CJC Chinese Journal of Chemistry 中国化学 - An International Journal

For submission: https://wiley.atyponrex.com/journal/CJOC
For published articles: https://onlinelibrary.wiley.com/journal/16147065

Recent Advances

Cite this paper: *Chin. J. Chem.* **2025**, *43*, 3637—3658. **DOI: 10.1002/cjoc.70231**

Recent Progress on Nickel-Catalyzed Reductive Dicarbofunctionalization of Alkenes†

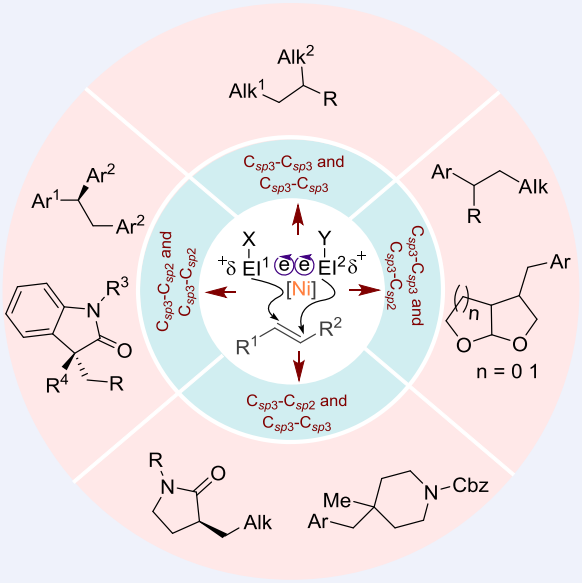
Yucheng Liu,[‡,a,b] Fu-Yu Li,[‡,a,b] Muneer-ul-Shafi Bhat,[‡,b] Lan Tian,[a,b] Hao-Ran Zhang,[a,b] Huan Meng,[b] Han-Tong Zhao,[b] Yu-Long Li,*[,a,c] and Wei Shu*[,b]

[a] *College of Chemistry and Environmental Engineering, Key Laboratory of Green Catalysis of Higher Education Institutes of Sichuan, Sichuan University of Science and Engineering, Zigong , Sichuan 643000, China*
[b] *Shenzhen Grubbs Institute, Department of Chemistry, Guangming Advanced Research Institute, and Guangdong Provincial Key Laboratory of Catalysis, Southern University of Science and Technology, Shenzhen, Guangdong 518055, China*
[c] *Key Laboratory of Advanced Energy Materials Chemistry (Ministry of Education), Nankai University, Tianjin 300071, China*

Keywords

Alkenes | Dicarbofunctionalization | Nickel catalysis | Reductive cross-coupling | C–C bond-forming process

Comprehensive Summary



As readily available and abundant industrial feedstocks, alkenes have emerged as versatile platform for constructing value-added targets. Transition metal-catalyzed dicarbofunctionalizations reactions forge two carbon-carbon bonds in one step with construction of two vicinal saturated carbon centers, providing profound synthetic potential in organic synthesis and pharmaceutical chemistry. In particular, nickel-catalyzed reductive dicarbofunctionalization of alkenes has witnessed remarkable progress in recent years. Compared to conventional redox-neutral dicarbofunctionalization strategy, reductive variant offers significant advantages, such as no use of pre-formed organometallic reagents, operational simplicity and mild reaction conditions. This review summarizes developments of nickel-catalyzed reductive dicarbofunctionalization of alkenes to forge diverse carbon-carbon bonds in the absence of stoichiometric carbon nucleophiles. The mechanistic considerations are comprehensively discussed, including two-electron migratory insertion and the single-electron radical addition pathways. Furthermore, we provide critical insights into future directions and potential challenges in this area, highlighting opportunities for further methodology development and applications for nickel-catalyzed reductive dicarbofunctionalization of alkenes.

*E-mail: yu_longli@suse.edu.cn; shuw@sustech.edu.cn
‡These authors contributed equally to this work.
†Dedicated to the Special Issue of Catalytic Alkene Functionalization.

Key Scientists

KEY PLAYERS in the field of nickel-catalyzed reductive dicarbofunctionalization of alkenes.

Hegui Gong
Shanghai University, China

2012 — Ni-catalyzed intramolecular reductive dialkylation of alkenes

Cristina Nevado
University of Zurich, Switzerland

2012 — Ni-catalyzed intermolecular reductive dicarbofunctionalization of alkenes

Yu Peng
Southwest Jiaotong University, China

2017 — Intramolecular reductive dicarbofunctionalization of alkenes

Tianning Diao
New York University, USA

2018 — Ni-catalyzed asymmetric reductive diarylation of alkenes

Wangqing Kong
Wuhan University, China

2019 — Enantioselective reductive diarylation of alkenes

Yifeng Chen
East China University of Science & Technology, China

2020 — Nickel-catalyzed enantioselective carbamoyl-alkylation of alkenes

Xingzhong Shu
Lanzhou University, China

2021 — Ni-catalyzed Enantioselective reductive divinylation of 2-bromo-1.6-dienes

Wei Shu
Southern University of Science and Technology, China

2022 — Ni-catalyzed three-component reductive dialkylation of unactivated alkenes (2022)
Ni-catalyzed site-divergent reductive dicarbofunctionalization of alkenes (2025)

David W. C. MacMillan
Princeton University, USA

2024 / 2025 — Ni-catalyzed dicarbofunctionalization of alkenes via triple radical sorting

Stories to be Continued ...

Contents

1. Introduction

Carbon-carbon bonds are fundamental building blocks in organic molecules. The direct functionalization of these bonds has garnered significant attention, as it opens new avenues for constructing otherwise challenging or inaccessible molecular frameworks by modifying the carbon backbone. In the past two decades, considerable progress has been made in transition-metal-catalyzed cross-coupling reactions by enabling selective C–C bond formation from simple precursors.[1] However, traditional cross-coupling reactions utilizing transition metals typically forge one C–C bond per transformation and often demand prefunctionalized substrates and a multistep synthetic sequence to achieve complex molecular architectures. As a result, growing attention has turned toward reaction platforms that can simultaneously construct two C–C bonds in a single operation to enhance molecular complexity and synthetic efficiency.[2] This shift has paved the way for diverse alkene difunctionalization strategies that streamline the synthesis of complex molecules.

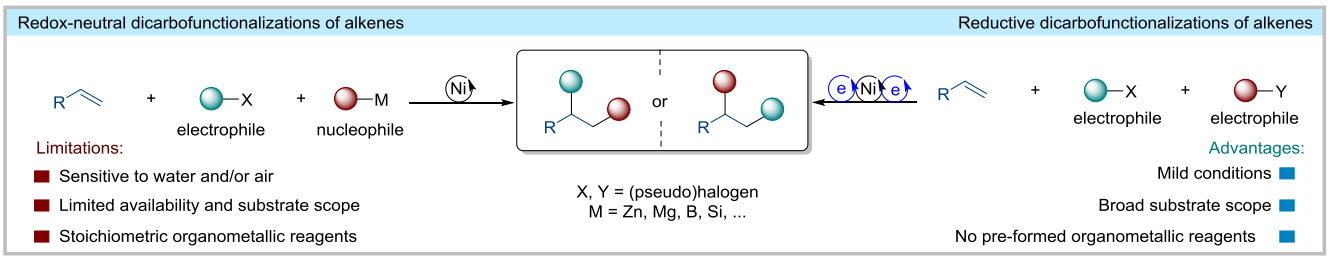
Alkenes, as one of the most abundant feedstock chemicals, play a central role in these transformations due to their inherent reactivity, electronic tunability, and structural diversity, which make them ideal substrates for a broad range of catalytic processes. Owing to their nucleophilic behavior, alkenes readily undergo reactions with electrophilic partners or can be activated by transition metals and radicals to engage in more complex multicomponent processes. In recent years, this reactivity has been leveraged in the development of alkene dicarbofunctionalization reactions, wherein two carbon-based groups are installed across a carbon–carbon double bond in a single transformation.[3] As a result, these reactions enable high atom- and step-economy and has become a versatile and efficient tool for the synthesis of pharmaceuticals, natural products, and functional materials.

Among alkene difunctionalization strategies, transition metal-catalyzed dicarbofunctionalization stands out for its ability to simultaneously forge two C–C bonds with precise regio- and stereocontrol. These reactions are generally categorized based on the redox interplay of the coupling partners into redox-neutral, reductive, and oxidative manifolds. Each mode introduces distinct mechanistic paradigms and synthetic challenges. In redox-neutral dicarbofunctionalization, an alkene reacts with one electrophile and one nucleophile, commonly an organic halide and an organometallic reagent (*e.g.*, Grignard, organozinc, or boron compounds). While often effective, these reactions are limited by their reliance on pre-formed organometallic nucleophiles, which are frequently air- and moisture-sensitive, incompatible with various functional groups, and challenging in terms of scalability and operational practicality (Scheme 1). To address these limitations, reductive dicarbofunctionalization has emerged as a robust alternative, wherein two electrophilic coupling partners, typically organic halides or redox-active esters, are combined across an alkene in the presence of a stoichiometric reductant. By avoiding the use of stoichiometric organometallic reagents, reductive protocols offer new chemical space for difunctionalizations of alkenes.[4] Recent advances have demonstrated broad substrate scopes, including challenging unactivated alkenes and sterically hindered systems. Nonetheless, the inherent similarity in reactivity between two electrophiles introduces a significant challenge in achieving high levels of chemo- and regioselectivity, especially when competitive oxidative addition pathways or radical recombination steps are involved. In contrast, oxidative dicarbofunctionalization remains significantly underdeveloped and falls outside the scope of this review.[5]

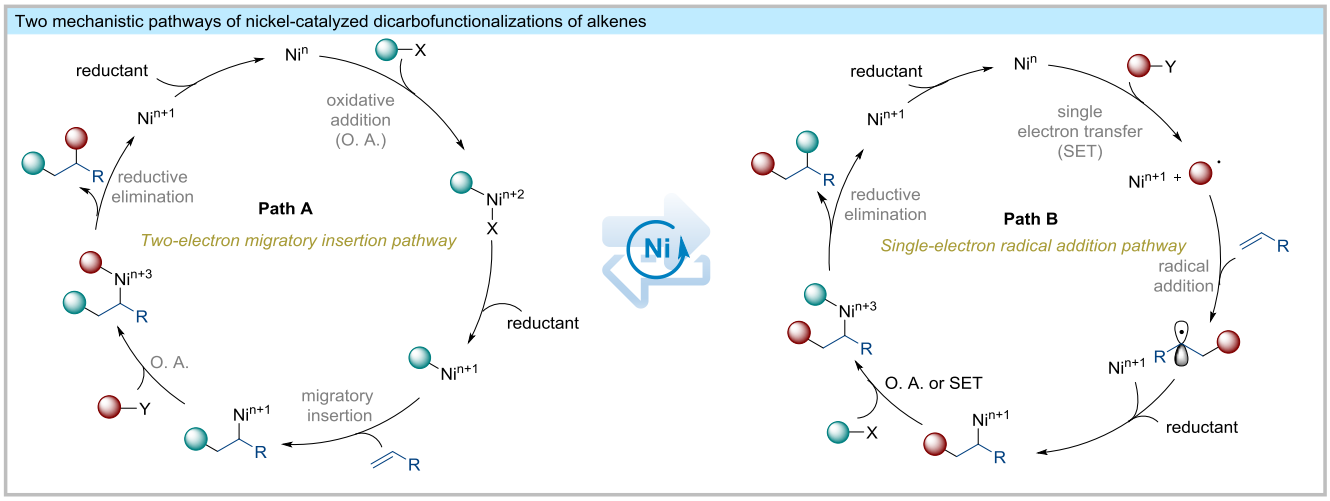
Building on the growing interest in alkene dicarbofunctionalization, recent advances have demonstrated the unique potential of nickel catalysis in promoting such transformations. The growing preference for nickel stems from several distinct advantages that make it particularly suited for these multicomponent couplings. First, nickel catalysts with lower reduction potential, smaller atomic radius, and reduced electronegativity compared to palladium enable Ni(0) species to undergo oxidative addition with a broader range of substrates, including those that are typically inert toward Pd(0). This expands the accessible chemical space for cross-coupling. Second, the open-shell electronic structure of nickel allows it to mediate reactions via both classical two-electron oxidative addition and single-electron transfer (SET) pathways, the latter being particularly advantageous for engaging alkyl electrophiles through radical intermediates. Third, nickel exhibits a higher barrier to β-hydride elimination in alkylnickel intermediates compared to palladium, thus minimizing undesired side reactions and enabling the construction of otherwise labile C_{sp^3}–C_{sp^3} bonds (Scheme 2a).[6] Together, these advantages make nickel particularly well-suited for reductive dicarbofunctionalization, where precise control over selectivity and radical intermediates is essential. This reactivity can be rationalized by examining the established mechanistic framework that underlies alkene difunctionalization catalyzed by late transition metals. Although the general difunctionalization catalytic cycle follows four key steps: oxidative addition, migratory insertion, transmetalation, and reductive elimination (Scheme 2b), the performance of individual metals can differ significantly. For example, Pd-catalyzed systems often suffer from two major limitations: First, the relatively slow oxidative addition of electrophiles to palladium species leads to the undesired direct cross-coupling between the two partners. Second, the alkylpalladium intermediates formed during the reaction are prone to β-hydride elimination, resulting in the formation of Heck-type byproducts.[7]

In contrast, the unique properties of nickel, its variable oxidation states, compatibility with single-electron and two-electron

Scheme 1 Overview of Ni-catalyzed dicarbofunctionalizations of alkenes



Scheme 2 Representative pathways for Ni-catalyzed dicarbofunctionalizations of alkenes



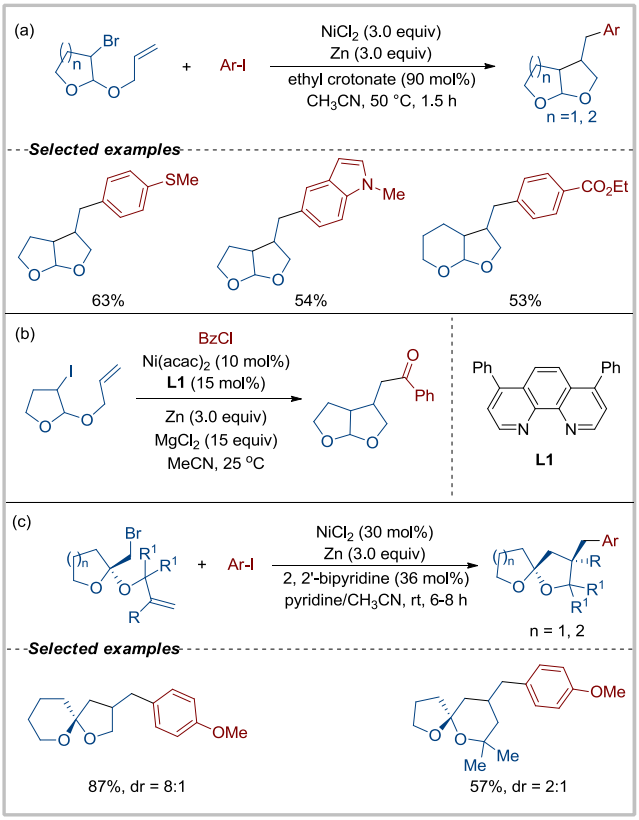
processes, and its ability to engage a wide range of electrophiles have enabled the development of diverse mechanistic strategies for alkene dicarbofunctionalization. These reactions typically proceed through two distinct mechanistic paradigms, each offering new opportunities and challenges for C–C bond formation: (a) Two-electron migratory insertion pathway (Path A, Scheme 2b): The catalytic cycle typically initiates with the oxidative addition of a C_{sp^2}-electrophile to a nickel(0) species, forming a nickel(II) complex. Subsequent migratory insertion of the alkene into the Ni–C bond generates a key alkyl-nickel intermediate, which then couples with a second electrophile to produce the dicarbofunctionalization product by reductive elimination. This pathway offers excellent control over regio- and stereoselectivity. (b) Single-electron radical addition pathway (Path B, Scheme 2b): The unique redox properties of nickel facilitate SET activation of C_{sp^3}-electrophiles, generating reactive alkyl radicals. These radicals add to the alkene, forming carbon-centered alkyl radical intermediates that are subsequently captured by nickel species, which undergo cross-coupling with the second carbo-electrophiles to yield the final product *via* reductive elimination.[8] While this pathway expands reaction scope and functional group compatibility, it also introduces significant challenges in controlling regio- and stereoselectivity. This review systematically summarizes recent advances in nickel-catalyzed reductive dicarbofunctionalization of alkenes, with an emphasis on nickel-catalyzed reductive dicarbofunctionalization of alkenes via reductive elimination to forge the second carbon-carbon bond.

2. Construction of C_{sp3}-C_{sp3} Bonds and C_{sp3}-C_{sp2} Bonds by Ni-catalyzed Dicarbofunctionalization of Alkenes

Nickel-catalyzed alkyl-arylation of alkenes offers a more efficient route to simultaneously forge C_{sp^3}–C_{sp^3} and C_{sp^3}–C_{sp^2} bonds. This enhanced reactivity profile stems from fundamental differences in the kinetic parameters of the coupling partners. This inherent selectivity paradigm enables access to structurally complex architectures that would otherwise require multi-step syntheses.

In 2012, Peng and co-workers reported a nickel-mediated intramolecular cyclizative alkylarylation of alkenes with tethered alkyl bromides and aryl iodides under reductive conditions (Scheme 3a).[9] This transformation under mild conditions provides access to stereochemically complex fused or spirocyclic scaffolds. This system works well with a wide range of functional groups and allows for late-stage modifications. Its tandem cyclization coupling method creates complex fused or spirocyclic structures with excellent control over stereochemistry, even on a gram scale. Remarkably, this unique intramolecular coupling method enables to form two C–C bonds and four connected stereocenters in one step, providing a simple and effective way to build complex polycyclic structures.

Scheme 3 Nickel-mediated/catalyzed two-component reductive alkylarylation of unactivated alkenes



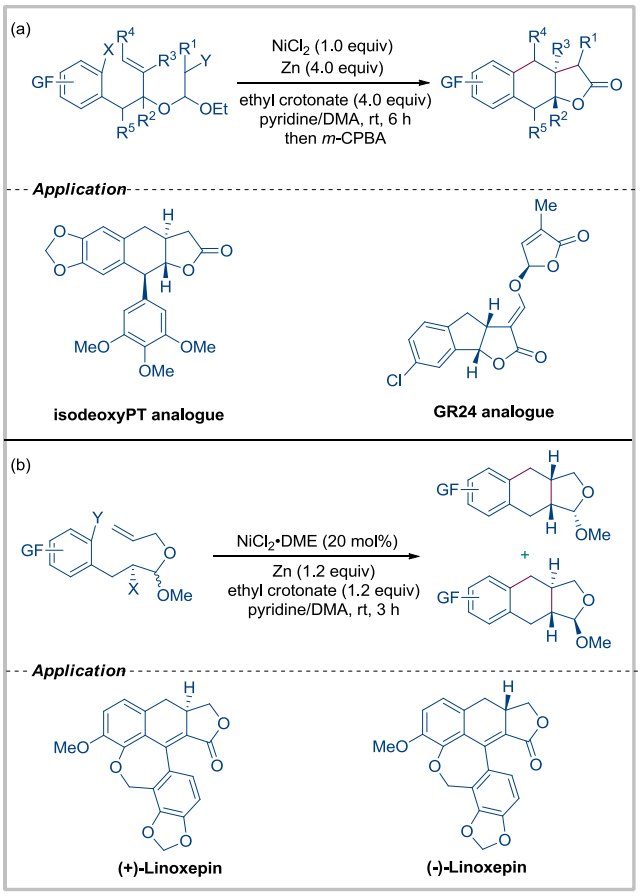
In 2013, Gong and co-workers developed a nickel catalyzed two-component alkylacylation of alkenes (Scheme 3b).[10] This reaction realized the reductive ring closing/ketone formation by utilizing benzoyl chloride as electrophilic coupling partner. In 2014, Peng group explored this nickel-catalytic system to synthesize a range of dioxygen-containing spiro compounds (Scheme 3c).[11] Based on their previous success with complex fused and spirocy-

clic structures, they were able to efficiently and selectively synthesize various dioxygen spirocycles under mild conditions. Notably, this system demonstrates the utility of this approach for the construction of complex challenging structural motifs encountered in natural products and bioactive agents.

