of benzoyl fluoride (**2**) did not proceed regardless of photoirradiation (**Scheme 7**b). Therefore, the author considered that the benzoyl radical was generated *via* a single-electron reduction of benzoyl fluoride (**2**), rather than a Ni–C bond homolysis of the oxidative addition complex. When benzoyl cyanide (**5**) was used instead of benzoyl fluoride (**2**), the product **3** was not obtained (**Scheme 7**c). A radical clock experiment gave a ring-opening product **7** in 24% yield, which revealed the presence of benzylic radical intermediates (**Scheme 7**d).

Scheme 7. Mechanistic Studies

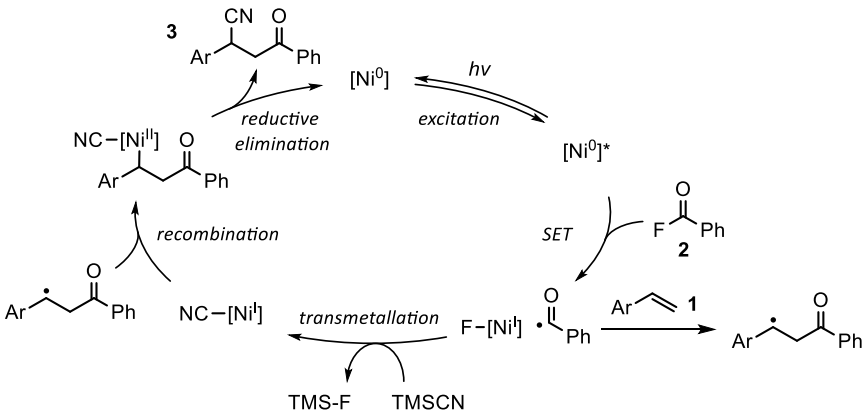


■ Proposed Mechanism

Based on the mechanistic studies, the author proposed the reaction mechanism shown in **Scheme 8**. Initially, the nickel(0) complex is excited under visible-light irradiation. Then, an oxidative quenching of photoexcited nickel(0) complex by benzoyl fluoride (**2**) occurs to furnish a benzoyl radical and a nickel(I) fluoride complex. The resulting benzoyl radical adds to 4-cyanostyrene (**1**) to give a benzylic radical intermediate. On the other hand, the nickel(I) fluoride

complex undergoes a transmetalation with TMSCN to form a nickel(I) cyanide complex. The benzylic radical intermediate is combined with the nickel(I) cyanide complex, generating a nickel(II) alkyl cyanide complex. Finally, a reductive elimination produced the difuctionalized product **3** with a regeneration of the nickel(0) complex. The pathway in which the benzylic radical intermediate adds to a copper-bound cyano ligand cannot be ruled out.

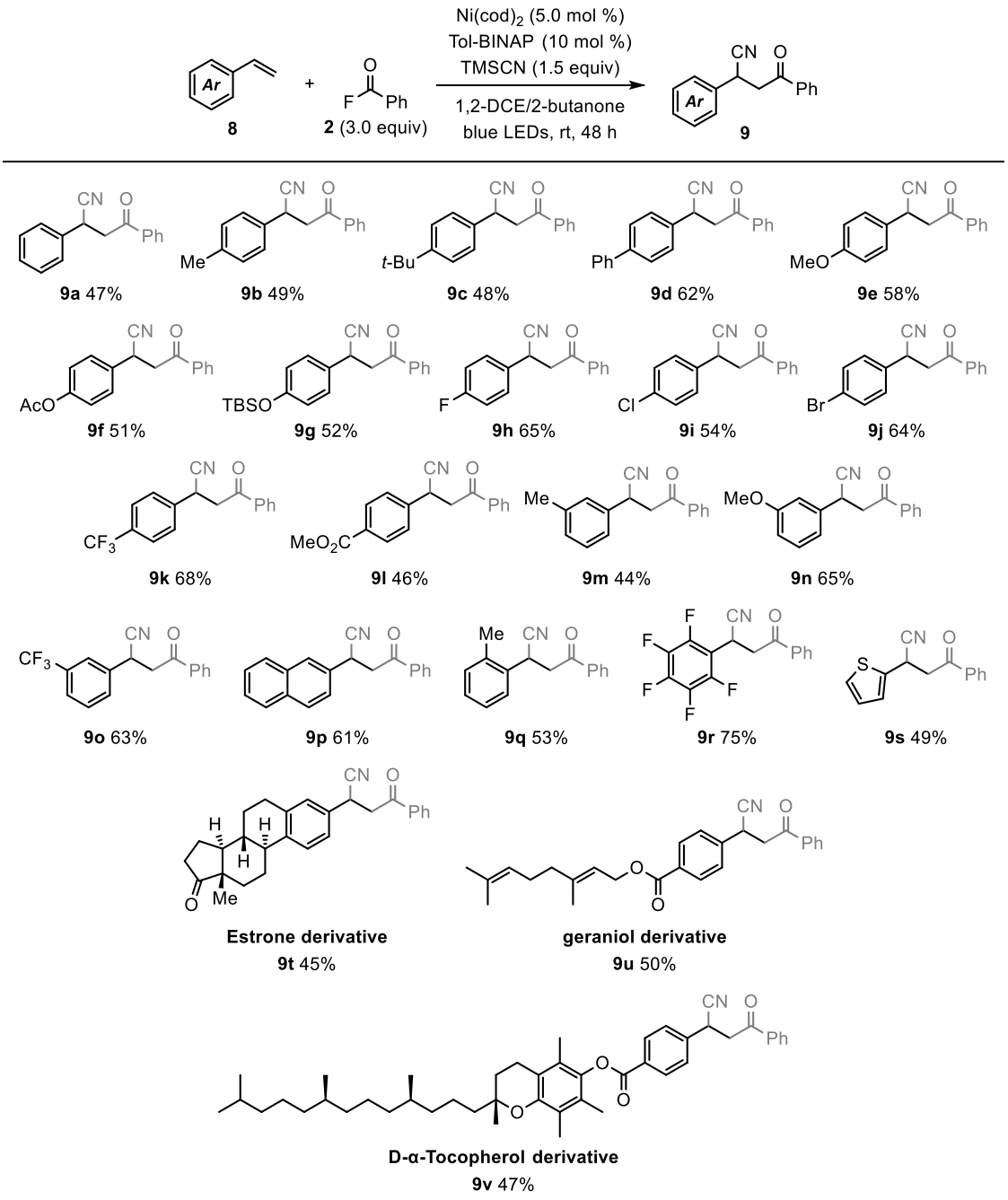
Scheme 8. Proposed Mechanism



■ Substrate Scope

The scope of vinylarenes **8** was examined in the acylcyanation reaction with benzoyl fluoride (**2**) (**Table 2**). Various vinylarenes bearing electron-donating or electron-withdrawing substituents at *para* positions participated in the reaction and gave the corresponding products **9a–9l** in moderate to high yields. *Meta*- and *ortho*-substituted vinylarenes were also suitable substrates. 2,3,4,5,6-Pentafluorostyrene and 2-vinylthiophene reacted well. This protocol showed a high functional group tolerance, so applied to the late-stage functionalization of naturally derived substrates. Estrone, geraniol, and D-α-Tocopherol derivatives were converted into the desired products **9t–9v**.

Table 2. Reaction with Various Vinylarenes 8[a]

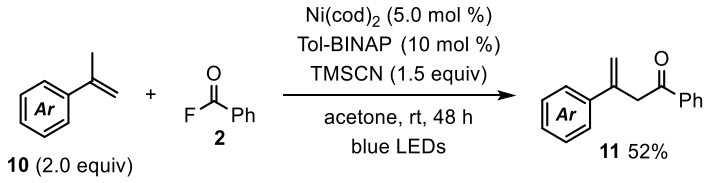


[a]On a 0.30 mmol scale. Isolated yields after preparative thin-layer chromatographic purification.

Although the substituents on the aromatic rings didn't significantly affect the efficiency of the reaction, the substituent pattern on the alkenes is essential. When the reaction was conducted with β-substituted styrenes, no desired products were obtained (see the Experimental

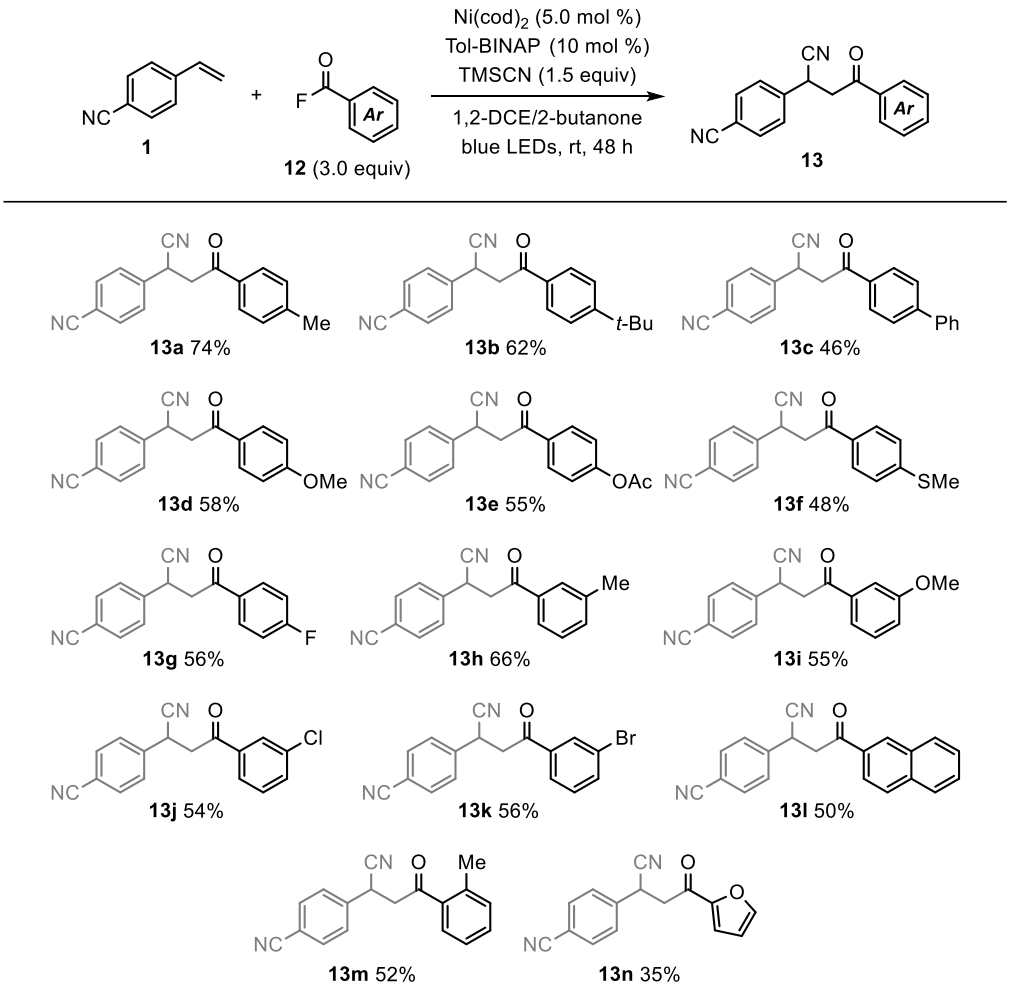
Section). Moreover, α-methylstyrene (**10**) was converted into β,γ-unsaturated ketone **11** under the modified reaction conditions (**Scheme 9**). The difficulty in forming C–CN bonds at the sterically hindered tertiary benzylic position probably gave the product **11**.

