

A review of enantioselective dual transition metal/photoredox catalysis

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Transition metal catalysis is one of the most important tools to construct carbon-carbon and carbon-heteroatom bonds in modern organic synthesis. Visible-light photoredox catalysis has recently drawn considerable attention of the scientific community owing to its unique activation modes and significance for the green synthesis. The merger of photoredox catalysis with transition metal catalysts, termed metallaphotoredox catalysis, has become a popular strategy for expanding the synthetic utility of visible-light photocatalysis. This strategy has led to the discovery of novel asymmetric transformations, which are unfeasible or not easily accessible by a single catalytic system. This contemporary area of organic chemistry holds promise for the development of economical and environmentally friendly methods for the asymmetric synthesis of chiral compounds. In this review, the advances in the enantioselective metallaphotoredox catalysis (EMPC) are summarized.

transition metal catalysis, photoredox catalysis, dual catalysis, asymmetric catalysis

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1 Introduction

It has long been recognized that transition metal catalysis is one of the most important tools to construct carbon-carbon bond and carbon-heteroatom bond in modern organic synthesis. Three Nobel Prizes have been awarded in this field since 2000: Knowles, Noyori and Sharpless for stereoselective catalysis in 2001 [1]; Chauvin, Grubbs and Schrock for olefin metathesis in 2005 [2]; and Heck, Suzuki and Negishi for palladium-catalyzed cross-coupling in 2010 [3]. In spite of these achievements, transition metal catalysis is still an important source of innovation in synthetic chemistry, especially for the synthesis of optically active molecules.

Visible-light photoredox catalysis has recently drawn considerable attention of the scientific community owing to its unique activation modes and significance for the green

synthesis [4–10]. Comparing to non-photochemical strategies, photocatalysis provides a direct means to access highly reactive intermediates, such as free radicals and radical ions. These species cannot readily be generated using non-photochemical strategies. The high activity of these intermediates renders the controlling of selectivity, especially stereoselectivity, synthetically challenging [11–14].

The combination of photoredox catalysis with well-established asymmetric catalysis, such as transition metal catalysis, organocatalysis and biocatalysis, provides a potential solution to stereoselective photochemistry [15–19]. In this dual catalysis, the photocatalyst is responsible for the photochemical process and a chiral catalytic system enables the asymmetric bond formation. In this regard, the merger of photoredox catalysis with transition metals, termed metallaphotoredox catalysis by MacMillan *et al.* [20], becomes a popular strategy for expanding the synthetic utility of visible-light photocatalysis. This synergistic catalytic strat-

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egy leads to the discovery of novel asymmetric transformations, which are unfeasible or not easily accessible by a single catalytic system (Figure 1). This contemporary area of organic chemistry holds promise for the development of economical and environmentally friendly methods for the enantioselective synthesis of chiral compounds. In this review, we summarize the recent advances in the enantioselective metallaphotoredox catalysis (EMPC). The combined transition metal-based Lewis acids and photoredox catalytic systems have been well-reviewed elsewhere [18] and are not included in this review.

2 Enantioselective metallaphotoredox catalysis

2.1 Enantioselective nickel metallaphotoredox catalysis (Ni-EMPC)

Metallaphotoredox catalysis is particularly effective in C(sp³) fragment couplings, which are traditionally challenging to engage with transition metals alone. Nickel is one of the most widely used metals in these cross couplings because of (1) its demonstrated competence in room-temperature oxidative addition with alkyl electrophiles, (2) its favorable single-electron redox potentials, and (3) its lower susceptibility to undergo problematic β-hydride elimination steps. The pivotal studies of Molander *et al.* [21], Doyle and MacMillan *et al.* [22] merged the use of photoredox catalysis in the single-electron transmetalation for the cross-coupling catalyzed by nickel [23].

In 2014, Molander *et al.* [21] introduced a Ni/photoredox cocatalyzed cross coupling using benzyl potassium trifluoroborate salts as radical precursors (Scheme 1). The mildness of the reaction conditions contrasts sharply with those previously reported for conventional cross-couplings of benzylboron reagents, leading to improved tolerance of sensitive functional groups. Mechanistically, Ni(0) complex first engages the aryl bromide 2 in oxidative addition to afford aryl Ni(II) complex A. In the meantime, the reductive quenching process of the visible-light excited Ir(III)* by alkyl trifluoroborate 1 leads to an alkyl radical 4 that is rapidly captured by the Ni(II) complex A. Reductive elim-

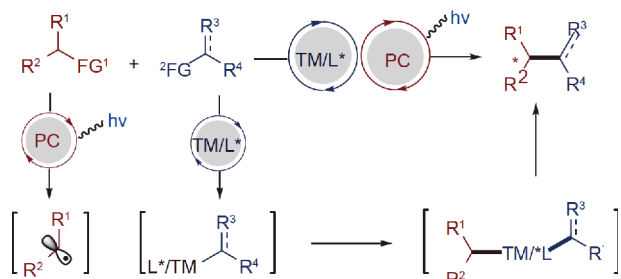
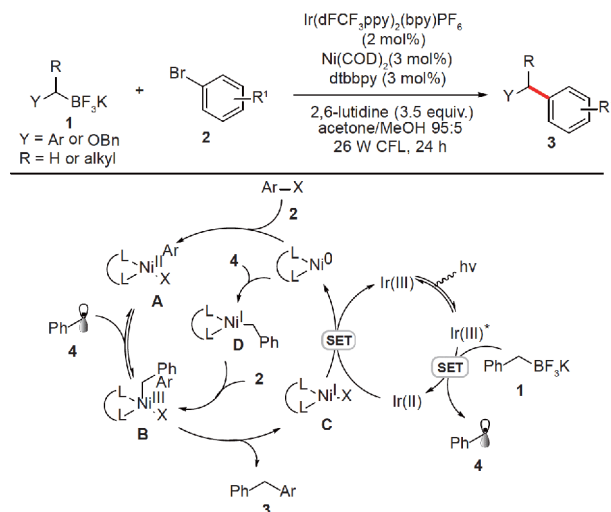


Figure 1 The general rationale for enantioselective metallaphotoredox catalysis (color online).



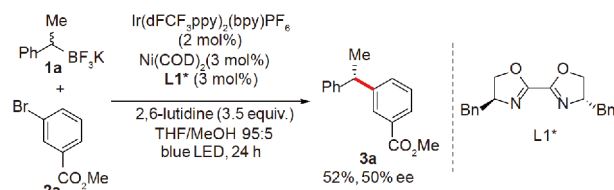
Scheme 1 Organoboron cross coupling by Ni-MPC (color online).

ination from the resultant Ni(III) species B yields the cross coupled product 3 and Ni(I) complex. Finally, single-electron reduction of Ni(I) species C by low-valent Ir(II) complex simultaneously regenerates the Ni(0) catalyst and the ground state photocatalyst. Alternatively, alkyl radical 4 could add to Ni(0) complex firstly to generate Ni(I)-alkyl species D. Subsequent oxidative addition into aryl bromide would afford high-valent Ni(III) complex B, reductive elimination from which would give the product (Scheme 1).

