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Review

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Three-component cross-coupling reactions involving alkenes enabled by visible-light and earth-abundant-metal-catalysis

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Abstract

Catalytic difunctionalizations of alkenes represent one of the most straightforward and efficient ways to build molecular complexity due to the simultaneous installation of two vicinal chemical bonds onto alkenes, providing profound chemical space for selective transformations in organic synthesis. Over the past decade, the merge of visible-light catalysis and earth-abundant-metal catalysis has taken advantage of green catalysis, thus evolving into an enabling platform for difunctionalization of alkenes. This dual catalytic mode facilitates the construction of multiple chemical bonds over the π-bond of alkenes in one step, providing a mild and straightforward method for the rapid construction of sp^3-rich structures in a selective manner. In this review, we systematically summarized the progress of three-component cross-coupling reaction of olefins catalyzed by visible-light and first-row transition metal over the past decade. The combination of visible-light with different first-row transition metals, such as copper, nickel, chromium, titanium, manganese and iron, is discussed, along with the detailed reaction mechanisms. The scope of alkenes in this review includes alkenes, 1,3-dienes and 1,3-enynes. Moreover, the future directions and efforts in visible-light and earth-abundant-metal-catalyzed three-component reactions of alkenes are also discussed.

Keywords: Photocatalysis, earth-abundant transition-metal catalysis, alkenes, three-component reaction, cross-coupling

INTRODUCTION

Transition-metal-catalyzed cross-coupling reactions have fundamentally changed the strategy in organic synthesis and are among the most efficient and straightforward ways to construct diverse chemical bonds, which have significantly enhanced the ability to access complex organic molecules and found broad applications in the synthesis of natural products and functional materials[1-5]. Over the past few decades, significant advancements have been made in noble-transition-metal-catalyzed cross-coupling reactions to form C–C and C–heteroatom bonds[6-10]. However, the use of precious metals such as platinum, palladium, and rhodium hampered their further applications due to their high cost, toxicity, and rarity[11]. In this regard, earth-abundant transition metals, such as iron, cobalt, nickel, and copper, are becoming increasingly important for the sustainable future of organic synthesis and manufacturing due to their low cost, low toxicity, and abundance[12-17]. The development of efficient methodology based on these earth-abundant transition metals offers potential synthetic methods with environmental and economic benefits and provides opportunities to discover new chemical space in bond-forming processes and synthesis.

Given the abundant and renewable nature of visible light, photochemistry and photocatalysis [via photoinduced electron transfer (PET)] have been proven to be a powerful tool for organic synthesis[18-25]. To this end, the combination of photoredox and earth-abundant transition metals offers a new and enabling platform for new methodology development, which provides great potential for the development of more sustainable and cost-effective synthetic methodologies in organic synthesis and opens up new avenues for exploring catalysis in diverse chemical spaces[26-34].

On the other hand, as abundant and readily available feedstocks, alkenes have been recently utilized as prominent platforms for the diverse transformation and precursors for other functional groups with the formation of C–Y (Y = C, N, O, X, S, *etc.*) bonds[35-37]. Among these, catalytic three-component difunctionalization of alkenes represents a powerful and efficient technology for the rapid construction of molecular complexity in a single operation due to the simultaneous formation of two vicinal chemical bonds[38-41]. Over the past decade, three-component difunctionalizations of alkenes enabled by the merger of photoredox and earth-abundant transition-metal catalysis have gained great attention from the community and achieved significant progress.

In this review, the progress in merging visible-light and earth-abundant-transition-metals (Cu, Ni, Cr, Ti, Mn and Fe) catalyzed three-component difunctionalizations of alkenes over recent years has been summarized. The reactions and the mechanistic aspects are discussed to provide insight into the reaction development. Moreover, further efforts and directions in this area are also discussed. In addition, the review is divided into different categories based on the types of earth-abundant transition metals.

1. Photoredox and copper-catalyzed three-component difunctionalizations of alkenes:
1.1 Three-component cross-coupling involving monoalkenes.
1.2 Three-component cross-coupling involving 1,3-diene/enyne.
2. Photoredox and nickel-catalyzed three-component difunctionalizations of alkenes.
3. Photoredox and chromium-catalyzed three-component difunctionalizations of alkenes.

4. Photoredox and titanium-catalyzed three-component difunctionalizations of alkenes.
5. Photoredox and manganese-catalyzed three-component difunctionalizations of alkenes.
6. Photoredox and iron-catalyzed three-component difunctionalizations of alkenes.

PHOTOREDOX AND COPPER-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

Copper is emerging as a viable transition metal for catalytic cross-coupling reactions to forge carbon-carbon and carbon-heteroatom bonds. Moreover, excited copper complexes have strong reducing ability, sufficient lifetime and high luminescence intensity, which make them ideal candidates as photosensitizers[42,43]. Accordingly, different reaction mechanisms and roles for copper could be possible in copper-catalyzed reactions under visible-light irradiation, which significantly broadens the chemical space for synthesis. In 2022, Engl *et al*. summarized the concept, application and opportunities of atom transfer radical addition (ATRA) of copper-photocatalytic alkenes[44]. In terms of photoredox and copper-catalyzed three-component difunctionalizations of alkenes, typical general mechanisms are proposed and depicted in Scheme 1.

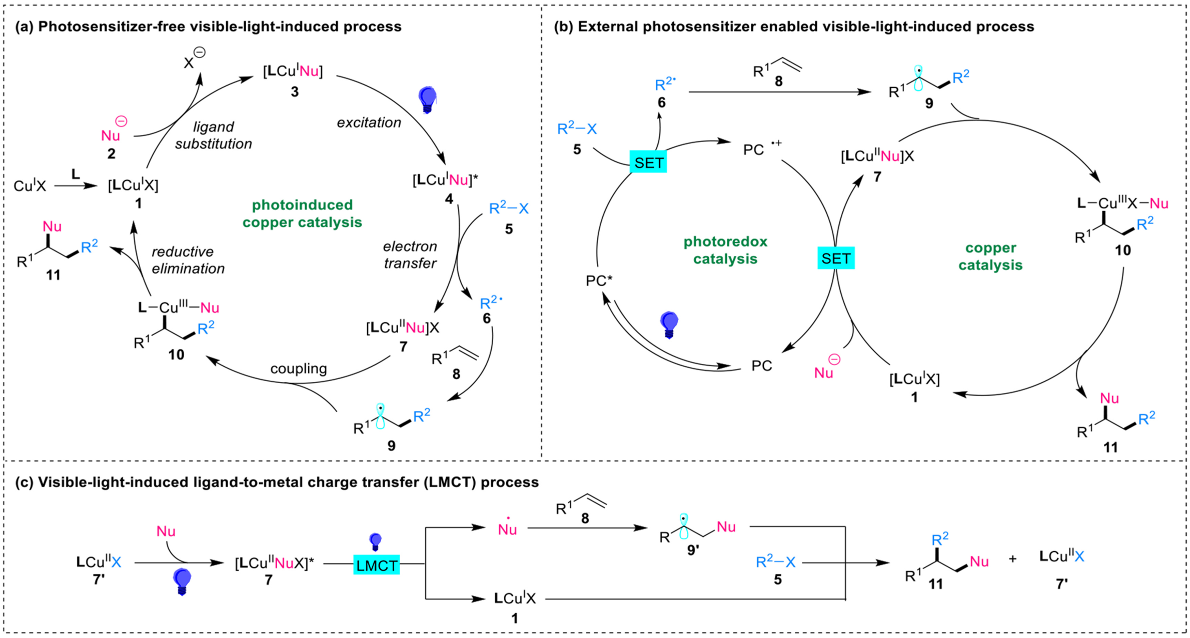
The first general pathway for copper-catalyzed alkene-involved three-component cross-coupling reactions under visible-light irradiation proceeds in the absence of external photocatalysts (PCs) [Scheme 1(a)]. First, cupric salt CuX and ligand **L** generate intermediate **1** *in situ*, which reacts with nucleophile **2** by ligand substitution to afford Cu^I-Nu adduct **3**. Upon irradiation, complex **3** absorbs light energy to become the excited-state complex **4**, which undergoes single electron transfer (SET) with electrophile **5** (such as alkyl halide) to deliver a carbon-centered radical **6** along with Cu^{II}-Nu species **7**. Next, the radical **6** is subsequently captured by alkenes **8** to generate a new radical intermediate **9**, which recombines with Cu^{II}-Nu species **7** to form Cu^{III} species **10**. Lastly, the trivalent copper species **10** undergoes reductive elimination to provide the final coupling product **11** and regenerate cupric salt CuX. In this reaction pathway, copper acts as both PC and transition-metal catalyst.

The second general pathway for copper-catalyzed alkene-involved three-component cross-coupling reactions under visible-light irradiation proceeds in the presence of an external PC [Scheme 1(b)]. First, the excited-state PC^* oxidizes the electrophilic reagents **5** to generate a carbon-centered radical **6** through a single-electron oxidation process, which then adds to the alkenes **8** to give new radicals **9**. Then, the Cu^{II}-Nu complex **7** is intercepted by radical **9** to furnish Cu^{III} species **10**, which undergoes rapid reductive elimination to deliver final product **11** and Cu^I complex **1**. Finally, **1** binds to the nucleophile Nu^-, which is then oxidized by $PC^{+\bullet}$ to regenerate Cu^{II} species **7** and ground-state PC, thereby finishing two catalytic cycles.

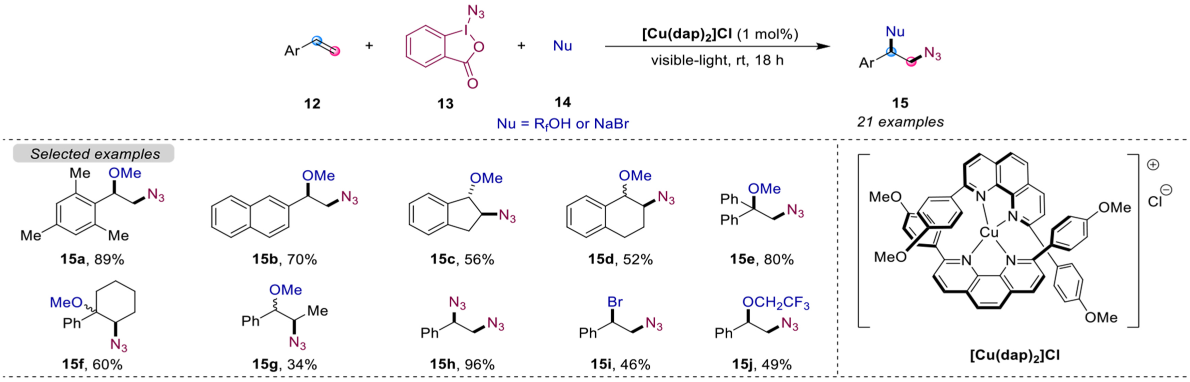
The above-mentioned pathways are initiated by radical generation along with the formation of Cu^{II} from Cu^I. The third pathway is generation of radicals by ligand-to-metal charge-transfer (LMCT) process to generate Cu^I from Cu^{II} [Scheme 1(c)][45-49]. Upon irradiation, $\mathbf{L}Cu^{II}NuX$ **7** is excited to undergo LMCT to generate radical $Nu^\bullet$ and $\mathbf{L}Cu^I$. Next, $Nu^\bullet$ is intercepted by alkenes to generate a new carbon-centered radical **9'**, which combines with electrophiles to afford the desired product **11** in the presence of $\mathbf{L}Cu^I$.

Three-component cross-coupling involving monoalkenes

In 2015, Fumagalli *et al.* developed a photoredox copper-catalyzed three-component reaction of styrenes **12** with Zhdankin reagent **13** and nucleophile **14** (ROH or NaBr) to afford nitrogen-containing small molecule building blocks **15** in 34%-96% yields [Scheme 2][50]. This transformation generates azide radicals from **13** under photocatalytic conditions, followed by the addition of alkenes **12** to obtain carbon-centered radicals, which are ultimately captured by polar molecules to deliver the final product **15**. Notably, this catalytic



Scheme 1. Typical pathways for photoinduced copper-catalyzed three-component cross-coupling of alkenes.

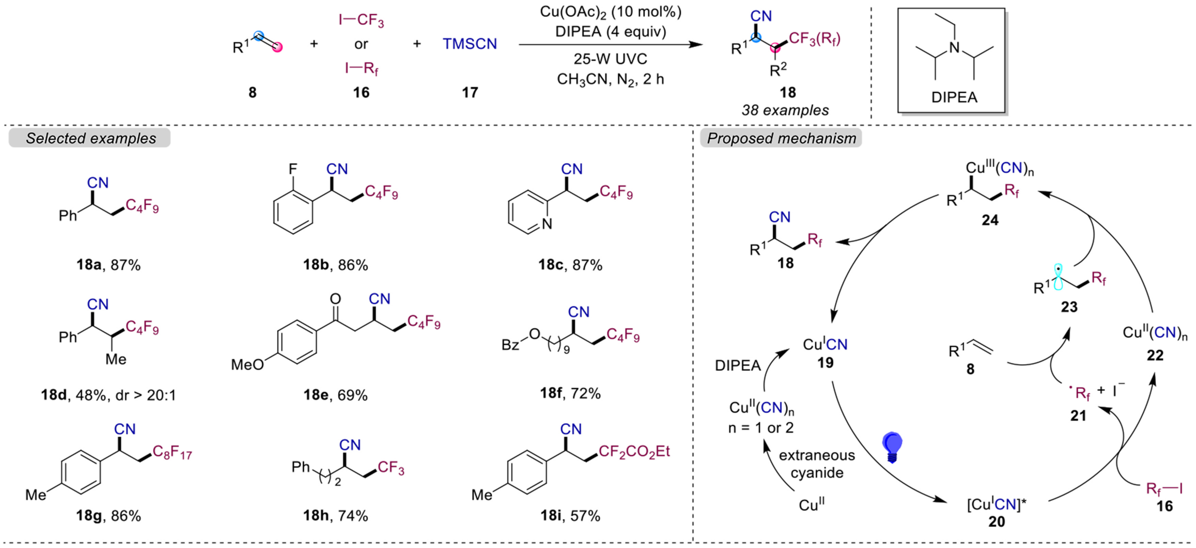


Scheme 2. Three-component azidation of styrenes with Zhdankin reagent and nucleophiles.

system is applicable only to aromatic alkenes as radical acceptors and methanol, trifluoroethanol, and sodium bromide as nucleophiles.

Moreover, [Cu(dap)$_2$Cl] can mediate the LMCT pathway. In 2018, Hossain *et al.* developed a photoinduced Cu-catalyzed oxo-azidation of arylalkenes with TMSN$_3$ and O$_2$ to give α-N$_3$-substituted aromatic ketones[51]. The reaction undergoes a LMCT process to generate radicals [Scheme 1(c)], where $N_3^{\bullet}$ is captured by styrenes to generate benzyl radicals. Interception of benzylic radicals by O$_2$ to produce the final products. In 2023, He *et al.* reported a visible-light-induced copper-catalyzed three-component reaction of arylalkenes with MgCl$_2$ and O$_2$ to deliver α-chloroketones[52].

In 2017, Guo *et al.* reported the first example of photoinduced, copper-catalyzed three-component cyanofluoroalkylation of alkenes using fluoroalkyl iodides **16** as fluoroalkylation reagents [Scheme 3][53]. With a compact fluorescent light bulb irradiation, alkenes **8** react with fluoroalkyl iodides **16** and



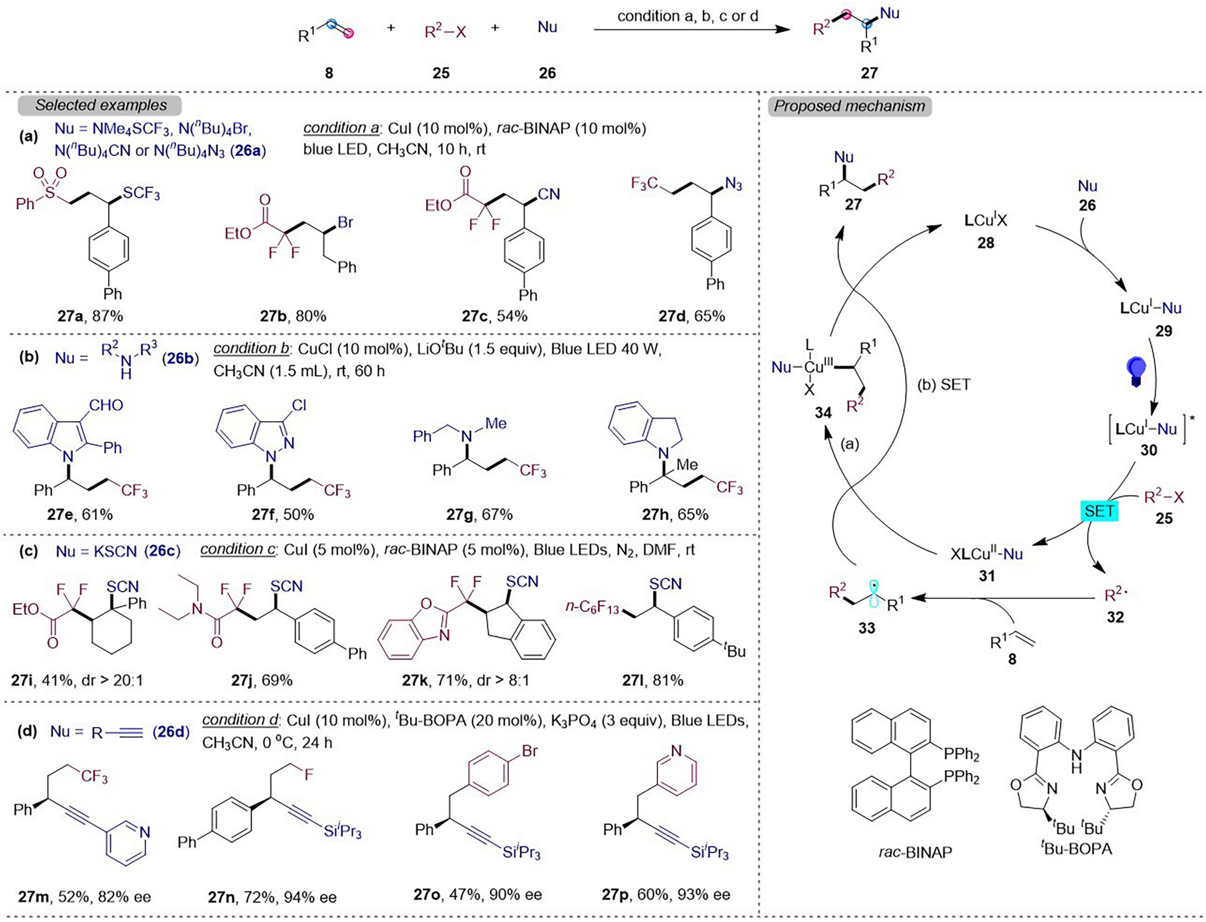
Scheme 3. Photoinduced and copper-catalyzed cyanofluoroalkylation of alkenes.

trimethylsilyl cyanide (TMSCN) **17** to give difunctionalization product **18** in 48%-91% yields. The strategy uses *N*,*N*-diisopropylethylamine (DIPEA) as a sacrificial reducing agent, and is applicable to both alkyl and aryl alkenes. Moreover, using inexpensive and readily available fluorinated alkyl iodides instead of Togni's or Umemoto's reagents as fluoroalkyl precursors renders the reaction suitable for large-scale synthesis.

Copper acetate [$Cu(OAc)_2$] and extraneous cyanide TMSCN **17** undergo rapid ligand exchange and are followed by SET with electron-rich DIPEA to form $Cu^{I}CN$ **19**, which is converted into its triplet state $[Cu^{I}CN]^*$ **20** by 25 W ultraviolet-C (UVC) irradiation. Then, the oxidative quenching step switched **16** into alkyl radical **21** and iodine ion along with recycling of $Cu^{II}(CN)_n$ **22**. Subsequently, alkene **8** captures **21** to generate a new radical **23**, which rebounds with **22** to form key intermediate Cu^{III} species **24**. Finally, reductive elimination of **24** delivers the desired product **18** and regenerates **19** to complete the catalytic cycle. Notably, Cu^{I} and Cu^{II} salts showed good catalytic activities; these results indicated that the catalytic cycle could be initiated either from Cu^{II} or from Cu^{I}.

In 2018, He *et al.* described a visible-light-promoted Cu^{I}/BINAP catalyzed three-component cross-coupling of alkenes (including styrenes and electron-poor alkenes) **8** with alkyl halides **25** and nucleophiles **26a** (trifluoromethylthiolate, bromide, cyanide and azide) to afford **27** in 54%-98% yields [Scheme 4(a)][54]. In this process, a photoexcited $LCu^{I}Nu$ complex served as a reductant to generate an alkyl radical from alkyl halides. Moreover, this catalytic system is suitable for styrenes or electron-poor alkenes, but the alkyl halides require strong electron-withdrawing groups at β-position, such as carbonyl, fluorine or sulfone groups.

In 2019, Xiong *et al*. reported a visible-light-mediated copper-catalyzed carboamination of alkenes with alkyl halides and primary/secondary amines to give alkylamination with 30%-86% yields [Scheme 4(b)][55]. In this reaction, CuCl serves as both PC and cross-coupling catalyst. This method is suitable for aryl alkenes and 1,3-dienes and tolerates both primary and secondary amines under mild conditions. Notably, a catalytic amount of ligand (*rac*-BINOL) is needed for this transformation when non-carbazole secondary amines are used as coupling partners.



Scheme 4. Visible-light-induced, copper-catalyzed three-component cross-coupling of alkenes with alkyl halides and nucleophiles.

In 2023, Hu *et al.* reported a photoinduced and Cu-catalyzed three-component cross-coupling reaction of styrenes with KSCN and fluorinated alkyl halide to give difluorothiocyanate compounds in 41%-82% yields [Scheme 4(c)][56]. CuI/*rac*-BINAP plays a dual role as photoredox catalyst for electron transfer and cross-coupling catalyst for C–SCN bond formation. Notably, this catalytic system is compatible with various 1-, 1,2-, 1,1-, and 1,1,2-substituted styrenes and directed aliphatic alkenes. Moreover, activated alkyl halides are suitable alkyl radical precursors for this reaction.

Similarly, Zhang *et al.* reported a photoinduced, Cu-catalyzed three-component cross-coupling of aryl alkenes with terminal alkynes and aryl/alkyl iodides to form propargylic skeleton in 40%-93% yields[57]. This method uses 2,2':6',2"-terpyridine as a ligand and is applicable to hetero/aryl alkenes, terminal aryl/alkylalkynes, and aryl/alkyl iodides. Later, Zhang *et al.* developed visible-light-mediated Cu-catalyzed enantioselective alkylalkynylation and arylalkynylation of styrenes with terminal alkynes and alkyl/aryl iodides to afford chiral propargylic building blocks in 13%-87% yields with up to 98% ee [Scheme 4(d)][58]. Chiral Cu^I/^{t}Bu-BOPA complexes act as both PC and transition-metal catalysts to induce the enantioselectivity of the products. This method is compatible with styrenes with diverse substitution patterns, terminal alkynes, and aryl and alkyl iodides. Unfortunately, aliphatic alkenes fail to undergo this enantioselective process.

The general mechanism of the reaction between alkenes, alkyl halides, and nucleophiles is described in Scheme 4. Firstly, the Cu^{I} complex **28** underwent ligand exchange with nucleophiles **26** to form intermediate Cu^{I}-nucleophile complex **29**, which was converted to excited-state Cu^{I} species **30** under light radiation. Then, alkyl halides **25** interacted with **30** by SET to generate Cu^{II}-nucleophile complex **31** and alkyl radicals **32**. Alkyl radicals **32** were captured by alkenes **8** to form a new radical species **33**. Two possible pathways may lead to the formation of the target products **27** from **33**. Radicals **33** rebounded with Cu^{II} species **31** to generate Cu^{III} complex **34**, followed by reductive elimination to provide the products **27** and regenerate Cu^{I} species **28** (path a). Alternatively, radicals **33** could directly coupling with **31** through a SET process to deliver the target products **27** and Cu^{I} species **28** (path b).

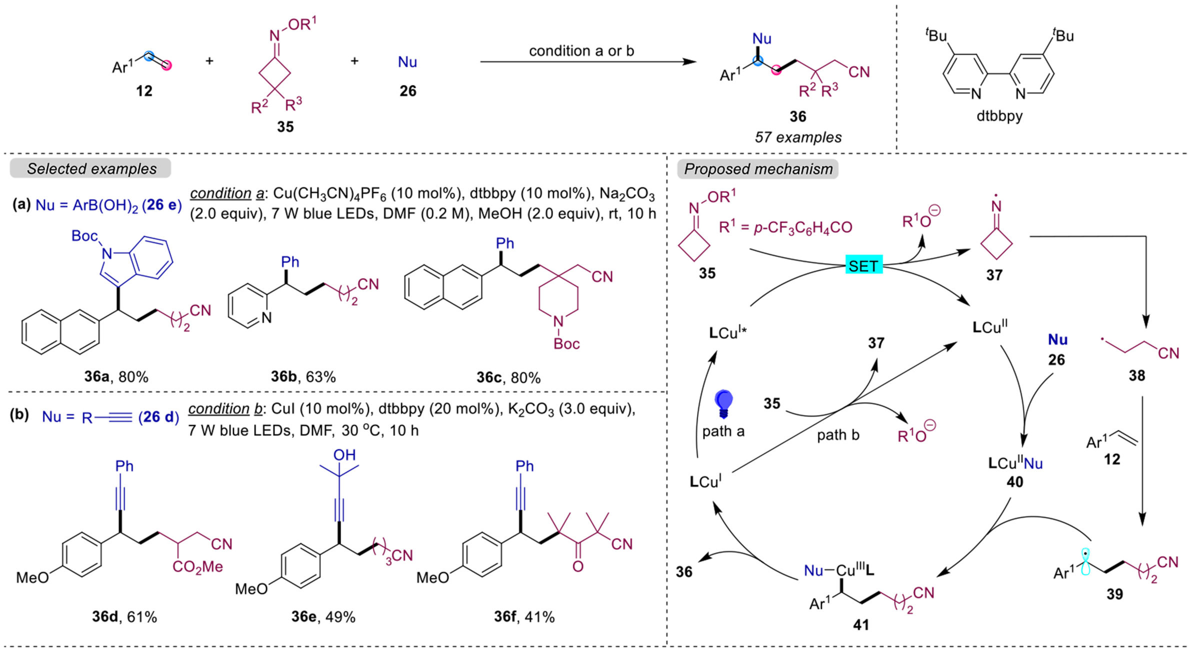
In 2018, Yu *et al.* developed a visible-light-promoted Cu/dtbbpy catalyzed three-component cross-coupling of styrenes **12** with oxime esters **35** and nucleophiles aryl/vinyl boronic acids **26e**, providing 1,1-diarylmethane containing alkylnitriles **36** in 20%-90% yields [Scheme 5(a)][59]. This protocol is applicable to various aromatic alkenes, aryl and vinyl boronic acids. However, only oxime esters derived from cyclobutanones are suitable for this reaction. Very recently, a general visible-light-promoted copper-catalyzed asymmetric three-component cross-coupling of alkenes with oxime carbonates and aryl boronic acids has been developed, delivering chiral benzylic alkynes and allenes in 19%-87% yields with 30%-96% ee[60]. Notably, copper/Box complexes play a dual role in both alkyl radical generation and subsequent asymmetric cross-coupling with aryl boronic acids.

Moreover, using terminal alkynes **26d** instead of arylboronic acids, reaction can be conducted under similar conditions to afford alkylalkynylation of styrenes in 14%-76% yields [Scheme 5(b)][61]. This strategy combines photoinduced iminyl radical mediated C–C bond cleavage with copper-catalyzed C(sp^3)–C(sp) cross-coupling.

These reactions utilized oxime esters as cyanoalkyl radical precursors, which underwent SET with ligated Cu^{I} species to give Cu^{II} species and iminyl radicals **37**, followed by ring-opening of four-membered ring to give cyanoalkyl radicals **38**. Radical addition of **38** onto styrenes **12** generated benzylic radicals **39**. Recombination of **39** with Cu^{II}-Nu species **40**, generated from transmetalation of ligated Cu^{II} species with nucleophiles **26** (aryl boronic acids or terminal alkynes), gave Cu^{III} species **41**. Reductive elimination of **41** delivered the final products and the regeneration of ligated Cu^{I} species.

In 2019, Lv *et al*. developed a visible-light-promoted copper-catalyzed three-component coupling of alkenes **8** with aryl boronic acids **26e** and α-bromocarbonyl precursors **42** to synthesize γ arylated carbonyls **43** in 45%-88% yields [Scheme 6][62]. In the absence of a directing group, the protocol allows for the sequential formation of C(sp^3)–C(sp^3) and C(sp^3)–C(sp^2) bonds under ambient conditions. Additionally, this catalytic method is compatible with a wide range of aryl and alkyl alkenes, aryl boronic acids, and α-bromo-carbonyls.

Under visible-light irradiation, the ground-state photocatalyst Ir^{III} was converted into its excited-state Ir^{III*}, which interacted with α-bromocarbonyl precursor **42** by SET process to afford an alkyl radical **44** and Ir^{IV}. Then, intermediate **44** was trapped by alkene **8** to give a new alkyl radical **45**. Meanwhile, Cu^{I} transmetalated with aryl boronic acid **26e** in the presence of a base to provide Ar-Cu^{I} intermediate **46**. Rebound of **46** with alkyl radical **45** formed Cu^{II} intermediate **47**, which further underwent SET to reduce Ir^{IV} to ground-state Ir^{III}, followed by reductive elimination to deliver the final products **43** and Cu^{I} species to close the catalytic cycles.

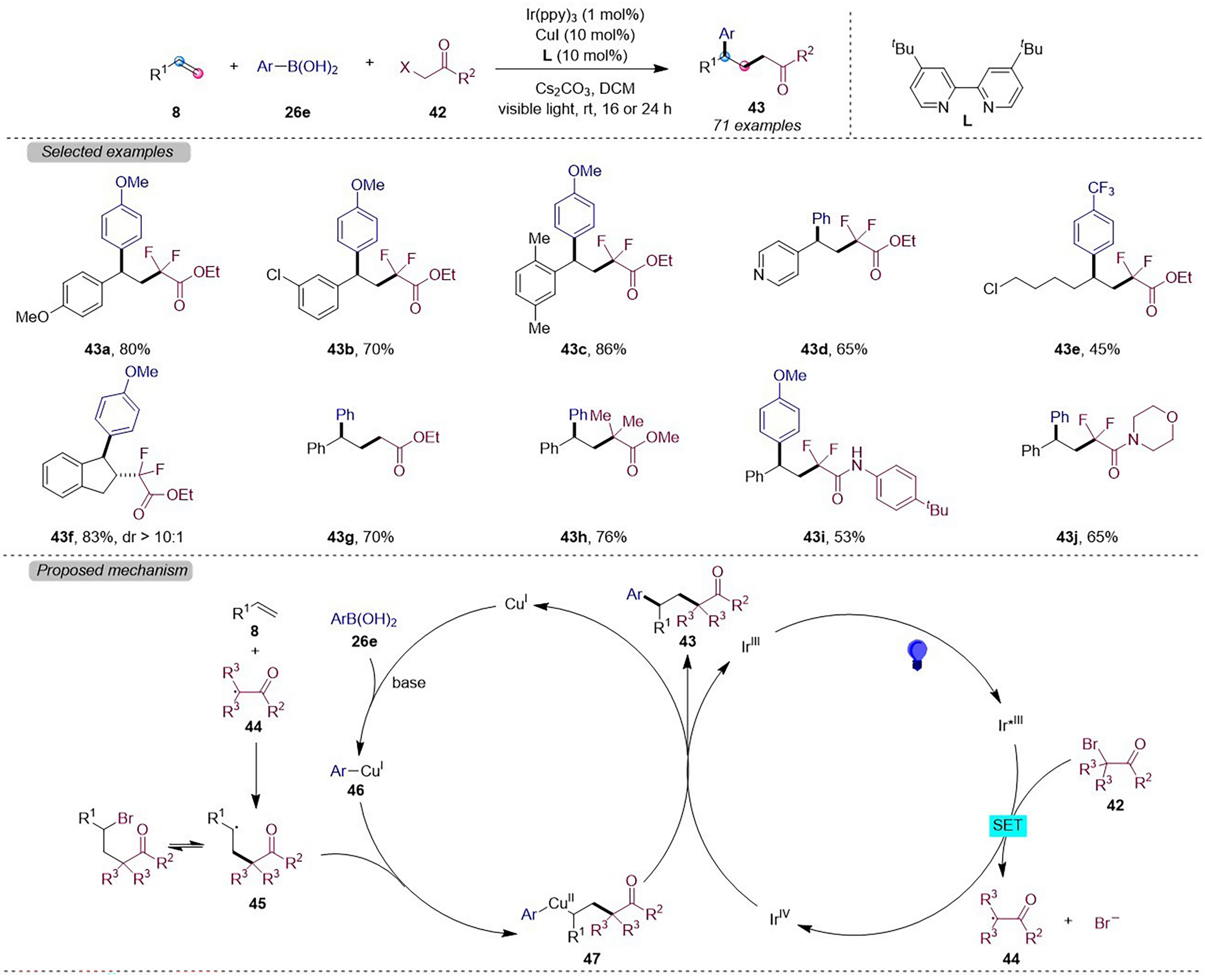


Scheme 5. Photoinduced copper-catalyzed cross-coupling of styrenes with oxime esters and nucleophiles.

Then, Lv *et al.* further described a visible-light and copper dual-catalyzed three-component cross-coupling of alkenes **8** with α-bromocarbonyl precursors **42** and terminal alkyne silicates **48** to furnish γ-alkynylated esters, acids, amides, ketones and aldehydes **49** in 33%-80% yields [Scheme 7][63]. The strategy is operationally simple and does not require a directing group, and a series of readily available starting materials can be assembled at the γ-position of the carbonyl group. Cu^{I}**L** complex **50** coordinates with alkynes to form alkynyl Cu^{I} species **51**, which interacts with α-bromocarbonyl precursors **42** to give alkyl radicals **52** and alkynyl Cu^{II} **53**. Then, alkyl radicals add to the C=C double bond of alkenes **8** to provide benzyl radicals **54**, which are then intercepted by **53** to afford key intermediate Cu^{III} species **55**. Finally, Cu^{III} species **55** are excited by Ir^{III} photocatalyst to generate $[Cu^{III}]^{*}$ species **56**, followed by accelerated reductive elimination to produce desired products **49**.

In 2021, Wang *et al.* developed a photoredox and copper-catalyzed three-component enantioselective carbocyanation of styrenes **12** with redox-active oxime esters (**57** or **35**) and TMSCN **17** to provide β-cyano ketones (**58**) and 1,5-dinitriles (**59**) in 24%-86% yields with 82%-97% ee [Scheme 8][64]. The success of this process hinges on the chemoselective addition of acyl and cyanoalkyl radicals to styrenes, which are generated *in situ* by the C–C bond cleavage triggered by the photocatalytic nitrogen-centered iminyl radical of the redox-active oxime ester. This reaction tolerates a range of styrenes, yet fails to aliphatic alkenes.

