

Base Metal Catalysis in Nitrene Transfer Reactions

Hillol Khatua, Anogh Ghosh, Subrata Das, Sima Patra, Souvik Nandi, and Buddhadeb Chattopadhyay*



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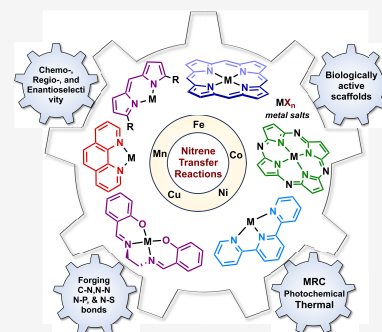


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ABSTRACT: Leveraging base metal catalysis to transform small organic molecules by forging X–N bonds (X = C, N, P, S) through nitrene transfer reactions (NTRs) renders a robust and sustainable paradigm shift for preparing valuable amine building blocks. Over the last four decades, 3d metal-catalyzed NTRs have received significant attention in the field of organic synthesis. This review will thoroughly discuss the manipulation of various complexes of base metals, such as Mn, Fe, Co, Ni, and Cu, to control the reaction pathways for X–N bond formation using different nitrene precursors. This review will encompass exemplary, pioneering, and pertinent synthesis in this area and will comprehensively elucidate the mechanistic rationale behind each 3d metals. The reactivity, regioselectivity, chemo-selectivity and enantioselectivity of those novel base-metal catalysts are an inevitable part of this discussion. We will also address the inherent limitations and potential opportunities within this specific field of study.



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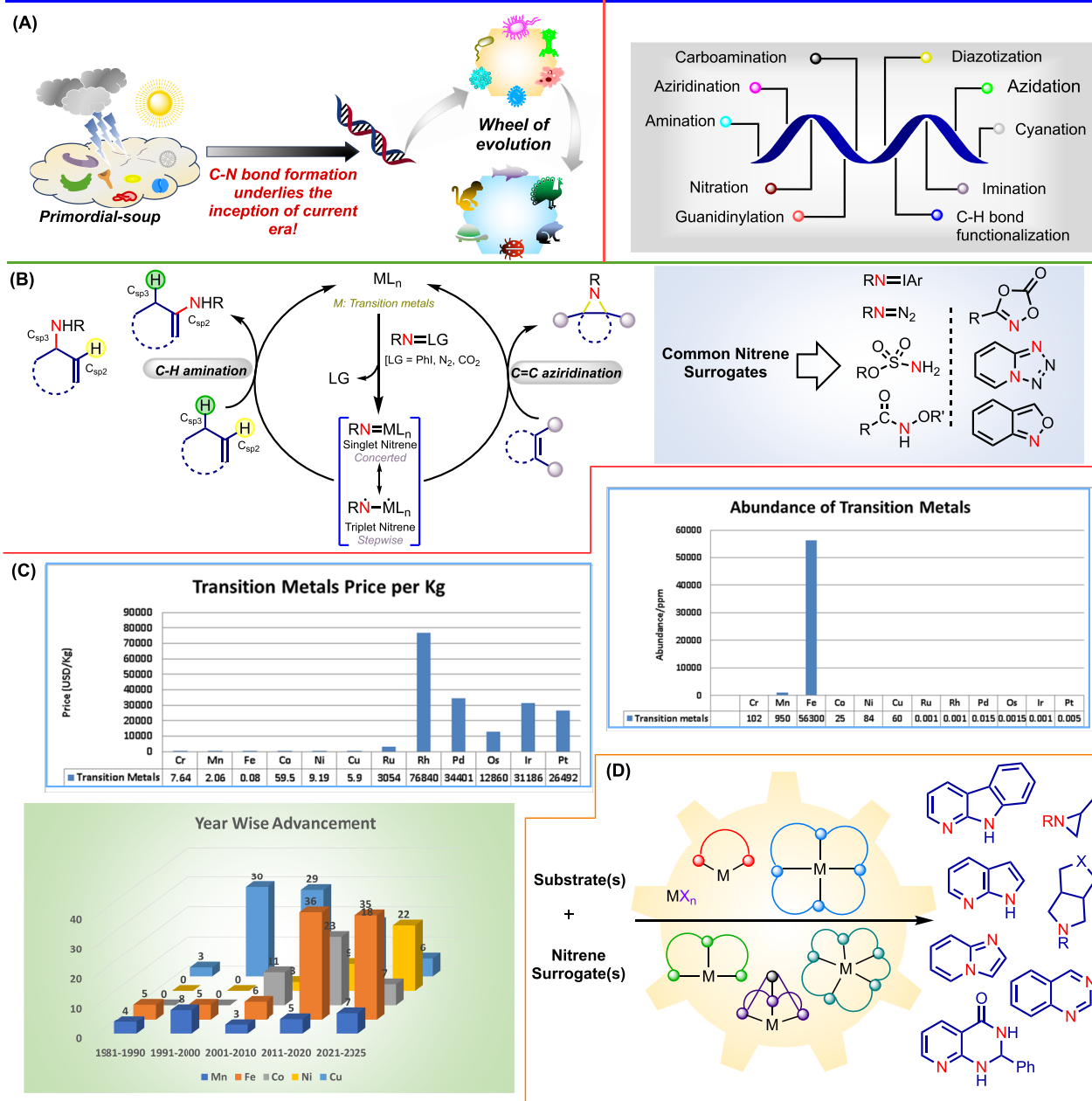
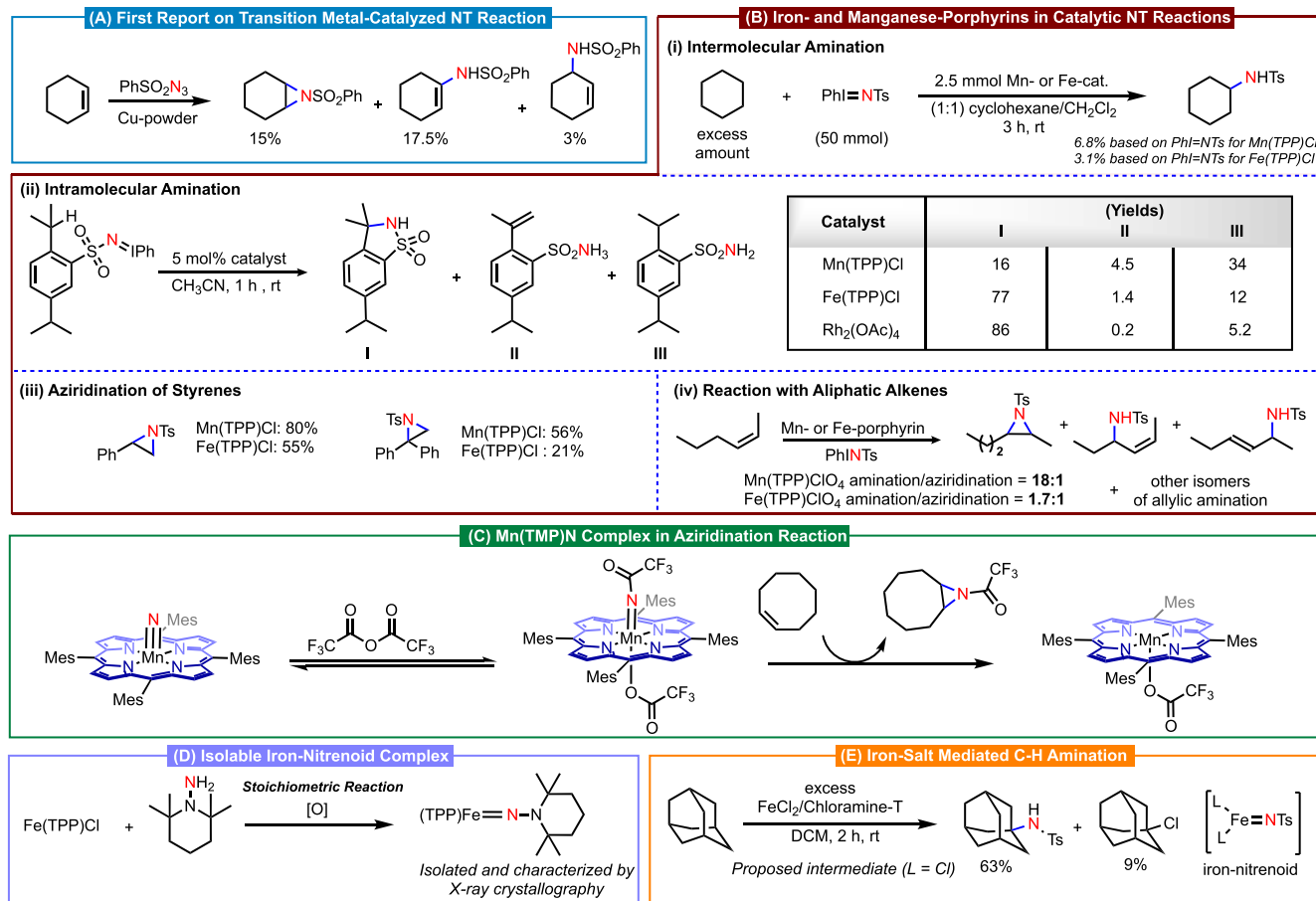


Figure 1. A prelude and conspectus about base-metal-catalyzed NTRs.

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Scheme 1. Seminal Examples in Base-Metal-Catalyzed NTRs



1. INTRODUCTION

It is well documented that the C–N bond is one of the most fundamental building blocks for countless molecular scaffolds necessary for life and technology, such as medicines, agrochemicals, natural products, advanced materials, and so on. The formation of C–N bonds is key to make nitrogen-containing molecular scaffolds such as amines, amides, heterocycles, peptides, and many more, which exhibit diverse biological activities and industrial applications. Thus, creating effective and sustainable approaches for establishing C–N bonds is a primary emphasis in synthetic organic chemistry.^{1,2} Over the past decades, a series of C–N bond forming reactions, viz., nitration, cyanation, azidation, amination, cycloadditions, classical cross-coupling, and most notably C–H functionalization, has collectively redefined the boundaries of molecular design and late-stage diversification [Figure 1A].^{3–5} Among these, C–H functionalization strategies have emerged as exceptionally powerful because they bypass prefunctionalized starting materials and enable direct conversion of inert C–H bonds into value-added C–N bonds [Figure 1A].^{6–11} A defining breakthrough within this broader landscape has been the development of nitrene-transfer reactions (NTRs), which provide streamlined and modular access to nitrogen-containing motifs through the intermediacy of reactive metal-nitrenoid species.^{12–20} These reactions proceed primarily through two manifolds: (1) aziridination of C=C double bonds, and (2) C–H bond amination, both of which share the formation of a metal-nitrenoid species as the key intermediate [Figure 1B]. The nitrenoid intermediate may

engage either a π -bond or a σ -bond, and its stereoelectronic profile, governed by metal identity, ligand architecture, and nitrene precursor, determines whether the ensuing transformation unfolds through a concerted or a stepwise mechanistic pathway. It can acquire a radical character referred to as “iminyl” species, and it can be described as “imido” species or “imido-like” species based on the characteristics of the σ -bond and π -bond. Typically, metal-nitrenoid species also occur in singlet and triplet states, similar to nitrenes. Interestingly, singlet nitrenoid species adhere to the concerted mechanism, whereas triplet nitrenoid species follow a radical intermediate pathway, specifically involving hydrogen atom abstraction and simultaneous radical substitution.²¹ This ability to oscillate between discrete electronic manifolds grants NTRs exceptional finesse in modulating regioselectivity, stereoselectivity, and chemoselectivity through judicious catalyst and ligand design.

The overwhelming influence of transition metal catalysis in the catalytic dynasty is unequivocal.²² In this context, NTRs catalyzed by transition metals are no exception. Notably, the dominance of noble metal catalysts of palladium and iridium is undeniable in the field of organic synthesis. The emergence of base-metal catalysts (Mn, Fe, Co, Ni, Cu) has redefined the landscape by offering sustainable, cost-effective, and environmentally benign alternatives to the noble metals [Figure 1C].^{23–26} Owing to their unique electronic structures and accessible redox states, base metals often engage in single-electron transfer (SET) processes that promote stepwise amination through hydrogen atom abstraction and radical

substitution. Additionally, electrophilic substitution (S_NAr) and electrocyclozation pathways have been identified in aryl C–H amination, depending on the substrate and nitrenoid electronic characteristics. Such reactivity is particularly favored at benzylic, allylic, and tertiary C–H bonds due to their lower bond dissociation energies. Importantly, the discovery of nitrene transfer reactions by biomimicked iron and manganese porphyrin complexes by Breslow provided a conceptual bridge between enzymatic NTRs and synthetic catalysis.²⁷ Over time, this area has found its significant value in C–N bond formation reactions that continues to thrive with further advancements. Since then, base-metal porphyrin and related complexes have emerged as versatile and tunable catalysts, significantly broadening the scope of sustainable C–N bond formation [Figure 1D].^{28,29}

In this context, it is worth noting that base-metal catalysis for the NTRs have seen significant advancements that have been documented in numerous excellent review articles.^{30–48} For example, Gallo et al. reported a comprehensive review of metallo-porphyrins mediated strategies for creating the C–N bond via base metal catalysis.³⁰ Che group has published several review articles, with an emphasis on Fe-nitrene/imido complexes.^{31,37,41,46,47} Deng et al. also explored³² a related area utilizing iron catalysis, while the Bi group⁴³ reviewed nitrene transfer methods to prepare aliphatic azides. In the same line, Chattopadhyay group¹⁸ conducted an extensive assessment of Fe-catalyzed C–N bond formation through NTRs. In that vein, while Procter et al. highlighted³⁶ the significance of Co-based metalloradical catalysis, the Perez group³⁸ evaluated the importance of Cu-catalyzed $C(sp^3)$ –H functionalization, and Orru et al. reviewed²⁰ particularly NTRs to carbon monoxide and isocyanides by iron, nickel, and copper catalysis. On the other hand, asymmetric C–N bond formation exploiting metal-nitrenoids was efficiently surveyed by the Ohe,³⁴ Pelliser,³⁵ Uchida,¹⁵ Schomaker,²¹ and Phipps⁴⁵ groups, respectively. Visible-light-induced nitrene transfer reactions were reviewed by Koeing and his team.¹⁷ The feasibility of different dipyrin-based and copper-scorpionate metal complexes in nitrene transfer reactions was surveyed by Baudron et al.⁴⁰ and Perez et al.⁴² Regarding emerging nitrene precursors, de Bruin³⁹ and Xu et al.⁴⁸ showcased their contextual significance in NTRs. Furthermore, Dauban et al.³³ highlighted the imminent infancy, and Power et al.⁴⁴ assessed the difficulties and challenges in this context. Notably, regardless of all these significant accounts, articles encompassing different base metals and their achievements in the domain of NTRs are still lacking. Given the substantial advancement and great potential of base metals in facilitating nitrene transfer reactions, we present comprehensive information on this topic, covering the range of reactions, mechanistic details, the development of catalysts and critical aspects of the developed nitrene transfer reactions. Furthermore, this review discusses transformations with metal nitrene intermediates, encompassing C–H amination, aziridination, annulation, cross-coupling, rearrangement, and S–N/N–N/P–N bond formation, intending to provide readers a comprehensive and critical overview of advancements in this promising area. We restrict our discussion to homogeneous base metal catalysis, while enzyme catalytic transformations fall outside the purview of this review.

2. PIONEERING DISCOVERIES IN NITRENE TRANSFER REACTIONS

The inception of metal-catalyzed nitrene transfer reactions (NTRs) was reported by Kwart and Khan (Scheme 1A).⁴⁹ They showed that benzenesulfonyl azide was able to transfer a nitrogen atom to cyclohexene with copper powder under heating conditions. This reaction produced a mixture of aziridine, allylic C–H insertion and vinylic C–H insertion products. Crucially, their findings emphasized that metal catalysts like copper may reduce the activation energy for azide decomposition, enabling C–N bond formation through metal-nitrenoid inserting into σ - or π -bonds. On the other hand, in 1982, Breslow and Gellman made a groundbreaking report on the application of biomimicked iron and manganese porphyrin complexes in C–H amination for the first time (Scheme 1B).²⁷ They used $PhI=NTs$ as the nitrogen source for the amination of cyclohexane. Even though the yields were not significant, $Mn(TPP)Cl$ outperformed $Fe(TPP)Cl$ in intermolecular C–H amination (Scheme 1B(i)). Notably, for intramolecular amination, $Fe(TPP)Cl$ exhibited greater efficiency (Scheme 1B(ii)).⁵⁰ In 1984, Mansuy and co-workers reported the aziridination of styrenes with iron and manganese porphyrin complexes. $Mn(TPP)Cl$ showed much greater efficiency than its iron equivalent (Scheme 1B(iii)).⁵¹ They further expanded their studies to aliphatic alkenes and discovered that the chemoselectivity of NT reactions was highly dependent on the metal center. $Mn(TPP)ClO_4$ favored allylic C–H amination, whereas $Fe(TPP)ClO_4$ delivered nonselective outcomes (Scheme 1B(iv)). This was preliminarily attributed to the greater electrophilicity of iron-nitrenoids relative to Mn-nitrenoids, which led to both the aziridination and allylic C–H amination reactions.⁵² At the same time (in 1983), Groves and Takahashi first time reported the metal nitride activation to generate aziridine scaffolds (Scheme 1C).⁵³

They discovered that when $Mn(TMP)N_3$ was irradiated in benzene, it yielded an isolable manganese(V) nitride, $Mn(TMP)N$. This species, identified as diamagnetic with a low-spin d^2 configuration, efficiently underwent the aziridination of cyclooctene (yielding 84–92%) at room temperature in the presence of trifluoroacetic anhydride. The mechanistic studies suggested the formation of manganese(V)-imido complex, which formed in situ from the reaction of trifluoroacetic anhydride with $Mn(TPP)N$ that was further supported by the kinetic study of Bottomley and Neely.⁵⁴ Around the same time, Mansuy and co-workers also reported the synthesis of iron porphyrin-nitrene complexes.⁵⁵ When iron porphyrin [$Fe(TPP)Cl$] was treated with 1-amino-2,2,6,6-tetramethylpiperidine in the presence of either dioxygen or iodosobenzene, they obtained a stable pentacoordinate iron-nitrene complex (Scheme 1D). This was characterized by X-ray crystallography, revealing a linear Fe–N–N unit, with bond lengths indicative of multiple bond character (Fe–N: 1.809 Å; N–N: 1.232 Å) and an $S = 2$ spin state for the iron center. In another noteworthy study, Motherwell and coworkers⁵⁶ discovered that $FeCl_2$ can facilitate the amination of hydrocarbons using Chloramine-T as the aminating agent (Scheme 1E). They obtained 63% yield of monoaminated adamantane using almost four equivalents of $FeCl_2$ and Chloramine-T compared to adamantane. The reaction was proposed to proceed via an iron-nitrenoid intermediate. However, a minor amount of chlorinated adamantane was also observed as a side product.

To further investigate the reaction pathway, they conducted an experiment using 1-chloroadamantane as the substrate with FeCl_2 and Chloramine-T. This resulted in the formation of 1,3-dichloroadamantane (19%) and monoaminated adamantane (49%) as the primary products. Based on these observations, they proposed an alternative reaction mechanism involving an initial chlorination step mediated by FeCl_2 /Chloramine-T, followed by nucleophilic displacement of chlorine by nitrogen to form the C–N bond. These early findings established the foundation for the advancement of iron-catalyzed nitrene transfer reactions. In the early 1990s, the Evans group^{57,58} achieved notable progress in the aziridination of olefins using Cu(I) and Cu(II) catalysts. All these pioneering and seminal studies laid a strong underpinning for the development of modern catalytic systems for nitrene transfer reactions.

3. NITRENE TRANSFER REACTIONS TO FORM C–N BONDS

3.1. Manganese Catalysis (Mn)

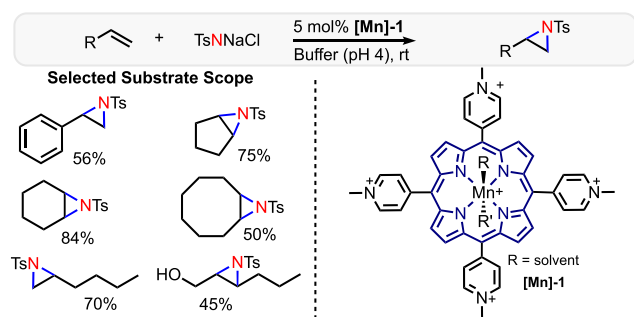
In the field of organic synthesis, owing to the broad redox range, manganese plays a significant role as various catalysts. Manganese and its corresponding complexes can undergo single-electron transfer processes (SETs) and two-electron processes as well. These complexes became a sustainable choice due to the high abundance and low toxicity. Therefore, in the realm of base-metal-catalyzed nitrene transfer reactions, the idea of manganese-catalysis is highly warranted for progressing the area of NTRs.

3.1.1. Manganese-Catalyzed Aziridination Reactions.

Aziridines are the smallest and simplest saturated three-membered nitrogen heterocycle. Compared to their cousin epoxides, this N-heterocycle is less explored.⁵⁹ Aziridines tethered natural products, active pharmaceutical ingredients and polymers are common. Consequently, because of the distinct characteristics of this scaffold, there is an ongoing necessity to identify an appropriate and sustainable approach to provide this synthetically valuable molecule.

3.1.1.1. Exploiting Tosyl Amines. Although there are multiple useful approaches to produce the aziridine moiety, but they are in constant odds with the sustainable paradigms.⁴³ In that regard, inspired by the initial studies by Breslow, Gellman and Mansuy, Stokes and co-workers⁶⁰ reported a water-soluble manganese porphyrin-based complex ([Mn]-1) as a catalyst for the aziridination reaction, utilizing Chloramine-T as the nitrene precursor (Scheme 2). The catalytic efficiency was found to be pH-dependent, with slightly acidic to neutral conditions yielding the highest conversions. The

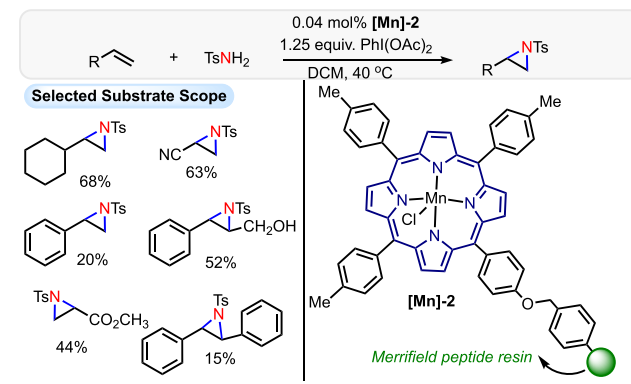
Scheme 2. Aziridination Catalyzed by a Water-Soluble Manganese-Porphyrin Complex



method was found effective for the aziridination of both aliphatic and aromatic alkenes. Notably, for aliphatic alkenes, no allylic aminations were observed.

In 2005, Yu group reported a Merrifield's peptide resin (MPR)-supported manganese-porphyrin system ([Mn]-2) for the aziridination of alkenes using a combination of $\text{PhI}(\text{OAc})_2$ and TsNH_2 in a dichloromethane solvent (Scheme 3).⁶¹ While

Scheme 3. Aziridination Catalyzed by a Polymer-Supported Manganese Porphyrin Catalyst



good yields were achieved for the aziridination of aliphatic alkenes, but moderate yields were obtained for aromatic alkenes (conversion ranging from 20% to 85%). Furthermore, the catalyst demonstrated efficiency for both benzylic and allylic amination reactions.

3.1.1.2. Incorporating Iminoiodinanes. Realizing the great importance of the aziridine scaffold in organic transformations, synthetic chemists endeavored to achieve the asymmetric synthesis of aziridine scaffolds. In 1993, Katsuki and co-workers introduced manganese-salen catalysis for asymmetric aziridination (Scheme 4). Their initial study with ([Mn]-3) yielded only 9% of the aziridination from styrene with moderate enantioselectivity (61%).⁶²

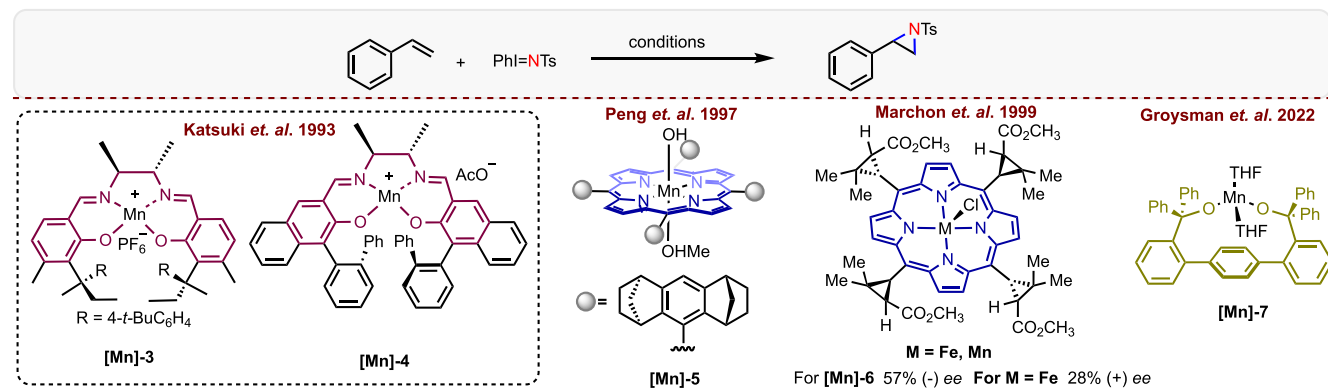
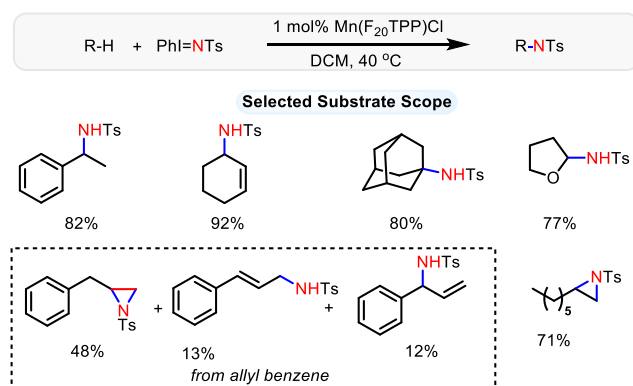
To improve, they modified the salen complexes by incorporating optically active binaphthyl groups as chiral elements ([Mn]-4), which afforded enantioselectivity of up to 94%.⁶³ Later, Peng and co-workers in 1997 demonstrated an asymmetric aziridination strategy using a D_4 -symmetric Halterman manganese-porphyrin catalyst ([Mn]-5).⁶⁴ The reaction produced good yield and moderate enantioselectivity (*ee* 40–68%) with 20 times excess of alkene with respect to $\text{PhI}=\text{NTs}$, and 0.5 mol % of the catalyst (Scheme 4).

Marchon group investigated the asymmetric aziridination reaction using manganese and iron porphyrins having meso-chiral cyclopropyl moieties (Scheme 4).⁶⁵ Recently, Groysman et al. reported a new manganese complex ([Mn]-7) ligated with a bulky chelating bis(alkoxide) ligand for a similar type of aziridination reaction (Scheme 4).⁶⁶

3.1.2. Manganese-Catalyzed $\text{C}(\text{sp}^3)\text{--H}$ Amination (Intermolecular).

3.1.2.1. Exploiting Iminoiodinanes. Che and co-workers developed an efficient C–H bond amination strategy using $\text{Mn}(\text{F}_{20}\text{TPP})\text{Cl}$ as a catalyst (Scheme 5).⁶⁷ A diverse array of C–H bonds, including benzylic, allylic, etheral and tertiary C–H bonds were aminated using this method. However, substrates containing allylic C–H bonds showed no clear trend toward either aziridination or allylic amination. For instance, allyl benzene yielded a mixture of products, whereas 1-octene underwent exclusive aziridination.

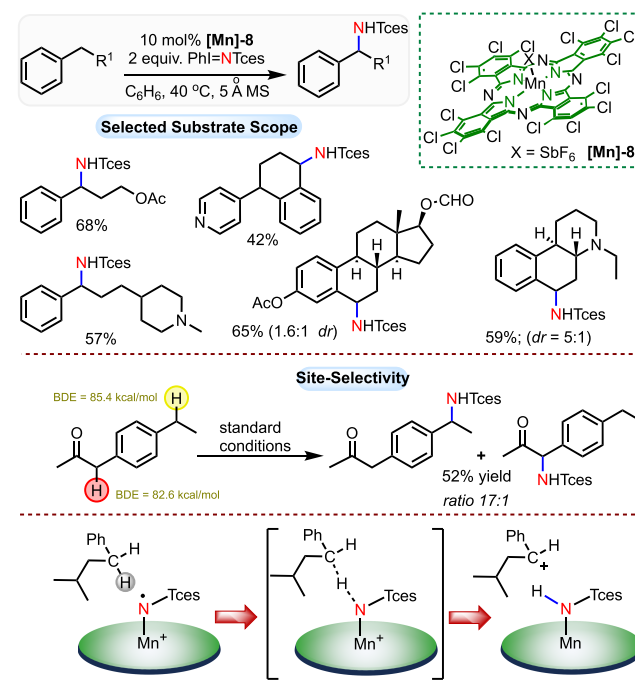
Scheme 4. Manganese-Catalyzed Aziridination Reactions

Scheme 5. Mn(F₂₀TPP)Cl Catalyzed Aminations and Aziridinations using PhI=NTs

Later, the Katsuki group developed an asymmetric amination using optically active cationic Mn(salen) complexes bearing electron-withdrawing substituents.⁶⁸

In 2018, White et al. reported a highly selective benzylic amination catalyzed by ([Mn]-8) (Scheme 6).⁶⁹ This amination reaction was found to be so selective that only the benzylic C–H bonds underwent activation and amination even in the presence of multiple reactive C–H bonds. This developed strategy overcomes the challenge in Rh-catalyzed intermolecular amination reactions,⁷⁰ where a mixture of products is typically formed due to poor site selectivity. Notably, substrates-containing basic nitrogen, masked by both Brønsted and Lewis acids, are well tolerated, enabling access to aminated *N*-heterocycles. Furthermore, the reaction exhibits high efficacy in the selective benzylic amination of bioactive complex molecules. Parallel competition kinetic isotope effect (KIE) measurements (2.5 ± 0.2) and intramolecular competition KIE (3.0 ± 0.1) suggest that C–H bond cleavage is likely the rate-determining step. Contemporary DFT studies by the Wang group⁷¹ unveiled that the C–H cleavage occurs via an ionic mechanism rather than a radical pathway, i.e., hydride transfer (HYT) rationale involving concerted hydrogen atom and electron transfers.

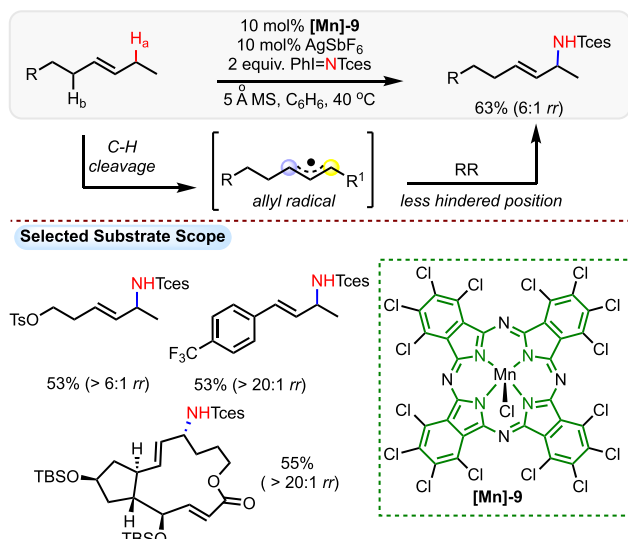
In this context, it is important to note that the nitrene transfer to alkene having allylic C–H bond poses a formidable challenge of chemo-selectivity between competitive aziridination and allylic amination. Generally, aziridination is preferred over allylic amination in both intermolecular and intramolecular reaction under a Rhodium-based catalytic system. Importantly, the White group demonstrated a highly site-

Scheme 6. Manganese-Catalyzed Intermolecular Benzylic C(sp³)–H Amination

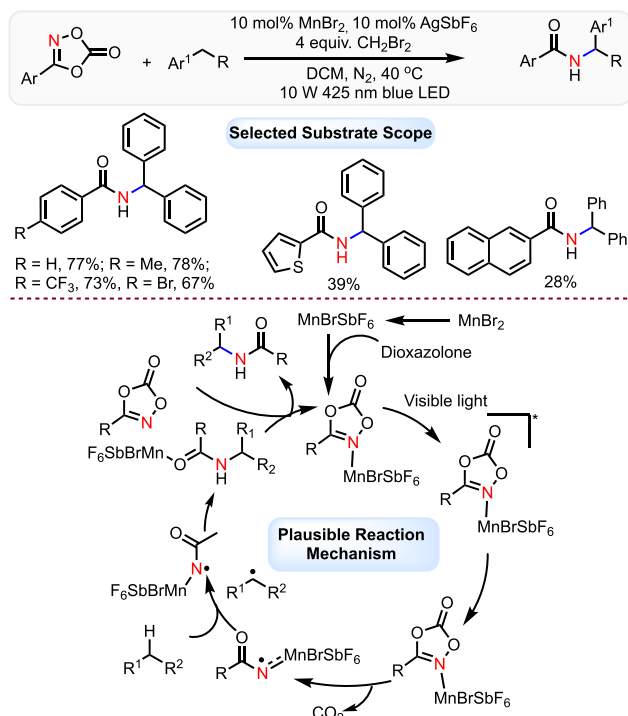
selective and chemo-selective intermolecular allylic amination of a diverse array of alkenes using a manganese-phthalocyanine catalyst ([Mn]-9) (Scheme 7).⁷² The exceptional site selectivity and chemo-selectivity are attributed to the bulky and electrophilic nature of the phthalocyanine ligand, which preferentially activates the less hindered allylic C–H bonds while suppressing aziridination. This rationale was supported by DFT calculations conducted by the Qian group.⁷³ It has been found that the developed amination strategy is broadly applicable, accommodating cyclic, acyclic, linear, and styrenyl olefins. Additionally, its utility has been showcased in the late-stage modification of complex natural product derivatives.

3.1.2.2. Incorporating Dioxazolones. In 2023, Bao et al. reported a manganese-catalyzed, visible-light-promoted paradigm-shift for the benzylic amination using dioxazolone as the nitrene source (Scheme 8).⁷⁴ While the reaction exhibits broad functional group tolerance, but its application is limited to only activated diarylmethane and cyclic etheral C–H bonds. Mechanistic studies, supported by both experiment and theory

Scheme 7. Chemoselective and Site-Selective Intermolecular Allylic Amination



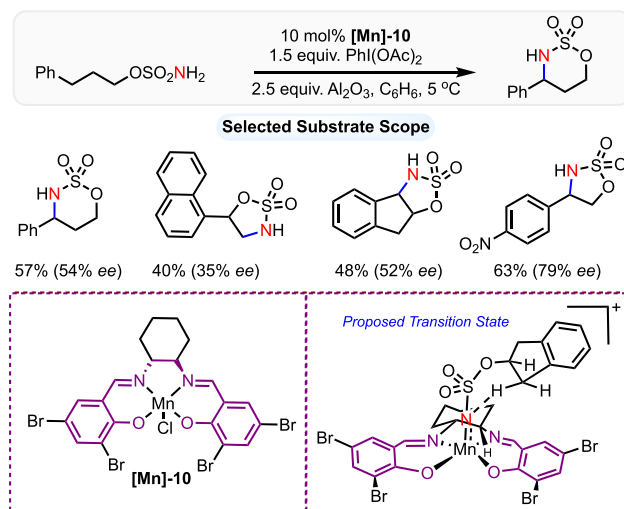
Scheme 8. Visible-Light-Induced Manganese-Catalyzed Amidation using Dioxazolone



indicated that the formation of a Mn-acyl nitrene intermediate and follows a stepwise radical pathway.

3.1.3. Manganese-Catalyzed C(sp³)-H Amination (Intramolecular). In 2005, the Che group⁷⁵ reported first chiral metallosalen-catalyzed enantioselective intramolecular amidation of sulfamate esters under mild conditions accomplishing moderate enantioselectivity (up to 79%) with exclusive *cis*-selectivity (Scheme 9). Interestingly, although the neutral [Mn]-10 complex shows optimal performance for this amidation reaction in the presence of Al₂O₃, it was previously found to be less effective in intermolecular C-H amination reaction.⁶⁸ The trend in the *ee* values suggests that through-

Scheme 9. Mn-catalyzed Enantioselective Intermolecular Amination of Sulfamate Esters

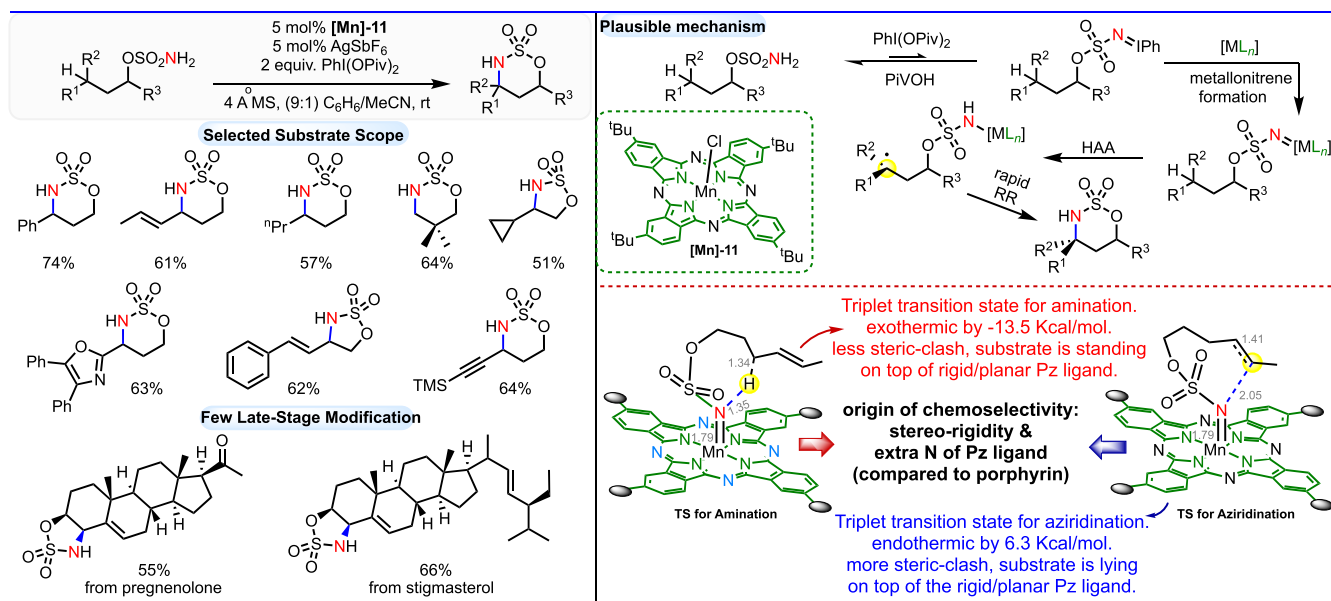
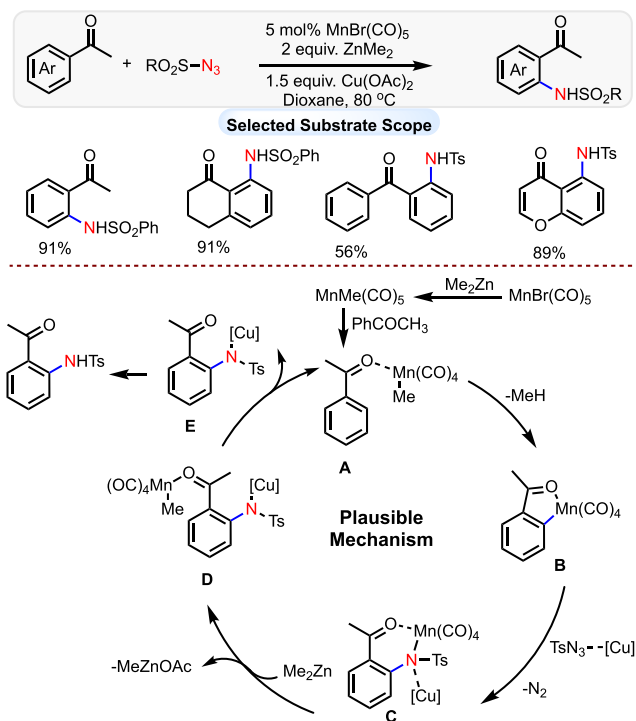


space electrostatic interaction (field effect) as well as steric effect is responsible for chiral induction.

In 2015, White and co-workers reported a highly chemo-selective intramolecular C(sp³)-H amination using manganese-phthalocyanine ([Mn]-11) as a catalyst (Scheme 10).⁷⁶ Traditional noble metal rhodium catalysts, which stereospecifically functionalize aliphatic C-H bonds (secondary and tertiary), often suffer from poor chemo-selectivity due to competitive oxidation of π -bonds. In contrast, Mn catalysts demonstrate high chemo-selectivity for allylic C-H amination compared to the aziridination but exhibit only moderate reactivity toward stronger aliphatic C-H bonds.

This iron catalyzed method efficiently aminates a broad range of allylic C-H bonds, including primary aliphatic and propargylic C-H bonds. Additionally, this method demonstrated excellent competence for the late-stage modification of complex molecules; specifically, sulfamate ester-derived steroids like pregnenolone and stigmasterol efficiently underwent aminative cyclization, producing five-membered heterocycles with good yields. Notably, the ([Mn]-11) catalyst showed good reactivity and exceptional chemoselectivity with a ratio of >20:1, which stands in stark contrast to the 1:1 ratio observed when using the rhodium catalyst [Rh₂(esp)₂] (bis[rhodium-($\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,3-benzenedipropionic acid)]).⁷⁶ Mechanistic investigations suggest a stepwise pathway involving hydrogen atom abstraction followed by a rapid radical rebound process. This mechanism is supported by Hammett correlation data and olefin isomerization experiments. In a recent computational study by the Zhan group,⁷⁷ delineated the good planarity, skeletal-nitrogen atoms and good stereorigidity of the macrocyclic ligand renders the metallonitrene adequately electrophilic and make it enough susceptible to undergo amination over aziridination. Despite these advancements, the lack of an enantioselective version of this reaction limits its applicability in medicinal chemistry and drug discovery. Therefore, the development of an enantioselective variant is highly desirable.

3.1.4. C(sp²)-H Amination. In 2018, the Xu group developed an efficient manganese-catalyzed ortho C(sp²)-H amidation of aromatic ketones using sulfonyl azides (Scheme 11).⁷⁸ A diverse range of ketones, including fused and biaryl systems smoothly transformed to the desired product under

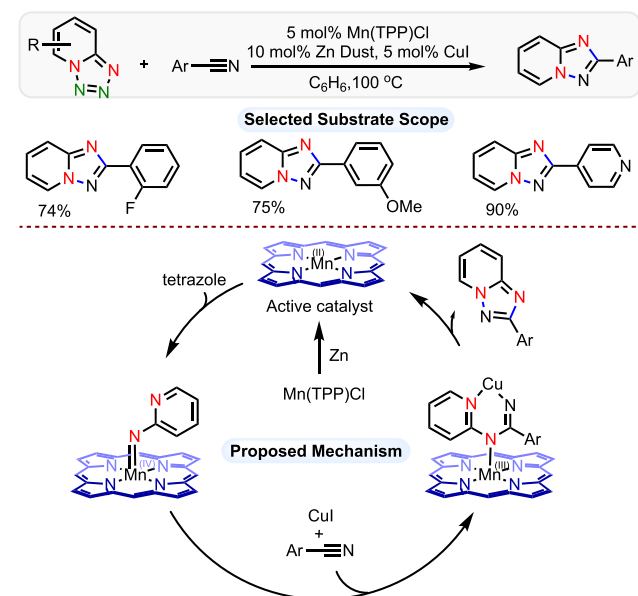
Scheme 10. Chemoselective Intramolecular C(sp³)-H Amination Catalyzed by Manganese-Phthalocyanine ComplexScheme 11. Manganese-Catalyzed *ortho*-C-H Amidation of Aromatic Ketones

the reaction conditions. The developed protocol addresses the key limitation in the previously reported method where late-transition metals (Ru, Ir) were used.^{79,80} Based on the literature precedents, a mechanistic pathway was proposed. The catalytic cycle begins with the formation of MnMe(CO)₅ through transmetalation of MnBr(CO)₅ with Me₂Zn, accompanied by the release of methane gas. Intermediate (A) is generated through the complexation of MnMe(CO)₅ with acetophenone. Subsequent *ortho*-C(sp²)-H metalation of (A) leads to the formation of manganacycle intermediate (B). The reversible coordination of tosyl azide to the manganese center,

followed by amido insertion, results in Mn-intermediate (C) with the concurrent release of N₂. The subsequent transmetalation of intermediate (C) with Me₂Zn forms intermediate (D), which undergoes ligand exchange with acetophenone to regenerate intermediate (A), thus propagating the catalytic cycle. Simultaneously, intermediate (E) is formed and undergoes hydrolysis to yield the final amination product.

3.1.5. Manganese-Catalyzed Annulation Reaction (Leveraging Tetrazoles). In 2021, the Chattopadhyay group reported a manganese-catalyzed denitrogenative annulation reaction involving benzonitrile and pyridotetrazole (Scheme 12).⁸¹ The reaction employs a catalytic combination of Mn(TPP)Cl, Zn dust, and CuI. Mechanistic studies revealed that Zn dust reduces Mn(III) to Mn(II) in situ, generating

Scheme 12. Mn-Catalyzed Denitrogenative Annulation of Tetrazole with Nitriles



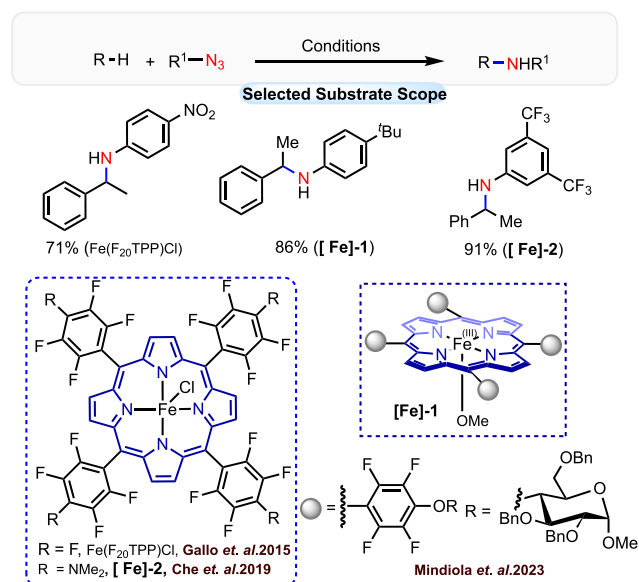
Mn(II)(TPP) as the active catalyst. This Mn(II) species facilitates the denitrogenation of the tetrazole to generate a 2-pyridyl nitrene intermediate. Simultaneously, CuI coordinates with the nitrile group, enhancing its electrophilicity and enabling the manganese-nitrene species to add to the nitrile π -system, leading to the annulated product. While the developed method exhibited broad substrate scope with various tetrazoles and aryl nitriles, it was ineffective with aliphatic nitriles, which failed to yield the desired products.

3.2. Iron Catalysis (Fe)

Due to the high abundance, minimal hazardousness, variable formal oxidation states and especially low-cost renders, iron catalysis is a perfect choice for many important synthetic transformation. Among them, iron-catalyzed nitrene transfer reactions have achieved significant interest as a sustainable and efficient strategy for introducing amine functionalities into organic molecules, owing to its high abundance and versatile reactivity.^{37,41,46,47}

2.1. Iron-Catalyzed C(sp³)-H Amination (Intermolecular). **3.2.1.1. Utilizing Organic Azides.** In 2010, the Che group studied an iron porphyrin-catalyzed C-H bond amination reactions using aryl azides.⁸² They introduced the electron-deficient iron porphyrin complex Fe(F₂₀TPP)Cl (F₂₀TPP = 5,10,15,20-tetrakis(perfluorophenyl)porphyrin) for the C-H bond amination reactions (Scheme 13).

Scheme 13. Fe-Porphyrin-Catalyzed Intermolecular Amination



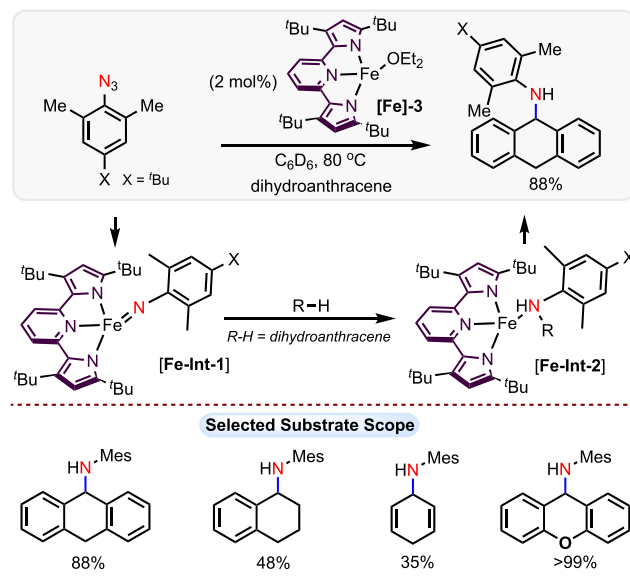
It was observed that while the intermolecular C-H aminations of sulfonyl azides provided poor yields, significant improvements were observed when 4-nitrophenyl azide was employed. The scope of the reaction was demonstrated through the amination of both benzylic and stronger aliphatic C-H bonds, including the challenging substrates such as cycloheptane, cyclooctane, and adamantane.

Importantly, the efficiency of the Fe(F₂₀TPP)Cl-catalyzed amination reactions can be dramatically enhanced (up to 14-fold) under microwave irradiation. This is due to the rapid activation of both the catalyst and the azide under microwave irradiation, which improves the reaction kinetics. In 2015, Lay and Gallo et al. also reported the catalytic C-H bond

amination by modifying an iron-porphyrin catalyst. The modified catalyst ([Fe]-1), featuring tetrafluorophenyl glycoside units attached to the porphyrin core, demonstrated high efficiency for the benzylic C-H bond aminations (Scheme 13).⁸³ After four years, Che et al. revisited the C-H bond amination reaction catalyzed by Fe(F₂₀TPP)Cl due to its moderate yield and low catalytic efficiency, particularly for unactivated C-H bonds. To enhance the catalytic performance of the porphyrin system, they further modified the catalyst structure of Fe(F₂₀TPP)Cl by replacing the *para*-F groups of F₂₀TPP ligand with *N,N*-dimethylamino groups, developing the catalyst [Fe(TF₄DMAP)Cl] ([Fe]-2) (Scheme 13).⁸⁴

In most iron-catalyzed nitrene transfer reactions, the iron-nitrene intermediates have not been isolated for direct characterization. Instead, they are typically studied through indirect control experiments or spectroscopic analysis. However, Mindiola and co-workers successfully isolated the key intermediates involved in the intermolecular reaction catalyzed by ([Fe]-3) (Scheme 14).⁸⁵ The intermediate [Fe-

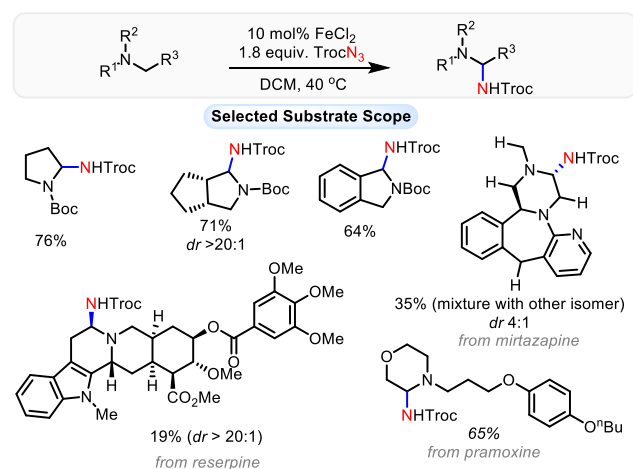
Scheme 14. Isolable Iron-Imido Intermediate in Amination Reaction



[Fe-Int-1] was obtained via a stoichiometric reaction between ([Fe]-3) and 4-*t*-Bu-C₆H₄N₃. Spectroscopic analysis confirmed its S = 1 spin state and an iron center with (+4) oxidation state. Furthermore, the isolated imido complex (Fe-Int-1) underwent reaction with dihydroanthracene, yielding the adduct (Fe-Int-2). These intermediates were identified as essential species in catalytic intermolecular amination catalyzed by ([Fe]-3).

Very recently, Baudoin and Geraci reported an elegant method for the site-selective intermolecular C(sp³)-H amination of *N*-heterocycles (Scheme 15).⁸⁶ This method circumvents the need for the less practical *N*-chloro-*N*-sodiocarbamate reagent for α -amination of heterocycles developed by Chang and co-workers.⁸⁷ Instead, the use of TrocN₃ as the nitrogen source, in combination with an inexpensive FeCl₂ catalyst, offers a more efficient and operationally simple alternative. This approach is compatible with a wide range of amines, including pharmaceutically relevant compounds and complex molecules such as dextro-

Scheme 15. Site Selective Intermolecular C(sp³)-H Amination of *N*-Heterocycles Catalyzed by FeCl₂



methorphan, vortioxetine, reserpine, and mirtazapine. Notably, the selectivity trend observed in this reaction is distinct and complementary to other Fe-catalyzed C-H amination methods, which typically favor benzylic C-H bonds. When substrates containing two heteroatoms, amination occurred exclusively at the α -position to the most electron-rich nitrogen atom. For example, mirtazapine, which contains six potentially reactive C(sp³)-H bonds, underwent selective amination at the most accessible α -methylene position adjacent to the electron-rich nitrogen, despite variations in bond dissociation energies (BDEs).