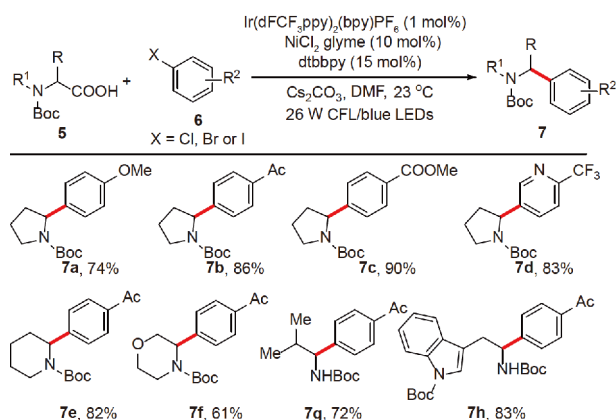
When chiral ligand L1* was added to the Ni(COD)₂ catalyst, racemic trifluoroborate 1a was engaged in stereoconvergent cross-coupling with methyl 3-bromobenzoate 2a, affording enantio-enriched product 3a (Scheme 2, 52% yield, 50 ee). In their successive study [24], the authors explained that stereoconvergence did not arise from facial-selective addition to the Ni center, but rather from the reductive elimination step.

MacMillan and Doyle *et al.* [22] published a concurrent Ni/photoredox cocatalyzed cross coupling that employs carboxylic acids in place of organoboron reagents (Scheme 3).

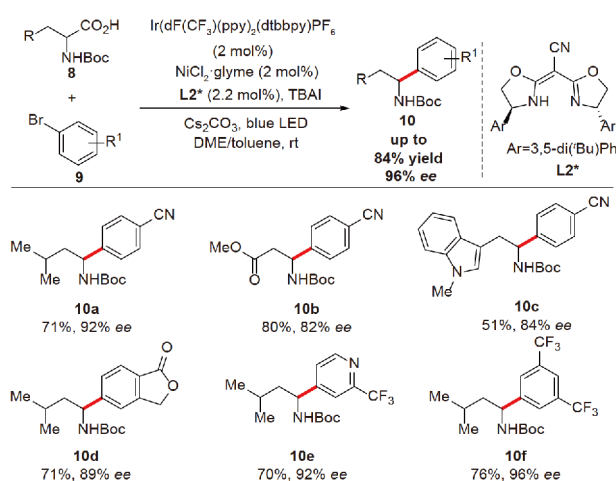
On the basis of this work, MacMillan, Fu and co-workers [25] realized the highly enantioselective decarboxylative cross-coupling with carbamate-protected amino acids by using a chiral cyano-bisoxazoline ligand L2* (Scheme 4). The asymmetric decarboxylation cross-coupling was de-



Scheme 2 Stereoconvergent cross-coupling of a racemic trifluoroborate with an aryl bromide (color online).



Scheme 3 Decarboxylation cross coupling by Ni-MPC.

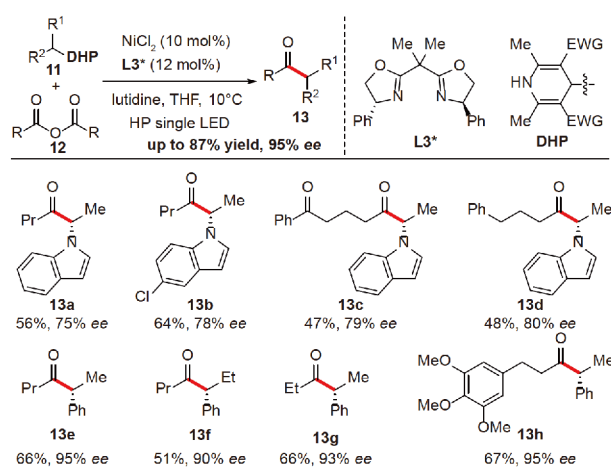


Scheme 4 Enantioselective decarboxylation cross coupling by Ni-EMPC (color online).

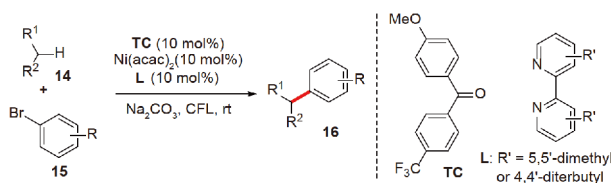
monstrated with a wide scope of *N*-Boc protected α -amino acids **8** and many functional groups were tolerated, delivering various enantioenriched benzylic amine products **10**.

Melchiorre *et al.* [26] reported an asymmetric Ni/photoredox cocatalyzed cross-coupling of anhydrides **12** and 4-alkyl dihydropyridines (DHPs) **11**. This reaction does not require exogenous photocatalysts. It is triggered by the direct excitation of DHPs, which act as radical sources and reductants, facilitating the turnover of the chiral catalytic nickel complex (Scheme 5).

From the perspective of atom economy and synthetic efficiency, C–H arylation reactions via hydrogen atom transfer (HAT) process have their own unique advantages [27–29]. In 2018, Martin *et al.* [30] described a Ni/photoredox/HAT cocatalyzed C(sp³)–H arylation and alkylation, in which simple and easily accessible diaryl ketones were utilized as photocatalysts and HAT catalysts (Scheme 6). Mechanistically, oxidative addition of Ni(0) into an aryl halide **15** would produce aryl nickel(II) complex **E**. Concurrently, electron-rich alkyl radical would be generated upon HAT from long-lived triplet excited **H** along with the formation of



Scheme 5 Enantioselective acyl cross coupling by Ni-EMPC (color online).

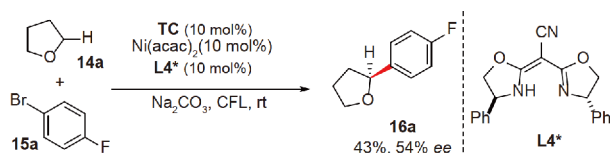
Scheme 6 C(sp³)–H arylation enabled by the synergy of triplet excited ketones and nickel catalysts (color online).

a ketyl radical **I**. The Ni(II) complex **E** captures the alkyl radical rapidly and might generate discrete Ni(III) species **F**, which would undergo reductive elimination to deliver the targeted C–H functionalization product and Ni(I) intermediate **G**. Finally, the two catalytic cycles could be inter-

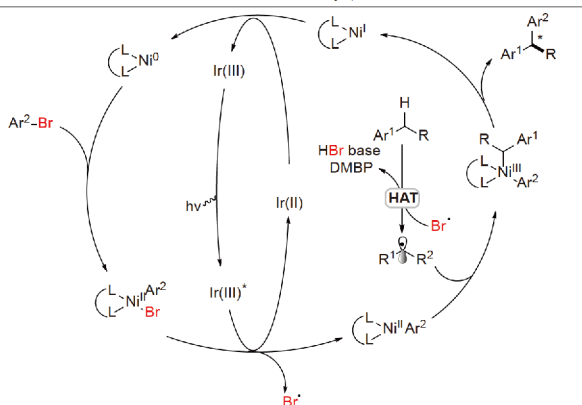
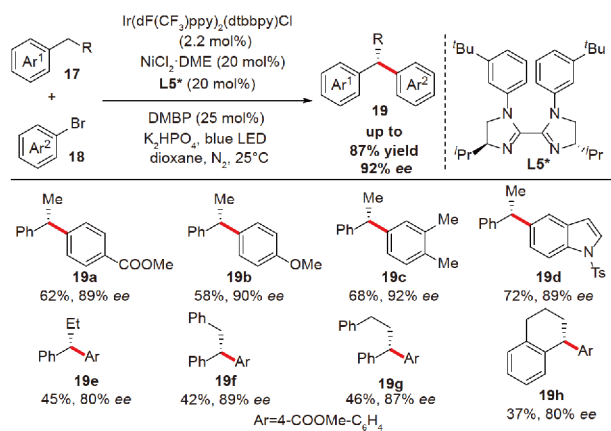
faced under basic conditions by a SET from the ketyl radical **I** to Ni(I) intermediate **G** (Scheme 6).