Scheme 9. Reaction with α-Methylstyrene



Next, the scope of acyl fluorides **12** was evaluated in the reaction with 4-cyanostyrene (**1**) (**Table 3**). An electronically diverse array of *para*-substituted acyl fluoride was examined, and it was found that the electron-rich or non-biased fluorides were applicable to the reaction. However, electron-deficient fluorides were unsuitable reactants, probably due to the unstability of acyl radicals (see the Experimental Section).[12] *Meta*- or *ortho*-substituents didn't cause any problems with the reaction. Although *meta*-chloro and *meta*-bromo benzoyl fluorides were a little electron-poor, the reaction proceeded and gave the corresponding products **13j** and **13k**. Heteroaryl-acyl fluoride could react with **1** albeit in a lower yield.

Table 3. Reaction with Various Acyl Fluorides[a]



[a]On a 0.30 mmol scale. Isolated yields after preparative thin-layer chromatographic purification.

Conclusion

In summary, the author has developed the photoexcited nickel-catalyzed acylcyanation of vinylarenes. The oxidative quenching of the photoexcited nickel(0) complex is the key to the reaction. This finding would expand the possibility of utilizing photoexcited nickel catalysis in organic synthesis.

Experimental Section.

■ General Methods.

All reactions were carried out under a nitrogen atmosphere unless otherwise noted. IR measurements were performed on a JASCO FTIR-4X with ATR Pro 4X. UV-vis absorption spectra were recorded on a HITACHI U-1900 Spectrophotometer. Irradiation of photoreactions was carried out using a HepatoChem lamp (EvoluChem LED 425PF) or a Kessil lamp (PR160L-456nm). ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a JEOL ECS 400 MHz spectrometer. NMR data were obtained in $CDCl_3$ unless otherwise noted. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm ($CHCl_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm ($CDCl_3$). High-resolution mass spectra were recorded on ESI-TOF mass spectrometers, Bruker Daltonics microTOF II. Preparative thin-layer chromatography (PTLC) was performed on silica gel plates with silica gel 60 PF254 indicator (Sigma-Aldrich). Flash silica gel column chromatography was performed with silica gel 60N (Kanto). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9210 (JAIGEL-H).

■ Materials.

All chemicals and anhydrous solvents were obtained from commercial suppliers and used without further purification unless otherwise noted. Anhydrous 1,2-dichloroethane (Kanto), 2-butanone (FUJIFILM Wako), acetone (FUJIFILM Wako), and acetonitrile (Kanto) were degassed before use. $Ni(cod)_2$ (Kanto), Tol-BINAP (TCI), and TMSCN (Kanto) were obtained from commercial suppliers.

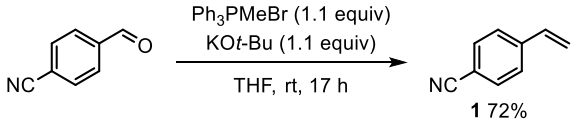
Vinylarenes **8a–8c**, **8e**, **8i–8k**, **8p**, **8r**, and **10** were obtained from commercial suppliers and used after removing polymerization inhibitors. [styrene, 4-methylstyrene, 4-*tert*-butylstyrene,

4-methoxystyrene, 4-chlorostyrene, 4-bromostyrene, and 4-trifluoromethylstyrene (TCI). 2-vinylnaphthalene (Aldrich). 2,3,4,5,6-pentafluorostyrene (FUJIFILM Wako)]. 4-cyanostyrene (**1**), 4-phenylstyrene (**8d**), 4-acetoxystyrene (**8f**), 4-(*tert*-butyl-dimethylsiloxy)styrene (**8g**), 4-fluorostyrene (**8h**), methyl 4-vinylbenzoate (**8l**), 3-methylstyrene (**8m**), 3-methoxystyrene (**8n**), 3-trifluoromethylstyrene (**8o**), 2-methylstyrene (**8q**), 2-vinylthiphene (**8s**), Estrone derivative **8t**, geraniol derivative **8u**, and D-α-Tocopherol derivative **8v** were prepared as shown below.

Benzoyl fluoride (**2**) was obtained from a commercial supplier (TCI) and used without further purification. Benzoyl cyanide (**5**) was prepared as shown below. 4-methylbenzoyl fluoride (**12a**), 4-*tert*-butylbenzoyl fluoride (**12b**), 4-phenylbenzoyl fluoride (**12c**), 4-methoxybenzoyl fluoride (**12d**), 4-acetoxybenzoyl fluoride (**12e**), 4-thiomethoxybenzoyl fluoride (**12f**), 4-fluorobenzoyl fluoride (**12g**), 3-methylbenzoyl fluoride (**12h**), 3-methoxybenzoyl fluoride (**12i**), 3-chlorobenzoyl fluoride (**12j**), 3-bromobenzoyl fluoride (**12k**), 2-naphthoyl fluoride (**12l**), 2-methylbenzoyl fluoride (**12m**), and 2-froyl fluoride (**12n**) were prepared as shown below.

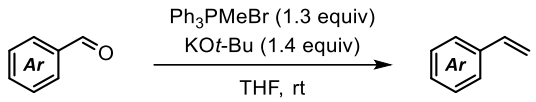
■ Substrate Preparation.

4-cyanostyrene (1):



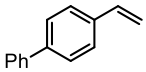
4-Cyanostyrene (**1**) was prepared according to the literature procedure.[13] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (2.0 g, 5.5 mmol, 1.1 equiv), KO*t*-Bu (620 mg, 5.5 mmol, 1.1 equiv), and THF (16 mL, 0.30 M). The mixture was stirred at 0 °C for 15 minutes. Then, 4-cyanobenzaldehyde (660 mg, 5.0 mmol, 1.0 equiv) was added to the mixture and warmed to room temperature. After 17 hours, the mixture was passed through a pad of Celite, and the residue was concentrated under reduced pressure. The

crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **1** as a colorless oil (470 mg, 3.6 mmol, 72% yield). The analytical data of **1** matched well with the reported one.



Vinylarenes **8d**, **8h**, **8l–8o**, and **8q** were prepared according to the following procedure. To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (1.3 equiv), KO*t*-Bu (1.4 equiv), and THF (0.25 M). The mixture was stirred at 0 °C for 15 minutes. Then, the carbonyl compound (1.0 equiv) was added to the mixture and warmed to room temperature. After complete consumption of the carbonyl compound, the mixture was passed through a pad of Celite, and the residue was concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography.

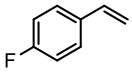
4-phenylstyrene (8d):



The reaction was carried out using 4-phenylbenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane) to give **8d** in 87% yield. The analytical data of **8d** matched well with the already reported one.[14] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.66–7.55 (m, 4H), 7.54–7.39 (m, 4H), 7.34 (t, 1H, *J* = 8.8 Hz), 6.76 (dd, 1H, *J* = 17.2, 10.4 Hz), 5.79 (d, 1H, *J* = 18.0 Hz), 5.27 (d, 1H, *J* = 10.8 Hz).

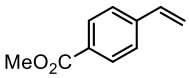
4-fluorostyrene (8h):



The reaction was carried out using 4-fluorobenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give **8h** in 70% yield. The analytical data of **8h** matched well with the already reported one.[15] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.38 (dd, 2H, *J* = 8.8, 5.6 Hz), 7.01 (t, 2H, *J* = 8.8 Hz), 6.68 (dd, 1H, *J* = 18.0, 11.2 Hz), 5.67 (d, 1H, *J* = 18.0 Hz), 5.22 (d, 1H, *J* = 10.4 Hz).

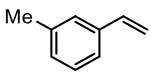
methyl 4-vinylbenzoate (8l):



The reaction was carried out using methyl 4-formylbenzoate on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **8l** in 68% yield. The analytical data of **8l** matched well with the already reported one.[14] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.00 (d, 2H, *J* = 8.8 Hz), 7.46 (d, 2H, *J* = 8.0 Hz), 6.75 (dd, 1H, *J* = 17.2, 10.4 Hz), 5.86 (d, 1H, *J* = 17.6 Hz), 5.38 (d, 1H, *J* = 10.8 Hz), 3.91 (s, 3H).

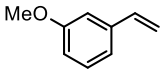
3-methylstyrene (8m):



The reaction was carried out using 3-methylbenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (pentane) to give **8m** in 61% yield. The analytical data of **8m** matched well with the already reported one.[16] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.25–7.19 (m, 3H), 7.11–7.05 (m, 1H), 6.70 (dd, 1H, *J* = 17.2, 10.4 Hz), 5.74 (d, 1H, *J* = 17.6 Hz), 5.23 (d, 1H, *J* = 10.4 Hz), 2.36 (s, 3H).

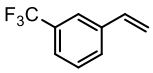
3-methoxystyrene (8n):



The reaction was carried out using 3-methoxybenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **8n** in 93% yield. The analytical data of **8n** matched well with the already reported one.[17] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.25 (t, 1H, *J* = 8.0 Hz), 7.01 (d, 1H, *J* = 7.2 Hz), 6.95 (s, 1H), 6.82 (dd, 1H, *J* = 8.4, 2.8 Hz), 6.69 (dd, 1H, *J* = 17.6, 10.8 Hz), 5.75 (d, 1H, *J* = 17.6 Hz), 5.25 (d, 1H, *J* = 10.8 Hz), 3.83 (s, 3H).

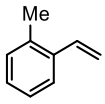
3-trifluoromethystyrene (8o):



The reaction was carried out using 3-trifluoromethylbenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane) to give **8o** in 39% yield. The analytical data of **8o** matched well with the already reported one.[18] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (s, 1H), 7.58 (d, 1H, *J* = 8.0 Hz), 7.51 (d, 1H, *J* = 7.6 Hz), 7.44 (t, 1H, *J* = 7.6 Hz), 6.75 (dd, 1H, *J* = 18.0, 11.2 Hz), 5.83 (d, 1H, *J* = 17.2 Hz), 5.36 (d, 1H, *J* = 10.4 Hz).

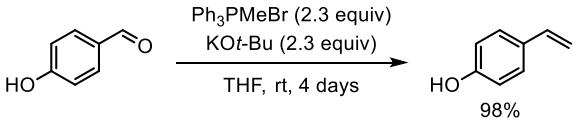
2-methylstyrene (8q):



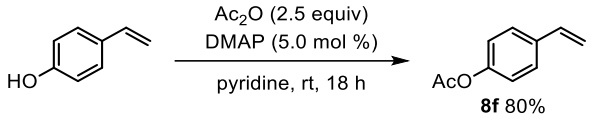
The reaction was carried out using 2-methylbenzaldehyde on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane) to give **8q** in 66% yield. The analytical data of **8q** matched well with the already reported one.[16] Therefore, only the ^{1}H NMR data is presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.52–7.45 (m, 1H), 7.22–7.12 (m, 3H), 6.96 (dd, 1H, *J* = 17.6, 11.2 Hz), 5.65 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.30 (dd, 1H, *J* = 11.2, 1.6 Hz), 2.36 (s, 3H).

4-acetoxystyrene (8f):

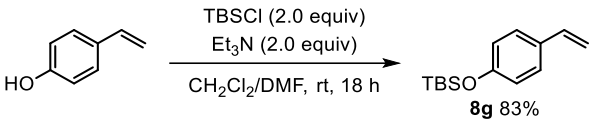


4-Hydroxystyrene was prepared according to the literature procedure.[19] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (13.2 g, 37 mmol, 2.3 equiv), KO*t*-Bu (4.1 g, 37 mmol, 2.3 equiv), and THF (120 mL, 0.13 M). The mixture was stirred at 0 °C for 15 minutes. Then, 4-hydroxybenzaldehyde (2.1 g, 16 mmol, 1.0 equiv) was added to the mixture and warmed to room temperature. After 4 days, H_2O was added to the mixture and extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (CH_2Cl_2) to give the desired product (2.0 g, 16 mmol, 98% yield). The analytical data matched well with the reported one.