3.2.1.2. Leveraging Tetrazoles. Furthermore, iron-porphyrins were found to be highly effective for the activation of pyridotetrazole to furnish 2-pyridyl nitrene intermediates. An intermolecular benzylic C(sp³)-H bond amination using tetrazole under iron-porphyrin metalloradical catalysis was reported by the Chattopadhyay group (Scheme 16).⁸⁸ The method enabled the direct installation of 2-pyridyl amine units at the benzylic positions of hydrocarbon substrates, which is

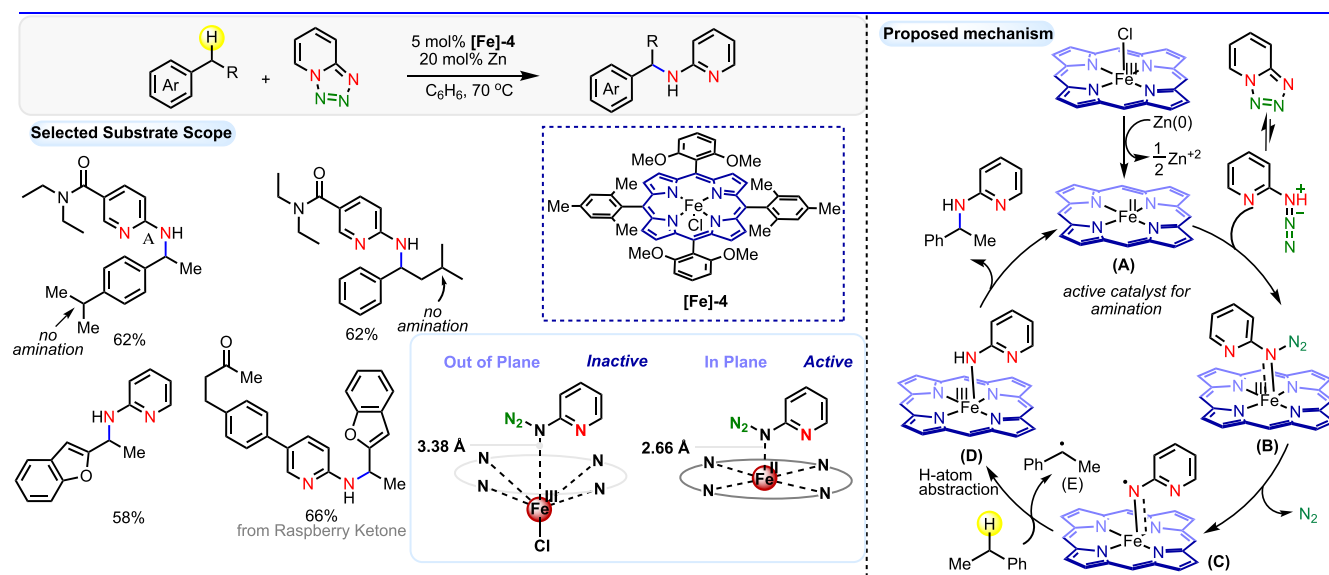
highly beneficial in complex molecular scaffolds for the late-stage amination.

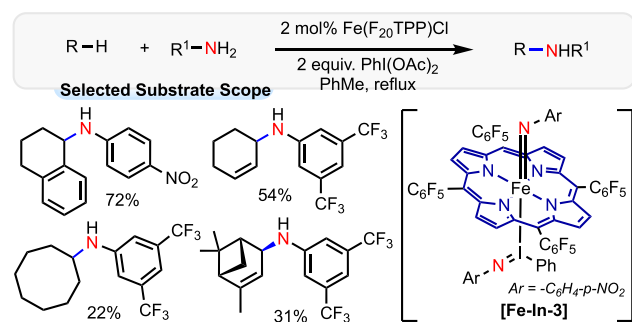
A distinguishing feature of this strategy lies in the in situ generation of Fe(II) porphyrin as the catalytically active species, deviating from conventional nitrene transfer methods that predominantly employ Fe(III) porphyrin complexes for active catalyst. Recently, Mondal and co-workers, through DFT studies, showed⁸⁹ that Fe(III)-porphyrin is catalytically inactive due to its out-of-plane Fe center, leading to a high nitrene formation barrier (35.9 kcal/mol). In contrast, the planar Fe(II)-porphyrin exhibits a much lower barrier (21.4 kcal/mol), accounting for its catalytic activity. The optimal catalyst for this transformation was an iron-porphyrin complex ([Fe]-4) featuring mesityl and 2,6-dimethoxy substituents at the periphery of the porphyrin. The reaction exhibited high selectivity for amination at secondary benzylic positions over tertiary and primary ones. Experimental studies support the formation of a benzylic radical intermediate during the reaction, with hydrogen atom abstraction identified as the rate-limiting step. A mechanism for the amination reaction is displayed in Scheme 16. Initially, Zn reduces the Fe(III)-porphyrin catalyst to its active Fe(II)-porphyrin (A) form via single-electron transfer. The open form of tetrazole then coordinates with the iron center, generating a metal-bound azide complex (B) that leads to the formation of an iron-iminyl radical intermediate (C). This nitrene intermediate subsequently abstracts a benzylic C(sp³)-H hydrogen, yielding intermediates (D and E). Finally, recombination of these intermediates (D and E) affords the aminated product, thereby completing the catalytic cycle. Despite these advancement, use of moderately high temperature limits its application.

Recent surge of photoredox catalysis brought new dimension to organic syntheses. In this vein, Yu, Li, and co-workers reported a visible-light-driven FeCl₃-catalyzed benzylic amination using tetrazole.⁹⁰

3.2.1.3. Incorporating Amines. The Che group employed a “metal catalyst + PhI(OAc)₂ + primary arylamines” amination protocol for C-H bond amination reactions (Scheme 17).⁹¹ This approach streamlined the amination method by eliminating the need for the ex situ generation of nitrene

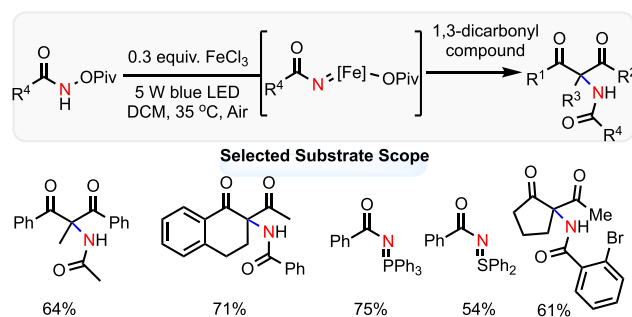
Scheme 16. Iron-Catalyzed Benzylic Amination Using Tetrazole as Nitrene Precursor



Scheme 17. In Situ-Generated Iminoiodinane in Iron-Catalyzed C–H Bond Amination

precursors. This method was found to be effective for the amination of both activated and unactivated C–H bonds. ESI-MS analysis and DFT calculations provided evidence supporting the involvement of an iron-nitrene intermediate (**Fe-Int-3**) in the catalytic cycle.

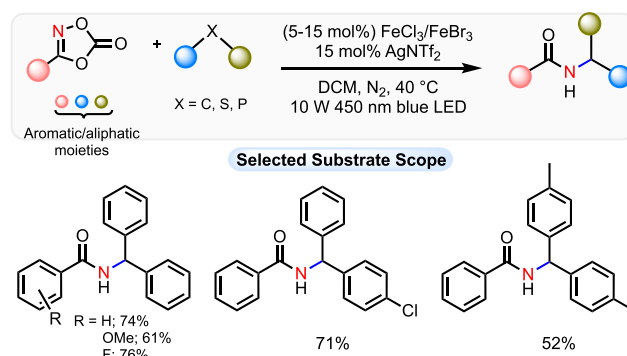
3.2.1.4. Exploiting Carboxamides. Building on the C–H amination studied by Motherwell and co-workers,⁵⁶ Qiu and co-workers developed an efficient FeCl₃-photoredox catalytic method for amide synthesis from readily available *N*-acyloxy benzamides (**Scheme 18**).⁹² Under iron-photoredox catalysis,

Scheme 18. FeCl₃-Photoredox for the Amination of 1,3-Dicarbonyl Compounds

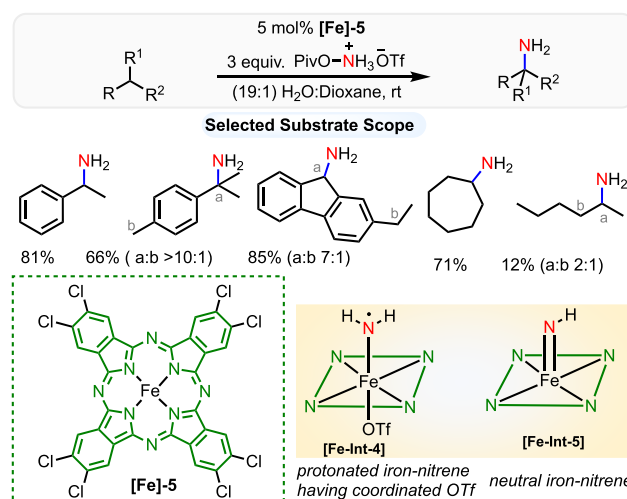
N-acyloxy benzamides generated an iron-benzoyl nitrenoid intermediate, which inserted into the C(sp³)–H bond of 1,3-dicarbonyl compounds, yielding monoamidated dicarbonyl products. This strategy was successfully extended to acyl nitrene insertion into various bonds, including C(sp²)–H, benzylic C(sp³)–H, sulfur- and phosphorus-containing molecules.

3.2.1.5. Utilizing Dioxazolones. In 2021, the Bao group reported a synergistic report on visible light promotion and iron catalysis for intermolecular nitrene transfer reactions incorporating dioxazolones to forge C(sp³)–N, N=S, and N=P bonds (**Scheme 19**).⁹³ This synthetic maneuver is devoid of any exogenous-ligands and excellently compatible with almost more than 100 substrates under ambient reaction conditions. DFT study and other experimental reports bolstered the intervention of radical pathway and degree of decarboxylation highly depends on the conversion of ground state sextet of the intermediated dioxazolone-bound iron species to the quartet spin state via visible-light irradiation through intersystem crossing.

3.2.1.6. Using Hydroxylamine Esters. Iron-phthalocyanine catalysis has proven highly effective for the direct installation of primary amines at various types of C(sp³)–H bonds, including

Scheme 19. Visible-Light and Iron Catalysis for Nitrene Transfer Reactions of Dioxazolones

benzylic, allylic and aliphatic C–H bonds introducing hydroxylamine ester (**Scheme 20**).⁹⁴ Conventional nitrene

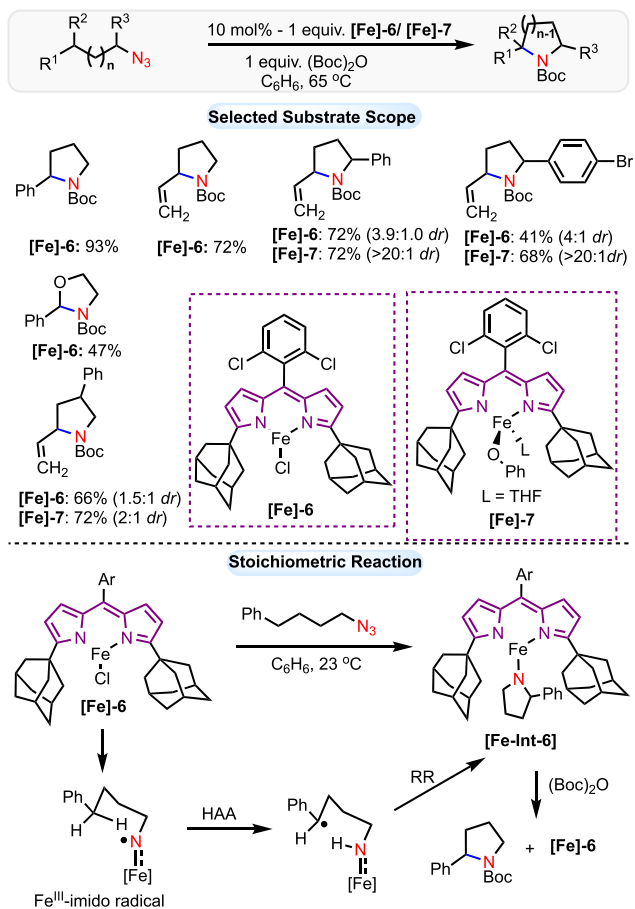
Scheme 20. Iron-Catalyzed Primary Amination of C(sp³)–H Bonds

transfer reactions typically proceed via *N*-protected metal-nitrene intermediates, thereby requiring additional deprotection steps to access primary amines. In contrast, this method bypasses such limitations by utilizing unprotected metal-nitrene species, allowing direct and efficient synthesis of primary amines. However, poor chemo- and regioselectivity were observed, particularly for allylic and aliphatic chain substrates. DFT calculations suggest that the active intermediate in the amination reaction is a protonated iron-nitrene species, denoted as [(Cl₈PcFeNH₂)⁺(OTf)[−]], in which the triflate anion (TfO[−]) coordinates to the iron center ([**Fe-Int-4**]). This protonated species is energetically more favorable than the neutral iron-nitrene [[**Fe-Int-5**]] analogue (neutral iron-nitrene was generally proposed for enzymatic C–H primary amination reactions) by 27.5 kcal/mol. Moreover, the reaction works well and is also amenable to late-stage functionalization.

3.2.2. Iron-Catalyzed C(sp³)–H Amination (Intramolecular). **3.2.2.1. Leveraging Organic Azides.** In 2011, Betley and co-workers demonstrated that exposure of an iron(III)-dipyrinato complex to aryl or alkyl azides generated an Fe(III)-dipyrinato imido radical species. This species underwent hydrogen atom abstraction (HAA) and radical

recombination (RR), facilitating insertion into the benzylic C–H bond of toluene (Scheme 21).⁹⁵ Subsequently, they

Scheme 21. Iron-Dipyrrinato Complex in Intramolecular Alkyl Azide Amination



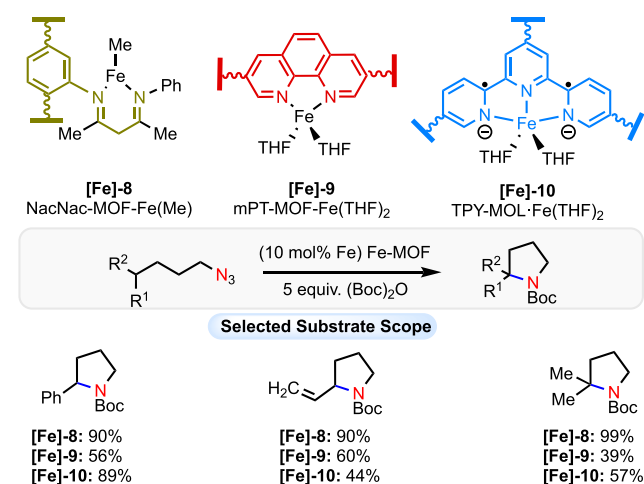
extended this strategy to the intramolecular amination of alkyl azides.⁹⁶ Interestingly, the initial reaction was limited to a stoichiometric process, as catalytic turnover failed in the intramolecular amination. This was attributed to the inhibition of the catalytic cycle by the resulting *N*-heterocycle, which coordinated with the iron-dipyrrinato species to form a stable complex ([Fe]-6). The structure of complex [Fe-Int-6] was confirmed by X-ray crystallography. To overcome this limitation, (Boc)₂O proved to be an efficient additive. It reacted with the pyrrolidine product, reducing its nucleophilicity, thereby preventing the formation of complex [Fe-Int-6]. As a result, the catalytic efficiency of the iron-dipyrrinato complex ([Fe]-6) was restored. This catalytic system exhibited broad substrate scope, tolerating various types of C–H bonds, including benzylic, allylic and aliphatic secondary and tertiary positions. The corresponding amination products were obtained in moderate to high yields. To investigate the mechanism, radical clock experiments were performed, which revealed no detectable ring-opening products. This suggests that if a radical intermediate is involved, its lifetime is short due to a rapid recombination process. However, the possibility of the direct C–H amination pathway also may not be ruled out.

It was observed that the intramolecular amination using the catalyst ([Fe]-6) shows low diastereoselectivity. To improve the diastereoselectivity, Betley et al. screened various

dipyrrinato iron-alkoxide and aryloxide complexes (Scheme 21).⁹⁷ They discovered that the phenolate complex ([Fe]-7) efficiently catalyzed the cyclization of alkyl azides with allylic and benzylic C–H bonds, yielding *syn*-2,5-disubstituted pyrrolidines with excellent diastereoselectivity. DFT calculations suggest that the observed diastereoselectivity arises from interactions between the phenolate ligand and the iron center, likely involving π -bonding. These interactions create increased steric hindrance with the substrate, influencing the diastereoselective outcome of the reaction.

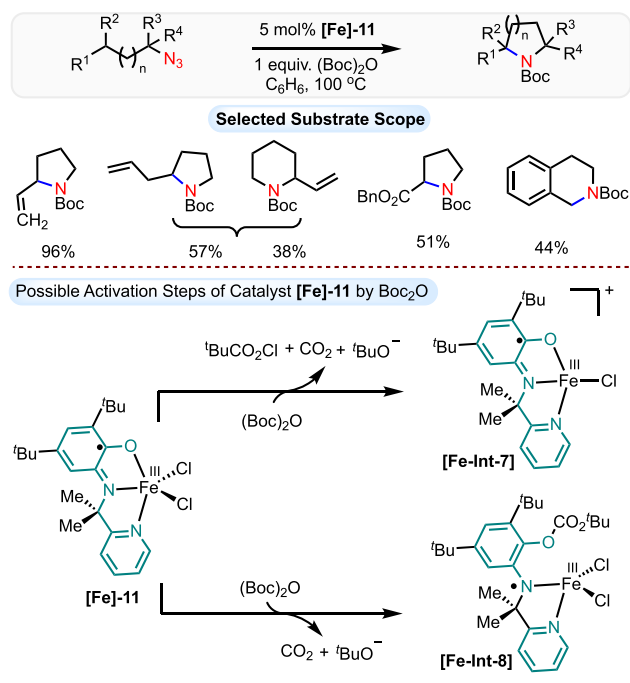
In 2016, Lin and co-workers developed UiO-type MOFs functionalized catalysts using (β -diketimate)iron,⁹⁸ (phenanthroline)iron,⁹⁹ and (terpyridine)iron¹⁰⁰ to facilitate intramolecular C(sp³)–H bond amination of organic azides (Scheme 22).

Scheme 22. Iron-MoF-Catalyzed Intramolecular Amination



These catalysts efficiently facilitated the amination of aliphatic azides, yielding α -substituted pyrrolidines with satisfactory yields. The analysis of substrate scope showed that whereas these MOF-based catalysts successfully aminated benzylic and allylic C(sp³)–H bonds, but their effectiveness in amination of secondary and tertiary aliphatic C(sp³)–H bonds was only moderate. Notably, the MOF-supported catalysts outperformed their homogeneous counterparts. For example, while sterically hindered substrates were found to be well tolerated that afforded gem-disubstituted pyrrolidines in quantitative yield, but analogous homogeneous catalysts failed to provide the desired product. Furthermore, the MOF-supported catalysts exhibited excellent recyclability, maintaining their catalytic efficiency even after a second reuse with no significant decrease in performance.

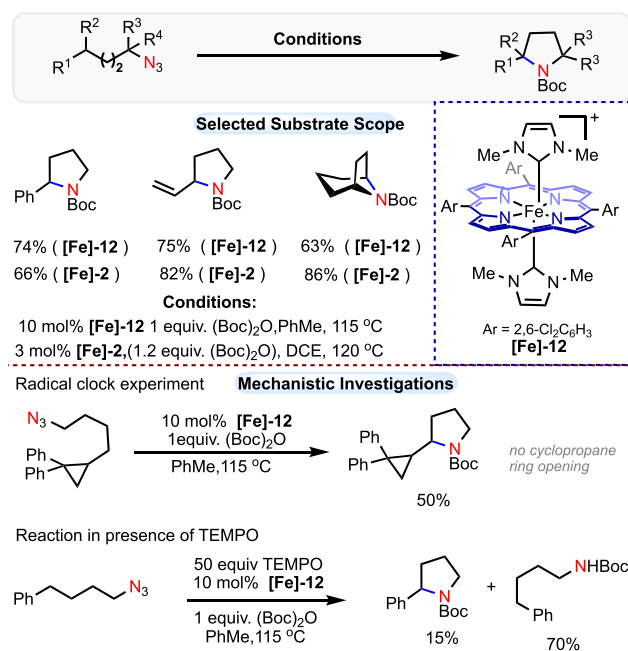
In 2017, de Bruin, van der Vlugt, and co-workers developed a novel, air-stable, high-spin iron(III) complex [Fe(NNOISQ)-Cl₂] ([Fe]-11) (ISQ = iminosemiquinonato) featuring a redox-active pyrido-aminophenol ligand for the intramolecular C–H bond amination of alkyl azides (Scheme 23).¹⁰¹ The radical in the ligand is antiferromagnetically coupled with the high-spin iron(III) center, resulting in an overall spin state of *S* = 2. In combination with (Boc)₂O, the catalyst efficiently generated pyrrolidine products from alkyl azides. However, in nearly all cases, significant amounts of linear amine byproducts were also observed. The reaction was hypothesized to proceed via iron-imido species as key intermediates, though their structural characteristics remained unclear. Kinetic studies

Scheme 23. $[\text{Fe}(\text{NNO}^{\text{ISQ}})\text{Cl}_2]$ -Catalyzed Intramolecular Amination

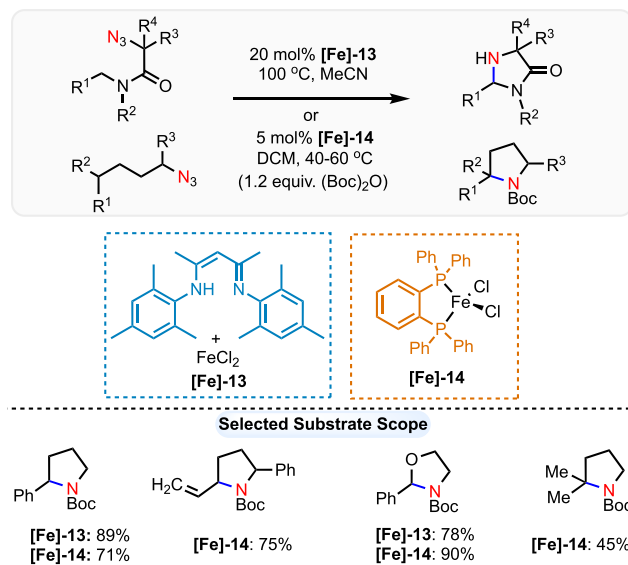
were conducted to identify the rate-determining step of the amination reaction. Surprisingly, the reaction followed zero-order kinetics with respect to the azide substrate, while being first-order in both the iron catalyst and $(\text{Boc})_2\text{O}$. Two possible active catalysts (**Fe-Int-7** and **Fe-Int-8**) were proposed, both generated through the reaction between $(\text{Boc})_2\text{O}$ and the precatalyst (**[Fe]-11**).

In 2018, the Che group demonstrated that iron-porphyrins are among the most effective catalysts for intramolecular $\text{C}(\text{sp}^3)\text{-H}$ amination of aliphatic azides. In particular, an iron-porphyrin complex $[\text{Fe}(\text{TDCPP})(\text{NHC})_2]\text{I}$ (**[Fe]-12**) featuring an axial *N*-heterocyclic carbene (NHC) ligand showed high efficiency in aminating a broad range of C-H bonds, including benzylic, allylic, tertiary, secondary, and even primary $\text{C}(\text{sp}^3)\text{-H}$ bonds, affording the corresponding pyrrolidines in high yields (Scheme 24).¹⁰²

Furthermore, mass spectrometry and DFT studies suggested that the catalytic cycle begins with thermally induced dissociation of one NHC ligand from the iron center of the catalyst, yielding the $[\text{Fe}(\text{TDCPP})(\text{NHC})]^\dagger$ species. This species interacts with an alkyl azide to form $[\text{Fe}(\text{TDCPP})(\text{NHC})(\text{N}_3\text{R})]^\dagger$ followed by azide decomposition and subsequent nitrene insertion into C-H bond, ultimately yielding the amination product. DFT calculations supported the importance of NHC ligand, as it helps to attain the ruffled conformation of the entire porphyrin system thereby it kicks the $\text{Fe}(\text{III})$ out of the plane and make the azide adduct formation slightly exergonic. Furthermore, because of the high efficiency of $[\text{Fe}(\text{TDCPP})(\text{NHC})_2]$ in aminating diverse C-H bonds, the species was utilized for the synthesis of complex nitrogen-containing heterocyclic compounds. In a subsequent study, the same group found that the catalyst $[\text{Fe}(\text{TF}_4\text{DMAP})\text{-Cl}]$ (**[Fe]-2**) displayed significantly higher efficiency in intramolecular C-H bond amination of alkyl azides in comparison to $[\text{Fe}(\text{TDCPP})(\text{NHC})_2]\text{I}$ (**[Fe]-12**), requiring only 1 mol % catalyst loading (reduced from 10 mol %).¹¹⁵ In

Scheme 24. Iron-Porphyrin(NHC)-Complex in C-H Bond Amination

2019 Yu et al. developed a straightforward method for the preparation of poly substituted imidazolinones from alkyl azides using a combination of FeCl_2 and a β -diketiminate ligand (Scheme 25).¹⁰³ While this catalytic system benefits

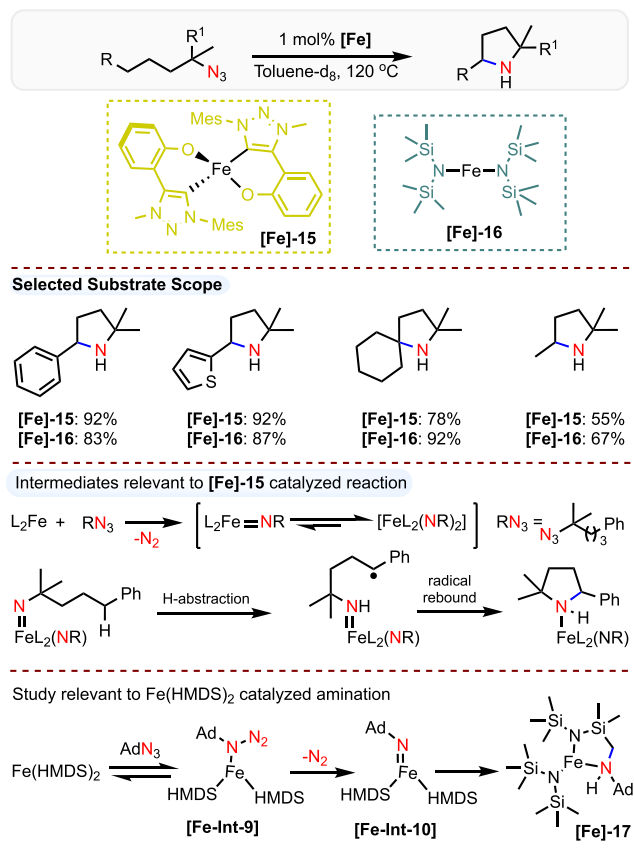
Scheme 25. Synthesis of Imidazolinones via Iron-Catalyzed Nitrene Transfer Reaction of Alkyl Azides

from its simplicity, it requires high reaction temperatures (100 °C) and a relatively high catalyst loading (20 mol %) to achieve complete conversion and high yields.

To overcome these limitations, the same group introduced a more efficient iron-phosphine complex (**[Fe]-14**), which operates at a lower temperature (40 °C) and with a reduced catalyst loading (5 mol %).¹⁰⁴ This improved catalytic system delivered imidazolinone products in comparable yields to those obtained with the FeCl_2 - β -diketiminate catalyst. Most

importantly, the amination reaction did not necessitate (Boc)₂O as an additive in case of tertiary alkyl azides, this is possibly because of the sterically crowded N-atoms that facilitate the product elimination from the catalyst pocket. Further, Liu and co-workers found that FeBr₂ can also facilitate C(sp³)-H amination of primary alkyl azides to produce imidazolinones without the employment of external ligand.¹⁰⁵ In 2021, the Albrecht group reported a homoleptic C,O-chelating mesoionic carbene-iron complex ([Fe]-15) for the amination of tertiary alkyl azides (Scheme 26).¹⁰⁶ Due to the

Scheme 26. Iron-Mesoionic Carbene Complex and Fe(HMDS)₂ for Catalytic Intramolecular C–H Amination



presence of a tertiary group adjacent to the nitrogen atom, this reaction did not require additional protecting groups. The catalytic method facilitated the activation of a broad range of C–H bonds, including benzylic, primary, secondary and tertiary C–H bonds. Kinetic studies revealed a first-order and half-order dependence on substrate and catalyst concentration respectively, suggesting a unique mechanistic pathway in which a Fe-bis-nitrene intermediate was formed by consecutive N₂ extrusions. The Fe-bis-nitrene proceeds via H-abstraction/radical rebound, affording the final amination products.

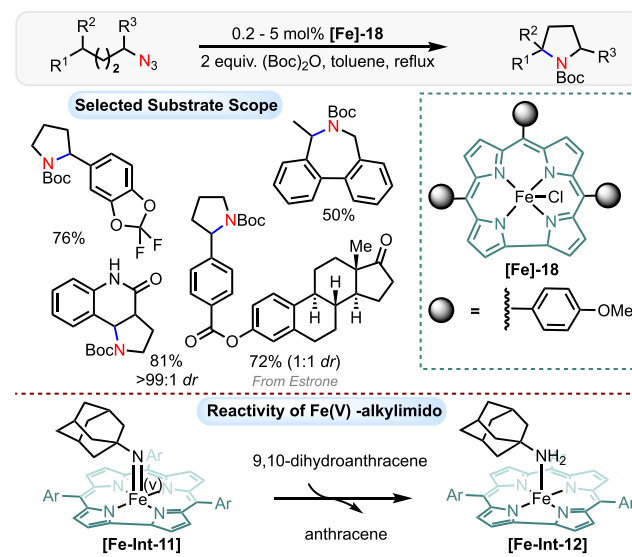
The reaction mechanism was further supported by the DFT studies, which revealed that the second N₂ elimination was the rate-limiting step of the whole reaction.¹⁰⁷ They further reported silicone-based ligand containing iron catalysts, which were devoid of multistep synthesis of the ligand precursors (Scheme 26).¹⁰⁷ They showed that the air-sensitive iron complex Fe(HMDS)₂ (HMDS = bis(trimethylsilyl)amine) could efficiently catalyze the intramolecular C–H amination of alkyl azides, achieving catalytic efficiencies comparable to those

observed with the homoleptic C,O-chelating mesoionic carbene-iron complex ([Fe]-15).

To address the air sensitivity of Fe(HMDS)₂, the same group identified an alternative, commercially available iron salt, FeI₂, which rapidly and selectively catalyzed the amination of various C–H bonds.¹⁰⁸ To gain mechanistic insight into the Fe(HMDS)₂-catalyzed reaction, they performed a stoichiometric reaction between Fe(HMDS)₂ and AdN₃, leading to the isolation of a stable iron α -N-coordinated organoazide complex ([Fe]-Int-9), which was characterized via spectroscopic analysis. Photocrystallographic studies revealed that ([Fe]-Int-9) gradually loses N₂, resulting in Fe–N bond shortening and the formation of an iron imido/nitrene complex ([Fe]-Int-10). In solution, the nitrene moiety is inserted into a C–H bond of the N(SiMe₃)₂ ligand, yielding a C–H bond amination product ([Fe]-17), which was also characterized spectroscopically. However, efforts to isolate an Fe(NAD) complex ([Fe]-Int-10) were unsuccessful.

While Fe(III)(NR) and Fe(IV)(NR) complexes have been extensively studied for C(sp³)-H functionalization, the use of high-valent Fe(V)(NR) species remained largely unexplored. Such species can provide valuable insights into the structure–reactivity relationships in Fe(III)-catalyzed C–H aminations as well as other nitrene transfer reactions. In this context, very recently, Che and co-workers studied the C(sp³)-H amination by using iron corrole complex that operates via an iron(V)-alkylimido intermediate (Scheme 27).¹⁰⁹ The iron corrole

Scheme 27. Iron Corrole-Catalyzed Intramolecular Amination of Alkyl Azide

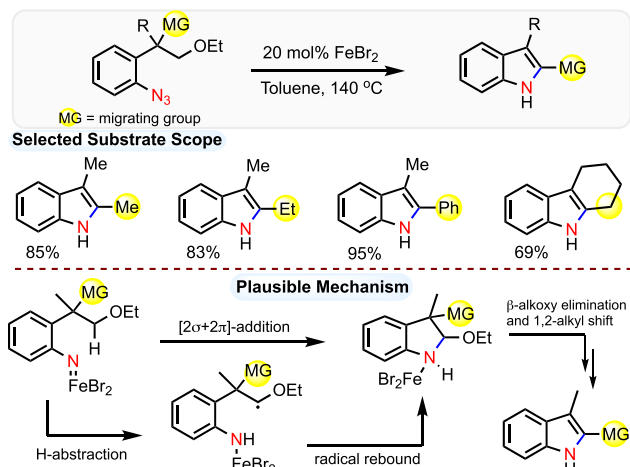


complex ([Fe]-18) was found to be highly effective for amination of diverse C–H bonds which requires only 0.2 mol % of catalyst loading. The catalyst was also found to generate several TON (up to 3880) for C–H amination reaction which was in general rare for this type of reaction. Additionally, the reaction yielded excellent diastereoselectivities (99:1 dr) in all cases and was successfully applied to the late-stage modification of various complex natural products and drug molecules.

In 2013, Driver and co-workers discovered that under FeBr₂ catalysis, phenyl azides bearing *ortho*-alkoxy groups underwent conversion to 2,3-disubstituted indoles via a tandem process

involving etheral C–H bond amination, β -alkoxy elimination, and a 1,2-alkyl shift (Scheme 28).¹¹⁰ This reaction proceeded via a concerted $[2\sigma + 2\pi]$ addition between the iron-imido species and the C–H bond, leading to C–N bond formation.

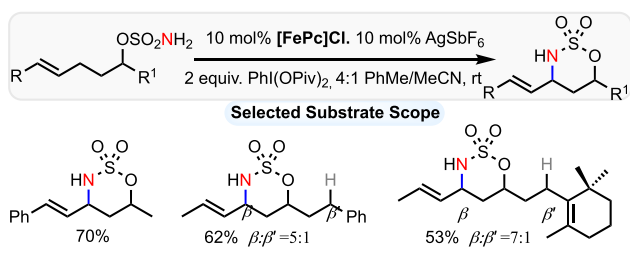
Scheme 28. FeBr₂-Catalyzed Intermolecular C–H Amination of *ortho*-Substituted Aryl Azides



The preference for the 1,2-shift followed the trend: Me < 1° < 2° < Ph. Later, Ren et al. investigated the reaction mechanism through DFT studies.¹¹¹ Their study revealed that the C–H amination did not follow the classical radical rebound pathway. Instead, it proceeded via a concerted $[2\sigma + 2\pi]$ addition between the iron-imido species and the C–H bond, leading to C–N bond formation.

3.2.2.2. Incorporating Sulfonamides. In 2012, White and Paradine reported a highly selective allylic C–H amination of sulfamate esters using an iron-phthalocyanine catalyst (Scheme 29).¹¹² This system exhibited a strong preference for allylic C–

Scheme 29. Fe-Catalyzed Intramolecular Allylic C–H Amination



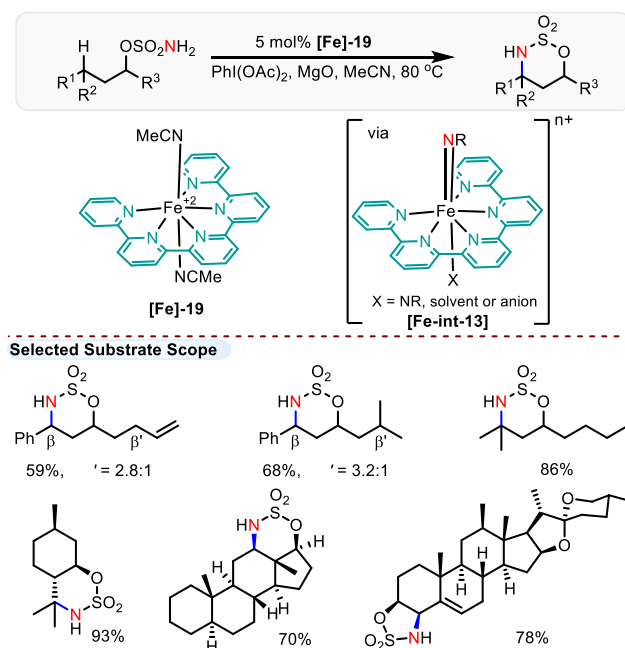
H bond amination over other C–H bonds, following the selectivity trend: allylic > benzylic > etheral > 3° > 2° $\gg$ 1°. The site selectivity was further influenced by steric and electronic factors. For instance, substrates with electron-withdrawing groups adjacent to the allylic C–H bond showed lower amination efficiency. Consistently, in polyolefin-containing substrates, amination occurred preferentially at the more electron-rich allylic C–H bond.

When sterically distinct allylic C–H sites were present, the reaction favored the less hindered position. A radical pathway was proposed for this transformation. To probe the mechanism, the amination of (*Z*)-hept-5-en-2-yl sulfamate (*Z*/*E* > 20:1) was examined, resulting in a significant decrease in the *Z*/*E* ratio (to 9:1), suggesting the formation of a

stabilized allyl radical. Additionally, an intermolecular kinetic isotope effect (KIE) of 2.5 was observed, supporting a mechanism involving hydrogen abstraction and radical rebound. Interestingly, a direct comparison between the iron-phthalocyanine and Rh₂(OAc)₄ catalysis highlights the key differences in reactivity. While the iron catalyst strongly favored allylic C–H amination, the rhodium system led to a considerable amount of aziridination. Furthermore, the [FeIII(Pc)] catalyst demonstrated superior selectivity in distinguishing between energetically distinct C–H bonds compared to Rh₂(OAc)₄.¹¹²

In 2013, Che et al. described the intramolecular amination of sulfamate esters using a seven-coordinate quinquepyridine-supported iron complex ([Fe]-19) (Scheme 30).¹¹³ This

Scheme 30. Iron-Catalyzed Intramolecular Amination of Sulfamate Esters

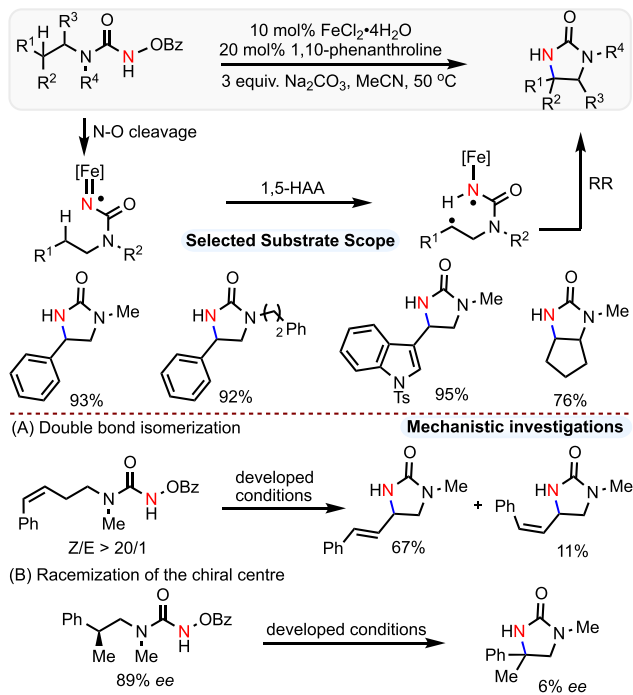


complex exhibited high efficiency in facilitating the amination of various substrates, including benzylic and allylic sulfamate esters even in the presence of multiple C–H bonds within a substrate. Notably, benzylic C(sp³)–H bonds were preferentially aminated over tertiary C(sp³)–H bonds, benzylic C(sp³)–H bonds over allylic C(sp³)–H bonds, and tertiary C(sp³)–H bonds over secondary C(sp³)–H bonds. Furthermore, this amination method was successfully applied to substrates with complex molecular architectures, such as isononane, menthane, spirost-5-ene, choline, and androstane frameworks, consistently affording high yields of the aminated products. The catalytic activity of the iron complex Fe(qpy)-(MeCN)₂₂ was attributed to the formation of a reactive cationic seven-coordinate iron-imido/nitrene intermediate, [Fe(qpy)(NR)(X)]ⁿ⁺ (where X represents NR, solvent, or an anion) ([Fe]-Int-13).

This conclusion was supported by experimental evidence, including ESI-MS analysis, and followed by DFT studies. Additionally, computational studies revealed that the iron-imido intermediate exhibited radical character at the imido moiety, highlighting its unique electronic structure and reactivity.

3.2.2.3. Utilizing Carboxamides. In 2021, the Meggers group reported an efficient iron-catalyzed C(sp³)–H amination using a simple catalyst system comprising iron(II) chloride and 1,10-phenanthroline (Scheme 31).¹¹⁴ This

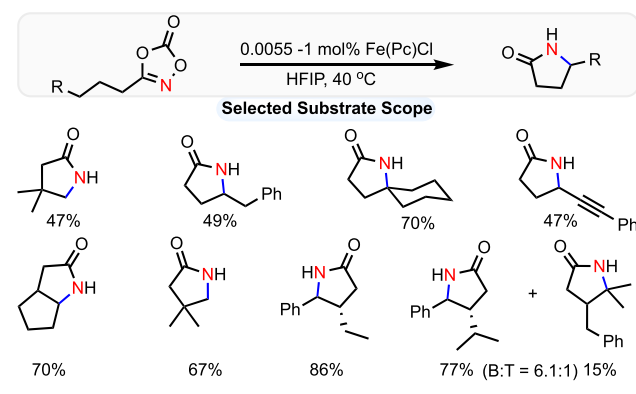
Scheme 31. Iron-Catalyzed Amination of Activated and Unactivated C(sp³)–H Bonds



method enables the direct C–H amination of *N*-benzoyloxycarbonyl ureas to afford imidazolidin-2-ones in high yields. The reaction is highly effective for the benzylic, allylic, propargylic and even nonactivated aliphatic C(sp³)–H bonds. Notably, this amination proceeds under open-flask conditions. A proposed mechanism is shown in Scheme 31. This involves the coordination of the active Fe(II) species to *N*-benzoyloxycarbonyl urea, followed by base-induced deprotonation and benzoate elimination to generate an iron nitrenoid intermediate. In its triplet state, this intermediate undergoes 1,5-hydrogen atom transfer (HAT), forming a radical intermediate, which rapidly undergoes radical rebound to form the C–N bond. Several control experiments supported this mechanistic proposal. For example, in the allylic C–H amination of a *Z*-alkene, the reaction resulted in isomerization of the double bond, indicating the generation of an allylic radical intermediate. Furthermore, loss of stereochemical integrity in the C–H amination of a substrate with a chiral center reinforced the stepwise nature of hydrogen abstraction followed by radical rebound, ruling out a concerted nitrene insertion mechanism.

3.2.2.4. Involving Dioxazolones. Using dioxazolone precursors, Chang and Kweon developed an iron-phthalocyanine-catalyzed intramolecular C–H amidation for the preparation of γ -lactam derivatives (Scheme 32).¹¹⁵ This method showcased the initial instance of lactam preparation through direct C–H amination utilizing an iron-acyl nitrenoid intermediate, which successfully inhibited the competitive Curtius-type rearrangement. The reaction was highly efficient, requiring extremely low catalyst loading (0.0055 mol % of PcFe(III)Cl) under an air atmosphere. This method enabled the amidation of primary

Scheme 32. Iron-Phthalocyanine-Catalyzed Intramolecular C–H Amidation



and secondary aliphatic, secondary benzylic and propargylic C(sp³)–H bonds. The catalytic system showed selectivity in the order of benzylic > tertiary >> secondary C(sp³)–H bonds. Experimental and computational studies suggested that the reaction proceeded via an iron-imidyl radical intermediate, followed by hydrogen atom abstraction and rapid radical rebound. The key C–N bond-forming step occurs in a stepwise manner via this radical intermediate. The remarkably high turnover numbers (up to 47 000) observed for the catalytic system are attributed to its durability in the presence of oxygen and efficient catalyst regeneration.

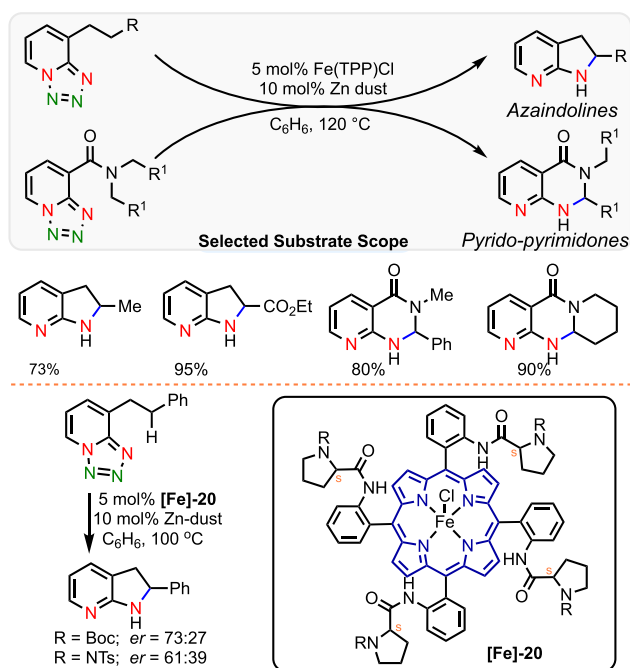
Additionally, the catalyst's high activity is rationalized by the facile spin interconversion of the iron species, which enhances the overall catalytic efficiency.

3.2.2.5. Introducing Tetrazoles. The Chattopadhyay group demonstrated that 1,2,3,4-tetrazoles can easily be employed as aminating reagent for a series of reactions using iron-porphyrin metalloradical catalysis. It was reported that an iron-porphyrin can efficiently be used for the intramolecular sp³ C–H amination reaction of 1,2,3,4-tetrazoles bearing unactivated primary, secondary, and tertiary C–H bonds (Scheme 33).¹¹⁶ This method enabled the efficient synthesis of a diverse array of aza-indoline derivatives in high yields. The reaction tolerated not only alkyl chain substitution at the C8 position of the tetrazole but also tetrazoles featuring an amide unit, where α -C–H bonds adjacent to the amide were effectively aminated, affording pyridopyrimidones as the final desired product. The potential of this method for enantioselective C(sp³)–H amination was also explored. After screening several chiral catalysts, it was found that ([Fe]-20) catalyzed the reaction quantitatively, yielding the aminated product with an enantiomeric ratio of 73:27, which suggested that upon suitable catalyst design through ligand modification, enantioselective may be improved significantly. A radical rebound mechanism was proposed for the transformation.

3.2.3. Enantioselective C(sp³)–H Amination. While racemic Fe-catalyzed nitrene transfer (NT) reactions have been widely explored, there are only a few reports of asymmetric NT reactions catalyzed by nonenzymatic iron complexes.

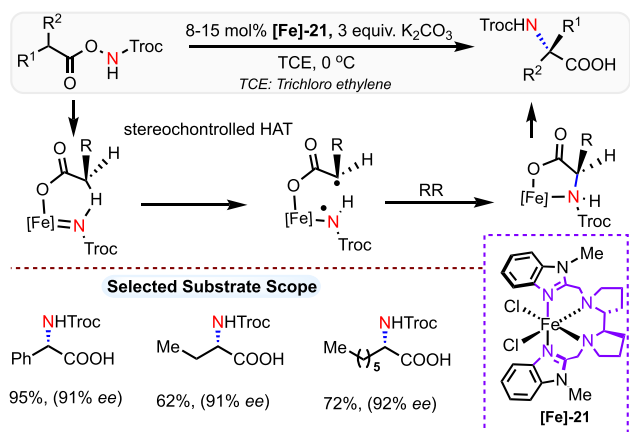
3.2.3.1. Using Carboxamides. In 2022 Meggers et al. expanded the scope of iron-catalyzed nitrene transfer reactions to prepare optically active α -amino acids via a stereocontrolled 1,3-nitrogen shift (Scheme 34).¹¹⁷ In this approach, abundant and readily available carboxylic acids served as starting

Scheme 33. Iron-Catalyzed Amination of Strong Aliphatic C(sp³)-H Bonds



materials, which were first functionalized into their corresponding azanyl ethers.

Scheme 34. Stereocontrolled 1,3-Nitrogen Migration for Synthesizing Chiral α -Amino Acids

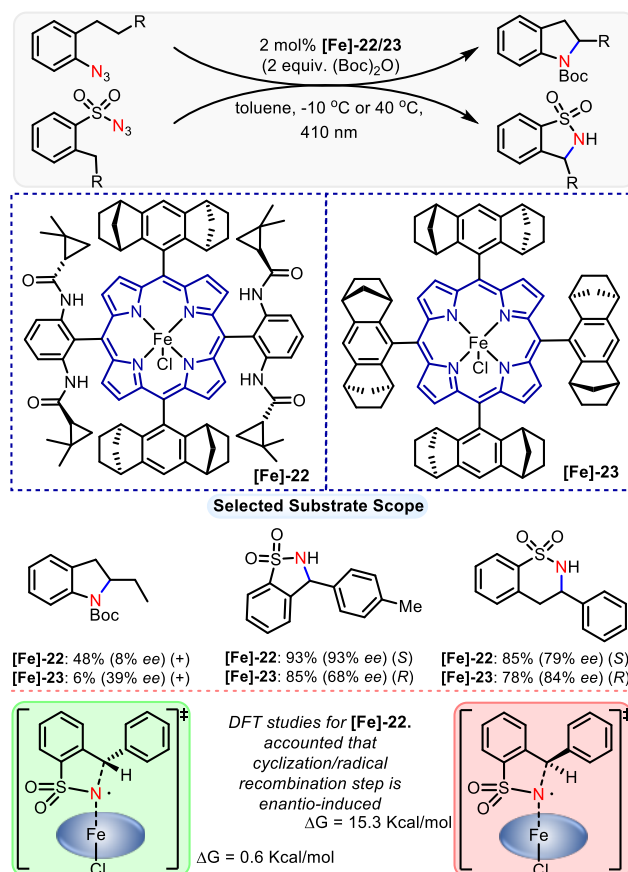


The azanyl ethers then underwent an intramolecular, highly regio- and stereocontrolled 1,3-amine transfer, yielding chiral α -amino acid derivatives under the influence of the iron catalyst (*R,R*)-FeBIP (BIP = 2,2'-bipyrrrolidine). The (*R,R*)-FeBIP catalyst demonstrated exceptional efficiency in producing chiral α -amino acids, irrespective of the side chains (activated and nonactivated). In contrast, ruthenium catalysis gave optimal results only when the substrate contained activated side chains, such as aryl, allyl, or propargyl groups. A mechanism for the 1,3-nitrogen shift reaction is shown in Scheme 34. This strategy allows enantioselective amination of carboxylic-acid-containing drugs and natural products, and enables the synthesis of unnatural α -amino acids.

3.2.3.2. Leveraging Organic Azides. In 2023, Che group reported a photoinduced asymmetric intramolecular C(sp³)-

H amination catalyzed by chiral iron complexes based on meso- and β -substituted porphyrins (Scheme 35).¹¹⁸ This

Scheme 35. Chiral Iron Porphyrins-Catalyzed Enantioselective Intramolecular C(sp³)-H Bond Amination

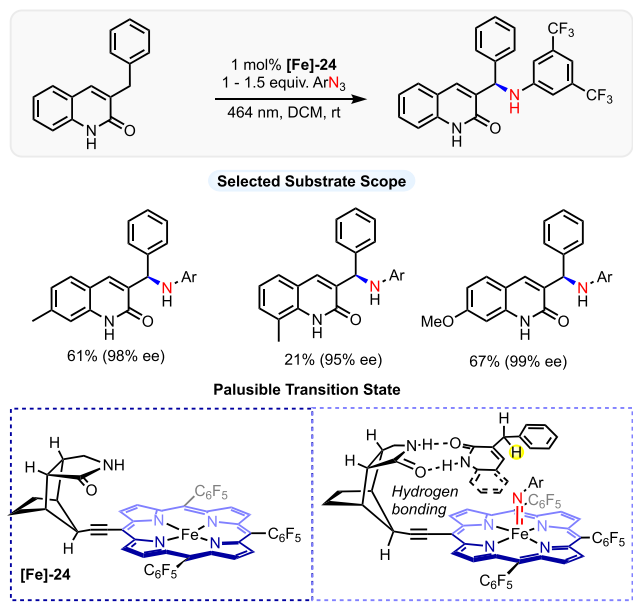


method enables the synthesis of chiral indolines and benzofused cyclic sulfonamides from aryl and arylsulfonyl azides, delivering up to 93% *ee*. Upon photoradiation, the azide functionality is activated to form an iron-nitrenoid intermediate. This reactive species stereoselectively abstracts a hydrogen atom from the C-H bond, followed by radical recombination to forge the desired C-N bond. DFT studies revealed that enantioselectivity arises from cooperative non-covalent interactions particularly hydrogen bonding and steric effects between the Fe(NSO₂Ar) unit and the peripheral substituents on the chiral porphyrin scaffold. Substrate scope analysis showed that high enantioselectivity was achieved with substrates bearing activated C-H bonds adjacent to aryl groups.

In contrast, substrates with unactivated C(sp³)-H bonds, lacking nearby aromatic rings afforded only moderate enantioselectivity. These findings suggested that there might be π - π interactions between the porphyrin ligand and substrate's aryl unit that significantly contributed to the stereochemical outcome of the reaction.