Asymmetric cross coupling reaction via this photocatalytic HAT process is quite challenging. When utilizing a chiral ligand **L4***, moderate enantioselectivity and yield could be accessed (43% yield, 54% ee, Scheme 7).

Benzylic C–H arylation of ethylbenzene derivatives with aryl halides is still a challenge. Recently, Lu *et al.* [31] developed a direct enantioselective benzylic C–H arylation under photoredox/nickel dual catalysis by using their designed chiral biimidazoline (BiIM) ligand **L5*** (Scheme 8). Different from the mechanism proposed in Scheme 6, the HAT process of this reaction occurred between bromine-free radical and alkyl benzene. This protocol could be used for the preparation of useful chiral 1,1-diaryl alkanes **19**, starting from readily available alkyl benzenes **17** and aryl bromides **18** with various functional group tolerance.



Scheme 7 Enantioselective C(sp³)-H arylation by Ni-EMPC (color online).

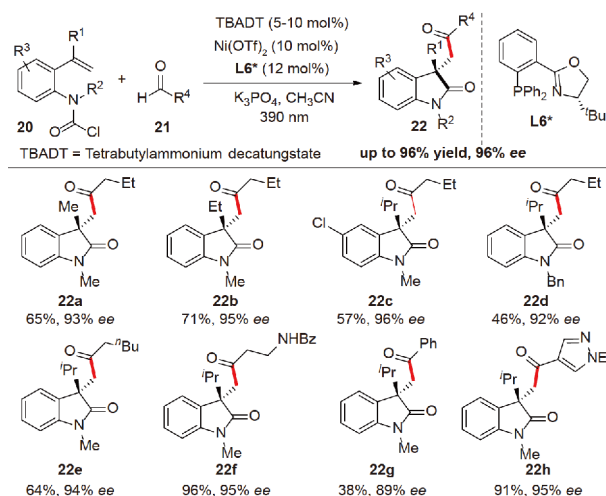


Scheme 8 Enantioselective benzylic C–H arylation by Ni-EMPC (color online).

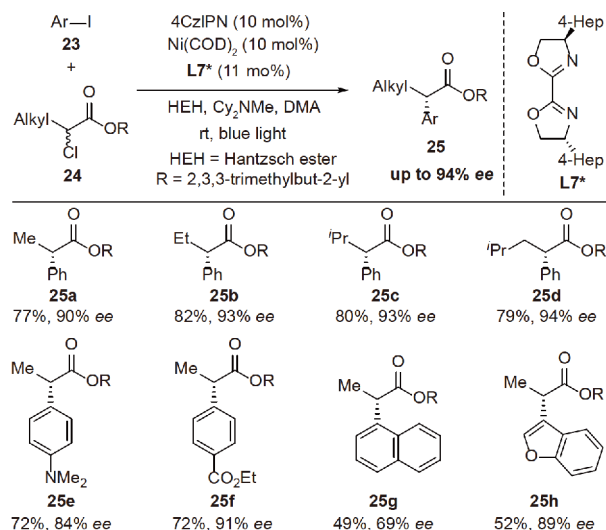
Wang *et al.* [32] introduced an asymmetric difunctionalization of alkenes via the merger of nickel and photocatalysis. In this cooperative catalysis, easily accessible starting materials aldehydes serve as an appealing acyl source through tetrabutylammonium decatungstate (TBADT) catalyzed acyl C–H activation. This new method enables the highly enantioselective synthesis of diverse 3,3-disubstituted oxindoles (Scheme 9).

Very recently, Mao, Walsh and co-workers [33] reported the first dual nickel/photoredox catalyzed asymmetric reductive cross-coupling of racemic α -chloro esters with aryl iodides (Scheme 10). A diverse array of valuable α -aryl esters are formed with high enantioselectivities and good yields. This novel synergistic strategy expands the scope of Ni-catalyzed asymmetric reductive cross-coupling reactions.

In addition to the above-mentioned direct construction of chiral centers using chiral nickel complex, asymmetric de-



Scheme 9 Enantioselective acyl-carbamoylation of alkenes by Ni-EMPC (color online).



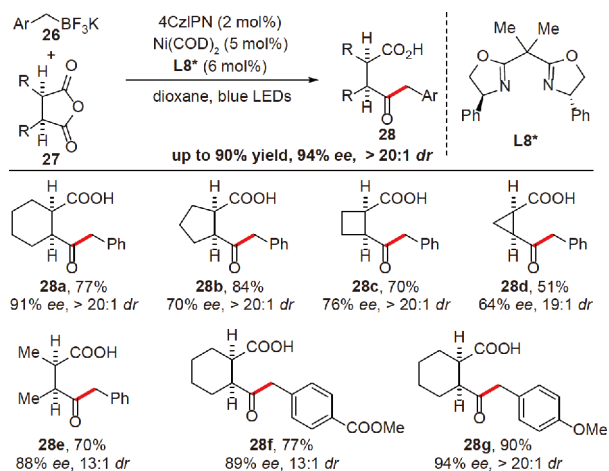
Scheme 10 Enantioselective reductive cross-coupling by Ni-EMPC.

symmetrization of symmetric prochiral substrates is another useful strategy for the enantioselective dual Ni/photoredox catalysis. In 2018, Rovis and Doyle *et al.* [34] described an enantioselective desymmetrization of cyclic *meso*-anhydrides **27** with benzyl trifluoroborates **26** under photoredox/nickel dual catalysis (Scheme 11). This reaction tolerates a variety of sterically and electronically different trifluoroborates, as well as structurally unique cyclic anhydrides. They proposed a Ni(0/I/III) mechanism similar to that in Scheme 1. As such, enantioselective oxidative addition of Ni(0) to the anhydride, followed by interception of the benzylic radical on a Ni(II) species to afford Ni(III) complex, reductive elimination from the Ni(III) complex would give the product.