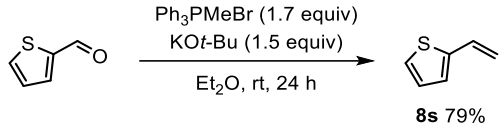
4-Acetoxystyrene (**8f**) was prepared according to the literature procedure.[20] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ac_2O (1.2 mL, 13 mmol, 2.5 equiv), DMAP (31 mg, 0.25 mmol, 5.0 mol %), 4-hydroxybenzaldehyde (610 mg, 5.0 mmol, 1.0 equiv), and pyridine (25 mL, 0.20 M). The reaction mixture was stirred at room temperature. After 18 hours, saturated aqueous solution of $CuSO_4$ was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was washed with H_2O, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give **8f** (660 mg, 4.1 mmol, 80% yield). The analytical data of **8f** matched well with the reported one.

4-(*tert*-butyl-dimethylsiloxy)styrene (8g):



4-(*tert*-Butyl-dimethylsiloxy)styrene (**8g**) was prepared according to the literature procedure.[21] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added TBSCl (1.5 g, 10 mmol, 2.0 equiv), Et_3N (1.4 mL, 10 mmol, 2.0 equiv), 4-hydroxybenzaldehyde (610 mg, 5.0 mmol, 1.0 equiv), and CH_2Cl_2/DMF (19 + 2.0 mL, 0.24 M). The reaction mixture was stirred at room temperature. After 18 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **8g** (990 mg, 4.2 mmol, 83% yield).The analytical data of **8g** matched well with the reported one.

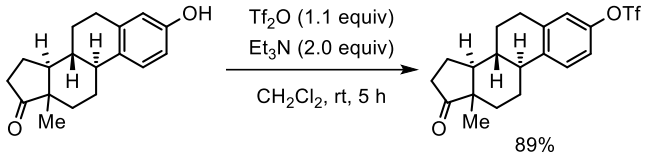
2-vinylthiophene (8s):



8s 79%

2-Vinylthiophene (**8s**) was prepared in 79% yield according to the literature procedure.[22] To an oven-dried 50 mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (1.8 g, 5.1 mmol, 1.7 equiv), KO*t*-Bu (510 mg, 4.5 mmol, 1.5 equiv), 2-thiophenecarboxaldehyde (340 mg, 3.0 mmol, 1.0 equiv), and Et_2O (30 mL, 0.10 M). The reaction mixture was stirred at room temperature. After 24 hours, saturated aqueous solution of NH_4Cl was added to the mixture and extracted with Et_2O × 3 times. The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (pentane) to give **8s** (260 mg, 2.4 mmol, 79% yield). The analytical data of **8s** matched well with the reported one.

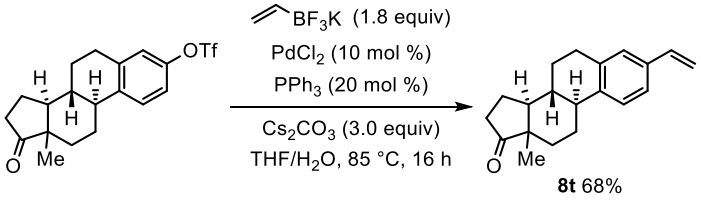
Estrone derivative 8t:



89%

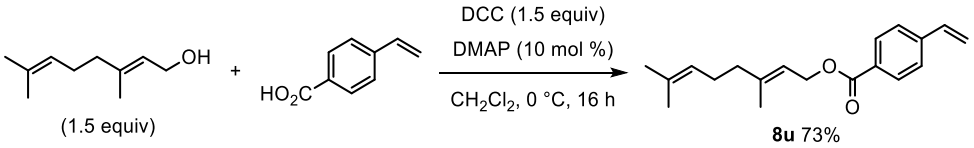
The Estrone derivative **8t** was prepared according to the literature procedure.[23] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added estrone (1.7 g, 6.0 mmol, 1.0 equiv) and CH_2Cl_2 (40 mL, 0.20 M). Then, Et_3N (1.2 g, 12 mmol, 2.0 equiv) and Tf_2O (1.1 mL, 6.6 mmol, 1.1 equiv) were added dropwise at 0 °C. The reaction mixture was stirred at room temperature. After 5 hours, saturated aqueous solution of $NaHCO_3$ was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over

$MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give the product (2.2 g, 5.4 mmol, 89% yield). The analytical data matched well with the reported one.



To an oven-dried 100 mL two-necked round-bottom flask equipped with a stirrer bar were added triflated-estrone (2.1 g, 5.3 mmol, 1.0 equiv), potassium vinyl trifluoroborate (1.3 g, 9.5 mmol, 1.8 equiv), Cs_2CO_3 (5.1 g, 16 mmol, 3.0 equiv), $PdCl_2$ (94 mg, 0.53 mmol, 10 mol %), PPh_3 (170 mg, 0.64 mmol, 12 mol %), and THF/H_2O (10 + 1.4 mL, 0.45 M). The reaction mixture was stirred at 85 °C in an oil bath. After 16 hours, H_2O was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give **8t** (1.0 g, 3.6 mmol, 68% yield). The analytical data of **8t** matched well with the reported one.

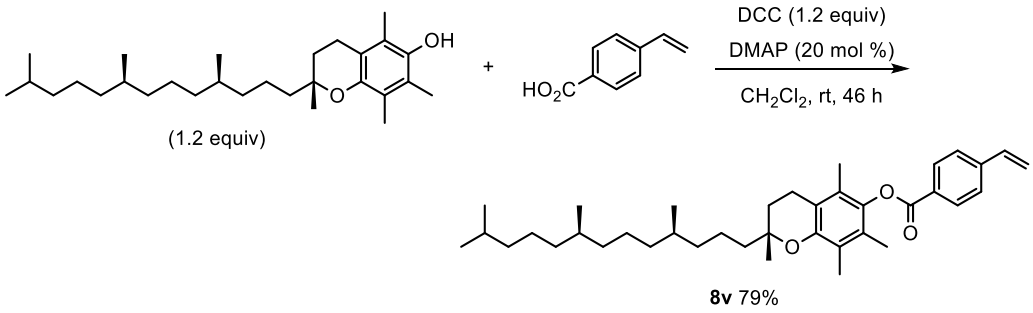
geraniol derivative 8u:



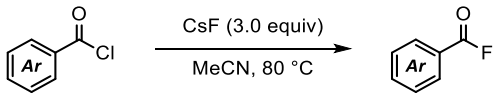
The geraniol derivative **8u** was prepared according to the literature procedure.[24] To an oven-dried 100 mL three-necked round-bottom flask equipped with a stirrer bar were added 4-vinylbenzoic acid (890 mg, 6.0 mmol, 1.0 equiv), DCC (1.9 g, 9.0 mmol, 1.5 equiv), DMAP (74 mg, 0.60 mmol, 10 mol %), and CH_2Cl_2 (36 mL, 0.17 M). Then, geraniol (1.5 g, 9.0 mmol, 1.5

equiv) was added to the mixture at 0 °C. The reaction mixture was stirred at 0 °C. After 16 hours, the solvent was removed under reduced pressure, and the residue was filtered through a pad of Celite. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 60:1) to give **8u** (1.3 g, 4.4 mmol, 73% yield).The analytical data of **8u** matched well with the reported one.

D-α-Tocopherol derivative 8v:



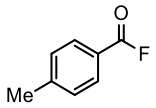
The D-α-Tocopherol derivative **8v** was prepared according to the literature procedure.[25] To an oven-dried 200 mL two-necked round-bottom flask equipped with a stirrer bar were added 4-vinylbenzoic acid (1.2 g, 8.0 mmol, 1.0 equiv), D-α-Tocopherol (4.2 g, 9.6 mmol, 1.2 equiv), DCC (2.0 g, 9.6 mmol, 1.2 equiv), DMAP (200 mg, 1.6 mmol, 20 mol %), and CH_2Cl_2 (80 mL, 0.10 M). The reaction mixture was stirred at room temperature. After 46 hours, the solvent was removed under reduced pressure. The residue was dissolved with AcOEt and passed through a pad of Celite. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **8v** (3.5 g, 6.2 mmol, 77% yield). The analytical data of **8v** matched well with the reported one.



Acyl fluoride **12a**, **12c**, **12d**, **12g–12j**, **12l**, and **12n** were prepared according to the

literature procedure.[26] To an oven-dried two-necked round-bottom flask equipped with a stirrer bar were added aroyl chloride (1.0 equiv), CsF (3.0 equiv), and MeCN (0.50 M). The mixture was stirred at 80 °C. After complete consumption of the aroyl chloride, the mixture was passed through a pad of Celite, and the residue was concentrated under reduced pressure. The crude mixture was purified by bulb-to-bulb distillation.

4-methylbenzoyl fluoride (12a):

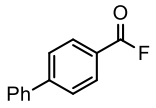


The reaction was carried out using 4-methylbenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12a** (710 mg, 5.1 mmol, 51% yield). The analytical data of **12a** matched well with the already reported one.[27]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.94 (d, 2H, *J* = 8.4 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 2.46 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 17.5 (s, 1F).

4-phenylbenzoyl fluoride (12c):

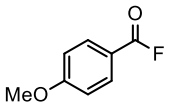


The reaction was carried out using 4-phenylbenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12c** (1.1 g, 5.7 mmol, 56% yield). The analytical data of **12c** matched well with the already reported one.[27]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.12 (d, 2H, *J* = 8.0 Hz), 7.75 (d, 2H, *J* = 7.2 Hz), 7.67–7.61 (m, 2H), 7.53–7.41 (m, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.2 (s, 1F).

4-methoxybenzoyl fluoride (12d):

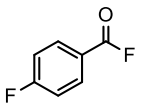


The reaction was carried out using 4-methoxybenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12d** (1.1 g, 7.0 mmol, 70% yield). The analytical data of **12d** matched well with the already reported one.[27]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (d, 2H, *J* = 8.4 Hz), 6.98 (dd, 2H, *J* = 8.8, 1.2 Hz), 3.90 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 16.1 (s, 1F).

4-fluorobenzoyl fluoride (12g):

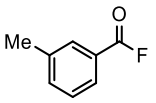


The reaction was carried out using 4-fluorobenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12g** (540 mg, 3.8 mmol, 38% yield). The analytical data of **12g** matched well with the already reported one.[28]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.08 (dd, 2H, *J* = 8.8, 5.2 Hz), 7.25–7.16 (m, 2H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.1 (s, 1F), -100.5 (s, 1F).

3-methylbenzoyl fluoride (12h):



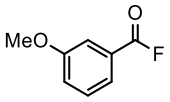
The reaction was carried out using 3-methylbenzoyl chloride on a 10 mmol scale. The

crude mixture was purified by bulb-to-bulb distillation to give **12h** (760 mg, 5.5 mmol, 55% yield). The analytical data of **12h** matched well with the already reported one.[28]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.86 (s, 1H), 7.85 (d, 1H, *J* = 7.6 Hz), 7.51 (d, 1H, *J* = 7.2 Hz), 7.41 (t, 1H, *J* = 8.0 Hz), 2.44 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.4 (s, 1F).