Bach and co-workers reported an asymmetric amination of 3-benzylquinolones mediated by visible light and a chiral iron porphyrin complex (Scheme 36).¹¹⁹ They showed that a chiral iron porphyrin catalyst ([Fe]-24), featuring a lactam moiety as a two-point hydrogen bonding site, effectively facilitates the intermolecular amination of various heterocyclic substrates

Scheme 36. Iron Porphyrin-Catalyzed Intermolecular Enantioselective Amination Reactions Mediated by Visible Light

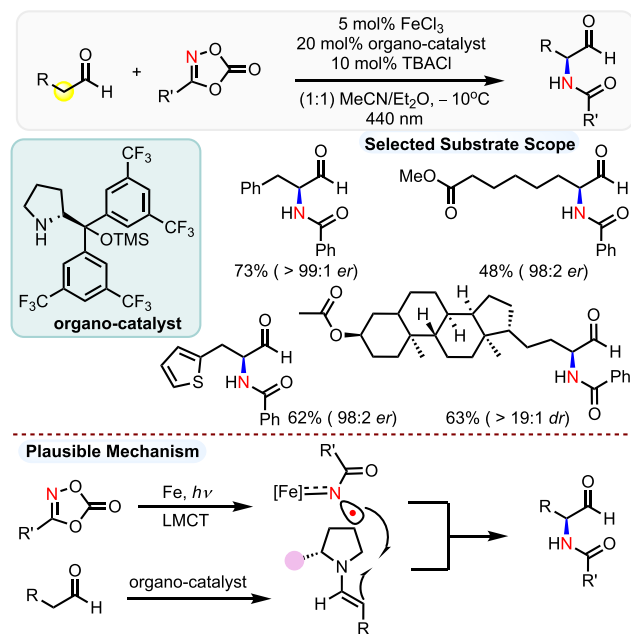


with high enantioselectivity. The two-point hydrogen bonding interactions between the substrate and the porphyrin ligand framework governs the enantioselectivity of the reaction proficiently. Notably, the corresponding manganese porphyrin complex was found to be completely inactive in the amination reaction.¹¹⁹

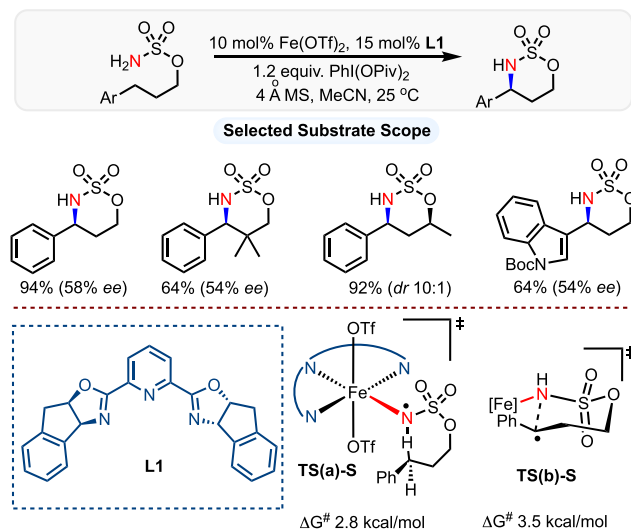
3.2.3.3. Incorporating Dioxazolone. Leveraging dual iron and chiral enamine catalysis, the Chang group reported¹²⁰ an enantioselective α -amination of aldehydes. They used FeCl_3 in combination with a chiral enamine catalyst. This method demonstrated broad substrate scope and high enantioselectivity. The α -amination was successfully applied to a variety of bioactive aldehydes. Mechanistic studies revealed that visible-light-promoted the LMCT to in situ generation of $[\text{Fe}(\text{II})-\text{Cl}_3^-]$ which efficiently activates dioxazolones to generate an iron-acyl nitrenoid radical intermediate. This reactive intermediate subsequently inserts into the chiral enamine, delivering the α -amination product. Importantly, this method is an excellent example for a suitable merger of Fe-nitrenoid with chiral enamine catalysis. The proposed mechanism is illustrated in Scheme 37.

3.2.3.4. Utilizing Sulfonamides. Recently, Schomaker, Liu, and co-workers reported¹²¹ an $\text{Fe}(\text{OTf})_2$ catalyst supported by a chiral Indane-derived PyBOX ligand (L1) for the enantioselective intramolecular NT of homo- and bis-homobenzylic sulfamates (Scheme 38). Computational studies revealed that the radical rebound step is enantio-determining and is influenced by key noncovalent interactions (NCIs) between the ligand and the aryl moiety of the substrate that govern the observed enantioselectivity. A chairlike transition state, as shown in Scheme 38, was proposed as the energetically exergonic. Kinetic isotope effect (KIE) studies—both intramolecular ($\text{KIE} = 1.56$) and competitive intermolecular—indicate that hydrogen atom transfer (HAT) is unlikely to be the rate-determining step, suggesting that formation of the iminoiodinane intermediate may be rate-limiting.

Scheme 37. Organo-Iron Dual Catalysis in Visible-Light-Promoted Enantioselective α -Amination of Aldehydes



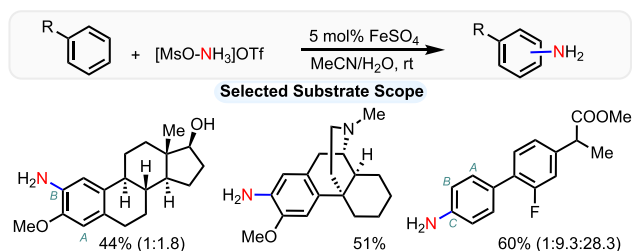
Scheme 38. Asymmetric Intramolecular Iron-Catalyzed Nitrene Transfer into Benzylic C–H Bonds



3.2.4. Iron-Catalyzed $\text{C}(\text{sp}^2)\text{--H}$ Amination (Intermolecular). The direct installation of an amine functionality through nitrene transfer is a powerful strategy for accessing aniline derivatives in a single step. In 2016, Morandi and co-workers reported a method wherein FeSO_4 serves as the catalyst and $[\text{MsO-NH}_3]\text{OTf}$ acts as the amine source, enabling the synthesis of a wide range of primary anilines without the need for directing groups (Scheme 39).¹²²

This method was successfully applied to the late-stage functionalization of bioactive molecules. Mechanistic studies showed that electron-rich substituents on the aryl ring accelerated the reaction rate, whereas electron-withdrawing groups significantly slowed it down. A kinetic isotope effect ($\text{KIE} = 1$) indicated that C–H bond cleavage is not the rate-limiting step. These findings support the electrophilic aromatic substitution (EAS) pathway for the reaction. In a related study,

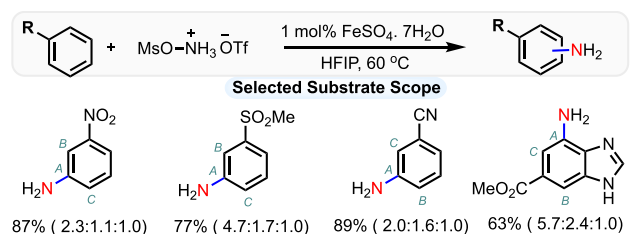
Scheme 39. Synthesis of Primary Anilines through Iron-Catalyzed C–H Bond Amination



Morandi's group demonstrated the synthesis of *N*-methylanilines using $[\text{NsO}-\text{NH}_2\text{Me}]\text{OTf}$ as the aminating agent.¹²³ Jiao and co-workers also developed an arene C–H amination strategy employing a redox-active aminating reagent $[\text{RCO}_2-\text{NH}_3]\text{OTf}$ featuring a *p*-nitrobenzoate residue.¹²⁴ This reagent proved effective for the amination of both aryl and heteroaryl compounds. Furthermore, Loh and co-workers reported arene C–H bond amination using 4-nitrobenzenesulfonyl azide (NsN_3) as the aminating agent.¹²⁵ However, all these methods share common limitations: electron-poor substrates typically result in lower yields and regioselectivity remains a challenge.

In 2019, Ritter and co-workers resolved the low yielding issue related to the electron-deficient arenes (Scheme 40).¹²⁶

Scheme 40. Electron-Deficient Arene C–H Bond Amination

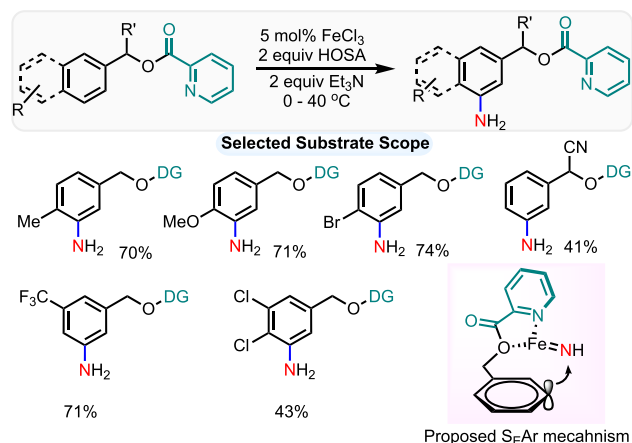


They demonstrated that use of HFIP as solvent enhances the efficiency the iron-catalyzed amination for electron-deficient arenes such as, nitrobenzene, benzonitrile, (methylsulfonyl)-benzene and others. Through the hydrogen bonding interactions with the anionic counterparts of the aminating reagent, HFIP increases the electrophilicity of cationic aminating part which in turn leads to the amination of electron-deficient arenes.

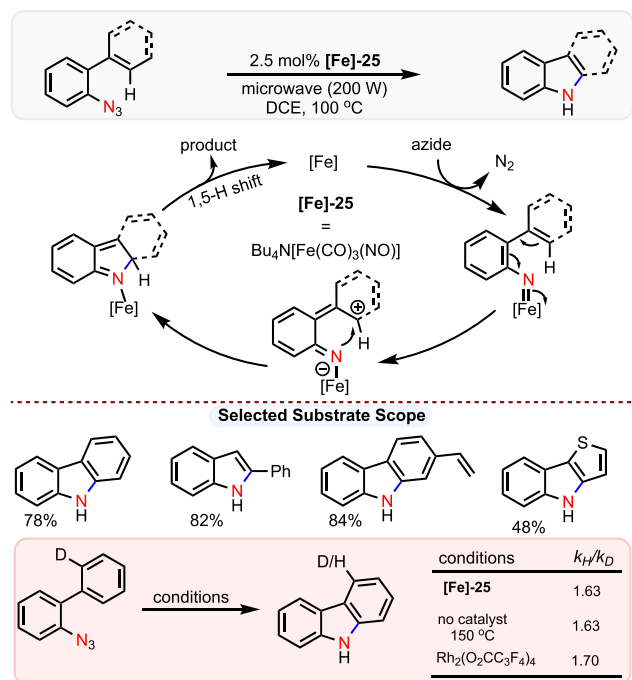
In the next year, the Flack group addressed the challenge associated with the regioselectivity issue (shown in Scheme 39 and 40) by developing a picolinate-directed arene C–H amination strategy, in which amination selectively occurred at the *meta*-position (Scheme 41).¹²⁷ Mechanistic investigations, including kinetic isotope effect (KIE) experiments, yielded a KIE value of 1, indicating that C–H bond cleavage is not the rate-determining step. This observation rules out organometallic C–H activation pathways. Among various pathways for C–H bond amination, the electrophilic aromatic substitution pathway was most consistent with the observed *meta*-selective amination.

3.2.5. Iron-Catalyzed $\text{C}(\text{sp}^2)$ –H Amination (Intramolecular). 3.2.5.1. *Leveraging Organic Azides.* Plietker and Alt reported a nucleophilic iron complex ($[\text{Fe}]\text{-25}$), $[\text{Bu}_4\text{N}][\text{Fe}(\text{CO})_3(\text{NO})]$, for the intramolecular $\text{C}(\text{sp}^2)$ –H amination of α -azidobiaryls and (azidoaryl)alkenes (Scheme 42).¹²⁸ Under thermal or microwave irradiation, the iron

Scheme 41. Directing-Group Assisted *meta*-Selective C–H Bond Amination



Scheme 42. Iron-Catalyzed Intramolecular $\text{C}(\text{sp}^2)$ –H Amination of α -Azidobiaryls



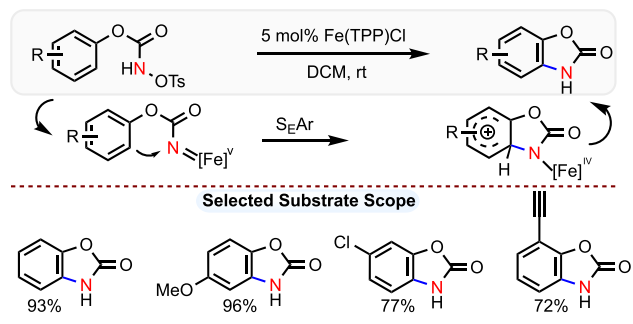
complex efficiently generated carbazoles and indoles from their respective azide precursors. Mechanistic investigations exhibited a moderate kinetic isotope effect (KIE) of 1.63 for α -monodeuterated 2-azidobiphenyl, a value comparable to those observed in the noncatalyzed thermal reaction and Rh-catalyzed amination developed by Driver and co-workers.¹²⁹

Further studies showed that both *E*- and *Z*-configured (azidoaryl)alkenes reacted with similar efficiency. Even trisubstituted olefins were found to be reactive under these conditions. Based on these observations, the authors proposed an electrocyclization mechanism. Initially, the anionic iron complex reacts with the azide forming a nitrene intermediate, which due to the electron-accepting ability of the ligands, generates a zwitterionic mesomeric structure. It is propensity for MLCT sets the stage for C–N bond formation, and consecutive 1,5-H shift leads to carbazole or indole formation. In another study, the Plietker group utilized their nucleophilic

iron complex $[\text{Bu}_4\text{N}][\text{Fe}(\text{CO})_3(\text{NO})]$ (**[Fe]-25**) to catalyze the intramolecular amination of saturated C–H bonds.¹³⁰ This approach enabled the synthesis of substituted indoline and tetrahydroquinoline derivatives, employing aryl azides as nitrogen sources.

3.2.5.2. Utilizing Carbamates. In 2018, Singh and co-workers reported an efficient strategy for the intramolecular nitrene transfer/cyclization of *N*-tosyloxyarylcarbamate substrates using an iron-porphyrin catalyst (Scheme 43).¹³¹

Scheme 43. Iron-Catalyzed Arene C–H Amidation using Functionalized Hydroxyl Amines

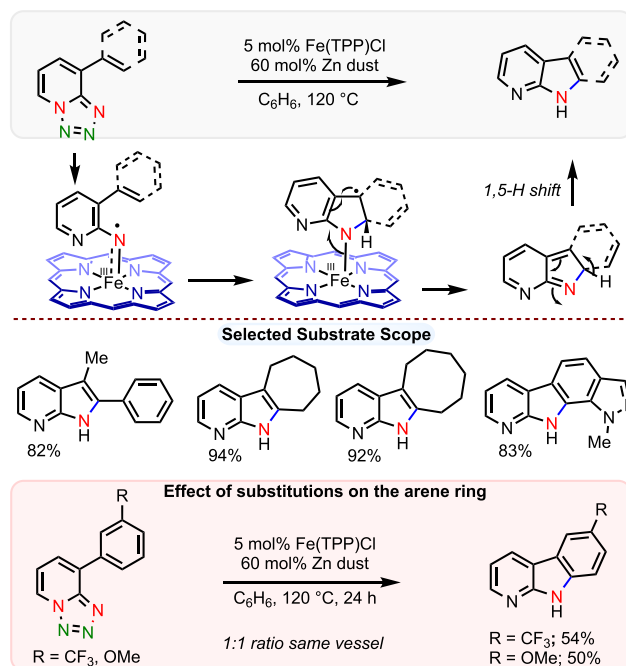


This method enabled the synthesis of benzoxazolone derivatives in high yield; however, the reaction was primarily limited for substrates with electron-donating substituents. In contrast, strong electron-withdrawing groups such as NO_2 and CF_3 completely suppressed product formation. Furthermore, the reaction exhibited high selectivity for aryl C–H amination over $\text{C}(\text{sp}^3)\text{--H}$ bond amination. This selectivity was supported by DFT calculations, which revealed that the energy barrier for aryl C–H bond amination was lower than that for alkyl C–H bond amination. Based on both theoretical and experimental studies, a plausible reaction mechanism was proposed. The reaction proceeds via the formation of an $\text{Fe}(\text{V})$ -nitrenoid intermediate, which undergoes electrophilic aromatic substitution, ultimately leading to the formation of benzoxazolone products.

3.2.5.3. Introducing Tetrazoles. In 2022, the Chattopadhyay group developed an iron metalloradical-catalyzed intramolecular $\text{C}(\text{sp}^2)\text{--H}$ amination using C8-aryl- or C8-alkene-substituted tetrazoles (Scheme 44).¹³² This method provided easy access to two important classes of *N*-heterocycles, α -carbolines and 7-azaindoles, with high functional group tolerance. Moreover, the reaction was successfully applied to achieve complex molecular scaffolds. Control experiments were conducted to elucidate the reaction mechanism. Kinetic isotope effect (KIE) studies using intramolecular dideuterated and intermolecular monodeuterated tetrazoles gave a KIE value of 2.0. Furthermore, a competition experiment between substrates bearing electron-donating (OMe) and electron-withdrawing (CF_3) groups showed no significant difference in product conversion, indicating that electronic effects do not influence the reaction.

This finding ruled out an electrophilic aromatic substitution (EAS) mechanism. Interestingly, when the reaction was performed in the presence of the radical scavenger TEMPO, no product formation was observed. Based on these collective findings, a metalloradical activation mechanism was proposed for the $\text{C}(\text{sp}^2)\text{--H}$ amination. This mechanism was further supported by DFT calculations, which revealed that the

Scheme 44. Iron Porphyrin-Catalyzed Intramolecular $\text{C}(\text{sp}^2)\text{--H}$ Amination

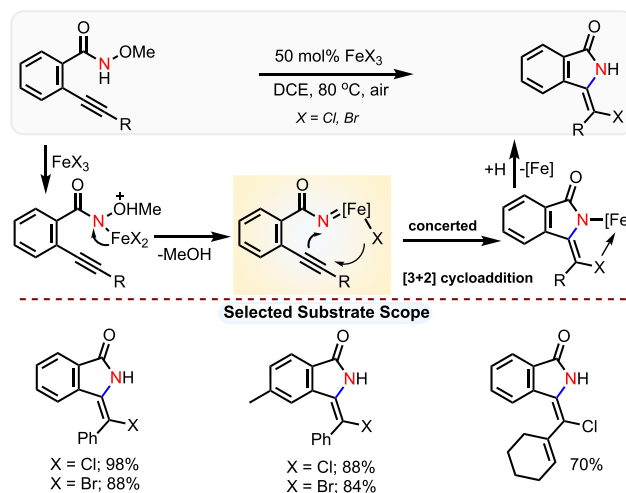


involvement of a triplet spin state for the nitrene radical intermediate was energetically more favorable.

3.2.6. Functionalization of Alkenes and Alkynes.

3.2.6.1. Intramolecular Examples. In 2021, the Qiu group reported an iron-catalyzed haloamidation of alkynes using *N*-methoxybenzamide as an acyl nitrene precursor (Scheme 45).¹³³ The reaction underwent efficiently without requiring

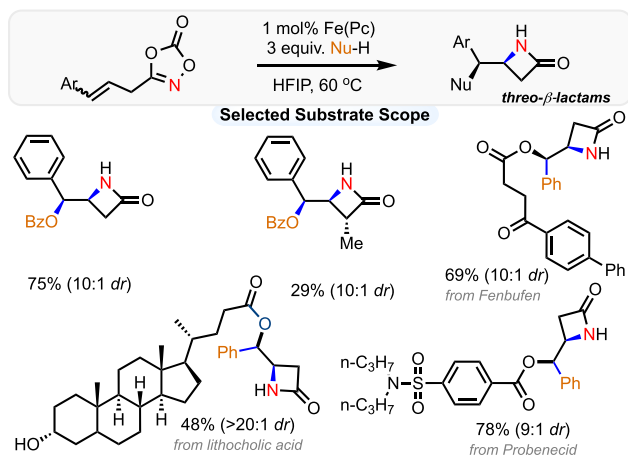
Scheme 45. Iron-Catalyzed Stereoselective Haloamidation of Amide-Tethered Alkynes



additional additives, delivering high yields in the presence of 50 mol % FeCl_3 or FeBr_3 . Although this method requires substoichiometric catalysts loading, it enabled the selective synthesis of *cis*-chloro- and *cis*-bromo-containing isoindolin-5-ones exclusively without the formation of *trans* isomer. Based on these preliminary findings, a halo anion-assisted concerted $[3 + 2]$ cyclization mechanism was proposed to explain the observed selectivity.

In 2022, Chang and co-workers reported a unique oxyamidation strategy for olefin functionalization using an iron-phthalocyanine catalyst (Scheme 46).¹³⁴ This approach

Scheme 46. Iron-Catalyzed Olefin Oxyamidation



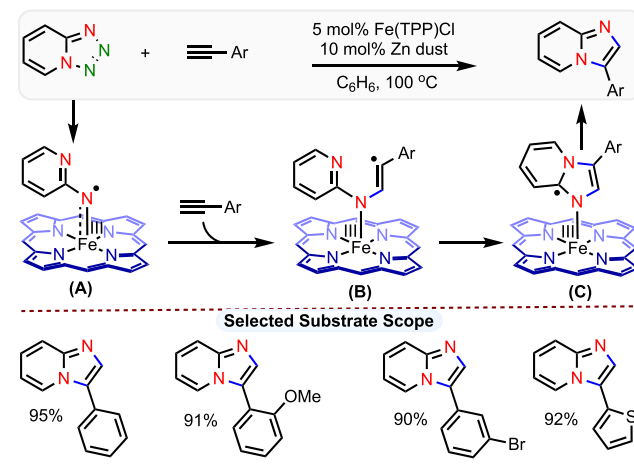
utilizes olefin substrates tethered with 1,4,2-dioxazol-5-ones to synthesize β -lactam scaffolds. In the presence of an external oxygen nucleophile, the reaction predominantly yields the threo-isomer of β -lactam with notable diastereoselectivity.

Mechanistic studies supported by the DFT calculations provided evidence for the key triplet iron-imidyl radical intermediate, highlighting the crucial role of the phthalocyanine ligand's high π -accepting ability in facilitating 4-*exo-trig* lactamization. This, in turn, enables the incorporation of oxygen nucleophiles with high diastereoselectivity. Furthermore, this strategy was successfully extended to γ -lactam synthesis, proceeding with high efficiency. The method demonstrated broad functional group tolerance and efficiently applied to the late-stage modification of natural products and drug molecules, including fenbufen, lithocholic acid, and probenecid.

3.2.6.2. Intermolecular Examples. 3.2.6.2.1. Leveraging Tetrazoles. Using tetrazole as a nitrene precursor in 2019, the Chattopadhyay group reported an iron-porphyrin-metalloradical catalyzed nitrene transfer/annulation reaction between tetrazoles and terminal aryl alkynes (Scheme 47).¹³⁵ A major challenge in this transformation was the competing azide-alkyne cycloaddition between the azido form of tetrazole and the alkyne, which predominantly led to the formation of 1,2,3-triazoles as side products. This study led to the development of an iron(II)-porphyrin catalyst system that effectively suppressed this cycloaddition while promoting the denitrogenative annulation between tetrazole and alkyne. It has been shown that the method can afford a diverse range of substituted imidazopyridines in high yields. However, the reaction was found to be ineffective with aliphatic alkynes and internal alkynes. To rationalize the product formation, a radical activation mechanism was proposed, which was supported by electron paramagnetic resonance (EPR) spectroscopy and radical trapping experiments.

The radical activation mechanism of this reaction is presented in Scheme 47. At first, Zn reduces the ferric oxidation state of iron-porphyrin to ferrous oxidation state via a single-electron transfer, which was confirmed by a UV red shift. Then, the coordination with the nitrogen atom of the azide, it forms an α -Fe(III)-nitrene radical (A) after dinitrogen

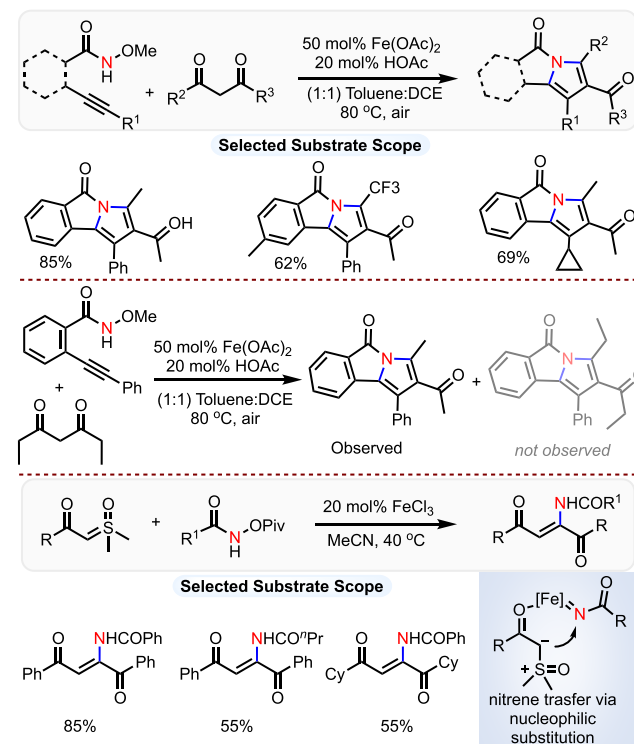
Scheme 47. Iron-Porphyrin-Catalyzed Nitrene Transfer/Annulation Reaction Between Tetrazole and Terminal Aryl Alkynes



loss. Trapping with an alkyne produces γ -Fe(III)-vinyl radical (B), which undergoes intramolecular radical addition to the C=N bond, yielding β -Fe(III)-alkyl radical (C) and constructing a fused five-membered ring. Finally, the intermediate (C) undergoes β -radical scission, breaking the N-Fe bond and forming a C=N bond, completing the catalytic cycle.

3.2.6.2.2. Utilizing Carbamates. In 2021, the Qiu group developed an Fe(acac)₃-catalyzed intramolecular acyl nitrene insertion into an alkyne moiety to prepare pyrrolo[2,1-*a*]isoindol-5-ones (Scheme 48).¹³⁶ It has been proposed that the acetylacetonate ligand of the catalyst served as a nucleophile in the reaction. To validate this mechanism, a control experiment was conducted under standard conditions

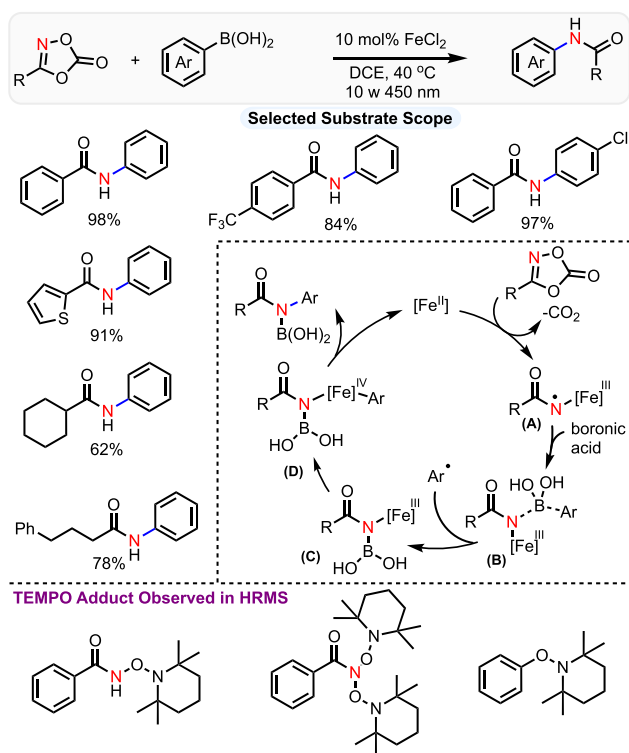
Scheme 48. Fe(acac)₃-Catalyzed Intramolecular Acyl Nitrene Insertion



in the presence of heptane-3,5-dione. Interestingly, the reaction yielded only the desired product, without the formation of the cross-cycloaddition product, which suggested that the transformation proceeds via a counteranion participating addition pathway. Furthermore, the addition of 2 equiv of TEMPO had minimal impact on the reaction outcome, further indicating that a radical pathway is unlikely to be involved. These experimental findings support a 5-*exo-dig* acyl nitrene/alkyne metalation mechanism, where a counteranion-participating acyl nitrene/alkyne metalation accounts for the formation of pyrrolo[2,1-*a*]isoindol-5-ones. Recently, the same group demonstrated an iron-catalyzed nitrene transfer reaction to synthesize enamides from sulfur ylides (Scheme 48).¹³⁷ The reaction was ascribed to nucleophilic substitution of iron-acyl nitrene with sulfur ylides followed by rearrangement leading to the product formation.

3.2.7. Cross-Coupling Reaction. **3.2.7.1. Utilizing Dioxazolones.** In 2021, Bao and co-workers developed a visible light-mediated, iron(III)-catalyzed decarboxylative cross-coupling reaction between boronic acids and dioxazolones (Scheme 49).¹³⁸ This method encompasses broad range of dioxazolones and aromatic boronic acids but aliphatic boronic acids proved incompetent.

Scheme 49. Visible-Light-Promoted Iron-Catalyzed Decarboxylative *N*-Arylation

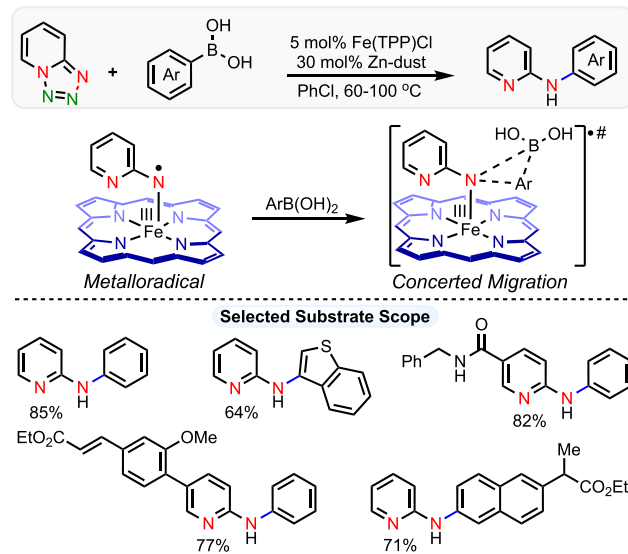


Mechanistic studies, including radical trapping experiments, led to the mass spectrometric identification of several TEMPO-trapped adducts, supporting the involvement of a radical pathway. Based on these experimental findings, a plausible reaction mechanism was proposed (Scheme 49). Upon photoexcitation in the presence of the iron catalyst, the dioxazolone undergoes decarboxylation to generate an iron-bound aminyl radical intermediate (A). This species subsequently reacts with the arylboronic acid via a nucleo-

homolytic substitution pathway, leading to the formation of an aryl radical and an iron complex (C). The aryl radical is then rapidly captured by this iron species to form a new organoiron intermediate (D), which undergoes reductive elimination, followed by hydrolysis furnish the desired cross-coupling product.

3.2.7.2. Leveraging Tetrazoles. In 2023, exploiting an iron-porphyrin catalyst, the Chattopadhyay group developed a denitrogenative cross-coupling reaction between tetrazoles and boronic acids (Scheme 50).¹³⁹ This method enabled the

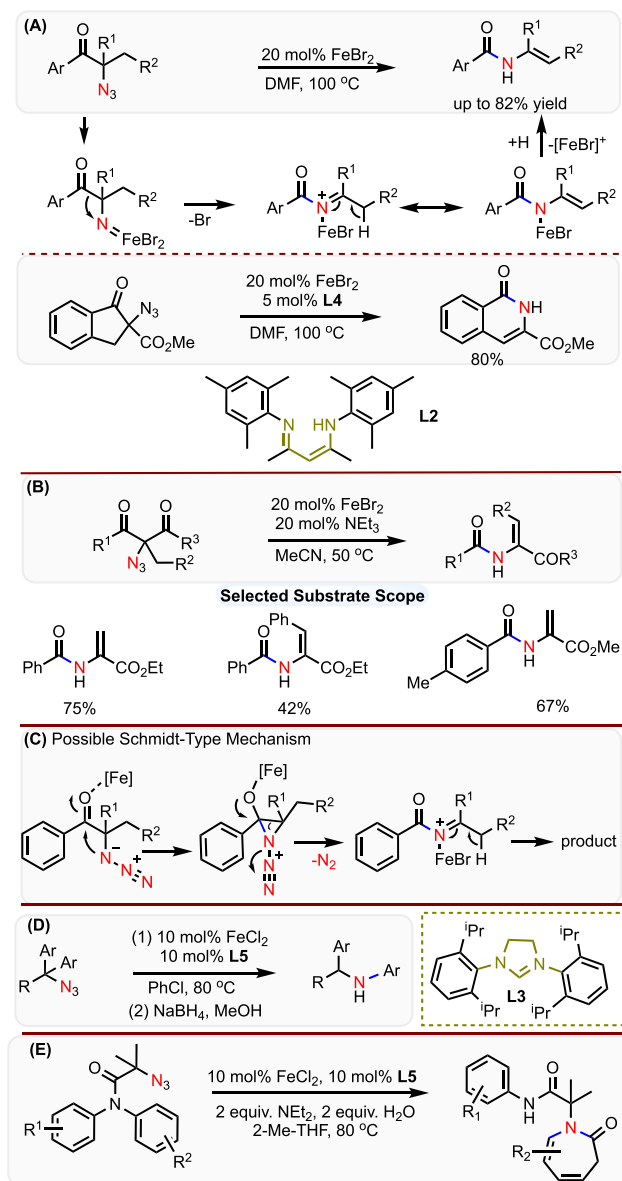
Scheme 50. Iron Porphyrin-Catalyzed Cross-Coupling Reaction Between Tetrazole and Boronic Acid



efficient synthesis of a broad range of *N*-pyridyl aryl amines with high functional group tolerance using diverse tetrazoles, aromatic and aliphatic azides with only aromatic boronic acid as the coupling partner. The reaction proceeds via a metalloradical activation mechanism, distinguishing it from the conventional metal-catalyzed C–N cross-coupling strategies. Furthermore, DFT calculations indicated that the aryl migration step follows a concerted pathway (Scheme 50)—a mechanistic feature that differs from the findings reported by Bao and co-workers (Scheme 49).

3.2.8. Rearrangement Reaction. **3.2.8.1. Leveraging Organic Azides.** In 2018, the Yu group demonstrated the ability of iron salts to activate the tertiary azides toward nitrene-mediated rearrangement reactions. They reported that in the presence of FeBr₂, tertiary α -azidyl ketones underwent an 1,2-acyl migration, enabling the efficient synthesis of enamides and isoquinolones in good to excellent yields (Scheme 51A).¹⁴⁰ For open-chain tertiary α -azidyl phenyl ketones, high yields of enamides were achieved using only a catalytic amount of FeBr₂. However, for cyclic tertiary α -azidyl ketones, the inclusion of ligand L2 was necessary to obtain optimal yields of isoquinolones. Moreover, functionalized 2-benzazepin-1-ones were synthesized under similar conditions, albeit in lower yields. In a subsequent study, Yu and co-workers found that the catalytic combination of FeBr₂ and triethylamine provided greater reactivity than the FeBr₂ alone (Scheme 51B).¹⁴¹ From a mechanistic perspective, this acyl migration rearrangement is intriguing. Product formation may occur via either a pathway analogous to the Schmidt

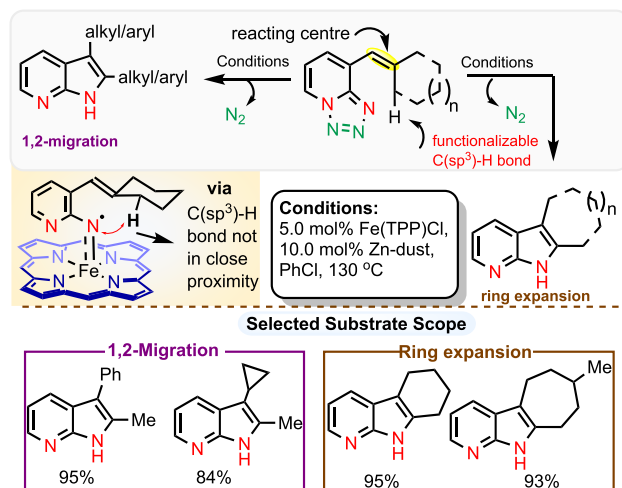
Scheme 51. Fe-Salt-Catalyzed 1,2-Acyl Migration of Tertiary α -Azidyl Ketones



rearrangement (Scheme 51C) or through an acyl migration involving an iron-nitrene intermediate (Scheme 51A). To investigate this, the reaction was tested with various Lewis acids, including FeCl_3 , $\text{BF}_3 \cdot \text{OEt}_2$, TiCl_4 , $\text{Zn}(\text{OTf})_2$, and $\text{Sc}(\text{OTf})_3$. Since these acids are typically more effective than FeBr_2 in promoting Schmidt rearrangements, their inability to yield the desired product ruled out this mechanism. Further supporting the iron-nitrene pathway, a control experiment with a substrate containing a functionalizable benzylic C–H bond led to the formation of a C–H amination product alongside the expected enamine derivatives. This result strongly suggests that the acyl migration proceeds via an iron-nitrene intermediate rather than a Schmidt-type rearrangement. Thereafter, they expanded the scope of nitrene-mediated rearrangement reactions to α, α -diaryl-tertiary azides (Scheme 51D)¹⁴² and subsequently reported a unique skeletal rearrangement involving the migration of a phenyl ring from the amido nitrogen in 2-azido-*N,N*-diphenyl amides to the azido nitrogen (Scheme 51E).¹⁴³

3.2.8.2. *Introducing Tetrazoles.* In 2021, the Chattopadhyay group reported an iron-porphyrin-catalyzed rearrangement reaction of C8-methylene cyclohexane-tethered tetrazole substrates (Scheme 52).¹⁴⁴ Despite the presence of $\text{C}(\text{sp}^3)\text{--H}$

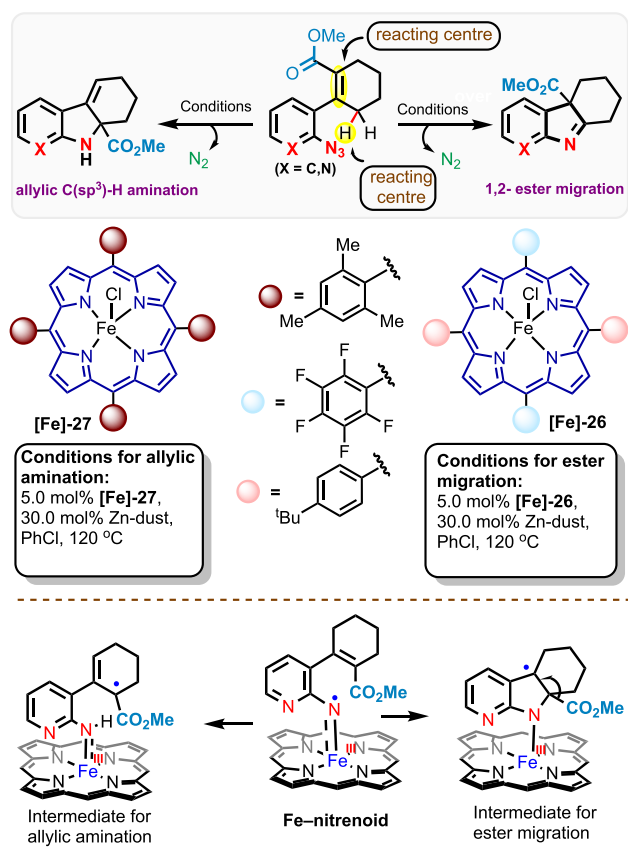
Scheme 52. Iron-Catalyzed Radical Activation Mechanism for Denitrogenative Rearrangement Over $\text{C}(\text{sp}^3)\text{--H}$ Amination



bonds available for amination, the reaction favored nitrene attack at the methylene π -cloud over $\text{C}(\text{sp}^3)\text{--H}$ amination. This preference arises because the cyclohexane adopts a stable chair conformation, positioning the functionalizable $\text{C}(\text{sp}^3)\text{--H}$ bonds away from the reacting radical center, making them less accessible for amination. This strategy enabled the synthesis of a diverse array of 2,3-disubstituted azaindoles with high functional group tolerance. Based on various control experiments, including radical trapping studies, analysis of electronic effects, and ring-opening experiments, a metalloradical activation pathway was proposed for the bond migration/rearrangement process. Notably, high reaction temperature was one of the major issues of this transformation. However, exploration of different porphyrin ligands with varied steric and electronics could lower the reaction temperature which was out of scope of this work.

Inspired from this chemoselective rearrangement overriding competing $\text{C}(\text{sp}^3)\text{--H}$ amination, Chattopadhyay and co-workers were curious to merge Fe-MRC (iron-metalloradical catalysis) with chemodivergence, to chemoselectively access both the plausible products from the same substrate. In a recent study, they also showcased catalyst-enabled chemodivergent metalloradical activation for molecular rearrangement via ester migration and allylic $\text{C}(\text{sp}^3)\text{--H}$ amination (Scheme 53).¹⁴⁵ To achieve such chemodivergent outcomes, they aimed to modulate the electronic properties of the catalyst to direct the reaction pathway of substrates featuring multiple competitive reactive sites. Therefore, after extensive screening by tuning ligand environment, they found that $[\text{Fe}]\text{-26}$ resulted in ester migration as major product while $[\text{Fe}]\text{-27}$ shifted the product distribution toward allylic $\text{C}(\text{sp}^3)\text{--H}$ amination. The scope of the reactions has been demonstrated by the use of a wide number of tetrazoles and aryl azides. Based on literature precedents and control experiments, such as, radical trapping experiment, EPR experiment, analysis of electronic effect via Hammett plot, a metalloradical activation

Scheme 53. Iron-Catalyzed Chemodivergent 1,2-Ester Migration and Allylic C(sp³)-H Amination



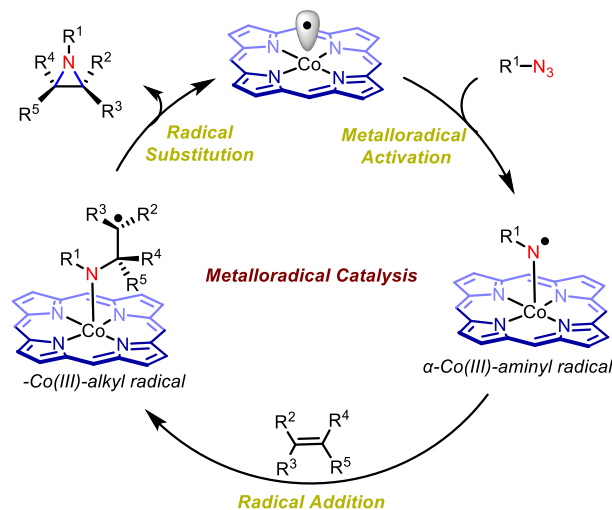
mechanism has been proposed. This observed switch in chemoselectivity can be rationalized by considering the steric and electronic nature of the iron–nitrenoid intermediate. As a reasoning of such chemodivergent outcomes, they postulated that the iron complex ([Fe]-26) bearing two $-\text{C}_6\text{F}_5$ substituents renders the iron–nitrenoid intermediate highly electrophilic, thereby promoting nitrene addition across the double bond. In contrast, the catalyst ([Fe]-27) featuring electron-donating substituents on the porphyrin ligand makes the iron–nitrenoid intermediate energetically favorable toward allylic C(sp³)-H abstraction. Using the developed strategies, different *N*-heterocycles having a quaternary carbon center attached with a modifiable ester group for further synthetic transformation have been achieved that were inaccessible by previously reported methods.

3.3. Cobalt Catalysis (Co)

Cobalt-catalyzed nitrene transfer reactions have emerged as robust and eco-friendly methods for constructing diverse and valuable C–N bonds. The groups of Zhang, de Bruin, and subsequently others have extensively explored this area, using cobalt catalysts in nitrene transfer reactions and significantly advancing the field of Co-nitrene chemistry. One key development from this group is the concept of metalloradical catalysis (MRC), a unique mechanistic pathway exhibited by Co(porphyrin) complexes.¹⁴⁶ MRC leverages the potential of metal-centered radicals as open-shell one-electron catalysts. These radicals enable the homolytic activation of substrates, generating metal-entangled organic radicals that dictate reaction pathways and influence the stereochemical outcomes of catalytic radical processes.

3.3.1. Cobalt-Catalyzed Aziridination Reactions (Intermolecular). Co-metalloradical catalysis has shown remarkable efficiency in aziridination reactions. Upon exposure to organic azides, the cobalt catalyst generates a nitrogen-centered radical intermediate, $[\alpha\text{-Co(III)}\text{-aminyl radical}]$, which was characterized through a combination of spectroscopic analyses and DFT calculations.^{147,148} This reactive intermediate undergoes radical addition to alkenes, forming a $\gamma\text{-Co(III)}\text{-alkyl radical}$ that subsequently undergoes a 3-*exo-tet* radical cyclization to furnish the aziridine product (Scheme 54). In 2005, the Zhang group demonstrated the cobalt-

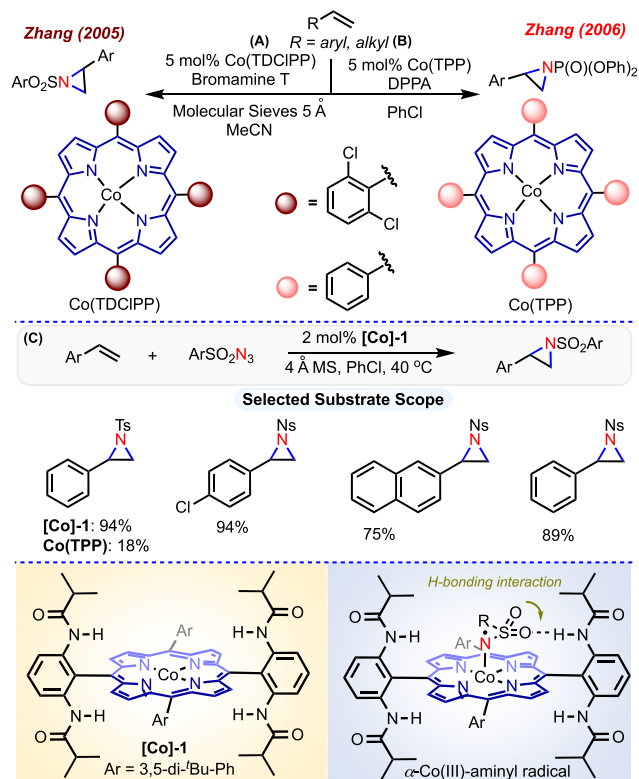
Scheme 54. General Mechanism for Cobalt-Catalyzed Aziridination Reactions



catalyzed aziridination reaction using bromamine-T (Scheme 55 (A)).¹⁴⁹ The cobalt-catalyst, Co(TDCIPP) was found highly effective for the aziridination of aryl and alkyl alkenes, including internal, sterically hindered, or electron-deficient alkenes.

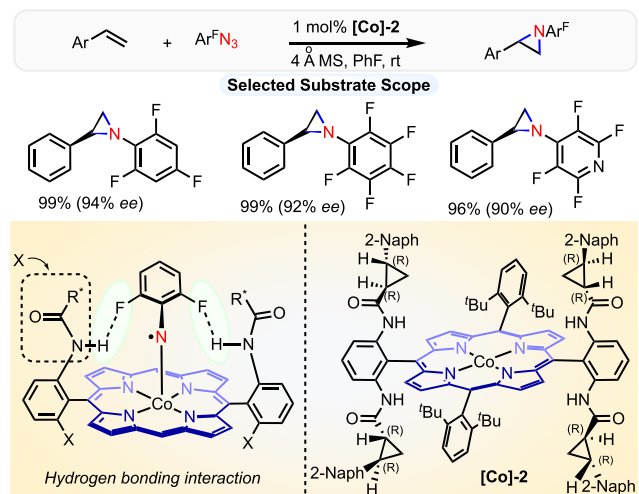
It was found that electron-rich porphyrins produced lower yield whereas electron deficient porphyrins were proved to be more efficient toward aziridination probably due to the electrophilic nature of the key $\alpha\text{-Co(III)}\text{-aminyl radical}$ intermediate in the catalytic cycle. The Zhang group also reported a series of aziridination reaction using Co-catalysis varying different nitrene source and porphyrin catalysts. Though diphenylphosphoryl azide (DPPA) as the nitrene precursor tolerated well under Co(TPP) catalysis (Scheme 55 (B)),¹⁵⁰ sulfonyl azide resulted in poor yield in aziridination reaction. This cobalt-catalyzed aziridination involves a key electrophilic cobalt-nitrene intermediate. Consequently, substituents or ligand environments that stabilize this intermediate and enhance its electrophilicity are expected to promote its formation and accelerate the overall catalytic cycle. The D_{2h} -symmetric porphyrin-containing amide functional groups at the ortho positions of meso-phenyl groups was designed to invoke a potential hydrogen bonding interaction between the S=O and N–H unit in the nitrene intermediate of ([Co]-1) (Scheme 55 (C)).¹⁵¹ As a result of this stabilization and activation from the hydrogen-bonding interaction, ([Co]-1) was expected to be a superior catalyst, in comparison with Co(TPP) and Co(TDCIPP), for aziridination with sulfonyl azides. In 2008, Cenini et al. reported the compatibility of *p*-nitrophenylazide with other catalysts, albeit with poor yield.¹⁵²

Scheme 55. Cobalt-Catalyzed Olefin Aziridination using Sulfonyl Azides



In 2013, Zhang et al. in a subsequent report, demonstrated a cobalt–porphyrin-catalyzed asymmetric aziridination of alkenes using fluoroaryl azides as nitrene precursors (Scheme 56).¹⁵³ The cobalt catalyst (**[Co]-2**) was identified as optimal,

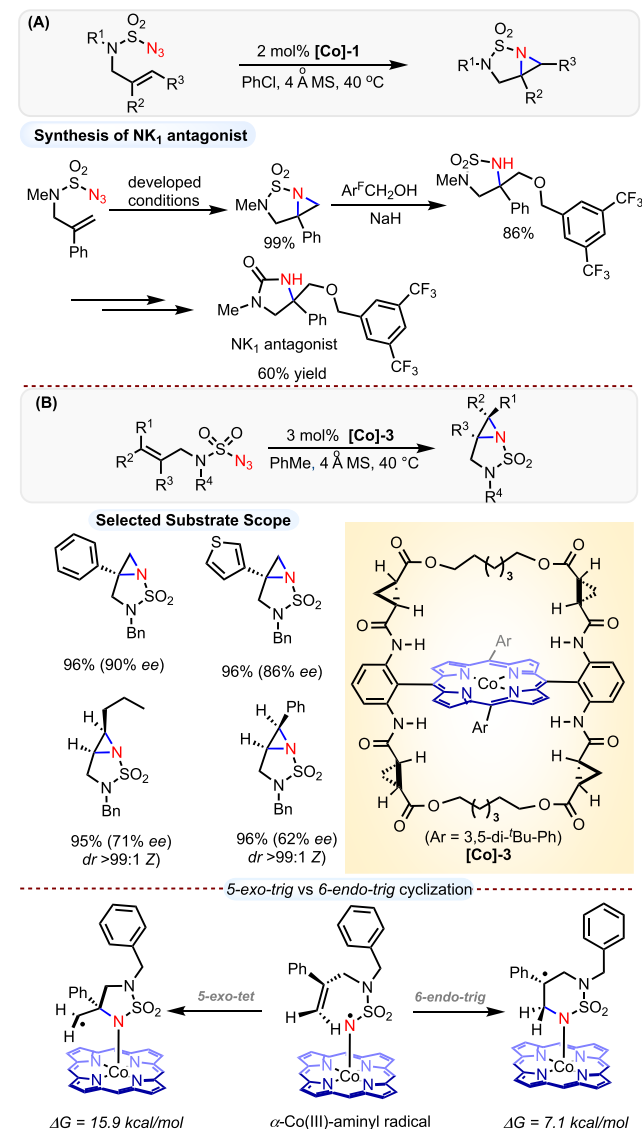
Scheme 56. Asymmetric Cobalt-Catalyzed Aziridination of Alkenes with Fluoroaryl Azides



delivering the aziridinated product in 94% yield and 90% ee with only 1 mol % catalyst loading, without the need for additional additives to activate the olefins. The enhanced reactivity and stereoselectivity were attributed to N–H...F hydrogen-bonding interactions (as highlighted in Scheme 56) within the Co(III)–nitrene radical intermediate.