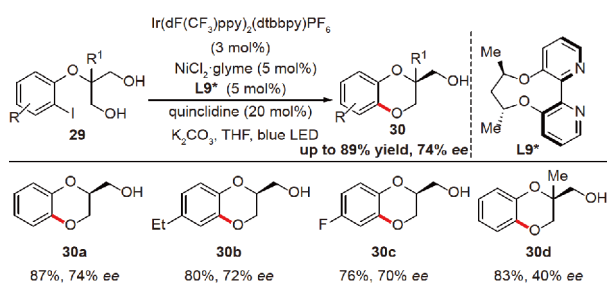
Xiao *et al.* [35] published a concurrent report of a Ni/photoredox cocatalyzed desymmetric C–O coupling reaction (Scheme 12). By using a novel axially chiral 2,2'-bipyridine ligand **L9***, a series of chiral 1,4-benzodioxanes **30** were afforded in high yields and moderate to good enantioselectivity under mild reaction conditions.

2.2 Enantioselective palladium metallaphotoredox catalysis (Pd-EMPC)

Palladium, one of the most widely used transition metals, has



Scheme 11 Enantioselective desymmetrization of cyclic *meso*-anhydrides by Ni-EMPC (color online).

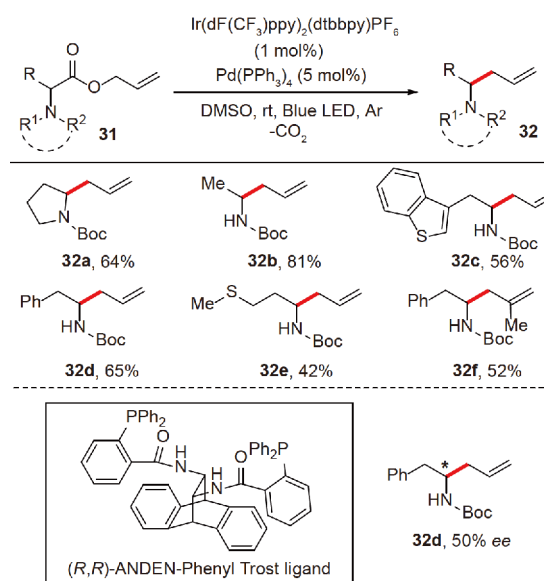


Scheme 12 Enantioselective desymmetric C–O coupling by Ni-EMPC (color online).

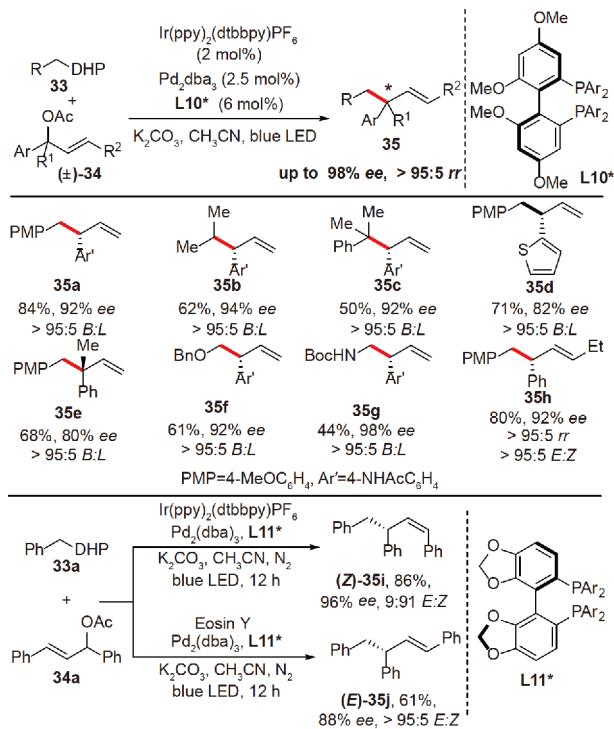
been investigated concomitantly with photoredox catalysis. However, the reports of enantioselective reactions under these dual catalysis conditions are rare.

Pd-catalyzed asymmetric allylic alkylations (AAA) are highly valuable transformations in organic synthesis (Tsuji-Trost allylation) [36–38]. Pd-catalyzed AAA reactions with “hard” or nonstabilized alkyl nucleophiles ($pK_a > 25$) are especially challenging [39–43]. In 2015, by using a unified palladium catalyst and photocatalyst, Tunge *et al.* [44,45] achieved a radical decarboxylative allylation of *N*-protected α -amino and phenylacetic allyl esters (Scheme 13). In this reaction, radical decarboxylation overcomes the inherent difficulties that are associated with anionic metal-mediated decarboxylation of aliphatic acids, and expands the scope of allylic alkylation chemistry. Efforts were also made to achieve asymmetric version of this reaction. When Trost ligand was used, moderate enantioselectivity (50% ee) was observed.

Very recently, our group described a highly regio- and enantioselective visible-light-induced allylic alkylation reaction with 4-alkyl-1,4-dihydropyridines **33** (Scheme 14) [46]. Alkyl radicals generated from 4-alkyl-1,4-dihydropyridines act as coupling partners with the π -allyl palladium complexes. The allylic acetate **34** could be alkylated with primary, secondary, and tertiary alkyl radicals. In particular, the thermodynamically less stable *Z*-isomer of alkylation product **35i** can be obtained as the major product. Photochemical isomerization of (*E*)-**35j** led to (*Z*)-**35i** in the presence of Ir-based photocatalyst. Replacing photocatalyst to Eosin Y, which is ineffective in the photochemical isomerization, (*E*)-isomer **35j** was isolated as the sole product. In addition, the regioselectivity and dynamic kinetic resolution effect of this reaction are different from the tradi-



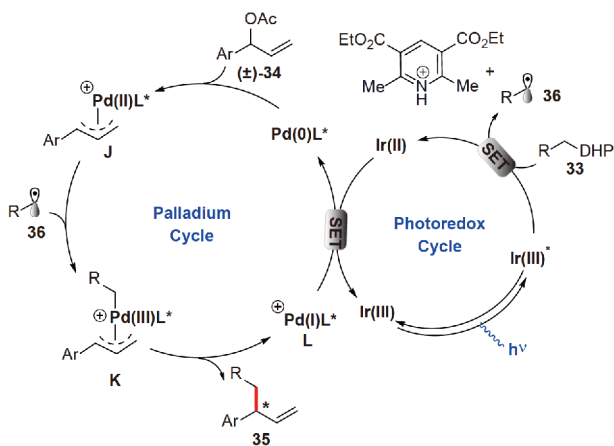
Scheme 13 Decarboxylative allylations of α -amino acids by dual Pd/photoredox catalysis (color online).



Scheme 14 Asymmetric allylic alkylation by Pd-EMPC (color online).

tional palladium catalyzed AAA reactions. Non-symmetrical monosubstituted allylic electrophiles typically affords achiral linear products except that prochiral nucleophiles are employed, and control of regioselectivity to afford chiral branched products remains a key challenge in this field. Many factors may affect the regioselectivity of this reaction, such as ligand, solvent, and photocatalyst. Among these, we believe that ligand effect is one of the most important factors.

A plausible mechanism is proposed (Scheme 15), as in the classical AAA reaction, oxidative addition of Pd(0) into allyl ester **34** forms an allyl Pd(II) species **J**, which is able to trap an alkyl radical **36** derived by the photocatalytic oxidation of dihydropyridine **33**. Reductive elimination of Pd(III) species



Scheme 15 Proposed mechanism for AAA reaction by Pd-EMPC (color online).