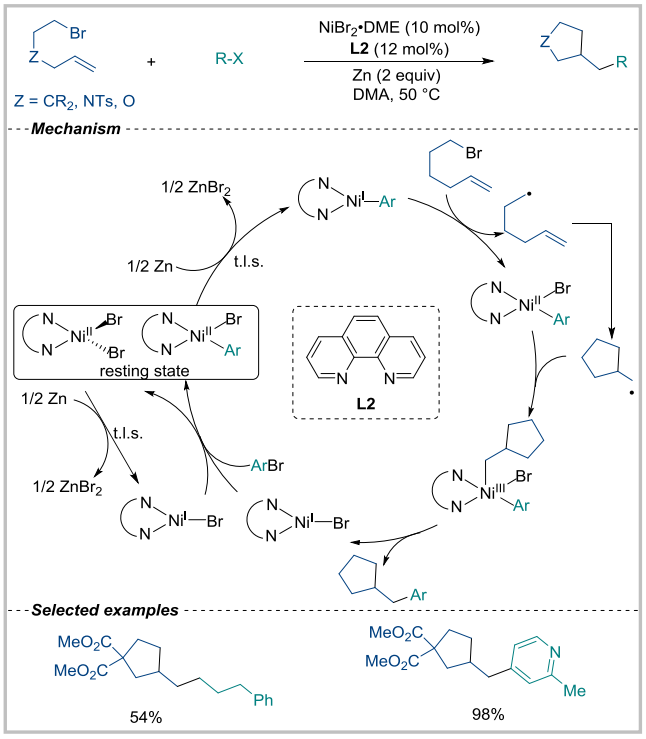
In 2016, Peng group utilized a similar reaction strategy to realize the stereoselective synthesis of *trans*-tetrahydronaphthalene-[2,3-*b*]furans (Scheme 4a).[12] The method displays a broad substrate scope and was successfully used to create the aromatic strigolactone analogue GR24, as well as new therapeutic (iso)deoxypodophyllotoxin derivatives. Moreover, this approach displays the *in situ* reductive intramolecular alkylarylation of alkenes with a tertiary alkyl bromide and an aryl iodide to access challenging complex lactones bearing multiple quaternary stereocenters, such as spirocyclic and adjacent ones. Mechanistic studies indicated that the cyclization selectivity was governed by substrate control and revealed that the stereochemical effects of the alkene and halide tethers played a crucial role in directing the reaction pathway. Subsequently, the same group further expanded this catalytic system to achieve the facile construction of a variety of tetrahydronaphtho[2,3-*c*]furan compounds (Scheme 4b).[13] The method offers a high tolerance for a variety of functional groups, allowing numerous substitution patterns on the fused core with consistently high yields. Moreover, conformational control was the decisive factor in regulating the formation of the *trans*- or *cis*-fusion in tandem cyclization/cross-coupling. Remarkably, the ester function, such as in tricyclic acetal, was also tolerated under the mild reductive conditions, whereas this type of electrophilic group is generally not compatible in the classical cross-coupling reactions due to the presence of organometallic reagent. Furthermore, the versatility of this approach was also highlighted by its successful application in the enantiodivergent total synthesis of linoxepin, showing its synthetic utility in the synthesis of complex natural products.

In 2018, Diao and co-workers developed a nickel-catalyzed reductive dicarbofunctionalization of unactivated alkenes. The reaction proceeds efficiently under mild conditions with both electron-rich and electron-deficient aryl bromides, giving the cyclizative alkylarylation products in excellent yields (Scheme 5).[14] Furthermore, the method demonstrated a broad substrate scope and strong functional group compatibility, making it suitable for the preparation of various carbocyclic and heterocyclic compounds. Contrary to previous 2-component difunctionalization systems, which were primarily confined to 5-membered ring formation, this methodology enables effective formation of 6-membered heterocycles, providing direct access to biologically relevant piperidine and tetrahydrofuran derivatives, demonstrating its synthetic and medicinal relevance. Subsequently, to understand the mechanistic pathway, the group later in 2019 carried out detailed mechanistic investigations supported by kinetic, spectroscopic, and organometallic studies. These insights revealed a unique sequential reduction pathway, in contrast to a typical radical chain mechanism. The observed key findings include: (1) the reduction of Ni^{II} to Ni^{I} by Zn was identified as the rate-determining step, with the resting state of the catalyst being a mixture of (phen)$Ni^{II}Br_2$ and (phen)Ni^{II}(Ar)Br; (2) Zn can only reduce (phen)Ni^{II} to (phen)Ni^{I}, without detection of any (phen)Ni^{0} intermediates, indicating a non-classical reduction profile for the Ni species; (3) formation of the alkyl radicals resulted from a bimolecular oxidative addition of the aryl bromides to (phen)Ni(I)–Br, a two-electron step that was uncommon for radical-forming processes. Additionally, the study elucidated the intrinsic mechanisms governing the activation order and selectivity of different electrophiles.

Scheme 4 Ni-mediated/catalyzed stereospecific one-component arylalkylation of alkenes



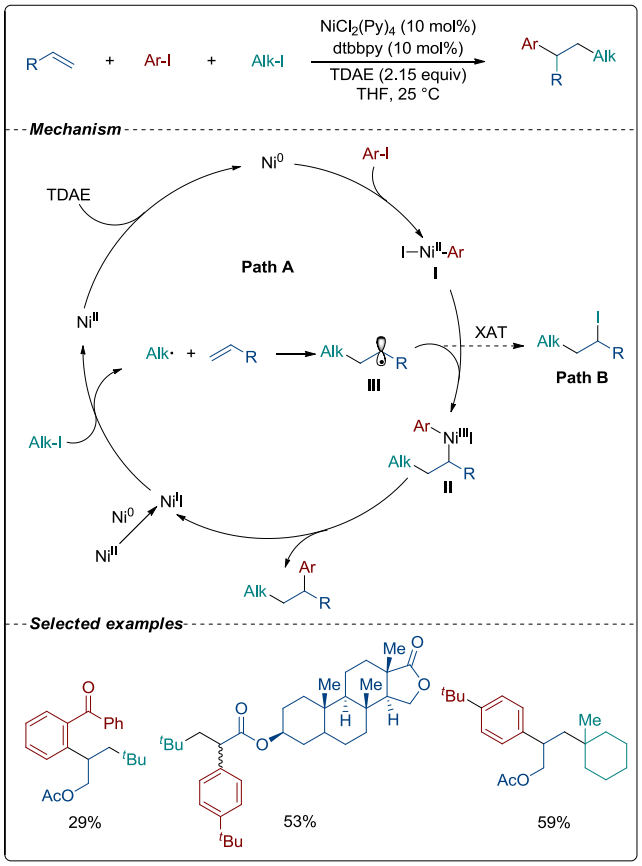
Scheme 5 Ni-catalyzed two-component reductive alkylarylation of alkenes



In 2017, Nevado and co-workers reported the first example of intermolecular three-component reductive dicarbofunctionalization of activated alkenes to facilitate the simultaneous installation of C_{sp3}-C_{sp3} and C_{sp3}-C_{sp2} bonds (Scheme 6).[15] Both electron-rich and electron-deficient alkenes are good substrates for this al-

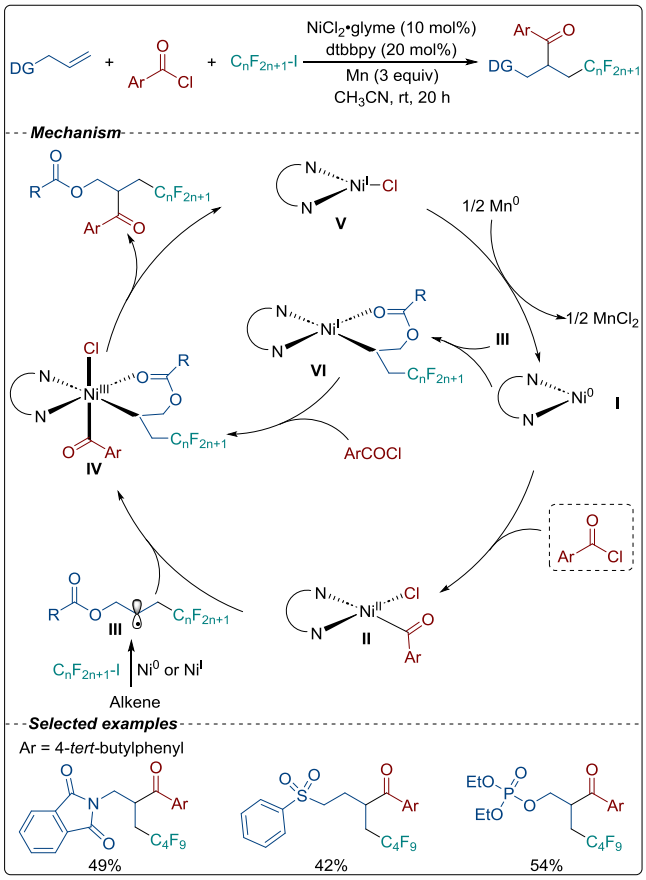
kylarylation process. The reaction in the presence of $NiCl_2(Py)_4$ and TDAE catalytic system enables the coupling of alkyl iodides, alkenes, and aryl iodides in a flexible way, displaying good chemo- and regioselectivity and high functional group compatibility. Importantly, using tertiary alkyl iodides and aryl iodides was key to achieving efficient cross-selectivity and reducing unwanted side reactions like alkyl–alkyl or aryl–aryl homocoupling. Moreover, control experiments involving radical traps and radical clock substrates firmly support C-centered radical intermediates, and stoichiometric studies support the involvement of ArNi(II) species in the catalytic cycle. Based on the experimental evidences, a possible pathway would involve the *in-situ* formation of Ni(0) which would undergo oxidative addition with aryl iodide to generate ArNi(II) intermediate; meanwhile, Ni(I) would activate the alkyl iodide to give rise to alkyl radical, while it adds to the alkene to furnish the radical intermediate, which subsequently combines with the ArNi(II) to access the Ni(III) intermediate, followed by a reductive elimination to release the dicarbofunctionalized product, and to regenerate the Ni(I). Additionally, the control experiments exclude the possibility of a stepwise pathway through secondary alkyl iodide intermediates and favor the direct radical relay mechanism through the ArNi(II) species. The group then advanced this strategy to achieve preferential functionalization of alkenes to give dinucleophilic products through nickel-catalyzed reductive dicarbofunctionalization.[16] A directing group was essential to guide the regioselectivity as well as to avoid undesired side reactions. This facile and versatile strategy was nicely applicable to various substrates and was extremely tolerant to many functional groups; it could be used to rapidly construct diverse carbon–carbon backbones from easily accessible precursors.

Scheme 6 Ni-catalyzed reductive three-component alkylarylation of activated alkenes



In 2018, the Chu group disclosed a nickel-catalyzed radical-relay three-component strategy for carboacylation of unactivated alkenes (Scheme 7).[17] The reaction utilizes the ester group as the directing group, perfluoroalkyl iodine and acyl chloride as coupling reagents to provide access to a wide range of β-fluoroalkyl ketones. This transformation facilitates the efficient construction of C_{sp3}-C_{sp3} and C_{sp3}-C_{sp2} bonds with excellent regioselectivity under mild reaction conditions. Moreover, the method is effective with alkenes containing chelating moieties such as esters, carbonates, and phosphates, highlighting the broad compatibility throughout a wide range of substrates and functional groups. The success of this reaction is strongly dependent on the chelation assistance, and both the six- and seven-membered directing groups exhibit high efficiency, whereas non-chelating or five-membered/strained directing groups give poor or no reactivity. Furthermore, the strong guiding effect also gives access to high site-selectivity, even for substrates that possess multiple alkenes, such as those present in complex bio-derived molecules. Mechanistic investigations suggest that the reaction proceeds through a radical-relay pathway wherein a fluoroalkyl radical, generated *via* single-electron reduction of fluoroalkyl iodides by low-valent nickel species or manganese, adds to the alkene to form a secondary carbon-centered radical. The intermediate is then trapped by an acylnickel(II) complex to provide a β-fluoroalkyl ketone by reductive elimination.

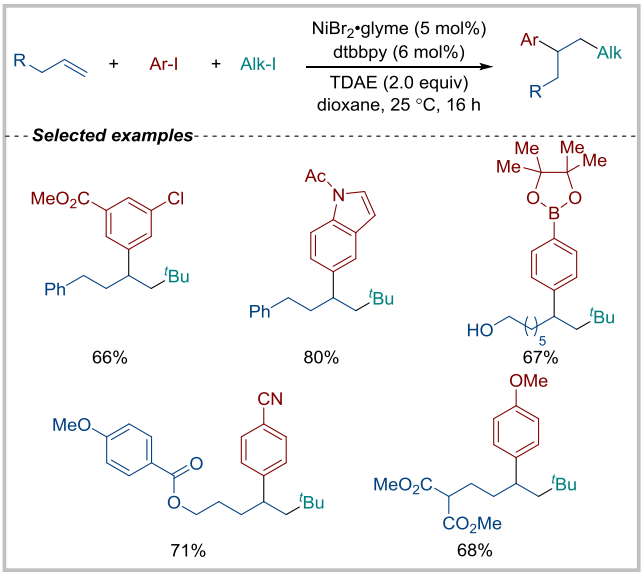
Scheme 7 Ni-catalyzed reductive fluoroalkylacylation of alkenes



Nevado group in 2019 introduced a three-component reductive alkyl arylation reaction of unactivated alkenes with two electrophilic carbon sources (Scheme 8).[18] By fine-tuning the reaction parameters, the method allowed for the efficient addition of aryl and alkyl iodides to a wide range of unactivated alkenes and 1,*n*-dienes. Notably, this transformation exhibited excellent chemoselectivity and functional group tolerance, enabling the incorporation of diverse aryl iodides, including electron-rich, electron-poor, sterically hindered, and heterocyclic substrates, into dicarbofunctionalized products in good to high yields. The key

advantage of this methodology is that it proceeds without the requirement of directing groups. Mechanistic insight supported by control experiments and density functional theory (DFT) calculations revealed the feasibility of a radical-based mechanism involving two interconnected Ni^{I}/Ni^{III} processes and demonstrated the different abilities of Ni^{II} species and $PhNi^{I}$ to reduce C_{sp3}-I bonds. The role of reducing agent TDAE was further studied, revealing that it plays a crucial role in governing the high levels of chemoselectivity. These observations provided new ideas for the development of related reductive coupling reactions, where an efficient transformation avoids the need for pre-activation of the substrates.

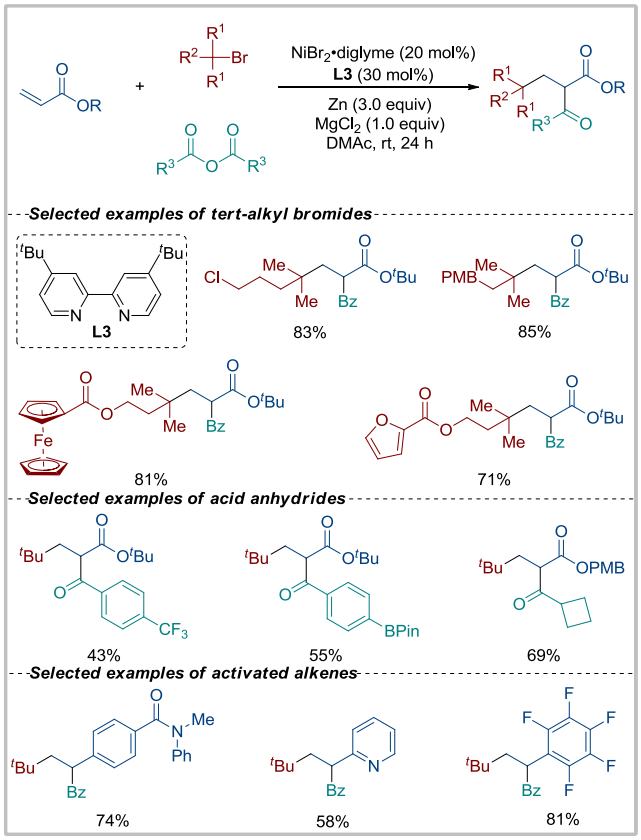
Scheme 8 Ni-catalyzed reductive alkylarylation of non-directed aliphatic alkenes



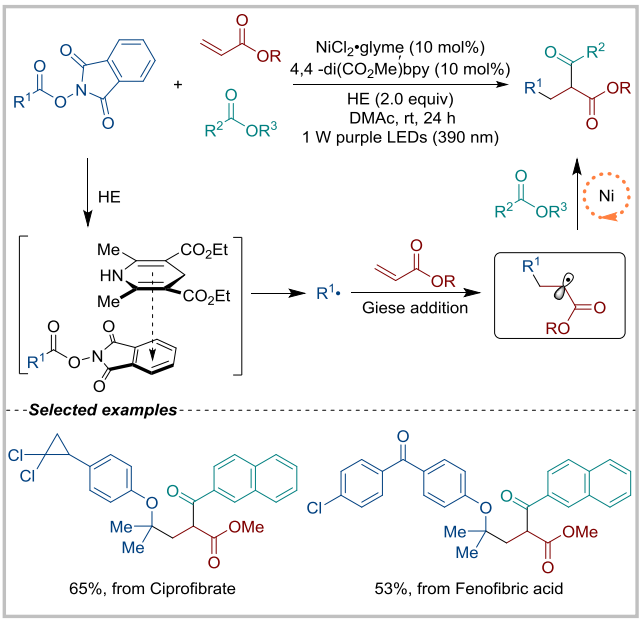
In 2020, Wang and co-workers proposed a three-component reductive alkylacylation of electron-deficient activated alkenes with tertiary alkyl bromides and acid anhydrides *via* nickel catalysis (Scheme 9).[19] The method provides the efficient construction of C_{sp3}–C_{sp3} and C_{sp3}–C_{sp2} bonds under mild conditions. Furthermore, the strategy shows the compatibility with a variety of acid anhydrides and alkenes, including α-substituted acrylates and electron-deficient styrenes, while enabling the formation of quaternary centers and scalable synthesis. Mechanistic investigation supported by a series of control experiments, suggested that the reaction proceeds *via* a radical pathway. The authors demonstrated that the synergistic interaction between $MgCl_2$ and Zn effectively cleaves the C–Br bond, generating a *tert*-butyl radical, which undergoes radical addition onto the electron-deficient alkene to form a carbon-centered radical. This radical was subsequently captured by Ni^{II} species, formed from the oxidative addition of the anhydride into the Ni^{0} catalyst. Reductive elimination from the resulting Ni^{III} intermediate furnishes the target product and regenerates the Ni^{I} species, followed by the reduction with Zn to complete the catalytic cycle. This method offers a flexible and selective way to make β-functionalized carbonyl compounds from simple starting materials and highlights the utility of radical and metal cooperation in nickel-catalyzed multicomponent reactions.