3-methoxybenzoyl fluoride (12i):

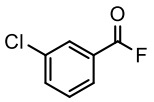


The reaction was carried out using 3-methoxylbenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12i** (490 mg, 3.2 mmol, 64% yield). The analytical data of **12i** matched well with the already reported one.[28]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (d, 1H, *J* = 8.0 Hz), 7.53 (t, 1H, *J* = 2.0 Hz), 7.46–7.39 (m, 1H), 7.24 (ddd, 1H, *J* = 8.4, 2.8, 0.8 Hz), 3.87 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.7 (s, 1F).

3-chlorobenzoyl fluoride (12j):

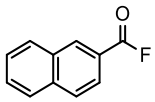


The reaction was carried out using 3-chlorobenzoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12j** (1.1 g, 7.0 mmol, 70% yield). The analytical data of **12j** matched well with the already reported one.[29]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.03 (t, 1H, *J* = 2.0 Hz), 7.94 (d, 1H, *J* = 8.0 Hz), 7.71–7.64 (m, 1H), 7.49 (dt, 1H, *J* = 7.6, 1.6 Hz).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 19.2 (s, 1F).

2-naphthoyl fluoride (12l):

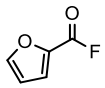


The reaction was carried out using 2-naphthoyl chloride on a 10 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12l** (520 mg, 3.0 mmol, 30% yield). The analytical data of **12l** matched well with the already reported one.[27]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.65 (s, 1H), 8.05–7.89 (m, 4H), 7.72–7.65 (m, 1H), 7.65–7.58 (m, 1H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.2 (s, 1F).

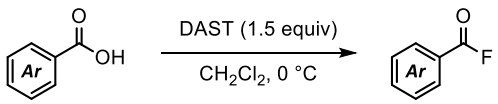
2-froyl fluoride (12n):



The reaction was carried out using 2-froyl chloride on a 5.0 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12n** (380 mg, 3.3 mmol, 67% yield). The analytical data of **12n** matched well with the already reported one.[30]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.76–7.73 (m, 1H), 7.42 (d, 1H, J = 3.6 Hz), 6.64–6.61 (m, 1H).

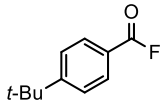
^{19}F NMR ($CDCl_3$, 396 MHz): δ = 15.4 (s, 1F).



Acyl fluoride **12b**, **12e**, **12f**, **12k**, and **12m** were prepared according to the literature procedure.[31] To an oven-dried two-necked round-bottom flask equipped with a stirrer bar were

added benzoic acid (1.0 equiv) and CH_2Cl_2 (0.33 M). Then, DAST (1.5 equiv) was added slowly at 0 °C. The mixture was stirred at 0 °C. After complete consumption of the benzoic acid, saturated aqueous solution of $NaHCO_3$ was added to the mixture and extracted with CH_2Cl_2 × 3 times. The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography or bulb-to-bulb distillation.

4-*tert*-butylbenzoyl fluoride (12b):

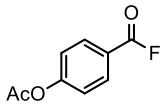


The reaction was carried out using 4-*tert*-butylbenzoic acid on a 5.0 mmol scale. The crude mixture was purified by bulb-to-bulb distillation to give **12b** (740 mg, 4.1 mmol, 83% yield). The analytical data of **12b** matched well with the already reported one.[29]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (d, 2H, *J* = 8.4 Hz), 7.54 (dd, 2H, *J* = 8.4, 1.2 Hz), 1.36 (s, 9H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 17.8 (s, 1F).

4-acetoxybenzoyl fluoride (12e):

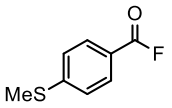


The reaction was carried out using 4-acetoxybenzoic acid on a 10 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give **12e** (1.8 g, 9.7 mmol, 97% yield). The analytical data of **12e** matched well with the already reported one.[32]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.08 (d, 2H, *J* = 8.8 Hz), 7.31–7.25 (m, 2H), 2.34 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 18.3 (s, 1F).

4-thiomethoxybenzoyl fluoride (12f):

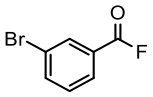


The reaction was carried out using 4-thiomethoxybenzoic acid on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 5:1) to give **12f** (670 mg, 3.9 mmol, 78% yield). The analytical data of **12f** matched well with the already reported one.[33]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.92 (d, 2H, *J* = 8.4 Hz), 7.30 (d, 2H, *J* = 7.6 Hz), 2.54 (s, 3H).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 16.7 (s, 1F).

3-bromobenzoyl fluoride (12k):

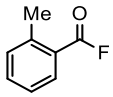


The reaction was carried out using 3-bromobenzoic acid on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give **12k** (780 mg, 3.8 mmol, 77% yield). The analytical data of **12k** matched well with the already reported one.[30]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.18 (s, 1H), 7.99 (d, 1H, *J* = 8.0 Hz), 7.86–7.90 (m, 1H), 7.42 (dt, 1H, *J* = 7.6, 1.2 Hz).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 19.2 (s, 1F).

2–methylbenzoyl fluoride (12m):

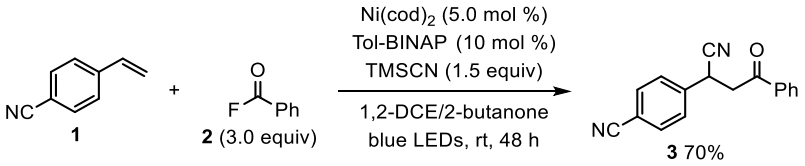


The reaction was carried out using 2-methylbenzoic acid on a 5.0 mmol scale. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 30:1) to give **12m** (540 mg, 3.9 mmol, 79% yield). The analytical data of **12m** matched well with the already reported one.[27]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.02–7.97 (m, 1H), 7.55 (dt, 1H, *J* = 8.0, 1.2 Hz), 7.37–7. 30 (m, 2H), 2.66 (d, 3H, *J* = 2.0 Hz).

^{19}F NMR ($CDCl_3$, 396 MHz): δ = 29.3 (s, 1F).

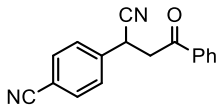
■ Typical Procedure for the Photoexcited Nickel-Catalyzed Acylcyanation.



In a nitrogen-filled glove-box, $Ni(cod)_2$ (4.1 mg, 0.015 mmol, 5.0 mol %), 1,2-DCE (750 μL), and 2-butanone (750 μL) were added to 4-cyanostyrene (38.5 mg, 0.30 mmol, 1.0 equiv), benzoyl fluoride (111.7 mg, 0.90 mmol, 3.0 equiv), Tol-BINAP (20.4 mg, 0.030 mmol, 10 mol %), and TMSCN (44.6 mg, 0.45 mmol, 1.5 equiv) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred under blue LEDs (HepatoChem, 425 nm) irradiation with a fan. After 48 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **3** as a white solid (54.4 mg, 0.21 mmol, 70% yield).

■ **Characterization of the Products 3, 9a–9v, 13a–13n.**

3:

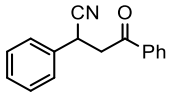


The analytical data of **3** matched well with the already one.[10c] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91 (d, 2H, *J* = 7.2 Hz), 7.70 (d, 2H, *J* = 8.4 Hz), 7.64–7.56 (m, 3H), 7.48 (t, 2H, *J* = 8.0 Hz), 4.66 (dd, 1H, *J* = 6.8, 6.8 Hz), 3.76 (dd, 1H, *J* = 17.6, 6.8 Hz), 3.55 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.8, 140.4, 135.5, 134.2, 133.0, 128.9, 128.6, 128.1, 119.5, 118.0, 112.6, 43.9, 31.8.

9a:

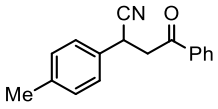


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9a** as a white solid (33.4 mg, 0.14 mmol, 47% yield). The analytical data of **9a** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.96–7.89 (m, 2H), 7.60 (t, 1H, *J* = 7.6 Hz), 7.51–7.31 (m, 7H), 4.58 (dd, 1H, *J* = 7.6, 6.0 Hz), 3.73 (dd, 1H, *J* = 17.6, 7.6 Hz), 3.51 (dd, 1H, *J* = 18.0, 6.0 Hz),

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ = 194.6, 135.7, 135.2, 133.9, 129.3, 128.8, 128.4, 128.1, 127.5, 120.6, 44.5, 31.9.

9b:

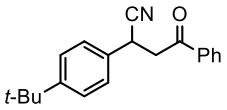


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9b** as a white solid (37.0 mg, 0.15 mmol, 49% yield). The analytical data of **9b** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.89 (m, 2H), 7.59 (t, 1H, *J* = 7.2 Hz), 7.47 (t, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.19 (d, 2H, *J* = 8.4 Hz), 4.53 (dd, 1H, *J* = 8.0, 6.4 Hz), 3.71 (dd, 1H, *J* = 18.0, 8.0 Hz), 3.49 (dd, 1H, *J* = 18.0, 6.4 Hz), 2.35 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.7, 138.3, 135.7, 133.9, 132.2, 129.9, 128.8, 128.1, 127.3, 120.8, 44.6, 31.5, 21.1.

9c:

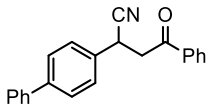


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9c** as a white solid (41.9 mg, 0.14 mmol, 48% yield). The analytical data of **9c** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (d, 2H, *J* = 7.2 Hz), 7.59 (t, 1H, *J* = 7.6 Hz), 7.47 (t, 2H, *J* = 7.6 Hz), 7.41 (d, 2H, *J* = 8.0 Hz), 7.36 (d, 2H, *J* = 8.4 Hz), 4.55 (dd, 1H, *J* = 8.0, 6.0 Hz), 3.72 (dd, 1H, *J* = 18.0, 8.0 Hz), 3.50 (dd, 1H, *J* = 17.6, 6.0 Hz), 1.31 (s, 9H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.7, 151.5, 135.7, 133.8, 132.2, 128.8, 128.1, 127.2, 126.2, 120.8, 44.6, 34.6, 31.4, 31.2.

9d:

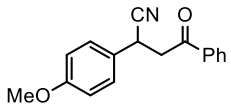


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9d** as a white solid (57.8 mg, 0.19 mmol, 62% yield). The analytical data of **9d** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, 2H, *J* = 7.2 Hz), 7.64–7.55 (m, 5H), 7.54–7.42 (m, 6H), 7.37 (t, 1H, *J* = 7.2 Hz), 4.63 (dd, 1H, *J* = 7.6, 6.4 Hz), 3.77 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.56 (dd, 1H, *J* = 17.6, 6.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.6, 141.4, 140.1, 135.7, 134.2, 133.9, 128.9, 128.8, 128.1, 127.9, 127.7, 127.1, 120.6, 44.5, 31.6.

9e:

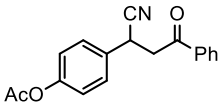


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **9e** as a white solid (46.2mg, 0.17 mmol, 58% yield). The analytical data of **9e** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92 (d, 2H, *J* = 7.2 Hz), 7.59 (t, 1H, *J* = 7.2 Hz), 7.47 (t, 2H, *J* = 7.6 Hz), 7.35 (d, 2H, *J* = 8.4 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 4.52 (t, 1H, *J* = 6.8 Hz), 3.80 (s, 3H), 3.69 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.49 (dd, 1H, *J* = 18.0, 6.4 Hz).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 194.8, 159.5, 135.7, 133.9, 128.8, 128.7, 128.1, 127.2, 120.9, 114.6, 55.3, 44.6, 31.1.