K leads to alkylation product **35** and a Pd(I) complex **L**, which is reduced by the photocatalyst to regenerate the starting Pd(0) complex, thereby also closing the photoredox cycle.

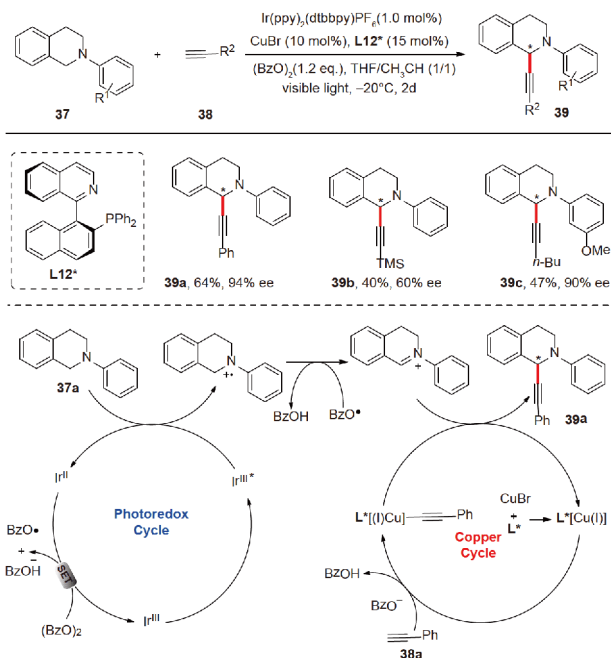
2.3 Enantioselective copper metallaphotoredox catalysis (Cu-EMPC)

The combination of photocatalysts with copper catalysts has emerged as an efficient dual catalytic system for incorporating functional groups into organic molecules. Recently, some reviews have summarized the photoredox and copper co-catalyzed radical mediated transformations and provided an overview of the emerging applications in organic synthesis [47–49]. The copper described here is used as the metal center, which could efficiently intercept organic radical intermediates generated by the photoredox catalysis and get stabilized, instead of Lewis acid or photocatalysts only in the copper catalysis cycle. This synergistic mechanistic prototype involves the generation of radical species through the reduction of organic substrates upon photoexcitation and capture of the radical intermediates in a rebound process. The resulting copper intermediate then undergoes reductive elimination to give the final products. Nevertheless, asymmetric radical reactions via this synergistic photoredox/copper catalysis are much less developed.

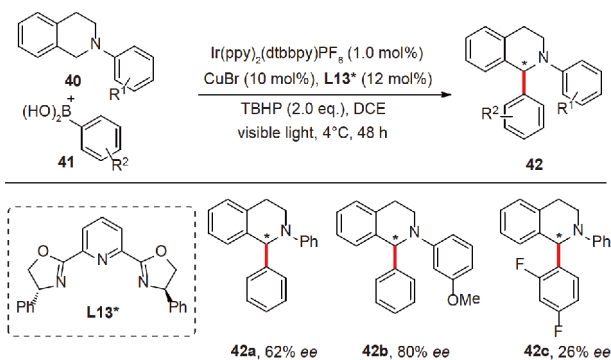
In 2015, Li *et al.* [50] reported a synergistic photoredox and copper catalysis mediated highly efficient catalytic asymmetric cross-dehydrogenative-coupling reaction, using Ir(ppy)₂(dtbbpy)PF₆ together with the CuBr/L12* as the catalytic system and benzoyl peroxide as the terminal oxidant. Optically active 1-alkynyl tetrahydroisoquinolines **39** was given in good yields and excellent enantioselectivities. This strategy features low photocatalyst loading, the convenience of using visible light and avoiding pre-functionalization of the starting material, and places this reaction in the green chemist's synthetic toolbox (Scheme 16).

Li *et al.* [51] then introduced a highly enantioselective oxidative C(sp³)–H arylation of *N*-aryltetrahydroisoquinolines through the combination of the photoredox and copper catalysis. In this reaction, they used L13* as the chiral ligand, and good enantiomeric ratios were obtained (Scheme 17).

Liu and Lin *et al.* [52] reported in 2017 an asymmetric radical decarboxylative cyanation reaction of *N*-hydroxyphthalimide (NHP) esters with trimethylsilyl cyanide (TMSCN) by merging photoredox catalysis with copper catalysis. This method features good functional group tolerance and broad substrate scope, and provides a straightforward access to chiral alkyl nitriles with high yields and enantioselectivity under mild reaction conditions, regardless of the poor enantioselectivity was obtained for the non-benzylic carbon radicals. In addition, different from the



Scheme 16 Asymmetric cross-dehydrogenative-coupling of alkynes and tetrahydroisoquinolines by Cu-EMPC (color online).

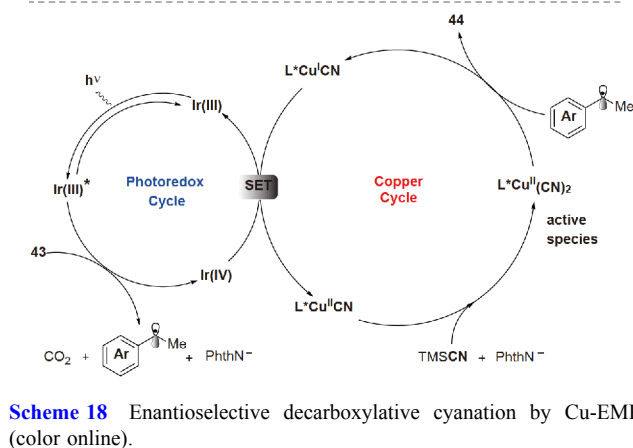
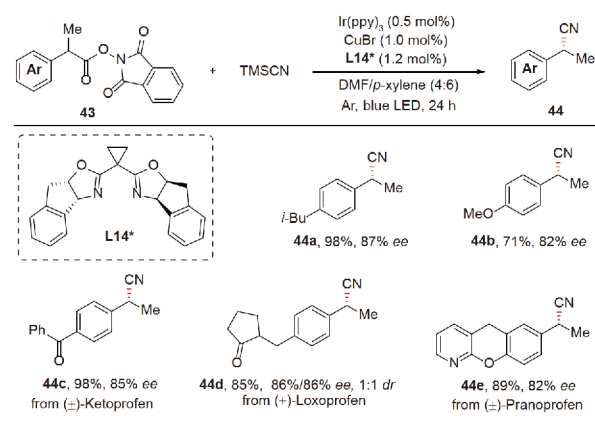


Scheme 17 Asymmetric C(sp³)-H arylation of tetrahydroisoquinolines mediated by Cu-EMPC (color online).