Photoredox/Ni dual catalysis has attracted considerable interest over the past few years, providing novel activation modes to afford C_{sp3}-C_{sp3} and C_{sp3}-C_{sp2} bonds in a controlled manner under considerably milder conditions. In a notable work by Yuan and co-workers, wherein nickel-catalyzed, three-component reductive 1,2-alkylacylation of electron-deficient alkenes was achieved by activation through an electron donor-acceptor (EDA) complex (Scheme 10).[20] The process involves the use of NHPI esters and

Scheme 9 Ni-catalyzed three-component reductive alkylacylation of electron-deficient alkenes



Scheme 10 Light-promoted Ni-catalyzed reductive alkylacylation of alkenes

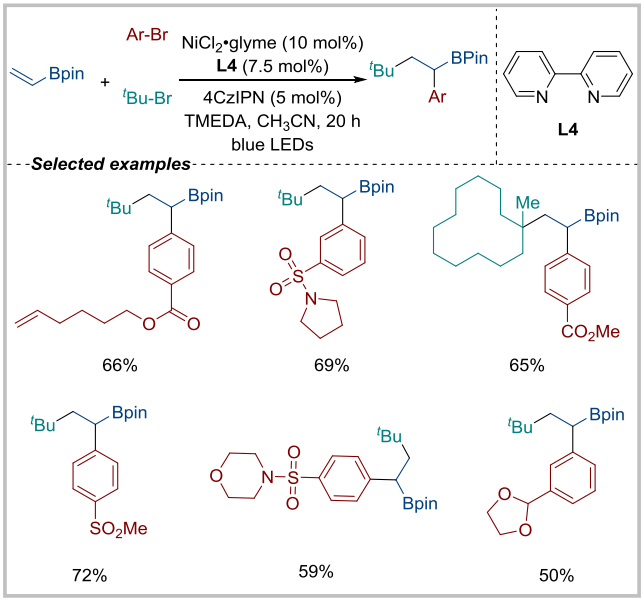


2-pyridyl esters as alkyl and acyl radical precursors. Importantly, this process bypasses the requirement of an external photocatalyst and stoichiometric metal reductant. The reaction exhibits a wide range of substrate generality and is tolerant to various functional groups, including esters, amides, cyano, and halides. It also enables late-stage modifications of complex bioactive molecules and scalable synthesis of versatile β-ketoesters. To check the nature of reaction pathway, control experiments, including UV-vis

spectroscopy and radical trapping, revealed the formation of the EDA complex between the NHPI ester and Hantzsch ester as the source of alkyl radicals. This rules out the involvement of Ni(II) acyl intermediates and supports a photoinitiated radical pathway as the key step in this Ni-catalyzed alkylacylation. The reaction initiates with the formation of EDA complex between NHPI ester and Hantzsch ester. This complex leads to the generation of an alkyl radical, which subsequently adds to the alkene and is intercepted by the Ni^0 to form Ni^I species. This undergoes oxidative addition with an acyl electrophile or *via* a 2-pyridyl ester pathway to produce a Ni^{III} species, which upon reductive elimination delivers the corresponding product.

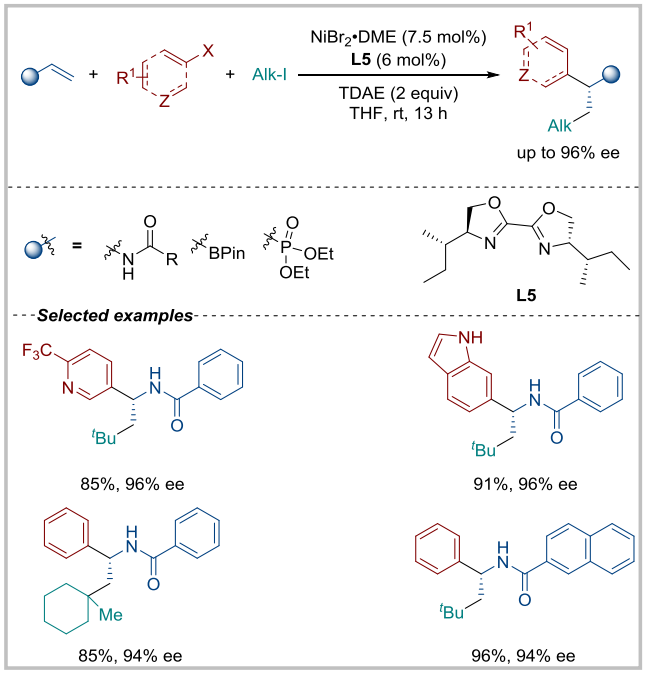
In 2020, Martin and co-workers reported a site-selective 1,2-dicarbofunctionalization of vinyl boronates through photoredox/Ni dual catalysis (Scheme 11).[21] The process is based on the regioselective addition of an aryl and tertiary alkyl group to the alkene functionality of vinyl boronates, with bromoarenes and tertiary alkyl bromides as electrophilic partners. This method under mild conditions demonstrates high levels of chemo and regioselectivity and tolerates a wide range of functional groups, including esters, nitriles, and heterocycles. Furthermore, this tandem catalytic protocol not only results in multiple downstream functional group modifications of the alkylboron products through C–B bond manipulation but also proceeds *via* a reductive-quenching pathway with *in situ*-formed alkyl radicals and Ni(0)/Ni(II) catalytic cycle. The methodology represents an attractive tool for the modular preparation of densely functionalized alkylboron reagents, which are valuable intermediates in cross-coupling and late-stage functionalization.

Scheme 11 Ni-catalyzed reductive 1,2-alkylarylation of vinyl boronates



The construction of enantioenriched, complex molecules from easily accessible alkenes and commercially available electrophiles using asymmetric intermolecular nickel-catalyzed reductive dicarbofunctionalization is a modular and efficient strategy. In 2020, Nevado group established a nickel-catalyzed protocol to facilitate the efficient asymmetric intermolecular reductive dicarbofunctionalization of alkenes (Scheme 12).[22] The reaction features the installation of two different readily available electrophiles (alkyl iodides and aryl iodides) across a variety of alkenes, including vinyl boranes, vinyl amides, and vinyl phosphonates, furnishing the desired products with high levels of regio- and enantioselectivity. Moreover, the existence of coordination sites on the (*S*,*S*)-*sec*-Bu-BiOx chiral ligand and alkenes was the key to the success of the reaction. Additionally, the results of density functional theory (DFT) calculations confirmed that the weak interaction between the amide group and the nickel center contributed to the formation of the *R*-configuration of the product. Remarkably, the multiple transformations of chiral amides obtained in this process showed the potential of this new method in the direct assembly of chiral building blocks such as primary amines, secondary amines, and oxazolines, highlighting its synthetic practicality.

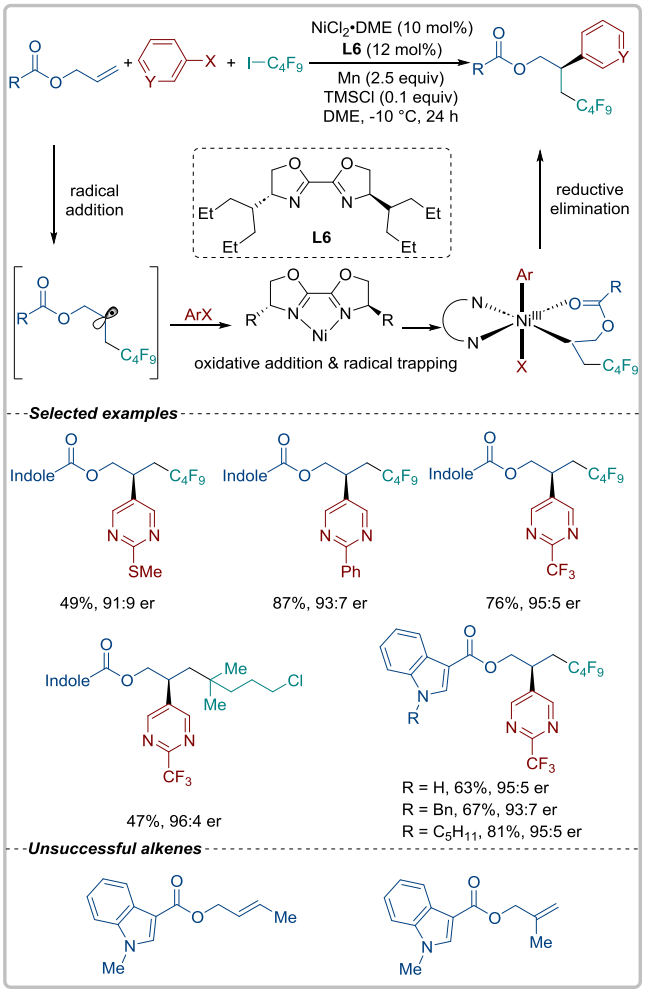
Scheme 12 Ni-catalyzed reductive asymmetric alkylarylation of *N*-acylenamines



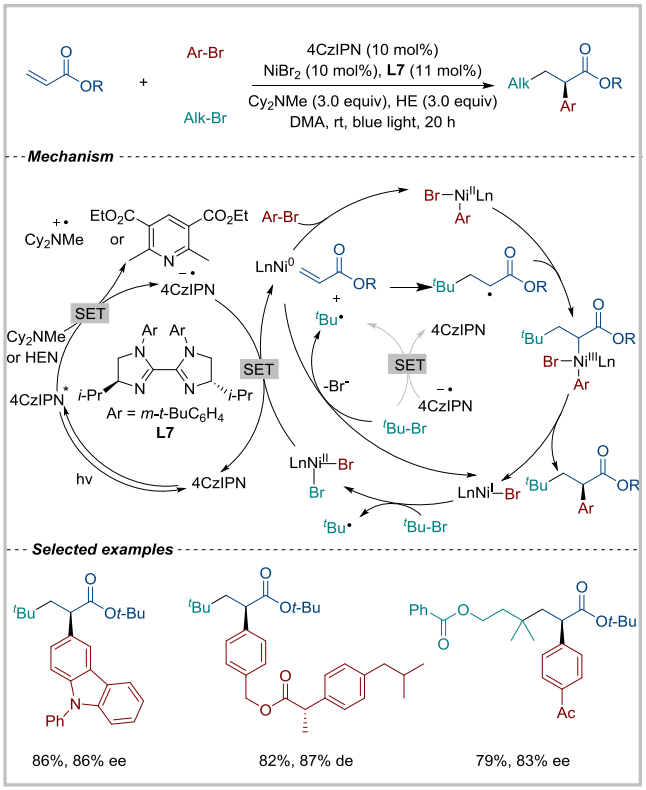
Inspired by the significance of chelation-assisted strategies in regio- and site-selective difunctionalization, Chu and co-workers further explored this protocol by disclosing a chiral BiOx ligand to develop a nickel-catalyzed enantioselective fluoroalkylarylation of unactivated alkenes with aryl halides and perfluoroalkyl iodides as coupling partners (Scheme 13).[23] This approach offers the efficient synthesis of a variety of functionalized β-fluoroalkyl arylalkanes from readily available simple alkenes in a mild manner with high yield and excellent enantioselectivity (up to 97 : 3 er). It is worth mentioning that the ester group not only served as a weakly coordinating directing group to control regioselectivity, but also acted as a versatile synthetic handle, allowing for easy post-modifications to access diverse chiral fluorinated scaffolds. Mechanistic studies indicated that the transformation was likely to proceed through a radical process that was triggered by a fluoroalkyl radical formation and subsequently involved migratory insertion and cross-coupling with aryl halides by a Ni(I)/Ni(III) catalytic cycle. This work demonstrates that the combination of ligand development and substrate control is a powerful tool to facilitate asymmetric difunctionalizations of unactivated alkenes.

In 2021, Mao group devised a visible-light-driven photordox/nickel dual catalytic protocol for the regio and enantioselective three-component dicarbofunctionalization of acrylates using aryl and alkyl bromides (Scheme 14).[24] This transformation provides an efficient route to construct enantioenriched nonsteroidal anti-inflammatory drug (NSAID) derivatives. The method avoids the use of organometallic precursors and instead achieves reductive activation with an organic electron donor, the Hantzsch ester, rather than traditional metal reductants. The process shows great tolerance for different functional groups and delivers excellent

Scheme 13 Ni-catalyzed three-component reductive asymmetric fluoroalkylarylation of allylic esters



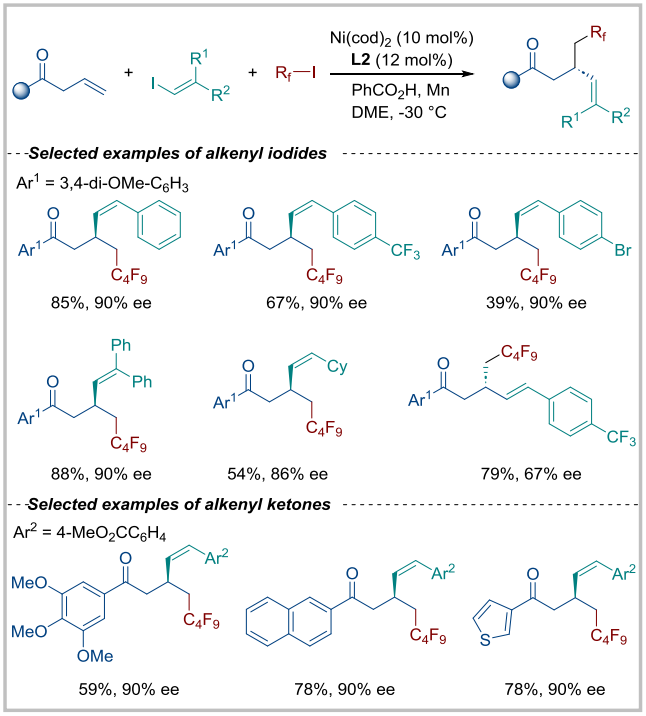
Scheme 14 Light-promoted Ni-catalyzed enantioselective reductive alkylarylation of acrylates



enantioselectivity across many substrates, including drug-like molecules such as Flurbiprofen and Naproxen derivatives. Mechanistic investigations revealed that the reaction pathway likely begins with the excitation of photocatalyst 4CzIPN under visible-light irradiation. The excited state photocatalyst, upon reductive quenching by the Hantzsch ester, forms the 4CzIPN$^{\bullet-}$ species. This species, in turn, reduces Ni^{II} to Ni^{0} *via* two SET steps, generating catalytically active $LnNi^{0}$ species. The resulting $LnNi^{0}$ catalyst thus underwent oxidative addition with an aryl bromide to yield the $LnNi^{II}(Ar)Br$ complex. Meanwhile, the alkyl bromide undergoes SET with either Ni or the reduced photocatalyst 4CzIPN$^{\bullet-}$ to generate a tertiary alkyl radical. This tertiary alkyl radical adds to the acrylate, furnishing an α-carbonyl radical, which was intercepted by the $LnNi^{II}(Ar)Br$ complex to produce a reactive Ni^{III} species. Finally, this Ni^{III} intermediate underwent reductive elimination to yield the target product. Subsequently, Maji and co-workers developed a similar visible-light-promoted strategy for 1,2-dicarbofunctionalization of unactivated alkenes, employing alkyl bromides and aryl iodides as electrophiles.[25] Recently, Mao's team extended this catalytic system to vinyl phosphonates, reported a highly enantioselective domino alkyl-arylation that produces α-aryl phosphonates.[26] This difunctionalization three-component strategy employs aryl bromides, tertiary alkyl bromides, and vinyl phosphonates under mild conditions with Hantzsch ester as terminal reductant. The key advantage of this process is that it eliminates the need for preformed organometallics and phosphorus halides.

In 2022, Chu and co-workers developed a Ni-catalyzed enantioselective three-component reductive alkylalkenylation of

Scheme 15 Ni-catalyzed three-component reductive alkylalkenylation of directed alkenes



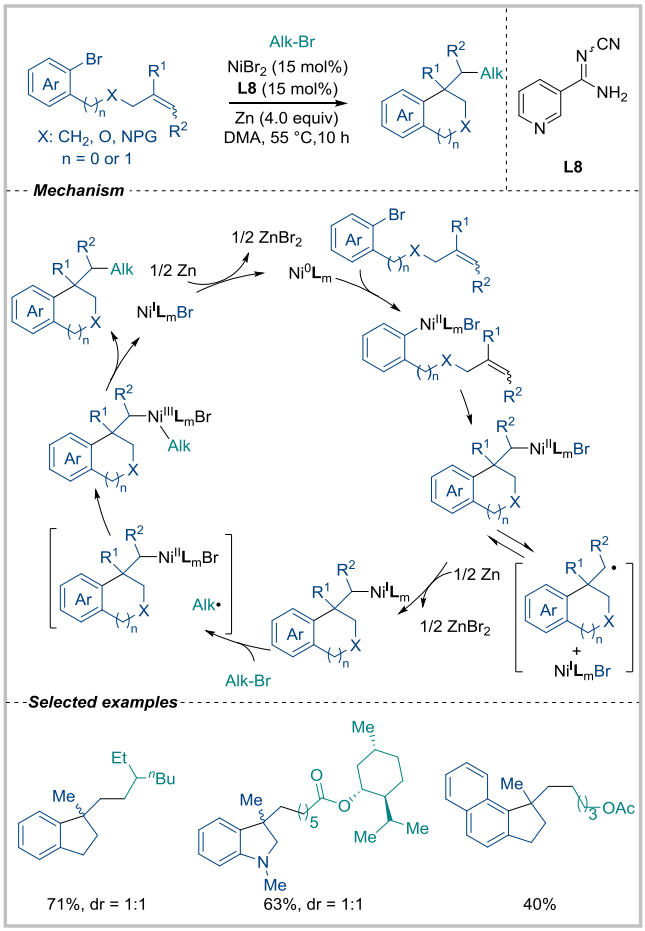
electronically unbiased alkenes using carbonyl-directed nickel catalysis (Scheme 15).[27] This method enables simultaneous regioselective construction of C(sp³)–C(sp³) and C(sp³)–C(sp²) bonds under mild conditions using Mn as a reductant and benzoic acid as an additive. Leveraging five-membered nickelacycles stabilized by pendant ketone coordination and chiral bis(oxazoline) (BiOx) ligands, the reaction couples β,γ-unsaturated ketones, *cis*-alkenyl

iodides, and fluoroalkyl iodides to deliver enantioenriched β-alkenyl ketones in high yields and excellent enantioselectivity. The work establishes a strategy for enantioselective alkene dialkylalkenylation by weak carbonyl-directed chelation to form a key five-membered nickelacycle intermediate, which governs stereocontrol at the allylic carbon. The protocol accommodates diverse functional groups and was extended to racemic alkylalkenylation of unbiased alkenes bearing ketones, esters, ethers, or amides at room temperature, highlighting its broad synthetic utility.

