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# Metal-to-Ligand Ratio-Dependent Chemodivergent Asymmetric Synthesis

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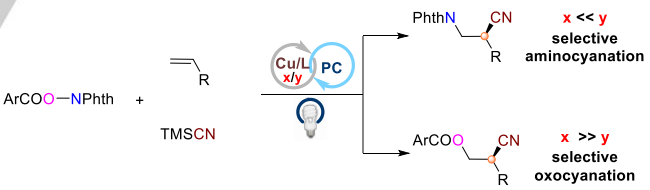
**Abstract:** The metal-to-ligand ratio is an important variable in the field of asymmetric organometallic catalysis. An unsuitable metal-to-ligand ratio can reduce the catalytic activity and/or the asymmetric induction. Herein, we report a chemodivergent asymmetric synthesis achieved by tuning the metal-to-ligand ratio in an organometallic catalytic system. Using N-(aroyloxy)phthalimide as the precursor of either an oxygen-centered aroyloxy radical or a nitrogen-centered phthalimidyl radical, enantioselective oxocyanation or aminocyanation of alkenes was achieved separately through a dual photoredox and copper catalysis. It was found that the metal-to-ligand ratio can exert chemoselective control while retaining the high enantiopurity of divergent products. In addition to tolerating many functional groups and working well with a wide range of alkenes, both reactions proceed efficiently with catalyst loading as low as 0.2 mol% and can be performed on a gram scale without loss of chemoselectivity or enantioselectivity. Chemodivergent asymmetric 1,5-aminocyanation or 1,5-oxocyanation of vinylcyclopropane can also be realized by this protocol. Mechanistic investigations involving electron paramagnetic resonance (EPR) experiments were performed to shed light on the stereochemical and chemodivergent results. The reactions deliver a diverse range of optically active compounds and also provide a new scenario which allows optimization of the reaction conditions in asymmetric organometallic catalysis.

## Introduction

Organometallic catalysts are important in both academic and industrial chemistry[1] and can improve reaction efficiency, tune reaction selectivity and facilitate new reaction pathways with fundamentally different mechanisms. The metal itself is often the focus of a catalytic reaction, but the ligand is also a key factor which controls the reactivity and selectivity, especially in asymmetric catalysis.[2] The metal-to-ligand ratio in such situations is an important variable and its optimization is normally pursued in the field of asymmetric catalysis.[3] Excess ligand occupies the reactive site of the metal center and can reduce the catalytic activity. On the other hand extra metal is generally avoided since the background reaction and side reactions can be induced by a ligand-free metal, leading to low enantioselectivity and yield. Consequently, a slight excess of ligand is generally used to facilitate the reactivity and enantioselectivity in asymmetric catalysis.[2]

Because compounds containing oxygen and/or nitrogen are common in biologically active molecules and functional materials, the development of novel synthetic methods and strategies involving the construction of C−N and C−O bonds is the focus of intense research efforts. Radical reactions have been going through a renaissance due to their distinctive selectivity, high reactivity and functional group tolerance,[4] and are being used increasingly as conventional synthetic tools, complementary to ionic reactions.[5] In this context, N-centered radicals are often considered to be irreplaceable intermediates in the construction of C−N bonds.[6] Progress involving N-centered radicals however is slow when compared with carbon-centered radicals because of a dearth of convenient access to them and a lack of awareness of their reactivity.[7] Compared with N-centered radicals whose reactivity can be modified by two substituent groups, O-centered radicals, such as alkyloxy[8] and acroyloxy[9] radicals are more electrophilic and reactive, and this leads to difficulties in controlling their reaction selectivity.[10] The construction of C–O bonds based on O-centered radicals has been less explored and the development of a general method for intermolecular asymmetric reactions involved O-centered radicals remains an major challenge.




**Scheme 1.** Metal-to-ligand ratio-dependent chemodivergent asymmetric synthesis (this work).

The difunctionalization of alkenes involving heteroatom-centered radicals is one of most important methods to construct heteroatom-containing compounds.[11] The regioselectivity of these reactions generally follows the anti-Markovnikov rule,[12] and complements the ion chemistry which follows the Markovnikov rule. In this report, we disclose a metal-to-ligand ratio-dependent generation of either an O-centered aroyloxy radical or an N-centered phthalimidyl radical from *N*-(aroyloxy)-phthalimides ($ArCO_2NPhth$) *via* merged copper and photoredox catalysis,[13,14] leading to enantioselective oxocyanation and aminocyanation of alkenes respectively (Scheme 1). The most important factor controlling the chemoselectivity of the reaction is