9f:

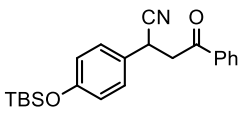


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **9f** as a white solid (44.5 mg, 0.15 mmol, 51% yield). The analytical data of **9f** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^1H NMR ($CDCl_3$, 400 MHz): δ 7.96–7.89 (m, 2H), 7.60 (t, 1H, J = 7.2 Hz), 7.51–7.43 (m, 4H), 7.13 (d, 2H, J = 8.8 Hz), 4.59 (dd, 1H, J = 7.6, 6.0 Hz), 3.73 (dd, 1H, J = 18.4, 8.0 Hz), 3.50 (dd, 1H, J = 18.0, 6.0 Hz), 2.30 (s, 3H).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 194.4, 169.3, 150.6, 135.6, 134.0, 132.8, 129.0, 128.7, 128.1, 122.5, 120.4, 44.6, 31.3, 21.1.

9g:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9g** as a white solid (57.1 mg, 0.16 mmol, 52% yield).

IR (ATR, cm^{-1}): 2957, 2927, 2856, 2243, 1684, 1508, 1250, 910, 839, 779, 600.

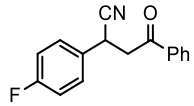
^1H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.89 (m, 2H), 7.59 (t, 1H, J = 8.0 Hz), 7.47 (t, 2H, J = 8.0

Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 6.83 (d, 2H, *J* = 8.4 Hz), 4.50 (dd, 1H, *J* = 7.6, 6.0 Hz), 3.69 (dd, 1H, *J* = 17.6, 7.6 Hz), 3.48 (dd, 1H, *J* = 18.0, 6.0 Hz), 0.98 (s, 9H), 0.19 (s, 6H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.8, 155.7, 135.8, 133.8, 128.8, 128.6, 128.1, 127.8, 120.9, 120.7, 44.6, 31.2, 25.6, 18.2, -4.45.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{27}NO_2SiNa^+$ 388.17; Found 388.1686.

9h:

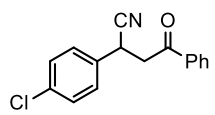


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9h** as a white solid (49.3 mg, 0.19 mmol, 65% yield). The analytical data of **9h** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.89 (m, 2H), 7.60 (t, 1H, *J* = 8.0 Hz), 7.48 (t, 2H, *J* = 8.0 Hz), 7.43 (d, 1H, *J* = 8.8 Hz), 7.41 (d, 1H, *J* = 8.8 Hz), 7.08 (t, 2H, *J* = 8.8 Hz), 4.57 (t, 1H, *J* = 6.8 Hz), 3.71 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.51 (dd, 1H, *J* = 18.0, 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.4, 162.5 (d, *J* = 249.5 Hz), 135.6, 134.0, 131.0 (d, *J* = 2.9 Hz), 129.3 (d, *J* = 8.6 Hz), 128.9, 128.1, 120.5, 116.2 (d, *J* = 22.1 Hz), 44.4, 31.2.

9i:



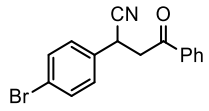
The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9i** as a white

solid (43.5 mg, 0.16 mmol, 54% yield). The analytical data of **9i** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94–7.89 (m, 2H), 7.60 (t, 1H, *J* = 7.2 Hz), 7.47 (t, 2H, *J* = 8.0 Hz), 7.41–7.33 (m, 4H), 4.56 (t, 1H, *J* = 6.8 Hz), 3.71 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.51 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.3, 135.5, 134.4, 134.0, 133.7, 129.4, 128.94, 128.86, 128.1, 120.2, 44.3, 31.3.

9j:

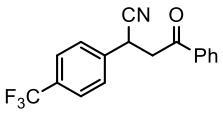


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9j** as a white solid (60.1 mg, 0.19 mmol, 64% yield). The analytical data of **9j** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94–7.88 (m, 2H), 7.60 (t, 1H, *J* = 7.2 Hz), 7.52 (d, 2H, *J* = 8.8 Hz), 7.47 (t, 2H, *J* = 8.4 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 4.55 (t, 1H, *J* = 6.8 Hz), 3.71 (dd, 1H, *J* = 17.6, 7.2 Hz), 3.50 (dd, 1H, *J* = 18.0, 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.3, 135.5, 134.3, 134.0, 132.4, 129.2, 128.8, 128.1, 122.5, 120.1, 44.2, 31.3.

9k:

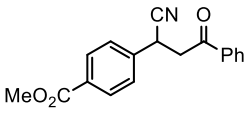


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9k** as a white solid (62.7 mg, 0.21 mmol, 68% yield). The analytical data of **9k** matched well with the already reported one.[10c] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92 (d, 2H, *J* = 6.8 Hz), 7.70–7.55 (m, 5H), 7.48 (t, 2H, *J* = 8.0 Hz), 4.67 (t, 1H, *J* = 6.8 Hz), 3.76 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.55 (dd, 1H, *J* = 18.0, 6.8 Hz)

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.1, 139.2, 135.4, 134.1, 130.8 (q, *J* = 32.7 Hz), 128.9, 128.1, 126.3 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 274.5 Hz), 119.9, 44.2, 31.7.

9l:

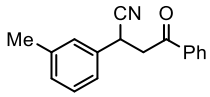


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **9l** as a white solid (40.2 mg, 0.14 mmol, 46% yield). The analytical data of **9l** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06 (d, 2H, *J* = 8.4 Hz), 7.94–7.89 (m, 2H), 7.60 (t, 1H, *J* = 7.2 Hz), 7.53 (d, 2H, *J* = 8.0 Hz), 7.47 (t, 2H, *J* = 7.6 Hz), 4.64 (dd, 1H, *J* = 7.2, 6.4 Hz), 3.92 (s, 3H), 3.75 (dd, 1H, *J* = 17.6, 7.2 Hz), 3.53 (dd, 1H, *J* = 17.6, 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.2, 166.3, 140.1, 135.5, 134.0, 130.5, 130.3, 128.9, 128.1, 127.6, 120.0, 52.3, 44.2, 31.8.

9m:

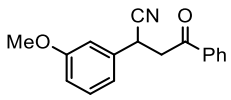


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9m** as a white solid (32.7 mg, 0.13 mmol, 44% yield). The analytical data of **9m** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (dd, 2H, *J* = 8.4, 1.2 Hz), 7.60 (t, 1H, *J* = 8.0 Hz), 7.47 (t, 2H, *J* = 8.4 Hz), 7.25 (dt, 3H, *J* = 18.8, 8.0 Hz), 7.15 (d, 1H, *J* = 7.6 Hz), 4.53 (dd, 1H, *J* = 8.4, 6.0 Hz), 3.72 (dd, 1H, *J* = 18.4, 8.0 Hz), 3.49 (dd, 1H, *J* = 18.4, 6.0 Hz), 2.37 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.7, 139.2, 135.7, 135.2, 133.9, 129.14, 129.12, 128.8, 128.12, 128.08, 124.5, 120.7, 44.6, 31.8, 21.4.

9n:

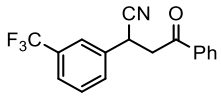


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **9n** as a white solid (52.8 mg, 0.20 mmol, 65% yield). The analytical data of **9n** matched well with the already reported one.[34] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (dd, 2H, *J* = 8.4, 1.2 Hz), 7.60 (t, 1H, *J* = 7.2 Hz), 7.47 (t, 2H, *J* = 7.6 Hz), 7.30 (t, 1H, *J* = 8.0 Hz), 7.01 (d, 1H, *J* = 7.6 Hz), 6.97 (dd, 1H, *J* = 1.6, 1.6 Hz), 6.87 (dd, 1H, *J* = 8.4, 2.0 Hz), 4.54 (dd, 1H, *J* = 8.4, 6.0 Hz), 3.82 (s, 3H), 3.73 (dd, 1H, *J* = 17.6, 8.0 Hz), 3.50 (dd, 1H, *J* = 18.0, 6.0 Hz).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 194.6, 160.1, 136.7, 135.6, 133.9, 130.3, 128.8, 128.1, 120.5, 119.6, 133.7, 133.2, 55.3, 44.5, 31.9.

9o:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9o** as a white solid (57.6 mg, 0.19 mmol, 63% yield).

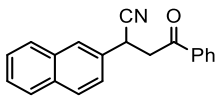
IR (ATR, cm^{-1}): 3338, 2958, 2249, 1677, 1333, 1117, 687.

^1H NMR ($CDCl_3$, 400 MHz): δ 7.93 (d, 2H, *J* = 7.2 Hz), 7.71 (s, 1H), 7.67 (d, 1H, *J* = 7.6 Hz), 7.61 (t, 2H, *J* = 6.4 Hz), 7.55 (d, 1H, *J* = 7.2 Hz), 7.48 (t, 2H, *J* = 8.0 Hz), 4.66 (t, 1H, *J* = 6.8 Hz), 3.77 (dd, 1H, *J* = 18.4, 8.0 Hz), 3.54 (dd, 1H, *J* = 17.6, 6.4 Hz).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 194.2, 136.4, 135.5, 134.2, 131.8 (q, *J* = 32.7 Hz), 131.2, 130.0, 129.0, 128.2, 125.5 (q, *J* = 3.9 Hz), 124.5 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 274.4 Hz), 120.0, 44.4, 31.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{12}NOF_3Na^+$ 326.08; Found 326.0733.

9p:



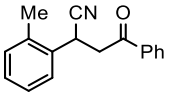
The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9p** as a white solid (52.3 mg, 0.18 mmol, 61% yield). The analytical data of **9p** was matched well with the

already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.93 (m, 3H), 7.87 (d, 1H, *J* = 8.0 Hz), 7.85 (dt, 2H, *J* = 6.8, 3.2 Hz), 7.59 (t, 1H, *J* = 7.2 Hz), 7.55–7.45 (m, 5H), 4.75 (dd, 1H, *J* = 7.6, 6.0 Hz), 3.81 (dd, 1H, *J* = 17.6, 7.6 Hz), 3.51 (dd, 1H, *J* = 18.0, 6.0 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.6, 135.6, 133.9, 133.3, 132.9, 132.5, 129.3, 128.8, 128.1, 127.9, 128.7, 126.8, 126.7, 126.6, 124.8, 120.6, 44.5, 32.0.

9q:

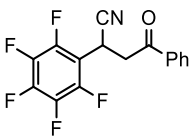


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9q** as a white solid (39.4 mg, 0.16 mmol, 53% yield). The analytical data of **9q** was matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98–7.92 (m, 2H), 7.61 (t, 1H, *J* = 7.2 Hz), 7.53–7.44 (m, 3H), 7.31–7.19 (m, 3H), 4.72 (dd, 1H, *J* = 8.8, 4.8 Hz), 3.74 (dd, 1H, *J* = 18.0, 8.8 Hz), 3.42 (dd, 1H, *J* = 18.0, 5.2 Hz), 2.42 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.7, 135.7, 135.3, 133.9, 133.4, 131.3, 128.8, 128.5, 128.1, 127.5, 127.0, 120.7, 43.1, 28.7, 19.2

9r:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9r** as a white solid (73.4 mg, 0.23 mmol, 75% yield).

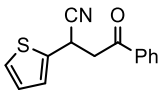
IR (ATR, cm^{-1}): 2954, 2851, 2248, 1684, 1505, 1130, 1122, 994, 689.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (dd, 2H, *J* = 8.4, 1.2 Hz), 7.63 (t, 1H, *J* = 7.2 Hz), 7.50 (t, 2H, *J* = 7.6 Hz), 4.90 (dd, 1H, *J* = 8.4, 8.0 Hz), 3.87 (dd, 1H, *J* = 18.0, 8.4 Hz), 3.73 (dd, 1H, *J* = 18.4, 8.0 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz): δ -139.9 (s, 2F), -151.7 (t, 1F, *J* = 23.1 Hz), -159.9 (t, 2F, *J* = 23.1 Hz).