The reaction is initiated by the excitation of the PC to PC^{*} under purple light-emitting diode (LED) irradiation. Redox-active oxime esters **57** or **35** went through a SET reduction process with PC^{*} to afford iminyl radicals **60** or **37** along with carboxylic anions and oxidized photocatalyst $PC^{\bullet+}$. Next, iminyl radicals underwent C–C bond β-cleavage to form acyl and cyanoalkyl radicals **61** and **38**, which were trapped by styrenes **12** through radical addition to deliver benzylic radicals **62**. Meanwhile, initially released carboxylic anion promoted the ligand exchange between $\mathbf{L}Cu^{I}$ species and TMSCN **17** to furnish $\mathbf{L}Cu^{I}CN$ complex **63**, which interacted with $PC^{\bullet+}$ to generate $\mathbf{L}Cu^{II}(CN)_2$ complex **64** and regenerate PC in the presence of TMSCN. Next, pro-chiral benzylic radicals **62** rebounded with **64** to form chiral high-valent Cu^{III} complex

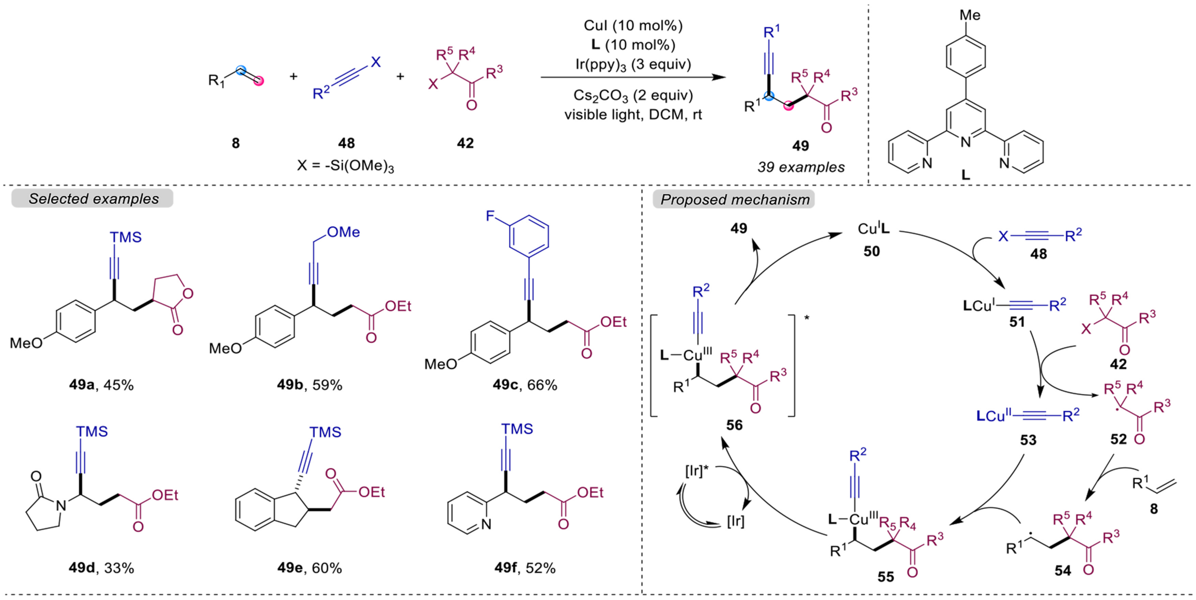


Scheme 6. Photoinduced and copper-catalyzed radical relay alkylarylation of alkenes.

65, followed by reductive elimination to give enantioenriched β-cyano ketones **58** or alkyldinitriles **59** and regenerate Cu^I species **63**.

As a class of zwitterions, the transformation of sulfur ylides through ion pathways has been widely studied. However, there are relatively few reports on sulfur ylides as radical precursors. In 2022, Yan *et al.* developed a photoinduced and stoichiometric $Cu(TFA)_2 \cdot H_2O$ mediated three-component radical addition/hydroxylation reaction of styrenes **12** with sulfur ylides **66** to deliver γ-hydroxy carbonyl compounds **67** in 44%-99% yields in the presence of water [Scheme 9][65]. α-Carbonyl carbon-centered radicals **70** were the key intermediate in the transformation, which was formed by the proton-coupled electron transfer (PCET) of sulfur ylides **66** in a mixed solvent [CF_3CH_2OH/dichloromethane (DCM) = 4:1] via **68** to release dimethyl sulfide **69**. Addition of **70** to styrenes **12** led to the formation of benzylic radicals **71**, which was oxidized to benzylic cations **72** enabled by stoichiometric $Cu(TFA)_2 \cdot H_2O$. In the presence of water, **72** was quenched to deliver the final product **67**. Moreover, this protocol is suitable for styrenes, yet not for aliphatic alkenes.

Atom transfer radical addition (ATRA) reaction or Kharasch addition was first discovered by Kharasch *et al.* in the 1940s[66-68]. In 2022, Wang *et al.* described a photoinduced Cu-catalyzed asymmetric ATRA-type reaction of styrenes **12** with carboxylic acids **73** and radical precursors **74** to deliver enantioenriched



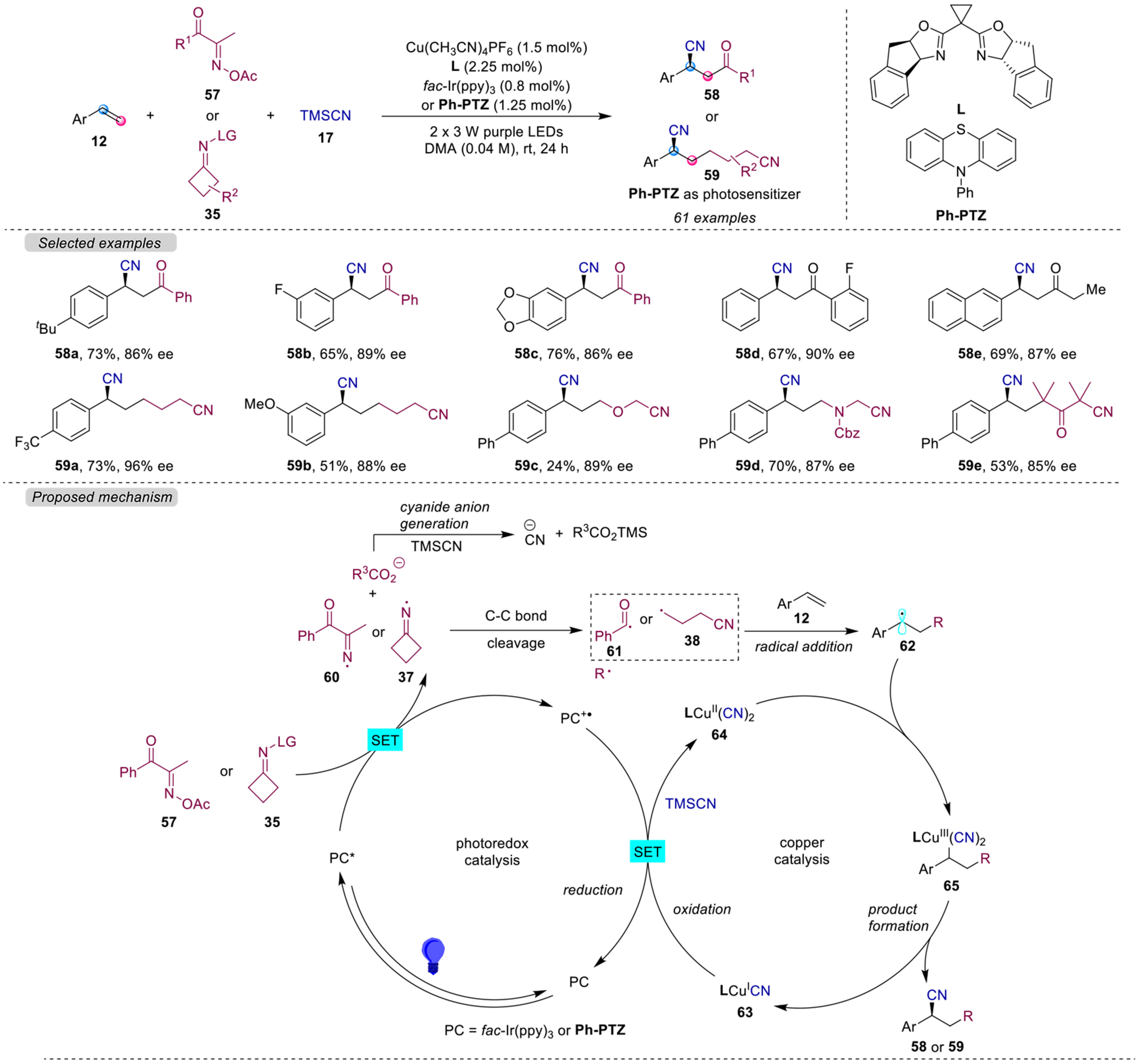
Scheme 7. Visible-light-induced copper-catalyzed alkylalkynylation of styrenes.

benzylic alcohol derived esters **75** in 46%-92% yields with 55%-97% ee [Scheme 10][69]. This method is compatible with terminal styrenes and a wide range of aromatic/aliphatic carboxylic acids. In addition, radical precursors may include cyclobutanone-derived oxime esters, alkylsilyl peroxides, and lauroyl peroxides.

The transformation proceeds under redox-neutral conditions without the use of external oxidants. First, the ligand exchange between the complex of $Cu(CH_3CN)_4PF_6$/(*S*,*S*)-**L** and carboxylic acids **73** provided light-absorbing intermediate [**L**/Cu^I/X] (X = PF_6^- or $ArCO_2^-$) species **76**. Upon purple light irradiation, **76** was excited to its excited-state $[\mathbf{L}/Cu^I/X]^*$ **77**, followed by SET with oxime esters **35** to furnish iminyl radicals **37** and [**L**Cu^{II}/O_2CAr]X **78** along with the formation of carboxylic anion ($BocO^-$). Driven ring strain release, **37** underwent β–C–C bond cleavage to afford cyanoalkyl radicals **38**, which further added to styrenes **12** to form benzylic radicals **79**. Subsequently, **78** recombined with benzylic radicals **79** to provide Cu^{III} species **80** via a radical rebound process. Finally, intermediate **80** went through reductive elimination to forge enantioselective C–O bond to give final products **75** and regenerate **76**.

To date, synthesis of highly functionalized acyclic (hetero)arylethylamines remains challenging. Cai *et al.* described a visible-light-induced and copper-catalyzed three-component reaction of alkenes **8** with arylthianthrenium salts **81** and sodium azide **82** to deliver functionalized acyclic (hetero)arylethylamine scaffolds **83** in 36%-73% yields [Scheme 11][70]. Importantly, *rac*-BINAP coordinated with $Cu(CH_3CN)_4BF_4$ and NaN_3 *in situ* to form *rac*-BINAP-Cu^I-N_3 **84** as photoactive catalytic species, and its structure was confirmed by X-ray diffraction analysis. Notably, this strategy can be applied to both aryl and aliphatic alkenes.

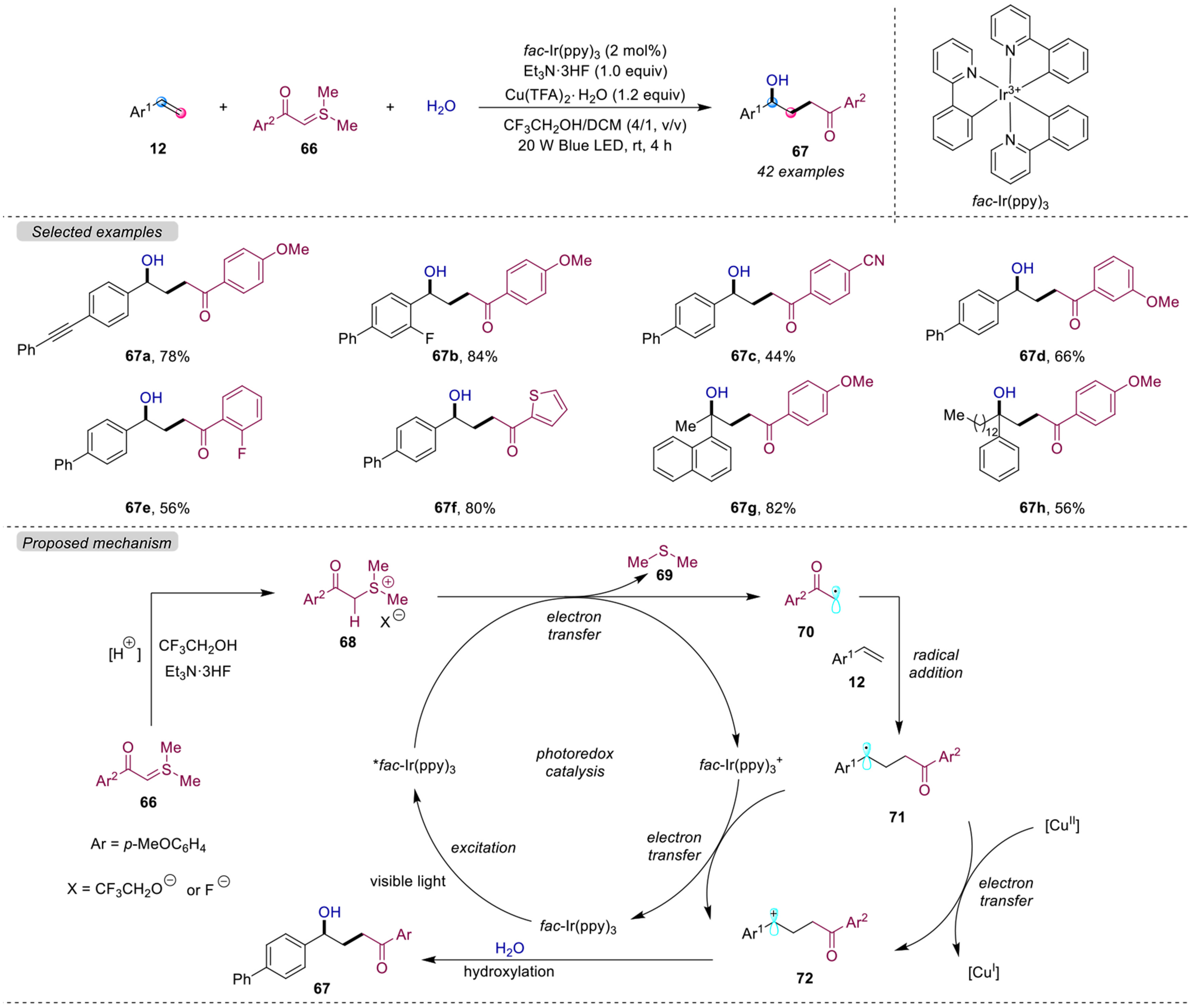
Upon visible-light irradiation, *rac*-BINAP-Cu^I-azide **84** was converted to its excited-state **85**, followed by reaction with arylthianthrenium salts **81** by single-electron reduction to form aryl radicals **86** and Cu^{II} complex **87** or its cationic counterpart. Next, aryl radicals **86** were captured by carbon-carbon double bonds of alkenes **8** to produce alkyl radicals **88**, which underwent azido transfer from **87** via an outer-sphere route to afford the products **83** and regenerate photoactive catalytic species **84**.



Scheme 8. Photoinduced Cu-catalyzed asymmetric three-component carbocyanation of styrenes.

In 2024, Zhang *et al.* developed a visible-light-promoted and copper-catalyzed enantioselective cyanofunctionalization of styrenes **12** with electrophiles (H^+, D^+, CO_2) **89** and nucleophiles **90** to deliver a series of chiral cyanides **91** with 23%-97% yields and 64%-99% ee [Scheme 12][71]. This dual catalytic strategy generates alkene radical anions, achieving regio-, chemo-, and enantioselective hydrocyanation, deuterocyanation and cyanocarboxylation of styrenes. Additionally, this method is suitable for various terminal and internal styrenes under mild conditions.

The catalytic cycle begins with the excitation of PC to PC^*, which interacted with styrenes **12** by a SET process to produce the key intermediate alkene radical anion **92** and oxidized-state $PC^{\bullet+}$. Subsequently, protonation of alkene radical anion **92** by **89** (such as H_2O or HCN, which was generated *in situ* from TMSCN and H_2O) delivered benzylic radicals **93**. Meanwhile, CuTc coordinated with ligand and underwent further ligand exchange with TMSCN to form the $\mathbf{L}Cu^ICN$ species **94**, followed by a SET pathway with oxidized $PC^{\bullet+}$ to provide $\mathbf{L}Cu^{II}(CN)_2$ species **95** and PC. Finally, benzylic radical **93** rebounded with **95** to

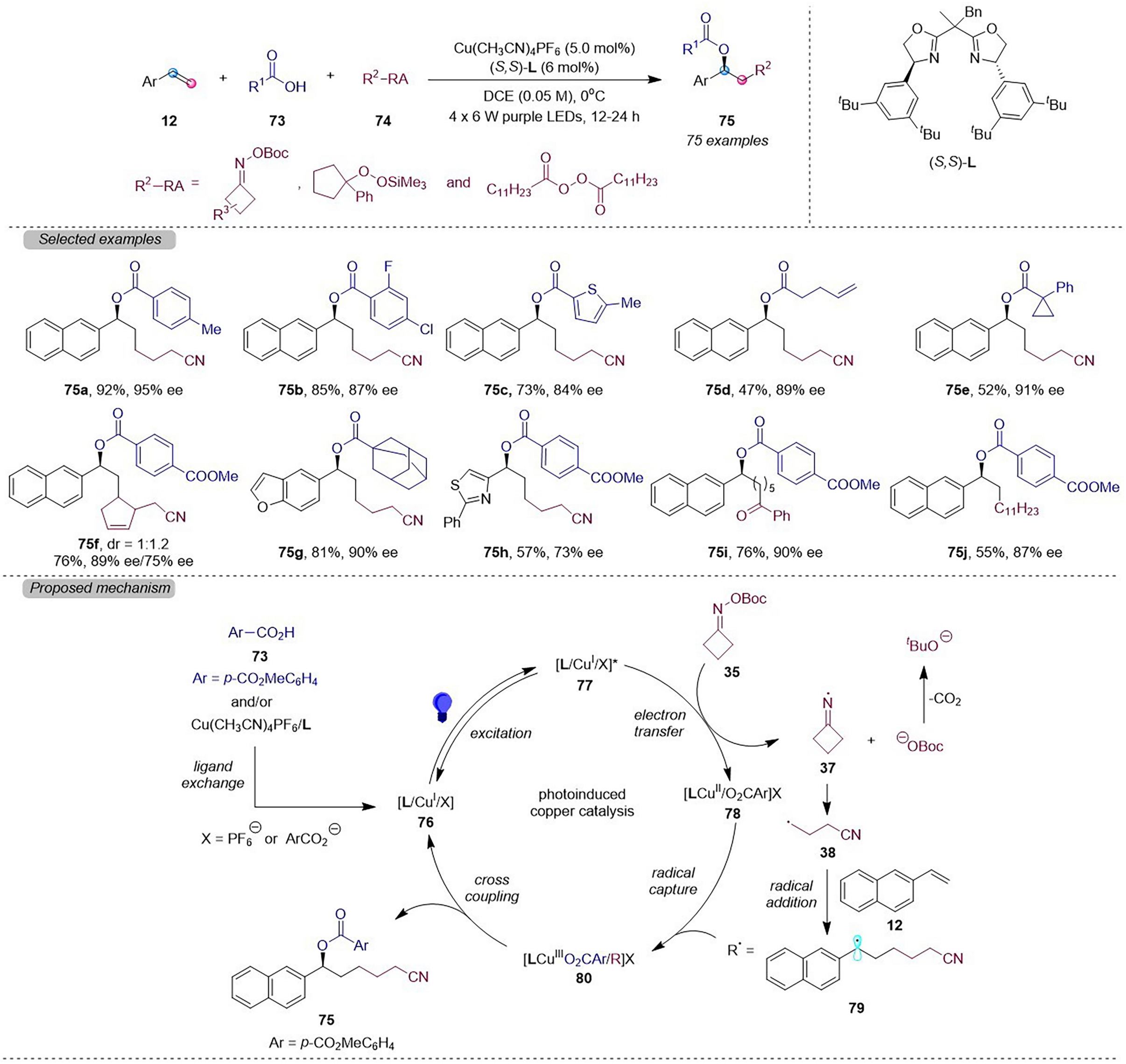


Scheme 9. Visible-light and copper mediated alkylhydroxylation of styrenes.

give key Cu^{III} complex **96**. Further reductive elimination of **96** furnished the final products **91** and catalytic species **94**.

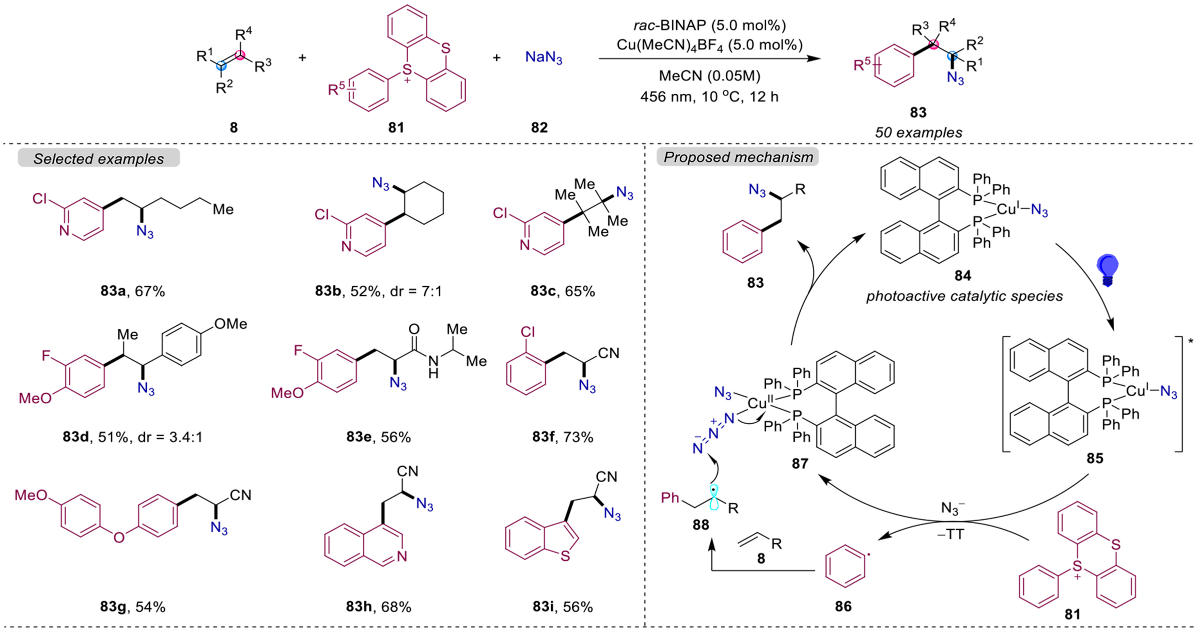
Three-component cross-coupling involving 1,3-diene/enyne

Compounds 1,3-dienes are widely used in the synthesis of various value-added architectures. There are two reaction modes: 1,2- and 1,4-difunctionalizations of 1,3-dienes via allyl intermediates. Recently, the use of 1,3-dienes to build molecular complexity has been studied extensively. In 2021, Wang *et al.* reported a visible-light-mediated and Cu-catalyzed three-component coupling reaction of 1,3-dienes **97a** with oxime esters **35** and carboxylic acids **73** to furnish a series of chiral esters in 63%-89% yields with 37%-96% ee under mild conditions [Scheme 13(a)][72]. Importantly, this protocol can be applied to Kharasch-Sosnovsky reaction. Moreover, this strategy was featured with mild reaction conditions, operational simplicity, inexpensive substrates, and compatibility with aryl 1,3-dienes, aryl/alkyl carboxylic acids, and cyclobutanone-type oxime esters. Unfortunately, the catalytic system has poor regioselectivity (rr = 1:1) and enantioselectivity (39% ee) for alkyl 1,3-dienes.



Scheme 10. Photoinduced Cu-catalyzed enantioselective alkylesterificaiton of styrenes.

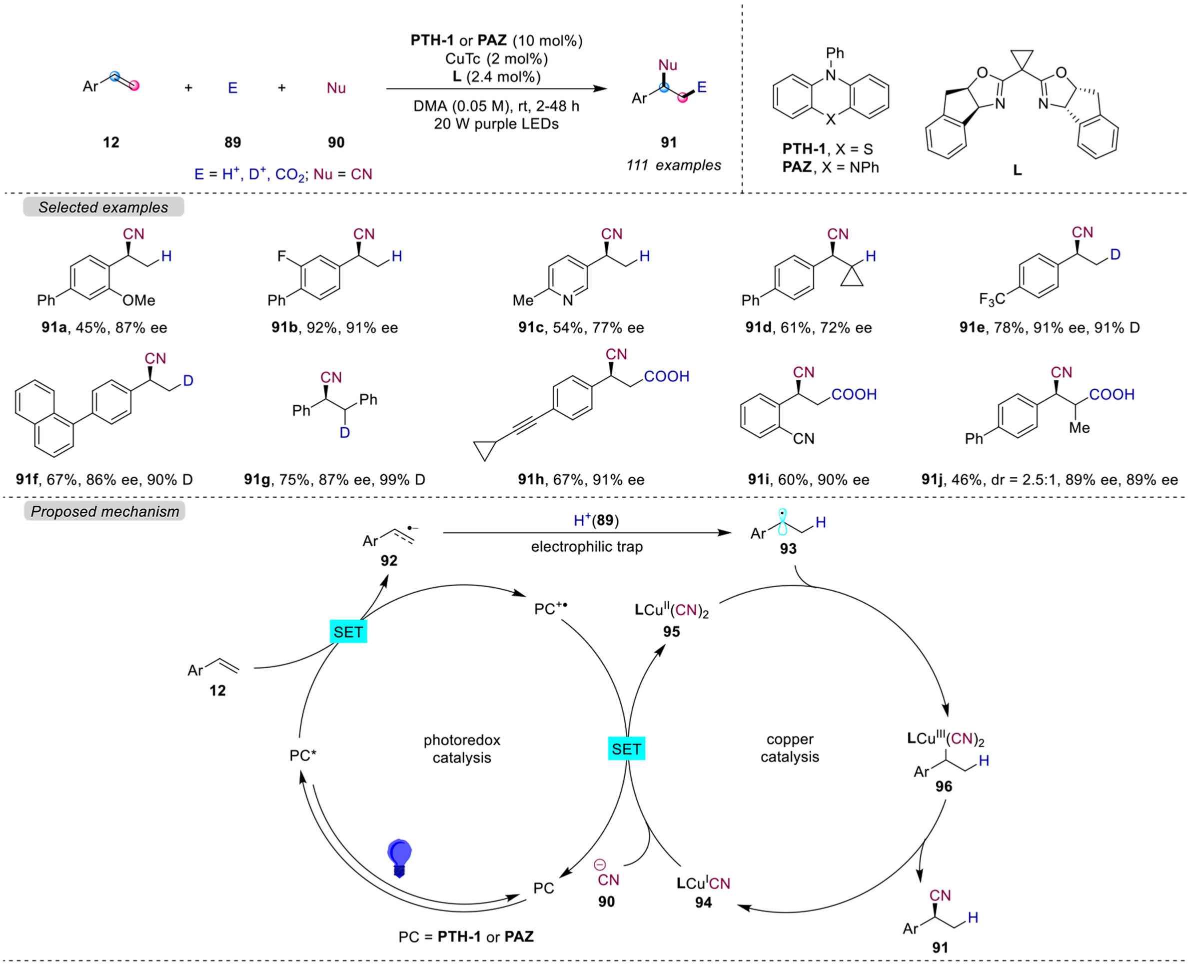
Building blocks, 1,3-enynes, can quickly and efficiently construct complex and functionalized molecules. The presence of both carbon-carbon double bonds and carbon-carbon triple bonds in 1,3-enynes facilitates their use in the synthesis of 1,3-dienes, allenes and propargyl compounds. Therefore, the challenge in organic synthesis is to accurately control chemo-, regio- and enantioselectivity when 1,3-enynes are involved. In 2023, Li *et al.* developed a visible-light-promoted Cu-catalyzed regio- and enantioselective radical coupling of 1,3-enynes **97b** with oxime esters **35** and carboxylic acids **73** to form cyanoalkylated propargylic esters with 61%-95% yields and 18%-99% ee [Scheme 13(b)][73]. This protocol is compatible with a range of aryl-substituted 1,3-enyne, aryl/alkyl carboxylic acids, and oxime esters derived from cyclobutanone. However, it should be noted that the enantioselectivity of alkyl-substituted 1,3-enyne is significantly reduced.



Scheme 11. Photoinduced copper-catalyzed arylazidation of alkenes.

The radical-involved multi-component bifunctionalization of 1,3-dienes has recently emerged as a promising strategy for the rapid synthesis of valuable allyl compounds in one-pot. However, expanding the scope of accessible radicals and achieving precise enantiomeric control remain major challenges. In 2024, Li *et al.* described a visible-light-mediated copper-catalyzed enantioselective three-component cross-coupling of 1,3-dienes **97a** with azidobenziodazolone reagent (Ts-ABZ) **98** and carboxylic acids **73** to obtain the final product **99** with 27%-80% yield and 62%-98% ee [Scheme 13(c)][74]. The results of mechanistic studies have demonstrated that chiral copper complexes not only function as PCs, generating azide radicals, but also act as catalysts for enantioselective radical C–O cross-coupling. Moreover, this dual catalytic system has been demonstrated to be suitable for the synthesis of various aryl-substituted 1,3-butadiene and aryl/alkyl carboxylic acids. However, the reaction of alkyl-substituted 1,3-butadiene has not yet been successful.

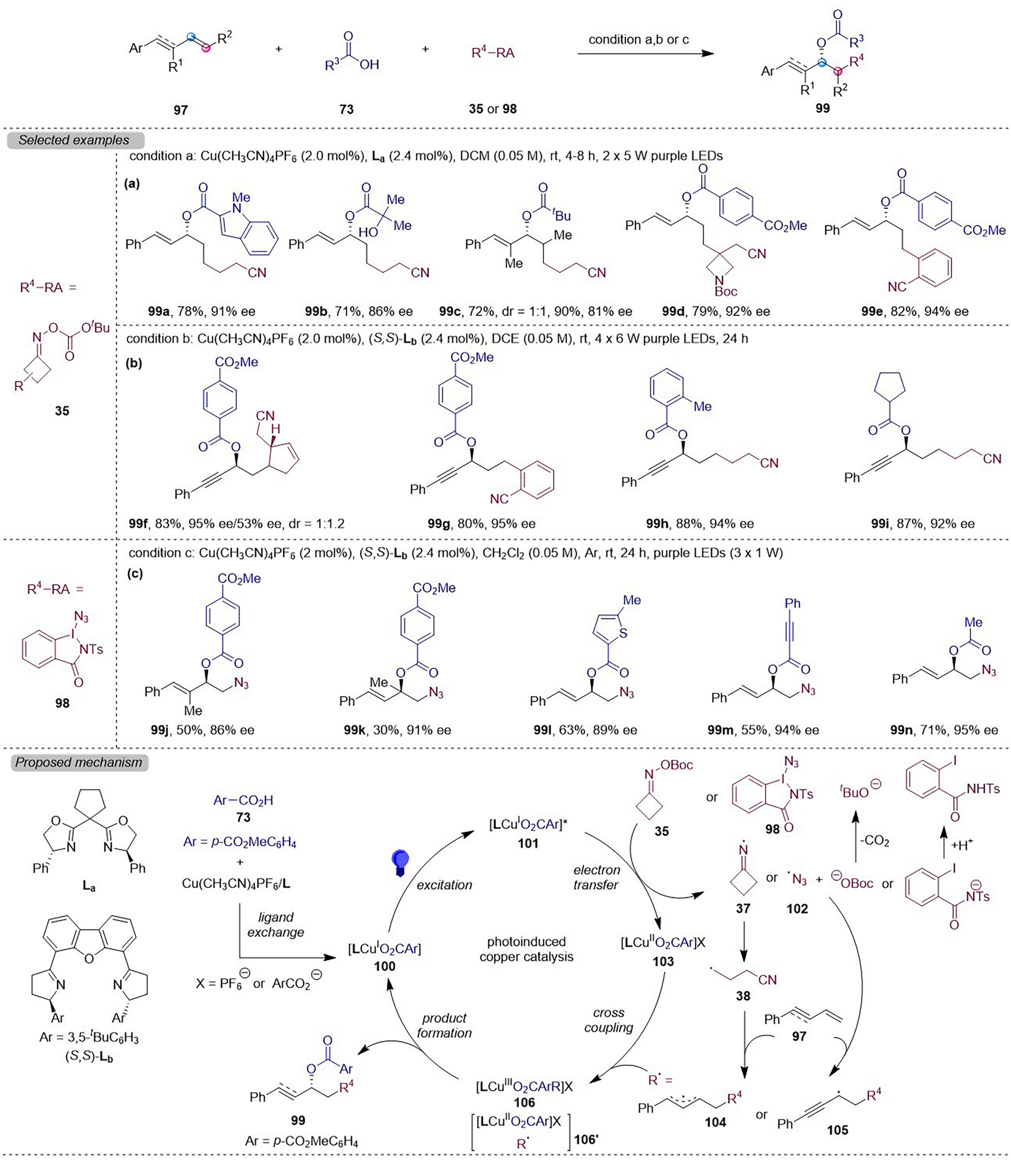
The general mechanism of visible-light-induced Cu-catalyzed reactions of 1,3-diene/1,3-enynes with carboxylic acids and radical precursors is illustrated in Scheme 13. The catalytic cycle starts with ligand exchange between carboxylic acids **73** and $Cu(CH_3CN)_4PF_6$/**L** to generate [**L**/Cu^IO_2CAr] species **100**, which transforms to its excited-state **101** under purple light irradiation, followed by engaging in SET pathway with oxime esters **35** or Ts-ABZ **98** to give iminyl radicals **37** or azidyl radical **102**, Cu^{II} species **103** and a carboxylic anion ($BocO^-$). Subsequently, iminyl radicals **37** undergo a ring strain-driven β–C–C bond cleavage, resulting in the formation of cyanoalkyl radicals **38,** which combine with 1,3-dienes **97a** to provide the relatively stable allylic radicals **104.** On the other hand, azidyl radical **102** is captured by 1,3-enynes **97b** to form stabilized propargyl radicals **105**. Then, **104** or **105** are intercepted by Cu^{II} species **103** via a radical rebound process, resulting in the formation of π-allyl Cu^{III} complex **106.** This complex undergoes reductive elimination, leading to the generation of the final product **99** in an enantioselective manner, while simultaneously regenerating **100** and completing the catalytic cycle. Notably, π-allyl Cu^{III} complex **106** also might exist in equilibrium with hybrid allylic Cu^{II} radical **106'**.



Scheme 12. Photoinduced copper-catalyzed enantioselective cyanofunctionalization of styrenes.

The emergence of bifunctional reagents that serve as dual coupling partners with an activating species has become valuable synthetic tools in organic chemistry. Such reagents permit the development of various reaction modes with enhanced efficiency and structural variability, which is highly sought after for atom-economic and sustainable synthesis. Chen *et al.* reported a visible-light-promoted copper-catalyzed regio- and enantioselective 1,2-dicarbofunctionalization of 1,3-dienes **97a** with oxime esters **35** to simultaneously construct C–C and C–O bonds to deliver allylic esters in 24%-94% yields with 17%-95% ee [Scheme 14][75]. As a bifunctional reagent, the redox oxime esters form a π-allyl copper complex with 1,3-dienes **97a** through a radical polarity crossing process. Furthermore, the copper-based chiral catalyst functions as both the photoredox catalyst for radical formation and the source of asymmetric induction in C–O coupling. This strategy is applicable to aryl 1,3-dienes under mild conditions. However, the regioselectivity and enantioselectivity of alkyl-substituted 1,3-dienes are poor.