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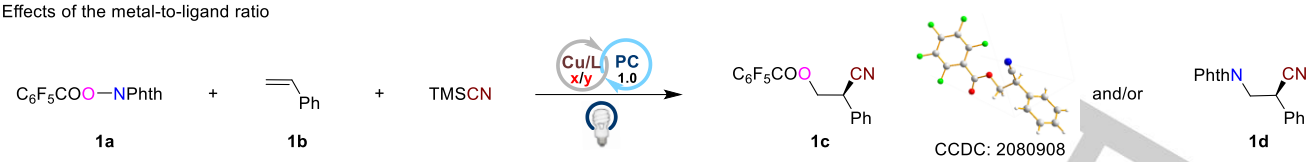
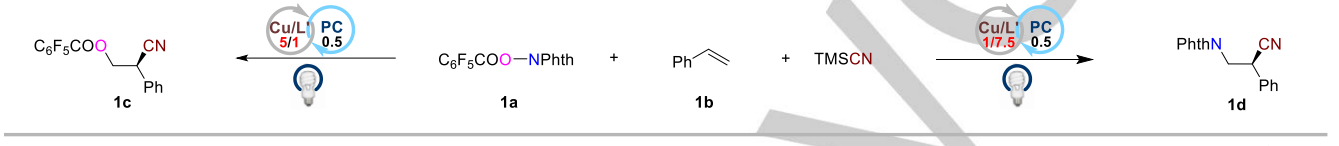
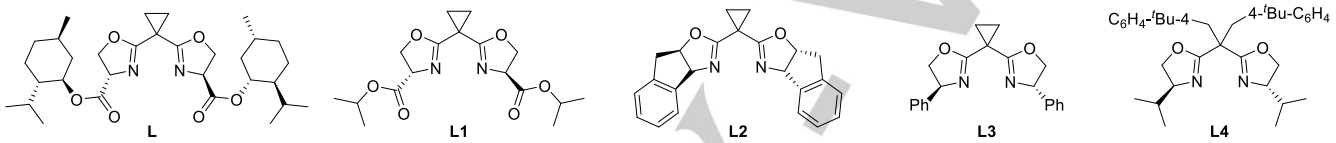
**A.** Effects of the metal-to-ligand ratio




| Entry | 1 | 2 | 3 | 4 | 5[a,b] | 6 | 7 | 8 | 9[b] |
|---|---|---|---|---|---|---|---|---|---|
| **x** (mol%)/**y** (mol%) | **1/1** | 2/1 | 5/1 | 7/1 | **5/1** | 1/2 | 1/5 | 1/7.5 | **1/7.5** |
| $CH_3CN$ (mL) | 7 | 7 | 7 | 7 | **2** | 7 | 7 | 7 | **7** |
| yield (**1c** + **1d**) | **68%** | 77% | 84% | 83% | **83%**[c] | 62% | 62% | 62% | **59%**[d] |
| **1c**/**1d** | **1/2.1** | 1.1/1 | 3.9/1 | 5.4/1 | **> 14/1** | 1/5.0 | 1/6.9 | 1/20 | **< 1/20** |
| ee (**1c**)\|ee (**1d**) | **95%\|83%** | 95%\|85% | 95%\|84% | 95%\|85% | **96%\|--** | 97%\|87% | 97%\|87% | --\|90% | **--\|91%** |

**B.** Effects of the ligand **L'**




**1c**, 83%y,[a,c] > 14/1,[e] 96% ee; **1d**, 59%y,[d] < 1/20,[e] 91% ee

**1c**, 80%y,[a,c] > 14/1,[e] 90% ee; **1d**, 60%y,[d] < 1/20,[e] 77% ee

**1c**, 77%y,[a,c] > 14/1,[e] 81% ee; **1d**, 60%y,[d] < 1/20,[e] 65% ee

**1c**, 72%y,[a,c] > 14/1,[e] 80% ee; **1d**, 55%y,[d] < 1/20,[e] 67% ee

**1c**, 44%y,[a,c] > 14/1,[e] 82% ee; **1d**, messy

Reaction conditions: **1a** (0.2 mmol), **1b** (0.5 mmol), TMSCN (0.3 mmol), $Cu(CH_3CN)_4BF_4$ (x mol%), **L** (y mol%), PC (3DPA2FBN, 2,4,6-Tris(diphenylamino)-3,5-difluorobenzonitrile, 1.0 mol%), $CH_3CN$ (7 mL), blue LEDs (24 W), Argon, at 5 °C, 12 h. Yield determined by crude NMR with $CH_2Br_2$ as an internal standard. Ee values were determined by HPLC on a chiral stationary phase. [a] $CH_3CN$ (2 mL). [b] PC (0.5 mol%). [c] Isolated yield of **1c**. [d] Isolated yield of **1d**. [e] Ratio of **1c**/**1d**.

**Scheme 2.** Reaction discovery and optimizing conditions

indeed the metal-to-ligand ratio which, if tuned, can provide a straightforward chemodivergent asymmetric synthetic route.[15]

## Results and Discussion

The limited number of easily accessible, suitable reactive and reliable radicals is a major issue which has limited the development of radical chemistry.[4,5] Recently, because of the mild reaction conditions involved, radicals generated from visible-light induced single electron reduction of redox activated esters such as N-hydroxyphthalimide esters (NHP esters, N-(acyloxy)phthalimides) have received more attention.[16] The reduction of aliphatic NHP esters generates alkoyloxy radical intermediates which decompose to alkyl radicals through an intrinsic decarboxylation process, leading to a series of alkylation reactions.[17] Using NHP esters derived from pentafluorophenyl or trifluoromethyl carboxylic acids, the reduction reactions result in a phthalimidyl radical, which can lead to radical amination processes.[18] The generation of acroyloxy or phthalimidyl radicals is determined by the relative electronegativity of the acroyloxy segment and the phthalimidyl fragment, and this limits the production of target radicals or requires the preparations of well-designed NHP esters. In the other hand, Liu et al.[19] and other groups[20] recently developed a series of elegant copper-catalyzed asymmetric radical cyanation reactions.[21] The optically pure organonitriles that are obtained are present in many bioactive compounds and therapeutic agents[22] but can also be easily transformed to other useful functional groups.[23] The aromatic NHP ester (*N*-(aroyloxy)-phthalimide, $ArCO_2NPhth$) **1a** derived from pentafluorophenyl carboxylic acid was initially selected as an amino radical source for the development of radical-involved asymmetric 1,2-aminocyanation of alkenes shown in Scheme 2 (for details of the optimization, see Table S1 in Supporting Information-SI).[24] The reaction was first performed with a copper to ligand **L** ratio of 1/1 and photoredox catalysis (Scheme 2A, entry 1). The oxocyanation product **1c** was obtained together with the desired aminocyanation product **1d**, suggesting that both the aroyloxy radical and the phthalimidyl radical may be present under the reaction conditions. This result conflicts with the report that under visible-light photocatalysis, **1a** generates a phthalimidyl radical exclusively.[17e] Interestingly, upon increasing the loading of copper from 1 mol% to 7 mol% and maintaining the loading of **L** at 1 mol%, the ratio of **1c**/**1d** was increased to 5.4/1 (entries 2-4). Upon reducing the volume of the solvent from 7 mL to 2 mL and loading of the photocatalyst (PC) from 1 mol% to 0.5 mol%, the **1c**/**1d** ratio reached 14/1 and **1c** could be isolated in 83% yield