3. Construction of C_{sp3}-C_{sp2} Bonds and C_{sp3}-C_{sp3} Bonds by Ni-catalyzed Dicarbofunctionalization of Alkenes

In 2019, Wang group disclosed a nickel-catalyzed reductive arylalkylation of unactivated alkenes with primary alkyl bromides as coupling partners (Scheme 16).[28] This transformation provides a library of benzene-fused carbocyclic and heterocyclic compounds such as indanes, isochromanes, indolines, and tetrahydroisoquinolines. The reaction exhibits a wide substrate scope and high diastereoselectivity. The method avoids the use of organometallic reagents and displays a high functional group tolerance (alcohol, boronate, acetal, imide, nitrile, esters, aldehydes, ketone). A series of mechanistic insights, corroborated by control experiments, indicates that the catalytic cycle likely proceeds *via* dual oxidative addition, migratory insertion, and reductive elimination pathways. Later that year, the wang group introduced highly enantioselective nickel-catalyzed asymmetric reductive dicarbofunctionalization of unactivated alkenes to enable the efficient construction of a series of benzene-fused cyclic compounds bearing quaternary stereocenters directly from aryl and alkyl halides without the need for

Scheme 16 Ni-catalyzed two-component reductive arylalkylation of alkenes



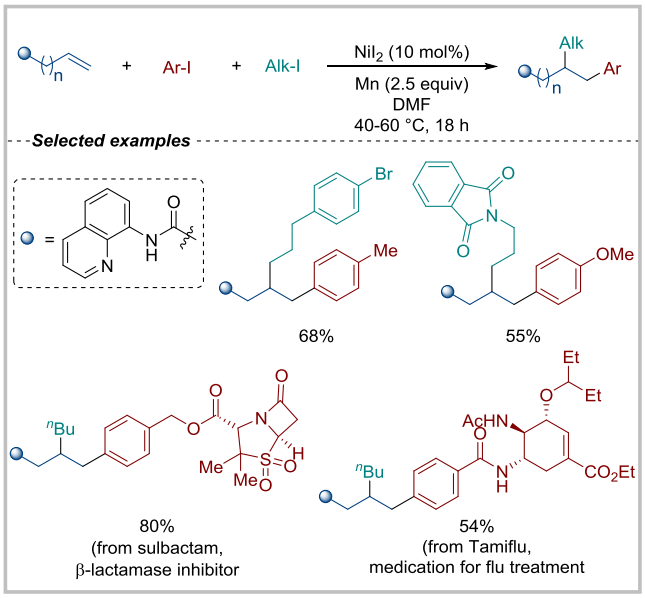
organometallic reagents.[29] Notably, this method offers improved step economy and broad functional group compatibility by eliminating the need for preformed organometallic reagents. To further explore the reductive dicarbofunctionalization strategy, the Wang group made an important breakthrough by developing *N*-hydroxyphthalimide (NHP) esters and benzyl chlorides as alternative coupling partners.[30-31] This method allows for the efficient construction of a wide array of benzene-fused carbocyclic and heterocyclic compounds under mild conditions with high tolerance to diverse functional groups such as esters, nitriles, halides, and ketones. In a subsequent contribution, Zhou and co-workers reported an efficient nickel-catalyzed desymmetric reductive cyclization of 1,6-dienes, to afford direct access to chiral tertiary alcohols. This method enables the simultaneous construction of both chiral tertiary alcohols and all-carbon quaternary stereocenters with excellent diastereoselectivity and high enantioselectivity, highlighting its synthetic efficiency and stereochemical precision. Significantly, this method was proven to be effective in late-stage modification of natural products and complex bioactive molecules, including the plant essence antibacterial Linolenic acid, Indomethacin, and Osotrazine.[32]

In the same year, the Chen group discovered a highly efficient and enantioselective nickel-catalyzed reductive dicarbofunctionalization of 1,1-disubstituted enamide by employing unactivated alkyl iodides as coupling reagents, and Bn-Biox as the chiral ligand. This methodology provides facile access to isoquinolinone derivatives containing all-carbon quaternary stereocenters with excellent efficiency (up to 99% yield) and enantioselectivities (up to 99% ee), highlighting its potential for the asymmetric synthesis of valuable *N*-heterocycles under mild reductive conditions.[33] Building on the development of enantioselective reductive dicarbofunctionalizations, independent studies by the Gong[34] and Wang[35] groups further explored the scope of nickel-catalyzed reductive arylalkylation reactions using *N*-arylacrylamides as radical acceptors. Gong utilized the alkylpyridinium salts as alkyl radical precursors under mild reaction conditions to facilitate the synthesis of benzene-fused isoquinolinone derivatives containing all-carbon quaternary centers with good efficiency. Parallelly, Wang and co-workers employed easily accessible free alcohols, which were *in-situ* converted to alkyl radicals through halogen atom transfer (XAT), thereby affording efficient access to similar carbocyclic motifs.

Koh and Wang have independently reported their work on Ni-catalyzed reductive arylalkylation of alkenes involving sequential addition of two different organohalides using 8-aminoquinoline (AQ) and bidentate quinolinamide (QA) as directing group (Scheme 17).[36] Koh group showed that the AQ moiety efficiently directed nickel catalysts to mediate selective migratory insertion and cross-electrophile coupling reaction, enabling the formation of a variety of β- and γ-substituted amide products with high regioselectivity and functional group compatibility. On the other hand, the Wang group extended this approach to include aryl and alkyl halides, demonstrating the broad scope of this methodology and its tolerance to sterically and electronically diverse coupling partners. This method employs the bidentate quinolinamide (QA) directing group to govern the selectivity of reductive dicarbofunctionalization of alkenyl amines. Together, these studies demonstrated the utility of AQ-assisted nickel catalysis for the predictable dicarbofunctionalization through single cross-electrophile coupling manifolds. To further investigate the applicability of 8-aminoquinoline as a bidentate directing group, Chen and co-workers proposed a nickel-catalyzed three-component strategy employing the AQ directing group. This includes asymmetric reductive arylalkylation of nonactivated alkenes with aryl and alkyl electrophiles as cross-coupling partners.[37] The approach follows a Ni(0)/Ni(II)/Ni(III) catalytic cycle through carbometalation and radical cross-coupling to construct β-arylalkylated amides with high regio and enantioselectivity. Mechanistic studies and DFT

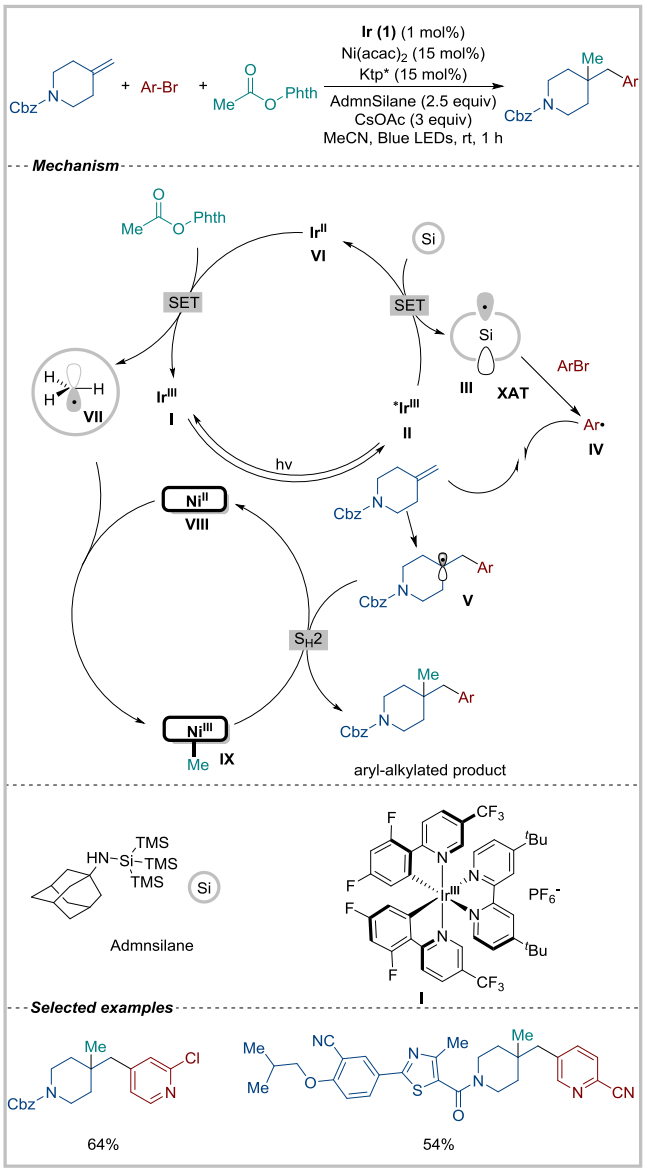
calculations revealed that the hemilabile coordination behaviour of the PHOX ligand was a key factor for the success of the reaction, and the Heck-type migratory insertion was the rate- and enantio-determining step, establishing a strong correlation between ligand dynamics and reaction selectivity. Concurrently, Shu group introduced a nickel-catalyzed reductive approach that allows for controllable 1,2- and 1,3-arylalkylation of *N*-acyl allylic amines, representing the first site-divergent migratory difunctionalization of alkenes under cross-electrophile coupling conditions.[38] The method works well with a wide range of substrates, shows good functional group tolerance, and provides a flexible way to build complex aryl–alkyl structures from simple, easy-to-find starting materials.

Scheme 17 Ni-catalyzed reductive arylalkylation of directed alkenes



Recent contributions from the MacMillan group have demonstrated that radical sorting is a viable method for alkene difunctionalization, allowing for the introduction of both aryl–alkyl and dialkyl moieties by judicious control of radical reactivity, polarity, and ultimately, selectivity. This led to the development of a triple-radical sorting strategy that facilitates the metallophotoredox catalyzed aryl-alkylation of unactivated alkenes using aryl bromides and primary alkyl groups as coupling reagents to construct C_{sp3}-C_{sp2} and C_{sp3}-C_{sp3} bonds (Scheme 18).[39] The protocol under mild conditions worked well with a wide range of unsaturated alkenes, aryl bromides, and alkyl compounds. Alkenes containing carbamates, alkyl chlorides, free alcohols, or nitriles exhibited relatively low reactivity, while many structurally complex bromides, including heteroaryl amines, and bromides derived from glipizide and tolazamide showed high potential for application. Mechanistic studies revealed that the reaction proceeds *via* the excitation of photocatalyst Ir^{III} **I** to its triplet excited state $^*Ir^{III}$ **II**, which is then reductively quenched by adamantylamino-supersilane, followed by aza-Brook rearrangement to generate the silyl radical **III**. Radical **III** undergoes halogen atom transfer (XAT) with aryl bromide to form the aryl radical **IV**. This aryl radical adds to an unactivated alkene, producing the alkyl radical **V**. To complete the catalytic cycle, Ir^{II} **VI** reduces a redox-active ester, generating the primary alkyl radical **VII**, which is captured by the S_H2 radical-sorting catalyst **VIII**. Finally, the alkyl radical **V** and the alkyl-metal complex **IX** undergo an S_H2 reaction to furnish the target product. The innovation of this strategy lies in its ability to create the simultaneous generation of three distinct radical species: aryl radical, primary alkyl radical, and hindered alkyl radical, providing a new method for the synthesis of complex drug molecules and bioactive intermediates.

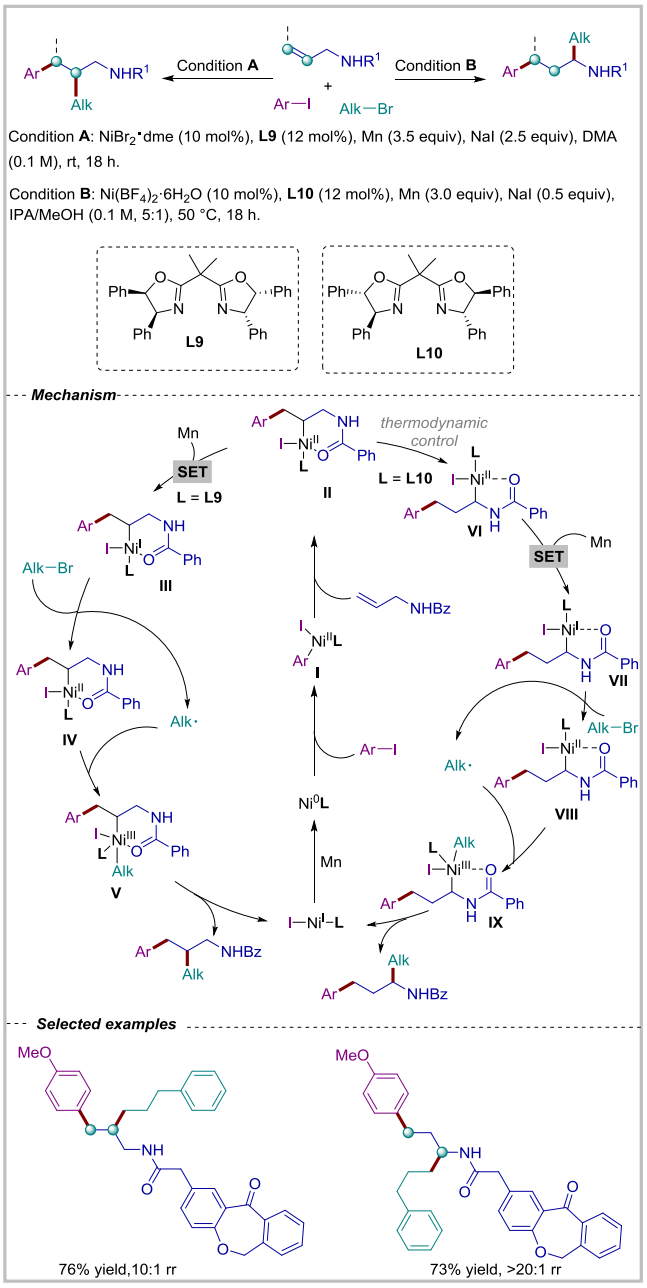
Scheme 18 Light-promoted Ni-catalyzed arylalkylation of alkenes by triple radical sorting



In 2025, Shu and co-workers developed a Ni-catalyzed reductive three-component coupling enabling site-divergent arylalkylation of unactivated allylic amines with aryl and alkyl halides (Scheme 19).[40] By modulating ligands and conditions, the reaction selectively delivers either 1,2-arylalkylation products (aryl at distal alkene carbon) or 1,3-migratory arylalkylation products (aryl migration via β-H elimination) from identical substrates. This strategy represents the first controlled migratory difunctionalization of alkenes under reductive conditions, offering versatile routes to architecturally distinct amines from simple precursors. Mechanistic studies revealed that the Ni-catalyzed transformation proceeds through ligand-controlled pathways: (i) under Conditions A (**L10**), Ni^0 undergoes oxidative addition with aryl iodides, followed by stereospecific alkene carbometallation to form a chelated alkyl-Ni^{II} intermediate **II**; this is reduced to Ni^I intermediate III by Mn, which reacts with alkyl bromides to generate alkyl radicals that are captured to afford Ni^{III} species **V**. The reductive elimination of species **V** affords 1,2-arylalkylation product. (ii) under Conditions B (**L11**), the initial alkyl-Ni^{II} intermediate undergoes

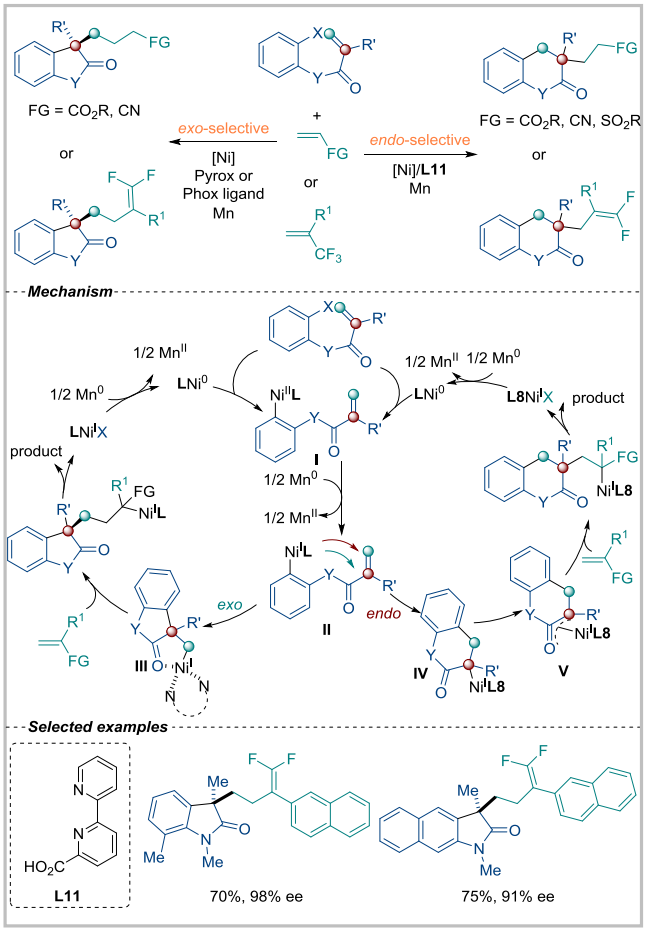
intramolecular β-H elimination/insertion to migrate Ni to the distal carbon; subsequent alkyl radical capture and reductive elimination deliver 1,3-migratory arylalkylation. Radical involvement was confirmed by cyclopropylmethyl bromide ring-opening experiments, while deuterium labeling and crossover studies verified irreversible, intramolecular Ni-migration. The Mn/NaI system facilitates Ni^{I}/Ni^{III} redox cycles which is critical for both pathways.

Scheme 19 Ni-catalyzed regioselective and site-divergent reductive arylalkylations of alkenes



Synthesis of cyclic structures containing quaternary carbon stereocenters through Ni-catalyzed dicarbofunctionalization of alkenes has received significant interest. However, the majority of the reported procedures mainly afford the *exo*-cyclization/cross-coupling products, and the *endo*-selective versions are relatively limited.[41] To address this gap, Kong group established the first example of ligand-controlled, nickel-catalyzed regioselective reductive dicarbofunctionalization of alkenes to access both five- and six-membered benzo-fused lactams (Scheme 20).[42] By employing chiral Pyrox- or Phox-type bidentate ligands, they achieved highly enantioselective 5-*exo* cyclization/cross-coupling to produce indolin-2-ones. Alternatively, switching to an achiral 2,2′-bipyridine ligand allowed a regioselectivity switch to favor the 6-*endo* cyclization/cross-coupling, producing 3,4-dihydroquinolin-2-ones in good yields. Mechanistic investigations supported by control experiments reveal that the reaction proceeds *via* the *in-situ* generation of Ni^{0} under reductive conditions, which undergoes oxidative addition with ArBr to form an $ArNi^{II}X$ intermediate **I**, followed by the reduction with Mn^{0} to generate an $ArNi^{I}$ intermediate **II**. The ligand environment controls the regioselectivity of the cyclization (*exo vs endo*), leading to the corresponding cross-coupled products with high selectivity.