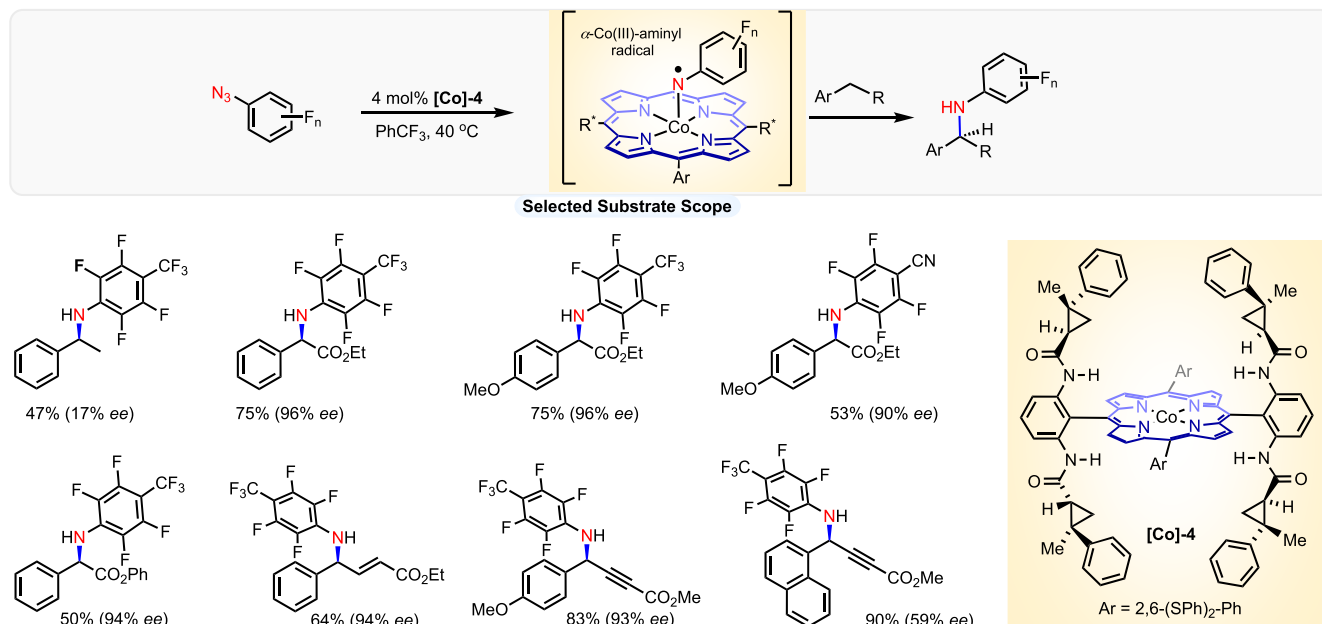
3.3.2. Cobalt-Catalyzed Aziridination Reactions (Intramolecular). Cobalt-catalyzed aziridination was further applied to prepare strained heterobicyclic aziridines. For example, the (**[Co]-1**) catalyst was used for the intramolecular radical aziridination of allylic sulfamoyl azides to make highly strained 2-sulfonyl-1,3-diazabicyclo [3.1.0] hexanes in high yields (Scheme 57A).¹⁵⁴ Importantly, to showcase the

Scheme 57. Cobalt-Catalyzed Intramolecular Aziridination of Allylic Sulfonyl Azides

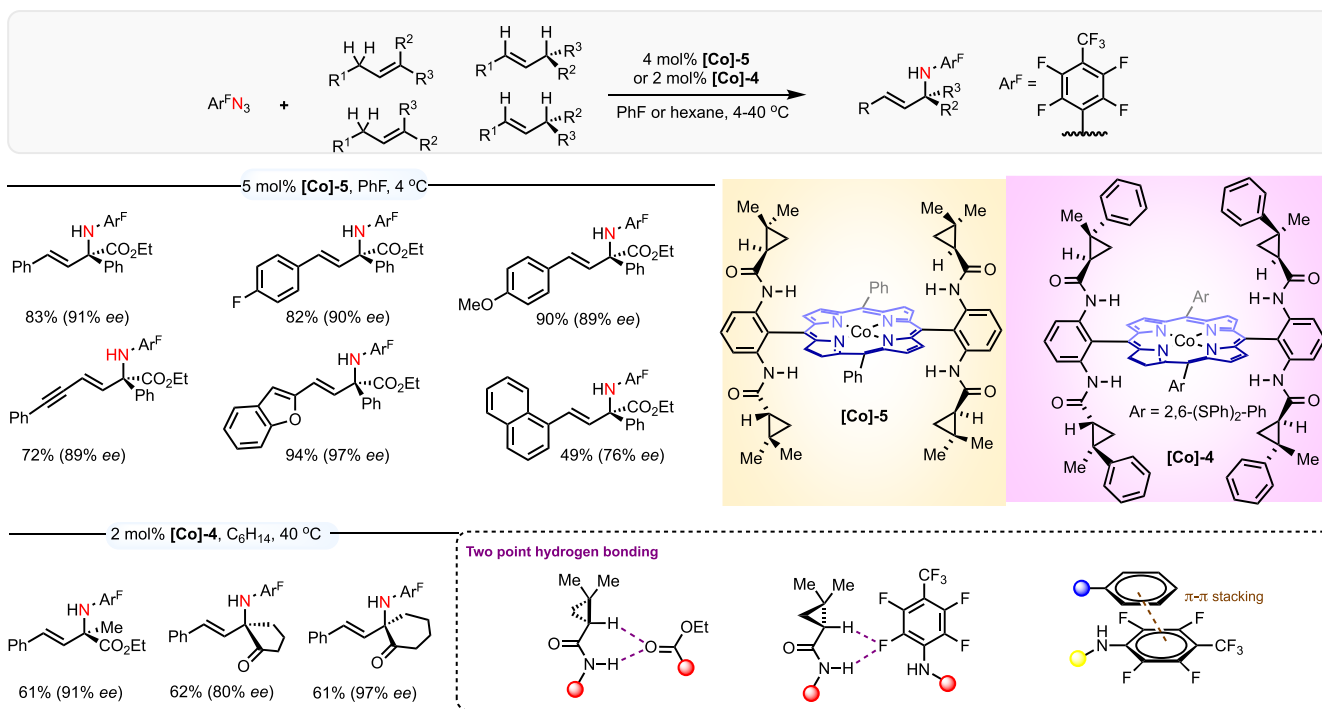


efficiency of the developed aziridination reaction, a potent neurokinin 1 (NK1) antagonist has been synthesized using this method as one of the key synthetic steps that provided 60% overall yield of the target product. The enantioselective version of this intramolecular aziridination was further explored by utilizing a chiral Co(II) amidoporphyrin catalyst (**[Co]-3**) with a tunable pocket-like environment as the supporting ligand (Scheme 57B).¹⁵⁵

The C6-bridged alkyl chains containing catalyst (**[Co]-3**) enabled the transformation in excellent yields with high diastereo- and enantioselectivity. Regarding the nitrene addition in initial C–N bond forming step, the α -Co(III)-aminyl radical can undergo either 5-exo-tet or 6-endo-trig

Scheme 58. Co-Catalyzed Enantioselective Intermolecular C(sp³)-H Amination

Scheme 59. Cobalt-Catalyzed Site-Selective Allylic C-H Amination

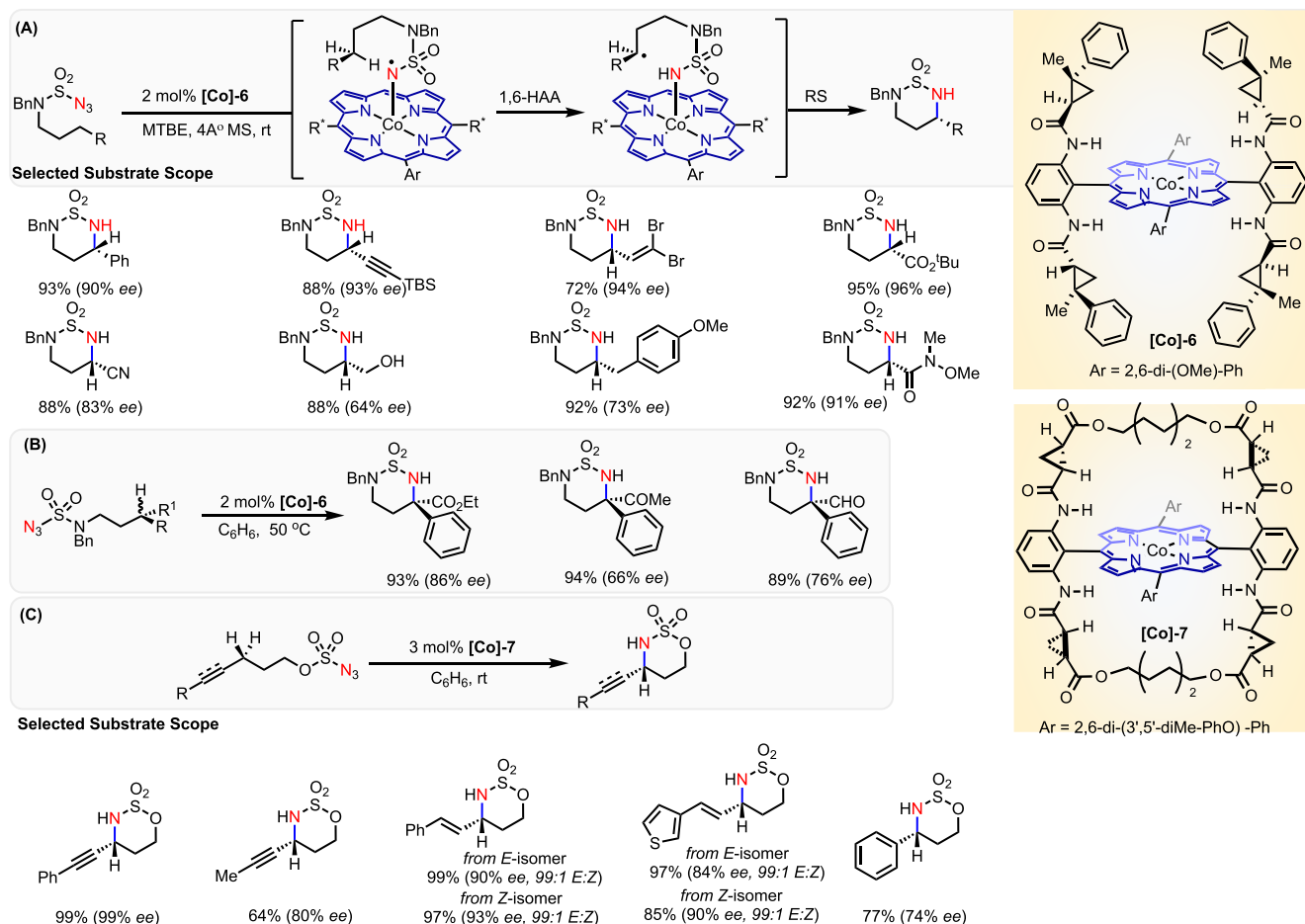


cyclization. The regioselectivity of the radical addition (*exo*- vs *endo*-cyclization) plays a crucial role in asymmetric induction, influencing stereochemical control during catalysis. The DFT calculations indicate that α -Co(III)-aminyl radical intermediate prefers 6-*endo*-*trig* cyclization via the 6-membered transition state (T.S.) substantially over 5-*exo*-*trig* cyclization via the 5-membered T.S. by 8.8 kcal/mol. Notably, mechanistic intricacies revealed that kinetic stability of the initially generated chiral radical center on the ring plays pivotal role in the enantio-determining step, e.g., for kinetically labile prochiral radical center the final step of radical substitution is expected to determine the enantioselectivity whereas if the

stereo configuration of the prochiral radical center is kinetically stable relative to the rate of the following RS, the first step of *endo* addition is anticipated to determine the enantioselectivity.

3.3.3. Cobalt-Catalyzed C(sp³)-H Amination (Intermolecular). The Co-MRC (Cobalt-Metalloradical Catalysis) platform has shown excellent synthetic applications in the C-H bond amination reactions. Zhang and co-workers employed an α -Co(III) aminyl radical to initiate a hydrogen atom transfer (HAT) process, thereby generating an alkyl radical species. Subsequent radical substitution afforded the C-H bond amination product.

Scheme 60. Cobalt-Catalyzed 1,6-C–H Amination of Sulfamoyl Azides



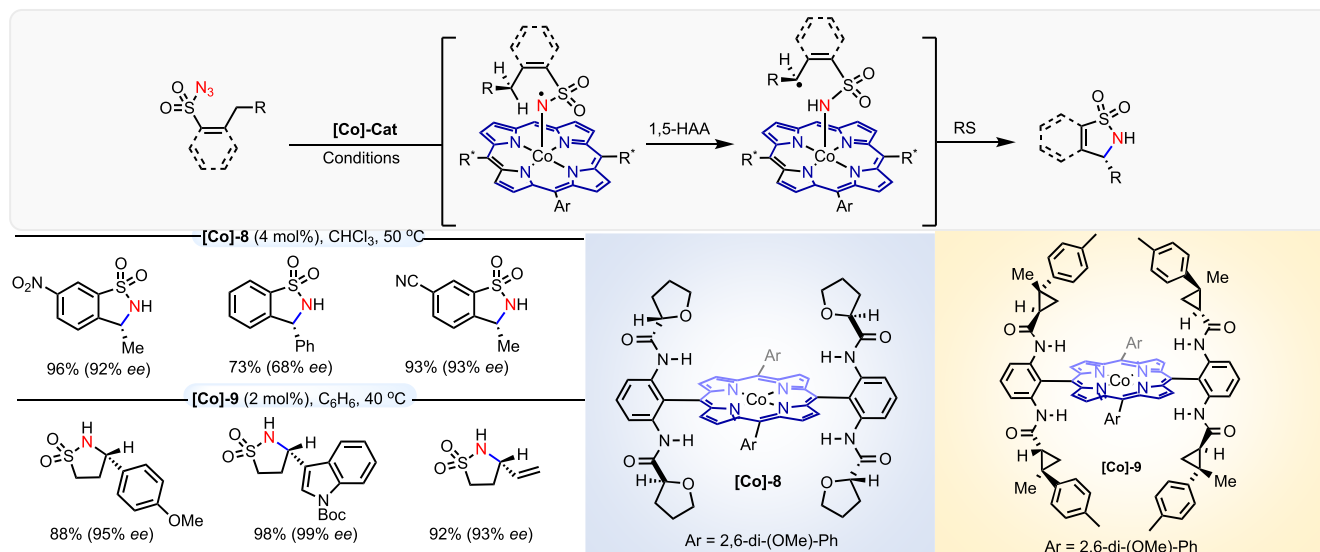
In 2007, Zhang reported a C–H bond amination reaction using bromamine-T.¹⁵⁶ Among the cobalt porphyrin catalysts tested, Co(TDCIPP) bearing 2,6-dichlorophenyl porphyrin ligand exhibited the highest efficiency in catalyzing the C(sp³)–H amination of aromatic hydrocarbons into their corresponding benzyl amine derivatives. The substrate scope was further expanded using 2,2,2-trichloroethoxycarbonyl azide (TrocN₃) under Co(TPP) catalysis.¹⁵⁷ However, other azides such as sulfonyl, phosphoryl, and carbonyl azides gave poor yields under the developed conditions. In 2020, the same group developed an enantioselective version of the intermolecular C–H amination reaction (Scheme 58).¹⁵⁸ Although achieving high enantioselectivity in intermolecular transformations is highly challenging, they succeeded by incorporating cooperative noncovalent interactions between a D₂-symmetric chiral amidoporphyrin ligand (as in [Co]-4) and the substrate. This strategy enabled a highly enantioselective amination of benzylic C–H bonds in carboxylic acid esters using fluorinated azides. Notably, when ethylbenzene, lacking hydrogen-bonding capability with the chiral ligand, was used as the substrate, only 17% ee was obtained. Mechanistic investigations, including EPR spectroscopy, mass spectrometry, and radical trapping experiments, supported a stepwise radical pathway.

The kinetic isotope effect (KIE = 8.1) revealed that the C–H bond cleavage is the rate-limiting step. Furthermore, the substitution pattern of fluorinated azides proved critical for reactivity. While 2,4,5-trifluorophenyl azide gave only trace

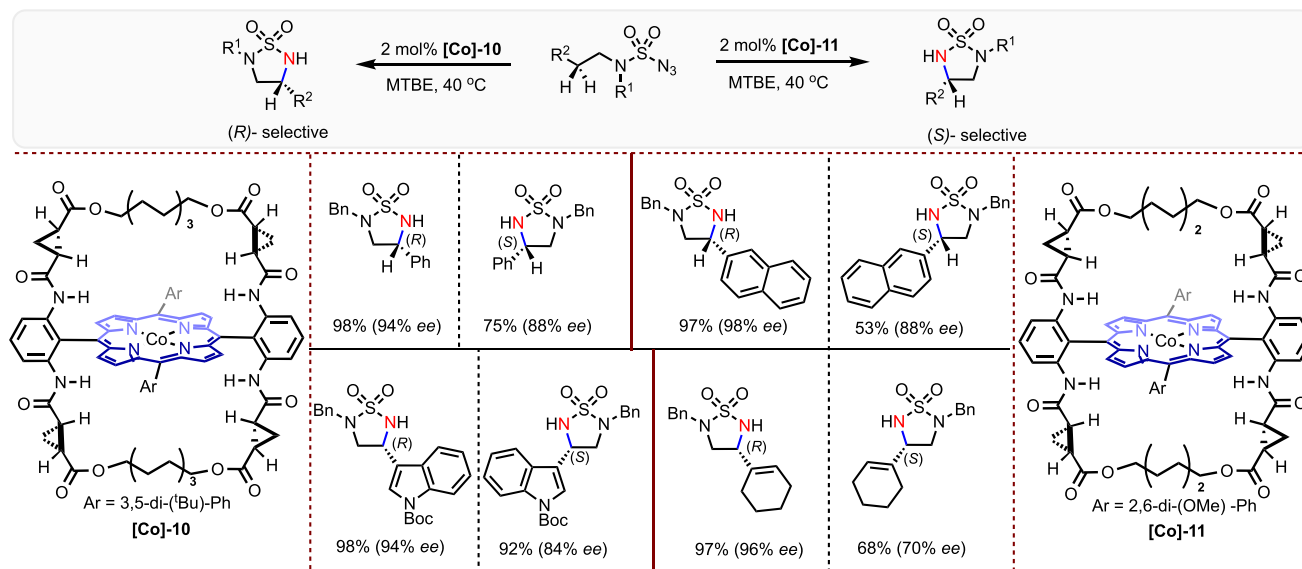
amount of the C–H amination product, 3,4,5-trifluorophenyl azide showed no reactivity under identical conditions, highlighting the importance of 2,6-substitution in enabling key noncovalent interactions. Thus, development of asymmetric strategies devoid of fluorinated azides still remain apparent; pose a significant challenge in this domain.

Co(II)-based metalloradical catalysis also enables radical chemoselective intermolecular amination of allylic C–H bonds. The use of (D₂)-symmetric chiral Co-porphyrin, featuring a tunable pocket-like environment, provides a remarkable convergence of regioselectivity, diastereoselectivity, and enantioselectivity in the allylic amination of substrates bearing benzylic positions (Scheme 59).¹⁵⁹ Notably, while the first-generation catalyst, ([Co]-5) exhibits limited control over enantioselectivity in the asymmetric synthesis of chiral α-tertiary amino carbonyl compounds with α-alkyl substituents, this limitation is addressed by the second-generation chiral metalloradical catalyst, ([Co]-4), which enhances stereocontrol for diverse allylic substrates. DFT calculations reveal that a network of multiple attractive noncovalent interactions (NCIs) holds the two reacting partners in close proximity and orients them appropriately within the catalyst pocket. This organized environment facilitates C–N bond formation with high regioselectivity and induces strong asymmetric induction. Importantly, the formation of α-tertiary amines is favored by 3.2 kcal mol^{−1} over that of α-secondary amines. Alkane amination often faces the problem of site selectivity and overreaction under photocatalytic conditions. In contrast, the

Scheme 61. Cobalt-Catalyzed Enantioselective 1,5-C–H Amination of Sulfonfyl Azides



Scheme 62. Cobalt-Catalyzed Enantiodivergent 1,5-C–H Amination



use of transition metal with fine-tuning of ligand have potential to overcome the existing limitations.

3.3.4. Cobalt-Catalyzed C(sp³)–H Amination (Intramolecular). In radical chemistry, 1,5-HAT and 1,6-HAT processes are frequently exploited in intramolecular amination reactions.¹⁶⁰ Taking this into account, Zhang and co-workers developed an asymmetric metalloradical catalysis (MRC) strategy for the enantioselective construction of heterocyclic compounds via 1,6-HAT, followed by a 6-*exo-tet* radical cyclization (Scheme 60 (A)).¹⁶¹

A well-designed cobalt catalyst, [Co]-6, was employed to activate sulfamoyl azides that generates a α -Co(III)-aminyl radical. Importantly, cooperative hydrogen-bonding interactions between the catalyst and substrate played a crucial role in controlling the stereochemistry of the radical substitution step. This method enables the amination of a broad range of C(sp³)–H bonds, including benzylic, allylic, and propargylic positions, with excellent regio- and enantioselectivities. A variety of functional groups—including alcohols, bromo,

esters, amides, and cyano groups—were well tolerated, affording the desired products in high yields and with high enantiomeric excess. Notably, the reaction exhibits remarkable regioselectivity for 1,6-HAT over 1,5-HAT. Furthermore, the resulting optically active heterocycles can be readily transformed into chiral 1,3-diamines upon desulfonylation. Mechanistic studies support the suggested pathway: a kinetic isotope effect (KIE) of 6.6 strongly indicates C–H bond cleavage through hydrogen atom abstraction, while EPR spectroscopy offered proof for the formation of the α -Co(III)-aminyl radical intermediate. The synthetic potential of chiral MRC was further highlighted by the deracemization of racemic tertiary C(sp³)–H bonds, enabling the enantioconvergent construction of quaternary stereogenic centers (Scheme 60(B)).¹⁶² They also reported a highly selective radical 1,6-C(sp³)–H amination of alkoxysulfonyl azides via a Co(II)-based metalloradical catalysis (MRC) system (Scheme 60 (C)).¹⁶³ The key to this transformation is a cavity-shaped ligand environment provided

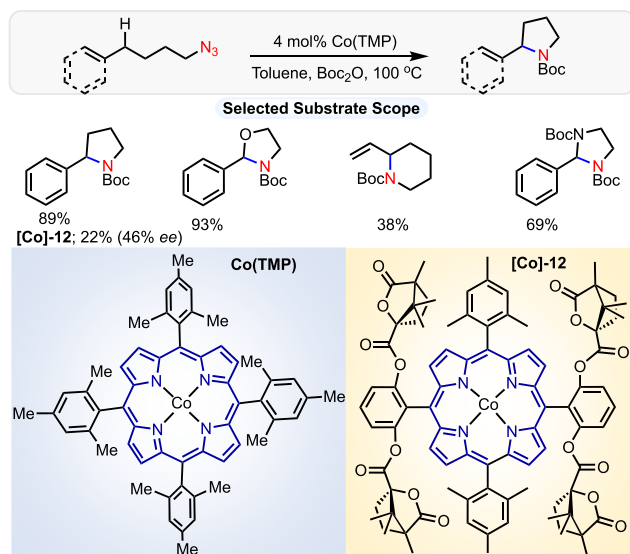
by the C6-bridged metalloradical catalyst ([Co]-7), which features 2,6-diaryloxyphenyl substituents. This unique catalyst enables efficient intramolecular C–H amination at room temperature, affording six-membered sulfamidates with remarkable enantioselectivity (up to 99% *ee*) at propargylic, allylic, and benzylic stereogenic centers, while simultaneously installing an additional amino functionality. In a subsequent study, Zhang and co-workers extended this strategy to the synthesis of five-membered *N*-heterocycles via 1,5-HAA followed by radical substitution (Scheme 61).¹⁶⁴ To achieve this, they designed substrates lacking a hydrogen at the 1,6-position, thereby exclusively favoring 1,5-HAA, which led to five-membered ring formation. The ([Co]-8) catalyst was found to be highly effective, delivering fused benzene and cyclic sulfonamides in high yields with excellent enantioselectivities. For aliphatic substrates containing benzylic or allylic hydrogens, the use of a modified catalyst, ([Co]-9), proved to be essential for achieving optimal reactivity and selectivity.

In a parallel study, the Zhang group demonstrated an unprecedented mode of asymmetric induction in 1,5-amination involving enantiodifferentiative hydrogen atom abstraction (HAA) and stereoretentive radical substitution (RS) (Scheme 62).¹⁶⁵ Utilizing a Co(II)-based metalloradical system supported by bridged ligands, they achieved remarkable control over both enantioselectivity and reactivity in catalytic radical C–H amination reactions. These chiral ligands featured tunable cavities, modulated by varying the distal alkyl bridges and remote nonchiral aryl substituents. Notably, the catalyst [Co]-10, bearing a C8-alkyl bridge and a 3,5-*di*-*tert*-butylphenyl group, promoted *R*-selective cyclization with high yield and enantioselectivity.

In contrast, the catalyst [Co]-11, containing a C6-alkyl bridge and a 2,6-dimethoxyphenyl group, directed the cyclization toward the *S*-selective product with similarly impressive efficiency and enantiocontrol.

de Bruin and co-workers addressed this issue and reported that Co(TMP) (TMP = tetramesitylporphyrin) can catalyze intramolecular benzylic amination reactions of alkyl azides at elevated temperature (100 °C) (Scheme 63).¹⁶⁶

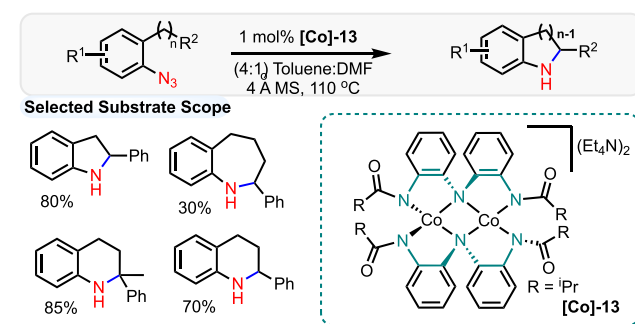
Scheme 63. Cobalt-Catalyzed Intramolecular Benzylic Amination of Alkyl Azides



This reaction enables the direct synthesis of various nitrogen-containing heterocycles from aliphatic azides. A range of heterocycles—including pyrrolidines, oxazolidines, imidazolidines, isoindolines, and tetrahydroisoquinolines may be obtained in good to excellent yields. Notably, the use of *di*-*tert*-butyl dicarbonate (Boc₂O) is essential, as it prevents coordination of the resulting *N*-heterocycles to the cobalt-porphyrin catalyst. Furthermore, poor enantioselectivities (up to 46% *ee*) were achieved in the ring-closing reaction of (4-azidobutyl)benzene using a cobalt-porphyrin catalyst functionalized with four (1*S*)-(-)-camphanic ester groups ([Co]-12). This approach integrates the enantioselective radical 1,5-C(sp³)-H amination of alkoxysulfonyl azides via Co(II)-MRC with an enantiospecific ionic ring-opening of the resulting five-membered chiral sulfamidates by nucleophiles. The process provides enantioselective β-C–H amination of simple alcohols, simultaneously converting hydroxyl groups into diverse functionalities through formal nucleophilic substitution. The success of this method depends on the fine-tuning of the Co(II)-based metalloradical catalyst. Specifically, the cavity size of the porphyrin ligand and the nature of the nonchiral aryl substituents played critical roles in determining both yield and enantioselectivity. Among the catalysts tested, ([Co]-11), featuring a C6-alkyl bridge and 2,6-dimethoxyphenyl groups, delivered the highest levels of reactivity and enantioselectivity. Remarkably, this catalyst system demonstrated broad substrate scope, efficiently engaging benzylic, allylic, propargylic, and even unactivated C–H bonds.

Beyond Co(II) complexes stabilized by macrocyclic porphyrin ligands, various other cobalt catalysts have also been reported to promote nitrene C(sp³)-H insertion reactions. Blakey, Macbeth, and co-workers developed an intramolecular C–H amination using a dinuclear Co(II) complex ([Co]-13), supported by a modular and tunable redox-active ligand (Scheme 64).¹⁶⁷ This strategy enabled the

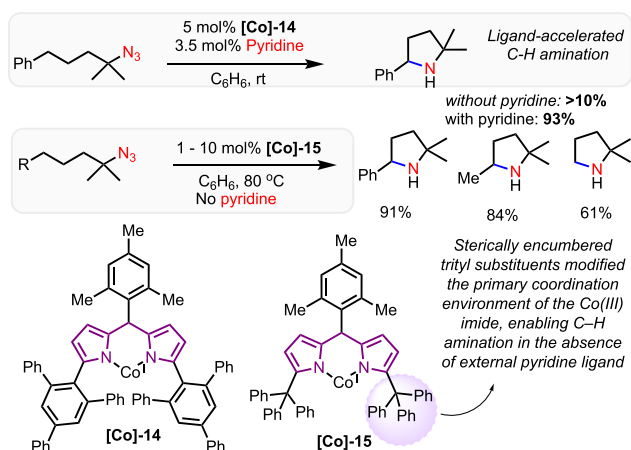
Scheme 64. Dinuclear Cobalt-Catalyzed C(sp³)-H Amination using Aryl Azides



efficient synthesis of indolines and 5-, 6-, and 7-membered nitrogen-containing heterocycles from aryl azides. The reaction proceeded effectively with a low catalyst loading (1 mol %). A kinetic isotope effect study (KIE 3.4) suggested a hydrogen atom abstraction followed by a radical substitution mechanism.

Betley and co-workers demonstrated that Co(I)-dipyrromethene complexes can catalyze the intramolecular C(sp³)-H amination of alkyl azides, delivering unprotected pyrrolidine products in high yields (Scheme 65).^{168,169} Interestingly, this transformation proceeds without the need for Boc₂O to liberate the amine product from the catalyst pocket. While the addition of pyridine accelerated the reaction with catalyst

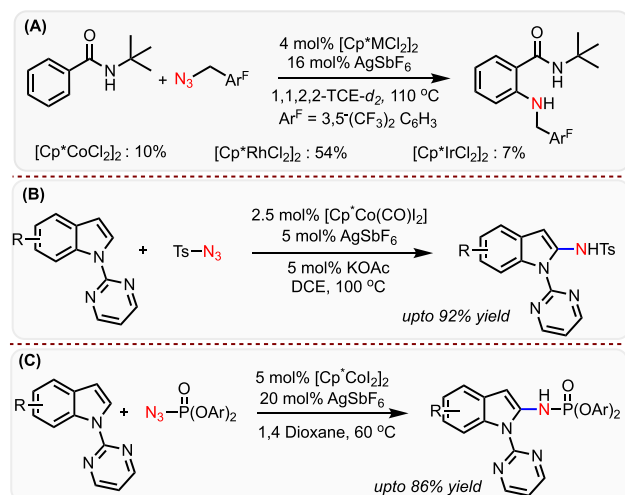
Scheme 65. C(sp³)-H Amination Catalyzed by Co(I) Dipyrrin Complexes with Alkyl Azides



([Co]-14), it had no effect when using ([Co]-15). The ligand framework of ([Co]-15), bearing sterically encumbered trityl substituents, imparts a unique structural environment around the Co(III)-imide. This subtle modification in ligand framework not only prevents catalyst degradation but also significantly enhances the efficiency of C-H amination.

3.3.5. Cobalt-Catalyzed C(sp²)-H Amination (Intermolecular). **3.3.5.1. Exploiting Organic Azides.** In comparison to its group 9 congeners (rhodium and iridium), cobalt catalysis generally exhibits significantly lower catalytic activity in C-H bond activation, particularly for directed C(sp²)-H amination reactions. A comparative study by Chang and co-workers investigated the differences in catalytic activity among Cp^{*}M(III) species (M = Co, Rh, Ir) in C-H amination (Scheme 66A).¹⁷⁰ DFT calculations for the amination of

Scheme 66. Cp^{*}-Based Group-9 Metal-Catalyzed C-H Bond Aminations

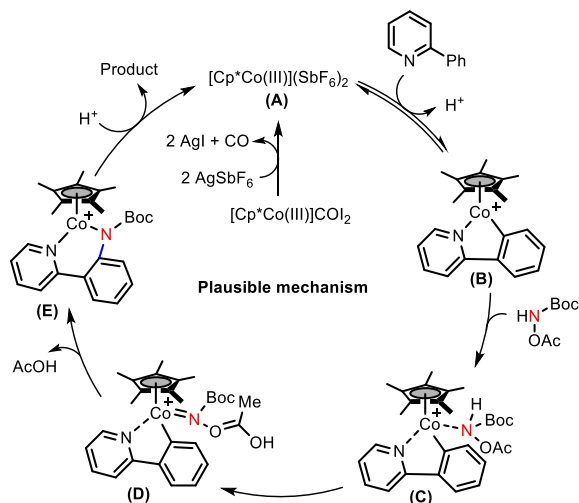
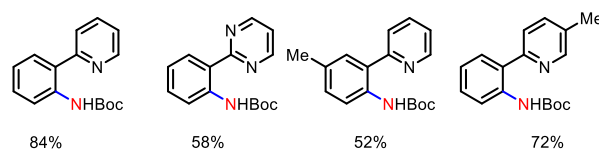
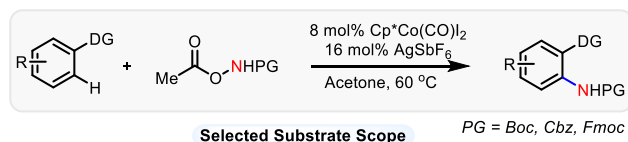


benzamides with alkyl azides revealed that cobalt showed inferior catalytic performance due to both kinetically and thermodynamically less favorable C-H bond cleavage, specifically the concerted metalation-deprotonation (CMD) process, compared to its rhodium analogue. Despite these limitations, a pioneering study by Kanai and co-workers demonstrated that Cp^{*}Co(CO)I₂ can catalyze the C2-selective

directed C-H amidation of indoles using sulfonyl azides (Scheme 66B).¹⁷¹ This method was later extended by the same group to include phosphoryl azides as amidating agents (Scheme 66C).¹⁷²

3.3.5.2. Introducing Acetoxycarbamates. Beyond organic azides, other nitrene sources have also been employed in cobalt-catalyzed C-H amination. The Chang group reported the use of O-acylcarbamates in Cp^{*}Co(III)-catalyzed C-H amination of arenes (Scheme 67).¹⁷³

Scheme 67. Cobalt-Catalyzed Arene C-H Bond Amination Using Acetoxycarbamates



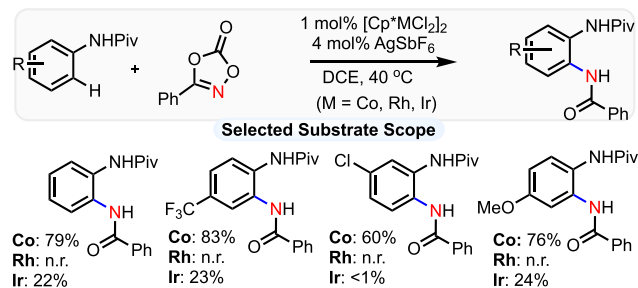
This method enabled the installation of amine functionalities bearing removable protecting groups such as *tert*-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), and fluorenylmethyloxycarbonyl (Fmoc). Interestingly, the developed method is also viable for the amidation reaction using biologically active purine as the directing group. A measured intermolecular kinetic isotope effect (KIE) of 1.1 suggested that C-H bond cleavage is unlikely to be involved in the turnover-limiting step.

The proposed catalytic cycle of the amidation involves the generation of a cationic cobalt(III) species (A), which undergoes C-H activation to form a five-membered cobaltacycle intermediate (B). Coordination of the amidating reagent to this metallacycle, followed by oxidative activation, leads to the formation of a nitrene species (C). Subsequent nitrene insertion into the arene yields a Co(III)-amido intermediate (D). Final protonolysis of this intermediate delivers the desired product and regenerates the cobalt catalyst (E), thus completing the catalytic cycle.

3.3.5.3. Utilizing Dioxazolones. Further expanding the scope for directing-group assisted C-H bond amination, the

Chang group employed dioxazolones as versatile acyl nitrene precursors in cobalt catalysis (Scheme 68).¹⁷⁴

Scheme 68. Comparative Catalytic Activity of Group-9 Cp^{*}M-complexes in C(sp²)-H Amination with Dioxazolones



Interestingly, a comparative study revealed that Cp^{*}Co(III) outperformed its Rh and Ir analogues in the C-H amidation of anilides, although the underlying reason for this enhanced activity remains unclear. Nevertheless, this observation underscores the growing potential of first-row transition metal catalysis. This cobalt-catalyzed method was also extended to a diverse range of substrates featuring various directing groups, including purine, pyridine, pyrimidine, ketoxime, pyrazole, and oxazolonyl motifs, with dioxazolones as effective amidating agents.^{175–180}

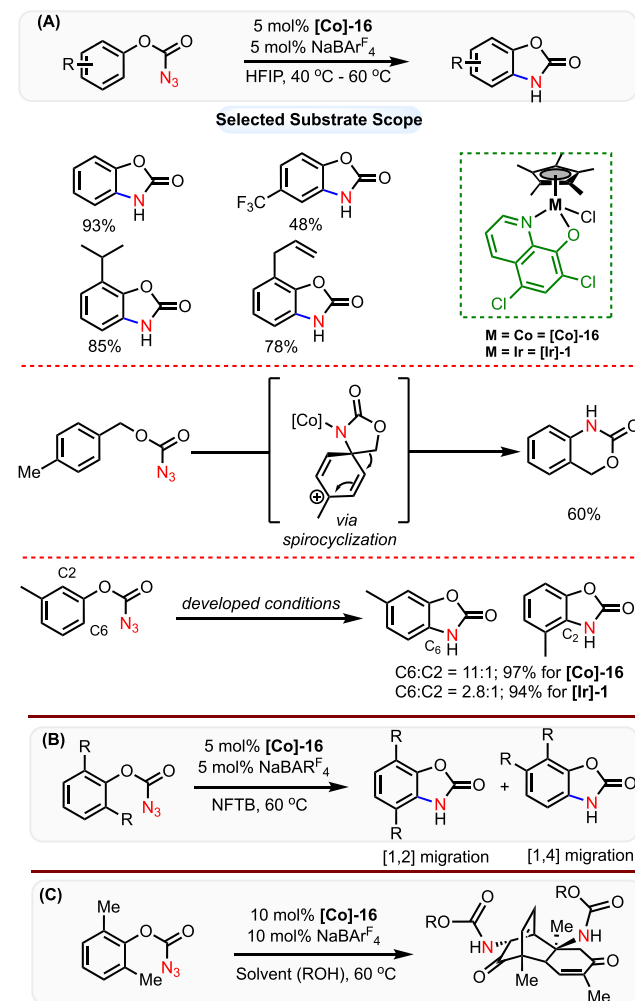
3.3.6. Cobalt-Catalyzed C(sp²)-H Amination (Intramolecular). The potential of Cp^{*}Co(III)-catalysis was further explored in the intramolecular C(sp²)-H amination of phenyl azidoformates to access benzo-fused cyclic carbamates (Scheme 69A).¹⁸¹ A tailored [Co]-16 catalyst proved to be effective for this transformation via an outer-sphere C-H amination pathway.¹⁸² Interestingly, when benzyl azidoformate was used, a spirocyclization followed by skeletal rearrangement (as highlighted in Scheme 69A) through C-C migration was observed, affording a six-membered cyclic carbamate. Importantly, the [Co]-16 catalyst showed high regioselectivity, preferentially aminating the less hindered C6 position over the C2 site in *meta*-substituted phenyl azidoformates. In contrast, the iridium-based counterpart ([Ir]-1) exhibited lower regioselectivity for C6/C2 amination. The X-ray crystallographic analysis of [Co]-16 revealed shorter bond lengths between the cobalt center and its ligands compared to the iridium catalyst. This tighter coordination environment likely increases steric repulsion, thereby favoring insertion of the key metal-nitrenoid at the less hindered C6 position.

The development of the Cp^{*}Co (N,O) system for outer-sphere C(sp²)-H amidation was further explored by the same group for cobalt-nitrenoid transfer in more specialized aromatic systems (Scheme 69B).¹⁸³ While nonafluoro-*tert*-butanol (NFTB) proved to be effective for amidative alkyl migration, switching the solvent to hexafluoroisopropanol (HFIP) dramatically altered the reaction outcomes (Scheme 69C).¹⁸⁴

3.4. Nickel Catalysis (Ni)

The surge of base-metal-catalyzed NTRs received significant invigoration by nickel-mediated nitrene transfer reactions to forge C-N bonds. In general, Ni-catalyzed hydroamination reactions have prevailed more compare to other base metals, which is as follows.

Scheme 69. Cp^{*}-Cobalt-Catalyzed Intramolecular C(sp²)-H Amination of Arylazidoformates

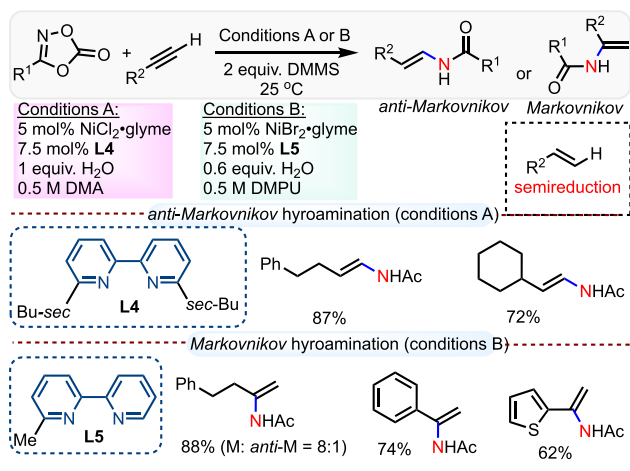


3.4.1. NiH-Catalyzed Hydroamination Reactions (Intramolecular). **3.4.1.1. Leveraging Dioxazolones.** Nickel-catalyzed hydroaminations of alkynes garnered significant attention due to its high regioselectivity.

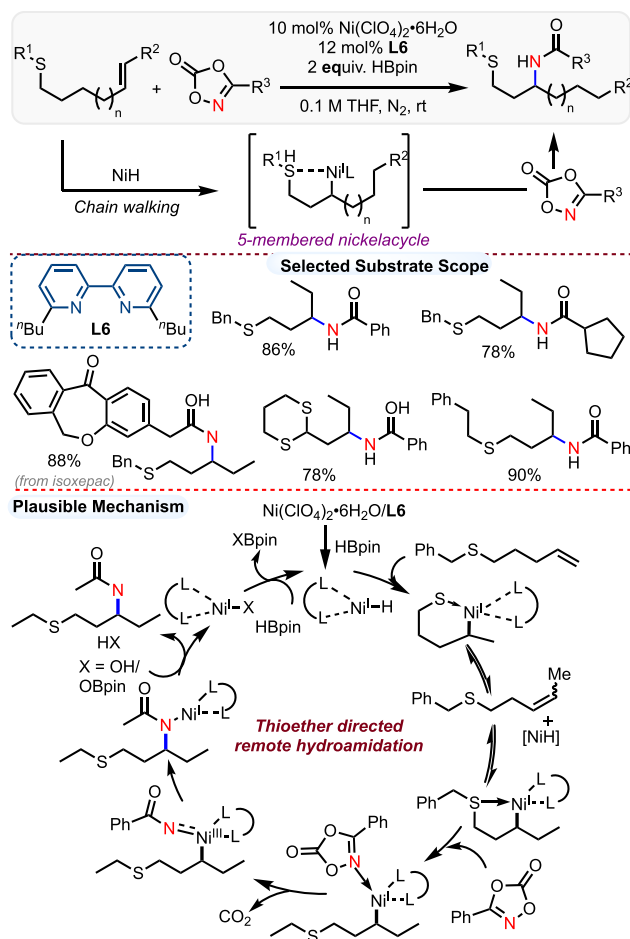
In this vein, Chang, Seo, and co-workers demonstrated a ligand-controlled hydro-nickelation pathway that enables access to both (*E*)-anti-Markovnikov and Markovnikov hydroaminations product of terminal alkynes with good to excellent regioselectivity (Scheme 70).¹⁸⁵ They observed that sterically more encumbered ligand (L4) directed terminal metalation, thus provided anti-Markovnikov product. In the contrary, strictly less demanding ligand (L5) allowed innate Markovnikov hydrometalation. Notably, the addition of H₂O significantly increased the turnover number. Combined theoretical and experimental studies suggest that water facilitates the transmetalation step.

Alike alkynes, NiH-catalyzed hydroamination reactions of alkenes are quite interesting due to their high regioselectivity aspect. In that regard, thioether-directed highly γ -selective remote Markovnikov-hydroamidation reaction of unactivated alkene using NiH-catalysis was reported by Yu and co-workers (Scheme 71).¹⁸⁶ They utilized [Ni(ClO₄)₂]-6H₂O catalyst in combination with 2,9-dibutyl-1,10-phenanthroline ligand (L6) and dioxazolone as an amidation agent. It was observed that this method competently provided hydroamidation product of

Scheme 70. NiH-Catalyzed Regiodivergent Hydroamidation of Alkenes



Scheme 71. NiH-Catalyzed $\text{C}(\text{sp}^3)\text{-H}$ -Selective Migratory Hydroamidation of Unactivated Alkenes

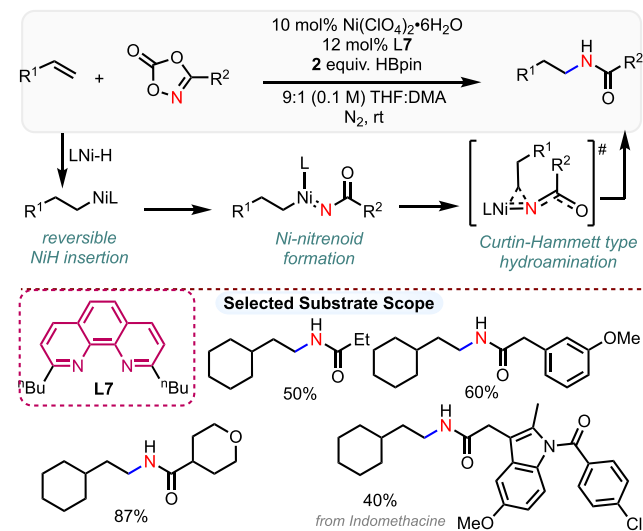


diverse classes of alkenes with excellent yield and regioselectivity. While both benzylic and aliphatic thioethers afforded high regioselectivity, a notable decline in reaction efficiency was observed with increasing distance between alkene and sulfur atom. Upon careful investigation and previous literature precedents, they proposed that at first NiH-catalyst is inserted into the alkene and the corresponding stable five-membered nickelacycle effectively halts the chain-walking isomerization at

a specific γ -methylene site, which consequently leads to regioselective γ -functionalization as shown in Scheme 71.

Using the same catalytic conditions, the Yu group further expanded the hydroaminations reactions for the *anti*-Markovnikov amination of unactivated alkenes (Scheme 72).¹⁸⁷ The steric bulk of the ligand plays a crucial role to

Scheme 72. NiH-Catalyzed *anti*-Markovnikov Hydroamidation of Unactivated Terminal Alkenes

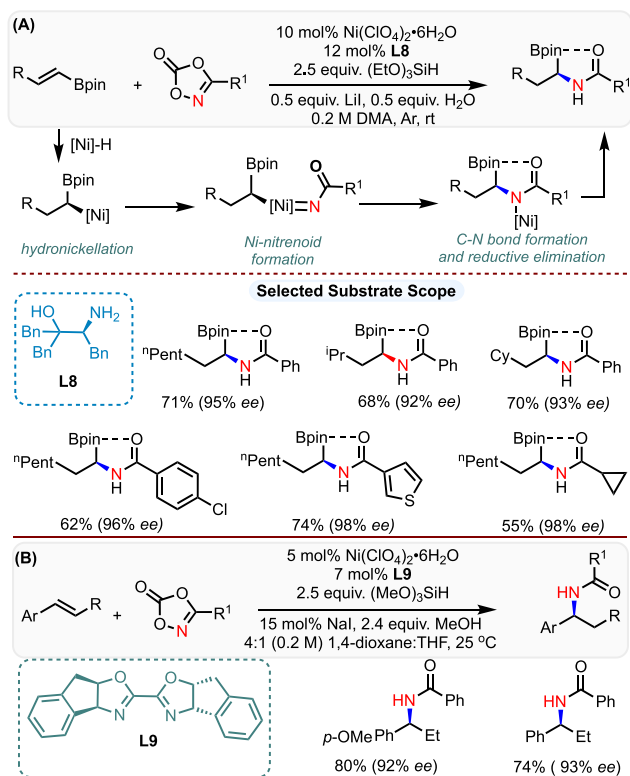


guide the *anti*-Markovnikov-type insertion of the metal into the alkene. Mechanistic insights, supported by DFT calculations, indicated that the reaction proceeded via an initial reversible insertion and elimination of the $[\text{NiH}]$ species into the alkene. This was followed by an irreversible Curtin–Hammett type hydroamidation step,¹⁸⁸ leading to the formation of *N*-alkyl amides. Crossover experiments and deuterium-labeling studies provided further evidence for the observed *anti*-Markovnikov regioselectivity.

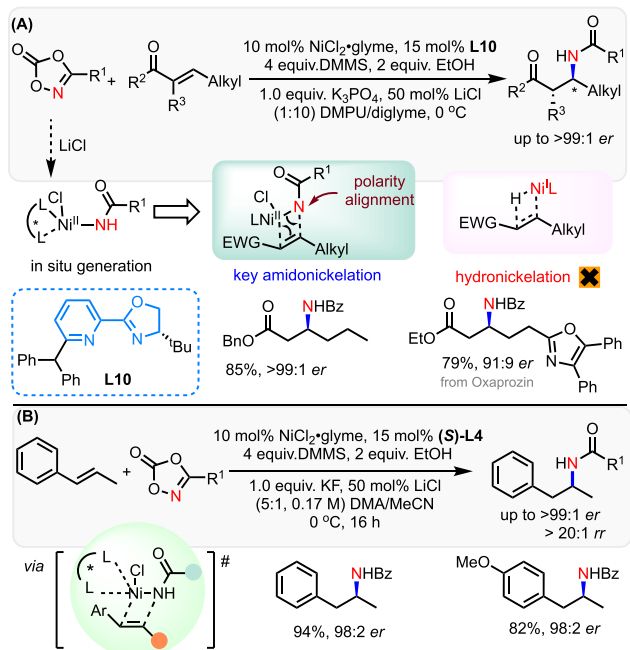
Contemporarily, Zhu and co-workers in 2022, reported the asymmetric hydroamidation of alkenyl boronates using NiH-catalysis (Scheme 73 (A)).¹⁸⁹ This approach used a simple amino alcohol ligand (**L8**), which was competent enough to provide high enantioselectivity under mild reaction conditions. This method proved to be versatile, yielding a variety of α -aminoboronates and a biologically active pharmacophore in excellent yields and with remarkable enantioselectivities. Mechanistic studies revealed that the transformation proceeds through an enantioselective hydrometalation step, followed by inner-sphere nitrenoid transfer, resulting a C–N bond formation. Finally reductive elimination to complete the catalytic cycle. In another study, utilizing bioxazoline ligand (**L9**) in NiH catalysis, the Zhu group demonstrated the enantioselective benzylic amidation of styrenes (Scheme 73 (B)).¹⁹⁰ They observed that an underlying enantioselective *syn*-hydronickellation step plays a crucial role in the chiral induction of the developed reaction.

In 2024, Chang and co-workers disclosed a β -selective chiral hydroamidation of α,β -unsaturated carbonyl compounds. The $\text{NiCl}_2 \cdot \text{glyme}$ catalyst in combination with a (*tert*-Bu)-substituted chiral pyridineoxazoline (PyOX) ligand (**L10**) enabled high enantioselectivity (up to >99:1 *er*) for aminating various alkyl-substituted olefins conjugated to esters, amides, thioesters, and ketones at the β -positions (Scheme 74 (A)).¹⁹¹

Scheme 73. NiH-Catalyzed Asymmetric Hydroamidation of Vinyl Boronates and Vinylarenes



Scheme 74. NiH-Catalyzed Formal Olefinic Hydroamidation and Asymmetric Homobenzylic Hydroamidation of Aryl Alkenes

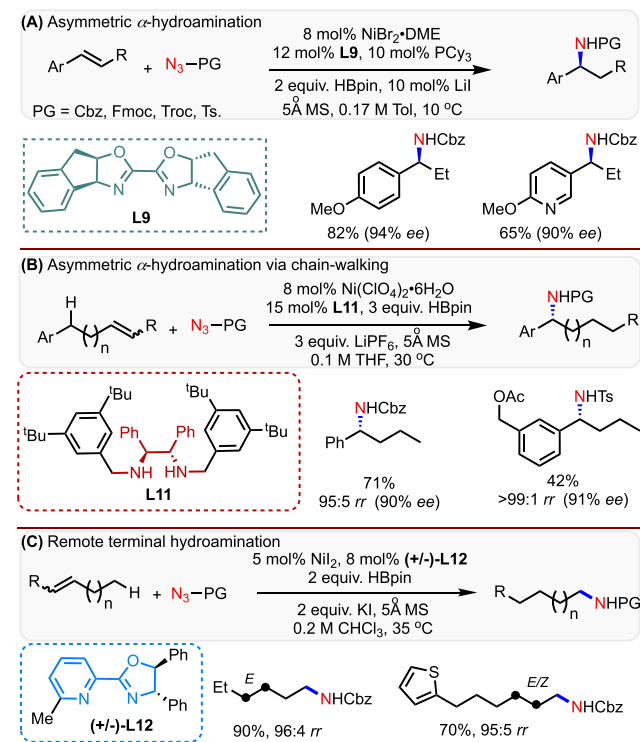


Experimental findings complemented by DFT calculations revealed that the reaction does not proceed via a direct hydronickelation pathway, which would lead to α -metalation. Instead, the process involves olefin amidonickelation of the Ni-amido intermediate, generated in situ from the dioxazolone. This mechanism was driven by a polar-matched migratory

olefin insertion, that accounts for the high regioselectivity and asymmetric induction. Using a similar mechanistic approach, very recently, the same group expanded the Ni-catalysis for regio- and enantioselective homobenzylic hydroamination of aryl alkene (Scheme 74 (B)).¹⁹²

3.4.1.2. Incorporating Organic Azides. Apart from dioxazolone, organic azides can also serve as nitrene precursors for hydroamidation reactions under the domain of nickel catalysis. In that regard, the group of Wang and Zhu introduced a NiH-catalyzed strategy for *ipso*- and remote hydroamination of proximal or distant alkenes, enabling the regio- and enantioselective synthesis of both linear and α -branched primary amines in 2024 (Scheme 75 (A)).¹⁹³ In

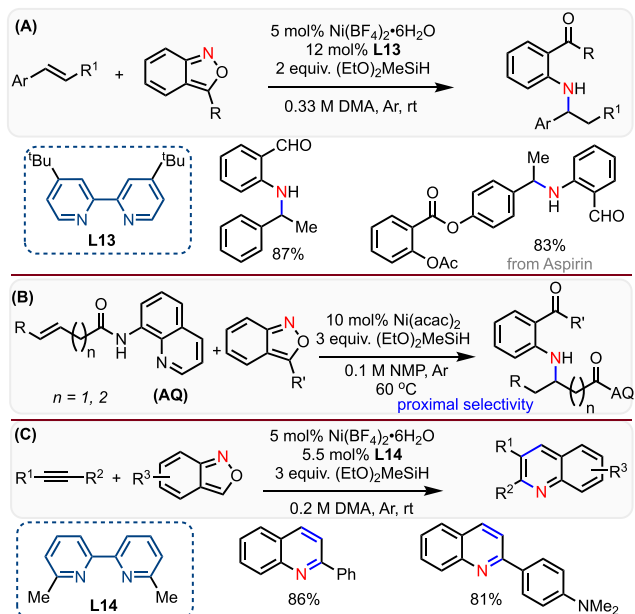
Scheme 75. NiH-Catalyzed *ipso*- and Remote Hydroamination



contrast to the extensively studied CuH species, NiH species exhibit markedly lower nucleophilicity, rendering them compatible with carbonyl groups and amenable to a wider array of electrophilic amination reagents. For instance, nitroarenes, which are prone to reduction by CuH, serve as effective aryl-aminating agents in NiH catalysis. Hence, it was hypothesized that NiH species could generate promising results in the presence of sensitive azides.¹⁹³ Through systematic optimization, the authors discovered that use of $\text{NiBr}_2 \cdot \text{dimethoxyethane}$ (DME) in combination with a chiral bisoxazoline ligand (**L9**) can generate excellent yield and high enantioselectivity. For the more challenging asymmetric remote hydroamination, they utilized a dual-function chiral diamine ligand (**L11**), which proved essential for both chain-walking and subsequent regio- and enantioselective amination (Scheme 75 (B)). This approach was successful even with remote terminal or internal unactivated olefinic substrates. Altering the reaction conditions, terminal-selective remote hydroaminations were also achieved (Scheme 75 (C)).