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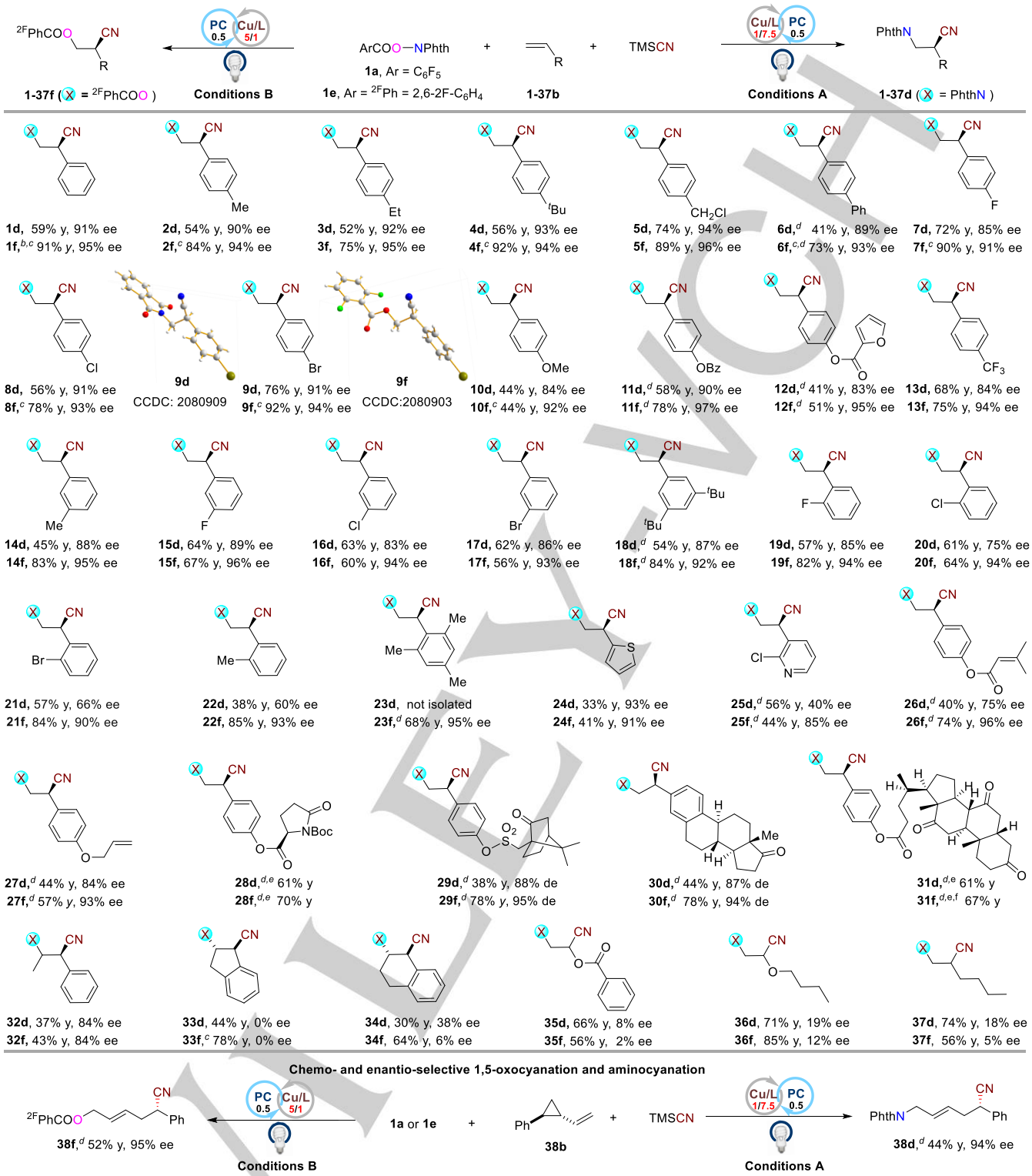


[a] Conditions A: **1a** (0.2 mmol), alkene **1-38b** (0.5 mmol), TMSCN (0.3 mmol), $CH_3CN$ (7 mL), PC (3DPA2FBN, 0.5 mol%), $Cu(CH_3CN)_4BF_4$ (1 mol%) and **L** (7.5 mol%), irradiated by blue LEDs (24 W) at 5 °C for 12 h. Conditions B: **1e** (0.2 mmol), alkene **1-38b** (0.5 mmol), TMSCN (0.3 mmol), $CH_3CN$ (2 mL), PC (3DPA2FBN, 0.5 mol%), $Cu(CH_3CN)_4BF_4$ (5 mol%) and **L** (1 mol%), irradiated by blue LEDs (24 W) at 5 °C for 12 h. The isolated yield of the single isomer product, and ee and de values were determined by HPLC on a chiral stationary phase. See SI for experimental details. [b] The **1f**/**1d** ratio is 29/1, which is determined by $^1H$ NMR of the reaction mixture. [c] The reaction was conducted in 2.0 mmol scale of **1a** or **1e**. [d] With 1.5 equiv of olefin **b**. [e] Ee or de were not determined. [f] $CH_3CN$ (5 mL).