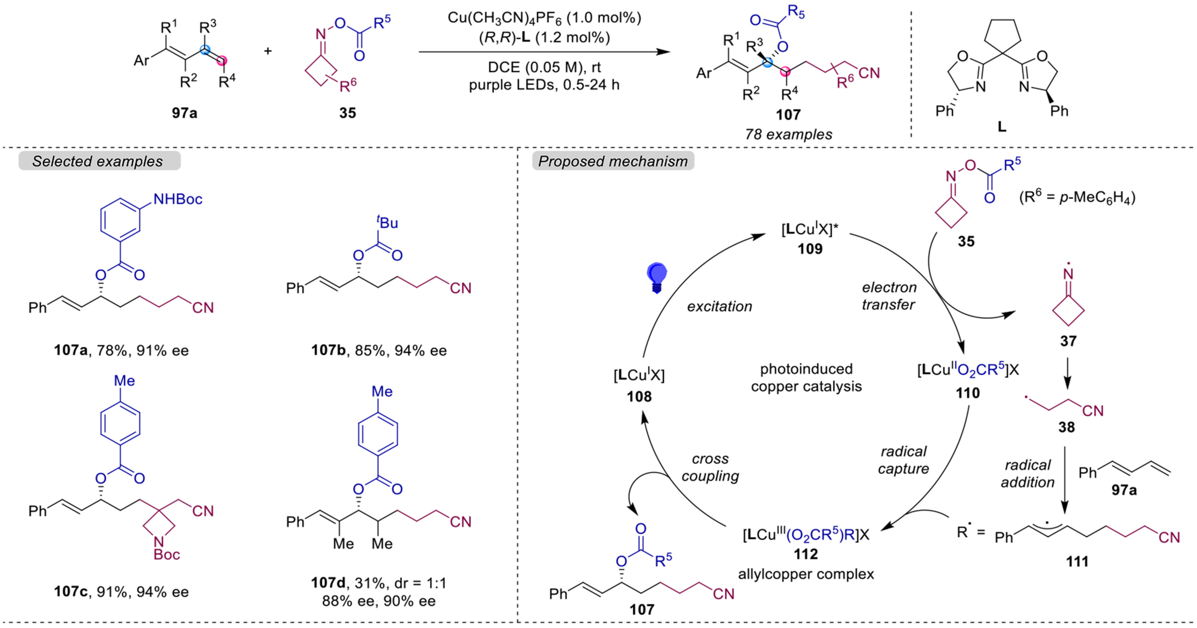
The process begins with $\mathrm{Cu(CH_3CN)_4PF_6}$ coordinating with (*R*,*R*)-**L** to generate **L**$\mathrm{Cu^I}$X **108**, which is excited by purple light resulting in the formation of $[\mathrm{LCu^IX}]^*$ **109**. Similarly, through a SET process, redox-active oximes **35** react with **109** to yield iminyl radicals **37** and $\mathrm{Cu^{II}}$-nucleophile complex **110**. Notably, $\mathrm{Cu^{II}}$ complex **110** is derived from **109** and carboxylic anion released by oxime esters. Then, iminyl radicals **37** undergo β–C–C bond cleavage and radical addition with 1,3-dienes **97a** to furnish allyl radical species **111**, which are captured by intermediate **110** to generate π-allyl $\mathrm{Cu^{III}}$ complex **112**. Finally, the reductive



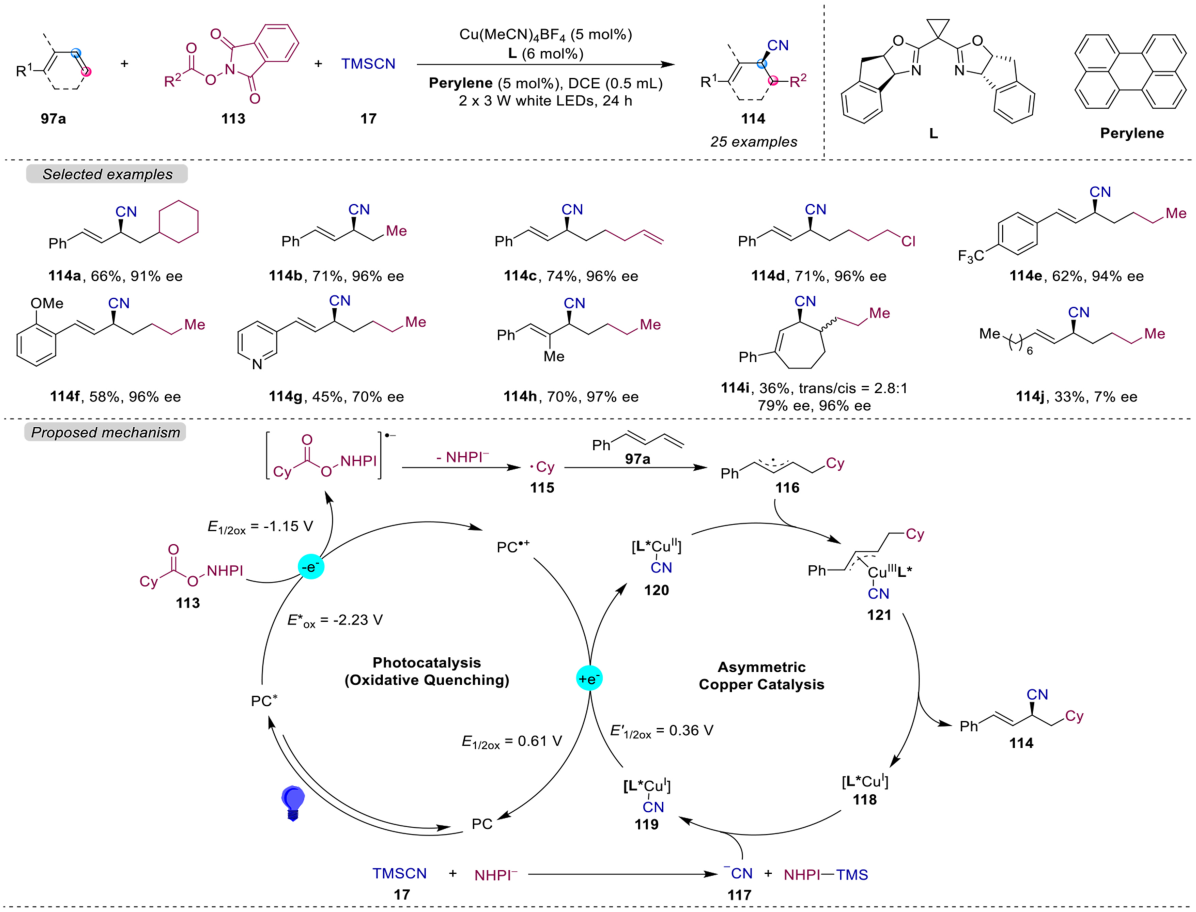
Scheme 13. Photoinduced copper-catalyzed asymmetric 1,2-alkylesterification of 1,3-dienes.

elimination of π-allyl Cu^{III} complex **112** provides allylic esters **107** and regenerates **108**.

Lu *et al.* reported a visible-light-mediated copper-catalyzed three-component enantioselective carbocyanation of 1,3-dienes **97a** with *N*-hydroxyphthalimide (NHPI) esters **113** and TMSCN **17**, yielding chiral allyl cyanides in 33%-79% yields with 7%-97% ee [Scheme 15][76]. The conditions are applicable to aromatic substituted 1,3-dienes. Unfortunately, the yield and enantioselectivity of alkyl-substituted 1,3-



Scheme 14. Photoinduced copper-catalyzed asymmetric 1,2-alkylesterification of 1,3-dienes using oxime esters as a difunctional reagent.



Scheme 15. Photoinduced copper-catalyzed asymmetric 1,2-carbocyanation of 1,3-dienes.

diene substrates are unoptimized.

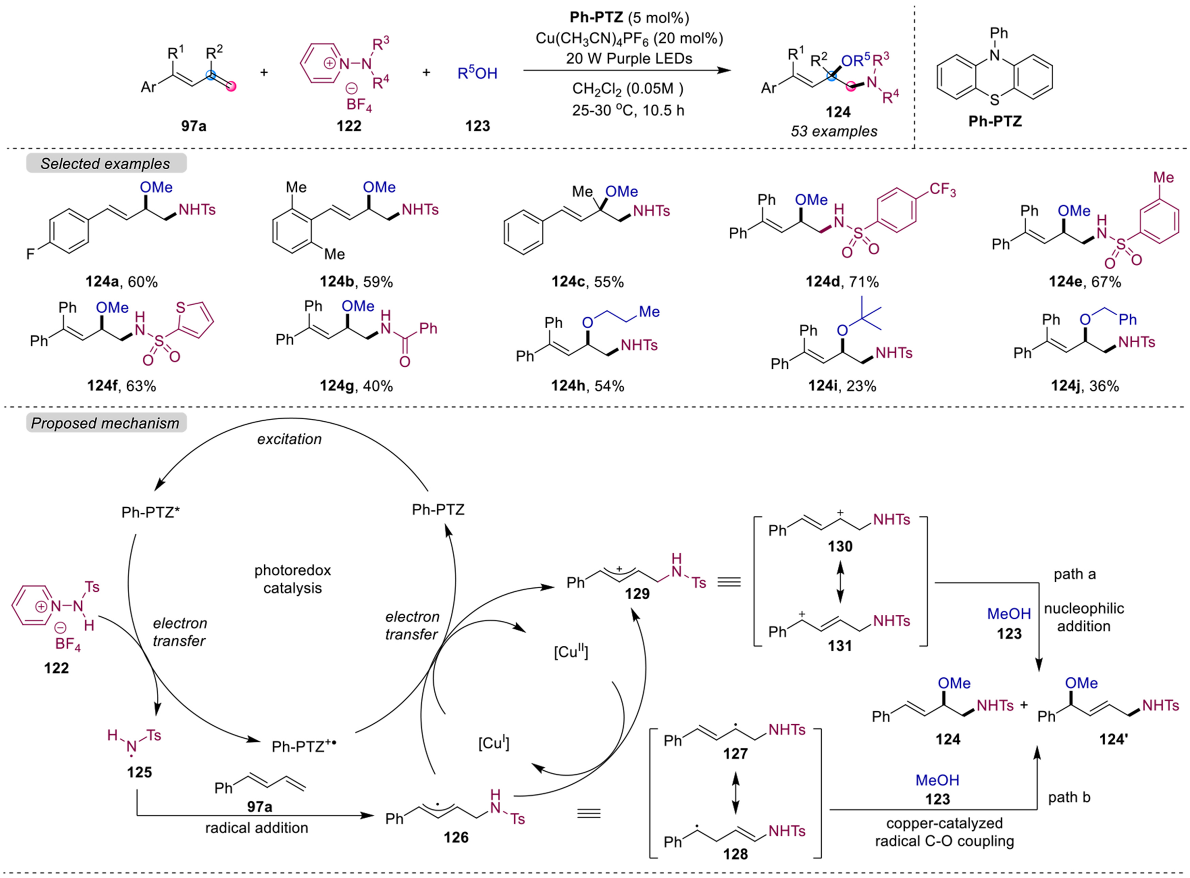
A possible reaction mechanism is proposed based on control experiments. Firstly, the PC perylene is transformed into PC* under visible-light irradiation. The redox-active NHPI esters **113** are reduced by PC* to give alkyl radicals **115** and PC$^{\bullet+}$, by releasing CO_2 and NHPI$^-$. Subsequently, the alkyl radicals **115** are trapped by 1,3-dienes **97a**, forming allyl radicals **116**. Additionally, NHPI$^-$ interacts with TMSCN **17** to generate cyano radical **117**, which coordinates with the chiral $\mathbf{L}^*Cu^I$ **118** complex to form the intermediate $\mathbf{L}^*Cu^I$-CN **119**. Next, PC$^{\bullet+}$ oxidizes **119** to form the $\mathbf{L}^*Cu^{II}$-CN species **120** and PC. Finally, the allyl radicals **116** are intercepted by **120**, resulting in the formation of the pivotal chiral allyl Cu^{III} complex **121**. This complex then undergoes a rapid reductive elimination to generate chiral allyl cyanides **114** and regenerate **118**.

N-Aminopyridinium salts have been demonstrated as nitrogen-centered radical precursors in cross-coupling reactions. In 2022, Wu *et al.* reported a photoredox and $Cu(CH_3CN)_4PF_6$ catalyzed regioselective three-component reaction of 1,3-dienes **97a** with *N*-aminopyridinium salts **122** and alcohols **123** to deliver 1,2-aminoalkoxylation products **124** in 23%-71% yields [Scheme 16][77]. In this process, *N*-aminopyridine salts **122** act as the precursor of nitrogen-centered radicals, and alcohols **123** act as oxygen nucleophiles. This catalytic system is compatible with a series of aryl-substituted 1,3-dienes and aliphatic alcohols.

Under purple lights irradiation, the ground-state 10-phenylphenothiazine (Ph-PTZ) is excited to Ph-PTZ* [$E_{1/2}$(Ph-PTZ/Ph-PTZ*) = -2.1 V *vs.* saturated calomel electrode (SCE)], which initiates the catalytic cycle. Subsequently, through a thermodynamically favored SET process, *N*-aminopyridinium salts **122** interact with Ph-PTZ* to generate amidyl radicals **125** and oxidized-state Ph-PTZ$^{\bullet+}$. Radicals **125** are captured by1,3-dienes **97a** to deliver relatively stabilized carbon radicals **126**, which might consist of a pair of resonant structures (allylic carbon radicals **127** and benzylic radicals **128**). Then, Ph-PTZ$^{\bullet+}$ [$E_{1/2}$(Ph-PTZ$^{\bullet+}$/Ph-PTZ) = +0.68 V *vs.* SCE] oxidizes radicals **126** to carbocations **129** via SET approach. There are also two resonant structures: allylic cations **130** and benzylic cations **131** in carbocations **129**. The nucleophilic attack of **129** with alcohols **123** results in the formation of 1,2-addition products **124**, whereas **131** undergoes a similar reaction to yield 1,4-addition products **124'** (path a). Notably, the Ph-PTZ$^{\bullet+}$ could also oxidize the Cu^I catalyst to the Cu^{II} species, which also can oxidize the carbon radicals **126** to the carbon cations **129**. Copper-catalyzed direct C–O bond coupling of radicals **126** with alcohols **123** is an unfavorable reaction pathway (path b). $Cu(CH_3CN)_4PF_6$ plays an important role in improving 1,2-regioselectivity.

The light-driven, earth-abundant-metal-catalyzed 1,2-selective three-component cross-coupling reaction of 1,3-dienes has been widely reported, whereas the 1,4-addition reaction has been less frequently reported. In 2022, Bi *et al.* continued to report a photoinduced copper-catalyzed three-component selective 1,4-difluoroalkylesterification of 1,3-dienes **97a** with carboxylic acid **73** and CF_2-reagents **42** to afford allyl ester products **132** in a yield of 37%-85% [Scheme 17][78]. Upon light irradiation, the *in situ* afforded excited-state Ir^{III*} [$E_{1/2}$(Ir^{IV}/Ir^{III*}) = -1.73 V *vs.* SCE in CH_3CN] undergoes a thermodynamically favorable SET pathway with CF_2-reagents **42** to give difluoroalkyl radicals **133** and the oxidized-state Ir^{IV} [$E_{1/2}$(Ir^{IV}/Ir^{III}) = 0.77 V *vs.* SCE in CH_3CN]. The subsequent conversion mechanism is analogous to that described in Scheme 16. It is noteworthy that the formation of 1,4-selectivity is attributed to the greater stability of benzyl carbocations compared to allyl carbocations.

In 2023, Liu *et al.* reported a visible-light-promoted $Cu(CH_3CN)_4PF_6$ catalyzed three-component reaction of 1,3-dienes **97a** with carboxylic acids **73** and *N*-aminopyridinium tetrafluoroborate salts **122**, which delivered a series of allyl carboxylic esters and tertiary ethers **134** with yields ranging from 36% to 94% [Scheme 18][79]. Upon light irradiation, copper catalysts exhibit a dual effect, acting as PC to generate nitrogen radicals and



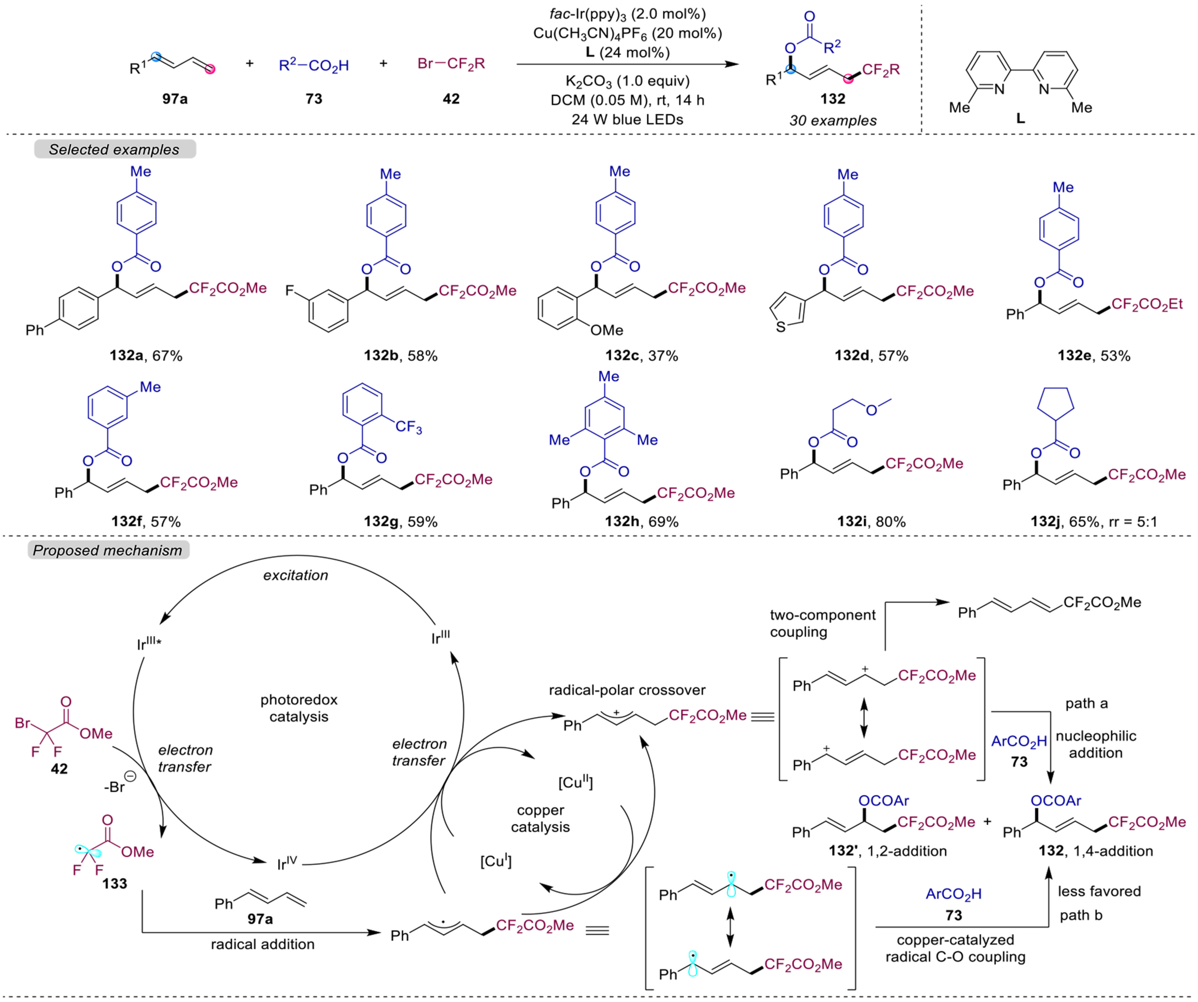
Scheme 16. Photoinduced copper-catalyzed 1,2-aminoalkoxylation of 1,3-dienes.

reacting with allyl radicals through a SET process. Notably, this strategy effectively constructs a series of tertiary carbon centers. This reaction can function with diverse substrates, including a series of aryl/alkyl carboxylic acids and alkyl substituted 1,3-dienes.

The mechanism investigation shows that the catalytic cycle begins when ground-state LCu^{I} **135** is excited by visible-light to **136**, which interacts with *N*-aminopyridinium tetrafluoroborate salts **122** via SET process to deliver nitrogen-centered radicals **137** and LCu^{II} species **138**. Then, radical **137** is trapped by isoprene **97a** to furnish a stable allyl radical **139**, which combines with **138** by another SET approach to form allyl carbocations **140**, followed by undergoing a nucleophilic attack with the carboxylic acids **73** to obtain final products **134** and regenerate ground-state LCu^{I} **135**.

PHOTOREDOX AND NICKEL-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

As one of the earth-abundant metals, nickel has attracted considerable attention from the chemical research community due to its favorable cost, low toxicity and distinctive catalytic activity. Nickel metal has rich valence states (Ni^0/Ni^I/Ni^{II}/Ni^{III}/Ni^{IV}) and high energy barriers of β-hydrogen elimination, making it a promising candidate for cross-coupling reactions[40,80]. The combination of photoredox and nickel catalysis has further accelerated the development of nickel-catalyzed cross-coupling reactions, enabling challenging transformations that are difficult to achieve in a single catalytic cycle under mild reaction conditions.The three-component cross-coupling reaction of alkenes catalyzed by dual visible-light and nickel has also been

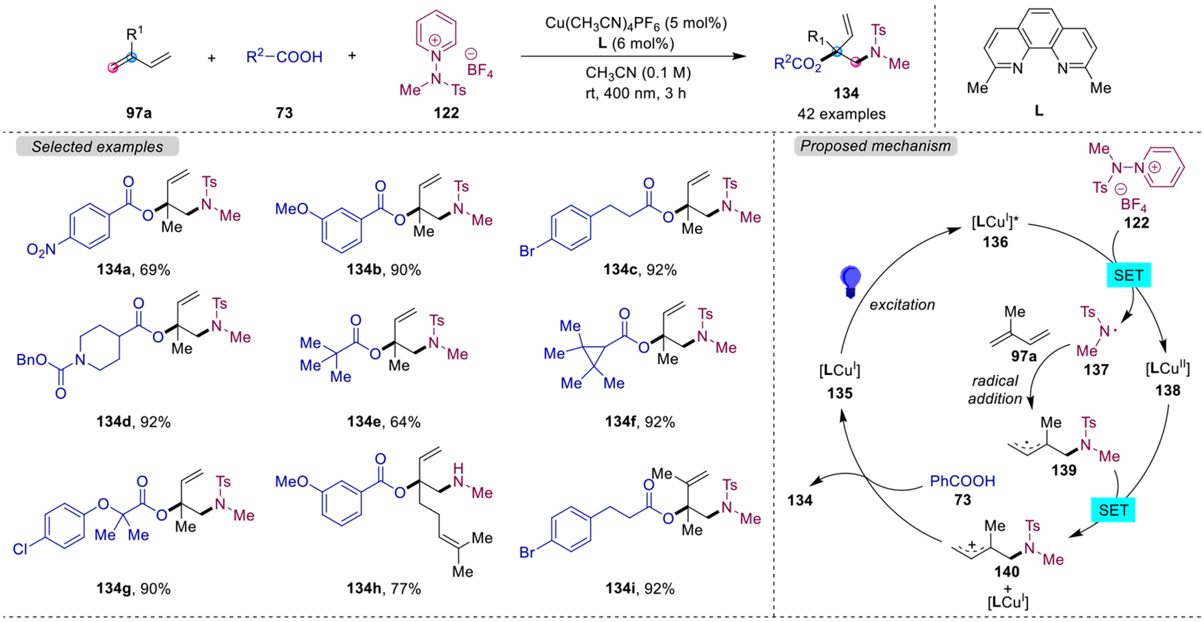


Scheme 17. Photoinduced copper-catalyzed 1,4-difluoroalkylesterification of 1,3-dienes.

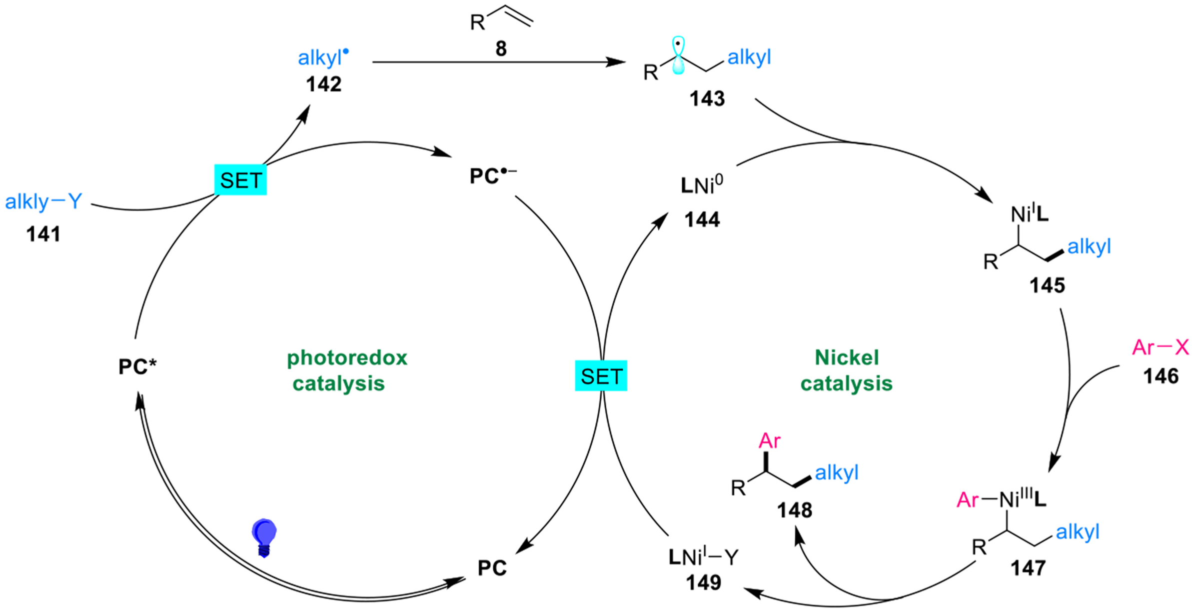
the subject of extensive investigation over the past decade.

While there may be discrepancies in the specifics, the overarching mechanism of the three-component cross-coupling reaction of alkenes synergistically catalyzed by photoredox and nickel can be summarized as illustrated in Scheme 19. In the visible-light irradiation, the ground-state PC is converted to PC^*, which then reacts with coupling substrate **141** by SET process to generate radical **142** and reduced $PC^{\bullet -}$. Then, radical **142** is trapped by alkene **8** by radical addition to deliver carbon-centered radicals **143**, which are intercepted by Ni^0 species **144** to give Ni^I intermediate **145**, followed by oxidative addition with another coupling substrate **146** to afford Ni^{III} complex **147**. Subsequently, the Ni^{III} intermediate **147** undergoes reductive elimination, resulting in the formation of the final product **148** and the generation of the Ni^I species **149**. Ultimately, the reduced $PC^{\bullet -}$ reduces **149** to **144** via another SET, thereby regenerating the ground-state PC and closing two catalytic cycles.

In 2019, García-Domínguez *et al.* reported a visible-light-induced and nickel-catalyzed three-component difunctionalization reaction of conjugated alkenes **150** with aryl halides **151** and nucleophiles **152** to provide desired product **153** in 15%-74% yields [Scheme 20][81]. The process does not contain stoichiometric additives, the coupling agent is easy to handle, and the operation is simple. Furthermore, conjugated alkenes



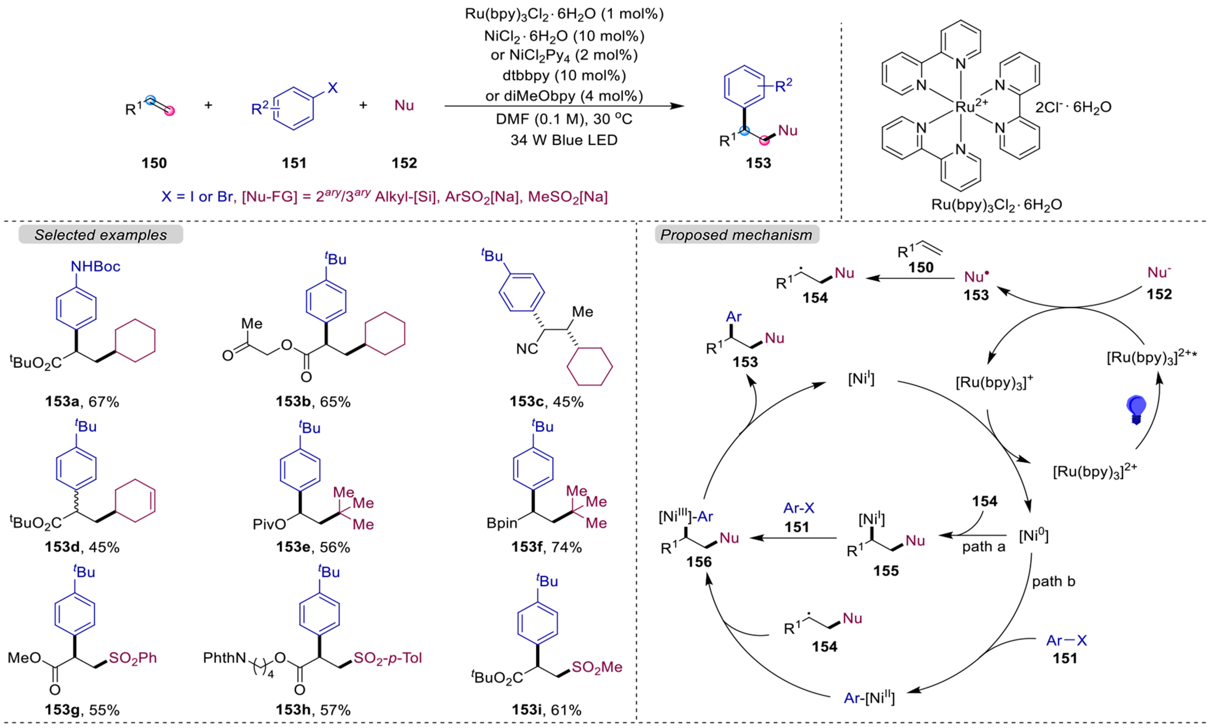
Scheme 18. Photoinduced copper-catalyzed 1,2-aminoesterification of 1,3-dienes.



Scheme 19. Possible pathway for photoinduced and nickel-catalyzed three-component difunctionalization of alkenes.

encompass acrylic esters, acrylonitrile, and other related compounds. Nucleophilic reagents include alkylsilicates and sulfinates, which are responsible for the production of secondary and tertiary alkyl and sulfonyl radicals, respectively.

The reaction begins when the ground-state PC $[Ru(bpy)_3]^{2+}$ is excited to an excited-state $[Ru(bpy)_3]^{2+*}$ by visible-light, which oxidizes the nucleophiles **152** to afford the radicals **153**. These are subsequently trapped by conjugated alkenes **150**, thereby providing the secondary carbon-centered radical **154**. Meanwhile, Ni^I is

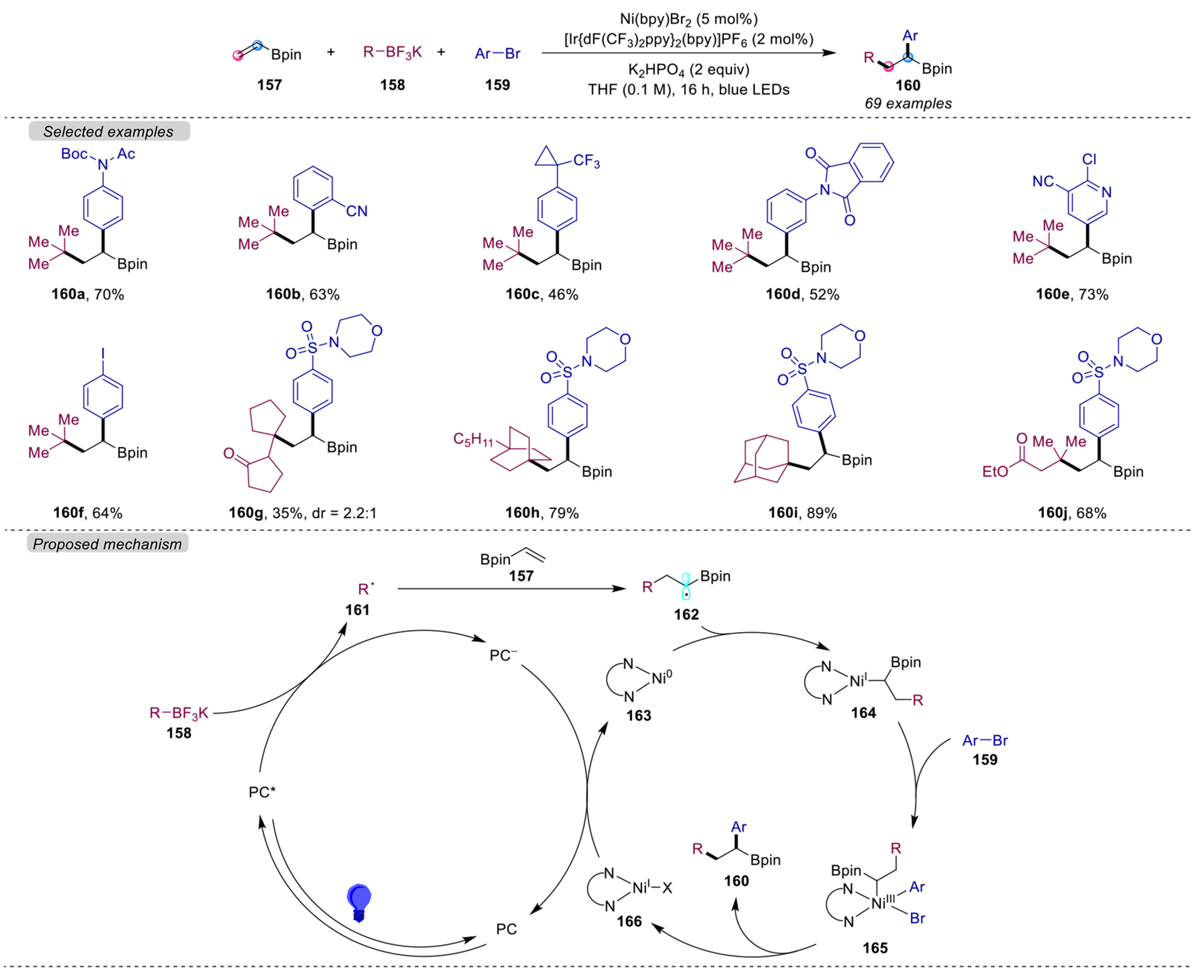


Scheme 20. Photoredox/nickel-catalyzed alkyl/sulfonylarylation of alkenes.

reduced by $[Ru(bpy)_3]^+$ to obtain Ni^0, which reacts with radical **154** to generate alkyl-Ni^I complex **155**. This is followed by oxidative addition with the aromatic halides **151**, resulting in the formation of the Ar-Ni^{III}-alkyl species **156** (path a). Alternatively, the intermediate **156** can be formed by Ni^0 oxidative addition with aromatic halides **151**, followed by radical recombination with **154** (path b). Finally, Ar-Ni^{III}-alkyl species **156** undergo reductive elimination to form the final products **153** and Ni^I complex. The next step of the two catalytic cycles is similar, both involving the oxidation of Ru^I species by Ni^I, which regenerates the ground-state PC $[Ru(bpy)_3]^{2+}$ and the Ni^0 catalyst, respectively.

The reaction of organoboron compounds exhibits tunable reactivity, ease of handling, and product stability, rendering it an optimal synthon for the construction of molecular complexity. In 2019, Campbell *et al.* described a Ni/photoredox dual catalyzed cross-coupling of vinyl boronic esters **157** with trifluoroborates **158** and aryl bromides **159** to afford α-arylboronic acid esters **160** in 35%-98% yields [Scheme 21][82]. The rapid addition of 3° radicals to alkenes and their reluctance toward single-electron metalation to Ni complexes represent a significant advancement in the field of regioselective alkylation and arylation of alkenes. Furthermore, this catalytic system is compatible with a range of aryl bromides and secondary/tertiary radical precursors, facilitating the formation of a series of tertiary/quaternary carbon centers.