3.4.1.3. Utilizing Anthranils. Anthranils were also employed as the nitrene source for the hydroamidation reaction. In 2021, Hu et al. disclosed the NiH-catalyzed hydroamination of olefins using anthranil as electrophilic aminating agent for the synthesis of *N*-alkyl-2-aminobenzophenones and *N*-alkyl-2-aminobenzaldehydes (Scheme 76 (A)).¹⁹⁴ Combining the

Scheme 76. NiH-Catalyzed Hydroamination of Olefins Using Anthranils

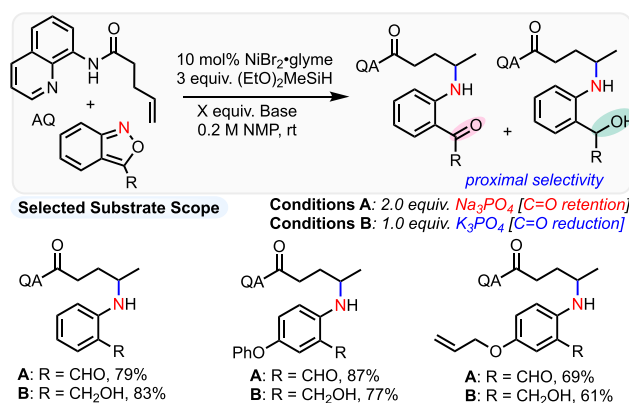


Ni(BF₄)₂·6H₂O catalyst and bipyridine ligand (**L15**) in the presence of hydrosilane, as reducing agent, provides the desired products in good to excellent yield. One unique feature of this strategy is its distinctive reaction outcome compared with the previously developed CuH catalysis. While the Cu-catalyzed method¹⁹⁵ gives rise to a complete reduction resulting in benzyl alcohol, this strategy provides the retention of the carbonyl group. The mechanism suggested that the reaction proceeds through NiH-insertion into the olefin, and further, in the presence of anthranil, the Ni-nitrenoid is formed. Finally, after reductive elimination, the desired product is formed. Subsequently, Hu and co-workers expanded their NiH-catalyzed hydroamination strategy for directing group assisted proximal selective functionalization of unactivated alkenes using anthranil (Scheme 76 (B)).¹⁹⁶ The high regioselectivity of the product is due to the presence of a bidentate 8-aminoquinoline (AQ) directing group via the formation of nickellacycle intermediates. Furthermore, the Hu group developed a NiH-catalyzed cascade hydroamination/cyclization of both terminal and internal alkynes with anthranils, providing an efficient route to highly substituted quinolines (Scheme 76 (C)).¹⁹⁷

In 2023, Wang et al. reported that the nature of the base used for hydrosilylation can alter the chemoselectivity of directing group assisted proximal selective functionalization of unactivated alkenes using anthranil (Scheme 77).¹⁹⁸ When Na₃PO₄ was used as base, the carbonyl group was retained. On the other hand, K₃PO₄ provided carbonyl reduction via a base-catalyzed hydrosilylation process.

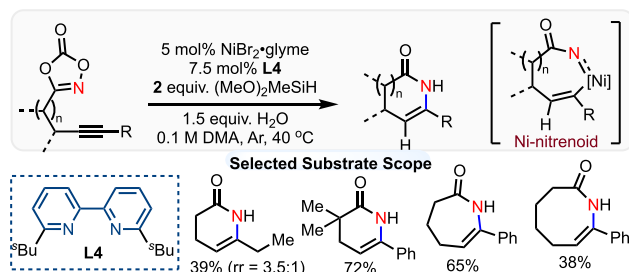
3.4.2. NiH-Catalyzed Hydroamination Reactions (Intramolecular). In 2022, after developing the intermolecular

Scheme 77. NiH-Catalyzed Proximal Selective Divergent Hydroamination



hydroamidation of alkynes, the Chang group explored intramolecular hydroamidation of alkynyl dioxazolones to achieve the regioselective synthesis of six- to eight-membered enamides (Scheme 78).¹⁹⁹ Remarkably, the reaction favored

Scheme 78. NiH-Catalyzed Endo-Selective Intramolecular Hydroamidation of Alkynes

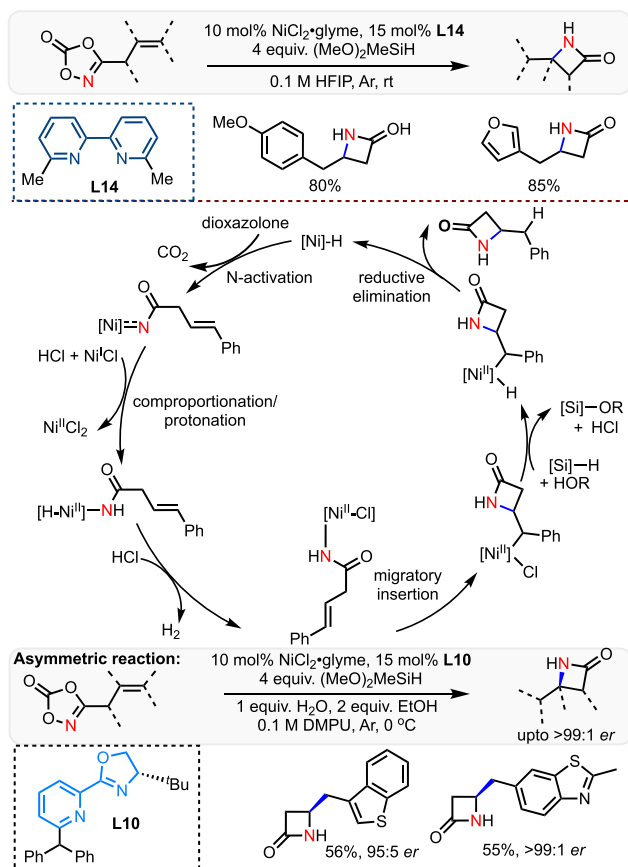


the endocyclic pathway over the exocyclic one, delivering products with excellent regioselectivity. They proposed that Ni(I) hydride species acts as the active catalyst. The proposed catalytic cycle involves key steps such as *syn*-hydronickelation, alkenylnickel isomerization, oxidative activation of the dioxazolone, and inner-sphere nitrenoid transfer, culminating in *endo*-selective C–N bond formation. The critical alkenylnickel isomerization step was shown to proceed through an η^2 -vinyl-like transition state.

The same group further explored the NiH-catalyzed intramolecular hydroamination to prepare β -lactam scaffolds with remarkable regioselectivity (Scheme 79).²⁰⁰ The formation of β -lactams occurred exclusively through proximal C–N bond formation, effectively suppressing the distal selectivity that would yield γ -lactams.

Using a NiCl₂·glyme catalyst in combination with a 6,6'-dimethyl bipyridine ligand (**L14**), a broad range of aryl, alkyl, and heteroaryl alkene substrates were successfully converted to the desired β -lactam products with high regioselectivity. Furthermore, replacing the bipyridine ligand with a chiral ligand (**L10**) resulted in highly enantioenriched β -lactams with moderate yields. Importantly, the enantioselectivity can be altered by changing the stereochemistry of the ligand. For example, the use of an (*S*)-**L10** ligand led to the formation of (*R*)- β -lactam products and vice versa. The reaction proceeded through an unconventional pathway, bypassing the traditional transition metal hydride (TMH) mechanism. Instead, the process was initiated by a kinetically controlled *N*-activation

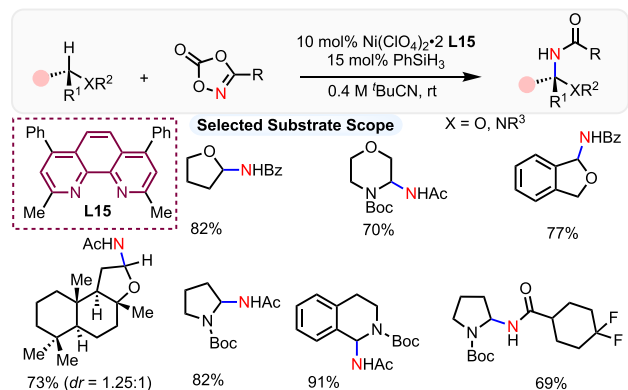
Scheme 79. NiH-Catalyzed Intramolecular Asymmetric Hydroamidation



step involving a Ni-nitrenoid species. This was followed by the formation of alkenylamido-Ni(II) intermediates, which facilitated regioselective intramolecular amidonickelation to yield the β -lactam products.

3.4.3. Ni-Catalyzed $\text{C}(\text{sp}^3)$ -H Amination (Intermolecular). In 2022, Martin and co-workers demonstrated an intermolecular $\text{C}(\text{sp}^3)$ -H amination using nickel-catalysis and dioxazolone as nitrene precursor (Scheme 80).²⁰¹ Under the reaction conditions, amidation took place adjacent to the nitrogen or oxygen atom of the saturated heterocyclic compounds. Kinetic analysis using deuterated substrates

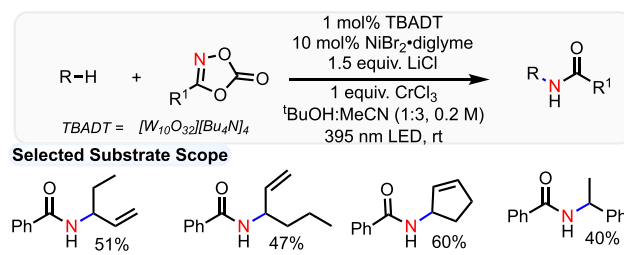
Scheme 80. Nickel-Catalyzed Site-Selective Intermolecular $\text{C}(\text{sp}^3)$ -H Amidation



revealed a KIE of 3.8, suggested that $\text{C}(\text{sp}^3)$ -H cleavage is the rate-limiting step.

Hydrosilane played an important role in reducing the oxidation state of nickel. EPR analysis suggested that Ni(II) converted to active Ni(I) species by PhSiH_3 , which is the active catalytic species for the transformation (Scheme 80). Although, this method can tolerate diverse class of substrates, but it requires excess amount of heterocyclic partners. Recently, this limitation was overcome by the Baudoin group using iron catalysis.¹¹⁷ In the same year, Wang et al. unveiled a tungsten/nickel cocatalyzed strategy for the amidation of inert $\text{C}(\text{sp}^3)$ -H bonds using photoexcitation strategy (Scheme 81).²⁰² A KIE of 1.25 was observed for the reaction, suggesting

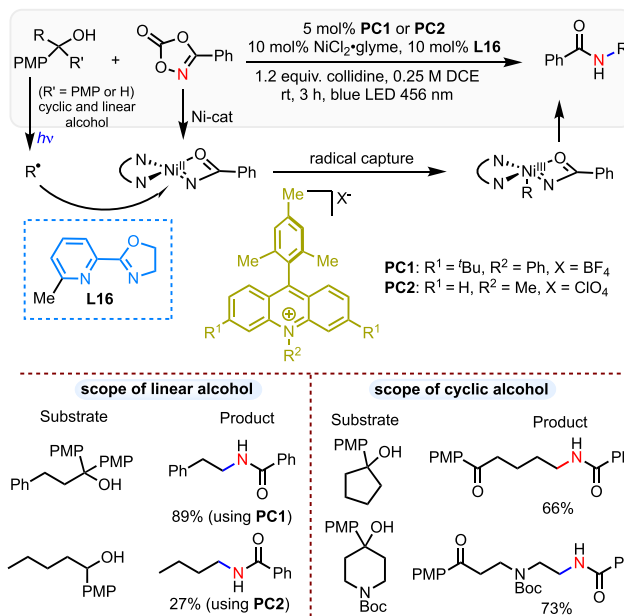
Scheme 81. Photoexcited Amidation of Inert $\text{C}(\text{sp}^3)$ -H Bonds



that homolytic C-H bond cleavage is not the rate-limiting step, instead, they found that the regeneration of TBADT and NiI_2 is the rate-determining step.²⁰² The Bao group also reported²⁰³ a similar kind of direct intermolecular $\text{C}(\text{sp}^3)$ -H amidation reaction via synergistic decatungstate anion photocatalysis and nickel catalysis.

Recently, Chang group reported a photoredox/Ni dual-catalyzed strategy for $\text{C}(\text{sp}^3)$ -N coupling, leveraging dioxazolones as precursors for Ni(II)-nitrenoid species (Scheme 82).²⁰⁴ This approach facilitates the synthesis of versatile *N*-alkyl amides, enabling $\text{C}(\text{sp}^3)$ -amidation reactions with both

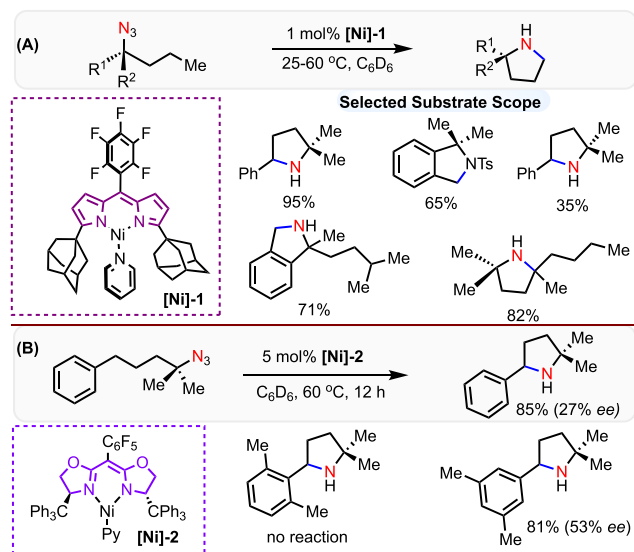
Scheme 82. Synthesis of *N*-Alkyl Amide via Dual Photoredox PCET/Ni-Catalysis



cyclic and acyclic alcohols. Experimental and computational investigations revealed that photoredox-mediated proton-coupled electron transfer (PCET) plays a key role in generating alkyl radicals from alcohols. The resulting carbon-centered radicals are efficiently captured by the (κ^2 -N,O)Ni(II)-nitrenoid intermediate, which subsequently undergoes reductive elimination to yield aliphatic amides containing C(sp³)–N bonds. This method is the first example of PCET/Ni-catalyzed amidative β -scission using alcohols.

3.4.4. Ni-Catalyzed C(sp³)–H Amination (Intramolecular). In 2020, Betley and co-workers studied the intramolecular C(sp³)–H amination reaction of tertiary aliphatic azides using Ni-dipyrrin catalysis (Scheme 83 (A)).²⁰⁵ The

Scheme 83. Ni-Catalyzed C(sp³)–H Amination

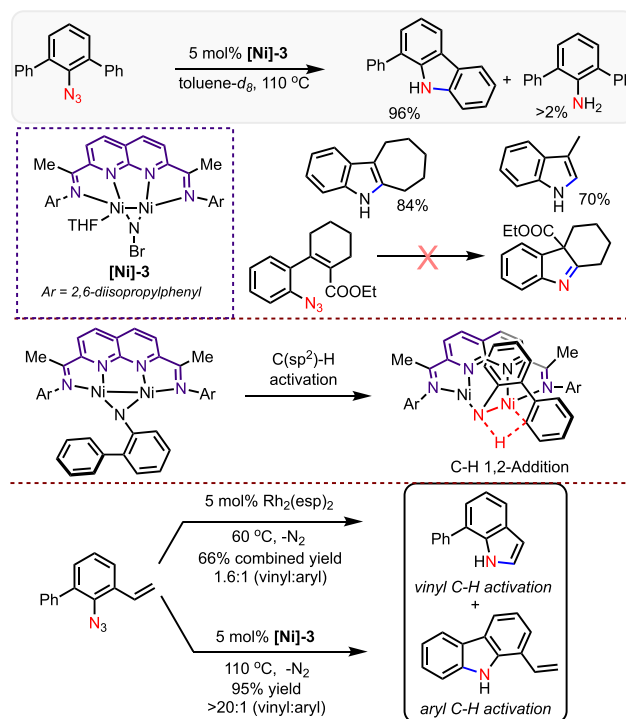


catalyst ([Ni]-1) showed excellent reactivity toward primary, secondary, tertiary, and benzylic C–H bonds. A remarkably high primary kinetic isotope effect (KIE) value of 31.9 ± 1 was observed. A radical mechanism was proposed for the reaction comprising hydrogen atom transfer and radical recombination steps. An enantioselective version of this transformation was also attempted using a ([Ni]-2) catalyst; however, the enantioselectivity remained low (Scheme 83 (B)).²⁰⁶ Notably, substrate scope analysis revealed that increasing the steric bulk at the meta positions on the aryl substituents leads to a higher ee.

3.4.5. Nickel-Catalyzed C(sp²)–H Amination. In 2020, Uyeda and co-workers reported a Ni-catalyzed intramolecular C(sp²)–H amination enabled by a dinuclear nickel complex, ([Ni]-3), using a naphthyridine-diimine (NDI) ligand (Scheme 84).²⁰⁷

This catalyst system activates aryl and vinyl C(sp²)–H bonds for nitrene insertion via a distinct C–H bond activation pathway, diverging from the conventional electrocyclic mechanism observed with Rh-catalyzed systems. Notably, the dinickel catalyst ([Ni]-3) outperforms the widely used Rh-based catalyst [Rh₂(esp)₂] in achieving chemoselective amination of azide substrates bearing both α -phenyl and α -vinyl groups. While [Rh₂(esp)₂] affords a mixture of aryl and vinyl C–H amination products, the dinickel catalyst exhibits high selectivity, favoring vinyl C–H functionalization with a ratio >20:1 (vinyl C–H/aryl C–H). DFT studies reveal that

Scheme 84. Dinickel-Catalyzed Intramolecular C(sp²)–H Amination



the cationic Ni₂(μ -NAr) complex undergoes endothermic cleavage of its metal–metal bond, creating an open coordination site that accommodates the substrate's C–H σ -bond. This coordination facilitates a kinetically favorable 1,2-addition of the C–H bond to the dinickel imide, leading to a metallacyclic intermediate. The transition state for vinyl C–H activation is calculated to be 9.1 kcal/mol lower in energy than that for aryl C–H activation, explaining the observed selectivity.

3.5. Copper Catalysis (Cu)

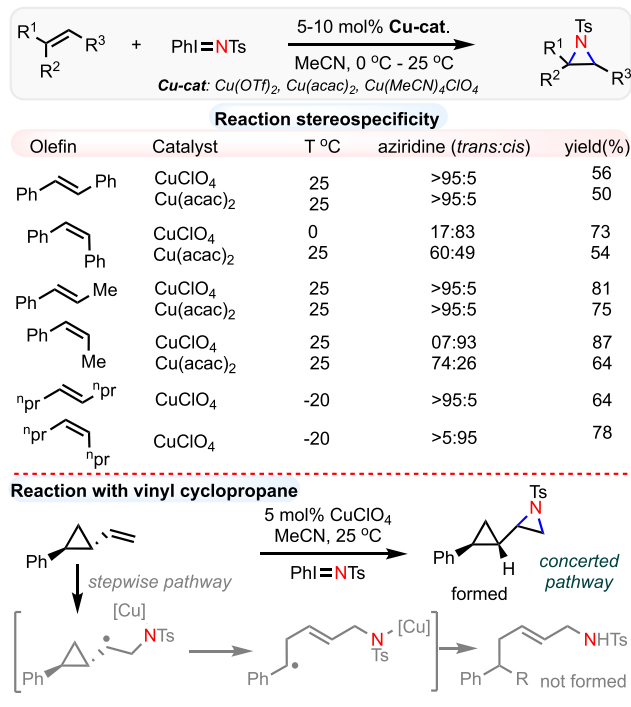
Over the years, the discovery and design of novel copper complexes have enabled the precise and efficient incorporation of nitrene intermediates into organic frameworks, addressing longstanding challenges in nitrogen-functionalization chemistry.

3.5.1. Copper-Catalyzed Aziridination Reactions.

3.5.1.1. Exploiting Iminoiodinanes. In early 1990s, the Evans group^{57,58} made significant advancements in olefin aziridination using Cu(I) and Cu(II) catalysis. They utilized PhI=NTs as a nitrogen source for aziridination and showed that copper catalysts like Cu(OTf)₂, Cu(acac)₂, and Cu(MeCN)₄ClO₄ were more effective than other metal complexes, such as Fe(TPP)Cl, Mn(TPP)Cl, Co(acac)₂, and Rh(OAc)₄ which often led to a mixture of aziridination and amination products.

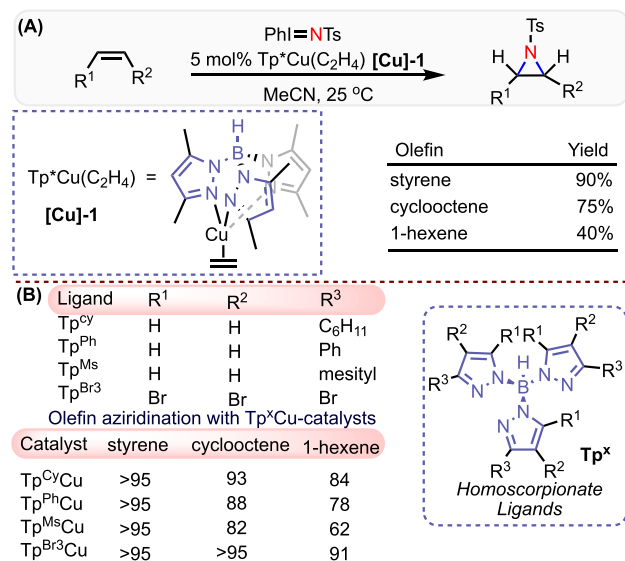
Investigations into substrate scope revealed that the aziridination reaction was effective across a broad range of electron-rich and electron-deficient olefins. Additionally, they found that olefin geometry and substituent nature had a significant impact on the stereoselectivity of the aziridination (Scheme 85).²⁰⁸ The reaction exhibited high stereospecificity with *trans*-1,2-disubstituted alkenes and *cis*-1,2-alkyl-substituted alkenes. However, phenyl substitution on the olefin seems to alter the aziridination from a stereospecificity to a

Scheme 85. Copper-Catalyzed Stereospecific Aziridination



nonstereospecificity manifold as demonstrated for *cis*-stilbene and *cis*- β -methylstyrene. To gain insight into the reaction mechanism, a reaction was conducted with vinyl cyclopropane that resulted in exclusively aziridination product with cyclopropane ring intact. This finding supported a concerted nature of the reaction pathway or a rapid radical rebound. In 1993, Templeton, Brookhart and Perez demonstrated that the poly(pyrazolyl)borate-Cu(I) complex, Tp^{*}Cu(C₂H₄) ([Cu]-1) (where Tp^{*} is hydro-tris(3,5-dimethyl-1-pyrazolyl)borate), served as an effective catalyst for the aziridination of styrene, 1-hexene, and *cis*-cyclooctene with PhI=NTs as the nitrogen source (Scheme 86 (A)).²⁰⁹ Almost after one decade, the Perez group further explored a series of poly(pyrazolyl)borate-

Scheme 86. Copper-Homoscaptopionate in Aziridination Reactions



Cu(I) complexes in aziridination reaction and discovered that the perbromo catalyst, TpBr₃Cu, achieved remarkably high yields of aziridines, even when using equimolar mixtures of olefin and PhI=NTs, along with a low catalyst loading of just 1% (Scheme 86 (B)).²¹⁰ Later, Lovely and co-workers showed that copper complexes of fluorinated tris(pyrazolyl)borates serve as more versatile alternatives for aziridination reactions compared to their nonfluorinated counterparts.²¹¹ Subsequently, incorporating iminoiodinanes as nitrene surrogate, aziridination of styrene and its derivatives were reported using different copper catalysts.^{212,213}

3.5.1.2. Incorporating Organic Azides. Most Cu-catalysts described for the aziridination of olefins typically require 5 mol % loading relative to the nitrogen sources. However, in 1999, an exception was noted by Halfen et al., who utilized ([Cu]-2) in catalytic amounts of just 0.5 mol %, which is 10–20 times less than what is needed for other most used copper catalysts (Scheme 87).²¹² Similarly, in 2017, Che reported that tripodal S-ligand complex of copper(I) ([Cu]-8) could catalyze aziridination reactions with only 1 mol % catalyst loading.²¹³ A list of copper-complexes^{214–218} has been displayed in Scheme 87, which showed remarkable efficiency in aziridination reaction. Furthermore, different amine precursors were also used for aziridination reactions.^{219–221}

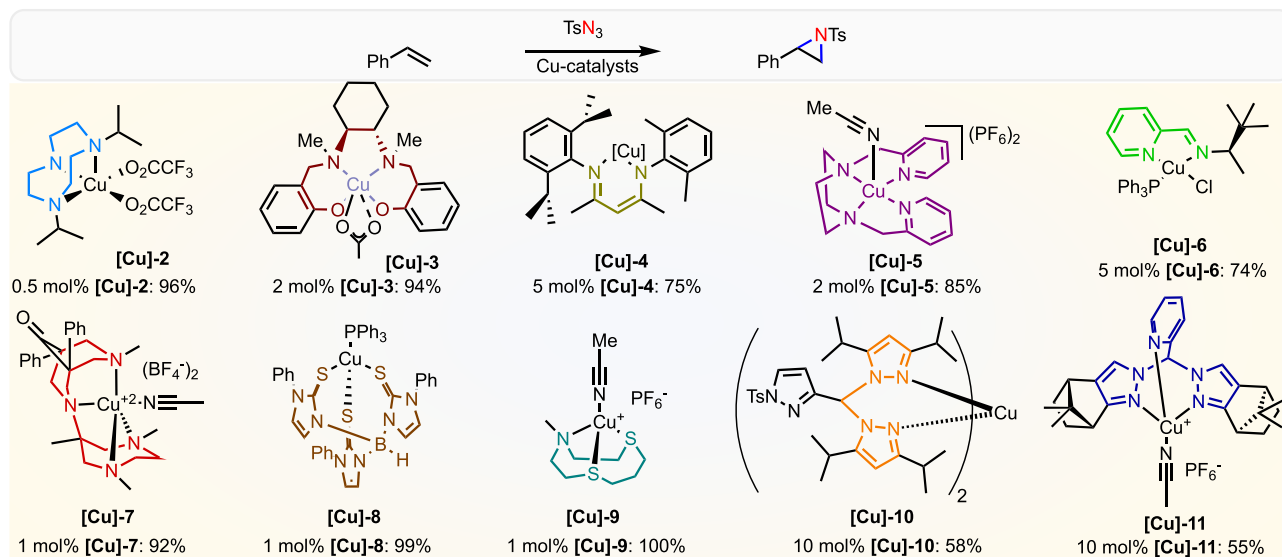
3.5.1.3. Utilizing Sulfonamides. In 2010, a diastereoselective copper-catalyzed alkene aziridination has been reported by the Dauban group using chiral nitrenes generated from sulfonimides in the presence of an iodine(III) oxidant (Scheme 88).²²² The reaction involves the interaction of iodosylbenzene, an iodine(III) oxidant, with a sulfonimide in the presence of a copper catalyst, leading to the formation of a highly reactive chiral metallanitrene intermediate. This metallanitrene reacts with various olefins, used in stoichiometric amounts, to produce aziridines in excellent yields, reaching up to 96%. The addition of the nitrene derived from *p*-nitrosulfonimide to *tert*-butyl acrylate demonstrates an optimized diastereomeric excess (*de*) of 94%. Stereoselectivity in the aziridination was further refined through the combination of the sulfonimide with a chiral copper catalyst, enabling matching and mismatching effects. Notably, this stereocontrol was observed predominantly with styrene and its derivatives. A significant feature of this transformation is the preferential addition of the electron-deficient nitrene species to electron-poor olefins, showcasing its unique reactivity profile.

In 2011, Dodd and co-workers reported a copper(I)-catalyzed aminolactonization reaction involving various 4-aryl-pent-4-enoates and in situ-generated nosyliminoiodane, producing 5-aryl-5-nosylamidomethylbutyrolactones (Scheme 89).²²³ This reaction was proposed to proceed through an aziridine intermediate. Efforts to introduce chirality into the process were explored using chiral salen and BOX (L17) ligands. Notably, the use of a chiral BOX ligand achieved poor enantiomeric excess (*ee*) of up to 48% with yields up to 90%.

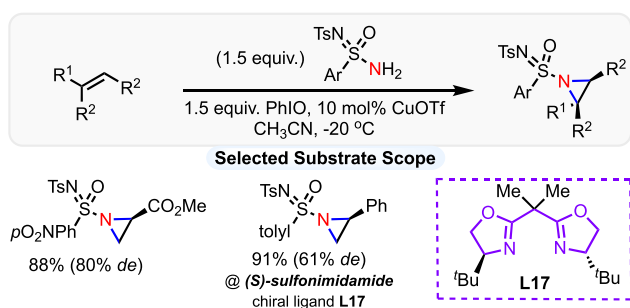
3.5.2. Copper-Catalyzed Asymmetric Aziridination Reaction. In 1993, Jacobsen²²⁴ and Evans²²⁵ independently developed copper-catalyzed enantioselective aziridination reactions (Scheme 90).

Evans used a C₂-symmetric chiral bis-oxazoline ligand (L18) in copper catalysis, which promoted the aziridination of styrene with remarkable enantioselectivity (up to 97% *ee*). On the other hand, Jacobsen introduced benzylidene derivatives of 1,2-diaminocyclohexane (L19) as chiral ligands, achieving high

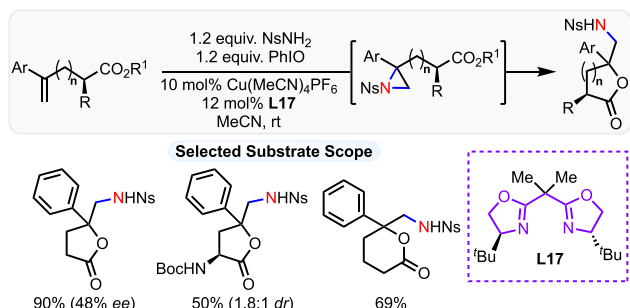
Scheme 87. Copper-Complexes used in Aziridination Reaction



Scheme 88. Copper-Catalyzed Aziridination with Chiral Sulfonimidamides



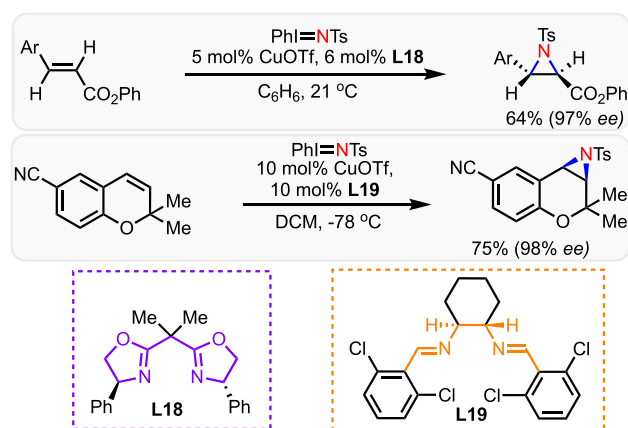
Scheme 89. Copper-Catalyzed Aminolactonization of Olefins



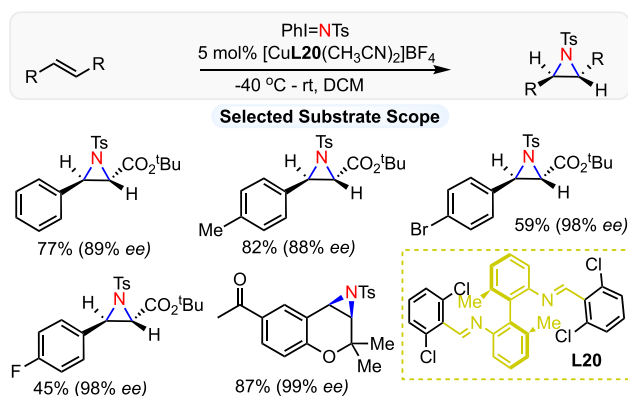
enantioselectivity, with *ee* up to 98%. Furthermore, Jacobsen and co-workers investigated the mechanistic aspects of the (diamine)copper-catalyzed aziridination reaction and provided compelling evidence supporting a nitrene-transfer pathway.²²⁶ Their studies suggested that the copper catalyst activates the nitrene precursor, enabling selective transfer of the nitrene group to the alkene, leading to the formation of the aziridine with high enantiocontrol. These initial studies pave the way for the development of new catalytic systems for enantioselective aziridination reactions.^{227,228}

In the same year, Scott et al. disclosed a highly enantioselective aziridination of olefins achieved with chiral biaryldiimine/Cu(I) catalyst system (Scheme 91).²²⁹ In

Scheme 90. Evans and Jacobsen's Copper-Catalyzed Asymmetric Aziridination



Scheme 91. Chiral Biaryldiimine Ligated Copper Complex in Enantioselective Aziridination



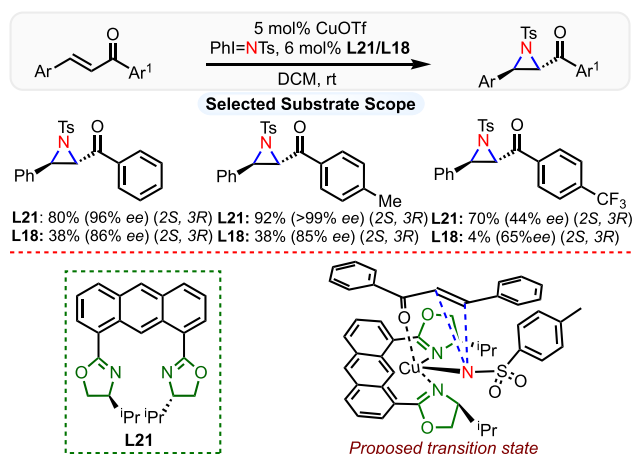
particular, the imine ligand (L20) in combination with Cu(I) or Cu(II) generated up to 99% *ee* in the aziridination of 6-acyl-2,2-dimethylchromene and 88–98% *ee* for a range of cinnamate esters.

Styrenes and other alkenes are converted with lower enantioselectivities (5–54%). Structural analysis of the catalyst

revealed two classes of structures; bimetallic double helices ($[\text{Cu}_2\text{L}_2]^{2+}$) and monometallic ($[\text{CuL}]^+$). Ligand steric governs the structural preference; ortho disubstitution at the aryl imine is required to furnish monometallic, active system. The monometallic form is found to be more efficient in the aziridination of alkenes than the bimetallic one in terms of rate, turnover, and enantioselection. Inspired by Scott's work, both the Shi²³⁰ and Suga²³¹ groups later developed copper-catalyzed enantioselective aziridination reactions using chiral salen-type ligands, which also delivered high *ee* values for cinnamate aziridinations.

In 2005, a highly enantioselective aziridination of chalcones was reported by the Xu group utilizing novel 1,8-bisoxazolidinylanthracene (L21) ligand (Scheme 92).^{232,233} The enantioselective outcome for ligand L21 found opposite to that of the ligand used by Evans (L18).

Scheme 92. Copper-Catalyzed Asymmetric Aziridination of Chalcones



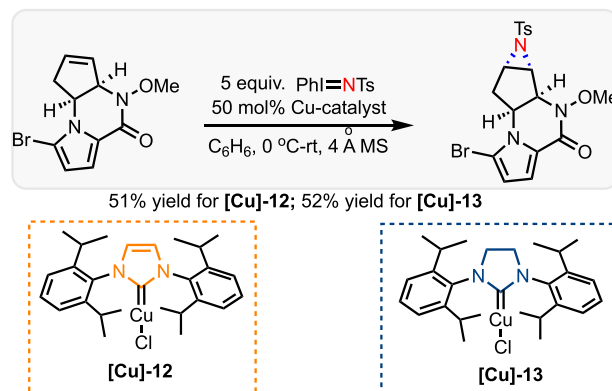
It was observed that the enantioselectivity is highly substituent dependent. Chalcones with electron-donating substituents show higher enantioselectivities due to the stronger Lewis basicity of the oxygen of their carbonyl groups than those with electron-withdrawing substituents.

A transition state for the asymmetric aziridination was proposed where the nitrene attacks from the top and implicates a copper-nitrene species chelated to the ligand nitrogen atoms and to the chalcone carbonyl group.²³⁴ Subsequently, Xu and co-workers demonstrated that cyclohexane-linked bis-oxazoline ligands could also deliver high enantioselectivity in chalcone aziridination.^{235,236} In a related study, they showed that the same ligand (L21) could effectively promote regio- and stereoselective aziridination of 1,3-dienes bearing carbonyl functionalities.²³⁷

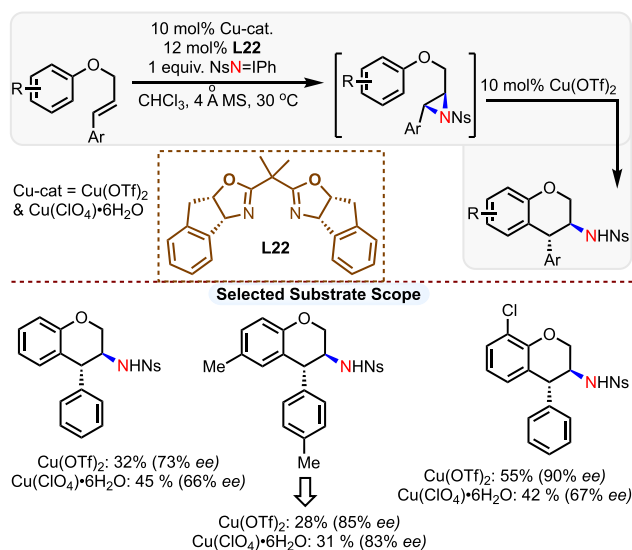
In 2006, Trost and Dong reported an asymmetric aziridination reaction using an NHC-copper catalyst (Scheme 93).^{238,239} This synthetic maneuver proved effective as one of the key steps for the total synthesis of agelastatin A.

In 2011, Sinha and Hajra reported a one-pot azidoarylation reaction of aryl cinnamyl ethers using a copper catalyst in combination with chiral bis-oxazoline ligands (Scheme 94).²⁴⁰ This method afforded 3-amino-4-arylchromans with excellent regioselectivity, diastereoselectivity (*dr* > 99:1), and enantioselectivity (up to 95% *ee*), although the yields were moderate for most substrates. A variety of bis-oxazoline ligands, the indenyl-derived BOX ligand, in particular, exhibited the highest

Scheme 93. NHC-Copper-Catalyzed Aziridination Reaction



Scheme 94. Copper-Catalyzed Enantioselective Aziridoarylation Reaction



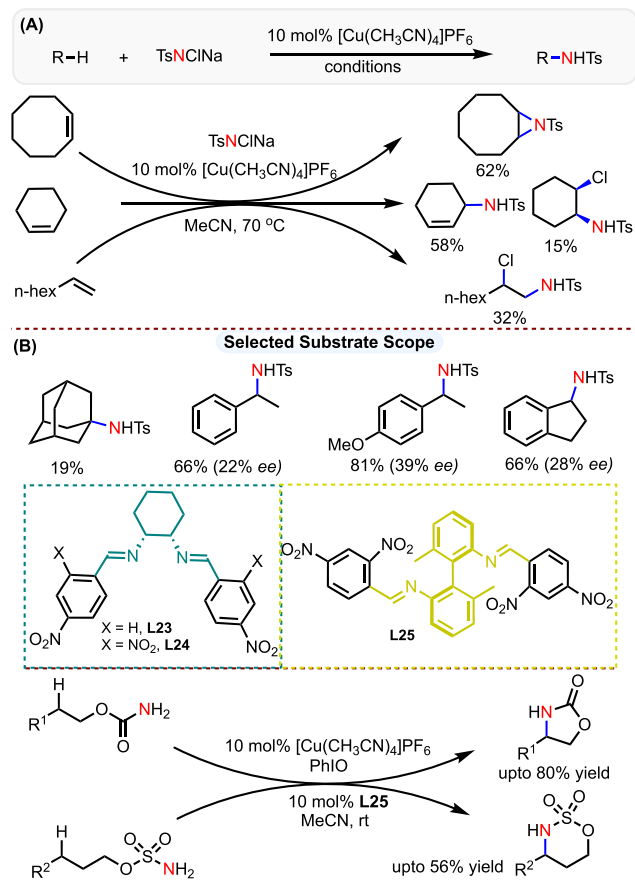
enantioselectivity. Interestingly, an inverse stereoinduction was observed when the PhBOX/copper complex was employed for the catalytic asymmetric azidoarylation.²⁴¹ It was noted that cyclization occurred only when an aryl substitution was present on the double bond of the starting material. In contrast, allyl phenyl ether failed to undergo cyclization, leading to aziridination. A similar strategy comprising aziridination followed by ring expansion of cyclopropanes was reported by Yu and co-workers.²⁴²

3.5.3. Copper-Catalyzed C(sp³)–H Amination Reaction (Intermolecular)

3.5.3.1. Exploiting Chloramine-T. In 1998, Taylor and co-workers reported an intermolecular catalytic amination of benzylic and allylic C(sp³)–H aminations employing copper(I) triflate as catalyst with chloramine-T as nitrogen source.²⁴³ While the study did not delve deeply into the synthetic scope, it underscored the potential of copper complexes as effective catalysts for C–H amination.

In 2007 Nicholas and Bhuyan increased the efficiency of the amination reaction by utilizing $[\text{Cu}(\text{NCMe})_4]\text{PF}_6$ as catalyst and anhydrous chloramine-T (Scheme 95 (A)).²⁴⁴ The reaction showed high efficacy for electron-rich substrates, while electron-deficient substrates, such as 4-nitro-1-ethylbenzene, yielded significantly lower amination. Later, in 2010, the Nicholas group further explored enantioselective copper-

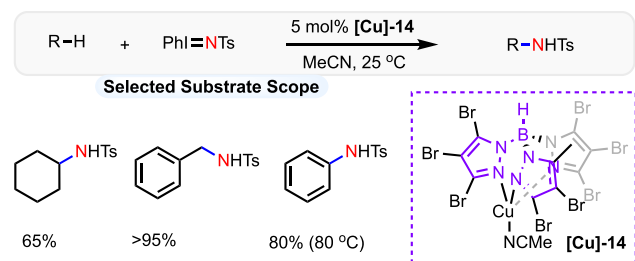
Scheme 95. $[\text{Cu}(\text{NCMe})_4]\text{PF}_6$ -Catalyzed Amination Reaction



catalyzed benzylic amination by evaluating various chiral ligand classes, including α -amino acids, diamines, bis-oxazolines, and diimines (Scheme 95 (B)).²⁴⁵ While these ligands (L23 and L24) facilitated the amination process, the reactions exhibited only low to moderate enantioselectivity. In a separate study, they reported intramolecular C–H amination of carbamates and sulfamates using PhIO as the oxidizing agent.²⁴⁶ However, the enantioselectivity is very low, with only 16% enantiomeric excess (ee) achieved for oxazolidinones.

3.5.3.2. Incorporating Iminoiodanes. The Pérez group demonstrated a C–H amination reaction using a copper catalyst with a homoscorpionate ligand.^{247,248} Their studies revealed that the complex $\text{TpBr}_3\text{Cu}(\text{NCMe})$ exhibits remarkable catalytic activity for nitrene transfer and subsequent insertion into C–H bonds across various substrates, including benzene, cyclohexane, and cyclic ethers (Scheme 96). This

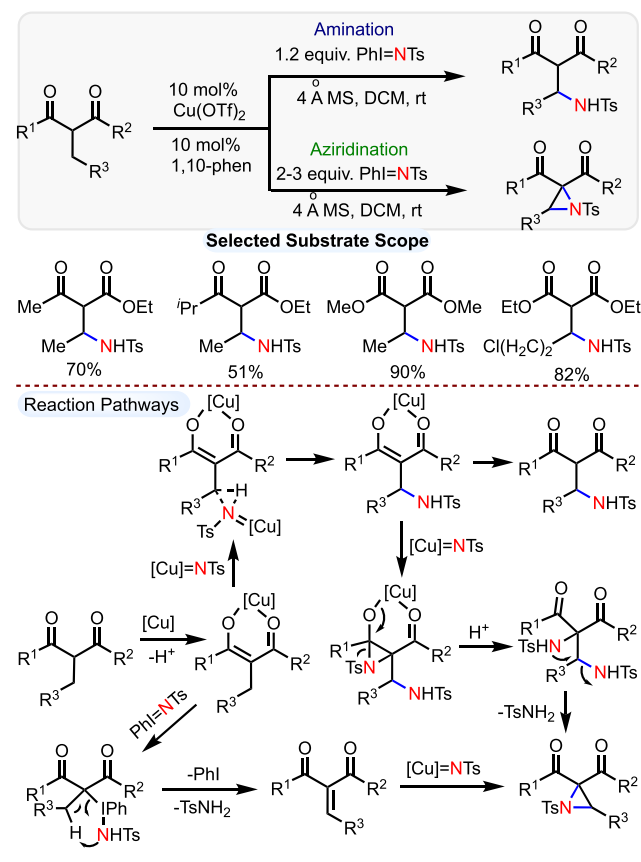
Scheme 96. Homoscorpionate Ligated Copper-Catalyzed C–H Amination Reactions



catalytic system provides a straightforward approach to arylamines without the need for prefunctionalization, overcoming the challenge posed by the high bond dissociation energy of aromatic C–H bonds. Both chloramine-T and PhI=NTs were found to be equally effective as nitrene sources for this reaction. Later, Bao and co-workers studied the computational analysis and unveiled the mechanism of this reaction.²⁴⁹

In 2012, the Chan group uncovered a product-switching reaction involving β -C–H amination and aziridination of 2-alkyl substituted 1,3-dicarbonyl compounds by employing $\text{Cu}(\text{OTf})_2/1,10$ -phen as catalyst and PhI=NTs as nitrogen source (Scheme 97).²⁵⁰ Slightly altered reaction conditions

Scheme 97. $\text{Cu}(\text{OTf})_2$ -Catalyzed Amination and Aziridination of 2-Alkyl Substituted 1,3-Dicarbonyl Compounds

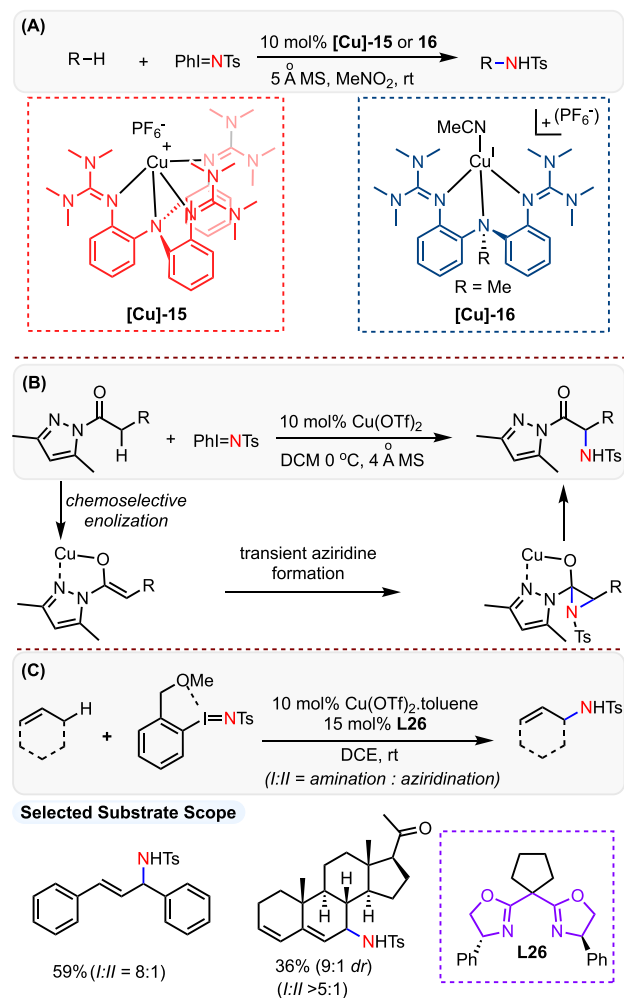


greatly influenced the type of products generation. When 1.2 equiv of the iminoiodane were used, the amination of the allylic C–H bond in the enolic form of the substrate, generated in situ via coordination to the Lewis acidic metal catalyst, selectively yields the β -aminated adduct. Conversely, increasing the nitrogen source from 1.2 to 2–3 equiv shifted the reaction toward the preferential formal aziridination of the C–C bond of the 2-alkyl substituent, resulting the aziridine product. Product formations are explained in Scheme 97. Further, the synthetic utility of this developed methodology is showcased by the efficient synthesis of the chiral *N*-acyl-protected quaternary α -aminoethyl ester with high yield and enantioselectivity. In a subsequent study, the Chan group reported the α -amination of 1,3-dicarbonyl compounds.²⁵¹ The reaction is believed to proceed via a mechanism involving aziridination of

the enolic form of the substrate, facilitated by a copper–nitrene or copper–imido species generated from the reaction of the metal catalyst with the iminoiodane, followed by ring opening of the aziridine to yield the α -aminated product.

In 2014, Stavropoulos and co-workers investigated a C_3 -symmetric tripodal copper(I) complex ([Cu]-15) featuring a Lewis basic guanidinato ligand for nitrene-transfer reactions between imidoiodinanes and substrates containing C–H and C=C bonds (Scheme 98 (A)).²⁵² The catalyst facilitates

Scheme 98. Copper-Catalyzed Amination Reactions Using PhINTs



amination of unfunctionalized hydrocarbons at tertiary and secondary C–H sites, while the primary C–H bonds remain unreacted. Benzylic and α -heteroatom-functionalized C–H bonds are aminated with high efficiency. Furthermore, the catalyst enables aziridination of both electron-poor and electron-rich olefins. Mechanistic studies, including Hammett analysis, kinetic isotope effects (KIE), radical clock experiments, electron paramagnetic resonance (EPR) spectroscopy, and theoretical calculations, provided insights into the active intermediates. Based on these studies, they proposed a reaction mechanism involving carbon-centered radicals during the C–H insertion process. The reactivity was attributed to a putative triplet copper–nitrene species, which serves as the key intermediate for the reaction.

Recently, the same group investigated copper-catalyzed nitrene transfer reactions using bipodal Cu(I) complexes ([Cu]-16).²⁵³ These compounds feature coordinated ligation comprising a diarylmethyl-amine or triaryl-amine residue, along with two imine groups supported by super basic TMG arms. In contrast to their previously studied tripodal catalyst, ([Cu]-15), the bipodal catalysts ([Cu]-16) exhibited lower yields for amination reactions. Mechanistic investigations suggest that, similar to the tripodal copper catalyst, the reaction proceeds via a putative metal–nitrene oxidant, generating an intermediate carbon-centered radical (or carbocation) during the process.

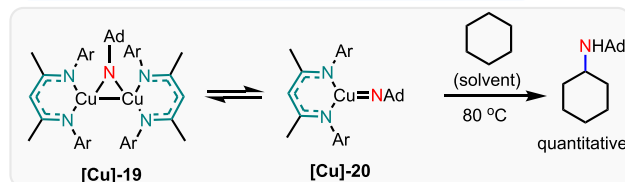
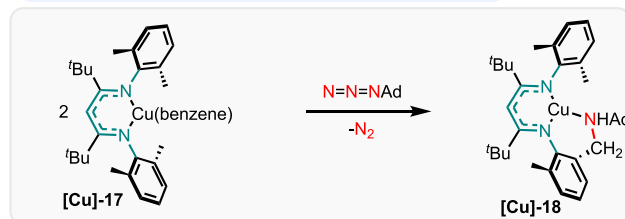
In 2016, Ohshima and co-workers reported a ligand free Cu(OTf)₂-catalyzed method for the chemo-selective α -amination of acylpyrazoles using iminoiodinane (Scheme 98 (B)).²⁵⁴ In this reaction, the copper catalyst plays a dual role by promoting the enolization of acylpyrazoles via bidentate coordination and generating a highly electrophilic copper nitrene.

In 2022, Zhu and co-workers reported a copper-catalyzed chemoselective allylic amination using *ortho*-methoxymethyl iminoiodinane as the nitrene precursor (Scheme 98 (C)).²⁵⁵ Interestingly, the authors also demonstrated that under photoirradiation and in the absence of a catalyst, the reaction selectively yielded the aziridination product, completely suppressing the amination pathway.