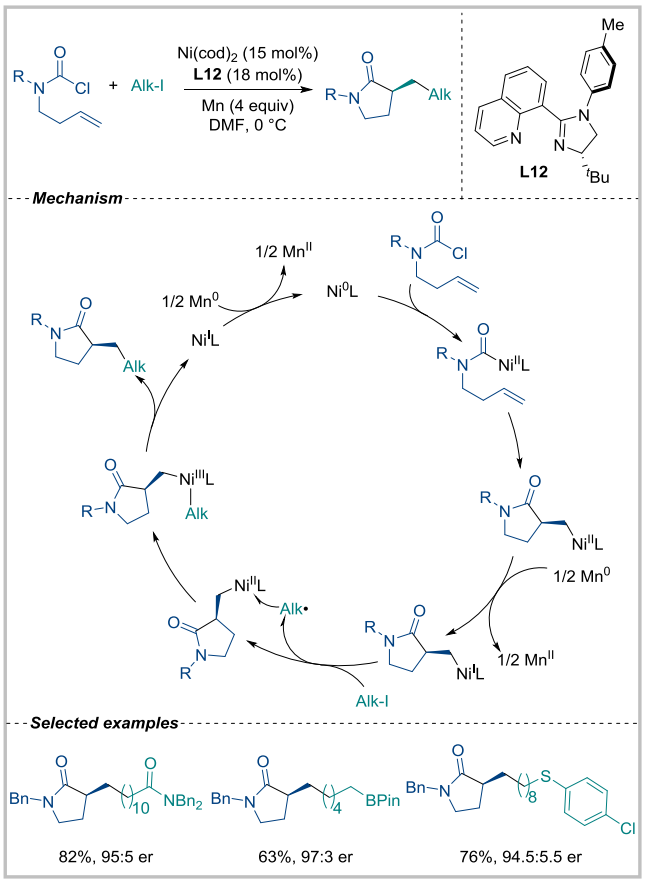
Scheme 20 Ligand-controlled Ni-catalyzed two-component regiodivergent reductive dicarbofunctionalization of alkenes



Another interesting work was described by Chen and co-workers for the synthesis of chiral non-aromatic heterocycles (Scheme 21).[43] This transformation involves the coupling of 3-butenyl carbamoyl chloride with unactivated alkyl iodides to produce chiral α-alkylated pyrrolidinone with broad substrate scope and high enantiomeric excess. Notably, a newly designed chiral ligand, 8-quinoline imidazoline, was critical for inducing high stereocontrol. The mechanistic studies supported by stoichiometric and radical cyclization experiments, revealed that the enantioselectivity-determining step (EDS) involved an intramolecular migratory insertion of the carbamoyl nickel intermediate into the alkene and that the reaction proceeded *via* a single electron transfer pathway to form radical species, which upon reductive elimination furnished the desired product as chiral pyrrolidinone. Building on their earlier success, the same group further extended their research in 2022 by replacing the chiral ligand with a newly designed 1-naphthyl-substituted quinoline-imidazoline ligand (NapQuinim), which significantly enhanced both diastereo- and enantioselectivity.[44] The method facilitates the efficient synthesis

of chiral pyrrolidinones containing two stereocenters. This modification enabled the highly selective coupling of α-substituted homoallylic carbamoyl chlorides with unactivated alkyl iodides to furnish *trans*-pyrrolidinones in high yields (up to 85%) with excellent diastereomeric ratios (dr >20 : 1) and enantiomeric excesses (up to 97% ee). In the same year, the Chen group further modified the substrate framework by developing a desymmetric dicarbofunctionalization of 1,6-dienes *via* nickel-catalyzed reductive cross-coupling. The method provides facile access to functionalized pyrrolidinones containing two non-adjacent stereocenters, along with a challenging remote tertiary stereocenter.[45] Subsequently, both the Chen and Wang groups independently explored the scope of this methodology to the enantioselective synthesis of nitrogen containing heterocycles using different chiral ligands to achieve the synthesis of *δ*-lactams, *γ*-lactam, and oxindoles.[46-48]

Scheme 21 Ni-catalyzed two-component asymmetric reductive alkylcarbamoylation of alkenes

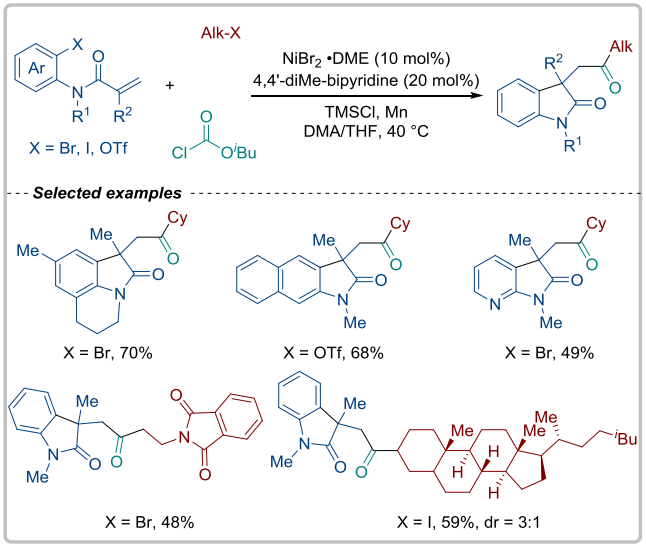


4. Construction of C_{sp3}-C_{sp2} Bonds and C_{sp3}-C_{sp2} Bonds by Ni-catalyzed Dicarbofunctionalization of Alkenes

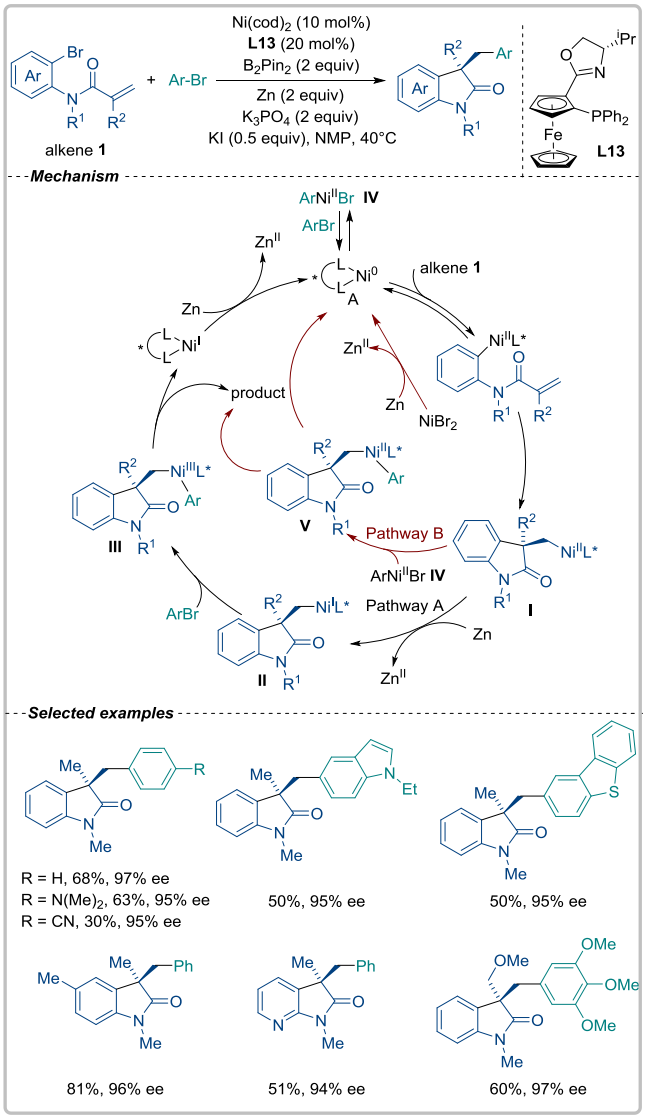
In 2019, Kong and co-workers described a nickel-catalyzed three-component reductive arylacylation of alkenes using readily available *N*-aryl acrylamides, isobutyl chloroformate as a CO source, and alkyl halides as electrophiles (Scheme 22).[49] This transformation facilitates the effective and rapid construction of 3,3-disubstituted oxindoles. The crucial advantage of this methodology is that it avoids using toxic CO gas or metal carbonyl reagents, making it safer and better for the environment. Additionally, the process works well with a wide range of substrates, including primary, secondary, and complex alkyl halides, as well as benzyl and cholesterol-derived compounds.

In 2018, Kong group developed an enantioselective reductive diarylation of *N*-aryl acrylamides with aryl bromides as coupling

Scheme 22 Ni-catalyzed reductive arylacylation of alkenes toward oxindoles



Scheme 23 Ni-catalyzed two-component asymmetric reductive diarylation of activated alkenes by domino cyclization/cross-coupling



partners (Scheme 23).[50] The methodology provided access to

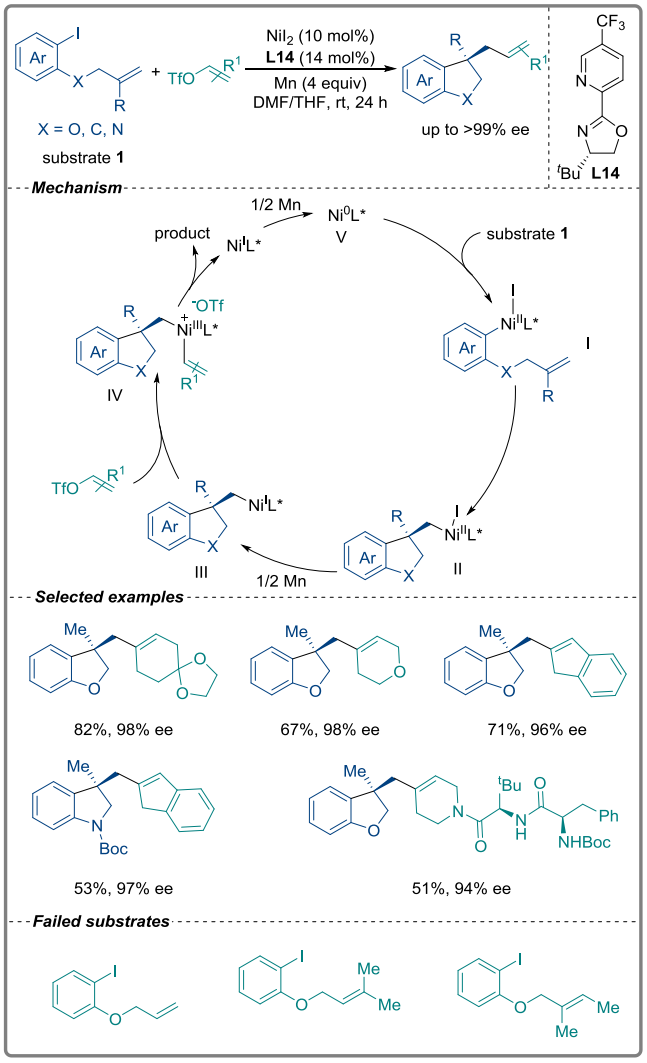
indolinone derivatives containing all-carbon quaternary centers with excellent yields and high levels of enantioselectivity. This method works under mild conditions and tolerates a wide range of functional groups and substrates, making it an efficient way to access oxindole and azaoxindole structures, which are important in pharmaceutical chemistry. Importantly, the reaction avoids the use of preformed organometallic reagents. Mechanistic studies revealed that the catalytic reaction involves a σ-alkyl-Ni(II) complex formed through oxidative addition and migratory insertion, while ruling out arylzinc and arylboronate pathways and suggesting the enantioselective step likely happens during the irreversible migratory insertion. The reaction likely occurs through two distinct pathways: In path A, the *in situ* generated Ni^0 species undergoes oxidative addition with alkene **1**, followed by intramolecular migratory insertion to form a $Ni^{II}X$ species **I**. This species undergoes reduction by Zn/Pin_2B_2 to produce a Ni^I intermediate **II**, which, upon further oxidative addition with aryl bromide, followed by the reductive elimination, yields the target product while regenerating the Ni^0 catalyst. In path B, $Ni^{II}X$ species **I** and **IV** undergo transmetalation to form a $Ni^{II}ArX$ species **V**, which subsequently undergoes reductive elimination to furnish the desired product. The group later explored the scope of enantioselective reductive difunctionalization by replacing aryl bromides with alkenyl bromides, alkynyl bromides, alkenes, and alkenyl fluorides, utilizing different Ni/chiral ligand catalytic systems, thereby allowing for the construction of various types of C_{sp3}-C_{sp2} and C_{sp3}-C_{sp2} bonds in a modular fashion.[51-53] Notably, this catalytic system was also applied to the arylcyanation of alkenes using *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS) as a cyanating reagent to construct C_{sp^3}-C_{sp^2} and C_{sp^3}-C_{sp} bonds.[54]

In 2019, Shu and co-workers disclosed an enantioselective cross-electrophilic aryl-alkenylation of unactivated alkenes with alkenyl triflates using NiI_2 as the catalyst, Mn as the reductant, and pyrox as the chiral ligand (Scheme 24).[55] This method provides access to various biologically active chiral molecules, including dihydrobenzofurans, indolines, and indanes, with high levels of enantioselectivity. The protocol shows a wide substrate scope and was found compatible with a broad range of substrates, including alkenes, aryl iodides, and alkenyl triflates. Remarkably, the synthetic utility was further demonstrated by successful late-stage modifications of complex bioactive molecules, such as peptides, indomethacin, and steroids. Moreover, mechanistic studies supported by control experiments revealed that the reaction occurs through initial oxidative addition of Ar–I to Ni(0), followed by intramolecular migratory insertion and reductive coupling with alkenyl triflate, rather than activation of the alkenyl–OTf.

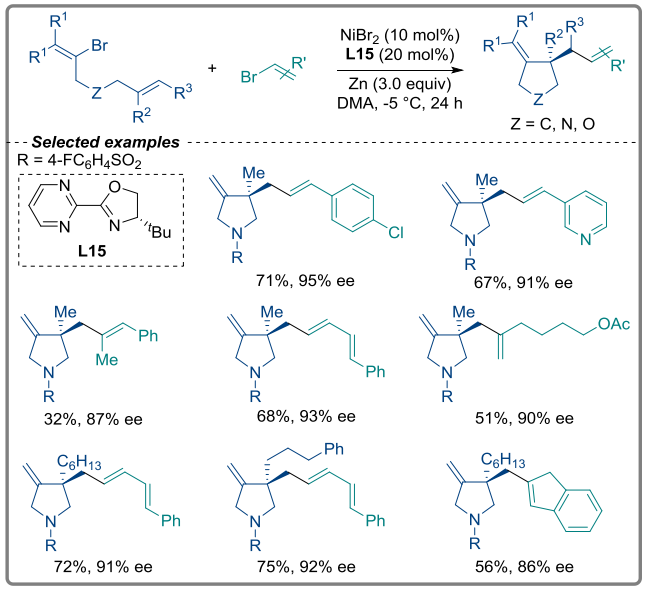
Later in 2021, Shu group introduced a modified nickel-catalyzed strategy by replacing the chiral pyrox-ligand with *t*-Bu-pmrox, thereby achieving an efficient reductive cyclization/vinylation of 2-bromo-1,6-dienes with bromoalkenes (Scheme 25).[56] This represented the first example of reductive asymmetric divinylation of unactivated alkenes, enabling the effective construction of a variety of enantioenriched 5-membered carbocycles and heterocycles. The reaction exhibits high levels of diastereo- and enantioselectivity under mild reaction conditions. The method provides a new way to synthesize novel chiral cyclic compounds.

The three-component cross-coupling strategy has become an effective way to construct C_{sp3}-C_{sp2} and C_{sp3}-C_{sp2} bonds with high efficiency and selectivity. In 2019, Diao and co-workers devised a nickel-catalyzed approach for the asymmetric diarylation of styrenes. The reaction facilitates the efficient construction of chiral α,α,β-triaryl ethane frameworks, commonly found in bioactive molecules and natural products (Scheme 26).[57] This method proceeds under operationally simple conditions, exhibits wide substrate scope and high functional group tolerance. Remarkably, the enantioselectivity of this transformation was highly influenced by the size and electronic nature of the *N*-oxyl radical additives,

Scheme 24 Ni-catalyzed two-component enantioselective reductive arylalkenylation of unactivated alkenes



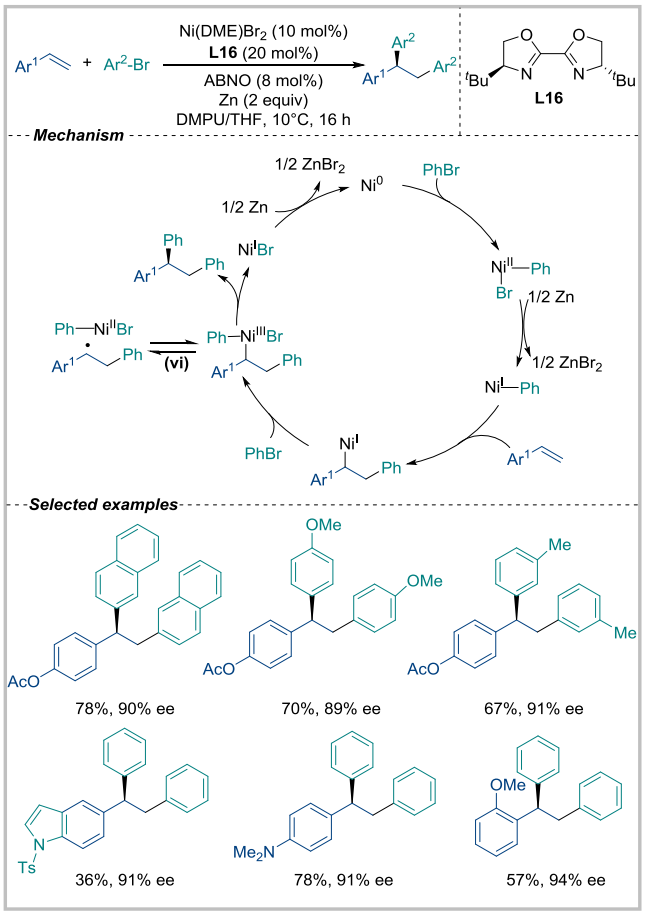
Scheme 25 Ni-catalyzed enantioselective reductive divinylation of unactivated alkenes



with a multivariate analysis showing a strong link between enan-

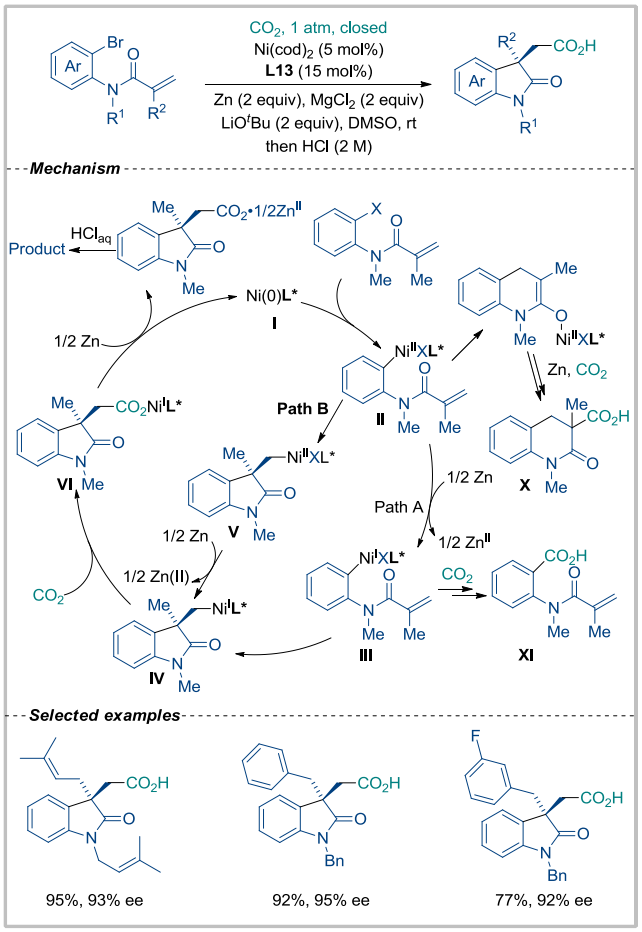
tioselectivity and steric factors, highlighting ABNO's (9-azabicyclo-[3.3.1]nonan-3-one *N*-oxyl) important role as a key ligand-like additive in the catalytic cycle. The reaction mechanism likely occurs via a radical pathway involving benzylic intermediates and 1 : 1 Ni/ligand ratio in the enantio-determining step.