The general mechanism of the reaction process is given by the authors. Upon exposure to visible-light, PC is converted to PC*, which then reacts with trifluoroborates **158** via reductive quenching by SET process, forming radicals **161**. These radicals then engage in a Giese-type addition with vinyl boronic esters **157**, generating radicals **162**. Subsequently, the single-electron metalation of radicals **162** to Ni^0 species **163** results in the formation of an alkyl-Ni^I complex **164**, which then undergoes oxidative addition with aryl bromides **159** to yield a Ni^{III} complex **165**. Reductive elimination produces the final products **160** and Ni^I species **166**. Lastly, the Ni^I species **166** undergoes SET reduction by PC⁻, thereby regenerating the ground-

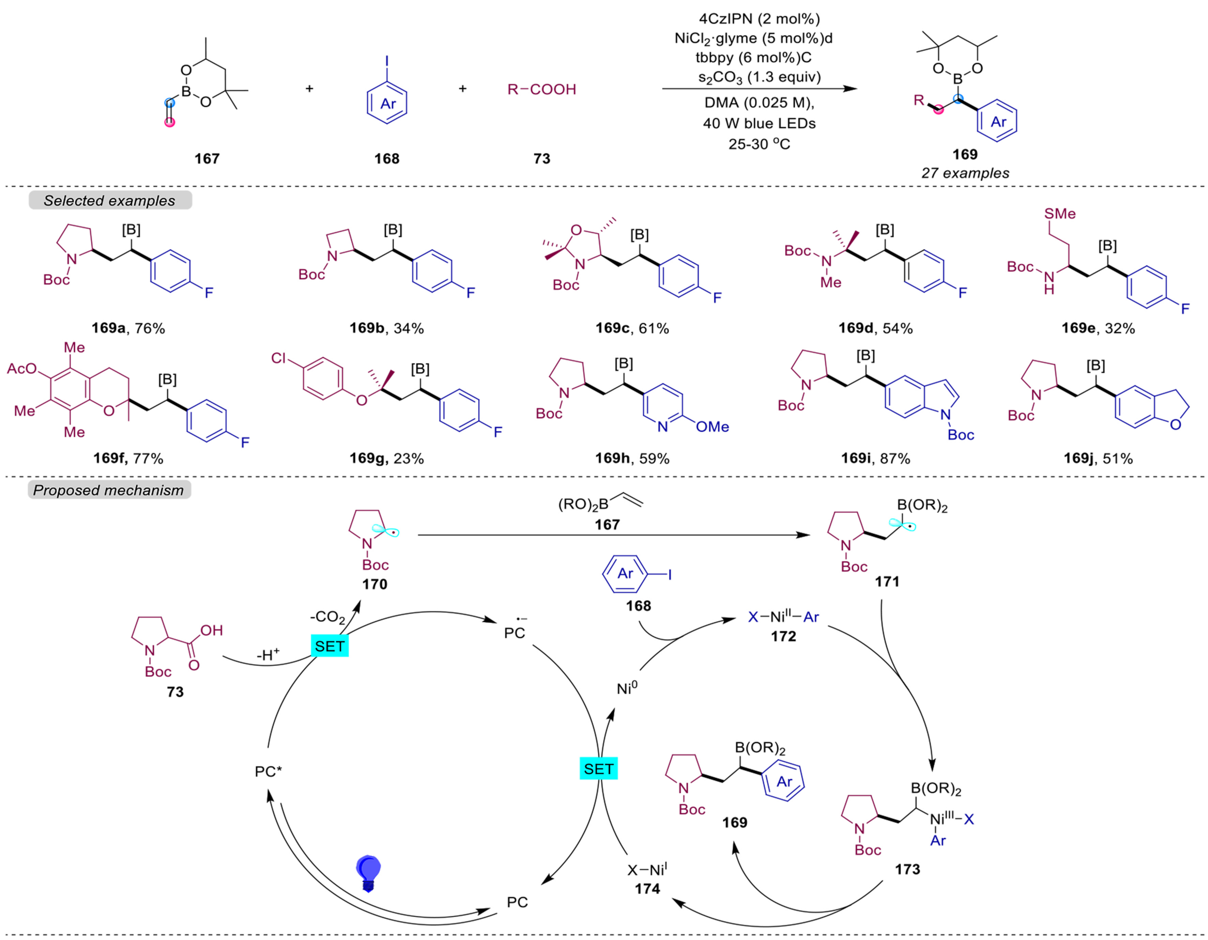


Scheme 21. Three-component dicarbofunctionalization of vinyl boronates by nickel/photoredox catalysis.

state PC and the Ni^0 species **163**, thus closing the two catalytic cycles. It is noteworthy that this process depends on the selective addition of radicals **161** to alkenes **157**, rather than direct cross-coupling to Ni^0 species **163** through single-electron metalation.

In 2020, Mega *et al.* developed a photoredox nickel-catalyzed decarboxylative conjunctive cross-coupling of vinyl boronic esters **167** with alkyl carboxylic acids **73** and aryl iodides **168**[83]. This process afforded alkyl boronic esters **169** in yields ranging from 11% to 87% [Scheme 22]. This protocol is applicable to a range of radical precursors and aryl iodides under mild conditions. It is important to note that this transformation process presents two significant challenges. Firstly, the rate of radical **170** addition to vinyl borates **167** must exceed its rate of addition to the Ni^{II} complex **172** to avoid the formation of the two-component coupling product. This is challenging as the rate of alkyl radical addition to vinyl borates **167** is 20 times lower than to acrylate. Secondly, the reaction rate of α-boryl radicals **171** and **172** must be faster than the SET between **171** and the $PC^{\bullet-}$. This is necessary to prevent the formation of the Giese product.

Mechanism exploration indicates that the catalytic cycle commences when PC is excited to PC^* under 40 W blue LED irradiation. Concurrently, the carboxylic acids **73** are converted into their conjugated bases in the presence of Cs_2CO_3, which interact with PC^* through a SET pathway and decarboxylate to give nucleophilic

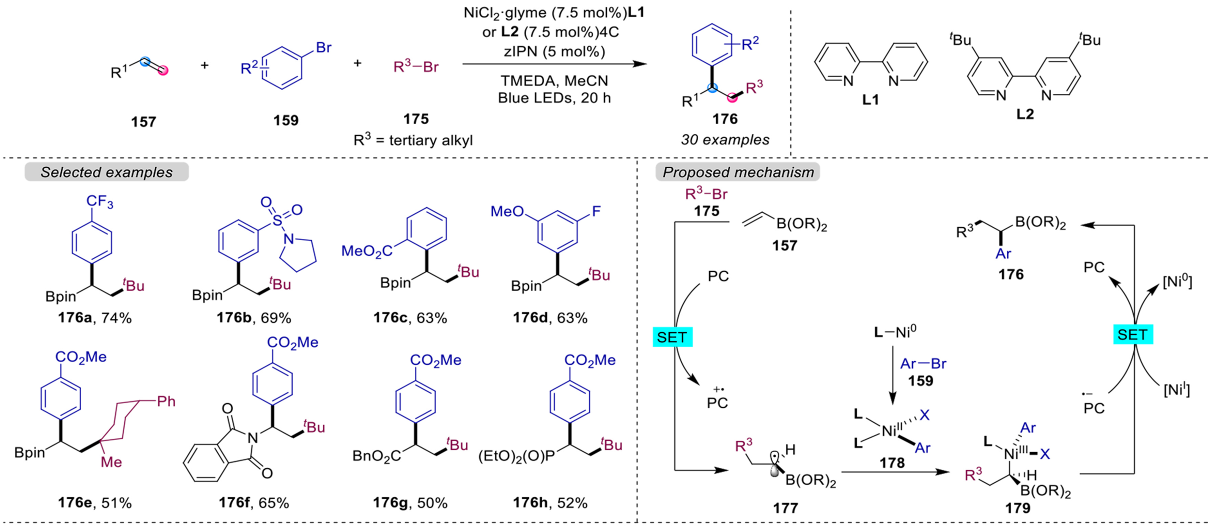


Scheme 22. Photoredox/nickel-catalyzed decarboxylative alkylarylation of vinyl boronates.

α-amino radicals **170**. These radicals then add to vinyl boronic ester **167**, forming stabilized α-boryl radicals **171**. Meanwhile, the oxidative addition of Ni^{0} catalyst with aryl iodide **168** provides Ni^{II} complex **172**, which is then intercepted by α-boryl radicals **171** to form Ni^{III} species **173**. This subsequently undergoes reductive elimination, providing the desired conjunctive products **169** and the Ni^{I} complex **174**. Finally, the SET reaction between PC$^{\bullet -}$ and Ni^{I} complex **174** regenerates the ground-state PC and Ni^{0} species, thereby completing two catalytic cycles.

In 2020, Sun *et al*. reported a visible-light-promoted and nickel dual catalyzed chemo- and site-selective cross-electrophile coupling reaction of vinyl boronates **157** with aryl bromides **159** and alkyl bromides **175**, which resulted in the delivery of organoboron compounds in 50%-81% yields [Scheme 23][84]. In essence, this strategy demonstrates the viability of reductive cross-coupling involving three distinct electrophilic partners in a synergistic manner. In addition to vinyl boronic acid esters, this system is compatible with other conjugated alkenes, including acrylamide, acrylic esters, and vinyl phosphate esters. Moreover, aryl bromides also have a wide range of potential substrates, although radical precursors are limited to tertiary substituted alkyl bromides.

The alkyl bromides **175** and the excited-state photocatalyst PC$^{\bullet +}$ facilitate the generation of nucleophilic alkyl radicals through the SET process. These radicals then add to the vinyl borate ester **157**, providing



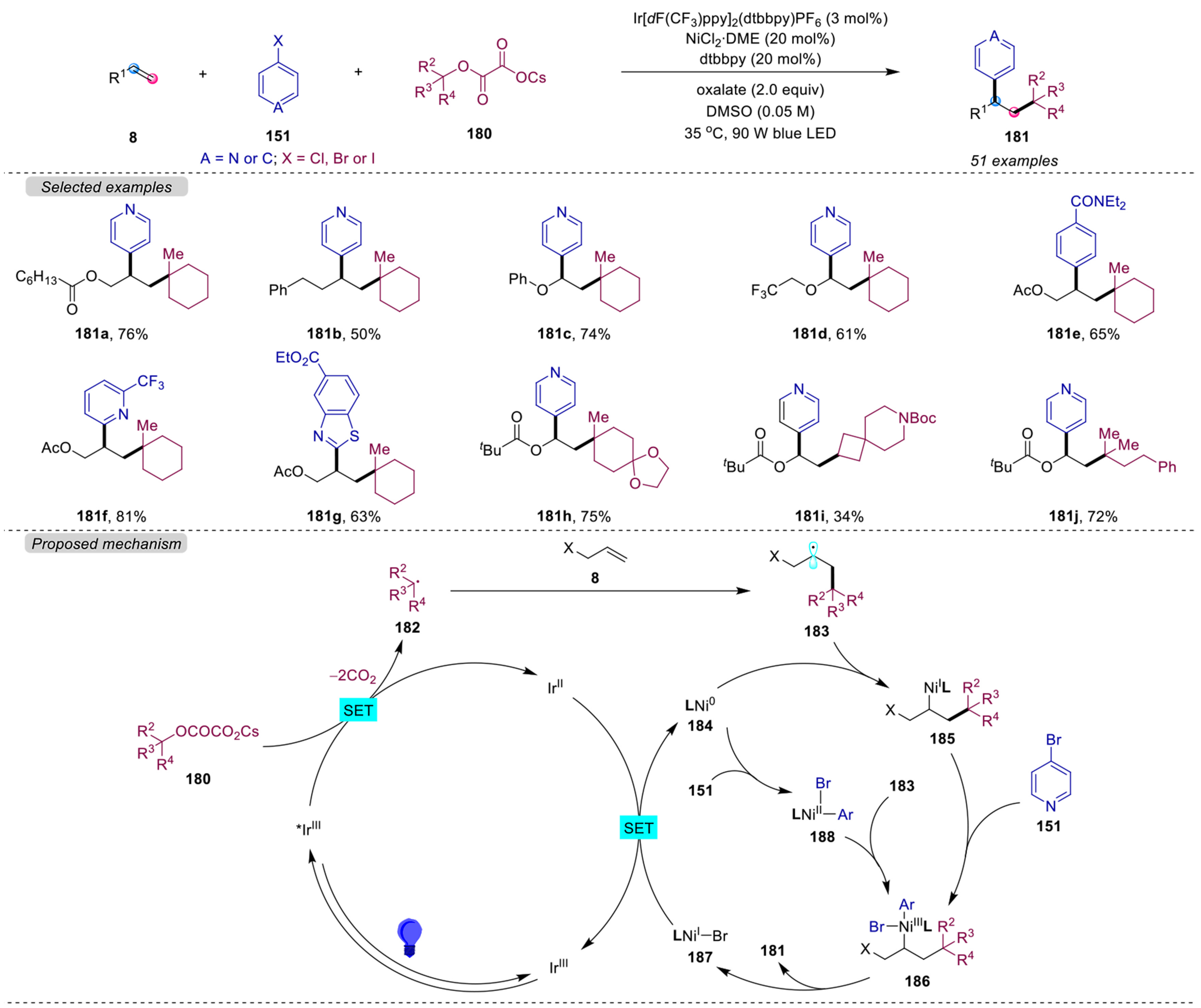
Scheme 23. Photoredox/nickel-catalyzed 1,2-alkylarylation of vinyl boronates.

intermediates **177**. It is of particular significance to note that the stability of the intermediates **177** is contingent upon the effective delocalization of the radical through the vacant p-orbital of the boron atom. Concurrently, oxidative addition of aryl bromides **159** to **L**Ni^0 results in electrophilics Ni^{II} entity **178**. The recombination of **177** with **178**, which occurs in a polarity-matched manner, results in the formation of the Ni^{III} species **179**. This is followed by a reductive elimination route, ultimately leading to the generation of the targeted product **176** and the Ni^I intermediate. Lastly, the SET pathway between Ni^I species and PC$^{\bullet-}$ results in the formation of the ground-state PC and **L**Ni^0 species.

In 2019, Guo *et al.* described a photoredox/nickel dual-catalyzed three-component regioselective 1,2-alkylarylation of alkenes **8** with aryl halides **151** and alkyl oxalates **180** to give desired coupling products **181** in 34%-92% yields [Scheme 24][85]. This method forms two continuous C–C bonds involving radical addition and nickel-assisted coupling. The catalytic system is suitable for both activated and non-activated alkenes, as well as for (hetero)aryl halides. However, the radical precursors are limited to tertiary substituted alkyl oxalates.

A plausible catalytic cycle of the three-component reaction is illustrated in Scheme 24. Initially, photoexcited catalyst *Ir^{III} oxidizes oxalate **180**, resulting in the generation of tertiary alkyl radicals **182** and the release of two CO_2 molecules. The former is subsequently added to alkenes **8**, forming nucleophilic secondary alkyl radicals **183**. These radicals are then captured by Ni^0 species **184**, ultimately leading to the formation of a Ni^I complex **185**. Subsequently, aryl halides **151** undergo oxidative addition with intermediates **185** to form key (aryl)(alkyl)Ni^{III} species **186**. This is followed by a rapid reductive elimination, which affords the final products **181** and Ni^I complex **187**. An alternative potential pathway for the formation of intermediate **188** is the oxidative addition of Ni^0 **184** with aryl halides **151** to give Ni^{II} species **188**, which is then intercepted by radicals **183**. Lastly, single-electron reduction of **187** by reducing Ir^{II} to regenerate the ground-state PC Ir^{III} and Ni^0 species **184**, thereby closing two catalytic cycles.

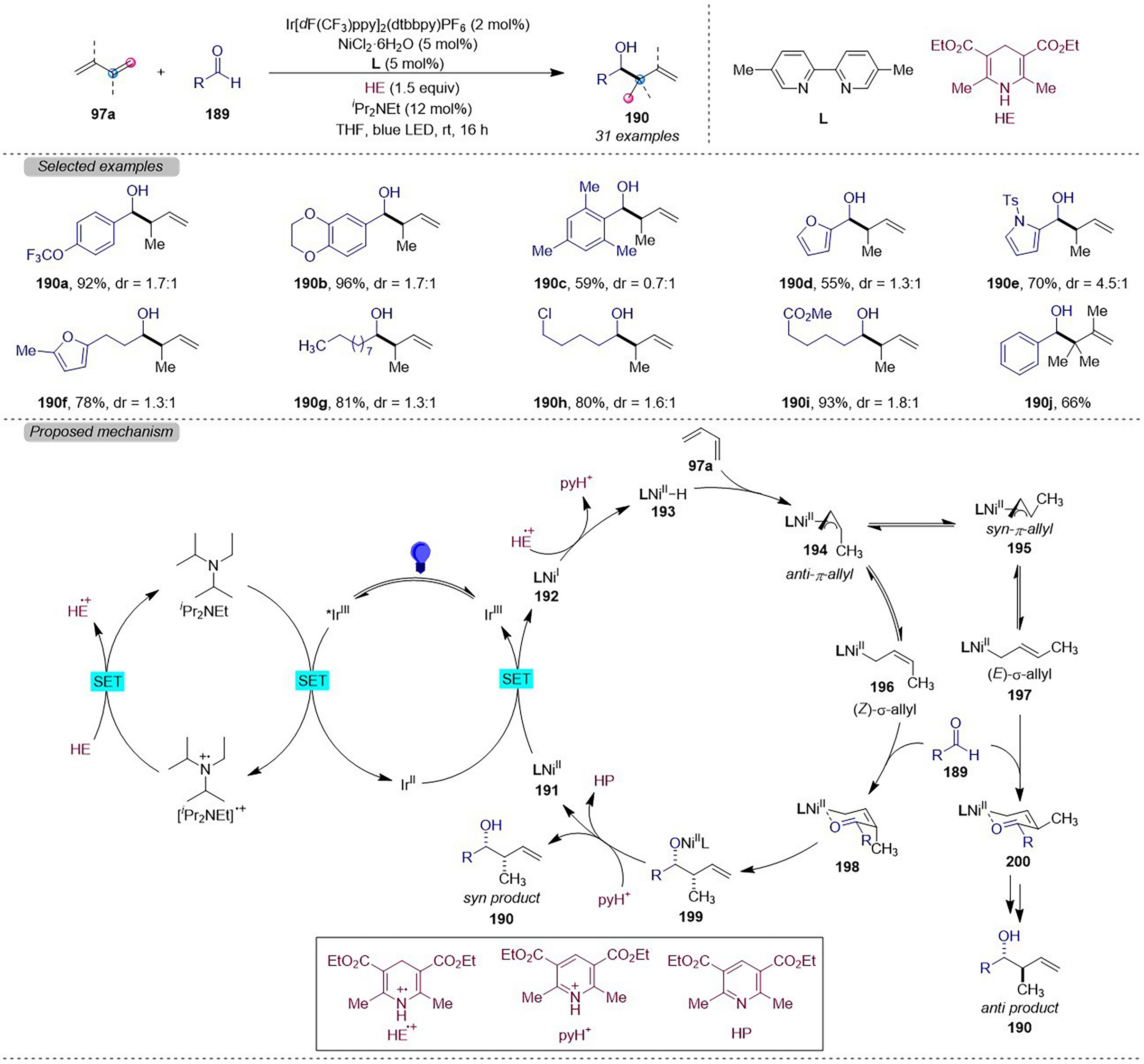
Nickel-catalyzed reductive coupling reactions have attracted considerable attention because they rely solely on organo-electrophiles, eliminating the need for stepwise pre-synthesis of organometallic reagents. In 2020, Li *et al.* reported a visible-light-induced Ni-catalyzed reductive coupling of 1,3-dienes **97a** with aldehydes **189**, which resulted in the delivery of homoallylic alcohols **190** in yields ranging from 34% to 99% under



Scheme 24. Photoredox/nickel-catalyzed decarboxylative alkylarylation of alkenes.

mild conditions [Scheme 25][86]. The authors employ the Hantzsch ester (HE) as the hydrogen radical source to facilitate the oxidation of the low-valent nickel salt, thereby yielding the Ni-H species. Furthermore, this dual catalytic system is compatible with aryl or alkyl aldehydes. However, the regioselectivity for asymmetric 1,3-dienes is only 1.9:1, indicating that additional optimization is necessary to enhance the asymmetric induction.

The reaction pathway begins with the formation of an excited PC *Ir under visible-light irradiation, which then undergoes reduction by $^{i}Pr_2NEt$ [E_{ox} ($^{i}Pr_2NEt$) = +0.65 V] via SET process to form a highly reducing Ir^{II} species and [$^{i}Pr_2NEt$]$^{\bullet+}$, the latter accepting one electron from HE to regenerate $^{i}Pr_2NEt$ and the $HE^{\bullet+}$. The reduction potential of Ir^{*} is $E_{1/2}^{red}$ [$^{*}Ir^{III}/Ir^{II}$] = +1.21 V *vs.* SCE in MeCN. Meanwhile, Ni^{II} complex **191** is reduced by Ir^{II} [$E_{1/2}^{red}$ (Ir^{III}/Ir^{II}) = -1.37 V *vs.* SCE in MeCN], affording Ni^{I} species **192** [$E_{1/2}^{red}$ (Ni^{II}/Ni^{I}) = -0.68 V *vs.* SCE in DMSO] and regenerating ground-state Ir^{III}, thus closing the photocatalytic cycle. Ni^{I} species **192** then combines with $HE^{\bullet+}$ to deliver key intermediate Ni-H species **193** and pyridinium ion pyH^{+}. The Ni-H species is captured by *s-cis* configuration 1,3-dienes **97a** to produce the key *anti*-π-allyl-nickel intermediate **194**, which can isomerize to *syn*-π-allyl-nickel intermediate **195** rapidly. Intermediates **194** and **195** are subsequently converted to *Z*- and *E*-σ-allyl nickel intermediates **196** and **197**. Next,



Scheme 25. Photo- and nickel-catalyzed reductive 1,2-hydroalkyaltion of 1,3-dienes with aldehydes.

intermediates **197** react with aldehydes **189** and, through the Zimmerman-Traxler transition state **198**, form *syn*-homoallylic nickel alkoxides **199**, which are protonated by pyH$^+$ to yield *syn*-homoallylic alcohols **190** and regenerate Ni^{II} complex **191** along with HP. Moreover, *E*-σ-allyl nickel intermediates **197** follow a comparable pathway, resulting in the formation of *anti*-homoallylic alcohols **190**. The authors believe that the crotyl methyl group placed pseudoaxially in transition state **198** may serve to mitigate gauche interactions between this group and the substituent of the aldehydes **189**, as observed in certain reactions. This may explain why transition state **198** is more favorable than **200** in this reaction. Furthermore, the latter transition state model results in *anti*-diastereoselectivity.

Additionally, sodium sulfinate can function as a radical precursor in the nickel-catalyzed three-component cross-coupling reaction under photochemical or electrochemical conditions. In 2020, Huang *et al*. reported a visible-light-induced and nickel-catalyzed cascade cross-coupling process of dienes **201** with sodium sulfinates **202** and aryl halides **151**, which delivered a series of saturated five-membered ring compounds in

46%-99% yields [Scheme 26][87]. This process synthesizes three new chemical bonds (one C–S and two C–C bonds) in one step, facilitating the rapid construction of complex molecules from commercially available feedstock chemicals. Notably, this strategy is compatible with 1,3/1,4/1,5/1,6-diene, aryl halides, and sodium aryl/alkyl sulfinates.

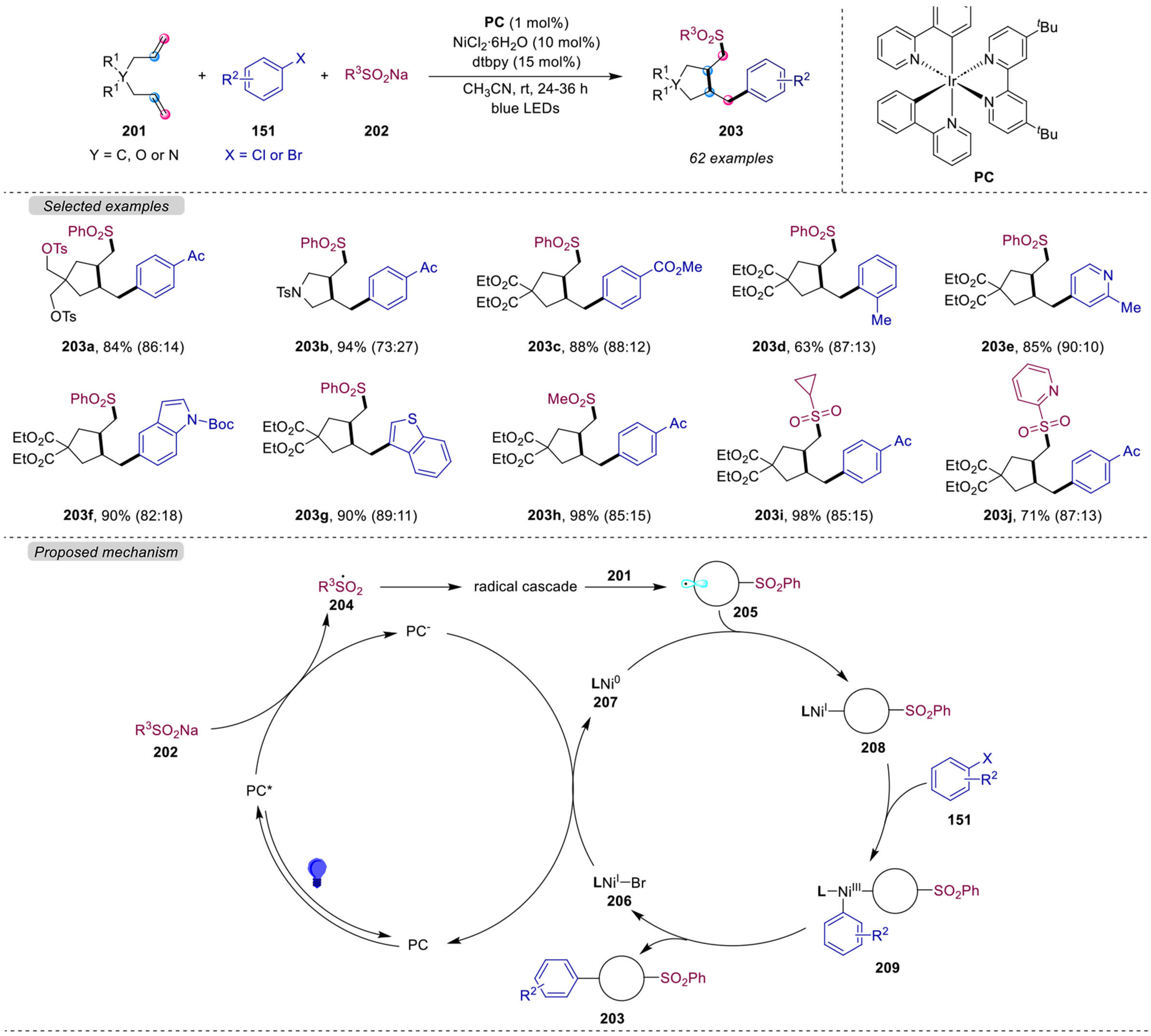
The conversion process is initiated when photosensitizer PC is excited to highly oxidizing excited-state PC^* under visible-light irradiation. Radical precursor sodium sulfinate **202** is oxidized by PC^* via SET process to form sulfonyl radical **204**, accompanied by the generation of photocatalyst PC^-. Subsequently, the PC^- reduced Ni^I complex **206** is reduced by another SET process, resulting in the formation of the $\mathbf{L}Ni^0$ species **207**. This process ultimately returns the system to its ground-state PC. Meanwhile, the sulfur-centered radical **204** is captured by the dienes **201** and undergoes a radical cascade cyclization reaction to furnish the cyclic radical intermediates **205**, which combine with $\mathbf{L}Ni^0$ species **207** to form alkyl-Ni^I intermediates **208**, followed by oxidative addition with aryl halides **151** to give Ni^{III} complex **209**. Lastly, intermediate **209** undergoes reductive elimination to deliver desired product **203** and Ni^I species **206**.

Silicon-containing compounds have a broad of applications in the fields of organic synthesis, medicinal chemistry, and material science. Zhang *et al*. reported a photoredox and nickel-catalyzed three-component carbosilylation of electron-deficient alkenes **150** with aryl bromides **159** and $(TMS)_3SiH$ **210** to deliver organosilicon compounds with 14%-84% yields [Scheme 27][88]. The silylation reaction involves the participation of photogenerated silicon radical intermediates, whereas the arylation process is conducted through the utilization of nickel-catalyzed cross-coupling. The arylsilylation system of alkenes is compatible with (hetero)aryl bromides, although the alkenes are limited to activated ones.

The coupling conversion is carried out under visible-light irradiation with $Ir(dF\text{-}Me\text{-}ppy)_2(dtbbpy)(PF_6)$ as PC and $Ni(cod)_2$ as nickel catalyst. First, Ni^0 species **212** and aryl bromides **159** undergo oxidative addition, forming Ni^{II} intermediate **213**. Concurrently, the Ir^{III} PC is excited by blue LED light, resulting in the formation of the excited-state $^*Ir^{III}$. This is then reductively quenched by Br^- of **213**, generating Ir^{II} and bromide radicals **214**. Subsequently, a hydrogen atom is abstracted from $(TMS)_3SiH$ **210**, producing a silyl radical **215**. Following that, methyl acrylate **150** captures silyl radical **215** to generate β-silyl alkyl radicals **216**, which is trapped by Ni^{II} species **213** to afford Ni^{III} complex **217**. Then, C–C reductive elimination from **217** yields the final products arylsilylation **211** and Ni^I species **218**. Lastly, the Ir^{II} complex reduces Ni^I **218**, thereby regenerating both the Ni^0 catalyst and the PC Ir^{III}.

Notably, the addition of chiral ligands in the visible-light and nickel co-catalytic system can also result in asymmetric cross-coupling reactions of alkenes. In 2020, Guo *et al.* developed a visible-light-induced photoredox/nickel dual-catalyzed enantioselective three-component alkylarylation reaction of activated alkenes **150** with secondary or tertiary alkyl trifluoroborates **158** and aryl bromides **159** to deliver β-alkyl-α-arylated carbonyls, phosphonates and sulfones with 16%-92% yields and 15%-97% ee [Scheme 28][89]. The catalytic cycling mechanism follows that of $Ni^0/Ni^{II}/Ni^{III}$, with the stereo-determining step being the addition of radicals to tetrahedral Ni^{II} species.

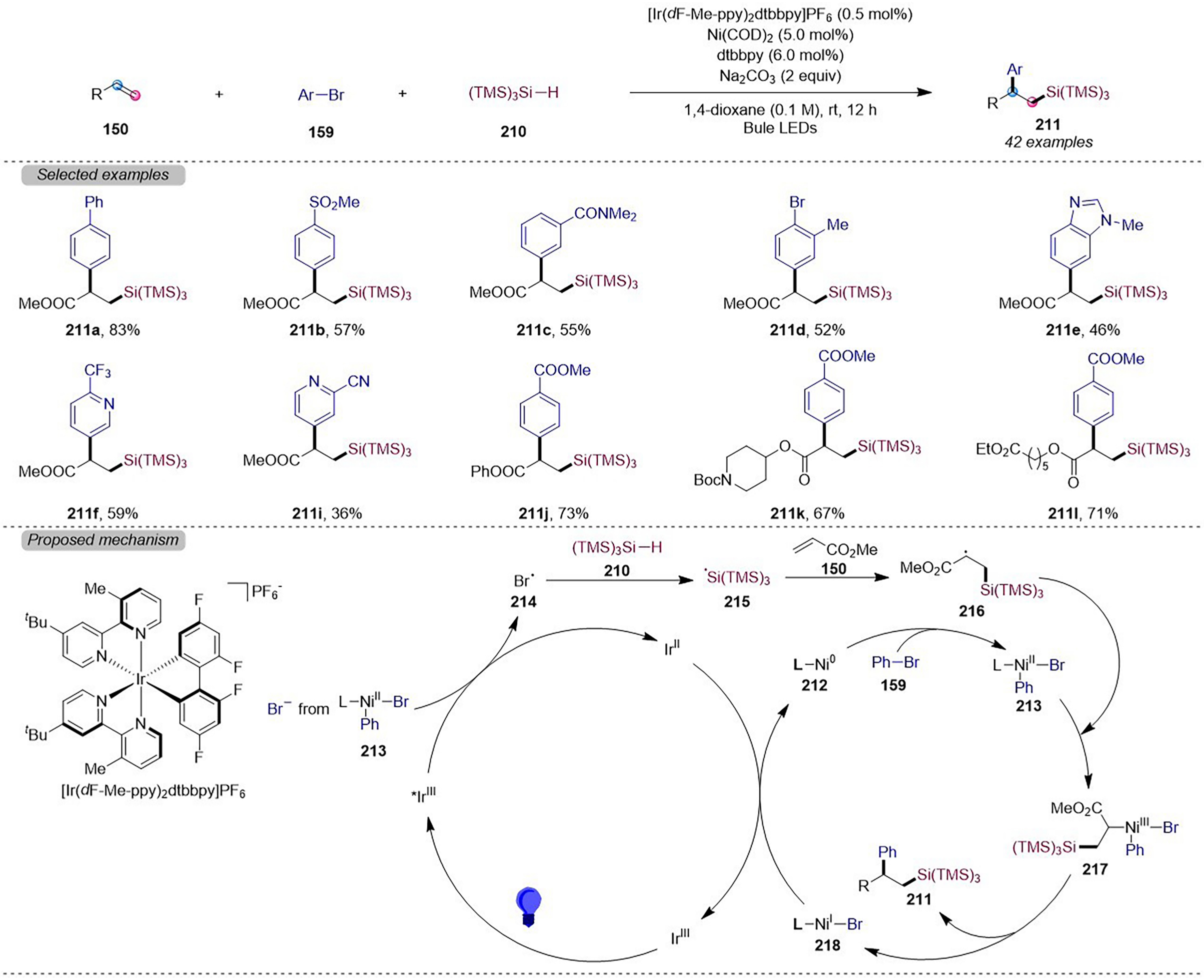
Based on [UB3LYP-D3(BJ)/def2-SVP-CPCM(THF)] calculations, the authors put forth a proposed mechanism for this transformation. Upon irradiation, photosensitizer Ir^{III} was excited to $^*Ir^{III}$, which proceeded to oxidize alkyl trifluoroborate reagent **158** to alkyl radicals **220** and Ir^{II} by single-electron oxidation. Then, alkyl radicals **220** undergo rapid and irreversible radical addition to acrylates **150**, resulting in the formation of α-ester radicals **221**. Meanwhile, the photosensitizer Ir^{II} facilitated the reduction of the bipyridyl-Ni^I **222** complex to Ni^0 **223**, which was then subjected to a rapid oxidative addition with aromatic



Scheme 26. Photo- and nickel-catalyzed cyclization sulfonylarylation of 1,6-dienes.

bromides **159** to provide a square planar singlet Ni^{II} species **224**. Additionally, alkyl radicals **221** were observed to be captured by the **223**, resulting in the formation of a Ni^{I}-alkyl species **225**. This subsequently underwent an oxidative addition with aromatic bromides **159**, generating a Ni^{III} species **226**. It is noteworthy that the Ni^{III} species **226** undergoes reversible radical dissociation, forming a square planar singlet Ni^{II} species **224**. This species can subsequently undergo isomerization and intersystem crossing, leading to the emergence of the more stable tetrahedral triplet spin state Ni^{II} **227** species. Lastly, **227** rapidly and irreversibly combines with the α-ester radicals **221** to obtain Ni^{III} species **226'**, resulting in the formation of the alkylarylation products **219** and Ni^{I} complex **222**. The authors found that the energy of the radical addition step (**227** to **226'**) is greater than that of the reductive elimination transition state (**226'** to **222**). The results demonstrate that the stereo-determining step of this process is the radical addition of the tetrahedral Ni^{II} center, rather than reduction elimination.