**Scheme 3**. Scope of oxocyanation and aminocyanation reactions[a]

with 96% ee (entry 5). The **1c**/**1d** ratio was decreased when increasing the loading of ligand **L** (entries 6-8). When **L** was used at 7.5 mol% (entries 8 and 9), the oxocyanation product **1c** was essentially absent and the aminocyanation product **1d** was isolated with 59% yield and 91% ee (entry 9). Excess ligand or excess copper failed to influence the high enantioselectivity but controlled the chemoselectivity significantly. Several control experiments were performed (Table S1 in SI). In absence of light, photocatalyst or copper, no desired products were achieved from either of the aminocyanation and oxocyanation reactions. Without the assistance of a ligand, only the oxocyanation product **1c** could be obtained, in 25% yield. In the optimization of reaction conditions, aryl C–H amination products N-(4-vinylphenyl)-phthalimide and N-(2-vinylphenyl)-phthalimide were observed as major side products in the aminocyanation reaction (Table S2 in SI). Different NHP esters ($ArCO_2NPhth$) derived from 3,5-ditrifluoromethylphenyl, 4-fluorophenyl, 2,6-dichlorophenyl, 4-trifluoromethylphenyl, and phenyl carboxylic acid were examined (Table S3 in SI). The chemoselective oxocyanation products were achieved exclusively with good to high yield (48-89%) under conditions B, and the chemoselectivities of the reactions under conditions A varied, depending on the aryl structure. Several Box ligands were investigated, giving the selected results in Scheme 2B (for details of screening ligands, see Table S4 in SI) and it was found that the new serine-derived bisoxazoline ligand **L** whose design was based on the Song's research[25] is the best ligand in both the aminocyanation and oxocyanation reactions. The ester group in the serine-derived BOX scaffold can further stabilize the copper species and increase the rigidity of the transition state,[25] which may improve the efficiency and enantioselectivity in both the aminocyanation and oxocyanation reactions (Table S4 in SI).

With the optimal reaction conditions in hand, the scope of alkenes was explored under conditions A with excess ligand, or conditions B with excess copper (Scheme 3). Because the pentafluorophenyl carboxylic acid derived product **1c** decomposed easily to 2-phenylacrylonitrile during the purification, the 2,6-difluorophenyl carboxylic acid derived NHP ester **1e** was used in place of **1a** when exploring the substrate scope of the oxocyanation reactions. The reaction of **1e** with styrene under conditions B could produce the desired oxocyanation product **1f** with high yield (91%), high enantioselectivity (95% ee) and high chemoselectivity (**1f**/**1d**, 29/1). Neither electron-rich or electron-deficient substituents in the *para*- and/or the *meta*-position of styrene influenced the reactions. Both aminocyanation products (**1-18d**, 42-76% yield, 83-94% ee) and those from oxocyanation (**1-18f**, 44-92% yield, 92-96% ee) were formed in good yields and with high enantioselectivities. In the reactions of compounds with an *ortho*-halogen, such as fluoro, chloro or bromo substituted styrenes, the aminocyanation products were produced with moderate enantioselectivities (**19-21d,** 57-61% yield, 67-85% ee) and oxocyanation products were formed with high enantio-selectivities (**19-21f**, 90-94% ee) and isolated in 64-84% yield. Since the N-centered radical is a less electrophilic and reactive species than an O-centered radical, sterically hindered substrates might be not suitable for the aminocyanation reaction. With *ortho*-methyl or *ortho*-dimethyl styrenes as examples, the reactions produced the oxocyanation products with good yields and high enantioselectivities (**22f**, 85% yield, 93% ee; **23f**, 68% yield, 95% ee) but little or no aminocyanation products (**22d**, 38% yield; **23d**, yield undetermined) were obtained. In addition to the styrene derivatives, heteroaryl alkenes, such as 2-vinylthiophene and 2-chloro-3-vinylpyridine were suitable substrates for both the aminocyanation (**24d**, 33% yield, 93% ee; **25d**, 56% yield, 40% ee) and the oxocyanation reactions (**24f**, 41% yield, 91% ee; **25f**, 44% yield, 85% ee). Various functional groups, such as alkyl (**2b**, **3b**, **4b**, **14b**, **18b**, **22b**, **23b**), chloromethyl (**5b**), phenyl (**6b**), fluoro (**7b**, **15b**, **19b**), chloro (**8b**, **16b**, **20b**), bromo (**9b**, **17b**, **21b**), alkoxy (**10b**), aryloxyl (**11b**, **12b**) and trifluoromethyl (**13b**) are tolerated. For substrates containing additional olefinic groups such as acryl (**26b**) or alkyl alkenyl (**27b**) groups, both aminocyanation (**26d**, 40% yield, 75% ee; **27d** 44% yield, 84% ee) and oxocyanation (**26f**, 74% yield, 96% ee; **27f**, 57% yield, 93% ee) of aryl olefins could be achieved selectively. The vinylbenzenes derived from natural products such as an α-amino acid (**28b**), camphorsulfonic acid (**29b**), estrone (**30b**) or dehydrocholic acid (**31b**) went through the chemodivergent asymmetric process smoothly, and both the aminocyanation (**28-31d**, 38-61% yield) and oxocyanation products (**28-31f**, 64-78% yield) were isolated with high diastereoselectivity, indicating that this protocol may have significant potential in late stage functional group transformations. In the reaction of *β*-methyl styrene (**32b**), a single diastereomeric product (**32d**, 37% yield, 84% ee; **32f**, 43% yield, 84% ee) could be isolated with moderate yields and enantioselectivities. When cyclic 1,2-disubstituted alkenes, such as indene (**33b**) and 1,2-dihydronaphthalene (**34b**) were used as substrates, both the aminocyanation (**33d**, 44% yield; **34d**, 30% yield) and oxocyanation products (**33f,** 78% yield; **34f**, 64% yield) were isolated but with little or no enantioselectivity. Other type of alkenes, such as vinyl ethers (**35**-**36b**) and unactivated alkyl alkenes (**37b**) were also adequate substrates, providing the desired aminocyanation (**35-37d**, 66-74% yield) and oxocyanation (**35-37f**, 56-85% yield) products in reasonable yields although with no or low enantioselectivity. Asymmetric 1,5-bifunctionalization still remains a challenge.[26] Recently, Wang et al. reported enantioselective 1,5-cyanotrifluoromethylation of vinylcyclo-propanes, which afforded easy access to useful chiral allyl nitriles.[27] Inspired by these reactions, the radical probe vinylcyclopropane **38b** was used as a substrate. The desired 1,5-aminocyanation product (**38d**, 44% yield, 94% ee) and the 1,5-oxocyanation product (**38f**, 52% yield, 95% ee) were obtained with high enantioselectivity under either conditions A or B. The allyl amine or allyl alcohol substructures are common in bioactive compounds and are frequently used as synthetic building blocks in organic synthesis. The chiral center present in the allylic position increases the utility of these allyl amines and allyl alcohol. The absolute configurations of typical products were confirmed by X-ray crystallographic analysis.[28]