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_8NOF_5Na^+$ 348.04; Found 348.0416.

9s:

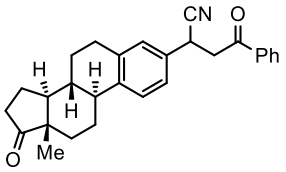


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9s** as a white solid (35.1 mg, 0.15 mmol, 49% yield). The analytical data of **9s** matched well with the already reported one.[10b] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98–7.93 (m, 2H), 7.62 (t, 1H, *J* = 7.6 Hz), 7.49 (t, 2H, *J* = 7.6 Hz), 7.28 (dd, 1H, *J* = 5.2, 0.8 Hz), 7.19–7.14 (m,1H), 6.98 (dd, 1H, *J* = 5.6, 3.6 Hz), 4.87 (t, 1H, *J* = 6.8 Hz), 3.77 (dd, 1H, *J* = 18.0, 7.2 Hz), 3.63 (dd, 1H, *J* = 18.0, 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.2, 137.0, 135.5, 134.0, 128.9, 128.1, 127.2, 126.7, 125.9, 119.7, 44.6, 27.2.

9t:

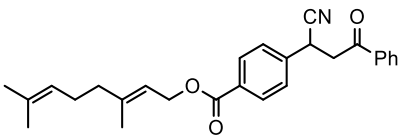


The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9t** as a white solid (55.7 mg, 0.14 mmol, 45% yield). The analytical data of **9t** matched well with the already reported one.[10a] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (d, 2H, *J* = 7.2 Hz), 7.60 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.47 (t, 2H, *J* = 8.0, 8.0 Hz), 7.21 (d, 1H, *J* = 8.0 Hz), 7.19 (d, 2H, *J* = 9.6 Hz), 4.51 (dd, 1H, *J* = 7.6, 6.0 Hz), 3.72 (dd, 1H, *J* = 17.6, 8.0 Hz), 3.49 (dd, 1H, *J* = 18.4, 6.0 Hz), 2.94-2.91 (m, 2H), 2.51 (dd, 1H, *J* = 18.8, 8.8 Hz), 2.41 (dt, 1H, *J* = 8.8, 5.6 Hz), 2.32–2.24 (m, 1H), 2.20–2.02 (m, 3H), 1.97 (dd, 1H, *J* = 12.0, 2.8 Hz), 1.69–1.42 (m, 6H), 0.91 (s, 3H) .

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 220.6, 194.7, 140.0, 137.6, 135.7, 133.9, 132.6, 128.8, 128.1, 128.0, 126.3, 124.8, 120.8, 50.4, 47.9, 44.5, 44.2, 38.0, 35.8, 31.5, 31.4, 29.3, 26.3, 25.6, 21.5, 13.8.

9u:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9u** as a colorless oil (62.5 mg, 0.15 mmol, 50% yield).

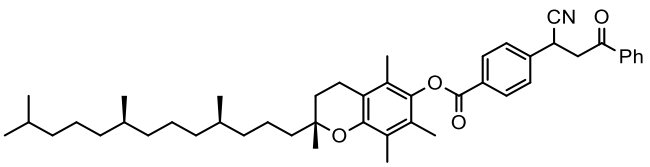
IR (ATR, cm^{-1}): 3060, 2966, 2916, 2855, 2245, 1713, 1686, 1612, 1597, 1254, 1100, 731, 688.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07 (d, 2H, *J* = 8.4 Hz), 7.92 (d, 2H, *J* = 7.6 Hz), 7.60 (dd, 1H, *J* = 7.2, 7.2 Hz), 7.52 (d, 2H, *J* = 8.0 Hz), 7.47 (dd, 2H, *J* = 8.0, 8.0 Hz), 5.45 (dd, 1H, *J* = 6.4, 6.4 Hz), 5.09 (dd, 1H, *J* = 5.2, 4.4 Hz), 4.84 (d, 1H, *J* = 6.8 Hz), 4.64 (dd, 2H, *J* = 6.8, 6.8 Hz), 3.74 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.54 (dd, 1H, *J* = 18.0, 6.0 Hz), 2.13–2.05 (m, 4H), 1.76 (s, 3H), 1.67 (s, 3H), 1.61 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.2, 165.8, 142.7, 139.9, 135.5, 134.0, 131.9, 130.7, 130.5, 128.9, 128.1, 127.6, 123.7, 120.0, 118.1, 77.2, 62.1, 44.2, 39.5, 31.8, 26.3, 25.7, 17.7, 16.6.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{27}H_{29}NO_3Na^+$ 438.20; Found 438.2043.

9v:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **9v** as a white solid (98.0 mg, 0.14 mmol, 47% yield).

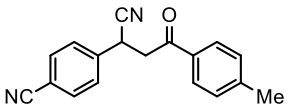
IR (ATR, cm^{-1}): 2949, 2924, 2866, 2360, 1732, 1686, 1449, 1273, 1236, 1091, 751, 688.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 2H, *J* = 8.4 Hz), 7.94 (d, 2H, *J* = 7.6 Hz), 7.62 (dt, 3H, *J* = 7.6, 3.6 Hz), 7.49 (dd, 2H, *J* = 7.6, 7.6 Hz), 4.70 (dd, 1H, *J* = 6.4, 6.4 Hz), 3.79 (dd, 1H, *J* = 17.6, 7.2 Hz), 3.59 (dd, 1H, *J* = 18.0, 6.4 Hz), 2.61 (dd, 2H, *J* = 6.8, 6.8 Hz), 2.12 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.87–1.78 (m, 2H), 1.57–1.01 (m, 32H), 0.87–0.84 (m, 15H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 194.1, 164.4, 149.6, 140.6, 140.5, 135.5, 134.1, 131.1, 129.8, 128.9, 128.1, 127.9, 126.8, 125.0, 123.2, 120.0, 75.1, 44.2, 19.4, 37.4, 37.3, 32.8, 31.9, 28.0, 24.8, 24.4, 22.7, 22.6, 21.0, 20.6, 19.7, 19.6, 13.0, 12.2, 11.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{46}H_{61}NO_4Na^+$ 714.45; Found 714.4467

13a:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **13a** as a white solid (60.2 mg, 0.22 mmol, 74% yield).

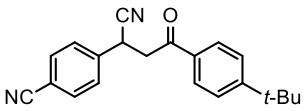
IR (ATR, cm^{-1}): 3040, 2924, 2361, 2229, 1675, 1604, 1181, 810, 587.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, 2H, *J* = 8.4 Hz), 7.69 (d, 2H, *J* = 8.4 Hz), 7.58 (d, 2H, *J* = 8.8 Hz), 7.27 (d, 2H, *J* = 6.8 Hz), 4.65 (t, 1H, *J* = 6.4 Hz), 3.72 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.52 (dd, 1H, *J* = 18.0, 7.6 Hz), 2.41 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.4, 145.3, 140.5, 132.9, 132.8, 129.6, 128.5, 128.2, 119.6, 118.0, 112.5, 43.8, 31.8, 21.7.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2ONa^+$ 297.10; Found 297.0977.

13b:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13b** as a white solid (58.5 mg, 0.18 mmol, 62% yield).

IR (ATR, cm^{-1}): 2957, 2906, 2868, 1358, 2230,1677, 1606, 1407, 984, 830, 570.

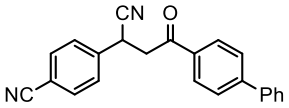
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (d, 2H, *J* = 8.0 Hz), 7.69 (d, 2H, *J* = 8.4 Hz), 7.59 (d, 2H, *J*

= 8.4 Hz), 7.48 (d, 2H, *J* = 8.4 Hz), 4.67 (t, 1H, *J* = 6.4 Hz), 3.72 (dd, 1H, *J* = 18.0, 6.8 Hz), 3.54 (dd, 1H, *J* = 18.0, 6.8 Hz), 1.33 (s, 9H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.4, 158.2, 140.5, 132.9, 132.7, 128.6, 128.1, 125.9, 119.6, 118.0, 112.5, 43.8, 35.2, 31.8, 31.0.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{20}N_2ONa^+$ 339.15; Found 339.1471.

13c:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (CH_2Cl_2) to give **13c** as a white solid (46.2 mg, 0.14 mmol, 46% yield).

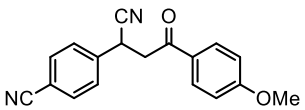
IR (ATR, cm^{-1}): 3063, 2917, 2359, 2228, 1675, 1603, 1406, 1254, 998, 825, 770, 705.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, 2H, *J* = 8.4 Hz), 7.74–7.67 (m, 4H), 7.64–7.58 (m, 4H), 7.48 (t, 2H, *J* = 6.8 Hz), 7.42 (t, 1H, *J* = 7.6 Hz), 4.69 (t, 1H, *J* = 6.8 Hz), 3.79 (dd, 1H, *J* = 18.0, 6.8 Hz), 3.58 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.4, 147.0, 140.4, 139.4, 133.9, 133.0, 129.0, 128.7, 128.6, 127.5, 127.3, 119.5, 118.0, 112.6, 44.0, 31.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{16}N_2ONa^+$ 359.1155; Found 359. 1124.

13d:



The reaction was carried out following the typical procedure. The crude mixture was

purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **13d** as a white solid (50.2 mg, 0.17 mmol, 58% yield).

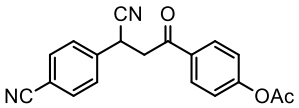
IR (ATR, cm^{-1}): 2228, 1672, 1598, 1509, 1251, 1168, 829, 587.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, 2H, *J* = 9.2 Hz), 7.69 (d, 2H, *J* = 6.4 Hz), 7.58 (d, 2H, *J* = 8.0 Hz), 6.94 (d, 2H, *J* = 9.2 Hz), 4.66 (t, 1H, *J* = 6.8 Hz), 3.87 (s, 3H), 3.69 (dd, 1H, *J* = 18.0, 6.8 Hz), 3.49 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 192.2, 164.3, 140.6, 132.9, 130.4, 128.58, 128.3, 119.6, 118.0, 114.1, 112.5, 55.6, 43.5, 31.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2O_2Na^+$ 313.0947; Found 313.0945.

13e:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13e** as a white solid (52.2 mg, 0.16 mmol, 55% yield).

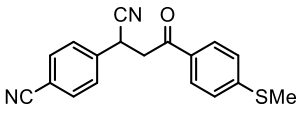
IR (ATR, cm^{-1}): 3077, 2927, 2359, 2235, 1753, 1674, 1220, 1203, 1171, 995, 835, 604.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, 2H, *J* = 8.4 Hz), 7.70 (d, 2H, *J* = 8.8 Hz), 7.58 (d, 2H, *J* = 8.0 Hz), 7.22 (d, 2H, *J* = 8.8 Hz), 4.65 (t, 1H, *J* = 6.8 Hz), 3.73 (dd, 1H, *J* = 18.4, 6.8 Hz), 3.53 (dd, 1H, *J* = 18.0, 6.4 Hz), 2.33 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 192.6, 168.6, 155.2, 140.3, 133.0, 132.8, 129.8, 128.5, 122.2, 119.4, 118.0, 112.7, 43.9, 31.8, 21.1.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{14}N_2O_3Na^+$ 341.09; Found 341.0906.

13f:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13f** as a white solid (44.3 mg, 0.14 mmol, 48% yield).