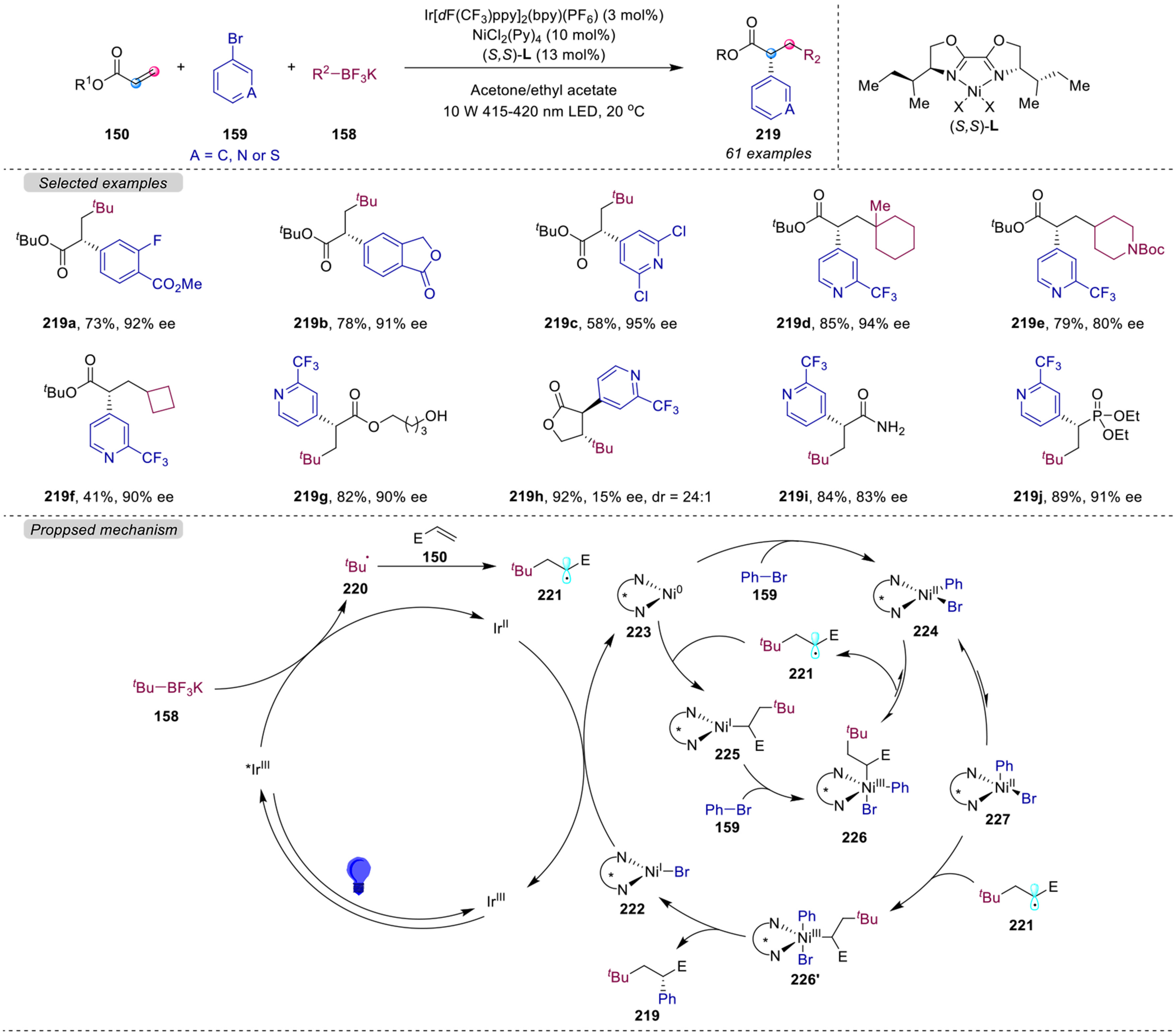
The poor stability of primary alkyl radicals, which are produced by photoredox/nickel dual catalysis, makes this process relatively difficult. Zheng *et al.* developed a photoinduced Ni-catalyzed chemo- and regioselective reductive conjugate cross-coupling reaction of alkenes **150** with aryl halides **151** and α-silyl



Scheme 27. Photo- and nickel-catalyzed silylarylation of electron-deficient alkenes.

amines **228**, enabling the synthesis of α-aryl substituted γ-amino acid derivatives in 20%-90% yields [Scheme 29][90].Importantly, this method uses α-silyl amines as a radical precursor to achieve the synthesis of primary alkyl radicals substituted by amines. The challenge of this transformation is to reduce the two-component side reactions caused by the high activity of primary carbon radicals and the dehalogenation of aryl halides. Moreover, aryl halides are compatible with a diverse range of substrates in this catalytic system. However, the use of α-silyl amines is confined to tertiary amines.

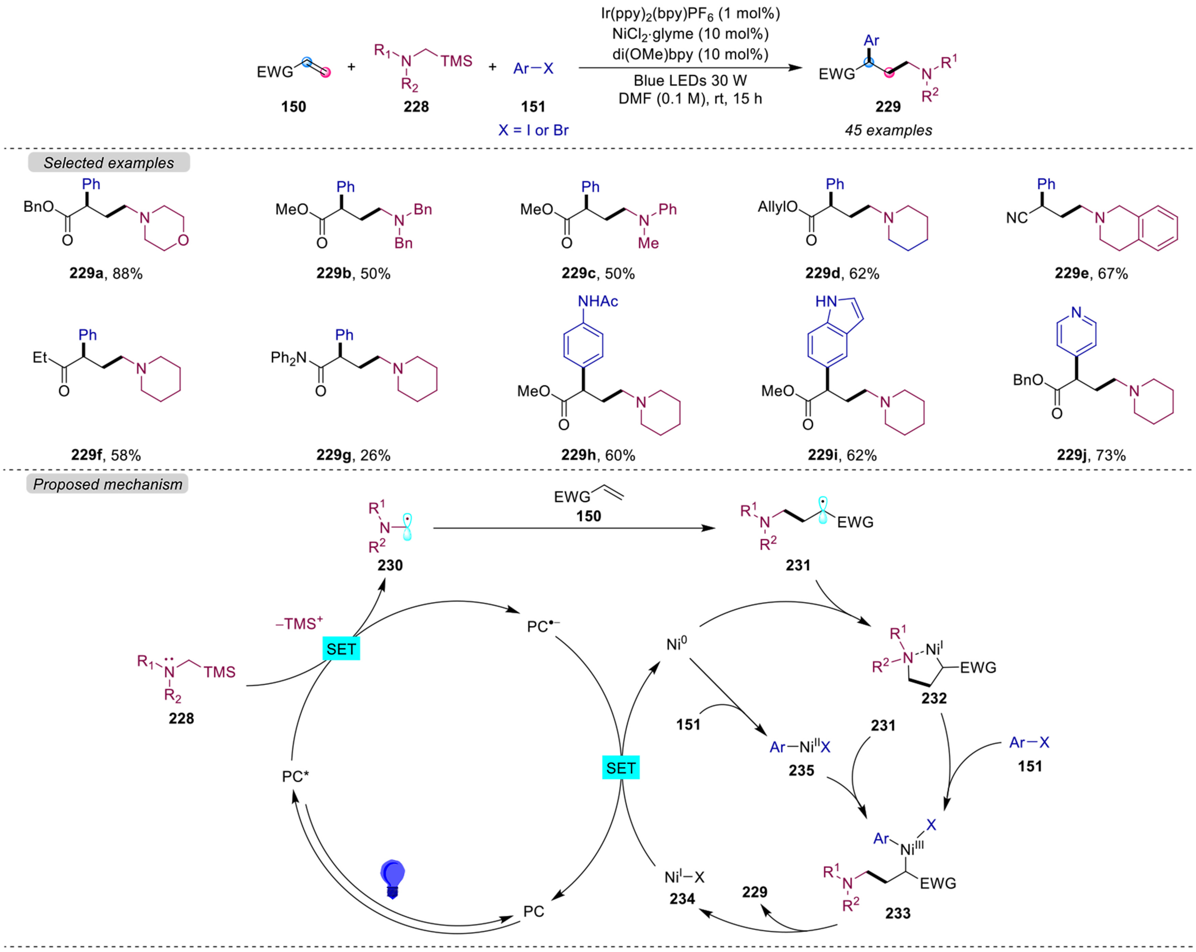
The proposed mechanism is illustrated in Scheme 29. α-Silyl amines **228** are oxidized by excited-state PC* via SET route to give primary α-amino radicals **230**, which rapidly undergo Giese-type addition to form β-amino radicals **231**, followed by intercepted by Ni^0 species to afford alkyl-Ni^I complex **232**. Then, **232** undergoes oxidative addition with aryl halides **151** to generate the key Ni^{III} species **233** (path a), which is followed by a facile reductive elimination to deliver the final conjunctive cross-coupled products **229** and Ni^I intermediate **234**. Ultimately, the SET reaction between the reduced state of PC$^{\bullet-}$ and **234** restores the ground state of PC and Ni^0, thereby completing both catalytic cycles. An alternative mechanism proposes that the Ni^{III} complex **233** is formed by the recombination of radical **231** with Ni^{II} species **235**, which arises from the oxidative addition of Ni^0 active species with aryl halides **151** (path b).



Scheme 28. Photo- and nickel-catalyzed enantioselective three-component alkylarylation of alkenes.

The use of unactivated C(sp^3)-hybridized centers from the hydrocarbon skeleton as radical precursors will lead to a simpler photo/nickel dual-catalyzed three-component cross-coupling reaction. In 2021, Xu *et al.* described a visible-light-induced nickel-catalyzed three-component dicarbofunctionalization of conjugated alkenes **150** with C(sp^3)-hybridized centers compounds **236** and aryl halides **151** to afford α-aryl esters in trace to 82% yields [Scheme 30][91]. The protocol employs an inexpensive and readily synthesizable decatungstate [tetrabutylammonium decatungstate (TBADT)] as a PC and abundant hydrocarbons as radical precursors, facilitating the installation of a diverse array of highly functionalized tertiary, secondary, and primary C(sp^3)-hybridization centers. Furthermore, this strategy is compatible with a series of activated alkenes, aryl halides, and secondary or tertiary C–H bonds under mild conditions.

As shown in Scheme 30, the authors proposed a possible catalytic pathway. Under visible-light irradiation, TBADT is excited to its excited-state $^*[W_{10}O_{32}]^{4-}$, which then abstracts a hydrogen atom from unactivated hydrocarbon substrates **236** to provide reduced decatungstate $[W_{10}O_{32}]^{5-}H^+$ and alkyl radicals **238**. Then, methyl acrylate **150** captures alkyl radicals **238** to give another alkyl radicals **239**, which are intercepted by LNi^0 species **240** to provide alkyl-Ni^I intermediate **241**. Subsequently, oxidative addition with aryl halides

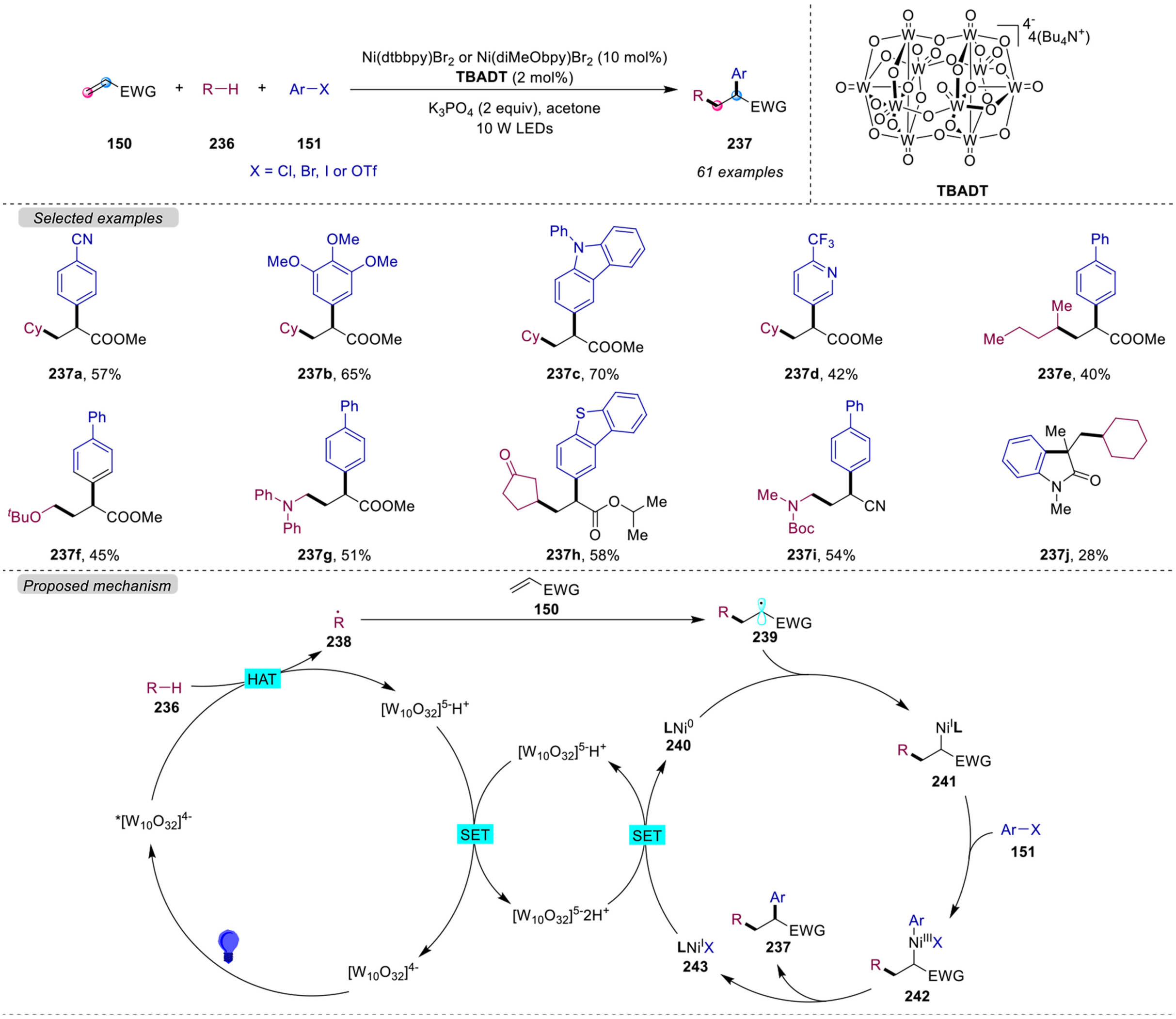


Scheme 29. Photo- and Ni-catalyzed 1,2-aminomethylarylation of electron-deficient alkenes.

151 generates crucial alkyl-Ni^{III}-aryl complex **242**, which, through reduction elimination, delivers the final products **237** and LNi^{I}X **243**. Next, two molecules $[W_{10}O_{32}]^{5-}H^+$ interact via SET process to form ground-state PC $[W_{10}O_{32}]^{4-}$ and $[W_{10}O_{32}]^{5-}2H^+$, thereby completing the photocatalytic cycle. Lastly, following another SET pathway, **243** is reduced to **240** by $[W_{10}O_{32}]^{5-}2H^+$, thus closing nickel catalytic cycle.

Similarly, Campbell *et al.* developed a visible-light-induced photoredox/nickel-catalyzed three-component cross-coupling of activated alkenes **150** with aryl bromides **159** and C–H bonds building blocks (alcohols, ethers lactones and lactams) **244** to afford dicarbofunctionalization products **245** in 31%-96% yields [Scheme 31][92]. It is of particular significance to note that the hydrogen bonding between the radical precursors containing an -OH group and the acrylic esters plays a pivotal role in determining the selectivity of the products in this protocol. In addition to chain-like activated alkenes, this strategy is also applicable to cyclic alkenes and a series of (hetero)aromatic bromides.

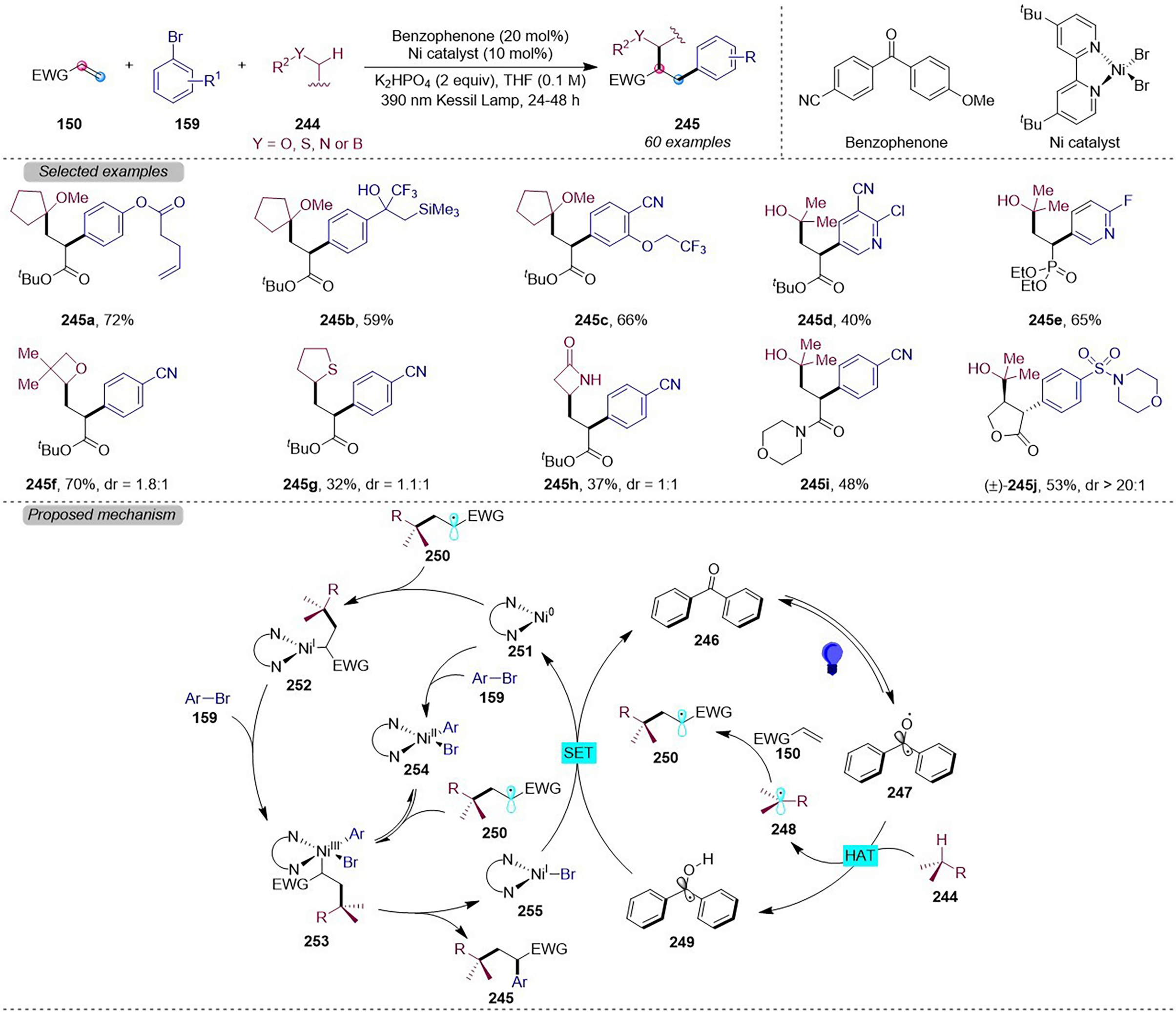
Mechanism studies have shown that this process involves hydrogen bond-assisted radical addition. Firstly, upon irradiation, diaryl ketone **246** is excited to triplet-state diradical **247**, which interacts with **244** to afford carbon-centered radicals **248** and ketyl radicals **249** through selective homolysis of an activated C–H bond. Subsequently, the alkyl radicals **248** undergo a regioselective Giese addition reaction with activated alkenes **150**, forming the radical adducts **250**. These are captured by a Ni^0 species **251**, resulting in the formation of



Scheme 30. Photoinduced tungsten- and Ni-catalyzed 1,2-alkylarylation of electron-deficient alkenes via aliphatic C–H cleavage.

the $\mathrm{Ni^I}$ complex **252**. Finally, oxidative addition with aryl bromides **159** occurs, leading to the generation of the $\mathrm{Ni^{III}}$ intermediate **253**. Conversely, $\mathrm{Ni^0}$ may also undergo oxidative addition directly with aryl bromides **159**, yielding tetrahedral $\mathrm{Ni^{II}}$ intermediates **254**. These could then combine with radicals **250** to form the $\mathrm{Ni^{III}}$ intermediates **253**. Next, reductive elimination from **253** would produce the final products **245** and $\mathrm{Ni^I}$ species **255**. Ultimately, the ketyl radical **249** reduces the $\mathrm{Ni^I}$ species **255**, thereby regenerating the $\mathrm{Ni^0}$ species **251** and returning the ground-state diaryl ketone **246** to its original state through SET process.

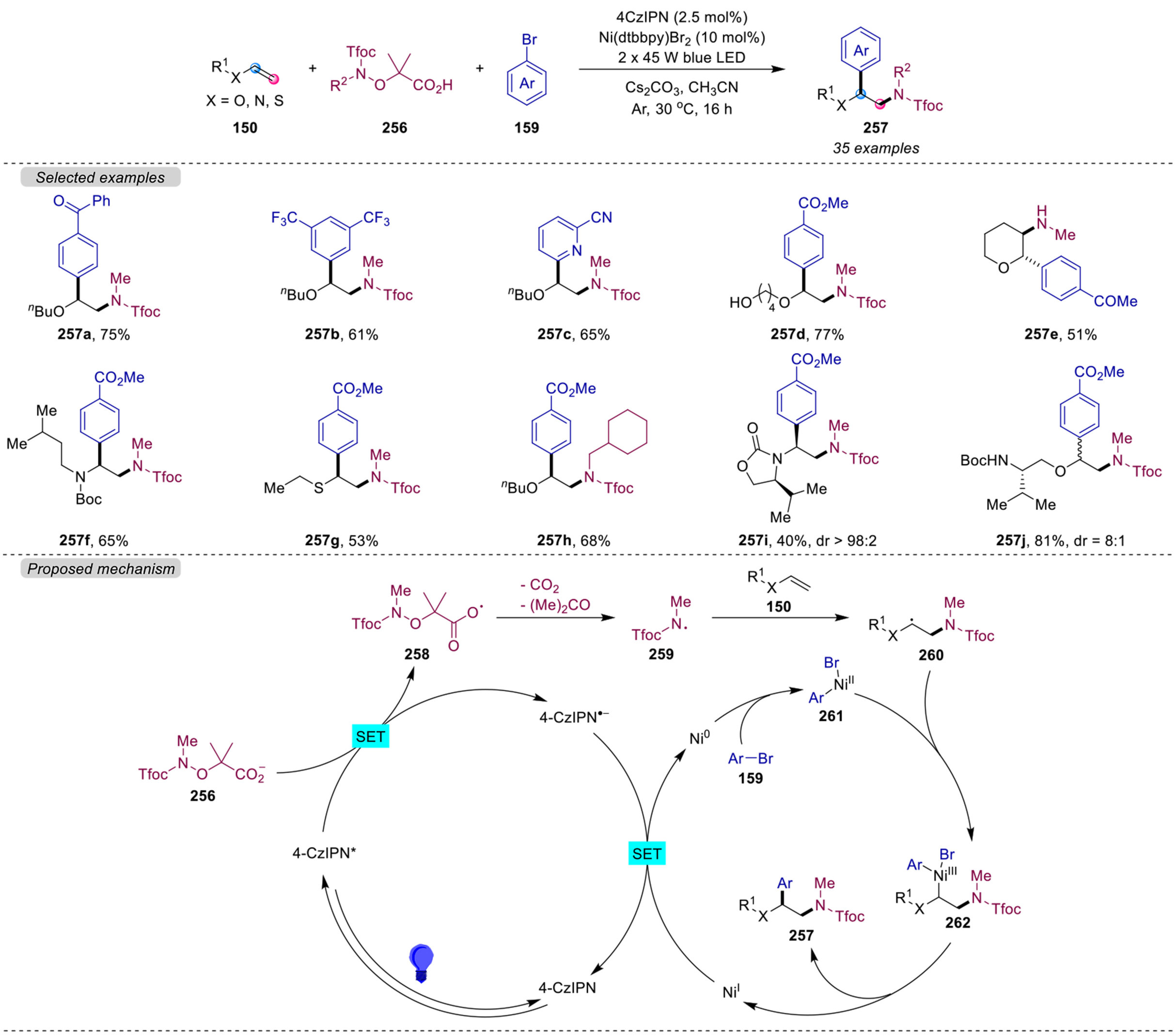
Jiang *et al.* reported a photoredox and nickel-catalyzed three-component aminoarylation of electron-rich alkenes **150** with 2,2,2-trifluoroethoxy carbonyl protected α-amino-oxy acids **256** and aryl bromides **159**, which provide 1,2-aminoarylation products **257** in 37%-89% yields [Scheme 32][93]. The *anti*-Markovnikov addition of the amidyl radicals derived from **256** to the alkenes **150** and Ni-mediated radical/transition metal crossover result in the formation of 1,2-aminoarylation product. The category of electron-rich alkenes encompasses a number of different compounds, including vinyl ethers, vinyl amides, vinyl amines and vinyl thioethers.



Scheme 31. Photoinduced ketone and Ni-catalyzed 1,2-alkylarylation of electron-deficient alkenes by C–H cleavage.

The catalytic process commences with the photoexcitation of 4CzIPN upon irradiation to generate the excited redox catalyst 4CzIPN*, which oxidizes deprotonated **256** by SET pathway, resulting in the formation of carboxyl radicals **258** and reduced 4CzIPN$^{\bullet -}$. The cleavage of radicals **258** results in the formation of nitrogen-centered radicals **259**, accompanied by the release of CO_2 and acetone. Subsequently, electron-rich alkenes **150** are captured by radicals **259** via radical addition, affording the radical adducts **260**. Concurrently, the reduced photosensitizer 4CzIPN$^{\bullet -}$ reduces Ni^I species to Ni^0 and returns to the ground-state 4CzIPN, closing the photocatalytic cycle. Next, Ni^0 undergoes oxidative addition with aryl bromide **159** and combines with radical adducts **260** to form key Ni^{III} complex **262**, which is then subjected to reductive elimination to afford final products **257** and a Ni^I species, completing the nickel catalysis cycle.

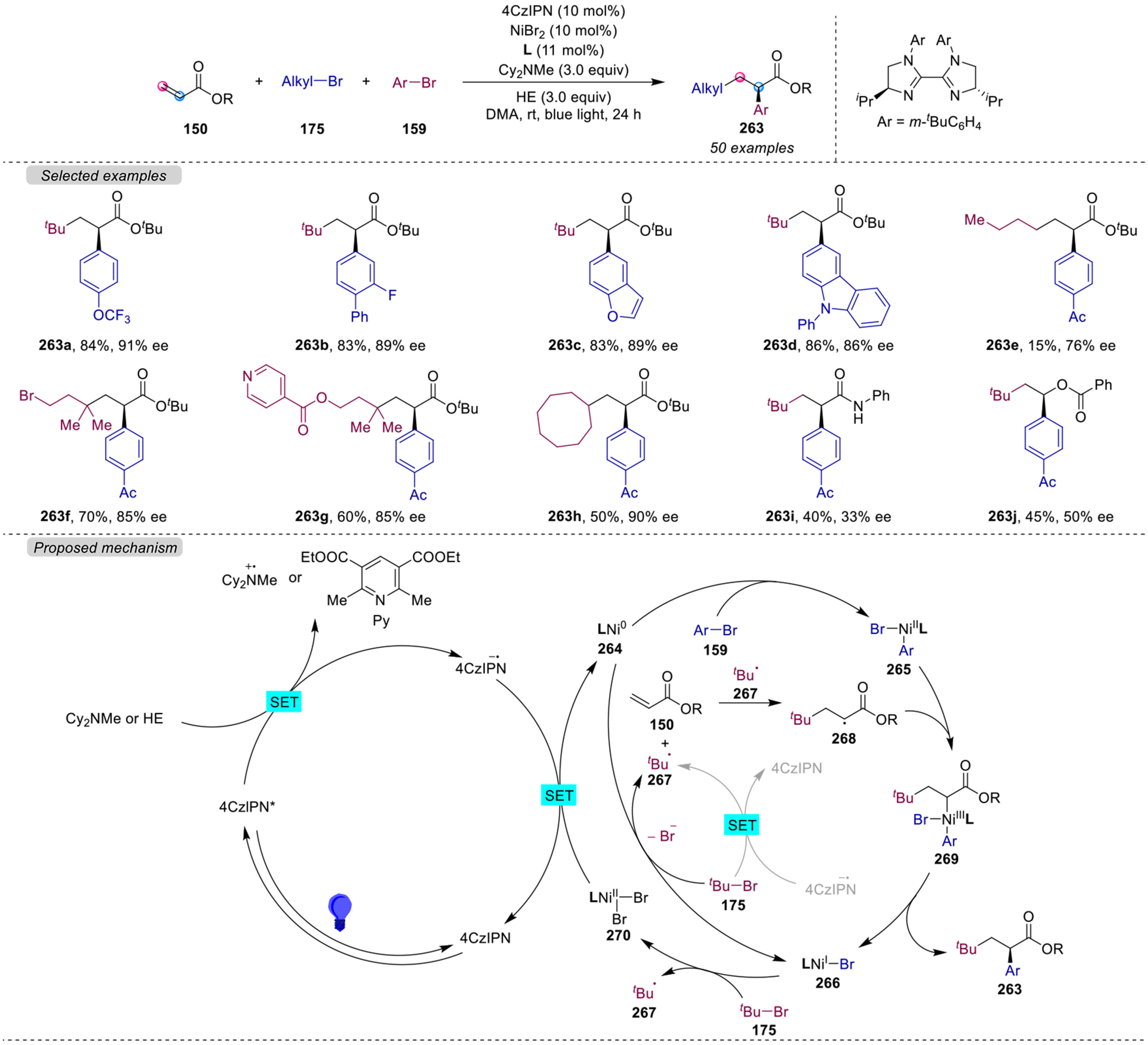
Enantioenriched α-aryl propionic acid is an important structural unit of nonsteroidal *anti*-inflammatory medications (NSAIDs). Qian *et al*. reported a visible-light-promoted photoredox/nickel dual catalyzed three-component reductive coupling reaction of acrylates **150** with alkyl halides **175** and aryl bromides **159**, which afforded enantioenriched α-arylpropionate esters **263** with 15%-90% yields and 33%-93% ee [Scheme 33][94]. Notably, key steps of this protocol include the reduction of alkyl bromide to the alkyl radical, which is then added to acrylate by Giese addition followed by capture by the enantioenriched nickel



Scheme 32. Photo- and Ni-catalyzed 1,2-aminoarylation of electron-rich alkenes.

catalyst, thus affording the desired product. Furthermore, this strategy is applicable to acrylic esters or acrylamide and a range of alkyl and aryl bromides.

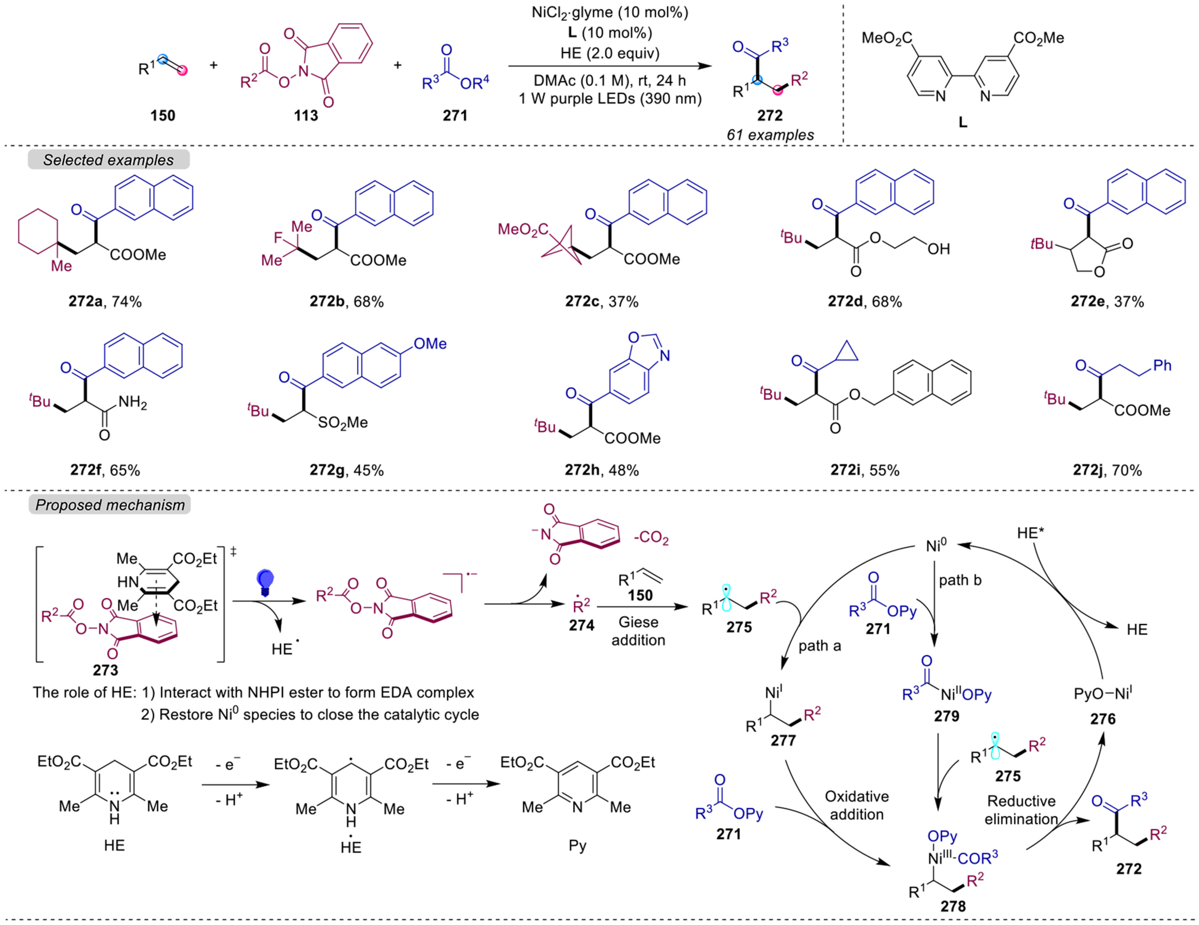
The plausible mechanism of this reaction is proposed in Scheme 33. The reduced PC 4CzIPN$^{\bullet-}$ via two SET processes *in situ* provides LNi^0 species **264**, which undergoes oxidative addition with the aryl bromides **159** to yield the LNi(Ar)^{II}Br complex **265**. Meanwhile, the alkyl bromides **175** undergo a SET process by either the **264** or reduced 4CzIPN$^{\bullet-}$ to generate alkyl halide radical anions, which then undergo a loss of bromide, generating the tertiary radicals **267**, being tapped by acrylate **150** and deliver α-carbonyl radical **268**. Subsequently, radical **268** is intercepted by **265** to form Ni^{III} complex **269**, which undergoes rapid reductive elimination to give the final products **263** and Ni^I species **266**. In the photoredox cycle, photoexcited *4CzIPN reacts with HE or Cy$_2$NMe to give 4CzIPN$^{\bullet-}$. The generated 4CzIPN$^{\bullet-}$ is oxidized by nickel catalyst (Ni^{II}/Ni^I) and/or **175** to regenerate 4CzIPN.



Scheme 33. Photo- and Ni-catalyzed enantioselective 1,2-alkylarylation of acrylates under reductive conditions.

In the reported visible-light-mediated/nickel dual-catalyzed alkenes three-component cross-coupling reactions, many catalytic systems require the introduction of PCs to initiate the reaction. Interestingly, the difunctionalization of alkenes can also be achieved without the use of external PCs through the ingenious design of substrates. In 2022, Xi *et al*. developed a visible-light-induced nickel-catalyzed three-component net-reduction 1,2-alkylacylation of activated alkenes **150** with NHPI esters **113** and 2-pyridyl esters **271** to furnish a series 1,3-dicarbonyl compounds **272** with 30%-81% yields [Scheme 34][95]. Notably, the reductive coupling generates electron donor-acceptor (EDA) complexes *in situ*, obviating the need for the addition of external PCs and stoichiometric metal reducing agents. Additionally, this reaction is applicable to a range of activated alkenes, NHPI esters, and 2-pyridine esters under mild conditions.