Several experiments were performed in an effort to further understand the reaction mechanism (Scheme 4 and Figures S1-S2 in SI). Quenching experiments were performed and are shown in Figure S1. The fluorescence of PC (3DPA2FBN) was not quenched by either TMSCN, styrene, TMSOTf, $Cu(MeCN)_4BF_4$[29] or a mixture of $Cu(MeCN)_4BF_4$ and the ligand **L**. In contrast, the fluorescence was quenched by **1a** or a mixture of **1a** and TMSOTf with defined Stern–Volmer kinetics. Under conditions B, the side product TMSNPhth was detected by both GCMS and HRMS (Figure S2 in SI). Electron paramagnetic resonance (EPR) spectra were recorded using 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) for spin trapping (Scheme 4A).

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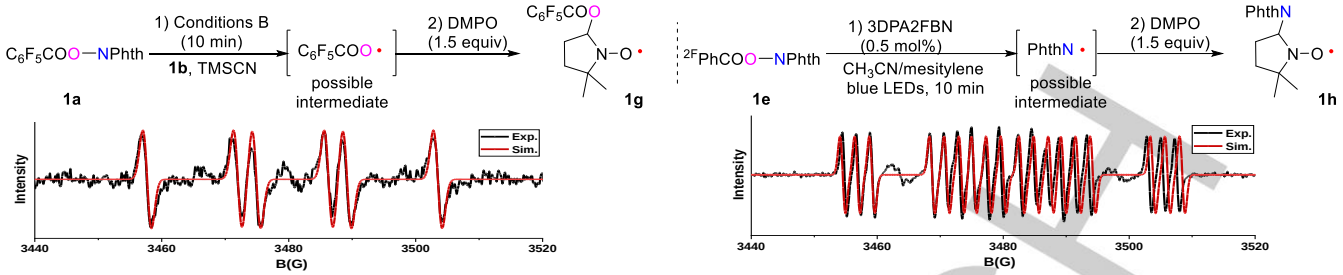
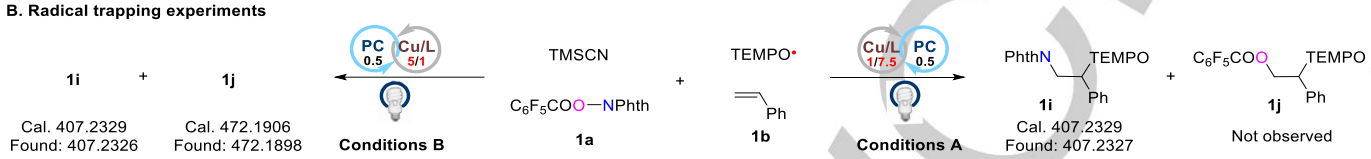
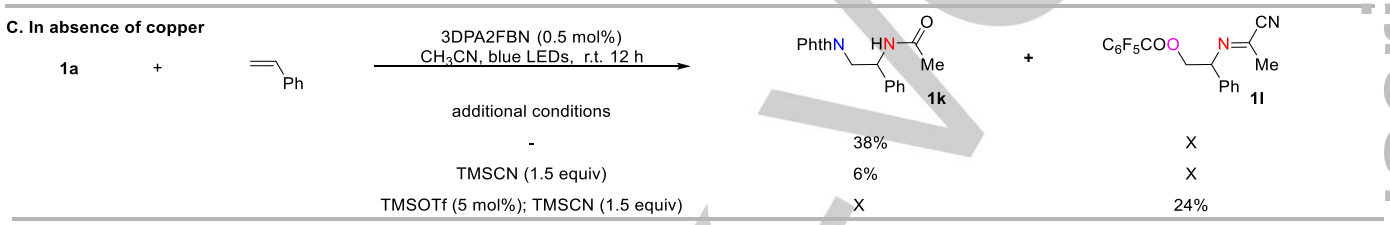
**A. EPR experiments**