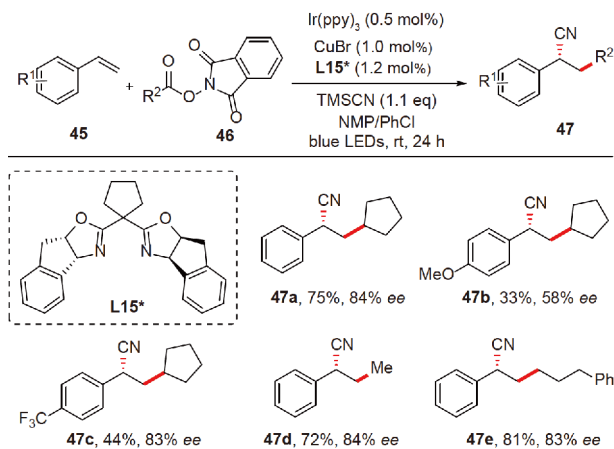
oxidant of electrophilic F⁺ reagents or CF₃⁺ reagents they previously used, the relatively inert N–O bond of NHP ester failed to oxidize L^{*}Cu(I)CN, and thus photocatalyst Ir(ppy)₃ was used to initiate the radical decarboxylation of the NHP ester and generate L^{*}Cu(II)CN species. Moreover, the key step of the oxidation of L^{*}Cu(I)CN through Ir(IV) makes the resulting oxidative quenching cycle different from the mechanisms of their previous studies. Mechanistically, the NHP ester, upon single-electron transfer (SET) reduction by the excited photocatalyst Ir(III)*, forms a benzylic radical and Ir(IV). The oxidized photocatalyst Ir(IV) could oxidize L^{*}Cu(I)CN to generate L^{*}Cu(II)CN in the presence of TMSCN. Radical rebound of benzylic radical with L^{*}Cu(II)CN and then reductive elimination deliver the decarboxylative cyanation products with the concurrent release of L^{*}Cu(I)CN (Scheme 18).

Independently, Han and Mei *et al.* [53] developed a novel photoredox and copper co-catalyzed asymmetric cyanoalkylation of alkenes with primary, secondary, and tertiary alkyl substituted NHP esters. In this radical cyanoalkylation reaction, the photoredox induced alkyl radical adds to styrene, and the generated benzylic radical couples with a chiral Box/Cu(II) cyanide complex to achieve the asymmetric radical difunctionalization of alkenes (Scheme 19).

In 2019, Xiao, Lan and Lu *et al.* [54] reported a catalytic asymmetric propargylic radical cyanation via a synergetic photoredox/copper catalysis strategy. Ph-PTZ is used as an organic photocatalyst, which serves to generate propargyl radicals and oxidize Cu(I) species to Cu(II) species. This strategy provides an unprecedented access to optically enriched propargyl cyanides with generally high reaction efficiency and enantioselectivity under mild conditions. An excited Ph-PTZ* reduces propargyl ester 48, followed by fragmentation to reveal a propargyl radical, which can be captured in a stereoselective manner by L^{*}Cu(II)(CN)₂ to form chiral Cu(III) species. Then reductive elimination of chiral Cu(III) species delivers the final chiral propargyl cyanide 49 and regenerates the chiral Cu(I) catalyst. With the assistance of the carboxylic anion LG⁻, cyanide anion (CN⁻) can be slowly released from TMSCN, which can be coordinated to the chiral Cu(I) catalyst to form L^{*}Cu(I)(CN)₂ species. Mechanistic investigation, including control ex-



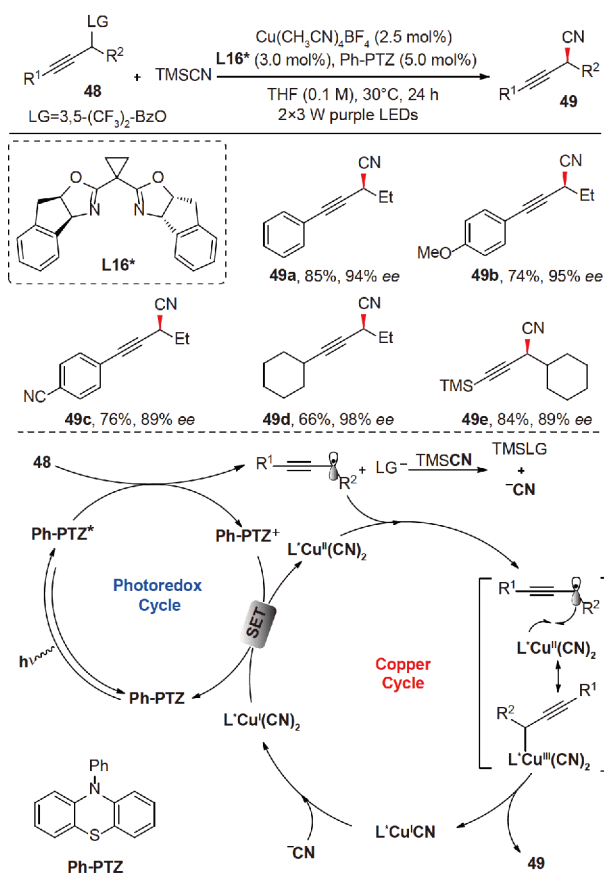
Scheme 18 Enantioselective decarboxylative cyanation by Cu-EMPC (color online).



Scheme 19 Asymmetric cyanoalkylation reaction of alkenes by Cu-EMPC (color online).

periments and DFT calculations, shows that the enantioselectivity is determined by the reductive elimination step, and the higher energy barrier was observed in reductive elimination for the *R*-product compared with that for the *S*-product (Scheme 20).

In 2019, Zhu *et al.* [55] realized a reaction of *N*-alkoxyppyridinium salts **50** with commercially available TMSCN under the conditions of 1,10-Phen as ligand, Ir(ppy)_3 and

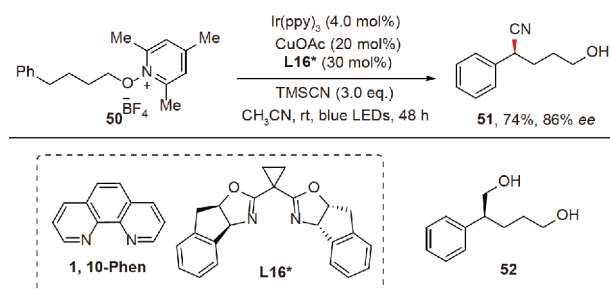


Scheme 20 Catalytic asymmetric propargylic radical cyanation by Cu-EMPC (color online).

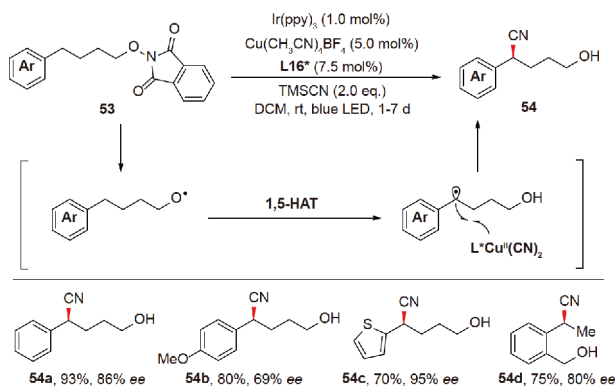
CuOAc as catalyst. δ -azido, δ -cyano, and δ -thiocyanato alcohols were afforded in high yields. This reaction went through the process of alkoxy radical generation, 1,5-hydrogen atom transfer (1,5-HAT) and copper catalyzed functionalization of the resulting C-centered radical. The catalytic enantioselective cyanation protocol could be realized when **L16*** was used as the ligand instead of 1,10-Phen, and **51** was obtained in 74% yield with 86% ee. The (*S*)-absolute configuration of **51** was determined by comparing the specific optical rotation of its derivative **52** with the known compound (Scheme 21).