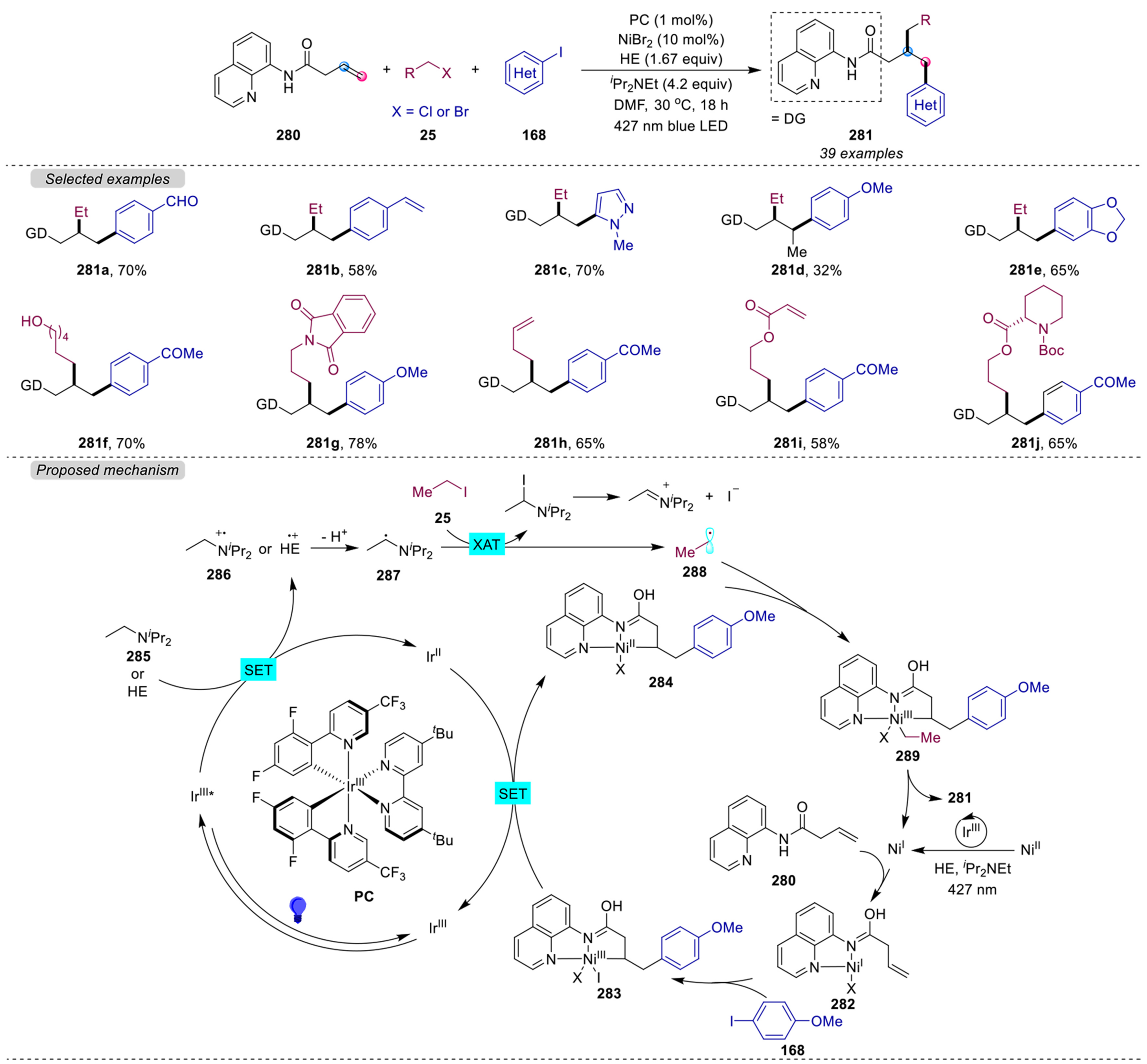
The mechanism study shows that the reaction begins with the coordination of NHPI esters **113** and HE to form photoactive EDA complex **273** under visible-light irradiation, which results in the extrusion of CO_2 and phthalimide anion and subsequently generates alkyl radical **274**. The latter is then captured by activated alkenes **150** through Giese addition, leading to the formation of radical intermediates **275**. Meanwhile, the



Scheme 34. Photo- and Ni-catalyzed 1,2-alkylacylation of electron-deficient alkenes.

catalytically active Ni^0 is formed by the reduction of Ni^{II} pre-catalyst **276** with the excited state of HE*. Then, Ni^0 species combine with alkyl radical **275** to provide the Ni^I complex **277**, which undergoes oxidative addition with the ester **271** leading to the generation of Ni^{III} intermediate **278**. An alternative pathway involves the direct oxidative addition of Ni^0 to 2-pyridyl esters **271**, resulting in the formation of Ni^{II} complex **279**. This complex then interacts with alkyl radicals **275**, generating Ni^{III} intermediates **278**. Finally, species **278** undergo reductive elimination to furnish the 1,3-dicarbonyl compounds **272** and Ni^I species **276**. Lastly, the excited state of HE* reduces **276**, thereby regenerating active Ni^0 species and closing the catalytic cycle.

In general, the regioselectivity of electronically unbiased alkyl alkenes is challenging to control. However, this can be addressed by introducing directing groups into the raw materials, which allows for greater control over the reaction outcome. Dey *et al*. reported a visible-light-mediated and nickel dual catalyzed three-component 1,2-dicarbofunctionalization of unactivated alkenes **280** with alkyl bromides/iodides **25** and aryl iodides **168** to deliver coupling products **281** in 32%-84% yields [Scheme 35][96]. Notably, 8-aminoquinoline serves the dual function of a directing group and a ligand, thereby driving the process. This strategy is applicable to both terminal and internal unactivated alkenes, along with various alkyl/aryl halide reagents.



Scheme 35. Photo- and Ni-catalyzed 1,2-arylalkylation of unactivated alkenes.

The transformation is initiated by visible-light. Upon irradiation, Ni^{II} from NiBr$_2$ is reduced to Ni^{I} species by PC Ir^{III}, which coordinates with 8-aminoquinoline and then tethers unactivated alkenes **280** to generate Ni^{I} complex **282**, followed by sequential oxidative addition and migration insertion providing Ni^{III} complex **283**. Next, the reduced-state Ir^{II} undergoes SET process to reduce **283** to Ni^{II} species **284**, accompanied by the generation of ground-state Ir^{III}. Meanwhile, tertiary amine **285** or HE reacts with *Ir^{III} via a SET pathway to obtain α-amino radical cations **286** or HE$^{\bullet+}$, which undergo a rapid deprotonation process leading to the generation of α-amino radicals **287**. Subsequently, they interact with alkyl halides **25** through halogen atom transfer (XAT), producing alkyl radicals **288**. Lastly, alkyl radicals **288** are trapped by intermediates **284** to give Ni^{III} species **289**, which then undergo reductive elimination to deliver final products **281**.

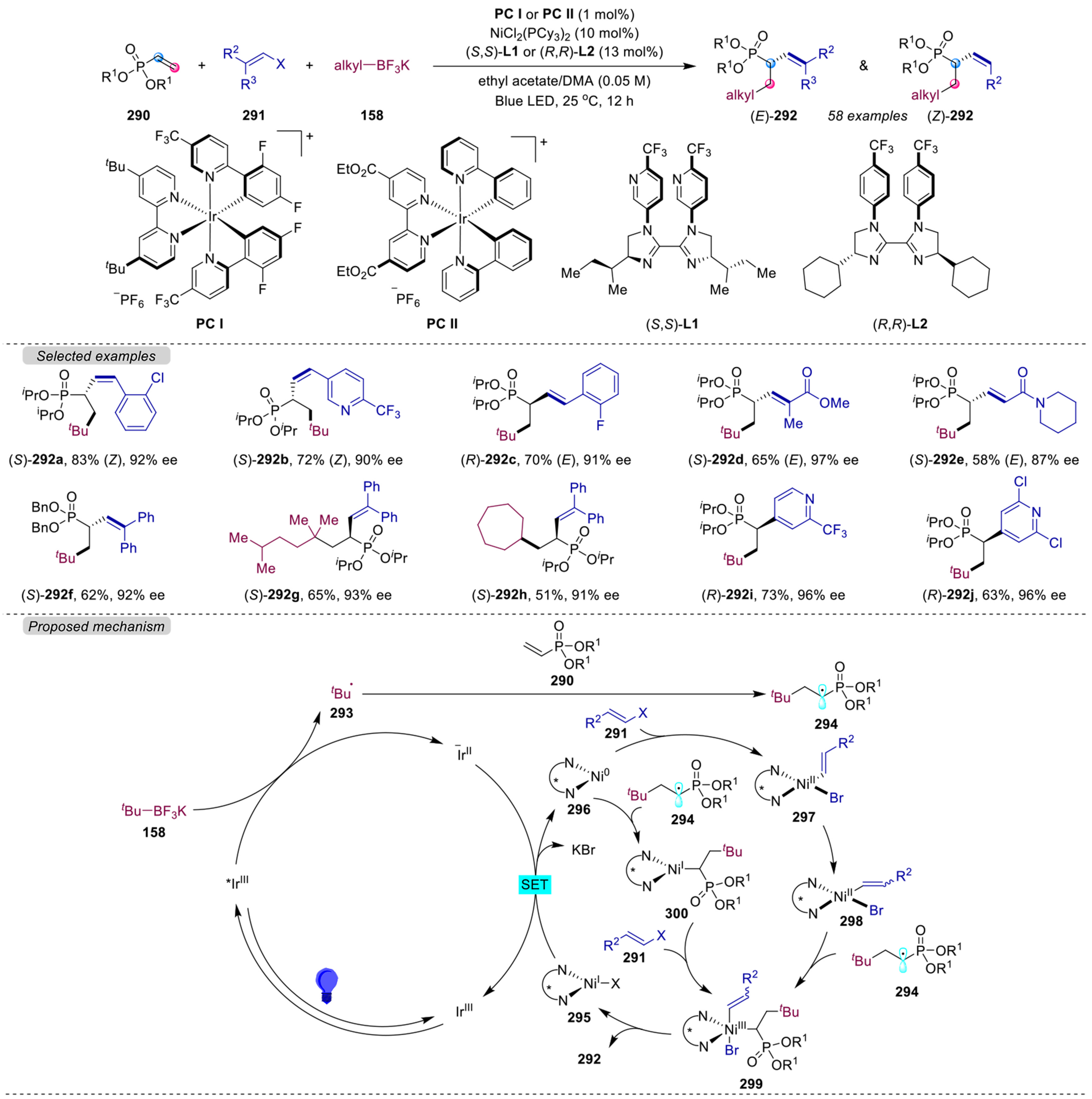
The exceptionally high reactivity of open-shell radical species has resulted in the catalytic asymmetric multicomponent cross-coupling involving radicals remaining largely underdeveloped. In 2023, Li *et al.* reported a nickel metallaphotoredox catalyzed chemo-, regio-, stereo-, and enantioselective three-component cross-coupling reaction of vinyl phosphonates **290** with alkenyl halides **291** and alkyl trifluoroborates **158** to produce a series of enantioenriched α-alkenyl phosphonates **292** with 43%-89% yields and 85%-98% ee [Scheme 36][97]. Moreover, by modifying the triplet energy of the PC, it is possible to achieve the divergent formation of enantio-enriched trans and cis α-alkenyl phosphonates. The strategy is compatible with various alkenyl halides **291** and alkyl trifluoroborates **158** under mild conditions, with the exception that the alkene contains a vinyl phosphate ester.

The possible mechanism of this three-component reaction is shown in Scheme 36. Upon irradiation, ground-state PC $\mathrm{Ir^{III}}$ is converted into its excited-state $^*\mathrm{Ir^{III}}$, which oxidizes alkyl trifluoroborates **158** to alkyl radicals **293** by single-electron oxidation. This is followed by a fast and irreversible Giese addition to vinyl phosphonates **290**, which affords α-phosphonate alkyl radicals **294**. Simultaneously, generated $\mathrm{Ir^-}$ reduces $\mathrm{Ni^I}$ complex **295**, which is derived from nickel coordinating with chiral ligands to the $\mathrm{Ni^0}$ species **296** along with the regeneration of the ground-state $\mathrm{Ir^{III}}$ and the termination of the photocatalytic cycle. Then, $\mathrm{Ni^0}$ species **296** engage with vinyl bromides **291**, resulting in direct oxidative addition to generate singlet spin-state, square-planar $\mathrm{Ni^{II}}$ **297**. This then undergoes isomerization to the tetrahedral, triplet spin-state $\mathrm{Ni^{II}}$ **298**, followed by the capture of α-phosphonate alkyl radicals **294**, which affords the crucial $\mathrm{Ni^{III}}$ species **299**. An alternative pathway involves the direct combination of $\mathrm{Ni^0}$ with alkyl radicals **294** via radical addition, resulting in the formation of $\mathrm{Ni^I}$ complex **300**. This complex then undergoes oxidative addition with vinyl bromides **291**, leading to the generation of $\mathrm{Ni^{III}}$ species **299**. Finally, $\mathrm{Ni^{III}}$ species **299** undergoes reversible radical dissociation prior to productive reductive elimination to give the desired products **292** and regenerate $\mathrm{Ni^I}$ complex **295**, thereby closing the nickel catalytic cycle.

At present, there are still rare reports on the three-component cross-coupling reaction of aromatic alkenes that employ a combination of photoredox and nickel catalysis. In 2023, Liu *et al.* developed a visible-light-induced and nickel-catalyzed three-component enantioselective transformation of aryl alkenes **12** with alkenyl halides **291** and sodium sulfinates **202** to afford enantioenriched β-chiral sulfones **301** in 45%-90% yields and 72%-94% ee [Scheme 37(a)][98]. This dual catalytic strategy allows for a one-step reaction in the presence of chiral ligands while controlling enantioselectivity, and thus enables the direct obtaining of the target product from readily available starting materials. Moreover, this protocol is applicable to a range of alkenyl halides and sodium aryl/alkyl sulfinates, although the alkenes are limited to terminal aromatic alkenes.

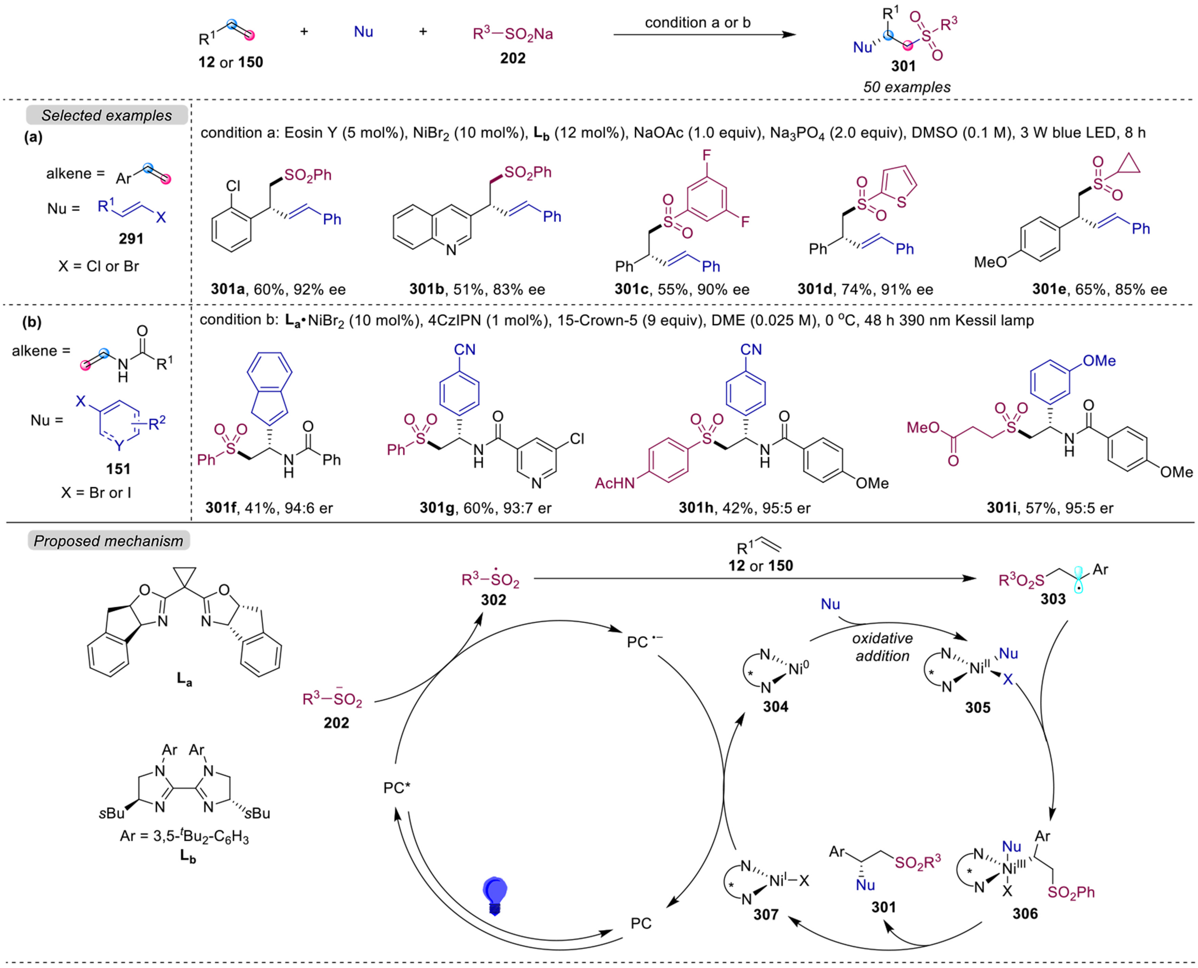
This process is initiated by the PC Eosin Y being excited to excited-state Eosin $\mathrm{Y^*}$ under visible-light irradiation. This results in the oxidation of sulfinates **202**, which deliver the radical anion Eosin $\mathrm{Y^{\bullet-}}$ and sulfonyl radicals **302**. The latter is trapped by styrenes **12**, leading to the formation of benzylic radicals **303**. Meanwhile, active species $\mathrm{Ni^0}$ **304** reacts with alkenyl halides **291** by oxidative addition to form alkenyl nickel intermediates **305**. These selectively rebond with benzylic radicals **303** to form $\mathbf{L^*}\mathrm{Ni^{III}}$ complex **306**, which then undergoes reductive elimination to provide the final β-chiral alkenyl sulfones **301** and $\mathbf{L^*}\mathrm{Ni^IX}$ species **307**. Lastly, $\mathbf{L^*}\mathrm{Ni^IX}$ is reduced by Eosin $\mathrm{Y^{\bullet-}}$ to regenerate $\mathbf{L^*}\mathrm{Ni^0}$ species **304** and ground-state Eosin Y, and accompanied by the close of two catalytic cycles.

Similarly, Du *et al.* described a nickel/photoredox dual-catalyzed asymmetric three-component carbonsulfonylation of *N*-vinylamide **150** with (hetero)aryl halides **151** and sodium sulfinates **202**[99]. This process simultaneously forms C–C and C–S bonds, allowing the synthesis of β-aryl and β-alkenyl sulfones in 40%-92% yields and 88:12-99:1 er [Scheme 37(b)]. The strategy employed 4CzIPN as the PC, chiral biimidazoline as the ligand, and is completed through $\mathrm{Ni^0/Ni^I/Ni^{III}}$ work pathway. Differently, secondary alkyl radicals **303** are rapidly captured by $\mathbf{L^*}\mathrm{Ni^0}$ complex **304** to afford (alkyl)$\mathrm{Ni^I}$ species. Next, aryl halides **151** and (alkyl)$\mathrm{Ni^I}$ species undergo oxidative addition to give (aryl)(alkyl)$\mathrm{Ni^{III}}$ intermediates **306**.

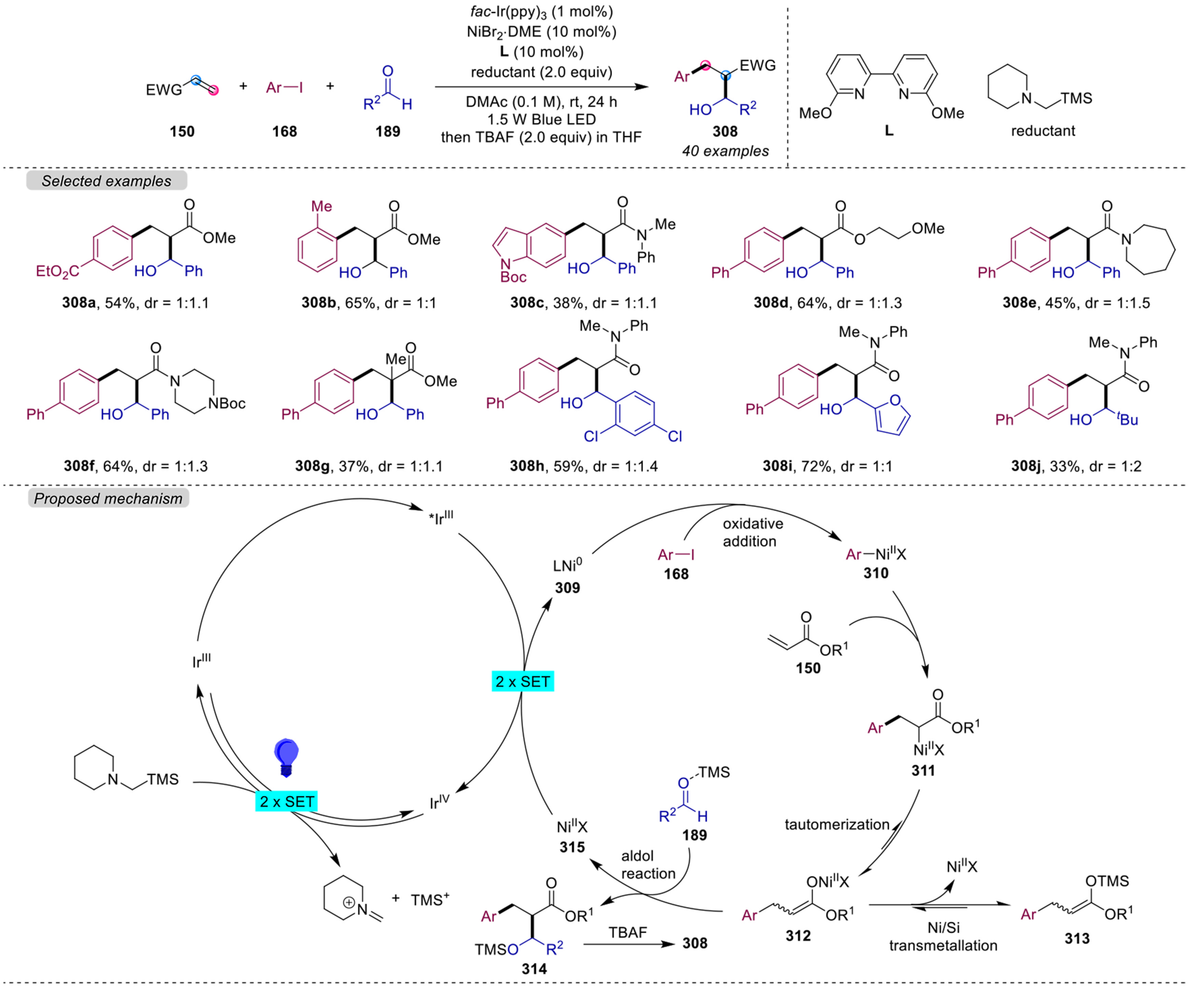


Scheme 36. Photo- and Ni-catalyzed enantioselective 1,2-alkylalkenylation of vinylphosphonates.

In accordance with the general mechanism proposed in Scheme 19, radical precursors are typically assembled at the distal carbon of alkene, while aromatic groups are located at the proximal carbon. Consequently, the alternative assembly mode, in which the radical precursor is attached to the proximal carbon of the olefin and the aryl group is attached to the distal carbon of the alkene, can facilitate the formation of more flexible and diverse coupling products. In 2023, Zhao *et al.* developed a nickel/photoredox dual catalyzed three-component reductive cross-coupling of electron-deficient alkenes **150** with aryl iodides **168** and aldehydes **189** [Scheme 38][100]. This process afforded β-hydroxy ester/amide compounds **308** with 30%-81% yields and 1:1-1:1.8 dr. Notably, the success of this coupling/tandem transformation hinges on the identification of α-silylamine as the organic reductant. This enables the release of silylium ions in lieu of protons, thereby preventing any unwanted protonation processes. Additionally, it serves as a Lewis acid to facilitate the *in situ* activation of aldehydes. The method is applicable to a range of



Scheme 37. Ni-organophotocatalyzed enantioselective sulfonylalkenylation of styrenes.

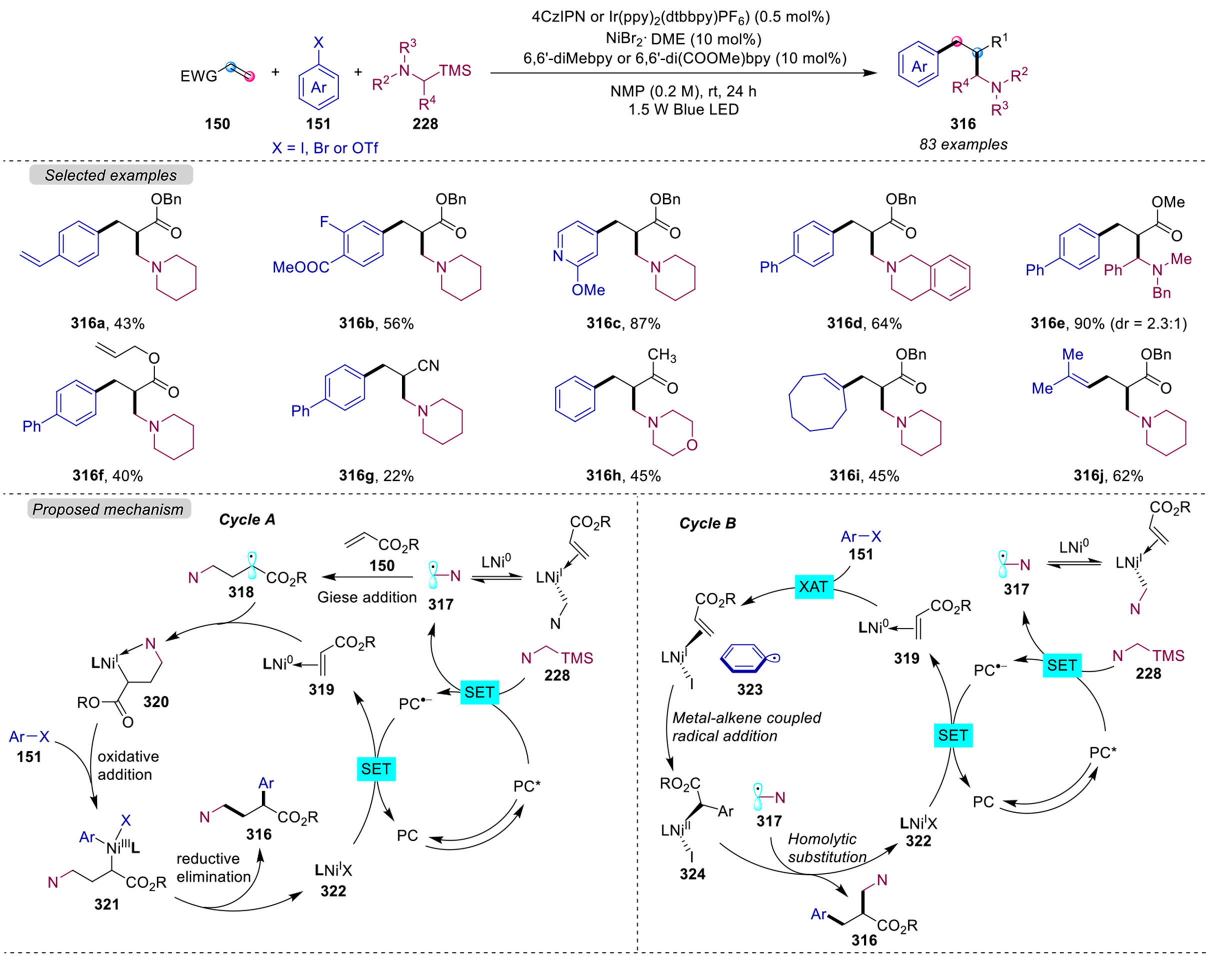


Scheme 38. Photo- and Ni-catalyzed reductive arylalkylation of alkenes with aldehydes.

substrates, including acrylic esters and amides, along with alkyl and aryl aldehydes.

A possible reaction mechanism is shown in Scheme 38. Initially, two SET processes occur between the photoexcited $^{*}Ir^{III}$ ($E^{IV/*III}_{1/2}$ = -1.73 V *vs.* SCE) and Ni^{II} [$E_{1/2}(Ni^{II}/Ni^{0})$ = -1.2 V *vs.* SCE] resulting in the generation of Ir^{IV} and $\mathbf{L}Ni^{0}$ species. The latter exhibits strong reductive potential Ir^{IV} ($E^{IV/III}_{1/2}$ = +0.77 V *vs.* SCE), which can oxidize α-silylamine ($E^{ox}_{1/2}$ = +0.71 V *vs.* SCE) to get iminium ion and TMS^{+} through another two SET processes, along with ground-state Ir^{III}. Concurrently, Ni^{0} species **309** undergoes oxidative addition with aryl iodides **168** to afford Ni^{II} species **310**, of which the migration insertion into C=C bond of **150** occurred to give α-carbonyl-Ni^{II} complex **311**. An equilibrium exists between Ni^{II} oxygen enolate **312** and carbon enolate **311** tautomers, which could be further transformed into a more stable silyl ketene acetal **313** via a Ni/Si transmetallation. Lastly, the aldol reaction, which is promoted by Lewis acidic silylium ions, delivers intermediates and regenerates the Ni^{II} catalyst. The removal of TMS, performed using tetrabutylammonium fluoride (TBAF), provides the final products.

In 2024, Ye *et al.* developed a visible-light-induced photoredox/nickel dual catalyzed ligand-controled regioreversed 1,2-arylalkylation of activated alkenes **150** with aryl halides **151** and α-silylamines **228**[101]. This process furnished β-amino esters/amides **316** in 22%-92% yields [Scheme 39]. Notably, this strategy involves



Scheme 39. Photo- and Ni-catalyzed alkylaminoarylation of electron-deficient alkenes.

the generation of phenyl radicals for the attachment of the phenyl group on the distal carbon of alkene, rather than the conventional Giese addition. Through mechanism studies, the authors identified *ortho*-substituted bipyridine ligands as the key factor in regulating regioselectivity. In addition, this strategy is suitable for both aryl halides and vinyl halides under mild conditions, although it is not compatible with primary or secondary amines.

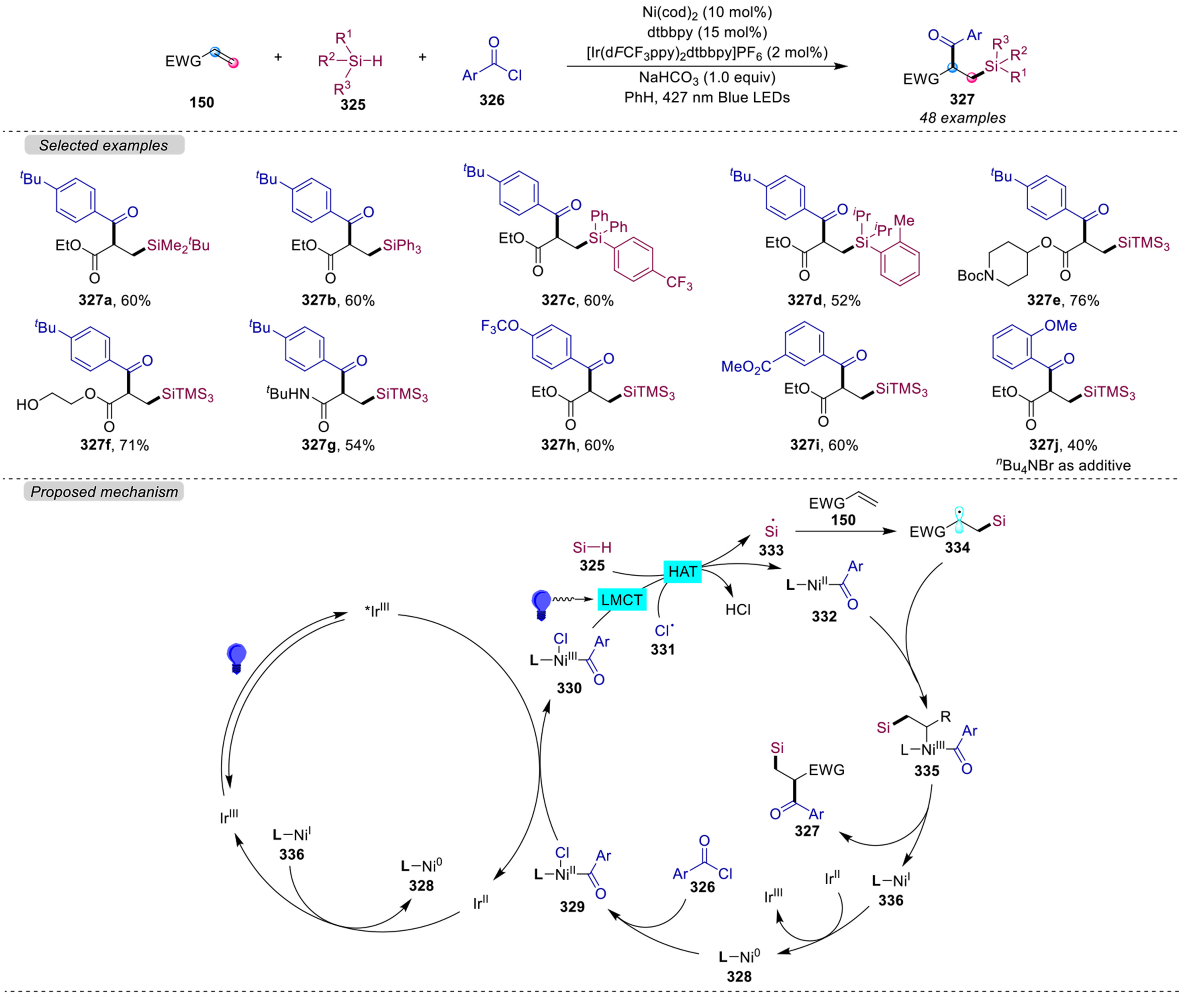
The authors put forth two possible reaction pathways. In cycle A, the excited photosensitizer PC* reacts with α-silylamines **228** by single electron reduction to form α-amino radicals **317**. These radicals are then trapped by alkenes **150** by Giese addition to form α-carbonyl radicals **318**, followed by combining with Ni^0 complex **319** to give Ni$^{\mathrm{I}}$ intermediates **320**. Subsequently, oxidative addition of **320** with aryl halides **151** results in the formation of Ni$^{\mathrm{III}}$ intermediates **321**, which undergo reductive elimination to yield the 1,2-aminoalkylarylation products **316** and Ni$^{\mathrm{I}}$ complex **322**. Finally, the SET process between Ni$^{\mathrm{I}}$ **322** and the reduced state PC$^{\bullet-}$ to regenerate ground-state PC and **319**. Notably, the use of bpy ligands with strong coordination ability inhibits the competitive XAT pathway for the reaction of aryl halides with Ni^0 complexes. Furthermore, the *ortho*-substituted bpy ligand weakens the coordination affinity of alkenes to the Ni^0 center, thus enhancing the reactivity of XAT to generate aryl radicals **323**, which in turn trigger the 1,2-arylaminealkylation process (cycle B). Therefore, the reaction is preferentially initiated by the metal-alkene coupling radical addition reaction of **323**, forming triplet alkyl Ni$^{\mathrm{II}}$ **324**. This then undergoes homolytic substitution with α-amino radicals **317**, resulting in the formation of the 1,2-arylaminoalkylation products **316**.

The chlorine radical is widely acknowledged as an effective electrophilic hydrogen atom abstractor. In 2024, Koo *et al.* reported a nickel/photoredox-catalyzed three-component silylacylation of acrylates **150** with hydrosilyl compounds **325** and aryl acyl chlorides **326**, which provided 1,3-dicarbonyl compounds **327** in 40%-79% yields under redox-neutral conditions [Scheme 40][102]. The protocol employs LMCT to facilitate the cleavage of Ni^{III}-Cl, thereby generating chlorine radicals. These radicals then activate Si–H bonds through hydrogen atom transfer (HAT), resulting in the generation of silicon radicals. Notably, acyl chlorides serve the dual function of acylating agents and chloride donors throughout the process. Additionally, this catalytic system is suitable for the conversion of acrylic esters and amides, but only compatible with arylacyl chlorides and tertiary silanes.