Scheme 26 Ni-catalyzed asymmetric reductive homo-diarylation of styrenes



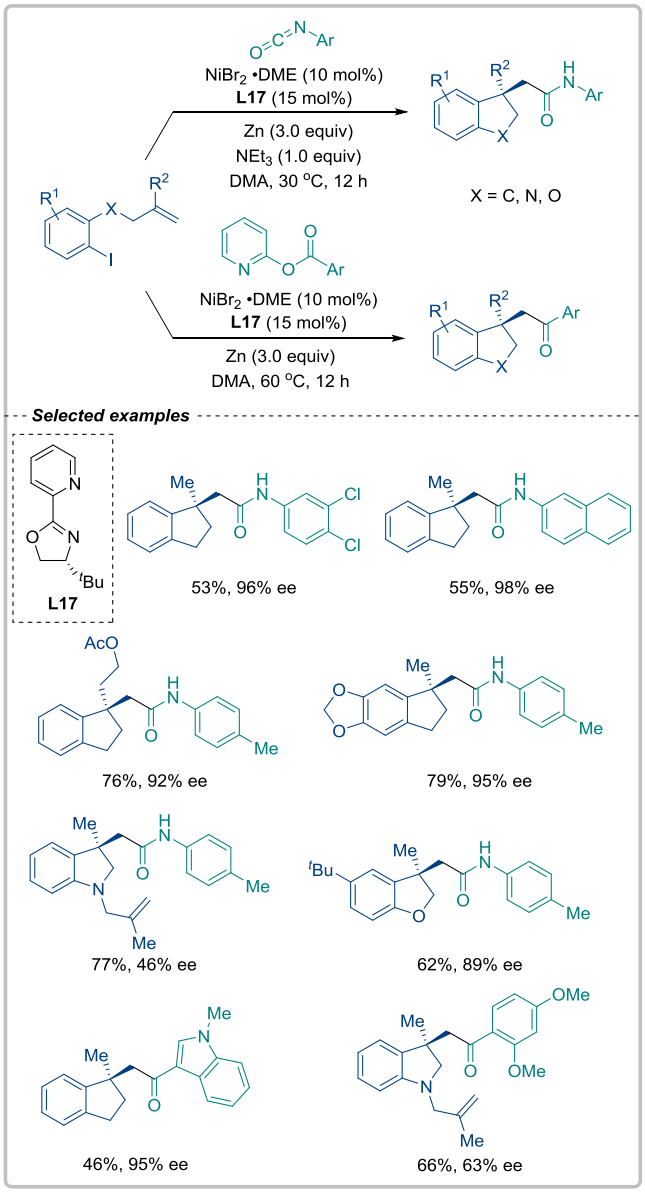
Although there has been recent progress in nickel catalysis, the reductive carbo-carboxylation of alkenes using CO_2 remains a tough challenge in synthesis. Most existing methods depend on stoichiometric organometallic reagents or focus on non-enantioselective processes, and Ni-catalyzed enantioselective CO_2 incorporation into unsaturated hydrocarbons is still largely unexplored. In 2021, Kong, Yu and co-workers, discovered a nickel-catalyzed methodology for asymmetric reductive carbo-carboxylation of alkenes using CO_2 (Scheme 27).[58] This approach allows for easy access to valuable oxindole-3-acetic acid derivatives. The reaction tolerates a wide array of substrates, including various substituted *N*-aryl acrylamides and aryl (pseudo)halides, with excellent chemo-, regio-, and enantioselectivity. The strategy shows its further utility by transforming a wide range of products into various chiral natural products, such as (−)-Debromoflustramine B and (+)-Coixspirolactam A. The reaction mechanism supported by control experiments suggested that the pathway begins with the oxidative addition of aryl halide to Ni^0 species, generating Ar-$Ni^{II}L^*$, which undergoes single-electron reduction by Zn to produce Ar-$Ni^{I}L^*$ intermediate **IV**. Subsequently, intermediate **IV** undergoes nucleophilic attack on CO_2 to form Ar-Ni^{I} carboxylate **VI**, which is further reduced and transmetalated to yield carboxylate **VII** and regenerates the reactive Ni^0L^***I**. Finally, hydrolysis yields the target product. Meanwhile, Ar-$Ni^{II}L^*$ **II** undergoes 6-endo cyclization to form byproduct **X**, and Ar-$Ni^{I}L^*$ **III** undergoes carboxylation by CO_2 to yield byproduct **XI**. In the same year, the Bandini group reported a nickel-catalyzed enantioselective CO_2 fixation approach by utilizing pyridyl imidazolines as chiral ligands and alkyl-substituted alkenes as substrates, achieving an elegant Heck-type coupling/carboxylation cascade reaction. This method allows for direct access to a series of benzofuran-3-ylacetic acid compounds with high levels of enantioselectivity.[59] The work signifies an important milestone in asymmetric CO_2 utilisation and provides a rare example of enantioselective carboxylation by a cascade radical-polar crossover strategy, entailing an excellent pathway for the construction of chiral carboxylic acid frameworks from simple starting materials.

Scheme 27 Ni-catalyzed asymmetric reductive arylcarboxylation of alkenes with carbon dioxide

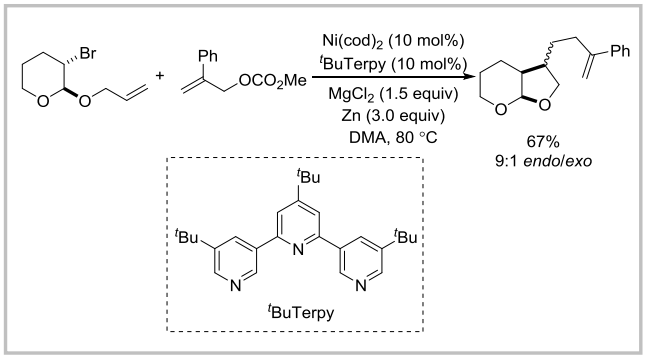


In 2022, Wang group reported a nickel-catalyzed asymmetric two-component reductive aryl-acylation and aryl-carbamoylation of unactivated alkenes.[60] This method employs *ortho*-iodoaryl-tethered unactivated alkenes as substrates and utilizes either *ortho*-pyridinyl esters or isocyanates as electrophilic acyl or carbamoyl source, respectively. Using Ni(II)/Pyrox complex as catalyst under mild conditions, the reaction efficiently constructs chiral indanes, indolines, and dihydrobenzofurans bearing a quaternary stereogenic center. The process demonstrates broad substrate scope, accommodating various electron-donating and electron-withdrawing substituents on both the aryl iodide and the acyl/carbamoyl coupling partners, including esters and nitriles. Excellent enantioselectivities were achieved alongside moderate to high yields. This strategy offers significant advantages over previous methods by avoiding preformed organometallics, toxic carbon monoxide gas, strong bases, enabling direct access to enantioenriched carbonyl-containing cyclic scaffolds. The synthetic utility was further highlighted through diverse derivatizations of the products.

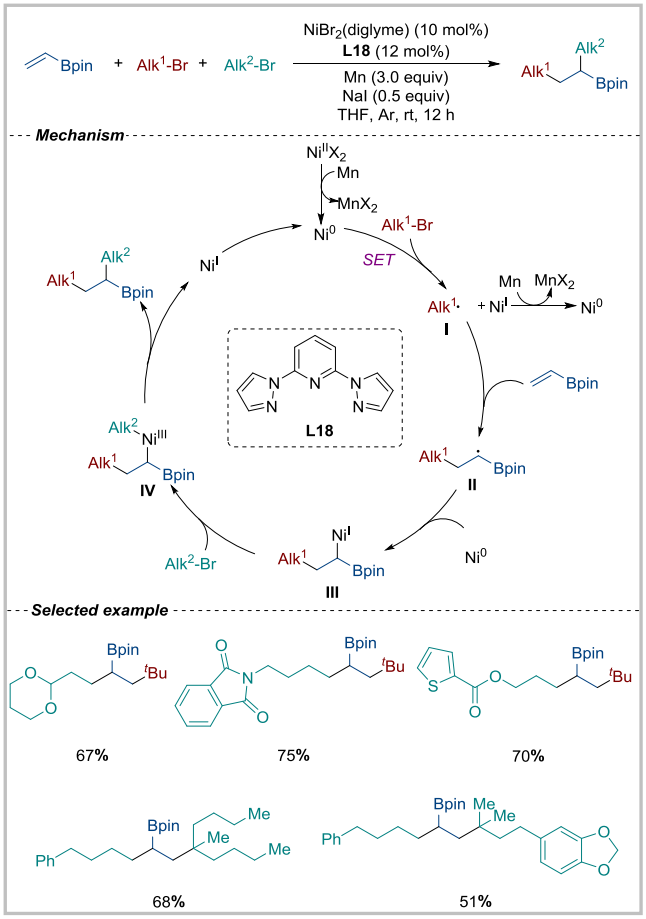
Scheme 28 Ni-catalyzed two-component asymmetric reductive aryl-acylation and aryl-carbamoylation of alkenes



Scheme 29 Ni-catalyzed two-component reductive dialkylation of alkenes



Scheme 30 Ni-catalyzed three-component reductive dialkylation of vinyl boronates



5. Construction of C_{sp3}-C_{sp3} Bonds and C_{sp3}-C_{sp3} Bonds by Ni-catalyzed Dicarbofunctionalization of Alkenes

The construction of dual C_{sp3}–C_{sp3} bonds *via* nickel-catalyzed dialkylation of alkenes remains a significant challenge in cross-coupling chemistry, primarily due to two intrinsic limitations: (1) the relatively low reactivity of alkyl halides in oxidative addition to nickel centers compared to their aryl or alkenyl counterparts, and (2) the propensity of alkylnickel intermediates to undergo β-hydride elimination, leading to undesired side reactions. Despite these inherent difficulties, recent advances have demonstrated that judicious selection of alkyl halide substrates, particularly through the pairing of differentially reactive partners (*e.g.*, tertiary versus primary alkyl halides), can effectively overcome these limitations.

In 2012, Gong group reported a nickel-catalyzed two-component dialkylation of alkenes by cyclization/alkyl-alkyl coupling process (Scheme 29).[61] The reaction employed a terpyridine derivative as ligand. One example was demonstrated for the synthesis of fused scaffolds by constructing two alkyl-alkyl bonds over the double bond of alkenes.

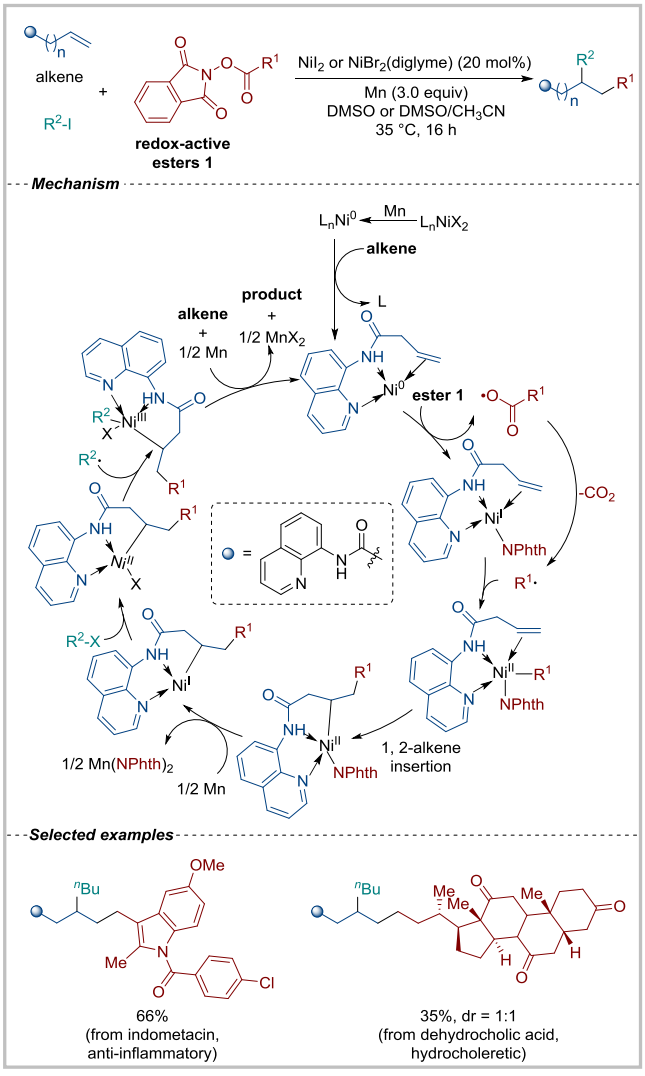
In 2020, Fu and co-workers devised a nickel-catalyzed three-component reductive dicarbofunctionalization of alkenes for the construction of alkyl borates using alkyl bromides as coupling reagents (Scheme 30).[62] The method under mild reductive conditions demonstrated the wide substrate scope and high chemoselectivity, accommodating a variety of functional groups, such as esters, halides, and heterocycles. The method was successfully applied to the late-stage functionalization of complex molecules such as glucose, indomethacin, and oleic acid derivatives. The mechanistic studies supported by competitive and radical clock experiments revealed that the reaction favors a single-electron transfer (SET) pathway for alkyl bromide activation, in which electron-deficient olefins showed greater reactivity, while tertiary alkyl bromides exhibited increased efficiency for radical addition. Additionally, the control experiment involving the use of TDAE, a

non-metal reductant, instead of Mn^0 suggested that the activation of alkyl bromides takes place by single-electron transfer (SET) rather than the *in-situ* formation of alkyl manganese reagents. Based on these observations, a plausible reaction mechanism was proposed: initially, Ni^0 and the more reactive tertiary alkyl bromide undergo a single-electron transfer to form the tertiary alkyl radical I. This radical I undergoes Giese-type addition to the electron-deficient alkene to form the stabilized secondary alkyl radical II, which is subsequently intercepted by the Ni catalyst. Finally, reductive elimination furnishes the desired target product and regenerates the Ni^0 species.

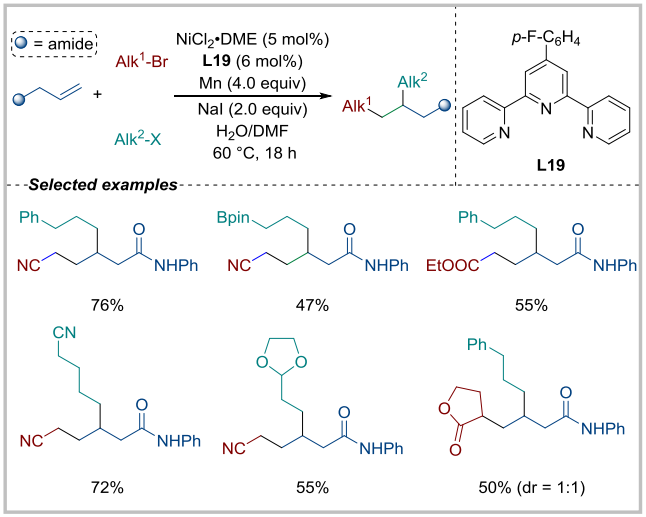
In the same year, Koh and co-workers described a Ni-catalyzed three-component strategy for regioselective dialkylation of unactivated alkenes with organohalides and redox-active esters. The reaction under mild conditions facilitates the effective construction of two different C_{sp3}-C_{sp3} bonds in a modular fashion (Scheme 31).[63] This protocol shows applicability to a wide range of substrates and excellent functional group tolerance with high levels of regioselectivity. Moreover, it accommodates a variety of aliphatic redox-active esters and alkyl iodides in combination with alkenyl amides, even when the substrates have sensitive motifs or complex molecular structures. A notable feature of this methodology is its high regioselectivity, which is ascribed to the orthogonal reactivity of the electrophiles where NHP esters tend to add to the Ni^0 center through a single-electron transfer (SET) process, forming alkyl–Ni(I) species, while the organohalide partner follows a different reaction path. Remarkably, the synthetic utility of this approach was further explored by the successful late-stage modification of drug molecules and natural products.

In 2022, Shu and co-workers developed a modular strategy for reductive 1,2-cross-dialkylation of unactivated aliphatic alkenes *via* nickel-catalysis (Scheme 32).[64] The method employs two distinct alkyl bromides under mild conditions to enable the effective construction of C_{sp3}-C_{sp3} bonds with excellent chemo- and regioselectivity. A notable feature of this methodology is that it avoids the use of preformed alkyl nucleophiles, thus improving the substrate scope and functional group tolerance. Significantly, this approach was further applied to its successful late-stage modifications of some complex molecules, such as menthol- and (+)-borneol-derived alkyl bromides, highlighting the synthetic utility of this protocol. Mechanistic studies supported by radical clock and inhibition experiments revealed that the reaction likely proceeds through a single-electron transfer (SET) process, wherein Ni^0 facilitates the formation of alkyl radicals, followed by sequential addition and coupling steps to yield the final product. The strategy considerably widens the avenues for alkene dicarbofunctionalization by tackling major issues posed by the construction of C_{sp^3}–C_{sp^3} bonds and opening other new possibilities for the expedient assembly of complex molecular scaffolds.

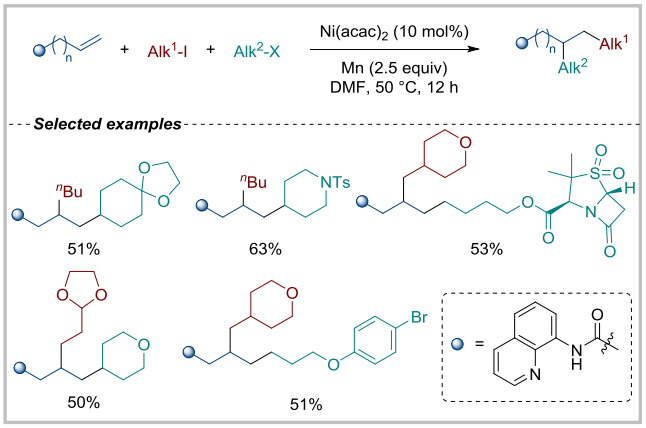
Scheme 31 Ni-catalyzed reductive dialkylation of unactivated alkenes with electrophilic NHPI esters and haloalkanes



Scheme 32 Ni-catalyzed reductive 1,2-cross-dialkylation of unactivated alkenes



Scheme 33 Ni-catalyzed reductive cross-dialkylation of alkenes with unactivated alkyl electrophiles



Recently, Yang and co-workers developed a new method for the reductive cross-dialkylation of aliphatic alkenes using two

unactivated electrophiles (Scheme 33).[65] This nickel-catalyzed reaction uses primary alkyl (pseudo)halides and secondary alkyl iodides as coupling partners under mild conditions, allowing for the efficient formation of two C_{sp3}-C_{sp3} bonds. The reaction shows compatibility with a numerous variety of substrates and exhibits high tolerance to different functional groups with excellent regioselectivity. The synthetic utility of this method was further demonstrated by its application in the late-stage modification of complex molecules and the easy synthesis of bioactive intermediates.

6. Conclusions and Perspectives

Ni-catalyzed reductive dicarbofunctionalizations of alkenes represent a dynamic area for the construction of sp^3-rich architectures from readily available and cost-effective electrophiles with alkenes. This reaction mode circumvents the use of stoichiometric organometallic species, which has the advantage of operational simplicity, easy availability, cost-effectiveness, and broad functional group tolerance.

This review summarizes recent progress in nickel-catalyzed reductive dicarbofunctionalization of alkenes by forging two saturated carbon-carbon bonds. Diverse dicarbofunctionalizations, such as diarylation, dialkylation, alkylarylation, acylalkylation, acylarylation, acylcarbamoylation, deliver a wide range of sp^3-rich structures from alkenes in a single step, which highlights the profound potential of reaction mode for organic synthesis and further applications. However, significant limitations and challenges remain with this reaction mode. First, most studies are focused on intramolecular dicarbofunctionalizations of alkenes; intermolecular versions of this reaction mode are less explored, particularly for non-directed unactivated alkenes. Second, asymmetric dicarbofunctionalizations of alkenes still remain challenging. Only asymmetric arylation/acylation reactions were realized with limited scope. Other types of asymmetric dicarbofunctionalization reactions of alkenes remain unsolved. Moreover, three-component asymmetric dicarbofunctionalizations of alkenes are also challenging. Third, the types of carbo-coupling partners are still limited.

Further efforts in this area should be made in the following directions to develop more general dicarbofunctionalization protocols of alkenes. First, Ni-catalyzed asymmetric dicarbofunctionalizations of alkenes should be designed to forge tertiary and quaternary stereogenic carbon centers with different substitution patterns. Second, the combination of visible-light catalysis, electrochemical catalysis, and cooperative catalysis with Ni-catalysis will offer new chemical space for reductive dicarbofunctionalizations of alkenes. Moreover, further insights into the reaction mechanisms using computational studies, crystallography, and experimental investigations may provide a better understanding of the reaction mechanism and further enhance reaction design and discovery for new Ni-catalyzed reductive dicarbofunctionalizations of alkenes. We anticipate that the Ni-catalyzed reductive dicarbofunctionalizations of alkenes will expand the synthetic toolbox for alkene transformations and provide complementary strategies for organic synthesis, medicinal chemistry, and material sciences.

Acknowledgement

Financial support from National Natural Science Foundation of China (22171127, 22371115, and 22373056), Natural Science Foundation of Sichuan Province (25NSFSC2247), Sichuan Science and Technology Program (2024ZYD0017), Shenzhen Science and Technology Innovation Committee (JCYJ20240813094226034, JCYJ20230807093522044), the Pearl River Talent Recruitment Program (2019QN01Y261), Guangdong Provincial Key Laboratory of Catalysis (2020B121201002), Scientific Research and Innovation Team Program of Sichuan University of Science and Engineering (No. SUSE652A014), and the Innovation Fund of Postgraduate from Sichuan University of Science & Engineering (Y2024079, Y2024087) is thanked. This research is supported by the SUSTech-NUS Joint Research Program. We acknowledge the assistance of the SUSTech Core Research Facilities.