Independently, Liu *et al.* [56] reported a catalytic asymmetric cyanation of remote $\text{C(sp}^3\text{)-H}$ bonds by merging photoredox catalysis with copper catalysis. This reaction provides an efficient pathway to synthesize chiral δ -cyano alcohols. The key step to govern the reactivity and site selectivity was initiated with an intramolecular 1,5-HAT process (Scheme 22).

In 2019, Chen *et al.* [57] and Wang *et al.* [58] independently reported enantioselective radical ring-opening cyanation of four and five-membered cycloketone oxime esters to access chiral 1,5- and 1,6-dinitriles by dual photoredox and copper catalysis. Chen used Ph-PTZ as the organic photocatalyst whereas iridium photocatalyst was used by Wang. Both of these reactions show good functional group tolerance and broad substrate scope, producing a wide range of optically active alkyl dinitriles with high yields and ex-



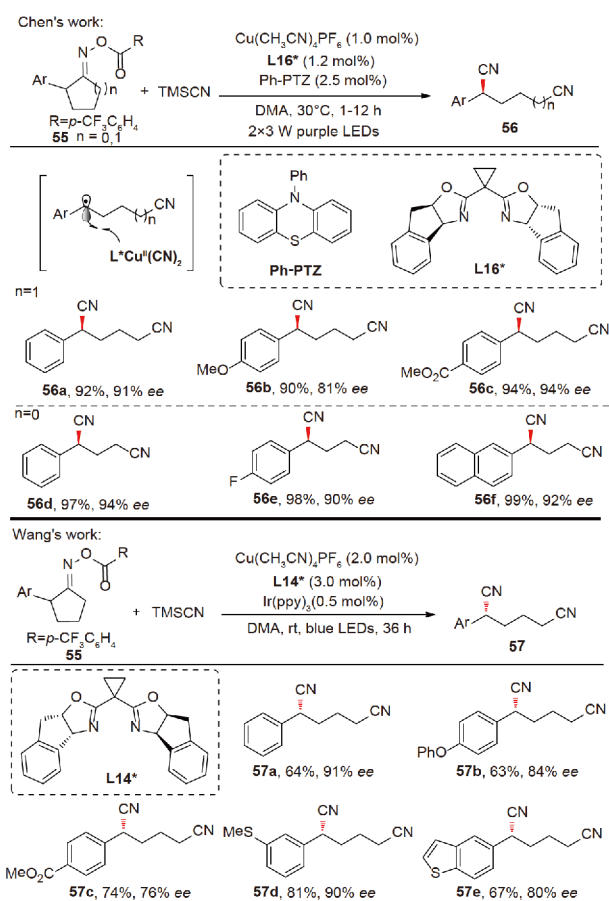
Scheme 21 Asymmetric cyanation of remote C-H bonds by Cu-EMPC (color online).



Scheme 22 Enantioselective cyanation of remote C-H bonds by Cu-EMPC (color online).

cellent enantioselectivities. Chen *et al.* also demonstrated that the model reaction could be carried out under sunlight exposure when replacing Ph-PTZ with Ir(ppy)₃, and the catalytic system could be applied to the three-component enantioselective ring opening cross-coupling of cyclobutane oxime ester. Wang *et al.* observed that unlike the dual photoredox and copper catalysis for the enantioselective ring opening cyanation of the cyclopentanone oxime esters, the asymmetric cyanation of cyclobutanone oxime esters could be realized by copper catalysis alone (Scheme 23).

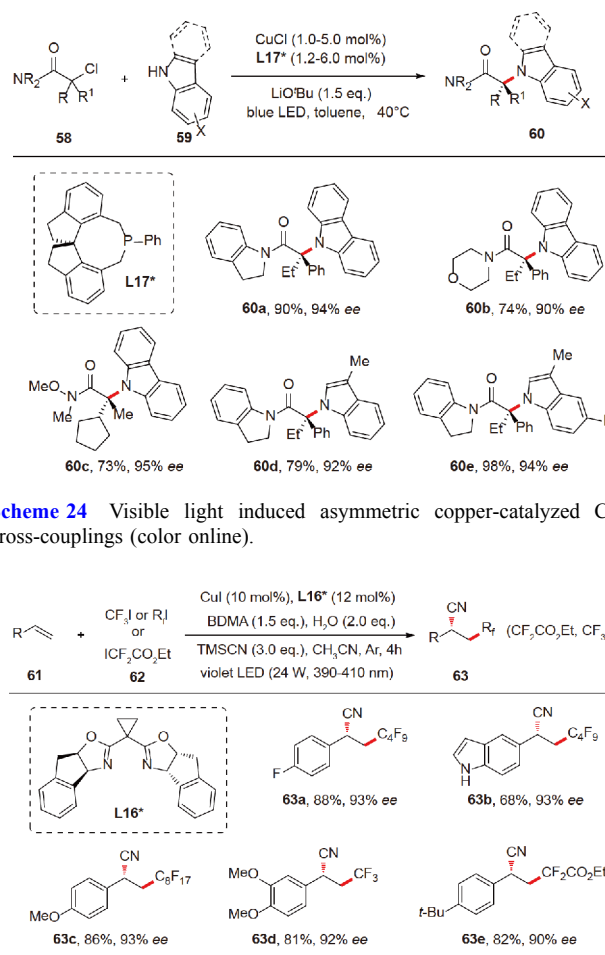
In addition to the synergetic photoredox/copper catalysis mediated asymmetric radical reactions described above, which the photocatalyst mediates the electron transfer and copper-based chiral catalyst devotes to introducing the enantioselectivity, the copper-based chiral complex alone could also be served as both the photo sensitizer and the catalyst for asymmetric cross-coupling reactions. In 2016, Fu and Peters *et al.* [59] established a photoinduced copper catalyzed method in which copper acted as both the photocatalyst and the source of asymmetric induction, for coupling readily available racemic tertiary alkyl chloride electrophiles with amines to generate fully substituted stereocenters with high enantioselectivity. This protocol comprises the area of the



Scheme 23 Enantioselective radical ring-opening cyanation of redox-active oxime esters by Cu-EMPC (color online).

enantiocovergent synthesis of secondary and tertiary C–heteroatom bonds enabled by visible light induced transition metal catalyzed couplings of alkyl halides (Scheme 24).