The reaction is initiated by the oxidative addition reaction of LNi^0 **328** with aryl acyl chlorides **326** to form Ni^{II} **329**, which undergoes single-electron oxidation by the excited PC $^*Ir^{III}$ ($^*E_{1/2}$ = +1.21 V *vs.* SCE in MeCN), leading to the formation of Ni^{III} species **330**. Upon visible-light irradiation, the Ni^{III} complex **330** engages in LMCT, resulting in the photoelimination of a chlorine radical **331** and the regeneration of a Ni^{II} complex **332**. This chlorine radical then interacts with hydrosilanes **325** by HAT, affording silyl radicals **333**. These are subsequently captured by α,β-unsaturated alkenes **150** to give alkyl radicals **334**, followed by combining with **332** to yield Ni^{III} species **335**. This then undergoes reductive elimination to produce the 1,3-dicarbonyl compounds **327** and a Ni^I complex **336**. Finally, the reduction of Ir^{II} ($E_{1/2}$ = -1.37 V *vs.* SCE in MeCN) by Ni^I (E_p = -1.17 V *vs.* SCE in THF) via SET results in the regeneration of ground-state Ir^{III} and the formation of Ni^0 species **328**, thereby completing the dual catalytic cycle.

The construction of $C(sp^3)$–$C(sp^3)$ bonds represents a significant challenge in cross-coupling chemistry. In 2024, Cong *et al.* reported a photoredox/nickel dual catalyzed trimolecular cross-coupling of unactivated alkenes **8** with alkyl halides **25** and hypervalent iodine-based reagents **337** to deliver dicarbofunctional products **338** in 29%-94% yields [Scheme 41][103]. Notably, the approach undergoes a bimolecular homolytic substitution (S_H2) mechanism and chemoselective XAT to achieve regioselectivity without the assistance of a directing group and simultaneously constructing two $C(sp^3)$–$C(sp^3)$ bonds.

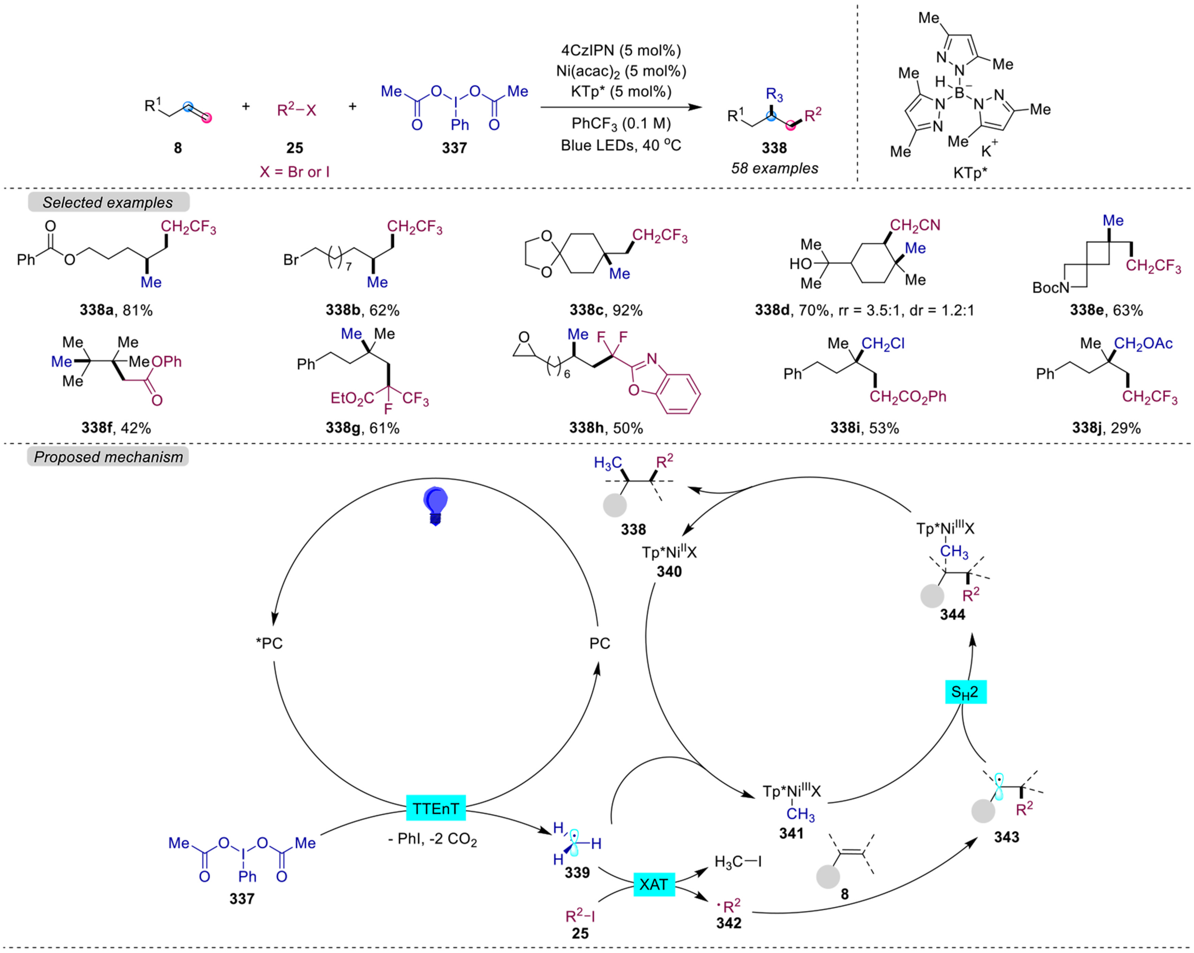
Irradiation of the PC 4CzIPN with blue light resulted in the conversion of 4CzIPN into a high-energy triplet state 4CzIPN*. This energy transfer to the iodine (III) compound **337** was facilitated by triplet-triplet energy transfer (TTenT), leading to the homolysis of the I–O bond and the subsequent formation of carboxyl radicals. These radicals fragment to release methyl radical **339**, iodobenzene, and CO_2. Subsequently, the nucleophilic and unhindered **339** is trapped by the *in situ*-generated Ni^{II} species **340** to form the Ni^{III} species **341**. Meanwhile, another equivalent of methyl radical engages with the electron-poor alkyl iodides **25** by chemoselective XAT to afford an electrophilic alkyl radical **342** and an iodomethane byproduct. Alkyl radicals **342** are regioselectively intercepted by the unactivated C=C bond of **8** (polarity matching) to form a sterically more congested alkyl radical **343**, which favors S_H2 coupling with **341** to afford Ni^{III} complex **344**. This complex is then delivered to final dialkylation products **338** and regenerate **340**, thereby shutting off the nickel catalytic cycle. It is crucial to note that the success of this dialkylation process depends on the ability of the organonickel-catalyzed species to discern between various radical intermediates **339**, **342** and **343** (the nucleophilic and unhindered **339** preferentially associates with the Ni center in **340**), and the key role of the electrophilic reagents **342** is to facilitate the nucleophile **339** induced selective XAT formation reaction with **25**.



Scheme 40. Photo- and Ni-catalyzed silylacylation of acrylates.

Wang *et al*. reported a visible-light-induced nickel-catalyzed three-component arylalkylation of unactivated alkenes **8** with aryl bromides **159** and NHPI esters **113** to afford desired products **345** in 41%-83% yields [Scheme 42][104]. This protocol employs a high-energy aryl radical, a primary radical and a hindered alkyl radical sorting mechanism to construct C(sp^3)–C(sp^3) bonds and C(sp^3)–C(sp^2) bonds. This conversion overcomes the issues of uncontrolled radical recombination and disproportionation through a nickel-catalyzed S$_H$2 step.

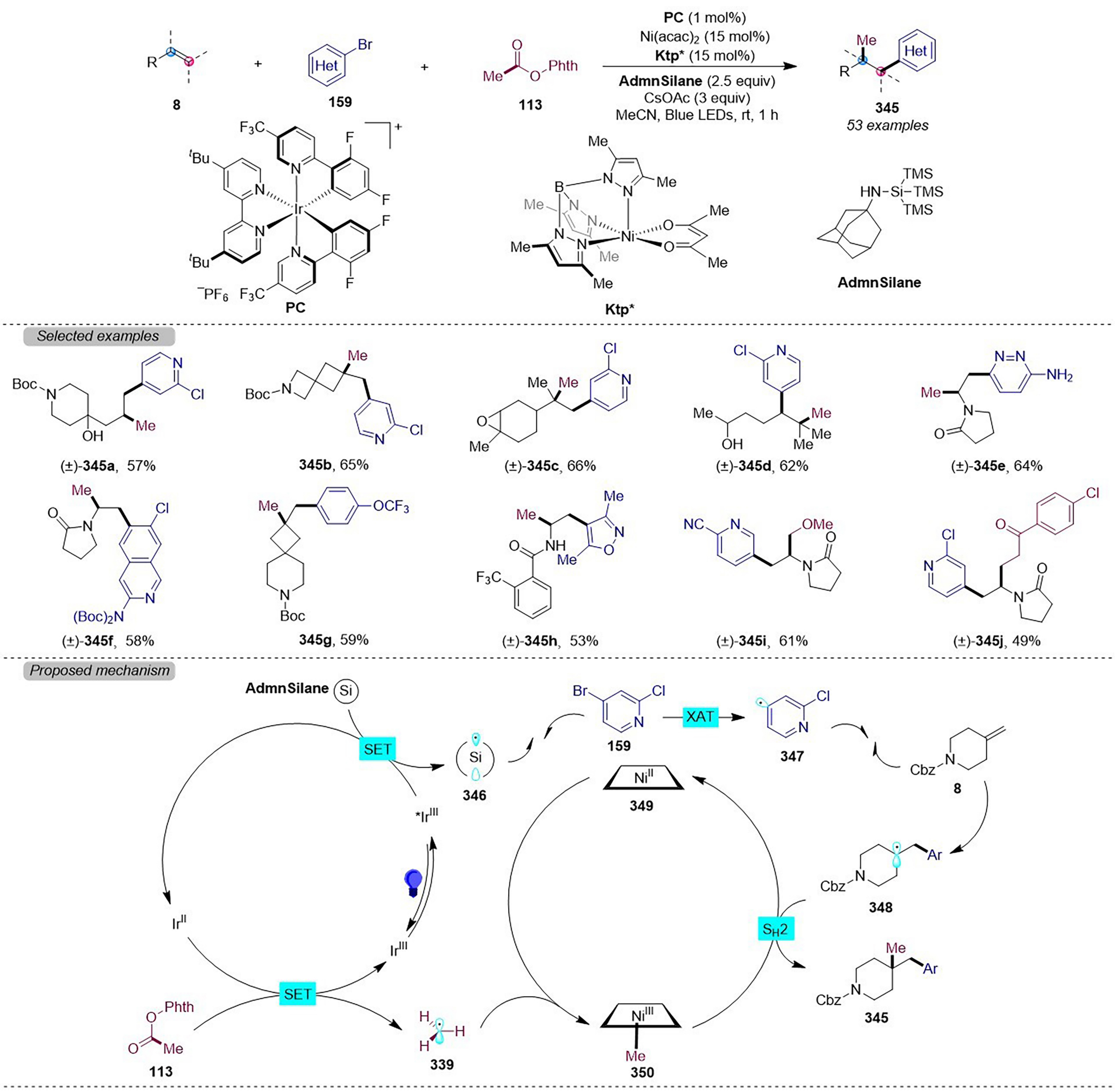
The process starts with the iridium PC Ir^{III} being excited to long-lived triplet excited-state *Ir^{III}[$E_{1/2}^{red}$ (*Ir^{III}/Ir^{II}) = +1.21 V *vs*. SCE in MeCN]. This is then reductively quenched by Adamantylaminosupersilane (Admn silane) [E_{pa} = +0.86 V *vs*. SCE in *N,N*-dimethylacetamide (DMA)/*tert*-amyl alcohol], after which it undergoes rapid aza-Brook rearrangement to yield a silyl radicals **346**. Subsequently, radical species **346** react with aryl bromides **159** by XAT process affording key aryl radicals **347**, which then adds to C=C bonds of alkene **8** to provide hindered alkyl radicals **348**. Meanwhile, Ir^{II} reduces redox-active NHPI esters **113**, subsequently undergoing decarboxylation to yield primary alkyl radicals **339**. These are captured by the S$_H$2 radical-sorting catalyst **349**, forming an alkyl metal complex **350**. Lastly, the hindered alkyl radicals **348** combine with alkyl metal complex **350** by S$_H$2 reaction, thereby delivering the final products **345** and regenerating the catalyst **349**.



Scheme 41. Photo- and Ni-catalyzed dialkylation of unactivated alkenes.

In 2024, Hu *et al*. described a visible-light-promoted and nickel-catalyzed asymmetric three-component dicarbofunctionalization of alkene **150** with C(sp^3)–H nucleophiles **236** and aryl bromides **159** to provide α-aryl/alkenyl carbonyls and phosphonates in 25%-92% yield and 59:41-98:2 er [Scheme 43][105]. This protocol provides an efficient platform for the installation of C(sp^3)–C(sp^3) bonds and C(sp^3)–C(sp^2) bonds with chemo-, regio- and enantioselectivity from ubiquitous alkane, ether and alcohol feedstocks. Furthermore, the photoredox/nickel catalytic system is compatible with activated alkenes, styrene-type alkenes, and a series of (hetero)aryl bromides.

The catalytic mechanism is illustrated in Scheme 43. First, ground-state PC $[W_{10}O_{32}]^{4-}$ is stimulated to excited-state $^*[W_{10}O_{32}]^{4-}$ by visible-light, which then abstracts a hydrogen atom from C(sp^3)-H nucleophiles **236**, resulting in the formation of alkyl radicals **352** and singly reduced $[W_{10}O_{32}]^{5-}H^+$. The disproportionation of $[W_{10}O_{32}]^{5-}H^+$ results in the formation of doubly reduced $[W_{10}O_{32}]^{6-}2H^+$ and the regeneration of ground-state $[W_{10}O_{32}]^{4-}$. The photocatalytic cycle was completed. Subsequently, carbon-centered radicals **352** are intercepted by alkenes **150** via radical addition to another alkyl radical **353**. The latter species is then trapped by Ni^0 species **354**, resulting in the formation of alkyl-Ni^I species **355**, which undergoes oxidative addition with alkenyl bromides **159** to generate alkyl-Ni^{III}-aryl complex **356**. Alternatively, Ni^I species **357** could combine with alkyl radicals **353** to form alkyl-Ni^{II} species **358**, which are converted to alkyl-Ni^I species **355** via single-electron reduction. Finally, intermediates **356** undergo reductive elimination to produce the final



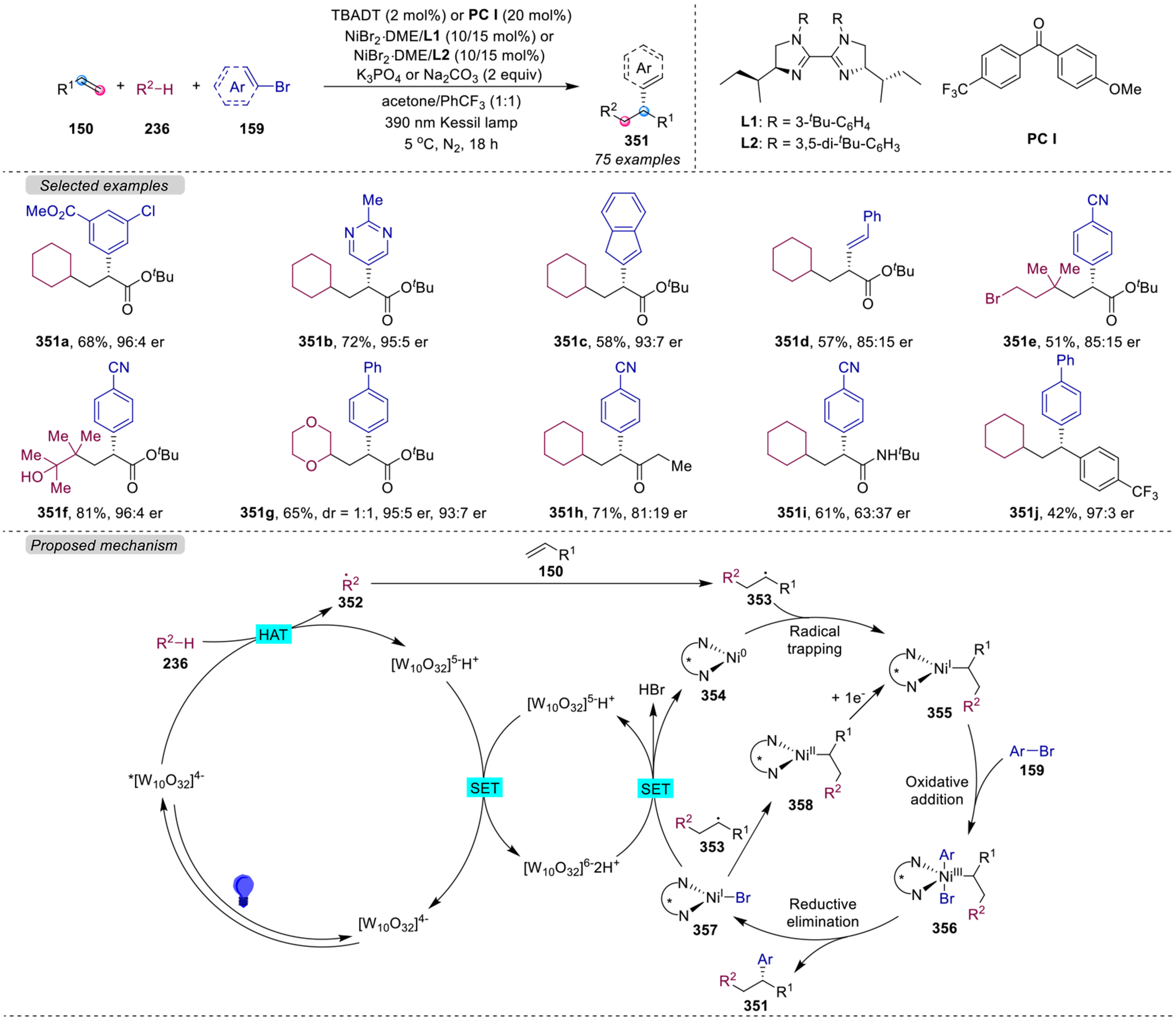
Scheme 42. Photo- and Ni-catalyzed arylmethylation of alkenes.

products **351** and Ni^I species **357**, which interact with doubly reduced $[W_{10}O_{32}]^{6-}2H^+$ via a SET route, thereby regenerating the active Ni^0 catalyst **354** and singly reduced $[W_{10}O_{32}]^{5-}H^+$.

PHOTOREDOX AND CHROMIUM-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

In recent years, chromium catalysis has attracted considerable interest due to its distinctive reactivity[13]. However, three-component cross-coupling reaction of alkenes catalyzed by the combination of chromium and visible-light remains underdeveloped.

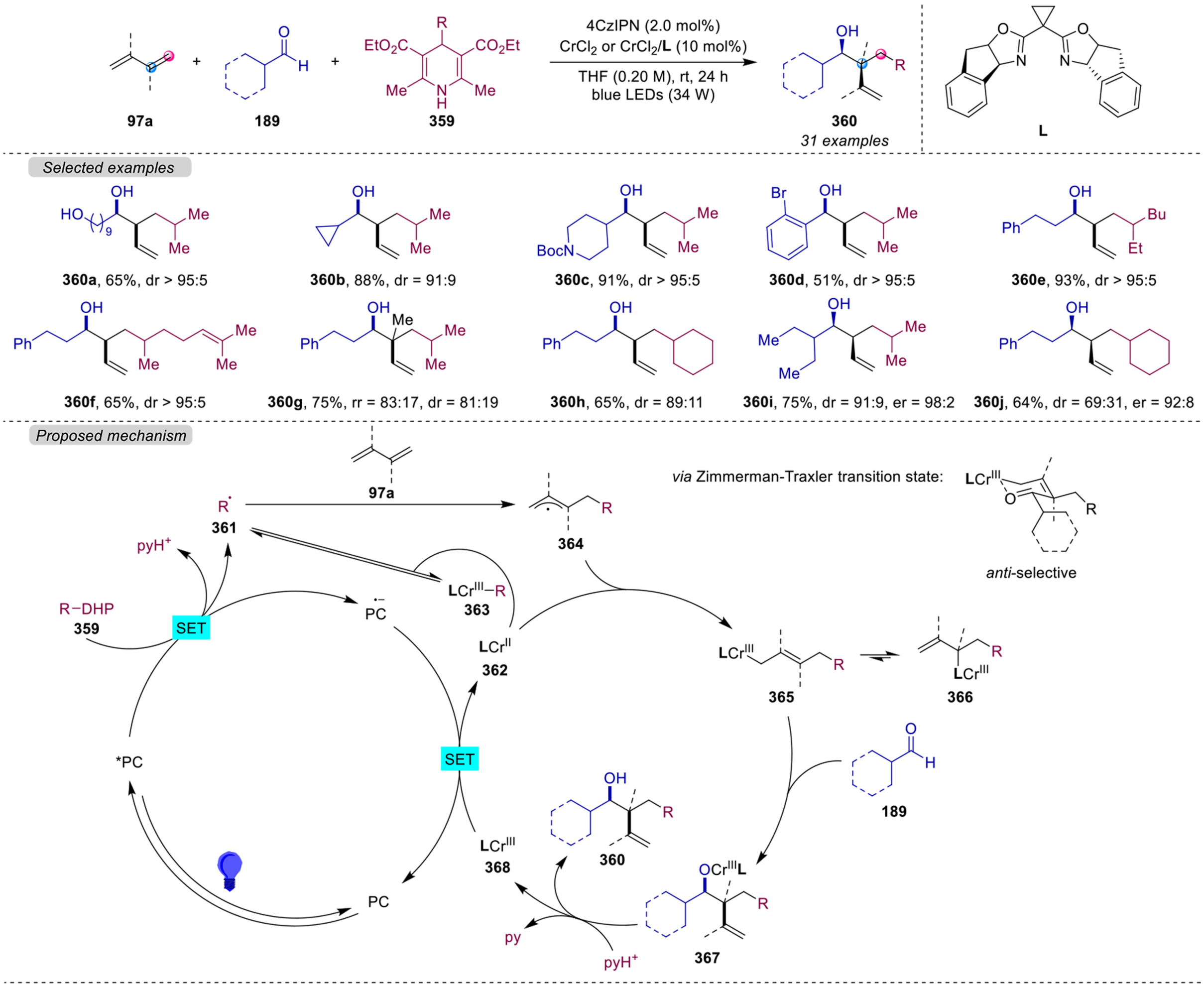
In 2020, Schwarz *et al.* developed a photoredox and chromium-catalyzed regioselective and diastereoselective dialkylation of 1,3-dienes **97a** with aldehydes **189** and 4-alkyl HEs **359** to deliver



Scheme 43. Photo- and Ni-catalyzed enantioselective alkylarylation of alkenes.

homoallylic alcohols **360** in 51%-95% yields and 70:30 to > 95:5 dr [Scheme 44][106]. Moreover, enantioselective synthesis of homoallylic alcohols can be achieved by incorporating chiral bisoxazoline ligands into the catalytic system. This approach is applicable to diverse alkyl/aryl aldehydes, 4-alkyl HEs and alkyl-substituted 1,3-dienes.

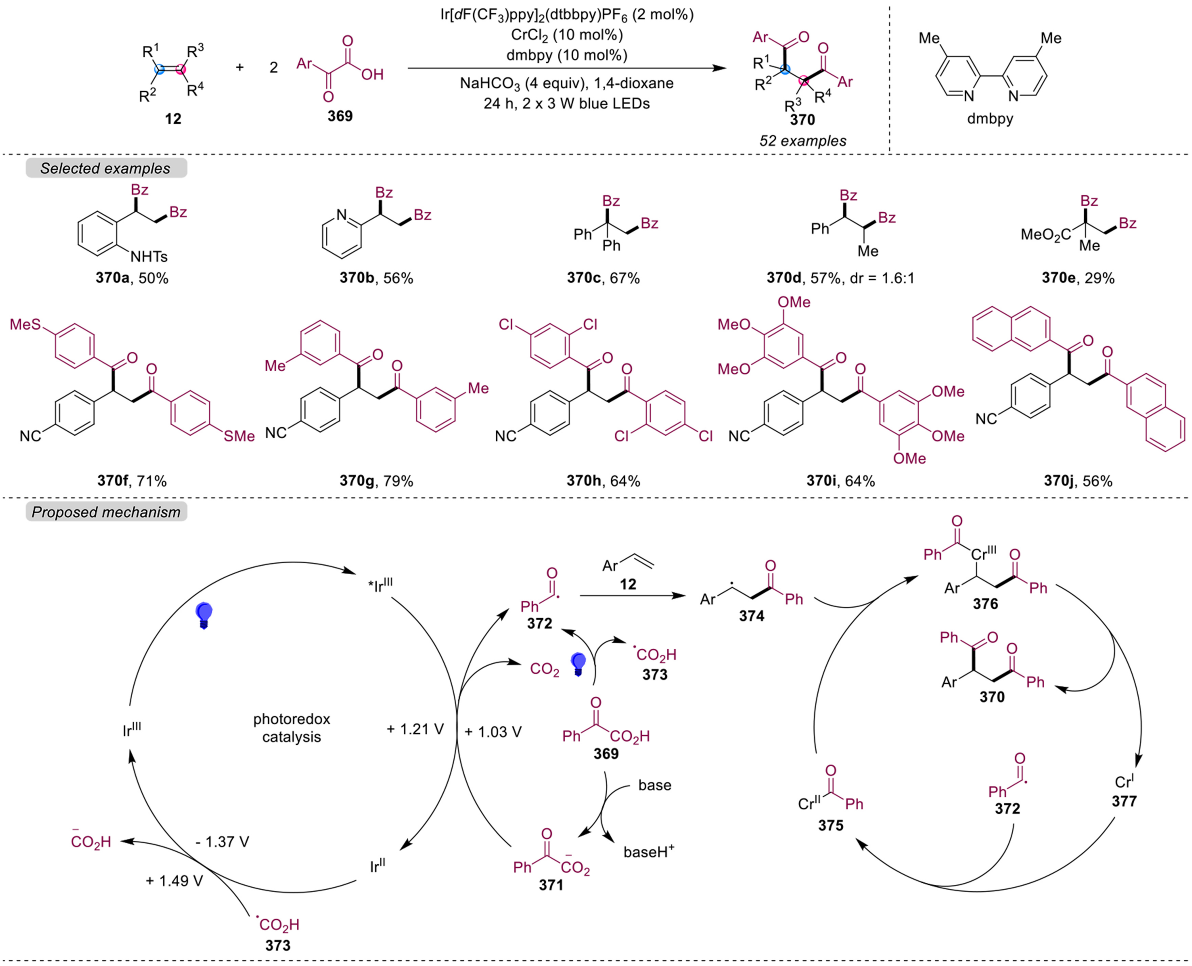
Mechanistic studies indicate that the coupling reaction begins with the excitation of PC to its highly oxidizing excited-state PC*, which is quenched by 4-alkyl HEs **359** to generate alkyl radicals **361** and pyridinium species pyH$^+$, along with the reduced photocatalyst PC$^{\bullet-}$. Subsequently, the alkyl radicals **361** could either reversibly interact with low-valent **L**Cr^{II} species **362** to give an off-cycle **L**Cr^{III} species **363** or react with 1,3-dienes **97a** to give allyl radicals **364**. The allyl radicals **364** were captured by **L**Cr^{II} species **362** to afford the Cr^{III} allyl species **365** and **366**. Notably, the formation of chromium alkoxide **367** via a six-membered Zimmerman-Traxler transition state would occur in a regioselective and *anti*-selective manner. Subsequently, hydrolysis of **367** by pyH$^+$ gives the formation of products **360** and **L**Cr^{III} complex **368**. A SET process between the PC$^{\bullet-}$ and **368** regenerates the PC and **L**Cr^{II} **362**.



Scheme 44. Photo- and Cr-catalyzed 1,2-dialkylation of 1,3-dienes.

In 2022, Liu *et al*. reported a flexible visible-light-mediated chromium-catalyzed radical diacylation of alkenes **12** or 1,3-dienes with α-keto acids **369**, which afforded dione compounds **370** in 29%-81% yields [Scheme 45][107]. This protocol uses styrenes, 1,3-diene, and vinylcyclopropane to synthesize 1,4-, 1,6-, and 1,7-diketones under mild conditions, respectively.

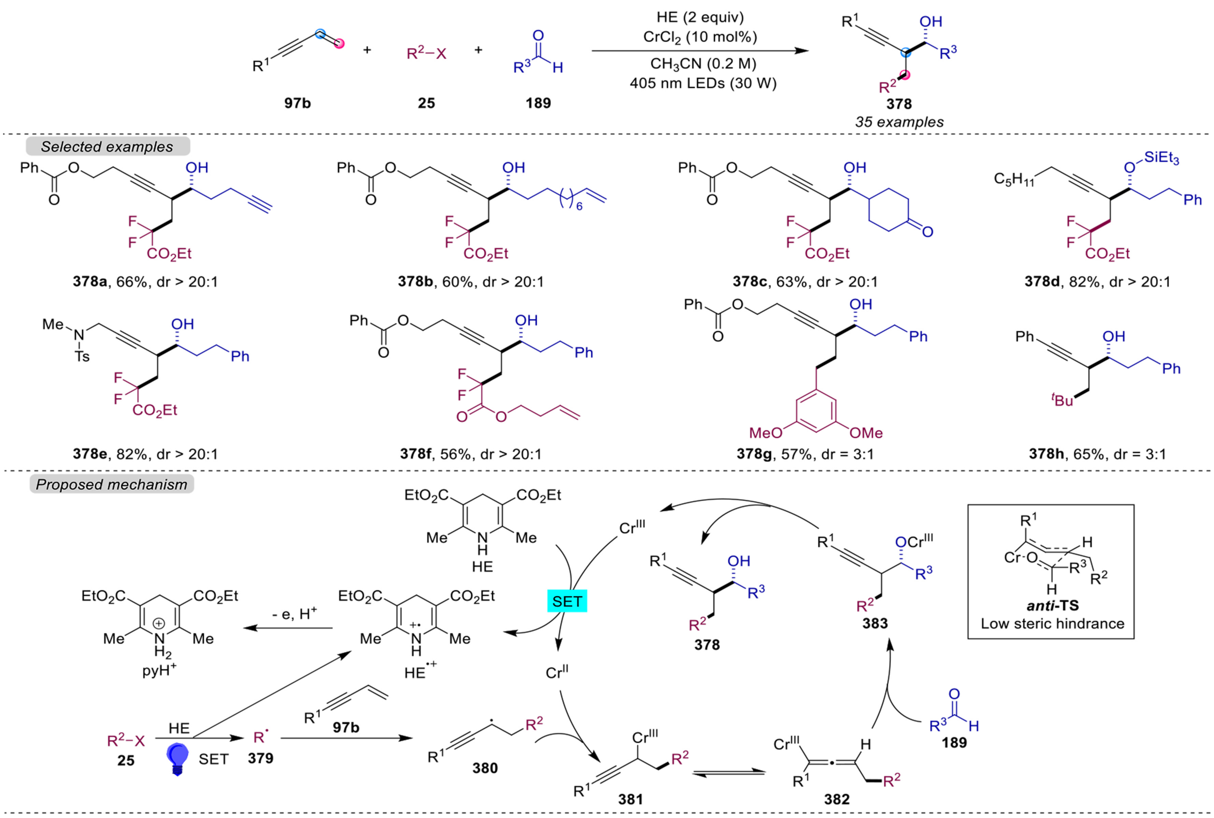
The plausible mechanism of this reaction is also illustrated [Scheme 45]. First, PC Ir^{III} is transformed to its excited state *Ir^{III} under visible-light irradiation. Meanwhile, base-mediated deprotonation of phenylglyoxylic acid **369** results in the formation of α-oxocarboxylate **371**, which is then oxidized to acyl radicals **372** by *Ir^{III} by releasing CO$_2$ as a byproduct. Alternatively, arylglyoxylic acids **369** could be responsible for producing acyl radicals **372** and carboxyl radicals **373**. Carboxyl radicals **373** can oxidize Ir^{II} PC back to Ir^{III}, thus completing the photocatalytic cycle. On the other hand, acyl radicals **372** are intercepted by aryl alkenes **12** to yield benzyl radicals **374**. In parallel, anionic Cr^{I} species may be produced via the single-electron reduction of Cr^{II} catalyst by PC Ir^{II}, which combine with acyl radicals **372** to form Cr^{II} complex **375** and further trapped benzyl radicals **374** to form stable quartet Cr^{III} intermediates **376**. Finally, Cr^{III} intermediates **376** undergo reductive elimination to form the final 1,4-dione products **370** and a Cr^{I} species **377**.



Scheme 45. Photo- and Cr-catalyzed diacylation of alkenes.

In 2024, Wu *et al*. developed a visible-light and chromium-catalyzed regio- and diastereoselective radical three-component cross-coupling reaction of 1,3-enynes **97b** with alkyl halides **25** and aldehydes **189** to provide a series of homopropargylic alcohols **378** in 43%-85% yields with 3:1 to > 20:1 dr [Scheme 46][108]. Importantly, the dialkylation of 1,3-enynes proceeds in the absence of external PCs, stoichiometric metal reductants, and additives. This protocol could be applied to 1,3-enynes and alkyl electrophilic reagents.

The possible mechanism of the three-component reaction involving 1,3-enyne is illustrated in Scheme 46. Initially, upon irradiation with blue light, HE is transformed into its active state HE^*, which then reduces alkyl halides **25** by a SET process to form the alkyl radicals **379** and $HE^{•+}$. Akyl radicals are further captured by C=C bonds of 1,3-enynes **97b** to give the propargyl radicals **380**. Meanwhile, $HE^{•+}$ loses an electron and a proton, resulting in the formation of the pyridinium pyH^+. Next, the propargyl radicals **380** are intercepted by Cr^{II} species to yield the nucleophilic propargylic Cr^{III} complex **381**. This complex is in equilibrium with the resonance form of the allenic Cr^{III} complex **382**, which thereafter interacts with aldehydes **189** by nucleophilic addition, leading to the generation of the intermediate **383** with high diastereoselectivity via an *anti*-transition six-membered cycle. Subsequently, the homopropargylic alcohols **378** and Cr^{III} species are formed by the hydrolysis of the O–Cr^{III} bond in **383** by the pyH^+. Finally, the excited HE^* reduces Cr^{III} to Cr^{II}, thereby completing the catalytic cycle.

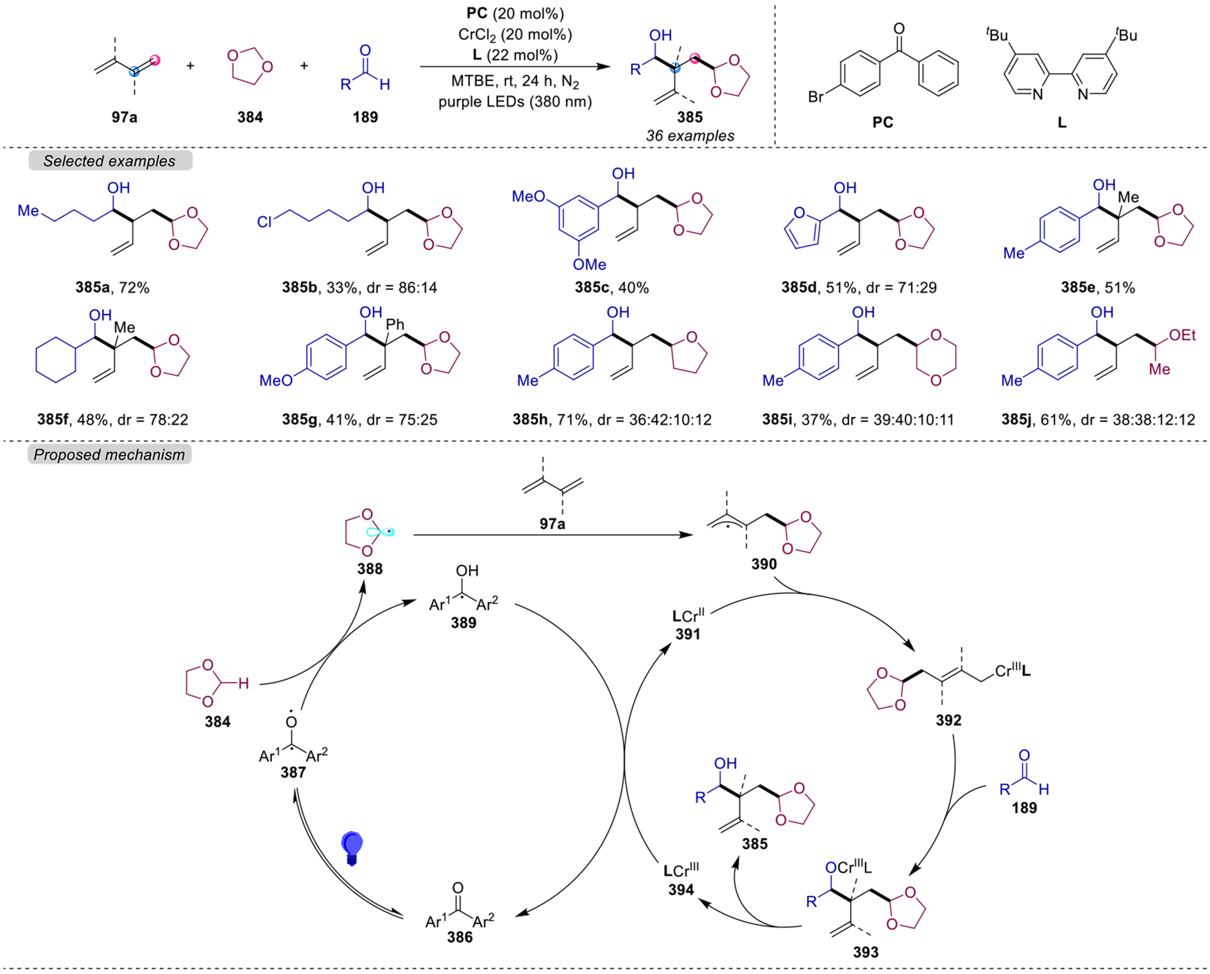


Scheme 46. Photo- and Cr-catalyzed reductive 1,2-dialkylation of 1,3-enynes.