3.5.3.3. Utilizing Organic Azides. In 2008, Warren, Cundari, and co-workers reported a catalytic C–H amination using a β -diketiminate dicopper catalyst (Scheme 99).²⁵⁶ It

Scheme 99. β -Diketimate-Copper Complex in Nitrene Transfer Reaction

(A) Intramolecular C–H amination with a β -diketiminate ligand

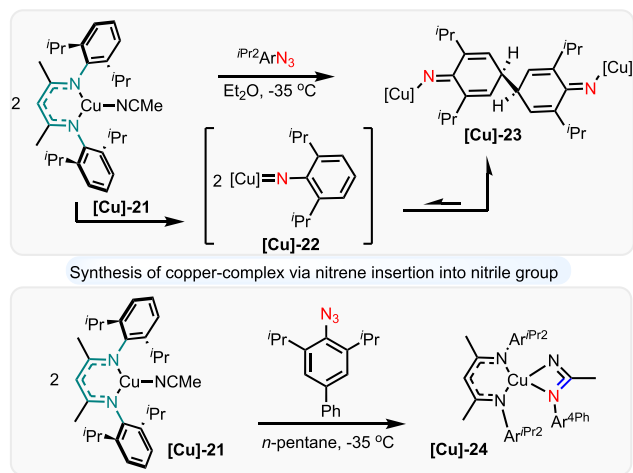


was found that a methyl group on the aryl substitution of the β -diketiminate copper complex ([Cu]-17), promotes intramolecular ligand methyl C–H bond amination with azide as the aminating agent to generate the copper complex ([Cu]-18). This intramolecular ligand amination hindered the formation of the critical nitrene intermediate necessary for substrate amination. This challenge was addressed by employing a 2,6-dichloro-substituted ligand. Notably, when a dicopper complex with a 2,6-dichloro-aryl substituted β -diketiminate ligand was reacted with an equimolar amount of alkyl azide, a dicopper nitrene species ([Cu]-19) was formed, as confirmed by X-ray crystallographic analysis, which revealed a symmetrically bridging nitrene moiety between the two copper centers.

Thermolysis of ([Cu]-20) in the presence of cyclohexane yielded the corresponding C–H amination product quantitatively. Using this copper catalyst, intermolecular C–H amination was successfully achieved with benzylic substrates, cyclohexane, and aldehydic C–H bonds. Further kinetic and computational studies indicated that the C–H amination proceeded through a terminal copper alkynitrene ([Cu]-20) intermediate and C–H amination takes place via a stepwise HAA/RR mechanism.

In 2017, the same group explored how the steric bulk of substituents on the β -diketiminate ligand and aryl azides affects the reactivity of the copper-nitrene intermediate (Scheme 100).²⁵⁷ The reaction of a sterically encumbered copper(I) β -

Scheme 100. Reaction of Terminal Copper-Nitrene Intermediates

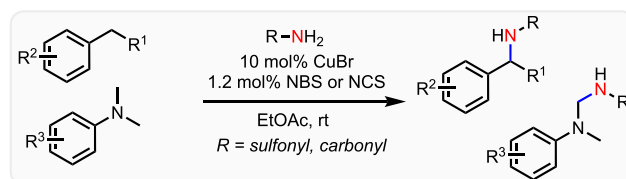


diketiminate complex ([Cu]-21), with bulky aryl azides ($N_3Ar^{iPr_2}$) generates terminal nitrenes, $[iPr_2NN]Cu = NAr$ ([Cu]-22). These nitrenes can either dimerize via C–C bond formation at the *para* position of the aryl nitrene, yielding the dicopper(II) diketimide ([Cu]-23) ($Ar = 2,6\text{-}iPr_2C_6H_3$), or undergo nitrile insertion to form diazametallocyclobutene ([Cu]-24) ($Ar = 4\text{-}Ph\text{-}2,6\text{-}iPr_2C_6H_2$). Importantly, reactivity studies revealed that both ([Cu]-23) and ([Cu]-24) function as “masked” forms of the terminal nitrenes, $[iPr_2NN]Cu = NAr$. These intermediates effectively transfer the nitrene group to PMe_3 , $tBuNC$, and can even facilitate C–H amination of benzylic $C(sp^3)$ –H bonds.

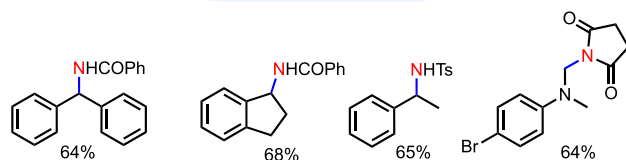
3.5.3.4. Using Amines. Zhao and co-workers reported an efficient approach for benzylic C–H bond amination using carboxamides or sulfonamides in combination with *N*-halosuccinimides and copper bromide (Scheme 101).²⁵⁸ In this reaction, NBS reacts with the amine functionality of carboxamides or sulfonamides to generate *N*-bromocarboxamides or *N*-bromosulfonamides. These intermediates then interact with the copper salt to form a Bromamine-T-like reagent, which serves as a nitrene precursor. This method proved highly effective for the amination of the *N*-methyl group in *N,N*-dimethylanilines. Moreover, the reaction demonstrated broad substrate compatibility, accommodating various carboxamides, including aryl amides, aliphatic amides, and lactam derivatives.

3.5.4. Copper-Catalyzed $C(sp^3)$ –H Amination Reaction (Intramolecular). A highly regio- and stereoselective intramolecular C–H amination of dioxazolones under copper

Scheme 101. Copper-Catalyzed Amination using *N*-Halosuccinimide as Oxidant

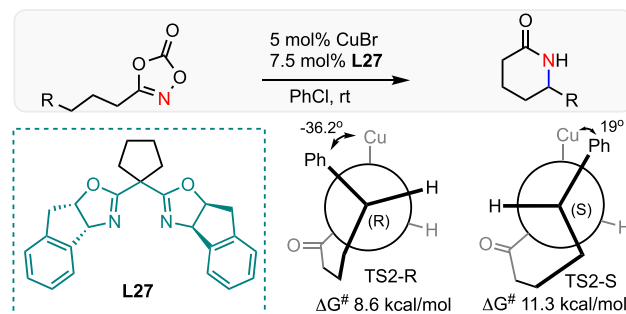


Selected Substrate Scope

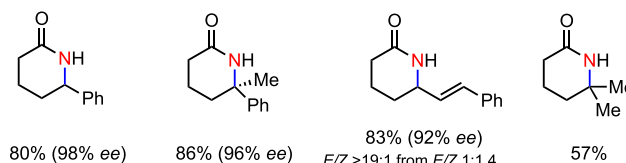


catalysis was demonstrated by the Chang group (Scheme 102).²⁵⁹ The reaction exhibited exceptional selectivity for δ -

Scheme 102. Regio- and Enantioselective Catalytic δ -C–H Amination of Dioxazolones using Copper Catalysis



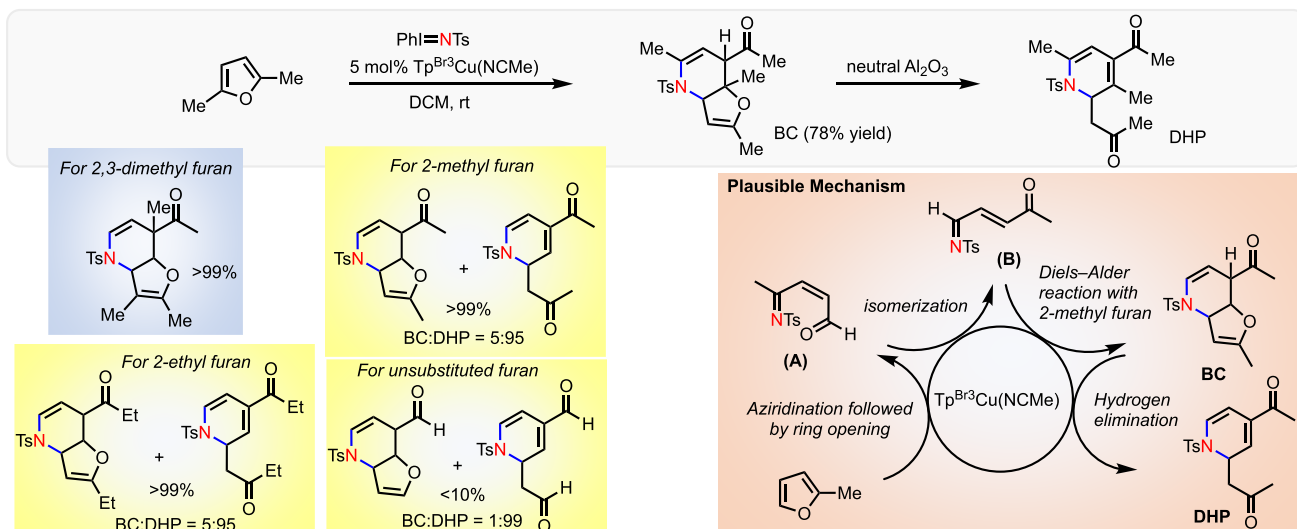
Selected Substrate Scope



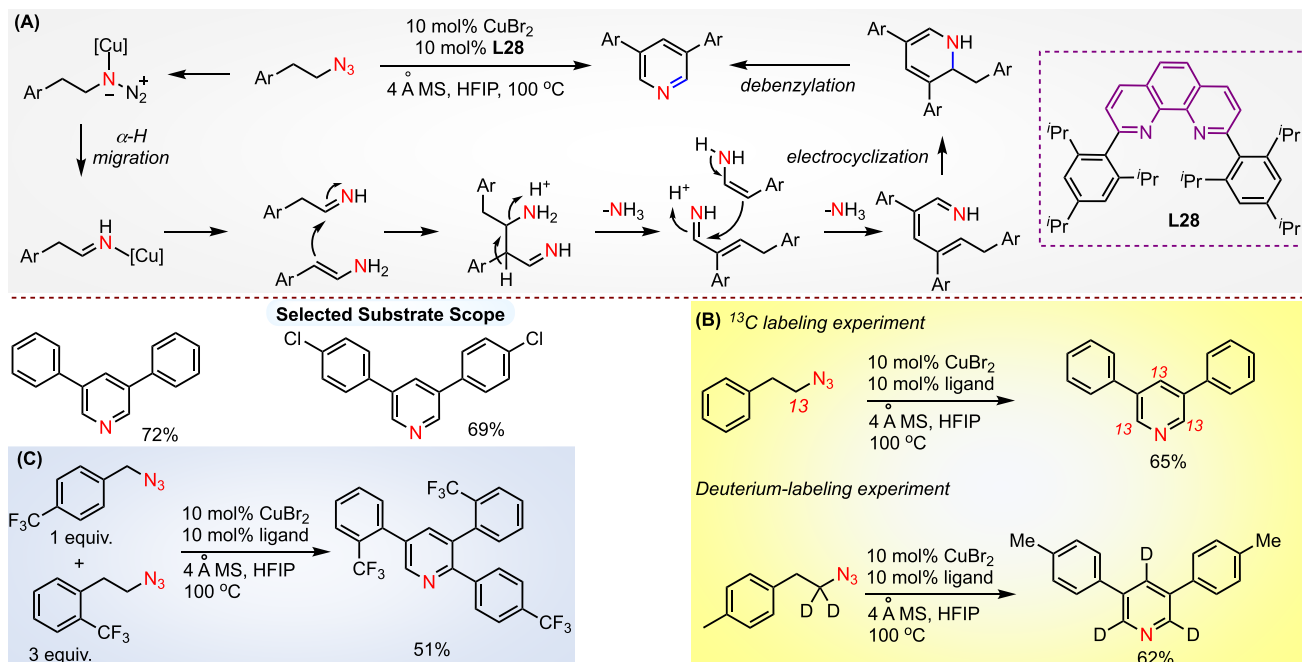
C–H bonds, even in the presence of competing γ -C–H bonds. This method enables the efficient synthesis of the chiral six-membered lactam with quaternary stereogenic carbon centers with high enantioselectivity. Mechanistic studies revealed that open-shell nature of the Cu-nitrenoid intermediate plays a crucial role in the selective hydrogen atom abstraction from the δ -C–H bond. This selectivity is further supported by DFT calculations, which showed that the δ -C–H bond abstraction is energetically favored, being 1.8 kcal/mol lower in activation energy compared to γ -C–H abstraction. The enantioselective radical rebound step was also investigated computationally. The free energy difference between the two diastereomeric transition states, TS2-R and TS2-S, was calculated to be 2.7 kcal/mol, which correlates well with the experimentally observed enantioselectivity (99:1 *er*). Moreover, the resulting chiral δ -lactams were further elaborated into various medically relevant compounds.

3.5.5. Miscellaneous Examples Involving Copper-Nitrenoid Intermediates. The Perez group unveiled a nitrene-mediated rearrangement reaction of furans using copper catalysis (Scheme 103).^{260,261} The reaction yielded either bicyclic compounds (BC) or dihydropyridines (DHP)

Scheme 103. Copper-Nitrene Mediated Rearrangement Reaction of Furans



Scheme 104. Copper-Catalyzed Synthesis of Multisubstituted Pyridines from Homo Aryl Azides



depending upon (i) the acidic nature of the column chromatography static phase used for the purification step, and (ii) the nature of the substituted furan in the precursor. When the reaction was performed with 2,5-dimethylfuran and PhI=NTs using TpBr₃Cu(NCMe) as the catalyst, the product obtained after silica gel chromatography was a bicyclic compound (BC). However, when neutral alumina was used, the product shifted to dihydropyridine (DHP). A range of TpxCu complexes exhibited similar behavior, consistently producing BC unless Al₂O₃ was employed for purification. The high acidity of Al₂O₃ promoted hydrogen elimination from the β-carbonyl position of BC, leading to the formation of DHP. The reaction was further explored with different furans, yielding intriguing results (Scheme 103). For example, 2,3-dimethylfuran produced only BC due to the absence of a β-hydrogen for elimination. In contrast, monosubstituted furans, such as 2-methyl- or 2-ethylfuran, led to a product mixture

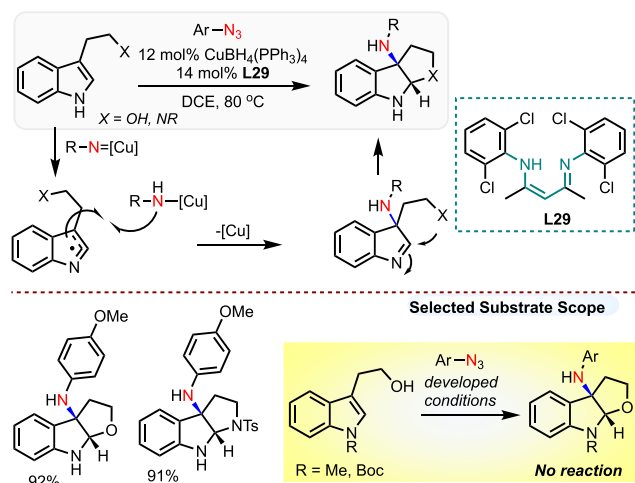
with a ~5:95 molar ratio of BC to DHP. Unsubstituted furan resulted in only 10% DHP formation in a low-yield transformation. To understand the mechanism of the transformation, a reaction with equimolar amounts of PhI=NTs and 2-methylfuran was monitored by ¹H NMR, which revealed the formation of intermediates (A) and (B). Over time, (A) was converted into (B), and additional NMR experiments demonstrated that the disappearance rate of (B) increased with catalyst concentration, highlighting the noninnocent role of the copper complex in its reaction with a second furan unit to form BC. The proposed mechanism consists of four catalytic cycles: (1) aziridination of the furan, (2) transamination to generate (A) and (B), (3) an inverse electron-demand Diels-Alder reaction forming BC, and (4) metal-catalyzed hydrogen elimination yielding the final product (DHP) (Scheme 103).

Traditionally, the preparation of unsymmetrical 3,5-diarylpyridines relies on palladium-catalyzed Suzuki–Miyaura cross-coupling reactions, which involve multistep protocols and expensive palladium catalysts.²⁶² Moreover, such pyridines cannot be synthesized using the conventional abnormal Chichibabin pyridine synthesis.^{263,264} In 2017, Liao and co-workers developed an efficient copper-catalyzed method for synthesis of 3,5-diarylpyridines and 2,3,5-trisubstituted pyridines from readily available homo aryl azides (Scheme 104).²⁶⁵

The key step in this transformation involves the generation of *N*-unsubstituted aliphatic imines from azides, which subsequently undergo an addition–elimination sequence followed by rearrangement to afford the pyridine derivatives. Reaction optimization identified a customized phenanthroline-based ligand (L33) as optimal for the synthesis of multi-substituted pyridines and indole derivatives (Scheme 104 (A)). Interestingly, it was found that solvents such as toluene, THF, and dioxane were ineffective for this reaction, whereas HFIP proved to be crucial. This can be attributed to the ability of HFIP to stabilize the *N*-unsubstituted imine intermediate, facilitating the reaction. To elucidate the reaction mechanism, isotopic labeling experiments were conducted. A ¹³C-labeled azide was synthesized and subjected to the optimized reaction conditions, yielding 2,4,6-¹³C-labeled pyridine. Similarly, when an α -deuterated azide was used, the reaction produced 2,4,6-deuterated pyridine (Scheme 104 (B)). These results indicated that the transformation involves three-molecules of azides. Furthermore, when a mixture of benzyl azide and homo benzyl azide (1:3 ratio) was subjected to the developed reaction conditions, 2,3,5-trisubstituted pyridines were successfully synthesized (Scheme 104 (C)).

In 2019, the Deng group reported a copper-catalyzed nitrene transfer and cyclization reaction of tryptophols and tryptamines, employing aryl azides as the nitrogen source (Scheme 105).²⁶⁶ This method enabled the synthesis of a variety of indole alkaloids in excellent yields (up to 99%) using CuBH₄(PPh₃)₂ as the catalyst and a β -diketiminate ligand (L29). To elucidate the intermediates involved in the cyclization process, several control experiments were conducted. When the reaction was carried out in the presence of

Scheme 105. Copper-Catalyzed Nitrene Transfer/Cyclization Reaction to Synthesize Indole Alkaloids

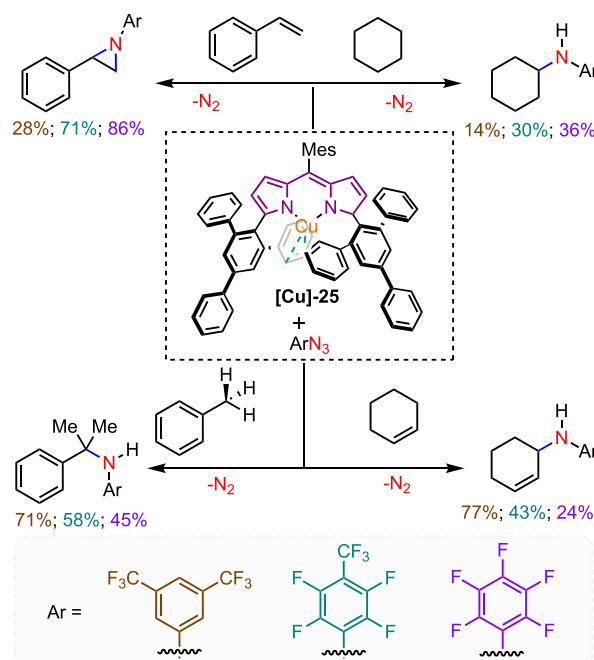


radical quenchers, like 2,2,6,6-tetramethyl-1-(BHT) significantly inhibited the reaction.

These results strongly suggested the intermediacy of radical intermediates in the reaction. When *N*-protected tryptophols were tested under the reaction conditions, no desired product was observed, indicating that the N–H bond of the indole is essential for nitrene transfer. These findings excluded a possible aziridination/cyclization pathway, and instead supported a mechanism involving radical addition followed by cyclization.

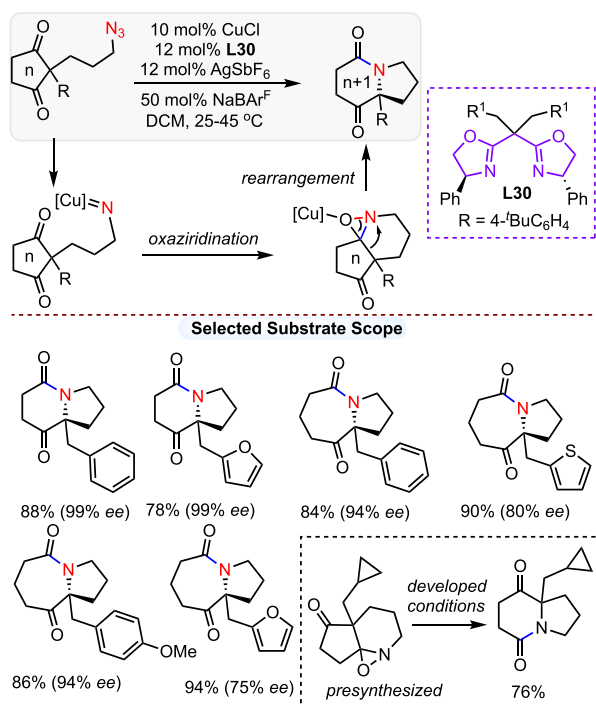
In 2019, Betley et al. reported a synthetic paradigm of copper(I) dipyrin complex ([Cu]-25).²⁶⁷ They assessed the reaction of aryl azides with ([Cu]-25) can culminate into a terminal triplet nitrene intermediate, upon X-ray absorption spectroscopy and quantum chemistry calculations. They also proved the competency of the nitrene adducts with a moderate to good nitrene transfer reaction profile with amination and aziridination of different substrates (Scheme 106). A unique

Scheme 106. Dipyrin Ligated Cu(I)-Catalyzed Amination and Aziridination Reaction



aspect of this reaction is the isolation and crystallographic characterization of the Cu-nitrene intermediate. Notably, the copper complex does not exhibit Cu–N multiple bond character; instead, the bonding is better described as a radical delocalized into the aromatic ring.

In 2021, Zhang and co-workers developed a novel copper-catalyzed intramolecular tandem oxaziridination/1,2-alkyl rearrangement of cyclic diketones with alkyl azides, enabling the synthesis of chiral fused bicyclic lactam derivatives (Scheme 107).²⁶⁸ High enantioselectivity was achieved using the chiral ligand L30. To investigate the involvement of an oxaziridine intermediate in the reaction mechanism, a reaction was conducted with a presynthesized oxaziridine under the developed conditions, yielding the racemic fused bicyclic lactam in 76% yield. This result provided indirect evidence that the oxaziridine serves as a key intermediate, which undergoes subsequent rearrangement to form the lactam derivatives.

Scheme 107. Copper-Catalyzed Oxaziridination/1,2-Alkyl Rearrangement of 1,3-Diketones


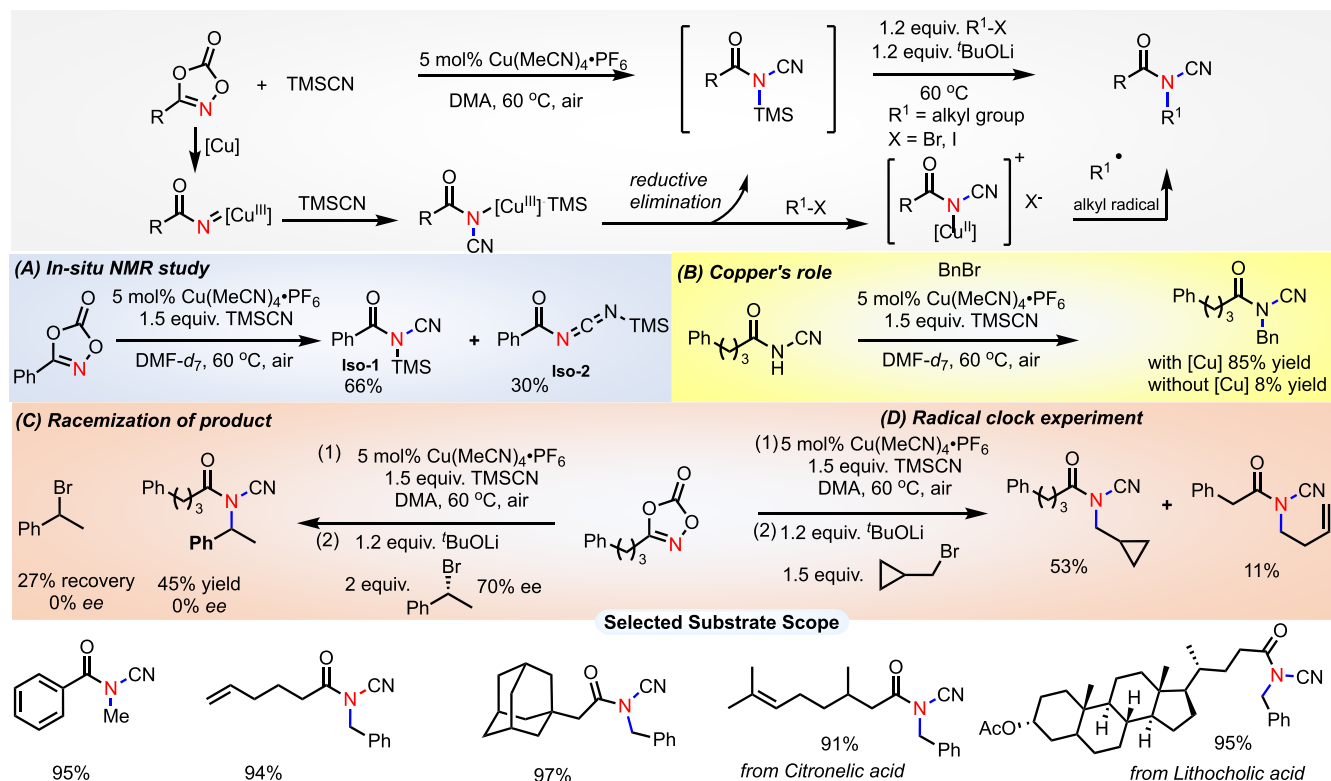
In 2024, Norton and co-workers developed an innovative copper-catalyzed method for synthesizing alkylated *N*-acyl cyanamides via a nitrogen umpolung strategy (Scheme 108).²⁶⁹ This approach consists of two distinct reaction pathways: (i) a Cu-nitrene transfer and (ii) a Cu-catalyzed *N*-

alkylation. The method utilizes dioxazolones, trimethylsilyl cyanide (TMSCN), and alkyl halides as key reagents. To elucidate the mechanism of the nitrene transfer reaction, an *in situ* NMR study was performed using dioxazolone and TMSCN in the presence of copper-catalysis, revealing the formation of two isomers, Iso-1 and Iso-2, in nearly equimolar amounts (Scheme 108 (A)).

The formation Iso-1 and Iso-2 can be explained by the nucleophilic addition of cyanide into the Cu-nitrenoid species. For *N*-alkylation step, control experiments demonstrated the crucial role of Cu(MeCN)₄PF₆ (Scheme 108 (B)). Without the Cu-catalyst, only 8% alkylated product was achieved by the reaction of BnBr with ^tBuOLi. However, the addition of 5 mol % Cu(MeCN)₄PF₆ increased the yield to 85%. Further, the radical clock experiment with (bromomethyl)cyclopropane produced 11% yield of the ring-opening product, suggesting a radical mechanism (Scheme 108 (C)). While (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) failed to trap radical species, use of enantioenriched (1-bromoethyl)benzene gave the racemic *N*-acyl cyanamide (2% ee), along with the recovery of racemic (1-bromoethyl)benzene (27%), further supporting a radical pathway (Scheme 108 (D)). Importantly, this copper-catalyzed strategy enables the late-stage functionalization of natural products and pharmaceuticals, highlighting its utility in complex molecule synthesis.

4. NITRENE TRANSFER REACTIONS TO FORM N–N BONDS

The N–N linkages are key structural motifs in many natural products, imparting diverse and intriguing chemical and biological properties.²⁷⁰ Despite the extensive development of methods for constructing C–N bonds, strategies for N–N bond formation remain relatively underexplored. Traditional

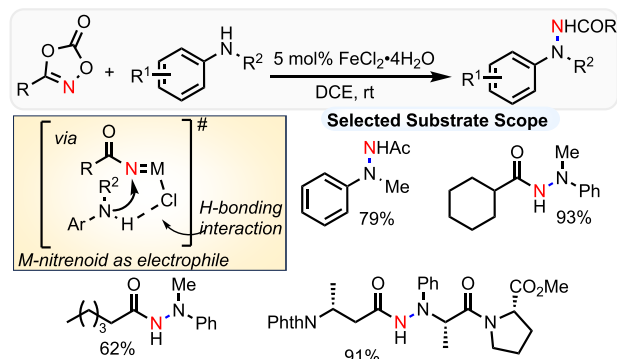
Scheme 108. Copper-Catalyzed C–N Coupling for the Synthesis of Alkylated *N*-Acyl Cyanamides


approaches to N–N bond construction largely rely on prefunctionalized precursors such as hydrazines or diazo compounds.²⁷¹ In contrast, direct N–N coupling via nitrene transfer offers a more convergent and flexible synthetic strategy, enabling broader retrosynthetic options.

4.1. Iron Catalysis (Fe)

One promising approach involves the nucleophilic attack of amines on electron-deficient nitrene intermediates to forge N–N bonds. In this context, in 2021, Chang, Chen, and co-workers have developed a simple and highly efficient iron-catalyzed protocol for synthesizing a wide range of hydrazides from readily available carboxylic acids and amines (Scheme 109).²⁷² The reaction proceeds smoothly at room temperature

Scheme 109. Iron-Catalyzed Nitrene-Mediated N–N Coupling for Efficient Synthesis of Hydrazides



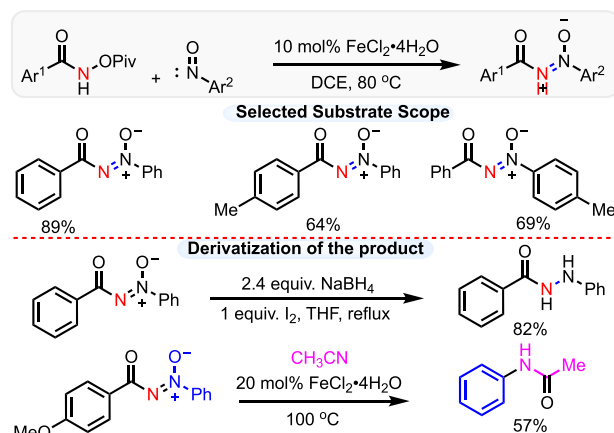
with only a catalytic amount of ferrous chloride (FeCl_2). Mechanistic studies indicate that the transformation involves a highly electrophilic acyl nitrene intermediate, which undergoes nucleophilic attack by arylamines, likely facilitated by $\text{Cl}\cdots\text{HN}$ hydrogen bonding. Notably, although Cp^*IrCl_2 can also promote the N–N coupling efficiently, sterically hindered dioxazolones derived from α -substituted carboxylic acids exhibit significantly improved reactivity under the iron-catalyzed conditions. Interestingly, primary aryl amines and aliphatic amines are incompetent under the developed conditions.

In 2024, the Xia group reported a nitrene transfer reaction between nitrosobenzenes and *N*-acyloxycarbonyl amides catalyzed by ferrous chloride (Scheme 110).²⁷³ This method enables the efficient synthesis of *N*-acyl azoxy compounds via N=N bond formation. The reaction is proposed to proceed through an iron-nitrene intermediate, which undergoes nucleophilic addition by nitrosobenzene to afford the desired product. Notably, the synthetic utility of this transformation has been demonstrated through further derivatizations: the resulting azoxy compounds can be reduced to hydrazides and employed as novel aryl transfer reagents in reactions with nitriles.

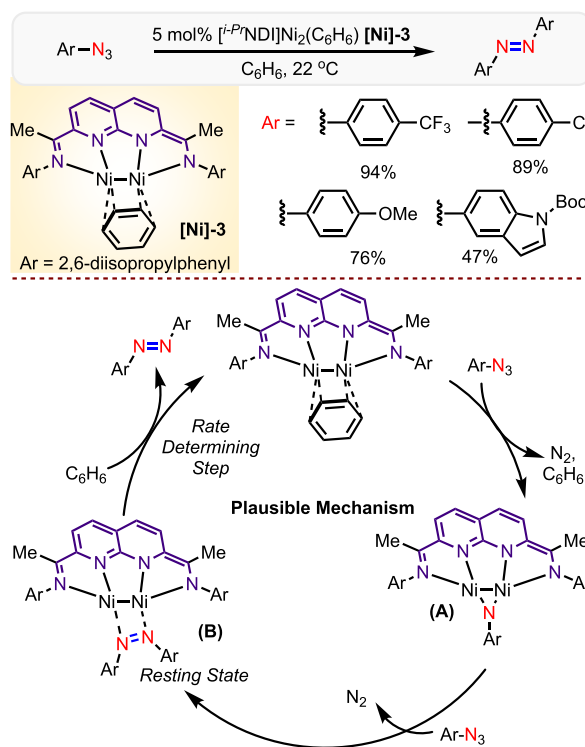
4.2. Nickel Catalysis (Ni)

In 2018, the Uyeda group reported a dinuclear nickel-catalyzed method for the preparation of a variety of azoarenes from aryl azides (Scheme 111).²⁷⁴ Because the reaction proceeds without requiring an external redox reagent, it is highly compatible with a wide range of organic functional groups, providing azoarene products in excellent yields. A mononuclear nickel catalyst is ineffective here, as it binds strongly to the azoarene product, preventing catalytic turnover. In contrast, the dinickel catalyst demonstrates high efficiency

Scheme 110. Iron-Catalyzed Nitrene Transfer Reaction of Nitrosobenzenes with *N*-Acyloxycarbonyl Amides



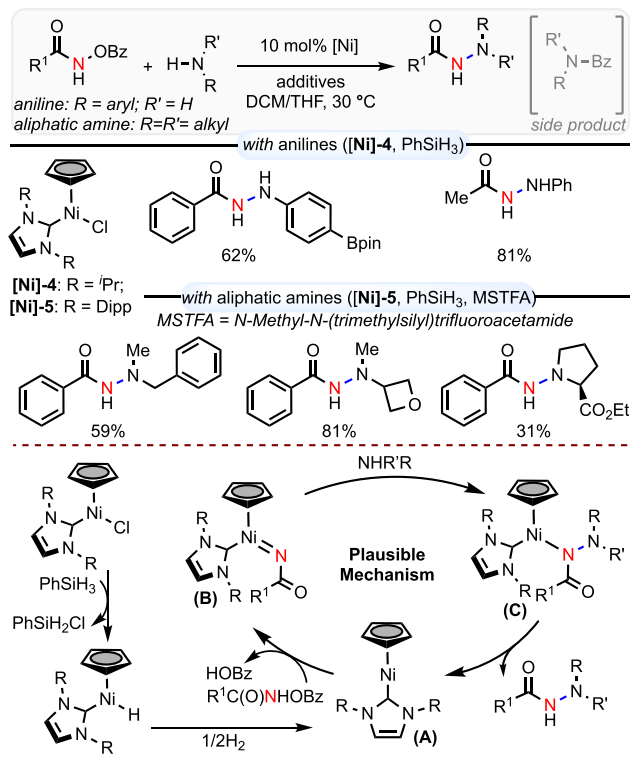
Scheme 111. Dinuclear Ni Complex-Catalyzed Azoarene Synthesis from Aryl Azides



due to its weaker coordination with the product. Mechanistic studies indicate that the reaction initiates with the formation of a $\mu\text{-NAr}$ intermediate, which subsequently reacts with another equivalent of aryl azide to form a $\mu\text{-N}_2\text{Ar}_2$ complex. Finally, in the presence of benzene, the weakly coordinated azoarene product is released, allowing the dinickel catalyst to regenerate and re-enter the catalytic cycle. The structure and reactivity of these proposed intermediates reveal two essential features of the dinickel active site that are critical for efficient catalytic turnover. First, the reactive imido species is stabilized through π -interactions with the Ni–Ni bond, which helps suppress unwanted hydrogen atom abstraction. Second, the azoarene product binds only weakly to the Ni–Ni bond, a consequence of its enforced, high-energy cis conformation.

The preparation of hindered azoarenes has long been a significant challenge, with established oxidative and reductive coupling methods, yielding poor results. To address this issue, in 2023, the Stoltz group reported an efficient nickel-catalyzed strategy for N–N bond formation to synthesize hydrazide derivatives (Scheme 112).²⁷⁵

Scheme 112. Ni-Catalyzed Hydrazine Synthesis through Nitrene Transfer Reaction

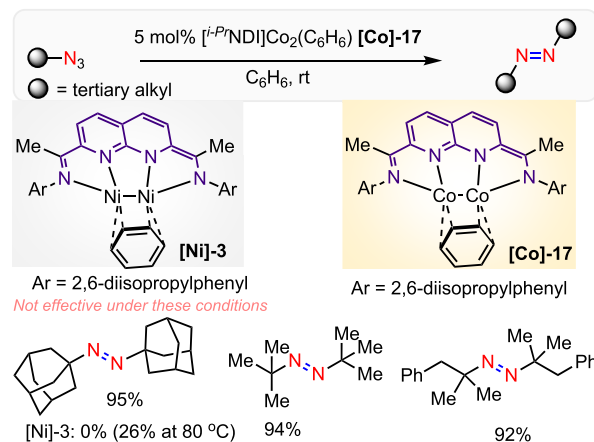


In this transformation, O-benzoylated hydroxamates served as nitrene precursors. The reaction was enabled by an air-stable Ni(II) half-sandwich precatalyst ([Ni]-4 and [Ni]-5), which, upon silane-mediated reduction, generated a mononuclear Ni(I) species (A) identified as the catalytically active form. In the presence of hydroxamate, this Ni(I) species formed an electrophilic, Ni-stabilized acyl nitrenoid intermediate (B). Subsequent outer-sphere N–N bond formation with an amine, followed by proton transfer and product dissociation, delivered the hydrazide products. Notably, the reaction displayed a broad scope, accommodating both aryl and aliphatic amines with high efficiency, which was previously inaccessible by Chang's protocol (Scheme 109).

4.3. Cobalt Catalysis (Co)

Recently (2025), Uyeda and co-workers found that Ni-catalysis was ineffective for the synthesis of azoalkanes via the dimerization of alkyl azides.²⁷⁶ For instance, the coupling of adamantyl azide failed to produce azoadamantane at room temperature, and only afforded a low yield of 26% at 80 °C (Scheme 113). In striking contrast, the isostructural (NDI)-Co₂(C₆H₆) complex ([Co]-17) proved to be a highly efficient catalyst for the dimerization of tertiary alkyl azides, delivering the corresponding azoalkanes in excellent yields at room temperature. Critical to the N=N coupling reactivity is the formation of a dicobalt imido intermediate that is resistant to undergoing competing H atom abstraction. These azoalkanes

Scheme 113. Dimerization of Azides by Dicobalt Catalysis



serve as valuable precursors to tertiary alkyl radicals, which can participate in C–C bond-forming reactions to construct sterically congested quaternary carbon centers.

5. NITRENE TRANSFER REACTIONS TO FORM P–N BONDS

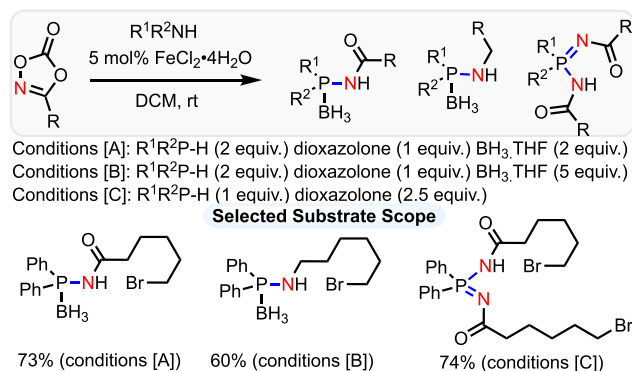
The P–N motif has gained increasing attention in the design of organic ligands for both organo- and metal-catalyzed transformations.²⁷⁷ However, the development of efficient P–N bond-forming reactions has lagged behind over the past few decades.²⁷⁸ Classical approaches—such as the Staudinger condensation between phosphines and azides, and nucleophilic substitution between phosphorus halides and amines—remain the primary methods for P–N bond construction. While valuable, these strategies often require harsh conditions and involve hazardous or moisture-sensitive reagents. An attractive alternative is the metal-nitrene-mediated insertion of amine functionality into P–H bonds, offering a direct route to P–N bond formation. Despite its potential, this approach has seen limited exploration in the literature.

5.1. Iron Catalysis (Fe)

In 2022, Wang and Chen reported an excellent method for metal-nitrene-mediated P–N bond formation, using catalytic FeCl₂ and dioxazolones as nitrene precursors (Scheme 114).²⁷⁹

This strategy enables the efficient and versatile synthesis of a wide array of P–N-containing compounds, including amidophosphines, iminophosphonamides, aminophosphines, and

Scheme 114. Nitrene-Mediated P–N Coupling Under Iron Catalysis

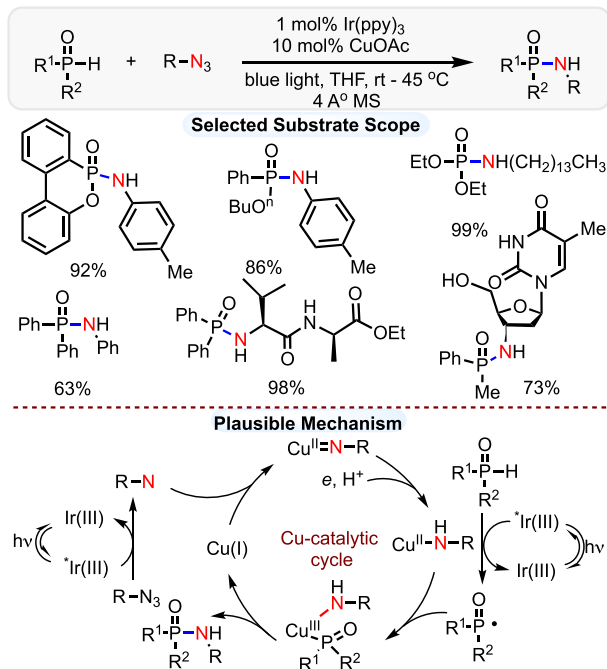


iminophosphoranes, starting from readily available phosphorus substrates. The reaction is proposed to proceed via the formation of an Fe–acylnitrenoid intermediate, which facilitates nitrogen atom transfer to the phosphorus center.

5.2. Copper Catalysis (Cu)

A notable example is the work by Lu and co-workers, who developed a dual copper/photoredox catalytic system for the synthesis of P(O)–N bonds via the coupling of P(O)–H compounds with organic azides (Scheme 115).²⁸⁰

Scheme 115. Dual Copper and Photoredox Catalysis for P(O)–N Coupling between P(O)–H Compounds and Azides



Under visible-light irradiation, where Ir(ppy)₃ acts as a photocatalyst to simultaneously promote the decomposition of the azide to generate a triplet nitrene and the homolytic cleavage of the P(O)–H bond to yield a phosphinoyl radical. The triplet nitrene then reacts with Cu(I) to form a Cu(III)–nitrene intermediate, which undergoes radical addition of the phosphinoyl species followed by reductive elimination to afford the desired P–N bond. Importantly, this method demonstrates a broad substrate scope, tolerating a variety of P(O)–H compounds—including diaryl-, dialkyl-, and dialkoxy-phosphine oxides—as well as both aryl and alkyl azides, underscoring the versatility and generality of the transformation. Furthermore, an asymmetric variant of the reaction was developed by employing an appropriate chiral ligand. The reaction was also shown to be fully compatible with flow chemistry using a microchannel reactor.

6. NITRENE TRANSFER REACTIONS TO FORM S–N BONDS

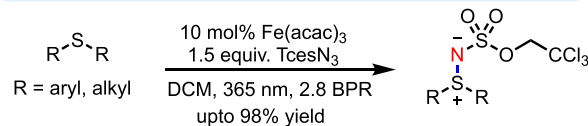
6.1. Iron Catalysis

6.1.1. Exploiting Azides. Incorporating a photochemical (UVA) continuous flow technique and Fe(acac)₃ as catalyst, Lebel and co-workers reported the imidation of sulfoxides and sulfides with trichloroethoxysulfonyl azide (TcesN₃) (Scheme

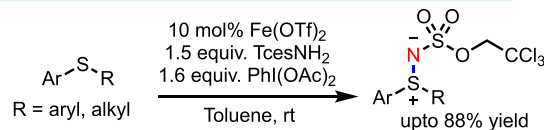
116 (A)).²⁸¹ The reaction conditions proved effective for both alkyl and aromatic sulfoxides and sulfides. Taking inspiration

Scheme 116. TcesN₃ Mediated Iron-Catalyzed Imidation of Sulfides

(A) Amination of sulfides using TcesN₃ under photocatal flow process



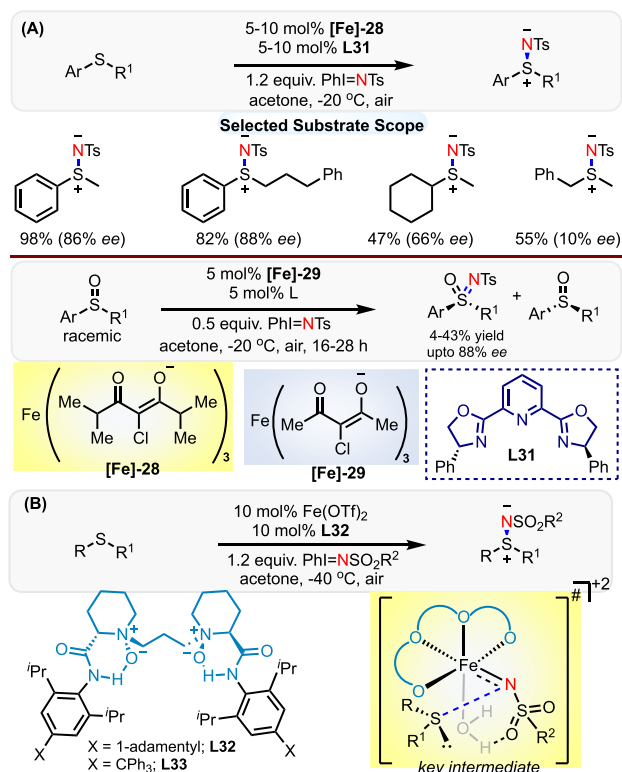
(B) Amination of sulfides using TcesNH₂ under batch process



from this work in 2024, the Bolm group employed TcesNH₂ as an aminating agent instead of TrocN₃ to mitigate the potential risks associated with the latter (Scheme 116 (B)).²⁸² Among the catalysts tested, Fe(OTf)₂ proved to be the most effective, outperforming Rh-based catalysts (Rh₂(esp)₂ and Rh₂(OOCCH₃)₂) as well as Cu-based catalysts. But, the reaction scope was limited to aryl alkyl or diaryl sulfides, no scope was found for dialkyl sulfides.

6.1.2. Utilizing Iminoiodinanes. Bolm et al. also achieved the enantioselective imidation of sulfides using an iron catalyst ([Fe]-28) in combination with a chiral ligand (L31) (Scheme 117 (A)).²⁸³ While various iron salts such as Fe(acac)₃, Fe(OTf)₂, and Fe(ClO₄)₂, as well as other metal acetylacetonates (Cu(acac)₃, Mn(acac)₃, and Ru(acac)₃), failed to

Scheme 117. Iron(III)-Catalyzed Enantioselective Sulfur Imidation

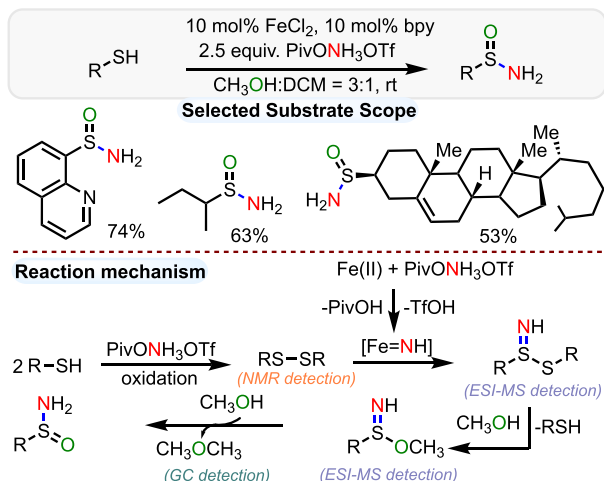


deliver high enantioselectivity, [Fe]-28 featuring a 4-chloro-substituted heptanedionate ligand provided excellent enantiomeric excess (*ee*) for alkyl aryl sulfinamides. In a subsequent study, Bolm's group developed a sulfimination-based kinetic resolution process for the synthesis of enantioenriched sulfoximines from racemic sulfoxides.²⁸⁴ Using the [Fe]-29 catalyst in combination with (*R,R*)-L32, racemic sulfoxides were converted into the corresponding optically active sulfoximines in yields of up to 43% with an *ee* of 88%.

In 2024, Feng et al. reported a highly enantioselective imidation of both dialkyl and alkyl aryl sulfides by using Fe(OTf)₂ in combination with a chiral *N,N'*-dioxide ligand (L33 (Scheme 117 (B))).²⁸⁵ The weak-field interaction of the chiral L33 ligand facilitated the formation of a water-coordinated high-spin iron nitrenoid species that was supported by the DFT calculations and CSI-MS analysis.

6.1.3. Incorporating Amines. Bolm also reported an iron-catalyzed nitrene transfer method for synthesizing free NH-sulfoximines using a readily available and self-stable hydroxylamine triflic acid salt.²⁸⁶ In 2021, Morandi and co-workers demonstrated an iron-catalyzed nitrene transfer method for the selective conversion of thiols (–SH) into sulfinamides (–SONH₂) (Scheme 118).²⁸⁷ This transformation forms two

Scheme 118. Iron-Catalyzed Thiol Amino-Oxidation

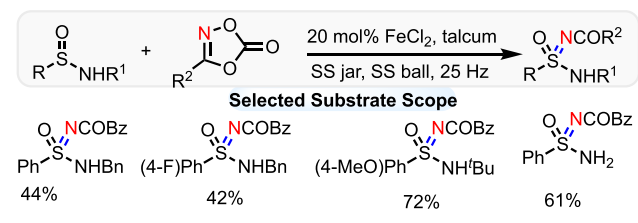


distinct bonds (S=O and S–N) in a single step, enabling the chemoselective synthesis of valuable, unprotected sulfinamides. PivONH₃OTf is proposed to react with the iron catalyst, generating an iron-nitrene (Fe=NH) intermediate, which then engages with the in situ-formed bisulfide to produce a transient sulfimide intermediate. Subsequent attack by methanol leads to the formation of a sulfoximine-ether intermediate, which undergoes a second methanol-mediated transformation, forming the S=O bond and releasing dimethyl ether. ESI-MS analysis confirmed the characterization of key reaction intermediates.

6.1.4. Introducing Dioxazolones. The Bolm group also reported a ball-milling approach for the synthesis of *N*-acyl sulfoximines using iron catalysis and dioxazolone as nitrene source (Scheme 119).²⁸⁸ This solvent-free method, conducted under ambient conditions, demonstrated broad substrate tolerance, accommodating a wide range of sulfinamides with various substituents.

Notably, *N*-unsubstituted (primary) sulfinamides also underwent imidation. However, despite its high synthetic utility, the

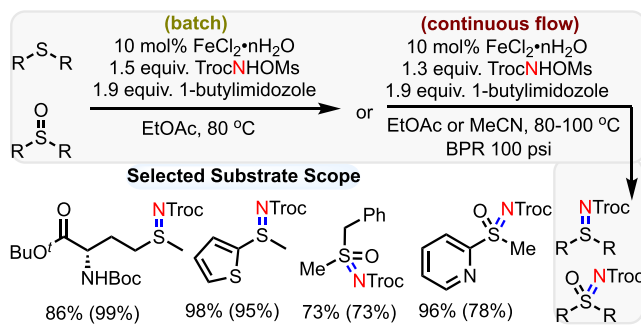
Scheme 119. Mechanochemical Iron-Catalyzed Nitrene Transfer to Sulfinamides



reaction showed lower yields with aliphatic side chain-containing dioxazolones. For instance, cyclohexyl-dioxazolone afforded only 29% yield, while *tert*-butyl-dioxazolone failed to produce any product. Additionally, substrates bearing electron-withdrawing substituents on either the sulfoxide unit or dioxazolone exhibited lower yields compared to their electron-donating counterparts.

6.1.5. Using Carboxamides. In 2019, Lebel and co-workers reported a straightforward and highly efficient strategy for synthesizing sulfilimines and sulfoximines using *N*-mesyloxycarbamates as aminating agents and FeCl₂ as a catalyst (Scheme 120).²⁸⁹

Scheme 120. Iron-Catalyzed Batch and Continuous Flow Process for Sulfur Imidation



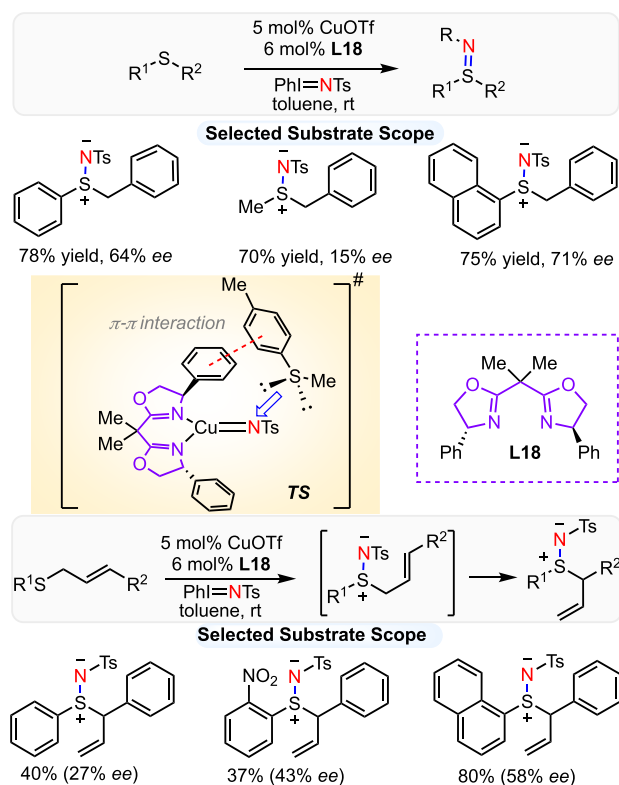
The reaction proceeded rapidly, requiring just 15 to 60 min. The reaction also successfully carried out in continuous flow process further enabled the rapid synthesis of a broad range of products within 1–10 min, achieving high yields with excellent reproducibility and scalability. Notably, the use of 1-butylimidazole, an ionic-liquid-forming base, was crucial in preventing the formation of an insoluble byproduct salt.