**B. Radical trapping experiments**

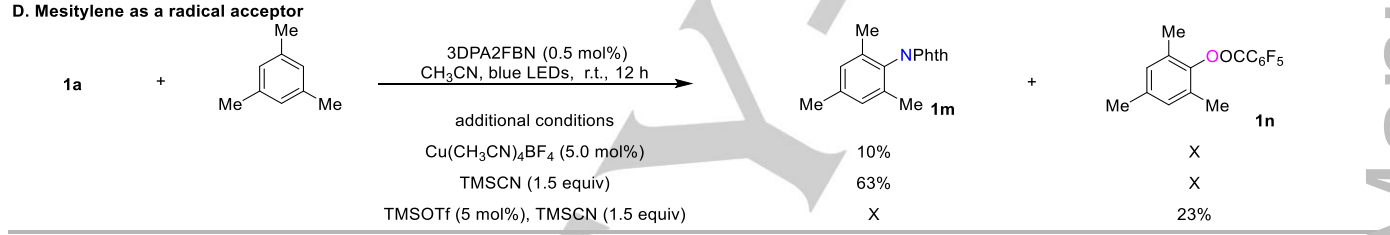



**C. In absence of copper**



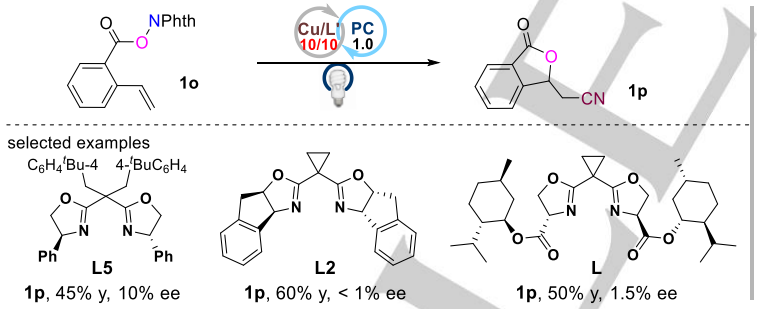

| additional conditions | 1k | 1l |
|---|---|---|
| - | 38% | X |
| TMSCN (1.5 equiv) | 6% | X |
| TMSOTf (5 mol%); TMSCN (1.5 equiv) | X | 24% |

**D. Mesitylene as a radical acceptor**

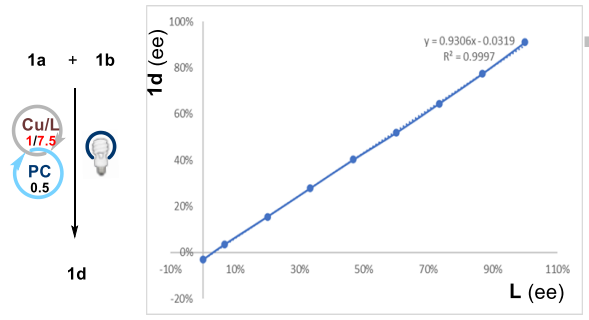



| additional conditions | 1m | 1n |
|---|---|---|
| $Cu(CH_3CN)_4BF_4$ (5.0 mol%) | 10% | X |
| TMSCN (1.5 equiv) | 63% | X |
| TMSOTf (5 mol%), TMSCN (1.5 equiv) | X | 23% |