In 2024, Hu *et al.* described a dual visible-light-induced chromium catalyzed three-component Nozaki-Hiyama-Kishi type reaction of 1,3-butadienes **97a**, 1,3-dioxolane **384**, and aldehydes **189** to afford homoallylic alcohols **385** in yields ranging from 29% to 84% [Scheme 47][109]. Notably, the photocatalyst diaryl ketone serves two distinct roles: first, in the HAT process, and second, in facilitating the turnover of the chromium catalyst. Additionally, aryl/alkyl aldehydes are suitable substrates for combination with 1,3-butadienes and 1,3-dioxolane.

Mechanistic studies have confirmed that the reaction is initiated by the excitation of photocatalyst diaryl ketone **386** to oxygen radical **387**, which results in the abstraction of a hydrogen atom from 1,3-dioxolane **384** to give radical intermediate **388**. The generation of ketyl radical **389** is a concomitant effect of this reaction. Then, the addition of **388** to 1,3-butadienes **97a** affords allyl radicals **390**, which interact with LCr^{II} species **391** to form π-allyl chromium species **392**. This is followed by a nucleophilic addition to aldehydes **189**, forming Cr^{III} species **393**. Finally, final products **385** and LCr^{III} **394** are obtained through the protonation reaction of free protons or protonated diaryl ketones. The reduction reaction between ketyl radicals **389** and **394** results in the regeneration of ground-state diaryl ketone **386** and Cr^{II} species **391**, thereby closing two catalytic cycles.

Interestingly, chromium can also serve as a catalyst for the three-component reaction of alkenes in the presence of other earth-abundant metals under light irradiation. In 2024, Yan *et al.* developed a photoredox chromium and cobalt dual catalyzed allylation reaction of 1,3-butadienes **97a** with aldehydes **189**, which resulted in the delivery of homoallylic alcohols **395** with 45%-95% yields and 3:1 to > 20:1 dr [Scheme 48][110]. This approach is catalyzed by CoPor and CrCl$_3$ and the reaction is completed through a metal-hydride HAT



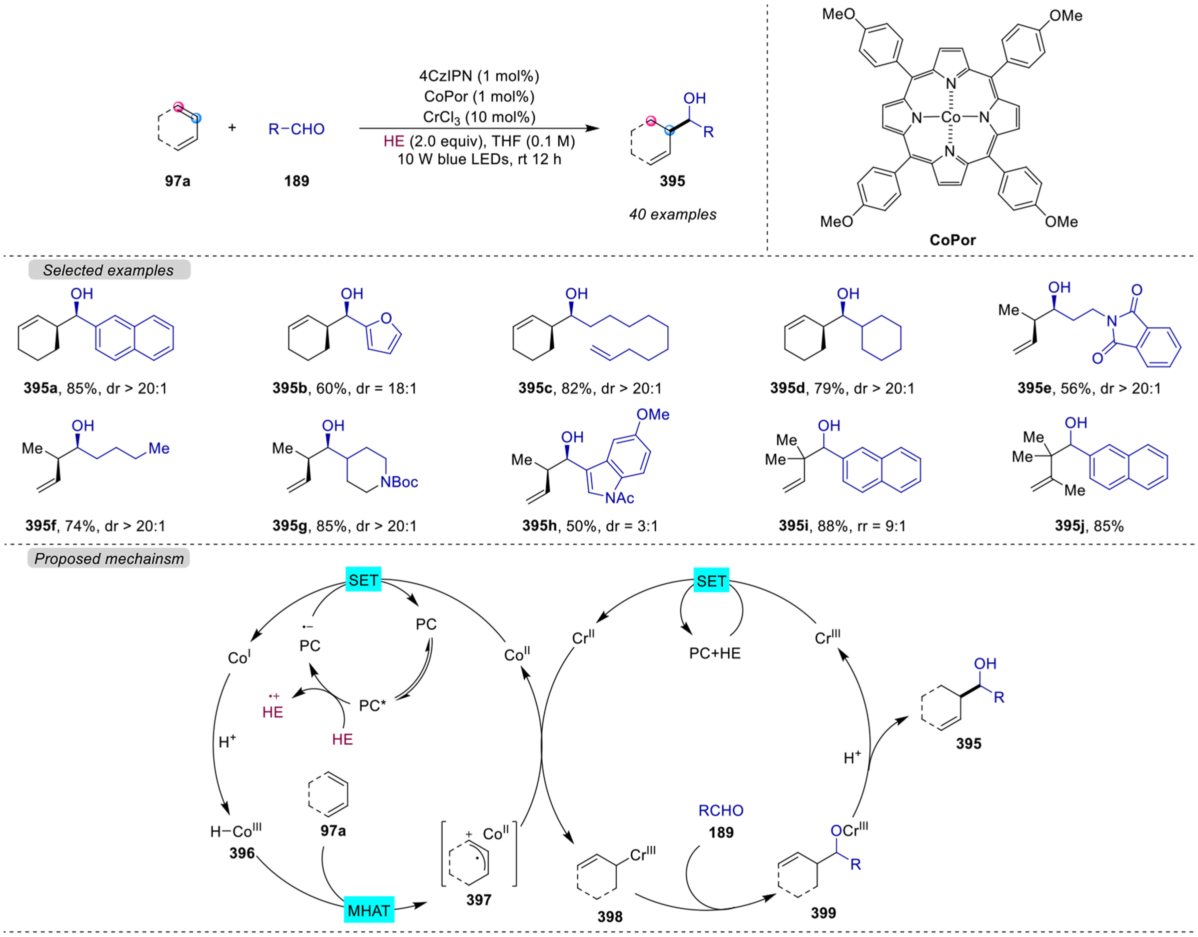
Scheme 47. Photo- and Cr-catalyzed 1,2-dialkylation 1,3-dienes enabled by hydrogen atom transfer.

(MHAT) pathway under illumination. Moreover, this process is compatible with aryl/alkyl aldehydes and cyclic/acyclic 1,3-butadienes.

As shown in Scheme 48, a possible catalytic cycle is proposed. Upon visible-light irradiation, 4CzIPN is excited to 4CzIPN*, which interacts with HE by SET to form 4CzIPN$^{\bullet-}$ and HE$^{\bullet+}$; the latter continues to participate in the reaction by losing electrons and protons. The reduction of Co^{II} and Cr^{III} to Co^{I} and Cr^{II}, respectively, by 4CzIPN$^{\bullet-}$ is followed by the capture of a proton by Co^{I}, leading to the formation of the Co^{III}-H species **396**. This species then undergoes a MHAT-mediated conversion of 1,3-butadienes **97a** into allyl radicals **397**, which are rapidly intercepted by Cr^{II} to form an allyl-Cr^{III} species **398**. Subsequently, **398** is added to aldehydes **189** and undergoes hydrolysis to yield the final product homoallyl alcohols **395**, while releasing the Cr^{III}. Of particular note is the Zimmerman-Traxler transition state, which elucidates the mechanism of diastereoselectivity.

PHOTOREDOX AND TITANIUM-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

In 2021, Li *et al.* reported a visible-light-mediated titanium-catalyzed three-component reaction of 1,3-dienes **97a** with alkyl bromides **175** and aldehydes/ketones **189**[111,112]. This process was shown to be

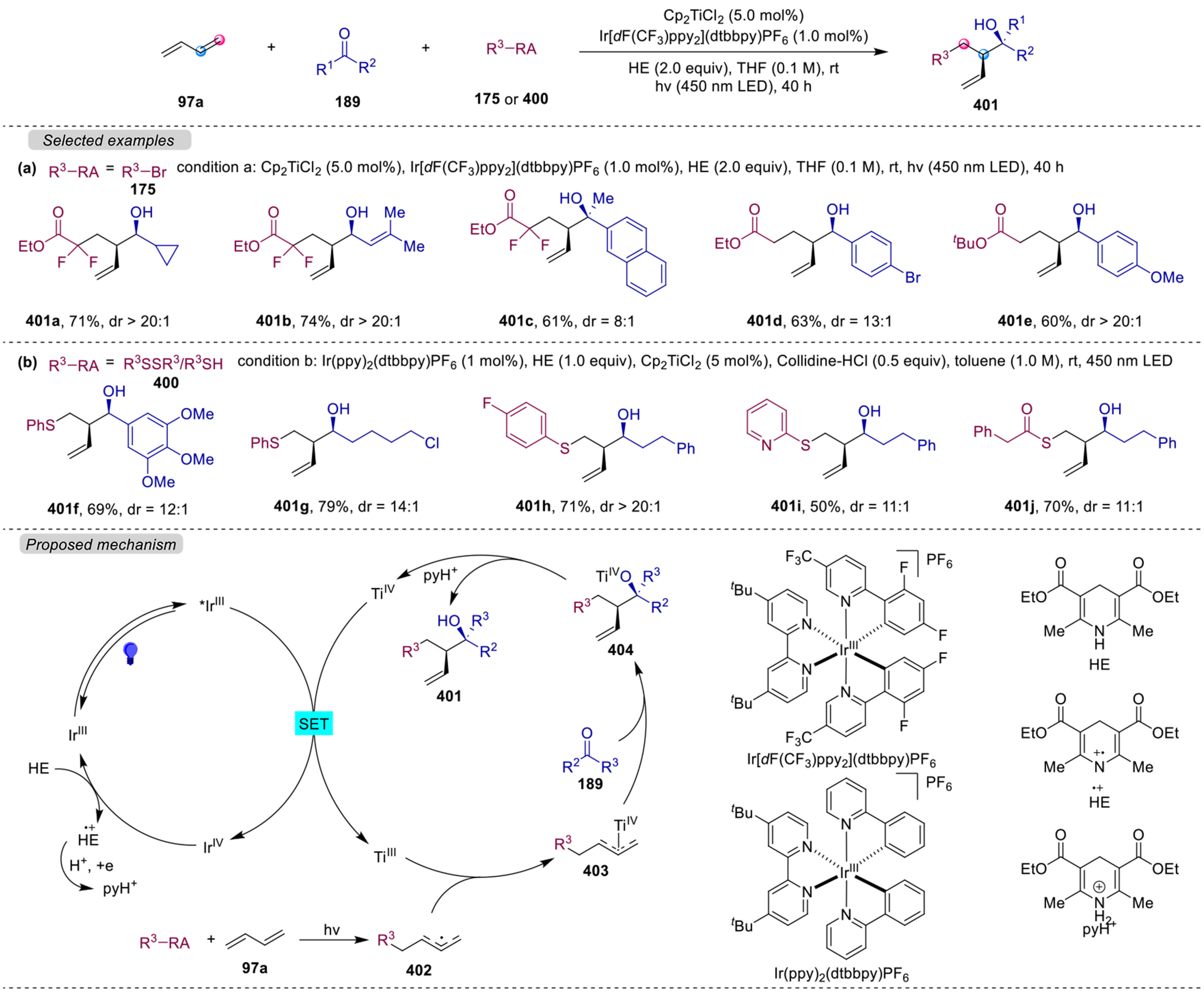


Scheme 48. Photo- and Cr-catalyzed hydroalkylation of 1,3-dienes with aldehydes.

effective in the synthesis of a series of homoallylic alcohols in 44%-92% yields and 5:1 to > 20:1 dr [Scheme 49(a)]. Following dual photoredox/titanium catalysis, the key intermediate π-allyltitanium complexes are formed. Additionally, the regio- and diastereoselectivity of this method are comparable to those of the chromium-catalyzed Nozaki-Hiyama-Kishi allylation reaction.

Under visible-light irradiation, the ground-state PC Ir^{III} is excited to excited-state $^*Ir^{III}$ to initiate the catalytic cycle. $^*Ir^{III}$ can reduce alkyl halides **175** via a SET pathway, forming alkyl radicals. These radicals are then rapidly trapped by 1,3-dienes **97a**, generating the allyl radicals **402**. Then, allyl radicals **402** combine with Ti^{III} to afford key intermediate π-allyltitanium complexes **403**, which undergo nucleophilic addition with aldehydes or ketones **189** to afford Ti^{IV} species **404**. Subsequently, following hydrolysis by pyH^+, the homoallylic alcohols **401** are formed and release a free Ti^{IV}; the latter is reduced to Ti^{III} by another $^*Ir^{III}$ through SET process and accompanied by the formation of strong oxidant Ir^{IV}. Lastly, the Ir^{IV} species is reduced by HE to ground-state Ir^{III}, producing $HE^{\bullet+}$. This can further participate in electron transfer events, ultimately leading to the production of pyH^+. Notably, the *anti*-selectivity of homoallylic alcohols can be explained by Zimmerman-Traxler transition state.

The next reaction involved the use of thioethers or thiols in place of alkyl halides, leading to the discovery of a three-component regio- and diastereoselectivity process for 1,3-butadiene **97a** with thioethers/thiols **400**

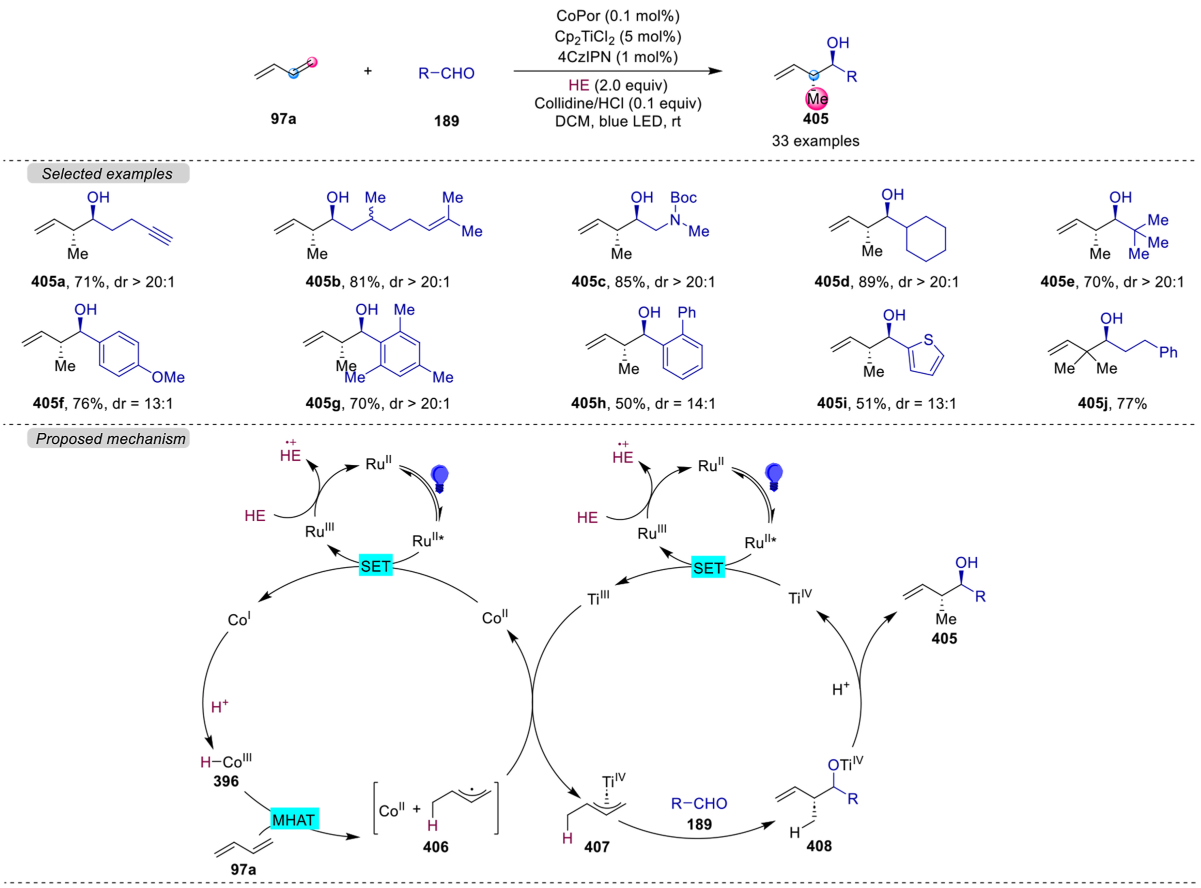


Scheme 49. Photo- and Ti-catalyzed of 1,2-dialkylation of 1,3-dienes.

and aldehydes **189** under visible-light and titanium catalysis. This process resulted in the formation of γ-hydroxy thioether compounds with 50%-94% yields and 5:1 to > 20:1 dr [Scheme 49(b)][113]. In addition, both thioether and thiol are appropriate substrates for combination with 1,3-butadienes. Under light irradiation, the disulfide bonds undergo homolytic cleavage resulting in the trapping of 1,3-dienes **97a**. This process gives rise to the formation of allyl radicals **402** and thiyl radicals.

Yan *et al*. developed a photoredox CoPor and Cp_2TiCl_2 dual catalyzed radical reaction of 1,3-butadienes **97a** with aldehydes **189**, which afforded homoallylic alcohols **405** with 38%-92% yields and 9:1 to > 20:1 dr [Scheme 50][114]. This strategy employs HE as the hydrogen source, thereby providing the products through the MHAT mechanism. Moreover, this protocol is compatible with a range of alkyl/aryl aldehydes and alkyl-substituted 1,3-butadienes under mild conditions.

The plausible mechanism of the above transformation is shown in Scheme 50. First, the photoexcited $^*Ru(bpy)_3^{2+}$ is oxidized by Co^{II} and Ti^{IV} to give the strong oxidant $Ru(bpy)_3^{3+}$, which could further oxidize HE to form radical cation $HE^{•+}$, donating an electron and generating pyH^+. Then, H^+ from $HE^{•+}$ or pyH^+ is reduced by the Co^I to yield Co^{III}-H species **396**, which is then transferred to a hydrogen atom to



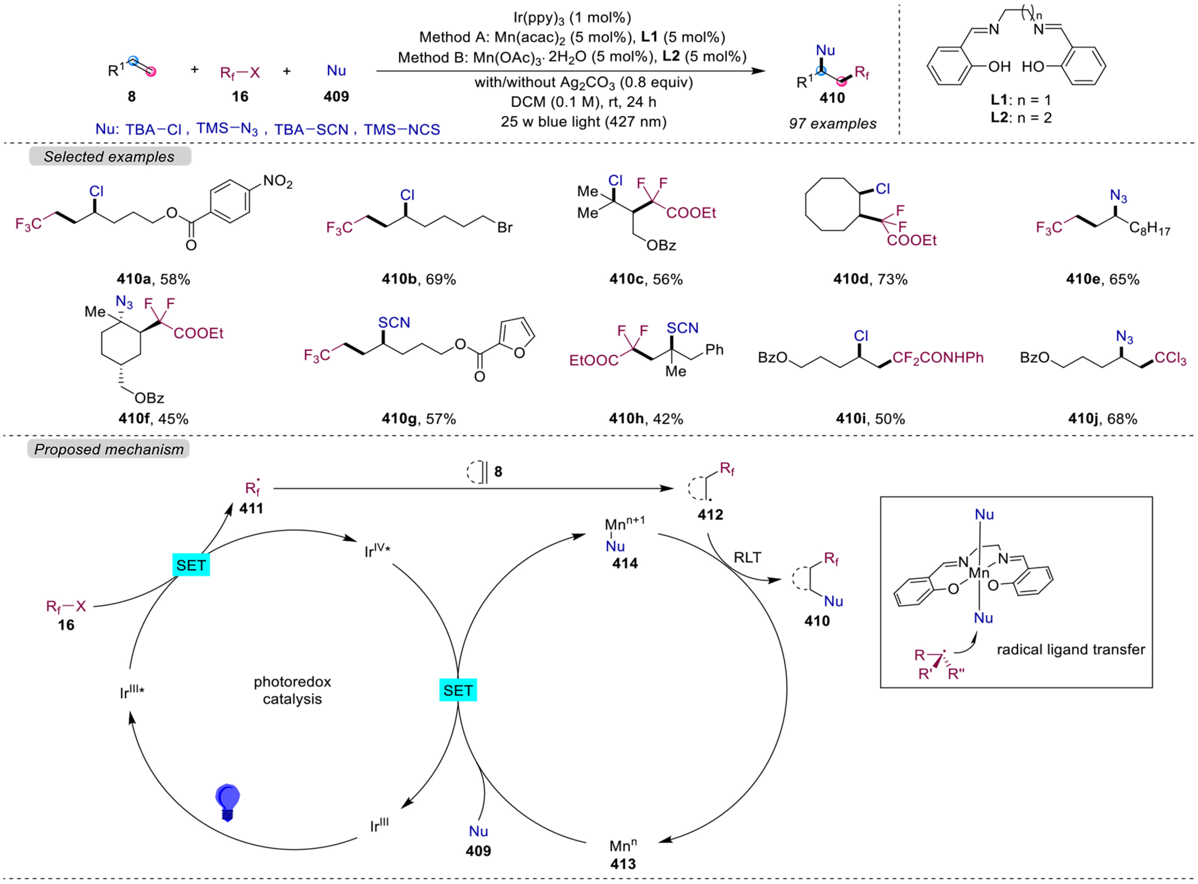
Scheme 50. Photo- and Ti-catalyzed crotylation of aldehydes with 1,3-butadiene.

1,3-butadienes **97a** and generate allyl radicals **406** and Co^{II} via the MHAT process. The allyl radicals **406** are rapidly captured by Ti^{III} to give nucleophilic π-allyltitanium species **407**, which further combine with the aldehydes **189** to give Ti^{IV} intermediates **408**. Protonation by pyH$^+$ occurs to furnish the products **405**. Identically, the Zimmerman-Traxler transition state also exhibits diastereoselectivity.

PHOTOREDOX AND MANGANESE-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

In 2022, the significant reactivity of cytochrome P450 hydroxylases and non-heme iron-dependent oxygenases inspired further research. Bian *et al.* first developed visible-light-induced and manganese-catalyzed difunctionalization of unactivated alkyl alkenes **8** with fluoroalkylation reagents **16** and anionic nucleophiles **409** by ATRA-diverting radical ligand transfer (RLT), affording difunctionalization products **410** in 42%-92% yields [Scheme 51][115]. The nucleophiles, including TBA-Cl, TMS-N_3, TBA-SCN and TMS-NCS, realized chloro-, azido-, and thiocyanato(fluoro)alkylation of unactivated alkenes. Additionally, this RLT elementary step involves a coordinated nucleophile rebounding to a carbon-centered radical, forming a new C–X bond in analogy to the radical rebound step observed in metalloenzymes.

In 2023, Li *et al.* reported a visible-light-promoted manganese-catalyzed hydrosulfonylation of alkenes **8** with sulfonyl chlorides **415** and $(TMS)_3$Si-H **210**, which provides sulfonyl-containing compounds in 35%-97% yields without external PC [Scheme 52][116]. Compared to the existing photocatalytic alkenes



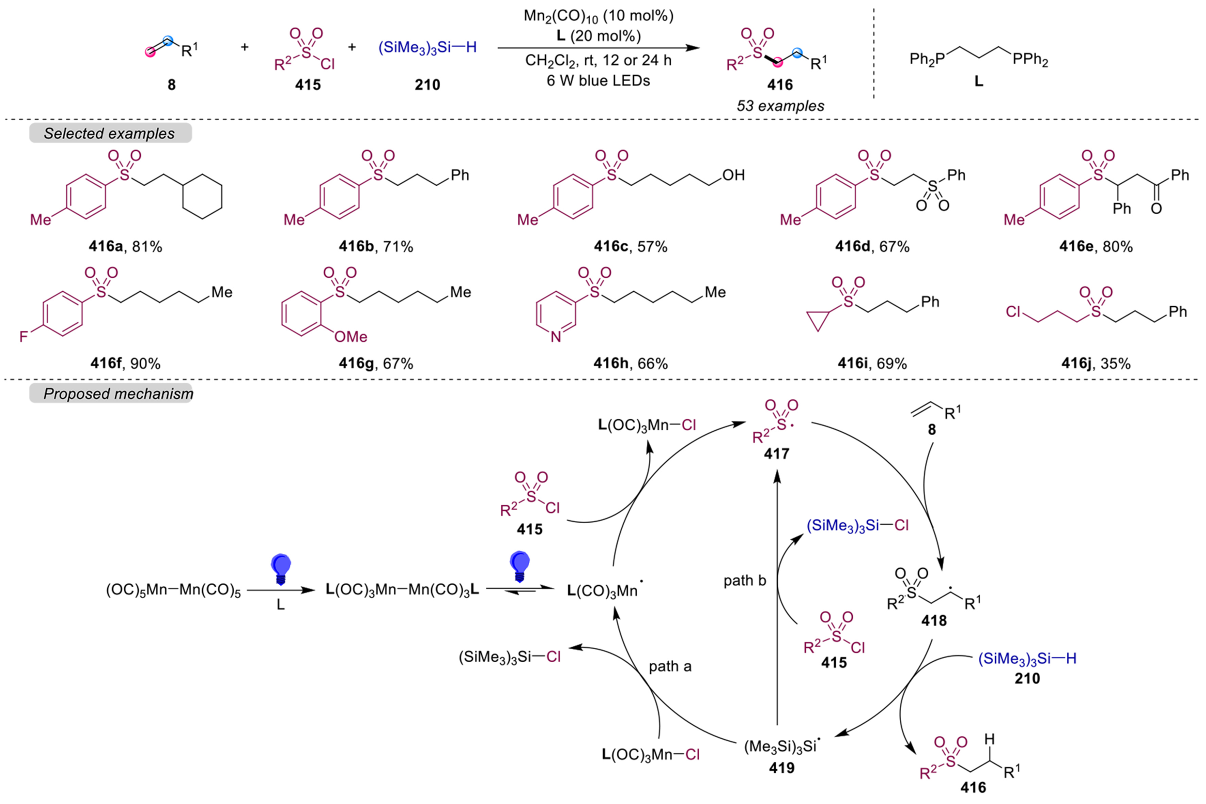
Scheme 51. Photo- and Mn-catalyzed alkylchorination of unactivated alkenes.

sulfonylation methods, this technique avoids the utilization of toxic 4-hydroxythiophenol, thereby offering a green and sustainable alternative method for alkene sulfonylation. Moreover, this approach exhibits a broad substrate scope, encompassing a range of alkyl/aryl alkenes and alkyl/aryl sulfonyl chlorides.

As shown in Scheme 52, the authors proposed a possible mechanism for this conversion. The Mn–Mn bond in $L_2Mn_2(CO)_6$ is cleaved under 6 W blue LEDs, resulting in the formation of $LMn(CO)_3^{\bullet}$. This subsequently abstracts a Cl atom from sulfonyl chloride **415**, leading to the generation of the sulfonyl radical **417** and the production of $LMn(CO)_3Cl$. Then, sulfonyl radicals **417** undergo radical addition, which is trapped by alkenes **8** to yield the carbon-centered radicals **418**. These then abstract the hydrogen atom from $(Me_3Si)_3SiH$ **210**, resulting in the formation of products **416** and the silyl radicals **419**. Radical $LMn(CO)_3^{\bullet}$ regeneration occurs via two distinct pathways. Firstly, **419** abstracts the Cl atom from $LMn(CO)_3Cl$ thereby providing $(Me_3Si)_3SiCl$ as well as regenerating $LMn(CO)_3^{\bullet}$ (path a). Secondly, the transfer of the Cl atom from sulfonyl chloride **415** to **419** affords $(Me_3Si)_3SiCl$ and regenerates **417** (path b).

PHOTOREDOX AND IRON-CATALYZED THREE-COMPONENT DIFUNCTIONALIZATIONS OF ALKENES

To date, there are few reports on the three-component cross-coupling reaction of alkenes by merging photoredox and iron catalysis. In 2024, Tang *et al.* described a photoredox and iron-catalyzed three-component 1,2-thiosulfonylation of aryl alkenes **8** with thiophenols **420** and sulfonyl chlorides **415**, affording β-sulfur substituted sulfone compounds **421** in 40%-85% yields [Scheme 53][117]. This strategy uses



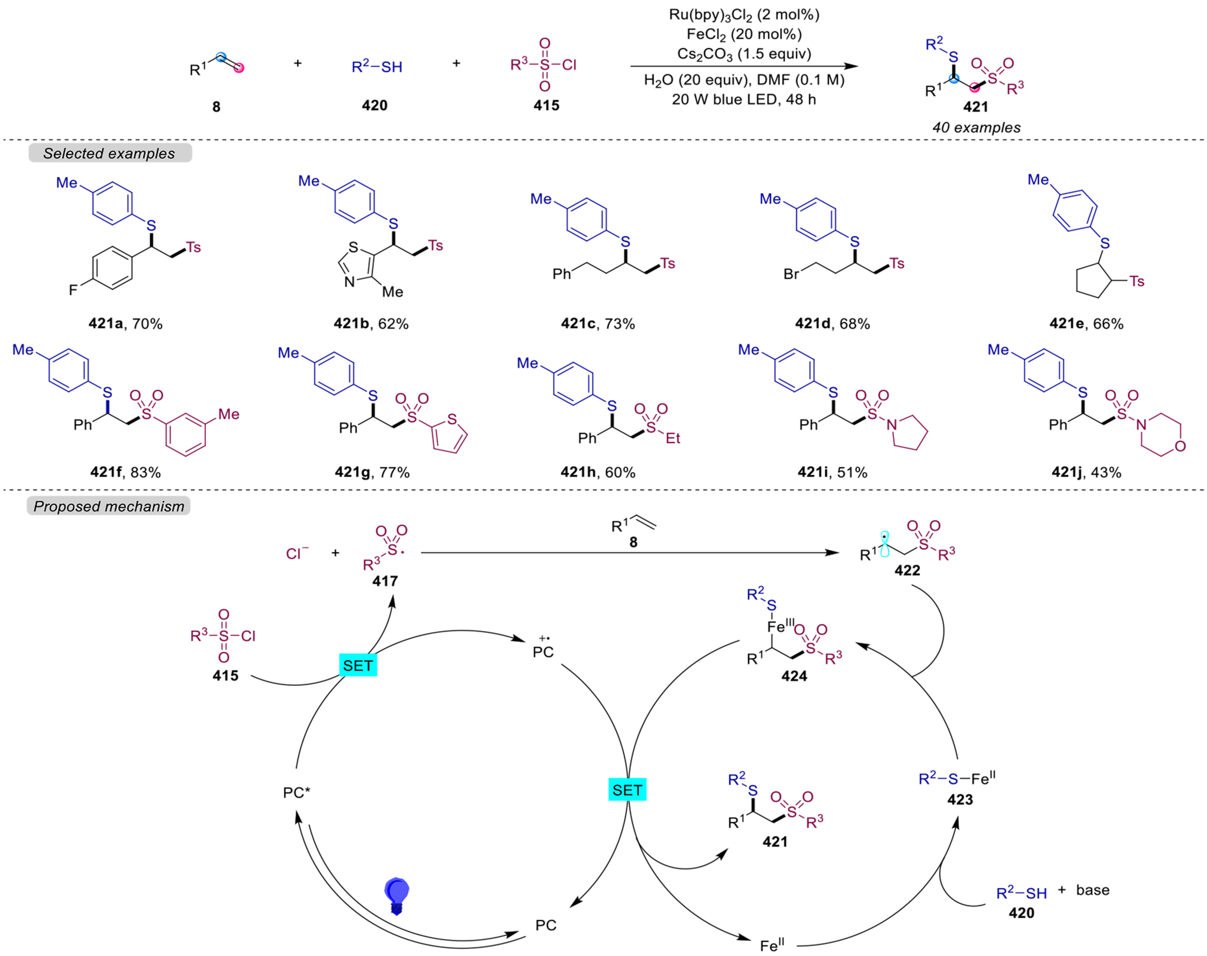
Scheme 52. Photo- and Mn-catalyzed hydrosulfonylation of alkenes.

readily available sulfonyl chlorides as the sulfonation reagent, enabling the simultaneous construction of two $C(sp^3)$–S bonds, avoiding the pre-synthesis of thiosulfates. Moreover, this method is applicable to a wide range of aryl/alkyl alkenes, aryl/alkyl sulfonyl chlorides, and arylthiophenols.

The catalytic process of this reaction is proposed. First, PC is stimulated to its excited state PC^*, which reacts with sulfonyl chlorides **415** to give the sulfonyl radicals **417** and a $PC^{\bullet+}$. Then, the resulting sulfonyl radicals **417** add to alkenes **8** by radical addition, thereby generating more stable benzyl radicals **422**. Simultaneously, the thiophenols **420** interact with Fe^{II} catalyst to form an iron-sulfur intermediate **423**. This intermediate subsequently rebounds with the benzyl radicals **422**, leading to the generation of Fe^{III} species **424**. Lastly, intermediate **424** undergoes reductive elimination and subsequent SET to $PC^{\bullet+}$, delivering the final products **421** and regenerating Fe^{II} catalyst to close the catalytic cycle.

CONCLUSION AND OUTLOOK

Over the past decades, visible-light and earth-abundant-metal enabled synergistic catalytic three-component cross-coupling reaction involving alkenes has emerged as a platform for the development of novel and highly enabling synthetic methodologies, enabling the advancement of chemical transformations that are difficult to achieve with a single catalytic cycle. Multiple chemical bonds, including carbon-carbon and carbon-heteroatom bonds, are forged in one step under mild conditions to provide rapid access to molecular complexity in a selective manner. However, research in the three-component reaction area remains quite limited. First, the combination of visible-light with copper and nickel is more investigated, yet the combination of visible-light with other earth-abundant transition metals, such as scandium, vanadium, cobalt, iron, chromium, and manganese, has received less attention. Second, the reaction mode is limited to



Scheme 53. Photo- and Fe-catalyzed 1,2-thiosulfonylation of alkenes.

the interaction with alkenes to form more stabilized alkyl radicals, which are then trapped by the transition metal to catalyze the bond-forming process. Moreover, only carbon-carbon bond formations are intensively investigated in the transition-metal-catalyzed step. Third, most three-component reactions are limited to biased alkenes or alkenes with a directing group. Aliphatic alkenes without electronic bias or directing groups present ongoing challenges regarding reactivity and selectivity control. Fourth, catalytic enantioselective transformations using three-component reactions from alkenes remain underexplored. Most future efforts should focus on solving these limitations, enabling the forging of diverse carbon-carbon and carbon-heteroatom bonds. We hope the visible-light mediated earth-abundant transition-metal catalyzed three-component reaction of alkenes will evolve into a powerful and adaptive tool for the constructing of molecular complexity from readily available starting materials with the control of chemo-, regio-, and enantioselectivities.

DECLARATIONS

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Authors' contributions

Writing the manuscript: Jia, J.S.
Revising the manuscript: Chen, X.Y.; Li, Y.L.; Shu, W.
Guiding the work: Li, Y.L.; Shu, W.

Availability of data and materials

Not applicable.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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