6.2. Copper Catalysis

6.2.1. Exploiting Iminoiodinanes. Copper(I) and copper(II) complexes have been shown to effectively catalyze nitrene transfer from imidoiodinanes to sulfides and sulfoxides. Uemura and co-workers demonstrated that a catalytic amount of Cu(OTf) efficiently facilitated the imidation of sulfides with PhI=NTs at room temperature, yielding the corresponding *N*-Ts sulfinamides in moderate to good yields.^{290–292} Building on this, they²⁹³ reported that prochiral sulfides could be transformed into chiral sulfinamides using PhI=NTs in the presence of a catalytic amount of a copper salt and chiral 4,4'-disubstituted bis(oxazoline) ligand (L18) (Scheme 121).

Among the copper salts tested, Cu(OTf) was found to be the most effective, delivering both the highest yield (78%) and the best enantioselectivity (65% *ee*) in comparison to CuPF₆(CH₃CN)₄ and Cu(OTf)₂. Solvent polarity was also a critical factor in optimizing enantioselectivity. In coordinating

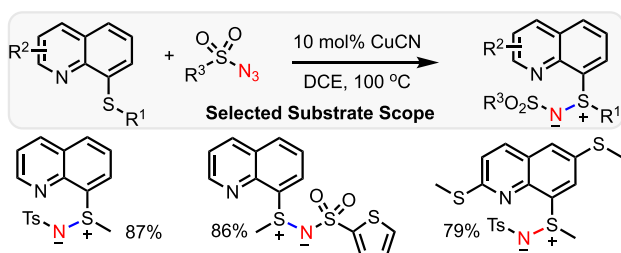
Scheme 121. Copper-Catalyzed Nitrene Transfer Reaction to Sulfides and Sulfoxides



solvents like acetonitrile, the enantiomeric excess was low (less than 22% ee), whereas switching to toluene significantly improved the ee. The best enantioselectivities were achieved with sulfides bearing two aromatic (or partially aromatic) substituents. It is hypothesized that the 4,4'-disubstituted bis(oxazoline) ligands may engage in π -stacking interactions, effectively blocking access to the catalytic site along the plane containing the C2 axis, thereby enhancing the enantioselectivity. Additionally, for allylic sulfides, the imidation reaction yielded the corresponding allylic sulfonamides. This transformation was attributed to a [2,3]-sigmatropic rearrangement of the initially formed allylic sulfimide intermediates.

6.2.2. Utilizing Organic Azides. In 2019, Li and co-workers described a directing-group-assisted copper-catalyzed imidation of 8-quinolylsulfides using sulfonyl azides as nitrene sources (Scheme 122).²⁹⁴ Among the copper(I) salts tested, CuCN exhibited superior catalytic performance compared to CuI and CuCl. The quinoline nitrogen played a pivotal role in the reaction by coordinating with the copper catalyst, thereby facilitating nitrene transfer to the sulfur atom at the C8

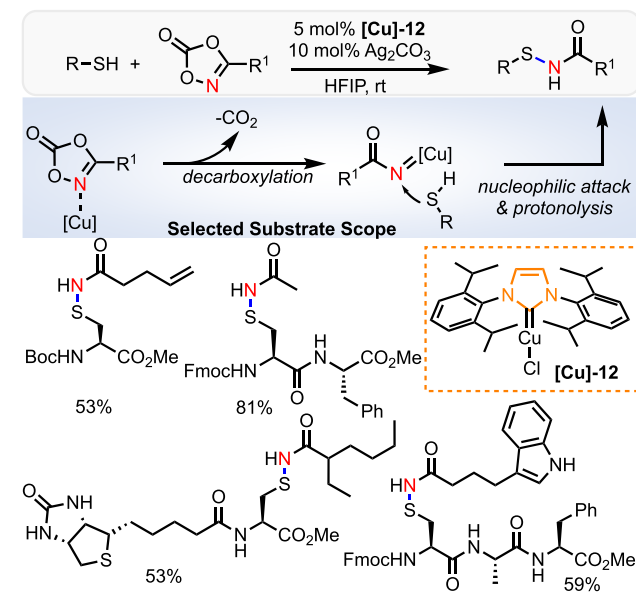
Scheme 122. Cu-Catalyzed Quinoline-N Directed Nitrene Transfer Reactions



position. Notably, substrates bearing multiple methylthio substituents, such as 2,6,8-tris(methylthio)quinoline, displayed exceptional chemoselectivity. Sulfimidation occurred exclusively at the C8 position, yielding the monosulfimide in 79% yield.

6.2.3. Introducing Dioxazolones. Chen and co-workers reported an efficient copper-catalyzed S-amidation of thiols with dioxazolones, yielding N-acyl sulfenamides.²⁹⁵ The copper catalyst ([Cu]-12) featuring an N-heterocyclic carbene (NHC) ligand outperformed other metal complexes, including Ir, Fe, Rh, Co, and Ni. This method is practical, broad in scope, and convenient. As illustrated in Scheme 123, the

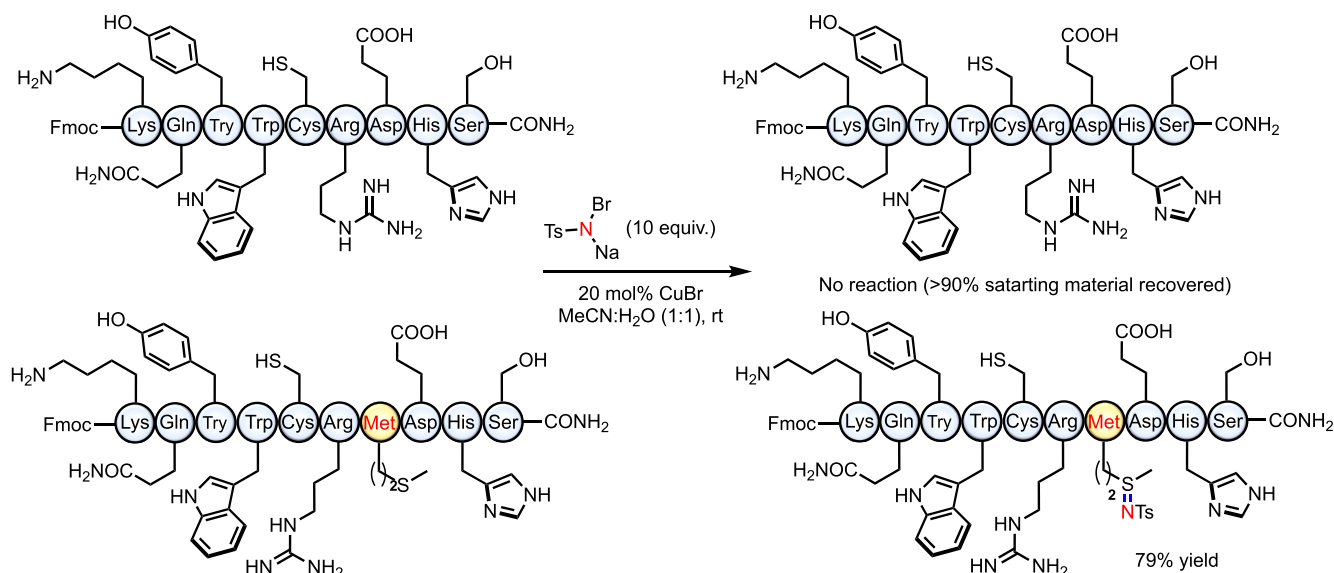
Scheme 123. Copper-Catalyzed Nitrene-Mediated S-Amidation Reaction of Thiols



catalytic cycle involves (i) dioxazolone decarboxylation at the Cu center, (ii) nucleophilic attack of the thiol on the Cu-nitrenoid intermediate, and (iii) protonolysis. Notably, the resulting N-acyl sulfenamides serve as potent S-sulfonylation reagents, enabling the synthesis of unsymmetrical disulfides under mild conditions. The developed strategy addresses challenges in synthesizing sterically hindered disulfides, which are typically difficult to access by conventional methods.^{296,297}

6.2.4. Using Bromamine-T. Recently, Raj and co-workers have developed a Cu-catalyzed nitrene transfer reaction for chemoselective methionine profiling (Scheme 124) in bioactive peptides, proteins, and complex cell lysate mixtures.²⁹⁸ Among various tested catalysts, CuBr exhibited superior activity delivering the sulfonyl sulfimide product with 88% yield. Alternative catalysts based on iron (Fe) and palladium (Pd) were found to be less effective. To understand the chemoselective nature of the reaction, a nonapeptide (Fmoc-KQYWCREHS-CONH₂) lacking methionine was tested under the standard reaction conditions, revealing no modifications even after prolonged exposure (24 h), and the peptide was recovered in >90% yield. While, the decapeptide (Fmoc-KQYWCRMEHS-CONH₂), which includes a methionine residue, underwent single-site modification with a yield of 79%. Energy evaluations further supported the reaction's chemoselectivity. The analysis revealed that the energy gap between the HOMO of methionine and the LUMO of the

Scheme 124. Copper-Catalyzed Chemoselective Nitrene Transfer to Methionine



MeCN-bound copper-nitrene complex was the lowest among all reactive amino acid residues, except for tryptophan. This minimal energy gap facilitated the selective functionalization of the methionine residue.

7. CONCLUSION AND OUTLOOK

This Review aims to provide a comprehensive overview of the use of base metal catalysis in nitrene transfer reactions that have emerged as a powerful and versatile method for the synthesis of nitrogen-containing molecules. The transition from precious metals to more abundant first-row transition metals (3d metals)—like manganese, iron, cobalt, nickel, and copper—has resulted in significant developments in creating affordable and sustainable catalytic systems. These base metals have shown remarkable chemo-, regio-, and stereoselectivity in nitrene transfer reactions, such as aziridination, C–H amination, rearrangements, cyclization-induced C–N bond formation, synthesis of heterocycles and other *N*-heteroatom bond forming transformations. As a result, the review also offers an extensive compilation and overview of base-metal-catalyzed nitrene transfer (NT) reactions.

A subtle demarcation of 3d transition metals can be early (Sc–Cr), mid (Mn–Co), and late (Ni–Zn). Across this period their characteristic properties change, so do the corresponding metal-nitrene species [M(NR)]. Early 3d metals provides highly polarized, nucleophilic dianionic imido ligands (NR²⁻) with electrophilic metal center, consequence of a significant energy gap of the valence orbitals of the metal and the nitrene precursor. These imido complexes prefer to undergo 1,2-addition with the multiple bonds due to their innate polar nature.²⁹⁹ Regarding the mid 3d metals, due to the resemblance of the energy profile of the valence orbitals of both the species, they tend to bind with covalent mode of linkage with the nitrene precursors. The reactivity profiles of these metal-nitrene complexes are very acute to the electronic structure; whereas low-spin electronic configuration renders stability,³⁰⁰ high-spin (open-shell) analogues enforce reactivity for nitrene transfer catalysis.³⁰¹ In the case of late 3d metals, due to the high density of d electrons and simultaneous increase in electronegativity, an inversion of the metal and ligand (NR) valence orbital energy is possible. This turn of

event can render the metal center more reduced with ligand dominated frontier molecular orbitals (FMOs).³⁰² Thus, although the bond order of the complex remains unaltered but reactivity profile gets discrepant. In general, upon coordinating with an open-shell transition metal species (3d metals) nitrene can manifest a range of covalent type of interactions between the metal center and nitrogen atom of the nitrene. The resulting metal-nitrenoid species can have one σ -bond; these kinds of species can invoke radical nature and routinely described as “iminyl” species. On the other hand, metal-nitrenoid species featuring both σ - and π -bonds considered as “imido” species.³⁰³ A third category could be, where metal-nitrenoid species acquire a σ -bond and a weakened π -bond due to the occupancy in the antibonding π^* orbital, described as “imido-like” species.³⁰⁴

In terms of the metal core, earlier mention in Scheme 1B (iv) highlights that altering the metal core can significantly change the reactivity and thus can provide a different outcome. Where Mn(TPP)ClO₄ favored the allylic C–H amination over aziridination, Fe(TPP)ClO₄ is nonselective due to the higher electrophilicity of the corresponding metal-nitrenoids. From White's initial reports with [Mn]-11 catalyst (Scheme 10) highlights that more electrophilic metal-nitrenoid species are suitable to break stronger C–H bond. As a result, replacing Mn(III) (d⁴) with Fe(III) (d⁵) resulted in reduced reactivity due to strong π -back bonding with the ligand scaffolds. In the case of C(sp³)–H amination manifold, both Fe (Scheme 14) and Co (Scheme 58 and 59) favor benzylic/allylic C–H bond, in contrast Cu favors the less sterically hindered C(sp³)–H bond.³⁰⁵

It indicates the steric effect is more vivid in Cu-nitrenoid species, albeit radical stability guides the choice for Fe- and Co-nitrenoid species. Another investigation by the Deng group also shed light on how the oxidation state of cobalt-imido complexes can affect the C–H activation, where Co(IV)-imido showed competency, contrary to the analogous Co(V)-imido species.³⁰⁶

Regarding the mode of electronic nature/valence center, the redox property of the nitrene N atom in the metal-nitrenoid can also alter the course of reaction. In that vein, Betley et al. showed superior efficacy of Fe-based iminyl species over

imido-analogue.³⁰⁷ Deng and his team demonstrated that a tethered-electron withdrawing fragment in Fe(IV)-imido species can promote the hydrogen atom abstraction by lowering the activation barrier.³⁰⁸ Mondal et al. concluded a (TPP)Co-iminyl species performed inferiorly compare to the (TPP)-Fe-imido-like congener for the course of aziridination reaction.³⁰⁴

Needless to say, the choice of ligand is game changer. In 2015, White et al. reported superiority of the porphyrazine (Pz) ligand compare to porphyrin (Por), as already stated in details (Scheme 10). Extra four nitrogen atoms in the skeleton of the ligand (Pz) renders strong π -back bonding from the metal and render the corresponding metal-nitrenoid complex more electronegative, enforcing the efficacy to aminate stronger C(sp³)-H bond. In Betley's work on diastereoselective C-H bond amination to furnish disubstituted pyrrolidines (Scheme 21), an extensive impact of the auxiliary ligand has been noticed. Che et al. demonstrated the undeniable significance of the axial coordinated NHC-moiety to the Fe-metal center (Scheme 24). It has been proposed that the presence of the NHC-moiety ruffles out the entire geometry of the porphyrin skeleton, thereby kicking out the Fe-metal from the ligand plane and helping the metal-nitrenoid formation step. The Chattopadhyay group showed that changing the iron-porphyrin stereoelectronics by ligand tuning can switch the chemoselectivity (Scheme 53). The Zhang group demonstrated that changing the cavity size formed by the *exo*-skeleton of the ligand framework by altering the number of carbon atoms can switch the enantioselectivity (Scheme 62). In general, (Por)Co-nitrene undergoes a metalloradical mode of activation with substrate, and subsequent HAA and radical recombination produce the amination or aziridination product. Albeit the Uyeda group demonstrated that [Co]-17 rather undergoing the MRC-activation/HAA/RR, the complex rendered a different mode of activation and produced dimerized product (Scheme 113). Regarding the role of ligands in nickel- and copper-catalysis in NTRs, we already discussed in detail in section 3.4 and 3.5.

The selection of the nitrene precursor is also crucial for the desired outcomes. As we entailed in section 3.1, Mn prefers the iminoiodinanes more compared to the other precursors. Similarly, Co and Ni prefer electron-deficient aryl azides (section 3.3) and dioxazolones (section 3.4), respectively. Although Fe and Cu have relatively no such strong preference, section 3.2 and section 3.4, respectively. Ultimately, about the mode of reaction among the coupling partners, Mn, Fe, and Co prefer C-H amination over aziridination in general. Likewise, Ni favors hydroamination unlike other base metals, and Cu has a propensity to undergo aziridination.

Over the years, several pioneering groups have shaped the domain of base-metal-catalyzed nitrene-transfer reactions (NTRs). The White group established Mn-catalyzed C-H amination across diverse scaffolds; the de Bruin group advanced Co-metalloradical catalysis (Co-MRC) and its mechanistic foundation; the Zhang group exploited Co-MRC for enantioselective C-N bond formation; the Chang group introduced dioxazolones as versatile nitrene surrogates; and the Chattopadhyay group developed a distinct Fe-based metalloradical activation strategy. Collectively, these catalysts have delivered impressive chemo-, regio-, and stereoselectivity across aziridination, C-H amination, rearrangements, and heterocycle synthesis. Despite significant advances, key challenges persist. Structurally well-defined metal-nitrenoid or

metal-imido intermediates remain scarce, forcing reliance on spectroscopic, kinetic, and computational inference. This obscures the C-N bond-forming steps, the roles of metal-ligand electronics in chemo- and regioselectivity, and the true oxidation states of reactive species. Stereoselectivity in base-metal NTRs is linked to noncovalent interactions; however, electronic influences remain elusive, limiting a comprehensive mechanistic understanding. These mechanistic and characterization challenges will be key to unlocking its full potential in both synthetic and biological applications.

As a future direction, progress will hinge on rational ligand design, control of metal reactivity, and development of highly selective C-H amination strategies suitable for late-stage augmentation of bioactive molecules. Scaling these methods to industrially relevant conditions, coupled with deeper mechanistic insight and commitment to green-chemistry principles, will be essential for establishing robust, sustainable, and economically viable base-metal-catalyzed processes.

AUTHOR INFORMATION

Corresponding Author

Buddhadeb Chattopadhyay – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India;  orcid.org/0000-0001-8473-2695; Email: buddhadeb.c@iiserpune.ac.in, buddhachem12@gmail.com

Authors

Hillol Khatua – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India

Anogh Ghosh – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India

Subrata Das – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India

Sima Patra – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India

Souvik Nandi – Department of Chemistry, Indian Institute of Science Education and Research Pune, Pune 411008 Maharashtra, India

Complete contact information is available at:

<https://pubs.acs.org/10.1021/acs.chemrev.5c00503>

Author Contributions

CRedit: **Hillol Khatua** formal analysis, writing - review & editing; **Anogh Ghosh** formal analysis, writing - review & editing; **Subrata Das** writing - review & editing; **Sima Patra** writing - review & editing; **Souvik Nandi** writing - review & editing; **Buddhadeb Chattopadhyay** conceptualization, supervision, writing - original draft, writing - review & editing.

Notes

The authors declare no competing financial interest.

Biographies

Hillol Khatua completed his Ph.D. in 2024 under the supervision of Professor Chattopadhyay at the CBMR, Lucknow. His doctoral research centered on metal-catalyzed nitrene-mediated C-N bond-forming reactions. Currently, Dr. Khatua is serving as an Assistant

Professor at the Government General Degree College at Keshiary, West Bengal.

Anogh Ghosh is currently pursuing his Ph.D. at the Indian Institute of Science Education and Research (IISER) Pune under the supervision of Professor Chattopadhyay. His research interest lies in 3d-metal-catalyzed C–H functionalization and asymmetric C–H activation.

Subrata Das completed his Ph.D. under the supervision of Professor Chattopadhyay. His research focuses on developing denitrogenative and decarboxylative nitrene transfer reactions for the formation of C–N and N–N bonds.

Sima Patra joined Professor Chattopadhyay's group for her Ph.D. Her research interest centered on base-metal-catalyzed nitrene-transfer reaction toward C–N bond-formation and mechanistic investigation.

Souvik Nandi is currently pursuing his Ph.D. at the Indian Institute of Science Education and Research (IISER) Pune under the supervision of Professor Chattopadhyay. His research is centered on transition-metal-catalyzed nitrene transfer reactions.

Buddhadeb Chattopadhyay received his M.Sc. in Chemistry from Visva-Bharati University, India, in 2003 and Ph.D. in 2009 from the University of Kalyani with Professor K. C. Majumdar. Following his doctoral studies, he spent nearly six years as postdoctoral research associate—at the University of Illinois at Chicago (USA) and at Michigan State University, Michigan (USA). In August 2014, he started his independent academic career at the Centre of Biomedical Research (CBMR) in Lucknow, India. Before joining the Indian Institute of Science Education and Research Pune (IISER Pune), Buddhadeb served for more than ten years at the Centre of Biomedical Research (CBMR), Lucknow, in the positions of Assistant Professor, Associate Professor and Additional Professor. Since January 2025, he has been serving as an Associate Professor in the Department of Chemistry at the Indian Institute of Science Education and Research (IISER), Pune. His research interest includes the catalyst/ligand engineering for the C–H bond activation/functionalization, especially C–H bond borylations of organic molecules and metal-nitrene/carbene chemistry via metalloradical catalysis by means of denitrogenative transformations to make high-valued nitrogen heterocycles. Dr. Chattopadhyay is a Fellow of the Royal Society of Chemistry, London, UK (FRSC) and Fellow of the National Academy of Sciences (FNASc). Dr. Chattopadhyay has been serving as Associate Editor, *Organic Chemistry Frontiers* (OCF), RSC.

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■ REFERENCES

- (1) Pulletikurti, S.; Yadav, M.; Springsteen, G.; Krishnamurthy, R. Prebiotic Synthesis of α -Amino Acids and Orotate from α -Ketoacids Potentiates Transition to Extant Metabolic Pathways. *Nat. Chem.* **2022**, *14*, 1142–1150.
- (2) Ward, B.; et al. Denitrification as the Dominant Nitrogen Loss Process in the Arabian Sea. *Nature* **2009**, *461*, 78–81.
- (3) Erdik, E.; Ay, M. Electrophilic Amination of Carbanions. *Chem. Rev.* **1989**, *89*, 1947–1980.
- (4) Hartwig, J. F. Evolution of a Fourth Generation Catalyst for the Amination and Thioetherification of Aryl Halides. *Acc. Chem. Res.* **2008**, *41*, 1534–1544.
- (5) Kim, S.; Loose, F.; Chirik, P. J. Beyond Ammonia: Nitrogen-Element Bond Forming Reactions with Coordinated Dinitrogen. *Chem. Rev.* **2020**, *120* (12), 5637–5681.
- (6) Collet, F.; Lescot, C.; Dauban, P. Catalytic C–H Amination: the Stereoselectivity Issue. *Chem. Soc. Rev.* **2011**, *40*, 1926–1936.
- (7) Park, Y.; Kim, Y.; Chang, S. Transition Metal-Catalyzed C–H Amination: Scope, Mechanism, and Applications. *Chem. Rev.* **2017**, *117*, 9247–9301.
- (8) Bisht, R.; Haldar, C.; Hassan, M. M. M.; Hoque, M. E.; Chaturvedi, J.; Chattopadhyay, B. Metal-Catalysed C–H Bond Activation and Borylation. *Chem. Soc. Rev.* **2022**, *51*, 5042–5100.
- (9) Das, S. K.; Roy, S.; Khatua, H.; Chattopadhyay, B. Ir-Catalyzed Intramolecular Transannulation/C(sp²)-H Amination of 1,2,3,4-Tetrazoles by Electrocyclization. *J. Am. Chem. Soc.* **2018**, *140*, 8429–8433.
- (10) Chattopadhyay, B.; Gevorgyan, V. Transition Metal Catalyzed Denitrogenative Transannulation: Converting Triazoles into Other Heterocyclic Systems. *Angew. Chem., Int. Ed.* **2012**, *51*, 862–872.
- (11) Das, S. K.; Roy, S.; Chattopadhyay, B. Transition Metal-Catalyzed Denitrogenative Annulation to Access High-Valued N-Heterocycles. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202210912.
- (12) Müller, P.; Fruit, C. Enantioselective Catalytic Aziridinations and Asymmetric Nitrene Insertions into C–H Bonds. *Chem. Rev.* **2003**, *103*, 2905–2920.
- (13) Shin, K.; Kim, H.; Chang, S. Transition-Metal-Catalyzed C–N Bond Forming Reactions Using Organic Azides as the Nitrogen Source: A Journey for the Mild and Versatile C–H Amination. *Acc. Chem. Res.* **2015**, *48*, 1040–1052.
- (14) Alderson, J. M.; Corbin, J. R.; Schomaker, J. M. Tunable, Chemo- and Site-Selective Nitrene Transfer Reactions through the Rational Design of Silver(I) Catalysts. *Acc. Chem. Res.* **2017**, *50*, 2147–2158.
- (15) Hayashi, H.; Uchida, T. Nitrene Transfer Reactions for Asymmetric C–H Amination: Recent Development. *Eur. J. Org. Chem.* **2020**, *2020*, 909–916.
- (16) Roy, S.; Das, S. K.; Khatua, H.; Das, S.; Chattopadhyay, B. Road Map for the Construction of High-Valued N-Heterocycles via Denitrogenative Annulation. *Acc. Chem. Res.* **2021**, *54*, 4395–4409.
- (17) Empel, C.; Koenigs, R. M. Visible-Light-Mediated Amination Reactions via Nitrene Intermediates. *Chem. Catalysis.* **2022**, *2*, 2506–2514.
- (18) Khatua, H.; Das, S.; Patra, S.; Nandi, S.; Chattopadhyay, B. Iron-Catalysed Nitrene Transfer Reaction to Form C–N Bonds. *Tetrahedron Lett.* **2024**, *144*, 155136.
- (19) Roy, S.; Das, S. K.; Chattopadhyay, B. Cobalt(II)-Based Metalloradical Activation of 2-(Diazomethyl)pyridines for Radical Transannulation and Cyclopropanation. *Angew. Chem., Int. Ed.* **2018**, *57*, 2238–2243.
- (20) Roose, T. R.; Verdoorn, D. S.; Mampuy, P.; Ruijter, E.; Maes, B. U. W.; Orru, R. V. A. Transition Metal-Catalysed Carbene- and Nitrene Transfer to Carbon Monoxide and Isocyanides. *Chem. Soc. Rev.* **2022**, *51*, 5842–5877.
- (21) Ju, M.; Schomaker, J. M. Nitrene Transfer Catalysts for Enantioselective C–N Bond Formation. *Nat. Rev. Chem.* **2021**, *5*, 580–594.
- (22) Docherty, J. H.; Lister, T. M.; McArthur, G.; Findlay, M. T.; Domingo-Legarda, P.; Kenyon, J.; Choudhary, S.; Larrosa, I. Transition-Metal-Catalyzed C–H Bond Activation for the Formation of C–C Bonds in Complex Molecules. *Chem. Rev.* **2023**, *123*, 7692–7760.
- (23) Wang, D.; Astruc, D. The Recent Development of Efficient Earth-Abundant Transition-Metal Nanocatalysts. *Chem. Soc. Rev.* **2017**, *46*, 816–854.
- (24) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackerman, L. 3d Transition Metals for C–H Activation. *Chem. Rev.* **2019**, *119*, 2192–2452.
- (25) Feng, Y.; Long, S.; Tang, X.; Sun, Y.; Luque, R.; Zeng, X.; Lin, L. Earth-Abundant 3d-Transition-Metal Catalysts for Lignocellulosic biomass conversion. *Chem. Soc. Rev.* **2021**, *50*, 6042–6093.

- (26) Muller, P.; Fruit, C. Enantioselective Catalytic Aziridinations and Asymmetric Nitrene Insertions into CH Bonds. *Chem. Rev.* **2003**, *103*, 2905–2919.
- (27) Breslow, R.; Gellman, S. H. Tosylamidation of Cyclohexane by a Cytochrome P-450 Model. *J. Chem. Soc., Chem. Commun.* **1982**, 1400–1401.
- (28) Lu, H.; Zhang, X. P. Catalytic C-H Functionalization by Metalloporphyrins: Recent Developments and Future Directions. *Chem. Soc. Rev.* **2011**, *40*, 1899–1909.
- (29) Che, C. M.; Lo, V. K. Y.; Zhou, C. Y.; Huang, J. S. Selective Functionalisation of Saturated C-H Bonds with Metalloporphyrin Catalysts. *Chem. Soc. Rev.* **2011**, *40*, 1950–1975.
- (30) Fantauzzi, S.; Caselli, A.; Gallo, E. Nitrene Transfer Reactions Mediated by Metallo-Porphyrin Complexes. *Dalton Trans.* **2009**, 5434–5443.
- (31) Che, C.-M.; Zhou, C.-Y.; Wong, E. L.-M. Catalysis by Fe=X Complexes (X = NR, CR₂). In *Iron Catalysis: Fundamentals and Applications*; Plietker, B., Ed.; Top. Organomet. Chem.; Springer Berlin Heidelberg: Berlin, Heidelberg, 2011; pp 111–138.
- (32) Zhang, L.; Deng, L. C-H bond amination by iron-imido/nitrene species. *Chin. Sci. Bull.* **2012**, *57*, 2352–2360.
- (33) Dequierez, G.; Pons, V.; Dauban, P. Nitrene chemistry in organic synthesis: still in its infancy? *Angew. Chem., Int. Ed.* **2012**, *51*, 7384–7395.
- (34) Shimbayashi, T.; Sasakura, K.; Eguchi, A.; Okamoto, K.; Ohe, K. Recent Progress on Cyclic Nitrenoid Precursors in Transition-Metal-Catalyzed Nitrene-Transfer Reactions. *Chem. Eur. J.* **2019**, *25*, 3156–3180.
- (35) Pellissier, H. Recent Developments in Enantioselective Cobalt Catalyzed Transformations. *Coord. Chem. Rev.* **2018**, *360*, 122–168.
- (36) Huang, H.-M.; Garduño-Castro, M. H.; Morrill, C.; Procter, D. J. Catalytic Cascade Reactions by Radical Relay. *Chem. Soc. Rev.* **2019**, *48*, 4626–4638.
- (37) Liu, Y.; You, T.; Wang, T.-T.; Che, C.-M. Iron-Catalyzed C-H Amination and Its Application in Organic Synthesis. *Tetrahedron* **2019**, *75*, 130607.
- (38) Díaz-Requejo, M. M.; Pérez, P. J. The TpxM Core in Csp³-H Bond Functionalization Reactions: Comparing Carbene, Nitrene, and Oxo Insertion Processes (Tpx = Scorpionate Ligand; M = Cu, Ag). *Eur. J. Inorg. Chem.* **2020**, *2020*, 879–885.
- (39) van Vliet, K. M.; de Bruin, B. Dioxazolones: Stable Substrates for the Catalytic Transfer of Acyl Nitrenes. *ACS Catal.* **2020**, *10*, 4751–4769.
- (40) Baudron, S. A. Dipyrin Based Metal Complexes: Reactivity and Catalysis. *Dalton Trans.* **2020**, 49, 6161–6175.
- (41) Liu, Y.; You, T.; Wang, H.-X.; Tang, Z.; Zhou, C.-Y.; Che, C.-M. Iron- and Cobalt-Catalyzed C(sp³)-H Bond Functionalization Reactions and Their Application in Organic Synthesis. *Chem. Soc. Rev.* **2020**, *49*, 5310–5358.
- (42) Rodríguez, M. R.; Díaz-Requejo, M. M.; Pérez, P. J. Development of Molecular Complexity through Nitrene-Transfer Reactions Catalyzed by Copper and Silver Scorpionate Complexes. *Synlett* **2021**, *32*, 763–774.
- (43) Sivaguru, P.; Ning, Y.; Bi, X. New Strategies for the Synthesis of Aliphatic Azides. *Chem. Rev.* **2021**, *121*, 4253–4307.
- (44) Cosio, M. N.; Powers, D. C. Prospects and challenges for nitrogen-atom transfer catalysis. *Nat. Rev. Chem.* **2023**, *7*, 424–438.
- (45) Fanourakis, A.; Phipps, R. J. Catalytic, Asymmetric Carbon-Nitrogen Bond Formation Using Metal Nitrenoids: From Metal-Ligand Complexes via Metalloporphyrins to Enzymes. *Chem. Sci.* **2023**, *14*, 12447–12476.
- (46) Liu, Y.; Shing, K.-P.; Lo, V. K.-Y.; Che, C.-M. Iron- and Ruthenium-Catalyzed C-N Bond Formation Reactions. Reactive Metal Imido/Nitrene Intermediates. *ACS Catal.* **2023**, *13*, 1103–1124.
- (47) Wu, K.; Che, C.-M. Iron-Catalysed Intramolecular C(sp³)-H Amination of Alkyl Azides. *Chem. Commun.* **2024**, *60*, 13998–14011.
- (48) Bao, M.; Dong, S.; Chen, K.; Xu, X. Recent Advances in Nitrene Chemistry with Emerging Precursors. *Chem. Asian J.* **2025**, *20*, No. e202401521.
- (49) Kwart, H.; Khan, A. A. Copper-Catalyzed Decomposition of Benzenesulfonyl Azide in Cyclohexene Solution. *J. Am. Chem. Soc.* **1967**, *89*, 1951–1953.
- (50) Breslow, R.; Gellman, S. H. Intramolecular Nitrene Carbon-Hydrogen Insertions Mediated by Transition-Metal Complexes as Nitrogen Analogs of Cytochrome P-450 Reactions. *J. Am. Chem. Soc.* **1983**, *105*, 6728–6729.
- (51) Mansuy, D.; Mahy, J. P.; Dureault, A.; Bedi, G.; Battioni, P. Iron- and manganese-porphyrin catalysed aziridination of alkenes by tosyl- and acyl-iminiodobenzene. *J. Chem. Soc., Chem. Commun.* **1984**, 1161–1163.
- (52) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. Allylic amination of alkenes by tosyliminiodobenzene: manganese porphyrins as suitable catalysts. *Tetrahedron Lett.* **1988**, *29*, 1927–1930.
- (53) Groves, J. T.; Takahashi, T. Activation and Transfer of Nitrogen from a Nitridomanganese(V) Porphyrin Complex. Aza analog of epoxidation. *J. Am. Chem. Soc.* **1983**, *105*, 2073–2075.
- (54) Bottomley, L. A.; Neely, F. L. Nitrogen Atom Activation: the Influence of Porphyrin Ring Structure on the Kinetics of the Reaction of Trifluoroacetic Anhydride with Nitrido Manganese(V) Porphyrins. *J. Am. Chem. Soc.* **1988**, *110*, 6748–6752.
- (55) Mansuy, D.; Battioni, P.; Mahy, J. P. Isolation of an Iron-Nitrene Complex from the Dioxygen- and Iron Porphyrin-Dependent Oxidation of a Hydrazine. *J. Am. Chem. Soc.* **1982**, *104*, 4487–4489.
- (56) Barton, D. H. R.; Hay-Motherwell, R. S.; Motherwell, W. B. Functionalisation of Saturated Hydrocarbons. Part 1. Some Reactions of a Ferrous Chloride-Chloramine-T Complex with Hydrocarbons. *J. Chem. Soc., Perkin Trans. 1* **1983**, 445–451.
- (57) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. Copper-Catalyzed Aziridination of Olefins by (N-(p-Toluenesulfonyl)imino)-phenyliodinane. *J. Org. Chem.* **1991**, *56*, 6744–6746.
- (58) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. Development of the Copper-Catalyzed Olefin Aziridination Reaction. *J. Am. Chem. Soc.* **1994**, *116*, 2742–2753.
- (59) Sweeney, J. B. Aziridines: Epoxides' Ugly Cousins? *Chem. Soc. Rev.* **2002**, *31*, 247–258.
- (60) Wolgemuth, D. K.; Elmore, S. D.; Cope, J. D.; Sheridan, P. E.; Stokes, S. L.; Emerson, J. P. Manganese-catalyzed Aziridination of Olefins with Chloramine-T in Water and Buffered Aqueous Solutions. *Catal. Commun.* **2021**, *150*, 106275–106279.
- (61) Zhou, Z.-W.; Zhao, Y.-C.; Yue, Y.; Wu, J.; Yang, M.; Yu, X.-Q. Aziridination and Amidation Catalyzed by Polymer-Supported Metalloporphyrins with PhI(OAc)₂ and TsNH₂. *ARKIVOC* **2005**, *2005*, 130.
- (62) Noda, K.; Hosoya, N.; Irie, R.; Ito, Y.; Katsuki, T. Asymmetric Aziridination by using Optically Active (Salen) Manganese(III) Complexes. *Synlett* **1993**, *1993*, 469–471.
- (63) Nishikori, H.; Katsuki, T. Catalytic and Highly Enantioselective Aziridination of Styrene Derivatives. *Tetrahedron Lett.* **1996**, *37*, 9245–9248.
- (64) Lai, T.-S.; Che, C.-M.; Kwong, H.-L.; Peng, S.-M. Catalytic and Asymmetric Aziridination of Alkenes Catalysed by a Chiral Manganese Porphyrin Complex. *Chem. Commun.* **1997**, 2373–2374.
- (65) Simonato, J.-P.; Pecaut, J.; Marchon, J.-C.; Robert Scheidt, W. Antagonistic Metal-Directed Inductions in Catalytic Asymmetric Aziridination by Manganese and Iron Tetramethylchiorporphyrins. *Chem. Commun.* **1999**, 989–990.
- (66) Kurup, S.; Woodland, N.; Lord, R.; Groysman, S. Aziridination Reactivity of a Manganese(II) Complex with a Bulky Chelating Bis(Alkoxide) Ligand. *Molecules* **2022**, *27*, 5751.
- (67) Yu, X.-Q.; Huang, J.-S.; Zhou, X.-G.; Che, C.-M. Amidation of Saturated C-H Bonds Catalyzed by Electron-Deficient Ruthenium and Manganese Porphyrins. A Highly Catalytic Nitrogen Atom Transfer Process. *Org. Lett.* **2000**, *2*, 2233–2236.
- (68) Kohmura, Y.; Katsuki, T. Mn(salen)-Catalyzed Enantioselective C-H Amination. *Tetrahedron Lett.* **2001**, *42*, 3339–3342.

- (69) Clark, J. R.; Feng, K.; Sookezian, A.; White, M. C. Manganese Catalyzed Benzylic C(sp³)-H Amination for Late-Stage Functionalization. *Nat. Chem.* **2018**, *10*, 583–591.
- (70) Roizen, J. L.; Zalatan, D. N.; Du Bois, J. Selective intermolecular amination of C-H bonds at tertiary carbon centers. *Angew. Chem., Int. Ed.* **2013**, *52*, 11343–11346.
- (71) Wang, J.; Zheng, K.; Li, T.; Zhan, X. Mechanism and Chemoselectivity of Mn-Catalyzed Intramolecular Nitrene Transfer Reaction: C-H Amination vs. C = C Aziridination. *Catalysts* **2020**, *10*, 292.
- (72) Ide, T.; Feng, K.; Dixon, C. F.; Teng, D.; Clark, J. R.; Han, W.; Wendell, C. I.; Koch, V.; White, M. C. Late-Stage Intermolecular Allylic C-H Amination. *J. Am. Chem. Soc.* **2021**, *143*, 14969–14975.
- (73) Wang, J.; Xiao, R.; Zheng, K.; Qian, L. Theoretical Studies on Mn-Catalyzed Intermolecular Allylic C-H Aminations of Internal Olefins: Mechanism, Chemo- and Regioselectivity. *Mol. Catal.* **2022**, *524*, 112278.
- (74) Du, Y.; Yu, X.; Tang, J.-J.; Li, Y.; Fan, J.; Li, F.; Bao, M. Visible-Light-Promoted Mn-Catalyzed C(sp³)-H Amidation with Dioxazolones. *Journal of Organic Chemistry* **2023**, *88*, 9783–9790.
- (75) Zhang, J.; Chan, P. W. H.; Che, C. M. Enantioselective Intramolecular Amidation of Sulfamate Esters Catalyzed by Chiral Manganese(III) Schiff-base Complexes. *Tetrahedron Lett.* **2005**, *46*, 5403–5408.
- (76) Paradine, S. M.; Griffin, J. R.; Zhao, J.; Petronico, A. L.; Miller, S. M.; White, M. C. A Manganese Catalyst for Highly Reactive yet Chemoselective Intramolecular C(sp³)-H Amination. *Nat. Chem.* **2015**, *7*, 987–994.
- (77) Wang, J.; Zheng, K.; Li, T.; Zhan, X. Mechanism and Chemoselectivity of Mn-Catalyzed Intramolecular Nitrene Transfer Reaction: C-H Amination vs. C = C Aziridination. *Catalysts* **2020**, *10*, 292.
- (78) Kong, X.-Q.; Xu, B. Manganese-Catalyzed ortho-C-H Amidation of Weakly Coordinating Aromatic Ketones. *Org. Lett.* **2018**, *20*, 4495–4498.
- (79) Bhanuchandra, M.; Ramu Yadav, M.; Rit, R. K.; Rao Kuram, M.; Sahoo, A. K. Ru(II)-catalyzed intermolecular ortho-C-H amidation of aromatic ketones with sulfonyl azides. *Chem. Commun.* **2013**, *49*, 5225–5227.
- (80) Kim, J.; Chang, S. Iridium-Catalyzed Direct C-H Amidation with Weakly Coordinating Carbonyl Directing Groups under Mild Conditions. *Angew. Chem., Int. Ed.* **2014**, *53*, 2203–2207.
- (81) Khatua, H.; Das, S. K.; Roy, S.; Chattopadhyay, B. Dual Reactivity of 1,2,3,4-Tetrazole: Manganese-Catalyzed Click Reaction and Denitrogenative Annulation. *Angew. Chem., Int. Ed.* **2021**, *60*, 304–312.
- (82) Liu, Y.; Che, C.-M. [Fe(III)(F₂₀-tpp)Cl] Is an Effective Catalyst for Nitrene Transfer Reactions and Amination of Saturated Hydrocarbons with Sulfonyl and Aryl Azides as Nitrogen Source under Thermal and Microwave-Assisted Conditions. *Chem. Eur. J.* **2010**, *16*, 10494–10501.
- (83) Tseberlidis, G.; Zardi, P.; Caselli, A.; Cancogni, D.; Fusari, M.; Lay, L.; Gallo, E. Glycopolyporphyrin Catalysts for Efficient C-H Bond Aminations by Organic Azides. *Organometallics* **2015**, *34*, 3774–3781.
- (84) Du, Y.-D.; Xu, Z.-J.; Zhou, C.-Y.; Che, C.-M. An Effective [Fe(III)(TF₄DMap)Cl] Catalyst for C-H Bond Amination with Aryl and Alkyl Azides. *Org. Lett.* **2019**, *21*, 895–899.
- (85) Zars, E.; Pick, L.; Swain, A.; Bhunia, M.; Carroll, P. J.; Munz, D.; Meyer, K.; Mindiola, D. J. Iron-Catalyzed Intermolecular C-H Amination Assisted by an Isolated Iron-Imido Radical Intermediate. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202311749.
- (86) Geraci, A.; Baudoin, O. Fe-Catalyzed α -C(sp³)-H Amination of N-Heterocycles. *Angew. Chem., Int. Ed.* **2025**, *64*, No. e202417414.
- (87) Lee, W.; Kim, D.; Seo, S.; Chang, S. Photoinduced α -C-H Amination of Cyclic Amine Scaffolds Enabled by Polar-Radical Relay. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202202971.
- (88) Khatua, H.; Das, S.; Patra, S.; Das, S. K.; Roy, S.; Chattopadhyay, B. Iron-Catalyzed Intermolecular Amination of Benzylic C(sp³)-H Bonds. *J. Am. Chem. Soc.* **2022**, *144*, 21858–21866.
- (89) Mahajan, M.; Mondal, B. Fe(II)-Porphyrin Catalysts Emulate Enzymatic Structural Features for C-H Amination Reactions. *Inorg. Chem.* **2025**, *64*, 16687.
- (90) Du, Y.; Tang, J.-J.; Wang, Y.; Hu, J.; Chen, C.; Xiong, Z.; Li, Y.; Fan, J.; Bao, M.; Yu, X. Visible-Light-Driven Iron-Catalyzed Intermolecular Benzylic C(sp³)-H Amination with 1,2,3,4-Tetrazoles. *Org. Lett.* **2024**, *26*, 664–669.
- (91) Liu, Y.; Chen, G.-Q.; Tse, C.-W.; Guan, X.; Xu, Z.-J.; Huang, J.-S.; Che, C.-M. [Fe(F₂₀TPP)Cl]-Catalyzed Amination with Arylamines and {[Fe(F₂₀TPP)(NAr)](PhI = NAr)} Intermediate Assessed by High-Resolution ESI-MS and DFT Calculations. *Chem. Asian J.* **2015**, *10*, 100–105.
- (92) Hou, M.; Zhang, Z.; Lai, X.; Zong, Q.; Jiang, X.; Guan, M.; Qi, R.; Qiu, G. Photoredox/Iron Dual-Catalyzed Insertion of Acyl Nitrenes into C-H Bonds. *Org. Lett.* **2022**, *24*, 4114–4118.
- (93) Tang, J.-J.; Yu, X.; Wang, Y.; Yamamoto, Y.; Bao, M. Interweaving Visible-Light and Iron Catalysis for Nitrene Formation and Transformation with Dioxazolones. *Angew. Chem., Int. Ed.* **2021**, *60*, 16426–16435.
- (94) Liu, Y.; Chen, Y.; Zhao, Y.-J.; Zhang, G.-Q.; Zheng, Y.; Yu, P.; Chen, P.; Jia, Z.-J. Iron-Catalyzed Primary Amination of C(sp³)-H Bonds. *J. Am. Chem. Soc.* **2024**, *146*, 24863–24870.
- (95) King, E. R.; Hennessy, E. T.; Betley, T. A. Catalytic C-H Bond Amination from High-Spin Iron Imido Complexes. *J. Am. Chem. Soc.* **2011**, *133*, 4917–4923.
- (96) Hennessy, E. T.; Betley, T. A. Complex N-Heterocycle Synthesis via Iron-Catalyzed, Direct C-H Bond Amination. *Science* **2013**, *340*, 591–595.
- (97) Iovan, D. A.; Wilding, M. J. T.; Baek, Y.; Hennessy, E. T.; Betley, T. A. Diastereoselective C-H Bond Amination for Disubstituted Pyrrolidines. *Angew. Chem., Int. Ed.* **2017**, *56*, 15599–15602.
- (98) Thacker, N. C.; Lin, Z.; Zhang, T.; Gilhula, J. C.; Abney, C. W.; Lin, W. Robust and Porous β -Diketiminato-Functionalized Metal-Organic Frameworks for Earth-Abundant-Metal-Catalyzed C-H Amination and Hydrogenation. *J. Am. Chem. Soc.* **2016**, *138*, 3501–3509.
- (99) Thacker, N. C.; Ji, P.; Lin, Z.; Urban, A.; Lin, W. Phenanthroline-Based Metal-Organic Frameworks for Fe-Catalyzed C_{sp³}-H Amination. *Faraday Discuss.* **2017**, *201*, 303–315.
- (100) Lin, Z.; Thacker, N. C.; Sawano, T.; Drake, T.; Ji, P.; Lan, G.; Cao, L.; Liu, S.; Wang, C.; Lin, W. Metal-Organic Layers Stabilize Earth-Abundant Metal-Terpyridine Diradical Complexes for Catalytic C-H Activation. *Chem. Sci.* **2018**, *9*, 143–151.
- (101) Bagh, B.; Broere, D. L. J.; Sinha, V.; Kuijpers, P. F.; van Leest, N. P.; de Bruin, B.; Demeshko, S.; Siegler, M. A.; van der Vlugt, J. I. Catalytic Synthesis of N-Heterocycles via Direct C(sp³)-H Amination Using an Air-Stable Iron(III) Species with a Redox-Active Ligand. *J. Am. Chem. Soc.* **2017**, *139*, 5117–5124.
- (102) Shing, K.-P.; Liu, Y.; Cao, B.; Chang, X.-Y.; You, T.; Che, C.-M. N-Heterocyclic Carbene Iron(III) Porphyrin-Catalyzed Intramolecular C(sp³)-H Amination of Alkyl Azides. *Angew. Chem., Int. Ed.* **2018**, *57*, 11947–11951.
- (103) Zhao, X.; Liang, S.; Fan, X.; Yang, T.; Yu, W. Iron-Catalyzed Intramolecular C-H Amination of α -Azidyl Amides. *Org. Lett.* **2019**, *21*, 1559–1563.
- (104) Liang, S.; Zhao, X.; Yang, T.; Yu, W. Iron-Phosphine Complex-Catalyzed Intramolecular C(sp³)-H Amination of Azides. *Org. Lett.* **2020**, *22*, 1961–1965.
- (105) Stroek, W.; Keilwerth, M.; Pividori, D. M.; Meyer, K.; Albrecht, M. An Iron-Mesoionic Carbene Complex for Catalytic Intramolecular C-H Amination Utilizing Organic Azides. *J. Am. Chem. Soc.* **2021**, *143*, 20157–20165.
- (106) Wang, J.; Xiao, R.; Lin, Z.; Zheng, Z.; Zheng, K. Mechanistic and Chemoselective Investigations on Nitrene Transfer Reactions Mediated by a Novel Iron-mesoionic Carbene Catalyst. *Molecular Catalysis* **2023**, *536*, 112922–112927.