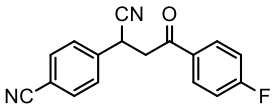
IR (ATR, cm^{-1}): 2360, 2341, 2221, 1998, 1672, 1587, 1091, 808, 668.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (d, 2H, *J* = 8.4 Hz), 7.68 (d, 2H, *J* = 8.0 Hz), 7.57 (d, 2H, *J* = 8.0 Hz), 7.24 (d, 2H, *J* = 8.8 Hz), 4.64 (t, 1H, *J* = 6.8 Hz), 3.70 (dd, 1H, *J* = 18.0, 7.6 Hz), 3.49 (dd, 1H, *J* = 18.0, 6.4 Hz), 2.50 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 192.7, 147.7, 140.4, 132.9, 131.4, 128.5, 128.4, 124.9, 119.6, 118.0, 112.5, 43.6, 31.8, 14.6.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2OSNa^+$ 329.0719; Found 329.0728.

13g:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13g** as a white solid (46.5 mg, 0.17 mmol, 56% yield).

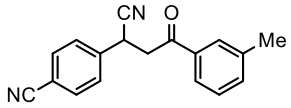
IR (ATR, cm^{-1}): 2360, 2340, 2224, 1682, 1594, 1504, 1216, 828, 583.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.97–7.92 (m, 2H), 7.70 (d, 2H, *J* = 8.8 Hz), 7.58 (d, 2H, *J* = 8.4 Hz), 7.18–7.12 (m, 2H), 4.64 (t, 1H, *J* = 7.2 Hz), 3.73 (dd, 1H, *J* = 18.0, 6.8 Hz), 3.51 (dd, 1H, *J* = 18.4, 6.8 Hz).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 192.3, 166.3 (d, J = 258.2 Hz), 140.2, 133.0, 131.7, 130.8 (d, J = 9.6 Hz), 128.5, 119.4, 118.0, 116.2 (d, J = 22.1 Hz), 112.6, 43.8, 31.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{11}FN_2ONa^+$ 301.0748; Found 301.0757.

13h:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13h** as a white solid (54.4 mg, 0.20 mmol, 66% yield).

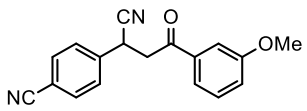
IR (ATR, cm^{-1}): 3097, 3061, 2920, 2246, 2228, 1670, 1362, 1262, 1161, 781, 690.

^1H NMR ($CDCl_3$, 400 MHz): δ 7.74–7.66 (m, 4H), 7.59 (d, 2H, J = 8.0 Hz), 7.42 (d, 1H, J = 7.6 Hz), 7.36 (t, 1H, J = 8.0 Hz), 4.65 (t, 1H, J = 7.2 Hz), 3.74 (dd, 1H, J = 18.0, 6.8 Hz), 3.54 (dd, 1H, J = 18.0, 7.2 Hz), 2.40 (s, 3H).

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 194.0, 140.5, 138.9, 135.3, 135.0, 133.0, 128.8, 128.6, 128.5, 125.3, 119.5, 118.0, 112.6, 43.9, 31.8, 21.3.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2ONa^+$ 297.10; Found 297.0978.

13i:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13i** as a white solid (48.4 mg, 0.17 mmol, 55% yield).

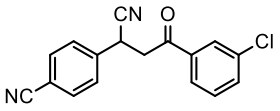
IR (ATR, cm^{-1}): 3084, 3063, 2925, 2838, 2360, 2341, 2224, 1682, 1469, 1431, 1265, 771, 789.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70 (d, 2H, *J* = 8.4 Hz), 7.59 (d, 2H, *J* = 8.0 Hz), 7.49–7.42 (m, 2H), 7.38 (t, 1H, *J* = 8.0 Hz), 7.15 (ddd, 1H, *J* = 8.4, 2.8, 0.8 Hz), 4.65 (t, 1H, *J* = 6.4 Hz), 3.85 (s, 3H), 3.74 (dd, 1H, *J* = 18.0, 7.2 Hz), 3.54 (dd, 1H, *J* = 18.4, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.7, 160.0, 140.4, 136.6, 133.0, 129.9, 128.5, 120.7, 120.6, 119.5, 118.0, 112.6, 112.4, 55.5, 44.0, 31.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2O_2Na^+$ 313.10; Found 313.0935.

13j:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13j** as a white solid (47.7 mg, 0.16 mmol, 54% yield).

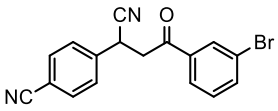
IR (ATR, cm^{-1}): 2232, 1780, 1683, 1572, 1506, 1414, 1248, 786, 730, 678, 570.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (s, 1H), 7.78 (d, 1H, *J* = 7.6 Hz), 7.70 (d, 2H, *J* = 8.4Hz), 7.58 (d, 3H, *J* = 8.4 Hz), 7.43 (t, 1H, *J* = 7.6 Hz), 4.63 (t, 1H, *J* = 7.2 Hz), 3.73 (dd, 1H, *J* = 17.6, 6.8 Hz), 3.52 (dd, 1H, *J* = 18.0, 6.4 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 192.7, 140.1, 136.7, 135.3, 134.1, 133.0, 130.3, 128.5, 128.2, 126.1, 119.3, 117.9, 112.7, 44.0, 31.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{11}ClN_2ONa^+$ 317.0452; Found 317.0450.

13k:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13k** as a white solid (55.7 mg, 0.16 mmol, 56% yield).

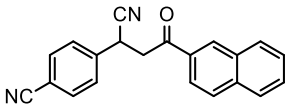
IR (ATR, cm^{-1}): 2229, 1689, 1608, 1566, 1506, 1413, 1247, 1206, 729, 676.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (s, 1H), 7.83 (d, 1H, *J* = 8.0 Hz), 7.74–7.69 (m, 3H), 7.58 (d, 2H, *J* = 8.4 Hz), 7.38–7.34 (m, 1H), 4.63 (t, 1H, *J* = 6.8 Hz), 3.73 (dd, 1H, *J* = 18.0, 7.2 Hz), 3.51 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 192.6, 140.0, 137.0, 136.8, 133.0, 131.1, 130.5, 128.5, 126.5, 123.2, 119.2, 117.9, 112.7, 43.9, 31.8.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{11}BrN_2ONa^+$ 360.9947; Found 360.9955.

13l:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **13l** as a white solid (48.0 mg, 0.15 mmol, 50% yield).

IR (ATR, cm^{-1}): 2227, 1681, 1607, 1504, 1355, 1185, 818, 749, 588, 477.

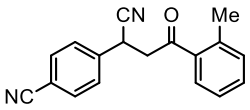
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41 (s, 1H), 7.98–7.87 (m, 4H), 7.70–7.55 (m, 6H), 4.71 (t, 1H, *J* = 6.8 Hz), 3.89 (dd, 1H, *J* = 18.0, 7.2 Hz), 3.69 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 193.8, 140.4, 135.9, 133.0, 132.6, 132.3, 130.1, 129.5, 129.1,

128.9, 128.6, 127.8, 127.2, 123.3, 119.6, 118.0, 112.6, 43.9, 31.9.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{14}N_2ONa^+$ 333.0998; Found 333.1003.

13m:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 3:1) to give **13m** as a white solid (42.8 mg, 0.16 mmol, 52% yield).

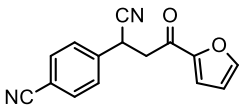
IR (ATR, cm^{-1}): 2955, 2925, 2359, 2228, 1681, 1340, 976, 833, 760, 603, 572.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70 (d, 2H, *J* = 8.8 Hz), 7.62–7.55 (m, 3H), 7.46–7.39 (m, 1H), 7.31–7.23 (m, 2H), 4.63 (t, 1H, *J* = 6.8 Hz), 3.68 (dd, 1H, *J* = 18.0, 7.2 Hz), 3.48 (dd, 1H, *J* = 18.0, 6.8 Hz), 2.49 (s, 3H).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 196.8, 140.4, 139.4, 135.3, 133.0, 132.6, 132.5, 128.7, 128.5, 126.0, 119.5, 118.0, 112.6, 46.1, 32.1, 21.6.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}N_2ONa^+$ 297.0998; Found 297.0995.

13n:



The reaction was carried out following the typical procedure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 2:1) to give **13n** as a white solid (26.8 mg, 0.11 mmol, 35% yield).

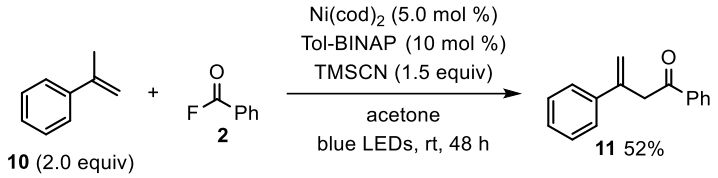
IR (ATR, cm^{-1}): 3340, 2358, 2329, 1666, 1468, 1261, 791.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 (d, 2H, *J* = 8.4 Hz), 7.62–7.55 (m, 3H), 7.27–7.24 (m, 1H), 6.58 (dd, 1H, *J* = 3.6, 1.6 Hz), 4.62 (t, 1H, *J* = 7.6 Hz), 3.61 (dd, 1H, *J* = 17.2, 6.8 Hz), 3.42 (dd, 1H, *J* = 18.0, 6.8 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 182.9, 151.6, 147.2, 140.1, 133.0, 128.5, 119.2, 118.3, 118.0, 112.9, 112.7, 43.3, 31.4.

HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{10}N_2O_2Na^+$ 273.06; Found 276.0616.

■ Typical Procedure for the Photoexcited Nickel-Catalyzed Acyl-Hack Reaction.



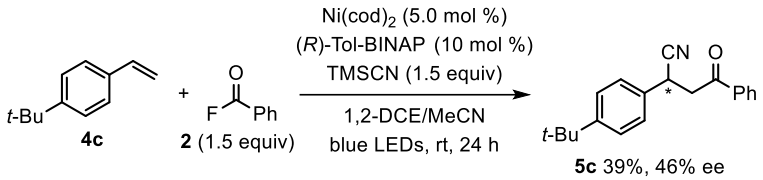
In a nitrogen-filled glove-box, $Ni(cod)_2$ (4.1 mg, 0.015 mmol, 5.0 mol %) and acetone (1.5 mL, 0.20 M) were added to α-methylstyrene (70.9 mg, 0.60 mmol, 2.0 equiv), benzoyl fluoride (37.3 mg, 0.30 mmol, 1.0 equiv), Tol-BINAP (20.4 mg, 0.030 mmol, 10 mol %), and TMSCN (44.6 mg, 0.45 mmol, 1.5 equiv) in an oven-dried 4 mL vial equipped with a stirrer bar. The vial was taken outside the glove-box. The reaction mixture was stirred under blue LEDs (Kessil, 456 nm) irradiation with a fan. After 48 hours, the mixture was passed through a pad of Florisil® with AcOEt. The filtrate was concentrated under reduced pressure. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **11** as a colorless oil (35.0 mg, 0.16 mmol, 52% yield). The analytical data of **11** was matched well with the already reported one.[35] Therefore, only the NMR data are presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02–7.95 (m, 2H), 7.57 (t, 1H, *J* = 7.6 Hz), 7.50–7.38 (m, 4H), 7.35–7.24 (m, 3H), 5.61 (s, 1H), 5.18 (s, 1H), 4.17 (d, 2H, *J* = 0.80 Hz).