In 2019, Xu, Wang and Liu *et al.* [60] disclosed a visible light-induced, copper catalyzed photoredox enantioselective cyanofluoroalkylation of alkenes by directly employing fluoroalkyl iodides as fluoroalkylation reagents. In this reaction, copper-based single catalyst played not only the photoredox catalyst for the outer-sphere electron transfer, but also the asymmetric cross-coupling catalyst for enantioselective C–CN bond formation. A plausible mechanism was proposed in Scheme 25. The rapid ligand exchange



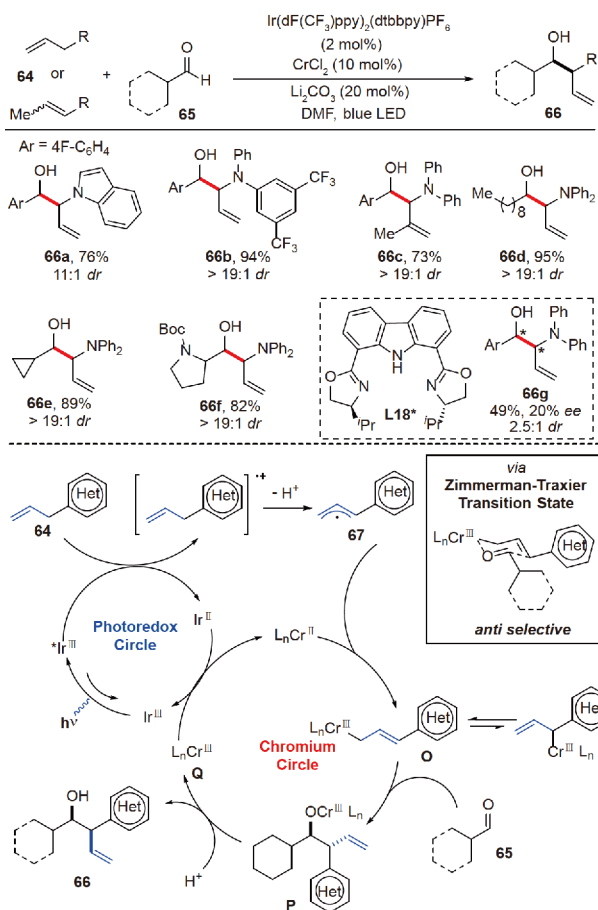
Scheme 24 Visible light induced asymmetric copper-catalyzed C–N cross-couplings (color online).

Scheme 25 Asymmetric cyanofluoroalkylation of alkenes by dual functional chiral copper catalysis. BDMA = *N*, *N*-dimethylbenzylamine (color online).

of TMSCN with $L^*Cu^I X$ delivered $L^*Cu^I CN$ species, which was excited to its excited state $[L^*Cu^I CN]^*$ under visible light irradiated. Through oxidative quenching step, $R_f\dot{I}$ was converted to $\bullet R_f$, and $[L^*Cu^I CN]^*$ was oxidized to $[L^*Cu^{II}(CN)_2]$ intermediate. At the same time, the addition of $\bullet R_f$ to alkene gave the radical intermediate **M**. It then reacted with $[L^*Cu^{II}(CN)_2]$ to form a chiral Cu^{III} intermediate **N**. Finally, the desired product was obtained by reductive elimination with high enantioselectivity.

2.4 Enantioselective chromium metallaphotoredox catalysis (Cr-EMPC)

The Nozaki-Hiyama-Kishi (NHK) reaction is a well-established chromium mediated allylation of aldehyde [61,62]. Glorius and coworkers [63] have recently published a diastereoselective allylation of aldehydes with unfunctionalized allyl (hetero-) arenes by the combination of photoredox and chromium catalysis, which significantly extends the scope of the venerable NHK reaction (Scheme 26). They proposed a plausible mechanism. Cr(II) captures allyl radical **67** generated from the reductive quenching of the excited photocatalyst by an allyl (hetero-) arene **64** to form Cr(III) allyl



Scheme 26 Allylation of aldehydes by Cr/photoredox cocatalysis (color online).

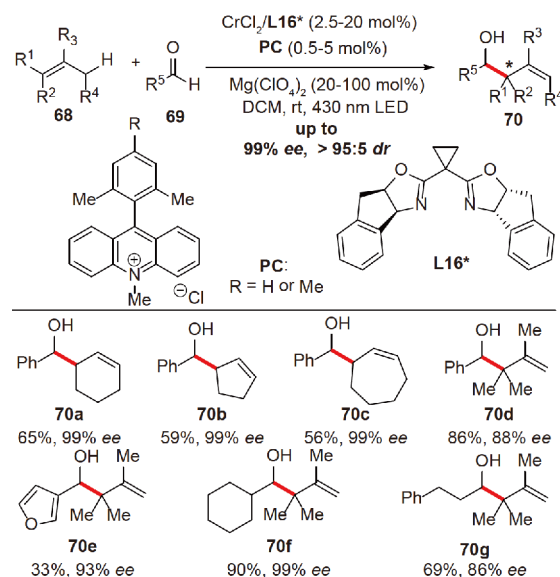
species **O**, which would react with an aldehyde **65** via a six-membered Zimmerman-Traxler transition state to generate Cr(III) species **P** in an *anti*-selective fashion. Then the product **66** is obtained by protonation of **P**. Finally, the two catalytic cycles could be interfaced under basic conditions by a final SET between the reduced Ir(II) photocatalyst and Cr(III) **Q**. The addition of a chiral bisoxazoline ligand **L18*** in a test reaction gave a moderate enantioselectivity (20% ee).

The Cr/photoredox cocatalyzed enantioselective NHK-type allylations was employed by Mitsunuma and Kanai (Scheme 27) [64]. They found that the addition of $Mg(ClO_4)_2$ markedly enhanced both the reactivity and enantioselectivity.

3 Conclusions

The use of two catalysts in a single chemical reaction is a powerful strategy. This strategy can enable transformations which are either difficult or impossible to achieve otherwise. This review demonstrates that the combination of transition metals (Ni, Pd, Cu, and Cr) with photoredox catalysis enhances the control of stereoselectivity in this dual catalytic system and expands the scope of the traditional transition metal and photoredox catalysis. This state of the art synthetic technology provides a new solution to access organic compounds in an enantioselective manner.

Although significant progress in the metallaphotoredox catalysis has been made in recent years, enantioselective versions are still limited. It is clear that several important frontiers still exist for further research in this field to deeply investigate the potential of enantioselective metallaphotoredox catalysis: (1) The design of cooperative catalytic systems with different transition metals, as the successful



Scheme 27 Enantioselective allylation of aldehydes by Cr-EMPC (color online).

examples so far are based on Ni, Pd, Cu, and Cr. (2) Enriching the modes of reactions enabled by metallaphotoredox catalysis. (3) Expanding and generalizing the scope of existing reactions. (4) Increasing mechanistic understanding of the underlying electron transfer processes. (5) Enantioselective photoexcited-state transition-metal catalysis with a chiral ligand, wherein a single transition-metal complex works as both the internal photocatalyst and asymmetric cross-coupling catalyst, is more sustainable and efficient, and will be a new trend in this field [65,66]. Enantioselective metallaphotoredox catalysis (EMPC) provides great chance to develop new reaction modes in asymmetric catalysis and needs to be further investigated.

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Conflict of interest The authors declare that they have no conflict of interest.

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