- (107) Stroek, W.; Albrecht, M. Discovery of a Simple Iron Catalyst Reveals the Intimate Steps of C-H Amination to form C-N bonds. *Chem. Sci.* **2023**, *14*, 2849–2859.
- (108) Stroek, W.; Hoareau, L.; Albrecht, M. From the Bottle: Simple Iron Salts for the Efficient Synthesis of Pyrrolidines via Catalytic C-H Bond Amination. *Catal. Sci. Technol.* **2023**, *13*, 958–962.
- (109) You, T.; Shing, K.-P.; Wu, L.; Wu, K.; Wang, H.-H.; Liu, Y.; Du, L.; Liang, R.; Phillips, D.-L.; Chang, X.-Y.; Huang, J.-S.; Che, C.-M. Iron Corrole-Catalyzed Intramolecular Amination Reaction of Alkyl Azides. Spectroscopic Characterization and Reactivity of [Fe V (Cor)](NAD)]. *Adv. Sci.* **2024**, *11*, 2401420–2401429.
- (110) Nguyen, Q.; Nguyen, T.; Driver, T. G. Iron(II) Bromide-Catalyzed Intramolecular C-H Bond Amination [1,2]-Shift Tandem Reactions of Aryl Azides. *J. Am. Chem. Soc.* **2013**, *135*, 620–623.
- (111) Ren, Q.; Shen, X.; Wan, J.; Fang, J. Density Functional Theory Study of the Mechanisms of Iron-Catalyzed Intramolecular C-H Amination [1,2]-Shift Tandem Reactions of Aryl Azides. *Organometallics* **2015**, *34*, 1129–1136.
- (112) Paradine, S. M.; White, M. C. Iron-Catalyzed Intramolecular Allylic C-H Amination. *J. Am. Chem. Soc.* **2012**, *134*, 2036–2039.
- (113) Liu, Y.; Guan, X.; Wong, E. L. M.; Liu, P.; Huang, J. S.; Che, C.-M. Nonheme Iron-Mediated Amination of C(sp³)-H Bonds. Quinquepyridine-Supported Iron-Imide/Nitrene Intermediates by Experimental Studies and DFT Calculations. *J. Am. Chem. Soc.* **2013**, *135*, 7194–7204.
- (114) Jarrige, L.; Zhou, Z.; Hemming, M.; Meggers, E. Efficient Amination of Activated and Non-Activated C(sp³)-H Bonds with a Simple Iron-Phenanthroline Catalyst. *Angew. Chem., Int. Ed.* **2021**, *60*, 6314–6319.
- (115) Kweon, J.; Chang, S. Highly Robust Iron Catalyst System for Intramolecular C(sp³)-H Amidation Leading to γ -Lactams. *Angew. Chem., Int. Ed.* **2021**, *60*, 2909–2914.
- (116) Das, S. K.; Roy, S.; Khatua, H.; Chattopadhyay, B. Iron-Catalyzed Amination of Strong Aliphatic C(sp³)-H Bonds. *J. Am. Chem. Soc.* **2020**, *142*, 16211–16217.
- (117) Ye, C.-X.; Shen, X.; Chen, S.; Meggers, E. Stereocontrolled 1,3-Nitrogen Migration to Access Chiral α -Amino Acids. *Nat. Chem.* **2022**, *14*, 566–573.
- (118) Wang, H.-H.; Shao, H.; Huang, G.; Fan, J.; To, W.-p.; Dang, L.; Liu, Y.; Che, C.-M. Chiral Iron Porphyrins Catalyze Enantioselective Intramolecular C(sp³)-H Bond Amination Upon Visible-Light Irradiation. *Angew. Chem., Int. Ed.* **2023**, *62*, e202218577.
- (119) Ahmed, H.; Ghosh, B.; Breitenlechner, S.; Feßner, M.; Merten, C.; Bach, T. Intermolecular Enantioselective Amination Reactions Mediated by Visible Light and a Chiral Iron Porphyrin Complex. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202407003.
- (120) Hore, S.; Jeong, J.; Kim, D.; Chang, S. Visible-Light-Promoted Enantioselective α -Amidation of Aldehydes by Harnessing Organo-Iron Dual Catalysis. *J. Am. Chem. Soc.* **2024**, *146*, 22172–22179.
- (121) Seo, K.; Zhang, Y.; Trinh, T. A.; Kim, J.; Qi, L.; Guzei, I. A.; Clark, J. R.; Liu, P.; Schomaker, J. M. Mechanistic and Computational Insights into Asymmetric Intramolecular Iron-Catalyzed Nitrene Transfer into Benzylic C-H Bonds. *ACS Catal.* **2025**, *15*, 3789–3798.
- (122) Legnani, L.; Cerai, G. P.; Morandi, B. Direct and Practical Synthesis of Primary Anilines through Iron-Catalyzed C-H Bond Amination. *ACS Catal.* **2016**, *6*, 8162–8165.
- (123) Falk, E.; Gasser, V. C. M.; Morandi, B. Synthesis of N-Alkyl Anilines from Arenes via Iron-Promoted Aromatic C-H Amination. *Org. Lett.* **2021**, *23*, 1422–1426.
- (124) Liu, J.; Wu, K.; Shen, T.; Liang, Y.; Zou, M.; Zhu, Y.; Li, X.; Li, X.; Jiao, N. Fe-Catalyzed Amination of (Hetero)Arenes with a Redox-Active Aminating Reagent under Mild Conditions. *Chem. - Eur. J.* **2017**, *23*, 563–567.
- (125) Ding, Y.; Zhang, S. Y.; Chen, Y. C.; Fan, S. X.; Tian, J. S.; Loh, T. P. Regioselective C-H Amidation of (Alkyl)arenes by Iron(II) Catalysis. *Org. Lett.* **2019**, *21*, 2736–2739.
- (126) D'Amato, E. M.; Börgel, J.; Ritter, T. Aromatic C-H Amination in Hexafluoroisopropanol. *Chem. Sci.* **2019**, *10*, 2424–2428.
- (127) Anugu, R. R.; Munnuri, S.; Falck, J. R. Picolinate-Directed Arene Meta-C-H Amination via FeCl₃ Catalysis. *J. Am. Chem. Soc.* **2020**, *142*, 5266–5271.
- (128) Alt, I. T.; Plietker, B. Iron-Catalyzed Intramolecular C(sp²)-H Amination. *Angew. Chem., Int. Ed.* **2016**, *55*, 1519–1522.
- (129) Stokes, B. J.; Richert, K. J.; Driver, T. G. Rh₂(II)-Catalyzed Synthesis of Carbazoles from Biaryl Azides. *J. Org. Chem.* **2009**, *74*, 6442–6451.
- (130) Alt, I. T.; Guttroff, C.; Plietker, B. Iron-Catalyzed Intramolecular Aminations of C(sp³)-H Bonds in Alkylaryl Azides. *Angew. Chem., Int. Ed.* **2017**, *56*, 10582–10586.
- (131) Prasanthi, A. V. G.; Begum, S.; Srivastava, H. K.; Tiwari, S. K.; Singh, R. Iron-Catalyzed Arene C-H Amidation Using Functionalized Hydroxyl Amines at Room Temperature. *ACS Catal.* **2018**, *8*, 8369–8375.
- (132) Das, S. K.; Das, S.; Ghosh, S.; Roy, S.; Pareek, M.; Roy, B.; Sunoj, R. B.; Chattopadhyay, B. An Iron(II)-Based Metalloradical System for Intramolecular Amination of C(sp²)-H and C(sp³)-H Bonds: Synthetic Applications and Mechanistic Studies. *Chem. Sci.* **2022**, *13*, 11817–11828.
- (133) Liu, J.-B.; Ren, M.; Lai, X.; Qiu, G. Iron-Catalyzed Stereoselective Haloamidation of Amide-Tethered Alkynes. *Chem. Commun.* **2021**, *57*, 4259–4262.
- (134) Kweon, J.; Kim, D.; Kang, S.; Chang, S. Access to β -Lactams via Iron-Catalyzed Olefin Oxyamidation Enabled by the π -Accepting Phthalocyanine Ligand. *J. Am. Chem. Soc.* **2022**, *144*, 1872–1880.
- (135) Roy, S.; Khatua, H.; Das, S. K.; Chattopadhyay, B. Iron(II)-Based Metalloradical Activation: Switch from Traditional Click Chemistry to Denitrogenative Annulation. *Angew. Chem., Int. Ed.* **2019**, *58*, 11439–11443.
- (136) Lai, X.; Liu, J.-B.; Wang, Y.-C.; Qiu, G. Iron-Catalyzed Intramolecular Acyl Nitrene/Alkyne Metalation for the Synthesis of Pyrrolo[2,1-a]isoindol-5-ones. *Chem. Commun.* **2021**, *57*, 2077–2080.
- (137) Song, H.; Chen, N.; Cao, B.; Hou, M.; Qiu, G. A Metal-Catalyzed Tunable Reaction of Ylides with Hydroxylamine Derivatives. *Org. Lett.* **2025**, *27*, 3261–3266.
- (138) Tang, J.-J.; Yu, X.; Yamamoto, Y.; Bao, M. Visible-light-Promoted Iron-catalyzed N-Arylation of Dioxazolones with Arylboronic Acids. *ACS Catal.* **2021**, *11*, 13955–13961.
- (139) Das, S.; Ehlers, A. W.; Patra, S.; de Bruin, B.; Chattopadhyay, B. Iron-Catalyzed Intermolecular C-N Cross-Coupling Reactions via Radical Activation Mechanism. *J. Am. Chem. Soc.* **2023**, *145*, 14599–14607.
- (140) Yang, T.; Fan, X.; Zhao, X.; Yu, W. Iron-Catalyzed Acyl Migration of Tertiary α -Azidyl Ketones: Synthetic Approach toward Enamides and Isoquinolones. *Org. Lett.* **2018**, *20*, 1875–1879.
- (141) Yang, T.; Lin, Y.; Yang, C.; Yu, W. Iron-Catalyzed 1,2-Acyl Migration of tertiary α -Azido Ketones and 2-Azido-1,3-Dicarbonyl Compounds. *Green Chem.* **2019**, *21*, 6097–6102.
- (142) Wei, K.; Yang, T.; Chen, Q.; Liang, S.; Yu, W. Iron-Catalyzed 1,2-Aryl Migration of tertiary Azides. *Chem. Commun.* **2020**, *56*, 11685–11688.
- (143) Wei, K.; Liang, S.; Yang, T.; Yu, W. Iron-Catalyzed 1,4-Phenyl Migration/Ring Expansion of α -Azido N-Phenyl Amides. *Org. Lett.* **2021**, *23*, 8650–8654.
- (144) Roy, S.; Das, S. K.; Khatua, H.; Das, S.; Singh, K. N.; Chattopadhyay, B. Iron-Catalyzed Radical Activation Mechanism for Denitrogenative Rearrangement Over C(sp³)-H Amination. *Angew. Chem., Int. Ed.* **2021**, *60*, 8772–8780.
- (145) Patra, S.; Das, S.; Nandi, S.; Khatua, H.; Chattopadhyay, B. Catalyst-Enabled Chemoselective Metalloradical Activation for Molecular Rearrangement via Ester Migration and Allylic C(sp³)-H Amination. *J. Am. Chem. Soc.* **2025**, *147*, 30582–30590.
- (146) Lee, W.-C. C.; Zhang, X. P. Metalloradical Catalysis: General Approach for Controlling Reactivity and Selectivity of Homolytic Radical Reactions. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202320243.

- (147) Goswami, M.; Lyaskovskyy, V.; Domingos, S. R.; Buma, W. J.; Woutersen, S.; Troeppner, O.; Ivanovic-Burmazovic, I.; Lu, H.-J.; Cui, X.; Zhang, X. P.; Reijerse, E. J.; DeBeer, S.; van Schooneveld, M. M.; Pfaff, F.; Ray, K.; de Bruin, B. Characterization of Porphyrin-Co(III)-'Nitrene Radical' Species Relevant in Catalytic Nitrene Transfer Reactions. *J. Am. Chem. Soc.* **2015**, *137*, 5468–5479.
- (148) Suarez, A. I. O.; Jiang, H. L.; Zhang, X. P.; de Bruin, B. The Radical Mechanism of Cobalt(II) Porphyrin-Catalyzed Olefin Aziridination and The Importance of Cooperative H-Bonding. *Dalton Trans.* **2011**, *40*, 5697–5705.
- (149) Gao, G.-Y.; Harden, J. D.; Zhang, X. P. Cobalt-Catalyzed Efficient Aziridination of Alkenes. *Org. Lett.* **2005**, *7*, 3191–3193.
- (150) Gao, G.-Y.; Jones, J. E.; Vyas, R.; Harden, J. D.; Zhang, X. P. Cobalt-Catalyzed Aziridination with Diphenylphosphoryl Azide (DPPA): Direct Synthesis of N-Phosphorus-Substituted Aziridines from Alkenes. *J. Org. Chem.* **2006**, *71*, 6655–6658.
- (151) Ruppel, J. V.; Jones, J. E.; Huff, C. A.; Kamble, R. M.; Chen, Y.; Zhang, X. P. A Highly Effective Cobalt Catalyst for Olefin Aziridination with Azides: Hydrogen Bonding Guided Catalyst Design. *Org. Lett.* **2008**, *10*, 1995–1998.
- (152) Caselli, A.; Gallo, E.; Fantauzzi, S.; Morlacchi, S.; Ragaini, F.; Cenini, S. Allylic Amination and Aziridination of Olefins by Aryl Azides Catalyzed by CoII(tpa): A Synthetic and Mechanistic Study. *Eur. J. Inorg. Chem.* **2008**, *2008*, 3009–3019.
- (153) Jin, L.-M.; Xu, X.; Lu, H.; Cui, X.; Wojtas, L.; Zhang, X. P. Effective Synthesis of Chiral N-Fluoroaryl Aziridines through Enantioselective Aziridination of Alkenes with Fluoroaryl Azides. *Angew. Chem., Int. Ed.* **2013**, *52*, 5309–5313.
- (154) Jiang, H.; Lang, K.; Lu, H.; Wojtas, L.; Zhang, X. P. Intramolecular Radical Aziridination of Allylic Sulfamoyl Azides by Cobalt(II)-Based Metalloradical Catalysis: Effective Construction of Strained Heterobicyclic Structures. *Angew. Chem., Int. Ed.* **2016**, *55*, 11604–11608.
- (155) Xu, H.; Wang, D.-S.; Zhu, Z.-Y.; Deb, A.; Zhang, X. P. New Mode of Asymmetric Induction for Enantioselective Radical N-Heterobicyclization via Kinetically Stable Chiral Radical Center. *Chem.* **2024**, *10*, 283–298.
- (156) Harden, J. D.; Ruppel, J. V.; Gao, G.-Y.; Zhang, X. P. Cobalt-Catalyzed Intermolecular C-H Amination with Bromamine-T as Nitrene Source. *Chem. Commun.* **2007**, 4644–4646.
- (157) Lu, H.; Subbarayan, V.; Tao, J.; Zhang, X. P. Cobalt(II)-Catalyzed Intermolecular Benzylic C-H Amination with 2,2,2-Trichloroethoxycarbonyl Azide (TrocN₃). *Organometallics* **2010**, *29*, 389–393.
- (158) Jin, L.-M.; Xu, P.; Xie, J.; Zhang, X. P. Enantioselective Intermolecular Radical C-H Amination. *J. Am. Chem. Soc.* **2020**, *142*, 20828–20836.
- (159) Xu, P.; Xie, J.-J.; Wang, D.-S.; Zhang, X. P. Metalloradical Approach for Concurrent Control in Intermolecular Radical Allylic C-H Amination. *Nat. Chem.* **2023**, *15*, 498–507.
- (160) Han, J.-F.; Guo, P.; Zhang, X.-G.; Liao, J.-B.; Ye, K.-Y. Recent Advances in Cobalt-Catalyzed Allylic Functionalization. *Org. Biomol. Chem.* **2020**, *18*, 7740–7750.
- (161) Li, C.-Q.; Lang, K.; Lu, H.-J.; Hu, Y.; Cui, X.; Wojtas, L.; Zhang, X. P. Catalytic Radical Process for Enantioselective Amination of C(sp³)-H Bonds. *Angew. Chem., Int. Ed.* **2018**, *57*, 16837–16841.
- (162) Lang, K.; Li, C.-Q.; Kim, I.; Zhang, X. P. Enantioconvergent Amination of Racemic Tertiary C-H Bonds. *J. Am. Chem. Soc.* **2020**, *142*, 20902–20911.
- (163) Zhu, Y.; Lee, W.-C. C.; Zhang, X. P. Catalytic Metalloradical System for Radical 1,6-C(sp³)-H Amination with Concurrent Control of Site-, Chemo-, and Enantio-selectivity. *J. Am. Chem. Soc.* **2025**, *147*, 15755–15766.
- (164) Hu, Y.; Lang, K.; Li, C.-Q.; Gill, J. B.; Kim, I.; Lu, H.-J.; Fields, K. B.; Marshall, M. K.; Cheng, Q.-G.; Cui, X.; Wojtas, L.; Zhang, X. P. Enantioselective Radical Construction of 5-Membered Cyclic Sulfonamides by Metalloradical C-H Amination. *J. Am. Chem. Soc.* **2019**, *141*, 18160–18169.
- (165) Lang, K.; Torker, S.; Wojtas, L.; Zhang, X. P. Asymmetric Induction and Enantiodivergence in Catalytic Radical C-H Amination via Enantiodifferentiative H-Atom Abstraction and Stereoretentive Radical Substitution. *J. Am. Chem. Soc.* **2019**, *141*, 12388–12396.
- (166) Kuijpers, P. F.; Tiekink, M. J.; Breukelaar, W. B.; Broere, D. L. J.; van Leest, N. P.; van der Vlugt, J. I.; Reek, J. N. H.; de Bruin, B. Cobalt-Porphyrin-Catalyzed Intramolecular Ring-Closing C-H Amination of Aliphatic Azides: A Nitrene-Radical Approach to Saturated Heterocycles. *Chem. - Eur. J.* **2017**, *23*, 7945–7952.
- (167) Villanueva, O.; Weldy, N. M.; Blakey, S. B.; MacBeth, C. E. Cobalt Catalyzed sp³ C-H Amination Utilizing Aryl Azides. *Chem. Sci.* **2015**, *6*, 6672–6675.
- (168) Baek, Y.; Betley, T. A. Catalytic C-H Amination Mediated by Dipyrin Cobalt Imidos. *J. Am. Chem. Soc.* **2019**, *141*, 7797–7806.
- (169) Baek, Y.; Hennessy, E. T.; Betley, T. A. Direct Manipulation of Metal Imido Geometry: Key Principles to Enhance C-H Amination Efficacy. *J. Am. Chem. Soc.* **2019**, *141*, 16944–16953.
- (170) Figg, T. M.; Park, J.; Chang, S.; Musaev, D. G. Comparative Investigations of Cp*-Based Group 9 Metal-Catalyzed Direct C-H Amination of Benzamides. *Organometallics* **2014**, *33*, 4076–4085.
- (171) Sun, B.; Yoshino, T.; Matsunaga, S.; Kanai, M. Air-Stable Carbonyl(pentamethylcyclopentadienyl)Cobalt Diodide Complex as a Precursor for Cationic (Pentamethylcyclopentadienyl)Cobalt(III)-Catalysis: Application for Directed C-2 Selective C-H Amidation of Indoles. *Adv. Synth. Catal.* **2014**, *356*, 1491–1495.
- (172) Sun, B.; Yoshino, T.; Matsunaga, S.; Kanai, M. A Cp*CoI₂-Dimer as a Precursor for Cationic Co(III)-Catalysis: Application To C-H Phosphoramidation of Indoles. *Chem. Commun.* **2015**, *51*, 4659–4661.
- (173) Patel, P.; Chang, S. Cobalt(III)-Catalyzed C-H Amidation of Arenes using Acetoxycarbamates as Convenient Amino Sources under Mild Conditions. *ACS Catal.* **2015**, *5*, 853–858.
- (174) Park, J.; Chang, S. Comparative Catalytic Activity of Group 9 [Cp*M III] Complexes: Cobalt-Catalyzed C-H Amidation of Arenes with Dioxazolones as Amidating Reagents. *Angew. Chem., Int. Ed.* **2015**, *54*, 14103–14107.
- (175) Liang, Y.; Liang, Y.-F.; Tang, C.; Yuan, Y.; Jiao, N. Cationic Cobalt(III)-Catalyzed Aryl and Alkenyl C-H Amidation: A Mild Protocol for the Modification of Purine Derivatives. *Chem. - Eur. J.* **2015**, *21*, 16395–16399.
- (176) Mei, R.; Loup, J.; Ackermann, L. Oxazolynyl-Assisted C-H Amidation by Cobalt(III) Catalysis. *ACS Catal.* **2016**, *6*, 793–797.
- (177) Yu, Y.; Bai, J.; You, M.; Yu, J.; Li, W.; Xiao, Y.; Zhang, S.; Xiong, Z.; Tan, Z. Cp*Co(III)-catalyzed C-H amidation of 2-arylimidazo[1,2-*a*]pyridines with dioxazolones. *Tetrahedron* **2025**, *171*, 134420–134427.
- (178) Shi, X.; Xu, W.; Wang, R.; Zeng, X.; Qiu, H.; Wang, M. Ketone-Directed Cobalt(III)-Catalyzed Regioselective C2 Amidation of Indoles. *J. Org. Chem.* **2020**, *85*, 3911–3920.
- (179) Huang, J.; Ding, J.; Ding, T.-M.; Zhang, S.; Wang, Y.; Sha, F.; Zhang, S.-Y.; Wu, X.-Y.; Li, Q. Cobalt-Catalyzed Ortho-C(sp²)-H Amidation of Benzaldehydes with Dioxazolones Using Transient Directing Groups. *Org. Lett.* **2019**, *21*, 7342–7345.
- (180) Wang, H.; Lorion, M. M.; Ackermann, L. Overcoming the Limitations of C-H Activation with Strongly Coordinating N-Heterocycles by Cobalt Catalysis. *Angew. Chem., Int. Ed.* **2016**, *55*, 10386–10390.
- (181) Lee, J.; Lee, J.; Jung, H.; Kim, D.; Park, J.; Chang, S. Versatile Cp*Co(III)(LX) Catalyst System for Selective Intramolecular C-H Amidation Reactions. *J. Am. Chem. Soc.* **2020**, *142*, 12324–12332.
- (182) Lee, J.; Chang, S. Versatile Utility of Cp*Co(III) Catalysts in C-H Amination under Inner- and Outer-Sphere Pathway. *Synlett* **2023**, *34*, 1356–1366.
- (183) Lee, J.; Kang, B.; Kim, D.; Lee, J.; Chang, S. Cobalt-Nitrenoid Insertion-Mediated Amidative Carbon Rearrangement via Alkyl-Walking on Arenes. *J. Am. Chem. Soc.* **2021**, *143*, 18406–18412.

- (184) Lee, J.; Kang, B.; Kim, D.; Chang, S. Alcohol-Incorporating Diels-Alder Dimerization of In Situ Formed ortho-Quinamine via Co-Nitrenoid Insertion. *Org. Lett.* **2022**, *24*, 5845–5850.
- (185) Lyu, X.; Zhang, J.; Kim, D.; Seo, S.; Chang, S. Merging NiH Catalysis and Inner-Sphere Metal-Nitrenoid Transfer for Hydroamidation of Alkynes. *J. Am. Chem. Soc.* **2021**, *143*, 5867–5877.
- (186) Du, B.; Ouyang, Y.; Chen, Q.; Yu, W.-Y. Thioether-Directed NiH-Catalyzed Remote γ -C(sp³)-H Hydroamidation of Alkenes by 1,4,2-Dioxazol-5-ones. *J. Am. Chem. Soc.* **2021**, *143*, 14962–14968.
- (187) Du, B.; Chan, C.-M.; Ouyang, Y.; Chan, K.; Lin, Z.; Yu, W.-Y. NiH-Catalyzed anti-Markovnikov Hydroamidation of Unactivated Alkenes with 1,4,2-Dioxazol-5-ones for the Direct Synthesis of N-Alkyl Amides. *Commun. Chem.* **2022**, *5*, 176–188.
- (188) Seeman, J. Effect of Conformational Change on Reactivity in Organic Chemistry. Evaluations, Applications, and Extensions of Curtin-Hammett/Winstein-Holness Kinetics. *Chem. Rev.* **1983**, *83*, 83–134.
- (189) Zhang, Y.; Qiao, D.; Duan, M.; Wang, Y.; Zhu, S. Enantioselective Synthesis of α -Aminoboronates by NiH-Catalyzed Asymmetric Hydroamidation of Alkenyl Boronates. *Nat. Commun.* **2022**, *13*, 5630.
- (190) Meng, L.; Yang, J.; Duan, M.; Wang, Y.; Zhu, S. Facile Synthesis of Chiral Arylamines, Alkylamines and Amides by Enantioselective NiH-Catalyzed Hydroamination. *Angew. Chem., Int. Ed.* **2021**, *60*, 23584–23589.
- (191) Lyu, X.; Jung, H.; Kim, D.; Chang, S. Enantioselective Access to β -Amino Carbonyls via Ni-Catalyzed Formal Olefin Hydroamidation. *J. Am. Chem. Soc.* **2024**, *146*, 14745–14753.
- (192) Lyu, X.; Jeon, E.; Seo, C.; Kim, D.; Chang, S. Nickel-Catalyzed Asymmetric Homobenzylic Hydroamidation of Aryl Alkenes to Access Chiral β -Arylamides. *J. Am. Chem. Soc.* **2025**, *147*, 8928–8938.
- (193) Wang, S.-C.; Liu, L.; Duan, M.; Xie, W.; Han, J.; Xue, Y.; Wang, Y.; Wang, X.; Zhu, S. Regio- and Enantioselective Nickel-Catalyzed Ipso- and Remote Hydroamination Utilizing Organic Azides as Amino Sources for the Synthesis of Primary Amines. *J. Am. Chem. Soc.* **2024**, *146*, 30626–30636.
- (194) Gao, Y.; Cui, Y.; Huo, Y.; Chen, J.; She, M.; Li, X.; Chen, Q.; Hu, X. Q. Nickel-Catalyzed Hydroamination of Olefins with Anthranils. *J. Org. Chem.* **2021**, *86*, 12107–12118.
- (195) Xie, F.; Shen, B.; Li, X. Enantioselective Copper-Catalyzed Hydroamination of Vinylarenes with Anthranils. *Org. Lett.* **2018**, *20*, 7154–7157.
- (196) Cui, Y.; Gao, Y.; Zhao, W.; Luo, Y.; Xie, H.; Huo, Y.; Hu, X.-Q. NiH-Catalyzed Proximal-Selective Hydroamination of Unactivated Alkenes with Anthranils. *J. Org. Chem.* **2022**, *87*, 14861–14869.
- (197) Gao, Y.; Yang, S.; Huo, Y.; Chen, Q.; Li, X.; Hu, X.-Q. NiH-Catalyzed Hydroamination/Cyclization Cascade: Rapid Access to Quinolines. *ACS Catal.* **2021**, *11*, 7772–7779.
- (198) Zheng, Y.-L.; Liang, D.-Y.; Ma, H.-B.; Meng, F.-C.; Wang, T. Regio- and Chemoselective Hydroamination of Unactivated Alkenes with Anthranils via NiH-Catalysis. *Chem. Commun.* **2023**, *59*, 2751–2754.
- (199) Choi, H.; Lyu, X.; Kim, D.; Seo, S.; Chang, S. Endo-Selective Intramolecular Alkyne Hydroamidation Enabled by NiH Catalysis Incorporating Alkenyne Nickel Isomerization. *J. Am. Chem. Soc.* **2022**, *144*, 10064–10074.
- (200) Lyu, X.; Seo, C.; Jung, H.; Faber, T.; Kim, D.; Seo, S.; Chang, S. Intramolecular Hydroamidation of Alkenes Enabling Asymmetric Synthesis of β -Lactams via Transposed NiH Catalysis. *Nat. Catal.* **2023**, *6*, 784–795.
- (201) Chen, J.; Wang, H.; Day, C. S.; Martin, R. Nickel Catalyzed Site-Selective Intermolecular C(sp³)-H Amidation. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202212983.
- (202) Wang, Q.; Ni, S.; Yu, L.; Pan, Y.; Wang, Y. Photoexcited Direct Amination/Amidation of Inert Csp³-H Bonds via Tungsten-Nickel Catalytic Relay. *ACS Catal.* **2022**, *12*, 11071–11077.
- (203) Zhou, S.; Liu, T.; Bao, X. Direct Intermolecular C(sp³)-H Amidation with Dioxazolones via Synergistic Decatungstate Anion Photocatalysis and Nickel Catalysis: A Combined Experimental and Computational Study. *J. Catal.* **2022**, *415*, 142–152.
- (204) Keum, H.; Ryoo, H.; Kim, D.; Chang, S. Amidative β -Scission of Alcohols Enabled by Dual Catalysis of Photoredox Proton-Coupled Electron Transfer and Inner-Sphere Ni-Nitrenoid Transfer. *J. Am. Chem. Soc.* **2024**, *146*, 1001–1008.
- (205) Dong, Y. Y.; Clarke, R. M.; Porter, G. J.; Betley, T. A. Efficient C-H Amination Catalysis Using Nickel-Dipyrrin Complexes. *J. Am. Chem. Soc.* **2020**, *142*, 10996–11005.
- (206) Dong, Y. Y.; Lund, C. J.; Porter, G. J.; Clarke, R. M.; Zheng, S. L.; Cundari, T. R.; Betley, T. A. Enantioselective C-H Amination Catalyzed by Nickel Iminyl Complexes Supported by Anionic Bisoxazoline (BOX) Ligands. *J. Am. Chem. Soc.* **2021**, *143*, 817–829.
- (207) Powers, I. G.; Andjaba, J. M.; Zeller, M.; Uyeda, C. Catalytic C(sp²)-H Amination Reactions Using Dinickel Imides. *Organometallics* **2020**, *39*, 3794–3801.
- (208) von Fraunberg, K.; Huisgen, R. Copper-Catalyzed Decomposition Reactions of Imidazides; Reactions of Copper Azenes. *Tetrahedron Lett.* **1969**, *10*, 2599–2602.
- (209) Pérez, P. J.; Brookhart, M.; Templeton, J. L. A copper(I) Catalyst for Carbene and Nitrene Transfer to form Cyclopropanes, Cyclopropenes, and Aziridines. *Organometallics* **1993**, *12*, 261–262.
- (210) Mairena, M. A.; Díaz-Requejo, M. M.; Belderráin, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. Copper-Homoscorpionate Complexes as Very Active Catalysts for the Olefin Aziridination Reaction. *Organometallics* **2004**, *23*, 253–256.
- (211) Dias, H. V. R.; Lu, H.-L.; Kim, H.-J.; Polach, A. S.; Goh, T. K. H. H.; Browning, R. G.; Lovely, C. J. Copper(I) Ethylene Adducts and Aziridination Catalysts Based on Fluorinated Tris(pyrazolyl)-borates [HB(3-(CF₃),5-(R) Pz)₃][−] (where R = CF₃, C₆H₅, H; Pz = pyrazolyl). *Organometallics* **2002**, *21*, 1466–1473.
- (212) Halfen, J. A.; Hallman, J. K.; Schultz, J. A.; Emerson, J. P. Remarkably Efficient Olefin Aziridination Mediated by a New Copper(II) Complex. *Organometallics* **1999**, *18*, 5435–5437.
- (213) Lam, T. L.; Tso, K. C.-H.; Cao, B.; Yang, C.; Chen, D.; Chang, X.-Y.; Huang, J.-S.; Che, C.-M. Tripodal S-Ligand Complexes of Copper(I) as Catalysts for Alkene Aziridination, Sulfide Sulfimidation, and C-H Amination. *Inorg. Chem.* **2017**, *56*, 4253–4257.
- (214) Comba, P.; Merz, M.; Pritzkow, H. Catalytic Aziridination of Styrene with Copper Complexes of Substituted 3,7-Diazabicyclo[3.3.1]nonanones. *Eur. J. Inorg. Chem.* **2003**, *2003*, 1711–1718.
- (215) Amisal, L. D.; Dai, X.; Kinney, R. A.; Krishnaswamy, A.; Warren, T. H. Cu(I) β -Diketiminates for Alkene Aziridination: Reversible Cu-Arene Binding and Catalytic Nitrene Transfer from PhI = NTs. *Inorg. Chem.* **2004**, *43*, 6537–6539.
- (216) Conry, R. R.; Tipton, A. A.; Striejskewicz, W. S.; Erkizia, E.; Malwitz, M. A.; Caffaratti, A.; Natkin, J. A. Copper Complexes with N-Alkylated NS₂-Macrocyclic Ligands: Synthesis, Characterization, and Capabilities as Aziridination Precatalysts. *Organometallics* **2004**, *23*, 5210–5218.
- (217) Sun, W.; Herdtweck, E.; Kühn, F. E. Catalytic Aziridinations with Copper(II) Salen Complexes. *New J. Chem.* **2005**, *29*, 1577–1580.
- (218) Pérez, J.; Morales, D.; García-Escudero, L. A.; Martínez-García, H.; Miguel, D.; Bernad, P. Synthesis of New Copper(I) Complexes with Tris(2-pyridyl) Ligands. Applications to Carbene and Nitrene Transfer Reactions. *Dalton Trans.* **2009**, 375–382.
- (219) Dauban, P.; Dodd, R. H. PhI = NSes: A New Iminoiodinane Reagent for the Copper-Catalyzed Aziridination of Olefins. *J. Org. Chem.* **1999**, *64*, 5304–5307.
- (220) Leca, D.; Toussaint, A.; Mareau, C.; Fensterbank, L.; Lacote, E.; Malacria, M. Efficient Copper-Mediated Reactions of Nitrenes Derived from Sulfonimidamides. *Org. Lett.* **2004**, *6*, 3573–3575.
- (221) Ando, T.; Minakata, S.; Ryu, I.; Komatsu, M. Nitrogen Atom Transfer to Alkenes Utilizing Chloramine-T as a Nitrogen Source. *Tetrahedron Lett.* **1998**, *39*, 309–312.

- (222) Robert-Peillard, F.; Di Chenna, P. H.; Liang, C.; Lescot, C.; Collet, F.; Dodd, R. H.; Dauban, P. Catalytic stereoselective alkene aziridination with sulfonimidamides. *Tetrahedron: Asymmetry* **2010**, *21*, 1447–1457.
- (223) Karila, D.; Leman, L.; Dodd, R. H. Copper-Catalyzed Iminoiodane-Mediated Aminolactonization of Olefins: Application to the Synthesis of 5,5-Disubstituted Butyrolactones. *Org. Lett.* **2011**, *13*, 5830–5833.
- (224) Li, Z.; Conser, K. R.; Jacobsen, E. N. Asymmetric Alkene Aziridination with Readily Available Chiral Diimine-Based Catalysts. *J. Am. Chem. Soc.* **1993**, *115*, 5326–5327.
- (225) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. Bis(oxazoline)-Copper Complexes as Chiral Catalysts for the Enantioselective Aziridination of Olefins. *J. Am. Chem. Soc.* **1993**, *115*, 5328–5329.
- (226) Li, Z.; Quan, W.; Jacobsen, E. N. Mechanism of the (Diimine)Copper-Catalyzed Asymmetric Aziridination of Alkenes. Nitrene Transfer via Ligand-Accelerated Catalysis. *J. Am. Chem. Soc.* **1995**, *117*, 5889–5890.
- (227) Södergren, M. J.; Alonso, D. A.; Andersson, P. G. Readily Available Nitrene Precursors Increase the Scope of Evans' Asymmetric Aziridination of Olefins. *Tetrahedron: Asymmetry* **1997**, *8*, 3563–3565.
- (228) Bertilsson, S. K.; Tedenborg, L.; Alonso, D. A.; Andersson, P. G. Chiral N,N' - and N,O -Bidentate Anionic Ligands. Preparation, Metal Complexation, and Evaluation in the Asymmetric Aziridination of Olefins. *Organometallics* **1999**, *18*, 1281–1286.
- (229) Sanders, C. J.; Gillespie, K. M.; Bell, D.; Scott, P. Structural Origins of a Dramatic Variation in Catalyst Efficiency in Enantioselective Alkene Aziridination: Implications for Design of Ligands Based on Chiral Biaryldiamines. *J. Am. Chem. Soc.* **2000**, *122*, 7132–7133.
- (230) Shi, M.; Wang, C.-J.; Chan, A. S. C. Axially Dissymmetric Binaphthyl-diimine Chiral Salen type Ligands for Copper-Catalyzed Asymmetric Aziridination. *Tetrahedron: Asymmetry* **2001**, *12*, 3105–3111.
- (231) Suga, H.; Kakehi, A.; Ito, S.; Ibata, T.; Fudo, T.; Watanabe, Y.; Kinoshita, Y. Asymmetric Cyclopropanation and Aziridination Reactions of Olefins Catalyzed by Cu(I)-Binaphthyl-diimine Complexes. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 189–199.
- (232) Xu, J.; Ma, L.; Jiao, P. Asymmetric Aziridination of Chalcones Catalyzed by a Novel Backbone 1,8-Bisoxazolinylnanthracene (AnBOX)-Copper Complex. *Chem. Commun.* **2004**, 1616–1617.
- (233) Ma, L.; Jiao, P.; Zhang, Q.; Xu, J. Rigid Backbone 1,8-Anthracene-Linked Bis-Oxazolines (AnBOXes): Design, Synthesis, Application and Characteristics in Catalytic Asymmetric Aziridination. *Tetrahedron: Asymmetry* **2005**, *16*, 3718–3734.
- (234) Ma, L.; Jiao, P.; Zhang, Q.; Du, D.-M.; Xu, J. Ligand and Substrate π -Stacking Interaction Controlled Enantioselectivity in the Asymmetric Aziridination. *Tetrahedron: Asymmetry* **2007**, *18*, 878–884.
- (235) Ma, L.; Du, D.-M.; Xu, J. Rational Tuning Chelate Size of Bis-Oxazoline Ligands to Improve Enantioselectivity in the Asymmetric Aziridination of Chalcones. *J. Org. Chem.* **2005**, *70*, 10155–10158.
- (236) Ma, L. G.; Du, D. M.; Xu, J. X. Effect of chelate size of bisoxazolines on the asymmetric aziridination. *Chin. J. Org. Chem.* **2006**, *26*, 568–572.
- (237) Ma, L.; Du, D.-M.; Xu, J. Asymmetric Aziridination of 1,3-Dienes Catalyzed by Bisoxazoline-Copper Complexes. *Chirality* **2006**, *18*, 575–580.
- (238) Trost, B. M.; Dong, G. New Class of Nucleophiles for Palladium-Catalyzed Asymmetric Allylic Alkylation. Total Synthesis of Agelastatin A. *J. Am. Chem. Soc.* **2006**, *128*, 6054–6055.
- (239) Trost, B. M.; Dong, G. A Stereodivergent Strategy to Both Product Enantiomers from the Same Enantiomer of a Stereoinducing Catalyst: Agelastatin A. *Chem. Eur. J.* **2009**, *15*, 6910–6919.
- (240) Hajra, S.; Sinha, D. Catalytic Enantioselective Aziridoarylation of Aryl Cinnamyl Ethers Toward Synthesis of *trans*-3-Amino-4-Arylchromans. *J. Org. Chem.* **2011**, *76*, 7334–7340.
- (241) Hajra, S.; Maji, B.; Mal, D. A Catalytic and Enantioselective Synthesis of *trans*-2-Amino-1-Aryltetralins. *Adv. Synth. Catal.* **2009**, *351*, 859–864.
- (242) Liang, Y.; Jiao, L.; Wang, Y.; Chen, Y.; Ma, L.; Xu, J.; Zhang, S.; Yu, Z.-X. Nitrene Equivalent Mediated Metal-Free Ring Expansions of Alkylidenecyclopropanes and an Alkylidenecyclobutane. *Org. Lett.* **2006**, *8*, 5877–5879.
- (243) Albone, D. P.; Aujla, P. S.; Taylor, P. C.; Challenger, S.; Derrick, A. M. A Simple Copper Catalyst for Both Aziridination of Alkenes and Amination of Activated Hydrocarbons with Chloramine-T Trihydrate. *J. Org. Chem.* **1998**, *63*, 9569–9571.
- (244) Bhuyan, R.; Nicholas, K. M. Efficient Copper-Catalyzed Benzylic Amidation with Anhydrous Chloramine-T. *Org. Lett.* **2007**, *9*, 3957–3959.
- (245) Barman, D. N.; Nicholas, K. M. Ligand-assisted, copper-catalyzed enantioselective benzylic amination. *Tetrahedron Lett.* **2010**, *51*, 1815–1818.
- (246) Barman, D. N.; Nicholas, K. M. Copper-Catalyzed Intramolecular C-H Amination. *Eur. J. Org. Chem.* **2011**, *2011*, 908–911.
- (247) Caballero, A.; Diaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Perez, P. J. Highly Regioselective ? Functionalization of Aliphatic Carbon-Hydrogen Bonds with a Perbromohomoscorpionate Copper(I) Catalyst. *J. Am. Chem. Soc.* **2003**, *125*, 1446–1447.
- (248) Frutos, M. R.; Trofimenko, S.; Diaz-Requejo, M. M.; Perez, P. J. Facile Amine Formation by Intermolecular Catalytic Amidation of Carbon-Hydrogen Bonds. *J. Am. Chem. Soc.* **2006**, *128*, 11784–11791.
- (249) Hou, K.; Hrovat, D. A.; Bao, X. Computational Exploration of the Mechanism of Copper-Catalyzed Aromatic C-H Bond Amination of Benzene via a Nitrene Insertion Approach. *Chem. Commun.* **2015**, *51*, 15414–15417.
- (250) Ton, T. M. U.; Tejo, C.; Tiong, D. L. Y.; Chan, P. W. H. Copper(II) Triflate Catalyzed Amination and Aziridination of 2-Alkyl Substituted 1,3-Dicarbonyl Compounds. *J. Am. Chem. Soc.* **2012**, *134*, 7344–7350.
- (251) Ton, T. M. U.; Himawan, F.; Chang, J. W. W.; Chan, P. W. H. Copper(II) Triflate Catalyzed Amination of 1,3-Dicarbonyl Compounds. *Chem. Eur. J.* **2012**, *18*, 12020–12027.
- (252) Bagchi, V.; et al. A Versatile Tripodal Cu(I) Reagent for C-N Bond Construction via Nitrene-Transfer Chemistry: Catalytic Perspectives and Mechanistic Insights on C-H Aminations/Amidations and Olefin Aziridinations. *J. Am. Chem. Soc.* **2014**, *136*, 11362–11381.
- (253) Sahoo, S. K.; Harfmann, B.; Bhatia, H.; Singh, H.; Balijapelly, S.; Choudhury, A.; Stavropoulos, P. A Comparative Study of Cationic Copper(I) Reagents Supported by Bipodal Tetramethylguanidinylligands as Nitrene-Transfer Catalysts. *ACS Omega* **2024**, *9*, 15697–15708.
- (254) Tokumasu, K.; Yazaki, R.; Ohshima, T. Direct Catalytic Chemoselective α -Amination of Acylpyrazoles: A Concise Route to Unnatural α -Amino Acid Derivatives. *J. Am. Chem. Soc.* **2016**, *138*, 2664–2669.
- (255) Xing, Q.; Jiang, D.; Zhang, J.; Guan, L.; Li, T.; Zhao, Y.; Di, M.; Chen, H.; Che, C.; Zhu, Z. Combining Visible-Light Induction and Copper Catalysis for Chemo-selective Nitrene Transfer for Late-stage Amination of Natural Products. *Commun. Chem.* **2022**, *5*, 79.
- (256) Badiel, Y. M.; Dinescu, A.; Dai, X.; Palomino, R. M.; Heinemann, F. W.; Cundari, T. R.; Warren, T. H. Copper-Nitrene Complexes in Catalytic C-H Amination. *Angew. Chem., Int. Ed.* **2008**, *47*, 9961–9964.
- (257) Bakhoda, A.; Jiang, Q.; Bertke, J. A.; Cundari, T. R.; Warren, T. H. Elusive Terminal Copper Arylnitrene Intermediates. *Angew. Chem., Int. Ed.* **2017**, *56*, 6426–6430.
- (258) Liu, X.; Zhang, Y.; Wang, L.; Fu, H.; Jiang, Y.; Zhao, Y. General and Efficient Copper-Catalyzed Amidation of Saturated C-H Bonds Using N-Halosuccinimides as the Oxidants. *J. Org. Chem.* **2008**, *73*, 6207–6212.

- (259) Kim, S.; Song, S. L.; Zhang, J.; Kim, D.; Hong, S.; Chang, S. Regio- and Enantioselective Catalytic δ -C-H Amidation of Dioxazolones Enabled by Open-Shell Copper-Nitrenoid Transfer. *J. Am. Chem. Soc.* **2023**, *145*, 16238–16248.
- (260) Fructos, M. R.; Álvarez, E.; Díaz-Requejo, M. M.; Pérez, P. J. Selective Synthesis of N-Substituted 1,2-Dihydropyridines from Furans by Copper-Induced Concurrent Tandem Catalysis. *J. Am. Chem. Soc.* **2010**, *132*, 4600–4607.
- (261) Maestre, L.; Fructos, M. R.; Díaz-Requejo, M. M.; Pérez, P. J. Copper-Catalyzed Nitrene Transfer as a Tool for the Synthesis of N-Substituted 1,2-Dihydro- and 1,2,3,4-Tetrahydropyridines. *Organometallics* **2012**, *31*, 7839–7843.
- (262) Blachut, D.; Szawka, J.; Czarnocki, Z. A Convenient Route to Symmetrically and Unsymmetrically Substituted 3,5-Diaryl-2,4,6-Trimethylpyridines via Suzuki-Miyaura Cross-Coupling Reaction. *Beilstein J. Org. Chem.* **2016**, *12*, 835–845.
- (263) Li, Z. Y.; Huang, X. Q.; Chen, F.; Zhang, C.; Wang, X. Y.; Jiao, N. Cu-Catalyzed Concise Synthesis of Pyridines and 2-(1H)-Pyridones from Acetaldehydes and Simple Nitrogen Donors. *Org. Lett.* **2015**, *17*, 584–587.
- (264) Xiang, J.-C.; Wang, M.; Cheng, Y.; Wu, A.-X. Molecular Iodine-Mediated Chemoselective synthesis of Multisubstituted Pyridines Through Catabolism and Reconstruction Behaviour of Natural Amino Acids. *Org. Lett.* **2016**, *18*, 24–27.
- (265) Hu, L.; Liu, Y. A.; Liao, X. In Situ Generation of N-Unsubstituted Imines from Alkylazides and Their Applications for Imine Transfer via Copper Catalysis. *Sci. Adv.* **2017**, *3*, No. e1700826.
- (266) Zhang, G.-Y.; Peng, Y.; Xue, J.; Fan, Y.-H.; Deng, Q.-H. Copper-Catalyzed Nitrene Transfer/Cyclization Cascade to Synthesize 3a-Nitrogenous Furoindolines and Pyrroloindolines. *Org. Chem. Front.* **2019**, *6*, 3934–3938.
- (267) Carsch, K. M.; DiMucci, I. M.; Iovan, D. A.; et al. Synthesis of a Copper-Supported Triplet Nitrene Complex Pertinent to Copper-Catalyzed Amination. *Science* **2019**, *365*, 1138–1143.
- (268) Han, X.; Shan, Li-X.; Zhu, J.-X.; Zhang, C.-S.; Zhang, X.-M.; Zhang, F.-M.; Wang, H.; Tu, Y.-Q.; Yang, M.; Zhang, W.-S. Copper-Nitrene-Catalyzed Desymmetric Oxaziridination/1,2-Alkyl Rearrangement of 1,3-Diketones toward Bicyclic Lactams. *Angew. Chem., Int. Ed.* **2021**, *60*, 22688–22692.
- (269) Wan, Y.; Zhang, H. K.; Qian, J.; Aliyu, M. A.; Norton, J. R. Copper-Catalyzed C-N Cross-Coupling for Construction of Alkylated N-Cyanamide Derivatives via Nitrogen Umpolung. *Chem.* **2024**, *10*, 2538–2549.
- (270) Blair, L. M.; Sperry, J. Natural Products Containing a Nnitrogen-Nitrogen Bond. *J. Nat. Prod.* **2013**, *76*, 794–812.
- (271) Ragnarsson, U. Synthetic Methodology for Alkyl Substituted Hydrazines. *Chem. Soc. Rev.* **2001**, *30*, 205–213.
- (272) Wang, H.; Jung, H.; Song, F.; Zhu, S.; Bai, Z.; Chen, D.; He, G.; Chang, S.; Chen, G. Nitrene-Mediated Intermolecular N-N Coupling for Efficient Synthesis of Hydrazides. *Nat. Chem.* **2021**, *13*, 378–385.
- (273) Huang, W.; Yan, H.; Wang, Q.; Chen, J.; Luo, Y.; Xia, Y. An Iron-Catalyzed Nitrene Transfer Reaction of Nitrosobenzenes with N-Acyloxamides for Accessing N-Acyl Azoxy Molecules. *Org. Chem. Front.* **2024**, *11*, 2561–2565.
- (274) Powers, I. G.; Andjaba, J. M.; Luo, X.; Mei, J.; Uyeda, C. Catalytic Azoarene Synthesis from Aryl Azides Enabled by a Dinuclear Ni Complex. *J. Am. Chem. Soc.* **2018**, *140*, 4110–4118.
- (275) Barbor, J. P.; Nair, V. N.; Sharp, K. R.; Lohrey, T. D.; Dibrell, S. E.; Shah, T. K.; Walsh, M. J.; Reisman, S. E.; Stoltz, B. M. Development of a Nickel-Catalyzed N-N Coupling for the Synthesis of Hydrazides. *J. Am. Chem. Soc.* **2023**, *145*, 15071–15077.
- (276) Brook, K. B.; Sahoo, S. R.; Uyeda, C. Dicobalt-Catalyzed N = N Coupling Reactions of Tertiary Alkyl Azides to form Azoalkanes. *Chem.* **2025**, *11*, 102437–102444.
- (277) Melen, R. L. Frontiers in Molecular p-Block chemistry: From Structure to Reactivity. *Science* **2019**, *363*, 479–484.
- (278) Zhu, Y.-Y.; Niu, Y.; Niu, Y.-N.; Yang, S.-D. Recent Advances in the Synthesis and Applications of Phosphoramides. *Org. Biomol. Chem.* **2021**, *19*, 10296–10313.
- (279) Bai, Z.; Song, F.; Wang, H.; Cheng, W.; Zhu, S.; Huang, Y.; He, G.; Chen, G. Nitrene-Mediated P-N Coupling Under Iron Catalysis. *CCS Chem.* **2022**, *4*, 2258–2266.
- (280) Wu, Y.; Chen, K.; Ge, X.; Ma, P.; Xu, Z.; Lu, H.; Li, G. Redox-Neutral P(O)-N Coupling between P(O)-H Compounds and Azides via Dual Copper and Photoredox Catalysis. *Org. Lett.* **2020**, *22*, 6143–6149.
- (281) Lebel, H.; Piras, H.; Borduy, M. Iron-catalyzed amination of sulfides and sulfoxides with azides in photochemical continuous flow synthesis. *ACS Catal.* **2016**, *6*, 1109–1112.
- (282) Periasamy, K.; Gordeeva, S.; Bolm, C. Syntheses of Sulfilimines by Iron-Catalyzed Iminations of Sulfides with 2,2,2-Trichloroethyl Sulfamate. *J. Org. Chem.* **2024**, *89*, 9705–9709.
- (283) Wang, J.; Frings, M.; Bolm, C. Enantioselective Nitrene Transfer to Sulfides Catalyzed by a Chiral Iron Complex. *Angew. Chem., Int. Ed.* **2013**, *52*, 8661–8665.
- (284) Wang, J.; Frings, M.; Bolm, C. Iron-Catalyzed Imidation Kinetic Resolution of Racemic Sulfoxides. *Chem. Eur. J.* **2014**, *20*, 966–969.
- (285) Liu, Z.; Wu, H.; Zhang, H.; Wang, F.; Liu, X.; Dong, S.; Hong, X.; Feng, X. Iron-Catalyzed Asymmetric Imidation of Sulfides via Sterically Biased Nitrene Transfer. *J. Am. Chem. Soc.* **2024**, *146*, 18050–18060.
- (286) Yu, H.; Li, Z.; Bolm, C. Three-Dimensional Heterocycles by Iron-Catalyzed Ring-Closing Sulfoxide Imidation. *Angew. Chem., Int. Ed.* **2018**, *57*, 12053–12056.
- (287) Chatterjee, S.; Makai, S.; Morandi, B. Hydroxylamine-Derived Reagent as a Dual Oxidant and Amino Group Donor for the Iron-Catalyzed Preparation of Unprotected Sulfinamides from Thiols. *Angew. Chem., Int. Ed.* **2021**, *60*, 758–765.
- (288) Pan, S.; Mulks, F. F.; Wu, P.; Rissanen, K.; Bolm, C. Mechanochemical Iron-Catalyzed Nitrene Transfer Reactions: Direct Synthesis of N-Acyl Sulfonimidamides from Sulfinamides and Dioxazolones. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202316702.
- (289) Lai, C.; Mathieu, G.; Tabarez, L. P. G.; Lebel, H. Batch and Continuous-Flow Iron(II)-Catalyzed Synthesis of Sulfilimines and Sulfoximines using N-Mesyloxycarbamates. *Chem. Eur. J.* **2019**, *25*, 9423–9426.
- (290) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S. Novel Asymmetric Catalytic Synthesis of Sulfimides. *Chem. Commun.* **1996**, 931–932.
- (291) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S.; Baird, C. P.; Sparey, T. J.; Taylor, P. C. Catalytic Asymmetric Sulfimide. *J. Org. Chem.* **1997**, *62*, 6512–6518.
- (292) Takada, H.; Oda, M.; Oyamada, A.; Ohe, K.; Uemura, S. Catalytic Diastereoselective Sulfimide of Diaryl Sulfides and Application of Chiral Sulfimides to Asymmetric Allylic Alkylation. *Chirality* **2000**, *12*, 299–312.
- (293) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S.; Baird, C. P.; Sparey, T. J.; Taylor, P. C. Catalytic Asymmetric Sulfimide. *J. Org. Chem.* **1997**, *62*, 6512–6518.
- (294) Xiao, X.; Huang, S.; Tang, S.; Jia, G.; Ou, G.; Li, Y. Ligand-Free, Quinoline N-Assisted Copper-Catalyzed Nitrene Transfer Reaction to Synthesize 8-Quinolylsulfimides. *J. Org. Chem.* **2019**, *84*, 7618–7629.
- (295) Bai, Z.; Zhu, S.; Hu, Y.; Yang, P.; Chu, X.; He, G.; Wang, H.; Chen, G. Synthesis of N-acyl sulfenamides via Copper Catalysis and Their Use as S-sulfonylating Reagents of Thiols. *Nat. Commun.* **2022**, *13*, 6445–6453.
- (296) Wu, Z.; Pratt, D. A. Radical substitution provides a unique route to disulfides. *J. Am. Chem. Soc.* **2020**, *142*, 10284–10290.
- (297) Gao, W. C.; Tian, J.; Shang, Y. Z.; Jiang, X. Steric and stereoscopic disulfide construction for cross-linkage via N-dithiophthalimides. *Chem. Sci.* **2020**, *11*, 3903–3908.

- (298) Sahu, S.; Emenike, B.; Beusch, C. M.; Bagchi, P.; Gordon, D. E.; Raj, M. Copper(I)-Nitrene Platform for Chemoproteomic Profiling of Methionine. *Nat. Commun.* **2024**, *15*, 4243–4260.
- (299) Mindiola, D. J. Oxidatively Induced Abstraction Reactions. A Synthetic Approach to Low-Coordinate and Reactive Early Transition Metal Complexes Containing Metal-Ligand Multiple Bonds. *Acc. Chem. Res.* **2006**, *39*, 813–821.
- (300) Nugent, W. A.; Mayer, J. M. Metal-Ligand Multiple Bonds: The Chemistry of Transition Metal Complexes Containing Oxo, Nitrido, Imido, Alkylidene, or Alkylidyne Ligands (Wiley Interscience, 1988).
- (301) King, E. R.; Sazama, G. T.; Betley, T. A. Co(III) Imidos Exhibiting Spin Crossover and C-H Bond Activation. *J. Am. Chem. Soc.* **2012**, *134*, 17858–17861.
- (302) Hoffmann, R.; Alvarez, S.; Mealli, C. From Widely Accepted Concepts in Coordination Chemistry to Inverted Ligand Fields. *Chem. Rev.* **2016**, *116*, 8173–8192.
- (303) Hong, S.; Sutherlin, K. D.; Vardhaman, A. K.; et al. A Mononuclear Nonheme Iron(V)-Imido Complex. *J. Am. Chem. Soc.* **2017**, *139*, 8800–8803.
- (304) Mahajan, M.; Mondal, B. Origin of the Distinctive Electronic Structure of Co- and Fe-Porphyrin-Nitrene and Its Effect on Their Nitrene Transfer Reactivity. *Inorg. Chem.* **2023**, *62*, 5810–5821.
- (305) Bakhoda, A.; Jiang, Q.; Badiei, Y. M.; Bertke, J. A.; Cundari, T. R.; Warren, T. H. Copper-Catalyzed C(sp³)-H Amidation: Sterically Driven Primary and Secondary C-H Site-Selectivity. *Angew. Chem., Int. Ed.* **2019**, *58*, 3421–3425.
- (306) Zhang, L.; Liu, Y.; Deng, L. Three-Coordinate Cobalt(IV) and Cobalt(V) Imido Complexes with N-Heterocyclic Carbene Ligation: Synthesis, Structure, and their Distinct Reactivity in C-H Bond Amination. *J. Am. Chem. Soc.* **2014**, *136*, 15525–15528.
- (307) Wilding, M. J. T.; Iovan, D. A.; Wrobe, A. T.; et al. Direct Comparison of C-H Bond Amination Efficacy through Manipulation of Nitrogen-Valence Centered Redox: Imido versus Iminyl. *J. Am. Chem. Soc.* **2017**, *139*, 14757–14766.
- (308) Liu, Q.; Long, L.; Ma, P.; Ma, Y.; Leng, X.; Xiao, J.; Chen, H.; Deng, L. Synthesis, structure, and C-H bond activation reaction of an iron(IV) terminal imido complex bearing trifluoromethyl groups. *Cell Rep. Phys. Sci.* **2021**, *2*, 100454.