^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.7, 141.8, 140.3, 136.6, 133.2, 128.6, 128.4, 127.7, 125.8,

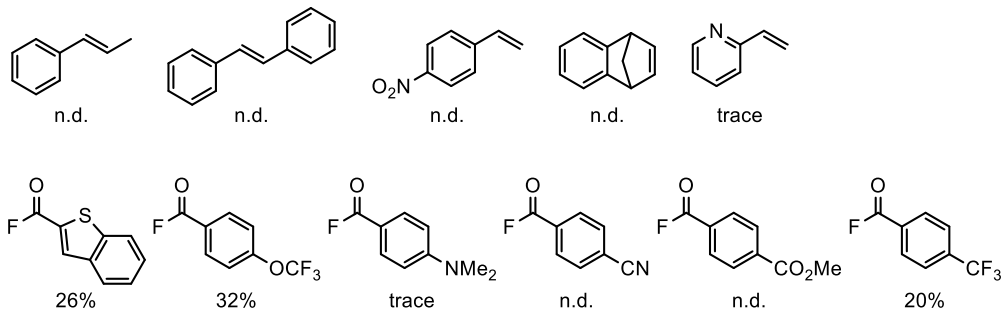
116.5, 45.3.

■ **Asymmetric Acylcyanation of 4-*tert*-butylstyrene.**

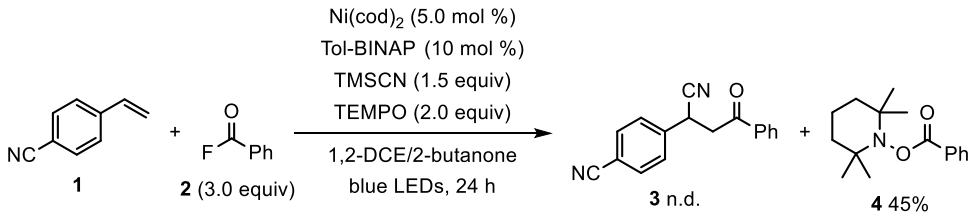


The reaction was carried out on a 0.20 mmol scale using 1.5 equiv of benzoyl fluoride (**2**), (*R*)-Tol-BINAP instead of (*rac*)-Tol-BINAP, and 1,2-DCE/MeCN (1:1, 0.10 M) instead of 1,2-DCE/2-butanone. The reaction time was 24 hours. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 5:1) to give **5c** (22.5 mg, 0.077 mmol, 39%, 46% ee). The *ee* value was determined by chiral HPLC analysis (Daicel Chiralpak IG, hexane/isopropyl alcohol = 90/10, flow rate = 0.6 mL/min, λ = 254 nm), t^1 = 28.4 min (minor), t^2 = 30.8 min (major).

■ **Substrate Scope: Limitation.**

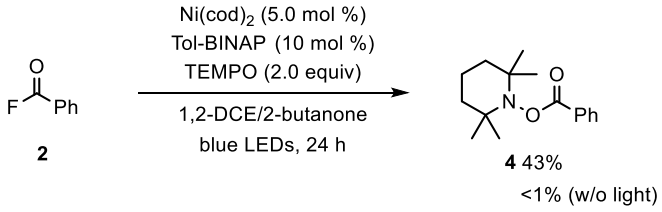


■ **Reactions in the Presence of TEMPO.**



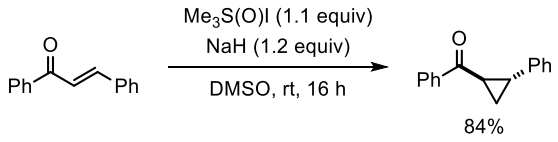
The reaction was carried out with 2.0 equiv of TEMPO on a 0.20 mmol scale. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 20:1) to give **4** as a white solid (47.3 mg, 0.18 mmol, 45% yield based on TEMPO). The analytical data of **4** matched well with the already reported one.[16b] Therefore, only the ^{1}H NMR data was presented here.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.14 (d, 2H, *J* = 7.6 Hz), 7.63 (t, 1H, *J* = 7.2 Hz), 7.52 (t, 2H, *J* = 7.2 Hz), 1.92–1.59 (m, 5H), 1.57–1.48 (m, 1H), 1.34 (s, 6H), 1.18 (s, 6H).

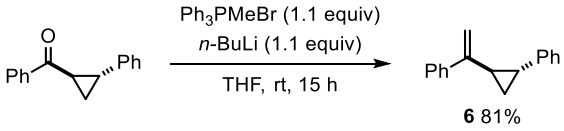


The reaction was carried out on a 0.20 mmol scale. The crude mixture was purified by preparative thin-layer chromatography (hexane/AcOEt = 10:1) and GPC.

■ **Ring-Opening Reaction.**

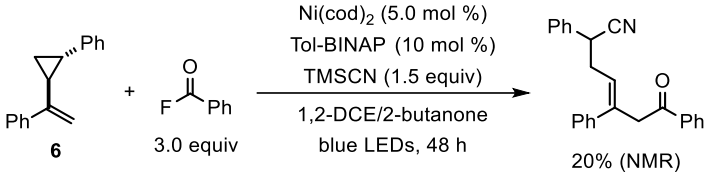


The substrate **6** was prepared according to the literature procedure.[14a,36] To an oven-dried 50mL two-necked round-bottom flask equipped with a stirrer bar were added sodium hydride (60% in oil, 12 mmol, 1.2 equiv), trimethylsulfoxonium iodide (11 mmol, 1.1 equiv), and DMSO (18 mL). After stirring at room temperature for 1 hour, the flask was cooled to 0 °C and a solution of chalcone (10 mmol, 1.0 equiv) in DMSO (5.0 mL) was added. The mixture was stirred at room temperature. After 16 hours, H_2O was added to the mixture and the mixture was extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 10:1) to give the product in 84% yield.



To an oven-dried 100mL two-necked round-bottom flask equipped with a stirrer bar were added Ph_3PMeBr (9.2 mmol, 1.1 equiv) and THF (30 mL). Then *n*-BuLi (1.6 M in hexane, 9.2 mmol, 1.1 equiv) was added to the mixture at -78 °C, and the substrate (8.4 mmol, 1.0 equiv) in THF (12 mL) was added dropwise at 0 °C. After stirring at room temperature for 16 hours, saturated aqueous solution of NH_4Cl was added to the mixture and the mixture was extracted with AcOEt × 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 20:1) to give **6** in 81% yield. The analytical data of **6** matched

well with the reported one.



The ring-opening reaction was carried out according to the typical procedure. The crude mixture was analyzed by ^{1}H NMR using 1,1,2,2-tetrabromoethane as an internal standard. The analytical data of the ring-opening product matched well with the already reported one.[14a]

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Chapter 6

Summary of This Dissertation

Single-electron transfer by transition metal catalysts is a useful tool to generate various radical ions, and numerous chemical transformations based on it have been reported. Synthetic methods *via* SET by transition metal catalysts are attracting attention by researchers in order to achieve difficult transformation under mild conditions. The research reported in this dissertation focused on the development of useful chemical transformations and new catalytic systems using single-electron transfer by transition metal catalysts.

In Chapter 2, the copper-catalyzed aminoalkoxylation of alkylarenes *via* formal double C(sp^3)–H functionalization was described. The reaction proceeded in three steps. (1) Copper-catalyzed benzylic alkoxylation of ethylarenes; (2) The elimination of the alkoxy group from resulting benzylic alcohols to give vinylarenes; (3) Copper-catalyzed aminoalkoxylation of the intermediary vinylarenes to give arylethanolamines. *N*-centered radicals generated *via* single-electron transfer from the copper(I) catalyst to *N*-fluorobenzenesulfonimide acted as hydrogen-absorbing reagents and amination reagents. This method presents a new strategy to synthesize valuable molecules from alkylarenes, which are cheaper and more readily available than vinylarenes.

In Chapter 3, the development of the new copper(II) photoredox catalyst and its application to *anti*-Markovnikov hydration of vinylarenes were described. The copper(II) photoredox catalyst exhibited a strong oxidizing ability, so the photoexcited catalyst could oxidize vinylarenes to generate their radical cations *via* single-electron transfer. Direct addition of H_2O to the resulting radical cations gave the product. This is the first example of a bimolecular quenching of photoexcited copper(II) complexes. This work provides deep insight for the development of photoredox catalysts using inexpensive and earth-abundant first-row transition metals.

In Chapter 4, the photoexcited palladium catalyzed Suzuki-Miyaura cross-coupling reaction of α-chlorocarbonyl compounds with arylboronic acids. Single-electron reduction of α-

chlorocarbonyl compounds by photoexcited palladium catalyst enabled the formal oxidative addition of the chlorides, less reactive than bromides and iodides. The catalytic cycle consisted of single-electron and two-electron processes. This work offered easy access to bioactive α-arylacetic acid derivatives from readily available α-chlorocarbonyl compounds for the coupling reaction under mild conditions.

In Chapter 5, the photoexcited nickel-catalyzed acylcyanation of vinylarenes with acyl fluorides and TMSCN was described. The oxidative quenching of the photoexcited nickel(0) catalyst generates acyl radicals from acyl fluorides. The resulting acyl radicals added to vinylarenes to generate benzylic radicals, and the formation of C–CN bond at the benzylic positions gave the product. Photoexcited nickel catalysis is still an under-researched area, so this work helps deep understanding of the photoreactivity of nickel complexes.

Through this dissertation based on single-electron transfer by transition metal catalysts, the author developed practical synthetic methods using readily available starting materials, and new catalysis to generate radicals using earth-abundant transition metals, such as copper and nickel. These studies reiterate the value of synthetic methods using transition metal-catalyzed single-electron transfer processes and are crucial for the establishment of sustainable synthetic chemistry. The author wishes the discovery he made would benefit the further progress of fine organic synthesis.

List of Publications

Chapter 2:

"Cu-Catalyzed Double C(sp^3)–H Functionalization of Ethylarenes to Form Arylethanolamines"

Naoki Oku and Tomoya Miura. *J. Org. Chem.* **2023**, *88*, 7592–7596.

Chapter 3:

"Copper Photoredox Catalyst Exhibiting Strong Oxidizing Ability for *anti*-Markovnikov Hydration"

Naoki Oku, Keito Fuke, Ken Yamazaki, Yasunori Matsui, Hiroshi Ikeda, and Tomoya Miura. *Manuscript in preparation.*

Chapter 4:

"Photoassisted Cross-Coupling Reaction of α-Chlorocarbonyl Compounds with Arylboronic Acids"

Naoki Oku, Masahiro Murakami, and Tomoya Miura. *Org. Lett.* **2022**, *24*, 1616–1619.

Chapter 5:

"Photoinduced Nickel-Catalyzed Acylcyanation of Vinylarenes with Acyl Fluorides and TMSCN"

Naoki Oku, Reo Saeki, Yuriko Doi, and Tomoya Miura. *Manuscript in preparation.*

Other publications:

"Diastereo- and Enantioselective Synthesis of (*E*)-δ-Boryl-Substituted *anti*-Homoallylic Alcohols in Two Steps from Terminal Alkynes"

Tomoya Miura, Naoki Oku, and Masahiro Murakami. *Angew. Chem. Int. Ed.* **2019**, *58*, 14620–14624.

"**Regioselective 1,3-Dipolar Cycloaddition of Nitriles with Nitrile Imines Generated from Tetrazoles**"

Tomoya Miura, Kohei Hagiwara, Takayuki Nakamuro, Yuuya Nagata, Naoki Oku, and Masahiro Murakami. *Chem. Lett.* **2021**, *50*, 131–135.

"Stereo- and Enantioselective Synthesis of Propionate-Derived Trisubstituted Alkene Motifs"

Tomoya Miura, Naoki Oku, Yota Shiratori, Yuuya Nagata, and Masahiro Murakami. *Chem. Eur. J.* **2021**, *27*, 3861–3868.

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