References

[1] (a) Heck, R. F.; Nolley, J. P. Palladium-catalyzed vinylic hydrogen substitution reactions with aryl, benzyl, and styryl halides. *J. Org. Chem.* **1972**, *37*, 2320–2322; (b) Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.-i.; Nakajima, I.; Minato, A.; Kumada, M. Nickel-phosphine complex-catalyzed Grignard coupling. I. cross-coupling of alkyl, aryl, and alkenyl Grignard reagents with aryl and alkenyl halides: general scope and limitations. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958–1969; (c) Baba, S.; Negishi, E. A novel stereospecific alkenyl-alkenyl cross-coupling by a palladium- or nickel-catalyzed reaction of alkenylalanes with alkenyl halides. *J. Am. Chem. Soc.* **1976**, *98*, 6729–6731; (d) Milstein, D.; Stille, J. K. Palladium-catalyzed coupling of tetraorganotin compounds with aryl and benzyl halides. synthetic utility and mechanism. *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998; (e) Ren, Y.-F.; Chen, B.-H.; Chen, X.-Y.; Du, H.-W.; Li, Y.-L.; Shu, W. Direct synthesis of branched amines enabled by dual-catalyzed allylic C–H amination of alkenes with amines. *Sci. Adv.* **2024**, *10*, eadn1272; (f) Wang, Y.; Meng, H.; Li, S.-F.; Shu, W. Nitrogenation and oxygenation of an unstrained C–C bond enabled by the merger of visible-light and Cu-catalysis. *ACS Catal.* **2024**, *14*, 2402–2408; (g) Wang, S.; Shi, L.; Chen, X.-Y.; Shu, W. Catalyst-controlled regiodivergent and enantioselective formal hydroamination of *N*,*N*-disubstituted acrylamides to α-tertiary-α-aminolactam and β-aminoamide derivatives. *Angew. Chem. Int. Ed.* **2023**, *62*, e202303795; (h) Wang, S.; Zhang, J.-X.; Zhang, T.-Y.; Meng, H.; Chen, B.-H.; Shu, W. Enantioselective access to chiral aliphatic amines and alcohols via Ni-catalyzed hydroalkylations. *Nat. Commun.* **2021**, *12*, 2771; (i) Yang, P.-F.; Zhu, L.; Liang, J.-X.; Zhao, H.-T.; Zhang, J.-X.; Zeng, X.-W.; Ouyang, Q.; Shu, W. Regio- and enantioselective hydroalkylations of unactivated olefins enabled by nickel catalysis: reaction development and mechanistic insights. *ACS Catal.* **2022**, *12*, 5795–5805; (j) Yang, P.-F.; Shu, W. Orthogonal access to α-/β-branched/linear aliphatic amines by catalyst-tuned regiodivergent hydroalkylations. *Angew. Chem. Int. Ed.* **2022**, *61*, e202208018; (k) Zhang, J.-X.; Yang, P.-F.; Shu, W. Access to dialkylated allylic stereogenic centers by Ni-catalysed enantioselective hydrovinylation of unactivated alkenes. *Chem. Sci.* **2022**, *13*, 11405–11410; (l) Zhao, W.-T.; Zhang, J.-X.; Chen, B.-H.; Shu, W. Ligand-enabled Ni-catalysed enantioconvergent intermolecular alkyl-alkyl cross-coupling between distinct alkyl halides. *Nat. Commun.* **2023**, *14*, 2398; (m) Zeng, X.-W.; Lin, J.-N.; Shu, W. Hydrogen source tuned regiodivergent asymmetric hydroalkylations of 2-substituted 1,3-dienes with aldehydes by cobalt-catalysis. *Angew. Chem. Int. Ed.* **2024**, *63*, e202403073; (n) Zhao, W.-T.; Shu, W. Enantioselective C_{sp3}-C_{sp3} formation by nickel-catalyzed enantioconvergent cross-electrophile alkyl-alkyl coupling of unactivated alkyl halides. *Sci. Adv.* **2023**, *9*, eadg9898; (o) Liu, M.-S.; Min, L.; Chen, B.-H.; Shu, W. Dual catalysis relay: coupling of aldehydes and alkenes enabled by visible-light and NHC-catalyzed cross-double C-H functionalizations. *ACS Catal.* **2021**, *11*, 9715–9721; (p) Shi, L.; Xing, L.-L.; Hu, W.-B.; Shu, W. Regio- and enantioselective Ni-catalyzed formal hydroalkylation, hydrobenzylation, and hydropropargylation of acrylamides to α-tertiary amides. *Angew. Chem. Int. Ed.* **2021**, *60*, 1599–1604.

[2] (a) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. Cascade reactions in total synthesis. *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186; (b) Touré, B. B.; Hall, D. G. Natural product synthesis using multicomponent reaction strategies. *Chem. Rev.* **2009**, *109*, 4439–4486; (c) Ruijter, E.; Scheffelaar, R.; Orru, R. V. A. Multicomponent reaction design in the quest for molecular complexity and diversity. *Angew. Chem. Int. Ed.* **2011**, *50*, 6234–6246; (d) Plesniak, M. P.; Huang, H.-M.; Procter, D. J.

Radical cascade reactions triggered by single electron transfer. *Nat. Rev. Chem.* **2017**, *1*, 1–16; (e) Zhan, Y.-Z.; Xiao, N.; Shu, W. Ni-catalyzed regio- and stereo-defined intermolecular cross-electrophile dialkylation of alkynes without directing group. *Nat. Commun.* **2021**, *12*, 928; (f) Du, Y.-M.; Chen, X.-Y.; Li, Y.-L.; Koh, M. J.; Shu, W. Rapid assembly of enantioenriched α-arylated ketones via Ni-catalyzed asymmetric cross-hydrocarbonylation enabled by alkene sorting. *Nat. Commun.* **2025**, *16*, 4163; (g) Du, Y.-M.; Lin, J.-N.; Li, Y.-L.; Yu, Q.; Shu, W. Nickel-catalyzed adaptive migration-enabled asymmetric cross-hydrocarbonylation of unactivated alkenes. *J. Am. Chem. Soc.* **2025**, *147*, 18944–18952; (h) Chen, X.-Y.; Yu, Q.; Shu, W. Synthesis of α-*N*-heteroaryl ketones by nickel-catalyzed chemo-, regio- and enantioselective carbonylation of alkenes and *N*-alkenyl heteroarenes. *Angew. Chem. Int. Ed.* **2025**, *63*, e202423426.

[3] (a) Mc Donald, R. I.; Liu, G.; Stahl, S. S. Palladium(II)-catalyzed alkene functionalization via nucleopalladation: stereochemical pathways and enantioselective catalytic applications. *Chem. Rev*. **2011**, *111*, 2981–3019; (b) Chatterjee, T.; Iqbal, N.; You, Y.; Cho, E. J. Controlled fluoroalkylation reactions by visible-light photoredox catalysis. *Acc. Chem. Res.* **2016**, *49*, 2284–2294; (c) Koike, T.; Akita, M. New horizons of photocatalytic fluoromethylative difunctionalization of alkenes. *Chem* **2018**, *4*, 409–437; (d) Lin, J.; Song, R.-J.; Hu, M.; Li, J.-H. Recent advances in the intermolecular oxidative difunctionalization of alkenes. *Chem. Rec.* **2019**, *19*, 440–451; (e) Diccianni, J.; Lin, Q.; Diao, T.-N. Mechanisms of nickel-catalyzed coupling reactions and applications in alkene functionalization. *Acc. Chem. Res*. **2020**, *53*, 906–919; (f) Tu, H.-Y.; Zhu, S.-Q.; Qing, F.-L.; Chu, L.-L. Recent advances in nickel-catalyzed three-component difunctionalization of unactivated alkenes. *Synthesis* **2020**, *52*, 1346–1356; (g) Ping, Y.-Y.; Kong, W.-Q. Ni-catalyzed reductive difunctionalization of alkenes. *Synthesis* **2020**, *52*, 979–992; (h) Huang, B.-B.; Sun, Z.-M.; Sun, G.-B. Recent progress in cathodic reduction-enabled organic electrosynthesis: Trends, challenges, and opportunities. *eScience* **2022**, *2*, 243–277; (i) Ping, Y.-Y.; Song, H.-X.; Kong, W.-Q. Recent advances in Ni-catalyzed asymmetric reductive difunctionalization of alkenes. *Chin. J. Org. Chem.* **2022**, *42*, 3302–3321; (j) Zeng, Y.; Zhao, M.-T.; Zeng, H.-L.; Jiang, Q.; Ming, F.-W.; Xi, K.; Wang, Z.-C.; Liang, H.-F. Recent progress in cathodic reduction-enabled organic electrosynthesis: Trends, challenges, and opportunities. *eScience* **2023**, *3*, 100156. (k) Pan, Q.; Ping, Y.-Y.; Kong, W.-Q. Nickel-catalyzed ligand-controlled selective reductive cyclization/cross-couplings. *Acc. Chem. Res.* **2023**, *56*, 515–535; (l) Zhao, H.-T.; Lin, J.-N.; Shu, W. Visible-light mediated nickel-catalyzed asymmetric difunctionalizations of alkenes. *Chem. Eur. J.* **2024**, *30*, e202402712.

[4] (a) Knappke, C. E. I.; Grupe, S.; Gärtner, D.; Corpet, M.; Gosmini, C.; Wangelin, A. J. Reductive cross-coupling reactions between two electrophiles. *Chem. Eur. J.* **2014**, *20*, 6828–6842; (b) Weix, D. J. Methods and mechanisms for cross-electrophile coupling of Csp^2 halides with alkyl electrophiles. *Acc. Chem. Res*. **2015**, *48*, 1767–1775; (c) Liu, J.; Ye, Y.; Sessler, J. L.; Gong, H. Cross-electrophile coupling of activated and sterically hindered alkyl halides and C-O bonds. *Acc. Chem. Res.* **2020**, *53*, 1833–1845; (d) Xue, W.; Jia, X.; Wang, X.; Yin, Z.; Gong, H. Nickel-catalyzed all-carbon quaternary centers formation with tertiary alkyl electrophiles. *Chem. Soc. Rev.* **2021**, *50*, 4162–4184; (e) Ehehalt, L. E.; Beleh, O. M.; Priest, I. C.; Mouat, J. M.; Olszewski, A. K.; Ahern, B. N.; Cruz, A. R.; Chi, B. K.; Castro, A. J.; Kang, K.; Wang, J.; Weix, D. J. Cross-electrophile coupling: principles, methods, and applications in synthesis. *Chem. Rev*. **2024**, *124*, 13397–13569; (f) You, L.-X.; Tian, L.; Guo, C.-L.; Li, S.-Y.; Liu, Y.-C.; Li, Y.-L.; Shu, W. Ni-catalyzed cross-electrophile alkyl-alkyl Coupling Reactions. *Sci. China Chem.* **2025**, *68*, doi: 10.1007/s11426–024–2438-x.

[5] (a) Trejos, A.; Fardost, A.; Yahiaoui, S.; Larhed, M. Palladium(II)-catalyzed coupling reactions with a chelating vinyl ether and arylboronic acids: a new Heck/Suzuki domino diarylation reaction. *Chem. Commun.* **2009**, *2009*, 7587–7589; (b) Yahiaoui, S.; Fardost, A.; Trejos, A.; Larhed, M. Chelation-mediated palladium(II)-catalyzed domino Heck-Mizoroki/Suzuki-Miyaura reactions using arylboronic acids: increasing scope and mechanistic understanding. *J. Org. Chem.* **2011**, *76*, 2433–2438; (c) Urkalan, K. B.; Sigman, M. S. Palladium-catalyzed oxidative intermolecular difunctionalization of terminal alkenes with organostannanes and molecular oxygen. *Angew. Chem. Int. Ed.* **2009**, *48*, 3146–3149; (d) Kusunuru, A. K.; Jaladanki, C. K.; Tatina, M. B.; Bharatam, P. V.; Mukherjee, D. TEMPO-promoted domino Heck-Suzuki arylation: diastereoselective *cis*-diarylation of glycals and pseudoglycals. *Org. Lett.* **2015**, *17*, 3742–3745.

[6] (a) Batsanov, S. S. Van der waals radii of elements. *Inorg. Mater.* **2001**, *37*, 871–885; (b) Mann, J. B.; Meek, T. L.; Knight, E. T.; Capitani, J. F.; Allen, L. C. Configuration energies of the *d*-block elements. *J. Am. Chem. Soc.* **2000**, *122*, 5132–5137; (c) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. Recent advances in homogeneous nickel catalysis. *Nature* **2014**, *509*, 299–309; (d) Poremba, K. E.; Dibrell, S. E.; Reisman, S. E. Nickel-catalyzed enantioselective reductive cross-coupling reactions. *ACS Catal*. **2020**, *10*, 8237–8246; (e) Yang, P.-F.; Liang, J.-X.; Zhao, H.-T.; Shu, W. Access to enantioenriched 1,*n*-diamines via Ni-catalyzed hydroamination of unactivated alkenes with weakly coordinating groups. *ACS Catal*. **2022**, *12*, 9638–9645; (f) Ke, Y.; Li, W.; Liu, W.-F.; Kong, W.-Q. Ni-catalyzed ligand-controlled divergent and selective synthesis. *Sci. China Chem*. **2023**, *66*, 2951–2976; (g) Zhao, W.-T.; Meng, H.; Lin, J.-N.; Shu, W. Ligand-controlled nickel-catalyzed regiodivergent cross-electrophile alkyl-alkyl couplings of alkyl halides. *Angew. Chem. Int. Ed.* **2023**, *62*, e202215779; (h) Liu, M.-S.; Shu, W. Rapid synthesis of β-chiral sulfones by Ni-organophotocatalyzed enantioselective sulfonylalkenylation of alkenes. *JACS Au* **2023**, *3*, 1321–1327; (i) Yang, P.-F.; Zhao, H.-T.; Chen, X.-Y.; Shu, W. Enantioselective alkyl–alkyl coupling by Ni-catalysed asymmetric cross-hydrodimerization of alkenes. *Nat. Synth.* **2024**, *3*, 1360–1368; (j) Zi, Q.-X.; Shu, W. Asymmetric synthesis of dialkyl carbinols by Ni-catalyzed reductive-oxidative relay of distinct alkenes. *Adv. Sci.* **2024**, *11*, 202409592; (k) Zou, J.-Y.; Xing, F.-L.; Zi, Q.-X.; Du, H.-W.; Chen, M.; Shu, W. Asymmetric alkyl-alkyl coupling between electron-deficient and unactivated alkenes to access α-chiral phosphines by Ni catalysis. *Sci. Adv.* **2025**, *11*, eadv6571.

[7] (a) Dhungana, R. K.; Kc, S.; Basnet, P.; Giri, R. Transition metal-catalyzed dicarbofunctionalization of unactivated alkenes. *Chem. Rec.* **2018**, *18*, 1314–1340; (b) Giri, R.; Kc, S. Strategies toward dicarbofunctionalization of unactivated alkenes by combined Heck carbometalation and cross-coupling. *J. Org. Chem*. **2018**, *83*, 3013–3022; (c) Wickham, L. M.; Giri, R. Transition metal (Ni, Cu, Pd)-catalyzed alkene dicarbofunctionalization reactions. *Acc. Chem. Res*. **2021**, *54*, 3415–3437.

[8] (a) Badir, S. O.; Molander, G. A. Developments in photoredox/nickel dual-catalyzed 1,2-difunctionalizations. *Chem* **2020**, *6*, 1327–1339; (b) Derosa, J.; Apolinar, O.; Kang, T.; Tran, V. T.; Engle, K. M. Recent developments in nickel-catalyzed intermolecular dicarbofunctionalization of alkenes. *Chem. Sci.* **2020**, *11*, 4287–4296; (c) Luo, Y.-C.; Xu, C.; Zhang, X. Nickel-catalyzed dicarbofunctionalization of alkenes. *Chin. J. Chem.* **2020**, *38*, 1371–1394; (d) Qi, X.; Diao, T. Nickel-catalyzed dicarbofunctionalization of alkenes. *ACS Catal.* **2020**, *10*, 8542–8556; (e) Tu, H.-Y.; Zhu, S.; Qing, F.-L.; Chu, L. Recent advances in nickel-catalyzed three-component dicarbofunctionalization of unactivated alkenes. *Synthesis* **2020**, *52*, 1346–1356; (f) Zhu, S.; Zhao, X.; Li, H.; Chu, L. Catalytic three-component dicarbofunctionalization reactions involving radical capture by nickel. *Chem. Soc. Rev*. **2021**, *50*, 10836–10856.

[9] Yan, C.-S.; Peng, Y.; Xu, X.-B.; Wang, Y.-W. Nickel-mediated inter-and intramolecular reductive cross-coupling of unactivated alkyl bromides and aryl iodides at room temperature. *Chem. Eur. J*. **2012**, *18*, 6039–6048.

[10] Lu, W.-B.; Liang, Z.-Y.; Zhang, Y.-W.; Wu, F.; Qian, Q.; Gong, H.-G. Gram-scale ketone synthesis by direct reductive coupling of alkyl Iodides with acid chlorides. *Synthesis* **2013**, *45*, 2234–2240.

[11] Peng, Y.; Xu, X.-B.; Xiao, J.; Wang, Y.-W. Nickel-mediated stereocontrolled synthesis of spiroketals via tandem cyclization-coupling of β-bromo ketals and aryl iodides. *Chem. Commun.* **2014**, *50*, 472–474.

[12] (a) Peng, Y.; Xiao, J.; Xu, X.-B.; Duan, S.-M.; Ren, L.; Shao, Y.-L.; Wang,

Y.-W. Stereospecific synthesis of tetrahydronaphtho[2,3‐*b*]furans enabled by a nickel-promoted tandem reductive cyclization. *Org. Lett*. **2016**, *18*, 5170–5173; (b) Xiao, J.; Wang, Y.-W.; Peng, Y. Nickel-promoted reductive cyclization cascade: a short synthesis of a new aromatic strigolactone analogue. *Synthesis* **2017**, *49*, 3576–3581.

[13] (a) Xiao, J.; Cong, X.-W.; Yang, G.-Z.; Wang, Y.-W.; Peng, Y. Stereoselective synthesis of a podophyllum lignan core by intramolecular reductive nickel-catalysis. *Chem. Commun*. **2018**, *54*, 2040–2043; (b) Liu, Z.-H.; Xiao, J.; Zhai, Q.-Q.; Tang, X.; Xu, L.-J.; Zhuang, Z.-Y.; Wang, Y.-W.; Peng, Y. Intramolecular Ni-catalyzed reductive coupling enables enantiodivergent synthesis of linoxepin. *Chem. Commun*. **2024**, *60*, 694–697.

[14] (a) Kuang, Y.-L.; Wang, X.-F.; Anthony, D.; Diao, T.-N. Ni-catalyzed two-component reductive dicarbofunctionalization of alkenes via radical cyclization. *Chem. Commun.* **2018**, *54*, 2558–2561; (b) Lin, Q.; Diao, T.-N. Mechanism of Ni-catalyzed reductive 1,2-dicarbofunctionalization of alkenes. *J. Am. Chem. Soc.* **2019**, *141*, 17937–17948.

[15] García-Domínguez, A.; Li, Z.; Nevado, C. Nickel-catalyzed reductive dicarbofunctionalization of alkenes. *J. Am. Chem. Soc.* **2017**, *139*, 6835–6838.

[16] García-Domínguez, A.; Nevado, C. Transforming alkenes into dinucleophiles. *Chimia* **2018**, *72*, 212–215.

[17] Zhao, X.; Tu, H.-Y.; Guo, L.; Zhu, S.; Qing, F.-L.; Chu, L.-L. Intermolecular selective carboacylation of alkenes via nickel-catalyzed reductive radical relay. *Nat. Commun.* **2018**, *9*, 3488.

[18] Shu, W.; García-Domínguez, A.; Quirós, M. T.; Mondal, R.; Cárdenas, D. J.; Nevado, C. Ni-catalyzed reductive dicarbofunctionalization of nonactivated alkenes: scope and mechanistic insights. *J. Am. Chem. Soc.* **2019**, *141*, 13812–13821.

[19] Wang, L.; Wang, C. Nickel-catalyzed three-component reductive alkylacylation of electron-deficient activated alkenes. *Org. Lett.* **2020**, *22*, 8829–8835.

[20] Xi, X.-X; Chen, Y.-K.; Yuan, W.-M. Nickel-catalyzed three-component alkylacylation of alkenes enabled by a photoactive electron donor-acceptor complex. *Org. Lett.* **2022**, *24*, 3938–3943.