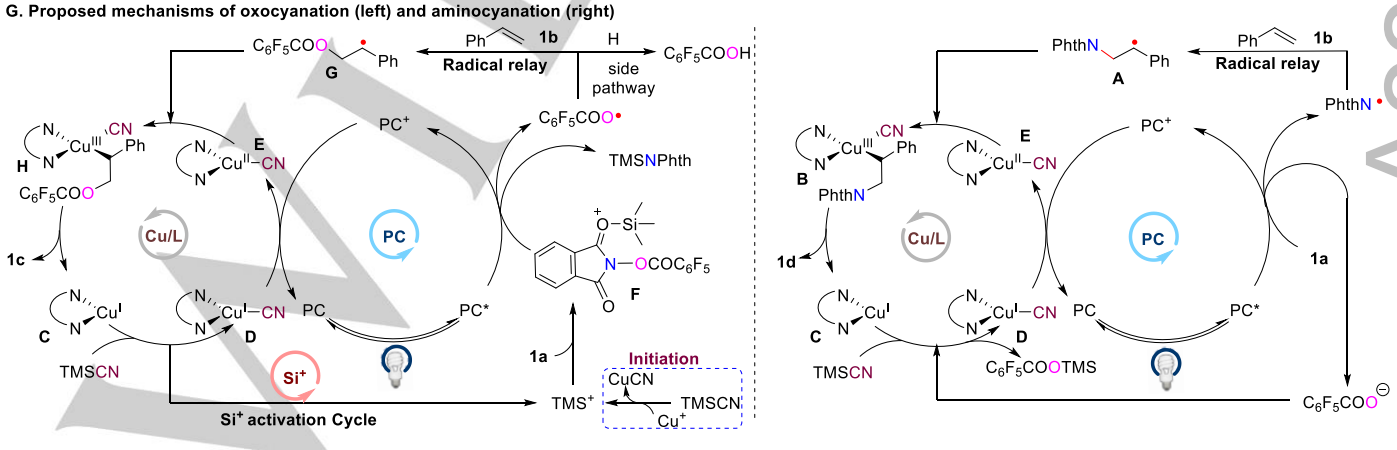
**E. Intramolecular reaction**




**F. Non-linear effect investigation**




**G. Proposed mechanisms of oxocyanation (left) and aminocyanation (right)**




**Scheme 4.** Mechanistic studies

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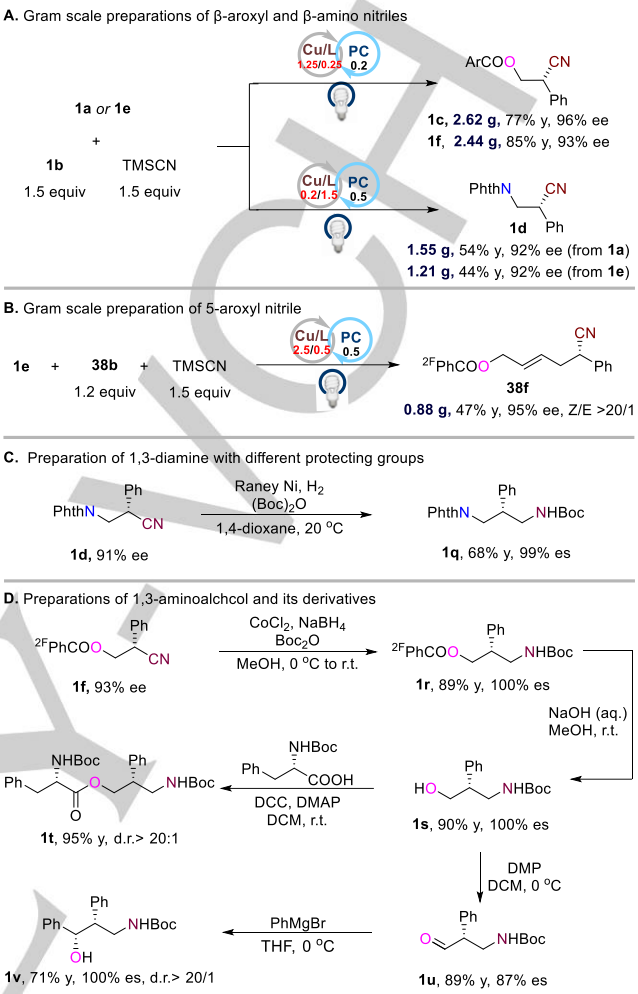
In the reaction of **1a** under conditions B, formation of the DMPO-spin adduct **1g** indicates that benzoyloxyl radical was selectively generated.[30] In the reaction of **1e** in the absence of copper and TMSCN, the resulting spectra showed that the DMPO-spin adduct **1h** is consistent with the trapping of the phthalimidyl radical. The radical trapping reactions of **1a** were performed using TEMPO as a radical scavenger (Scheme 4B). Both two catalytic reactions were inhibited by TEMPO, no **1c** and **1d** being observed by TLC and $^1$H NMR spectra. The TEMPO captured products **1i** and **1j** were detected by HRMS under the conditions B, and only **1i** was observed under conditions A. This agrees with the observation that almost no oxocyanation product **1c** was produced in the reaction of the NHP ester **1a** with styrene (Scheme 2A, entry 9). When the reaction was performed under the photoredox conditions in the presence or absence of TMSCN (Scheme 4C), the side diamination product **1k** (38% and 6% respectively) was obtained and is believed to have been produced from the cascade phthalimidyl radical addition to styrene and a Ritter type reaction. It is known that proton[31] or boron reagents[32] can drive photoinduced electron transfer between photoexcited catalysts and aliphatic NHP esters, and thus the cations present in this reaction system may play a role similar to that of the proton or boron reagents. Consequently, a catalytic amount of TMSOTf was added to the photoredox reaction and a 1,2-hydroxylamino product **1l** was isolated but the alternative product **1k** was not observed. Compound **1l** was thought to be produced from a Ritter type reaction involving benzoyloxyl radical. When the reaction was performed under conditions A with an additional 2.5 mol% of TMSOTf, both the oxocyanation product **1c** (18%) and the aminocyanation product **1d** (43%) were observed. The reaction (entry 1 in Scheme 2A, metal/ligand = 1/1, total yield 68%, **1c**/**1d** = 1/2.1) with an additional 10 mol% of potassium phthalate, as a sacrificial Lewis base to capture $TMS^+$, was performed, no oxocyanation product **1c** was observed and the aminocyanation product **1d** was achieved in 41% yield. When mesitylene was used in place of styrene as the radical acceptor (Scheme 4D). Under the photoredox conditions in the presence of copper or TMSCN, the amination product **1m** which is thought to originate from phthalimidyl radical, was formed. In contrast, the acetoxylated product **1n** was isolated in the presence of a catalytic amount of TMSOTf while formation of **1m** was not observed. Thus, the evidence for the selective formation of benzoyloxyl radical and phthalimidyl radical respectively under different metal-to-ligand ratios appears strong. These results also indicate that $TMS^+$ plays a key role in the formation of the benzoyloxyl radical. Only the phthalimidyl radical was formed in the absence of $TMS^+$. The aminocyanation and oxocyanation products **33** and **34** from the reactions of cyclic 1,2-disubstituted alkenes are racemic or minimally enantiomeric (Scheme 3). To further understand the stereochemical outcomes of the reaction, the substrate **1o** was designed for intramolecular oxocyanation reactions with different ligands (Scheme 4E, see details in Table S5 in SI), and led to the desired product **1p** which was formed with moderate yield and almost no enantioselectivity (< 10% ee). These results suggest that there is almost no asymmetric induction during the formation of C−O or C−N bonds. The ee values of the aminocyanation and oxocyanation products were almost unchanged when altering the metal/ligand ratio from 1/7 to 7.5/1 (Scheme 2A). Furthermore, the ee of the chiral ligand **L** is proportional to that of the product **1d** under the conditions which used an excess of **L** (Scheme 4F), indicating that the progress of the reaction depends on a metal-to-ligand (1/1 ratio) species.[33]




**Scheme 5.** Synthetic applications

Based on our experiments and earlier reports[20, 34], a proposed mechanism was developed and is shown in Scheme 4G. Under the conditions B with excess ligand (right cycle), the direct oxidative quenching of the excited photocatalyst furnishes a phthalimidyl radical which adds to the styrene to form a radical intermediate **A**. The addition reaction of **A** with the ligand/$Cu^{II}$(CN) complex **E** furnishes the high valent Cu(III) species **B**. Reductive elimination of **B** yields the desired aminocyanation product **1d**. Under conditions A with excess $Cu^+$ (left cycle), the reaction of excess $Cu^+$ and TMSCN initially generates the $TMS^+$ ion which may coordinate with the carbonyl group of **1a** to form the complex **F**, thus supporting an increased positive charge in the phthalimidyl group. SET reduction of complex **F** generates an aroyloxy radical which leads to the final oxocyanation reaction. The $TMS^+$ ion can be regenerated from the reaction of the ligand/$Cu^+$ complex species **C** with TMSCN, completing the $Si^+$ activation cycle.[35] Since an oxygen-centered radical is a very reactive species which could abstract a hydrogen atom from the reaction system as a side reaction pathway,[9] increasing the concentration of the reaction benefits the desired intermolecular radical oxocyanation reaction (entry 4 *vs* 5, Scheme 2A).

We studied the synthetic applications of the reactions (Scheme 5). When gram scale preparations are conducted in the oxocyanation reactions, the load of catalyst can be further reduced to 1.25 mol% of copper, 0.25 mol% of ligand **L** and 0.2 mol% of the photocatalyst 3DPA2FBN (Scheme 5A), providing the β-aroxyl nitriles **1c** (2.62 g, 77% yield, 96% ee, from **1a**) and **1f** (2.44 g, 85% yield, 93% ee, from **1e**) respectively. Similarly, for the aminocyanation reactions, the catalyst loading of copper could be reduced to 0.2 mol%, and the β-amino nitrile **1d** is formed in moderate yields with high enantioselectivity (1.55 g, 54% yield, 91% ee from **1a**; 1.21 g, 44% yield, 91% ee from **1e**). For the 1,5-oxocyanation reaction on a gram scale (Scheme 5B), 0.5 mol% of **L** is enough to promote the reaction, providing 5-aroxyl nitrile **38f** in high enantioselectivity (0.88 g, 47% yield, 95% ee and >20/1 (Z/E)), demonstrating the practicality of the method. Reduction of the cyano group in **1d** efficiently generated an optically active 1,3-diamine **1q** with different protecting groups (Scheme 5C). Reduction of **1f** provided the protected 3-amino alcohol **1r** in good yield (Scheme 5D). Selective deprotection of the aroyl group in **1r** formed an alcohol **1s**, which can couple with an α-amino acid to generate the ester **1t.** Oxidation of **1s** provided the β-amino α-chiral aldehyde **1u** with some loss of the original enantiopurity. This aldehyde **1u** was attacked by a phenyl Grignard reagent, a nucleophile, to provide 1,3-amino alcohol **1v** with adjacent stereogenic centers. Since the fragments of 1,3-amino alcohols and 1,3-diamines are present in natural products and many useful compounds, and are employed as useful building blocks in organic synthesis, these chemical transformations will extend the applications of this reaction.

## Conclusion

In summary, we have developed a novel strategy for chemodivergent asymmetric synthesis through a dual photoredox and copper catalysis. The reaction depends on the metal-to-ligand ratio. Using *N*-(aroyloxy)phthalimide as the aroyloxy or phthalimidyl source, enantioselective oxocyanation or aminocyanation of alkenes can be independently realized by tuning the metal-to-ligand ratio. In addition to tolerating many functional groups and proceeding with a wide range of alkenes, the reactions are highly efficient. They use a catalyst loading as low as 0.2 mol% and can be performed at the gram scale without losing efficiency or enantioselectivity. Mechanistic investigations including EPR experiments, were performed to illustrate the possible reaction pathway and the process of stereoinduction. The organic photocatalyst serves either with excess copper to generate an O-centered aroyloxy radical or with excess ligand to produce the N-centered phthalimidyl radical. The copper/ligand complex functions as an organometallic catalyst, installing a cyano group in an enantiocontrolled manner. This protocol provides unprecedented access to a diverse range of optically active difunctionalized compounds (77 examples, up to 91% yield and up to 97% ee), which has great potential in pharmaceutical chemistry and natural product synthesis. The current study reveals that the metal-to-ligand ratio can contribute substantially to chemoselective control while retaining the high enantiopurity of the divergent products, which provides a new scenario when optimizing metal-to-ligand ratio in asymmetric catalysis.

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**Keywords:** Radical • Asymmetric • Cyanation • Catalytic • Chemodivergent

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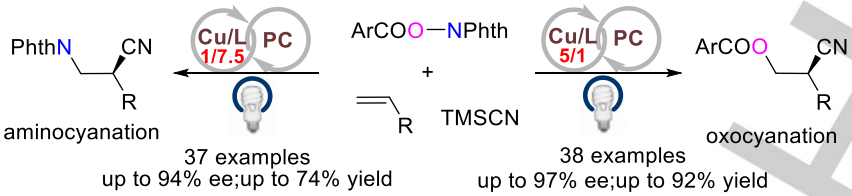


A chemodivergent asymmetric synthesis can be achieved by tuning the metal-to-ligand ratio in an organometallic catalytic system.