[21] Sun, S.-Z.; Duan, Y.; Mega, R. S.; Somerville, R. J.; Martin, R. Site-selective 1,2-dicarbofunctionalization of vinyl boronates through dual catalysis. *Angew. Chem. Int. Ed.* **2020**, *59*, 4370–4374.

[22] Wei, X.; Shu, W.; García-Domínguez, A.; Merino, E.; Nevado, C. Asymmetric Ni-catalyzed radical relayed reductive coupling. *J. Am. Chem. Soc.* **2020**, *142*, 13515–13522.

[23] Tu, H.-Y.; Wang, F.; Huo, L.-P.; Li, Y.-B.; Zhu, S.-Q.; Zhao, X.; Li, H.; Qing, F.-L.; Chu, L.-L. Enantioselective three-component fluoroalkylarylation of unactivated alkenes through nickel-catalyzed cross-electrophile coupling. *J. Am. Chem. Soc.* **2020**, *142*, 9604–9611.

[24] Qian, P.-C.; Guan, H.-X.; Wang, Y.-E.; Lu, Q.-Q.; Zhang, F.; Xiong, D.; Walsh, P. J.; Mao, J.-Y. Catalytic enantioselective reductive domino alkyl arylation of acrylates via nickel/photoredox catalysis. *Nat. Commun.* **2021**, *12*, 6613.

[25] Dey, P.; Jana, S. K.; Rai, P.; Maji, B. Dicarbofunctionalizations of an unactivated alkene via photoredox/nickel dual catalysis. *Org. Lett.* **2022**, *24*, 6261–6265.

[26] Lin, T.-Z.; Li, G.-R.; Lu, Q.-Q.; Zhang, C.; Wang, Y.-E.; Xing, F.; Xu, Y.-D.; Yang, K.; Xiong, D.; Xu, X.-F.; Walsh, P. J.; Mao, J.-Y. Enantioselective domino alkyl arylation of vinyl phosphonates by combining photoredox and nickel catalysis. *Green Synth. Catal.* **2025**, *6*, 289–296.

[27] Wang, F.; Pan, S.-W.; Zhu, S.-Q.; Chu, L.-L. Selective three-component reductive alkylalkenylation of unbiased alkenes via carbonyl-directed Nickel Catalysis. *ACS Catal.* **2022**, *12*, 9779–9789.

[28] Jin Y.-X.; Wang, C. Ni-catalysed reductive arylalkylation of unactivated alkenes. *Chem. Sci.* **2019**, *10*, 1780–1785.

[29] Jin Y.-X.; Wang, C. Nickel-catalyzed asymmetric reductive arylalkylation of unactivated alkenes. *Angew. Chem. Int. Ed.* **2019**, *58*, 6722–6726.

[30] Jin Y.-X.; Yang, H.-B.; Wang, C. Nickel-catalyzed reductive arylalkylation via a migratory insertion/decarboxylative cross-coupling cascade. *Org. Lett.* **2019**, *21*, 7602–7608.

[31] Jin Y.-X.; Yang, H.-B.; Wang, C. Nickel-catalyzed asymmetric reductive arylbenzylation of unactivated alkenes. *Org. Lett.* **2020**, *22*, 2724–2729.

[32] Zhao, T.-Y.; Xiao, L.-J.; Zhou, Q.-L. Nickel-catalyzed desymmetric reductive cyclization/coupling of 1,6-dienes: an enantioselective approach to chiral tertiary alcohol. *Angew. Chem. Int. Ed.* **2022**, *61*, e202115702.

[33] Fang, K.; Huang, W.-Y.; Shan, C.-X.; Qu, J.-P.; Chen, Y.-F. Synthesis of 3,3-dialkyl-substituted isoindolinones enabled by nickel-catalyzed reductive dicarbofunctionalization of enamides. *Org. Lett.* **2021**, *23*, 5523–5527.

[34] Yang, J.; Yang, L.-N.; Gu, J.; Shuai, L.; Wang, H.; Ouyang, Q.; Li, Y.-L.; Liu, H.-B.; Gong, L. Nickel-catalyzed reductive cascade arylalkylation of alkenes with alkylpyridinium salts. *Org. Lett.* **2022**, *24*, 2376–2380.

[35] Zhao, C.; Ge, Z.-L.; Hu, J.-H.; Tian, H.-J.; Wang, X.-M. Enantioselective reductive aryl-benzylation of alkenes by a nickel-titanium bimetallic system. *Cell Rep. Phys. Sci.* **2023**, *4*, 101474.

[36] (a) Yang, T.; Chen, X.-X.; Rao, W.-D.; Koh, M. J. Broadly applicable directed catalytic reductive difunctionalization of alkenyl carbonyl compounds. *Chem* **2020**, *6*, 738–751; (b) Zhao, L.; Meng, X.; Zou, Y.-F.; Zhao, J.-S.; Wang, L.-L.; Zhang, L.-L.; Wang, C. Directed nickel- catalyzed diastereoselective reductive difunctionalization of alkenyl amines. *Org. Lett.* **2021**, *23*, 8516–8521.

[37] Dong, Z.; Xu, C.-Y.; Chang, J.-C.; Zhou, S.-T.; Sun, P.-P.; Li, Y.-Q.; Chen, L.-A. Enantioselective directed nickel-catalyzed three-component reductive arylalkylation of alkenes via the carbometalation/radical cross-coupling sequence. *ACS Catal.* **2024**, *14*, 4395–4406.

[38] Meng, H.; Jia, J.-S.; Yang, P.-F.; Li, Y.-L.; Yu, Q.; Shu, W. Ni-catalyzed regioselective and site-divergent reductive arylalkylations of allylic amines. *Chem. Sci.* **2025**, *16*, 4442–4449.

[39] (a) Wang, J. Z.; Lyon, W. L.; MacMillan, D. W. C. Alkene dialkylation by triple radical sorting. *Nature* **2024**, *628*, 104–109; (b) Wang, J. Z.; Mao, E.; Nguyen, J. A.; Lyon, W. L.; MacMillan, D. W. C. Triple radical sorting: aryl-alkylation of alkenes. *J. Am. Chem. Soc*. **2024**, *146*, 15693–15700.

[40] Meng, H.; Jia, J.-S.; Yang, P.-F.; Li, Y.-L.; Shu, W. Ni-catalyzed regioselective and site-divergent reductive arylalkylations of allylic amines. *Chem. Sci*. **2025**, *16*, 4442–4449.

[41] (a) Ping, Y.-Y.; Xiao Li, X.; Pan, Q.; Kong, W.-Q. Ni-catalyzed divergent synthesis of 2-benzazepine derivatives via tunable cyclization and 1,4-acyl transfer triggered by amide N-C bond cleavage. *Angew. Chem. Int. Ed.* **2022**, *61*, e202201574; (b) Ping, Y.-Y.; Pan, Q.; Guo, Y.; Liu, Y.-L.; Li, X.; Wang, M.-Y.; Kong, W.-Q. Switchable 1,2-rearrangement enables expedient synthesis of structurally diverse fluorine-containing scaffolds. *J. Am. Chem. Soc.* **2022**, *144*, 11626–11637; (c) Liu, W.-F.; Xing, Y.-X.; Yan, D.-H.; Kong, W.-Q.; Shen, K. Nickel-catalyzed electrophiles-controlled enantioselective reductive arylative cyclization and enantiospecific reductive alkylative cyclization of 1,6-enynes. *Nat. Commun*. **2024**, *15*, 1787; (d) Liu, W.-F.; Li, W.; Xu, W.-P.; Wang, M.-Y.; Kong, W.-Q. Nickel-catalyzed switchable arylative/endo cyclization of 1,6-enynes. *Nat. Commun.* **2024**, *15*, 2914; (e) Liu, Y.-L.; Ping, Y.-Y.; Kong, W.-Q. Nickel-catalyzed ligand-controlled switchable skeletal rearrangements: divergent synthesis of isoquinoline-1,3-diones, cyclohexenols, cycloheptenols, and 2-benzazepin-5-ones. *Sci. China Chem*. **2025**, *68*, 2541–2551.

[42] Pan, Q.; Ping, Y.-Y.; Wang, Y.-F.; Guo, Y.; Kong, W.-Q. Ni-catalyzed ligand-controlled regiodivergent reductive dicarbofunctionalization of alkenes. *J. Am. Chem. Soc.* ***2021***, *143*, 10282–10291.

[43] Wu, X.-Q.; Qu, J.-P.; Chen, Y.-F. Quinim: a new ligand scaffold enables nickel-catalyzed enantioselective synthesis of α‐alkylated γ‐lactam. *J. Am. Chem. Soc.* **2020**, *142*, 15654–15660.

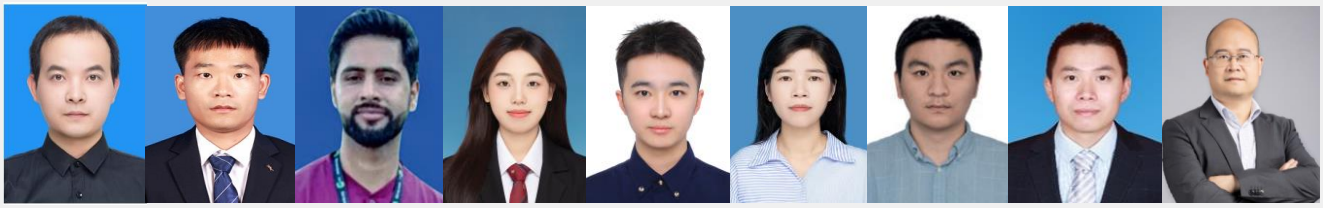
[44] Wu, X.-Q.; Turlik, A.; Luan, B.-X.; He, F.; Qu, J.-P.; Houk, K. N.; Chen, Y.-F. Nickel-catalyzed enantioselective reductive alkyl-carbamoylation of internal alkenes. *Angew. Chem. Int. Ed.* **2022**, *61*, e202207536.

[45] Wu, X.-Q.; Luan, B.-X.; Zhao, W.-Y.; He, F.; Wu, X.-Y.; Qu, J.-P.; Chen, Y.-F. Catalytic desymmetric dicarbofunctionalization of unactivated alkenes. *Angew. Chem. Int. Ed.* **2022**, *61*, e202111598.

[46] Zhang, C.-H.; Wu, X.-Q.; Xia, T.-T.; Qu, J.-P.; Chen, Y.-F. Ni-catalyzed

carbamoylation of unactivated alkenes for stereoselective construction of six-membered lactams. *Nat. Commun.* **2022**, *13*, 5964.
[47] Wu, L.-C.; Wu, X.-Q.; Qu, J.-P.; Chen, Y.-F. Exploration of quinim Ligand in Ni-catalyzed enantioselective reductive carbamoyl-alkylation of alkene. *Chin. J. Org. Chem*. **2023**, *43*, 4239–4250.
[48] Lan, Y.; Wang, C. Nickel-catalyzed enantioselective reductive carboacylation of alkenes. *Commun. Chem*. **2020**, *3*, 45–53.
[49] Xu, S.; Wang, K.; Kong, W.-Q. Ni-catalyzed reductive arylacylation of alkenes toward carbonyl-containing oxindoles. *Org. Lett.* **2019**, *21*, 7498–7503.
[50] Wang, K.; Ding, Z.-T.; Zhou, Z.-J.; Kong, W.-Q. Ni-catalyzed enantioselective reductive diarylation of activated alkenes by domino cyclization/cross-coupling. *J. Am. Chem. Soc.* **2018**, *140*, 12364–12368.
[51] Ping, Y.-Y.; Wang, K.; Pan, Q.; Ding, Z.-T.; Zhou, Z.-J.; Guo, Y.; Kong, W.-Q. Ni-catalyzed regio- and enantioselective domino reductive cyclization: one-Pot synthesis of 2,3-fused cyclopentannulated indolines. *ACS Catal.* **2019**, *9*, 7335–7342.
[52] Ma, T.; Chen, Y.-T.; Li, Y.-X.; Ping, Y.-Y.; Kong, W.-Q. Nickel-catalyzed enantioselective reductive aryl fluoroalkenylation of alkenes. *ACS Catal.* **2019**, *9*, 9127–9133.
[53] Li, Y.-X.; Ding, Z.-T.; Lei, A.-W.; Kong, W.-Q. Ni-catalyzed enantioselective reductive aryl-alkenylation of alkenes: application to the synthesis of (+)-physovenine and (+)-physostigmine. *Org. Chem. Front.* **2019**, *6*, 3305–3309.
[54] Li, H.-X.; Chen, J.-C.; Dong, J.-Q.; Kong, W.-Q. Ni-catalyzed reductive arylcyanation of alkenes. *Org. Lett*. **2021**, *23*, 6466–6470.
[55] Tian, Z.-X.; Qiao, J.-B.; Xu, G.-L.; Pang, X.-B.; Qi, L.-L.; Ma, W.-Y.; Zhao, Z.-Z.; Duan, J.-C.; Du, Y.-F.; Su, P.-F.; Liu, X.-Y.; Shu, X.-Z. Highly enantioselective cross-electrophile aryl-alkenylation of unactivated alkenes. *J. Am. Chem. Soc.* **2019**, *141*, 7637–7643.
[56] Qiao, J.-B.; Zhang, Y.-Q.; Yao, Q.-W.; Zhao, Z.-Z.; Peng, X.-J.; Shu, X.-Z. Enantioselective reductive divinylation of unactivated alkenes by nickel-catalyzed cyclization coupling reaction. *J. Am. Chem. Soc.* **2021**, *143*, 12961–12967.
[57] Anthony, D.; Lin, Q.; Baudet, J.; Diao, T.-N. Nickel-catalyzed asymmetric reductive diarylation of vinylarenes. *Angew. Chem. Int. Ed.* **2019**, *58*, 3198–3202.
[58] Chen, X.-W.; Yue, J.-P.; Wang, K.; Gui, Y.-Y.; Niu, Y.-N.; Liu, J.; Ran, C.-K.; Kong, W.-Q.; Zhou, W.-J.; Yu, D.-G. Nickel-catalyzed asymmetric reductive carbo-carboxylation of alkenes with CO_2. *Angew. Chem. Int. Ed.* **2021**, *60*, 14068–14075.
[59] Cerveri, A.; Giovanelli, R.; Sella, D.; Pedrazzani, R.; Monari, M.; Faza, O. N.; López, C. S.; Bandini, M. Enantioselective CO_2 fixation via a Heck-coupling/carboxylation cascade catalyzed by nickel. *Chem. Eur. J.* **2021**, *27*, 7657–7662.
[60] Jin, Y.-X.; Fan, P.; Wang, C. Nickel-catalyzed reductive asymmetric aryl-acylation and aryl-carbamoylation of unactivated alkenes. *CCS Chem.* **2022**, *4*, 1510–1518.
[61] Dai, Y.-J.; Wu, F.; Zang, Z.-H.; You, H.-Z.; Gong, H.-G. Ni-catalyzed reductive allylation of unactivated alkyl Halides with allylic carbonates. *Chem. Eur. J*. **2012**, *18*, 808–812.
[62] Wang, X.-X.; Lu, X.; He, S.-J.; Fu, Y. Nickel-catalyzed three-component alkene reductive dicarbofunctionalization to access alkylborates. *Chem. Sci.* **2020**, *11*, 7950–7956.
[63] Yang, T.; Jiang, Y.; Luo, Y.-X.; Lim, J. J. H.; Lan, Y.; Koh, M. J. Chemoselective union of alkenes, organohalides, and redox-active esters enables regioselective alkene dialkylation. *J. Am. Chem. Soc.* **2020**, *142*, 21410–21419.
[64] Zhang, J.-X.; Shu, W. Ni-catalyzed reductive 1,2-cross-dialkylation of unactivated alkenes with two alkyl bromides. *Org. Lett.* **2022**, *24*, 3844–3849.
[65] Yang, H.-X.; Zhang, Z.-M.; Cao, P.-T.; Yang, T. Nickel-catalyzed reductive alkene cross-dialkylation with unactivated alkyl electrophiles. *Org. Lett.* **2024**, *26*, 1190–1195.

Manuscript received: June 30, 2025
Manuscript revised: July 14, 2025
Manuscript accepted: July 24, 2025
Version of record online: XXXX, 2025



Left to Right: Yucheng Liu, Fu-Yu Li, Muneer-ul-shafi Bhat, Lan Tian, Hao-Ran Zhang, Huan Meng, Han-Tong Zhao, Yu-Long Li, Wei Shu

Yucheng Liu is an assistant professor in the College of Chemistry and Environmental Engineering at Sichuan University of Science and Engineering (SUSE, P. R. China). He obtained his bachelor's degree in Yangtze University. Then, he obtained a master degree under the supervision of professor Peiqiang Huang and professor Xiao Zheng at Xiamen University. In 2023, he received Ph.D. under the supervision of professor Hang Shi at Zhejiang University. In 2024, he joined SUSE. His current research interests focus on visible-light photoredox catalysis and transition-metal catalysis.

Fuyu Li obtained the bachelor's degree from Chongqing Normal University in 2019. In 2024, he obtained the Ph.D. at the Chengdu Institute of Organic Chemistry (Chinese Academy of Sciences) under the supervision of professor Xiaomei Zhang and professor Jiyu Wang. Subsequently, He joined the College of Chemistry and Environmental Engineering at Sichuan University of Science & Engineering (SUSE) as a lecturer. His current research focuses on transition metal-catalyzed radical chemistry and organic synthetic chemistry.

Muneer-ul-Shafi Bhat obtained his Ph.D. from the CSIR-Indian Institute of Integrative Medicine (India) under the supervision of Dr. Bhahwal Ali Shah. Later, he joined SUSTech as a postdoctoral fellow, collaborating with Wei Shu. His current research focuses on metal-catalyzed hydrofunctionalization of alkenes.

Lan Tian obtained her bachelor's degree from Jiangxi Science and Technology Normal University in 2024, and she is a master candidate under the supervision of professor Yulong Li at Sichuan University of Science and Engineering (SUSE). Her current research direction is organic synthetic chemistry.

Haoran Zhang obtained his bachelor's degree from Sichuan University in 2023, and he is a master candidate under the supervision of professor Yulong Li at Sichuan University of Science and Engineering (SUSE).

Huan Meng obtained her bachelor's degree from Zhengzhou University, followed by a master degree from Shanghai University. In 2020, she joined Southern University of Science and Technology (SUSTech) as s Ph.D. candidate under the supervision of Professor Wei Shu. She focuses on nickel-catalyzed difunctionalizations of alkenes.

Han-Tong Zhao obtained his bachelor's degree from Southern University of Science and Technology (SUSTech) in 2023, and he is a master candidate under the supervision of Professor Wei Shu at Southern University of Science and Technology (SUSTech). He is working on the nickel-catalyzed hydrofunctionalization of alkenes.

Yu-Long Li is a full professor in the College of Chemistry and Environmental Engineering at Sichuan University of Science and Engineering (SUSE). In 2005, he obtained a bachelor's degree, and then obtained the Ph.D. in 2010 under the supervision of professor Licheng Song and professor Qingmei Hu at Nankai University. In 2014, He was a postdoctoral fellow and visiting scholar at the University of Illinois at Urbana-Champaign (USA), collaborating with Thomas B. Rauchfuss. His current research focus on organic synthesis chemistry, visible light catalysis chemistry, radical chemistry.

Wei Shu is a Principal investigator with tenure in the Department of Chemistry at Southern University of Science and Technology (SUSTech). He received his bachelor's degree from Nankai University. He continued his graduate studies at the Shanghai Institute of Organic Chemistry (SIOC), Chinese Academy of Sciences under the supervision of Profs. Shengming Ma and Guochen Jia. He started his independent research at SUSTech in 2018 after postdoctoral stints at University of Zurich (Cristina Nevado), Princeton University (David W. C. MacMillan), and Massachusetts Institute of Technology (Stephen L. Buchwald). His research fields span over transition-metal catalysis, asymmetric catalysis, visible-light catalysis, microfluidic chemistry, and medicinal chemistry.